

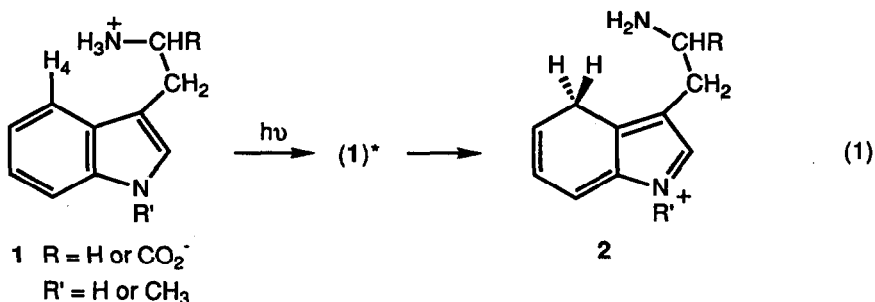
## FLASH PHOTOLYSIS OBSERVATION AND LIFETIMES OF THE CATION INTERMEDIATES IN THE INTRAMOLECULAR PHOTOPROTONATION OF TRYPTAMINE, TRYPTOPHAN AND THEIR N-METHYL DERIVATIVES

Frances Cozens,<sup>1a</sup> Robert A. McClelland<sup>1a</sup> and Steen Steenken<sup>1b</sup>

Department of Chemistry, University of Toronto, Toronto, Ontario, Canada M5S 1A1 and Max-Planck-Institut für Strahlenchemie, Mulheim D-4330, West Germany

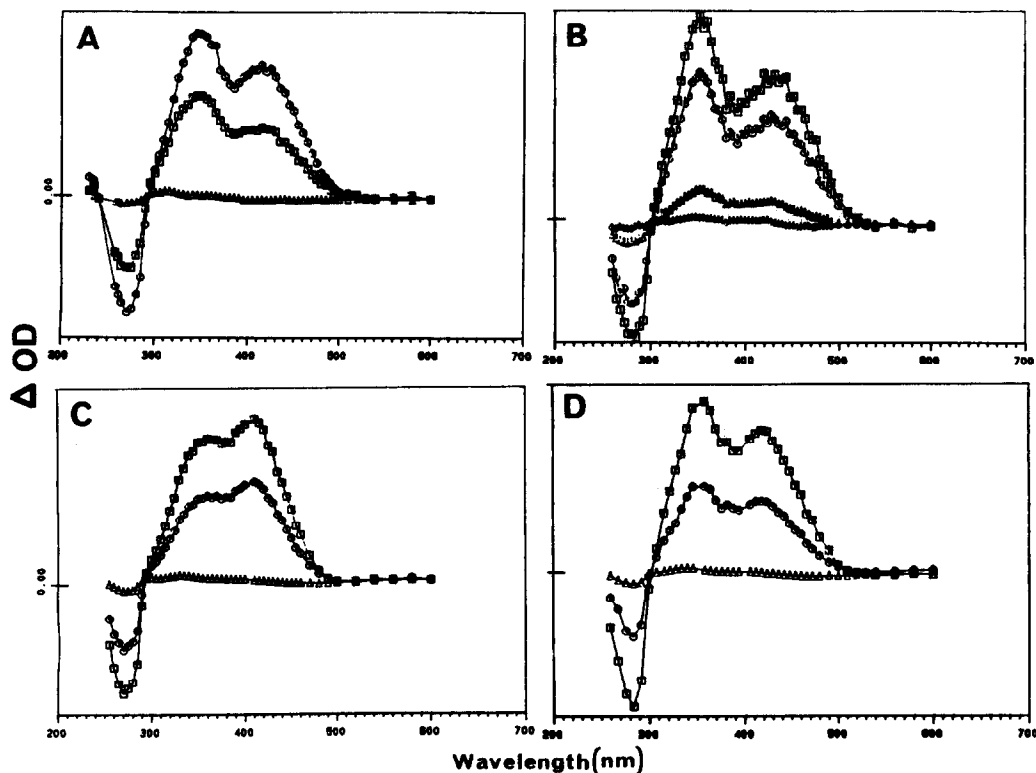
**Summary** Photolysis of the four title compounds in trifluoroethanol results in transient cyclohexadienyl-type cations ( $\lambda_{\max} \sim 350$  nm, 420 nm) arising from photoprotonation at H-4. Lifetimes are 300 - 500 ns, and are considerably shortened by the addition of water and acetate base. For the two parent compounds there is evidence in acetate buffered solutions for N-H deprotonation resulting in the tautomeric form of the parent compound.

Tryptamine (1, R = H, R' = H), tryptophan (1, R = CO<sub>2</sub><sup>-</sup>, R' = H) and related indole derivatives have been shown to undergo regioselective hydrogen-deuterium exchange at C4 upon irradiation in water and water:methanol.<sup>2</sup> A mechanism has been suggested<sup>2c</sup> with intramolecular proton transfer from the side chain ammonium group to the excited aromatic, generating the cyclohexadienyl-type cations 2 as intermediates.



This photosubstitution, which results in no net reaction other than the hydrogen exchange, is suggested as a major pathway for the non-radiative decay of the singlet excited state of these important indole derivatives. Although the cation 2 is necessary to explain the exchange, there is no other evidence for its intermediacy. Nanosecond laser flash photolysis experiments with tryptophan in aqueous solution produced a number of transients, but none were assigned to the cation 2.<sup>3</sup> In flash photolysis studies of simple carbenium ions, we have found that the cations are

kinetically more stable in fluorinated alcohol solvents such as trifluoroethanol (TFE).<sup>4</sup> We have therefore investigated the photolysis of the title indole derivatives in this solvent, and find that there is a transient, formed almost exclusively, whose properties are consistent with the cation 2.



**Figure 1.** Transient absorption spectra following 248 nm excitation (20 ns pulses) tryptamine (A), N-methyltryptamine (B), tryptophan (C) and N-methyltryptophan (D) in trifluoroethanol containing 1 - 10 mM acid. Rate constants for transient decay -  $1.8 \times 10^6 \text{ s}^{-1}$  (A),  $2.9 \times 10^6 \text{ s}^{-1}$  (B),  $2.5 \times 10^6 \text{ s}^{-1}$  (C) and  $2.6 \times 10^6 \text{ s}^{-1}$  (D). Initial spectra were obtained 20 ns after the laser pulse, final spectra at 1000 ns and intermediate spectra at 65 ns (A), 50 ns, 300 ns (B), 55 ns (C) and 55 ns (D).

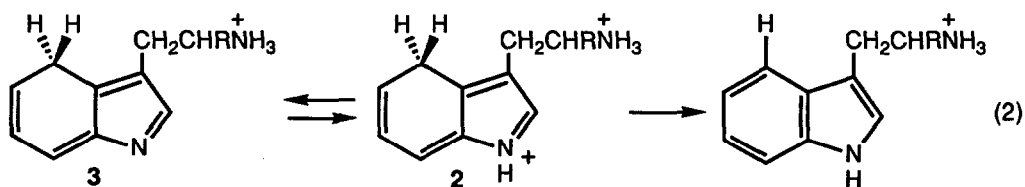
Results of experiments carried out in solutions containing a small amount of acid ( $\text{HClO}_4$  or  $\text{H}_2\text{SO}_4$ ) are shown in Figure 1. The behavior of all four compounds is very similar. After the 20 ns laser pulse there is a broad absorption from 300 nm to 500 nm with  $\lambda(\text{max})$  near 350 nm and 420 nm. The kinetic behavior across this region is identical and thus a single transient species is responsible. A negative signal representing bleaching of the absorbance of the precursor is observed below 300 nm. This absorbance returns with an identical rate as that above 300 nm decays, with a good isosbestic point near 300 nm. After about 1  $\mu\text{s}$ , there is little net change in optical density across the entire spectrum.<sup>5</sup> The absorbance changes follow exponential kinetics, and the overall behavior, both in terms of rate constants and initial  $\Delta\text{OD}$ , is the same in argon- and oxygen-saturated solutions. The latter observation implies that the transient is not a radical or

triplet. Interestingly, there is little indication of the previously reported triplet,<sup>3</sup> even in the argon-saturation experiments. The initial  $\Delta OD$  follows a linear dependency on laser dose, showing that that the transient forms in a monophotonic process. The return of OD below 300 nm implies that the parent is reforming. That this is the case is further demonstrated by the observation that repeated pulsing with one second between pulses of a stationary solution results in little change in the initial absorbance of the transient.<sup>6</sup>

These results are consistent with the transient being the cation **2**.<sup>7,8</sup> Further evidence for the photoprotonation mechanism comes from experiments with tryptamine involving 254 nm lamp photolysis in  $CF_3CH_2OD$ <sup>9</sup> (97% D). These were conducted as previously described for  $D_2O$  and MeOD -  $D_2O$  solutions,<sup>2</sup> with the tryptamine being isolated by evaporation of the solvent after various irradiation times, and 400 MrHz NMR spectra recorded in  $D_2O$ . Selective replacement of H4, the downfield signal in the aromatic region,<sup>2</sup> was observed.<sup>10</sup>

The rate constants for the decays of the cations obtained with the four precursors are very similar (figure caption), with the lifetime being 300 - 500 ns. It can be noted that with lifetimes of this order of magnitude, the cation is very likely a fully relaxed ground state species. Addition of water causes the rate to increase, and by 60% by volume water, the cations form and decay within the laser pulse. Experiments were also performed in acetate buffered (1:1 and 2:1  $CH_3COOH:CH_3COONa$ ) TFE and show a pronounced rate acceleration attributable to the acetate component, with  $k(\text{acetate}) = 1.0 \times 10^9 \text{ M}^{-1}\text{s}^{-1}$  for the cation from N-methyltryptamine. This presumably arises from acetate acting as a base to deprotonate the cation.

The close similarity in both the spectra and decay kinetics for the compounds with  $R' = H$  and Me show that the former produce cations, and not their tautomeric forms **3**. There is, however, good indication that the latter are formed from **2** in the acetate buffered solutions. While the decay of the N-methyl derivatives in these solutions follows excellent exponential kinetics, both tryptamine and tryptophan exhibit biphasic decays. This is observed only below 400 nm. The fast component has a rate constant that is identical to that of the single component decay observed above 400 nm. This rate constant is also very similar to that for the N-methyl analog. The second component observed below 400 nm is 10 - 20 times slower.



Our explanation is that in these solutions the initially formed **2** partly<sup>11</sup> reacts by N-H deprotonation to form **3**. The latter absorbs below 400 nm and is more slowly converted back to **1**, presumably reacting by way of **2**. In more acidic solutions **3**, if formed, is rapidly converted back to **2** because of the higher  $H^+$  concentration and single exponential behavior is observed.

The cations **2** are not observed on photolysis in 100% aqueous solution of comparable acidity, even though the observation of H<sub>4</sub>-exchange<sup>2</sup> implies that they should be present. The results of this study indicate that the cations simply decay too rapidly in water for detection with nanosecond flash photolysis equipment. With tryptophan, a transient identical to that observed here has been reported for photolysis in very acidic aqueous solutions (pH < 1).<sup>3</sup> This was assigned a structure of a protonated triplet. Our results suggest that it was indeed the ground-state cation **2**. In acids, the activity of water is lowered through a salt effect, and cations become much longer lived.<sup>12</sup>

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### References

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5. There is small additional absorbance near 300 nm that increases at higher laser doses, suggestive of a cation radical (or subsequent product) produced by two photon ionization.
6. This is less true at higher laser doses.
7. We presume that in the acidic solutions employed in this study the side chain NH<sub>2</sub> group has become protonated after the initial H<sup>+</sup> transfer.
8. Cyclohexadienyl-type cations of structure **2** have not previously been characterized. Their spectra are however similar to those observed in strong acids for protonated aminobenzenes and polycyclic arenes. V. A. Koptug, *Topics Current Chem.* **122**, 100 - 106 (1984).
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10. This is the same observation as made in D<sub>2</sub>O/D<sup>+</sup>,<sup>2</sup> and it constitutes one of the principal pieces of evidence for the proton transfer occurring from the intramolecular NH<sub>3</sub><sup>+</sup>. Indole itself undergoes photo-exchange in CF<sub>3</sub>CH<sub>2</sub>OD/D<sup>+</sup>, but the process is non-selective, as is the case also in D<sub>2</sub>O/D<sup>+</sup>.<sup>2b</sup> The flash photolysis experiments with indole in trifluoroethanol reveal transients with spectra similar to those in Figure 1, but the decay is multi-exponential, consistent with the production of several cyclohexadienyl-type cations.
11. The similar rate constants of the fast decay and for the N-methyl derivative imply that the C-H deprotonation must still be important for the N-H compounds.
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