

Transient Resonance Raman and Density Functional Theory Investigation of the 4-Acetamidophenylnitrenium Ion

Pik Ying Chan, Shing Yau Ong, Peizhi Zhu, King Hung Leung, and David Lee Phillips*

Department of Chemistry, The University of Hong Kong, Pokfulam Road,
Hong Kong S. A. R., P. R. China

phillips@hkucc.hku.hk

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This paper reports a transient resonance Raman and density functional theory study of the 4-acetamidophenylnitrenium ion in a mostly aqueous solvent. The transient Raman bands combined with results from density functional theory calculations indicate that the spectrum should be assigned to the singlet state of the 4-acetamidophenylnitrenium ion. The 4-acetamidophenylnitrenium ion was found to have a substantial iminocyclohexadienyl character comparable to previously studied *para*-phenyl-substituted phenylnitrenium ions and noticeable charge on both the acetamido and nitrenium moieties. The structure and properties of the 4-acetamidophenylnitrenium ion are compared to those of other aryl nitrenium ions. We briefly discuss the chemical reactivity and selectivity of the *para*-acetamido-substituted phenylnitrenium ions compared to *para*-phenyl- or *para*-alkoxy-substituted phenylnitrenium ions.

Introduction

The properties and chemical reactions of aryl nitrenium ions have long been of intense interest because they are thought to be key intermediates in chemical carcinogenesis.^{1–18} Aromatic amines may be enzymatically transformed into sulfate esters of the corresponding *N*-hydroxylamines and in aqueous environments will spontaneously produce an aryl nitrenium ion and a sulfate ion.^{13,17} Aryl nitrenium ions such as the 2-fluorenylnitrenium ion can be selectively trapped by guanine bases in DNA and make adducts, and these kinds of reactions are

believed to lead to carcinogenic mutations.^{8–10,14,18} Aryl nitrenium ions are very reactive and hence short-lived species that are generally difficult to study. Several photochemical methods have been developed in order to allow laser spectroscopic techniques to directly probe the spectroscopy and kinetics of aryl nitrenium ions in room-temperature solutions.^{19–33} The rate constants for reactions with other molecules and the lifetimes of aryl nitrenium ions have been obtained for a number of systems using time-resolved transient absorption spectroscopy.^{19–27,29,30} More recently, time-resolved vibrational spectroscopic techniques such as time-resolved infrared (TRIR) absorption spectroscopy and time-resolved resonance Raman

* To whom correspondence should be addressed. Fax: 852-2857-1586.

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(TR³) spectroscopy have been used to directly probe the structure of arylnitrenium ions in both organic and largely aqueous solvents.^{28,31–33} These investigations showed that several arylnitrenium ions have significant iminocyclohexadienyl character to differing degrees that depend on their structures and substituents.^{28,31–33} Several acetamido-substituted phenylnitrenium ions and their reactions with other molecules have been studied using transient absorption spectroscopy.³⁴ This work suggested that 4-(*N*-methylacetamido)phenylnitrenium ion has a significant positive charge on the *N*-methylacetamido group and had a very long lifetime of 5 ms in water.³⁴ The 4-(*N*-acetamido)phenylnitrenium ion has a lifetime about 5000 times longer than that found for the 4-methoxyphenylnitrenium ion^{35,36} even though the 4-methoxy substituent is more electron-donating on the basis of the σ^+ values (-0.78 for methoxy and -0.60 for methylacetamido). This remarkable reversal of expected trends provides an intriguing example of the failure of arylnitrenium ions to follow the carbocation scale.³⁴

In this paper, we report the first transient resonance Raman spectrum for an acetamido-substituted phenylnitrenium ion and directly probe its structural properties. The transient resonance Raman spectrum for 4-acetamidophenylnitrenium ion shows several Raman bands in a largely aqueous solution at room temperature. The Raman bands observed have vibrational frequencies and intensities that agree noticeably better with those predicted from (U)BPW91/cc-PVDZ calculations for the singlet state than the triplet state of the 4-acetamidophenylnitrenium ion. This and the large singlet–triplet energy gap from the (U)BPW91/cc-PVDZ computations indicate that the 4-acetamidophenylnitrenium ion is in its singlet state. Our results indicate that the 4-acetamidophenylnitrenium ion has substantial iminocyclohexadienyl character with significant positive charge on both the acetamido and nitrenium moieties. The structure and properties of the 4-acetamidophenylnitrenium ion are compared to those of other arylnitrenium ions recently characterized by time-resolved vibrational spectroscopy. We briefly discuss the failure of the 4-acetamido-substituted phenylnitrenium ions to follow the carbocation scale and why the 4-(*N*-methylacetamido)phenylnitrenium ion has a remarkably long lifetime in water solvent compared to other arylnitrenium ions such as the 4-methoxyphenylnitrenium ion. We also briefly discuss the chemical reactivity and selectivity toward water and deoxyguanosine of the *para*-acetamido-substituted phenylnitrenium ions compared to *para*-phenyl or *para*-alkoxy-substituted phenylnitrenium ions.

Results and Discussion

A. Transient Resonance Raman Spectrum and Density Functional Theory Results for the 4-Acetamidophenylnitrenium Ion. Previous work by McClelland and co-workers³⁴ demonstrated that flash photolysis of 4-(*N*-methylacetamido)phenyl azide in an aqueous solution produced the 4-(*N*-methylacetamido)phen-

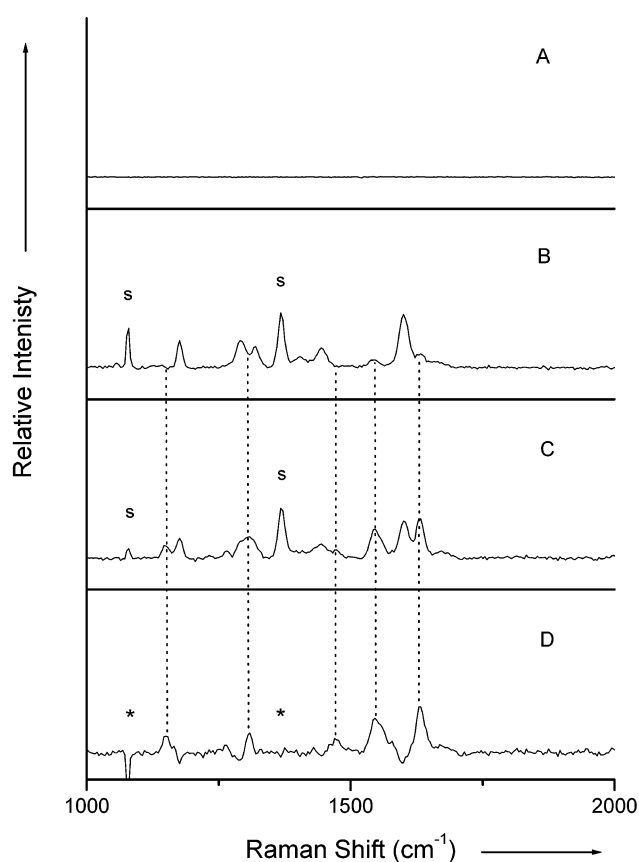


FIGURE 1. Examples of a typical 266 nm pump-only spectrum in the probe wavelength region (A), a 320 nm probe-only Raman spectrum (B), a pump–probe spectrum (C), and the resulting transient resonance Raman spectrum (D) of the 4-acetamidophenylnitrenium ion. “S” marks solvent bands (in B and C), while the asterisks mark solvent subtraction artifacts in the transient spectrum (D). The 1000–2000 cm^{-1} region is shown since this is where noticeable transient Raman bands were observed.

ylnitrenium ion very fast and that it absorbs strongly with a transient absorption maxima ~ 310 nm. Since the 4-acetamidonitrenium ion is very similar to the 4-(*N*-methylacetamido)phenylnitrenium ion, we used a 320 nm probe excitation wavelength to obtain its transient resonance Raman spectrum (see Figures 1 and 2) following 266 nm photolysis of a 4-acetamidophenyl azide precursor in a 60% water/40% acetonitrile mixed solvent. Figure 1 presents a typical pump-only spectrum in the probe wavelength region (A), a probe-only Raman spectrum (B), a pump–probe Raman spectrum (C), and a transient Raman spectrum (D) of the 4-acetamidophenylnitrenium ion. The transient Raman spectrum was obtained by subtracting the probe-only spectrum and the pump-only spectrum from the pump–probe spectrum. Figure 2 shows an expanded view of the transient resonance Raman spectrum of the 4-acetamidophenylnitrenium ion presented in Figure 1. Comparison of the experimental band vibrational frequencies and intensities to those predicted from density functional theory (DFT) or ab initio calculations for probable photoproduct species have been used to successfully assign time-resolved infrared (TRIR) and time-resolved resonance Raman (TR³) spectra to arylnitrenium ions, arylnitrenes, and

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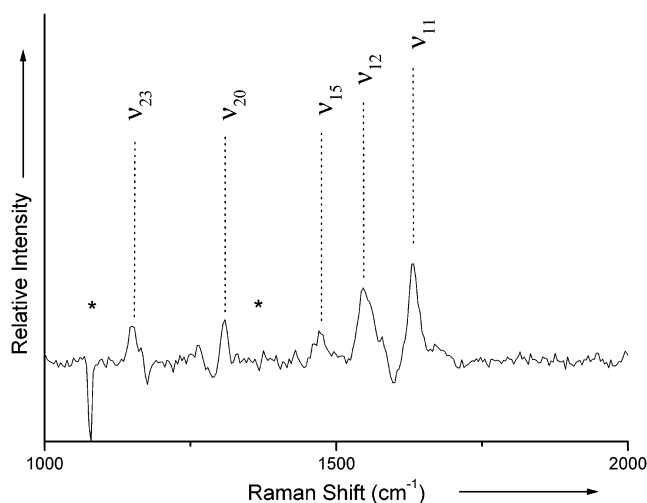


FIGURE 2. Expanded view of the transient resonance Raman spectrum of the 4-acetamidophenylnitrenium ion obtained using a 320 nm probe and 266 nm pump excitation wavelengths. The assignments of the larger Raman bands are labeled (see text and Table 1 for more details). The asterisks mark solvent and/or parent band subtraction artifacts.

other chemical intermediates.^{28,31–33,37–42} A similar methodology will be used to assign the TR³ spectra shown in Figures 1 and 2.

Toscano, Cramer, Falvey, and co-workers^{28,31} previously found that BPW91/cc-PVDZ calculations provided excellent estimates (within several cm⁻¹) of the vibrational frequencies they observed in the TRIR spectra for several arylnitrenium ions. We have also found that BPW91/cc-PVDZ computations gave good estimates of the vibrational frequencies (generally within 5–20 cm⁻¹ of the experimental values) observed in the TR³ spectra of several arylnitrenium ions.^{32,33,46} Since BPW91/cc-PVDZ calculations have given good estimates of the vibrational frequencies for about 10 other arylnitrenium ions studied previously,^{8,31–33,46} (U)BPW91/cc-PVDZ computations were done for the singlet and triplet states of the 4-acetamidophenylnitrenium ion as well as the 4-(*N*-methylacetamido)phenylnitrenium ion (for comparison purposes) to obtain their total energy, optimized geometry, and vibrational frequencies and intensities. Table 1 compares the experimental transient resonance Raman vibrational frequencies to those predicted from the DFT calculations for the singlet and triplet states of the 4-acetamidophenylnitrenium ion. Figure 3 shows simple schematic diagrams of the singlet and triplet states of the

4-acetamidophenylnitrenium and 4-(*N*-methylacetamido)phenylnitrenium ions with selected DFT optimized geometry bond lengths indicated next to the appropriate bonds. Examination of Figure 3 shows that the singlet states of the 4-acetamidophenylnitrenium and 4-(*N*-methylacetamido)phenylnitrenium ions have significantly more imine character (stronger C=N bonds) at both the acetamido and nitrenium moieties accompanied by more cyclohexadienyl character (e.g., greater carbon–carbon bond length alternation) in the phenyl ring compared to their respective triplet states. These differences in structure lead to noticeable differences in the vibrational frequencies of the singlet and triplet states, and this can help to distinguish them from one another by employing vibrational spectroscopy. Substituents *para* to the nitrenium ion moiety may noticeably change the singlet–triplet gap. For example, the π -donating character of the substituent at the *para* position can substantially stabilize the singlet state relative to the triplet state.^{31,43} We found singlet–triplet energy gaps of 27.6 kcal/mol for the 4-acetamidophenylnitrenium ion and 27.8 kcal/mol for the 4-(*N*-methylacetamido)phenylnitrenium ion from the (U)BPW91/cc-PVDZ computations with the singlet species being more stable. This indicates that the singlet states of these acetamidophenylnitrenium ions are significantly more stable than their triplet states. This and the fast formation of the nitrenium ions by protonation of the initially produced singlet arylnitrene precursor³⁴ suggest the transient resonance Raman spectra shown in Figures 1 and 2 are due to the singlet state of the 4-acetamidophenylnitrenium ion. This is similar to the assignments made previously for *para*-phenyl-substituted phenylnitrenium ions such as the 2-fluorenylnitrenium and 4-biphenylnitrenium ions.^{19,22,32,33}

Examination of Table 1 reveals that the transient Raman vibrational band frequencies are in noticeably better agreement with the frequencies predicted for the singlet 4-acetamidophenylnitrenium ion than for the corresponding triplet state. The singlet-calculated vibrational frequencies are different from the experimental Raman frequencies by about 13 cm⁻¹ on average compared to differences of about 19 cm⁻¹ on average for the triplet. Figure 4 compares the calculated vibrational frequencies and Raman intensities for the singlet and triplet states of the 4-acetamidophenylnitrenium ion to the experimental transient Raman spectrum vibrational frequencies and relative intensities in the 1000–2000 cm⁻¹ region. Examination of Figure 4 reveals that the experimental Raman vibrational frequencies and intensity pattern display a reasonable correlation with those computed for the singlet 4-acetamidophenylnitrenium ion but not for the triplet state.

The DFT computed Raman intensity for the C–O stretch mode in the 1760–1801 cm⁻¹ region compared to intensities of the modes in the 1400–1650 cm⁻¹ region is useful to distinguish the singlet- and triplet-state spectra for the 4-acetamidophenylnitrenium ion. The 1763 cm⁻¹ C–O stretch mode is computed to be the most intense Raman band and substantially more intense than the Raman bands in the 1470–1620 cm⁻¹ region of the triplet-state spectrum. However, the experimental transient Raman spectrum has no discernible mode in the C–O stretch region and the most intense bands are in the 1450–1650 cm⁻¹ region. This indicates that the

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TABLE 1. Experimental Raman Vibrational Frequencies Observed in the Time-Resolved Resonance Raman Spectra of 4-Acetamidophenylnitrenium Ion Shown in Figure 2^a

triplet 4-acetamidophenylnitrenium ion		singlet 4-acetamidophenylnitrenium ion		experiment
vibrational mode, possible description	UBPW91/cc-PVDZ calcd value (in cm ⁻¹)	vibrational mode, possible description	BPW91/cc-PVDZ calcd value (in cm ⁻¹)	10 ns time-resolved Raman frequency shift (in cm ⁻¹)
ν_{26} , CH ₃ bend	1001	ν_{28} , CH ₃ bend	1003	
ν_{25} , N–H bend + C–H bend	1098	ν_{27} , C–H bend	1008	
ν_{24} , C–H bend + CH ₃ bend	1134	ν_{26} , N–H bend + C–H bend	1072	
ν_{23} , C–H bend	1164	ν_{25} , N–H bend	1114	
ν_{22} , C–H bend + N–H bend	1240	ν_{24} , N–H bend + C–H bend	1140	
ν_{21} , N–H bend + C–H bend	1257	ν_{23}, C–H bend	1160	1150
ν_{20} , C–H bend	1304	ν_{22} , N–H bend + C–H bend	1253	
ν_{19} , CH ₃ bend	1330	ν_{21} , N–H bend + C–H bend	1299	
ν_{18} , C–N stretch + C–H bend	1348	ν_{20}, CH₃ bend	1329	1309
ν_{17} , CH ₃ bend	1390	ν_{19} , N–H bend + C–H bend	1359	
ν_{16} , CH ₃ bend	1406	ν_{18} , CH ₃ bend	1390	
ν_{15} , N–H bend + C–H bend	1410	ν_{17} , CH ₃ bend	1403	
ν_{14} , C–H bend + C–N stretch	1448	ν_{16} , N–H bend + C–H bend	1409	
ν_{13} , C–C stretch + N–H bend	1467	ν_{15}, C–N stretch	1464	1470
ν_{12} , N–H bend + C–C stretch	1504	ν_{14} , N–H bend	1491	
ν_{11} , C–C stretch (ring)	1606	ν_{13} , C–C stretch (ring) + N–H bend	1553	
ν_{10} , C–O stretch	1763	ν_{12}, C–N stretch	1571	1546
		ν_{11}, C–C stretch (ring)	1639	1633
		ν_{10} , C–O stretch	1801	

^a Experimental vibrational frequencies are compared to those from (U)BPW91/cc-PVDZ computations for the singlet and triplet states of 4-acetamidophenylnitrenium ion. See text for more details. Possible vibrational band assignments are also shown based on comparison to calculated vibrational frequencies from UBWP91/cc-PVDZ or BPW91/cc-PVDZ computations in the 1000–2000 cm⁻¹ fingerprint region for the ground singlet and triplet states of 4-acetamidophenylnitrenium ion (see text).

experimental transient Raman spectrum is very likely not due to the triplet state of the 4-acetamidophenylnitrenium ion. In contrast, the singlet state 1801 cm⁻¹ C–O stretch mode is predicted to have substantially less intensity than the 1450–1650 cm⁻¹ Raman bands. This is reasonably consistent with the transient Raman spectra where the largest bands are the 1450–1650 cm⁻¹ Raman bands and the 1801 cm⁻¹ band is not clearly observed. The computed 1571 cm⁻¹ ν_{12} Raman band (associated with mainly the C–N stretch mode) is predicted to have a much higher intensity than the computed 1553 cm⁻¹ ν_{13} mode (associated with the C–C stretch + N–H bend mode). Therefore, the experimental Raman band observed at 1546 cm⁻¹ is attributed to be mainly due to the ν_{12} 1571 cm⁻¹ computed Raman band. However, the ν_{15} C–N stretch mode and the ν_{14} N–H bend mode are predicted to have a similar intensity in the computed Raman spectrum but the experimental transient resonance Raman has only one clear band in this region. This may be due to the resonance enhancement of the experimental spectrum being more for the ν_{15} mode than the ν_{14} mode. This is consistent with the greater intensity observed for the ν_{12} C–N stretch mode relative to the ν_{11} C–C stretch in the experimental resonance Raman spectrum than predicted from the DFT calculated normal Raman spectrum for the singlet state. An alternative possibility is that the experimental vibrational frequencies of the ν_{15} and ν_{12} modes are closer together and not clearly resolved in the experimental spectrum. We note that almost all of the BPW91/cc-PVDZ calculations previously reported for arylnitrenium ions typically predict the characteristic symmetric stretch C–C mode within <8 cm⁻¹. The BPW91/cc-PVDZ calculations predict the singlet state ν_{11} mode within 6 cm⁻¹ of the experimental 1633 cm⁻¹ Raman band, while the predicted triplet-state ν_{11} mode is 27 cm⁻¹ away. This further supports the assignment of the transient reso-

nance Raman spectrum to a singlet-state 4-acetamidophenylnitrenium ion. The large calculated singlet–triplet energy gap with the singlet state being more stable and the reasonable agreement between the computed and experimental Raman vibrational frequencies and intensities prompts us to assign the transient Raman spectra in Figures 1 and 2 to the singlet state of the 4-acetamidophenylnitrenium ion.

We used DFT computations at the random-phase approximation⁴⁵ (RPA) to estimate the electronic transition energies and oscillator strengths for the singlet-state 4-acetamidophenylnitrenium and 4-(*N*-methylacetamido)phenylnitrenium ions, and these are listed in Table 2. Examination of Table 2 shows that the singlet-state 4-acetamidophenylnitrenium and 4-(*N*-methylacetamido)phenylnitrenium have only one large oscillator strength electronic transition at ~323 and ~336 nm, respectively, in the 200–1000 nm region. These results are consistent with the previous observation of a strong transient absorption band with a maxima of ~310 nm for the 4-(*N*-methylacetamido)phenylnitrenium ion.³⁴ This is consistent with and indirectly provides further support for our assignment of the transient Raman spectra shown in Figures 1 and 2 to the singlet state of the 4-acetamidophenylnitrenium ion.

B. Comparison of the Structure and Properties of the 4-Acetamidophenylnitrenium Ion to Several Other Arylnitrenium Ions. It is instructive to compare the structural characteristics of the singlet 4-acetamidophenylnitrenium ion to those found for the 4-(*N*-methylacetamido)phenylnitrenium ion and other previously studied arylnitrenium ions. All of the structural comparisons discussed here are based on the same BPW91/cc-PVDZ level of theory for the computed structures.^{28,31–33} The imine character of the singlet 4-acetamidophenylnitrenium ion is very strong (C⁸=N¹¹ bond length of 1.305 Å) for the nitrenium ion group and is even

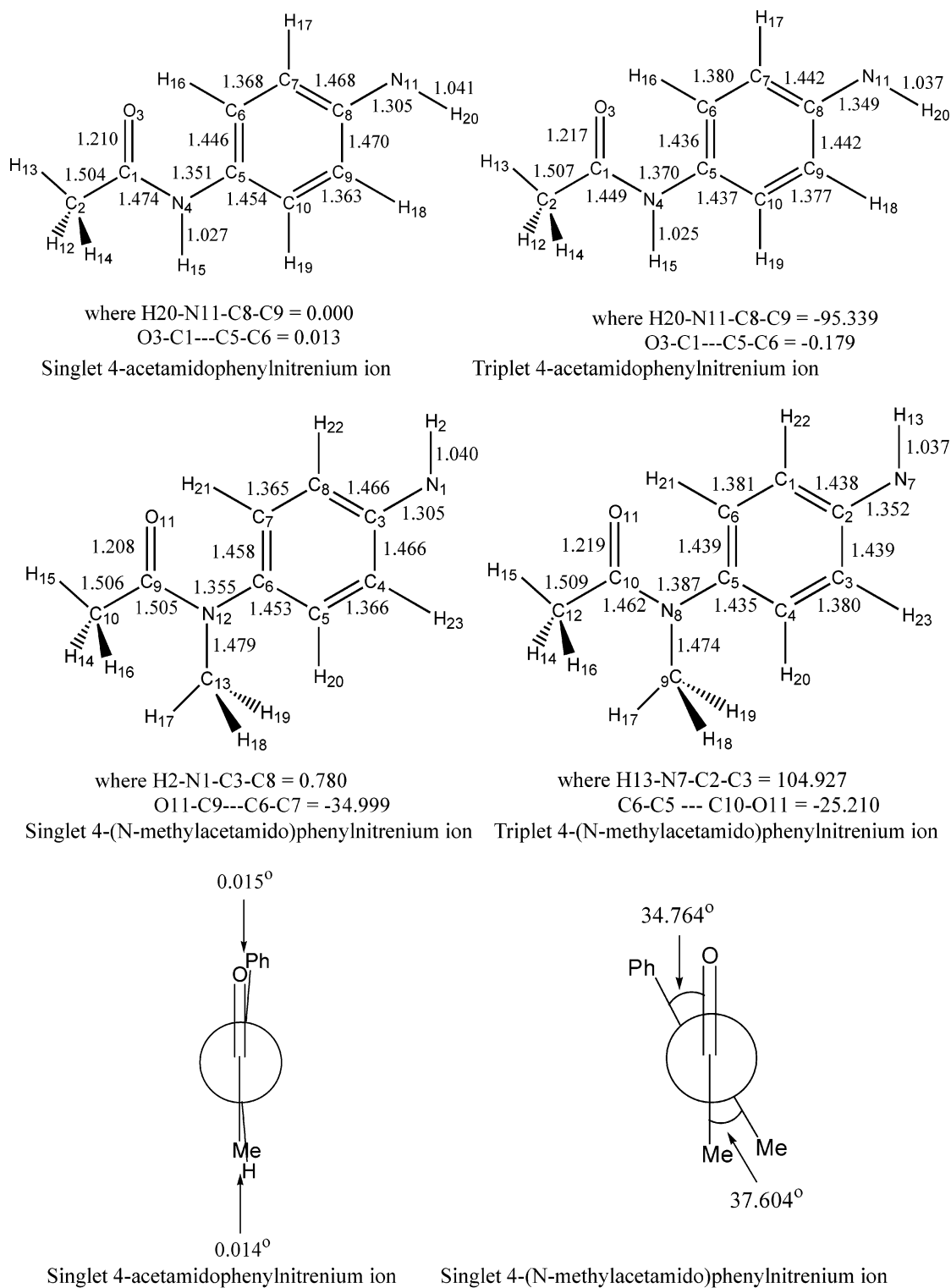


FIGURE 3. Diagrams of the singlet and triplet states of the 4-acetamidophenylnitrenium and 4-(*N*-methylacetamido)-phenylnitrenium ions with the atoms numbered. Selected bond lengths are shown (in Å) from the (U)BPW91/cc-PVDZ computations.

somewhat stronger than that found previously for the 2-fluorenylnitrenium ion (C=N bond length of about 1.308 Å).^{32,33} The C=N bond lengths are similar for both the 4-acetamidophenylnitrenium ion (1.305 Å) and the 4-(*N*-methylacetamido)phenylnitrenium ion (1.305 Å), but these are noticeably stronger than those for four other phenyl-substituted phenylnitrenium ions: 4-biphenyl-

nylnitrenium ion (1.308 Å),³³ diphenylnitrenium ion (1.351 Å),³³ *N*-(4-biphenyl)-*N*-methylnitrenium ion (1.321 Å),³¹ *N*-(4-methylphenyl)-*N*-methylnitrenium ion (1.323 Å),³¹ *N*-(4-chlorophenyl)-*N*-methylnitrenium ion (1.323 Å),³¹ and *N*-(4-methoxyphenyl)-*N*-methylnitrenium ion (1.317 Å).³¹ Similarly, the degree of C-C bond alternation (cyclohexadienyl character) in the phenyl ring to which

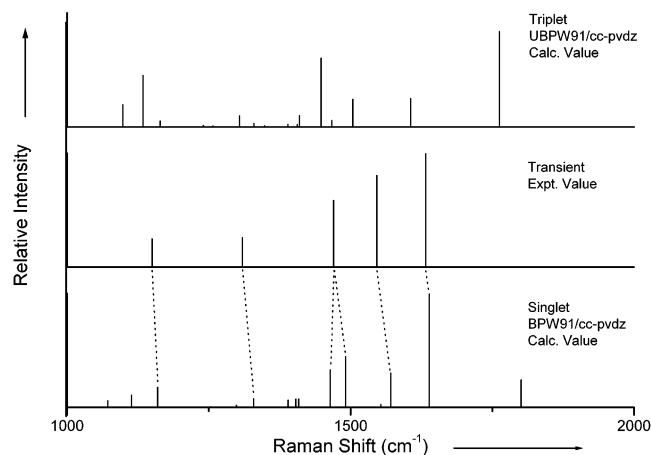


FIGURE 4. Comparison of the experimental transient Raman vibrational frequencies and relative intensities (from Figure 2) to those calculated for the singlet and triplet states of the 4-acetamidophenylnitrenium ion. The Raman band in the 1600 cm^{-1} region is scaled to be 100 for the experimental and singlet-state calculated spectra. The triplet-state calculated spectrum has the 1600 cm^{-1} region mode scaled to 25 so the large bands in the 1440 and 1760 cm^{-1} regions of the triplet spectrum can be shown relative to the other bands. Only Raman bands with an intensity >1 are shown. The dashed lines help indicate the correlation between the spectra. Only the 1000–2000 cm^{-1} region is shown because this is where noticeable transient Raman bands were observed.

TABLE 2. Electronic Transition Energies and Oscillator Strengths Obtained from RPA/cc-PVDZ Calculations Using the BPW91/cc-PVDZ Optimized Geometry for the Singlet 4-Acetamidophenylnitrenium and 4-(*N*-Methylacetamido)phenylnitrenium ions

species	singlet transition energies	oscillator strength	
4-acetamidophenylnitrenium ion	721 nm	0.0000	
	575 nm	0.0006	
	412 nm	0.0129	
	323 nm	0.4147	
	285 nm	0.0791	
	280 nm	0.0001	
	273 nm	0.0000	
	259 nm	0.0000	
	4-(<i>N</i> -methylacetamido)phenylnitrenium ion	614 nm	0.0004
		549 nm	0.0008
406 nm		0.0122	
336 nm		0.4347	
283 nm		0.0199	
276 nm		0.0142	
270 nm		0.0079	
261 nm		0.0111	

the nitrenium moiety is attached is also very strong in the two 4-acetamidophenylnitrenium ions examined and comparable to that found in the 2-fluorenylnitrenium ion.^{32,33} For example, the first phenyl ring in the 2-fluorenylnitrenium ion has bond lengths of $\text{C}^{12}-\text{C}^{11} = 1.473 \text{ \AA}$; $\text{C}^{11}-\text{C}^{10} = 1.370 \text{ \AA}$; $\text{C}^{10}-\text{C}^7 = 1.437 \text{ \AA}$ and $\text{C}^{12}-\text{C}^{13} = 1.470 \text{ \AA}$; $\text{C}^{13}-\text{C}^8 = 1.368 \text{ \AA}$; and $\text{C}^8-\text{C}^9 = 1.512 \text{ \AA}$ (see Scheme 1 in ref 33) compared to bond lengths of $\text{C}^9-\text{C}^8 = 1.470 \text{ \AA}$; $\text{C}^9-\text{C}^{10} = 1.363 \text{ \AA}$; $\text{C}^{10}-\text{C}^5 = 1.454 \text{ \AA}$ and $\text{C}^8-\text{C}^7 = 1.468 \text{ \AA}$; $\text{C}^7-\text{C}^6 = 1.368 \text{ \AA}$; and $\text{C}^6-\text{C}^5 = 1.446 \text{ \AA}$ for the singlet 4-acetamidophenylnitrenium ion (see Figure 3). Our results clearly indicate that the acetamidophenylnitrenium ions have a large degree of iminocy-

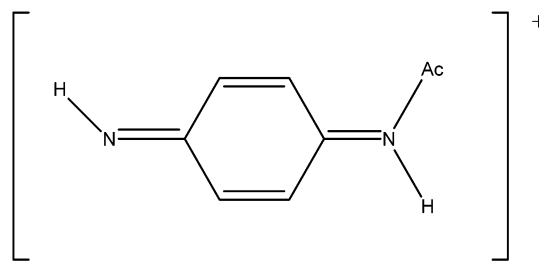


FIGURE 5. Schematic diagram of the 4-acetamidophenylnitrenium ion described as an acyliminium ion of cyclohexadienyl character with two $\text{C}=\text{N}$ bonds *para* to one another (see text for more details).

clohexadienyl character with an amount similar to the 2-fluorenylnitrenium ion for the $\text{C}=\text{N}$ bond of the nitrenium ion moiety. This is consistent with the similarity of the experimental resonance Raman vibrational frequencies of the symmetric aromatic $\text{C}=\text{C}$ stretch mode that is observed at 1633 cm^{-1} in the 4-acetamidophenylnitrenium ion compared to 1633 or 1637 cm^{-1} in the 2-fluorenylnitrenium ion.^{32,33} The symmetric aromatic $\text{C}=\text{C}$ stretch vibrational mode in the 1568 cm^{-1} to 1650 cm^{-1} region has been shown to display a good correlation with the amount of iminocyclohexadienyl character for a number of aryl nitrenium ions,^{28,31–33} and the acetamidophenylnitrenium ions examined here also display this correlation.

The large amount of iminocyclohexadienyl character observed for the 2-fluorenylnitrenium ion was mainly caused by the substitution of a second phenyl ring *para* to the nitrenium ion and the tendency of the biphenyl-like rings to tend toward a more quinoidal-like structure as charge delocalized into the phenyl rings, as well as the locking fluorene bridge that enhances this interaction between the two phenyl rings.^{32,33} However, the acetamidophenylnitrenium ions do not have this second phenyl ring and it is the acetamido moiety that induces the charge delocalization of the iminocyclohexadienyl character of the phenylnitrenium ion. The C^5-N^4 bond length of 1.351 \AA associated with the acetamido group attached to the phenyl ring in the singlet 4-acetamidophenylnitrenium ion has noticeable double-bond character as well. This indicates that the 4-acetamidophenylnitrenium ion may be described as an acyliminium ion of cyclohexadienyl character with two $\text{C}=\text{N}$ bonds *para* to one another (see Figure 5), and this facilitates charge delocalization so that both N atoms have noticeable charges.

The bottom part of Figure 3 shows a view of the singlet 4-acetamidophenylnitrenium and 4-(*N*-methylacetamido)phenylnitrenium ions along their $\text{C}-\text{N}$ bond where the carbon atom is that of the $\text{C}=\text{O}$ group and the N atom is that of the acetamido moiety attached to the phenyl ring. Comparison of the singlet 4-acetamidophenylnitrenium and 4-(*N*-methylacetamido)phenylnitrenium ions in Figure 3 reveals they have very similar iminocyclohexadienyl character even though the planarity of the $\text{C}=\text{O}$ bond of the acetamido group relative to the phenyl ring changes significantly from about 0.015° for the $\text{C}^5-\text{N}^4-\text{C}^1-\text{O}^3$ torsion angle to about 35° for the $\text{C}^6-\text{N}^{12}-\text{C}^9-\text{O}^{11}$ torsion angle, respectively. This suggests that the relative position of the $\text{C}=\text{O}$ group does not substantially influence the degree of iminocyclohexadi-

enyl character of these acetamidophenylnitrenium ions. The shortest distance between the H atoms on the methyl moiety attached to the C atom of the C=O group and the H atom attached to the N⁴ atom of the acetamido moiety is about 2.542 Å for H¹²–H¹⁵ of the singlet 4-acetamidophenyl nitrenium ion. The shortest distances between the H atoms on the methyl moiety attached to the C atom of the C=O group and the nearest H atom attached to the other methyl group of the acetamido moiety are about 2.257 and 2.406 Å the for H¹⁶–H¹⁷ and H¹⁴–H¹⁷ distances, respectively, for the singlet 4-(*N*-methylacetamido)phenylnitrenium ion. These H–H atom distances between the two methyl groups of the singlet 4-(*N*-methylacetamido)phenylnitrenium ion are a little shorter than the nearest analogous H–H distance of the 4-acetamidophenylnitrenium ion. The H–H atom distances between the two methyl groups of the singlet 4-(*N*-methylacetamido)phenylnitrenium ion would be even shorter if the torsion angle C⁶–N¹²–C⁹–O¹¹ was close to that of the 4-acetamidophenylnitrenium ion, and this indicates that the *N*-methyl substitution on the acetamido group causes the 4-(*N*-methylacetamido)phenylnitrenium ion to have the C=O group nonplanar relative to the phenyl ring due to some steric interaction between the two methyl groups. The rotation of the C=O bond away from the phenyl group in the singlet 4-(*N*-methylacetamido)phenylnitrenium ion makes the π molecular orbital of the C=O bond less parallel to the phenyl ring and have less electron withdrawal and/or resonance interaction with the phenyl ring. However, changing the H atom attached to the acetamido nitrogen in the 4-acetamidophenylnitrenium ion to a methyl group in the 4-(*N*-methylacetamido)phenylnitrenium ion leads to a smaller inductive and/or electron-donating interaction (the H atom has higher electron-donating ability than the methyl group). The competition between the C=O electron withdrawal and H versus methyl group electron donation interactions appear to largely balance each other. This enables the observed rotation of the C=O bond due to the methyl–methyl steric interaction, leading to similar iminocyclohexadienyl character on the two acetamidophenylnitrenium ions shown in Figure 3.

It is interesting to compare the structures of the singlet 4-acetamidophenylnitrenium and 4-(*N*-methylacetamido)phenylnitrenium ions to that recently found for the 4-methoxyphenylnitrenium ion.⁴⁶ The C=N bond of the nitrenium ion moiety is about 1.305 and 1.305 Å, respectively, for the 4-acetamidophenylnitrenium ions and almost the same as the 1.034 Å found for the 4-methoxyphenylnitrenium ion.⁴⁶ Similarly, the C–C bond alternation (or cyclohexadienyl character) of the phenyl ring is about the same in the 4-acetamidophenylnitrenium ions as it is in the 4-methoxyphenylnitrenium ion. In addition, the symmetric aromatic stretch vibrational frequencies (a good indicator of the degree of iminocyclohexadienyl character in aryl nitrenium ions) are about the same for the 4-acetamidophenylnitrenium ion (1633 cm⁻¹ from the transient Raman spectrum of Figure 2 and calculated to be at 1639 cm⁻¹ from the DFT calculations), the 4-(*N*-methylacetamido)phenylnitrenium ion (1638 cm⁻¹ from the DFT calculations), and the 4-methoxyphenylnitrenium ion (1632 cm⁻¹ from the transient Raman spectrum and 1639 cm⁻¹ from the DFT calculations of ref 46). This indicates that these arylni-

trenium ions have almost the same degree of iminocyclohexadienyl character. This suggests that the chemical reactivity of the nitrenium ion part of these ions are very similar to one another. However, the lifetime of the 4-(*N*-methylacetamido)phenylnitrenium ion is 5000 times longer than that for the 4-methoxyphenylnitrenium ion in water. Why are the lifetimes so different for these aryl nitrenium ions when they appear to have almost the same iminocyclohexadienyl character? This is discussed further in the next section.

C. Properties and Chemical Reactivity of the *para*-Acetamido Substituent and Comparison to *para*-Phenyl- and *para*-Alkoxy-phenylnitrenium Ion Reactions with Water and Deoxyguanosine. It has been noted that the 4-methoxy substituent is more electron donating than the 4-*N*-methylacetamido substituent from σ^+ values of -0.78 and -0.60, respectively, and that the lifetimes of the *N*-(*N*-methylacetamido)phenylnitrenium and 4-methoxyphenylnitrenium ions in water fail to follow the carbocation scale.³⁴ Ruane and McClelland³⁴ also noted that it is not surprising that this aryl nitrenium ion correlation is poor because σ^+ calibrates the effect of the substituent on the transition state for developing positive charge on the benzylic carbon. Since the phenylnitrenium parts of these *para*-substituted aryl nitrenium ions have almost the same iminocyclohexadienyl character, the chemical reactivity of the *N*-methylacetamido and the methoxy moieties must be very different from one another, with the 4-methoxy moiety being significantly more reactive toward water, and this helps to determine the relative lifetimes of the 4-(*N*-methylacetamido)phenylnitrenium and 4-methoxyphenylnitrenium ions in water. The barrier to reaction with water for oxocarocations are lower for those with greater charge on the oxocarbo group compared to those with less charge.⁴⁷ The oxocarocation character of the 4-methoxyphenylnitrenium ion was found to be substantial from the transient Raman spectra and DFT computed structure.⁴⁶ The reaction of the 4-methoxyphenylnitrenium ion with water is much faster ($k_w \approx 2.7 \times 10^6 \text{ s}^{-1}$) than the reaction of the 4-(*N*-methylacetamido)phenylnitrenium ion with water ($k_w = 2 \times 10^2 \text{ s}^{-1}$).^{34,36} The charge on the oxocarocation part of these kinds of aryl nitrenium ions can be lowered by adding a spacer phenyl group between the methoxy group and the phenylnitrenium ion as in the 4'-methoxybiphenyl-4-yl nitrenium ion, and this leads to a longer lifetime on the order of milliseconds.²⁹ Thus, the reactivity of the *para*-substituent toward water can significantly influence the lifetimes of *para*-substituted phenylnitrenium ions with an increase in their reactivity toward nucleophiles such as water, thereby decreasing their lifetimes.

The variation in the lifetimes of aryl nitrenium ions can also influence the selectivity of the substituted phenylnitrenium ion toward 2'-deoxyguanosine (denoted here as $k_{dG}:k_w$ selectivity). For example, we have found that the 4-acetamidophenylnitrenium, 4-(*N*-methylacetamido)phenylnitrenium, and 4-methoxyphenylnitrenium ions all have about the same iminocyclohexadienyl character for their phenylnitrenium moieties. They also have similar reaction rates toward 2'-deoxyguanosine with $k_{dG} = 9 \times$

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$10^6 \text{ M}^{-1} \text{ s}^{-1}$ for the 4-(*N*-methylacetamido)phenylnitrenium ion³⁴ and $k_{\text{dG}} = 2 \times 10^7 \text{ M}^{-1} \text{ s}^{-1}$ for the 4-methoxyphenylnitrenium ion.^{35,36} However, their reaction rates toward water are substantially different and can vary by a factor of more than 10 000: $k_{\text{w}} = 2.7 \times 10^6 \text{ s}^{-1}$ for the 4-methoxyphenylnitrenium ion to only $2 \times 10^2 \text{ s}^{-1}$ for the 4-(*N*-methylacetamido)phenylnitrenium ion.^{34–36} This leads to a $k_{\text{dG}}:k_{\text{w}}$ selectivity of about $4.5 \times 10^4 \text{ M}^{-1}$ for the 4-(*N*-methylacetamido)phenylnitrenium ion, and this is close to values in the 2 to $4 \times 10^4 \text{ M}^{-1}$ range found for some 4-biphenyl derivatives of aryl nitrenium ions.^{30,34,48} While the 4-(*N*-methylacetamido)phenylnitrenium ion exhibits significant selectivity toward 2'-deoxyguanosine, the 4-methoxyphenylnitrenium ion exhibits very little selectivity, with a $k_{\text{dG}}:k_{\text{w}}$ value of about 7.4 M^{-1} . This illustrates how a highly reactive *para*-substituent can alter the lifetime and 2'-deoxyguanosine selectivity of *para*-substituted phenylnitrenium ions. It appears that the relative competition between the substituent site and the nitrenium moiety of *para*-substituted aryl nitrenium ions for reaction with water is important for determining the lifetimes of these species in aqueous environments and the selectivity for reaction with 2'-deoxyguanosine and probably related groups in reactions with DNA.

Conclusion

An experimental transient resonance Raman spectrum was obtained for the 4-acetamidophenylnitrenium ion in a largely aqueous solvent. (U)BPW91/cc-PVDZ density functional theory calculations were also reported for the 4-acetamidophenylnitrenium and 4-(*N*-methylacetamido)phenylnitrenium ions. The transient resonance Raman vibrational frequencies and intensities in conjunction with results from the (U)BPW91/cc-PVDZ calculations indicate that the experimental Raman spectrum is due to the singlet state of the 4-acetamidophenylnitrenium ion. The singlet 4-acetamidophenylnitrenium ion has noticeable charge on both the acetamido and nitrenium moieties and has significant iminocyclohexadienyl character to a degree comparable to those previously reported for several *para*-phenyl-substituted phenylnitrenium ions. The chemical reaction rates of several *para*-acetamido, *para*-phenyl, and *para*-alkoxy-substituted phenylnitrenium ions with water and 2-deoxyguanosine substrates reported in the literature were compared to the structural properties of these aryl nitrenium ions. These aryl nitrenium ions were observed to have similar iminocyclohexadienyl character and reaction rates with 2'-deoxyguanosine but have a much wider range of reaction rates with water depending on the nature of the *para*-substituent. This suggests that relative competition between the substituent site and the nitrenium moiety of *para*-substituted aryl nitrenium ions for reaction with water helps determine the lifetimes of these species in aqueous environments and may affect the selectivity of the aryl nitrenium ions for reaction with 2'-deoxyguanosine and related groups in DNA.

Experimental and Computational Section

The 4-acetamidophenyl azide precursor compound was synthesized following a previously reported method for making azide compounds,⁴⁹ and details are provided in Supporting

Information. Samples of 4-acetamidophenyl azide were prepared with concentrations of about 2.5 mM in a 60% water/40% acetonitrile mixed solvent by volume with an acetate buffer (2 mM) and a pH of 3.5. The transient resonance Raman spectrum was obtained using an experimental apparatus and methods described elsewhere,^{32,33,37–40} so only a short description will be given here. The harmonics of a pulsed Nd:YAG laser and its hydrogen Raman-shifted laser lines provided the pump (266 nm) and probe (320 nm) excitation wavelengths for the transient Raman experiments. An optical time delay of about 5–10 ns between the pump and probe laser pulses was used in the experiments with the pump and probe beams lightly focused onto a flowing liquid stream of sample in a near collinear and backscattering geometry. The Raman scattering was then collected with reflective optics and imaged through a depolarizer and entrance slit of a 0.5 m spectrograph, whose grating dispersed the light onto a liquid cooled CCD detector mounted on the exit port. The CCD acquired the Raman signal for about 300–600 s before being read out to an interfaced PC computer, and about 10–20 of these readouts were added together to obtain a spectrum. Pump-only, probe-only, and pump–probe spectra were taken, and a background scan was also acquired. The known Raman band vibrational frequencies for the water/acetonitrile solvent were used to calibrate the Raman shifts of the spectra. Subtraction of a probe-only spectrum from the pump–probe spectrum was done so as to extract solvent and precursor Raman bands from the transient spectrum. The pump-only spectrum and background scans were then also subtracted to finally obtain the transient Raman spectrum of interest.

All of the density functional theory calculations given here made use of the Gaussian 98W program suite.⁵⁰ Complete geometry optimization and vibrational frequency calculations were done analytically using the (U)BPW91 method^{51,52} and the cc-PVDZ basis set.⁵³ The S^2 values for the unrestricted wave function calculations done for the triplet states were 2.0053 and 2.0056 for the 4-acetamidophenylnitrenium and 4-(*N*-methylacetamido)phenylnitrenium ions, respectively. These S^2 values are very close to the expected value of 2 and indicate that spin contamination was not appreciable for the triplet state calculations. Density functional theory calculations at the random-phase approximation⁴⁵ were also done in order to estimate the electronic transition energies and oscillator strengths for the 4-acetamidophenylnitrenium and 4-(*N*-methylacetamido)phenylnitrenium ions.

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Supporting Information Available: Description of the synthesis and characterization of the 4-acetamidophenyl azide precursor compound used in the transient resonance Raman experiments and selected output from the (U)BPW91/cc-PVDZ calculations showing the Cartesian coordinates, total energies, and vibrational zero-point energies for the

singlet and triplet states of the 4-acetamidophenylnitrenium ion and the 4-(*N*-methylacetamido)phenylnitrenium ion. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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