ABSTRACT

Title of Dissertaion: PHOTOLYTIC GENERATION OF NITRENIUM IONS: KINETIC STUDIES AND POLYMERIZATION REACTIONS

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Nitrenium ions are highly reactive transient species that contain a positively charged and dicoordinate nitrogen atom. The nitrogen atom contains only six electrons in its valence shell and thus the nitrogen is electron deficient and bears a positive charge. Nitrenium ions are of interest due to their suspected role in carcinogenesis since amines are known to form covalent bonds to DNA. The synthesis and photolysis of 1-(*N*-methyl-*N*-(1-naphthyl)amino)-2,4,6-trimethylpyridinium tetrafluoroborate, by laser flash photolysis, allowed for the direct observation of *N*-methyl-1-naphthylnitrenium ion as well as measurements of *N*-methyl-1-naphthylnitrenium ion's lifetime and trapping rate constants. It was determined that *N*-methyl-1-naphthylnitrenium ion has an absorption maximum centered around 500 nm and a lifetime of 835 ns. The trapping rate constants

with simple nucleophiles, such as chloride, alcohols, and amines, were determined to be on the order of 10^8 - 10^9 $M^{-1}s^{-1}$. These trapping rate constants were compared to other arylnitrenium ion systems to determine what factors contribute to a chemical's inherent carcinogenicity. The synthesis and photolysis of 1-(*N*-methyl-*N*-(2-naphthyl)amino)-2,4,6-trimethylpyridinium tetrafluoroborate was also performed. Although no transient intermediate was observed, products from photolysis are consistent with arylnitrenium ion products.

Nitrenium ions are also of interest due to their possible role in the polymerization of aniline to form polyaniline (PANI). PANI is of interest because of it is an electronically conducting polymer with many commercial aspects and the mechanism of formation has been under dispute for decades. Although it is generally agreed that the initial dimerization step is due to radical cation coupling, the mechanism for aniline polymerization is argued as proceeding through either a radical cation mechanism or via a nitrenium ion mechanism. Synthesis of a photochemical precursors of an aniline dimer 4-(*N*-anilino)phenyl azide produced what is believed to be a 4-(*N*-anilino)phenylnitrenium ion which has an absorption maximum centered around 490 nm. Spectroscopic analysis by MALDI-TOF-MS and X-ray photoelectron spectroscopy (XPS), shows that PANI is a photoproduct. The extrapolated data and results from similar systems, supports the hypothesis that polymerization involves a nitrenium ion intermediate.

PHOTOLYTIC GENERATION OF NITRENIUM IONS: KINETIC STUDIES AND POLYMERIZATION REACTIONS

by

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2005

DEDICATION

This work is dedicated to my parents, Dr. Shain-Dow and Helen Kung, for their support ever since I can remember. I would really like to thank my father for teaching me by example, that the only thing greater than the pursuit of knowledge is family.

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1.1: Nitrenium Ions Defined

Reactive intermediates have been a topic of study for decades. One interesting class of reactive intermediates are the nitrenium ions.[1] Nitrenium ions are highly reactive electron deficient nitrogen compounds with the general formula of $RR'N^+$ and the nitrogen contains six electrons in its valence shell; thus, the nitrogen bears a positive charge.[2,3] Nitrenium ions are isoelectronic with nitrenes (R-N), carbenium ions ($RR'R''C^+$), and carbenes ($RR'C$) (Figure 1.1).

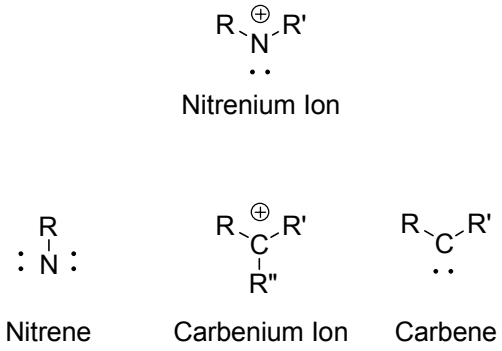


Figure 1.1: Nitrenium ions and isoelectronic species.

Nitrenium ions are similar to nitrenes because, in both cases, the nitrogen has six valence electrons but nitrenes are monovalent and neutral whereas nitrenium ions are divalent and cationic. Nitrenium ions are also similar to carbenium ions because they are both cationic but have different atoms bearing the positive charge. While nitrenium ions resemble carbenium ions in their chemical behavior, nitrenium ions are much more reactive. Due to their electronic structure, nitrenium ions are very strong electrophiles

and are short-lived at room temperature in solution. Nitrenium ions are also similar to carbenes because they are both divalent with two bonding orbitals and two nonbonding electrons.

Much like carbenes and nitrenes, the two non-bonding electrons allow the nitrenium ion to have two low energy electronic states, a singlet state and a triplet state (Figure 1.2). There is the triplet state, (σp), in which two non-bonding electrons have parallel spins in separate orbitals, one electron occupying the non-bonded σ-orbital and the other electron occupying the non-bonded p orbital. There is the singlet state, (σ^2), in which the two non-bonding electrons are paired in the same non-bonded σ-orbital. The reactivity of nitrenium ions can be attributed to these two non-bonding electrons and the two non-bonding orbitals on the nitrogen.[4] There are two other possible configurations for the singlet state which are the σp and the p^2, but these two states are much higher in energy and are therefore not considered greatly relevant to the chemical behavior of nitrenium ions.

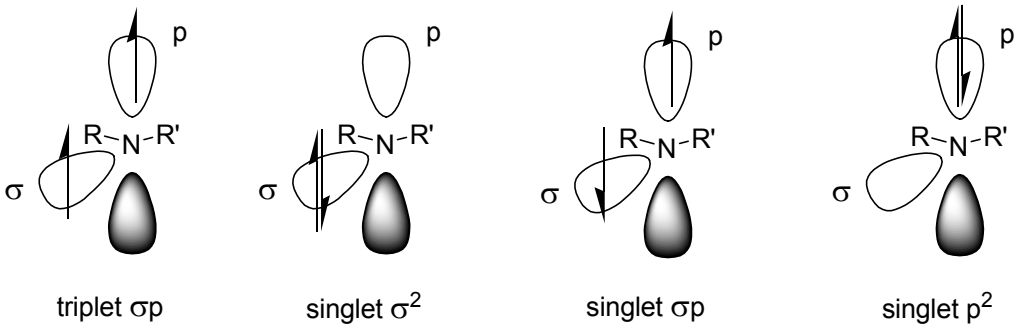


Figure 1.2: Electronic configurations of simple nitrenium ions.

The energy difference between the singlet and the triplet states is determined by the energy difference between the two non-bonding orbitals. This difference can be based on such factors as electron repulsion, electron exchange energy, and coulombic forces. A schematic representation of the energy difference is given in Figure 1.3.

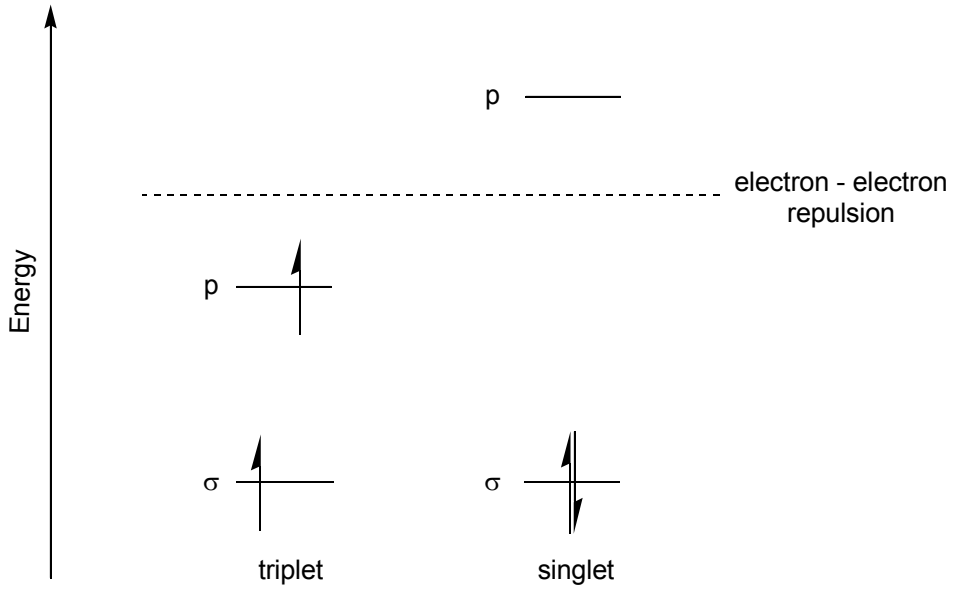


Figure 1.3: Factors affecting the singlet-triplet energy gap.

Although it appears that the singlet state (σ^2) should always be the lowest energy state since it has more s character (σ^2), there are other factors which affect the energy ordering. The two most prominent factors that affect the ground state are Hund's rule and electron-electron repulsion, both of which would favor the triplet state (σp). It turns out that the most stable state depends upon the substituents and substitution pattern of the nitrenium ion. The singlet state is favored when the p-orbital is destabilized and the σ-orbital is stabilized, such that the $\Delta E_{\sigma p}$ is greater than the electron repulsion, electron exchange energy, and coulombic forces. This allows for the pairing of the electrons in

the σ-orbital. The triplet state is favored when the p-orbital is stabilized and the σ-orbital is destabilized, such that $\Delta E_{\sigma p}$ is less than the electron repulsion, electron exchange energy, and coulombic forces. This allows for the unpairing of the electrons in both the σ and p-orbitals. Therefore, substituents that destabilize the p-orbital or stabilize the σ-orbital will favor the singlet state and vise versa.

The simplest example of a nitrenium ion is NH_2^+, also known as an imidogen ion, and commonly referred to as the parent nitrenium ion. The parent nitrenium ion (NH_2^+) has been extensively studied by theoretical methods and there is good agreement between calculated and high-resolution gas-phase spectra which show it to be a ground state triplet with a singlet-triplet energy gap (ΔE_{st}) of +29.16 and quasi-linear with a central bond angle of roughly 152º.[5-15] The reported values of ΔE_{st} are positive when the ground state is a triplet whereas negative values of ΔE_{st} indicate that the ground state is a singlet.

Nitrenium ions can be classified based on their substituents as aryl, alkyl, halo, or heteroarylnitrenium ions. Alkylation of the nitrenium ion's nitrogen allows for hyperconjugation which reduces the singlet-triplet gap as electron density is donated into the empty p-orbital. The electron donation stabilizes the closed-shell singlet state relative to the triplet state by increasing the energy splitting between the two orbitals.[15,16] This trend can be seen in Table 1.1 by comparing the first three entries. The ΔE_{st} values, by which the triplet state is favored, decreases for each subsequent addition of a methyl group.

Table 1.1: Singlet-triplet energy gaps and geometries for simple nitrenium ions.[8,12,15,17]

R_1	R_2	ΔE_{st} (kcal/mol)	Central Angle (°) Triplet/Singlet
H	H	+29.16	152.82/108.38
CH_3	H	+13.2	150.4/112.1
CH_3	CH_3	+8.6	143/119.7
F	H	-0.29	125.7/105.1
Cl	H	+5.02	133.7/108.7
CN	H	+27.5	180.0/120.4
F	F	-57.3	124.8/107.6
Cl	Cl	-19.8	137.0/117.3

The singlet and triplet ground state depend on the nature of the substituents on the nitrogen and their geometry about the central atom. Aromatic substituents efficiently stabilize the singlet state relative to the triplet state.[18-20] Early computations revealed that phenylnitrenium ion is planar and a ground state singlet. This allows for effective charge delocalization. The p-orbitals on the aromatic ring raise the energy of the unfilled out-of-plane p-orbital relative to the in plane σ-orbital, thus favoring electron pairing and stabilizing the singlet. Substituents on the ring, such as π-donating groups, further stabilize the singlet, whereas π-withdrawing groups counteract the effect and destabilize the singlet.[21-25]

Adding more electron-donating substituents on the ring can also destabilize the singlet relative to the triplet because the additional substituent increases the nitrenium ion's steric bulk. This is due to the fact that the more bulky substituents would force a greater central bond angle about the nitrogen and would give more p character to the σ-non-bonding orbital. This raises the σ-orbital energy and brings it closer to the p-non-bonding orbital. Thus, it reduces the $\Delta E_{\sigma p}$ and the orbitals become more and more

degenerate. Such is the case with bis(2,6-di-*tert*-butylphenyl)nitrenium ion, which is favored to be a ground state triplet (ΔE_{st} = +7.3 kcal/mol) because the steric bulk of the ortho *t*-butyl groups force the central angle to become nearly linear (150º) and favor the triplet state.[26] The ΔE_{st} and central angles of other nitrenium ions are listed in Table 1.1.

1.2: Reactions of the Singlet and Triplet States

Since singlet nitrenium ions are analogous to carbenium ions, nitrenium ions undergo similar reactions, such as 1,2-alkyl and hydride shifts.[15,16,24,27-30] Singlet arylnitrenium ions have been generated in aqueous solutions with simple nucleophiles and the primary decay routes have shown to be trapping at the ortho and para positions of the aromatic ring, with regard to the nitrenium ion center.[31-37] From these trapping studies, it can be generalized that if a nitrenium ion is very reactive, it is less selective and a mixture of ortho and para substituted products is generated. On the other hand, if the nitrenium ion is less reactive, then the nitrenium ion is more selective towards nucleophiles and the para product is predominantly formed.

Simple nucleophiles attack at the ring carbons because of charge delocalization and places significant amounts of charge at the para and ortho positions.[21,25,34,38-40] Since many arylnitrenium ions can be likened to 4-imine-2,5-cyclohexadienylcation, which has been confirmed by time-resolved infrared spectroscopy (TRIR), the preferential sites of attack are the para and ortho positions.[41]

Electron-rich π systems, including the DNA base guanosine, add to the nitrogen of the nitrenium ion but it is still unclear why.[20,40,42-48] There are several arguments as to

whether attack, by π-nucleophiles, on nitrenium ions is a concerted process or a stepwise process.[1,49-51] Triplet nitrenium ions can be considered to behave like free radicals due to having two unpaired electrons. In fact, the major decay pathway for these species seems to be by H-atom transfer.[41,52]

In recent years, laser flash photolysis (LFP) has become a major technique to study the formation and lifetime of nitrenium ion intermediates. LFP is an approach for the direct study of intermediate cations and has the advantage of providing detailed kinetic information. In this technique, a stable photochemical precursor is excited with light from a pulsed laser.[3] The laser pulse initiates a photochemical process that creates the short-lived intermediate. The intermediate is then detected via its UV-vis absorption spectrum using a probe beam from a continuous lamp and fast detector. A more detailed discussion of LFP is presented in Chapter 2.

Arylnitrenium ions have been proposed as intermediates in DNA damaging reactions which lead to convert a normal cell into a cancer cell.[53-57] It has been known for many years that arylnitrenium ions, from aromatic amines and amides, have mutagenic properties and implications as "ultimate carcinogens" which cause DNA damage.[58-60] Thus, nitrenium ions not only spark interest in chemical aspects, but in biochemical aspects as well. A more in-depth discussion of nitrenium ions as carcinogens is presented in Chapter 3.

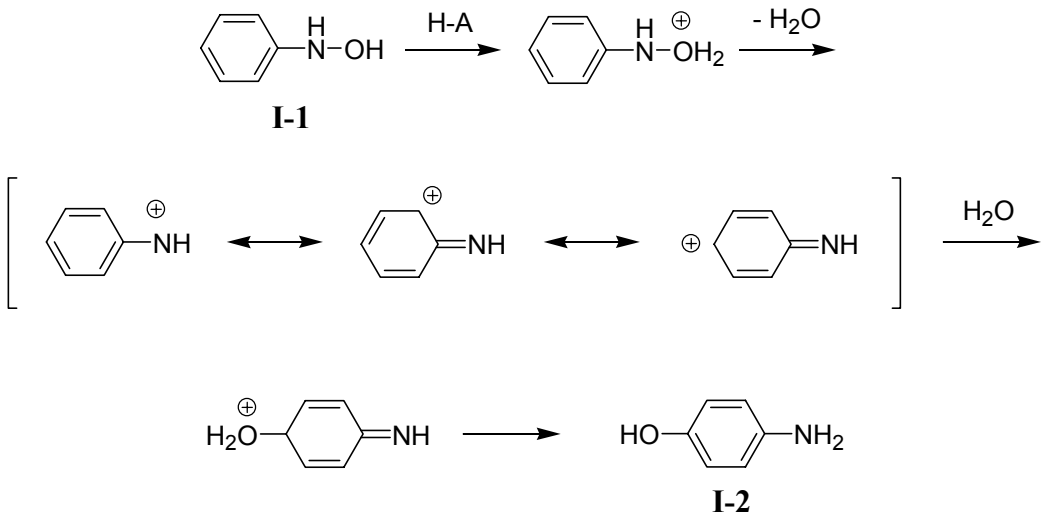
Nitrenium ions are also of interest due to their suspected role as an intermediate in the polymerization of aniline to form polyaniline (PANI). Polyaniline and its derivatives are of interest because they are electrically conductive when they are doped with oxidants. PANI can be prepared via oxidation of aniline either electrochemically,

enzymatically, or with chemical reagents.[61-78] PANI can be thought of as a polymer of phenylnitrenium ion where a phenylnitrenium ion can add to aniline yielding phenylbenzidine and the chain can elongate via this nitrenium ion coupling or via radical cation coupling.[61,63,64,72,73] A more detail discussion of nitrenium ions in polymerization reactions is presented in Chapter 4.

1.3: Historical Background

In order to discuss nitrenium ions in current applications, one must understand its beginnings. Before the 1980s, many scientists questioned the existence of nitrenium ions as discreet intermediates. Because the data from experimentation were ambiguous, researchers were unable to determine whether the products were from a concerted process or a step-wise process which would have the nitrenium ion as a true intermediate. Although not known as a nitrenium ion at the time, Bamberger mentions a reactive intermediate of the same general structure as a nitrenium ion in 1898.[79] The Bamberger rearrangement involves the acid-induced rearrangement of arylhydroxylamines.[80,81] When treated with aqueous sulphuric acid, phenylhydroxylamine (**I-1**) is converted to *p*-aminophenol (**I-2**). This reaction is known as the Bamberger rearrangement (Scheme 1.1).[82-84]

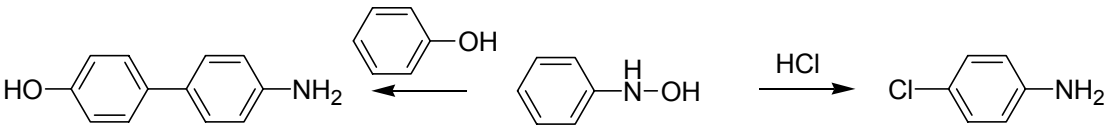
Scheme 1.1: The Bamberger rearrangement.



I-1 **I-2**

Originally, it was thought that an intermediate HO^+ was transferred but that was never observed. However, the attachment of many nucleophilies to the phenyl ring was observed. For example, if phenol is used as the nucleophile, its *p*-carbon becomes attached to the *p*-carbon of the phenylhydroxylamine, giving 4'-amino[1,1'-biphenyl]-4-ol (**I-3**) and the rearrangement of phenylhydroxylamine in the presence of hydrochloric acid gives *p*-chloroaniline (**I-4**) (Scheme 1.2).[82]

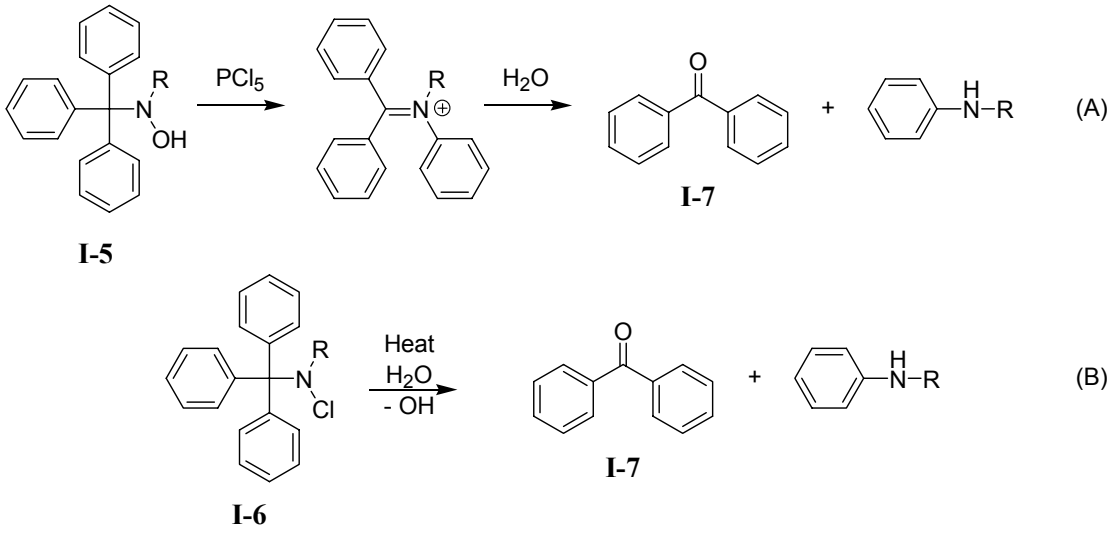
Scheme 1.2: Examples of the Bamberger rearrangement reacting with nucleophiles.



I-3 **I-1** **I-4**

Fifteen years later, in 1913, Stieglitz published a series of papers on the rearrangement of substituted hydroxylamines and *N*-chloroamines. It was found that upon hydrolysis, tritylhydroxylamines (**I-5**) and trityl-*N*-chloroamines (**I-6**) rearranged to give benzophenone (**I-7**) and aniline derivatives (Scheme 1.3).[1,85-87]

Scheme 1.3: Stieglitz's rearrangement study.

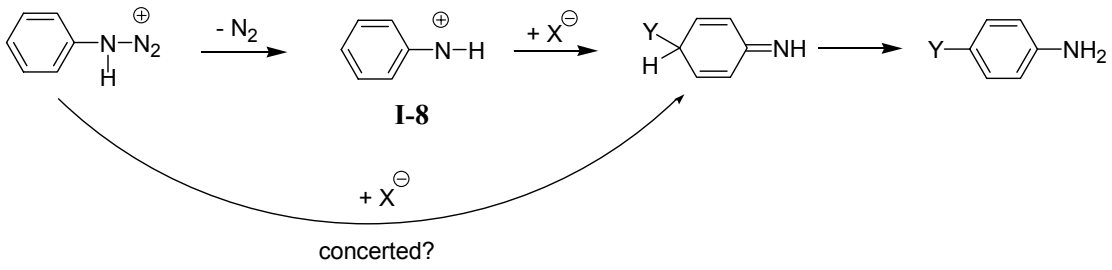


Reactions 1.3 A and B were reported to be facile when the R group was hydrogen, but reaction 1.3 B failed to occur with the R group was methyl. Therefore, Stieglitz concluded that the rearrangement was occurring through the intermediacy of a monovalent nitrogen (nitrene) species. Further research by Conley and Brandman found that reaction 1.3 B does occur when the R group is methyl, thus favoring the hypothesis that the reaction proceeds through a divalent electron-deficient nitrogen intermediate (nitrenium ion) instead of the previously thought nitrene.[88] This hypothesis was also supported by the research of Newman and Hay when they studied the migratory aptitudes

of aryl groups in the rearrangement of tritylhydoxylamines.[89] It was not until 1951 when Heller first reported kinetic data for a nitrenium ion intermediate.[32]

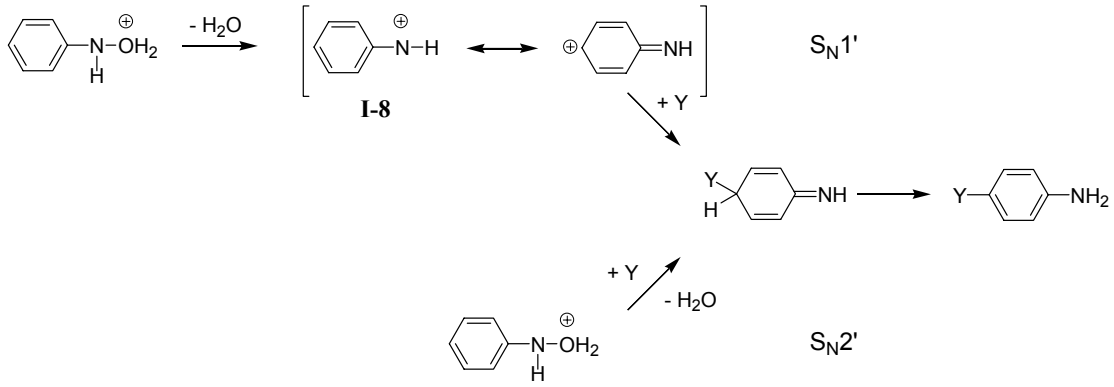
Abramovitch and Davis published a review article about the preparation and properties of nitrenes, known at that time as imido intermediates (imidogens) in 1964.[90] Abramovitch studied the reactions of aryl azides in acidic solutions and also determined that the reaction may either be a two-step or concerted process (Scheme 1.4).

Scheme 1.4: Abramovitch's proposed concerted and step-wise pathways.



From Scheme 1.5, one can see that the reaction can also be thought of as an S_N1' or as an S_N2' type process. A kinetic study indicated that a proton was involved in the rate-determining step and that the rate of the HCl catalyzed reaction was independent of the chloride concentration. Thus, the process was determined to be an S_N1' process via a discrete phenylnitrenium ion (**I-8**).

Scheme 1.5: S_N1' and S_N2' pathways.



McEwan studied acid-catalyzed unsymmetrical benzhydryl azides and the aryl migration showed little discrimination between aryl rings with electron-donating and electon-withdrawing groups.[91] Since the concerted process should be more selective with electron-donating substituents, it was proposed that the reaction occurred as a stepwise process rather than a concerted process and that the nitrenium ion was a discrete intermediate.

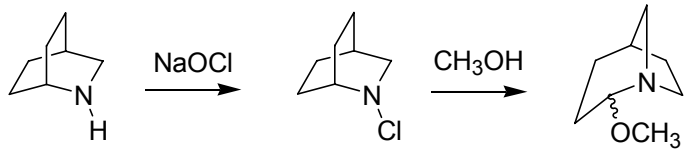
1.4: Gassman's Studies

As the evidence for the existence of nitrenium ions increased, so did the research into this reactive intermediate. In 1970, Gassman published product and kinetic studies of nitrenium ions. The basis of the product studies was that alkyl migration could occur to a divalent electron-deficient nitrogen species where both substituents on nitrogen were alkyl groups.[1,49,92] This approach was based on the tendency of alkyl groups to migrate to cationic centers but not to radical centers. This is in contrast to aryl groups and

hydrogen, which are known to migrate to both cationic and radical centers. Therefore, the migration of an alkyl group from carbon to nitrogen would suggest that the nitrogen was electron-deficient.

Since nitrenium ions resemble carbenium ions, systems in which carbenium ions have been studied can be used to study nitrenium ions, such as bridged bicyclic skeletons. With this in mind, Gassman converted the bridged bicyclic system isoquinuclidine (**I-9**), into *N*-chloroisoquinuclidine (**I-10**), and investigated its silver ion catalyzed solvolytic behavior and found that it produced **I-11** (Scheme 1.6).

Scheme 1.6: Gassman's initial product study.

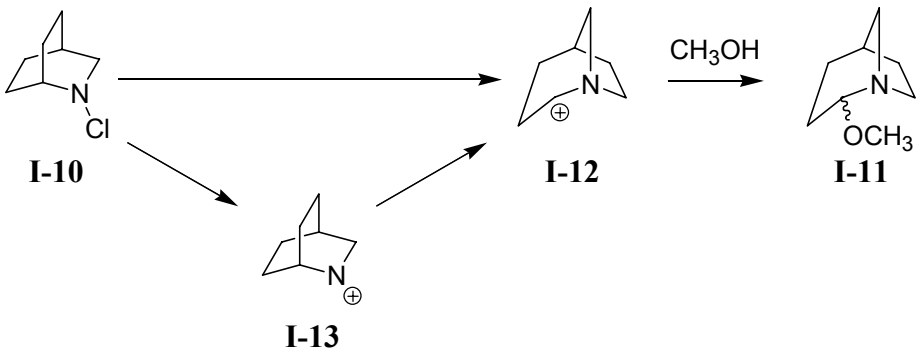


I-9 **I-10** **I-11**

The rearrangement from a 2-azabicyclo[2.2.2]octane system to a 1-azabicyclo[3.2.1]octane system does involve the migration of an alkyl group with its electron pair from carbon to nitrogen. This poses the question of how the rearrangement occurred. One can imagine the rearrangement proceeding through two possible pathways (Scheme 1.7). The first possible pathway is the heterolytic N-Cl cleavage by cationic silver to form a discrete nitrenium ion intermediate (**I-13**), which can undergo an alkyl migration to produce **I-12**. The nucleophilic addition of solvent to the resulting carbenium ion, **I-12**, would yield **I-11**. The second possible pathway is a concerted loss

of chloride and migration of the alkyl group with its pair of bonding electrons to yield **I-12**, which can undergo nuclephilic attack by the solvent to yield **I-11**.

Scheme 1.7: Two possible pathways for the formation of I-11.

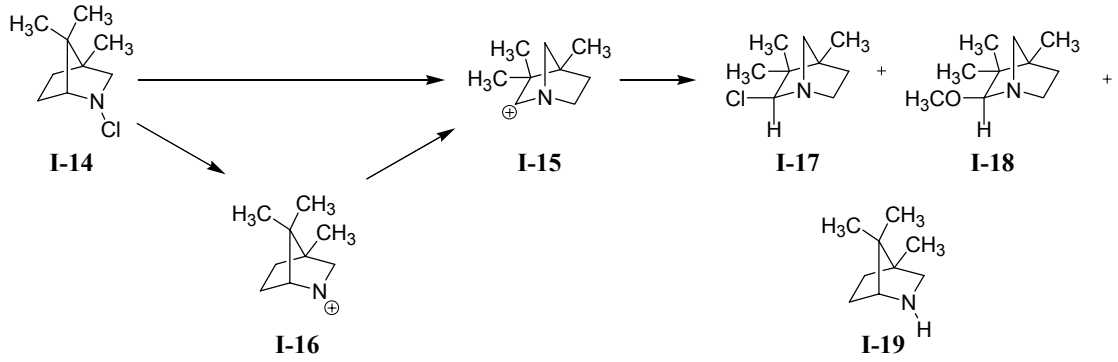


Upon the rearrangement of **I-10** to yield **I-12** one cannot unambiguously say that **5** is a discrete intermediate or not. It can be inferred that somewhere along the reaction pathway, there is the formation of an electron-deficient nitrogen since the alkyl group migrated with its electron pair. Since the product (**I-11**) requires an alkyl group to rearrange, with its electrons, it shows that there was an electron-deficient nitrogen along the pathway.

Two other examples where an alkyl migration to divalent nitrogen species by silver ion catalyzed solvolysis are the product studies of 4,7,7-trimethyl-2-chloro-2-azabicyclo[2.2.1]heptane (**I-14**) and 1,7,7-trimethyl-2-chloro-2-azabicyclo[2.2.1]heptane (**I-20**).[93] Upon refluxing **I-14** in methanol, three products were detected **I-17**, **I-18**, and **I-19** (Scheme 1.8). Again, the formation of **I-17** and **I-18** shows that an electron-deficient nitrogen was formed since the alkyl group migrated with its electron pair. The resulting carbenium ion was then either trapped by solvent or by chloride, which was generated by

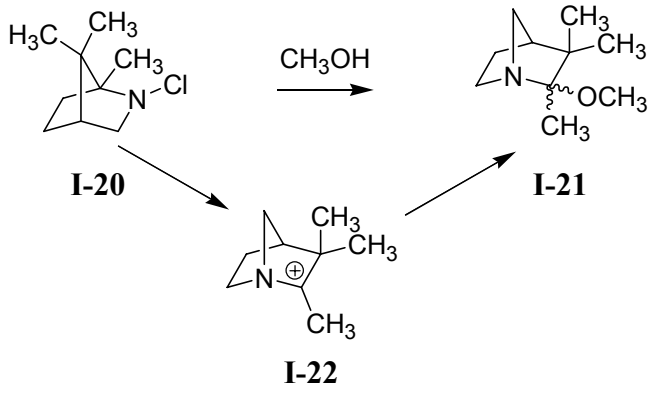
the heterolysis of the N-Cl bond. But, this product distribution did not answer the question whether the nitrenium ion is a discrete intermediate or not.

Scheme 1.8: Gassman's product study supporting rearrangements.



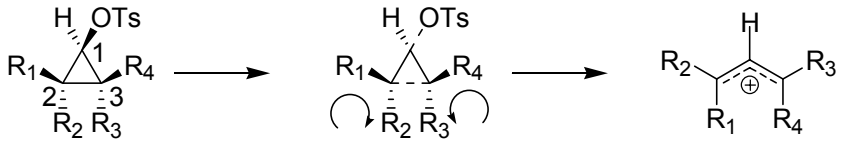
As presented in Scheme 1.9, the transformation of **I-20** to **I-21** shows a complete loss of chloride from the product and is consistent with a heterolytic cleavage of the N-Cl bond. The carbenium ion that is formed from this rearrangement would be the tertiary carbenium ion **I-22** and the addition of solvent to **I-22** yielding **I-21**, is consistent with expectations based on nitrenium ion concepts.

Scheme 1.9: Variation on Gassman's product study.



The kinetic rate data and the observed thermodynamic parameters for the solvolysis of **I-14** and **I-20** support a mechanism which involves a separation of charged ions. More kinetic evidence for the heterolytic cleavage of the N-Cl bond was provided by a study of the kinetics of *N*-chloroaziridine ionization in polar solvents. The use of *N*-chloroaziridines was based on observations that solvolytic ring opening of cyclopropyl tosylate and chloride derivatives (**I-23**) are actually concerted electrocyclic ring openings of cyclopropyl cations (**I-24**) to allylic cations (**I-25**) (Scheme 1.10).[94-97] This fact is key in demonstrating that a nitrenium ion is formed from the heterolytic cleavage of the N-Cl bond because the rearrangement follows the molecular orbital symmetry considerations of Woodward and Hoffman.[98] Cyclopropyl tosylate and chloride derivatives (**I-23**) ionize with concerted cleavage of the C_2-C_3 bond in a disrotatory process with outward rotation of the groups trans to the leaving group (**I-24**) to yield **I-25**.

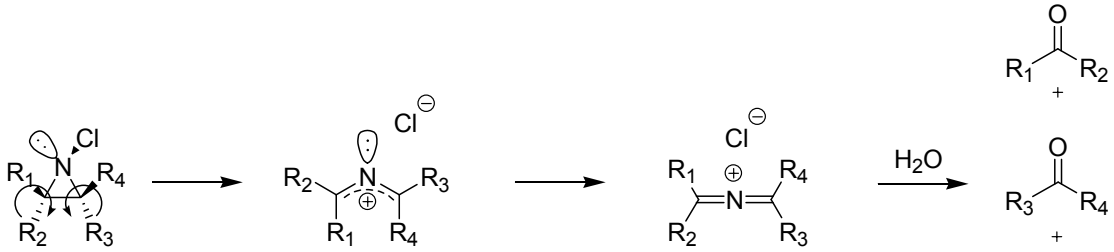
Scheme 1.10: Concerted disrotatory ring opening of cyclopropyl tosylates.



I-23 **I-24** **I-25**

The analogous *N*-chloroaziridines were used to see if this would generate the electron deficient nitrenium ion. Kinetic studies of *N*-chloroaziridines have shown that solvolysis occurs in a stereospecific fashion, with cleavage of the C_2-C_3 bond of the three-membered ring occurring in a concerted disrotatory fashion (Scheme 1.11).[1,99]

Scheme 1.11: Gassman's kinetic studies using *N*-chloroaziridines.



I-26 **I-27** **I-28**

Concerted ionization-ring cleavage of **I-26** would be expected to give an intermediate (**I-28**) which can hydrolyze to give two moles of carbonyl compounds and ammonium chloride.[100] The six derivatives of **I-26** are listed in Table 1.2 along with their relative rates of solvolysis. The results can be explained on the basis of increasing steric strain in the transition state or relief of steric compression in the ground state. It

could also be due to the effect of the methyl groups in stabilizing the developing positive charge on carbon during the disrotatory C_2-C_3 cleavage.

Table 1.2: Kinetic data from the *N*-chloroaziridine ring opening.

Compound	R_1	R_2	R_3	R_4	k_{rel}
I-26a	H	H	H	H	1
I-26b	H	H	H	CH_3	15
I-26c	H	H	CH_3	H	210
I-26d	H	CH_3	H	CH_3	1,490
I-26e	H	H	CH_3	CH_3	1,860
I-26f	H	CH_3	CH_3	H	155,000

The results are consistent with a concerted ionization-ring cleavage as expected on the basis of a disrotatory ring opening. Between compounds **I-26a** and **I-26b**, the partial positive charge in the transition state is distributed between two primary carbons whereas in **I-26b**, the distribution is between a primary and a secondary carbon. The increased stabilization provided by the secondary carbon is countered by the increased steric bulk in the concerted ionization and thus an increase in rate is small. Comparing **I-26b** and **I-26c**, the rate increases dramatically because the methyl group in **I-26b** is rotated inwards which increases steric interactions between a methyl group and a hydrogen atom. On the other hand, in **I-26c**, the methyl group is rotated outwards, decreasing steric interactions, thus the rate is increased by a factor of 14. Compound **I-26d** has two secondary carbon centers to distribute the positive charge and therefore the rate is much faster than compound **I-26c**, even though **I-26d** has a methyl – hydrogen interaction. The rate of solvolysis of compound **I-26e** is faster than that of **I-26d** because there is a tertiary carbon center, which stabilizes the positive charge. The rate of

solvolysis for compound **I-26f** is the fastest because the methyl - methyl group interaction is diminished due to the outward rotation of the methyl groups as required by the molecular orbital symmetry considerations for a process involving heterolytic cleavage of the N-Cl bond.

Results from both the product and kinetic studies provide evidence for heterolytic cleavage of the N-Cl bond producing an electron-deficient nitrogen species under solvolytic conditions. A study of the heavy atom effect was used to determine if the electron-deficient nitrogen was in fact the fully cationic divalent nitrenium ion or a slightly electron-deficient nitrogen species encountered during a transition state. As previously stated, nitrenium ions can exist in either the singlet or triplet states. The singlet will react much like a carbenium ion and undergo nucleophilic attack, while the triplet would react like a nitrogen radical cation and abstract hydrogen atoms. It has been established that heavy atom solvents can catalyze spin inversion by a factor of Z^4, where Z is the atomic number.[99,101] Therefore, using heavy atom solvents, one should be able to see the different products produced through the singlet and the triplet states of the nitrenium ion and provide evidence to the existence of the true nitrenium ion (Scheme 1.12 and Table 1.3).[92]

Scheme 1.12: Gassman's heavy atom solvent effect product study.

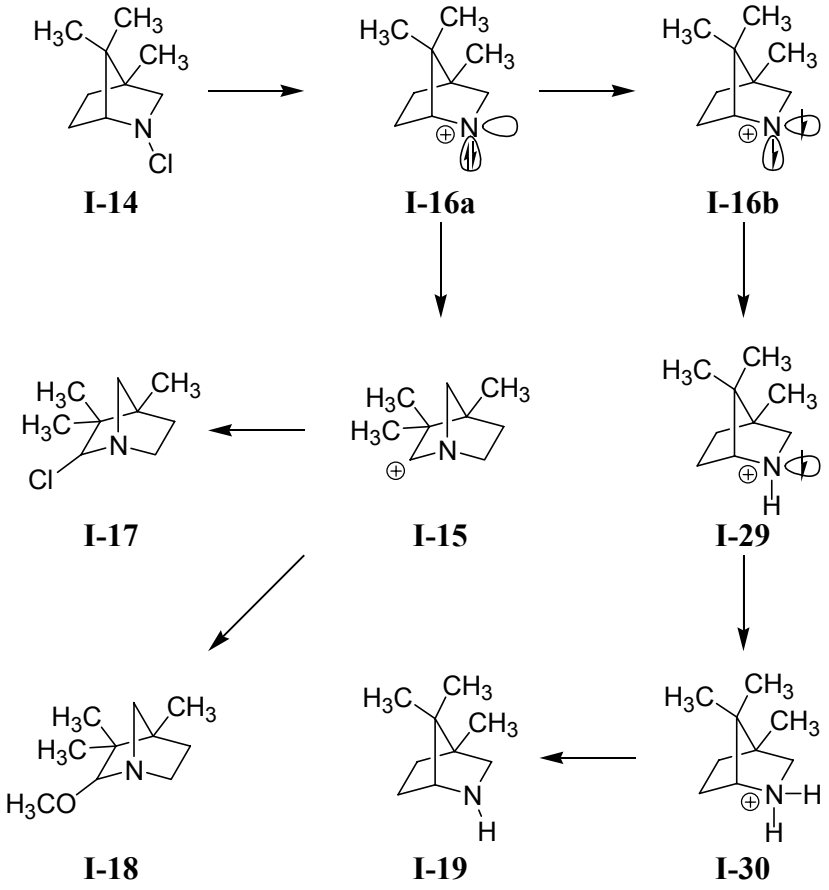


Table 1.3: Products from heavy atom solvolysis of I-14.

Solvent System	% Yield of I-17	% Yield of I-18	% Yield of I-19	% Yield of Singlet Products	Singlet /Triplet Product Ratio
CH_3OH-C_6H_{12}	56	10	8	66	8.2
CH_3OH- *p*-$C_6H_4Br_2$	33	10	25	43	1.7
CH_3OH-CCl_4	13	<1	59	13	0.22
CH_3OH- $CHCl_3$	4	<1	63	4	0.06
CH_3OH-$CHBr_3$	~1	<<1	45	1	0.02
CH_3OH- CH_3OH	59	20	7	79	11.3

From solvolysis of **I-14**, the singlet state of the nitrenium ion intermediate **I-16a** is formed which can undergo alkyl rearrangement to form carbenium ion **I-15**. This intermediate can then be trapped by chloride ion to form the chloro adduct **I-17** or by the solvent methanol to form the methoxy adduct **I-18**. The singlet state (**I-16a**) can undergo intersystem crossing (ISC) to the triplet state (**I-16b**). The triplet (**I-16b**) will act as a radical and abstract a hydrogen atom from the solvent to produce the radical cation **I-29**, which can abstract another hydrogen atom to yield the protonated amine **I-30**. Neutralization of **I-30** would give triplet product **I-19**.

As the solvent system is changed from a methanol/hexane mixture to a methanol/heavy atom solvent (*p*-dibromobenzene, bromoform, chloroform, and carbon tetrachloride), the yield of triplet product (**I-19)** increases. Therefore, one can infer that either there is a nitrenium ion intermediate or the initial N-Cl bond cleavage is homolytic and the triplet product is obtained by hydrogen atom abstraction from solvents, *p*-dibromobenzene, bromoform, chloroform, and methanol. But the same increase in the triplet product is observed when carbon tetrachloride, which cannot act as a hydrogen source, is used. In order for the heavy atom solvent effect to be applicable, there needs to be an intermediate that can exist in both the singlet and triplet states. Since the product study shows an increase in triplet products when heavy atom solvents are used, it can be determined that the nitrenium ion is a discrete entity.

Alkylnitrenium ions from silver ion solvolysis of various cyclic and bicyclic *N*-chloroamine supported the formation of nitrenium ions as legitimate intermediates.[49,92,102] In these reactions, the silver ion abstracts chloride from the nitrogen creating the singlet nitrenium ion. Products from such reactions include products from 1,2-alkyl shifts,

solvent trapping and chloride trapping. The free amine was also a product and supported the notion that the nitrenium ion reaction is step-wise and not concerted. The free amine came from the triplet state via intersystem crossing (ISC) accelerated by the heavy atom effect, which is common in photochemistry and photophysics.[103-105]

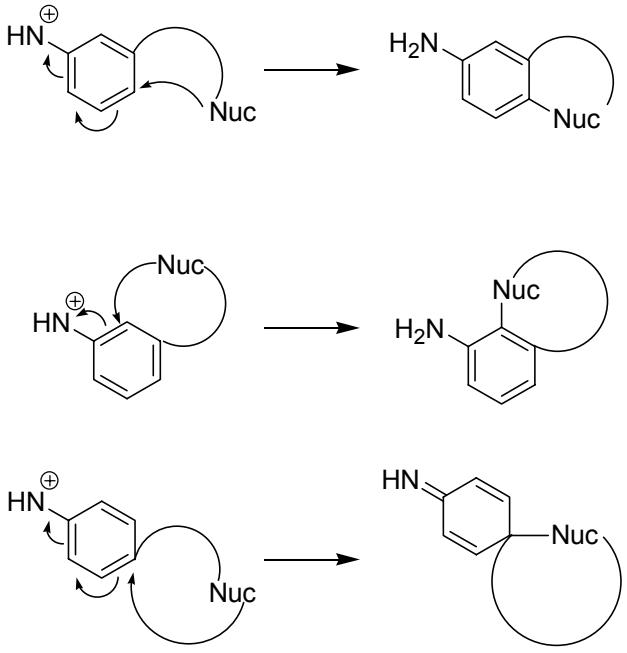
Gassman showed through product and kinetic studies that there was an electron-deficient nitrogen in the reaction pathway and that the initial N-Cl bond proceeded through a heterolytic cleavage. Through heavy atom solvent studies, Gassman reinforced that idea of heterolytic cleavage and determined that the nitrenium ion is an actual intermediate.

Gassman produced more evidence as to the presence of a discreet intermediate by kinetic studies on the solvolysis rates of a series of substituted *N*-chloroaniline derivatives. Gassman performed numerous early studies on nitrenium ions and LAH.[31,34,49,50,106,107] *N*-Chloroamines and *N*-hydroxylamine esters yield nitrenium ions in polar solutions. Their rate constants for solvolysis were measured and analyzed using the Hammett relationship and showed strong dependence on the electron-donating and the electron-accepting characteristics of the substituent and the electronegativity of the substituents.[39,49,92,108] An observed ρ^+ value of -6.35 indicated that a positively charged intermediate was formed.[31] Since then, several similar studies have been examined for other arylnitrenium ion systems.[37,38,109-114]

1.5: Contemporary Studies

In recent years, nitrenium ions have also been studied for their utility in organic synthesis.[2,60,115] Both aryl and alkoxynitrenium ions have found use in chemical synthesis by their incorporation into complex molecules. In general, they serve as nitrogen-based electrophiles and form bonds either at the nitrogen or an electropositive carbon center.[116-118] The most synthetically useful reactions are when the nitrenium ion center is covalently attached to a π-nucleophile via a long tether (Scheme 1.13).[74,75,119]

Scheme 1.13: General ipso- and spiro-substitution pathways with tethered nucleophiles.

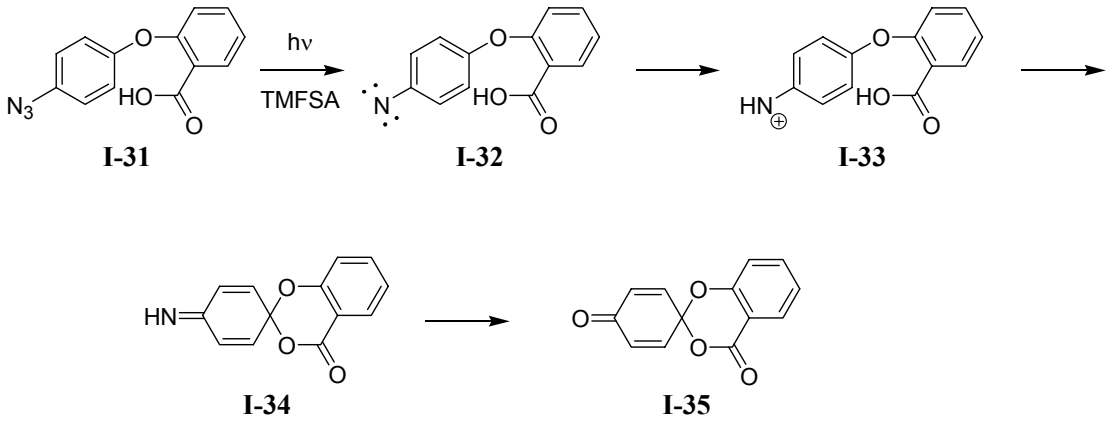


Reactions of nitrenium ions with π–nucleophiles can serve synthetic uses, some of which have been exploited by Wardrop and his group. Their reactions use the unique electronic effects of nitrenium ions to induce a spirocyclization of acylalkoxynitrenium ions which serve as intermediates in the synthesis of several interesting natural products.[74,75] These spirocycliazations are analogous to the methods employed by Abramovitch to yield macrocycles.[119,120] Other studies have also shown that nitrenium ions are trapped by alkenes.[121,122]

Abramovitch studied the acid catalyzed decomposition of arylnitrenium ions as useful intermediates in intramolecular cyclization reactions. Abramovitch has studied arylnitrenium ions in the formation of five and six membered lactones and seven membered rings.[123,124] There have also been studies in which nitrenium ions are used in the pathway to form *ipso*-substitution and in spirolactone formation (Schemes 1.13 and 1.14).[125]

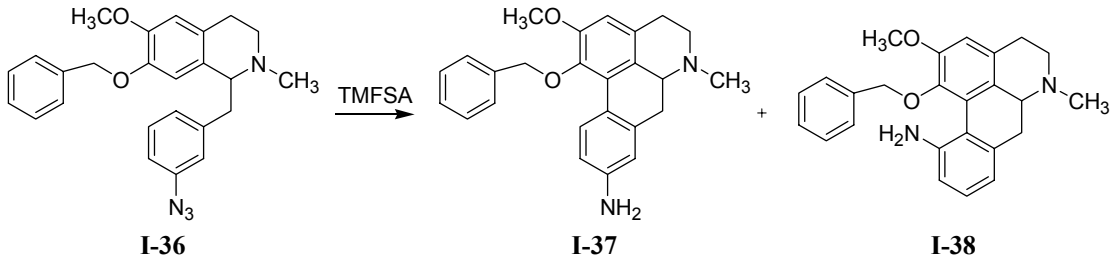
The *spiro*-trapping of arylnitrenium ions has been extended to the synthesis of the parent ring system of geodoxin. 4′-Azido-2-carboxydiphenyl ether (**I-31**) was decomposed with trifluoromethanesulphonic acid (TMFSA) to yield the spirolactone (**I-32**) (Scheme 1.14).[60,125] Photolysis of **I-31** yields nitrene **I-32**, which is protonated by TFSA to nitrenium ion **I-33**. The electron deficient nitrogen induces a spirocyclization ring closure and subsequent hydrolysis of the imine (**I-34**) to yield the final spirolactone (**I-35**).

Scheme 1.14: Formation of the parent ring of the natural product Geodoxin by nitrenium ion spirocyclization.



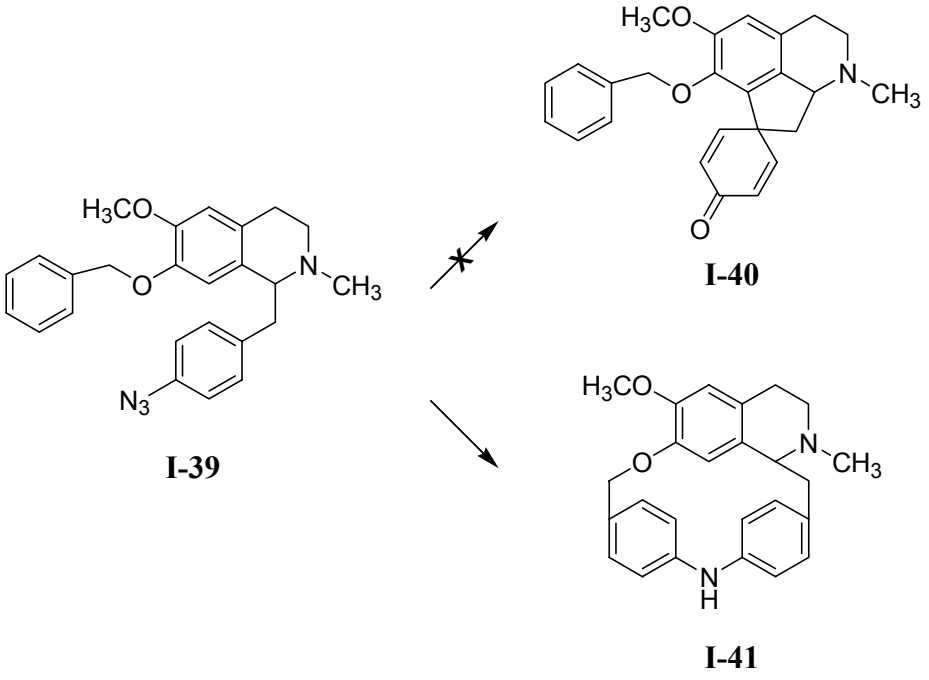
The synthetic use of nitrenium ions found new utility in later experiments performed by Abramovitch. From previous studies, it is clear how **I-36** can be transformed into **I-37** and **I-38** as an *ipso*-substitution (Scheme 1.15).[115]

Scheme 1.15: Formation of ipso-substitution products.



Using the same theory, one would also guess that the acid-catalyzed decomposition of **I-39** would presumably yield the *spiro*-substituted dienone (**I-40**) (Scheme 1.16). But in this case, the product yielded is **I-41**, a 16-membered macrocycle. The formation of this 16-membered macrocycle was one of the first moderately large ring formations observed that resulted from intramolecular electrophilic attack by a nitrenium ion upon an aromatic carbon.

Scheme 1.16: Expected spiro-substitution product (I-40) and actual macrocycle product (I-41).

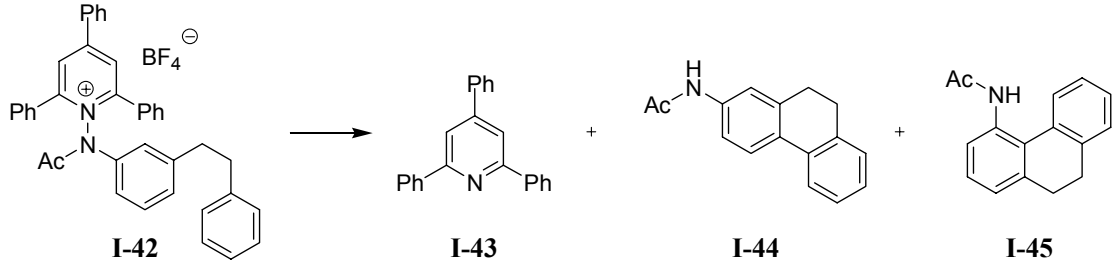


New technologies have been incorporated in further studies. With the synthesis of pyridinium salts, Abramovitch started to look at the thermolysis of pyridinium tetrafluoroborates as a new and synthetically useful source of arylnitrenium ions under non-acidic conditions.[59] Before this technique, studies were done with the acidic

decomposition of arylnitrenium ions and restricted the compounds to those without acid-sensitive moieties.

Pyridinium tetrafluoroborate salts have been decomposed to produce various products.[59] It was seen that the kinetics of formation of these products are consistent with the production of nitrenium ions. This led Abramovitch *et al.* to explore the use of pyridinium ions as the leaving group in a remote intramolecular functionalization (Scheme 1.17).

Scheme 1.17: Abramovitch's ipso-substitutions from pyridinium salts.



I-42 **I-43** **I-44** **I-45**

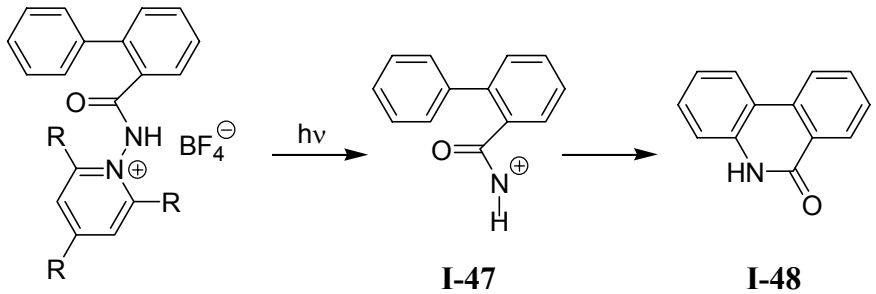
Pyridinium salt **I-42**, upon hydrolysis yields the neutral leaving group 2,4,6-triphenylcollidine (**I-43**) and the two ortho cyclized products that were expected from the ring closures (**I-44** and **I-45**).

One can now employ intramolecular cyclizations like those used in acid-catalyzed decompositions of aryl azides, but under initially non-acidic conditions. This promoted further study by Abramovitch and his group. Through these studies with intramolecular remote functionalization of arylnitrenium ions, it was determined that this method can be used in reactions as a useful and versatile method of forming homo- and heterocyclic

rings, such as six and seven membered ring, lactones, dihydrophenanthridines and benzo[c]chromens.[123,124,126] The *ipso*-substitution has also been demonstrated, and has been applied to the synthesis of prostaglandin photoaffinity probes.[125]

Abramovitch also studied the effects of different substituents on the pyridine leaving group of the pyridinium salt (Scheme 1.18).[127,128] Both **I-46a** and **I-46b** were decomposed to yield **I-48** and the simplest way to account for these results is to assume the formation of the acylnitrenium **I-47** by the photoheterolysis of the N-N bond. Unlike the thermolysis, which had been used before, no rearrangement products were observed.

Scheme 1.18: Experiments with substituted pyridine as the leaving group.



I-46

a: R = CH_3

b: R = Ph

I-47

I-48

Meanwhile, Novak's studies included the synthesis of ring-substituted *N*-sulfonoxyacetanilides (**I-49**) and their solvolysis reactions in aqueous and alcohol solvents.[35] From this experiment, the kinetic and product studies provided evidence for the solvolysis of the N-O bond cleavage in aqueous solution with the generation of tight

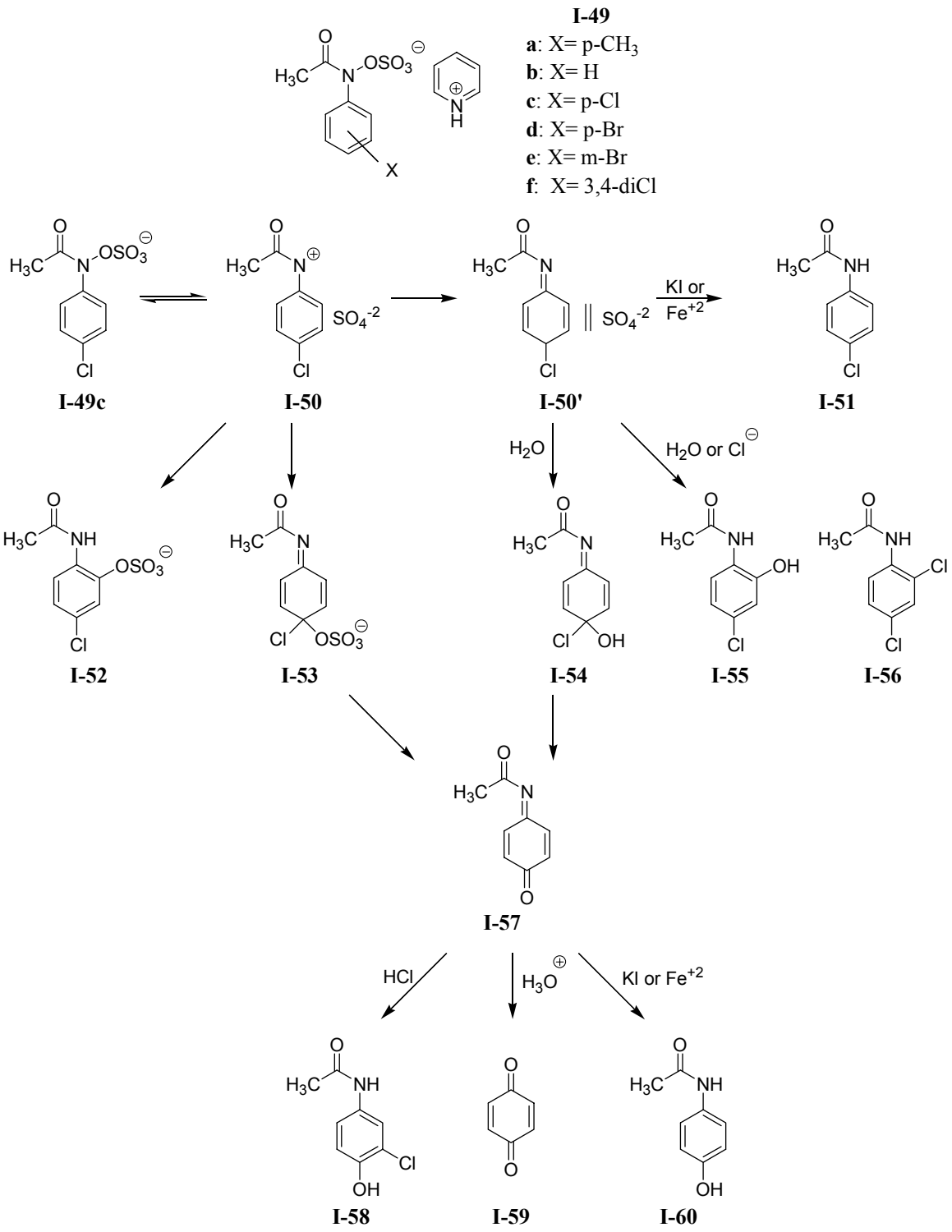
ion pairs and solvent separated ion pairs. Then, depending upon the type of solvent effect, one can see the many different products that can be synthesized (Scheme 1.19).

The entire scheme is based upon the formation of the nitrenium ion intermediate. The tight ion pair will add the SO_4^{-2} either at the *ortho*- (**I-52**) or *para*-position (**I-53**). The solvent separated ion pair can either be attacked by water to yield **I-54** and **I-55** or with chloride to yield **I-56**; reduction of **I-50b** would yield **I-51**. Both **I-53** and **I-54** and be oxidized to **I-57**, which can then be trapped with nucleophiles, such as chloride to yield **I-58**, or undergo hydrolysis of the imine to yield **I-59**, or reduction to yield **I-60**.

Upon synthesizing the *N*-sulfonoxyacetanilides (**I-49**) as their pyridinium salts, their solvolysis reactions in aqueous and alcoholic solvents were explored. In aqueous solvent, the correlation of log k_{obs} vs. σ^+ yields a ρ value of –4.5 which indicates that the solvolysis proceeds through a heterolytic cleavage of the N-O bond with the development of a positive charge on nitrogen as the rate determining step.

Other experiments performed by Novak *et al.* examined the rates of formation of several nitrenium ions via solvolysis. It was concluded that although the rates of formation of nitrenium ions generated by the heterolysis of an N-X bond may correlate to σ^+, the reactivity of the nitrenium ion itself has no correlation.[35,37] This was determined by studying different *N*-arylnitrenium ions derived from esters and then observing their rates of formation and product distribution via solvolysis.

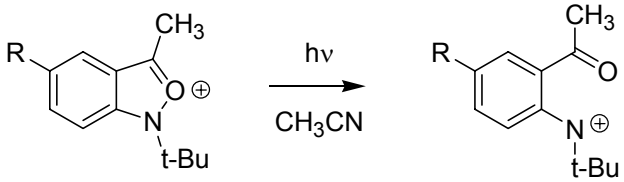
Scheme 1.19: Series of synthesized *N*-sulfonoxyacetanilides by Novak.



1.6: Recent Falvey Group Research

Research performed by the Falvey group produced the first reported successful application of LFP for direct observation of a nitrenium ion. This experiment involved the irradiation of **I-61** in anhydrous acetonitrile (CH_3CN) to give nitrenium ions **I-62** (Scheme 1.20).[58,128] This reaction is a photoheterolysis with a neutral methyl ketone as the leaving group.

Scheme 1.20: Photoheterolysis with a neutral leaving group.



I-61

a: R= H
b: R= Cl
c: R= Br
d: R= CH_3
e: R= Ph

I-62

a: R= H
b: R= Cl
c: R= Br
d: R= CH_3
e: R= Ph

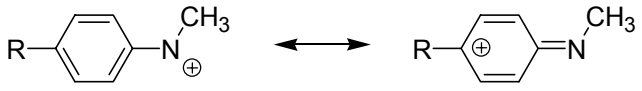
The Falvey group used LFP to study the lifetimes of the various nitrenium ions and different substituent effects on the lifetime of nitrenium ions. Study of the difference in the singlet and triplet energies of various types of nitrenium ions has also been pursued.

Some early work of substituent effects on the lifetimes and reactivities of arylnitrenium ions was performed in the early and mid-1990s. In these studies, the

researchers examined different substituted arylnitrenium ions by analyzing product studies and using different traps, such as water and alcohol. Laser flash photolysis, photothermal beam deflection, as well as kinetic studies on the reactions of arylnitrenium ions with nucleophiles have been made.

With the use of LFP and photothermal beam deflection investigations of 4-substitued *t*-butyl phenylnitrenium ions, many interesting observations have been made. It has been shown that a 4-phenyl substituent stabilizes the nitrenium center to a greater extent than for a 4-methyl or 4-halo group and almost the same extent as a 4-methoxy group. The 4-unsubstituted and 4-cyano systems are shown to be less stable than any of the other systems, including the 4-halo. Therefore, it was concluded that the simple quantitative models used for carbenium ions cannot be readily extrapolated to the nitrenium ion.[29]

Another important breakthrough, in the detection of nitrenium ions, is the use of time-resolved infrared (TRIR) to confirm the time scale and the structure of intermediates. LFP-TRIR spectroscopy was used to experimentally confirm the 4-iminocyclohexa-2,5-dienyl cation-like structure of arylnitrenium ions (**I-63′**) (Figure 1.4).[129]



I-63 **I-63'**

a: R= Ph **a**: R= Ph
b: R= Cl **b**: R= Cl
c: R= OCH_3 **c**: R= OCH_3
d: R= CH_3 **d**: R= CH_3

Figure 1.4: Structures of 4-substituted *N*-methylphenylnitrenium ions which can be viewed as 4-iminocyclohexa-2,5-dienyl cations.

LFP with TRIR detection allowed for structural characterization of the nitrenium ions through observation of a symmetrical aromatic C=C stretch in the region 1580 – 1628 cm^{-1}. The specific frequencies reflect the degree of quinoidal character present in each phenylnitrenium ion, that is, the degree to which the nitrenium ion resembles a 4-iminocyclohexa-2,5-dienyl cation. Quantum calculations using density functional theory (BPW91/cc-pVDZ) were carried out on the singlet and triplet nitrenium ions **I-63a-d** and the theoretically derived IR frequencies showed excellent quantitative agreement with the experimentally derived IR frequencies for the singlet nitrenium ions (Table 1.4).[130] On the other hand, the theoretically derived IR frequencies for the triplet states were not close to the experimentally derived IR frequencies and were off by 20 – 30 cm^{-1}, which highlights the agreement for the singlet state.

Table 1.4: LFP-TRIR for selected harmonic vibrational frequencies for *para*-substituted *N*-methylphenylnitrenium ions.

Nitrenium Ion	Experimental Symmetrical Aromatic C=C Stretching (cm^{-1})	Calculated Symmetrical Aromatic C=C Stretching (cm^{-1})
I-63a	1612, 1584	1619, 1601
I-63b	1604	1604
I-63c	1628	1629
I-63d	1616	1619

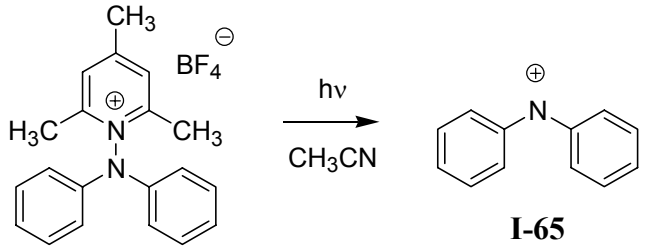
In terms of geometries, nitrenium ion **I-63a-d** show higher degrees of bond length alternation, which signifies more of a cyclohexadienyl cation character, than *N*-methyl-*N*–(1-naphthyl)nitrenium ion. In an ideal benzene structure, all of the ring carbon-carbon bond lengths would be nearly equal, whereas in a 1,4-cyclohexadienyl cation, the bond lengths between carbons 1 and 2, carbons 3 and 4, carbon 4 and 5, and carbons 6 and 1

would be longer than the bond lengths between carbons 2 and 3 and carbons 5 and 6. This is the case for all four nitrenium ions **I-63a-d**, where the difference between the average of the four long bonds and the average of the two short bonds for **I-63a-d** are 0.088 Å, 0.066 Å, 0.081 Å, and 0.069 Å, respectively (Figure 1.4). Also, calculated C-N bond lengths for the singlet nitrenium ions **I-63a-d** are 1.320 $\pm$ 0.003 Å, which is closer to typical values for a C=N bond (1.28 Å) than for a C-N bond (1.40 Å).[131]

Thus, it was verified that arylnitrenium ions are the primary products of photolysis of 1-(*N*-arylamino)pyridinium ions. Also, density functional theory (DFT) calculations have reliably reproduced key structural features of these intermediates. There was support for the theoretical calculations that **I-63a-d** are ground state singlets. And both infrared (IR) and DFT calculations indicate that these arylnitrenium ions possess structures that can be considered 4-iminocyclohexa-2,5-dienyl cations (**I-63′a-d**).[130]

Using LFP, a diarylnitrenium ion system, *N*,*N*-diphenylnitrenium ion (**I-65**) was generated from 1-(*N*,*N*-diphenyl)amino-2,4,6-trimethylpyridinium tetrafluoroborate (**I-64**) (Scheme 1.21).[122,132]

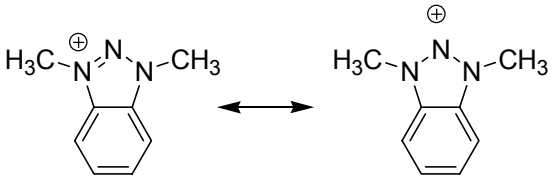
Scheme 1.21: Photochemical generation of *N*,*N*-diphenylnitrenium ion.



I-64 **I-65**

Diarylnitrenium ions (Ar_2N^+) form products from nucleophilic addition of various π–nucleophiles (electron rich alkenes) to the *ortho*- and *para*-positions of one of the phenyl rings. There does not seem to be effects associated with either the charge distribution of the LUMO that would strongly influence *ortho*-/*para*-/N selectivity for the nucleophilic trapping as calculated through a number of electronic structure calculations at different levels of molecular orbital and density functional theory.[132]

The Falvey group also studies the singlet-triplet energy gaps of the nitrenium ions. For example, the first experimental determination of a singlet-triplet energy gap (ΔE_{st}) for an organic nitrenium ion was made for 1,3-dimethylbenzotriazolium ion (**I-66, I-66′**) (Figure 1.5). LFP was used to determine the ΔE_{st} and was in agreement with DFT calculations.[133]



I-66 **I-66'**

Figure 1.5: The first experimentally measured ΔE_{st} was of 1,3-dimethylbenzotriazolium ion (I-66).

This experimental measurement of the singlet-triplet state energy gap was significant because such parameters that can be conveniently calculated from quantum mechanics (ΔE_{st}, equilibrium geometries, etc.) are extremely difficult to determine experimentally, especially for transient molecules in solution. Conversely, the sorts of

data readily available from experiments (UV-vis absorption spectra, reaction rate constants, stable product distributions) are difficult and/or expensive to accurately compute.

1.7: Conclusions

During the past hundred years, the study of nitrenium ions has evolved from speculation and hypothesis to observation and detection. Nitrenium ions can be observed from a variety of precursors and studied in various ways as well. Its study has developed from experimentation to prove its existence as a discreet intermediate to using nitrenium ions in the synthesis of natural products. Major advances in nitrenium ion chemistry has boomed from its beginnings by Bamberger and Stieglitz, with their initial nitrenium ion studies, to Gassman's seminal review on nitrenium ions in the 1970s, to the current leaders in nitrenium ion chemistry which include Abramovitch, Novak, and Falvey. Indeed, nitrenium ions have come to be full of promise considering their humble beginnings.

1.8: References

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Chapter 2: Laser Flash Photolysis

2.1: Brief History of Laser Flash Photolysis

There are two main techniques to characterize the lifetimes and reaction rate constants of nitrenium ions in solution.[1-3] The first method is the oldest and the most used and it involves measuring the relative yields of the stable products. The ratio of rate constants can then be inferred from the product ratio. These techniques were used with the thermal acid-catalyzed dehydroxylation of *N*-hydroxylamines, decomposition of azides under acidic conditions, heterolytic cleavage of *N*-chloroamines, heterolytic cleavage of hydroxylamine esters, and thermolysis of *N*-aminopyridinium ions.[1-30]

The second technique is laser flash photolysis (LFP) which employs short laser pulses to create a high concentration of the transient nitrenium ion and fast detection technology to characterize its spectrum and lifetime. Photochemistry has become an extraordinary tool in studying reactive intermediates such as carbenes, diradicals, and nitrenes because of their applications with LFP and low temperature matrices allow for photochemical generation and detection. Time-resolved UV-vis spectroscopy (TRUV) is the most commonly used technique is because of its high sensitivity but reveals little information as to the transient's actual chemical structure.

LFP is a way to observe short-lived intermediates that do not exist on the normal laboratory time scale of seconds to days. Previously, one would use experimental conditions, such as cryogenics to observe short-lived intermediates. But with the development of LFP, both the detection techniques as well as the fast generation of the intermediates could be accelerated. In 1967, the Nobel Prize was awarded to Norrish and

Porter for their work with flash phololysis methods.[31] In this method, the reactive intermediates were generated following excitation by the light pulse and millisecond and microsecond resolution was achieved. The invention of the laser in the early 1960s allowed for these faster detection methods. Lindqvist first reported LFP by a 337 nm nitrogen laser excitation source and was able to detect the acridine triplet.[32] Nanosecond LFP developed with the introduction of computer control and data acquisition. The first system was built at the University of Notre Dame in the late 1970s by Small and Scaiano.[33]

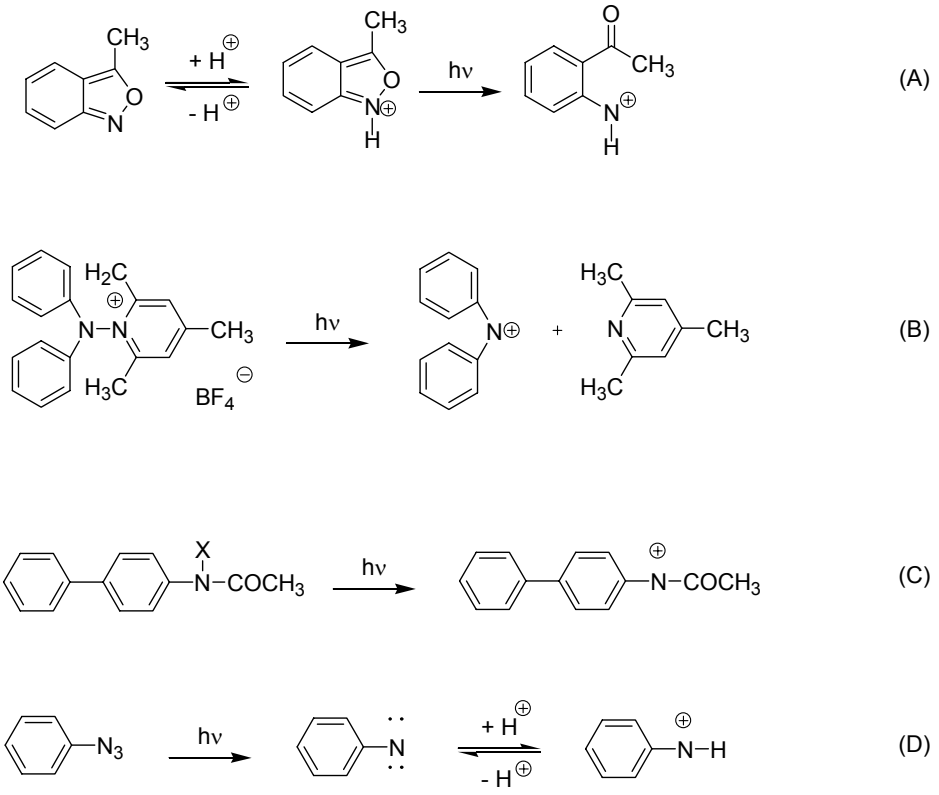
2.2: Photochemical Methods to Generate Nitrenium Ions

The study of nitrenium ions experienced a rebirth with the development of LFP because it allowed for the direct observation of signals related to these reactive intermediates. Previously, the studies of nitrenium ions mainly relied on product studies and comparative kinetic trapping rates. The first nitrenium ion examined by LFP was 4-dimethylaminophenylnitrenium ion in 1971, but was not considered as a true nitrenium ion but rater more of a quinonediimine.[34] It was not until twenty years later that *N*-*t*-butyl-(2-acetyl-4-chlorophenyl)nitrenium ion and *N*-*t*-butyl-(2-acetyl-4-bromophenyl)nitrenium ion became the first nitrenium ions directly observed by transient LFP-TRUV methods.[35] These nitrenium ions were generated by the photoisomerization of anthranilium ions of *N*-*t*-butyl-5-halo-3-methylanthranilium ion precursors and several other arylnitrenium ions were later observed using the same general method.[35-37]

In order to progress with the study of nitrenium ions, a reliable photochemical process was needed to generate the nitrenium ion, which leaves a positive charge on an

electronegative nitrogen atom. There are now several reliable photochemical pathways in which one can apply LFP for detection and kinetic characterization. There are many techiniques for generation of nitrenium ions such as photoisomerization of anthranilium ions, photofragmentation of *N*-aminopyridinium ions, photoheterolysis of hydroxylamine esters and *N*-chloroamines, and protonation of nitrenes generated from azide photolysis (Scheme 2.1).[26,29,30,35,38-70]

Scheme 2.1: Photochemical generation of nitrenium ions including (A) photoisomerization of anthranilium ions, (B) photofragmentation of *N*-aminopyridiniumions, (C) photoheterolysis of hydroxylamines esters and *N*-chloroamines, and (D) protonation of nitrenes generated from azide photolysis.



The photoisomerization of anthranilium ions, which was the first reported photochemical method to yield arylnitrenium ions, results in nitrenium ions via an N-O bond scission. This method has high quantum yields but has its limitations, including that the central nitrogen with an aromatic ring must contain a carbonyl substituent in the ortho position and that the photoisomerization may be reversible. The photofragmentation of *N*-aminopyridiniumions has a broader applicability as it allows for the formation of either primary or secondary nitrenium ions using near UV, low wavelength visable pulses. The nitrenium ion is produced via N-N bond scission and yields neutral pyridine as a by-product. This process can take place in non-protic and non-nucleophilic media. This method can be used to observe trapping of the nitrenium ions as well as the study of diarynitrenium ions, such as *N*,*N*-diphenylnitrenium ion.[46,47,54,71] Disadvantages include the relatively low yields from the multi-step synthesis of the aminopyridinium precursors and potential secondary reactions of the primary photoproducts by oxidation of the precursor. Photoheterolysis of hydroxylamine esters and *N*-chloroamines produces similar product distributions between thermolytic and photochemical methods. But, this method suffers from competing processes and the instability of the precursors. The photolysis of azides yields the corresponding nitrene, which in protic media, allows for the formation of primary nitrenium ion via protonation of the nitrene. Thus, there is a net replacement of N_2 with a proton. These precursors are easily synthesized and are readily accessible but the limits of this method are that only primary nitrenium ions can be generated, they must be generated in polar protic media, the need to employ low wavelength pulses, and competitive reactions of the nitrenen,

including ring expansion of the singlet nitrene and intersystem crossing to the triplet nitrene.

In all of these photochemical processes, the stable photochemical precursor is excited with light from a pulsed laser beam. The laser beam initiates a photochemical process that creates the short-lived intermediate nitrenium ion which is detected by its UV-vis absorption spectrum. This LFP technique has a few restrictions such that the intermediate under study must be photochemically generated from a stable precursor quickly and with high quantum yields. The intermediate must also be longer lived than the time resolution of the instrument and the intermediate must have a distinct absorption spectum, different from its precursor and have a high molar absorptivity to be observed with a good signal-to-noise ratio.

2.3: Laser Flash Photolysis – Time-Resolved Ultraviolet-Visible (LFP-TRUV)

Nanosecond LFP is a contemporary tool for kinetic studies. The laser set-up used in these studies is a simple pump beam/probe beam system (Figure 2.1). The sample cell is excited by a neodymium yttrium aluminium garnet (Nd:YAG) nanosecond laser (pump beam). The pump beam is reflected by dichroic mirrors and through a concave lens to disperse the excitation photon horizontally across the sample. The xenon arc lamp (probe beam) is regulated by a shutter, which opens prior to the laser pulse and closes after the end of the measurement. The shutter controls the amount of light passing through the sample and opening and closing when the laser beam is pulsed. It is not beneficial to

have the probe beam continuously pass though the sample because it can photolyze the sample and damage the photomultiplier tube (PMT).

The probe beam is then reflected by a plane mirror through the first focusing lens to the sample at which the pump beam and the probe beam intersect perpendicularly. The orthogonality of the pump and probe beam is to ensure that the amount of light scattering from the laser is kept to a minimum. After the probe beam passes through the second focusing lens, it is narrowed down to a single wavelength of light by the monochromator. This monochromatic light is changed into voltage via the PMT, whose signal is then seen on the oscilloscope. Transient waveforms are recorded with a LeCroy 9420 digital oscilloscope, which digitizes at a rate of 1 point/10 ns with a bandwidth of 350 MHz.

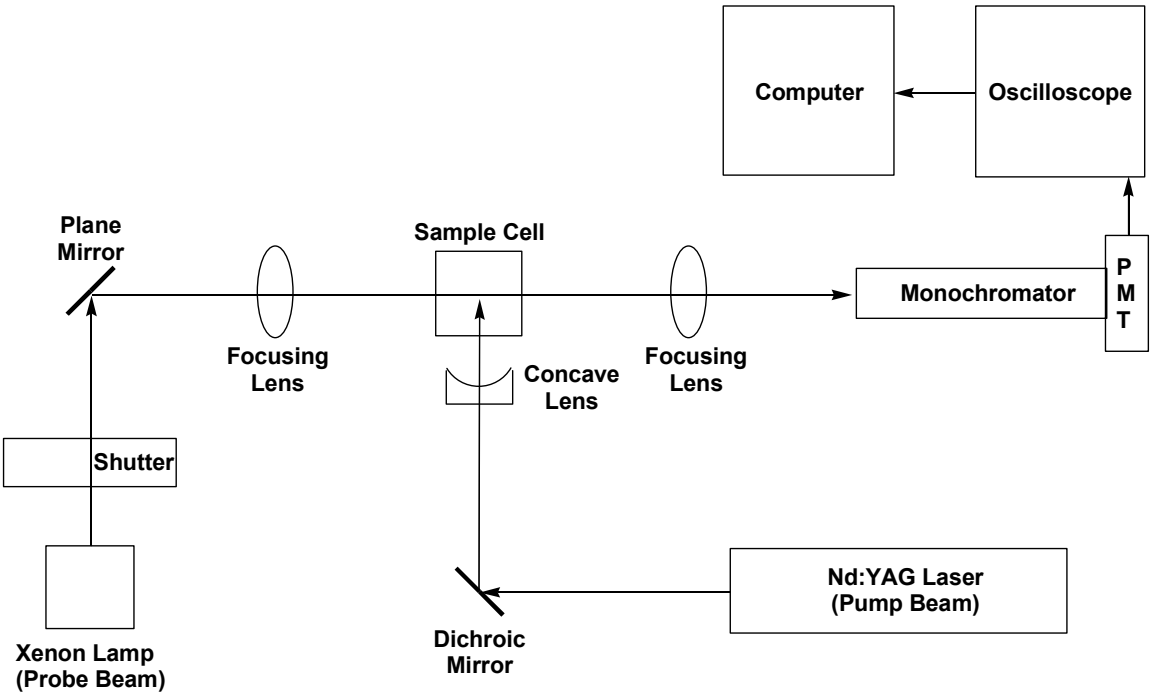


Figure 2.1: Laser flash photolysis (LFP) schematic.

Data from the laser flash photolysis with time-resolved ultraviolet-visible absorption detection experiments were collected using a Nd:YAG laser (Continuum Surelite II-10) as the pulsed excitation source. In the case of solid state lasers, such as the Nd:YAG laser employed in our laboratory, most of the useful wavelengths are obtained by generation of harmonics from the fundamental wavelengths. Second, third, and fourth harmonic generator crystals were used to create output wavelengths at 532, 355, and 266 nm. Other excitation wavelengths can also be employed by using a dye laser system or other types of lasers. Table 2.1 gives the typical wavelengths available from various lasers.

Table 2.1: Common lasers used for LFP.

Laser	Fundamental (nm)	Harmonic (nm)
Nitrogen	337	
Excimer	157	
	193	
	248	
	308	
	351	
Ruby	694	347
Nd:YAG	1064	532, 355, 266

The transient absorptions are monitored using a probe beam from an Oriel 350-W xenon arc lamp, which passes through the sample cuvette perpendicular to the excitation beam. A xenon arc lamp is used for the probe beam for UV-vis detection because of its ability to produce light at various wavelengths, emitting from 260 nm – 850 nm. Cut-off filters of varying wavelengths were also employed to prevent unwanted photolysis of the precursor by the probe beam. The detection system consists of a monochromator, which discriminates the selected wavelength of light allowed to enter the detector, which is a

PMT. The PMT, which is wired for fast response, responds to changes in probe light intensity within nanoseconds and sends the output voltages to an oscilloscope that captures and stores the data. The output has the shape shown in Figure 2.2. Note that increasing probe light intensity results in a negative signal and the voltage signals from photomultipliers are negative. The laser fires at time t = 0 and causes an increase in absorbance in the sample, thus the intensity of the light reaching the detector decreases. Although LFP is a single-beam spectrophotometer, it also acts as a dual-beam spectrophotometer with the reference separated by time and not by space.

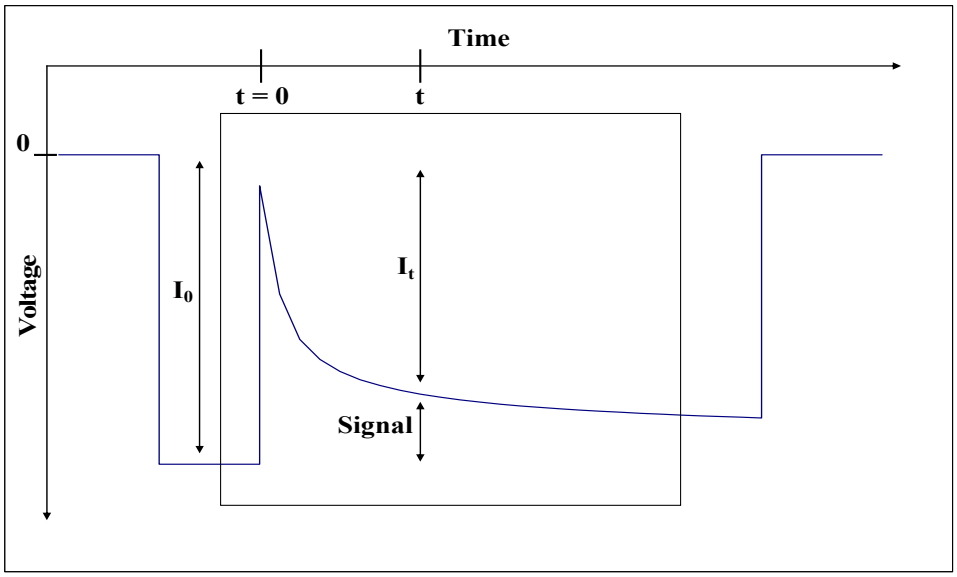


Figure 2.2: Time evolution of the photomultiplier output as a transient signal is generated and decays.

The reference is acquired before the laser pulse and yields I_0. The absorbance at time t is given by equation 1.

$$\text{Absorbance Change} = \text{Change in Optical Density } (\Delta\text{O.D.}) = \log\left(\frac{I_0}{I}\right) = -\log\left(1-\frac{\text{signal}}{I_0}\right) \quad (1)$$

In this technique, the reference beam is the same signal prior to the laser pulse and measures the changes in absorbance, abbreviated as Δ O.D. (optical density). The portion of the decay observed on the oscilloscope is boxed in Figure 2.2 where the points before the laser pulse at t = 0 are averaged to obtain I_0. The difference in the terms absorbance versus O.D. is significant because absorbance is defined as the difference in light intensities due to absorption where O.D. is defined as the light not transmitted and may included light scattering and other processes. In Figure 2.2, the decay signal does not return to the pre-excitation level which indicates that a new product has been formed and absorbs light. The LFP spectrum can become complicated by signals from the accumulated photoproducts. It is for this reason that flow cells are used when full-spectrum transients are produced. A flow cell rapidly introduces fresh samples into the irradiated zone and replaces the photolyzed material which is discarded (Figure 2.3).

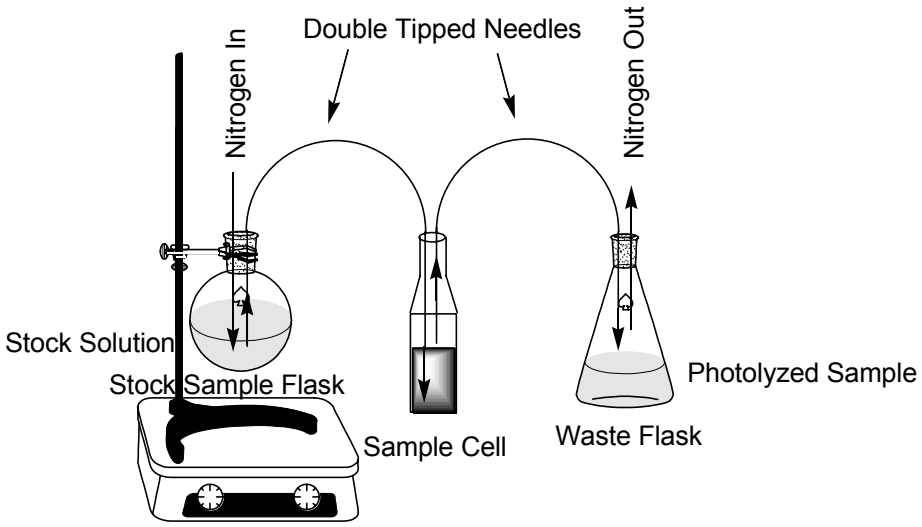


Figure 2.3: Flow cell set-up.

Two-photon processes are caused by absorption of photons by reaction intermediates and excited states. These processes can interfere with the observation of the intermediate of interest by the formation of new reaction intermediates and the partial depletion of intermediates formed. To minimize these problems, a higher laser power than required to obtain a good signal-to-noise ratio should not be used and the laser beam should not be focused too tightly. The purpose of the concave lens is to act as a beam spreader in order to increase the signal-to-noise ratio by diffusing the laser beam such that acoustic waves are prevented. Acoustic waves are repetitive and attenuated signals every few microseconds and are generated when a significant fraction of the laser pulse energy is absorbed in a small volume. The waves can be caused by a variety of problems, including tight focusing of the laser beam, high absorption by the sample at the laser wavelength, high absorption by reaction intermediates at the laser wavelength, and absorbing defects on the surface of the sample cuvette.

Figure 2.4: Focusing of the laser beam without (A) and with (B) the concave lens.

The signal detection is a function of time at selected wavelengths. The spectra are constructed by monitoring time-resolved traces at many wavelengths and then extracting Δ O.D. data at a given time from each trace. The data is collected in a three-dimensional (3D) matrix where the vertical axis is signal intensity and the other two axes are time and wavelength as shown in Figure 2.5.

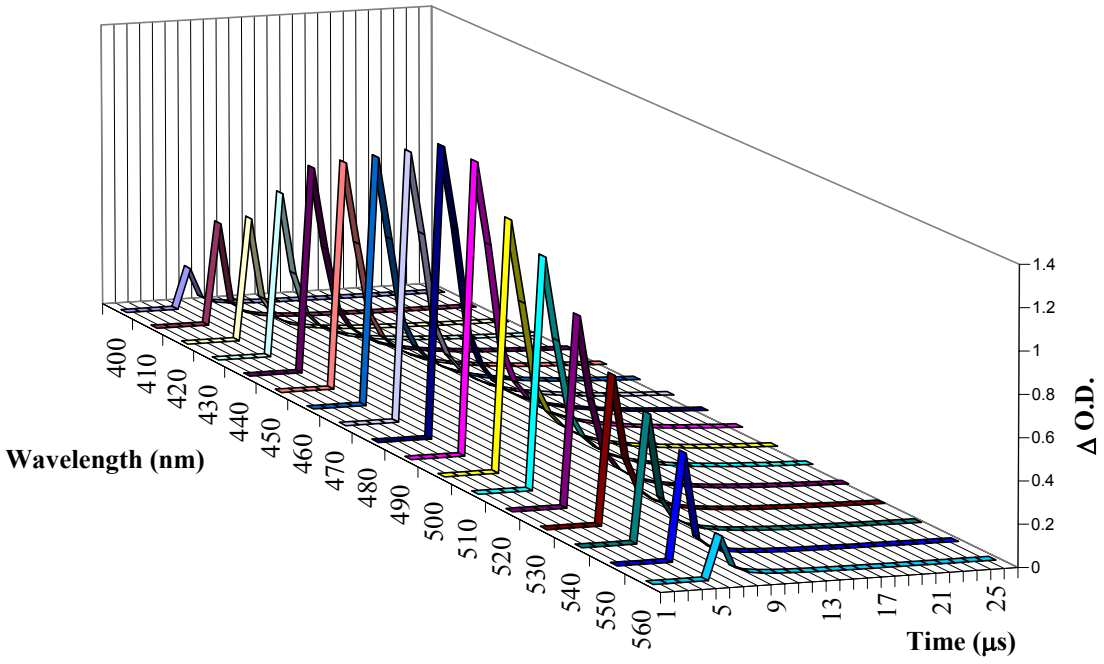


Figure 2.5: Example of a 3D matrix of a transient absorption spectrum.

Once the data is collected for all of the wavelengths of interest, the full transient spectrum can be created in a two-dimensional (2D) output with the y-axis as Δ O.D. and the x-axis is wavelength (nm). The data collected at different times can be represented with different series as shown in Figure 2.6.

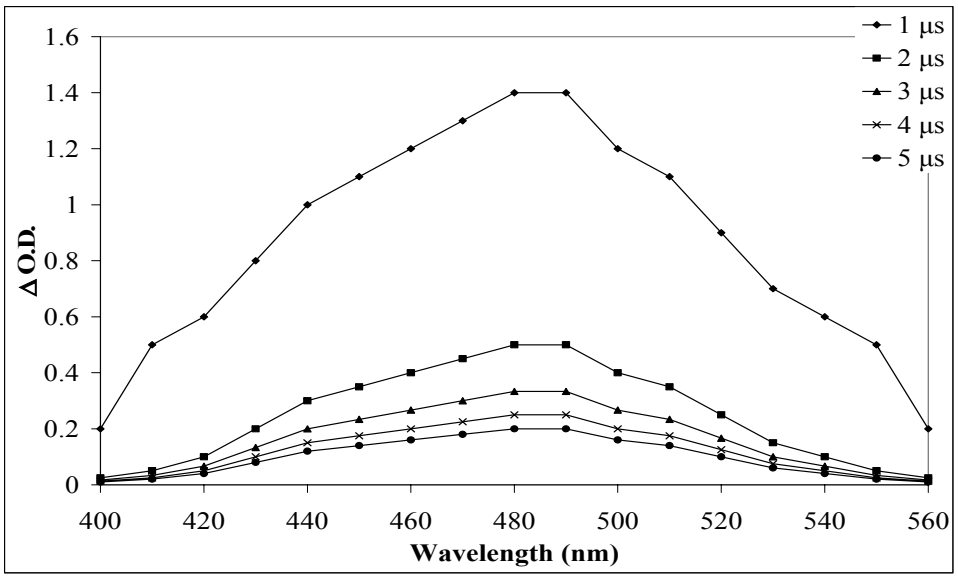


Figure 2.6: Example of a 2D transient UV-vis extrapolated from a 3D matrix of a transient absorption spectrum.

The resulting plot is of the change in optical density versus time. The experiment is repeated at different wavelengths and this data can then be used to determine the wavelength of maximum absorption (λ_{max}) and lifetime (τ) of any new transient species. The lifetime is a rough indication of stability because nitrenium ions are sensitive to changes in the medium as well as impurities in the medium. Therefore, τ is only meaningful if the nitrenium ions are measured under the same conditions. If the photolysis is of clean first-order kinetics, the decay follows simple first-order kinetics in

equation 2, where the subscript 0 indicates initial conditions, *t* after time *t*, and [R] is the transient concentration.

$$\ln\left(\frac{[R]_0}{[R]_t}\right)=\ln\left(\frac{[\Delta\ O.D]_0}{[\Delta\ O.D.]_t}\right)= - kt \quad (2)$$

It can be seen from equation 2 that there is no difference if concentration or O.D. is used for calculation plots. The lifetime of the intermediate is given by equation 3 where k_0 is the decay rate without any quencher. The half-life ($t_{1/2}$) can be determined from equation 4.

$$\tau = \frac{1}{k_0} \quad (3)$$

$$t_{\frac{1}{2}} = \frac{\ln 2}{k_0} = 0.69\tau = \frac{0.69}{k_0} \quad (4)$$

For pseudo-first-order behavior, the intermediates are present in micromolar concentrations and the molecules that they react with, denoted as Q for quencher, are present in concentrations in several orders of magnitude greater, therefore the concentration of the trap remains nearly consistent. It can be said that the Δ [Intermediate] >>> Δ [Q] that comparatively the Δ [Q] = 0. Thus, this follows common pseudo-first-order kinetics.

Quenching decay rate constants can be determined by fitting the data to equation 5, where $\Delta O.D._0$ is the maximum change in optical density at t = 0, k_{obs} is equal to the rate constant for the observed decay of the transient intermediate, and b is the baseline.

$$\Delta \text{ O.D.} = \Delta \text{ O.D.}_{\cdot 0} e^{-tk_{obs}} + b \quad (5)$$

The data analysis uses computer fitting which creates a theoretical curve using these three variables (ΔO.D.$_{\cdot 0}$, k_{obs}, and b) and performs many iterations to where the summation of the standard deviation of the best fit line of the data from n = 0 to n = t is zero, or a minimum, as shown in equation 6.

$$\sum_{n=0}^{n=t} \left[\Delta \text{ O.D.}_{\cdot \text{experimental}}(t) - \Delta \text{ O.D.}_{\cdot \text{theoretical}}(t) \right]^2 = 0 \quad (6)$$

To determine the reactivity of the intermediate, one can use different classes of quenchers or nucleophiles to determine how quickly they trap the reactive intermediate. This is done by measuring the relationship between k_{obs} with varying concentrations of trap and then fitting it to a second order decay function. To determine the trapping rate, k_{obs} can be substituted into equation 7 where k_0 is the decay rate without any quencher and k_q is the rate constant for trapping.

$$k_{obs} = k_0 + k_q [Q] \quad (7)$$

The trapping rate constant (k_q) is determined by plotting the concentration of quencher used versus k_{obs}. The resulting slope, determined by linear regression, is the trapping rate constant (k_q) and the y-intercept is k_0, given in terms of $M^{-1}s^{-1}$. Take for example the trapping of *N*-methyl-4-chlorophenylnitrenium ion with 1,4-

diazabicyclo[2.2.2]octane (DABCO) in CH_3CN. Figure 2.7 shows the kinetic behavior of *N*-methyl-4-chlorophenylnitrenium ion, which was directly observed by its absorbance detection at 480 nm. Monitoring at 480 nm, a series of waveforms were obtained with varying concentrations of DABCO (0.00 - 0.54 mM). The waveforms show the increased decay rates as the concentration of DABCO is increased and thus the k_{obs} also increased.

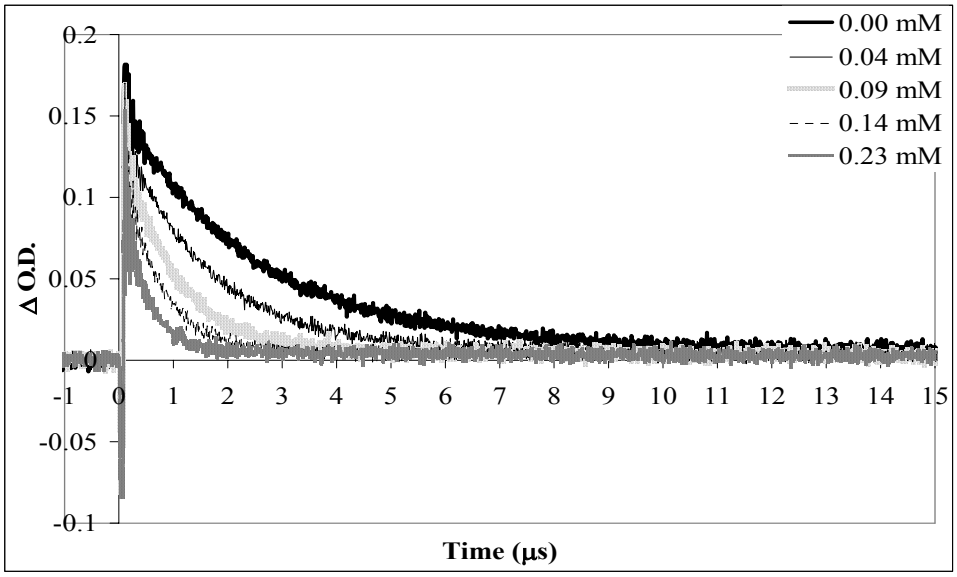


Figure 2.7: Experimental trapping waveforms of 4-chloro-*N*-methylphenylnitrenium ion trapped with varying concentration of 1,4-diazabicyclo[2.2.2]octane (DABCO).

The values of these trapping rates are plotted as a function of the concentration of DABCO to obtain the linear relationship shown in Figure 2.8. In this case, the slope of the line, which is the trapping rate constant, k_q, was determined to be 8.32×10^9 $M^{-1}s^{-1}$.

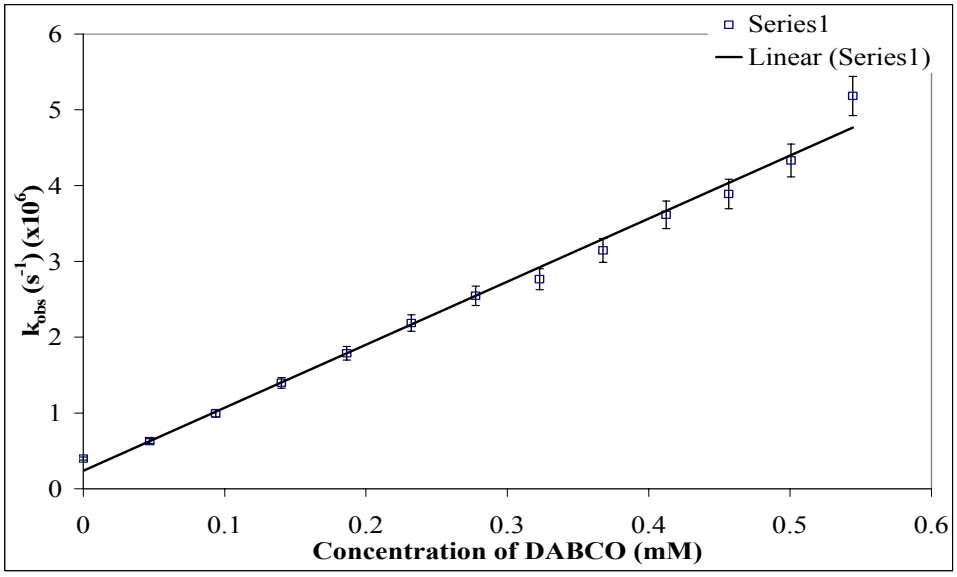


Figure 2.8: Experimental nucleophilic trapping rate constant of 4-Chloro-*N*-methylphenylnitrenium ion with varying concentrations of DABCO.

LFP has become a standard tool in photochemistry and physical organic chemistry and has made great advances in the past 35 years. The field continues to evolve with current techniques in picosecond and femtosecond LFP systems and by introducing vibrational spectroscopy, such as laser flash photolysis time-resolved infrared (LFP-TRIR) and laser flash photolysis time-resolved resonance Raman (LFP-TRRR), which provide detailed structural information but suffer from lower sensitivity than LFP-TRUV.[72-74] Great progress has also been made in the agreement and understanding of nitrenium ions as discreet intermediates due to their direct detection and characterization through LFP. LFP experiments provided the first direct evidence about UV-vis spectra, lifetimes, and reaction rate constants.

There have been many advances in the technologies involved with the experimentation of nitrenium ions, such as the use of non-acidic conditions by using pyridinium salts and laser flash photolysis to observe the nanosecond lifetimes of the

reactive intermediates. With such intense and interesting work being performed worldwide, much more information will be obtained and knowledge will be learned. Theoretical treatments of nitrenium ioins are able to calculate the geometry, charge distribution, heats of formation, and the relative energies of the singlet and triplet states. Generally, experiments measure a nitrenium ion's product distribution, reaction rate constants, and electronic spectra. Therefore, these theoretical treatments can be used to both predict and complement experimental measurements.

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Chapter 3: Photogenerated *N*-Methyl-*N*-(1-naphthyl)nitrenium Ion and *N*-Methyl-*N*-(2-naphthyl)nitrenium Ion

3.1: Carcinogenic History

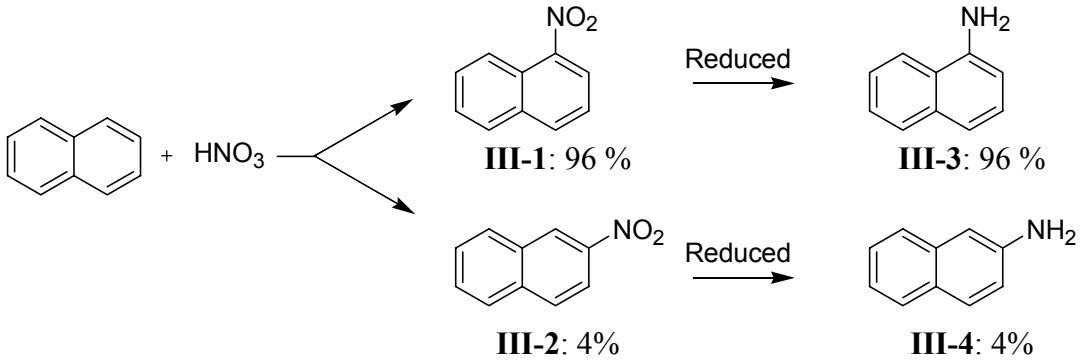
2-Naphthylamine was one of the first reported carcinogens, but the toxicity of its isomer, 1-naphthylamine, has been a topic of ongoing debate for decades. In 1895, Rehn reported the exposure effects of a group of chemical workers to certain aromatic amines, most notably the unexpected findings of four cases of bladder tumor thought to be caused by aniline.[1] In 1898, Leichtenstern proposed that it was exposure to naphthylamines, not aniline, that caused bladder tumors.[2] Evidence started to accumulate and supported the notion that naphthylamines and benzidine were involved with 38 cases of bladder tumors in a subsequent report by Rehn in 1906.[3] With the mainstream development of both the dyestuff and rubber industries by the 1920s, more cases of bladder tumors were documented in workers of these industries.[4,5]

1-Naphthylamine was used for the manufacture of azo dyes and the chemical construction of antioxidants for the rubber industry while its isomer 2-naphthylamine was used in the large scale manufacture of rubber industry antioxidants. Other aromatic amines, such as benzidine, biphenylamine, and *N*,*N*-diphenylamine were also widely used to make azo dyes, used in the rubber industry as antioxidants, and used as a hardener and a constituent of adhesives and plastics. Heuper described the series of epidemics of bladder cancer that followed the induction of synthetic dye manufacturing around the world, including Germany, Switzerland, England, the United States, Italy, France, the

Soviet Union, Japan, Austria, Poland, Czechoslovakia, India, and Sweden. The world-wide record of occupational cancers of the urinary system among dye workers, rubber workers, and others in contact with various carcinogenic aromatic amines, may be estimated between 2,500 and 3,000 cases from its discovery in 1895 to 1969. Because bladder cancers have a distinctly higher death rate than cutaneous cancers, they are more dangerous than the majority of the cancers elicited by coal tar and mineral oils.[6,7]

The industrial manufacture of 1-naphthylamine is performed by the nitration of naphthalene to 1-nitronaphthalene and then subsequent reduction to yield the free amine. Yet, when naphthalene is nitrated, the product consisted of about 90-96% of 1-nitronaphthalene (**III-1**) and about 10-4% of 2-nitronaphthalene (**III-2**) (Scheme 3.1). Therefore, subsequent reduction yielded the corresponding proportions of 1-naphthylamine (**III-3**) and 2-naphthylamine (**III-4**). The manufacture of 1-naphthylamine with 2-naphthylamine as an impurity was kept down to about 4% in 1962 and is now less than 0.5% under present day conditions.[8]

Scheme 3.1: Previous industrial manufacturation of 1-naphthylamine with 2-naphthylamine impurities.

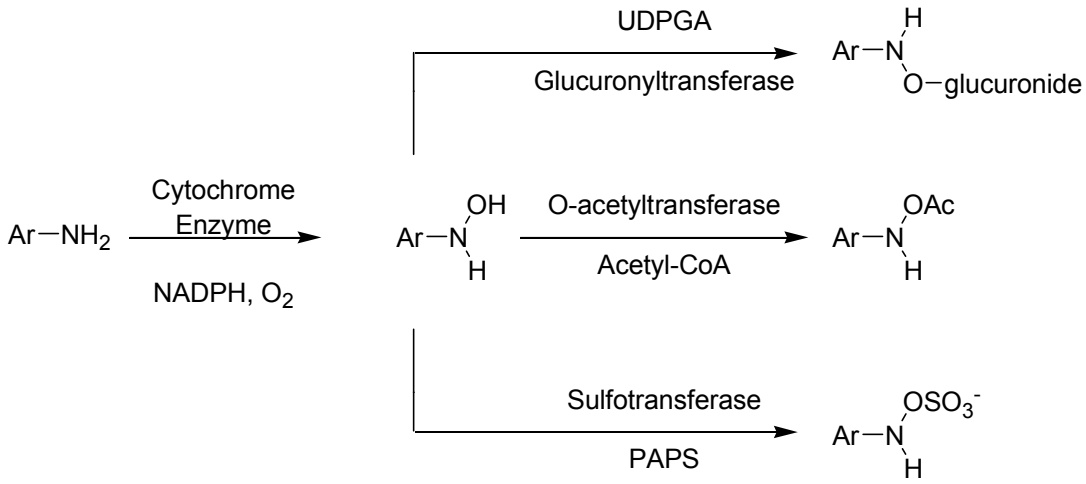


From the inception of the synthetic dye manufacturing industry in the United States, which began during World War I to 1948, 139 workers at the E. I. duPont de Nemours and Company had developed bladder cancer.[9] An assessment of a cohort study of 1,385 workers from the Augusta Chemical Company exposed to 2-naphthylamine between January 1, 1940 and December 31, 1972, identified a total of 13 confirmed cases of bladder cancer.[10] Those who worked in the 2-naphthylamine grinding room, which was reportedly a high-exposure area in the plant, were at the highest risk. In Japan, of the 100 cases of occupational bladder cancer reported between 1949 and 1970 by large companies producing dyes, 23 were attributed to 2-naphthylamine.[8]

The carcinogenicity of 1-naphthylamine has not been as readily accepted as that of 2-naphthylamine despite the number of cases which have been attributed to it in many countries. Therefore, 1-naphthylamine may not be a carcinogen *per se*, but its carcinogenicity may have been due to its 2-naphthylamine content.[11] Thus, the number of bladder tumor cases attributed to 1-naphthylamine before 1959 may have actually been due to 2-naphthylamine. Since the 1- and 2-naphthylamine systems are similar in structure, one would expect that both the 1- and 2-naphthylamine systems would have similar reactivity. The only difference between these two systems is their substitution patterns and this may be the definitive difference. Some of the best characterized examples of arylamines with significantly lower mutagenic activity than their isomeric relatives are 1-naphthylamine, 1-anthracenylamine, and 2-biphenylylamine. All of these aromatic amines have a point of ring fusion adjacent to the substituted carbon, Their isomers, 2-naphthylamine, 2-anthracenylamine, and 4-biphenylylamine, are significantly more mutagenic.[12]

Since the discovery of these chemicals as human carcinogens, many have wondered why is it that these chemicals are target specific. In other words, why does 2-naphthylamine only induce tumors in the bladder and at no other site in the body? It has been found that in humans and experimental animals, many aromatic amine carcinogens induce tumors in tissues distant from the sites of entry, but not at these sites. In general, aromatic amines are thought to play a role in DNA damage caused by enzymatically activated arylamine carcinogens.[13,14] The enzymatic activation of amines is cancerous due to the propagation of DNA-amine adducts into mutations and cellular transformations. In 1941, 2-acetylaminofluorene (2-AAF), a proposed insecticide, was shown to be carcinogenic to the liver, mammary glands, and urinary bladder of rats after dietary administration.[15] Subsequently, the *N*-hydroxy metabolite of 2-AAF was found to be more carcinogenic than the parent compound. The idea that these compounds require metabolic activation has been considered for many years and it was determined that the ultimate carcinogen was being generated at the same tissue site where they initiate carcinogenesis by reaction with functional cellular macromolecules.[16,17] Understanding of the mechanism of aromatic amine-induced carcinogenesis came from the discovery of *N*-hydroxylation of the compounds by the liver's endoplasmic reticulum mixed-function peroxidases or cytochrome P-450 (P-450 1A2 for 2-naphthylamine) [18] as the initial step in the activation of these carcinogens, which can then be converted to electrophiles via *N*-acetylation or *N*-sulfonation (Scheme 3.2).[13,19-22]

Scheme 3.2: Common metabolic pathway for activation of aromatic amines.

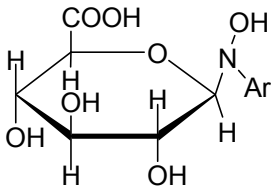


The liver is the main organ for the processing of nitrogenous wastes and contains enzymes normally involved in the detoxification of foreign compounds. Usually this process involves the production of a less toxic compound, such as the conversion of aniline to *p*-aminophenol. This is done to convert these compounds into more polar molecules and thus facilitating their excretion in the urine and feces.[22] Since the kidneys can excrete hydrophilic compounds more readily than hydrophobic compounds, several metabolic pathways in the liver seek to convert hydrophobic compounds into hydrophilic species. Occasionally, this attempted detoxification process will instead lead to the formation of reactive electrophilic metabolites which can covalently bind DNA and proteins. Therefore, many hydrophobic compounds are inadvertently converted to chemical species with increased toxicity.[23]

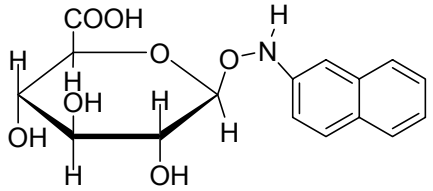
Although 2-naphthylamine is a potent bladder carcinogen in humans and dogs, it is virtually noncarcinogenic in rats and rabbits. These differences suggest that aromatic amines need species specific metabolic activation to induce tumors and it is not the

compounds themselves that are carcinogenic.[22] But then how are these insoluble *N*-hydoxylated metabolites formed in the liver transferred to the bladder as the site of carcinogenesis? Many studies have demonstrated the presence of stable glucuronic acid conjugates of *N*-hydroxy aryl amines (Figure 3.1), such as *N*-(β-1-glucosiduronyl)-*N*-hydroxy-2-naphthylamine, which are then transported through the blood and excreted by the kidneys to the bladder via the urine.[19,24,25] They are then chemically or enzymatically hydrolyzed in the acidic urine (pH 5-6) to form free *N*-hydroxyaromatic amine.[19] This free *N*-hydroxyaromatic amine is then converted to the ultimate carcinogen, via N-O bond heterolysis, which reacts with critical cellular macromolecules in the bladder epithelium initiating the carcinogenic process (Scheme 3.3).

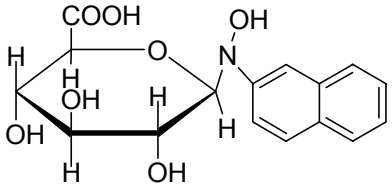
Since the late 1970s, the beagle has shown itself to be a viable test subject for the study of carcinogenicity of chemicals as it pertains to humans. Numerous studies have involved feeding varying amounts of 1- and 2-naphthylamines to beagles over a number of years and collecting the metabolites in their urine as well as sacrificing the dogs in order to make visual observations of the bladder for tumors.[26] Radomski studied six beagles that were fed purified 1-naphthylamine and collected urine metabolites over a nine year period, after which, the dogs were sacrificed and their bladders were examined grossly and microscopically.[20] The urine analysis showed *N*-oxidation products (1-nitrosonaphthalene and *N*-hydroxy-1-naphthylamine) but upon examination of the bladder tissue no abnormalities were found. This suggests that even though *N*-oxidation products of 1-naphthylamine are formed, they are not or are weakly carcinogenic as compared to 2-naphthylamine.



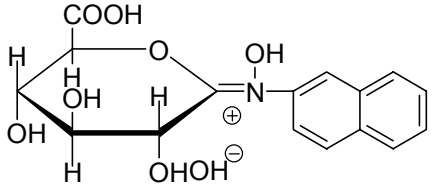
N-C glucuronides



N-(β-1-glucosiduronyloxy)-2-naphthylamine



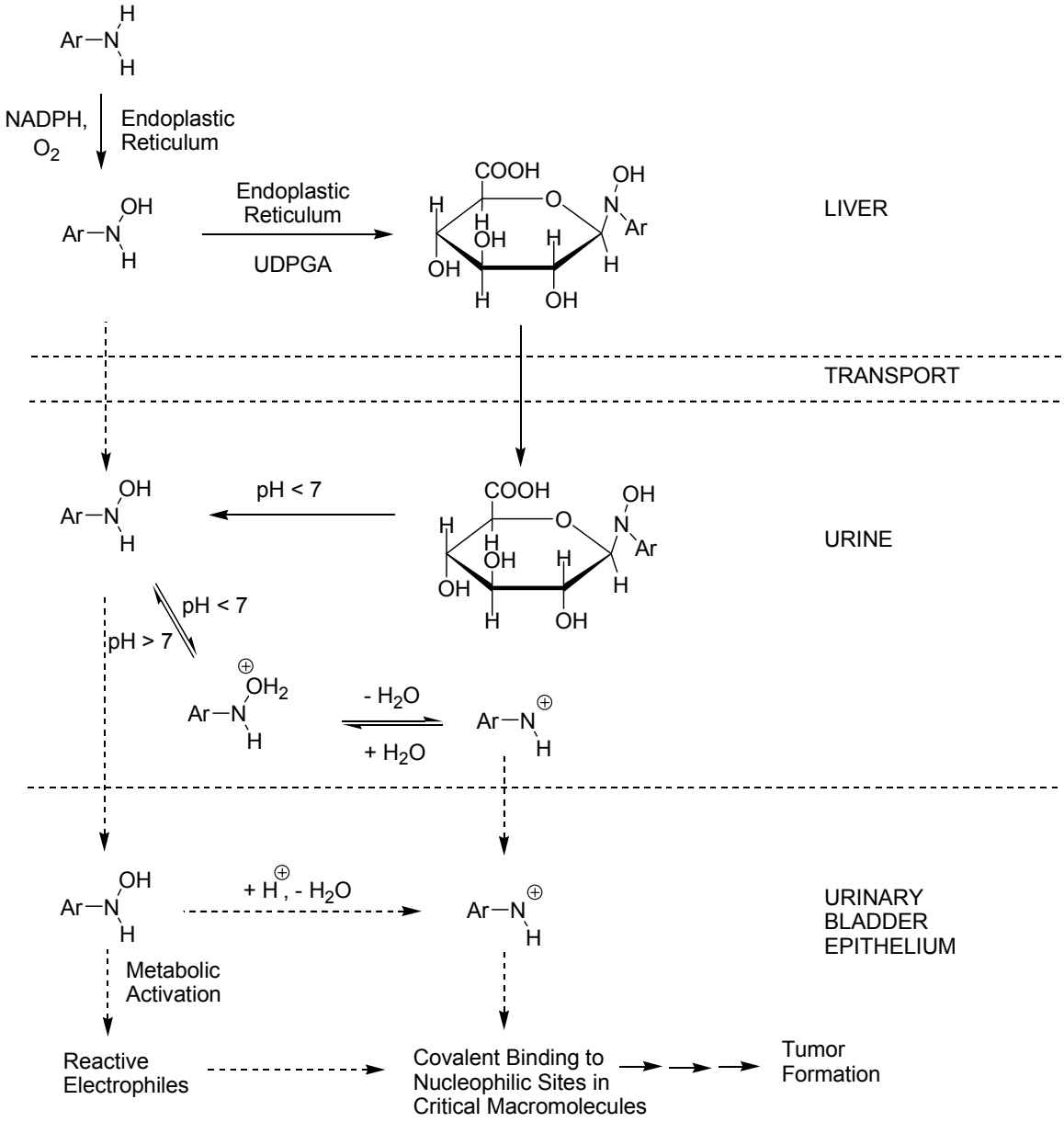
N-(β-1-glucosiduronyl)-*N*-hydroxy-2-naphthylamine



N-(1-glucosiduronylidene)-2-naphthylamine *N*-oxide hydrate

Figure 3.1: General and specific structures of adducts of glucuronide and *N*-hydroxy-2-naphthylamine *in vitro*.

Scheme 3.3: Formation and transport of possible proximate and ultimate carcinogenic metabolites of arylamines for the induction of urinary bladder cancer.



A similar, but more comprehensive study, was performed by Purchase when he tested mixtures of 1- and 2-naphthylamines.[27] In his dog study that lasted 128 months, those fed pure 2-naphthylamine developed transitional-cell carcinomas (a malignant tumor arising from a transitional type of stratified epithelium) of the bladder within 25-47 months. Of the dogs that ingested a mixture of 6% 2-aminonaphthalene in 1-naphthylamine, only 2 of the 8 dogs developed early carcinomas and of the group given a 0.5% mixture of 2-naphthylamine in 1-naphthylamine, only 2 of the 8 dogs developed hemangiona (a benign tumor of dilated blood vessels) of the bladder. Both of these conditions were found near the end of the study at 128 months. The test group fed pure 1-naphthylamine showed no signs of neoplasia (a new and abnormal formation of tissue as a tumor). This data suggests that 1-naphthylamine is at least 200 times less carcinogenic than 2-naphthylamine and demonstrates the potency between 1- and 2-naphthylamine. The urine of the dogs was also studied and the carcinogenicity of 2-naphthylamine was attributed to its metabolism in the liver to *N*-nitroso-2-naphthylamine and *N*-hydroxy-2-naphthylamine, which were then excreted via the urine and hydrolyzed in the acidic conditions of the bladder. [20]

The difference in the metabolism of 1- and 2-naphthylamine can also be seen in their reaction with the DNA of the urothelium. DNA-2-naphthalene adducts could be detected in the urothelium, 18.5 adducts/10^8 nucleotides, two days after administration of 2-naphthylamine to a dog, but no adducts were detected after administration of 1-naphthylamine.[27] The main DNA-2-naphthalene adducts observed *in vitro* were 1-(deoxyguanosin-N^2-yl)-2-naphthylamine, 1-(deoxyadenosin-N^6-yl)-2-naphthylamine, and

an imidazole ring-opened derivative of *N*-(deoxyguanosin-8-yl)-2-naphthylamine (Figure 3.2).[21,28,29]

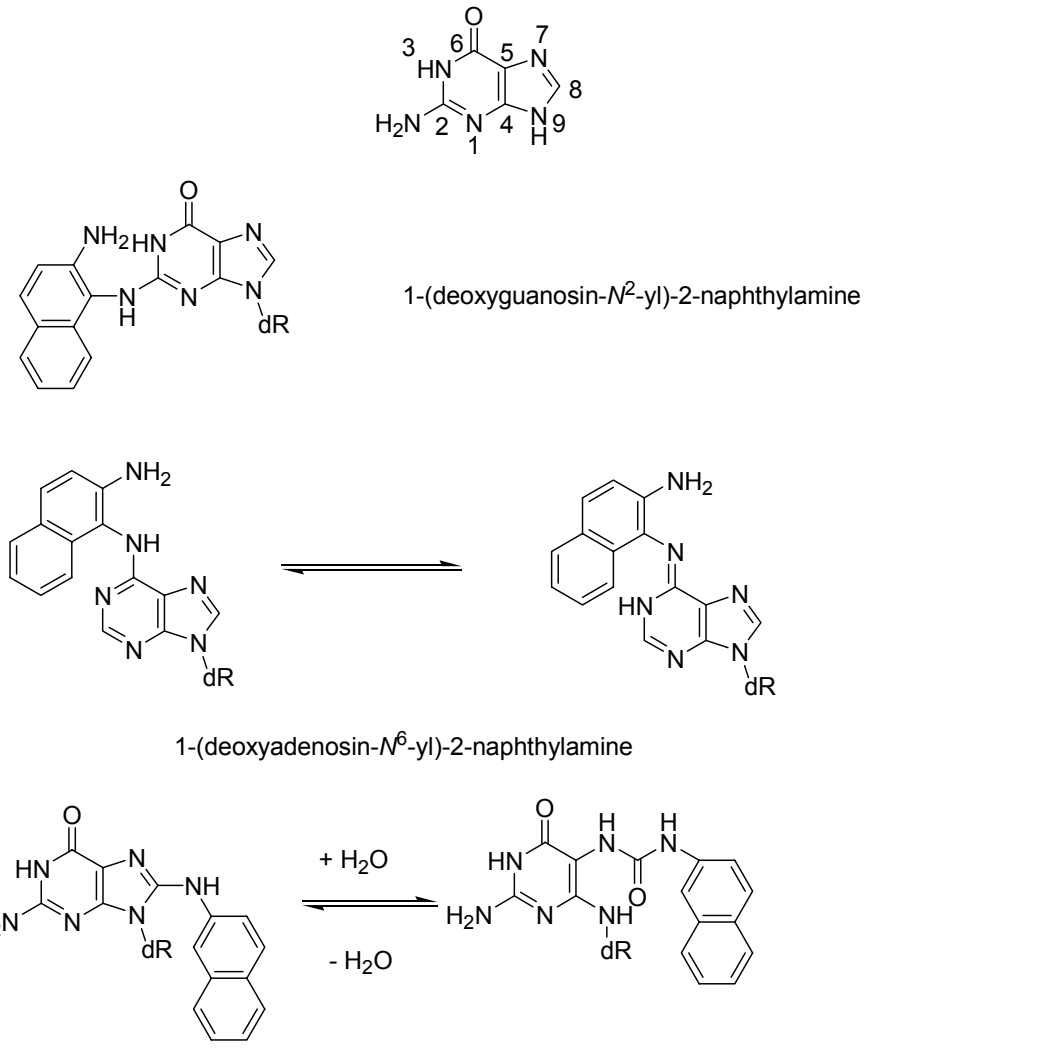
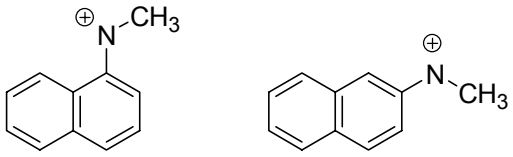


Figure 3.2: Adducts of *N*-hydroxy-2-naphthylamine with 2′-deoxyguanosine (dG) *in vitro*.

Since 2-naphthylamine is site specific, there was a difference in the amount of DNA-2-naphthylamine adducts between the urothelium (target) and liver tissues (non-target), such that the level of binding to DNA was 4-fold higher in the urothelium at 2 days and 8-fold higher at 7 days after dosing. This greater persistence of the C-8-guanine adduct in the urothelium as compared to the liver suggests that the susceptibility of the bladder to 2-naphthylamine induced tumors may be a direct consequence of the higher binding levels and greater persistence of DNA-2-naphthylamine adducts in this tissue.[21] On the other hand, similar experiments with 1-naphthylamine failed to produce binding in urothelial DNA.

Although the metabolic pathway for transport to the bladder may be agreed upon, the challenge still remains as to what is the active carcinogen of these aromatic amines. It has been suggested that *N*-hydroxylation of aromatic amines is required for potent carcinogenicity.[22] Another prerequisite is that the aromatic amine have at least two aromatic rings, either fused as in the case of 2-naphthylamine or joined as in the case of 4-biphenylamine. The conversion of certain *N*-hydroxy arylamines to arylnitrenium ions or carbocation electrophiles under acidic conditions was first proposed by Yukawa and Ingold in the 1950s and by Boyland and Kriek in the 1960s.[30-33] Miller and Miller relate that although there is a wide range of structures of known chemical carcinogens, their common feature is that their ultimate forms are electrophilic reactants and usually arise though metabolism *in vivo*.[34] The more complicated structural requirement is probably necessary to stabilize a positive charge on the amine nitrogen.[22,32] Thus, the covalent reactions of these electrophilic derivatives of carcinogens with DNA are the major cause of mutations.[21] Such electrophilic species can be seen in Figure 3.3.



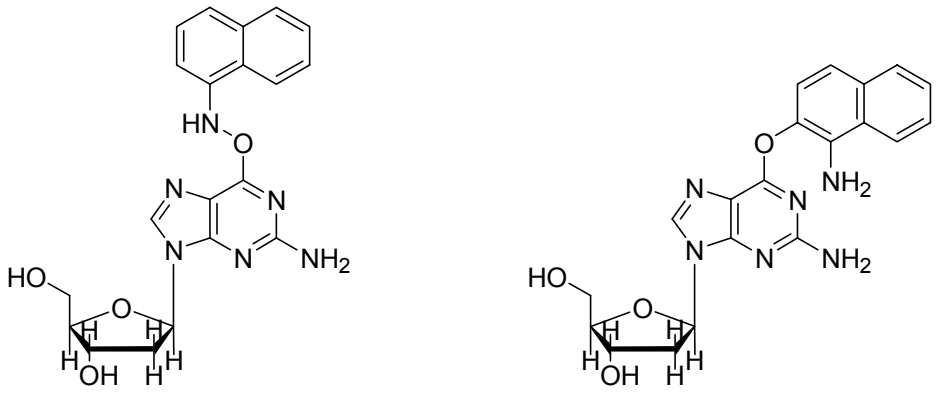
III-5 **III-6**

Figure 3.3: Structures of *N*-methyl-*N*-(1-naphthyl)nitrenium ion (III-5) and *N*-methyl-*N*-(2-naphthyl)nitrenium ion (III-6).

It is thought that *N*-hydroxy-2-naphthylamine is converted to an arylnitrenium ion-carbocation electrophile that is capable of binding to cellular macromolecules.[24,28,29] The arylnitrenium ion could result from acidic hydrolysis of the *N*-glucuronides, followed by protonation of the *N*-hydroxy groups of the resulting *N*-hydroxy amines, and then loss of water, as depicted in Scheme 3.3. These lipophilic cations may have detergent–like properties that facilitate their entry into the connected cellular membranes. Then they may be transported by diffusion through these membranes to critical cellular macromolecules.[24] *N*-Glucuronides are formed enzymatically by uridine diphosphate glucuronyltransferase (UDPGA) or are generated spontaneously from the arylamine and D-glucuronate, which are easily hydrolyzed in weakly acidic media.[35] The nucleophilic sites which are substituted must depend on the formation site of the electrophile and the extent to which the stability, solubility, and charge of the electrophile permit its movement within the cell.[36]

N-Hydroxy-1-naphthylamine in reaction with DNA *in vitro* yields adducts identified as *N*-(deoxyguanosin-O^6-yl)-1-naphthylamine, 2-(deoxyguanosin-O^6-yl)-1-naphthylamine, and its decomposition product (Figure 3.4). Since O^6-substituted deoxyguanosine adducts represent potential mispairing lesions, the formation of these 1-

naphthylamine-DNA adducts *in vivo* may constitute the initiation step in carcinogenesis.[28,37] In contrast to *N*-hydroxy-1-naphthylamine which reacts with DNA at the O^6 position of the guanine base, *N*-hydroxy-2-naphthylamine reacts at exocyclic amino groups of guanine and adenine and at the C-8 position of guanine (Figure 3.4).[28]



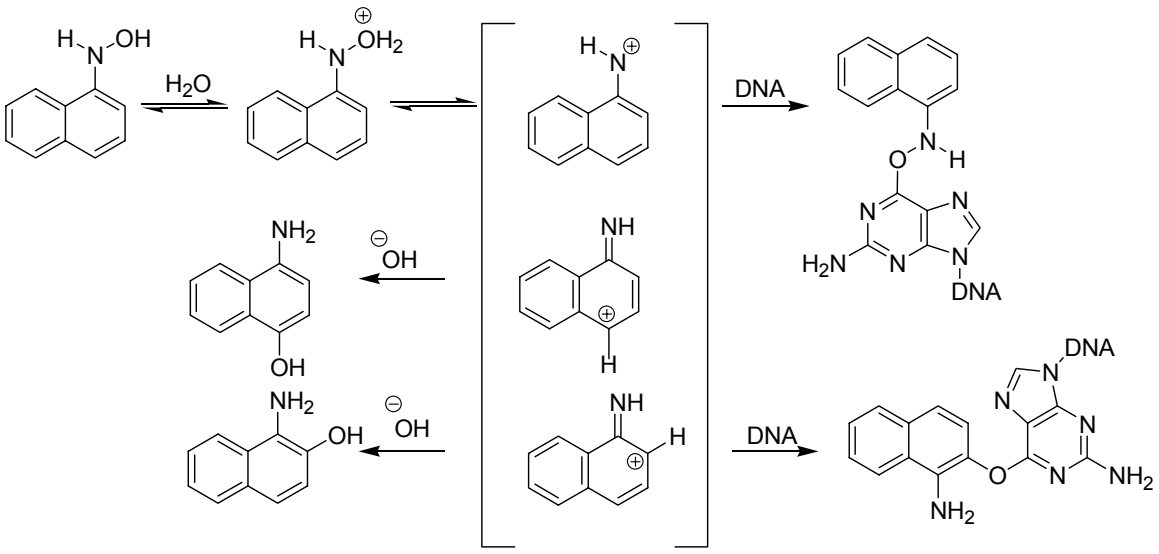
N-(Deoxyguanosin-O^6-yl)-1-naphthylamine 2-(Deoxyguanosin-O^6-yl)-1-naphthylamine

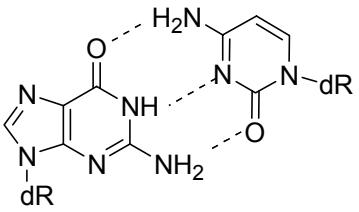
Figure 3.4: Adducts of *N*-hydroxy-1-naphthylamine with deoxyguanosine *in vitro*.

Direct evidence for the acid-dependent arylnitrenium ion formation was obtained by isotope exchange upon solvolysis of *N*-hydroxy-1-naphthylamine in acidic $H_2{}^{18}O$ and carbocation formation was indicated by the formation of the solvolysis products, 1-amino-2-naphthol and 1-amino-4-naphthol (Scheme 3.4). These studies demonstrated the conversion of a carcinogenic *N*-hydroxyl arylamine to electrophilic arylnitrenium ion and carbocation species that display high selectivity toward macromolecules. [37] The DNA may assist in adduct formation at the *N*-naphthyl and 2-naphthyl positions through steric interactions such as intercalation, hydrogen bonding, or kinking. The DNA may also stereochemically assist in directing the electrophilic region of the carcinogen to the O^6-

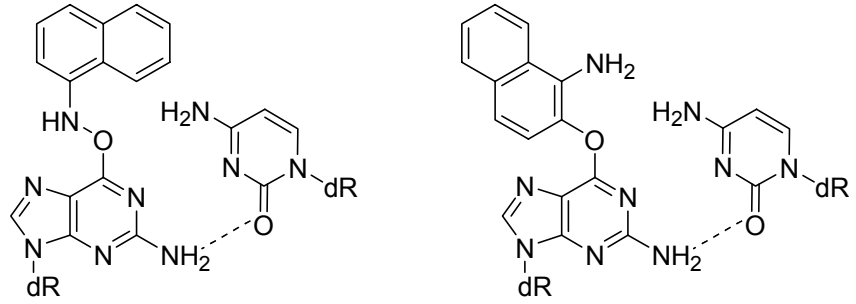
guanine atom and thus promote the selectivity of the reaction and the O^6-guanine-substituted adducts would interfere with normal Watson-Crick base pairing and could provide the initial step toward neoplasia. Computer-generated graphic models show that these adducts would cause relatively little distortion in the macromolecule and may not be recognized by repair enzymes. The *N*-hydroxy-1-naphthylamine-DNA adduct might also incur the possibility of mispairing with a thymine base during replication (Figure 3.5).[37]

Scheme 3.4: Proposed mechanism for reaction of *N*-hydroxy-1-naphthylamine with DNA.

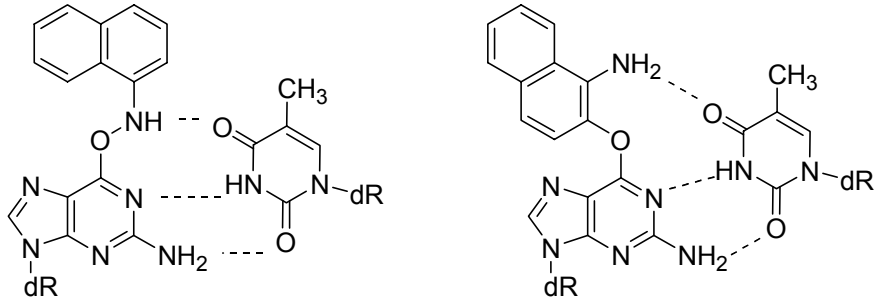




Normal G-C pairing



Carcinogen Modified G-C pairing



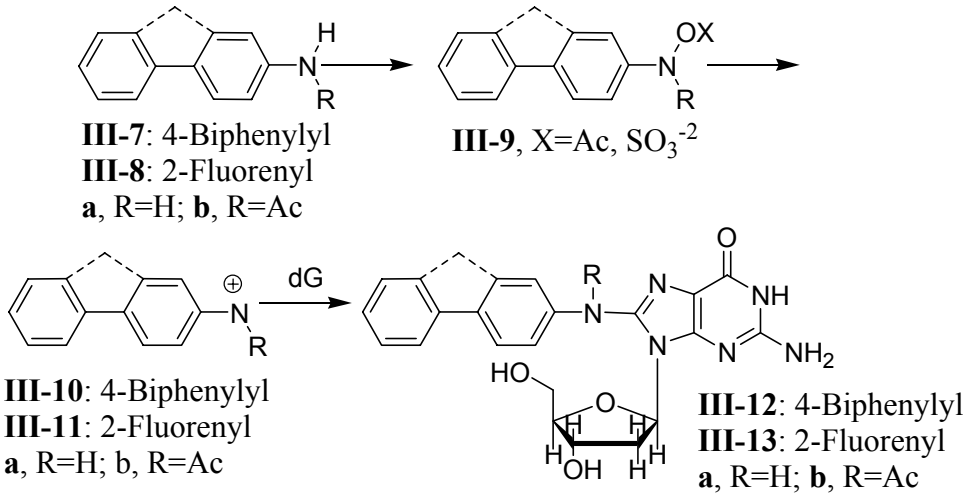
Carcinogen-Induced G-T mispairing

Figure 3.5: Possible effects of covalently bound 1-naphthylamine residues in DNA on Watson-Crick base pairing (dR = deoxyribonucleoside).

The arylnitrenium ion produced *in vivo* could react in an electrophilic substitution reactions at C-8 of guanine, which is the most likely to be attacked by an electrophilic agent.[33,38] Boche carried out detailed studies of the decomposition reactions of various *N*-hydroxylamine esters in the presence of DNA and dG and characterized the adducts that resulted from these reactions.[14,39] McClelland has shown that nitrenium ions have an affinity for guanine and guanine derivatives by forming covalent adducts where the C-8 position of guanine is linked to the nitrenium ion's nitrogen.[40,41] Such arylamination at guanine C-8 is typical of arylamine carcinogens and is attributed to an arylnitrenium ion as the guanine-binding electrophile.[42] It was stated that the C-8 position is the most electron-rich in purine, not necessarily in the ground state, but when excited by the approach of an electrophilic reagent. This example can be seen when guanine is easily brominated in the C-8 position while adenine resists bromination completely.[38]

Over the years, McClelland and his group have studied the most extensively studied carcinogens 4-biphenylamine (**III-7a**) and 2-fluorenylamine (**III-8a**). These compounds are highly toxic because they are relatively long-lived in water (> 1 μs) but react with DNA near the diffusion limit. It is interesting to note that pyrimidines do not react wih nitrenium ions at a rate faster than water, but guanine traps at a rate constant of 10^9 $M^{-1}s^{-1}$ whereas the other purines are one-tenth as reactive.[40,43-45] These carcinogens undergo activation to O-acetate or O-sulfate esters, followed by N-O bond heterolysis to yield arylnitrenium ions and form DNA adducts with the aryl nitrogen attached to the C-8 of guanine residues (Scheme 3.5). [44,46]

Scheme 3.5: Reactions of 4-biphenyl and 2-fluorenylnitrenium ions with dG.



III-7: 4-Biphenylyl
III-8: 2-Fluorenyl
a, R=H; **b**, R=Ac

III-9, X=Ac, SO_3^{-2}

III-10: 4-Biphenylyl
III-11: 2-Fluorenyl
a, R=H; b, R=Ac

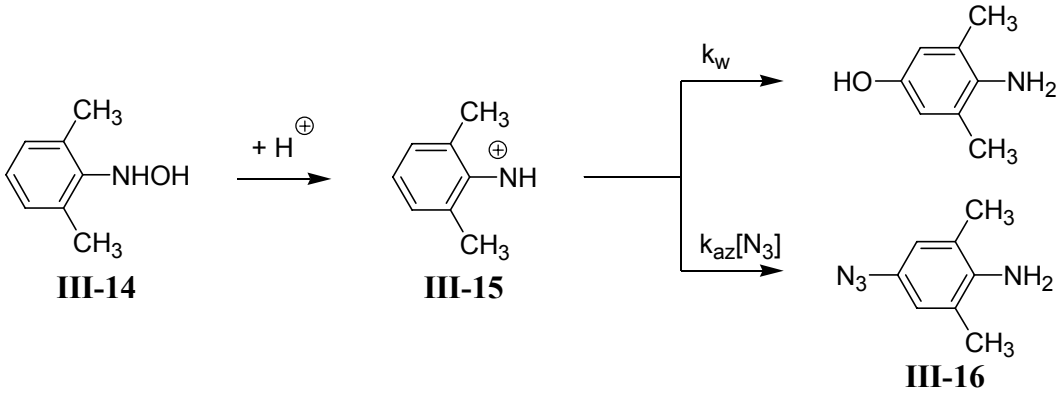
III-12: 4-Biphenylyl
III-13: 2-Fluorenyl
a, R=H; **b**, R=Ac

Major questions answered by McClelland *et al.* were: 1) whether the lifetimes of the arylnitrenium ion were sufficient enough to be considered viable intermediates, 2) if nitrenium ions show any reaction with guanine in competition with the solvent, and 3) if the nitrenium ion does add to guanine, by forming the C-8 adduct.[44] The selective trapping of **III-10** and **III-11** with dG could not occur if trapping by H_2O was not relatively slow. Hard nucleophiles attack nitrenium ions at the aromatic ring thus aromaticity is lost which contributes to the barrier to the reaction.[47] It has been suggested that the long lifetime of nitrenium ions in H_2O compared to similar carbenium ions is due to this barrier.[43] This long lifetime is critical which allows **III-10** and **III-11** to react selectively with relatively weakly nucleophilic dG. The carcinogenic potential of **III-10** and **III-11** appears to be related to the very high selectivity for C-8 of dG in aqueous solutions.

To determine if the lifetimes of **III-10** and **III-11** are sufficient in aqueous solution to be viable intermediates, McClelland performed azide-clock experiments and

found that the formation of **III-16** increases with increasing concentration of azide, but does not increase the rate of the reaction, which signifies that there is an intermediate cation (Scheme 3.6).[44,48] Since the rate does not increase with increasing concentration of azide, the reaction mechanism must be an S_N1 type reaction with the formation of the arylnitrenium ion and not a bimolecular reaction.

Scheme 3.6: Azide clock experiment.



III-14 **III-15** **III-16**

Through LFP, McClelland was able to observe the nitrenium ion intermediate through UV-vis spectroscopy.[44] The nitrenium ion was also seen as a stable intermediate in comparison to the carbenium ion counterpart. It was seen that the nitrenium ion was more stable in water with both water and azide as traps than the analogous carbenium ion. The rate of hydrolysis in aqueous solution for water as the trap for **III-11a** is $k_w = 3.4x10^4\ s^{-1}$ while the rate for **III-17** is $k_w = 1.5x10^7\ s^{-1}$ when R = Ph and $k_w \sim 10^9\ s^{-1}$ when R = H.[44] The longer lifetime of the 2-fluorenylnitrenium ion was given to the observation that the trap was reacting with the internal carbon of the aromatic ring; thus, it took longer to react because it had to break the aromaticity of the ring. This is in comparison to the analogous carbenium ion where the trap reacted with the external carbon of the carbenium ion; thus, its time of reaction was much shorter (Figure 3.6).

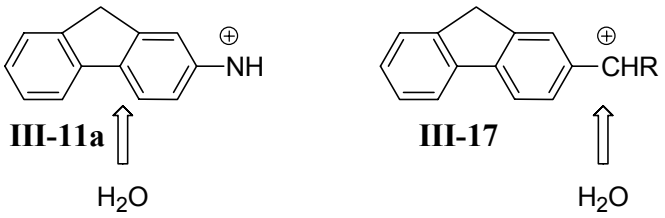


Figure 3.6: Difference in the active site between 2-fluorenylnitrenium ion (III-11a) and its corresponding carbenium ion (III-17).

Also noted was that arylnitrenium ions have several different carbenium ion resonance hybrids with the positive charge delocalized in the aromatic ring (Figure 3.7). The nitrenium ion can also be thought of as a cyclohexadienyl cation bearing an imine substituent.[40,48-50] This has also been experimentally supported through the use of time-resolved infrared spectroscopy (TRIR).[51-53] Therefore, the experimental site of reactivity correlates well with the calculated site of reactivity.

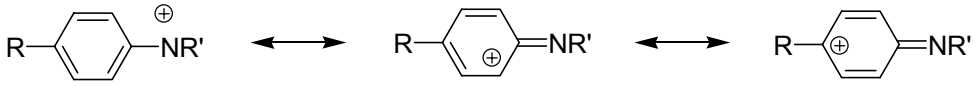


Figure 3.7: Nitrenium ion viewed as 4-iminocyclohexa-2,5-dienyl cations.

Although the lifetimes of the nitrenium ions were longer than originally thought, the lifetimes are still relatively small, but these small lifetimes (>1 μs) are long enough for the nitrenium ions to react with guanine.[54,55] Novak *et al.* were able to detect the reaction of the nitrenium ion with guanine. McClelland *et al.* were able to support this observation through LFP and rate studies.[40,41,56] The rate studies showed that if the

concentration of the 2′-deoxyguanosine (dG) trap was increased, the trapping rate increased as well, showing the second-order nature of the reaction. So the arylnitrenium ions do react with guanine to form the C-8 adduct. The rates for different arylnitrenium ions with water and dG are shown in Table 3.1.[41] An interesting point was that the carbenium ions did not react with dG to form the C-8 adduct. This may be in part to a combination of two factors: first, there may be enhanced guanine reactivity for the nitrenium ions and secondly, there is an unusually low water reactivity with the intermediate.

Table 3.1: Reactivities of arylnitrenium ions with water and dG.

Nitrenium Ion	k_w (s^{-1})	k_{dG} ($M^{-1}s^{-1}$)
4-biphenylyl (III-10a)	1.8×10^6	2×10^9
4′-methyl-4-biphenylyl	2.7×10^5	1.5×10^9
2-fluorenyl (III-11a)	2.7×10^4	7.6×10^8
4′-methoxy-4-biphenylyl	1.6×10^3	3.6×10^7

The mechanism of nitrenium ion addition is continuously under debate because trapping with dG yields C8-*N*-adducts while simple nucleophiles react at the ring's carbon atoms. Takeuchi *et al.* used a product study of phenylnitrenium ions to observe their reaction pathways.[57] According to MNDO molecular orbital calculations, it can be seen that the phenylnitrenium ion has resonance forms in which the positive charge is mainly delocalized in the *para*- and *ortho*-positions rather than the nitrogen atom itself.[58] Therefore, upon nucleophilic attack on these ring positions, one would expect to see products that are coupled to these positions. But, many diarylamines products have been observed with *N*-substitution by the phenylnitrenium ion (Scheme 3.7).[57] It was thought that the reaction would proceed either through a nitrenium ion or through an aromatic

S_N2-type reaction. A comparative experiment of *N*-phenylhydroxylamine (**III-18**) and phenyl azide (**III-19**) shows the product ratios are very similar, suggesting that both reaction pathways are via nitrenium ion intermediates produced by acid-catalyzed decomposition (Table 3.2).[57] From the partial rate factors (f_p) and the correlation between log f_p and σ_p^+ gives a linear plot with $\rho = -4.5$. This large negative value of ρ indicates that the diarylamines are produced via *N*-substitution of the phenylnitrenium ion onto the aromatics. The rate constants that were calculated indicate that the rate is first-order, thus ruling out the possibility of an S_N2-type reaction. Therefore, the reaction of the phenyl azide spontaneously losses a nitrogen molecule in the rate determining step to yield the phenylnitrenium ion.

Scheme 3.7: Direct amination using phenylnitrenium ion.

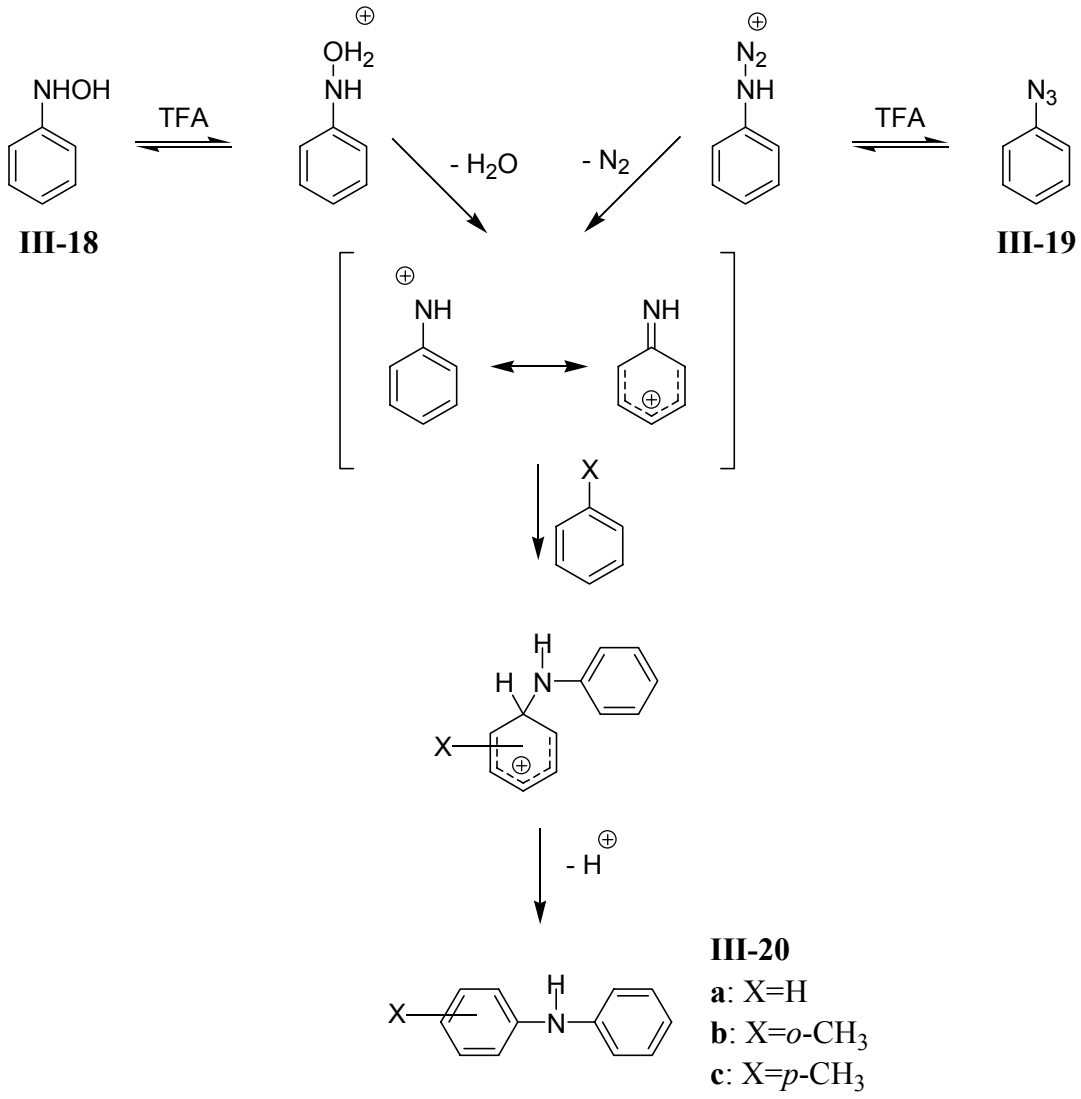
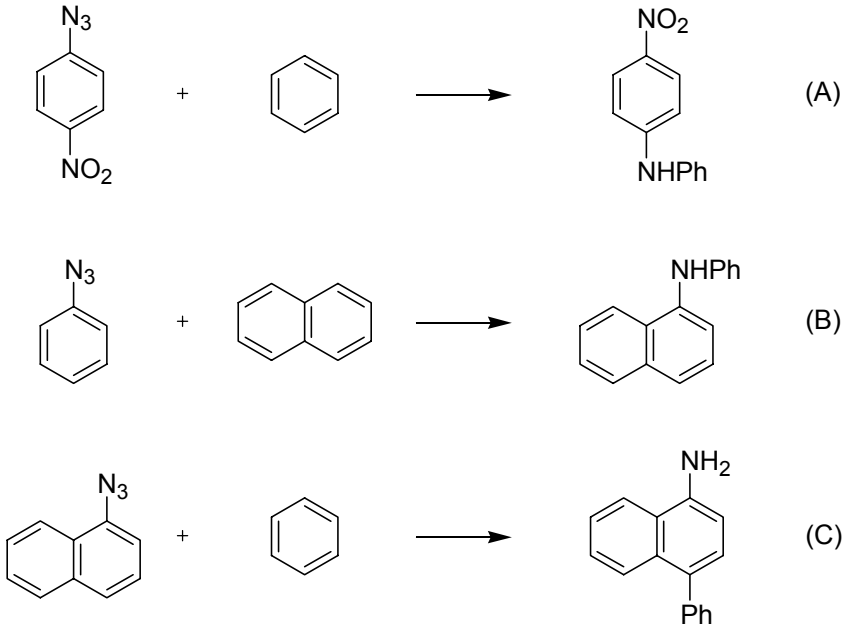


Table 3.2: Product distribution of direct amination using phenylnitrenium ion.

Substrate	% Yield III-20a	% Yield III-20b	% Yield III-20c
Benzene	55	---	---
Toluene	---	30	31

When benzene was used as the substrate, the major product was the *N*-adduct, diphenylamine (**III-20a**), with the carbon adducts as the minor products, 2-biphenylamine (11%) and 4-biphenylamine (12%). Toluene as the substrate afforded the two isomeric forms in about equal amounts of *N*-adducts (**III-20b** and **III-20c**). Naphthalene was also used as the substrate and the major products from that reaction were *N*-adducts *N*-phenyl-1-naphthylamine (41%) and *N*-phenyl-2-naphthylamine (8.2%). From the obtained results, one would assume that if naphthyl azide reacted with benzene, the major product would be the *N*-adduct, but as is shown in Scheme 3.8, the *para*-product is formed.[59]

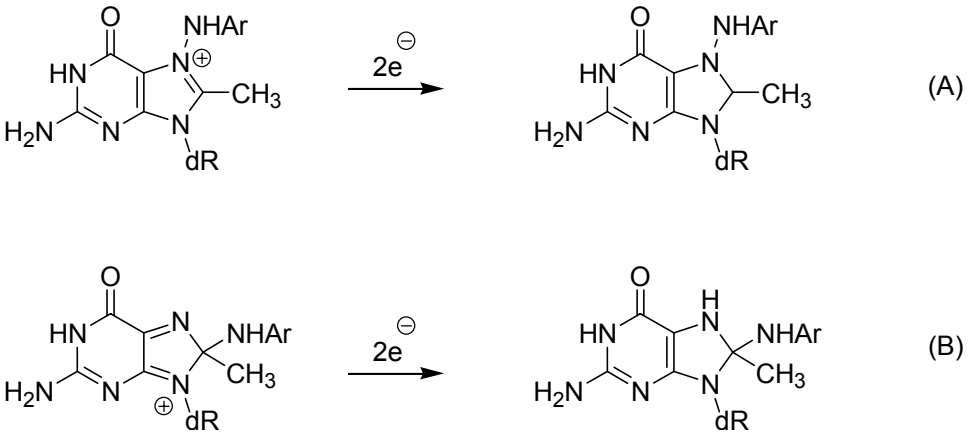
Scheme 3.8: Reactions and products using phenylnitrenium ions with naphthalene and naphthylnitrenium ions with benzene with TFA.



Equations A and B from Scheme 3.8 follow what would be expected with *N*-substitution in the product. On the other hand, equation C does not follow the same pattern. This preferential C-substitution by the 1-naphthylnitrenium ion may result from the favorable population of the positive charge at the 4-position of the ring rather than at the nitrogen.[58]

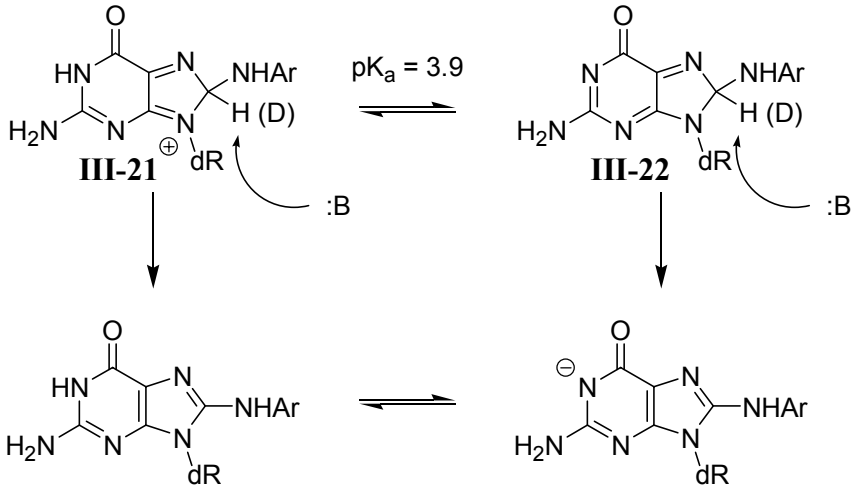
Experiments performed *in vitro* have shown that 2′-deoxyguanosine (dG) is an efficient trap for nitrenium ions. It has been reported that the C-8 is not regarded as the normal position of electrophilic addition in guanine for the *N*-adduct. Humphreys, Kadlubar and Guengerich found experimental evidence for the initial bond formation at N-7.[41,60] While on the other hand, Kennedy, Novak, and Kolb performed similar experiments and observed that the initial bond formation as an unstable species and its reduction product at C-8 (Scheme 3.9).[41,61]

Scheme 3.9: Addition pathways observed by Humphreys, Kadlubar and Guengerich (Equation A, Ar = 2-fluorenyl) and Kennedy, Novak, and Kolb (Equation B, Ar = 4-biphenylyl*)*.



This confusion prompted McClelland to study the mechanism of the formation of the C-8 adduct. McClelland *et al.* spectroscopically characterized the initial C-8 intermediate of 2-fluorenylnitrenium ion with 2′-deoxyguanosine.[41] Through LFP experiments, they could observe the growth of the intermediate and through lamp flash photolysis, they could observe the decay of the intermediate. Utilizing the decay of the intermediate, they performed kinetic studies with rate-pH profiles, buffer catalysis, aryl substituent effects, and C-8 deuterium isotope effect. From these studies, McClelland *et al.* postulated that the pathway that most agrees with the data collected is shown in Scheme 3.10.[41]

Scheme 3.10: Deuterium isotope effect in determining the C-8 adduct addition pathway.

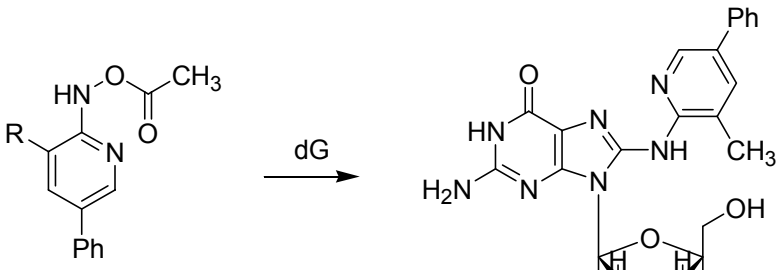


The irradiation of 2-fluorenyl azide in aqueous solutions containing dG results in significant yields of the C-8 adduct and flash photolysis revealed two intermediates of the

reaction. One is the nitrenium ion and the second, longer-lived species, is the C-8 adduct prior to the loss of the C-8 proton. This exists in a cationic acid form (**III-21**) and a neutral conjugate base form (**III-22**), with a pK_a of 3.9. The base is a tautomer of the final product and is the species present at pH 7. The C-8 intermediate appears to form directly in the nitrenium:dG reaction, which indicates that the substitution of $ArNH^+$ for H^+ at the C-8 position of a guanine derivative is a straightforward electrophilic aromatic substitution.

Not only are nitrenium ions from industry a concern, but more recently, attention has turned to the reactions of heteroarylnitrenium ions.[13,62] These intermediates are derived from the activation of heterocyclic amines which are created in cooked foodstuffs through the high-temperature thermolysis of amino acids or proteins. Nitrenium ions from food-derived heterocyclic arylamine mutagens derived from esters have been used to test the affinity of the nitrenium ion as a reactive intermediate in the formation of DNA adducts.[54,63] The ester (**III-23**) was decomposed to generate the nitrenium ion which, when reacted with 2′-deoxyguanosine (dG), formed the C-8-DNA adduct (Scheme 3.11). The adduct was the predominant form and was similar in structure to most other aromatic amine carcinogens.

Scheme 3.11: Heterocyclic nitrenium ion DNA adduct.



III-23

The International Agency for Research on Cancer (IARC) has categorized 2-naphthylamine into group 1, which represents sufficient evidence of carcinogenicity in humans, signifying that a causal relationship has been established between the agent and human cancer in studies in which chance, bias, and confounding can be excluded with reasonable confidence.[23,64] Besides initiating the formation of cancer cells and mutations, 2-naphthylamine can induce genetic damage including DNA strand breaks and chromosomal aberrations (changes in chromosome structure or number). Other types of genetic damage include micronucleus formation (a sign of chromosome damage or loss), aneuploidy (extra or missing chromosomes), sister chromatid exchange, and cell transformation (a step in tumor formation). On the other hand, 1-naphthylamine is categorized in group 3, which represents that the agent (mixture or exposure circumstance) is whose carcinogenicity to humans is not classifiable. Although the commercial production of 2-naphthylamine has been regulated for some time, some current sources for these carcinogenic aromatic amines include cigarette smoke condensate and the particulate phase of tobacco smoke.[23,65] Smoking and ingestion of charbroiled foods, broiled, and fried meat and other protein containing foods exposes an individual to arylamines that are activated by P-450 1A2, in addition to inducing the enzyme.[13] There is strong evidence that P-450 1A2 appears to be the major enzyme in human and animal liver involved in the bioactivation of genotoxic components of cigarette smoke condensate.[18]

Many research groups are trying to determine assays, both chemical and biological, that can determine a chemical compound's carcinogenic ability. Some of the chemically based assays include the k_e test which employs pulse-conducting technique

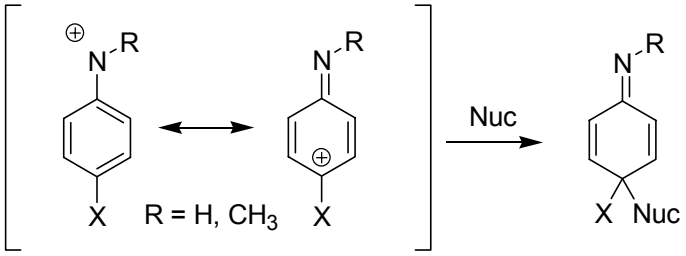
based on electron-solute interactions, taking into account the effective toxicity based on the octanol-water partition coefficient, or calculations of HOMO vs. LUMO gap between the electrophile and the nucleophile. [23,66,67] Some biologically based assays include the Syrian hamster embryo (SHE) cell transformation assay, testing viability against Chinese hamster V79 cells and *Salmonella typhimurium*, or using *in vivo* biochemical parameters to test against Ames test false positives.[68-70]

3.2: *N*-Methyl-*N*-1-naphthylnitrenium ion

3.2.1: *N*-Methyl-*N*-1-naphthylnitrenium ion: History and Introduction

Arylnitrenium ions are known to have short lifetimes in solution. However, monoarylnitrenium ions with π–donating substituents in the *para* position are highly stabilized to addition of simple nucleophiles, such as water, thereby increasing their lifetimes. The latter adds to the ring carbons as illustrated in Scheme 3.12.

Scheme 3.12: General addition of nucleophiles to nitrenium ions.



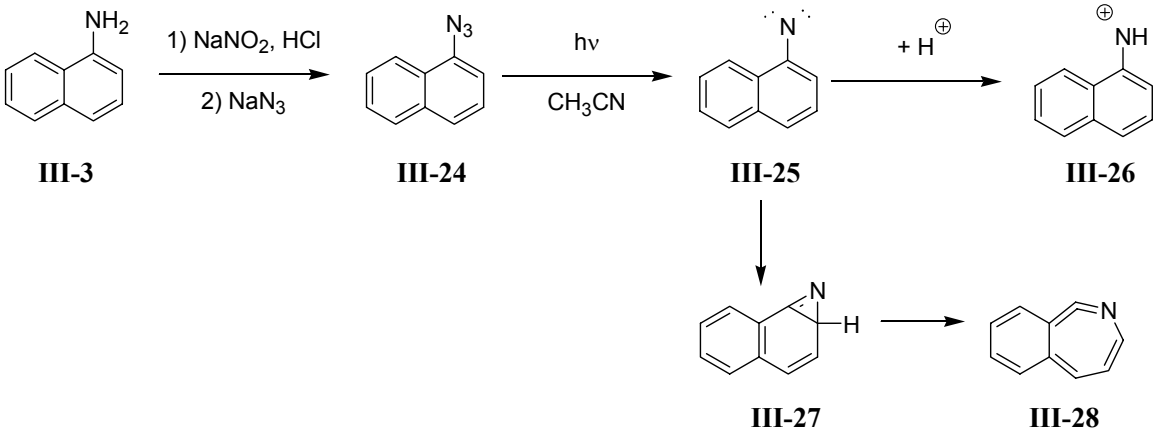
In contrast, π–nucleophiles, such as guanine bases in DNA, can add to the nitrogen. Monoarylnitrenium ions without the *para*-substitution pattern have subnanosecond lifetimes in solution. The stability of arylnitrenium ions with respect to nucleophiles has important implications in chemical toxicology. As a rule, it seems that arylnitrenium ions lacking stabilizing substituents in the *para* position react so rapidly with water that their ability to damage DNA is negligible. In contrast, conjugated aryl substituents in the *para* position stabilize arylnitrenium ions to water addition and leave its reactivity to aromatic nucleophiles (such as DNA bases) relatively unaffected. This leads to the question whether this observation is a steric or an electronic effect.

It is reasonable to suspect that increasing the π–conjugation of the system would stabilize the nitrenium ion, prolonging its lifetime. To test this hypothesis, *N*-methyl-*N*-(1-naphthyl)nitrenium ion was studied. This nitrenium ion benefits from the stabilizing electronic effect of benzannulation, while the *para* position is allowed to be kept open. This is in contrast to *N*-methyl-*N*-(4-biphenylyl)nitrenium ion, which has a π–conjugating phenyl group at the *para* position, which also increases steric bulk. Thus, the electronic effect of π–conjugation in the absence of significant steric effects can be studied and the relationship between the two can be determined using this *N*-methyl-*N*-(1-naphthyl)nitrenium ion system.

3.2.2: Synthesis of Photochemical Precursor to the Nitrenium Ion

There are two widely used photochemical routes for generating nitrenium ions. One method is to photolyze an azide in aqueous solution. Under these conditions, the resulting singlet nitrene can be rapidly protonated, yielding the corresponding nitrenium ion.[45,46,71-73] But this pathway is limited because the nitrenium ion produced by irradiation will only be a primary system. Thus, we examined the photolysis of 1-naphthyl azide in aqueous solution by laser flash photolysis (LFP). 1-Naphthyl azide was synthesized via a one-pot reaction, in which the first step was nitrosation of the primary amine followed by formation of the azide with sodium azide (Scheme 3.13).

Scheme 3.13: Synthetic and photolytic reaction pathways of 1-naphthyl azide.



III-3 **III-24** **III-25** **III-26** **III-27** **III-28**

LFP was performed with 1-naphthyl azide in anhydrous acetonitrile (CH_3CN) with sulfuric acid (H_2SO_4) as the proton source. The LFP spectrum can become complicated by signals from the accumulated photoproducts. To avoid this problem, it is

customary to use a flow cell which rapidly introduces fresh samples into the irradiated zone and replaces the photolyzed material which is discarded.

When these LFP experiments were performed, a broad signal was produced from 350 – 500 nm (Figure 3.8). When the photolysis was performed in CH_3CN alone, with no proton source, the observed broad signal ranged from 350 – 500 nm (Figure 3.9) and did not differ significantly from those generated in protic solution. In fact, the signals detected have been previously observed and are attributed to the well-known ring expansion intermediates from the nitrene (Scheme 3.13).[74-77]

For this reason, it was concluded that the unimolecular reactions of the singlet nitrene, including cyclization and intersystem crossing, were faster than the competing proton transfer. Therefore, another precursor to generate the nitrenium ion was used.

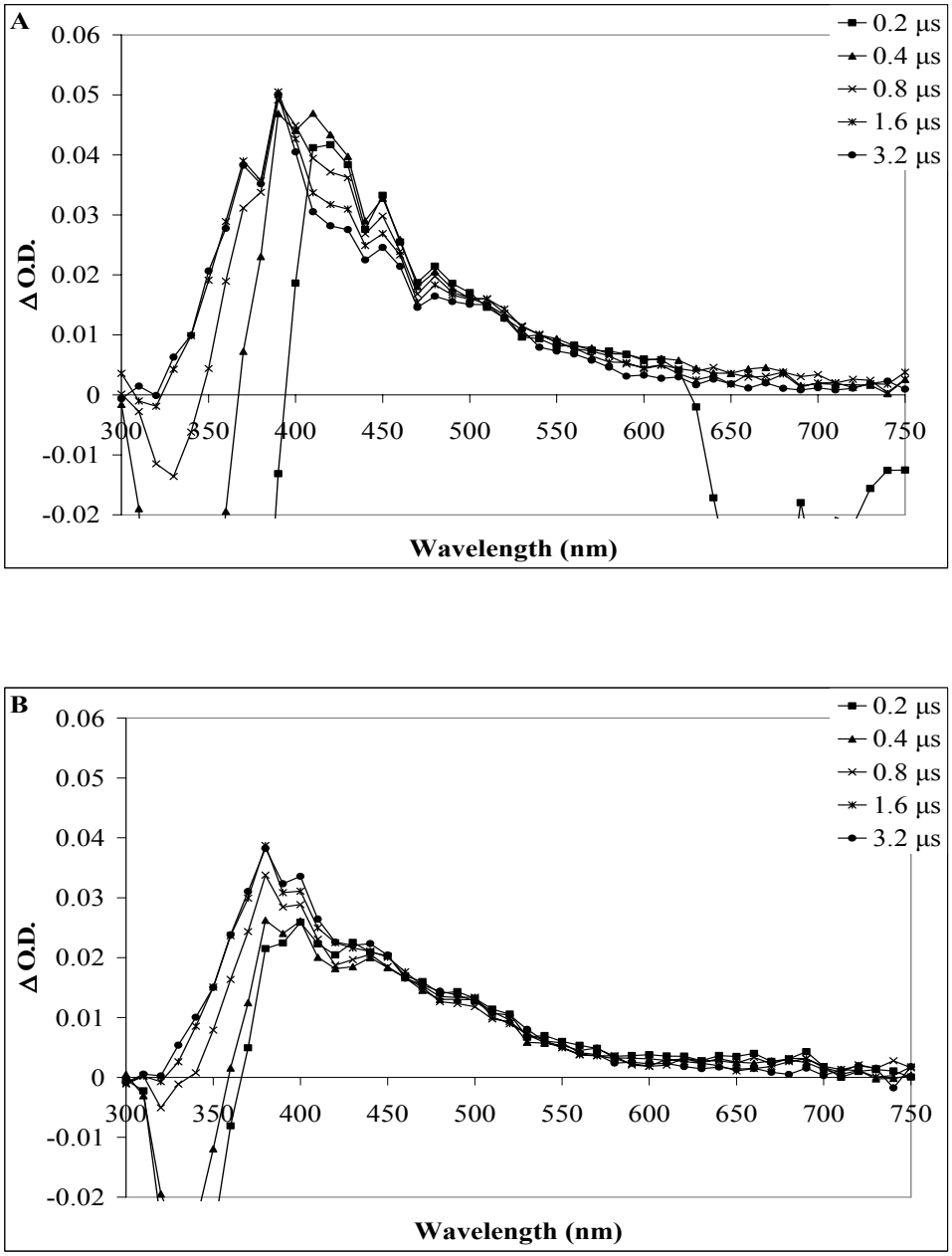


Figure 3.8: Transient UV-vis absorption spectra generated from LFP (266 nm, 4-6 ns, 3-5 mJ/pulse) of III-24 in anhydrous CH_3CN and H_2SO_4 taken 0.2, 0.4, 0.8, 1.6, and 3.2 μs after the laser pulse under (A) nitrogen (N_2) purge and (B) oxygen (O_2) purge.

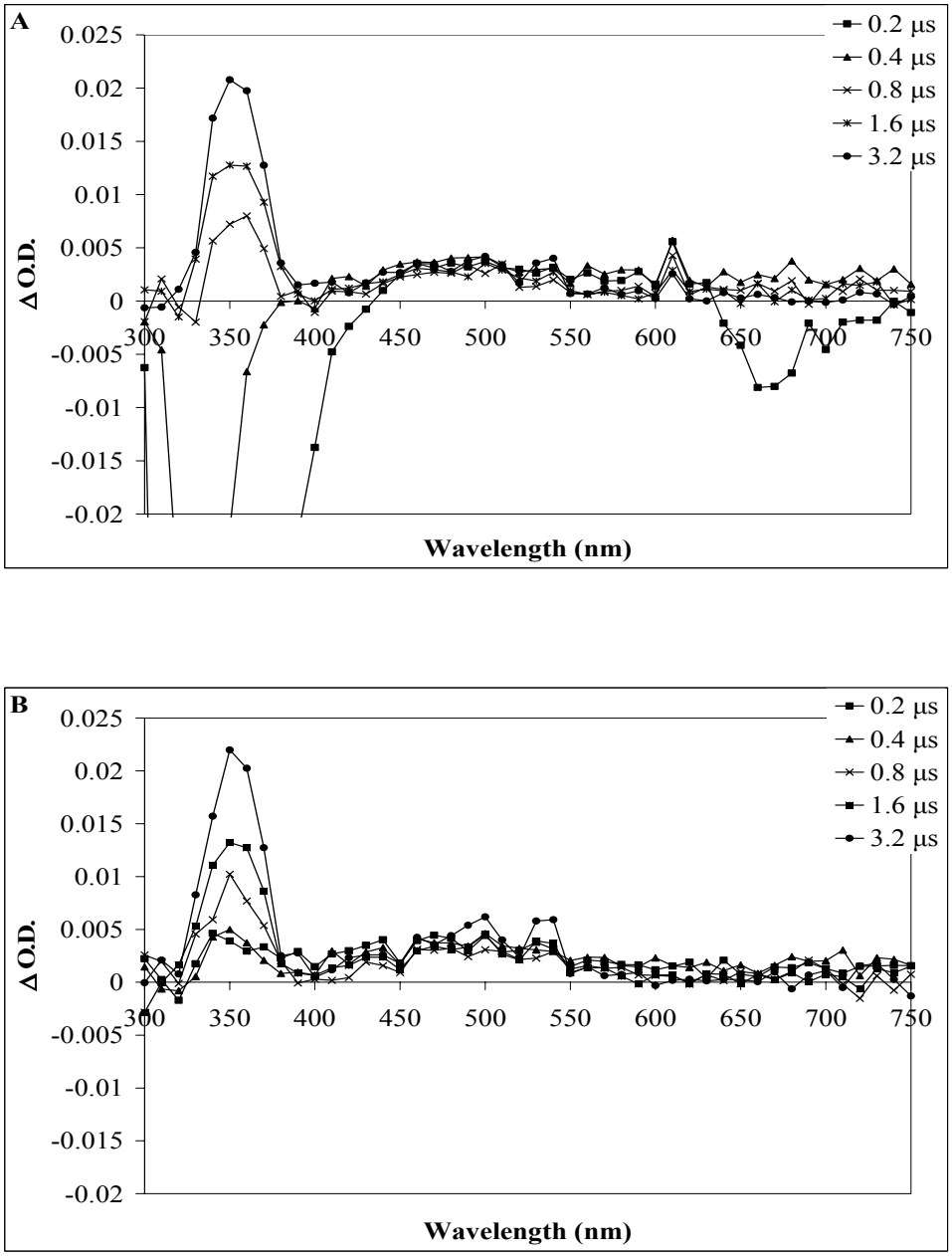
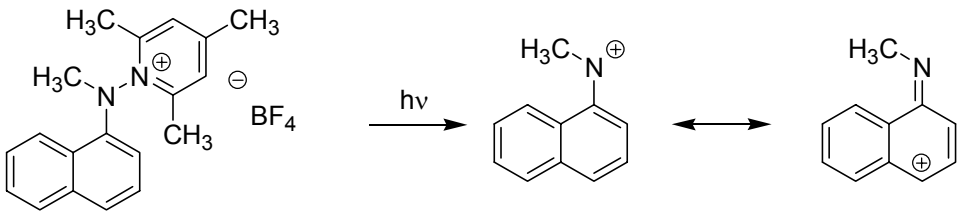


Figure 3.9: Transient UV-vis absorption spectra generated from LFP (266 nm, 4-6 ns, 3-5 mJ/pulse) of III-24 in CH_3CN taken 0.2, 0.4, 0.8, 1.6, and 3.2 μs after the laser pulse under (A) N_2 purge and (B) O_2 purge.

Previous studies have shown that arylnitrenium ions can be efficiently generated through photolysis from their substituted *N*-amino pyridinium salts and allows the formation of a secondary nitrenium ion due to the heterolytic scission of the N-N bond (Scheme 3.14).[53,56,78-80]

Scheme 3.14: Photolysis of 1-(*N*-methyl-*N*-(1-naphthyl)amino)-2,4,6-trimethylpyridinium tetrafluoroborate yielding *N*-methyl-*N*-(1-naphthyl)nitrenium ion.

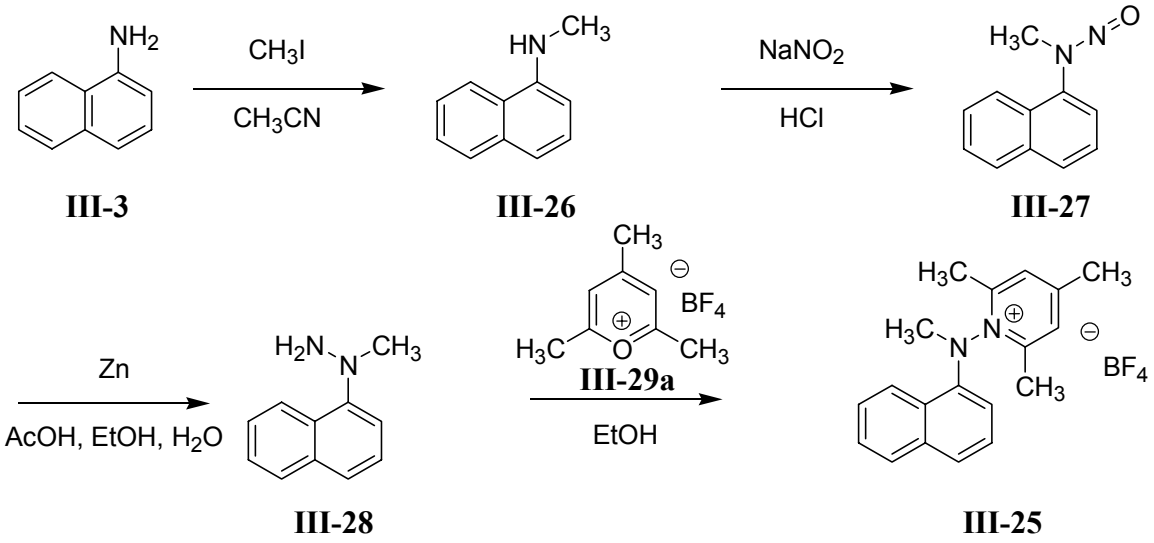


III-25 **III-5** **III-5a**

Thus, for this study, 1-(*N*-methyl-*N*-(1-naphthyl)amino)-2,4,6-trimethylpyridinium tetrafluoroborate was synthesized via this well-known and successful synthetic pathway (Scheme 3.15). *N*-Methyl-1-naphthylamine (**III-26**) was synthesized by direct methylation of 1-naphthylamine. Although this method suffers from producing the dimethylated side-product, it proved to be more convenient than other methods. In principle, one could imagine an alternate route of first protecting the amine with an acetyl group, methylating the amide, then deprotecting the acetyl group to give a higher yield of the mono-methylated product. In terms of practicality, the direct methylation provided similar yields and had the advantage of fewer steps. The secondary

amine (**III-26**) was then nitrosated with a sodium nitrite solution in the presence of hydrochloric acid to give *N*-methyl-*N*-nitroso-1-naphthylamine (**III-27**).

Scheme 3.15: Synthesis of 1-(*N*-methyl-*N*-(1-naphthyl)amino)-2,4,6-trimethylpyridinium tetrafluoroborate.



The latter compound was then reduced in the presence of zinc (Zn) and acetic acid (AcOH) to generate the 1-methyl-1-(1-naphthyl)hydrazine intermediate (**III-28**). This reduction step is particularly sensitive to the reaction conditions such that compound (**III-26**), resulting from over-reduction, is formed along with the desired hydrazine (**III-28**). Purification of this mixture was not performed due to the instability of the hydrazine. Instead, a substoichiometric amount, as determined by ^{1}H-NMR, of freshly prepared 2,4,6-trimethylpyrylium tetrafluoroborate (**III-29a**) was added in situ to the reduction mixture, yielding the final pyridinium salt (**III-25**). It is important that excess pyrylium salt (**III-29a**) is avoided as it is very difficult to separate the pyrylium salt from the

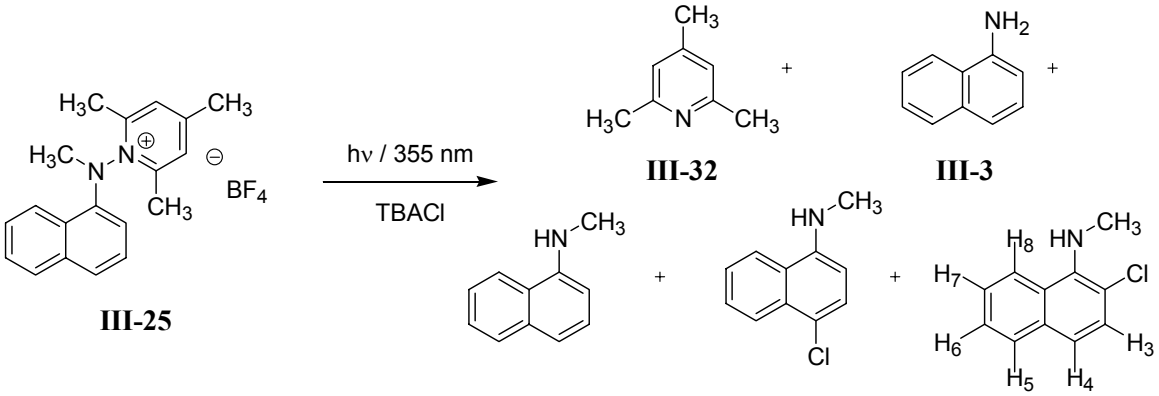
pyridinium salt. The pyridinium salt was then recrystallized, first from ethanol, then from methanol, and characterized by the customary spectroscopic methods (^{1}H-NMR, ^{13}C-NMR, and HRMS).

3.2.3: Stable Photoproducts

In order to verify that the nitrenium ion was generated, photolysis experiments were performed with 1-(*N*-methyl-*N*-(1-naphthyl)amino)-2,4,6-trimethylpyridinium tetrafluoroborate and tetrabutylammonium chloride (TBACl), as an efficient nucleophilic trapping agent. Studies on related nitrenium ions, as well as LFP studies on the current system, show that chloride is an efficient trap of aromatic nitrenium ions. As a general rule, all but the most stable nitrenium ions react with anionic nucleophiles, such as chloride, at the diffusion-limited rate.[81,82] Therefore, we photolyzed the pyridinium salt (**III-25**) with 5.42 mM TBACl as the chloride source, in a CH_3CN solution at 355 nm and analyzed the resulting photoproducts. Photolysis of 1-(*N*-methyl-*N*-(1-naphthyl)amino)-2,4,6-trimethylpyridinium tetrafluoroborate yielded *N*-methyl-*N*-(1-naphthyl)nitrenium ion through N-N bond heterolysis, which gave products characteristic of those expected from a singlet arylnitrenium ion. From the photolysis mixture five products were formed (Scheme 3.16): 2,4,6-collidine (**III-32**), 1-naphthylamine (**III-3**), *N*-methyl-1-naphthylamine (**III-26**), 4-chloro-*N*-methyl-1-naphthylamine (**III-30**), and 2-chloro-*N*-methyl-1-naphthylamine (**III-31**). Compounds **III-3**, **III-26**, and **III-30** were isolated and characterized by ^{1}H-NMR and GC analysis and compared to readily available standards. Photoproduct **III-31** was isolated and characterized through ^{1}H-NMR, ^{13}C-NMR, GC

analysis, and HRMS. Since no readily available standard was available for comparison, COSY-NMR, was critical in the determination of the location of the chloro substituent (Figure 3.10). 2,4,6-collidine (**III-32**) was characterized by GC analysis and GC/MS, but was not isolated.

Scheme 3.16: Photoproducts from III-25 and 5.42 mM TBACl in CH_3CN.



From the COSY-NMR spectrum, the doublets at 7.38 ppm and 7.41 ppm couple with and lean towards each other and no other signals. This would suggest that they are on the same ring, isolated from other protons. Thus, these signals were determined to be H_4 and H_3, respectively. The doublet at 8.13 ppm correlates to the triplet of doublets at 7.49 ppm while the doublet at 7.77 ppm correlates to the triplet of doublets at 7.45 ppm and both triplets of doublets couple to each other. With this correlation and splitting pattern, it was deduced that the signal at 8.13 ppm is H_8, the signal at 7.77 ppm is H_5, the signal at 7.49 ppm is H_7 an the signal at 7.45 ppm is H_6. This supported the conclusion that this was the 2-chloro-N-methyl-1-naphthylamine and not another isomer.

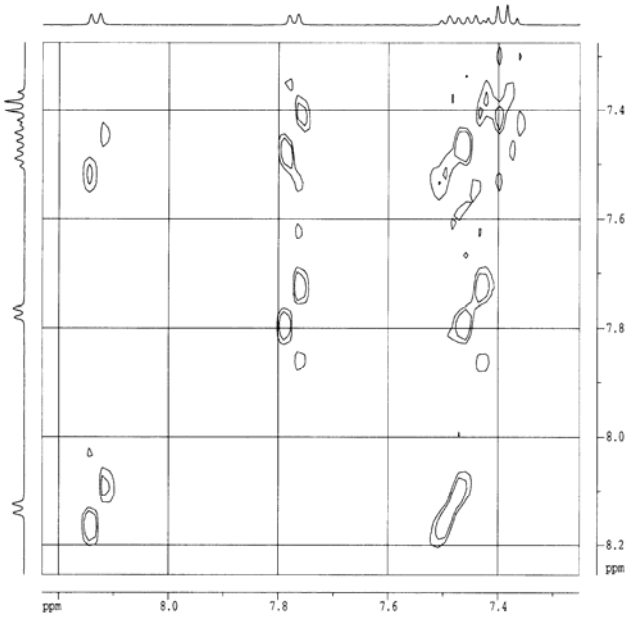


Figure 3.10: COSY-NMR spectrum of photoadduct 2-chloro-*N*-methyl-1-napththylamine (III-31).

From the mass balance results in Table 3.3, it can be seen that 2-chloro-*N*-methyl-1-naphthylamine (**III-31**) and 4-chloro-*N*-methyl-1-napththylamine (**III-30**), which are due to the chloride trapping at the *ortho*- and *para*- positions, are generated preferentially over the photoreduction products. The photoreduction products (**III-3**) and (**III-26**) are the minor products from possible hydride transfers. Overall, *N*-methyl-*N*-(1-naphthyl)nitrenium ions (**III-5**) is similar in reactivity to other nitrenium ion systems that have been previously studied. The mmols recovered were based on weights collected via column chromatography and the percent recovered was based on 21% conversion by photolysis, as monitored via ^{1}H NMR

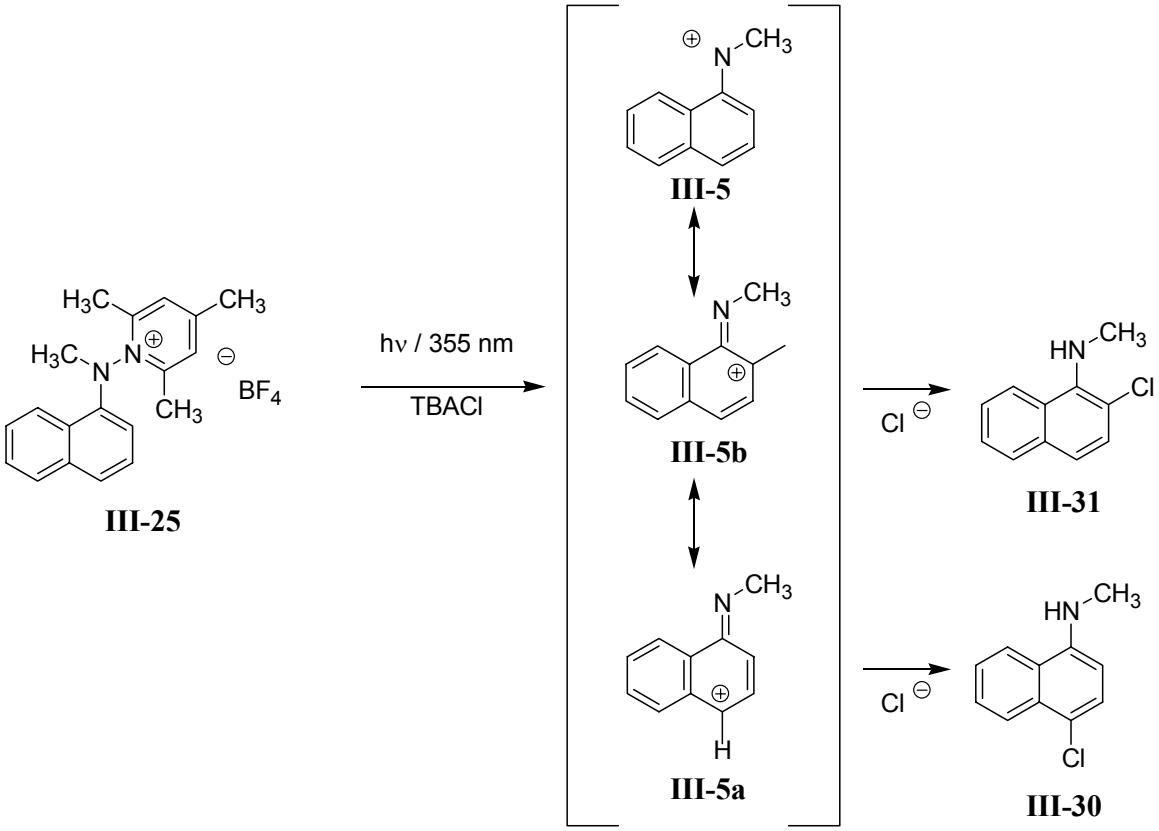
Table 3.3: Product study mass balance.

Compound	mmols Recovered	Percent Recovered
1-naphthylamine (III-3)	0.028	20
***N*-methyl-1-naphthylamine (III-26)**	0.025	18
4-chloro-*N*-methyl-1-naphthylamine (III-30)	0.039	28
2-chloro-*N*-methyl-1-naphthylamine (III-31)	0.032	23
Total	**0.124**	**89**

All of the detected products were consistent with the formation of a nitrenium ion. Photoproducts **III-30** and **III-31** represent photoadducts that are formed through the nucleophilic aromatic substitution of chloride (Scheme 3.17). The chloride forms adducts at either the *ortho*- or the *para*- position to the nitrogen and is in agreement to photoadducts of other similar nitrenium ion systems, such as *N*-methyl-*N*-phenylnitrenium ion.[51,83] Substitution at the 2- and 4-positions is supported by the observations made by Kadlubar, Novak, and Underwood groups through solvolysis reactions of differently *N*-substituted 1-naphthylamines.[37,84,85]

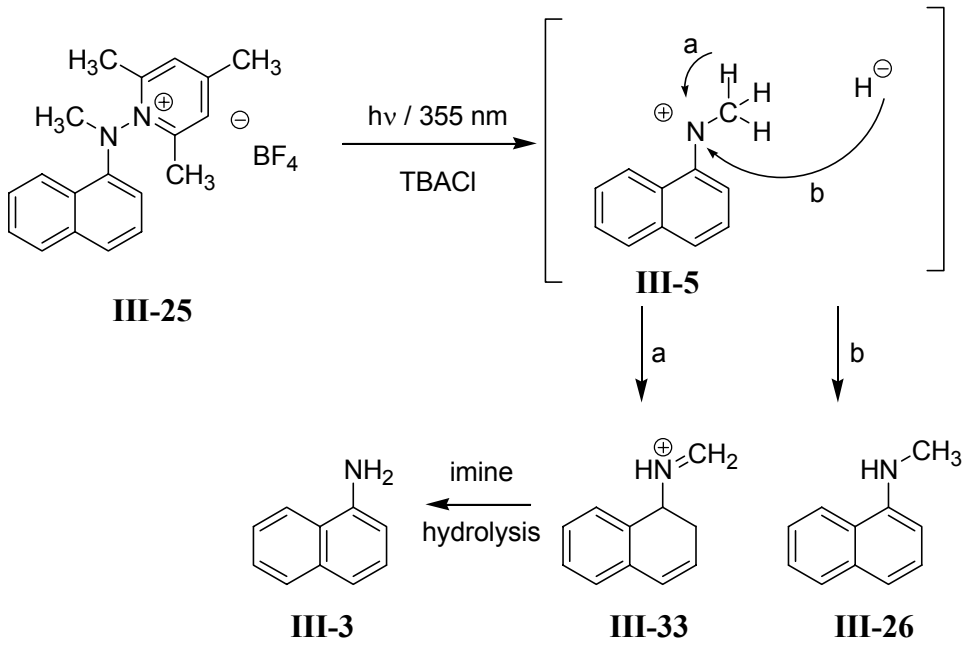
Another observation can be made from the product distribution and it is that there is almost no ortho-/para-adduct selectivity which suggests that the trapping process occurs with little or no activation barrier.[86] This signifies that trapping of the nitrenium ion is not selective in its trapping mechanism/pathway and thus would not be selective to different types of nucleophiles, such as water, proteins, or DNA. Therefore it would not tend to be very carcinogenic or mutagenic.

Scheme 3.17: Formation of 4-chloro-*N*-methyl-1-naphthylamine (III-30) and 2-chloro-*N*-methyl-1-naphthylamine (III-31).



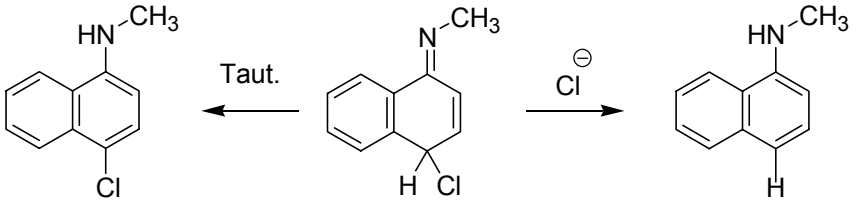
Photoproducts (**III-3)** and (**III-26**) are photoreduction products and may have occurred by several pathways (Scheme 3.18). The transformation of **III-5** to yield **III-3** may come from a 1,2-hydride transfer from the *N*-methyl group to the electron deficient nitrogen. This would form the iminium ion (**III-33**), which is reactive to hydrolysis through aqueous workup to yield the starting material (**III-3**). A similar process has been observed with *N*-methyl-*N*-phenylnitrenium ion.[83]

Scheme 3.18: Formation of the photoreduction products III-3 and III-26.



Photoproduct **III-26** may occur through hydrogen abstraction from the solvent or through secondary photolysis/electron transfer pathway of either of the chloro adducts. 4-Chloro-*N*-methyl-1-naphthylamine (**III-30**) and 2-chloro-*N*-methyl-1-naphththylamine (**III-31**) may be irradiated to homolytically cleave the C-Cl bond. This would be followed by an H-atom abstraction to yield the mono-methylated product **III-26**. Another explanation for formation of **III-26** is that the initial trapping of the nitrenium ion would produce **III-34** (Scheme 3.19). This adduct can undergoes tautomerization to yield 4-chloro-*N*-methyl-1-naphthylamine (**III-30**) or reaction with second chloride ion to yield *N*-methyl-1-naphthylamine (**III-26**).[47,48,52] The same process can occur if the initial trapping with chloride ion is at the ortho position.

Scheme 3.19: Possible route to *N*-methyl-1-naphthylamine (III-26).



III-30 **III-34** **III-26**

3.2.4: Laser Flash Photolysis – Time Resolved UV-vis (LFP-TRUV)

By analogy to previous studies, it was expected that LFP of this tetrafluoroborate salt would provide the nitrenium ion (**III-5**). LFP (355 nm, 4-6ns, 8-10 mJ/pulse) of 1-(*N*-methyl-*N*-(1-naphthyl)amino)-2,4,6-trimethylpyridinium tetrafluoroborate (**III-25**) in CH_3CN gives a short-lived visible absorption band with λ_{max} = 500 nm and a lifetime of 835 ns. On the basis of the previous experiments and reactivity patterns described below, this signal at 500 nm is ascribed to the *N*-methyl-*N*-(1-naphthyl)nitrenium ion (**III-5**). Figure 3.11 shows transient absorption spectra under both N_2 purged and O_2 purged conditions to observe any differences due to the triplet quenching ability of oxygen. The observed transient signal is insensitive to the presence of O_2, a well-known triplet quencher, since no significant differences are observed between the two spectra. This lack of difference provides support that the transient signal is not due to the triplet state of the precursor, but the singlet nitrenium ion is observed at 500 nm.

Also considered was the possibility that the signal at 500 nm was due to the radical cation of (**III-26**). To test this possibility, **III-26** was irradiated in the presence of

a well-known single electron acceptor, 1,4-dicyanobenzene (1,4-DCB). Excited state electron transfer from the amine to 1,4-DCB is expected to generate the radical cation of **III-26** and the radical anion of 1,4-DCB. The resulting LFP spectra, under both N_2 and O_2 purged conditions, are shown in Figure 3.12. The transient absorption spectra show an absorption band at 624 nm, which is much different from the absorption band at 500 nm from Figures 3.11 A and B. This difference in absorption shows that the absorption at 500 nm of Figure 3.11 is not due to the radical cation species of the precursor. The signals at 395 nm and 427 nm in Figures 3.12 A and B, are due to the radical anion of 1,4-DCB[87].

Excited triplet states and neutral radicals perform electron transfer to O_2, thereby creating the radical species. Both the lifetime and the spectrum are identical in both the N_2 purged and the O_2 purged systems, thus alternative assignments were excluded. The difference in intensities between Figures 3.12 A and B of the 395 nm and 427 nm signals may be due to the effect of oxygen preferentially quenching the radical anion of 1,4-DCB over the radical cation of **III-26**.

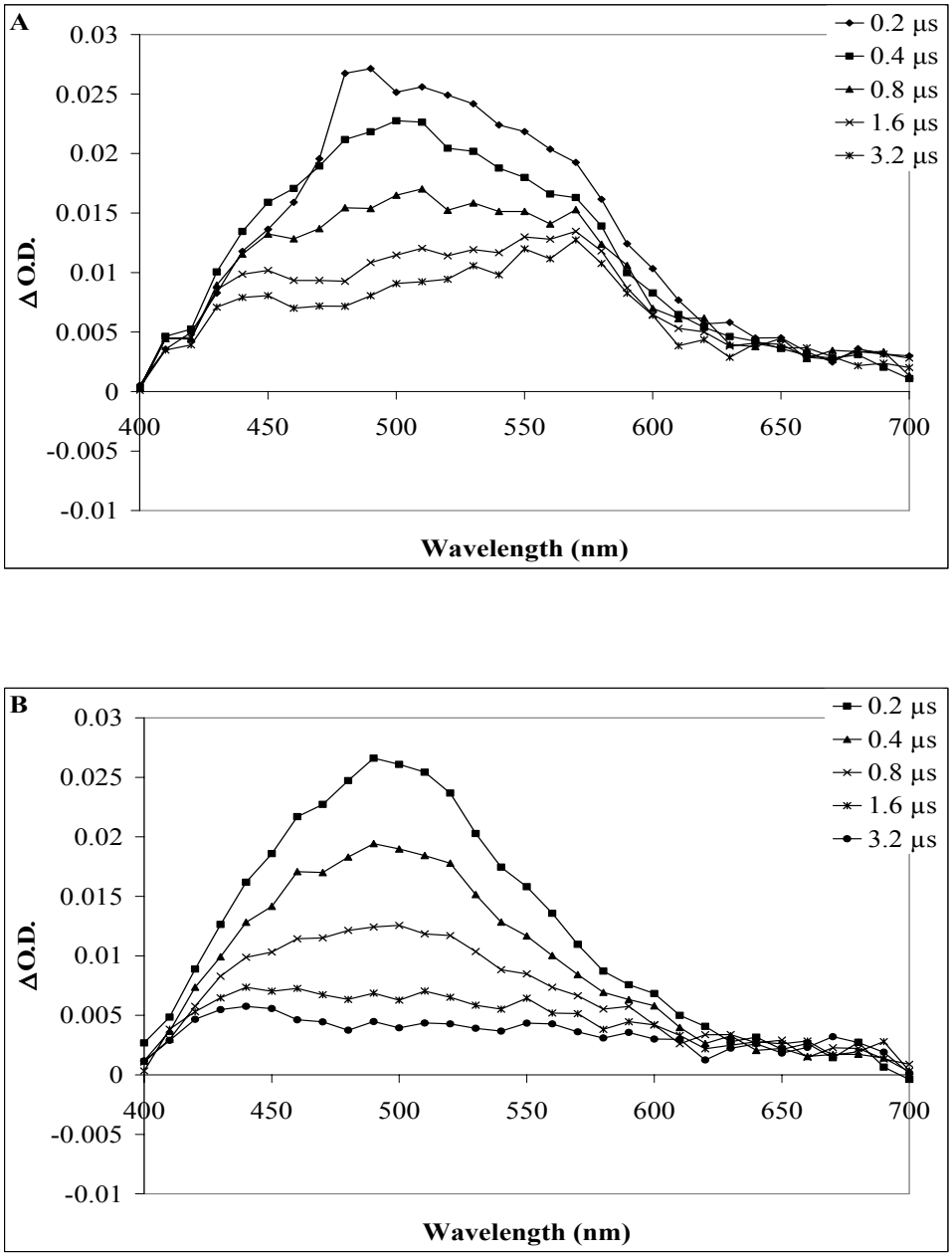


Figure 3.11: Transient UV-vis absorption spectra generated from LFP (355 nm, 4-6 ns, 8-10 mJ/pulse) of III-25 in CH_3CN taken 0.2, 0.4, 0.8, 1.6, and 3.2 μs after the laser pulse under (A) N_2 purge and (B) O_2 purge.

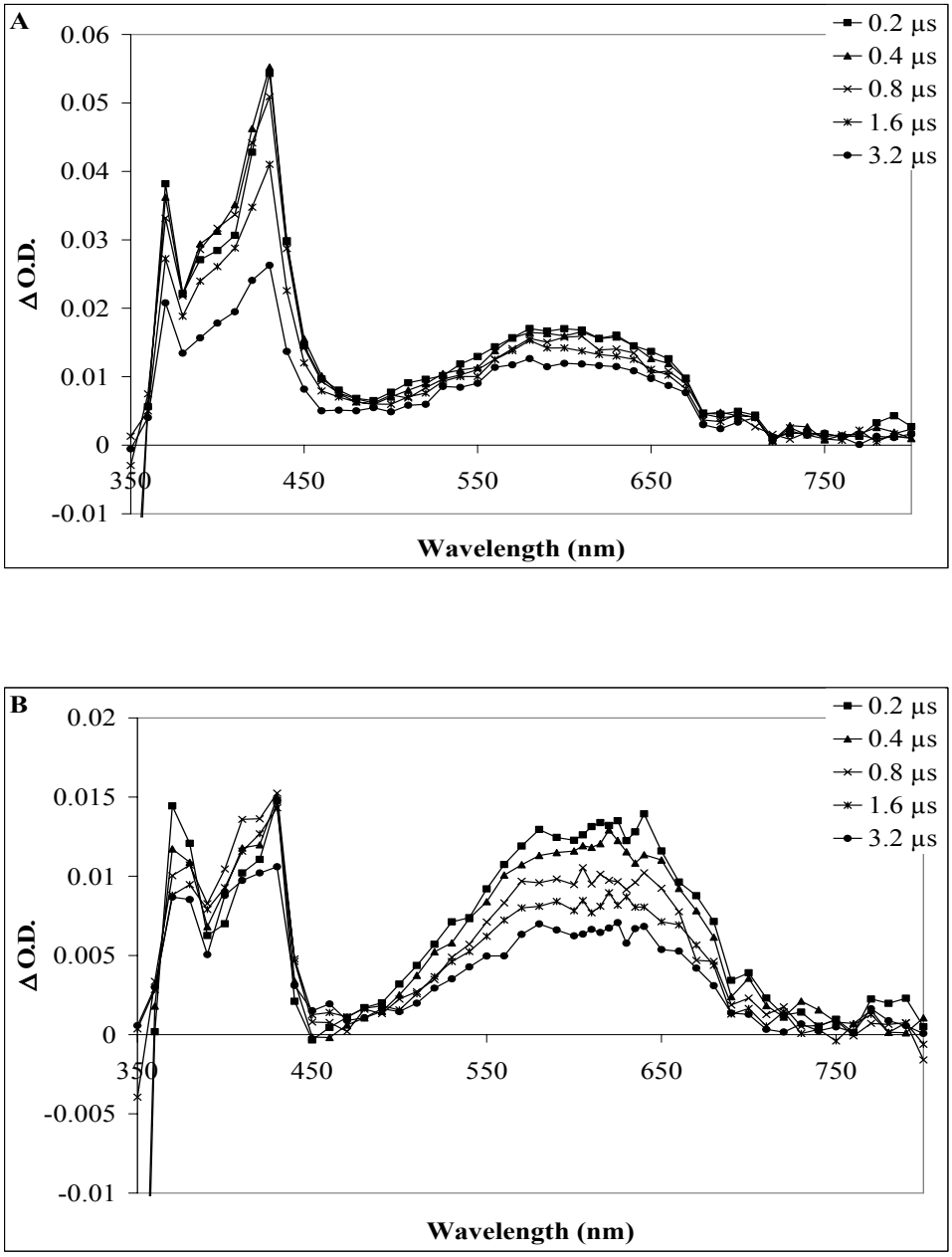
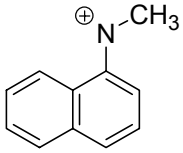


Figure 3.12: Transient UV-vis absorption spectra generated from LFP (355 nm, 4-6 ns, 8-10 mJ/pulse) of III-26 in the presence of 1,4-DCB in CH_3CN taken 0.2, 0.4, 0.8, 1.6, and 3.2 μs after the laser pulse under (A) N_2 purge and (B) O_2 purge.

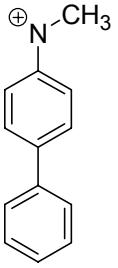
3.2.5: Trapping Rates

LFP was used to study the reactivity, lifetime, and trapping rates of *N*-methyl-*N*–(1-naphthyl)nitrenium ion (**III-5**) with different classes of nucleophiles (Table 3.4). Trapping rate constants were determined from the decay of the nitrenium ion's absorption band at 500 nm by varying the concentration of nucleophile. The observed transient absorption is due to the singlet arylnitrenium ion. This is supported by the fact that the lifetime of the transient species are diminished upon the addition of relatively weak nucleophiles, but not by oxygen.[80,88,89] In each case, the pseudo-first-order decay rates were found to depend in a linear fashion on the concentration of nucleophile. Previous studies have shown that anionic nucleophiles, such as chloride and azide, have trapping rate constants near the diffusion limit.[46,81]

To put these data in perspective, the trapping data for *N*-methyl-*N*–(1-naphthyl)nitrenium ion (**III-5**) and *N*-methyl-*N*-(4-biphenylyl)nitrenium ion (**III-35**) will be compared (Figure 3.13). These two systems are good for comparison since they are both highly conjugated π-systems and they differ in their substitution patterns.



III-5



III-35

Figure 3.13: Structures of *N*-methyl-*N*–(1-naphthyl)nitrenium ion (III-5) and *N*-methyl-*N*-(4-biphenylyl)nitrenium ion (III-35).

Table 3.4: Observed second-order trapping rate constants (k_{nuc}) of different nucleophiles with nitrenium ions III-5 and III-35, measured in $M^{-1}s^{-1}$.[81,90]

Nucleophile	(III-5) k_{nuc} ($M^{-1}s^{-1}$)	(III-35) k_{nuc} ($M^{-1}s^{-1}$)
Cl^- (TBACl)	$(2.76 \pm 0.02) \times 10^{10}$	$(7.7 \pm 1.2) \times 10^{9}$
H_2O	$(1.7 \pm 1.4) \times 10^{8}$	$(9.3 \pm 0.6) \times 10^{4}$
MeOH	$(1.6 \pm 0.3) \times 10^{9}$	$(3.8 \pm 1.1) \times 10^{5}$
EtOH	$(7.8 \pm 1.0) \times 10^{8}$	$(3.0 \pm 0.1) \times 10^{5}$
DABCO	$(8.7 \pm 0.9) \times 10^{9}$	$(8.8 \pm 0.3) \times 10^{9}$
n$BuNH_2$	$(1.0 \pm 0.2) \times 10^{10}$	$(5.8 \pm 0.2) \times 10^{9}$
t$BuNH_2$	$(1.0 \pm 0.07) \times 10^{10}$	$(3.8 \pm 0.6) \times 10^{9}$
Et_3N	$(1.1 \pm 0.05) \times 10^{10}$	$(3.0 \pm 0.4) \times 10^{9}$
Diisopropylamine	$(8.8 \pm 0.6) \times 10^{9}$	$(1.59 \pm 0.02) \times 10^{9}$
Aniline	$(9.6 \pm 1.6) \times 10^{9}$	$(1.18 \pm 0.2) \times 10^{10}$

Looking at the trapping rates for the *N*-methyl-*N*-(4-biphenylyl)nitrenium ion system (**III-35**), previously synthesized and studied by the Falvey group and similar to the work of McClelland lacking the *N*-methyl group, one can see that the less sterically hindered amines such as, *n*-butylamine (*n*$BuNH_2$), *t*-butylamine (*t*$BuNH_2$), and triethylamine (Et_3N), have rate constants around 1.0×10^{10} $M^{-1}s^{-1}$, which is near the diffusion limit of acetonitrile (2×10^{10} $M^{-1}s^{-1}$).[52,90,91] In contrast, the more hindered amines, such as, DABCO, diisopropylamine (*i*Pr_2NH), and aniline, have trapping rate constants that are slightly slower than those of the less hindered amines. The amine trapping rate constants are faster (at a rate 10^4 times faster) than those of the alcohols tested methanol (MeOH), ethanol (EtOH), and H_2O. It can be seen that water has the slowest trapping rate constant while EtOH is slightly faster. MeOH, the less hindered alcohol, has the fasted trapping rate constant of the alcohols at $(3.8 \pm 1.1) \times 10^5$ $M^{-1}s^{-1}$. If one were to extrapolate these trapping rate constants to neat 55 M H_2O, the lifetime of the nitrenium ion would decrease down to the nanosecond scale.

On the other hand, when comparing the rates of the *N*-methyl-*N*–(1-naphthyl)nitrenium ion system (**III-5**), one can see that there is no such dramatic difference between the rates of the amines (10^9 $M^{-1}s^{-1}$), the stronger nucleophiles and those of the alcohols (10^8 $M^{-1}s^{-1}$), the weaker nucleophiles. This minimal difference in trapping rates may be due to the substitution pattern of the nitrenium ion. The *N*-methyl-*N*–(1-naphthyl)nitrenium ion is a bicyclic system that is fused *ortho*- and *meta*- to the nitrenium ion nitrogen; therefore, the more reactive and preferred site of attack, the *para*-position, is unsubstituted. With the unsubstituted *para*- position, any nucleophile can effectively trap the nitrenium ion at a rate near the diffusion limit. Since the trapping rates are high, one can say that the nitrenium ion is short-lived thus, is less selective. With regards to *N*-methyl-*N*-(4-biphenylyl)nitrenium ion, the nitrenium ion is *para*-substituted with respect to the nitrenium ion nitrogen, which is the preferred site for nucleophilic attack. Since the *para*- position is substituted, the nitrenium ion is longer lived than if the *para*- position were unsubstituted. This difference in rate not only suggests that the nitrenium ion is long-lived but is selective as well. The combination of lifetime and selectivity supports the idea that *N*-methyl-*N*-(4-biphenylyl)nitrenium ion is a powerful carcinogen towards DNA.[5] On the other hand, the *N*-methyl-*N*–(1-naphthyl)nitrenium ion system may not be a powerful carcinogen since it is short-lived and may not be selective towards DNA. This idea is echoed in the testing of 4-biphenylamine and 4-biphenylacetamide, both of which have moderate carcinogenicity in the rat, but in the same experiment 3- and 2-biphenylacetamide appeared to be only weakly carcinogenic. This result reflects the general observation that aromatic amines

with a conjugated *para*-substituent in the same ring tend to be more carcinogenic than amines with this substituent in other positions or absent.[22]

If the trapping rate is small, the nitrenium ion is long-lived and may be a stronger carcinogen. Thus it follows that a shorter lived nitrenium ion has a higher trapping rate constant and thus is less carcinogenic. Miller stated that during the administration of the carcinogens to tissues, the electrophilic reactants encounter extracellular nucleophiles such as water and proteins before they enter the cell.[17] If a nitrenium ion has a large trapping rate with water or any other nucleophile, it would most likely be trapped before its entry into the cell and thus will not form adducts with DNA. Yet, if the nitrenium ion has a small trapping rate constant with water or other nucleophiles, it will have a longer lifetime and thus be able to enter the cell and form DNA adducts. Nitrenium ions that undergo slow reactions with solvent are selectively trapped by biologically relevant nucleophiles such as 2′-deoxyguanosine.[86] Such nitrenium ions as *N*-acetyl-*N*-(4-biphenylyl)- and *N*-acetyl-*N*-(2-fluorenyl)nitrenium ions are efficiently trapped by 2′-deoxyguanosine in aqueous solution so these ions could be responsible for the carcinogenic effects. As the nitrenium ions become more reactive with solvent, their reactions with nucleophiles such as 2′-deoxyguanosine must become less selective. The low efficiency of the trapping reactions may be related to the low carcinogenic potential.

One can see that substitution patterns, with respect to the nitrenium ion nitrogen, play an important role in the lifetime and selectivity. Monoaryl nitrenium ions with *para*- substituents are highly stabilized to the addition of nucleophiles whereas other monoaryl nitrenium ions without the *para*- substitution pattern have subnanosecond

lifetimes in solution. This may be why 4-biphenylamine is well known as a carcinogen and why it has been debated whether or not the 1-naphthylamine is also a carcinogen.[11]

3.2.6: Calculations

To examine these differences further, density functional theory (DFT) calculations (B3LYP/6-31G(d,p)) were carried out on two nitrenium ions as well as their hydroxide adducts. In *N*-methyl-*N*-(4-biphenylyl)nitrenium ion, the positive charge is strongly localized at the reactive center. Analysis of the charge distribution in both systems by using the generalized atomic polar tensor (GAPT) methods reveals a larger charge (+1.104) on the *para* carbon of the less reactive arylnitrenium ion than on the corresponding carbon of the more reactive *N*-methyl-*N*–(1-naphthyl)nitrenium ion (+0.670) as shown in Figure 3.14.

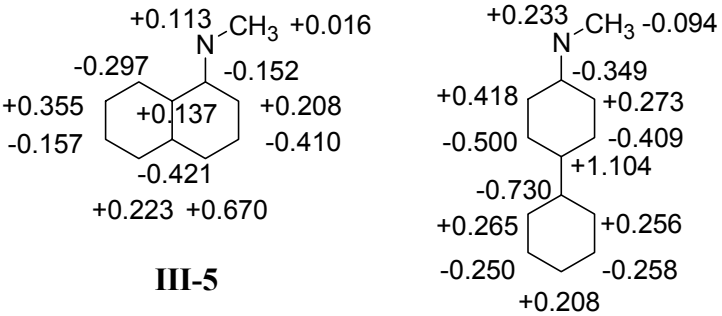
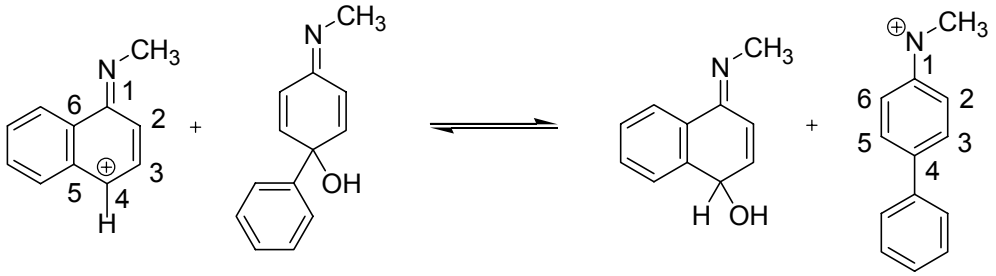


Figure 3.14: Generalized atomic polarization tensors (GAPT) charge distribution of III-5 and III-35.

In terms of geometries, *N*-methyl-*N*-(4-biphenylyl)nitrenium ion shows a higher degree of bond length alternation, which signifies more cyclohexadienyl cation character, than *N*-methyl-*N*–(1-naphthyl)nitrenium ion. In an ideal benzene structure, all of the ring carbon-carbon bond lengths would be nearly equal, whereas in a 1,4-cyclohexadienyl cation, the bond lengths between carbons 1 and 2, carbons 3 and 4, carbon 4 and 5, and carbons 6 and 1 would be longer than the bond lengths between carbons 2 and 3 and carbons 5 and 6. This is the case for both species where the difference between the average of the four long bonds and the average of the two short bonds for *N*-methyl-*N*–(1-naphthyl)nitrenium ion is 0.035 Å, whereas the difference for *N*-methyl-*N*-(4-biphenylyl)nitrenium ion is 0.088 Å (Scheme 3.20).

Scheme 3.20: Isodesmic reaction of III-5a and III-35 with water.



III-5a **III-36** **III-37** **III-35**

ΔE = -10.3 kcal/mol

At first glance, one may conclude that the difference in reactivity between these two nitrenium ion systems is based only on steric factors. Yet, there are other examples that show simple steric effects are not the complete explanation. McClelland and Ren used LFP to measure aqueous lifetimes for a series of 4′-substituted biphenylylnitrenium

ions.[45] In this series, the 4′-substitutent can be presumed to have a negligible steric effect on the addition reaction. What was observed as an electronic effect on the reactivity within this series of 4′-substituted biphenylylnitrenium ions that was dependent upon the 4′-substituent. A linear free energy analysis of these rate constants using the Hammett substituent parameter σ^+ gives a ρ value of +1.8 which demonstrates a measurable electronic effect. Also, the 4-methyl and 4-halo analogues of *N*-(4-biphenylyl)-*N*-methyl nitrenium ion are much more reactive than 4′-substituted biphenylnitrenium ions, even though these substituents exert comparable steric barriers to addition.

One way to explain the difference between *N*-methyl-*N*-(4-biphenylyl)nitrenium ion and *N*-methyl-*N*–(1-naphthyl)nitrenium ion is to take into account both of the nitrenium ions and their adducts with water (Scheme 3.20). One of the stabilizing effects in *N*-methyl-*N*-(4-biphenylyl)nitrenium ion is the conjugation afforded to it by the substitution of the phenyl ring to the arylnitrenium ion ring. Upon addition of a nucleophile at the 4-position, the conjugation between the two rings is lost. The carbon-carbon bond joining the phenyl ring to the arylnitrenium ion center increases by almost 0.1 Å upon addition of water. The phenyl ring also twists from a nearly coplanar dihedral of 20º in the nitrenium ion to being nearly perpendicular in the water adduct (Figure 3.15). This change in dihedral angle has been observed via calculations of analogous systems.[12,50] In contrast to this large reorganization by the phenyl ring, *N*-methyl-*N*–(1-naphthyl)nitrenium ion does not reorganize to nearly the same extent upon addition of water. In the *N*-methyl-*N*–(1-naphthyl)nitrenium ion system, the major change seems to be the restoration of aromaticity to the fused benzene ring (Figure 3.16).

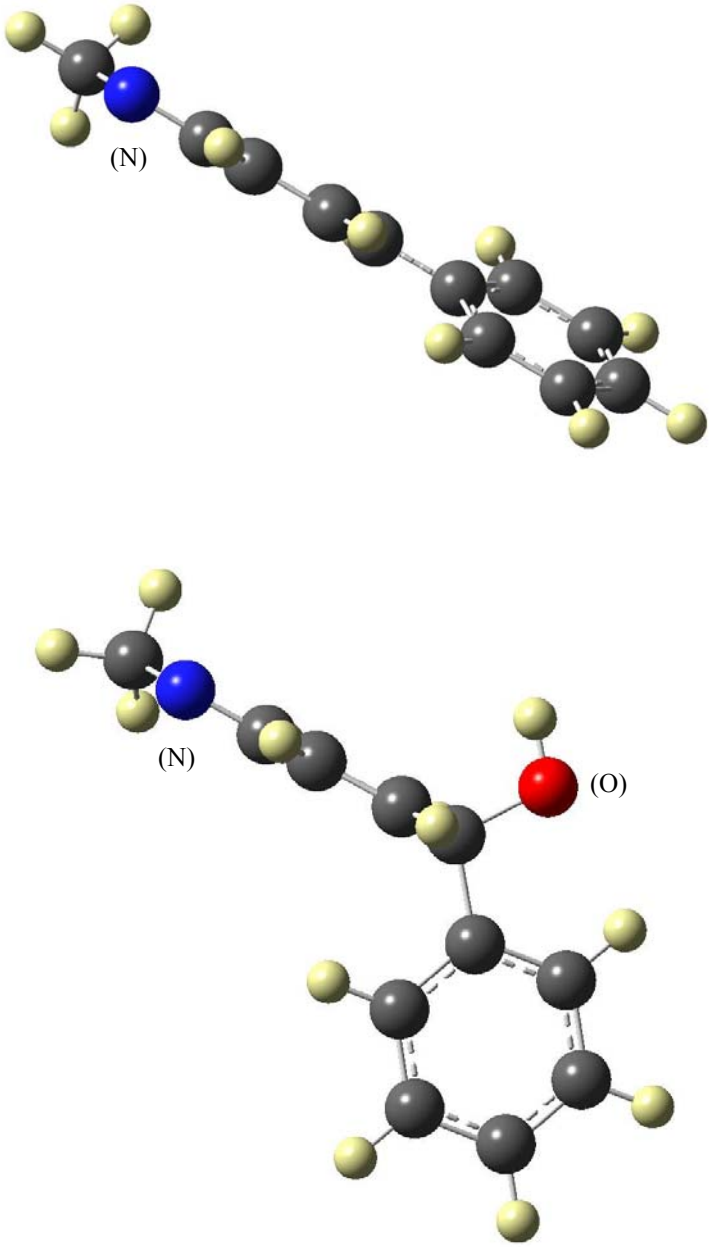


Figure 3.15: Calculated geometries of III-35 and III-36 illustrating the nearly coplanar dihedral of 20° in the nitrenium ion to being nearly perpendicular in the water adduct.

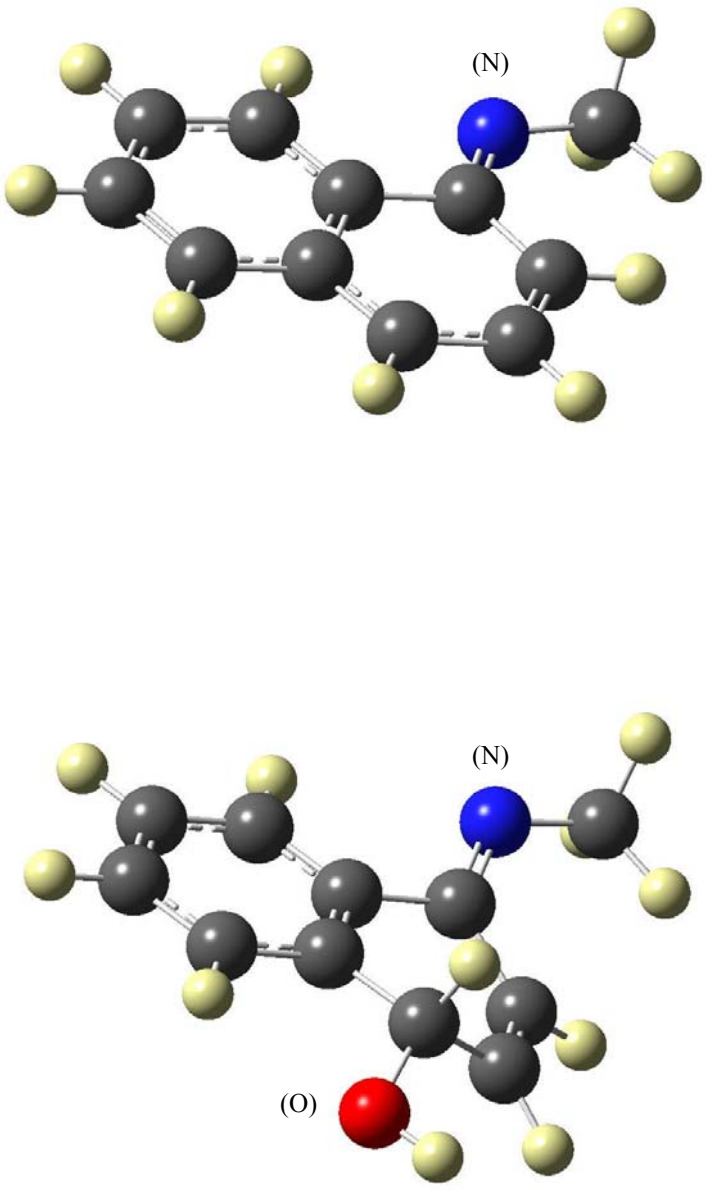
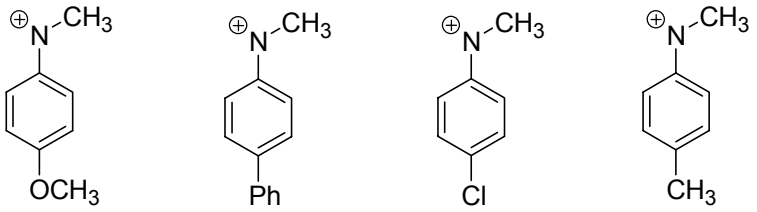


Figure 3.16: Calculated geometries of III-5a and III-37 illustrating *N*-methyl-*N*–(1-naphthyl)nitrenium ion system, the major change being the restoration of aromaticity to the fused benzene ring.

Novak and Lin performed a series of experiments to determine the azide/water selectivity ratio (S) for a large number of arylnitrenium ions.[50] Their studies generated the nitrenium ions in aqueous solutions and the selectivity ratio was derived from product analysis data. S is a reasonable substitute for the rate constant for the addition of water to the nitrenium ions if it is assumed that the azide trapping is diffusion limited for the series that is being studied. Their values correlated well with theoretical (HF/3-21G//(6-31G*)) relative hydroxide addition energies, derived from a series of isodesmic hydroxide transfer reactions. DFT (B3LYP/6-31G(d,p)) calculations were carried out on both *N*-methyl-*N*-(4-biphenylyl)nitrenium ion and *N*-methyl-*N*–(1-naphthyl)nitrenium ion, as well as the *para*- adducts of water. The energies from these computations agree reasonably well with those reported by Novak and Lin.[50] For instance, the B3LYP ΔE value for the isodesmic reaction involving *N*-methyl-*N*–(1-naphthyl)nitrenium ion and *N*-methyl-*N*-(4-biphenylyl)nitrenium ion is -10.3 kcal/mol, which is similar to the HF value of -10.8 kcal/mol. In the latter case, the *N*-substituent is an acetyl moiety while in the former case, the *N*-substituent is a methyl moiety, which may incur this difference. Therefore, both DFT and HF agree that *N*-methyl-*N*–(1-naphthyl)nitrenium ion derivatives are less stable to the addition of water than are the *N*-methyl-*N*-(4-biphenylyl)nitrenium ion derivatives. The loss of aromaticity upon the formation of stable adducts upon addition of water may be due to the fact that hydroxide is a poor leaving group.[13] Hence, the reaction would not be reversible and once the hydroxyl adduct is formed, aromaticity would not be able to be restored.

3.2.7: Trapping Rates of Comparable Nitrenium Ions

Aryl nitrenium ions generally have short lifetimes in solution. It is reasonable to suspect that increasing the π-conjugation of the system would stabilize the nitrenium ion, prolonging its lifetime. To test this hypothesis, the effects of benzannulation on the lifetime and reactivity of the nitrenium ion was studied. As previously stated, both the *N*-methyl-*N*-(4-biphenylyl)nitrenium ion and *N*-methyl-*N*–(1-naphthyl)nitrenium ion systems are highly conjugated π systems. One might think that this high degree of conjugation may aid in the stabilization of the nitrenium ion intermediate, as in the case of carbocations. Yet, it has been seen that this is not the case. McClelland has stated that carbocations and nitrenium ions have different reactivities and that arylcarbocations, in general, react at the external carbon, so that the product is aromatic.[40] This is in contrast to nitrenium ions which generally reacts at the ring *para*- position (Figure 3.6). It can be seen in Table 3.5 and Figure 3.17 that increasing the conjugation of the system or inducing a shift in the wavelength of maximum absorption to a longer wavelength (bathochromic shift) does not have the stabilization effect that one would expect.



III-38 **III-35** **III-39** **III-40**

Figure 3.17: Structures of *N*-methyl-*N*-(4-methoxyphenyl)-, -(4-biphenyl)-, (4-chlorophenyl)- and, -(4-methylphenyl)nitrenium ions.

Table 3.5: Observed second order trapping rate constants (k_{nuc}) of H_2O with nitrenium ions III-38, III-35, III-39, III-40, III-5 and their respective λ_{max} (nm).[81]

	4-Methoxy (III-38)	4-Phenyl (III-35)	4-Chloro (III-39)	4-Methyl (III-40)	1-Naphthyl (III-5)
k_{H2O} ($M^{-1}s^{-1}$)	(1.3±0.1) x 10^4	(9.3±0.6) x 10^4	(8.9±2.5) x 10^6	(2.32±0.08) x10^7	(1.7 + 1.4) x 10^8
λ_{max} (nm)	320	480	350	325	500

Five different nitrenium ions are compared with their trapping rates with H_2O and their wavelength of maximum absorption (λ_{max}). As the trapping rates increase from 10^4 $M^{-1}s^{-1}$ for the *N*-methyl-*N*-(4-chlorophenyl)nitrenium ion (**III-39**) to 10^8 $M^{-1}s^{-1}$ for the *N*-methyl-*N*–(1-naphthyl)nitrenium ion (**III-5**), we can see that their λ_{max} do not correlate. Their λ_{max} are sporadic and jump from 320 nm (**III-38**) to 480 nm (**III-35**) then back down to 350 nm (**III-39**) and 325 nm (**III-40**), until finally increasing to 500 nm for **III-5**. One can also conclude from Table 3.5 that increasing the conjugation does not exactly correlate to the lifetime of the intermediate. This trend is in agreement with previous reports of a lack of correlation of the trapping rates with substituent σ^+ values.[92] In the case of **III-38** and **III-35**, the *N*-methyl-*N*-(4-methoxyphenyl)nitrenium ion and *N*-methyl-*N*-(4-biphenylyl)nitrenium ion groups in the *para*- position can aid in the stabilization of the nitrenium ion, and the intermediate is longer lived in water than compounds **III-39** and **III-40** with chlorine and methyl in the *para*- position. The *N*-methyl substituted nitrenium ion systems show that the methyl group may help to stabilize the electron deficient nitrogen center through hyperconguation effects. Other nitrenium ion systems without the *N*-methyl substituent would have a shorter lifetime due to electronic and hyperconguation effects. Therefore, the trapping rate for these systems

with only an acetyl or a hydrogen atom should be much faster in the presence of H_2O due to electron donation abilities.

It is interesting to compare a series of 4-substituted arylnitrenium ions as those shown above. In this series (Table 3.6), in combination with Table 3.4, the reactivity of the 4-substituted aryl nitrenium ion systems with weak nucleophiles is shown to be in the order of 4-chloro ~ 4-methyl > 4-phenyl > 4-methoxy.

Table 3.6: Observed second-order trapping rate constants (k_{nuc}) of different nucleophiles with nitrenium ions III-39, III-40, and III-38 measured in $M^{-1}s^{-1}$.[81,90]

Nucleophile	4-Chloro (III-39) k_{nuc} ($M^{-1}s^{-1}$)	4-Methyl (III-40) k_{nuc} ($M^{-1}s^{-1}$)	4-Methoxy (III-38) k_{nuc} ($M^{-1}s^{-1}$)
Cl^- (TBACl)	$(2.8 \pm 0.3) \times 10^{10}$	$(2.3 \pm 0.2) \times 10^{10}$	$(1.7 \pm 0.1) \times 10^{10}$
H_2O	$(8.9 \pm 2.5) \times 10^{6}$	$(2.32 \pm 0.08) \times 10^{7}$	$(1.3 \pm 0.1) \times 10^{4}$
MeOH	$(7.0 \pm 1.0) \times 10^{7}$	$(6.0 \pm 1.6) \times 10^{7}$	$(3.4 \pm 0.8) \times 10^{4}$
EtOH	$(2.6 \pm 0.5) \times 10^{7}$	$(2.0 \pm 0.1) \times 10^{7}$	$(1.1 \pm 0.2) \times 10^{4}$
DABCO	$(8.3 \pm 0.3) \times 10^{9}$	$(6.6 \pm 0.6) \times 10^{9}$	$(1.97 \pm 0.09) \times 10^{9}$
*n*BuNH$_2$	$(7.2 \pm 0.4) \times 10^{9}$	$(8.6 \pm 0.7) \times 10^{9}$	$(3.8 \pm 0.2) \times 10^{9}$
*t*BuNH$_2$	$(3.1 \pm 0.06) \times 10^{10}$	$(1.6 \pm 0.2) \times 10^{10}$	$(6.3 \pm 2.6) \times 10^{8}$
Et_3N	$(4.4 \pm 0.3) \times 10^{9}$	$(8.5 \pm 1.1) \times 10^{9}$	$(3.8 \pm 0.6) \times 10^{8}$
Diisopropylamine	$(2.72 \pm 0.04) \times 10^{9}$	$(3.0 \pm 0.1) \times 10^{9}$	$(4.7 \pm 1.6) \times 10^{7}$
Aniline	$(6.8 \pm 0.7) \times 10^{9}$	$(1.1 \pm 0.1) \times 10^{10}$	$(1.88 \pm 0.06) \times 10^{9}$
Pyridine	$(1.1 \pm 0.04) \times 10^{10}$	$(7.9 \pm 0.4) \times 10^{9}$	$(1.90 \pm 0.06) \times 10^{9}$

These four nitrenium ions react rapidly with chloride ions, but vary when trapped by neutral oxygen nucleophiles. As can be seen, both the *N*-methyl-*N*-(4-methoxyphenyl)nitrenium ion and *N*-methyl-*N*-(4-biphenylyl)nitrenium ion are relatively slow to react with water with trapping rate constants on the order of 10^4 $M^{-1}s^{-1}$ whereas the *N*-methyl-*N*-(4-chlorophenyl)nitrenium ion and *N*-methyl-*N*-(4-methylphenyl)nitrenium ion are on the order of 10^7 $M^{-1}s^{-1}$. This reactivity trend is in

agreement with previous studies of the effect of ring substituents on arylnitrenium ions. For example, the 4-phenyl group stabilizes the arylnitrenium ions to a greater extent than it stabilizes an arylcarbenium ion which illustrates that substitutent effects on aryl cations cannot be directly applied to nitrenium ions.[93] Also, the 4-methyl group greatly stabilizes arylcarbenium ions, yet the same type of stabilization is not seen and induces greater activity than the 4-phenyl group and is about as reactive as the 4-chloro group. This shows how *para*-position π–donor substituents have unusually large stabilizing effects on nitrenium ions.

Although the extent of 4-iminocyclohexa-2,5-dienyl cation character depends on the substituent in the *para*-position as well as the *N*-substituent, which can be seen in the C=C frequency and C-N bond lengths. The 4-methoxy derivative shows the highest frequency indicating that this strongly π–electron-donating substituent imparts more quinoidal character and the 4-chloro derivative shows the lowest frequency, suggesting that it possesses the least quinoidal character. The computed structures show significant bond length alternation in the phenyl rings, shortened C-N bond lengths, and substantial positive charge delocalization into the phenyl rings. All of these effects are more pronounced with increasing π-donating character of the ring substituent.[52] Also shown was that 4-biphenylylnitrenium ion has more iminocyclohexadienyl character than *N*-methyl-*N*-(4-biphenylyl)nitrenium ion.[53] This may be another factor in determining the reactivity of arylnitrenium ions as well as their carcinogenicity.

Amines were used as nucleophiles since amines are abundant in biomolecules. Generally, amines react with arylnitrenim ions near the diffusion limit and is demonstrated with *N*-methyl-*N*-(4-methoxyphenyl)nitrenium, *N*-methyl-*N*-(4-

chlorophenyl)nitrenium ion and *N*-methyl-*N*-(4-methylphenyl)nitrenium ion. But as can been seen from Table 3.6, there is a deviation from this trend with the least reactive nitrenium ion tested, which is the *N*-methyl-*N*-(4-methoxyphenyl)nitrenium ion. With this derivative, the differences in the classes of amines are observed through their trapping rate constants. For the primary amine, 1-butylamine, and the cyclic diamine 1,4-diazabicyclo[2.2.2]octane (DABCO), the trapping rate constants are near the diffusion limit. This is also true for the aromatic amine, aniline, and the nitrogen heterocycle, pyridine, whose trapping rate constants did not differ greatly from the diffusion limit. Although these traps also absorb light at 266 nm, the concentration was kept low enough that the photo-precursors absorbed greater than 90% of the excitation energy. The significant difference can be seen with the sterically hindered amines, such as *tert*-butylamine, diisopropylamine, and triethylamine, whose trapping rate constants slowed to the scale of $10^7 - 10^8$ $M^{-1}s^{-1}$. This suggests that for typical trapping between amines and arylnitrenium ions, these addition reactions will show little selectivity.

A link between a series of polycyclic and monocyclic aromatic amines and their carcinogenicities was studied by Novak by a correlation of the nitrenium ion's azide/solvent selectivies with mutagenicities by testing against *Salmonella typhimurium* TA 98 and TA 100.[84] Quantitative carcinogenicity data are difficult to obtain, but quantitative mutagenicity data from Ames tests of the amine are readily available. A limited correlation of mutagenicity data with azide/solvent selectivity data for polycyclic amines can be demonstrated. Polycyclic amines do show reasonable correlations of log(mutagenicity) (log(m)) with log(S). The mutagenicity data are expressed in terms of log[(histidine revertants)/(nmol of amine)] for two *Salmonella typhimurium* strains (TA

98 and TA 100) commonly used in Ames tests.[94] Log(S) is calculated from the azide/solvent selectivity (S), which was estimated from a fit of the solvent derived products and azide derived products.

There is a good correlation of log(m) with log(S) for both TA 98 TA 100 among the five polycyclic amines. The correlation is reasonable because ions with long lifetimes in aqueous solution (large log(S)) should be able to react more selectively with nucleophilic sites on DNA. This is definitely true for reactions with monomeric deoxyguanosine.[43,61] Of the five polycyclic ions that were tested by Novak, four had positive values for log(S), as shown in Table 3.7. Of the four polycyclic amines with positive values for log(S), three of the polycyclic amines tested, all well known carcinogens, had values of log(S) > 2.00. It is surprising that 2-naphthylamine does not have a greater vale of log(S), but a distinct difference can be seen between 1-naphthylamine, which has a negative value of log(S), and the other four polycyclic amines. The negative value of log(S) may show that 1-naphthylamine contains inherently different properties based on electronics or substitution patterns. If other factors do not interfere, the more selective ions should generate a higher yield of DNA-carcinogenic adducts and lead to a greater level of mutagenicity.

Table 3.7: Mutagenicity and azide/solvent selectivity for aromatic amines.[84]

Amine	Log(S)	Log(m) TA 98	Log(m) TA 100
2-fluorenylamine	4.77	1.75 ± 0.18	1.44 ± 0.29
4-biphenylamine	2.97	0.72 ± 0.27	1.23 ± 0.27
4-stilbenylamine	2.45	0.46 ± 0.30	1.10 ± 0.60
1-naphthylamine	-0.15	-0.65 ± 0.22	-0.34 ± 0.35
2-naphthylamine	0.18	0.14 ± 0.33	0.83 ± 0.19
4-ethoxyphenylamine	2.73	-2.3 ± 0.2	-0.6 ± 0.2
4-chlorophenylamine	0.46	-2.5 ± 0.1	-1.5 ± 0.2
phenylamine	-0.15	< -3.3	< -2.7

This trend is reflected in Tables 3.4 and 3.7 by comparing the reactivity of 4-methoxyphenyl- (as it relates to 4-ethoxyphenyl-), 4-biphenylyl- , and 4-chlorophenylnitrenium ions to their log(S) values. From the trapping rate constants, it was determined that the reactivity of the 4-substituted aryl nitrenium ion systems with weak nucleophiles was in the order of 4-chloro > 4-phenyl > 4-methoxy. From Table 3.7 4-chloro has a log(S) value of 0.46 while both 4-ethoxy, (comparable to 4-methoxy), and 4-biphenylyl have much larger log(S) values of 2.73 and 2.97 respectively. These two nitrenium ions with log(S) values greater than 2.00 were also slowly trapped by water, it suggests that these two nitrenium ions are also selective. These results suggest that nitrenium ion selectivity is one of several factors that determine the mutagenicity of aromatic amines.

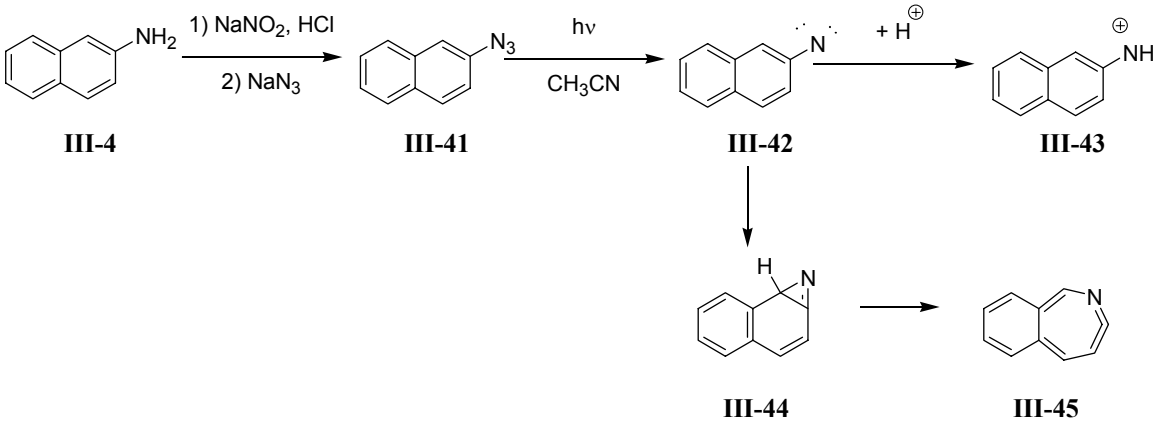
Monocyclic nitrenium ions are considerably less mutagenic than their analogues that generate polycyclic ions of similar log(S). It could be due to different transport properties for the more hydrophilic monocyclic amines and their metabolites, to different rates of metabolism, to faster repair rates for the DNA adducts of the less bulky amine, or to smaller genetic effects of the less bulky adducts. Also, there can be considerable differences in the efficiency of the *N*-oxidation and subsequent esterification for individual amines.

3.3: Attempted Observation of *N*-methyl-*N*-(2-naphthyl)nitrenium ion

With extensive data collected for the *N*-methyl-*N*-(1-naphthyl)nitrenium ion system, attention was turned to the more carcinogenic isomer, the *N*-methyl-*N*-(2-naphthyl)nitrenium ion system. 2-Naphthyl azide was synthesized in the same manner as

the 1-naphthyl azide system (Scheme 3.21). 2-Naphthylamine was nitrosated with sodium nitrite in the presence of hydrochloric acid. The second step of this one-pot synthesis was the addition of sodium azide which generated 2-naphthyl azide.

Scheme 3.21: Synthetic and photolytic reaction pathways of 2-naphthyl azide.



The LFP of 2-naphthyl azide in CH_3CN, with H_2SO_4 as the proton source, produced a broad transient absorption band from 370 – 500 nm under N_2 and O_2 (Figure 3.18A & B). When the photolysis was performed in CH_3CN alone, with no proton source, the observed signal was broad and ranged from 370 – 500 nm (Figure 3.19), did not differ significantly from those generated in protic solution (Figure 3.18). These signals have been previously observed and are attributed to the well-known ring expansion intermediates from the nitrene.[74,77,95]

Much like in the case of 1-naphthyl azide, the transient spectra of 2-naphthyl azide suggest that unimolecular reactions of the singlet nitrene, including cyclization and intersystem crossing, are faster than the competing proton transfer. Since the protonation of the nitrene pathway did not produce the desired nitrenium ion, another precursor to generate the nitrenium ion was used.

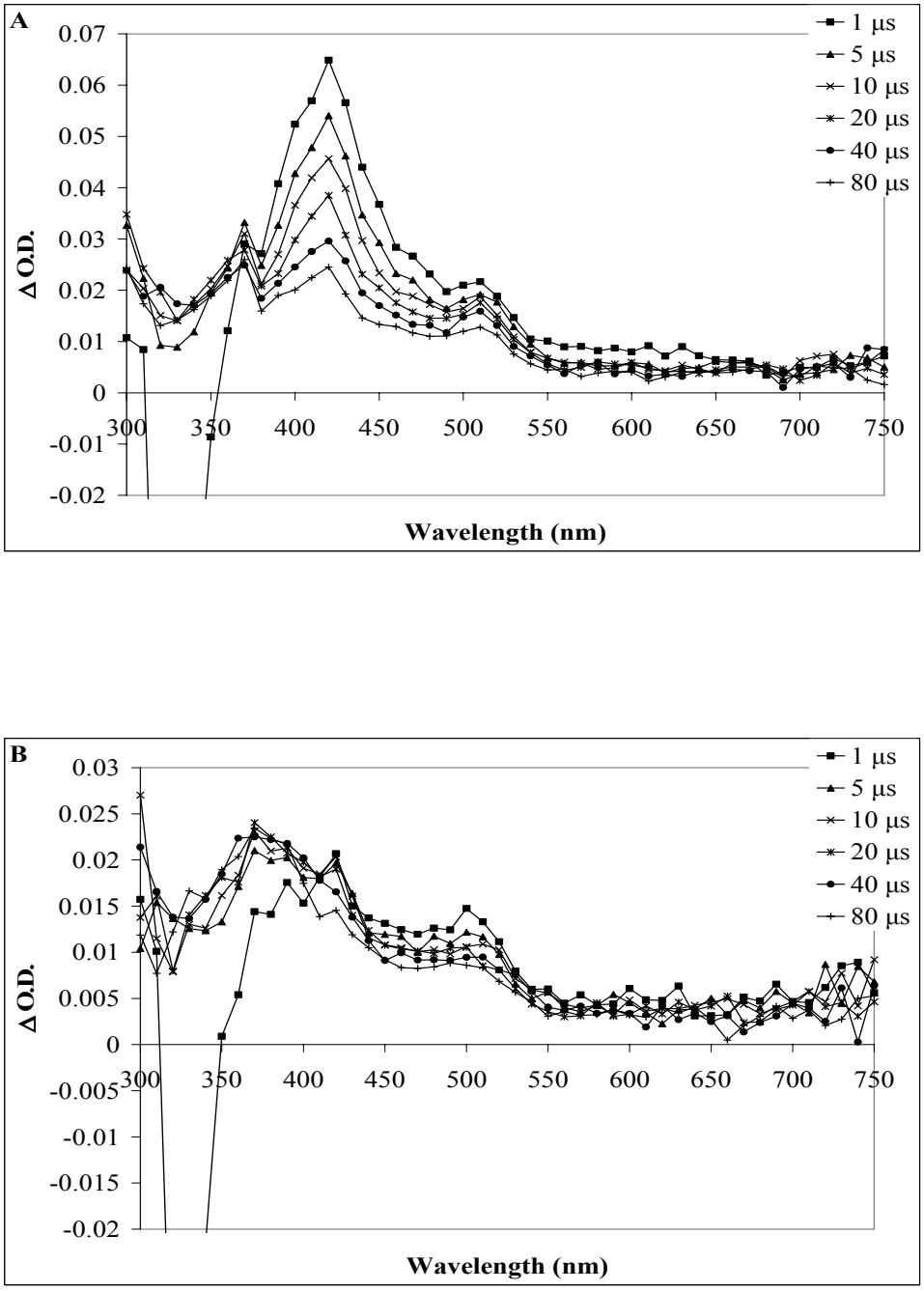


Figure 3.18: Transient UV-vis absorption spectra generated from LFP (266 nm, 4-6 ns, 3-5 mJ/pulse) of III-41 in CH_3CN and H_2SO_4 taken 1, 5, 10, 20, 40, and 80 μs after the laser pulse under (A) N_2 purge and (B) O_2 purge.

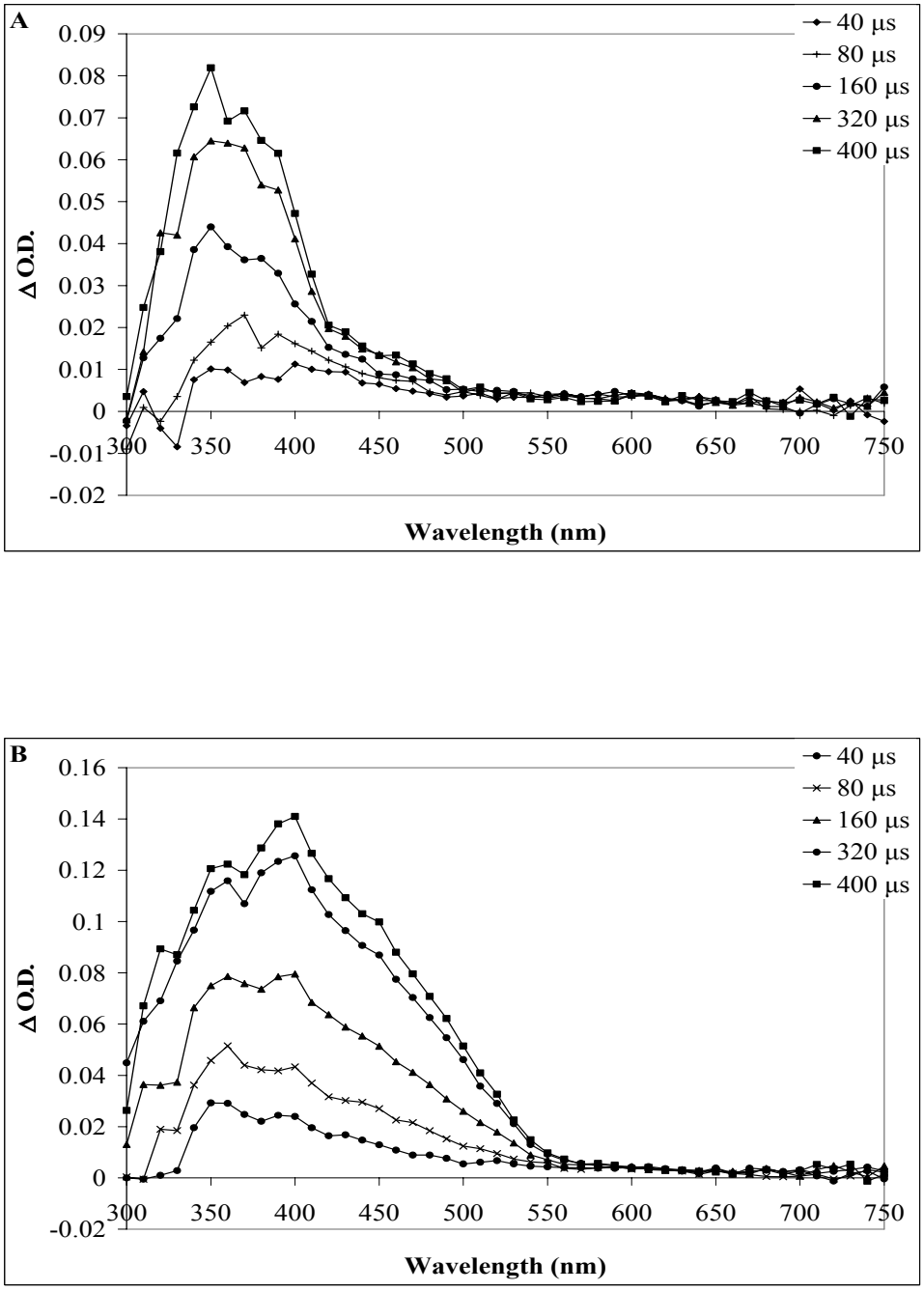
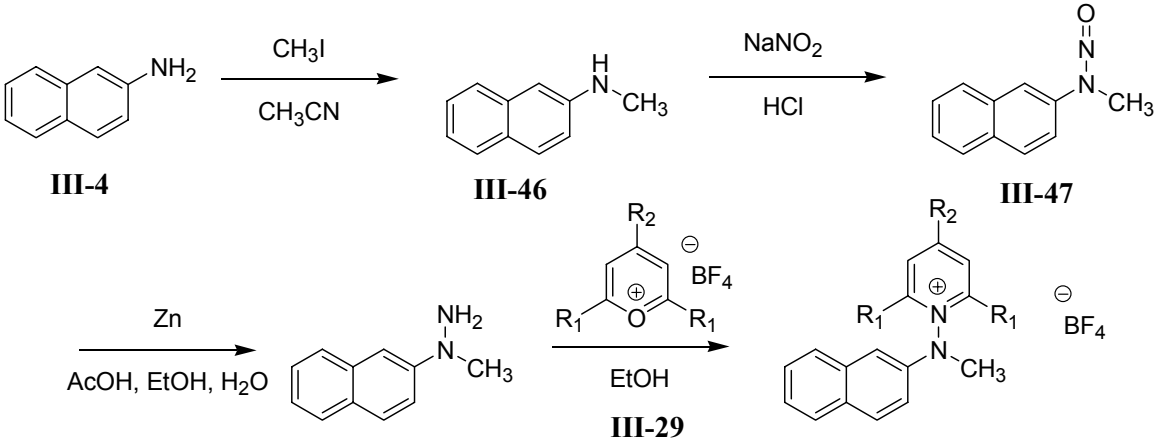


Figure 3.19: Transient UV-vis absorption spectra generated from LFP (266 nm, 4-6 ns, 3-5 mJ/pulse) of III-41 in CH_3CN taken 40, 80, 160, 320, and 400 μs after the laser pulse under (A) N_2 purge and (B) O_2 purge.

To parallel the 1-(*N*-methyl-*N*-(1-naphthyl)amino)-2,4,6-trimethylpyridinium tetrafluoroborate system, 1-(*N*-methyl-*N*-(2-naphthyl)amino)-2,4,6-trimethylpyridinium tetrafluoroborate was synthesized via the same scheme used for LFP studies (Scheme 3.22). *N*-Methyl-2-naphthylamine (**III-46**) was synthesized by direct methylation of 2-naphthylamine. The secondary amine (**III-46**) was then nitrosated with a sodium nitrite solution in the presence of hydrochloric acid to give *N*-methyl-*N*-nitroso-2-naphthylamine (**III-47**).

Scheme 3.22: Synthesis of 1-(*N*-methyl-*N*-(2-naphthyl)amino)-2,4,6-trimethylpyridinium tetrafluoroborate and derivatives.



The latter was then reduced in the presence of Zn and AcOH to generate the 1-methyl-1-(2-naphthyl)hydrazine intermediate (**III-48**). This reduction step is particularly sensitive to the reaction conditions such that compound (**III-46**), resulting from over-

reduction, is formed along with the desired hydrazine (**III-48**). Purification of this mixture was not performed due to the instability of the hydrazine. Instead, a substoichiometric amount, as determined by ^{1}H-NMR, of freshly prepared 2,4,6-trimethylpyrylium tetrafluoroborate (**III-29a**) was added *in situ* to the reduction mixture, yielding the final pyridinium salt (**III-49**). It is important that excess pyrylium salt (**III-29 a-d**) is avoided as it is very difficult to separate the pyrylium salt from the pyridinium salt. The pyridinium salt was then recrystallized, first from ethanol, then from methanol, and characterized by the customary spectroscopic methods (^{1}H-NMR, ^{13}C-NMR, and HRMS).

To rule out the possibility of observing the radical cation of *N*-methyl-2-naphthylamine (**III-46**), it was irradiated in the presence of 1,4-DCB. The excited state electron transfer from the amine to 1,4-DCB is expected to generate the radical cation of the amine and the radical anion of 1,4-DCB. The resulting LFP spectra are shown in Figures 3.20 A and B. The transient absorption spectra show an absorption band ranging form 450 – 570 nm and the signal is assigned to the radical cation of *N*-methyl-2-naphthylamine. The absorption signals at 395 and 427 nm are due to the radical anion of 1,4-DCB. The difference in the intensities between Figures 3.20 A and B of the 395 nm and 427 nm signals are due to the preferential quenching of the radical anion of 1,4-DCB over the radical cation of *N*-methyl-2-naphthylamine by oxygen.

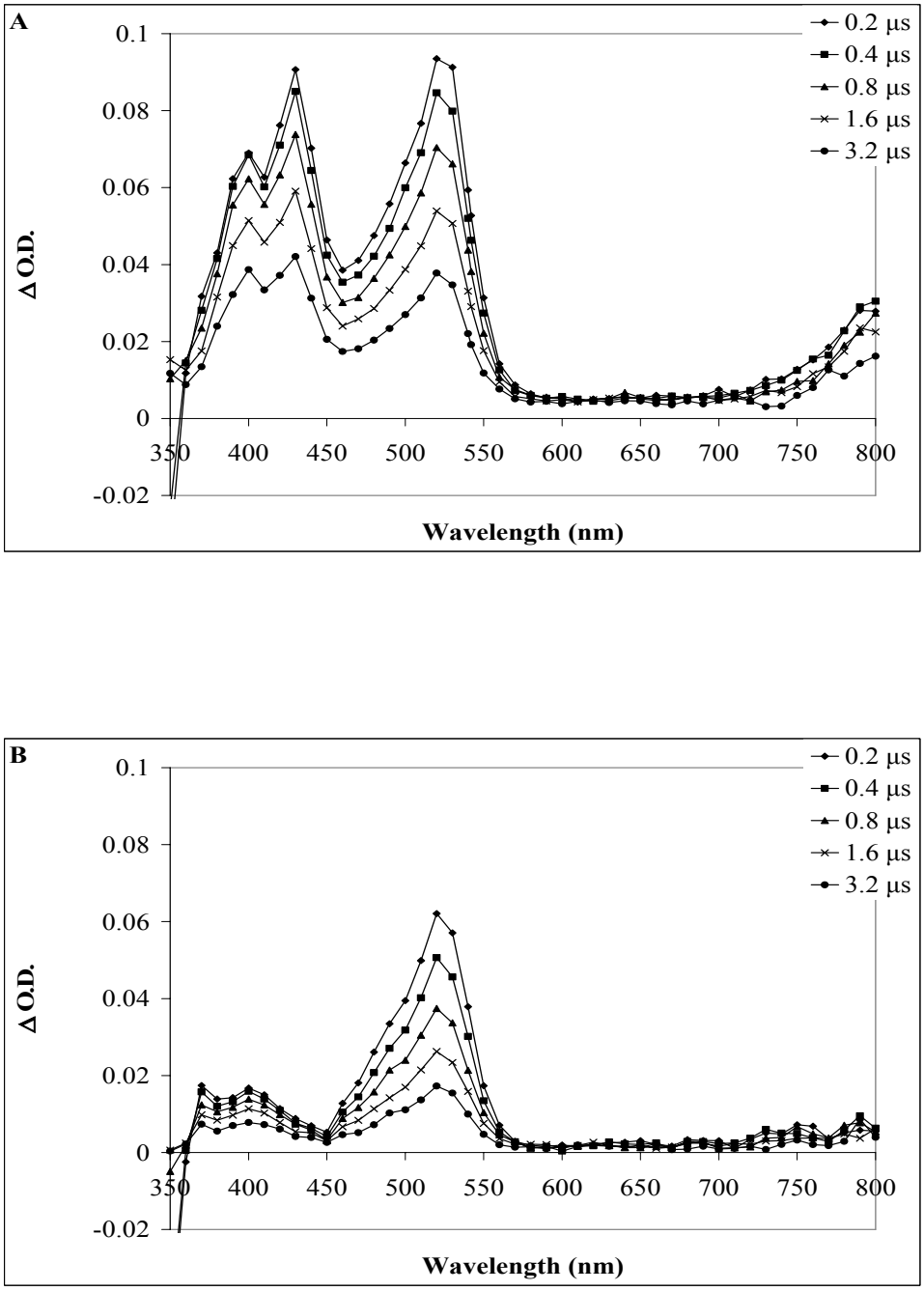


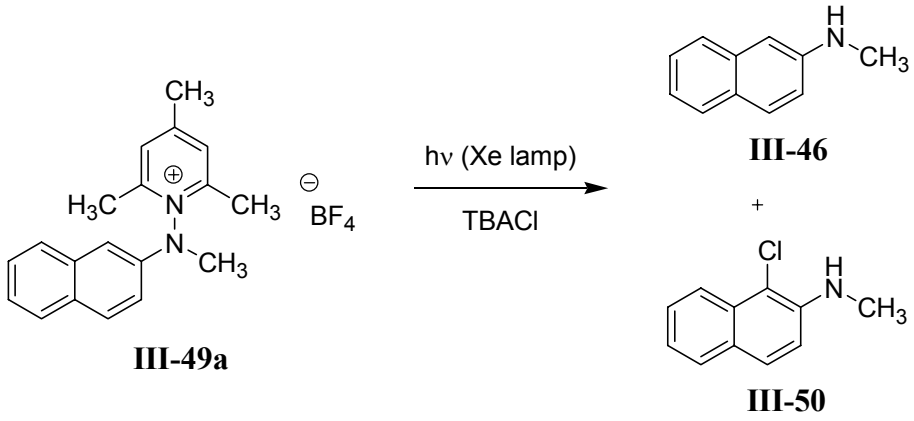
Figure 3.20: Transient UV-vis absorption spectra generated from LFP (355 nm, 4-6 ns, 8-10 mJ/pulse) of III-46 in the presence of 1,4-DCB in CH_3CN taken 0.2, 0.4, 0.8, 1.6, and 3.2 μs after the laser pulse under (A) N_2 purge and (B) O_2 purge.

Analogous to previous studies, it was expected that LFP of 1-(*N*-methyl-*N*-(2-naphthyl)amino)-2,4,6-trimethylpyridinium tetrafluoroborate (**III-49a**) would provide *N*-methyl-*N*-(2-naphthyl)nitrenium ion (**III-6**). LFP (355 nm, 4-6 ns, 8-10 mJ/pulse) of 1-(*N*-methyl-*N*-(2-naphthyl)amino)-2,4,6-trimethylpyridinium tetrafluoroborate (**III-49a**) in CH_3CN gave no reproducible transient absorption spectrum. Therefore, the excitation wavelength was changed from 355 nm to 266 nm for LFP. LFP (266 nm, 4-6 ns, 3-4 mJ/pulse) of 1-(*N*-methyl-*N*-(2-naphthyl)amino)-2,4,6-trimethylpyridinium tetrafluoroborate (**III-49a**) in CH_3CN also yielded no reproducible transient absorption spectrum. When the photolysis using excitation at 355 nm or 266 nm produced no observable signal, derivatives were synthesized using 2,6-dimethyl-4-(phenyl)pyrylium tetrafluoroborate (**III-29b**) and 2,6-dimethyl-4-(biphenylyl)pyrylium tetrafluoroborate (**III-29c**) salts (Scheme 3.22) instead of the 2,4,6-trimethylpyrlium tetrafluoroborate salt.[96] These derivatives were synthesized in order to increase their conjugation and thus increasing the wavelength of absorption of their chromophore. In doing so, the 355 nm excitation beam, which is more stable than 266 nm excitation, could be employed and thus yield better transient signals. Yet, this was not the case because under the experimental parameters, LFP of these two derivatives (**III-49b** and **III-49c**) did not produce any consistent transient absorption spectra that could be ascribed to the *N*-methyl-*N*-(2-naphthyl)nitrenium ion. The synthesis of the pyridinium salt using 2,4,6-triphenylpyrylium tetrafluoroborate (**III-29d**) was also attempted, but did not yield the desired product due to solubility issues.

After these four different pathways failed to yield any type of reproducible transient absorption signal, experiments were performed to test for the stable

photoproducts expected from the nitrenium ion. When 1-(*N*-methyl-*N*-(2-naphthyl)amino)-2,4,6-trimethylpyridinium tetrafluoroborate was photolyzed in CH_3CN in the presence of TBACl, the two main photoproducts obtained were 2-naphthylamine and 1-chloro-2-naphthylamine which were compared to the ^{1}H-NMR of standards (Scheme 3.23).

Scheme 3.23: Photoproducts from III-49a and 89.4 mM TBACl in CH_3CN.



III-49a **III-46** **III-50**

The photoproduct 1-chloro-*N*-methyl-2-naphthylamine (**III-50**) is an expected product because a strong nucleophile attack on most carbocyclic nitrenium ions occurs predominately at a position *ortho* to the nitrenium ion center if the *para* position is blocked.[13] So the photolysis of the pyridinium salt yielded expected nitrenium ion products. Even though the *N*-methyl-*N*-(2-naphthyl)nitrenium ion is not observed, it does produce the expected nitrenium ion products. These results are supported the observations made by Novak during his study of solvolysis reactions competition reactions between solvent and azide trap. Solvolysis of *N*-sulfonatooxy-*N*-acetyl-2-naphthylamine in a buffer solution resulted in 25 $\pm$ 2 % of *N*-acetyl-1-hydroxy-2-

naphthylamine while solvolysis of *N*-sulfonatooxy-*N*-acetyl-2-naphthylamine with an azide trap yielded 30.8 $\pm$ 1.5% *N*-acetyl-1-azido-2-naphthylamine, 9.1 $\pm$ 0.5% *N*-acetyl-6-azido-2-naphthylamine, and 6.0 $\pm$ 0.5% of *N*-acetyl-4-azido-2-naphthylamine, likely from an addition-elimination pathway, which is unusual, but not unprecedented.[86,97] Although no synthesized derivatives yielded direct observation of 2-naphthylnitrenium ion, similar products and product distribution are recorded with the 1-positional adduct as the major product and the 4-positional and 6-positional adducts as the minor products.

3.4: Conclusions

Hence, one can see that the *N*-methyl-*N*-(1-naphthyl)nitrenium ion (**III-5**) is cleanly generated by photolysis of 1-(*N*-methyl-*N*-(1-naphthyl)amino)-2,4,6-trimethylpyridinium tetrafluoroborate (**III-25**) and was observed to have a lifetime of 835 ns and a λ_{max} of 500 nm in CH_3CN. The *N*-methyl-*N*-(1-naphthyl)nitrenium ion (**III-5**) is efficiently trapped by chloride at the diffusion limit and from the product study analysis, it can be seen that chloride traps the nitrenium ion to yield two photoadducts, the 2-chloro-*N*-methyl-1-naphthylamine (**III-31**) and the 4-chloro-*N*-methyl-1-naphthylamine (**III-30**) isomers. The nitrenium ion is also efficiently trapped by other nucleophiles, such as alcohols and amines near the diffusion limit. This suggests that the nitrenium ion is very reactive and thus not selective to any particular nucleophile. This would also extend to DNA as a nucleophile and would suggest that this nitrenium ion has a low selectivity and high reactivity with DNA. The results from this study emphasize the importance of *para*- substitution in determining the lifetimes of monoaryl nitrenium ions

in the presence of nucleophiles. There is also the concept of increased conjugation having an effect on the lifetime of the nitrenium ion. This increase in conjugation is seen in their spectra but not in their lifetimes of chemistry and shows that the *para*- position is important to the lifetime and reactivity of the nitrenium ion. In conclusion, this nitrenium ion displays similar reactivity to other known nitrenium ion systems.

Thus, it is reasonable to infer that *N*-methyl-*N*-(1-naphthyl)nitrenium ion would have a very short lifetime in an aqueous environment and be only weakly mutagenic, if at all.[43,61] This would be consistent with earlier animal studies.[20,27] The mutagenicity or carcinogenicity of any compound is a function of a large number of variables. Included among these are the rates and efficiencies of metabolism of the compound into the ultimate mutagenic or carcinogenic species, the chemical stability of that metabolite, its transport properties across membranes, the efficiency of the metabolite's reactions with DNA, the genetic effect of the specific DNA adduct formed, and the susceptibility of that adduct to the organism's DNA repair machinery. Clearly, there is no single chemical or physical property that will perfectly correlate with a biological effect such as mutagenicity or carcinogenicity. Given this complexity, it is remarkable that mutagenicity can be correlated to any single chemical or physical property of a series of compounds, or even to multiple properties.[12]

There are several possibilities as to why *N*-methyl-*N*-(2-naphthyl)nitrenium ion was not observed. One possibility is that the quantum yield is too low to produce a viable signal. One can look at the transient LFP spectrum of *N*-methyl-*N*-(1-naphthyl)nitrenium ion (Figure 3.11) and see that the Δ O.D. reaches a maximum value of 0.03. Therefore, it is possible that the signal for *N*-methyl-*N*-(2-naphthyl)nitrenium

ion is below the detection limit of the instrument. Another possibility is that *N*-methyl-*N*-(2-naphthyl)nitrenium ion is too short-lived and cannot be recorded on the nanosecond time scale of our laser system. The final possibility is that the transient absorption signal of *N*-methyl-*N*-(2-naphthyl)nitrenium ion does not occur within the UV-visable range. The transient absorption spectrum may absorb in the deep UV or the near IR, although ZINDO calculations estimate that the signal would absorb at either 359.83 nm, 294.51 nm, or 567.94 nm with probabilities of 0.6084, 0.1817, and 0.1083, respectively. Through experimental LFP studies, no consistent or unambiguous transient signals were observed at any of these wavelengths, but the expected photoproducts upon trapping with chloride were observed.

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Chapter 4: Nitrenium Ions and Polymerization Reactions

4.1: Introduction to Polymers

A polymer is a relatively high molecular weight substance composed of repetitively linked small molecules, called monomeric units, in sufficient number such that the addition or removal of one or several units does not change the properties of the substance. An oligomer resembles a polymer, except that the number of linked units is considerably smaller and removal of one or a few units does affect its properties. Thus, there is no specific number of units that must be linked to qualify the substance as a polymer. Polymers composed of as few as 30 and as many as 100,000 units are not uncommon, whereas oligomers range from four to about fifteen linked monomers.[1]

The word polymer is derived from the Greek *poly*, meaning many and *mer*, meaning part and was first used by the Swedish chemist Berzelius in 1833.[2] The term macromolecule is synonymous with polymer and throughout the nineteenth century, chemists worked with macromolecules without having any clear understanding of their structure. Some modified natural polymers were commercialized, such as nitrated cellulose, which was marketed under such names as Celluloid and gun cotton. As long ago as 1839, the polymerization of styrene was reported and during the 1860s, the synthesis of polyethylene glycol and polyethylene succinate were published with the correct structures.[2]

The first completely synthetic polymer used on a commercial scale was a phenol-formaldehyde resin, the first synthetic plastic, commercially known as Bakelite. It was developed in the early 1900s by the Belgian-born chemist Leo Baekeland and by the

1920s, Bakelite had found its way into a wide spectrum of consumer products.[2] Time Magazine called Baekeland "The King of Plastics" and put him on the cover of its September 22, 1924 issue while dubbing Bakelite "The material with a thousand uses". Yet, despite such commercial successes, most scientists had no clear concept of basic polymeric structure. The prevailing theory was that polymers were aggregates of small molecules, much like colloids, but were held together by some mysterious secondary force.

This aggregation or association theory eventually gave way to the theories of the German chemist Hermann Staudinger, who attributed the remarkable properties of polymers to ordinary intermolecular forces between molecules of very high molecular weight. Staudinger also introduced the term *makromolekül*.[2] In recognition of his contributions, Staudinger was awarded the Nobel Prize in Chemistry in 1953. In the 1930s, the work of American chemist Wallance Hume Carothers placed the theories of Staudinger on a firm experimental basis and led to the commercial development of neoprene rubber and polyamide (nylon) fibers.

World War II led to significant advances in polymer chemistry, particulary with the development of synthetic rubber when the natural rubber-growing regions of the Far East became inaccessible to the Allies. Among the more significant developments were the discovery by Karl Ziegler in Germany of new coordination catalysts for initiating polymerization reactions and the application by Giulio Natta in Italy of these new systems to the development of polymers with controlled stereochemistry.[3,4] Their work revolutionized the polymer industry and the importance of their discoveries was recognized when the Nobel Prize in Chemistry was awarded jointly to Ziegler and Natta

in 1963.[2,5] Equally significant to the development of polymers was the work of Paul Flory (Nobel Prize 1974), who established a quantitative basis for polymer behavior, such as the physical properties of macromolecules in bulk or solution and chemical phenomena, such as crosslinking and chain transfer.[2,5,6]

More recently, there have been a number of important advances in polymer science. Today's research includes: polymers having excellent thermal and oxidative stability for use in high-performance aerospace applications; engineering plastics which are polymers designed to replace metals; and polymers for a broad spectrum of medical applications, from degradable sutures to artificial organs as well as polymers in other fields. Conducting polymers which exhibit electrical conductivities comparable to those of metals are widely studied and so are polymers that serve as insoluble support for catalysts or for automated protein or nucleic acid synthesis as noted by Bruce Merrifield, who originated solid-phase protein synthesis, and was awarded the Nobel Prize in Chemistry in 1984.[2]

4.2: Introduction to Polyaniline (PANI)

Electronically conductive polyaniline (PANI) is the simple 1,4-coupling product of monomeric aniline molecules. The general structure of PANI consists of two principle units, the completely reduced form of a repeat unit containing two benzenoid rings and the completely oxidized form of a repeat unit containing one benzenoid ring and one quinoid ring throughout the backbone of the polymer. The oxidation state of PANI depends on the relative percentages of each unit. PANI is part of a class of polymers

with the general formula as shown in Figure 4.1 containing y reduced and 1-y oxidized repeating groups. The value of y can be varied continuously from one, the completely reduced material, to zero, the completely oxidized polymer, yielding many different states of PANI. The emeraldine oxidation state, where y = 0.5, consists of alternating reduced and oxidized groups. The several forms of PANI may exist or co-exist in the polymer chains such as aromatic rings, quinoid rings, and free amine, imine, and protonated structures.[7]

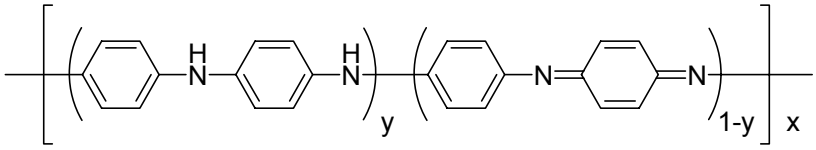


Figure 4.1: General formula of PANI.

PANI exists in various forms which differ in the oxidation state and degree of protonation of the main chain. The common oxidation states are shown in Figure 4.2. The leucoemeraldine form, when y = 1, the fully reduced form of PANI consisting solely of benzenoid units, is colorless, and acts as an insulator. Likewise, the pernigraniline form, when y = 0, is the fully oxidized form of PANI consisting solely of quinoid units, is purple, and acts as an insulator.[2,8,9] PANI in its neutral form is blue, but upon protonation it turns green, hence the names emeraldine for the protonated salt and emeraldine base for its blue precursor.

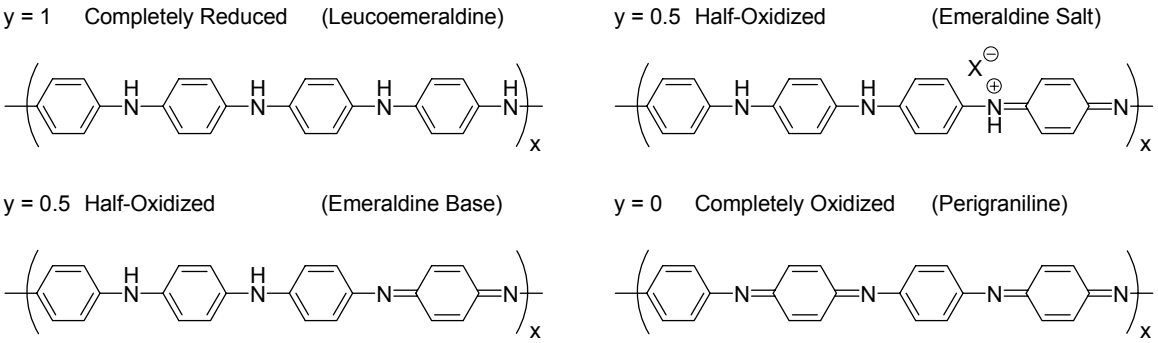


Figure 4.2: Structures of PANI.

The emeraldine base form of the polymer, when y = 0.5, consists of equal numbers of benzenoid and quinoid units and is thusly partially oxidixed. Emeraldine base is blue and acts as an insulator.[2] The emeraldine base form of PANI is the first well established example of the doping of an organic polymer to a highly conducting compound by a process in which the number of electrons associated with the polymer remains unchanged during the doping process. This is accomplished by treating emeraldine base with aqueous protic acids yielding the emeraldine salt by protonation of its basic sites (amine and imine groups).[9-13] The emeraldine salt is more stable, partially oxidized, and it exhibits higher conductivity.[2,14]

It is well known that the chemistry of PANI is more complex than the chemistry of other conducting polymers and is unique among all conducting polymers since the electrical conductivity and other properties of PANI and its derivatives are highly dependent on its oxidation states and the level of protonation.[15-17] PANI exhibits multiple color changes which depend on the oxidation states, which are both pH and potential dependent and demonstrates that besides the dopants (counterions), the presence of protons has an invariable pronounced effect on the conductivity.[18-23]

PANI was first discovered in 1835 as "aniline black", a term used for any product obtained by the oxidation of aniline.[24] A few years later, Fritsche carried out the tentative analysis of the products obtained by the chemical oxidation of this aromatic amine.[25] Thereafter, Letheby discovered that the final product of anodic oxidation of aniline at a platinum electrode, in an aqueous sulphuric acid solution, was a dark blue-green powdery precipitate.[26] Letheby also reported in 1862 on the electrochemical oxidation product of aniline and its color changes during different pH treatments which was verified by subsequent investigators.[26] The first directed study of PANI was performed in 1910 by Green and Woodhead and since then, there have been numerous articles and reviews covering this polymer.[27-31]

In the first decade of the 1900s, there were a number of studies on the synthesis and characterization of PANI and its derivatives in an effort to produce dyes. After a quiet period of over 50 years, it was reported that PANI had high electrical conductivity in 1968.[32] Although PANI has been known since the end of the 19th century, the most intensive research has been done in the last 30 years. Research interest was rekindled recently by MacDiarmid *et al.* whose investigations showed that this material is a conducting polymer.[33,34] Current research has focused on PANI because of the applicability PANI as an electrically conductive polymer, owing to its interesting electronic, optical, and electrochemical properties and to the potentially significant technological applications.[8,32,33,35-37]

The technological potential of PANI is due to its remarkable stability and processibility.[30] In commercial applications, polyamine solutions would provide a form more amenable to conventional plastics processing technology. It has become common

practice to remove insoluble material and use the soluble, possibly lower-molecular-weight fractions for the preparation of films.[38]

The potential of conducting polymers was recognized by awarding the 2000 Nobel Prize in Chemistry to Heeger, MacDiarmid, and Shirakawa for the discovery and development of conducting polymers. PANI, the oldest organic polymer ever synthesized, is interesting because of its chemistry/physics and its potential/practical applications in electrical devices.[39] PANI is interesting due to its moderately high conductivity upon doping with simple non-oxidizing Brönsted acids, such as HCl, and tunability since the conductivity has been found to depend on the redox state, the doping level, and moisture content of the polymer.[21,34] It is the emeradine state of PANI, obtained by oxidation of leucoemeraldine base or by protonation of pernigraniline, which gives PANI its electrical conductivity and other useful properties.[40,41] Its advantages as a conducting polymer include the low cost of aniline and the stability of PANI to oxygen, moisture, and elevated temperatures.[10,13,33,42,43]

There are several different commercial uses of PANI, including electronic devices such as rechargeable batteries, organic light emitting devices (OLEDs), photoconductivity, chemical sensors, and many others.[11,28,29,34,44-57] Its applications as energy storage media, photoelectrochemical assemblies, photochemical devices, and electrochromic devices has also been presented.[22,32,35,36,44,58-81] As far as the last application is concerned, some authors have even proposed different oxidation states of PANI to obtain the three fundamental colors of the chromatic circle.[71] It is also used commercially as an antistatic additive to plastics.[82-84]

PANI films or solutions can be used as an indicator since they can undergo multiple color changes in different pH ranges.[23,85,86] In the oxidized state, PANI films are colored and highly conductive, while in the reduced state, they are optically transparent with low conductivity.[59-61] The color of PANI films is reversibly changed to green by oxidation and to transparent yellow by reduction in 1 M HCl in the potential range from -0.2 V to +0.6 V vs SCE.[60,61]

PANI shows potential for use as a support for ion exchange chromatography because the equilibration by acid solution imposes the anion in the polymer and thus has been the basis for the use of PANI as an anion exchange polymer.[87] PANI can also act as a catalyst for fuel cell electrode and has important catalytic behavior in the decomposition of nitrous oxide and in the isomerization of butadiene. [88,89]

Not only is PANI receiving much attention, but so are many heterocyclic nitrogen compounds because they can be chemically polymerized to yield materials with interesting properties, particularly for photoconduction.[90] Electronic devices have been shown to behave like a diode and a transistor.[91] These polymer-based, transistor-like devices can be turned 'on' and 'off' by electrical or chemical signals that oxidize and reduce the polymer.

4.3: Mechanistic Controversy

PANI has been extensively studied due to its commercial importance as a conductive polymer due to its straightforward methods of preparation and stability of its conductive form in air.[32,35,37,58] Despite much research concerning its preparative methods and various properties, the mechanism of PANI polymerization remains uncertain. The mechanism of formation of PANI has been disputed for decades and is

still an active area of research and controversy. The two main polymerization mechanisms that are supported and argued over, are through one of two reactive species. Both a nitrenium ion and an anilinium radical cation have been proposed as propagating intermediates. Percec and Hill have recently reviewed these various mechanistic proposals.[42]

In terms of the reaction mechanism of the PANI synthesis, there is no comprehensive picture that can be found in the literature, even though the synthesis of PANI under various conditions has been carried out for more than 140 years, starting with the synthesis by Letheby.[26] Moreover, even the suppliers of commercial grades of PANI are not sure about the mechanism of the synthesis.[92]

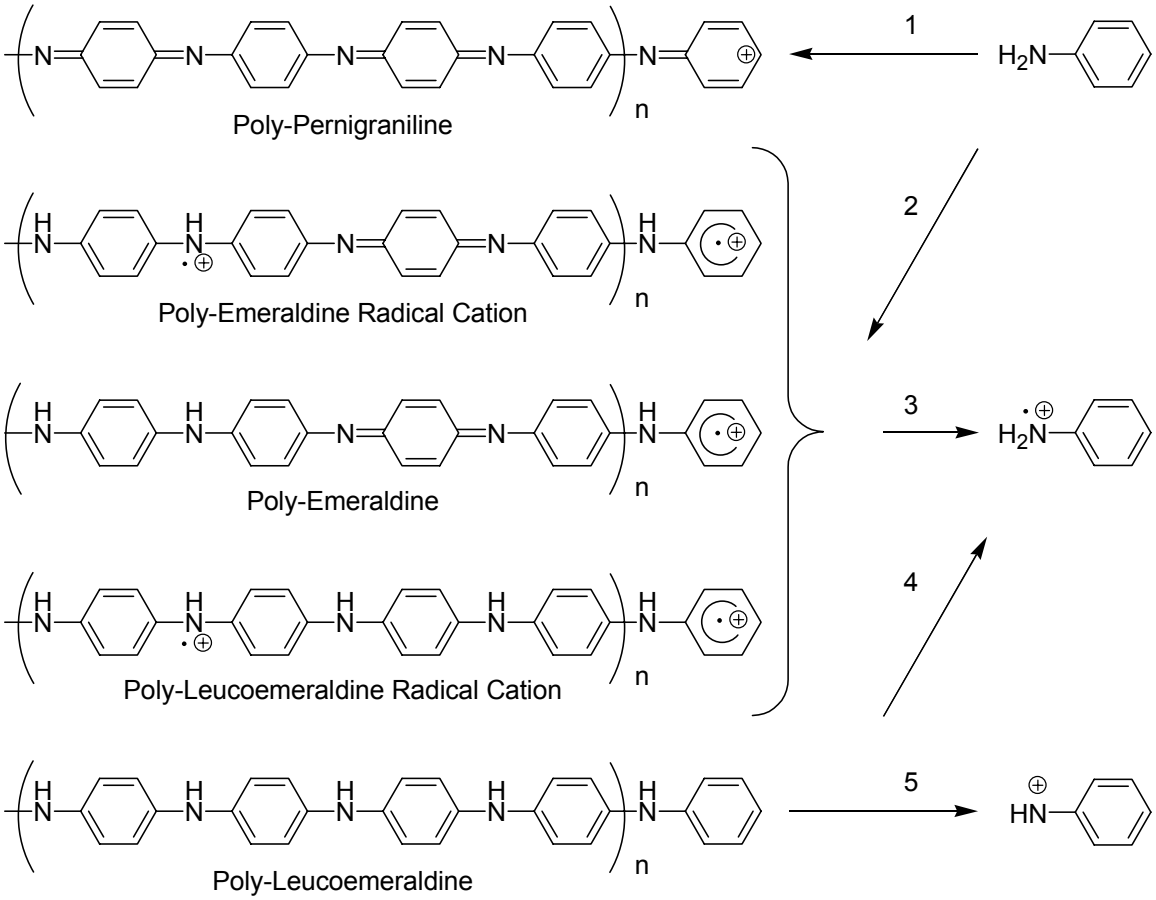
The two most common modes of synthesis are classical chemical synthesis and electrochemical synthesis of PANI.[28] PANI can be prepared by direct oxidation of aniline using an appropriate chemical oxidant or by electrochemical oxidation on different electrode materials in aqueous or nonaqueous media by the oxidation of aniline monomer.[32,35,37,58] Only those prepared in aqueous acidic media have a conducting form. Most of the information concerning the formation of PANI has been through electrochemical studies while chemical investigations concerning the kinetics of PANI formation are few and far between. Therefore, it is difficult to create a cogent argument from chemical synthesis results alone. Thus, it is customary to assume that both the electrochemical and chemical synthesis take the same pathway and the combination of results in both areas of study are allowed. However, one should bear in mind that the conditions of the electrochemical syntheses can be different from those of the chemical

syntheses, simply because the spatial situation in front of the working electrodes is quite different from the spatial situation encountered in chemical experiments.

Chemical synthesis of PANI is achieved typically via an oxidation of aniline by a strong oxidant, e.g., ammonium persulfate at ca. 0-5 ºC in an aqueous solution of a protic acid, typically in 1M HCl, but chemical methods of preparation lack the control of reaction conditions.[93] Chemical synthesis provides powder material, whereas electrochemical synthesis yields thin films on a conducting substrate. Electrochemical synthesis of PANI is generally carried out by either potentiostat or cyclic potential sweep techniques in an electrolyte consisting of aqueous solution of aniline and an acid.[8,36] One of the disadvantages associated with the use of high applied potentials and strong oxidants are side reactions, such as cross-linking and degredation of the polymers.[46,60,94,95] Both the chemical and electrochemical polymerization of aniline have proposed the incorporation of neutral aniline monomer into the growing polymer chain end via an electrophilic substitution reaction.

The simplified attack mechanisms, shown in Scheme 4.1, clearly demonstrate the importance of the reactivity of the aniline monomer and can occur by different reaction sequences. The pathways include nucleophilic addition of an aniline monomer on a nitrenium ion polymer end (1), anilinium radical cation addition (2, 3, 4), and electrophilic addition of phenylnitrenium ion, the oxidized form of the aniline monomer (5).

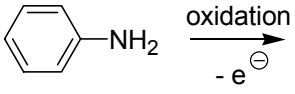
Scheme 4.1: Possible polymerization mechanisms of PANI.

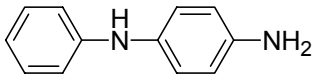


4.3.1: Evidence for Radical Cation Intermediates

The first step and rate-determining step in the electrochemical polymerization of aniline involves the oxidation of the neutral aniline monomers to radical cations, which leads to formation of dimeric species. These dimeric species, *p*-aminodiphenylamine (ADPA; **IV-1**) (head-to-tail), 1,2-diphenylhydrazine (**IV-2**) (head-to-head), and benzidine (**IV-3**) (tail–to-tail) can be formed via radical coupling among various resonance forms of the radical cation (Scheme 4.2).[37,46,96-98]

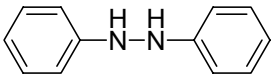
Scheme 4.2: Oxidation of aniline to dimeric species.





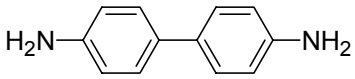
ADPA

IV-1



1,2-Diphenylhydrazine

IV-2



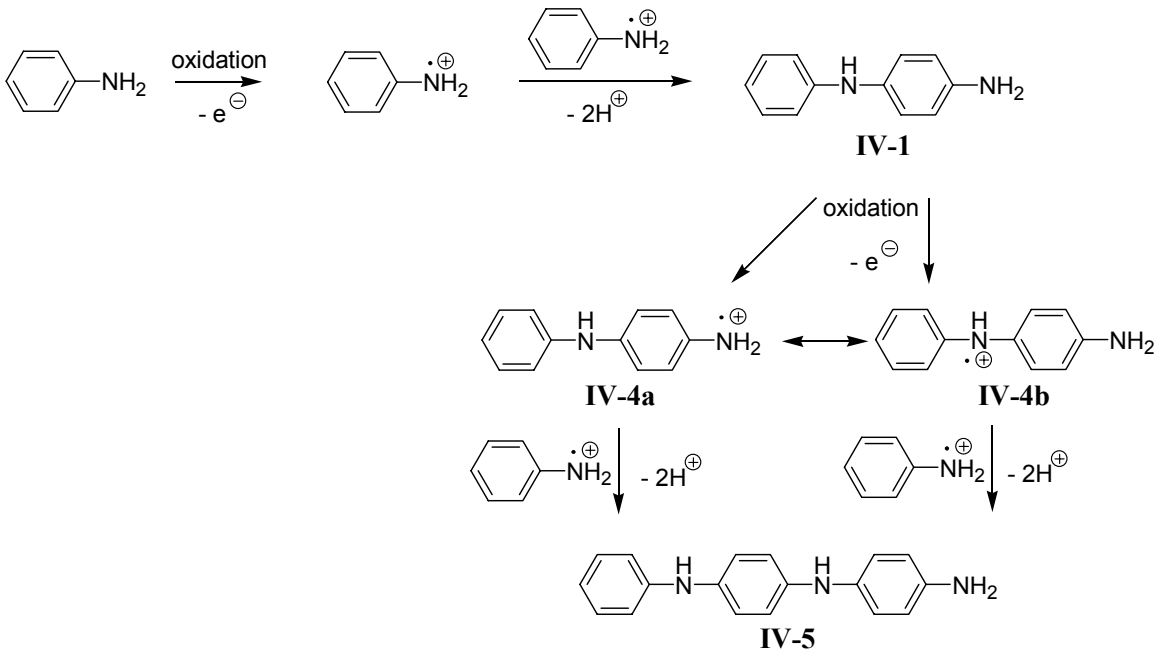
Benzidine

IV-3

The mechanism of polymerization, past the initial dimerization step, is not very well understood. Although previously, it was thought that the formation of PANI proceeded through head to tail coupling of the aniline radical cations.[37,46,98-110]

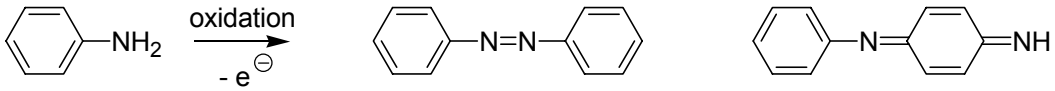
In general, polymerization proceeds via the radical cation of the monomer, which then reacts with a second radical cation of the monomer to give a dimer by eliminating two protons (Scheme 4.3). At the potential required to oxidize the monomer, the dimer or higher oligomers would also be oxidized, and thus, could react further with the radical cation of the monomer to build up the aniline chain. In this mechanism, one can argue that the oxidized polymer molecule, instead of adding to the neutral aniline monomer, catalytically oxidizes the neutral molecule of aniline in the presence of acid. Combination of the resulting radical cations leads to the formation of a growing polymer chain by losing two protons.[111]

Scheme 4.3: Oxidation of aniline dimers.



The electrochemical oxidation of organic compounds is a very complex subject especially with regard to the difficulty in relating the electrochemical results with those obtained chemically.[112] The electrochemical oxidation of aniline, at varying pH, also yields azobenzene (**IV-6**) and *N*-phenylquinonediimine (**IV-7**) (PQDI), via a radical cation mechanism (Scheme 4.4). The products of oxidation of PQDI and aniline occurred at the same potential or at a less positive potential suggesting that the oligomers are easier to oxidize and would involve chain growth leading to PANI.

Scheme 4.4: Oxidation of aniline to azobenzene and *N*-phenylquinonediimine (PQDI).



IV-6 **IV-7**

Since ADPA is an oxidation product of aniline, the intermediate steps in the polymerization of anilne lead to the oxidation of ADPA to give the radical cation and subsequent formation of the quinone dication. For this reason, it has been concluded that if these steps lead to oxidation reactions which are easier than the oxidation of aniline, then the oxidation of aniline is a determining reaction governing the efficiency and kinetics of the polymerization process. The next steps in the polymerization of ADPA are rapid and Mohilner *et al.* have proposed that the process occurs by the formation of the tetramer, then formation of the octamer, which polymerizes even further resulting in a polymer whose basic structure is that of emeraldine.[37]

The most overwhelming evidence for the presence of the anilinium radical cation is from the work of Ding, Padias, and Hall Jr.[113] In their experiments, the oxidative polymerization of aniline in aqueous acidic solution was carried out in the presence of a variety of organic compounds as potential traps for the postulated intermediates. The polymerization was inhibited by hindered phenols and electron-rich alkenes, which are traps for radical cations. However, PANI was still obtained in the presence of electron-rich arenes, such as 1,3-dimethoxybenzene (1,3-DMB) and 1,4-dimethoxybenzene (1,4-DMB), known as excellent traps for nitrenium ions. Their results have led to the proposed radical cation polymerization mechanism of aniline, in which the

polymerization is a chain growth reaction through the combination of a polymeric radical cation and an anilinium radical cation. The nitrenium ion mechanism was further rejected by the fact that attempted polymerization of *N*-phenylhydroxylamine, which forms authentic nitrenium ions in acid, failed to give polymer. Therefore, many research groups have adopted the anilinium cation radical mechanism even though there is still disagreement about the exact steps involved in chain growth.[37,92,111,113-115]

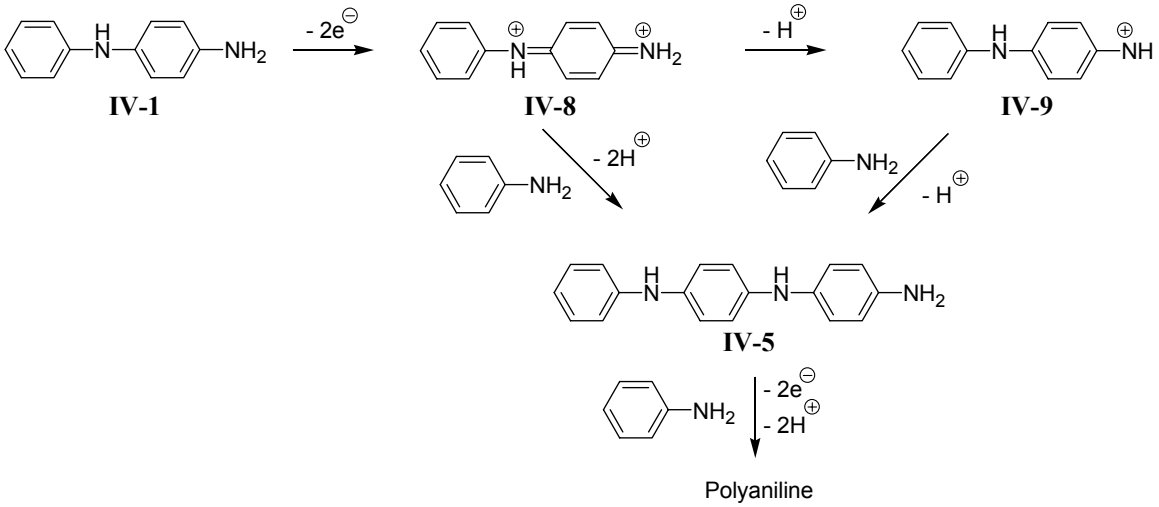
4.3.2: Evidence for Nitrenium Ion Intermediates

Originally, it was thought that the formation of the ADPA resulted from reaction of the electrophilic nitrenium ion with another molecule of aniline. Now, most researchers agree that the first step in aniline polymerization is the formation of a radical cation.[28]

In contrast to the radical cation initiated polymerization, an alternate mechanism for the polymerization of aniline has been proposed. Once ADPA is formed from aniline, it is oxidized via a single two-electron step to a quinoidal diimine form because of its lower oxidation potential in comparison with aniline.[37,116-118] The proposed mechanism in which polymer growth occurs by the coupling reaction of neutral monomer with a growing polymer chain containing a terminal iminium or nitrenium group. Two electron oxidation of ADPA produces quinoidal diiminium ion (**IV-8**) (Scheme 4.5). There are two reaction pathways available to **IV-8** that involve reactions with neutral monomer to produce the aniline trimer (**IV-5**). The electrophilic attack of **IV-8** upon aniline followed by loss of two protons results in the formation of **IV-5**. Alternatively, the deprotonation

of **IV-8** produces a nitrenium ion (**IV-9**) which can also react electrophilically with aniline to give **IV-5**. Stable nitrenium ions have been detected in other reaction media.[105]

Scheme 4.5: Possible mechanism of PANI formation via nitrenium ion intermediates.



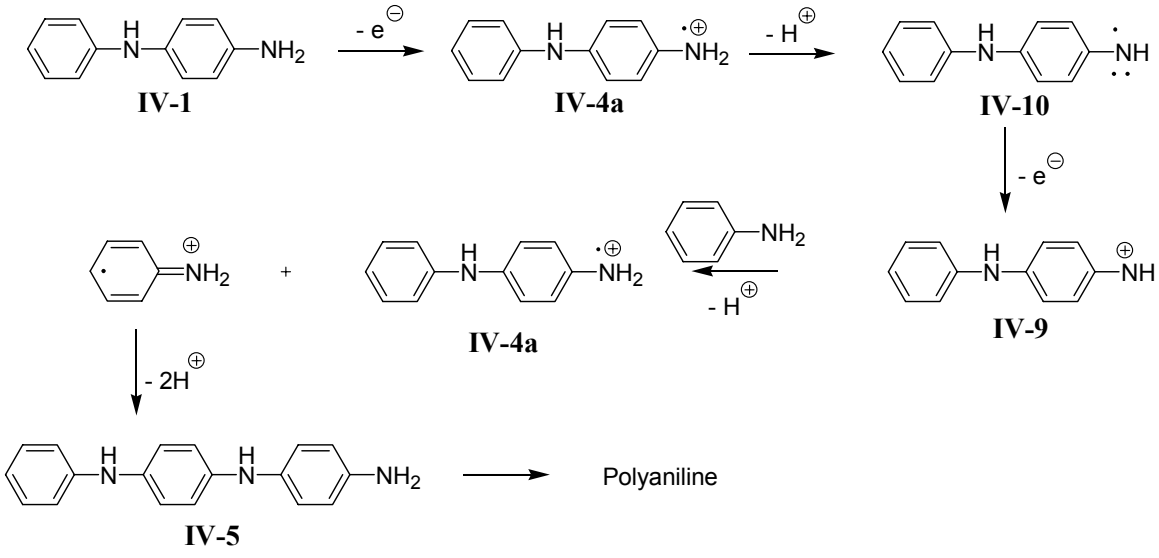
Wei proposed that the dimer loses two electrons to form a diiminium dication or a stable nitrenium cation which could be readily generated from the deprotonation of the diiminium ions.[109] The dication molecule, because of its significant positive charge, is rapidly deprotonated, yielding a nitrenium ion.[119] The presence of the stable nitrenium ion in the reaction medium was reported by Genies and Lapkowski.[104]

Based mainly on kinetic studies of the electrochemical polymerization of aniline, a new mechanism for aniline polymerization was proposed.[120] In this mechanism, the growth of polymer chains is achieved mainly via electrophilic aromatic substitution on neutral monomers by the oxidized growing polymer chain ends. The oxidized oligomeric species or their nitrenium forms, could react with neutral aniline monomers via an

electrophilic aromatic substitution.[109] The reaction system has been monitored by UV-vis spectroscopy and confirmed the existence of various oligmeric species during the reaction stage. Small green/blue particles started to appear in the solution and on the Pt electrode. These particles are the pernigraniline form of PANI according to Manohar *et al.*[121] Because the oxidation potential of aniline is higher than those of the dimers upon formation, the dimers are immediately oxidized and then react with an aniline monomer via an electrophilic aromatic substitution followed by further oxidation and deprotonation to afford the trimers and subsequent oligomers and polymers,

A similar reaction mechanism was proposed by Bodalia and Duran.[111] The oxidation of ADPA (**IV-1**) would be followed by deprotonation and further oxidation would yield nitrenium ion **IV-9** (Scheme 4.6). The acid-catalyzed oxidation of aniline by **IV-9** yields ADPA radical cation and aniline radical cation. The coupling of these two species followed by deprotonation gives **IV-5**.

Scheme 4.6: Possible mechanism of PANI formation via radical cation and nitrenium ion intermediates.



Breitenbach and Hecker propose that the oxidation mechanism of aniline in an acetonitrile/pyridine medium is similar to that in an acidic medium as described by Mohilner.[37,116,117] They suggested that the oxidation step is followed by abstraction of a proton from the nitrogen atom by more basic molecules like water or unprotonated aniline, resulting in the appearance of the neutral aniline radical. The neutral aniline radical can then undergo another oxidative attack, leading to another divalent cation carrying two free electrons at the nitrogen atom, a nitrenium ion.

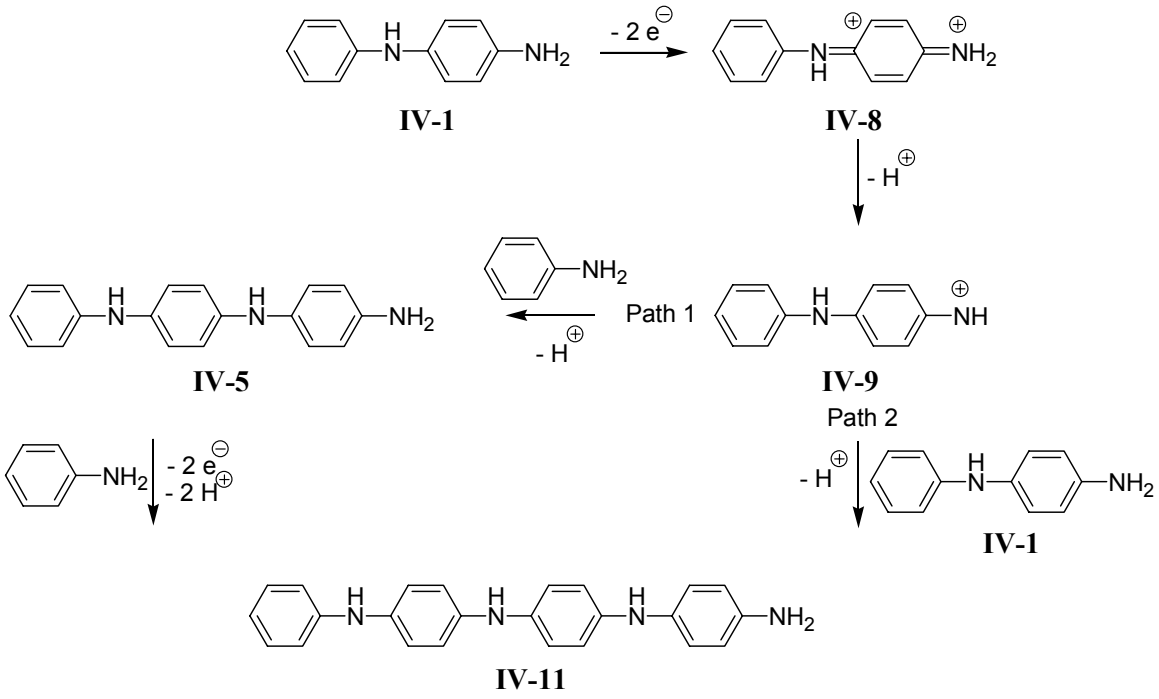
Polymerization of aniline and its derivatives in which the initial formation of the aniline dimers is slow in comparison with the succeeding growth of the polymer chains via an electrophilic substitution reaction with aniline. Soon after formation, the two dimers will be oxidized to their diimine forms which could be deprotonated to afford nitrenium ions.[105,108,117,118] An electrophilic attack of aniline monomers by the diimines of the nitrenium ions would accomplish a growth step and lead to the final polymer.

A possible mechanism for the reaction involved an electrophilic aromatic substitution of nitrenium ion to aromatic amines.[98,108,109,120,122,123] In acidic media, diprotonated PQDI (**IV-8**) (Scheme 4.7) can be deprotonated to generate a nitrenium ion at the chain end. This nitrenium ion could function as a strong electrophile and thus add to the aromatic ring.

Since the nitrenium ion may be a stronger electrophile than the iminium cation, this latter reaction is more plausible and is consistent with Genies' observations.[105,124] At this point there are two paths leading to polymer and they could be in competition as shown in Scheme 4.7. In path 1, nitrenium ion **IV-9** reacts with a neutral aniline via an electrophilic aromatic substitution reaction to form a trimer (**IV-5**). Since the oxidation

potential of the oligomers or polymers decreases in the order monomer > dimer > trimer . . . > polymer, the trimer could be readily oxidized and converted to the nitrenium ion followed by addition of another aniline monomer to form tetramer and eventually lead to the polymer.[125] This mechanism is consistent with the results from the kinetic study of the polymerization of aniline that the rate of polymerization is first order in both the aniline concentration and the amount of the polymer formed.[98]

Scheme 4.7: Possible mechanism of PANI formation via a nitrenium ion reacting with aniline (path 1) or ADPA (path 2).



At the beginning of polymerization, path 1 may be predominant because the concentration of aniline is higher and the difference between the oxidation potentials of aniline and the growing polymer chains is higher. Path 2 is also important in the later

stage of the polymerization because the nitrenium ion could react with another dimer to form tetramer. As most of the aniline has been consumed in the later stage of the polymerization, path 2 could become more predominant. The dimer could also be incorporated into the growing end of the oligomer to form the polymer.

This mechanism is further supported by the spectroelectrochemical experiments of Genies and Lapkowski.[104,105] Based on spectrophotochemical studies of aniline oxidation, Genies and Lapkowski observed a short lived intermediate which was created before the formation of PANI. The intermediate was diamagnetic and based on experimental results, it was proposed that the intermediate was the phenylnitrenium ion. Since nitrenium ions can also arise from the two-electron oxidation of amines, cyclic voltammetery (CV) can be used to detect and observe UV-vis absorption bands and correlate the absorbing species to the oxidation state.[126,127] During the spectrophotochemical oxidation of aniline, Genies and Lapkowski observed a low intensity band around 670 nm, which is characteristic of PANI but were surprised to see a strong absorption band associated with the existence of a soluble intermediate located at 420 nm, which gradually disappeared with a simultaneous increase in the intensity of the 670 nm band.[104] This indicated that the intermediate was involved in the reaction leading to the formation of the polymer. It was observed that the evolution of the 670 nm band is characteristic of the growth of PANI and that the polymer starts to grow after an induction time associated with the formation of the intermediate. The polymer continues to grow even without the potential applied due to the reaction with the intermediate present in the solution. Two possibilities were that it could be the anilinium radical cation or the phenylnitrenium ion. During an electron paramagnetic resonance (EPR)

spectroscopy experiment, no EPR signal was observed and thus spectroscopic evidence for the nitrenium ion mechanism became clear. Through CV experiments, a reduction peak was observed to be the reduction of the phenylnitrenium ion to the neutral aniline radical. This type of behavior has been observed with pyrazoline derivatives.[128] The CV also added support for the formation of the phenylnitrenium ion in the mechanism of PANI where the nitrenium ion acts as an electrophile and aniline acts as a nucleophile.

Another spectroscopic study of the polymerization mechanism of aniline by Genies *et al.* permitted them to demonstrate that at low oxidation potentials (+0.7 V versus Cu/CuF_2), the PANI formed from the polymerization of the monomer radical cation. On the contrary, if the potential is slightly higher than +0.7 V, the aniline is directly oxidized with the loss of two electrons and one proton to form the corresponding nitrenium ion, which is relatively stable in this solution and has been detected by visible spectroscopy.[100] The absorbance seen at 650 nm is characteristic of the growing film, while that at 420 nm is mainly due to a soluble intermediate with only a slight contribution due to the film. The ratio of the quantity of film formed to the quantity of soluble intermediate is much weaker when the oxidation is effected at 1 V. This soluble intermediate which absorbs at 420 nm was thought to be the phenylnitrenium ion which reacts slowly with aniline to form a polymer having a more poorly defined structure. Hence the chemical composition of the resulting material depends on the method of synthesis, be it chemical or electrochemical, and on the synthesis of conditions such as pH, concentration of reactants and products, oxidation potential, and other variables.

In the early studies by Mohilner and Bacon and Adams, it was shown that the formation of a radical cation upon oxidation of aniline is the rate-limiting step. The

radical cation thus formed leads to dimerization products such as benzidine and ADPA.[37,96] This indicates that the absorption band at 430 nm observed during the PANI synthesis arises from either the benzidine quinoid, an intermediate, or both. It is believed that both the benzidine quinoid and the solution intermediate species, which will be discussed later, are responsible for this electronic absorption.[101]

As the number of cycling increases, the longer wavelength peak increases and also shows continuous red shifts until the PANI spectrum is eventually obtained. All dimers appear to be produced as intermediate electrolysis products of aniline and any dimer is capable of growing into the polymers by producing their oxidized state.[101] The middle CV peaks and some spectroscopic behavior observed during the PANI growth are explained by the redox reactions of these dimers, quinoneimine produced from the incomplete hydrolysis of the quinoid form of PANI, the *p*-benzoquinone/hydroquinone pair and some oligomers. Since the acidity of the radical cation is not expected to be strong enough to be deprotonated in 1 M H_2SO_4 solution, it is reasonable that the free radical should not be produced in significant amounts for further electron transfer reactions. Futhermore, the generation of free radicals as intermediate species would have given EPR signals. Thus, the species that is responsible for the electronic tranisition at 430 nm should be the nitrenium ion. This nitrenium ion must be responsible for the transient absorption band at 430 nm observed during the oxidation of aniline.

Taking into account all the works cited, it is evident that much important progress has been made on the study of PANI. Although the polymerization mechanism has not been determined, the majority of authors believe that the initial dimerization occurs by radical coupling as Genies *et al.* have previously proposed for polypyrrole. Much

progress has also been made in preparing polymers with more well-defined structures and which possess the lowest possible degree of irregularity. Careful choice of solvent, electrolyte, reactant concentrations and synthesis conditions is important in order to obtain a regular polymer with the highest possible molecular mass.[73,105,129]

4.3.2: Research Foundation

The CV peaks observed during the PANI synthesis in the middle potential regions were shown to arise from the redox reactions of these dimers, oligomers, and degradation products of PANI including quinoneimines and *p*-benzoquinone.[101] It has also been reported that the dimer, trimer, oligomers, and higher polymers have lower oxidation potentials than the monomer. So, once oligomers are formed in the reaction medium, they can oxidize faster than the monomer and the reaction rate accelerates.

It was thought that if the dimeric species is initially introduced into the aniline polymerization system, the slow step in the polymerization could be avoided and the overall rate of polymer formation should be significantly increased.[109] The rate of PANI formation is generally in the following order: *p*-phenylaminediamine > benzidine > ADPA > 1,2-diphenylhydrazine > *p*-phenoxyaniline > aniline without any additive > hydroquinone > *N*,*N*-diphenylamine. Because the dimeric species have lower oxidation potentials than aniline, the oxidation will occur immediately after their formation to yield their corresponding quinoidal diiminium ions. An electrophilic attack by aniline monomer or ADPA on either the diiminuim ion or a nitrenium ion, which could be

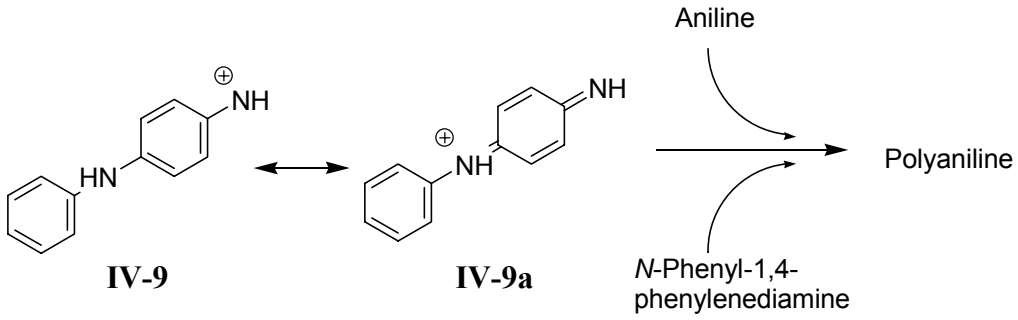
readily generated from a deprotonation of the diiminium ions, would accomplish a polymer growth step (Scheme 4.7, paths 1 and 2).[104,105,108,117,118]

This experimental scheme would be building upon the basis of ADPA, as suggested by Mohilner, Volkov, and Mengoli.[37,130,131] The dimeric species ADPA can be oxidized to similar quinoidal diiminium (or iminium), and subsequently the nitrenium ions at lower potentials than that for the aniline monomer. The additives which enhance the rate of PANI formation could, therefore, effectively function as initiators in the polymerization systems. Therefore, ADPA was used to observe polyaminodiphenylamine chains which are relatively short, having molar masses between 2,800 and 30,00 g, whereas the molar masses of PANI chains are around 80,000 g.[132] This would provide more evidence for the role of nitrenium ions in the polymerization of aniline.

4.4: Synthesis and Photolysis of 4-(*N*-Anilino)phenyl Azide

The initial goal was to research the role of nitrenium ions in the polymerization of PANI and to shed some light onto the mechanism of PANI formation. Since most authors agree that the dimerization step is via a radical cation mechanism, we started our research with ADPA as a starting point. The first step was to produce a suitable photochemical precursor to observe the resulting nitrenium ion and then study its photophysical properties. In general, we wanted to photolytically create a nitrenium ion that would take part in the polymerization of PANI as shown in Scheme 4.8.

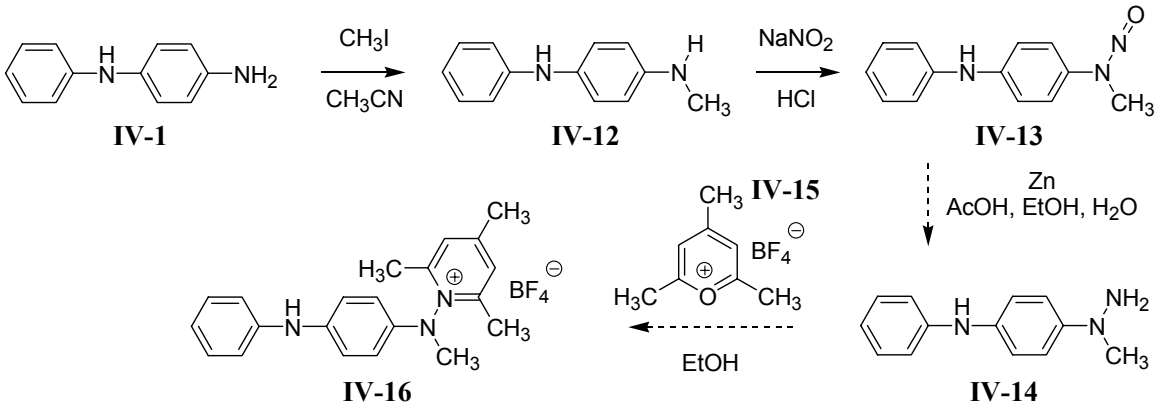
Scheme 4.8: Proposed research pathway.



4.4.1: Synthetic Schemes and Laser Flash Photolysis

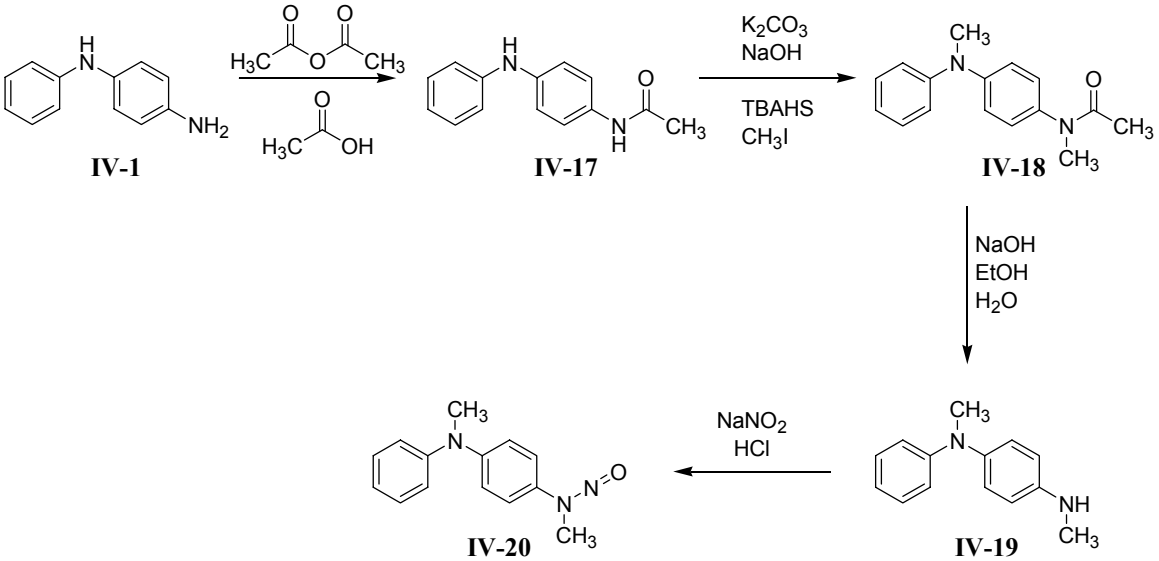
The original synthesis of the photochemical precursor included the use of the familiar *N*-pyridinium tetrafluoroborate salts. The proposed synthesis included methylating ADPA with methyl iodide (Scheme 4.9). The secondary amine (**IV-12**) was then nitrosated with a sodium nitrite solution in the presence of hydrochloric acid to give *N*-methyl-*N*-nitroso-*N*′-phenyl-1,4-phenylenediame (**IV-13**). It was thought that the reduction of **IV-13** would yield the corresponding hydrazine (**IV-14**), which could then be coupled to 2,4,6-trimethylpyrylium tetrafluoroborate (**IV-15**) to yield the final pyridinium tetrafluoroborate salt (**IV-16**). Yet, the reduction of the nitroso compound in the presence of zinc (Zn) and acetic acid (AcOH) to generate the corresponding hydrazine (**IV-14**) proved to be quite elusive, even after several months of attempting the reduction under different conditions. Another method that was attempted was the synthesis without the initial methylation, but that too had difficulties with the reduction of the corresponding nitroso compound to the hydrazine; therefore, other methods were pursued.

Scheme 4.9: Attempted synthesis of pyridinium tetrafluoroborate photoprecursor.



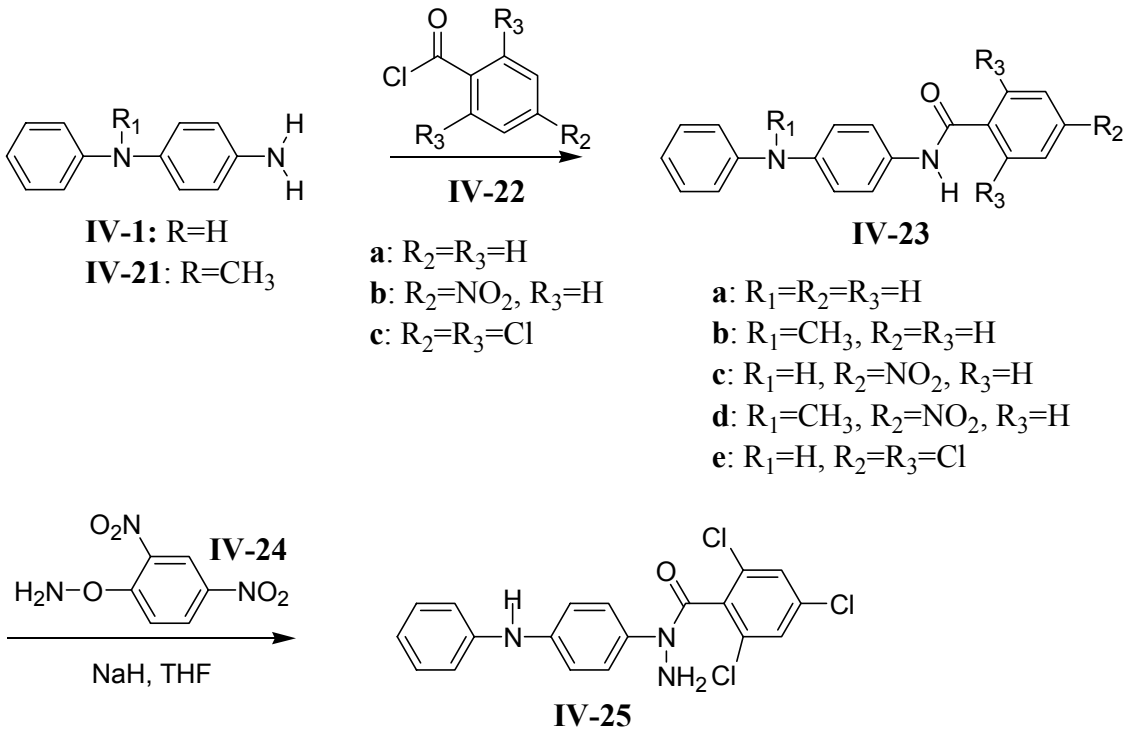
It was hypothesized that the internal secondary amine nitrogen was somehow problematic by acting as a nucleophile or as an electron donating group. Therefore, the methylation of the internal nitrogen was undertaken to minimize the electron donating effect. An alternate method included the protection of ADPA with acetic anhydride in the presence of AcOH to yield **IV-17** (Scheme 4.10). The methylation of both nitrogens to **IV-18** was performed with potassium carbonate, sodium hydroxide, tetrabutylammonium hydrogen sulfate and iodomethane. The deprotection step of **IV-18** with sodium hydroxide in EtOH and distilled water yielded **IV-19**, which was nitrosated with a solution of sodium nitrite in the presence of HCl to yield *N*,*N*′-dimethyl-*N*′-nitroso-*N*-phenyl-1,4-benzenediamine (**IV-20**). It was unfortunate that the attempts to reduce **IV-20** to the corresponding hydrazine proved to be too powerful, which resulted in *N*,*N*′-dimethyl-*N*-phenyl-1,4-benzenediamine (**IV-19**). Again, another synthetic procedure was undertaken to yield the desired pyridinium salt.

Scheme 4.10: Attempted synthesis of dimethylated pyridinium tetrafluoroborate photoprecursor.



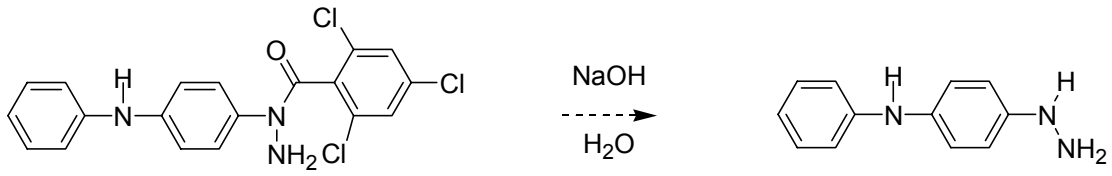
Another such method that was attempted is shown in Scheme 4.11. ADPA was protected with benzoyl chloride (**IV-22a**), *p*-nitrobenzoyl chloride (**IV-22b**), and 2,4,6-trichlorobenzoyl chloride (**IV-22c**) and *N*-methyl-*N*-phenyl-1,4-phenylenediamine (**IV-21**) was protected with benzoyl chloride (**IV-22a**) and *p*-nitrobenzoyl chloride (**IV-22b**) to afford the corresponding amide. This allowed the amide's proton to become relatively acidic so that it would be deprotonated with sodium hydride. The anion could then perform an S_N2 attack on *O*-(2,4-dinitrophenyl)hydroxylamine, which was synthesized according to publish procedures, to yield the corresponding hydrazine.[133]

Scheme 4.11: Synthesis of hydrazines via *O*-(2,4-dinitropheny)lhydroxylamine.



As it turned out, the deprotonation of the amide and nucleophilic attack proved to be a tedious task as the conditions needed to be anhydrous and under constant inert atmosphere. Unfortunately, the synthesis of the hydrazine proved to be difficult after many attempts with four the derivatives **IV-23a-d**. Fortunately, **IV-23e** did afford the corresponding hydrazine (**IV-25**). Once the hydrazine was synthesized, it was thought that the deprotection in refluxing acid or base would yield the free hydrazine base (**IV-26**) (Scheme 4.12), which could then be coupled to 2,4,6-trimethylpyrylium tetrafluoroborate (**IV-15**).

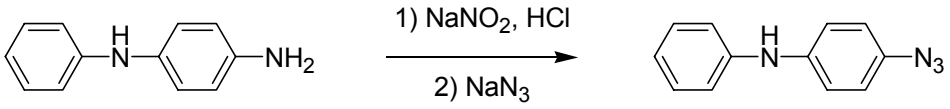
Scheme 4.12: Attemped synthesis of hydrazine free base.



IV-25 **IV-26**

Unfortunately, the attempt to make the hydrazine free base (**IV-26**) proved nearly impossible since refluxing in acid or base for more than 48 hours did not produce the desired product. Therefore, another synthetic pathway was needed to produce the desired photolysis precursor to yield 4-anilinophenylnitrenium ion (**IV-9**). As it turned out, the synthesis of the azide precursor was straight forward and produced the desired photoprecursor as seen in Scheme 4.13.

Scheme 4.13: One pot synthesis of 4-(*N*-anilino)phenyl azide.

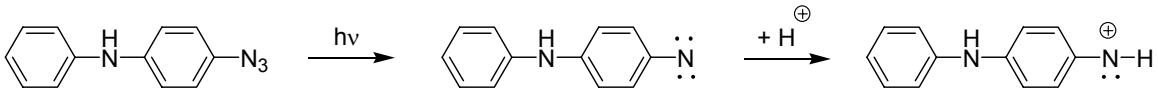


IV-1 **IV-27**

ADPA was nitrosated with sodium nitrite in the presence of hydrochloric acid. The second step of this one-pot synthesis was the addition of sodium azide, which generated 4-(*N*-anilino)phenyl azide (**IV-27**). Therefore, the azide photochemical precursor was used. As shown in Scheme 4.14, the azide can be photolyzed to produce the resulting nitrene (**IV-28**) and upon protonation, yield the nitrenium ion intermediate

(**IV-9**). The resulting nitrenium ion can undergo polymerization with either aniline monomers or other dimers.

Scheme 4.14: Photolysis of 4-(*N*-anilino)phenyl azide yielding the corresponding nitrenium ion via protonation of the nitrene.



IV-27 **IV-28** **IV-9**

To achieve a better understanding of the photochemistry of this compound, LFP of the azide (**IV-27**) was performed in a series of solvent systems. The first solvent in the series was CH_3CN, a polar aprotic solvent. Photolysis in CH_3CN would yield a reference transient absorption spectrum of the corresponding nitrene and nitrene products, such as ring expansion. These types of processes were seen in the cases of 1- and 2-naphthyl azides (Schemes 3.13 and 3.21 and Figures 3.8, 3.9, 3.18, 3.19). As can be seen in Figure 4.3A, the photolysis of the precursor yielded the spectrum with and initial absorbance band centered around 350 and 500 nm with a growth absorption band centered around 425 nm. This spectrum is attributed to the nitrene which can then form the aziridine ring and then undergo ring expansion, hence the growth.[134,135]

The radical cation of ADPA was observed in this solvent system when photolyzed in the presence of the electron acceptor 1,4-dicyanobenzene (1,4-DCB). The observed radical cation is shown in Figure 4.3B and has a transient absorption from 500 – 600 nm. The observed negative ΔO.D. in Figure 4.3B may be from absorption of accumulated photoproducts.

Photolysis of the azide (**IV-27**) in a mixture of 30% CH_3CN/70% H_2O afforded the generation of the nitrene which, in the presence of a proton source H_2O, would have afforded the corresponding nitrenium ion. The absorption band that was produced was centered around 420 nm and quite long-lived as can be seen in Figure 4.4A. Again, the radical cation of ADPA was ascertained to have a reference spectrum in this solvent mixture and was generated by the photolysis of the photochemical precursor in the presence of methyl picolyl perchlorate (MP) as shown in Figure 4.4B.

Because of the experiences with the 1- and 2-naphthyl systems, the addition of H_2SO_4, a stronger proton source than H_2O, was added to the CH_3CN/H_2O solution, to observe the nitrenium ion (**IV-9**). Figure 4.5A shows the transient absorption spectrum of the photoprecursor in the CH_3CN/H_2O solution with added acid and the resulting transient absorption shows that there is a large signal that is centered around 490 nm. The observation of the radical cation of ADPA was also attempted in the presence of MP (Figure 4.5B), but the photolysis also yielded the same broadness in the absorption spectrum as seen in Figures 4.3B and 4.4B. It is with these results that the 490 nm signal is ascribed to the nitrenium ion (**IV-9**) since its transient is markedly different than Figures 4.3A and 4.4A in differing solvent systems.

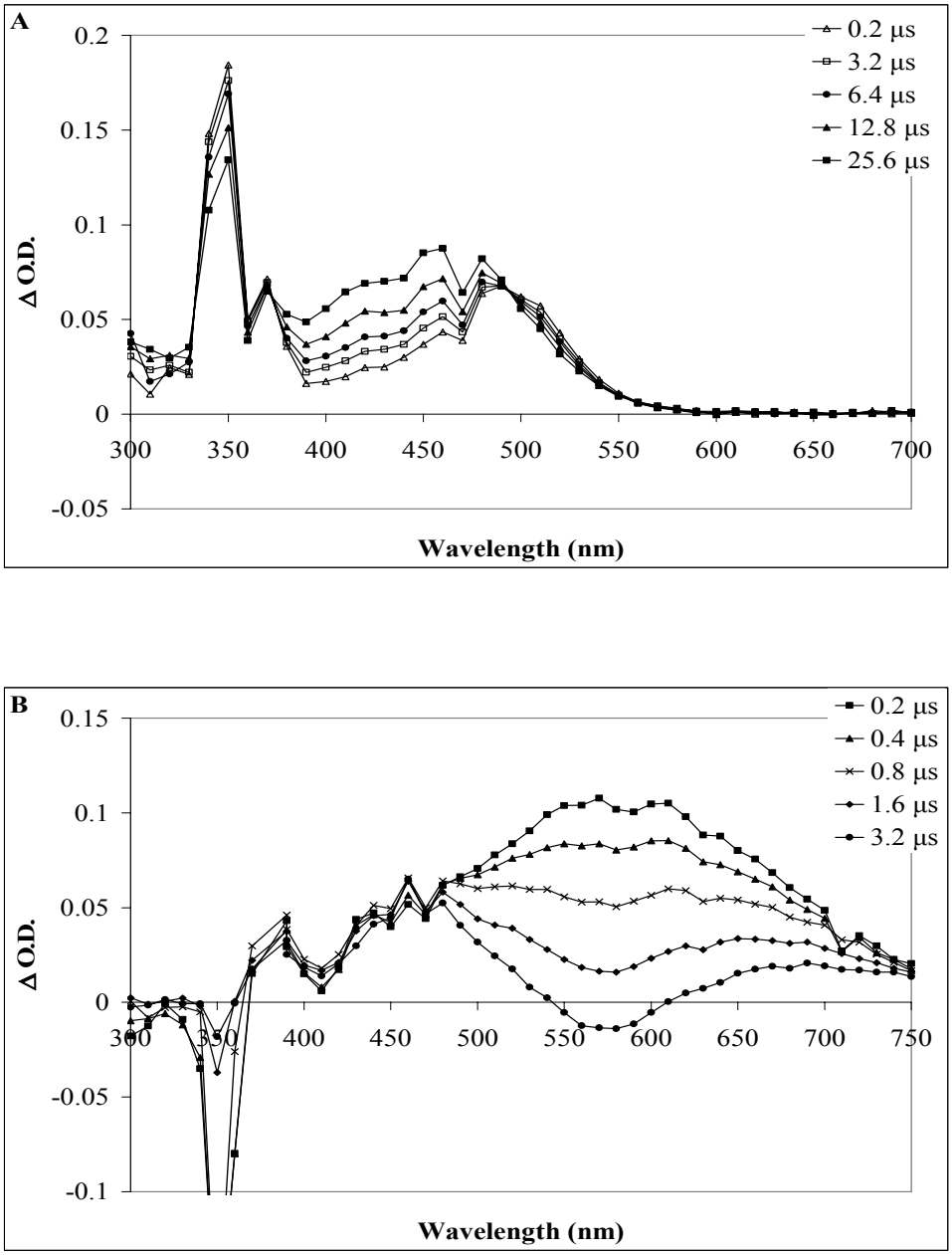


Figure 4.3: Transient UV-vis absorption spectra generated from LFP (266 nm, 4-6 ns, 3-5 mJ/pulse) of (A) IV-27 in CH_3CN, taken 0.2, 3.2, 6.4, 12.8, and 25.6 μs after the laser pulse under N_2 purge and (B) IV-1 in CH_3CN with 1,4-DCB, taken 0.2, 0.4, 0.8, 1.6, and 3.2 μs after the laser pulse under O_2 purge.

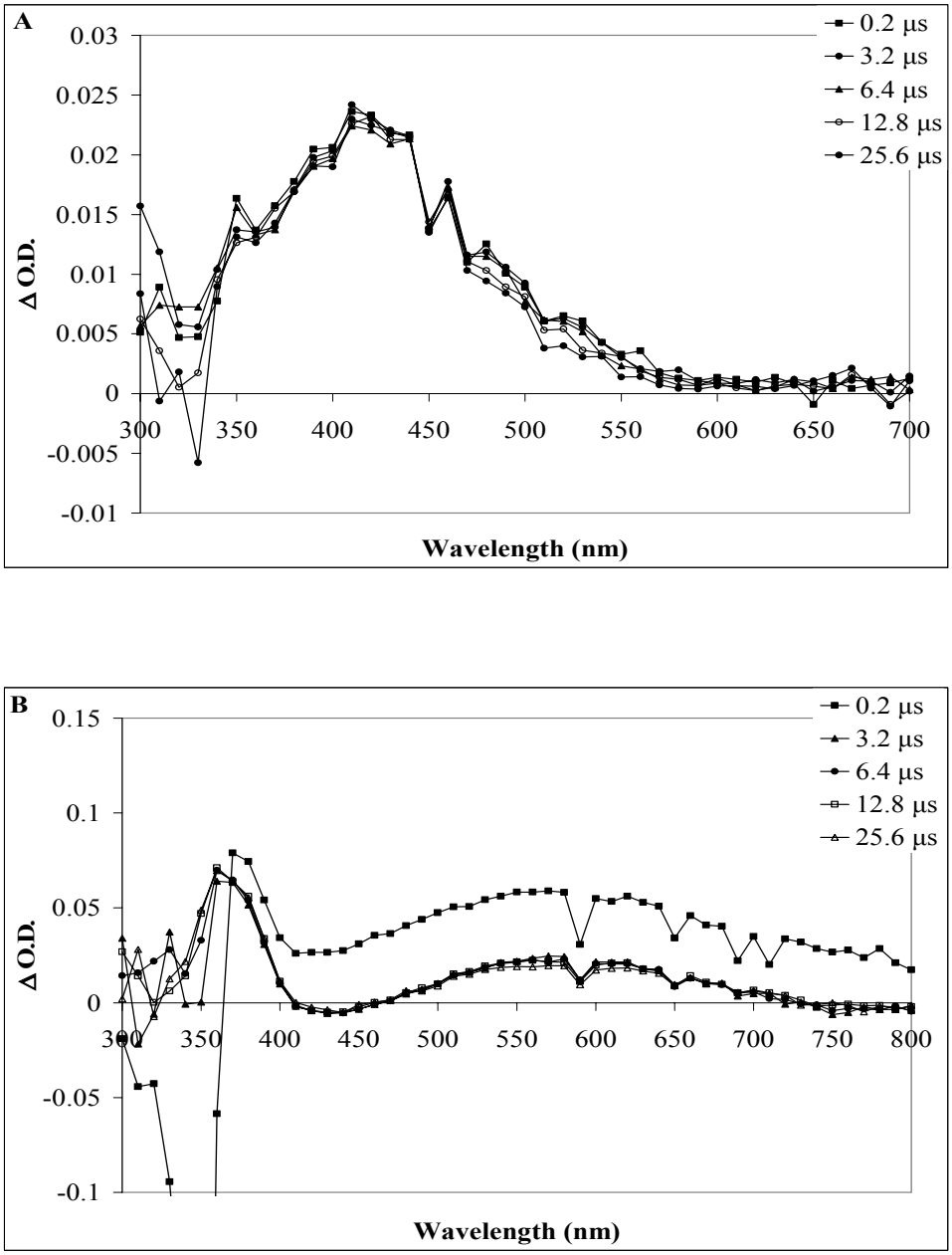


Figure 4.4: Transient UV-vis absorption spectra generated from LFP (266 nm, 4-6 ns, 3-5 mJ/pulse) of (A) IV-27 in CH_3CN/H_2O under N_2 purge and (B) IV-1 in CH_3CN/H_2O with MP, under O_2 purge taken 0.2, 3.2, 6.4, 12.8, and 25.6 μs after the laser pulse.

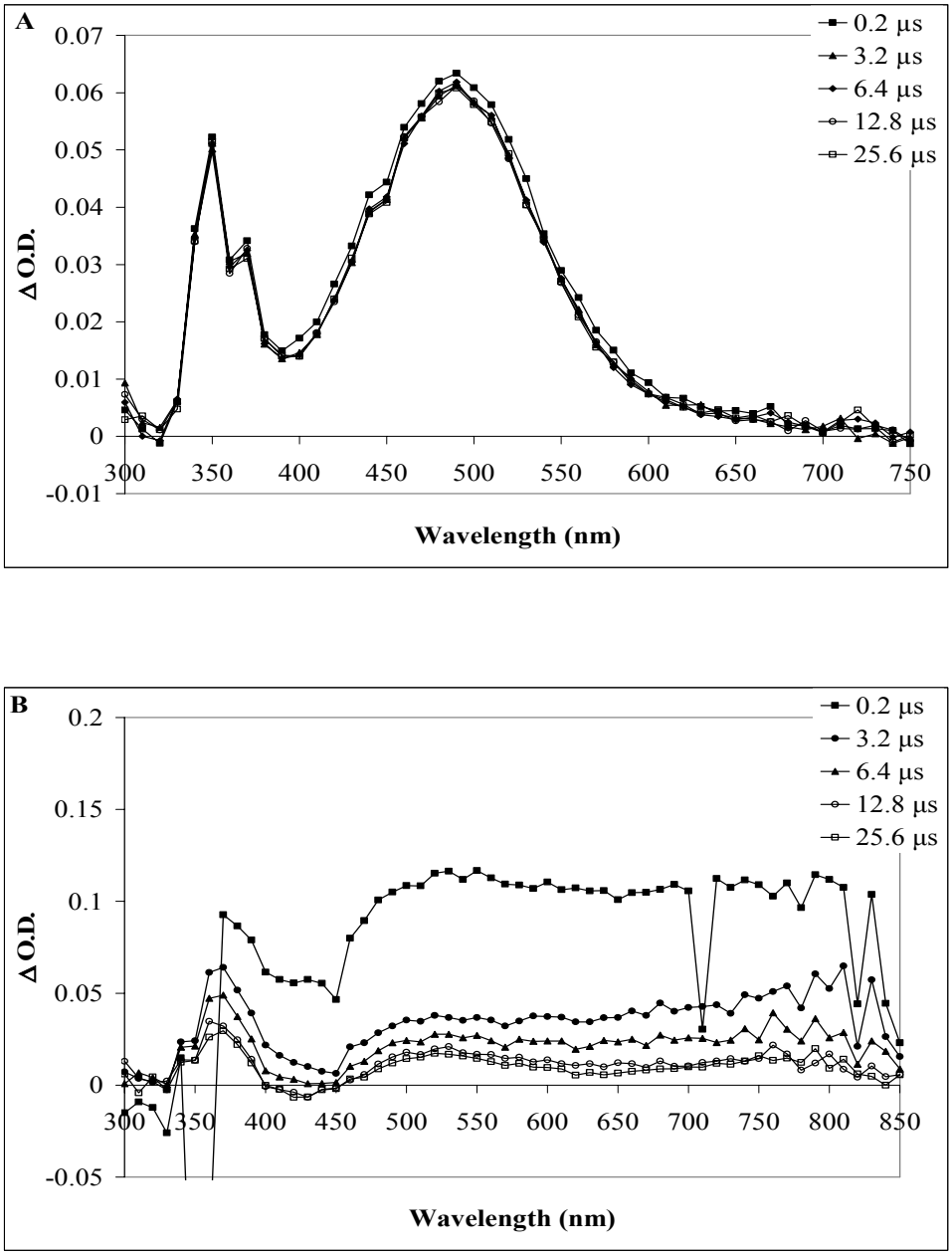


Figure 4.5: Transient UV-vis absorption spectra generated from LFP (266 nm, 4-6 ns, 3-5 mJ/pulse) of (A) IV-27 in CH_3CN/H_2O with acid, under N_2 purge and (B) IV-1 in CH_3CN/H_2O with MP and acid, under O_2 purge taken 0.2, 3.2, 6.4, 12.8, and 25.6 μs after the laser pulse.

The question arose as to the difference in the transient absorption spectra between the CH_3CN/H_2O spectrum and the CH_3CN/H_2O with acid spectrum. To answer this question, the photostability of the 420 nm intermediate under steady-state dark control was studied. The photochemical precursor (**IV-27**) was photolysed in CH_3CN/H_2O and its UV-vis spectrum was recorded after a series of laser pulses. It can be seen from Figure 4.6A that the 420 nm peak grows in as the sample is irradiated with more 266 nm laser pulses. After 1200 laser pulses, the sample was kept in the dark and periodically, its UV-vis spectrum was recorded. It can be seen, in Figure 4.6B, that the maximum wavelength of the intermediate shifted from 420 nm to 444 nm over time. Since the photolysis of the precursor allowed for a limited number of possibilities and that *N*-phenylquinone diimine (PQDI) is a well known oxidation product of ADPA, the 420 nm intermediate was determined to be PQDI.[62,63,130,131,136-140] The presence of PQDI is also supported by previous reports of the UV-vis of a quinine diimine compound centered at 444 nm.[141] Since PQDI can undergo hydrolysis, the intermediate that absorbs at 444 nm was determined to be *N*-phenyliminocyclohexa-2,5-dienone (**IV-29**). The sample was analyzed by mass spectroscopy and the resulting product returned with a mass-to-charge ratio (m/z) of 183.068 which added more evidence that the intermediate that absorbs at 420 nm is able to undergo hydrolysis and was PQDI, as seen in Scheme 4.15. As was shown by Kitani *et al.* and Gospodinova *et al.*, the new peaks in the spectra of Genies and Lapkowski can also be explained by the appearance of the oxidized form of ADPA, i.e. PQDI.[103,142-144] Support for the formation and hydrolysis of PQDI is seen in other cases.[46,145-147]

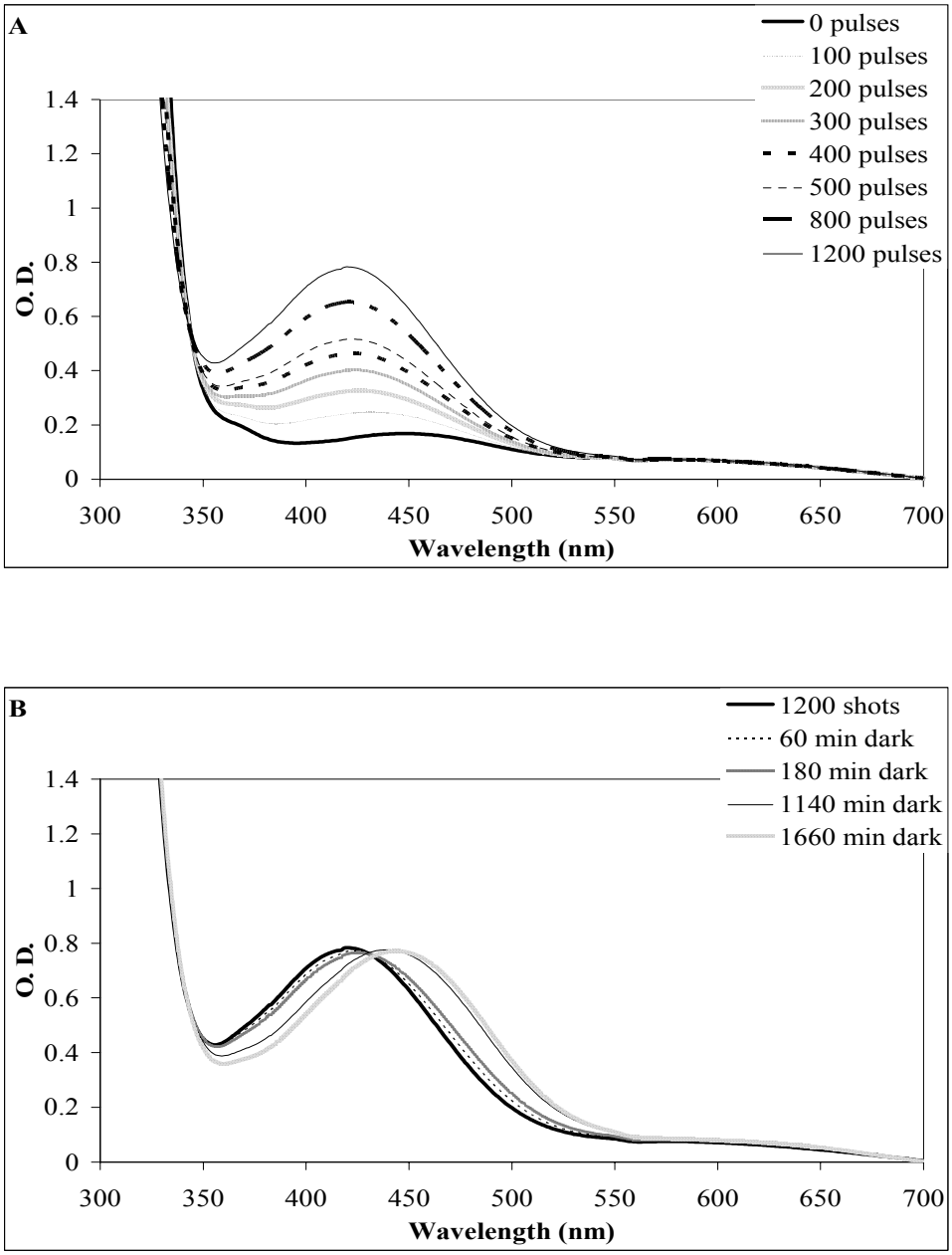
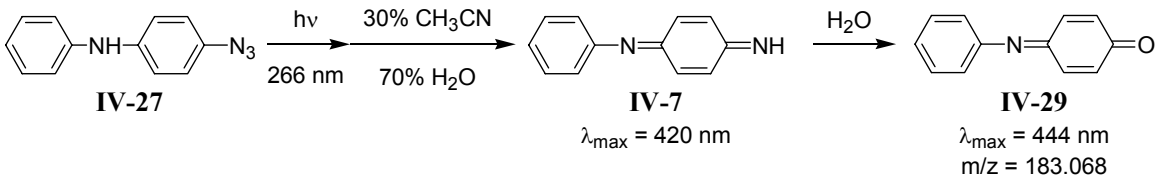


Figure 4.6: Experiment to study the steady-state dark control photostability of IV-7. Upon irradiation of IV-27 in CH_3CN/H_2O there is an increase of IV-7, which over time hydrolyzes to IV-29.

Scheme 4.15: Photoproducts PQDI (IV-7) and 4-phenyiminocyclohexa-2,5-dienone (IV-29).



The proposal that the 420 nm peak observed by Genies was really PQDI and not the nitrenium ion as previously thought has been adopted by Genies and Lapkowski in a subsequent paper.[105] It is interesting to note that in Figure 4.6B there is an isosbestic point at 345 nm. When only two compounds in chemical equilibrium are responsible for whole optical absorption in a given spectral region and the stoichiometry is 1:1, then there will be a wavelength in which the two species absorptivities are equal.[148] In other words, the point at which the spectra of the two species intercross is known as the isosbestic point. While the existence of this point is not proof of the absence of a third compound because the point could present null absorptivity in that particular frequency. The absence of an isosbestic point is definitely proof of the presence of more than two compounds.[148,149]

Another experiment involving the irradiation of the azide (**IV-27**) allowed for the formation of the PQDI at 420 nm, which upon addition of acid, yielded an intermediate that absorbed at 490 nm (Figure 4.7). Upon a subsequent rescan of the spectrum, one can see that the 490 nm peak disappeared and is replaced by an absorption centered at 780 nm, which is characteristic of PANI. PQDI is susceptible to dimerization if it is stored in an acidic medium of a sufficient pH, without the need for an oxidizing agent. This observation was first made by Willstätter and coworkers.[92] Absorption peaks, which are

characteristic of emeraldine salt, can be seen in the spectra at 420-430 nm and 685-750 nm. [8,9] They are due to polaron band transitions in the PANI film. In terms of UV-vis absorption, the position of the exciton band is also dependent on the chain length, as well as on the distribution of benzenoid and quinoid rings.[150] The polymerization conditions determine the structural characteristics, oxidation state, and degree of protonation. The UV-vis absorption spectra of the composite materials are affected by acid/base treatment in the same manner as pure PANI. A shift of about 160 nm of the 784 nm peak occurs over the pH range 1.5-8.5. The shift of this broad transition is primarily responsible for the observed color change of the film (blue to green) associated with changing pH.[151]

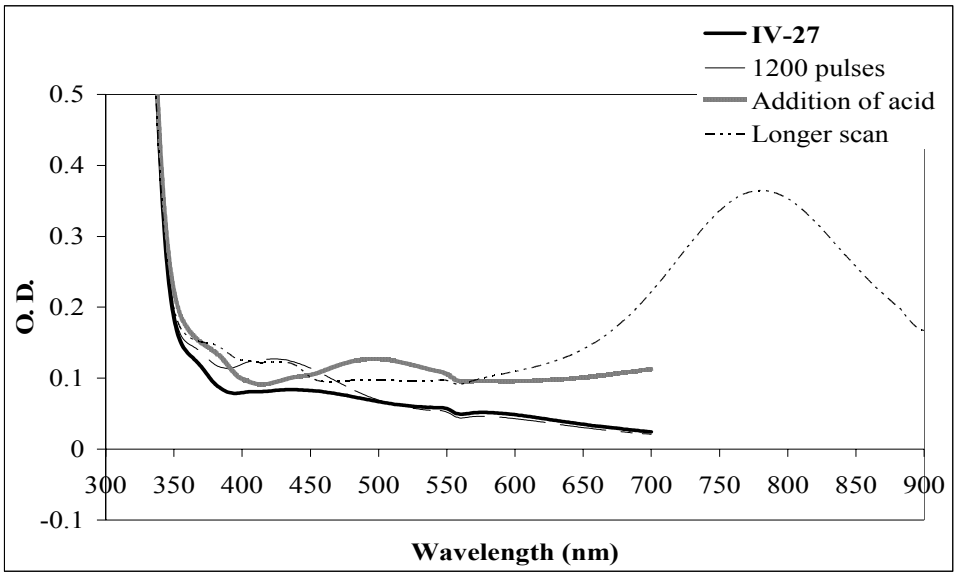


Figure 4.7: Photolysis of 4-(*N*-Anilino)phenyl azide (IV-27) in CH_3CN/H_2O to yield PQDI (IV-7). Addition of acid to yield 4-(*N*-Anilino)phenylnitrenium ion (IV-9) and eventually PANI.

Different polymer conformations are responsible for these two totally different spectra. Three distinctive peaks at 360 nm, 440 nm, and 780 nm are consistent with a localized polaron structure (shorter conjugation length) and a coil-like conformation for the polymer chain, while with a peak at 330 nm and a "free carrier tail", which is consistent with a delocalized polaron band structure (longer conjugation length) and an expanded coil-like conformation for the polymer chain, commencing at ~ 1000 nm which increased steadily in intensity to ~ 2600 nm.[14,152-155]

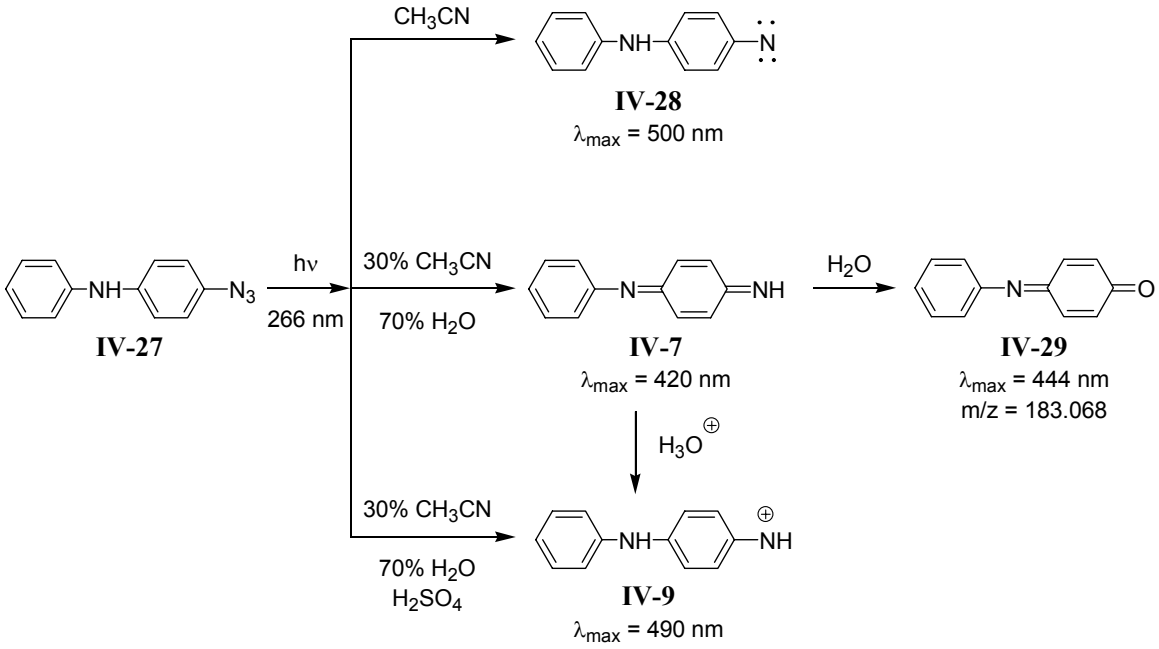
From the optical spectrum it is possible to identify, with reasonable accuracy, the oxidation state of PANI.[15] In its reduced leucoemeraldine form an absorption band at 320 nm is observed. The conducting emeraldine and the fully oxidized pernigraniline forms exhibit absorptions between 400 and 800 nm.[74]

The maximum absorbance due to dark green PANI occurs at 720 nm and agrees with published spectra of PANI films formed in H_2SO_4 with bands around 750 nm.[101,119,156,157] As the visible absorption spectrum of PANI is different for different oxidation states.[158,159]

With all of these results in hand, the photolysis pattern can be summarized in Scheme 4.16. In polar aprotic solvents, photolysis yields the corresponding nitrene and ring expansion products. In a polar weakly protic solvent system, PQDI (absorption maximum at 420 nm) is formed which can then undergo hydrolysis over time to 4-phenyliminocyclohexa-2,5-dienone (absorption maximum at 444 nm). In a polar strongly protic solvent system, when acid is present, the nitrenium ion formed by azide precursor with absorption maximum at 490 nm. PQDI can also be made *in situ* and then addition of

acid also produces the nitrenium ion, which quickly undergoes polymerization as seen by its UV-vis absorption bands.

Scheme 4.16: Summary of photolysis of IV-27 in different solvent systems and the intermediates they produce.



During oxidative condensation of aniline, the solution progressively becomes colored and yields a black precipitate. The coloration of the solvent is probably due to the soluble oligomers. The intensity of coloration depends on the nature of the medium and the concentration of the oxidant.

The properties of the obtained PANI depend strongly on the type of the oxidizing agent, solvent, temperature, electrode potential, the type of the electrode, pH, etc.[119] A transient absorption band in the visible spectrum, 720 nm, of the oxidized form of PANI was observed by Shim *et al.*[101] Moreover, it has been reported that the conductivity of

some conducting polymers depends strongly on the redox state, the doping level, and moisture content of the polymer matrix.[160]

Observing the formation of PANI on the basis of its UV-vis spectrum is difficult because the electronic spectra change regularly with the ratio of benzenoid to quinoid phenyl ring units as the visible absorption spectrum of PANI is different for different oxidation states.[159,161] Many wavelengths have been published include three absorbance peaks at 410, 800, and 1100 nm on the spectrum which is in accord with the spectrum of PANI with the chloride counterion.[158,159,161]

A wide range of colors from pale yellow to blue for both thin and thick polymer films on various types of electrodes have been observed such as blue with a thin layer of green product on the surface.[12,22,36,60,61,65,162] Analysis has revealed that the green product has a well-defined polymeric structure with the polymeric charges perfectly delocalized over the polymer backbone, whereas the blue product has chemically different nitrogen atoms. Recent Raman spectroscopic studies by certain authors have revealed that significant changes in absorption occur both in the near-IR beyond 800 nm and in the UV regions below 300 nm as the oxidation state of the film is changed. The oxidation and the reduction of PANI can be effected chemically or electrochemically, regardless of the method employed for the synthesis.[163] This series of color changes was also seen with all samples upon addition of acid then addition of base.

4.4.2: Analysis of Precipitated Photoproducts

Analysis of photoproducts may be difficult but modern analytical methods including matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS), X-ray photoelectron spectroscopy (XPS), X-ray diffraction (XRD) spectroscopy, and infrared spectroscopy (IR) can aid in the determination the product formed. However, the majority of authors admit that the characteristics of the polymer depend of the mode of synthesis.[28]

4.4.2.1: Matrix-Assisted Laser Desorption/Ionization Mass Spectrometry (MALDI)

In 1987, a new method for the determination of the molecular mass of polymers, matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS) was developed.[164] It has been noted that MALDI-TOF-MS is a direct, accurate, and rapid tool for the analysis of monodispersed PANI oligomers.[165] MALDI coupled to time-of-flight (TOF) has become the major method of analyzing synthetic polymers with mass spectrometry.[166,167] This analytical technique generates a mass spectrum that can give information about repeat units, end groups, and the molecular weight distribution of the polymer.[168,169] Intact, singly charged gas-phase ions of high molecular weight analytes are generated with this technique when utilizing proper sample preparation methods. In the current study, the products of photolyses were analyzed by MALDI to determine if PANI was actually formed.

The determination of a polymer's characteristics, both in structure and properties, is not always easy. One of the main problems related to the characterization of conducing polymers is the determination of their molecular mass and polydispersity because of the unsuitability of standard methods (gel permeation chromatography, vapor-phase deposition, etc.) for their determination.[170] Futhermore, as only a small part of the polymer is dissolved, this will probably correspond to the shortest chains, and then, even if the concentration is high enough to obtain a correct detection, the molecular mass obtained will be lower than the real value.[30] One would observe low MALDI peaks because of solubility issues.

The most important aspect of this experiment is the sample preparation process. In the most commonly employed technique, the "dried droplet method", the polymer is dissolved in a few microliters of a suitable solvent and then diluted with excess matrix solution.[171] Approximately one microliter of this final solution is spotted onto the sample plate and allowed to air dry. One of the major problems with this technique involves sample and matrix solubility and compatibility with each other. In order for them to co-crystallize on the sample plate, they must both be uniformly dissolved in the solvent system. For insoluble or slightly soluble samples, this becomes a major problem that leads to sensitivity, selectivity, and reproducibility issues.[172]

One of the main experimental parameters which must be optimized is the matrix used to provide the ionization of the sample, which has to be compatible with the sample in the solid state in order to provide a good mixture with the analyte. It also has to exhibit high electronic absorption at the laser wavelength (337 nm) resulting in good desorption/ionization of the sample. Another important factor to be controlled is the

solvent used in the deposition of the sample. An appropriate choice has to be made, because of the possible incompatibility of the solvent with both the sample and the matrix and in order to avoid any discrimination of molecules with different molecular masses or structures.[173,174] In these studies, the acidic matrix 2,5-dihydroxybenzoic acid (DHB) was used and the solvents used included 1-methyl-2-pyrrolidinone (NMP) and methansulfonic acid (MSA). The last two were employed because of their ability to dissolve PANI although they have high boiling points, thus making the evaporation of the solvent from the matrix-sample system difficult. Samples were prepared in two different ways. The first method was prepared by mixing equal parts of a solution of the polymer and a solution of the matrix being used. The second method was prepared by adding a solution of the sample to about 10 mg of the solid matrix. A two microliter volume of the final solution was then deposited on a stainless-steel sample holder and the solvent was evaporated in an oven at 35ºC.[175] Samples were prepared in both ways with both solvents and it was found that the use of NMP provided the best MALDI spectra as shown in the following Figures 4.8 and 4.9.

To demonstrate the ease of the photolysis, a hand-held short wave UV lamp was used to run the photolyses and two trials were run. The first trial was with the addition of acid just prior to the photolysis and the second trial was with the addition of acid just after photolysis. MALDI was run and the results are shown in Figures 4.8 and 4.9. From the MALDI one can see many major mass-to-charge (m/z) ratio distributions are present from four aniline units with a m/z ratio of 366 to nine aniline units with a m/z ratio of 824. Higher m/z values are also seen, but in much smaller intensities. These molecular weights are shown to be in agreement with previous studies on PANI and the

possible structures are shown in Figure 4.10. The fact that these two methods produce similar MALDI spectra show the versatility of nitrenium ions generated through photolysis.

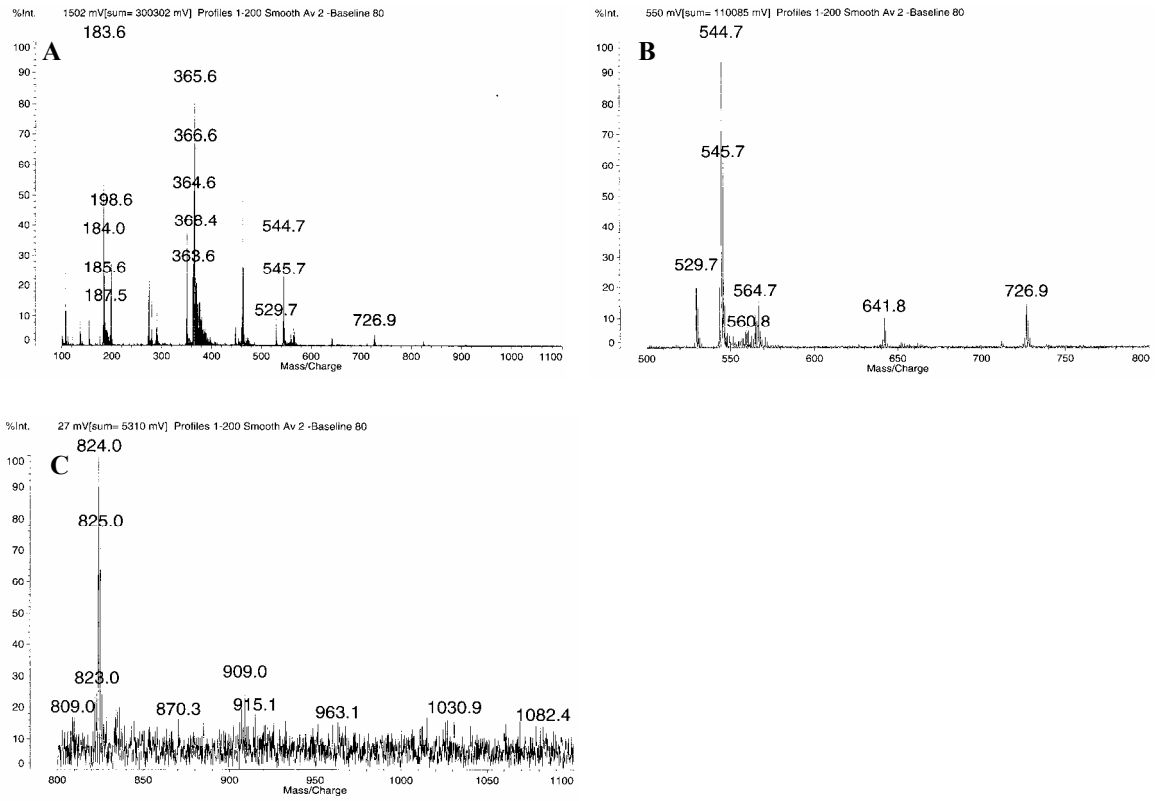


Figure 4.8: MALDI-TOF-MS spectra from the photolysis of 4-(*N*-anilino)phenyl azide (IV-27) in CH_3CN/H_2O with addition of TFA pre-photolysis.

Any peak in the MALDI is surrounded by a series of peaks differing from each other by one mass unit. This indicates that the theoretical distribution of benzenoid and quinoid units and that there are some molecules with slightly different distributions. Differences of +16 and -16 mass units and according to the structure of the sample, these differences can correspond to NH_2 groups. It is logical to think that the groups at -16

units may be due to the loss of a final amine group during fragmentation of the sample in the desoprtion/ionization process, although MALDI is a relatively soft ionization process.

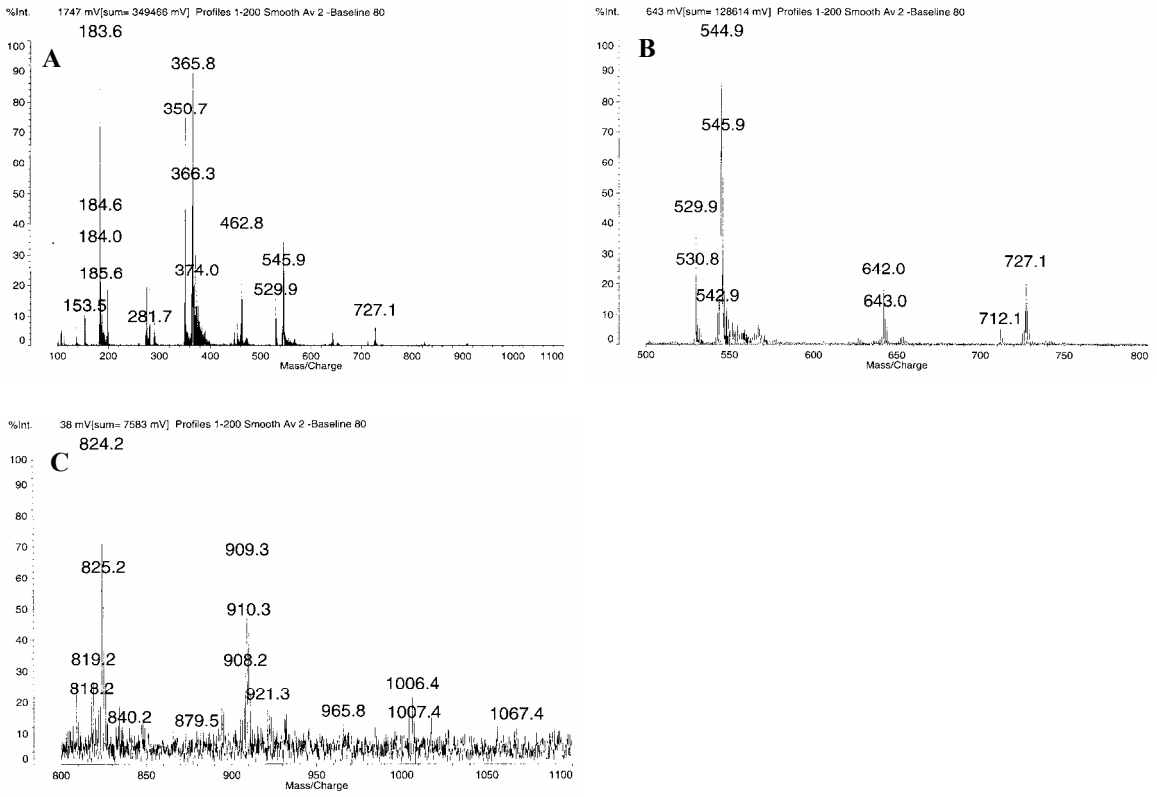


Figure 4.9: MALDI-TOF-MS spectra from photolysis of 4-(*N*-anilino)phenyl azide (IV-27) in CH_3CN/H_2O with addition of TFA post-photolysis.

The group at +16 units, correspondingly, should then be due to the loss of the final benzene group of the immediately higher oligomer in the fragmentation process. The series of peaks at differences of 14-16 mass units higher and lower from the main distribution, may be from fragmentation of the polymer during the desorption/ionization process. This spectrum shows that different oxidation states of each oligomer are present in the sample, as is shown by the two mass unit differences around major peaks. This is a

result of a benzenoid unit being converted into a quinoid unit with a subsequent loss of two protons or vice versa. The hydrogen ion in all of these structures is probably present on any one of the nitrogen atoms along the oligomer backbone, resulting in a positively charged quartenary nitrogen. The exact sequence of the benzenoid and quinoid units cannot be determined from these experiments and their location is arbitrarily shown in the structures in Figure 4.10. The peak present at m/z of 529.7 in Figure 4.8B can be assigned to the pentamer with an additional phenyl ring, which is due to the loss of the terminal aniline plus amine group. Another peak is assigned to the structure of the nine-mer with a terminal amine group that corresponds to 825 mass units.

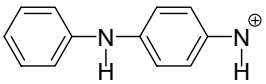
Therefore, there are a myriad of possible chemical structures for the polymeric backbone of PANI. Elucidation of the precise molecular arrangement is complicated by the fact that these structures are affected by both electronic excitation and reduction and by concomitant protonation and deprotonation of the nitrogen atoms in the polymer.

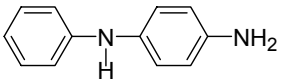
Although promising, the molecular mass obtained for the highest oligomers detected is lower than could be expected for these types of polymers, making any estimation of polydispersity impossible. This result could be due to poor dissolution of the high molecular mass polymer, fragmentation of the polymer under the experimental conditions, and poor volatilization of the high mass chains because of aggregation.[175]

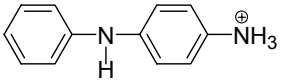
Analysis by mass spectrometry is challenging because of its poor solubility in conventional solvents. A few reports on the analysis of PANI with conventional spectrometry have been published over the last decade.[175-178] All of these results yielded low molecular weight oligomers, with molecular weights less than 2500 mass units. Room temperature synthesis of PANI, without the use of an ice bath results in the

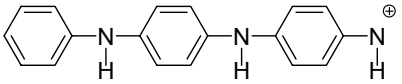
production of a larger quantity of lower molecular weight oligomers than the conventional synthesis. Another interesting result is the fragmentation occurring in the phenyl ring with the loss of one of the carbon atoms, followed by a rearrangement in order to produce a terminal five-membered ring as seen with the m/z of 712 in Figure 4.10.[179] It is possible for a loss of a methylene group and rearrangement to form a 5-membered ring because the synthesis of PANI is an extremely exothermic reaction that could supply enough energy to cleave the benzene ring.[180]

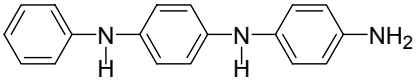
Another challenge using MALDI for the determination of PANI structures is that PANI has multiple protonation sites, such as neutral amine nitrogens or imine nitrogens. The protonation of these sites would increase both the oligomer's mass and charge by one, but would have a dramatic effect on the mass-to-charge ratio. An increase in the charge from one to two essentially halves the mass of the oligomer. Therefore, higher molecular weight oligomers may be hidden and mistakingly reported as lower weight oligomers. Such examples can be seen in the last three entries in Figure 4.10.

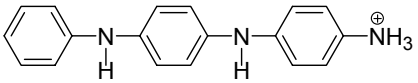
183 

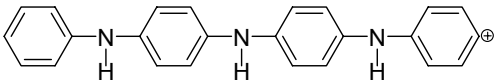
184 

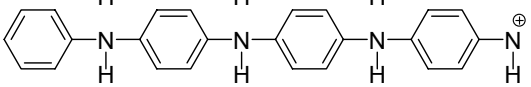
185 

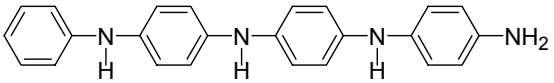
274 

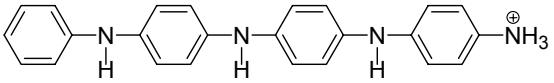
275 

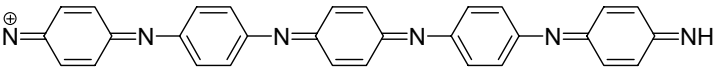
276 

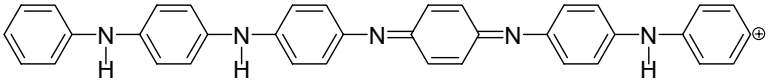
350 

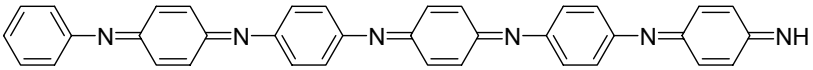
365 

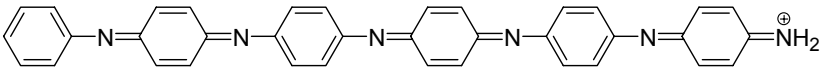
366 

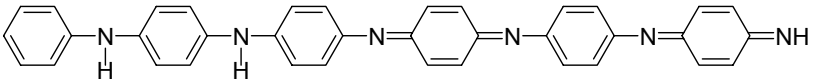
367 

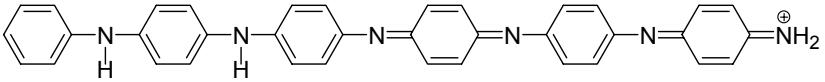
465 

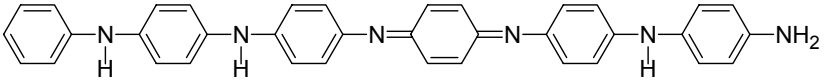
530 

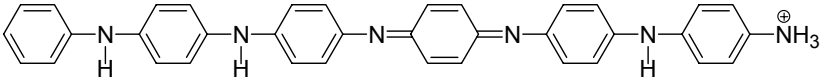
542 

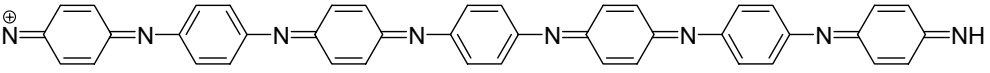
543 

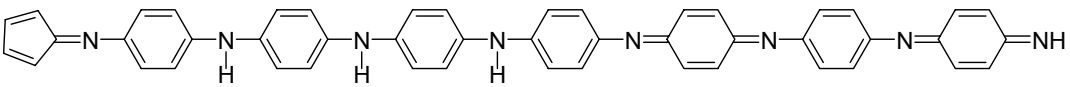
544 

545 

546 

547 

645 

712 

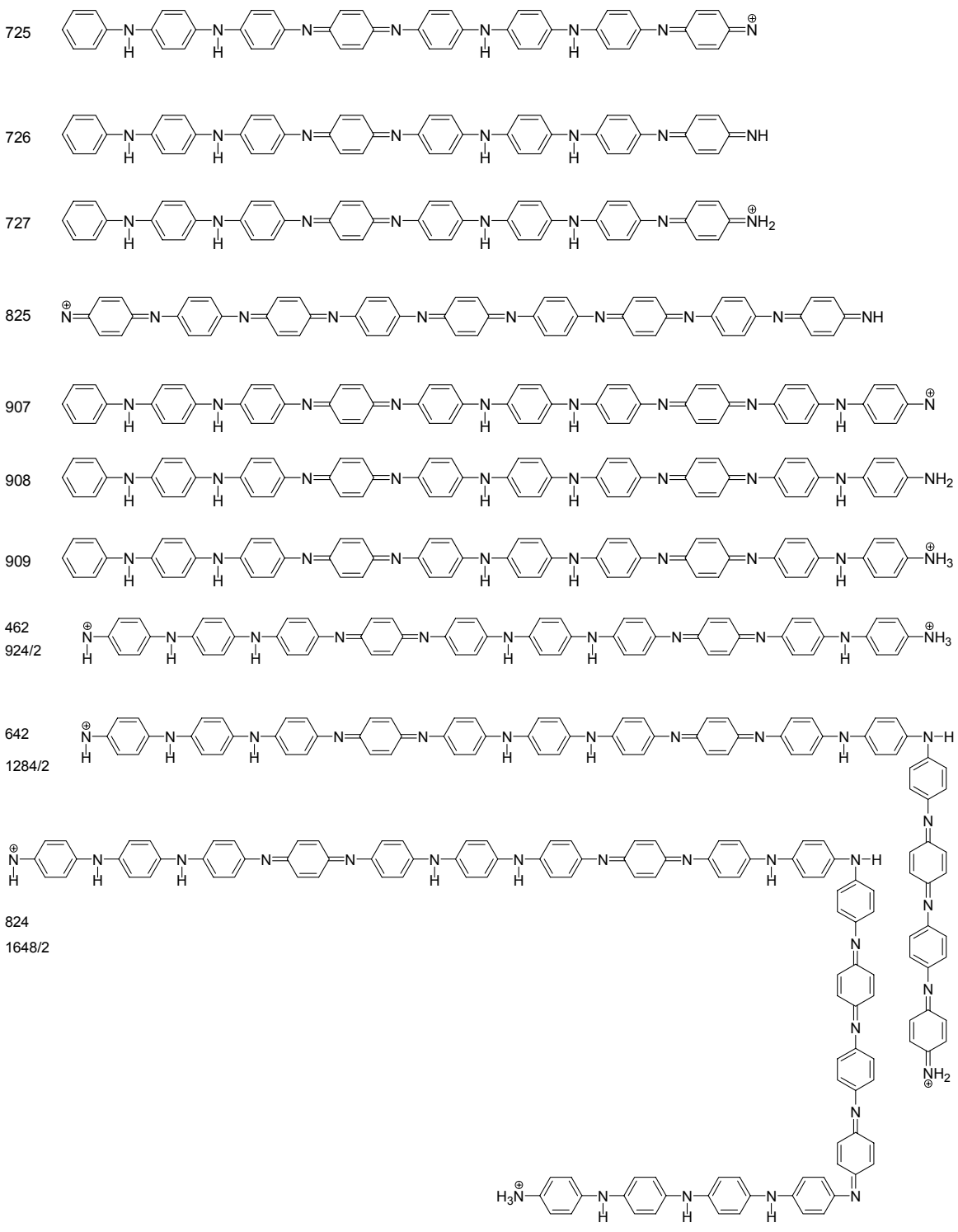
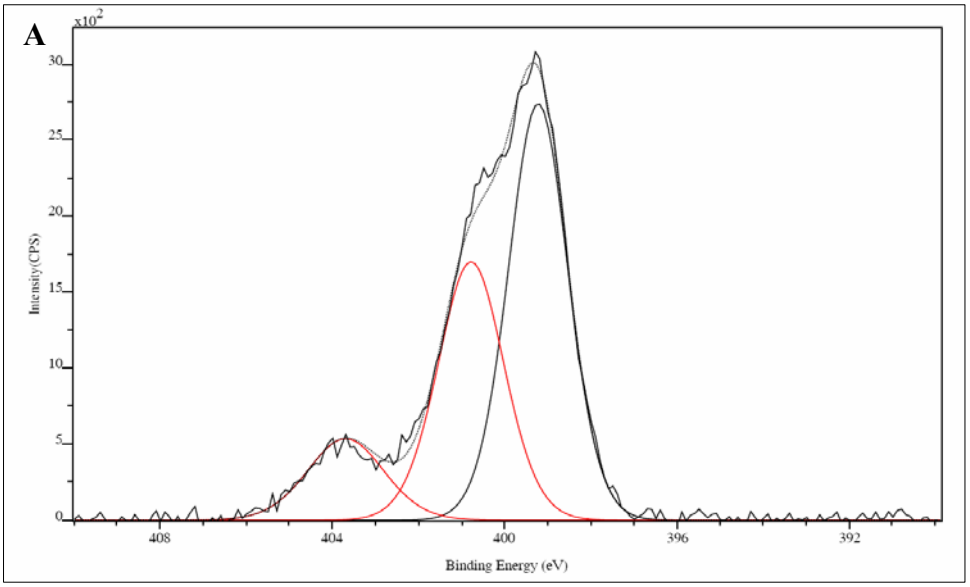


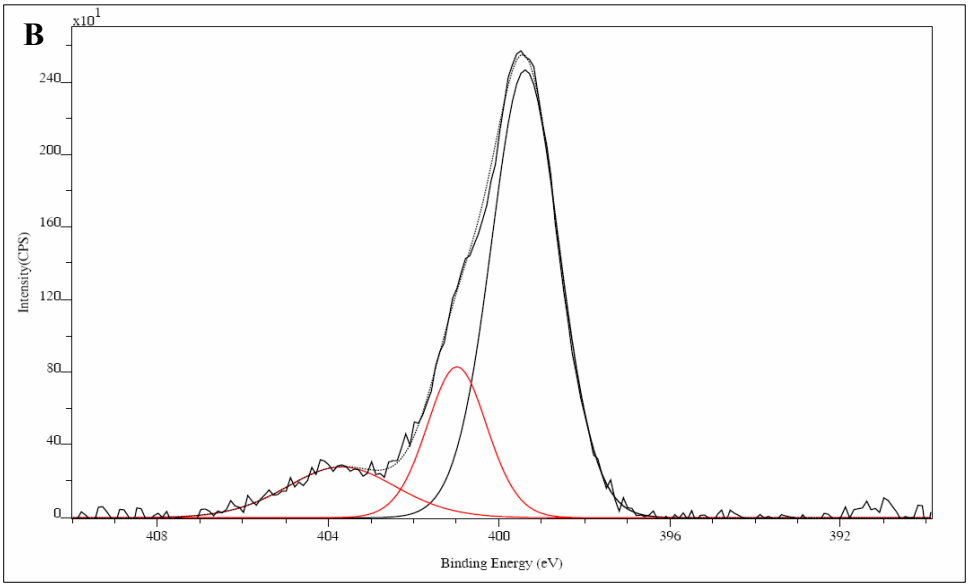
Figure 4.10: Postulated structures of PANI based on experimental mass-to-charge ratios, which are listed to the left of the structures.

4.4.3.2: X-ray Photoelectron Spectroscopy (XPS)

To provide additional evidence for the formation of oligomers of PANI, X-ray photoelectron spectroscopy (XPS) was utilized. From the XPS data, the binding energies of the core nitrogen (N) 1s and core carbon (C) 1s orbitals were obtained from three different sample of photochemically initiated polymerization of aniline. The photolysis was carried out in the similar fashion with a hand-held UV-lamp and the acid used was varied from trifluoroacetic acid (TFA) to hydrochloric acid (HCl) to sulfuric acid (H_2SO_4). The binding energies from all the acids gave similar binding energies to previously published binding energies of PANI.[92,181-184] Another useful point from XPS is that it can determine the type of nitrogens are in the sample. The protonation and/or oxidation to form the emeraldine salt can be followed by N 1s XPS investigations conducted on differently doped materials, as shown in Figures 4.11 A-C. The observed peaks can easily be assigned to nitrogen atoms with imine bonds (Eb = 398.1 eV), nitrogen atoms with amine bonds (Eb = 399.3 eV) and nitrogen atoms that are oxidized or protonated (Eb > 400.5 eV).[92] The experimentally observed N 1s binding energy are listed in Table 4.1.

Volkov *et al.* have confirmed these conclusions by carrying out studies on the oxidation products of aniline in spectroscopic and XPS methods.[131] The spectra of the anodic oxidative products of aniline are identical to those of the chemically prepared emeraldine. Using XPS spectroscopy, Volkov *et al.* have also identified ADPA as an intermediate product, thus reinforcing Mohilner's results.[37,131] The polymerization mechanism of aniline is more complex in acid medium than in basic medium since the aniline monomer can act as a base and deprotonate its own radical cation.


A
x10^2
30
25
20
15
10
5
0
Intensity(CPS)
408
404
400
396
392
Binding Energy (eV)


B
x10^1
240
200
160
120
80
40
0
Intensity(CPS)
408
404
400
396
392
Binding Energy (eV)

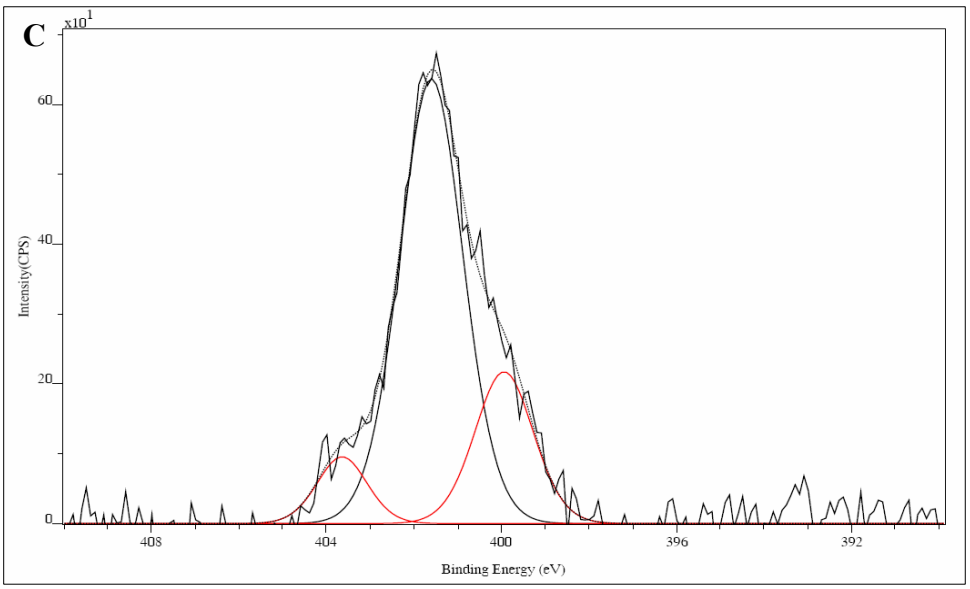


Figure 4.11: Experimentally observed N 1s XPS spectra of the photolysis of 4-(*N*-anilino)phenyl azide (IV-27) in CH_3CN/H_2O with post-photolysis addition of (A) HCl, (B) TFA, and (C) H_2SO_4.

Table 4.1 Experimentally observed N 1s XPS binding energies of the photolysis of photolysis of 4-(*N*-anilino)phenyl azide (IV-27) in CH_3CN/H_2O with post-photolysis addition of (A) HCl, (B) TFA, and (C) H_2SO_4.

Acid Used	N 1s Position Eb (eV)
HCl	399.2, 400.8, 403.7
TFA	399.4, 401.0, 403.7
H_2SO_4	399.9, 401.6, 403.6

It is evident that in all the cases the N 1s signal does not originate from a single nitrogen environment. A standard peak shape analysis with Gaussian fitting functions reveals that, in all three spectra, this peak can be resolved into three peaks. It is well documented that 398.5 eV is attributed to the neutral imine nitrogen. Although this imine binding energy is not overly expressed, the imine nitrogen may be present and have a different energy upon protonation. This is entirely consistent with the reports that the imine units of the polyemeraldine base are preferentially protonated by HCl and also gives further confirmation to the present peak assignments.[11,35] It was shown that the proportion of amine, imine, and positively charged nitrogen in PANI complexes could be quantitatively differentiated in the properly deconvoluted N 1s XPS core-level spectrum.[181]

The neutral amine nitrogen atoms was assigned to the peak at 399.5 eV and the higher binding energy peaks may be assigned successively to the increasingly positively charged nitrogen species.[184] The intensity of the 399.5 eV peak is at a maximum in the TFA sample and decreases in HCl and H_2SO_4. Published XPS N 1s spectrum of the freshly prepared leucoemeraldine sample exhibits only a single nitrogen environment at a binding energy of 399.3 eV, which is characteristic of the amine structure.[150,183,185,186]

The binding energies of 398.5, 399.5, 400.8, 402.2 eV correspond to N_1, the neutral imine nitrogen, N_2, the neutral amine nitrogen, N_3, delocalized polaron-type nitrogen, and N_4, the protonated imine nitrogen (localized bipolaron-type nitrogen), respectively as shown in Figure 4.12.

As for the C 1s spectra of the three samples (Figures 4.13 A-C), it is evident that in all the cases there are multiple contributions to the observed C 1s signals. The

published peaks include 284.5, 285.4, 286.4, and 287.4 eV and are seen in the experimental photoproducts (Table 4.2).[183,184] The first peak at the lowest binding energy is due to the neutral C-C or C-H bonds. The second peak at 285.4 eV is attributed to the carbon bonded with the neutral nitrogen atoms in N_1 and N_2 (Figure 4.12). Analogous to the N 1s peak assignment, the carbon atoms bonded to the polaronic type of nitrogen atoms could be attributed to the C_3 peak and the carbon atoms bonded to the N_4 type of nitrogen atoms are assigned to the C_4 level.[184]

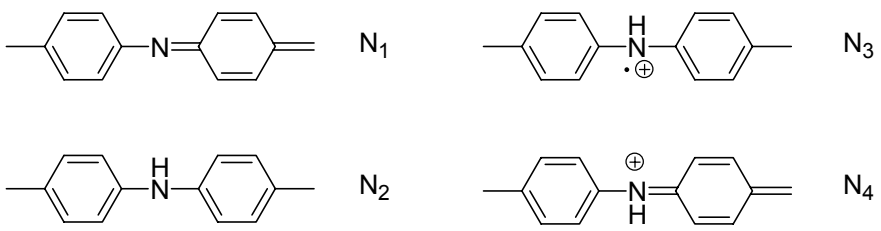
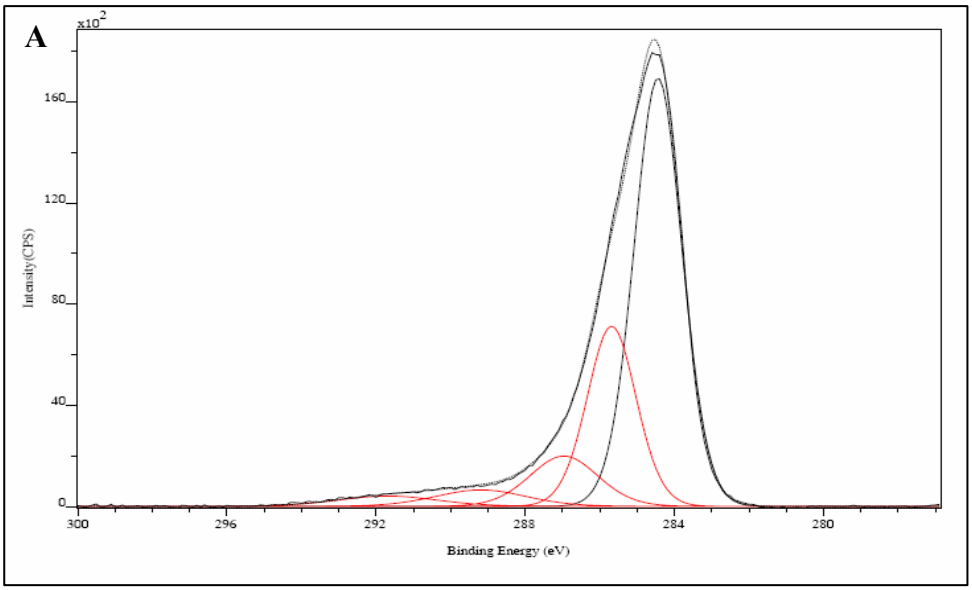
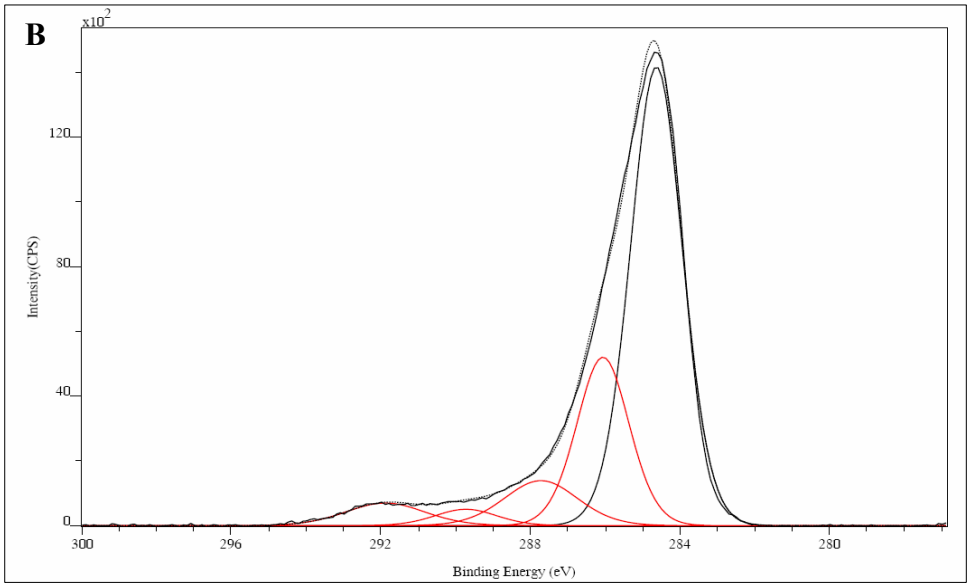


Figure 4.12: Proposed electrostatically inequivalent groups of nitrogen created in PANI.


A
x10^2
160
120
80
40
0
Intensity(CPS)
300
296
292
288
284
280
Binding Energy (eV)


B
x10^2
120
80
40
0
Intensity(CPS)
300
296
292
288
284
280
Binding Energy (eV)

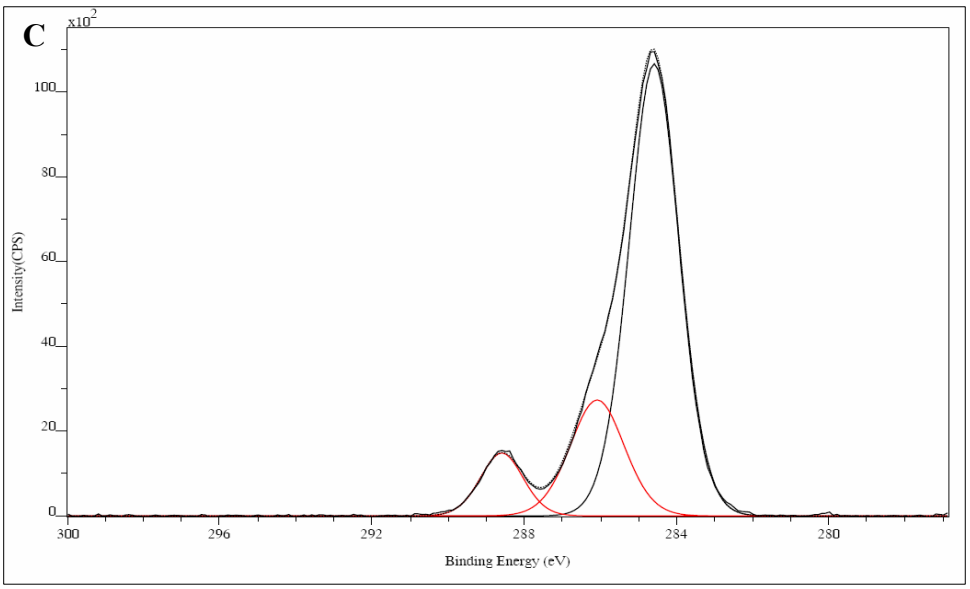


Figure 4.13: Experimentally observed C 1s XPS spectra of the photolysis of 4-(*N*-anilino)phenyl azide (IV-27) in CH_3CN/H_2O with post-photolysis addition of (A) HCl, (B) TFA, and (C) H_2SO_4.

Table 4.2: Experimentally observed C 1s XPS binding energies of the photolysis of photolysis of 4-(*N*-anilino)phenyl azide (IV-27) in CH_3CN/H_2O with post-photolysis addition of (A) HCl, (B) TFA, and (C) H_2SO_4.

Acid Used	C 1s Position Eb (eV)
HCl	284.4, 285.7, 286.9, 289.2, 291.8
TFA	284.7, 286.1, 287.7, 289.8, 291.9
H_2SO_4	284.6, 286.1, 288.6

The presence of the N_4 peak in the N 1s spectra in all of the three films suggests that the positive charge over the bipolaron nitrogen does not delocalize to the adjacent quinoid structure via conjugation. The N_4 peak is due mainly to the defect-induced

quinoid sites in the polymer chain. The lowest energy peak in the C 1s spectra at 284.5 eV is due to the C-H group in the aromatic ring.[184]

4.4.3.3: X-ray Diffraction Spectroscopy (XRD)

One of the greatest barriers limiting the information abstracted using conventional structural techniques such as X-ray diffraction spectroscopy (XRD), is the amorphous character of this polymer. Yet, Baughman *et al.* have recently used X-ray diffraction data to elucidate crystal structures of perchlorate and tetrafluoroborate salts of PANI.[187] They propose ring positions having a dihedral angle of +15 and -15 (alternately) with respect to a planar zigzag chain made by the nitrogen atoms.

Although mostly amorphous, XRD patterns for PANI have been reported in the literature. The experimentally produced PANI XRD patterns were run and compared to those published. The main reflections and angle of diffractions (2Θ), shown in Figure 4.14, were observed and are equal to 15.9º, 18º, 19.4º, 20º, 25º and are similar to published values.[92,188] The experimental XRD patterns also look similar to *in situ* doped PANI with toluene-4-sulfonic acid (TSA) with broad peaks at 2Θ equal to 13º, 20º, 25º, arising on an amorphous halo. Such a diffraction pattern is characteristic of doped PANI.

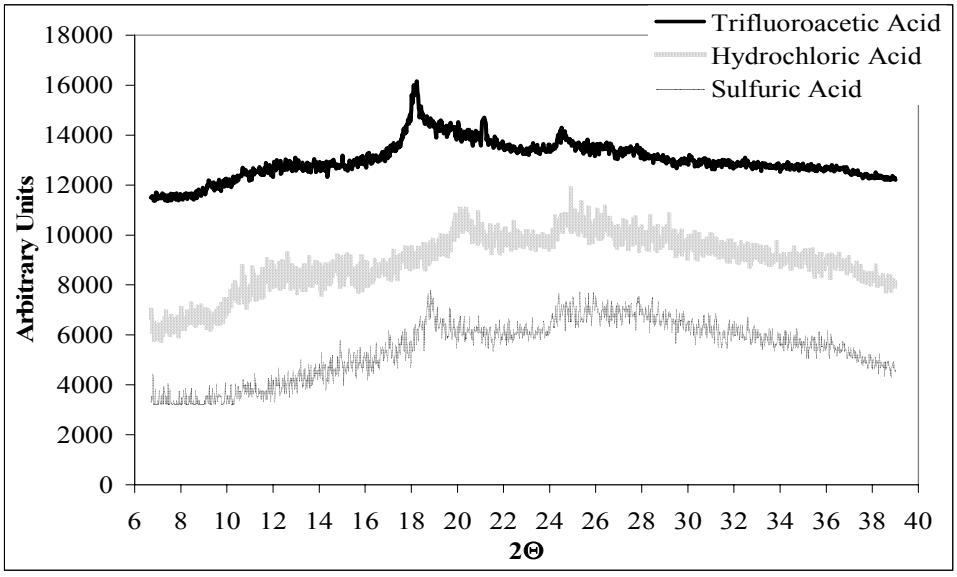


Figure 4.14: Experimentally observed X-ray diffraction spectra of the precipitates from the photolysis of 4-(*N*-anilino)phenyl azide in CH_3CN/H_2O with post-photolysis addition of (A) TFA, (B) HCl, and (C) H_2SO_4.

The angle of diffraction may not be as exact as the published results, but this may be due to that fact that the conducting form of PANI is suggested to be a "polaronic metal" where the defects (unpaired electrons and positive charges) are delocalized over the whole, undisturbed conjugation length resulting in semiquinoid distortions for all the ring structures ("polaron lattice").[16,189] X-ray methods have yielded general information on the bulk material but structural assignment at the molecular level is still somewhat controversial. It is the amorphous character of the polymer and the particular acid used and polymer process employed can affect the degree of crystallinity that limits the information that can be extracted using conventional structure-analysis methods.[57,190-192]

4.4.3.4: Infrared (IR) Spectroscopy

Infrared spectroscopy (IR) is another useful and well documented tool in examining the structure of PANIs. The literature puts forth that emeraldine has peaks that occur at approximately 1595, 1500, 1300, 1170, and 830 cm^{-1}.[37] For nigraniline the peaks occur at approximately 1590, 1502, 1305, 1150, and 830 cm^{-1}.[37] The major benzene breathing mode near 1590 cm^{-1} for the free amine can shift to lower frequency by about 30 cm^{-1} for salts.[193] For HCl doped sample, strong ammonium salt bands at 2892 and 2591 cm^{-1} and weak bands at 3401 and 3382 cm^{-1} characteristic of NH stretching modes in the neutral amine group were observed. Major peaks observed for oligomers were 1574, 1504, 1312, 1256, and 820 cm^{-1}, almost independent of the degree of oxidation.[159]

The IRs of experimentally photochemically induced PANI are shown in Figures 4.15 and 4.16 and look similar to those published of typical of polyemeraldine salt.[92,94,159,194-196] Their wavenumbers of importance are listed in Table 4.3 with published PANI wavenumbers and their interpretations.

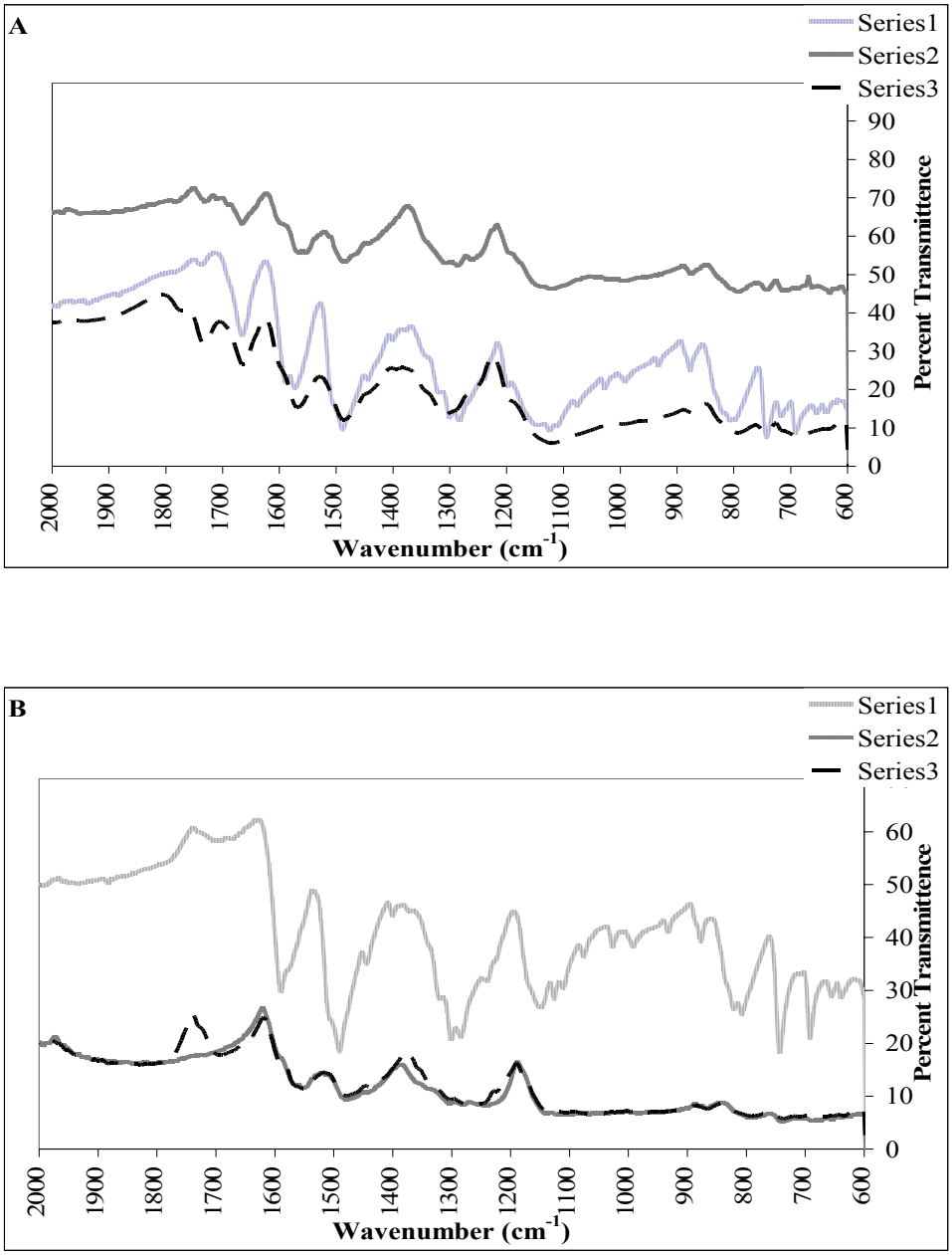
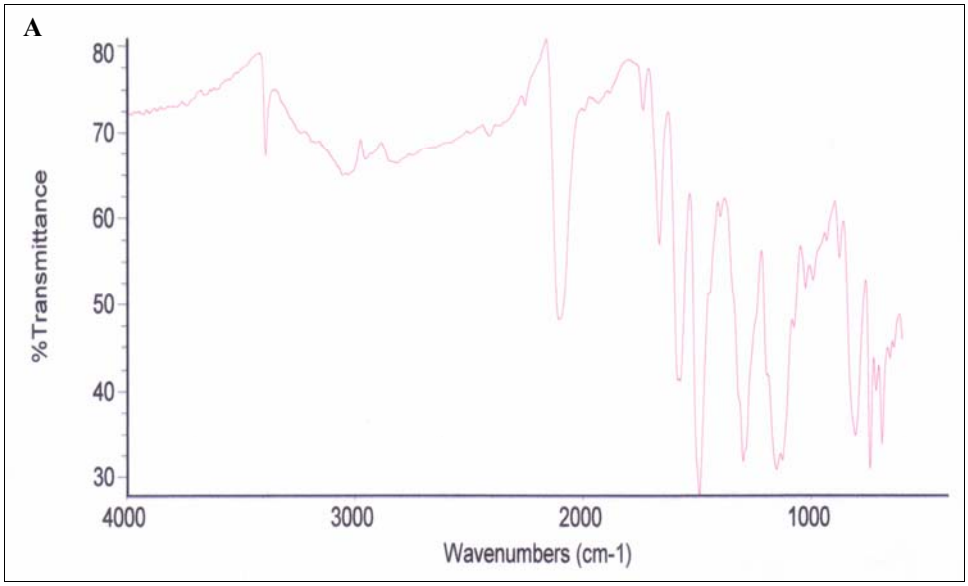
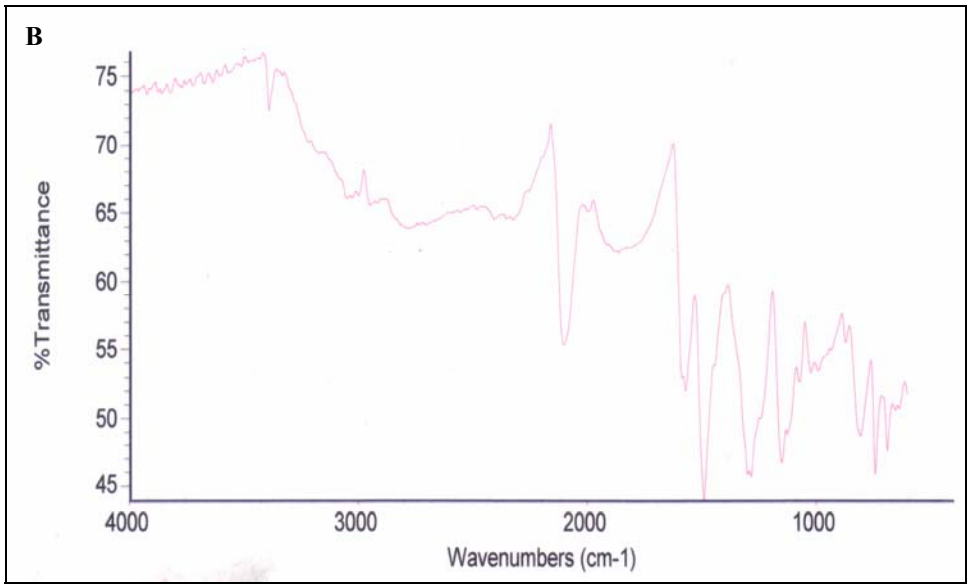


Figure 4.15: IR of photolysis product with addition of (A) TFA and with (B) HCl.





Figures 4.16: IR of photolysis product with addition of (A) TFA and with (B) HCl.

Table 4.3: Experimental and literature IR values.

Wavenumber (cm^{-1}) Experimental	Wavenumber (cm^{-1}) Published	Interpretation
1376, **1261**	1650, **1380**, 1355, 1319, 1311, 1310, **1260**, 1250	-C=N stretching
3392, 3386, **3315**	**3400**, 3310, **3300**-3200, 3000- 2860	-N-H stretching
1150, **1149**	1160, **1155**, **1150**, **1148**	C-H in-plane stretching
1589, 1578, 1571, 1567, 1563, 1534	1600, **1591**, 1510, 1502, 1500	Benzenoid ring stretching
877, **830**, **808**, **806**, **805**	**860**, 843, **830**, **810**, **800**	C-H out-of-plane stretching
1589, **1490**, **1488**	1610, **1600**, **1578**, 1502, **1500**, **1480**	quinoid ring stretching
3469, **3463**	**3460**	NH_2 asymmetric stretching
1030, **1002**, 999	1220, 1105, **1010**, 830	1,4-substitution C-H in plane stretching
821	843, 831, 828, **823**, 818	C-H out-of-plane bending
1150, **1149**	1154, **1159**, **1141**,1143, 1148	C-H in-plane bending
1376, **1371**, 1307, **1301**, **1299**, **1293**	**1377**, **1375**, 1337, 1319, 1309, 1306, **1301**, **1293**, 1250, 1248	CNC stretching
1589, **1578**, **1571**, 1567, **1490**	1616, **1591**, 1581, **1578**, **1576**, 1505, 1502, 1499, 1497, **1489**	Ring stretching
3380	**3380**	NH_2 symmetric stretching
3170	**3170**	=NH stretching
1589	**1587**	N=Q=N stretching
1400	**1410**	N-B-N stretching
1444	**1450**	benzene ring stretching
1240	**1240**	C-N str in BBB
745, 734, 695, 693, **690**	**740**, **690**	C-H op on 1,2 ring

For protonated PANI the quinoid (Q) and benzenoid (B) bands can shift about 10 cm^{-1} to the lower energy side with respect to that of the oligomers where 1490 cm^{-1} is the benzenoid ring vibration and the 1488 cm^{-1} band is assigned to a quinoid ring vibration.[159,197,198] The bands at 1587, 1490, and 1488 cm^{-1}, which are characteristic of the stretching vibrations of nitrogen atoms in aromatic and diimine units, are apparent in Figure 4.16. Peaks in the range between 400 and 800 cm^{-1} can be attributed to the ring

vibrations. The out-of-plane deformation vibrations of C-H bonds occur from 800 to 900 cm^{-1}.[94,122,132,199] The 3500 – 3100 cm^{-1} region is the N-H stretching region and the main absorption peaks are located at 3392 and 3315 cm^{-1} and are in agreement with published results.[197] The 3100 – 2800 cm^{-1} is the C-H stretching region and is barely observable at 3050 - 3030 cm^{-1} and 2960 – 2850 cm^{-1}.[197] The wavenumbers 1600 – 1450 cm^{-1} are the aromatic breathing, N-H deformation, and C=N stretching region while 1,4-disubstituted benzene ring may give absorption bands at 1600, 1580, and 1510 - 1500 cm^{-1} in PANI and is also mirrored in the experimental IRs.[197] The wavenumbers 1220 – 500 cm^{-1} are the region of in-plane and out-of-plane bending of C-H bonds on aromatic rings.[159,197,199]

Thus, it can be concluded that the IRs of the experimentally produce PANI sample are in agreement to those which have been previously studied.

4.4.4: Conclusions

Photolysis of 4-(*N*-anilino)phenyl azide in different solvents produce different products. In polar aprotic solvents, photolysis yields the corresponding nitrene and ring expansion products. In a polar weakly protic solvent system, PQDI is formed which can then undergo hydrolysis over time. In a strongly protic solvent system, when acid is present, the nitrenium ion formed by azide precursor with absorption band at 490 nm. PQDI can also be made *in situ* and then addition of acid also produces the nitrenium ion, which quickly undergoes polymerization as seen by its UV-vis absorption bands. Further evidence is provided by MALDI-TOF-MS which show products from four aniline units to eleven aniline units. XPS also shows that the binding energies of the N 1s and C 1s

orbitals are in agreement with published values of PANI of varying oxidation states. XRD and IR were used to show that the experimentally prepared samples were similar to published PANI by their angles of diffraction (2Θ) and stretching patterns. All of these observations provide evidence that PANI is a product of photoinitiated polymerization of aniline via the nitrenium ion intermediate.

Further studies are especially necessary concerning the reaction mechanism leading to PANI. Another serious problem is the fact that the polymerization of aniline is a heterogeneous reaction, that is, after reaching the tetrameric stage, the product molecules become insoluble in the acidic reaction medium and undergo precipitation. Afterwards, the production of larger molecules can only be accomplished via a boundary phase reaction at the solid-liquid interphase.[92]

4.5: 1-(*N*,*N*-Diphenylamino)-2,4,6-trimethylpyridinium tetrafluoroborate and Polymerization

4.5.1: Decay Pathways and Products

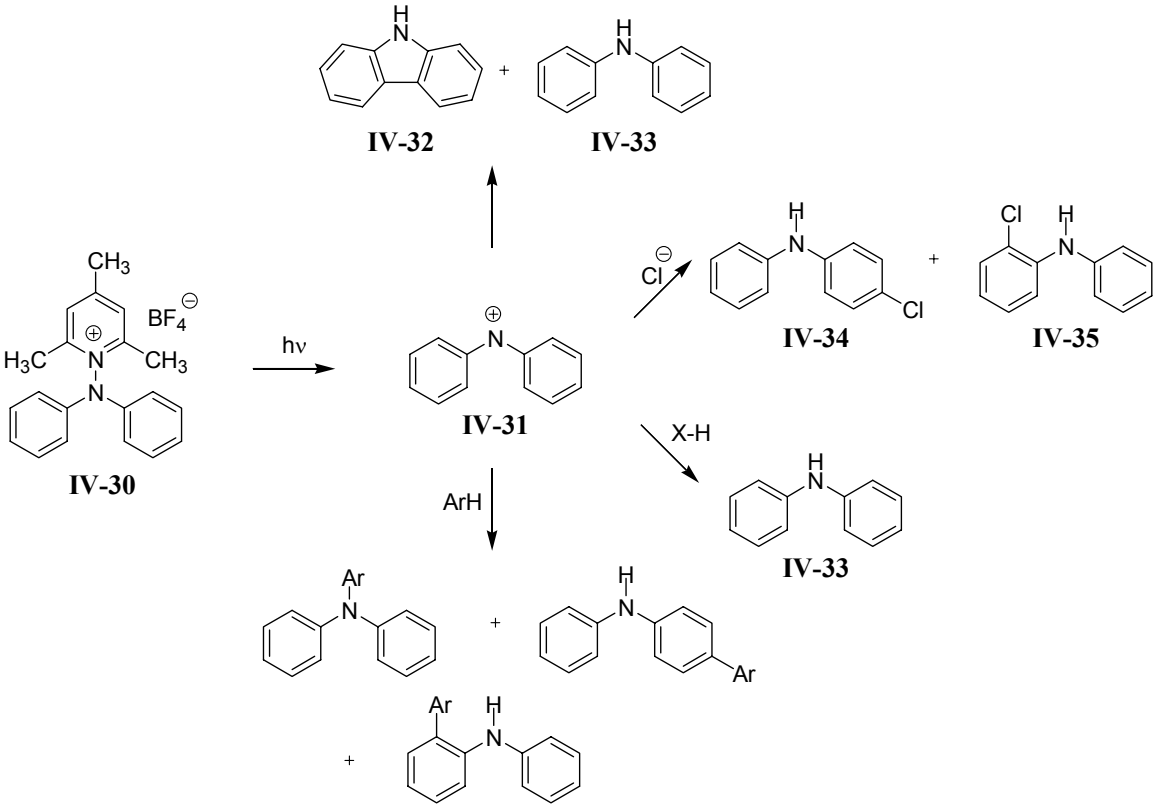
With the results from the polymerization of aniline, an interest in the role of nitrenium ions in mechanism of polymerization of *N*,*N*-diphenylnitrenium ion (DPN; **IV-31**) was revived. Previous studies using chemical trapping, LFP, TRIR, and TRRR have established that this species is generated upon photolysis of 1-(*N*,*N*-diphenylamino)-2,4,6-trimethylpyridinium tetrafluoroborate (**IV-30**) as shown in Scheme 4.17.[200-204] It

has been shown that *N*,*N*-diphenylnitrenium ion is a ground-state singlet like most simple aromatic nitrenium ions.[201,205-211]

DPN was first generated and characterized from the photolysis of its *N*-aminopyridinium ion precursor 1-(*N*,*N*-diphenylamino)-2,4,6-trimethrylpyridinium tetrafluoroborate. It was shown that nucleophiles such as chloride or methanol (CH_3OH) trap the singlet state nitrenium ions by attacking the aromatic ring.[201] Following the excitation laser pulse, transient absorption bands at 425 and 600-700 nm are observed. The 425 nm signal decays with a first order lifetime of 1.5 μs in CH_3CN. In the high wavelength region there is a broad absorption band that also decays with a 1.5 μs lifetime to give longer-lived bands at 325 and 680 nm. The long-lived peaks are assigned to the *N*,*N*-diphenylamine cation radical while the short-lived species that absorbs at 425 and at 660 nm is assigned to the singlet diphenylnitrenium ion.[201,212-214]

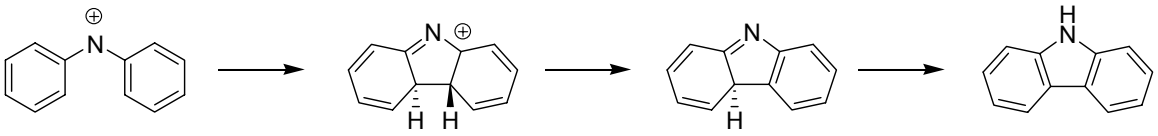
The decay pathways for *N*,*N*-diphenylnitrenium ion include addition of simple nucleophiles, such as halides and alcohols to the ortho and para positions on the phenyl rings, addition of electron-rich aromatic compounds to the nitrenium nitrogen atom via a σ-complex intermediate, and abstraction of hydride from a suitable donor (Scheme 4.17).[200-202,204,215]

Scheme 4.17: Decay pathways for *N*,*N*-diphenylnitrenium ion (IV-31) from photolysis of 1-(*N*,*N*-diphenylamino)-2,4,6-trimethrylpyridinium tetrafluoroborate (IV-30).



Diarylnitrenium ions have not been extensively studied, but research on *N*,*N*-diphenylnitrenium ion shows that without nucleophiles, the primary decay pathway is a cyclization reaction to form carbazole.[200,201] The formation of carbazole from *N*,*N*-diphenylnitrenium ion requires the loss of one aryl proton and the net migration of one proton from the phenyl ring to the nitrogen. One possible mechanism for this process would include an electrocyclization pathway, analogous to the Nazarov cyclization as shown in Scheme 4.18.

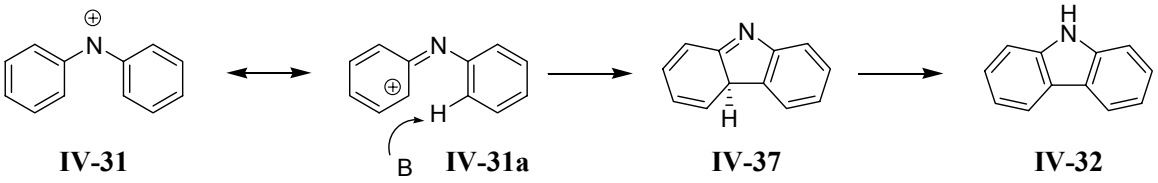
Scheme 4.18: Nazarov-Type cyclization of *N*,*N*-diphenylnitrenium ion to carbazole.



IV-31 **IV-36** **IV-37** **IV-32**

The initial ring closure would form the protonated carbazole tautomer **IV-36**. Conversion of this intermediate into stable products would require a deprotonation to give the carbazole tautomer **IV-37** followed by a net 1,7 proton shift to give the observed product. But, given that the neutral intermediate **IV-37** is observed to appear immediately following the decay of the nitrenium ion and that formation of **IV-36** is likely to be endothermic with a significant barrier, it is possible that **IV-37** could form through a concerted process. Therefore, a pathway in which the cyclization step is coupled to the proton loss as shown in Scheme 4.19 was considered. It was previously determined that based on thermodynamic and pK_a values, it was found that the mechanism for carbazole formation in solution is the cyclization reaction coupled to a transfer of the C2 proton of either the BF_4^- counterion or to the 2,4,6-trimethylpyridine leaving group.[216]

Scheme 4.19: Concerted proton transfer/cyclization mechanism.



It has been shown that when *N*,*N*-diphenylnitrenium ion is generated in the absence of trapping agents, stable photoproducts include diphenylamine (DPA) and carbazole, which are formed in relatively low yields.[201,216] The yields of carbazole are low because it reacts with nitrenium ions at the diffusion limited rate giving a poorly defined set of oxidized oligomeric products. Maximal yields of carbazole are obtained only when the reaction is carried out under highly dilute conditions.[200,201,216]

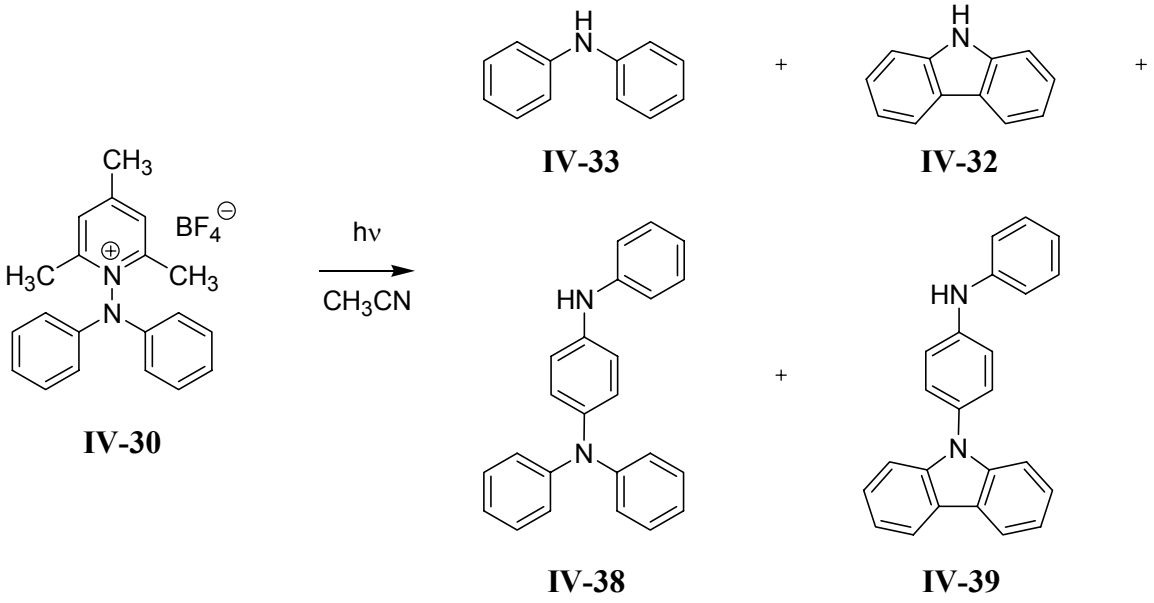
Along with these two products, large amounts of colored materials were formed which were assumed to be high molecular weight oligomers related to polydiphenylamine but had not been characterized. A goal was to determine the nature of the uncharacterized colored materials as well as the mechanism of their formation. The increasing commercial importance of PANI and its derivatives also served as inspiration to examine this process. Formation of polydiphenylamine in these reactions may also provide support for the possible involvement of nitrenium ions in PANI synthesis, as well as to help identify new methods by which these important polymers could be prepared.

To identify possible accumulated photoproducts, the photolysates from **IV-30** were analyzed in more detail. In particular we scaled up the reaction and carried out chromatographic separations on the mixture. These experiments reveal that, in addition

to the major photoproducts carbazole (**IV-32**) and DPA (**IV-33**), two dimeric species *N,N′,N′*-triphenyl-1,4-phenylenediamine (**IV-38**) and (4-carbazol-9-yl-phenyl)-phenyl-amine (**IV-39**) were also formed (Scheme 4.19). Product **IV-39** is derived from coupling between a diphenylnitrenium ion and carbazole. This adduct forms from the addition of the nitrogen of carbazole to the 4-position of the nitrenium ions arylsubstituent. This adduct was distinguished from its isomers by the number of signals in the ^{13}C NMR spectrum. Assuming rapid rotation about single bonds, product **IV-39** is predicted to give 14 unique signals and 14 unique signals are exactly what are observed. Also considered was the possible coupling of the nitrenium center with the 3-position on carbazole, which would have produced 16 unique signals. Coupling the 4-position of the nitenium ion fragment with the 3- or 1-positions of carbazole would each give 20 unique signals.

The other dimeric species, **IV-38**, is derived from the coupling of a nitrenium ion with diphenylamine. This was confirmed by photolysis experiments with added diphenylamine. Under these conditions, **IV-38** is the major product. As with **IV-39**, this species can be distinguished from its isomers by the number of signals in the ^{13}C NMR spectrum. Assuming rapid rotation about single bonds, product **IV-38** is predicted to give 12 unique signals and 12 unique signals are exactly what are observed. These products are similar to those observed by the chemical oxidation of carbazole to carbazole dimers whose NMR shifts were similar, but not exact.[217,218]

Scheme 4.20: Initial photoproducts of 1-(*N*,*N*-diphenylamino)-2,4,6-trimethylpyridinium tetrafluoroborate.



IV-30 **IV-33** **IV-32** **IV-38** **IV-39**

Arylnitrenium ions are electrophiles and have three distinct sites where positive charge is localized: at the nitrogen, at the para ring carbon, and at the ortho ring carbons. One might expect nucleophilic attack at any or all of these sites. Of course these same considerations apply to the isoelectronic carbenium ions. In practice, however, nucleophiles add almost excluseively to the exocyclic carbon atom of the carbenium ion.[219] In contrast, arylnitrenium ions are almost always attacked by simple nucleophiles at the ring carbons rather than the exocyclic nitrogen.[201,220,221] In fact, an examination of the literature reveals very few bona fide examples of nucleophilic addition to nitrogen. One significant exception to this is the reaction of guanosine with *N*-acyarylnitrenium ions.[222] In this case, a covalent bond is formed between the nitrogen of the nitrenium ion and the C-8 position of guanosine. Is it that guanosine is unique in adding to nitrogen or

will any π-nucleophile add to that site? Most, and in some cases all, nucleophilic addition occurs at the para position. More importantly, N-addition does not seem to be a general property of π-nucleophiles. In fact, only very electron rich alkenes add to the nitrogen of the nitrenium ion as determined from trapping with a variety of π-nucleophiles.[202]

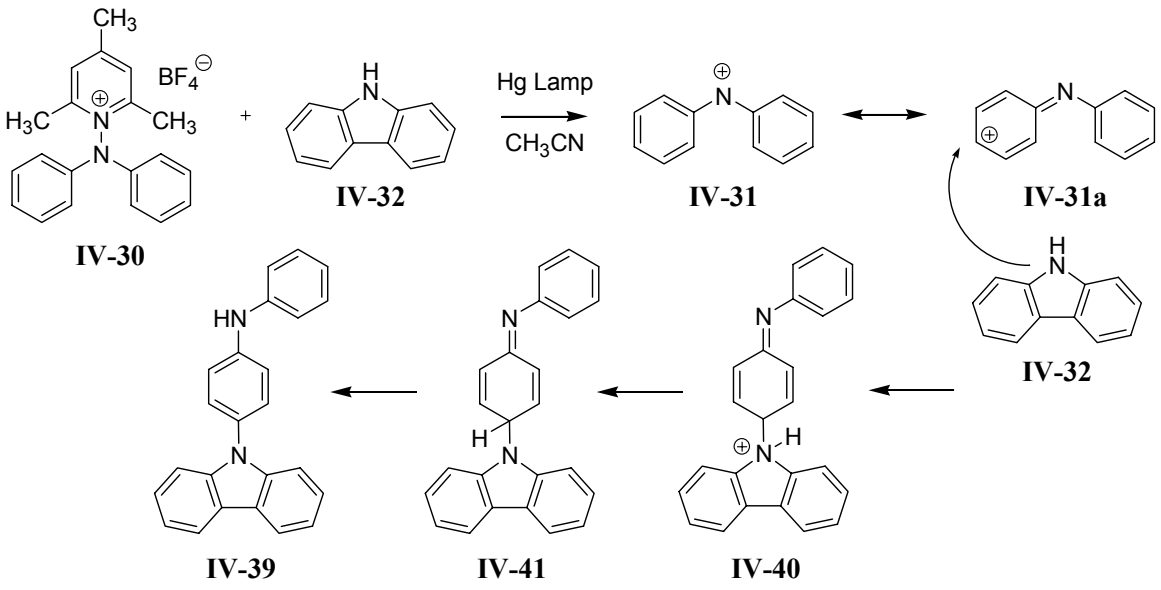
Since carbazole is expected to be the primary photoproduct, diphenylamine and **IV-39** would be derived from secondary reactions of **IV-31** with this product. The precursor was photolyzed in the presence of varying concentrations of carbazole and the product distributions were examined via gas chromatography (GC) (Table 4.4). As can be seen in Table 4.4, the yields of both the adduct **IV-33** and **IV-39** increase as the carbazole concentration is raised.

Table 4.4: Yields of diphenylamine (IV-33) and adducts IV-38 and IV-39 from photolysis of IV-30 in CH_3CN with varying concentrations of added carbazole.

Carbazole (IV-32) (μM)	Yield of IV-33 (μM)	Yield of IV-39 (μM)	Yield of IV-38 (μM)
266	52	110	26
1700	78	320	Trace
4800	99	830	Trace

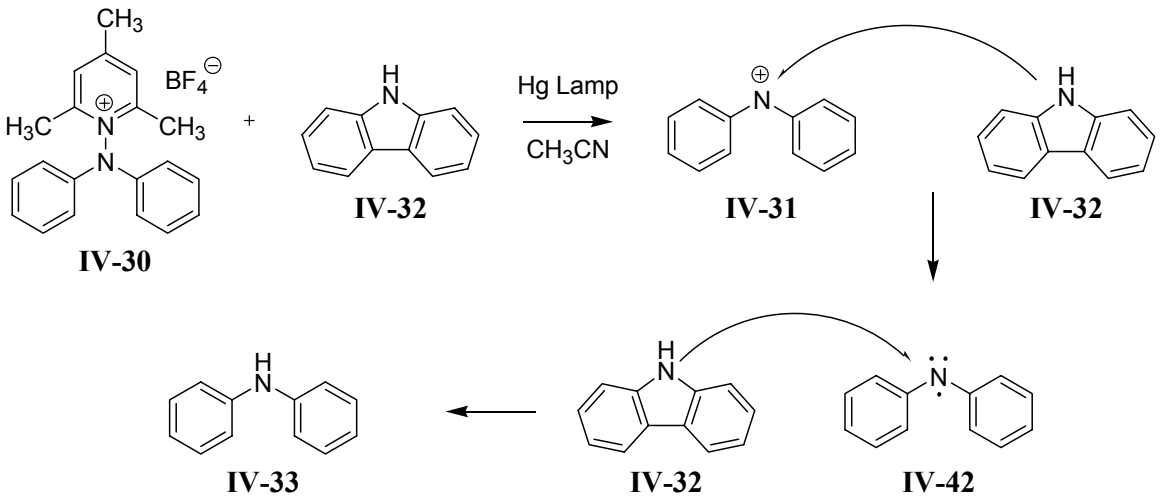
The mechanism of formation of **IV-33** and **IV-39** are illustrated in Schemes 4.21 and 4.22. Once the precursor is photolyzed, *N*,*N*-diphenylnitrenium ion is generated in the presence of carbazole. Carbazole can then attack the para-position to the nitrogen of the nitrenium ion since this has been shown to be the carbon with the most positive charge. Once the initial adduct is formed, the final product is attained via two deprotonation steps.

Scheme 4.21: Proposed mechanism for the formation of IV-39.



The mechanism for **IV-33** is quite different than the nucleophilic attack by carbazole as seen in Scheme 4.22. To produce diphenylamine, carbazole undergoes an oxidation and donates an electron to the diphenylnitrenium ion, thus forming a neutral diphenylamine radical and a carbazole radical cation. The newly formed neutral diphenylamine radical can then abstract a hydrogen atom from another carbazole molecule to yield diphenylamine.

Scheme 4.22: Proposed mechanism for the formation of diphenylamine.



To test for the probability of this mechanism, the observation of the carbazole radical cation was attempted with the LFP of 1-(*N*,*N*-diphenylamino)-2,4,6-trimethylpyridinium tetrafluoroborate in the presence of carbazole. Unfortunately, the resulting transient spectrum masked the wavelengths of where the carbazole radical cation would appear (663, 725, 810 nm) as shown in Figure 4.17.[212]

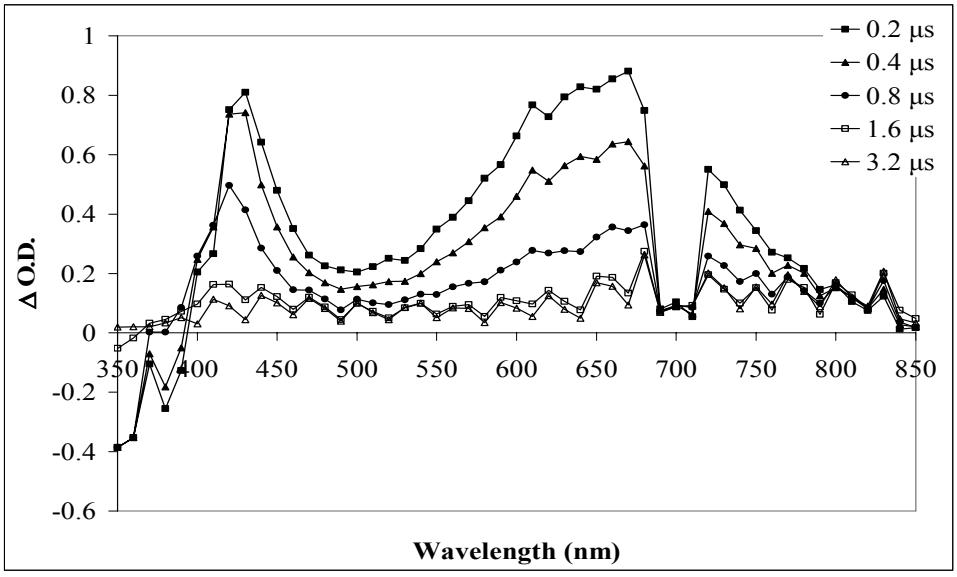


Figure 4.17: Transient UV-vis absorption spectra generated from LFP (355 nm, 4-6 ns, 8-10 mJ/pulse) of IV-30 with 1 mM carbazole in CH_3CN, taken 0.2, 0.4, 0.8, 1.6, and 3.2 μs after the laser pulse under N_2 purge. The errant absorption from 690 – 710 nm was also observed in rescans of the transient.

With this information in hand, another single electron donor, 1,4-dimethoxybenzene (1,4-DMB) was used to test the validity of the proposed mechanism. Again, 1-(*N*,*N*-diphenylamino)-2,4,6-trimethylpyridinium tetrafluoroborate was photolyzed in the presence of 1,4-DMB to observe the radical cation of 1,4-DMB which has reported absorbances at 443 and 475 nm (Figure 4.18).

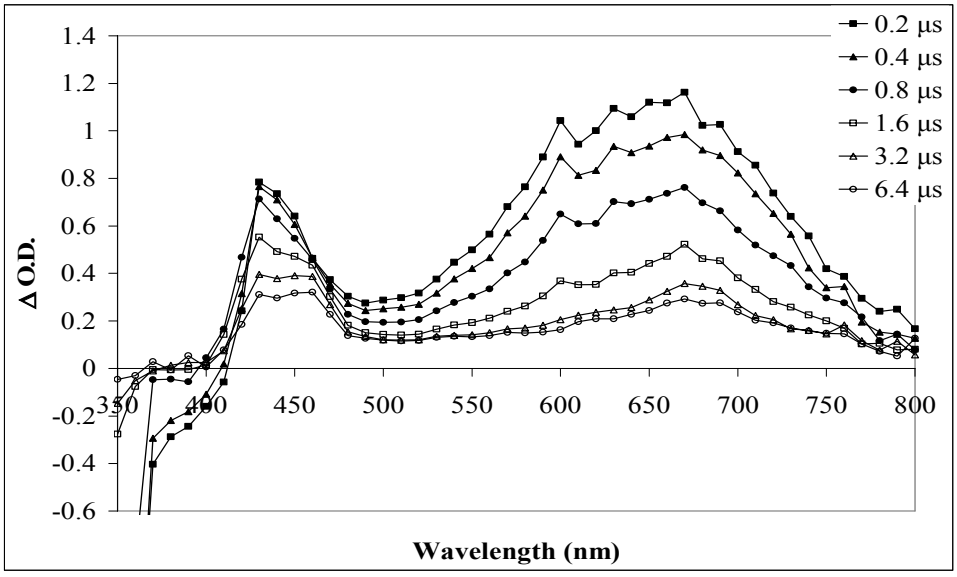


Figure 4.18: Transient UV-vis absorption spectra generated from LFP (355 nm, 4-6 ns, 8-10 mJ/pulse) of IV-30 with 1,4-DMB in CH_3CN, taken 0.2, 0.4, 0.8, 1.6, 3.2, 6.4 and 12.8 μs after the laser pulse under N_2 purge.

According to Shida, the 1,4-DMB radical cation shows absorbance bands at 443 and 475 nm.[212] At first glance, it seems as though this is just a transient absorption spectrum for diphenylnitrenium ion. But a more in depth look shows that the transient absorption band centered around 650 nm decays quite fast as compared to the transient absorption band centered around 430 and 460 nm (Figure 4.19). The 430 nm transient has a decay rate of 2.3 x 10^5 $M^{-1}s^{-1}$ and the 460 nm transient has a decay rate of 1.03 x 10^5 $M^{-1}s^{-1}$ while the 650 nm transient has a decay rate of 1.01 x 10^6 $M^{-1}s^{-1}$. This suggests that the radical cation of 1,4-DMB is generated and supports the mechanism that the coupling and the generation of the observed DPA is via a one electron transfer from the 1,4-DMB and forms the same dimeric species as observed with carbazole (Scheme 4.23).

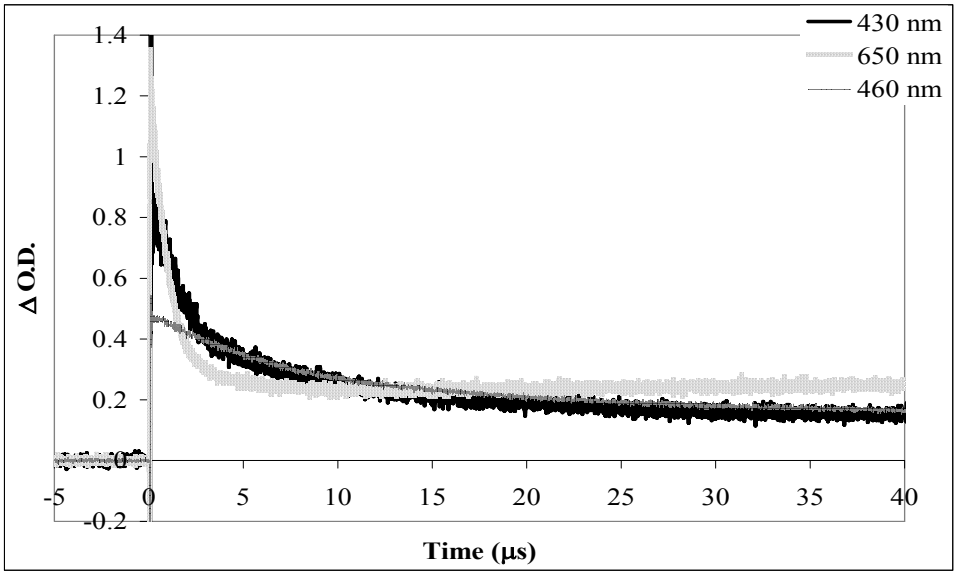
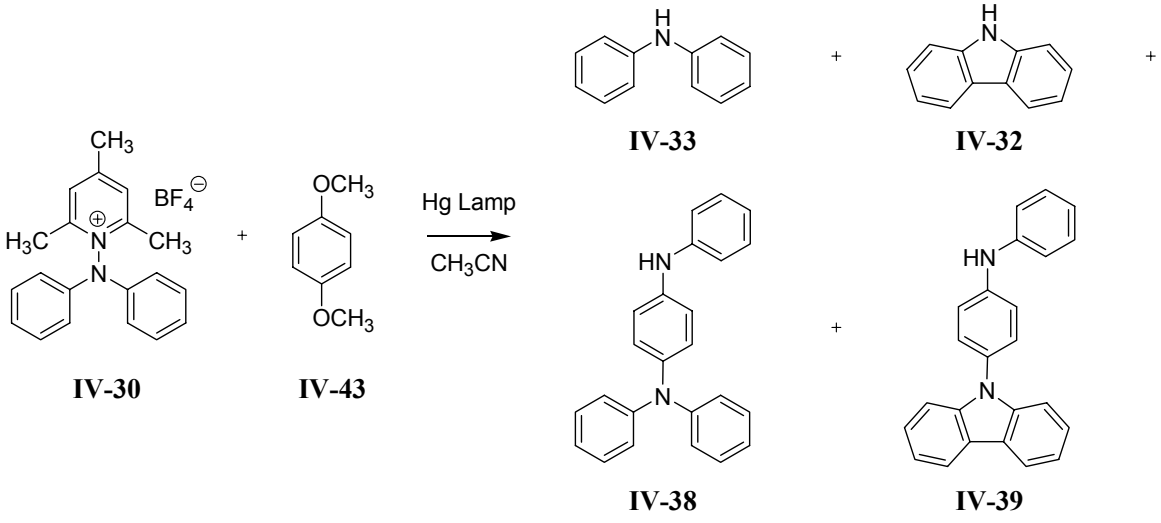


Figure 4.19: Decay waveforms of the 430, 460, and 650 nm transients of IV-30 with 1,4-DMB from Figure 4.18. The 430 nm transient has a decay rate of 2.3 x 10^5 $M^{-1}s^{-1}$ and the 460 nm transient has a decay rate of 1.03 x 10^5 $M^{-1}s^{-1}$ while the 650 nm transient has a decay rate of 1.01 x 10^6 $M^{-1}s^{-1}$.

Scheme 4.23: Photoproduct of 1-(*N*,*N*-diphenylamino)-2,4,6-trimethylpyridinium tetrafluoroborate with 1,4-DMB.



The structures of the two dimeric products suggested that the remaining material might be derived from higher order addition reactions creating mixed oligomers of carbazole and diphenylamine and two observations support this. Figure 4.20 shows the changes in the UV-vis spectra resulting from photolysis of **IV-30** in CH_3CN with a hand-held shortwave UV lamp. The product absorption band at 570 nm signals the formation of an extended π-system. Similar visible absorption bands are characteristic of both polydiphenylamine and poly-3,6-carbazole.[223]

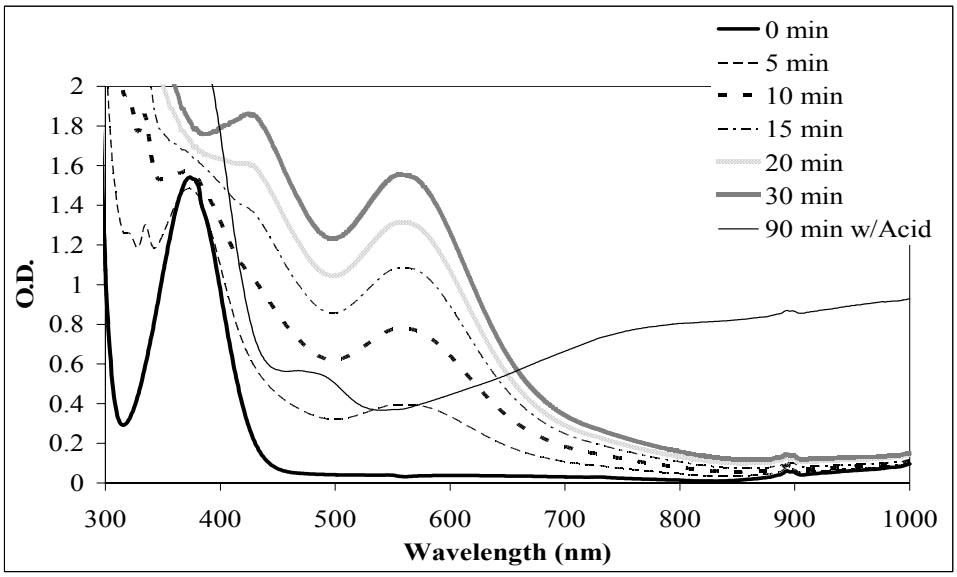


Figure 4.20: Steady-state UV-vis absorption spectra taken periodically following photolysis of IV-30 in a CH3CN solution.

An interesting note is that upon addition of acid, the UV-vis absorption shifts to the red and shows an increasing absorption from 780 nm, which is the random coil, or localized polaron, of PANI. The additional increase in absorbance around 1000 nm, which is the extended conformation of PANI, represents the "free carrier tail", which is characterisctic of metallic conductive material.[188]

The details of the secondary decay pathways have not been fully elucidated. However, it is reasonable to assume that the colored products are oligomers and polymers of these species and their corresponding cation radical. This assignment was later confirmed by time-resolved IR.[204] *N*,*N*-Diphenylnitrenium ion has been extensively characterized by theoretical calculations ΔE_{st} = -11.6 kcal/mol, TRIR, and UV-vis spectroscopy.[211] *N*,*N*-Diphenylnitrenium ion has formed σ-adducts with arenas (1,3,5-trimethoxybenzene (1,3,5-TMB) and 1,3-dimethoxybenzene (1,3-DMB))[215] Most abundant trapping at the para position and others at the ortho and N.

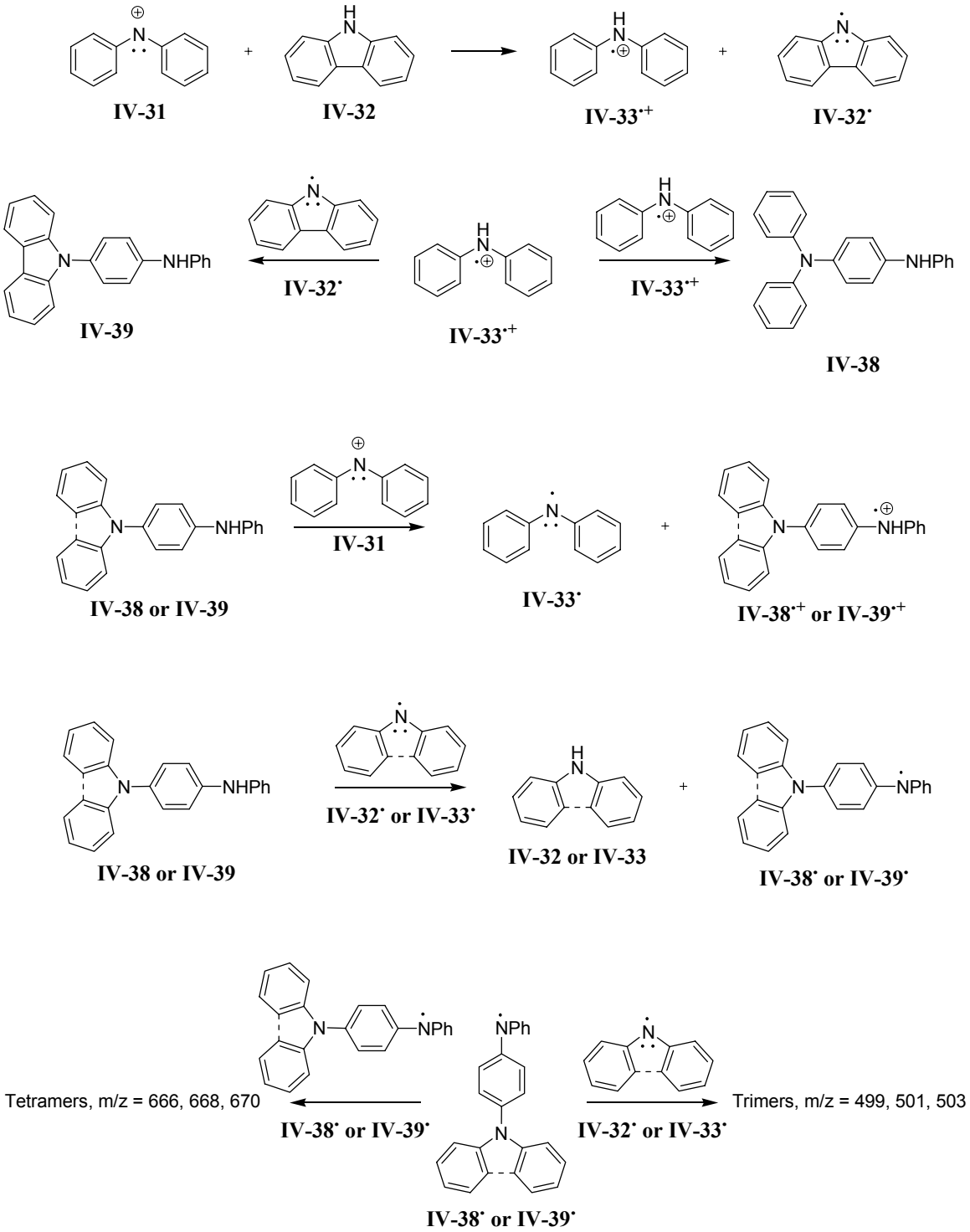
Previous CV studies has shown the oxidation of diphenylamine in a large excess of trichloro or trifluoroacetic acids form *N*,*N*,*N*′-triphenyl-*p*-phenylenediamine via two oxidations to yield the nitrenium ion.[96,224] It has been observed that the only polymer obtained after electrochemical oxidation of diphenylamine, in organic solvents, is a conducting polymer film.[137,225,226] The structure of the obtained materials strongly depends on the applied potential necessary to make the anodic polymerization feasible.[224]

Since the generation of diphenylnitrenium ion in the absence of any efficient trapping agents provides a highly complex mixture of colored materials and diphenylamine and carbazole are detected in low yields, it is assumed that the intractable material consists of oligomers and polymers of carbazole and diphenylamine. Both

carbazole and DPA are known to polymerize under oxidizing conditions and both the pyridinium salt and the transient nitrenium ion can function as oxidants.[125,227] It is likely, therefore, that carbazole and DPA are formed as primary photoproducts which are then consumed by reactions with subsequently generated DPN and/or DPA radical. The carbazole product comes from a net deprotonation/rearrangement of DPN.

On the basis of LFP experiments and product analysis, the polymerization of diphenylamine is proposed in Scheme 4.24. Nitrenium ion **IV-31** forms carbazole in the absence of traps. As carbazole accumulates, **IV-31** reacts with this product via a net H atom abstraction. Coupling of the 9-carbazolyl radical with the diphenylamine radical cation forms the dimeric product **IV-39**. The radical cation of **IV-33** (**IV-33**$^{\bullet+}$) can then couple to another radical cation of (**IV-33**$^{\bullet+}$) to form **IV-38** or it can abstract an additional electron from the various photoproducts to form diphenylamine. Another reaction that can occur is that the carbazolyl radical (**IV-32**$^{\bullet}$) can oxidize any of the oligomers that have been formed. Oxidation of the dimeric product by **IV-31** is followed by coupling reactions creating trimers and tetramers. Higher order oligomers are generated by analogous oxidation/coupling processes. Therefore, each nitrenium ion is capable of oxidizing two oligomers, which can couple to form larger oligomeric species. The structures of these larger oligomers have not been identified because of their complexity, but the similarity of the UV-vis spectrum to polydiphenylamine suggests that their structures are analogous.

Scheme 4.24: Polymerization scheme of *N*,*N*-diphenylnitrenium ion to polydiphenylamine.



4.5.2: MALDI-TOF-MS

Since the use of MALDI-TOF-MS was extremely helpful in identifying high molecular weight oligomers of PANI, MALDI was also used for the detection of high molecular weight oligomers of polydiphenylamine. The existence of high molecular weight oligomers support the idea that polymers are formed in these reactions and LFP experiments provide some insight into the mechanism by which this occurs. Figures 4.21 and 4.22 show portions of the MALDI-TOF-MS of special interest because they provide evidence of high molecular weight photoproducts. These two spectra were obtained from the photolysis of 1-(*N*,*N*-diphenylamino)-2,4,6-trimethylpyridinium tetrafluoroborate with varying amounts of carbazole as the trapping agent. Figure 4.21 shows the weight distribution from a 6.1 mM concentration of carbazole as a trap while Figure 4.22 shows the weight distribution from a 21.5 mM concentration of carbazole as a trap. Peaks centered around 335 m/z correspond to dimeric species while peaks centered around 500 m/z correspond to trimers. Similar sets of peaks are detected around 665 m/z for tetramers and 833 m/z and 1000 m/z, which correspond to pentamers and hexamers respectively.

Figure 4.23 shows the MALDI spectra for the photolysis of 1-(*N*,*N*-diphenylamine)-2,4,6-trimethylpyridinium tetrafluoroborate with a 6.7 mM concentration of carbazole (Figures 4.23 A and B) and with a 10.8 mM concentration of diphenylamine (Figures 4.23 C and D). These spectra also show the characteristic peaks for the dimer, trimer, tetramer, pentamer, hexamer, and so on.

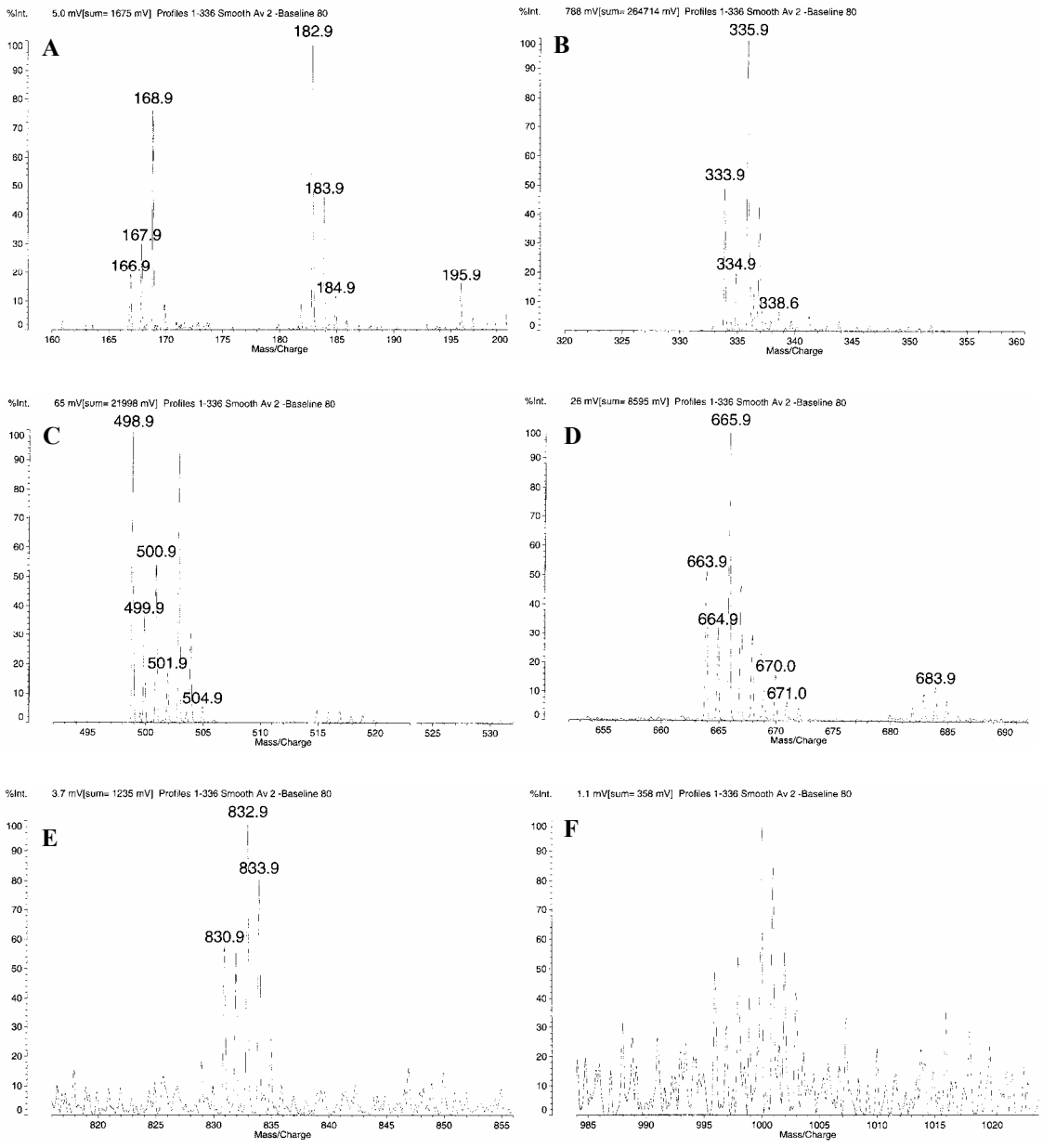


Figure 4.21: MALDI-TOF-MS of the photolysis of 1-(*N*,*N*-diphenylamino)-2,4,6-trimethylpyridinium tetrafluoroborate with 6.1 mM of carbazole. The presented mass ranges give m/z ratios of 336, 409, 604, 834, and 1001, which correspond to dimers, trimers, tetramers, pentamers and hexamers.

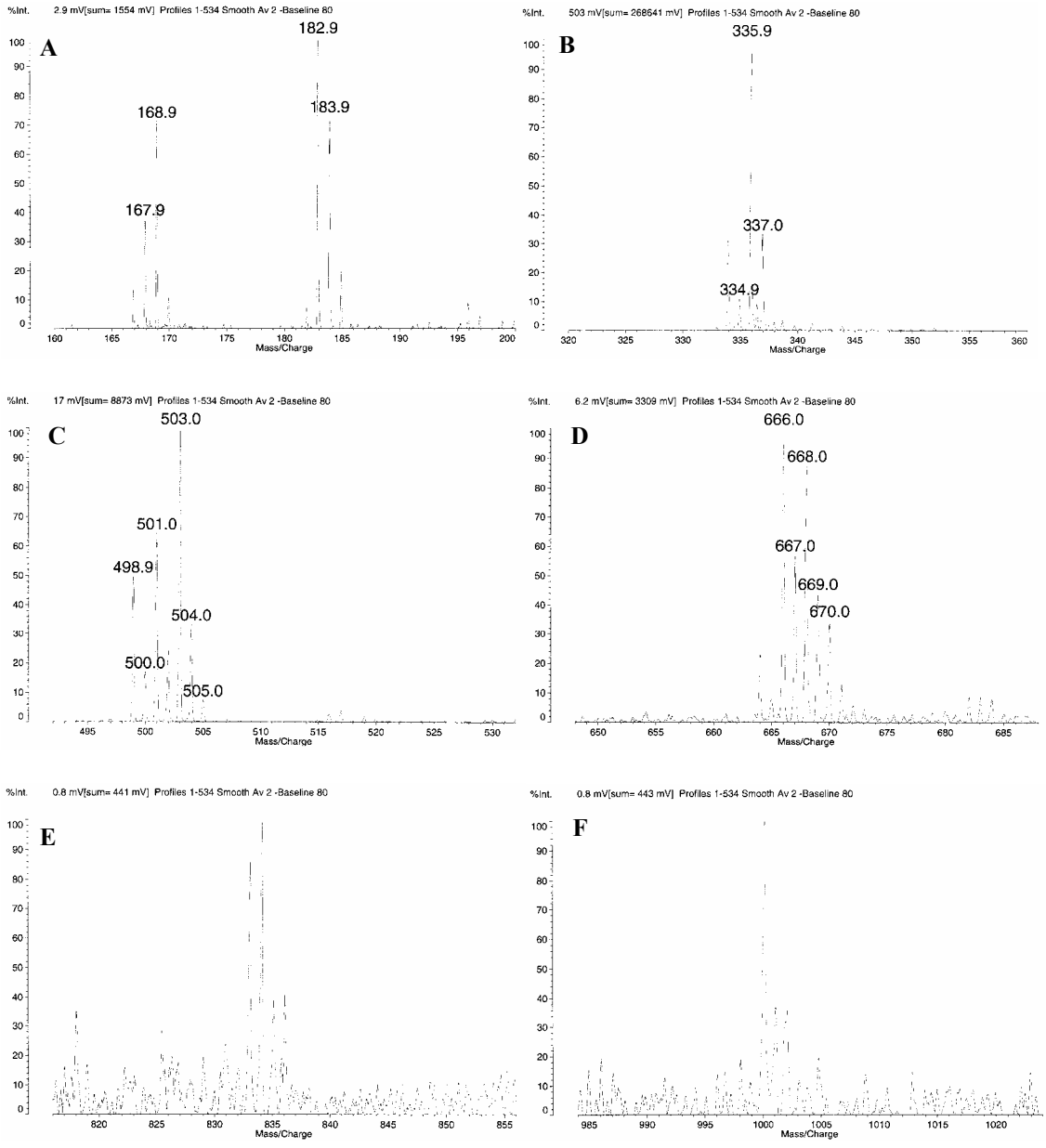


Figure 4.22: MALDI-TOF-MS of the photolysis of 1-(*N*,*N*-diphenylamino)-2,4,6-trimethylpyridinium tetrafluoroborate with 21.5 mM of carbazole. The presented mass ranges give m/z ratios of 336, 409, 604, 834, and 1001, which correspond to dimers, trimers, tetramers, pentamers and hexamers.

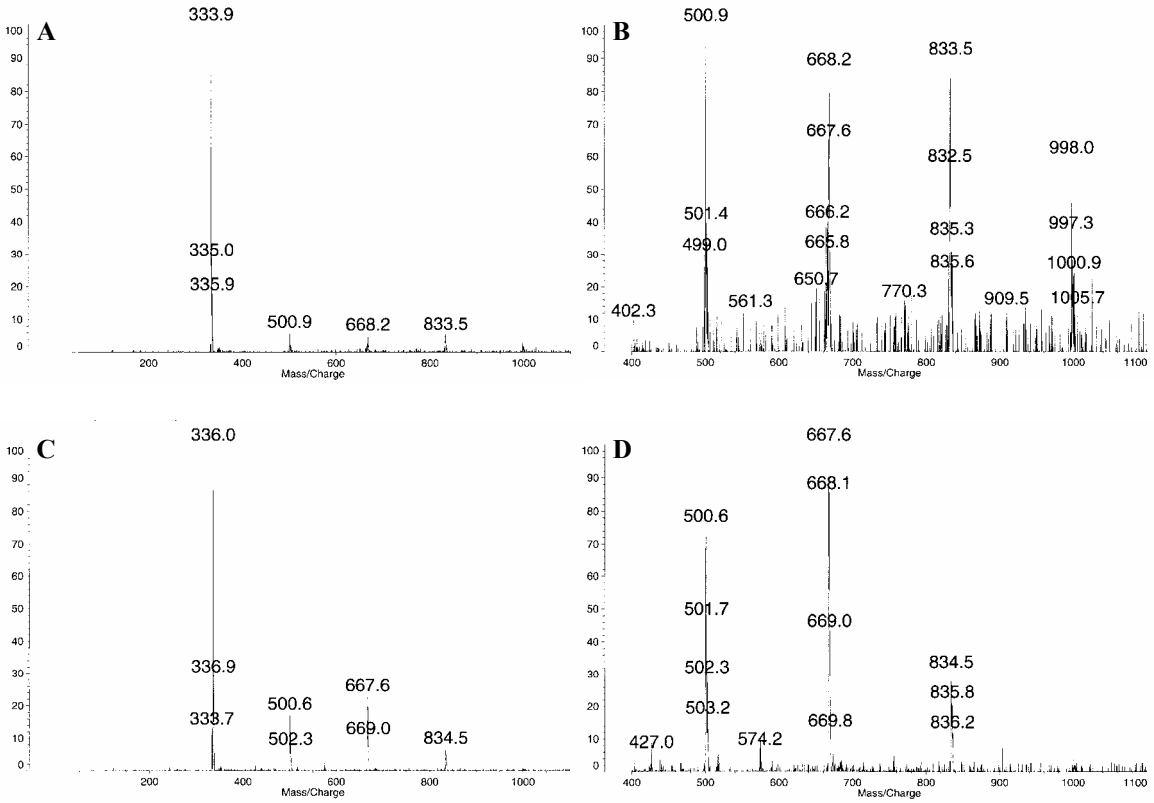
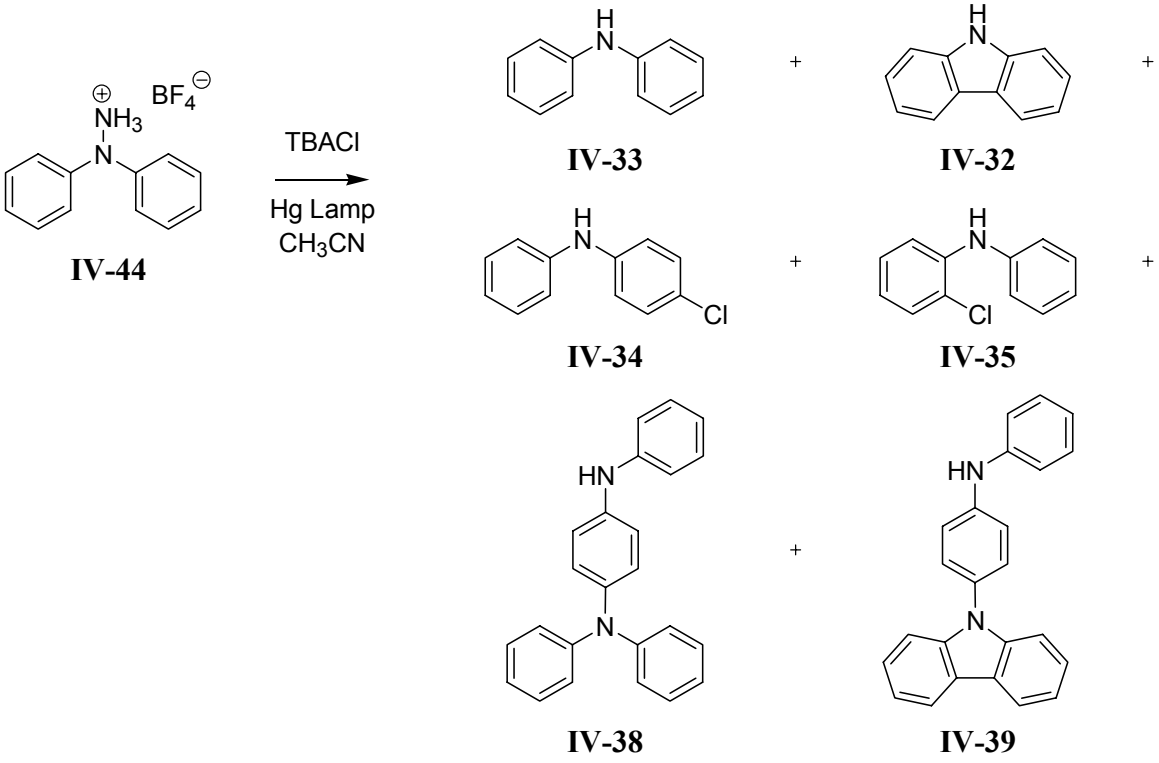


Figure 4.23: MALDI-TOF-MS of the photolysis of 1-(*N*,*N*-diphenylamino)-2,4,6-trimethylpyridinium tetrafluoroborate with (A) and (B) are from 6.7 mM carbazole trapping and (C) and (D) are from 10.8 mM diphenylamine trapping. The presented mass ranges give m/z ratios of 336, 409, 604, 834, and 1001, which correspond to dimers, trimers, tetramers, pentamers and hexamers.

4.5.3: 1,1-Diphenylhydrazinium Tetrafluoroborate Photolysis

A new photochemical precursor could be used which also yields the diphenylnitrenium ion. It has been shown that for diarylnitrenium ions, photolysis of their respective protonated hydrazines also yield the proposed diarylnitrenium ion by heterolysis of the N-N bond to yield ammonia.[228] Therefore, the polymerization of this photochemical precursor was also studied to add support for the polymerization scheme. It was found that photolysis of the protonated 1,1-diphenylhydrazine with TBACl also yields similar photoproducts seen with its pyridiunium tetrafluoroborate counterpart (Scheme 4.25). Photolysis of 1,1-diarylhydrazines, protonated with tetrafluoroboric acid (HBF_4), generates the corresponding nitrenium ion in high yields and give similar products when trapped with chloride yielding both ortho and para products. Photolysis of hydrazinium ions in CH_3CN produces stable products that are characteristic of the nitrenium ions.[201] The product mixtures were analyzed by GC and the products were identified by co-injections with authentic samples. The identities of the products determined by the GC studies were further corroborated by separating the components of the photolysate of precursor 0.0012 M with 1 equivalent of HBF_4 with 0.015 M TBACl in CH_3CN by flash chromatography and confirming the identity of the chloroadducts by ^1H NMR. The photolysis of diphenylhydrazinium ion in CH_3CN with added chloride as TBACl gives a mixture of 2- chloro-*N*-phenylaniline, 4-chloro-*N*-phenylaniline, and diphenylamine.

Scheme 4.25: Photoproducts of 1,1-diphenylhydrazinium tetrafluoroborate with chloride trap.



IV-44 **IV-33** **IV-32** **IV-34** **IV-35** **IV-38** **IV-39**

The MALDI-TOF-MS of the photolyzed 1,1-diphenylhydrazinium ions was also observed and it was clear that the resulting precipitates were also of high molecular weights, much like those from the photolysis of the corresponding pyridinium tetrafluoroborate, as can be seen in Figure 4.23. The MALDI spectra from the polymer from 1-(*N*,*N*-diphenylamino)-2,4,6-trimethylpyridinium tetrafluoroborate and from 1,1-diphenylhydrazinium ions all show peaks at around 335, 503, 666, 832 and 1001 (m/z), which correspond to diphenylamine dimers, trimers, tetramers, pentamers, hexamers.

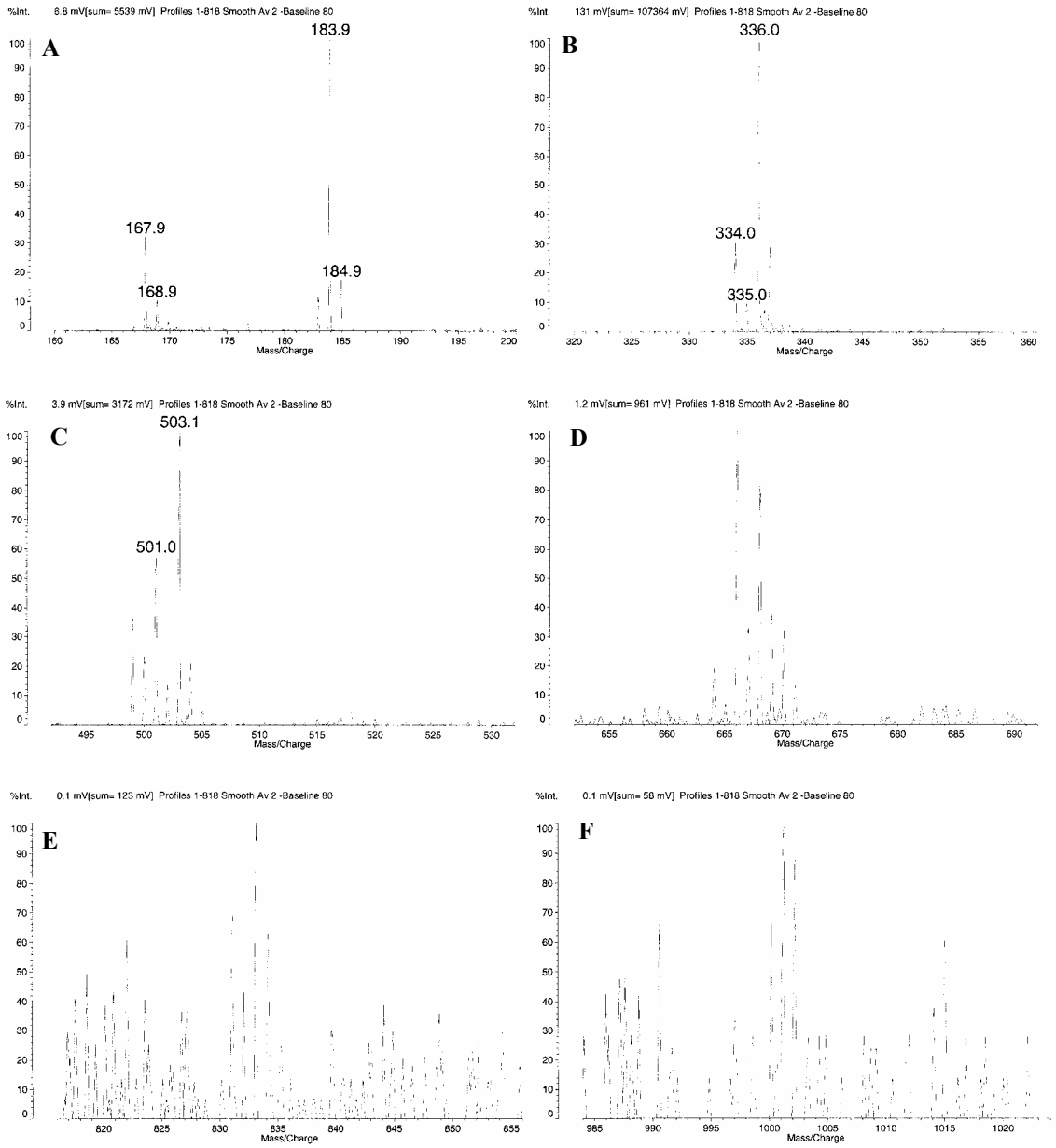


Figure 4.24: MALDI-TOF-MS of the photolysis of 1,1-diphenylhydrazinium tetrafluoroborate. The presented mass ranges give m/z ratios of 336, 409, 604, 834, and 1001, which correspond to dimers, trimers, tetramers, pentamers and hexamers.

4.5.4: Conclusions

The photolysis of 1-(*N*,*N*-diphenylamino)-2,4,6-trimethylpyridinium tetrafluoroborate yields *N*,*N*-diphenylnitrenium ion. In the absence of trapping agents, the primary decay pathway is the formation of carbazole and diphenylamine. It was reasoned that carbazole was not formed via a Nazarov type cyclization, but rather by a concerted deprotonation/cyclization process. The formation of diphenylamine was shown to occur via an electron donation of the formed carbazole to the nitrenium ion intermediate, followed by a hydrogen atom transfer. Photolysis of *N*,*N*-diphenylnitrenium ion also yielded two dimeric species which were identified as a carbazole-diphenylamine adduct and a diphenylamine dimer.

The experiments described here further develop the view of diphenylnitrenium ion chemistry. First, it is clear that the primary decay pathway (in solution) for diphenylnitrenium ion is a concerted electrocyclization/deprotonation reaction that provides carbazole via its H-4a tautomer (**IV-37**). The latter can be detected in LFP experiments. Laser flash photolysis experiments and product analysis show that with relatively easily oxidized arenes, the reaction with diphenylnitrenium ion goes through an initial electron transfer, rather than direct formation of a sigma complex. The electron transfer reactions lead to diphenylamine and, in many cases, oligomeric products derived from oxidation and coupling reactions. This appears to be the first direct observation of one-electron transfer reactions from a singlet nitrenium ion,

On the basis that dimeric compounds could be obtained, higher molecular weight compounds were also thought to arise from nitrenium ion intermediates. According to

the acquired MALDI spectra, high molecular weight materials were observed and were correlated to known oligomers of PANI and polydiphenylamine. Other analytical methods, such as XRD, XPS, and IR all correlate the photochemical products to varying forms of PANI and polydiphenylamine. These results fortify the theory that nitrenium ions have a role in the polymerization mechanism of aniline.

1,1-Diarylhydrazinium tetrafluoroborates have shown to be useful in the study of diarylnitrenium ions via the photolysis of their protonated hydrazine form. Photolysis of 1,1-diphenyllhydrazinium tetrafluoroborate has provided products similar to those observed with the photolysis of 1-(*N*,*N*-diphenylamino)-2,4,6-trimethylpyridinium tetrafluoroborate. The observed MALDI spectra also show high molecular weight materials which correspond to polydiphenylamine. These materials support the notion that nitrenium ions can play a role in the polymerization of aniline as well as aniline derivatives.

4.6: References

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Chapter 5: Experimental Methods

5.1: General Procedures

5.1.1: Solvents and General Chemicals

Unless otherwise stated, solvents and general chemicals were obtained from commercial suppliers and used without further purification. Solvents used in photochemical experiments were distilled under nitrogen atmosphere. CH_3CN was distilled from CaH_2 though a vacuum sealed column (30 cm) packed with glass helices. CH_2Cl_2 was distilled from CaH_2 and THF was distilled over sodium. Zinc was cleaned as per published procedures.[1] ^1H and ^{13}C nuclear magnetic resonance (NMR) spectra were obtained and chemical shifts are referenced to tetramethylsilane (TMS) and are reported in parts per million (□) downfield from ^1H and ^{13}C for TMS in CH_3CN or $CDCl_3$.

5.1.2: General LFP-TRUV Transient Absorption Spectra

Laser flash photolysis with time-resolved ultraviolet-visible absorption detection experiments were performed using a Nd:YAG laser as the pulsed excitation source. Second, third, and fourth harmonic generator crystals were used to create output wavelengths at 355 and 266 nm. The transient absorptions were monitored using a probe beam from a 350-W Xe arc lamp passed through the sample cuvette perpendicular to the excitation beam. Transient waveforms were recorded with a digital oscilloscope, which digitizes at a rate of 1 point/10 ns with a bandwith of 350 MHz. Samples for pulsed

irradiation were prepared such that the O.D. (optical density) of the photolabile substrate was approximately 1.5 -2.5 in anhydrous solvent at the excitation wavelength employed.

5.1.3: Trapping Rate Constants

A stock solution of substrate was made with anhydrous CH_3CN, such that the O.D. at the excitation wavelength was between 1.5 and 2.5. This would ensure that the substrate would absorb the pump pulsed beam and undergo photolysis. A 3 mL sample was transferred by syringe to a quartz cuvette and photolyzed without trap to measure k_0, the compound's decay rate without any trap. Trap from a millimolar stock solution in anhydrous CH_3CN was added to the sample via a microliter syringe in small aliquots, usually in 10 or 20 □L aliquots, and photolyzed to observe the new rate of decay. Consecutive additions of trap were monitored to collect many datum points.

Quenching decay rate constants can be determined by fitting the data to equation 1, where □O.D.$_0$ is the maximum change in optical density at t = 0, k_{obs} is equal to the rate constant for the observed decay of the transient intermediate, and b is the baseline.

$$\Delta \text{ O.D.}_{\cdot(t)} = \Delta \text{ O.D.}_{\cdot(0)} e^{-tk_{obs}} + b \quad (1)$$

The data analysis uses computer fitting which creates a theoretical curve using these three variables (□O.D.$_0$, k_{obs}, and b) and performs many iterations such that the summation of the standard deviation of the best fit line of the data from n = 0 to n = t is zero as shown in equation 2.

$$\sum_{n=0}^{n=t}\left[\Delta \text{ O.D.}_{\text{experimental}}(t) - \Delta \text{ O.D.}_{\text{theoretical}}(t)\right]^2 = 0 \quad (2)$$

□□ determine the reactivity of the intermediate, one can use different classes of quenchers or nucleophiles to determine how quickly they trap the reactive intermediate. This is done by measuring the relationship between k_{obs} with varying concentrations of trap and then fitting it to a second order decay function. To determine the trapping rate, k_{obs} can be defined by equation 3 where k_0 is the decay rate without any trap, k_q is the rate constant for trapping, and [Q] is the concentration of trap.

$$k_{obs} = k_0 + k_q[Q] \quad (3)$$

The trapping rate constant (k_q) is determined by plotting the concentration of quencher used versus k_{obs}. The resulting slope, determined by linear regression, is the trapping rate constant (k_q) and the y-intercept is k_0, given in terms of $M^{-1}s^{-1}$. The resulting trapping rate was reported with errors that were determined with a 95% confidence interval with Microsoft® Excel 98 computer software.

5.1.4: Radical Cation Transient Absorption Spectra

A stock solution of substrate was made with anhydrous CH_3CN, such that the O.D. at the excitation wavelength was between 1.5 and 2.5. This would ensure that the substrate would absorb the pump pulsed beam and undergo photolysis. The

concentration of the one-electron acceptor was calculated using the Stern-Volmer equation (4):

$$\frac{\Phi_0}{\Phi} = 1 + k_q \tau [Q] \quad (4)$$

where Φ_0 is the fluorescence without trap, Φ is the fluorescence with trap, k_q is the bimolecular rate constant, τ is the lifetime, and [Q] is the concentration of trap. For a value of 90% fluorescence quenching, equation 5 was used.

$$\frac{\Phi_0}{\Phi} = \frac{100}{10} = 10 = 1 + k_q \tau [Q] \quad (5)$$

The value for k_q was assumed to be 1 x 10^{10} $M^{-1}s^{-1}$ and τ was determined from literature values. Thus, the concentration of trap, [Q], was calculated. The spectral analysis was performed as described above in LFP-TRUV.

5.1.5: Calculations

All geometry optimizations and vibrational frequency calculations were carried out using the Gaussian 03 suite of programs.[2] The values were calculated using density functional theory, and in particular the hybrid B3LYP functional, comprised of Becke's B3 three-parameter gradient-corrected exchange functional with the LYP correlation functional of Lee, Yang, and Parr as originally described by Stephens *et al.*[3-6] For these calculations, the 6-31G(d,p) basis set was employed with the LYP correlation functional

of Lee, Yang, and Parr as originally described by Stephens *et al.* [7] The GAPT method for allocating partial charges has been described elsewhere.[8]

5.2: Synthesis of Photochemical Precursors

5.2.1: Synthesis of 1-Naphthyl azide (III-24)

Ice was added to 1-naphthylamine (4.88 g, 34.1 mmol), which was on an ice bath, and 30 mL of HCl was added dropwise. To this mixture, a solution of $NaNO_2$ (2.49 g, 36.1 mmol) in 20 mL of distilled water was added and stirred for 2 h. The solution was then neutralized to pH 7 with a saturated solution of $NaHCO_3$ and solid Na_2CO_3. A solution of NaN_3 (2.24 g, 34.5 mmol) and NaOAc (14.7 g, 179 mmol) in 50 mL of distilled water was added and stirred for 1 h. The solution was then extracted with CH_2Cl_2, dried over $MgSO_4$, filtered, and the solvent was removed under reduced pressure to yield a dark purple oil. The desired product was isolated by column chromatography (240 mm x 44 mm) and eluted with 5% ethyl acetate (EtOAc)/95% hexanes. The fractions were collected and the solvent was evaporated under reduced pressure to yield 3.72 g (22.1 mmol, 64%) of a dark purple solid. R_f: 0.76 (15% EtOAc/85% hexanes); ^{1}H NMR (400 MHz, CD_3CN) δ: 8.05 (d, J = 10.4 Hz, 1H), 7.88 (d, J = 8.4 Hz, 1H), 7.69 (d, J = 8.4, 1H), 7.57 – 7.48 (m, 3H), 7.34 (d, J = 7.6 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 136.9, 134.8, 128.1, 127.3, 126.6, 126.1, 125.1, 122.9, 114.3; UV-vis (CH_3CN) 222, 294, 326 nm; IR (CCl_4) 3389 (w), 3363 (w), 3317 (m), 3255 (w), 3089 (m), 3066 (s), 3049 (s), 2498 (m), 2420 (m), 2358 (m), 2289 (m), 2217 (w), 2145 (s), 2103 (s), 2044 (s), 1627 (m), 1591 (s), 1574 (s) 1502 (s), 1457 (s) cm^{-1}; MS (EI) m/z 169, 141, 140, 114, 113, 89, 71, 55, 41; HRMS (EI) calcd for $C_{10}H_7N_3$ 169.0639, found 169.0644.

5.2.2: Synthesis of 1-(*N*-Methyl-*N*-(1-naphthyl)amino)-2,4,6-trimethylpyridinium tetrafluoroborate (III-25)

***N*-Methyl-1-naphthylamine (III-26).** 1-Naphthylamine (**3**, 5.23 g, 36.6 mmol) was dissolved in 25 mL of anhydrous CH_3CN and then 5.01 g (35.3 mmol) of iodomethane was added to the solution while stirring. The solution was refluxed for 1 h with an ice water condenser. The mixture was then neutralized to pH 7 with a saturated solution of $NaHCO_3$ and extracted with CH_2Cl_2 until the organic layer was colorless. The combined organic extracts were then dried over $MgSO_4$, filtered, and the solvent was evaporated under reduced pressure to yield a dark purple oil. The mono-methylated compound (**4**) was isolated by column chromatography (240 mm x 44 mm) and eluted with 15% ethyl acetate/85% hexanes. The fractions were collected and the solvent was evaporated under reduced pressure to yield 2.72 g (17.4 mmol, 47%) of a dark purple oil. R_f: 0.54 (15% EtOAc/85% hexanes); ^{1}H NMR (400 MHz, CD_3CN) δ: 7.87 (d, J = 8 Hz, 1H), 7.76 (d, J = 8 Hz, 1H), 7.44-7.40 (m, 2H), 7.33 (t, J = 8 Hz, 1H), 7.15 (d, J = 8 Hz, 1H), 6.52 (d, J = 8 Hz, 1H), 5.08 (br s, 1H), 2.92 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 144.4, 134.1, 128.5, 126.6, 125.6, 124.5, 123.3, 119.8, 117.0, 103.6, 30.8; UV-vis (CH_3CN) 215, 248, 333 nm; IR (CCl_4) 3452 (m), 3068 (m), 3052 (m), 3013 (m), 2986 (m), 2940 (m), 2904 (m), 2881 (m), 2838 (m), 2815 (m), 1584 (s), 1522 (s) cm^{-1}; MS (EI) m/z 157, 156, 128, 115, 101, 89, 77, 63, 44; HRMS (EI) calcd for $C_{11}H_{11}N$ 157.0891, found 157.0886.

***N*-Methyl-*N*-nitroso-1-naphthylamine (III-27).** To 2.72 g (17.4 mmol) of the methylated compound (**4**), on an ice bath, 6 g of ice was added and 3 mL of HCl was added dropwise. Immediately to this solution, a solution of 1.51 g (21.9 mmol) $NaNO_2$

in 10 mL distilled water, which had been stirred for 10 min, was added and stirred for 40 min to produce a maroon oil. The mixture was filtered and washed with distilled water and CH_2Cl_2. The filtrate was neutralized to pH 7 with a saturated $NaHCO_3$ solution and extracted with CH_2Cl_2 until the organic layer was colorless. The combined organic extracts were then dried over $MgSO_4$, filtered, and the solvent was evaporated under reduced pressure. The nitrosated product (**5**) was isolated by column chromatography (240 mm x 44 mm) and eluted with 15% ethyl acetate/85% hexanes. The fractions were collected and the solvent was evaporated under reduced pressure to yield 2.64 g (14.19 mmol, 81.8 %) of a dark tangerine oil. R_f: 0.34 (15% EtOAc/85% hexanes); ^{1}H NMR (400 MHz, CD_3CN) δ: 8.06 – 7.96 (m, 2H), 7.70 – 7.28 (m, 5H), 3.51 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 138.9, 134.3, 129.8, 128.7, 128.4, 127.4, 126.7, 125.2, 123.3, 122.0, 36.1; IR (CCl_4) 3052 (s), 3017 (m), 2963 (m), 2931 (m), 2897 (m), 1953 (m), 1933 (m), 1809 (m) 1669 (m), 1596 (s), 1510 (s), 1448 (s), 1064 (s) cm^{-1}; MS (EI) m/z 186, 156, 128, 127, 115, 101, 77, 63, 44; HRMS (EI) calcd for $C_{11}H_{10}N_2O$ 186.0793, found 186.0781.

***N*-Methyl-*N*-(1-naphthyl)hydrazine (III-28).** A solution of 15 mLs each of acetic acid (AcOH), ethanol (EtOH), and distilled water was stirred together for 5 min and then added to 2.64 g (14.2 mmol) of the nitrosated compound (**5**) and stirred for 5 min. To this solution, 3.71 g (56.8 mmol, 4 equiv.) of Zn was added and stirred for 45 min. The solution was filtered to remove precipitated salts and rinsed with distilled water and CH_2Cl_2. The filtrate was neutralized to pH 7 with both solid Na_2CO_3 and aqueous $NaHCO_3$. The solution was extracted with CH_2Cl_2 until the organic layer was colorless. The combined organic extracts were dried over $MgSO_4$, filtered, and the solvent was

removed under reduced pressure yielding a dark purple oil. R_f: 0.16 (15% EtOAc/85% hexanes); ^{1}H NMR (400 MHz, CD_3CN) δ: 8.30 – 8.28 (m, 1H), 7.83 – 7.80 (m, 1H), 7.54 – 7.38 (m, 4H), 7.26 (d, *J* = 7.6 Hz, 1H), 3.90 (br s, 2H), 3.02 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 150.6, 134.6, 128.2, 128.1, 125.8, 125.5, 125.4, 123.99, 123.96, 113.0, 49.1; IR (CCl_4) 3351 (w) 3215 (w), 3048 (s), 2994 (m), 2947 (s), 2858 (w), 2838 (m), 2784 (s), 1914 (w), 1840 (w), 1813 (w), 1596 (s), 1572 (s), 1506 (s) cm^{-1}; MS (EI) m/z 172, 157, 156, 128, 127, 115, 102, 77, 75, 44; HRMS (EI) calcd for $C_{11}H_{12}N_2$ 172.1000, found 172.0998.

1-(*N*-Methyl-*N*-(1-naphthyl)amino)-2,4,6-trimethylpyridinium tetrafluoroborate (III-25). The percent yield of *N*-methyl-*N*-(1-naphthyl)hydrazine was determined by the ratio of NMR integrations. To this crude product mixture, 0.726 grams (3.47 mmol) of freshly prepared **III-29a** was added, followed by 10 mL of 100% EtOH. The solution was then stirred at room temperature for 2 h, cooled on an ice bath, and 200 mL of cold diethyl ether was added. Pale yellow crystals were isolated by filtration, giving 0.490 g. (1.34 mmol, 39%) of **1**: m.p. 116-120 °C (dec); ^{1}H NMR (400 MHz, CD_3CN) □: 7.96 (d, *J* = 8.4 Hz, 1H), 7.74 (d, *J* = 8.4 Hz, 1H), 7.65 (s, 2H), 7.55-7.37 (br m, 3H), 3.72 (s, 3H), 2.64 (s, 6H), 2.55 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) □: 159.8, 157.3, 140.4, 135.3, 130.1, 129.6, 126.9, 126.6, 125.86, 125.6, 125.2, 124.6, 113.6, 21.9, 20.5, 19.6; UV-vis (CH_3CN) 267, 281, 299, 347 nm; $\square_{266}$ = 7287 $M^{-1}cm^{-1}$, $\square_{355}$ = 2044 $M^{-1}cm^{-1}$; IR (nujol) 2959 (m), 2947 (m), 2924 (s), 2908, (m), 2889 (w), 2854 (m), 2842 (w), 1456 (m) 1374 (m) cm^{-1}; MS (FAB) m/z (relative intensity) 277.2 (14), 156.1 (100), 127 (3) ; HRMS (FAB) calcd for $C_{19}H_{21}N_2$ $[M - BF_4]^+$ 277.1704, found 277.1704.

5.2.3: Synthesis of 1-(*N*-(4-Methoxyphenyl)-*N*-methylamino)-2,4,6-trimethylpyridinium Tetrafluoroborate (photoprecursor to III-38)

Synthesized via previously published procedure.[9] The product was confirmed by ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.58 (s, 2H), 6.86 (d, J = 8 Hz, 2H), 6.27 (d, J = 8 Hz, 2H), 3.75 (s, 3H), 3.59 (s, 3H), 2.64 (s, 3H), 2.59 (s, 6H).

5.2.4: Synthesis of 1-(*N*-(4-Chlorophenyl)-*N*-methylamino)-2,4,6-trimethylpyridinium Tetrafluoroborate (photoprecursor to III-39)

Synthesis followed previously published procedure and supported with corresponding spectral analysis.[9] The product was confirmed by ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.69 (s, 2 H), 7.29 (d, J = 9 Hz, 2 H), 6.30 (d, J = 9 Hz, 2H), 3.61 (s, 3H), 2.65 (s, 3H), 2.58 (s, 6H).

5.2.5: Synthesis of 1-(*N*-Methyl-*N*-tolylamino)-2,4,6-trimethylpyridinium Tetrafluoroborate (photoprecursor to III-40)

Synthesis followed previously published procedure and supported with corresponding spectral analysis.[9] The product was confirmed by ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.69 (s, 2H), 7.12 (d, J = 8.5 Hz, 2H), 6.22 (br d, J = 8.5 Hz, 2H), 3.58 (s, J = 3H), 2.65 (s, 3H), 2.58 (s, 6H).

5.2.6: Synthesis of 2-Naphthylazide (III-41)

Synthesis followed previously published procedure.[10] To 2-naphthylamine (1.00 g, 7 mmol), 10 mL of HCl was added dropwise on ice with stirring. To this, a $NaNO_2$

solution (0.49 g, 7.1 mmol) in 10 mL distilled water was added and the resulting solution was stirred on an ice bath for 2 h. The reaction was neutralized to pH 7 with a saturated solution of $NaHCO_3$. A solution of NaN_3 (0.55 g, 8.5 mmol) and NaOAc (3.36 g, 40.9 mmol) in 10 mL distilled water was added and stirred for 1 h. The reaction was extracted with CH_2Cl_2, washed with distilled water, dried over $MgSO_4$, filtered, and the solvent was evaporated under reduced pressure to yield a yellow solid. The purified sample was isolated by column chromatography and eluted with 500 mL of 5% ethyl acetate/95% hexanes, then 500 mL of 10% ethyl acetate/90% hexanes, then 500 mL of 15% ethyl acetate/85% hexanes, then 500 mL of 20% ethyl acetate/80% hexanes. The fractions were collected and the solvent was evaporated under reduced pressure to yield 0.800 g (4.73 mmol, 67.6 %) of a yellow solid. R_f: 0.91 (15% EtOAc/85% hexanes); mp: 27-30 ºC; ^{1}H NMR (400 MHz, CD_3CN) δ: 7.92 – 7.82 (m, 3H), 7.56 – 7.44 (m, 3H), 7.21 (dd, *J* = 8.8 Hz, 2.6 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 137.5, 133.9, 131.0, 129.9, 127.9, 127.0, 126.9, 125.4, 118.8, 115.8; UV-vis (CH_3CN) 215, 247, 274, 283, 293, 317, 332 nm; IR (CCl_4) 3061 (w), 2384 (w), 2191 (w), 2107 (s), 1628 (w), 1598 (m), 1508 (m), 1284 (m), 1237 (w); MS (EI) m/z 169, 163, 141, 113, 99, 90, 71, 43; HRMS (EI) calcd for $C_{10}H_7N_3$ 169.0639, found 169.0632

5.2.7: Synthesis of 1-(*N*-Methyl-*N*-(2-naphthyl)amino)-2,4,6-trimethylpyridinium tetrafluoroborate (III-49)

***N*-methyl-2-naphthylamine (III-46).** 2-Naphthylamine (**16**, 5.45 g, 38.1 mmol) was crushed and dissolved in 30 mL of anhydrous CH_3CN and then 5.47 g (38.6 mmol) of iodomethane was added to the solution while stirring and a yellow precipitate formed.

The solution was refluxed for 45 min with an ice water condenser. The mixture was then neutralized to pH 7 with a saturated solution of $NaHCO_3$ and extracted with CH_2Cl_2 until the organic layer was colorless. The combined organic extracts were then dried over $MgSO_4$, filtered, and the solvent was evaporated under reduced pressure to yield a dark purple oil. The mono-methylated compound (**III-46**) was isolated by column chromatography (340 mm x 44 mm) and eluted with 10% ethyl acetate/90% hexanes. The fractions were collected and the solvent was evaporated under reduced pressure to yield 1.24 g (7.92 mmol, 21%) of a dark purple oil. R_f: 0.50 (15% EtOAc/85% hexanes); ^{1}H NMR (400 MHz, CD_3CN) δ: 7.64 (d, *J* = 8 Hz, 1H), 7.60 (d, *J* = 8 Hz, 1H), 7.59 (d, *J* = 8.8 Hz, 1H), 7.31 (t, *J* = 7 Hz, 1H), 7.13 (t, *J* = 7 Hz, 1H), 6.91 (dd, *J* = 8.8 Hz, 2.4 Hz, 1H), 6.74 (s, 1H), 4.62 (br s, 1H), 2.83 (s, 3H); ^{13}CNMR (400 MHz, $CDCl_3$) δ: 146.9, 135.2, 128.8, 127.6, 127.4, 126.3, 125.9, 121.9, 117.9, 103.7, 30.7; UV-Vis (CH_3CN) 212, 244, 281, 292, 350 nm; IR (CCl_4) 3436 (s), 3048 (s), 3017 (s), 2982 (s), 2908 (s), 2873 (s), 2807 (s), 2664 (w), 2617 (w), 1937 (m), 1903 (m), 1891 (m), 1627 (s), 1592 (s) cm^{-1}; MS (EI) m/z 157, 156, 128, 127, 115, 91, 77, 64, 44; HRMS (EI) calcd for $C_{11}H_{11}N$ 157.0891, found 157.0886.

***N*-methyl-*N*-nitroso-2-naphthylamine (III-47).** To 2.22 g (14.1 mmol) of the methylated compound (**III-46**), on an ice bath, 6 g of ice was added and 3 mL of HCl was added dropwise. Immediately to this solution, a solution of 1.04 g (15.1 mmol) $NaNO_2$ in 10 mL distilled water, which had been stirred for 10 min, was added and the solution turned into a orange/yellow emulsion and stirred for 1 h to produce a brownish-yellow oil. The solution was neutralized to pH 7 with a saturated $NaHCO_3$ solution and

extracted with CH_2Cl_2 until the organic layer was colorless. The combined organic extracts were then dried over $MgSO_4$, filtered, and the solvent was evaporated under reduced pressure to yield 2.56 g (13.8 mmol, 98%) of the brown solid nitrosated product (**18**). R_f: 0.43 (15% EtOAc/85% hexanes); mp: 76-80 ºC; ^{1}H NMR (400 MHz, CD_3CN) δ: 8.01 (d, *J* = 9.2. Hz, 1H), 7.97-7.89 (m, 4H), 7.60-7.52 (m, 2H), 3.52 (s, 3 H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 139.8, 133.3, 132.1, 129.6, 128.1, 127.8, 127.2, 126.3, 118.2, 116.1, 31.3; IR (CCl_4) 3064 (w), 2978 (s), 2935 (m), 2866 (s), 2803 (w), 2116 (w), 2054 (w), 1634 (m), 1600 (m), 1561 (s), 1467 (s), 1440 (s), 1122 (s), 1071 (s) cm^{-1}; MS (EI) m/z 186, 156, 121, 115, 91, 84, 66, 61; HRMS (EI) calcd for $C_{11}H_{10}N_2O$ 186.0793, found 186.0788.

***N*-Methyl-*N*-(2-naphthyl)hydrazine (III-48).** A solution of 25 mLs of each AcOH, EtOH, and distilled water was stirred together for 15 min and then added to 2.56 g (13.8 mmol) of the nitrosated compound (**III-47**) and stirred for 10 min. To this solution, 1.83 g (28.0 mmol, 2 equiv.) of Zn was added and stirred for 1 h. The solution was filtered to remove the Zn and rinsed with distilled water and CH_2Cl_2. The filtrate was neutralized to pH 7 with both solid Na_2CO_3 and aqueous $NaHCO_3$ and was extracted with CH_2Cl_2 until the organic layer was colorless. The combined organic extracts were dried over $MgSO_4$, filtered, and the solvent was removed under reduced pressure. The hydrazine compound (**III-48**) was isolated by column chromatography (340 mm x 44 mm) and eluted with 25% ethyl acetate/75% hexanes. The fractions were collected and the solvent was evaporated under reduced pressure to yield 0.65 g (3.8 mmol, 27%) of a dark purple oil. R_f: 0.11 (15% EtOAc/85% hexanes); ^{1}H NMR (400 MHz, CD_3CN) δ:

7.68 (t, *J* = 8.8 Hz, 3H), 7.49 (dd, *J* = 8.8, 2 Hz, 1H), 7.35 (t, *J* = 7.4 Hz, 1H), 7.209 (t, *J* = 7.4 Hz, 1H), 7.17 (d, *J* = 2 Hz, 1H), 3.97 (br s, 2 H), 3.14 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 150.4, 134.5, 128.6, 127.9, 127.6, 126.6, 126.2, 122.9, 117.3, 107.3, 44.8; IR (CCl_4) 3685 (s), 3541 (s), 3200 (m), 3165 (s), 2994 (s), 2939 (s), 2617 (m), 2400 (m), 2198 (w), 2062 (w), 1611, (s), 1429 (s), 1029 (s) cm^{-1}; MS (EI) m/z 172, 157, 156, 128, 127, 102, 101, 74, 64, 51, 50; HRMS (EI) calcd for $C_{11}H_{12}N_2$ 172.1000, found 172.0991.

1-(*N*-methyl-*N*-(2-naphthyl)amino)-2,4,6-trimethylpyridinium tetrafluoroborate (III-49a)

To the hydrazine (**III-48**), 0.56 grams (2.7 mmol) of freshly prepared **III-29a** was added, followed by 10 mL of 100% EtOH. The solution was then stirred at room temperature for 2 h, cooled on an ice bath, and 200 mL of cold diethyl ether was added. Bright yellow crystals were isolated by filtration, giving 0.96 g. (2.6 mmol, 99%) of **III-49a**: m.p. 146–148 °C (dec); ^{1}H NMR (400 MHz, CD_3CN) δ: 7.87 (d, *J* = 9.2 Hz, 1H), 7.82 (d, *J* = 8 Hz, 1H), 7.75 – 7.69 (m, 3H), 7.48 (t, *J* = 7.4 Hz, 1H), 7.38 (t, *J* = 7.4 Hz, 1H), 6.95 – 6.56 (br s, 2H), 3.63 (s, 3H), 2.62 (s, 3H), 2.55 (s, 6H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 161.3, 158.3, 141.3, 134.2, 131.1, 129.8, 128.8, 127.76, 127.70, 126.8, 124.7, 111.6, 105.9, 38.6, 22.2, 19.3; UV-vis (CH_3CN) 270, 330, 339, 365 nm; ε_{266} = 15391 $M^{-1}cm^{-1}$, ε_{355} = 660 $M^{-1}cm^{-1}$; IR (nujol) 2967 (s), 2951 (s), 2943 (s), 2928 (s), 2912 (s), 2842 (s) 2718 (w), 1634 (w), 1460 (s), 1374 (s), 1071 (m), 1033 (m) cm^{-1}; MS (FAB) m/z 277, 155, 119, 85; HRMS (FAB) calcd for $C_{19}H_{21}N_2$ $[M - BF_4]^+$ 277.1705, found 277.1699.

5.2.8: Synthesis of 2,6-dimethyl-4-phenylpyrylium tetrafluoroborate (III-29b)

Followed previously published synthetic method by Manoj and Gopidas with the exception of using tetrafluoroboric acid instead of perchloric acid.[11,12] ^{1}H NMR (400 MHz, CD_3CN) δ: 8.16 (s, 2H), 8.06 (d, J = 8 Hz, 2H), 7.81 (t, J = 8 Hz, 1H), 7.69 (t, J = 8 Hz, 2H), 2.87 (s, 6H); IR (neat) 1672 (m), 1638 (s), 158 (s), 1530 (s), 1452 (w), 1433 (w), 1337 (s), 1213 (s), 1012 (s), 877 (w), 777 (s), 681 (s) cm^{-1}; MS (FAB) m/z 185, 177, 133, 103, 89, 87, 45; HRMS (FAB) calcd for $C_{13}H_{13}O$ $[M - BF_4]^+$ 185.0966, found 185.0966.

5.2.9: Synthesis of 1-(*N*-Methyl-*N*-(2-naphthyl)amino)-2,6-dimethyl-4-phenylpyridinium tetrafluoroborate (III-49b)

To *N*-methyl-*N*-(2-naphthyl)hydrazine (**III-48**) (0.47 g, 2.7 mmol), freshly prepared 1-(*N*-methyl-*N*-(2-naphthyl)amino)-2,6-dimethyl-4-phenylpyrylium tetrafluoroborate (0.473 g, 1.74 mmol) was added, followed by 10 mL of 100% EtOH. The solution was then stirred at room temperature for 2 h, cooled on an ice bath, and 200 mL of cold diethyl ether was added. Dull yellow crystals were isolated and recrystallized from MeOH to yield (0.51 g, 1.2 mmol, 69%) light brown crystals. m.p. 186-188 ºC; ^{1}H NMR (400 MHz, CD_3CN) δ: 8.21 (s, 2H), 7.98 (d, J = 8 Hz, 2H), 7.89 (d, J = 8 Hz, 1H), 7.84 (d, J = 8 Hz, 1H), 7.75 – 7.65 (m, 4H), 7.49 (t, J = 7 Hz, 1H), 7.39 (t, J = 7 Hz, 1H), 6.83 (br s, 2H), 3.68 (s, 3H), 2.65 (s, 6H)**;** ^{13}C NMR (400 MHz, $CDCl_3$) δ: 159.5, 158.0, 141.5, 134.4, 134.0, 132.5, 131.2, 129.9, 129.0, 128.7, 127.9, 127.8, 126.9, 126.2, 124.8, 111.8, 106.1, 98.5, 38.8, 19.7; UV-vis (CH_3CN) 211, 234, 290, 398 nm; IR (neat) 3054 (w), 1622 (m), 1595 (m), 1557 (m), 1476 (m), 1433 (m), 1391 (w), 1340 (w), 1310 (m),

1144 (w), 1090 (w), 1032 (s), 947 (s), 827 (s), 800 (m), 769 (m), 677 (m) cm^{-1}; MS (FAB) m/z 339, 327, 263, 239, 219, 185, 177, 133, 89, 73, 45; HRMS (FAB) calcd for $C_{24}H_{23}N_2$ $[M - BF_4]^+$ 339.1861, found 339.1873

5.2.10: Synthesis of 2,6-dimethyl-4-biphenylylpyrylium tetrafluoroborate (III-29c)

Followed previously published synthetic method by Manoj and Gopidas with the exception of using tetrafluoroboric acid instead of perchloric acid.[11,12] ^1H NMR (400 MHz, CD_3CN) δ: 8.17 (d, *J* = 5.4 Hz, 4H), 7.99 (d, *J* = 5.4 Hz, 2H), 7.80 (d, *J* = 5.4 Hz, 2H), 7.56 – 7.49 (m, 3H), 2.87 (s, 6H); IR (neat) 1634 (s) 1595 (s), 1522 (s), 1452 (m), 1333 (s), 1201 (m), 1047 (s), 993 (s), 943 (w), 839 (m), 769 (s), 735 (m), 696 (m) cm^{-1}; MS (EI) m/z 261, 197, 155, 135, 119, 85, 57, 45; HRMS (EI) calcd for $C_{19}H_{17}O$ $[M - BF_4]^+$ 261.1279, found 261.1292.

5.2.11: Synthesis of 1-(*N*-Methyl-*N*-(2-naphthyl)amino)-2,6-dimethyl-4-biphenylylpyridinium tetrafluoroborate (III-49c)

To *N*-methyl-*N*-(2-naphthyl)hydrazine (**III-48**) (0.47 g, 2.7 mmol), freshly prepared 1-(*N*-methyl-*N*-(2-naphthyl)amino)-2,6-dimethyl-4-biphenylylpyrylium tetrafluoroborate (0.46 g, 1.7 mmol) was added, followed by 10 mL of 100% EtOH. The solution was then stirred at room temperature for 2 h, cooled on an ice bath, and 200 mL of cold diethyl ether was added. Dull yellow crystals were isolated and recrystallized from MeOH to yield (0.72 g, 1.4 mmol, 83%) golden brown crystals. m.p. 172-178 ºC; ^1H NMR (400 MHz, CD_3CN) δ: 8.26 (s, 2H), 8.08 (d, *J* = 8.8 Hz, 2H), 7.96 (d, *J* = 8.8, 2H), 7.90 (d, *J* = 8.8 Hz, 1H), 7.84 (d, *J* = 8 Hz, 1H), 7.83 – 7.76 (m, 3H), 7.56 – 7.45 (m,

4H), 7.39 (t, J = 8 Hz, 1H), 6.82 (br s, 2H), 3.7 (s, 3H), 2.66 (s, 6H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 159.4, 131.3, 129.2, 129.0, 128.7, 128.5, 127.9, 127.4, 126.9, 126.0, 124.9, 20.1; UV-vis (CH_3CN) 202, 238, 280, 290, 340 nm; IR (neat) 3633(w) 3552 (w), 3081 (w), 1626 (s), 1599 (s), 1568 (m), 1549 (m), 1510 (w), 1464 (m), 1337 (m), 1310 (m), 1209 (m), 1051 (s), 1028 (s), 831 (m), 769 (m), 731 (m) cm^{-1}; MS (FAB) m/z 415, 329, 309, 260, 155, 152, 119, 85; HRMS (FAB) calcd for $C_{30}H_{27}N_2$ $[M - BF_4]^+$ 415.2174, found 415.2159.

5.2.12: Synthesis of *O*-(2,4-Dinitrophenyl)hydroxylamine (IV-24)

Synthesis followed previously published procedure.[13] Product was confirmed by ^{1}H NMR (400 MHz, CD_3CN) δ: 8.69 (d, J = 5.6 Hz, 1H), 8.43 (dd, J = 9.2 Hz, 5.6 Hz, 1H), 8.00 (d, J = 9.6 Hz, 1H), 6.87 (s, 2H); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.83 (d, J = 2.4 Hz, 1H), 8.45 (dd, J = 9.2 Hz, 2.4 Hz, 1H), 8.06 (d, J = 9.6 Hz, 1H), 6.39 (s, 2H)

5.2.13: *N*-[4-(Methyl-phenyl-amino)-phenyl]-4-nitro-benzamide

Methyl-(4-nitro-phenyl)-phenyl-amine (precursor to IV-21). Synthesis followed previously published procedure.[14] *N*-Methyldiphenylamine (9.11 g, 49.7 mmol) was dissolved in 100 mL of acetic anhydride and the solution was stirred and heated to 50 ºC. Nitric acid (3 mL, 47 mmol) was added and the solution was stirred at 50 ºC for another 5 h. The solvent was then removed under reduced pressure. The desired product was isolated by column chromatography (340 mm x 44 mm) and eluted with 5% ethyl acetate/95% hexanes. The fractions were collected and the solvent was evaporated under reduced pressure to yield 4.65 g (20.4 mmol, 43%) of an orange-brown

oil and was confirmed by ^{1}H NMR. R_f: 0.22 (15% EtOAc/85% hexanes); ^{1}H NMR (400 MHz, CD_3CN) δ: 8.04 (d, *J* = 9.6 Hz, 2H), 7.49 (t, *J* = 7.8 Hz, 2H), 7.34 (t, *J* = 7.8 Hz, 1H), 7.29 (d, *J* = 7.8 Hz, 2H), 6.72 (d, *J* = 9.6 Hz, 2H), 3.39 (s, 3H); MS (FAB) m/z 228, 213, 181, 180, 134, 118, 84, 76, 58, 57, 47; HRMS (FAB) calcd for $C_{13}H_{12}N_2O_2$ 228.0898, found 228.0901.

***N*-Methyl-*N*-phenyl-1,4-benzenediamine (IV-21).** 25 mLs of each AcOH, EtOH, and distilled water was stirred together for 15 min and then added to methyl-(4-nitro-phenyl)-phenyl-amine (2.78 g, 12.2 mmol) and stirred for 10 min. To this solution, 1.595 g (24.5 mmol) of Zn was added and stirred for 5 h. The solution was filtered to remove the Zn and rinsed with distilled water and CH_2Cl_2. The filtrate was neutralized to pH 7 with both solid Na_2CO_3 and aqueous $NaHCO_3$ and was extracted with CH_2Cl_2 until the organic layer was colorless. The combined organic extracts were dried over $MgSO_4$, filtered, and the solvent was removed under reduced pressure. The desired product was isolated by column chromatography (340 mm x 44 mm) and eluted with 20% ethyl acetate/80% hexanes. The fractions were collected and the solvent was evaporated under reduced pressure to yield 1.66 g (8.38 mmol, 69%) of a dark purple oil. R_f: 0.1 (15% EtOAc/85% hexanes); ^{1}H NMR (400 MHz, CD_3CN) δ: 7.13 (t, *J* = 8 Hz, 2H), 6.90 (d, *J* = 8 Hz, 2H), 6.67 (t, *J* = 8 Hz, 5H), 4.05 (br s, 2H), 3.16 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 149.9, 143.3, 140.4, 130.5, 129.6, 129.1, 128.8, 127.0, 117.5, 116.1, 114.7, 40.4; MS (EI) m/z 198, 197, 183, 166, 154, 104, 91, 77, 65, 51, 39; HRMS (EI) calcd for $C_{13}H_{14}N_2$ 198.1157, found 198.1155.

***N*-[4-(Methyl-phenyl-amino)-phenyl]-4-nitro-benzamide (IV-23d).** Synthesis followed previously published procedure.[15] A solution of *p*-nitrobenzoyl chloride (1.84 g, 9.93 mmol) in 20 mL of CH_2Cl_2 was added dropwise over a period of 20 – 30 min to a stirred solution of *N*-methyl-*N*-phenyl-1,4-benzenediamine (1.48 g, 7.48 mmol) and triethylamine (0.87 g, 8.6 mmol) in 50 mL of CH_2Cl_2. After the addition was complete, the reaction mixture was refluxed overnight, with stirring. The reaction mixture was then cooled to room temperature and cold distilled water was added to precipitate the desired product which was then filtered to yield (4.32 g, 6.81 mmol, 91%) an orange solid. m.p. 216-220 ºC; ^{1}H NMR (400 MHz, CD_3CN) δ: 8.86 (br s, 1H), 8.33 (d, *J* = 8 Hz, 2H), 8.09 (d, *J* = 8.8 Hz, 2H), 7.63 (d, *J* = 8.8, 2H), 7.27 (t, *J* = 7.2 Hz, 2H), 7.06 (d, *J* = 8.8 Hz, 2H), 7.00 (d, *J* = 8 Hz, 2H), 6.93 (t, *J* = 7.2 Hz, 1H), 3.29 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 148.8, 130.5, 129.3, 128.2, 124.0, 121.8, 120.8, 120.5, 40.4; IR (neat) 3266 (m), 3054 (w), 1642 (m), 1591 (m), 1506 (s), 1410 (w), 1398 (w), 1348 (s), 1313 (s), 1252 (s), 1175 (w), 1101 (w), 1009 (m), 904 (w), 854 (s), 750 (s), 688 (s) cm^{-1}; MS (FAB) m/z 348, 347, 309, 309, 275, 197, 154, 119, 85, 57, 47; HRMS (FAB) calcd for $C_{20}H_{17}N_3O_3$ 347.1270, found 347.1287.

5.2.14: Synthesis of 4-Nitro-*N*-(4-phenylamino-phenyl)-benzamide (IV-23c)

Synthesis followed previously published procedure.[15] A solution of *p*-nitrobenzoyl chloride (3.37 g, 18.2 mmol) in 40 mL of CH_2Cl_2 was added dropwise over a period of 20 – 30 min to a stirred solution of 4-aminodiphenylamine (3.33 g, 18.1 mmol) and triethylamine (2.04 g, 21.1 mmol) in 40 mL of CH_2Cl_2. After the addition was complete, the reaction mixture was refluxed overnight, with stirring. The reaction

mixture was then cooled to room temperature and cold distilled water was added to precipitate the desired product which was then filtered to yield (2.16 g, 6.48 mmol, 36%) an orange-brown solid. m.p. 198-200 ºC; ^{1}H NMR (400 MHz, CD_3CN) δ: 8.83 (s, 1H), 8.33 (d, *J* = 8.8 Hz, 2H), 8.10 (d, *J* = 8.8 Hz, 2H), 7.60 (d, *J* = 8.8 Hz, 2H), 7.25 (t, *J* = 8 Hz, 2H), 7.13 – 7.07 (m, 4H), 6.88 (t, *J* = 7.2 Hz, 1H), 6.68 (s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ:140.6, 130.4, 129.4, 128.2, 124.0, 122.0, 121.2, 118.4, 117.7; IR (neat) 3355 (w), 3286 (w), 1630 (m), 1595 (s), 1506 (s), 1445 (m), 1395 (w), 1344 (s), 1317 (s), 1171 (m), 1105 (m), 1012 (m), 870 (m), 816 (m), 742 (s), 696 (s) cm^{-1}; HRMS (FAB) calcd for $C_{19}H_{15}N_3O_3$ 333.1113, found 333.1121.

5.2.15: Synthesis of *N*-(4-Phenylamino-phenyl)-benzamide (IV-23a)

Synthesis followed previously published procedure.[15] A solution of benzoyl chloride (4.61 g, 32.7 mmol) in 20 mL of CH_2Cl_2 was added dropwise over a period of 20 – 30 min to a stirred solution of 4-aminodiphenylamine (5.28 g, 28.7 mmol) and triethylamine (3.35 g, 33.1 mmol) in 100 mL of CH_2Cl_2. After the addition was complete, the reaction mixture was stirred at reflux overnight. The reaction mixture was then cooled to room temperature and cold distilled water was added to precipitate the desired product which was then filtered to yield (4.32 g, 15 mmol, 52%) a gray solid. m.p. 145-150 ºC; ^{1}H NMR (400 MHz, CD_3CN) δ: 8.65 (br s, 1H), 7.92 (d, *J* = 7.2 Hz, 2H), 7.58 (t, *J* = 8.8 Hz, 3H), 7.51 (t, *J* = 7.6 Hz, 2H), 7.24 (t, *J* = 7.6 Hz, 2H), 7.10 (d, *J* = 8.8 Hz, 2H), 7.06 (d, *J* = 7.6 Hz, 2H), 6.86 (t, *J* = 7.2 Hz, 1H), 6.64 (br s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 165.6, 143.4, 139.7, 135.0, 131.7, 131.5, 129.4, 128.8, 127.0, 121.8, 120.8, 118.8, 117.3; IR (neat) 3340 (w), 3293 (w), 3050 (w), 1630 (m), 1595 (m),

1522 (m), 1487 (m), 1441 (w), 1313(s), 1271 (m), 1167 (m), 1078 (w), 827 (w), 742 (m), 688 (s) cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{17}N_2O$ (MH^+) 289.13409, found 289.13415.

5.2.16: Synthesis of *N*-[4-(Methyl-phenyl-amino)-phenyl]-benzamide (IV-23b)

Synthesis followed previously published procedure.[15] A solution of benzoyl chloride (1.70 g, 12.1 mmol) in 20 mL of CH_2Cl_2 was added dropwise over a period of 20 – 30 min to a stirred solution of *N*-methyl-*N*-phenyl-1,4-benzenediamine (1.67 g, 8.42 mmol) and triethylamine (0.95 g, 9.35 mmol) in 20 mL of CH_2Cl_2. After the addition was complete, the reaction mixture was refluxed overnight, with stirring. The reaction mixture was cooled to room temperature and cold distilled water was added to precipitate a blue-gray solid. The desired product was isolated by column chromatography (340 mm x 44 mm) and eluted with 1 L of 10% ethyl acetate/90% hexanes, then 500 mL of 15% ethyl acetate/85% hexanes, then 500 mL of 20% ethyl acetate/80% hexanes, then 500 mL of 40% ethyl acetate/60% hexanes. The fractions were collected and the solvent was evaporated under reduced pressure to yield 1.66 g (5.5 mmol, 65.3 %) of an off-white solid. R_f: 0.06 (15% EtOAc/85% hexanes); m.p. 110-116 ºC; ^{1}H NMR (400 MHz, CD_3CN) δ: 8.71 (br s, 1H), 8.00 (d, J = 7.2 Hz, 2H), 7.93 (d, J = 7.6 Hz, 2H), 7.65 – 7.47 (m, 3H), 7.26 (t, J = 7.6 Hz, 2H), 7.06 (d, J = 8 Hz, 2H), 6.97 (d, J = 8 Hz, 2H), 6.89 (t, J = 7.2 Hz, 1H), 3.28 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 149.0, 148.2, 145.9, 135.0, 133.7, 132.1, 131.9, 131.7, 130.2, 129.2, 128.8, 128.4, 126.9, 123.4, 121.8, 121.6, 120.8, 119.5, 118.0, 40.3; IR (neat) 3324 (w), 3042 (w), 1645 (s), 1587 (s), 1510 (s), 1487 (s), 1321 (s), 1256 (s), 1175 (s), 1128 (s), 928 (s), 688 (s) cm^{-1}; MS (EI) m/z 302, 288, 197, 181, 154, 128, 105, 77, 51; HRMS (EI) calcd for $C_{20}H_{18}N_2O$ 302.1419, found 302.1411.

5.2.17: Synthesis of *N*,*N*′-Dimethyl-*N*′-nitroso-*N*-phenyl-1,4-benzenediamine (IV-20)

***N*′-Acetyl-*N*-phenyl-1,4-benzenediamine (IV-17).** Synthesis followed previously published procedure and supported with corresponding spectral analysis.[16] *N*-phenyl-1,4-benzenediamine (14.89 g, 80.8 mmol) and acetic anhydride (9.08 g, 88.9 mmol) were dissolved in 200 mL of acetic acid. The reaction mixture was refluxed for 3 h and cooled to room temperature. The mixture was concentrated and crystallized from toluene (14.93 g, 66.05 mmol, 82 %). ^{1}H NMR (400 MHz, CD_3CN) δ: 8.18 (br s, 1H), 7.41 (d, J = 8.8 Hz, 2H), 7.22 (t, J = 7.6 Hz, 2H), 7.02 (t, J = 8.8 Hz, 4H), 6.83 (t, J = 7.6 Hz, 1H), 6.56 (br s, 1H), 2.02 (s, 3H); MS (EI) m/z 226, 210, 185, 184, 167, 154, 130, 107, 103, 77, 63, 51, 44.

***N*′-Acetyl-*N*,*N*′-dimethyl-*N*-phenyl-1,4-benzenediamine (IV-18).** Synthesis followed previously published procedure and supported with corresponding spectral analysis.[16] *N*′-Acetyl-*N*-phenyl-1,4-benzediamine (14.93 g, 66.05 mmol), powdered sodium hydroxide (45.24 g, 1131 mmol) , powdered potassium carbonate (58.7 g, 425 mmol), tetrabutylammonium hydrogen sulfate (3.77 g, 11.08 mmol) and iodomethane (42 mL, 697 mmol) were added to 90 mL of toluene. The reaction mixture was refluxed for 18 h and cooled to room temperature. Ethyl acetate was added and the salts were removed by filtration. The residue was concentrated and crystallized from petroleum ether (60-80 ºC) resulting in pale yellow crystals (14.9 g, 58.9 mmol, 89%). ^{1}H NMR (400 MHz, CD_3CN) δ: 7.13 (t, J = 8.8 Hz, 2H), 6.06 (d, J = 8.8 Hz, 2H), 6.68 – 6.65 (m, 3H), 6.61 (d, J = 8.8 Hz, 2H), 3.17 (s, 3H), 2.75 (s, 3H).

***N*,*N*′-Dimethyl-*N*-phenyl-1,4-benzenediamine (IV-19).** Synthesis followed previously published procedure and supported with corresponding spectral analysis.[16] *N*′-Acetyl-*N*,*N*′-dimethyl-*N*-phenyl-1,4-benzediamine (14.9 g, 58.9 mmol) and sodium hydroxide (18.9 g, 472 mmol) were dissolved in ethanol/water (415 mL, 2:1 (v/v)). The reaction mixture was refluxed for 48 h and cooled to room temperature. The mixture was extracted with ethyl acetate, the combined organic layers were dried over $MgSO_4$, and the solvent was evaporated. The desired product was isolated by column chromatography (340 mm x 44 mm) and eluted with 15% ethyl acetate/85% hexanes. The fractions were collected and the solvent was evaporated under reduced pressure to yield 12.19 g (57.5 mmol, 97.7 %) of a dark purple oil. R_f: 0.26 (15% EtOAc/85% hexanes); ^{1}H NMR (400 MHz, CD_3CN) δ: 7.33 (t, *J* = 8 Hz, 2H), 7.14 – 7.03 (m, 5H), 6.95 (d, *J* = 8.8 Hz, 2H), 3.29 (s, 3H), 3.14 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 150.1, 146.6, 143.3, 139.1, 128.8, 127.4, 127.0, 117.2, 116.2, 114.7, 114.3, 113.3, 40.4, 31; MS (FAB) m/z 212, 211, 198, 197, 177, 146, 132, 107, 106, 89, 87, 55, 45; HRMS (FAB) calcd for $C_{14}H_{16}N_2$ 212.1313, found 212.1308.

***N*,*N*′-Dimethyl-*N*′-nitroso-*N*-phenyl-1,4-benzenediamine (IV-20).** To *N*,*N*′-dimethyl-*N*-phenyl-1,4-benzenediamine (3.41 g, 16.1 mmol), 6 g of ice was added and 4 mL of HCl was also added dropwise. To this mixture, a solution of $NaNO_2$ (1.27 g, 18.4 mmol) in 15 mL of distilled water was added and the resulting solution was stirred for 1 h. The solution was neutralized to pH 7 with a saturated solution of $NaHCO_3$, extracted with CH_2Cl_2, washed with distilled water, dried over $MgSO_4$, filtered, and the solvent was evaporated under reduced pressure to yield (3.53 g, 14.6 mmol, 91%) of a dark

brown solid. R_f: 0.3 (15% EtOAc/85% hexanes); ^{1}H NMR (400 MHz, CD_3CN) δ: 7.68 (d, *J* = 9.2 Hz, 1H), 7.59 (d, *J* = 7.6, 1H), 7.43 – 7.35 (m, 3H), 7.14 (d, *J* = 7.6 Hz, 2H), 7.04 (d, *J* = 10.4 Hz, 2H), 3.38 (s, 3H), 3.32 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 148.4, 134.8, 129.5, 129.1, 127.3, 123.4, 123.1, 122.6, 120.6, 120.4, 119.2, 118.5, 40.3, 32.2; MS (FAB) m/z 241, 239, 211, 195, 177, 151, 132, 118, 102, 89, 85, 45; HRMS (FAB) calcd for $C_{14}H_{16}N_3O$ (MH^+) 242.1293, found 242.1289.

5.2.18: Synthesis of 2,4,6-Trichloro-benzoic acid *N*-(4-phenylamino-phenyl)-hydrazide (IV-24)

2,4,6-Trichloro-*N*-(4-phenylamino-phenyl)-benzamide (IV-23e). A solution of 2,4,6-trichlorobenzoyl chloride (2.5 g, 10.24 mmol) in CH_2Cl_2 (10 mL) was added dropwise over a period of 20 – 30 min to a stirred solution of *N*-phenyl-1,4-benzenediamine (1.55 g, 8.43 mmol) and triethylamine (0.94 g, 9.3 mmol) in CH_2Cl_2 (10 mL). After the addition was complete, the reaction mixture was refluxed overnight, with stirring. The reaction mixture was then cooled to room temperature and extracted with CH_2Cl_2, washed with distilled water, dried over $MgSO_4$, filtered, and the solvent was evaporated under reduced pressure. The desired product was isolated by column chromatography (340 mm x 44 mm) and eluted with 1 L of 15% ethyl acetate/85% hexanes, then 1 L of 20% ethyl acetate/80% hexanes, then 500 mL of 40% ethyl acetate/60% hexanes, then 500 mL of 60% ethyl acetate/40% hexanes. The fractions were collected and the solvent was evaporated under reduced pressure to yield 1.7 g (4.4 mmol, 53%) of an off-white solid. R_f: 0.2 (15% EtOAc/85% hexanes); m.p. 188-192 ºC; ^{1}H NMR (400 MHz, CD_3CN) δ: 8.72 (br s, 1H), 7.57 (s, 2H), 7.49 (d, *J* = 8.8 Hz, 2H),

7.25 (t, *J* = 8.8 Hz, 2H), 7.11 – 7.06 (m, 4H), 6.87 (t, *J* = 7.6 Hz, 1H), 6.69 (br s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 161.5, 143.1, 140.6, 136.0, 134.5, 133.1, 130.2, 129.4, 128.2, 122.1, 121.2, 120.5, 118.5; IR (neat) 3347 (w), 3255 (w), 3073 (w), 1642 (s), 1591 (s), 1576 (s), 1545 (s), 1510 (s), 1364 (m), 1294 (s), 1186 (m), 1121 (m), 912 (w), 846 (m), 742 (s), 688 (s) cm^{-1}; MS (FAB) m/z 390, 357, 211, 183, 135, 85, 22, 55; HRMS (ESI) calcd for $C_{19}H_{14}N_2OCl_3$ (MH+) 391.01717, found 391.01841.

2,4,6-Trichloro-benzoic acid *N*-(4-phenylamino-phenyl)-hydrazide (IV-25). A published synthetic procedure for coupling the amide to *O*-(2,4-dinitrophenyl)hydroxylamine to yield the corresponding hydrazine was followed.[15] To three-necked round bottom flask purged with nitrogen, a solution of 2,4,6-trichloro-*N*-(4-phenylamino-phenyl)-benzamide (1.55 g, 8.43 mmol) in minimal anhydrous THF was added. A solution of sodium hydride (0.12 g, 2.8 mmol) in minimal anhydrous THF was added via cannula and the mixture was heated to 70 ºC and stirred for 1 h. The reaction mixture was cooled to room temperature and a solution of *O*-(2,4-dinitrophenyl)hydroxylamine (0.53 g, 2.6 mmol) in minimal THF was added and left to stir overnight. The reaction mixture was then extracted with CH_2Cl_2, washed with distilled water, dried over $MgSO_4$, filtered, and the solvent was evaporated under reduced pressure to yield a brown oil. The desired product was isolated by column chromatography (340 mm x 44 mm) and eluted with 20% ethyl acetate/80% hexanes. The fractions were collected and the solvent was evaporated under reduced pressure to yield 0.18 g (0.5 mmol, 19%) of a brown oil. R_f: 0.1 (15% EtOAc/85% hexanes);^{1}H NMR (400 MHz, CD_3CN) δ: 7.42 (d, *J* = 8 Hz, 2H), 7.36 (s, 2H), 7.20 (d, *J* = 8 Hz, 2H),

7.14 (t, *J* = 7.6 Hz, 3H), 7.05 (d, *J* = 7.6 Hz, 2H), 6.88 (d, *J* = 8 Hz, 1H), 6.75 (s, 1H), 5.06 (br s, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 171.5, 163.2, 144.2, 142.2, 135.8, 134.4, 133.0, 130.0, 128.3, 128.1, 127.0, 125.8, 124.2, 122.4, 119.6, 119.4, 118.8, 117.9, 116.5; MS (FAB) m/z 405, 391, 389, 355, 290, 255, 209, 198, 169, 155, 92, 85; HRMS (FAB) calcd for $C_{19}H_{14}N_3OCl_3$ 405.0202, found 405.0196.

5.2.19: Synthesis of 4-(*N*-anilino)phenyl azide (IV-27)

To *N*-phenyl-1,4-benzenediamine (3.44 g, 18.7 mmol), 6 g of ice was added and 5 mL of HCl was added dropwise with stirring. To this mixture, a $NaNO_2$ solution (1.34 g, 19.4 mmol) in 15 mL distilled water was added and the resulting solution was stirred on an ice bath for 2 h. The reaction was neutralized to pH 7 with a saturated solution of $NaHCO_3$. A solution of NaN_3 (1.24 g, 19 mmol) and NaOAc (6.3 g, 76 mmol) in 15 mL distilled water was added and stirred for 1 h. The reaction was extracted with CH_2Cl_2, washed with distilled water, dried over $MgSO_4$, filtered, and the solvent was evaporated under reduced pressure to yield a yellow solid. The purified sample was isolated by column chromatography and eluted with 15% ethyl acetate/85% hexanes. The fractions were collected and the solvent was evaporated under reduced pressure to yield 2.70 g (12.8 mmol, 69%) of a dark purple solid. R_f: 0.52 (15% EtOAc/85% hexanes); m.p. 52-62 ºC; ^{1}H NMR (400 MHz, CD_3CN) δ: 7.24 (t, *J* = 7.2 Hz, 2H), 7.09 (d, *J* = 8 Hz, 2H), 7.03 (d, *J* = 8 Hz, 2H), 6.95 (d, *J* = 8 Hz, 2H), 6.88 (t, *J* = 7.2 Hz, 1H), 6.67 (br s, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 143.1, 140.3, 132.6, 129.4, 121.1, 120.4, 119.9, 119.5, 117.5; UV-vis (CH_3CN) 244, 295 nm; IR (CCl_4) 3429 (w), 3231 (w), 3060 (w), 3029 (w), 2928 (w), 2850 (w), 2411 (w), 2256 (w), 2120 (s), 1596 (s), 1557 (m), 1541 (w), 1506

(s), 1444 (w), 1401 (w), 1285 (s), 1238 (m), 1176 (w) cm^{-1}; MS (FAB) m/z 210, 182, 155, 135, 119, 103, 85, 57, 47, 41**;** HRMS (FAB) calcd for $C_{12}H_{11}N_4$ (MH^+) 211.0984, found 211.0973.

5.2.20: Synthesis of 1-(*N*,*N*-diphenylamino)-2,4,6-trimethylpyridinium tetrafluoroborate (IV-30)

Synthesis followed previously published procedure and supported with corresponding spectral analysis.[17,18] The product was confirmed by ^1H NMR (400 MHz, CD_3CN) δ: 7.77 (s, 2H), 7.43 (t, *J* = 8 Hz, 4H), 7.22 (t, *J* = 8 Hz, 2H), 6.97 (d, *J* = 8 Hz, 4H), 2.63 (s, 3H), 2.50 (s, 6H).

5.3: Photoproduct Analysis

5.3.1: 1-(*N*-Methyl-*N*-(1-naphthyl)amino)-2,4,6-trimethylpyridinium tetrafluoroborate and TBACl

A solution of 245 mg (0.675 mmol) of **III-25** in 300 mL of CH_3CN was prepared and stirred for 10 min. To this solution, 452 mg (1.63 mmol) of TBACl was added and the solution was stirred under N_2 for 15 minutes. A 1 mL aliquot sample was retained as a dark control. 5 mL samples were transferred to a test tube and photolyzed with stirring under N_2 at 10 Hz with a Q-switch of 320 for 400 seconds. All the photolyzed samples were collected and stirred for 5 min and a 1 mL aliquot sample was retained as a photolyzed sample. The percent conversion was calculated through ^1H NMR integration between the dark control and the photolyzed sample against an internal standard of hexamethyldisiloxane. The rest of the photolyzed sample was neutralized with a

saturated solution of $NaHCO_3$, extracted with CH_2Cl_2, washed with distilled water, dried with $MgSO_4$, filtered, and then the solvent was removed under reduced pressure. The sample was separated via flash column chromatography (240 mm x 36 mm) with 2% ether/hexanes. Fractions were tested by GC and collected and the solvent was removed under reduced pressure and weighed. Isolated photoproducts included 1-naphthylamine, *N*-methyl-1-naphthylamine, 4-chloro-*N*-methyl-*N*-1-naphtylamine, and 2-chloro-*N*-methyl-*N*-1-naphthylamine.

4-Chloro-*N*-methyl-*N*-1-naphthylamine (III-30). 1-Amino-4-chloronaphthalene (0.82 g, 4.6 mmol) was dissolved in 25 mL of anhydrous CH_3CN and then 0.64 g (4.5 mmol, 0.98 eq.) of iodomethane was added to the solution while stirring. The solution was refluxed for 30 min. with an ice water condenser. The mixture was then neutralized to pH 7 with a saturated solution of $NaHCO_3$ and extracted with CH_2Cl_2 until the organic layer was colorless. The combined organic extracts were then dried over $MgSO_4$, filtered, and the solvent was evaporated under reduced pressure to yield a dark orange oil. The mono-methylated compound (**3**) was isolated by column chromatography (240 mm x 44 mm) and eluted with 15% ethyl acetate/85% hexanes. The fractions were collected and the solvent was evaporated under reduced pressure to yield 0.139 g (0.73 mmol, 16%) of a dark purple oil. R_f: 0.33 (15% EtOAc/85% hexanes); ^{1}H NMR (400 MHz, CD_3CN) δ: 8.14 (d, *J* = 8.4 Hz, 1H), 7.94 (d, *J* = 8.4 Hz, 1H), 7.60 (t, *J* = 8 Hz, 1H), 7.51 (t, *J* = 8 Hz, 1H), 7.43 (d, *J* = 8.4 Hz, 1H), 6.47 (d, *J* = 8 Hz, 1H), 5.24 (br s, 1H), 2.91 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 143.8, 131, 126.7, 125.3, 125.2, 124.4, 120.1, 119.9, 103.7, 31; IR (CCl_4) 3452 (m), 3075 (m), 3044 (m), 2982 (m), 2935 (s),

2904 (m), 2885 (w) 2819 (m), 1817 (w), 1572 (s), 1378 (s), 1079 (m), 1033 (m) cm^{-1}; MS (FAB) m/z 191, 176, 156; HRMS (FAB) calcd for $C_{11}H_{10}NCl$ 191.05017, found 191.05037.

2-Chloro-*N*-methyl-*N*-1-naphthylamine (III-31). A yellow oil was isolated. ^1H NMR (400 MHz, CD_3CN) δ: 8.15 (d, J = 8.4 Hz, 1H), 7.84 (d, J = 7.6 Hz, 1H), 7.54-7.39 (m, 4H), 4.29 (br s, 1H), 2.98 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 143.1, 133.5, 128.4, 126.8, 125.9, 123.8, 123.1, 121.9, 30.3; IR (CCl_4) 3646 (w), 3060 (w), 2959 (s), 2920 (s), 2858 (s), 1728 (w), 1553 (s), 1549 (s), 1258 (s), 1099 (s), 1013(s) cm^{-1}; MS (EI) m/z 191, 190, 176, 153, 149, 136, 126, 106, 89, 77, 75, 41, 28, 20; HRMS (EI) calcd for $C_{11}H_{10}NCl$ 191.0502, found 191.0504.

5.3.2: Photoproduct Analysis of 1-(*N*-Methyl-*N*-(2-naphthyl)amino)-2,4,6-trimethylpyridinium tetrafluoroborate and TBACl

A solution of 61.1 mg (0.059 mmol) of **III-49a** in 20 mL of anhydrous CH_3CN was prepared in a quartz tube and stirred for 10 min. To this solution, 0.495 g (1.79 mmol) of TBACl was added and wrapped in foil and the solution was stirred and purged under N_2 for 25 minutes. The foil was removed and the quartz tube was place in front of a Xe lamp for 4 h with stirring. The photolyzed sample was neutralized with a saturated solution of $NaHCO_3$, extracted with CH_2Cl_2, washed with distilled water, dried with $MgSO_4$, filtered, and the solvent was removed under reduced pressure. The sample was separated via preparative TLC plate with 10% ethyl acetate/90% hexanes. Fractions were

separated and isolated for analysis by ^{1}H NMR spectroscopy. The resulting identifiable compounds included *N*-methyl-2-naphthylamine and 1-chloro-*N*-methyl-2-naphthylamine as confirmed by ^{1}H NMR.

1-Chloro-*N*-methyl-2-naphthylamine (III-50). Chlorination procedure followed previously published method.[19] *N*-Methyl-2-naphthylamine (0.578 g, 3.68 mmol) was stirred and dissolved in 45 mL CCl_4 and warmed to 45-50 ºC. *N*-Chlorosuccinimide (0.504 g, 3.77 mmol) was added in small portions over 5 min. The solution was stirred an additional 20 min at 50 ºC, cooled, and filtered. The filtrate was neutralized to pH 7 with a saturated solution of $NaHCO_3$, extracted with CH_2Cl_2, washed with distilled water, dried over Na_2SO_4, filtered, and the solvent was evaporated under reduced pressure to yield (0.581 g, 3.07 mmol, 83.5%) of a dark purple oil. R_f: 0.35 (15% EtOAc/85% hexanes); m.p. 52-54 ºC, lit. 59-60 ºC[19]; ^{1}H NMR (400 MHz, CD_3CN) δ: 7.96 (d, *J* = 8 Hz, 1H), 7.76 (d, *J* = 8 Hz, 2H), 7.49 (t, *J* = 7.2 Hz, 1H), 7.25 (t, *J* = 7.2 Hz, 1H), 7.17 (d, *J* = 8 Hz, 1H), 2.97 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ: 141.9, 131.5, 128.1, 127.9, 127.8, 127.4, 122.5, 122.2, 113.6, 31.1; IR (CCl_4) 3440 (s), 3052 (m), 2986 (w), 2939 (w), 2908 (m), 2885 (m), 2831 (m), 1937 (w), 1721 (m), 1627 (m), 1510 (s), 1417 (s), 1335 (s), 1246 (m) cm^{-1}; MS (FAB) m/z 191, 154, 137, 136, 107, 89, 77, 39; HRMS (FAB) calcd for $C_{11}H_{10}ClN$ 191.0502, found 191.0512.

5.3.3: Photoproduct Analysis of 1,1-Diphenylhydrazinium tetrafluoroborate (IV-44) and TBACl

Used 77.7 mg (0.422 mmol) of 1,1-diphenylhydrazine free base in 3 mL anhydrous CH_3CN and added 95.3 mg HBF_4 (0.52 mmol) in 3 mL anhydrous CH_3CN and 0.242 g TBACl (0.873 mmol in 4 mL anhydrous CH_3CN, added together and stirred under N_2 purge for 15 min. Set in front of Hg lamp for 8 h. The photolysate was analyzed by a Shimadzu Corporation GC-17a equipped with a 15 m 0.25 mm I.D. 0.25 μm film DB-5 column was used. All injections were 1 μL, and the temperature/pressure program was, 60 °C at 67 kPa for 3 min ramp at a rate of 30 °C and 3.8 kPa per minute finishing at 300 °C and 97 kPa which was held for 9 minutes. The column flow rate was 1.9 mL/min. The compounds were detected using a flame ionization detector. The resulting retention times correlated to standards of diphenylamine, carbazole, 4-chlorodiphenylamine, 2-chlorodiphenylamine, (4-carbazol-9-yl-phenyl)-phenyl-amine, and *N,N′,N′*-triphenyl-1,4-phenylenediamine.

4-Chlorodiphenylamine (IV-34). Procedure was followed from Freeman *et al*.[20] and confirmed by ^{1}H NMR (400 MHz, CD_3CN) δ: 7.29 – 7.21 (m, 4H), 7.09 – 7.03 (m, 4H), 6.92 (t, J = 7.6 Hz, 1H), 6.74 (br s, 1H).

2-Chlorodiphenylamine (IV-35). Procedure was followed from Freeman *et al*.[20,21] and confirmed by ^{1}H NMR (400 MHz, CD_3CN) δ: 7.26-7.12 (m, 4H), 7.07 – 7.00 (m,2H), 6.86 (t, J = 7.4 Hz, 1H), 6.80 (d, J = 7.4 Hz, 1H), 6.63 (t, J = 7.4 Hz, 1H), 6.50 (br s, 1H).

5.3.4: Photoproduct Analysis of 1-(*N*,*N*-diphenylamino)-2,4,6-trimethylpyridinium tetrafluoroborate and Carbazole

In a 50 mL Erlenmeyer flask wrapped in aluminum foil, 20 mL of freshly distilled CH_3CN was added to 0.051 g (0.13 mmol) of 1-(*N*,*N*-diphenylamino)-2,4,6-trimethylpyridinium tetrafluoroborate. To this solution, 0.041 g (0.25 mmol) of carbazole was added and the Erlenmeyer flask was capped with a rubber septum. The light yellow solution was purged under N_2 for 10 min., unwrapped, and then allowed to sit under room light for 48 h. After the 48 h period, the solution was charcoal in color and the solvent was removed *in vacuo*.

A Shimadzu Corporation GC-17a equipped with a 15 m 0.25 mm I.D. 0.25 μm film DB-5 column was used. All injections were 1 μL, and the temperature/pressure program was, 60 °C at 67 kPa for 3 min ramp at a rate of 30°C and 3.8 kPa per minute finishing at 300 °C and 97 kPa which was held for 9 minutes. The column flow rate was 1.9 mL/min. The compounds were detected using a flame ionization detector. The GC trace of the photolysate showed four major peaks: one peak corresponding to diphenyl amine, one corresponding to carbazole, and two other products.

The remaining solid was taken up in a minimal amount of dichloromethane and added to a flash column (45 cm x 4 cm) that had been packed with 36 cm of silica gel, 40 mesh. The column was eluted with a gradual increase in polarity starting from 500 mL hexanes, then 500 mL 2% Et_2O/hexanes, then 500 mL 10% Et_2O/hexanes, then 1 L 20% Et_2O/hexanes. The collected fractions were analyzed by GC. The appropriate fractions were combined and concentrated under reduced pressure. The photoproduct was

determined to be (4-carbazol-9-yl-phenyl)-phenyl-amine by MS, ^{1}H NMR, ^{13}C NMR, and ^{13}C DEPT NMR.

(4-carbazol-9-yl-phenyl)-phenyl-amine (IV-39). ^{1}H NMR (400 MHz; CD_3CN): δ 8.18 (d, *J* = 7.6 Hz, 2H), 7.42 (t, *J* = 1.2 Hz, 4H), 7.36 (d, *J* = 4.8 Hz, 2H), 7.32-7.25 (m, 5H), 7.21 (d, *J* = 8.4 Hz, 2H), 6.97 (t, *J* = 7.2 Hz, 2H); ^{13}C NMR (400 MHz; CD_3Cl): δ 142.8, 142.4, 141.3, 130.0, 129.5, 128.3, 125.8, 123.0, 121.8, 120.2, 119.6, 118.6, 117.9, 109.8; ^{13}C DEPT NMR (400 MHz; CD_3Cl): δ 129.5, 128.3, 125.8, 121.8, 120.2, 119.6, 118.6, 117.9, 109.7; MS (FAB) m/z 334.5, 259.4, 241.4, 169.3, 168.3, 119.1, 85.1, 45.1; HRMS (FAB) calcd for $C_{24}H_{18}N_2$ 334.1470 found 334.1479

Concentration curves of diphenylamine, carbazole, and the photoproduct were created via GC and used to determine the yield of the photolysis. These curves were generated from solutions with concentrations ranging from $1.97x10^{-3}$ M to $1.84x10^{-1}$ M. The samples were analyzed via GC with the area underneath the curve for the compound recorded. The data were fit using a least-squares computer routine to obtain a straight line, y = mx + b, where y is the peak area and x is the concentration.

To determine that percent yield upon photolysis, another trial was performed with 60.7 mg (0.162 mmol) of 1-(*N*,*N*-diphenylamino)-2,4,6-trimethylpyridinium tetrafluoroborate in a 50 mL Erlenmeyer flask wrapped in aluminum foil and 20 mL of freshly distilled CH_3CN. To this solution, 45.5 mg (0.272 mmol) of carbazole was added and the Erlenmeyer flask was capped with a rubber septum. The light yellow solution was purged under N_2 for 10 min., unwrapped, and then allowed to sit under room light for 48 h. At this time the solution had changed to charcoal in color and 2 mL was removed for analysis. The solution was kept under room light for an additional 96 h.

After the total of 144 h, another sample was analyzed by GC. Assuming 100% photolytic conversion and using the previously calculated concentration curves, the percent of (4-carbazol-9-yl-phenyl)-phenyl-amine observed was 24% and the percent of diphenylamine observed was 51%.

5.3.5: Photoproduct Analysis of 1-(*N*,*N*-diphenylamino)-2,4,6-trimethylpyridinium tetrafluoroborate and 1,4-Dimethoxybenzene

In a 50 mL Erlenmeyer flask wrapped in aluminum foil, 20 mL of freshly distilled CH_3CN was added to 73.5 mg (0.196 mmol) of 1-(*N*,*N*-diphenylamino)-2,4,6-trimethylpyridinium tetrafluoroborate. To this solution, 78 mg (0.56 mmol) of 1,4-DMB was added and the Erlenmeyer flask was capped with a rubber septum. The light yellow solution was purged under N_2 for 10 min., unwrapped, and then allowed to sit under room light for 48 h. After the 48 h period, the solution was charcoal in color and the solvent was removed *in vacuo*.

A Shimadzu Corporation GC-17a equipped with a 15 m 0.25 mm I.D. 0.25 μm film DB-5 column was used. All injections were 1 μL, and the temperature/pressure program was, 60 °C at 67 kPa for 3 min ramp at a rate of 30 °C and 3.8 kPa per minute finishing at 300 °C and 97 kPa which was held for 9 minutes. The column flow rate was 1.9 mL/min. The compounds were detected using a flame ionization detector. The GC trace of the photolysate showed four major peaks: one peak corresponding to diphenyl amine, one corresponding to carbazole, one corresponding to (4-carbazol-9-yl-phenyl)-phenyl-amine, and one other product.

The remaining solid was taken up in a minimal amount of dichloromethane and added to a flash column (45 cm x 4 cm) that had been packed with 36 cm of silica gel, 40 mesh. The column was eluted with a gradual increase in polarity starting from 500 mL hexanes, then 500 mL 2% Et_2O/hexanes, then 500 mL 5% Et_2O/hexanes, then 500 mL 10% Et_2O/hexanes, then 500 mL 15% ether/hexanes, then 500 mL 20% ether/hexanes. The collected fractions were analyzed by GC. The appropriate fractions were combined and concentrated under reduced pressure. The remaining photoproduct was determined to be *N,N′,N′*-triphenyl-1,4-phenylenediamine as determined by ^{1}H NMR and MS as compared to previously published results.[17]

***N,N′,N′*-Triphenyl-1,4-phenylenediamine (IV-38).** Structure was confirmed based on comparison to previously published spectroscopic data.[17] ^{1}H NMR (400 MHz, CD_3CN) δ: 7.23 (t, J = 8.8 Hz, 6H), 7.12 – 6.94 (m, 12H), 6.85 (t, J = 7.2 Hz, 1H), 6.61 (br s, 1H); MS (EI) m/z 336.2, 355.1, 323.4, 267.3, 243.1, 211.3, 197.2, 167.1, 155.2, 127.2, 97.1, 71.1, 57.1, 43.2.

5.4: MALDI-TOF-MS Experiments

5.4.1: Preparative Photolysis of 4-(*N*-anilino)phenyl azide with Trifluoroacetic acid

Experiment one used 31.1 mg (0.15 mmol) of 4-(*N*-anilino)phenyl azide in 10 mL of 30% CH_3CN/70% distilled water in a Petri dish with a hand held shortwave UV-lamp placed on top of the dish for 5 min at which point the solution was brown. Trifluoroacetic acid was added and the solution turned purple with green precipitate. Experiment two used 34.8 mg (0.166 mmol) of 4-(*N*-anilino)phenyl azide in 10 mL of 30% CH_3CN/70% distilled water in a Petri dish with added trifluoroacetic acid. A hand

held shortwave UV-lamp was placed on top of the dish for 10 min at which point the solution turned purple with green precipitate. Both experiments were centrifuged to collect the precipitate for use in MALDI-TOF-MS analysis.

In these studies, the acidic matrix 2,5-dihydroxybenzoic acid (DHB) was used and the solvents used included 1-methyl-2-pyrrolidinone (NMP) and methansulfonic acid (MSA). The last two were employed because of their ability to dissolve PANI although they have high boiling points, thus making the evaporation of the solvent from the matrix-sample system difficult. Samples were prepared in two different ways: first by mixing equal parts of a solution of the polymer and a solution of the matrix being used, and second, by adding a solution of the sample to about 10 mg of the solid matrix. A two microliter volume of the final solution was then deposited on a stainless-steel sample holder and the solvent was evaporated in an oven at 35 ºC.[22] Samples were prepared in both ways with both solvents and it was found that the use of NMP provided the best MALDI spectra as shown in the following Figures 4.8 and 4.9.

5.4.2: Preparative Photolysis of 1-(*N*,*N*-diphenylamino)-2,4,6-trimethylpyridinium tetrafluoroborate

5.4.2.1: Preparative Photolysis of 1-(*N*,*N*-diphenylamino)-2,4,6-trimethylpyridinium tetrafluoroborate with Carbazole or Diphenylamine.

MALDI Sample Preparation: In each case, the solvent was removed under reduced pressure to allow for the collection of solid samples. The matrix used was 0.24 g of 2,5-dihydroxybenzoic acid (DHB) in 10 mL CH_3CN as the matrix. For each sample,

(carbazole, carbazole dark, diphenylamine, and diphenylamine dark), 0.5 mL of the sample and 0.5 mL of the matrix were mixed in a vial. To this mixture, a 1 μL aliquot of AcOH was added. A 1 μL aliquot of matrix alone was spotted on plate and allowed to air dry, at which point, another 1 μL aliquot of sample mixture was spotted and allowed to air dry.

5.4.2.1.1: MALDI Sample 1-(*N*,*N*-diphenylamino)-2,4,6-trimethylpyridinium tetrafluoroborate with Carbazole

Used 49.5 mg (0.132 mmol) 1-(*N*,*N*-diphenylamino)-2,4,6-trimethylpyridinium tetrafluoroborate and 22.4 mg (0.134 mmol) of carbazole in 20 mL anhydrous CH_3CN. The solution was wrapped in aluminum foil and purged under N_2 for 20 min. 1 mL was removed as a dark standard. The remaining solution was photolyzed with a Xe lamp for 3 h.

5.4.2.1.2: MALDI Sample 1-(*N*,*N*-diphenylamino)-2,4,6-trimethylpyridinium tetrafluoroborate with Diphenylamine

Used 51.9 mg (0.138 mmol) 1-(*N*,*N*-diphenylamino)-2,4,6-trimethylpyridinium tetrafluoroborate and 36.8 mg (0.217 mmol) of diphenylamine in 20 mL anhydrous CH_3CN. The solution was wrapped in aluminum foil and purged under N_2 for 20 min. 1 mL was removed as a dark standard. The remaining solution was photolyzed with a Xe lamp for 3 h.

5.4.2.2: 1-(*N*,*N*-diphenylamino)-2,4,6-trimethylpyridinium tetrafluoroborate Concentration Dependence

MALDI Sample Preparation: In each case, the solvent was removed under reduced pressure to allow for the collection of solid samples. The matrix used was 0.20 g of DHB in 10 mL CH_3CN. For each sample, (matrix, matrix with acid, low concentration, high concentration, hydrazine sample, low concentration dark, high concentration dark, polyaniline standard), 0.5 mL of the sample and 0.5 mL of the matrix were mixed in a vial. To this mixture, a 1 μL aliquot of AcOH was added. A 1 μL aliquot of matrix alone was spotted on plate and allowed to air dry at which point, another 1 μL aliquot of sample mixture was spotted and allowed to air dry .

5.4.2.2.1: 1-(*N*,*N*-diphenylamino)-2,4,6-trimethylpyridinium tetrafluoroborate Concentration Dependence: Low Concentration

Used 46.3 mg (0.123 mmol; 6.17 mM) of 1-(*N*,*N*-diphenylamino)-2,4,6-trimethylpyridinium tetrafluoroborate in 20 mL anhydrous CH_3CN and purged sample under N_2 for 15 min. 1 mL was removed as a dark standard. The remaining solution was photolyzed with a Xe lamp for 3 hours.

5.4.2.2.2: 1-(*N*,*N*-diphenylamino)-2,4,6-trimethylpyridinium tetrafluoroborate Concentration Dependence: High Concentration

Used 80.6 mg (0.2149 mmol; 21.49 mM) of 1-(*N*,*N*-diphenylamino)-2,4,6-trimethylpyridinium tetrafluoroborate in 10 mL anhydrous CH_3CN and purged sample under N_2 for 15 min. 1 mL was removed as a dark standard. The remaining solution was photolyzed with a Xe lamp for 3 hours.

5.4.3: Preparative Photolysis of 1,1-Diphenylhydrazinium tetrafluoroborate

Used 109.7 mg (0.596 mmol) of diphenylhydrazine in 10 mL anhydrous CH_3CN and added 0.12 g HBF_4 (48% by weight; 0.66 mmol) and purged sample under N_2 for 15 min. The solution was photolyzed with a Hg lamp for 6 h, neutralized to pH 7 with a saturated solution of $NaHCO_3$, extracted with DCM, dried over $MgSO_4$, solvent was evaporated under reduced pressure to 9 mL.

MALDI Sample Preparation: In each case, the solvent was removed under reduced pressure to allow for the collection of solid samples. The matrix used was 0.2013 g of DHB in 10 mL CH_3CN. For each sample, (matrix, matrix with acid, low concentration, high concentration, hydrazine sample, low concentration dark, high concentration dark, polyaniline standard), 0.5 mL of the sample and 0.5 mL of the matrix were mixed in a vial. To this mixture, a 1 μL aliquot of AcOH was added. A 1 μL aliquot of matrix alone was spotted on plate and allowed to air dry at which point, another 1 μL aliquot of sample mixture was spotted and allowed to air dry.

5.5: Other Spectroscopic Analyses of PANI

5.5.1: Confirmation of 4-Phenylimino-cyclohexa-2,5-dienone (IV-29)

The question arose as to the difference in the transient absorption spectra between the 30% CH_3CN/70% H_2O spectrum and the CH_3CN/H_2O with acid spectrum. To answer this question, the photostability of the 420 nm intermediate under steady-state dark control was studied. The photochemical precursor, 4-(*N*-anilino)phenyl azide, was photolysed in CH_3CN/H_2O and its UV-vis spectrum was recorded after a series of laser

pulses. It can be seen from Figure 4.6A that the 420 nm peak grows in as the sample is irradiated with more 266 nm light. After 1200 laser pulses, the sample was kept in the dark and periodically, its UV-vis spectrum was recorded. It can be seen, in Figure 4.6B, that the maximum wavelength of the intermediate shifted from 420 nm to 444 nm over time. Since the photolysis of the precursor allowed for a limited number of possibilities and that *N*-phenylquinone diimine (PQDI) is a well known oxidation product of ADPA, the 420 nm intermediate lent itself to be known as PQDI.[23-31] The presence of PQDI is also supported by previous reports of the UV-vis of a quinine diimine compound centered at 444 nm.[32] Since PQDI can undergo hydrolysis, the intermediate that absorbs at 444 nm was analyzed by MS and the resulting product returned as 183.068 mass-to-charge (m/z). This suggests that the intermediate that absorbs at 420 nm is able to undergo hydrolysis to yield 4-Phenylimino-cyclohexa-2,5-dienone, as seen in Scheme 4.14.

4-Phenylimino-cyclohexa-2,5-dienone (IV-29). UV-vis (CH_3CN/distilled water) 285, 444 nm; MS (EI) m/z 183, 182, 154, 151, 129, 125, 103, 92, 77, 63, 51, 44; HRMS (EI) calcd for $C_{12}H_9NO$ 183.0684, found 183.0688.

5.5.2: PANI Sample Preparation for XPS, XRD, and IR Analysis

5.5.2.1: PANI Sample Preparation for XPS, XRD, and IR Analysis with Trifluoroacetic Acid

52.8 mg (0.25 mmol) of 4-(*N*-anilino)phenyl azide was dissolved in 10 mL of 30% CH_3CN/70% distilled water in a Petri dish with a hand held shortwave UV-lamp placed on top of the dish for 1 h at which point the solution was brown. 1 mL of

trifluoroacetic acid was added and the solution turned purple with green precipitate. The sample was centrifuged to collect the precipitate for further analysis.

5.5.2.2: PANI Sample Preparation for XPS, XRD, and IR Analysis Hydrochloric Acid

50.7 mg (0.24 mmol) of 4-(*N*-anilino)phenyl azide was dissolved in 10 mL of 30% CH_3CN/70% distilled water in a Petri dish with a hand held shortwave UV-lamp placed on top of the dish for 1 h at which point the solution was brown. 1 mL of hydrochloric acid was added and the solution turned purple with green precipitate. The sample was centrifuged to collect the precipitate for further analysis.

5.5.2.3: PANI Sample Preparation for XPS, XRD, and IR Analysis Sulfuric Acid

50.9 mg (0.24 mmol) of 4-(*N*-anilino)phenyl azide was dissolved in 10 mL of 30% CH_3CN/70% distilled water in a Petri dish with a hand held shortwave UV-lamp placed on top of the dish for 1 h at which point the solution was brown. 1 mL of sulfuric acid was added and the solution turned purple with green precipitate. The sample was centrifuged to collect the precipitate for further analysis.

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Chapter 5

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