

**Understanding and Characterizing Excited State Electron  
Transfers in Catalysis and Nanomaterial Synthesis**

**Christopher Darrell McTiernan**

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**Department of Chemistry  
Faculty of Science  
University of Ottawa**

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## Abstract

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Over the past decade, there has been an ever-increasing interest in photochemical redox processes as a tool in organic syntheses. While the underlying mechanism of many of these transformations involves free radicals, the complex product mixtures and poor selectivity that are traditionally associated with these types of reaction can be in most cases avoided. In fact there are numerous examples of photoredox catalysis, which demonstrate that under well-selected conditions it is possible to obtain relatively clean products in high yields. Furthermore, photo-mediated reactions can typically be performed under milder conditions than thermal reactions, as the energy is supplied by light and heating is not required.

Despite recent advancements in the field, many of the new discoveries are accomplished using relatively expensive transition metal complexes of Ru and Ir as photocatalyst and tend to lack in-depth investigations into the corresponding excited-state kinetics or underlying mechanism of these transformations. While there are excellent reasons for employing polypyridyl Ru and Ir catalysts, such as strong visible light absorption, high photostability, and well known and documented excited state lifetimes and redox potentials; one of the aims of this thesis is to demonstrate that in many cases these Ru and Ir photocatalysts can be replaced with cheaper and in some cases metal-free and heterogeneous alternatives.

Herein, one will find examples of the use of the organic semiconductor,  $\alpha$ -



sexithiophene, as photocatalyst in the reductive dehalogenation of *vicinal*-dibromides and the singlet oxygen mediated oxidation of amines to their corresponding imines. We have also demonstrated that the inorganic semiconductor P25 TiO<sub>2</sub> can be used as an efficient heterogeneous photocatalyst for a variety of reductive transformations and that it is possible to employ it as photocatalyst under dual-photoredox/Ni catalysis conditions to perform the decarboxylative cross-coupling of carboxylic acids with aryl iodides.

In addition to this, the usefulness of kinetic analysis in improving and better understanding these transformations as well as the development of tools to characterize chain processes in these reactions are covered. Lastly, we also explore the role of excited state electron transfer from the triplet of benzophenone in the synthesis of colloidal gold nanoparticles.

Overall, the content of this thesis describes the development and improvement of several photoredox systems through either rational design, the development of new characterization tools, and in-depth kinetic and mechanistic analysis.

## **Acknowledgements**

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I am extremely grateful for having been given the opportunity to pursue my Ph.D studies in the Scaiano lab. Throughout the past few years I have gotten the chance to collaborate and interact with a group of great people and researchers from all around the world. I have learnt and experienced so much since joining the group and it is these experiences, which have shaped me into the researcher and person I am today. The lab space, equipment, and expertise available in the group itself and the department are second to none. Whether it was a piece of exotic glassware or a relatively obscure technique, chances are there was someone in the group who could point you in the right direction or drawer.

While there are many people to thank, I must say Tito has been an incredible supervisor and mentor. His curiosity and interest for science is contagious. I really appreciate that he has given me the freedom to explore and investigate a variety of different topics over the years. It is this hands-off approach to learning, which has allowed me to develop the knowledge and critical thinking skills, which are required to succeed at this level.

Thanks to all the current and previous Scaiano group members, who I have had the chance to work with, each of you has left a lasting impression on me. Thank you Betty Yakimenko, for making everything run so smoothly on the administrative side of things. Thank you to Michel Grenier, your help in setting up, designing, and troubleshooting instrumentation is much appreciated. Many of

the measurements and experiments presented within this thesis would not have been possible without your assistance.

I must also thank Spencer Pitre, whom I worked with very closely on a day-to-day basis. Our daily discussions on current trends in the field and problems we were having with our chemistry will be missed. I think we are a pretty good team and I hope that later on in our careers we can continue to collaborate.

Finally, I must also thank my family for all their support throughout this journey. While they might not always understand the path I have taken, they truly respect it. To my wife Amanda, thank you for being my best friend. I would never have been able to do this without you. I promise I will eventually get a “real job” but until then I know we will continue to enjoy the life we have made together.

Thank you all!!!

## Contribution Statement

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All of the projects presented within this thesis were completed under the supervision and guidance of professor Tito Scaiano. The large size and multidisciplinary nature of the Scaiano group has given me the freedom and opportunity to collaborate and contribute on a variety of different projects. Thus, while the majority of the work presented herein is the result of independent research, I believe it necessary to highlight both the intellectual and/or physical contributions of my collaborators. In the following section, I wish to highlight my direct contribution as well as the contributions of my fellow co-workers in each of the projects presented.

The use of  $\alpha$ -sexithiophene as photoredox catalyst in the reduction of *vicinal*-dibromides was a collaboration with fellow graduate student, Spencer Pitre. While I conceived the original idea of employing  $\alpha$ -sexithiophene as photoredox catalyst, Spencer synthesized some of the starting materials and was involved in many discussions revolving around the observed reactivity.

The singlet oxygen mediated oxidation of primary and secondary amines utilizing  $\alpha$ -sexithiophene as photocatalyst was an extension of the previous project. Recently, there has been a push to develop photocatalytic systems for these types of transformation. The idea was to demonstrate that a commercially available organic semiconductor, that requires no further modification, could be used to efficiently bring about the desired transformation.

The reductive dehalogenation and cyclization project was initiated by Hossein Ismaili, a former post-doctoral fellow in the Scaiano group. Myself, Hossein, and Spencer synthesized the required starting materials. In addition to synthesizing the starting materials, I prepared and characterized the platinized  $\text{TiO}_2$  catalyst. The photocatalytic reactions, product isolation, and characterization were performed by myself and Hossein.

The dual photoredox/Ni catalysis project was a result of several group discussions on the idea of heterogenizing these popular dual catalytic processes. Xavier Leblanc, a 4<sup>th</sup> year undergraduate student, played an important role in this project by synthesizing the Ni nanoparticle decorated  $\text{TiO}_2$  catalysts.

The work on polynuclear gold (I) complexes in photoredox catalysis was a collaboration with Barriault group from the University of Ottawa. Mathieu Morin and Terry McCallum, both graduate students in the Barriault group, prepared the gold complexes and performed the photocatalytic reactions. My role was performing the characterization and quenching experiments, while rationalizing the observed reactivity.

The section on probing chain reactions, describes work that was performed primarily by myself. While there was originally two portions of this work, the development of a  $\text{Ru}(\text{bpy})_3^{2+}$  based actinometer and an updated rotating sector method. The development of the  $\text{Ru}(\text{bpy})_3^{2+}$  based actinometer will not be discussed. Results of the actinometry experiments are mentioned and used as justification for the results of intermittent illumination experiments, however the development of the actinometer itself, which was a joint

collaboration between myself, Spencer, and RISE students Rebecca DiPucchio, and Wyatt Vine, will be presented in Spencer's thesis. It should also be mentioned that the electronics required for the intermittent illumination apparatus were designed and built by Michel Grenier, a technician in the Scaiano group.

The synthesis of gold nanoparticles using excited state benzophenone as reducing agent, was one of the first projects I worked on upon joining the Scaiano group. At this point I was being supervised by Geniece Tapley and Emilio Alarcon, both of whom are former post-doctoral fellows of the Scaiano group. They provided guidance and trained me on the use of the various equipment required to complete this project. Juliana Murillo-Lopez and Ramiro Arratia-Perez performed the theoretical calculations included in this section. Jose Carlos Netto-Ferreira, a visiting professor, provided valuable insights and trained me in the use of laser flash photolysis.

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## List of Abbreviations

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|                           |                                                          |
|---------------------------|----------------------------------------------------------|
| [ ]                       | concentration                                            |
| $^1\Delta_g$              | singlet oxygen                                           |
| 3,5-CF <sub>3</sub> -dppm | bis(bis(3,5-bis(trifluoromethyl)phenyl)phosphine)methane |
| A                         | absorbance                                               |
| Atm                       | atmosphere                                               |
| ATRC                      | atom transfer radical cyclization                        |
| bmimm                     | bis( <i>N</i> -methylimidazol-2-ylidene)methane          |
| BP                        | benzophenone                                             |
| C60                       | buckminsterfullerene                                     |
| CB                        | conduction band                                          |
| CD                        | circular dichroism                                       |
| CV                        | cyclic voltammetry                                       |
| D                         | donor                                                    |
| d                         | doublet                                                  |
| DABCO                     | 1,4-diazabicyclo[2.2.2]octane                            |
| DCM                       | dichloromethane                                          |
| DIPEA                     | diisopropylethylamine                                    |
| DMF                       | dimethylformamide                                        |
| dmpm                      | bis(dimethylphosphino)methane                            |
| DMSO                      | dimethylsulfoxide                                        |
| dppm                      | bis(diphenylphosphino)methane                            |
| e <sup>-</sup>            | electron                                                 |

|           |                                        |
|-----------|----------------------------------------|
| $E^*_S$   | singlet energy                         |
| $E^*_T$   | triplet energy                         |
| $E_{1/2}$ | half-wave potential                    |
| EA        | electron affinity                      |
| $E_{ox}$  | oxidation potential                    |
| EP        | electrostatic potential                |
| $E_{pa}$  | peak anodic potential                  |
| $E_{pc}$  | peak cathodic potential                |
| $E_{red}$ | reduction potential                    |
| ESR       | electron spin resonance                |
| eT        | electron transfer                      |
| Fc        | ferrocene                              |
| $h^+$     | hole                                   |
| HOMO      | highest occupied molecular orbital     |
| HPLC      | high performance liquid chromatography |
| Hz        | hertz                                  |
| $h\nu$    | light                                  |
| $I_{[q]}$ | intensity in presence of quencher      |
| $I_0$     | initial intensity                      |
| ICP       | inductively coupled plasma             |
| IP        | ionization potential                   |
| IRF       | instrument response function           |
| J         | Joule <i>or</i> coupling constant      |



|                  |                                       |
|------------------|---------------------------------------|
| $k_q$            | rate constant of quenching            |
| $K_{SV}$         | Stern-Volmer constant                 |
| LED              | light emitting diode                  |
| LFP              | laser flash photolysis                |
| LUMO             | lowest unoccupied molecular orbital   |
| m                | multiplet                             |
| MeCN             | acetonitrile                          |
| MeOH             | methanol                              |
| MV <sup>2+</sup> | methyl viologen                       |
| NHE              | normal hydrogen electrode             |
| NIR              | near infrared                         |
| nm               | nanometer                             |
| NMR              | nuclear magnetic resonance            |
| NP               | nanoparticle                          |
| NR               | no reaction                           |
| OD               | optical density                       |
| OLED             | organic light emitting diode          |
| OPV              | organic photovoltaic                  |
| PMT              | photomultiplier tube                  |
| ppm              | parts per million                     |
| PTLC             | preparative thin layer chromatography |
| q                | quartet                               |
| R <sub>3</sub> N | tertiary amine                        |

|                             |                                   |
|-----------------------------|-----------------------------------|
| s                           | singlet                           |
| SCE                         | standard calomel electrode        |
| SEM                         | scanning electron microscope      |
| SET                         | single electron transfer          |
| SHE                         | standard hydrogen electrode       |
| SOMO                        | singly occupied molecular orbital |
| SPB                         | surface plasmon band              |
| t                           | triplet                           |
| TLC                         | thin layer chromatography         |
| TMEDA                       | tetramethylenediamine             |
| TON                         | turn over number                  |
| tppm                        | tris(diphenylphosphino)methane    |
| UV                          | ultraviolet                       |
| VB                          | valence band                      |
| <i>vic</i> -Br <sub>2</sub> | <i>vicinal</i> -dibromide         |
| Vis                         | visible light                     |
| $\alpha$ -6T                | $\alpha$ -sexithiophene           |
| $\delta$                    | chemical shift                    |
| $\Delta E_{bg}$             | bandgap energy                    |
| $\Delta E_{coulombic}$      | coulombic energy                  |
| $\Delta G_{eT}$             | gibbs free energy                 |
| $\epsilon$                  | molar absorptivity coefficient    |
| $\eta$                      | refractive index                  |

|        |               |
|--------|---------------|
| $\tau$ | lifetime      |
| $\Phi$ | quantum yield |

# 1. Introduction

---

## 1.1. Opening Remarks

The work presented in this thesis is centered around the use of excited state electron transfers in both organic redox transformations and nanomaterial synthesis. The main objective is to demonstrate that through either rational design, the development of new characterization tools, and in-depth kinetic analysis, many of these excited state processes can be better understood and improved. Chapter 1 provides a brief background into the photophysics, photochemistry, and redox properties of photocatalysts typically used in these processes along with details relating to their measurement, which allow us to better understand the systems in question. Chapters 2 and 3 focus on the use of  $\alpha$ -sexithiophene, an organic semiconductor, as visible light photocatalyst in the reductive dehalogenation of *vicinal* dibromides to their corresponding alkenes and the oxidation of primary and secondary amines to their corresponding imines. Chapter 4 examines the use of TiO<sub>2</sub> as heterogeneous alternative to homogeneous Ru and Ir photocatalysts in a variety of reductive and oxidative transformations. Chapter 5 explores the reactivity of polynuclear gold (I) complexes towards light mediated reductive dehalogenations and cyclizations. In Chapter 6, we examine the use of intermittent illumination in probing light mediated chain processes. Finally, the role of excited state electron transfers in the synthesis of colloidal gold nanoparticles from triplet excited benzophenone is examined in Chapter 7.

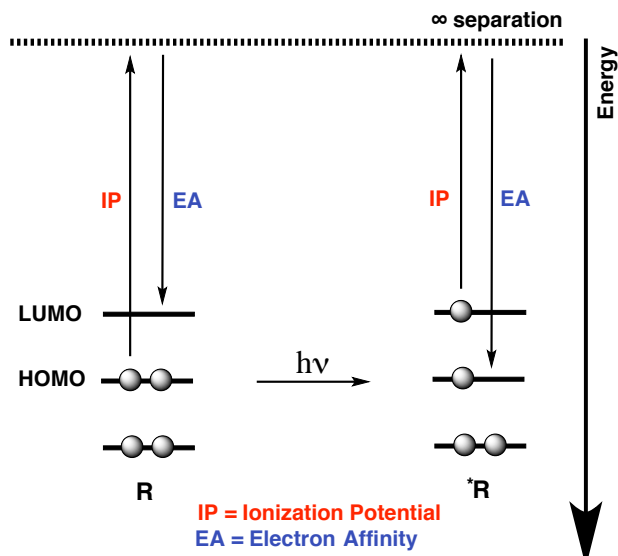
The basics presented in the next few sections will allow us to better frame the discussion of the results presented in subsequent chapters.

## 1.2. Understanding the Redox Properties of Excited States

Although many of the chemical transformations that can be attained through the use of photoredox chemistry have or can be accomplished using reagents which are either strong oxidants or reductants in their ground-states, many of these reagents are inherently difficult to work with, reflecting their high reactivity. One of the advantages photochemical reactions have over some of the more traditional oxidation or reduction reactions is that one can handle a relatively inert photocatalyst and generate the desired oxidizing and/or reducing agent *in-situ* by exciting the catalyst with light. It is partly this enhanced temporal control that makes photoredox chemistry so alluring.

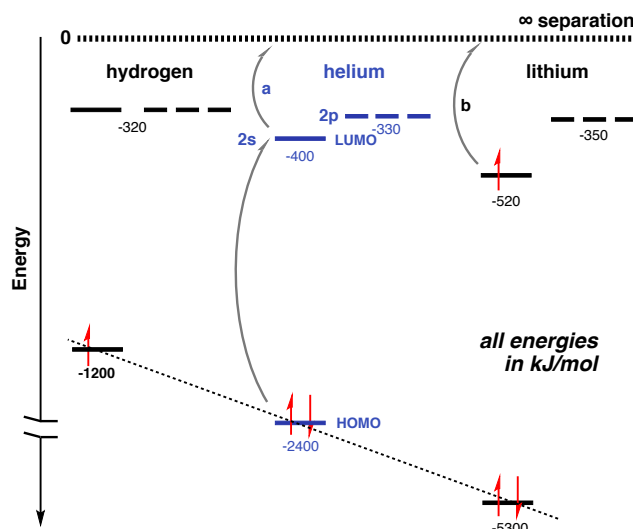
The recent photoredox literature, includes many instances in which it is stated that the photocatalyst becomes both a better electron donor and acceptor in its excited-state, however in most cases this behavior is followed by little or no explanation. What is important to realize is that this behavior is not limited to the popular photocatalysts and that any closed shell, diamagnetic molecule will display this behavior in either its singlet or triplet excited-state.<sup>1</sup> By simply comparing the ionization potential (IP) and electron affinity (EA) of an excited-state diamagnetic molecule with that of its corresponding ground state (Figure 1.1), it becomes evident that the EA of the excited-state molecule is higher than that in the ground-state, while the IP is lower. If we were to look at this situation thermodynamically, we would observe that the addition of an electron to the half-

filled HOMO of the excited molecule is more exothermic than its addition to the LUMO in the ground-state molecule, however it also apparent that the removal of an electron from the excited-state molecule becomes less endothermic. It is for these reasons excited diamagnetic molecules become both better reducing agents and oxidizing agents in their excited-state.



**Figure 1.1.** Orbital representations for the oxidation and reduction processes of ground-state and excited-state closed-shell species. Adapted with permission from Turro *et al.*<sup>1</sup> Copyright 2010 University Science Publishers.

To further emphasize that this behavior is not special to any particular set of molecules, we can use the helium atom as an example. As seen in Figure 1.2, if one were able to excite helium, the resulting excited helium atom would actually become even more reducing than ground state lithium. It is important to mention at this point that we are in no way suggesting that investigators begin using He as a reducing agent as its implementation would be impractical. Much of this impracticality stems from the fact that the 2000 kJ/mol energy difference between its HOMO and LUMO corresponds to an excitation wavelength of approximately 60 nm.<sup>2</sup>



**Figure 1.2.** Comparison of the orbital energy level diagrams of hydrogen, helium and lithium. Upon excitation of He, its IP (a) is less than the IP (b) of Li in the ground-state, corresponding to a more reductive species. Adapted with permission from Pitre *et al.*<sup>2</sup> Copyright 2016 American Chemical Society.

Interestingly this highlights one of the drawbacks of photoredox reactions, which is that problems with reagent or product degradation as well as competitive absorption by the solvent or reaction vessel will dictate which excitation wavelengths are attainable or useful. It also demonstrates that much of the costs associated with higher energy photons are actually related to the need for specialized equipment and unwanted side reactions. It is for these reasons that there is actually a finite amount of energy, which can be conferred to the photocatalyst for the subsequent oxidation or reduction reactions. Recently it has been suggested that one way around this limitation is through consecutive light-induced electron transfer processes.<sup>3,4</sup> It has been reported that through excitation of an open shell intermediate such as a radical anion one can accumulate sufficient energy to perform a reduction reaction, which would otherwise be unattainable. While this reactivity is interesting, the energy difference between the ground and excited state is typically small in open shell

systems.<sup>5</sup> In addition to this the excited state lifetime of open shell molecules tend to be quite short and therefore the reaction would likely time-out if the concentration of reactant was low.<sup>5-7</sup> It would therefore seem to be of more interest to accumulate energy through the excitation of molecules already in their excited singlet or triplet state, however this experiment would prove difficult as the initial transient would need to fulfill a variety of different criteria the least of which are a large extinction coefficient, and relatively long excited state lifetime.

As the initial electron transfer to or from the excited-state photocatalyst is the first step of the catalytic cycle, it is important to know whether or not it is thermodynamically feasible. This can be accomplished by calculating the Gibbs free energy for the electron transfer process. In the ground-state this can be calculated using the following equation:

$$\Delta G_{eT} = E_{1/2}^{\text{ox}}(D) - E_{1/2}^{\text{red}}(A) + \Delta E_{\text{Coulombic}} \quad (1.1)$$

where  $\Delta G_{eT}$  is the Gibbs free energy,  $E_{1/2}^{\text{ox}}(D)$  is the oxidation potential of the donor molecule,  $E_{1/2}^{\text{red}}(A)$  is the reduction potential of the acceptor molecule, and  $\Delta E_{\text{Coulombic}}$  is related to the dielectric constant of the solvent in which the reaction is performed. From this equation, we can see that in order for a reaction to be thermodynamically downhill or exothermic, the oxidation potential of the donor must be lower or more negative than the reduction potential of the acceptor.

One of the underlying principles behind photoredox catalysis is that through the use of photosensitizers, low-energy photons can be used to achieve high-energy processes. This implies that in general, electron transfer to or from the photocatalyst is thermodynamically uphill while the photocatalyst is in the



ground state. To account for the excited state energy of the photocatalyst, one can employ the following equation referred to as the Rehm-Weller equation:<sup>8,9</sup>

$$\Delta G_{eT} = E_{1/2}^{\text{ox}}(D) - E_{1/2}^{\text{red}}(A) - E_{\text{S or T}}^* (D \text{ or } A) + \Delta E_{\text{Coulombic}} \quad (1.2)$$

where  $E_{\text{S or T}}^* (D \text{ or } A)$  is the singlet or triplet excited state energy of the excited donor or acceptor molecule. From this, it is evident that the higher the excited state energy the more likely the reaction will be favorable.

### 1.3. Determining Oxidation and Reduction Potentials

In order to perform the calculations above it is necessary to know the corresponding oxidation and reduction potentials of the photocatalyst and reagents in the system. Although many of these values can be found in the literature or determined experimentally through the use of cyclic or differential pulse voltammetry, it is important that the potentials used in the calculation all be reported with respect to the same reference electrode. Although it is common to report potentials vs. aqueous reference electrode systems such as the standard hydrogen electrode (SHE), normal hydrogen electrode (NHE), standard calomel electrode (SCE), or the silver-silver chloride electrode (Ag/AgCl); due to the insolubility of many of the photocatalyst or reagents in aqueous solutions many of the measurements are performed in organic media. Frequently acetonitrile is employed as solvent with tetrabutylammonium salts being the preferred supporting electrolytes, as these systems tend to display some of the largest potential windows.<sup>10</sup> Typically the potentials in these systems will be measured with respect to an internal standard such as the ferrocene (Fc)/ferrocenium ( $\text{Fc}^+$ ) redox couple, however as  $E_{1/2}(\text{Fc}/\text{Fc}^+)$  is known with respect to a variety of

aqueous reference electrodes, one can easily convert the potentials between the different reference electrodes.<sup>11</sup> Another important thing to point out is that there is a difference between  $E_{1/2}$  potential, which corresponds to the mean value of the peak anodic potential ( $E_{pa}$ ) and peak cathodic potential ( $E_{pc}$ ) of a reversible redox couple, and the values of  $E_{pa}$  and  $E_{pc}$ , as they relate to irreversible processes.<sup>12</sup> The two values cannot be utilized interchangeably as they refer to two very distinct situations. Recently it has been suggested that it may be beneficial to report the measured potentials as  $E_{pc/2}$  or  $E_{pa/2}$  (that is, the potential at which the current reaches half the peak current of the irreversible oxidation or reduction), to account for the fact that in many cases the onset potential for these oxidations and reductions occur at significantly lower potentials.<sup>13</sup>

In many cases it is also convenient to know that there is 96 kJ/mol or 23 kcal/mol for every volt of single electron transfer, as this allows redox potentials to be converted into more conventional energy units.

#### **1.4. Determining Singlet and Triplet Energies**

In addition to redox potentials, it is also necessary to have reliable values for both the singlet and triplet excited state energy of the photocatalyst. Although many of these values can be found in the literature, there are instances, such as in the case of newly designed or modified catalyst where one must determine these experimentally. Typically singlet and triplet energies are reported as estimates of the lowest excited energy for each multiplicity, which tends to be the 0-0 vibronic transition.<sup>14</sup> In the case of the singlet one can estimate the energy from either the 0-0 band in the fluorescence or absorption spectrum. If however,

this band is indistinguishable in both spectra, it is acceptable to use the midpoint in between the absorption and fluorescence maxima as a rough estimate of the lowest singlet excited state energy.<sup>14</sup> As for the triplet energies, there are three different ways one can obtain this value experimentally.<sup>14</sup> The first involves obtaining singlet-triplet absorption spectra and estimating the energy from the 0-0 band. Although these transitions are exceedingly spin forbidden and tend to be very weak, in many cases it is possible to increase the intensity of these spectra through spin-orbit coupling in the presence of a paramagnetic species which tends to enhance intersystem crossing.<sup>15</sup> The second method, involves measuring the rate constant at which different acceptor molecules quench the excited triplet photocatalyst through energy transfer. Characteristically when the triplet energy of the donor is below that of the acceptor one will see a drastic decrease in the rate constant for energy transfer between the triplet donor and acceptor as the energy difference increases.<sup>14</sup> However, due to the fact that triplet-triplet energy transfer is a spin-allowed process, as long as the triplet energy level of the donor is above or matched to that of the acceptor, the rate constant for energy transfer will likely be approaching or at the diffusion controlled limit.<sup>15</sup> There are however problems with this technique, which relate to difficulties in selecting appropriate acceptors and that the resulting triplet energy is actually only a range of values. The third and most popular method, involves measuring the low-temperature phosphorescence spectra of the photocatalyst.<sup>8</sup> This is generally accomplished by preparing the sample in a solvent mixture which forms a glass upon freezing and then recording the spectra while the

samples is cooled at 77 K using a cold-finger trap filled with liquid N<sub>2</sub>.<sup>16</sup> From the 0-0 or shortest wavelength band of this spectrum, one can estimate the triplet energy. Although this 0-0 transition is as forbidden as that in the absorption spectra, detection of luminescence tends to be more sensitive. Also, even with the photocatalyst trapped in glass at the time of measurement, of the three methods the obtained values tend to be more accurate.

Recently, there have been a number of examples of photoredox reactions, which have proceeded quite efficiently despite the fact that the initial electron transfer to or from the excited state photocatalyst was determined to be endothermic.<sup>17</sup> Although this could perhaps be traced back to incorrect redox potentials or poor estimates of excited state energy, one might want to consider the differences between inner and outer-sphere electron transfer mechanisms.<sup>18</sup> Traditionally most photoredox transformations are treated as involving outer-sphere electron transfer, where there is no physical interaction between the photocatalyst and the corresponding donor or acceptor molecules. However, it should be pointed out that some of these processes might involve an inner-sphere process in which physical interaction between the photocatalyst and reagents may lead to some sort of activation of the substrate, which is not accounted for in the redox potentials or excited state energy.

Lastly, while this section has focused primarily on excited state electron transfer processes, in many examples the key electron transfer actually comes from either the reduced or oxidized ground state of the photocatalyst. Since photoredox reactions are typically catalytic in nature there is usually some type of

redox cycle employed. Although there are examples where both the oxidation and reduction portions of the photoredox cycle are used to bring about the desired transformation, certain systems require the use of sacrificial electron donors or acceptors for catalyst turnover. For the most part, reduced photocatalysts tend to become better reducing agents whereas the oxidized photocatalysts become better oxidizing agents. In many cases the reducing or oxidizing power of the reduced or oxidized catalyst rivals that of the excited state and due to their stability usually hold the advantage that the subsequent electron transfer is not racing against the clock.

### **1.5. Measuring Kinetics of Excited States**

Excited state kinetics can be used as a powerful tool to predict, rationalize, and optimize photoredox systems. Although the initial excited state oxidation or reduction may be thermodynamically favorable, this does not necessarily indicate that the reaction will occur. In order to determine if a proposed reaction or pathway is involved in a particular transformation we must turn to kinetics.

Through the use of steady state and time-resolved fluorescence, as well as laser flash photolysis (LFP) techniques we can study the kinetics of both the singlet and/or triplet excited states of the photocatalyst. Due to the short lifetime of singlet excited states (ps–ns) in comparison to the relatively long lifetime of triplet excited states ( $\mu$ s–ms), one might expect the majority of the chemistry to occur from the triplet manifold. However, this ultimately depends on the rate at which the different components of the system quench the excited state of the photocatalyst and on the concentrations employed.

One of the most convenient methods of determining singlet quenching values is by performing steady state fluorescence quenching studies. This is accomplished by monitoring the quenching of the photocatalysts fluorescence as a function of quencher concentration ([Q]) and employing Stern-Volmer analysis:<sup>19</sup>

$$\frac{I_0}{I_{[Q]}} = 1 + K_{SV}[Q] \quad (1.3)$$

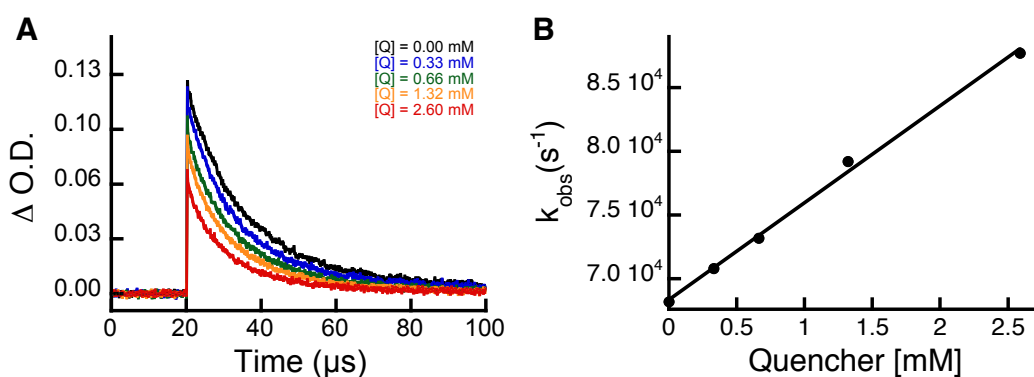
where  $I_0$  and  $I_{[Q]}$  are the fluorescence intensities in the absence and in the presence of quencher, [Q] is the concentration of quencher, and  $K_{SV}$  is the Stern-Volmer constant. Ideally, the Stern-Volmer plot ( $I_0/I_{[Q]}$  vs [Q]) should be linear and its slope corresponds to  $K_{SV}$ . In the case of dynamic quenching,  $K_{SV}$  is given by equation (1.4):

$$K_{SV} = k_q \tau_0 \quad (1.4)$$

where  $\tau_0$  is the fluorescence lifetime of the photocatalyst in the absence of a quencher. Using this equation, one can then determine the bimolecular quenching rate constant  $k_q$  ( $M^{-1}s^{-1}$ ) of the desired process. In some instances it may be determined that the resulting  $k_q$  is greater than the diffusion-controlled limit of the employed solvent. This is usually the result of static quenching, which arises due to a pre-association of the photocatalyst and quencher in the ground state.

In the case of triplet photosensitizers, their relatively long lifetime is attributed to the fact that their relaxation back to the singlet ground state is a spin forbidden process. Although many of the popular precious metal photocatalysts, such as  $Ru(bpy)_3Cl_2$ , have strongly emissive (phosphorescent) triplet states

whose kinetics can be evaluated using the same steady state and time-resolved techniques, there are many other sensitizers which have either weakly or non-emissive triplet states. In these instances, one can employ nanosecond LFP techniques to record time-resolved triplet-triplet transient absorption spectra, from which the kinetics of the system can be explored. Figure 1.3, depicts typical triplet decay traces obtained in the presence of increasing concentrations of quencher.



**Figure 1.3.** (A) Triplet decay traces in the presence of increasing concentration of quencher (q). All traces showing pseudo-first order decay (B) Corresponding kinetic quenching plot, the slope of which relates to the bimolecular rate constant for triplet quenching  $k_q$ . Adapted with permission from Pitre *et al.*<sup>2</sup> Copyright 2016 American Chemical Society.

By monitoring the rate of triplet decay as a function of [q], it is possible to determine the bimolecular rate constant for triplet quenching. When the triplet absorption decays with first-order or pseudo-first order kinetics, one can employ equation (1.5) to determine  $k_q$ :<sup>20</sup>

$$k_{obs} = \tau_0^{-1} + k_q[q] \quad (1.5)$$

where  $k_{obs}$  is the observed pseudo first order rate constant of triplet decay at a given concentration of quencher ( $\tau_{[q]}^{-1}$ ),  $\tau_0^{-1}$  is the inverse of the triplet lifetime in the absence of quencher, and [q] is the concentration of quencher. Employing

equation (1.5), one can plot  $k_{\text{obs}}$  versus  $[q]$  (Figure 1.3.B) and the slope of this plot will correspond to the bimolecular quenching constant  $k_q$ .

Using the techniques described above, one can determine the rate at which the different components of the system quench either the singlet and/or triplet excited state of the catalyst. Although the obtained rate constants can indicate whether or not a particular quencher is an efficient or inefficient quencher of a particular excited state, without accounting for the concentration of the quencher or the lifetime of the excited state, it is difficult to draw any conclusions about how the reaction is proceeding. A simple yet powerful way to exploit the obtained rate constant data is to calculate the percentage of excited states intercepted by a given quencher. This is accomplished by using equation (1.6):

$$\% \text{ } ^1 \text{ or } ^3\text{PC quenched by } Q_A = \frac{100 \times k_q^A [q_A]}{\tau_0^{-1} + k_q^A [q_A] + k_q^B [q_B] + k_q^C [q_C] + \dots} \quad (1.6)$$

where  $k_q^A$  is the bimolecular rate constant for the quencher of interest in  $\text{M}^{-1}\text{s}^{-1}$ ,  $[q_A]$  is the corresponding quencher concentration in M, and  $\tau_0^{-1}$  is the inverse of either the singlet or triplet lifetime in  $\text{s}^{-1}$ . Typically, when characterizing a photoredox system we would employ this equation under initial reaction conditions as it gives us a rough estimate of initial electron transfer efficiency. However, it can also be applied at any other point of the reaction given that all the corresponding rate constants and concentrations are known.

From equation (1.6), it becomes even more evident that although an excited state process is thermodynamically favorable, due to time constraints and



competition by other species, it will not necessarily occur. Nevertheless, we can ultimately use these data to optimize the system by modifying concentrations or eliminating possible quenchers. In practice, one of the simplest examples of such an optimization is the removal of  $O_2$  from a triplet-mediated transformation. Due to the fact that  $O_2$  tends to be a potent triplet state quencher, purging the reaction vessel of  $O_2$  can in many cases lead to dramatically increased yields. However, if  $O_2$ ,  $^1O_2$  or any other oxygen-derived species were to play a role in the reaction mechanism, this might not be the case.

As the experimentally determined rate constants ( $k_q$ ) incorporate all modes of deactivation of the excited state, the percentage of excited states quenched by either an electron donor or acceptor gives us only a rough estimate of the efficiency for this process, as not all quenching events lead to electron transfer. In order to have a better understanding of the system, we must be able to distinguish between energy and electron transfer events. In some cases, following an electron transfer the oxidized or reduced donor or acceptor molecule will give rise to a new absorption signal in the attainable portion of the spectrum. An excellent example of this is the reduction of methyl viologen ( $MV^{2+}$ ) to its radical cation ( $MV^{+\bullet}$ ), which has a strong absorption centered at 600 nm. However, in many cases the resulting reduced and/or oxidized species are not as strongly absorbing or as stable as  $MV^{+\bullet}$  as there may be many routes of deactivation. Through the use of LFP and transient spectroscopy, we can not only measure the absorption spectra of these intermediates but also monitor their growth and decay.

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## 2. Sexithiophene as Photoredox Catalyst

### Photocatalytic Dehalogenation of Vicinal Dibromo Compounds Utilizing Sexithiophene and Visible Light Irradiation

#### 2.1. Background

The protection and deprotection of olefinic functionalities through bromination and subsequent debromination can be a valuable tool in multi-step organic synthesis.<sup>1</sup> For the most part the protection of these groups as dibromides tends to be simple, straightforward and in most cases high yielding. However, the same cannot always be said of the deprotection process. Until recent developments, many routes to dehalogenation involved the use of highly toxic reductants, such as Zn, Fe, or organotin compounds, which due to their strongly reducing nature also suffer from selectivity issues and an incompatibility with a variety of functional groups.<sup>2-5</sup>

To overcome some of these disadvantages, several milder and selective electro- and photocatalytic reduction systems have been developed to convert *vicinal* dibromides (*vic*-Br<sub>2</sub>) to their corresponding alkenes with enhanced spatial and temporal control.<sup>6-10</sup> For the most part, the electrocatalytic systems have focused on direct two-electron electrochemical reduction, however the reduction can also be done indirectly through the electrochemical generation of reducing anion radicals or reduced metalloporphyrins.<sup>11,12</sup> The main advantage of the indirect systems being that the desired transformations can be brought about with less energy input due to the lower overpotentials required.

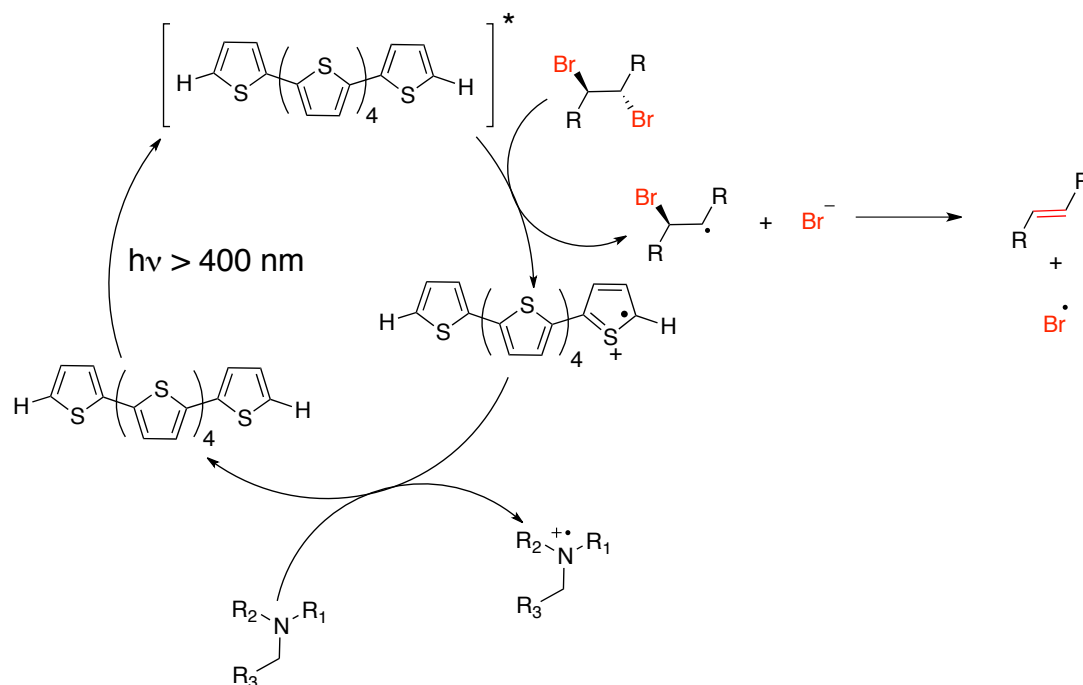
Similar transformations can also be accomplished through the use of high energy UV light, however problems with substrate and product degradation

as well as the need for expensive quartz glassware tend to make this route impractical.<sup>13,14</sup> For this reason the photocatalytic systems developed thus far for the dehalogenation of *vic*-Br<sub>2</sub> have focused primarily on the use of visible light (400-700 nm) absorbing transition metal photocatalysts, such as Ru(bpy)<sub>3</sub>Cl<sub>2</sub>. Though it has been over 20 years since it was first reported that a system comprising Ru(bpy)<sub>3</sub>Cl<sub>2</sub> as photosensitizer and triethylamine as sacrificial electron donor could be used to reductively dehalogenate *vic*-Br<sub>2</sub> compounds to their corresponding alkenes, there still remains considerable interest in this topic.<sup>10</sup> However, even with such interest, to the best of our knowledge there is yet to be a metal-free photocatalytic system developed for the reductive dehalogenation of *vic*-Br<sub>2</sub>.

With this in mind we set out to develop a novel metal-free photocatalytic system for the reductive dehalogenation of *vic*-Br<sub>2</sub>. Drawing inspiration from recent work published by McCulla and co-workers on the visible light promoted pinacol coupling of aryl aldehydes utilizing poly-(*p*)-phenylene as photocatalyst, we have decided to test the applicability of conjugated oligothiophenes, in particular  $\alpha$ -sexithiophene ( $\alpha$ -6T), as photoredox catalyst.<sup>15,16</sup>  $\alpha$ -6T is an oligomer consisting of 6-repeating thiophene units. Displaying properties representative of both oligothiophenes and organic semi-conductors, it is most commonly employed as an electron donor in organic photovoltaics (OPVs).<sup>17</sup> In addition, it is also well documented that excited state oligothiophenes are quite proficient reducing agents, which have been shown to reduce common electron acceptors such as methyl viologen (MV<sup>2+</sup>),<sup>18</sup> tetracyanoethylene, and C60.<sup>19</sup> It is

with this propensity for excited state electron transfer (eT) that we aimed to develop a photocatalytic system for the dehalogenation of *vic*-Br<sub>2</sub> based on the use of  $\alpha$ -6T as visible light photoredox catalyst and a tertiary amine as sacrificial electron donor (Scheme 2.1).

**Scheme 2.1.** Proposed Mechanism for the Photocatalyzed Reductive Dehalogenation



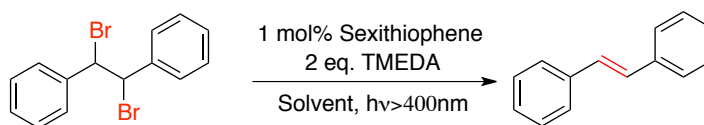
## 2.2. Optimization and Controls

We began our studies on the reductive dehalogenation of *vic*-Br<sub>2</sub> utilizing  $\alpha$ -6T as photocatalyst, TMEDA as sacrificial e<sup>-</sup> donor, and *meso*-1,2-dibromo-1,2-diphenylethane as our model substrate. In an attempt to optimize the reaction conditions for the dehalogenation reaction, we performed the test reaction under a variety of conditions (Table 2.1).

From these initial tests it was found that the optimal solvent for the dehalogenation is dimethylformamide (DMF) and that at the concentrations

employed, one can obtain near quantitative conversion of the model *vic*-Br<sub>2</sub> after only 1 hour of irradiation with two warm white LEDs (Table 2.1, entry 4). It is also observed that the reaction proceeds with reduced efficiency in the presence of O<sub>2</sub> (Table 2.1, entry 5). In addition to this, it is also evident that the photocatalyst, sacrificial amine, and light source are all critical components of the system as their omission results in little or no conversion of the starting material after 1 hour (Table 2.1, entry 6-8).

**Table 2.1.** Optimization of Reaction Conditions<sup>a</sup>



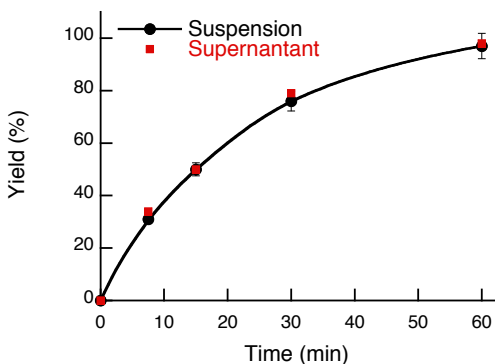
| Entry/Conditions | TMEDA | Solvent            | Atm.  | Time   | Isolated Yield |
|------------------|-------|--------------------|-------|--------|----------------|
| 1 (light)        | 2 eq. | CH <sub>3</sub> OH | Argon | 30 min | N.R.           |
| 2 (light)        | 2 eq. | CH <sub>3</sub> CN | Argon | 30 min | 18%            |
| 3 (light)        | 2 eq. | DMF                | Argon | 30 min | 76%            |
| 4 (light)        | 2 eq. | DMF                | Argon | 1 h    | >99%           |
| 5 (light)        | 2 eq. | DMF                | Air   | 1 h    | 68%            |
| 6 (dark)         | 2 eq. | DMF                | Argon | 1 h    | Trace          |
| 7 (no amine)     | -     | DMF                | Argon | 1 h    | Trace          |
| 8 (no catalyst)  | 2 eq. | DMF                | Argon | 1 h    | N.R.           |

<sup>a</sup>Reaction conditions: Substrate (60 mM), TMEDA (120 mM),  $\alpha$ -6T (0.01 eq.), solvent (5 mL). Irradiated with two warm white LEDs. Adapted with permission from McTiernan *et al.*<sup>20</sup> Copyright 2014 American Chemical Society.

### 2.3. Heterogeneous vs. Homogeneous Catalysis

One of the main drawbacks  $\alpha$ -6T as it relates to organic photovoltaics is its poor processability brought on by a lack of solubility in most organic solvents. It is however this same lack of solubility, which interested us in the possibility of developing the catalytic system as a heterogeneous one. To test the heterogeneity of our system, we have performed catalyst reusability studies and monitored the conversion of *meso*-1,2-dibromo-1,2-diphenylethane over time in

the presence and absence (catalyst added but removed prior to irradiation) of the suspended catalyst. Upon testing the reusability of the catalyst it was observed that over 5 trials there was no loss in activity. Although this could be indicative of a heterogeneous system it seemed almost too good to be true. A more likely scenario was that a small amount of leached  $\alpha$ -6T in solution was actually responsible for the observed catalysis. To test this idea we turn to the conversion vs. time traces shown in Figure 2.1.



**Figure 2.1.** Conversion vs. time of *meso*-1,2-dibromo-1,2-diphenylethane in the presence of suspended or leached  $\alpha$ -Sexithiophene. Adapted with permission from McTiernan *et al.*<sup>20</sup> Copyright 2014 American Chemical Society.

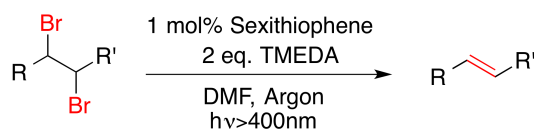
As expected the profile of the two plots are almost identical, indicating that indeed the leaching from the heterogeneous catalyst is triggering homogeneous catalysis. We have estimated that the leaching leads to an approximate homogeneous catalyst loading of 0.02 mol% (0.012 mM). However, since light scatter in the presence of the suspended photocatalyst did not affect the reaction rate, we decided to perform the reaction in the presence of suspended catalyst as it simplified sample preparation and maintains a saturation level of catalyst in solution.

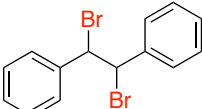
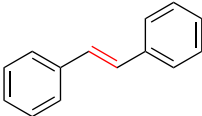
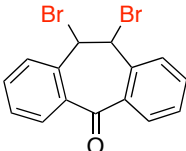
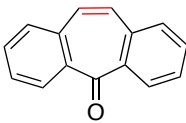
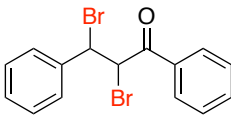
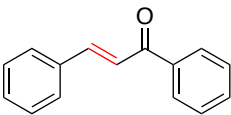
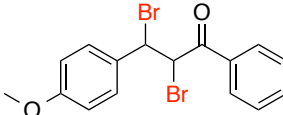
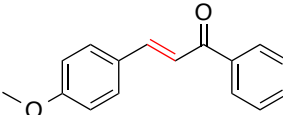
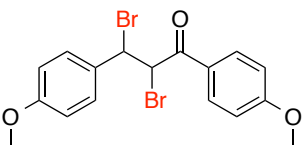
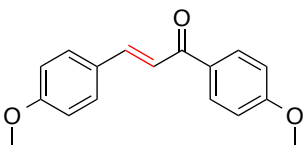
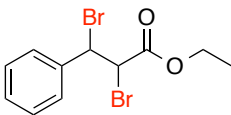
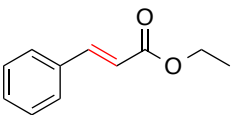
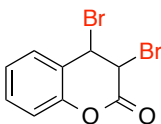
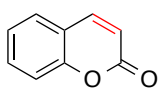
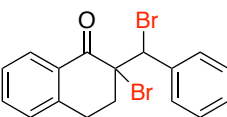
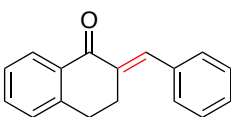
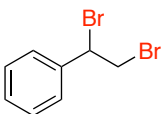
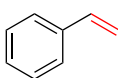
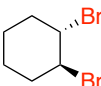


## 2.4. Substrate Scope

With the optimized conditions in hand, we then set out to test our system on a variety of different *vic*-Br<sub>2</sub> compounds. As illustrated in Table 2.1 our photocatalytic system can for the most part convert a number of activated *vic*-Br<sub>2</sub> to their corresponding alkene in good to excellent yields (65-99%) under short irradiation times (1-3 h). However, as shown by Table 2.2, entry 10, our system is unable to reduce the unactivated 1,2-dibromocyclohexane ( $E_{1/2}^{\text{red}} = -1.40 \text{ V vs. SCE}$ )<sup>11</sup> even after 3 hours of irradiation, most likely due to the fact that its reduction potential is outside the potential window attainable by the  $\alpha$ -6T photocatalyst.

**Table 2.2.** Photocatalyzed Reductive Dehalogenation of a Variety of *vic*-Dibromo Compounds<sup>a</sup>



| Entry | Substrate                                                                           | Product                                                                              | Time | % Yield          |
|-------|-------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|------|------------------|
| 1     |    |    | 1 h  | >99%             |
| 2     |    |    | 1 h  | >99%             |
| 3     |    |    | 1 h  | 84%              |
| 4     |    |    | 1 h  | 77%              |
| 5     |  |  | 1 h  | 79%              |
| 6     |  |  | 1 h  | 68%              |
| 7     |  |  | 2 h  | 88%              |
| 8     |  |  | 3 h  | 65%              |
| 9     |  |  | 3 h  | 57% <sup>b</sup> |
| 10    |  | -                                                                                    | 3 h  | N.R.             |

<sup>a</sup>Reaction conditions: Substrate (60 mM), TMEDA (120 mM),  $\alpha$ -6T (0.01 eq.). DMF (5mL) under Argon atmosphere. Irradiated with two warm white LEDs. Yields reported as isolated yields. <sup>b</sup>%Conversion by <sup>1</sup>H NMR. Adapted with permission from McTiernan *et al.*<sup>20</sup> Copyright 2014 American Chemical Society.

## 2.5. Probing The Mechanism

At this point, we became interested in examining the mechanism of these reductions in the hope of shedding light onto the origin of the high efficiency exhibited by our photocatalytic system. To accomplish this we have studied the thermodynamic feasibility and kinetics of the key mechanistic steps outlined in (Scheme 2.1) using *meso*-1,2-dibromo-1,2-diphenylethane as the model substrate.

### 2.5.A. Thermodynamic Analysis

As shown in (Scheme 2.1), the first step in the catalytic cycle upon excitation of  $\alpha$ -6T is an excited state electron transfer (eT) from the photocatalyst to the *vic*-Br<sub>2</sub> substrate, which results in the reduction of the *vic*-Br<sub>2</sub> and oxidation of the  $\alpha$ -6T leading to the formation of its radical cation ( $\alpha$ -6T<sup>•+</sup>). To demonstrate that indeed the excited state eT between the catalyst and the model *vic*-Br<sub>2</sub> is thermodynamically feasible, we can calculate the Gibbs free energy for eT from both the singlet and triplet excited state of the photocatalyst using equation (2.1).<sup>21,22</sup>

$$\Delta G_{eT} = E_{1/2}^{\text{ox}}(D) - E_{1/2}^{\text{red}}(A) - E_{S \text{ or } T}^*(D) + \Delta E_{\text{Coulombic}} \quad (2.1)$$

The results of the calculation for both the singlet and triplet states of  $\alpha$ -6T are shown in Table 2.3. These values indicate that eT from both the singlet and triplet state of  $\alpha$ -6T is exergonic. However, due to its higher excited state energy, eT from the singlet is more favorable by 17 kcal/mol.

**Table 2.3.** Thermodynamic Data for Electron Transfer From Excited  $\alpha$ -Sexithiophene to Model *vic*-Br<sub>2</sub> Compound

**Donor (D)**      **Acceptor (A)**

| Entry                     | Excited State | $E^*$            | $E_{1/2}^{ox}(D)^a$ | $E_{1/2}^{red}(A)^b$ | $\Delta G_{eT}$ |
|---------------------------|---------------|------------------|---------------------|----------------------|-----------------|
| (kcal mol <sup>-1</sup> ) |               |                  |                     |                      |                 |
| 1                         | Singlet       | 59 <sup>19</sup> | 10                  | -25                  | -24             |
| 2                         | Triplet       | 42 <sup>19</sup> |                     |                      | -7              |

<sup>a</sup>Oxidation potential of ground state donor (D)  $\alpha$ -6T = 0.415 V vs. SCE.<sup>23</sup> <sup>b</sup>Reduction potential of ground state acceptor (A) *vic*-Br<sub>2</sub> = -1.10 V vs. SCE.<sup>11</sup> Adapted with permission from McTiernan *et al.*<sup>20</sup> Copyright 2014 American Chemical Society.

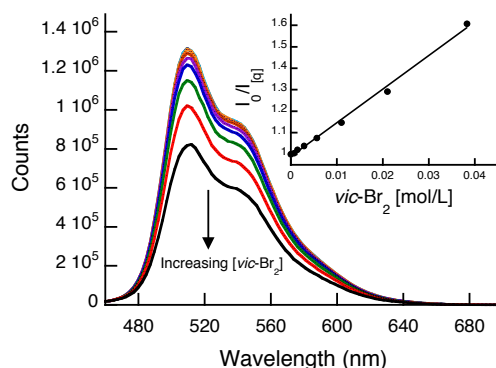
## 2.5.B. Kinetic Analysis

While the eT between <sup>1</sup> $\alpha$ -6T and *vic*-Br<sub>2</sub> is significantly more exothermic than that from the triplet state, given the short lifetime of the singlet ( $\tau_0$  = 0.81 ns) in comparison to that of the triplet ( $\tau_0$  = 16  $\mu$ s), one might still expect the majority of the chemistry to occur from the triplet manifold. However, this ultimately depends on the rate at which the different components of the system quench the excited states of the photocatalyst and on the concentrations employed. To determine these rates we have employed a combination of steady state/time resolved fluorescence and laser flash photolysis techniques.

To determine the singlet quenching values, we have performed steady state fluorescence quenching studies. By monitoring the quenching of  $\alpha$ -6T fluorescence emission as a function of quencher concentration [q] and employing the Stern-Volmer analysis of equation (2.2).<sup>24,25</sup>

$$\frac{I_0}{I_{[q]}} = 1 + K_{SV}[q] \quad (2.2)$$

where  $I_0$  and  $I$  are the fluorescence intensities in the absence and in the presence of quencher;  $[q]$  is the concentration of quencher and  $K_{SV}$  is the Stern-Volmer constant. From the slope of the linear Stern-Volmer quenching plot, one can obtain the corresponding  $K_{SV}$  value.



**Figure 2.2.** Kinetic analysis of the reaction between  $^1\alpha$ -6T and  $vic$ -Br $_2$ . Steady-state fluorescence spectrum of  $\alpha$ -6T ( $\lambda_{ex}$ =450 nm) in the presence of increasing concentrations of  $vic$ -Br $_2$ ; inset: Stern-Volmer plot displaying the decrease in fluorescence intensity as a function of  $vic$ -Br $_2$  concentration. Adapted with permission from McTiernan *et al.*<sup>20</sup> Copyright 2014 American Chemical Society.

For example, from the data shown in Figure 2.2, we find that  $K_{SV}$  for the model  $vic$ -Br $_2$  is  $15.6 \pm 1.56 \text{ M}^{-1}$ . However, for dynamic quenching  $K_{SV}$  is given by equation (2.3):

$$K_{SV} = k_q\tau_0 \quad (2.3)$$

where  $k_q$  is the quenching rate constant and  $\tau_0$  is the fluorescence lifetime of  $\alpha$ -6T in the absence of quencher, a value of  $k_q = 1.93 \pm 0.19 \times 10^{10} \text{ M}^{-1}\text{s}^{-1}$  can be calculated for the  $vic$ -Br $_2$ . Using this technique we have also determined  $k_q$  for other components of the system which may compete for  $^1\alpha$ -6T (Table 2.4).

**Table 2.4.** Singlet Quenching of  $\alpha$ -Sexithiophene

| Entry | Quencher [q]                | $K_{SV} (M^{-1})^a$ | $k_q (M^{-1}s^{-1})^b$           |
|-------|-----------------------------|---------------------|----------------------------------|
| 1     | <i>vic</i> -Br <sub>2</sub> | 15.6 $\pm$ 1.56     | 1.93 $\pm$ 0.19 $\times 10^{10}$ |
| 2     | TMEDA                       | 0.14 $\pm$ 0.01     | 1.69 $\pm$ 0.17 $\times 10^8$    |
| 3     | Alkene                      | 6.9 $\pm$ 0.7       | 8.50 $\pm$ 0.85 $\times 10^9$    |

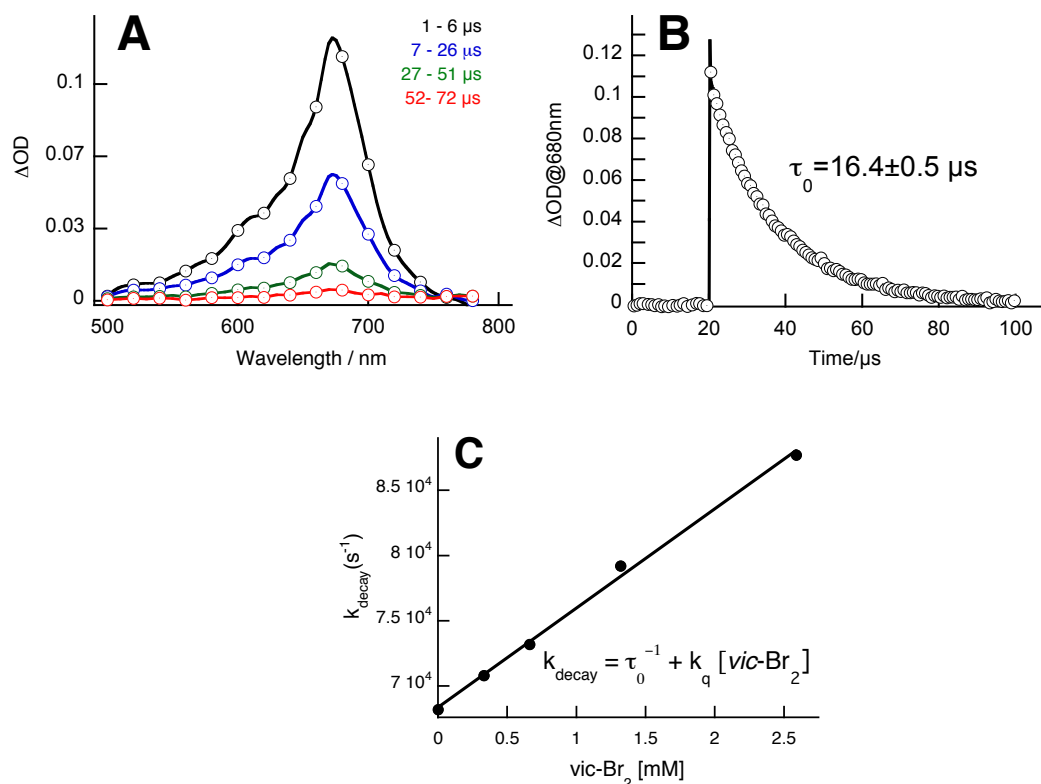
<sup>a</sup>Determined from the slope of the corresponding Stern-Volmer plot ( $I_0 / I_{[q]}$  vs. [q]). <sup>b</sup>Based on a fluorescence lifetime of  $\tau_0 = 0.81$  ns. Adapted with permission from McTiernan *et al.*<sup>20</sup> Copyright 2014 American Chemical Society.

From the data listed in Table 2.4, it can be seen that both the *vic*-Br<sub>2</sub> starting material and the alkene product are efficient quenchers of <sup>1</sup> $\alpha$ -6T, with bimolecular rate constants at or approaching the diffusion control limit. In comparison, TMEDA was found to react with <sup>1</sup> $\alpha$ -6T at a rate roughly two orders of magnitude slower than that of the *vic*-Br<sub>2</sub> starting material. It is however, important to mention that the quenching observed in the presence of TMEDA is unlikely to be due to electron transfer due to unfavorable thermodynamics. A likely scenario is that the singlet is being deactivated through a physical quenching process, such as the formation of an exciplex. From these data we were able to calculate that even with such a short lifetime, 49% of  $\alpha$ -6T singlets are intercepted by the *vic*-Br<sub>2</sub> under initial reaction conditions using equation (2.4):

$$\% ^1\alpha\text{-6T quenched by } vic\text{-Br}_2 = \frac{100 \times k_q^{vic\text{-Br}_2}[vic\text{-Br}_2]}{(\tau_0^{-1} + k_q^{vic\text{-Br}_2}[vic\text{-Br}_2] + k_q^{amine}[amine])} \quad (2.4)$$

With such a high percentage of singlets reacting with the *vic*-Br<sub>2</sub> it is likely that eT from <sup>1</sup> $\alpha$ -6T is playing a key role in our photocatalytic system. The fact that we also obtain a 68% conversion (Table 2.4, entry 5) in the presence of O<sub>2</sub>, a potent triplet quencher ( $k_q$  <sup>3</sup> $\alpha$ -6T = 3.0  $\pm$  0.3  $\times 10^9$  M<sup>-1</sup>s<sup>-1</sup>), is also in good agreement with our rationalization of the singlet quenching data. However, since we obtain a

>99% conversion (Table 2.4, entry 4) simply by purging the system of O<sub>2</sub>, it may be a combination of both singlet and triplet eT responsible for part of the efficiency of our system, with the <sup>3</sup>α-6T capable of reducing any *vic*-Br<sub>2</sub> that escapes reaction with the singlet. To test this idea we have performed time-resolved transient absorption spectroscopy on α-6T, using a nanosecond laser flash photolysis system, with the aim of determining the rate at which the different components of the system quench the α-6T triplet. Figure 2.3 shows the data from a typical quenching experiment used to determine the rate at which a *vic*-Br<sub>2</sub> reacts with <sup>3</sup>α-6T. These techniques were also applied to all other quenchers. Both the strong absorption and long lifetime of <sup>3</sup>α-6T greatly simplify these measurements.



**Figure 2.3.** Kinetic analysis of the reaction between  $^3\alpha\text{-6T}$  and  $\text{vic-Br}_2$ . A) Transient spectra showing the  $^3\alpha\text{-6T}$  signal at 680 nm obtained upon laser pulse excitation (355 nm, 10 mJ) of a  $\alpha\text{-6T}$  sample which had been purged of oxygen. B) Corresponding decay trace of  $^3\alpha\text{-6T}$  at 680 nm. C) Kinetic quenching plot showing the rate of  $^3\alpha\text{-6T}$  quenching as a function of  $[\text{vic-Br}_2]$ . The slope of this plot corresponds to the bimolecular rate constant for this reaction. Adapted with permission from McTiernan *et al.*<sup>20</sup> Copyright 2014 American Chemical Society.

As can be seen in Table 2.5,  $\text{O}_2$  is the only component that efficiently quenches the triplet of  $\alpha\text{-6T}$ . The  $\text{vic-Br}_2$  and its corresponding alkene react at rates around  $10^6 \text{ M}^{-1}\text{s}^{-1}$ , while the addition of TMEDA did not affect the rate of triplet decay.

**Table 2.5.** Triplet Quenching of  $\alpha\text{-Sexithiophene}$

| Entry | Quencher [q]      | $k_q (\text{M}^{-1}\text{s}^{-1})^a$ |
|-------|-------------------|--------------------------------------|
| 1     | $\text{vic-Br}_2$ | $7.6 \pm 0.8 \times 10^6$            |
| 2     | TMEDA             | $<5 \times 10^5$                     |
| 3     | Alkene            | $5.5 \pm 0.5 \times 10^6$            |
| 4     | $\text{O}_2$      | $3.0 \pm 0.3 \times 10^9$            |

<sup>a</sup>Determined from the slope of the corresponding kinetic quenching plot ( $k_{\text{decay}}$  vs. [q]). Adapted with permission from McTiernan *et al.*<sup>20</sup> Copyright 2014 American Chemical Society.



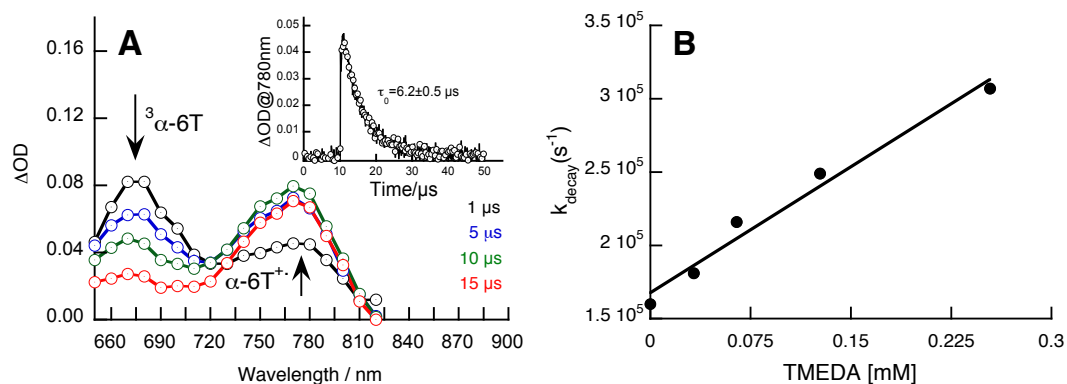
With these data on hand we are able to calculate, under initial reaction conditions, the percentage of triplets quenched by the *vic*-Br<sub>2</sub> in the presence and absence of O<sub>2</sub> using equation (2.5):<sup>26</sup>

$$\%{}^3\alpha\text{-6T quenched by } vic\text{-Br}_2 = \frac{100 \times k_q^{vic\text{-Br}_2}[vic\text{-Br}_2]}{(\tau_0^{-1} + k_q^{vic\text{-Br}_2}[vic\text{-Br}_2] + k_q^{amine}[amine] + k_q^{O_2}[O_2])} \quad (2.5)$$

Interestingly we find that in the presence of O<sub>2</sub> only 7% of triplets are quenched by *vic*-Br<sub>2</sub>. However upon removal of O<sub>2</sub> from the system, this number increases to 89%. These results are again in excellent agreement with the idea of a combination of singlet and triplet eT as well as the results observed in Table 2.5, entries 4 and 5.

Another key step in our proposed mechanism, which can influence the efficiency of our system, is catalyst turnover. Upon oxidation of the excited photocatalyst, the radical cation of  $\alpha$ -6T is formed. Although it has been previously observed that photochemical generation of oligothiophene radical cations can result in chain elongation through radical cation recombination,<sup>27-29</sup> the  $\alpha$ -6T<sup>•+</sup> appears to be quite stable ( $\tau_0 = 6 \mu\text{s}$ ). Therefore to regenerate the neutral photocatalyst we have included in our system TMEDA as sacrificial e<sup>-</sup> donor. Exploiting the fact that the 6T<sup>•+</sup> has a strong absorption at 780 nm, we can also determine the rate of catalyst turnover in the presence of TMEDA. Although the 6T<sup>•+</sup> can be generated through laser excitation of  $\alpha$ -6T in the presence of *vic*-Br<sub>2</sub> we have found substitution of the *vic*-Br<sub>2</sub> with MV<sup>2+</sup> results in more efficient production of the oxidized photocatalyst. By monitoring the rate of decay of the signal at 780 nm in the presence of increasing concentrations of TMEDA, we

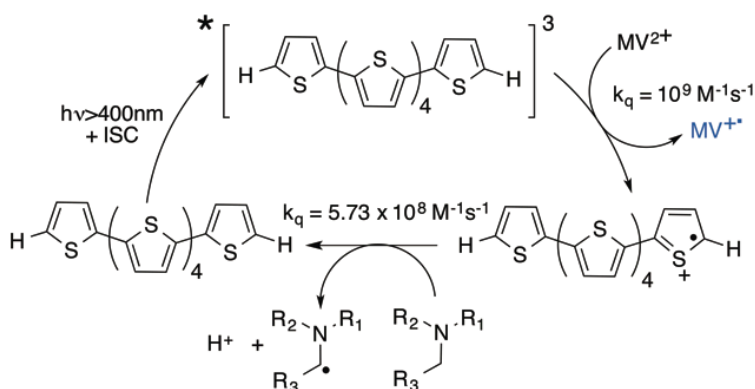
have been able to determine that TMEDA turns over the catalyst at a rate of  $5.7 \pm 0.6 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$ , justifying its selection as sacrificial electron donor.



**Figure 2.4.** Kinetic analysis of the reaction between  $\alpha\text{-6T}^{\bullet+}$  and TMEDA. A) Transient spectrum showing the decay of  $^3\alpha\text{-6T}$  at 680 nm and the growth of a signal centered at 780 nm, which is assigned to  $\alpha\text{-6T}^{\bullet+}$ . Spectra obtained upon laser pulse excitation (355 nm, 10 mJ) of a sample containing  $\alpha\text{-6T}$  and  $\text{MV}^{2+}$ , which had been purged of oxygen. The absorption of  $\text{MV}^{\bullet+}$  at 600 nm does not interfere with the measurement; inset: decay trace of  $\alpha\text{-6T}^{\bullet+}$  recorded at 780 nm. B) Stern-Volmer plot showing the rate of  $\alpha\text{-6T}^{\bullet+}$  quenching as a function of [TMEDA]. The slope of this plot corresponds to the bimolecular rate constant for this reaction. Adapted with permission from McTiernan *et al.*<sup>20</sup> Copyright 2014 American Chemical Society.

Up to this point we have been referring to TMEDA as solely a sacrificial  $e^-$  donor, whose role in the photocatalytic cycle is to simply turnover the photocatalyst from its oxidized to neutral state. However, recent publications from our group would suggest that this is most likely not the only role of TMEDA.<sup>30,31</sup> When tertiary aliphatic amines reductively quench a substrate under basic conditions the resulting amine-radical cation will readily deprotonate to give an  $\alpha$ -aminoalkyl radical, which due to its reductive nature ( $E_{1/2}^{\text{ox}} = -1.12 \text{ V vs. SCE}$ )<sup>32</sup>, can reduce a variety of organic substrates including *vic*-dibromides.

**Scheme 2.2.** Indirect Generation of  $\alpha$ -Sexithiophene Radical Cation and Subsequent Quenching by Amine<sup>a</sup>

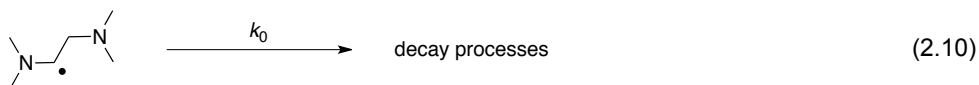
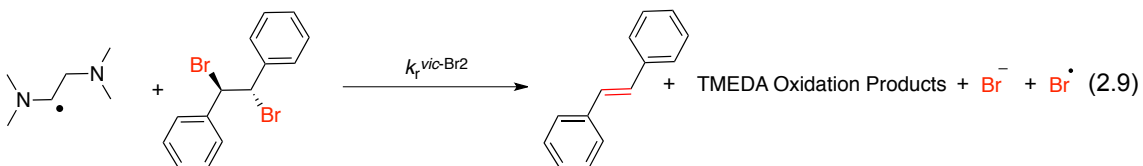
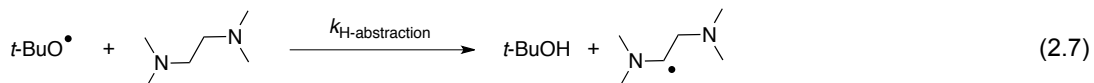


<sup>a</sup>Methyl viologen ( $MV^{2+}$ ) is used as electron acceptor to generate  $\alpha$ -6T $^{\bullet+}$  from  $^3\alpha$ -6T.  $E_{1/2}^{red}(MV^{2+}/MV^{\bullet+}) = -0.46$  V vs. SCE.<sup>33</sup> Quenching of  $\alpha$ -6T $^{\bullet+}$  through  $e^-$  transfer from a tertiary amine results in the regeneration of the neutral photocatalyst and an  $\alpha$ -aminoalkyl radical after proton loss.  $E_{1/2}^{ox}(R_3N/R_3N^{\bullet+}) = 0.50$  V vs. SCE.<sup>34</sup> Adapted with permission from McTiernan *et al.*<sup>20</sup> Copyright 2014 American Chemical Society.

Interested in examining the reactivity of the resulting TMEDA derived  $\alpha$ -aminoalkyl radicals with the model *vic*-Br<sub>2</sub> compound, we set out to study this reaction utilizing LFP. However, as neither the  $\alpha$ -aminoalkyl radical nor the product of its reaction with the *vic*-Br<sub>2</sub> give a signal in the attainable spectral region, we were required to use the probe technique.<sup>35</sup> It has been previously reported that  $\alpha$ -aminoalkyl radicals can be generated through reaction of the parent amine with *tert*-butoxyl radicals through H-abstraction and that the resulting  $\alpha$ -aminoalkyl radicals are potent reducers of  $MV^{2+}$  ( $k_r = 10^9$  M<sup>-1</sup>s<sup>-1</sup>).<sup>36</sup> Since *tert*-butoxyl radicals can be generated through direct photolysis of di-*tert*-butyl peroxide and reduced methyl viologen  $MV^{\bullet+}$  has a strong absorption at 600 nm, the reduction of  $MV^{2+}$  would appear to be an ideal probe for our system as any added *vic*-Br<sub>2</sub> would compete for the generated  $\alpha$ -aminoalkyl radicals.

When di-*tert*-butyl peroxide is photodecomposed in the presence of TMEDA, the  $MV^{2+}$  probe, and the model *vic*-Br<sub>2</sub>, the following reactions need to

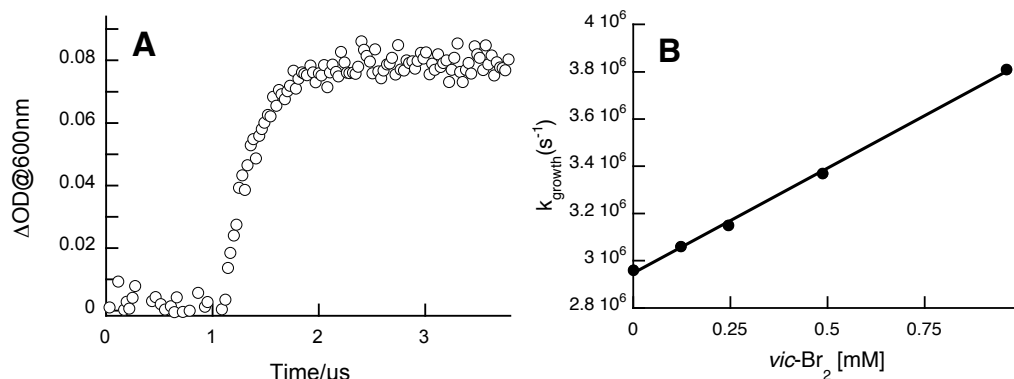
be taken into consideration in the time scale of our experiments:



According to the mechanism of reactions (2.6) – (2.10), the experimental pseudo-first-order rate constant ( $k_{\text{growth}}$ ) for build-up of the  $\text{MV}^{+\bullet}$  probe signal is given by equation (2.11):

$$k_{\text{growth}} = k_0 + k_r^{\text{MV}^{2+}} [\text{MV}^{2+}] + k_r^{\text{vic-Br}_2} [\text{vic-Br}_2] \quad (2.11)$$

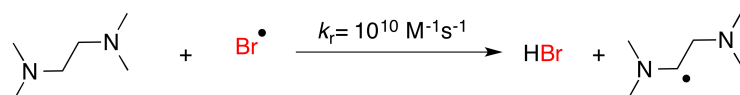
The value of  $k_r^{\text{vic-Br}_2}$  is thus obtained from the plot of  $k_{\text{growth}}$  vs. concentration of  $\text{vic-Br}_2$ , when the concentration of  $\text{MV}^{2+}$  is kept constant. From this we find that TMEDA derived  $\alpha$ -aminoalkyl radicals react with the model  $\text{vic-Br}_2$  at a rate of  $8.9 \pm 0.9 \times 10^8 \text{ M}^{-1}\text{s}^{-1}$ , which indirectly implies that some of the observed conversion may be due in part to reducing  $\alpha$ -aminoalkyl radicals formed upon catalyst turnover. It should however be mentioned that such a pathway is only likely to occur when the reaction is purged of  $\text{O}_2$ , as it is well known that  $\alpha$ -aminoalkyl radicals react quickly with  $\text{O}_2$  to give  $\alpha$ -aminoalkylperoxyl radicals ( $k_r \sim 10^9 \text{ M}^{-1}\text{s}^{-1}$ ), which eventually give rise to hydroperoxyl radicals.<sup>37</sup>



**Figure 2.5.** Kinetic analysis of the reaction between  $\alpha$ -aminoalkyl radicals of TMEDA and  $vic-Br_2$  using the probe technique. A) Growth of reduced  $MV^{2+}$  at 600 nm in the absence of  $vic-Br_2$ . B) Stern-Volmer plot showing the rate of growth at 600 nm as a function of  $[vic-Br_2]$ . The slope of this plot corresponds to the bimolecular rate constant for this reaction. Adapted with permission from McTiernan *et al.*<sup>20</sup> Copyright 2014 American Chemical Society.

Lastly, it should be noted that catalyst turnover is only one of two possible routes to the formation of  $\alpha$ -aminoalkyl radicals in our photocatalytic system. Previous reports have shown that  $Br^\bullet$  radicals, liberated upon initial reduction of the  $vic-Br_2$ , can abstract a hydrogen from aliphatic amines at diffusion-controlled rates to generate the corresponding  $\alpha$ -aminoalkyl radical (Scheme 2.3).

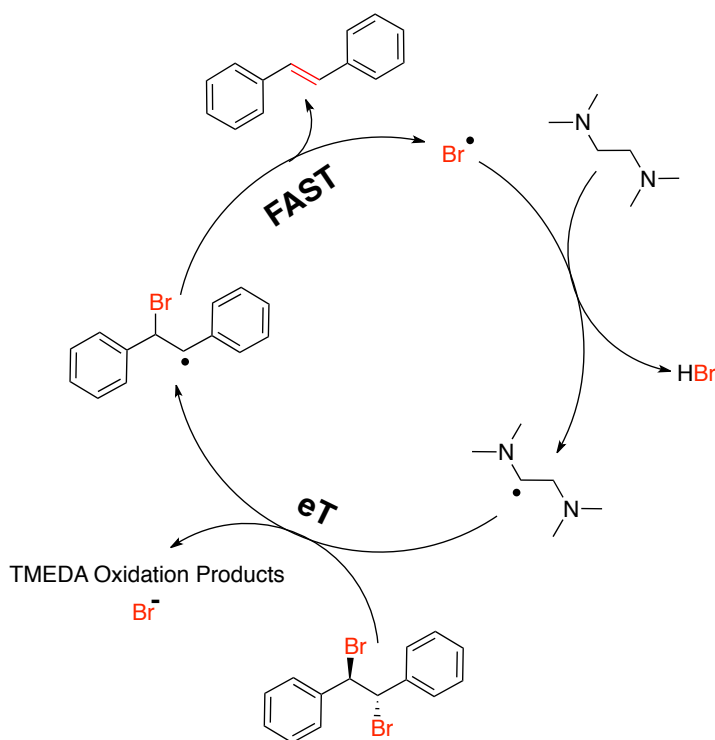
**Scheme 2.3.** Alternative Pathway for the Formation of  $\alpha$ -Aminoalkyl Radicals



However, it is not until you combine this route with the  $\alpha$ -aminoalkyl radicals ability to reduce  $vic-Br_2$  that it quickly becomes apparent that, depending on the reduction potential of the substrate, a chain reaction, as illustrated in Scheme 2.4, may be responsible for part of the observed conversion. In good agreement with this idea, we have found that under conditions of intermittent irradiation that there is a non-linear dependence between the rate of sample illumination and conversion (This will be discussed in detail in Chapter 6 – Probing Light-

Mediated Chain Processes). While it has been suggested that the liberated  $\text{Br}^\bullet$  radicals could perform a bromine atom abstraction to generate  $\text{Br}_2$  and propagate the chain, this seems unlikely owing to the enhanced stability of  $\text{HBr}$  in comparison to  $\text{Br}_2$ .

**Scheme 2.4.** Proposed Chain Reaction for the Dehalogenation of Vicinal Dibromides. Adapted with permission from McTiernan *et al.*<sup>20</sup> Copyright 2014 American Chemical Society.



## 2.6. Conclusions

We have demonstrated for the first time the use of  $\alpha$ -6T as a visible light photoredox catalyst in the reductive dehalogenation of *vic*-dibromides. The resulting photocatalytic system based on a combination of  $\alpha$ -6T, TMEDA, and visible light has been demonstrated to reductively dehalogenate a variety of different *vic*-dibromides in good to excellent yield under relatively short irradiation times. Through examination of the thermodynamic feasibility and rate constants of the key mechanistic steps we have been able to better understand the

underlying mechanisms, which contribute to the high efficiency of our catalytic system.

## **2.7. Appendix**

### **2.7.A. General Information**

Substrates and Reagents:  $\alpha$ -Sexithiophene, *N,N,N',N'*-tetramethylenediamine (TMEDA), Bromine, Sodium Thiosulphate, MeOH, and DMF were purchased from commercial suppliers (Sigma Aldrich, Alfa Aesar, and Fisher) and used with no further purification unless otherwise noted.

Light Source: Unless otherwise noted, was two warm-white 90 W LEDs, which were purchased from LedEngin.

Chromatography: Flash column chromatography was performed using 230-400 mesh silica gel. Preparatory thin layer chromatography (PTLC) was performed using 1000  $\mu$ m thick glass baked TLC plates purchased from Silicycle.

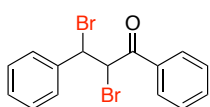
NMR: All  $^1\text{H}$  NMR were recorded on a Bruker AVANCE 400 spectrometer. Chemical shifts ( $\delta$ ) are reported in ppm from the solvent.

### **2.7.B. General Procedure for the Preparation of Vicinal-Dibromide Starting Materials**

The preparation of *vicinal*-dibromides from chalcones has previously been described. Briefly, the corresponding chalcone was dissolved or suspended in 10.0 mL of  $\text{CHCl}_3$  and cooled to 0°C. Once cooled, approx. 3.0 mL of freshly prepared bromine solution (0.56 M in  $\text{CHCl}_3$ ) was added dropwise to the stirring solution. The mixture was then allowed to warm to room temperature and the reaction was followed by TLC until completion. Once complete, the unreacted bromine was quenched through the addition of a saturated solution of sodium

thiosulfate. The reaction mixture was then extracted with  $\text{CHCl}_3$  (2 x 10.0 mL) and the combined organic layers were washed with brine (3 x 10 mL). The organic layer was dried over anhydrous  $\text{MgSO}_4$  and concentrated using a rotovap. Purification of the crude was accomplished by column chromatography (hexanes:ethylacetate).

**[Table 2.2, entry 3 Substrate]<sup>7</sup>**

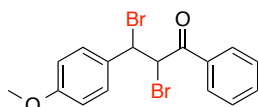


According to the general procedure, 1,3-diphenylprop-2-en-1-one (0.32 g, 1.53 mmol) and 3.10 mL of bromine solution (0.56 M in chloroform) afforded the desired product (0.42 g, 1.16 mmol, 76%) as white solid after column purification on silica gel.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 5.66 (d,  $J=11.0$  Hz, 1 H) 5.85 (d,  $J=11.0$  Hz, 1 H) 7.35 - 7.46 (m, 3 H) 7.52 - 7.59 (m, 4 H) 7.65 - 7.71 (m, 1 H) 8.07 - 8.16 (m, 2 H)

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 191.2, 138.2, 134.4, 134.2, 130.2, 129.3, 129.0, 128.9, 128.8, 128.5, 128.3, 49.8, 46.8

**[Table 2.2, entry 4 Substrate]<sup>38</sup>**

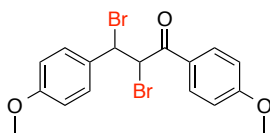


According to the general procedure, 3-(4-Methoxyphenyl)-1-phenyl-2-propen-1-one (0.36 g, 1.53 mmol) and 3.10 mL of bromine solution (0.56 M in chloroform) afforded the desired product (0.43 g, 1.10 mmol, 72%) as white solid after column purification on silica gel.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 3.92 (s, 3 H) 5.66 (d,  $J=11.5$  Hz, 1 H) 5.82 (d,  $J=11.5$  Hz, 1 H) 7.00 - 7.06 (m, 2 H) 7.38 - 7.47 (m, 3 H) 7.52 - 7.57 (m, 2 H) 8.08 - 8.13 (m, 2H)

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 189.6, 164.4, 138.4, 131.3, 129.2, 128.8, 128.3, 127.2, 114.2, 55.6, 50.0, 46.7

**[Table 2.2, entry 5 Substrate]<sup>39</sup>**



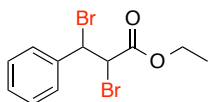
According to the general procedure, 1,3-Bis(4-methoxyphenyl)-2-propen-1-one (0.41 g, 1.53 mmol) and 3.10 mL of bromine solution (0.56 M in chloroform) afforded the desired product (0.43 g, 1.01 mmol, 66%) as pale yellow solid after column purification on silica gel.



$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 3.89 - 3.96 (m, 6 H) 5.55 - 5.65 (m, 1 H) 5.70 - 5.79 (m, 1 H) 6.88 - 6.96 (m, 2 H) 6.99 - 7.06 (m, 2 H) 7.43 (dd,  $J=8.5, 2.0$  Hz, 1 H) 7.74 (d,  $J=2.0$  Hz, 1 H) 8.03 - 8.14 (m, 2 H)

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 189.4, 164.5, 156.4, 133.1, 132.0, 131.4, 128.8, 127.0, 114.3, 112.0, 111.6, 56.3, 55.6, 49.0, 46.8

**[Table 2.2, entry 6 Substrate]<sup>40</sup>**

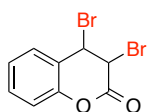


According to the general procedure, ethyl cinnamate (0.27 g, 1.53 mmol) and 3.10 mL of bromine solution (0.56 M in chloroform) afforded the desired product (0.43 g, 1.29 mmol, 84%) as white solid after column purification on silica gel.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 1.24 - 1.49 (m, 3 H) 4.37 (q,  $J=7.0$  Hz, 2 H) 4.85 (dd,  $J=12.0, 2.0$  Hz, 1 H) 5.36 (dd,  $J=12.0, 1.57$  Hz, 1 H) 7.29 - 7.55 (m, 5 H)

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 167.6, 137.5, 129.2, 128.8, 127.9, 62.5, 50.6, 46.9, 13.8

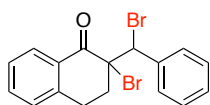
**[Table 2.2, entry 7 Substrate]<sup>41</sup>**



According to the general procedure, coumarin (0.22 g, 1.53 mmol) and 3.10 mL of bromine solution (0.56 M in chloroform) afforded the desired product (0.41 g, 1.35 mmol, 88%) as off-white solid after column purification on silica gel.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 4.94 (d,  $J=2.5$  Hz, 1 H) 5.33 (d,  $J=2.5$  Hz, 1 H) 7.04 - 7.32 (m, 2 H) 7.31 - 7.51 (m, 2 H)

**[Table 2.2, entry 8 Substrate]<sup>42</sup>**



According to the general procedure, 2-benzylidene-3,4-dihydro naphthalen-1(2H)-one (0.36 g, 1.53 mmol) and 3.10 mL of bromine solution (0.56 M in chloroform) afforded the desired product (0.49 g, 1.25 mmol, 82%) as off-white solid after column purification on silica gel.

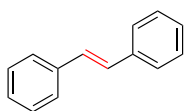
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 2.32 - 2.62 (m, 1 H) 2.83 - 3.35 (m, 3 H) 6.06 - 6.24 (m, 1 H) 7.18 - 7.71 (m, 8 H) 8.21 (dd,  $J=8.0, 1.0$  Hz, 1 H)

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 188.6, 142.4, 136.1, 134.2, 131.0, 131.0, 129.8, 129.3, 128.8, 128.6, 127.8, 127.2, 68.8, 55.3, 30.7, 26.1

**2.7.C. General Procedure for the Photocatalyzed Reductive Dehalogenations**

Substrate (0.3 mmol),  $\alpha$ -sexithiophene (1 mol%), and DMF (5 mL) were added to a 10 mL Schlenk tube. The reaction mixture was degassed with argon for 15 minutes, and TMEDA (90  $\mu$ L, 0.6 mmol) was added under argon. The reaction mixture was then irradiated for 1-3 hours. After irradiation the reaction was centrifuged (3000 rpm, 10 min) and the resulting supernatant was diluted in ether (25 mL), and washed with brine (4x, 25 mL). The organic layer was dried over anhydrous  $\text{MgSO}_4$  and concentrated using a rotovap. Purification of the crude was accomplished by PTLC (hexanes:ethylacetate). In all cases the *E/Z* ratio of the resulting alkenes were found to be > 10:1 through  $^1\text{H}$  NMR analysis.

**[Table 2, entry 1 Product]<sup>43</sup>**

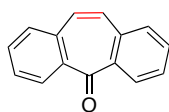


According to the general procedure, **1A** (0.102 g, 0.3 mmol),  $\alpha$ -sexithiophene (1 mol%), afforded **1B** (0.054 g, 0.3 mmol, >99%) as white solid after column purification on silica gel.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 7.11 (s, 2 H) 7.21 - 7.30 (m, 2 H) 7.36 (t,  $J=7.5$  Hz, 4 H) 7.52 (d,  $J=7.5$  Hz, 4 H)

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 137.3, 128.6, 128.6, 127.6, 126.5

**[Table 2, entry 2 Product]<sup>43</sup>**

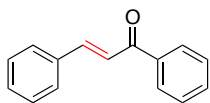


According to the general procedure, **2A** (0.110 g, 0.3 mmol),  $\alpha$ -sexithiophene (1 mol%), afforded **2B** (0.062 g, 0.3 mmol, >99%) as white solid after column purification on silica gel.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 7.06 (s, 2 H) 7.47 - 7.59 (m, 4 H) 7.59 - 7.68 (m, 2 H) 8.14 - 8.29 (m, 2 H)

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 195.3, 141.7, 138.4, 132.2, 130.3, 129.1, 126.4, 34.7

**[Table 2.2, entry 3 Product]<sup>43</sup>**

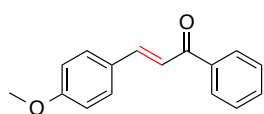


According to the general procedure, **3A** (0.110 g, 0.3 mmol),  $\alpha$ -sexithiophene (1 mol%), afforded **3B** (0.052 g, 0.25 mmol, 84%) as white solid after column purification on silica gel.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  ppm 7.37 - 7.70 (m, 9 H) 7.83 (d,  $J$ =15.5 Hz, 1 H) 8.00 - 8.10 (m, 2 H)

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  ppm 190.4, 144.7, 138.1, 134.8, 132.7, 130.4, 128.8, 128.5, 128.4, 128.3, 122.0

**[Table 2.2, entry 4 Product]<sup>44</sup>**

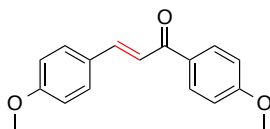


According to the general procedure, **4A** (0.120 g, 0.3 mmol),  $\alpha$ -sexithiophene (1 mol%), afforded **4B** (0.055 g, 0.23 mmol, 77%) as white solid after column purification on silica gel.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  ppm 3.90 (s, 3 H) 6.93 - 7.10 (m, 2 H) 7.36 - 7.47 (m, 3 H) 7.56 (d,  $J$ =15.68 Hz, 1 H) 7.63 - 7.73 (m, 2 H) 7.82 (d,  $J$ =15.48 Hz, 1 H) 7.97 - 8.13 (m, 2 H)

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  ppm 188.5, 163.3, 143.8, 135.0, 131.0, 130.7, 130.2, 128.8, 128.3, 121.8, 113.7, 55.4

**[Table 2.2, entry 5 Product]<sup>45</sup>**

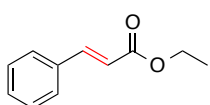


According to the general procedure, **5A** (0.128 g, 0.3 mmol),  $\alpha$ -sexithiophene (1 mol%), afforded **5B** (0.064 g, 0.24 mmol, 79%) as yellow solid after column purification on silica gel.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  ppm 3.88 (d,  $J$ =13.0 Hz, 6 H) 6.78 - 7.05 (m, 4 H) 7.44 (d,  $J$ =15.5 Hz, 1 H) 7.56 - 7.66 (m, 2 H) 7.79 (d,  $J$ =15.5 Hz, 1 H) 8.00 - 8.09 (m, 2 H)

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  ppm 188.6, 163.2, 161.4, 143.7, 131.3, 130.6, 130.0, 130.0, 127.7, 119.4, 114.3, 114.3, 113.7, 55.4, 55.3

**[Table 2.2, entry 6 Product]<sup>43</sup>**

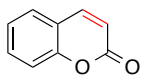


According to the general procedure, **6A** (0.101 g, 0.3 mmol),  $\alpha$ -sexithiophene (1 mol%), afforded **6B** (0.036 g, 0.20 mmol, 68%) as colourless oil after column purification on silica gel.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 1.35 (t,  $J=7.0$  Hz, 3 H) 4.27 (q,  $J=7.0$  Hz, 2 H) 6.45 (d,  $J=16.0$  Hz, 1 H) 7.27 - 7.42 (m, 3 H) 7.48 - 7.57 (m, 2 H) 7.70 (d,  $J=16.0$  Hz, 1 H)

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 166.8, 144.4, 134.4, 130.1, 128.8, 127.9, 118.2, 60.3, 14.2

**[Table 2.2, entry 7 Product]<sup>46</sup>**

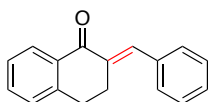


According to the general procedure, **7A** (0.092 g, 0.3 mmol),  $\alpha$ -sexithiophene (1 mol%), afforded **7B** (0.038 g, 0.26 mmol, 88%) as white solid after column purification on silica gel.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 6.40 (d,  $J=9.5$  Hz, 1 H) 7.20 - 7.36 (m, 2 H) 7.41 - 7.56 (m, 2 H) 7.69 (d,  $J=9.5$  Hz, 1 H)

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 160.5, 153.8, 143.3, 131.6, 127.7, 124.2, 118.6, 116.5, 116.3, 77.3

**[Table 2.2, entry 8 Product]<sup>47</sup>**

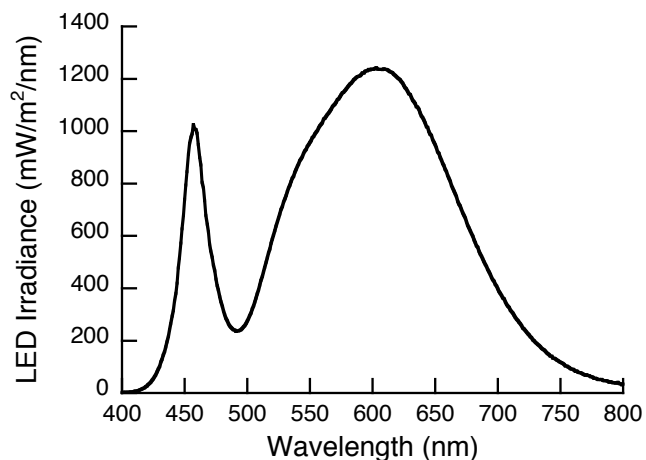


According to the general procedure, **8A** (0.118 g, 0.3 mmol),  $\alpha$ -sexithiophene (1 mol%), afforded **8B** (0.046 g, 0.20 mmol, 65%) as white solid after column purification on silica gel.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 2.85 - 3.04 (m, 2 H) 3.01 - 3.42 (m, 2 H) 7.08 - 7.59 (m, 8 H) 7.86 (s, 1 H) 8.12 (dd,  $J=8.0, 1.0$  Hz, 1 H)

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 187.7, 143.1, 136.5, 135.7, 135.4, 133.4, 133.2, 129.8, 128.4, 128.3, 128.1, 126.9, 28.7, 27.1

### 2.7.D. Output Spectrum of Warm White LEDs

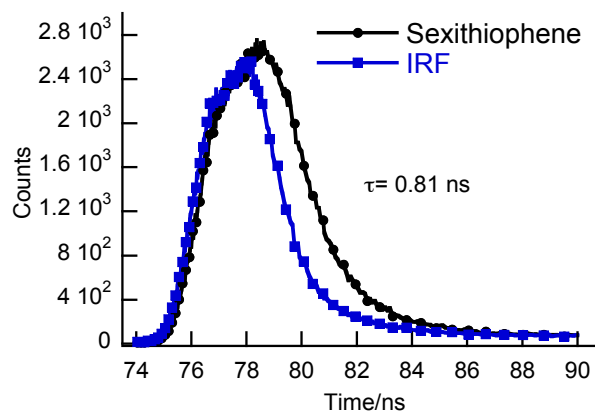


**Figure 2A.1.** Output spectrum of warm white LEDs used for irradiation of reaction mixtures.

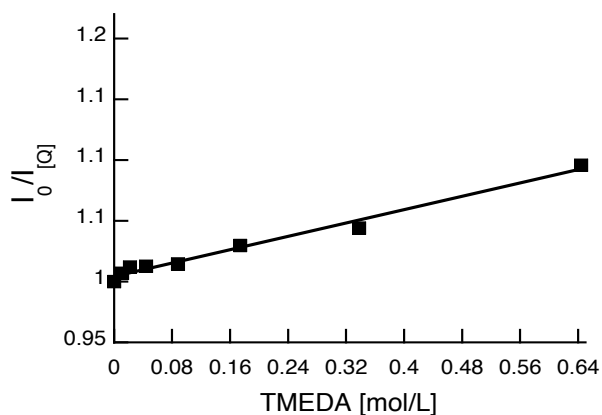
### 2.7.E. Steady-State and Time-Resolved Fluorescence Data

#### Quenching of singlet $\alpha$ -Sexithiophene:

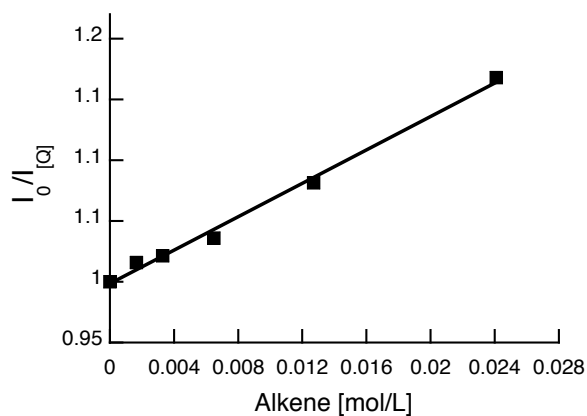
The fluorescence emission measurements required for the singlet quenching experiments of  $\alpha$ -6T were carried out in a Photon Technology International (PTI) QuantaMater spectrofluorimeter (bandwidth = 2 nm, excitation slits = 2 nm, emission slits = 2 nm) at room temperature using 1x1 cm quartz cuvettes. The fluorescence lifetime was measured in an Easy-Life (PTI) system using a 440 nm LED pulse excitation after which the lifetime was calculated using the integrated Easy-Life software. Samples of  $\alpha$ -6T were prepared in DMF with a final absorbance of  $\sim 0.1$  at 440 nm. The substrates used in the quenching studies were also prepared in this solution to ensure that the observed quenching is not due to dilution of the fluorophore



**Figure 2A.2.** Fluorescence lifetime of  $\alpha$ -6T in DMF. Measured at 510 nm upon 440 nm pulsed LED excitation. IRF trace corresponds to the instrument response function.



**Figure 2A.3.** Quenching of the  $\alpha$ -6T singlet by TMEDA. Stern-Volmer constant corresponds to the slope of this plot.

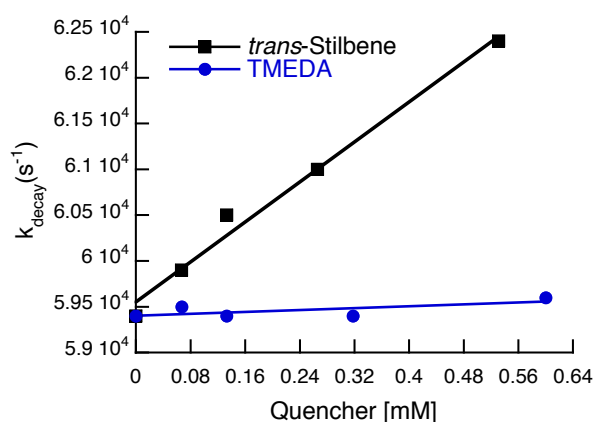


**Figure 2A.4.** Quenching of the  $\alpha$ -6T singlet by the alkene product. Stern-Volmer constant corresponds to the slope of this plot.

## 2.7.F. Laser Flash Photolysis Data

### Quenching of triplet $\alpha$ -Sexithiophene:

The triplet quenching experiments of  $\alpha$ -6T were performed using a Q-switched Nd:YAG-laser (355 nm, 10 mJ/pulse) in a LFP-111 laser-flash photolysis (LFP) system (Luzchem Research Inc., Ottawa, Canada) and 1×1 cm LFP-Luzchem cuvettes. Samples of  $\alpha$ -6T were prepared in DMF with a total volume of 3 mL and an absorbance of  $\sim 0.1$  at 355 nm. The samples were degassed with  $N_2$  for 30 minutes prior to use. The substrates used in the quenching studies were also prepared in DMF and degassed for the duration of the experiment.



**Figure 2A.5.** Quenching of the  $\alpha$ -6T triplet by *trans*-Stilbene and TMEDA. The bimolecular rate constant corresponds to the slope of this plot.

### Quenching of $\alpha$ -Sexithiophene radical cation:

The quenching experiments of the  $\alpha$ -6T radical cation were performed using a Q-switched Nd:YAG-laser (355 nm, 10 mJ/pulse) in a LFP-111 laser-flash photolysis (LFP) system (Luzchem Research Inc., Ottawa, Canada) and 1×1 cm LFP-Luzchem cuvettes. Samples of  $\alpha$ -6T containing 4 mM  $MV^{2+}$  (methyl viologen dichloride) were prepared in DMF with a total volume of 3mL and an absorbance

of  $\sim 0.1$  at 355 nm. The samples were degassed with  $N_2$  for 30 minutes prior to use. Upon excitation  $\alpha$ -6T donates an  $e^-$  to  $MV^{2+}$ , resulting in the production of  $MV^{+\bullet}$  and  $\alpha$ -6T $^{+\bullet}$ . Though  $MV^{+\bullet}$  has a strong absorption centered around 600 nm this does not overlap with the  $\alpha$ -6T $^{+\bullet}$  signal, which is found at 780 nm. By monitoring the decay rate of the signal at 780 nm in the presence of increasing concentrations of TMEDA we can determine the rate at which TMEDA turns over the catalyst.

Reactivity of TMEDA derived  $\alpha$ -aminoalkyl radicals with model vic-Br $_2$ :

The reactivity of TMEDA derived  $\alpha$ -aminoalkyl radicals with the model vic-Br $_2$  were performed using a Q-switched Nd:YAG-laser (355 nm, 10 mJ/pulse) in a LFP-111 laser-flash photolysis (LFP) system (Luzchem Inc., Ottawa, Canada) and 1×1 cm LFP-Luzchem cuvettes. Samples containing a constant concentration of TMEDA, 20% di-*tert*-butyl peroxide (v/v), and 4 mM  $MV^{2+}$  (methyl viologen dichloride) were prepared in MeCN:H $_2$ O (9:1). The water is required to solubilize the  $MV^{2+}$ . The samples were degassed with  $N_2$  for 30 minutes prior to use. At the concentrations employed, generation of the  $\alpha$ -aminoalkyl radicals can be considered almost instantaneous therefore greatly simplifying the kinetic analysis. Once formed the  $\alpha$ -aminoalkyl radicals will reduce the  $MV^{2+}$  to  $MV^{+\bullet}$  a process, which can be followed through the growth of a signal at 600 nm. By measuring the growth rate of the  $MV^{+\bullet}$  signal at 600 nm in the presence of increasing concentrations of vic-Br $_2$  one can measure the rate at which the TMEDA derived  $\alpha$ -aminoalkyl radicals react with the vic-Br $_2$ .



## 2.7.G. NMR Data

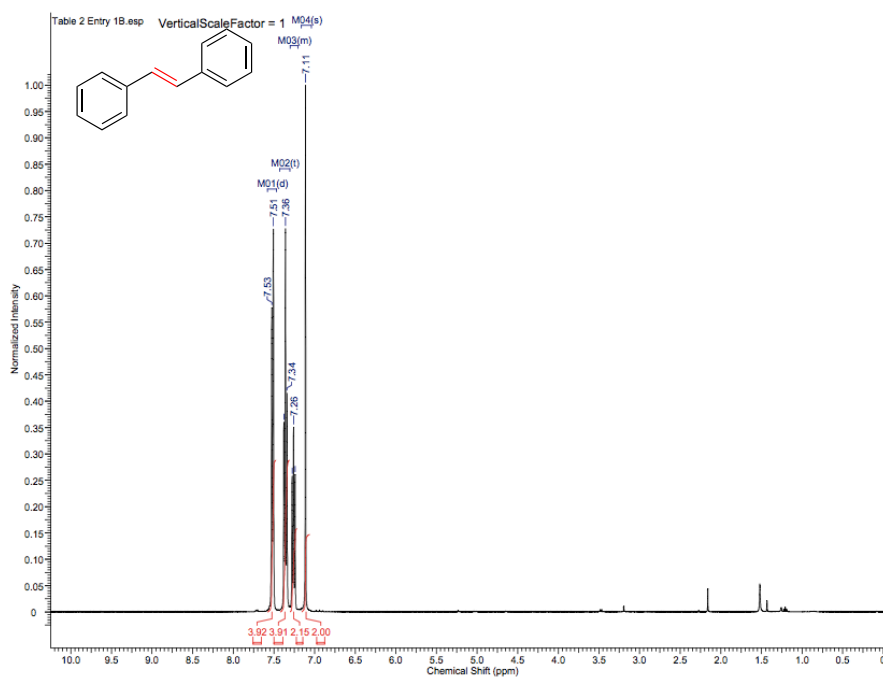


Figure 2A.6.  $^1\text{H}$  NMR of **1 Product** in  $\text{CDCl}_3$ .



Figure 2A.7.  $^{13}\text{C}$  NMR of **1 Product** in  $\text{CDCl}_3$ .

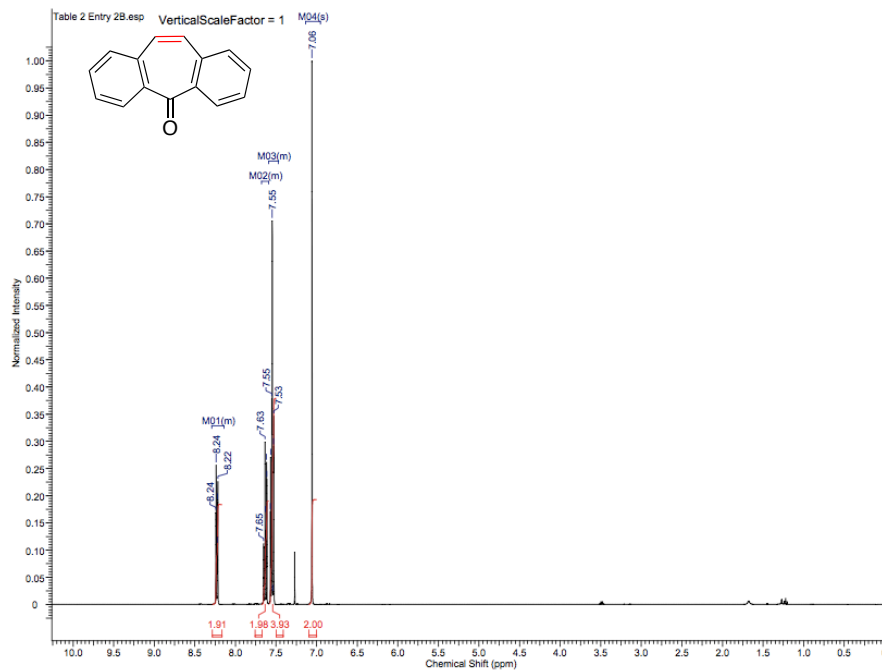


Figure 2A.8.  $^1\text{H}$  NMR of **2 Product** in  $\text{CDCl}_3$ .

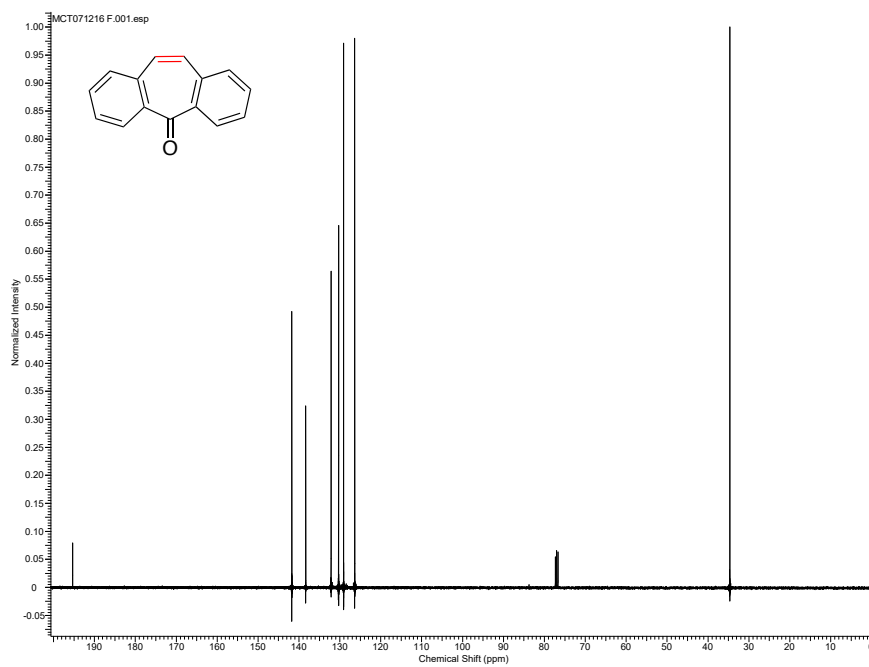


Figure 2A.9.  $^{13}\text{C}$  NMR of **2 Product** in  $\text{CDCl}_3$ .

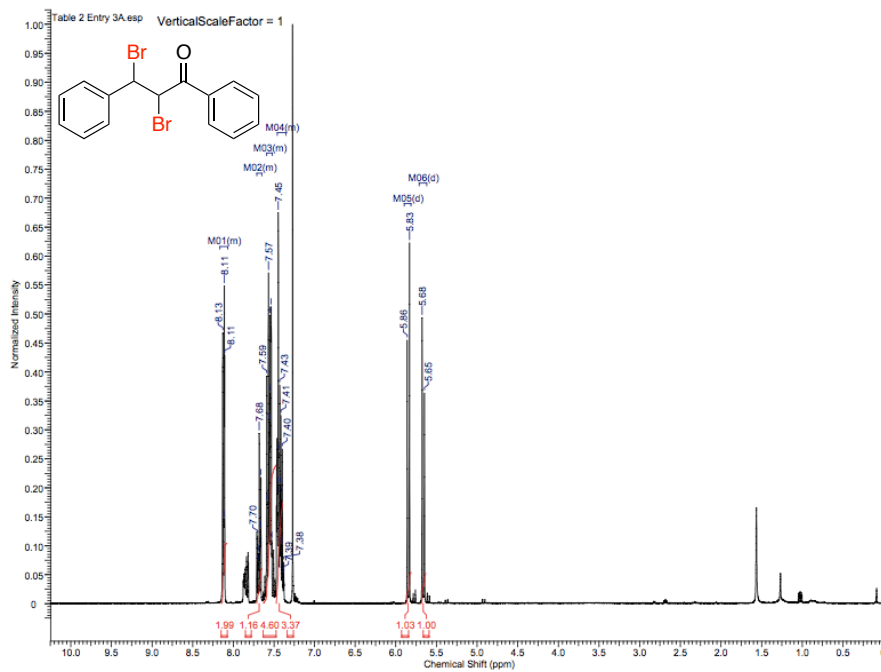


Figure 2A.10.  $^1\text{H}$  NMR of **3 Substrate** in  $\text{CDCl}_3$ .

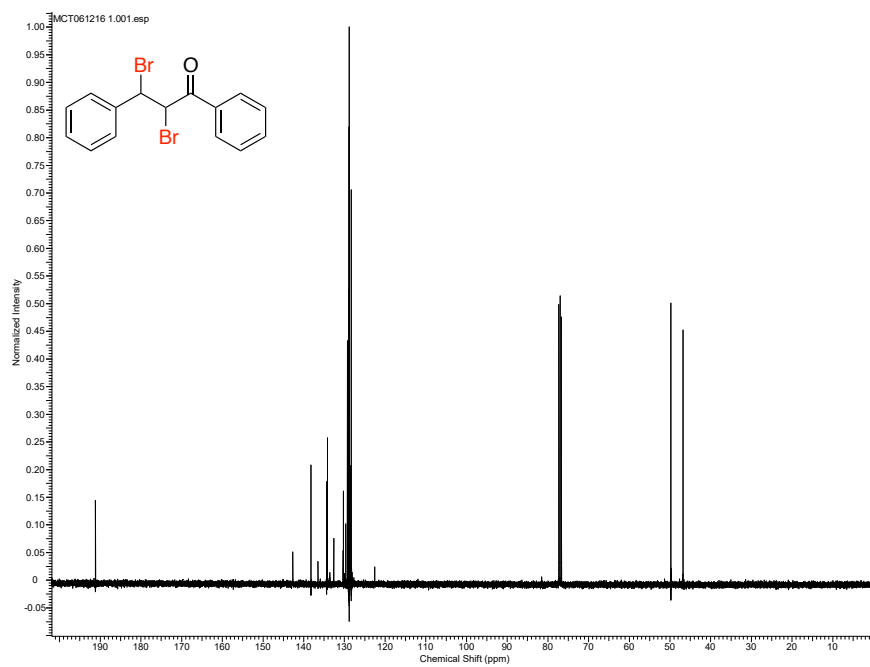
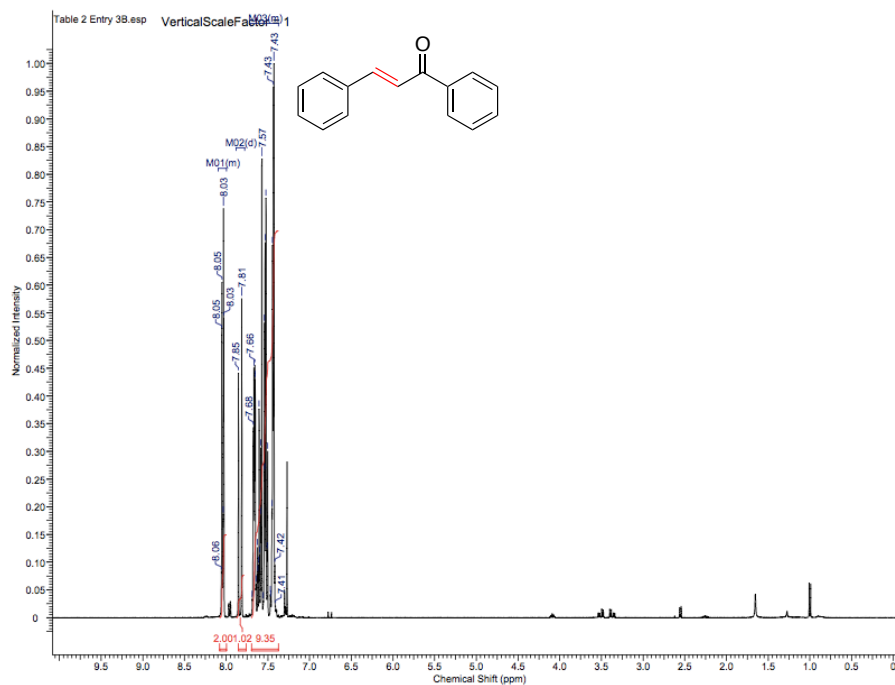
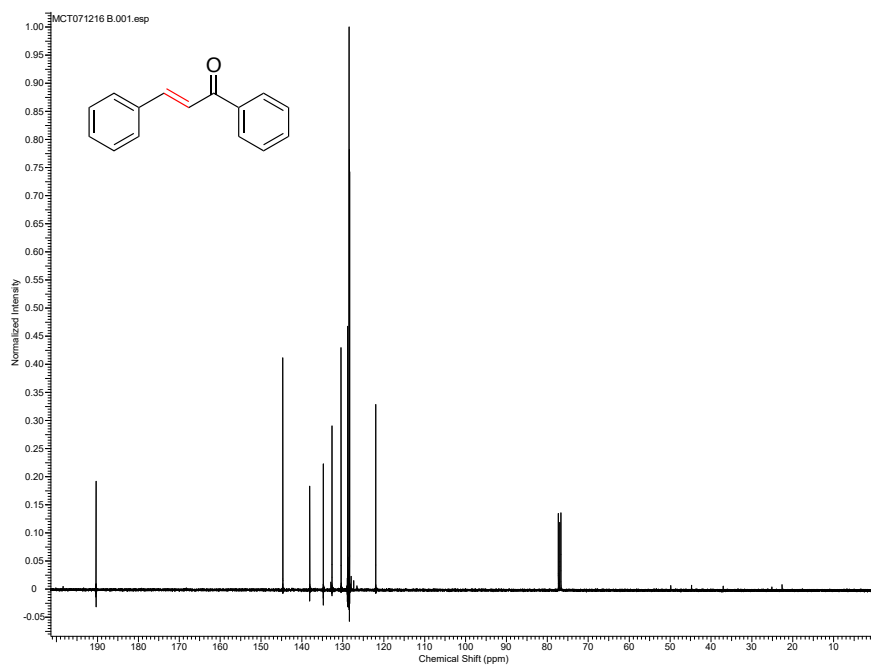


Figure 2A.11.  $^{13}\text{C}$  NMR of **3 Substrate** in  $\text{CDCl}_3$ .



**Figure 2A.12.**  $^1\text{H}$  NMR of **3 Product** in  $\text{CDCl}_3$ .



**Figure 2A.13.**  $^{13}\text{C}$  NMR of **3 Product** in  $\text{CDCl}_3$ .

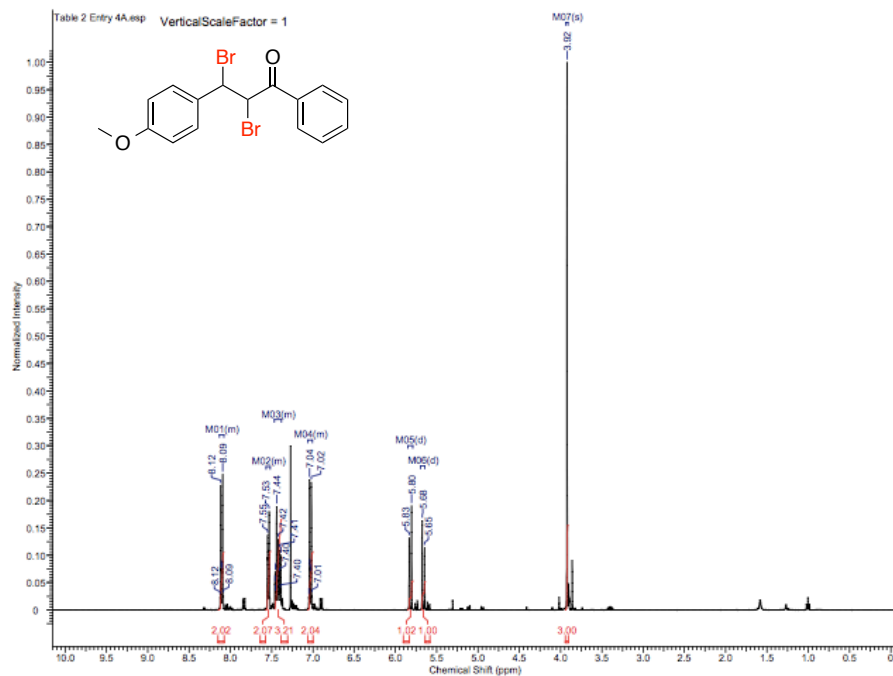


Figure 2A.14.  $^1\text{H}$  NMR of **4 Substrate** in  $\text{CDCl}_3$ .

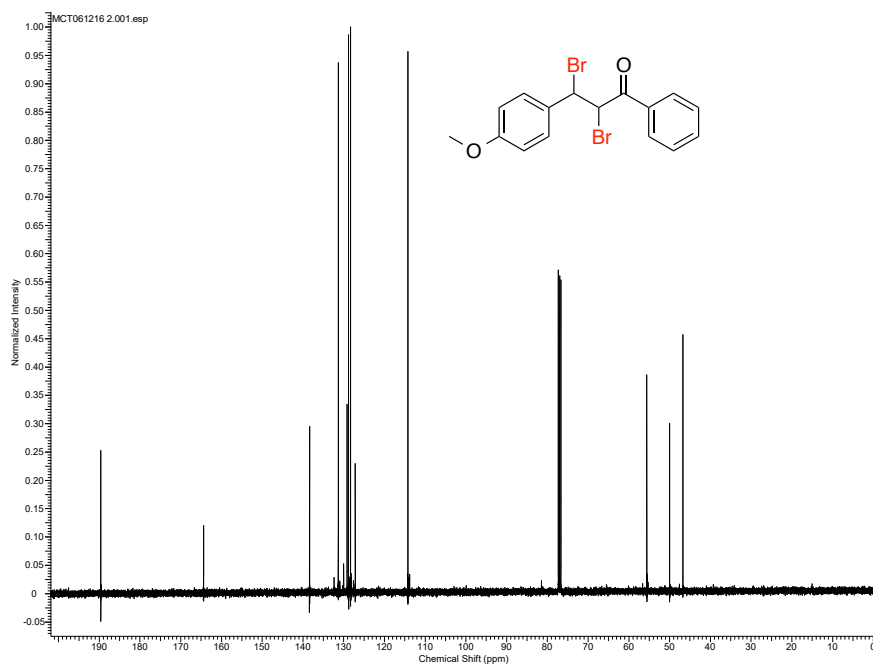


Figure 2A.15.  $^{13}\text{C}$  NMR of **4 Substrate** in  $\text{CDCl}_3$ .

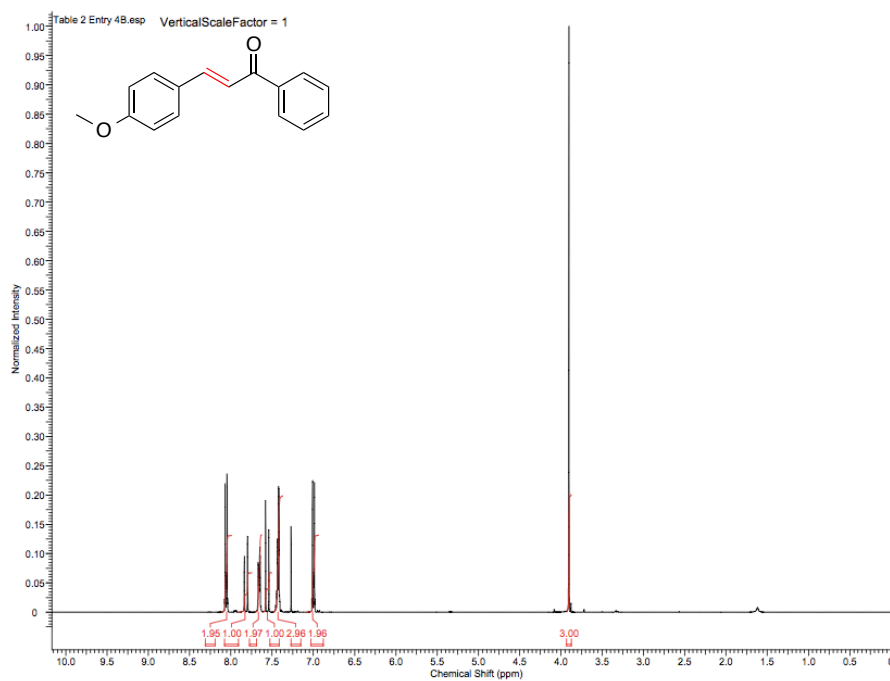


Figure 2A.16.  $^1\text{H}$  NMR of **4 Product** in  $\text{CDCl}_3$ .

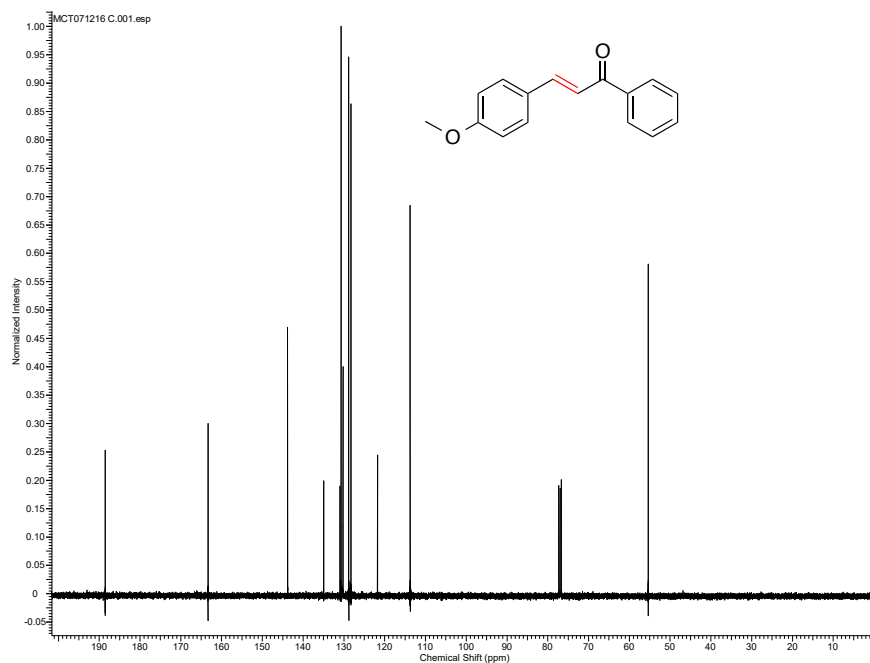


Figure 2A.17.  $^{13}\text{C}$  NMR of **4 Product** in  $\text{CDCl}_3$ .

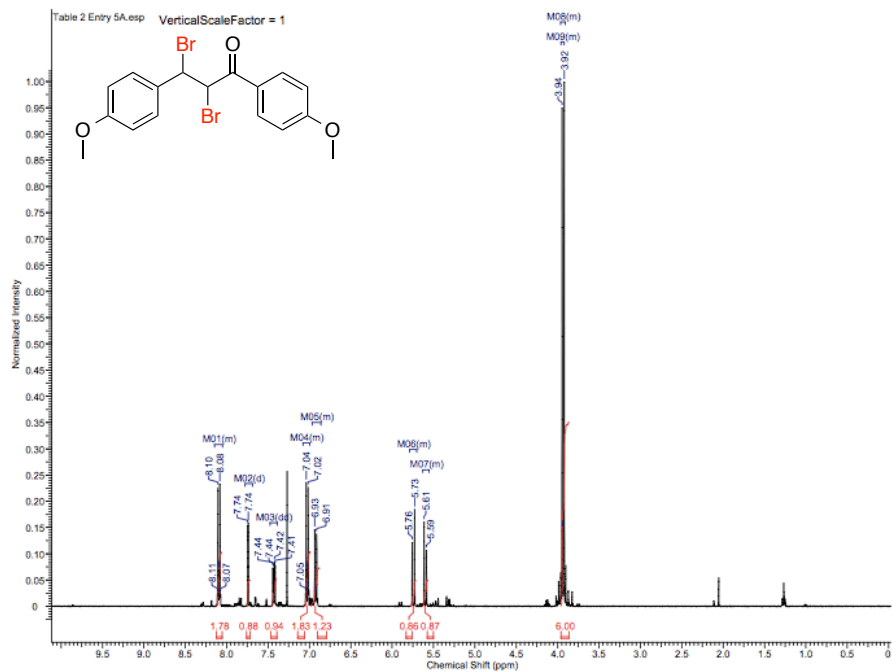


Figure 2A.18.  $^1\text{H}$  NMR of 5 Substrate in  $\text{CDCl}_3$ .

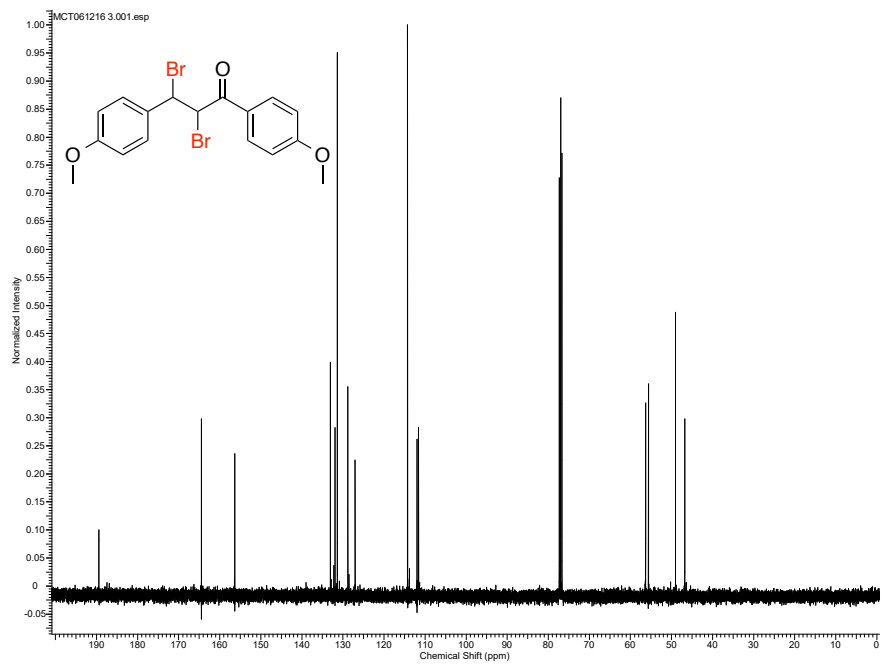


Figure 2A.19.  $^{13}\text{C}$  NMR of 5 Substrate in  $\text{CDCl}_3$ .

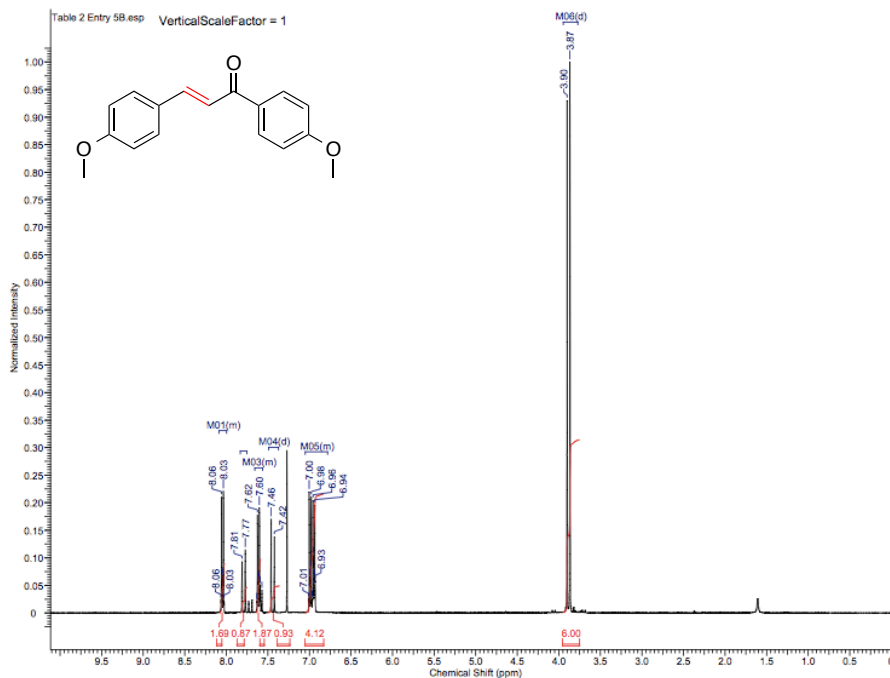


Figure 2A.20.  $^1\text{H}$  NMR of **5 Product** in  $\text{CDCl}_3$ .



Figure 2A.21.  $^{13}\text{C}$  NMR of **5 Product** in  $\text{CDCl}_3$ .



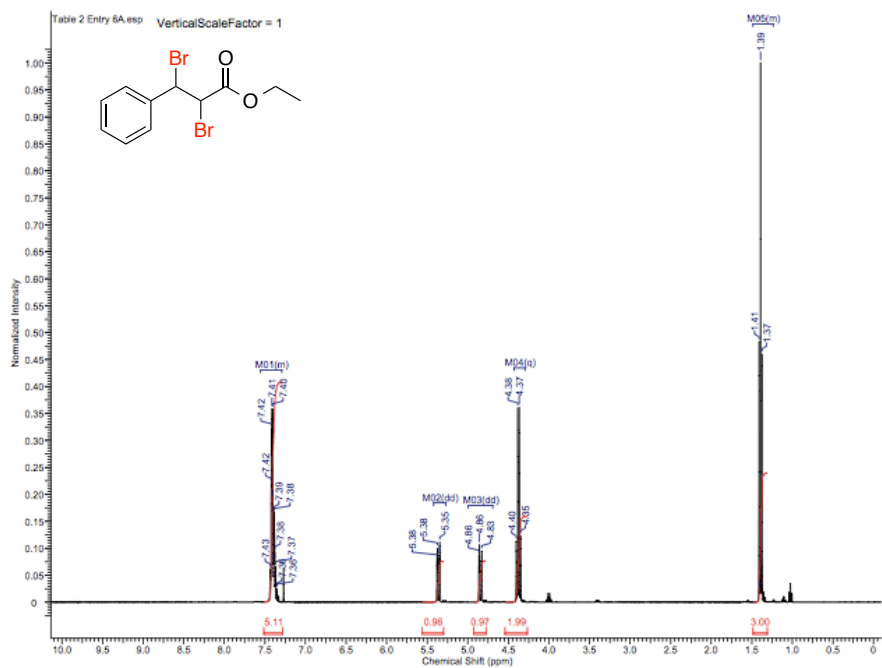


Figure 2A.22. <sup>1</sup>H NMR of **6 Substrate** in CDCl<sub>3</sub>.

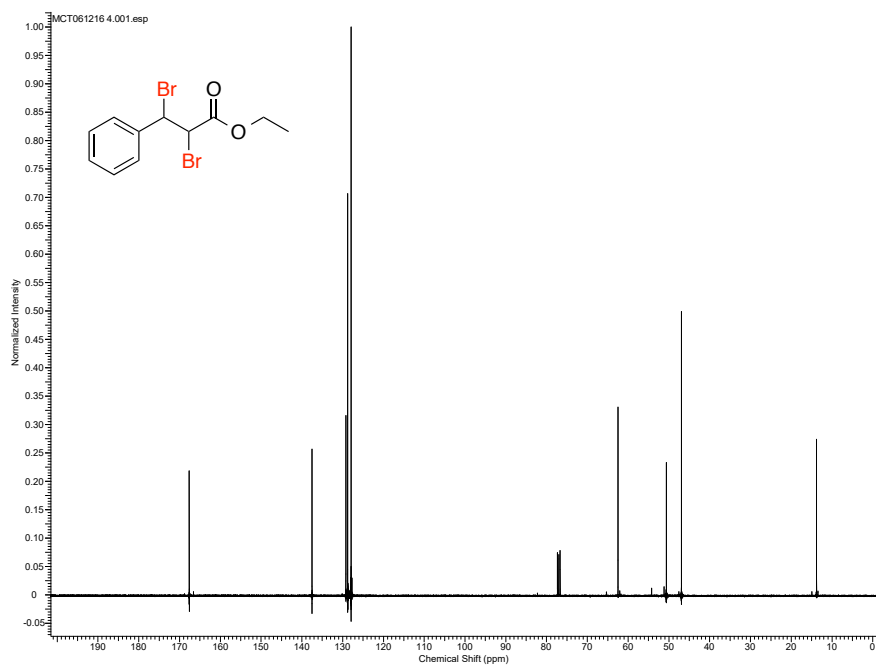


Figure 2A.23. <sup>13</sup>C NMR of **6 Substrate** in CDCl<sub>3</sub>.

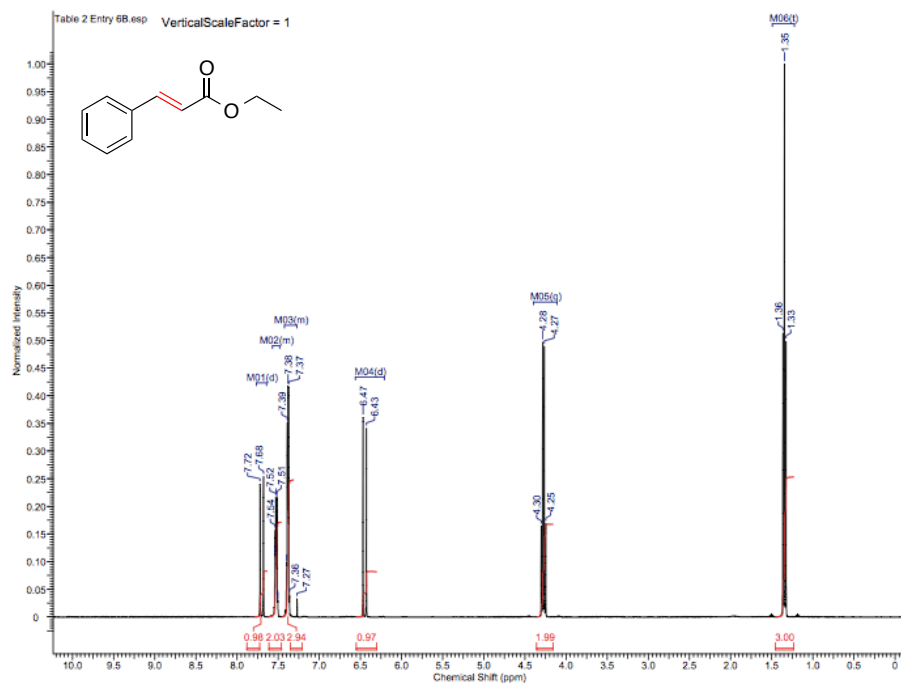


Figure 2A.24.  $^1\text{H}$  NMR of **6 Product** in  $\text{CDCl}_3$ .

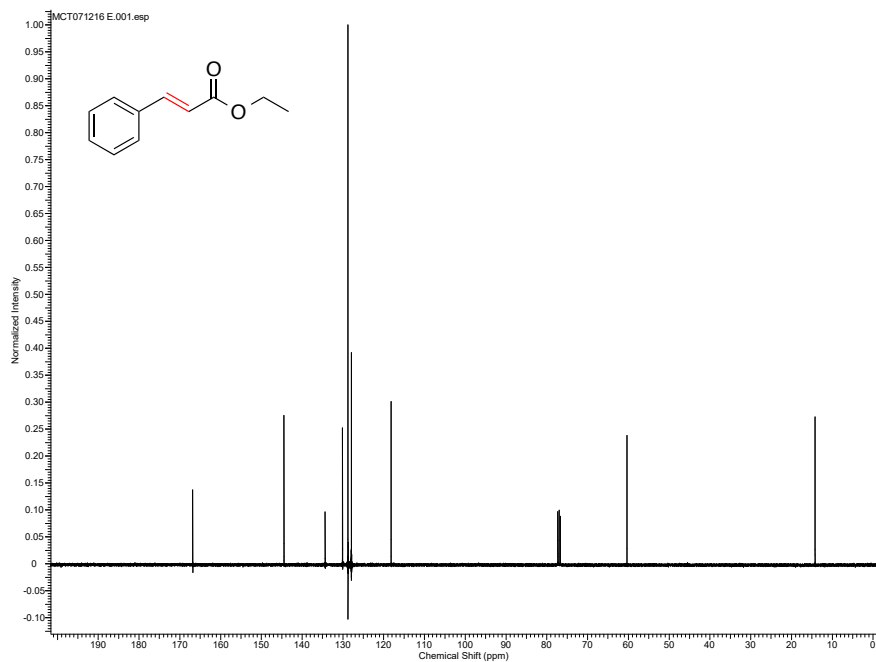


Figure 2A.25.  $^{13}\text{C}$  NMR of **6 Product** in  $\text{CDCl}_3$ .

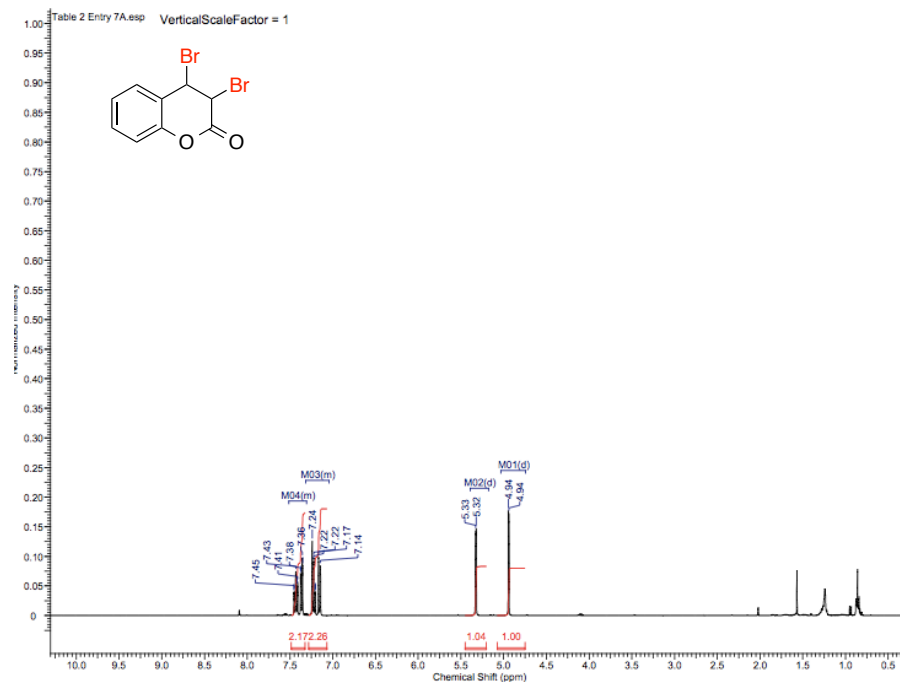


Figure 2A.26.  $^1\text{H}$  NMR of **7 Substrate** in  $\text{CDCl}_3$ .

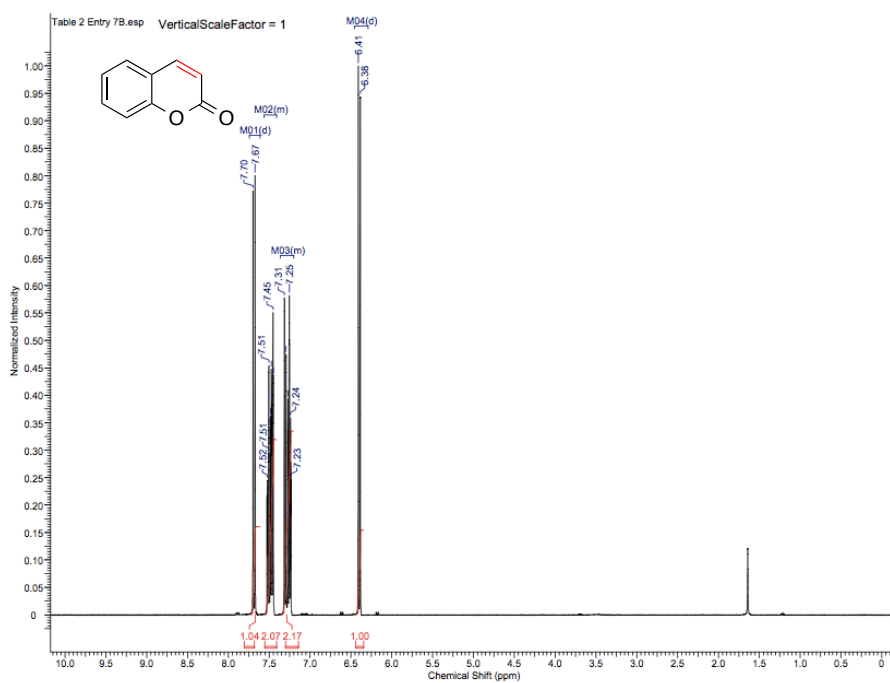


Figure 2A.27.  $^1\text{H}$  NMR of **7 Product** in  $\text{CDCl}_3$ .

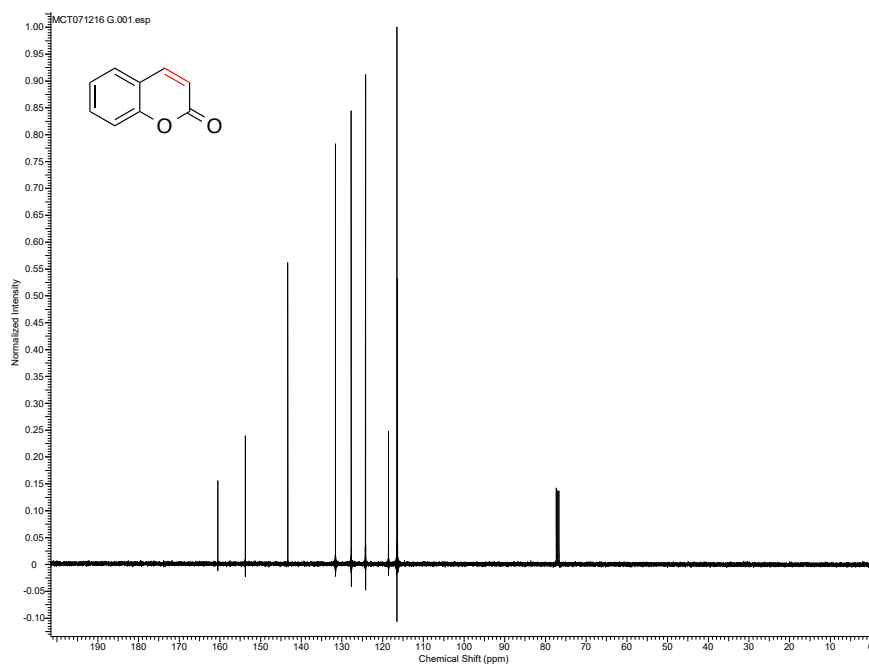


Figure 2A.28.  $^{13}\text{C}$  NMR of 7 Product in  $\text{CDCl}_3$ .

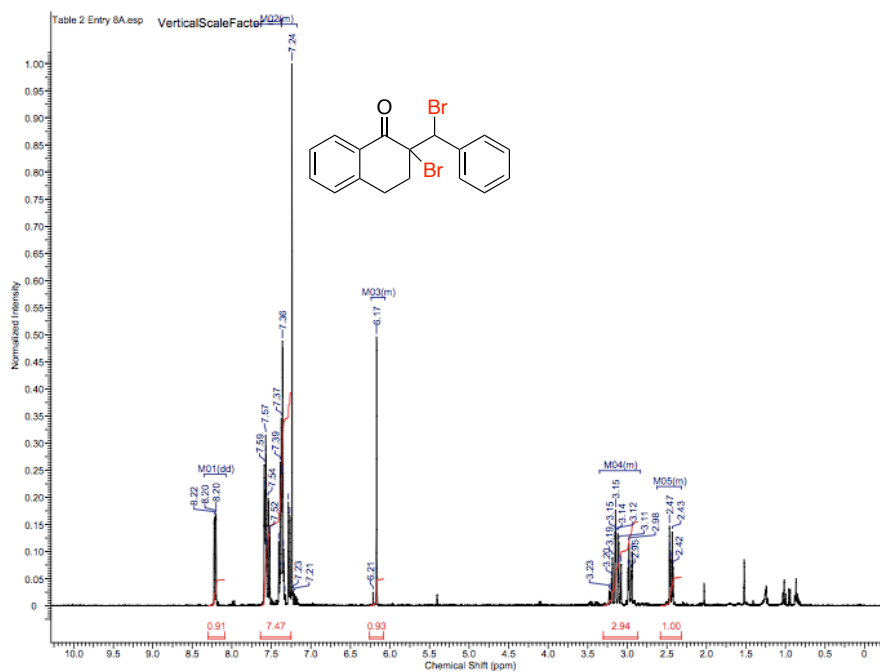


Figure 2A.29.  $^1\text{H}$  NMR of 8 Substrate in  $\text{CDCl}_3$ .



Figure 2A.30.  $^{13}\text{C}$  NMR of **8 Substrate** in  $\text{CDCl}_3$ .

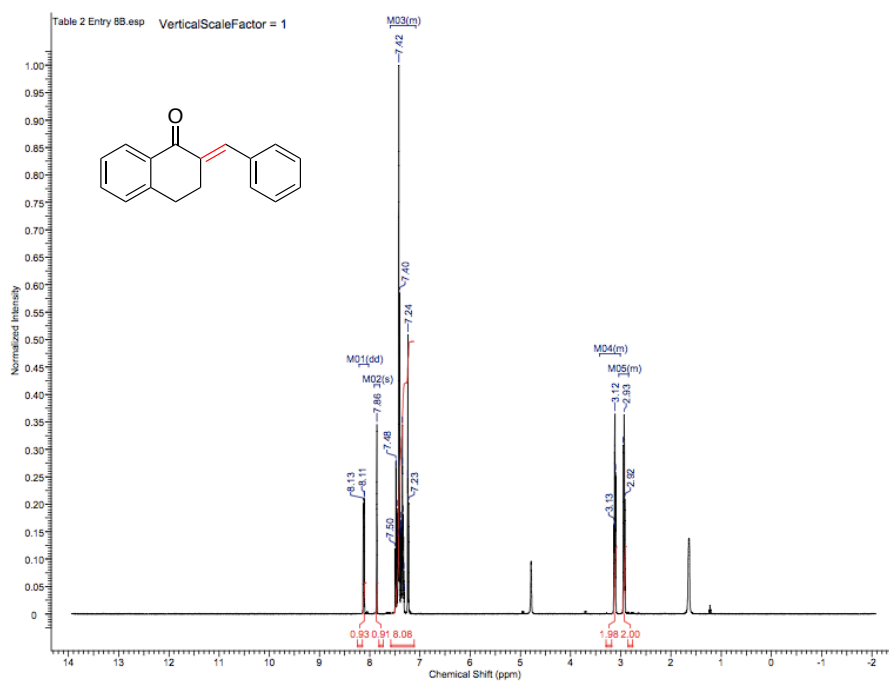


Figure 2A.31.  $^1\text{H}$  NMR of **8 Product** in  $\text{CDCl}_3$ .

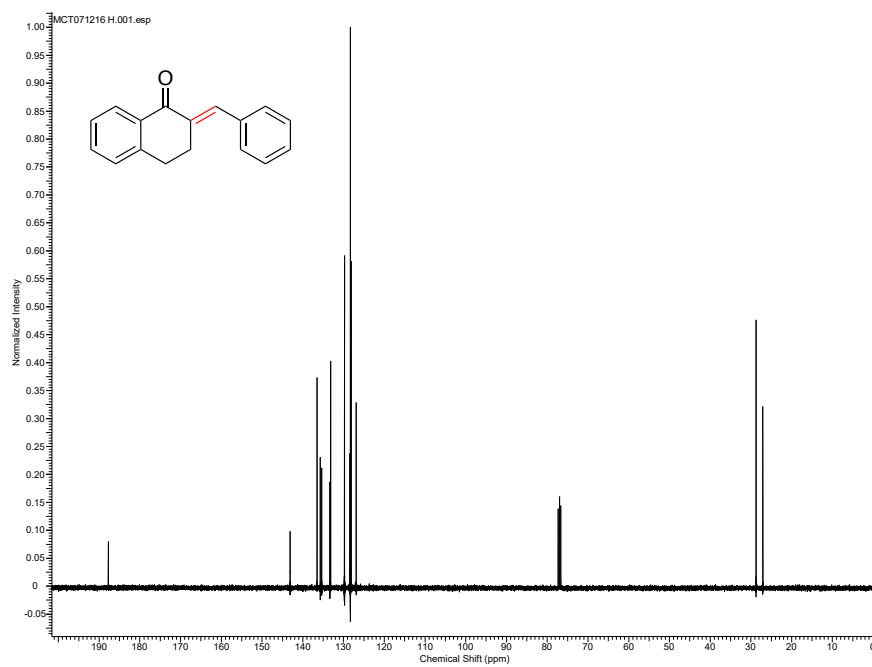


Figure 2A.32.  $^{13}\text{C}$  NMR of **8 Product** in  $\text{CDCl}_3$ .

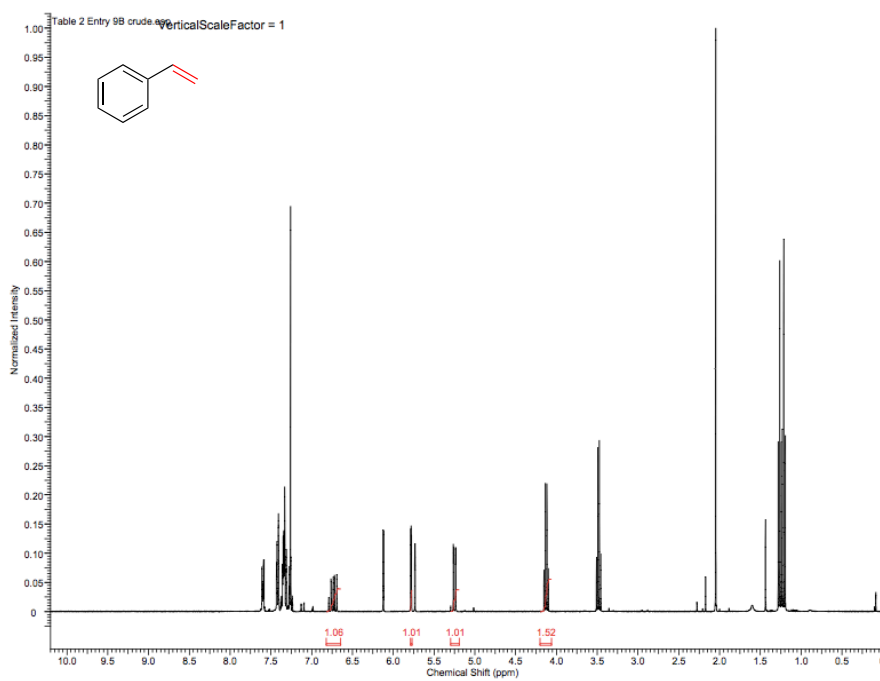


Figure 2A.33.  $^1\text{H}$  NMR of the crude reaction mixture for **9** in  $\text{CDCl}_3$ .

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### 3. Sexithiophene as $^1\text{O}_2$ Photosensitizer

#### Photocatalytic Oxidation of Amines Utilizing Sexithiophene and Visible Light Irradiation

##### 3.1. Background

In the previous chapter, we discussed the use of  $\alpha$ -sexithiophene ( $\alpha$ -6T) as photocatalyst in the light mediated reductive dehalogenation of *vic*-dibromides to their corresponding alkenes. Through exploitation of the relatively long-lived triplet of  $\alpha$ -6T (approx. 16  $\mu\text{s}$ ) and its propensity for excited state electron transfer, we were able to photocatalytically reduce a variety of *vic*-dibromides. With this being said, we also demonstrated that the triplet of  $\alpha$ -6T is readily quenched by oxygen at a rate of  $3.0 \times 10^9 \text{ M}^{-1}\text{s}^{-1}$  and as such the presence of oxygen will in most instances lead to drastically reduced reaction efficiencies when neither oxygen nor its corresponding reactive intermediates are involved in bringing about the desired transformation. For this reason, in many photoredox transformations, oxygen is excluded from the reaction mixture. However, the properties which make molecules ideal visible light photoredox catalysts, such as strong visible light absorption, long-lived triplet excited state, and high triplet energy; are typically the properties one looks for in visible light singlet oxygen ( $^1\text{O}_2$ ) sensitizers. In general as long as the triplet energy of the photosensitizer is above 22 kcal/mol it can excite triplet ground state oxygen to its corresponding singlet through an excited state energy transfer process.<sup>25</sup> When combined with the fact that  $^1\text{O}_2$  is a better oxidant ( $E_{\text{red}}^{1/2} [^1\text{O}_2/\text{O}_2^{\cdot-}] = 0.34 \text{ V vs. SCE in DMF}$  or  $0.79 \text{ V vs. SCE in H}_2\text{O}$ )<sup>48</sup> than ground state oxygen, it becomes apparent why

there has been a recent interest in employing  $^1\text{O}_2$  as the terminal oxidant in a variety of transformations.<sup>49</sup>

Interestingly, it has been previously shown that oligothiophenes are potent sensitizers of singlet oxygen, and that the pesticidal nature of many naturally occurring bithienyl and terthienyl analogues are due to this property.<sup>50</sup> As such, we set out to explore the use of  $\alpha$ -sexithiophene as heterogeneous photosensitizer of  $^1\text{O}_2$ . In order to evaluate its suitability for such a role, we have decided to employ it as photocatalyst in the oxidation of amines to imines.

Imines, commonly referred to as Schiff bases, can be important intermediates in the synthesis of fine chemicals, pharmaceuticals, and other biologically active compounds.<sup>51</sup> They are traditionally synthesized through condensation of amines with aldehydes or ketones in the presence of Lewis acid catalysts and dehydrating agents.<sup>51</sup> Those derived from aldehydes are referred to as aldimines, while those from ketones are called ketimines. Due to their importance, there has been a push to develop alternative strategies for their synthesis. One of these pathways involves the cross-coupling of alcohols with amines. While this strategy is capable of generating a variety of different symmetrically and unsymmetrically substituted imines from readily available starting materials, with water being one of the only by-products, it tends to be limited by challenges relating to the selective oxidation of alcohols into their corresponding aldehyde intermediate.<sup>52</sup> The other strategies have focused on the oxidative dehydrogenation of both primary and secondary amines.<sup>53</sup> It should be noted that while it may be possible to obtain hetero-coupled product through the

coupling of primary amines, this route tends to be lower yielding due to the intrinsic propensity of the amine coupling partners to self-couple.<sup>51</sup>

While all three of these methods show promise, in this chapter, we will focus solely on the generation of imines through the oxidation of both primary and secondary amines via photocatalytic methods. Over the last few years there have been a variety of different homogeneous and heterogeneous photocatalytic systems developed for imine formation based on the oxidation of amines. For the most part the heterogeneous systems have employed inorganic semiconductors such as  $\text{TiO}_2$ ,<sup>54,55</sup>  $\text{Nb}_2\text{O}_5$ ,<sup>56</sup>  $\text{CdS}$ ,<sup>57</sup>  $\text{ZnIn}_2\text{S}$ ,<sup>58</sup> and  $\text{BiVO}_4$ <sup>59</sup> as visible-light photocatalyst, giving rise to the corresponding self-coupled imine through a radical type pathway initiated through the direct oxidation of the amine by the excited photocatalyst. While many of the previously listed inorganic semiconductors are capable of excitation with visible-light, both  $\text{TiO}_2$  and  $\text{Nb}_2\text{O}_5$  are not typically considered visible light absorbers due to their relatively large band gap and the fact that their absorbance only tails into the visible portion of the electromagnetic spectrum. Interestingly, there are reports of both of these materials being used in visible-light promoted amine couplings.<sup>56,60</sup> Considering that one must absorb light to perform photochemistry, what they have proposed is that upon adsorption of the amine to the surface of these materials a colored charge-transfer complex is formed which can be used as an antenna allowing the system to absorb visible light. In addition to this, it also been demonstrated that decoration of  $\text{TiO}_2$  with plasmonic metal nanoparticles of Au, Ag, and Cu can be used to extend the absorption of the catalytic system into the visible region.<sup>61-63</sup>

While all three metals can bring about the desired coupling, Cu is the least efficient of the metals. This can be related back to the fact that of the three metals Cu is the most easily oxidized in the presence of oxygen. Interestingly Cu nanoparticles deposited on graphene have shown excellent activity and reuseability in the light mediated coupling of primary amines, which is likely related to graphene's ability to inhibit surface oxidation of the Cu nanoparticles.<sup>63</sup> Lastly, it has also been demonstrated that mesoporous graphitic carbon nitride can be used as a heterogeneous photocatalyst in these transformations.<sup>64</sup> While this material displays good activity and selectivity for the oxidation of both primary and secondary amines, it does require relatively high temperatures and pressures of oxygen to make the reaction proceed efficiently.<sup>64</sup>

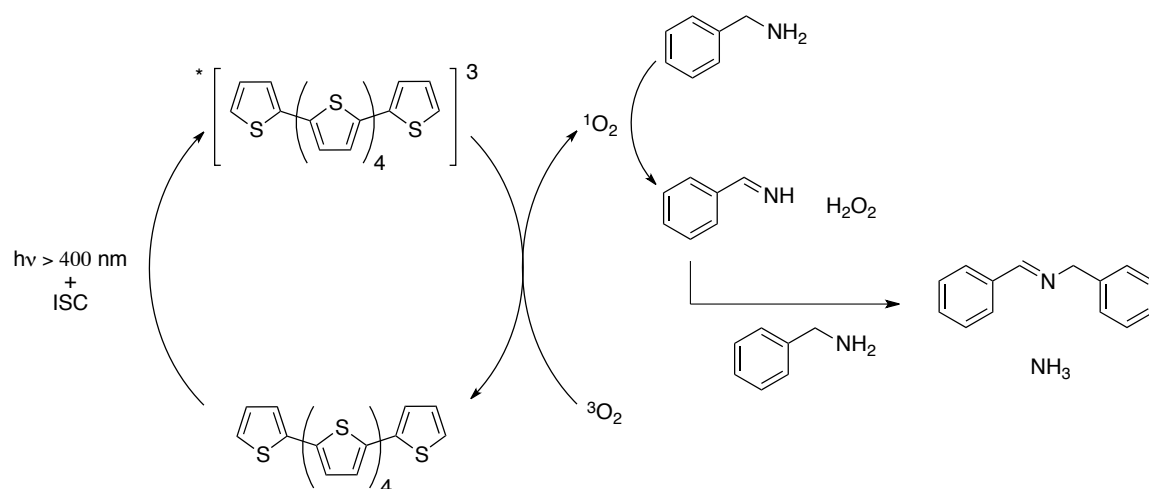
While the previous heterogeneous examples bring about the oxidation of amines through a direct electron transfer between the amine and the photocatalyst, it has been suggested that most examples employing homogeneous photocatalysts bring about the desired transformation via a singlet oxygen ( $^1\text{O}_2$ ) mediated pathway. For example both tetraphenylporphyrin and tetrapropylporphycene have been shown capable of oxidizing both primary and secondary amines to their corresponding imines through the sensitization of  $^1\text{O}_2$  from ground state triplet oxygen.<sup>65,66</sup> While both catalytic systems showed high reactivity for both electron rich primary and secondary amines, it was found that longer irradiation times or the presence of water in the system would yield high quantities of aldehyde as side-product.<sup>66</sup> Interestingly, when employing porphycene as photocatalyst it is possible to switch from the  $^1\text{O}_2$  mediated

pathway to the radical pathway by simply complexing the porphycene with tin(IV).<sup>66</sup> Through complexation of the porphycene with tin(IV) the redox properties of the catalyst are modified such that excited state electron transfer from the amine to the photocatalyst becomes more energetically favourable (exergonic) and thus outcompetes the sensitization of  $^1\text{O}_2$ .

More recently, it has been demonstrated that both derivatives of Bodipy<sup>67</sup> and phenothiazine<sup>68</sup> dyes can be used as singlet oxygen photosensitizer for the selective and efficient oxidation of both primary and secondary amines. While both dyes have long-lived triplet excited states which are efficiently quenched by  $^3\text{O}_2$  to generate  $^1\text{O}_2$  through a triplet-triplet energy transfer process, the functionalization of Bodipy dyes with an iodine atom enhances ISC leading to higher quantum yields for the generation of  $^1\text{O}_2$ .<sup>67</sup>

With this in mind we set out to develop a metal-free heterogeneous photocatalytic system for the  $^1\text{O}_2$  mediated oxidation of primary and secondary amines, using commercially available  $\alpha$ -sexithiophene as heterogeneous visible-light singlet oxygen sensitizer. The proposed mechanism for this transformation is shown in Scheme 3.1.

**Scheme 3.1.** Proposed Mechanism for the Photocatalyzed Oxidation of Amines to Imines



### 3.2. Optimization and Controls

We began our studies on the oxidation of amines utilizing  $\alpha$ -6T as photocatalyst and benzylamine as our model substrate. In an attempt to optimize the reaction conditions for the singlet oxygen mediated oxidations, we performed the test and control reactions under a variety of conditions (Table 3.1).

**Table 3.1.** Optimization of Reaction Conditions<sup>a</sup>

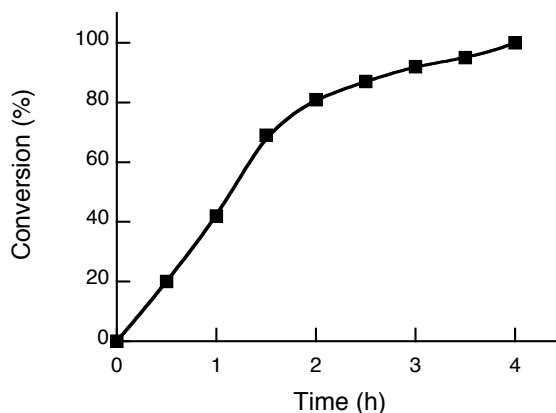
| Entry | Photocatalyst        | Solvent           | Atm.  | Time  | Yield             |
|-------|----------------------|-------------------|-------|-------|-------------------|
| 1     | 1 mol % $\alpha$ -6T | MeCN              | Air   | 4 h   | >99 %             |
| 2     | 1 mol % $\alpha$ -6T | MeCN              | Argon | 4 h   | NR                |
| 3     | No Catalyst          | MeCN              | Air   | 4 h   | NR                |
| 4     | 1 mol % $\alpha$ -6T | MeCN              | Air   | 4 h   | NR <sup>b</sup>   |
| 5     | 1 mol % $\alpha$ -6T | MeCN              | Air   | 1.5 h | 67 % <sup>c</sup> |
| 6     | 1 mol % $\alpha$ -6T | CHCl <sub>3</sub> | Air   | 1.5 h | 82 % <sup>d</sup> |

<sup>a</sup>Reaction conditions: Substrate (10 mM),  $\alpha$ -6T (0.01 eq.), solvent (5mL) under. Irradiated in photoreactor fitted with 14 Visible light bulbs. Yields determined through analysis of crude <sup>1</sup>H NMR. <sup>b</sup>Reaction performed under dark conditions. <sup>c</sup>[O<sub>2</sub>]<sub>MeCN</sub> and [O<sub>2</sub>]<sub>CHCl<sub>3</sub></sub> approx. 2.0 mM under air atmosphere.  $\tau(^1\Delta_r)_{CHCl_3}$ =207  $\mu$ s and  $\tau(^1\Delta_r)_{MeCN}$ =75  $\mu$ s

From these initial tests it was found that acetonitrile (MeCN) is a good solvent for the transformation and that oxygen, the  $\alpha$ -6T photocatalyst, and light are all necessary for the reaction to proceed (Table 3.1, entries 1,2,3, and 4). After 4 hours of irradiation in a photoreactor fitted with 14 visible light bulbs (see Appendix for irradiance and output spectrum) it was found that nearly all (>99%) of the benzylamine starting material was oxidized to its corresponding imine when MeCN is used as solvent (Table 3.1, entry 1). When we decrease the irradiation time in MeCN to 1.5 h the conversion drops down to 67% (Table 3.1, entry 5). Interestingly, the yield at 1.5 h of irradiation can be increased to 82% by switching to  $\text{CHCl}_3$  as solvent (Table 3.1, entry 6). Considering the concentration of dissolved oxygen in both solvents is similar, one of the more probable explanations for the enhanced reaction efficiency in  $\text{CHCl}_3$  is the longer lifetime of singlet oxygen in  $\text{CHCl}_3$  [ $\tau(^1\Delta_g)_{\text{CHCl}_3}=207 \text{ }\mu\text{s}$ ] in comparison to MeCN [ $\tau(^1\Delta_g)_{\text{MeCN}}=75 \text{ }\mu\text{s}$ ], thus providing evidence for the role of  $^1\text{O}_2$  in the oxidation process.

We have also followed the reaction progress of the model reaction as a function of time (Figure 3.1), under the previously optimized conditions. In Figure 3.1 it can be seen that the rate of reaction decreases as the reaction proceeds towards completion. As the reaction progresses the concentration of amine decreases, while the concentration of the corresponding imine product increases and considering that the imine is also capable of quenching  $^1\text{O}_2$  ( $k_q \text{ } ^1\Delta_g = 2.02 \pm 0.20 \times 10^5 \text{ M}^{-1}\text{s}^{-1}$ ), as its concentration increases it will begin to compete for some of the available singlet oxygen.





**Figure 3.1.** Conversion vs. Time profile for the oxidation of benzylamine to its corresponding imine. Conversion measured by  $^1\text{H}$  NMR. Each point corresponds to a separate reaction that was stopped at a different timepoint.

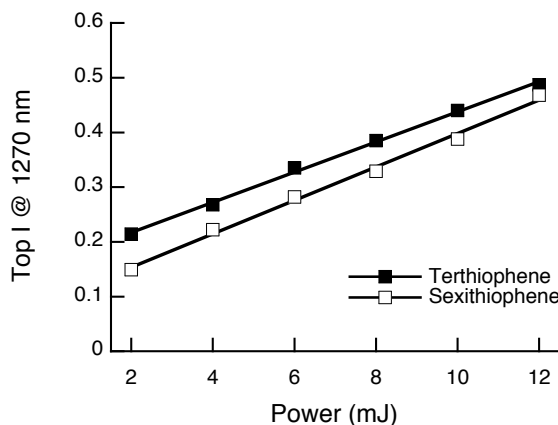
### 3.3. Substrate Scope

With the optimized conditions in hand, we then set out to test our system in the  $^1\text{O}_2$  mediated oxidation of both primary and secondary amines. As illustrated in Table 3.2 our photocatalytic system can for the most part convert a number of primary amines to their corresponding imine in moderate to excellent yields (39-99%) under short irradiation times (4 h). However, as shown by Table 3.2, entries 7-10 our system is not as efficient at oxidizing secondary amines, with the tetrahydroisoquinoline of entry 8 being the only secondary amine oxidized to a considerable extent within the series. In order to better understand the reactivity of our system we set out to characterize the underlying processes.



### 3.4. Quantum Yield of $^1\text{O}_2$ Generation

We began by examining the efficiency at which  $\alpha$ -6T generates  $^1\text{O}_2$ . Utilizing terthiophene as standard ( $\Phi_{\Delta\ 3\text{T}} = 0.86$ )<sup>50</sup> we have been able to determine the quantum yield of singlet oxygen generation from  $\alpha$ -6T. Briefly, by monitoring the phosphorescence (emission) of  $^1\text{O}_2$  at 1270 nm of optically matched and air equilibrated samples of terthiophene in  $\text{CDCl}_3$  and sexithiophene in MeCN, upon 355 nm laser pulse excitation of varying power intensities, we were able to produce the graph shown in Figure 3.2.



**Figure 3.2.** Intensity of phosphorescent signal at 1270 nm upon 355 nm laser excitation of Terthiophene in  $\text{CDCl}_3$  and  $\alpha$ -Sexithiophene in MeCN. (Absorbances at 355 nm matched at 0.1).

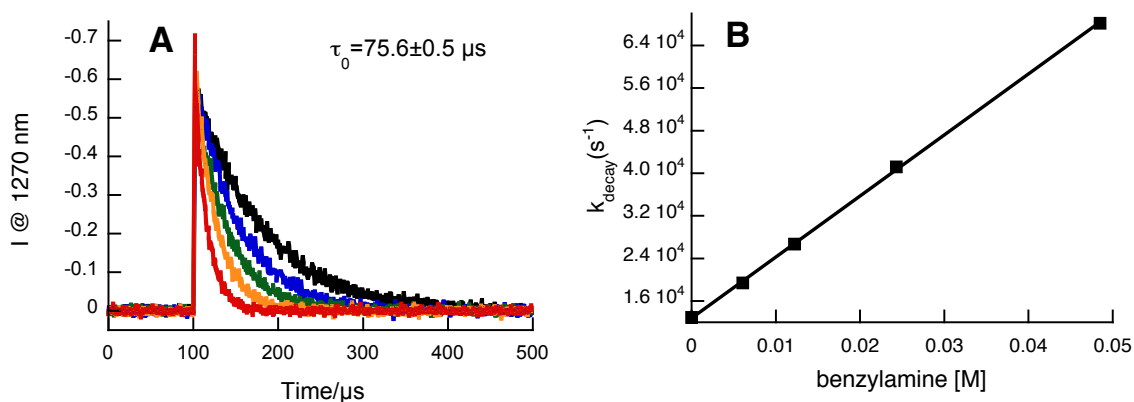
Utilizing equation 3.1, where  $\Phi_{\Delta\ 6\text{T}}$  is the quantum yield of  $^1\text{O}_2$  generation from  $\alpha$ -6T,  $\Phi_{\Delta\ 3\text{T}}$  is the quantum yield of  $^1\text{O}_2$  generation from terthiophene,  $\text{Grad}_{6\text{T}}$  and  $\text{Grad}_{3\text{T}}$  are the corresponding slopes from Figure 3.2, and  $\eta$  is the refractive index of the employed solvent, we were able to calculate the quantum yield of  $^1\text{O}_2$  generation for  $\alpha$ -6T as being 0.82. As such,  $\alpha$ -6T is a potent generator of  $^1\text{O}_2$ .

$$\Phi_{\Delta 6T} = \Phi_{\Delta 3T} \left( \frac{\text{Grad}_{6T}}{\text{Grad}_{3T}} \right) \left( \frac{\eta_{\text{MeCN}}^2}{\eta_{\text{CDCl}_3}^2} \right) \quad (3.1)$$

$$\Phi_{\Delta 6T} = 0.82$$

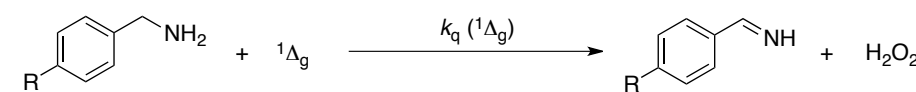
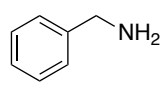
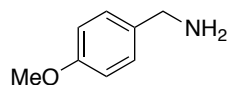
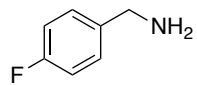
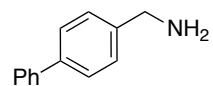
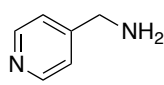
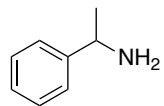
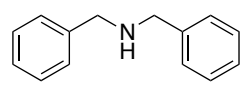
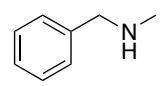
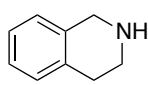
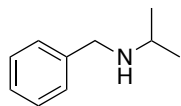
### 3.5. Quenching of $^1\text{O}_2$ by Primary and Secondary Amines

While the oxidation of primary and secondary amines to their corresponding imines has been previously explored, using a variety of different photosensitizers, it is currently difficult to find the bimolecular quenching rate constants for  $^1\text{O}_2$  and the amines utilized in this study. Considering that this reaction is a key process in the transformation, we decided to measure this rate constant for each of the employed amines (see Table 3.3). Typically the efficiency of  $^1\text{O}_2$  quenching by amines increases as the ionization potential decreases. Thus in general the rate constants of  $^1\text{O}_2$  quenching for amines decrease as follows:  $k_{\text{q tertiary}} > k_{\text{q secondary}} > k_{\text{q primary}}$ .<sup>69</sup>



**Figure 3.3.** Kinetic analysis of the reaction between  $^1\text{O}_2$  ( $^1\Delta_g$ ) and benzylamine. A) Decay of emission for  $^1\Delta_g$  at 1270 nm in the presence of increasing concentrations of benzylamine in MeCN. B) Kinetic quenching plot showing the rate of decay of the emission at 1270 nm as a function of [benzylamine]. The slope of this plot corresponds to the bimolecular rate constant for this reaction.

**Table 3.3.** Bimolecular Quenching Rate Constants for  $^1\text{O}_2$  and a Variety of Amines<sup>a</sup>

|  |                                                                                     |                                                |
|------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|------------------------------------------------|
| Entry                                                                              | Substrate                                                                           | $k_q (^1\Delta_g) \text{ M}^{-1}\text{s}^{-1}$ |
| 1                                                                                  |    | $1.15 \pm 0.12 \times 10^6$                    |
| 2                                                                                  |    | $2.01 \pm 0.20 \times 10^6$                    |
| 3                                                                                  |    | $9.57 \pm 0.96 \times 10^5$                    |
| 4                                                                                  |    | $3.50 \pm 0.35 \times 10^5$                    |
| 5                                                                                  |   | $6.45 \pm 0.65 \times 10^5$ <sup>b</sup>       |
| 6                                                                                  |  | $5.23 \pm 0.52 \times 10^5$                    |
| 7                                                                                  |  | $1.29 \pm 0.13 \times 10^7$                    |
| 8                                                                                  |  | $4.33 \pm 0.43 \times 10^7$                    |
| 9                                                                                  |  | $3.10 \pm 0.31 \times 10^7$                    |
| 10                                                                                 |  | $1.54 \pm 0.15 \times 10^7$                    |

<sup>a</sup> $^1\Delta_g$  was generated through 355 nm laser excitation (10 mJ per pulse) of an aerated solution of  $\alpha$ -Sexithiophene in MeCN. The phosphorescence of the  $^1\Delta_g$  was monitored at 1270 nm using a NIR-PMT.

<sup>b</sup>Due to the low solubility of 4-phenyl benzylamine in MeCN we have performed this experiment in  $\text{CHCl}_3$ .

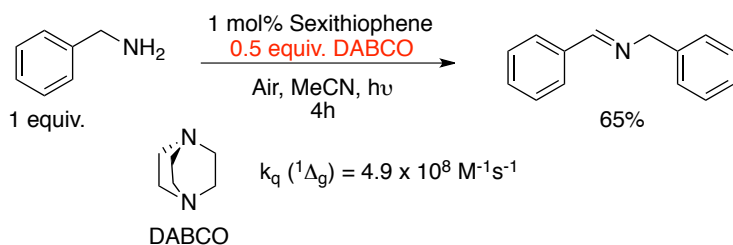
By monitoring the rate of decay for the emission of  $^1\text{O}_2$  at 1270 nm as a function of amine concentration (Figure 3.3.A) we can plot a corresponding kinetic quenching plot (Figure 3.3.B). The slope of the plots gives us the bimolecular rate constant of quenching for each of the amines. As expected the rate constants measured for the primary amines is approximately 2 orders ( $10^5 \text{ M}^{-1}\text{s}^{-1}$ ) of magnitude lower than that found for the secondary amines ( $10^7 \text{ M}^{-1}\text{s}^{-1}$ ). The bimolecular rate constants for  $^1\text{O}_2$  quenching for each of the amines studied can be found in Table 3.3. Interestingly we cannot make a direct correlation between the yield of imine obtained and the measured rate constants for singlet oxygen quenching, as one would expect that the yield of imines should be higher when secondary amines with higher  $k_q$  values are employed. However, from Table 3.3, we have found that the primary amines consistently give higher yields of the corresponding imines under our optimized reaction conditions. One of the most probable explanations for this difference in reactivity lies in the fact that perhaps the secondary amines are able to intercept the triplet of  $\alpha$ -6T, therefore decreasing the yield of singlet oxygen available to bring about the desired transformation.

### 3.6. Confirming the Role of Singlet Oxygen

While we have demonstrated the need for oxygen in the  $\alpha$ -6T catalyzed oxidation of amines and that the use of solvents with longer  $^1\text{O}_2$  lifetimes leads to higher yields, in order to confirm the role of  $^1\text{O}_2$  in our mechanism, we have performed some additional studies. One of these studies involved the addition of a  $^1\text{O}_2$  quencher to our model reaction. Through the addition of 0.5 equivalents of

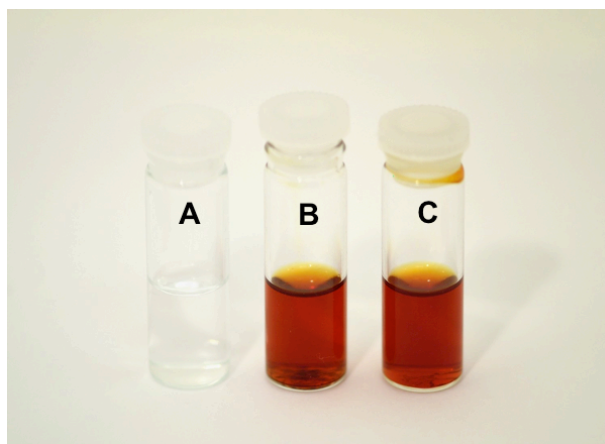
DABCO (1,4-diazabicyclo[2.2.2]octane), a potent quencher of  $^1\text{O}_2$  ( $k_q\ ^1\Delta_g = 4.9 \times 10^8\ \text{M}^{-1}\text{s}^{-1}$ )<sup>69</sup>, to the oxidation of benzylamine, we were able to decrease the 4 h yield from 99% to 65% (see Scheme 3.2). Thus confirming the role of singlet oxygen in the oxidation process.

**Scheme 3.2.** Inhibition of Benzylamine Oxidation Utilizing DABCO as Competitive Quencher of  $^1\Delta_g$ <sup>a</sup>



<sup>a</sup>Reaction conditions: benzylamine (10 mM),  $\alpha$ -6T (0.01 eq.), DABCO (0.5 eq.), MeCN (5mL) under Air atmosphere. Irradiated in photoreactor fitted with 14 Visible light bulbs. Yields determined through analysis of crude  $^1\text{H}$  NMR. As DABCO is an excellent quencher of  $^1\Delta_g$ , the observed decrease in efficiency upon its introduction is indicative of an oxidation mechanism involving  $^1\Delta_g$ .

In addition to the effect of DABCO, we have also detected the formation of  $\text{H}_2\text{O}_2$  using the Starch/KI/ $\text{CH}_3\text{COOH}$  test. Upon addition of the irradiated reaction mixture to a solution of Starch/KI/ $\text{CH}_3\text{COOH}$  we obtain a brown colour that is indicative of the presence of  $\text{H}_2\text{O}_2$  (Figure 3.4.B), which further confirms our proposed reaction mechanism. Interestingly, there are industrial processes to synthesize hydrazine from ammonia and hydrogen peroxide. However, considering that the reaction is not spontaneous and requires the presence of a ketone to activate the ammonia, we foresee no problems with performing this reaction on larger scales.



**Figure 3.4.** Photograph illustrating the results of the KI/Starch test for  $\text{H}_2\text{O}_2$ . A) Negative control: KI/Starch/Acetic Acid. B) KI/Starch/Acetic Acid + 200  $\mu\text{L}$  of benzylamine reaction mixture after 4 h of irradiation. C) Positive control: KI/Starch/Acetic Acid + 200  $\mu\text{L}$  of 30% w/w  $\text{H}_2\text{O}_2$ .

### 3.7. Conclusions

We have demonstrated the use of  $\alpha$ -6T as a visible light singlet oxygen catalyst in the oxidation of primary and secondary amines to their corresponding imines. While there are many singlet oxygen sensitizers,  $\alpha$ -6T is a commercially available organic semiconductor that requires no modification before use, and is a relatively potent generator of singlet oxygen, which can find applications in a variety of different transformations. In addition to demonstrating its usefulness in the oxidation of amines to imines, we have compiled the bimolecular rate constants for the reaction of  $^1\text{O}_2$  with a variety of different primary and secondary amines, which were currently missing in the literature.



### 3.8. Appendix

#### 3.8.A. General Information

Substrates and Reagents:  $\alpha$ -Sexithiophene, Amines, Acetonitrile, Chloroform, DABCO, Starch, Potassium Iodide, and Acetic acid were purchased from commercial suppliers (Sigma Aldrich, Alfa Aesar, and Fisher) and used with no further purification unless otherwise noted.

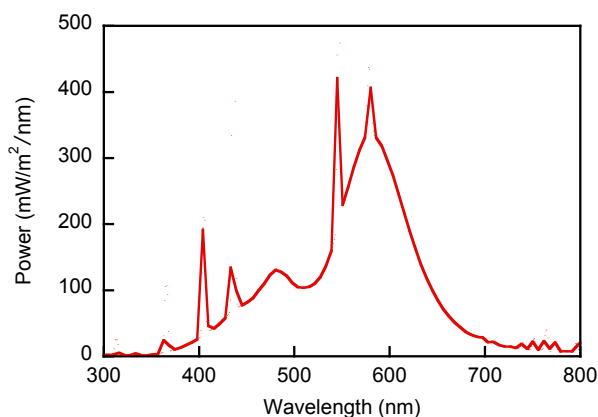
Light Source: All reactions were performed in a photoreactor (Luzchem Research Inc., Ottawa, Canada) fitted with 14 Visible light bulbs.

NMR: All  $^1\text{H}$  NMR were recorded on a Bruker AVANCE 400 spectrometer. Chemical shifts ( $\delta$ ) are reported in ppm from the solvent.

#### 3.8.B. General Procedure for the Oxidation of Primary and Secondary Amines

A 10 ml test tube was charged with  $\alpha$ -Sexithiophene (0.01 eq., 2.5 mg), the desired primary or secondary amine substrate (0.5 mmol), and 5 mL of MeCN. The mixture was then sonicated for 5 minutes. After the catalyst was dispersed, it was irradiated in a photoreactor fitted with 14 visible light bulbs for 4 hours with mechanical stirring. After irradiation the reaction mixture was centrifuged for 10 minutes at 3500 rpm. The supernatant was then evaporated and a  $^1\text{H}$  NMR of the crude reaction mixture was recorded in  $\text{CDCl}_3$ . The crude  $^1\text{H}$  NMRs of the imine products were compared to those obtained by Huang *et al.*<sup>21</sup>

### 3.8.C. Output Spectrum of Photoreactor with 14 Visible Light Bulbs



**Figure 3A.1.** Output spectrum of photoreactor with 14 visible light bulbs used for irradiation of reaction mixtures.

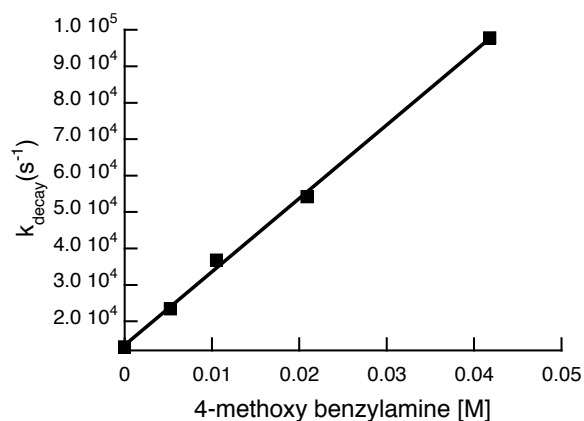
### 3.8.D. Laser Flash Photolysis Data

#### Quantum Yield of Singlet Oxygen Generation:

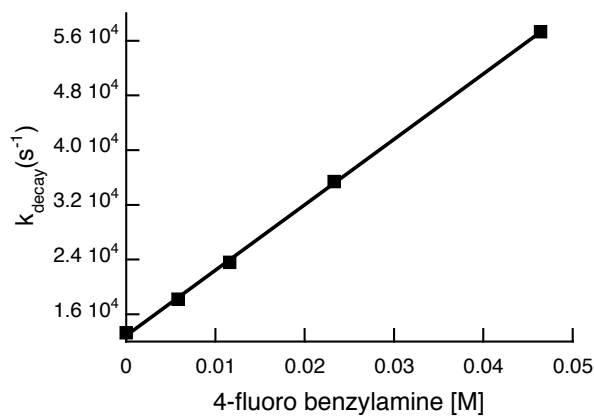
The singlet oxygen measurements for  $\alpha$ -6T were performed using a Q-switched Nd:YAG-laser (355 nm) in a LFP-111 laser-flash photolysis (LFP) system (Luzchem Research Inc., Ottawa, Canada) fitted with a NIR-PMT detector and 1×1 cm cuvettes. Samples of terthiophene and  $\alpha$ -6T were prepared in  $\text{CDCl}_3$  and MeCN, respectively with a total volume of 3 mL and an absorbance of  $\sim 0.1$  at 355 nm. The samples were purged with  $\text{O}_2$  for 20 minutes prior to use. The emission from  $^1\text{O}_2$  was monitored at 1270 nm.

### Quenching of Singlet Oxygen:

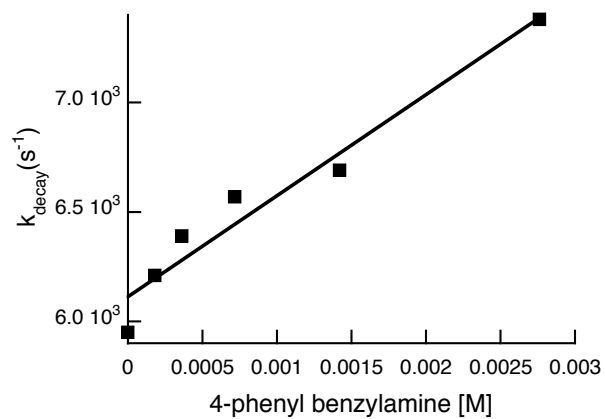
The quenching experiments of singlet oxygen were performed using a Q-switched Nd:YAG-laser (355 nm) in a LFP-111 laser-flash photolysis (LFP) system (Luzchem Research Inc., Ottawa, Canada) fitted with a NIR-PMT detector and 1×1 cm cuvettes. Samples of  $\alpha$ -6T were prepared in MeCN with a total volume of 3 mL and an absorbance of  $\sim 0.2$  at 355 nm. The samples were purged with O<sub>2</sub> for 20 minutes prior to use. The emission from <sup>1</sup>O<sub>2</sub> was monitored at 1270 nm.



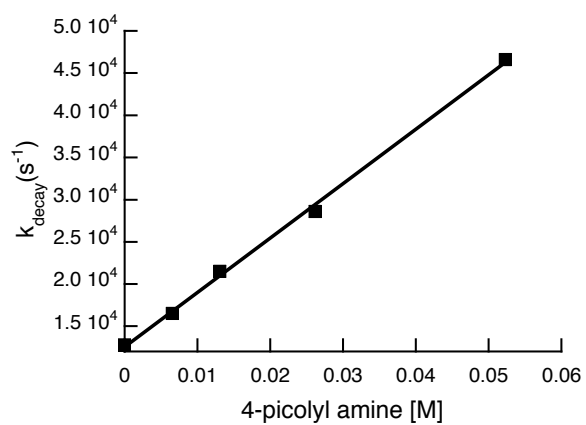
**Figure 3A.2.** Kinetic quenching plot for <sup>1</sup>Δ<sub>g</sub> and 4-methoxy benzylamine



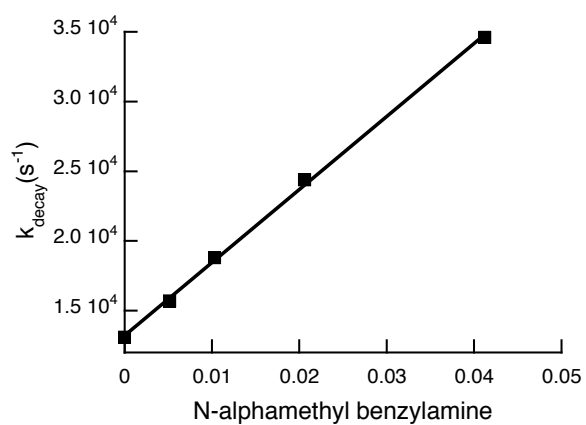
**Figure 3A.3.** Kinetic quenching plot for <sup>1</sup>Δ<sub>g</sub> and 4-fluoro benzylamine



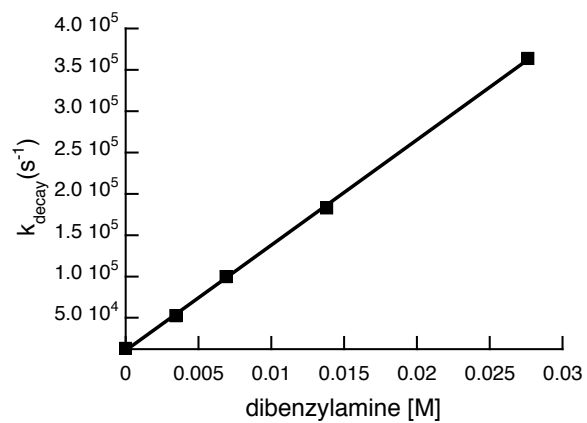
**Figure 3A.4.** Kinetic quenching plot for  $^1\Delta_g$  and 4-phenyl benzylamine



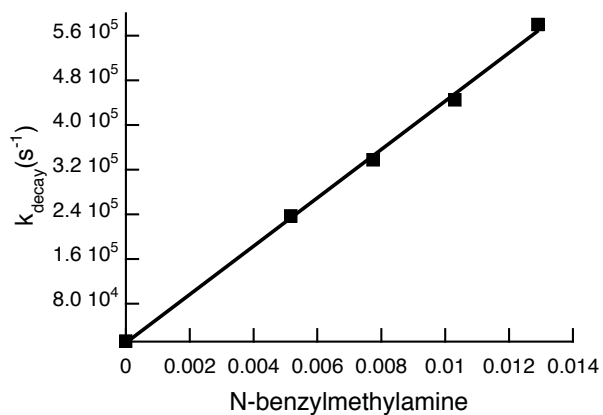
**Figure 3A.5.** Kinetic quenching plot for  $^1\Delta_g$  and 4-picolyl benzylamine



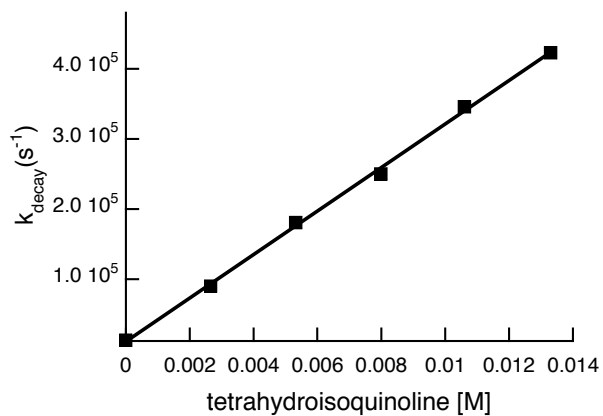
**Figure 3A.6.** Kinetic quenching plot for  $^1\Delta_g$  and N-alpha-methyl benzylamine



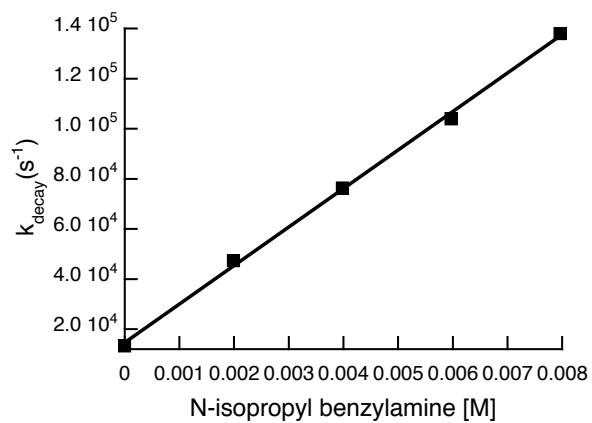
**Figure 3A.7.** Kinetic quenching plot for  $^1\Delta_g$  and dibenzylamine



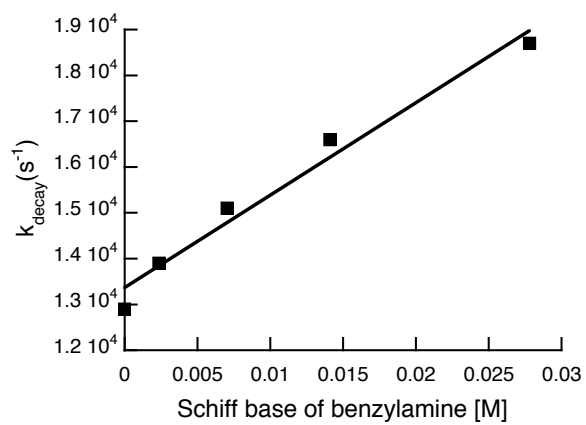
**Figure 3A.8.** Kinetic quenching plot for  $^1\Delta_g$  and N-benzylmethylamine



**Figure 3A.9.** Kinetic quenching plot for  $^1\Delta_g$  and tetrahydroisoquinoline

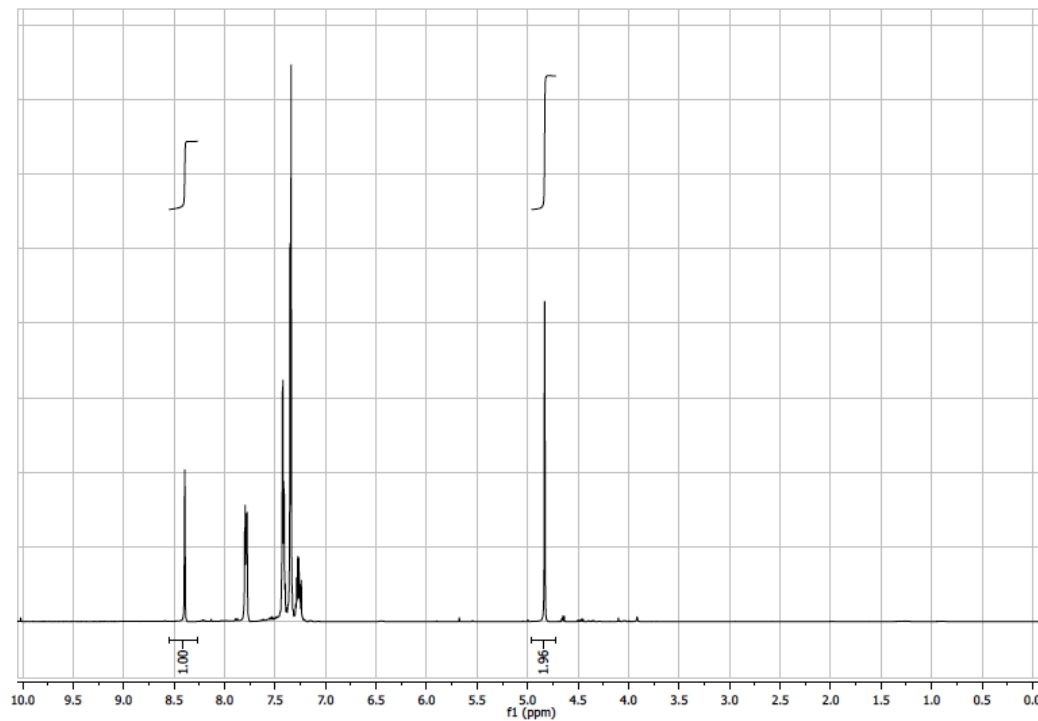


**Figure 3A.10.** Kinetic quenching plot for  $^1\Delta_g$  and N-isopropyl benzylamine

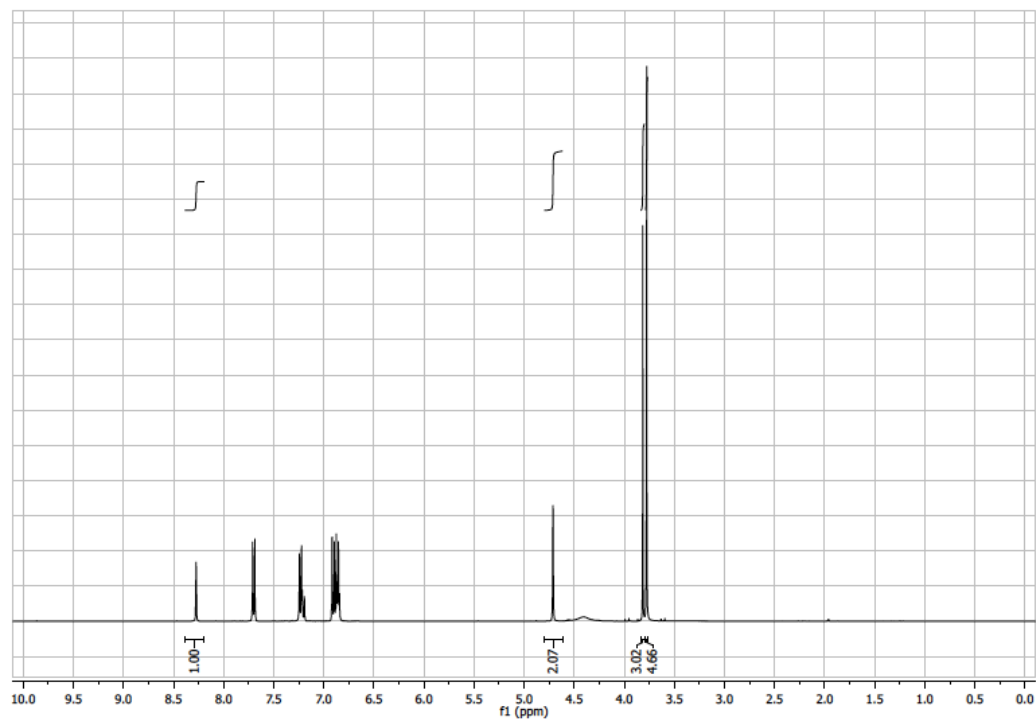


**Figure 3A.11.** Kinetic quenching plot for  $^1\Delta_g$  and Schiff base of benzylamine

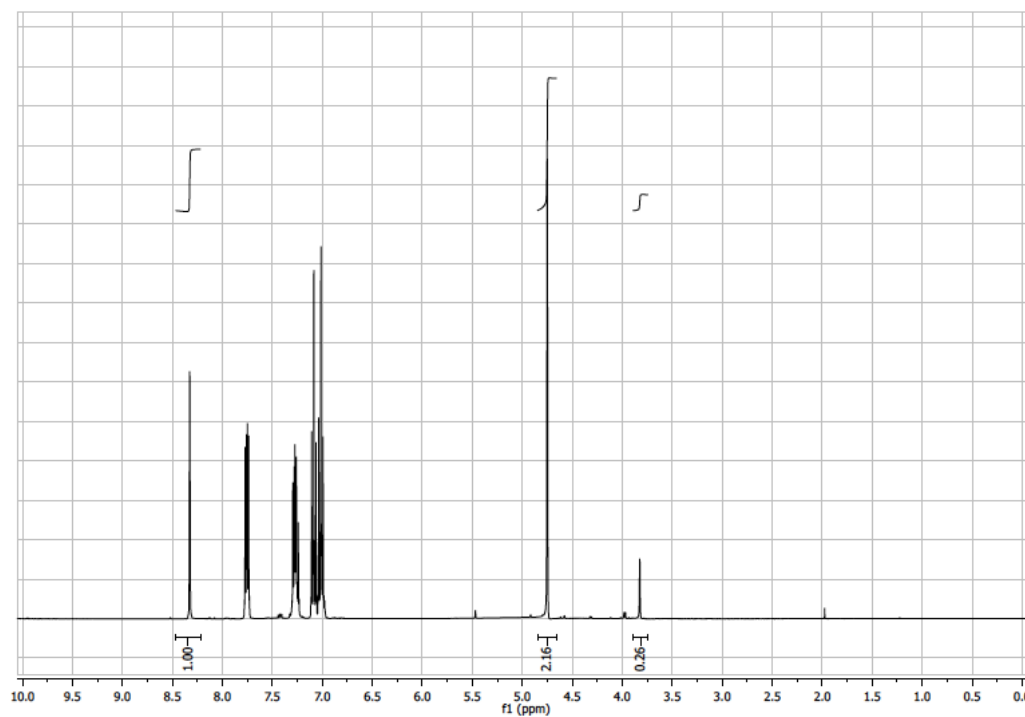
### 3.8.E. NMR Data



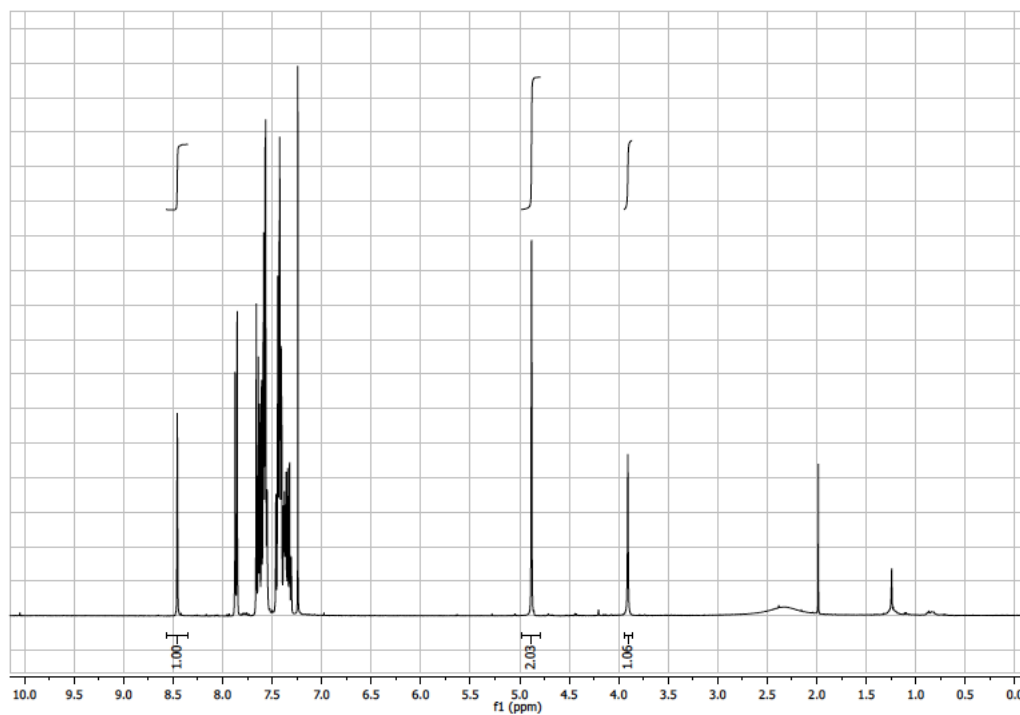
**Figure 3A.12.**  $^1\text{H}$  NMR spectrum of the crude from aerobic oxidative coupling of benzylamine 4h.



**Figure 3A.13.**  $^1\text{H}$  NMR spectrum of the crude from aerobic oxidative coupling of 4-methoxybenzylamine 4h.

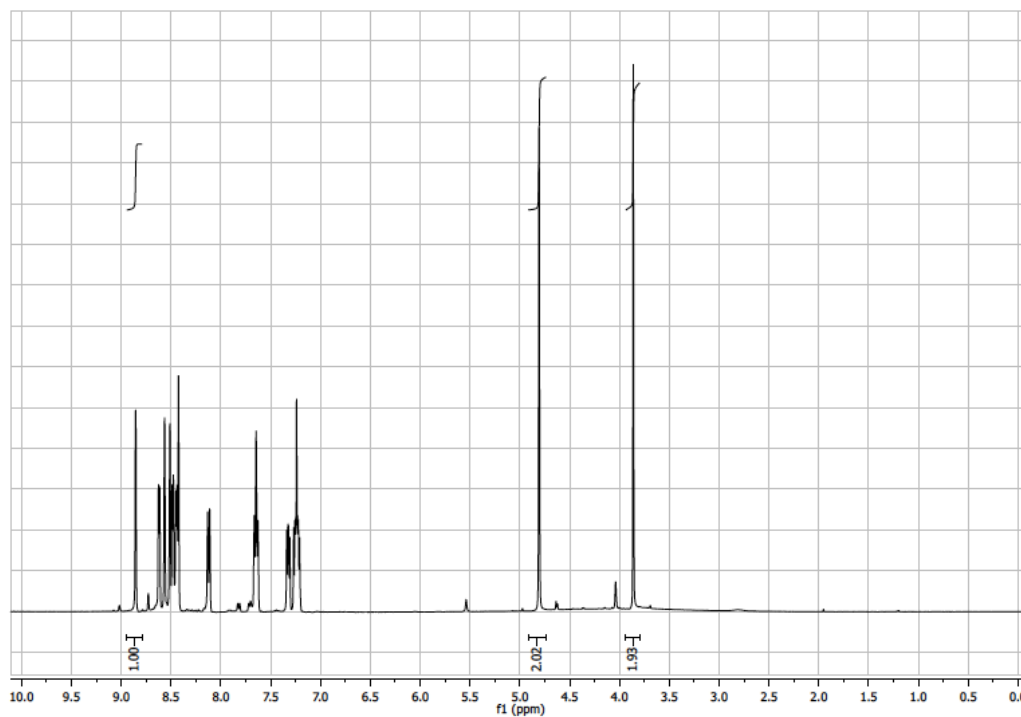


**Figure 3A.14.**  $^1\text{H}$  NMR spectrum of the crude from aerobic oxidative coupling of 4-fluoro benzylamine 4h.

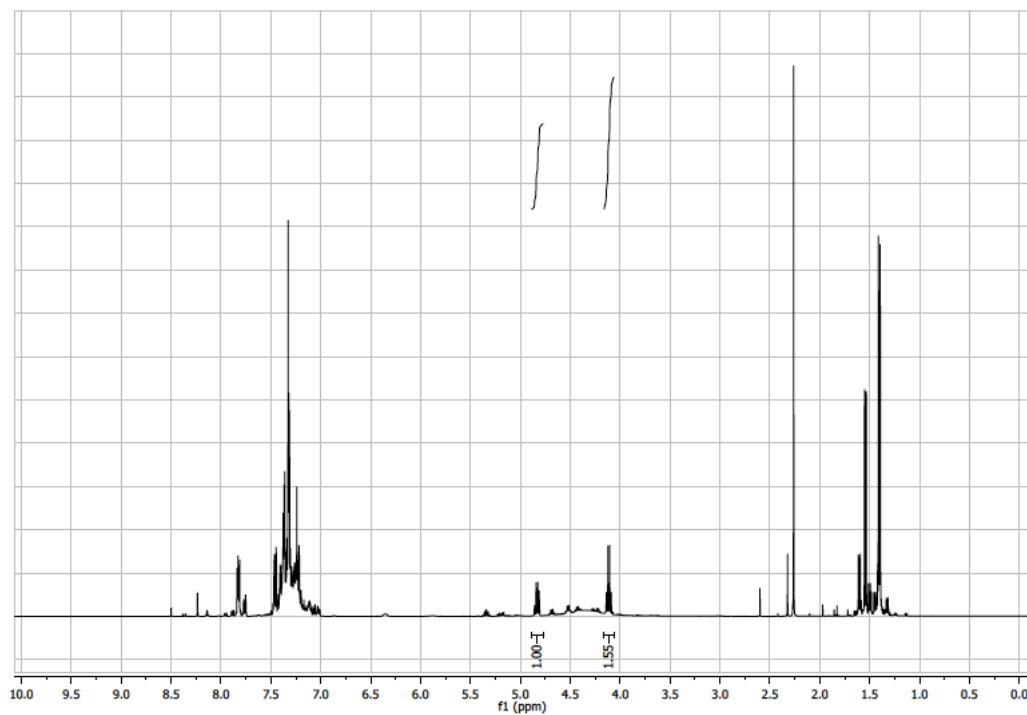


**Figure 3A.15.**  $^1\text{H}$  NMR spectrum of the crude from aerobic oxidative coupling of 4-phenyl benzylamine 4h.

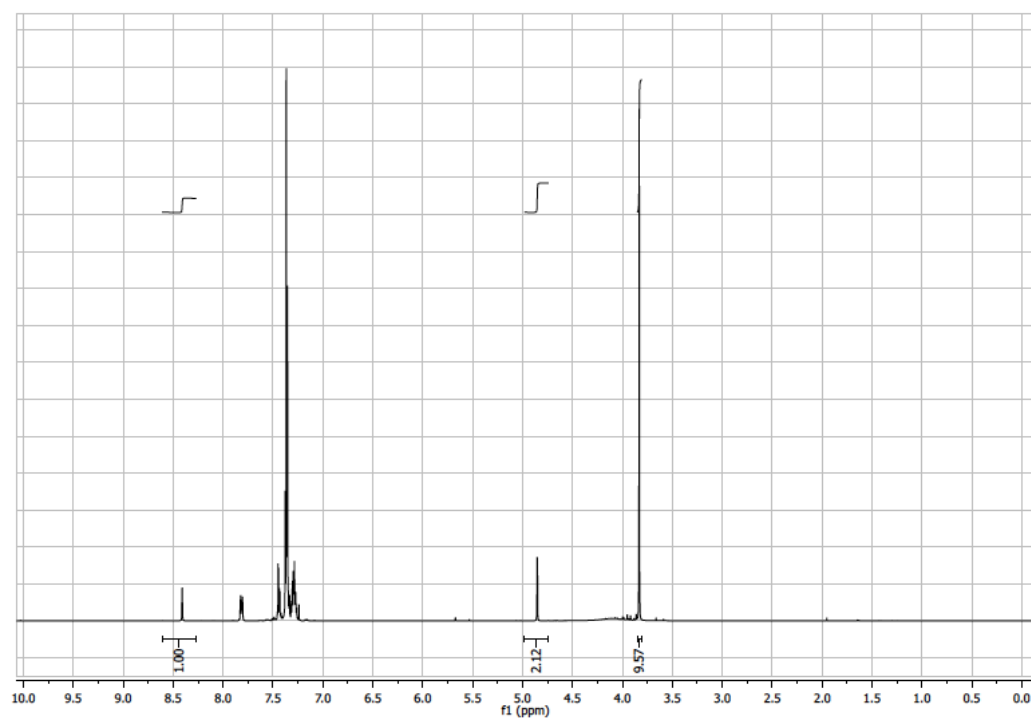




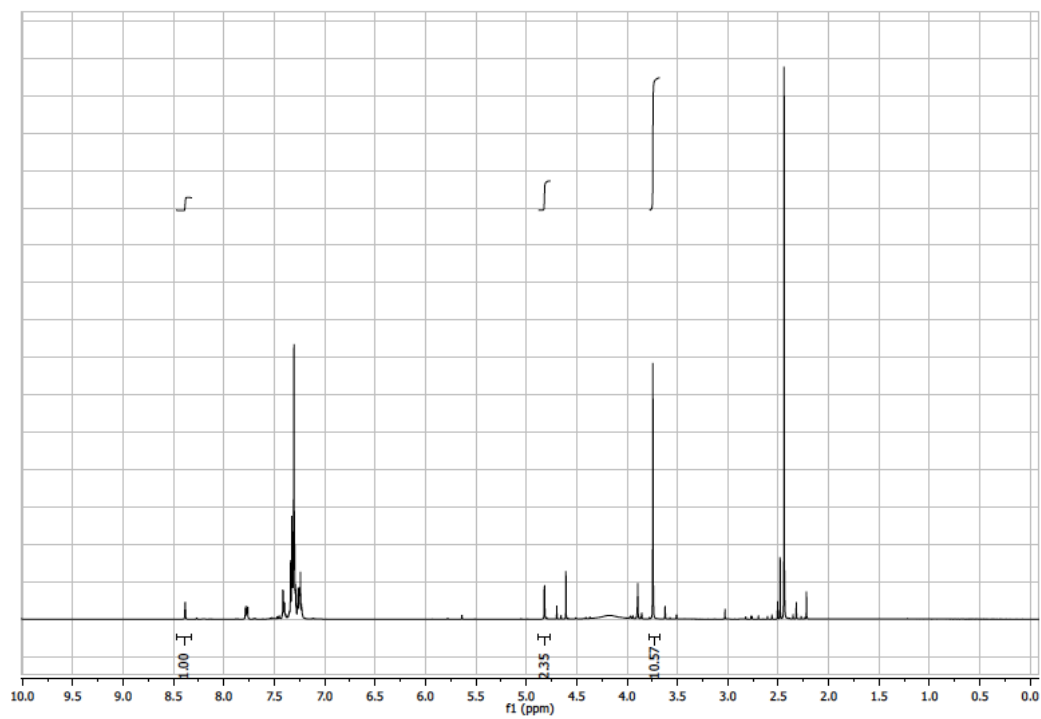
**Figure 3A.16.**  $^1\text{H}$  NMR spectrum of the crude from aerobic oxidative coupling of 4-picoly benzylamine 4h.



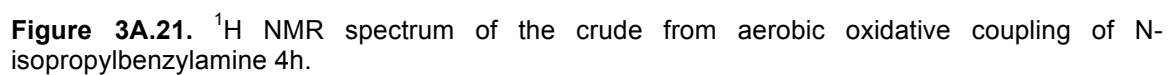
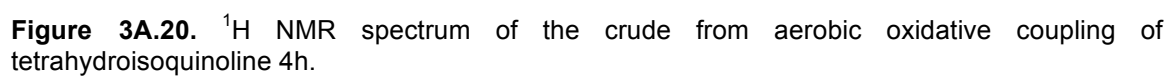
**Figure 3A.17.**  $^1\text{H}$  NMR spectrum of the crude from aerobic oxidative coupling of N-alpha-methyl benzylamine 4h.

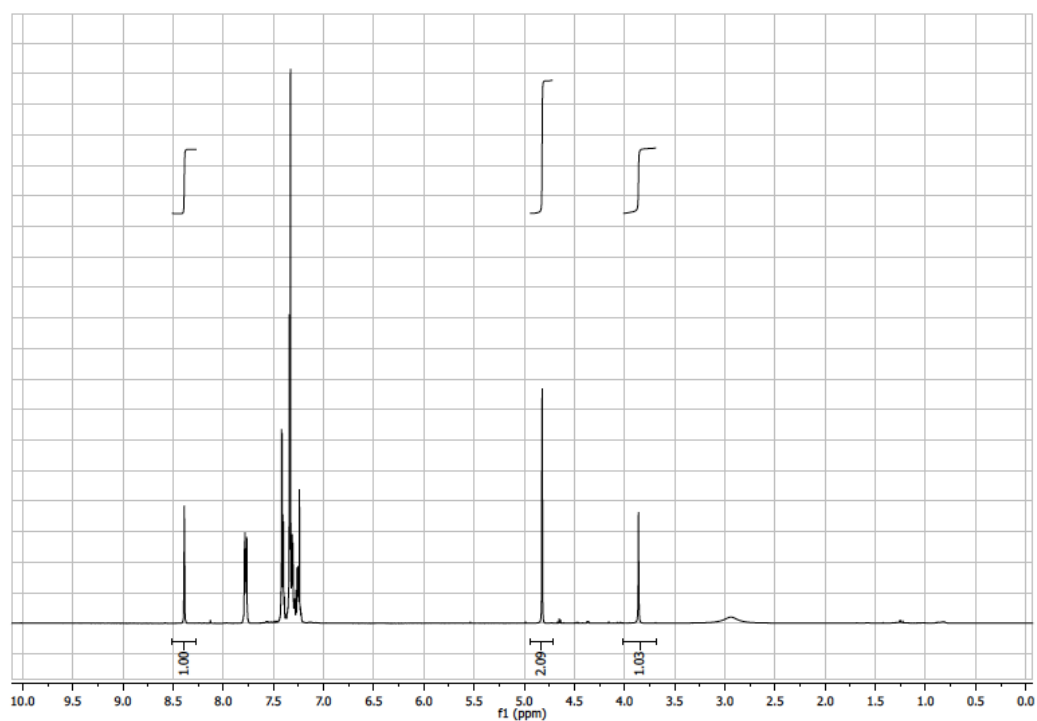


**Figure 3A.18.**  $^1\text{H}$  NMR spectrum of the crude from aerobic oxidative coupling of dibenzylamine 4h.

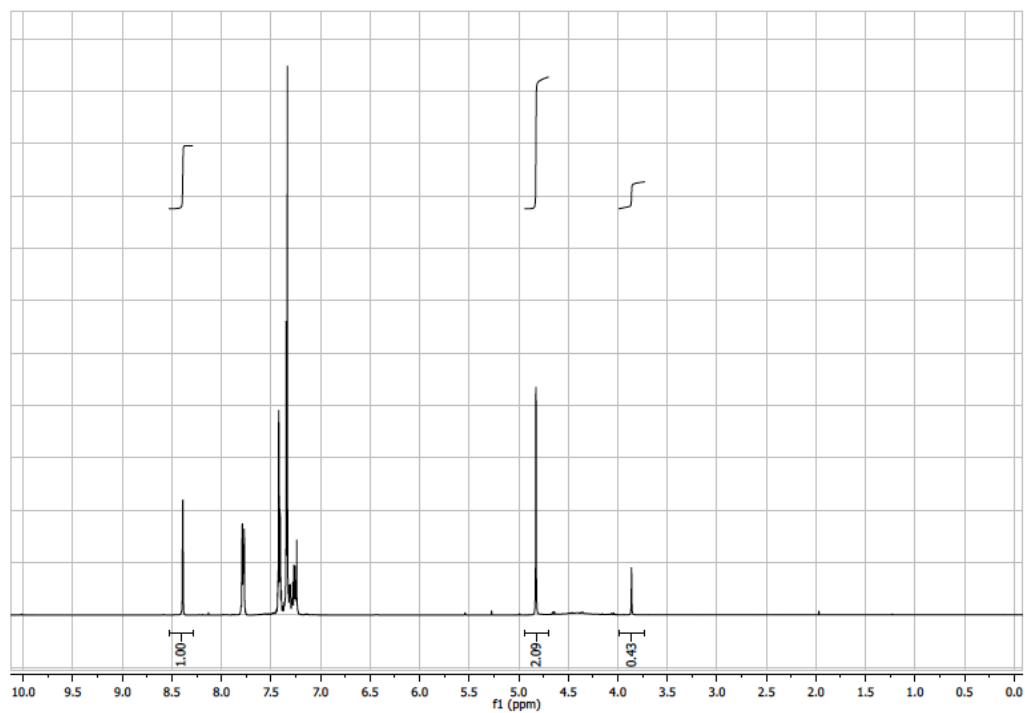


**Figure 3A.19.**  $^1\text{H}$  NMR spectrum of the crude from aerobic oxidative coupling of N-benzylmethylamine 4h.

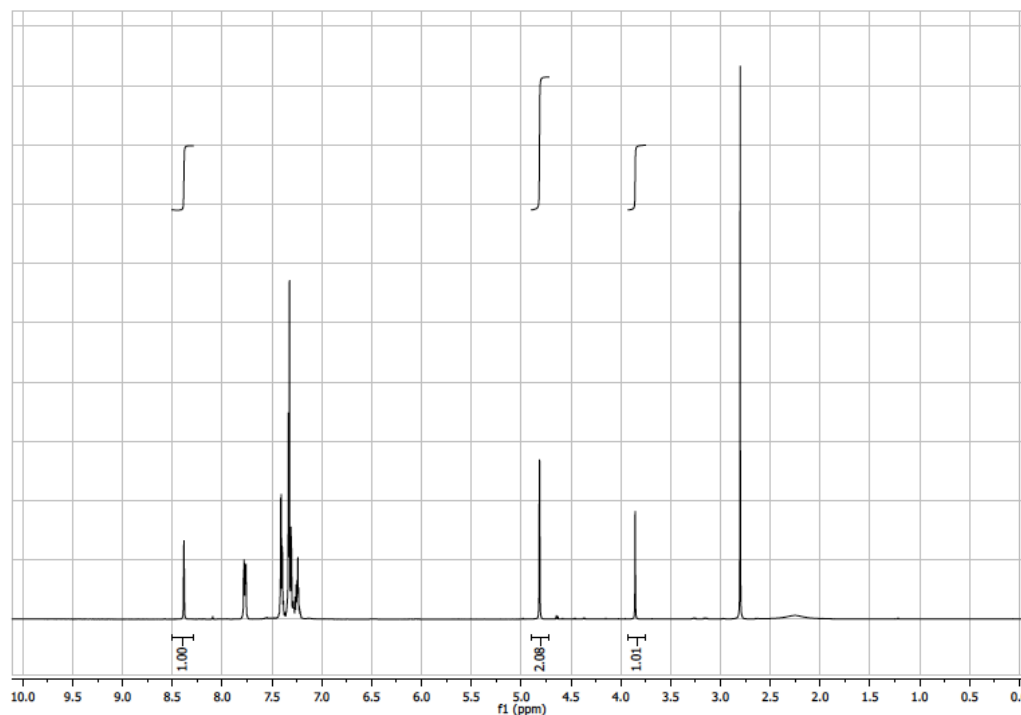




**Figure 3A.22.**  $^1\text{H}$  NMR spectrum of the crude from aerobic oxidative coupling of benzylamine in MeCN 1.5 h.



**Figure 3A.23.**  $^1\text{H}$  NMR spectrum of the crude from aerobic oxidative coupling of benzylamine in  $\text{CHCl}_3$  1.5 h.



**Figure 3A.24.**  $^1\text{H}$  NMR spectrum of the crude from aerobic oxidative coupling of benzylamine in MeCN 4 h with 0.5 equiv. of DABCO.

### 3.9. References

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## **4. Titania as Heterogeneous Photoredox Catalyst**

### **Heterogeneous Light-Mediated Reductive Dehalogenations and Cyclizations Utilizing Platinum Nanoparticles on Titania**

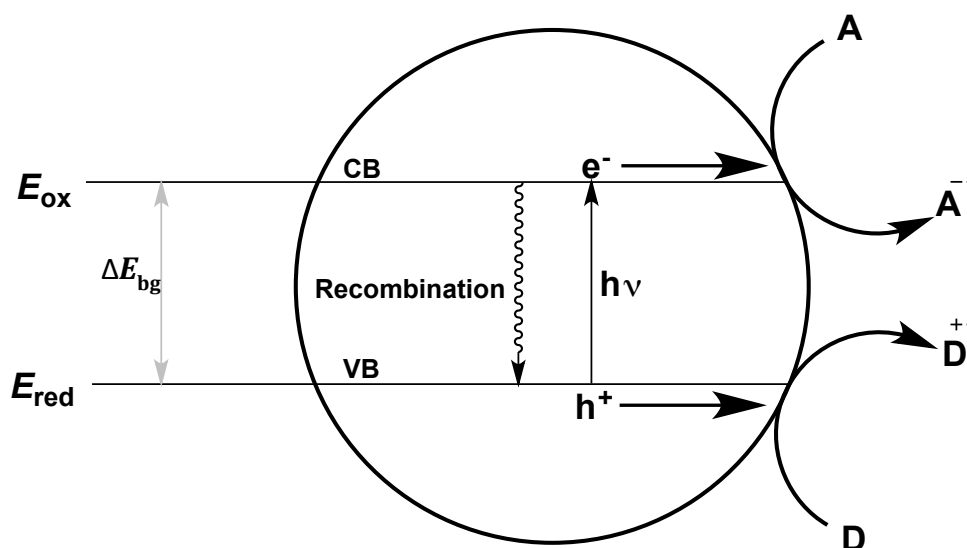
#### **4.1. Background**

As previously discussed, photoredox catalysis has attracted increasing amounts of attention because of the generally mild conditions required for substrate activation and its context in “green chemistry”.<sup>1</sup> In general, Ruthenium and Iridium complexes have been used as photosensitizers, as their long excited-state lifetime allow for intermolecular electron transfer to occur readily. However, these catalysts are not always readily removed and suffer from high cost (some of the more potent Ir complexes cost anywhere from \$1200 to \$1700 per gram), therefore the development of efficient, low cost photocatalytic systems with easily removable catalysts is imperative in further developing this field. One strategy that has been employed to counter these problems is the use of organic triplet photosensitizers, such as Eosin Y, Rose Bengal, 9-Mesityl-10-methylacridinium and Methylene Blue.<sup>2-5</sup>

Alternatively, another approach one can take to develop an efficient, low cost photoredox system is through heterogeneous semiconductor photocatalysis. Heterogeneous catalysis offers the advantage that the catalyst can be removed easily by either filtration or centrifugation, and one can choose semiconductors that absorb light near or in the visible region of the electromagnetic spectrum. One of the most popular semiconductors that fit these criteria is titanium dioxide (TiO<sub>2</sub>), which is gaining an increasing amount of interest in synthetic organic transformations.<sup>6-15</sup> TiO<sub>2</sub> can be easily removed by centrifugation or filtration, is

strongly reducing (when suspended in MeCN), has a broad absorption that extends weakly into the visible region, and is also inexpensive (\$0.94 per gram).<sup>16,17</sup>

**Scheme 4.1.** General TiO<sub>2</sub> Photoredox Scheme. Adapted with permission from McTiernan *et al.*<sup>18</sup> Copyright 2014 WILEY-VCH Verlag.



Upon excitation of TiO<sub>2</sub> with wavelengths of light having energy equal to or greater than its bandgap energy ( $\Delta E_{bg}$ ), an electron ( $e^-$ ) is promoted from the valence band (VB) to the conduction band (CB) (Scheme 4.1). In order to avoid recombination, the solution must contain both a donor (D) and an acceptor (A) with suitable redox potentials. This is analogous to general photoredox catalyzed processes, where a sacrificial electron donor with a suitable redox potential is used to reduce (or turn-over) the excited-state of the photocatalyst, and the reduced form of the photocatalyst donates that electron to an acceptor with a suitable redox potential. In this case, the sacrificial electron donor will be used to quench the holes ( $h^+$ ) formed upon excitation in order to reduce charge recombination. Typical photoredox sacrificial electron donors, such as amines,



can also be employed as hole quenchers for  $\text{TiO}_2$  photocatalysis. Hoffman et. al. have demonstrated the oxidation of amines by  $\text{TiO}_2$  to form  $\alpha$ -aminoalkyl radicals, which they have employed for radical additions to electron deficient alkenes and for radical tandem addition-cyclization reactions.<sup>19-21</sup> Therefore, using an amine as a sacrificial hole quencher for  $\text{TiO}_2$  photocatalysis has the advantage of reducing possible charge recombination, and gives the possibility for the participation of amine-derived radicals in the reaction.

One limitation of  $\text{TiO}_2$  is its lack of absorption in the visible region of the spectrum. Previous examples have shown that one can overcome this limitation through doping with nitrogen or hydrogen, or through decorating the  $\text{TiO}_2$  with metallic nanoparticles or organic dyes. For example, König et. al. have decorated  $\text{TiO}_2$  with Texas-Red, and have employed them in enantioselective alkylations and mannich type reactions.<sup>16,17</sup> However, dye molecules decorated on the surface are prone to oxidation by  $\text{TiO}_2$ , therefore limiting the possibility of catalyst reusability. On the other hand,  $\text{TiO}_2$  decorated with metallic nanoparticles are much more robust. In addition, previous examples have shown that platinum nanoparticles (PtNP) can be used to enhance the catalytic activity of  $\text{TiO}_2$  and extend its absorption closer to the visible region of the spectrum.<sup>22-25</sup>

In the following sections, the use of PtNP@ $\text{TiO}_2$  semiconductor particles for UVA/Vis-promoted heterogeneous photoredox radical transformations will be discussed.

## 4.2. Optimization and Controls

We began the initial assessment of our catalytic system using the hydrodehalogenation of ethyl 4-iodobenzoate to ethylbenzoate as a model reaction (Table 4.1). To our delight we found that under UVA/visible light irradiation (375-700 nm) and in the presence of di-isopropylethylamine (DIPEA) that the platinized  $\text{TiO}_2$  catalyst (Table 4.1, entry 4) significantly outperforms unmodified  $\text{TiO}_2$  under the same conditions (Table 4.1, entry 1). The higher activity of the  $\text{PtNP@TiO}_2$  catalyst ( $\text{TON} \approx 900$  with respect to Pt) can be simply explained by its ability to absorb a greater extent of the available photons (see Figure 4A.2), however the actual cause of the observed enhancement is most likely the result of efficient interfacial electron transfer from the conduction band of the  $\text{TiO}_2$  to the PtNP, which ultimately reduces electron-hole pair recombination making the process more efficient.<sup>25,26</sup> It has previously been reported that shuttling of CB  $e^-$  to Pt occurs on the picosecond timescale.<sup>16</sup> While the addition of Pt to the catalyst does increase its cost (approx. \$5.40 per gram) the increased efficiency of the resulting system more than makes up for this difference.

**Table 4.1.** Photoreduction of ethyl 4-iodobenzoate<sup>a</sup>

| Entry | Reductant                   | Conditions                | Conversion |
|-------|-----------------------------|---------------------------|------------|
| 1     | TiO <sub>2</sub>            | $h\nu > 375$ nm, DIPEA    | 53 %       |
| 2     | TiO <sub>2</sub>            | $h\nu > 375$ nm, No DIPEA | NR         |
| 3     | TiO <sub>2</sub>            | Dark, DIPEA               | NR         |
| 4     | PtNP(0.2%)/TiO <sub>2</sub> | $h\nu > 375$ nm, DIPEA    | 77 %       |
| 5     | PtNP(0.2%)/TiO <sub>2</sub> | $h\nu > 375$ nm, No DIPEA | NR         |
| 6     | PtNP(0.2%)/TiO <sub>2</sub> | Dark, DIPEA               | NR         |
| 7     | PtNP(0.2%)/TiO <sub>2</sub> | Dark, DIPEA, 50 °C        | NR         |
| 8     | PtNP(0.2%)/TiO <sub>2</sub> | $h\nu > 450$ nm, DIPEA    | 8 %        |

<sup>a</sup>Reaction conditions: ethyl 4-iodobenzoate (0.4 mmol), reductant (0.4 mmol), DIPEA (2.8 mmol), 5 mL MeCN, degassed with Argon for 15 min, and irradiated with a Luzchem solar simulator  $\lambda > 375$  nm for 15 h. Percent conversion was determined by <sup>1</sup>H NMR. Adapted with permission from McTiernan *et al.*<sup>18</sup> Copyright 2014 WILEY-VCH Verlag.

It should also be pointed out that the lack of conversion in the absence of DIPEA (Table 4.1, entries 2 and 5) provides strong evidence of its ability to inhibit electron-hole pair recombination through quenching of holes formed upon TiO<sub>2</sub> excitation. Entries 3 and 6 of Table 4.1 also confirms that excitation of the catalyst is required for the reaction to proceed. In addition, entry 7 of Table 4.1 in which the reaction was conducted under dark conditions at 50°C rules out a thermal pathway to the dehalogenated product. Lastly, entry 8 of Table 4.1 demonstrates that direct excitation of the PtNPs supported on TiO<sub>2</sub> also leads to product formation however under these conditions of irradiation the process is much less efficient.

### 4.3. Hydrodehalogenation of Aryl-Iodides

With the previous information in hand we then set out to test the ability of our optimized catalytic system to reduce both electron deficient and electron rich aryl iodides. As shown in Table 4.2 although we are capable of reducing both electron deficient (Table 4.2, entries 1, 2 and 3) and electron rich aryl iodides (Table 4.2, entry 4, 5 and 6), it takes for the most part significantly longer irradiation times to reach similar conversions for the electron rich substrate. In addition to this the versatility of the system is further highlighted by the observation that we can reduce aryl iodides in the presence of both aryl bromides and chlorides as well as common NHTs and NHBoc protecting groups. As expected, we were also able to dehalogenate an activated alkenyl iodide (Table 4.2, Entry 7) using our catalytic system, as activated alkenyl C-I bonds have similar reduction potentials as aryl C-I bonds.

**Table 4.2.** Hydrodehalogenation of iodo compounds<sup>a</sup>

| Entry | Substrate | Product | Time | Yield                     |
|-------|-----------|---------|------|---------------------------|
| 1     |           |         | 15 h | 74 %                      |
| 2     |           |         | 15 h | 70 %                      |
| 3     |           |         | 15 h | 87 %                      |
| 4     |           |         | 15 h | 72 % <sup>b</sup>         |
| 5     |           |         | 15 h | 54 % <sup>b</sup>         |
| 6     |           |         | 19 h | 71 %                      |
| 7     |           |         | 15 h | 63 %<br><i>E:Z</i> = 16:1 |

<sup>a</sup>Reaction conditions: iodo compound (0.4 mmol), PtNP(0.2%)/TiO<sub>2</sub> (0.4 mmol), DIPEA (2.8 mmol), 5 mL MeCN, degassed with Argon for 15 min, and irradiated with a Luzchem solar simulator  $\lambda > 375$  nm.

<sup>b</sup>Conversion by <sup>1</sup>H NMR. Adapted with permission from McTiernan *et al.*<sup>18</sup> Copyright 2014 WILEY-VCH Verlag.

#### 4.4. Dehalogenation and Cyclization of Iodo Compounds

Having demonstrated our system capable of reductively hydrodehalogenating aryl iodides we then set out to investigate its ability to promote the intramolecular cyclization of a variety of different unactivated alkyl, alkenyl, and aryl iodides (Table 4.3). Interestingly, after 18-24 h of irradiation we

were able to efficiently cyclize all of the substrates with the exception of the unactivated alkenyl iodides (Table 4.3, entries 7 and 8). In both cases there was no observable conversion of the starting material to either of its hydrodehalogenated or cyclized products after 24 h of irradiation. These results are most likely due to the higher dissociation energy of unactivated alkenyl C(sp<sup>2</sup>)-I bonds.<sup>16,17</sup> However as previously seen in Table 4.2, the activated alkenyl iodide (entry 7) is hydrodehalogenated in 63% yield after 15 hours of irradiation. In good agreement with these results, Stephenson and co-workers have shown that under their optimized conditions using *fac*-Ir(ppy)<sub>3</sub> as photocatalyst the same activated alkenyl iodide can be hydrodehalogenated in near quantitative yield with only 2.5 hours of irradiation, whereas it takes up to 60 hours of irradiation to achieve similar conversions for unactivated alkenyl iodides.<sup>27</sup>

For the most part the cyclizations of both the aryl and alkyl iodides occurred cleanly with little or no side products. However, upon irradiation of alkyl iodide 6a, we have isolated, in addition to the desired cyclized product, its alkenyl iodide analogue (Table 4.3, entry 6b). Interestingly, isolation of this alkenyl iodide would suggest that some of the observed cyclization efficiency might actually be due to a chain mechanism derived from an atom transfer radical cyclization (ATRC), shown in Scheme 4.2.

**Table 4.3.** Dehalogenation and cyclization of iodo compounds<sup>a</sup>

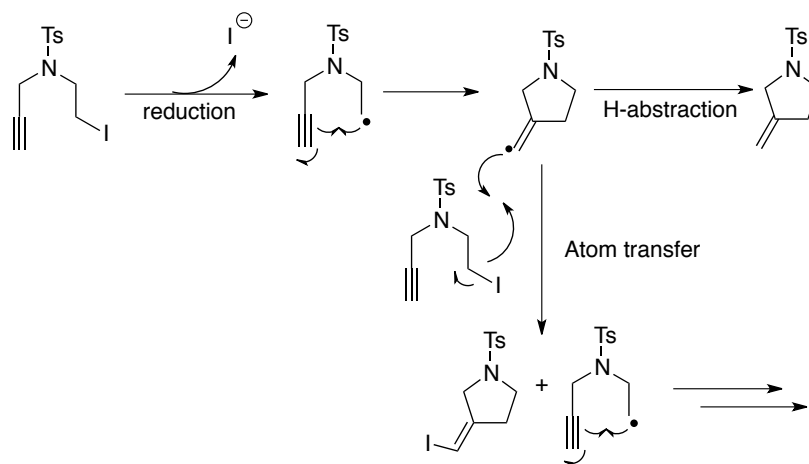
| Entry | Substrate | Product     | Time | Yield |
|-------|-----------|-------------|------|-------|
| 1     |           |             | 18 h | 74 %  |
| 2     |           |             | 20 h | 87 %  |
| 3     |           |             | 24 h | 71 %  |
| 4     |           |             | 24 h | 68 %  |
| 5     |           |             | 21 h | 73 %  |
| 6a    |           |             | 22 h | 71 %  |
| 6b    |           |             | 22 h | 9 %   |
| 7     |           | No Reaction | 24 h | NR    |
| 8     |           | No Reaction | 24 h | NR    |

<sup>a</sup>Reaction conditions: iodo compound (0.4 mmol), PtNP(0.2%)/TiO<sub>2</sub> (0.4 mmol), DIPEA (2.8 mmol), 5 mL MeCN, degassed with Argon for 15 min, and irradiated with a Luzchem solar simulator  $\lambda > 375$  nm. All yields are reported as isolated yields. Adapted with permission from McTiernan *et al.*<sup>18</sup> Copyright 2014 WILEY-VCH Verlag.

Although we have only been able to isolate the ATRC product for Table 4.3, entry 6, this may simply be due to the fact that our catalytic system cannot reduce the resulting alkenyl iodide. In other words, under the reductive conditions employed, the alkyl iodides that would form in Table 4.3, entries 1, 3-5 may be

absent due to the fact they are readily hydrodehalogenated. For this reason their absence does not necessarily rule out a possible mechanism involving ATRC.

**Scheme 4.2.** Plausible route to alkenyl iodide via ATRC. Adapted with permission from McTiernan *et al.*<sup>18</sup> Copyright 2014 WILEY-VCH Verlag.

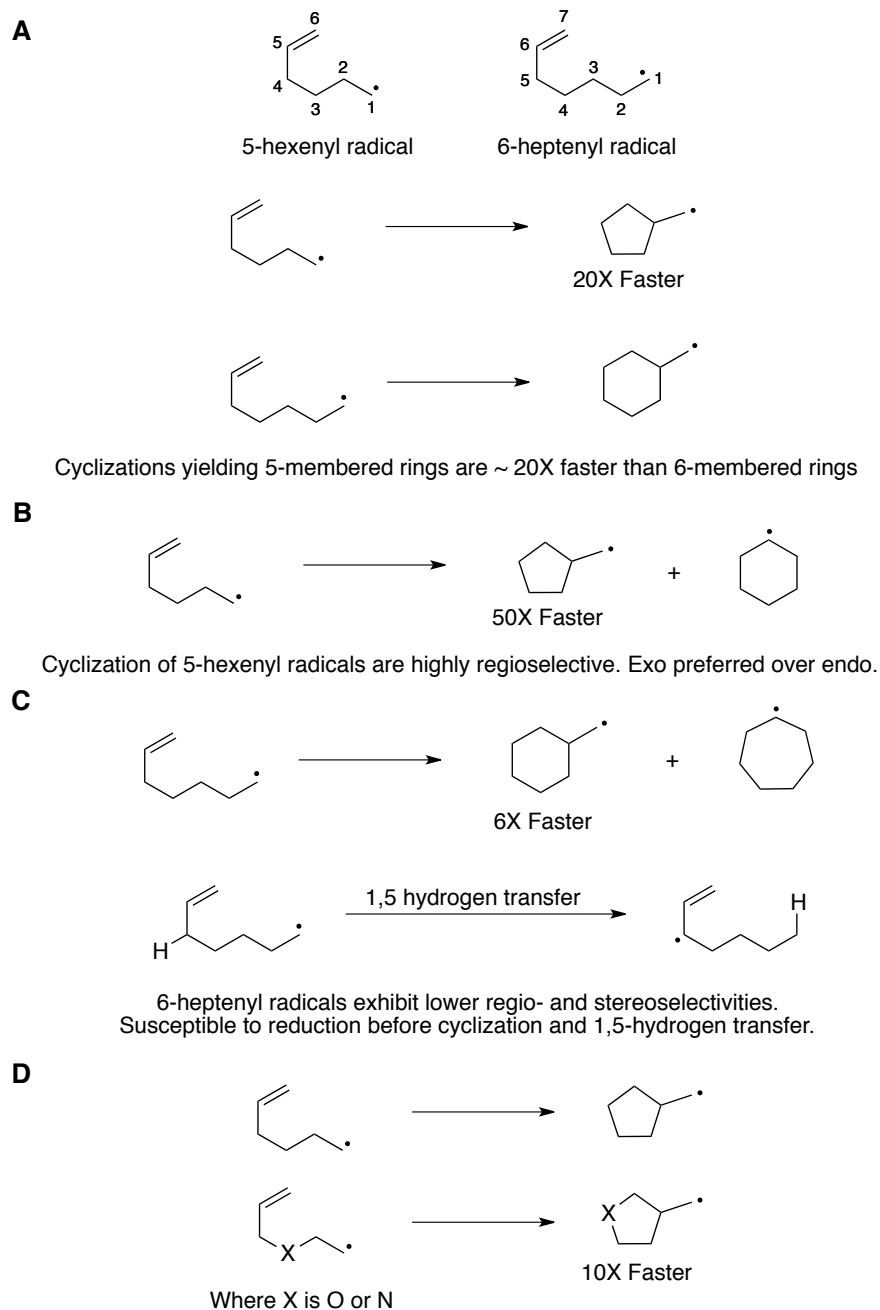


It should be mentioned that the cyclizations performed in Table 4.3 are well known reactions and that much is known about their kinetics, regioselectivity, and stereoselectivity. Upon reduction and cleavage of the C-I bond in the listed substrates one generates either 5-hexenyl or 6-heptenyl radicals. As expected, all examples of Table 4.3 that form 5-hexenyl radicals cyclize to give 5-membered rings, whereas 6-heptenyl radicals give rise to 6-membered rings. According to Beckwith the regioselectivity of the ring closure of 5-Hexenyl radicals and related species is controlled by the fact that these types of cyclizations require efficient overlap in the transition state structure between the semi-occupied molecular orbital (SOMO) and  $\pi^*$  orbitals.<sup>28,29</sup> In other words, the strain created within the 1,6-transition structure is much greater than that found in the 1,5-transition structure and that this strain energy is large enough to



outweigh the steric and thermodynamic factors that favour formation of the larger ring.<sup>28-31</sup> The regioselectivity in these types of cyclizations thus relate back to the rates at which the exo- and endo- reactions occur. It has been found that for the cyclization of 5-hexenyl radicals that the exo-mode of cyclization is approximately 50X faster than that of the endo-mode. While this difference is much smaller in 6-heptenyl radicals, with rate of formation of 6-membered species being 6X greater than that of 7-membered rings, it should be pointed out that cyclization to 5-membered rings is about 20X faster than that for 6-membered rings.<sup>32</sup> In addition to this, the cyclization of 5-hexenyl radicals are typically more stereoselective, with 1-,3-substituted analogues giving rise to cis- products and 2-,4-substituted analogues giving rise to trans- products. Part of the reason for the sluggish kinetics and lower regioselectivities and stereoselectivities in 6-membered ring formation has to do with the fact that in many cases the intermediate 6-heptenyl radical is reduced or undergoes 1,5- hydrogen transfer before the required cyclization occurs.<sup>32</sup> Interestingly, Ingold and Beckwith, have also shown that substitution of carbon for nitrogen or oxygen at the 3-position in 5-hexenyl radicals can accelerate the cyclization by a factor of 10. It is believed that the shortened C-O and C-N bonds and smaller C-O-C and C-N-C bond angles give rise to better overlap in the transition state, thus accelerating the rate of cyclization.<sup>33,34</sup> This acceleration in rate decreases the chance of hydrogen transfer and increases the regioselectivity of the cyclization as the rate of 6-endo cyclization is not enhanced.

**Scheme 4.3.** Cyclization of 5-hexenyl and 6-heptenyl radicals



Substitution of Oxygen or Nitrogen for Carbon at the 3 position of 5-hexenyl radicals accelerates cyclization 10 fold. The shortened C-O and C-N bonds as well as the smaller C-X-C angle lead to better overlap in the transition state.

## 4.5. Photocyclization of Bisenones

In addition to the cyclization of alkyl, and aryl iodides we have also been able to efficiently promote the intramolecular cyclization of aryl bisenones, which

have been previously accomplished both electrochemically and photocatalytically (Table 4.4).<sup>35,36</sup>

**Table 4.4.** Photocyclization of bisenones<sup>a</sup>

| Entry | Substrate | Product | Yield               |
|-------|-----------|---------|---------------------|
| 1a    |           |         | 51 %<br>d.r. > 10:1 |
| 1b    |           |         | 18 %<br>d.r. > 10:1 |
| 1c    |           |         | 25 %                |
| 2a    |           |         | 42 %<br>d.r. > 10:1 |
| 2b    |           |         | 31 %<br>d.r. > 10:1 |
| 2c    |           |         | 17 %                |

<sup>a</sup>Reaction conditions: bisenone ( $R^1 = \text{Ph}$ ,  $R^2 = p\text{-Cl-C}_6\text{H}_4$ ) (0.4 mmol), PtNP(0.2%)/TiO<sub>2</sub> (0.4 mmol), DIPEA (2.8 mmol), 5 mL MeCN, degassed with Argon for 15 min, and irradiated with a Luzchem solar simulator  $\lambda > 375 \text{ nm}$ . All yields are reported as isolated yields. Adapted with permission from McTiernan *et al.*<sup>18</sup> Copyright 2014 WILEY-VCH Verlag.

Upon 15 h of irradiation the bisenone substrates (Table 4.4, entries 1 and 2) undergo considerable conversion, however with little selectivity. In both cases we have been able to isolate a *cis* [2+2] cycloaddition product (Table 4.4, entries 1a and 2a), a simple reductive cyclization product (Table 4.2, entries 1b and 2b), and finally a [4+2] Diels-Alder cycloaddition product. In both cases we find the

[2+2] cycloaddition as the major isolated product. This reactivity can be explained by the presence of Lewis acidic sites on the surface of the  $\text{TiO}_2$  catalyst,<sup>37</sup> which would provide a pathway for the formation of the required radical anion upon one electron reduction.<sup>38</sup> However, we also obtain a considerable amount of the simple reductive cyclization product, which can be related to either the weak Lewis acidity of the  $\text{TiO}_2$  catalyst or the presence of reductive  $\alpha$ -aminoalkyl radicals formed upon amine oxidation. In good agreement, we have recently reported that  $\alpha$ -aminoalkyl radicals can induce the observed radical cyclization of bisenones.<sup>39</sup>

#### 4.6. Reusability

One of the major advantages of employing a heterogeneous catalyst in an organic transformation is its ease of removal and the subsequent potential for recyclability. As such, the ability of platinized  $\text{TiO}_2$  to be recovered and reused within the photoredox-mediated hydrodehalogenation of ethyl-4-iodobenzoate was examined. This substrate was selected as we had previously optimized its reaction conditions and found it to be quite selective. The PtNP@ $\text{TiO}_2$  mediated hydrodehalogenation of ethyl-4-iodobenzoate was examined over four trials using the same batch of catalyst. The conversion for each trial was obtained by  $^1\text{H}$ -NMR and calculated as 74%, 54%, 58%, and trace, respectively. The poor recyclability of the catalyst may be attributed to aggregation of the PtNP, as the aggregation of particles would lead to agglomerates, which are known to be less efficient at promoting interfacial electron transfers due to larger Schottky barriers.<sup>40</sup>

Although TEM images of the catalyst were obtained both before and after catalysis (Figure 4A.28), in neither case were we able to visualize the particles due to their small size and low loading. Therefore to confirm the presence Pt in the catalyst and to ensure that the observed decrease in efficiency was not due to leaching of Pt we have also performed ICP analysis and found that the Pt loading of the catalyst does not decrease appreciably over three trials (see appendix section for more details). The initial loading was found to be 178.5 mg Pt/100 g TiO<sub>2</sub> while the final loading after three reuses was 222.1 mg Pt/100 g TiO<sub>2</sub>. The fact that there is more Pt on the TiO<sub>2</sub> after the three reuses would indicate that there is considerable error associated with these measurements. This poor accuracy may be related to the fact that the loading of Pt on the TiO<sub>2</sub> is nearing the detection limit of the instrument.

It has also been suggested that fouling of the PtNP surface with iodine could also explain the observed decrease in efficiency. To test this hypothesis we have treated the used catalyst with potassium thiocyanate in the hope of removing any iodine bound to the surface of the PtNP. However, upon treatment not only did we not see a return to initial efficiency but the catalyst appeared to be even less efficient.

#### **4.7. Conclusions**

We have developed a highly reductive heterogeneous photoredox system around the ability of PtNP@TiO<sub>2</sub> to act as UVA/visible-light photocatalyst. Using a series of reductive transformation, which included the hydrodehalogenation of aryl and activated alkenyl iodides, the cyclization of aryl and alkyl iodides, and

lastly the cyclization of aryl bisenones; we have shown our system to be quite versatile and for the most part able to efficiently and cleanly promote the desired transformations, while offering the advantage of easy catalyst removal and simple purification.

## **4.8. Appendix**

### **4.8.A. General Information**

Substrates and Reagents: All reaction substrates were synthesized according to literature procedures or purchased from commercial suppliers and used without further purification. *N,N*-diisopropylethylamine (DIPEA) was purchased from Sigma Aldrich and purified by distillation before use. Acetonitrile (MeCN) was treated with potassium carbonate and activated 4 Å molecular sieves overnight, and was distilled under an argon atmosphere before use.

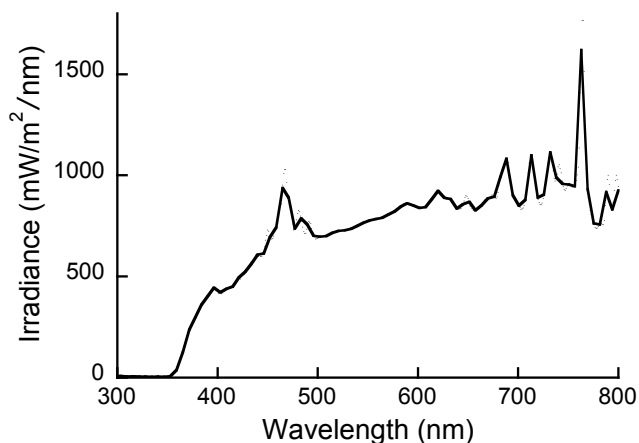
Light Source: All reactions were performed in a solar simulator (Luzchem Research Inc., Ottawa, Canada) fitted with a 375 nm long-pass cut off filter operating a power intensity of 12200 mW/m<sup>2</sup> in the UVA region and 231800 mW/m<sup>2</sup> in the visible region.

Chromatography: Flash column chromatography was performed using 230-400 mesh silica gel. Preparatory thin layer chromatography (PTLC) was performed using 1000 µm thick glass baked TLC plates purchased from Silicycle.

NMR: All <sup>1</sup>H and <sup>13</sup>C NMR were recorded on a Bruker AVANCE 400 spectrometer. Chemical shifts (δ) are reported in ppm from the solvent.

ICP: Analysis performed on a Perkin Elmer OPTIMA 2000 DV, samples were prepared via microwave-assisted acid digestion.

#### 4.8.B. Output Spectrum of Solar Simulator with 375 nm Long Pass Filter



**Figure 4A.1.** Output spectrum of solar simulator with 375 nm long pass filter used for irradiation of reaction mixtures.

#### 4.8.C. Synthesis of Pt(0.2%)NP@TiO<sub>2</sub>

A solution containing 60 mg of H<sub>2</sub>PtCl<sub>6</sub>, 60 ml of a 1% sodium citrate solution, and 240 ml of H<sub>2</sub>O were refluxed for 4 h. A third (100 ml) of the resultant Pt solution was stirred with 2 g of the TiO<sub>2</sub> (P25) and 10 g of NaCl was added. The suspension was stirred for 3 h and then subjected to centrifugation. The obtained Pt(0.2%)NP@TiO<sub>2</sub> powder was washed with water and dried at 40.0 °C.

#### 4.8.D. Diffuse reflectance spectrum of $\text{TiO}_2$ and $\text{Pt}(0.2\%)\text{NP@TiO}_2$

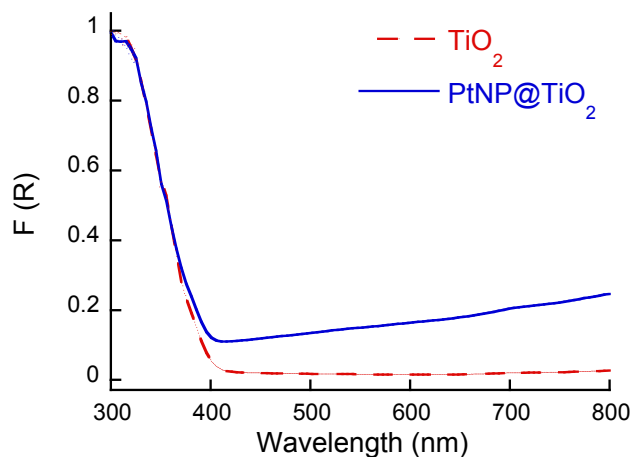


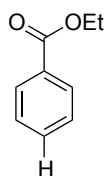
Figure 4A.2. Normalized diffuse reflectance spectrum of  $\text{TiO}_2$  and  $\text{PtNP@TiO}_2$

#### 4.8.E. General Procedure for the Photocatalyzed Reductive Dehalogenations and Cyclizations

A 10 mL schlenk tube was charged with  $\text{PtNP}(0.2\%)\text{@TiO}_2$  (32 mg, 0.4 mmol, 1 eq), substrate (0.4 mmol, 1 eq), and 5 mL of freshly distilled MeCN. The mixture was degassed with Ar for 30 min. Freshly distilled DIPEA (0.5 mL, 2.8 mmol, 7 eq) was added and the suspension was sonicated for 2 min. After dispersion of catalyst, the reaction mixture was irradiated with a solar simulator with 375 nm cut off filter for 15 h – 24 h. The solid catalyst was separated by centrifugation and crude product was obtained after solvent evaporation.

Control experiments (including using  $\text{TiO}_2$  (without PtNP), dark and no amine) were carried out under above conditions.

#### [Table 4.2, entry 1 Product]<sup>41</sup>



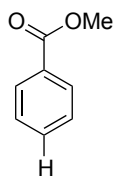
According to the general procedure, ethyl 4-iodobenzoate (110 mg, 0.4 mmol),  $\text{PtNP@TiO}_2$  (32 mg, 0.4 mmol) and DIPEA (0.5 mL, 2.8 mmol) in MeCN (5 mL) afforded the title compound (50 mg, 84% isolated yield) after purification by column chromatography (95:5 Hexanes:EtOAc).



$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 1.38 (t,  $J=7.0$  Hz, 3 H) 4.37 (q,  $J=7.0$  Hz, 2 H) 7.32 - 7.46 (m, 2 H) 7.48 - 7.58 (m, 1 H) 7.96 - 8.11 (m, 2 H)

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 166.4, 132.6, 130.4, 129.4, 128.2, 60.8, 14.2

**[Table 4.2, entry 2 Product]<sup>27</sup>**

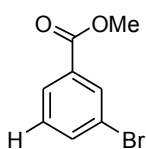


According to the general procedure, methyl 4-iodobenzoate (105 mg, 0.4 mmol),  $\text{PtNP@TiO}_2$  (32 mg, 0.4 mmol) and DIPEA (0.5 mL, 2.8 mmol) in MeCN (5 mL) afforded the title compound (38 mg, 70% isolated yield) after purification by column chromatography (4:1 Hexanes:EtOAc).

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 3.89 (s, 3 H) 7.38 - 7.44 (m, 2 H) 7.50 - 7.56 (m, 1 H) 8.00 - 8.04 (m, 2 H)

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 166.9, 132.7, 130.0, 129.4, 128.2, 51.9

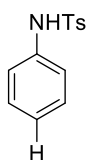
**[Table 4.2, entry 3 Product]<sup>27</sup>**



According to the general procedure, methyl 5-bromo-3-iodobenzoate (136 mg, 0.4 mmol),  $\text{PtNP@TiO}_2$  (32 mg, 0.4 mmol) and DIPEA (0.5 mL, 2.8 mmol) in MeCN (5 mL) afforded the title compound (75 mg, 87% isolated yield) after purification by column chromatography (95:5 Hexanes:EtOAc).

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 3.90 (s, 3 H) 7.30 (t,  $J=8.0$  Hz, 1 H) 7.62 - 7.70 (m, 1 H) 7.95 (dt,  $J=8.0, 1.5$  Hz, 1 H) 8.16 (t,  $J=1.5$  Hz, 1 H)

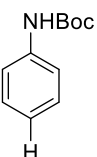
**[Table 4.2, entry 4 Product]<sup>27</sup>**



According to the general procedure, *N*-(4-iodophenyl)-4-methylbenzenesulfonamide (149 mg, 0.4 mmol),  $\text{PtNP@TiO}_2$  (32 mg, 0.4 mmol) and DIPEA (0.5 mL, 2.8 mmol) in MeCN (5 mL) afforded the title compound (72% conversion by  $^1\text{H}$  NMR).

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 2.39 (s, 3 H) 6.51-6.63 (br. s., 1 H), 7.07 (d,  $J=8.5$  Hz, 2 H) 7.12 (t,  $J=7.5$  Hz, 1 H) 7.21-7.27 (m, 4 H) 7.65 (d,  $J=8.5$  Hz, 2 H)

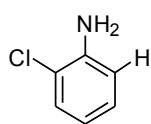
**[Table 4.2, entry 5 Product]<sup>27</sup>**



According to the general procedure, *tert*-butyl (4-iodophenyl)carbamate (128 mg, 0.4 mmol),  $\text{PtNP@TiO}_2$  (32 mg, 0.4 mmol) and DIPEA (0.5 mL, 2.8 mmol) in MeCN (5 mL) afforded the title compound (54% conversion by  $^1\text{H}$  NMR).

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ ppm 1.53 (s, 9 H) 6.45-6.55 (br. s., 1 H) 7.01-7.07 (m, 1 H) 7.27-7.32 (m, 2 H) 7.37 (d, *J*=8.0 Hz, 2 H)

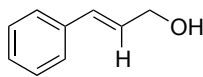
**[Table 4.2, entry 6 Product]<sup>27</sup>**



According to the general procedure, 2-chloro-6-iodoaniline (101 mg, 0.4 mmol), PtNP@TiO<sub>2</sub> (32 mg, 0.4 mmol) and DIPEA (0.5 mL, 2.8 mmol) in MeCN (5 mL) afforded the title compound (36 mg, 71% isolated yield) after purification by column chromatography (9:1 Hexanes:EtOAc).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ ppm 3.60 (br. s., 2 H) 6.54 (ddd, *J*=8.0, 2.0, 1.0 Hz, 1 H) 6.67 (t, *J*=2.0 Hz, 1 H) 6.70 - 6.77 (m, 1 H) 7.06 (t, *J*=8.0 Hz, 1 H)

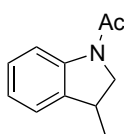
**[Table 4.2, entry 7 Product]<sup>27</sup>**



According to the general procedure, (z)-2-iodo-3-phenylprop-2-en-1-ol (104 mg, 0.4 mmol), PtNP@TiO<sub>2</sub> (32 mg, 0.4 mmol) and DIPEA (0.5 mL, 2.8 mmol) in MeCN (5 mL) afforded the title compound (34 mg, 63% isolated yield) after purification by column chromatography (4:1 Hexanes:EtOAc).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ ppm 1.53 (br. s., 1 H) 4.31 (dd, *J*=5.5, 1.5 Hz, 2 H) 6.36 (dt, *J*=16.0, 5.5 Hz, 1 H) 6.61 (d, *J*=16.0 Hz, 1 H) 7.19 - 7.23 (m, 1 H) 7.28 - 7.33 (m, 3 H) 7.35 - 7.39 (m, 2 H)

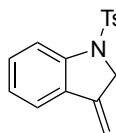
**[Table 4.3, entry 1 Product]<sup>17</sup>**



According to the general procedure, *N*-allyl-*N*-(2-iodophenyl)acetamide (120 mg, 0.4 mmol), PtNP@TiO<sub>2</sub> (32 mg, 0.4 mmol) and DIPEA (0.5 mL, 2.8 mmol) in MeCN (5 mL) afforded the title compound (55 mg, 78% isolated yield) after purification by column chromatography (9:1 Hexanes:EtOAc).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ ppm 1.36 (d, *J*=6.66 Hz, 3 H) 2.23 (s, 3 H) 3.45 - 3.54 (m, 1 H) 3.54 - 3.61 (m, 1 H) 4.21 (t, *J*=9.71 Hz, 1 H) 7.04 (t, *J*=7.38 Hz, 1 H) 7.14 - 7.23 (m, 3 H) 8.17 - 8.22 (m, 1 H)

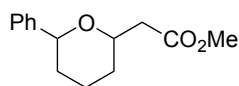
**[Table 4.3, entry 2 Product]<sup>42</sup>**



According to the general procedure, *N*-(2-iodophenyl)-4-methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide (165 mg, 0.4 mmol), PtNP@TiO<sub>2</sub> (32 mg, 0.4 mmol) and DIPEA (0.5 mL, 2.8 mmol) in MeCN (5 mL) afforded the title compound (86 mg, 75% isolated yield) after purification by column chromatography (9:1 Hexanes:EtOAc).

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 2.35 - 2.39 (m, 3 H) 4.54 (t,  $J=3.0$  Hz, 2 H) 4.98 (t,  $J=2.5$  Hz, 1 H) 5.37 (t,  $J=3.0$  Hz, 1 H) 7.01 (td,  $J=7.5$ , 1.0 Hz, 1 H) 7.20 - 7.29 (m, 3 H) 7.34 (dd,  $J=7.5$ , 0.5 Hz, 1 H) 7.66 - 7.74 (m, 3 H)

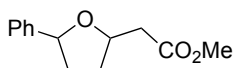
**[Table 4.3, entry 3 Product]<sup>17</sup>**



According to the general procedure, (*E*)-methyl 3-(4-iodo-1-phenylbutoxy)acrylate (144 mg, 0.4 mmol), PtNP@TiO<sub>2</sub> (32 mg, 0.4 mmol) and DIPEA (0.5 mL, 2.8 mmol) in MeCN (5 mL) afforded the title compound (59 mg, 63% isolated yield) after purification by column chromatography (5:1 Hexanes:EtOAc).

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 1.34 (dd,  $J=11.0$ , 4.0 Hz, 1 H) 1.42 - 1.54 (m, 1 H) 1.64 - 1.79 (m, 2 H) 1.80 - 1.89 (m, 1 H) 1.90 - 1.98 (m, 1 H) 2.47 (dd,  $J=15.0$ , 6.0 Hz, 1 H) 2.65 (dd,  $J=15.0$ , 7.0 Hz, 1 H) 3.66 (s, 3 H) 3.91 - 4.01 (m, 1 H) 4.39 (dd,  $J=11.0$ , 2.0 Hz, 1 H) 7.19 - 7.35 (m, 5 H)

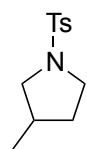
**[Table 4.3, entry 4 Product]<sup>17</sup>**



According to the general procedure, (*E*)-methyl 3-(3-iodo-1-phenylpropoxy)acrylate (138 mg, 0.4 mmol), PtNP@TiO<sub>2</sub> (32 mg, 0.4 mmol) and DIPEA (0.5 mL, 2.8 mmol) in MeCN (5 mL) afforded the title compound (60 mg, 68% isolated yield) after purification by column chromatography (5:1 Hexanes:EtOAc).

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 1.67 - 1.88 (m, 2 H) 2.16 - 2.23 (m, 1 H) 2.24 - 2.37 (m, 1 H) 2.59 (dd,  $J=15.0$ , 6.5 Hz, 1 H) 2.77 (dd,  $J=15.0$ , 6.5 Hz, 1 H) 3.69 (s, 3 H) 4.44 (p,  $J=6.5$  Hz, 1 H) 4.89 (t,  $J=7.0$  Hz, 1 H) 7.19 - 7.35 (m, 5 H)

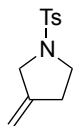
**[Table 4.3, entry 5 Product]<sup>27</sup>**



According to the general procedure, *N*-allyl-*N*-(2-iodoethyl)-4-methylbenzenesulfonamide (146 mg, 0.4 mmol), PtNP@TiO<sub>2</sub> (32 mg, 0.4 mmol) and DIPEA (0.5 mL, 2.8 mmol) in MeCN (5 mL) afforded the title compound (70 mg, 73% isolated yield) after purification by column chromatography (9:1 Hexanes:EtOAc).

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 0.91 (d,  $J=6.5$  Hz, 3 H) 1.28 - 1.41 (m, 1 H) 1.82 - 1.97 (m, 1 H) 2.11 (dd,  $J=15.0$ , 7.5 Hz, 1 H) 2.43 (s, 3 H) 2.74 (dd,  $J=9.5$ , 7.5 Hz, 1 H) 3.21 (ddd,  $J=9.5$ , 8.0, 7.5 Hz, 1 H) 3.34 (ddd,  $J=9.5$ , 8.0, 4.0 Hz, 1 H) 3.42 (dd,  $J=9.5$ , 7.5 Hz, 1 H) 7.27 - 7.37 (m, 2 H) 7.68 - 7.76 (m, 2 H)

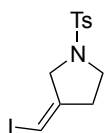
**[Table 4.3, entry 6a Product]<sup>27</sup>**



According to the general procedure, *N*-(2-iodoethyl)-4-methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide (145 mg, 0.4 mmol), PtNP@TiO<sub>2</sub> (32 mg, 0.4 mmol) and DIPEA (0.5 mL, 2.8 mmol) in MeCN (5 mL) afforded the title compound (67 mg, 71% isolated yield) after purification by column chromatography (7:1 Hexanes:EtOAc).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ ppm 2.40 - 2.43 (s, 3 H) 2.43 - 2.49 (m, 2 H) 3.23 - 3.36 (m, 2 H) 3.73 - 3.80 (m, 2 H) 4.84 - 4.95 (m, 2 H) 7.28 - 7.37 (m, 2 H) 7.62 - 7.77 (m, 2 H)

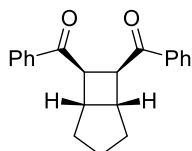
**[Table 4.3, entry 6b Product]<sup>27</sup>**



According to the general procedure, *N*-(2-iodoethyl)-4-methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide (145 mg, 0.4 mmol), PtNP@TiO<sub>2</sub> (32 mg, 0.4 mmol) and DIPEA (0.5 mL, 2.8 mmol) in MeCN (5 mL) afforded the title compound (13 mg, 9% isolated yield) after purification by column chromatography (7:1 Hexanes:EtOAc).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ ppm 2.45 (s, 3 H) 2.48 - 2.61 (m, 2 H) 3.41 (t, *J*=7.0 Hz, 2 H) 3.73 (dt, *J*=2.5, 1.5 Hz, 2 H) 6.00 (quin, *J*=2.5 Hz, 1 H) 7.36 (d, *J*=8.0 Hz, 2 H) 7.66 - 7.79 (m, 2 H)

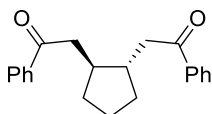
**[Table 4.4, entry 1a Product]<sup>36</sup>**



According to the general procedure, *E,E*-1,7-dibenzoyl-1,6-heptadiene (122 mg, 0.4 mmol), PtNP@TiO<sub>2</sub> (32 mg, 0.4 mmol) and DIPEA (0.5 mL, 2.8 mmol) in MeCN (5 mL) afforded the title compound (62 mg, 51% isolated yield) after purification by column chromatography (5:1 Hexanes:EtOAc).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ ppm 1.63 - 1.78 (m, 2 H) 1.81 - 1.90 (m, 2 H) 1.98 - 2.10 (m, 2 H) 3.21 (td, *J*=4.0, 2.5 Hz, 2 H) 3.86 (d, *J*=4.0 Hz, 2 H) 7.32 - 7.40 (m, 4 H) 7.42 - 7.49 (m, 2 H) 7.72 - 7.80 (m, 4 H)

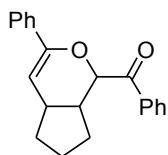
**[Table 4.4, entry 1b Product]<sup>36</sup>**



According to the general procedure, *E,E*-1,7-dibenzoyl-1,6-heptadiene (122 mg, 0.4 mmol), PtNP@TiO<sub>2</sub> (32 mg, 0.4 mmol) and DIPEA (0.5 mL, 2.8 mmol) in MeCN (5 mL) afforded the title compound (22 mg, 18% isolated yield) after purification by column chromatography (5:1 Hexanes:EtOAc).

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 1.28 - 1.35 (m, 2 H) 1.60 - 1.70 (m, 2 H) 1.95 - 2.05 (m, 2 H) 2.13 - 2.26 (m, 2 H) 2.96 (dd,  $J=16.5$ , 8.5 Hz, 2 H) 3.21 (dd,  $J=16.5$ , 4.5 Hz, 2 H) 7.43 - 7.50 (m, 4 H) 7.53 - 7.60 (m, 2 H) 7.96 (d,  $J=9.0$  Hz, 4 H)

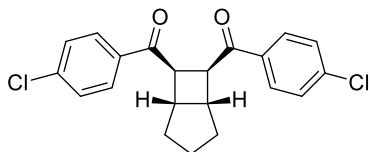
**[Table 4.4, entry 1c Product]<sup>36</sup>**



According to the general procedure, *E,E*-1,7-dibenzoyl-1,6-heptadiene (122 mg, 0.4 mmol), PtNP@TiO<sub>2</sub> (32 mg, 0.4 mmol) and DIPEA (0.5 mL, 2.8 mmol) in MeCN (5 mL) afforded the title compound (30 mg, 25% isolated yield) after purification by column chromatography (5:1 Hexanes:EtOAc).

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 1.36 - 1.82 (m, 4H) 2.01 (d,  $J=7.5$  Hz, 2 H) 2.70 (dd,  $J=7.0$ , 3.5 Hz, 2 H) 4.89 (d,  $J=7.0$  Hz, 1 H) 5.52 (d,  $J=4.0$  Hz, 1 H) 7.21 - 7.32 (m, 3 H) 7.44 - 7.53 (m, 4 H) 8.06 - 8.11 (m, 2 H)

**[Table 4.4, entry 2a Product]<sup>36</sup>**

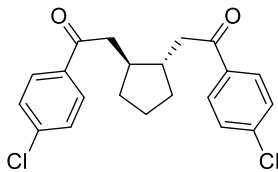


According to the general procedure, *E-E*-1,7-bis(4-chlorobenzoyl)-1,6-heptadiene (149 mg, 0.4 mmol), PtNP@TiO<sub>2</sub> (32 mg, 0.4 mmol) and DIPEA (0.5 mL, 2.8 mmol) in MeCN (5 mL) afforded the title compound (63 mg, 42% isolated yield) after purification by column chromatography (5:1

Hexanes:EtOAc).

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 1.62 - 1.77 (m, 3 H) 1.78 - 1.91 (m, 2 H) 1.95 - 2.09 (m, 2 H) 3.18 (td,  $J=4.5$ , 2.5 Hz, 2 H) 3.74 - 3.83 (m, 2 H) 7.29 - 7.38 (m, 4 H) 7.64 - 7.74 (m, 4 H)

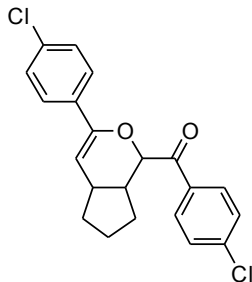
**[Table 4.4, entry 2b Product]<sup>36</sup>**



According to the general procedure, *E-E*-1,7-bis(4-chlorobenzoyl)-1,6-heptadiene (149 mg, 0.4 mmol), PtNP@TiO<sub>2</sub> (32 mg, 0.4 mmol) and DIPEA (0.5 mL, 2.8 mmol) in MeCN (5 mL) afforded the title compound (63 mg, 42% isolated yield) after purification by column chromatography (5:1 Hexanes:EtOAc).

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 1.27 (dq,  $J=12.5$ , 8.0 Hz, 2 H) 1.53 - 1.71 (m, 2 H) 1.97 (dq,  $J=13.0$ , 6.5 Hz, 2 H) 2.09 - 2.25 (m, 2 H) 2.91 (dd,  $J=16.5$ , 8.0 Hz, 2 H) 3.15 (dd,  $J=16.5$ , 5.0 Hz, 2 H) 7.36 - 7.48 (m, 4 H) 7.84 - 7.97 (m, 4 H)

**[Table 4.4, entry 2c Product]<sup>36</sup>**



According to the general procedure, E-E-1,7-bis(4-chlorobenzoyl)-1,6-heptadiene (149 mg, 0.4 mmol), PtNP@TiO<sub>2</sub> (32 mg, 0.4 mmol) and DIPEA (0.5 mL, 2.8 mmol) in MeCN (5 mL) afforded the title compound (63 mg, 42% isolated yield) after purification by column chromatography (5:1 Hexanes:EtOAc).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ ppm 1.29 - 1.50 (m, 2 H) 1.75 (dt, *J*=8.0, 4.0 Hz, 2 H) 1.92 - 2.10 (m, 2 H) 2.60 - 2.73 (m, 2 H) 4.81 (d, *J*=7.0 Hz, 1 H) 5.51 (d, *J*=4.0 Hz, 1 H) 7.16 - 7.30 (m, 4 H) 7.37 - 7.56 (m, 4 H) 7.96 - 8.08 (m, 2 H)

**4.8.F. Catalyst Reusability**

A 10 mL schlenk tube was charged with PtNP(0.2%)@TiO<sub>2</sub> (32 mg, 0.4 mmol, 1 eq), ethyl 4-iodobenzoate (110 mg, 0.4 mmol, 1 eq), and 5 mL of freshly distilled MeCN. The mixture was degassed with Ar for 30 min. Freshly distilled *i*Pr<sub>2</sub>NEt (0.5 mL, 2.8 mmol, 7 eq) was added and the suspension was sonicated for 2 min. After dispersion of catalyst, the reaction mixture was irradiated with a solar simulator with 375 nm cut off filter for 15 h. The solid catalyst was separated by centrifugation and crude product was obtained after solvent evaporation. The recovered PtNP@TiO<sub>2</sub> was then placed in a 10 mL schlenk tube and dried under ultra-high vacuum for roughly 30 minutes. This procedure was repeated for a total of three reusability trials.

#### 4.8.G. NMR Data

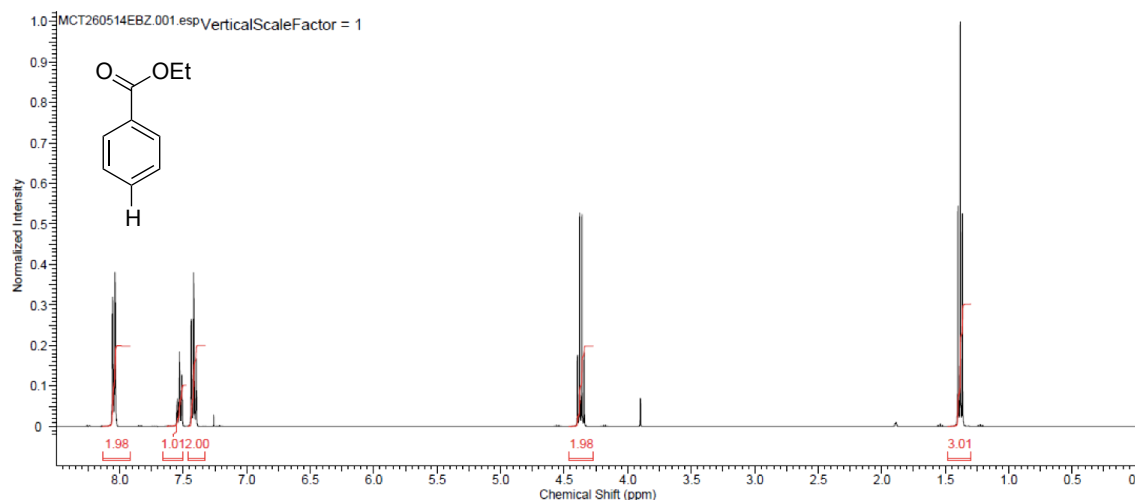


Figure 4A.6.  $^1\text{H}$  NMR of [Table 4.2 entry 1 Product] in  $\text{CDCl}_3$ .

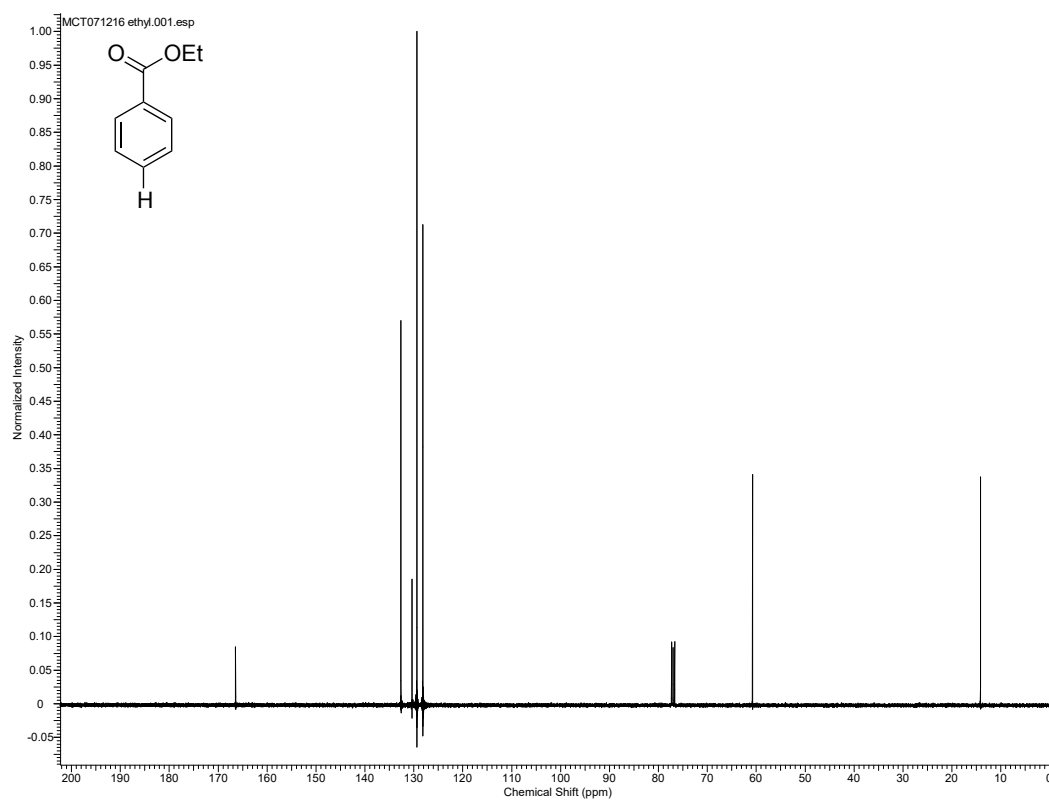
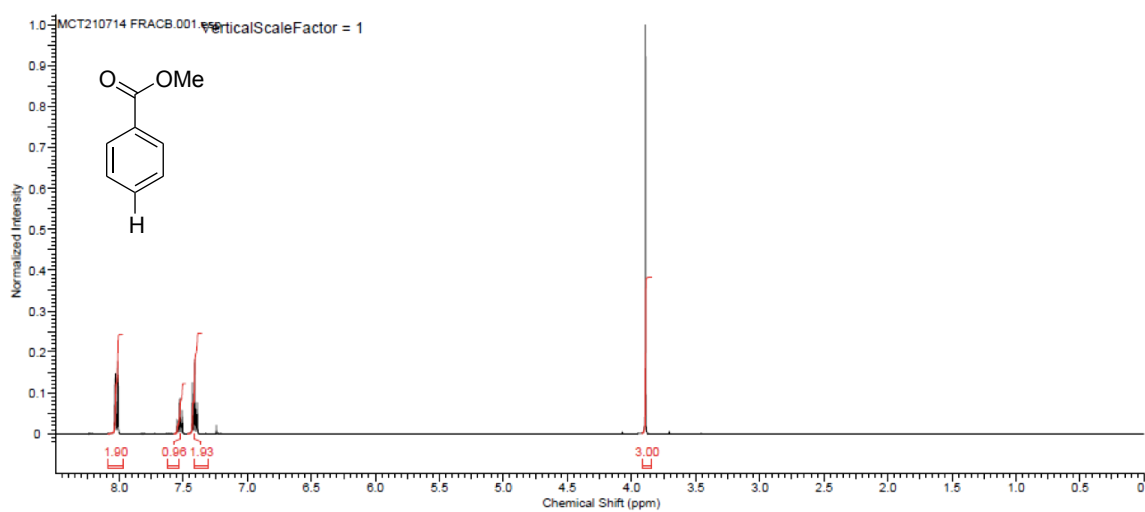
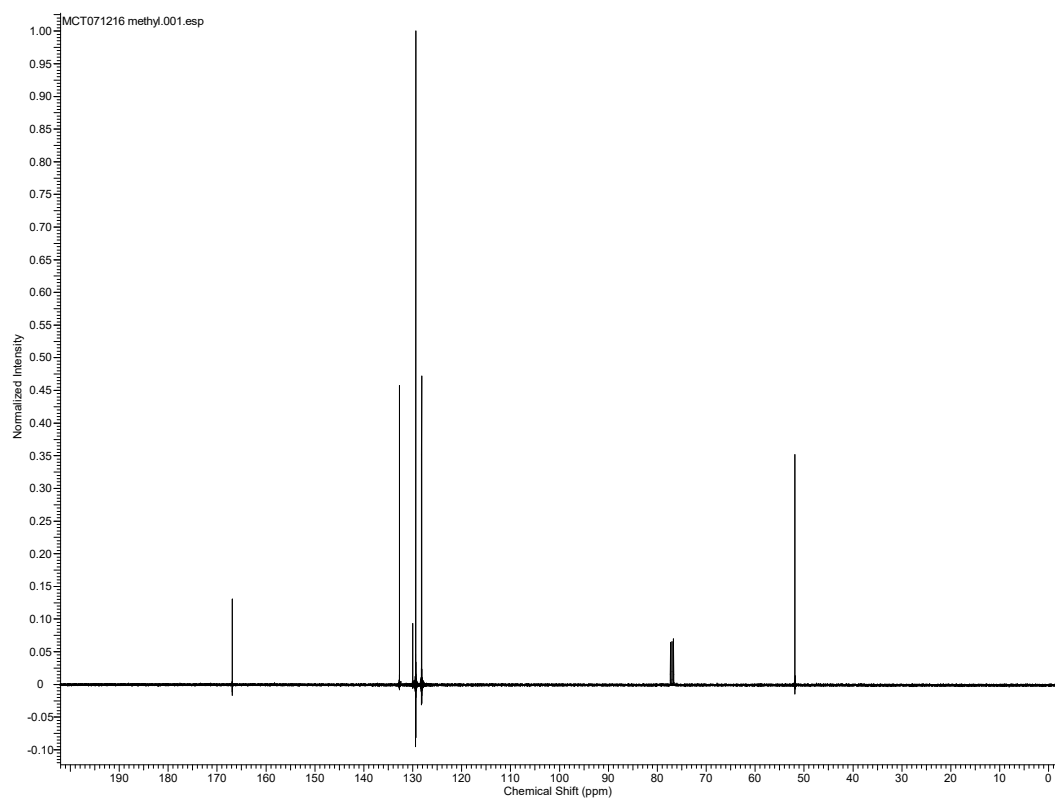


Figure 4A.7.  $^{13}\text{C}$  NMR of [Table 4.2 entry 1 Product] in  $\text{CDCl}_3$ .



**Figure 4A.8.**  $^1\text{H}$  NMR of [Table 4.2 entry 2 Product] in  $\text{CDCl}_3$ .



**Figure 4A.9.**  $^{13}\text{C}$  NMR of [Table 4.2 entry 2 Product] in  $\text{CDCl}_3$ .



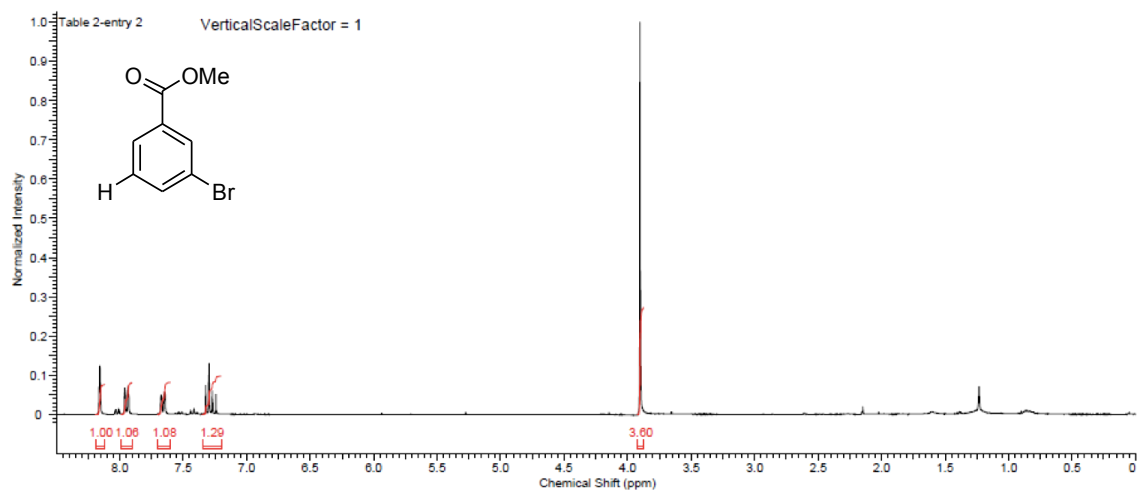


Figure 4A.10.  $^1\text{H}$  NMR of [Table 4.2 entry 3 Product] in  $\text{CDCl}_3$ .

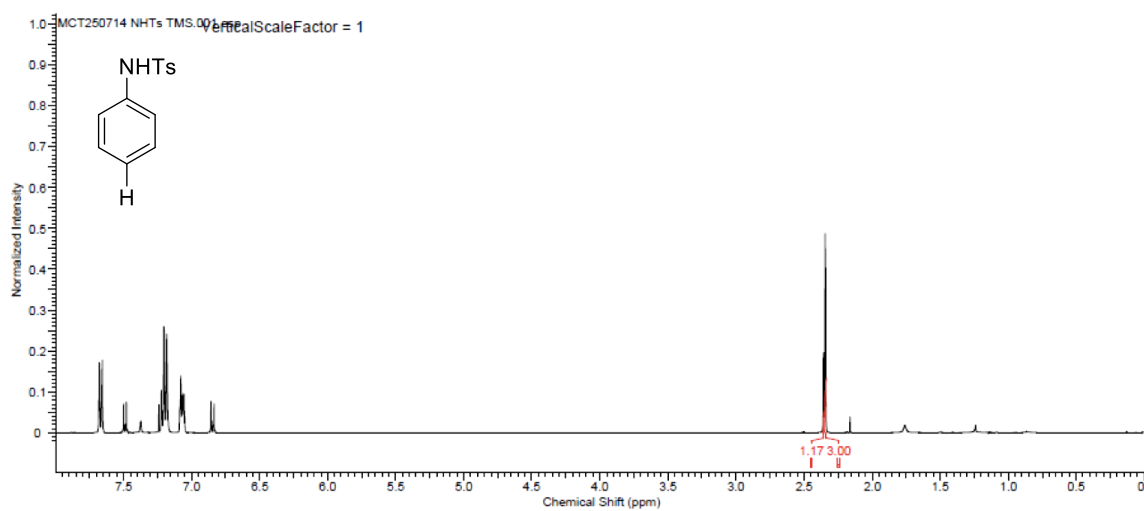


Figure 4A.11.  $^1\text{H}$  NMR of [Table 4.2 entry 4 Product] in  $\text{CDCl}_3$ .

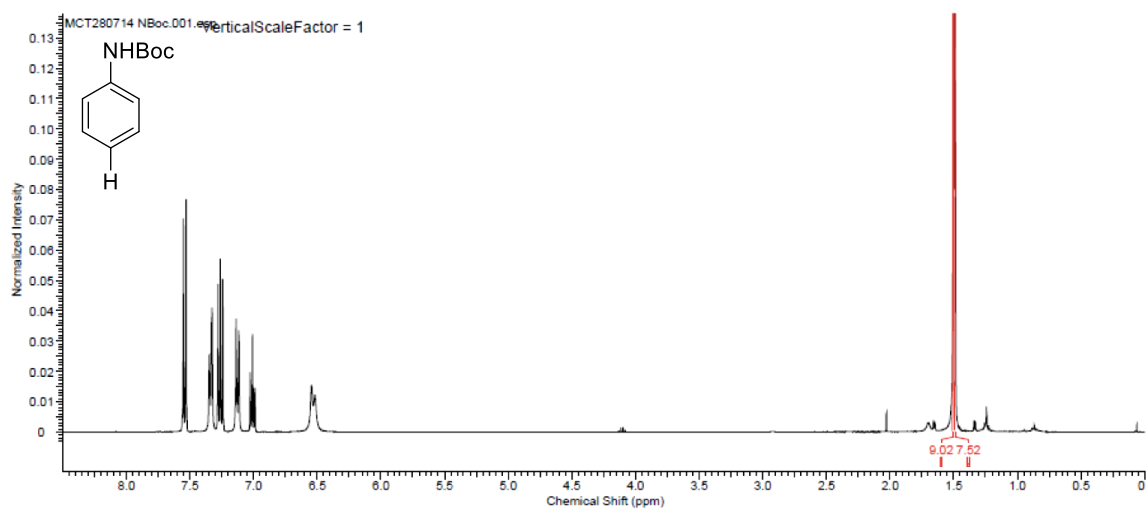


Figure 4A.12.  $^1\text{H}$  NMR of [Table 4.2 entry 5 Product] in  $\text{CDCl}_3$ .

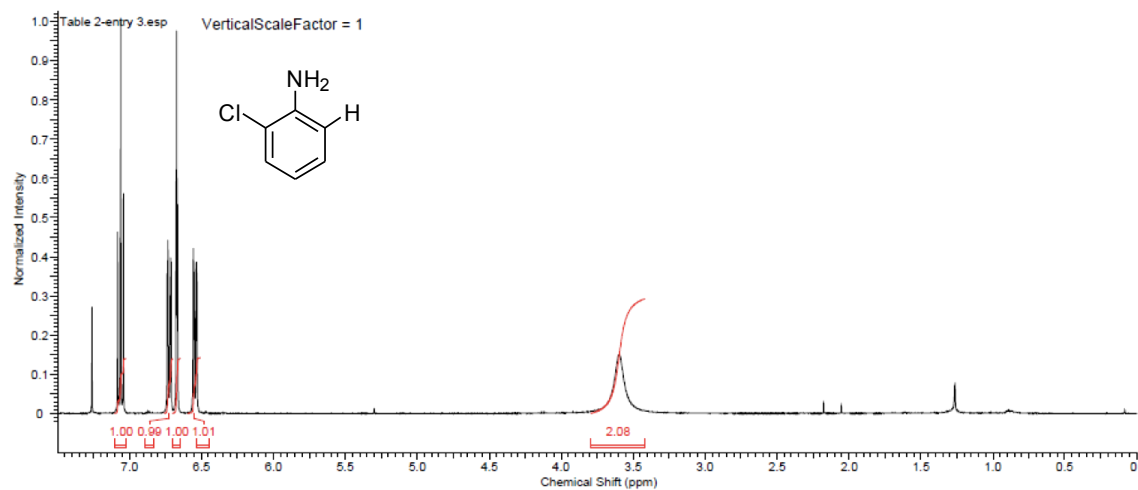


Figure 4A.13.  $^1\text{H}$  NMR of [Table 4.2 entry 6 Product] in  $\text{CDCl}_3$ .

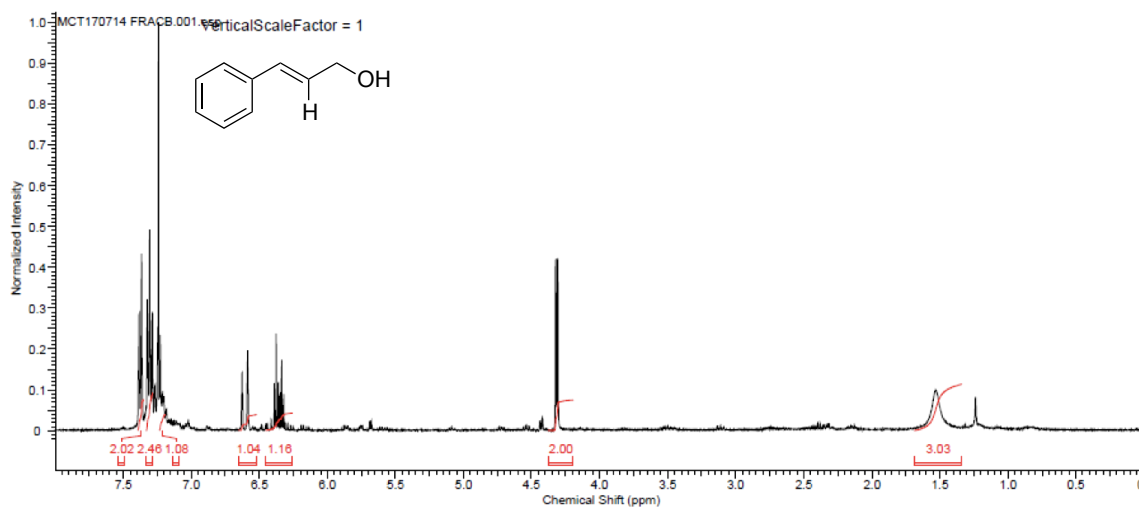


Figure 4A.14.  $^1\text{H}$  NMR of [Table 4.2 entry 7 Product] in  $\text{CDCl}_3$ .

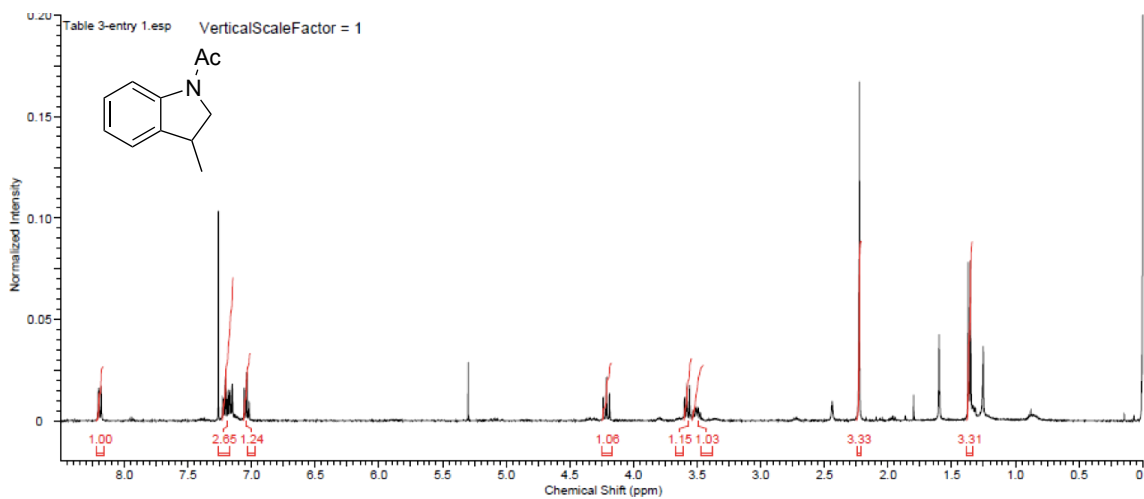


Figure 4A.15.  $^1\text{H}$  NMR of [Table 4.3 entry 1 Product] in  $\text{CDCl}_3$ .

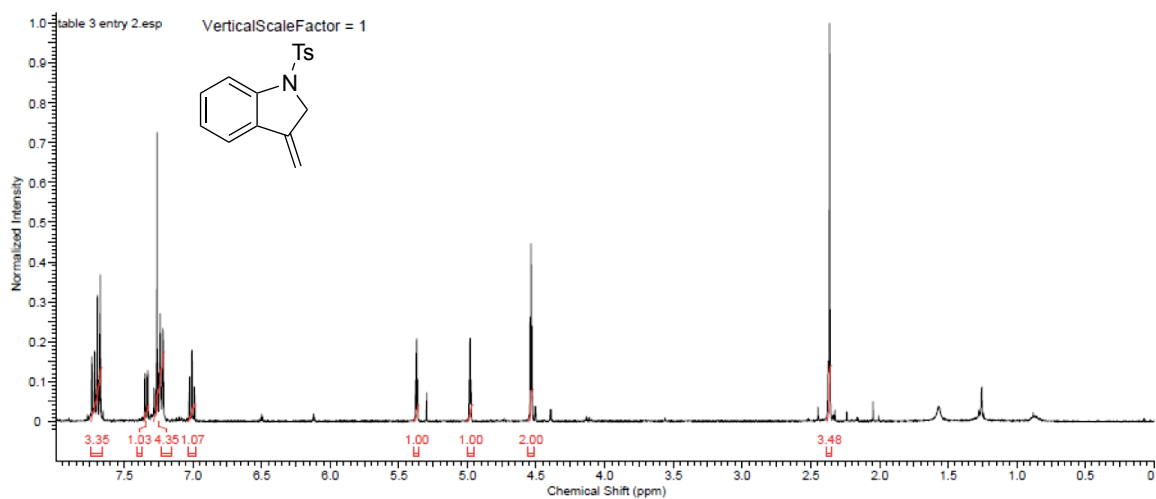


Figure 4A.16.  $^1\text{H}$  NMR of [Table 4.3 entry 2 Product] in  $\text{CDCl}_3$ .

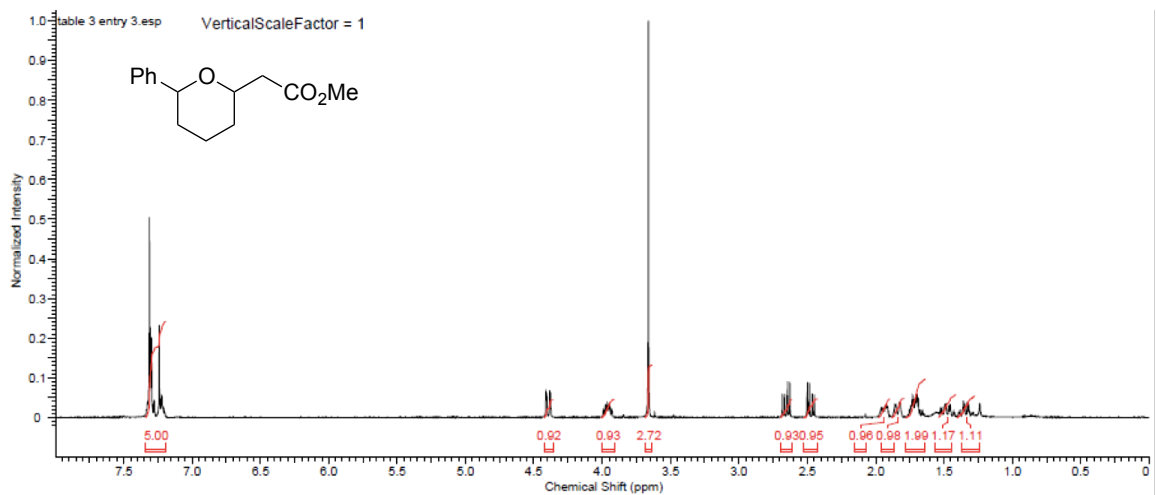


Figure 4A.17.  $^1\text{H}$  NMR of [Table 4.3 entry 3 Product] in  $\text{CDCl}_3$ .

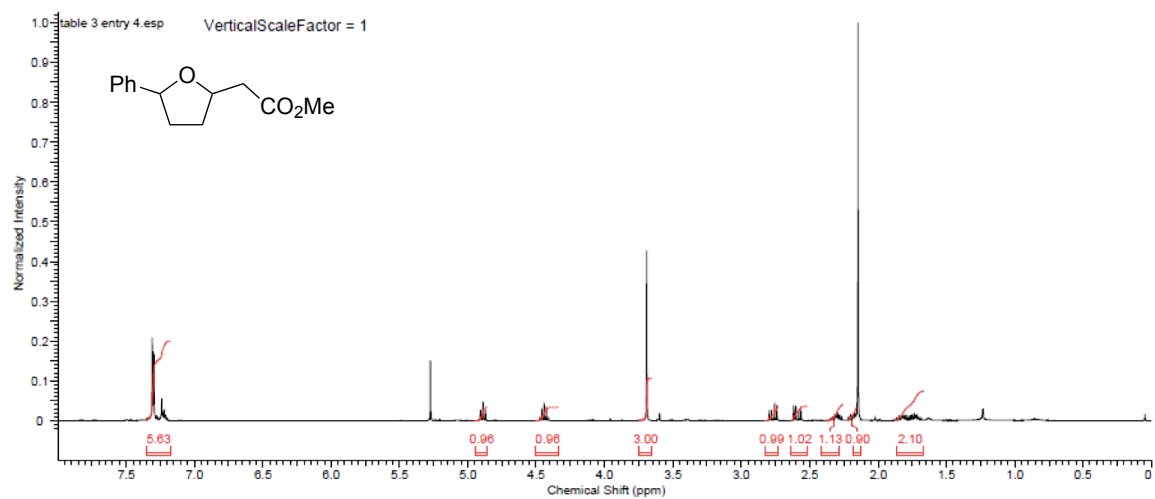


Figure 4A.18.  $^1\text{H}$  NMR of [Table 4.3 entry 4 Product] in  $\text{CDCl}_3$ .

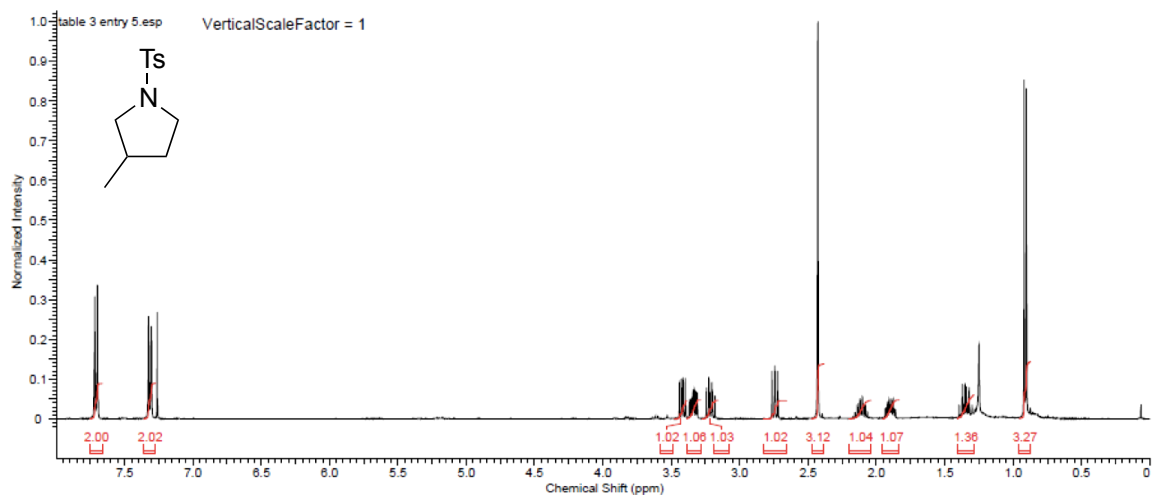


Figure 4A.19.  $^1\text{H}$  NMR of [Table 4.3 entry 5 Product] in  $\text{CDCl}_3$ .

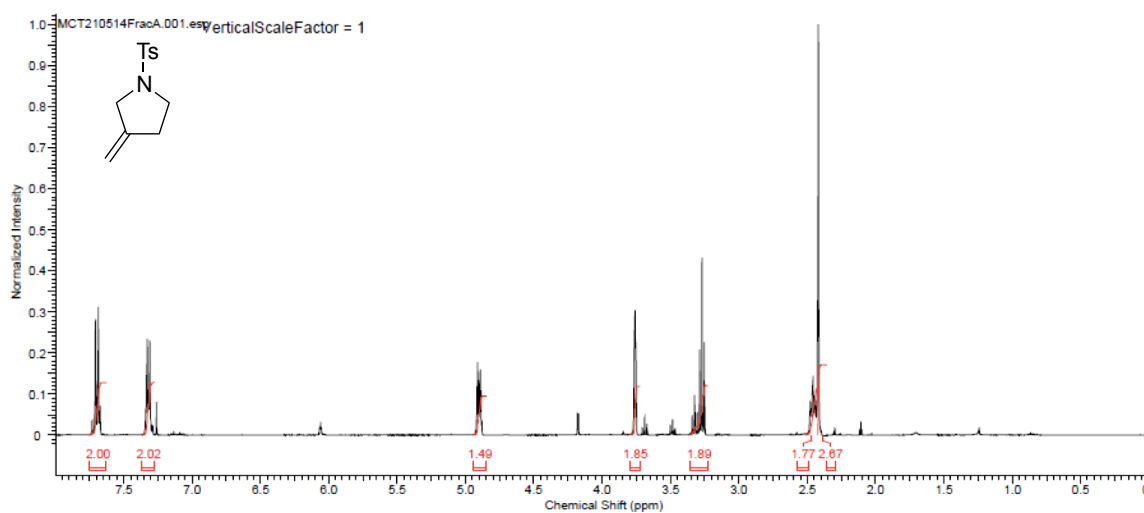


Figure 4A.20.  $^1\text{H}$  NMR of [Table 4.3 entry 6a Product] in  $\text{CDCl}_3$ .

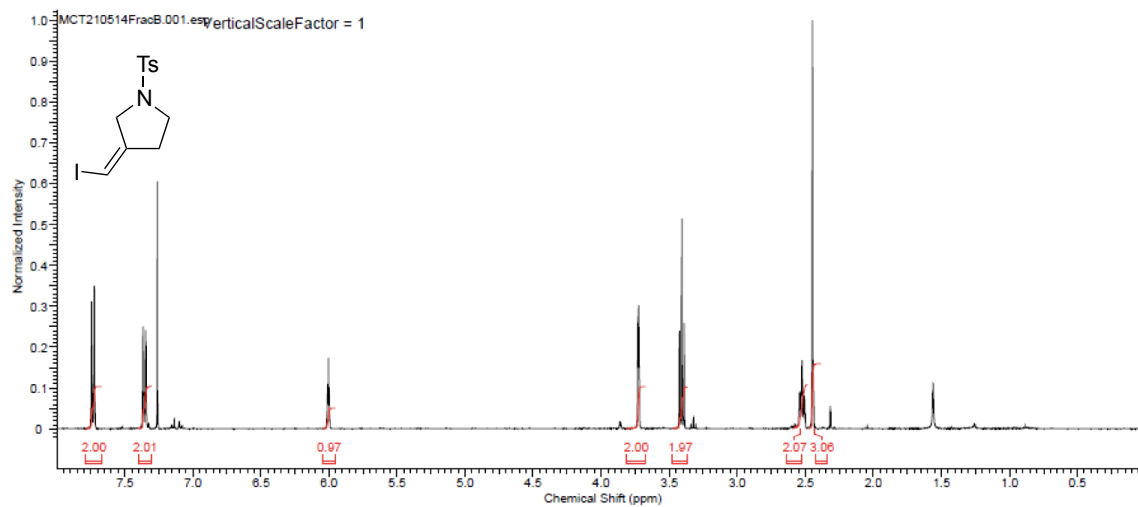


Figure 4A.21.  $^1\text{H}$  NMR of [Table 4.3 entry 6b Product] in  $\text{CDCl}_3$ .

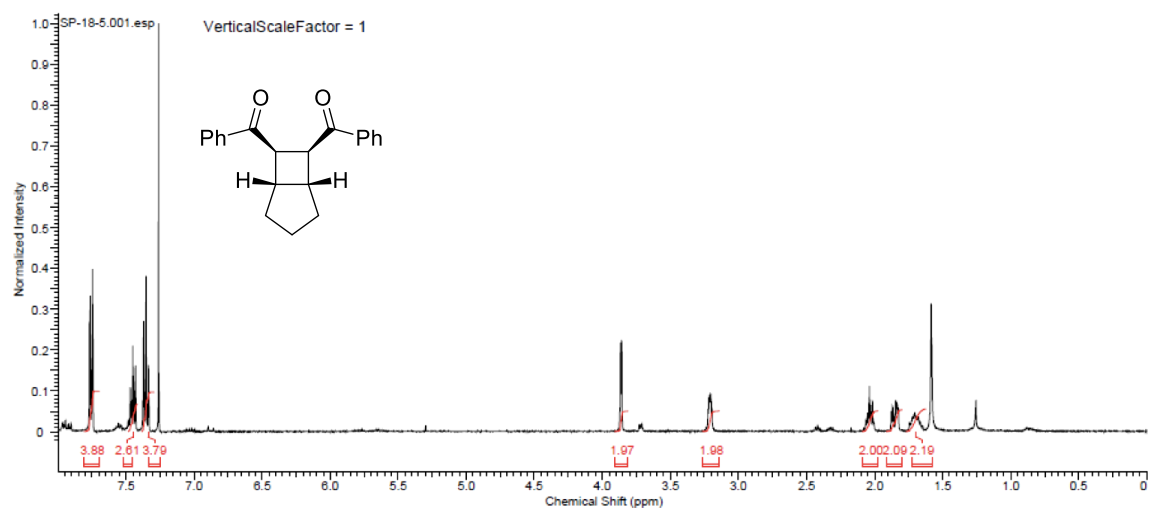


Figure 4A.22.  $^1\text{H}$  NMR of [Table 4.4 entry 1a Product] in  $\text{CDCl}_3$ .

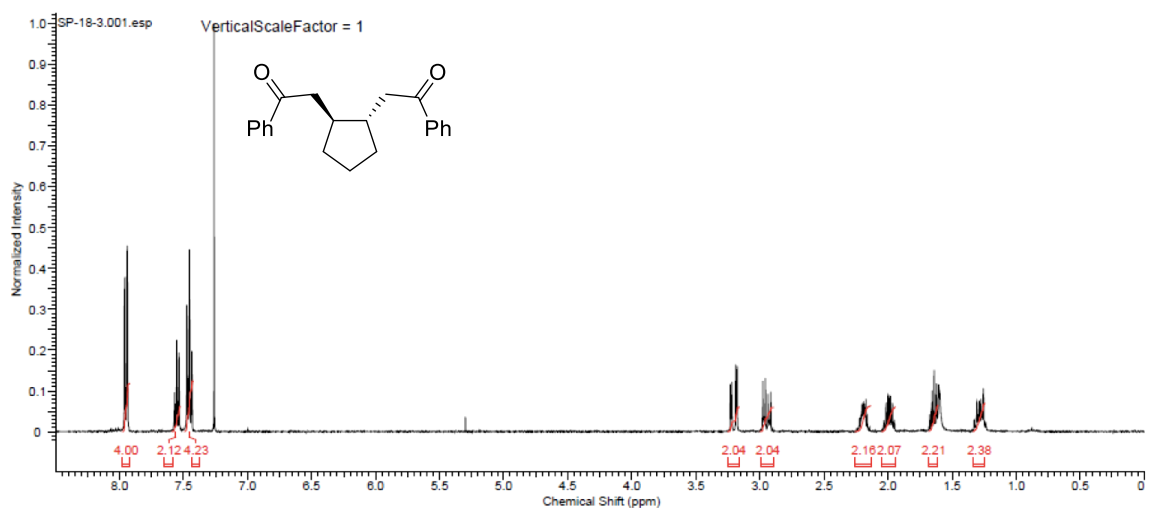


Figure 4A.23.  $^1\text{H}$  NMR of [Table 4.4 entry 1b Product] in  $\text{CDCl}_3$ .

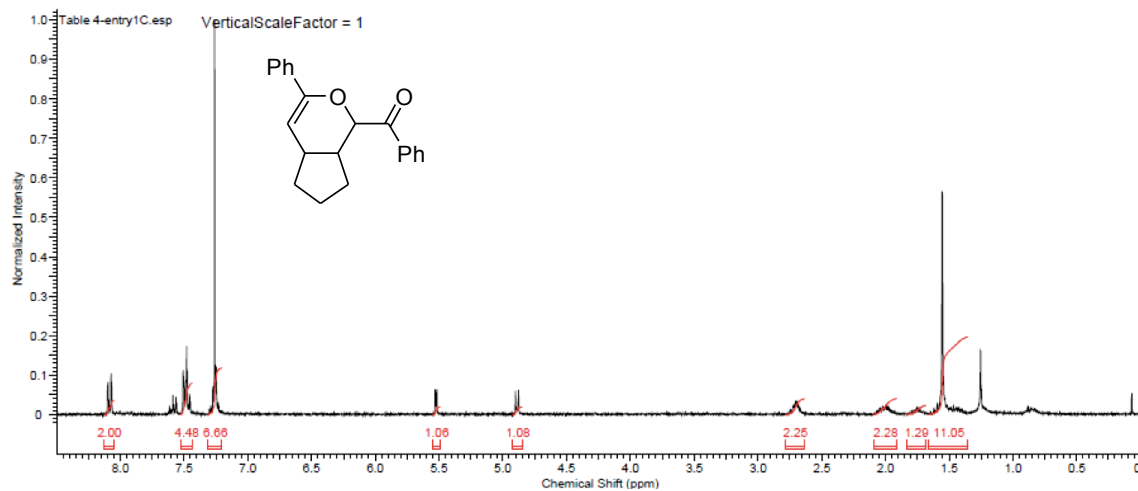


Figure 4A.24.  $^1\text{H}$  NMR of [Table 4.4 entry 1c Product] in  $\text{CDCl}_3$ .

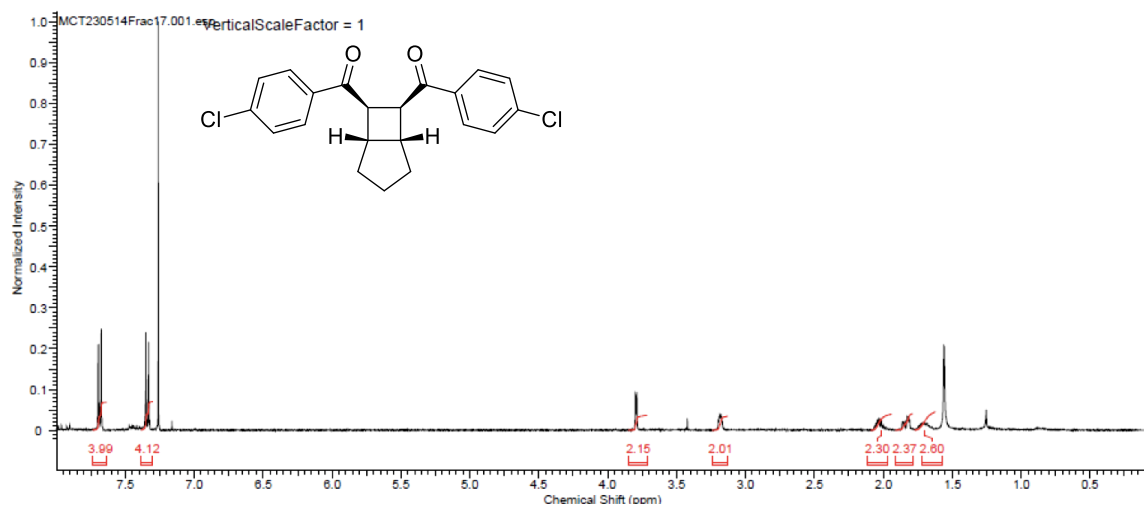


Figure 4A.25.  $^1\text{H}$  NMR of [Table 4.4 entry 2a Product] in  $\text{CDCl}_3$ .



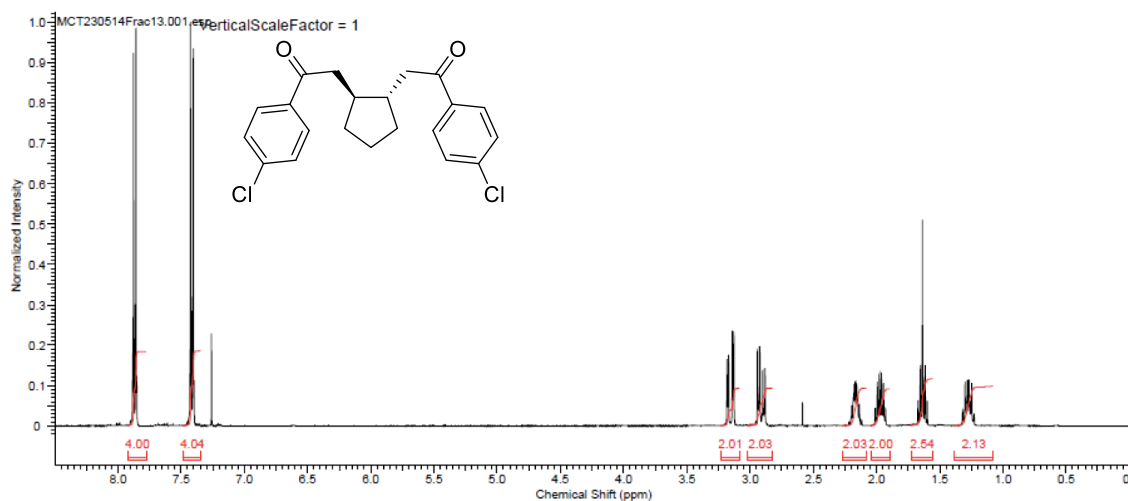


Figure 4A.26.  $^1\text{H}$  NMR of [Table 4.4 entry 2b Product] in  $\text{CDCl}_3$ .

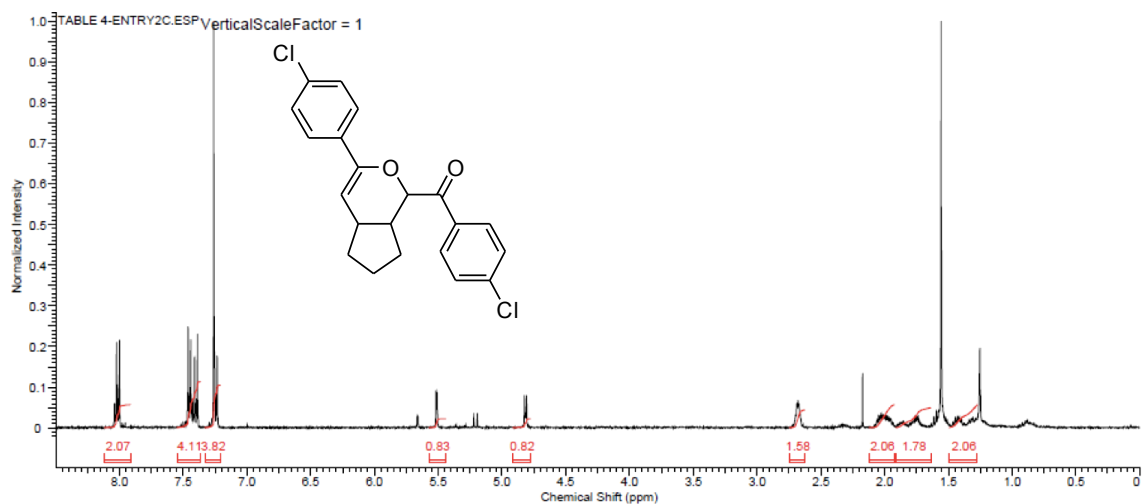
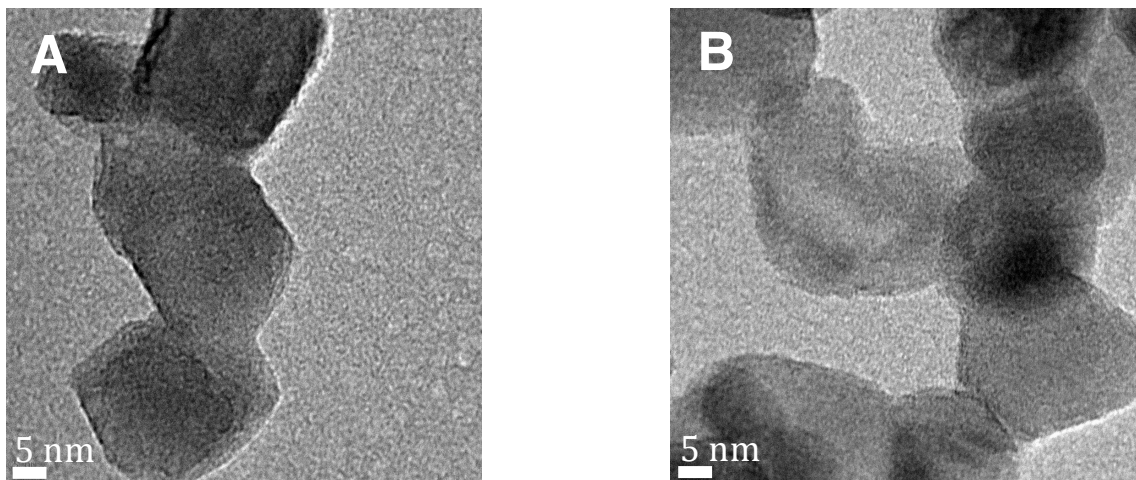


Figure 4A.27.  $^1\text{H}$  NMR of [Table 4.4 entry 2c Product] in  $\text{CDCl}_3$ .

#### 4.8.H. TEM Images of PtNP(0.2%)@TiO<sub>2</sub>



**Figure 4A.28.** TEM images of the PtNP@TiO<sub>2</sub> catalyst before (A) and after 3 reusability trials (B). Due to the small nature and low loading (0.2%) of the PtNPs, they could not be observed through conventional and high-resolution TEM imaging techniques.

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## Heterogeneous Titania-Photoredox/Nickel Dual Catalysis: Decarboxylative Cross-Coupling of Carboxylic Acids with Aryl Iodides

### 4.10. Background

When one thinks of important developments in synthetic organic chemistry, probably one of the most impactful has to be the introduction of transitional-metal catalyzed cross-coupling reactions. As a tool in forming C-C, C-N, and C-O bonds these methods have found applications in a variety of chemical syntheses, due to their well-known reliability, selectivity, and predictability. While there is currently a variety of different cross-coupling methods one can choose from (Mizoroki-Heck,<sup>1-5</sup> Suzuki-Miyaura,<sup>6</sup> Negishi,<sup>7-9</sup> Stille,<sup>10</sup> Kumada-Corriu,<sup>11-14</sup> Sonogashira,<sup>15</sup> Buchwald-Hartwig,<sup>16,17</sup> and Hiyama<sup>18</sup>) all of these methods require that the nucleophilic coupling partner be functionalized with transition-metal activated handles such as Grignards, Stannanes, and Boronic acids. While many of these reagents can be purchased or synthesized in few steps, they tend to be relatively expensive, may require harsh reaction conditions, and in some cases be difficult to handle due to their high reactivity. For these reasons, there has been a push to develop new techniques and methods, which would allow one to employ less expensive and readily available starting materials containing non-traditional leaving groups/handles (e.g. -COOH) as competent coupling partners in a variety of different cross-coupling reactions.

Over the last few years it has been shown that through a merger of visible-light photoredox and transition-metal catalysis one can create dual catalytic systems, which can be used to forge bonds between a variety of non-

conventional coupling partners.<sup>19-41</sup> While there has been a sudden surge in the use of Ni in these dual catalytic systems, other transition-metals such as Pd<sup>42-51</sup>, Cu,<sup>52</sup> and Au<sup>53-59</sup> have also been shown to act synergistically when coupled with appropriately selected photoredox systems.

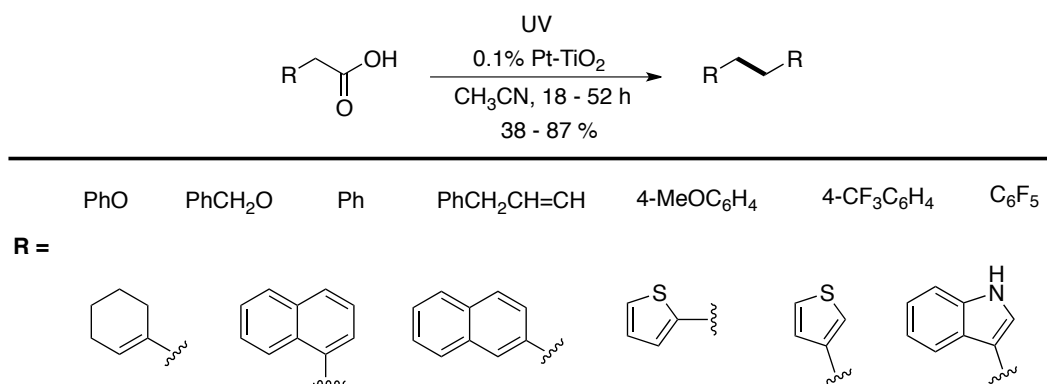
Since the work of Molander<sup>20</sup> and MacMillan<sup>41</sup> demonstrated that alkyl radicals generated through photoredox mediated single-electron transfer (SET) events could be efficiently intercepted by Ni(II) complexes and that the convergent Ni(III)(alkyl)(Ar) complex could undergo reductive elimination to furnish the desired cross-coupled product, there have been a number of publications which have looked to both better understand and expand on this chemistry.<sup>21-25,27,29-32,34,35,37-39,41</sup>

While the end product of these dual photoredox-Ni catalytic systems are quite diverse, the actual catalytic system employed to bring about these changes are quite conventional. That is most systems are derived from homogeneous Ir or Ru photoredox catalyst and some type of bipyridinium functionalized homogeneous Ni complex. The only criteria for the photocatalyst being that the SET redox potentials be favorable for both *in-situ* generation of the desired radical and for turnover of the Ni catalyst. Although the Ir and Ru photocatalysts have shown great promise in these dual catalytic systems, it is important to remember that we along with other groups have demonstrated that in many cases one can replace these relatively expensive transition-metal photocatalysts with cheaper alternative such as organic dyes (Methylene Blue,<sup>60,61</sup> Eosin-Y,<sup>62</sup> 9-Mesityl-10-methylacridinium<sup>63</sup>) and organic/inorganic semiconductors ( $\alpha$ -

Sexithiophene,<sup>64</sup> TiO<sub>2</sub><sup>65</sup>) to generate the required intermediates with little to no sacrifice in efficiency and in some cases these alternatives actually outperform their transition-metal counterparts.

As demonstrated in the previous section, both TiO<sub>2</sub> and Pt-modified TiO<sub>2</sub> can be used as efficient heterogeneous photoredox catalyst in the reductive dehalogenation and cyclization of a variety of different substrates. However, more recently it has been shown that these type of catalysts can also be used in the oxidative decarboxylation of carboxylic acids to generate homo-coupled products.<sup>66</sup>

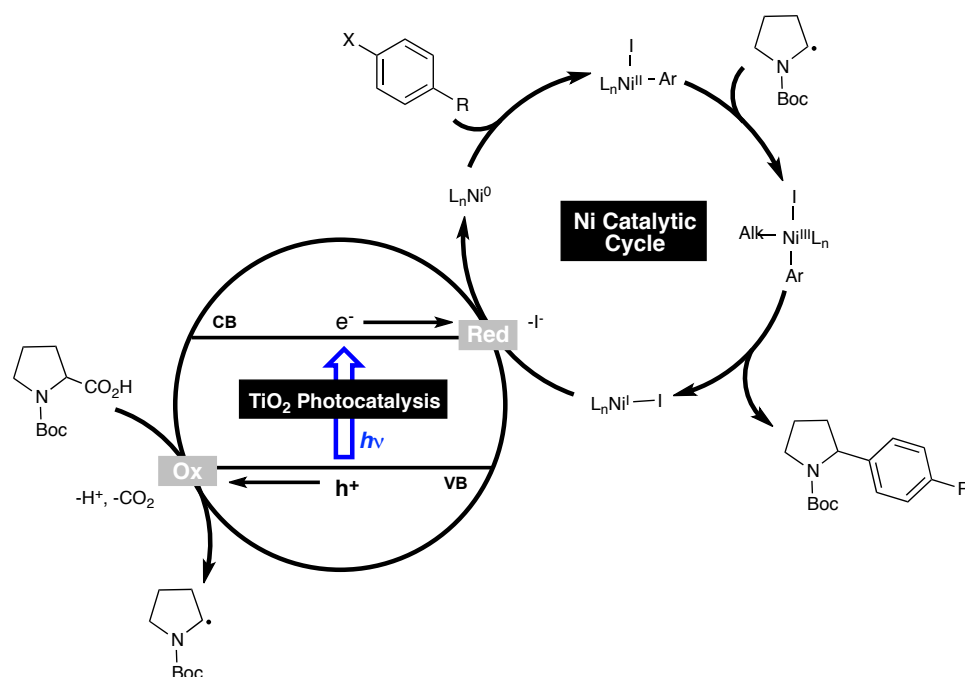
**Scheme 4.4.** Scope of Pt-TiO<sub>2</sub> Mediated Homo-Coupling of Carboxylic Acids<sup>66</sup>



As such we began to wonder whether we could substitute the highly oxidizing Iridium (III) photocatalyst Ir[dF(CF<sub>3</sub>)ppy]<sub>2</sub>(dtbbpy) PF<sub>6</sub>, typically used in the dual photoredox/Ni decarboxylative cross-couplings, with TiO<sub>2</sub>. Just as in the case of Ir, TiO<sub>2</sub> will be responsible for both generation of the alkyl radicals and turnover of the Ni catalytic cycle. The proposed mechanism for the dual TiO<sub>2</sub>-photoredox/Ni catalysis is presented in Scheme 4.5. The idea being that upon excitation of the TiO<sub>2</sub> photocatalyst the highly oxidizing holes in the valence band (VB) of the semiconductor would oxidatively decarboxylate the carboxylic acid to

furnish the alkyl radical, while the strongly reducing electrons in the conduction band (CB) would in turn provide a site for the reduction of the Ni(II) and Ni(I) complexes to their active Ni(0) species.

**Scheme 4.5.** Proposed Mechanism for the Dual TiO<sub>2</sub>-Photoredox-Ni-Catalyzed Decarboxylative Arylation.



In the next few sections, we will attempt to illustrate that one can replace the commonly employed Ir and Ru photocatalysts utilized in these dual-catalytic systems, with a relatively cheap, reusable, and environmentally benign photocatalyst such as P25 TiO<sub>2</sub>.

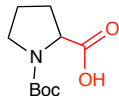
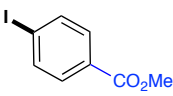
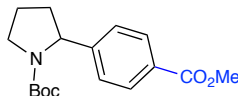
#### 4.11. Optimization and Controls

We began our studies on the decarboxylative cross-coupling of carboxylic acids with aryl-iodides using a catalytic system comprising P25 TiO<sub>2</sub> as photoredox catalyst, a variety of Ni(II) and Ni(0) precursor complexes, 4,4'-di-*tert*-butyl-2,2'-bipyridine (dtbbpy) as ligand for the complex, Cs<sub>2</sub>CO<sub>3</sub> as base, and a



UVA-Visible light source for irradiation (Luzchem Inc. Solar Simulator fitted with a longpass  $\lambda > 375$  nm filter). Utilizing N-Boc-Proline and methyl 4-iodobenzoate as model coupling partners, we performed test and control reactions under a variety of different conditions in order to optimize the procedure (Table 4.5).

**Table 4.5.** Optimization of Reaction Conditions and Controls<sup>a</sup>

| <div style="display: flex; align-items: center; justify-content: space-around;"> <div style="text-align: center;">  <p>Boc-Pro-OH<br/>0.6 mmol</p> </div> <div style="text-align: center;">  <p>Methyl 4-iodobenzoate<br/>0.4 mmol</p> </div> <div style="text-align: center;"> <p>0.5 eq. TiO<sub>2</sub><br/>10 mol% Ni Catalyst<br/>15 mol% dtbbpy, 1 eq CsCO<sub>3</sub><br/>5 mL Solvent, Atm<br/>Light Source</p> </div> <div style="text-align: center;">  </div> </div> |                          |         |       |      |                    |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------|---------|-------|------|--------------------|
| Entry                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Ni Catalyst              | Solvent | Atm.  | Time | Yield              |
| 1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | NiCl <sub>2</sub> •glyme | DMF     | Air   | 72 h | 0%                 |
| 2                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | NiCl <sub>2</sub> •glyme | DMF     | Argon | 72 h | 0%                 |
| 3                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | NiCl <sub>2</sub> •glyme | MeCN    | Air   | 36 h | 56%                |
| 4                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | NiCl <sub>2</sub> •glyme | MeCN    | Air   | 72 h | 93%                |
| 5                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | NiCl <sub>2</sub> •glyme | MeCN    | Air   | 72 h | 0% <sup>b</sup>    |
| 6                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | NiCl <sub>2</sub> •glyme | MeCN    | Air   | 72 h | 0% <sup>c</sup>    |
| 7                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | NiCl <sub>2</sub> •glyme | MeCN    | Argon | 3 h  | 19%                |
| 8                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | NiCl <sub>2</sub> •glyme | MeCN    | Argon | 6 h  | 61%                |
| 9                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | NiCl <sub>2</sub> •glyme | MeCN    | Argon | 18 h | 95%                |
| 10                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | NiCl <sub>2</sub> •glyme | MeCN    | Argon | 72 h | 0% <sup>b</sup>    |
| 11                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | NiCl <sub>2</sub> •glyme | MeCN    | Argon | 72 h | 0% <sup>c</sup>    |
| 12                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | NiCl <sub>2</sub> •glyme | MeCN    | Argon | 18 h | Trace <sup>d</sup> |
| 13                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | None                     | MeCN    | Argon | 18 h | 0%                 |
| 14                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | NiCl <sub>2</sub> •glyme | MeCN    | Argon | 18 h | Trace <sup>e</sup> |
| 15                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | NiCl <sub>2</sub> •glyme | MeCN    | Argon | 18 h | Trace <sup>f</sup> |
| 16                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Ni(acac) <sub>2</sub>    | MeCN    | Argon | 18 h | 8%                 |
| 17                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Ni(COD) <sub>2</sub>     | MeCN    | Argon | 18 h | >95%               |

<sup>a</sup>Reaction conditions: Boc-Pro-OH (0.6 mmol), methyl 4-iodobenzoate (0.4 mM), P25 TiO<sub>2</sub> (0.5 eq.), dtbbpy (15 mol%), CsCO<sub>3</sub> (1 eq.), solvent (5mL). Irradiated with solar simulator  $\lambda > 375$  nm. <sup>b</sup>no light. <sup>c</sup>no light and 50°C. <sup>d</sup>no base. <sup>e</sup>no P25 TiO<sub>2</sub>, <sup>f</sup>no base.

From these initial tests it was found that the optimal solvent for this particular catalytic system is acetonitrile (MeCN) (Table 4.5, entries 1 and 4) and that while the reaction can tolerate the presence of oxygen, its removal through a 20 minute Ar purge drastically increases the efficiency of the reaction (Table 4.5,

entries 2 and 8). While the drastically different results in dimethylformamide (DMF) and MeCN may be simply explained by interference due to the readily oxidizable amine impurities in the DMF,<sup>67</sup> the increase in efficiency observed in the absence of oxygen may be due to the fact that, when present oxygen can be readily reduced by electrons in the CB of TiO<sub>2</sub> ( $E^{\text{ox}} [\text{CB}] = -2.0 \text{ V vs. SCE}$ )<sup>68</sup> to give superoxide ( $\text{O}_2^{\bullet-}$ ) ( $E^{\text{red}} [\text{O}_2/\text{O}_2^{\bullet-}] = -0.8 \text{ V vs. SCE}$ )<sup>69</sup> which may disrupt the catalytic cycle directly or indirectly as it may compete with the reduction of the Ni(I) complex to its corresponding Ni(0) complex, a key step in the proposed mechanism (Scheme 4.3). Although the observed effect of O<sub>2</sub> in our system is opposite to that observed by Oderinde and co-workers for a similar transformation utilizing an Ir[dF(CF<sub>3</sub>)ppy]<sub>2</sub>(dtbbpy)PF<sub>6</sub>,<sup>35</sup> it should be pointed out that they believe that the presence of O<sub>2</sub> is assisting the intersystem crossing (ISC) process, resulting in a more efficient formation of the strongly oxidizing triplet excited state of <sup>\*</sup>Ir(III) ( $E_{1/2}^{\text{red}} [\text{Ir(III)}/\text{Ir(II)}] = 1.21 \text{ V vs. SCE}$ ).<sup>70</sup> While such an explanation is plausible for transition metal and organic based photocatalysts, as excitation of TiO<sub>2</sub> does not lead to the formation of singlet and triplet excited states, such an enhancement would not be expected in our system. However it should be pointed out that without a full examination of the underlying kinetics of the process it is difficult to envision how a reaction will be effected by the presence of oxygen. While O<sub>2</sub> could enhance ISC it would seem likely that the triplet of the Ir(III) ( $E_{1/2}^{\text{ox}} [\text{Ir(III)}/\text{Ir(IV)}] = -0.89 \text{ V vs. SCE}$ )<sup>71</sup> complex would be readily quenched by oxygen to generate either <sup>1</sup>O<sub>2</sub> or O<sub>2</sub><sup>•-</sup> and without knowing

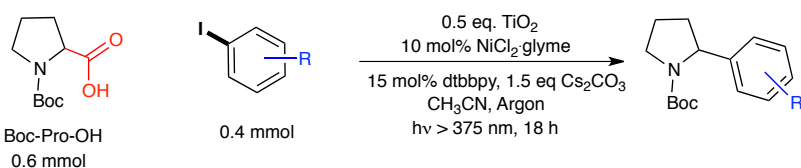
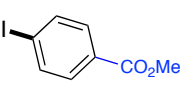
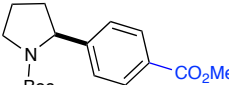
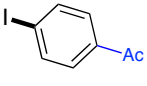
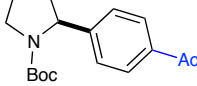
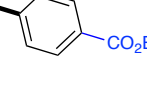
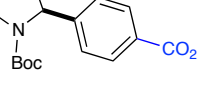
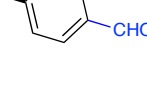
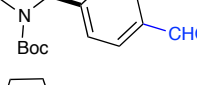
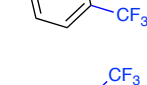
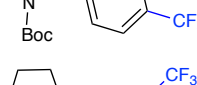
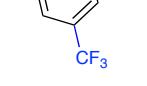
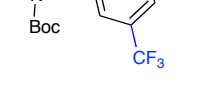
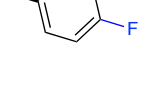
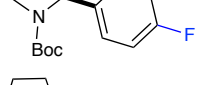
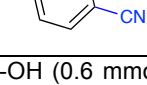
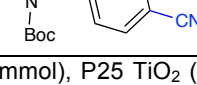
the associated rate constants of these processes it is difficult to estimate the enhancement one would expect with improved ISC.

In addition to solvent and atmosphere, we have also performed control reactions under dark conditions at both room temperature and 50 °C to ensure that it is excitation of the photocatalyst that brings about the desired transformation and not just heating caused by light absorption (Table 4.5, entries 5, 6, 10, and 11). From Table 4.5 it is also evident that the photocatalyst, Ni complex, dtbbpy ligand, and base are all critical components of the system as their omission results in little or no desired product even after 18 h of irradiation. Lastly, due to the fact that the added Ni complex is only a precursor for the  $\text{NiCl}_2 \cdot \text{dtbbpy}$  complex utilized in these transformations, we explored whether or not we could exchange the  $\text{NiCl}_2 \cdot \text{glyme}$  with other Ni sources such as  $\text{Ni}(\text{acac})_2$  and  $\text{Ni}(\text{COD})_2$ . As observed in Table 4.5, entry 16; when  $\text{Ni}(\text{acac})_2$  is used as precatalyst the efficiency of the reaction falls drastically with only 8% of the desired cross-coupled product obtained after 18 h of reaction. However, when we switch to the Ni(0) precatalyst,  $\text{Ni}(\text{COD})_2$ , there appears to be no observable change in the efficiency of the transformation. While the Ni(0) catalyst has the advantage that it does not require an initial reduction by the  $\text{TiO}_2$  to become active, this may not be that advantageous as reduction of Ni(II) to Ni(0) by the CB electrons is quite thermodynamically favorable ( $E_{1/2}^{\text{red}} [\text{Ni}^{\text{II}}/\text{Ni}^0] = -1.2 \text{ V vs. SCE}$ ).<sup>72</sup> The  $\text{Ni}(\text{COD})_2$  precatalysts is also air sensitive and therefore extra care must be taken when it is employed. For these reasons we have decided to move forward utilizing  $\text{NiCl}_2 \cdot \text{glyme}$  as our precatalyst.

## 4.12. Aryl Iodide Scope

With the optimized conditions in hand, we then set out to test our system in the cross-coupling of a variety of substituted aryl-iodides with our model alkyl

**Table 4.6.** TiO<sub>2</sub> Photoredox/Ni Dual Catalytic Decarboxylative Cross-Coupling: Aryl-Iodide Scope<sup>a</sup>

|  |                                                                                     |                                                                                      |       |
|------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|-------|
| Entry                                                                              | Aryl Iodide                                                                         | Product                                                                              | Yield |
| 1                                                                                  |    |    | 95 %  |
| 2                                                                                  |    |    | 88 %  |
| 3                                                                                  |   |   | 82 %  |
| 4                                                                                  |  |  | 79 %  |
| 5                                                                                  |  |  | 73 %  |
| 6                                                                                  |  |  | 77 %  |
| 7                                                                                  |  |  | 42 %  |
| 8                                                                                  |  |  | 68 %  |

<sup>a</sup>Reaction conditions: Boc-Pro-OH (0.6 mmol), aryl iodide (0.4 mmol), P25 TiO<sub>2</sub> (0.5 eq.), NiCl<sub>2</sub>·glyme (10 mol%), dtbbpy (15 mol%), Cs<sub>2</sub>CO<sub>3</sub> (1.5 eq.), 5 mL MeCN. degassed with Argon for 15 min, and irradiated with a solar simulator  $\lambda > 375$  nm. All yields are reported as isolated yields.

carboxylic acid (N-Boc-pro). As illustrated in Table 4.6 our dual-catalytic system is capable of coupling a number of electron-deficient aryl-iodides with N-Boc-proline in moderate to excellent yields (42-95%) under relatively short irradiation times (18h). As shown in Table 4.6, our procedure is tolerant to a variety of different functional groups, such as esters, acetyls, aldehydes, trifluoromethyl, fluorine, and nitriles. However, it should be mentioned that the presence of ether, alcohol, amine, or nitro functionalities on the aryl-iodide coupling partner either slow or completely shut down the catalytic cycle. While in a number of cases this may be due to the radical trapping ability of these functionalities, the electron donating nature of these substituents may also be inhibiting oxidative addition of the Ni(0) complex into the aryl-iodide preventing formation of the Ni(II) intermediate, which would then trap the alkyl radical formed upon oxidative decarboxylation. It is important to note that while we have previously illustrated that one can utilize TiO<sub>2</sub> as photoredox catalysts in the reductive dehalogenation of aryl-iodides, we have observed no corresponding hydrodehalogenated products under these reaction conditions. We do however find trace amounts of the corresponding phenol.

#### 4.13. Carboxylic Acid Scope

Once we had demonstrated that the aryl-iodide coupling partner could be modified, we set out to do the same thing with the carboxylic acid component. The holes produced in the VB ( $E^{\text{red}}$  [VB] = 1.0 V vs. SCE)<sup>68</sup> of TiO<sub>2</sub> upon excitation make it a moderately oxidizing inorganic semiconductor. Considering that the oxidation potential of N-Boc-pro ( $E_{1/2}^{\text{ox}}$  [N-Boc-pro] = 0.95 V vs. SCE)<sup>73</sup> is

just within the potential window of the  $\text{TiO}_2$  photocatalysts, it was necessary to find alkyl carboxylic acid type substrates which were more easily oxidized to expand the scope and illustrate the procedures broad applicability. With this in mind, we set out to cross-couple our model aryl-iodide (methyl 4-iodobenzoate) with a variety of substituted and unsubstituted phenylacetic acids. As can be observed in Table 4.7, we have successfully coupled various phenylacetic acid derivatives to methyl 4-iodobenzoate under our optimized conditions. As expected substrates bearing electron donating substituents gave the best results, owing to their lower oxidation potential. While the ability to cross-couple electron deficient phenylacetic acids is ultimately dependent on the oxidation potential of the substrate, it appears as though some withdrawing functionalities may be tolerated.

**Table 4.7.**  $\text{TiO}_2$  Photoredox/Ni Dual Catalytic Decarboxylative Cross-Coupling: Carboxylic Acid Scope<sup>a</sup>

| Entry | Carboxylic Acid | Product | Yield |
|-------|-----------------|---------|-------|
| 1     |                 |         | 62 %  |
| 2     |                 |         | 76 %  |
| 3     |                 |         | 73 %  |
| 4     |                 |         | 68 %  |

|    |  |  |      |
|----|--|--|------|
| 5  |  |  | 37 % |
| 6  |  |  | 44 % |
| 7  |  |  | 56 % |
| 8  |  |  | 48 % |
| 9  |  |  | 72 % |
| 10 |  |  | 83 % |
| 11 |  |  | 65 % |

<sup>a</sup>Reaction conditions: Carboxylic Acid (0.6 mmol), methyl 4-iodobenzoate (0.4 mmol), P25 TiO<sub>2</sub> (0.5 eq.), NiCl<sub>2</sub>•glyme (10 mol%), dtbbpy (15 mol%), Cs<sub>2</sub>CO<sub>3</sub> (1.5 eq.), 5 mL MeCN, degassed with Argon for 15 min, and irradiated with a solar simulator  $\lambda > 375$  nm. All yields are reported as isolated yields.

Interestingly many of the phenylacetic acid derivatives are classified as Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), as such this protocol provides a quick and simple route to their modification and functionalization with orthogonal handles for further modification. For the most part derivatives substituted in the alpha position display lower reactivity than their unsubstituted counterparts (Table 4.7, entries 6-8). While it would be easy to attribute this decrease in reactivity to steric effects, this is complicated by the fact that the

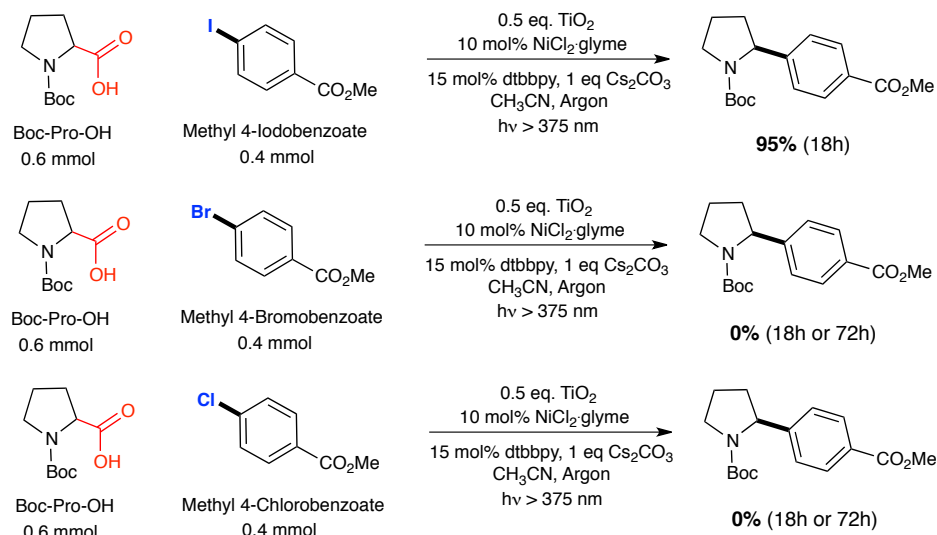
more sterically hindered diphenylacetic acid (Table 4.7, entry 9) appears to be a suitable coupling partner, giving similar yields to the unsubstituted derivatives. However, this difference in reactivity could possibly be related to the higher stability of the resulting diphenyl methyl radical.<sup>74</sup> Lastly, substrates containing aromatic ketone chromophores (Table 4.7, entry 10 and 11) are also exceptional coupling partners, giving moderate to good yields with little to no background reaction.

#### **4.14. Aryl Acid Scope**

In an attempt to broaden the applicability of this procedure we have attempted to swap the aryl iodide coupling partner with its bromide and chloride analogue. However after 72 hours of irradiation of N-Boc-Proline and either methyl 4-bromobenzoate or methyl 4-chlorobenzoate, under our optimized reaction conditions, we did not obtain any of the desired cross-coupled product. One possible explanation for the observed lack of reactivity may be that the reduction potential of the corresponding Ni(I)Cl or Ni(I)Br species (formed after the reductive elimination step) is outside the potential window attainable by the TiO<sub>2</sub> photocatalyst and thus the Ni(0) species required for the initial transmetallation step cannot be regenerated.



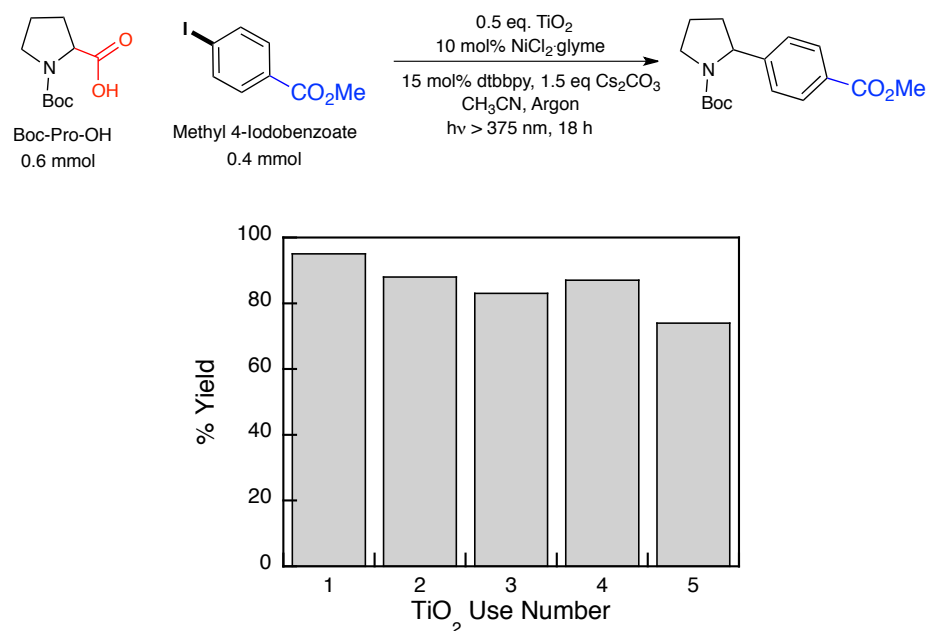
**Scheme 4.6.** TiO<sub>2</sub> Photoredox/Ni Dual Catalytic Decarboxylative Cross-Coupling: Aryl Halide Scope



#### 4.15. Reusability of TiO<sub>2</sub>

While easy photocatalyst removal is one of the main advantages of our semi-heterogeneous catalytic system, another benefit of heterogeneous catalysts is that in many cases they can be reused after isolation. While in some cases catalyst reusability has a large impact on the economical feasibility of a given protocol or its amenability to the industrial scale, due to the abundance and relatively low cost of TiO<sub>2</sub>, its reusability is not as critical. However, as the end goal of this work is to develop a completely heterogeneous system, for these transformations, in which the relatively expensive Ni catalyst is immobilized onto the TiO<sub>2</sub>, catalyst reusability will become more significant. Thinking also about environmental issues, we explored the reusability of the unmodified TiO<sub>2</sub> towards our model reaction, with the idea that it would provide us with insight into the likelihood of reusability for the Ni modified catalyst. As shown in Figure 4.1, the TiO<sub>2</sub> photocatalyst shows only a slight decrease in efficiency towards the cross-

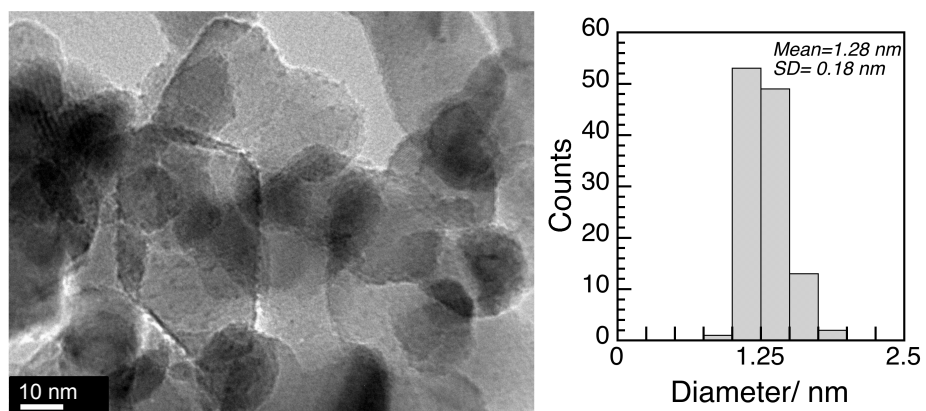
coupling reaction over 5 trials (approx. 15-20%), indicating that it is exceptionally reusable. It is important to note that in each trial 10 mol% of fresh  $\text{NiCl}_2\cdot\text{dtbbpy}$  complex was added.



**Figure 4.1.** Reusability of  $\text{TiO}_2$  in the photoredox/nickel dual catalytic decarboxylative cross-coupling of N-Boc-proline with methyl 4-iodobenzoate.

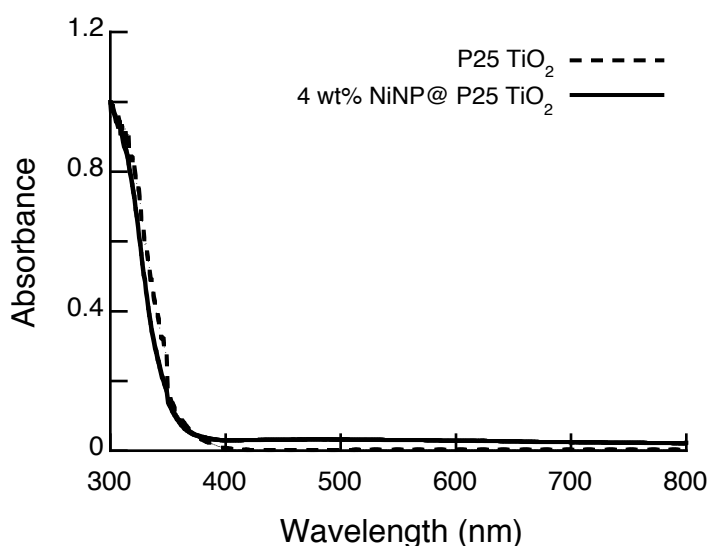
#### 4.16. Complete Heterogenization of Catalytic System

We thus became interested in whether or not we could replace the homogeneous  $\text{Ni(II)}$  complex with heterogeneous Nickel nanoparticles (NiNP) supported on the P25  $\text{TiO}_2$  photocatalyst. Utilizing a previously described method, we have photochemically deposited 1, 2, and 4 wt% NiNP on P25  $\text{TiO}_2$ . The resulting supported NiNP are roughly 1.3 nm in diameter as measured by TEM (Figure 4.2) and appear to be distributed evenly throughout the material.



**Figure 4.2.** TEM image of 4 wt% NiNP@P25 TiO<sub>2</sub> and corresponding size histogram illustrating the size distribution of the supported NiNP.

The resulting catalyst is grey in colour and as expected, has a strong absorption in the UVA and tails throughout the entire visible portion of the spectrum (for diffuse reflectance spectra of the 4 wt% NiNP @ TiO<sub>2</sub> see Figure 4.3).

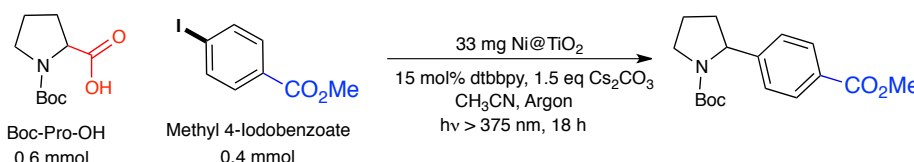


**Figure 4.3.** Normalized diffuse reflectance spectra for unmodified P25 TiO<sub>2</sub> and 4 wt% NiNP@P25 TiO<sub>2</sub>.

It should also be mentioned that previous reports indicate that the as synthesized NiNP are mainly Nickel oxide (NiO) with some Ni(0) by XPS analysis.<sup>75</sup> In order to examine the usefulness of these materials as

heterogeneous catalyst in the TiO<sub>2</sub>-photoredox/Ni mediated decarboxylative cross-coupling of carboxylic acids with aryl-iodides, we have again employed our model reaction as test reaction. As can be seen in Table 4.8, all three catalysts are able to bring about the desired transformation. However, after 18 hours of irradiation, the 4 wt% NiNP@P25 catalyst gave the best yield (Table 4.8, entry 3). Interestingly if we omit the dtbbpy ligand even after 72 h of irradiation we do not obtain any of the cross-coupled product. This would indicate that either the dtbbpy ligand is capable of interacting with the surface of the NiNP or perhaps that it is Ni leaching from the nanoparticles, which is responsible for the observed catalysis.

**Table 4.8.** Results of Model Reaction Using NiNP@P25 as Catalyst<sup>a</sup>

|  |              |        |      |       |
|-------------------------------------------------------------------------------------|--------------|--------|------|-------|
| Entry                                                                               | Catalyst     | Ligand | Time | Yield |
| 1                                                                                   | 1 wt% Ni@P25 | dtbbpy | 18 h | 24 %  |
| 2                                                                                   | 2 wt% Ni@P25 | dtbbpy | 18 h | 43 %  |
| 3                                                                                   | 4 wt% Ni@P25 | dtbbpy | 18 h | 68 %  |
| 4                                                                                   | 4 wt% Ni@P25 | none   | 72 h | < 5 % |

<sup>a</sup>Reaction conditions: Boc-Pro-OH (0.6 mmol), methyl 4-iodobenzoate (0.4 mmol), Ni@P25 TiO<sub>2</sub> (33 mg), dtbbpy (15 mol%), Cs<sub>2</sub>CO<sub>3</sub> (1.5 eq.), 5 mL MeCN. degassed with Argon for 15 min, and irradiated with a solar simulator  $\lambda > 375$  nm. All yields are reported as isolated yields.

In an attempt to better understand what was going on we attempted to reuse the 4 wt% Ni@P25 catalyst however we found a drastic decrease in the efficiency of the process upon recycling of the catalyst. While the material appears to be unchanged by its corresponding diffuse reflectance spectrum and TEM images, ICP analysis confirms that some of the Ni is leached from the

support under reaction conditions. However, even with this data it is difficult to attribute the complete loss in activity to leaching of the active species. A more likely scenario is that the surface of the NiNP are becoming deactivated through passivation with reaction intermediates which are difficult to remove between trials.

#### **4.17. Conclusions**

We have demonstrated that P25 TiO<sub>2</sub> can be utilized as an efficient heterogeneous photoredox catalyst in the decarboxylative cross-coupling of carboxylic acids with aryl iodides under dual photoredox/Ni catalysis conditions. While the system has some limitations in comparison to its homogeneous counterparts, the inexpensive and heterogeneous nature of the TiO<sub>2</sub> photocatalyst make the catalytic system quite attractive even without considering its reusability. We have also demonstrated that we can replace the homogeneous Ni(II) complex with Ni nanoparticles with only a slight decrease in reaction efficiency. As such we are currently searching for ways to improve both the synthesis and properties of the Ni-TiO<sub>2</sub> composites and in the process exploring whether such heterogeneous systems can be expanded to other dual photoredox/Ni transformations and if this strategy of heterogenization can be applied to other dual catalytic systems.

## 4.18. Appendix

### 4.18.A. General Information

Substrates and Reagents: P25 TiO<sub>2</sub>, NiCl<sub>2</sub>•glyme, Ni(acac)<sub>2</sub>, Ni(COD)<sub>2</sub>, CsCO<sub>3</sub>, and substrates were purchased from commercial suppliers (Sigma Aldrich, Alfa Aesar, Nippon Aerosil, Novabiochem and Fisher) and used with no further purification unless otherwise noted. All solvents were of HPLC grade and were passed through a solvent purification system before use.

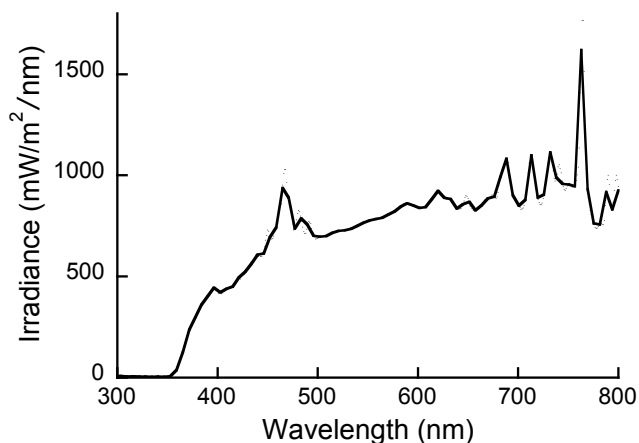
Light Source: All reactions were performed in a solar simulator (Luzchem Research Inc., Ottawa, Canada) fitted with a 375 nm long-pass cut off filter operating a power intensity of 12200 mW/m<sup>2</sup> in the UVA region and 231800 mW/m<sup>2</sup> in the visible region.

Chromatography: Flash column chromatography was performed using 230-400 mesh silica gel. Preparatory thin layer chromatography (PTLC) was performed using 1000 µm thick glass baked TLC plates purchased from Silicycle.

NMR: All <sup>1</sup>H NMR and <sup>13</sup>C were recorded on a Bruker AVANCE 400 spectrometer. Chemical shifts (δ) are reported in ppm from the solvent.

ICP: Analysis performed on a Perkin Elmer OPTIMA 2000 DV, samples were prepared via microwave-assisted acid digestion.

#### 4.18.B. Output Spectrum of Solar Simulator with 375 nm Long Pass Filter



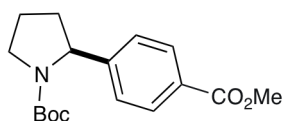
**Figure 4A.27.** Output spectrum of solar simulator with 375 nm long pass filter used for irradiation of reaction mixtures.

#### 4.18.C. General Procedure for the dual $\text{TiO}_2/\text{Ni}$ mediated decarboxylative cross-coupling of N-Boc-Proline with aryl iodides

Briefly, the  $\text{NiCl}_2 \cdot \text{dtbbpy}$  catalyst was assembled through the addition of 4.1 mg of  $\text{NiCl}_2 \cdot \text{glyme}$  and 5 mg of 4,4'-Di-*tert*-butyl-2,2'-dipyridyl (dtbbpy) to a 10 mL schlenk tube containing 3 mL of THF. The solution was then sonicated for 5 minutes and heated to boiling with a heat gun. At this point the mixture was concentrated using a rotovap and then allowed to dry under vacuum for 20 min. Once dry, N-Boc-proline (127 mg, 0.6 mmol),  $\text{Cs}_2\text{CO}_3$  (195 mg, 0.6 mmol),  $\text{TiO}_2$  (32 mg), aryl iodide (0.4 mmol), and 5 mL of freshly distilled MeCN. The resulting suspension was then sonicated for 2 min. The reaction mixture was then degassed with Ar for 20 minutes and then irradiated with a solar simulator fitted with a 375 nm cut off filter for 3-72 h while stirring at room temperature. The progress of the reaction was monitored by TLC. The solid catalyst was separated by centrifugation and the resulting supernatant was diluted in ether (25 mL), and washed with 10% NaOH (4x, 25 mL), Brine (2x, 25 mL),  $\text{H}_2\text{O}$  (2x, 25 mL). The

organic layer was dried over anhydrous  $\text{MgSO}_4$  and concentrated using a rotovap to yield the crude product. Purification of the crude was accomplished by column chromatography (hexanes:ethyl acetate).

**[Table 4.6, entry 1 Product]<sup>19</sup>**

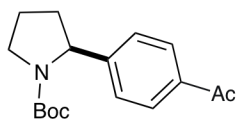


According to the general procedure, N-Boc-proline (127 mg, 0.6 mmol),  $\text{Cs}_2\text{CO}_3$  (195 mg, 0.6 mmol),  $\text{TiO}_2$  (32 mg),  $\text{Ni}\cdot\text{dtbbpy}$  (10 mol%), and 4-Iodomethylbenzoate (105 mg, 0.4 mmol), in MeCN (5 mL) afforded the title compound (116 mg, 95% isolated yield) after purification by column chromatography (5-20% EtOAc:Hexanes gradient).

$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.12 - 7.97 (m, 2 H), 7.21 - 7.11 (m, 2 H), 4.54 - 4.37 (m, 1 H), 3.93 - 3.81 (m, 3 H), 3.66 - 3.35 (m, 2 H), 2.46 - 2.25 (m, 1 H), 2.21 - 1.83 (m, 3 H), 1.44 (d,  $J$  = 9.5 Hz, 9 H)

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 171.3, 161.2, 154.5, 132.0, 131.5, 131.4, 128.1, 121.8, 121.4, 115.5, 80.8, 80.5, 59.5, 59.4, 52.5, 52.4, 52.0, 46.9, 46.8, 31.3, 30.2, 28.7, 24.8, 24.0

**[Table 4.6, entry 2 Product]<sup>19</sup>**



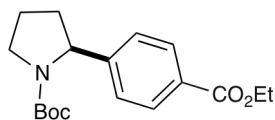
According to the general procedure, N-Boc-proline (127 mg, 0.6 mmol),  $\text{Cs}_2\text{CO}_3$  (195 mg, 0.6 mmol),  $\text{TiO}_2$  (32 mg),  $\text{Ni}\cdot\text{dtbbpy}$  (10 mol%), and 4-Iodoacetophenone (98 mg, 0.4 mmol), in MeCN (5 mL) afforded the title compound (102 mg, 88% isolated yield) after purification by column chromatography (5-20% EtOAc:Hexanes gradient).

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.02 - 7.92 (m, 2 H), 7.22 - 7.14 (m, 2 H), 4.54 - 4.40 (m, 1 H), 3.65 - 3.38 (m, 2 H), 2.60 - 2.55 (m, 3 H), 2.46 - 1.87 (m, 4 H), 1.50 - 1.39 (m, 9 H)

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 171.1, 154.2, 130.8, 130.7, 130.0, 129.9, 121.7, 121.3, 115.3, 80.4, 80.2, 59.2, 59.1, 46.6, 46.4, 31.0, 30.0, 28.4, 26.6, 24.5, 23.7



**[Table 4.6, entry 3 Product]**

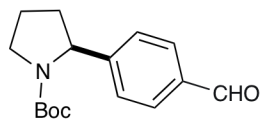


According to the general procedure, N-Boc-proline (127 mg, 0.6 mmol), Cs<sub>2</sub>CO<sub>3</sub> (195 mg, 0.6 mmol), TiO<sub>2</sub> (32 mg), Ni•dtbbpy (10 mol%), and 4-Iodoethylbenzoate (110 mg, 0.4 mmol), in MeCN (5 mL) afforded the title compound (105 mg, 82% isolated yield) after purification by column chromatography (5-20% EtOAc:Hexanes gradient).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ ppm 8.12 - 7.99 (m, 2 H), 7.20 - 7.10 (m, 2 H), 4.43 (dd, *J* = 4.5, 8.6 Hz, 1 H), 4.35 (dq, *J* = 4.0, 7.0 Hz, 2 H), 3.67 - 3.37 (m, 2 H), 2.48 - 1.85 (m, 4 H), 1.48 - 1.42 (m, 9 H), 1.37 (t, *J* = 7.0 Hz, 3 H)

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ ppm 166.5, 160.3, 154.1, 131.8, 131.2, 131.1, 122.6, 121.4, 121.1, 115.1, 80.5, 61.1, 60.6, 59.2, 59.1, 46.5, 31.0, 30.0, 28.4, 28.3, 24.5, 23.7, 14.3, 14.3

**[Table 4.6, entry 4 Product]**

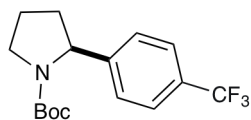


According to the general procedure, N-Boc-proline (127 mg, 0.6 mmol), Cs<sub>2</sub>CO<sub>3</sub> (195 mg, 0.6 mmol), TiO<sub>2</sub> (32 mg), Ni•dtbbpy (10 mol%), and 4-Iodobenzaldehyde (93 mg, 0.4 mmol), in MeCN (5 mL) afforded the title compound (73 mg, 79% isolated yield) after purification by column chromatography (5-20% EtOAc:Hexanes gradient).

<sup>1</sup>H NMR (400MHz, CDCl<sub>3</sub>) δ ppm 9.95 (d, *J* = 6.0 Hz, 1 H), 7.89 (dd, *J* = 8.5, 12.5 Hz, 2 H), 7.32 - 7.19 (m, 2 H), 4.55 - 4.39 (m, 1 H), 3.68 - 3.35 (m, 2 H), 2.48 - 1.85 (m, 4 H), 1.43 (d, *J* = 9.5 Hz, 9 H)

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ ppm 190.9, 190.7, 155.5, 155.2, 153.5, 134.0, 133.9, 131.2, 131.1, 122.2, 121.8, 80.3, 80.1, 59.1, 59.1, 46.6, 46.4, 31.0, 29.9, 28.3, 24.5, 23.7

**[Table 4.6, entry 5 Product]<sup>19</sup>**

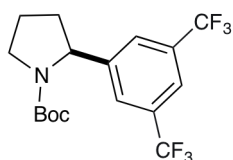


According to the general procedure, N-Boc-proline (127 mg, 0.6 mmol), Cs<sub>2</sub>CO<sub>3</sub> (195 mg, 0.6 mmol), TiO<sub>2</sub> (32 mg), Ni•dtbbpy (10 mol%), and 4-Iodobenzotrifluoride (109 mg, 0.4 mmol), in MeCN (5 mL) afforded the title compound (92 mg, 73% isolated yield) after purification by column chromatography (5-20% EtOAc:Hexanes gradient).

<sup>1</sup>H NMR (400MHz, CDCl<sub>3</sub>) δ ppm 7.62 (dd, *J* = 8.5, 13.1 Hz, 2 H), 7.26 - 7.17 (m, 2 H), 4.55 - 4.39 (m, 1 H), 3.68 - 3.36 (m, 2 H), 2.49 - 1.86 (m, 4 H), 1.44 (d, *J* = 8.5 Hz, 9 H)

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 159.2, 159.2, 127.0, 127.0, 126.9, 126.9, 125.9, 123.2, 122.4, 122.1, 115.5, 115.5, 115.5, 81.6, 81.1, 59.0, 47.0, 46.4, 30.7, 28.9, 28.3, 28.2, 24.2, 23.6

**[Table 4.6, entry 6 Product]<sup>19</sup>**

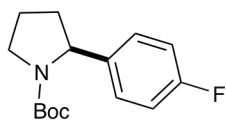


According to the general procedure, N-Boc-proline (127 mg, 0.6 mmol),  $\text{Cs}_2\text{CO}_3$  (195 mg, 0.6 mmol),  $\text{TiO}_2$  (32 mg),  $\text{Ni}\cdot\text{dtbbpy}$  (10 mol%), and 1-Iodo-3,5-bis(trifluoromethyl)benzene (136 mg, 0.4 mmol), in MeCN (5 mL) afforded the title compound (73 mg, 77% isolated yield) after purification by column chromatography (5-20% EtOAc:Hexanes gradient).

$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 7.73 (d,  $J$  = 14.0 Hz, 1 H), 7.59 (d,  $J$  = 15.5 Hz, 2 H), 4.58 - 4.41 (m, 1 H), 3.70 - 3.38 (m, 2 H), 2.51 - 1.90 (m, 4 H), 1.45 (d,  $J$  = 11.0 Hz, 9 H)

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 157.8, 133.5, 133.2, 132.9, 132.5, 127.6, 124.9, 122.2, 116.3, 116.2, 113.9, 113.8, 113.8, 81.7, 59.4, 47.4, 46.8, 31.0, 30.0, 28.7, 28.5, 24.5, 23.9

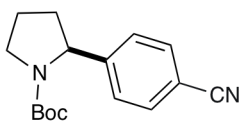
**[Table 4.6, entry 7 Product]<sup>19</sup>**



According to the general procedure, N-Boc-proline (127 mg, 0.6 mmol),  $\text{Cs}_2\text{CO}_3$  (195 mg, 0.6 mmol),  $\text{TiO}_2$  (32 mg),  $\text{Ni}\cdot\text{dtbbpy}$  (10 mol%), and 4-Fluoroiodobenzene (89 mg, 0.4 mmol), in MeCN (5 mL) afforded the title compound (45 mg, 42% isolated yield) after purification by column chromatography (5-20% EtOAc:Hexanes gradient)

$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 7.10 (dd,  $J$  = 5.5, 8.4 Hz, 2 H), 7.00 - 6.90 (m, 2 H), 4.72 (br. s., 1 H), 3.59 (br. s., 2 H), 2.29 (br. s., 1 H), 1.92 - 1.71 (m, 4 H), 1.48 - 1.39 (m, 4 H), 1.17 (br. s., 5 H)

**[Table 4.6, entry 8 Product]<sup>28</sup>**



According to the general procedure, N-Boc-proline (127 mg, 0.6 mmol),  $\text{Cs}_2\text{CO}_3$  (195 mg, 0.6 mmol),  $\text{TiO}_2$  (32 mg),  $\text{Ni}\cdot\text{dtbbpy}$  (10 mol%), and 4-Iodoacetophenone (98 mg, 0.4 mmol), in MeCN (5 mL) afforded the title compound (102 mg, 88% isolated yield) after purification by column chromatography (5-20% EtOAc:Hexanes gradient)

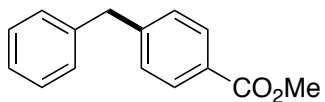
$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 7.67 (dd,  $J$  = 8.5, 13.1 Hz, 2 H), 7.28 - 7.19 (m, 2 H), 4.58 - 4.34 (m, 1 H), 3.71 - 3.37 (m, 2 H), 2.46 - 1.84 (m, 4 H), 1.44 (d,  $J$  = 12.0 Hz, 9 H)

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 160.4, 134.2, 119.4, 116.4, 103.1, 28.9, 28.4, 28.0

**4.18.D. General Procedure for the dual TiO<sub>2</sub>/Ni mediated decarboxylative cross-coupling of un-substituted and substituted phenylacetic acids with methyl 4-iodobenzoate.**

Briefly, the NiCl<sub>2</sub>•dtbbpy catalyst was assembled through the addition of 4.1 mg of NiCl<sub>2</sub>•glyme and 5 mg of 4,4'-Di-*tert*-butyl-2,2'-dipyridyl (dtbbpy) to a 10 mL schlenk tube containing 3 mL of THF. The solution was then sonicated for 5 minutes and heated to boiling with a heat gun. At this point the mixture was concentrated using a rotovap and then allowed to dry under vacuum for 20 min. Once dry, the phenylacetic acid derivative (0.6 mmol), Cs<sub>2</sub>CO<sub>3</sub> (195 mg, 0.6 mmol), TiO<sub>2</sub> (32 mg), methyl 4-iodobenzoate (105 mg, 0.4 mmol), and 5 mL of freshly distilled MeCN. The resulting suspension was then sonicated for 2 min. The reaction mixture was then degassed with Ar for 20 minutes and then irradiated with a solar simulator fitted with a 375 nm cut off filter for 3-72 h while stirring at room temperature. The progress of the reaction was monitored by TLC. The solid catalyst was separated by centrifugation and the resulting supernatant was diluted in ether (25 mL), and washed with 10% NaOH (4x, 25 mL), Brine (2x, 25 mL), H<sub>2</sub>O (2x, 25 mL). The organic layer was dried over anhydrous MgSO<sub>4</sub> and concentrated using a rotovap to yield the crude product. Purification of the crude was accomplished by column chromatography (hexanes:ethyl acetate).

**[Table 4.7, entry 1 Product]<sup>76</sup>**

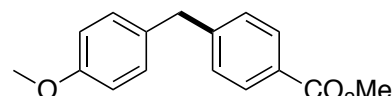


According to the general procedure, phenylacetic acid (82 mg, 0.6 mmol), Cs<sub>2</sub>CO<sub>3</sub> (195 mg, 0.6 mmol), TiO<sub>2</sub> (32 mg), Ni•dtbbpy (10 mol%), and 4-iodomethylbenzoate (105 mg, 0.4 mmol), in MeCN (5 mL) afforded the title compound (56 mg, 62% isolated yield) after purification by column chromatography (5-20% EtOAc:Hexanes gradient)

$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.07 - 8.00 (m, 2 H), 7.36 (d,  $J$  = 4.5 Hz, 4 H), 7.33 - 7.28 (m, 1 H), 7.16 - 7.09 (m, 2 H), 3.89 (s, 3 H), 3.86 (s, 2 H)

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 168.9, 166.7, 154.4, 132.3, 132.2, 131.5, 131.4, 128.7, 121.7, 52.5, 41.1

**[Table 4.7, entry 2 Product]<sup>77</sup>**

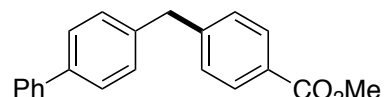


According to the general procedure, 4-methoxyphenylacetic acid (100 mg, 0.6 mmol),  $\text{Cs}_2\text{CO}_3$  (195 mg, 0.6 mmol),  $\text{TiO}_2$  (32 mg),  $\text{Ni}\cdot\text{dtbbpy}$  (10 mol%), and 4-iodomethylbenzoate (105 mg, 0.4 mmol), in MeCN (5 mL) afforded the title compound (135 mg, 76% isolated yield) after purification by column chromatography (5-20% EtOAc:Hexanes gradient)

$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.06 - 7.99 (m, 2 H), 7.30 - 7.25 (m, 2 H), 7.15 - 7.09 (m, 2 H), 6.91 - 6.86 (m, 2 H), 3.89 (s, 3 H), 3.80 (s, 5 H)

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 170.1, 166.6, 159.3, 154.7, 131.4, 130.7, 128.0, 125.4, 121.8, 114.5, 55.6, 52.5, 40.8

**[Table 4.7, entry 3 Product]**

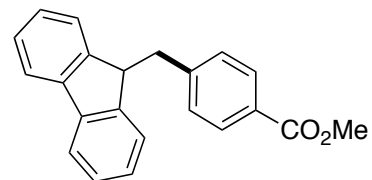


According to the general procedure, biphenylacetic acid (127 mg, 0.6 mmol),  $\text{Cs}_2\text{CO}_3$  (195 mg, 0.6 mmol),  $\text{TiO}_2$  (32 mg),  $\text{Ni}\cdot\text{dtbbpy}$  (10 mol%), and 4-iodomethylbenzoate (105 mg, 0.4 mmol), in MeCN (5 mL) afforded the title compound (88 mg, 73% isolated yield) after purification by column chromatography (5-20% EtOAc:Hexanes gradient)

$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.12 - 7.95 (m, 2 H), 7.66 - 7.53 (m, 4 H), 7.51 - 7.39 (m, 4 H), 7.38 - 7.29 (m, 1 H), 7.19 - 7.12 (m, 2 H), 3.90 (s, 2 H), 3.89 (s, 3 H)

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 169.4, 154.3, 140.6, 140.5, 132.0, 131.1, 129.7, 128.8, 127.8, 127.5, 127.4, 127.1, 121.5, 52.2, 41.0

**[Table 4.7, entry 4 Product]**

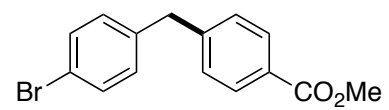


According to the general procedure, 9-fluoreneacetic acid (135 mg, 0.6 mmol),  $\text{Cs}_2\text{CO}_3$  (195 mg, 0.6 mmol),  $\text{TiO}_2$  (32 mg),  $\text{Ni}\cdot\text{dtbbpy}$  (10 mol%), and 4-iodomethylbenzoate (105 mg, 0.4 mmol), in MeCN (5 mL) afforded the title compound (86 mg, 68% isolated yield) after purification by column chromatography (5-20% EtOAc:Hexanes gradient)

$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.06 (d,  $J = 8.5$  Hz, 2 H), 7.77 (d,  $J = 7.5$  Hz, 2 H), 7.57 (d,  $J = 7.5$  Hz, 2 H), 7.43 - 7.29 (m, 4 H), 7.12 (d,  $J = 8.0$  Hz, 2 H), 4.49 (t,  $J = 6.5$  Hz, 1 H), 3.91 (s, 3 H), 3.08 (d,  $J = 7.0$  Hz, 2 H)

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 166.3, 154.2, 145.7, 140.9, 131.2, 127.8, 127.7, 127.3, 124.4, 121.5, 120.1, 52.2, 43.4, 38.7

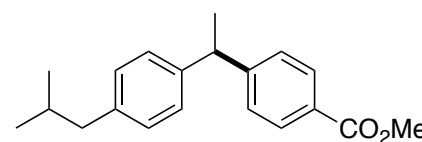
**[Table 4.7, entry 5 Product]<sup>78</sup>**

 According to the general procedure, 4-bromophenylacetic acid (129 mg, 0.6 mmol),  $\text{Cs}_2\text{CO}_3$  (195 mg, 0.6 mmol),  $\text{TiO}_2$  (32 mg),  $\text{Ni}\cdot\text{dtbbpy}$  (10 mol%), and 4-iodomethylbenzoate (105 mg, 0.4 mmol), in MeCN (5 mL) afforded the title compound (45 mg, 37% isolated yield) after purification by column chromatography (5-20% EtOAc:Hexanes gradient)

$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.08 - 7.98 (m, 2 H), 7.54 - 7.43 (m, 2 H), 7.30 - 7.20 (m, 5 H), 7.17 - 7.06 (m, 2 H), 3.91 - 3.87 (m, 3 H), 3.81 (s, 2 H)

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 169.8, 166.6, 154.6, 133.4, 131.4, 129.6, 129.1, 128.1, 127.8, 121.8, 52.5, 41.7

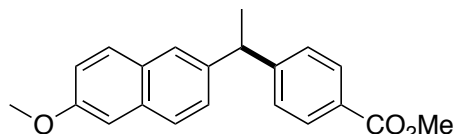
**[Table 4.7, entry 6 Product]**

 According to the general procedure, ibuprofen (124 mg, 0.6 mmol),  $\text{Cs}_2\text{CO}_3$  (195 mg, 0.6 mmol),  $\text{TiO}_2$  (32 mg),  $\text{Ni}\cdot\text{dtbbpy}$  (10 mol%), and 4-iodomethylbenzoate (105 mg, 0.4 mmol), in MeCN (5 mL) afforded the title compound (52 mg, 44% isolated yield) after purification by column chromatography (5-20% EtOAc:Hexanes gradient)

$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.03 - 7.98 (m, 2 H), 7.27 (d,  $J = 8.0$  Hz, 2 H), 7.13 (d,  $J = 8.0$  Hz, 2 H), 7.08 - 7.03 (m, 2 H), 3.93 (q,  $J = 7.0$  Hz, 1 H), 3.88 (s, 3 H), 2.45 (d,  $J = 7.3$  Hz, 2 H), 1.85 (td,  $J = 7.0, 13.6$  Hz, 1 H), 1.91 - 1.78 (m, 1 H), 1.59 (d,  $J = 7.0$  Hz, 3 H), 0.91 - 0.87 (m, 6 H)

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 172.7, 166.3, 154.5, 141.0, 131.1, 129.6, 127.6, 127.2, 121.4, 52.2, 45.3, 45.0, 30.2, 22.4, 18.4

**[Table 4.7, entry 7 Product]**

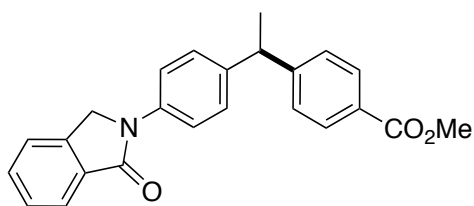


According to the general procedure, naproxen (138 mg, 0.6 mmol),  $\text{Cs}_2\text{CO}_3$  (195 mg, 0.6 mmol),  $\text{TiO}_2$  (32 mg),  $\text{Ni}\cdot\text{dtbbpy}$  (10 mol%), and 4-iodomethylbenzoate (105 mg, 0.4 mmol), in MeCN (5 mL) afforded the title compound (72 mg, 56% isolated yield) after purification by column chromatography (5-20% EtOAc:Hexanes gradient)

$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.06 - 7.93 (m, 2 H), 7.80 - 7.66 (m, 3 H), 7.47 (dd,  $J$  = 2.0, 8.6 Hz, 1 H), 7.20 - 7.00 (m, 4 H), 4.09 (q,  $J$  = 7.0 Hz, 1 H), 3.91 (s, 3 H), 3.87 (s, 3 H), 1.68 (d,  $J$  = 7.0 Hz, 3 H)

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 172.6, 166.3, 157.8, 154.5, 134.8, 133.9, 131.1, 129.3, 129.0, 127.6, 127.5, 126.2, 126.0, 121.4, 119.2, 105.6, 55.3, 52.1, 45.6, 18.4

**[Table 4.7, entry 8 Product]**

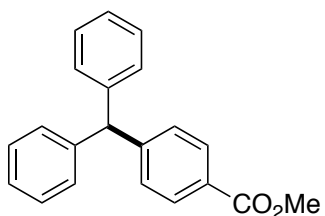


According to the general procedure, indoprofen (169 mg, 0.6 mmol),  $\text{Cs}_2\text{CO}_3$  (195 mg, 0.6 mmol),  $\text{TiO}_2$  (32 mg),  $\text{Ni}\cdot\text{dtbbpy}$  (10 mol%), and 4-iodomethylbenzoate (105 mg, 0.4 mmol), in MeCN (5 mL) afforded the title compound (71 mg, 48% isolated yield) after purification by column chromatography (5-20% EtOAc:Hexanes gradient)

$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.04 - 7.99 (m, 2 H), 7.94 - 7.85 (m, 3 H), 7.63 - 7.41 (m, 5 H), 7.10 - 7.04 (m, 2 H), 4.86 (s, 2 H), 4.01 - 3.94 (m, 1 H), 3.88 (s, 3 H), 1.62 (d,  $J$  = 7.0 Hz, 3 H)

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 167.5, 166.3, 154.4, 140.0, 138.9, 135.6, 132.2, 131.1, 128.5, 128.3, 127.7, 124.2, 122.6, 121.4, 119.8, 52.2, 50.7, 45.1, 18.4

**[Table 4.7, entry 9 Product]<sup>79</sup>**

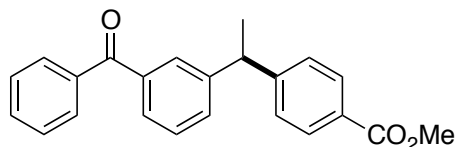


According to the general procedure, diphenylacetic acid (127 mg, 0.6 mmol),  $\text{Cs}_2\text{CO}_3$  (127 mg, 0.6 mmol),  $\text{TiO}_2$  (32 mg),  $\text{Ni}\cdot\text{dtbbpy}$  (10 mol%), and 4-iodomethylbenzoate (105 mg, 0.4 mmol), in MeCN (5 mL) afforded the title compound (87 mg, 72% isolated yield) after purification by column chromatography (5-20% EtOAc:Hexanes gradient)

$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.10 - 7.94 (m, 2 H), 7.45 - 7.25 (m, 10 H), 7.20 - 7.08 (m, 2 H), 5.25 (s, 1 H), 3.92 - 3.85 (s, 3 H)

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 170.5, 166.2, 154.3, 137.8, 131.1, 128.8, 128.6, 127.6, 121.4, 57.1, 52.2

**[Table 4.7, entry 10 Product]**

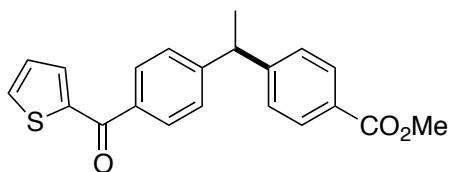


According to the general procedure, ketoprofen (153 mg, 0.6 mmol),  $\text{Cs}_2\text{CO}_3$  (195 mg, 0.6 mmol),  $\text{TiO}_2$  (32 mg),  $\text{Ni}\cdot\text{dtbbpy}$  (10 mol%), and 4-iodomethylbenzoate (105 mg, 0.4 mmol), in MeCN (5 mL) afforded the title compound (114 mg, 83% isolated yield) after purification by column chromatography (5-20% EtOAc:Hexanes gradient)

$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.05 - 8.00 (m, 2 H), 7.84 (t,  $J$  = 2.0 Hz, 1 H), 7.81 - 7.77 (m, 2 H), 7.71 (td,  $J$  = 1.5, 7.6 Hz, 1 H), 7.64 - 7.55 (m, 2 H), 7.51 - 7.42 (m, 3 H), 7.10 - 7.04 (m, 2 H), 4.04 (q,  $J$  = 7.0 Hz, 1 H), 3.88 (s, 3 H), 1.64 (d,  $J$  = 7.5 Hz, 3 H)

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 196.3, 172.0, 166.2, 154.2, 140.0, 138.1, 137.3, 132.5, 131.4, 131.1, 130.0, 129.3, 129.2, 128.8, 128.3, 127.7, 121.3, 52.1, 45.5, 18.4

**[Table 4.7, entry 11 Product]**



According to the general procedure, suprofen (104 mg, 0.6 mmol),  $\text{Cs}_2\text{CO}_3$  (195 mg, 0.6 mmol),  $\text{TiO}_2$  (32 mg),  $\text{Ni}\cdot\text{dtbbpy}$  (10 mol%), and 4-iodomethylbenzoate (105 mg, 0.4 mmol), in MeCN (5 mL) afforded the title compound (91 mg, 65% isolated yield) after purification by column chromatography (5-20% EtOAc:Hexanes gradient)

$^1\text{H}$  NMR (400MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 8.07 - 7.99 (m, 2 H), 7.90 - 7.85 (m, 2 H), 7.73 - 7.63 (m, 2 H), 7.51 (d,  $J$  = 8.0 Hz, 2 H), 7.15 (dd,  $J$  = 4.0, 5.0 Hz, 1 H), 7.10 - 7.05 (m, 2 H), 4.05 (q,  $J$  = 7.0 Hz, 1 H), 3.88 (s, 3 H), 1.66 (d,  $J$  = 7.0 Hz, 3 H)

$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  ppm 187.6, 171.8, 166.2, 154.2, 144.0, 143.4, 137.4, 134.8, 134.3, 131.1, 129.8, 128.0, 127.7, 121.3, 52.2, 45.7, 18.3

**4.18.E. General Procedure for the Photochemical Synthesis of NiNP @ P25  $\text{TiO}_2$ .**

Into a 100 mL Erlenmeyer flask, P25  $\text{TiO}_2$ , benzophenone (22 mg, 0.12 mmol),  $\text{Ni}(\text{acac})_2$  (31 mg, 0.12 mmol), and ethanol (100 mL) were added. The mixture was then sonicated for 10 minutes, to ensure complete dissolution of the

benzophenone and  $\text{Ni}(\text{acac})_2$  and dispersion of the  $\text{TiO}_2$ . The flask was stoppered and purged for 20 minutes with Argon. The solution was then irradiated for 6 hours under mechanical stirring in a Luzchem Inc. photoreactor, fitted with 14 UVA bulbs. As the reaction progressed the color of the solution changed from a light greenish-yellow to a dark grey. The solid was then isolated through centrifugation (20 min, 3500 RPM). This was then followed by 5 washes with 20 mL of ethanol, each time redispersing the pellet through sonication and reisolating the solid catalyst via centrifugation. The resulting slurry was then dried under vacuum for 72 hours to give a grey solid. The three different loadings were obtained by varying the amount of  $\text{TiO}_2$  added (50 mg – 4 wt%, 100 mg - 2 wt%, 200 mg – 1 wt%).

#### **4.18.F. General Procedure for the heterogeneous dual $\text{TiO}_2/\text{Ni}$ mediated decarboxylative cross-coupling of N-Boc-Proline with 4-methyl iodobenzoate**

Briefly, 33 mg of either 1 wt%, 2 wt%, or 4 wt%  $\text{NiNP@P25 TiO}_2$  and 5 mg of 4,4'-Di-*tert*-butyl-2,2'-dipyridyl (dtbbpy) to a 10 mL schlenk tube containing 3 mL of THF. The solution was then sonicated for 5 minutes and heated to boiling with a heat gun. At this point the mixture was concentrated using a rotovap and then allowed to dry under vacuum for 20 min. Once dry, N-Boc-proline (127 mg, 0.6 mmol),  $\text{Cs}_2\text{CO}_3$  (195 mg, 0.6 mmol),  $\text{TiO}_2$  (32 mg), aryl iodide (0.4 mmol), and 5 mL of freshly distilled MeCN. The resulting suspension was then sonicated for 2 min. The reaction mixture was then degassed with Ar for 20 minutes and then irradiated with a solar simulator fitted with a 375 nm cut off filter for 3-72 h while stirring at room temperature. The progress of the reaction was monitored by TLC.



The solid catalyst was separated by centrifugation and the resulting supernatant was diluted in ether (25 mL), and washed with 10% NaOH (4x, 25 mL), Brine (2x, 25 mL), H<sub>2</sub>O (2x, 25 mL). The organic layer was dried over anhydrous MgSO<sub>4</sub> and concentrated using a rotovap to yield the crude product. Purification of the crude was accomplished by column chromatography (hexanes:ethyl acetate).

## 4.18.G. NMR spectra

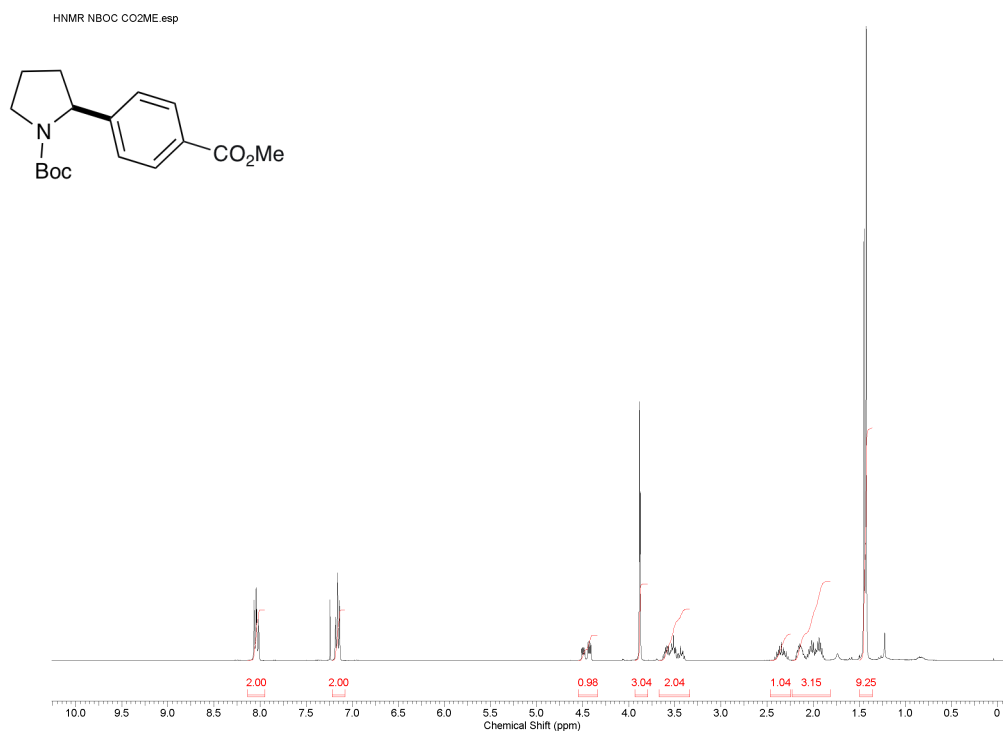


Figure 4A.28. <sup>1</sup>H NMR of [Table 4.6, entry 1 Product] in CDCl<sub>3</sub>.

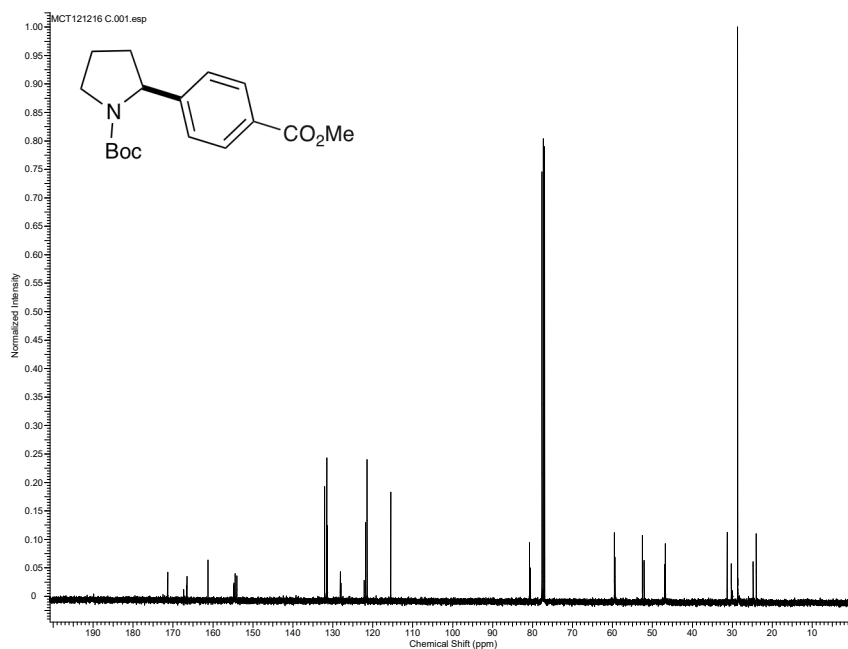


Figure 4A.29. <sup>13</sup>C NMR of [Table 4.6, entry 1 Product] in CDCl<sub>3</sub>.

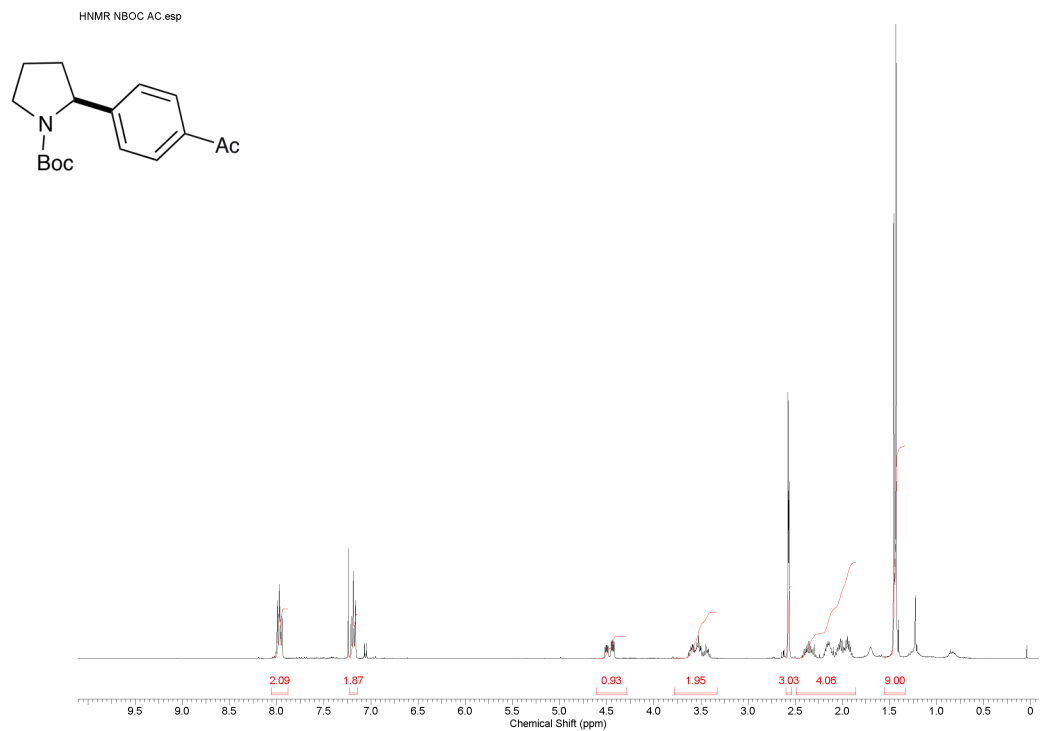


Figure 4A.30.  $^1\text{H}$  NMR of [Table 4.6, entry 2 Product] in  $\text{CDCl}_3$ .

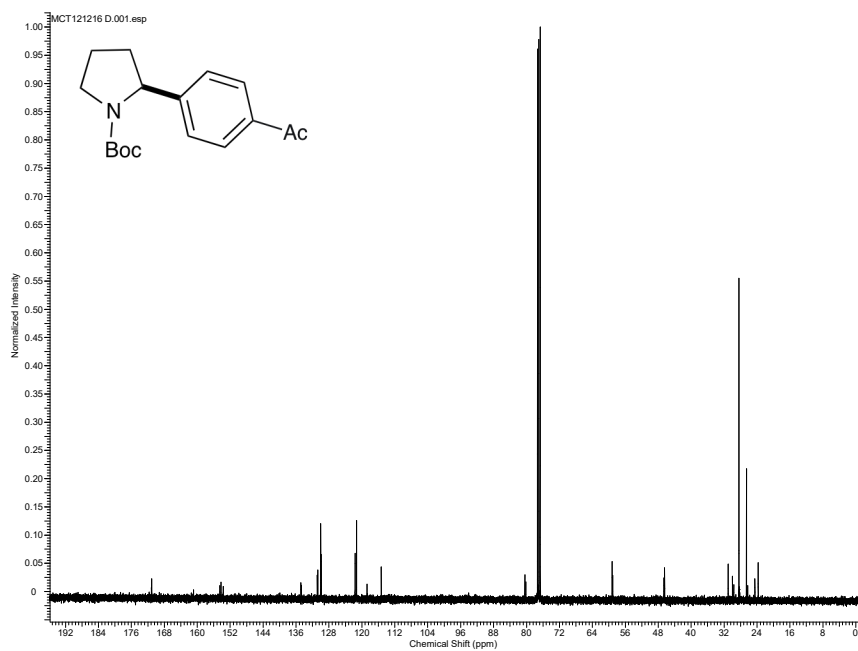


Figure 4A.31.  $^{13}\text{C}$  NMR of [Table 4.6, entry 2 Product] in  $\text{CDCl}_3$ .

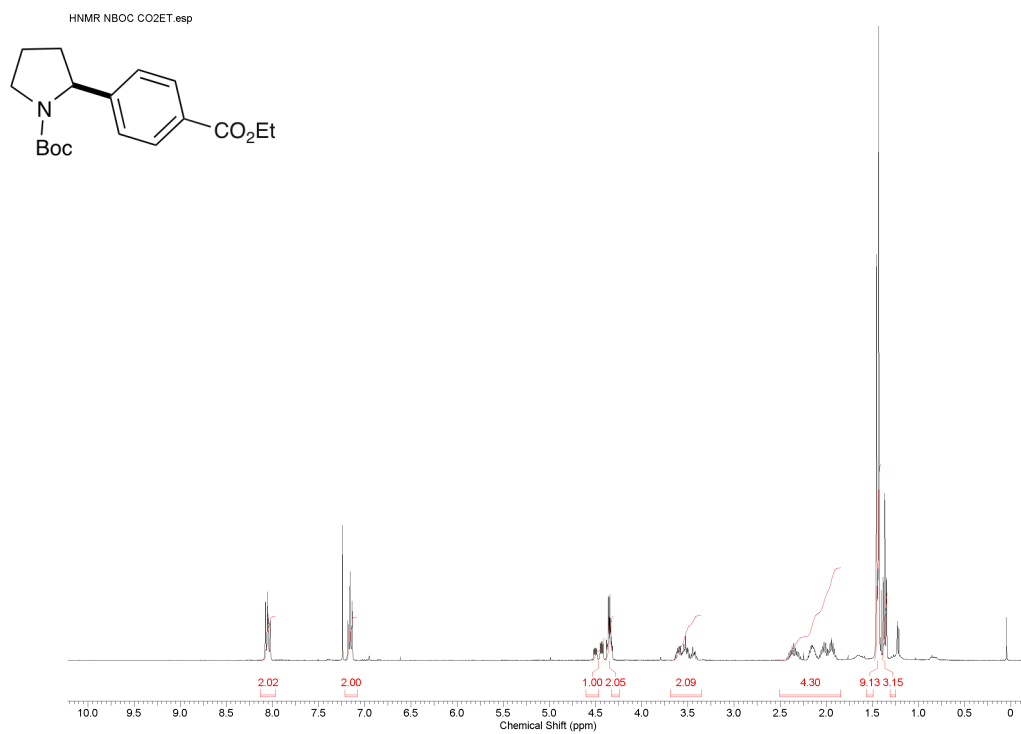


Figure 4A.32.  $^1\text{H}$  NMR of [Table 4.6, entry 3 Product] in  $\text{CDCl}_3$ .

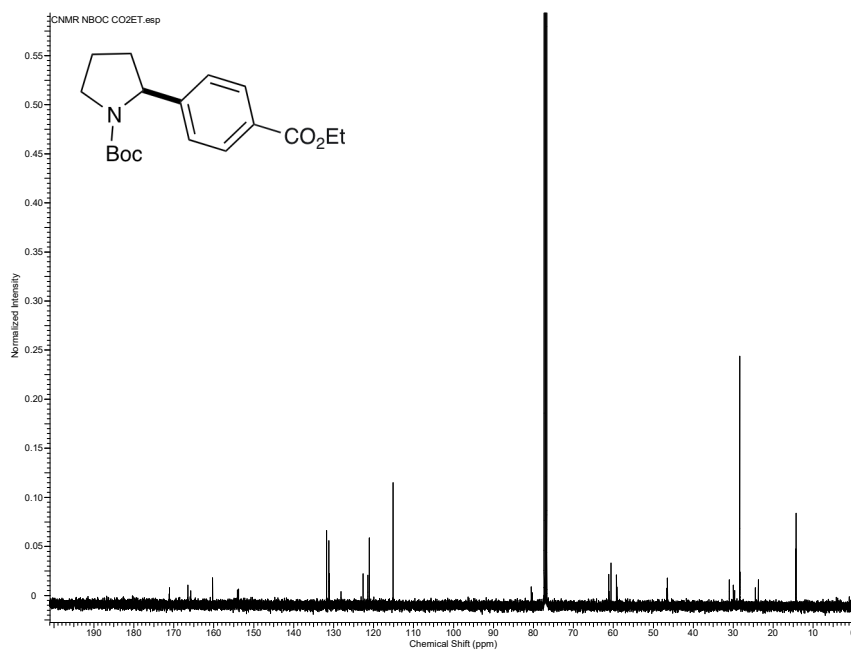


Figure 4A.33.  $^{13}\text{C}$  NMR of [Table 4.6, entry 3 Product] in  $\text{CDCl}_3$ .

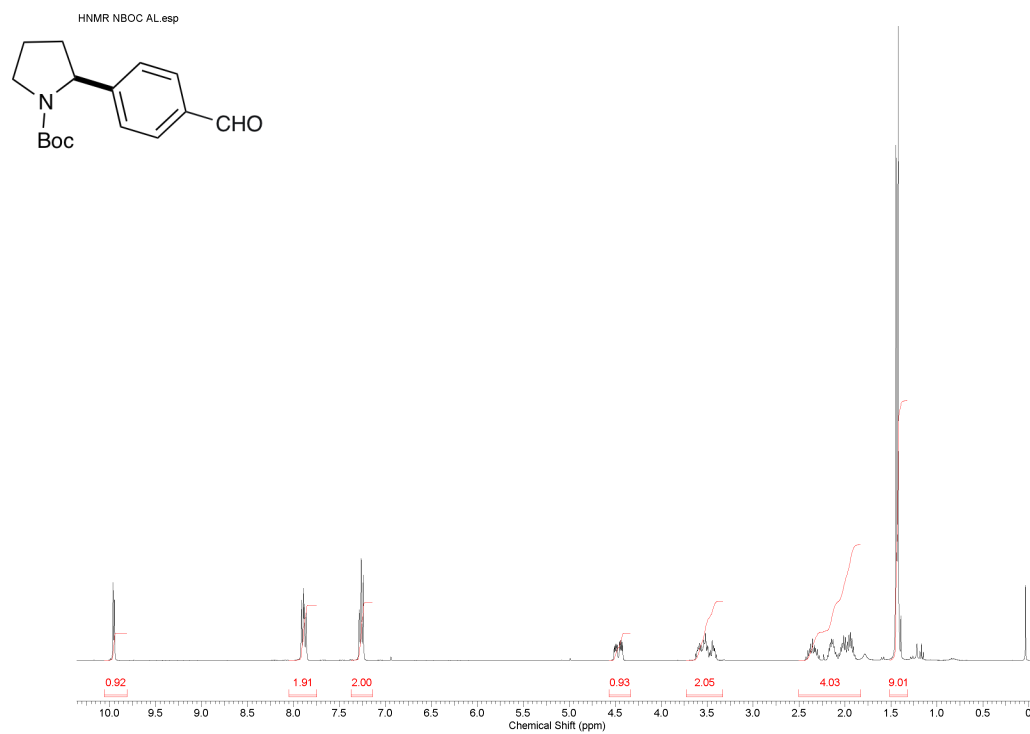


Figure 4A.34. <sup>1</sup>H NMR of [Table 4.6, entry 4 Product] in CDCl<sub>3</sub>.

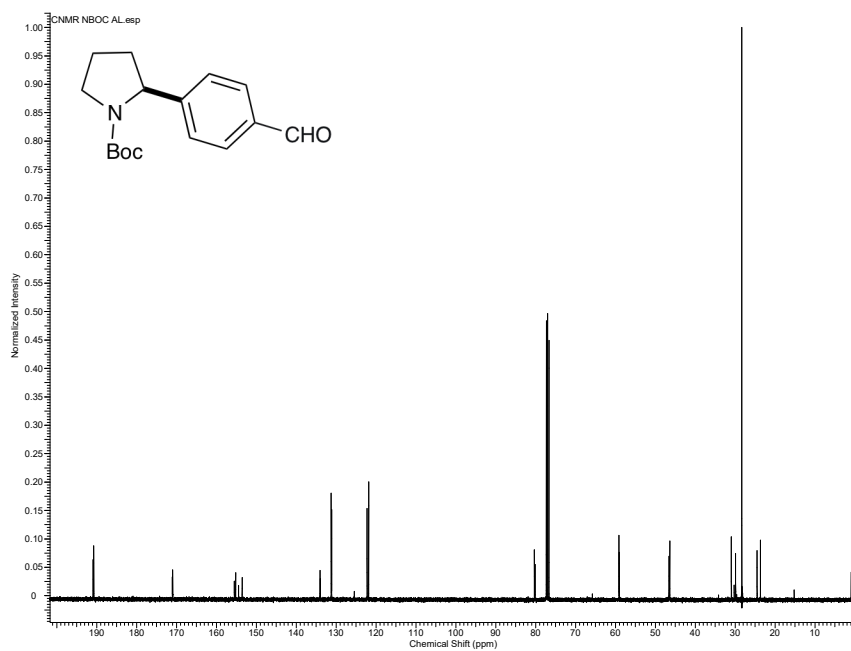


Figure 4A.35. <sup>13</sup>C NMR of [Table 4.6, entry 4 Product] in CDCl<sub>3</sub>.

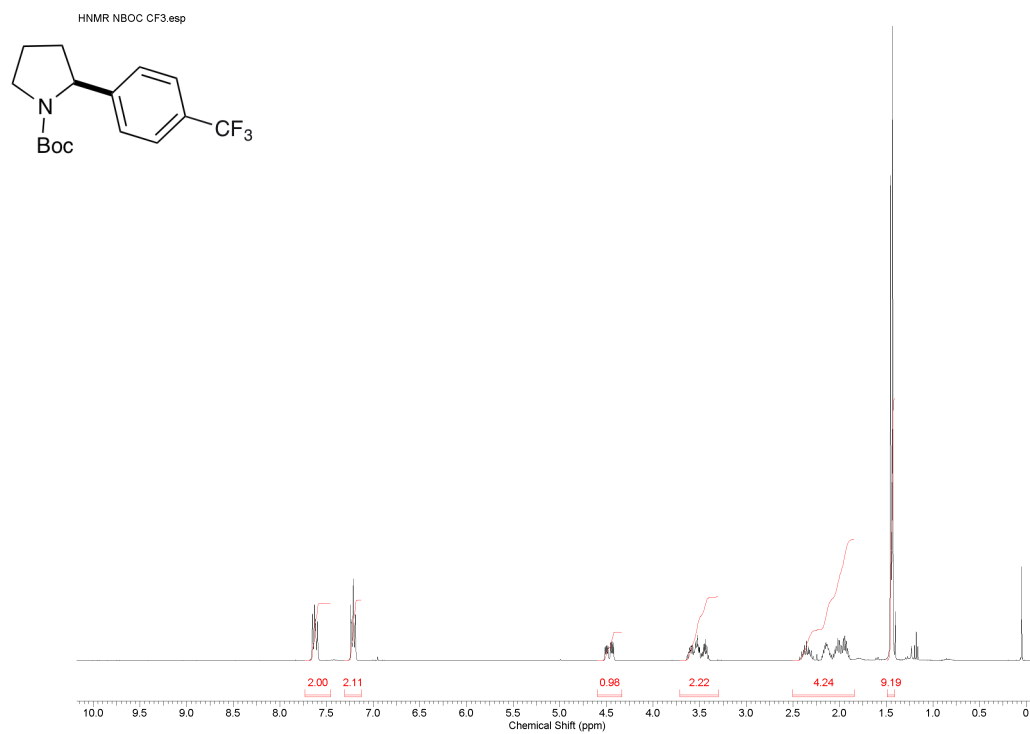


Figure 4A.36.  $^1\text{H}$  NMR of [Table 4.6, entry 5 Product] in  $\text{CDCl}_3$ .

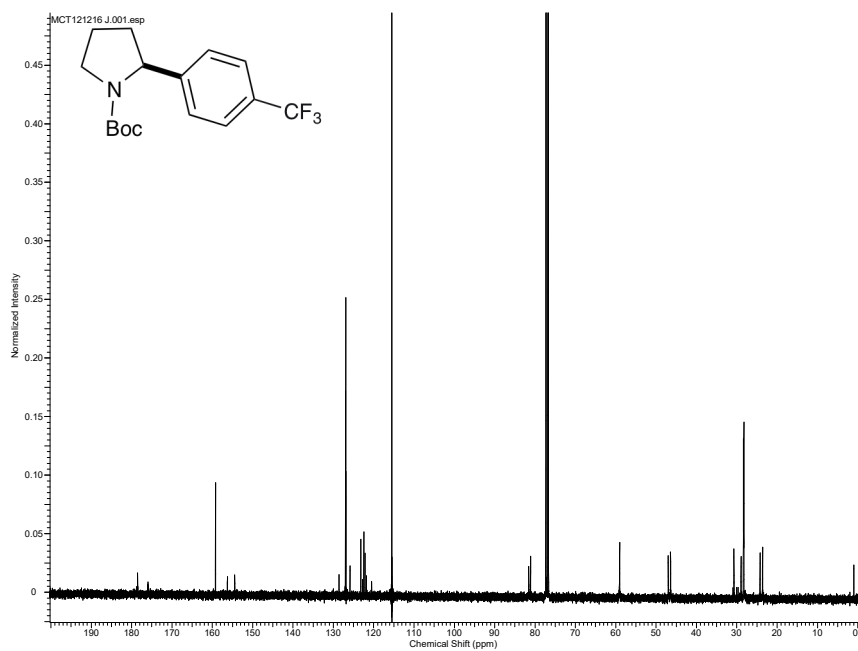


Figure 4A.37.  $^{13}\text{C}$  NMR of [Table 4.6, entry 5 Product] in  $\text{CDCl}_3$ .

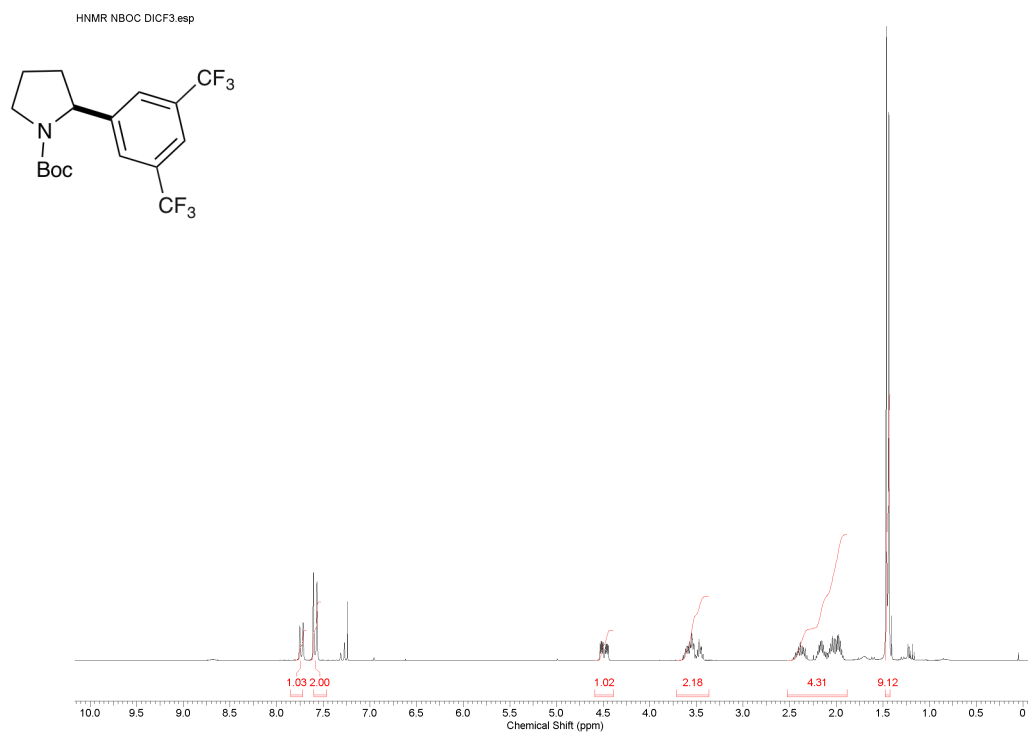


Figure 4A.38.  $^1\text{H}$  NMR of [Table 4.6, entry 6 Product] in  $\text{CDCl}_3$ .

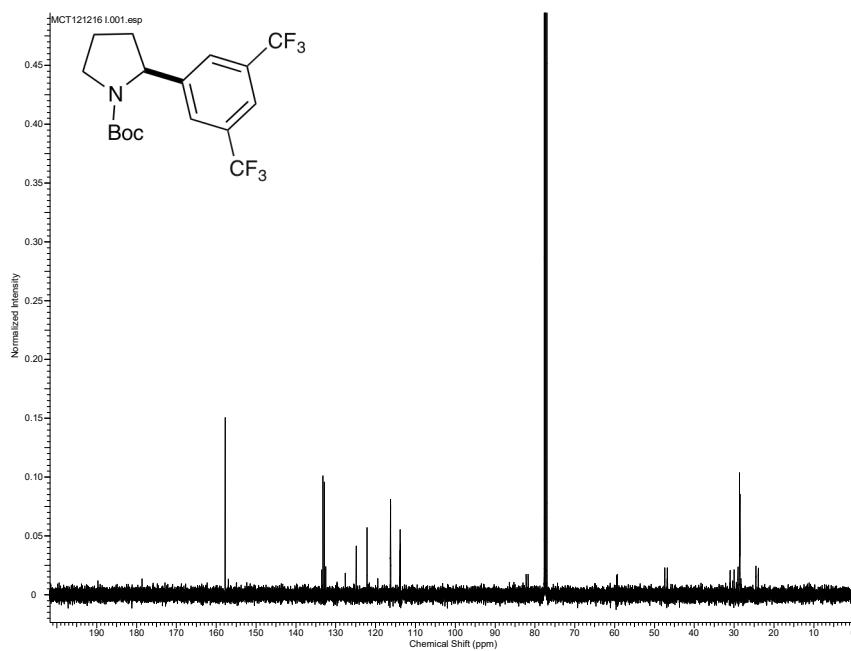
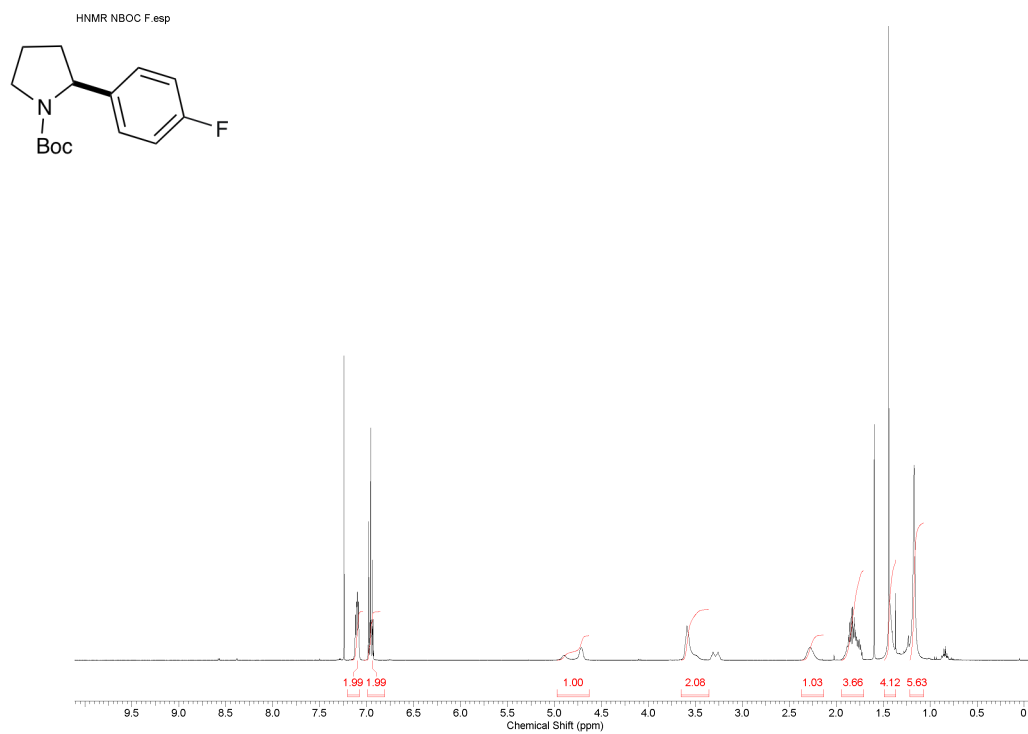
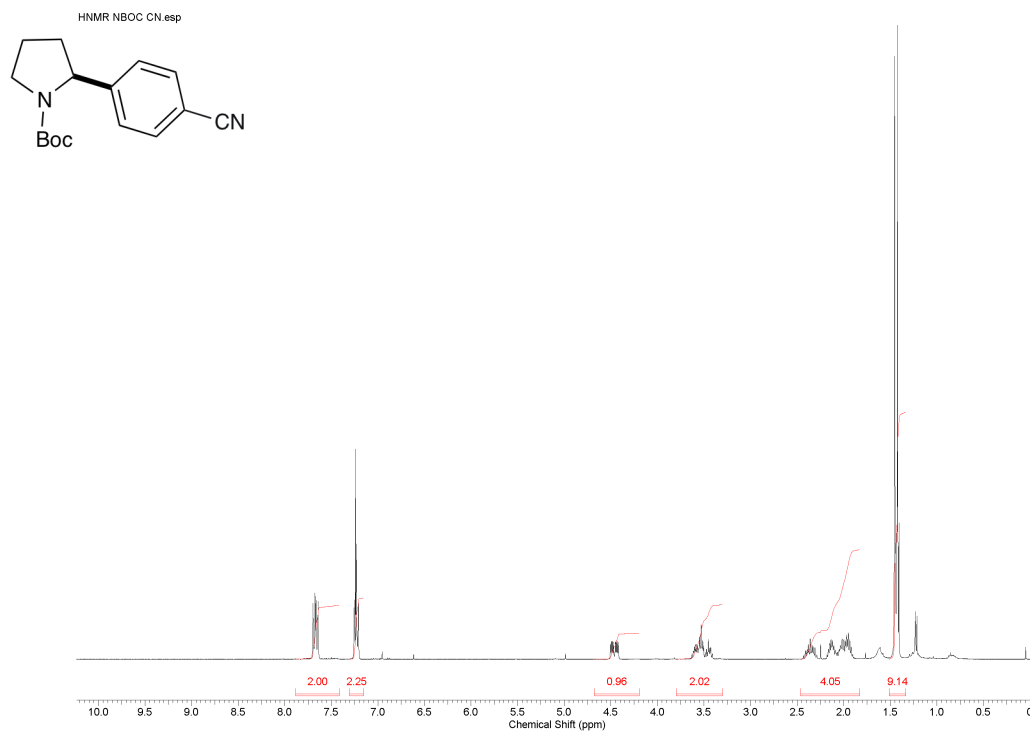


Figure 4A.39.  $^{13}\text{C}$  NMR of [Table 4.6, entry 6 Product] in  $\text{CDCl}_3$ .

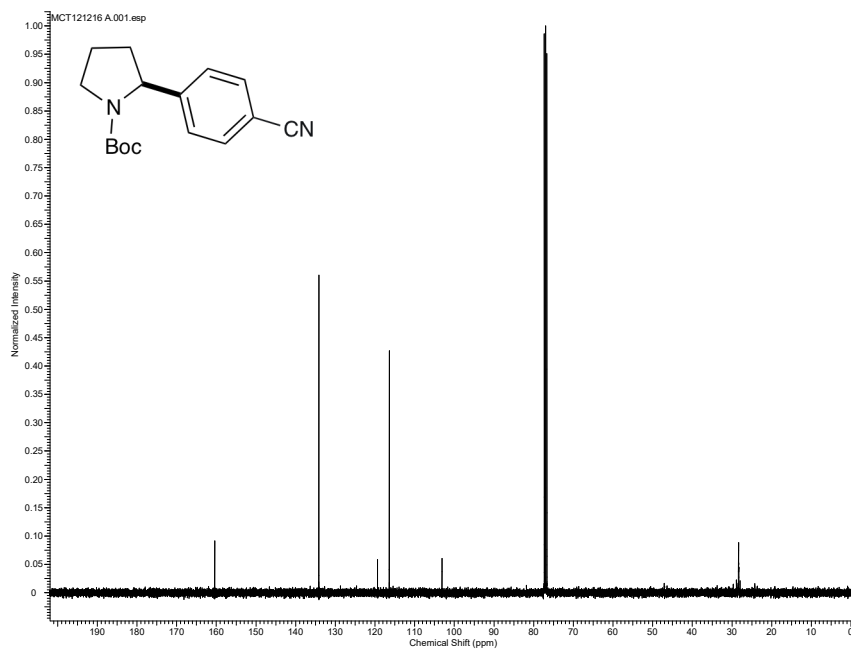


**Figure 4A.40.**  $^1\text{H}$  NMR of [Table 4.6, entry 7 Product] in  $\text{CDCl}_3$ .



**Figure 4A.41.**  $^1\text{H}$  NMR of [Table 4.6, entry 8 Product] in  $\text{CDCl}_3$ .

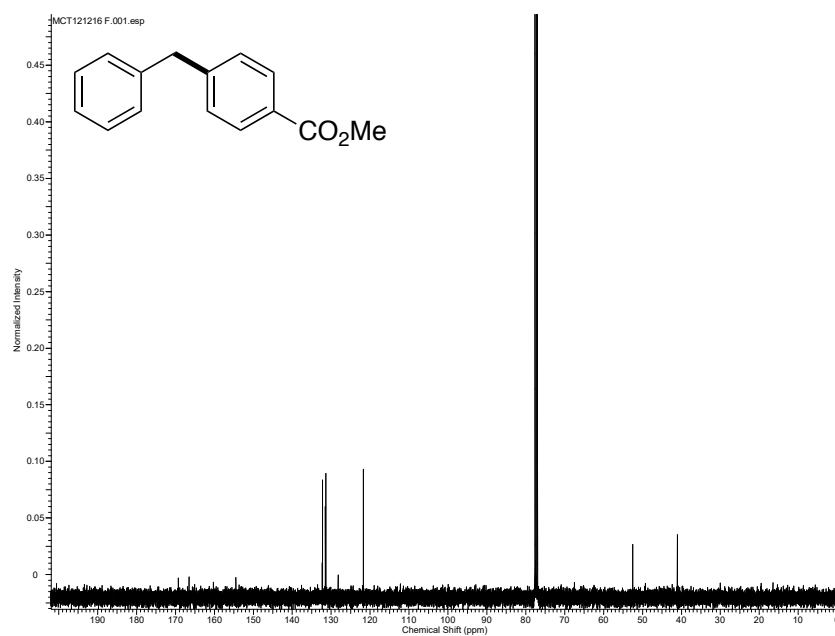




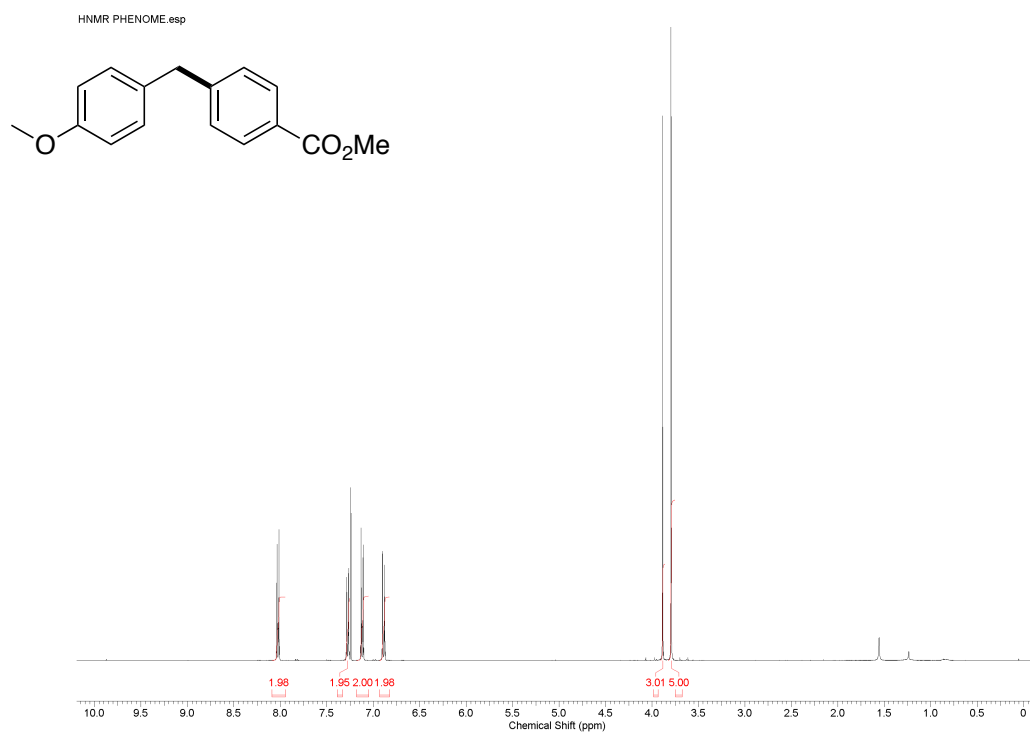
**Figure 4A.42.**  $^{13}\text{C}$  NMR of [Table 4.6, entry 8 Product] in  $\text{CDCl}_3$ .



**Figure 4A.43.**  $^1\text{H}$  NMR of [Table 4.7, entry 1 Product] in  $\text{CDCl}_3$ .



**Figure 4A.44.**  $^{13}\text{C}$  NMR of [Table 4.7, entry 1 Product] in  $\text{CDCl}_3$ .



**Figure 4A.45.**  $^1\text{H}$  NMR of [Table 4.7, entry 2 Product] in  $\text{CDCl}_3$ .

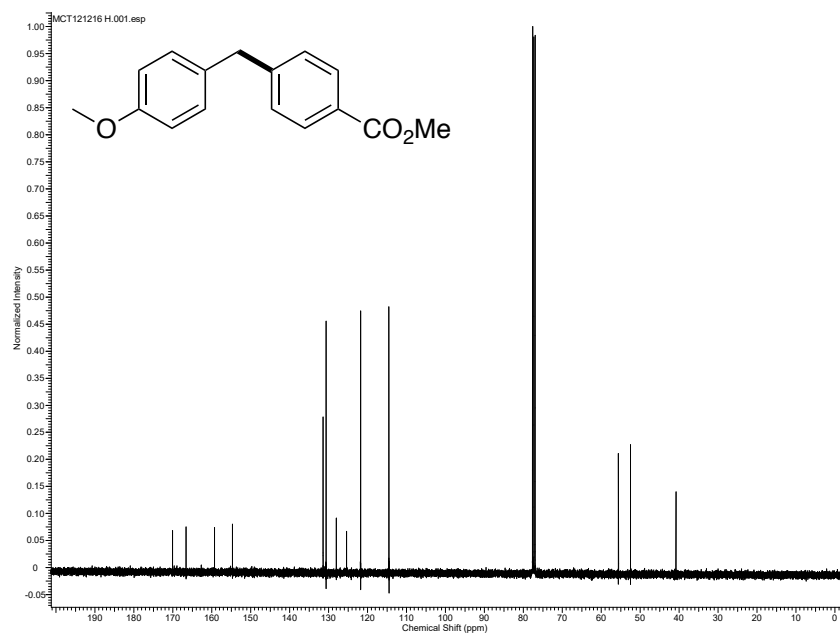


Figure 4A.46.  $^{13}\text{C}$  NMR of [Table 4.7, entry 2 Product] in  $\text{CDCl}_3$ .

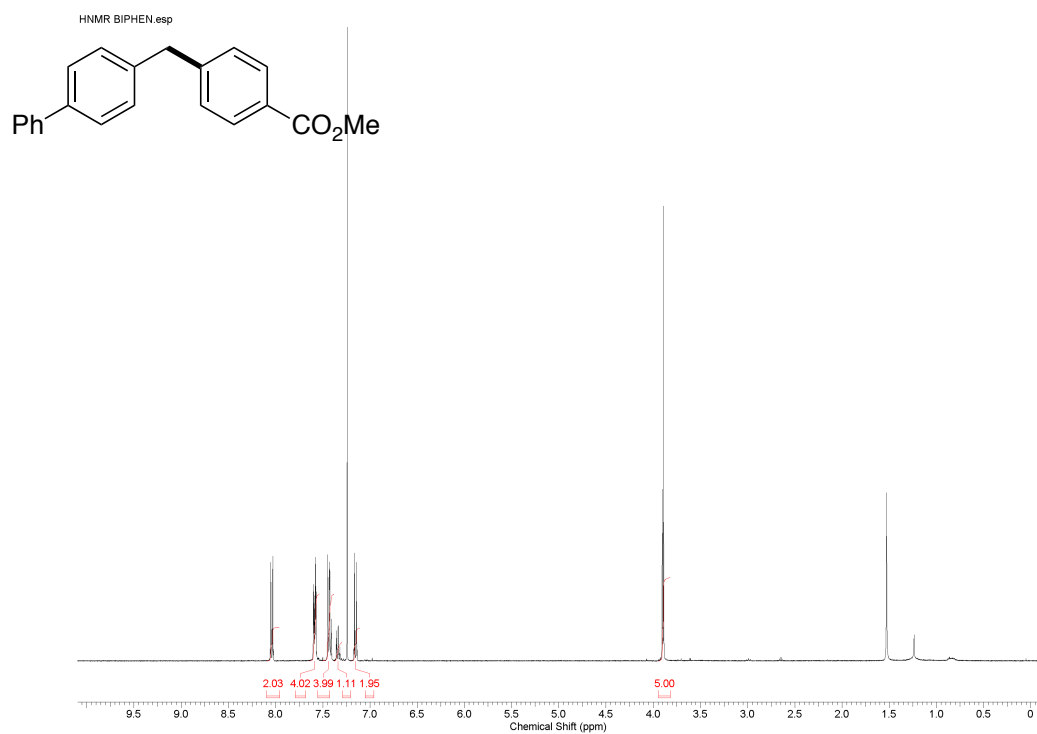
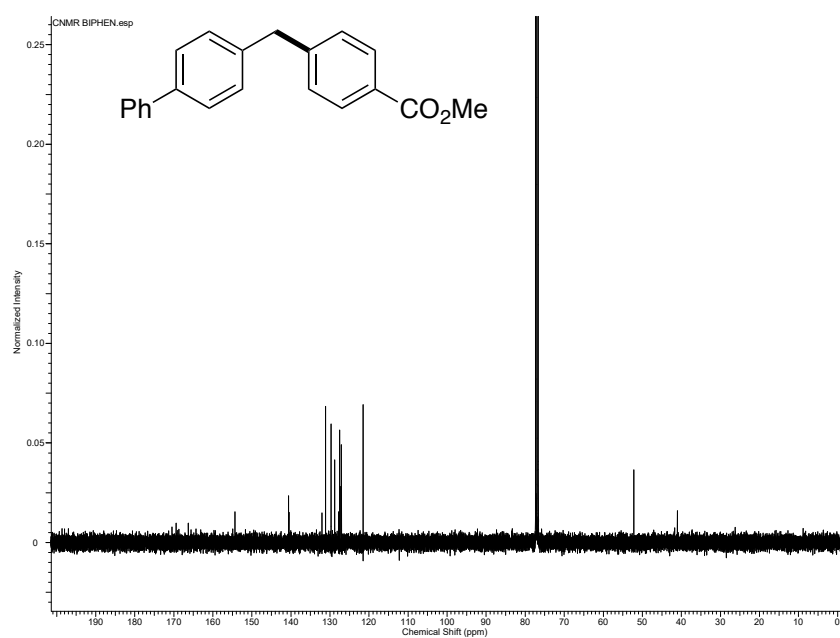
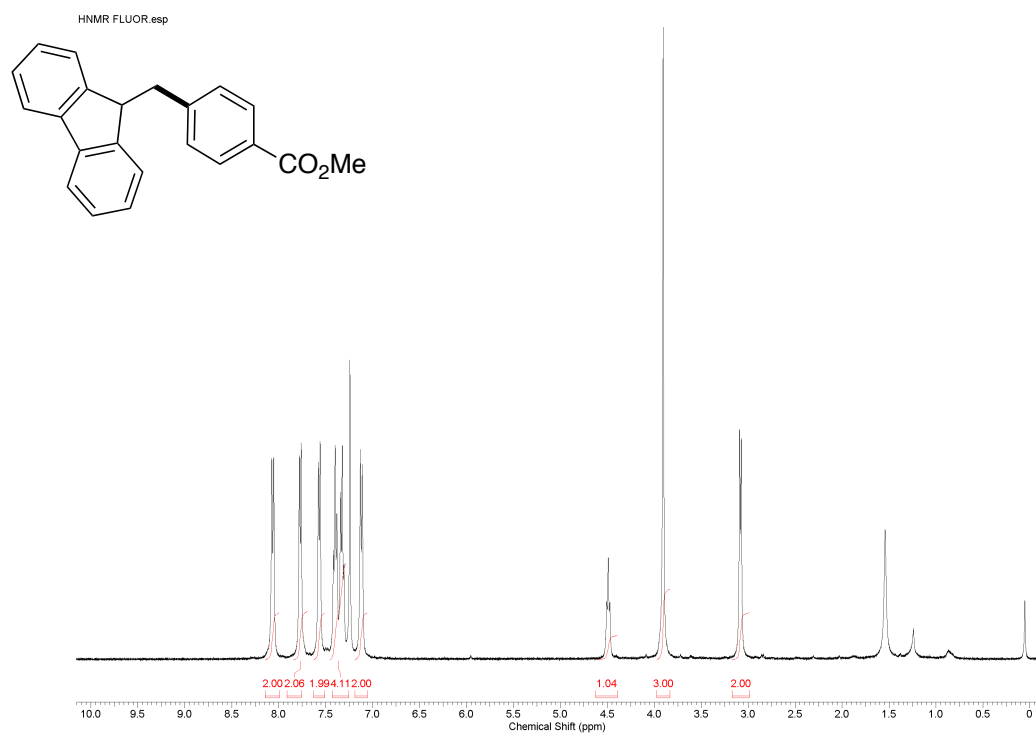


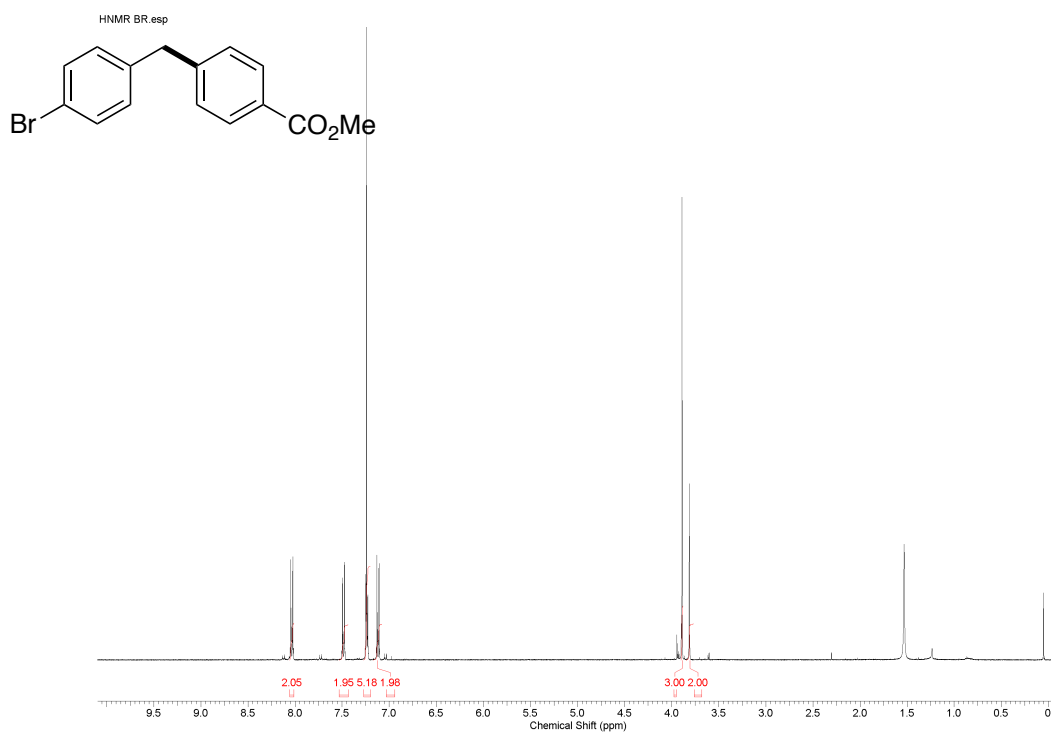
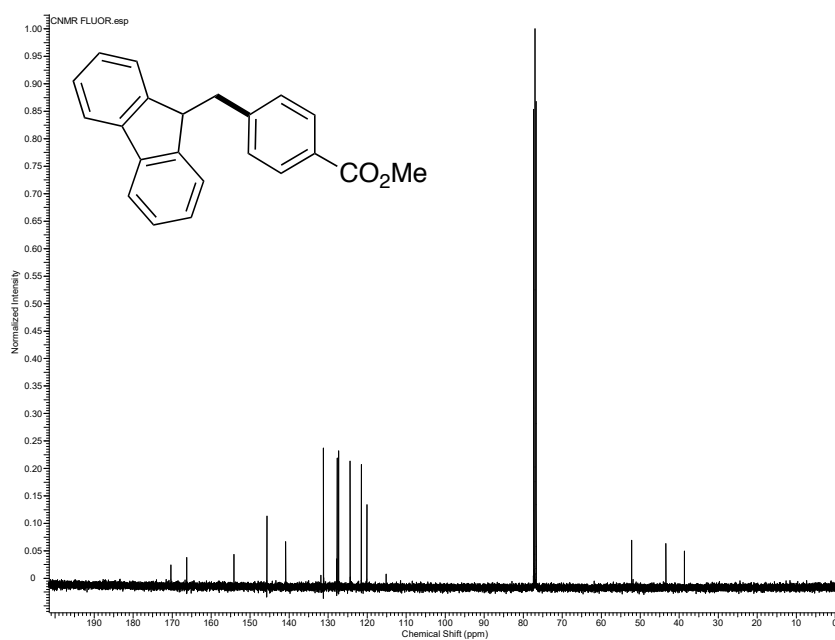
Figure 4A.47.  $^1\text{H}$  NMR of [Table 4.7, entry 3 Product] in  $\text{CDCl}_3$ .



**Figure 4A.48.** <sup>13</sup>C NMR of [Table 4.7, entry 3 Product] in CDCl<sub>3</sub>.



**Figure 4A.49.** <sup>1</sup>H NMR of [Table 4.7, entry 4 Product] in CDCl<sub>3</sub>.



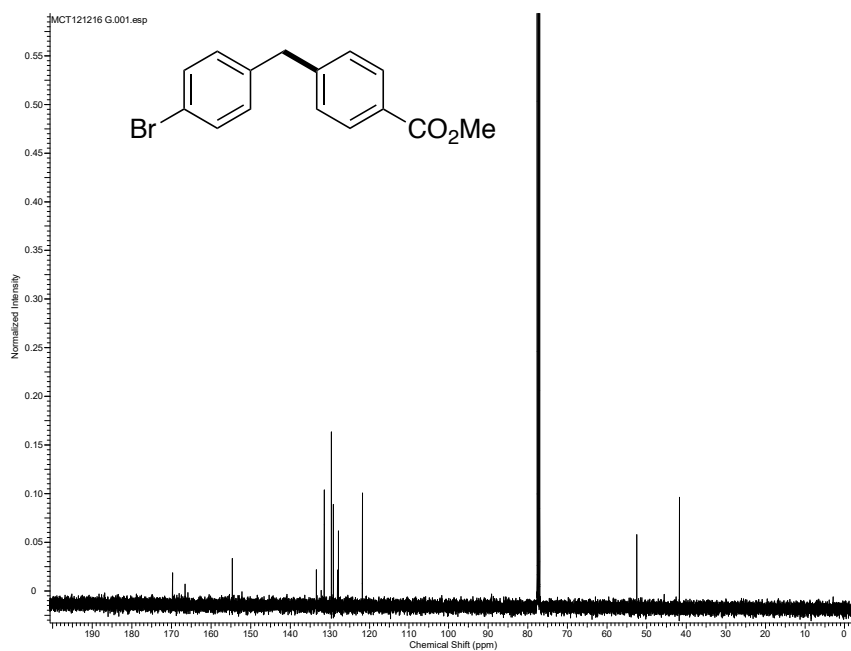


Figure 4A.52. <sup>13</sup>C NMR of [Table 4.7, entry 5 Product] in CDCl<sub>3</sub>.

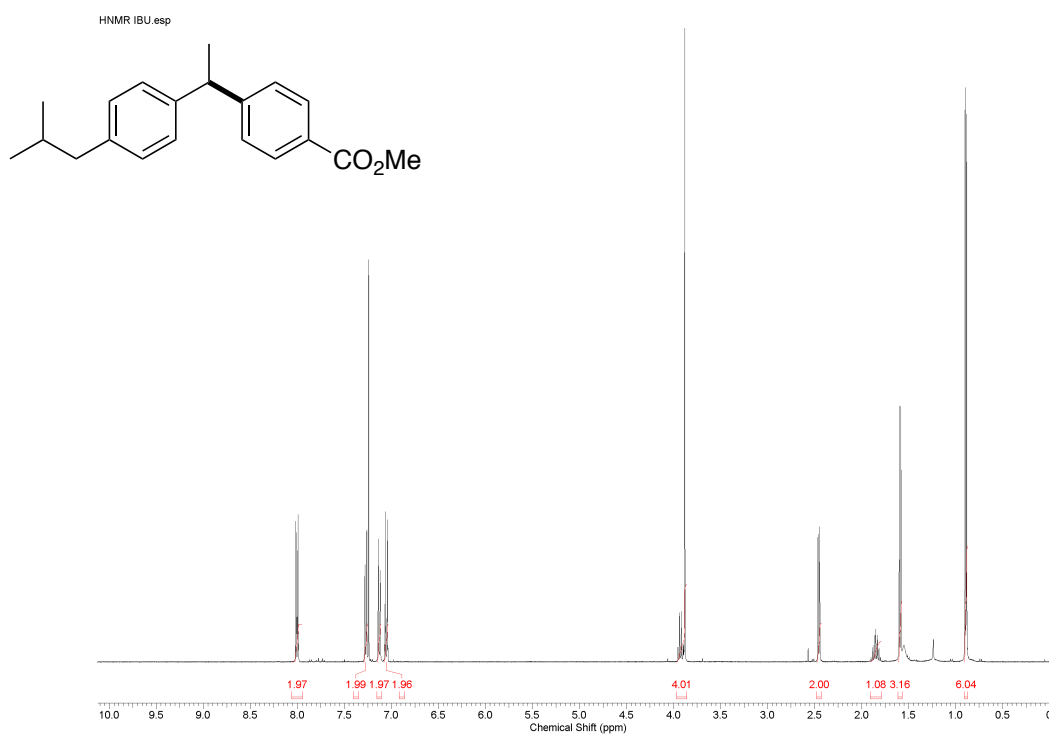


Figure 4A.53. <sup>1</sup>H NMR of [Table 4.7, entry 6 Product] in CDCl<sub>3</sub>.

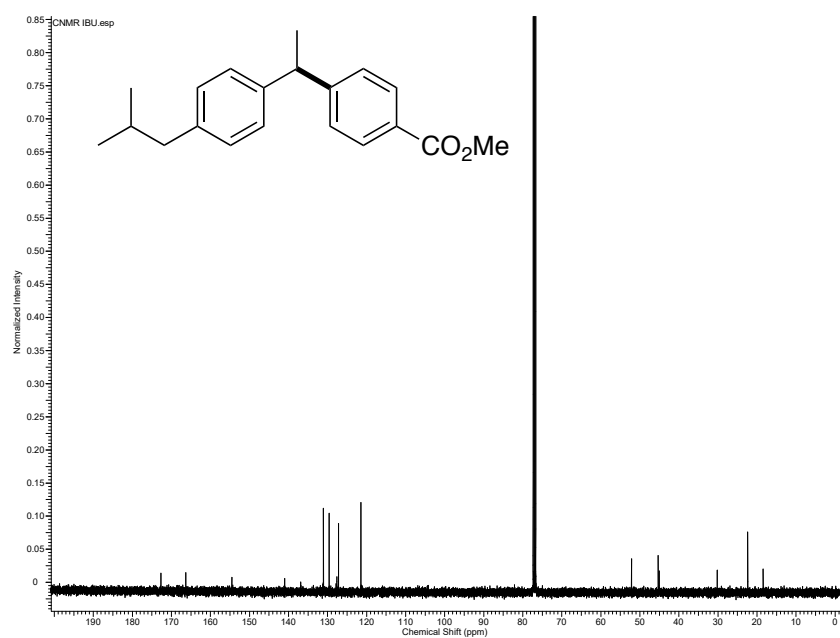


Figure 4A.54.  $^{13}\text{C}$  NMR of [Table 4.7, entry 6 Product] in  $\text{CDCl}_3$ .

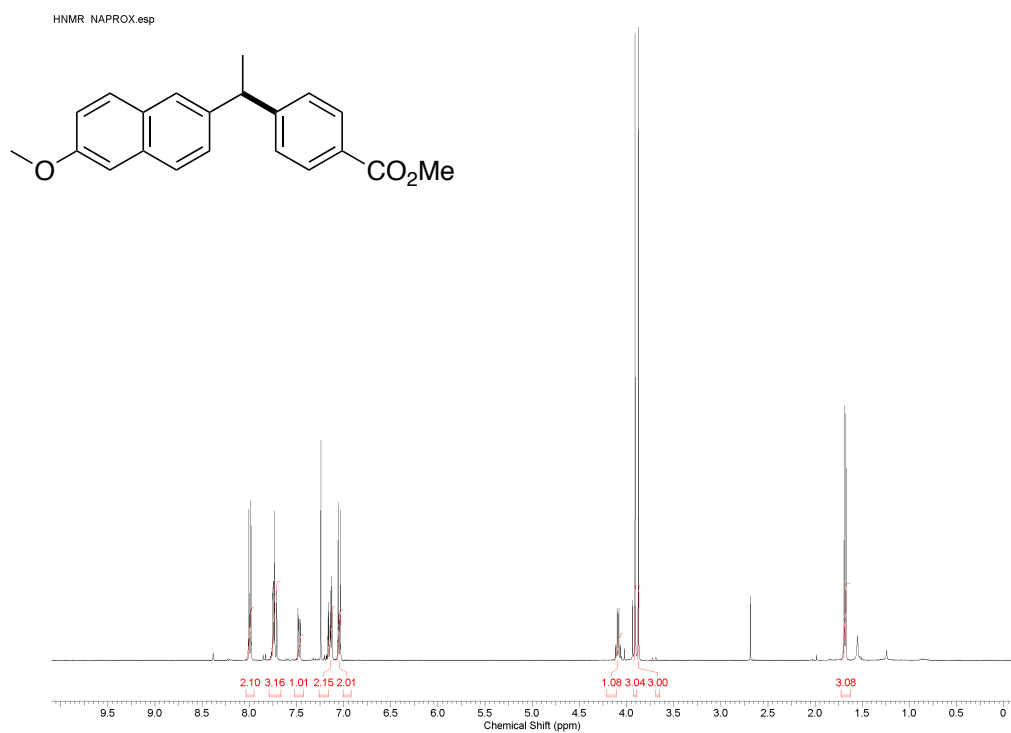


Figure 4A.55.  $^1\text{H}$  NMR of [Table 4.7, entry 7 Product] in  $\text{CDCl}_3$ .

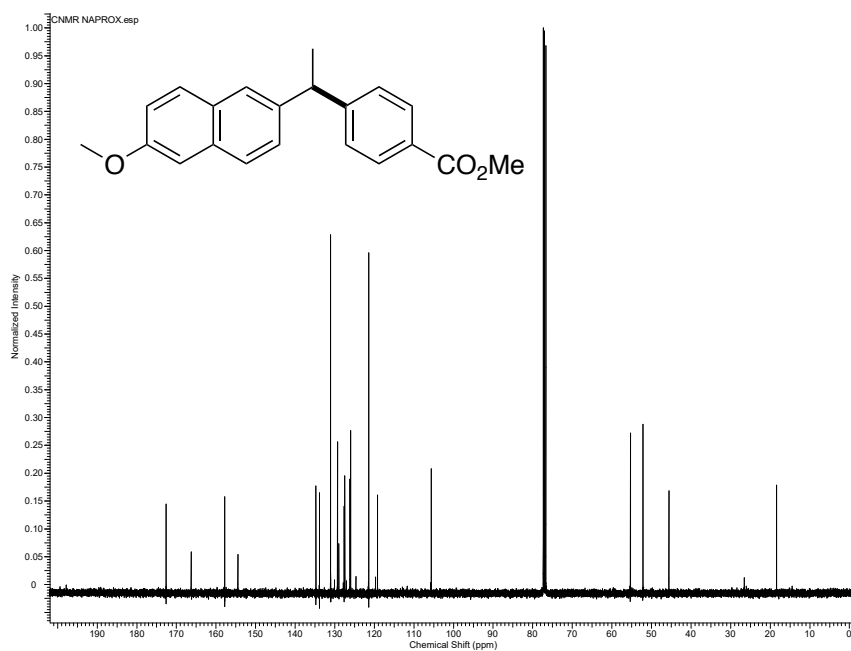


Figure 4A.56. <sup>13</sup>C NMR of [Table 4.7, entry 7 Product] in CDCl<sub>3</sub>.

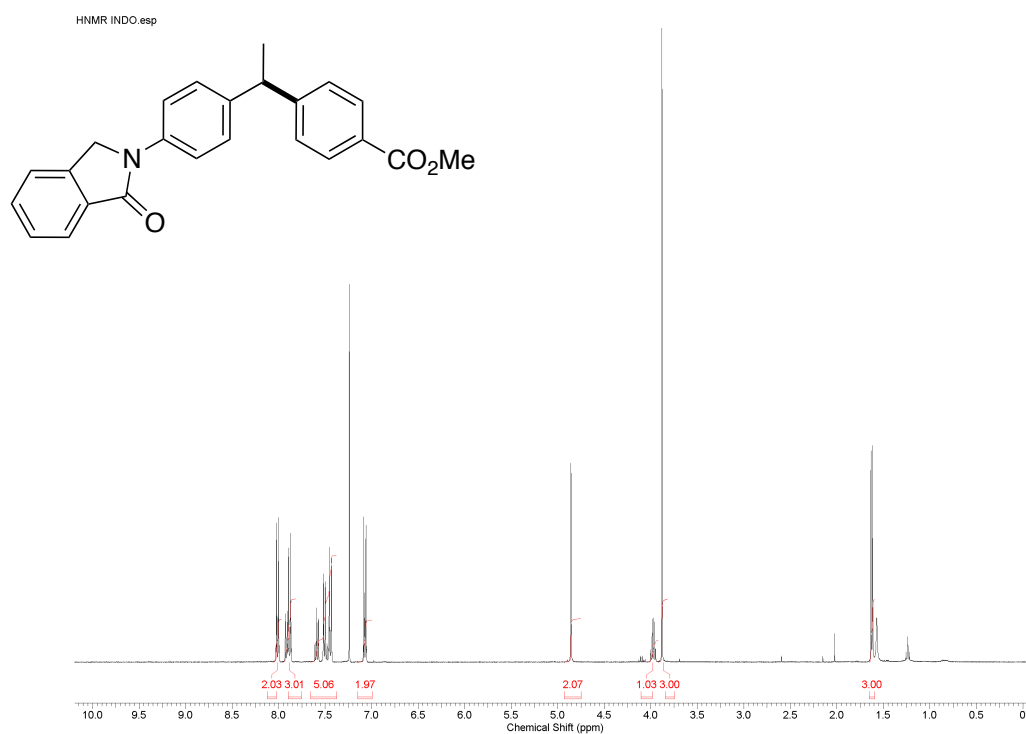
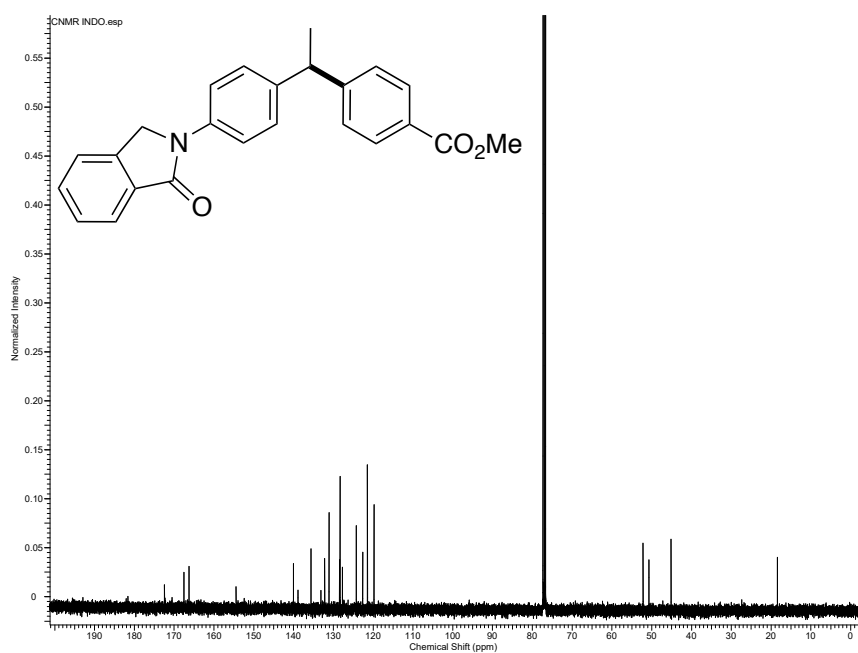
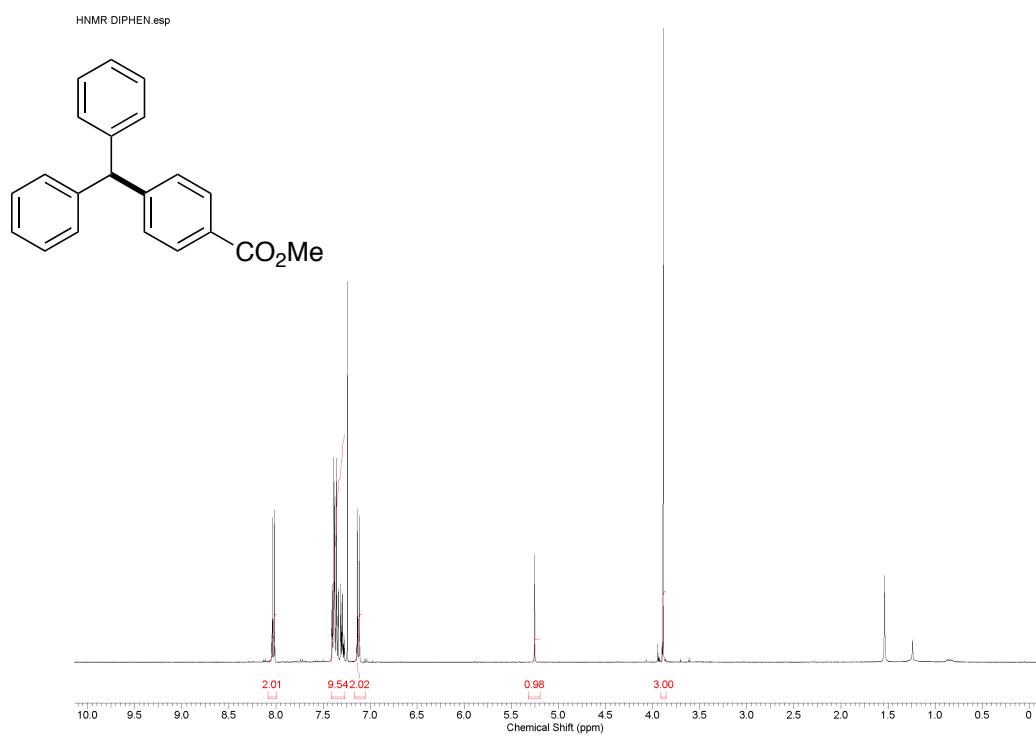


Figure 4A.57. <sup>1</sup>H NMR of [Table 4.7, entry 8 Product] in CDCl<sub>3</sub>.





**Figure 4A.58.** <sup>13</sup>C NMR of [Table 4.7, entry 8 Product] in CDCl<sub>3</sub>.



**Figure 4A.59.** <sup>1</sup>H NMR of [Table 4.7, entry 9 Product] in CDCl<sub>3</sub>.

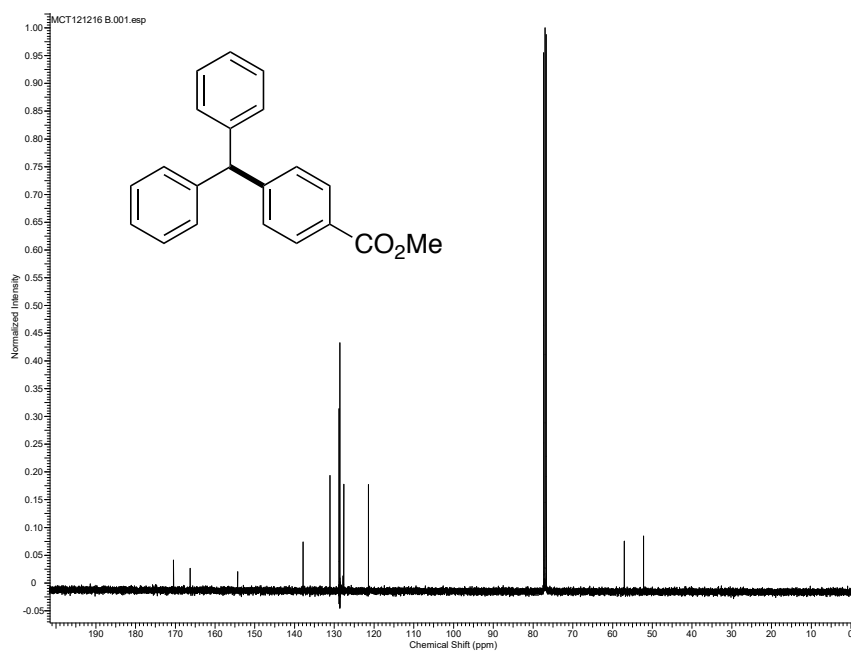


Figure 4A.60.  $^{13}\text{C}$  NMR of [Table 4.7, entry 9 Product] in  $\text{CDCl}_3$ .

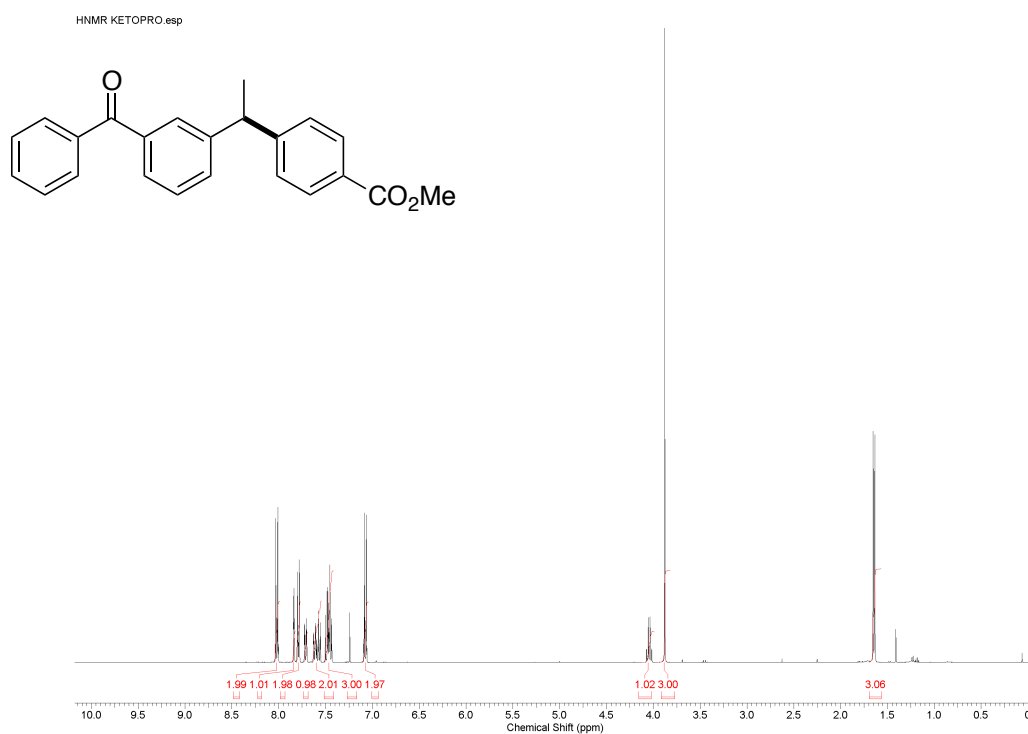


Figure 4A.61.  $^1\text{H}$  NMR of [Table 4.7, entry 10 Product] in  $\text{CDCl}_3$ .



Figure 4A.62.  $^{13}\text{C}$  NMR of [Table 4.7, entry 10 Product] in  $\text{CDCl}_3$ .

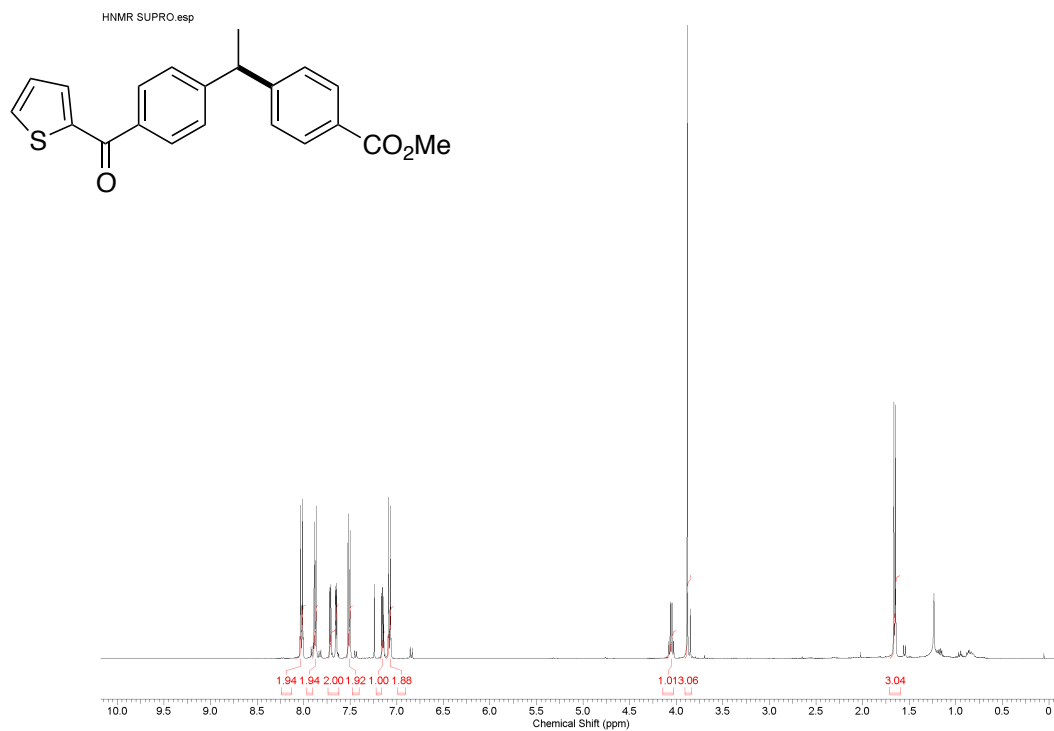


Figure 4A.63.  $^1\text{H}$  NMR of [Table 4.7, entry 11 Product] in  $\text{CDCl}_3$ .



**Figure 4A.64.** <sup>13</sup>C NMR of [Table 4.7, entry 11 Product] in CDCl<sub>3</sub>.

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## **5. Polynuclear Gold (I) Complexes in Photoredox Catalysis**

### **Understanding Their Reactivity Through Thermodynamic and Kinetic Analysis**

#### **5.1. Background**

Although the lustrous character of gold has captivated people for centuries, only in the past few decades have chemists harnessed the exciting chemical properties of gold complexes.<sup>1-7</sup> During this time the growing field of gold-catalyzed reactions has uncovered many complexes that serve as catalysts in a variety of reaction types, especially those requiring a Lewis acid.<sup>8-10</sup> More recently, studies involving highly luminescent polynuclear gold complexes have found a wealth of applications for both their photophysical and photochemical properties.<sup>8-13</sup> For example, their rich photochemistry has enabled their use in phosphorescent organic light-emitting diodes (OLEDs),<sup>14</sup> cellular imaging,<sup>15,16</sup> photocatalysis, and polymerization.<sup>17-21</sup>

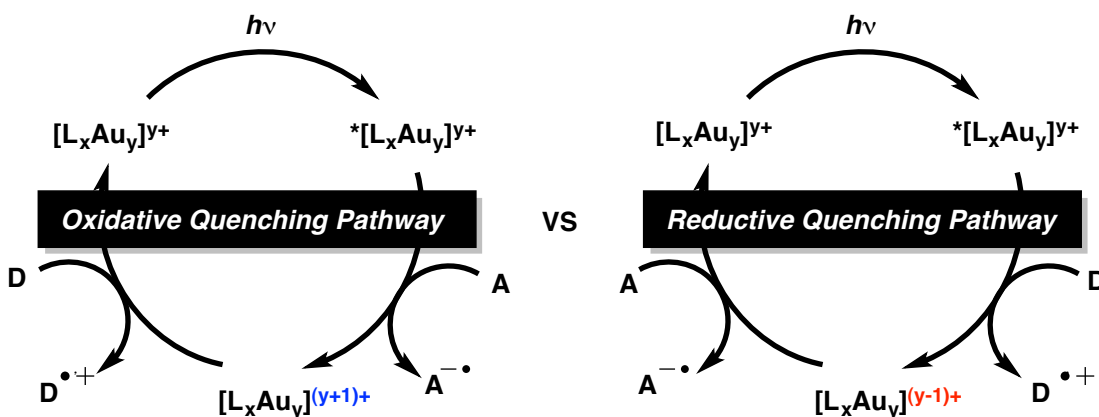
As demonstrated in the previous chapters, photoredox catalysis has offered chemists an array of new and mild ways to access highly reactive intermediates that were previously only attainable through the use of harsh conditions, when it comes to reductive dehalogenation reactions. While these techniques have resulted in the development of mild and highly efficient strategies for the generation of C-H, C-C, C-N and C-O bonds, the scope of these transformations tends to be limited to activated C-X bonds, such as polyhalomethanes, and alkyl/aryl iodides which are more easily reduced.<sup>22</sup>

Recently the Barriault group at the University of Ottawa has demonstrated that a photocatalytic system based on the phosphorescent dinuclear gold (I) complex  $[\text{Au}_2(\text{dppm})_2]^{2+}$  (**1**) (dppm = bis(diphenylphosphino)methane)<sup>23-26</sup> and *N,N*-diisopropylethylamine (DIPEA) as sacrificial electron donor is capable of reducing unactivated bromoalkanes and bromoarenes ( $\sim -1.9$  to  $-2.5$  V vs. SCE)<sup>24,26</sup> and that the ensuing radicals participate in ring-forming cyclization reactions, resulting in the formation of new C-C bonds.<sup>18,20</sup> Providing another alternative to some of the more commonly employed methods, which tend to involve harsh or chain propagating conditions.<sup>27-39</sup>

Although, similar light mediated transformations have been accomplished utilizing visible light absorbing Pt complexes<sup>40</sup> and perylene diimides<sup>41</sup> as photosensitizers, the reductive dehalogenation of unactivated C-Br bonds with photoexcited  $\text{Au}_2(\text{dppm})_2\text{Cl}_2$  (**1**) remained an interesting find, with many questions relating to the mechanism of these transformation remaining. As we have seen, photoredox catalysis can proceed through either an oxidative or reductive quenching pathway. In the reductive quenching pathway, the initial excited species is reduced through single electron transfer (SET) from a donor (D) molecule and the resulting reduced photocatalyst can then be oxidized in its ground state through subsequent reduction of an Acceptor (A) molecule. Opposite to this is the oxidative quenching pathway in which the initial excited state is oxidized through SET to an acceptor (A) molecule, and returned to its initial oxidation state through reduction by a donor (D) molecule. As we initiated this collaboration with the Barriault group they were unsure of the specific details

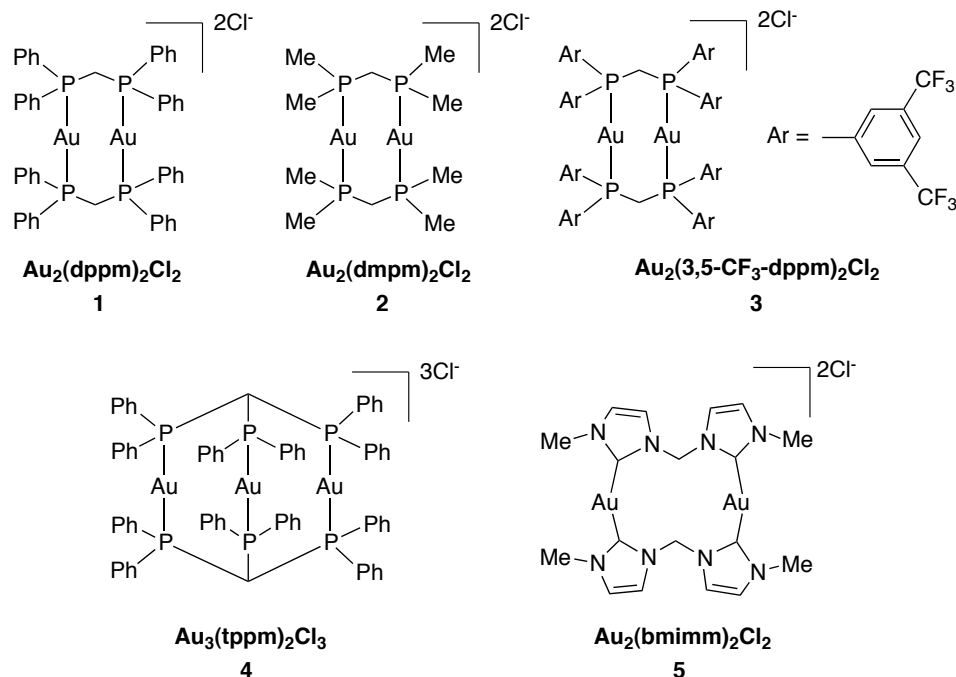
of the active pathway in their systems. Was dehalogenation achieved through a reductive or oxidative quenching pathway? Or Both? (Scheme 5.1) Also, many of the reduction potentials of the substrates fall outside the potential window attainable by the  $\text{Au}_2(\text{dppm})_2\text{Cl}_2$  photocatalytic system. Could this be explained due to differences between both inner and outer sphere electron transfer processes?

**Scheme 5.1.** Oxidative and Reductive Quenching Pathways for the Reductive Cyclizations and Dimerizations Catalyzed by Gold Complexes. Adapted with permission from McTiernan *et al.*<sup>42</sup> Copyright 2016 The Royal Society of Chemistry.



In an attempt to answer the above questions and gain further insight into the relevant excited state processes we set out to characterize the properties of a variety of polynuclear gold (I) complexes (Scheme 5.2), which we know are capable of bringing about the desired transformation. Through structural modification of the ligands and by changing the number of metal centers we were able to both satisfy our curiosity and explore the effect of electron donating and withdrawing ligands.

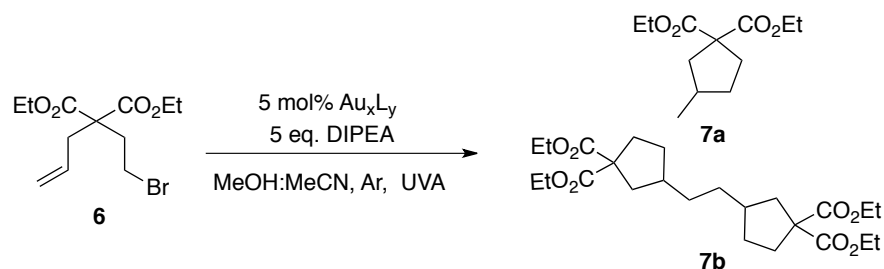
**Scheme 5.2.** Polynuclear Gold (I) Complexes in Photoredox Catalysis. Adapted with permission from McTiernan *et al.*<sup>42</sup> Copyright 2016 The Royal Society of Chemistry.



## 5.2. Polynuclear Gold (I) Complexes and Their Reactivity

In order to investigate the mechanism underlying these transformations, a series of structurally divergent Au (I) complexes were prepared. Through exchange of the dppm (**1**) ligand with either bis(dimethylphosphino)methane (dmpm) (**2**)<sup>43</sup>, or bis(bis(3,5-bis(trifluoromethyl)phenyl)phosphine)methane (3,5-CF<sub>3</sub>-dppm) (**3**) we can examine the effect of electron donating and withdrawing ligands, respectively. To study the effect of adding a third metal center to the complex they have also synthesized complex (**4**)<sup>44</sup> using tris(diphenylphosphino)methane (tppm) as ligand. Lastly, due to the success of N-heterocyclic carbene ligands in gold (I) Lewis acid catalysis complex (**5**)<sup>45</sup> with bis(*N*-methylimidazol-2-ylidene)methane (bmimm) as ligand was also prepared.

The activity of each of the structurally modified catalysts was compared for their activity in converting substrate (**6**) to products (**7a**) from reductive cyclization and (**7b**, as a mixture of diastereomers) from the unexpected coupling of two cyclized intermediates. Table 5.1, shows the conversion of substrate **6** utilizing the different polynuclear gold (I) complexes under their previously optimized conditions. Interestingly, all five of the complexes were able to promote the transformations, however some more efficiently than others. While complex **1** shows the highest reactivity, reaching completion in only 5 minutes of irradiation (Table 5.1, entry 1). Complex **2** and **4** with dmpm and tppm ligands, respectively, show modest reactivities, reaching completion in 2 hours (Table 5.1, entry 4 and 12). The trifluoromethylated dppm complex **3** shows the lowest reactivity taking 20 hours of irradiation to reach 82% conversion (Table 5.1, entry 9). Lastly, the bis-carbene complex **5** took 20 hours to reach complete conversion (Table 5.1, entry 17). Wanting to better understand these differences in reactivity, we set out to characterize the photophysical and electrochemical properties of all five complexes.

**Table 5.1.** Photoreduction of **6** Using Polynuclear Gold (I) Complexes<sup>a</sup>

| Entry | $\text{Au}_x\text{L}_y$ Complex                                      | Time (h) | Conversion (7a:7b) <sup>b</sup> % |
|-------|----------------------------------------------------------------------|----------|-----------------------------------|
| 1     | $\text{Au}_2(\text{dppm})_2\text{Cl}_2$ ( <b>1</b> )                 | 0.1      | >95(40:60) %                      |
| 2     | $\text{Au}_2(\text{dmpm})_2\text{Cl}_2$ ( <b>2</b> )                 | 0.1      | 21 %                              |
| 3     | $\text{Au}_2(\text{dmpm})_2\text{Cl}_2$ ( <b>2</b> )                 | 0.5      | 56 %                              |
| 4     | $\text{Au}_2(\text{dmpm})_2\text{Cl}_2$ ( <b>2</b> )                 | 2.0      | >95(73:27) %                      |
| 5     | $\text{Au}_2(3,5\text{-CF}_3\text{-dppm})_2\text{Cl}_2$ ( <b>3</b> ) | 0.1      | <5 %                              |
| 6     | $\text{Au}_2(3,5\text{-CF}_3\text{-dppm})_2\text{Cl}_2$ ( <b>3</b> ) | 0.5      | 11 %                              |
| 7     | $\text{Au}_2(3,5\text{-CF}_3\text{-dppm})_2\text{Cl}_2$ ( <b>3</b> ) | 2.0      | 27 %                              |
| 8     | $\text{Au}_2(3,5\text{-CF}_3\text{-dppm})_2\text{Cl}_2$ ( <b>3</b> ) | 8.0      | 55 %                              |
| 9     | $\text{Au}_2(3,5\text{-CF}_3\text{-dppm})_2\text{Cl}_2$ ( <b>3</b> ) | 20.0     | 82(54:46) %                       |
| 10    | $\text{Au}_3(\text{tppm})_2\text{Cl}_3$ ( <b>4</b> )                 | 0.1      | 12 %                              |
| 11    | $\text{Au}_3(\text{tppm})_2\text{Cl}_3$ ( <b>4</b> )                 | 0.5      | 41 %                              |
| 12    | $\text{Au}_3(\text{tppm})_2\text{Cl}_3$ ( <b>4</b> )                 | 2.0      | >95(63:37) %                      |
| 13    | $\text{Au}_2(\text{bmimm})_2\text{Cl}_2$ ( <b>5</b> )                | 0.1      | <5 %                              |
| 14    | $\text{Au}_2(\text{bmimm})_2\text{Cl}_2$ ( <b>5</b> )                | 0.5      | 28 %                              |
| 15    | $\text{Au}_2(\text{bmimm})_2\text{Cl}_2$ ( <b>5</b> )                | 2.0      | 35 %                              |
| 16    | $\text{Au}_2(\text{bmimm})_2\text{Cl}_2$ ( <b>5</b> )                | 8.0      | 67 %                              |
| 17    | $\text{Au}_2(\text{bmimm})_2\text{Cl}_2$ ( <b>5</b> )                | 20.0     | >95(80:20) %                      |

<sup>a</sup>Reaction conditions: Substrate (200 mM), DIPEA (5 eq.),  $\text{Au}_x\text{L}_y$  complex (5 mol%), MeOH:MeCN (1:1-1mL) under argon atmosphere. Irradiated with one UVA LED (365 nm). <sup>b</sup>% conversion by <sup>1</sup>H NMR. Adapted with permission from McTiernan *et al.*<sup>42</sup> Copyright 2016 The Royal Society of Chemistry.

### 5.3. Characterization of the Polynuclear Gold (I) Complexes and Rationalization of Their Reactivity

Through a combination of both steady-state and time-resolved absorption and emission measurements as well as cyclic voltammetry, we were able to

obtain the characterization data found in Table 5A.1 (See Appendix for experimental details)

From Table 5A.1 and the corresponding absorption spectra (see Figures 5A.1 – 5A.5) it can be seen that the majority of the Au complexes absorb strongly in the UVA region and tail towards the visible with the exception of complexes **2** and **5**, which only tail into the UVA region. It is believed that the observed absorption arises from a metal-to-metal charge transfer transition, due to the promotion of an electron from an antibonding  $5d_z^2$  orbital into the bonding  $6s/6p_z$  orbital. Although the lack of absorption in the visible could limit the scope of these transformations, the availability of modern light sources such as UVA LEDs enables one to easily perform irradiations in the spectral region that is absorbed only by the photocatalyst, thus avoiding direct irradiation of substrates or reaction products that could lead to degradation or side product formation. Further highlighting this idea is the recent work by the Hashmi group on the  $[\text{Au}_2(\text{dppm})_2]^{2+}$  catalyzed photoredox  $\alpha\text{-C}(\text{sp}^3)\text{-H}$  alkynylation of tertiary aliphatic amines.<sup>46</sup> Given that UVA radiation can readily pass through glass, no expensive, “special”, or quartz glassware is required to perform the reaction and in many cases the greater irradiance of specialized light sources can drastically reduce the required irradiation time. Interestingly, it should also be mentioned that photocatalytic systems requiring UVA excitation may in some cases be more potent excited state oxidizing and reducing agents than their visible light counterparts as the higher energy photons required for excitation would result in a higher excited state energy and more favourable redox processes.<sup>41</sup> However,



due to the fact that the chemistry likely occurs from the triplet manifold, some of this energy will be lost to competing radiative and non-radiative decay pathways, including intersystem crossing.<sup>41</sup> It is important to realize though, that it is the absorption and not the shorter wavelength that improves these processes. Meaning that a visible absorber does not become a better redox agent if you excite it with UVA light.

In Table 5.1 we observed that some of the catalysts were more efficient at bringing about the desired transformation. Although this could reflect that not all the catalysts absorb the same fraction of incident light, if we compare the efficiency of complex **2** and **4**, which have drastically different absorption spectra, we find that it takes both systems approximately 2 hours to reach quantitative conversion (Table 5.1, entry 4 and 12). Therefore, although preferential absorption of the incident light may be responsible for part of the differences observed in Table 5.1, it is likely that the thermodynamics and, in turn, the kinetics of the reaction, as well as other photophysical properties of the Au catalysts, such as the triplet quantum yield and lifetime, are responsible for much of the observed differences.

In order to understand the efficiency of these reductions, it is necessary to examine the thermodynamic feasibility and kinetics of the plausible mechanistic steps outlined in the oxidative and reductive quenching mechanisms of Scheme 5.1. As illustrated in Scheme 5.1, the catalytic cycle begins with either an electron transfer to or from the excited state of the catalyst. By determining the Gibbs free energy associated with each electron transfer process, it may be

possible to determine which pathway is more favorable. However, in order to make these calculations one requires the ground state oxidation and reduction potentials of the catalyst as well as their corresponding triplet energy along with the reduction potential of the acceptor molecule (**6**) and the oxidation potential of the donor molecule (DIPEA). Through the use of cyclic voltammetry we have been able to estimate the oxidation and reduction potentials of the Au catalysts in their ground state. Since all the Au complexes exhibited irreversible oxidation and reduction waves (See Appendix for experimental details and corresponding CV curves) we have used the peak anodic ( $E_{pa}$ ) and peak cathodic ( $E_{pc}$ ) potentials as estimates of the oxidation and reduction potentials, respectively. While the electrochemical irreversibility of the Au catalysts could suggest that they are merely precatalysts, when the reaction is followed by  $^{31}\text{P}$  NMR in  $\text{CD}_3\text{CN}$ , complex (**1**) is present and unchanged until full conversion is achieved. However, if irradiation of the sample is continued once the reaction has reached completion, the catalyst begins to decompose resulting in the appearance of secondary phosphine peaks, which correspond to free and oxidized ligand.

With the triplet energy ( $E_T^*$ ) of the Au catalysts obtained from 77 K phosphorescence measurements (see Appendix) we can employ equations 5.1 and 5.2 to determine the excited state oxidation ( $E_{ox}^*$ ) and reduction ( $E_{red}^*$ ) potentials.

$$E_{ox}^* = E_{pa} - E_T^* \quad (5.1)$$

$$E_{red}^* = E_{pc} + E_T^* \quad (5.2)$$

For example, in the case of  $[\text{Au}_2(\text{dppm})_2]^{2+}$  we find that  $E_{\text{ox}}^* = -1.53 \text{ V vs. SCE}$  and  $E_{\text{red}}^* = 0.60 \text{ V vs. SCE}$ . At  $-1.53 \text{ V vs. SCE}$  the calculated  $E_{\text{ox}}^*$  is in good agreement with the literature value of  $-1.6 \pm 0.1 \text{ V vs. SCE}$  obtained through excited state quenching studies employing a series of pyridinium acceptors with known reduction potential.<sup>47</sup> Since the reduction potential of substrate **6** is approximately  $0.50 \text{ V vs. SCE}$ <sup>48</sup> we can use equations 5.3 and 5.4 to determine the Gibbs free energy associated with either the oxidative or reductive quenching of the Au catalyst.

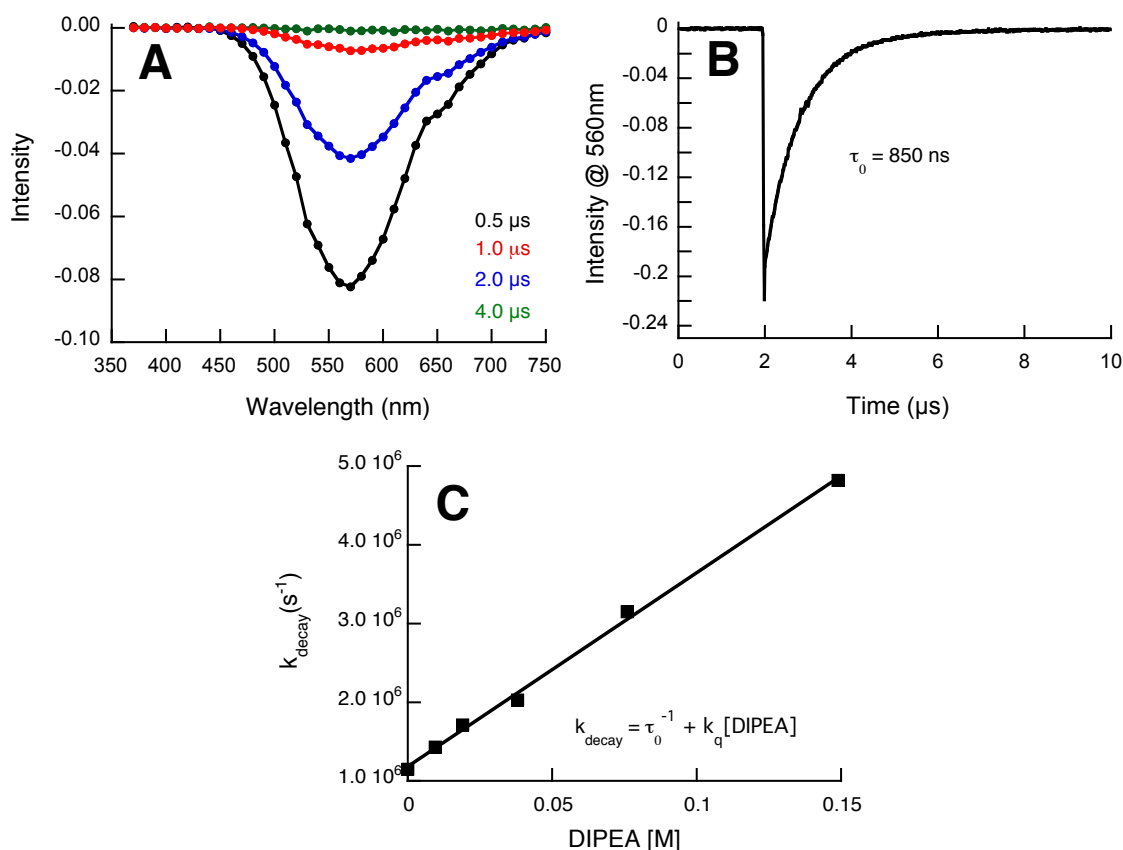
$$\Delta G_{\text{eT}}^{\text{ox quenching}} = E_{\text{ox}}^*(\text{Au}) - E_{\text{red}}(\mathbf{6}) \quad (5.3)$$

$$\Delta G_{\text{eT}}^{\text{red quenching}} = E_{\text{ox}}(\text{DIPEA}) - E_{\text{red}}^*(\text{Au}) \quad (5.4)$$

Continuing with the  $E_{\text{ox}}^*$  and  $E_{\text{red}}^*$  potentials of the  $[\text{Au}_2(\text{dppm})_2]^{2+}$  complex, we find that while the reductive quenching of complex **1** by DIPEA is thermodynamically favored by  $-0.1 \text{ eV}$ , the oxidative quenching by substrate **6** is actually thermodynamically uphill by  $0.37 \text{ eV}$ . Although this is a good indication that the reaction is proceeding through the reductive quenching mechanism when **1** is used as photocatalyst, it is important to remember that thermodynamics determine only if a reaction can take place and that there are examples in the photoredox literature in which reactions with significant free energy barrier proceed due to poor estimates of the redox potentials. Therefore we must turn to kinetics, as from the kinetics we can determine if a reaction does take place. Although there are only small differences between the  $E_{\text{red}}^*$  potentials of the Au complexes, there are some significant differences in their  $E_{\text{ox}}^*$  potentials. The most important of these oxidation potentials are that of complexes

**2** and **5**, which are negative enough to make the initial electron transfer from the excited photocatalyst to substrate **6** energetically favorable.

In order to study the kinetics of the excited state processes, we have performed time resolved transient spectroscopy on the Au complexes, using a nanosecond laser flash photolysis (LFP) system, with the aim of determining the rate at which the different components of the system quench the triplet of the Au complexes. Figure 5.1 shows the data used to determine the rate at which DIPEA reacts with the  $^3[\text{Au}_2(\text{dppm})_2]^{2+}$  complex; the same technique was applied to all quenchers and Au complexes.



**Figure 5.1.** Kinetic analysis of the reaction between  $^3\text{Au}_2(\text{dppm})_2\text{Cl}_2$  and DIPEA. A) Transient spectrum showing the  $^3\text{Au}_2(\text{dppm})_2\text{Cl}_2$  emission signal at 560 nm obtained upon laser pulse excitation (355 nm, 10 mJ) of a  $\text{Au}_2(\text{dppm})_2\text{Cl}_2$  sample which had been purged of oxygen. B) Corresponding decay trace of  $^3\text{Au}_2(\text{dppm})_2\text{Cl}_2$  at 560 nm. C) Kinetic quenching plot showing the rate of  $^3\text{Au}_2(\text{dppm})_2\text{Cl}_2$  quenching as a function of [DIPEA]. The slope of this plot corresponds to

Although we were not able to observe the growth of signals corresponding to either the reduced or oxidized forms of the Au complexes upon quenching by substrate **6** or DIPEA, the ability of the excited Au complexes to be quenched through electron transfer has been previously examined. Both methyl viologen ( $MV^{2+}$ ) a good electron acceptor  $E_{1/2}^{red}(MV^{2+}/MV^{+\bullet}) = -0.46$  V vs. SCE<sup>49</sup> and *N,N,N',N'*-tetramethyl-*p*-phenylenediamine (TMPD) a good electron donor  $E_{1/2}^{ox}(TMPD/TMPD^{+\bullet}) = 0.12$  V vs. SCE<sup>50</sup> quench  $^3[Au_2(dppm)_2]^{2+}$  at rates approaching diffusion control ( $k_q^{MV^{2+}} = 6.0 \times 10^9$  M<sup>-1</sup>s<sup>-1</sup> and  $k_q^{TMPD} = 6.6 \times 10^9$  M<sup>-1</sup>s<sup>-1</sup>)<sup>23</sup> and give rise to transient absorptions centered at 600 nm characteristic to their corresponding radical cations produced upon either reduction or oxidation. The fact that we do not see the growth of this signal may relate back to the instability of these complexes, a shift in the absorption of the transient, or a weakening of its absorption.

Table 5A.2 includes the bimolecular rate constant at which substrate **6**, DIPEA, and butyl bromide quench the triplet of the various Au complexes. Although butyl bromide ( $E_{red}^{1/2} = -2.5$  V vs. SCE) is not a component of the reaction mixture, we have included it here as reference. As one would expect, there is a strong relationship between the redox potentials of the quenchers and those of the Au complexes with the measured rate constants. For example, along the entire series of catalysts one finds that the rate constant for quenching by substrate **6** is greater than that of the more difficult to reduce butyl bromide. It is also observed that the rate of reductive quenching by DIPEA changes drastically

throughout the series, with differences of up to 3 orders of magnitude between the different complexes. These differences can be readily explained through the reduction potentials of the Au complexes, as the slowest rates were measured for complexes **1** and **2** and the fastest rate for complex **3**, the most difficult and easiest catalysts to reduce, respectively.

Although complex **1** is the most efficient of the catalysts, it displays some of the slowest rate constants in Table 5A.2. However, what this observation fails to account for is the excited state lifetime of the catalyst or the concentration of quencher present in solution, without which it is difficult to compare these values. One way to employ the data in Table 5A.2 is to use equations 5.5 and 5.6 to calculate the percentage of triplets quenched by either substrate **6** or DIPEA under initial reaction conditions.

%<sup>3</sup>Au<sub>x</sub> complex quenched by **6** =

$$\frac{100 \times k_q^6[\mathbf{6}]}{\tau_0^{-1} + k_q^6[\mathbf{6}] + k_q^{\text{DIPEA}}[\text{DIPEA}] + k_q^{\text{O}_2}[\text{O}_2]} \quad (5.5)$$

%<sup>3</sup>Au<sub>x</sub> complex quenched by DIPEA =

$$\frac{100 \times k_q^{\text{DIPEA}}[\text{DIPEA}]}{\tau_0^{-1} + k_q^6[\mathbf{6}] + k_q^{\text{DIPEA}}[\text{DIPEA}] + k_q^{\text{O}_2}[\text{O}_2]} \quad (5.6)$$

Included in both equations are terms corresponding to the concentration of oxygen and its bimolecular quenching constant. Since all the reactions have been purged with argon prior to irradiation, we can simply eliminate them from the equations. However, it is important to point out that due to the high solubility of O<sub>2</sub> in acetonitrile (approx. 1.6 mM under air) and its propensity for quenching triplets ( $k_q^{\text{O}_2} {}^3[\text{Au}_2(\text{dppm})_2]^{2+} = 2.0 \times 10^9 \text{ M}^{-1}\text{s}^{-1}$ )<sup>47</sup>, inefficient purging could lead to

drastically reduced yields as many of the triplets would be intercepted by oxygen through non productive quenching events.

When we employ equations 5.5 and 5.6 to calculate the percentage of  $^3[\text{Au}_2(\text{dppm})_2]^{2+}$  quenched by substrate **6** and DIPEA under initial reaction conditions we find that while 18% of triplets are quenched by **6**; the other 78% are intercepted by DIPEA. Even though the rate constants for both quenchers are similar, 78% was due to the fact that DIPEA was used in excess (5 times). When we combine this information with the fact that the reaction run with  $\text{Au}_2(\text{dppm})_2\text{Cl}_2$  as photocatalyst reaches completion in 5 minutes of irradiation, it would seem likely that in this case the reductive quenching pathway is the major route to product formation. However, if one were to do similar calculations for the other catalysts, this may not always be the case. While it is most likely that complexes **3** and **4** bring about the desired transformation through the reductive quenching pathway, as in both cases >99% of triplets are quenched by DIPEA; for complex **2** we find that 93% of its triplets are intercepted by substrate **6** and only 6% by DIPEA, the productive pathway may still be reductive in nature with the explanation for the sluggish reaction being the poor efficiency of quenching.

Lastly, for complex **5** it is difficult to determine the major pathway as 55% of triplets would be quenched by **6**, while another 34% by DIPEA. Thus if we were to assume that 100% of quenching events led to electron transfer (this is likely not the case) and that both the reductive and oxidative pathways were equally effective at bringing about the desired transformation, it would appear as though in addition to its poor UVA absorption, much of the inefficiency of complex

**5** can be attributed to its short excited state lifetime and the fact that a significant fraction of triplets escape quenching. Therefore, while we can conclude that the processes represented by equations 5.5 and 5.6 are kinetically competitive, it is becoming evident that these reductive transformations are quite complex with their being the possibility of both the oxidative and reductive quenching pathways leading to the formation of the desired product.

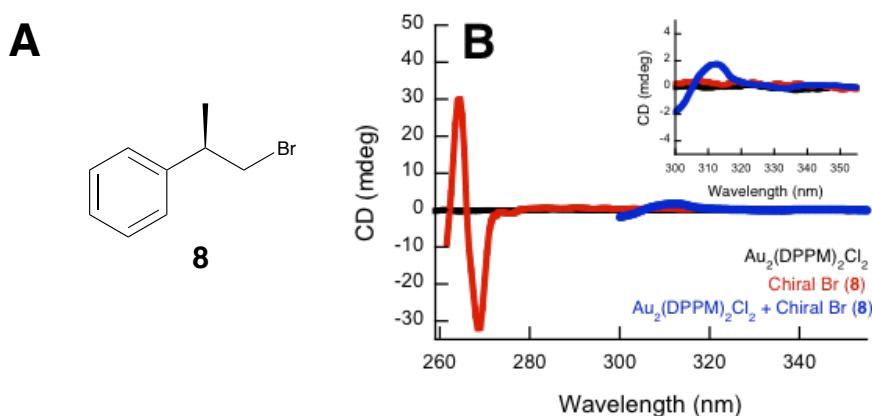
#### **5.4. Rationalizing the Reductive Strength of the Photocatalytic System**

Further highlighting the complexity of the systems, is the ability of the Au complexes to reduce substrate **6**, despite there being such a large barrier to electron transfer between the bromoalkanes redox potential and that of the excited state complex (**1**). There are two possible explanations for this behavior. The first is that much of this energy barrier would be eliminated if one were to utilize the onset outer sphere potentials in place of the peak potentials. The second explanation involves a potential interaction between the Au complex and the starting bromoalkane, which somehow activates the substrate.

Interestingly, it has been previously shown that  $[\text{Au}_2(\text{dppm})_2]^{2+}$  undergoes substrate binding with LiCl and LiBr salts.<sup>47</sup> In order to further explore this idea of substrate activation through catalyst interaction, we set out to examine the effect a chiral bromide substrate would have on the achiral  $\text{Au}_2(\text{dppm})_2\text{Cl}_2$ . The idea being that if there were some interactions between the two, perhaps the substrate would induce chirality within the Au complex. In order to test this hypothesis, chiral bromide (**8**) was synthesized and used to probe the potential interaction it and  $\text{Au}_2(\text{dppm})_2\text{Cl}_2$ , by measuring the circular dichroism spectrum of



**8** and complex **1** alone and in the presence of each other. In Figure 5.2, it is clear that in the presence of both **8** and  $\text{Au}_2(\text{dppm})_2\text{Cl}_2$  there is the appearance of a new CD signal centered at 312 nm, which can possibly be attributed to induction of chirality within the Au complex due to binding of substrate **8**. On the basis of this result, one can propose that the reduction of the carbon-bromide bond may proceed through an inner sphere mechanism. While such an inner sphere mechanism would make the measured outer sphere potentials irrelevant, there is no evidence to eliminate the possibility of a mechanism involving both an inner sphere and outer sphere pathway.



**Figure 5.2.** Probing substrate binding of  $\text{Au}_2(\text{dppm})_2\text{Cl}_2$  through induction of chirality. A) Structure of chiral bromide **8**. B) Circular dichroism (CD) spectra obtained of  $\text{Au}_2(\text{dppm})_2\text{Cl}_2$  alone (black), chiral Br (**8**) alone (red), and  $\text{Au}_2(\text{dppm})_2\text{Cl}_2$  in the presence of chiral Br (**8**) (blue) at 20 °C. Adapted with permission from McTiernan *et al.*<sup>42</sup> Copyright 2016 The Royal Society of Chemistry.

Finally, it should also be mentioned that due to the basic conditions of the reactions; the radical cation or DIPEA, formed upon reductive quenching, will readily deprotonate to give a strongly reducing  $\alpha$ -aminoalkyl radical ( $E_{1/2}^{\text{ox}} = -1.12 \text{ V vs. SCE}$ ).<sup>51</sup> Although it has been shown that these intermediates can actively participate in these types of transformations, they are not strong enough

reductants to access the unactivated bromoalkane and bromoarene ( $\sim -1.9$  to  $-2.5$  V vs. SCE) substrates of interest.

## 5.5. Conclusion

In this Chapter, we have characterized the photophysical and electrochemical properties of a series of polynuclear gold (I) complexes (**1-5**). Through careful examination of the thermodynamic feasibility and rate constants of the key mechanistic steps involved in the light mediated activation of a model bromoallylmalonate, it was demonstrated that the mechanism(s) involved in these photoredox mediated transformations are quite complex with there being the possibility of multiple competing reaction processes possible. While the results have provided insight into many of the questions we had posed, it also raises questions about the complexity of other systems, which involve the generation of long-lived, powerfully redox-versatile triplet excited states. Moving forward this data will not only help in reaction optimization but in rationalization of future applications. Through the combination of our own the skills and that of the Barriault group we have achieved a level of understanding in these processes, which otherwise would not have been attained.

## 5.6. Appendix

### 5.6.A. General Information

Substrates and Reagents: MeCN, MeOH, *N,N*-diisopropylethylamine (DIPEA), and all other reagents were purchased from commercial suppliers (Sigma Aldrich, Alfa Aesar, and Fisher) and used with no further purification unless otherwise noted.

Light Source: Unless otherwise noted, was one UVA (365 nm) LED, which was purchased from LedEngin.

### 5.6.B. Photophysical and Electrochemical Data of the Au<sub>x</sub> Complexes

**Table 5A.1.** Photophysical and Electrochemical Data of the Polynuclear Gold (I) Complexes

| Catalyst                                                                     | $\lambda_{\text{ex}}^a$ | $\epsilon_{\text{ex}} (\text{M}^{-1} \text{cm}^{-1})^a$ | $\lambda_{\text{em}}^a$ | $\Phi_{\text{em}}^b$ | ${}^3\tau_0^c$    | $E_{\text{T}}^* (\text{kJ Mol}^{-1})^d$ | $E_{\text{pa}} (\text{V vs SCE})^e$ | $E_{\text{pc}} (\text{V vs SCE})^e$ |
|------------------------------------------------------------------------------|-------------------------|---------------------------------------------------------|-------------------------|----------------------|-------------------|-----------------------------------------|-------------------------------------|-------------------------------------|
| (1) Au <sub>2</sub> (dppm) <sub>2</sub> Cl <sub>2</sub>                      | 355 nm                  | 73163                                                   | 560 nm                  | 0.137                | 850 ns            | 215                                     | 0.70                                | -1.63                               |
| (2) Au <sub>2</sub> (dmpm) <sub>2</sub> Cl <sub>2</sub>                      | 308 nm                  | 3813                                                    | 525 nm                  | 0.028                | 400 ns            | 228                                     | 0.49                                | -1.77                               |
| (3) Au <sub>2</sub> (3,5-CF <sub>3</sub> -dppm) <sub>2</sub> Cl <sub>2</sub> | 355 nm                  | 6539                                                    | 590 nm                  | 0.006                | 10 $\mu\text{s}$  | 203                                     | 1.41                                | -1.65                               |
| (4) Au <sub>3</sub> (tppm) <sub>2</sub> Cl <sub>3</sub>                      | 355 nm                  | 3780                                                    | 545 nm                  | 0.028                | 1.5 $\mu\text{s}$ | 220                                     | 1.09                                | -1.54                               |
| (5) Au <sub>2</sub> (bmimm) <sub>2</sub> Cl <sub>2</sub>                     | 308 nm                  | 491                                                     | 510 nm                  | 0.017                | 20 ns             | 235                                     | 0.34                                | -                                   |

<sup>a</sup> Measured in MeCN at 298 K. <sup>b</sup> Photoluminescence quantum yield determined relative to Ru(bpy)<sub>3</sub>Cl<sub>2</sub> as standard ( $\Phi_{\text{MeCN}} = 0.095$ ). <sup>c</sup> Triplet lifetime measured in N<sub>2</sub> degassed MeCN after 10 mJ laser pulse at  $\lambda_{\text{ex}}$ . <sup>d</sup> Triplet-state energy determined from the low temperature (77 K) phosphorescence spectra. <sup>e</sup> Determined using cyclic voltammetry. Conditions: scan rate = 100 mV s<sup>-1</sup>; 0.5-2.0 mM Au (I) complex in Ar degassed MeCN containing 100 mM Bu<sub>4</sub>NClO<sub>4</sub> supporting electrolyte; Pt wire working electrode; Pt wire counter electrode; Ag wire pseudo-reference electrode; Fc/Fc<sup>+</sup> redox couple as internal reference (0.41 V vs. SCE); oxidation and reduction potential reported as peak anodic ( $E_{\text{pa}}$ ) and peak cathodic ( $E_{\text{pc}}$ ) potentials due to their irreversible nature. Adapted with permission from McTiernan *et al.*<sup>42</sup> Copyright 2016 The Royal Society of Chemistry.

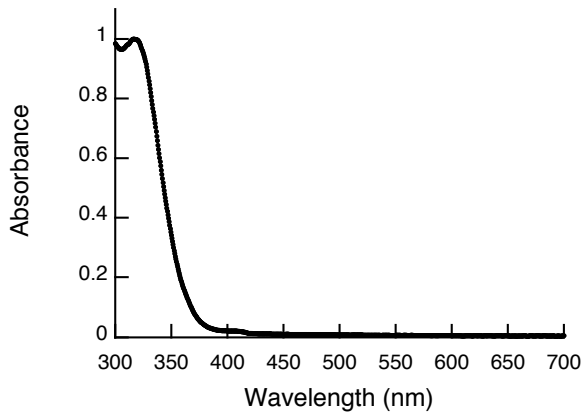
### 5.6.C. Rate Constants for the Triplet Quenching of the Au<sub>x</sub> Complexes

**Table 5A.2.** Triplet Quenching of Polynuclear Gold (I) Complexes (1-5)

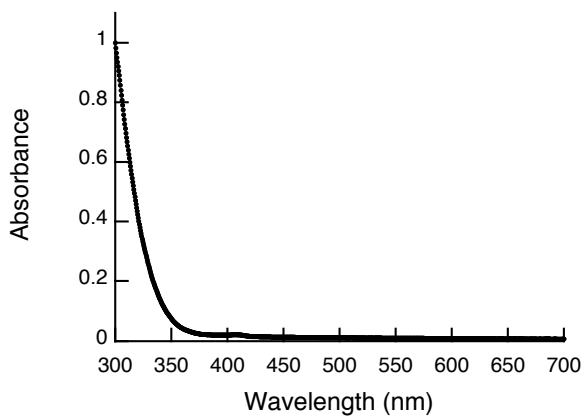
| Quencher | Au <sub>2</sub> (dppm) <sub>2</sub> Cl <sub>2</sub> ( <b>1</b> ) | Au <sub>2</sub> (dmpm) <sub>2</sub> Cl <sub>2</sub> ( <b>2</b> ) | Au <sub>2</sub> (3,5-CF <sub>3</sub> -dppm) <sub>2</sub> Cl <sub>2</sub> ( <b>3</b> )<br><i>k<sub>q</sub></i> (M <sup>-1</sup> s <sup>-1</sup> ) <sup>a</sup> | Au <sub>3</sub> (tppm) <sub>2</sub> Cl <sub>3</sub> ( <b>4</b> ) | Au <sub>2</sub> (bmimm) <sub>2</sub> Cl <sub>2</sub> ( <b>5</b> ) |
|----------|------------------------------------------------------------------|------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------|-------------------------------------------------------------------|
| ButylBr  | 2.9 x 10 <sup>6</sup>                                            | 1.1 x 10 <sup>9</sup>                                            | 4.8 x 10 <sup>5</sup>                                                                                                                                         | 4.5 x 10 <sup>6</sup>                                            | 1.2 x 10 <sup>9</sup>                                             |
| <b>6</b> | 3.1 x 10 <sup>7</sup>                                            | 1.7 x 10 <sup>9</sup>                                            | 5.1 x 10 <sup>6</sup>                                                                                                                                         | 2.8 x 10 <sup>7</sup>                                            | 1.3 x 10 <sup>9</sup>                                             |
| DIPEA    | 2.7 x 10 <sup>7</sup>                                            | 2.1 x 10 <sup>7</sup>                                            | 1.1 x 10 <sup>9</sup>                                                                                                                                         | 1.6 x 10 <sup>9</sup>                                            | 1.6 x 10 <sup>8</sup>                                             |

<sup>a</sup> Determined from the slope of the corresponding kinetic quenching plot (*k*<sub>decay</sub> vs. [Q]). Adapted with permission from McTiernan *et al.*<sup>42</sup> Copyright 2016 The Royal Society of Chemistry.

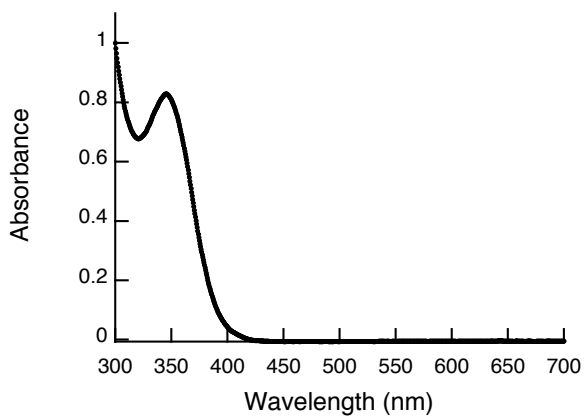
#### 5.6.D. Absorption Spectra of the Au<sub>x</sub> Complexes



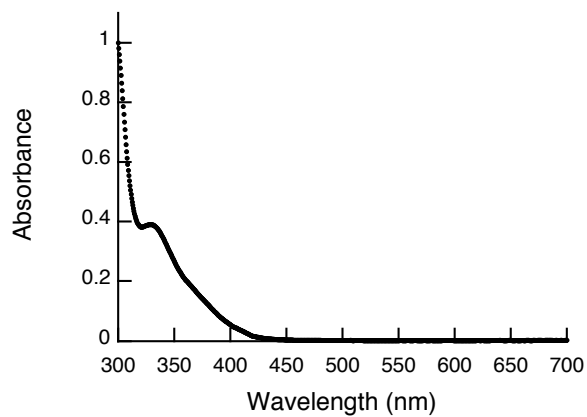
**Figure 5A.1.** Absorption spectrum of  $3.3 \times 10^{-3}$  mM  $\text{Au}_2(\text{dppm})_2\text{Cl}_2$  (1) in MeCN.



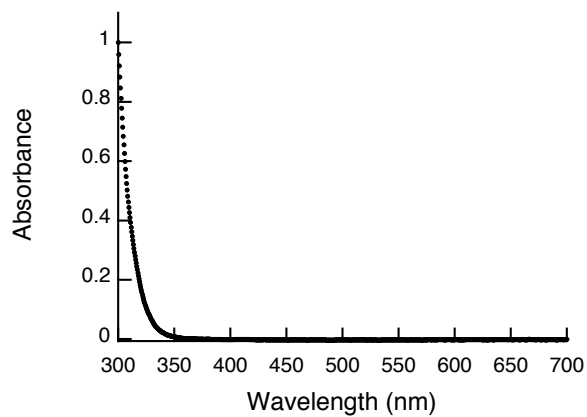
**Figure 5A.2.** Absorption spectrum of 0.20 mM  $\text{Au}_2(\text{dmpm})_2\text{Cl}_2$  (2) in MeCN.



**Figure 5A.3.** Absorption spectrum of 0.12 mM  $\text{Au}_2(3,5\text{-CF}_3\text{-dppm})_2\text{Cl}_2$  (3) in MeCN.

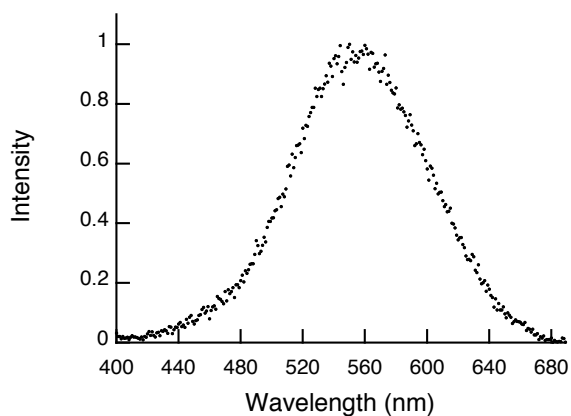


**Figure 5A.4.** Absorption spectrum of  $6.1 \times 10^{-2}$  mM  $\text{Au}_2(\text{tppm})_2\text{Cl}_2$  (**4**) in MeCN.

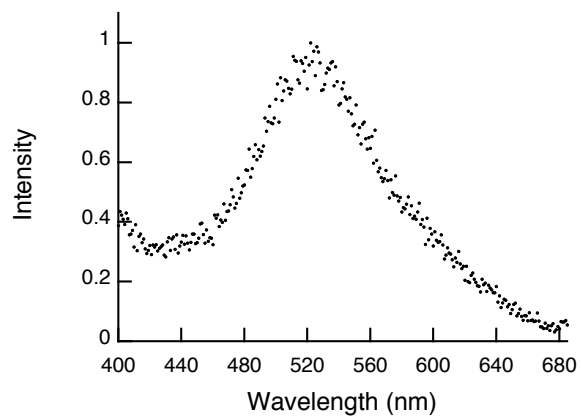


**Figure 5A.5.** Absorption spectrum of 1.02 mM  $\text{Au}_2(\text{bmim})_2\text{Cl}_2$  (**5**) in MeCN.

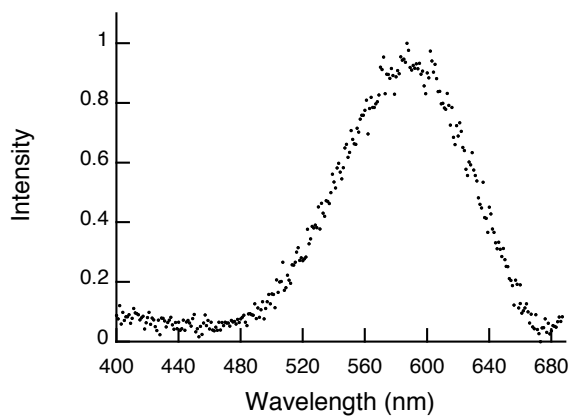
#### 5.6.E. 77 K Phosphorescence Spectra of the $\text{Au}_x$ Complexes



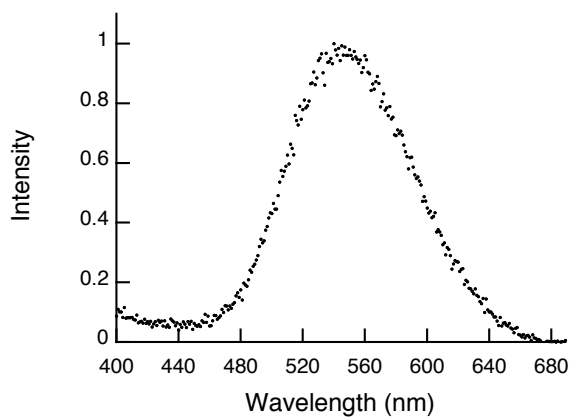
**Figure 5A.6.** 77 K phosphorescence spectrum of  $\text{Au}_2(\text{dppe})_2\text{Cl}_2$  (**1**) in EtOH:MeOH glass.



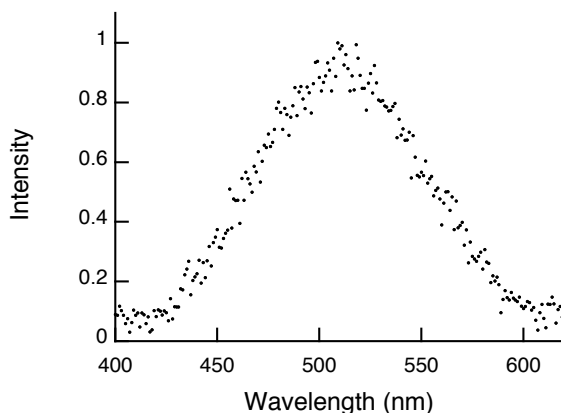
**Figure 5A.7.** 77 K phosphorescence spectrum of  $\text{Au}_2(\text{dmpm})_2\text{Cl}_2$  (**2**) in EtOH:MeOH glass.



**Figure 5A.8.** 77 K phosphorescence spectrum of  $\text{Au}_2(3,5\text{-CF}_3\text{-dppm})_2\text{Cl}_2$  (**3**) in EtOH:MeOH glass.



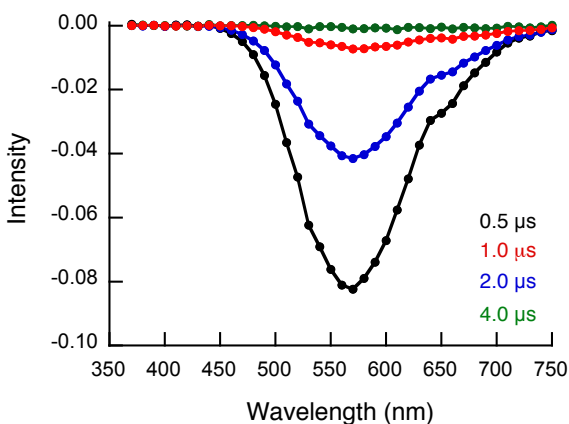
**Figure 5A.9.** 77 K phosphorescence spectrum of  $\text{Au}_2(\text{tppm})_2\text{Cl}_2$  (**4**) in EtOH:MeOH glass.



**Figure 5A.10.** 77 K phosphorescence spectrum of  $\text{Au}_2(\text{bmim})_2\text{Cl}_2$  (**5**) in EtOH:MeOH glass.

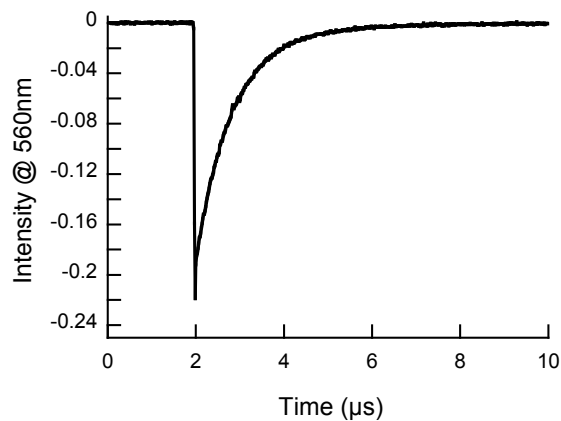
### 5.6.F. Laser Flash Photolysis Data of the $\text{Au}_x$ Complexes

Experiments were performed using either a Q-switched Nd:YAG-laser (355 nm, 10 mJ/pulse) or an excimer laser (308 nm, 10 mJ/pulse) in a LFP-111 laser-flash photolysis (LFP) system (Luzchem Research Inc., Ottawa, Canada) and 1 cm x 1 cm quartz cuvette (Luzchem). Samples of the  $\text{Au}_x$  complexes were prepared in MeCN with a total volume of 3 mL and an absorbance of  $\sim 0.1$  at 308 or 355 nm. The samples were degassed with  $\text{N}_2$  for 30 minutes prior to use. The substrates used in the quenching studies were also prepared in MeCN and were degassed for the duration of the experiment.

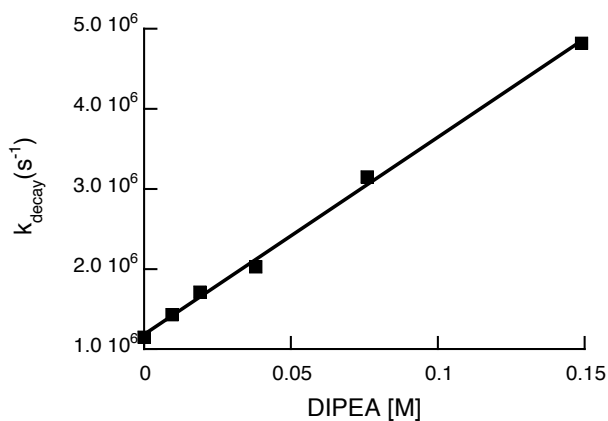


**Figure 5A.11.** Transient emission spectrum showing the  $^3\text{Au}_2(\text{dppm})_2\text{Cl}_2$  signal obtained upon laser pulse excitation (355 nm, 10 mJ) of a  $\text{Au}_2(\text{dppm})_2\text{Cl}_2$  sample which had been purged of oxygen.

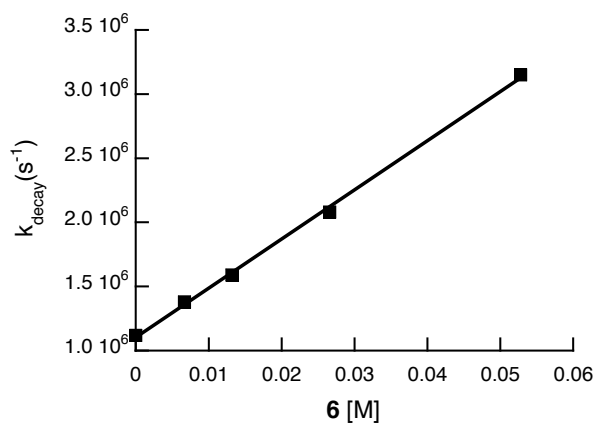




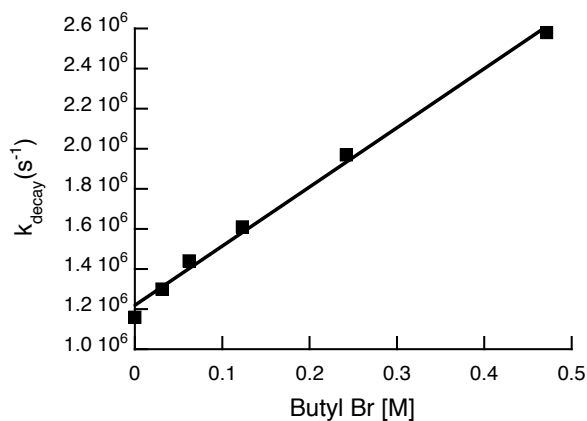
**Figure 5A.12.** Decay trace for the emission of  $^3\text{Au}_2(\text{dppm})_2\text{Cl}_2$  at 560 nm obtained upon laser pulse excitation (355 nm, 10 mJ) of a  $\text{Au}_2(\text{dppm})_2\text{Cl}_2$  sample which had been purged of oxygen.



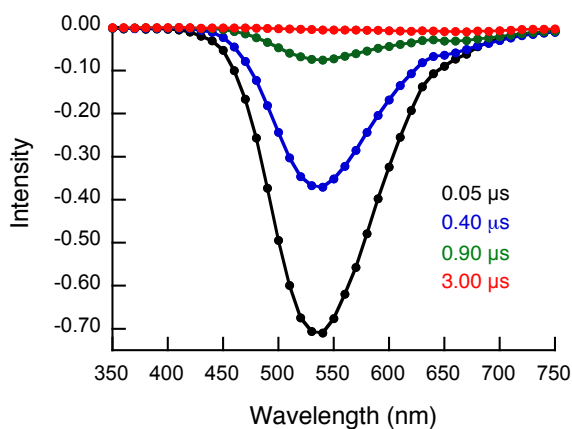
**Figure 5A.13.** Kinetic quenching plot showing the quenching of  $^3\text{Au}_2(\text{dppm})_2\text{Cl}_2$  by DIPEA. The slope of this plot corresponds to bimolecular rate constant.



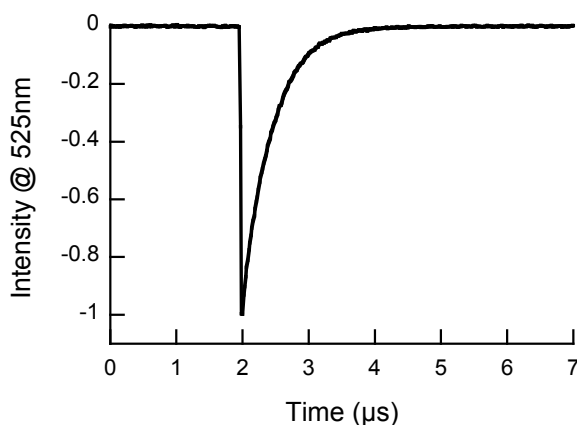
**Figure 5A.14.** Kinetic quenching plot showing the quenching of  $^3\text{Au}_2(\text{dppm})_2\text{Cl}_2$  by substrate **6**. The slope of this plot corresponds to bimolecular rate constant.



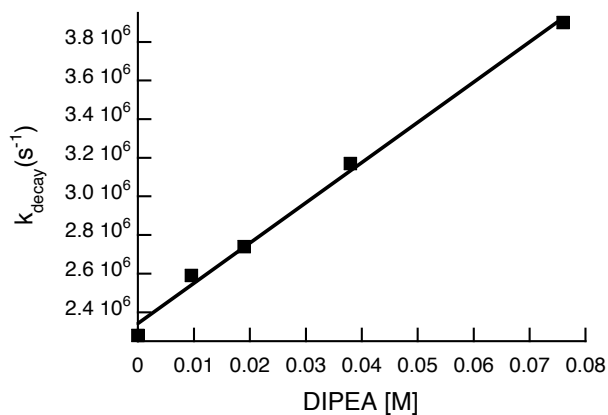
**Figure 5A.15.** Kinetic quenching plot showing the quenching of  $^3\text{Au}_2(\text{dppm})_2\text{Cl}_2$  by butyl bromide. The slope of this plot corresponds to bimolecular rate constant.



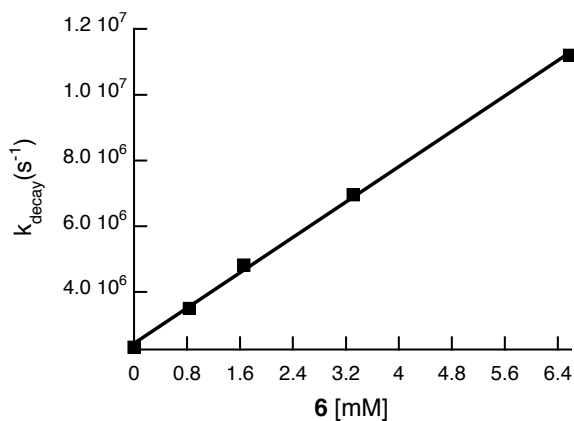
**Figure 5A.16.** Transient emission spectrum showing the  $^3\text{Au}_2(\text{dmpm})_2\text{Cl}_2$  signal obtained upon laser pulse excitation (308 nm, 10 mJ) of a  $\text{Au}_2(\text{dmpm})_2\text{Cl}_2$  sample which had been purged of oxygen.



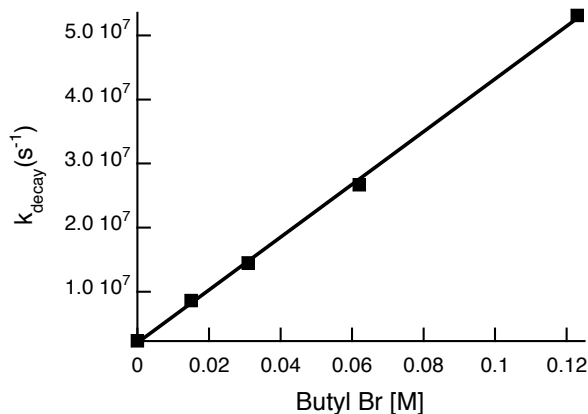
**Figure 5A.17.** Decay trace for the emission of  $^3\text{Au}_2(\text{dmpm})_2\text{Cl}_2$  at 525 nm obtained upon laser pulse excitation (308 nm, 10 mJ) of a  $\text{Au}_2(\text{dmpm})_2\text{Cl}_2$  sample which had been purged of oxygen.



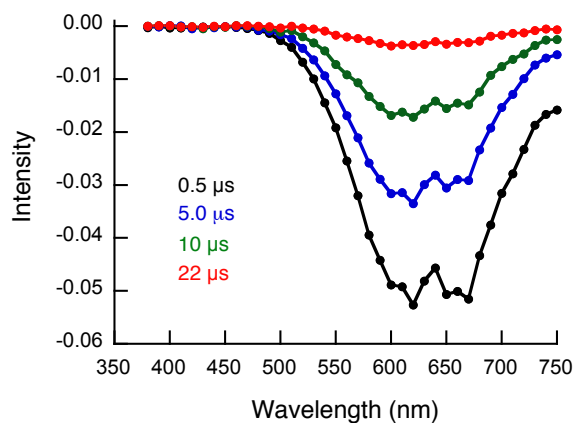
**Figure 5A.18.** Kinetic quenching plot showing the quenching of  $^3\text{Au}_2(\text{dmpm})_2\text{Cl}_2$  by DIPEA. The slope of this plot corresponds to bimolecular rate constant.



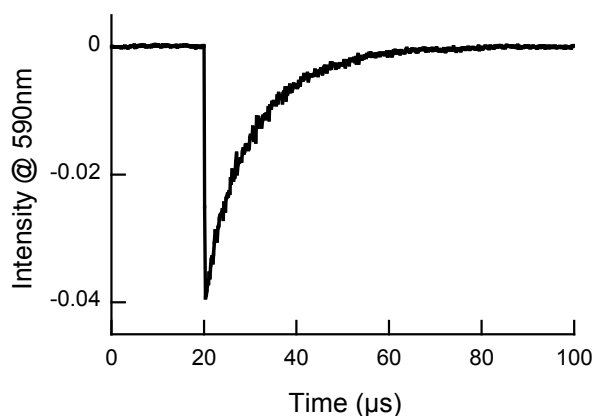
**Figure 5A.19.** Kinetic quenching plot showing the quenching of  $^3\text{Au}_2(\text{dmpm})_2\text{Cl}_2$  by substrate **6**. The slope of this plot corresponds to bimolecular rate constant.



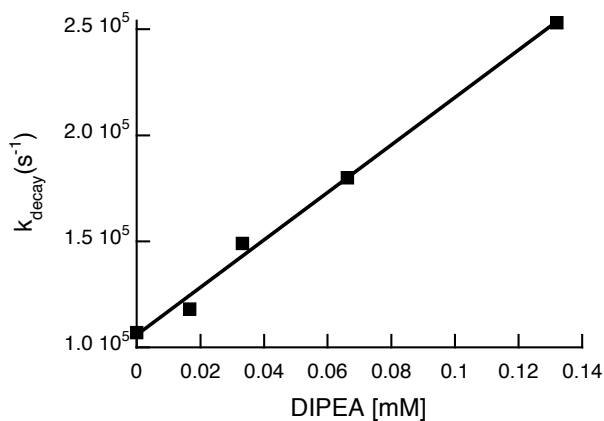
**Figure 5A.20.** Kinetic quenching plot showing the quenching of  $^3\text{Au}_2(\text{dmpm})_2\text{Cl}_2$  by butyl bromide. The slope of this plot corresponds to bimolecular rate constant.



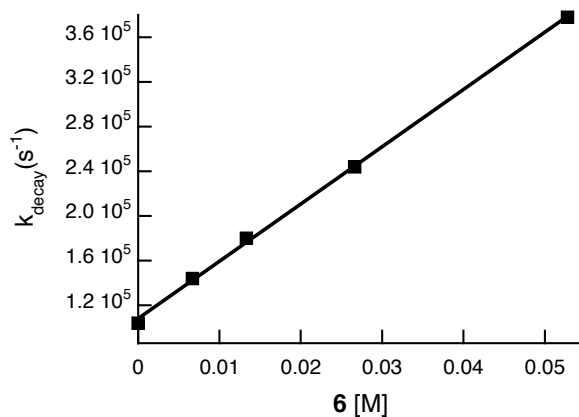
**Figure 5A.21.** Transient emission spectrum showing the  $^3\text{Au}_2(3,5\text{-CF}_3\text{-dppm})_2\text{Cl}_2$  signal obtained upon laser pulse excitation (355 nm, 10 mJ) of a  $\text{Au}_2(3,5\text{-CF}_3\text{-dppm})_2\text{Cl}_2$  sample which had been purged of oxygen.



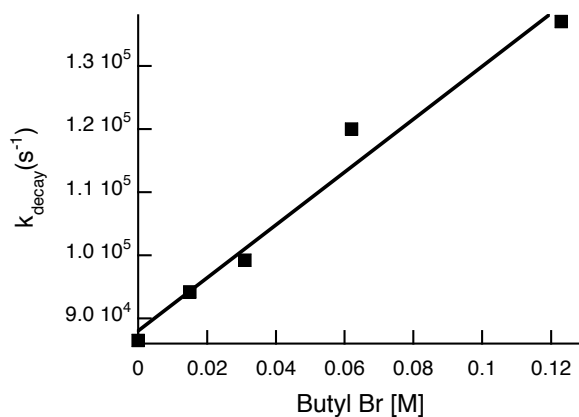
**Figure 5A.22.** Decay trace for the emission of  $^3\text{Au}_2(3,5\text{-CF}_3\text{-dppm})_2\text{Cl}_2$  at 590 nm obtained upon laser pulse excitation (355 nm, 10 mJ) of a  $\text{Au}_2(3,5\text{-CF}_3\text{-dppm})_2\text{Cl}_2$  sample which had been purged of oxygen.



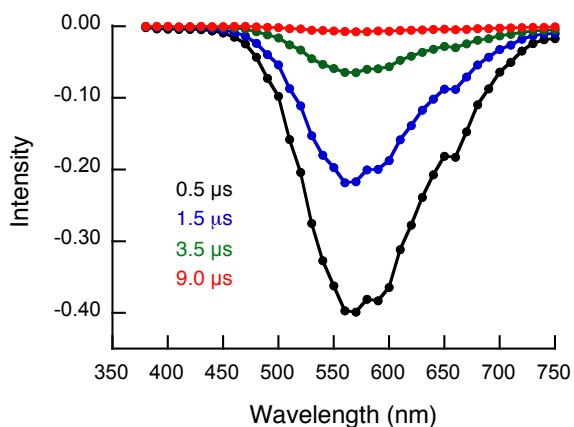
**Figure 5A.23.** Kinetic quenching plot showing the quenching of  $^3\text{Au}_2(3,5\text{-CF}_3\text{-dppm})_2\text{Cl}_2$  by DIPEA. The slope of this plot corresponds to bimolecular rate constant.



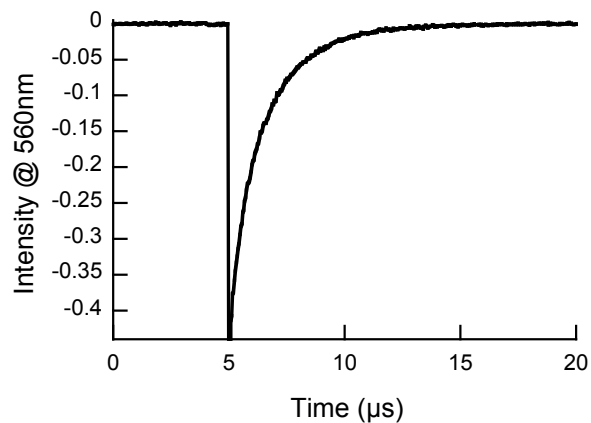
**Figure 5A.24.** Kinetic quenching plot showing the quenching of  $^3\text{Au}_2(3,5\text{-CF}_3\text{-dppm})_2\text{Cl}_2$  by substrate **6**. The slope of this plot corresponds to bimolecular rate constant.



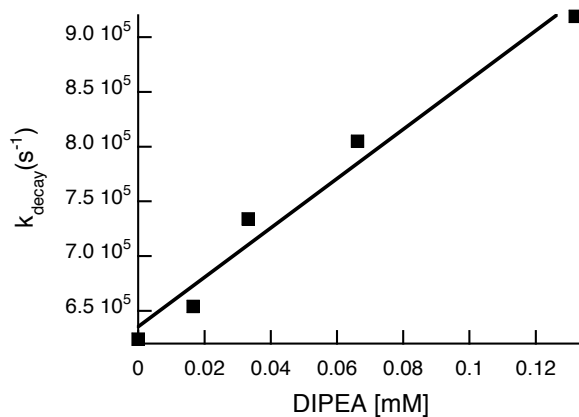
**Figure 5A.25.** Kinetic quenching plot showing the quenching of  $^3\text{Au}_2(3,5\text{-CF}_3\text{-dppm})_2\text{Cl}_2$  by butyl bromide. The slope of this plot corresponds to bimolecular rate constant.



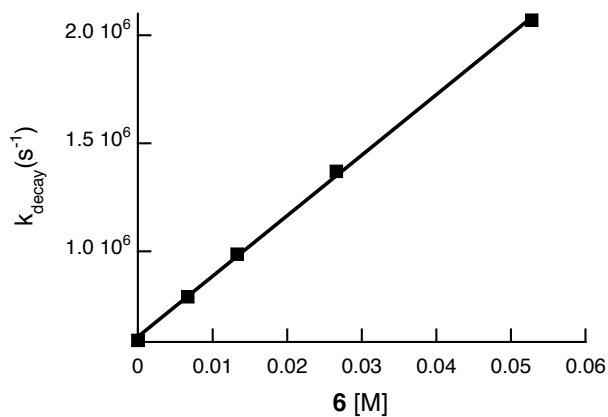
**Figure 5A.26.** Transient emission spectrum showing the  $^3\text{Au}_2(\text{tppm})_2\text{Cl}_2$  signal obtained upon laser pulse excitation (355 nm, 10 mJ) of a  $\text{Au}_2(\text{tppm})_2\text{Cl}_2$  sample which had been purged of oxygen.



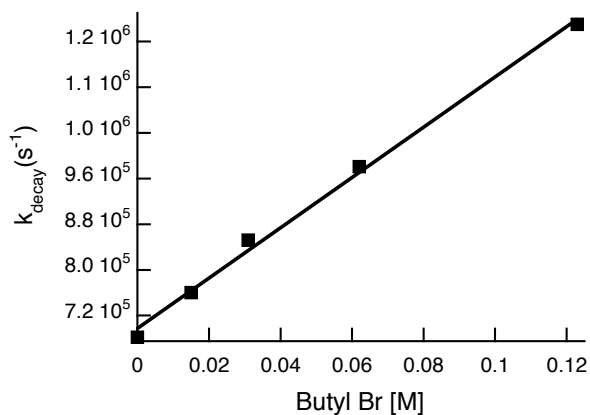
**Figure 5A.27.** Decay trace for the emission of  ${}^3\text{Au}_2(\text{tppm})_2\text{Cl}_2$  at 560 nm obtained upon laser pulse excitation (355 nm, 10 mJ) of a  $\text{Au}_2(\text{tppm})_2\text{Cl}_2$  sample which had been purged of oxygen.



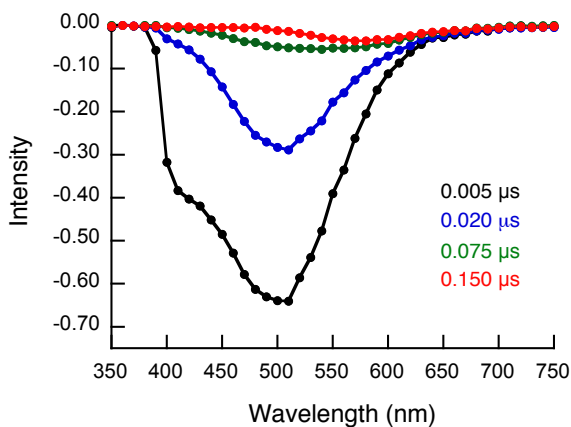
**Figure 5A.28.** Kinetic quenching plot showing the quenching of  ${}^3\text{Au}_2(\text{tppm})_2\text{Cl}_2$  by DIPEA. The slope of this plot corresponds to bimolecular rate constant.



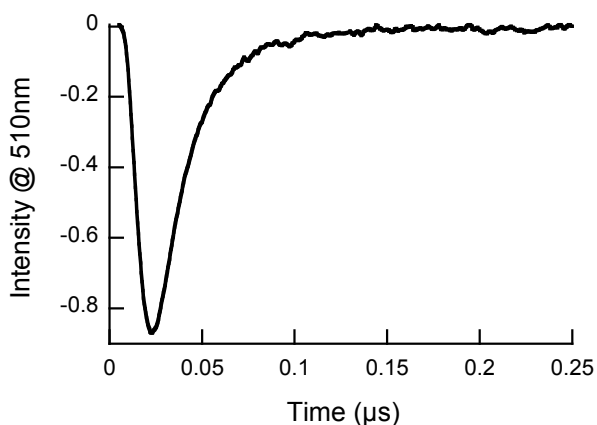
**Figure 5A.29.** Kinetic quenching plot showing the quenching of  ${}^3\text{Au}_2(\text{tppm})_2\text{Cl}_2$  by substrate **6**. The slope of this plot corresponds to bimolecular rate constant.



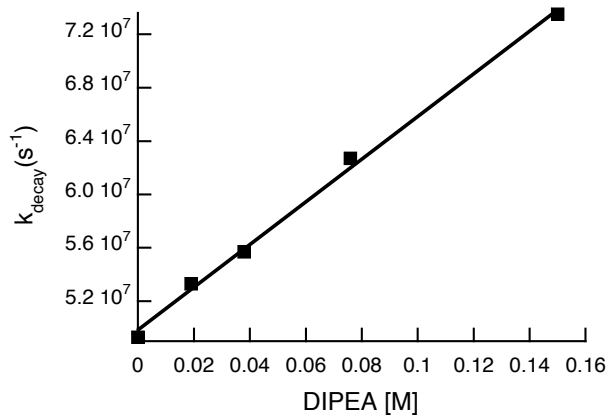
**Figure 5A.30.** Kinetic quenching plot showing the quenching of  $^3\text{Au}_2(\text{tppm})_2\text{Cl}_2$  by butyl bromide. The slope of this plot corresponds to bimolecular rate constant.



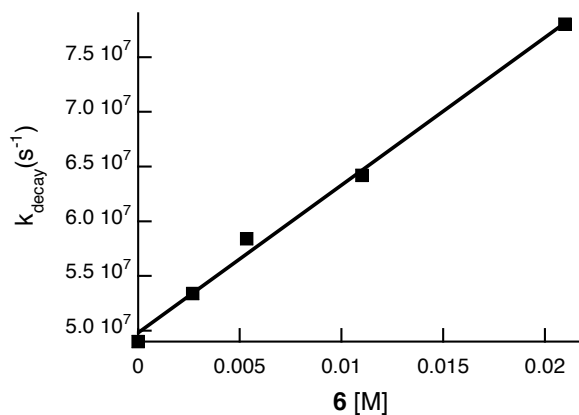
**Figure 5A.31.** Transient emission spectrum showing the  $^3\text{Au}_2(\text{bmimm})_2\text{Cl}_2$  signal obtained upon laser pulse excitation (308 nm, 10 mJ) of a  $\text{Au}_2(\text{bmimm})_2\text{Cl}_2$  sample which had been purged of oxygen.



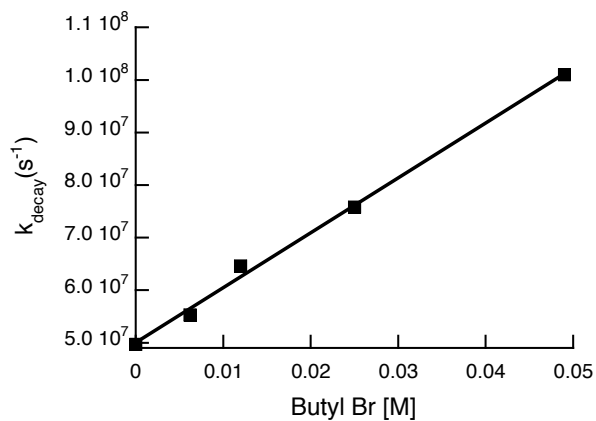
**Figure 5A.32.** Decay trace for the emission of  $^3\text{Au}_2(\text{bmimm})_2\text{Cl}_2$  at 510 nm obtained upon laser pulse excitation (308 nm, 10 mJ) of a  $\text{Au}_2(\text{bmimm})_2\text{Cl}_2$  sample which had been purged of oxygen. Curvature at the beginning of decay reflects that the short lifetime is close to the LFP rise time.



**Figure 5A.33.** Kinetic quenching plot showing the quenching of  $^3\text{Au}_2(\text{bmimm})_2\text{Cl}_2$  by DIPEA. The slope of this plot corresponds to bimolecular rate constant.



**Figure 5A.34.** Kinetic quenching plot showing the quenching of  $^3\text{Au}_2(\text{bmimm})_2\text{Cl}_2$  by substrate **6**. The slope of this plot corresponds to bimolecular rate constant.

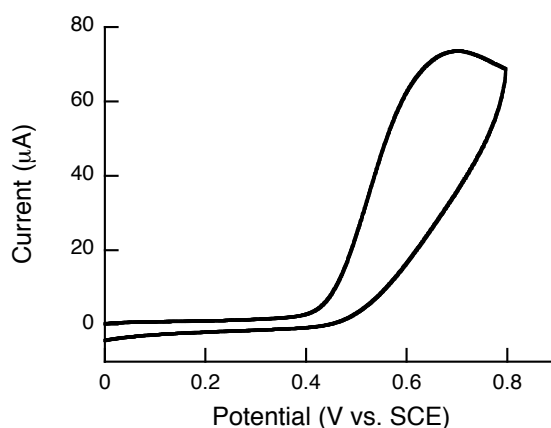


**Figure 5A.35.** Kinetic quenching plot showing the quenching of  $^3\text{Au}_2(\text{bmimm})_2\text{Cl}_2$  by butyl bromide. The slope of this plot corresponds to bimolecular rate constant.

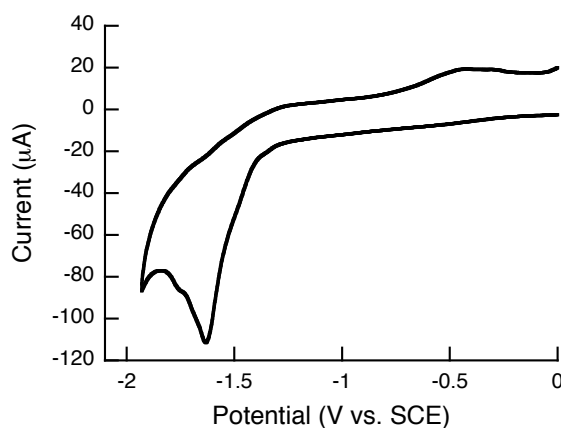


### 5.6.G. Cyclic Voltammetry Measurements of the Au<sub>x</sub> Complexes

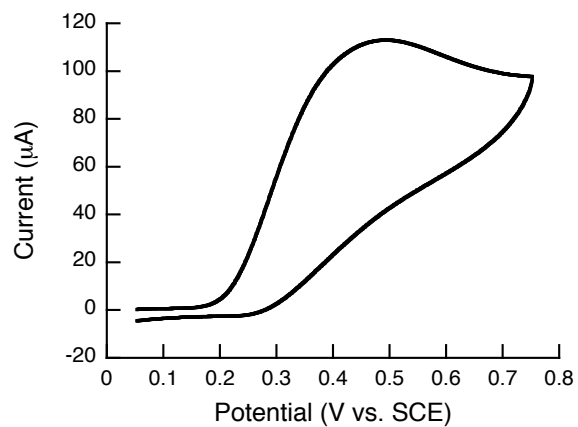
Conditions for cyclic voltammetry measurements: scan rate = 100 mV s<sup>-1</sup>; 0.5-2.0 mM Au (I) complex in Ar degassed MeCN containing 100 mM Bu<sub>4</sub>NClO<sub>4</sub> supporting electrolyte; Pt wire working electrode; Pt wire counter electrode; Ag wire pseudo-reference electrode; Fc/Fc<sup>+</sup> redox couple as internal reference (0.41 V vs. SCE); oxidation and reduction potential reported as peak anodic ( $E_{pa}$ ) and peak cathodic ( $E_{pc}$ ) potentials due to their irreversible nature.



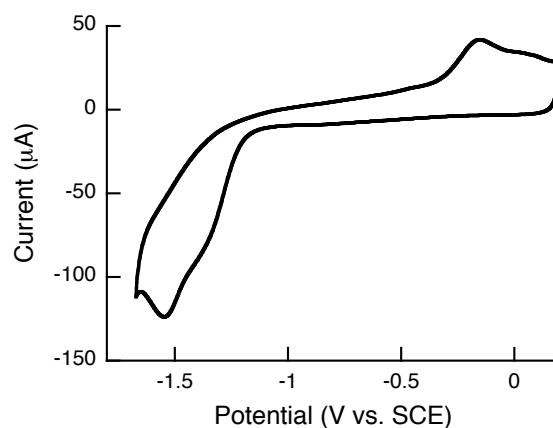
**Figure 5A.36.** Cyclic voltammogram of Au<sub>2</sub>(dppm)<sub>2</sub>Cl<sub>2</sub> [Anodic Scan].



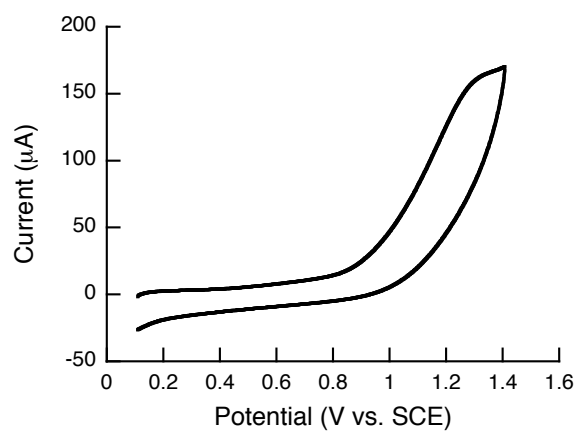
**Figure 5A.37.** Cyclic voltammogram of Au<sub>2</sub>(dppm)<sub>2</sub>Cl<sub>2</sub> [Cathodic Scan].



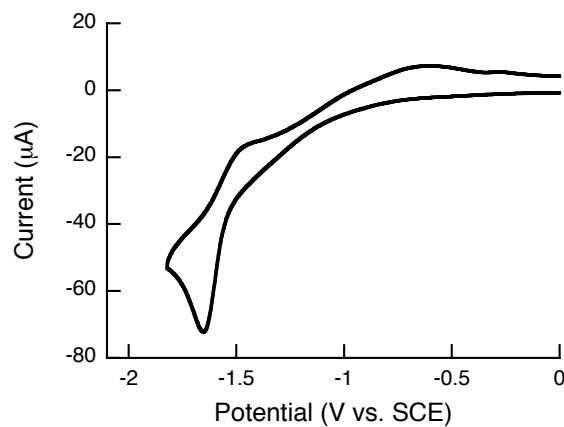
**Figure 5A.38.** Cyclic voltammogram of  $\text{Au}_2(\text{dmpm})_2\text{Cl}_2$  [Anodic Scan].



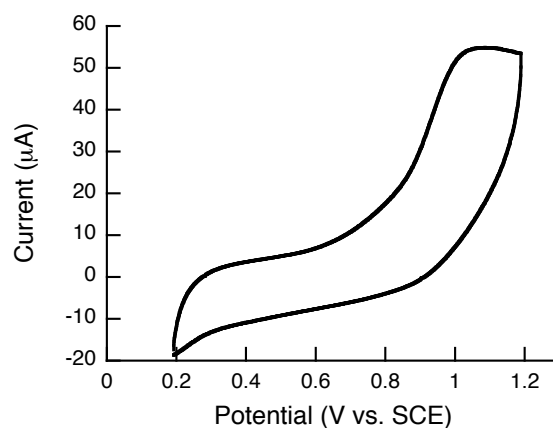
**Figure 5A.39.** Cyclic voltammogram of  $\text{Au}_2(\text{dmpm})_2\text{Cl}_2$  [Cathodic Scan].



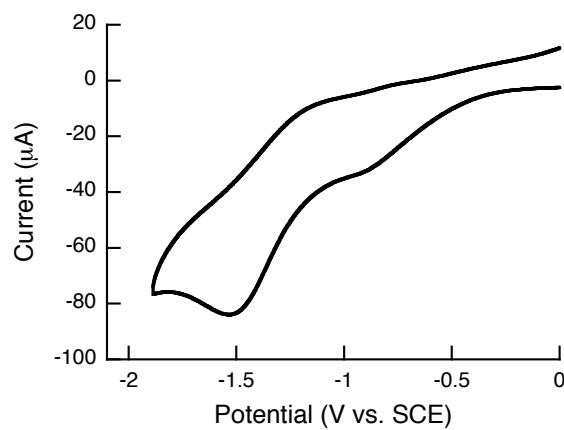
**Figure 5A.40.** Cyclic voltammogram of  $\text{Au}_2(3,5\text{-CF}_3\text{-dppm})_2\text{Cl}_2$  [Anodic Scan].



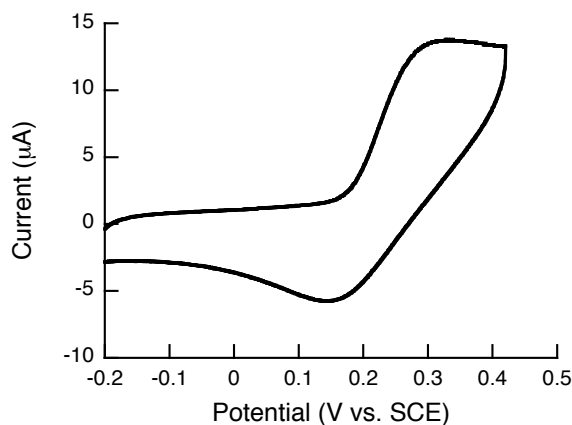
**Figure 5A.41.** Cyclic voltammogram of  $\text{Au}_2(3,5\text{-CF}_3\text{-dppm})_2\text{Cl}_2$  [Cathodic Scan].



**Figure 5A.42.** Cyclic voltammogram of  $\text{Au}_2(\text{tppm})_2\text{Cl}_2$  [Anodic Scan].



**Figure 5A.43.** Cyclic voltammogram of  $\text{Au}_2(\text{tppm})_2\text{Cl}_2$  [Cathodic Scan].



**Figure 5A.44.** Cyclic voltammogram of  $\text{Au}_2(\text{bmimm})_2\text{Cl}_2$  [Anodic Scan].

### 5.6.H. Calculating the Excited State Redox Potentials of the $\text{Au}_x$ Complexes

Using the triplet energy ( $E_T^*$ ) and ground state oxidation ( $E_{\text{pa}}$ ) and reduction ( $E_{\text{pc}}$ ) potentials of the  $\text{Au}_x$  complexes we can determine their corresponding excited state oxidation ( $E_{\text{ox}}^*$ ) and reduction ( $E_{\text{red}}^*$ ) potentials using the following equations:

$$E_{\text{ox}}^* = E_{\text{pa}} - E_T^*$$

$$E_{\text{red}}^* = E_{\text{pc}} + E_T^*$$

**Table 5A.3.** Excited State Redox Potentials of the Polynuclear Gold (I) Complexes

| Catalyst                                                    | $E_T^*$ (V) | $E_{\text{pa}}$ (V vs SCE) | $E_{\text{pc}}$ (V vs SCE) | $E_{\text{ox}}^*$ (V vs SCE) | $E_{\text{red}}^*$ (V vs SCE) |
|-------------------------------------------------------------|-------------|----------------------------|----------------------------|------------------------------|-------------------------------|
| (1) $\text{Au}_2(\text{dppm})_2\text{Cl}_2$                 | 2.23        | 0.70                       | -1.63                      | -1.53                        | 0.60                          |
| (2) $\text{Au}_2(\text{dmpm})_2\text{Cl}_2$                 | 2.36        | 0.49                       | -1.77                      | -1.87                        | 0.59                          |
| (3) $\text{Au}_2(3,5\text{-CF}_3\text{-dppm})_2\text{Cl}_2$ | 2.10        | 1.41                       | -1.65                      | -0.69                        | 0.45                          |
| (4) $\text{Au}_3(\text{tppm})_3\text{Cl}_3$                 | 2.28        | 1.09                       | -1.54                      | -1.19                        | 0.74                          |
| (5) $\text{Au}_2(\text{bmimm})_2\text{Cl}_2$                | 2.44        | 0.34                       | -                          | -2.10                        | -                             |

## 5.7. References

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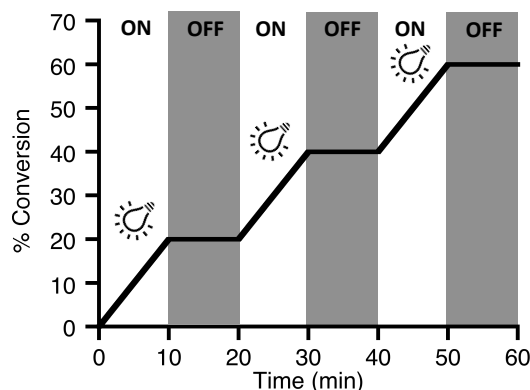
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## 6. Probing Light-Mediated Chain Processes

### 6.1. Background

Despite the recent advancements in the field of photoredox catalysis, many of the new discoveries are made in the absence of knowledge about excited-state kinetics as well as an understanding of the underlying mechanisms. As illustrated, in the previous chapters, we along with other groups, have demonstrated the usefulness of laser flash photolysis techniques in determining bimolecular rate constants of mechanistically key steps, which provide insights into the overall reaction mechanism.<sup>1-6</sup> However, we have also developed other powerful tools such as a Ru(bpy)<sub>3</sub>Cl<sub>2</sub> based visible light actinometer and an updated “rotating sector” method, which can be used to probe light-mediated chain processes.<sup>7</sup> While both actinometry and intermittent illumination are tried and tested methods when it comes to examining light-mediated chain reactions,<sup>8,9</sup> there are many examples in the current photoredox literature which propose chain propagation as a possible route to product formation, yet many fail to investigate this phenomena with these methods due to their time consuming nature and a lack of expertise. While one may find recent publications, which claim to probe chain reactions through intermittent illumination or light on-light off cycles as shown in Figure 6.1.<sup>10-19</sup> The problem with many of these investigations is that the employed light on-light off time scales are too long, typically on the minutes to tens of minutes time scale, to obtain any useful information regarding chain processes.





**Figure 6.1.** Typical light on-light off experiment employed to probe chain reactions in the current literature.

## 6.2. History and Theory Behind the Rotating Sector Method.

The use of intermittent illumination in photo-initiated reactions is in no way a new idea, having been initially suggested in 1929 by Briers, Chapman and Walters.<sup>20</sup> However, it was not until 1946 when Burnett and Melville expanded on the theory of intermittent illumination and applied it to the direct photopolymerization of vinyl acetate where it became evident that one could use such intermittent illumination to characterize chain reactions, in particular the average lifetime of a chain sequence.<sup>8</sup> The technique has since become known as the “rotating sector” method as at the time the simplest route to intermittent illumination was to place a rotating sector disk in the path of the light source. Using this set-up, one could control the light/dark ratio by controlling the size and/or number of sectors in the disk as well as the duration of the light-on and light-off periods through its speed of rotation.<sup>8</sup> Over the next few decades the theory and the instrumentation behind the technique expanded, as it was a relatively simple technique for obtaining kinetic data for photochemically initiated chain reactions exhibiting bimolecular chain termination. The technique eventually fell out of favour as it was demonstrated that electron spin resonance

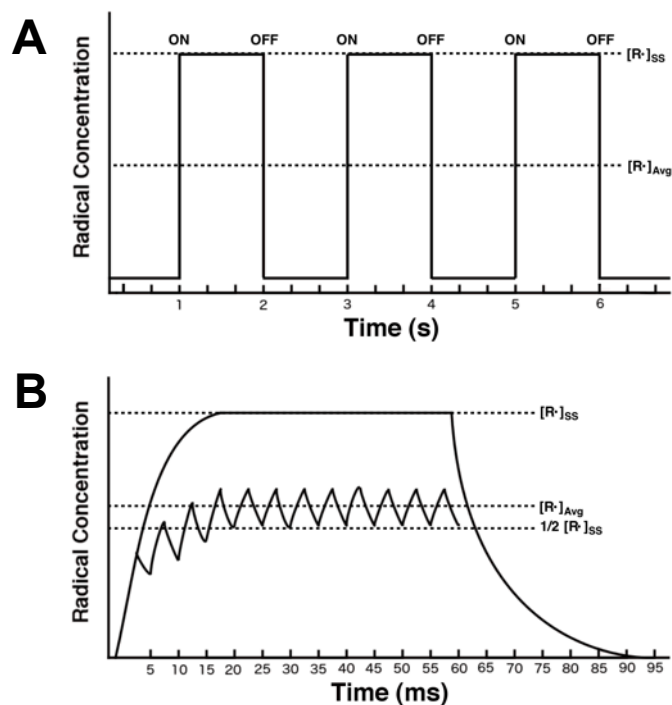
(ESR) spectroscopy could measure the rates of bimolecular radical reactions involved in both terminating and non-terminating chain events, some of which were only previously accessible through the use of intermittent illumination.<sup>21</sup>

Although the idea of utilizing a rotating sectored disk to intermittently irradiate a sample seems simple in principle, in practice its implementation is met with many difficulties the least of which is the procurement of a functioning rotating sector apparatus. Other challenges in its operation include its large physical footprint, the requirement of two different sectored disks (one for short pulses and one for long pulses)<sup>22</sup>, and poor control of the speed of rotation. High frequency of exposure also becomes difficult as fast rotating disks present safety risks.

In a typical rotating sector experiment the light is interrupted in such a way that the period of irradiation ( $t_{on}$ ) is followed by an off time ( $t_{off}$ ) that is equal to or longer than that of  $t_{on}$ . When the flashing rate is slow,  $t_{on}$  is much longer than the radical lifetime and because of this the radical concentration quickly increases to the value reached during steady-state irradiation  $[R\cdot]_{ss}$ . However, since the period over which the radicals decay is short in comparison to the dark period ( $t_{off}$ ), during the slow flashing cycle the radical concentration drops off to essentially zero whenever the light is off. The average concentration of radicals  $[R\cdot]_{avg}$  in the system throughout the experiment during slow flashing would thus be  $1/2[R\cdot]_{ss}$  if the period of light on and off were equal. Such a situation is depicted in Figure 6.2. On the other hand if the flashing rate is increased to the point where  $t_{on}$  is significantly shorter than  $\tau_s$  the situation is much different.

Under these conditions the radicals initiated during a single  $t_{\text{on}}$  period will continue to grow through several successive on-off cycles until they eventually level off. Since the radical concentrations does not reach the extreme high and low values it does when the flashing rate is slow, the  $[\text{R}\cdot]_{\text{Avg}}$  of the system approaches the steady-state concentration  $[\text{R}\cdot]_{\text{ss}}$  when the illumination is uninterrupted (Figure 6.2). From the plots in Figure 6.2, it becomes evident that as long as the intensity of irradiation and total irradiation time are kept constant, one should see a difference in the average rate of reaction for the fast and slow flashing regimes with the change in rate becoming apparent as the  $t_{\text{off}}$  time reaches that of the radical chain lifetime ( $\tau_s$ ).

One of the simplest ways to observe the change in reaction rate when moving from fast to slow flashing is to plot the percent conversion of the reaction versus  $\log(t_{\text{on}})$  of the flashing cycle. The point at which one observes a 50% change in the observed rate between slow and fast flashing in this plot corresponds to the average chain lifetime ( $\tau_s$ ). Although it may also be interesting to compare the conversions obtained under intermittent illumination with those obtained using steady-state illumination, it is not a requirement in the determination of  $\tau_s$ . In doing so it is also important to account for the fact that intermittently illuminated samples are only irradiated for one-half or one-third of the experiment depending on the on/off ratio used and therefore this should also be accounted for in the constant illumination of samples. It may also be important to monitor sample temperature as constant illumination may result in temperature increases, which may influence the observed rate of reaction.



**Figure 6.2.** Radical concentration versus time during intermittent illumination (a) Slow flashing,  $t_{on} \gg \tau_s$ . (b) Fast flashing,  $t_{on} \leq \tau_s$ . Adapted with permission from Pitre *et. al.*<sup>7</sup> Copyright 2015 Macmillan Publishers Limited.

### 6.3. Intermittent Illumination as a Chain Diagnostic Strategy: Revised Rotating Sector Method.

While the rotating sector method may not be as popular as it once was, it remains evident that many in the field of photoredox catalysis understand that one can probe a photo-initiated chain reaction through the use of intermittent illumination. However, as the lifetime of most chains are in the sub-second timescale, current attempts to establish whether or not a photoredox transformation involves a chain by testing the effect of switching the light source on and off on the time scale of minutes are futile. As might be expected, the more appropriate test for a chain reaction is conceptually the rotating sector method, where microsecond to second light pulses are employed,

Using existing LED technologies we envisioned the development of a new age rotating sector method in which the rotating sector would be replaced with a pulsed LED and that no moving parts would be involved. The LED would be powered by a constant current driver and controlled by a digital delay/pulse generator. Additional advantages of this system include a smaller physical footprint, digital control over the pulse length, light intensity, and light-to-dark ratio making the system quite versatile and user friendly. Note that in the traditional rotating sector method the light-to-dark ratio is fixed as it is determined by the configuration of open sectors in the rotating disk. For further details regarding the design of the apparatus, refer to Figure 6A.1 and its accompanying description.

Though the rotating sector experiment was and is designed to be quantitative, we envision it as being used as more a qualitative or semi-quantitative tool. For example, using the modified rotating sector experiment one could qualitatively define a reaction as involving a chain simply by demonstrating a non-linear dependence between conversion and the rate of sample illumination, as one would expect that the rate of photon delivery should have no effect on a system free of chain reactions. However, the rotating sector remains to be one of the easiest ways to experimentally determine the average lifetime of a propagating chain ( $\tau_s$ ). The  $\tau_s$  of a chain under steady state conditions is defined by equation 6.1.

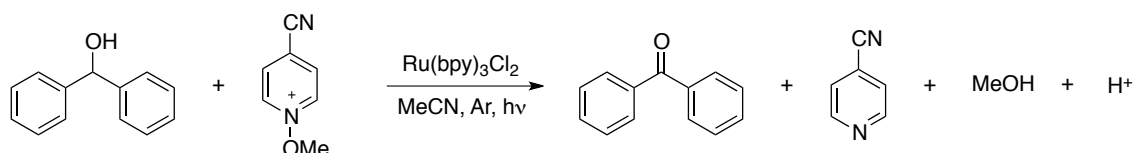
$$\tau_s = \frac{[ \text{ ] of steady-state chain-carrying radicals} }{\text{steady-state rate of radical removal due to termination}} \quad (6.1)$$

The problem with this is that under most conditions, the rate of the reaction is being measured under non-steady state conditions. Even though one of the main advantages of a light induced radical reaction is the ability to instantaneously initiate and interrupt radical formation by simply turning on or off the light source, there still remains a period of time between when the chain is initiated and realisation of the steady state, as well as another period of time between when the light is removed and the depletion of chain-carriers through termination reactions. Ideally one would determine  $\tau_s$  by measuring the rate of reaction over a given time after which the illumination has been terminated, however as  $\tau_s$  tends to be on the millisecond timescale and the amount of conversion during this time period would be minimal, it is difficult to accurately measure this value. Performing the rotating sector experiment makes this measurement viable as one can average the result over multiple on-off cycles.

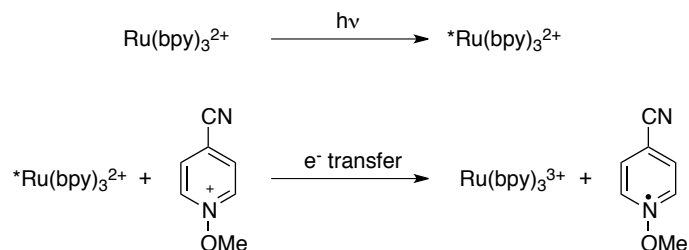
#### **6.4. Validation of the Updated Rotating Sector Method**

In order to validate the usefulness of our updated intermittent illumination experiment, it was important to use it in the characterization of a known chain reaction. It has been previously shown that in the presence of *N*-alkoxypyridinium salts the photocatalyzed oxidation of benzhydrol to benzophenone becomes a chain reaction (see Scheme 6.1 for proposed mechanism).<sup>23</sup>

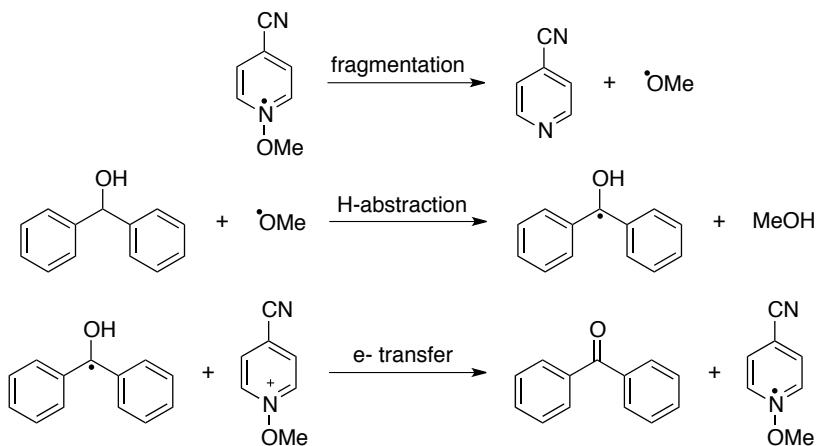
### Overall Reaction



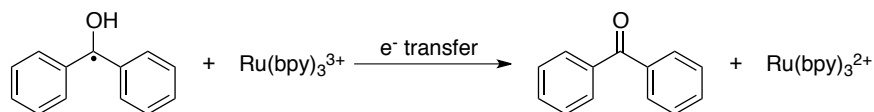
### Initiation



### Propagation



### Termination



**Scheme 6.1.** Proposed mechanism for the Ru(bpy)<sub>3</sub>Cl<sub>2</sub> mediated oxidation of benzhydrol in CH<sub>3</sub>CN. Note: The oxidation potential ( $E^{\text{ox}}$ ) of benzhydrol is > 2.04 V vs. SCE. Since the reduction potential of excited state  ${}^*\text{Ru(bpy)}_3^{2+}$  is [ $E^{\text{red}}(\text{II/I}) = + 0.77$  V vs. SCE] and that of oxidized Ru(bpy)<sub>3</sub><sup>3+</sup> is [ $E^{\text{red}}(\text{III/II}) = + 1.29$  V vs. SCE], electron transfer from benzhydrol to either  ${}^*\text{Ru(bpy)}_3^{2+}$  or Ru(bpy)<sub>3</sub><sup>3+</sup> is thermodynamically unfavourable.<sup>24</sup> Adapted with permission from Pitre *et. al.*<sup>7</sup> Copyright 2015 Macmillan Publishers Limited.

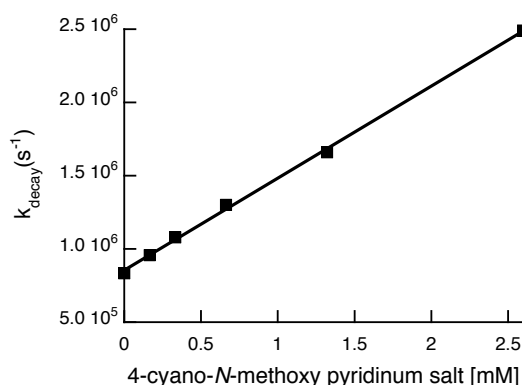
We thus decided that the oxidation of benzhydrol catalyzed by Ru(bpy)<sub>3</sub>Cl<sub>2</sub> in the presence of 4-cyano-*N*-methoxypyridinium tetrafluoroborate would be an ideal test reaction for the updated intermittent illumination apparatus. However, before we began our investigation of the light mediated chain, we examined whether or not the proposed oxidation of benzhydrol by Ru(bpy)<sub>3</sub>Cl<sub>2</sub> was thermodynamically and kinetically feasible.

If we calculate the Gibbs free energy for electron transfer between <sup>\*</sup>Ru(bpy)<sub>3</sub>Cl<sub>2</sub> and 4-cyano-*N*-methoxypyridinium tetrafluoroborate, we find that the initial electron transfer between <sup>\*</sup>Ru(bpy)<sub>3</sub>Cl<sub>2</sub> [*E*<sup>ox</sup>(III/<sup>\*</sup>II) = -0.81 V vs. SCE] and the pyridinium salt [*E*<sup>red</sup>(4-cyano-*N*-methoxypyridinium BF<sub>4</sub><sup>-</sup> salt) = -0.50 V vs. SCE] is exothermic by 0.31 V.<sup>24</sup> While this indicates that the initial excited state electron transfer is thermodynamically possible, it does not confirm that it is also kinetically favorable. Through the use of LFP, we have also determined that 4-cyano-*N*-methoxypyridinium tetrafluoroborate quenches <sup>3</sup>Ru(bpy)<sub>3</sub>Cl<sub>2</sub> at a rate of 6.9 × 10<sup>8</sup> M<sup>-1</sup>s<sup>-1</sup> (see Figure 6.3). Although we would expect the electron transfer to be diffusion controlled since it is exothermic by more than 0.2 V, the potential of the pyridinium salts is only an estimate based on its corresponding *N*-alkyl analogue. We have also determined that the triplet lifetime of Ru(bpy)<sub>3</sub>Cl<sub>2</sub> remains unchanged in the presence of benzhydrol. With this information in hand, the percentage of <sup>3</sup>Ru(bpy)<sub>3</sub>Cl<sub>2</sub> quenched by the pyridinium salt under initial reaction conditions can be calculated using the following equation:

$$\% \text{ } ^3\text{Ru(bpy)}_3^{2+} \text{ quenched by Salt} = \frac{100\% \times k_q^{\text{Salt}}[\text{Salt}]}{(\tau_0^{-1} + k_q^{\text{Salt}}[\text{Salt}])} \quad (6.2)$$



From this we calculate that 89.7% of  $\text{Ru}(\text{bpy})_3\text{Cl}_2$  triplets are quenched by the pyridinium salt under initial reaction conditions. When we combine this with the fact that the efficiency of intersystem crossing in  $\text{Ru}(\text{bpy})_3\text{Cl}_2$  is nearly unity ( $\eta_{\text{ISC}} \approx 1$ ), we find that the initiation efficiency of the reaction is approximately 0.90.



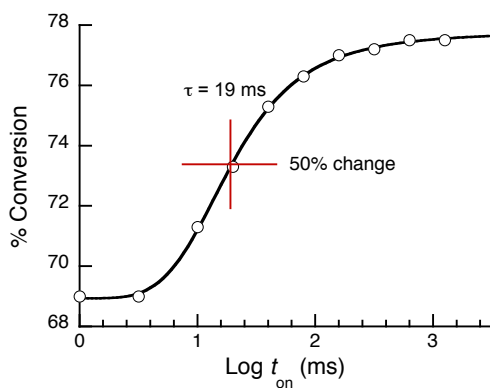
**Figure 6.3.** Quenching of  $^*\text{Ru}(\text{bpy})_3\text{Cl}_2$  by 4-cyano-*N*-methoxypyridinium tetrafluoroborate in  $\text{CH}_3\text{CN}$ . The bimolecular rate constant corresponds to the slope of this plot. Adapted with permission from Pitre *et. al.*<sup>7</sup> Copyright 2015 Macmillan Publishers Limited.

The oxidation of benzhydrol was carried out using 4-cyano-*N*-methoxypyridinium tetrafluoroborate (0.09 mmol, 20.0 mg), benzhydrol (0.09 mmol, 16.6 mg),  $\text{Ru}(\text{bpy})_3\text{Cl}_2$  (0.018 mmol, 13.5 mg) and 3 mL of  $\text{CH}_3\text{CN}$  in a 1 cm x 1 cm quartz cuvette fitted with a septa. The reaction was then degassed for 15 minutes and irradiated using a 460 nm LED for 2 minutes. Under these conditions we found that 77.4% of the benzhydrol was being converted to benzophenone during the 2 minutes of irradiation. Further details on sample preparation, yield/conversion determination, and the irradiation apparatus can be found in the appendix of this chapter. In order to determine whether or not the high efficiency of this reaction stems from an underlying chain mechanism we have examined this transformation utilizing both actinometric and intermittent illumination techniques. By determining the rate at which a 6.0 mM solution of

$\text{Ru}(\text{bpy})_3\text{Cl}_2$  absorbs photons under our geometry and conditions of irradiation, we could then determine the  $\Phi$  of the reaction. This task is greatly simplified using our newly developed  $\text{Ru}(\text{bpy})_3\text{Cl}_2$  based actinometer. By simply performing the actinometry experiment with a 6.0 mM solution of  $\text{Ru}(\text{bpy})_3\text{Cl}_2$ , we calculated that our sample absorbs  $1.53 \times 10^{-7}$  einsteins  $\text{s}^{-1}$ . We were then able to apply equation 6.2 to determine that the 77.4% conversion obtained in 2 minutes of irradiation corresponds to a quantum yield of 4.21 after correcting for the initiation efficiency of 0.90.

To further characterize and confirm the presence of a chain propagating mechanism we then employed our modified rotating sector method. Utilizing an on:off ratio of 1:2, we irradiated 10 samples, each for a total of 6 minutes (on+off time) at different flash rates. The results are displayed in Figure 6.4, in which conversion is plotted as a function of the  $\log(t_{\text{on}})$ . Qualitatively the fact that Figure 6.4 demonstrates a non-linear dependence between conversion and the rate of sample illumination reaffirms that indeed the studied reaction involves a chain mechanism. Quantitatively, we observe that there is an appreciable change in rate of conversion between 5 and 100 ms, indicating the  $\tau_s$  of the radical chain is somewhere between these two values. The lifetime of the chain can be approximated by using a sigmoidal curve fit, or simply determining graphically the point at which half of the total change in rate is observed. In the case of the benzhydrol oxidation this time corresponds to 19 ms. The fact that the total conversion during fast flashing is lower than that observed during slow flashing

reflects an increased number of termination events brought on by an increased concentration of propagating radicals.



**Figure 6.4.** Conversion of benzhydrol to benzophenone as a function of Log (light on period in milliseconds [ $t_{on}$ ]). Reaction Conditions:  $\text{Ru}(\text{bpy})_3\text{Cl}_2$  (6 mM), benzhydrol (30 mM), and 4-cyano-*N*-methoxypyridinium tetrafluoroborate (30 mM) in acetonitrile (3 mL) in a quartz cuvette were degassed with argon and irradiated with a 460 nm LED. Adapted with permission from Pitre *et al.*<sup>7</sup> Copyright 2015 Macmillan Publishers Limited.

## 6.5. Conclusion

In this Chapter, we have shown that one can easily update the rotating sector method utilizing readily available LED technologies and that the resulting system can be utilized to both qualitatively and quantitatively characterize light-mediated chain reactions. We envision that this method will have great implications on the field of photoredox catalysis, as it will provide researchers with a powerful and easily employed tool for the proper characterization chain mechanisms.

## 6.6. Appendix

### 6.6.A. General Information

Substrates and Reagents: Tris(bipyridine)ruthenium(II) chloride ( $\text{Ru}(\text{bpy})_3\text{Cl}_2$ ) was purchased from Fisher Scientific and used as received. Diphenylanthracene

(DPA), benzhydrol, 4-cyanopyridine *N*-oxide, and trimethyloxonium tetrafluoroborate were purchased from Sigma Aldrich and used as received.

Chromatography: Flash column chromatography was performed using 230-400 mesh silica gel. Preparatory thin layer chromatography (PTLC) was performed using 1000  $\mu$ m thick glass baked TLC plates purchased from Silicycle.

NMR: All  $^1\text{H}$  NMR were recorded on a Bruker AVANCE 400 spectrometer. Chemical shifts ( $\delta$ ) are reported in ppm from the solvent.

#### **6.6.B. Synthesis of 4-cyano-*N*-methoxypyridinium tetrafluoroborate**

An oven-dried 100 mL round bottom flask was charged with 4-cyanopyridine *N*-oxide (6 mmol, 720 mg) and trimethyloxonium tetrafluoroborate (11.37 mmol, 1.68 g). The contents were dissolved in 30 mL of dry DCM, and the reaction mixture was purged with argon for 15 minutes and stirred overnight. The reaction was quenched with 15 mL of MeOH, and the solvent was removed under reduced pressure. The crude solid was recrystallized in MeOH to afford 4-cyano-*N*-methoxypyridinium tetrafluoroborate as a white crystalline solid (910 mg, 68% isolated yield).

$^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta$  ppm 4.45 (s, 3 H) 8.64 - 8.98 (m, 2 H) 9.58 - 9.89 (m, 2 H)

$^{13}\text{C}$  NMR (101 MHz, DMSO- $d_6$ )  $\delta$  ppm 70.04, 114.94, 126.39, 132.93, 142.59

#### **6.6.C. General Procedure for Ru(bpy) $_3$ Cl $_2$ Laser Flash Photolysis Experiments**

The triplet quenching experiments of Ru(bpy) $_3$ Cl $_2$  were performed using a Nd-YAG laser (355 nm and 10 mJ/pulse) in a LFP-111 laser flash photolysis system (Luzchem Inc., Ottawa, Canada) and 1 x 1 cm quartz cuvettes. Samples of

$\text{Ru}(\text{bpy})_3\text{Cl}_2$  were prepared in acetonitrile with a total volume of 3 mL and an absorbance of 0.1 at 355 nm. The samples were deaerated with  $\text{N}_2$  30 minutes prior to use.

#### **6.6.D. General Procedure for the Oxidation of Benzhydrol**

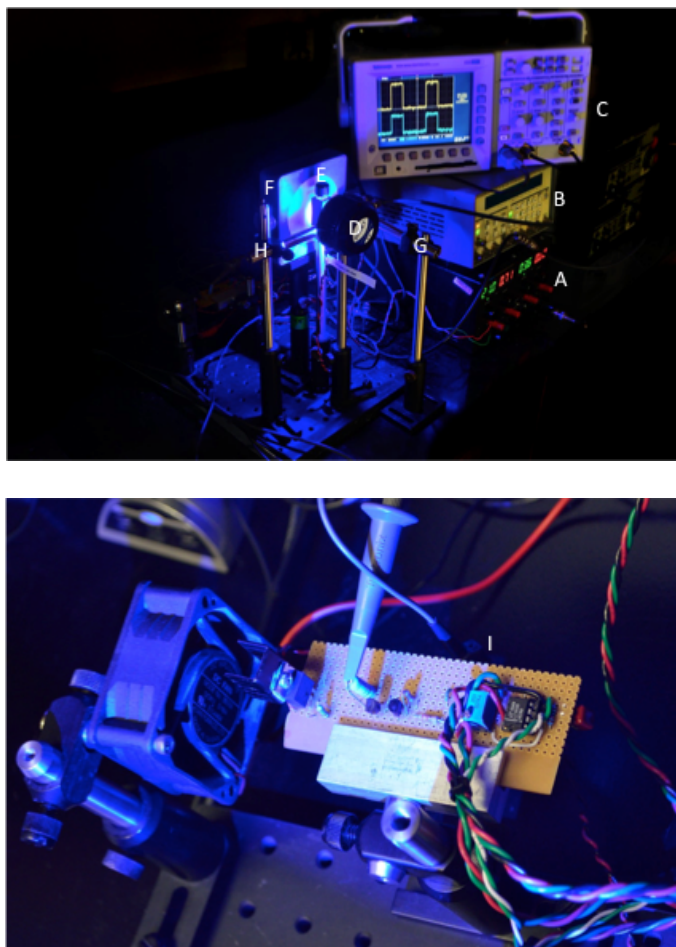
Typically, 4-cyano-*N*-methoxypyridinium tetrafluoroborate (0.09 mmol, 20.0 mg), benzhydrol (0.09 mmol, 16.6 mg),  $\text{Ru}(\text{bpy})_3\text{Cl}_2$  (0.018 mmol, 13.5 mg), and acetonitrile (3mL) were added to a 1 cm x 1 cm quartz cuvette fitted with a septa. The reaction mixture was then degassed with argon for 15 minutes. It was then subjected to 460 nm LED irradiation for 2 minutes. Upon completion of the irradiation, the reaction mixture was concentrated using a rotovap. The percent conversion was then determined using  $^1\text{H}$ -NMR, by monitoring the disappearance of the methoxy signal belonging to the pyridium salt and using dimethylsulfone as external standard.

#### **6.6.E. General Procedure for “Rotating Sector” Experiments for the Oxidation of Benzhydrol**

Typically, 4-cyano-*N*-methoxypyridinium tetrafluoroborate (0.09 mmol, 20.0 mg), benzhydrol (0.09 mmol, 16.6 mg),  $\text{Ru}(\text{bpy})_3\text{Cl}_2$  (0.018 mmol, 13.5 mg), and acetonitrile (3 mL) were added to a 1 cm x 1 cm quartz cuvette fitted with a septa. The reaction mixture was then degassed with argon for 15 minutes before it was intermittently irradiated for 6 minutes (light on+off time) using a pulsed 460 nm LED, which was powered by a constant current driver (designed and built in house) and controlled by a digital delay/pulse generator (Stanford Research System Inc.- MODEL DG535). In all cases the system was connected to an

oscilloscope (Tektronix – MODEL TDS3052), which monitored the delivered voltage and resulting current of the system. Using a photodiode we were able to monitor the shape and duration of the light pulse emitted from the LED. This allowed us to monitor the light pulse in real time to ensure that the appropriate light on:light off ratio was being employed. A light on:light off ratio of 1:2 was used in all trials, and the length of the on and off times were increased proportionally with each successive trial. After the irradiation, the reaction mixture was concentrated using a rotovap. The percent conversion was then determined using  $^1\text{H}$ -NMR, by monitoring the disappearance of the methoxy signal belonging to the pyridium salt and using dimethylsulfone as external standard.

#### 6.6.E. Photographs of the irradiation apparatus used for both steady-state and intermittent illuminations

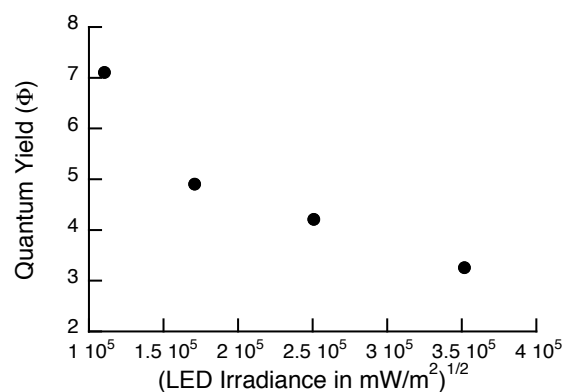


**Figure 6A.1.** Photographs of the irradiation apparatus used for both steady-state and intermittent illuminations. A) power supply, B) pulse generator, C) Oscilloscope, D) 460 nm LED, E) sample holder, F) magnetic stir plate, G) photodiode, H) removable notch filter, and I) constant current driver.

#### 6.6.F. Further examination of the quantum yield for the $\text{Ru}(\text{bpy})_3\text{Cl}_2$ mediated oxidation of benzhydrol

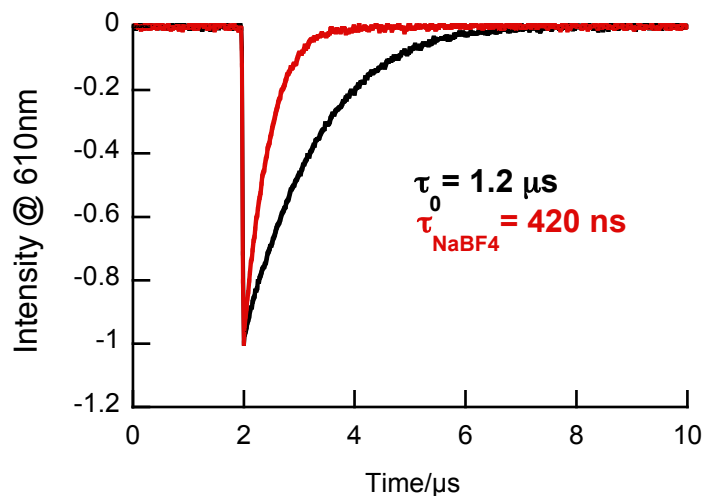
We have explored the dependency of the quantum yield on the power of irradiance, as well as the concentration of benzhydrol and 4-cyano-*N*-methoxypyridinium tetrafluoroborate. As the intensity of the absorbed light increases we have found that the quantum yield of the reaction decreases, and that there is a relationship between the square root of the light intensity and the

quantum yield of the chain (See Figure 6A.2). Although such a result would be unexpected in a direct photolysis experiment under photosensitized conditions this is anticipated. It is also seen that the quantum yield is independent of benzhydrol concentration but dependent on the concentration of the pyridinium tetrafluoroborate. Unexpectedly in the presence of 60 mM 4-cyano-*N*-methoxypyridinium tetrafluoroborate the conversion over 2 minutes is reduced to 43.2%. One would expect an increase in the concentration of the pyridinium salt to result in a decrease in termination events and therefore an increase the yield. A possible explanation for this observation is that the  $\text{BF}_4^-$  anion of the pyridinium salt is dynamically quenching or displacing the  $\text{Cl}^-$  counter-ion of the  $\text{Ru}(\text{bpy})_3^{2+}$  resulting in a drastically reduced excited state lifetime, which would ultimately decrease the initiation efficiency (see Figure 6A.3).



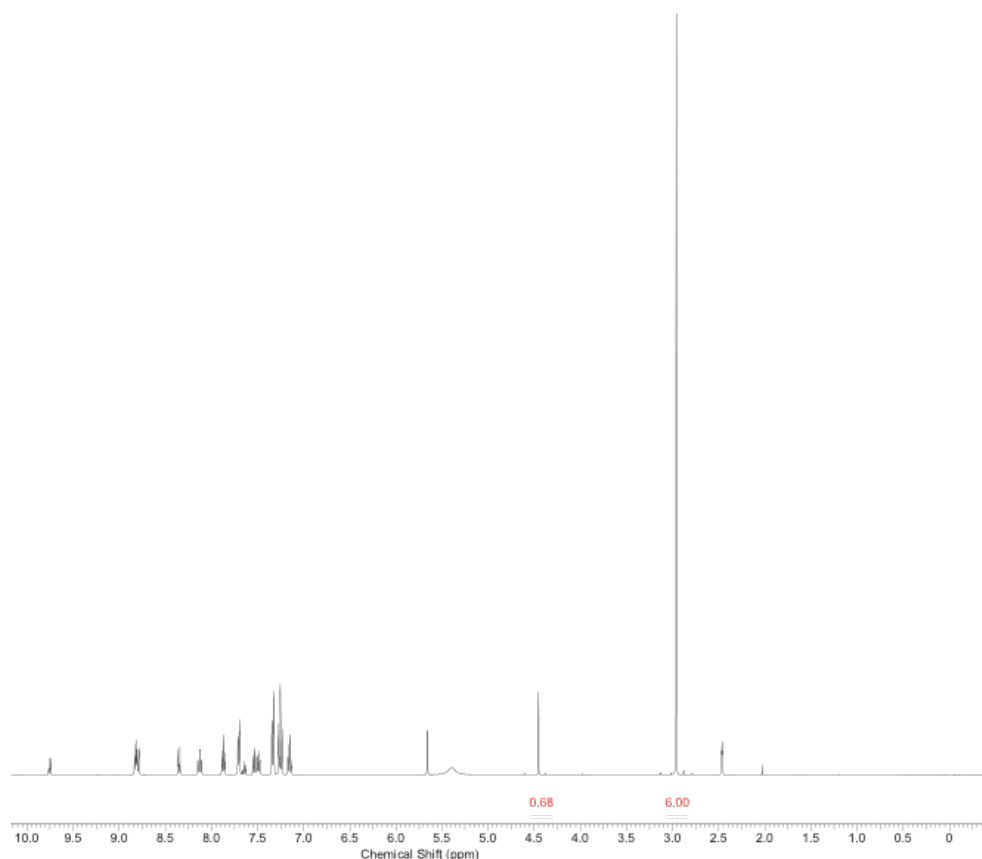
**Figure 6A.2.** Quantum Yield of the  $\text{Ru}(\text{bpy})_3\text{Cl}_2$  mediated oxidation of benzhydrol to benzophenone as a function of irradiation power (irradiance).



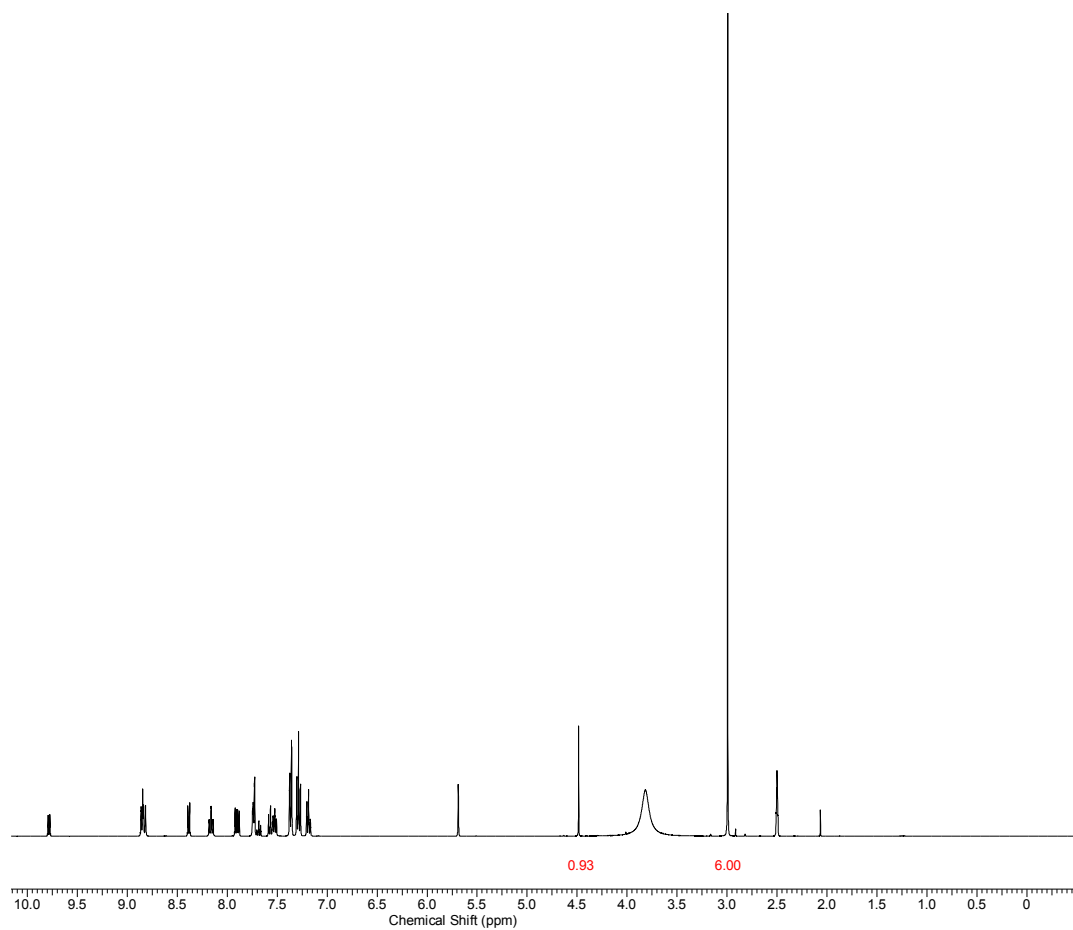


**Figure 6A.3.** Decay trace of the emission from  $^3\text{Ru}(\text{bpy})_3\text{Cl}_2$  @ 610 nm in  $\text{N}_2$  degassed acetonitrile, in the presence of 0 mM  $\text{NaBF}_4$  (black) and 0.03 M  $\text{NaBF}_4$  (red)

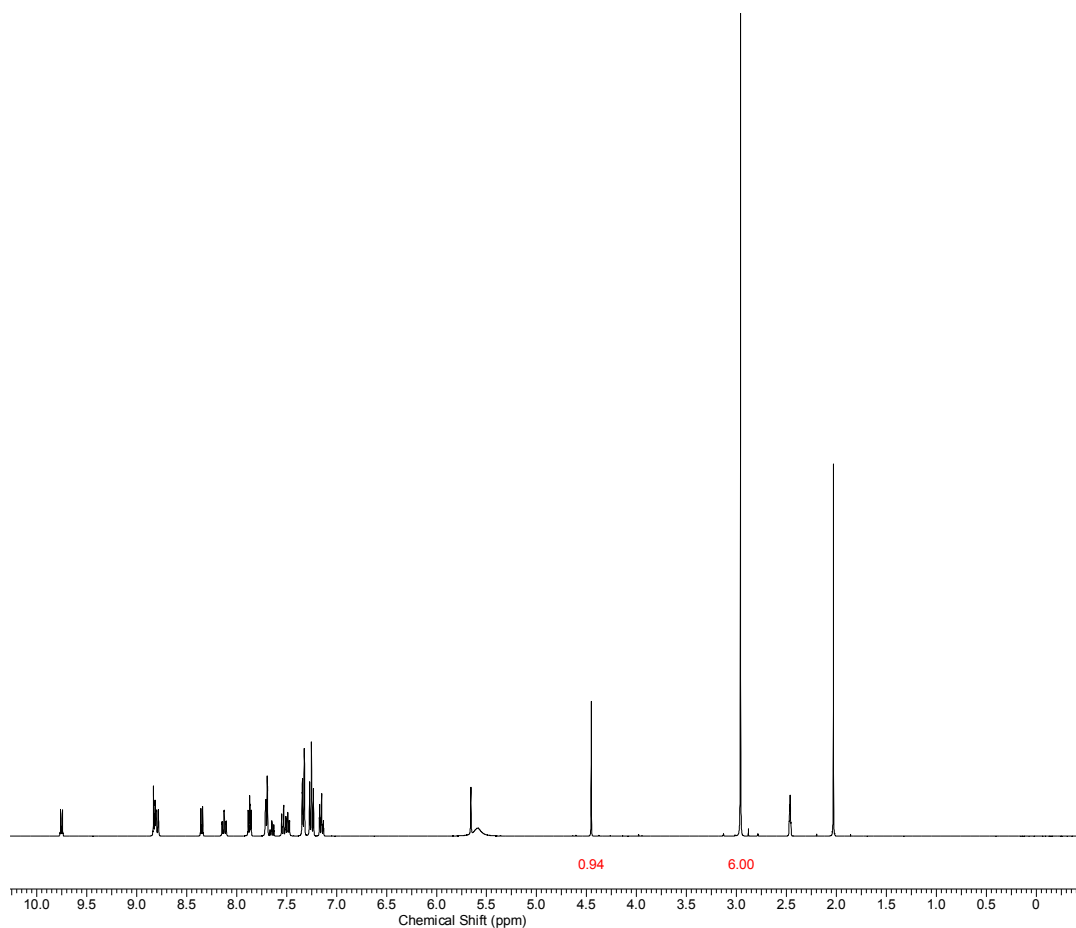
#### 6.6.G. $^1\text{H}$ and $^{13}\text{C}$ NMR Spectra



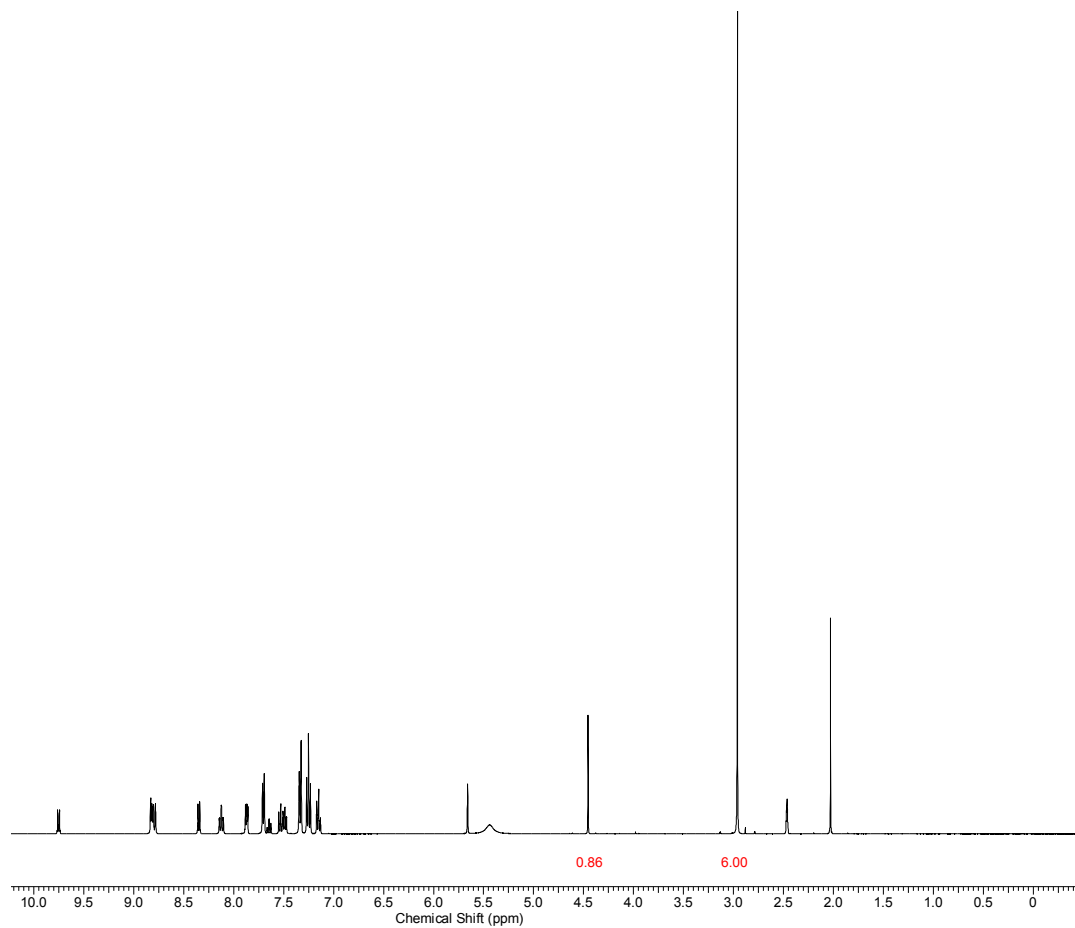
**Figure 6A.4.**  $^1\text{H}$ -NMR obtained after 2 min steady state irradiation [ $\text{Ru}(\text{bpy})_3\text{Cl}_2$  mediated oxidation of benzhydrol to benzophenone]



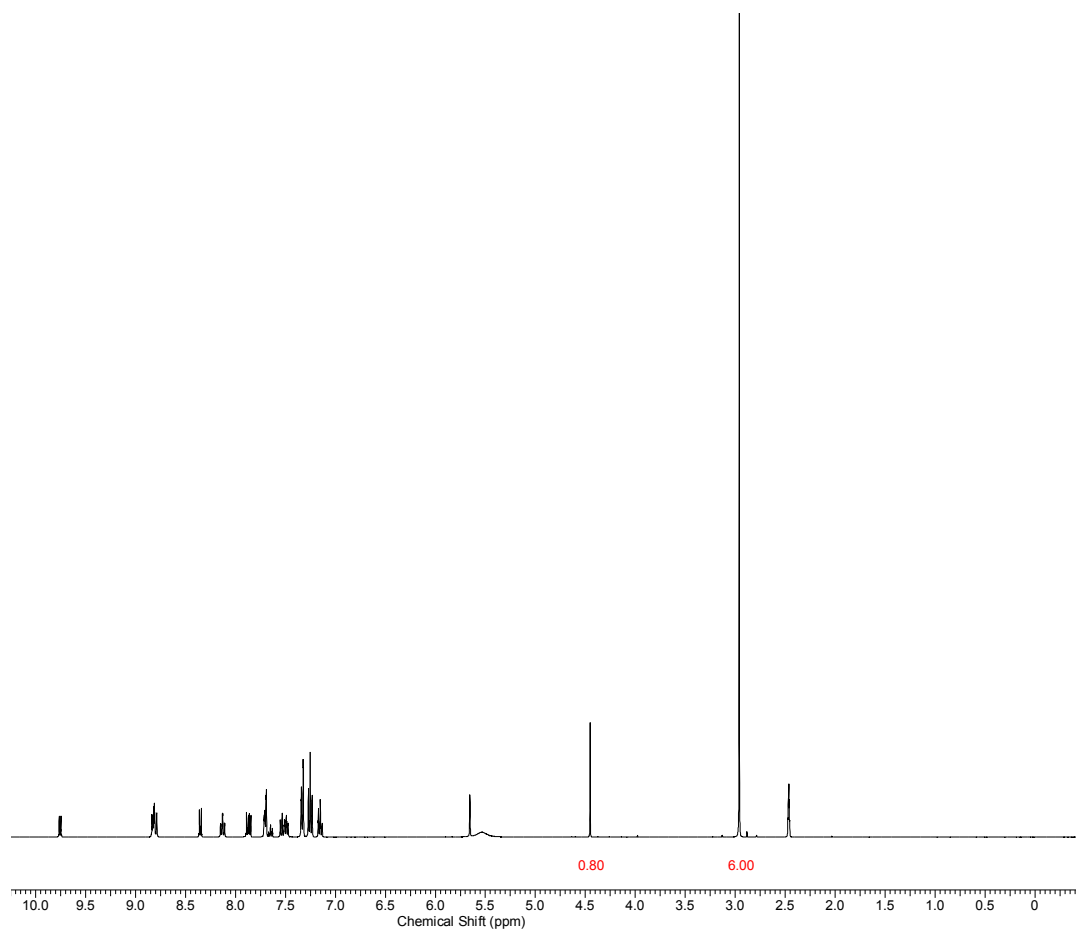
**Figure 6A.5.**  $^1\text{H}$ -NMR obtained after 6 min intermittent irradiation ( $t_{\text{on}} = 1$  ms)  $[\text{Ru}(\text{bpy})_3\text{Cl}_2]$  mediated oxidation of benzhydrol to benzophenone]



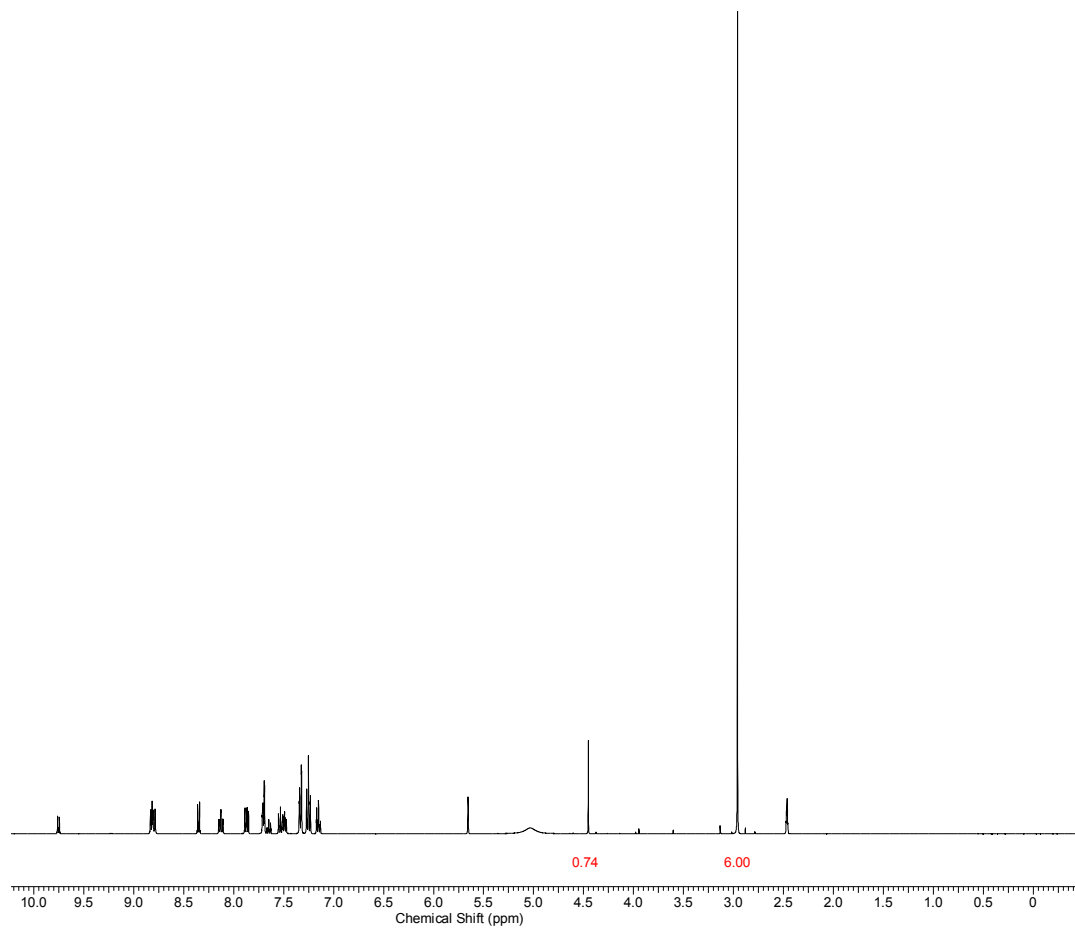
**Figure 6A.6.**  $^1\text{H}$ -NMR obtained after 6 min intermittent irradiation ( $t_{\text{on}} = 5$  ms)  $[\text{Ru}(\text{bpy})_3\text{Cl}_2]$  mediated oxidation of benzhydrol to benzophenone]



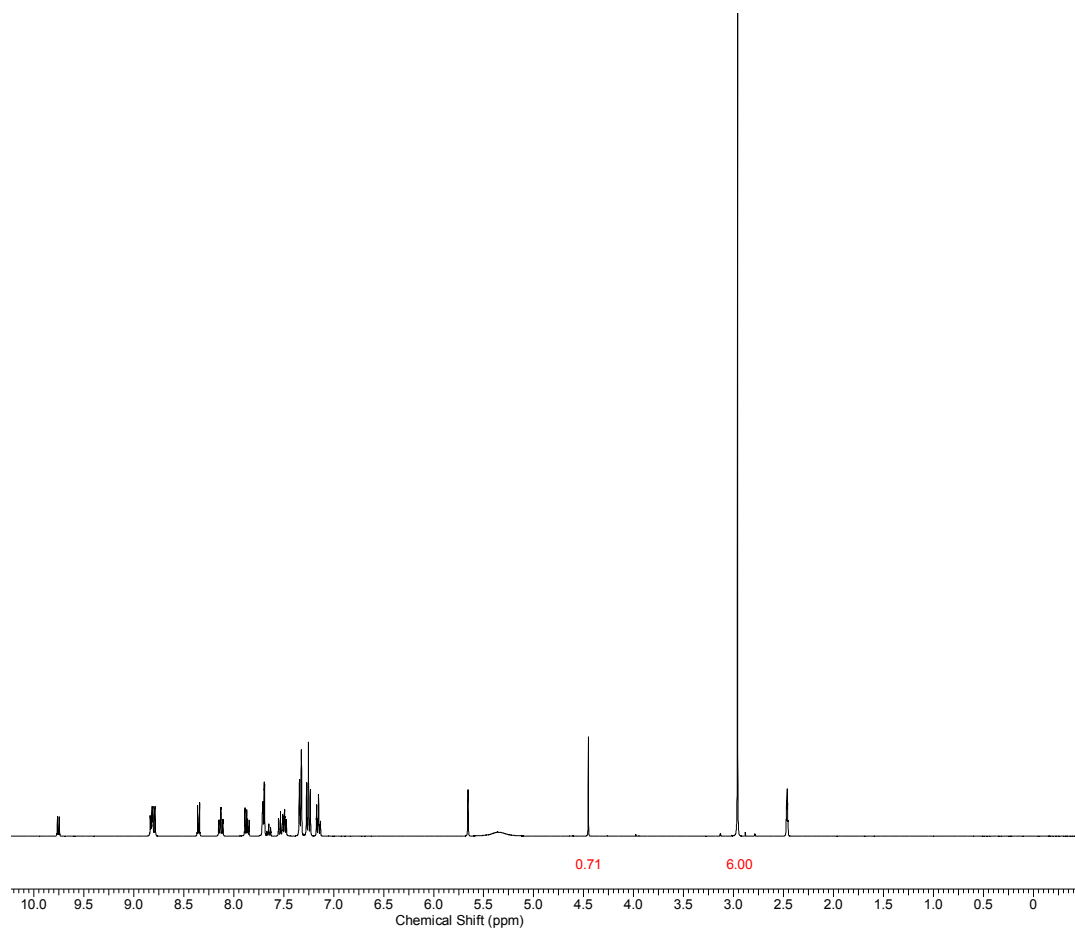
**Figure 6A.7.**  $^1\text{H}$ -NMR obtained after 6 min intermittent irradiation ( $t_{\text{on}} = 10$  ms)  $[\text{Ru}(\text{bpy})_3\text{Cl}_2]$  mediated oxidation of benzhydrol to benzophenone]



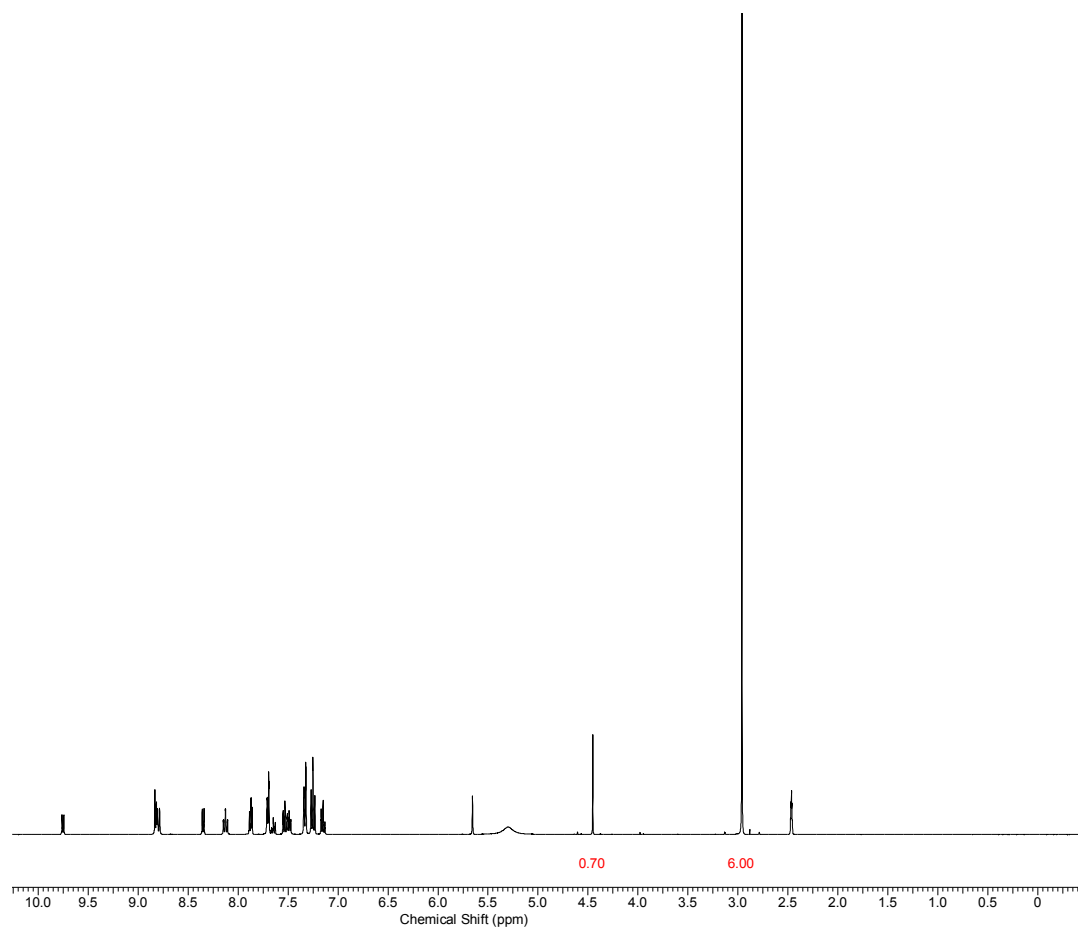
**Figure 6A.8.**  $^1\text{H}$ -NMR obtained after 6 min intermittent irradiation ( $t_{\text{on}} = 20$  ms)  $[\text{Ru}(\text{bpy})_3\text{Cl}_2]$  mediated oxidation of benzhydrol to benzophenone]



**Figure 6A.9.**  $^1\text{H}$ -NMR obtained after 6 min intermittent irradiation ( $t_{\text{on}} = 40$  ms)  $[\text{Ru}(\text{bpy})_3\text{Cl}_2]$  mediated oxidation of benzhydrol to benzophenone]

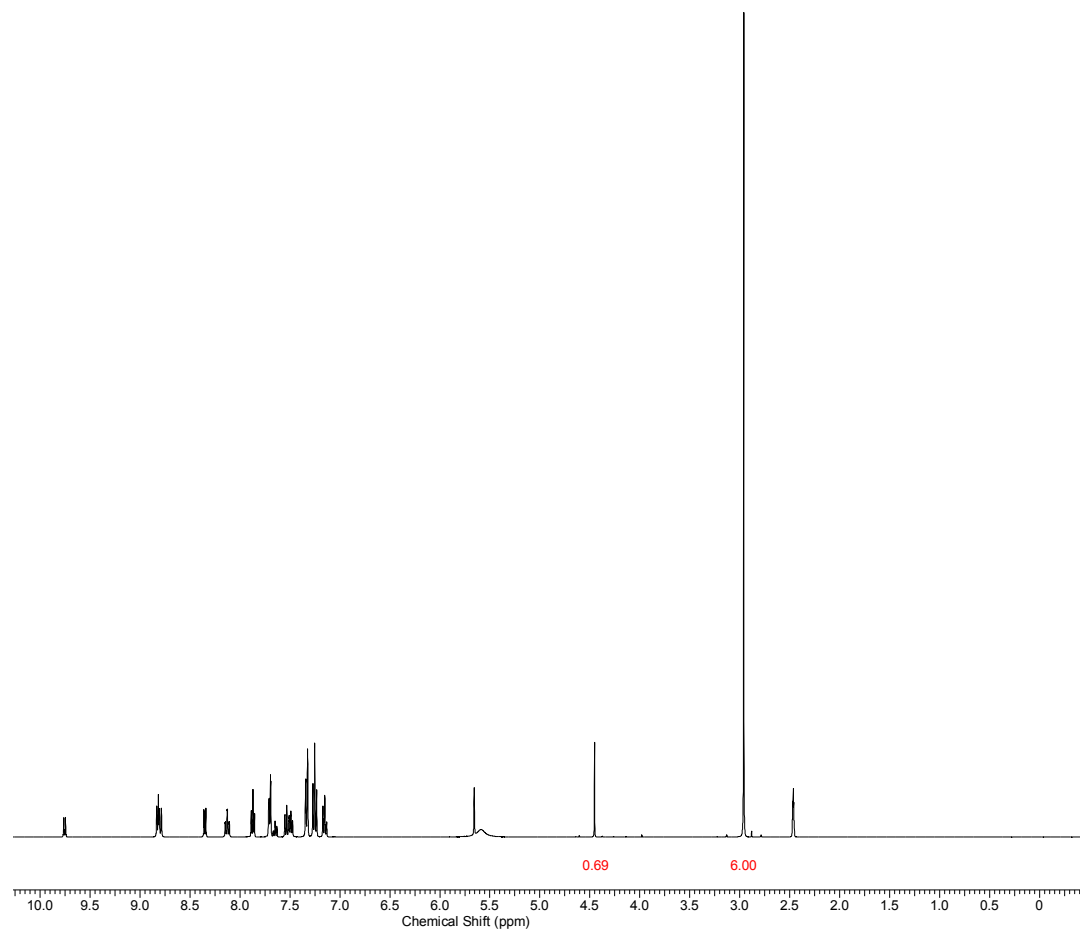


**Figure 6A.10.**  $^1\text{H}$ -NMR obtained after 6 min intermittent irradiation ( $t_{\text{on}} = 80$  ms)  $[\text{Ru}(\text{bpy})_3\text{Cl}_2]$  mediated oxidation of benzhydrol to benzophenone]

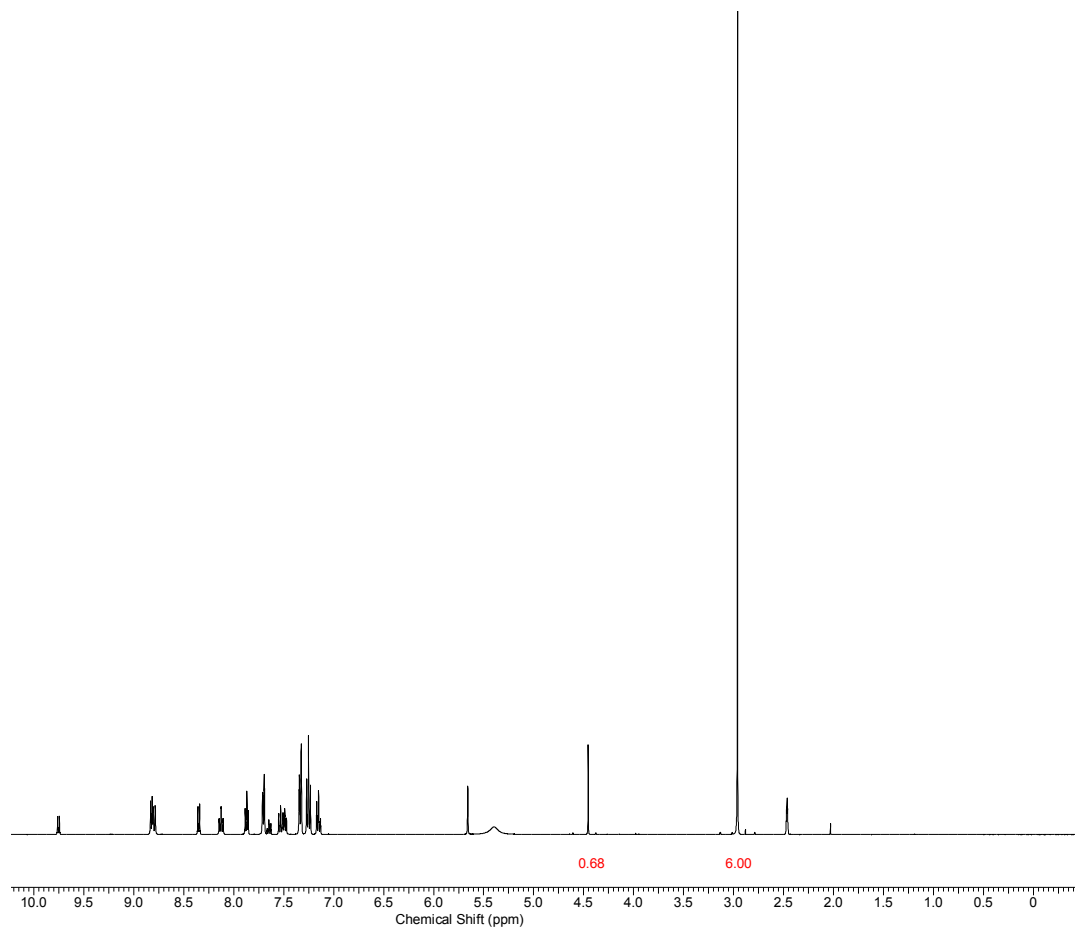


**Figure 6A.11.**  $^1\text{H}$ -NMR obtained after 6 min intermittent irradiation ( $t_{\text{on}} = 160$  ms)  $[\text{Ru}(\text{bpy})_3\text{Cl}_2]$  mediated oxidation of benzhydrol to benzophenone]

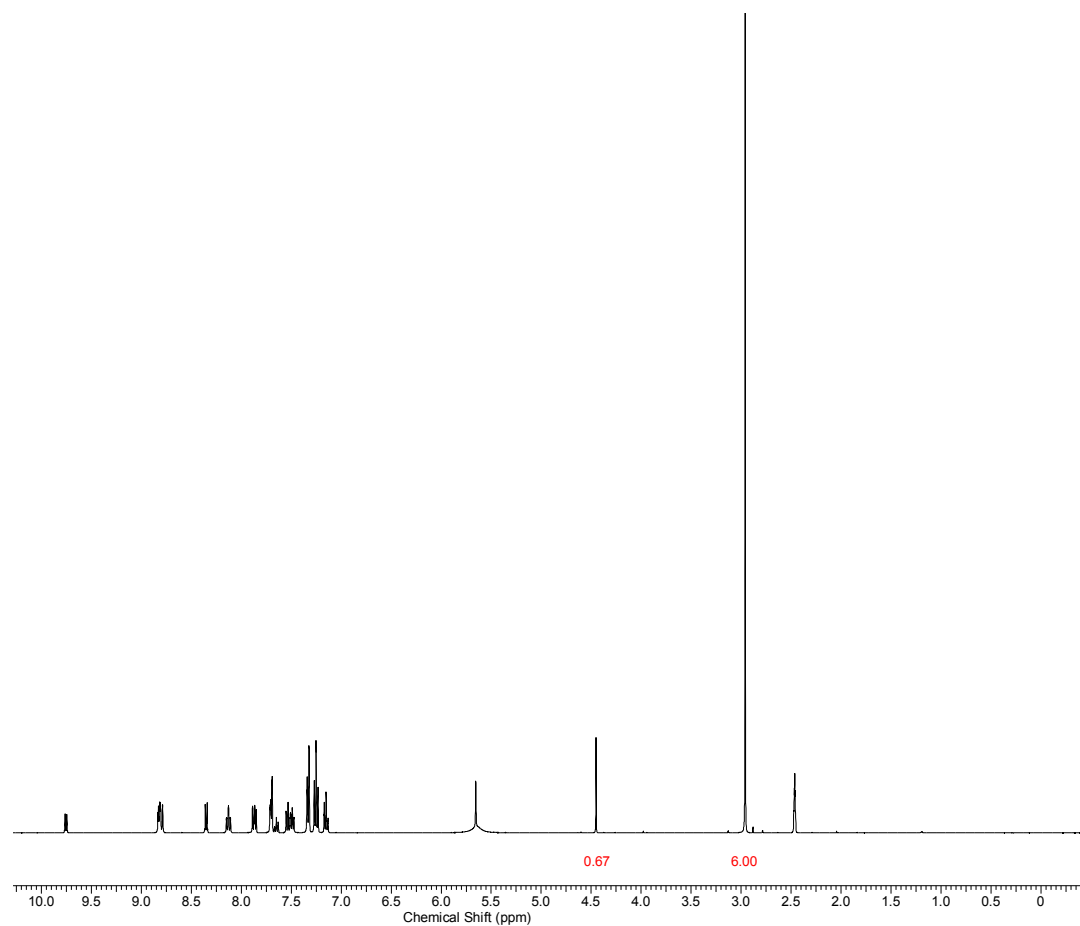




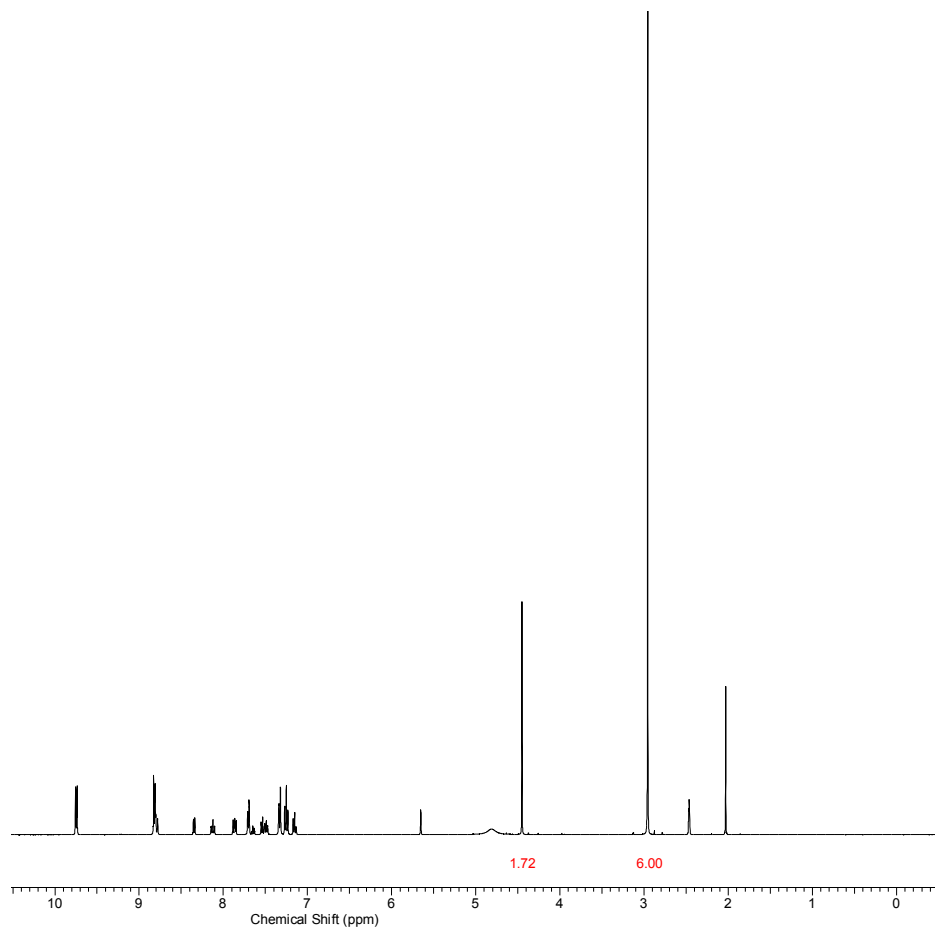
**Figure 6A.12.**  $^1\text{H}$ -NMR obtained after 6 min intermittent irradiation ( $t_{\text{on}} = 320$  ms)  $[\text{Ru}(\text{bpy})_3\text{Cl}_2]$  mediated oxidation of benzhydrol to benzophenone]



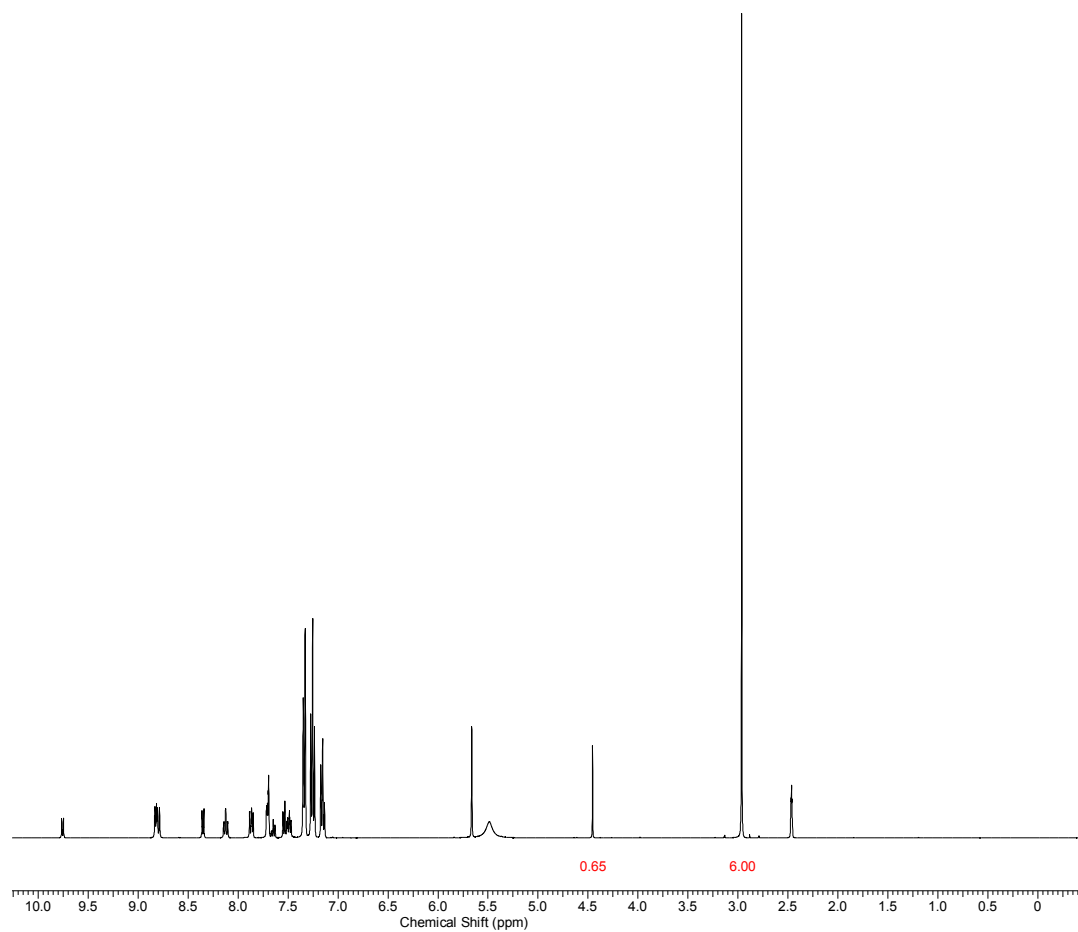
**Figure 6A.13.**  $^1\text{H}$ -NMR obtained after 6 min intermittent irradiation ( $t_{\text{on}} = 640$  ms)  $[\text{Ru}(\text{bpy})_3\text{Cl}_2]$  mediated oxidation of benzhydrol to benzophenone]



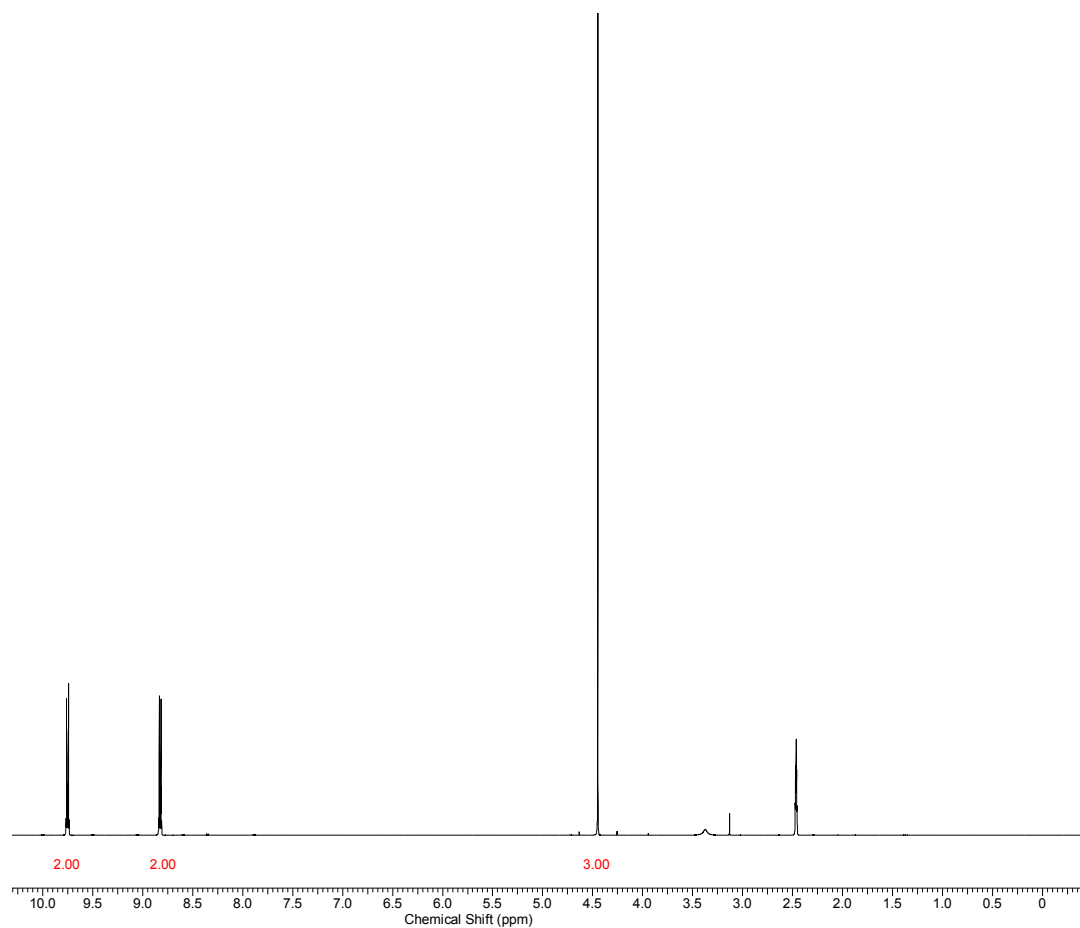
**Figure 6A.14.**  $^1\text{H}$ -NMR obtained after 6 min intermittent irradiation ( $t_{\text{on}} = 1280$  ms)  $[\text{Ru}(\text{bpy})_3\text{Cl}_2]$  mediated oxidation of benzhydrol to benzophenone]



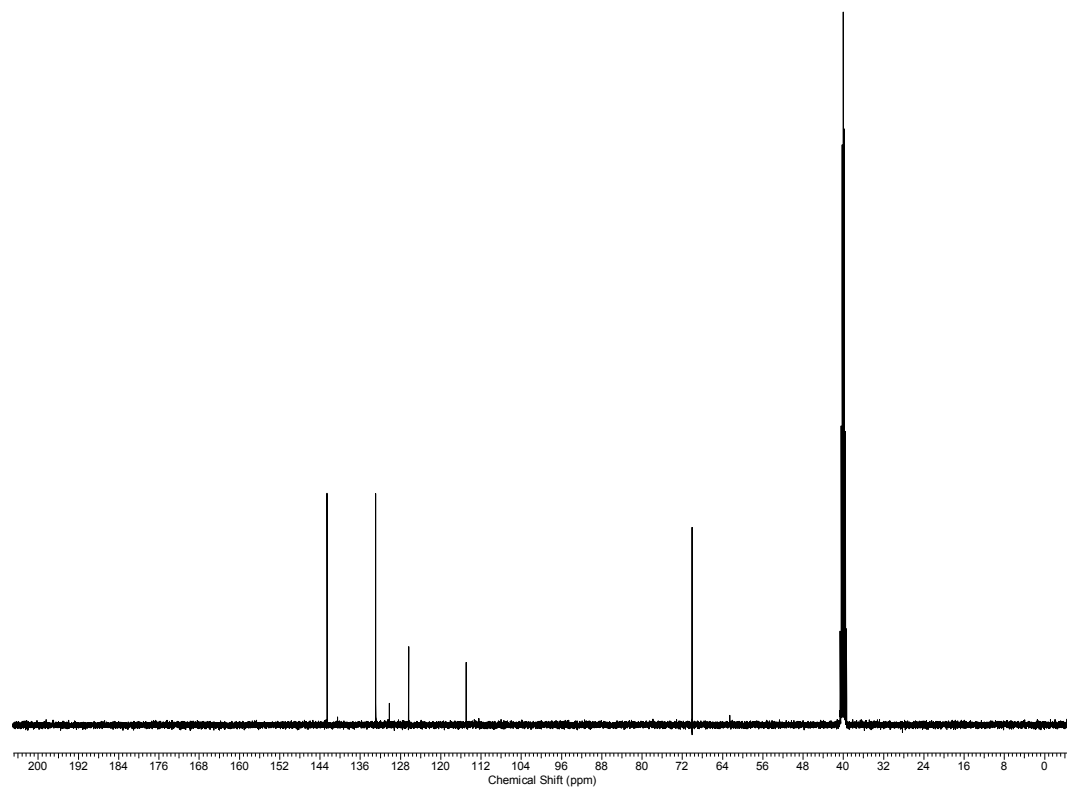
**Figure 6A.15.**  $^1\text{H}$ -NMR obtained after 2 min steady state irradiation  $[\text{Ru}(\text{bpy})_3\text{Cl}_2]$  mediated oxidation of benzhydrol to benzophenone] with 2X concentration of 4-cyano-*N*-methoxy pyridinium tetrafluoroborate



**Figure 6A.16.**  $^1\text{H}$ -NMR obtained after 2 min steady state irradiation  $[\text{Ru}(\text{bpy})_3\text{Cl}_2]$  mediated oxidation of benzhydrol to benzophenone] with 2X concentration of benzhydrol



**Figure 6A.17.**  $^1\text{H}$ -NMR of 4-cyano-*N*-methoxy pyridinium tetrafluoroborate in DMSO- $\text{d}_6$ .



**Figure 6A.18.**  $^{13}\text{C}$ -NMR of 4-cyano-*N*-methoxy pyridinium tetrafluoroborate in DMSO- $\text{d}_6$ .

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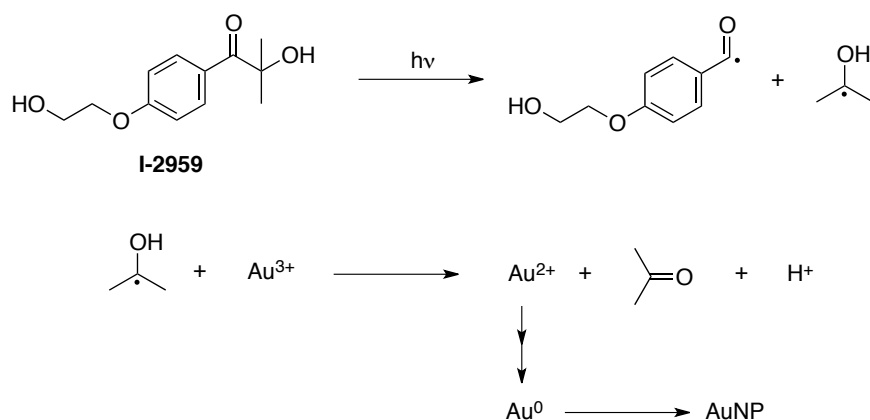
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## 7. Electron Transfer from the Benzophenone Triplet Controls AuNP Formation

### 7.1. Background

As a group we have recently reported a number of different methods for the photochemical generation of gold nanoparticles (AuNP) from  $\text{AuCl}_4^-$  salts.<sup>1,2</sup> One of the most notable involves the reduction of  $\text{AuCl}_4^-$  salt by reducing ketyl radicals formed upon photoinduced Norrish type I cleavage of I-2959 (Scheme 7.1).<sup>3</sup>

**Scheme 7.1.** Photodecomposition of I-2959 and subsequent multi-step reduction of  $\text{Au}^{3+}$  to  $\text{Au}^0$



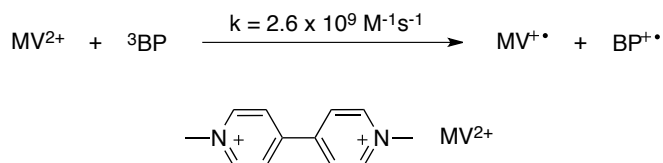
The high efficiency of this system arises due to the fact that the excited state precursor to the ketyl radical has a short triplet lifetime (11 ns).<sup>4</sup> This lifetime is ideal due to the fact that most transition-metal ions ( $\text{Au}^+$  and  $\text{Au}^3$  included) are excellent quenchers of excited states, with quenching rate constants in the range of  $10^9 \text{ M}^{-1}\text{s}^{-1}$ . This means that if the precursor were to have a long triplet lifetime ( $\mu\text{s}$ ), at the millimolar concentrations of metal ions used in the synthesis of AuNP, the excited precursor would be quenched before the required ketyl radicals could be generated. However, as we will see in this chapter, in some cases it may not

be essential for the excited state of the photoinitiator to be short lived since it is possible for the long lived triplet excited state of benzophenone to be quenched through an electron transfer by  $\text{Au}^{3+}$  and  $\text{Au}^+$  ions to produce metallic AuNP.

The electron accepting properties of the benzophenone (BP) triplet state are widely recognized and are reflected in its hydrogen and electron transfer reactions, as well in its interaction with  $\pi$ -systems. The  $n,\pi^*$  nature of the excited state causes its electron acceptor properties to be centred in the semi-occupied oxygen orbital.<sup>5</sup> It has long been recognized that this electronic configuration makes the reactivity of the benzophenone triplet very similar to that of an alkoxyl radical.<sup>6</sup>

However, as demonstrated throughout this thesis, excitation of any closed shell molecule causes its excited state to possess enhanced electron accepting and donating properties; and benzophenone is no exception. The electron donating character of the BP triplet is expected to display the reactivity of the singly occupied  $\pi^*$  orbital, somewhat delocalized between the carbonyl  $\pi$  system and one of the aromatic rings. Given that the benzophenone radical-cation is an unstable, and elusive species,<sup>7</sup> one expects electron donation from the benzophenone triplet to occur only in the presence of highly favourable electron acceptors. Such an example has been reported by Das in 1981,<sup>8</sup> where it was shown that methyl viologen ( $\text{MV}^{2+}$ ) was a good electron acceptor for the benzophenone triplet, leading to the characteristic methyl viologen radical cation (Scheme 7.2).<sup>8</sup>

**Scheme 7.2.** Photoreduction of  $MV^{2+}$  by triplet benzophenone. Adapted with permission from McTiernan *et al.*<sup>9</sup> Copyright 2014 The Royal Society of Chemistry.



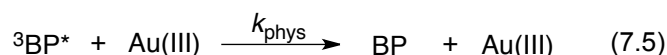
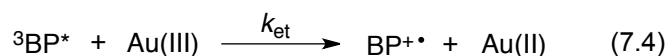
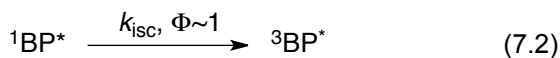
## 7.2. Thermodynamic Feasibility of the Reduction of $Au^{3+}$ to $Au^0$ by Triplet Benzophenone

The reduction potential of  $MV^{2+}$  is -0.45 V vs. SHE.<sup>10</sup> In the case of  $Au(III)$  the reduction potential to yield  $Au(I)$  is +0.93 V (in the  $AuCl_4^-$  form); while this suggests that reduction of  $Au(III)$  by the benzophenone triplet should be more favorable than for  $MV^{2+}$ , it should be noted that the reaction with  $Au(III)$  is likely to involve single electron transfer and thus yield the unstable  $Au(II)$ , for which no potentials appear to have been reported. Our own estimate is that for the  $Au(III)/Au(II)$  couple the reduction potential is between +0.35 and +0.71V, that is, making the reduction by the benzophenone triplet favourable.

## 7.3. Rate Constant and Nature of the Reaction Between Triplet Benzophenone and $Au^{3+}$

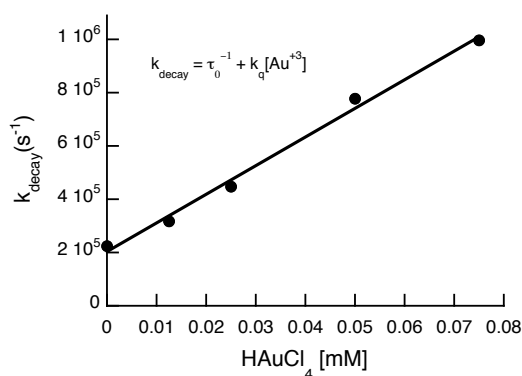
To study the nature and to determine a rate constant for the reaction between the triplet state of the benzophenone and the gold salt precursor, time resolved laser flash photolysis techniques were employed. Equations (7.1 – 7.5) describe the relevant photochemical process of the reaction. Triplet quenching studies, which allow one to determine the rate of excited state decay as a function of quencher concentration, were performed at room temperature in 3%  $CH_3CN$  in water monitoring the triplet state following 355 nm excitation. It should

be noted that the absorption at 355 nm is due exclusively to benzophenone, as  $\text{AuCl}_4^-$  is practically transparent at this wavelength due to its low concentration.



$$k_{\text{q}} = k_{\text{et}} + k_{\text{phys}}$$

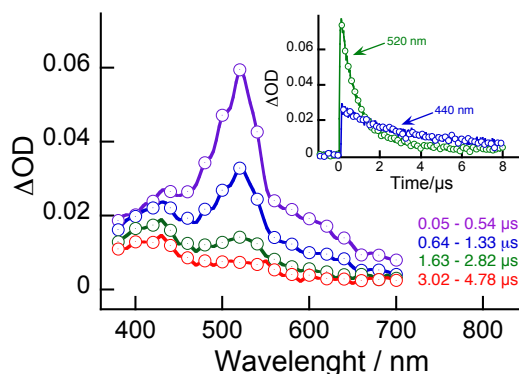
The corresponding quenching plot, monitoring  ${}^3\text{BP}^*$  at its 520 maximum, is shown in Figure 7.1.<sup>11</sup> From the slope of this plot we find a rate constant for the reaction of  $1.1 \times 10^{10} \text{ M}^{-1} \text{ s}^{-1}$ , or essentially diffusion controlled.



**Figure 7.1.** Observed decay rate constant of benzophenone triplet ( $\text{BP}^*$ ) as a function of added  $\text{HAuCl}_4$ . The sample absorbance was adjusted to 0.3 at 355 nm. The inset equation shows that the slope corresponds to the quenching rate constant,  $k_{\text{q}}$ . Adapted with permission from McTiernan *et al.*<sup>9</sup> Copyright 2014 The Royal Society of Chemistry.

The initial electron transfer from  $\text{BP}^*$  to  $\text{Au(III)}$  was also verified by the detection of a transient at 440 nm, (See Figure 7.2) present only upon addition of the  $\text{AuCl}_4^-$ , which has been previously assigned to the  $\text{BP}^{+\bullet}$ .<sup>7</sup> Detailed kinetic analysis of the 440 nm transient are difficult due to extensive overlap with  $\text{BP}^*$ ,

but the evidence for its formation is unequivocal. The inset of Figure 7.2 does not show the growth of the radical cation probably due to spectral overlap with other transients.

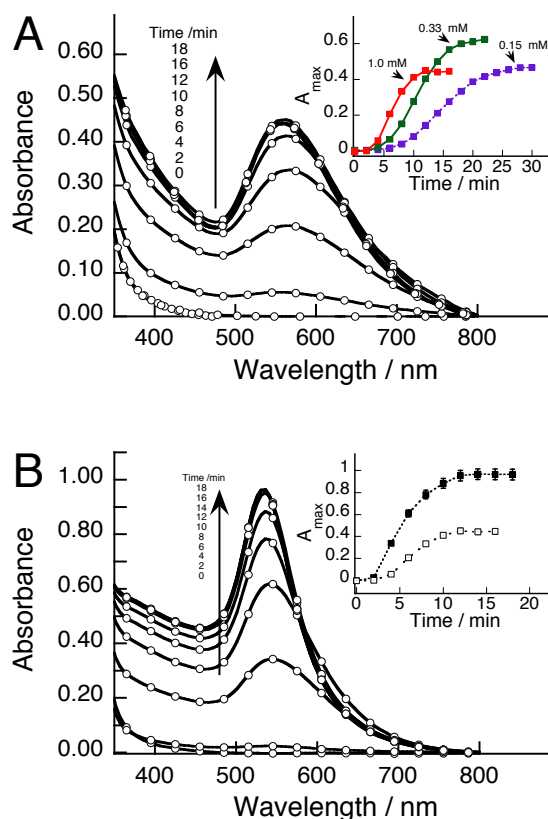


**Figure 7.2.** Transient spectrum showing the  $^3\text{BP}^*$  at 520 nm and the weak  $\text{BP}^{**}$  at 440 nm in the presence of  $\text{H[AuCl}_4\text{]}^-$ . Inset shows the decay trace of the  $^3\text{BP}^*$  at 520 nm and  $\text{BP}^{**}$  440 nm. Adapted with permission from McTiernan *et al.*<sup>9</sup> Copyright 2014 The Royal Society of Chemistry.

#### 7.4. Kinetics of AuNP Formation

In order to better understand the formation of AuNP under our experimental conditions, we set out to monitor the growth of the AuNP surface plasmon band (SPB) as a function of irradiation time and precursor concentration. As shown in Figure 7.3.A, when irradiating solutions containing 0.33 mM  $\text{AuCl}_4^-$  and variable concentrations of benzophenone (from 0.15 to 1.0 mM) with a 368 nm LED ( $167 \text{ W m}^{-2}$ ), the AuNP SPB appears at different times depending on the concentration of benzophenone. In all three examples it is clear that, upon LED irradiation AuNP formation exhibits a sigmoidal growth (see inset of Figure 7.3.A). Interestingly, we had previously observed this induction period in the formation of AuNP by photodecomposition of the photoinitiator Irgacure-2959 and attributed it to the formation of  $\text{Au}^+$  that does not absorb in this spectral region.<sup>1,3</sup> However, it was found that under similar conditions using 368

nm LED irradiation the induction time for Irgacure-2959 is shorter than that observed when identical concentrations of benzophenone are used as the photosensitizer as seen in Figure 7.3.B.

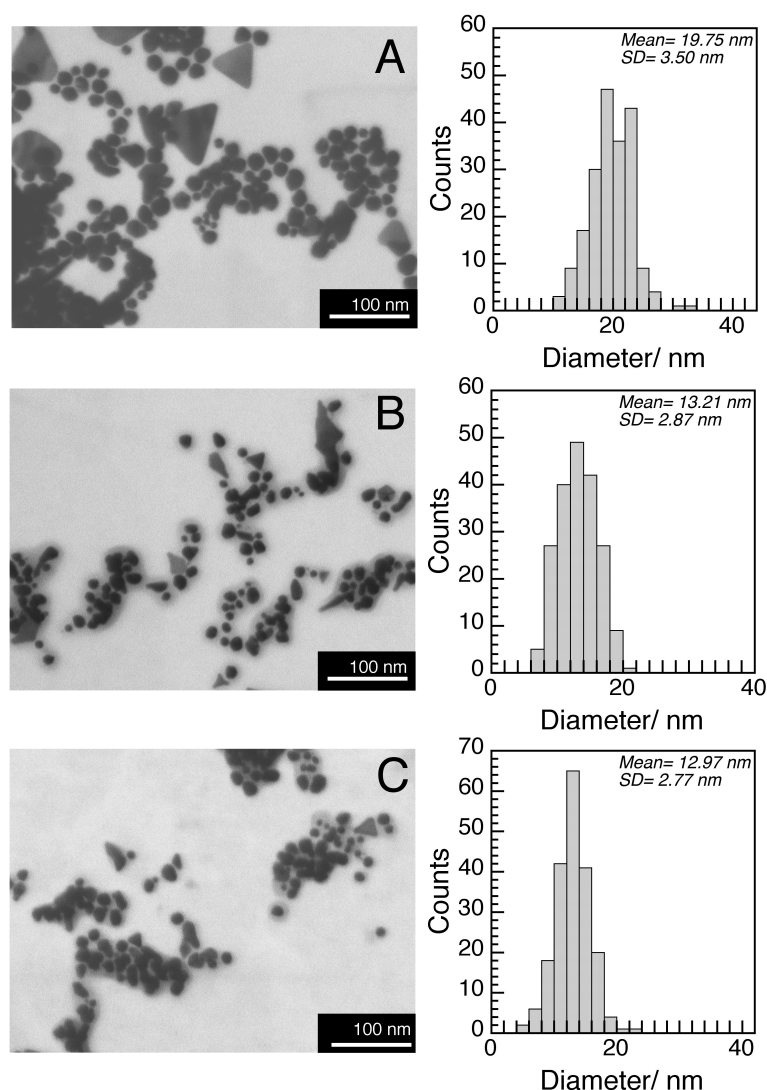


**Figure 7.3.** A) Changes in the absorption for 0.33 mM HAuCl<sub>4</sub> in water (with 3% CH<sub>3</sub>CN) upon 368 nm LED irradiation in the presence of 1.0 mM benzophenone at different times as indicated in each figure. Inset shows the increase at the maximum of AuNP SPB as a function of irradiation time obtained at different benzophenone concentrations as displayed in the figure. B) Changes in the absorption spectrum for 0.33 mM HAuCl<sub>4</sub> aqueous solutions (H<sub>2</sub>O) upon 368 nm LED irradiation in the presence of 1.0 mM I-2959 at different times as indicated in each figure. Inset shows the increase at the maximum of AuNP SPB as function of irradiation time obtained using either 1.0 mM I-2959 (squares) or benzophenone (circles). Adapted with permission from McTiernan *et al.*<sup>9</sup> Copyright 2014 The Royal Society of Chemistry.

In order to ensure that the period of lag was attributed to formation of Au<sup>+</sup> and not the active participation of the small amount of CH<sub>3</sub>CN, required for benzophenone solubilization, in the formation of AuNP we have performed a series of control experiments in which we have substituted the CH<sub>3</sub>CN for

CD<sub>3</sub>CN. If the excited benzophenone molecules were abstracting hydrogen from the CH<sub>3</sub>CN to generate reducing diphenyl ketyl radicals, upon substitution with CD<sub>3</sub>CN we would expect to see a considerable decrease in the rate of AuNP formation due to the increased activation energy required to cleave the C-D bond in comparison to the C-H bond.

### 7.5. Size and Morphology of Resulting AuNP



**Figure 7.4.** SEM images of AuNP prepared by 368 nm LED irradiation of aqueous solutions containing 0.33 mM HAuCl<sub>4</sub> and 0.15 mM (A), 0.33 mM (B) and 1.0 mM (C) of benzophenone (left) and corresponding size distribution histogram (right). Adapted with permission from McTiernan *et al.*<sup>9</sup> Copyright 2014 The Royal Society of Chemistry.



The AuNP formed using BP as an initiator are for the most part spherical with a few larger triangular plates as seen in the SEM images of Figure 7.4. As the concentration of benzophenone is increased in the average size of the particles is decreased and the amount of triangular plates present decreases. It is this second population of large triangular plates formed when BP is utilized which accounts for the broader plasmon absorption seen in Figure 7.3.A in comparison to Figure 7.3.B, which corresponds to the monodispersed AuNP formed when I-2959 is utilized. The fact that we observe smaller and monodisperse AuNP at higher concentrations of benzophenone is likely due to the fact that there is a higher concentration of capping agent (benzoic acid) which is capable of forming a protective layer that makes the nanoparticle surface unreactive towards agglomeration or the incorporation of precursors.

#### **7.6. Quantum Yield of Au Reduction**

Through the comparison of the signal derived from the triplet of benzophenone and that of the bleaching of Au(III) in the 300-320 nm region, during LFP experiments examining the electron transfer from BP\* to Au(III), we have been able to obtain a rough estimate of the quantum yield of the process . Assuming that the bleaching of Au(III) does not overlap with any BP or Au derived transient and that the photomultiplier response is linear at both 520 and 320 nm, and that changes in hydration of  $\text{HAuCl}_4$  do not introduce significant errors we can calculate the quantum yield of the electron transfer ( $\Phi_{\text{eT}}$ ) process using equation (7.6).

$$\Phi_{eT} = \frac{I_{\text{abs}}}{\text{Electron\_Transfer}} = \frac{\frac{\Delta OD_{520 \text{ nm}}}{\epsilon_{520 \text{ nm}}}}{\frac{\Delta OD_{320 \text{ nm}}}{\epsilon_{320 \text{ nm}}}} \quad (7.6)$$

Where  $I_{\text{abs}}$  and Electron\_Transfer are defined as the amount of light absorbed by benzophenone and the number of  $\text{Au}^{+3}$  reduced by the triplet excited state, respectively. We have replaced those by  $\Delta OD$  at 520 nm and 320 nm respectively as these wavelengths correspond to the maximum absorption for the benzophenone triplet excited state and the  $\text{HAuCl}_4$  ground state absorption. Having determined the extinction coefficients of the benzophenone triplet and the ground state benzophenone/ $\text{HAuCl}_4$  in 3%  $\text{CH}_3\text{CN}/\text{H}_2\text{O}$  to be  $\epsilon_{520 \text{ nm}}(5800 \text{ M}^{-1}\text{cm}^{-1})^{11}$  and  $\epsilon_{320 \text{ nm}}(2051 \text{ M}^{-1}\text{cm}^{-1})$ , respectively. Performing the calculation under conditions where almost 90% of the benzophenone triplet excited state is quenched by the gold salt we find the quantum yield for the one electron transfer of the reaction to be  $0.30 \pm 0.15$ , where the large errors reflect the uncertainties mentioned above.

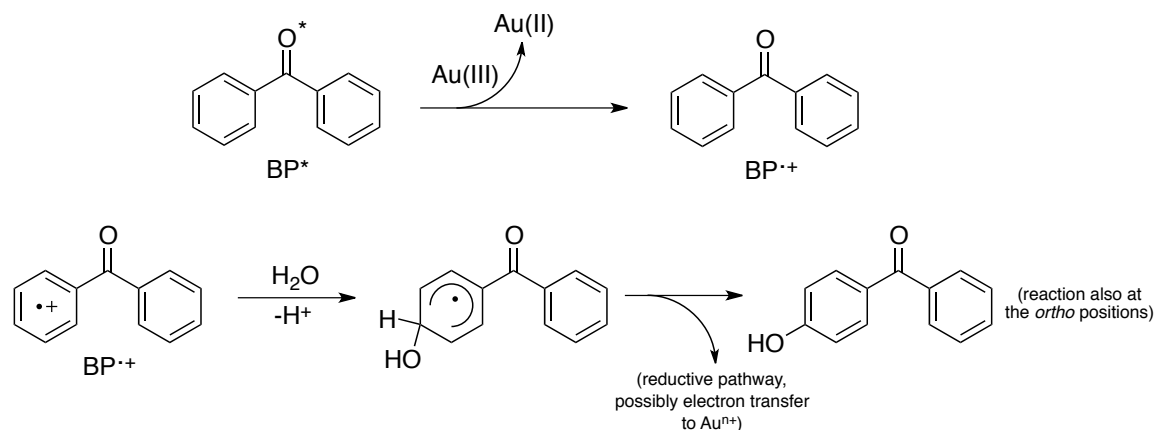
Since the reaction expressed by equation 7.5 refers only to the first electron transferred to  $\text{Au(III)}$  and we have shown in the inset of Figure 7.3.B that the overall reduction to yield AuNP is significantly less efficient than that of the much faster control experiment with I-2959, we can conclude that the reduction of  $\text{Au(I)}$  is rate limiting and that ketyl radicals are more potent reducing agents. Given that the quantum yield for the formation of ketyl radicals from I-2959 is 0.29.

### 7.7. Analysis of Benzophenone Oxidation Products

In good agreement with the excited state electron transfer and subsequent formation of the  $\text{BP}^{+\bullet}$  are the oxidation products (see Scheme 7.3) observed upon HPLC analysis of air equilibrated aqueous solutions containing only 1.0 mM benzophenone and 0.33 mM  $\text{HAuCl}_4$ , which had been LED irradiated for 20 minutes. The two main oxidation products observed were 4-hydroxybenzophenone and benzoic acid which can be explained through attack of water at the 2 and 4 position in the BP radical-cation, with the less hindered 4-position as the dominant reaction.

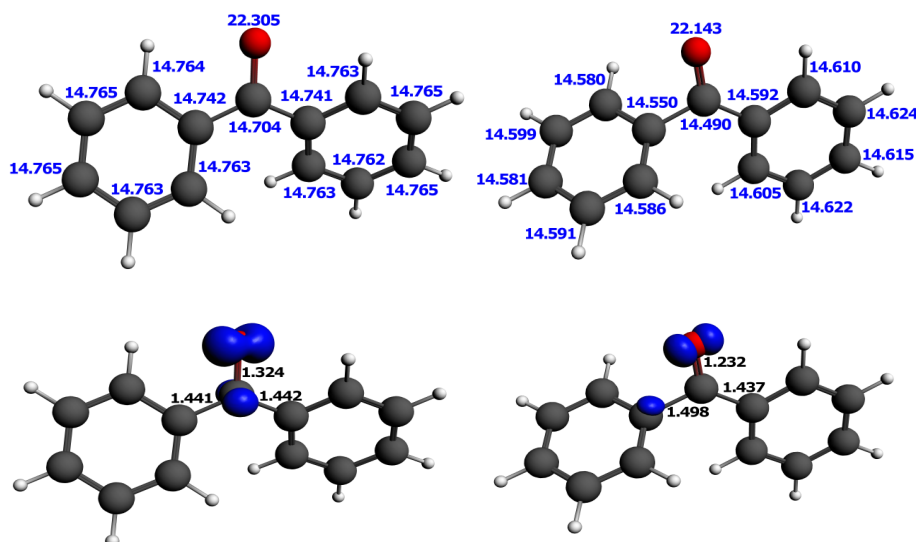
The release of a proton upon formation of both oxidation products coincides well with the fact that the pH of the irradiated solutions decreased upon AuNP formation (See Table 7A.1). We have also found that when solutions of 1.0 mM BP and 0.33 mM  $\text{HAuCl}_4$  are irradiated for 20 minutes under ambient conditions  $\approx 30\%$  of the benzophenone degrades with  $\approx 60\%$  of this oxidation occurring within the first two minutes (Table 7A.2), which also happens to be the amount of time it takes for the  $\text{AuCl}_4^-$  absorption to fade, presumably due to the formation of the non-absorbing Au(I) species.

**Scheme 7.3.** Proposed pathways for the formation of benzophenone by-products following 368 nm LED irradiation in the presence of  $\text{HAuCl}_4$ . Further oxidation and C-C bond cleavage are probably responsible for the formation of benzoic acid. Adapted with permission from McTiernan *et al.*<sup>9</sup> Copyright 2014 The Royal Society of Chemistry.



An electron spin density calculation was also performed with the aim of understanding the formation of the benzophenone triplet, its corresponding radical cation, and to help rationalize the observed oxidation products; all of which are in good agreement with the electrostatic potential (EP) at each nucleus and electron spin density calculations for the benzophenone radical-cation as depicted in Figure 7.5. The  $n, \pi^*$  nature of the benzophenone triplet leads to considerable radical character of the calculated C=O bond length of 1.324 Å and the experimental CO stretching frequency of  $1222\text{ cm}^{-1}$  (compared with  $1665\text{ cm}^{-1}$  for the ground state).<sup>12</sup> In contrast, for the BP radical-cation the calculated CO bond length is 1.232 Å, *i.e.*, showing double bond character and thus the cation character and reactivity are largely centered in the aromatic rings, as suggested also by the observed reactivity towards water. Comparing the EP before and after the electron transfer process (Figure 7.5) shows that the EP over the oxygen atom decreases, resulting from electron transfer. Further, the aromatic rings where the spin density accumulates in the radical cation show a reduction

in the EP on the C-atoms at the *o*- and *p*-positions, in agreement with the oxidation products observed.



**Figure 7.5.** *Top:* Calculated electrostatic potential at the nuclei of the benzophenone triplet excited state (left) and its corresponding cation radical (right). *Bottom:* Graphical representation of the electron spin density on the benzophenone triplet excited state (left) and its corresponding radical cation (right). The length (in Å) of selected bonds is also shown. Adapted with permission from McTiernan *et al.*<sup>9</sup> Copyright 2014 The Royal Society of Chemistry.

## 7.8. Conclusions

We show that AuNP can be prepared photochemically using the rarely recognized nucleophilic character of the benzophenone triplet. From our estimates of the Au(III) to Au(II) reduction potential (0.35-0.71 V vs. S.H.E.) as well as the well known reduction potential of Au(I) to Au(0) (1.15 V vs. S.H.E.), it is reasonable that BP\* is capable of reducing Au(III) to Au(II) as well as the Au(I), resulting from Au(II) disproportionation, to Au(0) due to its favourable reduction potential. From LFP experiments we have direct spectral evidence of the BP<sup>+</sup>. Whereas, from HPLC analysis we have indirect evidence of BP<sup>+</sup> formation from oxidation products likely formed from the nucleophilic addition of water to BP<sup>+</sup>, all of which are in good agreement with the spin density and electrostatic

potential calculations performed on the BP<sup>\*</sup> and BP<sup>+</sup>.

## 7.9. Appendix

### 7.9.A. General Information

Substrates and Reagents: All reagents were purchased from commercial sources and used as received unless otherwise stated. Benzophenone (BP) and gold (III) tetrachloroauric acid hydrate (HAuCl<sub>4</sub>•3H<sub>2</sub>O) were purchased from Sigma-Aldrich. Aqueous solutions were prepared daily using Milli-Q water, which had been previously treated for 24 hours with Chelex-100 in order to remove any metal traces. Optima grade CH<sub>3</sub>CN was purchased from Fisher Chemicals and deuterated acetonitrile (CD<sub>3</sub>CN 99.9%) and deuterated water (D<sub>2</sub>O 99.9%) were obtained from Cambridge Isotope Laboratories Inc.

Absorption Measurements: Absorption spectra were recorded using a Cary-50 UV-Visible spectrophotometer using 1×1 cm plastic cuvettes.

Synthesis and Characterization of Gold Nanoparticles: Experiments were conducted using a single 368 nm Synjet cooled LED (see Figure 7A.1). The irradiance of which was measured to be 167 W/m<sup>2</sup> with a Luzchem SPR-01 Spectroradiometer. A stock solution of 55 mM benzophenone was prepared in CH<sub>3</sub>CN from which 1.0 mM, 0.33 mM, and 0.15 mM aqueous solutions of benzophenone were prepared through dilution of an appropriate amount of the benzophenone stock solution with Chelex-100 treated Milli-Q H<sub>2</sub>O or D<sub>2</sub>O to a final volume of 15 mL. To all solutions 54 μL of a 91 mM solution of HAuCl<sub>4(aq)</sub> were added to give a final concentration of 0.33 mM. The HAuCl<sub>4(aq)</sub> solution was prepared in either H<sub>2</sub>O or D<sub>2</sub>O depending on the conditions of the reaction.

Irradiation of solutions at 368 nm were carried out under air in polystyrene cuvettes. The solutions were irradiated as 3.0 mL samples and a mini magnetic stirring bar was used to stir the solution. The AuNP formation was followed by UV-Vis, without dilution in the reaction cuvette. Once the intensity of the AuNP SPB had levelled off in the plateau region an aliquot was taken for SEM analysis and the samples were removed from the LED or photoreactor and stored in the dark. pH values recorded during AuNP formation were measured using a pH-meter 2000 (VWR scientific) electrode calibrated daily.

AuNP sizes were determined using a JSM-7500F field emission scanning electron microscope (SEM) from JEOL Ltd. Size distribution histograms and average particle size are based on the measurement of at least 200 particles per sample. Imaging software (ImageJ version 1.45s) was used to measure the size of the particles.

#### HPLC Analysis of Reaction Mixtures:

**Benzophenone Degradation** - Aqueous solutions containing 1.0 mM benzophenone and 0.33 mM  $\text{HAuCl}_4$  were irradiated with 368 nm LED light for varying periods of time corresponding to the induction period, linear growth phase, and plateau phase of AuNP growth, i.e. 2.0, 6.0 and 20 min, respectively. LED irradiations were conducted in the same fashion as described in the previous section (see Figure S1). The samples were transferred to 15 mL polystyrene centrifuge tubes and centrifuged at 3000 rpm for 20 min. The supernatant was then filtered through a 0.22  $\mu\text{m}$  syringe filter, of which 250  $\mu\text{L}$  was diluted with 4.75 mL of Milli-Q  $\text{H}_2\text{O}$  to give a final volume of 5.0 mL. 1.8 mL

of the solution was then transferred to an HPLC vial. Reverse phase analysis was performed on the samples using an Agilent Autosample 1100 with a Zorbax Extend C-18 – reverse phase column (3.5  $\mu\text{m}$ , 80 Å; 50 mm x 4.6 mm) C18 column. The autosampler and column temperature were set to 25 °C. The mobile phase consisted of 40/60-water/acetonitrile and the flow rate was set to 1.0 mL/min. The injection volume was 10  $\mu\text{L}$  and the detection wavelengths used were 220, 230, 260 and 285 nm. Benzophenone was followed at 260 nm.

**Oxidation Products** - To examine the oxidation products obtained upon irradiation of aqueous solutions containing benzophenone and  $\text{HAuCl}_4$  we have analyzed the products obtained following 20 min of 368 nm LED irradiation of an air equilibrated acetonitrile: $\text{H}_2\text{O}$  solution containing 1.0 mM and 0.33 mM  $\text{HAuCl}_4$ . After irradiation the sample was centrifuged at 3000 rpm for 20 minutes and 900  $\mu\text{L}$  of the supernatant was then diluted with 900  $\mu\text{L}$  of acetonitrile in an HPLC vial. Reverse phase analysis was performed on the samples using an Agilent Autosample 1100 with a Zorbax Extend C-18 – reverse phase column (3.5  $\mu\text{m}$ , 80 Å; 50 mm x 4.6 mm) C18 column. The autosampler and column temperature were set to 25 °C. The mobile phase consisted of 65/35-Water/Acetonitrile with 0.1% trifluoroacetic acid (TFA) and the flow rate was set to 1.0 mL/min. The injection volume was 10  $\mu\text{L}$  and the detection wavelengths used were 220, 240, 260 and 285 nm.

**HPLC Calibration Curve and Standards** – A 15 mL solution of a 1.0 mM benzophenone solution was prepared as described in the previous section. This stock solution was diluted to 50  $\mu\text{M}$  in Milli-Q  $\text{H}_2\text{O}$  and from here a series of



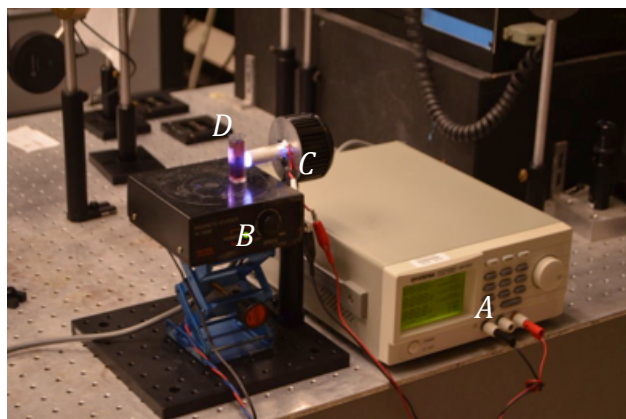
dilutions provided 40, 30, 20, and 10  $\mu\text{M}$  solutions which were analyzed via HPLC under the same conditions described above to construct a calibration curve for benzophenone at 260 nm. 50  $\mu\text{M}$  solutions of 4-chlorobenzophenone, 4-hydroxybenzophenone, and benzoic acid, as well as a 16.5  $\mu\text{M}$  solution of  $\text{HAuCl}_4$  were also submitted for HPLC analysis under the same conditions to determine their retention times. The concentrations of benzophenone, 4-hydroxybenzophenone, and benzoic acid found in the oxidation product study were determined from their molar absorptivity coefficient at 230nm.

Computational Details: The geometrical optimization of both the benzophenone triplet excited state and the radical cation formed after the electron transfer was done using the Amsterdam Density Functional (ADF) code. Both molecular structures were fully optimized by an analytical energy gradient method as implemented by Verluis and Ziegler, using the hybrid functional B3LYP with the triple- $\xi$  quality double plus polarization function (TZ2P) for all atoms.<sup>13</sup> In all cases, frequency analyses were performed after the geometry optimization, in which we obtained only positive frequencies, thus verifying local minima.

After the optimization procedure, the spin density was plotted by calculating the alpha spin density minus the beta spin density. Finally the electrostatic potential (EP) at each nucleus was determined by calculating the Coulomb potential of the molecule at the nuclear positions, where the contribution from the nucleus itself is omitted; in that way we obtained the EP at the nuclei due to valence electrons and other nuclei.

Quenching of Benzophenone by  $\text{HAuCl}_4$ : The triplet quenching experiments by  $\text{HAuCl}_4$  were performed using a Nd-YAG laser (355 nm, ca 10 ns, 10 mJ/pulse) in a LFP-111 laser-flash photolysis (LFP) system (Luzchem Inc., Ottawa, Canada) and 1×1 cm LFP cuvettes. Samples of benzophenone were prepared in solutions of 3% acetonitrile:water with a total volume of 3 mL and an absorbance of ~0.1 at 355 nm. The samples were degassed with  $\text{N}_2$  for 30 minutes prior to use. The solution of  $\text{HAuCl}_4$  used for the quenching study was prepared as a 91 mM solution in  $\text{H}_2\text{O}$ , which was also degassed for the duration of the experiment. Through serial additions of the quencher the quenching of the benzophenone triplet and the bleaching of the gold salt at 520 nm and 320 nm were monitored, respectively.

### 7.9.B. Apparatus Used for 368 nm LED Irradiation



**Figure 7A.1.** Photograph illustrating the experimental setup used for 368nm LED irradiation. The solutions were irradiated as 3.0 mL samples in polystyrene cuvettes and a mini magnetic stirring bar was used to agitate the solution. A is the power supply for the LED, B is a magnetic stirrer, C is the synjet cooled 368nm LED fitted with a tubular foil light collimator, and D is a polystyrene cuvette which contains the solution to be irradiated and a mini magnetic stir bar.

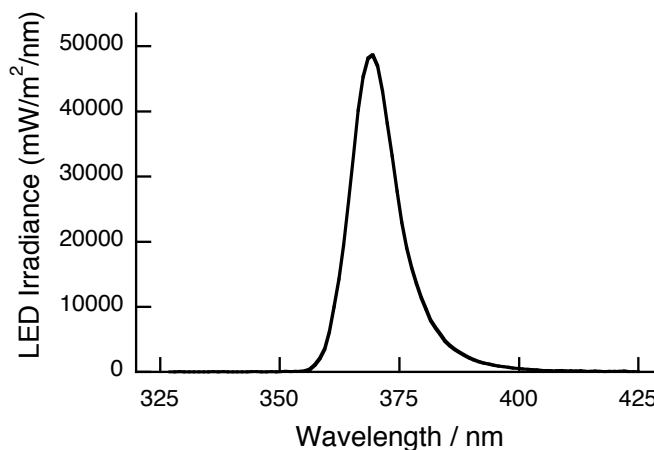


Figure 7A.2. Output spectrum of 368 nm LED used for irradiation of samples.

### 7.9.C. Changes in pH Upon 368 nm LED Irradiation

As previously mentioned in the main text one of the oxidation products, found upon 368 nm LED irradiation of aqueous solutions containing  $\text{HAuCl}_4$  and benzophenone, is 4-hydroxybenzophenone. It is proposed that this oxidation product is formed via a hydroxy-cyclohexyldienyl radical mediated gold salt reduction. Oxidation of the radical would result in 4-hydroxybenzophenone and

the release of a proton, which would most likely form HCl in solution resulting in a progressively more acidic solution as irradiation is continued. In good agreement with this are the pH of solutions containing 0.15, 0.33, or 1.0 mM benzophenone and 0.33mM H<sub>AuCl<sub>4</sub></sub> upon 368nm LED irradiation shown below in Table 7A.1.

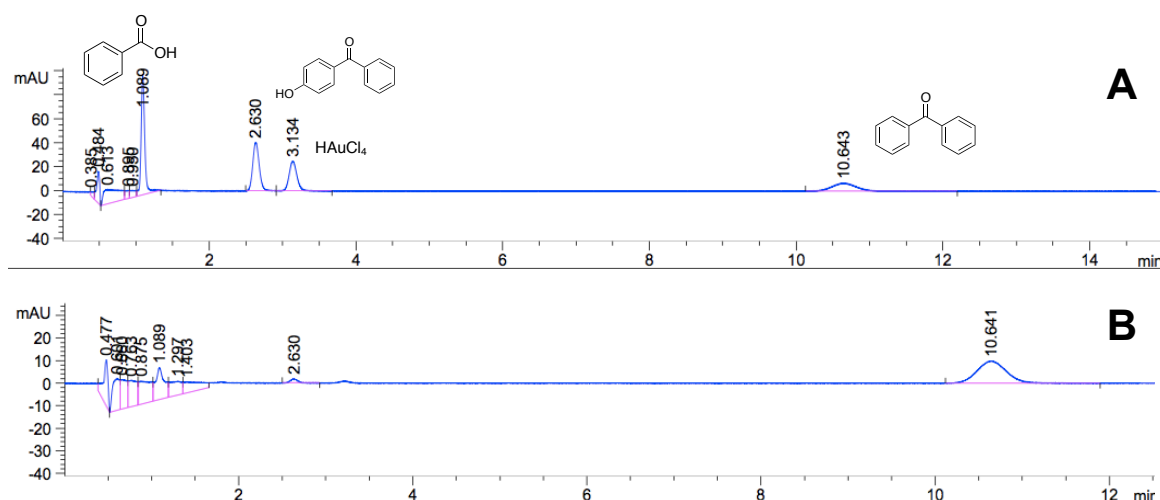
**Table 7A.1.** Changes in the pH of aqueous solutions containing 1.0 mM, 0.33 mM, or 0.15 mM benzophenone and 0.33 mM H<sub>AuCl<sub>4</sub></sub> upon irradiation with 368 nm LED.

| 1.0 mM Benzophenone |      | 0.33 mM Benzophenone |      | 0.15 mM Benzophenone |      |
|---------------------|------|----------------------|------|----------------------|------|
| Time (min)          | pH   | Time (min)           | pH   | Time (min)           | pH   |
| 0                   | 3.46 | 0                    | 3.41 | 0                    | 3.42 |
| 5                   | 3.28 | 5                    | 3.2  | 5                    | 3.26 |
| 10                  | 3.19 | 10                   | 3.04 | 10                   | 3.25 |
| 15                  | 2.98 | 15                   | 2.93 | 15                   | 3.12 |
| 20                  | 2.90 | 20                   | 2.90 | 20                   | 3.06 |
| 25                  | 2.87 | 25                   | 2.89 | 25                   | 2.98 |
| 30                  | 2.87 | 30                   | 2.90 | 30                   | 2.96 |

#### 7.9.D. HPLC Analysis of Benzophenone Degradation

To better understand the mechanism by which benzophenone reduces H<sub>AuCl<sub>4</sub></sub> upon 368nm LED irradiation we set out to monitor the degradation of benzophenone and the resulting oxidation products by HPLC. In Figure S4, one can find HPLC chromatograms extracted at a wavelength of 230 nm for (A) a standard mixture of starting materials (benzophenone and H<sub>AuCl<sub>4</sub></sub>) and possible oxidation products (4-hydroxybenzophenone and benzoic acid) and for (B) a 1mM benzophenone and 0.33 mM H<sub>AuCl<sub>4</sub></sub> aqueous solution which had been irradiated with a 368 nm LED for 20 minutes. In comparing the retention times of the standards with those from the actual reaction mixture, it can be seen that after irradiation there are peaks corresponding to benzophenone, 4-hydroxybenzophenone, and benzoic acid. The degree of degradation of benzophenone with respect to time upon 368nm LED irradiation of a 1 mM benzophenone and 0.33 mM H<sub>AuCl<sub>4</sub></sub> aqueous solution was also monitored by

HPLC, the results of which can be found in Table S2. As stated in the main text, after 20 minutes of irradiation approx. 30% of the benzophenone has been degraded. The concentrations of benzophenone and its oxidation products used to determine percent composition were determined using the molar absorptivity coefficient of each of the compounds at a wavelength of 230 nm. Sample prep and HPLC conditions for each of the HPLC analyses can be found in the corresponding figure caption or in the general information section of the appendix.

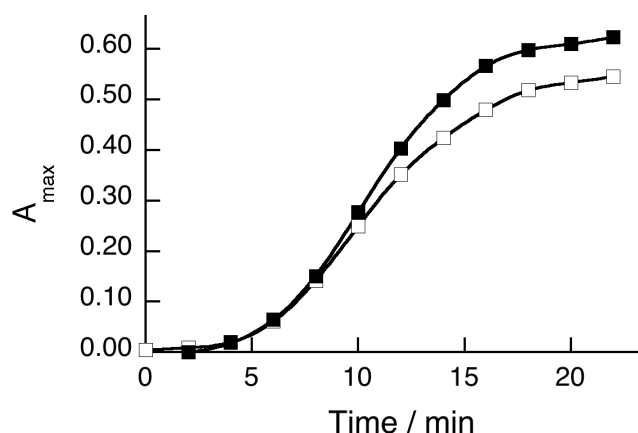


**Figure 7A.3.** HPLC chromatograms for (A) standard solution containing benzophenone [10.643 min], HAuCl<sub>4</sub> [3.134 min], 4-Hydroxybenzophenone [2.630 min], and benzoic acid [1.089 min] and (B) 1.00 mM benzophenone and 0.33mM HAuCl<sub>4</sub> aqueous solution irradiated for 20 minutes with 368 nm LED under air followed by 20 minutes of centrifugation at 3000 RPM and a 50:50 dilution in acetonitrile. Chromatograms were extracted at a wavelength of 230 nm. Reversed phase analysis was performed on the samples using an Agilent Autosample 1100 with a Zorbax Extend C-18 – reverse phase column (3.5  $\mu$ m, 80 Å; 50 mm x 4.6 mm) C18 column. The autosampler and column temperature were set to room temperature. The mobile phase consisted of 65/35-Water/Acetonitrile with 0.1% trifluoroacetic acid (TFA) and the flow rate was set to 1.0 mL/min. The injection volume was 10  $\mu$ L.

**Table 7A.2.** Concentration of benzophenone found by HPLC after 0, 2, 6, and 20 minutes of 368 nm LED irradiation of an aqueous solution containing 1.0 mM benzophenone and 0.33mM H<sub>2</sub>AuCl<sub>4</sub>. Reversed phase analysis was performed on the samples using an Agilent Autosampler 1100 with a Zorbax Extend C-18 – reverse phase column (3.5  $\mu$ m, 80 Å; 50 mm x 4.6 mm) C18 column. The autosampler and column temperature were set to room temperature. The mobile phase consisted of 40/60-Water/Acetonitrile and the flow rate was set to 1.0 mL/min. The injection volume was 10  $\mu$ L. Concentrations were determined using a calibration curve for benzophenone at a wavelength of 260 nm.

| Time (min) | [Benzophenone] mM |
|------------|-------------------|
| 0          | 1.00              |
| 2          | 0.83              |
| 6          | 0.82              |
| 20         | 0.70              |

#### 7.9.D. Substitution of CH<sub>3</sub>CN for CD<sub>3</sub>CN



**Figure 7A.4.** Effect of substitution of 3% CH<sub>3</sub>CN (open marker) for 3% CD<sub>3</sub>CN (filled marker) on the formation of AuNP under 368 nm LED irradiation.

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## 8. Summary and Future Directions

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### 8.1. Summary

This thesis has explored the use of excited state electron transfers in organic transformations and nanomaterial synthesis. Through the development of new photocatalytic systems along with in-depth kinetic and mechanistic analysis we have been able to better understand the nature of many different transformations as well as illustrate the ability to replace the commonly employed polypyridyl Ru and Ir photocatalysts, which tend to be relatively expensive, with cheaper and in some cases metal-free or heterogeneous alternatives. Interestingly, in many instances these alternatives outperform their precious metal counterparts.

While much of the advancements in the field have come in the form of unique reactivity, increased functional group tolerance, and the use of unconventional starting materials; many of these improvements have occurred in the absence of a better understanding of the underlying mechanism. As we look to expand and continue to improve on these chemistries, it would seem beneficial to have a better understanding of the underlying processes that control these transformations along with easy to employ characterization tools. As such, I believe the results and data presented within this thesis will have a considerable impact on the field. The intent of the following section is to summarize the various findings presented throughout the thesis.

In chapter 2 of this thesis we demonstrated that  $\alpha$ -sexithiophene, an organic semiconductor commonly used as an electron donor in organic



photovoltaic devices, can be employed as visible light photoredox catalyst in the reductive dehalogenation of *vicinal* dibromides to their corresponding alkenes. Through the use of steady-state and time resolved fluorescence techniques and laser flash photolysis we have been able to fully characterize the underlying mechanism for this transformation. In addition to characterizing the excited state electron transfer, we have demonstrated that the high efficiency of this system stems from the active participation of amine derived radicals and an underlying chain mechanism. While it was envisioned that the insolubility of  $\alpha$ -sexithiophene would give rise to a heterogeneous photocatalytic system, we have found that through the course of reaction some of the  $\alpha$ -sexithiophene is solubilized and it is this solubilized catalyst responsible for the observed conversions. The advantage of the employed system is that the insoluble portion of catalyst can be thought of as a reservoir of active catalyst in the case of deactivation or photobleaching and can be readily reused.

For chapter 3, we continued to examine the use of  $\alpha$ -sexithiophene as photocatalyst. Due to the high efficiency at which  $\alpha$ -6T generates  $^1\text{O}_2$ , we examined its ability to function as catalyst in the oxidation of primary and secondary amines to their corresponding imines. In addition to demonstrating the usefulness of the commercially available  $\alpha$ -6T as  $^1\text{O}_2$  sensitizer we have also measured the rate constant at which the employed amines intercept  $^1\text{O}_2$ , values that are missing from the current literature.

In chapter 4 we switched gears to examine the use of  $\text{TiO}_2$  as heterogeneous photoredox catalyst. Through decoration of P25  $\text{TiO}_2$  with Pt

nanoparticles, we have been able to push the absorption into the visible and decrease the probability of electron-hole pair recombination. The resulting photocatalytic system can bring about the efficient reductive hydrodehalogenation of aryl iodides as well as a variety of reductive cyclizations. While  $\text{Ru}(\text{bpy})_3^{2+}$  may bring about the desired transformations in shorter irradiation times, the inexpensive and heterogeneous nature of the  $\text{TiO}_2$  catalyst makes this method more economically viable. From here we then demonstrated that one can employ  $\text{TiO}_2$  as photocatalyst in the ever popular dual photoredox/Ni decarboxylative cross-couplings of carboxylic acids with aryl halides. Utilizing the oxidizing holes of the valence band to decarboxylate the carboxylic acid substrates and the reducing electrons of the conduction band to give rise to the active  $\text{Ni}(0)$  species, a variety of substituted aryl iodides were cross-coupled to either N-Boc proline or a variety of phenylacetic acid derivatives. The developed semi-heterogeneous protocol gives the desired products in moderate to excellent yields, while the results of the completely heterogeneous example, employing NiNP in place of the homogeneous Ni catalyst, indicates that there is room for improvement in many of these dual catalytic systems.

In chapter 5, the reactivity of polynuclear gold (I) complexes was explored. Through complete photochemical and electrochemical characterization of the employed complexes along with detailed kinetic analysis, we attempted to determine if the complexes brought about the reduction of C-Br bonds through either a reductive or oxidative quenching mechanism. Interestingly enough, what

we found is that in many cases the nature of these types of reactions are difficult to understand. While much of the current photoredox literature employs simplistic mechanistic schemes for these types of transformations, in many cases the reality is that many of these schemes are highly oversimplified considering the versatile nature of the highly redox active excited states involved. Even without taking into consideration the possibility of inner sphere electron transfer, which we have shown to be a possibility through induced chirality experiments, these transformations involve a number of competing and synergistic pathways. Having said this though the obtained data helped shed light on these transformations and will be highly useful in the optimization of future studies.

In chapter 6 we explored the characterization of light mediated chain reactions utilizing intermittent illumination. While there are many recent studies that claim to probe chain reactions through intermittent illumination or light on-light off studies, the employed pulse lengths are typically too long (minutes) to obtain any useful information. Considering the lifetime of the chains in these types of systems are in the range of ms to s, it is more appropriate to perform a rotating sector experiment, which employs light-on-light off sequences in this time scale. In order to simplify and update this method we have replaced the rotating sector disk with a pulsed LED system. Utilizing this updated system we have demonstrated that this method is capable of characterizing, both qualitatively and quantitatively, light mediated chain reactions. In particular we have examined the photocatalyzed oxidation of benzhydrol to benzophenone, a well known chain reaction.

Lastly, in chapter 7 we demonstrated that under certain conditions one can reduce  $\text{HAuCl}_4$  to metallic gold nanoparticles utilizing the rarely recognized nucleophilic character of the benzophenone triplet. Through a combination of laser flash photolysis studies and an analysis of the oxidation products we have strong evidence for the formation of the  $\text{BP}^{+\bullet}$  intermediate. In addition to being a new route to the synthesis of stable AuNP, it is one of few examples that takes advantage of the reducing nature of the benzophenone triplet.

## 8.2. Future Directions

While the work presented in this thesis has demonstrated that one can improve photoredox processes through both mechanistic analysis and heterogenization of the photocatalytic system, there remain many avenues through which these processes can be improved. For example, while heterogeneous catalysts have the added benefit of being easy to isolate and reuse, in many instances there are diffusional limitations in heterogeneous systems that result in reduced efficiency. Considering that one of the ways to get around these limitations is to employ the heterogeneous catalysts in continuous flow reactors, it would seem logical that the next step is to apply these catalytic systems in flow.

The preliminary results of the completely heterogenous dual photoredox/Ni catalysis system presented in chapter 4 are also quite interesting. Considering the attention these dual catalytic systems have received in the current literature, it will be interesting to examine the generality of these systems. Perhaps through the decoration of semiconductor photocatalyst, such as  $\text{TiO}_2$ ,

with metallic nanoparticles of either Au, Cu, Ni, Pt, or Pd or a combination of these metals, one can develop heterogeneous alternatives to many of the reported transformations.

### 8.3. Claims to Original Research

- Development of a photocatalytic system employing  $\alpha$ -sexithiophene as photoredox catalyst for the reductive dehalogenation of *vicinal* dibromides.
- Development of a photocatalytic system employing  $\alpha$ -sexithiophene as  $^1\text{O}_2$  sensitizer for the oxidation of primary and secondary amines to their corresponding imines.
- Development of a heterogeneous photocatalytic system for reductive dehalogenations and cyclizations employing PtNP@TiO<sub>2</sub> as photoredox catalyst.
- The first example of heterogeneous titania-photoredox/Ni dual catalysis for the decarboxylative cross-coupling of carboxylic acids with aryl iodides.
- Characterization of the photochemical and redox properties of a variety of polynuclear gold (I) complexes used in photocatalysis.
- Demonstrated that excited state electron transfer from the triplet excited state of benzophenone can direct the synthesis of gold nanoparticles.

### 8.4. Publications

*Publications resulting from work presented in this thesis*

- 1) **McTiernan, C. D.**; Morin, M.; McCallum, T.; Scaiano, J.C.; Barriault, L. (2016) "Polynuclear gold (I) complexes in photoredox catalysis: understanding their reactivity through characterization and kinetic analysis" *Catal. Sci. Technol.* **6**, 201-207.
- 2) Pitre, S. P.\*; **McTiernan, C. D.\***; Vine, W.; DiPucchio, R.; Grenier, M.; Scaiano, J.C. (2015) "Visible-Light Actinometry and Intermittent Illumination as Convenient Tools to Study Ru(bpy)<sub>3</sub>Cl<sub>2</sub> Mediated Photoredox Transformations" *Sci. Rep.* **5**, 16397. \*denotes equal contribution
- 3) **McTiernan, C. D.**; Pitre, S. P.; Ismaili, H.; Scaiano, J.C. (2014) "Heterogeneous Light-Mediated Reductive Dehalogenations and Cyclizations Utilizing Platinum Nanoparticles on Titania (PtNP@TiO<sub>2</sub>)" *Adv. Synth. Catal.* **356**, 2819-2824.

- 4) **McTiernan, C. D.**; Pitre, S.P.; Scaiano, J.C. (2014) "Photocatalytic Dehalogenation of Vicinal Dibromo Compounds Utilizing Sexithiophene and Visible-Light Irradiation". *ACS Catal.* **4**, 4014-4039.
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*Publications resulting from work not presented in this thesis*

- 1) Pitre, S.P.; **McTiernan, C.D.**; Scaiano, J.C. (2016) "A Library of Cationic Organic Dyes for Visible-Light Driven Photoredox Transformations" *ACS Omega.* **1**, 66-76.
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