INVESTIGATING THE MECHANISM AND EXPANDING THE REACTIVITY OF CU(I)-CATALYZED [2+2] PHOTOCYCLOADDITION REACTIONS OF OLEFINS

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INVESTIGATING THE MECHANISM AND EXPANDING THE REACTIVITY OF CU(I)-CATALYZED [2+2] PHOTOCYCLOADDITION REACTIONS OF OLEFINS

BY

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OF

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ABSTRACT

Light-matter interactions can change the physical and chemical properties of a substance. The energy of photons can be used to dissociate the chemical bonds as well as to generate new bonds. The work in this dissertation is an attempt to understand how photon energy governs the formation of new carbon bonds via alkene groups in the presence of copper catalyst.

Intermolecular and intramolecular \([2+2]\) photocycloaddition reactions facilitate the generation of cyclobutane moieties which are otherwise difficult to synthesize. Transition metal-based salts are used as catalysts to promote photocycloaddition reactions. The structure and the ring strain of a substrate can affect the reactivity and the rate of the photocycloaddition reactions. In this dissertation chapter 2 focuses on understanding the mechanism of Copper(I)-catalyzed intermolecular \([2+2]\) photocycloaddition reactions. We have used norbornene and cyclohexene as model substrates to explicate the mechanism of the Cu(I)-catalyzed intermolecular photocycloaddition reactions by using X-ray and optical transient absorption techniques. The mechanism for norbornene shows an initial metal to ligand charge transfer (MLCT) state which lasts for 18 ns prior to reverse electron transfer. Cyclohexene shows a change in metal-ligand bond strength instead of undergoing charge transfer. The evidence of the change in bond strength is consistent with the proposed idea of Salomon and Kochi for the formation of a more strained trans-cyclohexene intermediate.

The work presented in Chapter 3 of this dissertation focuses on understanding the mechanism of Cu(I)-catalyzed intramolecular \([2+2]\)
photocycloaddition reactions through the utilization of experimental and theoretical methods. The model substrates used for this study are 1,6-heptadiene, 1,7-octadiene, and 1,8-nonadiene which are linear alkenes with different carbon chain lengths. According to literature, only 1,6-dienes have been shown to undergo Cu(I)-catalyzed [2+2] photocycloaddition reactions. Theoretical DFT/TD-DFT calculations and experimental high energy resolution X-ray absorption spectroscopic studies are done to understand the structure-functional differences in photoreactive and nonreactive substrates. Based on the correlations observed between structure and photoreactivity, we have modified the structure of non-reactive substrates to adopt photoreactive conformations with steric modifications. Nuclear Magnetic Resonance (NMR) spectroscopy is used to confirm the photoreactivity of the alkene substrates.
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My appreciation also goes to my colleagues, friends, and family members, who provided me with moral support, encouragement, and motivation. Their unwavering belief in me and my abilities has kept me going during the challenging times.

Finally, I would like to dedicate this dissertation to the most precious people in my life, my father and mother, whose love, sacrifice, and unwavering support have been the bedrock of my success. I would like to express my gratitude to my beloved husband for being the best supporter, constructive critic, and for his love and care. Also, I would like to thank my sister and brother, who have stayed with me through thick and thin and have given me many cherished memories. The constant encouragement and the belief in me from my family have given me the strength to pursue my dreams and achieve my goals.
PREFACE

This dissertation is written in manuscript format. There are 3 chapters included in this dissertation. Chapter 1 is an introduction to photocycloaddition reactions, photocatalysts and ultrafast spectroscopic techniques. Chapter 2 is about Copper(I)-catalyzed [2+2] intermolecular photocycloaddition reactions and was published in the Journal of American Chemical Society. Chapter 3 is about Copper(I)-catalyzed [2+2] intramolecular photocycloaddition reactions and prepared to be submitted.
TABLE OF CONTENTS

ABSTRACT .......................................................................................................................... ii
ACKNOWLEDGMENTS ....................................................................................................... iv
PREFACE .......................................................................................................................... vi
TABLE OF CONTENTS ....................................................................................................... vii
LIST OF TABLES ............................................................................................................... ix
LIST OF FIGURES ............................................................................................................. x
CHAPTER 1 ....................................................................................................................... 1
Dissertation Introduction ................................................................................................. 1
INTRODUCTION ............................................................................................................... 2
THE [2+2] PHOTOCYCLOADDITION REACTIONS ......................................................... 3
X-RAY ABSORPTION SPECTROSCOPY (XAS) .............................................................. 6
HIGH-ENERGY RESOLUTION FLUORESCENCE DETECTION (HERFD) ............... 8
OPTICAL TRANSIENT ABSORPTION SPECTROSCOPY (OTA) ............................. 10
DENSITY FUNCTIONAL THEORY (DFT) ........................................................................ 11
REFERENCES ............................................................................................................... 13

CHAPTER 2 ....................................................................................................................... 19
Mechanisms of the Cu(I)-catalyzed intermolecular photocycloaddition reaction
revealed by optical and x-ray transient absorption spectroscopies. .......................... 19
ABSTRACT ..................................................................................................................... 20
INTRODUCTION ............................................................................................................. 21
EXPERIMENTAL SECTION .......................................................................................... 24
RESULTS AND DISCUSSION ....................................................................................... 31
CONCLUSIONS ............................................................................................................. 41
REFERENCES ............................................................................................................... 43
CHAPTER 3 ........................................................................................................... 58
Investigating the scope and limitations of Cu(I)-catalyzed intramolecular photocycloaddition of acyclic dienes using X-ray techniques and theoretical calculations to expand reaction boundaries. .................................................. 58

ABSTRACT ........................................................................................................... 59
INTRODUCTION .................................................................................................. 61
EXPERIMENTAL PROCEDURE .......................................................................... 66
RESULTS AND DISCUSSION ........................................................................... 70
CONCLUSIONS .................................................................................................. 78
REFERENCES ...................................................................................................... 80
LIST OF TABLES

**Table 3.1** DFT-optimized structures, energies, and dihedral angles of Cu(I)-olefin complexes. Dihedral angles are measured between Cu(I) coordinated terminal alkene groups and relative energies are calculated with respect to the lowest energy configurations of each ligand.......................... 98

**Table 3.2** Solvent phase DFT-optimized energies of the acyclic Cu(I)-olefin complexes. Relative energies (ΔE) are calculated with respect to the lowest energy configuration................................................................. 100

**Table 3.3** Coordinates of the optimized Cu(I)-1,6-heptadiene structure........ 101

**Table 3.4** Coordinates of the optimized Cu(I)-1,7-octadiene structure........ 102

**Table 3.5** Coordinates of the optimized Cu(I)-1,8-nonadiene structure ....... 103
LIST OF FIGURES

Figure 1.1 (A) Intermolecular and (B) intramolecular [2+2] photocycloaddition of olefins............................................................................................................................................ 4

Figure 1.2 Pre-edge, XANES and EXAFS spectral regions of the X-ray absorption spectrum................................................................................................................................. 8

Figure 1.3 Comparison between high energy resolution fluorescence detected (HERFD) spectra and total fluorescence yield (TFY) X-ray absorption (XAS) spectra of Cu(I)-1,6-heptadiene complex. .............................................................................. 9

Figure 1.4 Schematic representation of energy level diagram to illustrate ground state bleaching (GSB), excited state absorption (ESA) and stimulated emission (SE)........................................................................................................................................... 11

Figure 2.1 $^1$H NMR spectra of 0.6 M norbornene in THF with 3 mM (CuOTf)$_2$·toluene following irradiation at 270 nm in a photoreactor for various times. The spectrum of extracted product mixture after seven days is shown at the top. ................................................................................................................................................ 48

Figure 2.2 $^1$H NMR spectra of 0.6 M cyclohexene in THF with 3 mM (CuOTf)$_2$·toluene following irradiation at 270 nm in a photoreactor for various times. The spectrum of extracted product mixture after seven days is shown at the top. ................................................................................................................................................ 49

Figure 2.3 Optical absorption spectra of 6 mM CuOTf in THF alone and with 0.6 M norbornene or cyclohexene................................................................................................................................. 50

Figure 2.4. Ground state (GS) and difference Cu K-edge XANES spectra of 6 mM CuOTf in THF (A) and 6 mM CuOTf and 0.6 M norbornene in THF (B) at
several pump-probe delay times. The probe energies for which the short- and long-time kinetics are shown in Fig. 2-6 are indicated by vertical lines and bars, respectively. ................................................................. 51

**Figure 2.5** Transient Cu K-edge XANES spectra calculated from laser-on and laser-off spectra of 6 mM CuOTf in THF (A and B) and 6 mM CuOTf and 0.6 M norbornene in THF (C and D) obtained at several pump-probe delay times (cyan, green, and peach). Ground state spectra (black and blue) are also plotted for reference. The energy of the pre-edge feature that appears at 100 ps only in the sample with norbornene (8.977 keV) is indicated by a vertical arrow............. 52

**Figure 2.6** Fast (A) and slow (B) Cu K-edge kinetic traces measured for 6 mM CuOTf in THF (black) and 6 mM CuOTf and 0.6 M norbornene in THF (blue) and corresponding fits (red). The probe energies at which the traces were measured in panels A and B are indicated in Fig. 2-6 by vertical lines and bars, respectively. ................................................................. 53

**Figure 2.7** (A) – (C) X-ray transient absorption difference spectra of 3 mM CuOTf and 0.3 M cyclohexene in THF at various pump-probe delay times. (D) Short-time kinetic trace measured at the probe energy indicated by the vertical line in panels A-C. (E) Long-time kinetic trace averaged over the probe bandwidth indicated by the vertical bar in panels A-C................................. 54

**Figure 2.8** (A) Optical transient absorption spectra of 6 mM CuOTf and 0.6 M norbornene in THF at representative pump-probe delay times, showing the growth of the ESA signal over the first several ps. The -5 ps spectra of both the Cu + nb sample in THF (blue) and neat THF (gray) show a weak ESA signal
due to the multiphoton ionization of the solvent. The early-time kinetic trace taken from the probe region indicated by the vertical bar is shown in the inset with the corresponding multi-exponential fit. (B) Decay-associated spectra of CuOTf + nb obtained from a global fit of the optical transient absorption data.

Figure 2.9 (A) Optical transient absorption spectra of 6 mM CuOTf in THF (black), 6 mM CuOTf and 0.6 M norbornene in THF (blue), and 6 mM CuOTf and 0.6 M cyclohexene in THF (green) averaged over a pump-probe delay window of 2.8 to 3.8 ns. (B) Kinetic traces obtained by averaging over the probe window indicated by the vertical bar in panel (A). (C) Long-time kinetic traces of CuOTf alone scaled by a factor of 0.5 and CuOTf + nb, highlighting the identical kinetics observed on the µs time scale for the different samples. (D) Kinetic trace of CuOTf + nb with the contributions from multiphoton solvent ionization subtracted (blue) and the corresponding fit to a single exponential decay and a persistent offset.

Figure 2.10 Jablonski diagrams for the Cu(I)-catalyzed [2+2] photocycloaddition reactions of norbornene (left) and cyclohexene (right).

Figure 3.1 $^1$H NMR spectra of 0.2 M 1,6-heptadiene with 2 mM (CuOTf)$_2$·toluene in THF after excitation at 254 nm in a photoreactor for different irradiation times.

Figure 3.2 $^1$H NMR spectra of 0.2 M 1,7-octadiene with 2 mM (CuOTf)$_2$·toluene in THF after excitation at 254 nm in a photoreactor for different irradiation times.
Figure 3.3 $^1$H NMR spectra of 0.2 M 1,8-nonadiene with 2 mM (CuOTf)$_2$·toluene in THF after excitation at 254 nm in a photoreactor for different irradiation times.

Figure 3.4 $^1$H NMR spectra of 0.2 M 1,7-octadiene with 2 mM (CuOTf)$_2$·toluene after excitation at 254 nm in a photoreactor for nine days (without THF solvent).

Figure 3.5 Comparison of the HERFD-XANES and TFY-XANES of 1,6-heptadiene to illustrate the improved resolution of the HERFD at 1s → 4p region.

Figure 3.6 Comparison of the high-energy resolution fluorescence detected (HERFD) spectra of 50 mM (A) 1,6-heptadiene and 1,7-octadiene, (B) 1,6-heptadiene and 1,8-nonadiene (C) 1,6-heptadiene and norbornene with 2.5 mM (CuOTf)$_2$·toluene in anhydrous THF. 1,6-heptadiene and norbornene have a shoulder peak around 8.989 keV which is not prominent in 1,7-octadiene and 1,8-nonadiene.

Figure 3.7 High-energy resolution fluorescence detected (HERFD) spectral fittings of 50 mM 1,6-heptadiene with 2.5 mM (CuOTf)$_2$·toluene in anhydrous THF.

Figure 3.8 Optimized molecular structures of acyclic Cu(I) complexes and related dihedral angles between the two terminal alkenes. (A) Cu(I)-1,6-heptadiene, (B) Cu(I)-1,7-octadiene, (C) Cu(I)-1,8-nonadiene complexes. Atom labels: copper-maroon, carbon-blue, hydrogen-gray color.
Figure 3.9 Optimized molecular structure of the bicyclic Cu(I)-bis(norbornene) complex. Atom labels: copper-maroon, carbon-blue, hydrogen-gray color. ... 94

Figure 3.10 $^1$H NMR spectra of 0.2 M 4,8-dimethyl-1,7-nonadiene with 2 mM (CuOTf)$_2$·toluene in THF after excitation at 254 nm in a photoreactor for different irradiation times. ................................................................. 95

Figure 3.11 Comparison of the HERFD spectra of 50 mM (A) 1,6-heptadiene (B) 4,8-dimethyl-1,7-nonadiene (C) 2,5,9-trimethyl-2,8-decadiene with 2.5 mM (CuOTf)$_2$·toluene in anhydrous THF. 1,6-heptadiene and synthesized 4,8-dimethyl-1,7-nonadiene have a shoulder peak around 8.989 keV which is absent in synthesized 2,5,9-trimethyl-2,8-decadiene ligand................................................................. 96

Figure 3.12 Comparison of the HERFD spectra of 50 mM (A) 1,6-heptadiene (B) norbornadiene (C) 4-vinylcyclohexene with 2.5 mM (CuOTf)$_2$·toluene in anhydrous THF. All spectra have a shoulder peak around 8.989 keV. .......... 97
CHAPTER 1

Dissertation Introduction
INTRODUCTION

Synthesis of chemical compounds is an essential process in vast areas of fields such as pharmaceutical, medicinal, food industry, cosmetics, energy storage and more.\textsuperscript{1,2} Photon-mediated synthesis plays a crucial role as certain products cannot be obtained using thermal or electrochemical reaction conditions.\textsuperscript{3}

Photochemical reactions can occur via direct excitation, triplet sensitization and metal photocatalysis.\textsuperscript{1,4} Direct excitation could populates the first singlet excited state conserving the spin. Singlet states (s\textsubscript{1}) are known to have short lifetimes due to decay pathways such as fluorescence and internal conversion (IC) including structure mediated energy dissipation.\textsuperscript{2} Substituting direct excitation with the use of a triplet sensitizer or a transition metal photocatalyst could fulfill the efficiency of photocycloadditions by populating the long-lived triplet state.\textsuperscript{5} Triplet sensitizers have the ability to sensitize the triplet state of another molecule without exciting it through a singlet state.\textsuperscript{2} Ketones and aromatic ketones such as acetone, acetophenone and benzophenone are some triplet sensitizers which have higher triplet state energies and feasible intersystem crossing rates to sensitize nonconjugated molecules.\textsuperscript{2,6} Lower product yields and a mixture of many minor products result from photosensitized reactions.\textsuperscript{5,7}

Transition metal complexes are useful for selective excitations of π substrates to offer a single major product and enhance the lifetime of the reactive excited states of nonconjugated olefins to promote the electron transfer
towards bond formation. In comparison to the direct excitation of the substrates, excitation of the metal-substrate complex is identified as more reactive towards the formation of the product due to achievable metal-to-ligand charge transfer (MLCT) or ligand-to-metal charge transfer (LMCT) excitation states. Based on the excitation method, either direct excitation, triplet sensitization or metal catalysis, different photocycloaddition products can be obtained from the same starting material depending on the populated reactive singlet or triplet surfaces.

THE [2+2] PHOTOCYCLOADDITION REACTIONS

The discovery of photochemical reactions typically occurred after a compound underwent a physical change upon exposure to sunlight, either accidentally or intentionally due to curiosity. According to literature, the first reported [2+2] photocycloaddition reaction is the photodimerization of Thymoquinone upon exposure to sunlight, which was discovered in 1877 by Liebermann. In 1908, Ciamician and Silber made the first reported discovery of intramolecular [2+2] photocycloaddition, which entailed exposing carvone to sunlight and producing carvone camphor as a result.

The [2+2] photocycloaddition is a crucial step in synthesizing structurally complex and synthetically challenging molecules by allowing two π systems to interact with each other and form cyclobutane rings. Furthermore, the modified cyclobutane moieties resulting from ring expansion or fragmentation can serve as intermediate products in additional synthesis pathways. These [2+2] photocycloaddition reactions can be divided into two main categories as
Intermolecular and intramolecular cycloaddition. Intermolecular photocycloaddition requires two alkene groups in different molecules and intramolecular photocycloaddition requires two alkene groups within the same molecule to interact with each other to give the photoproduct (Figure 1.1). Intramolecular photocycloaddition reactions are identified to be more efficient and regioselective compared to intermolecular photocycloaddition reactions.¹⁴

![Diagram](A) Intermolecular and (B) intramolecular [2+2] photocycloaddition of olefins.

Nonconjugated alkenes have large energy gaps between the ground state and the first singlet excited state and hence require higher energies, typically around vacuum ultraviolet (VUV) wavelengths, for photoexcitation.¹³ The process of direct excitation or photosensitization is less efficient for nonconjugated π systems due to the demand of higher energies and lesser regio- and stereoselectivity, resulting in a large number of byproducts.⁴
Transition metal complexes selectively excite π substrates based on electron density, achieving higher regioselectivity and enhancing the reactivity of a wide range of π systems towards photocycloaddition.\textsuperscript{1,4} The [2+2] photocycloadditions are possible with alkene-alkene groups, enone groups, and mixed olefin groups. Carbonyl-olefin photocycloaddition is known as the Paterno-Büchi reaction which is named after great scientists Paterno, who observed the photoproduction in 1909 and Büchi who characterized the products after 45 years.\textsuperscript{4,11,14}

Several transition metal salts have been studied for olefin photocatalysis.\textsuperscript{1,15} Copper metal based salts such as copper(I) trifluoromethanesulfonate (CuOTf) is commonly used as a catalyst for photochemical reactions.\textsuperscript{2,4,16} The high abundance, low cost, redox properties, and feasibility of multiple ligand coordination have made copper an attractive catalyst.\textsuperscript{17} The high solubility in many organic solvents and the reduced competition with ligands from the weakly bound triflate anion have increased the yields of photoproducts when using CuOTf salt.\textsuperscript{5,16,18} Cu-catalyzed photochemical reactions are more common in the organic synthesis field over the decades of time.\textsuperscript{2}

To understand the mechanism, it is important to evaluate the reactive intermediate states and lifetimes. Excited state copper complexes have shorter lifetimes compared to the expensive iridium and ruthenium catalysts.\textsuperscript{19,20} Hence, to identify the intermediates and lifetimes of the Cu(I)-catalyzed [2+2] photocycloaddition reactions, use of an ultrafast characterization technique is important. The work in this dissertation mainly utilizes two ultrafast
characterizations spectroscopic techniques: X-ray transient absorption (XTA) and optical transient absorption (OTA) spectroscopic analysis.

Transient absorption spectroscopic techniques detect absorption changes and utilize them to understand the reaction intermediates and kinetics of a reaction. Spectroscopic analyses are conducted in a time-resolved manner using pump-probe techniques. A chemical reaction is initiated using a laser pump pulse, and changes are detected using another laser or X-ray pulse as a probe under different delay times. The pump-probe technique provides temporal resolution up to the femtosecond timescale, allowing the acquisition of data ranging from a few picoseconds to a couple of microseconds and beyond. Furthermore, absorption changes due to electronic transitions in the near UV to IR range can be detected using transient absorption techniques.

X-RAY ABSORPTION SPECTROSCOPY (XAS)

The X-ray absorption technique is an element-specific spectroscopic method, where we can selectively obtain information around the absorbing atom. This method provides detailed information about the electronic and molecular structure of a species in its solid, liquid or gaseous form. Furthermore, due to the higher penetration ability of X-rays, XAS provides information about transitions from deep core level orbitals to higher unoccupied orbitals up to the continuum. The three basic signal collection modes are transmission, fluorescence and photoelectron yield modes. The XAS spectra in this dissertation work are obtained by plotting total fluorescence emission.
(whose intensity is proportional to the Cu metal absorption)\textsuperscript{28} against the incident energy.

XAS spectrum has three main areas identified as the pre-edge region, X-ray absorption near edge structure (XANES) region and the extended X-ray absorption fine structure (EXAFS) region (Figure 1.2). The pre-edge region is assigned to $1s \rightarrow nd$ transitions in transition metal centers.\textsuperscript{29} The Copper pre-edge region is corresponding to the quadrupole-allowed dipole-forbidden $1s \rightarrow 3d$ transitions.\textsuperscript{22} This feature can be observed in $d^9$ Cu(II) complexes which have partially vacant 3d orbital. The intensity of this dipole forbidden peak is generated through 3d/4p orbital mixing, which is affected by the centrosymmetry of the complex.\textsuperscript{17,26,30} The XANES region, which corresponds to the dipole-allowed $1s \rightarrow 4p$ transitions, appears after the pre-edge region. Hence, XANES region probes the unoccupied orbitals in the metal center and provide information about the oxidation state, coordination geometry and bond strengths.\textsuperscript{31} With increasing incident energies, spectrum reaches to a highest intensity region known as the white line and proceeds towards the EXAFS to obtain data on multiple scatterings around the absorbing Cu atom.\textsuperscript{28,32}

Pump-probe delayed X-ray fluorescence detection provides information about the excited state dynamics and lifetimes through X-ray transient absorption (XTA) spectrum. The laser pump pulses and X-ray probe pulses are delayed relative to each other with respect to the repetition rates, in order to detect the changes in the excited states as snapshots over time.\textsuperscript{22} This pump-
probe XTA technique is complementary to the OTA technique which is discussed later in this dissertation.

Figure 1.2 Pre-edge, XANES and EXAFS spectral regions of the X-ray absorption spectrum.

HIGH-ENERGY RESOLUTION FLUORESCENCE DETECTION (HERFD)

In 1976, Eisenberg and co-workers evaluated the optimization of the resolution of X-ray resonant Raman scattering by using high intense synchrotron radiation. They observed when focusing on the $K\alpha_1$ region, linewidth of the emitted radiation is narrower than the conventional fluorescence linewidth due to lower lifetime broadening effect. In 1991, Hämäläinen and co-workers applied the removal of lifetime broadening phenomena to the X-ray absorption spectroscopy which is developed as the high-energy resolution fluorescence detection (HERFD) technique. Due to the minimization of core-hole lifetime broadening which limits the energy resolution in the XAS, HERFD
is more sensitive towards the structure determination and disclosure of additional spectral features compared to the conventional total fluorescence yield (TFY) XANES analysis.\textsuperscript{17,31,32,34} Figure 1.3 shows higher resolution at the HERFD-XANES region compared to the TFY-XANES region of the Cu(I)-1,6-heptadiene complex. Chapter 3 of this dissertation explains how we utilized HERFD to understand the Cu(I)-ligand coordination environments.

![Graph comparing HERFD and TFY spectra](image)

**Figure 1.3** Comparison between high energy resolution fluorescence detected (HERFD) spectra and total fluorescence yield (TFY) X-ray absorption (XAS) spectra of Cu(I)-1,6-heptadiene complex.
OPTICAL TRANSIENT ABSORPTION SPECTROSCOPY (OTA)

Optical transient absorption spectroscopy (OTA) is another ultrafast spectroscopic technique that can be used to obtain time-resolved data by using pump-probe delay times. In OTA, changes in absorption or optical density (ΔOD) of the pump excited samples are measured by detecting the transmitted probe intensities to understand the reaction intermediates and kinetics. The three main absorption changes and spectral regions that can be identified are: 1) ground state bleaching (GSB), which occurs due to the excitation of ground state atoms/molecules to the excited state; 2) excited state absorption (ESA), which occurs from the further promotion of excited molecules to higher excited states; and 3) stimulated emission (SE), which occurs from the probe inducing excited state atoms to relax back to the ground state (Figure 1.4).

Apparently, GSB and SE give negative feature and ESA gives a positive feature when deducing the ΔA (pump on – pump off) difference spectrum. The resulting ΔA spectrum can be convolved with several absorption peaks, including the reaction kinetics of electronic structure changes, solvent dynamics, the instrument response function (IRF), and scattering-mediated background noise (coherent artifact). Therefore, peak deconvolution using fitting parameters such as exponential decay, step functions, and global analysis is important for extracting the exact chemical reaction-mediated kinetics.
Optical laser setups have a higher temporal resolution compared to the X-ray absorption (XTA) technique described in the previous section. The OTA technique is successfully used to understand the transition-metal-mediated photophysical and photochemical studies.\textsuperscript{13,36–38} However, the disadvantage of OTA compared to XTA is that it is not element-specific, and we cannot obtain data specifically for a single element.\textsuperscript{13,36} Furthermore, spectroscopic results are limited to the transitions occurring at either the near UV, visible or infra-red (IR) region, depending on whether the probe pulses are in the visible or IR region.\textsuperscript{21,23}

**Figure 1.4** Schematic representation of energy level diagram to illustrate ground state bleaching (GSB), excited state absorption (ESA) and stimulated emission (SE).

Optical laser setups have a higher temporal resolution compared to the X-ray absorption (XTA) technique described in the previous section. The OTA technique is successfully used to understand the transition-metal-mediated photophysical and photochemical studies.\textsuperscript{13,36–38} However, the disadvantage of OTA compared to XTA is that it is not element-specific, and we cannot obtain data specifically for a single element.\textsuperscript{13,36} Furthermore, spectroscopic results are limited to the transitions occurring at either the near UV, visible or infra-red (IR) region, depending on whether the probe pulses are in the visible or IR region.\textsuperscript{21,23}

**DENSITY FUNCTIONAL THEORY (DFT)**

Computational chemistry is recognized as an essential tool besides synthesis and spectroscopy for atomic and electronic level understanding of
Density functional theory (DFT) is a computational method used to theoretically calculate the electronic structure and properties of molecules and materials. These calculations are based on total electron density and the electronic wave functions to compute energy. Evolving from the Schrödinger’s wave function in 1926 to the electron density variable in Thomas-Fermi (TF) theory, Kohn and Sham developed a mathematical equation in 1965 that paved the way to modern computational DFT calculations. Over time, a large number of density functionals such as B3LYP, hybrid meta-functionals and atomic basis sets like, 6-31G**, Sapporo-TZP-2012-diffuse have been developed as method combinations to improve quantum chemistry treatments for accurate and reliable results. Selecting the correct method combination is critical in obtaining accurate outcomes from calculations.

DFT is successfully used for the energy calculations of larger molecules and transition metal-mediated molecules due to its higher accuracy and lower computational cost compared to the other computational methods such as Hartree-Fock (HF). Chapter 3 of this dissertation shows how we utilized DFT calculations to deduce the conformational changes in the Cu(I)-olefin complexes to correlate structure-functional relationships towards photoreactivity.
REFERENCES


CHAPTER 2

Mechanisms of the Cu(I)-catalyzed intermolecular photocycloaddition reaction revealed by optical and x-ray transient absorption spectroscopies.

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ABSTRACT

The \([2 + 2]\) photocycloaddition provides a simple, single-step route to cyclobutane moieties that would otherwise be disfavored or impossible due to ring strain and/or steric interactions. We have used a combination of optical and x-ray transient absorption spectroscopies to elucidate the mechanism of the Cu(I)-catalyzed intermolecular photocycloaddition reaction, using norbornene and cyclohexene as model substrates. We find that for norbornene, the reaction proceeds through an initial metal-to-ligand charge transfer (MLCT) state that persists for 18 ns before returning to the monovalent oxidation state. The Cu K-edge spectrum continues to evolve until \(~5\) μs and then remains unchanged for the 50 μs duration of the measurement, reflecting product formation and ligand dissociation. We hypothesize that the MLCT transition and reverse electron transfer serve to sensitize the triplet excited state of one of the norbornene ligands, which then dimerizes with the other to give the product. For the case of cyclohexene, however, we do not observe a charge transfer state following photoexcitation and instead find evidence for an increase in the metal-ligand bond strength that persists for several ns before product formation occurs. This is consistent with a mechanism in which ligand photoisomerization is the initial step, which was first proposed by Salomon and Kochi in 1974 to explain the stereoselectivity of the reaction. Our investigation reveals how this photocatalytic reaction may be directed along strikingly disparate trajectories by only very minor changes to the structure of the substrate.
INTRODUCTION

The use of photochemistry in organic synthesis remains restricted to a small number of well-known reactions with relatively narrow scope. Among the group of established photochemical reactions in organic synthesis, “[t]he [2 + 2] photocycloaddition is undisputedly the most important and most frequently used,” according to a recent review by Bach and coworkers.1 This reaction is particularly useful in many natural product syntheses, where it provides a single-step route to challenging fused multicyclic and/or heterocyclic moieties,2–4 and it was famously used as a key step in the landmark syntheses of caryophyllene5 and cubane.6 More recently, Jiang et al.7 and Skubi et al.8 reported new catalytic platforms for the [2 + 2] photocycloaddition with unparalleled regio- and/or stereoselectivity, demonstrating that even after more than a century, the potential scope of this reaction has still not been fully explored.

Because the π-π* transitions of unconjugated olefins appear in the vacuum ultraviolet (UV) and exhibit poor intersystem crossing (ISC) yields, photocycloaddition of such substrates is typically accomplished using a triplet sensitizer or a Cu(I) salt as a catalyst. Cu(I) bis(olefin) complexes exhibit absorption bands in the near-UV that may be excited to drive the reaction with quantum yields greater than 60%,9 and a similar approach has been recently used to accommodate carbonyl substrates in a Cu(I)-catalyzed analog of the Paternò-Büchi reaction.10 Nevertheless, while this cheap, earth-abundant catalyst broadens the scope of this reaction, it also brings its own set of limitations. For example, intermolecular cycloadditions are only possible when
at least one of the substrates possesses ring strain at the position of the target alkene,\textsuperscript{11} while intramolecular cycloadditions are essentially only possible for 1,6-dienes.\textsuperscript{12} Although computational chemistry could help identify potential substrates and/or catalysts capable of overcoming these shortcomings, such work first requires a robust understanding of the reaction mechanism.

The Cu(I)-catalyzed intermolecular olefin photocycloaddition was first reported in 1965 by McKeon and coworkers, who used quantum yield measurements to conclude that the photocatalytic dimerization of norbornene in the presence of CuBr proceeds through photoexcitation of the 1:1 metal:ligand species, which then reacts with two additional norbornene molecules in solution to give the dimer and the ground state 1:1 complex.\textsuperscript{13,14} In 1973, Salomon and Kochi showed that the superior solubility of Cu(I) trifluoromethanesulfonate (CuOTf) and its olefin complexes in ethereal solvents results in an order of magnitude improvement in quantum yield over Cu(I) halides.\textsuperscript{15} The improved solubility also permitted a broader range of concentration-dependent quantum yield measurements, from which the authors concluded that the reaction actually proceeds exclusively from the pre-associated Cu(I) bis(norbornene) complex.\textsuperscript{9} Kochi and coworkers also explained the \textit{trans-anti-trans} stereoselectivity of the CuOTf-catalyzed photodimerizations of cyclohexene and cycloheptene by proposing a mechanism invoking an initial ligand photoisomerization followed by cycloaddition with a ground state substrate molecule,\textsuperscript{11} consistent with the
photoisomerization of the Cu(I) complex of cis-cis-1,5-cyclooctadiene to the cis-trans form observed earlier by Whitesides.\textsuperscript{16}

Despite this previous work, the mechanisms of these reactions remain unclear, with even the nature of the photochemically active optical transition(s) disputed. Salomon outlined several potential concerted and sequential mechanisms for the dimerization of norbornene invoking metal-to-ligand charge transfer (MLCT) or ligand-to-metal charge transfer (LMCT) states,\textsuperscript{17} with the formation of the organocopper carbenium intermediate via the latter pathway termed “photocupration”.\textsuperscript{18} In 1985, Geiger and Ferraudi performed flash photolysis studies of the Cu(I)-catalyzed photopolymerization of ethylene and photoisomerization of cyclooctadiene and observed transient species with lifetimes ranging from nanoseconds to milliseconds that they assigned primarily to biradical alkyl copper intermediates by comparison to stable organocopper species.\textsuperscript{19} This work strongly suggested that the metal plays a crucial role beyond simply templating the otherwise bimolecular reaction and/or promoting ISC following a ligand centered (\(\pi \rightarrow \pi^*\)) transition. Electronic structure calculations by Baerends and coworkers two years later provided compelling evidence for a mechanism in which such a Cu(I) biradical forms from an initially populated MLCT excited state,\textsuperscript{20} but to date there is still no direct experimental evidence for any single reaction mechanism.

While optical transient absorption (OTA) spectroscopy has been used to investigate metal-free photocycloadditions of enones\textsuperscript{21,22} and quinolones,\textsuperscript{23} similar efforts have not been reported for the Cu(I)-catalyzed photochemical
dimerization of olefins. In this work, we leverage the strengths of both OTA and X-ray transient absorption (XTA) to observe the excited state dynamics of such reactions in real time and thereby obtain clear pictures of their respective mechanisms. XTA allows us to track the oxidation state and ligation environment of the copper center, while OTA provides a probe of transient Cu(II) species with sub-ps resolution. We find that norbornene and cyclohexene, model substrates differing by only a single methylene bridge, exhibit strikingly disparate spectral features and dynamics. The distinct photodimerization mechanisms suggested by these results have important implications for understanding and expanding the scope of this class of reactions.

EXPERIMENTAL SECTION

Nuclear Magnetic Resonance Studies (1H NMR)

Photochemical reactor experiments were performed to analyze the photoreactivity of the substrates. Norbornene (0.56 g, 6 mmol) or cyclohexene (0.49 g, 6 mmol) and (CuOTf)2·toluene (0.015 g, 0.03 mmol; 0.06 mmol Cu(I)) were dissolved in 10 mL of anhydrous, air-free THF in a quartz reaction vessel with copper turnings under N2, and the vessel was sealed with a rubber septum and Parafilm. The vessel was transferred to a photoreactor (Rayonet RPR-100) equipped with sixteen 12 in, 14 W bulbs with emission at 254 nm (Rayonet RPR-2537 A) and stirred under constant irradiation for several days. The reaction temperature was maintained at approximately 35 °C using a cooling fan.
Small aliquots of the reaction mixtures were removed at various times using a syringe needle and used for $^1$H NMR analysis without any purification to avoid disproportionate loss of the volatile monomers and dimers during solvent evaporation. NMR samples were prepared by dissolving the reaction mixture in CDCl$_3$, and spectra were acquired using Bruker Avance III 300 MHz instrument. After seven days of irradiation, samples were filtered and extracted into pentane. The extract was washed with deionized water to remove the THF and residual copper salts and dried with anhydrous MgSO$_4$, and the pentane and residual THF were removed by rotary evaporation. NMR spectra of the reaction mixtures at several time points and the final extract are shown in Figures 2.1 and 2.2. All spectra of reaction mixtures were referenced and normalized to the internal THF peak at 3.67 ppm, and the extract spectra were referenced and normalized to the largest product peak in the 168 hours reaction mixture spectrum. The extracted spectra confirm the formation of the photocycloaddition products.

UV-Visible Absorption

Optical absorption spectra were acquired in a 2 mm pathlength fused quartz cuvette using a Shimadzu UV-3600 Plus spectrometer with a reference cuvette filled with THF. Samples were prepared as 6 mM solutions of CuOTf in THF alone or with 0.6 M norbornene or cyclohexene and always kept under N$_2$ to prevent oxidation. Following five minutes of sonication, each sample was passed through a 0.45 μm syringe filter to eliminate any undissolved particles. The spectra are plotted below in Figure 2.3.
X-ray Transient Absorption (XTA)

Total fluorescence yield copper K-edge transient absorption measurements were performed at beamline 11-ID-D at the Advanced Photon Source (APS, Argonne National Laboratory). All measurements were performed with the APS storage ring operating in 24-bunch mode, and the third harmonic of a regeneratively amplified Ti:sapphire laser system was used as the optical pump. A 3.0 kHz pulse train of 1 ps, 4 mJ pulses centered at 800 nm was produced by a Legend Elite Duo amplifier seeded by a Micra-5 oscillator and pumped by an Evolution intracavity-doubled, diode-pumped Nd:YLF Q-switched laser. The rf signal from the storage ring was used to phase lock the oscillator using the Synchrolock AP system (Coherent) and to trigger the Q-switch at a repetition rate of 3.0 kHz. The compression of the amplified laser pulse was intentionally detuned to give temporally chirped, ~1 ps pulses to increase the excited state fraction of the sample and minimize sample damage.

The third harmonic was obtained by passing the 800 nm beam through an 800 nm λ/2 waveplate, a Type 1 SHG BBO crystal, a calcite group delay compensation plate, a dual wavelength (800 and 400 nm) λ/2 waveplate, and a Type 1 THG BBO crystal and then dumping the first and second harmonics with a pair of harmonic separators reflective at 267 nm (Third Harmonic Femtokit, Eksma Optics). Further suppression of the lower harmonics was accomplished using a series of narrowband dielectric coated UV mirrors to direct the beam into the sample. The beam was focused with a 300 mm lens such that the beam reached the focal point behind the sample and the spot size at the position of
the liquid jet was 750 x 600 μm. The X-ray spot size was 500 x 200 μm. A λ/2 waveplate and polarizer places in the 800 nm beam before the third harmonic generation optics were used to control the excitation energy, which was 39 μJ/pulse at the sample position. The laser and X-ray beams overlapped at the sample position by aligning through a pinhole. A fast photodiode and 8 GHz oscilloscope (Infinium, Agilent) was then used to set the temporal overlap between the X-ray and laser pulses by adjusting the timing of the Synchrolock.

The X-ray probe pulses were generated using dual inline undulators followed by an actively stabilized dual crystal Si (111) monochromator. An upstream APD detector channel was used for pulse-by-pulse normalization of the fluorescence signal. A nickel Z-1 filter (3 absorption lengths) and soller slit assembly was mounted between the sample jet and each of two APD fluorescence detectors mounted at 90° relative to the X-ray beam to minimize background signal from elastic scattering. The signal of both APD channels was recorded at a 1 GHz sampling rate by a fast analyzer card (Agilent), and the data was processed in real time by software written by Dr. Guy Jennings (APS), which performs background subtraction, pulse shape fitting, and signal averaging. The signal from all X-ray pulses was recorded during all experiments to permit analysis of dynamics out to μs time scales. The energy axis was calibrated to the edge of a Cu foil reference spectrum measured simultaneously using the transmitted X-ray beam.

Norbornene (28.25 g, 0.3 mol) and CuOTf (0.775 g, 1.5 mmol; 3 mmol Cu(I)) or cyclohexene (12.25 g, 0.15 mol) and (CuOTf)$_2$·toluene (0.388 g, 0.75 mmol;
1.5 mmol Cu(I)) were dissolved in 500 mL of anhydrous, air-free THF in a 1 L glass reaction vessel with a PTFE-coated stir bar under an N₂ atmosphere inside a glove box. At this sample concentration, less than 5% of either substrate was estimated to be consumed throughout the measurement time of a single sample for a laser power of 115 mW. All glassware and stir bars were dried in an oven at 120 °C for at least 3 h prior to sample preparation. The vessel was sealed with a rubber septum and Parafilm and transferred to the beamline, where it was constantly purged with THF-saturated N₂. A peristaltic pump with PTFE tubing was used to circulate the sample, which was delivered to the X-ray beam from a steel tube as a 600-650 µm free-flowing liquid jet.

Optical Transient Absorption (OTA)

Femtosecond OTA measurements were performed using a commercial regeneratively amplified Ti:sapphire laser (Coherent Astrella) and home-written LabVIEW data acquisition code. A 1.0 kHz pulse train of 40 fs, 6.2 mJ pulses centered at 800 nm was produced by the Astrella amplifier, which was seeded by an oscillator (Coherent Vitara) and pumped by a diode-pumped Q-switched laser (Coherent Revolution). One sixth of the total power was used for the transient absorption experiments. The beam was split, with 90% of the beam used for the pump and 10% used for the probe. The pump beam was chopped at 500 Hz and delayed relative to the probe with a retroreflector mounted on a motorized delay stage before passing through the same series of third harmonic generation optics described above for the XTA measurements (Eksma Optics).
Neutral density was used in the pump line before the THG optics to adjust the pulse energy, and telescoping optics were used to reduce the beam waist to 2 mm. All fs OTA measurements were performed with a pump pulse energy of 0.25 µJ and a spot size of 300 µm (0.35 mJ/cm² fluence). The broadband probe was generated by focusing the probe beam into a sapphire plate and passing the white light through a high pass filter (750 nm cutoff) to give a continuum spanning from 440 to 750 nm. The pump and probe beams were focused and overlapped at the sample position, and the transmitted probe was focused into a fiber-coupled CMOS spectrometer (Avantes AvaSpec). A gaussian IRF of 310 fs (FWHM) was determined by measuring the nonresonant response of the blank solvent. OTA spectra were acquired with 2 s averaging at each time point, and all spectra and kinetic traces reported are the average of at least four scans.

Nanosecond OTA measurements were performed using a commercial tunable diode-pumped Q-switched Nd:YAG laser and optical parametric oscillator (Ekspla NT240) for the optical pump, a commercial broadband supercontinuum fiber laser (LEUKOS Disco-2-UV) for the optical probe, and home-written LabVIEW data acquisition code. The 1.0 kHz pump pulse train at 267 nm had a pulse duration of 3 ns, while the 2.0 kHz probe pulse train had a pulse duration of 0.8 ns and a continuous spectrum spanning 390-830 nm after passing through a hot mirror with a reflectivity cutoff of ~825 nm to eliminate the 1064 nm fundamental. The pump pulse energy was 10.0 µJ at the sample position with a rectangular spot size of 1.5 x 0.4 mm (1.7 mJ/cm² fluence). The probe laser operated at a repetition rate of 2.0 kHz and served as the master
clock, triggering the pump laser at a repetition rate of 1.0 kHz via a delay generator (SRS DG535), which also controlled the pump-probe delay time. The transmitted probe was focused into a fiber-coupled CMOS spectrometer (Avantes AvaSpec), and an instrument response function of ~3 ns was determined by measuring the rise time of the signal from a 2 mM sample of tris(bipyridine)ruthenium (II) chloride in MeOH. OTA spectra were acquired with 2 s averaging at each time point, and all spectra and kinetic traces reported are the average of at least six scans.

Sample preparation for the OTA measurements is similar to the XTA measurements. Norbornene (28.25 g, 0.3 mol) or cyclohexene (24.50 g, 0.3 mol) and CuOTf (0.775 g, 1.5 mmol; 3 mmol Cu(I)) were dissolved in 500 mL of anhydrous, air-free THF in a 1 L glass reaction vessel with a PTFE-coated stir bar under an N₂ atmosphere. At this sample concentration, less than 0.1% of either substrate was estimated to be consumed throughout the measurement time of a single sample for a laser power of 1 mW. All glassware and stir bars were dried in an oven at 120 °C for at least 3 h prior to sample preparation. The vessel was sealed with a rubber septum and Parafilm and transferred to the laser table, where it was constantly purged with N₂. A peristaltic pump with PTFE tubing was used to circulate the sample through a quartz flow cell with a pathlength of 0.5 mm.

Data Analysis

Data analysis was performed using MATLAB R2019a (MathWorks). Kinetic traces were fit to the sum of exponential decay components convolved with a
gaussian instrument response function (IRF) using the nonlinear least-squares fitting function lsqcurvefit. Normalization and background subtraction of XANES spectra was performed using Athena, a part of the Demeter 0.9.25 software package. NMR spectra were analyzed using the MestReNova 14.1.2-25024 software package.

RESULTS AND DISCUSSION

XTA measurements at the Cu K-edge were performed using a 6 mM solution of CuOTf in THF with no substrate or 0.6 M norbornene or cyclohexene was circulated using a peristaltic pump to deliver a liquid jet at the sample position, where the laser and X-ray beams were spatially overlapped at a shallow angle. The solutions were constantly purged with N₂ and the sample chamber was carefully sealed to prevent oxidation of Cu(I). The third harmonic of the 3 kHz output of a Ti:sapphire laser provided 100 fs pulses at 267 nm, which were used to trigger the photocycloaddition reaction. X-ray absorption near edge structure (XANES) spectra were then obtained by scanning the energy of the ~1 eV monochromatized X-ray beam and measuring the total X-ray fluorescence from the sample for each X-ray pulse (6.5 MHz) using avalanche photodiodes. Because XANES is an element-specific technique, samples could be prepared in 50-fold excess of substrate to drive the equilibrium⁹ between Cu⁺, [Cu(olefin)]⁺, and [Cu(olefin)₂]⁺ predominantly toward [Cu(olefin)₂]⁺ and keep the concentration of substrate approximately constant over 12 h measurement windows.
Ground state (i.e., “laser off”) XANES spectra of THF solutions of CuOTf alone and CuOTf with norbornene (nb) are shown in Figure 2.4 with difference spectra (“laser on” minus “laser off”) acquired at three pump-probe delay times. The CuOTf difference spectrum at 100 ps shows a broad excited state absorption (ESA) feature in the 1s→4p region along the edge as well as a sharp ground state bleach (GSB) at 8.981 keV and oscillatory features across the multiple scattering region. By the arrival of the subsequent probe pulse 153 ns later, the sharp GSB has mostly disappeared, while the other features have decayed only moderately. The bottom spectrum, which is averaged over 27 probe pulses spanning 2-6 µs to provide improved signal-to-noise, is essentially unchanged from the 153 ns spectrum. The CuOTf + nb difference spectrum at 100 ps, however, shows two prominent GSB peaks along the edge but no discernable features beyond the white line. By 153 ns the difference appears essentially flat, while the 2-6 µs averaged spectrum shows a weak but broad ESA feature in the 1s→4p region and a slight bleaching of the white line.

Approximate XANES spectra of the transient species (Figure 2.5) were obtained by subtracting a fractional amount of the “laser-off” spectra from the corresponding “laser-on” spectra and renormalizing the resulting data. An excited state fraction of 4% was used for all spectra, estimated from the laser pulse energy and spot size and sample optical density. Because both samples show no further spectral evolution after ~10 µs, a transient spectrum with excellent signal-to-noise could be obtained by averaging all 65 X-ray probe pulses arriving between 25 and 35 µs after the laser pump pulse.
The 100 ps CuOTf spectrum shows clear changes in the 1s→4p region but no apparent shift in the edge energy, as would be expected to accompany a charge transfer. There is also no evidence of a 1s→3d pre-edge feature at ~8.977 keV. Instead, a new peak appears at ~8.980 keV that is consistent with a Cu 1s→O n MLCT transition that gains intensity due to strong mixing between the O n and Cu 4pz orbitals, though detailed computational work is necessary to support such an assignment. By 153 ns, the spectrum appears essentially identical to that observed at all later times, with a prominent 1s→4p ESA and a bleaching of the white line but still no evidence of an edge shift. This spectrum and the corresponding difference spectra in Figure 2.4 are in excellent qualitative agreement with those presented by Solomon and coworkers for Cu(I) species with progressively lower coordination numbers. Thus, we conclude that the optical transition does not involve the Cu(I) center directly but is instead an n→3s transition at one of the weakly associated THF ligands, resulting in photodissociation. The lower-coordinate Cu(I) center then reaches a metastable state within 153 ns, and equilibration back to the fully coordinated ground state species does not occur within the 45 µs experimental window.

The 100 ps CuOTf + nb spectrum, however, shows the hallmarks of a 3d⁹ Cu(II) center: a pre-edge feature at 8.977 keV corresponding to the creation of a 3d hole, and a hypsochromic edge shift corresponding to the increase in oxidation state and stabilization of the 1s electrons. The shoulder at 8.9840 keV is also consistent with the characteristic 1s→4p + LMCT shakedown transition of Cu(II) species. Accordingly, we can unambiguously conclude that the
excited state of the \([\text{Cu(nb)}_2]^+\) complex 100 ps after excitation at 267 nm is an MLCT state. Within 153 ns, the transient spectrum is indistinguishable from the ground state spectrum, indicating that reverse electron transfer has returned the metal to a monovalent state. However, the spectrum continues to evolve over the next several \(\mu\)s, ultimately giving a metastable spectrum exhibiting the same 1s\(\rightarrow\)4p ESA and bleaching of the white line observed for the CuOTf sample. Because these features are consistent with decreased coordination number, the final spectrum may be assigned to the Cu(I) species present following product formation and dissociation. The Cu(I) species observed at 153 ns thus corresponds to a reaction intermediate that forms following reverse electron transfer from the initially prepared MLCT state.

Time scans with \(~\)50 ps resolution were also performed at the probe energy for which \(\Delta A\) at 100 ps was of greatest magnitude for each sample: 8.9944 keV for CuOTf, 8.9825 keV for CuOTf + nb, as shown in Figure 2.6A. Because these kinetic traces were acquired at different spectral regions for the two samples, caution must be used when making any direct comparison; nevertheless, each trace still provides important information on the excited state dynamics of the corresponding system. In particular, the bleach in the CuOTf sample recovers monoexponentially with a time constant of 320 ps (fit shown in red), while the bleach in the CuOTf + nb sample appears essentially static out to 2 ns. But while ps/ns dynamics could only be monitored at one probe energy at a time, the 6.5 MHz X-ray pulse train provides full XTA spectra out to 45 \(\mu\)s in steps of 153 ns. To improve signal-to-noise, the difference was integrated over the entire ESA
peak observed at >2 µs in both datasets, and the kinetic traces are plotted in Figure 2.6B. Both show a few-µs rise time (3.8 µs for CuOTf, 2.7 µs for CuOTf + nb), but CuOTf also shows a substantial impulsive ESA component. CuOTf + nb shows no evidence of an impulsive ESA, instead showing only an impulsive GSB that decays back to the baseline by the arrival of the next X-ray pulse due to the forward and reverse photoinduced electron transfer events. Thus, while some slow equilibration process likely occurs in the CuOTf sample on the µs time scale following excitation, ligand photodissociation occurs within only 320 ps. For CuOTf + nb, on the other hand, product formation and dissociation occur with a long time constant of 2.7 µs.

XTA difference spectra of CuOTf with cyclohexene (ch) at various delay times are presented in Figures 2.7A to 2.7C. The spectrum at 100 ps shows neither the pre-edge ESA at 8.977 keV nor the hypsochromic edge shift observed for CuOTf + nb, indicating that the optical transition is not an MLCT. There is no evidence either of a bathochromic edge shift, indicating that the transition is also not an LMCT. The only clear feature is a bleaching of the 1s → 4p peak at 8.9806 keV. By 153 ns, the difference spectrum appears essentially flat, while at later delay times it resembles the µs difference spectra of the CuOTf and CuOTf + nb systems. The GSB at 8.9806 keV partially recovers with a time constant of 280 ps but then persists beyond 2 ns (panel D), while the ESA observed at late delay times grows with a time constant of 5.5 µs (panel E). These observations are consistent with a change in the metal-ligand binding on
the ps and ns time scales and product formation and ligand dissociation at a rate comparable to that observed for CuOTf + nb.

Although it is that [Cu(nb)$_2$]$^+$ is in a Cu(II)* MLCT state at 100 ps, it is possible that a different state is populated immediately following photoexcitation. The temporal resolution achievable for XTA experiments at storage ring light sources such as the APS is typically limited to ~100 ps, and thus we investigated the ultrafast dynamics of the reaction using fs OTA. Although this method does not have the element specificity of XTA, the Cu(II)* state may be easily identified by the appearance of a band in the visible regime, across which the ground state [Cu(nb)$_2$]$^+$ complex exhibits no absorption. This band could correspond to the Cu(II) ligand field transition, absorption by the norbornene radical anion, or some combination of the two; further work is required for a conclusive assignment to be made.

OTA spectra at representative delay times are shown in Figure 2.8A. A persistent ESA is observed at negative delay times (blue), and it is also observed in neat THF (gray) at both positive and negative delay times. The increasing intensity of this ESA band at longer probe wavelengths is consistent with previously reported spectra of ionized THF generated by pulse radiolysis,$^{32,33}$ and thus we assign it to the long-lived species produced by multiphoton ionization of the solvent$^{41}$ (i.e., solvent radical cations and solvated electrons). A much stronger ESA band consistent with the Cu(II)* state, however, appears between 450 and 650 nm at positive times, growing in amplitude and shifting toward shorter wavelengths over the first several ps until reaching a
maximum amplitude at ~10 ps. This non-impulsive behavior is highlighted by
the kinetic trace shown in the inset (data averaged over the 468-482 nm probe
region indicated by the gray bar). After this time the spectrum remains
essentially unchanged, decaying only slightly over the 2 ns delay window.

The data beyond 1 ps may be fit across the entire probe spectrum with only
two components: a fast component with an average time constant of 4.2 ps
(black) and a slow component with a time constant much longer than the 2 ns
delay window (red). While the ESA on the red side of the 4.2 ps component
likely contains contributions from ionized solvent dynamics, the OTA signal at
wavelengths shorter than 500 nm may be ascribed entirely to the [Cu(nb)₂]⁺
complex. The negative signal in the 4.2 ps component in this region cannot be
assigned to the partial recovery of the GSB, as the steady-state optical spectrum
of this solution does not exhibit any absorption bands at visible wavelengths;
although some absorption is observed at wavelengths >450 nm, this simply
corresponds to the tail of the main UV absorption band, which decays smoothly
out to ~650 nm (Figure 2.3). However, because the sign of the OTA signal is
positive at all probe wavelengths, the non-impulsive growth of the signal
between 450 and 525 nm could correspond to 1) stimulated emission from the
thermalized singlet excited state and/or 2) spectral narrowing due to
intramolecular vibrational redistribution. Crucially, no spectral evolution is
observed after ~10 ps, meaning the 4.2 ps relaxation must yield the thermalized
³MLCT state observed by XTA at 100 ps. ISC rates of a few ps have been
reported for the MLCT states of many Cu(I) complexes,²⁶,³⁵–³⁷ but in the
absence of ultrafast emission spectra, we cannot conclusively assign the 4.2 ps component to either ISC from the thermalized \(^1\)MLCT state or thermalization of the \(^3\)MLCT state.

Because the XTA and fs-resolved OTA measurements could only provide lower and upper bounds for the lifetime of the \(^3\)MLCT state (2 and 153 ns, respectively), ns-resolved OTA is performed to determine the precise value. OTA spectra averaged over a delay window of 2-4 ns are shown in Figure 2.9 for CuOTf only (black) and CuOTf with norbornene (blue) and cyclohexene (green), and corresponding kinetic traces obtained by averaging over the probe spectral region indicated by the vertical bar are shown in panel B. The CuOTf sample provides a convenient means of eliminating contributions to the CuOTf + nb signal from multiphoton ionization of the solvent. Scaling the CuOTf signal by 50% gives a kinetic trace that matches that of CuOTf + nb nearly perfectly after 100 ns across the remainder of the 10 µs delay window (panel C). Accordingly, we may subtract the scaled CuOTf trace from the CuOTf + nb trace to isolate contributions from the photocatalytic species. While the subtraction likely introduces some artifacts in the data, we only seek to obtain the time constant unique to the CuOTf + nb sample that is also apparent in the raw data (panel B). The subtracted data (panel D, mustard circles) is fit well (red trace) by a single exponential decay and a persistent negative component, giving a reverse electron transfer rate of 18 ns.

Meanwhile, it is clear from Figure 2.9A-B that the ns-resolved OTA data obtained for CuOTf alone and CuOTf + ch are essentially identical to within a
scaling factor. The signal is ~30% weaker for CuOTf + ch, demonstrating that while multiphoton solvent ionization still occurs in this sample, many photons are now being absorbed instead by the copper species. The lack of the strong ESA signal centered at 500 nm observed for the CuOTf + nb sample provides further evidence that a Cu(II)^* transient species is not formed and thus the optical transition is not an MLCT. The OTA data alone for CuOTf + ch, however, are inconclusive.

Based upon the results presented above, we propose two distinct mechanisms for the [2+2] intermolecular photocycloaddition reactions of norbornene and cyclohexene, as illustrated by the Jablonski diagrams shown in Figure 2.10. In the case of norbornene, the relevant ground state species is the singlet [Cu(nb)_2]^+ complex, labeled 1S0. Photoexcitation at 267 nm brings this species to the Franck-Condon state on the 1MLCT potential energy surface, characterized by an oxidized Cu(II) center coordinated by a norbornene and a norbornene radical anion ligand. This species undergoes ISC to the thermalized 3MLCT state within 4.2 ps. Reverse electron transfer within 18 ns returns the copper center to the monovalent oxidation state, resulting in a reactive ligand-centered triplet biradical species (3LC). Finally, the cycloaddition reaction proceeds within 2.7 µs to give the norbornene dimer and a coordinatively unsaturated Cu(I) species. We note, however, that while we favor the mechanism in which photocycloaddition proceeds from the 3LC state as in the case of direct olefin excitation or triplet sensitization, we cannot rule out the
possibility that the first C-C bond formation occurs in the $^3$MLCT state prior to reverse electron transfer to give a metallacyclic intermediate.

While each of the intermediates and time constants given for norbornene are strongly supported by the XTA and OTA data, the cyclohexene system is notable for a lack of any clear OTA signal between 450 and 700 nm. Importantly, our NMR study of the photochemical dimerizations of norbornene and cyclohexene shows that the two compounds convert to product on comparable time scales. We may thus rule out the possibility that the cyclohexene system simply does not exhibit an OTA signal due to prohibitively unfavorable branching between an unreactive majority species and a reactive minority species in the excited state. In conjunction with the XTA data, this allows us to confidently say that the photochemically relevant excited state species is not a charge transfer state, and the reaction thus proceeds through an entirely different mechanism than in the case of norbornene.

The cyclohexene photocycloaddition mechanism proposed by Kochi and coworkers invokes the cis-trans photoisomerization of a cyclohexene ligand as the initial step, and this was later supported by further steady-state photochemical stereoselectivity experiments reported by Kropp et al. Copper(I) and other transition metals are known to stabilize strained trans-cycloalkenes to furnish isolable species, and thus a transient trans-cyclohexene intermediate is not unreasonable. Additionally, trans-cyclooctene exhibits stronger binding to Cu(I) than its cis counterpart, presumably due to relief of strain. While such an initial photoisomerization step is not directly
supported by our OTA and XTA data, it is consistent with all of our observations. Thus, we propose the mechanism illustrated in Figure 2.10, in which excitation at 267 nm yields a $^1\text{LC}$ ($\pi \rightarrow \pi^*$) Franck-Condon state. We tentatively assign the 280 ps time constant observed by XTA to the photoisomerization and re-binding of a cyclohexene ligand to give the $^1\text{S}_1$ intermediate, as the persistent bleaching of the 1s $\rightarrow$ 4p peak beyond this time is consistent with stronger coordination, and other solution-phase photoisomerization reactions are known to occur on similar time scales. However, it is also possible that the partial recovery of the bleach arises from differences in the coordination of the triplet and singlet ($\pi \rightarrow \pi^*$) states and thus corresponds to ISC, with isomerization and concomitant relaxation of the ($\pi \rightarrow \pi^*$) state occurring within the 2-153 ns window for which we do not have XTA data. Finally, as with norbornene, the cycloaddition reaction proceeds within a few µs to give the product and a coordinatively unsaturated Cu(I) species.

CONCLUSIONS

The Cu(I)-catalyzed [2+2] photocycloaddition of norbornene proceeds following the population of an initial Cu(II)$^*$ MLCT state that persists for 18 ns before relaxing to the LC state that ultimately combines with a ground state monomer to provide the dimer. The LC state is most likely a triplet biradical species, which suggests that the Cu(I) catalyst essentially serves as a pseudo-intramolecular triplet sensitizer. Because the $^1\text{MLCT}$ state may be accessed at near-UV wavelengths, it provides a path by which the high-energy (and presumably short-lived) $^1\text{LC}$ state may be bypassed, while the stronger spin-
orbit coupling in the copper complex compared to the bare olefin promotes efficient ISC. Additionally, the copper center likely serves as a template by holding the two monomers in position prior to excitation, though this latter function must be verified by careful quantum yield measurements. Once the $^3\text{LC}$ state is occupied, the cycloaddition reaction occurs on the time scale of a few $\mu$s.

Surprisingly, the dimerization of cyclohexene under the same conditions proceeds through an entirely distinct reaction mechanism that does not involve any charge transfer between the copper and the ligand(s). Although the XTA and OTA results presented here cannot unambiguously identify the intermediates in this reaction, all our observations are consistent with the mechanism proposed by Salomon and Kochi, in which absorption of a photon drives the cis-trans isomerization of a cyclohexene ligand to provide the reactive species. These results demonstrate that it is possible to take advantage of at least two starkly divergent photocycloaddition pathways using a Cu(I) catalyst and potentially even choose which pathway a particular reaction follows through judicious choice of substrate(s). We expect that these insights will inspire efforts to broaden the scope of both inter- and intramolecular photocycloaddition reactions while also steering them toward the desired stereo- and/or regioisomer(s) of interest.
REFERENCES


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Figure 2.1 $^1$H NMR spectra of 0.6 M norbornene in THF with 3 mM (CuOTf)$_2$-toluene following irradiation at 270 nm in a photoreactor for various times. The spectrum of extracted product mixture after seven days is shown at the top.
Figure 2.2 $^1$H NMR spectra of 0.6 M cyclohexene in THF with 3 mM (CuOTf)$_2$-toluene following irradiation at 270 nm in a photoreactor for various times. The spectrum of extracted product mixture after seven days is shown at the top.
Figure 2.3 Optical absorption spectra of 6 mM CuOTf in THF alone and with 0.6 M norbornene or cyclohexene
Figure 2.4 Ground state (GS) and difference Cu K-edge XANES spectra of 6 mM CuOTf in THF (A) and 6 mM CuOTf and 0.6 M norbornene in THF (B) at several pump-probe delay times. The probe energies for which the short- and long-time kinetics are shown in Fig. 2-6 are indicated by vertical lines and bars, respectively.
Figure 2.5 Transient Cu K-edge XANES spectra calculated from laser-on and laser-off spectra of 6 mM CuOTf in THF (A and B) and 6 mM CuOTf and 0.6 M norbornene in THF (C and D) obtained at several pump-probe delay times (cyan, green, and peach). Ground state spectra (black and blue) are also plotted for reference. The energy of the pre-edge feature that appears at 100 ps only in the sample with norbornene (8.977 keV) is indicated by a vertical arrow.
Figure 2.6 Fast (A) and slow (B) Cu K-edge kinetic traces measured for 6 mM CuOTf in THF (black) and 6 mM CuOTf and 0.6 M norbornene in THF (blue) and corresponding fits (red). The probe energies at which the traces were measured in panels A and B are indicated in Fig. 2-6 by vertical lines and bars, respectively.
Figure 2.7 (A) – (C) X-ray transient absorption difference spectra of 3 mM CuOTf and 0.3 M cyclohexene in THF at various pump-probe delay times. (D) Short-time kinetic trace measured at the probe energy indicated by the vertical line in panels A-C. (E) Long-time kinetic trace averaged over the probe bandwidth indicated by the vertical bar in panels A-C.
Figure 2.8 (A) Optical transient absorption spectra of 6 mM CuOTf and 0.6 M norbornene in THF at representative pump-probe delay times, showing the growth of the ESA signal over the first several ps. The -5 ps spectra of both the Cu + nb sample in THF (blue) and neat THF (gray) show a weak ESA signal due to the multiphoton ionization of the solvent. The early-time kinetic trace taken from the probe region indicated by the vertical bar is shown in the inset with the corresponding multi-exponential fit. (B) Decay-associated spectra of CuOTf + nb obtained from a global fit of the optical transient absorption data.
Figure 2.9 (A) Optical transient absorption spectra of 6 mM CuOTf in THF (black), 6 mM CuOTf and 0.6 M norbornene in THF (blue), and 6 mM CuOTf and 0.6 M cyclohexene in THF (green) averaged over a pump-probe delay window of 2.8 to 3.8 ns. (B) Kinetic traces obtained by averaging over the probe window indicated by the vertical bar in panel (A). (C) Long-time kinetic traces of CuOTf alone scaled by a factor of 0.5 and CuOTf + nb, highlighting the identical kinetics observed on the µs time scale for the different samples. (D) Kinetic trace of CuOTf + nb with the contributions from multiphoton solvent ionization subtracted (blue) and the corresponding fit to a single exponential decay and a persistent offset.
Figure 2.10 Jablonski diagrams for the Cu(I)-catalyzed [2+2] photocycloaddition reactions of norbornene (left) and cyclohexene (right).
CHAPTER 3

Investigating the scope and limitations of Cu(I)-catalyzed intramolecular photocycloaddition of acyclic dienes using X-ray techniques and theoretical calculations to expand reaction boundaries.

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ABSTRACT

The intramolecular [2+2] photocycloaddition reactions have higher regioselectivity and facilitate the synthesis of more challenging and complex products and intermediates compared to the intermolecular [2+2] cycloaddition. Transition metal salts are required to promote the [2+2] photocycloaddition of unconjugated olefins, which would otherwise require prohibitively high excitation energies. In the presence of catalytic copper(I) salts, intermolecular [2+2] photocycloaddition (i.e., dimerization) occurs for a broad range of cyclic monoolefins such as norbornene. On the other hand, intramolecular [2+2] photocycloaddition is only possible for 1,6-dienes, which have a three-atom tether. We have used 1,6-heptadiene, 1,7-octadiene, 1,8-nonadiene, and norbornene as model substrates to understand the origin of this strict selectivity using a combination of density functional theory (DFT) calculations and high energy resolution fluorescence detected X-ray absorption near-edge structure (HERFD-XANES) spectroscopy at the copper K-edge. The DFT-optimized structures of photochemically active 1,6-heptadiene and norbornene share a nearly coplanar olefin-olefin geometry about Cu(I), while the corresponding dihedral angles in the 1,7- and 1,8-diene complexes are substantially distorted toward a $D_{2d}$ local symmetry. The degree of distortion is also evident in the 1s$\rightarrow$4p region of the HERFD-XANES spectra, where the coplanar complexes exhibit a much more pronounced absorption band at 8.989 keV. Together, these computational and experimental results allow us to correlate coordination geometry with reactivity, and we conclude that the increased flexibility of the
alkyl tethers in 1,7- and 1,8-dienes results in an unfavorable orientation of the alkenyl molecular orbitals for photocycloaddition. We are able to sterically modify the unreactive structures in order to acquire a similar coordination geometry as that of the reactive substrates towards the cycloaddition. The $^1$H NMR spectra of the modified structures show a change in the chemical environment around the alkene groups in the presence of Cu(I) catalyst and UV irradiation.
INTRODUCTION

Organic synthesis plays an essential role in various fields such as pharmaceuticals, medicine, the food industry, and cosmetics. Photon mediated synthesis is important when the products are not achievable through thermal or electrochemical reaction conditions. Due to the feasibility and higher predictability, [2+2] photocycloaddition reaction is recognized as the most reliable and most synthetically useful photochemical reaction.\(^1,2\) We recently demonstrated that the Cu(I)-catalyzed photodimerization of cyclic alkenes can proceed through either charge transfer or ligand photoisomerization as the initial step, though many other aspects of the reaction mechanism remain unclear.\(^3\) Here we extend this work to understand the mechanisms and limitations of Cu(I)-catalyzed intramolecular cycloadditions.

The [2+2] photocycloaddition is a key step to synthesize structurally complex and synthetically challenging molecules by constructing a cyclobutane ring in a single step. These cyclobutane moieties can further convert as an intermediate product in another complex reaction through ring expansion or fragmentation to generate various new synthesis pathways.\(^2\) In the intramolecular case, two tethered alkene groups interact to give a fused cyclobutane product. The first known discovery of the intramolecular [2+2] photocycloaddition was reported by Ciamician and Silber in 1908, which involved the formation of carvone camphor by exposing carvone to sunlight.\(^4,5\) Unlike the intermolecular photocycloaddition, intramolecular reactions are more
predictable and have higher regio- and stereoselectivities determined by the number of atoms in the tether linkage and substituents on the tether.\textsuperscript{2,6,7}

Intramolecular cycloaddition reactions can generate two regioisomeric products either in a parallel (straight) or crossed fashion, based on the way the four alkene carbons connect with each other to form bonds.\textsuperscript{6,8} By studying the mercury sensitized photolysis of nonconjugated dienes, Srinivasan and coworkers proposed that 1,4- and 1,6-dienes undergo straight cycloaddition and 1,5-dienes undergo crossed cycloaddition.\textsuperscript{2,7} Based on the results, Srinivasan \textit{et al}. suggested that the initial step of an intramolecular photocycloaddition is the formation of a five-membered ring diradical intermediate,\textsuperscript{7,9} though some substrates such as photolysis of 1,8-divinylnapththalene deviate from this empirical “rule of five” depending on the structural arrangements\textsuperscript{5,9–11}

Direct excitation or photosensitization in [2+2] cycloaddition is mechanistically limited to coordinate electron-rich $\pi$ systems. Transition metal compounds are studied for their effective coordination with nonconjugated $\pi$ substrates, which enhances the lifetime of reactive excited states and promotes electron transfer in intermediate steps.\textsuperscript{12} Direct excitation is less efficient for unconjugated olefins due to the lesser ring strains and the challenges of using vacuum UV range excitation in the condensed phase. Earth-abundant, low-cost copper salts show remarkable activity as catalysts in the [2+2] photocycloaddition reactions of olefins.\textsuperscript{13–15} The charge transfer (CT) bands of Cu-coordinated olefinic complexes appear around 250 nm or above, and by exciting the complexes at these wavelengths, it is possible to drive
photocycloaddition of unconjugated compounds at comparatively lower energies than without the metal. In 1973, Salomon and Kochi introduced copper(I) trifluoromethanesulfonate (triflate, or OTf) as a superior catalyst for photocycloaddition of olefins. In 1978, Evers and Mackor reported the first observed Cu(I)-catalyzed intramolecular photocycloaddition reaction, which involved the photocycloaddition of diallyl ether.

However, Cu(I)-catalyzed photocycloadditions have their own limitations. Photoreaction of acyclic olefins is limited only to substrates with a three-atom tether between the two alkenes, i.e., 1,6-dienes, suggesting that olefins with longer or shorter tethers do not adopt the proper coordination geometry about the copper site. Nevertheless, the utility of this reaction is so great that 1,6-dienes have been retrosynthetically targeted in several natural product syntheses to enable the Cu(I)-catalyzed [2+2] photocycloaddition en route to the desired products.

Salomon et al. investigated the stereochemistry of the cyclohexene and cycloheptene by utilizing carbon-13 magnetic resonance (13C NMR) and X-ray crystallographic studies to propose a mechanism that explains the stereospecificity of the Cu(I)-catalyzed cycloolefin photodimers. Based on their observations, they proposed that concerted, orbital-symmetry controlled trans-cycloolefin intermediate formation governs the stereoselectivity of cyclohexene and cycloheptene photodimerization. Hence, the inability of larger ring size cycloalkenes and acyclic olefins to yield reactive trans-
intermediates, which would conserve orbital symmetry, results in their reluctance to undergo Cu(I)-catalyzed photodimerization.\textsuperscript{13,22}

While ligand geometry and \(\pi\)-orbital orientation has been invoked to justify the observation that intramolecular cycloadditions are only possible for 1,6-dienes,\textsuperscript{21} the reason for the inactivity of other acyclic olefins towards photocycloaddition has not been clearly elucidated. Several studies in literature were done to understand the coordination geometries of copper-olefin complexes by synthesizing, isolating and characterizing the coordinated structures.\textsuperscript{20,23,24} The results do not provide conclusive evidence to support the notion that acyclic dienes are less capable of coordinating with copper metal, or that their inactivity is attributable to unfavorable coordination around the Cu atom resulting from strain or geometrical flexibility.

In this work, we focus on the Cu(I)-catalyzed [2+2] photocycloaddition of 1,6-heptadiene, 1,7-octadiene and 1,8-nonadiene nonconjugated olefins. \(^1\text{H}\) NMR allows us to track the photoreactivity of the olefin complexes. Our results are consistent with the literature, which shows that only 1,6-dienes undergoes photocycloaddition. We used both theoretical and experimental approaches to understand the metal-coordinated environment and its effect on photoreactivity. High energy resolution fluorescence detected X-ray absorption near edge structure technique (HERFD-XANES) and density functional theory (DFT) calculations provide complementary structural probes of the Cu(I) complexes of the acyclic dienes as well as Cu(I) bis(norbornene), a complex that has been thoroughly studied as a model for intermolecular [2+2] photocycloaddition.\textsuperscript{18}
HERFD-XANES provides higher resolution and sensitivity towards the electronic structures compared to conventional total fluorescence yield (TFY-XANES) analysis.\textsuperscript{25–27} X-ray Raman scattering studies conducted by Eisenberg and co-workers showed that the measured linewidth is narrower than the conventional fluorescence linewidth when collecting only the Kα\textsubscript{1} emission due to the longer lifetime of the 2p core-hole state compared to the 1s core-hole state.\textsuperscript{28,29} Later, Hämäläinen \textit{et al.} took advantage of the same linewidth narrowing phenomenon to improve the resolution of X-ray absorption spectroscopy.\textsuperscript{25} Lancaster and coworkers have shown that HERFD gives improved resolution of the 1s $\rightarrow$ 4p spectral features in the spectra of copper complexes;\textsuperscript{29} here, we use the same approach to better understand the Cu(I)-olefin coordination.

Combining the HERFD technique with DFT calculations allows us to gain a more complete understanding of the structural arrangements involved. Furthermore, integrating HERFD-XANES with DFT calculations and conventional photochemistry allows us to correlate structure and reactivity in Cu(I)-catalyzed intramolecular photocycloadditions. We extended our computational work to simulate steric modifications of unreactive substrates that can adopt a coordination geometry similar to that of reactive substrates. We focused on synthetically feasible starting geometries in order to experimentally analyze the changes in photoreactivity of the substituted structures.
EXPERIMENTAL PROCEDURE

SYNTHETIC METHODS

All synthesis procedures were performed under inert conditions using N\textsubscript{2} and standard Schlenk line techniques. methyltriphenylphosphonium bromide (>98% purity), (±)-Citronellal (96% purity) were obtained from Alfa Aesar, and isopropyltriphenylphosphonium bromide (98% purity) was obtained from AmBeed. n-Butyllithium (1.6 M solution in hexanes), dichloromethane (DCM, stabilized with BHT) and tetrahydrofuran (THF, unstabilized) were purchased as anhydrous, air-free reagents from Thermo Scientific. Copper(I) trifluoromethanesulfonate toluene complex (2:1) (>98% purity) was obtained from Sigma Aldrich. All reagents were used as received. \textsuperscript{1}H NMR spectra were analyzed using the MestReNova 14.1.2-25024 software package.

4,8-dimethyl-1,7-nonadiene was prepared according to a modified literature procedure.\textsuperscript{30} A solution of 3.75 g (10.5 mmol) methyltriphenylphosphonium bromide in 8.0 mL of anhydrous DCM was prepared in a 50 mL round bottom flask under N\textsubscript{2}. The solution was cooled to 0 °C using an ice bath. Then, 7.0 mL of an n-butyllithium solution (1.6 M in hexane; 11.2 mmol) was added dropwise while stirring the DCM solution. After an hour, 2.4 mL (13.2 mmol) of citronellal was added. The solution was then stirred at room temperature for 24 h and subsequently cooled back to 0 °C before being quenched with 40 mL of aqueous saturated NH\textsubscript{4}Cl. The product was extracted to pentane, and the combined organic fractions were washed with brine and dried over anhydrous MgSO\textsubscript{4}. The solvent was removed by rotary evaporation, and the diene product was purified.
by column chromatography (silica; 100% pentane) followed by fractional
distillation to remove residual solvent to give the product as a colorless oil. \(^1\)H
NMR (400 MHz, CDCl\(_3\)) \(\delta \) 5.72 (ddt, \(J = 17.2, 10.0, 7.1 \) Hz, 1H), 5.10 – 5.00 (m, 
1H), 5.00 – 4.88 (m, 2H), 2.07 – 1.77 (m, 4H), 1.63 (d, \(J = 1.8 \) Hz, 3H), 1.55 (s, 
3H), 1.45 (dq, \(J = 13.3, 6.6 \) Hz, 1H), 1.35 – 1.23 (m, 1H), 1.09 (dddd, \(J = 13.4, 
9.0, 7.8, 6.0 \) Hz, 1H), 0.82 (d, \(J = 6.6 \) Hz, 3H). (Small amounts of H\(_2\)O and
pentane solvent peaks overlap with the product peaks in \(^1\)H NMR spectrum.)

2,5,9-trimethyl-2,8-decadiene was synthesized using the same procedure
but with isopropyltriphenylphosphonium bromide (4.00 g, 10.4 mmol) as the
ylide precursor. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta \) 5.06 (q, \(J = 8.7 \) Hz, 2H), 1.92 (dtp, 
\(J = 20.0, 14.1, 6.9 \) Hz, 3H), 1.76 (dt, \(J = 14.6, 7.6 \) Hz, 1H), 1.64 (d, \(J = 7.1 \) Hz, 
6H), 1.54 (d, \(J = 3.6 \) Hz, 6H), 1.40 (dp, \(J = 13.2, 6.6 \) Hz, 1H), 1.33 – 1.19 (m, 
1H), 1.14 – 1.00 (m, 1H), 0.81 (d, \(J = 6.6 \) Hz, 3H).

**COMPUTATIONAL METHODS**

DFT/TD-DFT calculations were performed using the GAMESS quantum
chemistry package. Geometry optimizations were carried out using the
generalized gradient approximation (meta-GGA) hybrid M-11 exchange-
correlation functional\(^{31}\) with the Slater-type 6-31G** basis set\(^{32-35}\) for C, H, and
O and the Sapporo-TZP-2012-diffuse basis set\(^{36}\) for Cu.\(^{37}\) All Cu(I) complexes
were taken to be in the +1 cationic singlet spin state, and calculations were done
both in vacuum and solvent phase. The Kirkwood-Onsager spherical cavity
model was used for the study of solvent effects.\(^{38-40}\) Coordinates of the
optimized geometries are provided in the Table 3.3-3.5.
STEADY STATE PHOTOCHEMISTRY

Photochemical reactor experiments were performed according to a modified literature procedure.\cite{ref3,ref18} Approximately 0.6 mmol of diene and 0.02 mmol of \((\text{CuOTf})_2\)·toluene (0.04 mmol of Cu(I)) were dissolved in 1.5 mL of dry, anhydrous THF under N\(_2\) in a quartz reaction vessel and sealed with a rubber septum and parafilm. The quartz vessels were then placed inside a photoreactor (Rayonet RPR-100) and irradiated with 254 nm using sixteen 12-inch, 14 W fluorescent bulbs. Reaction temperatures were maintained around 35 °C using a cooling fan. \(^1\text{H}\) NMR analysis was performed at various reaction times by taking small aliquots of the irradiated reaction mixtures. NMR samples were prepared in CDCl\(_3\) and measured using a Bruker Avance III 400 MHz instrument. After seven days of irradiation, samples were extracted into pentane, washed with deionized water to remove residual copper salts and THF solvent, dried over anhydrous MgSO\(_4\), and rotary evaporated.

HIGH-ENERGY RESOLUTION FLUORESCENCE DETECTION (HERFD)

Background subtraction and normalization of HERFD spectra was performed using Athena, a part of the Demeter 0.9.25 software package.\cite{ref41} Analysis of HERFD spectra was performed using MATLAB R2019a. All spectra were fit to the sum of four Gaussian functions plus an error function.

HERFD-XANES measurements were performed at the Inner Shell Spectroscopy beamline (8-ID) at the National Synchrotron Light Source II (NSLS-II) at Brookhaven National Laboratory. Details about the beamline instrumentation and data acquisition have been published elsewhere.\cite{ref42}
incident beam was focused to an 80 µm diameter circular Gaussian spot at the sample position using a polycapillary optic. The incident energy was scanned using a Si(111) monochromator, and the emission was monochromatized using a Johann (backscattering) spectrometer with a Ge-444 crystal. XANES spectra were acquired by collecting the peak of the of Kα₁ emission line with a Pilatus 100K detector (HERFD) and simultaneously collecting the total fluorescence using a passivated implanted planar silicon diode (TFY). The spectral resolution was determined to be 1.4 eV and 1.8 eV (FWHM), respectively. All spectra shown here are the average of at least 10 scans, and successive scans were constantly monitored to ensure the spectra were not changing due to oxidation from exposure to air and/or beam induced sample damage. A helium enclosure was placed between the sample, crystal, and detector to limit attenuation of the emission signal.

Samples were prepared in an argon-atmosphere glovebox at the beamline immediately before measuring. (CuOTf)₂·toluene (52 mg, 0.1 mmol) was dissolved in 40 mL of THF and filtered through 0.45 µm syringe filter. A portion of diene (2.0 mmol) was then added to give a solution that was 5.0 mM in Cu(I) and 50 mM in diene. In the case of norbornene, 4.0 mmol was added instead to give a solution that was 100 mM in monoolefin. Each sample was sealed with a rubber septum, transferred from the glovebox to the X-ray hutch, and delivered to the X-ray beam path using a recirculating peristaltic pump as a free-flowing 390 µm diameter liquid jet. The volume surrounding the sample jet was
enclosed with mylar film, and both the sample and the sample chamber were continuously purged with N₂ to prevent oxidation of the Cu(I).

RESULTS AND DISCUSSION

¹H NMR provides a straightforward means of tracking the progress of Cu(I)-catalyzed [2+2] photocycloadditions through the disappearance of the alkene peaks in the starting material and the appearance of new aliphatic peaks in the product(s). The time-course spectra of 1,6-heptadiene, 1,7-octadiene, and 1,8-nonadiene following irradiation at 254 nm in the presence of ~7 mol% CuOTf are shown in Figure 3.1-3.3. After only two days, the alkene peaks in 1,6-heptadiene have nearly disappeared. On the other hand, there is no evidence of any change in the spectra of the 1,7- and 1,8-dienes even after one week of irradiation. These results are consistent with previous studies¹,²,¹³,²⁰ and confirm that Cu(I)-catalyzed intramolecular photocycloaddition is only feasible for 1,6-dienes. We also irradiated a sample of neat 1,7-octadiene in the presence of catalytic CuOTf and still did not observe any changes in the NMR spectra (Figure 3.4).

In light of these results, we sought to analyze the coordination environment of the Cu(I)-diene complexes by measuring the corresponding Cu K-edge XANES spectra. Intensity and number of peaks in the 1s→4p transition region in the HERFD-XANES is also sensitive to the coordination environment of the Cu metal center, amount of overlap between the metal and ligand orbitals and oxidation state of the metal.³,⁴³,⁴⁴ A comprehensive analysis of the Cu K-edge XAS spectra carried out by Solomon and coworkers revealed that Cu(I)
complexes have signature features such as, peak shape, intensity, and energy position, in the $1s \rightarrow 4p$ transition region, which correlate with the oxidation state, geometry and coordination number of the metal center.\textsuperscript{43} They correlated ligand field theory with the interpretation of Cu(I) K-edge features in relation to the associated bond covalency and orbital overlap resulting from the ligand field splitting and degeneracy of the $4p_{x,y,z}$ orbitals. Solomon \textit{et al.} observed that as the energy splitting increases, the degree of covalent overlap between the ligand and metal orbitals also increases, leading to reduced transition intensities in comparison to those involving lower energy metal orbitals.\textsuperscript{43,45} Thus, in 2-coordinate linear Cu(I) complexes with $D_{\infty h}$ symmetry, the $1s \rightarrow 4p_z$ transition peak has a lower intensity and higher energy compared to the degenerate $1s \rightarrow 4p_{xy}$ transition peak, which appears at a relatively lower energy position on the X-ray absorption spectrum.\textsuperscript{43} Accordingly, tetrahedral ($T_d$) geometry with relatively similar energy $4p_{x,y,z}$ orbitals shows lower intense peaks at higher energies compared to the linear geometry.

Apparently, some Cu-mediated HERFD and TFY X-ray absorption studies have observed several new features in the $1s \rightarrow 4p$ transition region in addition to the major ligand field splitting related transitions.\textsuperscript{29,45} This includes the appearance of shoulder peaks and additional less intense peaks on the pre-edge and rising edge regions.\textsuperscript{29,45,46} These features cannot be explained by simple ligand field theory. The additional features observed are suggested to be a result of interactions between Cu $4p$ orbitals and unoccupied ligand orbitals, including symmetric or nonsymmetric Cu $4p$ and ligand orbital mixing such as
metal to ligand charge transfer (MLCT), as well as Cu 3d and low energy ligand orbital mixing. Peak broadening and splitting changes on the rising edge may also be influenced by the coordinated ligand and steric effects. Recent computational work by Rudolph and Jacob addressed the limitations of the ligand field model mentioned above and confirmed the earlier ligand field assignments for the major peaks while also explaining the new features observed in the XAS. Their calculations interpreted the peak broadening and splitting of differently coordinated Cu complexes and shows that $D_{2d}$ (i.e., flattened) four-coordinate Cu(I) complexes have a broader and bluer distribution of $1s \rightarrow 4p$ transitions than similarly tetrahedral complexes, in agreement with earlier work by Solomon and coworkers.

Accordingly, we chose to use HERFD-XANES measured at Cu Kα emission line to record these features with the best possible resolution and thereby learn about the metal-olefin coordination geometry. The improved resolution afforded by HERFD is highlighted in Figure 3.5, which shows both the HERFD and TFY XANES spectra of the 1,6-heptadiene complex of Cu(I).

HERFD spectra of Cu(I) coordinated by the unsubstituted 1,6-, 1,7-, and 1,8- linear dienes and norbornene in THF are presented in Figure 3.6. As expected, the spectra do not exhibit proper $1s \rightarrow 3d$ pre-edge peaks due to the $3d^{10}$ electron configuration of Cu(I). Instead, we observe several well-defined features along the rising edge that may be assigned to $1s \rightarrow 4p$ transitions. All spectra are well modeled by only four Gaussian peaks and an error function, allowing us to compare the individual peaks across the entire series of spectra.
The two lowest energy peaks are consistent in position, width, and magnitude for all complexes. However, the third peak is more prominent and hypsochromically shifted in the spectra of the 1,6-heptadiene and norbornene complexes, giving rise to a much stronger shoulder ~8 eV before the white line than observed for the 1,7- and 1,8-dienes. It is only with the superior resolution of the HERFD spectra that we are able to obtain reliable and quantitative fits of these features, demonstrating the power of the HERFD technique.

The substantially stronger shoulder in the spectra of the two photoreactive complexes (1,6-heptadiene and norbornene) supports the hypothesis that these substrates coordinated the Cu(I) center in a similar geometrical arrangement while 1,7-octadiene and 1,8-nonadiene adopt a different coordination geometry. Appearance of a shoulder peak can correlate with tetrahedral ($T_d$) geometry further distorted towards $D_{2d}$ twisted geometry and approaching a planar, rectangular shape $D_{2h}$ geometry in 1,6-heptadiene and norbornene Cu complexes, while 1,7-octadiene and 1,8-nonadiene relaxes at $D_{2d}$ symmetry which has deviated from planar geometrical arrangement compared to the $D_{2h}$. We cannot solely confirm the idea of having similar metal coordinated environments for the photoreactive and unreactive olefins only by analyzing HERFD-XANES data, but these spectral features are consistent with the literature studies discussed earlier regarding different geometric arrangements and additional spectral features appears in the XANES region of Cu complexes.

To support these experimental observations and gain a better understanding of our XANES data, we used DFT to calculate the optimized
structures and corresponding single point energies of the Cu(I) bis(olefin) complexes. DFT is recognized as a conventional tool for speculating on the structures, geometries, electronic properties, and other characteristics of transition metal-mediated compounds.\textsuperscript{47,48} This theory is beneficial for Cu systems and has been successfully applied in many Cu(I)-mediated calculations.\textsuperscript{49,50}

For each Cu(I) diene complex, we optimized the geometry starting from three initial structures: the monodentate, the mono(bidentate) with parallel terminal alkenes, and the mono(bidentate) with perpendicular terminal alkenes and as in a solvent and gaseous states. The optimizations converged to two distinct geometries depending on the initial structure: one with a nearly coplanar arrangement of the terminal alkenes about the Cu(I) center and one in which the alkenes are twisted out of plane toward a tetrahedral arrangement. Optimized structures with their energy values are summarized in Figure 3.8 and 3.9.

Based on the energies, more planar and parallel configuration around Cu(I) atom showed as the most favorable structure for 1,6-heptadiene. We calculated the dihedral angle between the two alkene groups coordinated to the metal center as 0.13°, which confirms the coplanar arrangement of the ligands. Although 1,7-octadiene exhibits a preference for the parallel geometry, we observed higher dihedral angles compared to 1,6-heptadiene and lesser relative energies between the parallel and perpendicular arrangements of the optimized 1,7-diene structures. Due to the negligible energy differences, the 1,7-parallel
and 1,7-perpendicular structures can interchange even at room temperature, which may negatively impact the reactivity of 1,7-octadiene by adopting a less favorable coordination environment. Both geometrical arrangements of 1,8-nonadiene showed larger dihedral angles compared to 1,6-heptadiene and favors the more twisted perpendicular coordination around the Cu metal. Similar to 1,6-heptadiene, norbornene shows smaller dihedral angles favoring the exo-configuration, which agrees with the experimental results of exo-trans-exo dimer as the major product.

We observed a similar energy minima pattern for the structures optimized in both the solvent state and the gaseous state calculations. The solvation model we used for the calculations is the Kirkwood-Onsager model, which simulates the solute as if it were inside a homogeneous spherical solvent cavity.\(^{38-40}\) We used a dielectric constant of 7.43 for the THF solvent and performed optimizations with different solvent radius values. We primarily considered the molecular area, collision distances, and accounted for Van der Waals forces to estimate the solvent cavity radius.\(^{51}\) We started the calculations from a 2 Å spherical cavity to obtain more accurate results. Interestingly, we observed similar energy patterns as gaseous phase for higher radii calculations compared to those for a 2 Å radius. Calculated energies with 3.5 Å radius are reported and compared in Table 3.2.

In agreement with the XANES analysis presented above, the alkene coplanarity in the lowest energy configurations appears to correlate well with photoreactivity. The dihedral angles between the alkenes in the geometries are
nearly 0° for all reactive ligands (0.13° for 1,6-heptadiene, 1.1° for norbornene) but quite large for all unreactive ligands (21.2° for 1,7-octadiene and 42.5° for 1,8-nonadiene). The similarity in the lower dihedral angles of the optimized structures in 1,6-heptadiene and norbornene supports the geometry arrangement of the D$_{2h}$ symmetry, which generates ligand field splitting of the 4$p_{x,y,z}$ orbitals, resulting an additional metal-ligand orbital overlaps. Hence, a common shoulder peak appears in the HERFD spectra for the same substrates could be due to higher energy 4$p_z$ overlaps with the lower lying ligand orbitals which increases the covalency of the bond. The higher dihedral angles calculated for 1,7-octadiene and 1,8-nonadiene are consistent with the D$_{2d}$ symmetry, which has a smaller splitting between the degenerate 4$p_{x,y}$ and 4$p_z$ orbitals compared to the D$_{2h}$ configuration. As a result, there is a lesser prominent appearance of an additional shoulder peak. This observation supports the hypothesis that photoreactive alkenes are coordinated to the Cu metal in a similar geometrical arrangement, which is different from that of unreactive substrates.

The reason for the alkenes to approach the metal center in different ways could be due to the steric related factors in the structure. Substituents on the structure can affect the coordination environment of the complex.\textsuperscript{2} We expanded our computational study to identify 1,7- or 1,8- dienes bearing additional steric bulk that enforces the putatively photoreactive coplanar coordination geometry, focusing on structures that are synthetically accessible from the commercially available starting materials in only a few steps to
determine if alkene arrangement is truly the determining factor for diene photoreactivity.

According to our DFT geometry optimizations, the Cu(I)-coordinated 4,8-dimethyl-1,7-nonadiene adopts a coplanar geometry with a 0.9° alkene-alkene dihedral angle, while 2,5,9-trimethyl-2,8-decadiene exhibits a 14° angle in its lowest energy configuration. These ligands were obtained in a single step from commercially available citronellal through a Wittig reaction with methyltriphenylphosphonium bromide or isopropyltriphenylphosphonium bromide in the presence of n-butyl lithium, as described above in the Synthetic Methods section. We evaluated the photoreactivity of the synthesized molecule using the photoreactor and ¹H NMR studies. Similar to the unsubstituted 1,7-diene, we did not observe any changes in the integration of the alkene or alkane peaks in the NMR spectra for 2,5,9-trimethyl-2,8-decadiene, even after seven days of irradiation. However, for 4,8-dimethyl-1,7-nonadiene, we observed changes in the peak multiplicity of the alkene peaks compared to the starting material (Figure 3.10). This change in peak multiplicity is related to the alteration in the chemical environment. The photochemically inert conditions observed for the sterically modified structures may be related to the unfavorable structural interconversion mediated by Cu and/or steric hindrance induced by the substituted groups. Alternatively, these conditions may require long and intense photon irradiation to reach higher energy barriers.

We also studied the HERFD spectra of the synthesized ligands (Figure 3.11), as well as commercially available photoreactive norbornadiene and 4-
vinylcyclohexene, to compare their spectral features (Figure 3.12). We observed the previously discussed common shoulder peak in the spectra of the synthesized 4,8-dimethyl-1,7-nonadiene, as well as in the spectra of the commercial photoreactive substrates. This observation further supports the hypothesis of a coplanar geometrical arrangement of the photoreactive olefins with Cu. However, for 2,5,9-trimethyl-2,8-decadiene, we observed a completely different HERFD-XANES region with no clear shoulder peak. Further studies are required to understand the geometrical arrangements and coordination environment around the Cu atom in order to extract the new features of the 2,5,9-trimethyl-2,8-decadiene HERFD spectrum.

To better understand the photoreactivity of the modified diene structures and their dependence on steric effects and geometrical arrangements, further computational and experimental photochemical analysis is necessary. These analyses will enable us to design new acyclic dienes with reactive trajectories, thereby achieving enhanced photoreactivity.

CONCLUSIONS

The Cu(I)-catalyzed [2+2] intramolecular photocycloaddition reactions are limited to three-atom tether dienes. By comparing the Cu K-edge HERFD-XANES spectra and DFT-optimized structures of the Cu(I) complexes of photoreactive 1,6-heptadiene and norbornene with those of unreactive 1,7-octadiene and 1,8-nonadiene, we have shown that to undergo Cu(I)-catalyzed [2+2] photocycloaddition, two alkene groups must coordinate the metal center in a coplanar arrangement. This geometric arrangement may facilitate close
proximity for orbital overlap, reduce steric hindrance, and promote favorable charge distribution for new bond formation. Steric modifications to the structures could promote the molecules towards cycloaddition reactions, while steric hindrance and geometry rearrangements in the presence of metal could reduce the reactivity and encourage unfavorable reaction pathways. When designing new structures to promote photocycloaddition, these factors should be carefully minimized through additional computational work and geometry optimization, followed by experimental evaluation.
REFERENCES


(7) Srinivasan, R.; Carlough, K. H. Mercury Photosensitized Internal Cycloaddition Reactions in 1,4-, 1,5-, and 1,6-Dienes. J. th 1967, 89 (19), 4932–4936.


(21) Subrata Ghosh, Swadesh R. Raychaudhuri, and R. G. S. Synthesis of Cyclobutanated Butyrolactones via Copper(1)-Catalyzed Intermolecular


Figure 3.1 $^1$H NMR spectra of 0.2 M 1,6-heptadiene with 2 mM (CuOTf)$_2$·toluene in THF after excitation at 254 nm in a photoreactor for different irradiation times.
Figure 3.2 $^1$H NMR spectra of 0.2 M 1,7-octadiene with 2 mM (CuOTf)$_2$·toluene in THF after excitation at 254 nm in a photoreactor for different irradiation times.
Figure 3.3 $^1$H NMR spectra of 0.2 M 1,8-nonadiene with 2 mM (CuOTf)$_2$-toluene in THF after excitation at 254 nm in a photoreactor for different irradiation times.
Figure 3.4 $^1$H NMR spectra of 0.2 M 1,7-octadiene with 2 mM (CuOTf)$_2$·toluene after excitation at 254 nm in a photoreactor for nine days (without THF solvent).
Figure 3.5 Comparison of the HERFD-XANES and TFY-XANES of 1,6-heptadiene to illustrate the improved resolution of the HERFD at $1s \rightarrow 4p$ region.
**Figure 3.6** Comparison of the high-energy resolution fluorescence detected (HERFD) spectra of 50 mM (A) 1,6-heptadiene and 1,7-octadiene, (B) 1,6-heptadiene and 1,8-nonadiene (C) 1,6-heptadiene and norbornene with 2.5 mM (CuOTf)$_2$·toluene in anhydrous THF. 1,6-heptadiene and norbornene have a shoulder peak around 8.989 keV which is not prominent in 1,7-octadiene and 1,8-nonadiene.
**Figure 3.7** High-energy resolution fluorescence detected (HERFD) spectral fittings of 50 mM 1,6-heptadiene with 2.5 mM (CuOTf)$_2$·toluene in anhydrous THF.
Figure 3.8 Optimized molecular structures of acyclic Cu(I) complexes and related dihedral angles between the two terminal alkenes. (A) Cu(I)-1,6-heptadiene, (B) Cu(I)-1,7-octadiene, (C) Cu(I)-1,8-nonadiene complexes. Atom labels: copper-maroon, carbon-blue, hydrogen-gray color.
Figure 3.9 Optimized molecular structure of the bicyclic Cu(I)-bis(norbornene) complex. Atom labels: copper-maroon, carbon-blue, hydrogen-gray color.
Figure 3.10 $^1$H NMR spectra of 0.2 M 4,8-dimethyl-1,7-nonadiene with 2 mM (CuOTf)$_2$·toluene in THF after excitation at 254 nm in a photoreactor for different irradiation times.
**Figure 3.11** Comparison of the HERFD spectra of 50 mM (A) 1,6-heptadiene (B) 4,8-dimethyl-1,7-nonadiene (C) 2,5,9-trimethyl-2,8-decadiene with 2.5 mM (CuOTf)$_2$·toluene in anhydrous THF. 1,6-heptadiene and synthesized 4,8-dimethyl-1,7-nonadiene have a shoulder peak around 8.989 keV which is absent in synthesized 2,5,9-trimethyl-2,8-decadiene ligand.
Figure 3.12 Comparison of the HERFD spectra of 50 mM (A) 1,6-heptadiene (B) norbornadiene (C) 4-vinylcyclohexene with 2.5 mM (CuOTf)$_2$·toluene in anhydrous THF. All spectra have a shoulder peak around 8.989 keV.
Table 3.1 DFT-optimized structures, energies, and dihedral angles of Cu(I)-olefin complexes. Dihedral angles are measured between Cu(I) coordinated terminal alkene groups and relative energies are calculated with respect to the lowest energy configurations of each ligand.

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<th>Single point energy (eV)</th>
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<td>Complex</td>
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<td>Error</td>
<td>Dihedral Angle</td>
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<td>----------------------------------------------</td>
<td>---------</td>
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<td>----------------</td>
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*NA-dihedral angle of mono-coordinated complexes are not applicable.*
Table 3.2 Solvent phase DFT-optimized energies of the acyclic Cu(I)-olefin complexes. Relative energies (ΔE) are calculated with respect to the lowest energy configuration.

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<th>ΔE in Solvent (eV)</th>
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Table 3.3 Coordinates of the optimized Cu(I)-1,6-heptadiene structure.

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Table 3.4 Coordinates of the optimized Cu(I)-1,7-octadiene structure

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Table 3.5 Coordinates of the optimized Cu(I)-1,8-nonadiene structure

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