

**N-Heterocyclic Carbenes for Applications in
Surface Enhanced Raman Spectroscopy,
Asymmetric Synthesis and Actinide Chemistry**

A Dissertation Presented for the
Doctor of Philosophy
Degree
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Joseph Felix DeJesus

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This work is dedicated to my late mother, Janet DeJesus.

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Abstract

N-Heterocyclic carbenes (NHCs) have been an incredibly important ligand in the field of organometallic chemistry for the last 25 years. The ability of this ligand platform to stabilize higher oxidation states on transition metals and to form highly stable metal carbon bonds has revolutionized organometallic chemistry by replacing ligands such as phosphines. While NHCs are highly effective for organometallic chemistry on transition metals, there are still several areas in which NHCs have had limited applications.

This dissertation covers research conducted towards remedying such shortcomings of NHCs in three specific fields: (1) modification of noble metal surfaces, (2) development of asymmetric variants of NHCs, and (3) the use of NHCs as ligands in actinide chemistry. First, two novel methods were developed to place NHCs on gold surfaces. Functionalized NHC precursors protected with carbon dioxide (CO_2) were applied to gold film over nanosphere (AuFON) surfaces. Alternatively, gold(I) NHC complexes, were synthesized and applied to gold nanoparticles (AuNPs). Both AuFONs and AuNPs were analyzed with surface-enhanced Raman spectroscopy (SERS) through a collaborative study. Second, the first examples of chiral macrocyclic tetra-NHCs were synthesized and characterized. These polydentate class of NHC ligands could be important for asymmetric catalysis. The oxidation chemistry of one ligand system ligated to iron(II) was studied extensively. Third, the first examples of uranium octa-NHC complexes were prepared. These uranium complexes have the most uranium-carbon bonds of any reported molecule.

Table of Contents

Chapter One: Introduction to N-Heterocyclic Carbene Chemistry and their Applications.....	1
Chapter Two: N-Heterocyclic Carbenes as a Robust Platform for Surface-Enhanced Raman Spectroscopy.....	21
Chapter Three: Facile Synthesis and in situ Chemical Transformations of SERS Active N Heterocyclic Carbene Functionalized Gold Nanoparticles.....	53
Chapter Four: A Chiral Macrocyclic Tetra-N-Heterocyclic Carbene Yields an “All Carbene” Fe(IV) Complex.....	92
Chapter Five: Towards a General Synthesis of C ₂ Symmetric Diimidazolium and Tetra-Imidazolium Macrocycles from Chiral 1,2-Diamines.....	154
Chapter Six: Disparate Azide Reactivity of a Chiral Iron(II) Tetra-NHC Complex.....	211
Chapter Seven: Octa-NHC U(IV) Complexes Isolated By Reactions with Dianionic Tetra-NHCs.....	248
Chapter Eight: Conclusion:.....	269
References:.....	272
Vita:.....	310

List of Tables

Table 4.1: Crystallographic data for complexes 4.4-4.9.	128
Table 4.2: Selected bond lengths and angles for compounds 4.6 – 4.9.....	129
Table 5.1: Optimization of desulfurization of 5.2-Thiourea to 5.2-Imidazole.....	166
Table 5.2: Isolated species with yields for chiral diimidazoles and macrocycles. Cells highlighted in yellow are in the process of being completed.	168
Table 6.1: Summary of Azide Reactivity Screen	232

List of Figures

Figure 1.1: General overview of NHC ligands.	3
Figure 1.2: Olefin metathesis mediated by Grubbs' ruthenium NHC complex.....	4
Figure 1.3: Facile functionalization of crystalline gold surfaces reported by Crudden and Horton.....	6
Figure 1.4: Diagram of basic SERS mechanism using a thiol ligand.....	7
Figure 1.5: Applications of NHC Functionalized Surfaces.	8
Figure 1.6: Required orbital orientation for NHCs to bind to a transition metal.....	10
Figure 1.7: Examples of high valent iron-NHC complexes.	11
Figure 1.8: Examples of utilization of macrocyclic tetra-NHC iron complexes for catalytic oxidative group transfer.	13
Figure 1.9: Examples of utilized chiral NHC metal complexes and their reactions.....	14
Figure 1.10: Novel reactivity promoted by actinide metal complexes.....	17
Figure 1.11: Examples of actinide NHC complexes.	17
Figure 1.12: Disparate areas of research from NHC ligands.....	19
 Figure 2.1: Raman spectrum of neat 2.1 (red trace) and Surface-enhanced Raman scattering spectrum (blue trace) of surface functionalized with 2.1.....	 30
Figure 2.2: Surface-enhanced Raman scattering spectra of films functionalized with 2.1 (orange trace), 2.8 (blue trace), 2.9 (red trace), 2.10 (green trace)	31
Figure 2.3: Reaction of carboxylate functionalized surfaces.	33

Figure 3.1: Examples of methods of NHC functionalized nanoparticle synthesis.....	57
Figure 3.2: Summary of NHC complexes used for SERS measurements and their corresponding numbers	60
Figure 3.3: Raman spectrum of 3.1-Cl/I alongside SERS of 3.1-AuNPs..	61
Figure 3.4: Raman spectrum of 3.3-Cl/I alongside SERS of 3.2-AuNPs..	64
Figure 3.5: TEM Images of AuNPs.....	66
Figure 3.6: SERS of reduction reactions forming 3.3-AuNPs..	67
Figure 3.7: SERS of coupling reactions forming 3.4-AuNPs (dotted black) and 3.4d ₅ - AuNPs (dotted blue) alongside Raman of benzoic acid (black) and Raman of deuterated benzoic acid (blue).....	69
Figure 4.1: Examples of chiral tetradentate ligands for chiral oxidative group transfer	95
Figure 4.2: X-ray crystal structure of ((S,S)-1,2-Cy,BMe ₂ TC ^H)Pd, 4.5.	101
Figure 4.3: X-ray crystal structure of [((S,S)-1,2-Cy,BMe ₂ TC ^H)Fe, 4.6..	102
Figure 4.4: X-ray crystal structure of [(((S,S)-1,2-Cy,BMe ₂ TC ^H)Fe) ₂ O], 4.7.....	105
Figure 4.5: X-ray crystal structures of [((S,S)-1,2-Cy,BMe ₂ TC ^H)Fe(N ₂ CPh ₂)], 4.8.	106
Figure 4.6: X-ray crystal structure [((S,S)-1,2-Cy,BMe ₂ TC ^H)Fe(CPh ₂)], 4.9.....	108
Figure 5.1. The most successful motif of chiral NHCs involving a monodentate NHC with chiral groups on the NHC backbone.	157
Figure 5.2: Methods to synthesize C ₂ symmetric 1,2-diamines.....	160
Figure 5.3: Attempted synthesis of 5.1 by all previously published routes for chiral diimidazoles.	161

Figure 5.4: Top: X-ray crystal structure of 5.15.	171
Figure 5.5: X-ray crystal structure of 5.16.	173
Figure 5.6: X-ray crystal structure of $[\{((S,S)\text{-}1,2\text{-DiCy,BMe}_2\text{TC}^H)\text{Fe}\}]$, 5.19.....	176
Figure 5.7: X-ray crystal structure of 5.20..	177
Figure 5.8: X-ray crystal structure of $[\{((R,R)\text{-}1,2\text{-DiCy,BMe}_2\text{TC}^H)\text{Fe}\}]$, 5.21.....	179
Figure 6.1: Previous aziridination catalysts.	213
Figure 6.2: X-ray crystal structure of $[\{((S,S)\text{-}1,2\text{-Cy,BMe}_2\text{TC}^H)\text{Fe-N-(}^t\text{Bu)-C(Cl)}\}]$, 6.1-Cl....	216
Figure 6.3: X-ray crystal structure of $[\{((S,S)\text{-}1,2\text{-Cy,BMe}_2\text{TC}^H)\text{Fe-N-(Octyl)-C(Cl)}\}]$, 6.2.	217
Figure 6.4: Overtime paramagnetic NMR of reaction of 4.6 with excess tert-butyl azide.	220
Figure 6.5: X-ray crystal structure of $[\{((S,S)\text{-}1,2\text{-Cy,BMe}_2\text{TC}^H)\text{Fe(NMes)}\}]$, 6.4.	223
Figure 6.6: X-ray crystal structure of $[\{((S,S)\text{-}1,2\text{-Cy,BMe}_2\text{TC}^H)\text{Fe}((\text{hex-1-ene})\text{N}_4(\text{hex-1-ene}))\}]$, 6.5.....	225
Figure 6.7: Overtime reaction of 4.6 with 6-azidohex-1-ene.....	226
Figure 6.8: X-ray crystal structure of $[\{((S,S)\text{-}1,2\text{-Cy,BMe}_2\text{TC}^H)\text{Fe-(N-(Tolyl)-C)}_2\}]$, 6.6.....	227
Figure 6.9: Comparison of different donation strength on reaction with 4.6.	229
Figure 6.10: X-ray crystal structure of $[\{((S,S)\text{-}1,2\text{-Cy,BMe}_2\text{TC}^H)\text{Co}\}]$, 6.10.....	231
Figure 6.11: Cyclic voltammetry trace of 4.6 in 0.1 M TBAPF ₆ in CH ₃ CN at 100 mV/s scan rate	233
Figure 6.12: Cyclic voltammetry trace of 6.10 in 0.1 M TBAPF ₆ in CH ₃ CN at 100 mV/s scan rate.....	233

Figure 6.13: Cyclic voltammetry trace of 4.10 in 0.1 M TBAPF ₆ in CH ₃ CN at 50 mV/s scan rate.....	234
Figure 6.14: Cyclic voltammetry trace of 6.4 in 0.1 M TBAPF ₆ in CH ₃ CN at 10 mV/s scan rate.	234
Figure 6.15: Pictorial summary of diverse azide reactivity of 4.6.....	236
Figure 7.1: Select examples of crystallographically characterized uranium(IV) NHC complexes involving tethered ligands to increase donation strength.	252
Figure 7.2: Crystal structure of (B ^{Me2,Me} TC ^H) ₂ U 7.1.	254
Figure 7.3: NMR comparison of 7.1 in CD ₃ CN (top, blue), CD ₂ Cl ₂ (middle, green) and C ₆ D ₆ (bottom, red).	256
Figure 7.4: VT NMR of 7.1 in CD ₃ CN.	258
Figure 7.5: Crystal structure of (B ^{Me2,Et} TC ^H) ₂ U, 7.2.	259
Figure 7.6: Widescan CV of 7.1 in THF with 0.1 M (TBA)(PF ₆) as the supporting electrolyte at 100 mV/s scanrate.....	262

List of Schemes

Scheme 2.1: Synthesis of CO ₂ adducts of NHCs.....	27
Scheme 3.1: Synthesis of gold(I) complexes 3.3-Cl/I, 3.3-I, 3.4-I and 3.4-Cl and attempted synthesis of CO ₂ -adduct of nitro functionalized NHC leading to decomposition product, 3.7.....	63
Scheme 3.2: Post-synthetic modification of 3.2-AuNP by reduction to 3.3-AuNPs and amide coupling to form 3.4-AuNPs.	66
Scheme 4.1: Synthesis of chiral macrocycle 4.4.	98
Scheme 4.2: Synthesis of metal complexes 4.5 and 4.6.	99
Scheme 4.3: Reactions of 4.6 with Me ₃ NO and Ph ₂ CN ₂	103
Scheme 4.4: Attempts at cyclopropanation with 4.6 and 4.9.	110
Scheme 5.1: General scheme of synthesis of various diimidazoles from diammonium chloride salt to the diimidazole.....	162
Scheme 5.2: Route for unexpected reaction pathways for 5.2-Thiourea.....	165
Scheme 5.3: Synthesis of a C ₂ diimidazolium salt from 5.2-Imidazole, 5.15.	170
Scheme 5.4: Synthesis of 5.16.....	172
Scheme 5.5: Synthesis of chiral macrocycles from C ₂ symmetric diimidazoles from reaction with bromodimethylborane in nitrile solvents.....	175
Scheme 5.6: Synthesis of C ₂ symmetric iron(II) complexes.	178

Scheme 6.1: Attempted aziridination catalysis with 4.6.	215
Scheme 6.2: Postulated imide insertion pathway.	221
Scheme 6.3: Proposed route towards bis-imide insertion.	228
Scheme 7.1: Synthesis of U(IV) complexes 7.1 and 7.2.	253
Scheme 7.2: Reactions of 7.1 with different reagents	260
Scheme 7.3: Attempted oxidations of 7.1 to uranium(V) species.	262

Chapter One: Introduction to N-Heterocyclic Carbene Chemistry and their Applications

Since the first isolation and characterization of an N-heterocyclic carbene (NHC) by Arduengo in 1991 (Figure **1.1A**),¹ NHCs have had increasing roles in synthetic chemistry.² While NHCs can stabilize main group elements³ and to act as organocatalysts,⁴ the vast majority of the NHC literature details their coordination with transition metals (Figure **1.1B**).^{2, 5-7} The key distinction of NHCs over other carbon ligands in organometallic chemistry is their singlet character of the carbene carbon, due to π -donation from the adjacent nitrogens into the empty p -orbital. This effect lead to strong σ -donation from the NHC to the metal (Figure 1.1B).⁸ In addition, the stabilized empty p -orbital results in much less π -backbonding.²

The most famous example of an NHC metal complex is the Grubbs-Hoyveda olefin metathesis catalyst. The discovery of this catalyst resulted in Grubbs being awarded a share of the 2005 Nobel Prize in Chemistry.⁹ The efficacy of the catalyst was related to the pendant NHC ligand stabilizing the necessary ruthenium(IV) intermediate for the reaction.^{10, 11} Indeed, while the pendant NHC results in facilitation of the reaction, the Schrock style carbene, which has no heteroatom donating to the empty p -orbital, can react to become the active intermediate for catalysis. This species can react with alkenes to form the metallocyclobutane intermediate (Figure **1.2D**) and with loss of ethylene forms the desired products. This catalyst has been used in cross metathesis to form products with two distinct olefins (Figure **1.2A**)¹², ring closing metathesis to form intramolecular alkenes of varying ring sizes (Figure **1.2B**)¹³ and also ring opening metathesis polymerization (ROMP, Figure **1.2C**)¹⁴, which facilitates polymers normally unavailable by other polymerization methods.

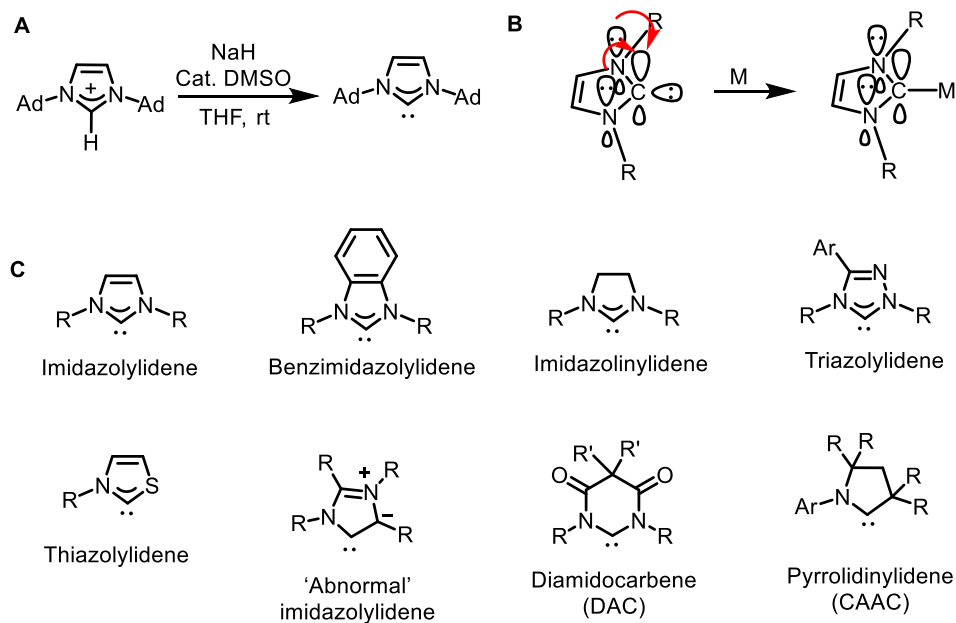


Figure 1.1: General overview of NHC ligands. **A:** Arduengo's original synthesis of the first isolated and characterized free NHC.¹ **B:** A schematic showing the electronic donation of the imidazole N₁ and N₃ donating into empty p-orbital, stabilizing the free singlet carbene in the s-orbital. This carbene can form a bond with primarily σ -bonding character with a metal, with minimal π -backbonding. **C:** The major classes of NHCs.²

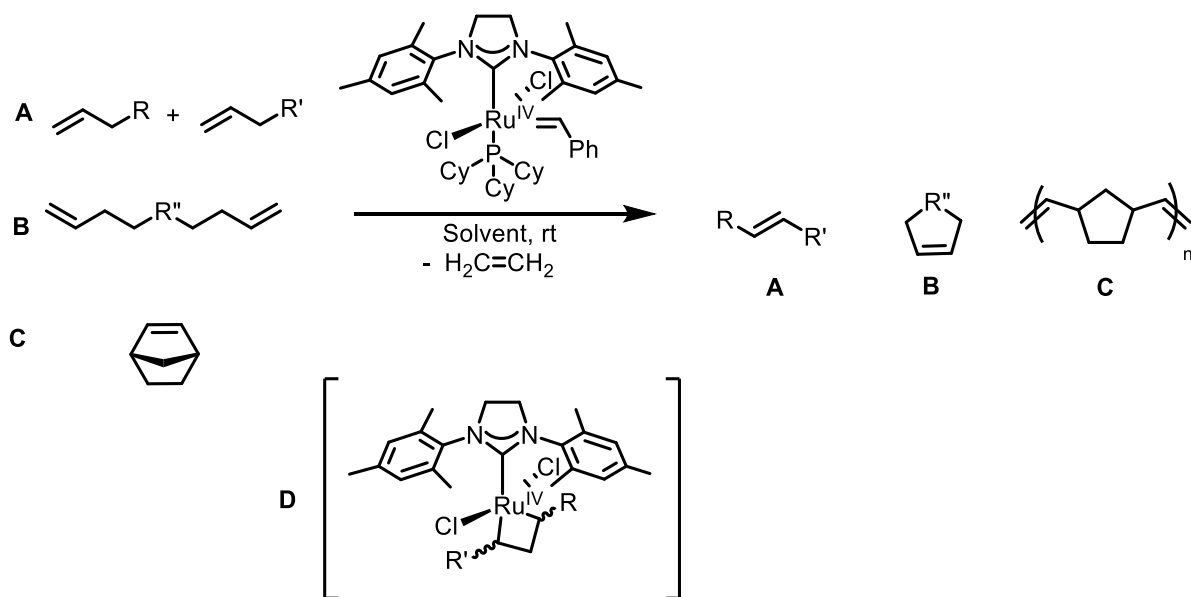


Figure 1.2: Olefin metathesis mediated by Grubbs' ruthenium NHC complex. All products are from corresponding reactions with loss of ethylene ($\text{CH}_2=\text{CH}_2$). **A:** Example of cross metathesis with two different alkenes. R and R' can be a variety of functional groups. **B:** Example of ring closing metathesis using two intramolecular alkenes. R'' can be a variety of atom lengths, as the reaction can form both thermodynamically unfavorable (7 membered) rings and very large (20+ atom) macrocycles. **C:** Example of ring opening metathesis polymerization (ROMP) using a norbornene monomer.

NHCs have another distinct advantage compared to some other carbon-based ligands; the ligand can be more readily modified to modulate reactivity. NHC ligands can be synthesized with a variety of alkyl groups placed on the “wing” nitrogen atoms, potentially favoring reductive elimination or providing sterically controlled reactivity at the metal center.^{2, 7} As alluded to in Figure **1.1C**, the electronics of the NHC can also be changed greatly by modifying the cyclic system by changing heteroatoms on the ring.^{15,}

16

While considering new applications of NHCs, there has recently been a newfound purpose of NHC as tethers for metal surfaces. The typical type of functional group that would tether these surfaces are thiol or amine functionalized ligands.^{17, 18} These ligands in a solvent would spontaneously react with the noble metal surface and self-assemble, to form self-assembled monolayers (SAMs). SAMs are unique in surface because the layers are a single unit of the ligand in thickness.¹⁹ SAMs have been utilized for a variety of applications, such as forming molecular functions, drug delivery and molecular recognition.¹⁷ The latter two applications have far reaching implications in real world applications of this monolayer technology. In recent years, there has been a number of reports by the Crudden, Johnson, Horton, Glorius and many other groups on utilizing NHCs to functionalize noble metal surfaces and nanoparticles, especially that of gold (Figure **1.3**).²⁰⁻²⁶

Drug delivery by use of nanoparticles has received a large amount of attention due to the ability to tailor the nanoparticles to particular cells due to the functionality.²⁷ There has been success in utilizing this approach for specialized treatment in cancer cells²⁸ and even Alzheimer's disease.²⁹ Additionally, nanoparticles made of gold have been

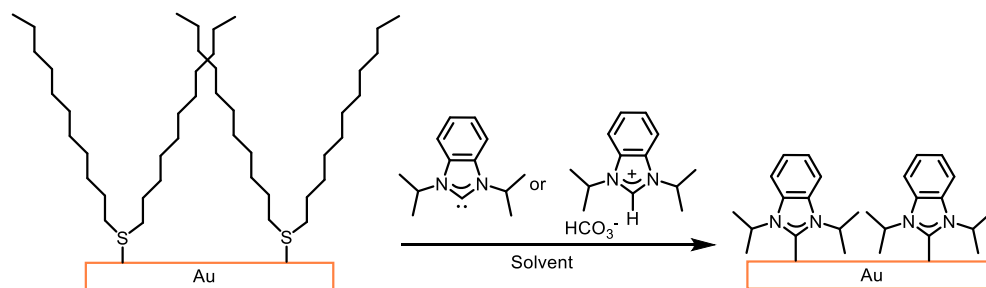


Figure 1.3: Facile functionalization of crystalline gold surfaces reported by Crudden and Horton.²² The dodecylsulfide capped surfaces could be reacted with either the free NHC or a protected bicarbonate-NHC salt in solution to append the NHC on the surface.

approved by the United States Food and Drug Association (FDA) for use *in vivo*, which expands the possibility for biological applications.³⁰ Such applications include molecular recognition in biological settings, like surface enhanced Raman spectroscopy (SERS).

SERS overcomes the signal limitations of normal solution state Raman spectroscopy by utilizing the surface the localized surface plasmonic resonance (LSPR) (Figure 1.4).³¹ Tethers bind the analyte close to the surface so the laser can take used for scattering to collect the Raman signal. While the LSPR effect necessitates the desired analyte being close to the surface, this provides unprecedented detection that has distinct advantage over other techniques like mass spectrometry. SERS can be done with portable spectrometers and provides vibrational signatures, which are both not possible with mass spectrometry.³²⁻³⁴

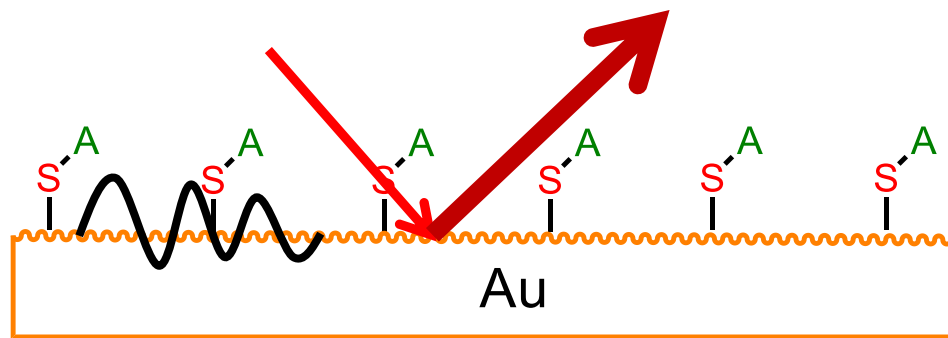


Figure 1.4: Diagram of basic SERS mechanism using a thiol ligand. The sulfur (**S**) is tethered to a gold surface, that is attached to an analyte (**A**). The incident radiation (smaller red arrow), excited the LSPR on the nano roughened surface (black wave) and results in a more intense scattered radiation that has a greater area of possible scattering on the analyte.

The biggest limitation for sensing with SERS is the thiol ligand dissociates too easily from the surface.¹⁸ Thiols, while having very great affinity to gold over other ligands, are easily dissociated from the surfaces in non-ideal conditions. In many organic solvents, at elevated temperatures, in oxidative and pH extremes thiols readily dissociate from the surface and rendered unusable.²¹ Their ease of dissociation is a severe limitation not just to SERS studies but any nanotechnology that requires these thiol SAMs. NHC SAMs may solve this critical problem. The strong σ -donation provides much stronger metal ligand bonds in many transition metals, like gold. This benefit allows NHCs to be more strongly bound to surfaces than thiols and be stable in many different conditions. Indeed, NHC functionalized surfaces have significantly greater robustness

compared to thiols, and have been found to be stable in acidic, basic and oxidizing conditions.²¹

With the discovery of the NHC SAMs, there has been significant effort to understand the properties of these surfaces.²⁰ However, there has been very little in the way of applications for these NHC SAMs to date. The applications of the NHC surfaces thus far are functionalizing HPA chips for biosensing by SPR^{35, 36} (Figure **1.5A**) and microcontact printing of NHCs on surfaces²⁶ (Figure **1.5B**). To date, NHC surfaces have

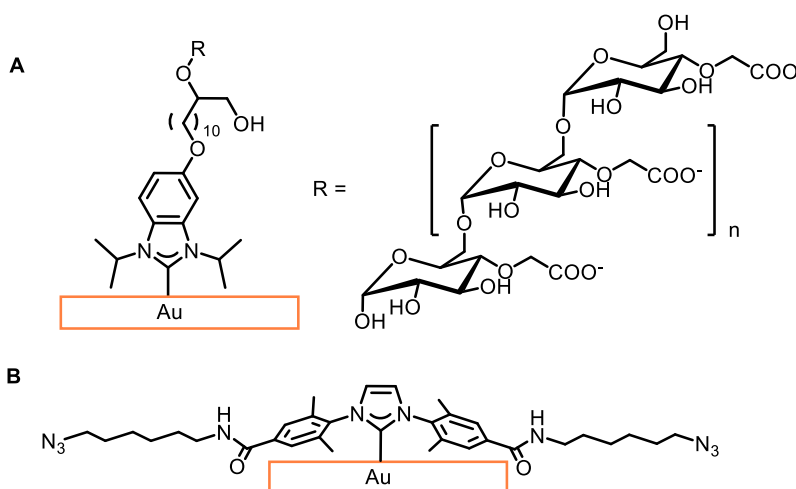


Figure 1.5: Applications of NHC Functionalized Surfaces. **A** is an example by Crudden and Horton which uses a dextran modified NHC on gold surfaces that can react with relevant biomolecules, like streptavidin and monitor it using SPR sensing.^{35, 36} **B** is an example by Ravoo and Glorius that utilize microcontact printing to append azide functionalized NHCs to perform click reactions with alkyne functionalized mannose and biotin.²⁶

not been applied for SERS. To use NHCs for SERS would necessitate the synthesis of functionalized NHCs, that would have distinct vibrational characterization.²⁰

NHCs are effective at stabilizing higher oxidation states on metals on 2nd and the 3rd row metals.³⁷ While this is more feasible and studied with 2nd and 3rd row transition metals, it is much more difficult to isolate higher oxidation states on 1st row transition metals in general. Iridium, for example, is known to access a wide variety of oxidation states, including iridium(IX).³⁸ However, for its first row analog cobalt, cobalt(IV) and cobalt(V) are rare oxidation states.³⁹⁻⁴¹ Second and third row Group 8-10 metals behave in a similar manner and are vital to some of the most critical reactions in synthetic chemistry.⁴²⁻⁴⁴ As a result, to promote a more sustainable catalytic reactions, there has been a push to utilize first row elements to circumvent the necessity of precious transition metals.^{45, 46}

Simply using a first-row transition metal in place of second and third row metals with the same ligand is highly challenging. One of the key differences between second and third transition metal complexes to their first row counterparts is attributed to the limited spatial extension of the 3d orbitals compared to that of the 4d and 5d.⁴⁶ This necessitates shorter metal-ligand bonds, which results in Pauli repulsion caused by the occupied s and p shells (Figure 1.6) destabilizing the bond due to causing 3d and ligand orbitals misaligning; this is further exacerbated for higher oxidation states on metals, which results in shorter bond lengths.^{47, 48} NHCs providing stronger σ -donation raise the energy of the HOMO of the ligand⁴⁹ and result in more favorable orbital overlap with 3d compared to that of nitrogenous or oxygen ligands.⁴⁶

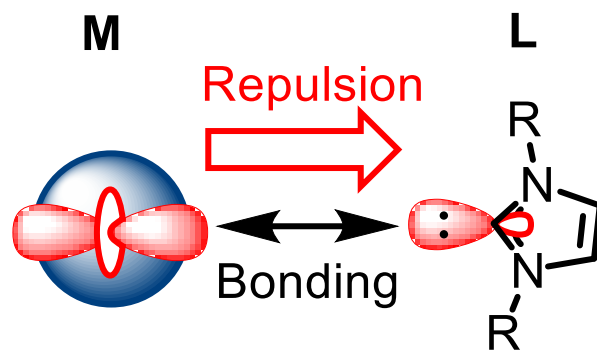


Figure 1.6: Required orbital orientation for NHCs to bind to a transition metal. The (n-1) s and p orbitals (blue sphere) can repel the incoming NHC due to Pauli repulsion. The orbitals (red orbitals) cannot overlap effectively when repelled, as the smaller 3d orbital requires a shorter bond than that of 4d and 5d metals.⁴⁶

While NHC metal complexes have been isolated with all first row transition metals, there has been significant effort towards understanding the chemistry of iron, the most abundant element in the earth's crust. Iron has rich redox chemistry, and have been ligated on NHC containing ligands from oxidation states from iron(0) to iron(V).⁴⁶ While the chemistry of iron(II) and iron(III) NHC complexes has been studied extensively,⁵⁰⁻⁵⁴ there are significantly fewer iron(IV) complexes with NHCs. For complexes utilizing one NHC ligand, both Deng^{55, 56} and Wolczanski⁵⁷ (Figure 1.7A, B and C) have isolated iron(IV) imido complexes. Both of these complexes utilized nitrene sources in form of organic azides, to form the desired imidos by a two-electron oxidation. This synthetic approach is highly desired and critical for applications in catalytic amination and aziridination, as the metal imido has been postulated as the necessary intermediate. The

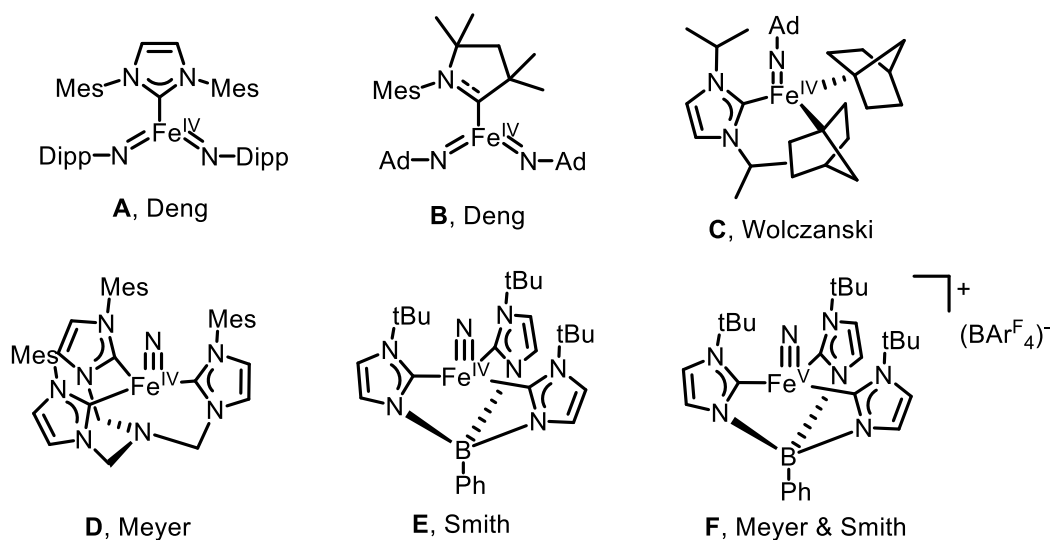


Figure 1.7: Examples of high valent iron-NHC complexes. Work by Deng (**A** and **B**)⁵⁶ involve synthesis of by oxidation of an iron(0) NHC using organic azides. Work by Wolczanski (**C**)⁵⁷ involved a similar approach using an iron(II) NHC precursor. The nitrido tripodal iron-NHC complexes by Meyer⁵⁸ and Smith⁵⁹ (**D** and **E**) were synthesized by reaction of the bound azide by ultraviolet light. The complex was able to access the rare iron(V) oxidation state (**F**)⁶⁰ which is the only isolated example using an NHC ligand.

ability to react these imidos with an alkene is an extremely desired transformation in organic chemistry.

Work by the Meyer and Smith groups (Figure **1.7D**, **E** and **F**) have used multidentate anionic NHC ligands to stabilize higher oxidation states on iron to form imidos and nitridos.⁵⁸⁻⁶⁵ In some cases, these nitrido complexes can transfer the nitrogen fragment to styrene and form aziridines after protecting the aziridine nitrogen.^{59, 65} This work has even resulted in rare iron(V) NHC complexes, in which the electron richness of the ligand as well as the sterics provided by the ligand protect the iron(V) complex.⁶⁰ These tris-NHC borate ligands utilized are isostructural to other scorpionate ligands that utilize phosphines and pyrazoles.^{66, 67} The NHC ligand variants are able to stabilize higher oxidation states in comparison.

In the same vein, the Jenkins (Figure **1.8A** and **B**) and Kühn groups (Figure **1.8C**) have done considerable work in stabilizing higher oxidation states on metals, especially iron, for use in oxidative group transfer.⁶⁸⁻⁷¹ Both groups use macrocyclic tetra-NHC complexes that are isostructural of porphyrins.^{54, 72} While porphyrin ligands have been successful for a wide variety of oxidative group transfer reactions,⁷³⁻⁷⁸ they are often limited by their ability to stabilize higher oxidation states on the metal centers.^{79, 80} Macrocyclic tetra-NHCs are more effective at stabilizing higher oxidation states⁷² and high coordinate iron oxos and imido complexes have been successfully isolated.^{54, 81} Some catalytic systems can support reactions like epoxidation and aziridination that may go through high oxidation states during the catalytic cycle.^{68, 69, 71}

Despite all these advantages, there are limitations for NHCs. For example, when compared to phosphines, chiral NHCs have not been as effective for asymmetric

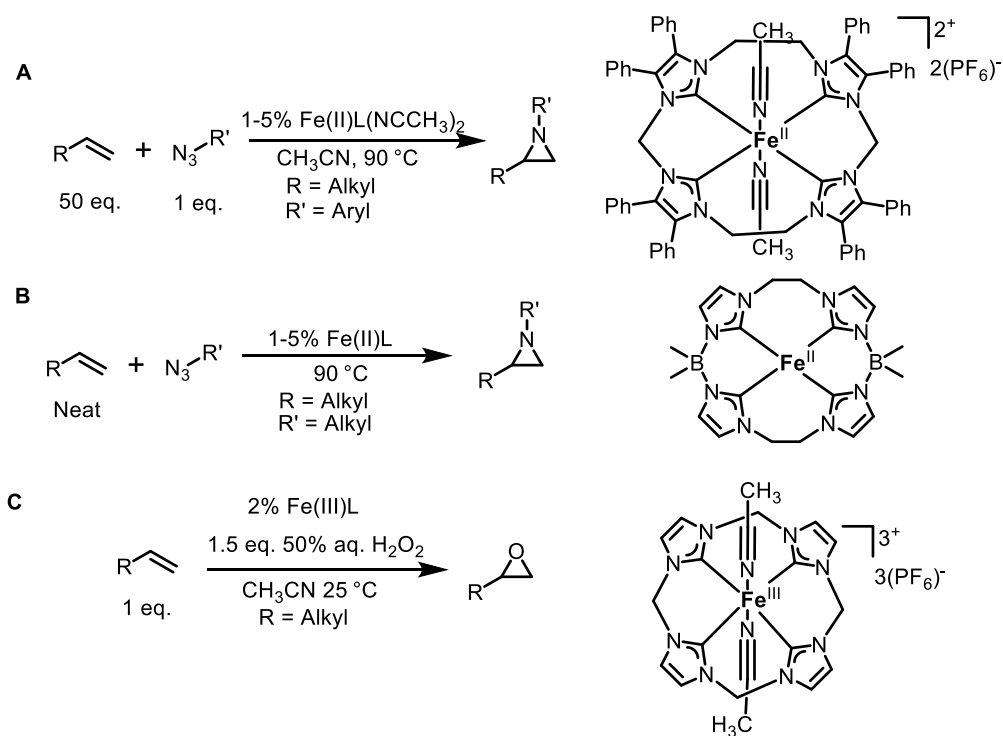


Figure 1.8: Examples of utilization of macrocyclic tetra-NHC iron complexes for catalytic oxidative group transfer. Examples **A** and **B** are done by the Jenkins' group by utilizing organic azides and unactivated alkenes to form aziridines.^{68, 69} **B** is the only example with unactivated azides. **C** is done by the Kühn group utilizing an iron(III) tetra-NHC complex to form epoxides from hydrogen peroxide solution.⁷¹

catalysis.⁸² Most new pharmaceuticals approved by the FDA are required to be single enantiomers.⁸³ As new pharmaceuticals may require many different stereocenters in a single molecule, effective asymmetric reactions necessitate robust functional group tolerance and the ability to synthesize chiral molecules from prochiral and achiral substrates, like that of aziridination.⁸⁴

The vast majority of chiral NHCs that have been utilized for asymmetric catalysis are monodentate NHC complexes largely due to the straightforward synthesis from chiral 1,2-diamines (Figure **1.9A**).^{82, 85} The lack of π -backbonding can allow for rotation on the metal carbon bond, eroding stereoretention⁸², which severely limits the utility for chiral NHCs for asymmetric reactions. There are very few asymmetric catalysis with NHCs using 1st row transition metals; the primary examples are on copper (Figure **1.9B**).⁸⁶

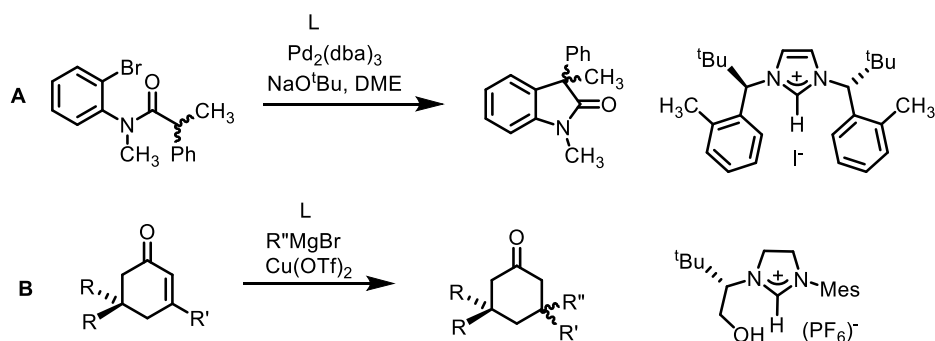


Figure 1.9: Examples of utilized chiral NHC metal complexes and their reactions. **A** is a palladium catalyzed intramolecular α -arylation. This is the most common test reaction for this style of monodentate NHC. **B** is one of the only examples of a first row transition metal (copper) being utilized in a chiral transformation using an NHC ligand.

One method that has been considered to circumvent this problem is switching to a bidentate ligand. Bidentate phosphines, like chiraphos, have been used successfully for asymmetric transformations.^{87, 88} However, this approach has been limited for NHCs due to both the inflexibility of the NHCs and the larger bite angle the bidentate of NHC's compared to phosphines.⁸² Finally, the synthesis of chiral bidentate NHCs is much more difficult compared to that of monodentate NHC ligands.⁸⁹⁻⁹¹ The standard imidazole condensation reaction is impacted greatly by the formation of an imidazole amine byproduct that lowers yield and makes it difficult to purify.⁹¹ Other methods result in cyclization that yields the motif for monodentate chiral NHCs.⁹² These shortcomings need to be overcome for asymmetric catalysis to be effective with NHCs.

NHCs have had other shortcomings incorporating highly electropositive metals, like the *f*-block elements.⁹³ Despite the misnomer of the "rare-earth elements", the lanthanides and actinides are more significantly more abundant than the aforementioned precious metals.⁴⁰ This abundance is desirable for being used for catalysis or other applications. Due to the lanthanide contraction, the *f*-electrons are not really valence electrons which has relegated these elements to Lewis acid catalyst or luminescent materials.^{94, 95} However, this *f*-electron contraction is not the case with the actinides, which have *f*-orbital valence electrons.

The actinides are often viewed as dangerous due to their intrinsic radioactivity. However, in the case of the actinides, thorium, uranium and americium, the α -emitting elements can have their radioactivity stopped by a piece of paper.^{40, 96} The only real danger from radioactivity is due to inhalation and ingestion, as the α -particles cannot penetrate the skin.⁹⁷ Due to considerable amount of left over depleted uranium, there is

significant interest in understanding its chemistry.⁴⁰ In the case of low valent uranium, it has been shown to perform small molecule activation, such as activating CO⁹⁸, CO₂⁹⁹, N₂¹⁰⁰ and arenes¹⁰¹ (Figures **1.10A**, **B**, **C** and **D**, respectively) , that is distinct from that of transition metals.⁹⁶

NHC actinide complexes are significantly more difficult to synthesize due to weak electrostatic attraction compared to transition metals to the neutral ligand.⁹³ Figure **1.11A** represents the first example of an actinide NHC complex. A noticeable aspect of this is that the uranium form was uranyl (UO₂), which has two electron rich oxo ligands attached to the uranium. For lower valent uranium without these oxo ligands, uranium NHC complexes cannot be made. A way around this shortcoming is to use strongly anionic ligands or anionic tethers attached to the NHC (Figure **1.11B**). The P. Arnold group have utilized NHCs with heteroatom tethers in the style of Figure **1.11B** to stabilize uranium NHC complexes, as well as other lanthanides.¹⁰²⁻¹⁰⁵ The anionic nature of the ligand allows the metal to become electron rich enough to form a stable bond with the NHC.

While utilizing this tether has been effective, it is a design limitation for NHC with actinides, and in some cases would be more favorable to avoid. Recently, there has been an example by the Long group¹⁰⁶ (Figure **1.11C**) and examples by the J. Arnold group¹⁰⁷⁻¹¹⁰ (Figure **1.11D**) in anionic NHC ligands utilizing a borate linker to form actinide NHC complexes. The borate linker makes the NHC ligand anionic, and the resulting ligand is significantly more electron rich. The examples utilizing these types of NHC complexes have been the only examples of using non-tethered NHC complexes for binding to low valent actinides. This discovery provides a promising example of utilizing NHC ligands

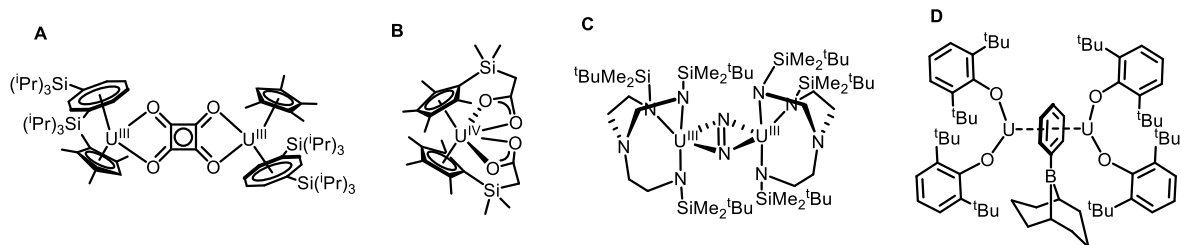


Figure 1.10: Novel reactivity promoted by actinide metal complexes. Each represents examples of small molecules being activated, such as CO (**A**), CO₂ (**B**), dinitrogen (**C**) and benzene (**D**).

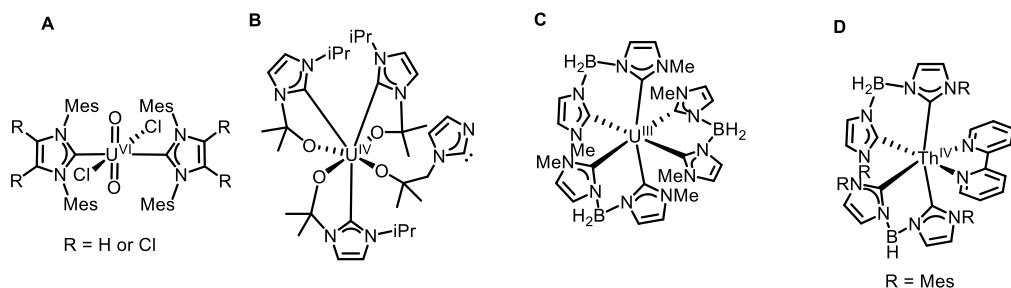


Figure 1.11: Examples of actinide NHC complexes. **A** is the first example of an actinide NHC complex reported by Costa that involved coordination to UO₂Cl₂.¹¹¹ **B** is an example of tethered NHCs that are used to stabilize low- to mid-valent uranium atoms.¹⁰² **C** and **D** show examples by Long¹⁰⁶ and J. Arnold¹⁰⁷ that utilize anionic bidentate NHCs to stabilize both U^{III} and Th^{IV}, respectively.

for a newfound purpose that previously wasn't obtainable, as the complexes result in unique magnetic molecules and promoting novel redox neutral reactivity.

The research presented in this dissertation takes steps to address these drawbacks and limitations of NHCs (Figure **1.12**). Chapters 2 and 3 involve the synthesis of bifunctional NHC precursors that can be easily used to functionalize gold surfaces with a variety of secondary functional groups off of the back of the NHC (Figure **1.12**, left). These were prepared by reaction of the free NHC with CO₂ and provides a method of forming these air stable precursors. The precursor was deposited using heat and vacuum and SERS confirmed that the functional groups are present and even chemical reactions can be monitored. This presents the first example of application of NHC functionalized surfaces for SERS and is a basis for further applications in functional surface chemistry for NHCs.

We also employed gold(I) NHC complexes to transfer of the functionalized NHC to citrate functionalized gold nanoparticles in benchtop conditions. This results in nanoparticles of sufficient size to be viable for SERS in biological media. It also allows for protic NHCs to be prepared, by the ability of problematic bifunctional NHCs to be synthesized to the gold(I) salt.

In Chapters 4, 5, and 6 (Figure **1.12**, right), we expand the possibilities of chiral NHC ligands through the novel synthesis of chiral tetra-NHC ligands and their resulting metal complexes. A novel route to form a variety of chiral diimidazoles, many of which are untenable by previously reported methods, is shown. The chiral ligands were utilized to synthesize a variety of chiral macrocyclic tetra-NHCs. The macrocycles and their subsequent metal complexes, of palladium, iron and cobalt, are the first reported chiral

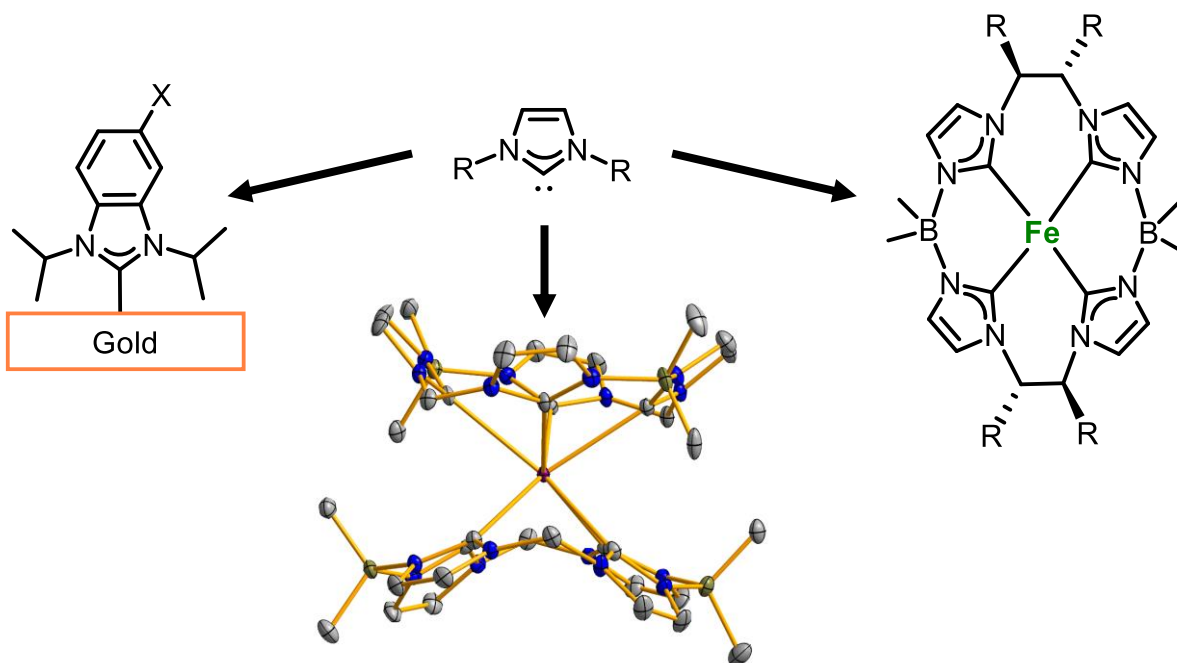


Figure 1.12: Disparate areas of research from NHC ligands. **Top Left:** Chapters 2 and 3. Bifunctional NHC ligands for surface modification. The label **X** corresponds to synthetic handles for surface functionality. **Top Right:** Chapters 4, 5 and 6. Synthesis of chiral macrocyclic tetra-NHCs and study of the oxidation chemistry of iron(II) variant. The label **R** corresponds to groups that impose chirality on the metal. **Bottom Middle:** Chapter 7. Octa-NHC uranium(IV) complex from macrocyclic tetra-NHC ligands.

macrocyclic tetra-NHCs. The oxidation chemistry and unprecedented reactivity of the iron(II) complexes are studied in detail. The starting iron(II) complex was able to stabilize both an iron diazo and an iron alkylidene with reaction of bisaryl diazoalkane. The resulting alkylidene is iron(IV) based on electrochemistry, which represents a very rare example of a high valent iron alkylidene. The same starting iron(II) complex was able to exhibit unprecedented activity with organic azides to form a five coordinate iron imido, iron metallotetrazene, and products of imido migratory insertion into the metal NHC bond.

Lastly, Chapter 7 details the synthesis of the first “octa-NHC” complex involving macrocyclic tetra-NHC ligands. This metal complex is the first example of a macrocyclic tetra-NHC bound to an actinide. The resulting complexes, both utilizing a 16- and 18-atom macrocyclic tetra-NHC have the most uranium carbon bonds in a single molecule. Despite being a relatively similar ligand, both ligands yield complexes with very different geometry and properties.

Chapter Two: N-heterocyclic Carbenes as a Robust Platform for Surface-Enhanced Raman Spectroscopy

A version of this chapter was originally published by Joseph F. DeJesus, Michael J. Trujillo, Jon P. Camden and David M. Jenkins as:

DeJesus Joseph F.; Trujillo Michael J.; Camden Jon P.; Jenkins David M. "N-heterocyclic Carbenes as a Robust Platform for Surface-Enhanced Raman Spectroscopy." *Journal of the American Chemical Society*, **2018**, 140, 1247-1250.¹¹²

The work presented in this chapter was part of a highly collaborative project in which both Michael J. Trujillo and I shared credit for first authorship. I did all the front-end synthetic work to make and characterize molecules **2.1** – **2.10** as well as worked in tandem with Michael J. Trujillo to figure out the how to reproducibly functionalize the gold film over nanosphere (AuFON) surfaces and do post synthetic functionalization. Michael J. Trujillo was responsible for all the synthesis of the substrates as well as all SERS spectra.

Abstract

Surface-enhanced Raman spectroscopy (SERS) underpins a wide range of commercial and fundamental applications. SERS often relies on ligands, usually thiols, bound to a noble metal surface to bring the analyte in close proximity. The difficulty of straightforward thiol synthesis combined with their instability on surfaces highlights the need for alternative ligand design. We present the first example of SERS utilizing N-heterocyclic carbene ligands. A general three step synthesis is presented for functionalized NHC-CO₂ adducts. These ligands are deposited on SERS-active gold film-over-nanosphere substrates (AuFONs) in solvent-free and base-free conditions which prevents fouling. The resulting films are found to be robust and capable of repeated post-synthetic modifications without degradation.

Introduction

Surface-enhanced spectroscopy is a versatile platform for low-concentration, non-destructive measurements of analytes ranging from heavy metals to biomarkers and proteins.^{32, 113, 114} The success of this approach relies on the extreme signal enhancement obtained by bringing the analyte in close proximity to a nanoscale roughened metal surface, usually Au or Ag.³¹ The surface enhancement, however, decays exponentially with distance from the surface, therefore, highlighting the importance of chemically modifying the nanostructures to increase analyte affinity and decrease non-specific binding.^{17, 115}

Although many chemical groups interact with noble-metal surfaces, thiols are almost exclusively employed for surface functionalization agents.¹¹⁶ Their extensive use results from their strong affinity towards noble metals (e.g. Ag and Au) and their spontaneous assembly to form compact and well-characterized monolayers.^{17, 19, 117, 118} The application of thiol-functionalized surfaces, however, is largely limited by (1) the stability of monolayers on the metal surface, particularly in biological settings or harsh chemical conditions,¹⁸ and (2) the difficulties associated with the synthesis of stable thiols, particularly without multiple protection and deprotection steps. In order to have robust and versatile monolayer-based plasmonic sensors, alternative surface functionalization schemes are needed to address these dual shortcomings.

N-heterocyclic carbenes (NHCs) are a highly influential class of ligands long known for their strong σ -bonds to transition metals.^{15, 119} While a plethora of molecular organometallic complexes have been prepared with NHCs,² only recently has it been demonstrated that NHCs form robust monolayers on crystalline gold surfaces.^{21, 23, 120} These monolayers showed markedly greater resilience to chemical conditions than thiols, specifically extreme pHs and strongly oxidizing conditions.^{21, 22, 121} The key disadvantage of NHC ligands compared to traditional thiol based ones are the necessity of rigorously air and water free conditions to form the reactive carbene. In addition, the imidazolium precursors, anions, or bases are liable to foul surfaces. As a result, synthetic chemists have attempted to find other methods for making air stable NHC-precursors for either surface functionalization or nanoparticle synthesis.^{21, 23, 19} However, to date, the synthesis of NHC-precursors with orthogonal functionalities are virtually unknown,¹²² nor have surface-enhanced Raman spectra (SERS) from NHC-monolayers been reported.

In this chapter, we provide a general method for synthesizing CO₂-adduct NHCs with orthogonal functional groups and report the corresponding NHC-SERS spectra. These NHC-CO₂ adducts are deposited on gold-film-over-nanosphere (AuFON) substrates in solvent-free and base-free conditions, which prevent fouling. The NHC films display excellent stability even when subject to harsh reactions conditions, including strong acids, bases, and reductants. The orthogonal functional groups allow for excellent SERS tags due to signals observed in the silent region of the Raman spectrum. Lastly, we utilize the chemical stability of our SERS-active NHC-films to demonstrate post-synthetic modifications of benzimidazolium NHCs films.

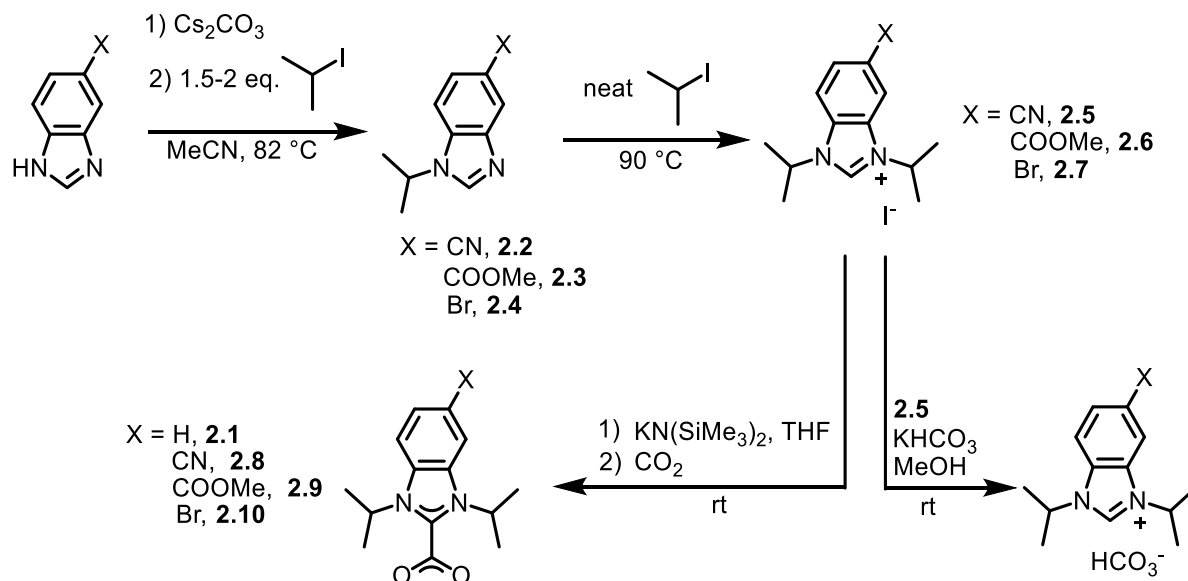
Results and Discussion

Carbenes, unlike thiols, must be deprotonated with a strong base prior to binding the metal surface. Deprotonation leads to counter ions and other residual chemicals that may contaminate the surface, although use of an air-stable “free” carbene can counter this drawback. Crabtree and Taton developed the initial synthesis of air stable CO₂- and [HCO₃]⁻ adducts for NHCs^{123, 124} and Crudden and Johnson demonstrated that both versions can bind to highly ordered gold surfaces, e.g. Au(111).^{22, 23} These adducts are advantageous when preparing functionalized surfaces, as CO₂ and H₂O are the only reaction byproducts and do not interfere with carbene binding to the metal surface.

The ability to place orthogonal functional groups near a metal surface is advantageous for SERS; therefore, we synthesized four different benzimidazoliums, each with a different functional group in the 5-position employing a general two step procedure. The synthesis of 1,3-diisopropyl-benzoimidazolium iodide has been previously reported,¹²⁵ but other substituted examples are generally not known. Addition of cesium

carbonate and 2-iodopropane to 5-cyano-1H-benzimidazole gave a mixture of 5/6-cyano-1-isopropyl-benzimidazole, **2.2**, (Scheme **2.1**) in 92% yield. Even though two isomers were present, it was not necessary to separate them since the compound was re-symmetrized in the following reaction. Appending the second equivalent of 2-iodopropane to form the benzimidazolium, however, was significantly more challenging. 5-cyano-1,3-diisopropyl-benzimidazolium iodide, **2.5**, was synthesized by addition of neat 2-iodopropane to **2.2** in a glass pressure tube. This tube was heated to 90 °C for four days. After a series of washing and precipitations, the product was recovered in 82% yield. The synthesis of the ester and bromide variants of the benzimidazoliums proceeded along the same lines as **2.5** (Scheme **2.1**). The two isopropyl groups were added to 5-methyl-carboxylate-1H-benzimidazole in subsequent steps in 76% and 75% yield, respectively, to give 5-methyl-carboxylate-1,3-diisopropyl-benzimidazolium iodide, **2.6**. Likewise, 5-bromo-1,3-diisopropyl-benzimidazolium iodide, **2.7** was formed in the same two steps in 79% and 61% yield, respectively.

We first attempted to form the $[\text{HCO}_3]^-$ adducts of the benzimidazoliums to circumvent the necessity of air-free synthesis.¹²³ Stirring 1,3-diisopropyl-benzimidazolium iodide in dry KHCO_3 in anhydrous methanol led to incomplete conversion while the same reaction with **2.5** caused significant degradation (Scheme **2.1**). Transient methoxide formed from either the KHCO_3 or the actual $[\text{HCO}_3]^-$ adduct of **2.5** caused degradation of the nitrile to the imino ester. While there are ways to circumvent



Scheme 2.1: Synthesis of CO_2 adducts of NHCs.

the issue of residual unreacted iodide (i.e. addition of H_2O_2 with CO_2),²² these necessitate the use of protic solvents which would degrade electron deficient functional groups by nucleophilic attack.

To circumvent the bicarbonate adducts we directly synthesized the NHC- CO_2 adducts. 1,3-diisopropyl-1H-benzimidazolium was deprotonated with potassium bis(trimethylsilyl)amide in THF and then CO_2 gas from a balloon was added at room temperature. Addition of CO_2 caused a white powder to precipitate from solution. After washing with diethyl ether, the air-stable product, 2-carboxy-1,3-diisopropylbenzimidazolium (**2.1**), was obtained in 64% yield (Scheme 2.1). Notably, the downfield imidazolium proton was absent in the ^1H NMR and large bands at 1625 cm^{-1} and 1369 cm^{-1} are seen in the IR which are evidence that the CO_2 adduct has been formed.

Compound **2.5** was converted into the NHC-CO₂ adduct by the same method as **1**, to give 2-carboxy-5-cyano-1,3-diisopropyl-benzimidazolium, **2.8**, in 77% yield as a white hygroscopic powder. Conspicuously, **2.8** displays three strong stretches in the IR at 2229 cm⁻¹, for the CN, and 1614 and 1373 cm⁻¹, for the CO₂ (Spectrum **3.3**). Deprotonation of **2.6** with potassium bis(trimethylsilyl)amide in THF followed by addition of CO₂ gas yielded 2-carboxy-5-methyl-carboxylate-1,3-diisopropyl-benzimidazolium, **9**. In the same manner as **2.1** and **2.5**, a significant CO₂ stretch is observed for **2.9** in the IR at 1609 and 1373 cm⁻¹ and an ester stretch is found at 1721 cm⁻¹ (Spectrum **3.6**). The same pathway to the bromide functionalized adduct gives **2.10** in 65% yield. While compound **1** is completely stable in air, compounds **2.8-2.10** very slowly degrade under atmospheric conditions over the course of months.

Previous work reported NHC monolayers on Au(111) surfaces, but gold surfaces lacking nanoscale roughness are not suitable for SERS.¹²⁶ Therefore, we developed a procedure to prepare NHC-functionalized surfaces on the well-studied gold film-over-nanosphere substrates (AuFONs). AuFONs are prepared by evaporation of gold (200 nm) on polystyrene nanospheres (600 nm diameter) using a chromium (5 nm) adhesion layer. AuFONs are easily prepared and commonly employed for SERS because of their uniform enhancement factors and reproducibility.¹²⁷

Initially, the AuFONs were soaked in either a solution of **2.1** or **2.8** in methanol. This method, however, yielded films with a weak and irreproducible SERS response. These issues were traced to degradation of **2.8** in methanol. NMR of **2.8** for prolonged periods in CD₃OD indicates that the carboxylate on the NHC-CO₂ adduct degrades the nitrile to an imino ester. Adopting a solvent free route to film deposition avoids this

dilemma. Directly placing the solid compound on the surface of the gold substrate and heating it under vacuum (5 torr, 120 °C) provides a simple procedure for surface functionalization for all NHC-CO₂ adducts while simultaneously retaining the functional groups (Figure **2.1** and **2.2**) and yields strong and reproducible NHC-SERS (*vide infra*). This solvent-free and reagent-free method prevents any inadvertent fouling of the SERS substrate by other reagents or ions.

Raman spectra of neat **2.1** and the SERS spectrum of AuFONs functionalized with **2.1** are displayed in Figure **2.1**. Although there are differences owing to the surface-selection rules, both the Raman and SERS spectra are dominated by the strong benzimidazolium ring modes. Furthermore, binding of the carbene to the gold surface is evidenced by the consistency of our SERS bands with previously reported frequencies obtained from HREELS of NHC films in vacuum.²² The observed red-shift (~30 cm⁻¹) of the stretching modes upon binding of the carbene to the AuFON surface is attributed to a weakening of bonds in the benzimidazolium ring as electron density is donated from the gold surface into the ring, in contrast to the electron withdrawing nature of the CO₂ adduct.

We then expanded our studies to include SERS measurements of the functionalized carbenes: **2.8**, **2.9**, and **2.10**. While Crudden reported surface plasmon resonance (SPR) measurements using NHC modified gold films, the vibrational fingerprint of individual functional groups have not been observed with NHC coated surfaces spectroscopically.¹¹⁷ Compounds **2.8**, **2.9** and **2.10** were deposited on AuFONs in the same manner as **1** and SERS spectra were collected (Figure **2.2**). Significantly, the functional groups for the nitrile (**2.8**) and ester (**2.9**) are readily apparent in the SERS

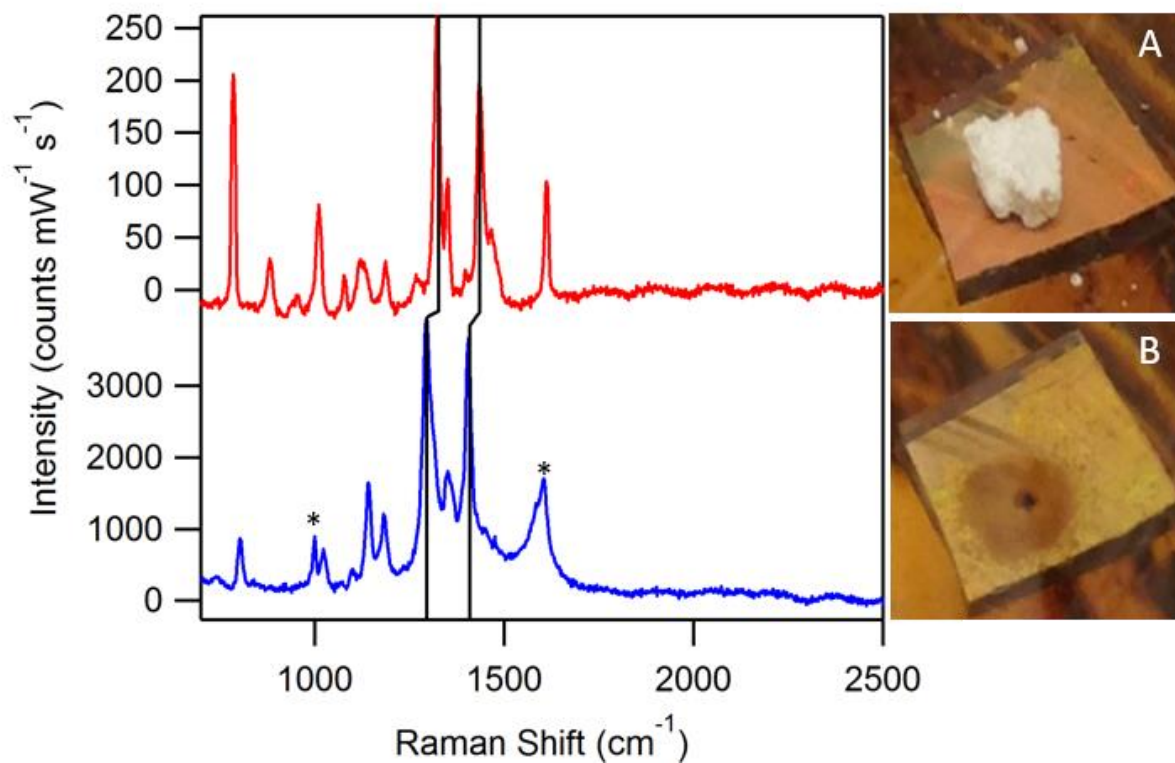


Figure 2.1: Raman spectrum of neat **2.1** (red trace) and Surface-enhanced Raman scattering spectrum (blue trace) of surface functionalized with **2.1**. Overlapping bands indicate the spectra are indeed of the characteristic benzimidazolium peaks, while much greater signal from the AuFON substrate indicates signal enhancement occurs. Asterisk (*) designates signals due to polystyrene. **A** and **B** are photos taken before and after heating on the surface under vacuum whereby **2.1** binds to the AuFONs.

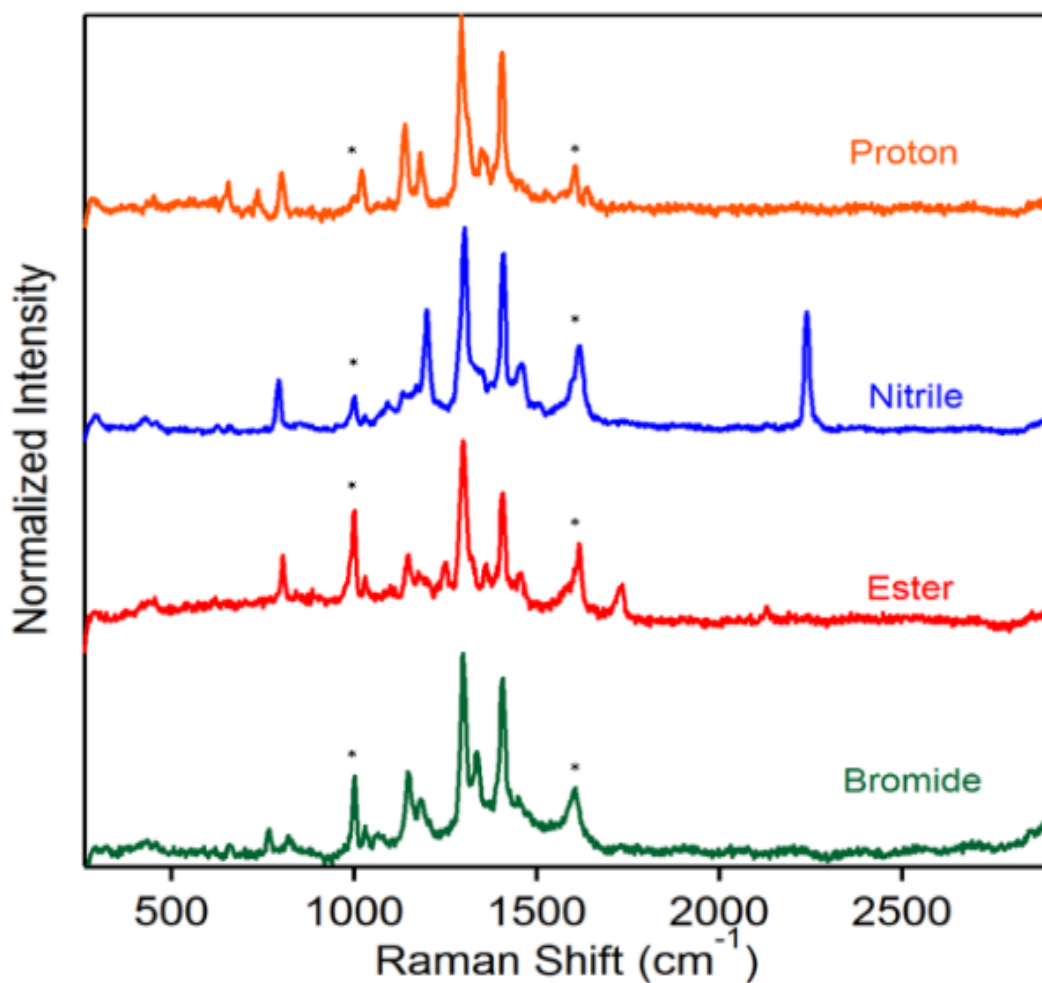


Figure 2.2: Surface-enhanced Raman scattering spectra of films functionalized with **2.1** (orange trace), **2.8** (blue trace), **2.9** (red trace), **2.10** (green trace). Asterisk (*) indicates contribution from polystyrene bands.

spectra at 2240 cm^{-1} and 1720 cm^{-1} , respectively. Nitriles and metal carbonyls have been extremely useful compounds for the preparation of SERS tags due to the signal observed in the silent region of the spectrum.¹¹³ These schemes, however, typically coat the particles with a metal or silica shell in order to achieve stability.²⁸ The inherent stability of carbenes on gold (discussed below) allows for a simpler synthesis of effective SERS tags that are bright in this silent region. Not surprisingly, the spectra for the bromide functionalized NHC (**2.10**), has signals that almost overlay **2.1**.

For NHCs to supplant thiol coated surfaces for SERS, they must show excellent stability under a variety of conditions. Slides with **2.1**-AuFONs were immersed in a variety of solvents, as well as acid and base for 24 hours at room temperature. In each case, no degradation was observed. The resistance to acid (1M) and base (5M) is particularly important for post-synthetic modification at a surface and detection applications in extreme environments. Remarkably, **2.1**-AuFON was stable to a reductant, as exposure to a 1% solution of NH_2OH showed no degradation.

Post-synthetic modification allows for building successive complex compounds on a surface or solid that may otherwise be highly challenging or unfeasible.^{126, 128} Post synthetic modification of **2.9**-AuFON is an excellent test case since the alkyl functionality of the ester can be removed to give the carboxylate which would be challenging to synthesize directly.¹²² An IR of **2.9** shows the signature ester stretch at 1720 cm^{-1} . A reaction of **2.9**-AuFONs and excess KOH in reagent-grade 95% ethanol showed elimination of the peak at 1720 cm^{-1} and retention of the other peaks. In particular, a change in the relative intensities of the bands near $1100\text{-}1200\text{ cm}^{-1}$ indicates hydrolysis of the ester to the carboxylate (Figure **2.3**). This reactivity was further confirmed by

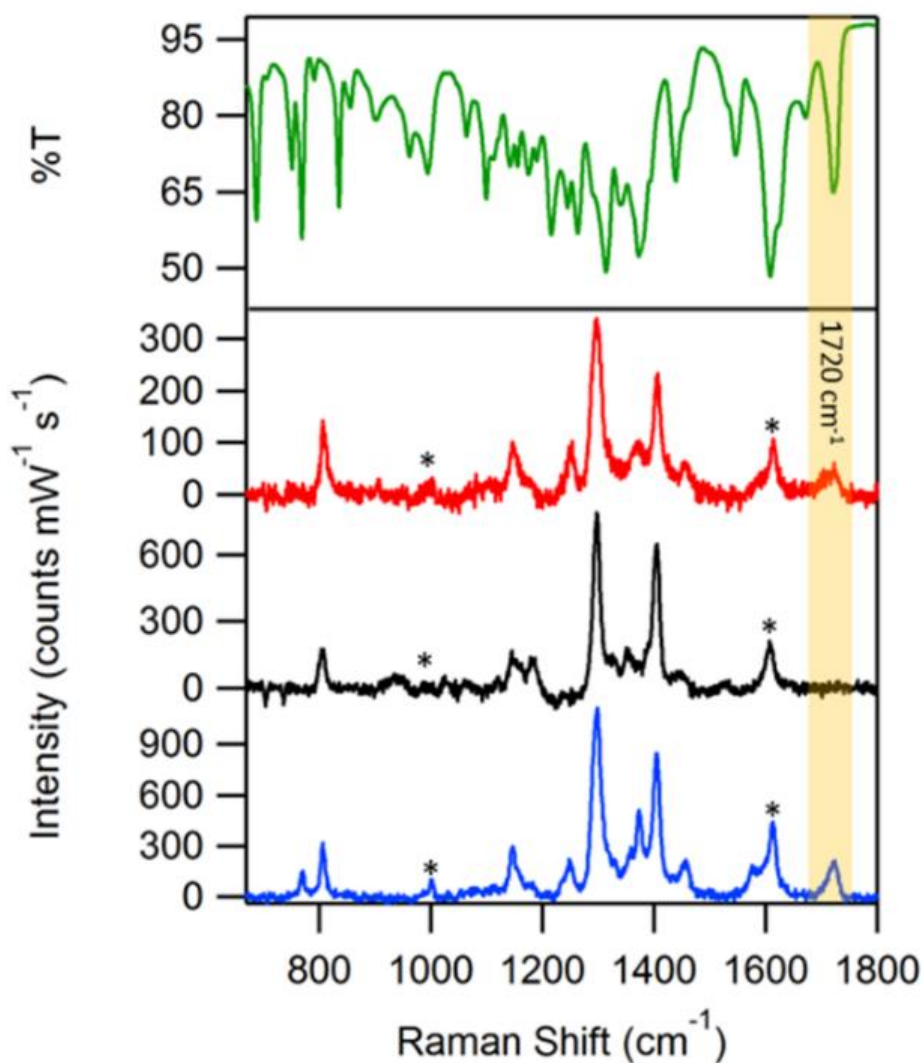


Figure 2.3: Reaction of carboxylate functionalized surfaces. After reaction surfaces functionalized with 2.9 with base (red trace to black trace), heating in a solution of EEDQ can reform the methyl ester (blue trace). Overlaid IR spectrum of 2.9 (green trace) corresponds to the signature ester peak. Asterisk (*) indicates contribution from polystyrene bands.

reformation of the original **2.9**-AuFON by addition of the commonly used coupling reagent, N-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline (EEDQ), in a methanol solution.³⁰ This pair of reactions shows that post-synthetic modifications are possible on an NHC modified surface for SERS applications.

Conclusion

In conclusion, we have demonstrated a general three step synthesis for preparing orthogonally functionalized, masked NHCs. These CO₂-adducted NHCs react in solvent free conditions under heating *in vacuo* on AuFONs to form NHC-functionalized substrates. The characteristic peaks from the benzimidazolium are SERS enhanced and represent the first NHC SERS spectra. Functional groups with clear vibrational modes in the silent region (such as nitrile) are easily prepared, which makes these species highly valuable as tags for a variety of SERS surfaces. The coated AuFONs are stable to a variety of solvents, acid, base, and reductants. This stability is in direct contrast to thiol coated AuFONs which are the current standard for functionalized detection with SERS. Finally, the stability of the NHC coated AuFONs allows for reactions to take place at the functional group off the benzimidazolium providing a simple route for post-synthetic modification of the surface. These factors, from ease of synthesis for functionalized NHCs, to improved stability, demonstrate that NHC's have great potential to supplant thiols for surface-enhanced spectroscopy applications in the near future.

Experimental

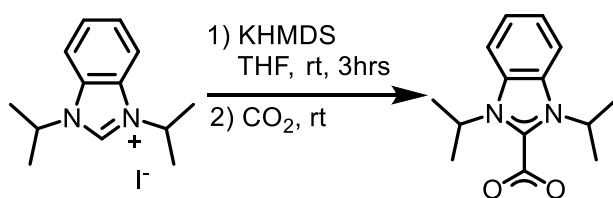
General Considerations for Synthesis:

All glassware for air and water sensitive reactions were dried at 170 °C overnight before use. All reactions were stirred vigorously with magnetic stirrers. A glovebox with a dinitrogen atmosphere was used for formation of the free carbenes for NHC-CO₂ adduct synthesis. Tetrahydrofuran used in NHC-CO₂ adduct reactions was dried on an Innovative Technologies (Newburyport, MA) Pure Solv MD-7 Solvent Purification System, degassed by three freeze-pump-thaw cycles on a Schlenk line to remove dioxygen and stored under activated 4 Å molecular sieves prior to use. Carbon dioxide gas was ultra pure grade from Airgas. Celite was dried at 240 °C under vacuum overnight and stored in a dinitrogen glovebox. The compounds 1,3-diisopropyl-benzoimidazolium iodide, **2.1** and 1H-benzoimidazole-5-carbonitrile, **2.2** were prepared from previous literature procedures or as described previously. All other compounds were purchased from commercial vendors at highest available purity and used without any further purification.

Solution ¹H NMR and ¹³C NMR were performed on a Varian VNMRS 500 MHz narrow-bore broadband system at 298 K. All ¹H and ¹³C shifts were referenced to the residual solvent. All solution 2D NMR experiments were performed on Varian VNMRS 600 MHz narrow-bore broadband system at 298 K. HSQC experiments were obtained on a Varian VNMRS 600 MHz narrow-bore broadband system at 298K. All mass spectrometry analyses were conducted at the Mass Spectrometry Center located in the Department of Chemistry at the University of Tennessee. The DART analyses on neutral organic

molecules were performed using a JEOL AccuTOF-D time-of-flight (TOF) mass spectrometer with a DART (direct analysis in real time) ionization source from JEOL USA, Inc. (Peabody, MA). The ESI/MS analyses on charged organic molecules were performed using a QSTAR Elite quadrupole time-of-flight (QTOF) mass spectrometer with an electrospray ionization source from AB Sciex (Concord, Ontario, Canada). Solutions for mass spectrometry with the NHC-CO₂ adducts were prepared in dichloromethane. All other solutions for mass spectrometry were prepared in methanol. Infrared spectra were collected on a Thermo Scientific Nicolet iS10 with a Smart iTR accessory for attenuated total reflectance (ATR) using the neat molecules.

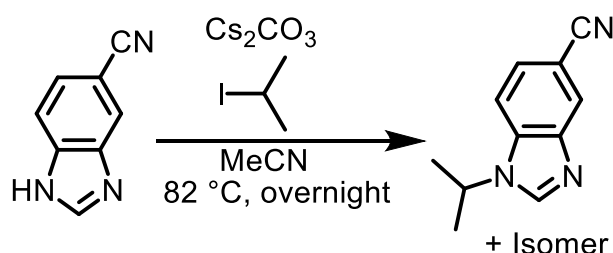
Synthesis of 2-carboxy-1,3-diisopropyl-benzimidazolium, 2.1:



1,3-diisopropyl-benzimidazolium iodide (0.5004 g, 1.515 mmol) was added to a 20 mL scintillation vial. Solid potassium bis(trimethylsilyl)amide (0.3059 g, 1.533 mmol) and then tetrahydrofuran (10 mL) were added to the vial. The solution was stirred at ambient temperature for 3 hours, and then was filtered over a short Celite plug into another 20 mL scintillation vial. A bonded septum cap was screwed onto the vial. The vial was taken out of the glovebox and a pre-purged needle with dinitrogen on a Schlenk line was inserted into the cap. A balloon attached to a luer-lock syringe was flushed with carbon dioxide three times and then inflated with carbon dioxide. This balloon was attached to a needle and inserted through the cap into the solution. Dinitrogen pressure was reduced and carbon dioxide was allowed to bubble through the solution with vigorous stirring. During

addition of carbon dioxide a solid precipitate formed. After full deflation of the balloon, an equal volume of diethyl ether was added to the solution and the solid was filtered over a fine porosity frit. The solid was washed with additional diethyl ether (40 mL) and then dried under vacuum which yielded a white powder. Yield: 0.241 g, 65%. **¹H NMR** (CD₃OD, 499.74 MHz): δ 8.04 (dd, $J_1 = 6.3$ Hz, $J_2 = 3.1$ Hz, 2H), 7.73 (dd, $J_1 = 6.3$ Hz, $J_2 = 3.1$ Hz, 2H), 5.08 (sept, $J = 6.9$ Hz, 2H), 1.74 (d, $J = 6.7$ Hz, 12H). **¹³C NMR** (CD₃OD, 125.66 MHz): δ 161.40, 138.95 (br), 132.57, 128.15, 114.96, 52.81, 22.11. **IR**: 2980, 2909, 2769, 2607, 1625, 1552, 1484, 1465, 1435, 1371, 1347, 1322, 1251, 1230, 1176, 1141, 1110, 1056, 995, 981, 881, 836, 756, 690, 647 cm⁻¹. **DART HR MS** (m/z): [M – CO₂ + H]⁺: 203.15407 (found), [C₁₃H₁₇N₂]⁺: 203.15482 (calculated).

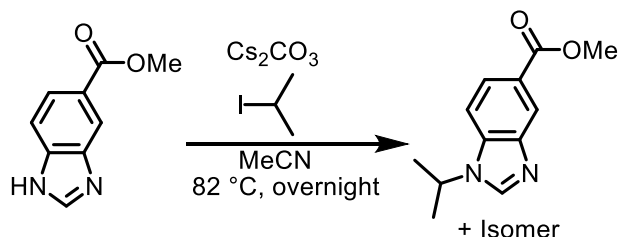
Synthesis of 5/6-cyano-1-isopropyl-benzimidazole, 2.2:



5-cyano-1H-benzimidazole (0.5008 g, 3.501 mmol) and cesium carbonate (1.142 g, 3.506 mmol) were added to a 50 mL round bottom flask. Acetonitrile (10 mL) was added to the flask, followed by the addition of 2-iodopropane (0.630 mL, 6.31 mmol). The reaction was heated to reflux at 82 °C under a dinitrogen atmosphere overnight. The volatiles were then removed in vacuo and the residual solid was extracted three times with ethyl acetate (3 x 20 mL). The ethyl acetate solution was then washed three times with water (3 x 25 mL) and a final time with brine solution (25 mL). The organic layer was then dried with anhydrous magnesium sulfate and then filtered over a medium porosity

frit and concentrated to dryness under vacuum. The resulting product, a tacky light pink solid, was used for the next reaction without further purification as the mixture of two isomers (43:57 ratio based on NMR integration). Yield: 0.597 g, 92%. **¹H NMR** (CDCl₃, 499.74 MHz): δ 8.15 (s, 1H), 8.12 (m, 2H), 7.85 (dd, *J*₁ = 8.5 Hz, *J*₂ = 0.5 Hz, 1H), 7.77 (dd, *J*₁ = 1.5 Hz, *J*₂ = 0.6 Hz, 1H), 7.54-7.48 (m, 3H), 4.66 (m, 2H), 1.65 (d, *J* = 6.8 Hz, 6H), 1.63 (d, *J* = 6.8 Hz, 6H). **¹³C NMR** (CDCl₃, 125.66 MHz): δ 147.03, 143.70, 143.47, 142.76, 136.09, 132.96, 126.10, 125.69, 125.61, 121.58 (overlapping), 119.90, 115.26, 111.26, 105.8, 105.53, 48.51, 48.38, 22.71 (overlapping). **IR**: 3086, 3061, 3027, 2982, 2942, 2219, 1781, 1614, 1491, 1483, 1468, 1408, 1373, 1352, 1332, 1304, 1288, 1273, 1240, 1224, 1169, 1128, 1105, 1031, 946, 892, 867, 823, 814, 753, 646 cm⁻¹. **DART HR MS** (m/z): [M+H]⁺: 186.10403 (found), [C₁₁H₁₂N₃]⁺: 186.10312 (calculated).

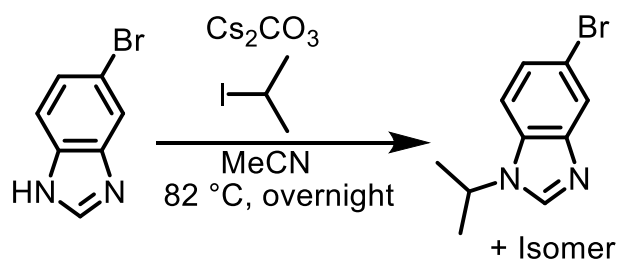
Synthesis of 5/6-methyl-carboxylate-1-isopropyl-benzimidazole, 2.3:



5-methyl-carboxylate-1H-benzimidazole- (4.996 g, 28.38 mmol) and cesium carbonate (9.253 g, 28.40 mmol) were added to a 250 mL round bottom flask. Acetonitrile (100 mL) was added to the flask, followed by the addition of 2-iodopropane (4.540 mL, 45.48 mmol). The reaction was heated to reflux at 82 °C under a dinitrogen atmosphere overnight. The volatiles were then removed in vacuo and the residual solid was extracted three times with ethyl acetate (3 x 70 mL). The ethyl acetate solution was then washed three times with water (3 x 80 mL) and a final time with brine solution (70 mL). The organic layer was

then dried with anhydrous magnesium sulfate and then filtered over a medium porosity frit and concentrated to dryness under vacuum. The resultant product, a viscous brown oil, was used for the next reaction without further purification as the mixture of two isomers (46:54 ratio based on NMR integration). Yield: 4.73 g, 76%. **¹H NMR** (CDCl₃, 499.74 MHz): δ 8.51 (dd, *J*₁ = 1.5 Hz, *J*₂ = 0.5 Hz, 1H), 8.19 (dd, *J*₁ = 1.5 Hz, *J*₂ = 0.5 Hz, 1H), 8.11 (s, 1H), 8.07 (s, 1H), 8.02 (dd, *J*₁ = 8.6 Hz, *J*₂ = 1.5 Hz, 1H), 7.98 (dd, *J*₁ = 8.5 Hz, *J*₂ = 1.6 Hz, 1H), 7.80 (dd, *J*₁ = 8.5 Hz, *J*₂ = 0.5 Hz, 1H), 7.44 (dd, *J*₁ = 8.6 Hz, *J*₂ = 0.5 Hz, 1H), 4.71 (sept, *J* = 6.8 Hz, 1H), 4.66 (sept, *J* = 6.7 Hz, 1H), 3.95 (s, 3H), 3.94 (s, 3H), 1.65 (d, *J* = 7.0 Hz, 6H), 1.63 (d, *J* = 7.0 Hz, 6H). **¹³C NMR** (CDCl₃, 125.66 MHz): δ 167.72, 167.65, 147.56, 143.75, 143.75, 142.87, 142.01, 136.59, 133.11, 124.70, 124.49, 124.34, 123.62, 122.97, 120.13, 112.62, 109.87, 52.30, 52.21, 48.18 (overlapped), 22.85, 22.74. **IR**: 3345, 2971, 1719, 1665, 1609, 1549, 1434, 1370, 1337, 1309, 1264, 1244, 1222, 1172, 1155, 1100, 1065, 992, 963, 906, 836, 792, 769, 748, 707, 688, 644 cm⁻¹. **DART HR MS** (m/z): [M+H]⁺: 219.11293 (found), [C₁₂H₁₅N₂O₂]⁺: 219.11335 (calculated).

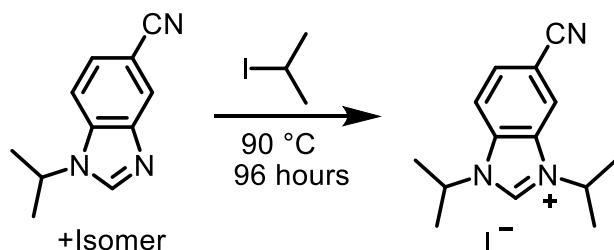
Synthesis of 5/6-Bromo-1-isopropyl-benzimidazole, 2.4:



5-bromo-1H-benzimidazole (2.500 g, 12.69 mmol) and cesium carbonate (4.136 g, 12.69 mmol) were added to a 250 mL round bottom flask. Acetonitrile (50 mL) was added to the flask, followed by the addition of 2-iodopropane (2.555 mL, 25.60 mmol). The reaction was heated to reflux at 82 °C under a dinitrogen atmosphere overnight. The

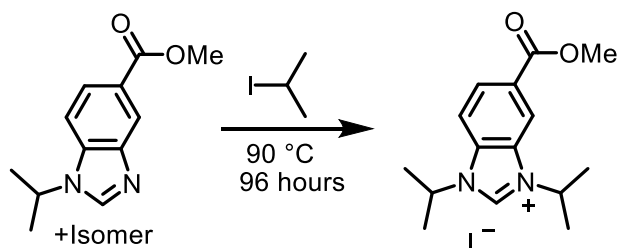
volatiles were then removed in vacuo and the residual solid was extracted three times with ethyl acetate (3 x 30 mL). The ethyl acetate solution was then washed three times with water (3 x 60 mL) and a final time with brine solution (60 mL). The organic layer was then dried with anhydrous magnesium sulfate and then filtered over a medium porosity frit and concentrated to dryness under vacuum. The resultant product, a viscous yellow brown oil, was used for the next reaction without further purification as the mixture of two isomers (48:52 ratio based on NMR integration). Yield: 2.41 g, 79%. **¹H NMR** (CDCl₃, 499.74 MHz): δ 7.98 (s, 1H), 7.97 (s, 1H), 7.96 (d, *J* = 1.7 Hz, 1H), 7.67 (d, *J* = 8.5 Hz, 1H), 7.59 (d, *J* = 1.7 Hz, 1H), 7.40 (dd, *J*₁ = 8.7 Hz, *J*₂ = 2.0 Hz, 1H), 7.38 (dd, *J*₁ = 8.7 Hz, *J*₂ = 1.8 Hz, 1H), 7.30 (d, *J* = 8.7 Hz, 1H), 4.61 (sept, *J* = 6.7 Hz, 1H), 4.59 (sept, *J* = 6.7 Hz, 1H), 1.63 (d, *J* = 6.8 Hz, 6H), 1.62 (d, *J* = 6.8 Hz, 6H). **¹³C NMR** (CDCl₃, 125.66 MHz): δ 145.28, 142.94, 141.20, 140.89, 134.36, 132.22, 125.70, 125.42, 123.17, 121.64, 115.99, 115.09, 113.23, 111.35, 48.01, 47.99, 22.57 (overlapping). **IR**: 3380, 3081, 2976, 2933, 1671, 1609, 1574, 1484, 1459, 1395, 1372, 1339, 1322, 1287, 1273, 1246, 1222, 1202, 1172, 1134, 1097, 1063, 1044, 901, 876, 843, 796, 754, 718, 635 cm⁻¹. **DART HR MS** (m/z): [M+H]⁺: 239.01914 (found), [C₁₀H₁₂N₂Br]⁺: 239.01839 (calculated).

Synthesis of 5-cyano-1,3-diisopropyl-benzimidazolium iodide, 2.5:



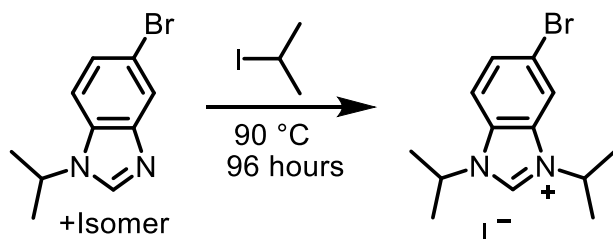
5/6-cyano-1-isopropyl-benzimidazole (**2.2**) (0.800 g, 4.32 mmol) was added to a 35 mL thick-walled glass pressure flask. Neat 2-iodopropane (8.625 mL, 86.41 mmol) was then added to the flask. The flask was sealed with a Teflon screw cap and stirred at 90 °C for 96 h. The flask was then cooled to room temperature and the solution was diluted with toluene (10 mL). The solid was then collected via filtration over a medium porosity frit and washed with additional toluene. The collected solid was then added to a 500 mL round bottom flask and 40 mL of acetonitrile was added which fully dissolved the solids. Approximately 300 mL of diethyl ether was then added to this solution and stirred until precipitation ceased. The solid was then collected via filtration over a medium porosity frit and washed with diethyl ether and dried in vacuo to give a fluffy white solid. Yield: 1.26 g, 82%. ¹H NMR (DMSO-d₆, 499.74 MHz): δ 9.97 (s, 1H), 8.89 (s, 1H), 8.37 (d, *J* = 8.8 Hz, 1H), 8.13 (d, *J* = 8.6 Hz, 1H), 5.10 (m, 2H), 1.66 (d, *J* = 6.2 Hz, 6H), 1.64 (d, *J* = 6.0, 6H). ¹³C NMR (DMSO-d₆, 125.66 MHz): δ 142.12, 133.21, 130.46, 129.49, 119.70, 118.08, 115.60, 108.79, 51.55, 51.37, 21.47 (overlapping). IR: 3107, 2987, 2231, 1823, 1626, 1553, 1490, 1459, 1436, 1412, 1390, 1374, 1355, 1314, 1297, 1254, 1222, 1159, 1133, 1099, 1065, 984, 938, 911, 832, 776, 679, 647 cm⁻¹. ESI HR MS (*m/z*): [M]⁺: 228.1505 (found), [C₁₄H₁₈N₂]⁺: 228.1501 (calculated).

Synthesis of 5-methyl-carboxylate-1,3-diisopropyl-benzimidazolium iodide, 2.6:



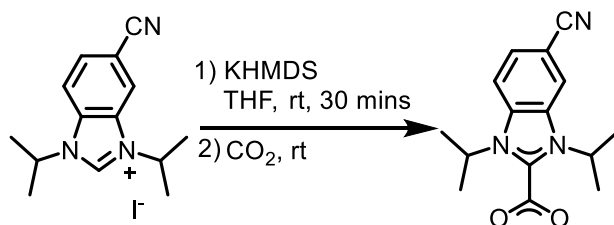
5/6-methyl-carboxylate-1-isopropyl-benzimidazole (**2.3**) (4.170 g, 19.28 mmol) was added to a 350 mL thick-walled glass pressure flask. Neat 2-iodopropane (38.50 mL, 385.7 mmol) was added to the flask. The flask was sealed with a Teflon screw cap and heated at 90 °C for 36 h. The flask was then cooled to room temperature and the solution was diluted with toluene (40 mL). The solid was then filtered over a medium porosity frit and washed with additional toluene. The solid residue was then added to a 1000 mL round bottom flask and 100 mL of methanol was added until the solids fully dissolved. Approximately 600 mL of diethyl ether was then added to this solution and stirred until precipitation ceased. The solid was then filtered over a medium porosity frit, washed with diethyl ether and dried in vacuo to give an off white powder. Yield: 5.64 g, 75%. **¹H NMR** (DMSO-d₆, 499.74 MHz): δ 9.93 (s, 1H), 8.67 (d, *J* = 0.8 Hz, 1H), 8.29 (d, *J* = 8.8 Hz, 1H), 8.23 (dd, *J*₁ = 8.8 Hz, *J*₂ = 1.4 Hz, 1H), 5.24 (sept, *J* = 6.6 Hz, 1H), 5.11 (sept, *J* = 6.6 Hz, 1H), 1.66 (d, *J* = 5.6 Hz, 6H), 1.64 (d, *J* = 5.6 Hz, 6H). **¹³C NMR** (DMSO-d₆, 125.66 MHz): δ 165.34, 141.43, 133.47, 130.76, 127.76, 126.81, 115.47, 114.52, 52.76, 51.27, 50.84, 21.74, 21.48. **IR**: 3108, 2978, 1822, 1723, 1625, 1604, 1556, 1463, 1433, 1415, 1400, 1388, 1362, 1345, 1294, 1270, 1243, 1222, 1184, 1148, 1136, 1117, 1085, 1072, 992, 962, 914, 889, 845, 794, 764, 758, 745, 648, 629 cm⁻¹. **ESI HR MS** (*m/z*): [*M*]⁺: 261.1610 (found), [C₁₅H₂₁N₂O₂]⁺: 261.1603 (calculated).

Synthesis of 5-bromo-1,3-diisopropyl-benzimidazolium iodide, 2.7:



5/6-Bromo-1-isopropyl-benzimidazole (**2.4**) (0.9950 g, 4.182 mmol) was added to a 100 mL thick-walled glass pressure flask. Neat 2-iodopropane (8.35 mL, 83.64 mmol) was added to the flask. The flask was sealed with a Teflon screw cap and heated at 90 °C for 36 h. The flask was then cooled to room temperature and the solution was diluted with toluene (20 mL). The solid was then filtered over a medium porosity frit and washed with additional toluene. The solid residue was then added to a 500 mL round bottom flask and 50 mL of methanol was added until the solids fully dissolved. Approximately 400 mL of diethyl ether was then added to this solution and stirred until precipitation ceased. The solid was then filtered over a medium porosity frit, washed with diethyl ether and dried in vacuo to give brown crystalline needles. Yield: 1.05 g, 61%. **¹H NMR** (DMSO-d₆, 499.74 MHz): δ 9.81 (s, 1H), 8.51 (d, *J* = 1.6 Hz, 1H), 8.13 (d, *J* = 8.5 Hz, 1H), 7.86 (dd, *J*₁ = 8.9 Hz, *J*₂ = 1.8 Hz, 1H), 5.07 (sept, *J* = 6.7 Hz, 1H), 5.06 (sept, *J* = 6.7 Hz, 1H), 1.63 (d, *J* = 6.8 Hz, 6H), 1.62 (d, *J* = 6.8 Hz, 6H). **¹³C NMR** (DMSO-d₆, 125.66 MHz): δ 140.39, 132.36, 130.29, 129.94, 119.53, 117.29, 116.35, 51.56, 51.37, 22.05, 21.97. **IR**: 3160, 3003, 2976, 2930, 2875, 1612, 1560, 1553, 1475, 1422, 1396, 1373, 1318, 1280, 1272, 1247, 1237, 1202, 1175, 1146, 1137, 1115, 1082, 1059, 982, 942, 883, 846, 814, 790, 772, 742, 641 cm⁻¹. **ESI HR MS** (*m/z*): [*M*]⁺: 281.0636 (found), [C₁₃H₁₈N₂Br]⁺: 281.0648 (calculated).

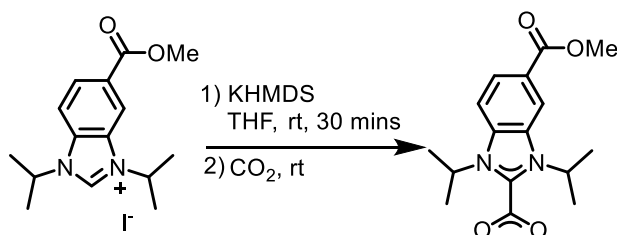
Synthesis of 2-carboxy-5-cyano-1,3-diisopropyl-benzimidazolium, 2.8:



5-cyano-1,3-diisopropyl-benzimidazolium iodide (**2.5**) (0.1990 g, 0.5602 mmol) was added to a 100 mL round bottom flask. Solid potassium bis(trimethylsilyl)amide (0.1132 g, 0.5675 mmol) and then tetrahydrofuran (20 mL) was added to the flask. The suspension was stirred for 30 min, and then was filtered over Celite and washed with additional tetrahydrofuran into another 100 mL round bottom flask. The flask was capped with a Suba-Seal septum and was taken out of the glovebox. A pre-purged needle with dinitrogen on a Schlenk line was inserted through the septum. A balloon attached to a luer-lock syringe was flushed with carbon dioxide three times and then inflated with carbon dioxide. This balloon was attached to a needle and inserted through the septum into the solution. Dinitrogen pressure was reduced and carbon dioxide was allowed to bubble through the solution with vigorous stirring. During addition of carbon dioxide, a solid began to precipitate from the solution. Following deflation of the balloon, an equal volume of diethyl ether was added to the solution and the solid was filtered over a fine porosity frit. The solid was washed with ether (40 mL) and then dried under vacuum to yield the dried NHC-CO₂ adduct as a white hygroscopic solid. The product was shortly dried under vacuum (no longer than 30 minutes) due to decomposition due to loss of CO₂ to form free carbene. Yield: 0.117 g, 77%. ¹H NMR (CD₃OD, 499.74 MHz): δ 8.65 (s, 1H), 8.24 (d, *J* = 8.4 Hz, 1H), 8.03 (d, *J* = 8.4 Hz, 1H), 5.12 (sept, *J* = 6.7 Hz, 1H), 5.11 (sept, *J* = 6.7 Hz, 1H), 1.75 (d, *J* = 6.4 Hz, 12H) (overlapping). ¹³C NMR (CD₃OD, 125.66

MHz): δ 161.40, 135.01, 132.51, 131.09, 120.49, 118.69, 116.55, 111.78, 53.60, 53.54, 22.20, 22.05. **IR**: 2980, 2642, 2229, 1614, 1551, 1494, 1441, 1373, 1348, 1248, 1176, 1140, 1115, 991, 904, 834, 686, 647 cm^{-1} . **DART HR MS** (m/z): $[\text{M} - \text{CO}_2 + \text{H}]^+$: 228.15028 (found), $[\text{C}_{14}\text{H}_{18}\text{N}_2]^+$: 228.15007 (calculated).

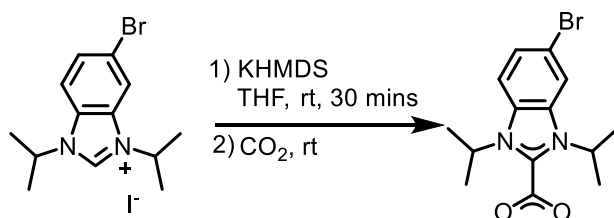
Synthesis of 2-carboxy-5-methyl-carboxylate-1,3-diisopropyl-benzimidazolium, 2.9:



5-methyl-carboxylate-1,3-diisopropyl-benzimidazolium iodide (**2.6**) (0.4994 g, 1.286 mmol) was added to a 100 mL round bottom flask. Solid potassium bis(trimethylsilyl)amide (0.2570 g, 1.288 mmol) and then tetrahydrofuran (50 mL) was added to this flask. The suspension was stirred for 30 min, and then was filtered over Celite and washed with additional tetrahydrofuran into another 100 mL round bottom flask. The flask was capped with a Suba-Seal septum and was taken out of the glovebox. A pre-purged needle with dinitrogen on a Schlenk line was inserted through the septum. A balloon attached to a luer-lock syringe was flushed with carbon dioxide three times and then inflated with carbon dioxide. This balloon was attached to a needle and inserted through the septum into the solution. Dinitrogen pressure was reduced and carbon dioxide was allowed to bubble through the solution with vigorous stirring. During addition of carbon dioxide, a solid began to precipitate from the solution. After deflation of the balloon, an equal volume of diethyl ether was added to the solution and the solid was filtered over a fine porosity frit. The solid was washed with additional ether (40 mL) and

then dried under vacuum to yield the dried NHC-CO₂ adduct as an off white hygroscopic solid. The product was shortly dried under vacuum (no longer than 30 minutes) due to decomposition due to loss of CO₂ to form free carbene. Yield: 0.284 g, 72%. **¹H NMR** (CD₃OD, 499.74 MHz): δ 8.67 (d, *J* = 0.6 Hz, 1H), 8.35 (dd, *J*₁ = 8.8 Hz, *J*₂ = 1.4 Hz, 1H), 8.16 (d, *J* = 8.7 Hz, 1H), 5.18 (sept, *J* = 6.7 Hz, 1H), 5.12 (sept, *J* = 6.7 Hz, 1H), 4.01 (s, 3H), 1.76 (d, *J* = 6.7 Hz, 6H), 1.75 (d, *J* = 6.7 Hz, 6H). **¹³C NMR** (CD₃OD, 125.66 MHz): δ 166.98, 161.39, 141.38, 135.35, 132.58, 130.34, 128.77, 116.69, 115.25, 53.34, 53.30, 53.14, 22.21, 22.07. **IR**: 2976, 2608, 1721, 1671, 1609, 1546, 1439, 1373, 1340, 1314, 1264, 1246, 1216, 1190, 1176, 1156, 1142, 1100, 1065, 995, 962, 902, 857, 836, 792, 770, 752, 689, 642 cm⁻¹. **DART HR MS** (*m/z*): [M – CO₂ + H]⁺: 261.16056 (found), [C₁₅H₂₁N₂O₂]⁺: 261.16030 (calculated).

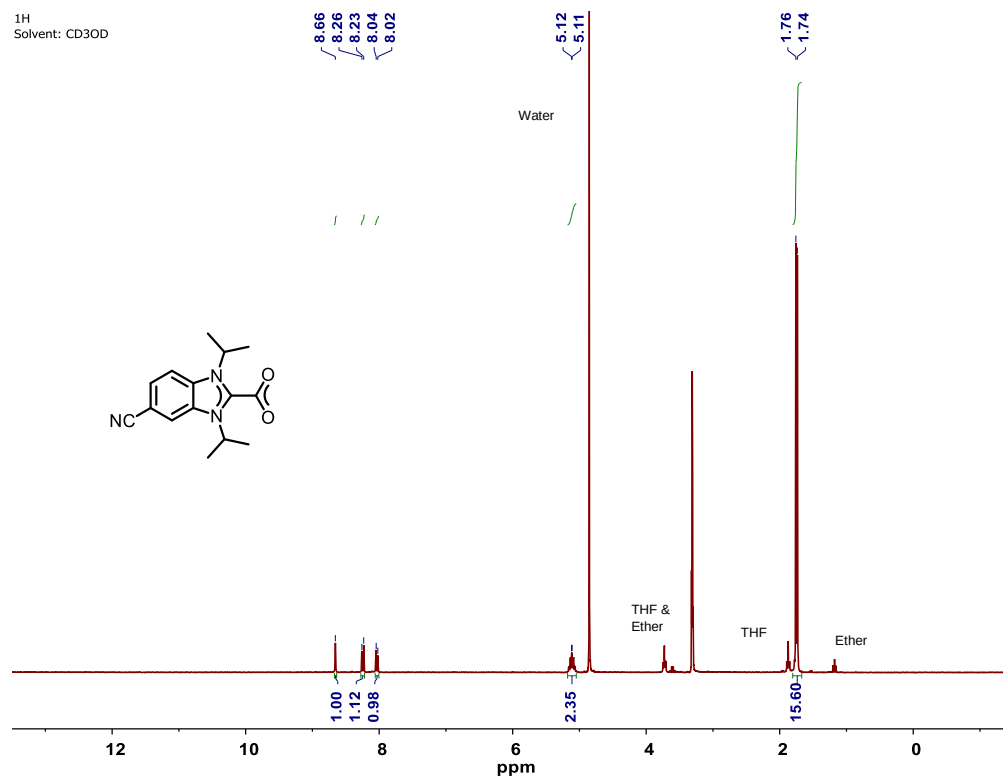
Synthesis of 5-bromo-2-carboxy-1,3-diisopropyl-benzimidazolium, **2.10**:



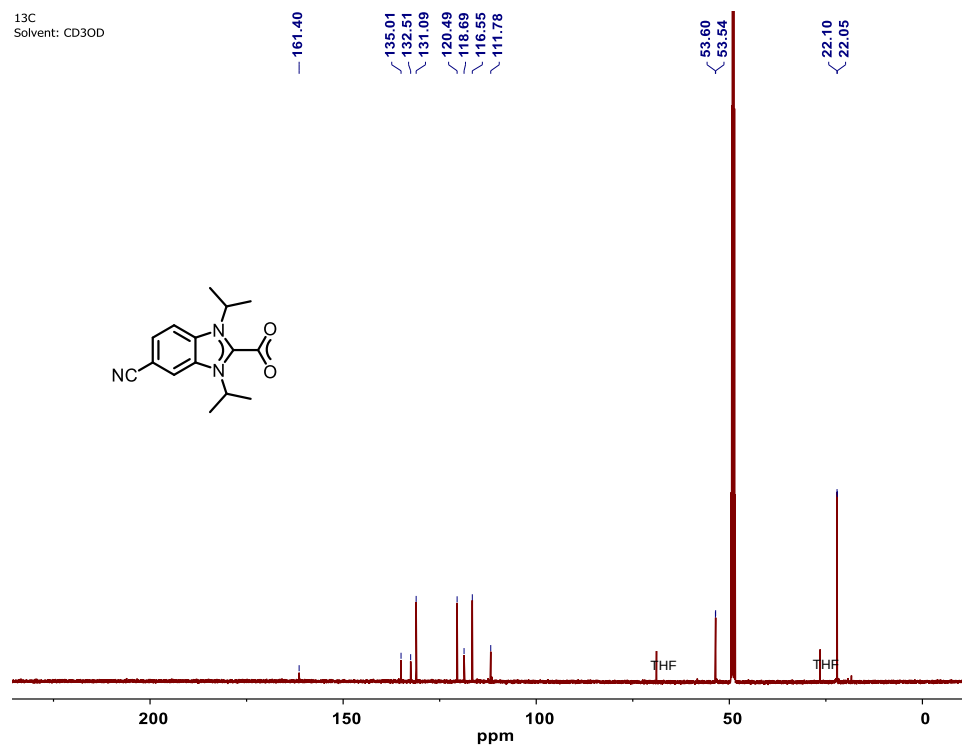
5-bromo-1,3-diisopropyl-benzimidazolium iodide (**2.7**) (0.4002 g, 0.9782 mmol) was added to a 100 mL round bottom flask. Solid potassium bis(trimethylsilyl)amide (0.1958 g, 0.9815 mmol) and then tetrahydrofuran (40 mL) was added to this flask. The suspension was stirred for 30 min, and then was filtered over Celite and washed with additional tetrahydrofuran into another 100 mL round bottom flask. The flask was capped with a Suba-Seal septum and was taken out of the glovebox. A pre-purged needle with dinitrogen on a Schlenk line was inserted through the septum. A balloon attached to a luer-lock syringe was flushed with carbon dioxide three times and then inflated with

carbon dioxide. This balloon was attached to a needle and inserted through the septum into the solution. Dinitrogen pressure was reduced and carbon dioxide was allowed to bubble through the solution with vigorous stirring. During addition of carbon dioxide, a solid began to precipitate from the solution. After deflation of the balloon, an equal volume of diethyl ether was added to the solution and the solid was filtered over a fine porosity frit. The solid was washed with ether (40 mL) and then dried under vacuum to yield the dried NHC-CO₂ adduct as a white hygroscopic solid. The product was shortly dried under vacuum (no longer than 30 minutes) due to decomposition due to loss of CO₂ to form free carbene. Yield: 0.207 g, 65%. **¹H NMR** (CD₃OD, 499.74 MHz): δ 8.34 (d, *J* = 1.5 Hz, 1H), 7.99 (d, *J* = 8.8 Hz, 1H), 7.86 (dd, *J*₁ = 8.9 Hz, *J*₂ = 1.6 Hz, 1H), 5.06 (sept, *J* = 6.7 Hz, 1H), 5.05 (sept, *J* = 6.7 Hz, 1H), 1.74 (d, *J* = 6.8 Hz, 6H), 1.72 (d, *J* = 6.8 Hz, 6H). **¹³C NMR** (CD₃OD, 125.66 MHz): δ 161.40, 133.72, 131.67, 131.48, 121.36, 118.05, 116.54, 53.21, 53.03, 22.10, 22.07. **IR**: 3028, 2974, 2629, 1627, 1551, 1445, 1376, 1329, 1288, 1249, 1221, 1187, 1145, 1112, 1060, 980, 908, 886, 835, 809, 771, 687, 644 cm⁻¹. **DART HR MS** (*m/z*): [*M* - CO₂ + H]⁺: 281.06562 (found), 281.0653 (calculated).

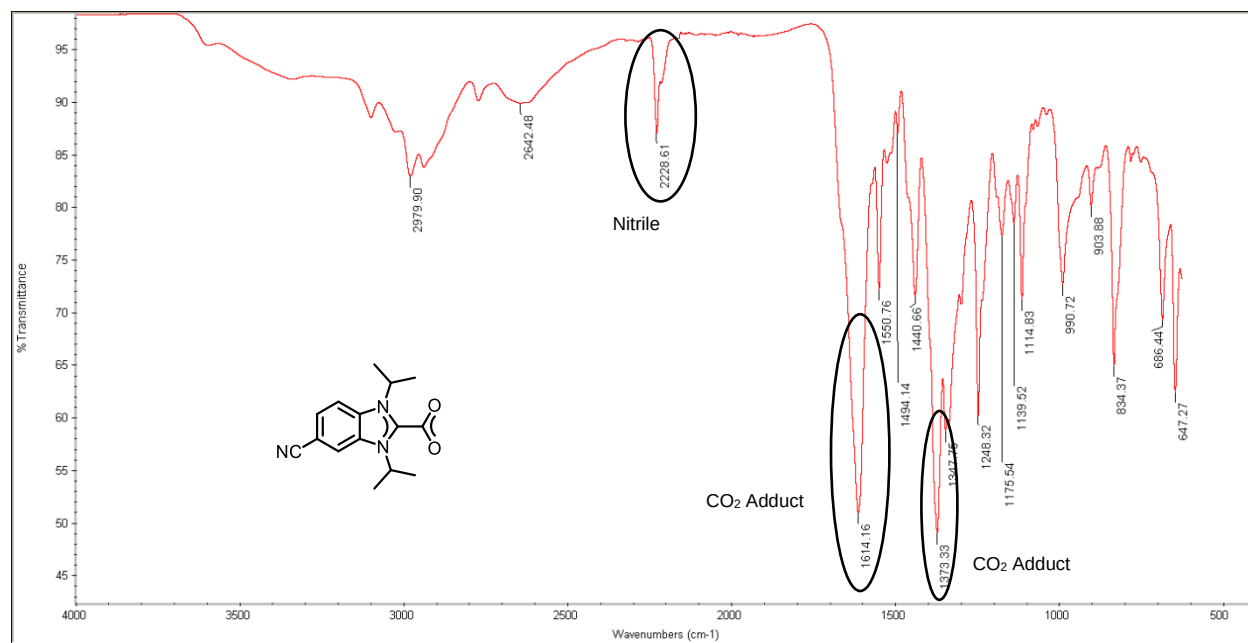
Selected Spectra Characterization:



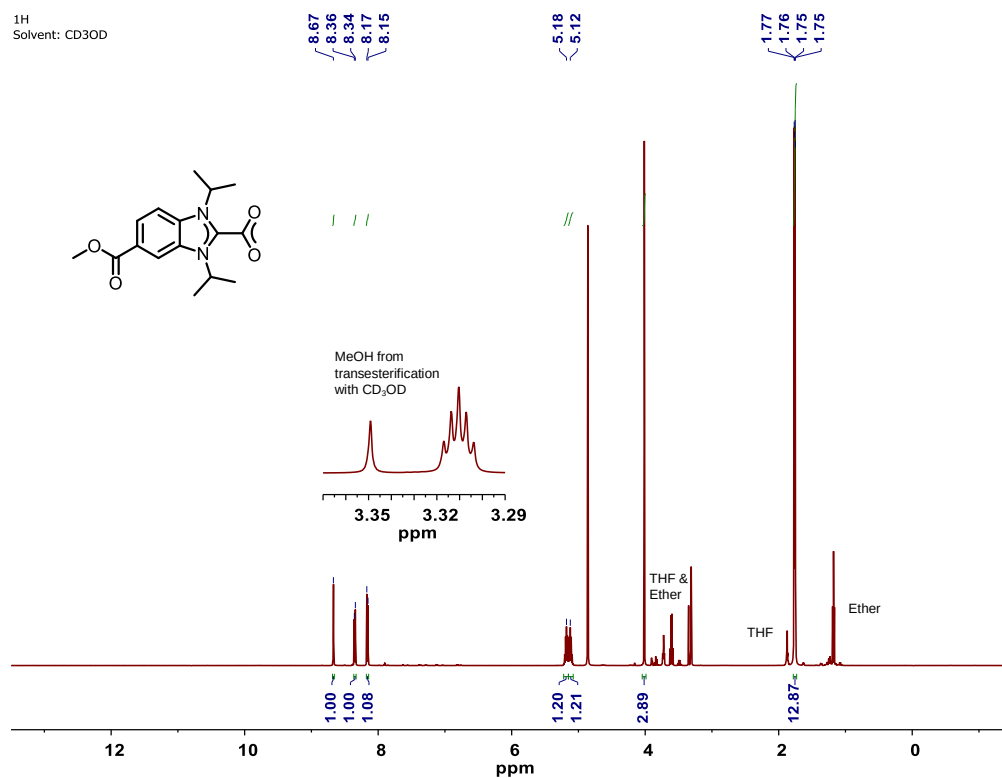
Spectrum 2.1: ¹H NMR of **2.8** in CD₃OD.



Spectrum 2.2: ¹³C NMR of **2.8** in CD₃OD.

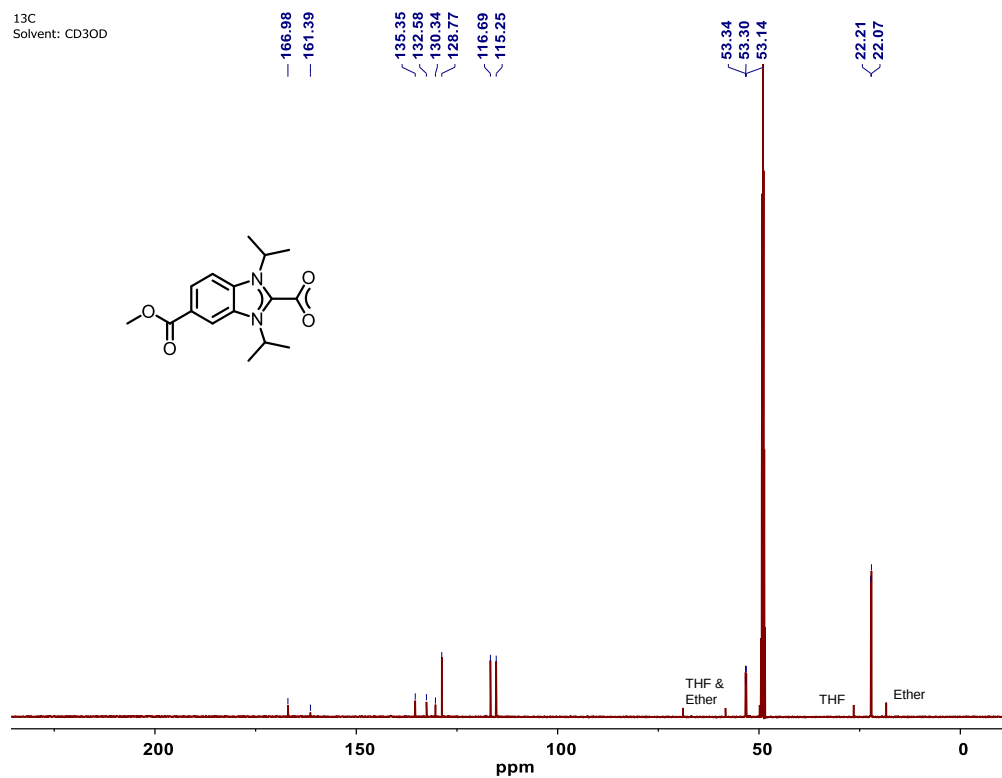


Spectrum 2.3: ATR-IR of **2.8**. Signature CO₂ adduct peaks are denoted by stretches at 1614 and 1373 cm⁻¹. Nitrile functional group is shown by the stretch at 2229 cm⁻¹.

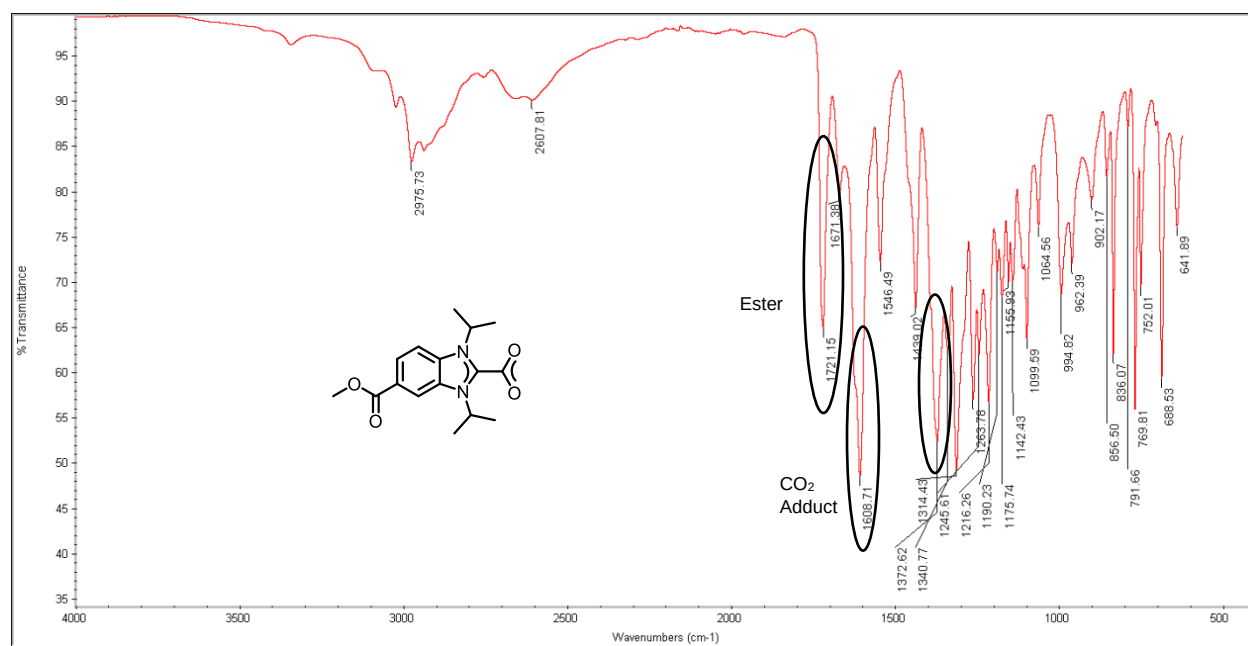


Spectrum 2.4: ¹H NMR of **2.9** in CD₃OD.

¹³C
Solvent: CD₃OD

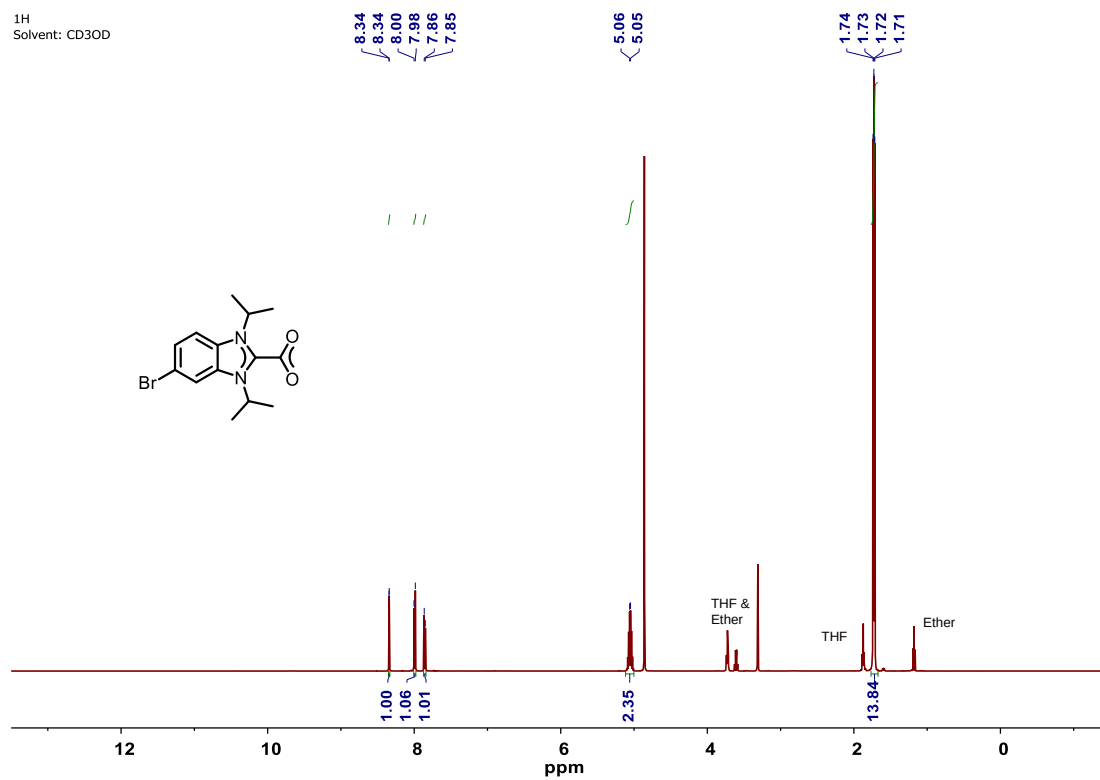


Spectrum 2.5: ¹³C NMR of **2.9** in CD₃OD.



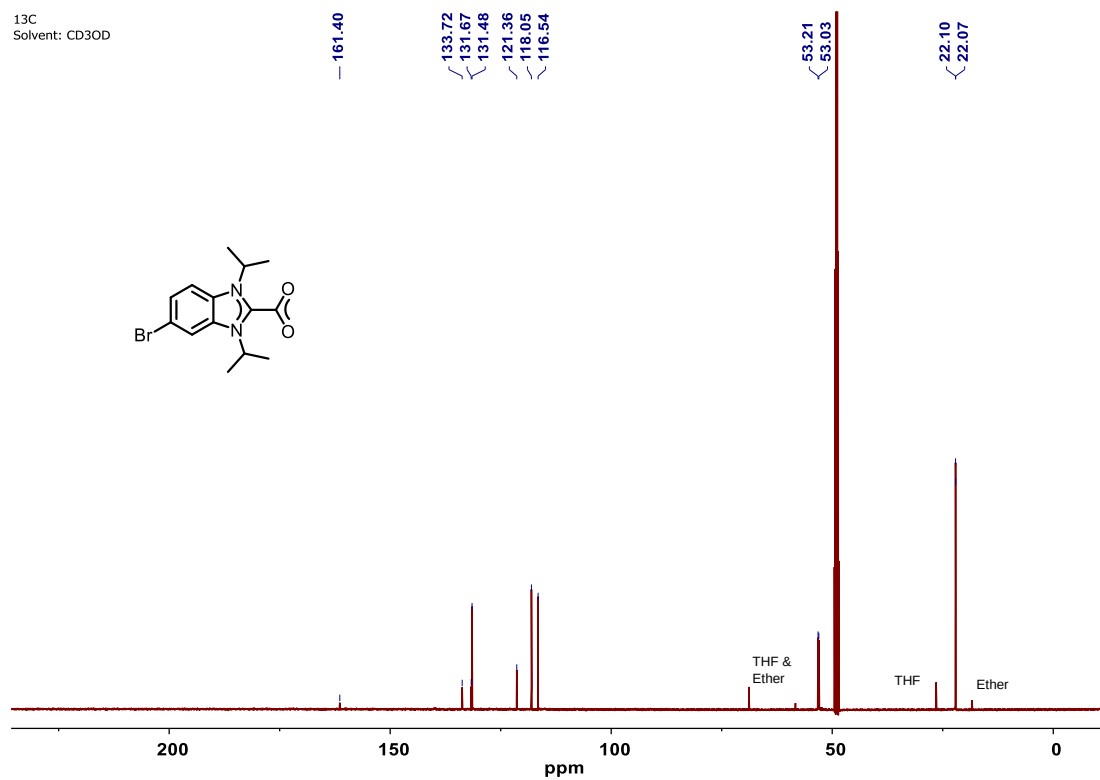
Spectrum 2.6: ATR-IR of **2.9**. Signature CO₂ adduct peaks are denoted by stretches at 1609 and 1373 cm⁻¹. Ester functional group is shown by stretch at 1721 cm⁻¹.

¹H
Solvent: CD₃OD

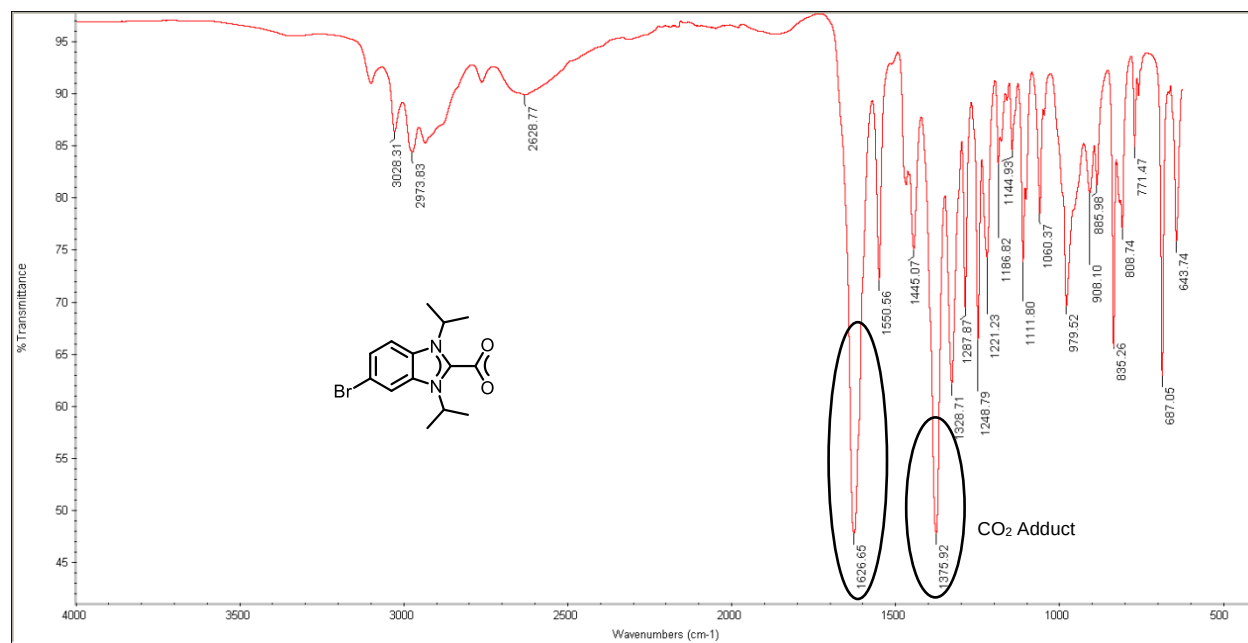


Spectrum 2.7: ¹H NMR of **2.10** in CD₃OD.

¹³C
Solvent: CD₃OD



Spectrum 2.8: ¹³C NMR of **2.10** in CD₃OD.



Spectrum 2.9: ATR-IR of **2.10**. Signature CO₂ adduct peaks are denoted by stretches at 1627 and 1376 cm⁻¹.

**Chapter Three: Facile Synthesis and *in situ* Chemical
Transformations of SERS Active N-Heterocyclic Carbene
Functionalized Gold Nanoparticles**

This work is done in collaboration with the authors Darius J. Yohannan, Joseph F. DeJesus, Leonhard F. P. Karger, Lindy M. Sherman, Jeffrey C. Becca, Shelby L. Strausser, Lasse Jensen, David M. Jenkins, and Jon P. Camden. A manuscript is in preparation with the same title as this Chapter.

My contribution was the initial idea and synthesis of the key ligands, NHC metal complexes and intermediates, which were fully characterized. The primary credit is shared with Darius J. Yohannan and Leonhard F. P. Karger from Dr. Jon Camden's group. Along with Lindy M. Sherman, they were responsible for all the AuNP synthesis involving these complexes and acquisition of the SERS spectra. The calculations were done by Jeffrey C. Becca from Dr. Lasse Jensen's group. Their contributions are necessary to the story of the chapter and are included.

Abstract

The remarkable resilience of N-heterocyclic carbene (NHC) gold bonds has quickly made NHCs a ligand of choice when functionalizing noble metal surfaces. Despite rapid progress using deposition from the free or CO₂-protected carbenes, synthetic challenges severely hinder the creation of NHC surfaces with protic functional groups, such as alcohols and amines, and the creation of larger NHC-protected nanoparticles. Using a simple and reproducible method we synthesize NHC-coated gold NPs (>15 nm diameter) from the gold(I) NHC complexes and aqueous NPs *without the need for external reductants or other chemicals*. This approach enables functional groups, such as a nitro-NHC, that cannot be prepared through the standard NHC-CO₂ adduct precursors. The resilience of the NHC-Au bond allows for a post-synthetic modification whereby the nitro is transformed into an amine, which is further shown capable of amide coupling with a carboxylic acid. The simplicity of our approach, its compatibility with aqueous nanoparticles solutions, and its ability to form protic functional groups on the NHC greatly expands the potential of NHC-functionalized noble-metal surfaces.

Introduction

It has long been known that N-heterocyclic carbenes (NHCs) form strong bonds with noble metals;^{22, 129} however, the extreme robustness of NHC self-assembled monolayers (SAMs) was only recently recognized.^{21, 26, 130, 131} The enhanced stability and accessibility for chemical modifications^{23, 26, 112} of NHC-SAMs is allowing NHCs to supplant thiols in applications from catalysis and biosensing to drug delivery.^{22, 35, 36, 132-137} NHC-coated materials are particularly appealing when non-ideal conditions, particularly swings in pH or temperature, are required.^{21, 22}

While NHC-CO₂ adducts or NHC bicarbonate salts are the most common method for populating noble metal surfaces,^{22, 23, 25, 112, 138} placing NHCs on nanoparticles is more challenging. Two complementary approaches for nanoparticle functionalization with NHCs have been developed. Either free NHCs can be added directly to preformed nanoparticles (Figure **3.1A**, left)^{139, 140} or gold NHC complexes can be reduced with borohydrides or boranes, forming NHC-functionalized gold nanoparticles under 10 nm (Figure 1A, right).^{122, 141} This small size of the AuNPs can limit their applications. For example, Surface-Enhanced Raman Spectroscopy (SERS) requires nanoparticles in the regime of 20-100 nm,¹⁴² while *in vivo* biological application require NPs greater than 10 nm to avoid rapid elimination by the kidneys.¹⁴³

In addition to the potential size restriction on the AuNPs, NHCs have another key limitation versus thiols, namely, functionalizing with protic groups require extra synthetic considerations. Protic groups on thiols, whether alcohol or amine, have been applied for sensing in SERS¹⁴⁴⁻¹⁴⁷ and as anti-bacterial agents in biological applications.^{148, 149} While thiols can be added to noble metal surfaces directly, free NHCs are not stable under ambient conditions. Indeed, many protic functional groups, such as alcohols and amines, are incompatible with the strong bases that are used to deprotonate the NHCs (Figure **3.1B**). In fact, to date, only carboxylic acids have been employed for functionalizing AuNPs. Crudden and coworkers ingeniously prepared a pendant carboxylic acid on the

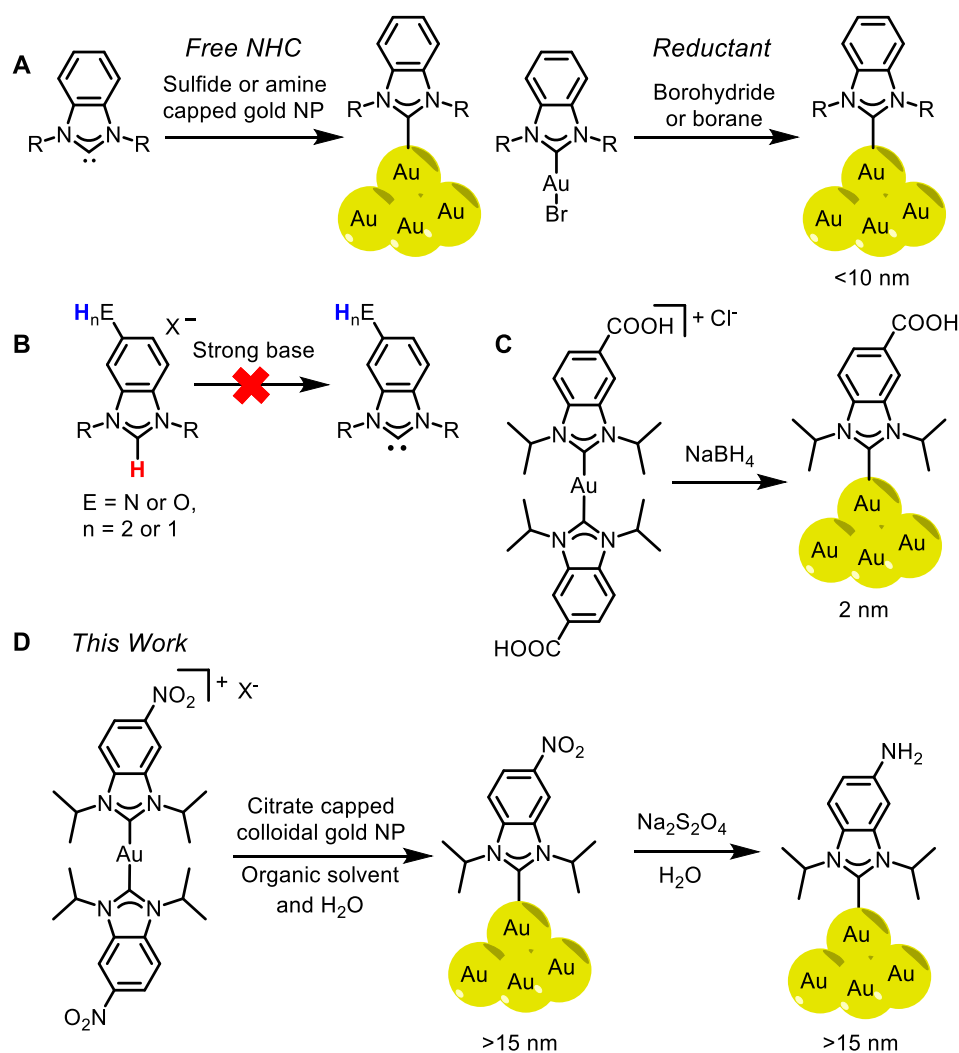


Figure 3.1: Examples of methods of NHC functionalized nanoparticle synthesis. **A** Two general methods for forming NHC-capped AuNPs with aprotic functional groups. **B** Forming free NHCs with protic functional groups is not possible since the protic proton (blue) is more readily deprotonated than the benzimidazolium proton (red). **C:** Crudden has formed small NPs with carboxylic acids on the backbone. **D** This work demonstrates a general method for NHC AuNP formation for large NPs that can undergo post synthetic modification to yield protic functional groups on the NHC.

back of the NHC gold complex precursor prior to reduction with sodium borohydride (Figure **3.1C**).¹²² However, even this case has constraints, as the carboxylic acid is resistant to the external reductant, and the functional group was prepared from the ester after formation of the gold NHC complex. Clearly for NHCs to reach their promise as versatile ligands for surfaces and NPs, a general, straightforward method for including protic functional groups on the NHC must be developed.

In this chapter, we report a general method for NHC coating of large NPs that allows access to protic functional groups on the surface (Figure **3.1D**). Addition of NHC gold(I) complexes to citrate-capped AuNPs (>15 nm diameter) leads to NHC coating of the NPs. Both functionalized and unfunctionalized NHCs can be transferred and this eliminates the need for NHC-CO₂ adducts, bicarbonate salts or external reductants. A post synthetic modification sequence demonstrates that amines can be formed which subsequently undergo amide coupling with a carboxylic acid. Critically, each step in the synthetic sequence on the AuNP was followed by SERS measurements, combined with isotope labeling and theoretical calculations, to confirm the progress of the chemical reactions on the AuNP.

Results and Discussion

While our goal was to introduce functionalized NHCs to nanoparticles, we had previously employed CO₂-protected NHCs to make SERS-active NHC-functionalized gold film-over-nanosphere (AuFONs).^{112, 138} Since this method of nanoparticle coverage has not been effective except for finite nanoclusters,¹⁵⁰ we believed that gold(I) complexes may allow for an effective method of transferring the NHC to the AuNP (Figure **3.2**). Stirring a dilute solution of the gold(I) salt (**3.1-CI/I**) in a biphasic mixture of

dichloromethane and water with citrate-capped nanoparticles successfully appended the NHC to the colloids without the need of an external reductant, forming **3.1-AuNPs** (Figure **3.2**). The NHC binding to the AuNP was confirmed after aggregation of the nanoparticles with sodium bromide and elucidation using SERS. The resulting spectrum (Figure **3.3**, red trace) was consistent with SERS spectra obtained with AuFONs functionalized with the same NHC.^{112, 138} Peaks at 1296 cm⁻¹ and 1403 cm⁻¹ are present in all SERS spectra, which identify the isopropyl and aryl stretching frequencies.³⁴ These peaks are red-shifted approximately 20 cm⁻¹ relative to the Raman spectra, owing to a decrease in electron density due to the presence of a metal. Switching the solvent of the reaction to acetonitrile also resulted in formation of **3.1-AuNPs** (Figure **3.3**, blue trace). We also found that this approach works with a monosubstituted gold(I) complex. We repeated the procedure with **3.2-Cl** (Figure **3.2**) and also succeed in preparing **3.1-AuNPs** (Figure **3.3**, green trace). These combined results are direct proof that the unfunctionalized NHC has been bound to the colloid, making **3.1-AuNPs**, and is effective over a variety of conditions.

This approach, however, is not amenable to the synthesis of an amine-functionalized surface due to the reactivity of the protic R-group. We reasoned that a nitro-NHC-functionalized gold surface could serve as a useful intermediate for an *in situ* reduction of the nitro-NHC to the amine-NHC. We synthesized the benzimidazolium iodide precursor, **3.6-I**, modifying from our previously reported method with other functional groups, in 70.3% yield over two steps from 5-nitro-benzimidazole (See SI).¹¹²

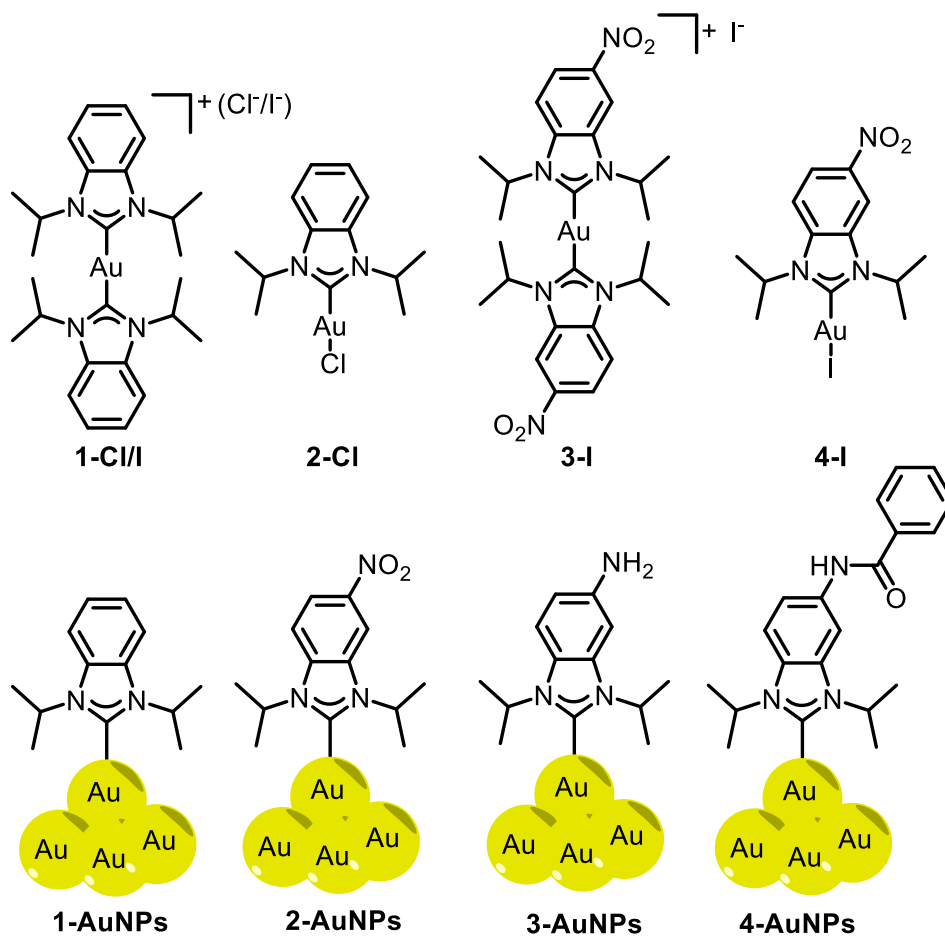


Figure 3.2: Summary of NHC complexes used for SERS measurements and their corresponding numbers. Complexes without colloids were synthesized and later added in a biphasic mixture of CH_2Cl_2 /water to **AuNPs**. SERS was taken of complexes with colloids.

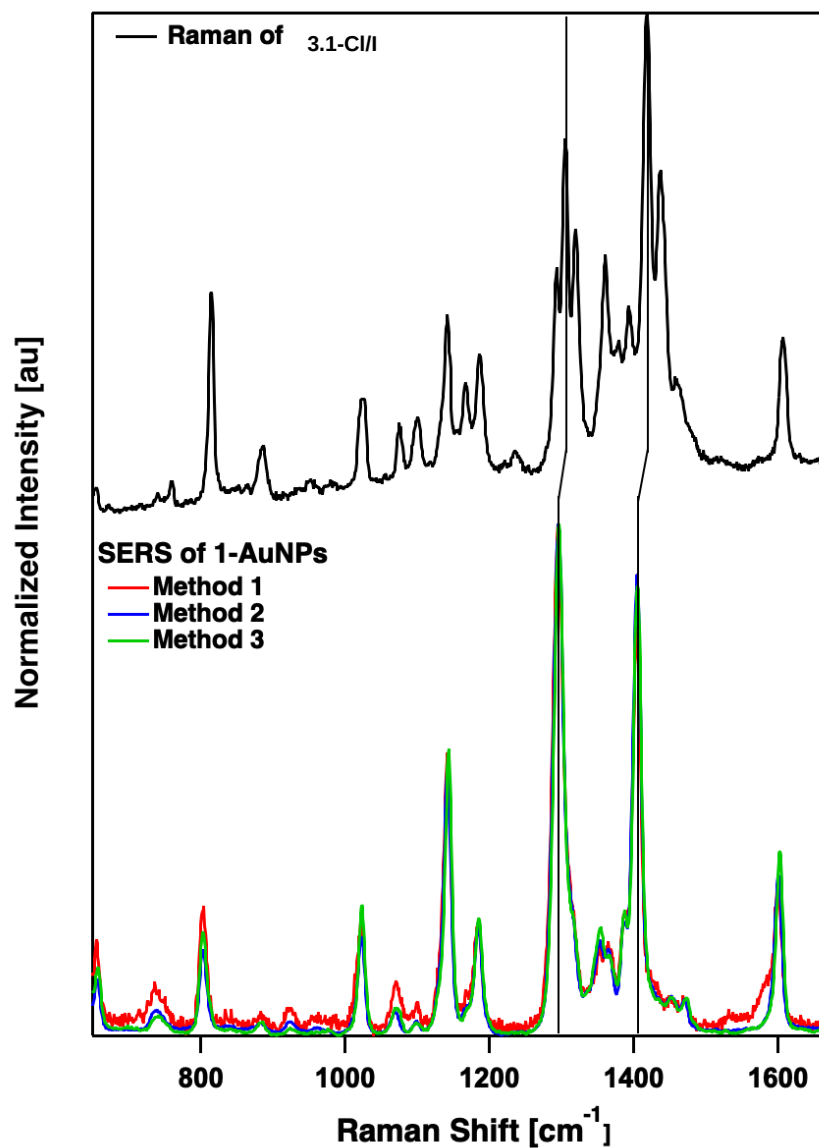


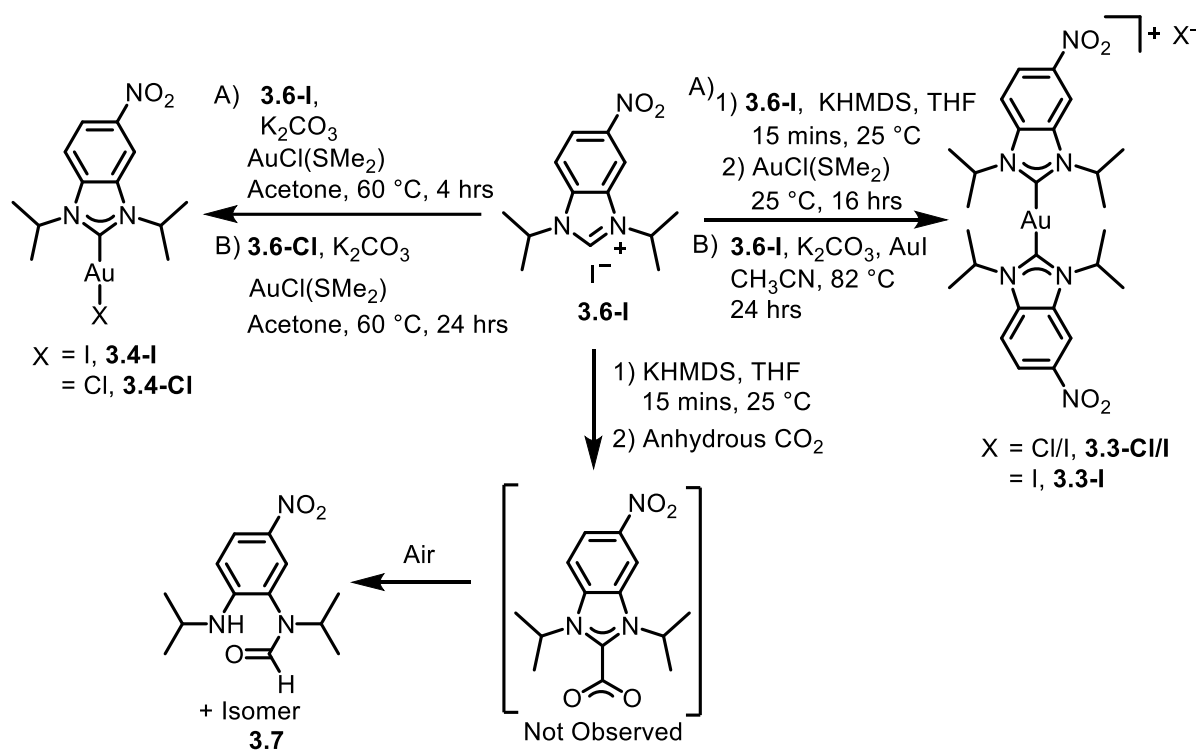
Figure 3.3: Raman spectrum of **3.1-CI/I** alongside SERS of **3.1-AuNPs**. Three methods were used to append NHCs to colloids, all presenting the same signatures for **3.1-AuNPs**. Red spectrum shows SERS of **3.1-AuNPs** functionalized with **3.1-CI/I** dissolved in CH_2Cl_2 . Blue spectrum shows SERS of **3.1-AuNPs** functionalized with **3.1-CI/I** dissolved in CH_3CN . Green **3.1-AuNPs** functionalized with **3.2-CI** dissolved in CH_2Cl_2 .

The bis-NHC gold complexes, **3.3-Cl/I** and **3.3-I**, could be prepared by both a strong base (Scheme 1A) and a mild base approach (Scheme **3.1B**) in 95.2% and 71.3% yield, respectively. The complexes were characterized by ^1H NMR (Spectra **3.5** and **3.9**), as well as HRMS (Spectra **3.8** and **3.14**) and X-ray crystallography. In addition, the IR spectra of all of these complexes show the characteristic 1523 and 1341 cm^{-1} N-O stretches (Spectra **3.7** and **3.13**), confirming that the NO_2 moiety is retained.

Since an unfunctionalized mono-NHC complex **3.2-Cl** was effective, we also prepared the nitro variants as well. **3.4-I** and **3.4-Cl** were synthesized in 52.7% and 24.6% yield, respectively, from the corresponding halide salts (Scheme **3.1**, see experimental for details). The gold complexes could be differentiated by ^{13}C NMR with the resonances at 194.80 ppm for **3.3-I** (Spectrum **3.11**), 191.46 (**3.4-I**, Spectrum **3.6**) and 182.03 (**3.4-Cl**, Spectrum **3.16**) ppm, respectively. The difference between the NHC complexes could be confirmed by HRMS as well (Spectra **3.9**, **3.5** and **3.15**, respectively).

Stirring biphasic solutions of **3.3-Cl/I** or **3.4-I** dissolved in CH_2Cl_2 resulted in the formation of **3.2-AuNPs** (Figure **3.2**). As before, the solvent for the gold complex did not have an appreciable effect as **3.3-I** dissolved in acetonitrile resulted in the formation of **3.2-AuNPs**. SERS of **3.2-AuNPs** revealed that this spectrum is reproducible and also comparable to **3.1-AuNPs** with the exception of the 1342 cm^{-1} peak appearing, which is attributed to the nitro stretch (Figure **3.4**).¹⁵¹ Similarly, peaks between 1100-1200 cm^{-1} and 1400 cm^{-1} have varying intensities, possibly owing to the decrease in electron density due to the nitro.

This facile route to forming **3.2-AuNPs** is particularly important for two reasons. First, this method does not require an external reductant, such as sodium borohydride,



Scheme 3.1: Synthesis of gold(I) complexes **3.3-Cl/I**, **3.3-I**, **3.4-I** and **3.4-Cl** and attempted synthesis of CO₂-adduct of nitro functionalized NHC leading to decomposition product, **3.7**.

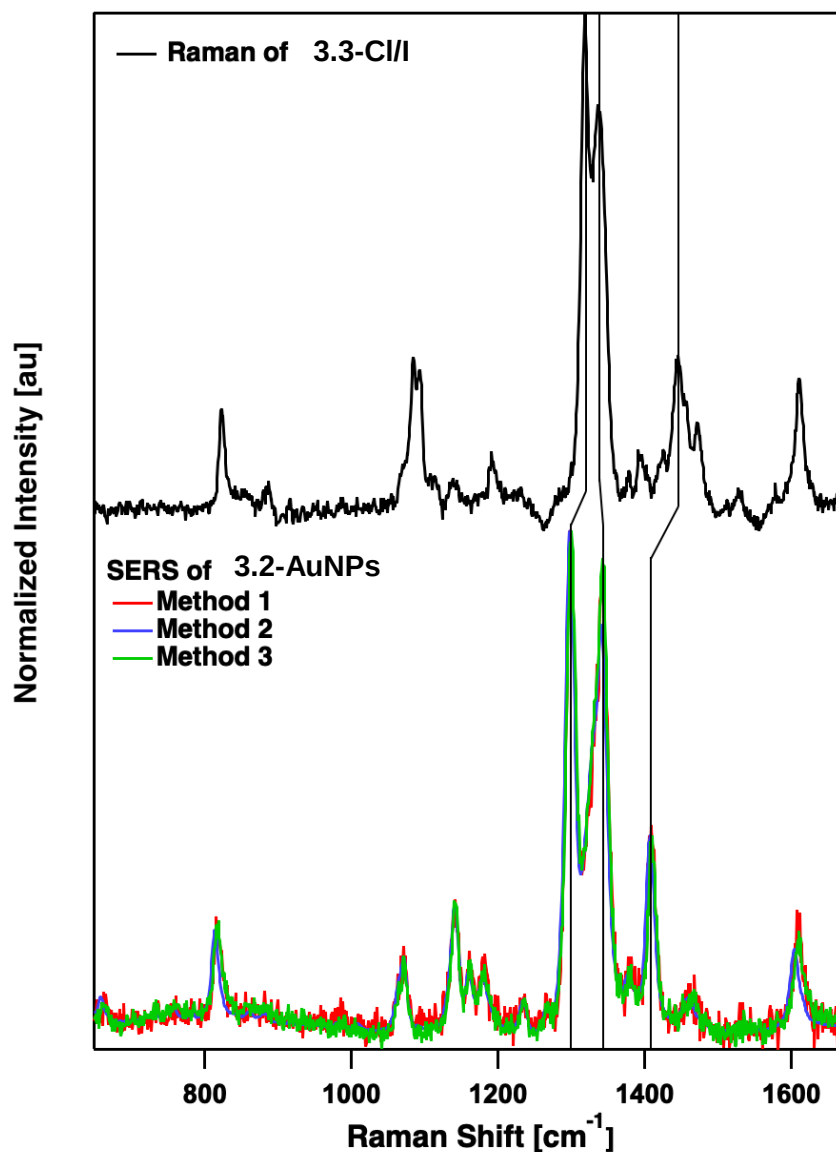


Figure 3.4: Raman spectrum of **3.3-Cl/I** alongside SERS of **3.2-AuNPs**. Three methods were used to append NHCs to colloids, all presenting the same signatures. Red spectrum shows SERS of **3.2-AuNPs** functionalized with **3.3-I** dissolved in CH_2Cl_2 . Blue spectrum shows SERS of **3.2-AuNPs** functionalized with **3.3-I** dissolved in CH_3CN . Green **3.2-AuNPs** functionalized with **3.4-I** dissolved in CH_2Cl_2 .

that would reduce the nitro group prematurely.¹⁵² Second, the CO₂-adduct for **3.6-I** could not be prepared since it is too electron poor (Scheme **3.1**). Indeed, only the ring opened product, compound **3.7**, was prepared.

The exact mechanism of how **3.1-AuNPs** and **3.2-AuNPs** are formed is not clear, but the process is highly general. The NHC transfer works with gold(I) NHC complexes with either one or two NHC ligands, and even confused anionic species, implies that the anion does not play a direct role. The only limitation that we noticed was the transfer failed when the concentration of **3.1** or **3.3** was greater than 200 nM due to spontaneously aggregation. During NMR analysis of the **3.1** and **3.3** in CDCl₃, a red discoloration appeared, possibly suggesting that the complexes were decomposing into nanoparticles in chlorinated solvents. While this may occur in dichloromethane, performing the same simple procedure acetonitrile provided comparable signal, indicating that the NHCs are binding directly to the nanoparticle as opposed to forming smaller nanoparticles and aggregating to the larger pre-formed ones. SEM and TEM measurements also confirmed that there are no visible changes to the size and structure of our AuNPs, providing further evidence that the NHCs are binding directly instead of forming smaller aggregates (Figure **3.5**).

To form the amine NHC-functionalized **3.3-AuNP**, we reduced the nitro group on the **3.2-AuNPs**. Tests with sodium borohydride degraded **3.2-AuNPs**, however a milder reducing agent, sodium hydrosulfite was effective (Scheme **3.2**). SERS analysis showed a decrease in the peak at 1342 cm⁻¹ and a shift of that peak to 1359 cm⁻¹ while all other peaks remained the same in location and relative intensity (Figure **3.6**), which indicates that the NHC was only modified at the nitro position forming **3.3-AuNPs**. In order to

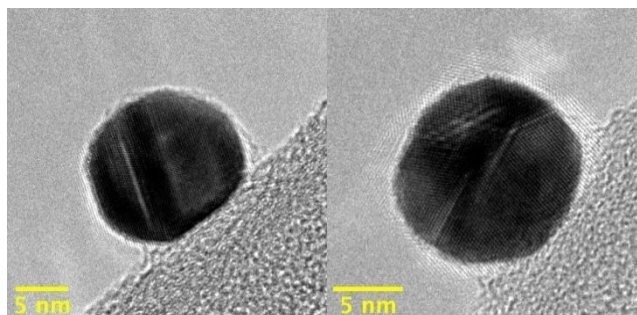
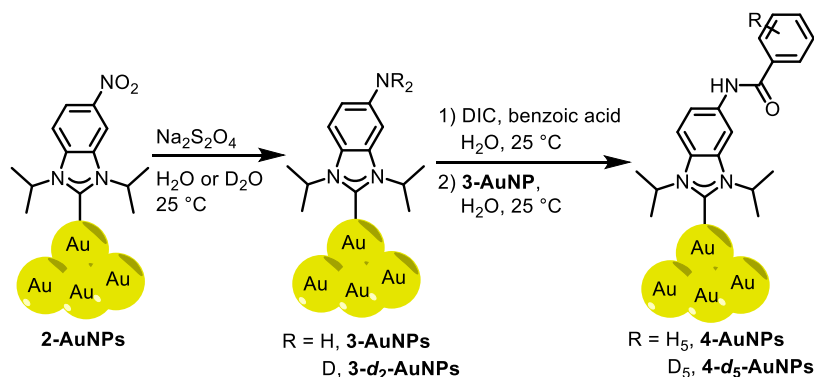


Figure 3.5: TEM Images of AuNPs. *Left:* TEM Image of nanoparticle before addition of nitro-NHC. *Right:* TEM Image of nanoparticle after addition of **3.3-I**. Size and shape of AuNPs stay the same before and after, indicating that NHCs are bound directly to colloid instead of forming small aggregates.



Scheme 3.2: Post-synthetic modification of **3.2-AuNP** by reduction to **3.3-AuNPs** and amide coupling to form **3.4-AuNPs**. Both protonated and deuterated versions were synthesized.

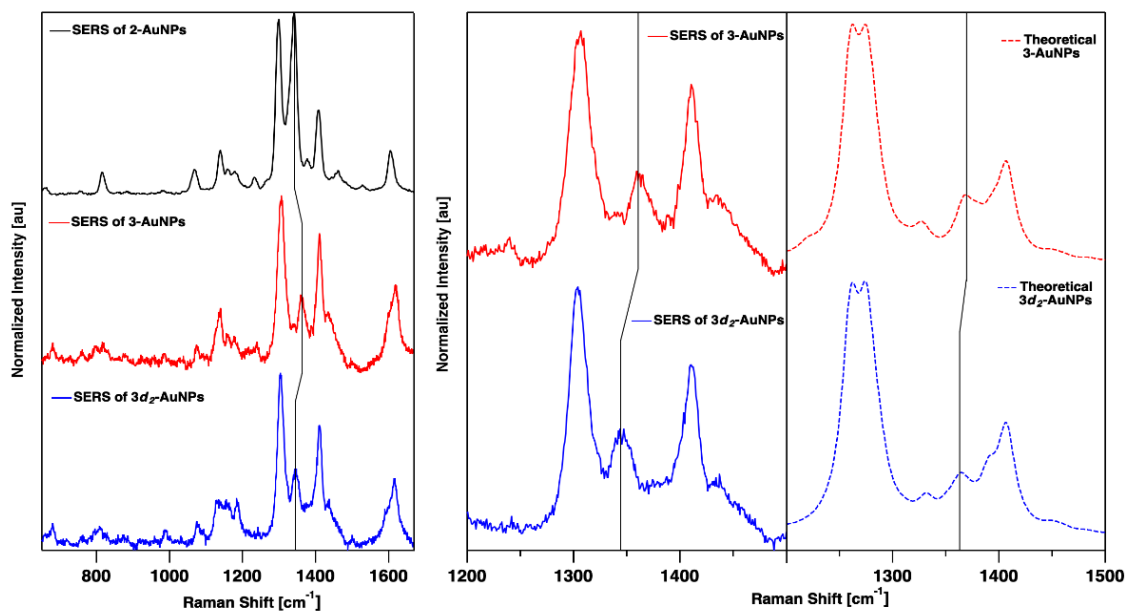


Figure 3.6: SERS of reduction reactions forming **3.3-AuNPs**. *Left:* SERS of **3.2-AuNPs** (black), SERS of **3.3-AuNPs** (red), and SERS of **3.3-d₂-AuNPs** (blue). Only peak associated with nitro or amine group shifts. *Right:* Highlight of area with amine peaks. The left spectra are the observed SERS spectra. The right spectra are from theoretical calculations.

confirm this result, we conducted the reduction again in the presence of D₂O. The peak associated with the amine would be red-shifted because of the difference in stretching frequencies for the two isotopes. After reduction of the NHC in D₂O, a new resonance was found at 1347 cm⁻¹, while all other peaks remained the same (Figure 3.6, left). Calculations of the SERS spectra show the same shift in the peak position (Figure 3.6, right).

With the amine coated **3.3-AuNPs**, we wanted to exploit this functional group by demonstrating an amide coupling to a carboxylic acids, which is a critical step for many surface and nanoparticle applications.¹²³ We chose benzoic acid for our test case since it has very distinct SERS signature ring mode at 1003 cm⁻¹ that does not overlap with any of the peaks on the NHC (Figure 3.7). A reaction with N,N'-diisopropylcarbodiimide (DIC) and benzoic acid in water at room temperature followed by the addition of **3.3-AuNPs** formed **3.4-AuNPs** (Scheme 3.2). SERS of **3.4-AuNPs** was reproducible and indicates that the coupling was successful as there is a peak at 1000 cm⁻¹ representative of the benzoic acid ring mode (Figure 3.7). As before, we employed isotopic labeling to confirm the reaction was effective. Substituting *d*₅-benzoic acid led to the same spectrum except the benzoic acid peak red-shifted to 985 cm⁻¹. The coupling clearly requires the DIC to react with the carboxylic acid in solution prior to coupling for two reasons. First, a reaction without DIC was ineffective (Figure 3.7). Second, we tried the same reaction with our previously reported in situ carboxylate surface and phenyl amine but no coupling was observed on gold FONs.^{112, 138}

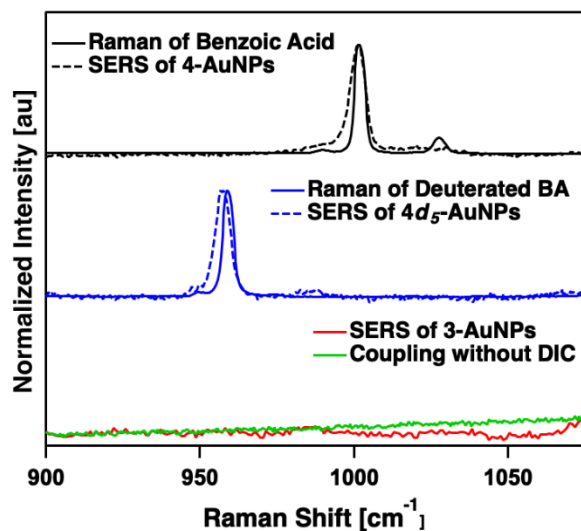


Figure 3.7: SERS of coupling reactions forming **3.4-AuNPs** (dotted black) and **3.4d₅-AuNPs** (dotted blue) alongside Raman of benzoic acid (black) and Raman of deuterated benzoic acid (blue). SERS of controls, **3.3-AuNPs** (red) and the coupling without DIC (green) indicate that there is no comparable peak between 1100-1200 cm⁻¹.

Conclusion

In conclusion, we have demonstrated a facile method to append NHCs to AuNPs resulting in the first SERS-active NHC-functionalized gold nanoparticles. This method is robust and reproducible, since it is effective for both di- and mono-NHC complexes with a variety of different anions that give identical SERS spectra. NHC complexes with reactive functional groups, such as a nitro, can be appended to the AuNPs. These nitro-functionalized AuNPs were reduced to form amine-functionalized gold colloids, that can undergo an amide coupling with carboxylic acids. This approach promises to leverage the

robustness of NHC gold bonds towards a plethora of new NP applications that were previously prohibited due to a lack of protic functional groups on the NHC coating.

Experimental

General Considerations for Synthesis:

All reactions and workups were conducted under air unless otherwise stated. All reagents and solvents were purchased and used as received from commercial vendors unless otherwise stated. All air sensitive reactions, workups and manipulations were done using standard Schlenk techniques under N₂ or in an MBraun Unilab glovebox under N₂. All glassware for aforementioned reactions were dried at 170 °C overnight before use. For air sensitive reactions, tetrahydrofuran (THF) was dried on an Innovative Technologies Pure Solv MD-7 Solvent Purification System, degassed by three freeze-pump-thaw cycles on a Schlenk line, and subsequently stored under activated 4 Å molecular sieves prior to use. Celite for air sensitive reactions was dried at 240 °C under vacuum overnight and stored in the glovebox. Carbon dioxide gas was ultra pure grade from Airgas. The compounds **3.1-Cl/I**, **3.1-Cl**, **3.1-PF₆** and **3.2-Cl** were prepared from previous literature procedures or as described previously.¹⁵³

General Considerations for Molecule Characterization:

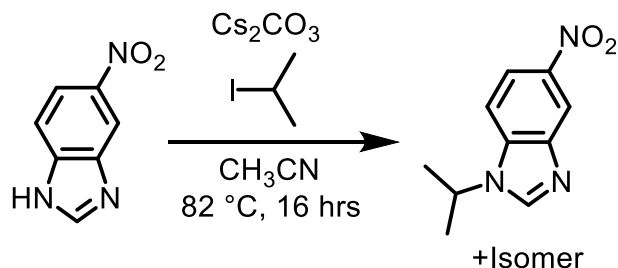
Solution ¹H NMR and ¹³C{¹H} NMR were performed on either a Varian Mercury 300 MHz or Varian VNMRs 500 MHz narrow-bore broadband system at 298 K. All ¹H and ¹³C shifts were referenced to the residual solvent. All solution 2D NMR experiments were performed on Varian VNMRs 600 MHz narrow-bore broadband system at 298 K. All mass spectrometry analyses were conducted at the Biological and Small Molecule Mass

Spectrometry Center located in the Department of Chemistry at the University of Tennessee. The DART analyses on neutral organic molecules were performed using a JEOL AccuTOF-D time-of-flight (TOF) mass spectrometer with a DART (direct analysis in real time) ionization source from JEOL USA, Inc. (Peabody, MA) using either dichloromethane or methanol as the solvent. Infrared spectra were collected on a Thermo Scientific Nicolet iS10 with a Smart iTR accessory for attenuated total reflectance (ATR) using the neat complexes. Carbon, hydrogen, and nitrogen analyses were obtained from Atlantic Microlab, Norcross, GA or Galbraith Laboratories Inc., Knoxville, TN.

General Considerations of X-ray Crystallography:

All X-ray data collections were performed on single crystals coated in Paratone oil on glass slides and mounted on nylon fibers. X-ray data for complex **3.3-I** was collected with the use of a Mo microsource on a Bruker D8 Venture diffractometer. Crystals were mounted in a 100 K cold stream provided by an Oxford Cryostream low-temperature apparatus. All data sets were reduced with Bruker SAINT and were corrected for absorption using SADABS. Structures were solved and refined using SHELXT and SHELXLE64, respectively.

Synthesis of 1-isopropyl-5/6-nitro-1H-benzimidazole,3.5:

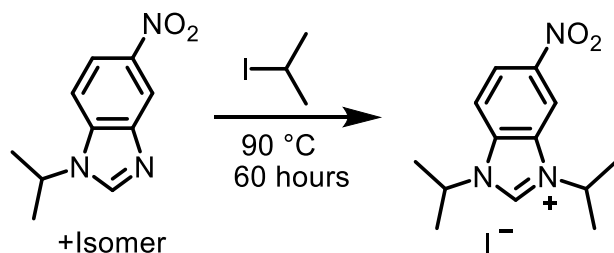


To a 250 mL round bottom flask, 5-nitro-1H-benzimidazole (1.999 g, 12.26 mmol, 1 eq.) and cesium carbonate (4.003 g, 12.29 mmol, 1 eq.) were added. To this was added 100 mL of acetonitrile followed by 2-iodopropane (2.210 mL, 22.07 mmol, 1.8 eq.). The flask was then heated at $82\text{ }^\circ\text{C}$ overnight. The solution was concentrated in vacuo and the residue was extracted with 100 mL ethyl acetate. The solution was washed with water (3 x 30 mL) followed by a final wash with brine (30 mL). The solution was dried with anhydrous magnesium sulfate and filtered. The filtrate was concentrated under vacuum and resulted in a tan-yellow solid as a mixture of isomers (46:54 based on NMR integration) (2.000 g, 97.4% yield). This solid was used without any further purification.

^1H NMR (CDCl_3 , 499.74 MHz): δ 8.70 (d, $J = 2.1\text{ Hz}$, 1H), 8.40 (d, $J = 2.4\text{ Hz}$, 1H), 8.23-8.17 (m, 4H), 7.84 (d, $J = 9.2\text{ Hz}$, 1H), 7.49 (d, $J = 8.7\text{ Hz}$, 1H), 4.73 (sept, $J = 6.8\text{ Hz}$, 1H), 4.70 (sept, $J = 6.8\text{ Hz}$, 1H), 1.68 (d, $J = 7.0\text{ Hz}$, 6H), 1.66 (d, $J = 6.6\text{ Hz}$, 6H). **^{13}C NMR** (CDCl_3 , 125.66 MHz): δ 148.47, 144.89, 143.79, 143.74, 143.47, 137.49, 132.69, 120.64, 118.61, 118.04, 117.33, 110.11, 107.25, 48.69, 48.63, 22.82, 22.73. **IR**: 3093, 2980, 1735, 1672, 1615, 1591, 1515, 1486, 1470, 1454, 1406, 1388, 1371, 1343, 1297, 1273, 1232, 1211, 1202, 1170, 1154, 1132, 1115, 1087, 1063, 1034, 935, 883, 842, 825,

819, 798, 758, 735, 720, 638 cm^{-1} . **DART HR MS** (m/z): $[\text{M}+\text{H}]^+$: 206.09268 (found), $[\text{C}_{10}\text{H}_{12}\text{N}_3\text{O}_2]^+$: 206.09240 (calculated).

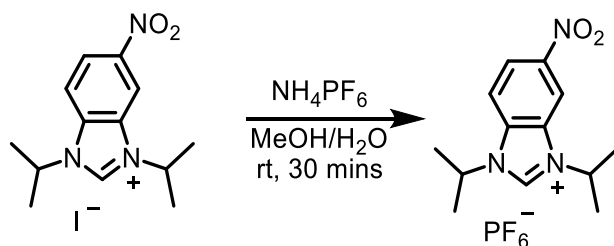
Synthesis of 1,3-diisopropyl-5-nitrobenzimidazolium iodide, 3.6-I:



In a 350 mL pressure vial, **3.5** (5.501 g, 26.81 mmol, 1 eq.) was added. To this was added neat 2-iodopropane (54 mL, 536.2 mmol, 20 eq.) and the tube was sealed with a Teflon screw cap. The reaction was heated and stirred at 90 °C for 60 hours, in which a solid began to precipitate. The solution was cooled to room temperature and diluted with 50 mL of toluene. This solution was filtered and washed with additional toluene. The solid was then dissolved in the minimal amount of acetonitrile (100 mL) and diethyl ether was added to precipitate a solid (300 mL). This solid was filtered over a 60 mL medium porosity frit and washed with additional diethyl ether. This was repeated if there was yellow color in the filtrate. The solid was then collected and dried, which resulted in **3.6-I** as bright yellow crystals (4.341 g, 43.2% yield). **^1H NMR** ($\text{DMSO}-d_6$, 499.74 MHz): δ 10.07 (s, 1H), 9.13 (d, $J = 2.1$ Hz, 1H), 8.52 (dd, $J_1 = 9.1$ Hz, $J_2 = 2.1$, 1H), 8.42 (d, $J = 9.2$ Hz, 1H), 5.29 (sept, $J = 6.6$ Hz, 1H), 5.16 (sept, $J = 6.9$ Hz, 1H), 1.68 (d, $J = 2.3$ Hz, 6H), 1.66 (d, $J = 2.2$ Hz, 6H). **^{13}C NMR** ($\text{DMSO}-d_6$, 125.66 MHz): δ 145.64, 143.27, 134.23, 130.61, 121.47, 115.24, 111.00, 51.68, 51.35, 21.74, 21.47. **IR**: 3130, 3067, 3025, 2984, 1931, 1618, 1551, 1531, 1432, 1375, 1347, 1330, 1283, 1241, 1213, 1191,

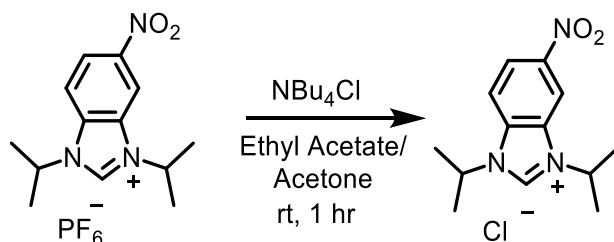
1175, 1147, 1134, 1118, 1089, 1070, 987, 879, 861, 848, 828, 803, 768, 753, 652, 627 cm^{-1} . **DART HR MS** (m/z): $[M]^+$: 248.14020 (found), $[\text{C}_{13}\text{H}_{18}\text{N}_3\text{O}_2]^+$: 248.13935 (calculated).

Synthesis of 1,3-diisopropyl-5-nitrobenzimidazolium hexafluorophosphate, 3.6-PF₆:



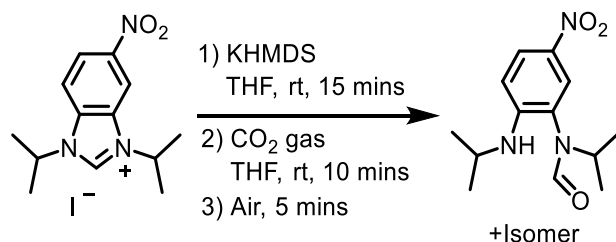
To a 20 mL scintillation vial containing **3.6-I** (1.039 g, 2.909 mmol, 1 eq.), 10 mL of methanol was added, and was stirred until full dissolution. In a 250 mL round bottom flask, NH_4PF_6 (0.5278 g, 3.238 mmol, 1.11 eq.) was added with 75 mL of water. This solution was vigorously stirred and to this the methanol solution of **3.6-I** was added dropwise resulting in an immediate precipitation of a white solid. After full addition, the mixture was stirred at room temperature for 30 minutes. The mixture was then filtered over a 60 mL fine porosity frit and washed with water (100 mL). The gummy residue was dissolved with acetone (80 mL) and filtered through the frit into a round bottom flask. The solution was concentrated and dried resulting in a white powder **3.6-PF₆** (1.069 g, 93.4% yield). **¹H NMR** (CD_3CN , 499.74 MHz): δ 9.15 (s, 1H), 8.84 (d, $J = 1.8$ Hz, 1H), 8.52 (dd, $J_1 = 9.2$ Hz, $J_2 = 2.1$ Hz, 1H), 8.10 (dd, $J_1 = 9.3$ Hz, $J_2 = 0.3$ Hz, 1H), 5.08 (sept, $J = 6.8$ Hz, 1H), 5.02 (sept, $J = 6.9$ Hz, 1H), 1.70 (d, $J = 3.7$ Hz, 6H), 1.69 (d, $J = 3.7$ Hz, 6H). **IR**: 3140, 1630, 1554, 1533, 1442, 1395, 1378, 1347, 1286, 1238, 1208, 1143, 1114, 1089, 991, 896, 876, 833, 768, 757, 738, 641 cm^{-1} .

Synthesis of 1,3-diisopropyl-5-nitrobenzimidazolium chloride, **3.6-Cl**:



Modified from a previously published procedure.¹⁵⁴ Tetrabutylammonium chloride, NBu₄Cl (1.064 g, 3.813 mmol, 3 eq.), was added to a 100 mL round bottom flask. To this flask was added 25 mL of ethyl acetate and it was stirred until full dissolution. In a 20 mL scintillation vial, **3.6-PF₆** (0.5002g, 1.271 mmol, 1 eq.) was dissolved in 20 mL of acetone with stirring. This solution was then quantitatively transferred dropwise to the ethyl acetate solution. After addition of about half of the acetone solution, a white precipitate formed. After full addition, the mixture was stirred at room temperature for 1 hour. Following this, the mixture was filtered over a 60 mL fine porosity frit and the solid was washed with 50 mL of 1:1 ethyl acetate: acetone solution. This was then washed with 30 mL of diethyl ether and thoroughly dried yielding the white powder **3.6-Cl** (0.1868 g, 17.3% yield). Full anion metathesis was confirmed by ¹⁹F NMR of **3.6-Cl** showing no signals for the PF₆ anion. ¹H NMR (DMSO-d₆ 499.74 MHz): δ 10.25 (s, 1H), 9.13 (d, *J* = 2.1 Hz, 1H), 8.52 (dd, *J*₁ = 9.2 Hz, *J*₂ = 2.2 Hz, 1H), 8.41 (d, *J* = 9.2 Hz, 1H), 5.30 (sept, *J* = 6.7 Hz, 1H), 5.17 (sept, *J* = 6.9 Hz, 1H), 1.67 (dd, *J*₁ = 6.8 Hz, *J*₂ = 0.9 Hz, 12H). IR: 3088, 2922, 2761, 1627, 1607, 1545, 1525, 1473, 1456, 1437, 1404, 1393, 1374, 1340, 1315, 1279, 1229, 1172, 1139, 1125, 1110, 1064, 984, 937, 873, 861, 839, 799, 765, 753, 736, 649, 632 cm⁻¹.

Synthesis of *N*-isopropyl-*N'*-(2-(isopropylamino)-5/6-nitrophenyl)formamide, **3.7**:

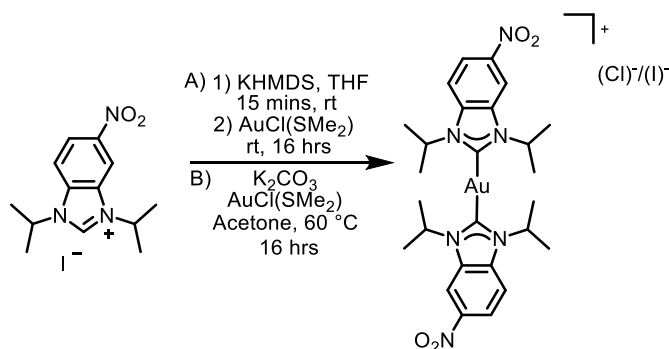


To a 20 mL scintillation vial in the glovebox, **3.6-I** (0.1003 g, 0.2665 mmol, 1 eq.) was added with 8 mL of THF. To this was added solid KHMDS (0.0533 g, 0.2665, 1 eq.) quantitatively transferred with 2 mL of THF. This solution was stirred at ambient temperature for 15 minutes. The resulting peach slurry was filtered quickly over a short Celite plug into another 20 mL scintillation vial. The vial was covered with a septa lined cap and taken outside the glovebox and a needle pre purged with dinitrogen on a Schlenk line was inserted. A balloon attached to a syringe was flushed 3x with CO₂ and then inflated and a needle was inserted into the cap. The gas was flushed over the solution for 10 minutes, resulting in no noticeable color change or precipitation. Following this, the cap was removed, and the solution was stirred for another 5 minutes, in which the solution went from peach to yellow. The solution was then concentrated by roto evaporation and was purified by gradient elution (0% to 2% MeOH:CH₂Cl₂) flash chromatography yielding **7** (0.0639 g, 90.4%) as a yellow powder which is a mixture of isomers (83:17 based on NMR integration). Position of formamide in major isomer is undetermined. ¹H NMR (CDCl₃, 499.74 MHz): δ 8.18 (d, *J* = 9.6 Hz, 1H), 7.97 (s, 1H), 7.93 (s, 1H), 6.69 (d, *J* = 9.6 Hz, 1H), 4.71 (m, 1H), 3.76 (sept, *J* = 6.5 Hz, 1H), 1.31 (d, *J* = 6.3 Hz, 3H), 1.26 (m, 6H), 1.11 (d, *J* = 6.8 Hz, 3H). Only major isomer labelled. ¹³C NMR (CDCl₃, 125.66 MHz): δ 163.72, 151.18, 136.68, 127.91, 127.07, 121.87, 109.85,

46.97, 44.55, 22.68, 22.46, 21.53, 19.52. Only major isomer labeled. **IR**: 3130, 3067, 3025, 2984, 1931, 1618, 1551, 1531, 1432, 1375, 1347, 1330, 1283, 1241, 1213, 1191, 1175, 1147, 1134, 1118, 1089, 1070, 987, 879, 861, 848, 828, 803, 768, 753, 733, 652, 627 cm^{-1} . **DART HR MS** (m/z): $[\text{M}+\text{H}]^+$: 266.15179 (found), $[\text{C}_{13}\text{H}_{20}\text{N}_3\text{O}_3]^+$: 266.15048 (calculated).

Synthesis of bis(1,3-diisopropyl-5-nitro-benzimidazolium)gold (I) chloride/iodide,

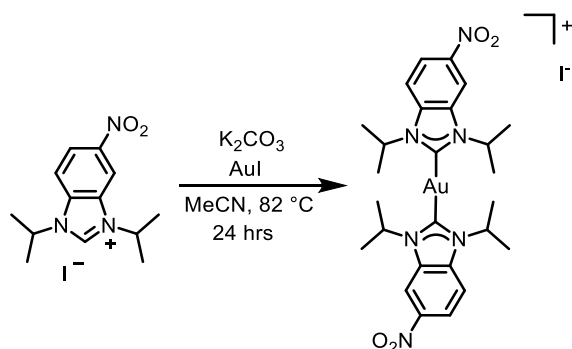
3.3-Cl/I:



Method A: To a 20 mL scintillation vial in the glovebox, **3.6-I** (0.2548 g, 0.6791 mmol, 2 eq.) was added. To this was added solid KHMDS (0.1354 g, 0.6787 mmol, 2 eq.) followed by 20 mL THF. This solution was stirred at RT for 15 minutes. To this, $\text{AuCl}(\text{SMe}_2)$ (0.100 g, 0.3395 mmol, 1 eq.) was added. The solution was stirred overnight at ambient temperature. Reaction was taken out of the glovebox and the THF was then removed in vacuum and the residue was taken up into CH_2Cl_2 . The solution was filtered over Celite and the filtrate was then layered hexanes and resulted in a red orange powder, **3.3-Cl/I**. This was used without any further purification (0.2646 g, 95.2% yield based on mass of **3.3-I**).

Method B: Modified from a previously reported procedure.¹²² In a round bottom flask, **3.6-I** (0.2016 g, 0.5599 mmol, 2 eq.), K₂CO₃ (0.1353 g, 1.008 mmol, 3.6 eq.) and AuCl(SMe₂) (0.0825 g, 0.2800 mmol, 1 eq.) were added. To this was added acetone (10 mL) and the solution was heated to 60 °C overnight. The slurry was cooled, followed by filtration over Celite. The filtrate was concentrated to dryness and taken up into 20 mL CH₂Cl₂. This solution was added to a short pad of Celite and allowed to be added dropwise to a stirring solution of diethyl ether (30 mL). The resulting dark red precipitate was then filtered over a fine porosity frit and washed with additional diethyl ether resulting in **3.3-CI/I** as a red powder (0.1635 g, 71.3% based on mass of **3.3-I**). ¹H NMR (CDCl₃, 499.74 MHz): δ 8.59 (d, *J* = 2.1 Hz, 2H), 8.33 (dd, *J*₁ = 9.1 Hz, *J*₂ = 2.0 Hz, 2H), 7.83 (d, *J* = 9.2 Hz, 2H), 5.77 (sept, *J* = 7.0 Hz, 2H), 5.71 (d, *J* = 7.1 Hz, 2H), 1.92 (d, *J* = 7.2 Hz, 12H), 1.89 (d, *J* = 7.2 Hz, 12H). ¹³C NMR (CDCl₃, 125.66 MHz): δ 194.91, 144.16, 136.77, 132.66, 119.63, 113.37, 109.40, 55.04, 54.99, 22.21, 22.12. IR: 3378, 2978, 2924, 1606, 1525, 1464, 1434, 1369, 1342, 1310, 1214, 1174, 1157, 1137, 1110, 1083, 1067, 988, 875, 819, 773, 754, 733 cm⁻¹.

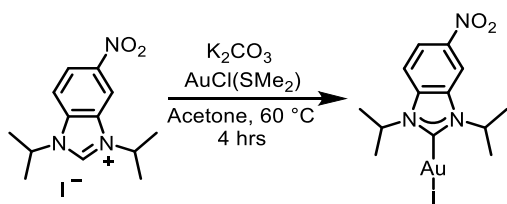
Synthesis of bis(1,3-diisopropyl-5-nitro-benzimidazolium)gold (I) iodide, **3.3-I**:



To a round bottom flask was added **3.6-I** (0.100 g, 0.2665 mmol, 2 eq.), K_2CO_3 (0.0663 g, 0.4797 mmol, 3.6 eq.) and AuI (0.0432 g, 0.1333 mmol, 1 eq.). To this was added acetonitrile (10 mL) and the solution was heated to $82\text{ }^{\circ}C$ for 24 hours. The mixture was then cooled to room temperature and filtered over a pad of Celite. The filtrate was then concentrated to dryness and taken up into CH_2Cl_2 . The solution was added dropwise into a stirring solution of diethyl ether and the red precipitate was collected and washed with additional ether. The resulting red powder was purified with flash chromatography with 10% $MeOH:CH_2Cl_2$ resulting in **3.3-I** as a brown/yellow solid (0.0573 g, 52.5% yield). Single crystals of **3.3-I** were grown by diffusing diethyl ether into an acetonitrile solution of **3.3-I** yielding yellow blocks. ^1H NMR ($CDCl_3$, 499.74 MHz): δ 8.59 (d, $J = 2.1$ Hz, 2H), 8.32 (dd, $J_1 = 9.0$ Hz, $J_2 = 2.0$ Hz, 2H), 7.81 (d, $J = 9.2$ Hz, 2H), 5.77 (sept, $J = 6.8$ Hz, 2H), 5.71 (sept, $J = 7.1$ Hz, 2H), 1.92 (d, $J = 7.1$ Hz, 12H), 1.89 (d, $J = 6.9$ Hz, 12H). ^1H NMR (CD_3CN , 499.74 MHz): δ 8.71 (d, $J = 2.0$ Hz, 2H), 8.36 (dd, $J_1 = 9.1$ Hz, $J_2 = 2.1$ Hz, 2H), 8.02 (d, $J = 9.2$ Hz, 2H), 5.48 (sept, $J = 7.1$ Hz, 2H), 5.44 (sept, $J = 6.9$ Hz, 2H), 1.86 (d, $J = 7.0$ Hz, 12H), 1.83 (d, $J = 7.0$ Hz, 12H). ^{13}C NMR ($CDCl_3$, 125.66 MHz): δ 194.80, 144.16, 136.78, 132.68, 119.62, 113.35, 109.41, 55.06, 55.00, 22.19, 22.10. ^{13}C NMR

(CD₃CN, 125.66 MHz): δ 193.17, 145.70, 137.28, 133.63, 120.74, 114.63, 110.33, 55.37, 54.66, 22.96, 22.52. **IR**: 3389, 2975, 1607, 1523, 1463, 1436, 1367, 1341, 1307, 1273, 1212, 1174, 1136, 1111, 1082, 1067, 988, 877, 862, 819, 777, 753, 734, 685 cm⁻¹. **DART HR MS** (m/z): [M-I]⁺: 691.23051 (found), [C₂₆H₃₄AuN₆O₄]⁺: 691.23071 (calculated).

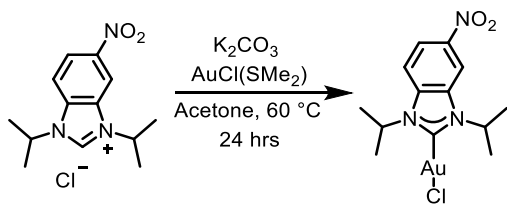
Synthesis of (1,3-diisopropyl-5-nitro-benzimidazolium)gold(I) iodide, **3.4-I**:



The molecule **3.4-I** was synthesized similarly to a previously published report, but resulted in the mono-NHC iodide complex.¹²² To a round bottom flask, **3.6-I** (0.1864 g, 0.4968 mmol, 1 eq.), K₂CO₃ (0.2322 g, 1.680 mmol, 3 eq.) and AuCl(SMe₂) (0.1537 g, 0.5599 mmol, 1 eq.) was added. To this was added acetone (10 mL) and the mixture was heated at 60 °C for 4 hours. The slurry was cooled to room temperature and was filtered over a pad of Celite. The filtrate was concentrated to dryness and taken up into CH₂Cl₂. The solution was filtered over a short Celite plug and added dropwise to a stirring solution of 1:1 diethyl ether and hexanes. The resulting white precipitate, **3.4-I**, was filtered over a fine porosity frit and washed with additional hexanes (0.1496 g, 52.7% yield). **¹H NMR** (CDCl₃, 499.74 MHz): δ 8.58 (s, 1H), 8.34 (d, J = 9.0, 1H), 7.78 (d, J = 9.2 Hz, 1H), 5.57 (m, 2H), 1.82 (d, J = 6.7 Hz, 6H), 1.78 (d, J = 6.9 Hz, 6H). **¹³C NMR** (CDCl₃, 125.66 MHz): δ 191.46, 144.50, 136.15, 132.11, 119.93, 113.24, 109.45, 54.77, 22.16, 22.01. **IR**: 3110, 2975, 2931, 1608, 1527, 1477, 1456, 1420, 1382, 1341, 1311, 1268, 1173, 1138, 1113,

1066, 889, 865, 823, 761, 736, 675, 651 cm^{-1} . **DART HR MS** (m/z): $[\text{M}+\text{H}]^+$: 572.01199 (found), $[\text{C}_{13}\text{H}_{18}\text{AuIN}_3\text{O}_2]^+$: 572.01037 (calculated).

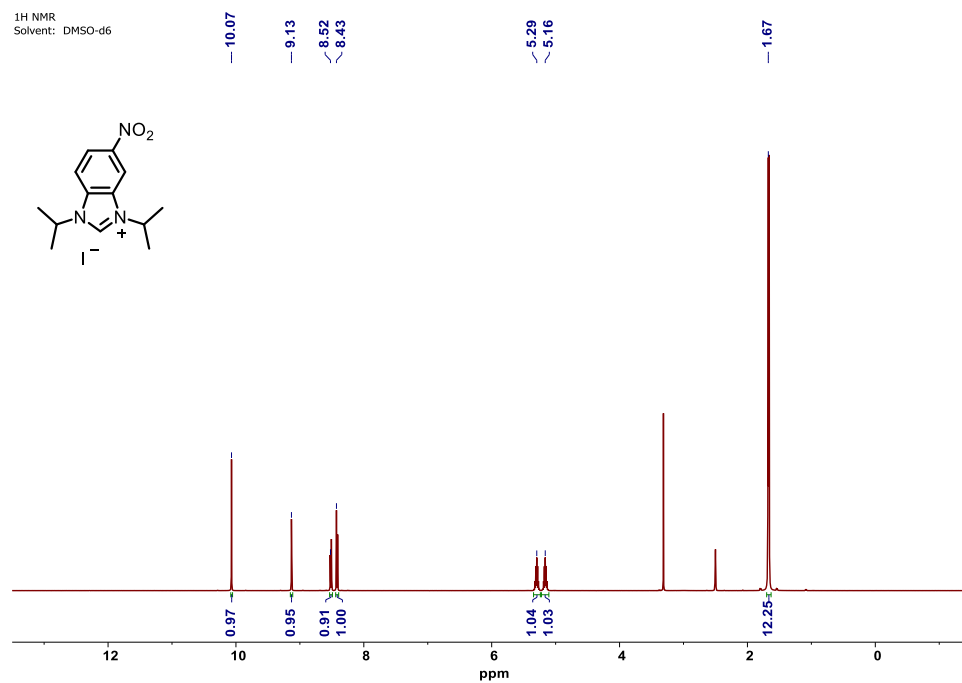
Synthesis of (1,3-diisopropyl-5-nitro-benzimidazolium)gold(I) chloride, 3.4-Cl:



Modified from a previously reported procedure.¹²² To a round bottom flask, **3.6-Cl** (0.1589 g, 0.5600 mmol, 2 eq.), K_2CO_3 (0.1393 g, 1.008 mmol, 3.6 eq.) and $\text{AuCl}(\text{SMe}_2)$ (0.1393 g, 1.008 mmol, 1 eq.) were added. To this was added acetone (10 mL) and the reaction was heated at $60\text{ }^\circ\text{C}$ for 24 hours. The mixture was then cooled to room temperature and filtered over a pad of Celite. The filtrate was dried and taken up into CH_2Cl_2 and filtered over a short pad of Celite into a stirring 1:1 solution of diethyl ether and hexanes. The solid was collected over a fine porosity frit and washed with additional hexanes. The product was purified by gradient elution flash chromatography (0% to 10% $\text{MeOH}:\text{CH}_2\text{Cl}_2$) to yield **3.4-Cl** as a white powder, (0.0331 g, 24.6%). **^1H NMR** (CDCl_3 , 499.74 MHz): δ 8.57 (d, $J = 2.2\text{ Hz}$, 1H), 8.33 (d, $J = 7.1\text{ Hz}$, 1H), 7.71 (d, $J = 9.2$, 1H), 5.58 (sept, $J = 6.7\text{ Hz}$, 1H), 5.56 (sept, $J = 6.9\text{ Hz}$, 1H), 1.81 (d, $J = 7.0\text{ Hz}$, 6H), 1.78 (d, $J = 7.0\text{ Hz}$, 6H). **^{13}C NMR** (CDCl_3 , 125.66 MHz): δ 182.03, 144.34, 136.22, 132.18, 119.90, 113.18, 109.35, 55.33, 20.22, 21.87. **IR**: 3116, 2976, 1606, 1523, 1476, 1458, 1419, 1382, 1343, 1309, 1268, 1175, 1137, 1113, 1068, 919, 899, 889, 865, 823, 760, 736 cm^{-1} . **DART HR MS** (m/z): $[\text{M}-\text{Cl}+\text{H}_2\text{O}]^+$: 462.11134 (found), $[\text{C}_{13}\text{H}_{19}\text{AuN}_3\text{O}_3]^+$: 462.10864 (calculated).

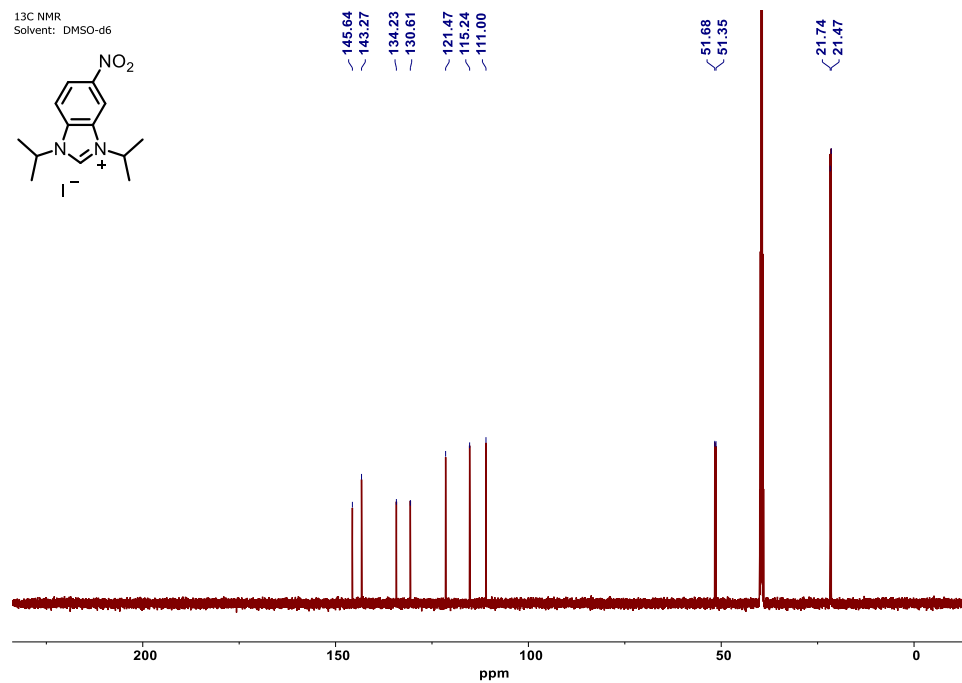
Selected Spectral Characterization:

¹H NMR
Solvent: DMSO-d₆

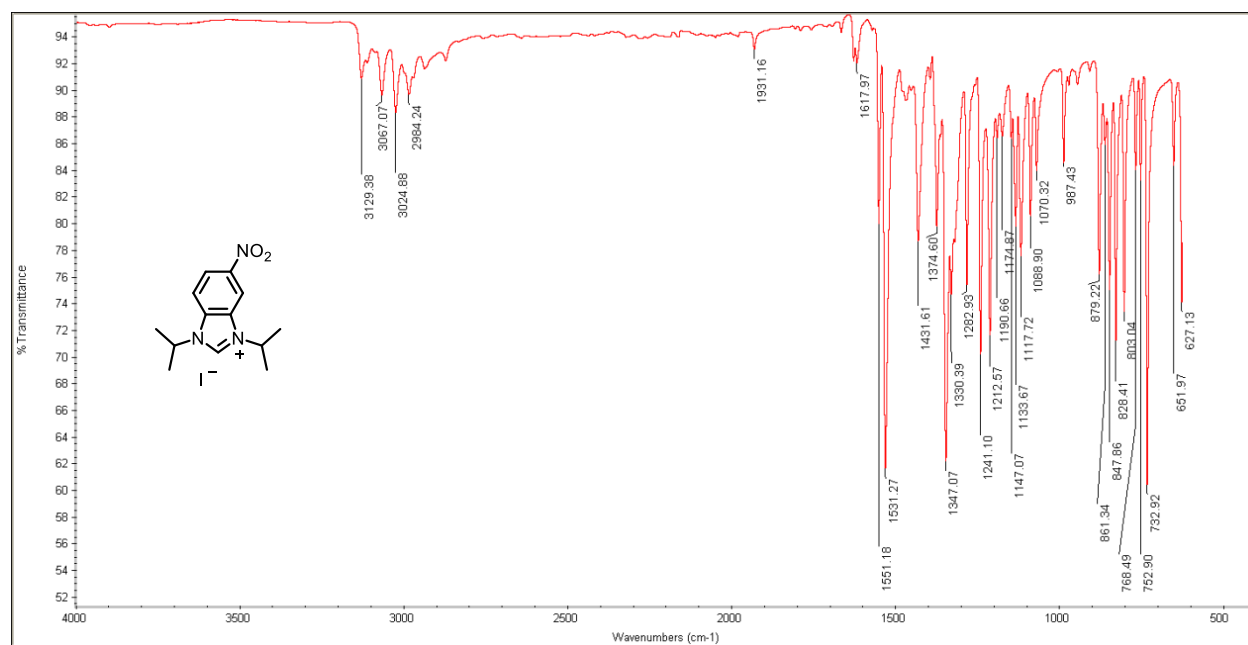


Spectrum 3.1: ¹H NMR of **3.6-I** in DMSO-d₆.

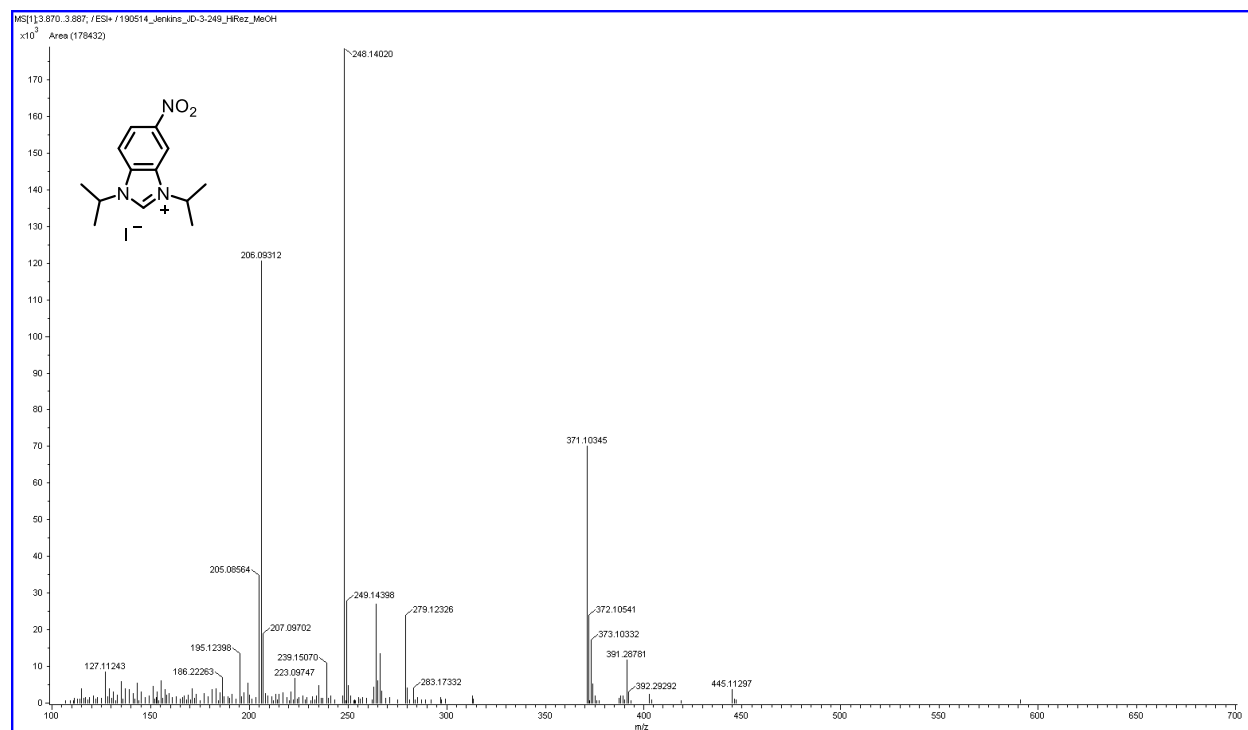
¹³C NMR
Solvent: DMSO-d₆



Spectrum 3.2: ¹³C NMR of **3.6-I** in DMSO-d₆.

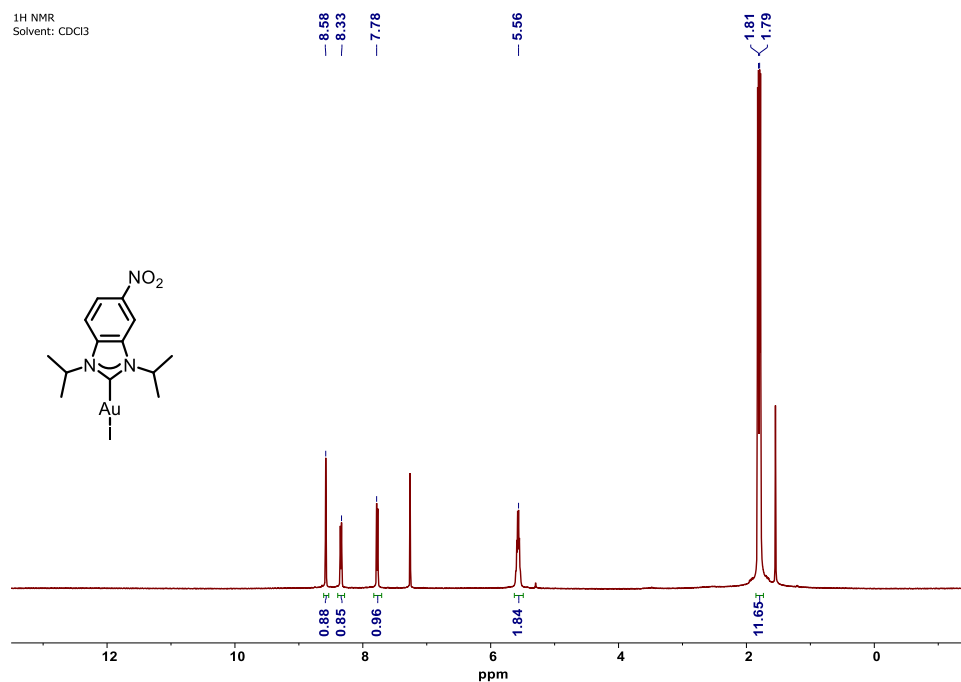


Spectrum 3.3: IR of **3.6-I**.



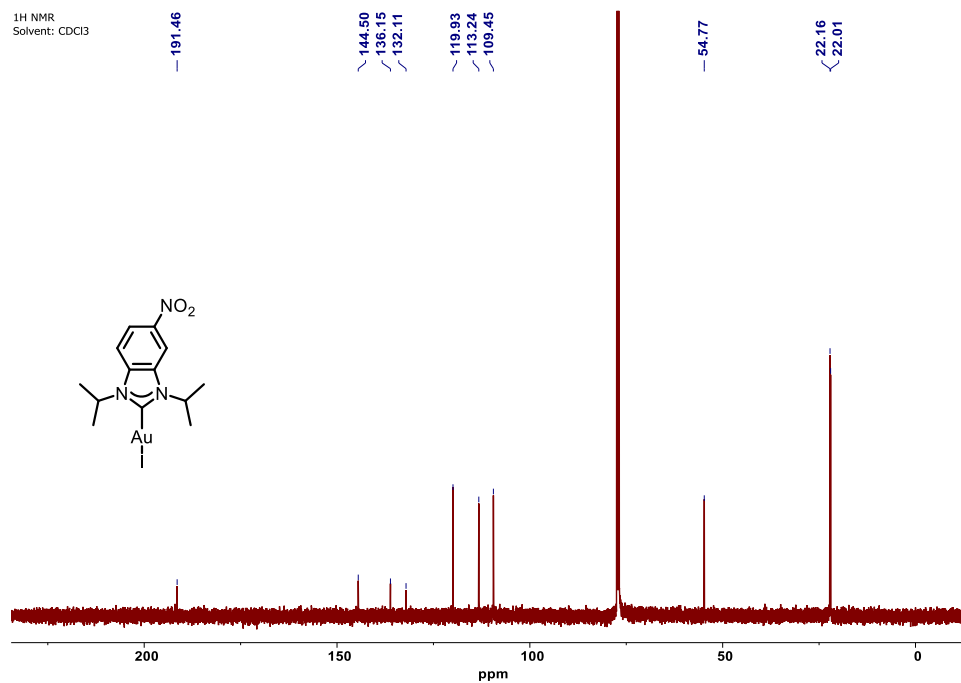
Spectrum 3.4: DART HRMS of **3.6-I**.

¹H NMR
Solvent: CDCl₃

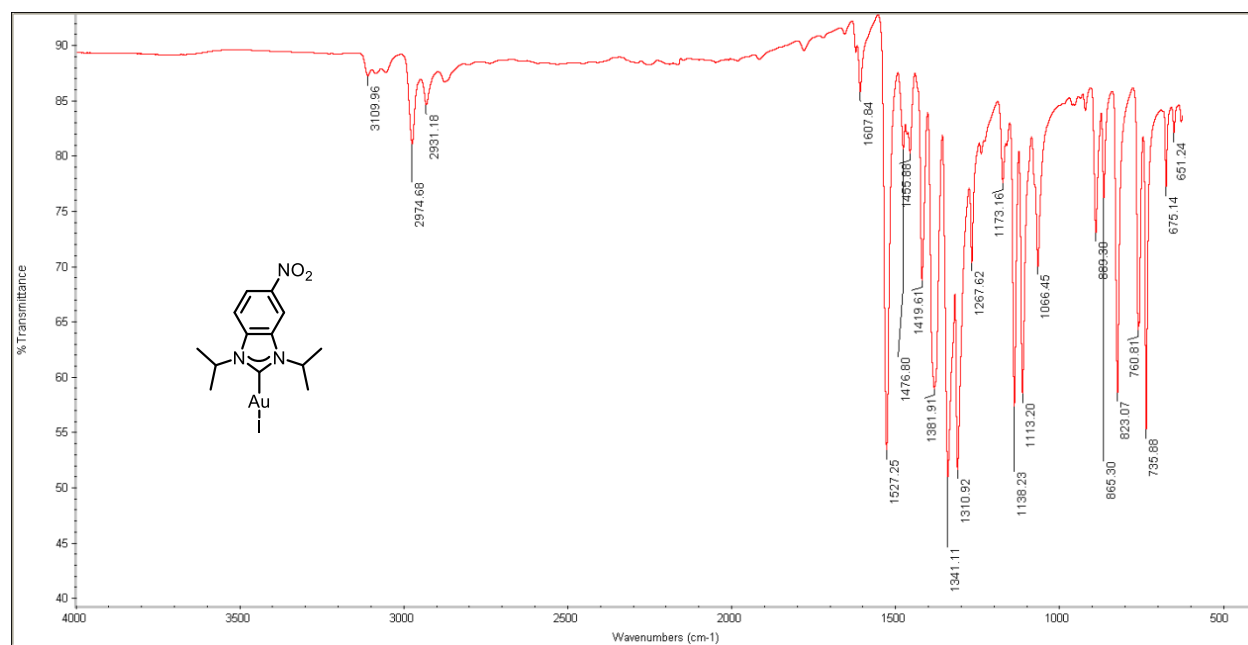


Spectrum 3.5: ¹H NMR of **3.4-I** in CDCl₃.

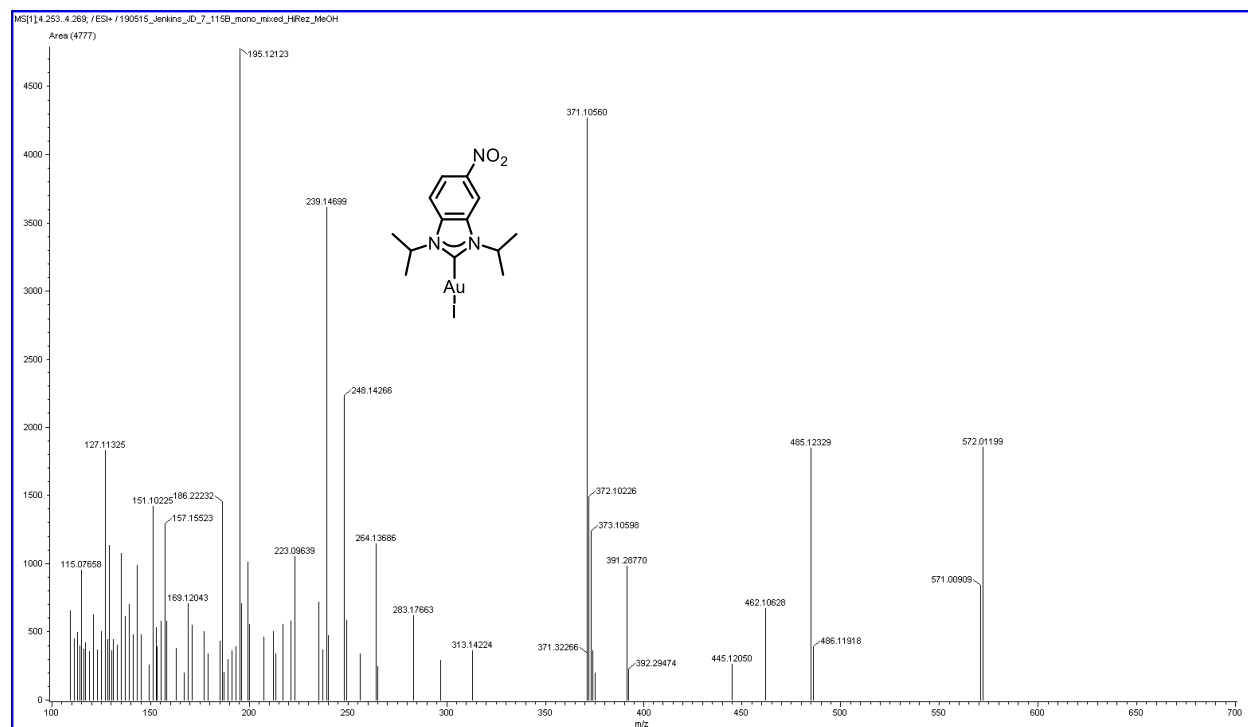
¹³C NMR
Solvent: CDCl₃



Spectrum 3.6: ¹³C NMR of **3.4-I** in CDCl₃.

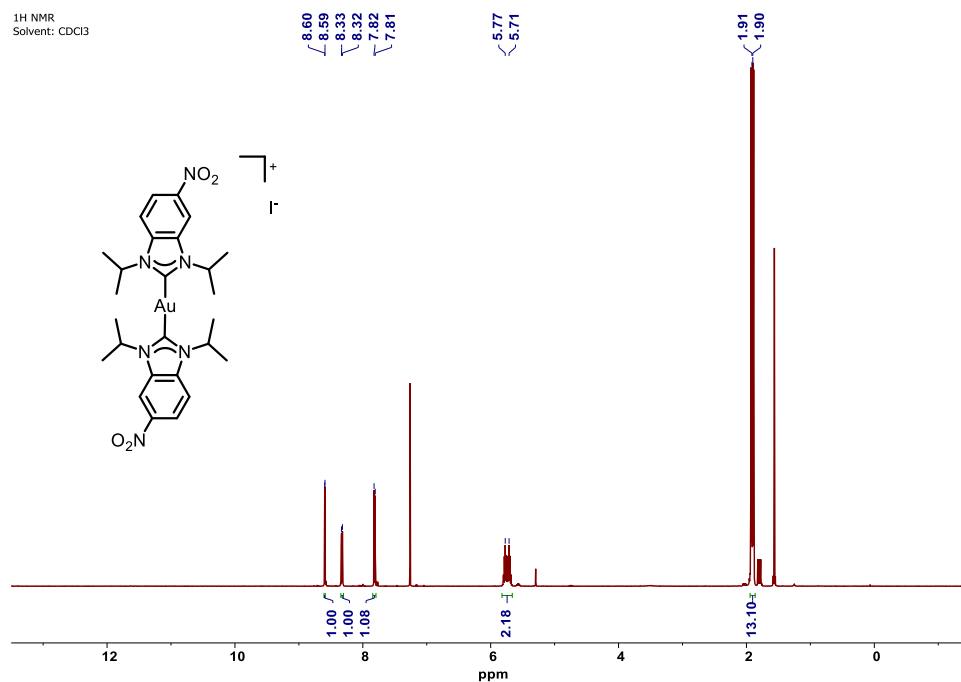


Spectrum 3.7: IR of **3.4-I**.



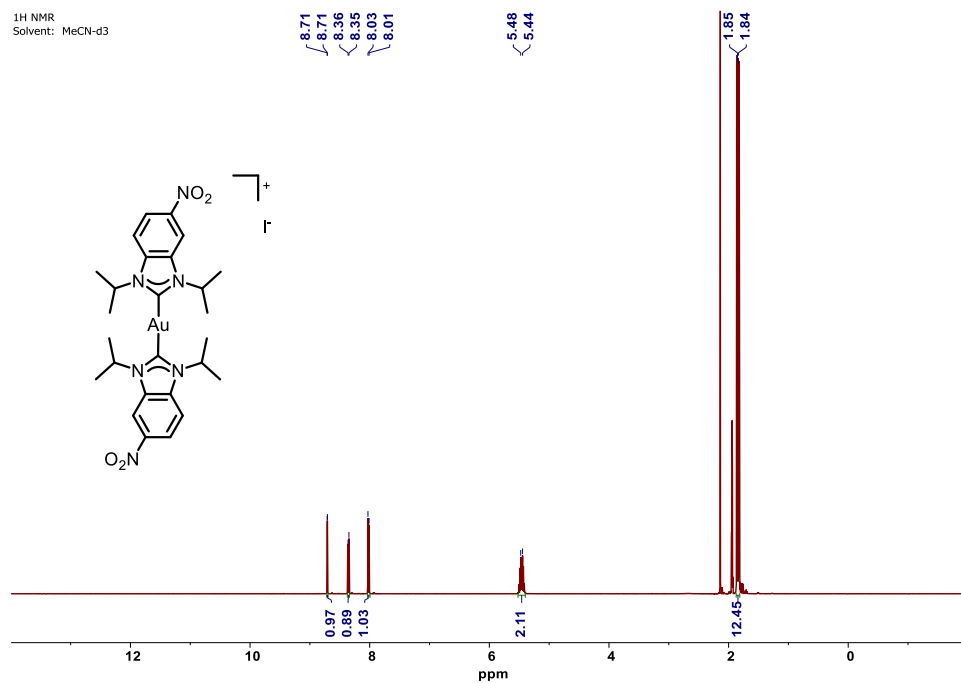
Spectrum 3.8: HR DART MS of **3.4-I**.

¹H NMR
Solvent: CDCl₃

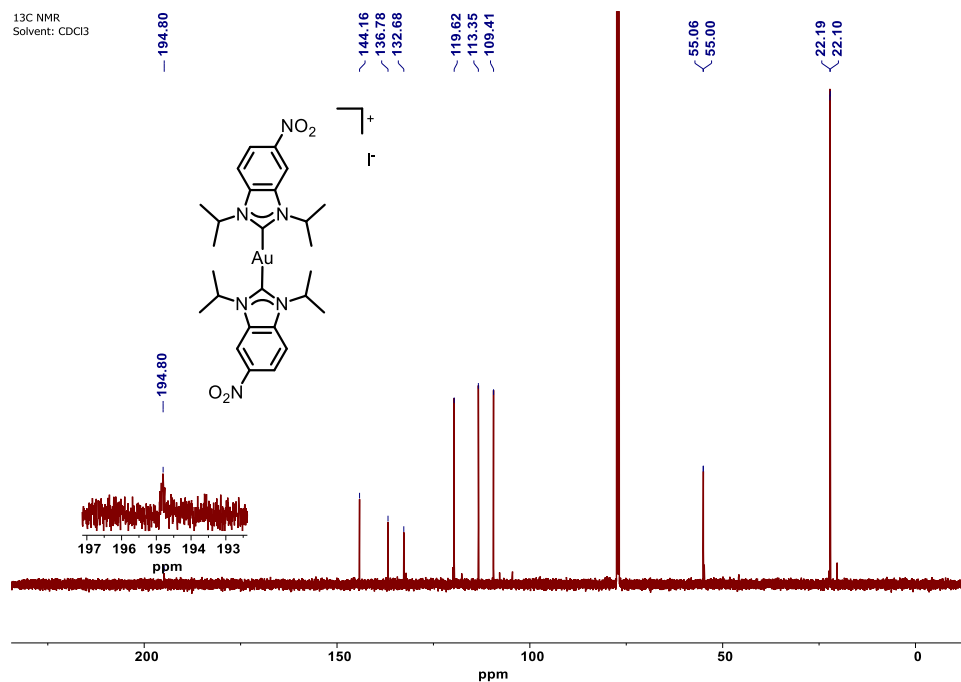


Spectrum 3.9: ¹H NMR of **3.3-I** in CDCl₃.

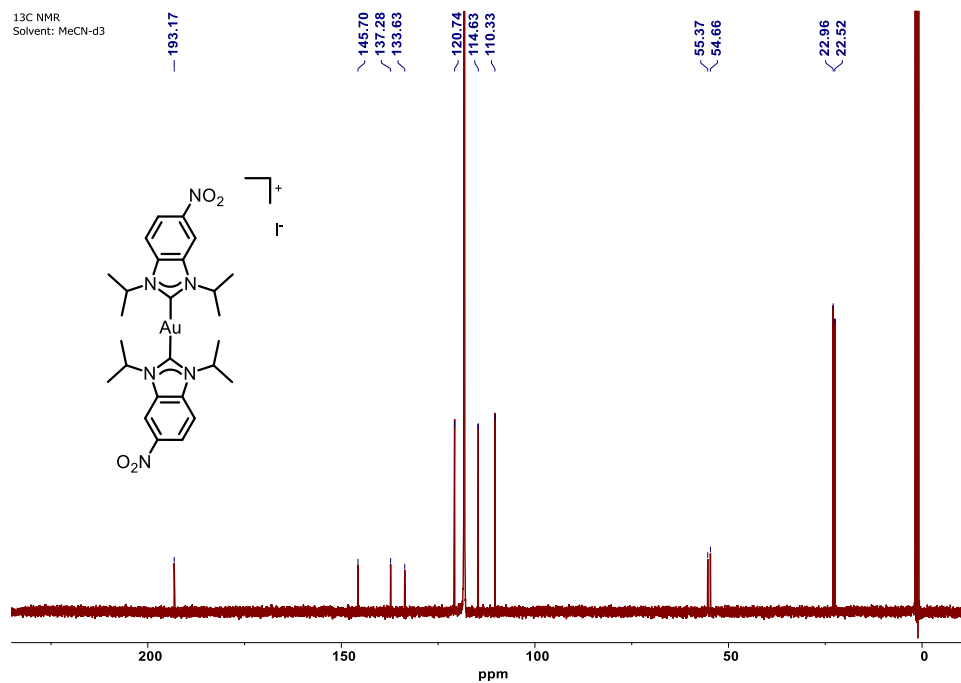
¹H NMR
Solvent: MeCN-d₃



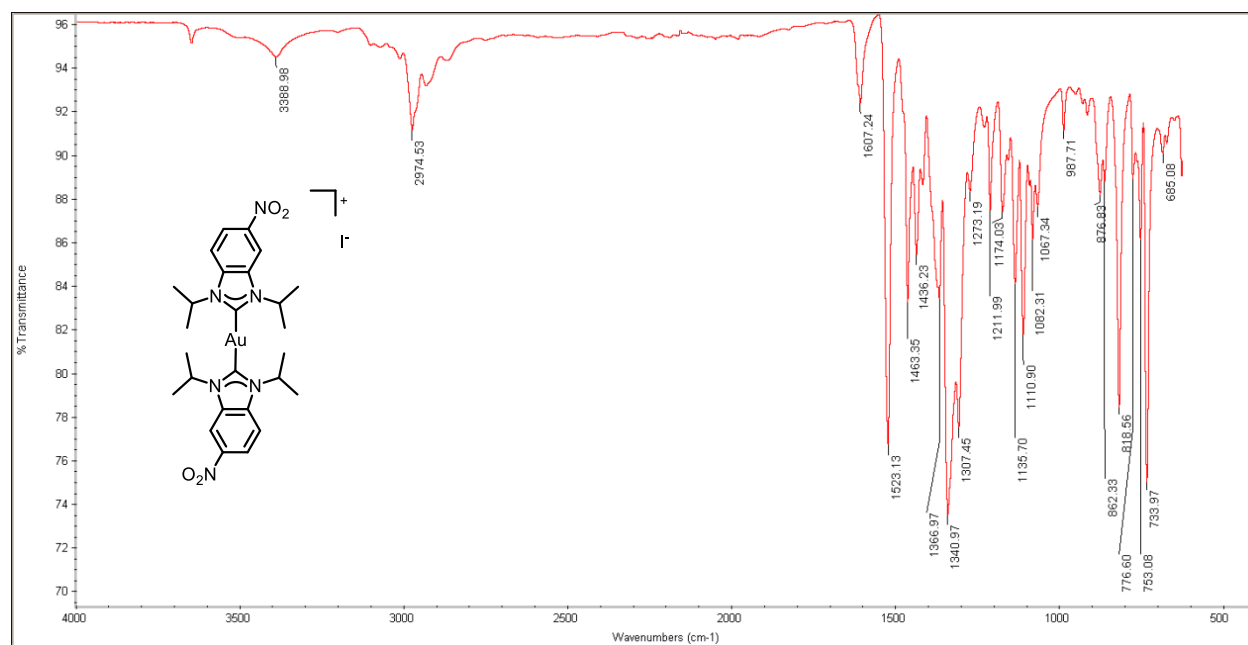
Spectrum 3.10: ¹H NMR of **3.3-I** in CD₃CN.



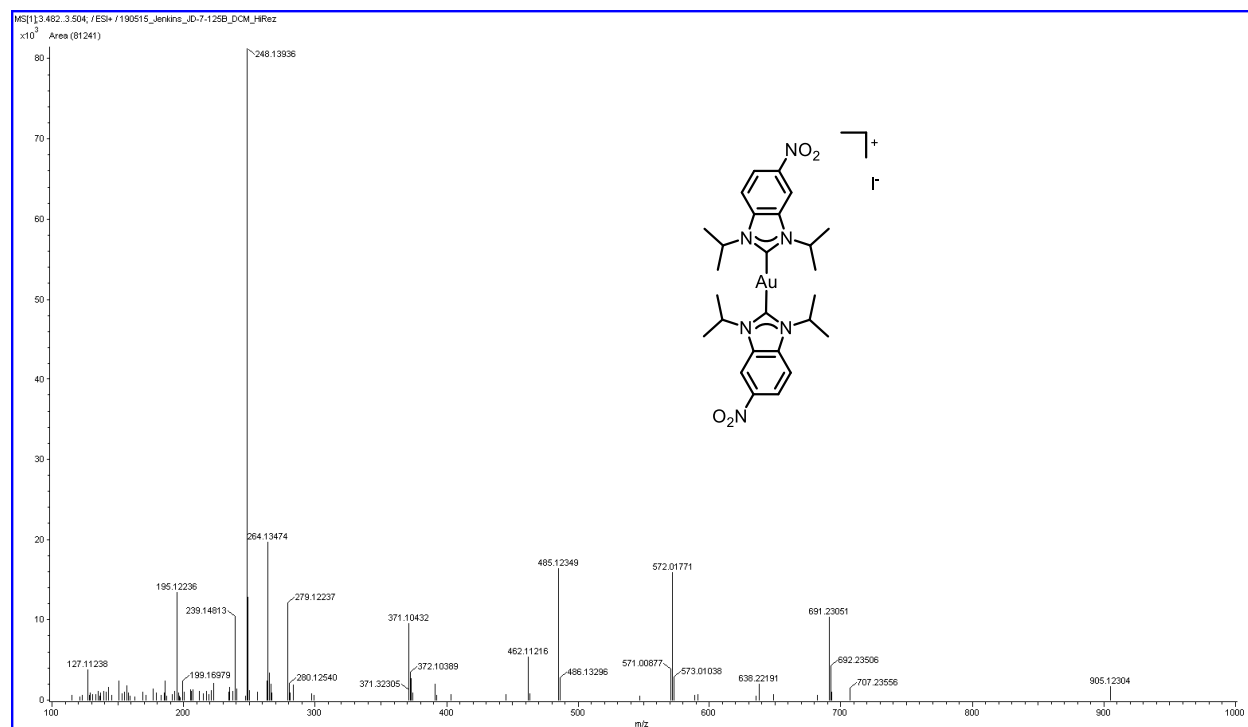
Spectrum 3.11: ¹³C NMR of **3.3-I** in CDCl₃.



Spectrum 3.12: ¹³C NMR of **3.3-I** in CD₃CN.

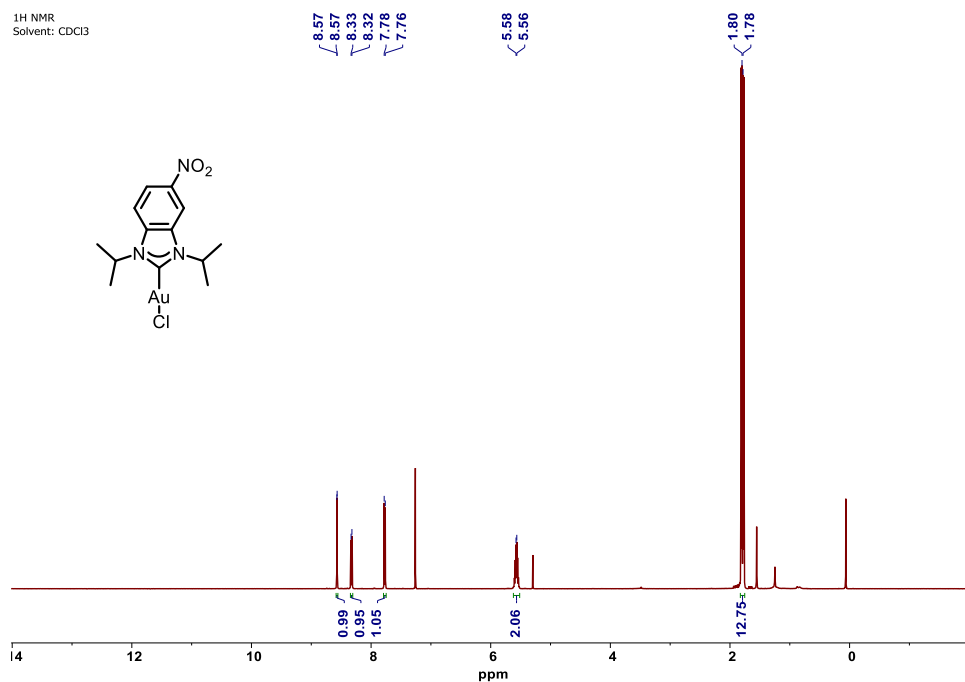


Spectrum 3.13: IR of **3.3-I**.



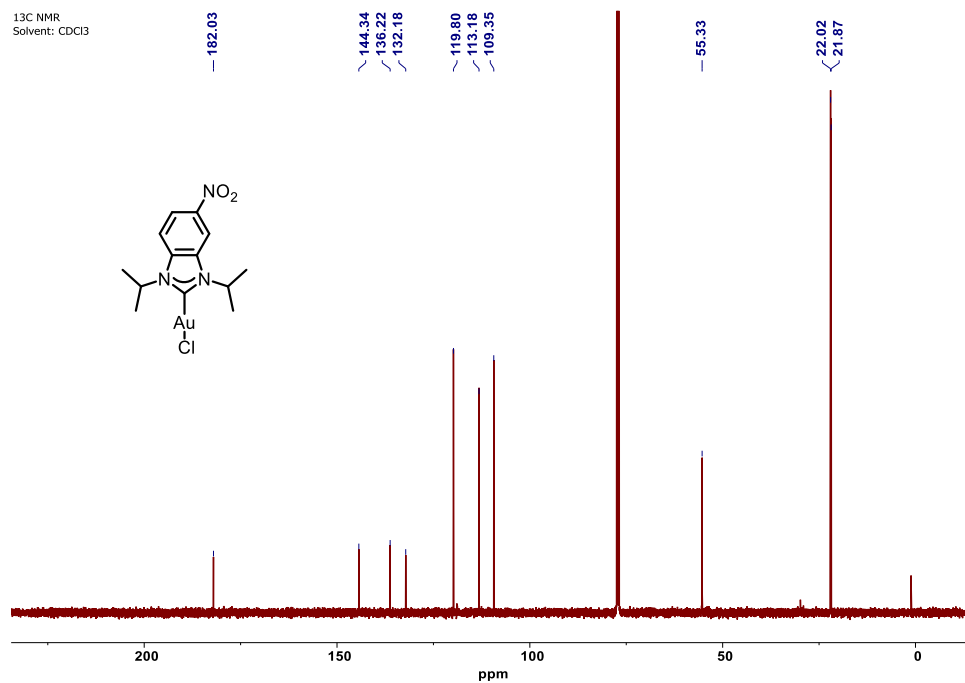
Spectrum 3.14: HR DART MS of **3.3-I**.

¹H NMR
Solvent: CDCl₃

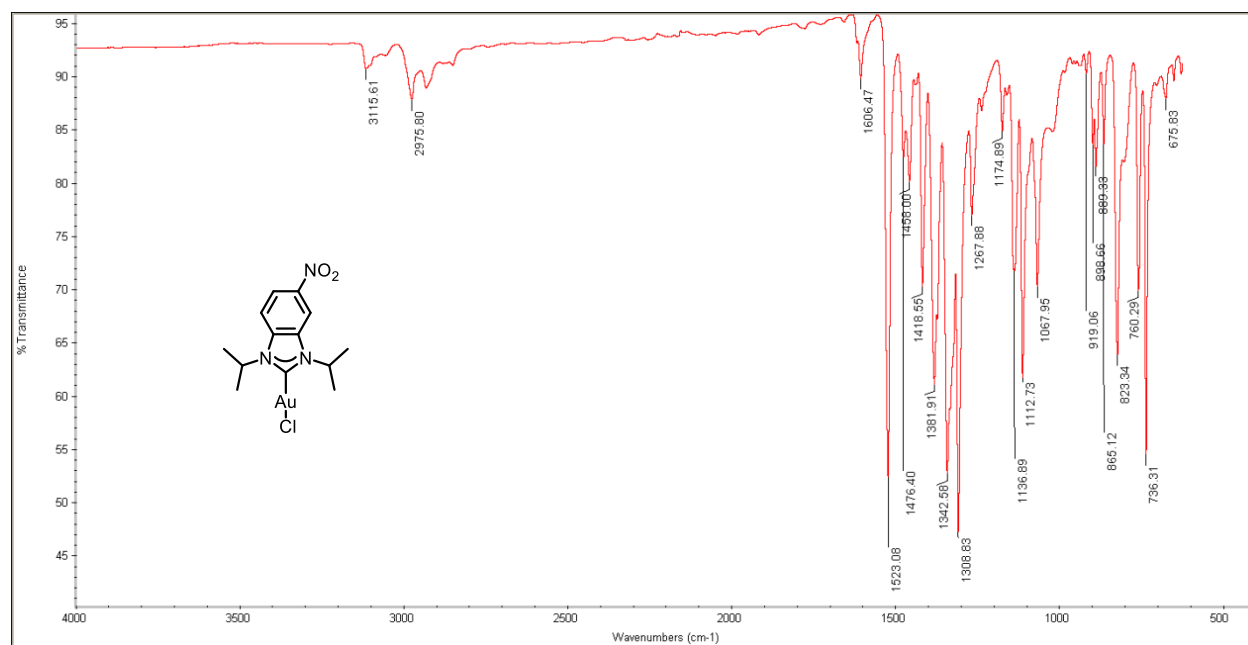


Spectrum 3.15: ¹H NMR of **3.4-Cl** in CDCl₃.

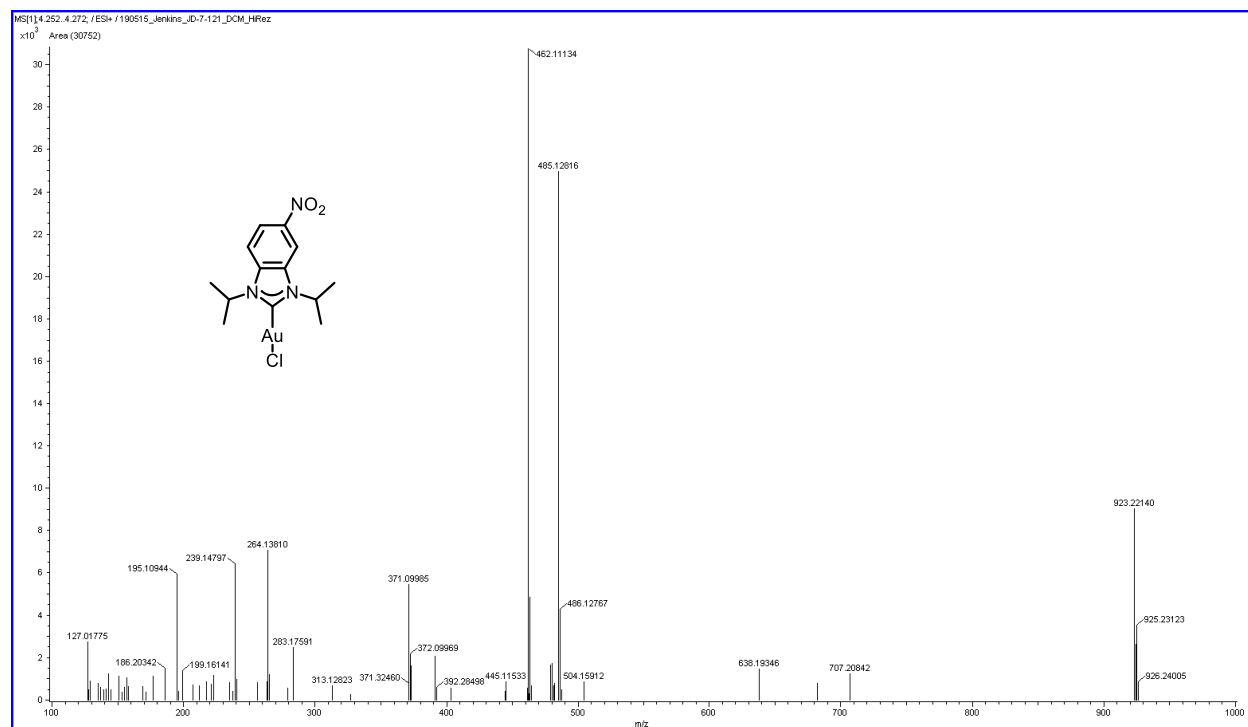
¹³C NMR
Solvent: CDCl₃



Spectrum 3.16: ¹³C NMR of **3.4-Cl** in CDCl₃.



Spectrum 3.17: IR of **3.4-Cl**.



Spectrum 3.18: HR DART MS of **3.4-Cl**.

**Chapter Four: A Chiral Macrocyclic Tetra-N-heterocyclic
Carbene Yields an “All Carbene” Fe(IV) Complex**

This work is currently been submitted for publication to *Angewandte Chemie International Edition* by Joseph F. DeJesus and David M. Jenkins as:

DeJesus, J. F.; Jenkins, D. M. A Chiral Macrocyclic Tetra-N-heterocyclic Carbene Yields an “All Carbene” Fe(IV) Complex.

Abstract

The first chiral macrocyclic tetra-N-heterocyclic carbene (NHC) ligand has been synthesized. The macrocycle, prepared in high yield and large scale, was ligated onto palladium and iron to give divalent C_2 -symmetric square planar complexes. Multinuclear NMR and single crystal X-ray diffraction demonstrated that there are two distinct NHCs on each ligand, due to the bridging chiral cyclohexane. Oxidation of the iron(II) complex with trimethylamine N-oxide yielded a bridging oxo complex. Diazodiphenylmethane reacted with the iron(II) complex at room temperature to give a paramagnetic diazoalkane complex; the same reaction yielded the iron(IV) alkylidene complex at elevated temperature. Notably, the diazoalkane complex can be directly transformed into the alkylidene complex, which had not been previously demonstrated on iron. Finally, a test catalytic reaction with a diazoalkane on the iron(II) complex does not yield the expected cyclopropane, but actually the azine compound.

Introduction

The ability to set stereochemistry during a catalytic reaction is a critical tool in synthetic chemistry, and three-membered ring formation is an increasingly active research topic.^{84, 155-157} The reason is that prochiral alkenes are widely abundant and can be combined with a variety of oxidants. The Jacobson-Katsuki epoxidation catalyst (Figure 4.1A) utilizes a tetradentate chiral salen ligand that promotes stabilization of the $Mn^V=O$ intermediate that asymmetrically transfers oxygen to alkenes.¹⁵⁸⁻¹⁶⁰ Research by Che established that chiral aziridines could be synthesized catalytically from single

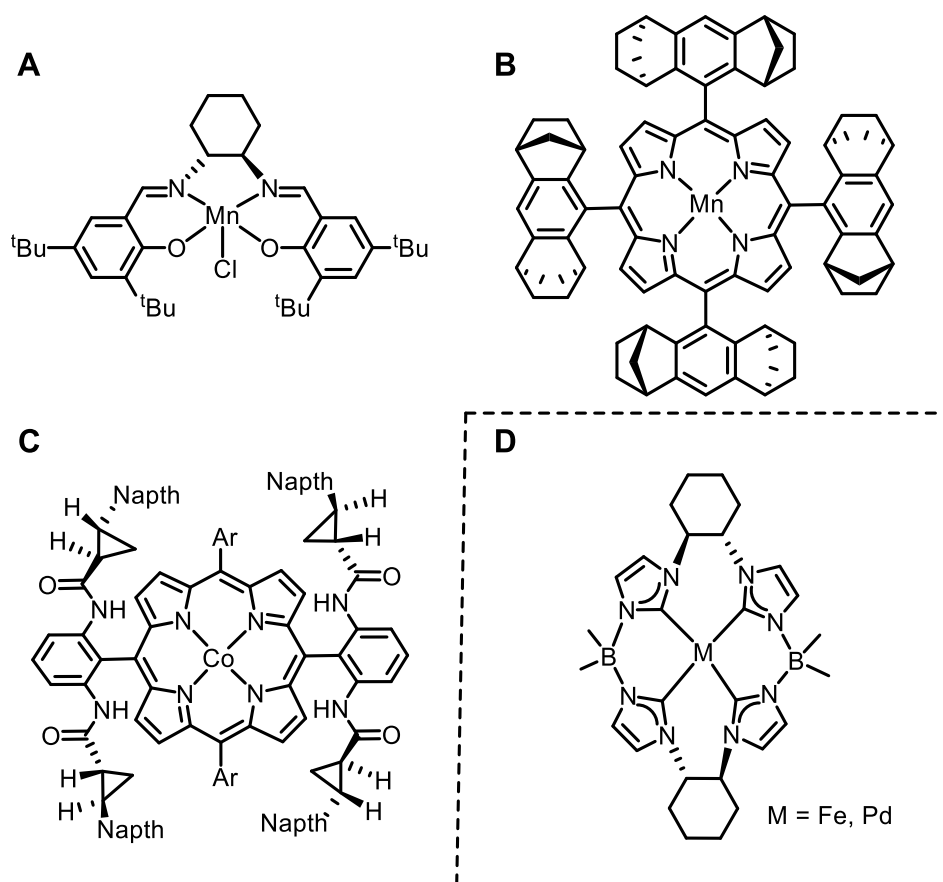


Figure 4.1: Examples of chiral tetradentate ligands for chiral oxidative group transfer.

4.1A-4.1C: Examples of chiral tetradentate ligands and complexes used in previous asymmetric group transfer catalysis. **4.1D:** New chiral ligand and complexes type presented in this work.

enantiomer porphyrin Mn or Ru complexes (Figure **4.1B**).^{73, 125} More recently, Zhang has employed chiral D_2 -symmetric porphyrin cobalt complexes (Figure **4.1C**) for enantioselective aziridination and cyclopropanation.^{76, 77, 161} Nonetheless, there are several drawbacks for these catalyst designs. First, they often require strong oxidants or have a limited substrates scope to form the required group (O, NR, or CR₂) that is to be selectively transferred to the alkene.^{162, 163} Second, the synthesis of the ligands, particularly chiral porphyrins, is often cumbersome; many require challenging multistep synthesis as well as a chiral resolution step.^{164, 165}

The first drawback has been mitigated with the development of macrocyclic tetra-N-heterocyclic carbenes (NHCs) that have allowed for weaker oxidants to be effective in catalysis.^{68, 71, 166} The increased electron donor strength of the NHCs stabilizes the required ligand multiple bond intermediates that are thought to be critical for these catalytic reactions.^{71, 161 60, 62, 167} For example, we have reported the synthesis of a neutral iron(II) complex utilizing a diborate tetra-NHC macrocyclic ligand that is able to activate completely aliphatic organic azides at room temperature, and perform catalytic aziridination to unactivated alkenes at elevated temperatures.⁶⁹ Furthermore, the Kühn group has demonstrated that macrocyclic tetra-NHC complexes are highly effective for epoxidation.⁷¹

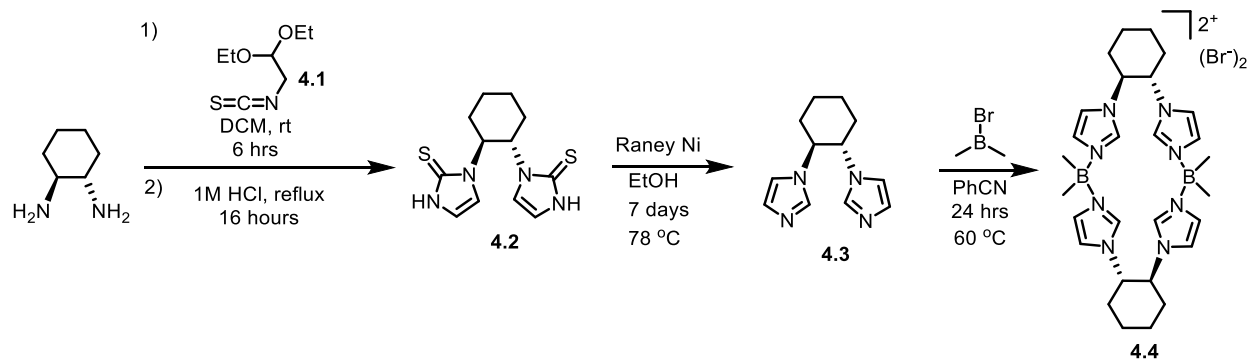
Despite their benefits, chiral tetradentate NHC ligands have lagged behind significantly compared to other ligands, such as porphyrins.⁸² The key obstacle to the synthesis of C_2 -symmetric bidentate NHC ligands is that the prototypical condensation reaction forms a 1:1 mixture of the imidazole amine species and the desired diimidazole. This mixture is difficult to purify, requires arduous column chromatography, and results in

low yields.^{89, 90, 168} While incomplete purification can be managed by alkylation for bidentate NHCs, for tetra-NHC macrocycles the presence of an impurity can lead to a mixture of species that is intractable to separate. Indeed, to date, no chiral tetra-NHC ligands have been synthesized.

This chapter explores the synthesis of the first chiral tetra-NHC macrocyclic ligand and its associated metal complexes. A scalable synthesis for a C_2 -symmetric chiral diimidazole is established that circumvents the typical byproduct complications. This key diimidazole is transformed into a chiral macrocycle that is then ligated to palladium(II) and iron(II). Initial oxidation reactions are explored with the iron complex which shows that an “all carbene” alkylidene complex can be formed from the addition of a diazoalkane with heat.

Results and Discussion

To develop a method for preparing a chiral macrocyclic tetraimidazolium, we desired to follow the route that we previously pioneered by reacting a diimidazole with a dielectrophile in a polar nitrile solvent.^{71, 169} Crucially, to synthesize these NHC macrocycles, we require an unsubstituted C_4 position on the imidazole, which renders some synthetic routes untenable.¹⁷⁰ Our approach to developing a robust and reliable route for preparing a chiral diimidazole, inspired by reports from Burgess and Kühn, would employ the formation of a bis-cyclic thiourea followed by reduction to yield the diimidazole (Scheme 4.1).^{91, 171}

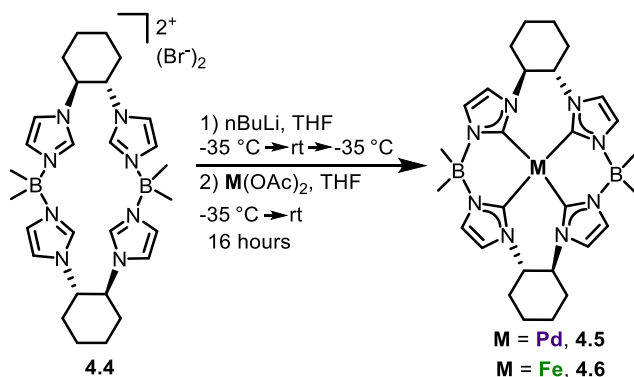


Scheme 4.1: Synthesis of chiral macrocycle **4.4**.

Addition of 1,1-diethoxy-2-isothiocyanatoethane (**4.1**) to (1*S*,2*S*)-1,2-diaminocyclohexane in dichloromethane led to the formation of the dithiourea 1,1'-((1*S*,2*S*)-cyclohexane-1,2-diyl)bis(3-(2,2-diethoxyethyl)thiourea), which was not isolated. The solvent was then removed and 1 M HCl was added and refluxed for 16 hours, leading to cyclization in 80% yield. Compound **4.2** formed as a white precipitate upon cooling and was collected by filtration. While some depictions of molecule **4.2** show it as the thiol tautomer,⁹¹ we believe—based on IR evidence of the broad N-H stretches at 3080 and 3016 cm⁻¹ and no presence of a S-H stretch—that it is primarily the thione form.¹⁷² The cyclic thiourea, **4.2**, was reduced with excess Raney nickel in refluxing ethanol over seven days to yield (1*S*,2*S*)-1,2-di(imidazole)cyclohexane, **4.3**, in 71% yield. Other desulfurization reagents such as hydrogen peroxide or benzoyl peroxide were ineffective.^{171, 173} Both key steps for forming the chiral diimidazole can be completed on 10+ gram scales with no chromatography and the resulting product is consistent with similar compounds.¹⁶⁸

The chiral macrocycle, ((*S,S*)-1,2-Cy,BMe₂TC^H)(Br)₂, **4.4**, was formed by reaction of **4.3** with bromodimethylborane in benzonitrile at 60 °C for 24 hours. The tan solid that was collected was washed with successively less polar solvents to yield a white powder in 81% yield. The absolute stereochemistry (*S,S,S,S*) of the macrocycle was confirmed by single crystal X-ray diffraction.

To assist with understanding the symmetry in solid state and solution, as well as its ability to support oxidative group transfer, we endeavored to synthesize palladium and iron complexes, respectively (Scheme **4.2**). Based on recent research using a similar 16-atom macrocycle, we knew that it was necessary to fully deprotonate the ligand, **4.4**, to prepare the metal complexes in high yield.⁷¹ Therefore, we used a similar methodology of deprotonating the macrocycle **4.4** with *n*BuLi beginning at a low temperature (-35 °C) and then warming to rt. The clear solution of deprotonated **4.4** was then cooled to -35 °C and the respective metal acetate salts were added. For Pd(OAc)₂ this gave a white powder, [(*S,S*)-1,2-Cy,BMe₂TC^H)Pd], **4.5**, in 72% yield, and for Fe(OAc)₂ this gave a neon



Scheme 4.2: Synthesis of metal complexes **4.5** and **4.6**.

yellow powder, $[(S,S)\text{-}1,2\text{-Cy,BMe}_2\text{TC}^H\text{Fe}]$, **4.6**, in 60% yield. Weaker lithium bases, such as lithium diisopropyl amide (LDA) or lithium bis(trimethylsilyl)amide (LiHMDS) were insufficiently strong to affect full deprotonation. Complex **4.5** is stable to atmospheric conditions while complex **4.6** is exceptionally air and moisture sensitive, consistent with other square planar tetra-NHCs we have prepared on these respective metals.^{71, 169}

Both the solution and solid state characterization of **4.5** and **4.6** demonstrate the rigid C_2 symmetry that the chiral ligand imposes. ^1H NMR of **4.5** in CDCl_3 shows two separate resonances at 5.61 and 4.16 ppm for the protons off the chiral carbons in the cyclohexane ring (Spectrum **4.5**). The 5.61 ppm resonance also does not shift appreciably in different polarity NMR solvents (Spectrum **4.34**), which shows that the C-H by the metal center is strongly influenced by proximity to the metal. Even more conspicuous is the NHC resonances that are split in the ^{13}C NMR as 176.9 and 165.6 ppm (Spectrum **4.6**). All previous diamagnetic macrocyclic tetra-NHC complexes have only shown one resonance in solution implying that they are all equivalent on NMR time scale.^{71, 169, 174-176} The split resonances of both the ^1H and ^{13}C NMR for **4.5** is a common trait of constrained geometry C_2 -symmetric bidentate NHC complexes, but for **4.5** the difference between the ^{13}C resonances are more pronounced.^{168, 177, 178} The solid state structure for **4.5** confirms this absolute C_2 symmetry and confirms that a single enantiomer is formed (Figure **4.2**,). Complex **4.5** has an average Pd-C bond distance of 2.01 Å which is consistent with its isostructural complexes and a τ_4 value of 0.07 showing that is close to the square planar ideal.^{114, 174}

The iron complex, **4.6** (Figure **4.3**), exhibits many of the same characteristics as **4.5**, but is complicated by its paramagnetism and extreme air sensitivity. Evans method

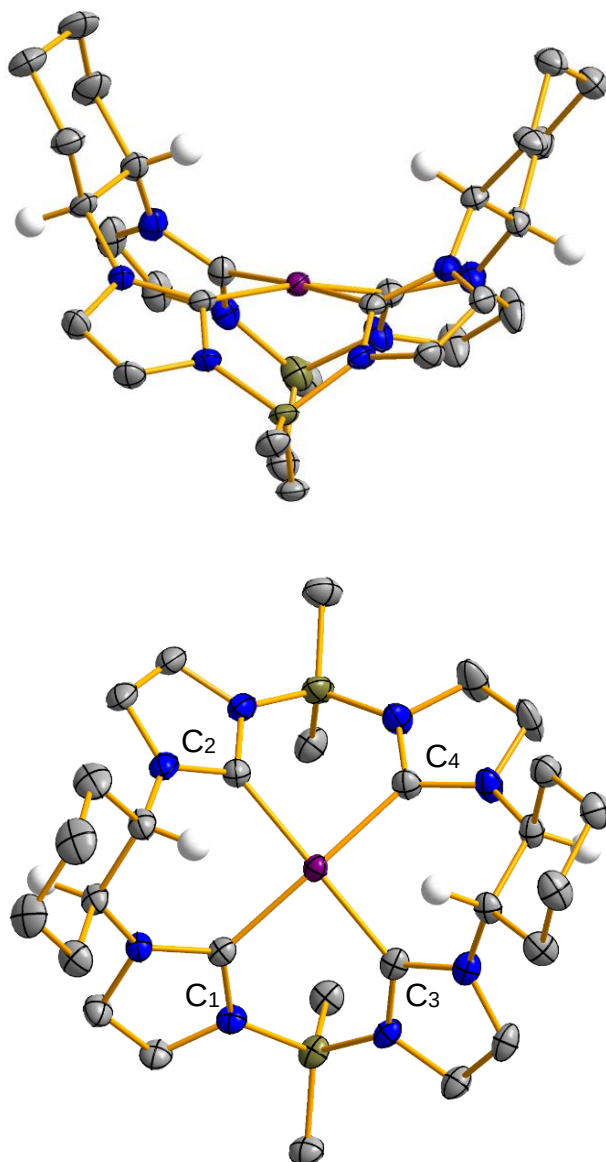


Figure 4.2: X-ray crystal structure of $((S,S)\text{-}1,2\text{-Cy,BMe}_2\text{TC}^H)\text{Pd}$, **4.5**. Purple, blue, gray, olive, and white ellipsoids (50% probability) represent Pd, N, C, B, and H atoms, respectively. Solvent molecules and non-chiral H atoms are omitted for clarity. ; Selected bond lengths (Å) and angles (°) are as followed: Pd-C₁: 2.020(3), Pd-C₂: 2.010(3), Pd-C₃: 2.040(3), Pd-C₄: 2.001(3), C₁-Pd-C₃: 167.88(12), C₂-Pd-C₄: 176.69(13).

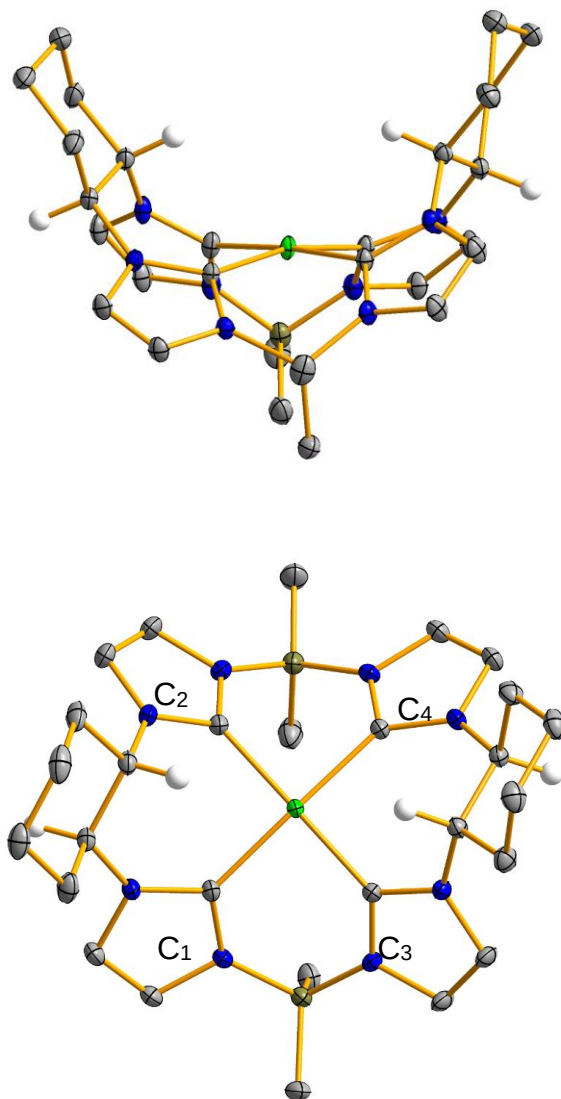
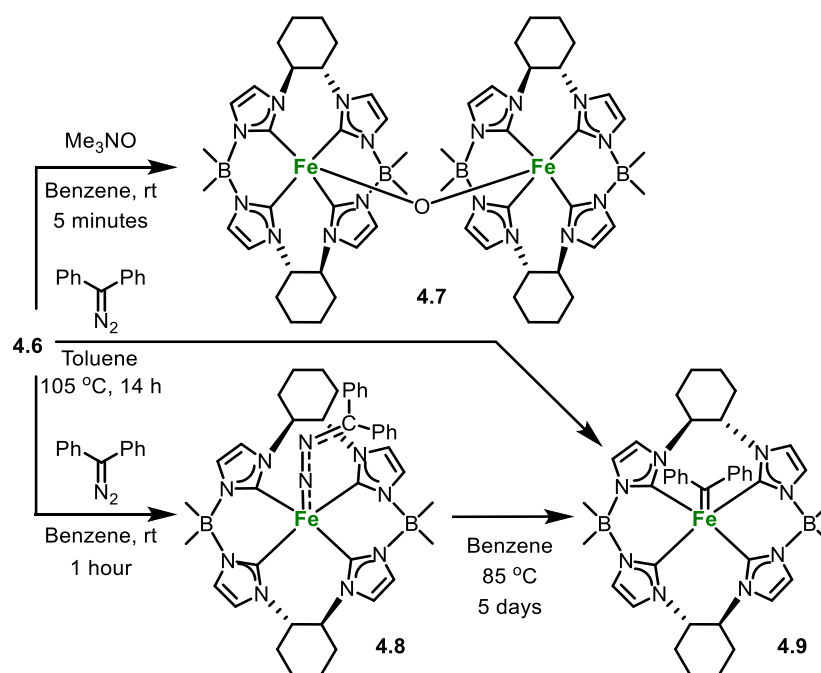


Figure 4.3: X-ray crystal structure of $[(S,S)\text{-}1,2\text{-Cy,BMe}_2\text{TC}^H)\text{Fe}$, **4.6**. Green, blue, gray, olive, and white ellipsoids (50% probability) represent Pd, N, C, B, and H atoms, respectively. Solvent molecules H-atoms not connected to stereogenic centers are omitted for clarity. Selected bond lengths (Å) and angles (°) are as followed: Fe-C₁: 2.0057(15), Fe-C₂: 1.9385(14), Fe-C₃: 2.0049(14), Fe-C₄: 2.0057(15), C₁-Fe-C₃: 166.64(6), C₂-Fe-C₄: 174.87(7).

measurements show two unpaired electrons, consistent with an isostructural iron complex, $[(^{\text{Et}},\text{BMe}_2\text{TC}^{\text{H}})\text{Fe}]$, that we reported previously.⁶⁹ All sixteen expected ^1H resonances for a C_2 symmetry are observed in a wide scan ^1H NMR for **4.6** (Spectrum **4.9**), and as for $[(^{\text{Et}},\text{BMe}_2\text{TC}^{\text{H}})\text{Fe}]$ donor solvents such as CH_3CN do not bind to the iron even at elevated temperature (Spectrum **4.11** and **4.35**). The X-ray crystal structure of **4.6** shows a similar square planar geometry with slightly greater distortion ($\tau_4 = 0.13$) and Fe-C bond distances that average 1.97 Å (Figure **4.3**).

Since divalent iron complexes supported by macrocyclic tetra-NHCs have been highly effective for oxidation catalysis,^{68, 69, 71} we tested the reactivity of **4.6** with oxidants (Scheme **4.3**). Reaction of complex **4.6** with trimethylamine N-oxide results in an



Scheme 4.3: Reactions of **4.6** with Me_3NO and Ph_2CN_2 .

immediate color change to red-brown. The X-ray crystal structure revealed that addition of oxygen led to a bridging oxo, $[\{((S,S)\text{-}1,2\text{-Cy,BMe}_2\text{TC}^H)\text{Fe}\}_2\text{O}]$ (**4.7**) (Figure 4.4).

Complex **4.7** is similar to other bridging iron oxo complexes supported by tetracarbene ligands have been reported by Meyer and our group.^{71, 175} The Fe-O bond lengths are each 1.816(2) Å and the Fe-O-Fe angle is nearly linear at 177.3(2)°. ¹H NMR of **4.7** showed a diamagnetic species similar to **4.5** (Spectrum 4.16). However, the broad peak at 6.59 ppm is highly shifted versus **4.5**. This resonance is attributed to the protons off the chiral cyclohexane that are pointed toward the oxo ligand. These protons appear to have significant hydrogen bonding character with the oxo, shifting them downfield.

Addition of diazodiphenylmethane to **4.6** caused a color change to dark brown with no apparent N₂ evolution. This paramagnetic product has a poorly resolved NMR, but intriguingly has a peak in the IR spectrum at 2038 cm⁻¹, suggesting that the N₂ moiety is still present (Spectrum 4.21). Single crystal X-ray confirmed that the N₂ from the diazoalkane had not been lost, and we had synthesized the diazoalkane complex, $[\{((S,S)\text{-}1,2\text{-Cy,BMe}_2\text{TC}^H)\text{Fe}(\text{N}_2\text{CPh}_2)]$ (**4.8**) (Figure 4.5). Diazoalkane binding to transition metals is quite complex,¹⁷⁹ and few diazoalkane complexes have been prepared on iron.¹⁸⁰⁻¹⁸³ Chirik and Albertin have synthesized linear diazoalkanes which bind as neutral adducts,^{180, 182} while Betley and Holland have prepared complexes where the ligand binds as a diazoalkanyl radicals.^{181, 183} For complex **4.8**, the key bond lengths (Fe-N, 1.779(4) Å; N-N, 1.215(5) Å; and N-C, 1.327(6) Å) are closer to the diazoalkanyl radical formulation (albeit with a slightly longer N-C bond). However, the ligand bond angles (Fe-N-N, 174.5(4)° and N-N-C, 140.4(5)°) are more consistent with a hydrazonido formulation.¹⁸³ Evans method measurements show a spin state of S = 1, which is consistent with either

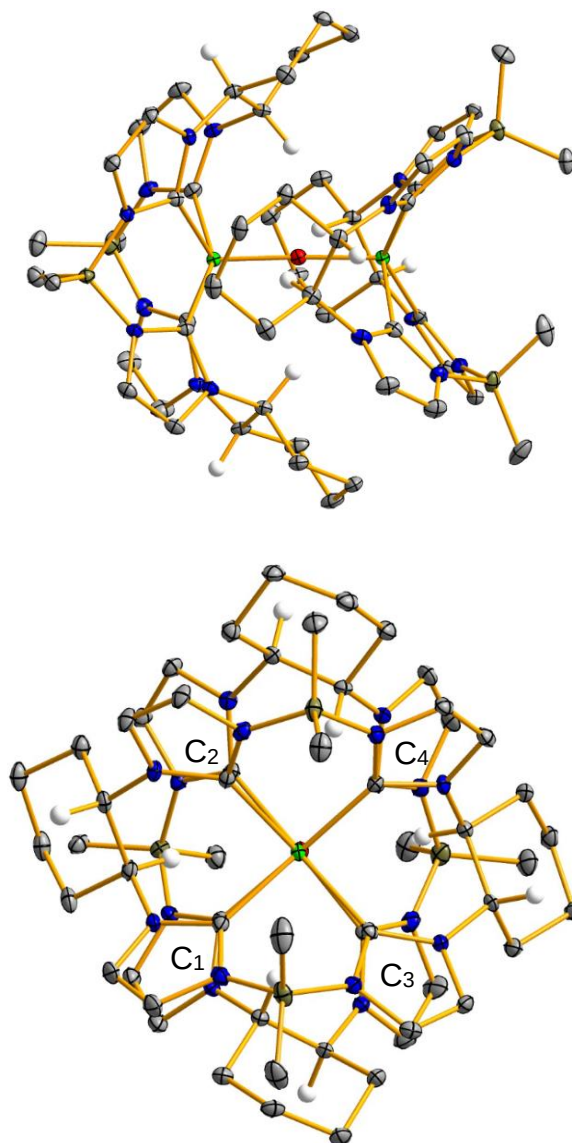


Figure 4.4: X-ray crystal structure of $[((S,S)\text{-}1,2\text{-Cy,BMe}_2\text{TCH})\text{Fe}]_2\text{O}$, **4.7**. Green, blue, gray, red, olive, and white ellipsoids (50% probability) represent Fe, N, C, O, B, and H atoms, respectively. Solvent molecules and H-atoms not connected to stereogenic centers are omitted for clarity. Selected bond lengths ($\text{\AA}$) and angles ($^\circ$) are as followed: Fe₁-C₁: 2.070(3), Fe₁-C₂: 2.017(3), Fe₁-C₃: 2.068(3), Fe₁-C₄: 2.014(3), Fe₁-O: 1.816(2), Fe₂-O: 1.816(2), C₁-Fe₁-C₃: 142.37(13), C₂-Fe₁-C₄: 152.07(14), Fe₁-O₁-Fe₂: 177.33(15).

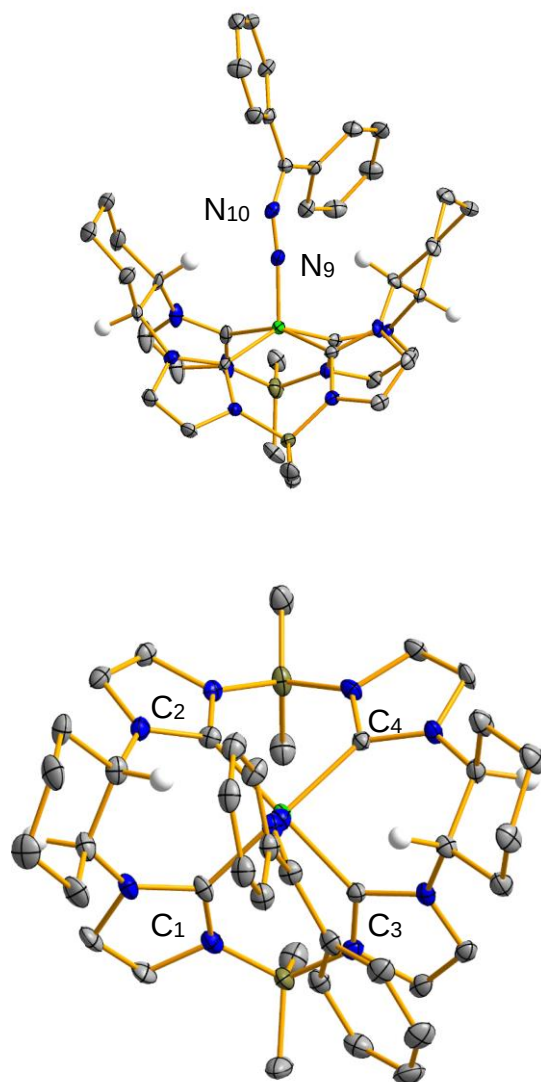


Figure 4.5: X-ray crystal structures of $[(S,S)\text{-}1,2\text{-Cy,BMe}_2\text{TC}^{\text{H}})\text{Fe}(\text{N}_2\text{CPh}_2)]$, **4.8**. Green, blue, gray, olive, and white ellipsoids (50% probability) represent Fe, N, C, B, and H atoms, respectively. Solvent molecules and H-atoms not connected to stereogenic centers are omitted for clarity. Selected bond length (Å) and angles (°) are as followed: Fe-C₁: 2.019(5), Fe-C₂: 1.900(5), Fe-C₃: 2.032(5), Fe-C₄: 1.978(5), Fe-N₉: 1.779(4), N₉-N₁₀: 1.215(5), N₁₀-C₂₉: 1.327(6), C₂₉-C₃₀: 1.477(8), C₂₉-C₃₆: 1.471(7).

formulation (i.e. intermediate spin Fe(IV) or intermediate spin Fe(III) with antiferromagnetic coupling to diazoalkanyl radical, $S = 3/2 - 1/2$). A final point of comparison is the average lengths of the Fe-NHC bonds since increasing the oxidation state in the same geometry should shorten the bonds. A comparison of **4.7**, **4.8**, and **4.9** (*vide infra*) indicates that the average Fe-C_{NHC} distances are 2.042 Å, 2.008 Å, and 1.995 Å, respectively. We believe that the evidence is in favor of the hydrazonido formulation for **4.8**, which is a similar spin state and oxidation state compared to our recently reported paramagnetic Fe(IV) imide complex, [(^{Me},^{BMe₂}TC^H)Fe(NDipp)].⁷¹

With the formation of the complex **4.8**, we endeavored to form the Schrock carbene to determine if these species would be effective for chiral carbene transfer reactions. Increasing the temperature of the reaction on **4.8** with diazoalkane to 105 °C in toluene led to a diamagnetic product which was consistent with the alkylidene complex (Figure **4.6** and Spectrum **4.38 - 4.43**), [(^(S,S)-1,2-Cy,^{BMe₂}TC^H)Fe(CPh₂)] (**4.9**). The ¹H NMR of **4.9** (Spectrum **4.24**) has similarities to that of **4.5** but the addition of the signals for the Ph groups on the alkylidene. Of note, the peak at 7.58 ppm is much broader than expected. Due to the integration of 4H and the expected ortho C-H doublet missing, it was thought these H's are fluxional in solution. Indeed, with the 2D-ROESY spectrum (Spectrum **4.29**) shows a cross peak to the C-H at 4.78 ppm. Along with other 2D NMR, this was absolutely assigned as the ortho C-H resonance on the alkylidene. ¹³C NMR (Spectrum **4.25**) showed inequivalent NHC resonances at 188.8 and 172.4 ppm and, strikingly, a resonance at 309.3 ppm, attributed to the alkylidene carbene carbon which could only be definitively observed by an increase of the relaxation delay. Lapinte, Floriani, Che, and Wolczanski have reported alkylidene resonances between 305 and 385 ppm.^{18, 184-186} A

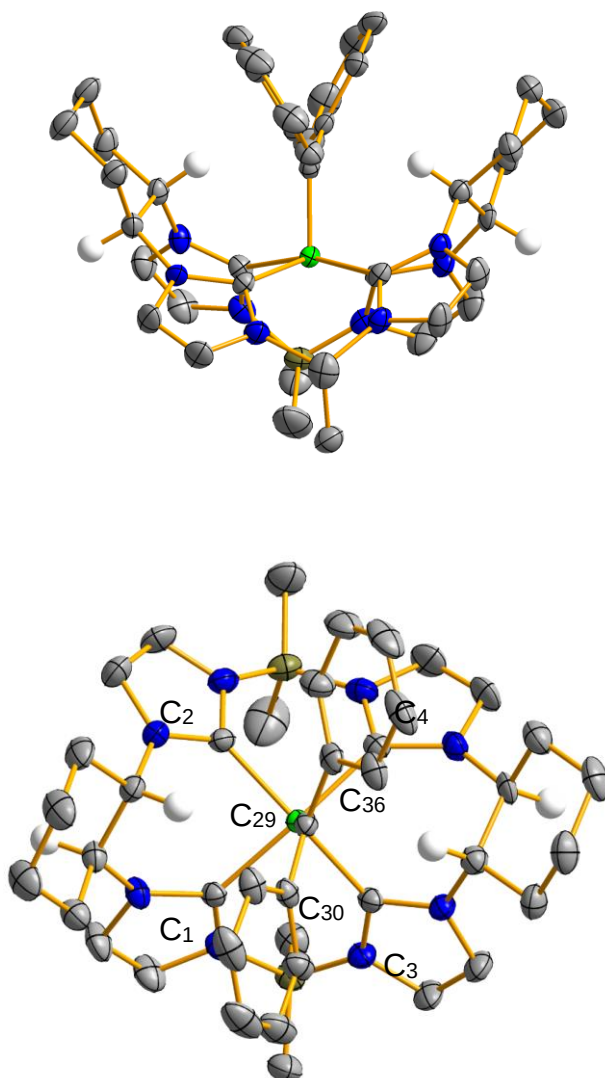
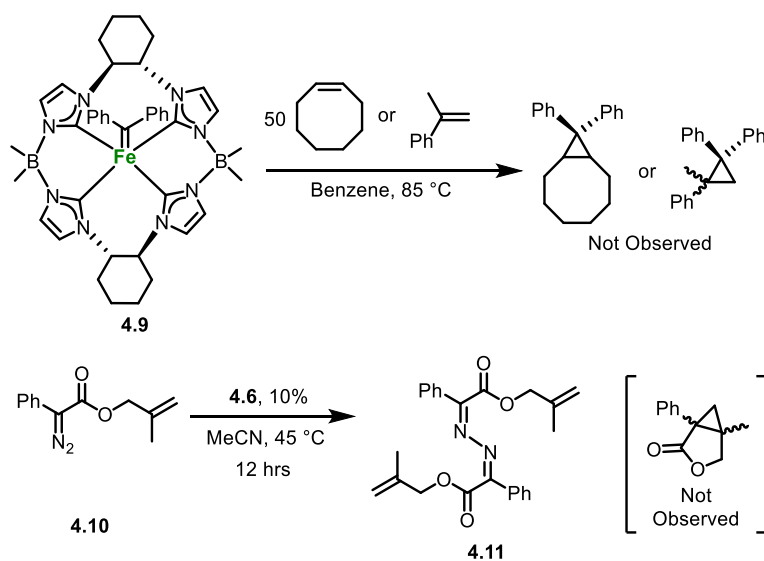


Figure 4.6: X-ray crystal structure $[(S,S)\text{-}1,2\text{-Cy,BMe}_2\text{TC}^H]\text{Fe}(\text{CPh}_2)$, **4.9**. Green, blue, gray, olive, and white ellipsoids (50% probability) represent Fe, N, C, B, and H atoms, respectively. Solvent molecules and H-atoms not connected to stereogenic centers are omitted for clarity. Selected bond lengths (Å) and angles (°) are as followed: Fe-C₁: 2.013(4), Fe-C₂: 1.977(3), Fe-C₃: 2.020(3), Fe-C₄: 1.969(4), Fe-C₂₉: 1.814(4), C₂₉-C₃₀: 1.508(5), C₂₉-C₃₆: 1.490(5).

single crystal X-ray analysis of **4.9** showed the first “all carbene” iron(IV) complex (Figure **4.6**). The Fe=C bond distance is 1.814(4) Å, making it slightly longer than examples with iron porphyrin complexes,^{18, 82, 187} but considerably shorter than examples by Chirik and Wolczanski.^{186, 188} Upon confirmation of the structure of **4.9**, we set up a degradation reaction of **4.8** with heating to see if **4.9** could be formed directly from the diazoalkane complex (Scheme **4.3**), which has never been observed on iron previously and rarely on other transition metals.^{183, 189-192} The reaction in C₆D₆ at 85 °C is quite complex and the alkylidene complex **4.9** starts to appear after four hours; however, after one day, **4.6** is also being formed (Spectra **4.36** and **4.37**). Five days were required to consume all of **4.8** and a mixture of **4.9** and **4.6** was still observed at that time. It was not clear what the organic byproduct was from the reaction, as no tetraphenylethylene was observed by NMR.

With the isolation of **4.9**, we were optimistic that this complex would be effective for chiral cyclopropanation. Regrettably, stoichiometric reactions of **4.9** with both cyclooctene and α -methylstyrene yielded no transfer of the carbene ligand (Scheme **4.4**). In addition, heating **4.9** in neat 1-decene at 170 °C did not result in cyclopropanation. Upon further examination, this is perhaps not too surprising since very few isolated iron alkylidene complexes transfer to give the cyclopropane, the notable exception being examples by Che.¹⁸ An examination of a space-filling model of the X-ray structure of **4.9** shows that there is relatively little space for disubstituted alkenes. However, a report by Zhu for intramolecular chiral cyclopropanation on iron inspired us to try a similar reaction to determine if **4.6** was an effective catalyst.¹⁹³ Reaction of 2-methylallyl 2-diazo-2-phenylacetate (**4.10**) with 10% **4.6** at 45 °C in CH₃CN did not form the expected



Scheme 4.4: Attempts at cyclopropanation with **4.6** and **4.9**.

intramolecular cyclopropane, but in fact formed the dimeric azine **4.11** in 81% yield. A control reaction of **4.10** without **4.6** showed no reaction after 16 hours. In addition, stoichiometric reaction of **4.10** with **4.6** in benzene formed the azine compound **4.11** in less than 15 minutes at room temperature. Sun found that Cp^*RhCl_2 catalyzed a similar reaction to form a similar azine from diphenyldiazomethane by diazo coupling, presumably from the Rh-carbene complex; we recently reported similar results with a less sterically encumbered tetra-NHC iron complex.^{71, 194}

Conclusion

In conclusion, we have synthesized the first chiral tetra-NHC macrocycle in three high yielding steps starting from (1*S*,2*S*)-1,2-diaminocyclohexane. This macrocycle was ligated onto palladium and iron in good yield through deprotonation with a strong base at low temperature. The diamagnetic palladium complex shows strict C_2 symmetry in the NMR spectra as evidenced by the two distinct NHC resonances in ^{13}C NMR. This C_2 symmetry is also observed in the single crystal X-ray structures of both the palladium and iron complexes. Two different oxidation reactions were tested on the iron complex due to the effectiveness of similar macrocyclic tetracarbene complexes in catalysis. A reaction with trimethylamine N-oxide led to the bridging oxo complex which has hydrogen bonding to four of the cyclohexane protons from the macrocyclic ligands. The addition of diphenyldiazomethane to the iron(II) complex at room temperature led to a rare diazoalkane iron complex, which appears to bind in the hydrazonido formulation. Most notably, heating the same reaction with a slight excess of diazoalkane leads to the formation of the Fe(IV) alkylidene complex, an “all carbene” complex. The diazoalkane complex can also be transformed into the alkylidene complex and this is the first system where this has been demonstrated on iron. While the iron(II) complex does not catalyze cyclopropanation, it does catalyze azine formation in a manner similar to Rh complexes. These results set the stage for further studies of chiral macrocyclic NHC complexes to complement porphyrin and salen complexes for oxidative group transfer reactions.

Experimental

General Considerations for Synthesis:

All reactions and workups for NHC ligands were conducted under air unless otherwise stated. All reactions, workups and manipulations involving the NHC metal complexes and subsequent reactions were done using standard Schlenk techniques under N₂ or in an MBraun Unilab glovebox under N₂ unless otherwise stated. All glassware for aforementioned reactions were dried at 170 °C overnight before use. For air sensitive reactions, tetrahydrofuran (THF), toluene, hexanes and were dried on an Innovative Technologies Pure Solv MD-7 Solvent Purification System, degassed by three freeze-pump-thaw cycles on a Schlenk line, and subsequently stored under activated 4 Å molecular sieves prior to use. Anhydrous acetonitrile (CH₃CN) was prepared by distillation over phosphorous pentoxide, followed by degassing by three freeze-pump-thaw cycles and stored over activated 4 Å molecular sieves prior to use. Benzene and pentane were purchased anhydrous from Sigma-Aldrich, degassed by three freeze-pump-thaw cycles and subsequently stored over activated 4 Å molecular sieves prior to use. For anhydrous NMR solvents, benzene-*d*₆ (C₆D₆), dichloromethane-*d*₂ (CD₂Cl₂) chloroform-*d* (CDCl₃) and acetonitrile-*d*₃ (CD₃CN) were degassed by three freeze-pump-thaw cycles and subsequently stored over activated 4 Å molecular sieves prior to use. Celite and silica gel used in the synthesis of metal complexes were dried overnight at 240 °C and subsequently stored in the glovebox prior to use. All reagents were purchased from commercial vendors at highest purity. (1*S*,2*S*)-(+)-1,2-Diaminocyclohexane was purchased from Combi-Blocks at highest available purity (96%). Raney Nickel (2800 mesh) was purchased from Oakwood and used within 2 months of opening.

Diphenyldiazomethane¹⁹⁵ and 2-methylallyl 2-diazo-2-phenylacetate (**4.10**)¹⁹⁶ were synthesized based on previously reported procedures.

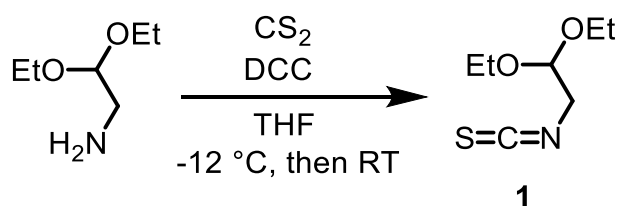
General Considerations for Molecule Characterization:

Solution ¹H NMR and ¹³CNMR were performed on either a Varian Mercury 300 MHz or Varian VNMRS 500 MHz narrow-bore broadband system at 298 K. All ¹H and ¹³C shifts were referenced to the residual solvent. All solution 2D NMR experiments were performed on Varian VNMRS 600 MHz narrow-bore broadband system at 298 K. All mass spectrometry analyses were conducted at the Biological and Small Molecule Mass Spectrometry Center located in the Department of Chemistry at the University of Tennessee. The DART analyses on neutral organic molecules were performed using a JEOL AccuTOF-D time-of-flight (TOF) mass spectrometer with a DART (direct analysis in real time) ionization source from JEOL USA, Inc. (Peabody, MA) using either dichloromethane or methanol as the solvent. The ESI/MS analyses on charged organic molecules were performed using an Exactive Plus OrbitrapTM Mass Spectrometer (Thermo Scientific, San Jose, CA, USA) with sheath gas set to 25 arbitrary units, auxiliary gas set to 10 arbitrary units, spray voltage to 4kV, capillary temperature set to 350 °C, and resolution of 140,000. Infrared spectra were collected on a Thermo Scientific Nicolet iS10 with a Smart iTR accessory for attenuated total reflectance (ATR) using the neat complexes. UV-vis measurements were taken inside a dry glovebox on an Ocean Optics USB4000 UV-vis system with 1 cm path length quartz crystal cell. Carbon, hydrogen, and nitrogen analyses were obtained from Atlantic Microlab, Norcross, GA, Galbraith Laboratories Inc., Knoxville, TN or Midwest Microlab, Indianapolis, IN.

General Considerations for Crystallography:

All X-ray data collections were performed on single crystals coated in Paratone oil on glass slides and mounted on nylon fibers. Crystals for **4.6**, **4.8** and **4.9** were coated in Paratone oil, which had previously been degassed with N₂ and dried with a piece of sodium metal inside the glovebox. X-ray data for complexes **4.6**, **4.7**, **4.8**, and **4.9** were collected with the use of a Mo microsource and X-ray data for **4.4** was collected using a Cu microsource on a Bruker D8 Venture diffractometer. Crystals were mounted in a 100 K cold stream provided by an Oxford Cryostream low-temperature apparatus. All data sets were reduced with Bruker SAINT and were corrected for absorption using SADABS. Structures were solved and refined using SHELXT and SHELXL64, respectively. Compounds **4.4** and **4.5** were treated with PLATON SQUEEZE command to remove nonsensical disordered solvent voids and remove heavily disordered toluene molecules, respectively.

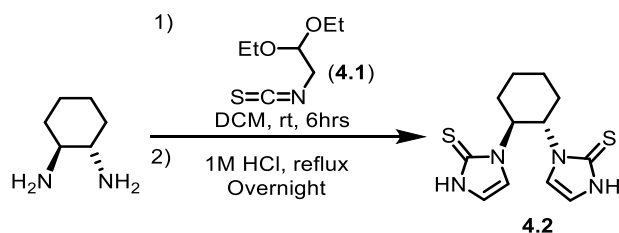
Synthesis of 1,1-diethoxy-2-isothiocyanatoethane, 4.1:



The synthesis of 1,1-diethoxy-2-isothiocyanatoethane was modified from a previously reported procedure. Dicyclohexyl carbodiimide (DCC) (77.46 g, 375.4 mmol, 1 eq.), THF (375 mL), and carbon disulfide (CS₂) (135 mL) were added to a 2 L round bottom flask. The 2 L flask was then attached to a drop addition funnel and the flask was cooled to -12 °C using an ice-salt cooling bath. Aminoacetaldehyde diethyl acetal (50.01 g, 375.5

mmol, 1 eq.) was added to the drop addition funnel. The amine was then added dropwise to the 2 L flask with vigorous stirring over 30-45 min. A large amount of white precipitate formed towards the end of addition. The funnel was removed, and the flask was covered. The flask was allowed to warm to ambient temperature overnight. The mixture was then filtered over a 350 mL medium porosity frit into another 2 L flask to remove the precipitate. The precipitate was washed with hexanes (500 mL) and then the filtrate concentrated in vacuo. The viscous yellow oil was then diluted with hexanes (800 mL), filtered over a second 350 mL medium porosity frit, and concentrated to a yellow oil. This oil was then stored in a -20 °C freezer overnight. The oil was then carefully transferred into a 250 mL round bottom flask by pipet without transferring any precipitated solid. The yellow oil was then purified by short path distillation and the first fraction was collected at 140 mTorr and 20 °C with an ice bath on the receiving end. The final pure product was a colorless oil (63.2 g, 96.1% yield). **¹H NMR** (CDCl₃, 499.74 MHz): δ 4.68 (t, *J* = 5.5 Hz, 1H), 3.66 (m, 4H), 3.56 (d, *J* = 5.5 Hz, 2H), 1.25 (t, *J* = 7.1 Hz, 6H). **¹³C NMR** (CDCl₃, 125.66 MHz): δ 133.56, 100.11, 63.12, 47.60, 15.39. **IR**: 2977, 2883, 2076, 1442, 1373, 1347, 1299, 1245, 1124, 1056, 934, 906, 816, 702 cm⁻¹. **DART HR MS** (*m/z*): [M+H]⁺: 176.07319 (found), [C₇H₁₄NO₂S]⁺: 176.07398 (calculated).

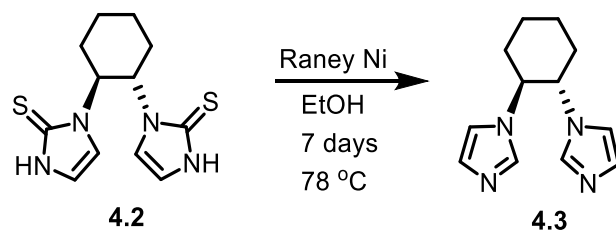
Synthesis of 1,1'-((1S,2S)-1,2-cyclohexanediyl)bis(1,3-dihydro-2H-imidazole-2-thione), 4.2:



(1S,2S)-1,2-Diaminocyclohexane (13.18 g, 115.4 mmol, 1 eq.) was added to a 1 L round bottom flask with 230 mL of CH₂Cl₂. 1,1-Diethoxy-2-isothiocyanatoethane (**4.1**) (40.45 g, 230.8 mmol, 2 eq.) was added quickly to the 1 L round bottom while stirring. The resulting solution began self-refluxing immediately. The reaction was allowed to cool to ambient temperature over 6 h. This solution was then concentrated in the round bottom flask under high vacuum, resulting in a sticky light-yellow foam. This foam turned into a viscous yellow oil quickly on exposure to air. The yellow oil was suspended in a 1M HCl solution (380 mL) and the biphasic mixture was refluxed at 100 °C overnight. [**Caution:** Unreacted **4.1** or other sulfur containing impurities will hydrolyze, releasing foul-smelling compounds. It is highly advisable to perform this reaction in a well-ventilated fume hood.] After 16 hours, a white precipitate formed. The reaction was then cooled to room temperature and kept in a -20 °C freezer overnight. The white precipitate was then filtered over a 150 mL medium porosity frit and washed with ice cold water (50x3 mL) which yielded **2** (26.15 g, 80.8% yield). ¹H NMR (DMSO-d₆, 499.74 MHz): δ 12.00 (s, 2H), 7.10 (t, *J* = 2.2 Hz, 2H), 6.80 (t, *J* = 2.4 Hz, 2H), 5.02 (m, 2H), 1.96 (d, *J* = 12.5, 2H), 1.79, (d, *J* = 4.8 Hz, 2H), 1.61 (m, 2H), 1.47 (m, 2H). ¹³C NMR (DMSO-d₆, 125.66 MHz): δ 160.46, 115.23, 114.55, 56.36, 31.81, 24.30. IR: 3142, 3080, 3017, 2923, 2859, 1577, 1528,

1481, 1447, 1425, 1407, 1390, 1345, 1335, 1307, 1299, 1279, 1261, 1225, 1153, 1138, 1108, 1053, 980, 954, 913, 850, 821, 785, 754, 716, 707, 679, 669 cm⁻¹. **DART HR MS** (*m/z*): [M+H]⁺: 281.08853 (found), [C₁₂H₁₇N₄S₂]⁺: 281.08891 (calculated).

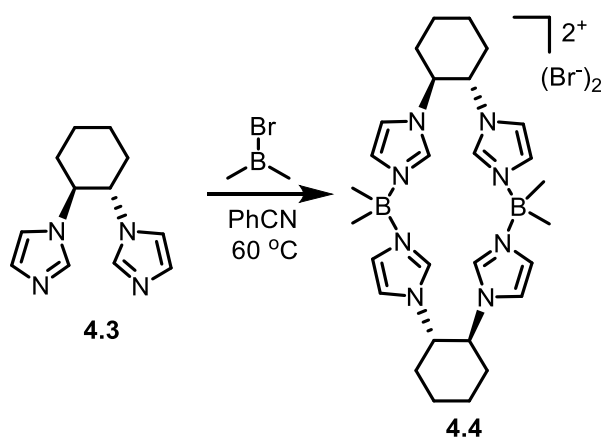
Synthesis of (1*S*,2*S*)-1,2-di(imidazole)cyclohexane, **4.3**:



Compound **4.2** (25.25 g, 90.15 mmol) was added to a 500 mL round bottom flask and dissolved in 200 mL of ethanol. 10 mL of activated Raney Nickel in water was added to the flask. The reaction was then heated under an N₂ atmosphere for 5 days at 78 °C with vigorous stirring. After 5 days, another 15 mL of Raney Nickel was added as some **4.2** remained (based on TLC and DART-MS measurements). After another 2 days, the reaction was cooled to room temperature. The slurry was then filtered over a plug of Celite on a 350 mL coarse filter frit and washed with methanol (600 mL). [**Caution:** The Raney Nickel collected was not allowed to run fully dry after filtering. The filtration flask was swapped out and the Raney Nickel was washed with 1M HCl followed by water.] The filtrate was then concentrated by rotary evaporation and then fully dried under high vacuum. The resulting black foamy residue was dissolved in 150 mL of CH₂Cl₂ and filtered over Celite to remove black solids. Diethyl ether was added to the solution until solid ceased precipitation. This was filtered and washed with additional diethyl ether resulting in a white powder after drying (14.01 g, 71.8% yield). **¹H NMR** (CDCl₃, 499.74 MHz): δ 7.13 (s, 2H), 6.94 (s, 2H), 6.65 (s, 2H), 3.95 (m, 2H), 2.28 (d, *J* = 13.6, 2H), 1.98

(m, 4H), 1.53 (m, 2H). ^{13}C NMR (CDCl_3 , 125.66 MHz): δ 135.67, 129.86, 116.50, 62.16, 32.69, 25.03. IR: 3128, 3095, 2948, 2867, 1627, 1497, 1449, 1406, 1281, 1236, 1228, 1111, 1102, 1092, 1084, 1030, 973, 955, 914, 877, 847, 826, 813, 766, 751, 734, 662, 643 cm^{-1} . DART HR MS (m/z): $[\text{M}+\text{H}]^+$: 217.14599 (found), $[\text{C}_{12}\text{H}_{17}\text{N}_4]^+$: 217.14532 (calculated).

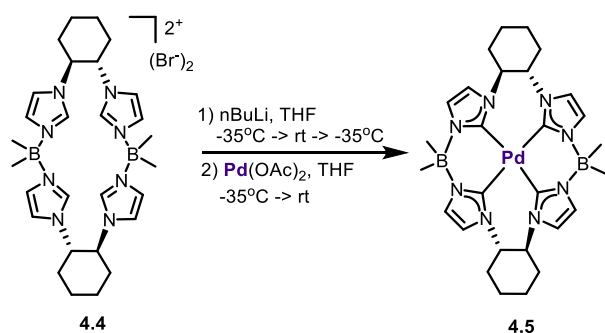
Synthesis of $((S,S)\text{-}1,2\text{-Cy,BMe}_2\text{TC}^H)(\text{Br})_2$, **4.4**:



Diimidazole **4.3** (3.038 g, 13.88 mmol, 2 eq.), was split into two equivalent portions. Half (1.519 g) was put into an oven-dried 250 mL round bottom flask inside the glovebox. To this round bottom flask, 60 mL of benzonitrile (PhCN) was added and the mixture was stirred until full dissolution. Bromodimethylborane (BrBMe_2) (1.40 mL, 14.34 mmol, 2.06 eq.) was added slowly by pipette to the round bottom flask. This solution was stirred for 30 minutes. The second portion of **4.3** (1.519 g) was then added to the flask and stirred for another 5 min. The flask was then covered with a septum, removed from the glovebox, and connected to a Schlenk line via a reflux condenser, put under N_2 , and heated at $60\text{ }^\circ\text{C}$ for 24 h. At the end of 24 h, the solution become a viscous tan slurry. The slurry was then cooled in an ice bath to $0\text{ }^\circ\text{C}$ and filtered over a fine porosity frit to remove the PhCN .

The collected solid was washed with CH₃CN (3x10 mL) until the tan sludge turned white. This white clumpy solid was triturated with THF (2x50 mL) and diethyl ether (3x50 mL). The solid was completely crushed into a fine powder and dried for at least 24 hours under high vacuum. These successive washings and drying resulted in a pure white solid (3.83 g, 81.8% yield). Single crystals of **4.4** were grown by dissolving **4.4** in roughly 0.5 mL of methanol, filtering any off particulates, adding two drops of methanol, followed by careful layering of 4 mL of diethyl ether resulting in colorless plates. **¹H NMR** (DMSO-d₆, 499.74 MHz): δ 8.59 (s, 4H), 7.45 (s, 4H), 7.13 (s, 4H), 4.83 (m, 4H), 2.19 (d, *J* = 12 Hz, 4H), 2.03 (m, 4H), 1.89 (m, 4H), 1.48 (m, 4H), 0.14 (s, 12H). **¹³C NMR** (DMSO-d₆, 125.66 MHz): δ 135.08, 122.80, 120.96, 61.03, 32.12, 23.98, 7.73. **IR**: 3405, 3103, 3050, 2932, 2860, 1621, 1536, 1448, 1355, 1315, 1283, 1261, 1129, 1112, 1086, 1022, 969, 948, 849, 793, 757, 679, 650 cm⁻¹. **ESI HR MS** (*m/z*): [M]²⁺: 257.1930 (found), [C₂₈H₄₄B₂N₈]²⁺: 257.1932 (calculated).

Synthesis of [(*(S,S)*-1,2-Cy,BMe₂TC^H)Pd], **4.5**:

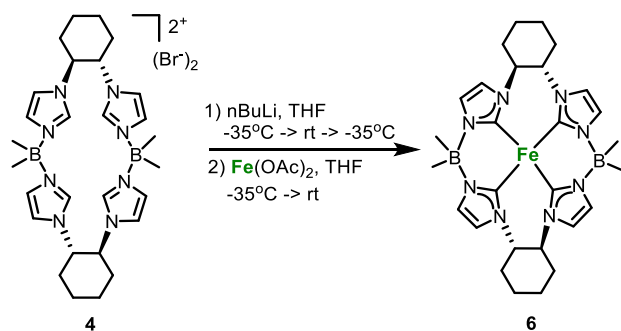


(*(S,S)*-1,2-Cy,BMe₂TC^H)(Br)₂ (0.2082 g, 0.3088 mmol, 1 eq.), **4.4**, was added to a 20 mL scintillation vial and 15 mL of THF was added. The vial was then cooled over 30 min to -35 °C in a freezer. A 2.5 M *n*BuLi solution in hexanes (0.5 mL, 1.250 mmol, 4.1 eq)

was then added to the vial, which was subsequently agitated and returned to the freezer. The suspension was manually agitated every 2 to 3 min over 5-10 mins, until the color changed to yellow. The vial was then allowed to warm up to ambient temperature until the suspension became a solution, approximately 45-60 min. The vial was then returned to the -35 °C freezer and cooled at least 30 min. A second 20 mL vial containing Pd(OAc)₂ (0.0697 g, 0.3096 mmol, 1 eq.) in 1 mL of THF was also cooled to -35 °C. The solution of the free NHC of **4.4** was then quantitatively transferred to the solution of Pd(OAc)₂ with stirring. The solution immediately turned brown and precipitated a grey solid shortly thereafter. The mixture was then allowed to stir for 24 h at rt. The reaction mixture was then filtered through a pad of silica gel on a 15 mL medium porosity frit that was followed by an additional 30 mL of THF. The THF solution was then concentrated and thoroughly dried to leave a white residue. The remaining THF was azeotroped with hexanes (3x10 mL) and the resulting solid residue was extracted with benzene (15 mL). This benzene extraction was concentrated to dryness under reduced pressure. The residue was triturated with hexanes (3x10 mL) which resulted in the pure white solid (0.137 g, 71.9% yield) after drying. Single crystals of **4.5** were grown by slow evaporation of a concentrated toluene/hexanes mixture in air to form colorless shards. ¹H NMR (CDCl₃, 499.74 MHz): δ 7.14 (d, *J* = 1.7 Hz, 2H), 7.06 (d, *J* = 1.7 Hz, 2H), 6.93 (d, *J* = 1.7 Hz, 2H), 6.74 (d, *J* = 1.7 Hz, 2H), 5.61 (dt, *J*₁ = 12 Hz, *J*₂ = 1.5 Hz, 2H), 4.16 (dt, *J*₁ = 11 Hz, *J*₂ = 4.1 Hz, 2H), 2.27 (t, *J* = 14 Hz, 4H), 1.99 (m, 4H), 1.87 (m, 2H), 1.61 (dt, *J*₁ = 3.3 Hz, *J*₂ = 13 Hz, 2H), 1.50 (m, 4H), 0.26 (s, 6H), 0.01 (s, 6H). ¹³C NMR (CDCl₃, 125.66 MHz): δ 176.86, 165.57, 123.12, 121.90, 119.99, 114.21, 64.58, 58.14, 37.88, 31.75, 25.30, 25.10, 16.14, 9.51. IR: 2923, 2853, 1679, 1559, 1450, 1430, 1399, 1355, 1337, 1279, 1241,

1207, 1155, 1124, 1113, 1066, 1039, 1015, 953, 943, 917, 874, 855, 823, 793, 754, 730 cm^{-1} . **DART HR MS** (m/z): $[\text{M}]^+$ 616.25973, $[\text{C}_{28}\text{H}_{40}\text{B}_2\text{N}_8\text{Pd}]^+$: 616.25969 (calculated). **CHN**: Calculated for $\text{C}_{28}\text{H}_{40}\text{B}_2\text{N}_8\text{Pd}$: C: 54.53, H: 6.54, N: 18.17. Found: C: 54.93, H: 6.45, N: 18.30.

Synthesis of $[(\text{(S,S)-1,2-Cy,BMe}_2\text{TC}^H)\text{Fe}]$, **4.6**:

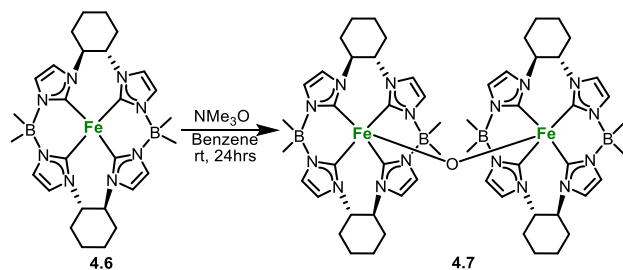


$(\text{(S,S)-1,2-Cy,BMe}_2\text{TC}^H)(\text{Br})_2$ (0.2082g, 0.3088 mmol, 1 eq.), **4.4**, was added to a 20 mL scintillation vial and 15 mL of THF is added. The vial was then cooled over 30 minutes to -35°C in a freezer. A 2.5 M $n\text{BuLi}$ solution in hexanes (0.500 mL, 1.25 mol, 4.1 eq.) was then added to the vial, which was subsequently agitated and returned to the freezer. The suspension was manually agitated every 2 to 3 min over 5-10 mins, until the color changed to yellow. The vial was then allowed to warm up to ambient temperature until the suspension became a solution, approximately 45-60 min. The vial was then returned to the -35°C freezer and cooled at least 30 min. A second 20 mL vial containing $\text{Fe}(\text{OAc})_2$ (0.0545 g, 0.3133 mmol, 1 eq.) with 1 mL of THF was also cooled to -35°C . The solution of the free NHC of **4.4** was then quantitatively transferred to the solution of $\text{Fe}(\text{OAc})_2$ with stirring. The solution immediately turned to an intense dark orange color. The solution was then allowed to stir for 24 hours at rt. Two identical reactions were set up in parallel.

The combined solutions were washed into a filter flask and the solution was concentrated under vacuum. The brown sludge was treated with pentanes (3 x 10 mL) to azeotrope off remaining THF, which left a brown-yellow powder. This powder was extracted with benzene (60 mL) and the filtrate was filtered over a short Celite plug and washed until no yellow solution was observed. The benzene solution was concentrated to about 20 mL, then frozen at -35 °C. The solution was then lyophilized, leaving a powder. The solid was then redissolved in minimal benzene (8 mL) and stirred until full dissolution. This was then filtered over another small Celite plug and was lyophilized again. This was repeated an additional time. The dried powder was triturated with hexanes (3x15 mL) and was dried under vacuum yielding neon yellow powder (0.317 g, 60.5% yield). Single crystals of **4.6** were obtained taking a precipitated solution of **4.6** in roughly 2 mL of benzene and 14 mL of hexanes and heating to reflux, decanting off the solution from the leftover solid. Cooling the solution to ambient temperature overnight formed neon yellow block crystals.

Widescan ¹H NMR (C₆D₆, 499.74 MHz): δ 78.42 (s, 2H), 35.85 (s, 2H), 30.09 (s, 2H), 29.20 (s, 2H), 27.26 (s, 2H), 15.00 (s, 2H), 9.04 (s, 6H), 8.85 (s, 2H), 6.79 (s, 2H), -5.94 (s, 2H), -13.39 (s, 2H), -17.42 (s, 2H), -19.13 (s, 2H), -23.08 (s, 2H), -74.77 (s, 6H), -90.24 (s, 2H). **Widescan ¹H NMR** (ACN-d₃, 599.74 MHz): δ 69.68 (s, 2H), 30.62 (s, 2H), 25.30 (s, 2H), 24.30 (s, 2H), 22.68 (s, 2H), 14.80 (s, 2H), 8.32 (s, 2H), 7.11 (s, 2H), 4.66 (s, 6H), -3.57 (s, 2H), -13.19 (s, 2H), -16.37 (s, 2H), -17.18 (s, 2H), -18.52 (s, 2H), -52.09 (s, 2H), -65.75 (s, 2H). **Evans Method**: 3.4 μB. **DART HR MS** (*m/z*): [M]⁺: 566.29171 (found), [C₂₈H₄₀B₂N₈Fe]⁺: 566.29115 (calculated). **UV-VIS** (THF): 365 nm (7300 L/mol*cm), 445 nm (4500 L/mol*cm).

Synthesis of $[[[(S,S)\text{-}1,2\text{-Cy,BMe}_2\text{TC}^H)\text{Fe}]_2\text{O}]$ **4.7**:

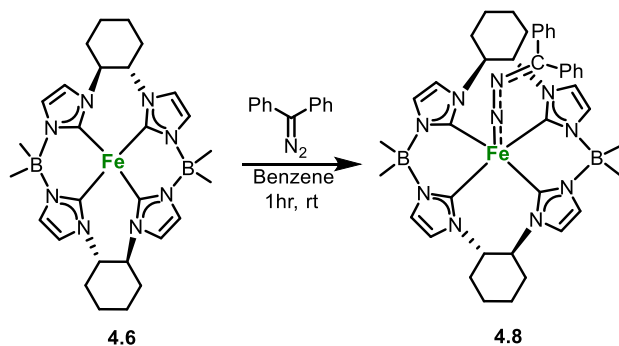


Trimethylamine N-oxide (0.0031 g, 0.0413 mmol, 1 eq.) was added to a 20 mL scintillation vial. To this was added **4.6** (0.0482 g, 0.0851 mmol, 2 eq.), dissolved in 10 mL of benzene. This solution was stirred at ambient temperature for 24 hours. Following this, the solution was filtered through a short pad of Celite and washed with an additional 5 mL of benzene, until no more color remained. This solution was thoroughly dried and hexanes were added to the residue and dried again (3x3 mL). This produced **4.7** as a brown powder (0.0432 g, 88.4% yield). Single crystals were grown by diffusing hexanes into a concentrated benzene solution of **4.7**, resulting in extremely dark red crystals. ^1H NMR (C_6D_6 , 599.74 MHz): δ 7.14 (s, 4H), 6.73 (s, 4H), 6.59 (bs, 4H), 6.07 (s, 4H), 3.40 (d, $J = 6.8$ Hz, 4H), 1.62 (d, $J = 9.0$ Hz, 4H), 1.45 (d, $J = 10.7$ Hz, 4H), 1.35-1.10 (m, 16H), 1.02 (d, $J = 12.2$ Hz, 4H), 0.93 (d, $J = 9.9$ Hz, 4H), 0.66 (s, 12H), -0.15 (s, 12H). ^1H NMR ($\text{CH}_3\text{CN-d}_3$, 599.74 MHz): δ 7.19 (s, 4H), 7.07 (s, 4H), 7.05 (s, 4H), 6.81 (s, 4H), 6.54 (bs, 4H), 3.87 (s, 4H), 1.63 (m, 4H), 1.32 (m, 22H), 1.05 (d, $J = 11.6$ Hz, 4H), 0.92 (m, 4H). ^{13}C NMR (CD_2Cl_2 , 149.94 MHz): 123.40, 122.86, 121.86, 117.50, 68.06, 37.65, 30.99, 25.91, 25.65, 17.32, 13.11 (Fe-C signals not observed due metal proximity with anti-ferromagnetic coupling). IR: 3140, 2931, 2857, 1555, 1448, 1424, 1398, 1348, 1323, 1290, 1273, 1239, 1229, 1208, 1170, 1157, 1135, 1124, 1113, 1045, 1034, 952, 943, 919,

879, 857, 826, 793, 719, 697, 691, 682, 641 cm^{-1} . **CHN**: Calculated for $\text{C}_{56}\text{H}_{80}\text{B}_4\text{Fe}_2\text{N}_{16}\text{O}$

• C_6H_6 : C: 60.72, H: 7.07, N: 18.27. Found: C: 60.50, H: 7.49, N: 16.59.

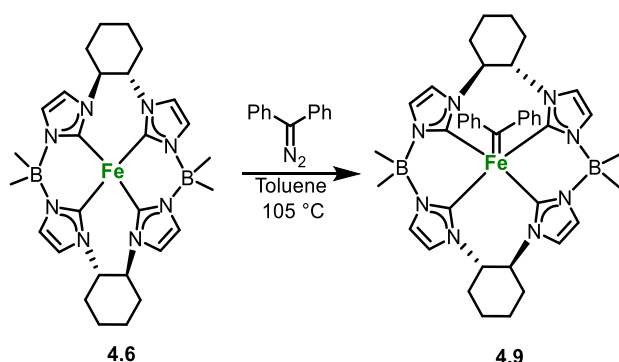
Synthesis of $[(S,S)\text{-}1,2\text{-Cy,BMe}_2\text{TC}^H]\text{Fe-N=N=CPh}_2$, **4.8:**



In a 20 mL scintillation vial, **4.6** (0.0746 g, 0.1318 mmol, 1 eq.) was added followed by the addition of benzene (5 mL). A solution of diphenyldiazomethane (0.0395 g, 0.2034 mmol, 1.54 eq.) in 2 mL of benzene was added, which caused an immediate color change to dark brown. This solution was then stirred at ambient temperature for 1 h. The solvent was removed under vacuum; hexanes were added to the vial and stirred. The solid was then allowed to settle and the solution was pipetted off. This was repeated 3 times with 10 mL of solvent, until no pink color appeared. The residue was then dissolved in 12 mL of 1:1 benzene:hexanes solution and filtered over a short pad of Celite. This was concentrated in vacuo; the solid was then redissolved in roughly 5 mL of toluene, layered with 15 mL of hexanes, and stored overnight at $-35\text{ }^\circ\text{C}$. The mother liquor was decanted off the precipitate. The crystals were washed 3 times with 5 mL of hexanes and dried under vacuum, yielding black crystals (0.0765 g, 76.3% yield). This solid was stored at $-35\text{ }^\circ\text{C}$ due to slow decomposition to **4.9**. Single crystals of **4.8** were grown by dissolving **4.8** in 0.5 mL of toluene and carefully layering 4 mL of hexanes into the solution at ambient

temperature overnight, yielding very dark red plates. **Widescan ^1H NMR** (C_6D_6 , 599.74 MHz): δ 46.95 (s), 22.35 (s), 11.51 (bs), 4.55 (s), 2.97 (s), 2.41 (s), 1.91 (s), 1.12 (s), 0.05 (s), -0.71 (s), -103.45 (s), -104.70 (s). **Evans Method**: 2.5 μB . **IR**: 3132, 2934, 2038, 1657, 1569, 1488, 1448, 1430, 1398, 1335, 1284, 1236, 1208, 1155, 1124, 1067, 1047, 944, 921, 878, 835, 824, 795, 765, 755, 724, 689, 637 cm^{-1} . **UV-Vis** (THF): 360 nm (19000 $\text{L}/\text{cm}^*\text{mol}$), 445 (7200 $\text{L}/\text{cm}^*\text{mol}$), 750 nm (1400 $\text{L}/\text{cm}^*\text{mol}$), 785 nm (1500 $\text{L}/\text{cm}^*\text{mol}$).

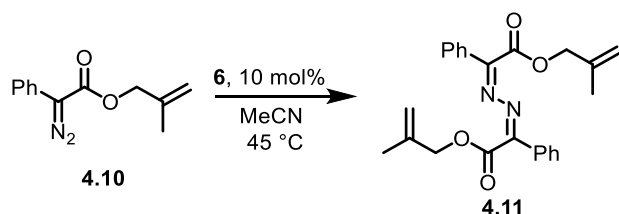
Synthesis of $[[[(S,S)\text{-}1,2\text{-Cy,BMe}_2\text{TC}^H)\text{Fe}=\text{CPh}_2]\text{ 4.9}:$



In a 200 mL Schlenk flask, **4.6** (0.1257 g, 0.2220 mmol, 1 eq.) was dissolved in 45 mL of toluene. To this solution, a toluene solution (5 mL) of diphenyldiazomethane (0.0970 g, 0.4884 mmol, 2.2 eq.) was added. The flask was sealed, removed from the glovebox, and heated in an oil bath at $105\text{ }^\circ\text{C}$ for 14 h. The flask was then cooled, dried under high vacuum, and brought back into the glovebox. The solid was treated with 20 mL of a 9:1 toluene:hexanes solution and filtered over a Celite plug. This was repeated three times more with 10 mL of the solution, until no green color was observed in the filtrate. The filtrate was concentrated to dryness, then 4 mL of CH_3CN was added. The solution was then cooled to $-35\text{ }^\circ\text{C}$ and allowed to settle. The acetonitrile was carefully pipetted off;

this was repeated four times total. The green solid was dried, redissolved in 3 mL of benzene, and lyophilized to yield **4.9** as a dark green powder (0.0984 g, 60.5% yield). Single crystals of **4.9** were grown by layering a concentrated solution of **4.9** in hexanes (1 mL) into acetonitrile (1 mL) at -35 °C, yielding dark green plates. **¹H NMR** (C₆D₆, 599.74 MHz): δ 7.59 (bs, 4H), 7.31 (s, 2H), 7.14 (s, 2H), 7.06 (t, *J* = 7.6 Hz, 2H), 6.73 (t, *J* = 8.0 Hz, 4H), 6.52 (s, 2H), 6.19 (s, 2H), 4.78 (dt, *J* = 11.8 Hz, *J* = 2.8 Hz, 2H), 3.29 (dt, *J* = 11.3 Hz, *J* = 3.7 Hz, 2H), 1.52 (s, 2H), 1.28 (d, *J* = 11.4 Hz, 2H), 1.22 (d, *J* = 12.4, 2H), 1.14 (d, *J* = 5.7 Hz, 2H), 1.06 (dq, *J* = 12.7 Hz, *J* = 3.0 Hz), 0.83 (s, 6H), 0.86 – 0.70 (m, 6H), 0.26 (s, 6H). **¹³C NMR** (C₆D₆, 149.94 MHz): δ 309.30, 188.82, 172.37, 160.34, 128.34, 126.29, 123.89, 123.85, 123.35, 123.28, 121.65, 114.83, 114.77, 65.66, 53.45, 53.40, 36.13, 30.66, 24.78, 24.37, 18.83, 13.02. **IR**: 3136, 2932, 2162, 2036, 1979, 1569, 1438, 1401, 1351, 1286, 1267, 1236, 1208, 1158, 1121, 1069, 1048, 946, 881, 852, 825, 797, 769, 729, 686, 638 cm⁻¹. **DART HRMS**: [M+H]⁺: 733.37506 (found), [C₄₁H₅₁B₂FeN₈]: 733.37722 (calculated). **UV-Vis** (THF): 420 nm (11000 L/cm²*mol), 635 nm (350 L/ cm²*mol), 745 nm (120 L/ cm²*mol). **CHN**: Calculated for C₄₁H₅₀B₂FeN₈: C: 67.24, H: 6.88, N: 15.30. Found: C: 66.91, H: 6.90, N: 15.22.

Catalytic Synthesis of **4.11**:



A solution of 2-methylallyl 2-diazo-2-phenylacetate (**4.10**) (0.1106 g, 0.5115 mmol, 1 eq.) in 4 mL of acetonitrile was added to **4.6** (0.0281 g, 0.496 mmol, 0.1 eq.) in a 20 mL

scintillation vial. The solution immediately turned dark green, then was heated at 45 °C for 12 h, during which the dark green color turned to yellow-orange. The solution was then concentrated under reduced pressure and the product was purified by silica gel flash chromatography with 9:1 hexanes:ethyl acetate to yield **4.11** as a tan-yellow solid (0.0837, 81.4%). Control reaction of **4.10** without **4.6** in CH₃CN showed no formation of **4.11** after 16 hours at 45 °C. **¹H NMR** (CDCl₃, 499.74 MHz): δ 7.80 (dd, *J* = 8.1 Hz, *J* = 1.3 Hz, 4H), 7.50 (tt, *J* = 8.4 Hz, *J* = 0.8 Hz, 2H), 7.43 (t, *J* = 7.8 Hz, 4H), 5.13 (s, 2H), 4.99 (s, 2H), 4.86 (s, 4H), 1.79 (s, 6H). **¹³C NMR** (CDCl₃, 149.94 MHz): δ 165.14, 162.30, 139.33, 132.17, 131.33, 128.87, 128.24, 128.20, 114.76, 68.87, 19.83. **IR**: 2922, 1727, 1656, 1605, 1574, 1495, 1446, 1366, 1325, 1303, 1198, 1178, 1157, 1073, 1033, 1012, 964, 919, 908, 863, 840, 811, 778, 746, 719, 682 cm⁻¹. **DART HRMS**: [M+H]⁺: 405.18192 (found); [C₂₄H₂₅N₂O₄]⁺: 405.18088 (calculated).

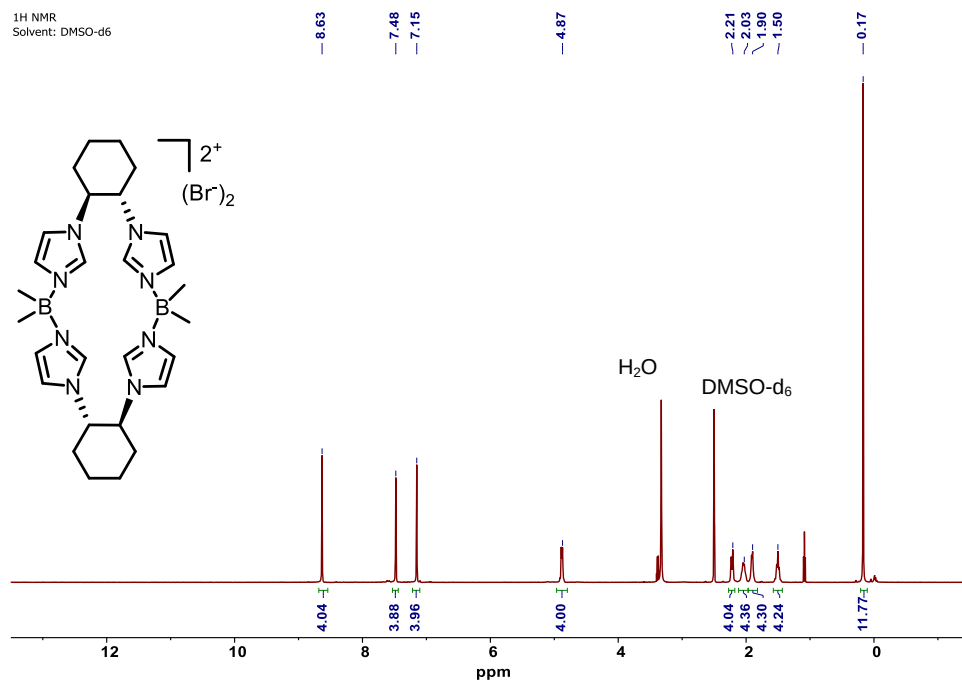
Table 4.1: Crystallographic data for complexes **4.4-4.9**.

Molecule	4	5	6	7	8	9
Empirical formula	C ₁₄ H ₂₂ BBrN ₄	C ₂₈ H ₄₀ B ₂ N ₈ Pd	C ₂₈ H ₄₀ B ₂ FeN ₈ , C ₆ H ₆	C ₅₆ H ₈₀ B ₄ Fe ₂ N ₁₆ O, C ₆ H ₆	C ₄₁ H ₅₀ B ₂ FeN ₁₀	C ₄₁ H ₅₀ B ₂ FeN ₈ , C ₂ H ₃ N
Color	Colorless	Colorless	Yellow	Red	Red	Green
Formula Weight	337.07	616.7	644.26	1226.4	760.38	773.41
Source, λ (Å)	Cu, 1.54178	Mo, 0.71073	Mo, 0.7103	Mo, 0.71073	Mo, 0.71073	Mo, 0.71073
Crystal System	Tetragonal	Monoclinic	Orthorhombic	Orthorhombic	Orthorhombic	Orthorhombic
Space group	I4 ₁ 22	P2 ₁	P2 ₁ 2 ₁ 2 ₁	P2 ₁ 2 ₁ 2 ₁	P2 ₁ 2 ₁ 2 ₁	P2 ₁ 2 ₁ 2 ₁
T(K)	100(2)	100(2)	100(2)	100(2)	100(2)	100(2)
a (Å)	15.7206(16)	21.2621(10)	13.8984(3)	12.5497(13)	15.5943(14)	11.266(4)
b (Å)	15.7206(16)	18.5788(9)	14.9407(3)	13.4906(13)	17.0596(16)	13.314(4)
c (Å)	24.616(3)	22.9415(11)	15.9817(3)	36.309(4)	29.618(2)	26.872(8)
α (°)	90	90	90	90	90	90
β (°)	90	116.0270(10)	90	90	90	90
γ (°)	90	90	90	90	90	90
V (Å ³)	6083.5(15)	8143.4(7)	3318.63(12)	6147.3(11)	7879.4(12)	4031(2)
Z	8	8	4	4	8	4
d _{calc} (g cm ⁻³)	0.736	1.006	1.289	1.325	1.282	1.274
μ (mm ⁻¹)	1.816	0.479	0.492	0.528	0.427	0.417
R ₁ /wR ₂	0.0324/0.0957	0.0367/0.0853	0.0321/0.0855	0.0534/0.1199	0.0604/0.1172	0.0530/0.1052
Flack Par.	< 0	0.000(12)	< 0	0.009(6)	0.023(10)	0.017(9)
Indep. Refl.	2983	54143	11057	20489	19374	9934

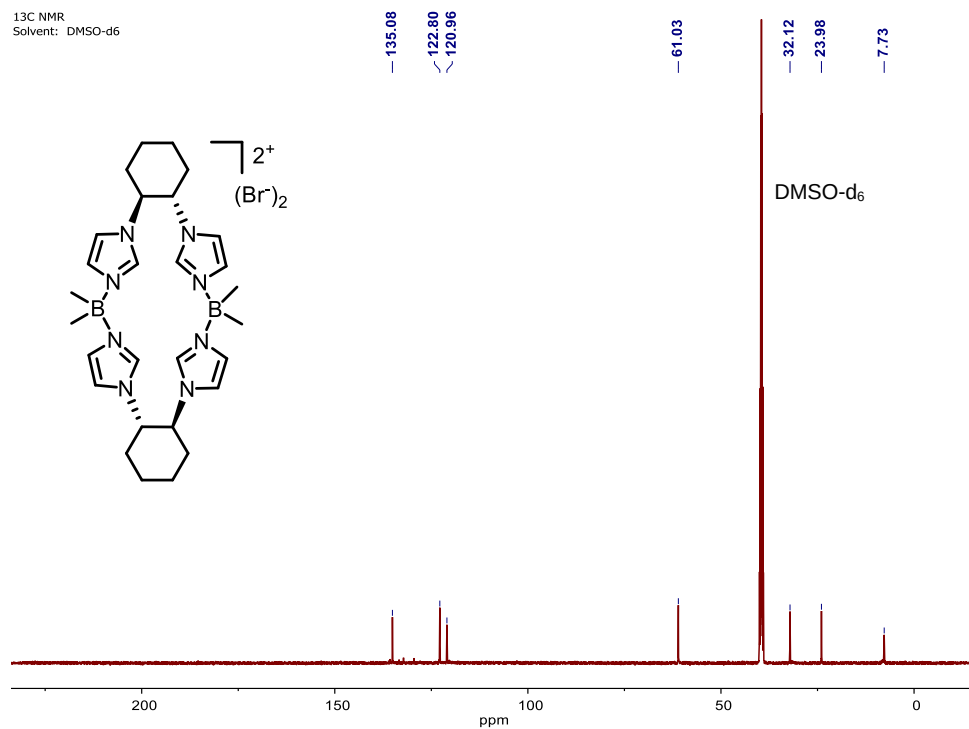
Table 4.2: Selected bond lengths and angles for compounds **4.6** – **4.9**. Note: **8_1** and **8_2** refer to the different residues in the asymmetric unit for **8**. These molecules are stereoisomers of one another due to free rotation on the bond of N₁₀.

	4.6	4.7	4.8	4.8_2	4.9
Bond Lengths (Å)					
Fe-C ₁	2.0057(15)	2.070(3)	2.023(5)	2.019(5)	2.013(4)
Fe-C ₂	1.9385(14)	2.017(3)	1.986(5)	1.990(5)	1.977(3)
Fe-C ₃	2.0049(14)	2.068(3)	2.044(5)	2.032(5)	2.020(3)
Fe-C ₄	2.0057(15)	2.014(3)	1.980(5)	1.978(5)	1.969(4)
Fe ₁ -O		1.816(2)			
Fe ₂ -O		1.816(2)			
Fe=N ₉			1.767(4)	1.779(4)	
N ₉ =N ₁₀			1.217(5)	1.215(5)	
N ₁₀ =C ₂₉			1.345(6)	1.327(6)	
C ₂₉ -C ₃₀			1.459(7)	1.477(8)	1.508(5)
C ₂₉ -C ₃₆			1.466(7)	1.471(7)	1.490(5)
Fe-C ₂₉					1.814(4)
Bond Angles (°)					
C ₁ -Fe-C ₂	91.50(6)	84.252	84.9(2)	85.9(2)	86.82(14)
C ₁ -Fe-C ₃	166.64(6)	142.387	143.6(2)	148.5(2)	153.98(15)
C ₁ -Fe-C ₄	87.73(6)	86.295	88.5(2)	87.5(2)	89.00(16)
C ₂ -Fe-C ₃	88.33(6)	86.634	86.7(2)	85.7(2)	88.69(14)
C ₂ -Fe-C ₄	174.87(7)	152.053	156.2(2)	152.6(2)	162.67(16)
C ₃ -Fe-C ₄	91.25(6)	84.961	85.1(2)	86.2(2)	87.71(15)
Fe ₁ -O-Fe ₂		177.334			
Fe=N ₉ =N ₁₀			173.8(4)	174.5(4)	
N ₉ =N ₁₀ =C ₂₉			138.1(4)	140.4(5)	
C ₃₀ -C ₂₉ -C ₃₆			124.0(5)	123.8(5)	114.4(3)
Fe-C ₂₉ -C ₃₀					123.3(3)
τ_4 or τ_5	0.14	0.13	0.22	0.07	0.14

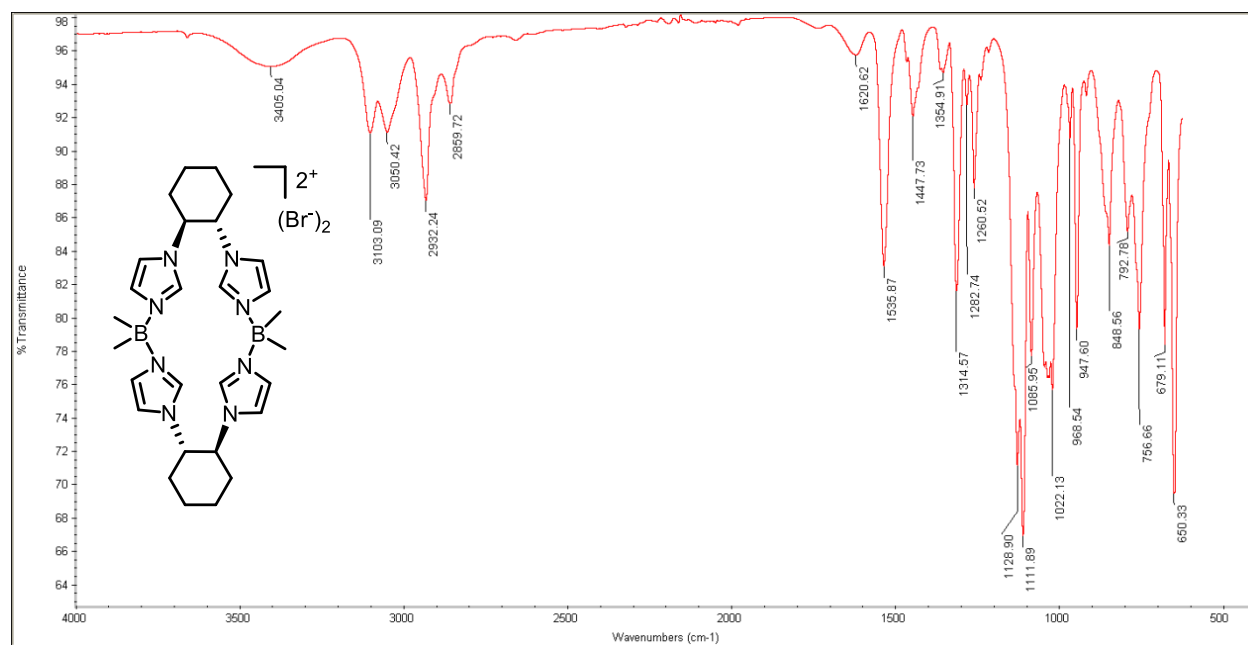
Selected Spectral Characterization:



Spectrum 4.1: ¹H NMR of **2.4** in DMSO-d₆.

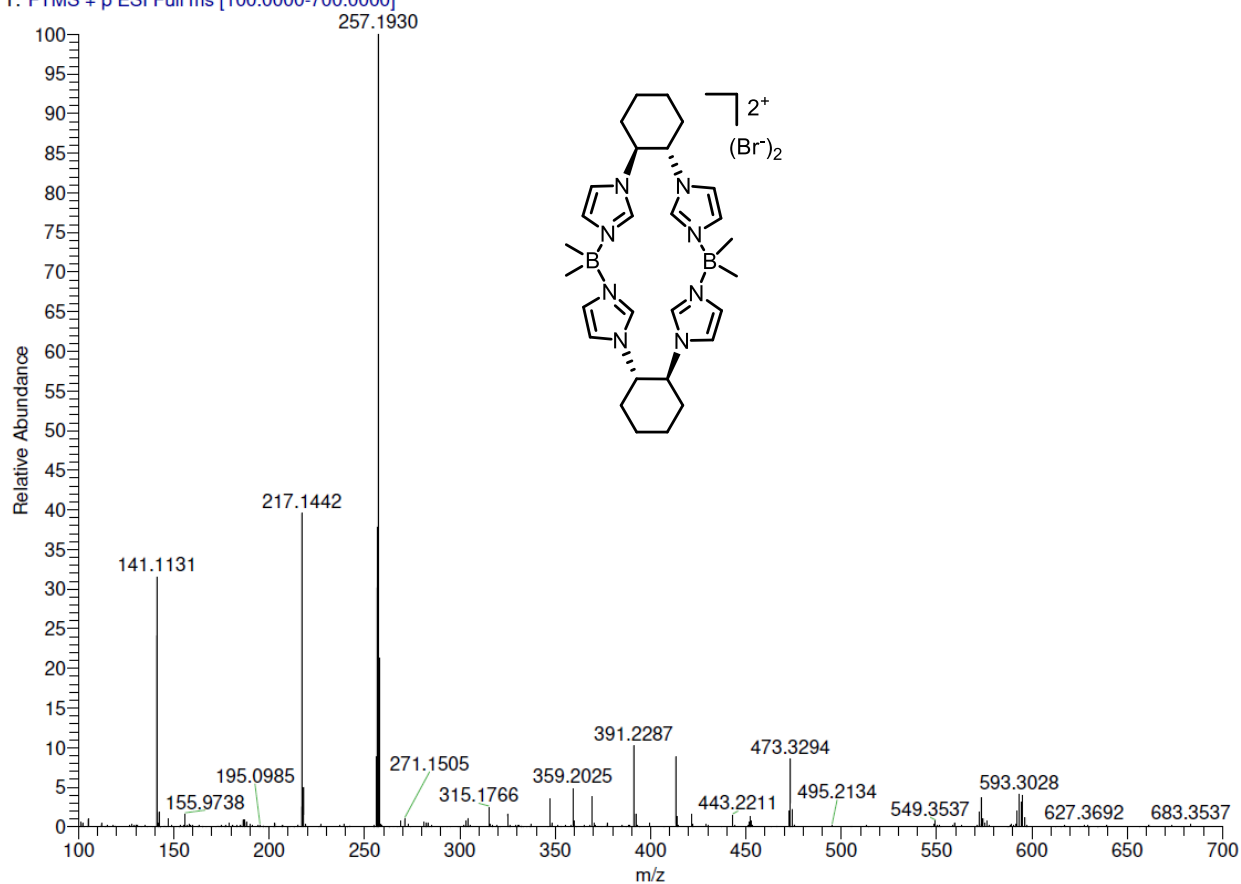


Spectrum 4.2: ¹³C NMR of **2.4** in DMSO-d₆.



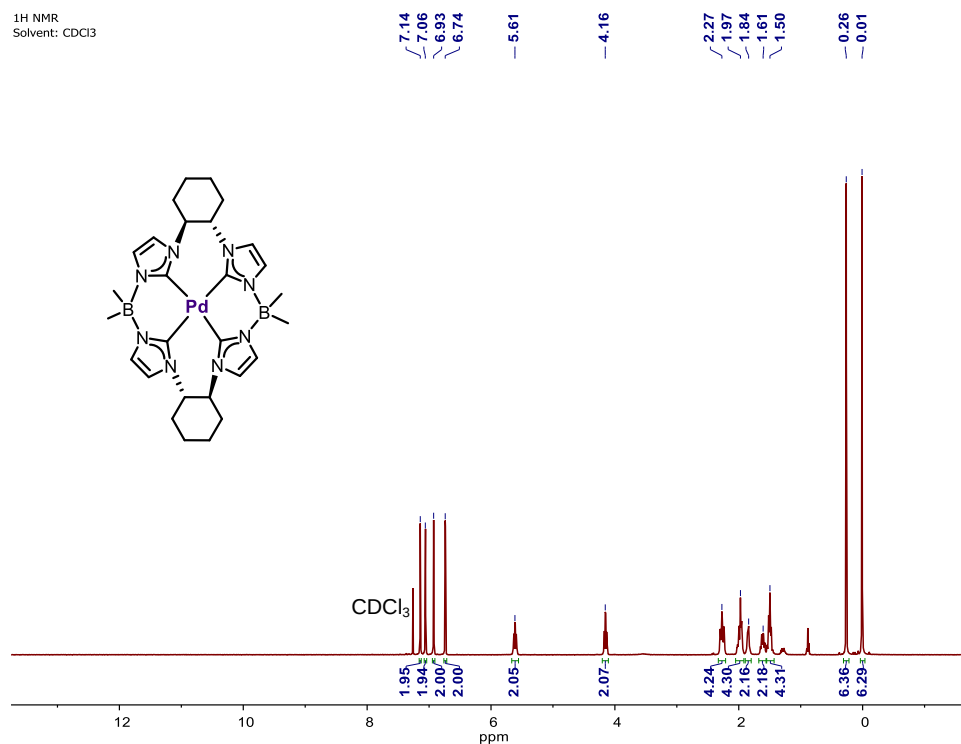
Spectrum 4.3: IR of 4.4.

2019_01_25_JD_6_17_2#35 RT: 0.99 AV: 1 NL: 1.25E9
T: FTMS + p ESI Full ms [100.0000-700.0000]



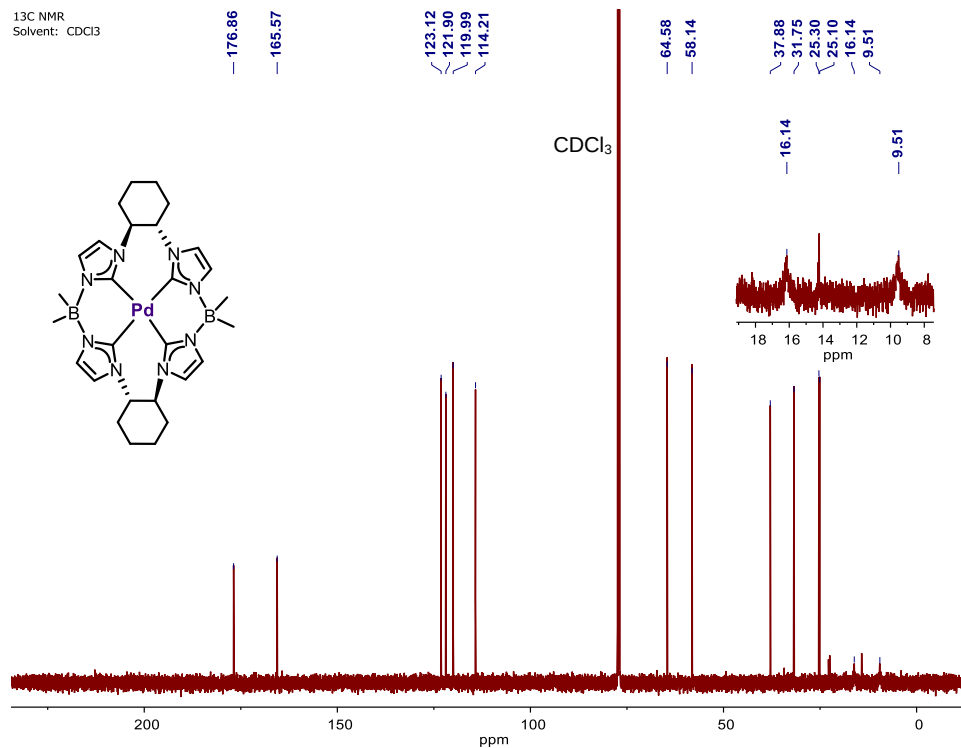
Spectrum 4.4: ESI HR MS of 4.4.

¹H NMR
Solvent: CDCl₃

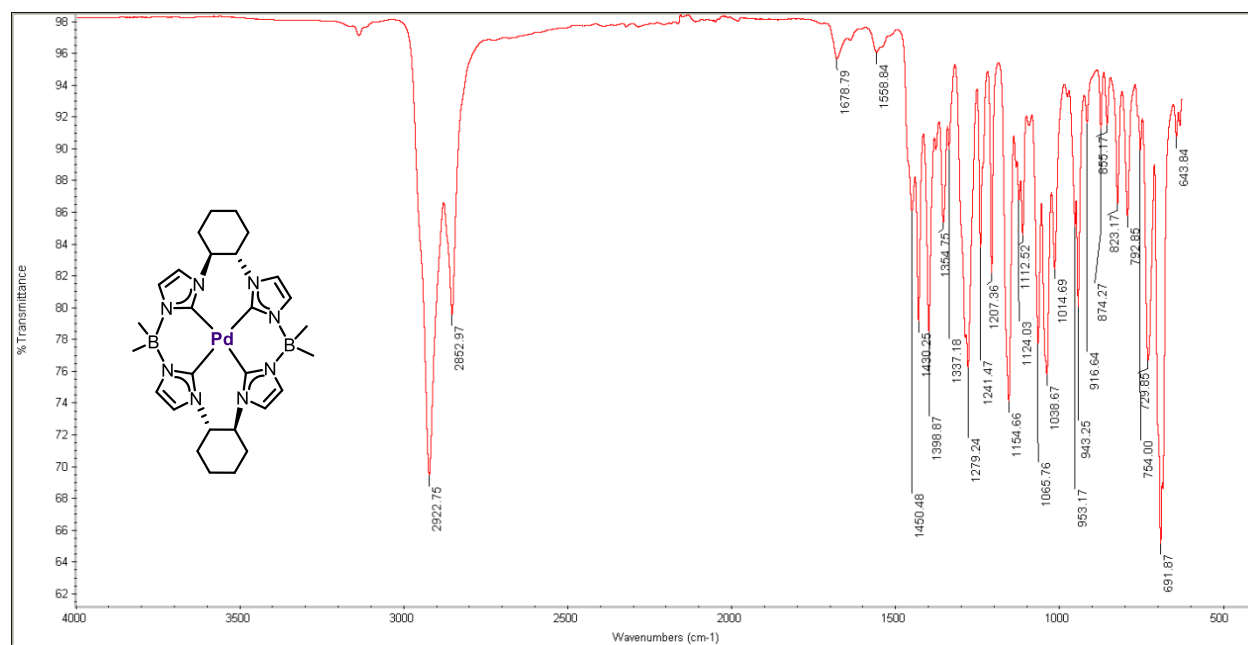


Spectrum 4.5: ¹H NMR of 4.5 in CDCl₃.

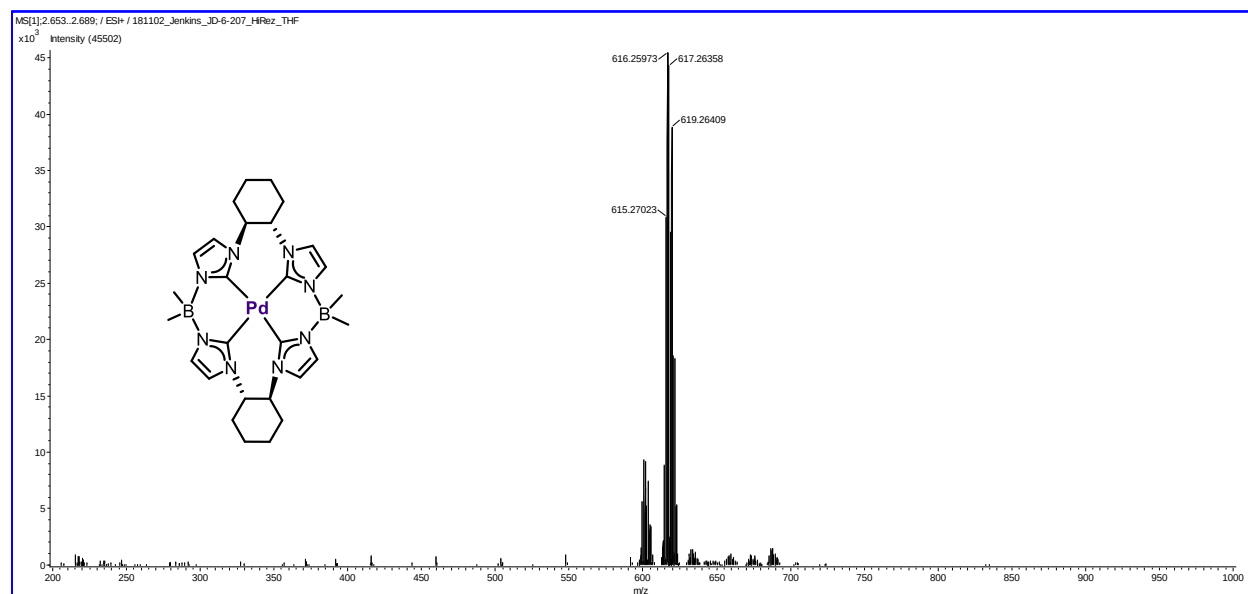
¹³C NMR
Solvent: CDCl₃



Spectrum 4.6: ¹³C NMR of 4.5 in CDCl₃.

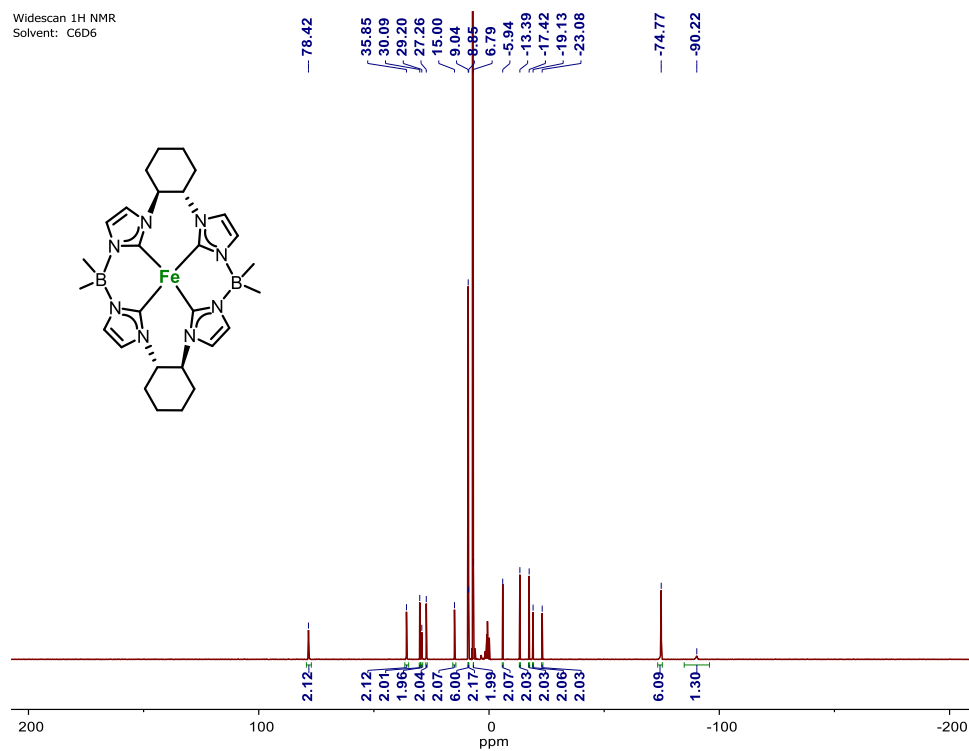


Spectrum 4.7: IR of 4.5.



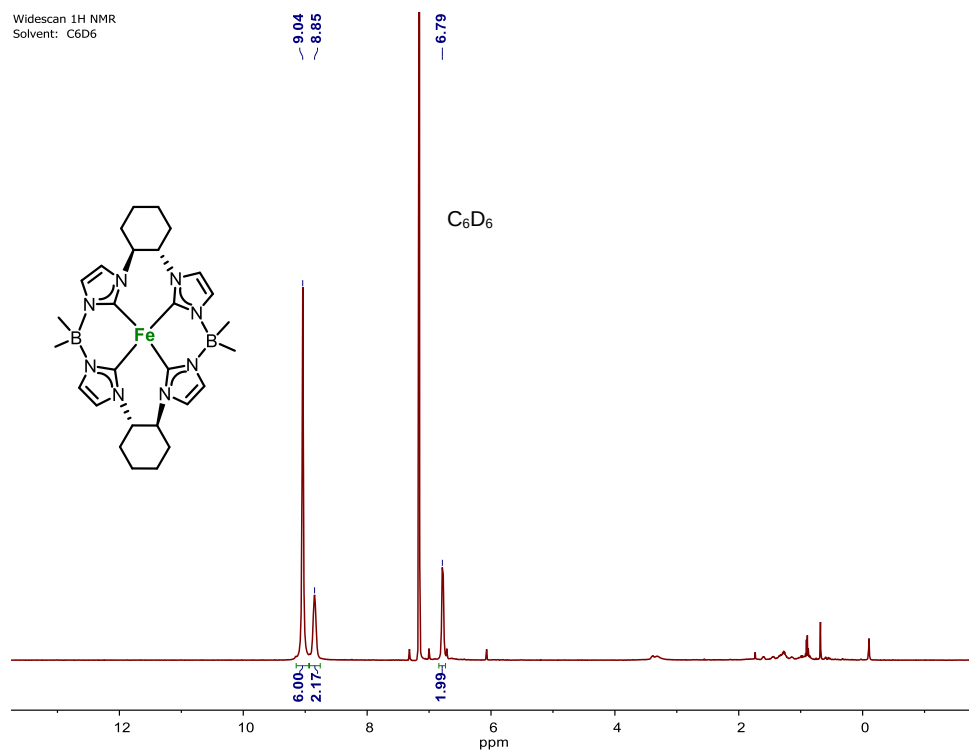
Spectrum 4.8: DART HR MS of 4.6

Widescan 1H NMR
Solvent: C6D6



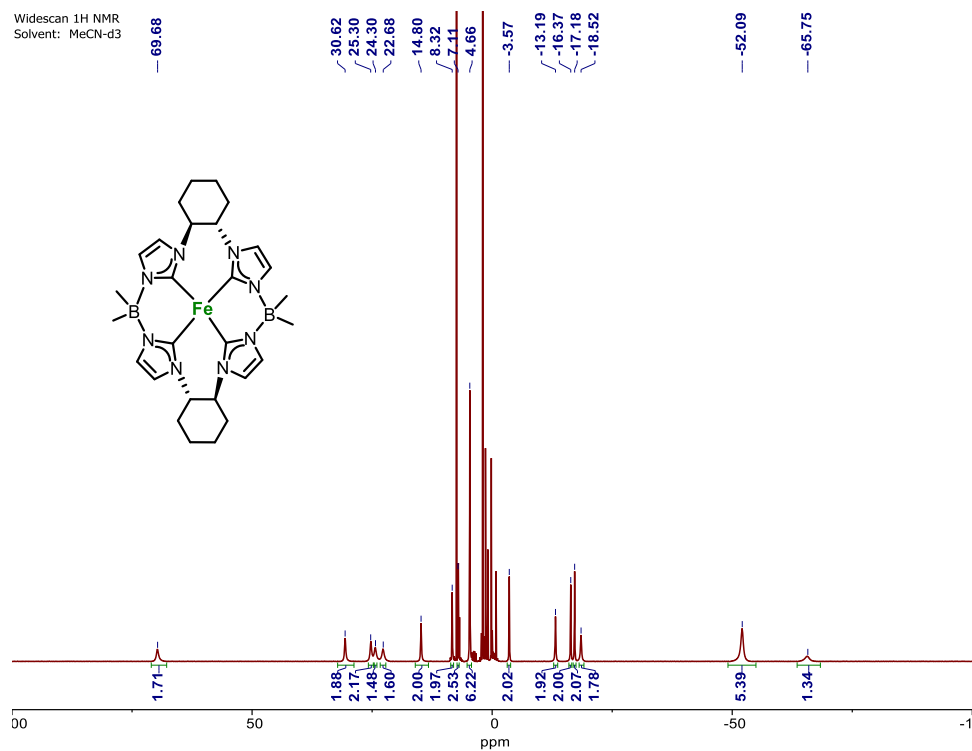
Spectrum 4.9: Widescan paramagnetic ^1H NMR of **4.6**.

Widescan 1H NMR
Solvent: C6D6

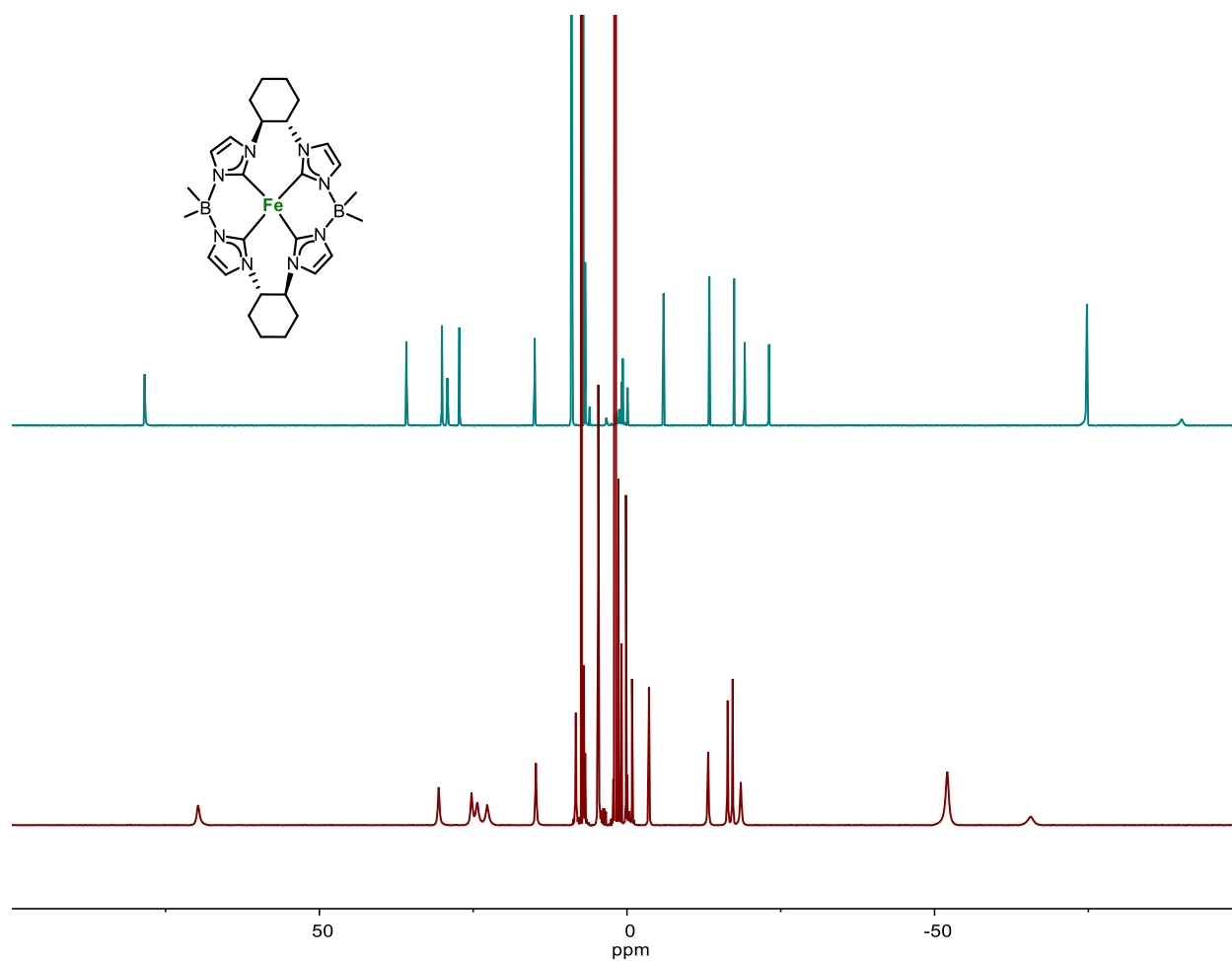


Spectrum 4.10: Expansion of diamagnetic region for **4.6**.

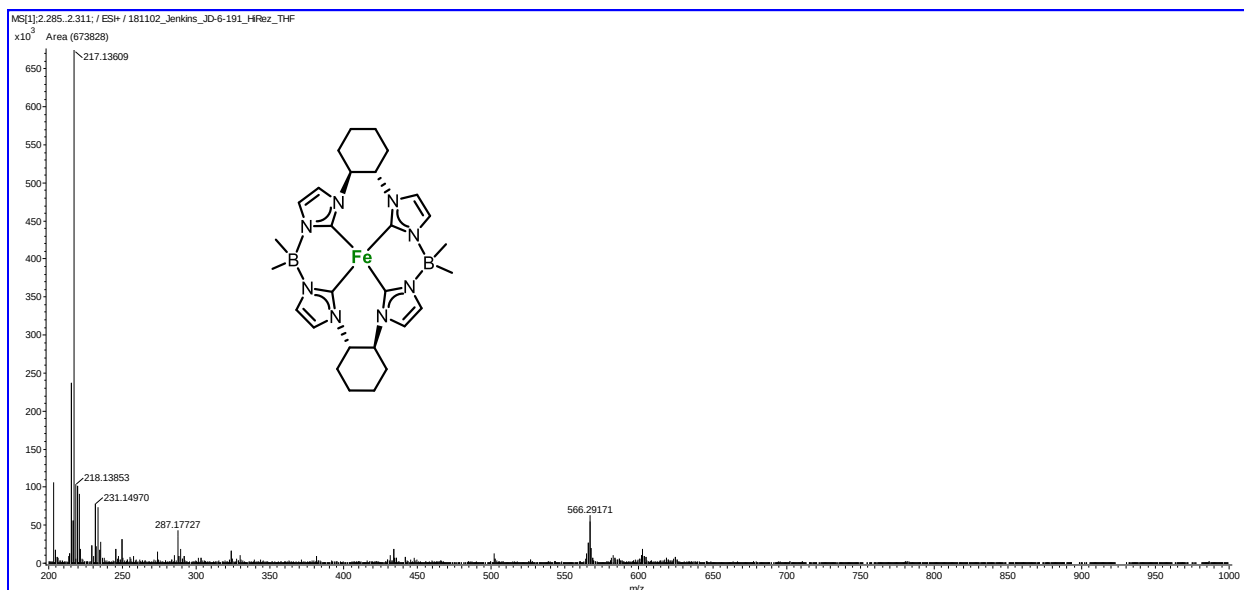
Widescan ^1H NMR
Solvent: MeCN-d_3



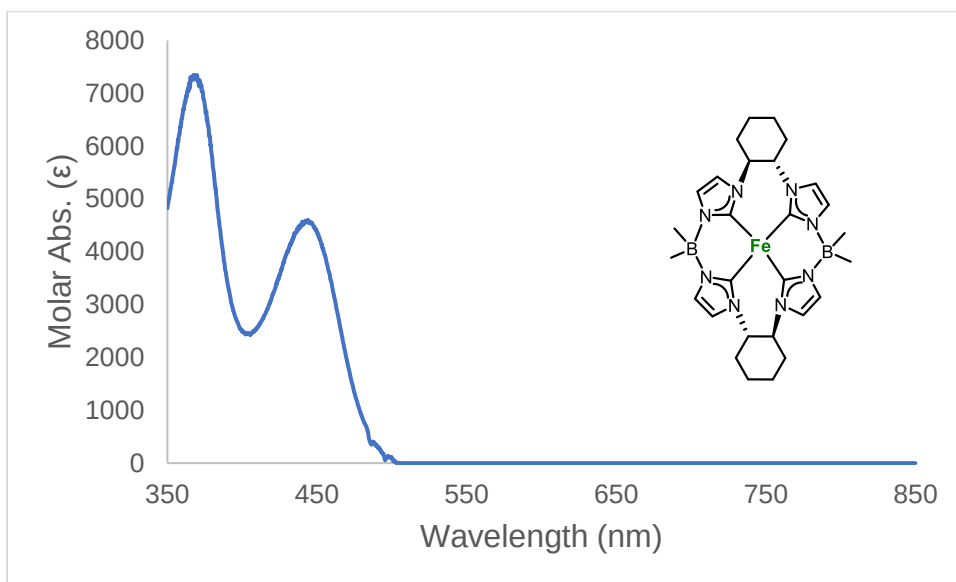
Spectrum 4.11: Widescan paramagnetic ^1H NMR of **4.6** in CD_3CN .



Spectrum 4.12: Stacked Widescan ¹H NMR Spectra of **4.6** in C₆D₆ (top, teal) and CD₃CN (bottom, red).

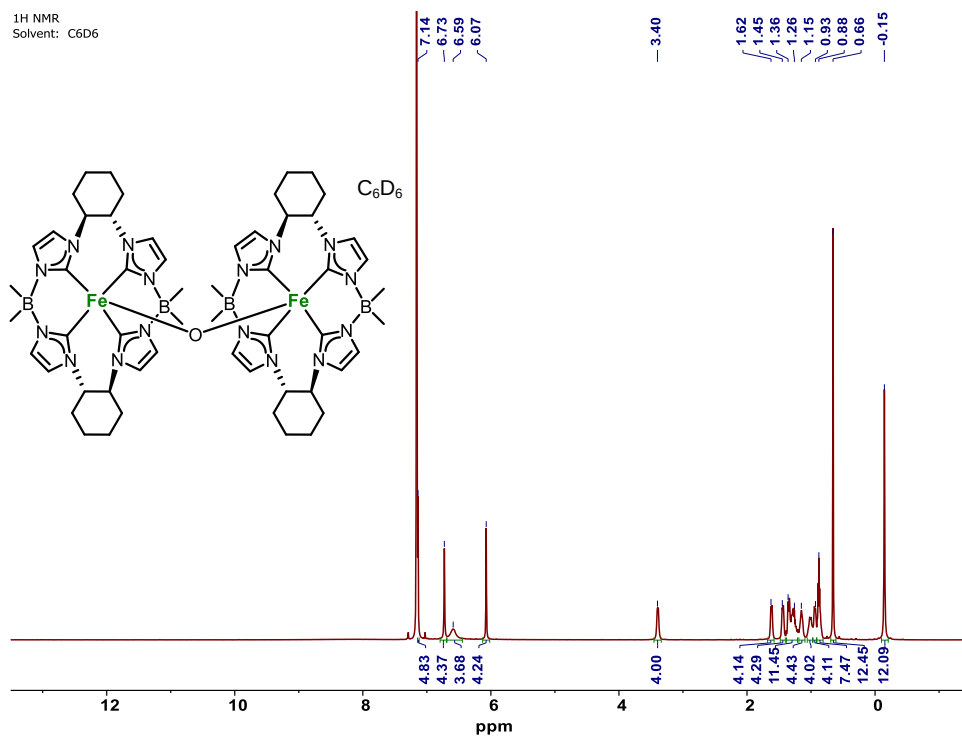


Spectrum 4.13: DART HR MS of **4.6**.



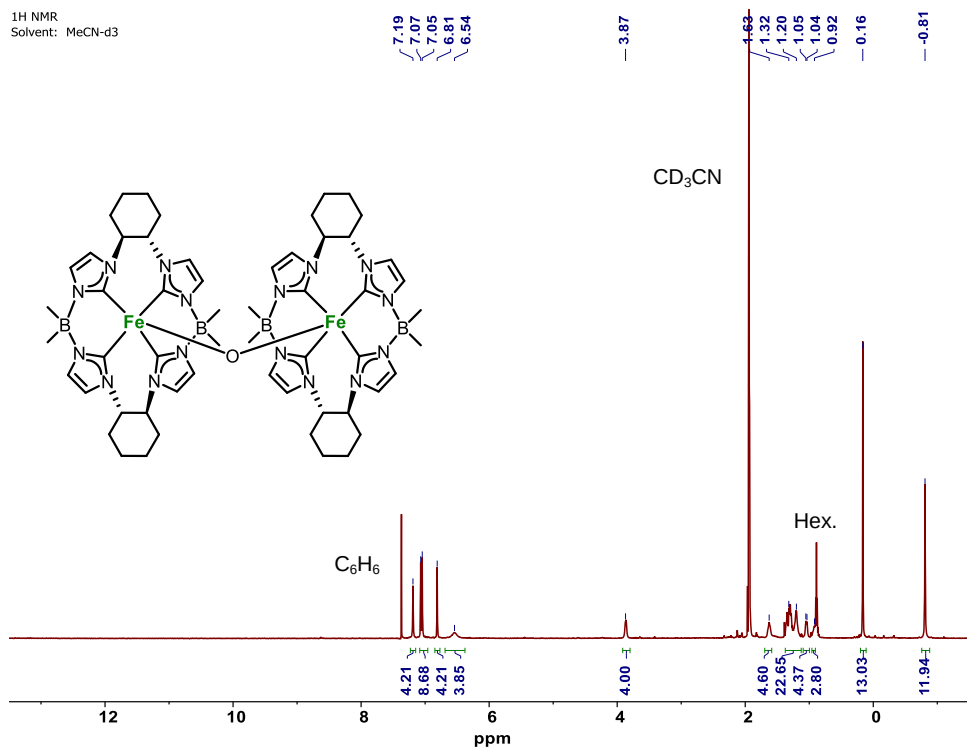
Spectrum 4.14: UV-Vis spectrum of **4.6** in THF.

¹H NMR
Solvent: C₆D₆

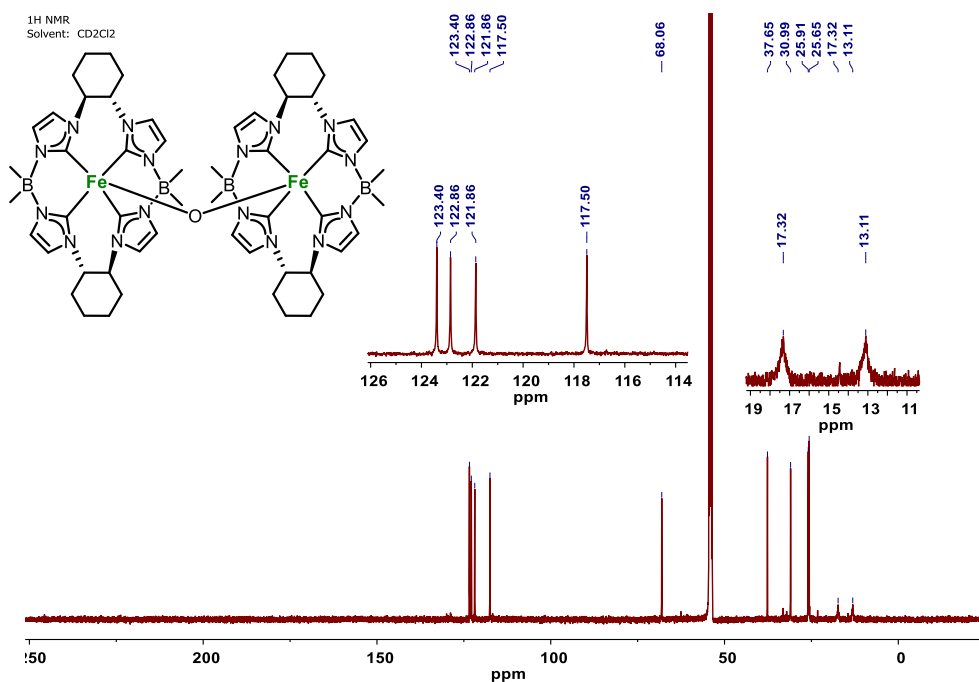


Spectrum 4.15: ¹H NMR of 4.7 in C₆D₆.

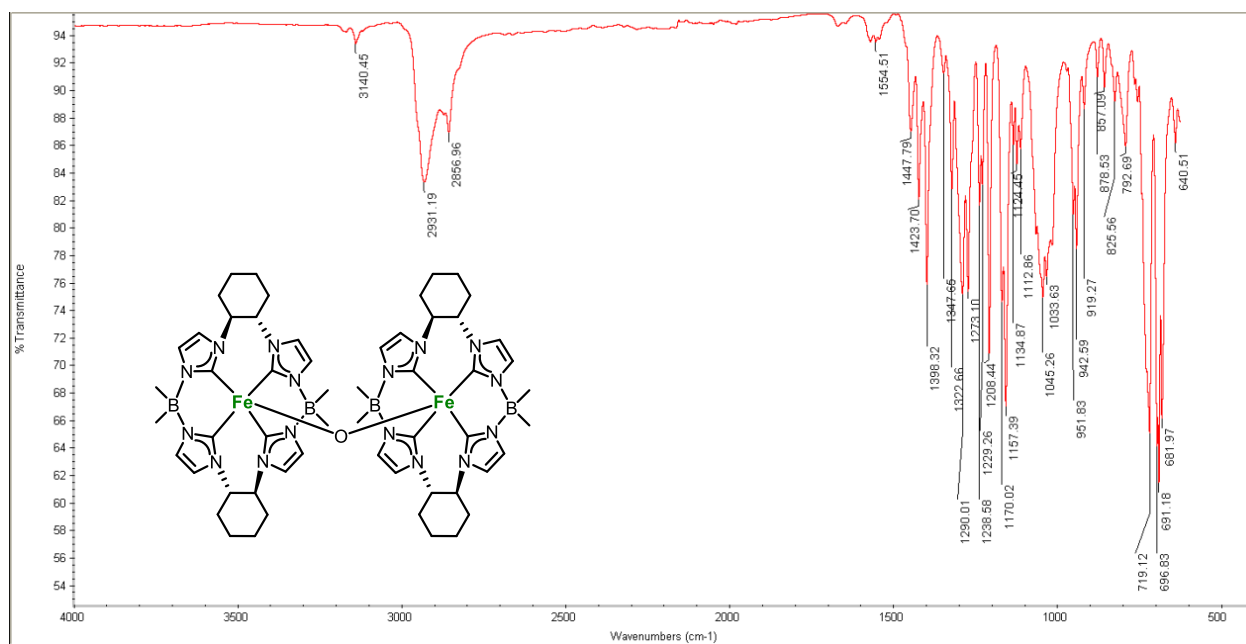
¹H NMR
Solvent: MeCN-d₃



Spectrum 4.16: ¹H NMR of 4.7 in CD₃CN.

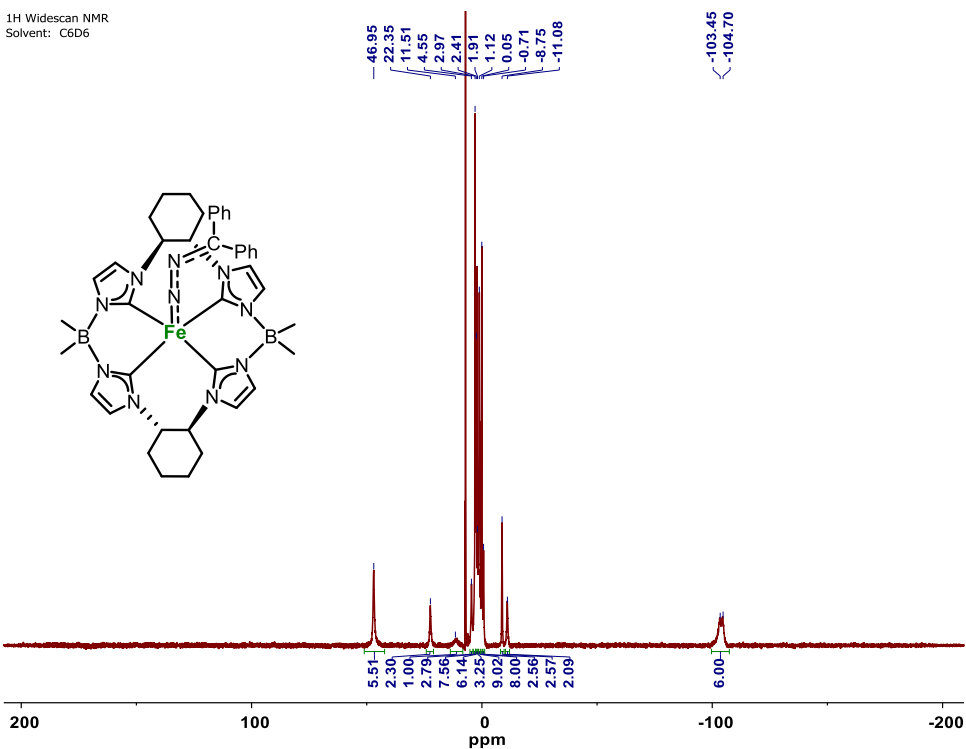


Spectrum 4.17: ¹³C NMR of 4.7 in CD₂Cl₂.



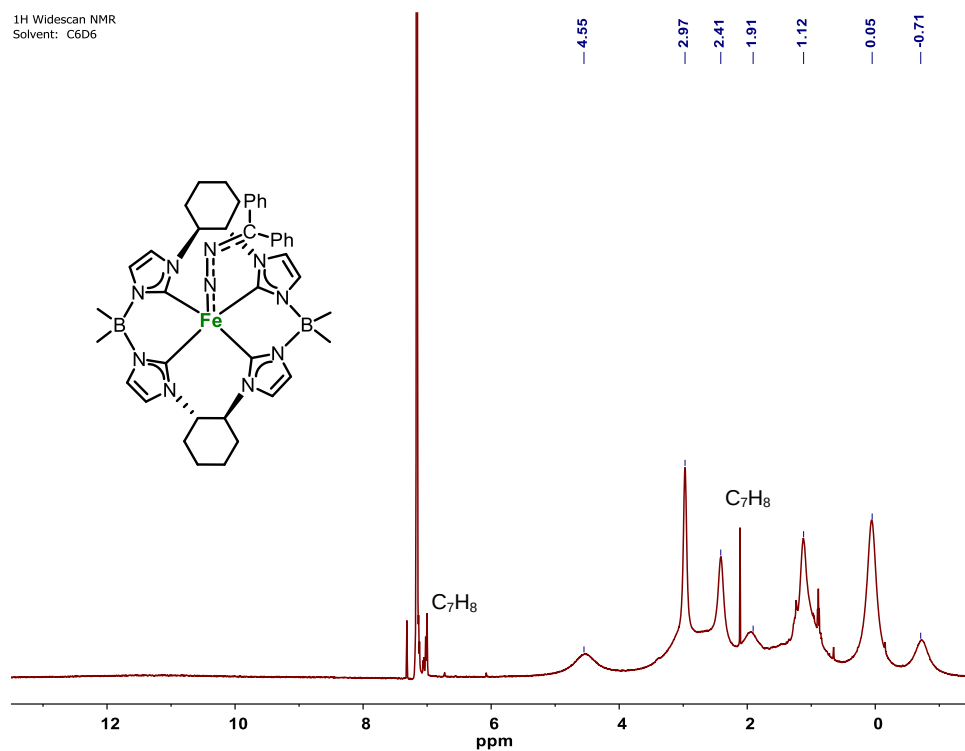
Spectrum 4.18: IR of 4.7.

¹H Widescan NMR
Solvent: C₆D₆

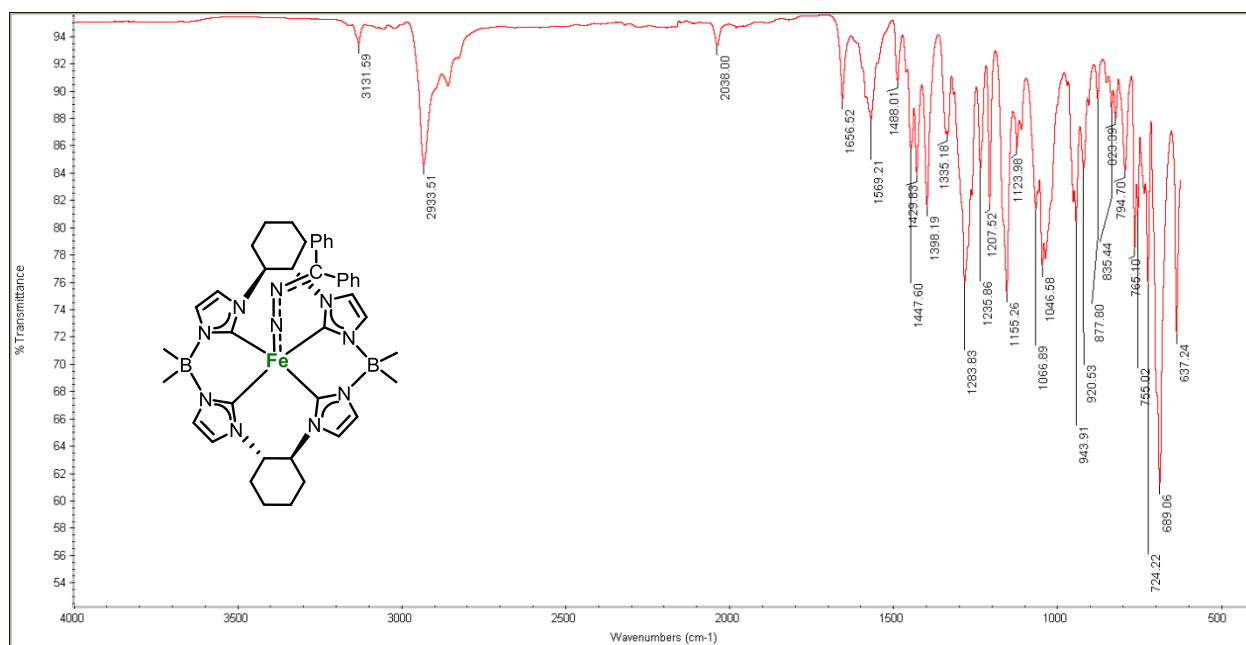


Spectrum 4.19: Widescan ¹H NMR for **4.8** in C₆D₆.

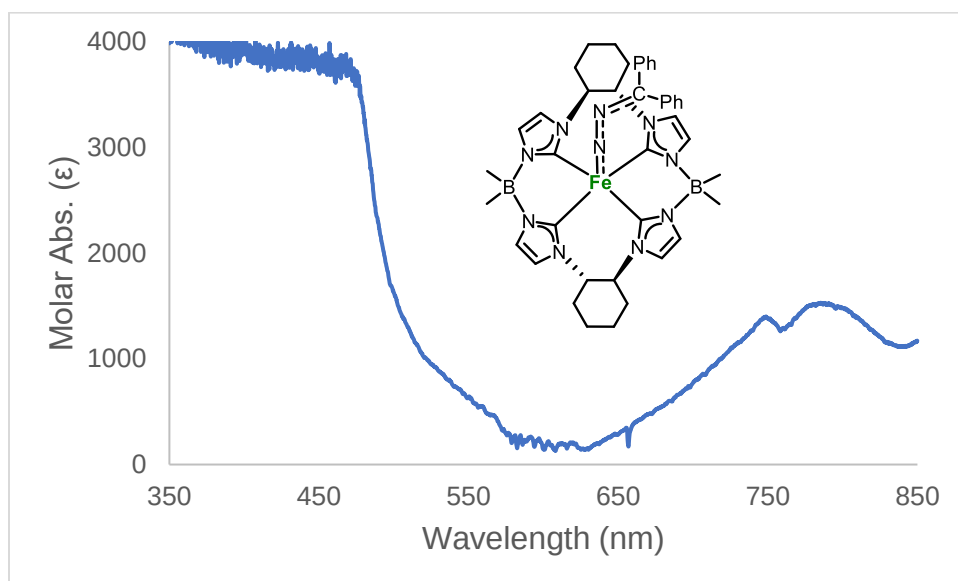
¹H Widescan NMR
Solvent: C₆D₆



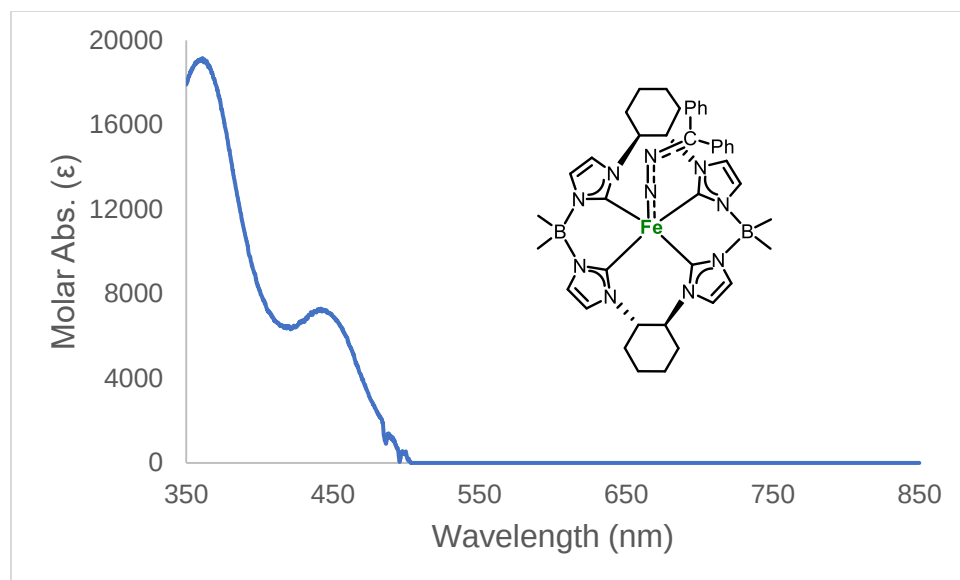
Spectrum 4.20: Expansion of Diamagnetic Region for **4.8** in C₆D₆.



Spectrum 4.21: IR of 4.8.

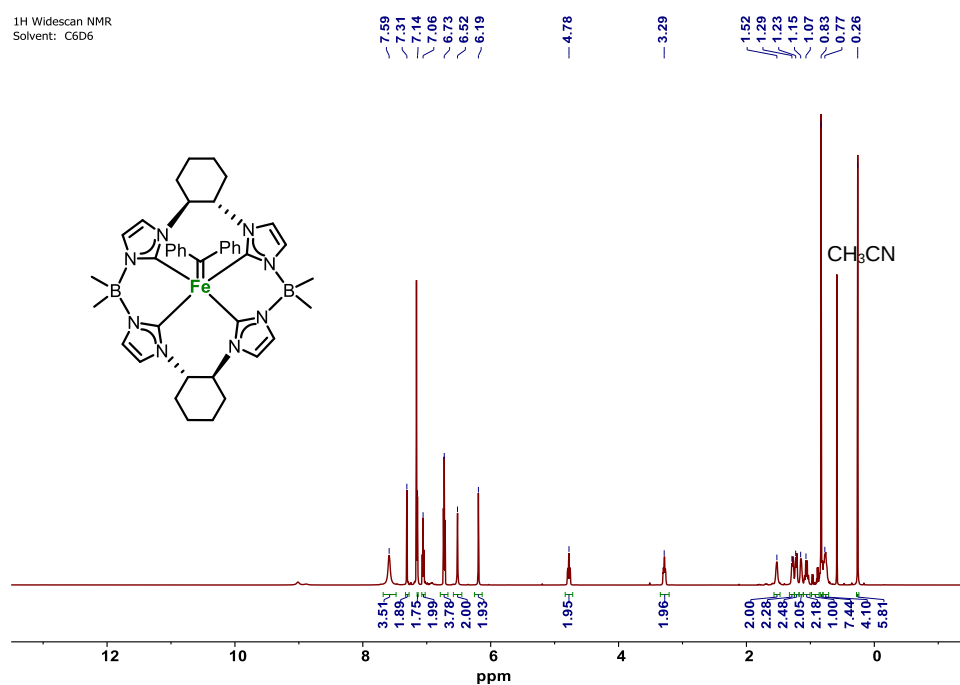


Spectrum 4.22: Concentrated (5.92×10^{-4} M) UV-Vis Spectrum in THF for 4.8.

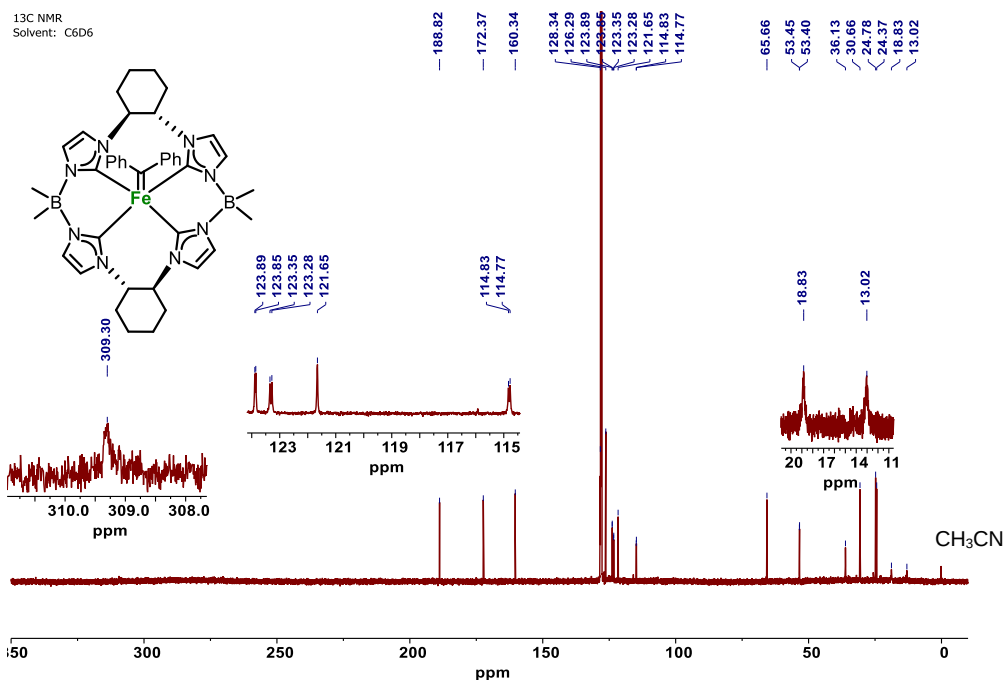


Spectrum 4.23: Dilute (4.384×10^{-5} M) UV-Vis Spectrum in THF for **4.8**.

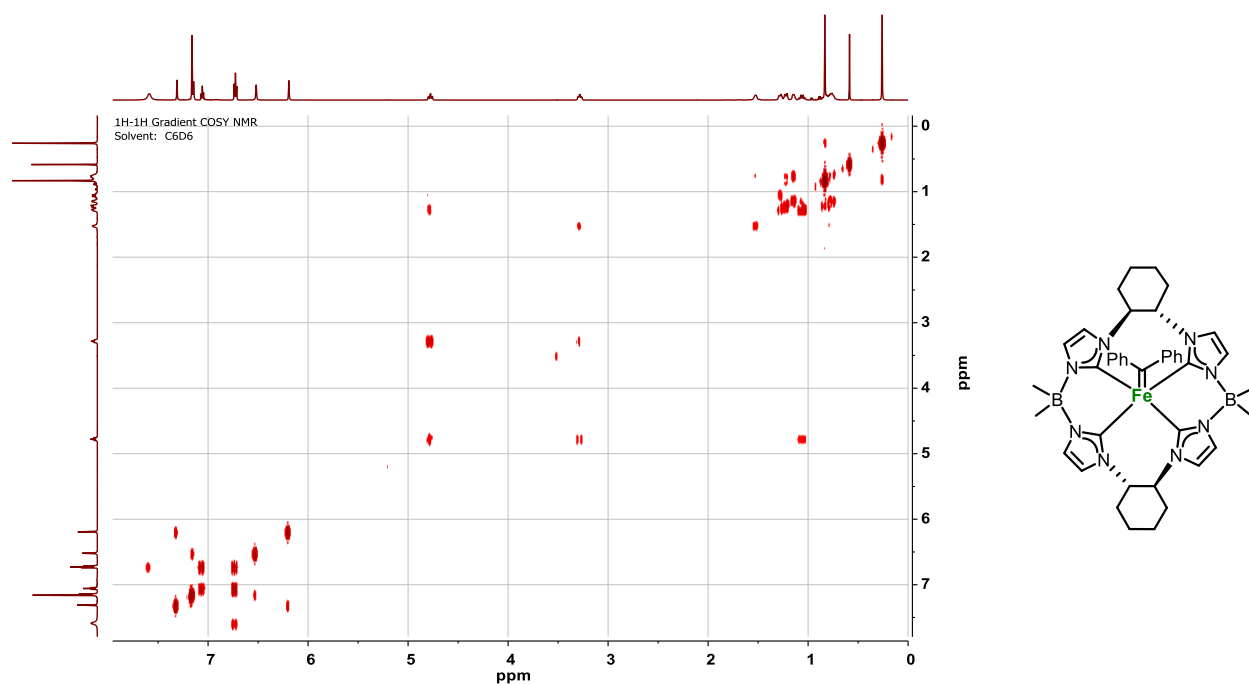
¹H Widescan NMR
Solvent: C₆D₆



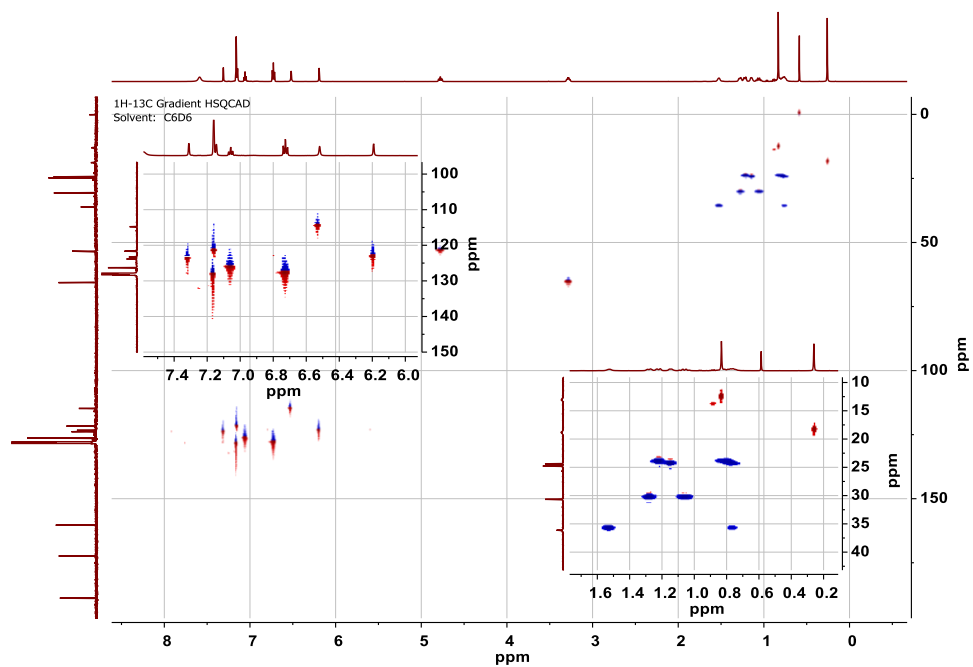
Spectrum 4.24: ¹H NMR of **4.9** in C₆D₆.



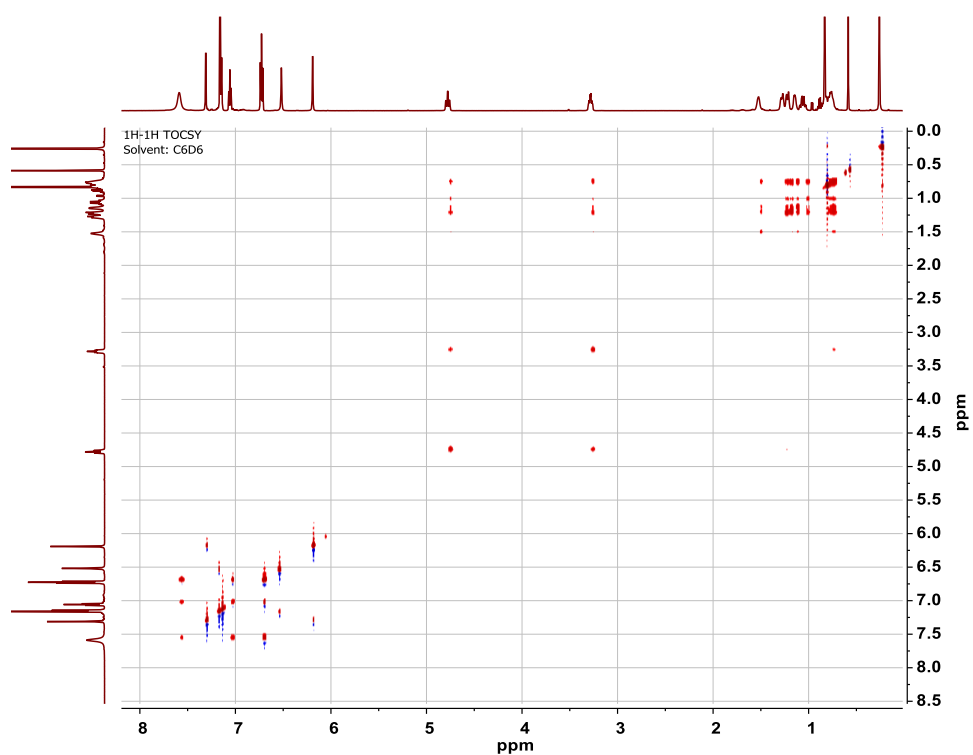
Spectrum 4.25: ¹³C NMR of **4.9** in C₆D₆. Insert of signal at 309.30 ppm is from ¹³C spectrum ran at 5 second relaxation delay.



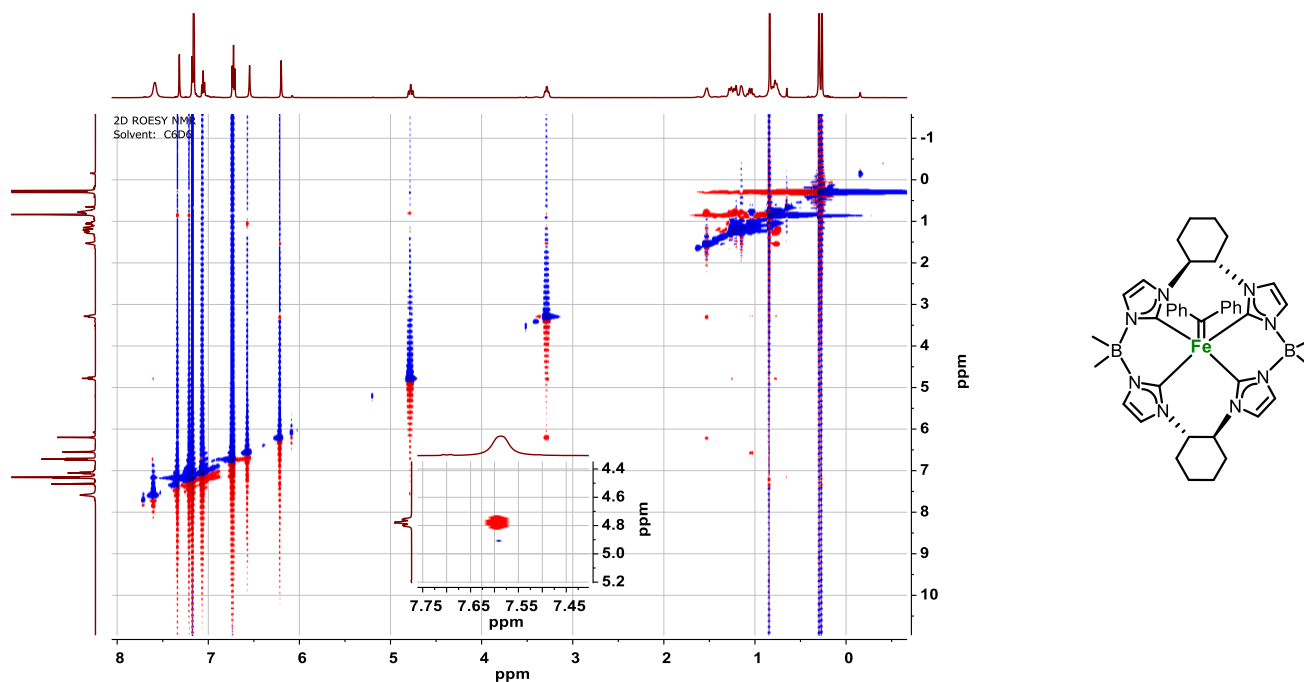
Spectrum 4.26: ¹H-¹H COSY Spectrum of **4.9** in C₆D₆.



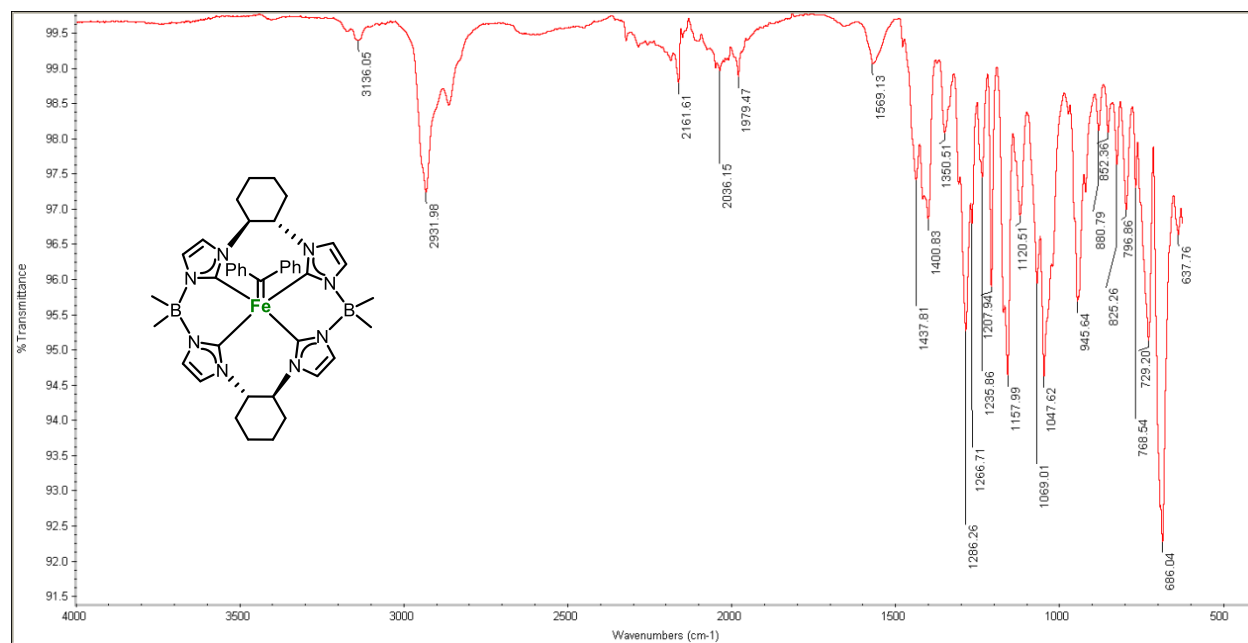
Spectrum 4.27: ^1H - ^{13}C HSQC Spectrum of **4.9** in C_6D_6 .



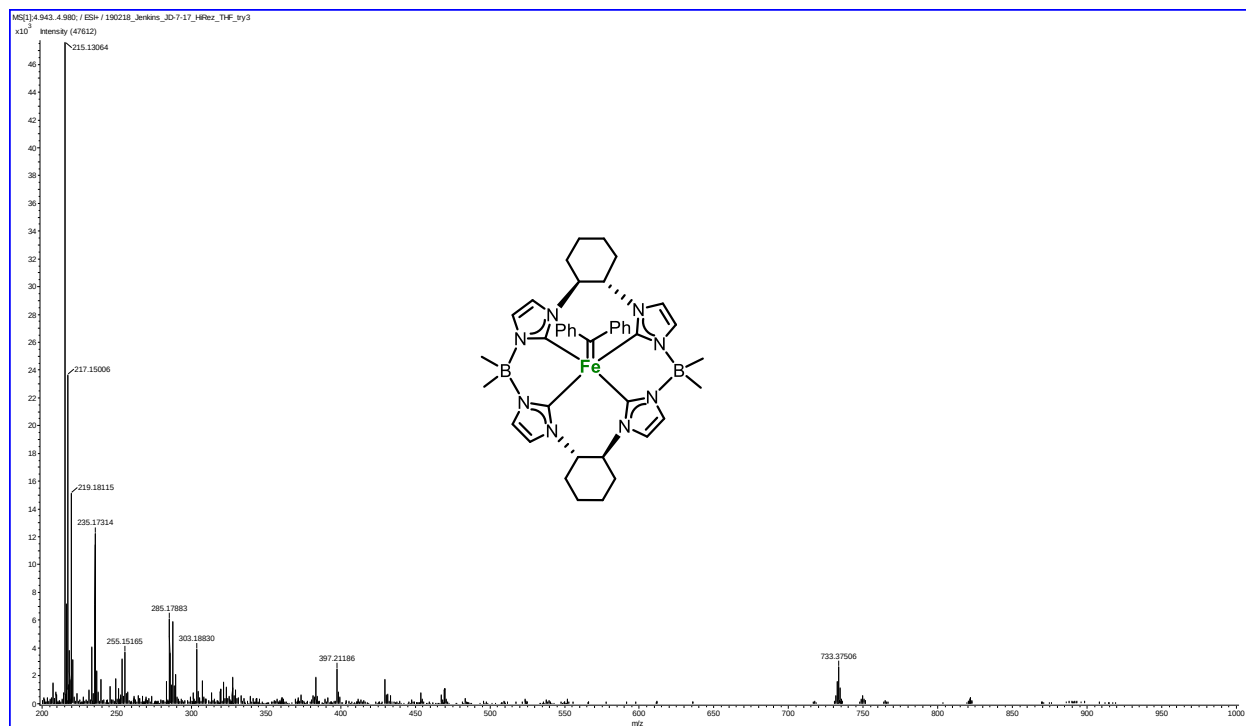
Spectrum 4.28: ^1H - ^1H TOCSY Spectrum of **4.9** in C_6D_6 .



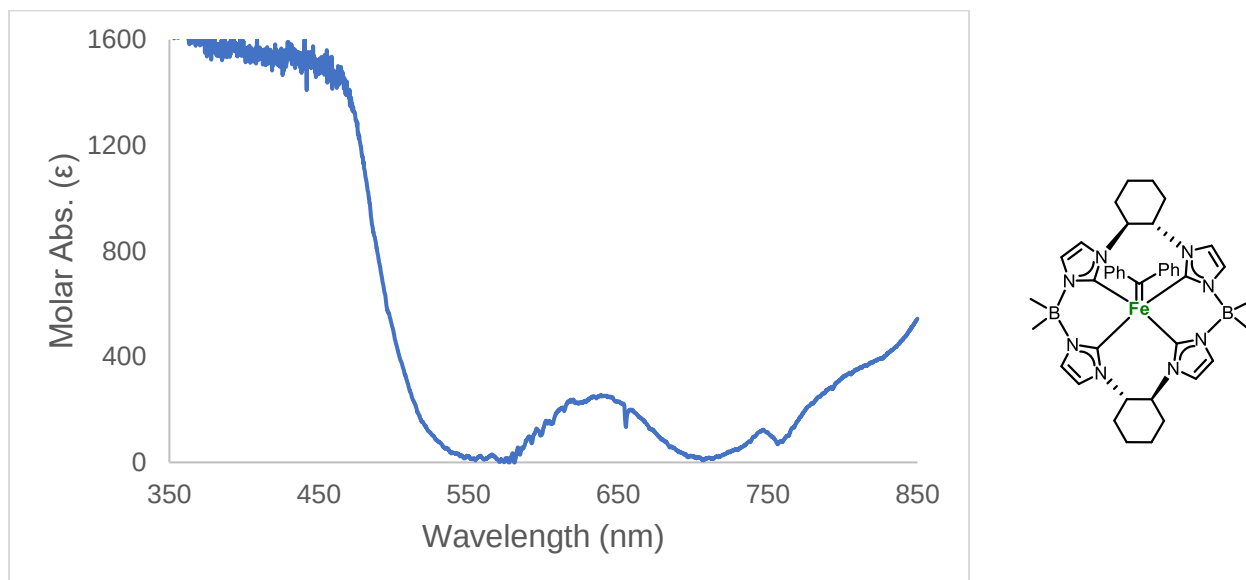
Spectrum 4.29: 2D-ROESY NMR Spectrum of **4.9** in C_6D_6 . Expanded region shows the crosspeak of the ortho C-H to the chiral C-H bond over the Fe center.



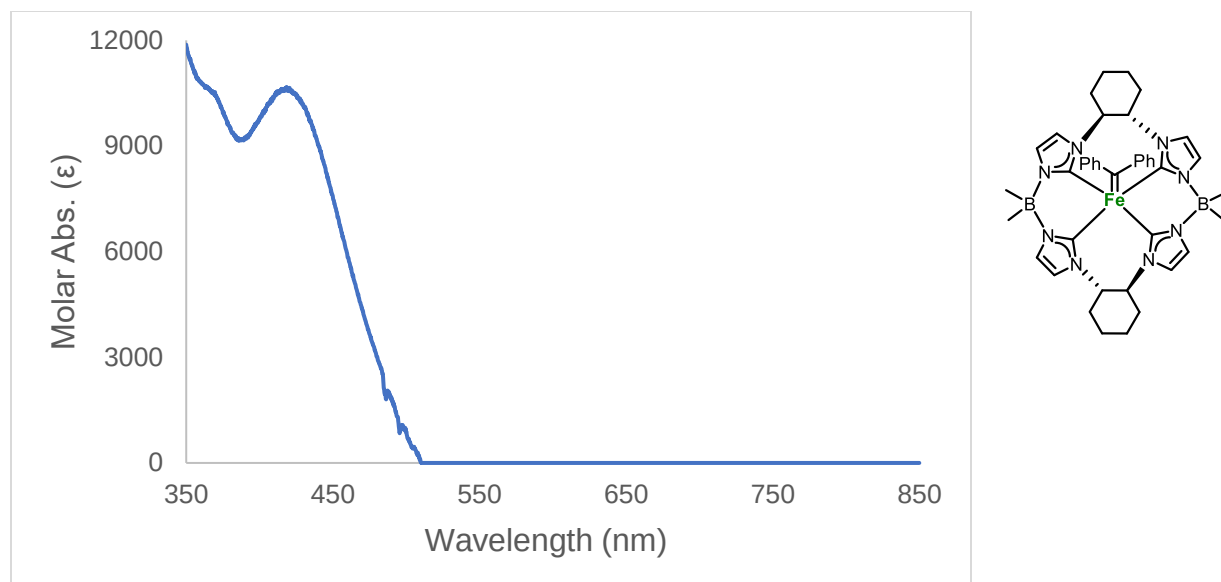
Spectrum 4.30: IR of **4.9**.



Spectrum 4.31: HR DART MS of **4.9**.

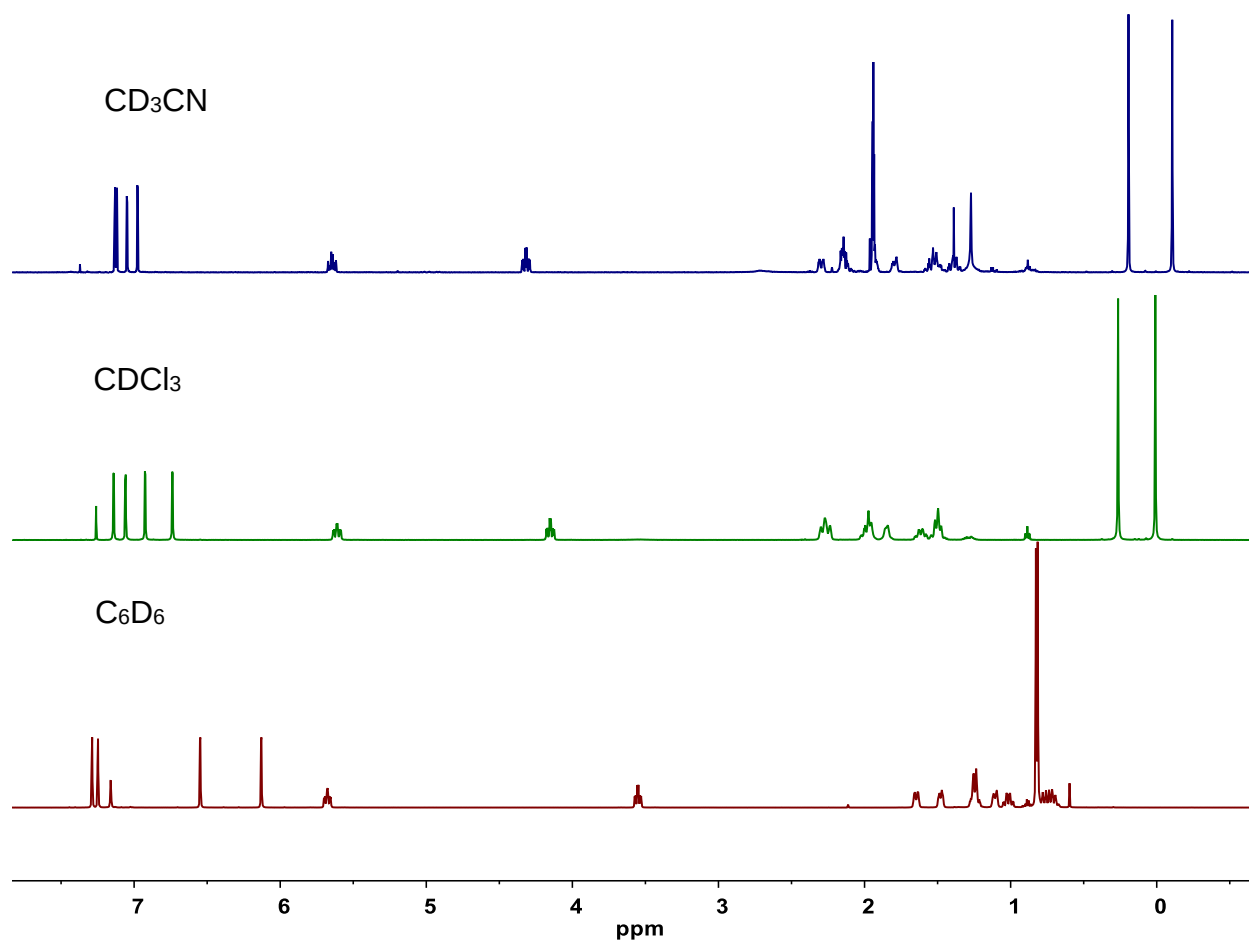


Spectrum 4.32: Concentrated (1.412×10^{-3} M) UV-Vis Spectrum of **4.9** in THF.

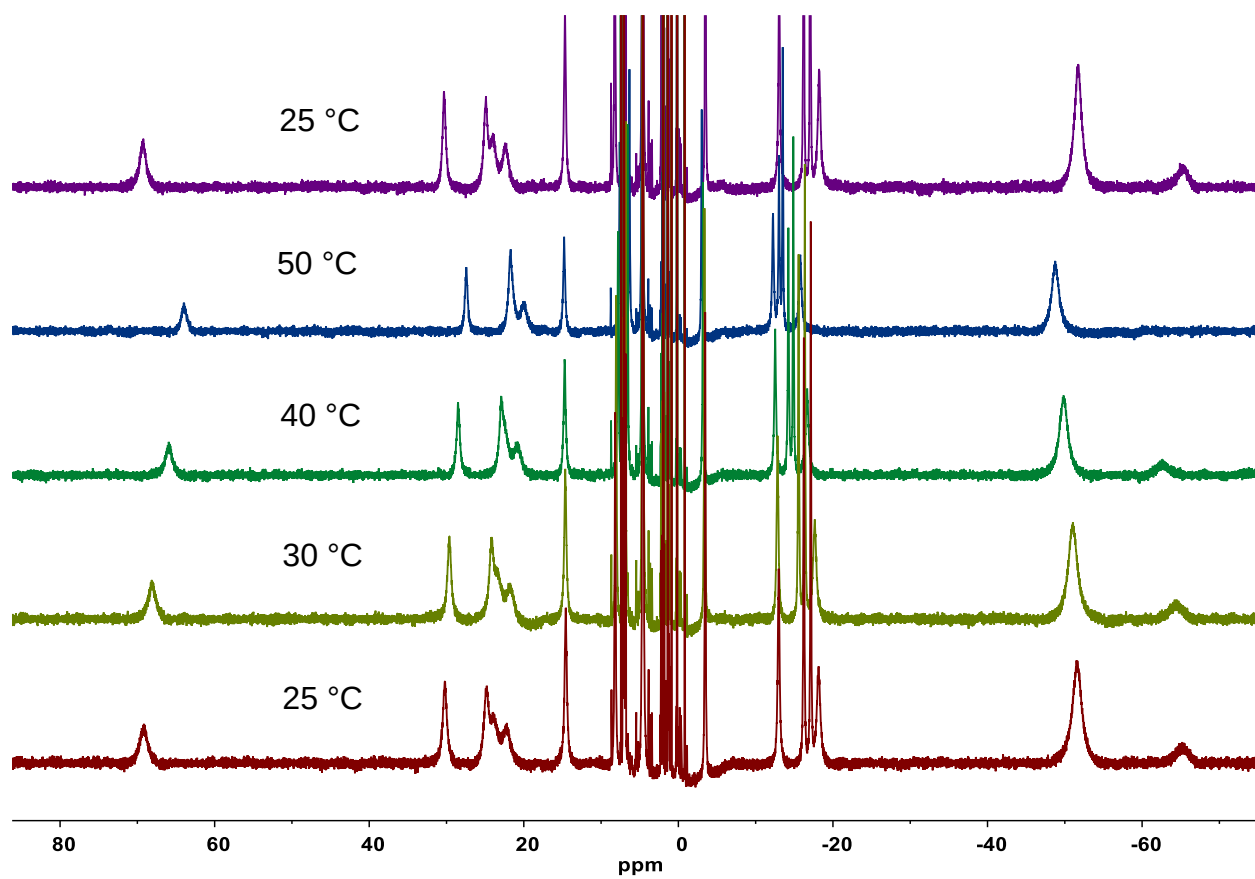


Spectrum 4.33: Dilute (7.587×10^{-5} M) UV-Vis Spectrum of **4.9** in THF.

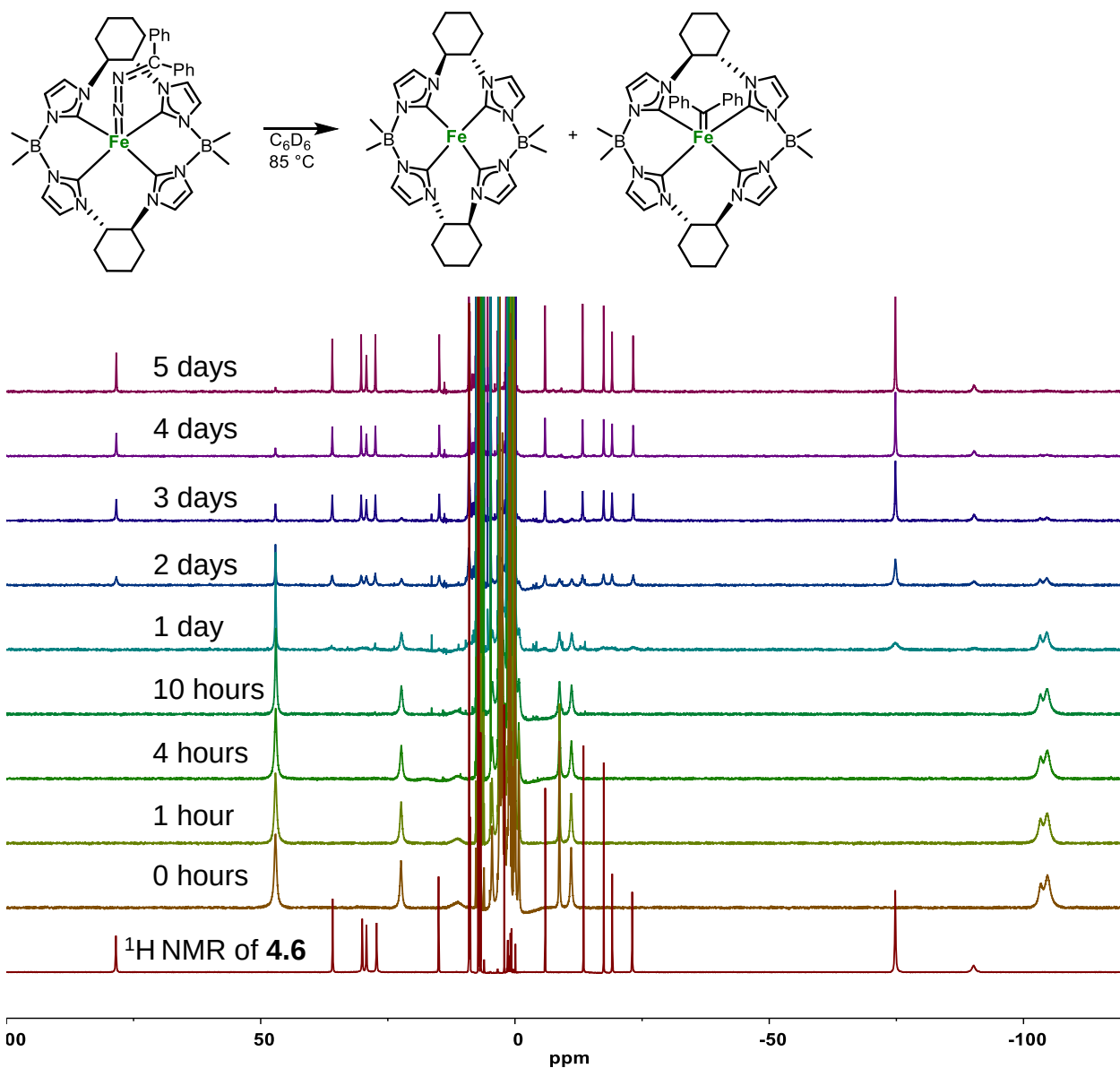
Additional NMRs for reactions



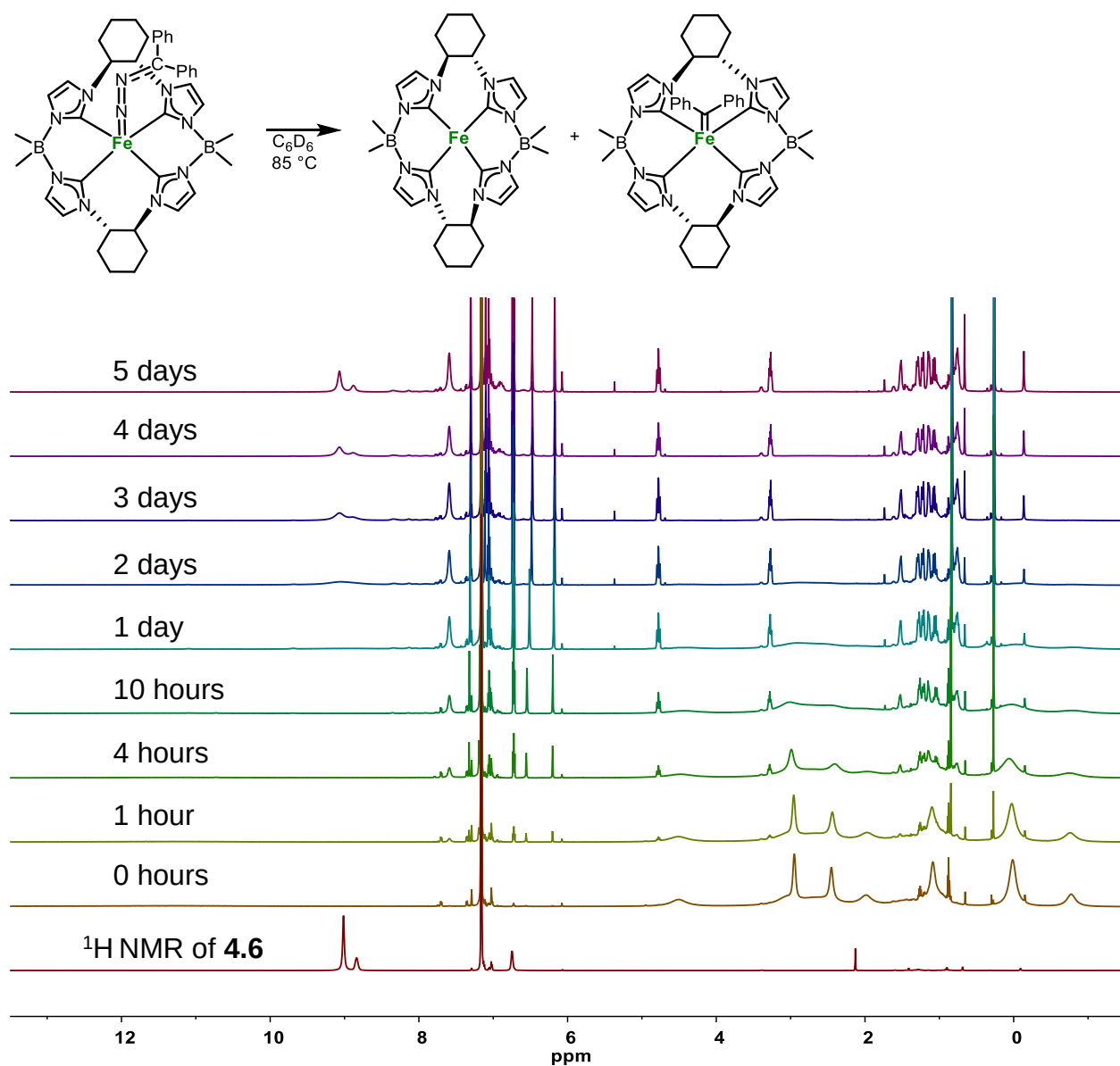
Spectrum 4.34: Comparison ^1H NMR of **4.5** in CD_3CN (top, blue), CDCl_3 (middle, green) and C_6D_6 (bottom, red).



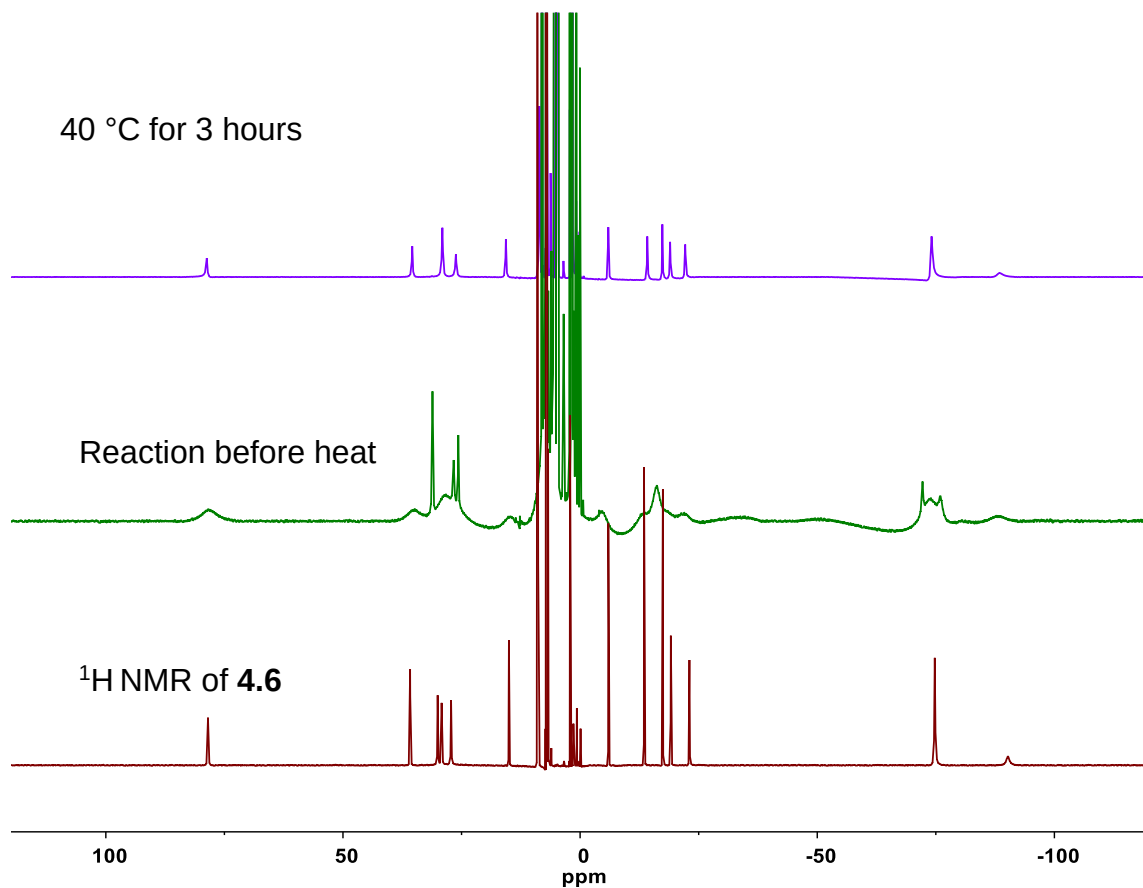
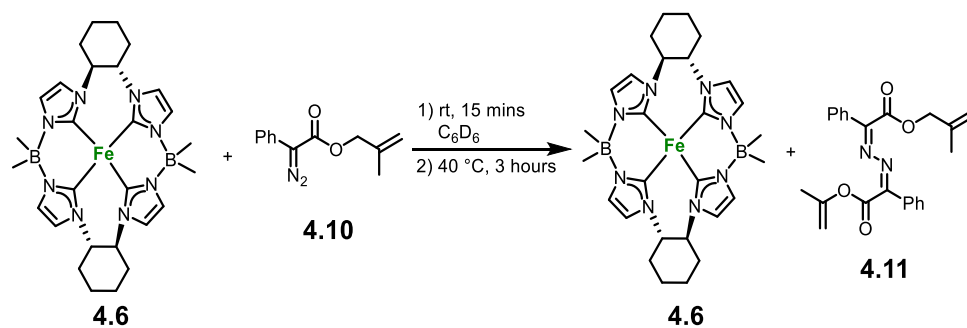
Spectrum 4.35: VT NMR of **4.6** in CD₃CN from 25 °C to 50 °C . **Purple** spectrum is after cooling the 50 °C run back to 25 °C.



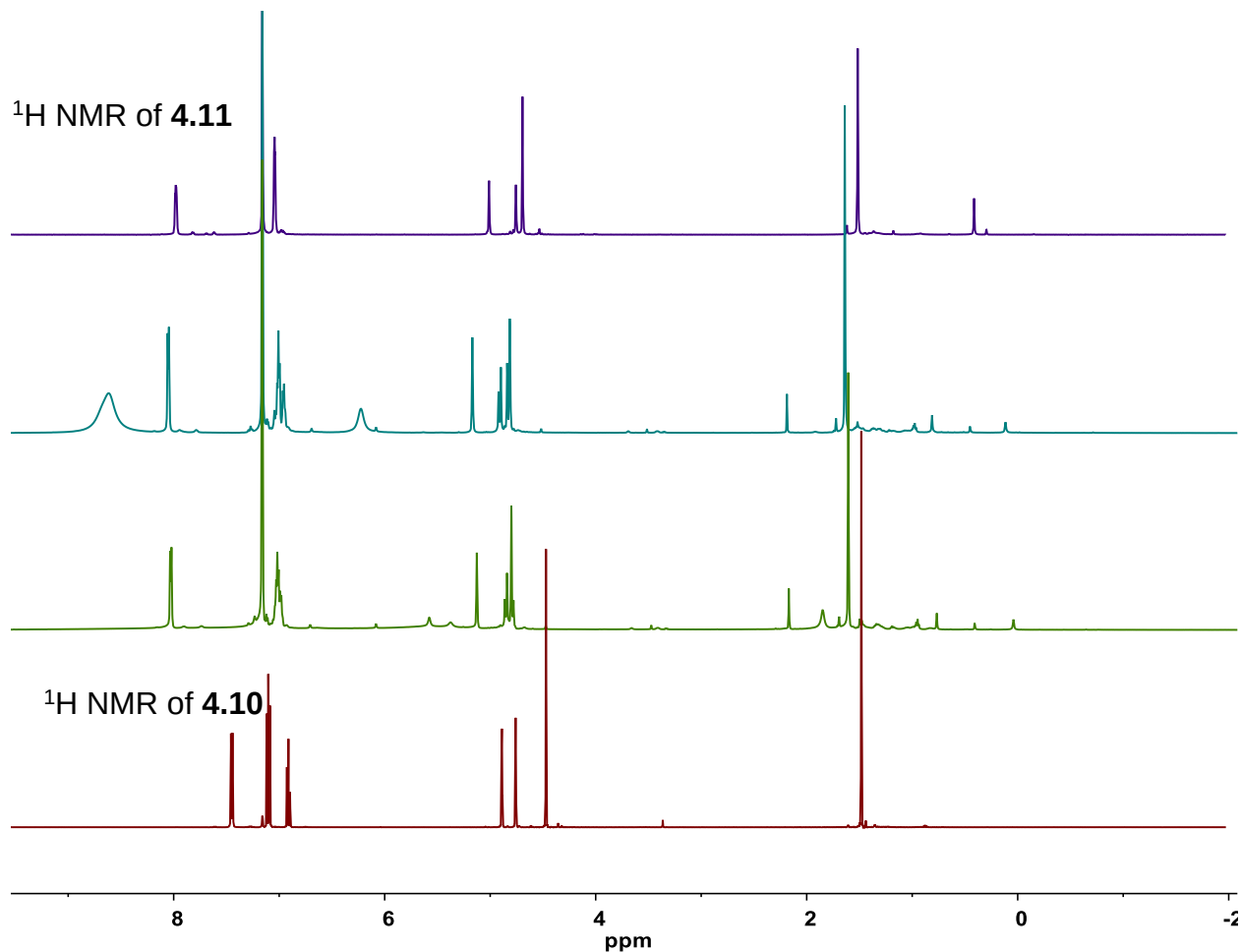
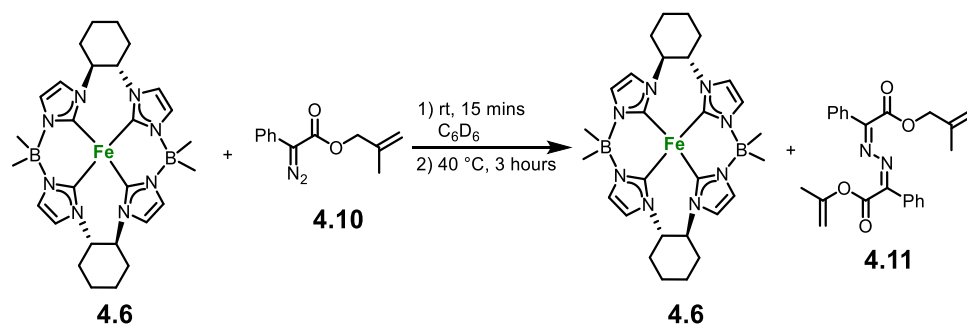
Spectrum 4.36: Thermal decomposition of **4.8** over 5 days in C_6D_6 . With time, NMR peaks corresponding to **4.6** appear in paramagnetic region.



Spectrum 4.37: Thermal Decomposition of **4.8** in C_6D_6 over 5 days. With time, peaks corresponding to **4.9** appear in the diamagnetic region.



Spectrum 4.38: Stoichiometric NMR scale reaction of **4.6** with **4.10** in C_6D_6 . Widescan shown here. Before heating (**green**) shows a paramagnetic species presumably the diazo adduct. Upon heating at 40 °C for 3 hours (**purple**), the only paramagnetic species is **4.6**.



Spectrum 4.39: Stoichiometric NMR scale reaction of **4.6** with **4.10** in C₆D₆. Diamagnetic regions shown here. Before heat (**green**), shows complete consumption of **4.10** and formation of **4.11**. Heating at 40 °C for 3 hours (**blue**) consumes the second paramagnetic species shown in Figure 4.38 and forms **4.6** and **4.11**.

**Chapter Five: Towards a General Synthesis of C_2 Symmetric
Diimidazolium and Tetra-Imidazolium Macrocycles from
Chiral 1,2-Diamines**

A portion of this work in this chapter was done by Nathaniel Dominique (REU student, University of Georgia) and Robert Ozburn (Undergraduate, University of Tennessee). Both completed the work under my direction and guidance for reproducing some of the diimidazoles in this chapter and advancing understanding of ways to efficiently synthesize them.

Abstract

Developing new chiral ligands to solve difficult transformations in organic chemistry is critical. N-heterocyclic carbenes (NHCs) have increasingly replaced phosphines in organometallic chemistry due to their stronger donor strength and resistance to oxidation. However, the application of NHC's in asymmetric catalysis are limited greatly in comparison to phosphines, as well as even salens and porphyrins. We have developed a general synthetic procedure for synthesis of C_2 symmetric diimidazoles from their corresponding diamines. This method provides a general route towards both alkyl and aryl diimidazoles. Initial reactions were performed to expand our library of chiral NHCs, making both bidentate and macrocyclic imidazoliums. We have also isolated an Fe(II) complex utilizing one of these new ligand types, which represents the closest example of a NHC analog of a chiral wall porphyrin.

Introduction

Asymmetric catalysis is at the forefront of new synthetic organic chemistry, as efficient isolation of single enantiomers in drug design is increasingly critical.^{43, 197, 198} A powerful way to stereoselectively form new chemical bonds is through transition metal catalysis using a chiral ligand reacting with achiral and prochiral substrates.¹⁹⁹ N-heterocyclic carbenes (NHCs) have increasingly been used for this process.⁸² The type of chiral NHC most used is the style shown in Figure 5.1A. The ligand incorporates sterically encumbering alkyl substituents on the nitrogens of the imidazole. The backbone can be functionalized with chiral directing groups, forming a " C_2 symmetric" complex. This propeller-like complex is among the most useful designs for inducing stereochemistry and

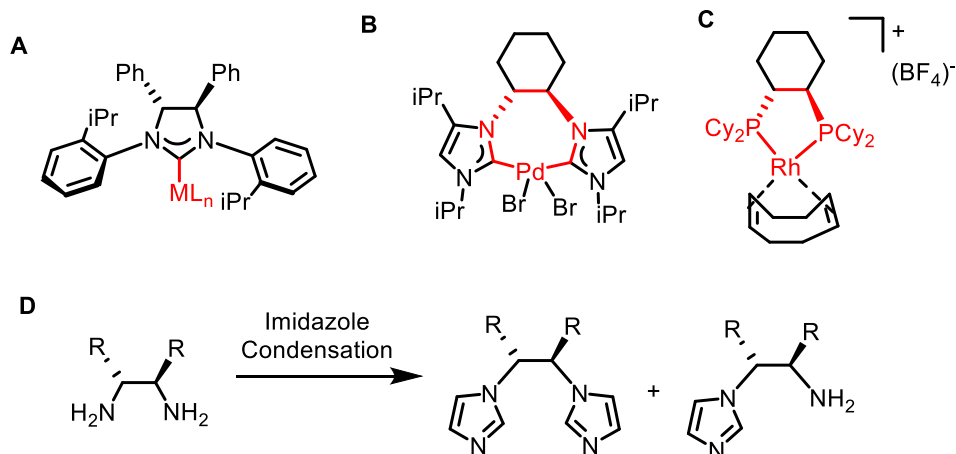


Figure 5.1. 5.1A: The most successful motif of chiral NHCs involving a monodentate NHC with chiral groups on the NHC backbone. Free rotation of the M-C bond (indicated in red) can erode stereoretention during catalysis. **5.1B:** Example of previously reported C_2 symmetric bidentate NHC. Bite angle is too large to prevent inversion of the stereo center, and groups are also oriented too far away so it has poor stereo induction. **5.1C:** Example of a similar bidentate phosphine catalyst that uses same diamine bridge but has good stereo induction due to tighter bite angle. **5.1D:** The most common example synthesis of bidentate NHCs using vicinal 1,2-diamines. This reaction always forms mixtures diimidazole and imidazole amine.

has been used in monodentate and bidentate ligands, metallocalen, and metalloporphyrin metal complexes.^{200, 201}

While monodentate NHCs are the most studied chiral NHCs, they often have significant drawbacks. The increased σ character and weaker π -backbonding of NHCs allow for the M-C bond to rotate freely; this may erode stereoretention in many systems. Bidentate ligands do not suffer from this problem and are thus more effective at preventing this (Figure 5.1B, left).⁸² However, the larger bite angle affects stereoiduction due to increased ligand flexibility. As a comparison, the similar bidentate phosphine complex in Figure 5.1B, right, which has a smaller bite angle, shows good stereoretention despite having the same type of chiral linker and C_2 symmetry.²⁰²

Currently, the synthesis of bidentate NHCs by standard routes is quite difficult and time consuming. The typical imidazole condensation (Figure 5.1C) always results in a 1:1 mixture of the desired diimidazole and the imidazole amine, complicating purification by column chromatography greatly.⁹¹ Therefore, a general method that tolerates a variety of diamines with simpler purification is highly desirable.

This chapter describes the development of a general synthetic procedure to synthesize new chiral bidentate NHCs. Our goal is to generate a class of new diimidazoles that can be used to synthesize macrocyclic tetra-NHCs as well as bidentate NHCs for chiral catalysis.

Results and Discussion

In order to develop a new library of chiral tetra-NHC ligands, we needed to first synthesize a variety of diamines. The general synthesis of diamines is given in Figure

5.2, which shows the different methods used. The most classical method involves the addition of an alkyl Grignard to an imine which contains a chiral auxiliary (Figure **5.2A**).²⁰³ This forms a diastereoselective secondary diamine, which can be subsequently reacted to cleave the auxiliaries, yielding the primary diamine. An alternative route involves synthesizing the diamine from the acid chloride. The acid chloride is subjected to sodium azide (NaN_3), thermally rearranging it to the isocyanide, and is then hydrolyzed to the free amine (Figure **5.2B**).²⁰⁴ One downfall of this approach is that it requires the use of a chiral acid to resolve the enantiomers, which can complicate purification. A recent third approach reacts (1*R*,2*R*)-1,2-bis(2-hydroxyphenyl)ethylenediamine (“mother diamine”) with aldehydes to perform a diimine condensation.^{92, 205} A [3,3]-diaza Cope rearrangement is then used to invert the stereochemistry, relative to starting material (Figure **5.2C**). This approach tolerates a variety of groups, including both aryl²⁰⁵ and alkyl⁹², as well as requires no chiral resolution. We envisioned this approach we be useful for making a variety of diimidazoles.

We chose the dicyclohexyl diamine (**5.1**) as our test case for developing a general synthesis. We felt this would be a valuable diimidazole to synthesize, as it is the most sterically encumbering diamine that can be made scalable due to cost restrictions.⁹² We initially attempted to synthesize the diimidazole by using all published methods for synthesizing C_2 symmetric diimidazoles (Figure **5.3**).^{90, 168, 170, 171} Unfortunately, none of these methods yielded the desired product, but, instead, yielded the compounds shown in red as the major products. Adjusting reaction conditions, such as temperature and the order of addition of reagents, did not yield favorable results for the synthesis of the diimidazole. Rather, all of the reactions yielded 5- or 6-membered rings in which a

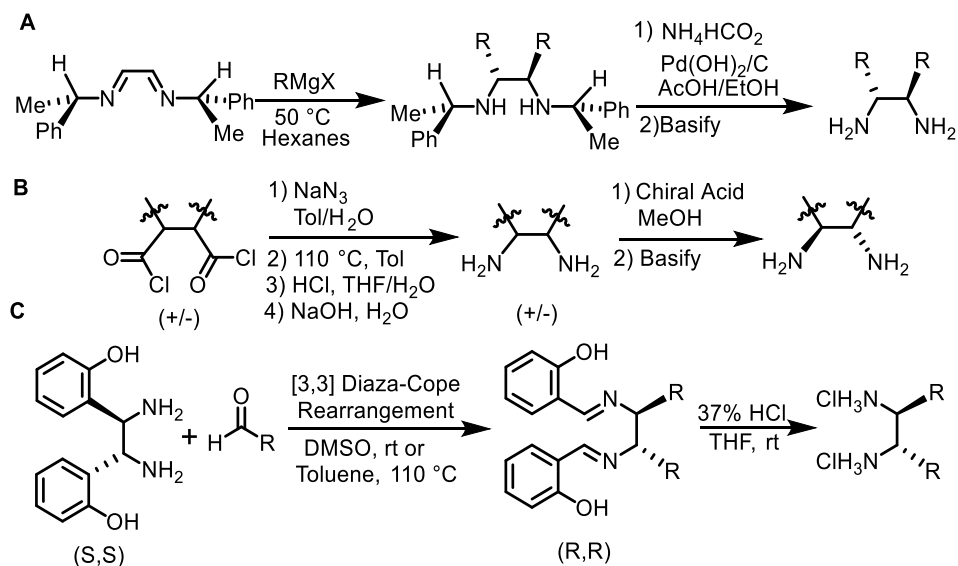


Figure 5.2: Methods to synthesize C_2 symmetric 1,2-diamines. **A:** Addition of an alkyl Grignard to bis-imine with a chiral auxiliary. **B:** Synthesis of acyl azide, followed by a Curtius rearrangement to yield the isocyanate, which is then hydrolyzed. This process requires a chiral acid to resolve enantiomers. **C:** [3,3] Diaza-Cope rearrangement from the "mother diamine" using aldehydes, followed by hydrolysis of the auxiliary. Reacting in $DMSO$ at room temperature is ideal for aryl aldehydes, while alkyl aldehydes require heating with loss of H_2O in toluene to perform the desired rearrangement.

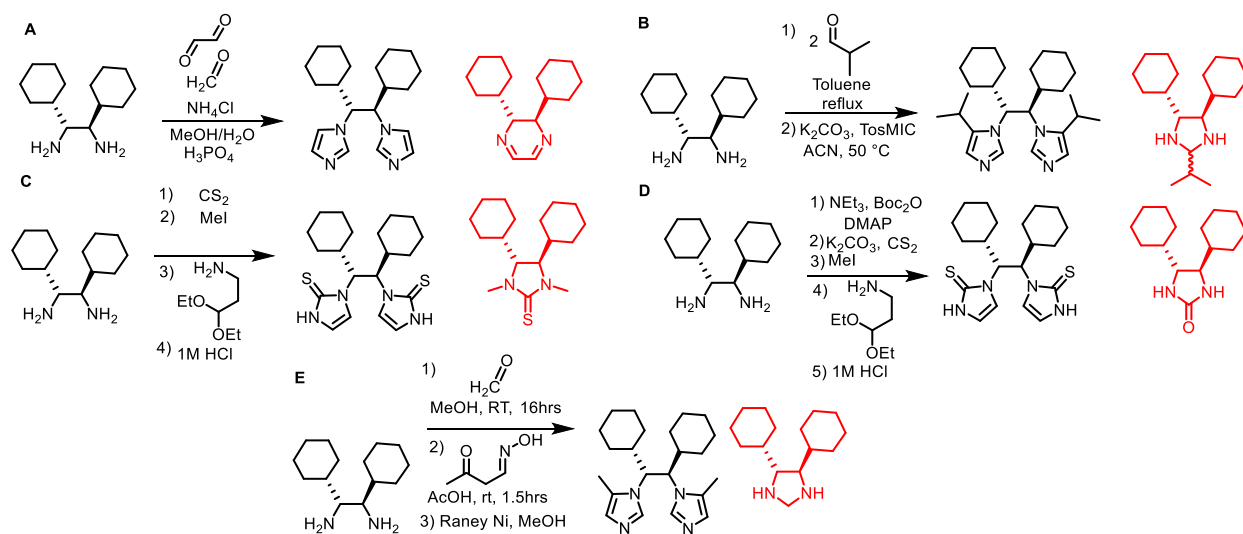
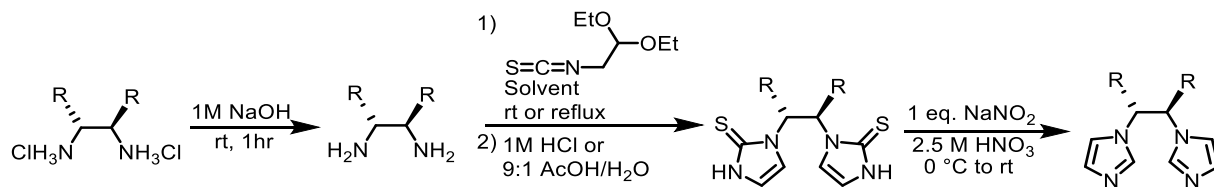


Figure 5.3: Attempted synthesis of **5.1** by all previously published routes for chiral diimidazoles. The molecule in red is the major product in each case, rather than the expected diimidazole.

molecule of water is eliminated (Figure 5.3A, 5.3B, and 5.3E) or lost a part of the molecule as a leaving group from intramolecular nucleophilic attack (Figure 5.3C and 5.3D).²⁰⁶

Given these problems, we envisioned synthesizing the diimidazole using the approach in Chapter 4. The thiourea is less likely to be nucleophilic and the NHR group is eliminated, thus making this route more advantageous. Indeed, we were able to synthesize **5.1-Imidazole** from **5.1-NH₃Cl** utilizing the route shown in Scheme 5.1. Some modifications have been made in the general synthesis relative to the route outlined in Chapter 4. The reaction involving **4.1** can be accomplished in the same way, but the acid is critical in step 2. Running the reaction with 1M HCl results in formation of **5.1-Thiourea** as a sticky brown residue, which is due to a large amount of a polymeric impurity.

Fortunately, using 9:1 AcOH/H₂O solution (Method B) keeps the residue in solution, but still forms the polymeric impurity. This species is hidden behind the peaks of the cyclohexyl ring from 1-2 ppm and results in the integration values being larger than expected. Spectrum 5.5 shows the characteristic NMR for **5.1-Thiourea**. There is a diagnostic peak at 10.72 ppm which corresponds to the acidic N-H, as well as the two



Scheme 5.1: General scheme of synthesis of various diimidazoles from diammonium chloride salt to the diimidazole.

peaks corresponding to C-H at 6.81 and 6.43 ppm. In addition, consistent with **4.3**, the chiral C-H's are shifted downfield to 5.42 ppm. The NMR provided in spectrum **5.5** is from Method C, in which dilution was ten times greater than normal (0.1 M vs 0.01 M), which resulted in much less of the intractable impurity, but it was not feasible for scale up. The yield reported for **5.1-Thiourea** (20.3%) contains the impurity, as column chromatography, attempted recrystallization, and sublimation were insufficient for purification.

The reaction to form **5.1-Imidazole** could be accomplished with Raney nickel as in Chapter 4, but we desired to move away from Raney nickel due to the large amount of pyrophoric nickel waste generated. We tried a number of conditions and found that using one equivalent of sodium nitrite in 2.5 M HNO₃ resulted in forming exclusively the **5.1-Imidazole** in 18.8% yield with the intractable impurity.²⁰⁷ The diagnostic change was the N-H peak has now disappeared and there are peaks that integrate to 2H corresponding to the new imidazole peaks (7.29, 7.01 and 6.52 ppm). In addition, the chiral C-H proton now has a similar quartet splitting at 4.21 ppm, similar to **4.3**, which is another indication that the desired diimidazole was made. The integration for the alkyl C-Hs was much higher than anticipated, which is an indication that the intractable impurity is still present. Attempts to remove this impurity were unsuccessful. **5.1-Imidazole** was found to be unstable on silica gel, deactivated silica gel, and basic or neutral alumina. In addition, many different crystallization solvent-system combinations were attempted, but the impurity had nearly identical solubility as **5.1-Imidazole**. The best route to purify the product was by sublimation, though a small amount of the impurity partially sublimed and some **5.1-imidazole** thermally decomposed. The best NMR obtained for this molecule is

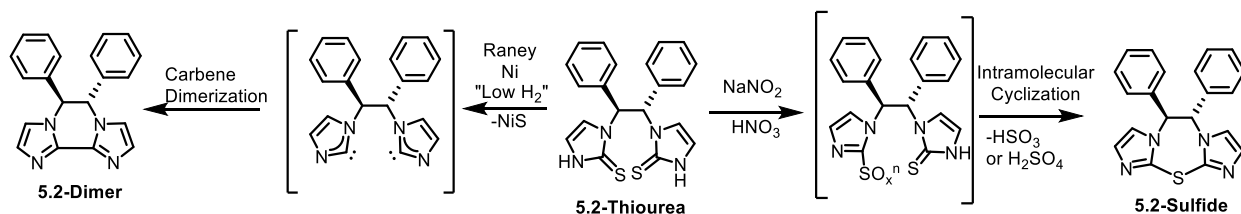
shown in spectrum **5.11**. Despite these shortcomings, this route is the only known way to synthesize chiral alkyl group containing diimidazoles, opening up a new ligand type to be used in asymmetric catalysis.

Given our success, we wanted to determine if this could be used as a general method to synthesize other diimidazoles. Thus, we utilized the commercially available (1*S*,2*S*)-diphenylethylene diamine (**5.2-NH₂**) to synthesize its imidazole (**5.2-Imidazole**), which had been previously described in low yield with incomplete purification.⁹⁰ We applied Method A to synthesize **5.2-Thiourea**, which was obtained in 92% yield. This ¹H NMR had a similar characteristic ¹H NMR as **5.1-Thiourea**, in which the N-H peak was shifted more downfield (11.19 ppm) and the backbone protons and chiral C-H's were also shifted downfield (6.44 ppm). This resonance is shifted more downfield than **4.2** and **5.1-Thiourea** which is a critical difference compared to the all alkyl derivatives (*vide infra*).

We employed the same reaction used to synthesize **5.1-Imidazole** in order to synthesize **5.2-Imidazole**. We found the reaction cleanly formed two distinct species which gave similar NMR spectra. Low resolution mass spectrometry (LRMS) and the symmetry of the compound in ¹H NMR (Spectrum **5.13**) indicate that the secondary compound formed is likely the bridging sulfide (**5.2-Sulfide**). We were surprised to isolate this compound, as there was no record of an analogous bridging sulfide in a 7-membered ring. We postulate that this is formed by oxidation of one of the sulfur atoms (Scheme **5.2**, right). Additionally, the Raney nickel desulfurization also resulted in the unexpected dimeric product (**5.2-Dimer**), confirmed by crude ¹H NMR and LRMS (Scheme **5.2**, left). In the case of Raney Nickel, the undesired product was largely the product formed in the reaction. As a result, we decided to optimize the NaNO₂ approach, as more of the desired

product could be isolated through this route. We modified our initial conditions, varying temperature, concentration, and time, to optimize the amount of yielded product.

The summary of the reaction screen is shown in Table **5.1**. Our initial conditions of using one equivalent of NaNO_2 to a cooled slurry of **5.2-Thiourea** followed by warming to ambient temperature, yielded the desired diimidazole in a 68:32 ratio based on the crude NMR following work-up, and in 40% yield based on the crude isolated product. It appeared that changing the equivalents of NaNO_2 and the temperature had little effect on the ratio of products but changing the concentration heavily affected yield. The ratio compared to the optimized conditions also was 22% less (68% vs. 44%). When the reaction was scaled up to isolate **5.2-Imidazole**, we found that it was stable on silica gel, and could be purified by gradient column chromatography to separate both species, isolating the diimidazole in 40.1% yield. The NMR of **5.2-Imidazole** is consistent with the similar reaction of **5.1-Imidazole** but with the chiral C-H shifted further downfield to 5.86 ppm (Spectrum **5.12**) and the presence of the phenyl C-H's.



Scheme 5.2: Route for unexpected reaction pathways for **5.2-Thiourea**.

Table 5.1: Optimization of desulfurization of **5.2-Thiourea** to **5.2-Imidazole**.

Equivalents of NaNO ₂	Temperature/ Time	% of Diimide. vs Bridging sulfide	Concentration of Thiourea	Yield (NMR Scale)
1	0 °C 10 mins, 25 °C 4 hours	68%	0.1 M	40%
2	0 °C 10 mins, 25 °C 4 hours	62%	0.1 M	25%
2	25 °C, 4 hours	58%	0.1 M	31%
1	0 °C, 4 hours	69%	0.1 M	22%
0.5	25 °C, 4 hours	61%	0.1 M	31%
1	25 °C, 4 hours	52%	0.05 M	10%
1	25 °C 4 hours	44%	0.2 M	26%
1	100 °C, 4 hours	60%	0.1 M	45%

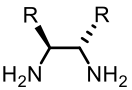
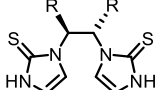
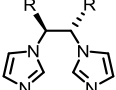
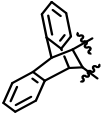
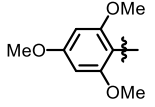
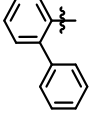
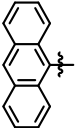
Since we had successfully demonstrated synthetic paths towards both aryl and alkyl diimidazoles, we wanted to expand our library of diimidazoles for chiral ligands. The results are shown in Table **5.2**. We decided to focus on alkyl groups first. We found that alkyl group **5.3** could similarly form the imidazole **5.3-Imidazole** through the same route at **5.1** in 51% overall yield. This product still had the intractable impurity, which could be clearly seen in the ^1H NMR (Spectrum **5.14**). The characteristic peaks for the imidazole are at 7.30, 7.00 and 6.55 ppm, while the chiral C-H peaks are at 4.10 ppm, which similar to **5.1-Imidazole**.

Attempts at forming an even bulkier diimidazole, we used the tert-butyl diamine **5.4-NH₂**.¹⁷⁰ We found, however, that utilizing this diamine was completely ineffective. The NMR from the conditions used in diamines **5.1** and **5.3** resulted in what appeared to be some unidentified ammonium salt. This showed that, in the case of alkyl diamines, there is a limit to how bulky the alkyl substituent can be. We are currently trying to use a primary diamine, **5.5-NH₂** to round out our library of alkyl diamines.

Similar to **4.3**, we wanted to also try diamines that had some rigidity in the backbone or chiral groups, as these have been shown to limit inversion in metal complexes for chiral NHCs. We utilized the diamines **5.6-NH₂**²⁰⁴, **5.7-NH₂**²⁰⁸, and **5.8-NH₂**²⁰⁹ towards this goal. While **5.7-Imidazole** and **5.8-Imidazole** have not been demonstrated before, **5.6-Imidazole** has been previously been reported based on the imidazole condensation reaction.^{89, 177}

We were successful in applying the synthesis of **5.6-Imidazole** from **5.6-NH₂** in 21.9% overall yield, which matches the published molecule.⁸⁹ We attempted synthesizing

Table 5.2: Isolated species with yields for chiral diimidazoles and macrocycles. Cells highlighted in yellow are in the process of being completed.

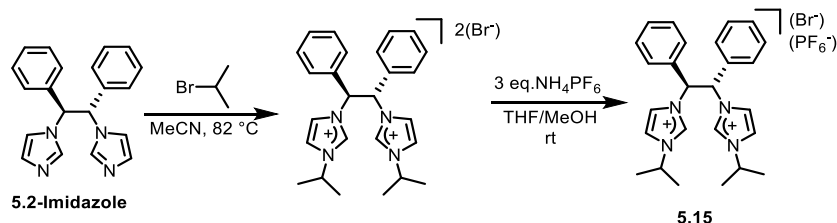
R group				Borate Macrocycle (BMe ₂)
 (5.1)	73.0%	20.3%*	18.8%*	32.2%
 (5.2)	Comm. Avail.	91.9%	40.1%	43.4%
 (5.3)	99.6%	80.2%*	21.9*	14.4%
 (5.4)	Literature ²⁰³	Decomp.	N/A	N/A
Heptyl-  (5.5)	Literature ²¹⁰			
 (+/-) (5.6)	Literature ²⁰⁴	18.8%	25.0%	46.0%
 (+/-) (5.7)	Literature ²⁰⁹	Decomp.	N/A	N/A
 (5.8)	70.9%			
 (5.9)	52.0%	53.5%		
 (5.10)	Comm. Avail.	22.3%		
 (5.11)	Decomposed	N/A	N/A	N/A
 (5.12)				
 (5.13)				
 (5.14)				

5.7-Imidazole through the same route as **5.1**, **5.3** and **5.4** however this resulted in an identical NMR as **5.4**'s case. It is unclear at this time why this occurs. **5.8-NH₂** was also attempted and resulted in formation of **5.8-Thiourea**. The NMR is consistent with the formed thiourea but contains another unidentified impurity.

Based on the literature, there are a much greater variety of aryl diamines available which can be tuned more effectively than alkyl diamines.^{205, 211} We wanted to expand this synthesis to different aryl diamines; no other aryl diimidazoles of this style have been reported. We initially settled on the diamines shown as **5.9-5.14**, as they contain a mix of steric parameters and possible tunability (**5.10**). The ammonium salts for **5.9-5.11**²⁰⁵ have been previously described, while **5.12-5.14** have not previously been described. We found that the **5.11-NH₂** was unable to be isolated and attempting in-situ deprotonation (Method C) to make **5.11-NH₂** was ineffective as well. This is likely due to extremely electron rich amines being unstable.

We were successful initially on synthesizing **5.9-Thiourea** and **5.10-Thiourea**. The NMRs for both (Spectrum **5.9** and **5.10**) are similar to **5.2**, with the exception of different aryl peaks and the presence of the O-H peak for **5.10-Thiourea** at 10.03 ppm. Significantly, this synthesis tolerates protic groups such as OH's, which can be functionalized later in the synthesis to add steric groups. We tried reducing **5.9-Thiourea** to **5.9-Imidazole** using the standard scheme, and the initial crude NMR showed the familiar mixture of the sulfide and imidazole. However, this product was not stable on silica gel, likely due to increased basicity of the imidazole nitrogen due to the extended conjugation on the naphthalene units.

Since we synthesized a variety of C_2 symmetric diimidazoles, we wanted to build our library of macrocyclic NHCs. First, we wanted to see if diimidazoliums with this winged motif could be made, since besides diimidazoles in the style of **4.3**^{168, 171} and **5.6-Imidazole**⁸⁹, as no similar diimidazoliums exist. We used **5.2-Imidazole** as our test case and reacted it with 2-bromopropane and dialkylated it to form the bidentate imidazolium salt (Scheme **5.3**). We found that the bromide salt was extremely hygroscopic, so we took the crude reaction mixture and reacted it with an excess of NH_4PF_6 under typical conditions²¹², to perform a full anion metathesis. However, we found that this only resulted in one bromide exchanging, resulting in **5.15**. The formation of the imidazolium was confirmed by the appearance of the peak at 8.73 ppm. This also was confirmed crystallographically by Figure **5.4**. Figure **5.4** shows the expected (*S,S*) stereochemistry is retained and incorporation of the isopropyl groups. However, looking at the expanded structure lattice (Figure **5.4** bottom), it shows that the bromide atom is stabilized by two different imidazolium through complex hydrogen bonding, which would explain why the bromide ion was not exchanged. Of note, the C-H on the chiral carbon is participating in



Scheme 5.3: Synthesis of a C_2 diimidazolium salt from **5.2-Imidazole**, **5.15**.

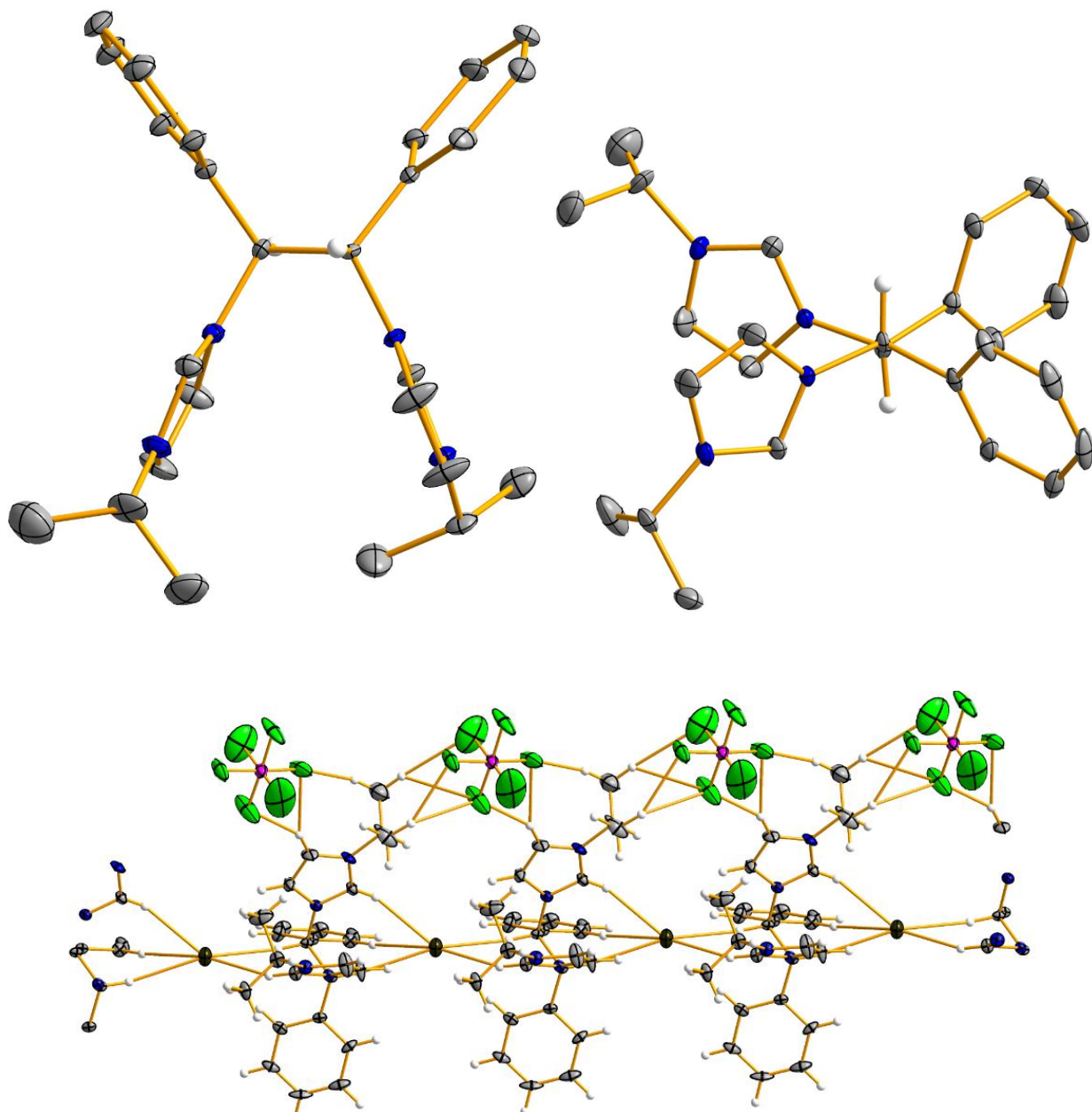
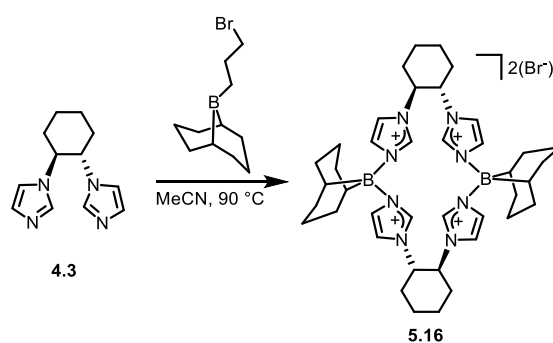


Figure 5.4: Top: X-ray crystal structure of **5.15**. Green, pink, blue, gray, dark olive, and white ellipsoids (30% probability) represent F, P, N, C, Br, and H atoms, respectively. Solvent molecules and H-atoms not connected to stereogenic centers are omitted for clarity. **Bottom:** Hydrogen bonding network shown by **5.15**, rationalizing remaining bromide anion.

hydrogen bonding, which implies that this atom has some acidity. The ^1H NMR for this proton is at 6.69 ppm, which is significantly shifted downfield for an alkyl C-H.

Next, we wanted to confirm that other boranes could be used to form these chiral macrocycles. To date, we have only shown that bromodimethylborane can be used to generate a boron-containing macrocycle that can be readily deprotonated to generate a tetra-NHC metal complex.^{69, 72, 169} We decided to use the 9-borabicyclo[3.3.1]nonane (9-BBN) analog²¹³, shown in **Scheme 5.4**. We were able to use the diimidazole **4.3**, forming the macrocycle in **Figure 5.5**.²¹⁴ The precipitated white solid washed and found to be sparsely soluble in most solvents besides methanol, in which it slowly decomposed. The ^1H NMR in DMSO- d_6 is shown in Spectrum **5.17** and has the characteristic imidazolium and chiral C-H peaks at 8.97, 7.42, 6.95, 5.04 ppm. The crystal structure shows a similar complex to **4.4**, in which the cyclohexane moieties are twisted and results in a 2-fold symmetry of the macrocycle.



Scheme 5.4: Synthesis of **5.16**.

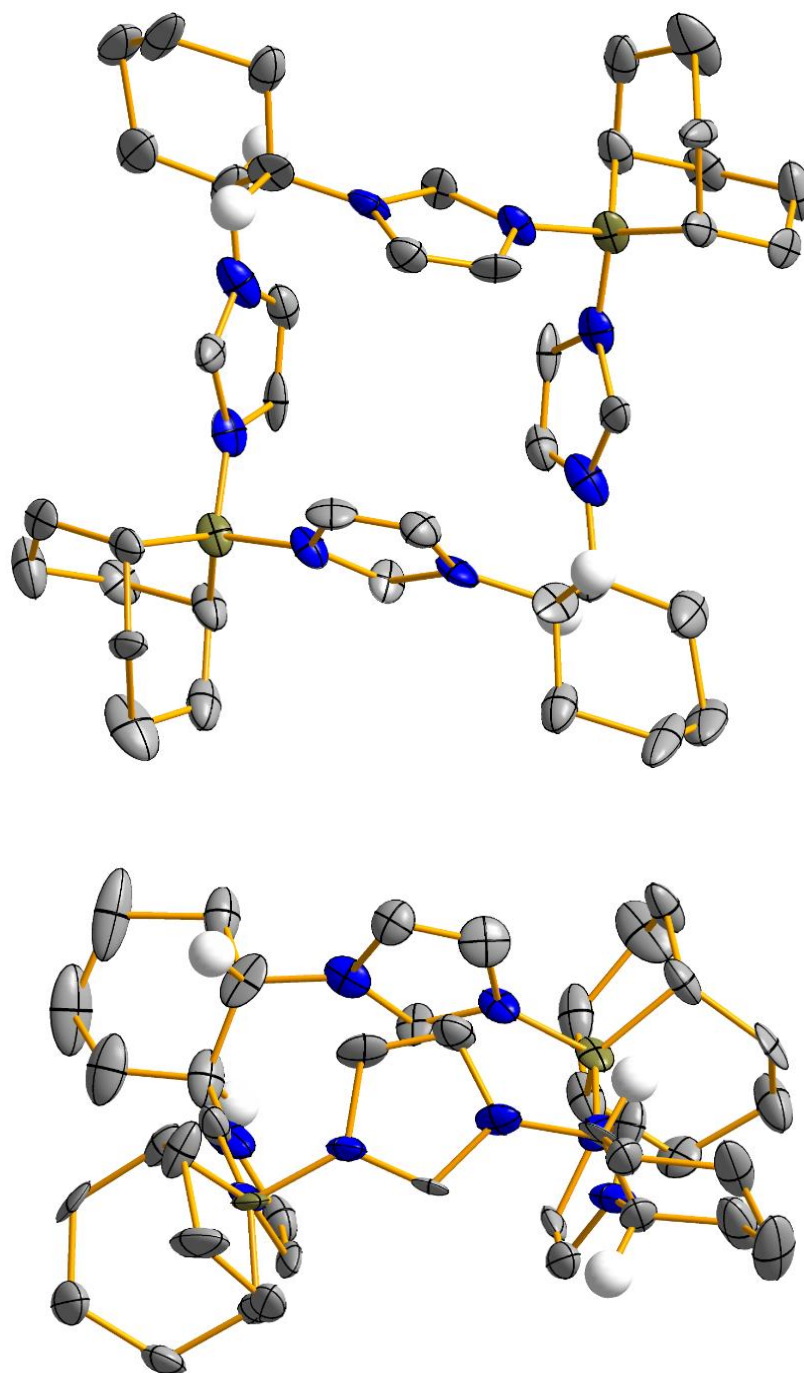
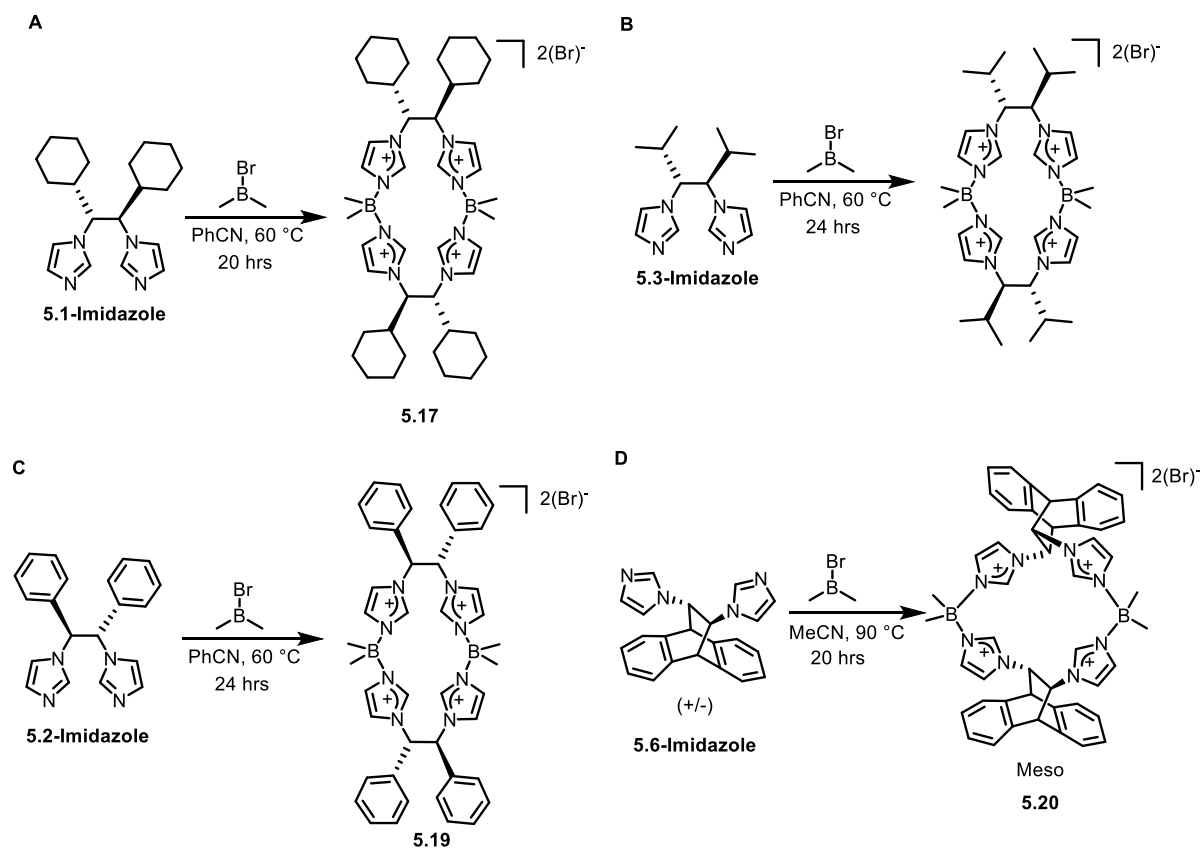


Figure 5.5: X-ray crystal structure of **5.16**. Blue, gray, olive, and white ellipsoids (30% probability) represent N, C, B, and H atoms, respectively. Solvent molecules, counteranions and H-atoms not connected to stereogenic centers are omitted for clarity.

With these considerations in mind, we decided to synthesize various dimethylborate macrocycles. The four isolated examples are shown by Scheme 5.5. For 5.17, 5.18 and 5.19, we found that using the less polar PhCN gave favorable results for synthesis of the macrocycles⁷², while for 5.20, CH₃CN was the optimal solvent for yield (46.0%). In the case of 5.17 and 5.18 we were initially confused and assumed that a dimeric macrocyclic system formed based on the crude NMR in DMSO-d₆ (Spectrums 5.18 and 5.20) as the two sets of signals were consistent with that. However, we grew crystals of 5.17 in methanol with ether diffusion and it resulted in the crystal structure in Figure 5.6. This proved that at least part of the isolated crude was a dimeric macrocycle. Upon closer inspection, fully dissolving the isolated molecule in MeOD-d₄ (Spectrum 5.19) resulted in the peaks coalescing into one species. It seems that 5.17 and 5.18 have some intramolecular hydrogen bonding that is quite strong. These are the first examples of these kind of macrocyclic tetra-NHCs.

We applied the borane from the synthesis of 5.19 and 5.20, which use aryl linkers for the diimidazole. This formed a similar type of NMR in both cases (Spectra 5.21 and 5.23). Notably, 5.19 seemingly had the chiral C-H protons missing. It was found through ¹H-¹³C HSQC (Spectrum 5.22) that the proton for the stereogenic carbons were at 7.39 ppm, which is very significantly shifted for an alkyl C-H bond. Similarly, we found that for 5.20 that the same type of alkyl C-H signal is significantly shifted to 6.65 ppm (Spectrum 5.23). Molecule 5.19 was attempted to be characterized crystallographically, but it had awful solubility in all organic solvents. We were able to crystallographically characterize 5.20, which is shown by Figure 5.7. We found that the main product in this reaction was the *meso* macrocycle, formed by the racemic mixture of the diimidazole. For unknown



Scheme 5.5: Synthesis of chiral macrocycles from C_2 symmetric diimidazoles from reaction with bromodimethylborane in nitrile solvents. **A-D** show four different diimidazoles that yielded recognizable borate macrocycles.

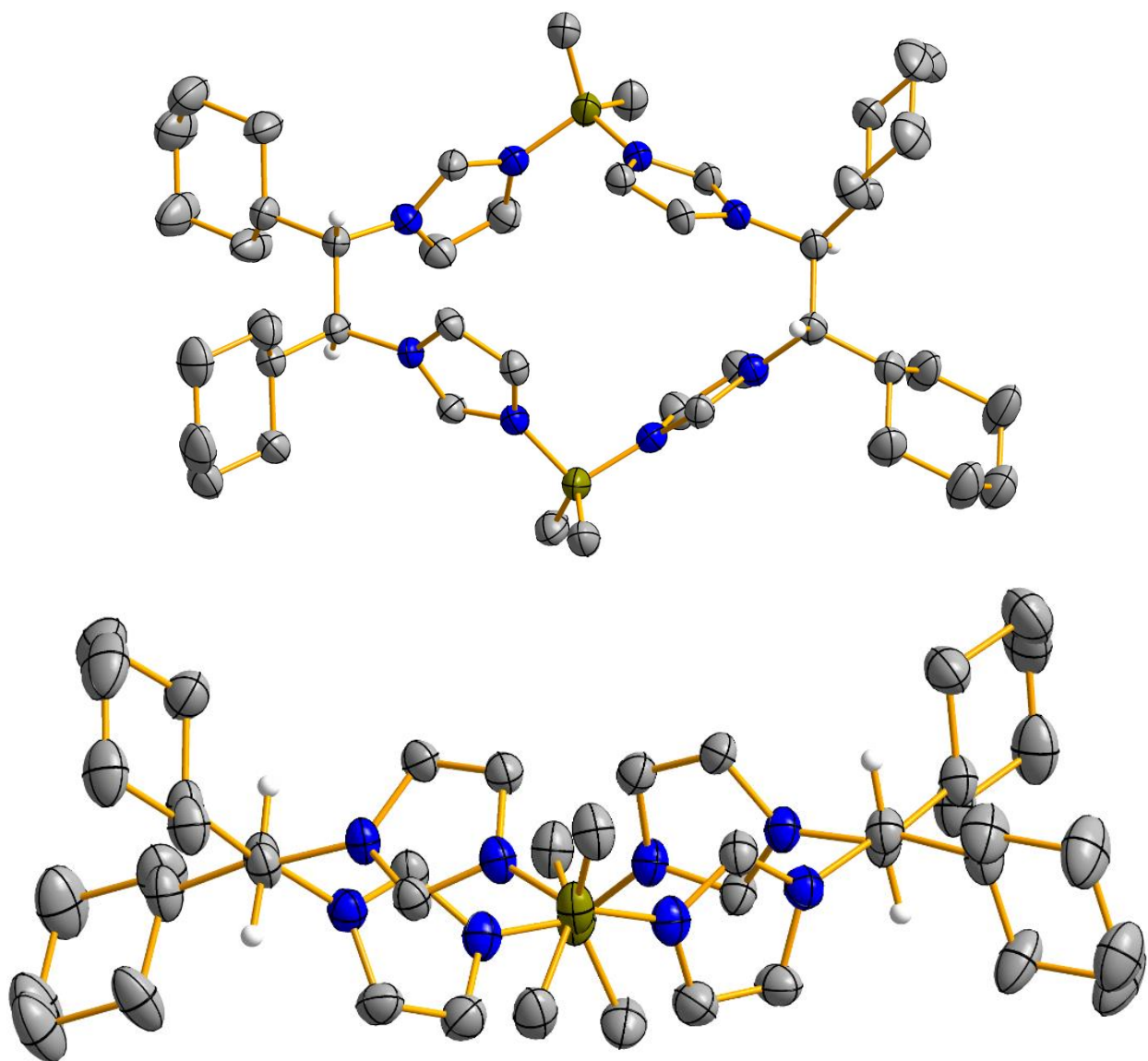


Figure 5.6: X-ray crystal structure of $[(\text{(S,S)-1,2-DiCy,BMe}_2\text{TC}^H)\text{Fe}]$, **5.19**. Blue, gray, olive, and white ellipsoids (50% probability) represent N, C, B, and H atoms, respectively. Solvent molecules, counteranions and H-atoms not connected to stereogenic centers are omitted for clarity.

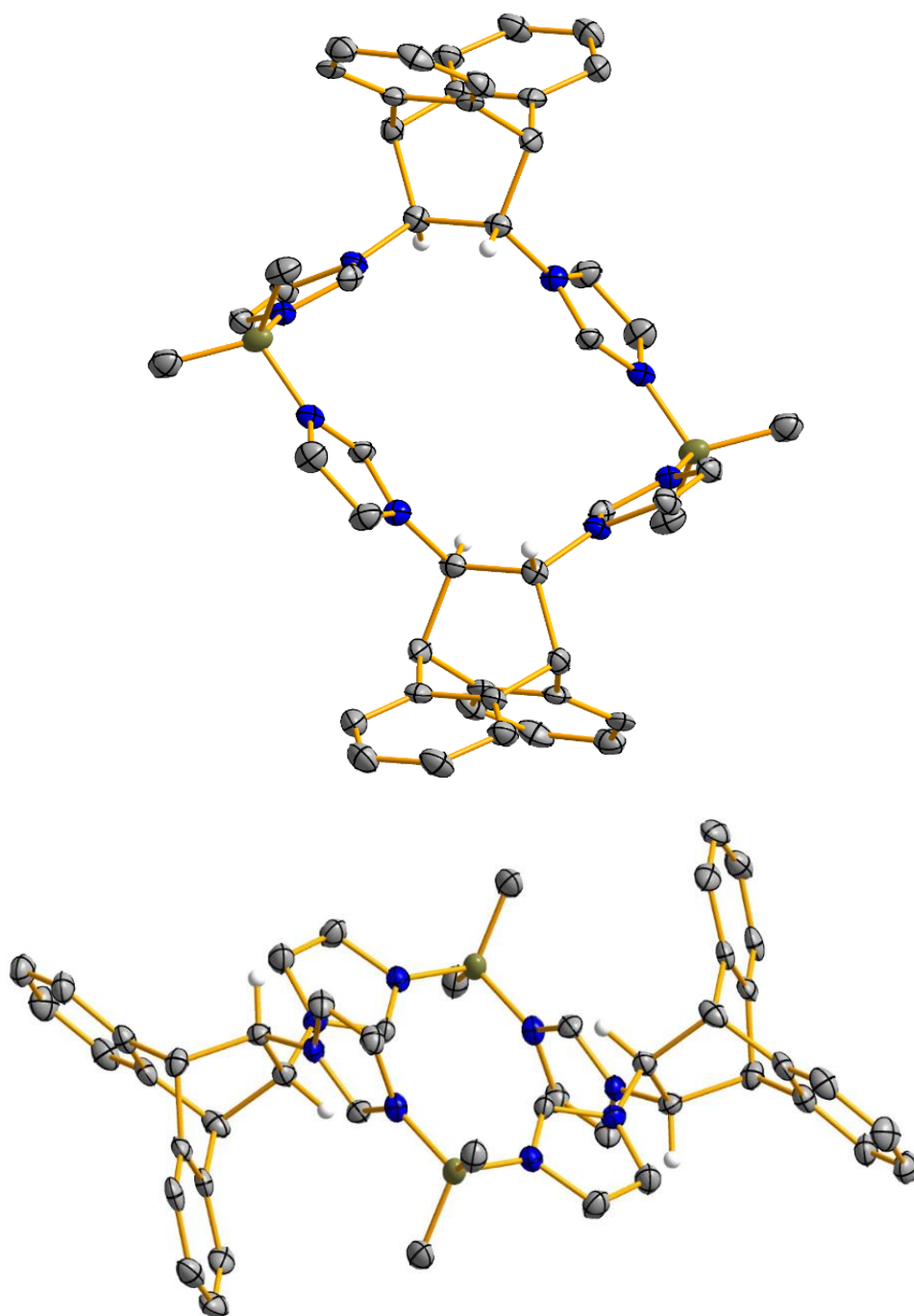
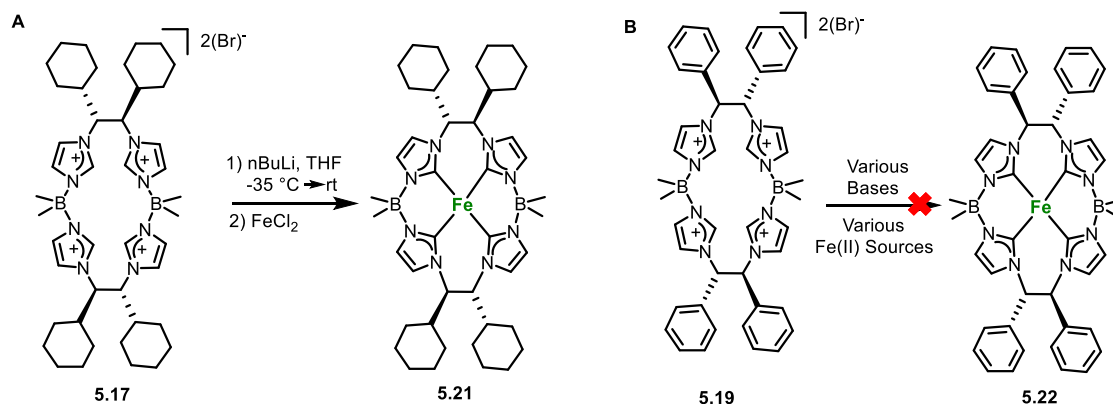


Figure 5.7: X-ray crystal structure of **5.20**. Blue, gray, olive, and white ellipsoids (50% probability) represent N, C, B, and H atoms, respectively. Solvent molecules, counteranions and H-atoms not connected to stereogenic centers are omitted for clarity.

reasons, this particular set of conditions formed only one product, whereas lower temperature and using PhCN resulted in a small amount of another macrocycle species forming, likely the racemic chiral macrocycle.

With both these new kinds of macrocycles in hand, we attempted to synthesize iron complexes (Scheme 5.6). With ligand **5.19**, we found that by applying the synthesis from Chapter 4, we were able to synthesize molecule **5.21**. The NMR we obtained was heavily paramagnetic, similar to **4.6**, which gave evidence that it was iron(II). We were able to crystallize **5.21** by diffusing a hexanes solution into acetonitrile, yielding the structure in Figure 5.8. This complex is the first example of a chiral NHC molecule that is analogous to a chiral wall porphyrin.^{76, 215} The average Fe-C bond length is 2.015 Å,



Scheme 5.6: Synthesis of C_2 symmetric iron(II) complexes. **A:** Synthesis of dicyclohexyl iron(II) complex, **5.21** from $n\text{BuLi}$ and iron(II) chloride. **B:** Attempted synthesis of **5.22** from **5.19**. Various bases ($n\text{BuLi}$, LDA, LiHMDS, KOtBu) and iron(II) sources (FeCl_2 , $[\text{Fe}[\text{N}(\text{SiMe}_3)_2]_2$, Fe_2Mes_4) and etherate solvents were ineffective at metalation.

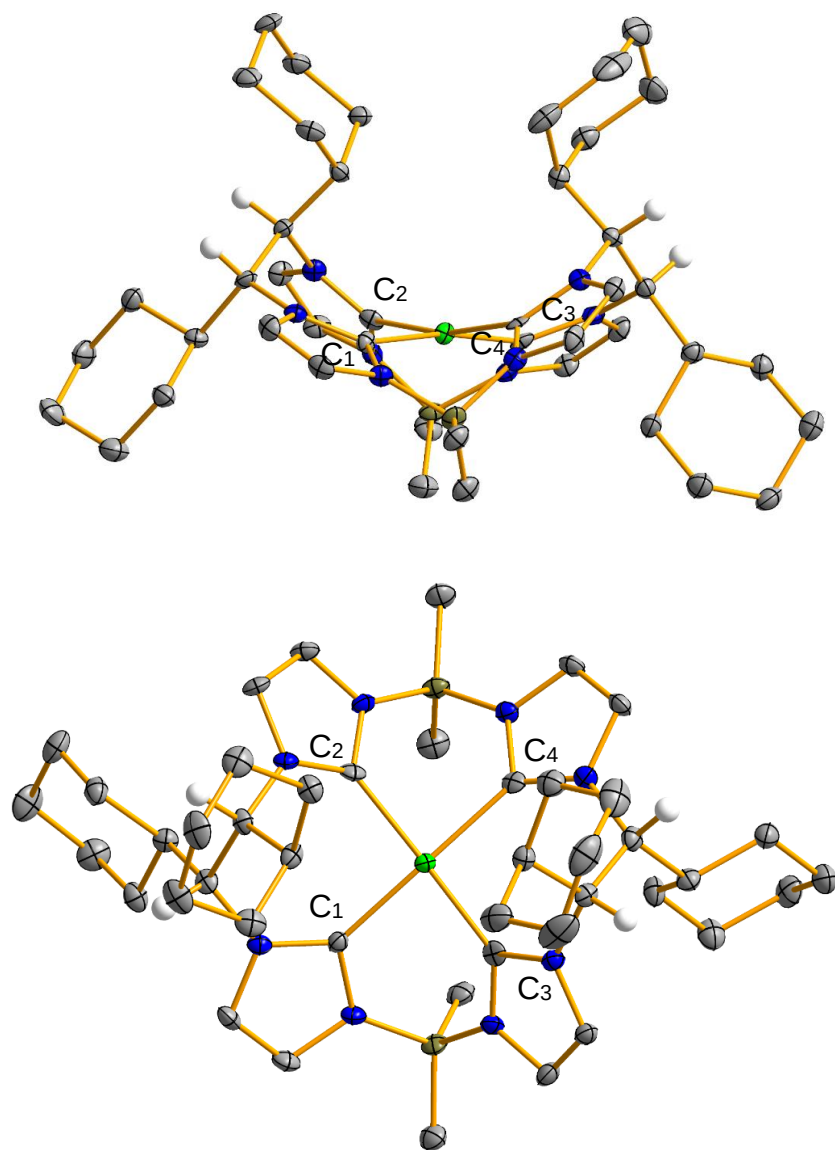


Figure 5.8: X-ray crystal structure of $[[((R,R)\text{-}1,2\text{-DiCy,BMe}_2\text{TCH})\text{Fe}]$, **5.21**. Green, blue, gray, red, olive, dark green, and white ellipsoids (50% probability) represent Fe, N, C, B, Cl, and H atoms, respectively. Solvent molecules and H-atoms not connected to stereogenic centers are omitted for clarity. Selected bond lengths (Å) and angles (°) are shown as followed: Fe-C₁: 1.993(5), Fe-C₂: 2.046(5), Fe-C₃: 1.984(5), Fe-C₄: 2.035(1), C₁-Fe-C₃: 167.24(19), C₂-Fe-C₄: 171.3(2).

which is much longer than **4.6** (0.045 Å longer) and has the longest Fe-C of any iron tetra-NHC to date.^{54, 68, 69, 72, 175} In addition, the τ_4 value is 0.029, which is much more square planar compared to **4.6**. With isolation of this, we are planning future work on this as an aziridination catalyst. Preliminary results show that this complex reacts with azides, but the reaction is extremely sluggish at room temperature compared to **4.6** (See Chapter 6).

We attempted the same reaction with **5.19** to form complex **5.22**, but we found that an insoluble precipitate formed when reacted with n BuLi. We were unable to conclusively determine why this occurred, but it appeared to be due to some sort of ligand decomposition, as it did not form any paramagnetic species on addition of iron chloride. Using weaker bases such as lithium diisopropyl amide (LDA), lithium bis(trimethylsilyl)amide (LiHMDS) and even potassium tert-butoxide (KOtBu), resulted in an intense dark purple solution upon immediate addition. Subsequent attempts at metalation did not result in this purple color disappearing and the resulting product did not have any paramagnetic peaks associated with it. We attempted *in-situ* deprotonation and metalation using reagents such as Ag₂O followed by FeCl₂, [Fe[N(SiMe₃)₂]₂]^{54, 175}, and [Fe₂Mes₄]²¹⁶, but no iron complex was formed. It is suspected that the chiral C-H is more acidic than the imidazolium protons, and results in degradation. Similarly, this same intense purple color is present in deprotonation of **5.20** which has not been metallated. Currently we are finding ways to circumvent this issue.

Conclusion

We have successfully utilized a previously described route to synthesize a variety of C₂ symmetric diimidazoles. The synthesis tolerates aryl, alkyl and fused vicinal 1,2-diamines. While this is the first method that tolerates all different types of diamines, there

are some limitations. For aryl derivatives, there can be different by products formed due to proximity of the imidazole moieties. For alkyl species, polymeric impurities are generated from the formation of the thiourea. Finally, for fused species, an ammonium-like impurity is observed as a result of the steric strain. The purified diimidazoles can be used to form both diimidazolium salts and macrocyclic tetra-imidazoliums from a borane source. We have been able to crystallographically characterize many of these ligands, and furthermore we have been able to synthesize and characterize the closest example of a chiral wall porphyrin analog as an iron(II) tetra-NHC complex.

Experimental

General Considerations for Synthesis:

All reactions and workups for NHC ligands were conducted under air, unless otherwise stated. All reactions, workups and manipulations involving the NHC metal complexes and subsequent reactions were done using standard Schlenk techniques under N₂ or in an MBraun Unilab glovebox under N₂, unless otherwise stated. All glassware for air sensitive reactions were dried at 170 °C overnight before use. For air sensitive reactions, tetrahydrofuran (THF), toluene, and hexanes were dried on an Innovative Technologies Pure Solv MD-7 Solvent Purification System, degassed by three freeze-pump-thaw cycles on a Schlenk line, and subsequently stored under activated 4 Å molecular sieves prior to use. Anhydrous acetonitrile (CH₃CN) was prepared by distillation over phosphorous pentoxide, followed by degassing by three freeze-pump-thaw cycles and stored over activated 4 Å molecular sieves prior to use. Benzene and pentane were purchased anhydrous from Sigma-Aldrich, degassed by three freeze-pump-thaw cycles and subsequently stored over activated 4 Å molecular sieves prior to use. Anhydrous benzene-*d*₆ (C₆D₆), was degassed by three freeze-pump-thaw cycles and subsequently stored over activated 4 Å molecular sieves prior to use. Celite and silica gel used in the synthesis of metal complexes were dried overnight at 240 °C and subsequently stored in the glovebox prior to use. All reagents were purchased from commercial vendors at highest purity. Raney Nickel (2800 mesh) was purchased from Oakwood and used within two months of opening. **5.1-NH₃Cl**⁹², **5.3-NH₃Cl**⁹², **5.4-NH₂**²⁰³, **5.5-NH₂**²¹⁰, **5.6-NH₂**²⁰⁴,

5.7-NH₂²⁰⁹, 5.8-NH₃Cl²⁰⁸, 5.9-NH₃Cl²⁰⁵, 5.11-NH₃Cl²⁰⁵ based on previously reported procedures.

General Considerations for Molecule Characterization:

Solution ¹H NMR and ¹³C NMR were performed on either a Varian Mercury 300 MHz or Varian VNMRs 500 MHz narrow-bore broadband system at 298 K. All ¹H and ¹³C shifts were referenced to the residual solvent. All solution 2D NMR experiments were performed on Varian VNMRs 600 MHz narrow-bore broadband system at 298 K. All mass spectrometry analyses were conducted at the Biological and Small Molecule Mass Spectrometry Center located in the Department of Chemistry at the University of Tennessee. The DART analyses on neutral organic molecules were performed using a JEOL AccuTOF-D time-of-flight (TOF) mass spectrometer with a DART (direct analysis in real time) ionization source from JEOL USA, Inc. (Peabody, MA) using either dichloromethane or methanol as the solvent. The ESI/MS analyses on charged organic molecules were performed using an Exactive Plus Orbitrap™ Mass Spectrometer (Thermo Scientific, San Jose, CA, USA) with sheath gas set to 25 arbitrary units, auxiliary gas set to 10 arbitrary units, spray voltage to 4kV, capillary temperature set to 350 °C, and resolution of 140,000. Infrared spectra were collected on a Thermo Scientific Nicolet iS10 with a Smart iTR accessory for attenuated total reflectance (ATR) using the neat complexes. UV-vis measurements were taken inside a dry glovebox on an Ocean Optics USB4000 UV-vis system with 1 cm path length quartz crystal cell. Carbon, hydrogen, and nitrogen analyses were obtained from Atlantic Microlab, Norcross, GA, Galbraith Laboratories Inc., Knoxville, TN or Midwest Microlab, Indianapolis, IN.

General Considerations for Crystallography:

All X-ray data collections were performed on single crystals coated in Paratone oil on glass slides and mounted on nylon fibers. Crystals for **5.21** were coated in Paratone oil, which had previously been degassed with N₂ and dried with a piece of sodium metal inside the glovebox. X-ray data for complexes **5.15**, **5.16**, **5.19**, **5.20** and **5.21** were collected with the use of a Mo microsource on a Bruker D8 Venture diffractometer. Crystals were mounted in a 100 K cold stream provided by an Oxford Cryostream low-temperature apparatus. All data sets were reduced with Bruker SAINT and were corrected for absorption using SADABS. Structures were solved and refined using SHELXT and SHELXL64, respectively.

Isolation of Diamines from Diammonium Chloride Salts:

The corresponding diammonium chloride salt was added to a round bottom flask. To this was added 1M NaOH solution. The mixture was stirred for 1 hour at room temperature. The slurry was diluted by half volume with H₂O and was added to a separatory funnel. The residue was washed with CH₂Cl₂ and the solution was extracted three times with CH₂Cl₂ (roughly 20 mL each extract per gram of diammonium chloride salt). The CH₂Cl₂ solution was dried with anhydrous MgSO₄, filtered and concentrated, yielding the free diamines.

General procedure of synthesis of aryl dithioureas (Method A):

In a round bottom flask, the corresponding free diamine was added with corresponding solvent (0.1M). To this solution was added isothiocyanate **4.1** (2 eq.) and the solution was either heated (2 hours) or stirred at room temperature (6 hours) depending on the conditions. The solution was concentrated and 1M HCl (0.1M) was added. The flask was

then heated overnight at 100 °C. The dithiourea precipitated out overnight. The solid was then filtered over a medium porosity frit and washed with copious amounts of water, yielding the pure dithiourea which was used without any further purification.

General procedure of synthesis of alkyl dithioureas (Method B):

To a round bottom flask, the free diamine was added with CH₂Cl₂ (0.1M concentration to diamine) followed by isothiocyanate **4.1** (2 eq.). The solution was stirred at room temperature for 6 hours. The CH₂Cl₂ was removed in vacuum, and then a 9:1 AcOH/H₂O solution (0.1M or 0.01M concentration to diamine) was added to the residue. The solution was heated at 100 °C overnight. The solution gradually turned dark brown. The solution was concentrated in vacuum and water was added to the solution. The same volume of ethyl acetate was added and the solution it was transferred to a separatory funnel. The solution was washed three times with H₂O and the ethyl acetate layer was dried with anhydrous MgSO₄, filtered and concentrated, yielding a dark brown foam. This foam typically contained an intractable impurity that could not be removed by chromatography, precipitation, crystallization or sublimation. The yields reported include this impurity in there but is indicated by an asterisk (*).

General procedure of synthesis of alkyl dithioureas from diammonium chloride salt (Method C):

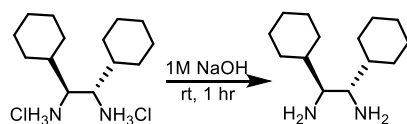
To a round bottom flask, the ammonium chloride salt was added in CH₂Cl₂ and stirred at room temperature. To the suspension, diisopropyl ethyl amine (DIEA, 2.1 eq.) was added and the solution was stirred for an addition 5-10 minutes. To this, the isothiocyanate **4.1** was added and the solution was allowed to stir at room temperature for 6 hours. The

CH₂Cl₂ was removed in vacuum and the solution. The 9:1 AcOH/H₂O (0.1 M) was added and the solution was heated overnight. The solution was then concentrated in vacuum and the residue was redissolved in ethyl acetate. This organic layer was washed 3 times with H₂O and the organic layer was dried with anhydrous MgSO₄, concentrated and dried yielding the product as a brown foam. The brown foam was triturated with diethyl ether to partially purify the species.

Procedure for desulfurization with NaNO₂ in HNO₃:

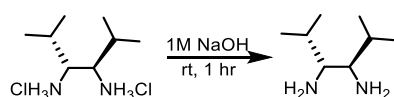
To a round bottom flask, the cyclic thiourea is added along with 2.5 M HNO₃ solution. The resulting slurry is stirred while cooling to 0 °C. To this solution, the NaNO₂ dissolved in a small amount of H₂O and was added. The solution was allowed to warm up to room temperature over 4 hours while cover with a septum. [**Caution**]: Over time, the sealed flask builds pressure due to NO_x gases formed. The flask must be vented periodically to prevent the septum bursting off and releasing NO_x gases. After the reaction completed, saturated K₂CO₃ was slowly added while stirring until the solution was fully basified. An equal volume of water was added and the solution was transferred to a separatory funnel using CH₂Cl₂ to wash in the water insoluble precipitate. The solution was extracted three times with CH₂Cl₂. The resulting solution was dried with anhydrous MgSO₄ and filtered and concentrated in vacuum to yield a foamy residue. This residue was purified by an appropriate method to yield the corresponding diimidazole.

Synthesis of 5.1-NH₂:



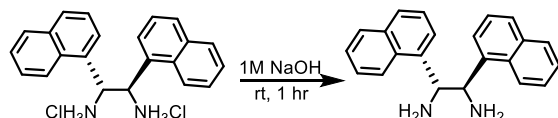
Based on general procedure using 6.1904 g of diammonium salt and 120 mL of 1M NaOH. Resulted in 3.412g of diamine as a fluffy white powder (73.0%). **¹H NMR** (CDCl₃, 499.74 MHz): δ 2.44 (dd, $J_1 = 9.2$ Hz, $J_2 = 3.0$ Hz, 2H), 1.84-1.71 (m, 6H), 1.70-1.63 (m, 4H), 1.37-1.08 (m, 12H), 1.00 (dq, $J_1 = 12.8$ Hz, $J_2 = 3.6$ Hz, 4H). Matches reported literature values.²¹⁷

Synthesis of 5.3-NH₂:



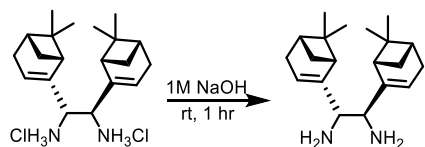
Based on general procedure using 4.177g of diammonium salt and 80 mL of 1M NaOH yielding 2.764 g of the diamine as a colorless oil (99.6%, quantitative). **¹H NMR** (CDCl₃, 499.74 MHz): δ 2.38 (dd, $J_1 = 4.4$ Hz, $J_2 = 1.4$ Hz, 2H), 1.73 (m, 2H), 1.25 (bs, 4H), 0.93 (d, $J = 6.7$ Hz, 6H), 0.89 (d, $J = 6.7$ Hz, 6H).

Synthesis of 5.9-NH₂:



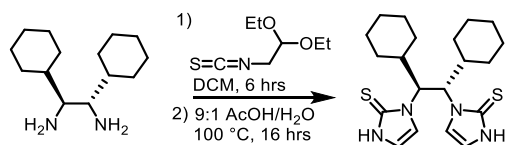
Based on general procedure using 0.200g of diammonium salt and 4 mL of NaOH yielding 0.0844 g of diamine as a white powder (52.0%). **¹H NMR** (CDCl₃, 499.74 MHz): δ 8.32 (d, $J = 8.5$ Hz, 2H), 7.88 (d, $J = 8.5$ Hz, 2H), 7.81 (d, $J = 7.3$, 2H), 7.77 (d, $J = 8.1$ Hz, 2H), 7.61-7.46 (m, 6H), 5.13 (s, 2H).

Synthesis of 5.8-NH₂:



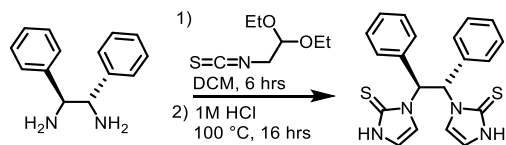
Synthesized based on general procedure using 0.2023g of ammonium salt in 8 mL of 1M NaOH solution yielding 0.1155g of a white powder (70.9%). ¹H NMR (CDCl₃, 499.74 MHz): δ 5.30 (m, 2H), 3.12 (s, 2H), 2.38 (t, *J* = 5.7 Hz, 1H), 2.35 (t, *J* = 5.7 Hz, 1H), 2.24-2.19 (m, 4H), 2.13 (dt, *J*₁ = 5.7 Hz, *J*₂ = 1.6 Hz, 2H), 2.10-2.03 (m, 2H), 1.28 (s, 6H), 1.26 (bs, 2H), 1.18 (d, *J* = 8.5 Hz, 2H), 0.83 (s, 6H).

Synthesis of 5.1-Thiourea:



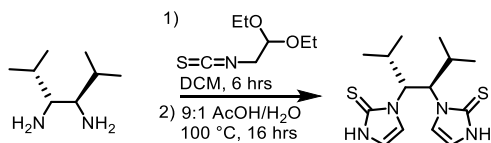
Synthesized based on **Method C** using 1.000g (3.365 mmol, 1 eq.), 1.198 mL of DIEA (6.730 mmol, 2 eq.), 1.179g of **4.1** (6.730 mmol, 2 eq.) and 34 mL of CH₂Cl₂. The concentration for the hydrolysis was 0.01M 9:1 AcOH/H₂O solution (336 mL). Yielded g of a brown powder (0.2671 g, 20.3%). ¹H NMR (CDCl₃, 499.74): δ 10.72 (s, 2H), 6.81 (s, 2H), 6.43 (s, 2H), 5.42 (s, 2H), 2.09 (d, *J* = 12.8 Hz, 2H), 1.96-1.55 (m, "22"H), 1.40-1.22 (m, "7"H), 1.18-0.79 (m, "13"H).

Synthesis of 5.2-Thiourea:



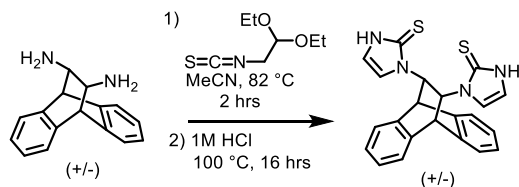
Synthesized based on **Method A** using diamine (10.00 g, 47.10 mmol) and isothiocyanate (16.51 g, 94.21mmol) in CH_2Cl_2 (236 mL) and stirred for 6 hours at room temperature. Part 2 used 236 mL of 1M HCl at 0.1 M concentration in relation to diamine yielding a white solid (16.37 g, 91.9%). $^1\text{H NMR}$ (CDCl_3 , 499.74 MHz): δ 11.19 (s, 2H), 7.56-7.51 (m, 4H), 7.31-7.20 (m, 6H), 7.16-7.12 (m, 4H), 6.44 (t, $J = 2.5$ Hz, 2H).

Synthesis of 5.3-Thiourea:



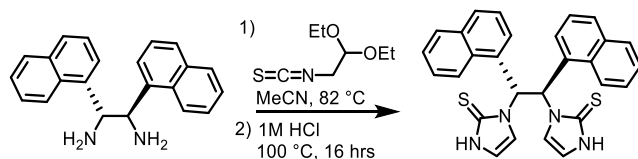
Synthesized using **Method B** using 2.764g of the free diamine (19.160 mmol, 1 eq.), in 192 mL CH_2Cl_2 and 6.7188g **4.1** (38.32 mmol, 2 eq.). Used 9:1 AcOH/ H_2O (0.1M, 192 mL) and yielded a fluffy brown solid (4.77 g, 80.2*%). $^1\text{H NMR}$ (CDCl_3 , 499.74 MHz): δ 10.82 (s, 2H), 6.85 (d, $J = 2.6$ Hz, 2H), 6.45 (d, $J = 2.6$ Hz, 2H), 5.40 (t, $J = 1.9$ Hz, 2H), 2.35 (sept, $J = 6.8$ Hz, 2H), 1.07 (d, $J = 6.9$ Hz, 6H), 1.03 (d, $J = 6.9$ Hz, 6H).

Synthesis of 5.6-Thiourea:



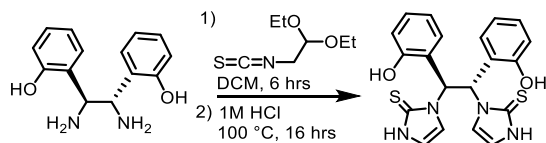
Synthesized using **Method A** using 0.5044g of diamine (2.134 mmol, 1 eq.) and 0.6881 (4.268 mmol, 2 eq.), and 21 mL of CH₃CN at reflux. Yielded the product as an off white solid (0.1621, 18.8%). ¹H NMR (DMSO-d₆, 499.74 MHz): δ 12.30 (s, 2H), 7.59 (d, *J* = 7.1 Hz, 2H), 7.37-7.20 (m, 6H), 6.76 (d, *J* = 2.5 Hz, 2H), 5.36 (s, 2H), 5.32 (t, *J* = 2.1 Hz, 2H), 4.54 (s, 2H).

Synthesis of 5.9-Dithiourea:



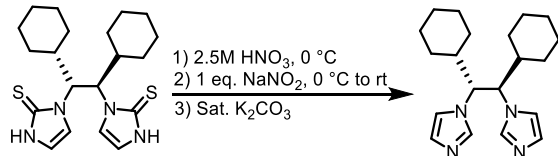
Synthesized using **Method A** using 0.0394 g of free diamine (0.1261 mmol, 1 eq.) and 0.0443 g of **4.1** (0.2522 mmol, 2 eq.) and 2 mL of CH₃CN at reflux. This yielded the product as a white solid (0.0256 g, 53.5%). ¹H NMR (DMSO-d₆, 499.74 MHz): δ 12.06 (s, 2H), 8.97 (d, *J* = 8.6 Hz, 2H), 8.06 (d, *J* = 7.4 Hz, 2H), 7.94 (s, 2H), 7.78 (d, *J* = 8.0 Hz, 2H), 7.72 (d, *J* = 8.0 Hz, 2H), 7.57-7.33 (m, 10H), 6.78 (t, *J* = 2.2 Hz, 2H).

Synthesis of 5.10-Thiourea:



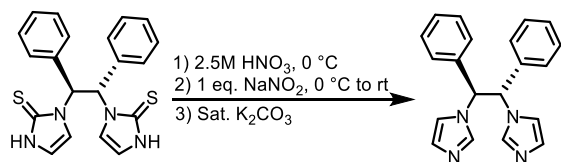
Synthesized based on **Method A** using 0.0244g (0.100 mmol, 1 eq.) of the free diamine and 0.0351 g of **4.1** (0.200 mmol, 2 eq.) and 1 mL of CH_3CN at reflux. This yielded the product as a light brown solid (0.0092 g, 22.3%). ^1H NMR ($\text{DMSO}-d_6$, 499.74 MHz): δ 11.92 (s, 2H), 10.03 (s, 2H), 7.52 (dd, $J_1 = 7.7$ Hz, $J_2 = 1.7$, 2H), 7.45 (t, $J = 2.2$ Hz, 2H), 7.43 (s, 2H), 6.95 (dt, $J_1 = 7.8$ Hz, $J_2 = 1.7$ Hz, 4H), 6.73 (t, $J = 2.5$ Hz, 2H), 6.67-6.54 (m, 6H).

Synthesis of 5.1-Imidazole:



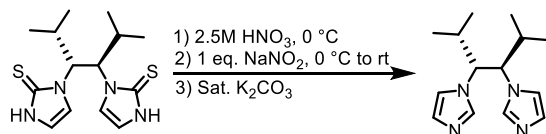
Based on general procedure using 6.846 g of **5.1-Thiourea** (17.53 mmol, 1 eq.) and 1.209 of NaNO_2 (17.53 mmol, 1 eq.) in 175 mL of 2.5 M HNO_3 . After the general work up, the fluffy solid was vacuum sublimed at 180-185 °C at 100 mtorr. The product deposited as a wax on the sublimation finger and was washed off with CH_2Cl_2 and concentrated yielding the product was a brown solid (1.079g, 18.9%). ^1H NMR (CDCl_3 , 499.74 MHz): δ 7.29 (s, 2H), 7.01 (s, 2H), 6.52 (s, 2H), 4.19 (d, $J = 8.4$ Hz, 2H), 2.05 (m, 2H), 1.90-1.60 (m, "25"H), 1.45-0.78 (m, "27"H).

Synthesis of 5.2-Imidazole:



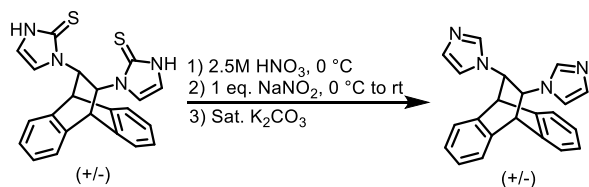
Based on the general procedure using 4.263 g of **5.2-Thiourea**, 0.6741 g of NaNO₂ and 67 mL of 2.5 M HNO₃. After general work up, the residue was purified using gradient column chromatography from 5% MeOH/CH₂Cl₂ to 10% MeOH/CH₂Cl₂, yielding the product 1.250g of a white powder (40.1%). ¹H NMR (CDCl₃, 499.74 MHz): δ 7.29-7.26 (m, 6H), 7.25-7.20 (m, 4H), 6.99 (t, *J* = 1.0 Hz, 2H), 6.75 (t, *J* = 1.4 Hz, 2H), 5.86 (s, 2H).

Synthesis of 5.3-Imidazole:



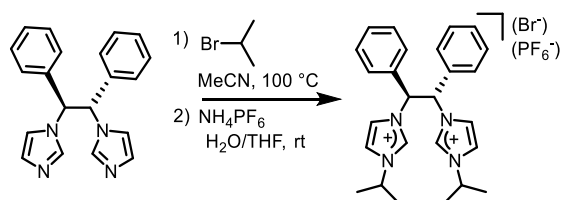
Based on the general procedure using 4.352 g of **5.3-Thiourea** (14.02 mmol, 1 eq.) and 0.9670 (14.02 mmol, 1 eq.) in 140 mL of 2.5 M HNO₃ solution. After the general work up, the product was vacuum sublimed at 90 °C at 85 mtorr. The product deposited as a wax on the sublimation finger and was washed off with CH₂Cl₂ and concentrated yielding the product as a brown wax (0.7420g, 21.5%). ¹H NMR (CDCl₃, 499.74 MHz): δ 7.30 (s, 2H), 7.00 (s, 2H), 6.55 (s, 2H), 4.09 (d, *J* = 8.5 Hz, 2H), 2.06 (sept, *J* = 7.1 Hz, 2H), 1.15 (d, *J* = 6.6 Hz, 6H), 0.77 (d, *J* = 6.6 Hz, 6H).

Synthesis of 5.6-Imidazole:



Based on general procedure using 0.2111 g of dithiourea (0.5244 mmol, 1 eq.) and 0.0036 (0.0524 mmol, 0.1 eq.) and 5 mL of 2.5 M HNO₃. This yielded a yellow foam that could be purified by crystallization using CH₂Cl₂ and ether yielding a off white powder (0.0509g, 25%). ¹H NMR matches literature values.⁸⁹

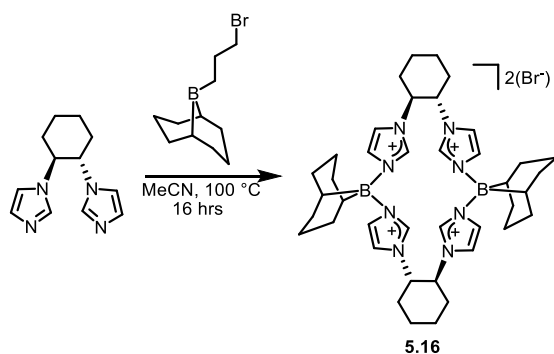
Synthesis of 5.15:



Diimidazole (0.9037, 2.880 mmol, 1 eq.) and isopropyl bromide (2.695 mL, 28.83 mmol, 10 eq.) were added in 15 mL of CH₃CN. The solution was heated at 100 °C for 16 hours. The reaction mixture was cooled and then diluted with an equal volume of diethyl ether. The solution was filtered over a medium porosity frit collected. The solid was dried and then redissolved in 16 mL of 1:1 H₂O/THF solution. This was added slowly dropwise to a solution of NH₄PF₆ in 40 mL of H₂O. The viscous suspension was filtered over a fine frit and washed with copious amounts of water. This residue was then dissolved in acetone and filtered through the same frit. The solution was concentrated and left with a fluffy off white solid (1.525g, 84.7%). Single crystals of **5.15** were grown by diffusion of diethyl ether into an acetonitrile solution of **5.15**. ¹H NMR (CD₃CN, 499.74 MHz): δ 8.73

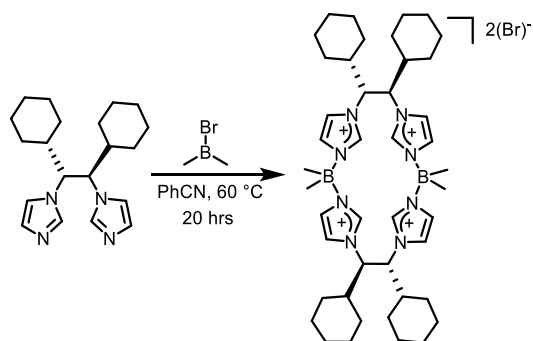
(t, $J = 1.7$ Hz, 2H), 7.61-7.56 (m, 6H), 7.50 (t, $J = 1.9$ Hz, 2H), 7.42-7.35 (m, 6H), 6.69 (s, 2H), 4.55 (sept, $J = 6.8$ Hz, 2H), 1.45 (d, $J = 3.4$ Hz, 6H), 1.44 (d, $J = 3.4$ Hz, 6H). ^{13}C NMR (CD_3CN , 124.94 MHz): δ 134.83, 133.32, 131.37, 130.69, 129.54, 123.19, 121.84, 66.11, 54.97, 30.84, 22.57, 22.55.

Synthesis of **5.16**:



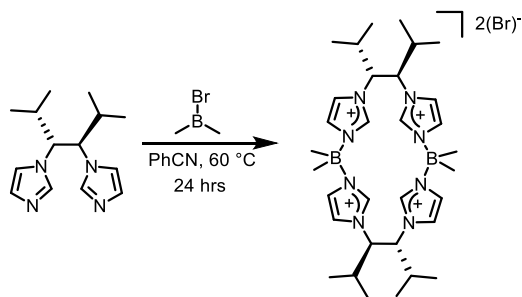
In a nitrogen filled glovebox, **4.3** (0.200 g, 0.9247 mmol, 1 eq.) was added to a thick-walled pressure vial. To this was added 3 mL of CH_3CN and stirred until full dissolution. To this solution was added the borane²¹³ (0.2247g, mmol, 1 eq.). The vial was sealed and removed from the glovebox and heated at 90 °C overnight, gradually resulting in light blue precipitate. This precipitate was washed with acetonitrile followed by ether resulting in the white powder (0.2036 g, 52.8%). Single crystals of **5.16** were grown by vapor diffusing diethyl ether into a solution of **5.16** in MeOH. ^1H NMR (DMSO-d_6 , 499.74 MHz): δ 8.97 (s, 4H), 7.42 (s, 4H), 6.95 (s, 4H), 5.04 (s, 4H), 2.30 (d, $J = 11.3$ Hz, 4H), 1.98-1.22 (m, 40H).

Synthesis of **5.17**:



In a nitrogen filled glovebox, **5.1-Imidazole** (0.500g, 1.531 mmol, 1 eq.) was dissolved in 10 mL PhCN in a 20 mL scintillation vial. To this, bromodimethylborane (180 μL , 1.837 mmol, 1.2 eq.) was added. The resulting slurry was heated for 20 hours at 60°C . The reaction was then taken out of the glovebox and precipitated with 10 mL of CH_3CN . This solid was filtered over a fine porosity frit and washed with additional CH_3CN (30 mL) and then diethyl ether (80 mL) yielding **5.17** as a white powder (0.2208 g, 32.2%). Single crystals were grown from a batch from another batch using the enantiomer by diffusing diethyl ether into a methanol solution of **5.17**. Minor peaks are *italicized*. ^1H NMR (DMSO- d_6 , 499.74 MHz): δ 8.74 (s, 4H), 8.66 (s, *4H*), 7.45 (s, 4H), 7.42 (s, *4H*), 6.95 (s, *4H*), 6.88 (s, 4H), 5.37 (s, *4H*), 5.25 (s, 4H). ^1H NMR (CD_3OD , 499.74 MHz): δ 8.63 (s, 4H), 7.44 (s, 4H), 7.02 (s, 4H), 5.20 (s, 4H),

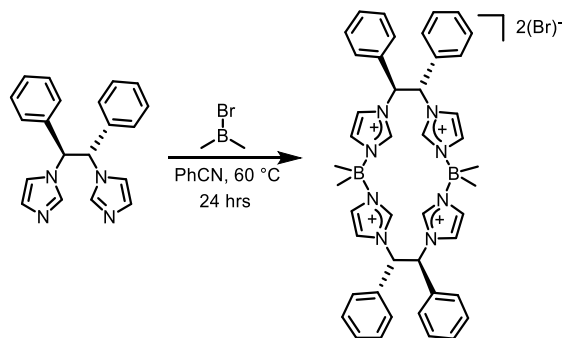
Synthesis of 5.18:



Reacted and worked up identically to **5.17** using 0.0412 g (0.1673mmol, 1 eq.) of **5.3-Imidazole**, 1 mL of PhCN and 30 uL of bromodimethylborane (0.3075 mmol, 1.8 eq.). Product was isolated as a white powder (0.0089 g, 14.4%). Minor peaks are *italicized*.

^1H NMR (DMSO- d_6 , 499.74 MHz): δ

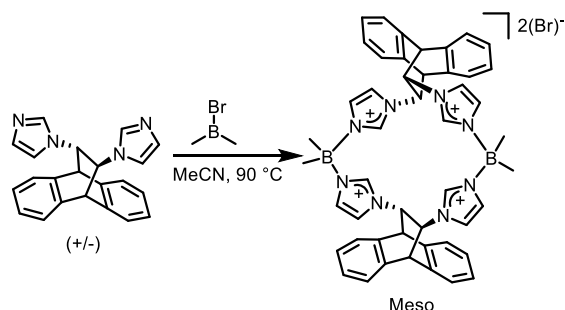
Synthesis of 5.19:



In a nitrogen filled glovebox, **5.2-Imidazole** (0.0795g, 0.2516, 1 eq.) was dissolved in 1 mL of PhCN in a 20 mL scintillation vial. To this, bromodimethylborane (25 uL, 0.2516 mmol, 1 eq.) was added. This resulting green slurry was stirred at 60 °C for 24 hours. The reaction was then taken outside the glovebox and filtered over a 15 mL fine porosity frit. The solid was then washed by CH₃CN (10 mL) followed by diethyl ether (30 mL), yielding 0.0477g of macrocycle (43.4%) as a white powder. ^1H NMR (DMSO- d_6 , 499.74

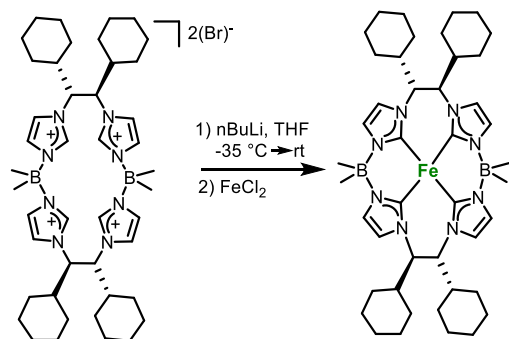
MHz): δ 9.38 (s, 4H), 8.19 (s, 4H), 7.77 (d, J = 8.2 Hz, 8H), 7.41-7.37 (m, 12H), 7.31 (t, J = 7.4 Hz, 4H), 7.17 (s, 4H), 0.22 (s, 12H).

Synthesis of **5.20**:



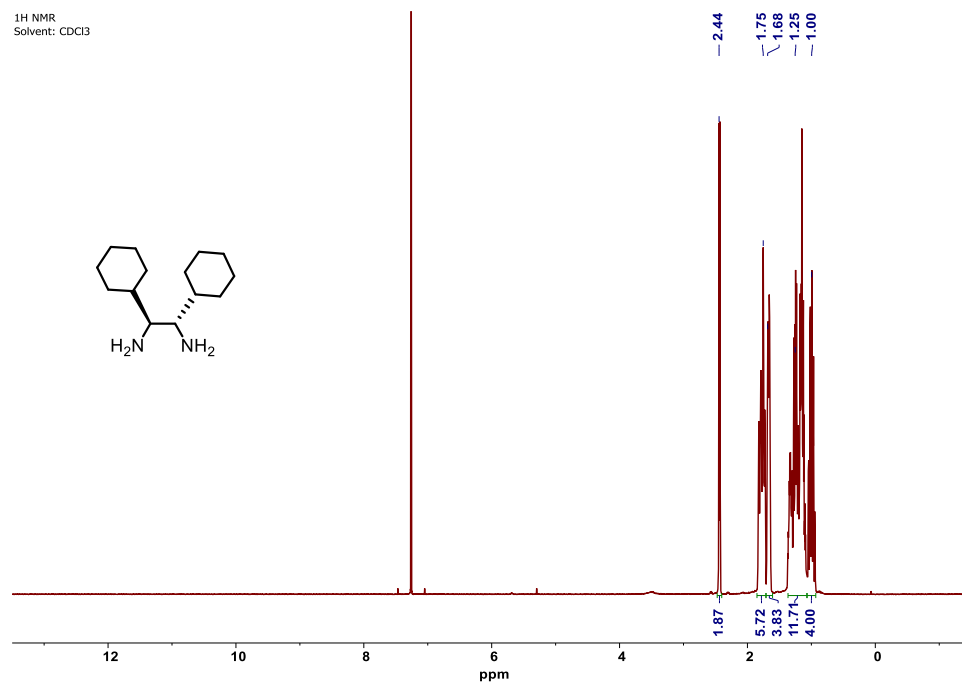
In a nitrogen filled glovebox, **5.6-Imidazole** (0.020g, 0.0591 mmol, 1 eq.) was dissolved in 1 mL of CH₃CN in a 20 mL scintillation vial. To this, bromodimethylborane (6 μ L, 0.0591, 1 eq.) was added. The slurry was then heated at 90 °C for 20 hours. The resulting solid was filtered over a fine porosity frit, washed with additional CH₃CN (10 mL) and diethyl ether (30 mL) resulting in **5.20** as a white solid (0.0125 g, 46%). Single crystals of **5.20** were grown by diffusion of diethyl ether in a solution of **5.20**. ¹H NMR (DMSO-d₆, 499.74 MHz): δ 7.59 (d, J = 7.5, 4H), 7.43 (d, J = 12.9 Hz, 8H), 7.37-7.32 (m, 4H), 7.27-7.23 (m, 8H), 6.65 (s, 4H), 5.19 (s, 4H), 4.82 (s, 4H), 0.13 (s, 6H), -0.20 (s, 6H).

Synthesis of **5.21**:

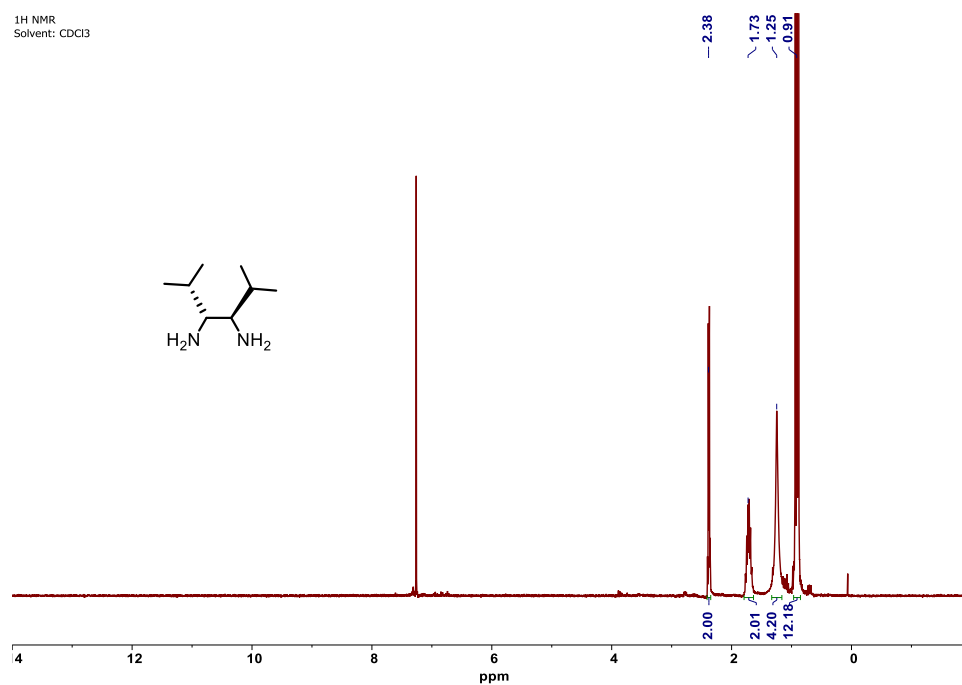


In a nitrogen filled glovebox, **5.17** (0.200 g, 0.2236 mmol, 1 eq.) was added to a 20 mL scintillation vial with 15 mL of THF and cooled to $-35\text{ }^{\circ}\text{C}$. To this, $n\text{BuLi}$ (0.367 mL, 0.9168 mmol, 4.1 eq.) was added and the solution was allowed to warm up to room temperature and all the solid went into solution over 1 hour. The solution was then quantitatively transferred to another vial containing and FeCl_2 (0.0327g, mmol, 1 eq.). The solution was then stirred at ambient temperature for 24 hours. THF was then removed in vacuum and pentane was added (5 mL x 3) and dried to thoroughly remove lingering THF. To this, 15 mL of hexanes were added, and the solution was filtered. The yellow solution was concentrated yielding **5.21** as an orange/yellow solid (0.0051 g, 2.90%). Single crystals were grown by slow diffusion of a hexanes solution of **5.21** into CH_3CN at $-35\text{ }^{\circ}\text{C}$. **^1H NMR** (C_6D_6 , 499.74 MHz): δ 50.04, 34.88, 31.05, 27.12, 22.30, 20.98, 20.68, 16.79, 15.09, 14.24, 10.98, 10.92, 10.28, 9.22, 7.45, 5.39, 5.21, 5.18, 4.86, 4.85, 0.17, -0.64, -1.50, -1.85, -2.20, -2.77, -3.17, -3.47, -4.04, -4.75, -4.99, -5.62, -6.13, -6.47, -6.60, -7.35, -9.13, -10.42, -13.19, -14.55, -16.41, -20.41, -20.50, -32.16, -39.85, -65.32, -70.10.

Selected NMR Spectra:

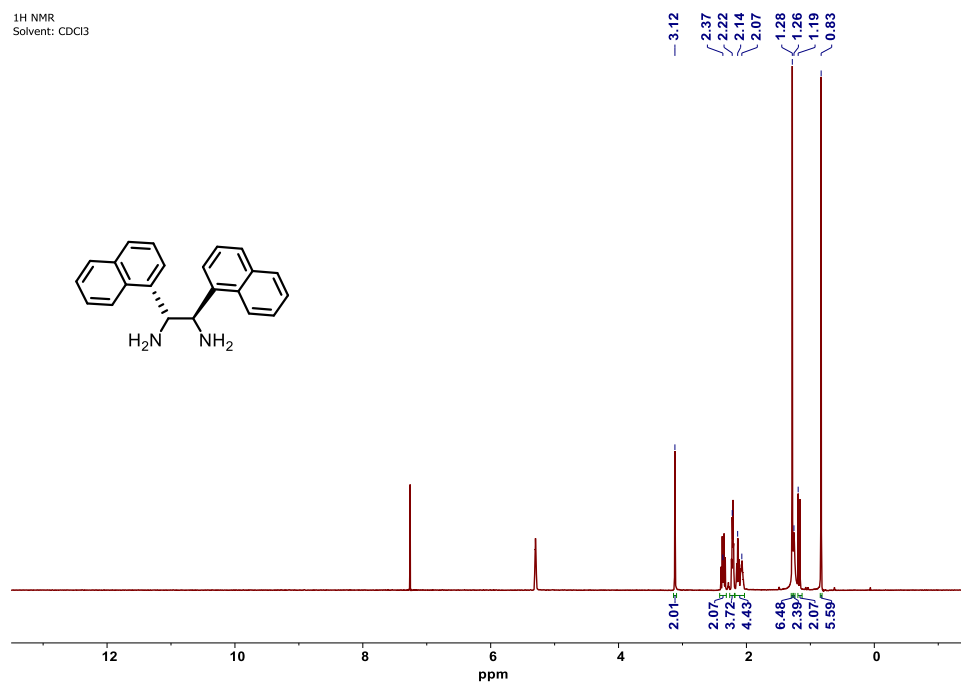


Spectrum 5.1: ¹H:



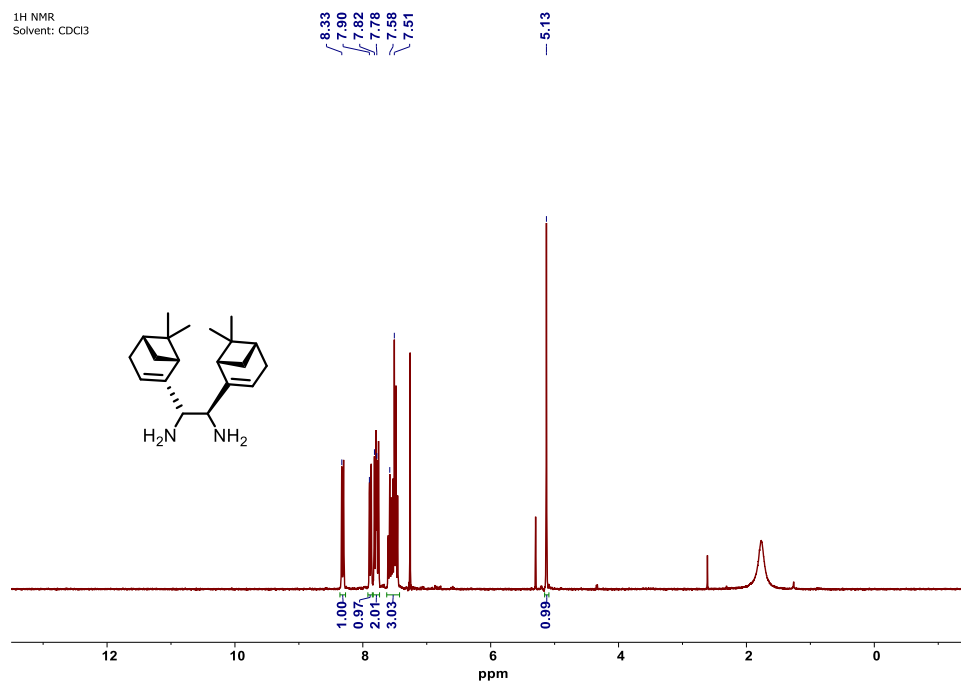
Spectrum 5.2: ¹H NMR of 5.3-NH₂ in CDCl₃.

¹H NMR
Solvent: CDCl₃

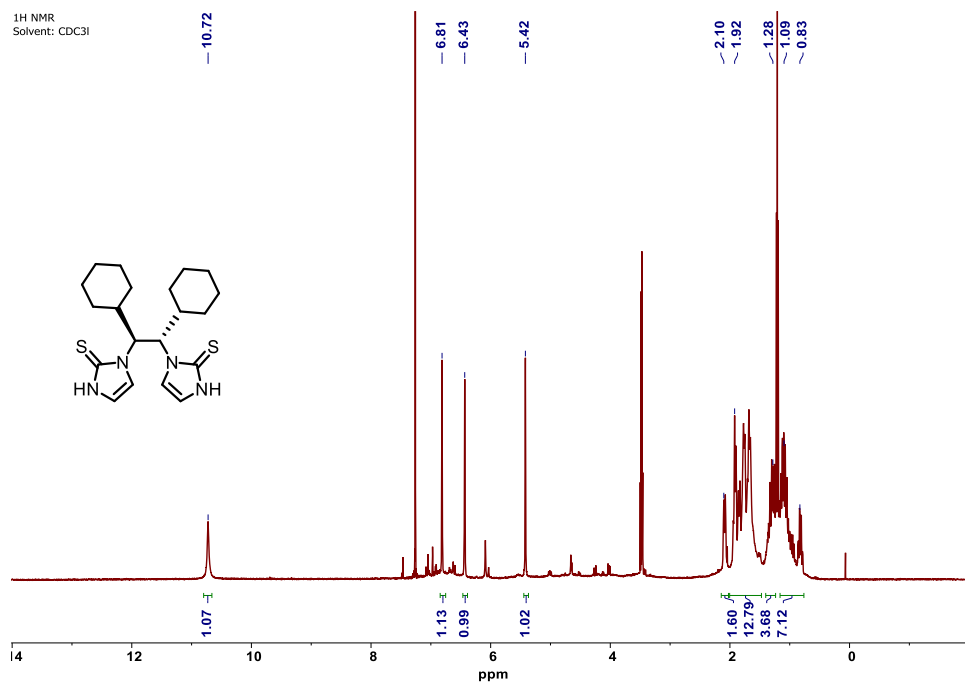


Spectrum 5.3: ¹H NMR of **5.8-NH₂** in CDCl₃.

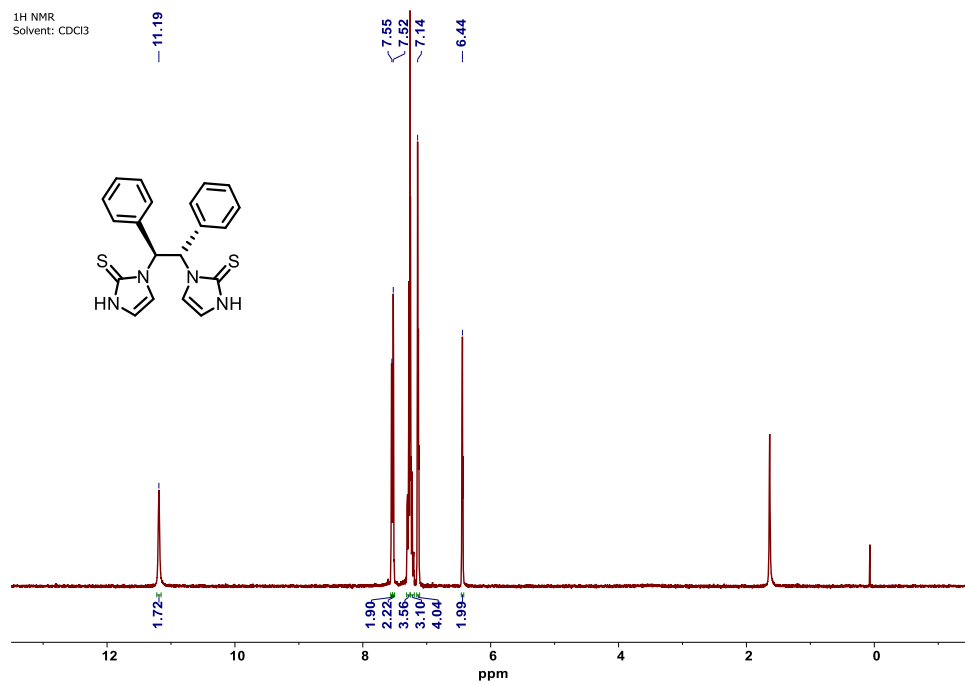
¹H NMR
Solvent: CDCl₃



Spectrum 5.4: ¹H NMR of **5.9-NH₂** in CDCl₃.

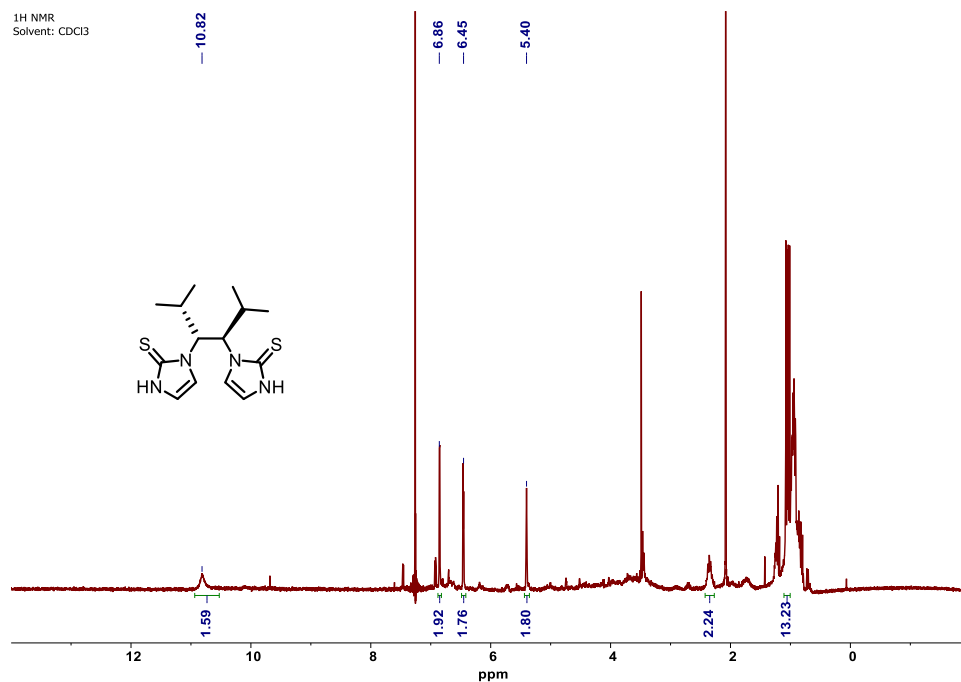


Spectrum 5.5: ¹H NMR of **5.1-Dithiourea** in CDCl₃



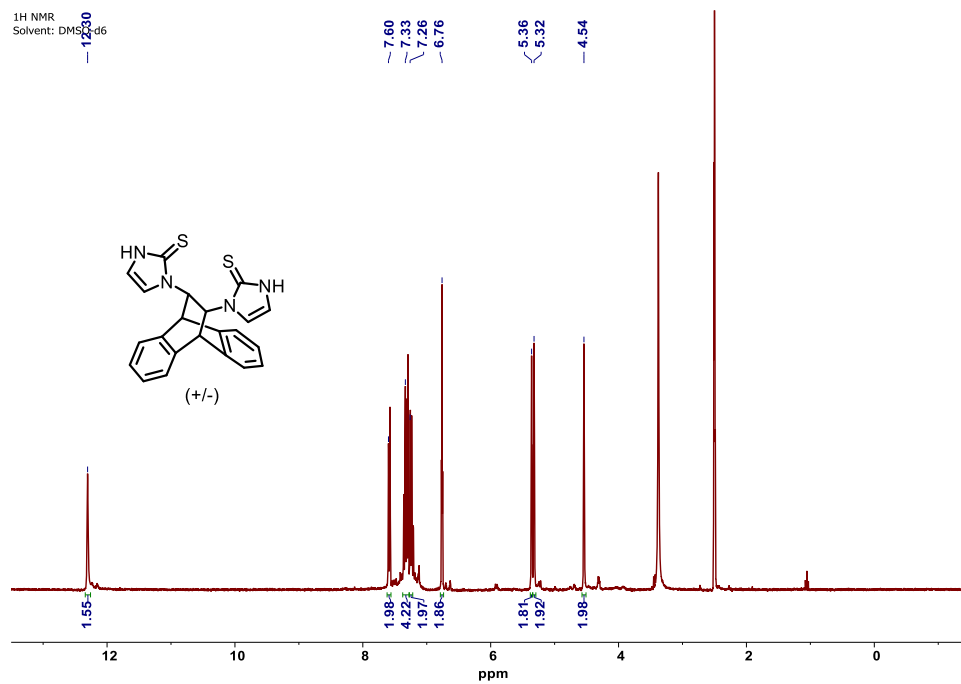
Spectrum 5.6: ¹H NMR of **5.2-Dithiourea** in CDCl₃.

¹H NMR
Solvent: CDCl₃

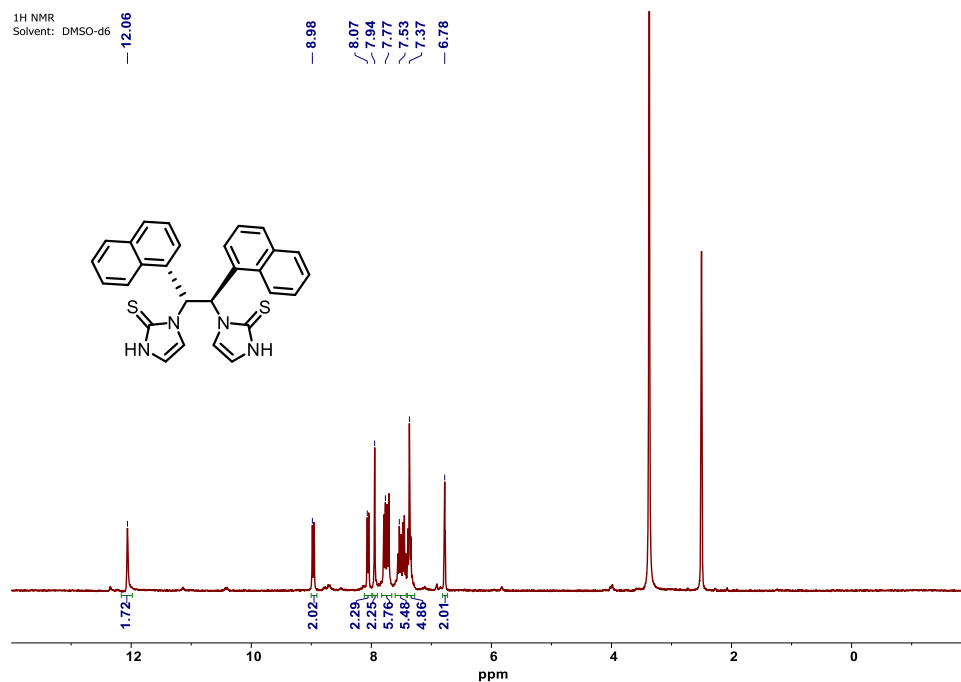


Spectrum 5.7: ¹H NMR of **5.3-Dithiourea** in CDCl₃.

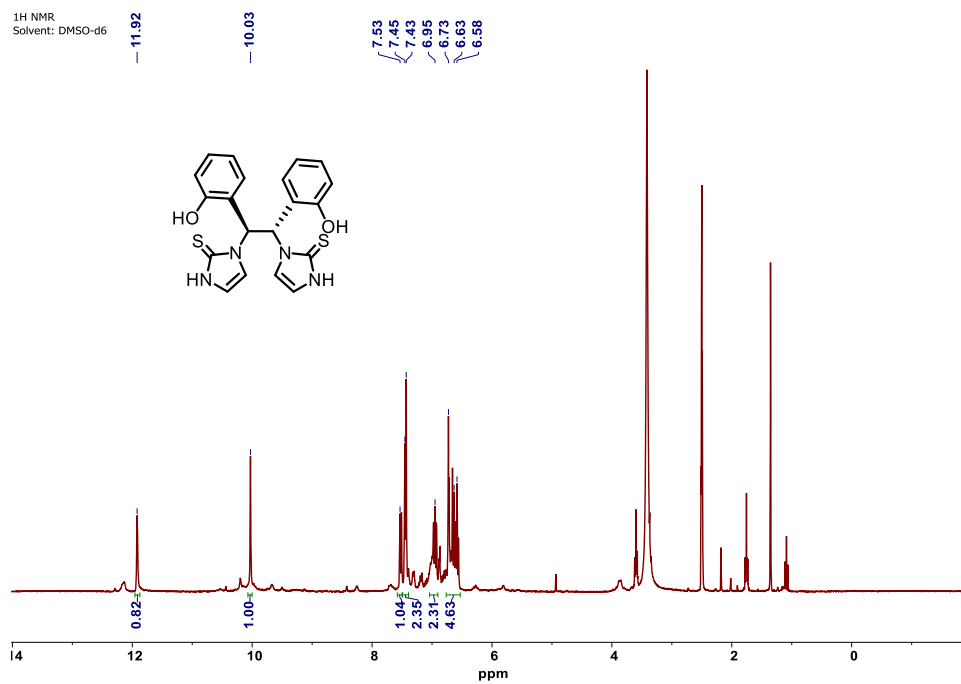
¹H NMR
Solvent: DMSO-d₆



Spectrum 5.8: ¹H NMR of **5.6-Dithiourea** in DMSO-d₆.

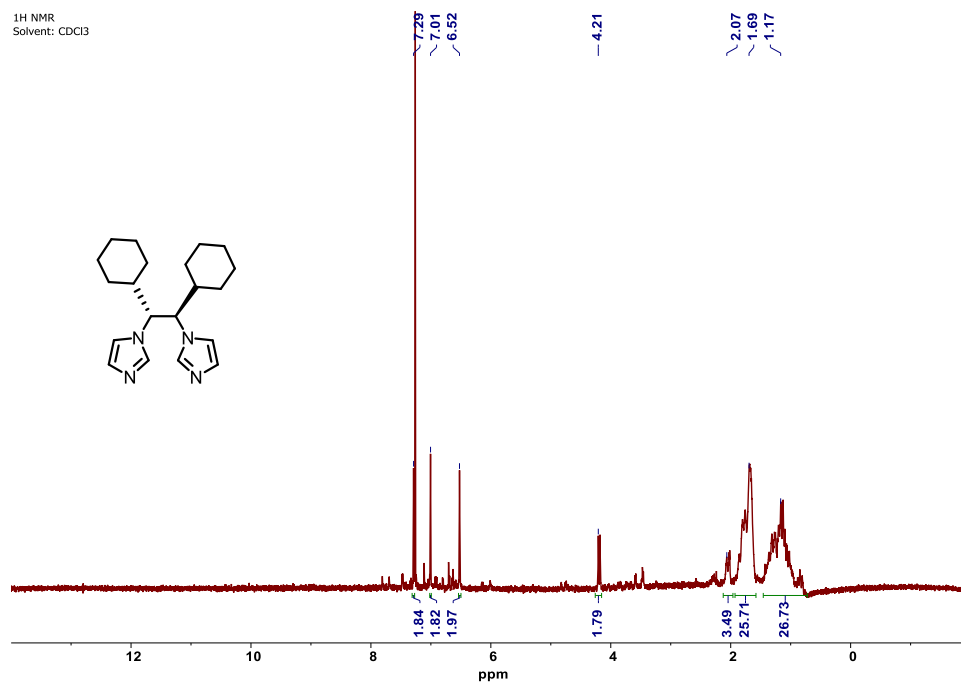


Spectrum 5.9: ¹H NMR of **5.9-Dithiourea** in DMSO-d₆.



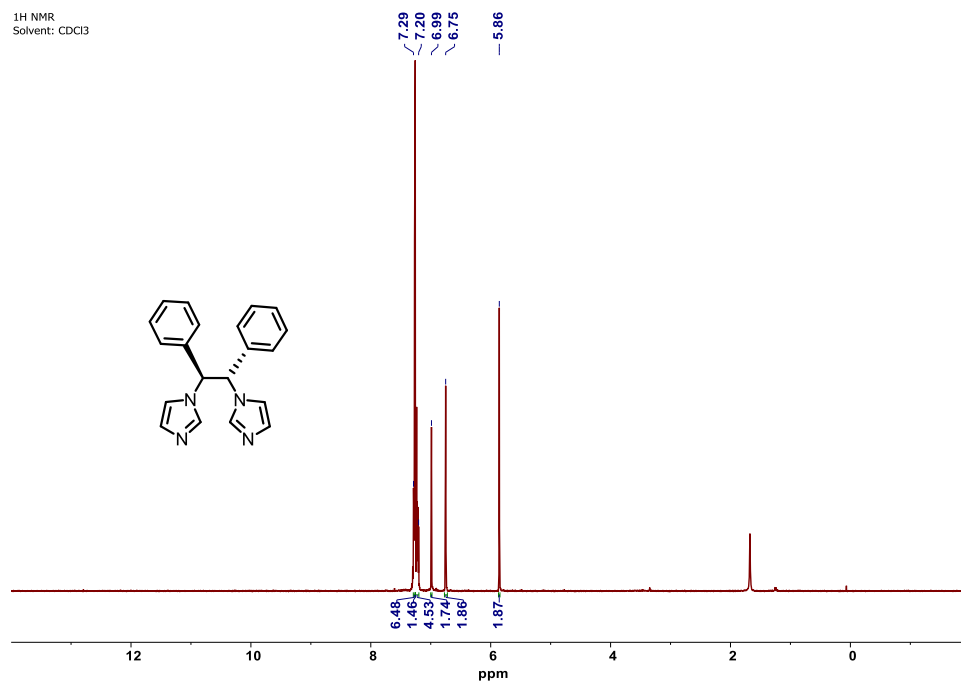
Spectrum 5.10: ¹H NMR of **5.10-Dithiourea** in DMSO-d₆.

¹H NMR
Solvent: CDCl₃



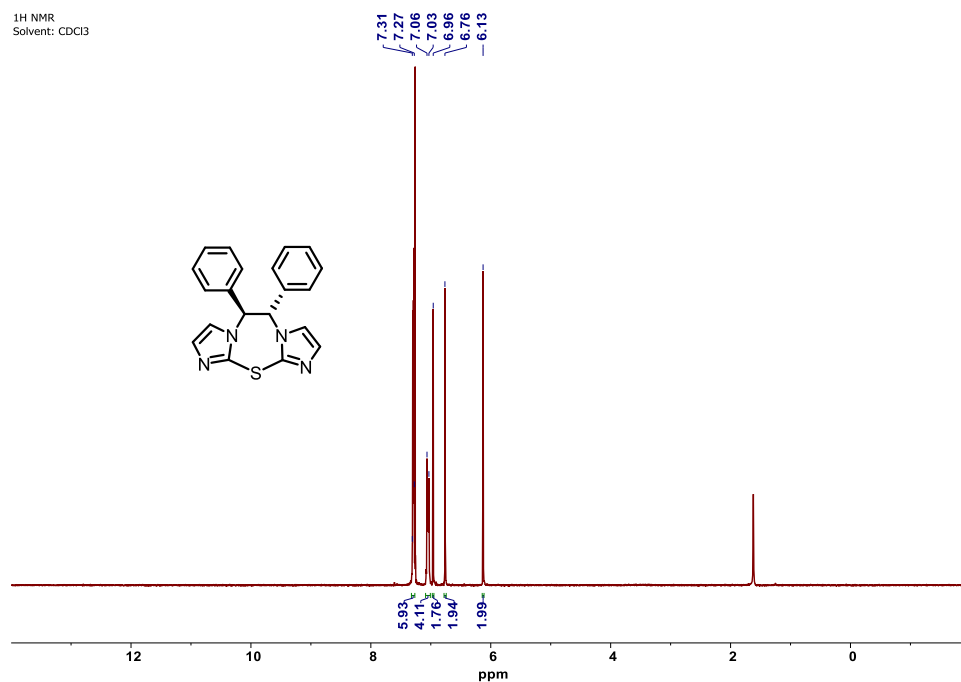
Spectrum 5.11: ¹H NMR of **5.1-Imidazole** in CDCl₃.

¹H NMR
Solvent: CDCl₃



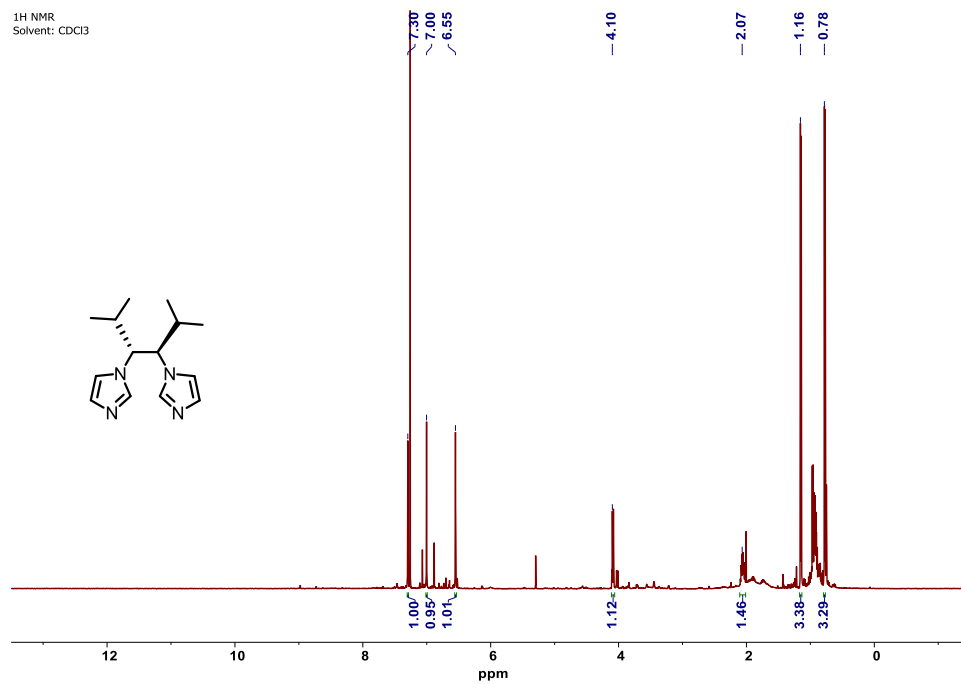
Spectrum 5.12: ¹H NMR of **5.2-Imidazole** in CDCl₃.

¹H NMR
Solvent: CDCl₃



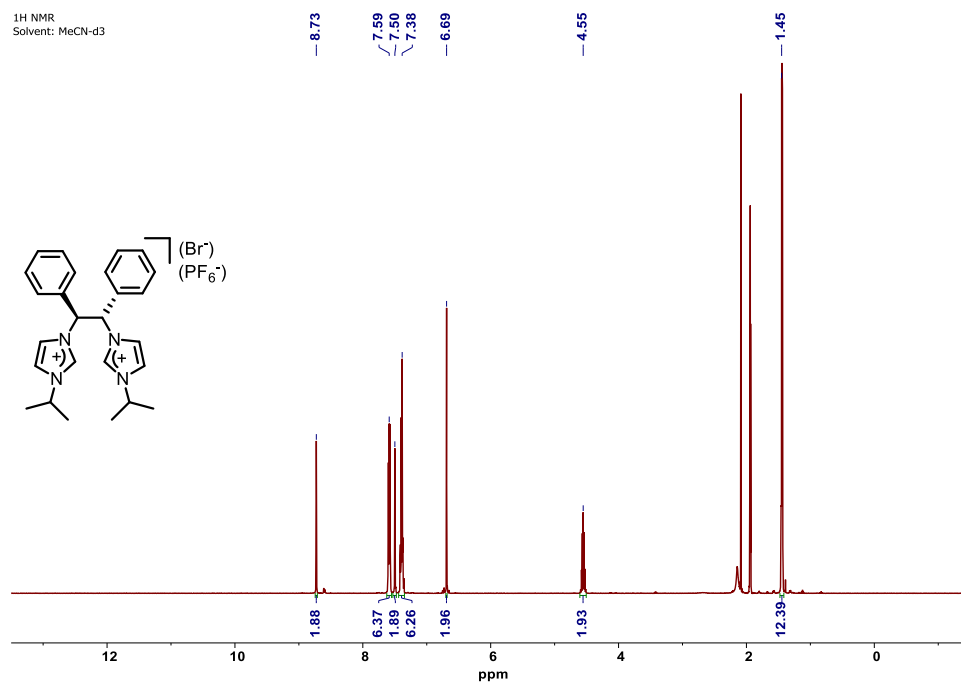
Spectrum 5.13: ¹H NMR of **5.2-Sulfide** in CDCl₃.

¹H NMR
Solvent: CDCl₃



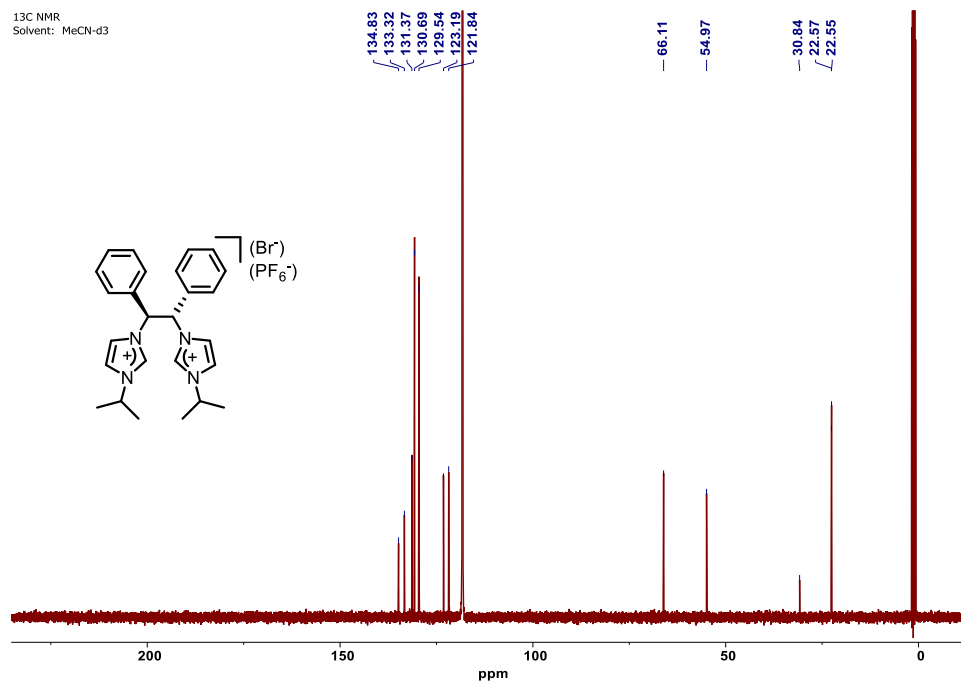
Spectrum 5.14: ¹H NMR of **5.3-Imidazole** in CDCl₃.

¹H NMR
Solvent: MeCN-d₃



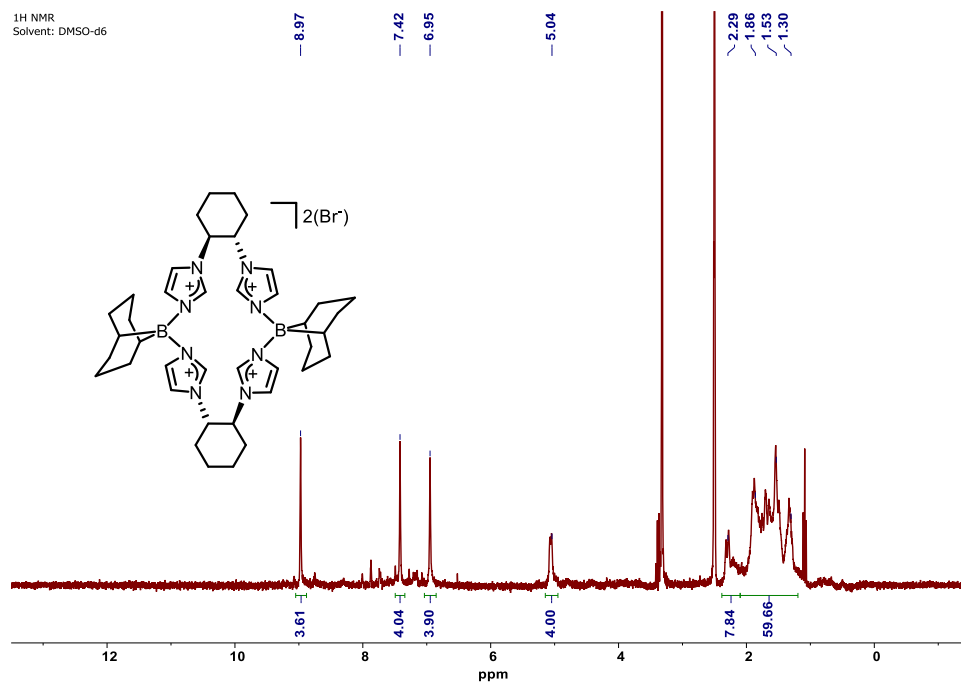
Spectrum 5.15: ¹H NMR of **5.15** in CD₃CN.

¹³C NMR
Solvent: MeCN-d₃



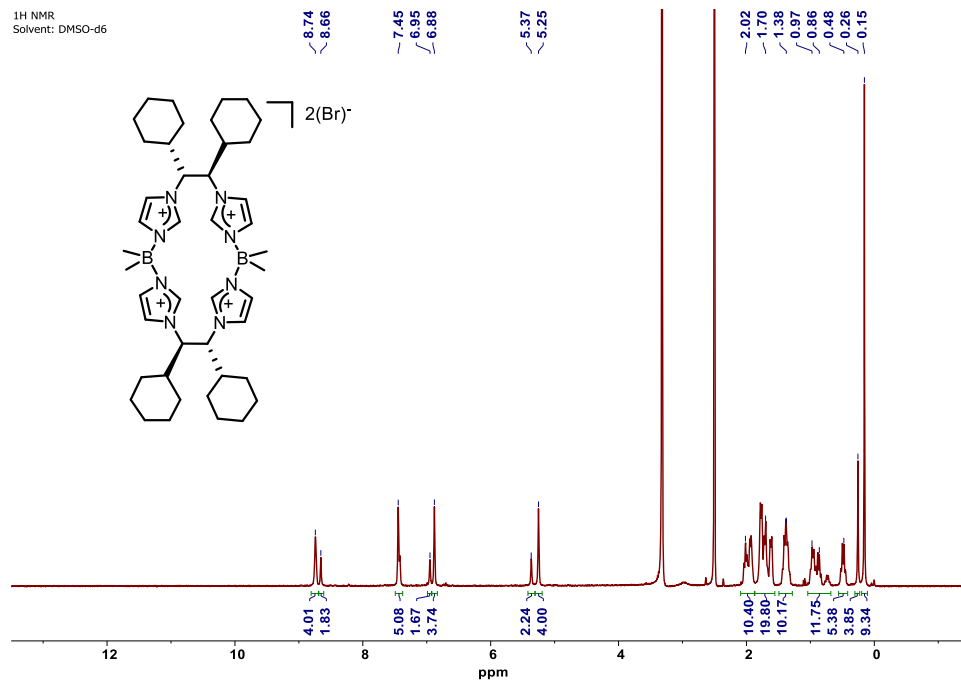
Spectrum 5.16: ¹³C NMR of **5.15** in CD₃CN.

¹H NMR
Solvent: DMSO-d₆



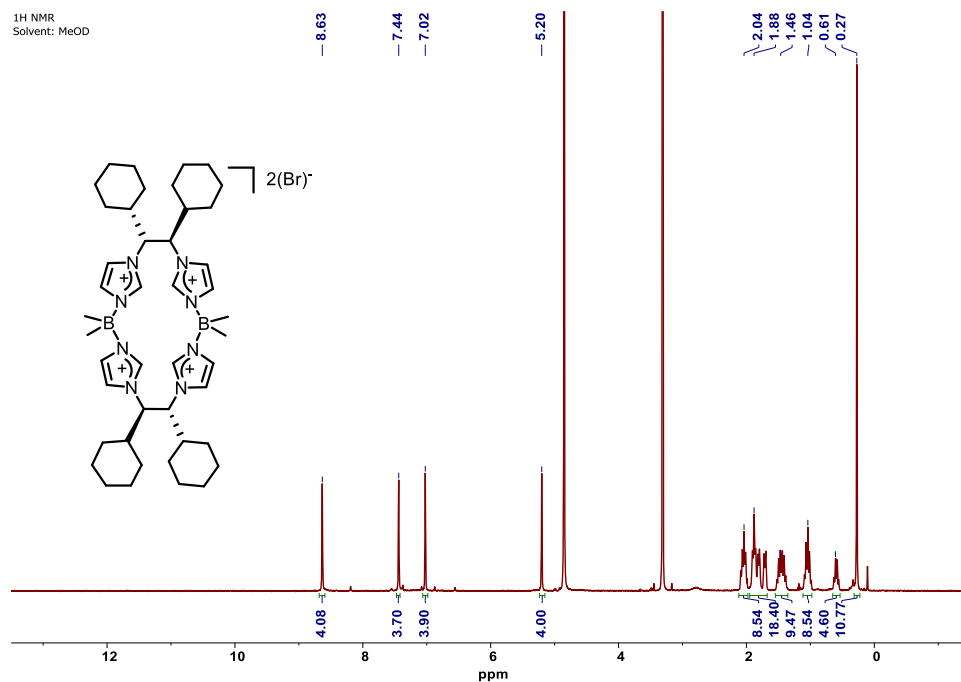
Spectrum 5.17: ¹H NMR of **5.16** in DMSO-d₆. Low signal to noise in NMR due to poor solubility.

¹H NMR
Solvent: DMSO-d₆



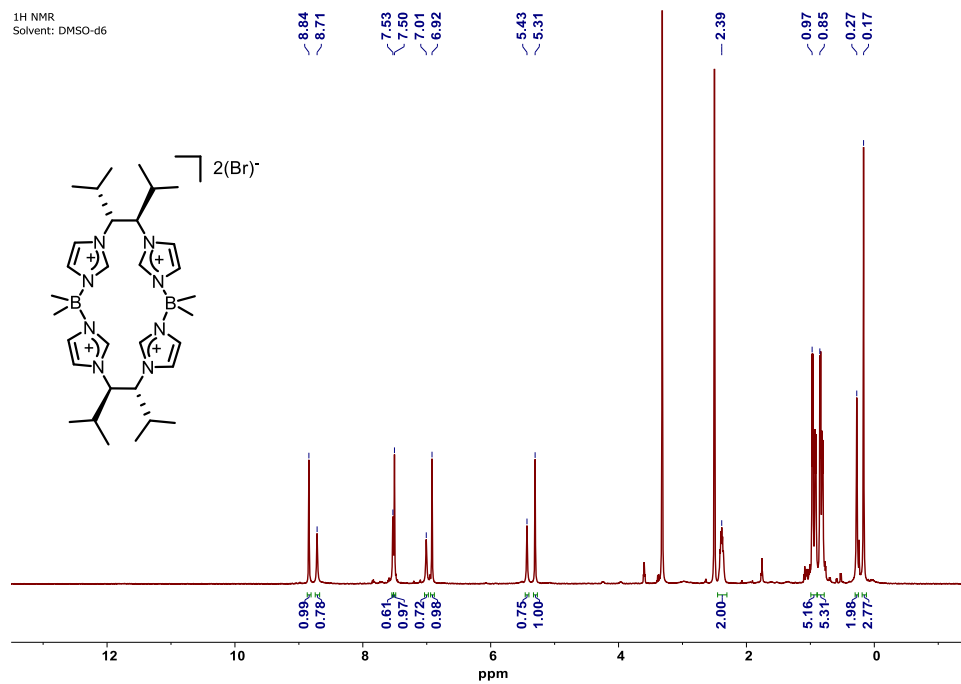
Spectrum 5.18: ¹H NMR of **5.17** in DMSO-d₆.

¹H NMR
Solvent: MeOD



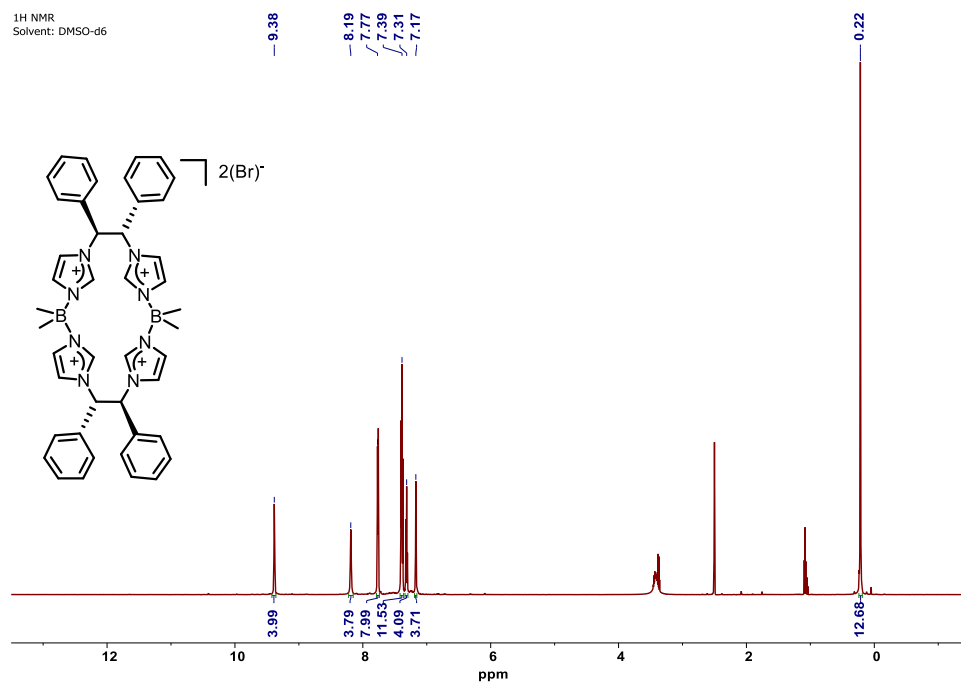
Spectrum 5.19: ¹H NMR of **5.17** in CD₃OD.

¹H NMR
Solvent: DMSO-d₆

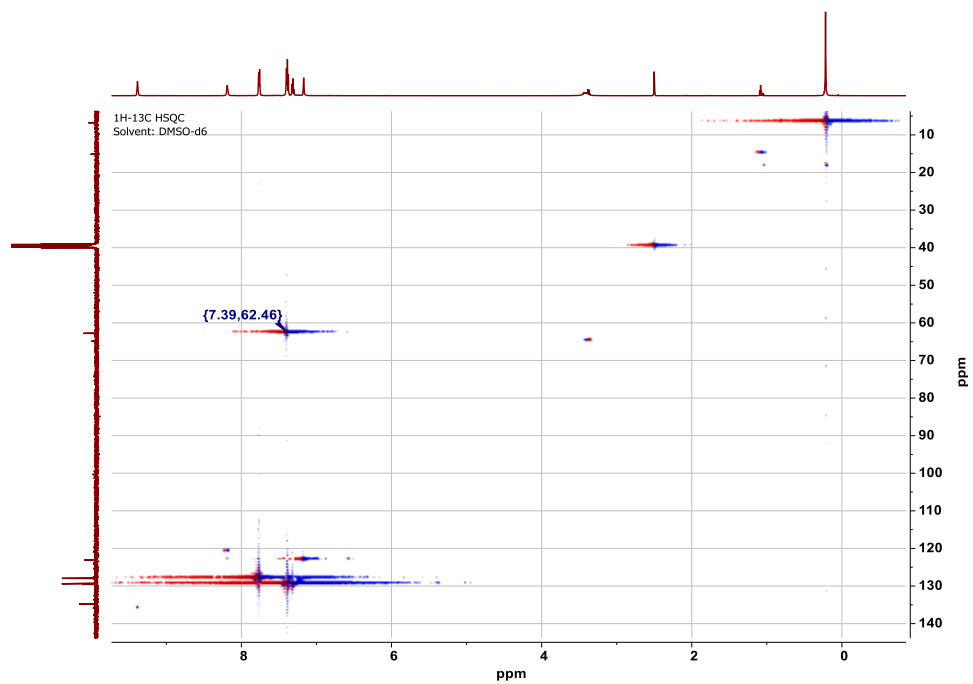


Spectrum 5.20: ¹H NMR of **5.18** in DMSO-d₆.

¹H NMR
Solvent: DMSO-d₆

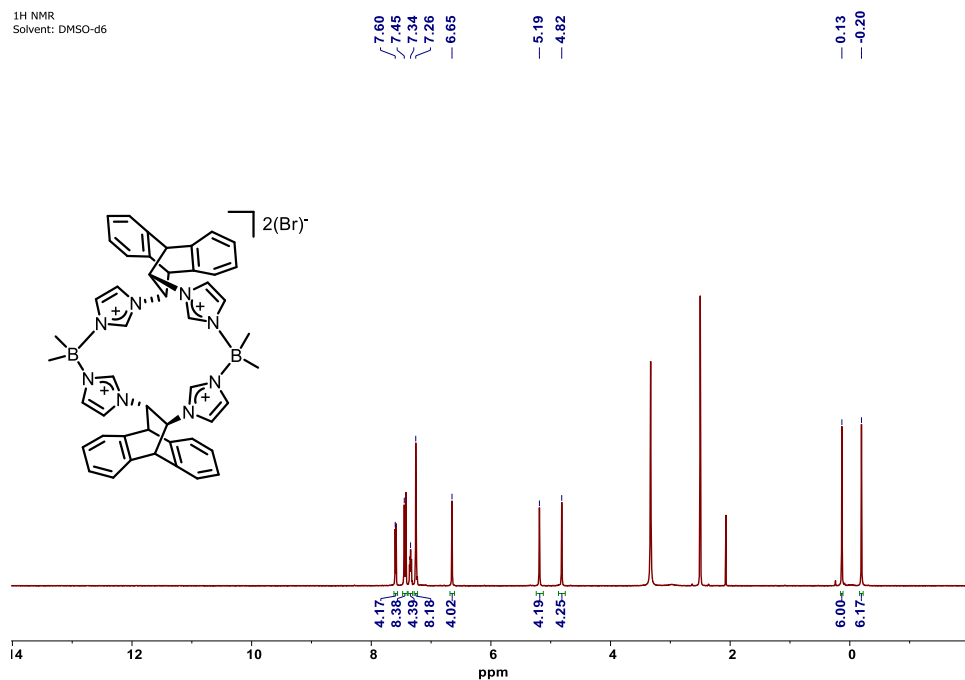


Spectrum 5.21: ¹H NMR of **5.19** in DMSO-d₆.



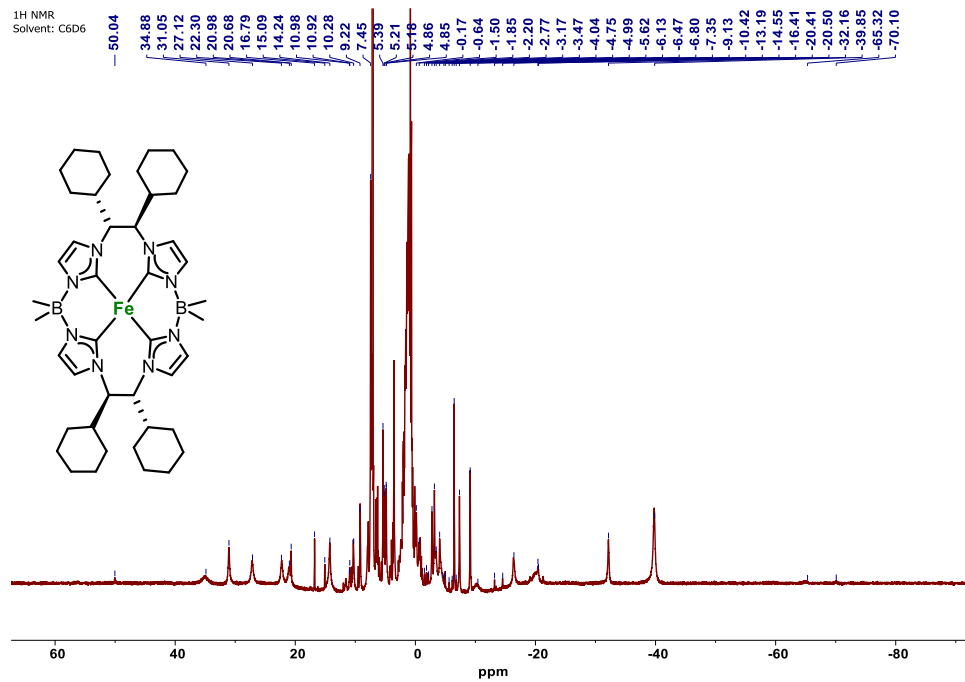
Spectrum 5.22: ¹H-¹³C HSQC Spectrum of **5.19** in DMSO-d₆. Picked peak corresponds to chiral alkyl C-H.

¹H NMR
Solvent: DMSO-d₆



Spectrum 5.23: ¹H NMR of 5.20 in DMSO-d₆.

¹H NMR
Solvent: C₆D₆



Spectrum 5.24: Widescan ¹H NMR of 5.21 in C₆D₆.

Chapter Six: Disparate Azide Reactivity of a Chiral Iron(II)

Tetra-NHC Complex

Abstract

The reactivity of the chiral iron(II) complex was tested with a variety of azides for preliminary studies on aziridination. Various azides led to distinctly different reactivity, including the formation of an iron imide and tetrazene. Notably, some organic azides led to an unexpected migratory insertion of the nitrene into one of the Fe-C NHC bonds. Each iron complex has been isolated and crystallographically characterized and solution NMR have been collected. These results suggest that insertion occurs from the iron(IV) imide. Some initial comparisons were made to other first row transition metals including, chromium, manganese and cobalt; however, insertion into the NHC bond was not observed for any of these cases. Electrochemical measurements of these complexes revealed that some iron(IV) complexes may be able to be oxidized to iron(V), which opens up the possibility for utilizing the $\text{Fe}^{3+}/\text{Fe}^{5+}$ redox cycle for catalytic aziridination.

Introduction

Aziridines are a valuable intermediate in synthetic organic chemistry, in particular pharmaceutical development, given their ease of ring opening and ring expansion reactions for synthesis of chiral amines and complex heterocycles, respectively.^{218, 219} The reactions of aziridines has been exploited in various total syntheses to generate complex natural products stereoselectively.⁸⁴ The versatility of this approach can be further increased by synthetic methods that generate a chiral aziridine, rather than setting stereochemistry during the reaction with a racemic aziridine.^{156, 157} While synthesis of chiral aziridines stoichiometrically has some precedence in organic chemistry, catalytic chiral aziridination, especially using atom economical alkenes and organic azides ($\text{C}_2 + \text{N}_1$ approach) lags behind considerably.^{156, 163}

To date, only three catalytic systems can perform chiral aziridination by the C₂ + N₁ approach (Figure 6.1). The first by Katsuki, utilizes a ruthenium(II) salen complex to catalyze the reaction of 2-(trimethylsilyl)ethanesulfonyl azide (SES-N₃) or tosyl azide (Ts-N₃) and activated acrylates to form aziridines (Figure **6.1A**).^{220, 221} The other two systems were developed by Zhang and feature cobalt(II) porphyrin catalysts (Figure **6.1B-C**). While both these systems are highly effective for the target substrates, they are severely limited in both azide and alkene breadth, in which they can only use perfluorinated azides⁷⁶ (to use H---F bonding to prevent racemization) or sulfonyl azides (easier to activate) and activated alkenes, like styrene or acrylates.⁷⁸

The macrocyclic tetra-NHC complexes synthesized by the Jenkins' group activate weakly oxidizing alkyl azides and undertake catalytic turnover to unactivated alkenes

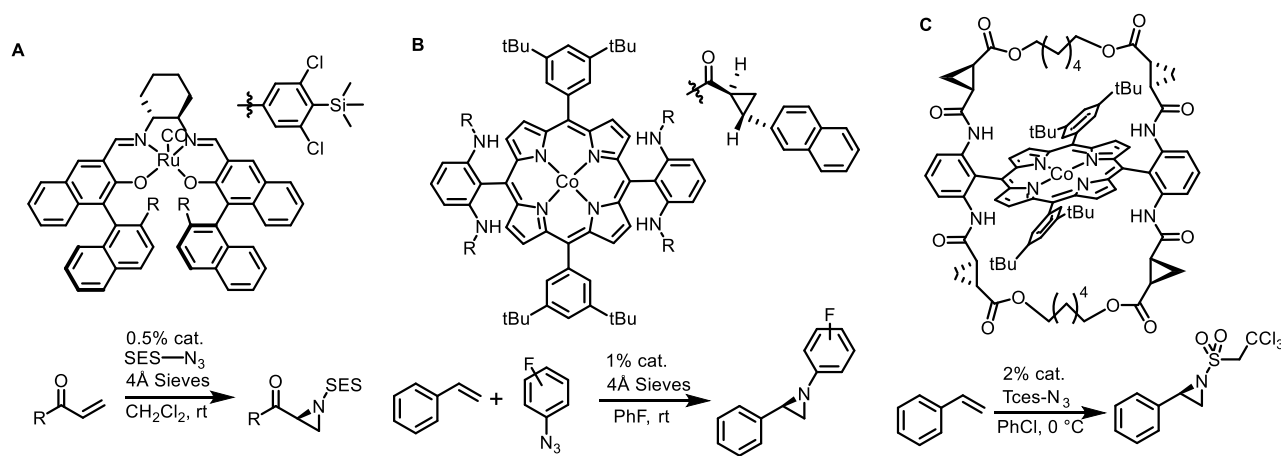


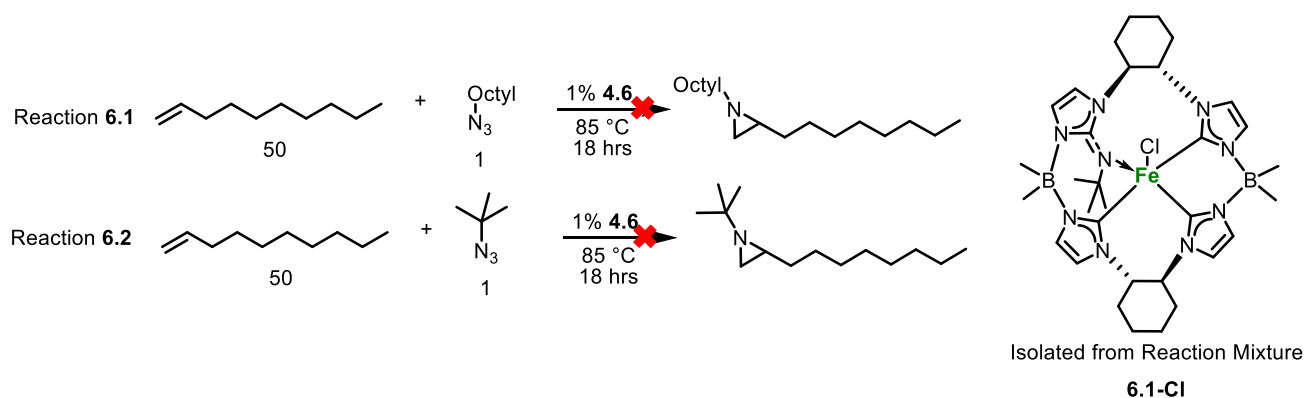
Figure 6.1: Previous aziridination catalysts. (A-C) Chiral aziridination catalysts using activated alkenes and specialized azides.

which suggests that we may be poised to prepare a broadly effective chiral aziridination catalyst.^{68, 69} We anticipated using $((S,S)\text{-}1,2\text{-Cy,BMe}_2\text{TC}^H)\text{Fe}$ (**4.6**) from Chapter 4 as a chiral aziridination catalyst for accomplish the similar aziridination as our previous iron(II) borate complex.⁶⁹ The reactivity of the azide towards the metal center is key to understanding potential limitations of the catalyst. For example, the rate limiting step for the catalytic cycles of our previous catalysts have shown to be the reaction of the iron(IV) imide with the alkene.²²² Because of this, excess azide can react with the imide and form a metallotetrazene, which reduces the efficacy of the catalysis.²²³ Therefore, understanding the fundamental reactivity of the azides with these complexes is critical to developing an effective catalyst.

Results and Discussion

Once the synthesis of **4.6** was established, I attempted aziridination on two different alkyl azides with 1-decene (Scheme 6.1). Alkyl azides are favorable for this reaction as the control reaction for aziridination is considerably lower compared to aryl or sulfonyl azides.^{68, 69} Indeed, when adding the azides from Scheme **6.1** to the solution of 1% **4.6** in neat 1-decene (50 eq.), the solutions changed from yellow to dark red. The octyl azide reaction occurred immediately, while the tert-butyl azide reaction was much slower.

We had hoped this reaction would work analogously to our previously reported work, in which the similar 18-atom catalyst $((\text{Et,BMe}_2\text{TC}^H)\text{Fe}$ resulted in yields of these aziridines in the analogous conditions at 82% and 49%, respectively.⁶⁹ However, we found that **4.6** was ineffective for aziridination under these conditions, as it only yielded



Scheme 6.1: Attempted aziridination catalysis with **4.6**.

control yields⁶⁹, <5% based on crude ^1H NMR. Fortuitously, we were able to pick a single dark red crystal in the reaction mixture tert-butyl azide reaction. What we observed was the nitrene fragment inserted into one of the Fe-C bonds and had scavenged a chloride contaminant, from previous iron complex synthesis (**Figure 6.2**). We attempted a reaction with just **4.6** and excess of octyl azide in C_6D_6 , which resulted in a dark red solution. The dark red solution was crystallized from a slow evaporation of benzene and hexanes solution to yield the structure in **Figure 6.3** as complex **6.2**. The product also incorporated a chloride contaminant and formed the same inserted species as the previous reaction. The ^1H NMR of the reaction mixture showed a large number of paramagnetic signals, which indicates the desymmetrization of the ligand. In addition, there was a large amount of decomposed ligand shown in the NMR, which showed that the product is not stable. Of note, the average bond lengths of the NHC bonds are 2.018 Å, which is slightly elongated compared to **4.6**. However, the $\text{N}_9\text{-C}_3$ bond length is 1.3703(32) Å, which is intermediary between what is expected for the C-N (1.465 Å) or

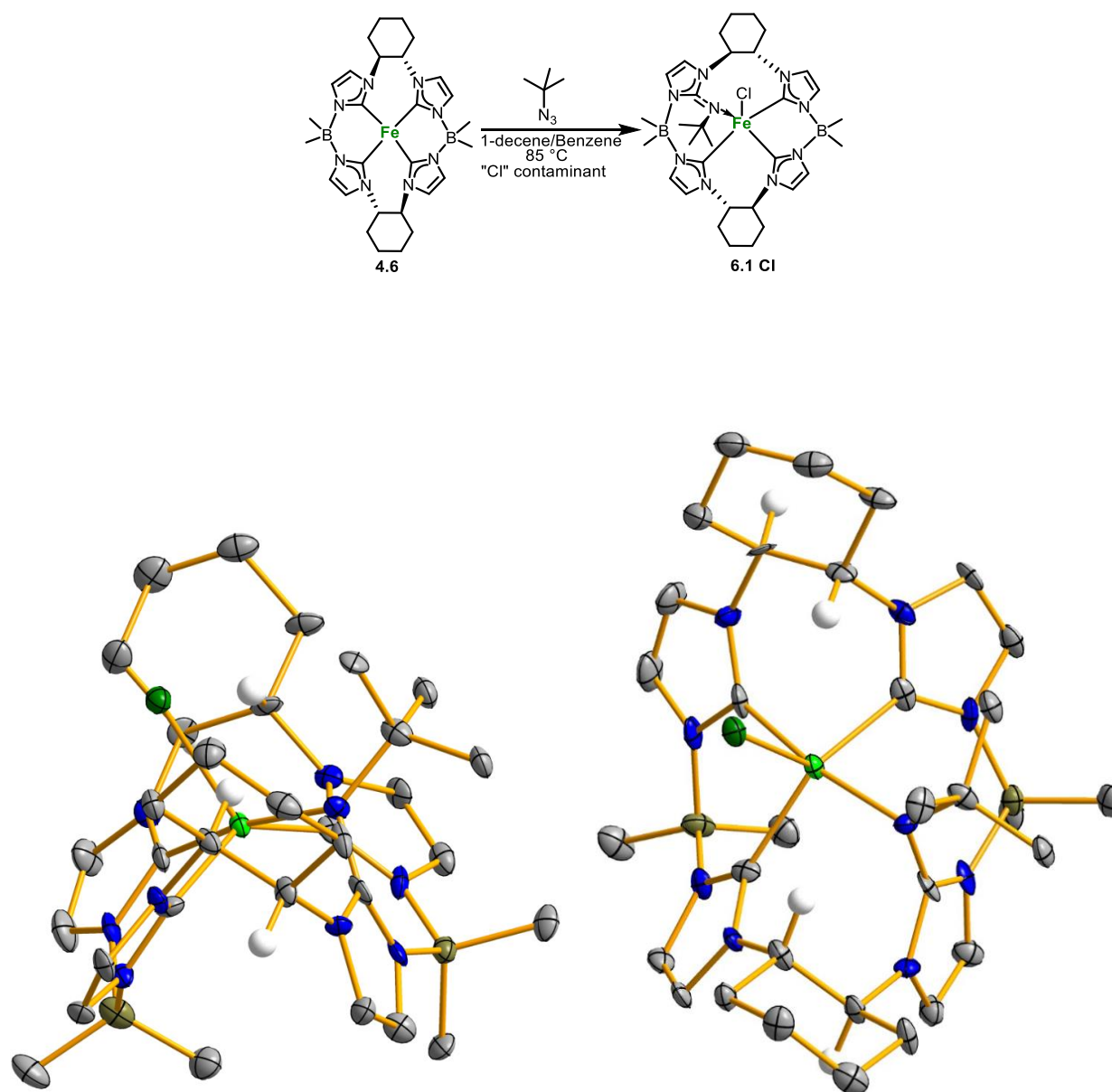


Figure 6.2: X-ray crystal structure of $[(\text{((S,S)-1,2-Cy, BMe}_2\text{TC}^H)\text{Fe-N-('Bu)-C(Cl)})]$, **6.1-Cl**. Green, blue, gray, red, olive, dark green, and white ellipsoids (50% probability) represent Fe, N, C, B, Cl, and H atoms, respectively. Solvent molecules and H-atoms not connected to stereogenic centers are omitted for clarity.

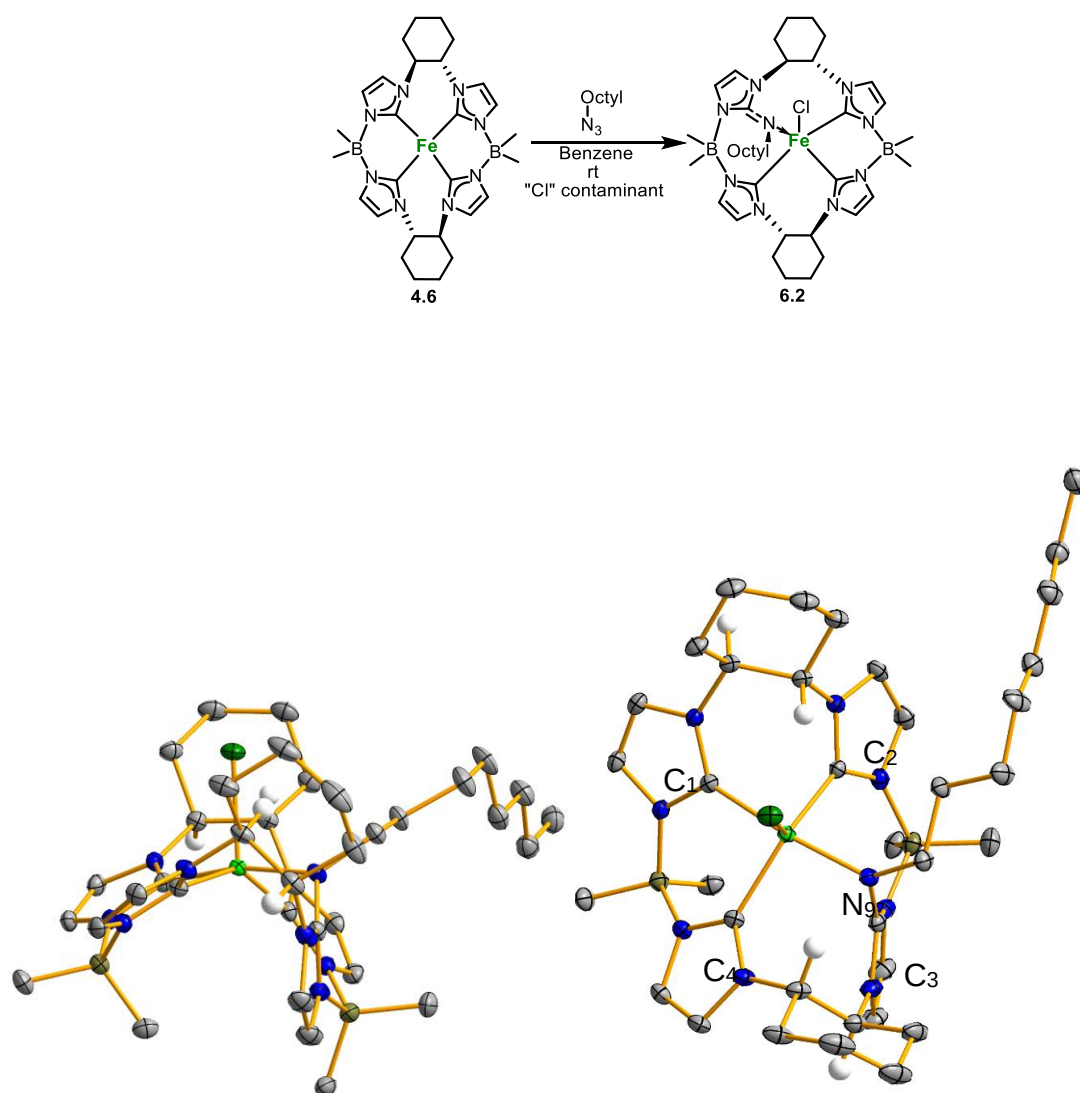


Figure 6.3: X-ray crystal structure of $[[((S,S)\text{-}1,2\text{-Cy,BMe}_2\text{TC}^H)\text{Fe-N}(\text{Octyl})\text{-C}(\text{Cl})]$, **6.2**. Green, blue, gray, red, olive, dark green, and white ellipsoids (50% probability) represent Fe, N, C, B, Cl, and H atoms, respectively. Solvent molecules and H-atoms not connected to stereogenic centers are omitted for clarity. Selected bond lengths (Å) and angles (°) are described as followed: Fe₁-C₁: 2.0075(24), Fe₁-C₂: 2.0003(21), Fe₁-C₄: 2.0483(23), Fe₁-N₉: 1.9574(23), Fe₁-Cl₁: 2.3534(6), N₉-C₃: 1.3703(32), C₁-Fe₁-N₉: 162.657(91), C₂-Fe₁-C₄: 139.927(96), Fe₁-N₉-C₃: 103.410(156).

C=N (1.279 Å) of an imine, which may be due to delocalization to the iron center. The Fe-N₉ bond length is 1.9574(23) Å, which is slightly longer than the similarly reported complex by Wolczanski.⁵⁷ This bears the most resemblance to a metal guanidine considering the N₉-C₃ length, but is slightly shortened compared to an iron(II) variant (2.0668(16)).²²⁴ This means that the isolated complexes are formally iron(III).

The isolation of this complex, as well as the failed aziridination reactions, prompted us to understand this insertion phenomena so we could circumvent it to promote effective catalysis. The migratory insertion of metal imides into M-C (NHC) bonds has not been observed often, but in the cases of it being reported, this occurrence was purported due to London dispersion forces of the ligand increasing the covalency of the metal imide.^{57, 225} This was quantified using calculations and bond dissociation energies (BDEs), which were more favorable towards the inserted imide species when the ligand had greater dispersion forces from the metal alkyl.^{225, 226} For these chiral tetra-NHC metal complexes, dispersion forces are likely to have large impact over the metal imides so understanding this is critical before developing further ligands.

Obviously, the most concerning problem with the discovery of **6.1** and **6.2** was that chloride was present in the mixture. We needed to determine if the chloride caused the insertion or was merely present as a donor ligand after the reaction occurred. We switched to Fe(OAc)₂ as the iron source to prepare **4.6** and used this complex for attempted aziridination. However, the catalysis still failed, and a large amount of insoluble precipitate was present in both cases. This result ruled out the role of the chloride for prohibiting catalysis.

It was further probed to see if these inserted species or an intermediate had radical character that could be exploited for productive reactivity by C-H activation similar to reports by the Betley group.^{181, 227, 228} We tried reacting **4.6** with octyl azide in presence of excess di-tert-butyl dicarbonate ((Boc)₂O) to trap the boc-protected pyrrole. We found no evidence of this occur, but the presence of unidentified paramagnetic and diamagnetic species. Attempts to characterize by X-ray crystallography have failed thus far.

We tried to determine if the insertion was due to the formation of the iron(IV) imide species analogous to Wolczanski's, or due to another mechanism such as inverted binding of the azide to the iron center (α vs γ binding).^{229, 230} We rationalized that the greater steric bulk of the tert-butyl group would allow us to monitor the reaction more effectively at ambient temperature. Adding 5 eq. of tert-butyl azide to **4.6** results in a large amount of unreacted **4.6**, but a new diamagnetic species appears. In particular, there are two sets of doublets of triplets at 4.05 and 3.40 ppm. These are indicative of a low spin square pyramidal iron(IV) species for this ligand system, similar to **4.10** and our previously reported imides.⁸¹ This is formed quickly at room temperature, but slowly decomposes to a paramagnetic species. The paramagnetic spectrum becomes much more complicated, and the paramagnetic signals become much weaker after 48 hours at ambient (Figure **6.4**), indicative of decomposition of the complex into dissociated ligand. This result shows implies that the iron imide is first formed, and then the imide inserts into the NHC bond (Scheme **6.2**).

In order to confirm the identity of the paramagnetic species, we attempted to synthesize **6.1** on scale and isolate it. The paramagnetic NMR (Spectrum **6.1**) of the isolated dark red solid (47.7% yield) was consistent with the paramagnetic species

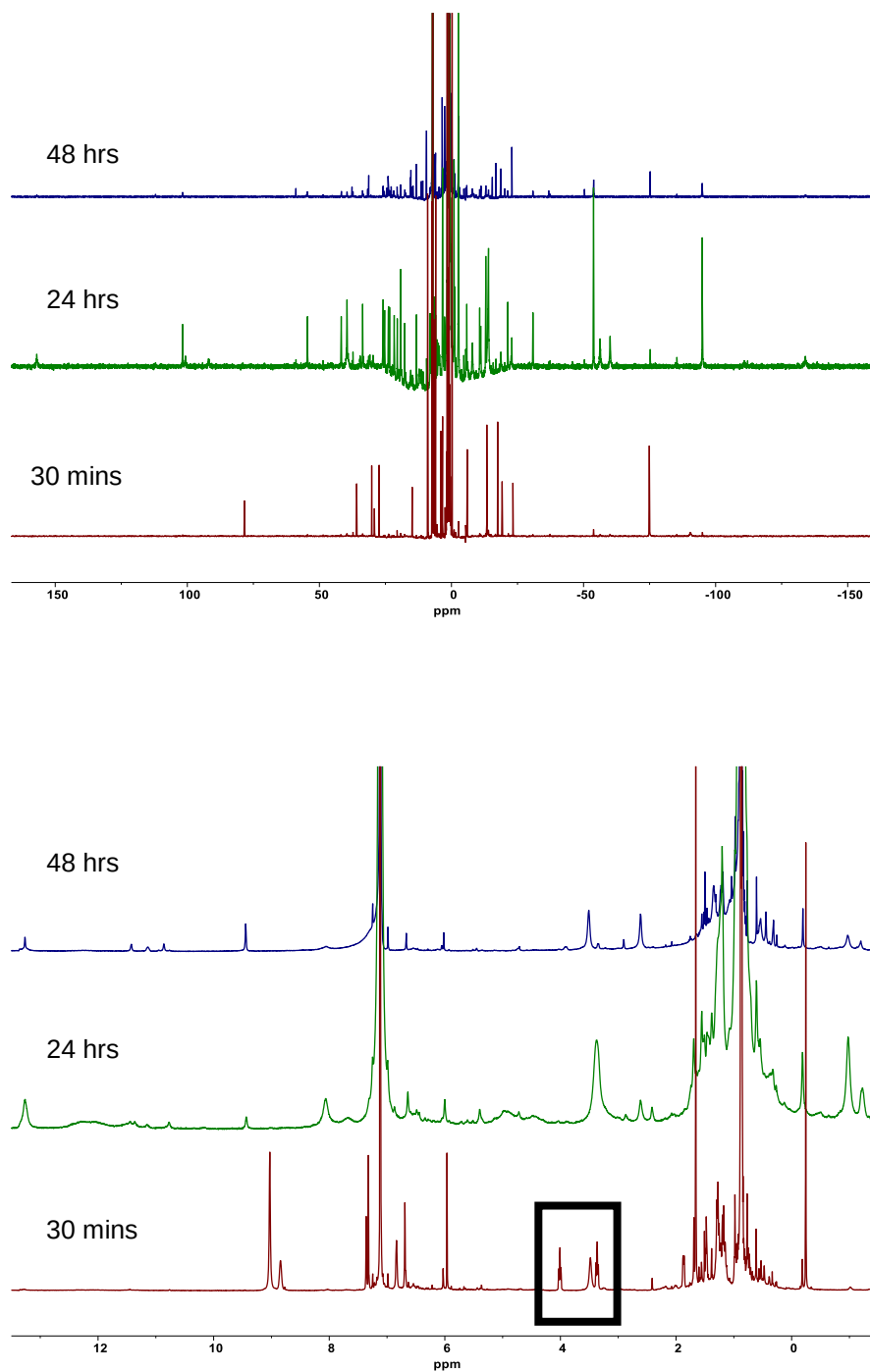
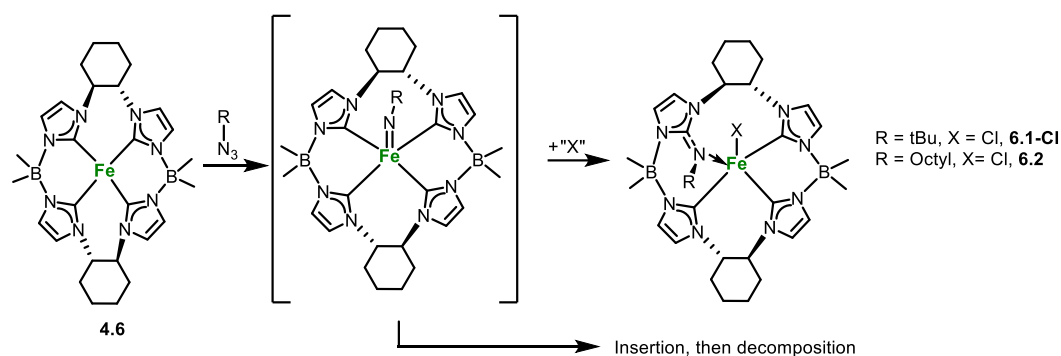


Figure 6.4: Overtime paramagnetic NMR of reaction of **4.6** with excess tert-butyl azide.

Bottom: Close up of diamagnetic region of reaction. Key diagnostic imide peaks indicated by the black box.



Scheme 6.2: Postulated imide insertion pathway.

observed after 24 hours, but the solid proved to be quite unstable and thermally decomposed even at $-35\text{ }^{\circ}\text{C}$ when trying to grow X-ray quality crystals. While it is possible that this is the inserted tert-butyl imide, we have not been able to conclusively prove at this time. We are intentionally synthesizing the species with an X type ligand, such as Cl, as conducting in the reaction in polar coordinating solvent results in complete decomposition of the species **6.1**.

We desired to get conclusive evidence of the formation of the iron(IV) imide and attempt stabilize the complex. We also expected that the use of an aryl azide would allow for a more stable inserted species and allow for conclusive characterization. Reacting **4.6** with 1-azido-2,6-diisopropylbenzene (Dipp azide) resulted in a small amount of paramagnetic species, but heating the reaction resulted in forming only **4.6** and azide decomposition. We tested the slightly less bulky 1-azido-2,4,6-trimethylbenzene (mesityl azide) and upon addition the solution immediately turned dark blue with bubbling. The solution resulting product was isolated as a dark blue/brown solid **6.4** in 67.4% yield. The

solid was crystallized at -35 °C as the aryl imide complex, shown in **Figure 6.5**. The resulting complex was a square pyramidal complex that was isostructural to our previously reported 5-coordinate iron(IV) imides. The Fe-N₉ bond is 1.758(4) Å in length and the Fe-N₉-C₂₉ angle is 162.224°, which is comparable to what we have previously reported.⁸¹ The Fe-N₉ bond length is also significant, as it is the longest Fe-N bond length on an iron(IV) imide that does not have significant imidyl character.^{55-57, 161, 227, 231} In addition, the ¹H NMR is paramagnetic, with peaks at 279 and 209 ppm. Despite the complexity, the corresponding paramagnetic peaks could be correlated to one another using ¹H DOSY NMR.

However, unlike the imides we have reported, these complexes are thermally unstable. Mild heating **6.4** (45 °C) does not result in degradation of the imide, but beyond that at 80 °C, the blue color disappears, and the solution forms a new paramagnetic species as a red brown solution in C₆D₆. While we have not determined what this species is, we were hopeful that this isolated imide could transfer the nitrene fragment to an alkene. Unfortunately, a stoichiometric reaction of **6.4** with 5 equivalents of 1-decene did not result in formation of the corresponding aziridine or any other discernable organic products.

With the confirmation of the iron(IV) imide being possible with isolation of **6.4** we concluded that utilizing **4.6** for intramolecular aziridination may be viable, if the energetic barrier for transferring the nitrene to alkene could be lowered. We reacted **4.6** with 6-azidohept-1-ene to see if it could afford aziridination. At room temperature for 1 hour, the NMR is asymmetrically paramagnetic and is red, very similarly to **6.1**. Mildly heating at 45 °C for 48 hours results in full conversion of this species to a diamagnetic species.

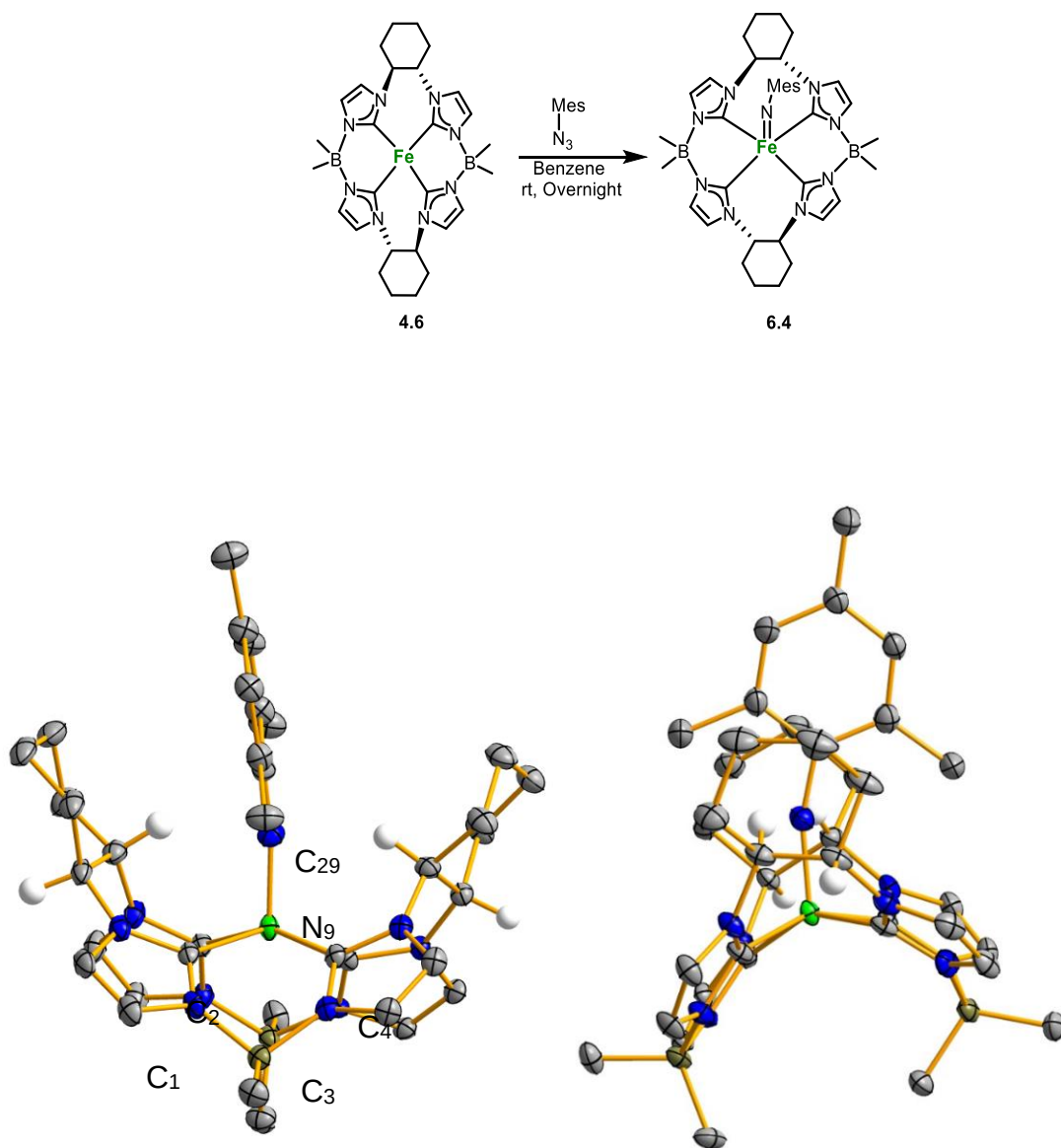


Figure 6.5: X-ray crystal structure of $[[((S,S)\text{-}1,2\text{-Cy,BMe}_2\text{TC}^H)\text{Fe}(\text{NMe}_3)]$, **6.4**. Green, blue, gray, red, olive, and white ellipsoids (50% probability) represent Fe, N, C, B, and H atoms, respectively. Solvent molecules and H-atoms not connected to stereogenic centers are omitted for clarity. Selected bond lengths ($\text{\AA}$) and angles ($^\circ$) are described as followed: Fe-C1: 2.003(4), Fe-C2: 1.981(4), Fe-C3: 2.025(4), Fe-C4: 1.969(4), Fe-N₉: 1.758(4), C1-Fe-C3: 148.51(15), C2-Fe-C4: 154.19(16), Fe-N₉-C₂₉: 162.3(7).

Stirring **4.6** at room temperature overnight also isolated the diamagnetic species in 47.9% yield after purification. The NMR has four different peaks for what appears to be the chiral C-H's at 4.16, 3.64, 2.95 and 2.03 ppm showing that the C_2 symmetry is broken. X-ray crystallography (Figure **6.6**) shows that the diamagnetic species is the metallotetrazene commonly seen in our systems with excess azide. The complex has a trigonal prismatic geometry, which is analogous to our previously reported tetrazenes. Surprisingly, this is not observed with the octyl azide case. Attempting a catalytic reaction of 10% **4.6** with the azide resulted in a significant amount of tetrazene, a large amount of unreacted azide (Figure **6.7**). There was a small amount of the product formed, but this is likely due to the control reaction.⁶⁹ To confirm this, we tried thermally decomposing **6.5** in C_6D_6 at 85 °C; after 48 hours there was only <5% conversion to an unidentified organic product, but not the aziridine.

Following these diverse results, we wanted to further understand the effect of the azide on how this insertion takes place and if it could be predicted. We reacted **4.6** with tolyl azide (Scheme **6.3**) and the crude NMR showed a mixture of paramagnetic and diamagnetic species. The yellow solid could be purified on a short silica gel plug with benzene elution to quench the paramagnetic species. This results solely the diamagnetic species as a yellow solid in 14.0% yield. Crystallization resulted in the structure of Figure **6.8**. This was initially misattributed to the tetrazene species similar to **6.5** but there is a distinct difference in location of the C-H on the chiral carbons at 2.75 and 0.36 ppm (Spectrum **6.6**). The crystal structure shows 4 coordinate Fe center which has a τ_4 value of 0.057. This is much more square planar compared to the base Fe(II) complex.

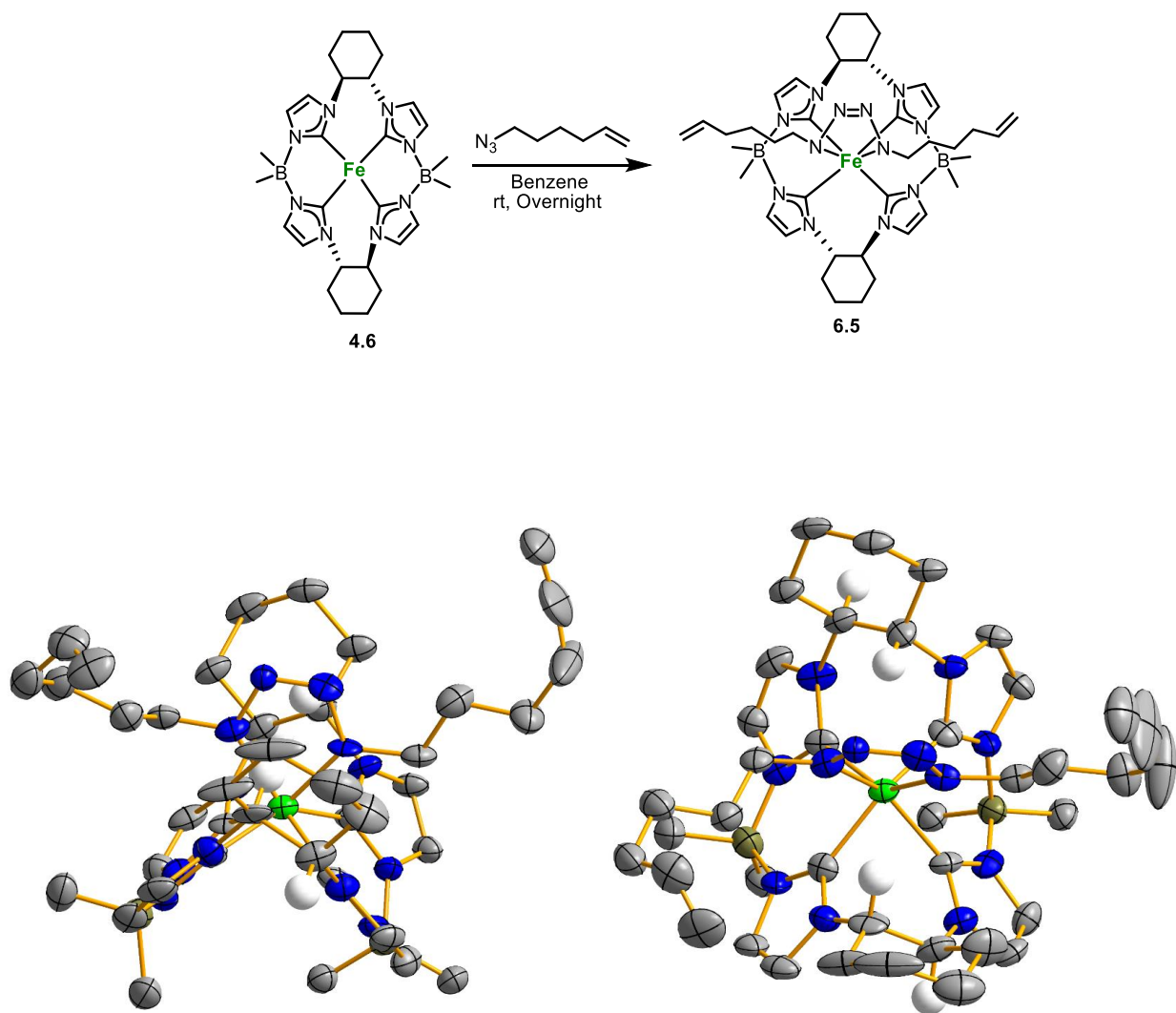


Figure 6.6: X-ray crystal structure of $[(\text{((S,S)-1,2-Cy,BMe}_2\text{TC}^H)\text{Fe}((\text{hex-1-ene})\text{N}_4(\text{hex-1-ene})))]$, **6.5**. Green, blue, gray, red, olive, and white ellipsoids (50% probability) represent Fe, N, C, B, and H atoms, respectively. Solvent molecules and H-atoms not connected to stereogenic centers are omitted for clarity.

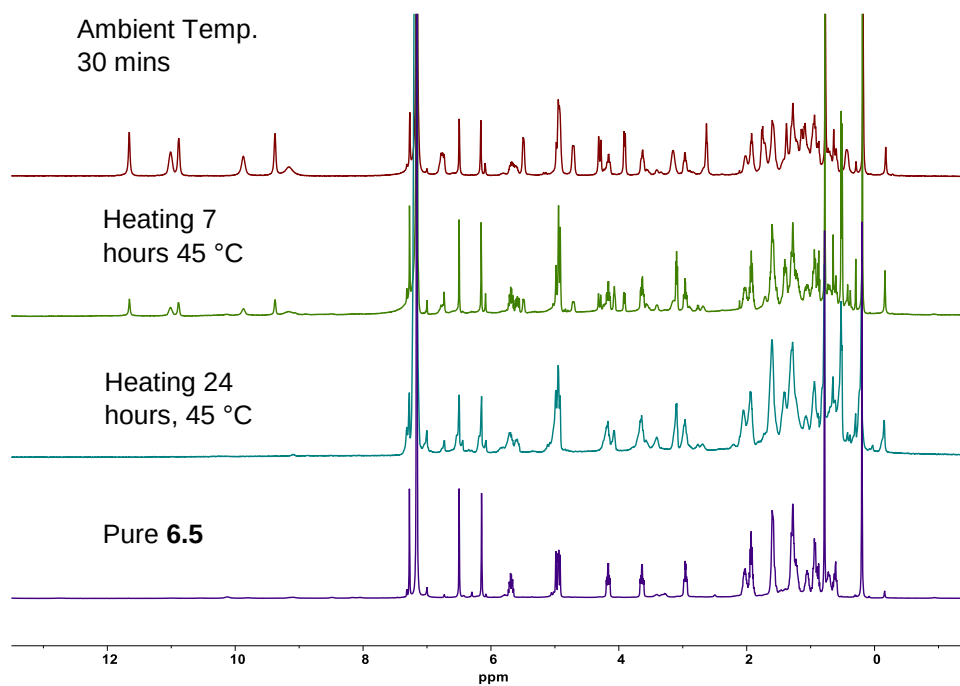
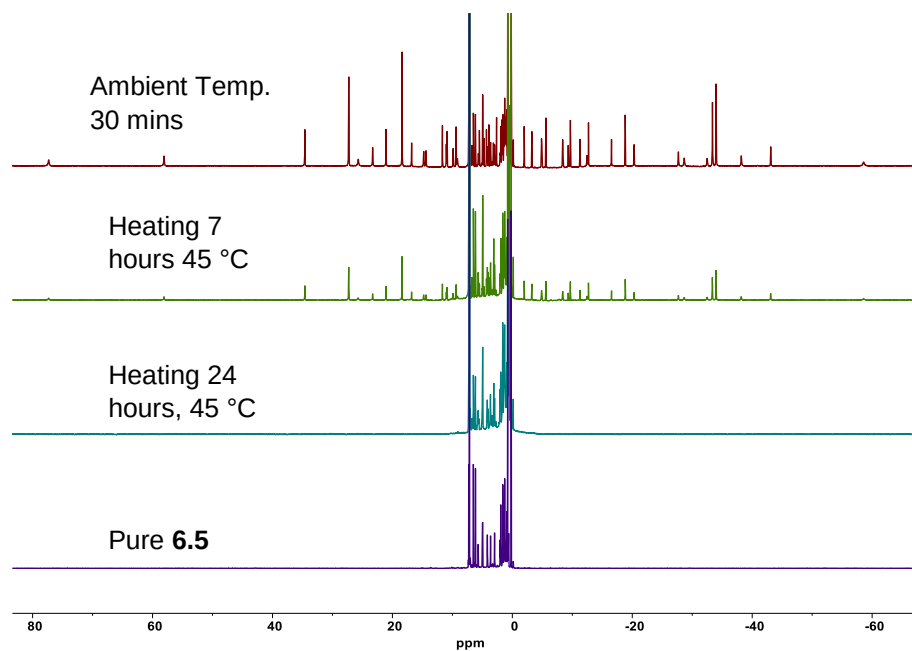


Figure 6.7: Overtime reaction of **4.6** with 6-azido-1-hexene. **Bottom:** Close up of diamagnetic region.

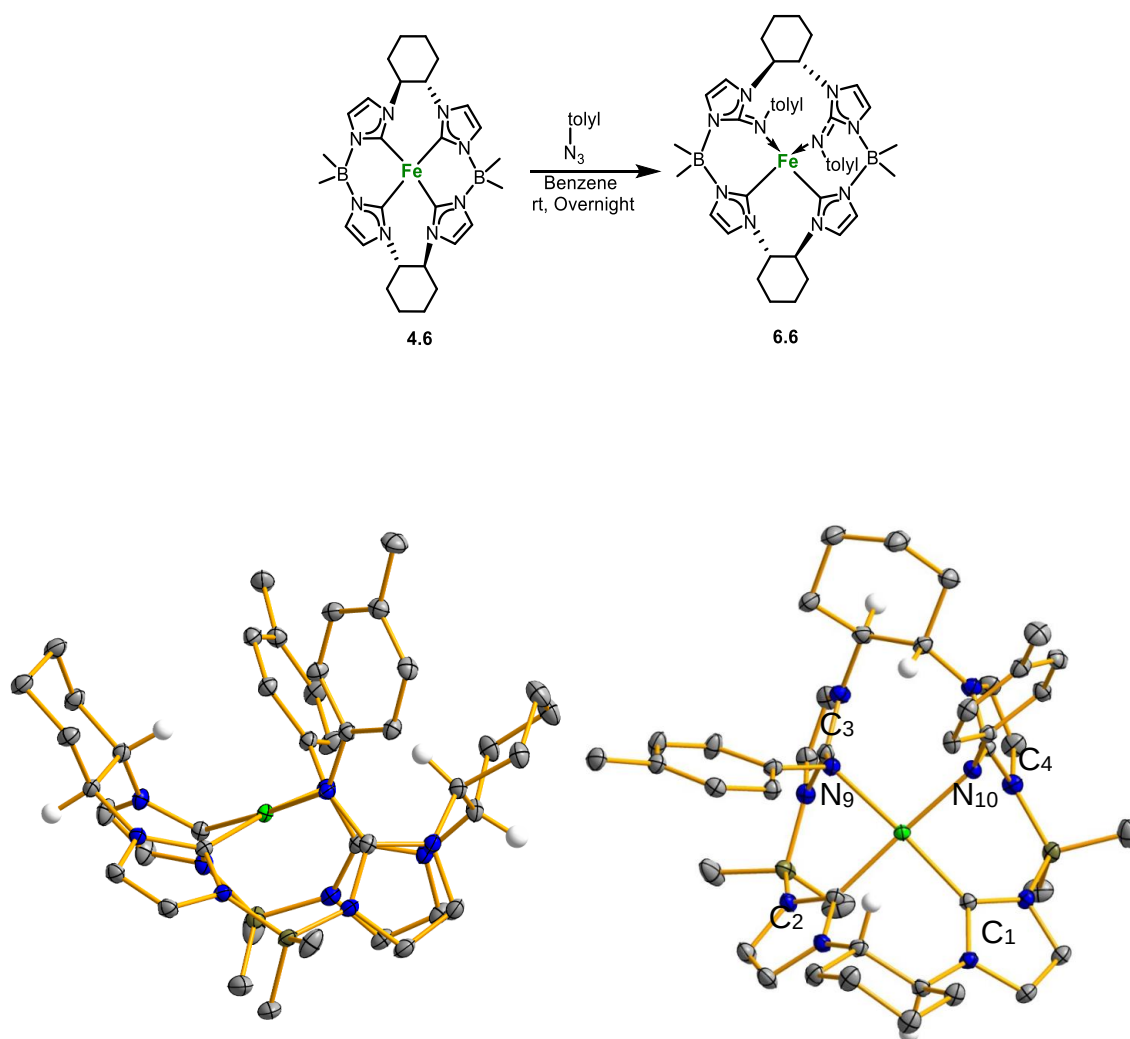
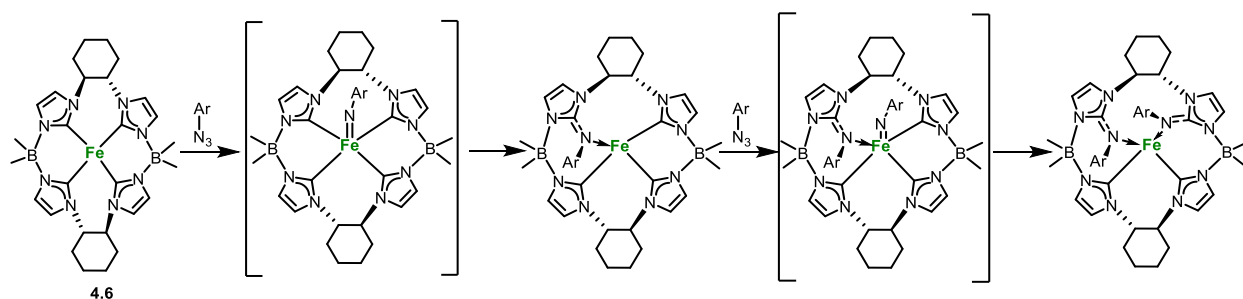


Figure 6.8: X-ray crystal structure of $[[((S,S)\text{-}1,2\text{-Cy,BMe}_2\text{TC}^H)\text{Fe}-(\text{N}-(\text{Tolyl})\text{-C})_2]$, **6.6**. Green, blue, gray, red, olive, and white ellipsoids (50% probability) represent Fe, N, C, B, and H atoms, respectively. Solvent molecules and H-atoms not connected to stereogenic centers are omitted for clarity. Selected bond lengths (Å) and angles (°) are described as followed: Fe₁-C₁: 1.9664(27), Fe₁-C₂: 1.9371(19), Fe₁-N₉: 1.9989(22), Fe₁-N₁₀: 1.9767(16), N₉-C₃: 1.3551(21), N₁₀-C₄: 1.3565(22), C₁-Fe₁-C₂: 91.546(90), C₁-Fe₁-N₉: 173.649(85), C₂-Fe₁-N₁₀: 178.266(79), Fe₁-N₉-C₃: 113.916(129), Fe₁-N₁₀-C₄: 102.426(121).

The Fe-C₁ and Fe-C₂ bonds are 1.966(2) Å and 1.937(2) Å in length. This implies that the oxidation state has increased to Fe(IV), but this cannot be conclusively determined without Mössbauer spectroscopy. In addition, the N₉-C₃ and N₁₀-C₄ lengths are 1.3551(21) and 1.3565(22) respectively, which is consistent with the guanidine character of the inserted species.²²⁴ This is the only example of a doubly inserted imide on an iron center. A postulated rationale for this mechanism is shown by Scheme 6.3. Trying other aryl azides resulted in a mixture of paramagnetic and diamagnetic species based on crude ¹H NMR. Due to the asymmetry and paramagnetism, we hypothesize that there is a mixture of mono- and bis-inserted imides. Increasing the electron donation strength of the azide *p*-methoxyazidobenzene, the diamagnetic species is more prevalent (6.7, Figure 6.9, top) while the using *p*-trifluoromethylazidobenzene (6.8, Figure 6.9, middle) results in solely the paramagnetic species. This observed trend implies that less electron rich imide is less likely to insert in the Fe-C bond. Reacting 4.6 with tosyl azide (6.9), which is a more electron withdrawing azide, results in dark red solution with a very weak paramagnetic spectrum which decomposes quickly.



Scheme 6.3: Proposed route towards bis-imide insertion.

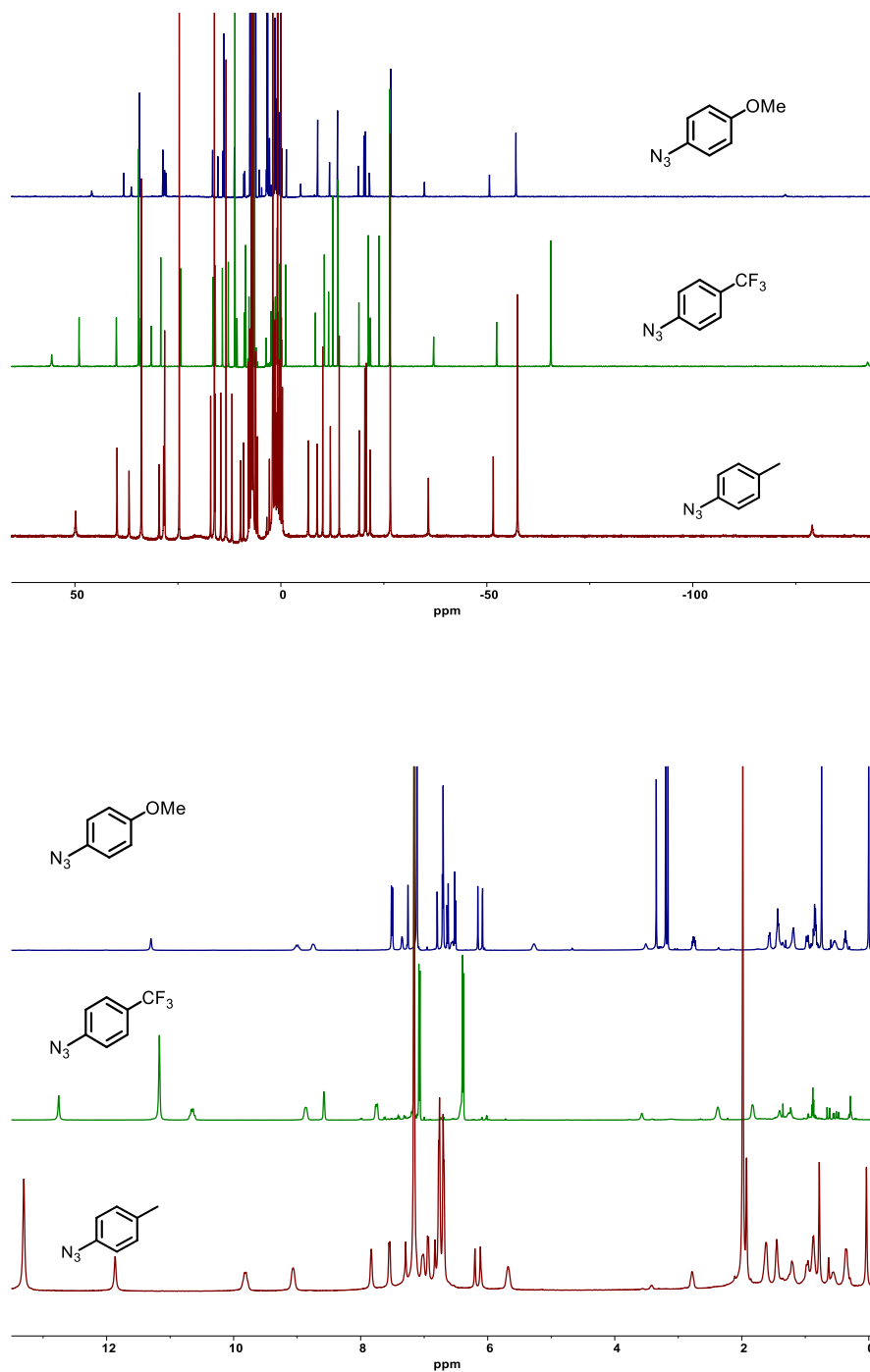


Figure 6.9: Comparison of different donation strength on reaction with **4.6**. Azide used is shown next to spectrum. All reactions are after 24 hours at ambient temperature. **Bottom:** Close up on diamagnetic region.

We wanted to see if the imide insertion was a general reaction with this ligand or exclusive to the iron complexes. We synthesized the Co(II) complex (**6.10**, 42.4%) shown in Figure **6.10**. The Co-C bond lengths average to 1.94 Å. The τ_4 value of the system is 0.096 which makes it more square planar compared to **4.5** and **4.6**. This complex was reacted with both tolyl and octyl azides but did not react and resulted in complex degradation at elevated temperature. The summary the azide reactivity is shown by Table **6.1**.

The electrochemistry of each of these complexes were examined next. The widescan cyclic voltammograms for **4.6** and **6.10** are shown in Figure **6.11** and **6.12** respectively. Both show a reversible oxidation wave a -0.84 V ($\text{Fe}^{2+}/\text{Fe}^{3+}$) and -0.184 V ($\text{Co}^{2+}/\text{Co}^{3+}$) respectively. In the case of **4.6**, this makes sense due to the great air sensitivity of the complex. Complex **6.10** is much more resistant to oxidation on air comparatively. This may be rationale for why the complex does not react with organic azides as readily as **4.6**.

Next we were interested in studying the electrochemistry of **6.4**. Comparing the CVs of **4.10** and **6.4**, it appears that both can access the iron(V) oxidation state. While with **4.10** the trace at -0.265 V is irreversible, for **6.4** it is at -0.64V and quasi reversible. Upon adding FcPF_6 to a solution of **6.4** in acetonitrile, there is an immediate change from dark blue to dark red, indicative of an oxidation state change. This is currently being examined as a possible way around, as going from a $\text{Fe}^{3+}/\text{Fe}^{5+}$ redox cycle may circumvent the insertion problem due to decreased electron richness of the complex and instability of iron(V) intermediates. This is also significant as there have been no structurally characterized or isolated mononuclear iron(V) imides using aryl azides.²³²

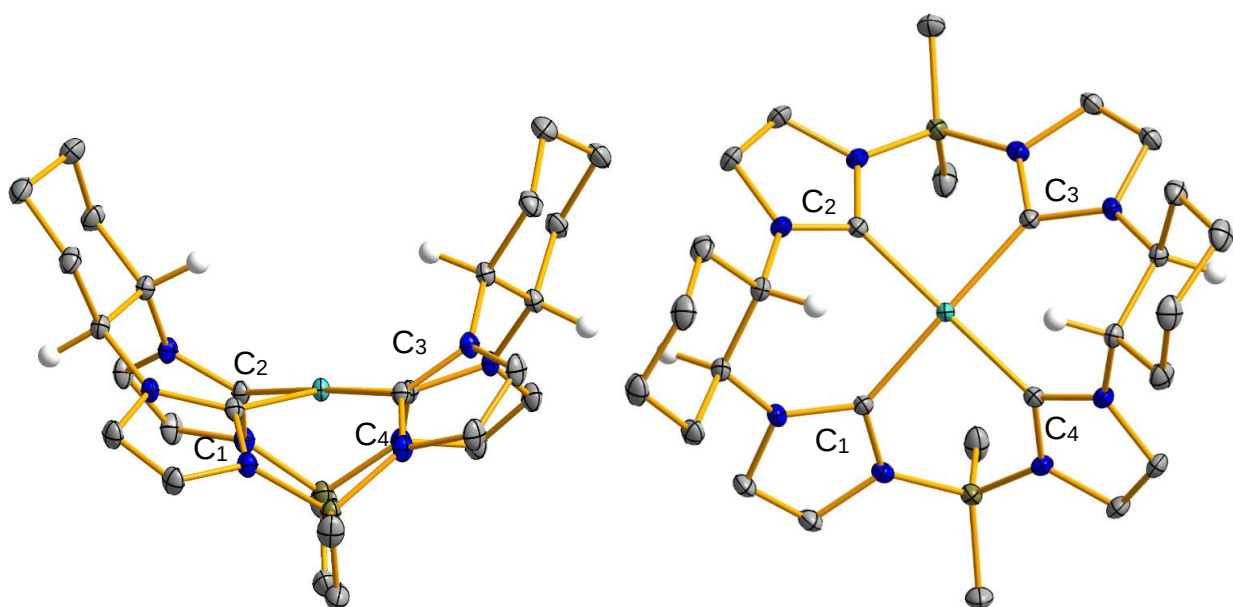
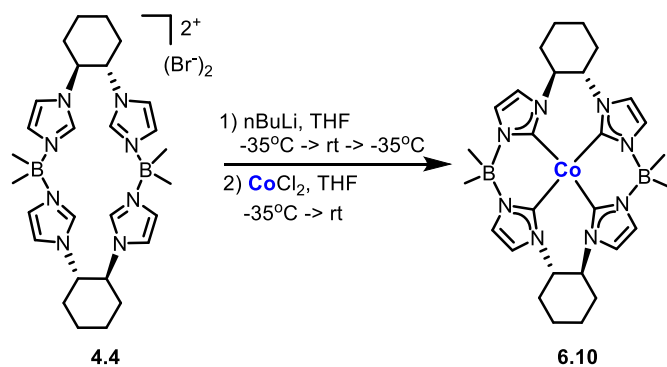
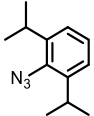
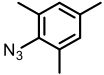
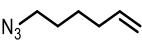
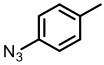
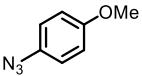
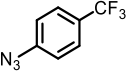
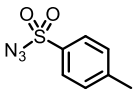


Figure 6.10: X-ray crystal structure of $[[((S,S)\text{-}1,2\text{-Cy,BMe}_2\text{TC}^H)\text{Co}]$, **6.10**. Light blue, blue, gray, red, olive, and white ellipsoids (50% probability) represent Co, N, C, B, and H atoms, respectively. Solvent molecules and H-atoms not connected to stereogenic centers are omitted for clarity. Selected bond lengths (Å) and angles (°) are as followed: Co₁-C₁: 1.9635(16), Co₁-C₂: 1.9181(14), C₁-Co₁-C₃: 169.768(66), C₂-Co₁-C₄: 176.629(60).

Table 6.1: Summary of Azide Reactivity Screen

Entry	Metal Complex	Azide	Azide Category	NMR	Color Change	Species
6.1	4.6		Alkyl	Asymmetric paramagnetic	Dark Red	Inserted (with "X")
6.2	4.6	N ₃ -Octyl	Alkyl	Asymmetric paramagnetic	Dark Red	Inserted (with "X")
6.3	4.6		Aryl	N/A	N/A	No reaction/ decomposition
6.4	4.6		Aryl	Paramagnetic	Dark Blue	Imide
6.5	4.6		Alkyl	Para- to Diamagnetic	Dark Red to Dark Blue	Tetrazene
6.6	4.6		Aryl	Mixture of Para- and Diamagnetic	Dark yellow/orange	Mono- and Bis Inserted (Major)
6.7	4.6		Aryl	Mixture of Para- and Diamagnetic	Dark Orange	Mono- and Bis Inserted (Major)
6.8	4.6		Aryl	Asymmetric Paramagnetic	Yellow	Mono Inserted
6.9	4.6		Sulfonyl	Broad Paramagnetic	Dark Red	??? then Decomposition
6.10	6.10	N ₃ -Octyl	Alkyl	N/A	N/A	Decomposition

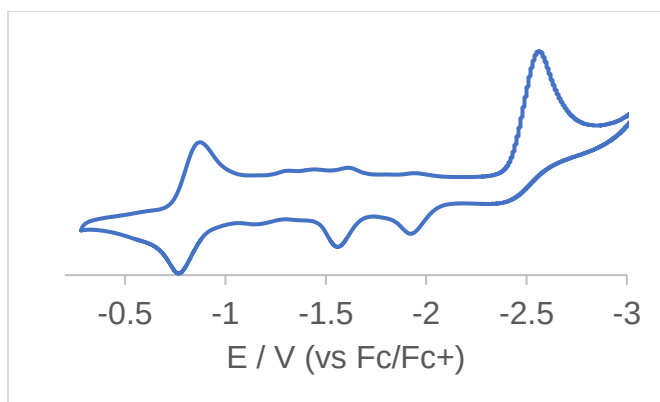


Figure 6.11: Cyclic voltammetry trace of **4.6** in 0.1 M TBAPF₆ in CH₃CN at 100 mV/s scan rate. Referenced to Fc/Fc⁺. Reversible Fe²⁺/Fe³⁺ redox cycle at -0.84V. Irreversible 2e⁻ reduction at -2.59 V and subsequent irreversible re-oxidation at -1.94V and -1.56 V.

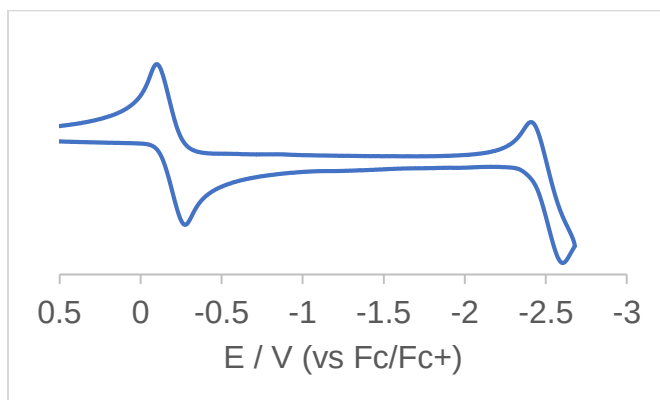


Figure 6.12: Cyclic voltammetry trace of **6.10** in 0.1 M TBAPF₆ in CH₃CN at 100 mV/s scan rate. Referenced to Fc/Fc⁺. Reversible Co²⁺/Co³⁺ redox cycle at -0.184V. Quasi-reversible reduction at -2.50 V.

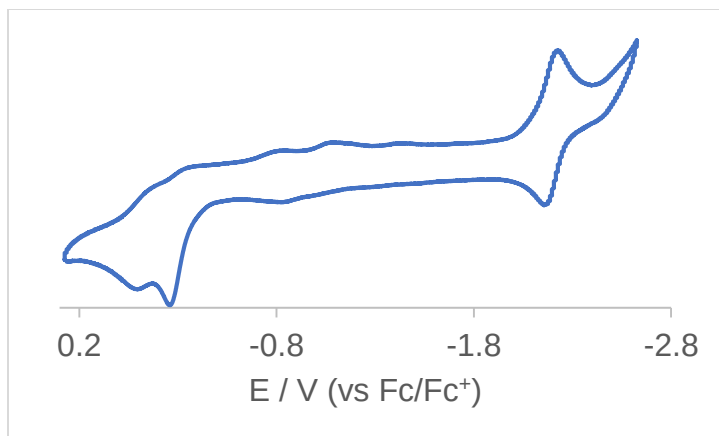


Figure 6.13: Cyclic voltammetry trace of **4.10** in 0.1 M TBAPF₆ in CH₃CN at 50 mV/s scan rate. Referenced to Fc/Fc⁺. Reversible reduction at -2.21 V. Complex irreversible oxidation at -0.265 V.

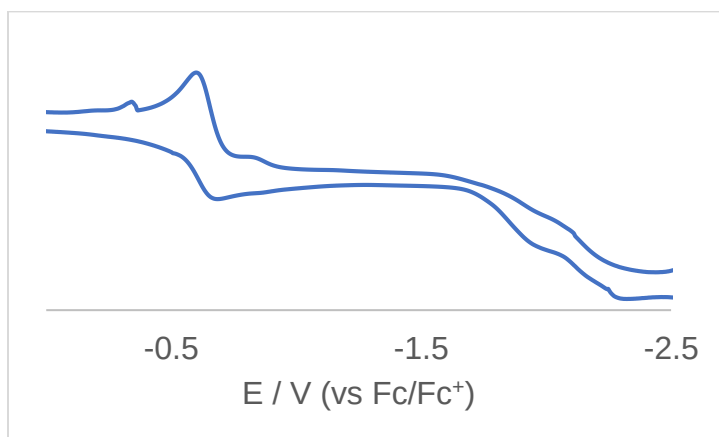


Figure 6.14: Cyclic voltammetry trace of **6.4** in 0.1 M TBAPF₆ in CH₃CN at 10 mV/s scan rate. Referenced to Fc/Fc⁺. Reversible oxidation at -0.64V.

Conclusion

While attempting to conduct catalytic aziridination with our new chiral iron(II) complex, **4.6**, we discovered that the iron(IV) imide undergoes a migratory insertion into one of the Fe-NHC bonds in the macrocycle. We found this phenomenon is prevalent for some different organic azides with this system. Strikingly, it appears that various azides react differently based on small changes to the azide itself or conditions the reaction occurs in. We found that steric bulk can affect the rate at which the insertion occurs, where the imide species can be observed at room temperature and even crystallographically characterized. Through a screen of different organic azides, it seems that also electron withdrawing azides may influence inserted species, as it prefers the paramagnetic mono-inserted species rather than the bis-inserted one. Based on these results, we are currently studying the possibility of obtaining iron(V) with the case of **6.4** to use as our intermediate for catalytic aziridination. Additionally, understanding the subtle reactivity of these azides would allow for greater understanding of improvements for chiral tetra-NHC ligand design (Figure **6.15**).

Experimental

General Considerations for Synthesis:

All reactions, workups and manipulations involving the NHC metal complexes and subsequent reactions were done using standard Schlenk techniques under N₂ or in an MBraun Unilab glovebox under N₂ unless otherwise stated. All glassware for aforementioned reactions were dried at 170 °C overnight before use. For air sensitive reactions, tetrahydrofuran (THF), toluene, hexanes and were dried on an Innovative Technologies Pure Solv MD-7 Solvent Purification System, degassed by three freeze-pump-thaw cycles on a Schlenk line, and subsequently stored under activated 4 Å molecular sieves prior to use. Anhydrous acetonitrile (CH₃CN) was prepared by distillation over phosphorous pentoxide, followed by degassing by three freeze-pump-thaw cycles and stored over activated 4 Å molecular sieves prior to use. Benzene and pentane were purchased anhydrous from Sigma-Aldrich, degassed by three freeze-pump-thaw cycles and subsequently stored over activated 4 Å molecular sieves prior to use. For anhydrous NMR solvents, benzene-*d*₆ (C₆D₆), chloroform-*d* (CDCl₃) and acetonitrile-*d*₃ (CD₃CN) were degassed by three freeze-pump-thaw cycles and subsequently stored over activated 4 Å molecular sieves prior to use. Celite and silica gel used in the purification of metal complexes were dried overnight at 240 °C and subsequently stored in the glovebox prior to use. All reagents were purchased from commercial vendors at highest purity. Octyl azide²³³, tert-butyl azide²³⁴, mesityl azide²³⁵, Dipp azide²³⁶, 6-azidohex-1-ene²²⁸, tolyl azide²³⁷, p-methoxyazidobenzene²³⁸, p-trifluoromethylazidobenzene²³⁹, and tosyl azide¹⁹⁶ were synthesized from previously

reported procedures. These azides were degassed by either sparging with N₂ for 30 minutes or by 3 freeze-pump-thaw cycle, and stored over activated 4 Å molecular sieves.

General Considerations of X-ray Crystallography:

All X-ray data collections were performed on single crystals coated in Paratone oil on glass slides and mounted on nylon fibers. X-ray data for complex **6.1-Cl**, **6.2**, **6.4**, **6.5**, **6.6**, **6.10** were collected with the use of a Mo microsource on a Bruker D8 Venture diffractometer. Crystals were mounted in a 100 K cold stream provided by an Oxford Cryostream low-temperature apparatus. All data sets were reduced with Bruker SAINT and were corrected for absorption using SADABS. Structures were solved and refined using SHELXT and SHELXLE64, respectively.

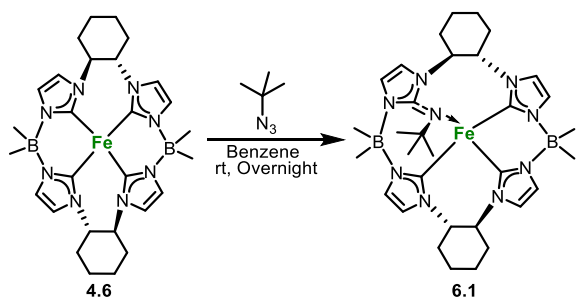
Procedure for Testing for Catalytic Activity

To a 20 mL scintillation vial, the appropriate metal complex was either weighed in as a solid (amounts greater than 0.005 g) or added as a 0.1 M stock solution in benzene (amounts less than 0.005 g). Following this, the alkene (50 eq. to the azide) was added to the vial. To this solution was added the azide was quantitatively transferred and the solution was heated at 80 °C in a heating block. The reaction was monitored for at most 48 hours by TLC.

General Procedure for NMR Screen for Reactivity with Azides

To a 4 mL shell vial, **4.6**, or **6.10** were added. To this was added roughly 0.6 mL of deuterated solvent and stirred until full dissolution. To this solution, a single drop of the neat azide was added. The physical change was noted, the solution was transferred to an NMR tube, sealed, and analyzed over a period of at least 24 hours by ^1H NMR. The solution was then concentrated to dryness and single crystals were grown by an appropriate method. Promising reactions demonstrating one organometallic species were scaled up and purified as described below.

Synthesis of $[[[(S,S)\text{-}1,2\text{-Cy,BMe}_2\text{TC}^H)\text{Fe-N-}(t\text{Bu})\text{-C}], \mathbf{6.1}$:

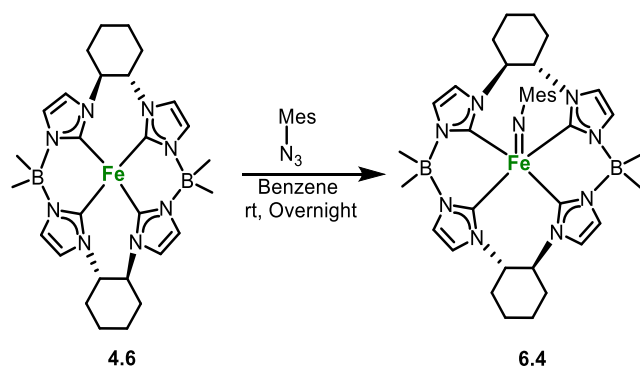


To a vial containing **4.6** (0.0482 g, 0.0851 mmol, 1 eq.) in 5 mL benzene was added tert-butyl azide (0.0253 g, 0.2532 mmol, 3 eq.). The solution gradually turned dark red overnight with no noticeable N_2 bubbling, with heavy amount of precipitate forming. The solution was diluted with 5 mL hexanes and filtered over Celite and concentrated which resulted in a dark red powder (0.0265 g, 47.7%). Stored at $-35\text{ }^\circ\text{C}$ to limit decomposition.

Widescan ^1H NMR (C_6D_6 , 499.74 MHz): δ 157.26, 112.08, 101.87, 58.91, 54.59, 41.78, 39.60, 37.68, 33.69, 31.76, 31.39, 30.55, 25.84, 25.28, 24.45, 23.97, 23.83, 23.44, 22.90, 21.39, 20.56, 19.29, 17.75, 17.44, 15.39, 13.30, 9.48, 8.09, 6.64, 6.01, 2.63, -0.95, -1.23, -1.46, -2.58, -5.80, -10.64, -11.01, -12.95, -14.04, -16.18, -18.66, -21.31, -22.81, -30.81,

-36.84, -45.73, -50.29, -53.75, -57.82, -75.22, -94.94, -133.73. IR: 3137, 2931, 2864, 1537, 1449, 1385, 1359, 1273, 1243, 1207, 1166, 1115, 1035, 944, 882, 829, 789, 723, 697, 663 cm⁻¹.

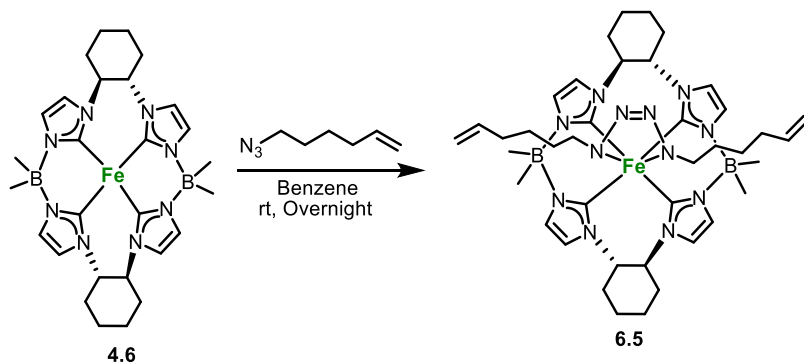
Synthesis of [((*S,S*)-1,2-Cy,BMe₂TC^H)Fe(NMes)], **6.4**:



To a solution containing **4.6** (0.0315 g, 0.0556 mmol, 1 eq.) in 5 mL benzene, neat 2,4,6-trimethylazidobenzene (mesityl azide, 0.0389 g, 0.2413 mmol, 5 eq.) was added at room temperature. The solution immediately changed to a dark blue color with mild N₂ bubbling. The solution was stirred for 16 hours at room temperature. Following this, 5 mL hexanes was added to the benzene and this dark blue solution was filtered over a pad of Celite. The solution was concentrated in vacuo, and hexanes was added to the solution and stirred. The solid was allowed to settle and the hexanes was carefully pipetted off. This was repeated two additional times, and the solid was dried, yielding **6.4** as a dark blue powder (0.0262 g, 67.4%). Single crystals were grown by keeping a solution of **6.14** in hexanes with 3 drops of toluene at -35 °C. **Widescan** ¹H NMR (C₆D₆, 499.74 MHz): δ 279.23, 202.80, 85.51, 61.95, 57.17, 25.07, 22.02, 20.81, 16.72, 15.84, 14.39, 13.33, 12.22, 11.86, 9.77, 8.90, 8.64, 6.55, 6.41, 5.85, 5.60, 4.66, 4.07, 3.18, 2.94,

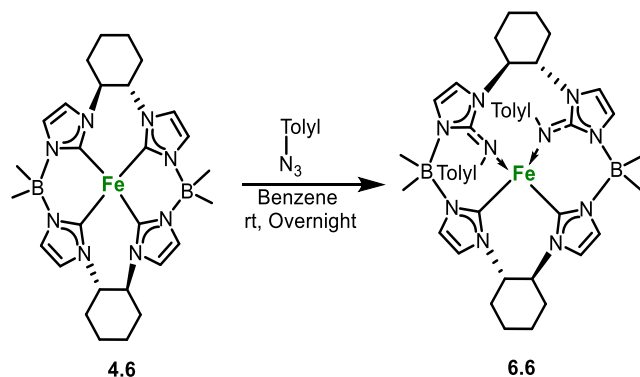
2.67, 2.45, 2.13, 1.68, 1.10, -0.38, -3.34, -3.49, -3.79, -5.92, -11.31, -13.44, -15.73, -19.32.

Synthesis of ((S,S)-1,2-Cy,BMe₂TC^H)Fe((hex-1-ene)N₄(hex-1-ene), **6.5:**



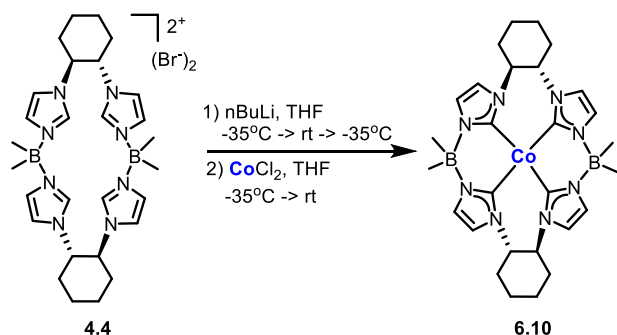
To a solution of **4.6** (0.0407 g, 0.0707 mmol, 1 eq.) in benzene (4 mL) was added 6-azido-1-hexene (0.0432 g, 0.0442 mmol, 5 eq.). The reaction immediately bubbled N₂ in addition turned a red solution then slowly turned to a brown orange solution with a precipitate overnight. The solution was diluted with 4 mL of hexanes and filtered over a short pad of Celite. The solution was concentrated and this yielded **6.5** as a brown/red powder (0.0267 g, 47.9%). Single crystals were grown by saturating a solution of **6.5** with hexanes, followed by addition of 3 drops of toluene, filtering and keeping in a freezer at -35 °C. ¹H NMR (C₆D₆, 499.74 MHz): δ 7.27 (s, 2H), 6.50 (s, 2H), 6.15 (s, 2H), 5.69 (m, 2H), 4.97 (d, *J* = 17 Hz, 2H), 4.93 (d, *J* = 11 Hz, 2H), 4.17 (dt, *J*₁ = 12 Hz, *J*₂ = 4.6 Hz, 2H), 3.64 (dt, *J*₁ = 12 Hz, *J*₂ = 4.8 Hz, 2H), 2.96 (dt, *J*₁ = 11 Hz, *J*₂ = 4.0 Hz, 2H), 2.07-1.98 (m, 2H), 1.93 (p, *J* = 7.4, 4H), 1.64-1.54 (m, 6H), 1.33-1.16 (m, 10H), 1.10-1.01 (m, 2H), 0.98-0.85 (m, 6H), 0.78 (s, 6H), 0.76-0.66 (m, 2H), 0.66-0.57 (m, 2H), 0.20 (s, 6H).

Synthesis of [(((*S,S*)-1,2-Cy,BMe₂TC^H)Fe-(N-(Tolyl)-C)₂], **6.6:**



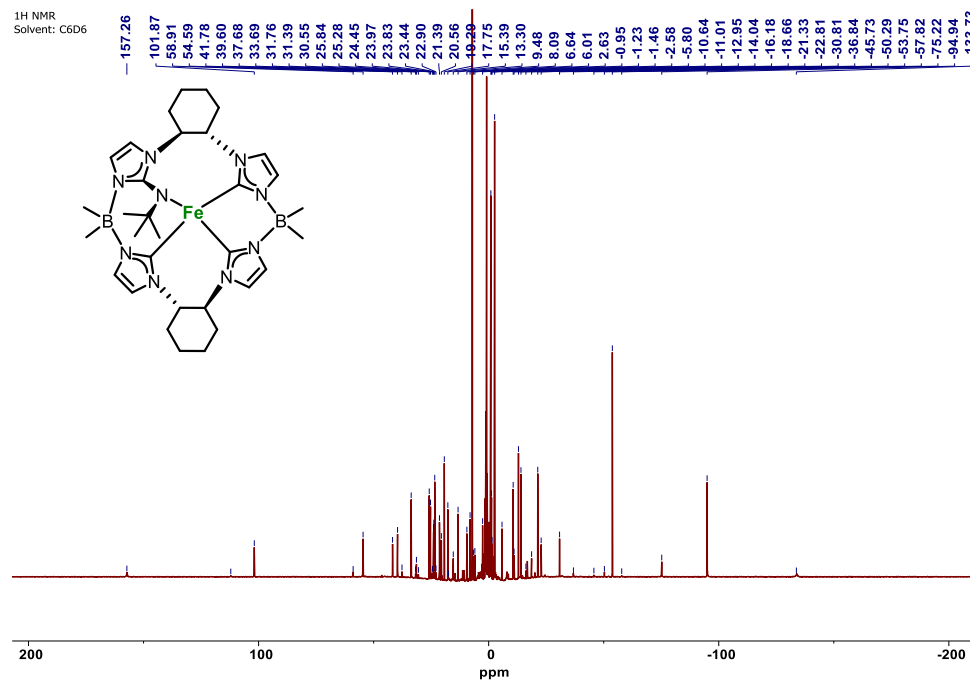
To a 20 mL scintillation vial, **4.6** (0.0507 g, 0.0883 mmol, 1 eq.) was added with 7 mL of benzene. To this was added tolyl azide (0.0616 g, 0.4626 mmol, 5.2 eq.) and the solution immediately turned dark green. The solution gradually turned dark orange with a precipitate overnight. The solution was diluted with 7 mL of hexanes and was filtered over a short Celite plug. The solution was concentrated leaving a yellow powder. The product was purified by column chromatography using benzene as the eluent, collecting the second yellow band, yielding the yellow powder, **6.6** (0.0096 g, 14.0%). ¹H NMR (C₆D₆, 499.74 MHz): δ 7.57 (d, *J* = 8.4 Hz, 4H), 7.32 (d, *J* = 2.4 Hz, 2H), 6.96 (d, *J* = 8.6 Hz, 4H), 6.85 (d, *J* = 2.1 Hz, 2H), 6.20 (d, *J* = 1.6 Hz, 2H), 6.10 (d, *J* = 1.6 Hz, 2H), 2.80-2.71 (m, 2H), 1.93 (s, 6H), 1.65-1.58 (m, 3H), 1.47-1.30 (m, 9H), 1.22-1.14 (s, 3H), 0.98-0.90 (m, 3H), 0.81 (s, 6H), 0.59-0.46 (m, 2H), 0.36 (dt, *J*₁ = 11 Hz, *J*₂ = 2.4 Hz, 2H), 0.07 (s, 6H).

Synthesis of $[(S,S)\text{-}1,2\text{-Cy,BMe}_2\text{TC}^H]\text{Co}$, **6.10**:

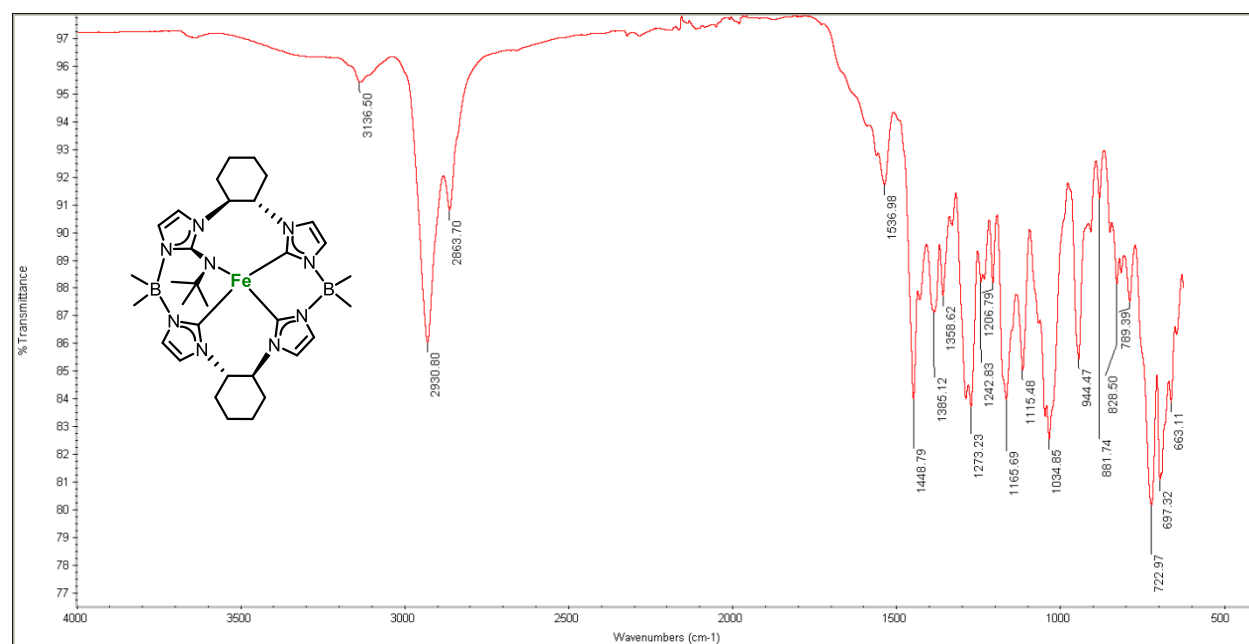


Synthesized similarly to **4.6** but with 0.2056 g of **4.4** (0.3049 mmol, 1 eq.) 0.5 mL of 2.5 M $n\text{BuLi}$ solution (1.25 mmol, 4.1 eq.) and 0.0396 g of CoCl_2 (0.3049 mmol, 1 eq.) to yield the pale yellow powder (0.0736 g, 42.4%) Single crystals were grown by slow evaporation of a solution of **6.10** in toluene and hexanes (1:3) yielding pale yellow needles. **Widescan ^1H NMR** (C_6D_6 , 499.74 MHz): δ 20.04, 17.93, 14.87, 12.00, 5.41, 3.80, -0.69, -0.74, -3.85, -7.21, -19.54.

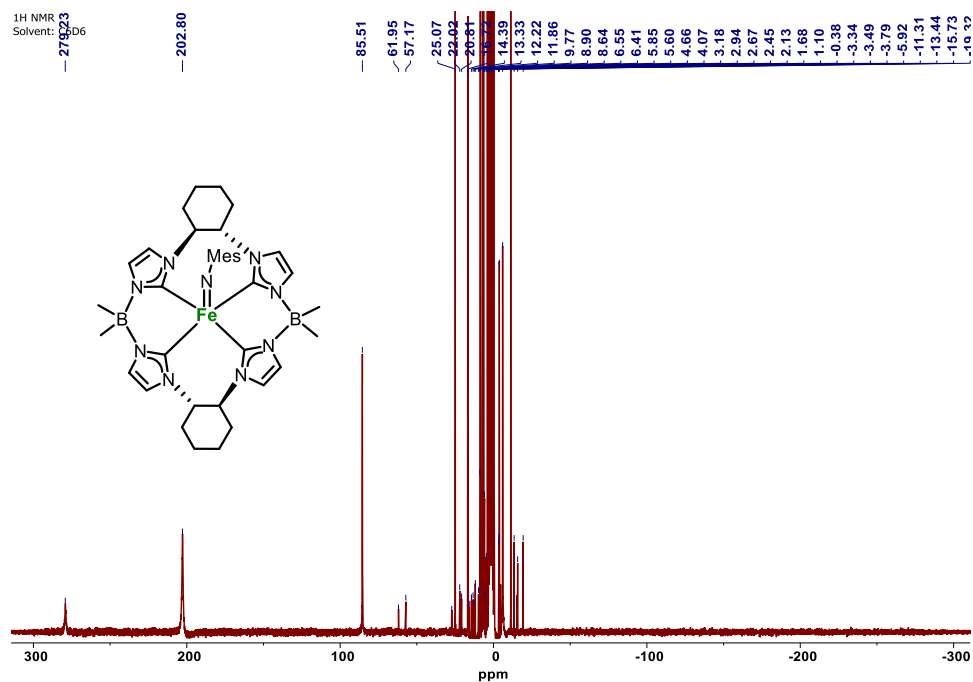
Selected Spectral Characterization:



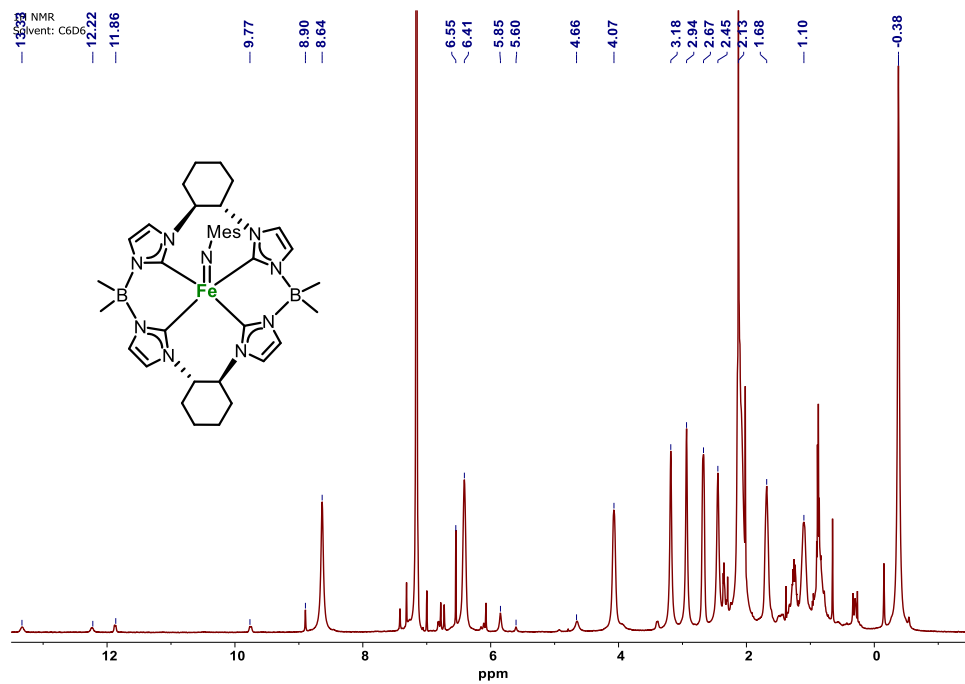
Spectrum 6.1: Isolated NMR of **6.1** in C₆D₆.



Spectrum 6.2: IR of **6.1**.

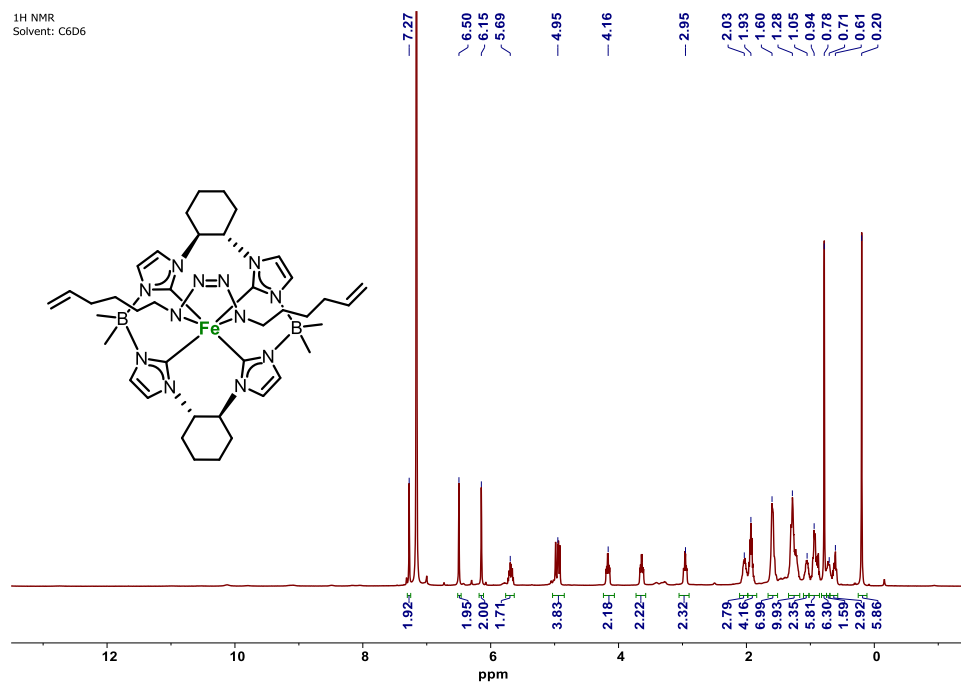


Spectrum 6.3: Paramagnetic NMR of **6.4** in C₆D₆.



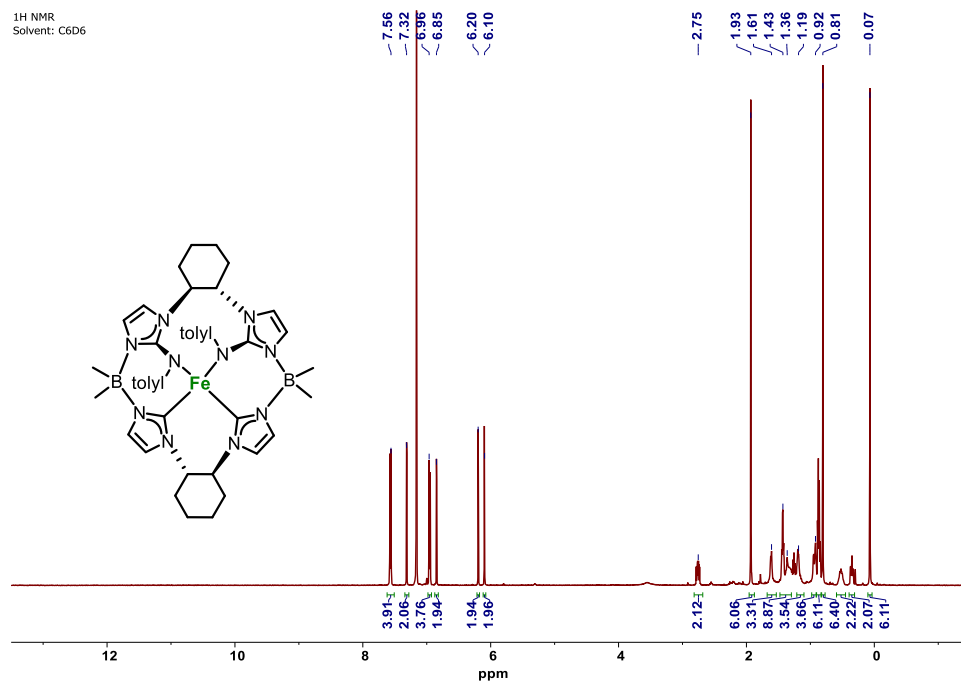
Spectrum 6.4: NMR of **6.4** in C₆D₆. ¹H DOSY confirms that diamagnetic peaks labelled belong to the same species.

¹H NMR
Solvent: C₆D₆



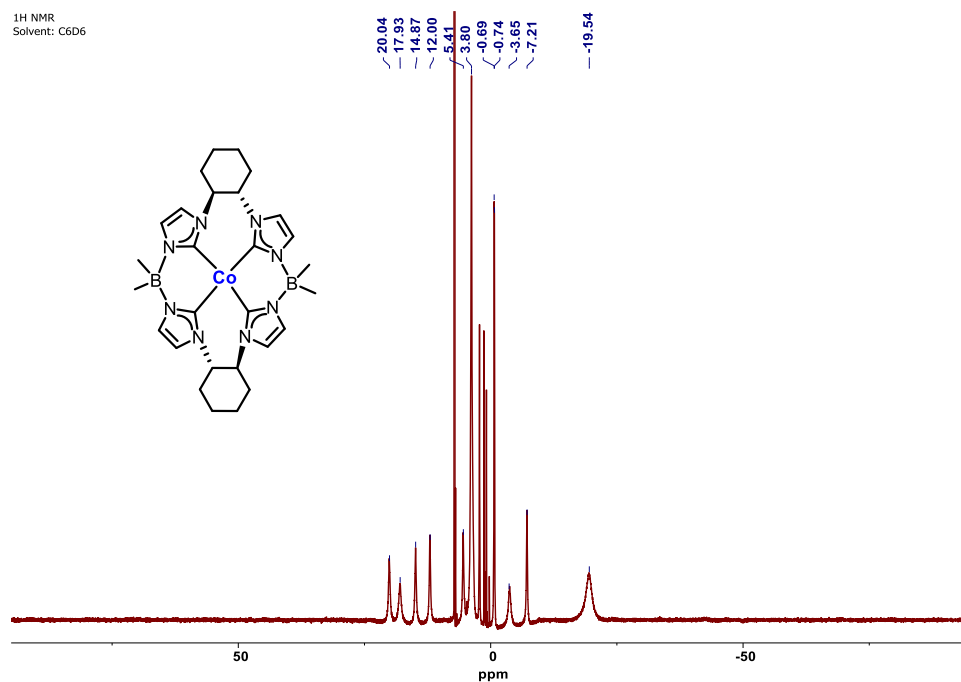
Spectrum 6.5: ¹H NMR of **6.5** in C₆D₆.

¹H NMR
Solvent: C₆D₆



Spectrum 6.6: ¹H NMR of **6.6** in C₆D₆.

¹H NMR
Solvent: C₆D₆



Spectrum 6.8: Widescan ¹H NMR of **6.10** in C₆D₆.

Chapter Seven: Octa-NHC U(IV) Complexes Isolated By

Reactions with Dianionic Tetra-NHCs

This work was done as a collaboration with Ryan W. F. Kerr and Dr. Polly L. Arnold at the University of Edinburgh. I did all the work presented in this chapter, but Ryan W. F. Kerr and Dr. Polly L. Arnold provided advice, mentorship and funding on getting this project started.

Abstract

In recent years there has been considerable research on organometallic actinide complexes; however, N-heterocyclic carbenes (NHCs) have had limited success in binding to f-block elements. Even for the examples that have been prepared, NHC ligands typically require an anionic tether for binding. Dianionic borate tetra-NHC macrocycles bind to uranium(IV) without a separate anionic tether. The isolated complexes are the first examples of an octa-NHC uranium(IV) complex. Changing the ligand size results in structures of two distinct geometries at the uranium center. Initial studies on reactivity of the scalable complex are also reported and discussed.

Introduction

Despite uranium having a low dose of inherent radioactivity, chemists frequently study dioxo-uranium(VI) ions (uranyl) in aqueous media.²⁴⁰⁻²⁴² Uranyl has two primary applications. First, it is a common ion for detecting actinide proliferation for nuclear weapons since it is a stable form of uranium.^{32, 243, 244} Second, it is the naturally occurring form of uranium in sea water, whereby its extraction could be a source for nuclear energy.^{245, 246} In addition to these aqueous studies, there has been a surge of research on non-aqueous low valent (less than tetravalent) uranium chemistry.⁹⁶ Low valent uranium complexes have been particularly effective in small molecule activation, and there is significant interest in using NHCs for catalytic small molecule activation²⁴⁷⁻²⁴⁹ and functionalization.^{250, 251} In particular, there has been significant research conducted in formation of organometallic uranium complexes.⁹⁶

Reacting neutral carbon-based ligands, such as NHCs, there is an electrostatic mismatch, which prevents straightforward ligation.⁹³ In order to overcome this problem, an anionic tether or an electron rich ligand is often incorporated, such as an alkoxide, amide, or cyclopentadienyl (Cp).^{102, 252-254} Examples of isolated and crystallographically characterized uranium(IV) NHC complexes are shown by Figure 7.1.^{102, 253, 255}

In recent years, there have been attempts to isolate thorium and uranium complexes with NHCs that do not contain an anionic tether. A single report by the Long group on uranium(III),¹⁰⁶ and multiple reports by the Arnold group on thorium(IV)¹⁰⁷⁻¹¹⁰, shows this is a proof of concept for NHC using an anionic linker can metallate actinides. Our dianionic borate macrocycles can metallate uranium(IV) salts yielding sandwich-like complexes with eight U-C bonds.

Results and Discussion

The uranium macrocyclic complexes were synthesized using sodium bis(trimethylsilyl)amide (HMDS) in an ethereal solvent to deprotonate the appropriate macrocycle, followed by addition of $\text{U}(\text{dioxane})_2$ to generate the uranium-NHC complex.

Metalation was also attempted using the approaches described in previous chapters (See Chapter 4 and Chapter 5 for examples). We found that almost all other bases were ineffective. Our previously most effective base for transition metals, $n\text{BuLi}$, did not result in any formation of paramagnetic peaks. The lack of NMR signals can be attributed to the propensity of uranium to form adducts with lithium salts.²⁵⁶ Thus, we attempted to deprotonate the macrocycle with non-lithium containing bases, in particular $n\text{BuNa}$ and benzyl sodium, but these did not result in productive deprotonation of the ligands. We also tried $\text{Li}(\text{HMDS})$ and $\text{K}(\text{HMDS})$ as well, but found that the sodium variant

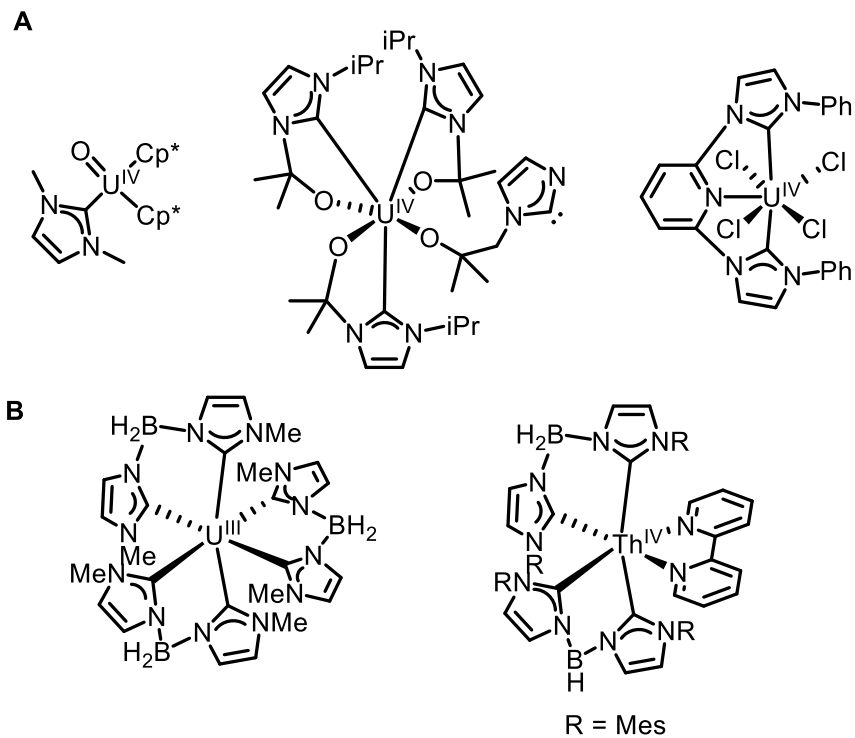
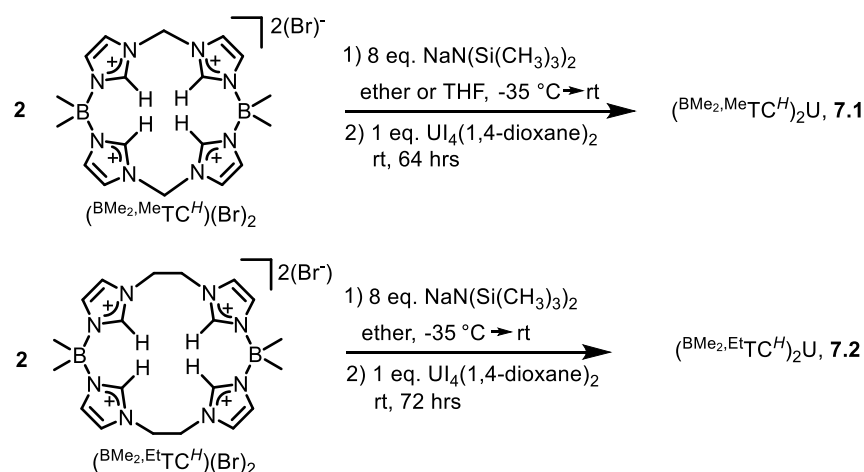


Figure 7.1: **A:** Select examples of crystallographically characterized uranium(IV) NHC complexes involving tethered ligands to increase donation strength. **B:** Examples from Long (left) and Arnold (right) of using borate bidentate NHCs to bind to uranium and thorium.

was the only base effective for metalation of the ligand (Scheme 7.1). We were able to isolate the complex $(\text{BMe}_2\text{MeTC}^H)_2\text{U}$, **7.1**, in 25% yield as a bright purple solid after purification. The crude solid was crystallized by diffusion of hexanes into a toluene solution of **7.1**. The crystals of **7.1** revealed the structure shown in Figure 7.2: the first structurally characterized uranium(IV) octa-NHC complex. The X-ray structure shows that the two macrocycles chelated to the uranium center in a square antiprismatic geometry. Each of the U-C bonds are slightly different from one another, averaging to 2.62 Å in length, which is comparable to the other few reported uranium(IV) NHC complexes^{102, 253, 255}, but short compared to uranium(III) examples.^{106, 257, 258} The C₁-U₁-C₃ and the C₂-U₁-C₄ angles on a single macrocycle are 107.36(8)° and 109.91(7)°, respectively, which implies great strain on the macrocycle when bound to the uranium. In addition, the angle across macrocycles is C₁-U₁-C₅ 138.84(8)°, consistent with a near



Scheme 7.1: Synthesis of U(IV) complexes **7.1** and **7.2**.

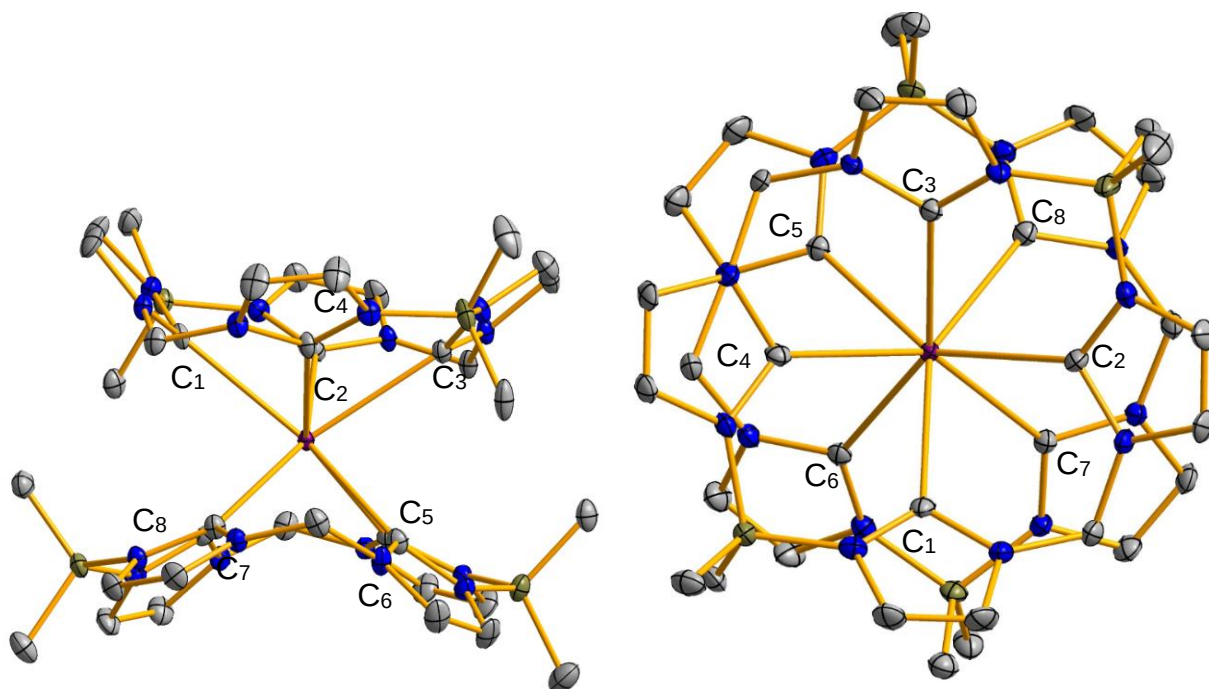


Figure 7.2: Crystal structure of $(^{\text{BMe}_2,\text{MeTCH}})_2\text{U}$ **7.1**. Purple, blue, gray, and olive ellipsoids (50% probability) represent uranium, nitrogen, carbon and boron. Hydrogen atoms omitted for clarity. Selected bond lengths ($\text{\AA}$) and angles ($^\circ$) are described as followed: U1-C1: 2.613(2), U1-C2: 2.625(2), U1-C3: 2.653(2), U1-C4: 2.632(2), U1-C5: 2.621(2), U1-C6: 2.617(2), U1-C7: 2.613(2), U1-C8: 2.620(2), C1-U1-C3: 107.36(8), C2-U1-C4: 109.90(7), C1-U1-C2: 70.35(8), C1-U1-C4: 69.64(8), C1-U1-C5: 138.84(8), C1-U1-C6: 149.11(8), C1-U1-C7: 85.24(8), C1-U1-C8: 81.52(8).

ideal staggered orientation. Curiously, the dimethyl borate units (BMe_2) are in close proximity to each other, rather than the expected staggered configuration.

The crude reaction contained a red paramagnetic species that was not identified. Fortuitously, the second paramagnetic species was air sensitive, in contrast to **7.1**, allowing us to purify the complex by brief exposure to air and subsequent extraction with toluene. Additionally, cooling the crude solution at $-35\text{ }^\circ\text{C}$ in toluene allowed us to purify the product without exposure to air, but did not result in complete separation of the paramagnetic species. The use of this alternative purification method led to loss of a small amount of the desired product due to its solubility. A third approach to purify our product involved using a small amount of silica gel to quench the reactive species and remove salts; the product had some instability on silica so using a minimal amount was crucial.

The ^1H NMR of pure **7.1** was paramagnetic (Spectrum **7.1**), which is characteristic of uranium(IV) complexes.¹⁰⁶ Based on ^1H DOSY NMR, there appears to be ten paramagnetic peaks corresponding to the complex, which is double of what is expected of paramagnetic metal complexes for this ligand.⁷² Similar to the crystal structure, it is likely that the macrocycles are locked in their staggered conformation, resulting in inequivalent signals. Comparing the ^1H NMR of **7.1** in different solvents showed that the complex remained paramagnetic, even in chlorinated and coordinating solvents (Figure **7.3**). Of note, the resonances at 8.36 and 7.97 in CD_2Cl_2 coalesce into one signal at 8.22 ppm in CD_3CN . The coalescence is an indication that the macrocycles are fluxional on the NMR time scale depending on the solvent. We have so far been unable to assign the NMR resonances.

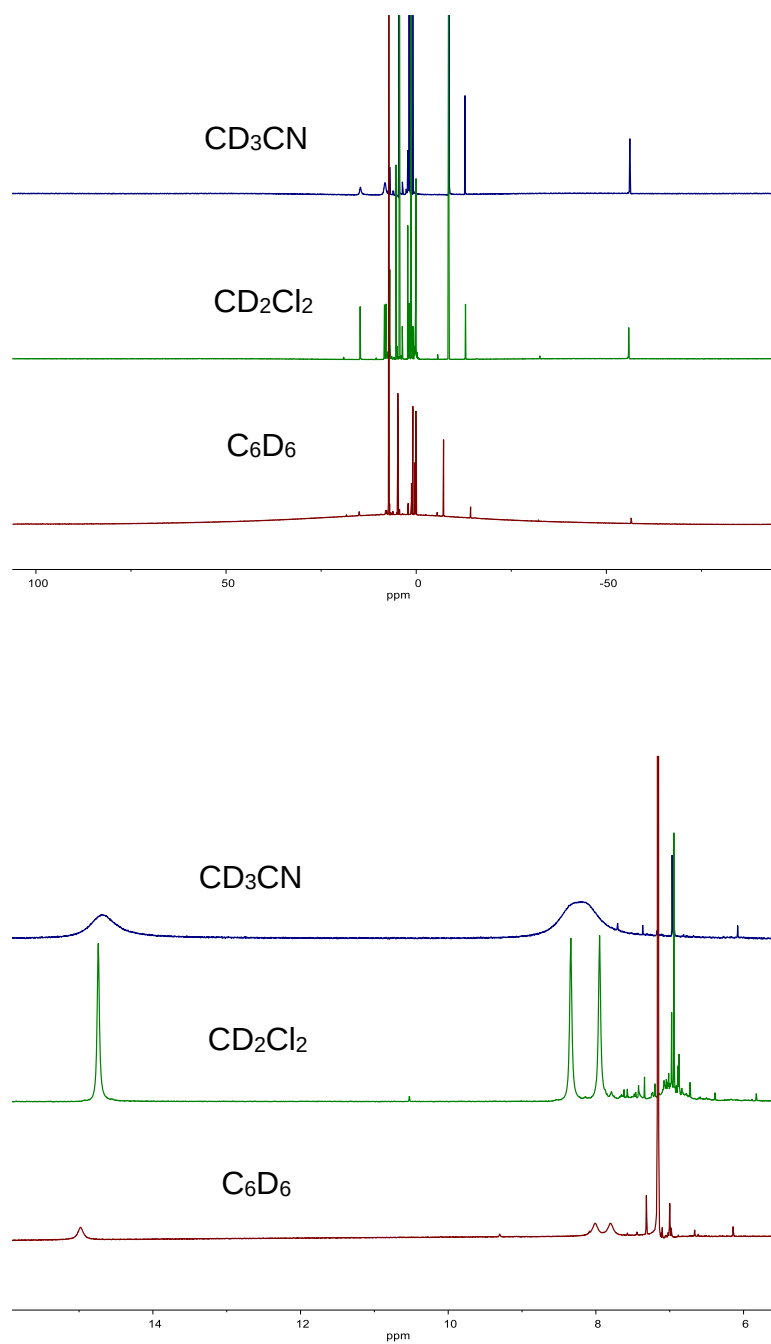


Figure 7.3: NMR comparison of **7.1** in CD_3CN (top, **blue**), CD_2Cl_2 (middle, **green**) and C_6D_6 (bottom, **red**).

Following this, VT NMR was run for **7.1** in CD₃CN (Figure **7.4**). It was shown that at higher temperatures, the peaks began to move towards the diamagnetic region, but the peak that coalesced (8.22 ppm) nearly disappeared at 50 °C. The shifting effect was reversible, as cooling down resulted in it returning to the original NMR spectrum (Figure **7.4**, top).

We applied the synthesis for **7.1** to the synthesis of the 18-atom ringed variant, **7.2** (Scheme **7.1**). We were able to isolate only one single crystal from a benzene and hexanes crystallization; the resulting structure is shown in Figure **7.5**. The isolated complex was also an octa-NHC complex, similar to **7.1**, but contained striking differences. The complex had a very high symmetry associated with it ($P2_1/c$ for **7.1** versus $Fddd$ for **7.2**). The two U-C bonds, U₁-C₁ and U₁-C₂ are 2.7136(1) Å and 2.6224(1) Å respectively. While the U₁-C₂ bond is comparable to molecule **7.1** in the U-C length, U₁-C₁ bond length is considerably longer than most uranium(IV) NHC complexes and is the second longest reported value.¹⁰² The geometry of the complex is square prismatic, where the NHC bonds are almost entirely eclipsed.²⁵⁹ As a consequence, the BMe₂ moieties are completely staggered. The macrocycle is has a similarly highly bent character to it (C₁-U₁-C₃ and C₂-U₁-C₄ angles are 106.488(1)° and 106.253(1), respectively), but, due to the larger macrocycle size, appears very unstable.

We have made significant efforts to reproduce this molecule on a measurable scale, but have not been successful so far. Modification of reaction solvent (THF, DME, 1,4-dioxane, Me-THF) and bases (*vide supra*) have not resulted in reproducible syntheses. It is likely that forming the 7-membered chelate for **7.2** is much more unfavorable compared to the 6-membered chelate for **7.1**. Due to the nature of uranium

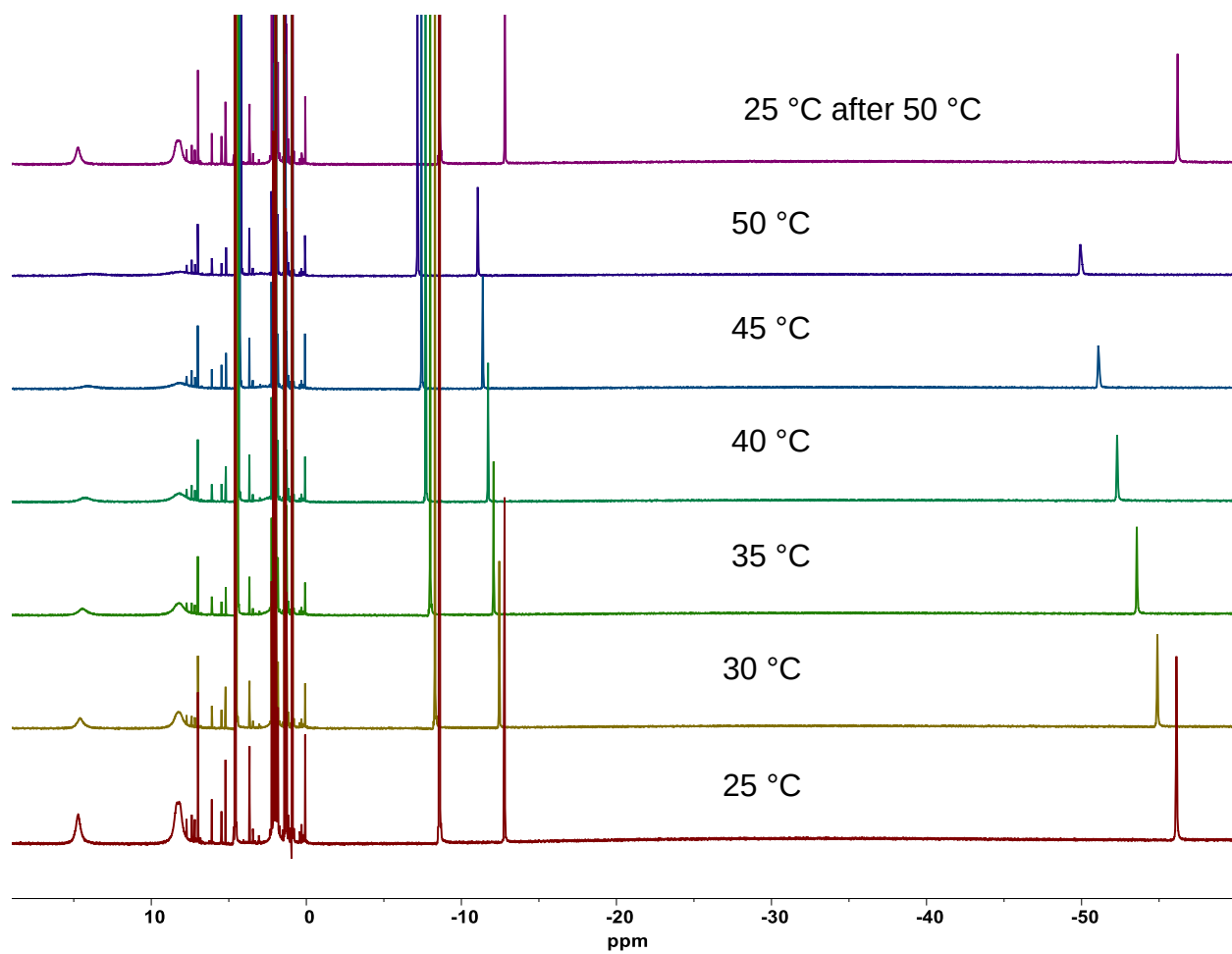


Figure 7.4: VT NMR of **7.1** in CD₃CN. Paramagnetic peaks are fully reversible after cooling back down to 25 °C (top, **purple**).

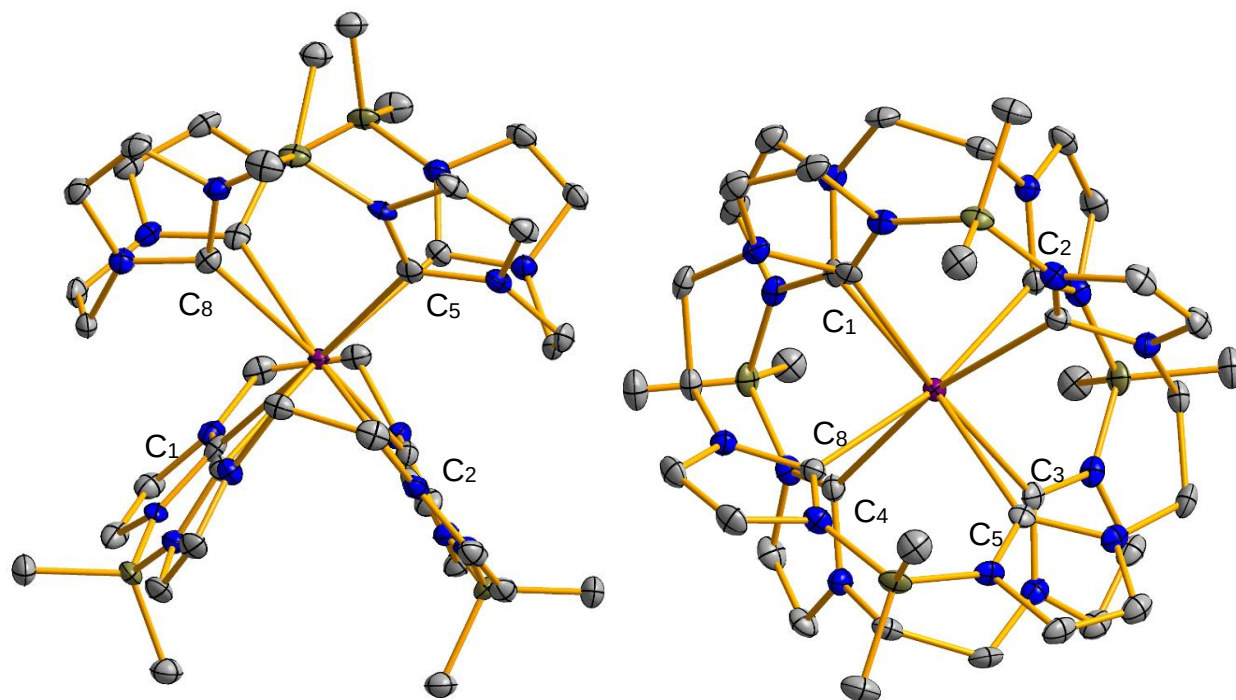
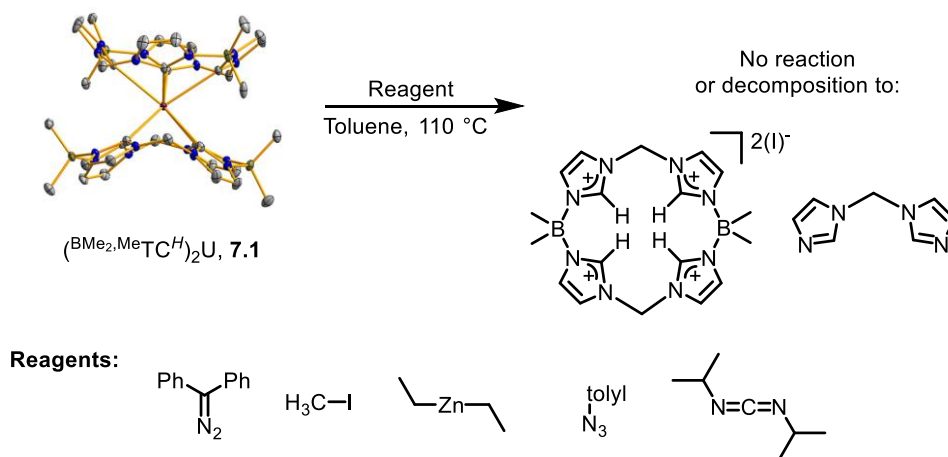


Figure 7.5: Crystal structure of $(^{\text{BMe}_2,\text{EtTC}^H})_2\text{U}$, **7.2**. Purple, blue, gray, and olive ellipsoids (50% probability) represent uranium, nitrogen, carbon and boron, respectively. Hydrogen atoms and solvent molecules are omitted for clarity. Selected bond lengths (Å) and angles (°) are described as followed: $\text{U}_1\text{-C}_1$: 2.7136(1), $\text{U}_1\text{-C}_2$: 2.6224(1), $\text{C}_1\text{-U-C}_2$: 66.190(1), $\text{C}_1\text{-U}_1\text{-C}_3$: 106.488(1), $\text{C}_2\text{-U}_1\text{-C}_4$: 106.253(1) $\text{C}_1\text{-U}_1\text{-C}_5$: 175.079(1), $\text{C}_2\text{-U}_1\text{-C}_8$: 168.706(1).

NHC complexes needing to eliminate an acid (HMDS for example) to metallate, this would make formation of **7.2** largely unfavorable due to ring strain. It is possible that an even larger NHC macrocycle may be able to circumvent this.

Since we are interested in group transfer reactions, we attempted to incorporate a ninth ligand onto **7.1**. The summary of the results is shown by Scheme 7.2. We tried a variety of reagents, including two electron oxidants, electrophiles, and nucleophiles, to try to form new complexes from **7.1**. Unfortunately, none of these resulted in constructive reactivity. In cases where reactivity was observed, NMR and X-ray crystallography were used to confirm either dissociation of the macrocycle (in the case of methyl iodide) or decomposition to the diimidazole. It seems, so far, that a ninth ligand cannot be incorporated without total decomposition of the complex.

The ability of **7.1** to not coordinate a ninth ligand is congruent with the air stability



Scheme 7.2: Reactions of **7.1** with different reagents

of the complex. In the solid state, **7.1** appears to be air stable for several months. An NMR tube containing **7.1** still has purple crystals after being on air for 12 months, but still has decomposed to some extent. The exhibited stability is incredibly unusual for a uranium(IV) complex and has only been reported for one other complex, a similar sandwich-like complex that uses a tetramethyltetraazaannulene (TMTAA) ligand.²⁶⁰

Given the inherent stability of **7.1**, we attempted electrochemistry of **7.1** in THF (Figure **7.6**). The widescan CV shows two specific redox events: a reversible oxidation at 0.055 V and a quasi-reversible reduction at -2.85 V. The observation of these waves implies that an electron can be added to or removed from the complex. The reduction to uranium(III) is at an exceedingly low potential, which shows that synthesizing the isostructural uranium(III) complexes would be very difficult.

The reasonably obtainable oxidation potential for **7.1** led us to attempt oxidation to uranium(V) using a silver salt.²⁶¹ Based on **Scheme 7.3**, we added silver hexafluorophosphate (AgPF₆) to a solution of **7.1** in THF; an immediate color change to pink with precipitation of silver metal was observed. Upon stirring overnight, however, the reaction congealed into a solid, indicative of THF polymerization, which is common for actinide species. Surprisingly, conducting this oxidation in CD₂Cl₂ to monitor by NMR resulted in no reactivity of **7.1**. We are currently redoing this oxidation in a non-cyclic glyme solvent, like 1,2-dimethoxyethane (DME), to confirm identity of the uranium(V) species. We have previously observed no redox character with the actual ligand before, so isolation of the likely uranium(V) species would be to our knowledge the first evidence of a uranium(V) NHC complex.

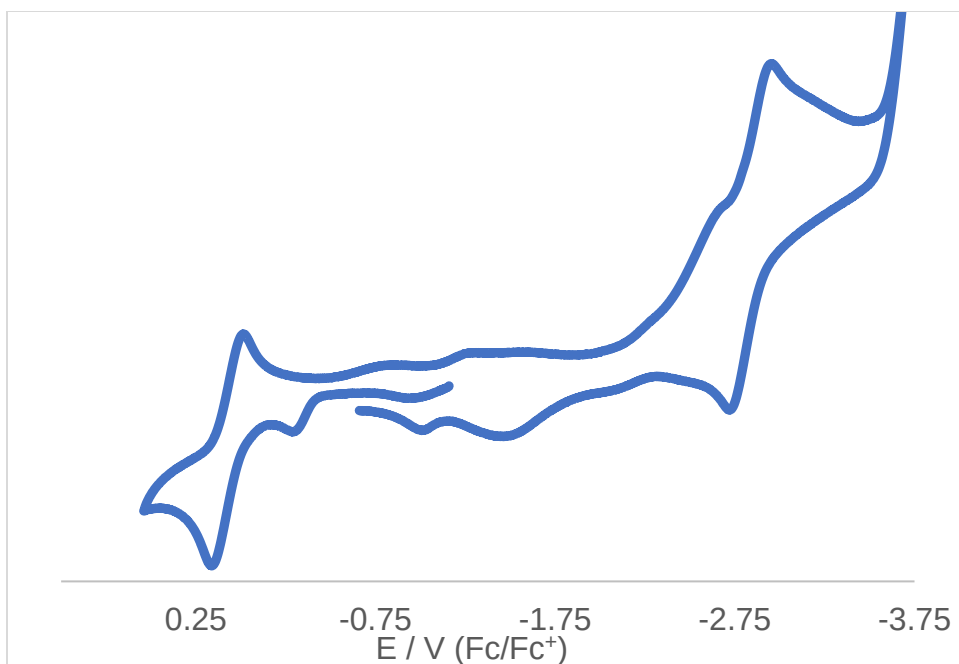
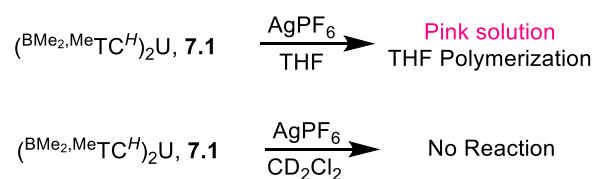


Figure 7.6: Widescan CV of **7.1** in THF with 0.1 M (TBA)(PF₆) as the supporting electrolyte at 100 mV/s scanrate. Reversible wave at 0.055 V and quasi-reversible wave at -2.85 V. Referenced to Fc/Fc⁺.



Scheme 7.3: Attempted oxidations of **7.1** to uranium(V) species.

Conclusion

We have synthesized the first uranium complexes using a macrocyclic tetra-NHCs. We found that adding two equivalents of the ligands ($^{\text{BMe}_2, \text{Me}}\text{TC}^{\text{H}}$) and ($^{\text{BMe}_2, \text{Et}}\text{TC}^{\text{H}}$) to $\text{U}(\text{I}_4(1,4\text{-Dioxane})_2$ resulted in isolation of ($^{\text{BMe}_2, \text{Me}}\text{TC}^{\text{H}}$) $_2\text{U}$ and ($^{\text{BMe}_2, \text{Et}}\text{TC}^{\text{H}}$) $_2\text{U}$. Despite having one atom difference in linker length, the molecules are strikingly different from one another, where one has a square antiprismatic geometry and the other has a square prismatic. Despite multiple attempts, reactions to incorporate a ninth ligand onto ($^{\text{BMe}_2, \text{Me}}\text{TC}^{\text{H}}$) $_2\text{U}$ were met with failure, and any reactivity resulted in ligand decomposition. Additionally, electrochemistry of ($^{\text{BMe}_2, \text{Me}}\text{TC}^{\text{H}}$) $_2\text{U}$ revealed that reversible and quasi-reversible oxidation and reductions are possible. Reacting ($^{\text{BMe}_2, \text{Me}}\text{TC}^{\text{H}}$) $_2\text{U}$ with AgPF_6 resulted in a distinct color change to the presumed uranium(V) complex, but this polymerized THF. Currently we are attempting to isolate the uranium(V) complex and understanding the magnetic properties of the uranium(IV) species.

Experimental

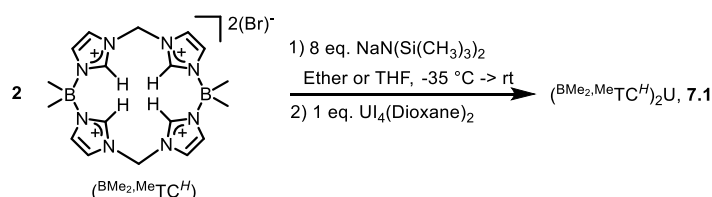
General Considerations for Synthesis:

All reactions, workups and manipulations involving the NHC metal complexes and subsequent reactions were done using standard Schlenk techniques under N₂ or in an MBraun Unilab glovebox under N₂ unless otherwise stated. All glassware for aforementioned reactions were dried at 170 °C overnight before use. For air sensitive reactions, tetrahydrofuran (THF), toluene, hexanes and diethyl ether were dried on an Innovative Technologies Pure Solv MD-7 Solvent Purification System, degassed by three freeze-pump-thaw cycles on a Schlenk line, and subsequently stored under activated 4 Å molecular sieves prior to use. Anhydrous acetonitrile (CH₃CN) was prepared by distillation over phosphorous pentoxide, followed by degassing by three freeze-pump-thaw cycles and stored over activated 4 Å molecular sieves prior to use. Benzene and pentane were purchased anhydrous from Sigma-Aldrich, degassed by three freeze-pump-thaw cycles and subsequently stored over activated 4 Å molecular sieves prior to use. For anhydrous NMR solvents, benzene-*d*₆ (C₆D₆), methylene chloride-*d*₂ (CD₂Cl₂) and acetonitrile-*d*₃ (CD₃CN) were degassed by three freeze-pump-thaw cycles and subsequently stored over activated 4 Å molecular sieves prior to use. Celite and silica gel used in the purification of metal complexes were dried overnight at 240 °C and subsequently stored in the glovebox prior to use. All reagents were purchased from commercial vendors at highest purity. $\text{U}(\text{1,4-Dioxane})_2$ ²⁶², $(\text{BMe}_2\text{MeTCH})_2(\text{Br})_2$ ⁷², $(\text{BMe}_2\text{EtTCH})_2(\text{Br})_2$ ¹⁶⁹ were prepared by previous literature procedure or as described previously.

General Considerations for X-ray Crystallography:

Crystallographic X-ray data for **7.1** and **7.2** were collected using Mo-K α radiation (λ = 0.71073) on an Oxford Diffraction Excalibur Eos CCD area detector diffractometer using ω scans at the University of Edinburgh, Scotland. Used absorption correction was “Analytical numeric absorption correction using a multifaceted crystal model”. Structures were solved using SHELX and SHELXE64 software. Molecule **7.1** was treated with PLATON SQUEEZE command to remove heavily disordered toluene molecule.

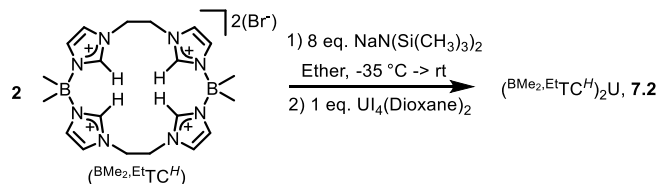
Synthesis of $(\text{BMe}_2, \text{MeTC}^H)_2\text{U}$, **7.1**:



To a 20 mL scintillation vial, $(\text{BMe}_2, \text{MeTC}^H)(\text{Br})_2$ (0.500 g, 0.930 mmol, 2 eq.) was added with 17 mL of THF. The reaction then cooled to -35°C in the freezer. The vial was then taken out of the freezer and solid sodium bis(trimethylsilyl)amide (0.6821 g, 3.720 mmol, 8 eq.) was added as one portion; the slurry began to gradually turn yellow/brown as it was warmed up to ambient temperature. Following this, solid $\text{UI}_4(1,4\text{-dioxane})_2$ (0.4286 g, 0.465 mmol, 1 eq.) was added as one portion and the residue was washed in with a small amount of THF. The solution immediately turned black and was stirred for 64 hours at room temperature. The solution was then filtered over a short plug of silica and washed with additional THF until the purple band stopped eluting. The resulting purple solution was then concentrated again and was taken up into toluene and filtered over a short pad of Celite. The toluene was concentrated and dried thoroughly, yielding **7.1** as a dark

purple powder (0.113 g, 25% yield). **Widescan ^1H NMR** (599.74 MHz, CD_2Cl_2): 14.76, 8.36, 7.97, 6.96, 4.45, 1.91, 0.18, -8.50, 12.94, -55.86. **UV-Vis (THF)**: 476 (210 L/cm * mol), 558 (920 L/cm * mol)

Synthesis of $\text{U(IV)}[(\text{BMe}_2, \text{EtTC}^H)]_2$, **7.2**:



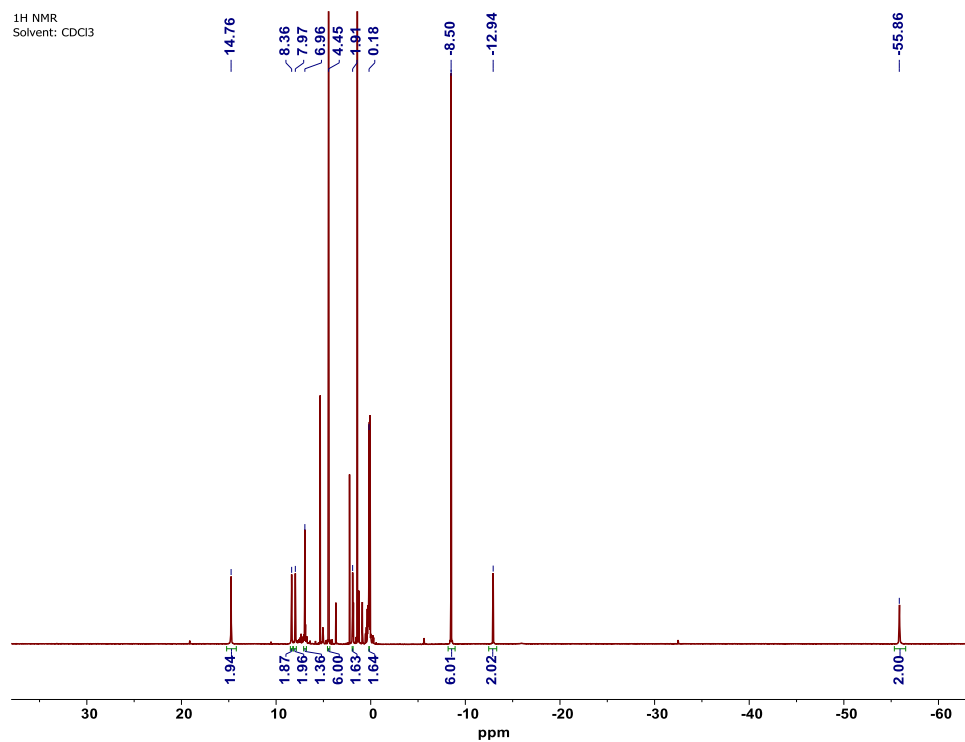
To an 8 mL scintillation vial, $(\text{BMe}_2, \text{EtTC}^H)(\text{Br})_2$ (0.0279g, 0.0442 mmol, 2 eq.) was added with 2 mL of diethyl ether and was cooled to -35°C . To this was added solid sodium bis(trimethylsilyl)amide (0.0324 g, 0.1767 mmol, 8 eq.) in one portion; the slurry gradually turned bright orange as it warmed to ambient temperature. $\text{U}_4(1,4\text{-dioxane})_2$ (0.0204 g, 0.0221 mmol, 1 eq.) was added as one portion, which it immediately turned black. The solution was stirred at ambient temperature for 72 hours. The solution was concentrated in vacuo and extracted with C_6D_6 and transferred to an NMR tube. After NMR analysis the solution was crystallized with a counter layer of hexanes resulting in a single dark orange crystal as **7.2**.

Attempts for Further Reactions with **7.1**:

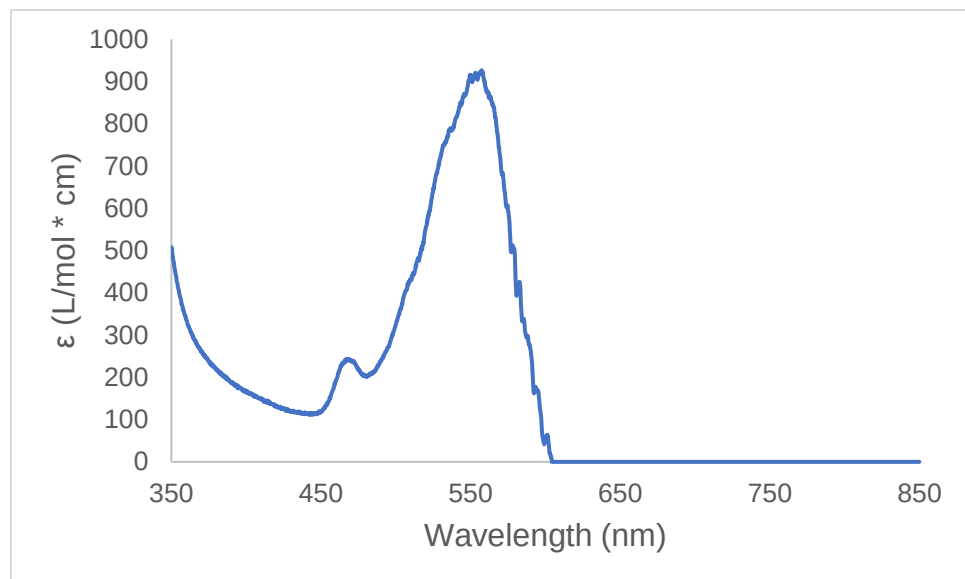
In a 20 mL scintillation vial, 0.005 g of **7.1** (0.05070 mmol, 1 eq.) was dissolved in 2 mL of toluene. To this solution was added 1 drop of the reagent for liquids or 5 equivalents of the solid. The solution was stirred for 16 hours at room temperature. None of these had any noticeable reaction. They were then and were then heated overnight at 110°C to try to promote reactivity. The solutions with a noticeable reaction had the toluene

removed in vacuo, and the residue was redissolved in either CH_2Cl_2 or CH_3CN and recrystallized with a counter layer of pentane or diethyl ether respectively.

Selected Spectral Characterization:



Spectrum 7.1: ¹H NMR of **7.1** in CD₂Cl₂. Peaks indicated correspond to the product as indicated by ¹H NMR.



Spectrum 7.2: UV-VIS spectrum of **7.1** in THF (8.450×10^{-4} M)

Chapter Eight: Conclusion

The first examples of synthesizing bifunctional N-Heterocyclic carbene (NHC)-CO₂ adducts and NHC-HCO₃ salts have been demonstrated. These NHC adducts were successfully used to functionalize gold film over nanosphere (AuFON) surfaces after heating the neat solid under vacuum on the surfaces. The surfaces were nano roughened and could be used for surface enhanced Raman spectroscopy (SERS). This enabled the first study of NHC functionalized surfaces using SERS. Post-synthetic functionalization of these surfaces could be monitored using SERS, including reactions that would normally decompose thiol functionalized surfaces, such as reactions with strong bases.

We also demonstrated a method of functionalizing gold nanoparticles (AuNPs) that were large enough to be SERS active, circumventing the AuNP size problem with previously NHC functionalized nanoparticles. A useful functional group, nitro, was reduced to an amine and further functionalized on surfaces, was reported. The gold(I) precursor synthesized circumvented a larger problem with NHC-CO₂ adduct synthesis, in which a strong base or a strong reductant like NaBH₄ was not needed. This approach will prove critical in applying functionalized NHC AuNPs for medical purposes, due to the ability to synthesize functionalized gold(I) complexes without harsh conditions.

The first chiral macrocyclic tetra-NHC was synthesized. A new synthetic route was designed for the necessary chiral diimidazole that circumvented scalability problems with typical diimidazole NHC precursors. The macrocycle could be formed by reaction with a borane dielectrophile and metallated with a strong base and a metal salt to form ((S,S)-1,2-Cy,BMe₂TC^H)Pd), ((S,S)-1,2-Cy,BMe₂TC^H)Fe and ((S,S)-1,2-Cy,BMe₂TC^H)Co, which are chiral divalent metal complexes.

$((S,S)\text{-}1,2\text{-Cy,BMe}_2\text{TC}^H)\text{Fe}$ exhibited unprecedented reactivity to form diazo $((S,S)\text{-}1,2\text{-Cy,BMe}_2\text{TC}^H)\text{Fe}(\text{N}_2\text{CPh}_2)$, alkylidene $((S,S)\text{-}1,2\text{-Cy,BMe}_2\text{TC}^H)\text{Fe}(\text{CPh}_2)$, imide $((S,S)\text{-}1,2\text{-Cy,BMe}_2\text{TC}^H)\text{Fe}(\text{NMe}_3)$, and tetrazene $((S,S)\text{-}1,2\text{-Cy,BMe}_2\text{TC}^H)\text{Fe}((\text{hex-1-ene})\text{N}_4(\text{hex-1-ene}))$, metal complexes from diazoalkanes or organic azides. The isolated diazo and alkylidene complexes are the first examples on an iron NHC complex. The iron alkylidene complex appears to be in the iron(IV) oxidation state, which an important species for iron-catalyzed olefin metathesis. The iron imide isolated has the longest Fe-N bond of any iron(IV) imide, and, based on electrochemistry, may be able to access the iron(V) oxidation state. Small organic azides lead to nitrene insertion into the NHC bond in the macrocycle, showing the first imide insertions into iron NHC bonds.

The synthesis used to generate the new chiral diimidazoles could be used for making a variety of C_2 symmetric diimidazoles. The synthetic route overcomes the major limitation of the reported syntheses, setting the stage for a new ligand class for asymmetric catalysis.

Finally, the first examples of uranium octa-NHC complexes, $(\text{BMe}_2,\text{MeTC}^H)_2\text{U}$ and $(\text{BMe}_2,\text{EtTC}^H)_2\text{U}$, have been synthesized. Two different complexes were isolated and have different geometries despite the small difference in macrocycle size. The complexes have the most uranium-carbon bonds of any compound reported to date.

References

1. Arduengo, A. J.; Harlow, R. L.; Kline, M., A stable crystalline carbene. *Journal of the American Chemical Society*. **1991**, *113*, 361-363.
2. Hopkinson, M. N.; Richter, C.; Schedler, M.; Glorius, F., An overview of N-heterocyclic carbenes. *Nature*. **2014**, *510*, 485.
3. Doddi, A.; Peters, M.; Tamm, M., N-Heterocyclic Carbene Adducts of Main Group Elements and Their Use as Ligands in Transition Metal Chemistry. *Chemical Reviews*. **2019**, *119*, 6994-7112.
4. Flanigan, D. M.; Romanov-Michailidis, F.; White, N. A.; Rovis, T., Organocatalytic Reactions Enabled by N-Heterocyclic Carbenes. *Chemical Reviews*. **2015**, *115*, 9307-9387.
5. Hahn, F. E.; Jahnke, M. C., Heterocyclic Carbenes: Synthesis and Coordination Chemistry. *Angewandte Chemie International Edition*. **2008**, *47*, 3122-3172.
6. Díez-González, S.; Marion, N.; Nolan, S. P., N-Heterocyclic Carbenes in Late Transition Metal Catalysis. *Chemical Reviews*. **2009**, *109*, 3612-3676.
7. Herrmann, W. A., N-Heterocyclic Carbenes: A New Concept in Organometallic Catalysis. *Angewandte Chemie International Edition*. **2002**, *41*, 1290-1309.
8. Jacobsen, H.; Correa, A.; Poater, A.; Costabile, C.; Cavallo, L., Understanding the M(NHC) (NHC=N-heterocyclic carbene) bond. *Coordination Chemistry Reviews*. **2009**, *253*, 687-703.
9. Grubbs, R. H., Olefin-Metathesis Catalysts for the Preparation of Molecules and Materials (Nobel Lecture). *Angewandte Chemie International Edition*. **2006**, *45*, 3760-3765.

10. Occhipinti, G.; Jensen, V. R., Nature of the Transition Metal–Carbene Bond in Grubbs Olefin Metathesis Catalysts. *Organometallics*. **2011**, *30*, 3522-3529.
11. Sanford, M. S.; Ulman, M.; Grubbs, R. H., New Insights into the Mechanism of Ruthenium-Catalyzed Olefin Metathesis Reactions. *Journal of the American Chemical Society*. **2001**, *123*, 749-750.
12. Galan, B. R.; Kalbarczyk, K. P.; Szczepankiewicz, S.; Keister, J. B.; Diver, S. T., A Rapid and Simple Cleanup Procedure for Metathesis Reactions. *Organic Letters*. **2007**, *9*, 1203-1206.
13. Polshettiwar, V.; Varma, R. S., Olefin Ring Closing Metathesis and Hydrosilylation Reaction in Aqueous Medium by Grubbs Second Generation Ruthenium Catalyst. *The Journal of Organic Chemistry*. **2008**, *73*, 7417-7419.
14. Årstad, E.; Barrett, A. G. M.; Hopkins, B. T.; Köbberling, J., ROMPgel-Supported Triphenylphosphine with Potential Application in Parallel Synthesis. *Organic Letters*. **2002**, *4*, 1975-1977.
15. Schuster, O.; Yang, L.; Raubenheimer, H. G.; Albrecht, M., Beyond Conventional N-Heterocyclic Carbenes: Abnormal, Remote, and Other Classes of NHC Ligands with Reduced Heteroatom Stabilization. *Chemical Reviews*. **2009**, *109*, 3445-3478.
16. Soleilhavoup, M.; Bertrand, G., Cyclic (Alkyl)(Amino)Carbenes (CAACs): Stable Carbenes on the Rise. *Accounts of Chemical Research*. **2015**, *48*, 256-266.
17. Love, J. C.; Estroff, L. A.; Kriebel, J. K.; Nuzzo, R. G.; Whitesides, G. M., Self-Assembled Monolayers of Thiolates on Metals as a Form of Nanotechnology. *Chemical Reviews*. **2005**, *105*, 1103-1170.

18. Schoenfish, M. H.; Pemberton, J. E., Air Stability of Alkanethiol Self-Assembled Monolayers on Silver and Gold Surfaces. *Journal of the American Chemical Society*. **1998**, *120*, 4502-4513.
19. Ulman, A., Formation and Structure of Self-Assembled Monolayers. *Chemical Reviews*. **1996**, *96*, 1533-1554.
20. Smith, C. A.; Narouz, M. R.; Lummis, P. A.; Singh, I.; Nazemi, A.; Li, C.-H.; Crudden, C. M., N-Heterocyclic Carbenes in Materials Chemistry. *Chemical Reviews*. **2019**, *119*, 4986-5056.
21. Crudden, C. M.; Horton, J. H.; Ebraliidze, I. I.; Zenkina, O. V.; McLean, A. B.; Drevniok, B.; She, Z.; Kraatz, H.-B.; Mosey, N. J.; Seki, T.; Keske, E. C.; Leake, J. D.; Rousina-Webb, A.; Wu, G., Ultra stable self-assembled monolayers of N-heterocyclic carbenes on gold. *Nature Chemistry*. **2014**, *6*, 409.
22. Crudden, C. M.; Horton, J. H.; Narouz, M. R.; Li, Z.; Smith, C. A.; Munro, K.; Baddeley, C. J.; Larrea, C. R.; Drevniok, B.; Thanabalasingam, B.; McLean, A. B.; Zenkina, O. V.; Ebraliidze, I. I.; She, Z.; Kraatz, H.-B.; Mosey, N. J.; Saunders, L. N.; Yagi, A., Simple direct formation of self-assembled N-heterocyclic carbene monolayers on gold and their application in biosensing. *Nature Communications*. **2016**, *7*, 12654.
23. Zhukhovitskiy, A. V.; Mavros, M. G.; Van Voorhis, T.; Johnson, J. A., Addressable Carbene Anchors for Gold Surfaces. *Journal of the American Chemical Society*. **2013**, *135*, 7418-7421.
24. MacLeod, M. J.; Johnson, J. A., PEGylated N-Heterocyclic Carbene Anchors Designed To Stabilize Gold Nanoparticles in Biologically Relevant Media. *Journal of the American Chemical Society*. **2015**, *137*, 7974-7977.

25. Wang, G.; Rühling, A.; Amirjalayer, S.; Knor, M.; Ernst, J. B.; Richter, C.; Gao, H.-J.; Timmer, A.; Gao, H.-Y.; Doltsinis, N. L.; Glorius, F.; Fuchs, H., Ballbot-type motion of N-heterocyclic carbenes on gold surfaces. *Nature Chemistry*. **2016**, 9, 152.
26. Nguyen, D. T.; Freitag, M.; Körsgen, M.; Lamping, S.; Rühling, A.; Schäfer, A. H.; Siekman, M. H.; Arlinghaus, H. F.; van der Wiel, W. G.; Glorius, F.; Ravoo, B. J., Versatile Micropatterns of N-Heterocyclic Carbenes on Gold Surfaces: Increased Thermal and Pattern Stability with Enhanced Conductivity. *Angewandte Chemie International Edition*. **2018**, 57, 11465-11469.
27. Saha, K.; Agasti, S. S.; Kim, C.; Li, X.; Rotello, V. M., Gold Nanoparticles in Chemical and Biological Sensing. *Chemical Reviews*. **2012**, 112, 2739-2779.
28. Ahmad, A.; Khan, F.; Mishra, R. K.; Khan, R., Precision Cancer Nanotherapy: Evolving Role of Multifunctional Nanoparticles for Cancer Active Targeting. *Journal of Medicinal Chemistry*. **2019**.
29. Wechsler, M. E.; Vela Ramirez, J. E.; Peppas, N. A., 110th Anniversary: Nanoparticle Mediated Drug Delivery for the Treatment of Alzheimer's Disease: Crossing the Blood–Brain Barrier. *Industrial & Engineering Chemistry Research*. **2019**.
30. Singh, P.; Pandit, S.; Mokkapati, V. R. S. S.; Garg, A.; Ravikumar, V.; Mijakovic, I., Gold Nanoparticles in Diagnostics and Therapeutics for Human Cancer. *International Journal of Molecular Sciences*. **2018**, 19.
31. Willets, K. A.; Van Duyne, R. P., Localized Surface Plasmon Resonance Spectroscopy and Sensing. *Annual Review of Physical Chemistry*. **2007**, 58, 267-297.

32. Trujillo, M. J.; Jenkins, D. M.; Bradshaw, J. A.; Camden, J. P., Surface-enhanced Raman scattering of uranyl in aqueous samples: implications for nuclear forensics and groundwater testing. *Analytical Methods*. **2017**, *9*, 1575-1579.
33. Hu, Q.; Tay, L.-L.; Noestheden, M.; Pezacki, J. P., Mammalian Cell Surface Imaging with Nitrile-Functionalized Nanoprobes: Biophysical Characterization of Aggregation and Polarization Anisotropy in SERS Imaging. *Journal of the American Chemical Society*. **2007**, *129*, 14-15.
34. Ren, X.; Tan, E.; Lang, X.; You, T.; Jiang, L.; Zhang, H.; Yin, P.; Guo, L., Observing reduction of 4-nitrobenzethiol on gold nanoparticles in situ using surface-enhanced Raman spectroscopy. *Physical Chemistry Chemical Physics*. **2013**, *15*, 14196-14201.
35. Li, Z.; Narouz, M. R.; Munro, K.; Hao, B.; Crudden, C. M.; Horton, J. H.; Hao, H., Carboxymethylated Dextran-Modified N-Heterocyclic Carbene Self-Assembled Monolayers on Gold for Use in Surface Plasmon Resonance Biosensing. *ACS Applied Materials & Interfaces*. **2017**, *9*, 39223-39234.
36. Li, Z.; Munro, K.; Narouz, M. R.; Lau, A.; Hao, H.; Crudden, C. M.; Horton, J. H., Self-Assembled N-Heterocyclic Carbene-Based Carboxymethylated Dextran Monolayers on Gold as a Tunable Platform for Designing Affinity-Capture Biosensor Surfaces. *ACS Applied Materials & Interfaces*. **2018**, *10*, 17560-17570.
37. Rogers, M. M.; Stahl, S. S., N-Heterocyclic Carbenes as Ligands for High-Oxidation-State Metal Complexes and Oxidation Catalysis. In *N-Heterocyclic Carbenes in Transition Metal Catalysis*, Glorius, F., Ed. Springer Berlin Heidelberg: Berlin, Heidelberg, 2007; pp 21-46.

38. Pyykkö, P.; Xu, W.-H., On the Extreme Oxidation States of Iridium. *Chemistry – A European Journal*. **2015**, *21*, 9468-9473.
39. Byrne, E. K.; Theopold, K. H., Redox chemistry of tetrakis(1-norbornyl)cobalt. Synthesis and characterization of a cobalt(V) alkyl and self-exchange rate of a Co(III)/Co(IV) couple. *Journal of the American Chemical Society*. **1987**, *109*, 1282-1283.
40. Greenwood, N. N.; Earnshaw, A., Chemistry of the Elements (2nd Edition). Elsevier: 1997.
41. Zhang, L.; Liu, Y.; Deng, L., Three-Coordinate Cobalt(IV) and Cobalt(V) Imido Complexes with N-Heterocyclic Carbene Ligation: Synthesis, Structure, and Their Distinct Reactivity in C–H Bond Amination. *Journal of the American Chemical Society*. **2014**, *136*, 15525-15528.
42. Biffis, A.; Centomo, P.; Del Zotto, A.; Zecca, M., Pd Metal Catalysts for Cross-Couplings and Related Reactions in the 21st Century: A Critical Review. *Chemical Reviews*. **2018**, *118*, 2249-2295.
43. Noyori, R., Asymmetric Catalysis: Science and Opportunities (Nobel Lecture). *Angewandte Chemie International Edition*. **2002**, *41*, 2008-2022.
44. Crabtree, R., Iridium compounds in catalysis. *Accounts of Chemical Research*. **1979**, *12*, 331-337.
45. Su, B.; Cao, Z.-C.; Shi, Z.-J., Exploration of Earth-Abundant Transition Metals (Fe, Co, and Ni) as Catalysts in Unreactive Chemical Bond Activations. *Accounts of Chemical Research*. **2015**, *48*, 886-896.

46. Cheng, J.; Wang, L.; Wang, P.; Deng, L., High-Oxidation-State 3d Metal (Ti–Cu) Complexes with N-Heterocyclic Carbene Ligation. *Chemical Reviews*. **2018**, *118*, 9930-9987.
47. Buijse, M. A.; Baerends, E. J., Analysis of nondynamical correlation in the metal–ligand bond. Pauli repulsion and orbital localization in MnO–4. *The Journal of Chemical Physics*. **1990**, *93*, 4129-4141.
48. Kaupp, M., The role of radial nodes of atomic orbitals for chemical bonding and the periodic table. *Journal of Computational Chemistry*. **2007**, *28*, 320-325.
49. Bernhammer, J. C.; Frison, G.; Huynh, H. V., Electronic Structure Trends in N-Heterocyclic Carbenes (NHCs) with Varying Number of Nitrogen Atoms and NHC–Transition-Metal Bond Properties. *Chemistry – A European Journal*. **2013**, *19*, 12892-12905.
50. Kernbach, U.; Ramm, M.; Luger, P.; Fehlhammer, W. P., A Chelating Triscarbene Ligand and Its Hexacarbene Iron Complex. *Angewandte Chemie International Edition in English*. **1996**, *35*, 310-312.
51. Przyojski, J. A.; Arman, H. D.; Tonzetich, Z. J., Complexes of Iron(II) and Iron(III) Containing Aryl-Substituted N-Heterocyclic Carbene Ligands. *Organometallics*. **2012**, *31*, 3264-3271.
52. Hashimoto, T.; Hoshino, R.; Hatanaka, T.; Ohki, Y.; Tatsumi, K., Dinuclear Iron(0) Complexes of N-Heterocyclic Carbenes. *Organometallics*. **2014**, *33*, 921-929.
53. McGuinness, D. S.; Gibson, V. C.; Steed, J. W., Bis(carbene)pyridine Complexes of the Early to Middle Transition Metals: Survey of Ethylene Oligomerization and Polymerization Capability. *Organometallics*. **2004**, *23*, 6288-6292.

54. Anneser, M. R.; Haslinger, S.; Pöthig, A.; Cokoja, M.; Basset, J.-M.; Kühn, F. E., Synthesis and Characterization of an Iron Complex Bearing a Cyclic Tetra-N-heterocyclic Carbene Ligand: An Artificial Heme Analogue? *Inorganic Chemistry*. **2015**, *54*, 3797-3804.
55. Zhang, H.; Ouyang, Z.; Liu, Y.; Zhang, Q.; Wang, L.; Deng, L., (Aminocarbene)(Divinyltetramethyldisiloxane)Iron(0) Compounds: A Class of Low-Coordinate Iron(0) Reagents. *Angewandte Chemie International Edition*. **2014**, *53*, 8432-8436.
56. Wang, L.; Hu, L.; Zhang, H.; Chen, H.; Deng, L., Three-Coordinate Iron(IV) Bisimido Complexes with Aminocarbene Ligation: Synthesis, Structure, and Reactivity. *Journal of the American Chemical Society*. **2015**, *137*, 14196-14207.
57. Jacobs, B. P.; Wolczanski, P. T.; Jiang, Q.; Cundari, T. R.; MacMillan, S. N., Rare Examples of Fe(IV) Alkyl-Imide Migratory Insertions: Impact of Fe—C Covalency in (Me₂IPr)Fe(=NAd)R₂ (R = neoPe, 1-nor). *Journal of the American Chemical Society*. **2017**, *139*, 12145-12148.
58. Vogel, C.; Heinemann, F. W.; Sutter, J.; Anthon, C.; Meyer, K., An Iron Nitride Complex. *Angewandte Chemie International Edition*. **2008**, *47*, 2681-2684.
59. Muñoz Iii, S. B.; Lee, W.-T.; Dickie, D. A.; Scepaniak, J. J.; Subedi, D.; Pink, M.; Johnson, M. D.; Smith, J. M., Styrene Aziridination by Iron(IV) Nitrides. *Angewandte Chemie International Edition*. **2015**, *54*, 10600-10603.
60. Scepaniak, J. J.; Vogel, C. S.; Khusniyarov, M. M.; Heinemann, F. W.; Meyer, K.; Smith, J. M., Synthesis, Structure, and Reactivity of an Iron(V) Nitride. *Science*. **2011**, *331*, 1049.

61. Bucinsky, L.; Breza, M.; Lee, W.-T.; Hickey, A. K.; Dickie, D. A.; Nieto, I.; DeGayner, J. A.; Harris, T. D.; Meyer, K.; Krzystek, J.; Ozarowski, A.; Nehr Korn, J.; Schnegg, A.; Holldack, K.; Herber, R. H.; Telser, J.; Smith, J. M., Spectroscopic and Computational Studies of Spin States of Iron(IV) Nitrido and Imido Complexes. *Inorganic Chemistry*. **2017**, 56, 4751-4768.
62. Nieto, I.; Ding, F.; Bontchev, R. P.; Wang, H.; Smith, J. M., Thermodynamics of Hydrogen Atom Transfer to a High-Valent Iron Imido Complex. *Journal of the American Chemical Society*. **2008**, 130, 2716-2717.
63. Cutsail Iii, G. E.; Stein, B. W.; Subedi, D.; Smith, J. M.; Kirk, M. L.; Hoffman, B. M., EPR, ENDOR, and Electronic Structure Studies of the Jahn–Teller Distortion in an FeV Nitride. *Journal of the American Chemical Society*. **2014**, 136, 12323-12336.
64. Lee, W.-T.; Juarez, R. A.; Scepianiak, J. J.; Muñoz, S. B.; Dickie, D. A.; Wang, H.; Smith, J. M., Reaction of an Iron(IV) Nitrido Complex with Cyclohexadienes: Cycloaddition and Hydrogen-Atom Abstraction. *Inorganic Chemistry*. **2014**, 53, 8425-8430.
65. Crandell, Douglas W.; Muñoz, S. B.; Smith, J. M.; Baik, M.-H., Mechanistic study of styrene aziridination by iron(IV) nitrides. *Chemical Science*. **2018**, 9, 8542-8552.
66. Trofimenko, S., Recent advances in poly(pyrazolyl)borate (scorpionate) chemistry. *Chemical Reviews*. **1993**, 93, 943-980.
67. Saouma, C. T.; Peters, J. C., ME and ME complexes of iron and cobalt that emphasize three-fold symmetry (E=O, N, NR). *Coordination Chemistry Reviews*. **2011**, 255, 920-937.

68. Cramer, S. A.; Jenkins, D. M., Synthesis of Aziridines from Alkenes and Aryl Azides with a Reusable Macrocyclic Tetracarbene Iron Catalyst. *Journal of the American Chemical Society*. **2011**, *133*, 19342-19345.
69. Chandrachud, P. P.; Bass, H. M.; Jenkins, D. M., Synthesis of Fully Aliphatic Aziridines with a Macrocyclic Tetracarbene Iron Catalyst. *Organometallics*. **2016**, *35*, 1652-1657.
70. Elpitiya, G. R.; Malbrecht, B. J.; Jenkins, D. M., A Chromium(II) Tetracarbene Complex Allows Unprecedented Oxidative Group Transfer. *Inorganic Chemistry*. **2017**, *56*, 14101-14110.
71. Kück, J. W.; Anneser, M. R.; Hofmann, B.; Pöthig, A.; Cokoja, M.; Kühn, F. E., Fighting Fenton Chemistry: A Highly Active Iron(III) Tetracarbene Complex in Epoxidation Catalysis. *ChemSusChem*. **2015**, *8*, 4056-4063.
72. Anneser, M. R.; Elpitiya, G. R.; Powers, X. B.; Jenkins, D. M., Toward a Porphyrin-Style NHC: A 16-Atom Ringed Dianionic Tetra-NHC Macrocycle and Its Fe(II) and Fe(III) Complexes. *Organometallics*. **2019**, *38*, 981-987.
73. Lai, T.-S.; Che, C.-M.; Kwong, H.-L.; Peng, S.-M., Catalytic and asymmetric aziridination of alkenes catalysed by a chiral manganese porphyrin complex. *Chemical Communications*. **1997**, 2373-2374.
74. Li, Y.; Huang, J.-S.; Zhou, Z.-Y.; Che, C.-M.; You, X.-Z., Remarkably Stable Iron Porphyrins Bearing Nonheteroatom-Stabilized Carbene or (Alkoxy carbonyl)carbenes: Isolation, X-ray Crystal Structures, and Carbon Atom Transfer Reactions with Hydrocarbons. *Journal of the American Chemical Society*. **2002**, *124*, 13185-13193.

75. Chan, K.-H.; Guan, X.; Lo, V. K.-Y.; Che, C.-M., Elevated Catalytic Activity of Ruthenium(II)–Porphyrin-Catalyzed Carbene/Nitrene Transfer and Insertion Reactions with N-Heterocyclic Carbene Ligands. *Angewandte Chemie International Edition*. **2014**, *53*, 2982-2987.
76. Jin, L.-M.; Xu, X.; Lu, H.; Cui, X.; Wojtas, L.; Zhang, X. P., Effective Synthesis of Chiral N-Fluoroaryl Aziridines through Enantioselective Aziridination of Alkenes with Fluoroaryl Azides. *Angewandte Chemie International Edition*. **2013**, *52*, 5309-5313.
77. Wang, Y.; Wen, X.; Cui, X.; Wojtas, L.; Zhang, X. P., Asymmetric Radical Cyclopropanation of Alkenes with In Situ-Generated Donor-Substituted Diazo Reagents via Co(II)-Based Metalloradical Catalysis. *Journal of the American Chemical Society*. **2017**, *139*, 1049-1052.
78. Hu, Y.; Lang, K.; Tao, J.; Marshall, M. K.; Cheng, Q.; Cui, X.; Wojtas, L.; Zhang, X. P., Next-Generation D2-Symmetric Chiral Porphyrins for Cobalt(II)-Based Metalloradical Catalysis: Catalyst Engineering by Distal Bridging. *Angewandte Chemie International Edition*. **2019**, *58*, 2670-2674.
79. Khade, R. L.; Fan, W.; Ling, Y.; Yang, L.; Oldfield, E.; Zhang, Y., Iron Porphyrin Carbenes as Catalytic Intermediates: Structures, Mössbauer and NMR Spectroscopic Properties, and Bonding. *Angewandte Chemie*. **2014**, *126*, 7704-7708.
80. Liu, Y.; Xu, W.; Zhang, J.; Fuller, W.; Schulz, C. E.; Li, J., Electronic Configuration and Ligand Nature of Five-Coordinate Iron Porphyrin Carbene Complexes: An Experimental Study. *Journal of the American Chemical Society*. **2017**, *139*, 5023-5026.
81. Anneser, M. R.; Elpitiya, G. R.; Townsend, J.; Johnson, E. J.; Powers, X. B.; DeJesus, J. F.; Vogiatzis, K. D.; Jenkins, D. M., Unprecedented Five-Coordinate Iron(IV)

Imides Generate Divergent Spin States Based on the Imide R-Groups. *Angewandte Chemie International Edition*. **2019**, 58, 8115-8118.

82. Janssen-Müller, D.; Schlepphorst, C.; Glorius, F., Privileged chiral N-heterocyclic carbene ligands for asymmetric transition-metal catalysis. *Chemical Society Reviews*. **2017**, 46, 4845-4854.

83. Calcaterra, A.; D'Acquarica, I., The market of chiral drugs: Chiral switches versus de novo enantiomerically pure compounds. *Journal of Pharmaceutical and Biomedical Analysis*. **2018**, 147, 323-340.

84. Dalpozzo, R.; Lattanzi, A.; Pellissier, H., Applications of Chiral Three-membered Rings for Total Synthesis: A Review. *Current Organic Chemistry*. **2017**, 21, 1143-1191.

85. Kündig, E. P.; Seidel, T. M.; Jia, Y.-x.; Bernardinelli, G., Bulky Chiral Carbene Ligands and Their Application in the Palladium-Catalyzed Asymmetric Intramolecular α -Arylation of Amides. *Angewandte Chemie International Edition*. **2007**, 46, 8484-8487.

86. Martin, D.; Kehrli, S.; d'Augustin, M.; Clavier, H.; Mauduit, M.; Alexakis, A., Copper-Catalyzed Asymmetric Conjugate Addition of Grignard Reagents to Trisubstituted Enones. Construction of All-Carbon Quaternary Chiral Centers. *Journal of the American Chemical Society*. **2006**, 128, 8416-8417.

87. Mauleón, P.; Alonso, I.; Rivero, M. R.; Carretero, J. C., Enantioselective Synthesis of Chiral Sulfones by Rh-Catalyzed Asymmetric Addition of Boronic Acids to α,β -Unsaturated 2-Pyridyl Sulfones. *The Journal of Organic Chemistry*. **2007**, 72, 9924-9935.

88. Akiyama, K.; Wakabayashi, K.; Mikami, K., Enantioselective Heck-Type Reaction Catalyzed by tropos-Pd(II) Complex with Chiraphos Ligand. *Advanced Synthesis & Catalysis*. **2005**, 347, 1569-1575.

89. Lowry, R. J.; Veige, M. K.; Clément, O.; Abboud, K. A.; Ghiviriga, I.; Veige, A. S., New Constrained-Geometry C₂-Symmetric Di-N-heterocyclic Carbene Ligands and Their Mono- and Dinuclear Rhodium(I) Complexes: Design, Synthesis, and Structural Analysis. *Organometallics*. **2008**, 27, 5184-5195.
90. Mechler, M.; Frey, W.; Peters, R., Macrocyclic Salen–Bis-NHC Hybrid Ligands and Their Application to the Synthesis of Enantiopure Bi- and Trimetallic Complexes. *Organometallics*. **2014**, 33, 5492-5508.
91. Perry, M. C.; Cui, X.; Powell, M. T.; Hou, D.-R.; Reibenspies, J. H.; Burgess, K., Optically Active Iridium Imidazol-2-ylidene-oxazoline Complexes: Preparation and Use in Asymmetric Hydrogenation of Arylalkenes. *Journal of the American Chemical Society*. **2003**, 125, 113-123.
92. Kim, H.; Staikova, M.; Lough, A. J.; Chin, J., Stereospecific Synthesis of Alkyl-Substituted Vicinal Diamines from the Mother Diamine: Overcoming the “Intrinsic Barrier” to the Diaza-Cope Rearrangement Reaction. *Organic Letters*. **2009**, 11, 157-160.
93. Arnold, P. L.; Casely, I. J., F-Block N-Heterocyclic Carbene Complexes. *Chemical Reviews*. **2009**, 109, 3599-3611.
94. Kobayashi, S.; Sugiura, M.; Kitagawa, H.; Lam, W. W. L., Rare-Earth Metal Triflates in Organic Synthesis. *Chemical Reviews*. **2002**, 102, 2227-2302.
95. Bünzli, J.-C. G., Lanthanide Luminescence for Biomedical Analyses and Imaging. *Chemical Reviews*. **2010**, 110, 2729-2755.
96. Liddle, S. T., The Renaissance of Non-Aqueous Uranium Chemistry. *Angewandte Chemie International Edition*. **2015**, 54, 8604-8641.

97. Craft, E. S.; Abu-Qare, A. W.; Flaherty, M. M.; Garofolo, M. C.; Rincavage, H. L.; Abou-Donia, M. B., DEPLETED AND NATURAL URANIUM: CHEMISTRY AND TOXICOLOGICAL EFFECTS. *Journal of Toxicology and Environmental Health, Part B*. **2004**, 7, 297-317.
98. Summerscales, O. T.; Cloke, F. G. N.; Hitchcock, P. B.; Green, J. C.; Hazari, N., Reductive Cyclotetramerization of CO to Squarate by a U(III) Complex: The X-ray Crystal Structure of $[(U(\eta\text{-C}_8\text{H}_6\{\text{SiPr}_3\text{-1,4}\}_2)(\eta\text{-C}_5\text{Me}_4\text{H}))_2(\mu\text{-}\eta^2\text{:}\eta^2\text{-C}_4\text{O}_4)]$. *Journal of the American Chemical Society*. **2006**, 128, 9602-9603.
99. Evans, W. J.; Siladke, N. A.; Ziller, J. W., Reactivity of the tethered alkyl uranium bonds of $(\eta^5\text{:}\kappa^1\text{-C}_5\text{Me}_4\text{SiMe}_2\text{CH}_2)_2\text{U}$. *Comptes Rendus Chimie*. **2010**, 13, 775-780.
100. Roussel, P.; Scott, P., Complex of dinitrogen with trivalent uranium. *Journal of the American Chemical Society*. **1998**, 120, 1070-1071.
101. Arnold, P. L.; Mansell, S. M.; Maron, L.; McKay, D., Spontaneous reduction and C–H borylation of arenes mediated by uranium(III) disproportionation. *Nature Chemistry*. **2012**, 4, 668.
102. Arnold, P. L.; Blake, A. J.; Wilson, C., Synthesis and Small Molecule Reactivity of Uranium(IV) Alkoxide Complexes with both Bound and Pendant N-heterocyclic Carbene Ligands. *Chemistry – A European Journal*. **2005**, 11, 6095-6099.
103. Arnold, P. L.; Turner, Z. R.; Germeroth, A. I.; Casely, I. J.; Nichol, G. S.; Bellabarba, R.; Tooze, R. P., Carbon monoxide and carbon dioxide insertion chemistry of f-block N-heterocyclic carbene complexes. *Dalton Transactions*. **2013**, 42, 1333-1337.
104. Arnold, P. L.; Cadenbach, T.; Marr, I. H.; Fyfe, A. A.; Bell, N. L.; Bellabarba, R.; Tooze, R. P.; Love, J. B., Homo- and heteroleptic alkoxycarbene f-element complexes

and their reactivity towards acidic N–H and C–H bonds. *Dalton Transactions*. **2014**, 43, 14346-14358.

105. Arnold, P. L.; Kerr, R. W. F.; Weetman, C.; Docherty, S. R.; Rieb, J.; Cruickshank, F. L.; Wang, K.; Jandl, C.; McMullon, M. W.; Pöthig, A.; Kühn, F. E.; Smith, A. D., Selective and catalytic carbon dioxide and heteroallene activation mediated by cerium N-heterocyclic carbene complexes. *Chemical Science*. **2018**, 9, 8035-8045.

106. Meihaus, K. R.; Minasian, S. G.; Lukens, W. W.; Kozimor, S. A.; Shuh, D. K.; Tyliczszak, T.; Long, J. R., Influence of Pyrazolate vs N-Heterocyclic Carbene Ligands on the Slow Magnetic Relaxation of Homoleptic Trischelate Lanthanide(III) and Uranium(III) Complexes. *Journal of the American Chemical Society*. **2014**, 136, 6056-6068.

107. Garner, M. E.; Hohloch, S.; Maron, L.; Arnold, J., A New Supporting Ligand in Actinide Chemistry Leads to Reactive Bis(NHC)borate-Supported Thorium Complexes. *Organometallics*. **2016**, 35, 2915-2922.

108. Garner, M. E.; Hohloch, S.; Maron, L.; Arnold, J., Carbon–Nitrogen Bond Cleavage by a Thorium-NHC-bpy Complex. *Angewandte Chemie*. **2016**, 128, 13993-13996.

109. Garner, M. E.; Arnold, J., Reductive Elimination of Diphosphine from a Thorium–NHC–Bis(phosphido) Complex. *Organometallics*. **2017**, 36, 4511-4514.

110. Garner, M. E.; Lohrey, T. D.; Hohloch, S.; Arnold, J., Synthesis, characterization, and epoxide ring-opening reactivity of thorium-NHC-bpy complexes. *Journal of Organometallic Chemistry*. **2018**, 857, 10-15.

111. Oldham, J. W. J.; Oldham, S. M.; Scott, B. L.; Abney, K. D.; Smith, W. H.; Costa, D. A., Synthesis and structure of π -heterocyclic carbene complexes of uranyl dichloride. *Chemical Communications*. **2001**, 1348-1349.
112. DeJesus, J. F.; Trujillo, M. J.; Camden, J. P.; Jenkins, D. M., N-Heterocyclic Carbenes as a Robust Platform for Surface-Enhanced Raman Spectroscopy. *Journal of the American Chemical Society*. **2018**, *140*, 1247-1250.
113. Huang, T.; Nallathamby, P. D.; Gillet, D.; Xu, X.-H. N., Design and Synthesis of Single-Nanoparticle Optical Biosensors for Imaging and Characterization of Single Receptor Molecules on Single Living Cells. *Analytical Chemistry*. **2007**, *79*, 7708-7718.
114. Qian, X.; Peng, X.-H.; Ansari, D. O.; Yin-Goen, Q.; Chen, G. Z.; Shin, D. M.; Yang, L.; Young, A. N.; Wang, M. D.; Nie, S., In vivo tumor targeting and spectroscopic detection with surface-enhanced Raman nanoparticle tags. *Nature Biotechnology*. **2007**, *26*, 83.
115. Malinsky, M. D.; Kelly, K. L.; Schatz, G. C.; Van Duyne, R. P., Chain Length Dependence and Sensing Capabilities of the Localized Surface Plasmon Resonance of Silver Nanoparticles Chemically Modified with Alkanethiol Self-Assembled Monolayers. *Journal of the American Chemical Society*. **2001**, *123*, 1471-1482.
116. Sun, F.; Galvan, D. D.; Jain, P.; Yu, Q., Multi-functional, thiophenol-based surface chemistry for surface-enhanced Raman spectroscopy. *Chemical Communications*. **2017**, *53*, 4550-4561.
117. Schwartz, D. K., MECHANISMS AND KINETICS OF SELF-ASSEMBLED MONOLAYER FORMATION. *Annual Review of Physical Chemistry*. **2001**, *52*, 107-137.

118. Vericat, C.; Vela, M. E.; Benitez, G.; Carro, P.; Salvarezza, R. C., Self-assembled monolayers of thiols and dithiols on gold: new challenges for a well-known system. *Chemical Society Reviews*. **2010**, 39, 1805-1834.
119. Lin, J. C. Y.; Huang, R. T. W.; Lee, C. S.; Bhattacharyya, A.; Hwang, W. S.; Lin, I. J. B., Coinage Metal–N-Heterocyclic Carbene Complexes. *Chemical Reviews*. **2009**, 109, 3561-3598.
120. Weidner, T.; Baio, J. E.; Mundstock, A.; Große, C.; Karthäuser, S.; Bruhn, C.; Siemeling, U., NHC-Based Self-Assembled Monolayers on Solid Gold Substrates. *Australian Journal of Chemistry*. **2011**, 64, 1177-1179.
121. Zhukhovitskiy, A. V.; MacLeod, M. J.; Johnson, J. A., Carbene Ligands in Surface Chemistry: From Stabilization of Discrete Elemental Allotropes to Modification of Nanoscale and Bulk Substrates. *Chemical Reviews*. **2015**, 115, 11503-11532.
122. Salorinne, K.; Man, R. W. Y.; Li, C.-H.; Taki, M.; Nambo, M.; Crudden, C. M., Water-Soluble N-Heterocyclic Carbene-Protected Gold Nanoparticles: Size-Controlled Synthesis, Stability, and Optical Properties. *Angewandte Chemie International Edition*. **2017**, 56, 6198-6202.
123. Fèvre, M.; Pinaud, J.; Leteneur, A.; Gnanou, Y.; Vignolle, J.; Taton, D.; Miqueu, K.; Sotiropoulos, J.-M., Imidazol(in)ium Hydrogen Carbonates as a Genuine Source of N-Heterocyclic Carbenes (NHCs): Applications to the Facile Preparation of NHC Metal Complexes and to NHC-Organocatalyzed Molecular and Macromolecular Syntheses. *Journal of the American Chemical Society*. **2012**, 134, 6776-6784.
124. Voutchkova, A. M.; Feliz, M.; Clot, E.; Eisenstein, O.; Crabtree, R. H., Imidazolium Carboxylates as Versatile and Selective N-Heterocyclic Carbene Transfer

Agents: Synthesis, Mechanism, and Applications. *Journal of the American Chemical Society*. **2007**, 129, 12834-12846.

125. Chen, W.-C.; Lai, Y.-C.; Shih, W.-C.; Yu, M.-S.; Yap, G. P. A.; Ong, T.-G., Mechanistic Study of a Switch in the Regioselectivity of Hydroheteroarylation of Styrene Catalyzed by Bimetallic Ni–Al through C–H Activation. *Chemistry – A European Journal*. **2014**, 20, 8099-8105.

126. Banholzer, M. J.; Millstone, J. E.; Qin, L.; Mirkin, C. A., Rationally designed nanostructures for surface-enhanced Raman spectroscopy. *Chemical Society Reviews*. **2008**, 37, 885-897.

127. Farcau, C.; Astilean, S., Mapping the SERS Efficiency and Hot-Spots Localization on Gold Film over Nanospheres Substrates. *The Journal of Physical Chemistry C*. **2010**, 114, 11717-11722.

128. Heutz, F. J. L.; Samuels, M. C.; Kamer, P. C. J., Solid-phase synthesis of recyclable diphosphine ligands. *Catalysis Science & Technology*. **2015**, 5, 3296-3301.

129. Lavrich, D. J.; Wetterer, S. M.; Bernasek, S. L.; Scoles, G., Physisorption and Chemisorption of Alkanethiols and Alkyl Sulfides on Au(111). *The Journal of Physical Chemistry B*. **1998**, 102, 3456-3465.

130. Qi, S.; Ma, Q.; He, X.; Tang, Y., Self-assembled monolayers of N-heterocyclic carbene on gold: Stability under ultrasonic circumstance and computational study. *Colloids and Surfaces A: Physicochemical and Engineering Aspects*. **2018**, 538, 488-493.

131. Lee, M.-T.; Hsueh, C.-C.; Freund, M. S.; Ferguson, G. S., Air Oxidation of Self-Assembled Monolayers on Polycrystalline Gold: The Role of the Gold Substrate. *Langmuir*. **1998**, 14, 6419-6423.

132. Li, Z.; Munro, K.; Ebralize, I. I.; Narouz, M. R.; Padmos, J. D.; Hao, H.; Crudden, C. M.; Horton, J. H., N-Heterocyclic Carbene Self-Assembled Monolayers on Gold as Surface Plasmon Resonance Biosensors. *Langmuir*. **2017**, *33*, 13936-13944.
133. Ferry, A.; Schaepe, K.; Tegeder, P.; Richter, C.; Chepiga, K. M.; Ravoo, B. J.; Glorius, F., Negatively Charged N-Heterocyclic Carbene-Stabilized Pd and Au Nanoparticles and Efficient Catalysis in Water. *ACS Catalysis*. **2015**, *5*, 5414-5420.
134. Mercks, L.; Albrecht, M., Beyond catalysis: N-heterocyclic carbene complexes as components for medicinal, luminescent, and functional materials applications. *Chemical Society Reviews*. **2010**, *39*, 1903-1912.
135. Cao, Z.; Kim, D.; Hong, D.; Yu, Y.; Xu, J.; Lin, S.; Wen, X.; Nichols, E. M.; Jeong, K.; Reimer, J. A.; Yang, P.; Chang, C. J., A Molecular Surface Functionalization Approach to Tuning Nanoparticle Electrocatalysts for Carbon Dioxide Reduction. *Journal of the American Chemical Society*. **2016**, *138*, 8120-8125.
136. Ernst, J. B.; Schwermann, C.; Yokota, G.-i.; Tada, M.; Muratsugu, S.; Doltsinis, N. L.; Glorius, F., Molecular Adsorbates Switch on Heterogeneous Catalysis: Induction of Reactivity by N-Heterocyclic Carbenes. *Journal of the American Chemical Society*. **2017**, *139*, 9144-9147.
137. Tegeder, P.; Freitag, M.; Chepiga, K. M.; Muratsugu, S.; Möller, N.; Lamping, S.; Tada, M.; Glorius, F.; Ravoo, B. J., N-Heterocyclic Carbene-Modified Au–Pd Alloy Nanoparticles and Their Application as Biomimetic and Heterogeneous Catalysts. *Chemistry – A European Journal*. **2018**, *24*, 18682-18688.
138. Trujillo, M. J.; Strausser, S. L.; Becca, J. C.; DeJesus, J. F.; Jensen, L.; Jenkins, D. M.; Camden, J. P., Using SERS To Understand the Binding of N-Heterocyclic

Carbenes to Gold Surfaces. *The Journal of Physical Chemistry Letters*. **2018**, 9, 6779-6785.

139. Hurst, E. C.; Wilson, K.; Fairlamb, I. J. S.; Chechik, V., N-Heterocyclic carbene coated metal nanoparticles. *New Journal of Chemistry*. **2009**, 33, 1837-1840.

140. Man, R. W. Y.; Li, C.-H.; MacLean, M. W. A.; Zenkina, O. V.; Zamora, M. T.; Saunders, L. N.; Rousina-Webb, A.; Nambo, M.; Crudden, C. M., Ultrastable Gold Nanoparticles Modified by Bidentate N-Heterocyclic Carbene Ligands. *Journal of the American Chemical Society*. **2018**, 140, 1576-1579.

141. Ling, X.; Schaeffer, N.; Roland, S.; Pileni, M.-P., Nanocrystals: Why Do Silver and Gold N-Heterocyclic Carbene Precursors Behave Differently? *Langmuir*. **2013**, 29, 12647-12656.

142. Israelsen, N. D.; Hanson, C.; Vargis, E., Nanoparticle Properties and Synthesis Effects on Surface-Enhanced Raman Scattering Enhancement Factor: An Introduction. *The Scientific World Journal*. **2015**, 2015, 12.

143. Hoshyar, N.; Gray, S.; Han, H.; Bao, G., The effect of nanoparticle size on in vivo pharmacokinetics and cellular interaction. *Nanomedicine (Lond)*. **2016**, 11, 673-692.

144. Sharma, B.; Bugga, P.; Madison, L. R.; Henry, A.-I.; Blaber, M. G.; Greeneltch, N. G.; Chiang, N.; Mrksich, M.; Schatz, G. C.; Van Duyne, R. P., Bisboronic Acids for Selective, Physiologically Relevant Direct Glucose Sensing with Surface-Enhanced Raman Spectroscopy. *Journal of the American Chemical Society*. **2016**, 138, 13952-13959.

145. Zhang, C.; Liang, X.; You, T.; Yang, N.; Gao, Y.; Yin, P., An ultrasensitive “turn-off” SERS sensor for quantitatively detecting heparin based on 4-mercaptobenzoic acid functionalized gold nanoparticles. *Analytical Methods*. **2017**, *9*, 2517-2522.
146. Gu, X.; Wang, H.; Schultz, Z. D.; Camden, J. P., Sensing Glucose in Urine and Serum and Hydrogen Peroxide in Living Cells by Use of a Novel Boronate Nanoprobe Based on Surface-Enhanced Raman Spectroscopy. *Analytical Chemistry*. **2016**, *88*, 7191-7197.
147. Lyandres, O.; Shah, N. C.; Yonzon, C. R.; Walsh, J. T.; Glucksberg, M. R.; Van Duyne, R. P., Real-Time Glucose Sensing by Surface-Enhanced Raman Spectroscopy in Bovine Plasma Facilitated by a Mixed Decanethiol/Mercaptohexanol Partition Layer. *Analytical Chemistry*. **2005**, *77*, 6134-6139.
148. Zhao, Y.; Tian, Y.; Cui, Y.; Liu, W.; Ma, W.; Jiang, X., Small Molecule-Capped Gold Nanoparticles as Potent Antibacterial Agents That Target Gram-Negative Bacteria. *Journal of the American Chemical Society*. **2010**, *132*, 12349-12356.
149. Li, X.; Robinson, S. M.; Gupta, A.; Saha, K.; Jiang, Z.; Moyano, D. F.; Sahar, A.; Riley, M. A.; Rotello, V. M., Functional Gold Nanoparticles as Potent Antimicrobial Agents against Multi-Drug-Resistant Bacteria. *ACS Nano*. **2014**, *8*, 10682-10686.
150. Narouz, M. R.; Osten, K. M.; Unsworth, P. J.; Man, R. W. Y.; Salorinne, K.; Takano, S.; Tomihara, R.; Kaappa, S.; Malola, S.; Dinh, C.-T.; Padmos, J. D.; Ayoo, K.; Garrett, P. J.; Nambo, M.; Horton, J. H.; Sargent, E. H.; Häkkinen, H.; Tsukuda, T.; Crudden, C. M., N-heterocyclic carbene-functionalized magic-number gold nanoclusters. *Nature Chemistry*. **2019**, *11*, 419-425.

151. Passingham, C.; Hendra, P. J.; Hodges, C.; Willis, H. A., The Raman spectra of some aromatic nitro compounds. *Spectrochimica Acta Part A: Molecular Spectroscopy*. **1991**, *47*, 1235-1245.
152. Fountoulaki, S.; Daikopoulou, V.; Gkizis, P. L.; Tamiolakis, I.; Armatas, G. S.; Lykakis, I. N., Mechanistic Studies of the Reduction of Nitroarenes by NaBH₄ or Hydrosilanes Catalyzed by Supported Gold Nanoparticles. *ACS Catalysis*. **2014**, *4*, 3504-3511.
153. Sivaram, H.; Tan, J.; Huynh, H. V., Syntheses, Characterizations, and a Preliminary Comparative Cytotoxicity Study of Gold(I) and Gold(III) Complexes Bearing Benzimidazole- and Pyrazole-Derived N-Heterocyclic Carbenes. *Organometallics*. **2012**, *31*, 5875-5883.
154. Peuntinger, K.; Pilz, T. D.; Staehle, R.; Schaub, M.; Kaufhold, S.; Petermann, L.; Wunderlin, M.; Görls, H.; Heinemann, F. W.; Li, J.; Drewello, T.; Vos, J. G.; Guldi, D. M.; Rau, S., Carbene based photochemical molecular assemblies for solar driven hydrogen generation. *Dalton Transactions*. **2014**, *43*, 13683-13695.
155. Doyle, M. P., Exceptional Selectivity in Cyclopropanation Reactions Catalyzed by Chiral Cobalt(II)–Porphyrin Catalysts. *Angewandte Chemie International Edition*. **2009**, *48*, 850-852.
156. Pellissier, H., Recent Developments in Asymmetric Aziridination. *Advanced Synthesis & Catalysis*. **2014**, *356*, 1899-1935.
157. Helene, P., Synthesis of Natural and/or Biologically Relevant Three-membered Heterocycles and Derivatives through Asymmetric Epoxidation, Aziridination, Azirination and Thiirination. *Letters in Organic Chemistry*. **2018**, *15*, 171.

158. Zhang, W.; Loebach, J. L.; Wilson, S. R.; Jacobsen, E. N., Enantioselective epoxidation of unfunctionalized olefins catalyzed by salen manganese complexes. *Journal of the American Chemical Society*. **1990**, *112*, 2801-2803.
159. Irie, R.; Noda, K.; Ito, Y.; Matsumoto, N.; Katsuki, T., Catalytic asymmetric epoxidation of unfunctionalized olefins using chiral (salen)manganese(III) complexes. *Tetrahedron: Asymmetry*. **1991**, *2*, 481-494.
160. Linker, T., The Jacobsen–Katsuki Epoxidation and Its Controversial Mechanism. *Angewandte Chemie International Edition in English*. **1997**, *36*, 2060-2062.
161. Searles, K.; Fortier, S.; Khusniyarov, M. M.; Carroll, P. J.; Sutter, J.; Meyer, K.; Mindiola, D. J.; Caulton, K. G., A cis-Divacant Octahedral and Mononuclear Iron(IV) Imide. *Angewandte Chemie International Edition*. **2014**, *53*, 14139-14143.
162. Chang, J. W. W.; Ton, T. M. U.; Chan, P. W. H., Transition-metal-catalyzed aminations and aziridinations of C–H and C–C bonds with iminoiodinanes. *The Chemical Record*. **2011**, *11*, 331-357.
163. Jenkins, D. M., Atom-Economical C2 + N1 Aziridination: Progress towards Catalytic Intermolecular Reactions Using Alkenes and Aryl Azides. *Synlett*. **2012**, *23*, 1267-1270.
164. Halterman, R. L.; Jan, S. T., Catalytic asymmetric epoxidation of unfunctionalized alkenes using the first D4-symmetric metallotetraphenylporphyrin. *The Journal of Organic Chemistry*. **1991**, *56*, 5253-5254.
165. Marchon, J.-C.; Ramasseul, R., Chiral Metalloporphyrins and Their Use in Enantiocontrol. **2003**, *11*, 75-132.

166. Keller, C. L.; Kern, J. L.; Terry, B. D.; Roy, S.; Jenkins, D. M., Catalytic aziridination with alcoholic substrates via a chromium tetracarbene catalyst. *Chemical Communications*. **2018**, 54, 1429-1432.
167. Kropp, H.; King, A. E.; Khusniyarov, M. M.; Heinemann, F. W.; Lancaster, K. M.; DeBeer, S.; Bill, E.; Meyer, K., Manganese Nitride Complexes in Oxidation States III, IV, and V: Synthesis and Electronic Structure. *Journal of the American Chemical Society*. **2012**, 134, 15538-15544.
168. Bonnet, L. G.; Douthwaite, R. E.; Hodgson, R., Synthesis of Constrained-Geometry Chiral Di-N-Heterocyclic Carbene Ligands and Their Silver(I) and Palladium(II) Complexes. *Organometallics*. **2003**, 22, 4384-4386.
169. Bass, H. M.; Cramer, S. A.; McCullough, A. S.; Bernstein, K. J.; Murdock, C. R.; Jenkins, D. M., Employing Dianionic Macrocyclic Tetracarbenes To Synthesize Neutral Divalent Metal Complexes. *Organometallics*. **2013**, 32, 2160-2167.
170. Mucha, P.; Mlostoń, G.; Jasiński, M.; Linden, A.; Heimgartner, H., A new approach to enantiomerically pure bis-imidazoles derived from trans-1,2-diaminocyclohexane. *Tetrahedron: Asymmetry*. **2008**, 19, 1600-1607.
171. Gigler, P.; Bechlars, B.; Herrmann, W. A.; Kühn, F. E., Hydrosilylation with Biscarbene Rh(I) Complexes: Experimental Evidence for a Silylene-Based Mechanism. *Journal of the American Chemical Society*. **2011**, 133, 1589-1596.
172. Bogatskii, A. V.; Luk'yanenko, N. G.; Kirichenko, T. I., Cyclic thioureas (review). *Chemistry of Heterocyclic Compounds*. **1983**, 19, 577-589.

173. Wolfe, D. M.; Schreiner, P. R., Facile Conversion of Amino Acids into 1-Alkyl Imidazole-2-thiones, and Their Oxidative Desulfurization to Imidazoles with Benzoyl Peroxide. *Synthesis*. **2007**, 2007, 2002-2008.
174. Bass, H. M.; Cramer, S. A.; Price, J. L.; Jenkins, D. M., 18-Atom-Ringed Macrocyclic Tetra-imidazoliums for Preparation of Monomeric Tetra-carbene Complexes. *Organometallics*. **2010**, 29, 3235-3238.
175. Meyer, S.; Klawitter, I.; Demeshko, S.; Bill, E.; Meyer, F., A Tetracarbene–Oxoiron(IV) Complex. *Angewandte Chemie International Edition*. **2013**, 52, 901-905.
176. Fei, F.; Lu, T.; Chen, X.-T.; Xue, Z.-L., Synthesis and structural characterization of metal complexes with macrocyclic tetracarbene ligands. *New Journal of Chemistry*. **2017**, 41, 13442-13453.
177. Jeletic, M. S.; Lower, C. E.; Ghiviriga, I.; Veige, A. S., Chemical Exchange Saturation Transfer (CEST) as a Tool to Measure Ligand Flexibility of Chelating Chiral Di-N-heterocyclic Carbene Complexes. *Organometallics*. **2011**, 30, 6034-6043.
178. Tang, J.; He, Y.; Yu, J.; Zhang, D., N,N'-Bisaryl Substituted Chiral Linker-Bridged Bis(N-Heterocyclic Carbene) Palladium Complexes: Design, Synthesis, and Catalytic Properties. *Organometallics*. **2017**, 36, 1372-1382.
179. Hillhouse, G. L.; Haymore, B. L., Diazoalkane complexes of molybdenum and tungsten. *Journal of the American Chemical Society*. **1982**, 104, 1537-1548.
180. Bart, S. C.; Bowman, A. C.; Lobkovsky, E.; Chirik, P. J., Iron Diazoalkane Chemistry: N–N Bond Hydrogenation and Intramolecular C–H Activation. *Journal of the American Chemical Society*. **2007**, 129, 7212-7213.

181. Sazama, G. T.; Betley, T. A., Multiple, Disparate Redox Pathways Exhibited by a Tris(pyrrolido)ethane Iron Complex. *Inorganic Chemistry*. **2014**, 53, 269-281.
182. Albertin, G.; Antoniutti, S.; Bortoluzzi, M.; Botter, A.; Castro, J.; Sibilla, F., Preparation of diazoalkane complexes of iron(ii). *RSC Advances*. **2016**, 6, 97650-97658.
183. Bonyhady, S. J.; DeRosha, D. E.; Vela, J.; Vinyard, D. J.; Cowley, R. E.; Mercado, B. Q.; Brennessel, W. W.; Holland, P. L., Iron and Cobalt Diazoalkane Complexes Supported by β -Diketiminato Ligands: A Synthetic, Spectroscopic, and Computational Investigation. *Inorganic Chemistry*. **2018**, 57, 5959-5972.
184. Mahias, V.; Cron, S.; Toupet, L.; Lapinte, C., Synthesis of Bis(methoxycarbene) and Bis(alkylidene) Ligands Bridging Two Iron Centers in the Cp*Fe(L1)(L2) Series. X-ray Crystal Structure of the Iron Alkylidene [Cp*Fe(dppe)(C(H)Me)][PF₆]. *Organometallics*. **1996**, 15, 5399-5408.
185. Klose, A.; Solari, E.; Floriani, C.; Re, N.; Chiesi-Villa, A.; Rizzoli, C., Iron–carbene functionalities supported by a macrocyclic ligand: iron–carbon double bond stabilized by tetramethyldibenzotetraazaannulene. *Chemical Communications*. **1997**, 2297-2298.
186. Lindley, B. M.; Jacobs, B. P.; MacMillan, S. N.; Wolczanski, P. T., Neutral Fe(iv) alkylidenes, including some that bind dinitrogen. *Chemical Communications*. **2016**, 52, 3891-3894.
187. Wang, H.; Schulz, C. E.; Wei, X.; Li, J., New Insights into the Ligand Nature of Carbene: Synthesis and Characterizations of Six-Coordinate Iron(II) Carbene Porphyrin Complexes. *Inorganic Chemistry*. **2019**, 58, 143-151.
188. Russell, S. K.; Hoyt, J. M.; Bart, S. C.; Milsman, C.; Stieber, S. C. E.; Semproni, S. P.; DeBeer, S.; Chirik, P. J., Synthesis, electronic structure and reactivity of

bis(imino)pyridine iron carbene complexes: evidence for a carbene radical. *Chemical Science*. **2014**, 5, 1168-1174.

189. Messerle, L.; Curtis, M. D., Reaction of diaryldiazomethanes with a metal-metal triple bond: synthesis, structural characterizations, and reactivity of novel bridging diazoalkane and alkylidene complexes. *Journal of the American Chemical Society*. **1980**, 102, 7789-7791.

190. Mindiola, D. J.; Hillhouse, G. L., Synthesis, Structure, and Reactions of a Three-Coordinate Nickel-Carbene Complex, {1,2-Bis(di-tert-butylphosphino)ethane}NiCPh₂. *Journal of the American Chemical Society*. **2002**, 124, 9976-9977.

191. Cohen, R.; Rybtchinski, B.; Gandelman, M.; Rozenberg, H.; Martin, J. M. L.; Milstein, D., Metallocarbenes from Diazoalkanes: An Experimental and Computational Study of the Reaction Mechanism. *Journal of the American Chemical Society*. **2003**, 125, 6532-6546.

192. Iluc, V. M.; Hillhouse, G. L., Three-Coordinate Nickel Carbene Complexes and Their One-Electron Oxidation Products. *Journal of the American Chemical Society*. **2014**, 136, 6479-6488.

193. Shen, J.-J.; Zhu, S.-F.; Cai, Y.; Xu, H.; Xie, X.-L.; Zhou, Q.-L., Enantioselective Iron-Catalyzed Intramolecular Cyclopropanation Reactions. *Angewandte Chemie International Edition*. **2014**, 53, 13188-13191.

194. Qiu, L.; Huang, D.; Xu, G.; Dai, Z.; Sun, J., Realized C–H Functionalization of Aryldiazo Compounds via Rhodium Relay Catalysis. *Organic Letters*. **2015**, 17, 1810-1813.

195. Miller, J., Notes- Preparation of Crystalline Diphenyldiazomethane. *The Journal of Organic Chemistry*. **1959**, 24, 560-561.
196. Keipour, H.; Ollevier, T., Iron-Catalyzed Carbene Insertion Reactions of α -Diazoesters into Si-H Bonds. *Organic Letters*. **2017**, 19, 5736-5739.
197. Huang, X.; Meggers, E., Asymmetric Photocatalysis with Bis-cyclometalated Rhodium Complexes. *Accounts of Chemical Research*. **2019**, 52, 833-847.
198. Przydacz, A.; Skrzyńska, A.; Albrecht, Ł., Breaking Aromaticity with Aminocatalysis: A Convenient Strategy for Asymmetric Synthesis. *Angewandte Chemie International Edition*. **2019**, 58, 63-73.
199. Liu, Y.; Han, S.-J.; Liu, W.-B.; Stoltz, B. M., Catalytic Enantioselective Construction of Quaternary Stereocenters: Assembly of Key Building Blocks for the Synthesis of Biologically Active Molecules. *Accounts of Chemical Research*. **2015**, 48, 740-751.
200. Desimoni, G.; Faita, G.; Jørgensen, K. A., C₂-Symmetric Chiral Bis(Oxazoline) Ligands in Asymmetric Catalysis. *Chemical Reviews*. **2006**, 106, 3561-3651.
201. Shaw, S.; White, J. D., Asymmetric Catalysis Using Chiral Salen-Metal Complexes: Recent Advances. *Chemical Reviews*. **2019**.
202. Demay, S.; Volant, F.; Knochel, P., New C₂-Symmetrical 1,2-Diphosphanes for the Efficient Rhodium-Catalyzed Asymmetric Hydroboration of Styrene Derivatives. *Angewandte Chemie International Edition*. **2001**, 40, 1235-1238.
203. Roland, S.; Mangeney, P.; Alexakis, A., A Practical and Efficient Synthesis of Enantiomerically Pure Di-tert-butyl-ethanediamine. *Synthesis*. **1999**, 1999, 228-230.

204. Coffinier, R.; Assal, M. E.; Peixoto, P. A.; Bosset, C.; Miqueu, K.; Sotiropoulos, J.-M.; Pouységu, L.; Quideau, S., Total Synthesis of (-)-Bacchopetiolone via an Asymmetric Hydroxylative Phenol Dearomatization/[4+2]-Dimerization Cascade Promoted by a Novel Salen-Type Chiral Iodane. *Organic Letters*. **2016**, *18*, 1120-1123.
205. Kim, H.; Nguyen, Y.; Yen, C. P.-H.; Chagal, L.; Lough, A. J.; Kim, B. M.; Chin, J., Stereospecific Synthesis of C2 Symmetric Diamines from the Mother Diamine by Resonance-Assisted Hydrogen-Bond Directed Diaza-Cope Rearrangement. *Journal of the American Chemical Society*. **2008**, *130*, 12184-12191.
206. Lou, Y.; Remarchuk, T. P.; Corey, E. J., Catalysis of Enantioselective [2+1]-Cycloaddition Reactions of Ethyl Diazoacetate and Terminal Acetylenes Using Mixed-Ligand Complexes of the Series Rh₂(RCO₂)_n (L*_{4-n}). Stereochemical Heuristics for Ligand Exchange and Catalyst Synthesis. *Journal of the American Chemical Society*. **2005**, *127*, 14223-14230.
207. Baumann, M.; Baxendale, I. R., A Continuous-Flow Method for the Desulfurization of Substituted Thioimidazoles Applied to the Synthesis of Etomidate Derivatives. *European Journal of Organic Chemistry*. **2017**, *2017*, 6518-6524.
208. Kim, H.; Choi, D. S.; Yen, C. P.-H.; Lough, A. J.; Song, C. E.; Chin, J., Diastereoselective diaza-Cope rearrangement reaction. *Chemical Communications*. **2008**, 1335-1337.
209. Groaz, E.; Banti, D.; North, M., Synthesis of N-heterocyclic compounds via ene-yne metathesis reactions. *Tetrahedron*. **2008**, *64*, 204-218.

210. Giri, N.; Davidson, C. E.; Melaugh, G.; Del Pópolo, M. G.; Jones, J. T. A.; Hasell, T.; Cooper, A. I.; Horton, P. N.; Hursthouse, M. B.; James, S. L., Alkylated organic cages: from porous crystals to neat liquids. *Chemical Science*. **2012**, *3*, 2153-2157.
211. Vemula, R.; Wilde, N. C.; Goreti, R.; Corey, E. J., A New, Short, and Stereocontrolled Synthesis of C₂-Symmetric 1,2-Diamines. *Organic Letters*. **2017**, *19*, 3883-3886.
212. Hollering, M.; Weiss, D. T.; Bitzer, M. J.; Jandl, C.; Kühn, F. E., Controlling Coordination Geometries: Ru–Carbene Complexes with Tetra-NHC Ligands. *Inorganic Chemistry*. **2016**, *55*, 6010-6017.
213. Braunschweig, H.; D'Andola, G.; Welton, T.; White, A. J. P., Synthesis and Structure of Novel Organocycloborates. *Chemistry – A European Journal*. **2006**, *12*, 600-606.
214. Toure, M.; Charles, L.; Chendo, C.; Viel, S.; Chuzel, O.; Parrain, J.-L., Straightforward and Controlled Shape Access to Efficient Macrocyclic Imidazolylboronium Anion Receptors. *Chemistry – A European Journal*. **2016**, *22*, 8937-8942.
215. Xu, Z.-J.; Fang, R.; Zhao, C.; Huang, J.-S.; Li, G.-Y.; Zhu, N.; Che, C.-M., cis- β -Bis(carbonyl) Ruthenium–Salen Complexes: X-ray Crystal Structures and Remarkable Catalytic Properties toward Asymmetric Intramolecular Alkene Cyclopropanation. *Journal of the American Chemical Society*. **2009**, *131*, 4405-4417.
216. Klose, A.; Solari, E.; Floriani, C.; Chiesi-Villa, A.; Rizzoli, C.; Re, N., Magnetic Properties Diagnostic for the Existence of Iron(II)-Iron(II) Bonds in Dinuclear Complexes

Which Derive from Stepwise Insertion Reactions on Unsupported Iron-Aryl Bonds. *Journal of the American Chemical Society*. **1994**, *116*, 9123-9135.

217. Hilgraf, R.; Pfaltz, A., Chiral Bis(N-sulfonylamino)phosphine- and TADDOL-Phosphite-Oxazoline Ligands: Synthesis and Application in Asymmetric Catalysis. *Advanced Synthesis & Catalysis*. **2005**, *347*, 61-77.

218. Hu, X. E., Nucleophilic ring opening of aziridines. *Tetrahedron*. **2004**, *60*, 2701-2743.

219. Njardarson, J. T., Catalytic Ring Expansion Adventures. *Synlett*. **2013**, *24*, 787-803.

220. Kawabata, H.; Omura, K.; Uchida, T.; Katsuki, T., Construction of Robust Ruthenium(salen)(CO) Complexes and Asymmetric Aziridination with Nitrene Precursors in the Form of Azide Compounds That Bear Easily Removable N-Sulfonyl Groups. *Chemistry – An Asian Journal*. **2007**, *2*, 248-256.

221. Fukunaga, Y.; Uchida, T.; Ito, Y.; Matsumoto, K.; Katsuki, T., Ru(CO)-salen-Catalyzed Synthesis of Enantiopure Aziridinyll Ketones and Formal Asymmetric Synthesis of (+)-PD 128907. *Organic Letters*. **2012**, *14*, 4658-4661.

222. Isbill, S. B.; Chandrachud, P. P.; Kern, J. L.; Jenkins, D. M.; Roy, S., Elucidation of the Reaction Mechanism of C2 + N1 Aziridination from Tetracarbene Iron Catalysts. *ACS Catalysis*. **2019**, *9*, 6223-6233.

223. Cramer, S. A.; Hernández Sánchez, R.; Brakhage, D. F.; Jenkins, D. M., Probing the role of an FeIV tetrazene in catalytic aziridination. *Chemical Communications*. **2014**, *50*, 13967-13970.

224. Glöge, T.; Petrovic, D.; Hrib, Cristian G.; Daniliuc, C.; Herdtweck, E.; Jones, Peter G.; Tamm, M., Synthesis and Structural Characterisation of an Isomorphous Series of Bis(imidazolin-2-imine) Metal Dichlorides Containing the First Row Transition Metals Mn, Fe, Co, Ni, Cu and Zn. *Zeitschrift für anorganische und allgemeine Chemie*. **2010**, 636, 2303-2308.
225. Cundari, T. R.; Jacobs, B. P.; MacMillan, S. N.; Wolczanski, P. T., Dispersion forces play a role in (Me₂IPr)Fe(η -NAd)R₂ (Ad = adamantyl; R = neoPe, 1-nor) insertions and Fe–R bond dissociation enthalpies (BDEs). *Dalton Transactions*. **2018**, 47, 6025-6030.
226. Liptrot, D. J.; Power, P. P., London dispersion forces in sterically crowded inorganic and organometallic molecules. *Nature Reviews Chemistry*. **2017**, 1, 0004.
227. King, E. R.; Hennessy, E. T.; Betley, T. A., Catalytic C–H Bond Amination from High-Spin Iron Imido Complexes. *Journal of the American Chemical Society*. **2011**, 133, 4917-4923.
228. Hennessy, E. T.; Betley, T. A., Complex N-Heterocycle Synthesis via Iron-Catalyzed, Direct C–H Bond Amination. *Science*. **2013**, 340, 591.
229. Zardi, P.; Pozzoli, A.; Ferretti, F.; Manca, G.; Mealli, C.; Gallo, E., A mechanistic investigation of the ruthenium porphyrin catalysed aziridination of olefins by aryl azides. *Dalton Transactions*. **2015**, 44, 10479-10489.
230. Hopmann, K. H.; Ghosh, A., Mechanism of Cobalt-Porphyrin–Catalyzed Aziridination. *ACS Catalysis*. **2011**, 1, 597-600.

231. Iovan, D. A.; Betley, T. A., Characterization of Iron-Imido Species Relevant for N-Group Transfer Chemistry. *Journal of the American Chemical Society*. **2016**, *138*, 1983-1993.
232. Hong, S.; Sutherlin, K. D.; Vardhaman, A. K.; Yan, J. J.; Park, S.; Lee, Y.-M.; Jang, S.; Lu, X.; Ohta, T.; Ogura, T.; Solomon, E. I.; Nam, W., A Mononuclear Nonheme Iron(V)-Imido Complex. *Journal of the American Chemical Society*. **2017**, *139*, 8800-8803.
233. Alvarez, S. G.; Alvarez, M. T., A Practical Procedure for the Synthesis of Alkyl Azides at Ambient Temperature in Dimethyl Sulfoxide in High Purity and Yield. *Synthesis*. **1997**, *1997*, 413-414.
234. Bottaro, J. C.; Penwell, P. E.; Schmitt, R. J., Expedient Synthesis of t-Butyl Azide. *Synthetic Communications*. **1997**, *27*, 1465-1467.
235. Lu, Y.; Wang, L.; Wang, X.; Xi, T.; Liao, J.; Wang, Z.; Jiang, F., Design, combinatorial synthesis and biological evaluations of novel 3-amino-1'-((1-aryl-1H-1,2,3-triazol-5-yl)methyl)-2'-oxospiro[benzo[a]pyrano[2,3-c]phenazine-1,3'-indoline]-2-carbonitrile antitumor hybrid molecules. *European Journal of Medicinal Chemistry*. **2017**, *135*, 125-141.
236. Guisado-Barrios, G.; Bouffard, J.; Donnadieu, B.; Bertrand, G., Crystalline 1H-1,2,3-Triazol-5-ylidenes: New Stable Mesoionic Carbenes (MICs). *Angewandte Chemie International Edition*. **2010**, *49*, 4759-4762.
237. Smith, P. A. S.; Brown, B. B., The Reaction of Aryl Azides with Hydrogen Halides^{1,2}. *Journal of the American Chemical Society*. **1951**, *73*, 2438-2441.

238. Subedi, Y. P.; Alfindie, M. N.; Shrestha, J. P.; Chang, C.-W. T., Tuning the biological activity of cationic anthraquinone analogues specifically toward *Staphylococcus aureus*. *European Journal of Medicinal Chemistry*. **2018**, *157*, 683-690.
239. Abramovitch, R. A.; Challand, S. R.; Scriven, E. F. V., Intermolecular aromatic substitution by aryl nitrenes. *The Journal of Organic Chemistry*. **1972**, *37*, 2705-2710.
240. Sessler, J. L.; Melfi, P. J.; Pantos, G. D., Uranium complexes of multidentate N-donor ligands. *Coordination Chemistry Reviews*. **2006**, *250*, 816-843.
241. Fortier, S.; Hayton, T. W., Oxo ligand functionalization in the uranyl ion (UO₂²⁺). *Coordination Chemistry Reviews*. **2010**, *254*, 197-214.
242. Andrews, M. B.; Cahill, C. L., Uranyl Bearing Hybrid Materials: Synthesis, Speciation, and Solid-State Structures. *Chemical Reviews*. **2013**, *113*, 1121-1136.
243. He, W.; Hua, D., Spectrographic sensors for uranyl detection in the environment. *Talanta*. **2019**, *201*, 317-329.
244. Lu, G.; Haes, A. J.; Forbes, T. Z., Detection and identification of solids, surfaces, and solutions of uranium using vibrational spectroscopy. *Coordination Chemistry Reviews*. **2018**, *374*, 314-344.
245. Bernstein, K. J.; Do-Thanh, C.-L.; Penchoff, D. A.; Alan Cramer, S.; Murdock, C. R.; Lu, Z.; Harrison, R. J.; Camden, J. P.; Jenkins, D. M., The synthesis and spectroscopic characterization of an aromatic uranium amidoxime complex. *Inorganica Chimica Acta*. **2014**, *421*, 374-379.
246. Chen, L.; Bai, Z.; Zhu, L.; Zhang, L.; Cai, Y.; Li, Y.; Liu, W.; Wang, Y.; Chen, L.; Diwu, J.; Wang, J.; Chai, Z.; Wang, S., Ultrafast and Efficient Extraction of Uranium

from Seawater Using an Amidoxime Appended Metal–Organic Framework. *ACS Applied Materials & Interfaces*. **2017**, 9, 32446-32451.

247. Leduc, J.; Frank, M.; Jürgensen, L.; Graf, D.; Raauf, A.; Mathur, S., Chemistry of Actinide Centers in Heterogeneous Catalytic Transformations of Small Molecules. *ACS Catalysis*. **2019**, 9, 4719-4741.

248. Gardner, B. M.; Liddle, S. T., Small-Molecule Activation at Uranium(III). *European Journal of Inorganic Chemistry*. **2013**, 2013, 3753-3770.

249. Arnold, P. L., Uranium-mediated activation of small molecules. *Chemical Communications*. **2011**, 47, 9005-9010.

250. Fox, A. R.; Bart, S. C.; Meyer, K.; Cummins, C. C., Towards uranium catalysts. *Nature*. **2008**, 455, 341.

251. Halter, D. P.; Heinemann, F. W.; Maron, L.; Meyer, K., The role of uranium–arene bonding in H₂O reduction catalysis. *Nature Chemistry*. **2017**, 10, 259.

252. Nakai, H.; Hu, X.; Zakharov, L. N.; Rheingold, A. L.; Meyer, K., Synthesis and Characterization of N-Heterocyclic Carbene Complexes of Uranium(III). *Inorganic Chemistry*. **2004**, 43, 855-857.

253. Pugh, D.; Wright, J. A.; Freeman, S.; Danopoulos, A. A., ‘Pincer’ dicarbene complexes of some early transition metals and uranium. *Dalton Transactions*. **2006**, 775-782.

254. Mehdoui, T.; Berthet, J.-C.; Thuéry, P.; Ephritikhine, M., The remarkable efficiency of N-heterocyclic carbenes in lanthanide(III)/actinide(III) differentiation. *Chemical Communications*. **2005**, 2860-2862.

255. Evans, W. J.; Kozimor, S. A.; Ziller, J. W., Bis(pentamethylcyclopentadienyl) U(III) oxide and U(IV) oxide carbene complexes. *Polyhedron*. **2004**, 23, 2689-2694.
256. Tondreau, A. M.; Duignan, T. J.; Stein, B. W.; Fleischauer, V. E.; Autschbach, J.; Batista, E. R.; Boncella, J. M.; Ferrier, M. G.; Kozimor, S. A.; Mocko, V.; Neidig, M. L.; Cary, S. K.; Yang, P., A Pseudotetrahedral Uranium(V) Complex. *Inorganic Chemistry*. **2018**, 57, 8106-8115.
257. Turner, Z. R.; Bellabarba, R.; Tooze, R. P.; Arnold, P. L., Addition-Elimination Reactions across the M–C Bond of Metal N-Heterocyclic Carbenes. *Journal of the American Chemical Society*. **2010**, 132, 4050-4051.
258. Gardner, B. M.; McMaster, J.; Liddle, S. T., Synthesis and structure of a bis-N-heterocyclic carbene complex of uranium tetrachloride exhibiting short Cl...Ccarbene contacts. *Dalton Transactions*. **2009**, 6924-6926.
259. Psillakis, E.; C. Jeffery, J., Square-prismatic vs. square-antiprismatic coordination in complexes of lead(II) with a simple bidentate chelating ligand; effects of intermolecular hydrogen bonding. *Chemical Communications*. **1997**, 1965-1966.
260. Hohloch, S.; Garner, M. E.; Booth, C. H.; Lukens, W. W.; Gould, C. A.; Lussier, D. J.; Maron, L.; Arnold, J., Isolation of a TMTAA-Based Radical in Uranium bis-TMTAA Complexes. *Angewandte Chemie International Edition*. **2018**, 57, 16136-16140.
261. Connelly, N. G.; Geiger, W. E., Chemical Redox Agents for Organometallic Chemistry. *Chemical Reviews*. **1996**, 96, 877-910.
262. Monreal, M. J.; Thomson, R. K.; Cantat, T.; Travia, N. E.; Scott, B. L.; Kiplinger, J. L., $\text{U}(\text{I})_4(1,4\text{-dioxane})_2$, $[\text{UCl}_4(1,4\text{-dioxane})]_2$, and $\text{U}(\text{I})_3(1,4\text{-dioxane})_{1.5}$: Stable and

Versatile Starting Materials for Low- and High-Valent Uranium Chemistry.
Organometallics. **2011**, 30, 2031-2038.

Vita

Joseph (Joe) DeJesus was born in Orlando, Florida on March 30th, 1991. He spent many years in Casselberry, Florida; a city that is part of the greater Orlando area. He attended the University of Central Florida for his bachelor's degree in chemistry, because he wanted to make beautiful molecules and math made his head hurt. He did undergraduate research with both Prof. Yi Liao's and Prof. Karin Chumbimuni-Torres' groups. He was involved in the synthesis and characterization of visible-light activated photoacids and ionophores for electrochemical sensors, respectively. Afterwards, he decided it was too dang hot in Florida, so he moved to Tennessee for his graduate studies at the University of Tennessee, where he worked in Prof. David Jenkins' research group. He learned a wide breadth of organic and organometallic chemistry towards modifying gold surfaces toward sensing, synthesizing novel chiral ligands and metal complexes, as well as stabilizing actinides with non-tradition ligands. He has attended and presented at multiple national conferences and has authored several papers in scientific journals during his time there.

Outside the lab, Joe enjoys activities like low-speed cycling, low-speed swimming, being terrible at video games and taking two years to finish reading a novel. Joe also enjoys "simple things in life" like cooking (and eating) delicious foods and enjoying a satisfying cup of coffee on a warm afternoon. Joe has a strong sense of wanderlust; he plans on visiting all seven continents and seeing many different countries and places in his lifetime.