Thermodynamically Favored vs. Kinetically Favored Carbon-Sulfur Bond Activation

David Hoeft
Carthage College
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Abstract

The study of carbon-sulfur bond activation is a topic that receives much attention because of its uses in the petroleum refining process through hydrodesulfurization (HDS). The carbon–sulfur bond activation of thioesters using (dippe)Pt(NBE)₂ was studied. It was found that the bond lengths of carbon groups attached to the central Platinum atom increase from 2.099(7) Å in the starting compound to 2.13(2) Å in the transition state. This is important because it helps understanding of sterics and mechanisms for the reaction. Next, the differences between kinetically favored and thermodynamically favored C-S bond activations were compared and one was found more favored as compared to the other. These data could lead to many advances in the study and uses of HDS.

Introduction

For decades, using transition-metal complexes to activate carbon–sulfur bonds has been a technique to study carbon-sulfur bond activation. A major reason carbon-sulfur bond activation has been under much study is to better understand the mechanism behind carbon-sulfur bond cleavage, also known as the hydrodesulfurization process or HDS process. An example of a HDS process can be seen in Scheme 1 below. This process is very important to study because HDS is one of the steps that takes place in processing petroleum. This thesis is
a discussion of work done by Matthew R. Grochowski et al. and Sabuj Kundu et al. in the lab of Dr. William D. Jones\textsuperscript{8,9}.

HDS, as stated earlier, is the process by which sulfur is removed from hydrocarbons during petroleum refinement. If the sulfur is not removed during this process, noxious sulfur oxides are produced during fuel combustion. This production of sulfur oxides is a major cause of air pollution, and there are now new environmental standards that are stricter on SO\textsubscript{2} emissions. Currently, the heterogeneous catalyst that is being used in HDS is Ni/Mo (or Mo/Co) sulfide. This catalyst is effective in removing most organo-sulfur compounds encountered in petroleum processing. Improvement in catalytic efficiency will require increased effectiveness toward the removal of the problematic remaining substituted thiophenes\textsuperscript{10}.

It is because of the goal to make HDS safer and to streamline it that research on carbon-sulfur bond activation is necessary. In some of the carbon-sulfur reactions studied in Dr. William D. Jones work the mechanisms contained the processes of methyl migration, oxidative addition, and decarbonylation.

A methyl migration is the process in which a methyl group migrates to the coordination site of the metal center during a reaction, an example of this is shown in Figure 1. Oxidative addition is the opposite process of reductive elimination, and is the process where the oxidation state and the coordination...
number on the metal center increase, an example of this is shown in Figure 2. Another process involved in reactions studied was decarbonylation, the process of an organic or inorganic substrate losing a carbon monoxide group. These processes help to explain the mechanisms of the reactions studied.

In order to study HDS, multiple experiments were carried out using different organometallic complexes and solvents to determine the best yield of carbon-sulfur bond activation. In order to determine the structure of the reactants, products, and the intermediates in these reactions $^1$H, $^{31}$P($^1$H), $^{13}$C($^1$H) NMR spectroscopy and X-ray crystallography were used.

NMR (nuclear magnetic resonance) spectrometry is a research technique that utilizes the magnetic properties of the atomic nuclei under study. By utilizing the magnetic properties of these nuclei it is possible to determine physical and chemical properties of the molecules. NMR spectrometry can provide very useful information about the structure and reaction state of the molecule or atoms that are being investigated.

$^1$H NMR spectrometry is the harnessing of the naturally occurring nuclear magnetic resonance in NMR spectroscopy with respect to hydrogen-1 nuclei of molecules in a substance and those hydrogen atoms effect on neighboring hydrogen atoms. These interactions allow a spectrum to be produced and trends to be analyzed in order to determine the structure of the
molecules. $^1$H NMR spectrometry is a very useful because it detects nearly all of the hydrogen atoms in a substance because nearly all hydrogen isotopes are $^1$H.

$^{13}$C NMR spectrometry is the application of nuclear magnetic resonance spectroscopy to the $^{13}$C isotope. $^{13}$C NMR is similar to $^1$H NMR because it allows the identification of carbon atoms in an organic molecule just as $^1$H NMR allows the identification of hydrogen atoms. $^{13}$C NMR is an important tool in chemical structure identification, but it normally is not the best way to identify compounds. $^{13}$C NMR detects only the $^{13}$C isotope of carbon; $^{13}$C is not the major isotope of carbon. $^{13}$C not being the major isotope is a deterrent because the natural abundance of the $^{13}$C isotope is only 1.1%, and therefore, not much is detected by the NMR spectrometry. $^{13}$C has to be the carbon isotope studied by NMR spectrometry because the main carbon isotope, $^{12}$C, has zero net spin, and therefore, is not detectable by NMR spectrometry. $^{13}$C is useful in another way because it allows the detection of metal-carbon bonds. These metal-carbon bonds show up on spectra and can be surrounded by satellite peaks. These satellites are just extra peaks that occur because of the metal interference in the noise of the NMR. $^{13}$C can be problematic because of its J-coupling. J-coupling is the coupling that occurs between two nuclear spins because of the influence of bonding electrons on the magnetic field that runs between the two nuclei. $^{13}$C is a useful technique in determining structure, however, it is not effective as a technique that can identify all the nuclei of a specific molecule.

$^{31}$P NMR spectroscopy is a technique that is comparable to both $^{13}$C NMR spectrometry and $^1$H NMR spectrometry. Unlike $^{13}$C NMR spectrometry, $^{31}$P NMR spectrometry is isotopically nearly 100% abundant. The $^{31}$P nucleus also has a spin of $\frac{1}{2}$, similar to the $^{13}$C nucleus. $^{31}$P NMR
Spectroscopy is useful to judge the purity of a compound and to assign structures of phosphorus-containing compounds because these signals are normally well resolved and often occur at routinely characteristic frequencies. If the sample under study is not pure it will have uncharacteristic peaks and will not be easily analyzed. Chemical shifts and coupling constants span a large range but sometimes are not readily predictable. The ordinary range of chemical shifts for $^{31}$P NMR spectrometry occurs from about δ250 to -δ250 ppm. This range is much wider than typical range for $^1$H NMR spectrometry. Also, $^{31}$P NMR spectrum shifts are primarily not determined by the magnitude of the diamagnetic shielding, like in $^1$H NMR spectrometry.

Diamagnetic shielding occurs when protons are surrounded by a cloud of charge because of adjacent bonds and atoms. This diamagnetic shielding causes the materialization of and induced field which opposes the applied field of the NMR. This changes the effective field at the nucleus of the atom. As far as J-coupling is concerned, phosphorus-carbon couplings are more complicated since the two-bond couplings are often larger than one-bond couplings which are seen in $^{13}$C NMR spectrometry. Also similar to $^{13}$C NMR spectrometry, $^{31}$P NMR spectrometry also has metal satellites for the same reasons, metal interference with the spectra. This technique, along with the other NMR techniques, was very useful in identifying products and intermediates during the reactions.

**X-ray crystallography** is a technique used to help determine the arrangement of atoms within a crystal which is useful in this study to determine structure. In this technique a beam of X-rays is directed at a crystal and the crystal causes the beam of light to spread into many specific directions leaving a shadow of the molecule. By comparing many diffraction patterns of the crystal a three dimensional structure of the molecule under study can be produced. X-ray
crystallography, inversely to NMR Spectrometry, can require a substantial investment of time after initial crystallization conditions are established to optimize the diffraction properties of a crystal. This process can take weeks to years, but once a well-diffracting crystal is obtained, and an anomalous scattering atom is incorporated, the structure determination is quite quick, some datasets of very high-resolution crystals can be confirmed within hours\textsuperscript{12}.

Using these techniques to assist in the study of carbon-sulfur bond activation yielded thermodynamic and kinetic answers to what type of reactants yield more helpful carbon-sulfur bond activations in the process of HDS. This data will be obtained by comparing kinetic and thermodynamic data obtained from carbon-sulfur bond activation to data obtained from carbon-carbon bond activation. This data will also be compared to Density Functional Theory (DFT) hypotheses. DFT is a quantum mechanical method used to investigate electronic structures of molecules.

Before DFT, calculation of the properties of molecules was based on trying to determine the motion of all available electrons, making it mathematically difficult when dealing with large molecules. Dr. Walter Kohn showed that knowing the motion of all electrons was not necessary, it is sufficient to only consider the average number of electrons located at any one point in space. DFT makes it possible to study very large molecules that contain many electrons. DFT is now one of the most widely used methods in quantum chemistry\textsuperscript{13}.

In this thesis the work of Dr. William D. Jones was examined, in correlation with other supplementary articles, to better comprehend carbon-sulfur bond activation. In the first article, multiple experiments were conducted with (dippe)Pt(NBE)\textsubscript{2} to study the carbon-sulfur bond
activation of both cyclic and acyclic thioesters. Dippe is also referred to as 1,2-Bis(diisopropylphosphino)ethane and is a bidentate ligand in coordination chemistry. The first experiment conducted is shown in Scheme 2 and explained below in the results and discussion.

**Results and Discussion:**

**Reaction with MeC(O)SMe (S-methyl thioacetate)**

In the first step of this experiment the 16-electron species (dippe)Pt(NBE)$_2$ (NBE = norbornene), complex 1, was treated with 5 equiv of S-methyl thioacetate in benzene at 100 °C for 25 minutes. This reaction gave what was described as a good yield of the complex (dippe)Pt(C(O)Me)(SMe), complex 2a, as shown in Scheme 2. Scheme 3 purports a possible mechanism for the reaction. The first step of the mechanism is the loss of the NBEs to form a 14-electron intermediate shown in Scheme 3. This reactive 14-electron intermediate then oxidatively adds the S-methyl thioacetate to form complex 2a. While adding more S-methyl thioacetate at 160°C for two days a methyl migration occurs bringing the methyl substituent to the metal center and allowing a decarbonylation to occur with the loss of Carbon Monoxide. Next, another oxidative addition occurs with another S-Methyl Thioacetate to form an 18-
electron intermediate complex. After this another methyl migration occurs followed by another decarbonylation yielding the final cis product 4a as shown in Scheme 3. The final product is cis because the dippe’s phosphorus atoms are bonded. Therefore, to each other so the other two substituent groups on the metal center must be cis.

Complex 2a was an off-white solid which was isolated from the rest of the byproducts. After it was isolated it was then analyzed by $^1$H, $^{13}$C($^1$H), and $^{31}$P($^1$H) NMR spectroscopy and X-ray crystallography. Figure 4 and Figure 5 represent the structure determined from the X-ray crystallography. The $^{31}$P($^1$H) NMR spectrum of 2a yielded two doublets. Along with these doublets were platinum satellites at δ 60.14 ($J_{P-P} = 3.9$ Hz, $J_{Pt-P} = 3018$ Hz) and 57.69 ($J_{P-P} = 3.9$ Hz, $J_{Pt-P} = 1413$ Hz). This is typical for platinum–phosphorus couplings to appear on phosphorus trans to thiolate and sp$^2$-carbon ligands$^{14}$. The structure of 2a shows square-planar Pt(II) geometry as supported by the bond angles around the platinum of 86.40(7)$^\circ$, 90.54(7)$^\circ$, 90.87(10)$^\circ$, and 92.16(18)$^\circ$.

The (dippe)Pt(NBE)$_2$ was then treated with 10 equiv of S-methyl thioacetate in $p$-xylene-$d_{10}$ at 160 °C for 2 days. This gave the complex (dippe)Pt(SMe)$_2$, characterized as complex 4a in Scheme 2, in good yield. An intermediate was observed using $^{31}$P NMR during early reaction
times, but after two days at 160°C the intermediate disappeared. The complex 4a was an off-white solid which was isolated from the rest of the byproducts. After it was isolated, it was then analyzed by $^1$H, $^{13}$C($^1$H), and $^{31}$P($^1$H) NMR spectroscopy and X-ray crystallography. As shown in Figure 6 below, complex 4a is a symmetric species much like complex 2a. The X-ray crystallography structure is supported by the $^{31}$P($^1$H) NMR spectrum, which has as a singlet at δ 68.79 ($J_{Pt-P} = 2681$ Hz). The byproducts of this reaction were analyzed using Gas Chromatography-Mass Spectrometry (GC-MS), and were concluded to be the organic products acetone and Me$_2$S. These products were in a 1.6 acetone:1 Me$_2$S ratio according to the GC-MS data.

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**Figure S.3** $^1$H NMR spectrum of 2a in CD$_2$Cl$_2$ (400 MHz): Complex 2a

**Figure S.6** $^1$H NMR spectrum of 4a in CD$_2$Cl$_2$ (400 MHz): Complex 4a

Comparison of the two $^1$H NMR spectra shows the disappearance of functional group containing the carbon bonded to a methyl and double bonded to an oxygen. This is why the two sets of peaks that occur around 2 ppm turn into one peak shifted up the spectrum. Adapted from C-S Bond Activation of Thioesters Using Platinum (0)"
The $^{31}$P NMR spectrum of complex 2a and complex 4a were compared to analyze the structures of the two complexes. The loss of the ketone from complex 2a and the addition of another S-methyl causes the molecule to have a plane of symmetry. This is supported by Figure 5 which shows the two phosphorus peaks and their four satellites in 2a’s NMR turning in to one peak with two satellites. Also, in 2a’s spectrum the intermediate, 3a, shows up in two labeled singlets at 66.605 and 64.234 ppm. The symmetry of 4a makes the two phosphorus atoms identical yielding one peak. The $^1$H NMR spectrum of complex 2a and complex 4a were compared to analyze the structures of the two complexes. In Complex 2a’s spectrum there are many peaks because there is a lack of symmetry in the molecule. This is
different in the final spectra of 4a where there are fewer, more defined peaks due to the symmetry. In order to identify the complex that was detected in the early stages of formulating complex 4a, complex 2a was heated at 160°C in the absence of any free thioesters for three days in a p-xylene-d$_{10}$ solution. The NMR data for all four spectra is located in Table 1 and Table 2, below.

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<th>Table 1. Assignment of 1H NMR Peaks for 2a and 4a</th>
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<td>Assignment of all peaks that occur in Figure 4. Location of peak, peak type, and the atom in the molecule that the peak corresponds to are all listed in the table. The numbers associated with the carbon atoms correspond to Figure 3 for Complex 2a and Figure 6 for Complex 4a. The hydrogen atoms attached to C15, C18, C21, and C24 are not visible because their peaks are overlapped by the CH3 peaks from the isopropyl groups. Adapted from supplemental data from C-S Bond Activation of Thioesters using Platinum (O)⁹.</td>
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<th>1H NMR Assignment</th>
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<tr>
<td>Complex 2a</td>
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<tr>
<td>Peak(s) Correspond To</td>
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<td>C22, C23, C25, C26 H's</td>
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<td>C16, C17 H's</td>
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<td>C19, C20 H's</td>
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<td>C3 H's</td>
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<td>C5, C18, C21, C24</td>
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This was done in the absence of thioesters to prevent any unwanted carbon-sulfur reactions from occurring. This reaction, shown below in Scheme 3, yielded complex 3a.

Complex 3a was isolated as the major component and was about 80% of the product. The other byproduct was a symmetrical dinuclear platinum complex. Complex 3a was also characterized by $^1$H, $^{13}$C{$^1$H}, and $^{31}$P{$^1$H} NMR spectroscopy and X-ray crystallography. Complex 3a had bond distances Pt–CH$_3$ = 2.13(2) Å. The Pt–CH$_3$ bond distance is longer in complex 3a as compared to complex 2a, Pt–C$_2$H$_4$O = 2.099(7) Å, due to the difference between sp$^3$ vs. sp$^2$ hybridization. In the $^{13}$C NMR spectrum Pt–CH$_3$ appeared as a doublet of doublets at $\delta$ –3.00 ($J_{P-C} = 7.6$ Hz, $J_{P-C} = 87.0$ Hz, $J_{Pt-C} = 535.3$ Hz). However, in the $^1$H NMR spectrum this data was obscured by overlap with the isopropyl signals from the complex. Complex 3a was the treated with excess S-methyl thioacetate in $p$-xylene-$d_{10}$ at 160 °C for 2 days and this caused complex 4a to form in good yield, as shown in Scheme 3. This shows that complex 3a is an intermediate involved in the
reaction leading to complex 4a in Scheme 2 above. In the reaction leading from complex 3a to complex 4a the organic products acetone and Me$_2$S were once again detected by GC-MS. The initial reaction with Pt$^0$ leads to the cleavage of the thioester C–S, which is followed by decarbonylation. The additional reaction with substrate is what eventually leads to the bis-thiolate product shown as complex 4a in both Scheme 2 and Figure 6.
These first sets of experiments discussed much information about C-S bond activation and their reaction processes. The following experiments performed by William D. Jones, Matthew R. Grochowski, Ting Li, and William W. Brennessel focus on the kinetics and thermodynamics products of C-S bonds and the effects these differences have on reactions. Products that form faster are kinetic products, and products that are more stable are the thermodynamic products.

**Reaction of complex 6 with 2-Cyanothiophene:**

The reaction of complex 6 with 2-cyanothiophene occurred quickly at room temperature in THF to give the C-S insertion complex \((\text{dippe})\text{Ni}(\kappa^2\text{-S,C-SCH═CHCH═C(CN)})\) \((2a)\). The complex 2a had a 93\% isolated yield. Adapted from Competitive Carbon-Sulfur vs Carbon-Carbon Bond Activation of 2-Cyanothiophene with \([\text{Ni}(\text{dippe})\text{H}]_2\).\(^8\) SCH═CHCH═C(CN)), complex 7a, at an isolated yield of 93\%. The insertion of the 2-cyanothiophene occurred exclusively at the C-S bond. This supports that the reaction first loses the H\(_2\) gas then opens the 2-cyanothiophene ring at the C-S bond. This would then follow a similar mechanism as shown in Scheme 3. The carbon bonded to the nickel on 2a is \(\eta^2\) giving the metal center a 16-electron count. The \(^{31}\text{P}\) NMR spectrum showed two doublets at \(\delta 73.06\) and 72.22 \((J_{p-p} = 34 \text{ Hz})\).
These doublets were very closely spaced indicating that there is high interaction between the two phosphorus atoms in the products. The structure of complex 2a is a nickel metallacycle product with square planar geometry around the Ni(II) center. This geometry is supported by the bond angles of 94.44°, 83.955°, 86.398°, and 95.26° around the Ni(II) center. Complex 7a was isolated as a solid, but it was only found to be stable in nitrogen while in solid form. If the compound was exposed to air it decomposed because of oxidation and the formation of dippe oxide. When exposed to air and monitored by $^{31}$P NMR spectroscopy dippe oxide could be observed at $\delta$ 52.9, THF. When 7a was heated in THF at 85 °C over a period of 13 hours, transformation of the compound occurred to give the C–CN bond-activated product (dippe)Ni(CN)(2-thiophene), complex 8, shown in Scheme 6 below. It is proposed that an intermediate is formed during this reaction and the mechanism is unclear. Complex 3 has important sterics because the sterics affect the ability of the molecule to react and the ability to measure the activation energy experimentally.
Observation of Intermediates at Low Temperature

No intermediates were observed at room temperature in the reaction of 6 with 2-cyanothiophene to form complex 7a because the reaction occurred so quickly. However, when the amount of 2-cyanothiophene was increased to 4 equivalents and added to complex 6 at -60 °C in THF-d_{8} many intermediates were observed as shown in Scheme 7 above. At low temperatures the structures that were most prevalent were the kinetically favored products, not the thermodynamically favored products.

The amount of 2-cyanothiophene was increased to 4 equivalents in this part of the experiment to cause more congestion and collisions of molecules in the reaction and allow the intermediates to be observed. When reacted at -60 °C, complex 7a was present, but only at about nine percent of the final product. However, this value is quite small compared to the percent yields of the other species. In previous studies with complex 6 a direct relationship between the P−P coupling constant and the nickel oxidation state has been observed\textsuperscript{15}.

According to these studies, a Ni(0) complex is identifiable by a P−P coupling constant of \( J \) greater than 60 Hz, whereas a Ni(II) complexes are typified by \( J \) less than 40 Hz. Complex 7a is a Ni(II) complex, and in addition to 7a, a second Ni(II) complex was present at about 19% yield.
This product appears to be the C—S-activated complex that comes from the insertion into the nonsubstituted C—S bond, (dippe)Ni(κ₂-S,C-SC(CN)═CHCH═CH). After integrating the collected NMR spectrum, a ratio of 2b:2a at −60 °C was determined to be 2:1. This observation is similar to the reaction involving the Pt–dippe analogue. The recorded observation leads to the idea that activation of the nonsubstituted C—S bond of 2-cyanothiophene is observed as a kinetic product which will eventually convert to the thermodynamically favored activation of the nitrile-substituted C—S bond.¹⁶

**Kinetic and Thermodynamic C—S Activations**

Based on experimental observations, the C—S activation product complex 7a is thermodynamically more stable than 7b. From the Density Functional Theory (DFT) calculations shown in Figure 7, 7a lies 6.3 kcal/mol lower in energy than 7b. When changing from the Ni(dmpe), Bis(Dimethylphosphino)ethane, to the Ni(dippe) fragment the DFT calculations show that 7a is still about 3 kcal/mol under 7b.

At room temperature, no resonances for 7b could be seen in the NMR spectrum. This data makes sense based on the hypothesis that 7a is the thermodynamic product and 7b is the
kinetic product. From the $\eta^2$-C,C-2-cyanothiophene complexes the activation barrier for the C−S activation leading to 7a is 13.7 kcal/mol, and that activation barrier for the 7b is only 9.6 kcal/mol. These DFT calculated values are congruent with the experimental results that 7b is the kinetic product while 7a is the thermodynamic product. This data is supported by the experimental data because 7b formed first. But 7a was more stable. This data also matches the previous results obtained with Pt(dmpe) and 2-cyanothiophene$^{13}$. These results show that Pt(dmpe) and 2-cyanothiophene tend to have a kinetic preference for cleavage of the unsubstituted C−S bond.

When complex 6, [Ni(dippe)H]$_2$, was reacted with 2-cyanothiophene at room temperature C−S bond activation occurred. This produced complex 7a, a Ni metallacycle product. Bond cleavage occurs on the nitrile-substituted side of the thiophene, in this reaction. In a reaction 7a was then heated in solution at 85 °C. While this heating took place, conversion to the C–CN activated product, complex 8, occurred. When complex 8 was cooled back to room temperature it did not form complex 7a. This data shows that complex 8 was more thermodynamically stable than 7a even though the DFT calculations predicted otherwise. The reasoning behind why this occurs is still unclear. What this did demonstrate is that C−S cleavage is kinetically favored over C−C cleavage. Conversely, C-C cleavage is thermodynamically favored over C-S cleavage. The reasoning behind this is breaking a C-C bond is more favorable than breaking a C-S bond with higher electron density. At −60 °C, when the reaction was monitored by NMR spectroscopy, several intermediates were observed to be in equilibrium. These intermediates included complex 7a and the isomer of complex 7a in which the alternate C–S bond had been cleaved, complex 7b. Activation from the nonsubstituted side
of the thiophene was kinetically preferred at low temperature over 7a at −60 °C. This data indicates that sterics contribute to the kinetic selectivity. The 7b is more sterically hindered because the CN is located on an alpha carbon to the sulfur whereas in 7a the CN is located on the other side of the metal. Over time conversion to cleavage of the substituted C−S bond occurs as the major thermodynamic product. These experiments and their observations show that C-S bond activation is a kinetically favored reaction rather than thermodynamically favored as compared to C-C bond activation in these experiments dealing with closed systems.

**Conclusion**

In the first set of experiments, (dippe)Pt(NBE)$_2$ was used to examine the carbon–sulfur bond activation of cyclic thioesters. By using multiple NMR techniques and X-ray crystallography many conclusions were made about the structure and the mechanism of these C-S activated thioesters. The first step of the mechanism was an oxidative addition of the acyl C-S bond of a molecule of thioester. This step led to formation of (dippe)Pt(acyl)(SR), complex 2a, from the starting material. Complex 2a then underwent a decarbonylation. Next, the activation of a second molecule of thioester led to the formation of the final product (dippe)Pt(SMe)$_2$, complex 4a, after the reductive elimination of ketone/alkane. The structure of 4a was a symmetrical species and was confirmed by X-ray crystallography. When the NMRs of 4a were compared to those of 2a noticeable differences were apparent because of the symmetry of 4a.

In the second set of experiments, C-S bond activation was tested to understand whether it is kinetically or thermodynamically favored over C-C bond activation. At room temperature, C-S bond activation occurred cleanly when complex 6 was reacted with 2-cyanothiophene. This
process produced a Ni metallacycle product that was labeled 7a. In this reaction, bond cleavage occurred on the nitrile-substituted side of the thiophene. After this, 7a was heated in solution at 85 °C. During the heating process the molecule converted to the C-CN activated product 8. Conversion to complex 8 demonstrated that C-S cleavage is kinetically favored over C-C cleavage. This conversely proved that C-C bond activation is thermodynamically preferred over C-S bond activation. This reaction was monitored at multiple temperatures to observe intermediates. When observed at −60 °C by NMR spectroscopy the isomer of 7a, 7b, was observed. 7b occurred when the alternate C–S bond had been cleaved. This activation that occurs from the nonsubstituted side of the thiophene, at low temperature (-60°C) shows that sterics contribute to the kinetic selectivity. These experiments let many conclusions about thermodynamically favored and kinetically favored C-S bond activation, and will lead to many future directions.

There is a large possibility for future experiments involving C-S bond activation and its thermodynamics. One possible experiment that could be performed is to perform the HDS process at multiple temperatures while monitoring the process with $^1$H NMR, $^{31}$P NMR, and X-ray crystallography. This would allow a clearer picture of the proper way to perform HDS and oil refining to decrease the amount of unwanted byproducts produced.
References

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