Synthesis and Reactivity Studies of Catalysts for Efficient C–C and C–H Bond Activation

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ABSTRACT

Understanding why and how chemical bonds are formed and broken will inform the design of new chemical transformations that are more sustainable and environmentally-friendly. The objective of this study is to synthesize and characterize platinum (II) complexes that can activate C–C and C–H bonds and to understand how these complexes react. We have proposed that coordinative unsaturation at an electrophilic metal center enables C–H bond activation. We have tested this hypothesis by synthesizing a cationic platinum (II) complex bearing a 2,2'-bipyridine ligand, phenyl group, and non-coordinating anion. Additionally, we have synthesized and investigated novel cyclopropane-containing olefins for reactivity with platinum (II) complexes. These studies help distinguish between different C–H bond activation mechanisms.

KEYWORDS

hydrocarbon functionalization, homogenous catalysis, platinum, rearrangement, organometallic chemistry

INTRODUCTION

Global warming is a direct result of society's energy consumption. Improving the efficiency of industrial processes can reduce energy-related greenhouse gas (GHG) emissions, mitigating global warming. Catalysts can provide this increase in efficiency by allowing chemical processes to be run at lower temperatures and pressures, and by minimizing chemical waste byproducts (World Resources Institute 2011). A catalyst is a chemical that facilitates a reaction and is not consumed in the process, allowing it, ideally, to be reused indefinitely (Nelson and Cox 2005). Catalysts reduce the energy required for chemical processes, speed reaction rates, and improve selectivity for desired products, ultimately minimizing waste (Bartholomew and Farrauto 2011). Designing catalytic reactions and understanding catalysts' roles in organic chemical reactions can improve large-scale processes used to synthesize pharmaceuticals, materials, plastics, and fuels, lowering costs and reducing environmental impacts (National Research Council 2003). Many of these processes require insertion of chemical groups into a molecule where they did not exist before, and modern techniques often requires several steps to transform unreactive bonds, such as carbon–carbon (C–C) and carbon–hydrogen (C–H) bonds, into desired functional groups (Bergman 2007). C–H bonds are "un-functional groups." This is exemplified by the standard representation of molecules in organic chemistry; C–H bonds are indicated by the absence of any other bond. The "invisibility" of C–H bonds in their notation is a reflection of their ubiquitous nature and their lack of reactivity (Goldman and Goldberg 2004). Furthermore, the high bond energy of C–C and C–H bonds contributes to their chemical inertness. The molecules do not have low-energy empty orbitals or high-energy filled orbitals that could readily participate in a chemical reaction (Labinger and Bercaw 2002). Thus, C–C and C–H bonds are important targets for catalysis, as direct activation of these bonds is especially useful for shortening multi-step syntheses. These activations have the potential to be achieved in a selective, energy- and material-efficient manner as we move to improve industrial catalytic processes to be more environmentally friendly.

Transitioning toward more economical and sustainable industrial processes requires us to expand our ability to catalyze chemical reactions. This requires a better understanding of how catalysts activate unreactive molecules and, fundamentally, why and how chemical bonds are broken and formed (National Research Council 2003). Better understanding of these

transformations will allow for improved control, and allow us to design new chemical syntheses, and improve those that exist, so that they are increasingly materials-efficient and environmentally-safe (Goldman and Goldberg 2004).

Platinum has been shown to be a promising metal for catalytic C–H and C–C bond activation (Luedtke and Goldberg 2008, Bowring et al. 2013a). More specifically, platinum complexes with bipyridine-based ligands have been shown to participate in catalytic transformations of organic substrates (Karshtedt et al. 2006). Platinum is a third-row transition metal, making strong bonds to carbon and hydrogen and thus better enabling C–C and C–H bond activation (Crabtree 2009). Platinum often prefers to form d^8, square planar complexes, which make substitution at the metal center easier than with octahedral complexes (Crabtree 2009). Properties of platinum, such as its ability to do C–C and C–H bond activation, allows us to synthesize a new molecule and broaden our knowledge about C–C and C–H bond activation.

The objective of this study is to synthesize and characterize complexes designed to activate C–C and C–H bonds and to investigate how these complexes function. What features enable a complex to activate C–C and C–H bonds? What allows a complex to act catalytically? How does the activation proceed? We propose that if we treat an organic substrate, with a cyclopropane ring and nearby double bond, with a platinum (II) complex composed of a 2,2'-bipyridine ligand, phenyl group, and non-coordinating anion, the platinum (II) complex will be able to catalytically activate C–H bonds and rearrange to a more stable isomer. This will lead to a better understanding of an existing rearrangement mechanism of a spirocyclopropane (Bowring et al. 2013a) and explore the potential of generalizing this mechanism to new substrates.

METHODS

General

Unless otherwise noted, we carried out all reactions in a Vacuum Atmospheres glovebox or used Schlenk techniques under a nitrogen atmosphere. We purchased triflimidic acid ($HNTf_2$) from Acros Organics and purified it by sublimation at 40 °C for five days. Pentane, hexanes, benzene, toluene, and 1,2-dichlorobenzene were purchased from Sigma Aldrich. Tetrahydrofuan (THF) was purchased from Macron Chemicals. We dried benzene and hexane with a Vacuum

Atmospheres solvent purifier system. We dried pentane, toluene, and THF with a JC Meyers Phoenix SDS solvent purification system. 1,2-dichlorobenzene was dried over calcium hydride (CaH_2). Benzene-d_6 was purchased from Cambridge Isotope Laboratories and dried over sodium-potassium (NaK) alloy, vacuum transferred, and freeze-pump-thawed four times. All NMR spectra were collected at ambient temperature on Bruker AVQ-400, AV-300, or AV-600 NMR spectrometers and referenced to the residual proteo solvent signals. Structures were visualized using the ChemBioDraw 13.0.2.3021 software (PerkinElmer Informatics 2013).

Study system

The objective of my study was to synthesize and characterize complexes for C–C and C–H bond activation and investigate the potential for these metal complexes to catalyze novel rearrangement reactions. The study system under investigation was a hydrocarbon substrate—a cyclopropane ring connected to a cyclopentene ring (Figure 1). We proposed that if we treated this hydrocarbon substrate with an in-house synthesized platinum (II) complex (Figure 2), we would be able to catalytically activate the C–H bonds of the cyclopropane and causing the molecule rearrange to form norbornene (Figures 3 and 4) at moderate temperatures and in halogenated aromatic solvents. We synthesized the platinum (II) complex was based on a published literature procedure (Bowring et al. 2013a). We synthesized the hydrocarbon substrate from allylzinc bromide and propargyl bromide, with ring-closing metathesis with the Hoveyda-Grubbs second generation catalyst (Sigma Aldrich). The synthesis of 1,1-diallylcyclopropane (Equations 1 and 2) was based on a published literature procedure (Frangin and Montigny 2005). The allyl bromide and propargyl bromide used to synthesize 1,1-diallylcyclopropane were purchased from Sigma Aldrich(St. Louis, MI). The ring-closing metathesis (Equation 3) with the Hoveyda-Grubbs second generation catalyst was based on a published literature procedure (Benedetti et al. 2012). We employed a series of characterization methods to identify the substrate.

Figure 1. Hydrocarbon substrate: spiro[2.4]hept-5-ene.

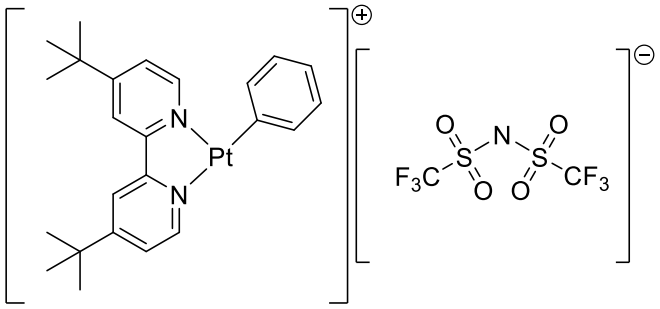


Figure 2. Platinum (II) catalyst.

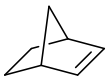


Figure 3. Norbornene.

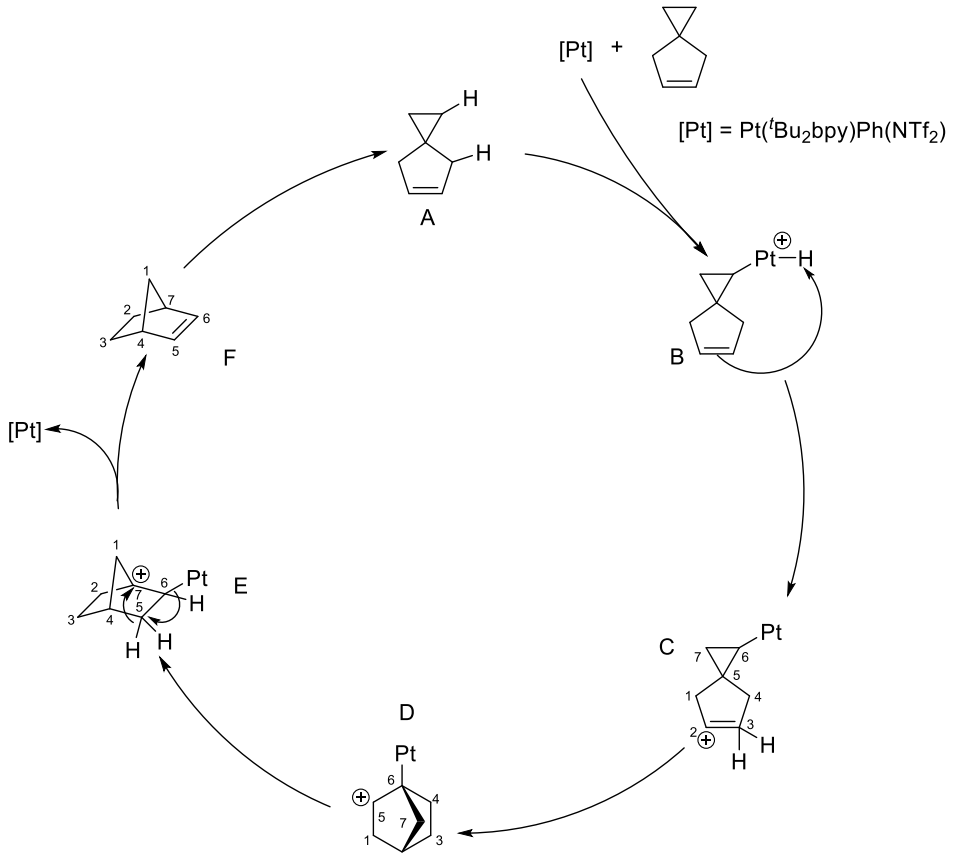


Figure 4. Proposed hydrocarbon substrate rearrangement mechanism.

Data collection methods

NMR Spectroscopy

Nuclear magnetic resonance (NMR) spectroscopy was the primary characterization tool in this study. We used Bruker AVQ-400 and AVB-400 MHz NMR spectroscopy instruments to characterize reaction mixtures, intermediates, and products. We prepared samples by dissolving approximately 0.010 g of the reaction mixture in approximately 0.5 mL of deuterated solvent (e.g. deuterated benzene). We transferred the sample to a thin-walled, borosilicate glass tube. Next, we lowered the sample into the NMR spectrometer. We first tuned the probe to the nucleus to be investigated and then homogenized the magnetic field across the sample, a process known as shimming. Then we employed standard fourier transform NMR pulse sequences to collect multiple

spectra, on average eight scans, and then averaged the spectra, which increased the signal-to-noise ratio. We then phased the averaged spectra and adjusted the baseline, which allowed us to analyze the NMR spectra of the sample. We analyzed the NMR spectra with the MestReNova 8.1 software package (Mestrelab Research R. L. 2013).

GC-MS

A second characterization tool we employed was gas chromatography-mass spectrometry (GC-MS). We collected data with an Agilent Technologies 6890N Network GC system and Agilent 5973 Network Mass Selective detector. We prepared the GC-MS sample by diluting a drop of the reaction mixture in a solvent (e.g. diethyl ether) and filtering out any solid material through a basic alumina plug. We collected data by injecting 1 μL of the sample into the instrument. The sample was separated into its components by gas chromatography, using helium as the mobile phase and a DB-5MS column as the stationary phase. Mass spectrometry analyzed a portion of the separated sample, recording a total ion chromatograph (TIC) that contained the mass spectra of the chromatographic product, a continuous process. We analyzed the TICs using Enhanced Data Analysis (Agilent Technologies 2001). GC-MS to identify the hydrocarbon substrate was performed by the QB3/Chemistry Mass Spectrometry Facility at the University of California, Berkeley.

Data analysis methods

We used NMR and mass spectrometry to confirm the identity of the hydrocarbon. NMR spectroscopy allows us to predict products' molecular structures based on where, relative to a reference, the resonances appeared in the spectrum (i.e. their chemical shift) and their integrals. We integrated all resonances, except those assignable to proteo solvent resonances and impurities present in the solvent used to prepare the NMR sample. The resulting integrals provided ratios of the number of nuclei that gave rise to each signal. We assigned observed resonances to nuclei in the molecules' predicted structures based on their chemical shifts and the aforementioned integrals.

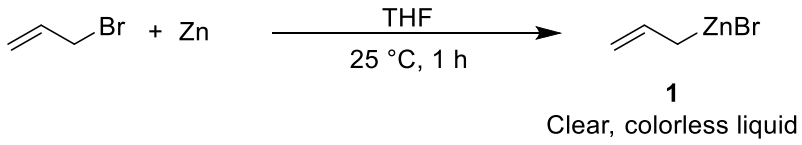
For each sample, GC-MS provided limited evidence of the products' purities, assuming that the species and any possible contaminants are separable by gas chromatography and ionizable

by electron impact. The peaks in a TIC correspond to components in the original mixture. A mass spectrum of a compound identified in the TIC contains information on that component's mass/charge ratio and/or gas phase fragmentation pattern. If the mass/charge ratio of the proposed product is not observed in the spectrum, different fragmentation products are hypothesized, given the proposed structure and compared to proposed mass spectrum. The structure is evidenced by the correspondence between the fragmentation pattern and the observed mass spectrum.

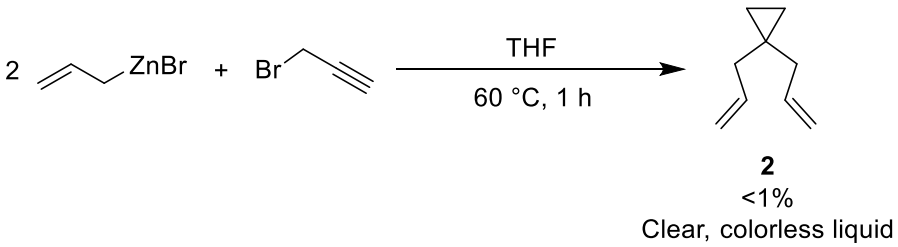
RESULTS

Synthesis of hydrocarbon substrate

We synthesized a series of organic compounds to make a hydrocarbon substrate. We generated allylzinc bromide (**1**) by a dropwise addition of allyl bromide in anhydrous THF to zinc dust (Equation 1). We added propargyl bromide dropwise to a solution of compound **1** at 60 °C to give 1,1-diallylcyclopropane (**2**) as a clear and colorless liquid (Equation 2, Figure 5). Reaction of compound **2** with Hoveyda-Grubbs second generation catalyst (5 mol %) (Figure 6) in *ortho*-dichlorobenzene gave the target cyclopentene compound (**3**) by ring-closing metathesis (Equation 3). We used ^{1}H NMR spectroscopy to characterize the compound (Figure 7).



Equation 1. Synthesis of allylzinc bromide.



Equation 2. Synthesis of 1,1-diallylcyclopropane.

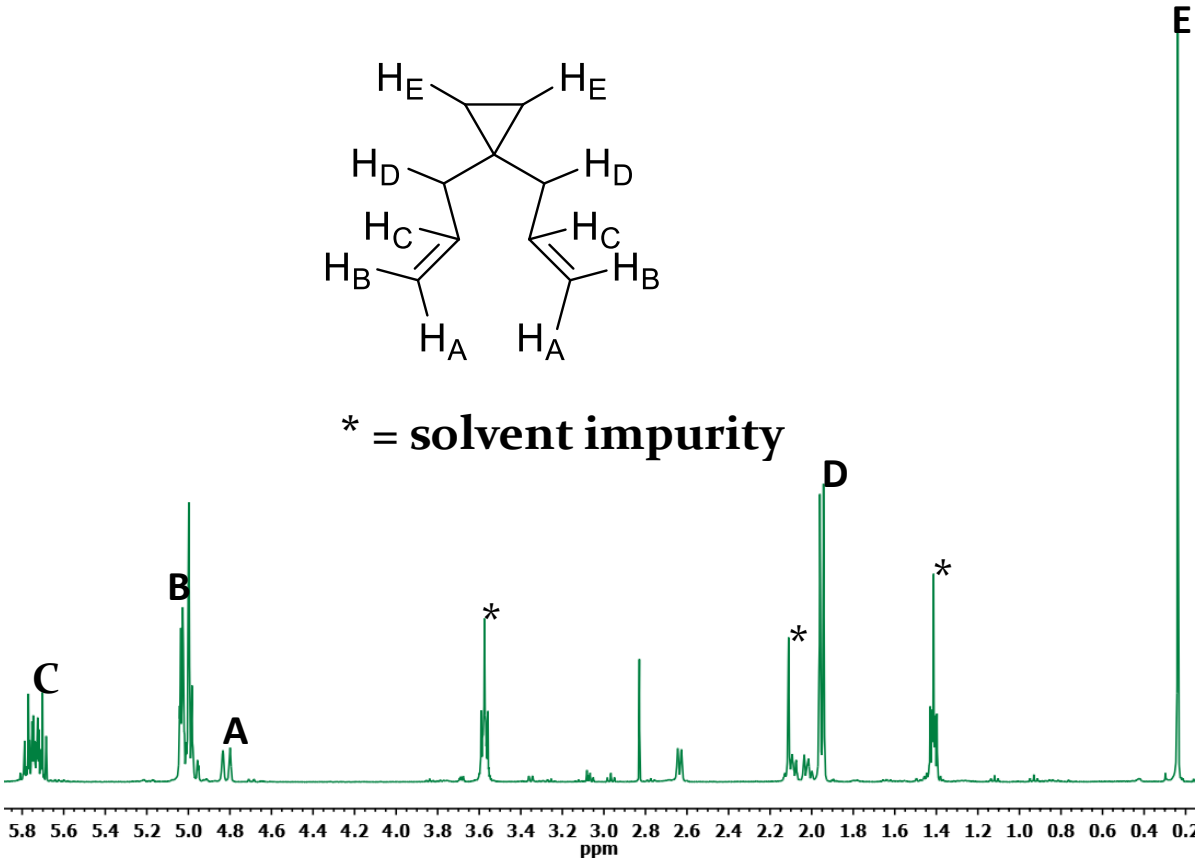


Figure 5. ^{1}H NMR spectrum of 1,1-diallylcyclopropane.

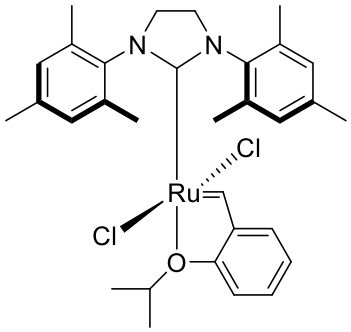
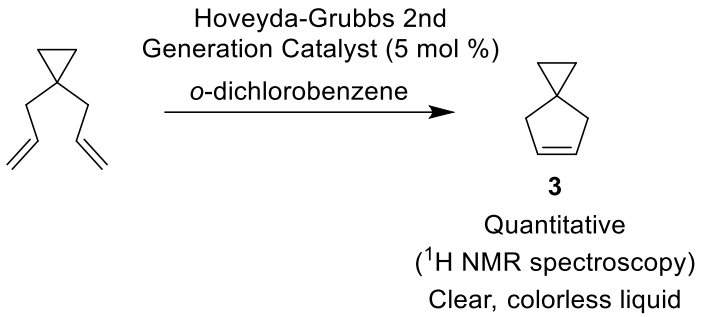


Figure 6. Hoveyda-Grubbs second generation catalyst.



Equation 3. Synthesis of spiro[2.4]hept-5-ene.

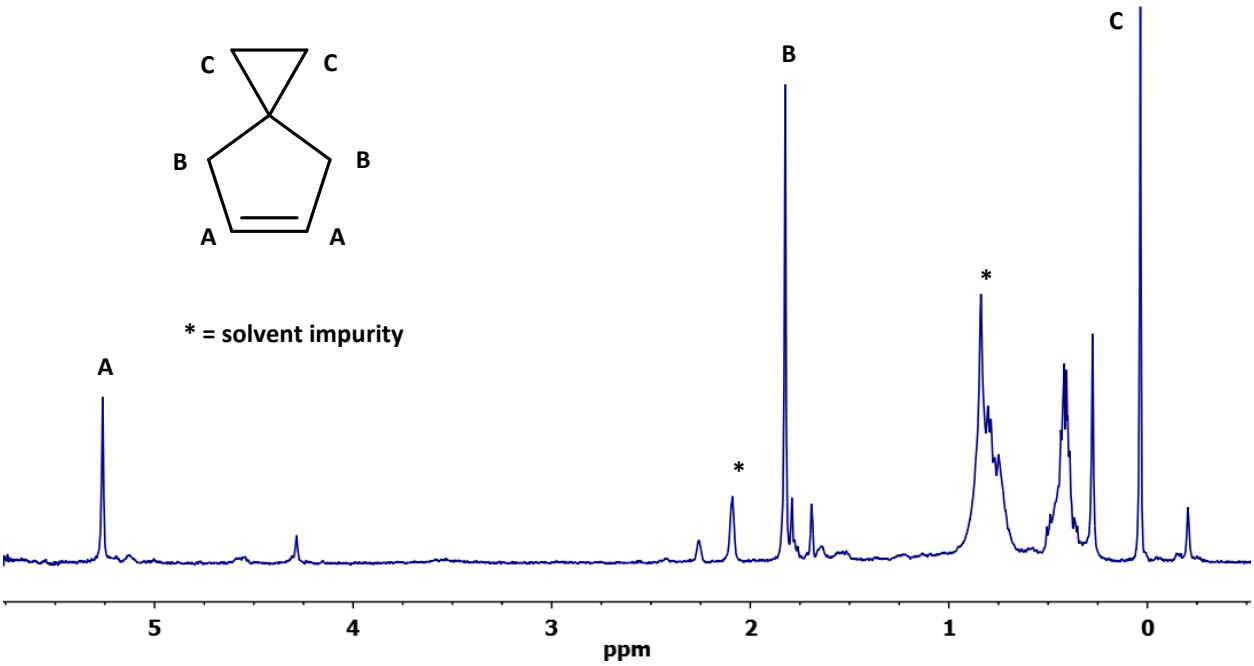
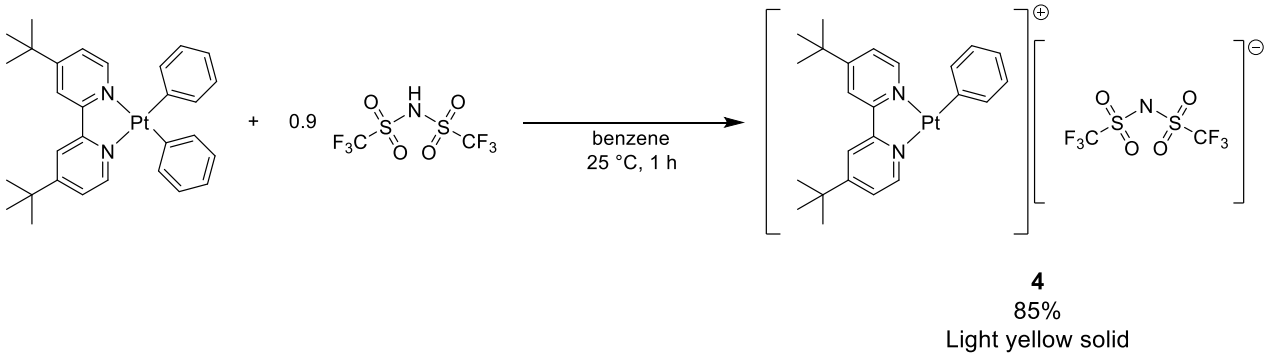


Figure 7. ^{1}H NMR of hydrocarbon substrate.

Synthesis of Pt(^{t}Bu$_2$bpy)Ph(NTf$_2$)

We synthesized a platinum (II) complex to attempt to activate the C–H and C–C bonds on the hydrocarbon substrate. Pt(^{t}Bu$_2$bpy)Ph$_2$ was synthesized previously (Hill et al. 2007, Rashidi et

al. 1990, Ong et al. 2003). We produced Pt(^{t}Bu$_2$bpy)Ph(NTf$_2$) (**4**) by adding a solution of HNTf$_2$ in benzene to a suspension of Pt(^{t}Bu$_2$bpy)Ph$_2$ in benzene (Eq. 4). The reaction was stirred for an hour and a light yellow precipitate formed. The reaction mixture was vacuum filtered and the precipitate was collected on a fine porosity fritted funnel. We used NMR spectroscopy to identify the product.

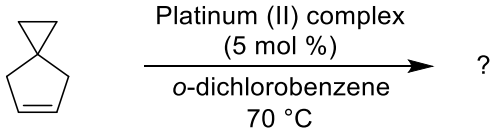


4
85%
Light yellow solid

Equation 4. Synthesis of Pt(^{t}Bu$_2$bpy)Ph(NTf$_2$).

Reaction of platinum (II) complex with hydrocarbon substrate

We used a platinum (II) complex to treat the hydrocarbon substrate (Equation 5).We added the internal standard 1,3,5-tris(trifluoromethyl)benzene (Figure 8) to compound **4**. We dissolved compound **4** in a solution of compound **3** in *ortho*-dicholorobenzene. We heated the sample to 70 °C. We monitored the reaction by NMR spectroscopy over a one week period and no reaction was observed (Figure 9).



Equation 5. Reaction of Pt (II) complex with hydrocarbon substrate.

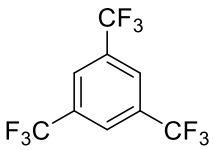


Figure 8. 1,3,5-tris(trifluoromethyl)benzene.

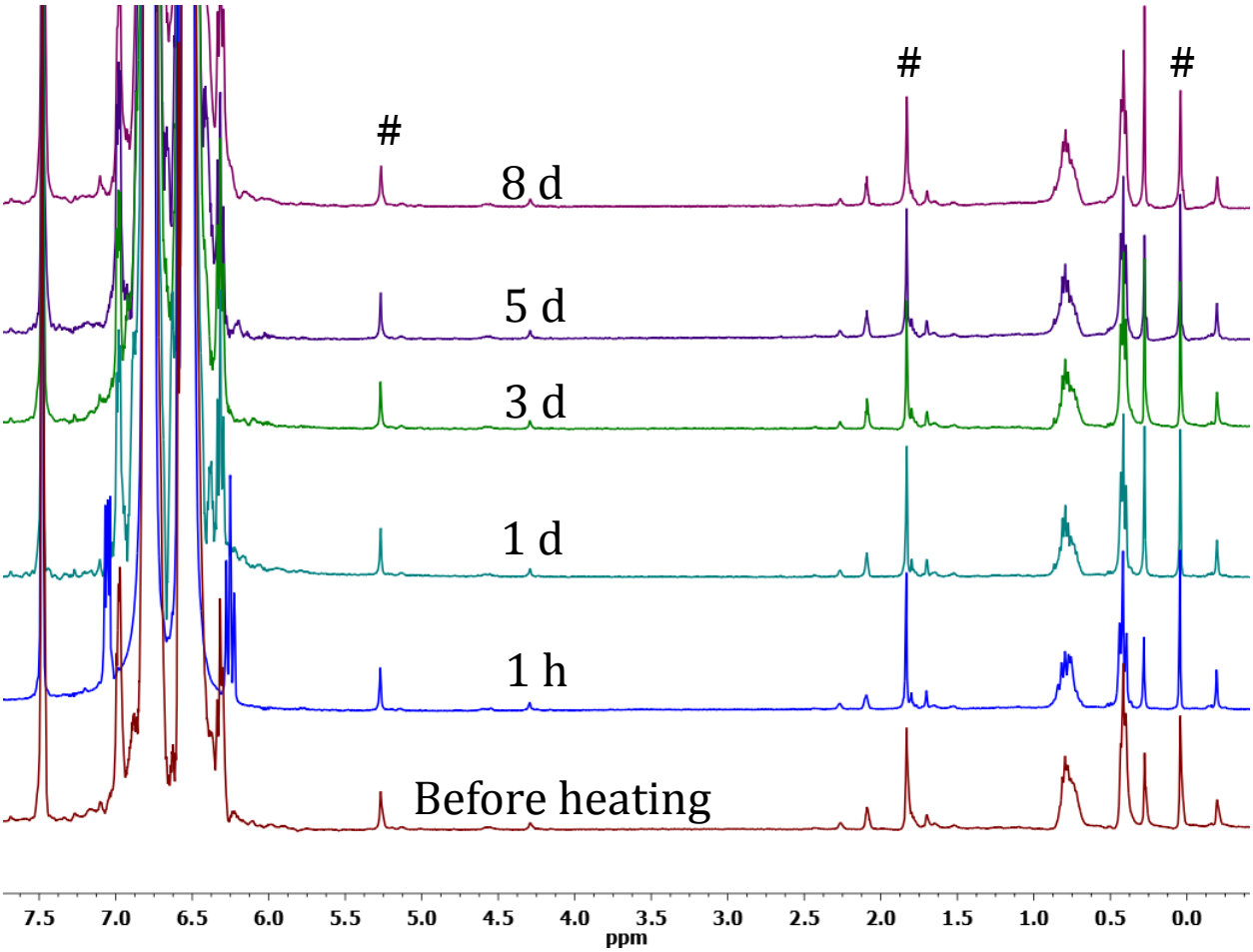


Figure 9. Monitoring reactivity by ^{1}H NMR. Stacked ^{1}H NMR spectra of the reaction mixture recorded over the course of eight days. We denoted the peaks we monitored with the number sign (#).

DISCUSSION

In this study, we synthesized and characterized a complex designed to catalytically activate C–C and C–H bonds and investigated how this complex functions. We have synthesized and characterized a new hydrocarbon substrate and platinum (II) complex. We treated the substrate with the platinum (II) complex to determine if C–H and C–C bond activation, presumably followed by substrate rearrangement, would occur.

Hydrocarbon substrate (spiro[2.4]hept-5-ene)

We synthesized the hydrocarbon substrate in three steps. First, we synthesized allylzinc bromide from allyl bromide and zinc dust according to the literature procedure (Frangin et al. 2005). We found that the reaction was able to proceed by to first activating the zinc dust, as suggested by the literature (Frangin et al. 2005). We prepared the activated zinc using an approach modified from Zhang et al. (2009). We activated the zinc dust by heating the zinc to 60-70 °C, adding 1,2-dibromoethane and THF dropwise, cooling to room temperature, and quenching with trimethylsilyl (TMS) chloride and THF.

Second, the reaction of allylzinc bromide with propargyl bromide produced 1,1-diallylcyclopropane via organozinc intermediates. We performed this reaction according to the literature procedure (Frangin et al. 2005) and adapted an isolation and purification procedure by Bellassoued and Frangin (1978).

Third, we employed the Hoveyda-Grubbs second generation catalyst to form the cyclopentene ring via ring-closing metathesis. The ^{1}H NMR spectra of the 1,1-diallylcyclopropane stock solution before and after the addition of the catalyst confirmed that the reaction of Hoveyda-Grubbs second generation catalyst with 1,1-diallylcyclopropane was completed in less than a minute at ambient temperature. This is an improvement of the suggested reaction conditions of 1 hour at 70 °C for ring-closing metathesis to form a five-membered nitrogen-containing ring (Benedetti et. al 2012).

Platinum (II) complex Pt(^{t}Bu$_2$bpy)Ph(NTf$_2$)

We synthesized the platinum (II) complex in a one-step process. We reacted Pt(^{t}Bu$_2$bpy)Ph$_2$ (Bowring et al. 2013b) with HNTf$_2$ to produce Pt(^{t}Bu$_2$bpy)Ph(NTf$_2$). We found the product to be mostly pure without recrystallization, as suggested by (Bowring et al. 2013a), by NMR spectroscopy.

Reactivity studies

Upon treating the hydrocarbon substrate with the platinum (II) complex, we found that the complex activated neither C–C nor C–H bonds. We did not observe any change in the resonances we monitored. We integrated the resonances, referenced the integrated values against the internal standard of 1,3,5-tris(trifluoromethyl)benzene, compared the spectra over time, and found no significant change in the peaks we monitored. The stability of the substrate upon treatment with the platinum (II) complex suggests that its C–C and C–H bonds remained unactivated.

Limitations

The synthesis of the platinum (II) complex resulted in significant delays to the progression of the project. We found that the proposed synthesis of the platinum (II) complex $Pt(Me_2bpy)Ph(NTf_2)$ by Bowring et. al (2013a) to be the most challenging. We found the reaction of $Pt(Me_2bpy)Ph_2$ and $HNTf_2$ to be incredibly sensitive. We hypothesize that small to trace amounts of olefin and thiophene were present in the benzene and pentane used, and these commonly found solvent impurities induced a series of side reactions that prevented the reaction of $Pt(Me_2bpy)Ph_2$ and $HNTf_2$ from going to completion. Given this significant delay, we moved to synthesize the platinum (II) complex $Pt(^tBu_2bpy)Ph(NTf_2)$, which proved to be a more manageable synthesis.

Future directions

We will continue to modify the reaction conditions and improve the synthetic methods in order to increase yields. Additionally, we will treat the hydrocarbon substrate with different platinum (II) complexes to further our understanding of its physical properties and stoichiometric reactivity. Additionally, we will explore the activation of other potentially informative hydrocarbon substrates.

Conclusion

We have examined the generalizability of the catalytic C–C and C–H bond activation reported by Bowring et al. (2013a), testing the hypothesis that if our hydrocarbon substrate were to be activated similarly, our hydrocarbon would rearrange to form norbornene. We synthesized a new hydrocarbon substrate via two organozinc intermediates and synthesized a platinum (II) complex. We identified the compounds by NMR spectroscopy and GC-MS. We monitored reactivity by NMR spectroscopy and found that the catalyst appeared to activate neither C–C nor C–H bonds in the novel substrate. These results suggest the reaction mechanism for C–C and C–H bond activation reported by Bowring et al. (2013a) may not be as broadly applicable as originally hypothesized.

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