UNIVERSITY OF CALIFORNIA SAN DIEGO

Synthetic and Mechanistic Studies on Ruthenium-accelerated 6π Electrocyclization Reactions of Conjugated Trienes

A Thesis submitted in partial satisfaction of the
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in

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by

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The Thesis of Yifan Li is approved, and is acceptable in quality and form for publication on microfilm and electronically:

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ABSTRACT OF THE THESIS

Synthetic and Mechanistic Studies on Ruthenium-accelerated 6*π* Electrocyclization Reactions of Conjugated Trienes

by

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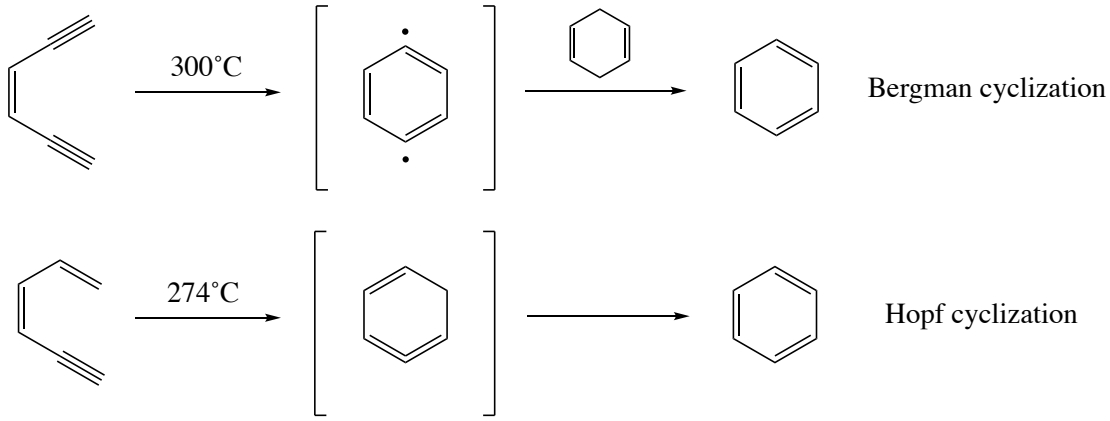
This work mainly focused on exploring mechanism of ruthenium triggered 6π electrocyclization of trienes. The first assignment is the synthesis of trienes, the thermal and photolysis reactions of the all protio terminal triene were carried out in order to compare the efficiency and effectiveness of the traditional cyclization process and the ruthenium mediated reaction. Based on all the results from the all-protio triene reactions, the η^4 and η^6 intermediates were discovered. Meanwhile, whether the ruthenium

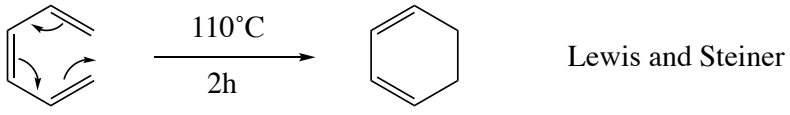
accelerated cyclization undergoes a disrotatory proceed is hard to judge. Therefore, deuterium labeled trienes were desired. Deuterium enriched trienes need to be employed as the substrates to clarify the stereochemistry. With the consistency of mechanism proposed by Stryker and the results obtained from the deuterium labelling studies, the ruthenium-mediated disrotatory cyclization process of trienes was demonstrated. Then the kinetic isotopic effect study was achieved, the competition reaction between all-protio triene and triene-d_2 demonstrated no isotopic effect appeared in this case, which indicated the rate determine step of the whole cyclization process is not the metal binding step. Lastly, the kinetic studies of terminal triene and three dimethyl triene synthesized by Li-An Wang were carried out to clarified the reacting rate of all these triene and to learn more about the mechanism occurred during the cyclization process.

A. Introduction

The thermal cyclization reaction of unsaturated organic molecules has a quite long history. For enediynes and dienynes, Bergman cyclization and Hopf cyclization are famous demonstrations.[1,2] (Scheme 1) The triene thermal cyclization hexatriene towards cyclohexadiene was reported in 1964 by Lewis and Steiner.[3] Not only is the high temperature a key element for overcoming the activation barriers, but a long period of time is required. (Scheme 2).

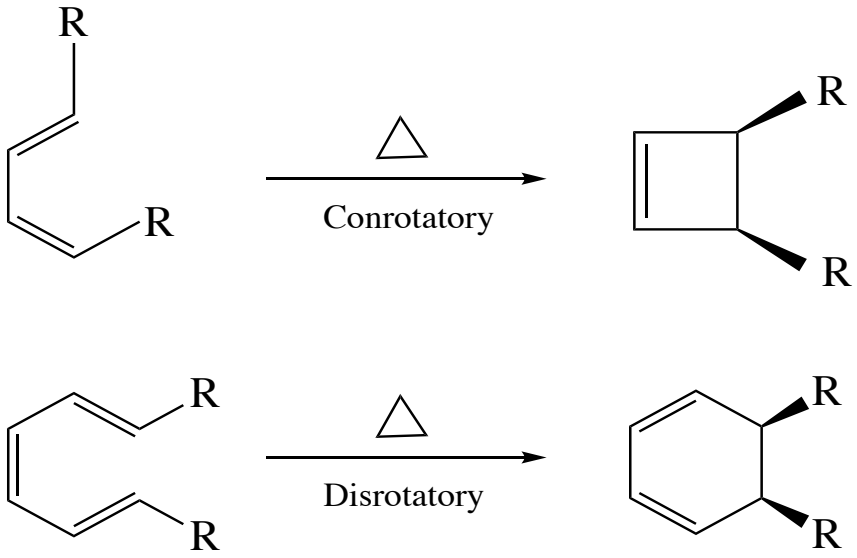


Scheme 1. Bergman cycloaromatization and Hopf cyclization.



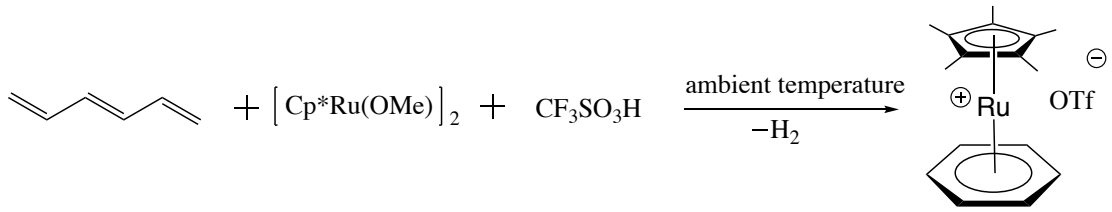
Scheme 2. Cyclization of *cis*-1,3,5-hexatriene to cyclohexadiene.

Until 1967, Woodward and Hoffmann accrued their results and those of other researchers to illustrated the stereochemistry rules for the unsaturated organic molecules cyclization process in the publication entitled “The Conservation of Orbital Symmetry”.[4] They concluded the different rotations of the reacting carbons are determined by the number of the *π*-electrons involved in the thermal cyclization process. The [4n] *π*-electron system leads to conrotatory ring closure wherein the reacting carbons rotate in the same direction, while the [4n+2] system leads to disrotatory ring closure wherein the reacting carbons rotate in different directions. (Scheme 3) Woodward and Hoffmann significantly impact the world of organic chemistry and provided the theory foundation that underpins the research in this thesis.



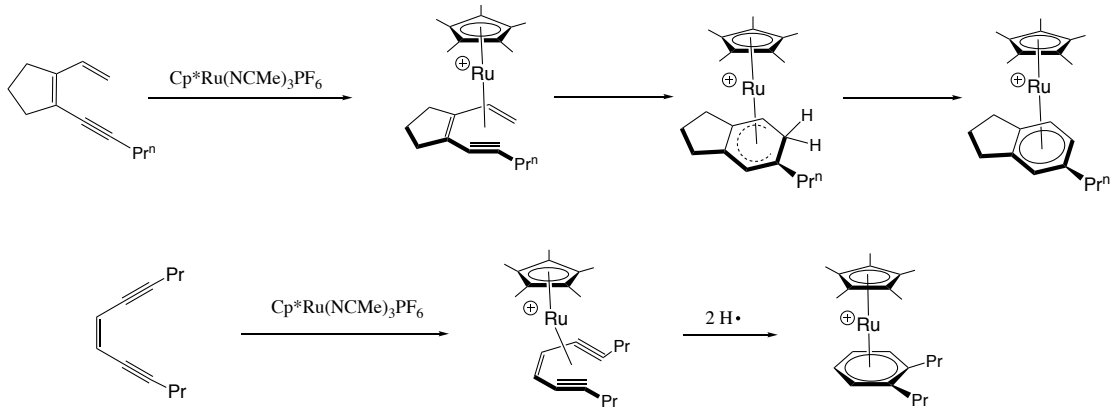
Scheme 3. Stereochemical outcomes of thermal cyclization of dienes and trienes based on the Woodward-Hoffmann rules.

Later in the 1990s, Cp*Ru$^+$ was introduced for the cyclization of (*E*)-1,3,5-hexatriene (Scheme 4). Due to its high Lewis acidity this electrophilic fragment lowers the energy barrier for C_6 ring aromatization reactions through an electron withdrawing effect. So, when hexatriene was treated with $[Cp^*Ru(OMe)]_2$ and CF_3SO_3H, the final product $[Cp^*Ru(\eta^6\text{-}C_6H_6)](CF_3SO_3)$ was obtained at ambient temperature. But they did not further examine the mechanism.[5]



Scheme 4. The cycloaromatization of (*E*)-1,3,5-hexatriene triggered by $[Cp^*Ru(OMe)]_2$/HOTf.

Cp*Ru$^+$ and CpRu$^+$ were employed to trigger cyclizations or cycloaromatizations of the conjugated dienynes[6] and enediynes[7] at ambient temperature in Professor O'Connor's lab (Scheme 5). And based on our results with dienyne and enediynes, the η_6 triene might be a key to the cycloaromatization of hexatriene mentioned above, and we further hypothesized that a disrotatory ring closure may also involve which has never been observed with 6π electrocyclization.



Scheme 5. The cycloaromatization of dienyne and enediyne triggered by $[Cp^*Ru(NCMe)_3]PF_6$ at ambient temperature.

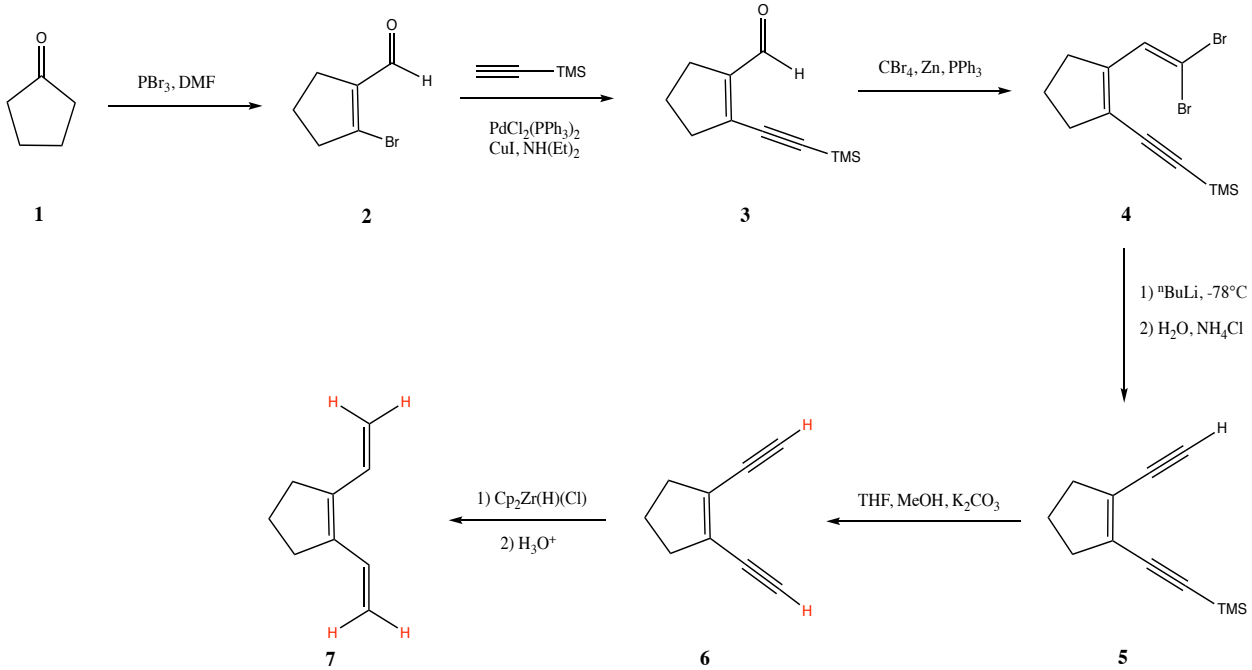
Inspired by pervious works done in Professor O'Connor's lab, and based on the Woodward-Hoffmann rules, we proposed that when conjugated trienes are treated with $CpRu(NCMe)_3PF_6$ a 6π electrocyclization and aromatization will occur rapidly at ambient temperatures.

B. Results and Discussion

1. Synthesis of Trienes

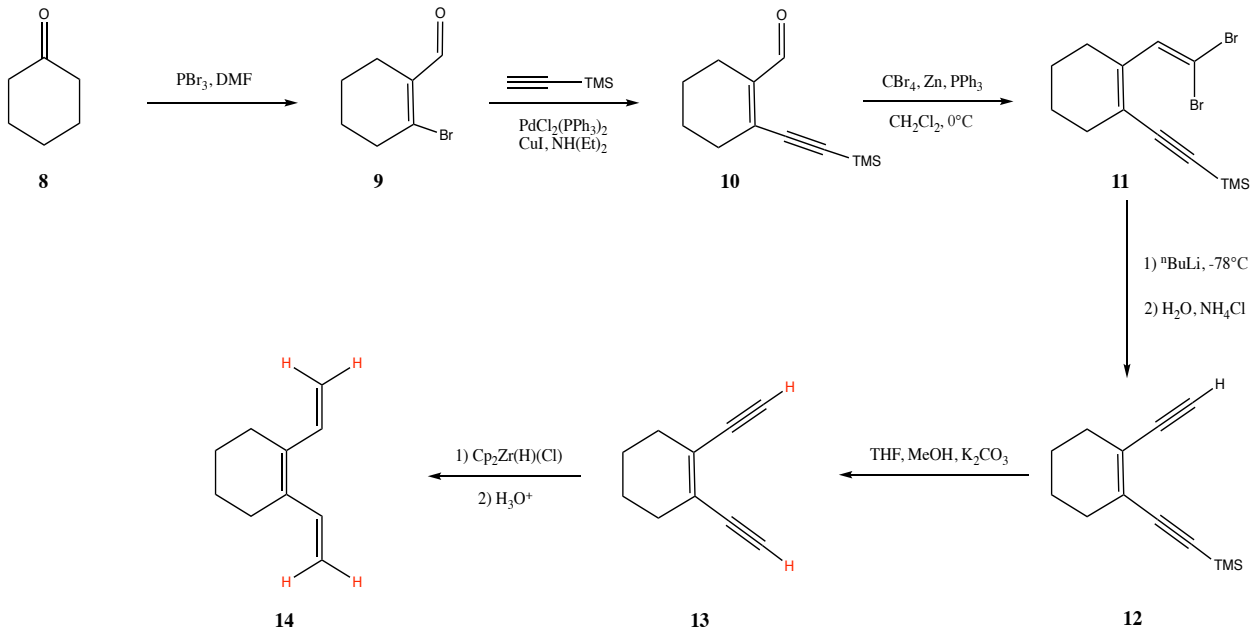
My role in the project started with the synthesis of trienes. At the beginning 1,2-divinylcyclopent-1-ene (**7)** was chosen to be the target compound based on a previous study from Dr. Cope's research in the O'Connor lab. To make **7**, we applied the route in Dr. Hitt's and Dr. Cope's theses. Cyclopentanone (**1**) was treated with PBr_3 and DMF to synthesize compound **2**. Sonogashira coupling of **2** with trimethylsilylacetylene afforded

compound **3** with excellent yield. Then another alkyne functional group was installed by Corey-Fuchs reaction, that was followed by the desilylation of compound **5** to generate enediyne **6**. Enediyne **6** was subsequently stirred in dry methylene chloride with $Cp_2Zr(H)(Cl)$ for an hour and quenched with the H_3O^+ to give **7** in 10% yield after aqueous workup and column chromatography on silica gel with hexanes (Scheme 6). Unfortunately, triene **7** is very volatile which leads to a difficult purification process. Substrate polymerization may have also contributed to our failure to isolation of triene **7.** The polymerization was observed as the generation of white solid while **7** should be clear oil, even when it was diluted by hexanes and kept at -20 ˚C, there was still white solids precipitated from the solution within a week. Therefore, we decided to prepare the six-membered ring triene 1,2-divinylcyclohex-1-ene (**14)** instead of **7** to increase the yield and purity.



Scheme 6. Synthetic route for triene **7**.

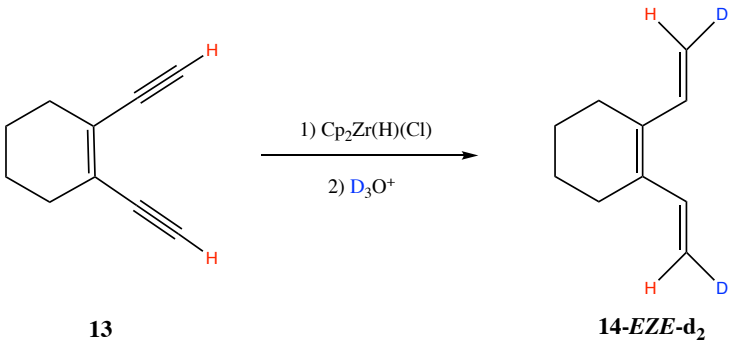
To procure the six-membered ring triene **14**, we utilized a route similar to that for the five-membered ring triene **7**. The route started with cyclohexanone (**8**), PBr_3 and DMF to afford aldehyde **9.** Compound **10** was converted from **9** through the Sonogashira coupling with trimethylsilylacetylene. Followed by the Corey-Fuchs reaction on **10** and desilylation of **12**, enediyne **13** was generated in 51% yield. Reduction of enediyne **13** with Schwartz's reagent in dry methylene chloride produced **14** with 50% yield after aqueous workup and column chromatography on silica gel with hexanes (Scheme 7).



Scheme 7. Synthetic route for triene **14**.

In order to study the stereochemistry of cyclization and aromatization process, deuterium-labeled trienes were also synthesized to carry out mechanism studies. Similar

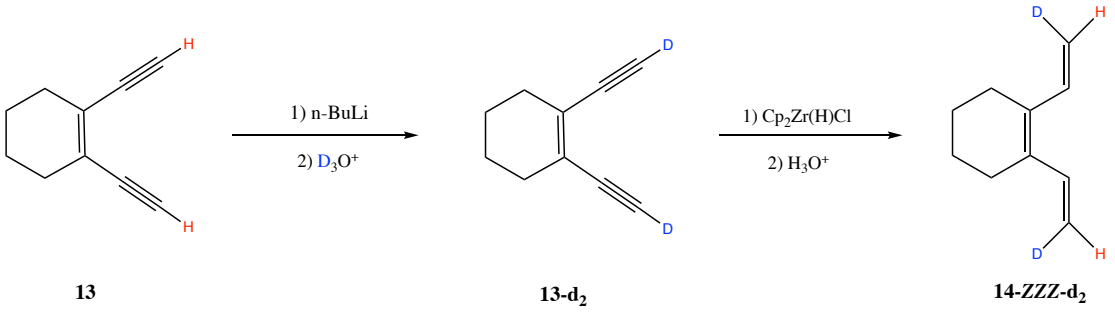
to the all-protio triene synthesis, we started from the cyclohexanone (**8**). After the same steps until the hydrozirconation the reaction was quenched with D_3O^+ to give **14-*EZE*-d_2** (> 72% deuterium enrichment) in 65% yield after column chromatography (Scheme 8).



13 **14-*EZE*-d_2**

Scheme 8. Synthetic route for deuterium-labeled triene 14-*EZE*-d_2.

To synthesize another deuterium-labeled triene isomer **14-*ZZZ*-d_2**, we followed Dr. Hitt's thesis route to obtain enediyne **13.** We deprotonated **13** with ^{n}BuLi in dry THF at -78 ˚C for an hour, and then the reaction mixture was subsequently quenched with D_3O^+ to produce deuterium-labeled enediyne **13-d_2** (> 95% deuterium enrichment) in 57% yield. The deprotonation was repeated to enhance the deuterium enrichment of **13-d_2**. After the hydrozirconation, **14-*ZZZ*-d_2** (> 92% deuterium enrichment) was obtained in 54% yield after silica gel chromatography (Scheme 9).

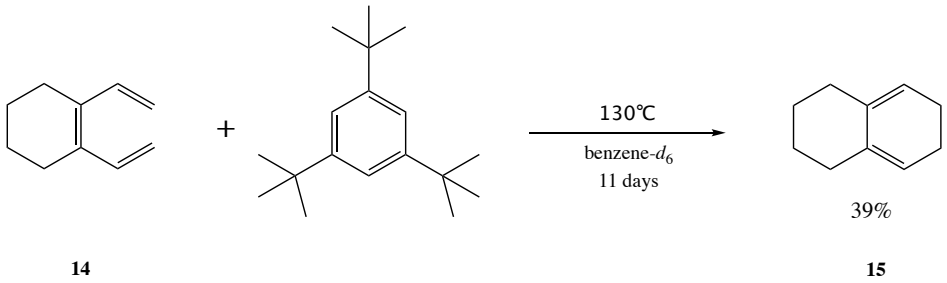


13 **13-d_2** **14-*ZZZ*-d_2**

Scheme 9. Synthetic route for deuterium-labeled triene **14-*ZZZ*-d_2**.

2. Thermal and photolysis Reactions of Trienes

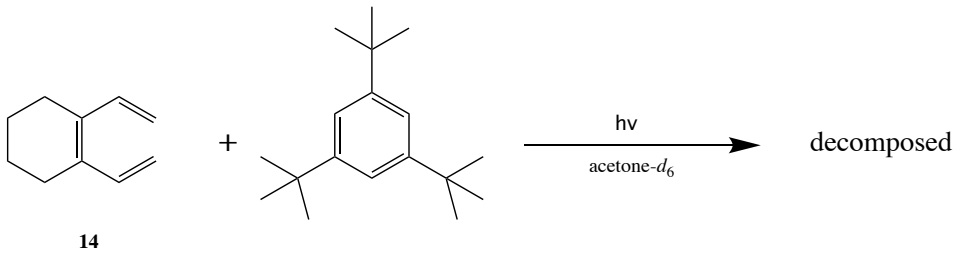
In order to compare with the cyclization triggered by the ruthenium complex, we carried out a thermal reaction to assess the thermal reactivity of triene **14**. **14** was dissolved in benzene-d_6 in a flame-sealed NMR tube, and initial NMR spectrum was recorded. Then the NMR tube was submerged into an oil bath at 130 ˚C, and the reaction was monitored by using ^{1}H NMR spectroscopy. After 11 days, all the starting triene was consumed according to the disappearance of the vinyl hydrogens resonances at δ 5.18 (d, 2H, J = 17.2 Hz) and δ 5.02 (d, 2H, J = 11.2 Hz), and the resonances of the product were also observed at δ 5.40 (m, 2H, vinyl-*H*), δ 2.25 (m, 4H, methylene-*H*), δ 2.02 (m, 4H, methylene-*H*), δ 1.62 (m, 4H, methylene-*H*). The yield (39%) of product was calculated by the integration of vinyl hydrogen resonance at δ 5.40 (d, 1H, J =15.6 Hz) related to internal standard resonance at δ 7.43 (s, 3H). (Scheme 10).



14 **15**

Scheme 10. Thermal reaction of triene **14**

A photolysis reaction of triene **14** was also carried out. A solution of **14** in acetone-d_6 was loaded into a J. Young NMR tube which was exposed to the UV light with λ centered at 254 nm in a Rayonette photoreactor. Triene **14** was observed to decompose at a slow rate under the UV light based on the decrease in the integration of the vinyl hydrogen resonance at δ 7.06 (dd, 2H, vinyl-*H*). After 8 days, all the starting materials were vanished without any evidence of formation of the desired cyclohexadiene product (Scheme 11).



14

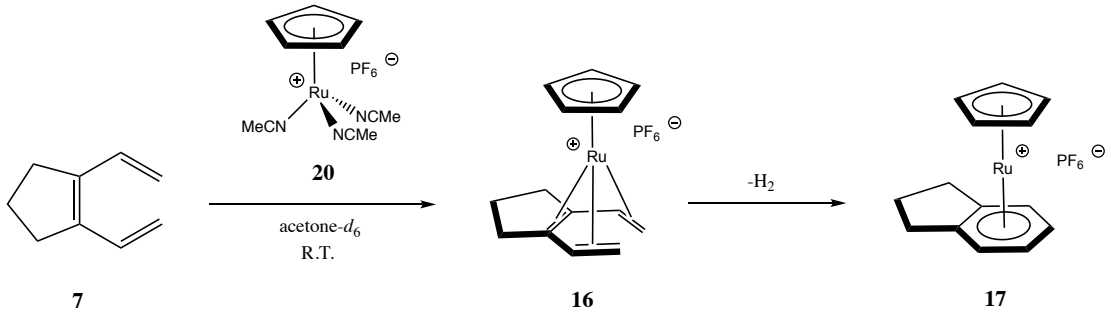
Scheme 11. Photochemical reaction of triene **14**

Based on the results above, both the thermal and the photochemical reactions did not provide satisfying results. The photolysis reaction simply leads to the decomposition of the triene. Even though the cyclized product was detected, the long reaction time and low yield make it a dubious method for further applications. Thus, research on other methods for decreasing the activation barrier is crucial.

3. Ruthenium-Catalyzed Cyclization/Cycloaromatizations of Trienes

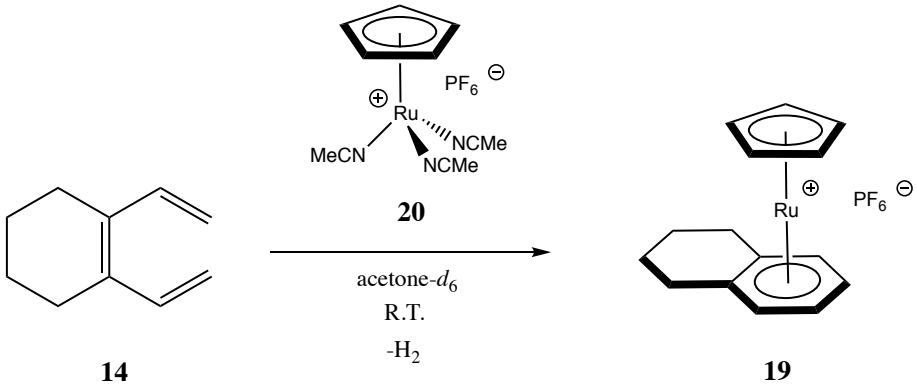
3.1. Mechanistic Study of Ruthenium-Triggered Cyclization and Aromatization of Trienes

Five-membered ring triene **7** was treated with ruthenium complex **20**. An oven-dried J. Young NMR tube containing **7**, $[CpRu(NCMe)_3]PF_6$ (**20)** and 1,3,5-tri-tert-butylbenzene as the internal standard in dry acetone-d_6 was allowed to react at ambient temperatures while monitored the progress of reaction by ^1H NMR spectroscopy. Two new Cp resonances at δ 5.45 (s, 5H) and δ 5.49 (s, 5H) were observed. After 30 minutes the Cp resonances at δ 5.45 (s, 5H) almost disappeared while the one at δ 5.49 (s, 5H) enlarged compared to the resonances of the internal standard. Which indicates that the Cp resonances at δ 5.45 (s, 5H) belongs to the intermediate **16** and the one at δ 5.49 (s, 5H) belongs to the final product **17** (Scheme 12).



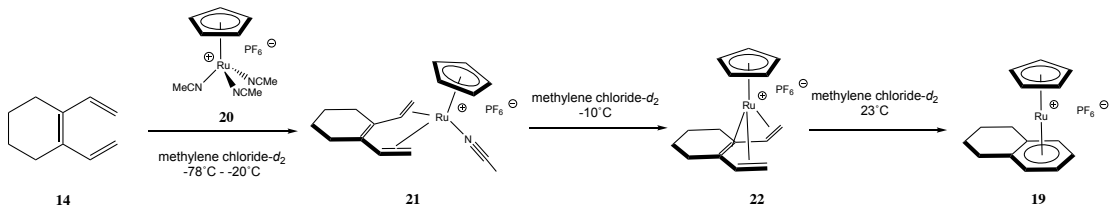
Scheme 12. Reaction of **7** with $[CpRu(NCMe)_3]PF_6$ (**20**) leading to intermediate **16** and then final product **17**.

After six-membered ring was synthesized, we duplicated the same ruthenium triggered reaction with **14**. An ambient temperature reaction of **14** and ruthenium complex **20** 1,3,5-tri-tert-butylbenzene as the internal standard dissolved in dry acetone-d_6 was set up and monitored by ^1H NMR spectroscopy. Majority of the triene was consumed within first 30 minutes, then the reaction was allowed to stand at ambient temperature for 9 more hours. The integration of Cp resonance of 19 indicates a 90.3% yield was achieved (Scheme 13).



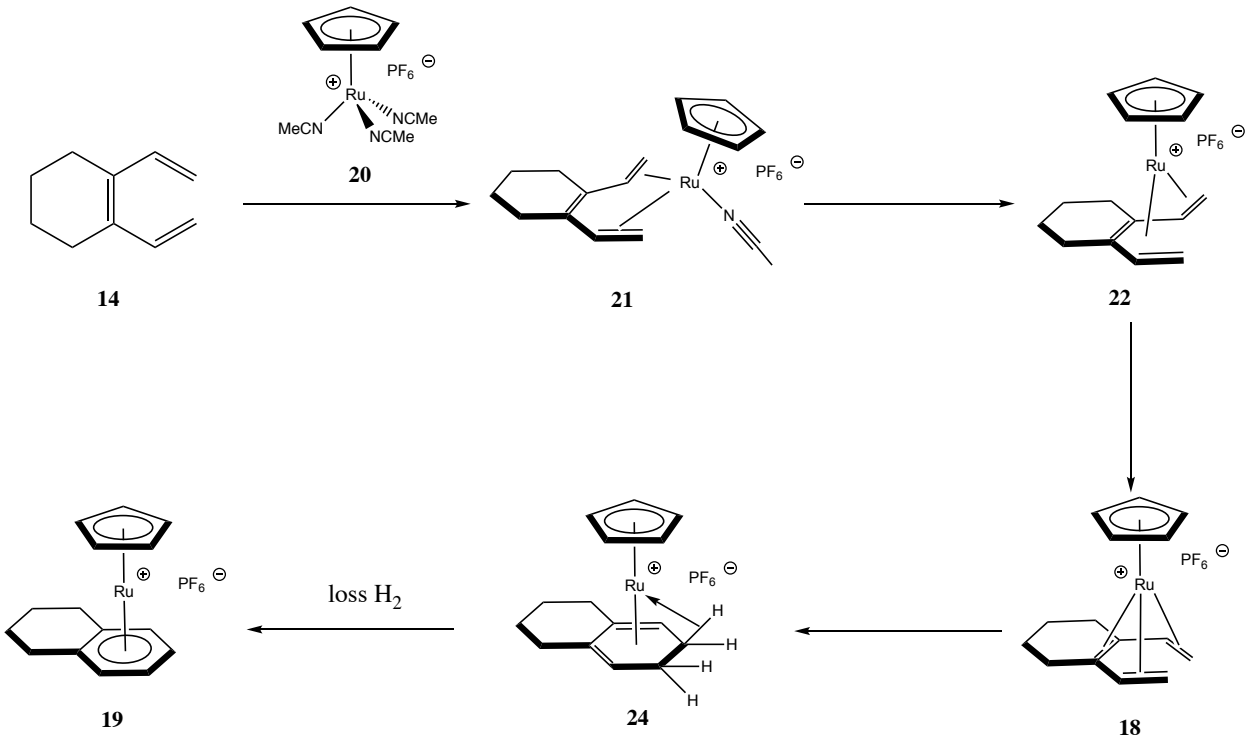
Scheme 13. Reaction of **14** with $[CpRu(NCMe)_3]PF_6$ (**20**) leading to final product **19**.

In order to discover the intermediate generated and the cycloaromatization mechanism occurred during the whole reacting process, the similar reaction was set up while reacted at lower temperature. Triene **14**, $[CpRu(NCMe)_3]PF_6$ **20**, and 1,3,5-tri-tert-butylbenzene as the internal standard were added into an oven-dried J. Young NMR tube. After dry methylene chloride-d_2 was distilled into the tube under vacuum. The J. Young tube was kept at -60 ˚C in the JEOL ECA500 NMR instrument equipped with a nitrogen-cooled Cold Probe, and an initial ^{1}H NMR spectrum was recorded immediately. Then the reaction mixture was monitored by ^{1}H NMR spectroscopy while temperature was slowly increasing. After 20 minutes, the resonances of intermediate **21** at *δ* 1.31 (m, 2H, methylene-*H*), 1.70 (m, 2H, methylene-*H*), 1.88 (m, 2H, methylene-*H*), 2.08 (m, 1H, methylene-*H*), 2.19 (m, 1H, methylene-*H*), 2.35 (s, 3H, NC*Me*), 2.75 (d, 1H, *J* = 11.5 Hz, vinyl-*H*), 3.36 (d, 1H, *J* = 13 Hz, vinyl-*H*), 3.99 (d, 1H, *J* = 9.0 Hz, vinyl-*H*), 4.12 (dd, 1H, J_1 = 8.5 Hz, J_2 = 13 Hz, vinyl-*H*), 4.15 (d, 1H, *J* = 8.5 Hz, vinyl-*H*), 4.28 (dd, 1H, J_1 = 9.0 Hz, J_2 = 11.5 Hz, vinyl-*H*), 5.12 (s, 5H, Cp) were observed at -20 ˚C. Then the reaction was warmed up to -10 ˚C. After 120 minutes, the resonances of the asymmetric intermediate **22** at *δ* 2.44 (d, 1H, *J* = 17.5 Hz, vinyl-*H*), 2.505 (d, 1H, *J* = 10 Hz, vinyl-*H*), 2.513 (d, 1H, *J* = 10.5 Hz, vinyl-*H*), 3.03 (dd, 1H, J_1 = 10 Hz, J_2 = 17.5 Hz, vinyl-*H*), 3.54 (dd, 1H, J_1 = 7 Hz, J_2 = 10.5 Hz, vinyl-*H*), 4.77 (d, 1H, *J* = 7 Hz, vinyl-*H*), 5.33 (s, 5H, Cp) were observed. Then the reacting mixture was warmed up and allowed to stand at ambient temperature for 12 hours. Then all the resonances of compound **21** and **22** were vanished, only compound **19** could be observed while gave the yield of **19** 90.3% (Scheme 14).



Scheme 14. Reaction of **14** with $[CpRu(NCMe)_3]PF_6$ (**20**) leading to intermediates **21**, **22** and then final product **19**.

Accordingly, we proposed the mechanism of the cyclization and aromatization of all-protio triene mediated by ruthenium complex **20** (Scheme 15). Firstly, a ligand change reaction occurred, two double bonds of the triene was bind to the ruthenium to form the η^4 intermediate **21**, then the rest double bond was coordinated to the ruthenium while all the acetonitrile ligands were unloaded to form the η^6 intermediate **22**. Then we hypothesized that 22 may isomerize into η^6 intermediate **18,** a 6π electrocyclization of **18** leads to cyclohexadiene intermediate **24**, that is followed by loss of H_2 to generate the final arene product **19**.



Scheme 15. Mechanism proposed for the reaction of **14** with $[CpRu(NCMe)_3]PF_6$ **20**.

Based on the results above, isolation of intermediates **21** and **22** were desired to conform the cycloaromatization mechanism proposed. We decided to attempt the crystallization method to isolate these two intermediates and the crystal structures would be a helpful indication of the mechanism study.

For crystallization of intermediate **21**, **14** (74.2 mg, 0.55 mmol) and **20** (200 mg, 0.46 mmol) were added into an oven-dried 100 mL Schlenk flask. The flask was cooled in a dry ice-acetone bath and placed under vacuum. After 20 mL of dry methylene chloride was distilled into the flask under vacuum. The Schlenk flask was kept at - 25 ˚C to react for 5 hours, followed by distillation of 50 mL dry hexane. Then the whole system was kept at - 78 ˚C for two weeks, while some solids precipitated from the solution were observed.

After the mixture was poured out from the Schlenk flask, only the crystals for intermediate **22** was observed while also in poor quality analyzed by X-ray crystallography (Figure 1). After that we tried several more times of crystallization of **21** but all failed. The reason of the vanishment of **21** might be once the crystal was exposed into the air, the η^4 intermediate will trasfer into η^6 rapidly, which is extremely active at ambiemt temperature.

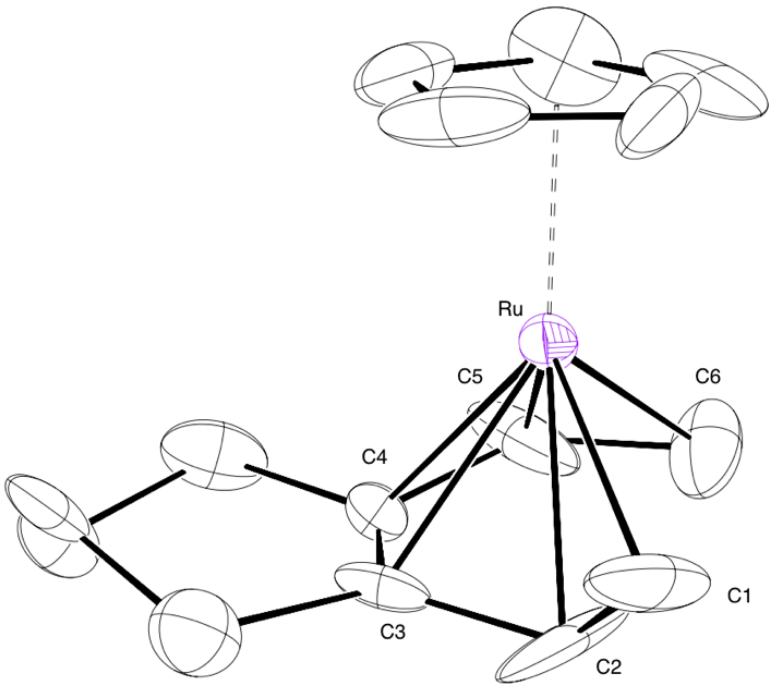


Figure 1. X-ray structure for intermediate **22**.

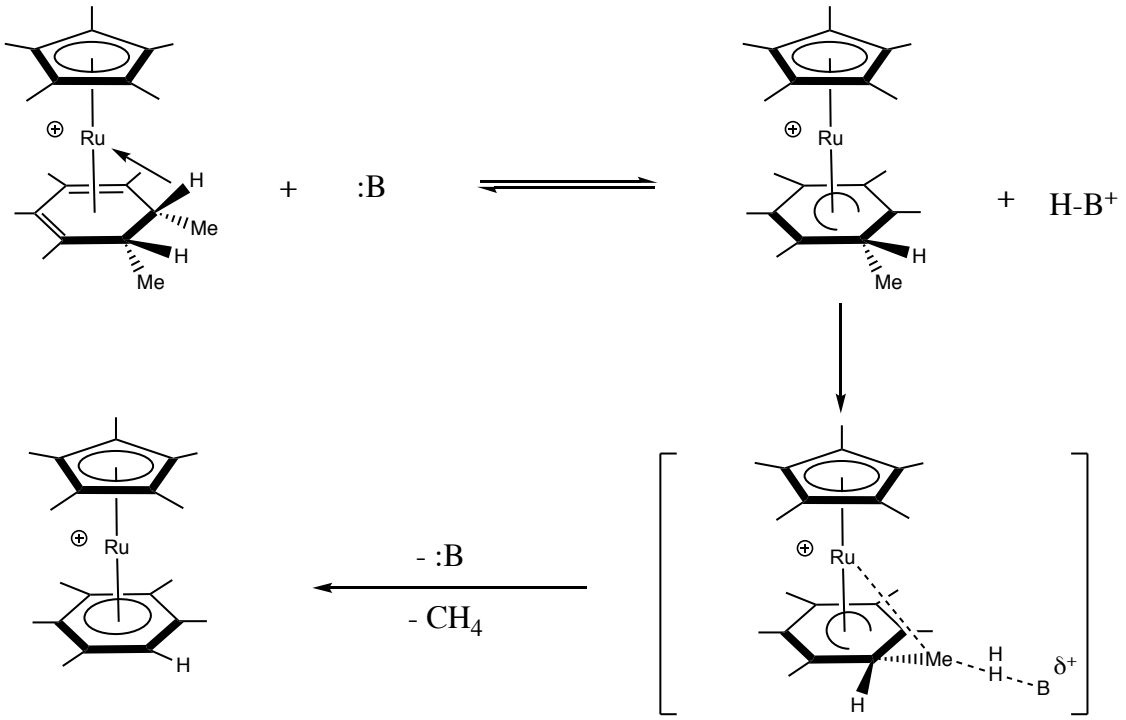
Table 1. Selected Bond Distances (Å) for intermediate **22**

Bond (A-B)	Length (Å)	Bond (A-B)	Length (Å)
Ru-C1	2.338	C1-C2	1.452
Ru-C2	2.173	C2-C3	1.410
Ru-C3	2.157	C3-C4	1.390
Ru-C4	2.282	C4-C5	1.464
Ru-C5	2.162	C5-C6	1.508
Ru-C6	2.207	C1-C6	3.331

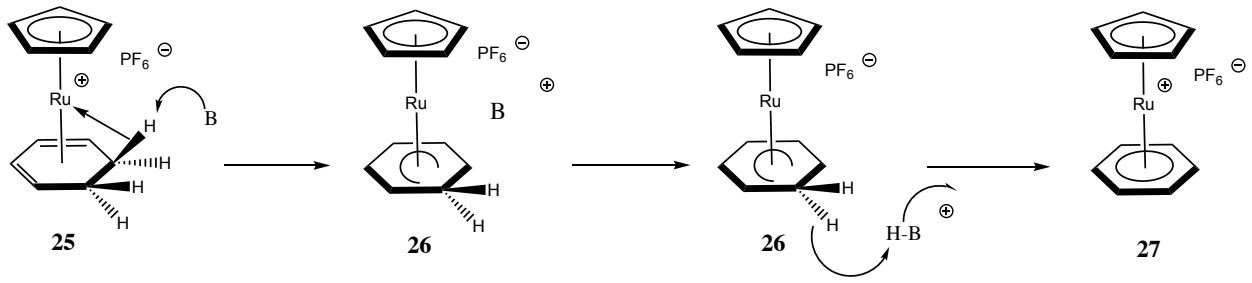
Encouraged by the result above, crystallization of η^6 intermediate **22** seems to be accessible. For better quality crystal of intermediate **22**, an oven-dried J. Young NMR tube with triene **14** and ruthenium complex **20** inside was placed under vacuum while kept at - 78 ˚C, after dry methylene chloride was distilled into, the tube was warmed up to - 15 ˚C to - 12 ˚C in a dry ice 2-propanol bath and the mixture was allowed to react for 5 hours. Then dry hexane was distilled into, the tube was kept at - 20 ˚C to induce crystallization of **22**. Unfortunately, no qualified crystals were detected by X-ray crystallography. We endeavored the crystallization for several more times, trying to obtain better qualified crystals by increasing the reaction time or changing the solvents added during the crystallization, but all failed.

3.2. Ruthenium-Triggered Cyclization and Aromatization of Deuterium labeled Trienes

In summary, ruthenium complex **20** was demonstrated to successfully accelerate the cycloaromatization process of conjugated trienes at ambient temperature within a few hours. However, the detailed mechanism of loss of hydrogen is still unclear, and a mechanical study is needed to unveil the mystery. According to Stryker's research[8], they proposed that the first deprotonation of the ruthenium-hydride complex was achieved by the base added to form a cyclohexadienyl ligand (Scheme 16). Then the *exo*-Me would be detached by liberated Bronsted acid via the ruthenium-assisted C-C cleavage to form the final arene product. The mechanism proposed for cycloaromatization of 25 is based on the mechanism from Stryker (Scheme 17). In order to explore the 6 π cyclization process in which a disrotatory mode is involved, deuterium enriched trienes need to be employed as the substrates to clarify the stereochemistry.



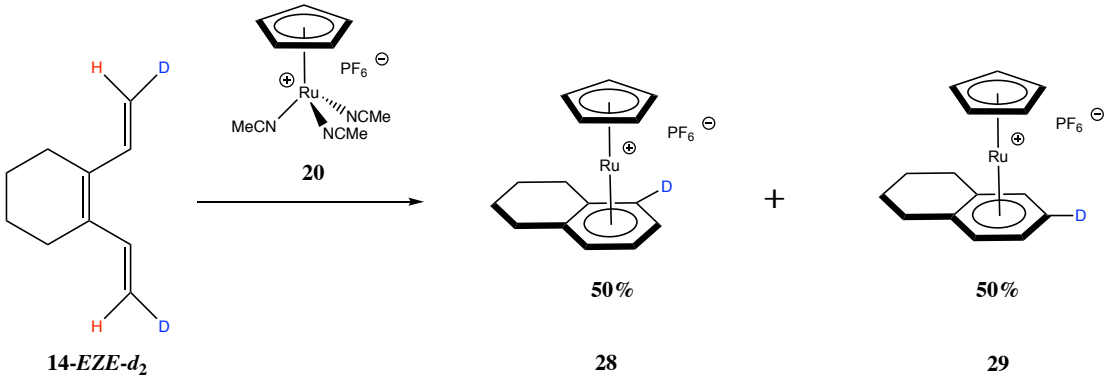
Scheme 16. Mechanism proposed by Stryker.



Scheme 17. Mechanism proposed by Stryker for aromatization of **25**.

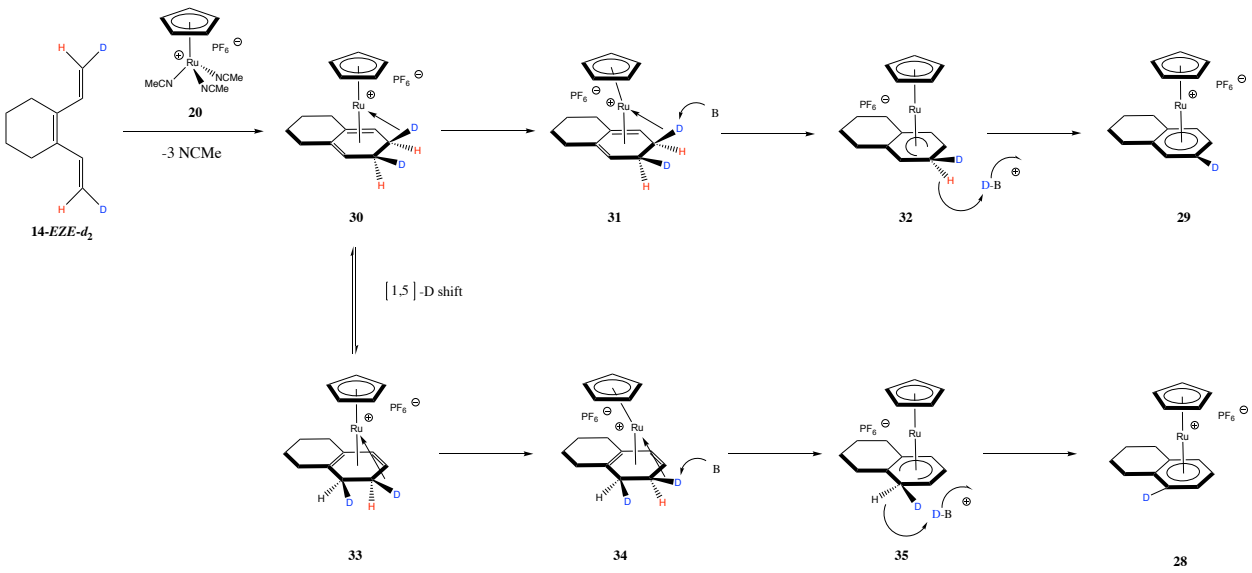
14-*EZE*-d_2 (0.083 M) was treated with ruthenium complex **20** (0.03 M) dissolved in dry methylene chloride-d_2 in an over-dried J. Young NMR tube. After reacting at ambient temperature overnight, methylene chloride-d_2 was pumped out under vacuum and dry acetone-d_6 was distilled in to the J. Young NMR tube. The formation of arene

compound **28** and **29** was observed by ^{1}H NMR spectroscopy, ^{2}H NMR spectroscopy and mass spectrometry. While the ratio of **28** and **29** was detected as 1: 1 as the integrations of two arene hydrogens' resonances at *δ* 6.18 (d, 1.5H, arene-*H*), 6.26 (d, 1.5H, arene-*H*) related to the resonance of Cp at *δ* 5.48 (s, 5H, Cp) is 1.5: 1.5: 5. The mass spectrum showed deuterium enrichment for final product is D1 70%, D0 30%. (Scheme 17)



Scheme 18. Reaction of **14-*EZE*-d_2** with [CpRu(NCMe)$_3$]PF$_6$ (**20**).

After the disrotatory 6*π* electrocyclization, a rapid [1,5] deuterium shift occurred, and thus an equilibrium can be established between intermediates **30** and **33**. The subsequent deprotonations of deuteriums that are *endo* to metal center in **30** and **33** by trace amount of base in the solution can generate intermediates **32** and **35**, respectively. The hydrogens that are *exo* to ruthenium leave as hydride to produce the ruthenium arene products **28** and **29** (Scheme 18).

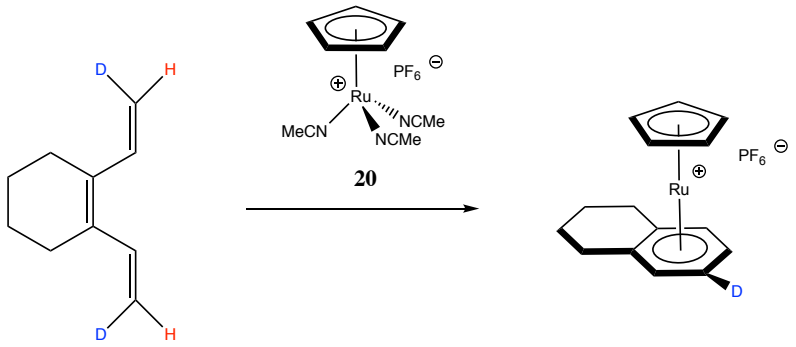


Scheme 19. Mechanism proposed for reaction of **14-*EZE*-d_2** with $[CpRu(NCMe)_3]PF_6$ (**20**).

In the Ruthenium triggered cycloaromatization of **14-*ZZZ*-d_2** we found that the concentration of the reactants will cause different final products or different ratios of the final products.

14-*ZZZ*-d_2 (0.010 M) was treated with ruthenium complex **20** (0.005 M) dissolved in dry methylene chloride-d_2 in an over-dried J. Young NMR tube. After reacting at ambient temperature overnight, methylene chloride-d_2 was pumped out under vacuum and dry acetone-d_6 was distilled in to the J. Young NMR tube. The resonances of arene compound **29** was observed by ^{1}H NMR spectroscopy at δ 1.79 (m, 2H, methylene-*H*), 1.85 (m, 2H, methylene-*H*), 2.69 (m, 2H, methylene-*H*), 2.83 (m, 2H, methylene-*H*), 5.26 (s, 5H, Cp), 5.99 (m, 1H, arene-*H*), 6.02 (m, 2H, arene-*H*), by ^{2}H NMR spectroscopy at δ

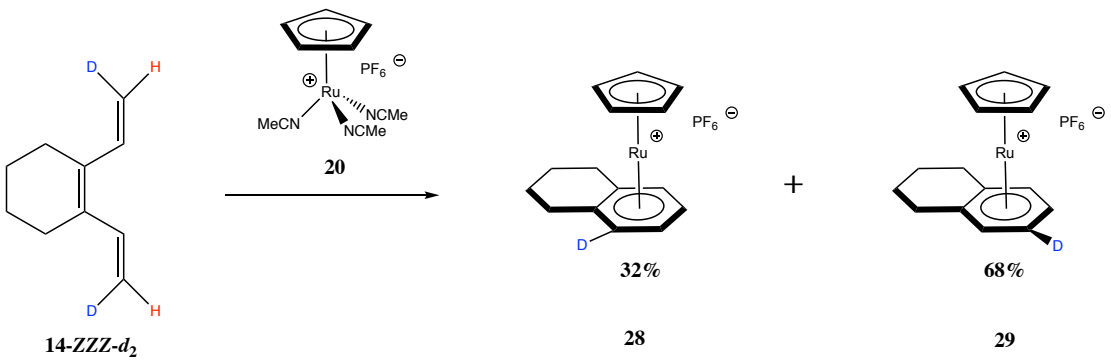
6.21 (s, 1D) and deuterium enrichment of final product **29** is measured by mass spectroscopy as D1 74%, D0 26% (Scheme 19).



14-*ZZZ*-d_2 **29**

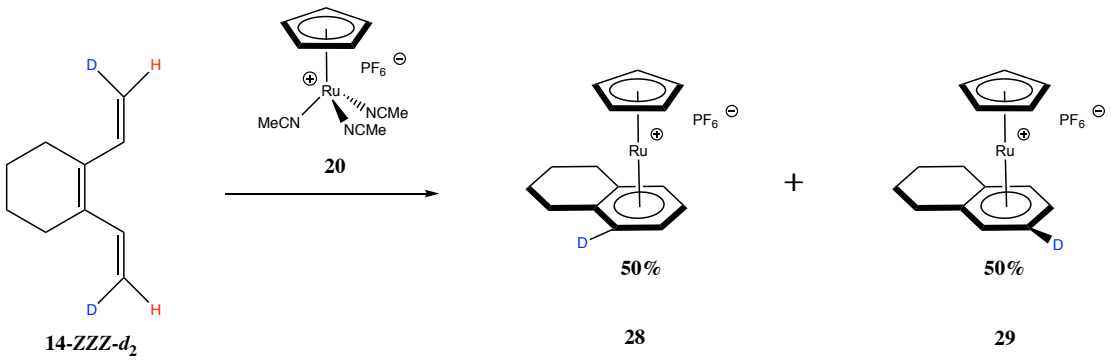
Scheme 20. Reaction of **14-*ZZZ*-d_2** (0.010 M) with [CpRu(NCMe)$_3$]PF$_6$ (**20**) (0.005 M).

14-*ZZZ*-d_2 (0.025 M) was treated with ruthenium complex **20** (0.013 M) dissolved in dry methylene chloride-d_2 in an over-dried J. Young NMR tube. After reacting at ambient temperature overnight, methylene chloride-d_2 was pumped out under vacuum and dry acetone-d_6 was distilled in to the J. Young NMR tube. The resonances of arene compound **28** and **29** was observed by ^{1}H NMR spectroscopy at δ 1.85 (m, 4H, methylene-*H*), 2.86 (m, 4H, methylene-*H*), 5.49 (s, 5H, Cp), 6.19 (m, 1H, arene-*H*), 6.27 (m, 2H, arene-*H*). The resonances observed by ^{2}H NMR spectroscopy at δ 6.17 (s, 1D), 6.25 (s, 1D), (Scheme 20) while the ratio of **28** and **29** was detected as nearly 32: 68.



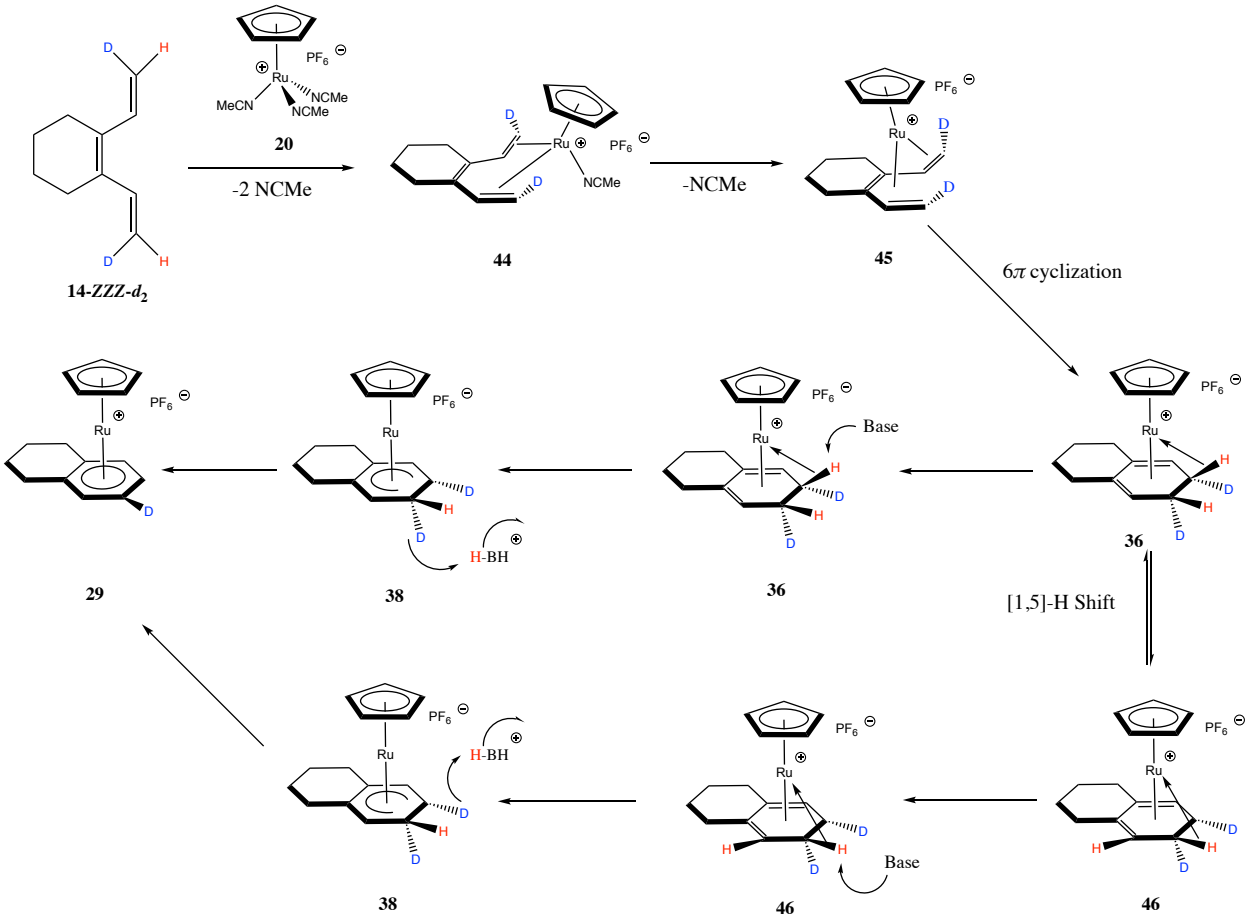
Scheme 21. Reaction of **14-ZZZ-d$_2$** (0.025 M) with [CpRu(NCMe)$_3$]PF$_6$ (**20**) (0.013 M).

14-*ZZZ*-d_2 (0.075 M) was treated with ruthenium complex **20** (0.038 M) dissolved in dry methylene chloride-d_2 in an over-dried J. Young NMR tube. After reacting at ambient temperature overnight, methylene chloride-d_2 was pumped out under vacuum and dry acetone-d_6 was distilled in to the J. Young NMR tube. The formation of arene compound **28** and **29** was observed by ^{1}H NMR spectroscopy at δ 1.85 (m, 4H, methylene-*H*), 2.85 (m, 4H, methylene-*H*), 5.48 (s, 5H, Cp), 6.18 (m, 1.5H, arene-*H*), 6.26 (m, 1.5H, arene-*H*), and observed by ^{2}H NMR spectroscopy at δ 6.20 (s, 1D), 6.28 (s, 1D), while the ratio of **28** and **29** was detected as 1: 1 (Scheme 21).

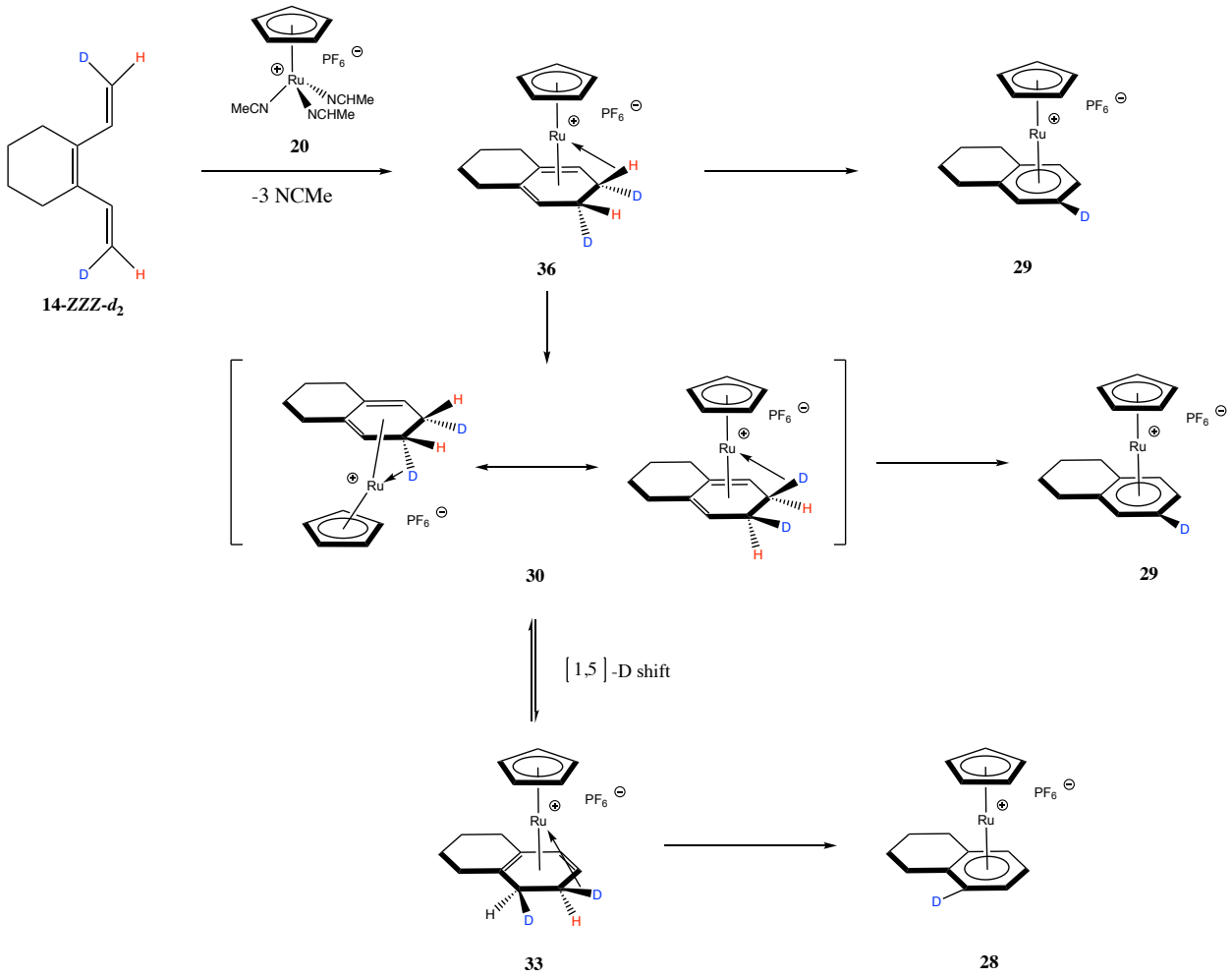


Scheme 22. Reaction of **14-*ZZZ*-d_2** (0.075 M) with [CpRu(NCMe)$_3$]PF$_6$ (**20**) (0.038 M).

When the concertation of acetonitrile in the reaction mixture was relatively low, a trace amount base in the solution will take off the ring hydrogen that is *syn* to the metal center upon the cyclization of the triene (Scheme 22), whereas the other *regio* isomer **33** will be generated in the presence of higher concentration of acetonitrile that triggers the dissociation of ruthenium from the cyclohexadiene followed by recoordination to the opposite site (Scheme 23).



Scheme 23. Mechanism proposed for reaction of **14-*ZZZ*-d_2** with [CpRu(NCMe)$_3$]PF$_6$ (**20**) when the concentration of acetonitrile is lower.



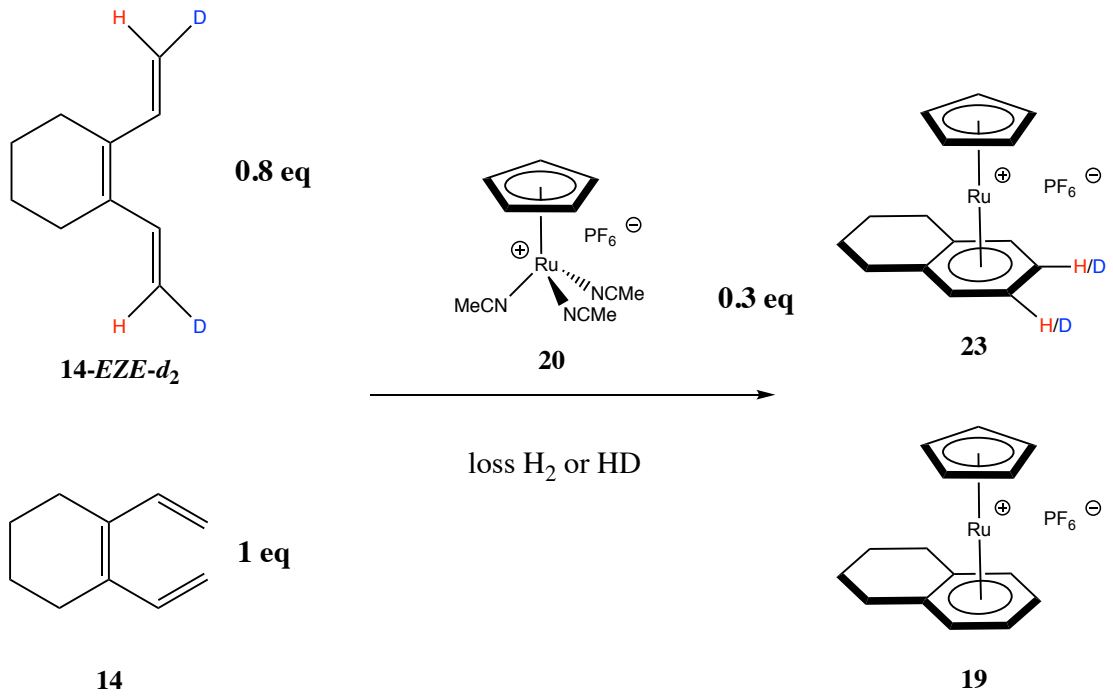
Scheme 24. Mechanism proposed for reaction of **14-*ZZZ*-d_2** with [CpRu(NCMe)$_3$]PF$_6$ (**20**) when the concentration of acetonitrile is higher.

Basically, the ruthenium-mediated disrotatory cyclization process of trienes was demonstrated by the deuterium labelling studies with the consistency of Stryker's mechanism. For the future direction, the low concentration of ruthenium complex 20

reactions with 14-*EZE*-d_2 are needed to carry out and the effects of acetonitrile concentration on the mechanism of cycloaromatization process should be explored.

3.3. Kinetic Isotopic effect study of Ruthenium-Triggered Cyclization and Aromatization of Trienes

To determine whether there is kinetic isotopic effect appeared during the ruthenium trigged cyclization and aromatization process, we set up a competition reaction between triene **14** and deuterated triene **14-*EZE*-d_2**. triene **14** (1 eq.) and triene **14-*EZE*-d_2** (0.8 eq.) and 1,3,5-tri-*tert*-butylbenzene as internal standard were adder into an oven dried J.Young NMR tube. The NMR tube was frozen in a dry ice-acetone bath and placed under vacuum, 0.5 mL dry acetone-d_6 was distilled into the tube. A ^{1}H NMR spectrum for these two trienes was recorded. Then $CpRu(NCMe)_3PF_6$ (0.3 eq.) was added into the tube inside a glovebox. The reaction mixture was monitored by ^{1}H NMR spectroscopy at ambient temperature. In the ^{1}H NMR spectrum for two trienes, the ratio of the integrations of the resonance of triene **14** at δ 5.05 and the resonance of triene **14** and **14-*EZE*-d_2** at δ 5.23 is 1.46: 1. The tube was allowed to stand in ambient temperature overnight. In the final ^{1}H NMR spectrum, the ratio of those two resonances is 1.45: 1, which is approximately same to the one from the two trienes spectrum. Accordingly, there is no kinetic isotopic effect occurred. Hence the binding step of trienes and ruthenium complex is not the rate determine step of the whole process (Scheme 24).



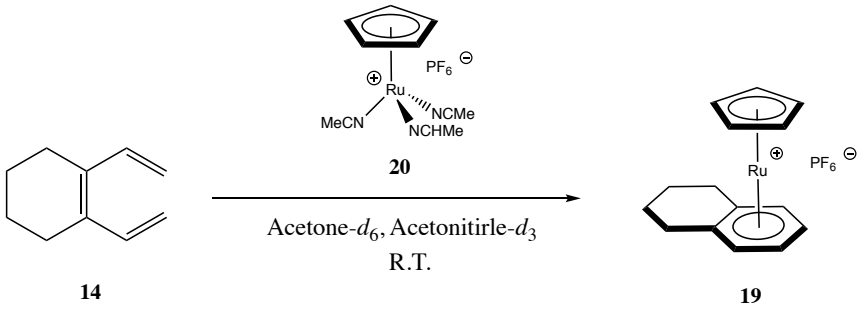
Scheme 25. Competition reaction of **14** and **14-*ZZZ*-d_2** with ruthenium complex (**20**) leading to final products **19** and **23**.

3.4. Kinetic studies of Ruthenium-Triggered Cyclization and Aromatization of Terminal Triene and Dimethyl trienes. (Cooperate with Li-An Wang and Jiyue Chen)

To compare the reacting rate of ruthenium mediated cycloaromatization, the kinetic studies are required. Due to the time scale of NMR spectroscopy, extra acetonitrile was added to slow down the reaction.

Frist of all, the amount of acetonitrile to add need to be determined. 1041, 741 and 678 times amount of acetonitrile-d_3 to the concentration of ruthenium complex **20** were added into the J. Young NMR tubes contain triene **14** and ruthenium complex **20** with 1,3,5-tri-tert-butylbenzene added as an internal standard (Scheme 25). After dry acetone-

d_6 was distilled into the tube under vacuum, the reactions were warmed to ambient temperature and monitored by ^{1}H NMR spectroscopy. According triene **14** consuming time and graph of the experimental results, 678 times amount of acetonitrile-d_3 were chosen to be the standard of the series of kinetic studies reactions.



Scheme 26. Relative race study of triene **14**.

When triene **14** was treated with ruthenium complex **20** and 678 times amount of acetonitrile-d_3, the k was measured as 0.0569 s^{-1} while the half-life of the **14** was 0.0034 hour (Figure 2).

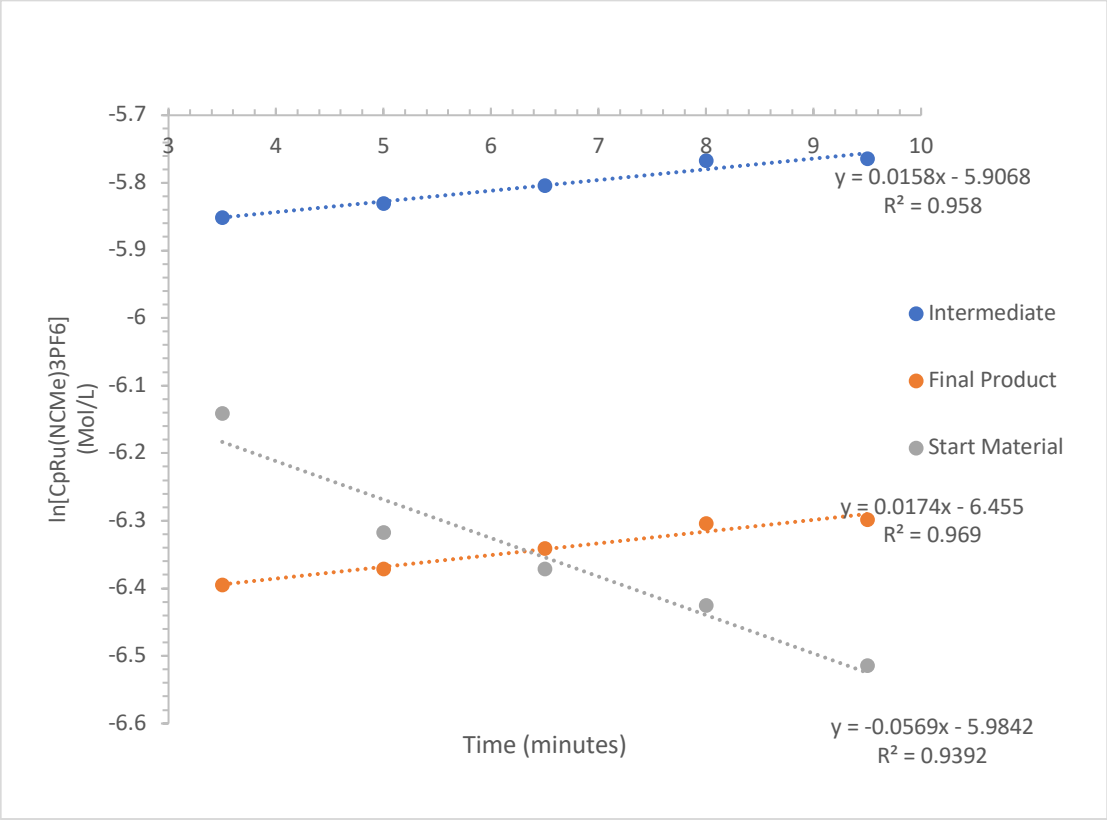
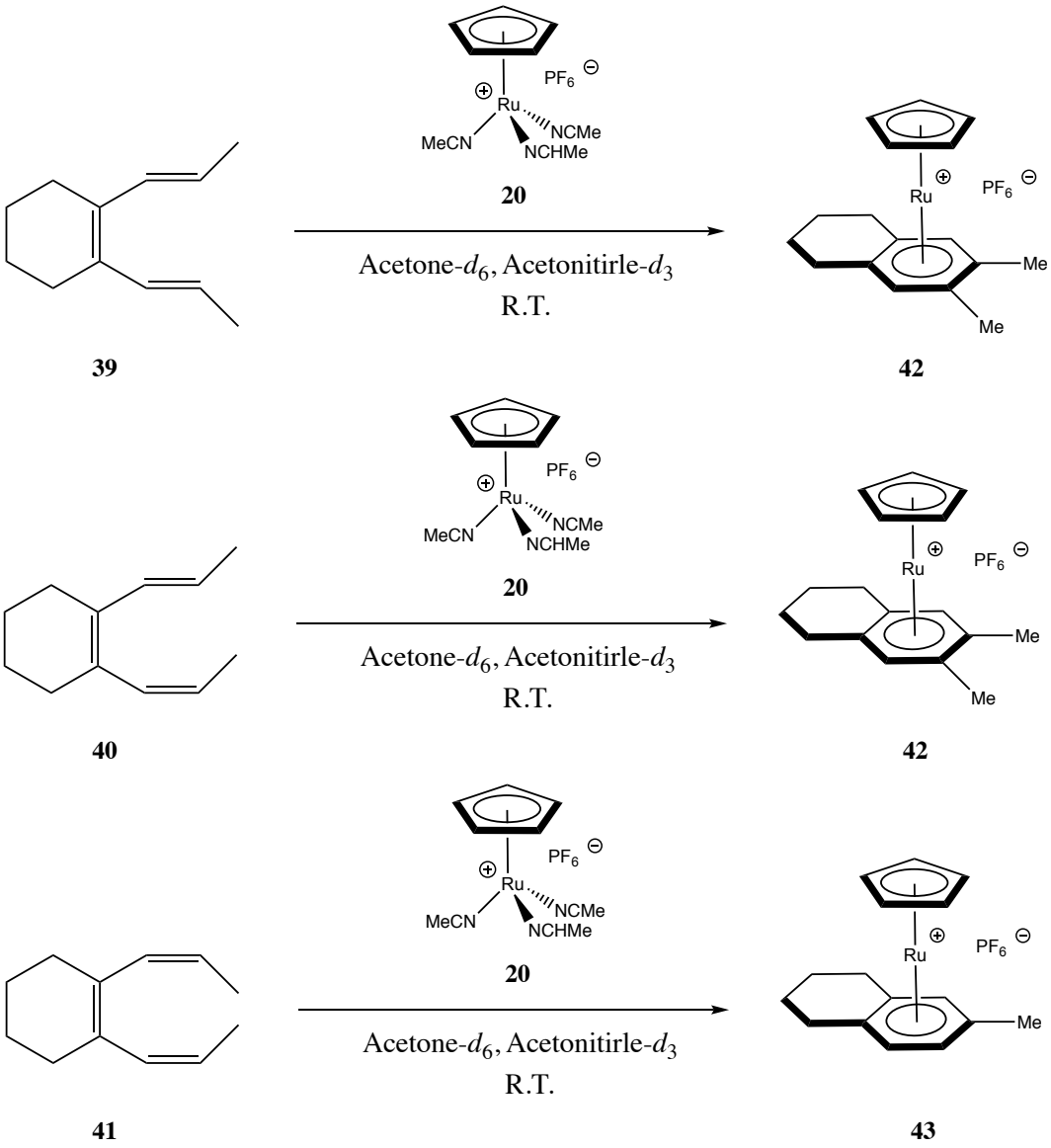


Figure 2. Natural logarithm concentration change of $CpRu(NCMe)_3PF_6$, intermediate and final product with time when **14** was employed as substrate.

Then three dimethyl trienes **39**, **40** and **41** which were synthesized by Li-An was treated with ruthenium complex 20 and 678 times amount of acetonitrile-d_3. After dry acetone-d_6 was distilled into the tube under vacuum, the reactions were warmed to ambient temperature and monitored by ^{1}H NMR spectroscopy (Scheme 26).



Scheme 27. Relative race study of dimethyl trienes **39**, **40** and **41**.

When dimethyl trienes **39**, **40** and **41** were treated with ruthenium complex **20** and 678 times amount of acetonitrile-d_3, The result shows: *EZ* triene **40** (k = 0.00012 s^{-1}, $t_{1/2}$ = 1.60 h); *ZZ* triene **41** (k = 0.0002 s^{-1}, $t_{1/2}$ = 0.875 h); *EE* triene **39** (k = 0.00030 s^{-1}, $t_{1/2}$ =

0.642 h) (Figure 3, 4, 5). The data showed that the reaction of *EZ* triene **40** was the slowest one, which might be attributed to the different stabilities of intermediates. The dimethyl trienes were synthesized by Li-An Wang, and the study of 41 was conducted by Jiyue.

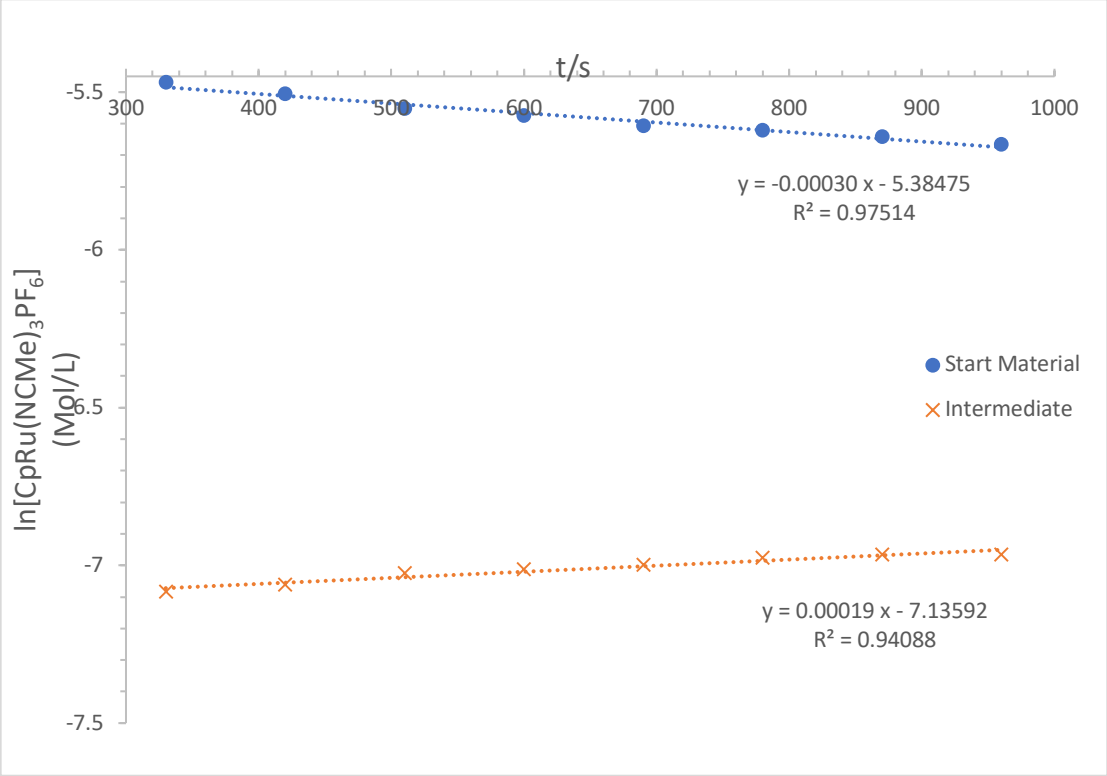


Figure 3. Natural logarithm concentration change of ruthenium complex **20** and intermediate with time when **39** was employed as substrate.

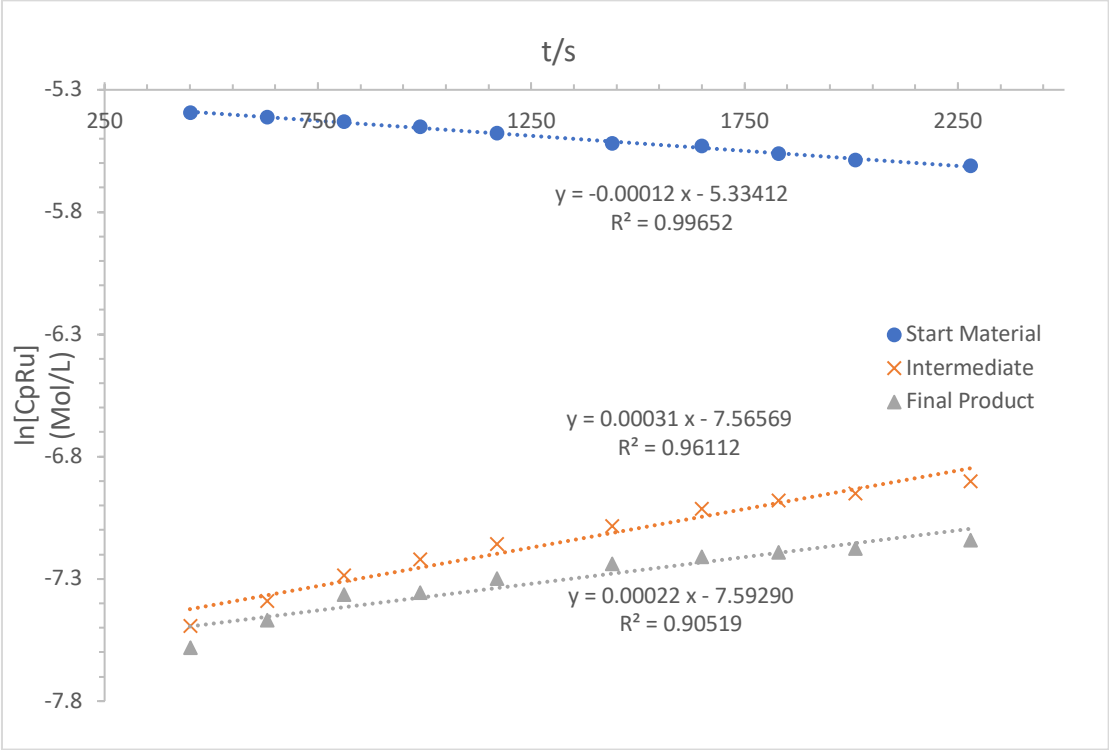


Figure 4. Natural logarithm concentration change of ruthenium complex **20** and intermediate with time when **40** was employed as substrate.

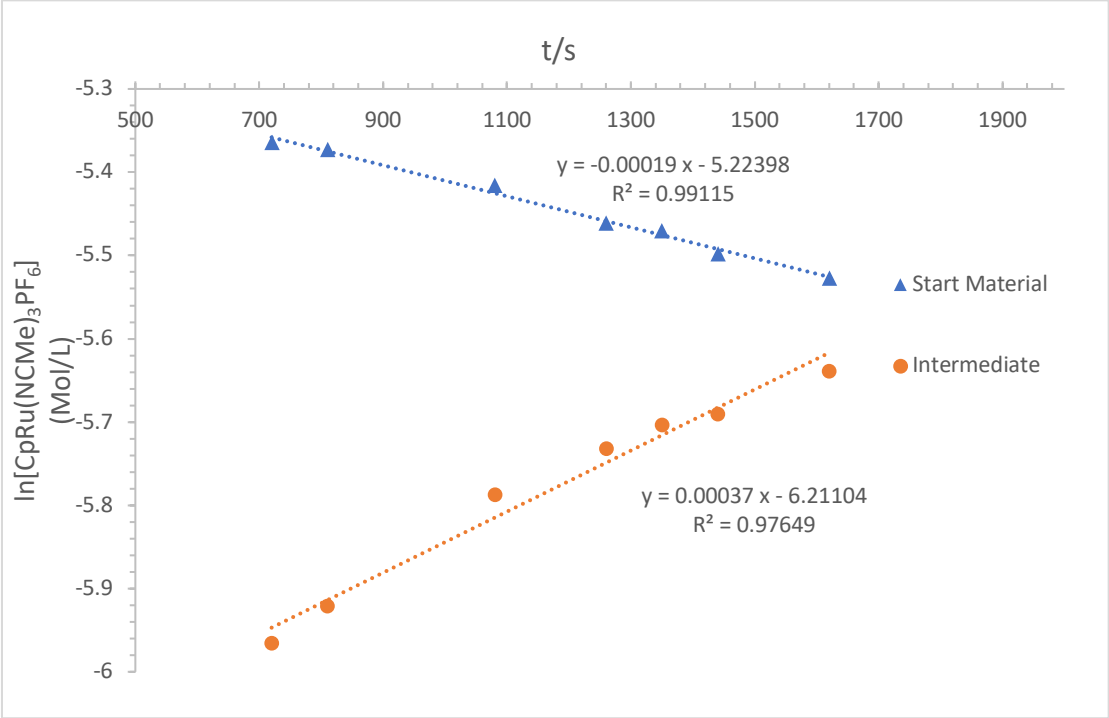


Figure 5. Natural logarithm concentration change of ruthenium complex **20** and intermediate with time when **41** was employed as substrate.

C. Conclusions

To sum up, the former ways of trienes cyclization like the thermal and photochemical only provided unsatisfied results due to the long time taken and the low yield occurred. Instead, $[CpRu(NCMe)_3]PF_6$ (**20**) carried out the 6π electrocyclizations when trienes served as substrates in a very effective and efficient way. The cyclization and cycloaromatization were achieved at ambient temperature within shorter time period. The trienes and deuterium labeled trienes substrates were synthesized and several intermediates were observed by ^{1}H NMR spectroscopy and X-ray crystallography to

explore the mechanism of the ruthenium mediated reactions. The deuterium labeled intermediates indicate the reacting carbons were rotating in a disrotatory fashion during the ring closure process which supports that the ruthenium triggered cycloaromatization follows the 6π electrocyclization fashion.

In the future, the crystallization of intermediates η^4-cyclohexadiene and η^6-cyclohexadiene might still need to be attempted to further support our proposal. Meanwhile, more substrates with different functional groups can be treated with the ruthenium complex to examine the steric and electronic effects on the cyclization process and to explore the extent of this annulation reaction.

D. Experimental Section

1. General Information:

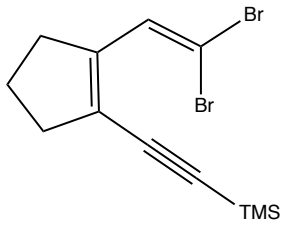
All organometallic reagents were manipulated under an inert gas atmosphere, using standard Schlenk techniques or a nitrogen-filled glove box. Solvents were dried by passage through an alumina column. Chloroform-*d* was refluxed over CaH_2 for two days and then freeze-pump-thaw-degassed prior to use. Benzene-d_6 was dried over sodium/benzophenone ketyl and distilled prior to use. Acetone-d_6 was dried over activated molecular sieves for 2 h before distillation into a dry Schlenk flask. Dichloromethane-d_2 was dried over activated molecular sieves for 12 h prior to use. NMR-tube-scale reactions were performed in J. Young NMR tubes equipped with a Teflon needle-valve adapter. Flash column chromatographic purifications were conducted using silica gel. ^1H and $^{13}C\{^1H\}$ NMR spectra were recorded on Varian Mercury 400 (^1H, 400

MHz; ^{13}C, 100.7 MHz), Varian VX500 (^{1}H, 500 MHz; ^{13}C, 126 MHz) or JEOL ECA500 (^{1}H, 500 MHz; ^{13}C, 126 MHz) spectrometers. ^{1}H and $^{13}C\{^{1}H\}$ NMR chemical shifts (δ) are reported relative to residual proton or carbon chemical shifts for the solvent. IR spectra were recorded on a Thermo-Nicolet iS10 FTIR spectrometer. Mass spectral analyses were performed by Chemistry and Biochemistry Molecular Spectrometry Facility at UC San Diego. Crystallography data were collected by Mo-Kα radiation (λ = 0.71073 Å) or Cu-Kα radiation (λ = 1.54178 Å) at the UC San Diego Crystallography laboratory.

2. Synthesis and Characterization Data

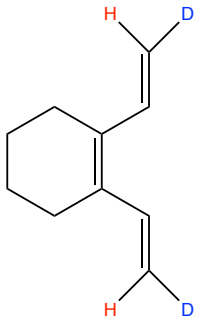
((2-(2,2-dibromovinyl)cyclopent-1-en-1-yl)ethynyl)trimethylsilane (4): Zn dust (8.03 g, 0.12 mol) and PPh3 (32.1 g, 0.12 mol) were strring in methylene chloride (120 mL) while CBr_4 (20.4 g, 0.06 mol) dissolved in methylene chloride (40 mL) was added dropwise at 0 ˚C. A solution of 2-((trimethylsilyl)ethynyl)cyclopent-1-ene-1-carbaldehyde (**3,** 5.9 g, 0.03 mol) in methylene chloride (100 mL) was added into the stirring reaction mixture over 15 minutes. The reaction was allowed to stir for 2 h while gradually warmed up to ambient temperature. The reaction mixture was filtered through celite, washed with water (3 x 100 mL), aq. 1 M HCl (2 x 50 mL) and brine (3 x 100 mL). Then the organic extracts were dried over anhydrous MgSO4, concentrated and purified by flash silica column chromatography (hexanes) to afford 4 as a yellow oil (9.1 g, 0.026 mol, 87.1% yield). IR (film, cm^{-1}) 3006, 2959, 2898, 2848, 2133, 1544, 1438, 1281, 1250, 1205, 986, 855, 753. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (s, 1H, vinyl-*H*), 2.93 (m, 2H, methylene-*H*), 2.40 (m, 2H, methylene-*H*), 1.90 (m, 2H, methylene-*H*), 0.21 (s, 3H, TMS-Me). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$): δ 145.9 (vinyl-*C*), 133.7 (vinyl-*C*), 128.4 (vinyl-*C*), 104.3 (*C*-TMS),

101.1 (vinyl-*C*), 89.9 (*C*≡C-H), 36.2 (methylene-*C*), 33.7 (methylene-*C*), 23.2 (methylene-*C*), 0.1 (TMS-*C*). HRMS for $[C_{12}H_{15}Br_2Si]^+$: 344.9304 (Theo. Mass), 344.9301 (Mass Measured), Delta (-0.9 ppm).



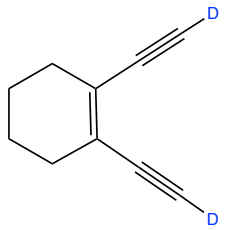
4

1,2-bis((E)-vinyl-2-d)cyclohex-1-ene (**14-*EZE*-d_2**): $Cp_2Zr(H)(Cl)$ (554 mg, 2.15 mmol) was weighed and transferred into a flask equipped with a stir bar and rubber septum in glovebox. Enediyne **13** (140 mg, 1.08 mmol) dissolved in dry dichloromethane (14 mL) was added into the flask. The bright yellow reaction mixture was allowed to stir for 1.5 h, while the solution became homogeneous and red. Then the solution was quenched with CF_3CO_2D (1 mL, diluted to 7.5 mL with D_2O) and allowed to stir for 10 minutes. The layers were partitioned and the aqueous layer was extracted with dichloromethane (3 x 50 mL). The combined organic extracts were washed with sat. aq. $NaHCO_3$ (2 x 50 mL), H_2O (2 x 50 mL), brine (2 x 50 mL) and dried over anhydrous $MgSO_4$. The volatiles were removed under vacuum and the residue was purified on a silica column with hexanes eluent to give the triene **14-*EZE*-d_2** as a clear oil (95 mg, 0.7 mmol, 65% yield，> 70% deuterium incorporation as determined by mass spectroscopy). Diagnostic resonances of triene **14-*EZE*-d_2** in ^1H NMR (400 MHz, $CDCl_3$) were observed at δ 1.66 (t, 4H, methylene-*H*), 2.28 (t, 4H, methylene-*H*), 5.21 (d, *J*= 17.2 Hz, 1H, vinyl-*H*), 7.06 (d, *J*= 17.2 Hz, 1H, vinyl-*H*).



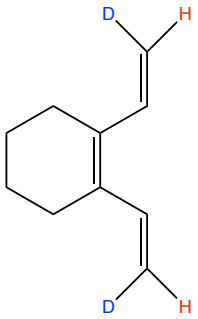
14-*EZE*-d_2

1,2-bis(ethynyl-d)cyclohex-1-ene (13-d_2): Enediyne **13** (1.1 g, 8.45 mmol) was dissolved in dry THF (60 mL) in an oven-dried flask equipped with a stir bar and rubber septum under dry N_2. The solution was cooled to -78 ℃ on a dry ice-acetone bath and then ^{n}BuLi (10 mL, 2 M in hexanes, 20 mmol) was added dropwise to the solution over 15 minutes. The reaction mixture was stirred at -78 ℃ for 1 h and then quenched with CF_3CO_2D (3 mL, 39.2 mmol, diluted to 15 mL with D_2O). The solution was allowed to warm to ambient temperature and stirred for 10 min. The layers were partitioned and the aqueous layer was extracted with Et_2O (3 x 25 mL). The combined organic extracts were washed with sat. aq. $NaHCO_3$ (3 x 50 mL), H_2O (3 x 50 mL), brine (3 x 50 mL) and dried over anhydrous $MgSO_4$. The volatiles were removed under vacuum and the residue was purified on a silica gel column with hexanes eluent. Repeated all the process above again in order to enhance the deuterium enrichment and give the enediyne **13-d_2** as a clean oil (640 mg, 4.84 mmol, 57% yield, > 85% deuterium incorporation as determined by ^{1}H NMR spectroscopy). Diagnostic resonances of enediyne **3** in ^{1}H NMR (400 MHz, $CDCl_3$) were observed at δ 1.430 (m, 4H, methylene-*H*), 1.57 (m, 4H, methylene-*H*).



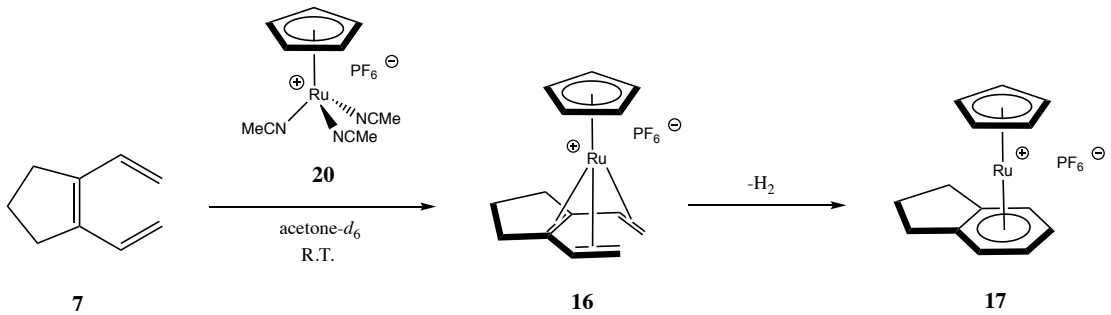
13-d_2

1,2-bis((Z)-vinyl-2-d)cyclohex-1-ene (14-*ZZZ*-d_2): $Cp_2Zr(H)(Cl)$ (2.83g, 11 mmol) was weighed and transferred into a flask equipped with a stir bar and rubber septum in glovebox. Enediyne **13-d_2** (640 mg, 4.84 mmol) dissolved in dry dichloromethane (50 mL) was added into the flask. The bright yellow reaction mixture was allowed to stir for 1.5 h, while the solution became homogeneous and red. Then the solution was quenched with CF_3CO_2H (4.5 mL, diluted to 30 mL with H_2O) and allowed to stir for 10 minutes. The layers were partitioned and the aqueous layer was extracted with dichloromethane (3 x 50 mL). The combined organic extracts were washed with sat. aq. $NaHCO_3$ (2 x 50 mL), H_2O (2 x 50 mL), brine (2 x 50 mL) and dried over anhydrous $MgSO_4$. The volatiles were removed under vacuum and the residue was purified on a silica column with hexanes eluent to give the triene **4** as a clear oil (355 mg, 2.61mmol, 54% yield，> 90% deuterium incorporation as determined by mass spectroscopy. Diagnostic resonances of triene **4** in ^1H NMR (400 MHz, $CDCl_3$) were observed at *δ* 1.66 (m, 4H, methylene-*H*), 2.28 (m, 4H, methylene-*H*), 5.05 (d, *J*= 11.2 Hz, 1H, vinyl-*H*), 7.05 (d, *J* = 11.2 Hz, 1H, vinyl-*H*).



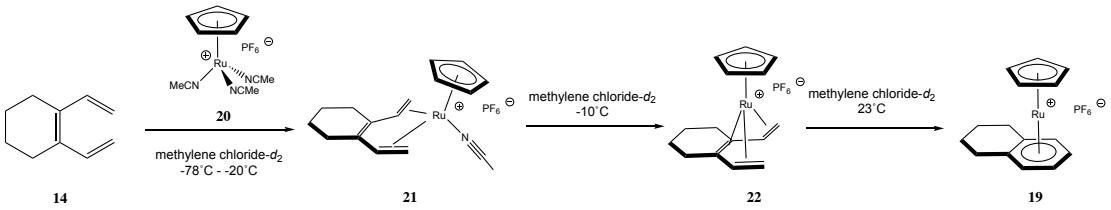
14-*ZZZ*-d_2

NMR-tube-scale reaction of 7 with [CpRu(NCMe)$_3$]PF$_6$ (20) to generate 17 in acetone-d_6: Triene **7** (15.2 mg, 0.10 mmol) and [CpRu(NCMe)$_3$]PF$_6$ (**20**; 5.5 mg, 0.01 mmol) were added into an oven-dried J. Young NMR tube, with 1,3,5-tri-tert-butylbenzene added as an internal standard. The tube was frozen by liquid nitrogen immediately and then placed under vacuum. After dry acetone-d_6 (0.5 mL) was distilled into the tube under vacuum, the tube was degassed via 3 cycles of freeze/pump/thaw/degas. The reaction was allowed to react at ambient temperature while monitored by ^{1}H NMR spectroscopy. After 30 min, nearly all [CpRu(NCMe)$_3$]PF$_6$ **20** was consumed based on disappearance of a Cp resonance at δ 5.31 (s, 5H), and the resonances for **17** were observed at δ 6.47 (s, 2H, aromatic-*H*), 6.16 (s, 2H, aromatic-*H*), 5.49 (s, 5H, Cp).

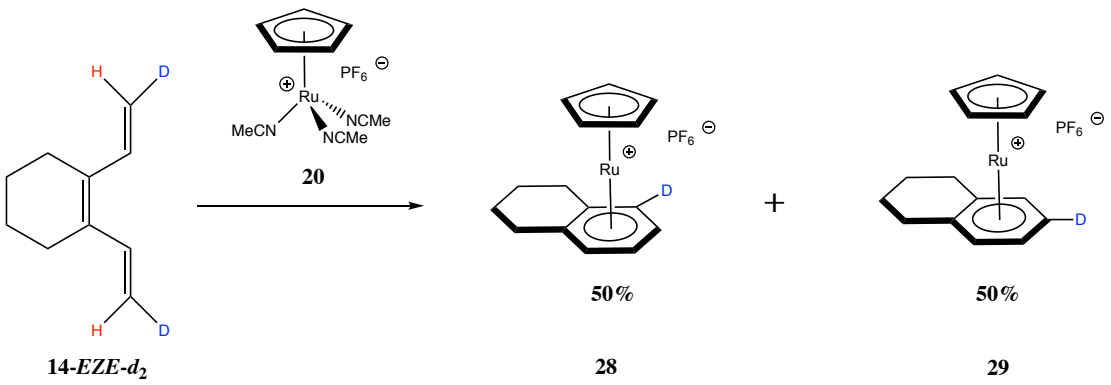


NMR reaction of $CpRu(NCMe)_3PF_6$ (20) triggered cycloaromatization of 1,2-divinylcyclohex-1-ene (14) via (η^5-cyclopentadienyl)(η^4-1,2-divinylcyclohex-1-ene) Ru acetonitrile hexafluorophosphate (21), and (η^5-cyclopentadienyl)(η^6-1,2-divinylcyclohex-1-ene) Ru hexafluorophosphate (22) as intermediates in dichloromethane-d_2: 6.8 mg of 1,2-divinylcyclohex-1-ene (**14**) (0.051mmol) and $CpRu(NCMe)_3PF_6$ (20 mg, 0.046 mmol) were added into an oven dried J.Y. NMR tube. The tube was frozen by liquid nitrogen immediately and then placed under vacuum. After 0.7 mL of dry dichloromethane-d_2 was distilled into the tube under vacuum, the tube was degassed via 3 cycles of freeze/pump/thaw/degas. The NMR tube was kept at -60 ˚C in the JEOL ECA500 NMR instrument equipped with a nitrogen-cooled Cold Probe, and an initial ^{1}H NMR spectrum was recorded immediately. Then the reaction mixture was monitored by ^{1}H NMR spectroscopy while slowly increasing temperature. After 70 minutes at -20 ˚C, a new set of resonances of intermediate **21** were observed at δ 1.31 (m, 2H, methylene-*H*), 1.70 (m, 2H, methylene-*H*), 1.88 (m, 2H, methylene-*H*), 2.08 (m, 1H, methylene-*H*), 2.19 (m, 1H, methylene-*H*), 2.35 (s, 3H, NC*Me*), 2.75 (d, 1H, J = 11.5 Hz, vinyl-*H*), 3.36 (d, 1H, J = 13 Hz, vinyl-*H*), 3.99 (d, 1H, J = 9.0 Hz, vinyl-*H*), 4.12 (dd, 1H, J_1 = 8.5 Hz, J_2 = 13 Hz, vinyl-*H*), 4.15 (d, 1H, J = 8.5 Hz, vinyl-*H*), 4.28 (dd, 1H, J_1 = 9.0 Hz, J_2 = 11.5 Hz, vinyl-*H*), 5.12 (s, 5H, Cp). Then the reaction was warmed up to -10 ˚C. After 120 minutes, the characteristic resonances of complex **22** were observed at δ 2.44 (d, 1H, J = 17.5 Hz, vinyl-*H*), 2.505 (d, 1H, J = 10 Hz, vinyl-*H*), 2.513 (d, 1H, J = 10.5 Hz, vinyl-*H*), 3.03 (dd, 1H, J_1 = 10 Hz, J_2 = 17.5 Hz, vinyl-*H*), 3.54 (dd, 1H, J_1 = 7 Hz, J_2 = 10.5 Hz, vinyl-*H*), 4.77 (d, 1H, J = 7 Hz, vinyl-*H*), 5.33 (s, 5H, Cp). Then the reaction mixture was warmed up to 23 ˚C. After 12 hours, all the resonances of **21** and **22**

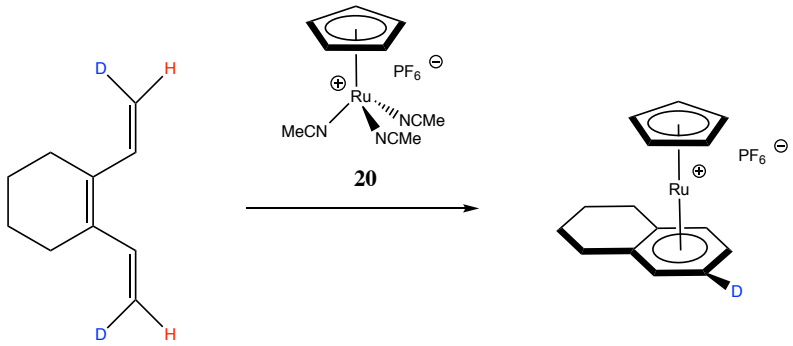
disappeared, and resonances of complex **19** were observed at *δ* 1.77 (m, 2H, methylene-*H*), 1.86 (m, 2H, methylene-*H*), 2.69 (m, 2H, methylene-*H*), 2.83 (m, 2H, methylene-*H*), 5.26 (s, 5H, Cp), 5.99 (m, 2H, arene-*H*), 6.02 (m, 2H, arene-*H*). When the reaction was carried out at ambient temperature, the yield of **19** (90.3%) was calculated by the integration of Cp resonance at *δ* 5.26 (s, 5H) relative to internal standard.



NMR-tube-scale reaction of 14-*EZE*-d_2 with [CpRu(NCMe)$_3$]PF$_6$ (20) to generate 28 and 29 in dichloromethane-d_2: Triene **14-*EZE*-d_2** (6.3 mg, 0.04 mmol, 0.050 M, deuterium enrichment D2 70%) and CpRu(NCMe)$_3$PF$_6$ (**20**; 9.7 mg, 0.02 mmol, 0.025 M) were added into an oven-dried J. Young tube. After the J. Young tube was frozen by liquid nitrogen and then placed under vacuum, 0.8 mL of dry dichloromethane-d_2 was distilled into the J. Young tube, the tube was then degassed via 3 cycles of freeze/pump/thaw/degas. After reacting at ambient temperature overnight, dichloromethane-d_2 was pumped out under vacuum and dry acetone-d_6 was distilled into the J. Young tube. The formation of the ruthenium combined **28** and **29** was observed by ^{1}H NMR spectroscopy, ^{2}H NMR spectroscopy and mass spectrometry. The ^{1}H NMR resonances for the reaction were observed at *δ* 1.85 (m, 4H, methylene-*H*), 2.85 (m, 4H, methylene-*H*), 5.48 (s, 5H, Cp), 6.18 (d, 1.5H, arene-*H*), 6.26 (d, 1.5H, arene-*H*). The ^{2}H NMR resonances for the reaction were observed at *δ* 6.20 (s, 1D), 6.28 (s, 1D). The deuterium enrichment is measured as: D1 70%, D0 30%. (ESI)

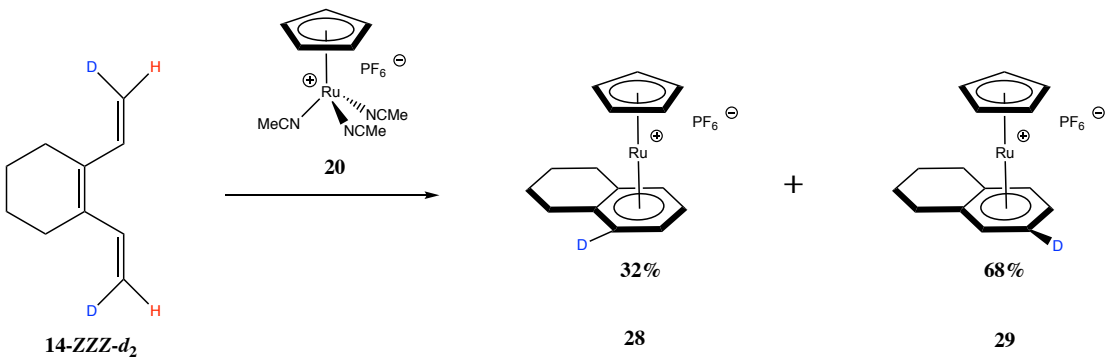


NMR-tube-scale reaction of 14-*ZZZ*-d_2 with [CpRu(NCMe)$_3$]PF$_6$ (20) to generate 28 and 29 in dichloromethane-d_2: Tirene **14-*ZZZ*-d_2** (3.1 mg, 0.02 mmol, 0.010 M, deuterium enrichment D2 92%) and CpRu(NCMe)$_3$PF$_6$ (**20**; 5 mg, 0.01 mmol, 0.005 M) were added into an oven-dried J. Young tube. After the J. Young tube was frozen by liquid nitrogen and then placed under vacuum, 2.2 mL of dry dichloromethane-d_2 was distilled into the J. Young tube, the tube was then degassed via 3 cycles of freeze/pump/thaw/degas. After reacting at ambient temperature overnight, dichloromethane-d_2 was pumped out under vacuum and dry acetone-d_6 was distilled into the J. Young tube. The formation of the ruthenium combined complex **6** was observed by ^{1}H NMR spectroscopy, ^{2}H NMR spectroscopy and mass spectrometry. The ^{1}H NMR resonances for the reaction were observed at δ 1.79 (m, 2H, methylene-*H*), 1.85 (m, 2H, methylene-*H*), 2.69 (m, 2H, methylene-*H*), 2.83 (m, 2H, methylene-*H*), 5.26 (s, 5H, Cp), 5.99 (m, 1H, arene-*H*), 6.02 (m, 2H, arene-*H*). The ^{2}H NMR resonance for the reaction was observed at δ 6.21 (s, 1D). The deuterium enrichment is measured as: D1 74%, D0 26%. (ESI).

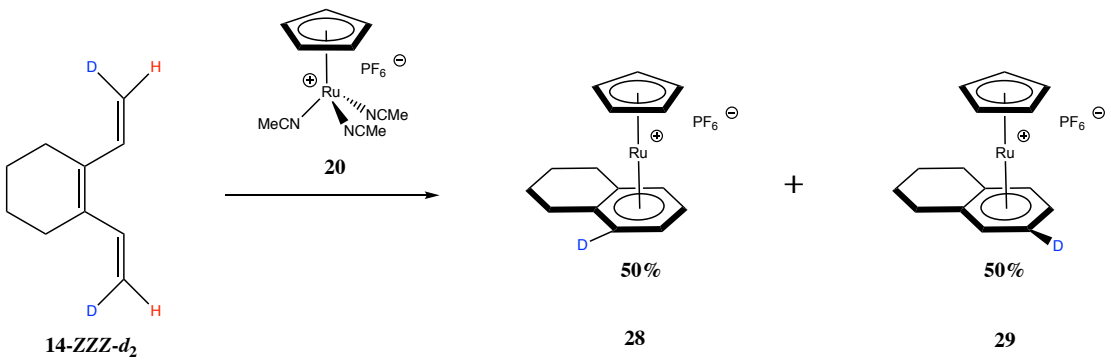


14-*ZZZ*-d_2 **29**

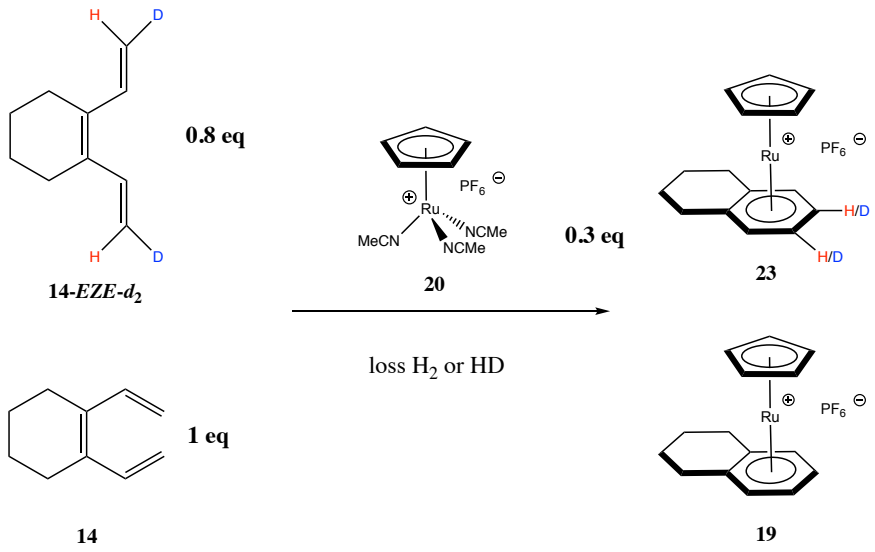
NMR-tube-scale reaction of 14-*ZZZ*-d_2 with $[CpRu(NCMe)_3]PF_6$ (20) to generate 28 and 29 in dichloromethane-d_2: Tirene **14-*ZZZ*-d_2** (3.1 mg, 0.02 mmol, 0.025 M, deuterium enrichment D2 92%) and $CpRu(NCMe)_3PF_6$ (5 mg, 0.01 mmol, 0.013 M) were added into an oven-dried J. Young tube. After the J. Young tube was frozen by liquid nitrogen and then placed under vacuum, 0.8 mL of dry dichloromethane-d_2 was distilled into the J. Young tube, the tube was then degassed via 3 cycles of freeze/pump/thaw/degas. After reacting at ambient temperature overnight, dichloromethane-d_2 was pumped out under vacuum and dry acetone-d_6 was distilled into the J. Young tube. The formation of the ruthenium combined complex **28** and **29** was observed by ^{1}H NMR spectroscopy and ^{2}H NMR spectroscopy. The ^{1}H NMR resonances for the reaction were observed at δ 1.85 (m, 4H, methylene-*H*), 2.86 (m, 4H, methylene-*H*), 5.49 (s, 5H, Cp), 6.19 (m, 1H, arene-*H*), 6.27 (m, 2H, arene-*H*). The ^{2}H NMR resonances for the reaction were observed at δ 6.17 (s, 1D), 6.25 (s, 1D).



NMR-tube-scale reaction of 14-*ZZZ*-d_2 with $[CpRu(NCMe)_3]PF_6$ (20) to generate 28 and 29 in dichloromethane-d_2: Tirene **14-*ZZZ*-d_2** (9.4 mg, 0.06 mmol, 0.075 M, deuterium enrichment D2 92%) and $CpRu(NCMe)_3PF_6$ (15 mg, 0.03 mmol, 0.038 M) were added into an oven-dried J. Young tube. After the J. Young tube was frozen by liquid nitrogen and then placed under vacuum, 0.8 mL of dry dichloromethane-d_2 was distilled into the J. Young tube, the tube was then degassed via 3 cycles of freeze/pump/thaw/degas. After reacting at ambient temperature overnight, dichloromethane-d_2 was pumped out under vacuum and dry acetone-d_6 was distilled into the J. Young tube. The formation of the ruthenium combined complex **28** and **29** was observed by ^{1}H NMR spectroscopy and ^{2}H NMR spectroscopy. The ^{1}H NMR resonances for the reaction were observed at δ 1.85 (m, 4H, methylene-*H*), 2.85 (m, 4H, methylene-*H*), 5.48 (s, 5H, Cp), 6.18 (m, 1.5H, arene-*H*), 6.26 (m, 1.5H, arene-*H*). The ^{2}H NMR resonances for the reaction were observed at δ 6.20 (s, 1D), 6.28 (s, 1D).



NMR-tube-scale competition reaction of 14-*EZE*-d_2 and 14 with [CpRu(NCMe)$_3$]PF$_6$ (20) to generate 23 and 19 in acetone-d_6: triene 14 (11 mg, 0.082 mmol, 1 eq.) and triene 14-*EZE*-d_2 (9 mg, 0.066 mmol, 0.8 eq.) and 1,3,5-tri-*tert*-butylbenzene as internal standard were adder into an oven dried J.Young NMR tube. The NMR tube was frozen in a dry ice-acetone bath and placed under vacuum, 0.5 mL dry acetone-d_6 was distilled into the tube, the tube was then degassed via 3 cycles of freeze/pump/thaw/degas. A ^{1}H NMR spectrum for these two trienes was recorded. Then CpRu(NCMe)$_3$PF$_6$ (2.0mg, 0.021 mmol, 0.3 eq.) was added into the tube inside a glovebox. Once the tube was moved out from the glovebox, an initial ^{1}H NMR spectrum was recorded, and then the reaction mixture was monitored by ^{1}H NMR spectroscopy at ambient temperature. In the initial ^{1}H NMR spectrum, the ratio of the integrations of the resonance of triene 14 at δ 5.05 and the resonance of triene 14 and 14-*EZE*-d_2 at δ 5.23 is 1.46: 1. The tube was allowed to stand in ambient temperature overnight. Then the final ^{1}H NMR spectrum was recorded. In the final ^{1}H NMR spectrum, the ratio of those two resonances is 1.45: 1, which is approximately same to the one from the two trienes spectrum.

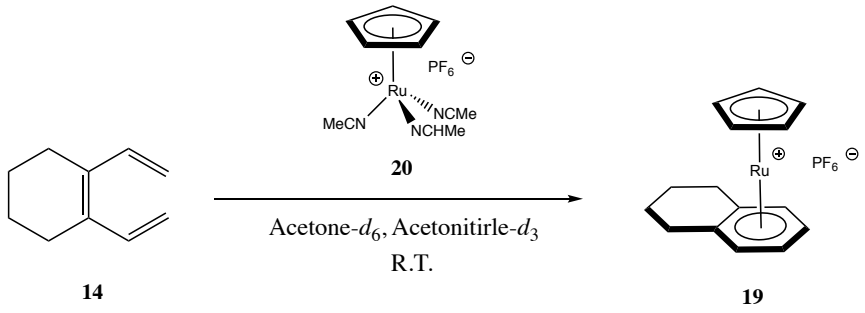


General methods of the kinetic studies of $CpRu(NCMe)_3PF_6$ with 1,2-divinylcyclohex-1-ene (14) at room temperature in acetone-d_6 solvent: triene 14 (9.8 mg, 0.073 mmol) was added into an oven dried J.Young NMR tube with $CpRu(NCMe)_3PF_6$ (2.0mg, 0.0046 mmol), acetonitrile-d_3 (128 mg, 3.12 mmol) and 1,3,5-tri-*tert*-butylbenzene as internal standard. After the NMR tube was frozen at -78 ˚C and placed under vacuum, acetone-d_6 was meticulously distilled into the NMR tubes until the total solution volume is 0.92 mL, the tube was then degassed via 3 cycles of freeze/pump/thaw/degas. The NMR tube was shaken and swirled to dissolve all the solid via using the vortex mixer while maintaining the temperature at -78 ˚C. The time recording started when the NMR tube was placed into a water bath to warmed up to 23 ˚C. The reaction was subsequently monitored by ^1H NMR spectroscopy under ambient temperature (23 ˚C). The consumptions of $CpRu(NCMe)_3PF_6$ were recorded by the integrating of Cp resonance at δ 4.31 (s, 5H) relative to internal standard. The

ln[CpRu(NCMe)$_3$PF$_6$]-Time plots were made to calculate the rate constant *k* and half-lives for 14. The result shows: triene 14 (k = 0.0569 s^{-1}, $t_{1/2}$ = 0.0034 h).

Table 2. Concentrations of CpRu(NCMe)$_3$PF$_6$ and their natural logarithms at different time points when 1,2-divinylcyclohex-1-ene (**14**) was employed as substrate

Time (seconds)	210	300	390	480	570
ln[CpRu(NCMe)$_3$PF$_6$] (mol/L)	-6.1417	-6.3172	-6.3720	-6.4252	-6.5146
ln[Intermediate] (mol/L)	-5.8518	-5.8306	-5.8047	-5.7671	-5.7647
ln[Final Product] (mol/L)	-6.3948	-6.3720	-6.3410	-6.3045	-6.2982

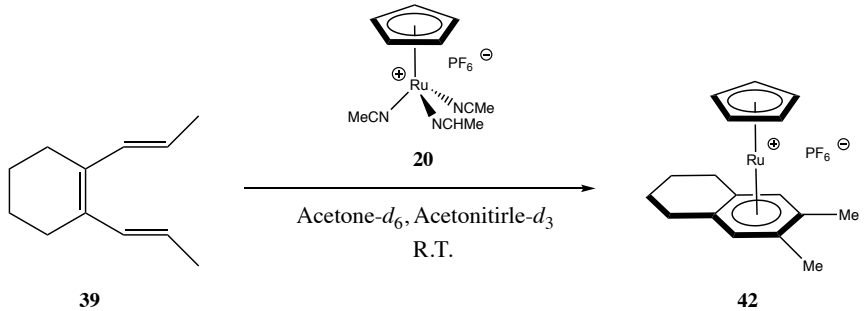


General methods of the kinetic studies of CpRu(NCMe)$_3$PF$_6$ with 1,2-di((*E*)-prop-1-en-1-yl)cyclohex-1-ene (*EE,* 39) at room temperature in acetone-d_6 solvent: triene (*EE*, 39) (18 mg, 0.111 mmol) was added into an oven dried J.Young NMR tube with CpRu(NCMe)$_3$PF$_6$ (2.0mg, 0.0046 mmol), acetonitrile-d_3 (128 mg, 3.12 mmol) and 1,3,5-tri-*tert*-butylbenzene as internal standard. After the NMR tube was frozen at -78 ˚C and placed under vacuum, acetone-d_6 was meticulously distilled into the NMR tubes until the total solution volume is 0.92 mL, the tube was then degassed via 3 cycles of

freeze/pump/thaw/degas. The NMR tube was shaken and swirled to dissolve all the solid via using the vortex mixer while maintaining the temperature at -78 ˚C. The time recording started when the NMR tube was placed into a water bath to warmed up to 23 ˚C. The reaction was subsequently monitored by ^{1}H NMR spectroscopy under ambient temperature (23 ˚C). The consumptions of $CpRu(NCMe)_3PF_6$ were recorded by the integrating of Cp resonance at δ 4.31 (s, 5H) relative to internal standard. The ln[$CpRu(NCMe)_3PF_6$]-Time plots were made to calculate the rate constant k and half-lives for 39. The result shows: *EE* triene (k = 0.00030 s^{-1}, $t_{1/2}$ = 0.642 h).

Table 3. Concentrations of $CpRu(NCMe)_3PF_6$ and their natural logarithms at different time points when 1,2-di((*E*)-prop-1-en-1-yl)cyclohex-1-ene (***EE*, 39**) was employed as substrate.

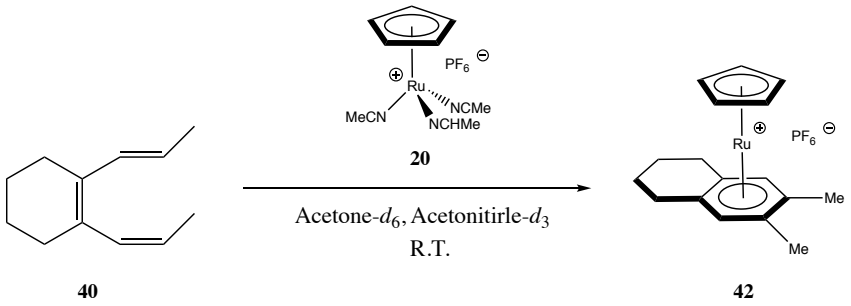
Time (seconds)	330	420	510	600	690	780	870	960
ln[$CpRu(NCMe)_3PF_6$] (mol/L)	-5.4697	-5.5065	-5.5521	-5.5744	-5.6063	-5.6220	-5.6419	-5.6650
ln[Intermediate] (mol/L)	-7.0846	-7.0621	-7.0240	-7.0133	-6.9976	-6.9770	-6.9668	-6.9668



General methods of the kinetic studies of $CpRu(NCMe)_3PF_6$ with 1-((*E*)-prop-1-en-1-yl)-2-((*Z*)-prop-1-en-1-yl)cyclohex-1-ene (*EZ,* 40) at room temperature in acetone-d_6 solvent: triene (***EZ*, 40**) (18 mg, 0.111 mmol) was added into an oven dried J.Young NMR tube with $CpRu(NCMe)_3PF_6$ (2.0mg, 0.0046 mmol), acetonitrile-d_3 (128 mg, 3.12 mmol) and 1,3,5-tri-*tert*-butylbenzene as internal standard. After the NMR tube was frozen at -78 ˚C and placed under vacuum, acetone-d_6 was meticulously distilled into the NMR tubes until the total solution volume is 0.92 mL, the tube was then degassed via 3 cycles of freeze/pump/thaw/degas. The NMR tube was shaken and swirled to dissolve all the solid via using the vortex mixer while maintaining the temperature at -78 ˚C. The time recording started when the NMR tube was placed into a water bath to warmed up to 23 ˚C. The reaction was subsequently monitored by ^{1}H NMR spectroscopy under ambient temperature (23 ˚C). The consumptions of $CpRu(NCMe)_3PF_6$ were recorded by the integrating of Cp resonance at δ 4.31 (s, 5H) relative to internal standard. The ln[$CpRu(NCMe)_3PF_6$]-Time plots were made to calculate the rate constant k and half-lives for 39. The result shows: *EZ* triene (k = 0.00012 s^{-1}, $t_{1/2}$ = 1.60 h).

Table 4 . Concentrations of $CpRu(NCMe)_3PF_6$ and their natural logarithms at different time points when 1-((*E*)-prop-1-en-1-yl)-2-((*Z*)-prop-1-en-1-yl)cyclohex-1-ene (***EZ*, 40**) was employed as substrate.

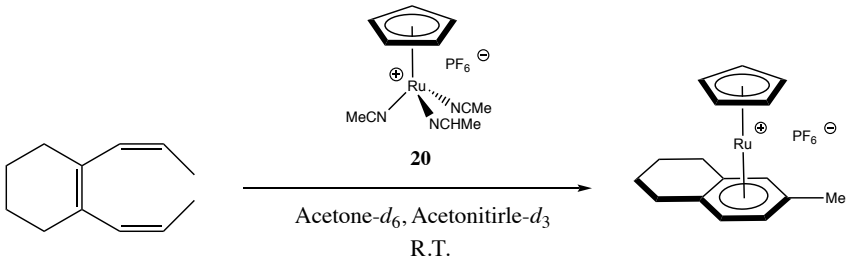
Time (seconds)	450	630	810	990	1170	1440	1650	1830	2100	2280
ln[$CpRu(NCMe)_3PF_6$] (mol/L)	-5.3933	-5.4121	-5.4314	-5.451	-5.4771	-5.5186	-5.5314	-5.6508	-5.5854	-5.6118
ln[Intermediate] (mol/L)	-7.4930	-7.3901	-7.2869	-7.2205	-7.1583	-7.0835	-7.0140	-6.9810	-6.9525	-6.9012
ln[Final Product] (mol/L)	-7.5812	-7.4709	-7.3647	-7.3581	-7.2998	-7.0239	-7.2096	-7.1925	-7.1757	-7.1429



General methods of the kinetic studies of $CpRu(NCMe)_3PF_6$ with 1,2-di((*Z*)-prop-1-en-1-yl)cyclohex-1-ene (*ZZ,* 41) at room temperature in acetone-d_6 solvent: triene (***ZZ*, 41**) (18 mg, 0.111 mmol) was added into an oven dried J.Young NMR tube with $CpRu(NCMe)_3PF_6$ (2.0mg, 0.0046 mmol), acetonitrile-d_3 (128 mg, 3.12 mmol) and 1,3,5-tri-*tert*-butylbenzene as internal standard. After the NMR tube was frozen at -78 ˚C and placed under vacuum, acetone-d_6 was meticulously distilled into the NMR tubes until the total solution volume is 0.92 mL, the tube was then degassed via 3 cycles of freeze/pump/thaw/degas. The NMR tube was shaken and swirled to dissolve all the solid via using the vortex mixer while maintaining the temperature at -78 ˚C. The time recording started when the NMR tube was placed into a water bath to warmed up to 23 ˚C. The reaction was subsequently monitored by ^1H NMR spectroscopy under ambient temperature (23 ˚C). The consumptions of $CpRu(NCMe)_3PF_6$ were recorded by the integrating of Cp resonance at δ 4.31 (s, 5H) relative to internal standard. The ln[$CpRu(NCMe)_3PF_6$]-Time plots were made to calculate the rate constant k and half-lives for 39. The result shows: ***ZZ*** triene (k = 0.0002 s^{-1}, $t_{1/2}$ = 0.875 h).

Table 5. Concentrations of $CpRu(NCMe)_3PF_6$ and their natural logarithms at different time points when 1,2-di((*Z*)-prop-1-en-1-yl)cyclohex-1-ene (***ZZ*, 41**) was employed as substrate.

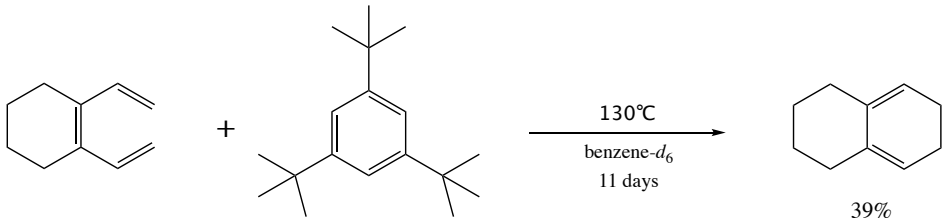
Time (seconds)	270	450	720	810	1080	1260	1350	1440	1620	1710
$CpRu(NCMe)_3PF_6$ (mol/L)	0.005341	0.005147	0.004679	0.004640	0.004445	0.004250	0.004211	0.004094	0.003977	0.003833
$\ln[CpRu(NCMe)_3PF_6]$ (mol/L)	-5.2323	-5.2694	-5.3647	-5.3731	-5.4160	-5.4609	-5.4701	-5.4983	-5.5273	-5.5642



41 **43**

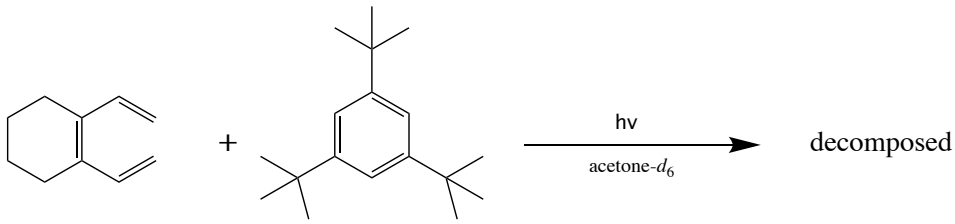
NMR-tube-scale thermal reaction of 1,2-divinylcyclohex-1-ene (14) in benzene-d_6: 1,2-divinylcyclohex-1-ene (**14**; 5 mg, 0.037 mmol) was added into a 5-mm medium-wall NMR tube, with added 1,3,5-tri-*tert*-butylbenzene as internal standard. The tube was cooled in a dry ice-acetone bath and placed under vacuum. After 0.7 mL of dry benzene-d_6 was distilled into the NMR tube under vacuum, the sample was degassed via 3 cycles of freeze/pump/thaw/degas. Then the NMR tube was flame-sealed and an initial ^{1}H NMR spectrum was recorded immediately. The tube was then placed into an oil bath at 130 ˚C, and the reaction progress was monitored by ^{1}H NMR spectroscopy. After 11 days, all the starting triene was consumed according to the disappearance of the vinyl hydrogens resonances at δ 5.18 (d, 2H, J = 17.2 Hz) and δ 5.02 (d, 2H, J = 11.2 Hz), and the resonances of 1,2,3,4,6,7-hexahydronaphthalene (**15**) were also observed at δ 5.40 (m, 2H, vinyl-H), δ 2.25 (m, 4H, methylene-*H*), δ 2.02 (m, 4H, methylene-*H*), δ 1.62 (m,

4H, methylene-*H*). The yield (39%) of 1,2,3,4,6,7-hexahydronaphthalene (**15**) was calculated by the integration of vinyl hydrogen resonance at *δ* 5.40 (m, 2H, vinyl-H) related to internal standard resonance at *δ* 7.43 (s, 3H).



14 **15**

NMR-tube-scale photolysis reaction of 1,2-divinylcyclohex-1-ene (14) in acetone-d_6: 1,2-divinylcyclohex-1-ene (**14**; 5 mg, 0.037 mmol) was added into a J. Young NMR tube, with added 1,3,5-tri-*tert*-butylbenzene as internal standard. The tube was cooled in a dry ice-acetone bath and placed under vacuum. After 0.65 mL of dry acetone-d_6 was distilled into the NMR tube, the sample was degassed via 3 cycles of freeze/pump/thaw/degas. An initial ^{1}H NMR spectrum was recorded immediately. Then the tube was placed in a Rayonette photoreactor equipped with UV broadband lamps with wavelengths centered at 254 nm, and the reaction was monitored by ^{1}H NMR spectroscopy. After 8 days, all the resonances of divinylcyclohex-1-ene (**14**) were vanished without any evidence of formation of the desired cyclohexadiene product.



14

3. ^{1}H and ^{13}C NMR Spectra:

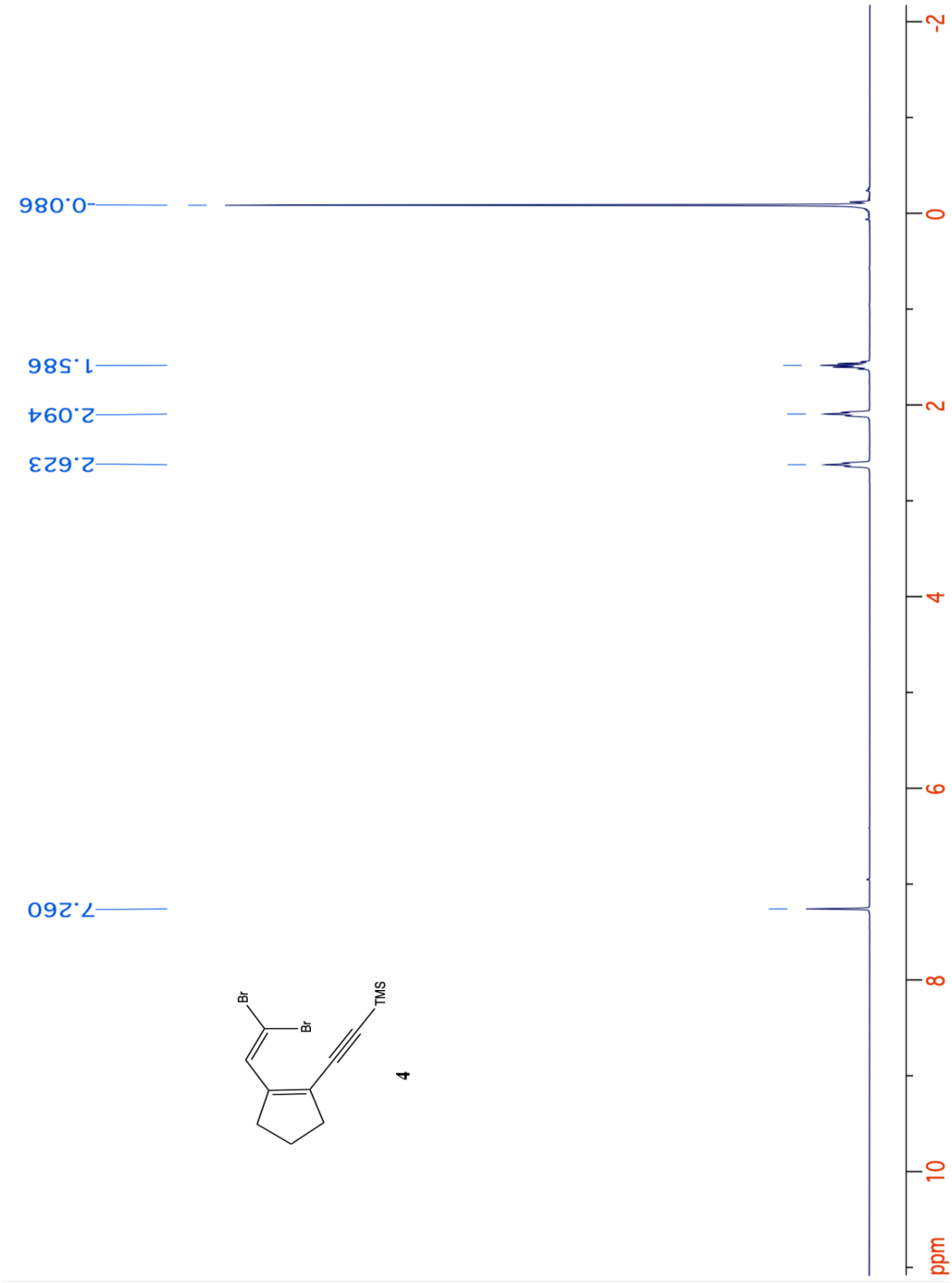


Figure 6. ((2-(2,2-dibromovinyl)cyclopent-1-en-1-yl)ethynyl)trimethylsilane (**4**), ^{1}H NMR spectrum (400 MHz, $CDCl_3$).

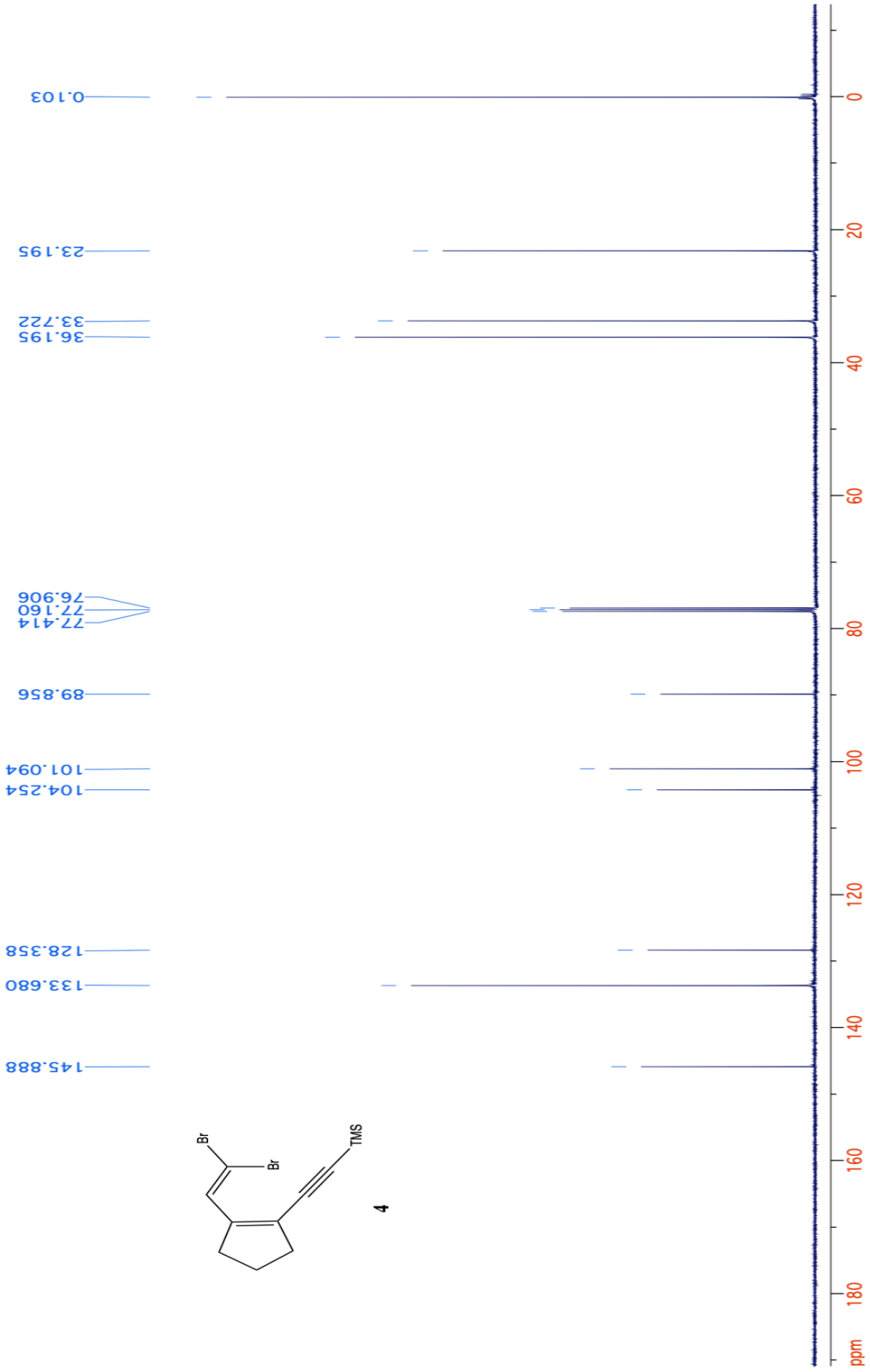


Figure 7. ((2-(2,2-dibromovinyl)cyclopent-1-en-1-yl)ethynyl)trimethylsilane (**4**), $^{13}C\{^{1}H\}$ NMR spectrum (500 MHz, $CDCl_3$).

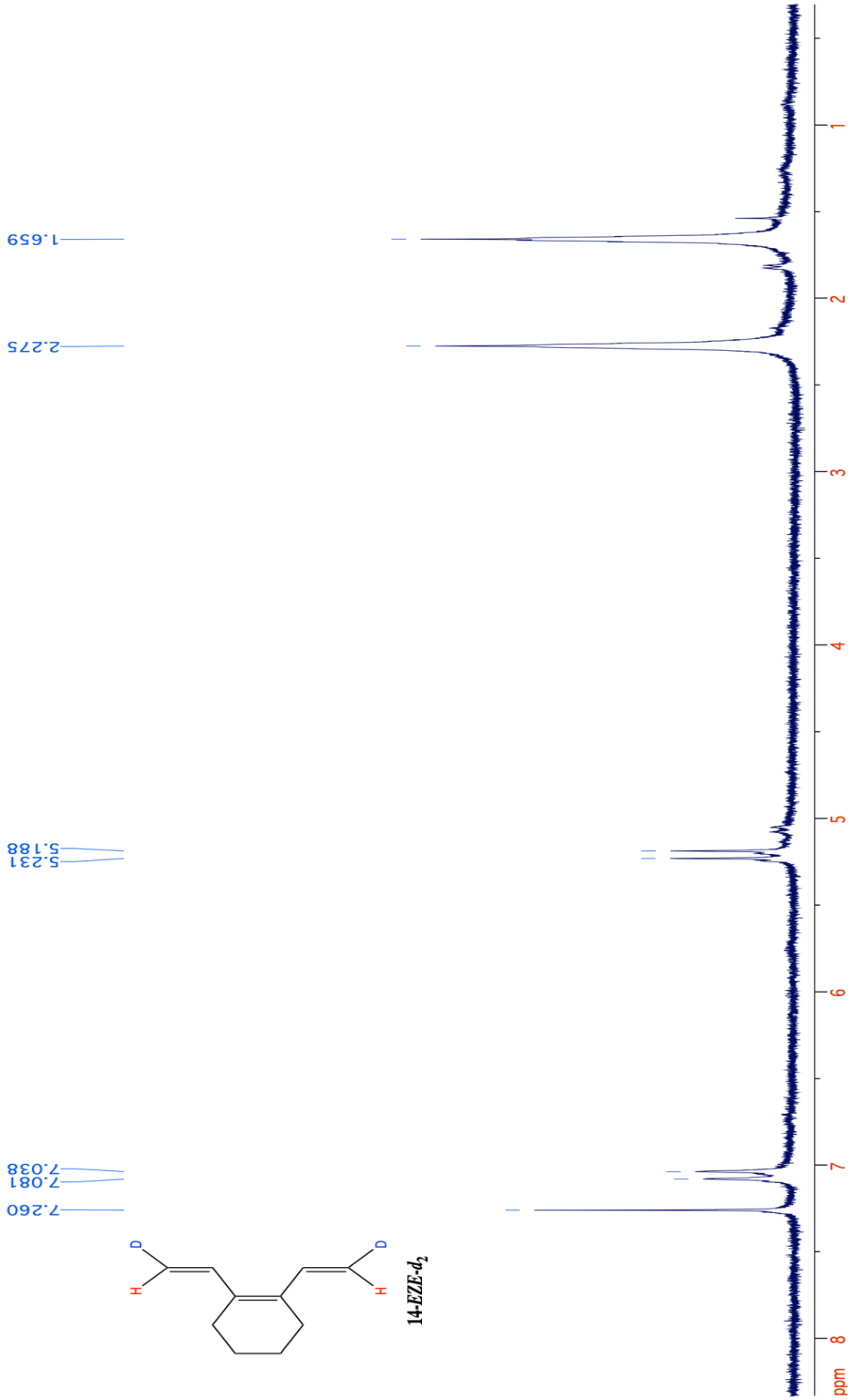


Figure 8. 1,2-bis((*E*)-vinyl-2-d)cyclohex-1-ene (**14-*EZE*-d_2**), ^{1}H NMR spectrum (400 MHz, $CDCl_3$).

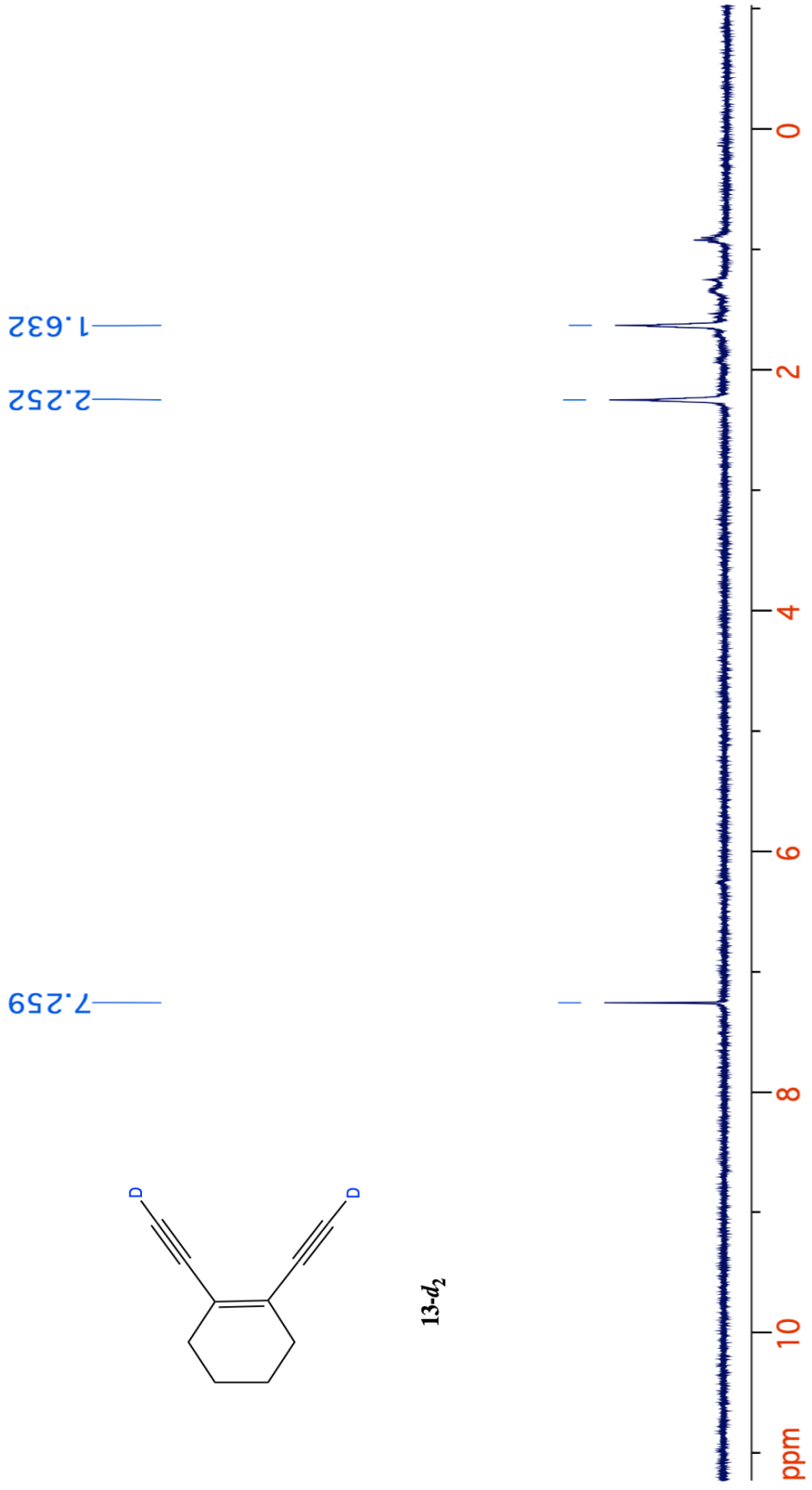


Figure 9. 1,2-bis(ethynyl-d)cyclohex-1-ene (**13-d_2**), ^{1}H NMR spectrum (400 MHz, $CDCl_3$).

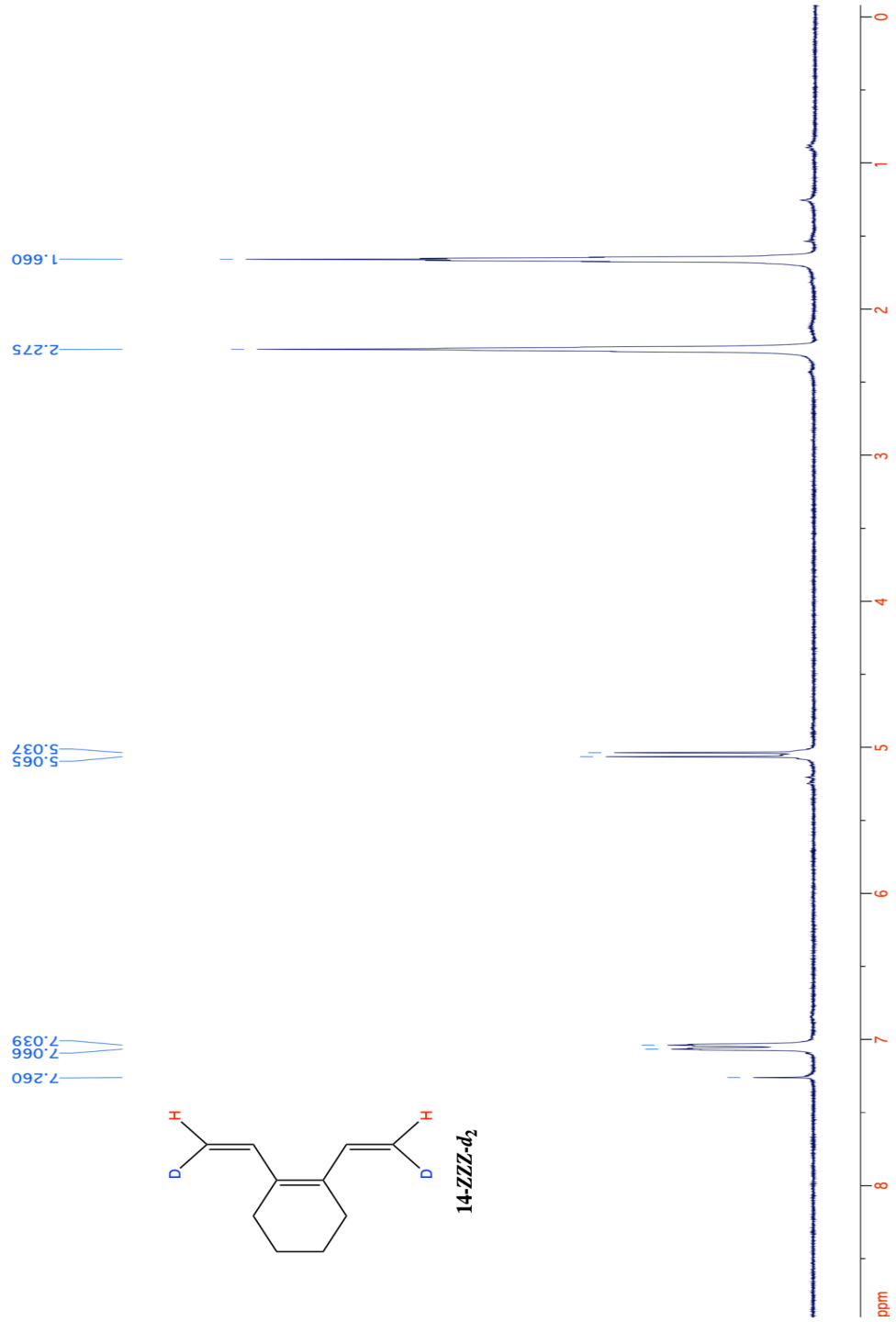


Figure 10. 1,2-bis((*Z*)-vinyl-2-d)cyclohex-1-ene (**14-ZZZ-d_2**), ^{1}H NMR spectrum (400 MHz, $CDCl_3$).

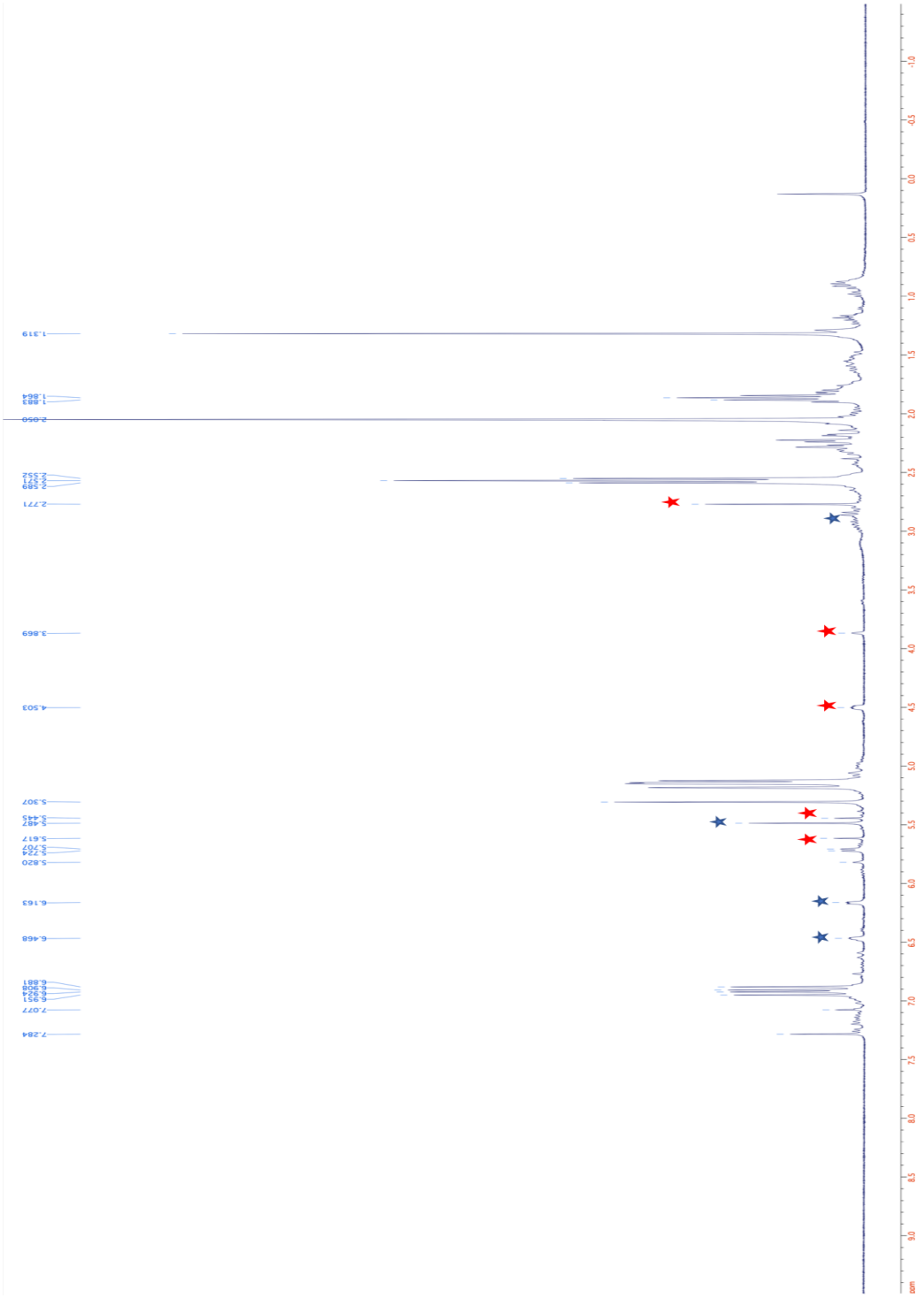


Figure 11. ^{1}H NMR spectrum (400 MHz, acetone-d_6) of crude reaction mixture of **7** with [CpRu(NCMe)$_3$]PF$_6$ to generate intermediate **16** (labeled with red star) and complex **17** (labeled with blue star) after 6 minutes.

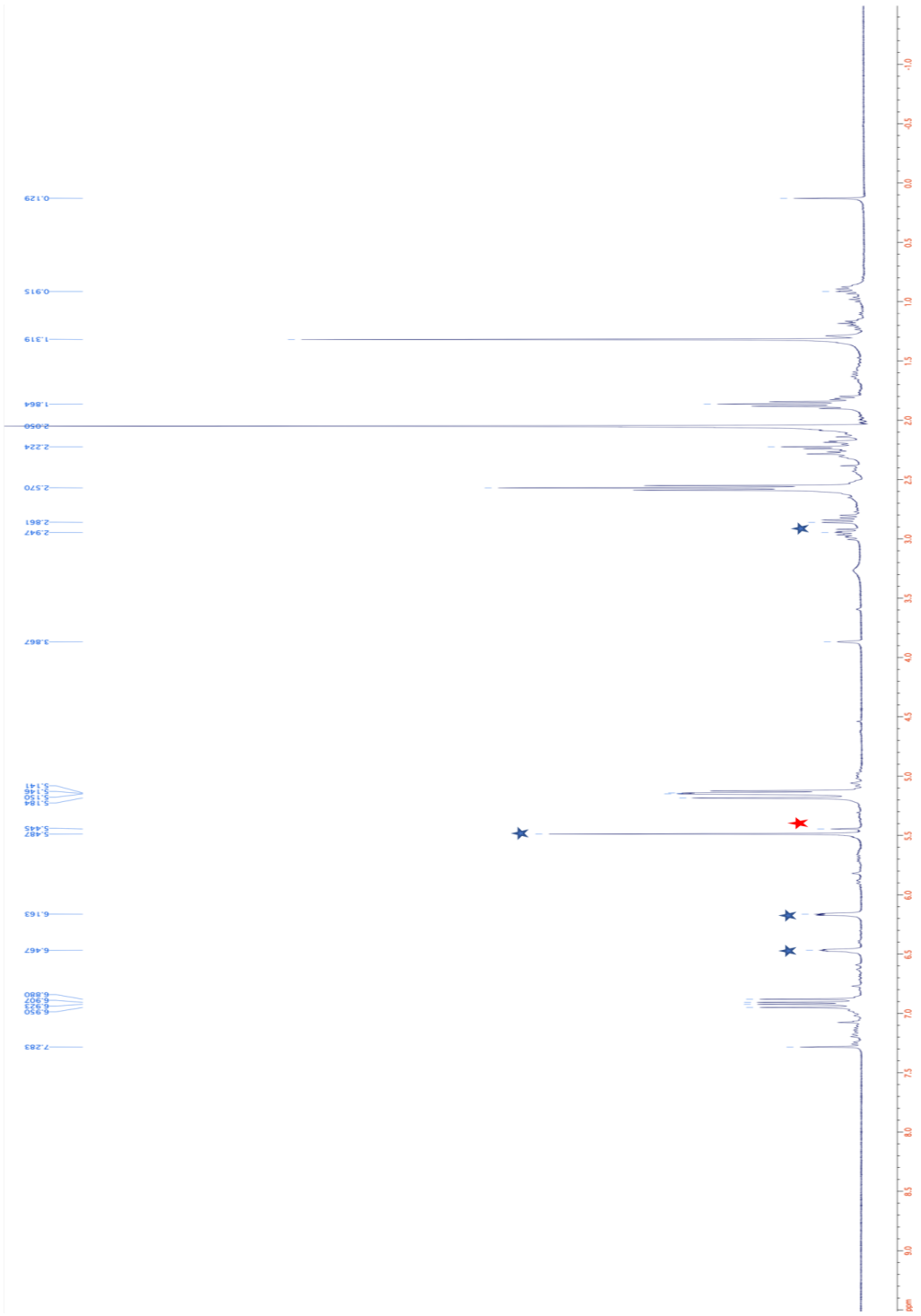


Figure 12. ^{1}H NMR spectrum (400 MHz, acetone-d_6) of crude reaction mixture of **7** with $[CpRu(NCMe)_3]PF_6$ to generate intermediate **16** (labeled with red star) and complex **17** (labeled with blue star) after 30 minutes.

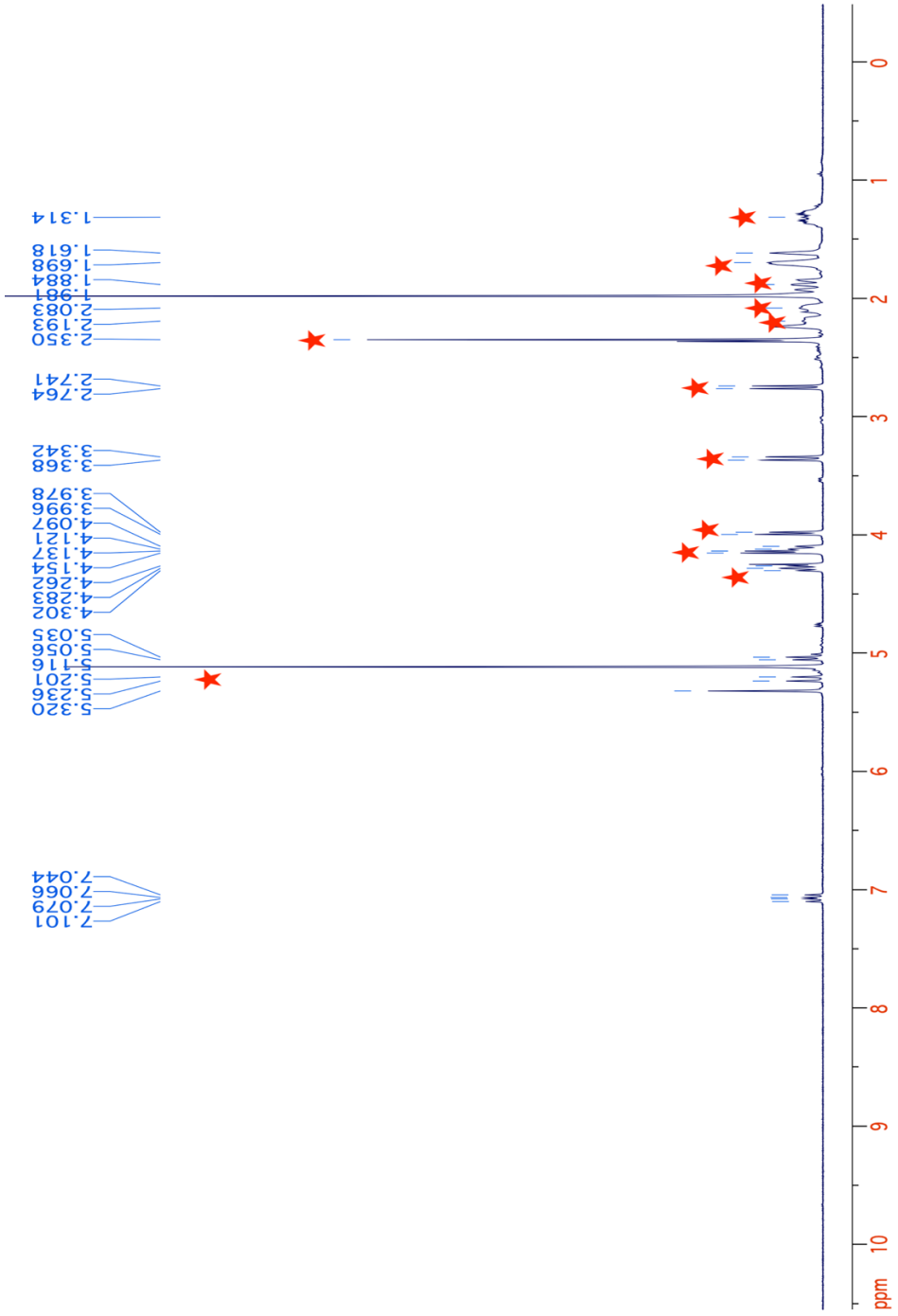


Figure 13. ^{1}H NMR spectrum (500 MHz, CD_2Cl_2) of crude reaction mixture of **14** with $CpRu(NCMe)_3PF_6$ to generate (η^5-cyclopentadienyl)(η^4-1,2-divinylcyclohex-1-ene) Ru acetonitrile hexafluorophosphate (**21**, labeled with red star) in dichloromethane-d_2 at − 20 ˚C.

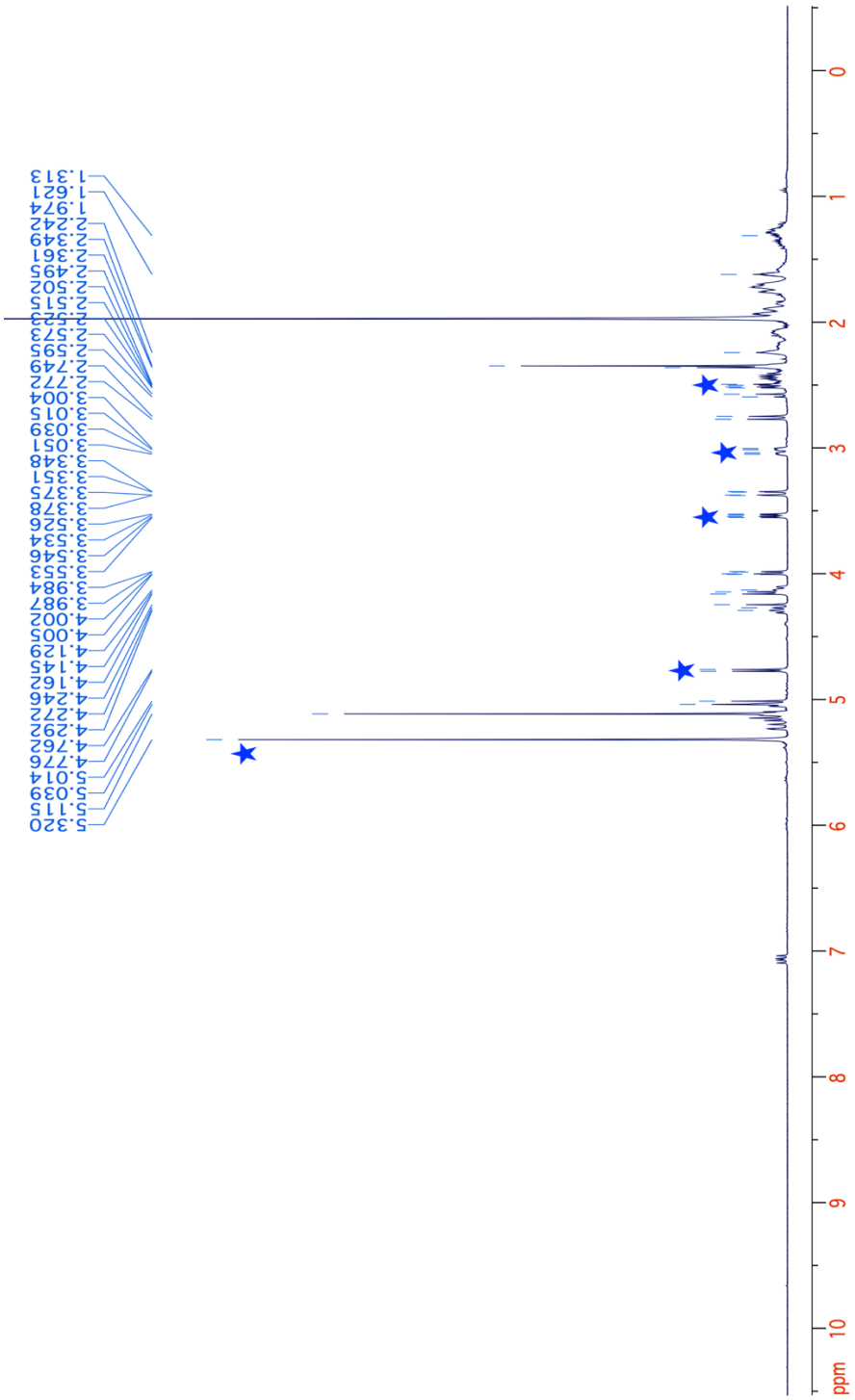


Figure 14. ^{1}H NMR spectrum (500 MHz, CD_2Cl_2) of crude reaction mixture of **14** with $CpRu(NCMe)_3PF_6$ to generate (η^5-cyclopentadienyl)(η^6-1,2-divinylcyclohex-1-ene) Ru hexafluorophosphate (**22,** labeled with blue star) in dichloromethane-d_2 at − 10 ˚C.

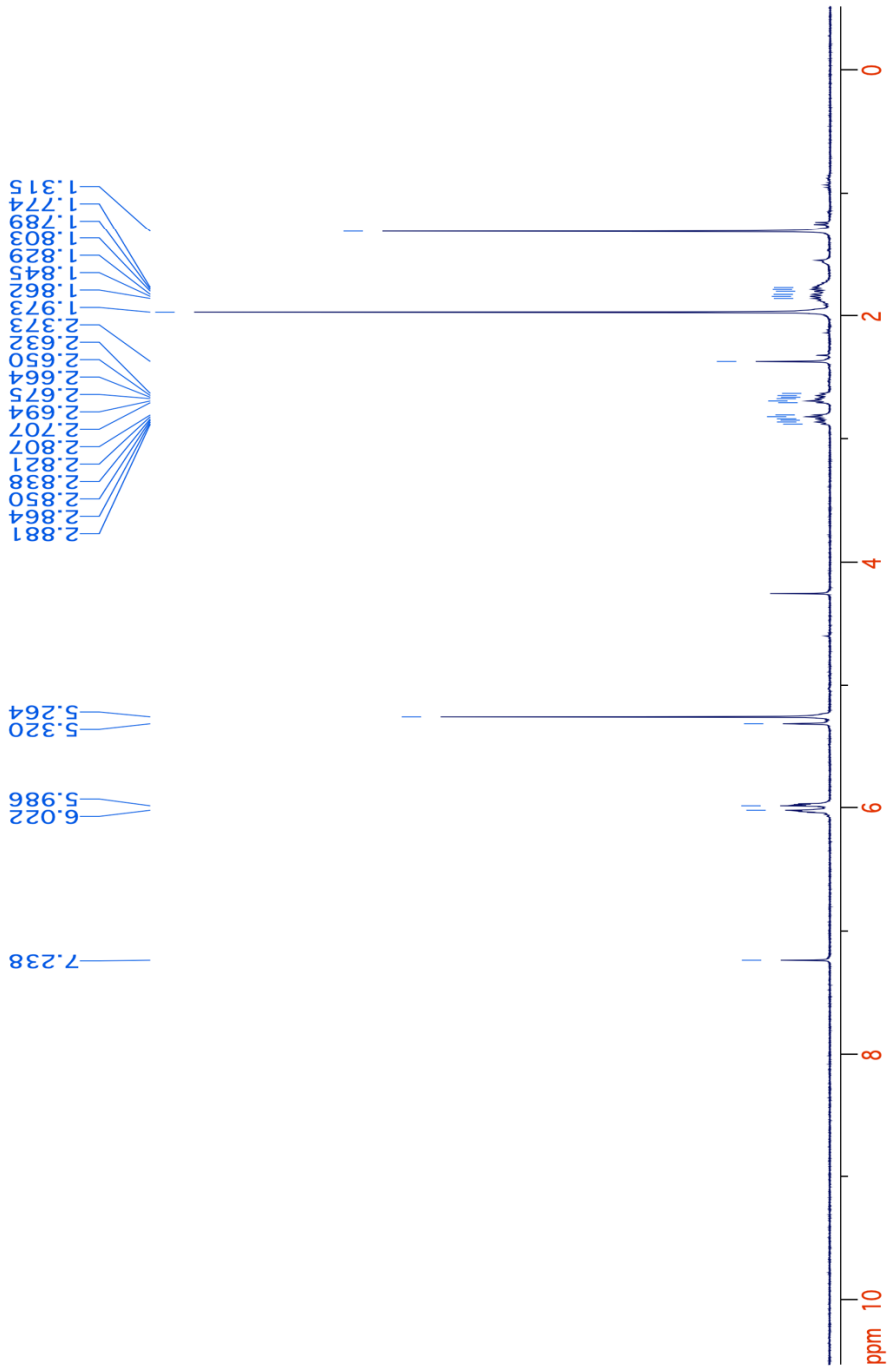


Figure 15. ^{1}H NMR spectrum (500 MHz, CD_2Cl_2) of crude reaction mixture of **14** with $CpRu(NCMe)_3PF_6$ to generate (η^5-cyclopentadienyl)(η^6-1,2,3,4-tetrahydronaphthalene) Ru hexafluorophosphate (**19**) in dichloromethane-d_2.

Figure 16. ^{1}H NMR spectrum (500 MHz, acetone-d_6) of crude reaction mixture of **14-*EZE*-d_2** (0.050 M) with $CpRu(NCMe)_3PF_6$ (0.025 M) to generate complex **28** and **29** in acetone-d_6.

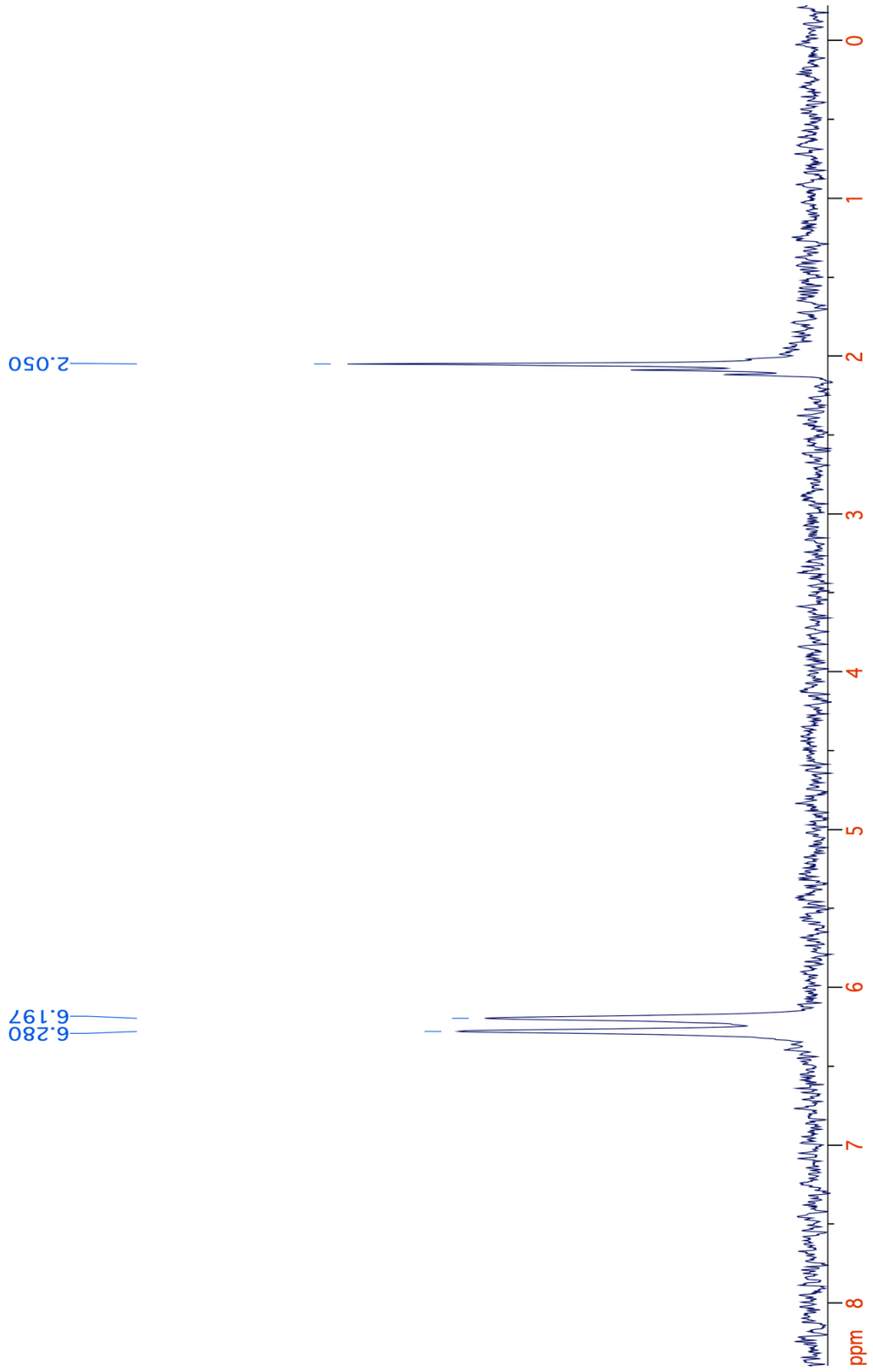


Figure 17. ^{2}H NMR spectrum (500 MHz, acetone) of crude reaction mixture of **14-*EZE*-*d*$_2$** (0.050 M) with $CpRu(NCMe)_3PF_6$ (0.025 M) to generate complex **28** and **29** in acetone.

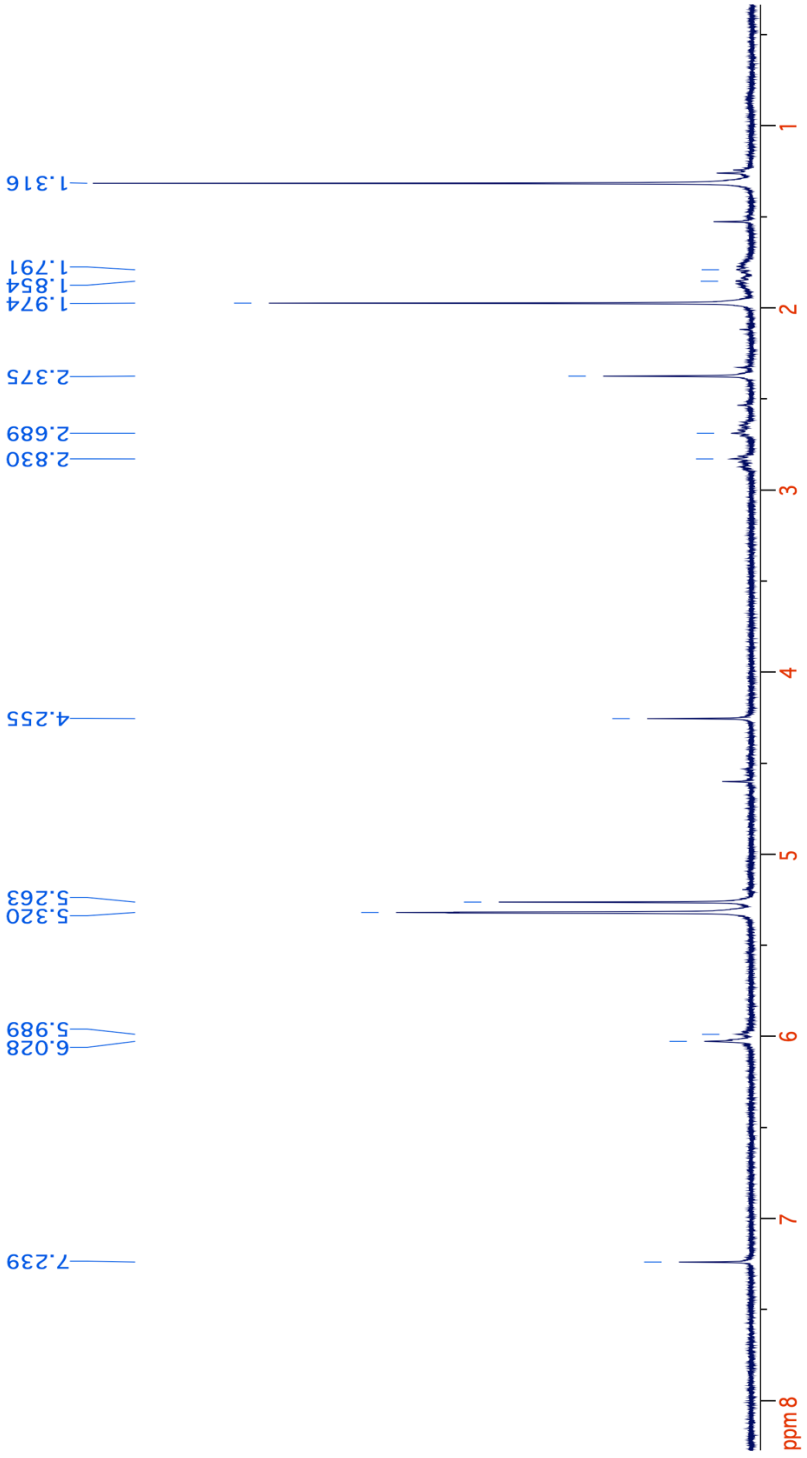


Figure 18. ^{1}H NMR spectrum (400 MHz, CD_2Cl_2) of crude reaction mixture of **14-*ZZZ*-d_2** (0.010 M) with $CpRu(NCMe)_3PF_6$ (0.005 M) to generate complex **29** in dichloromethane-d_2.

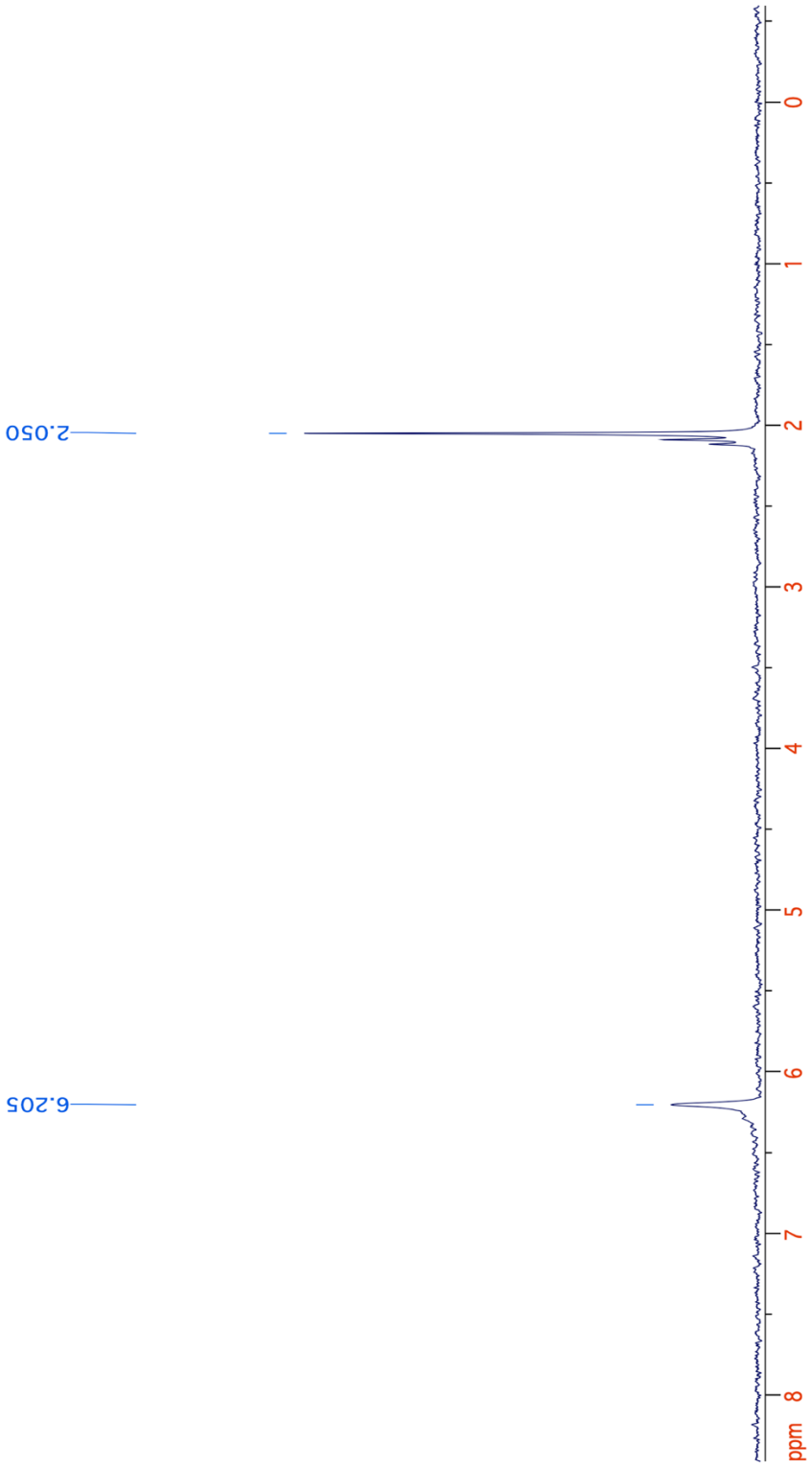


Figure 19. ^{2}H NMR spectrum (500 MHz, acetone) of crude reaction mixture of **14-*ZZZ*-*d*$_2$** (0.010 M) with $CpRu(NCMe)_3PF_6$ (0.005 M) to generate complex **29** in acetone.

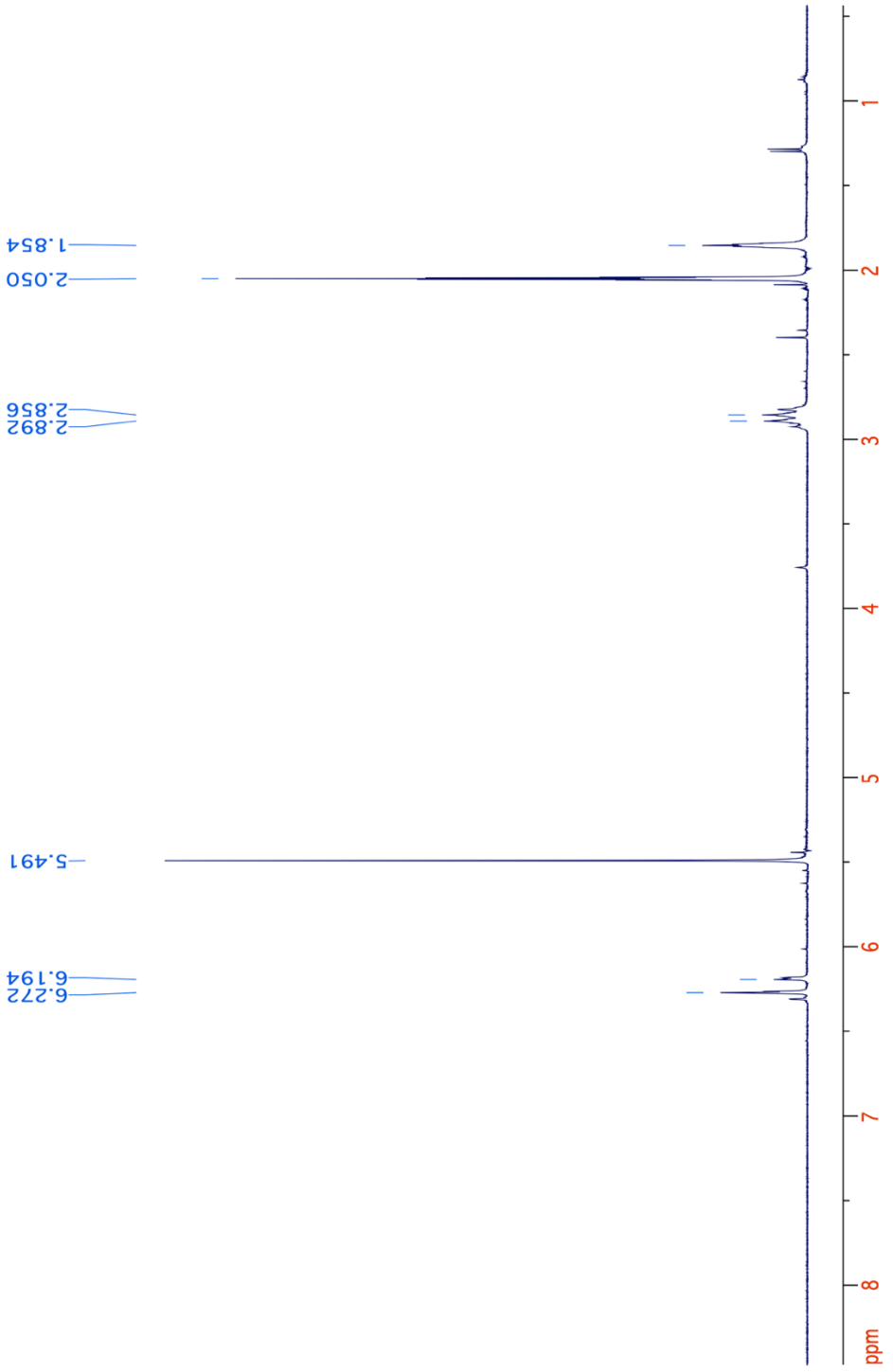


Figure 20. ^{1}H NMR spectrum (500 MHz, acetone-d_6) of crude reaction mixture of **14-*ZZZ*-d_2** (0.025 M) with $CpRu(NCMe)_3PF_6$ (0.013 M) to generate complex **28** and **29** in acetone-d_6.

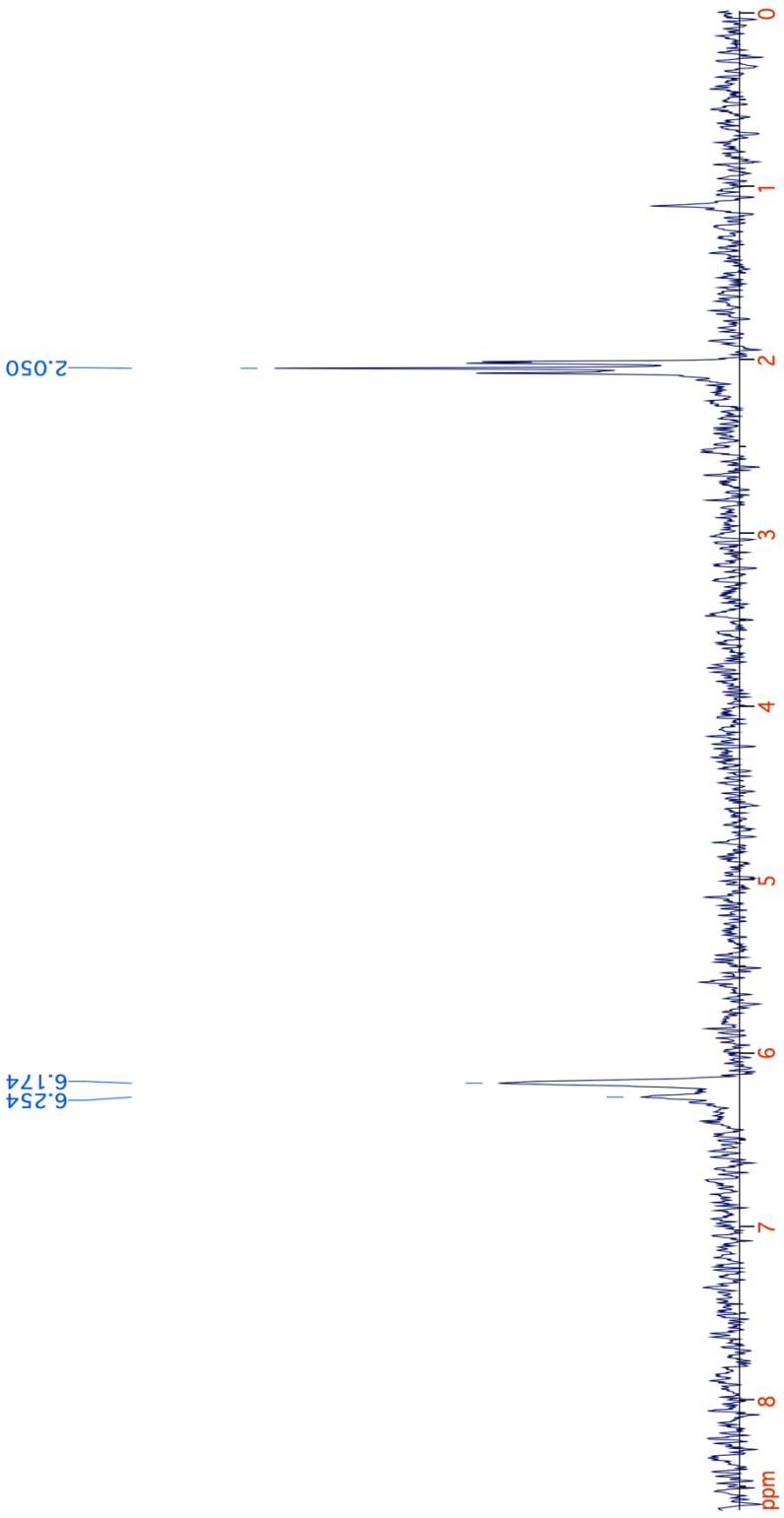


Figure 21. ^{2}H NMR spectrum (500 MHz, acetone) of crude reaction mixture of **14-*ZZZ*-*d*$_2$** (0.025 M) with $CpRu(NCMe)_3PF_6$ (0.013 M) to generate complex **28** and **29** in acetone.

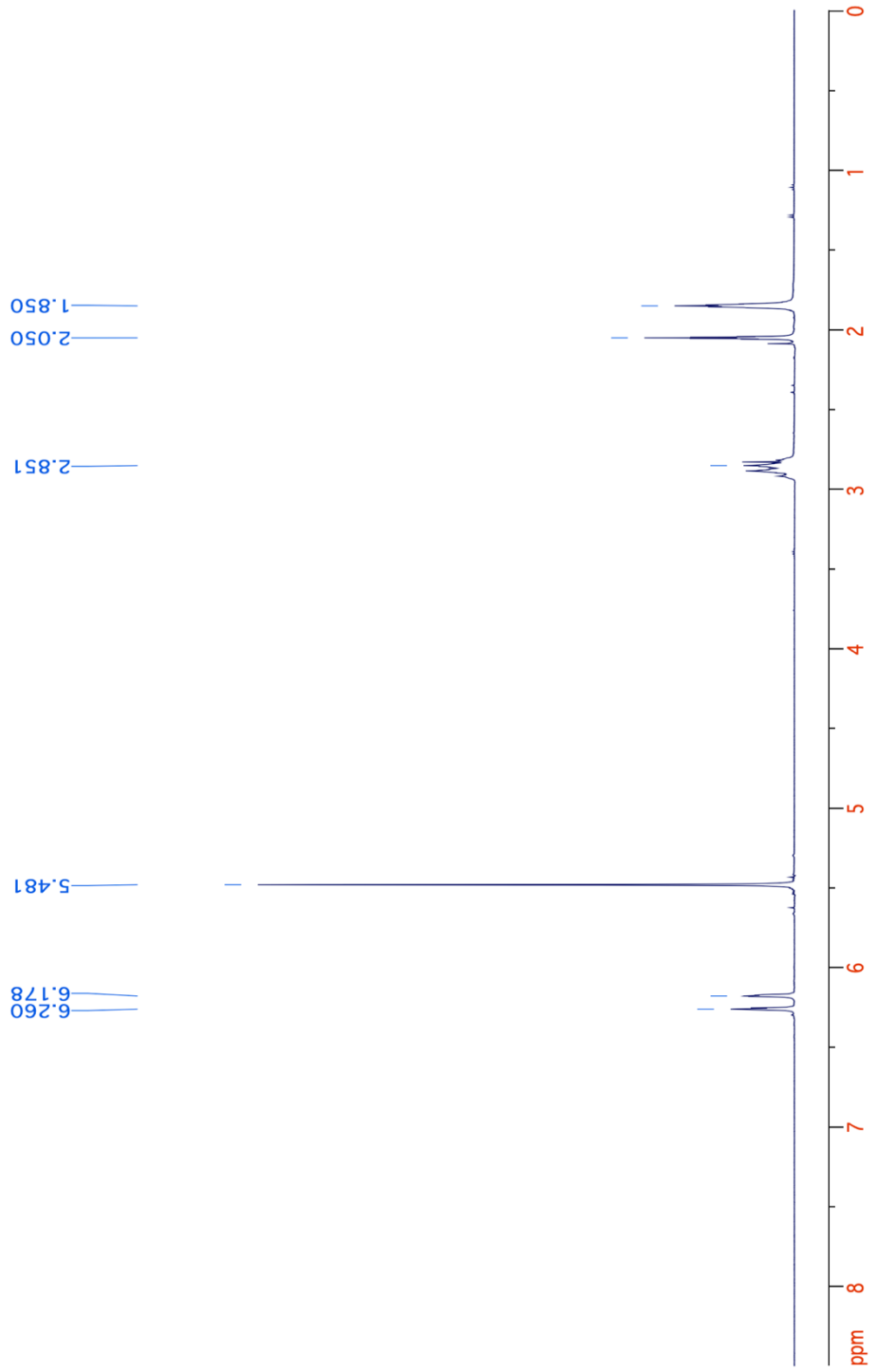


Figure 22. ^{1}H NMR spectrum (500 MHz, acetone-d_6) of crude reaction mixture of **14-ZZZ-*d*$_2$** (0.075 M) with CpRu(NCMe)$_3$PF$_6$ (0.038 M) to generate complex **28** and **29** in acetone-d_6.

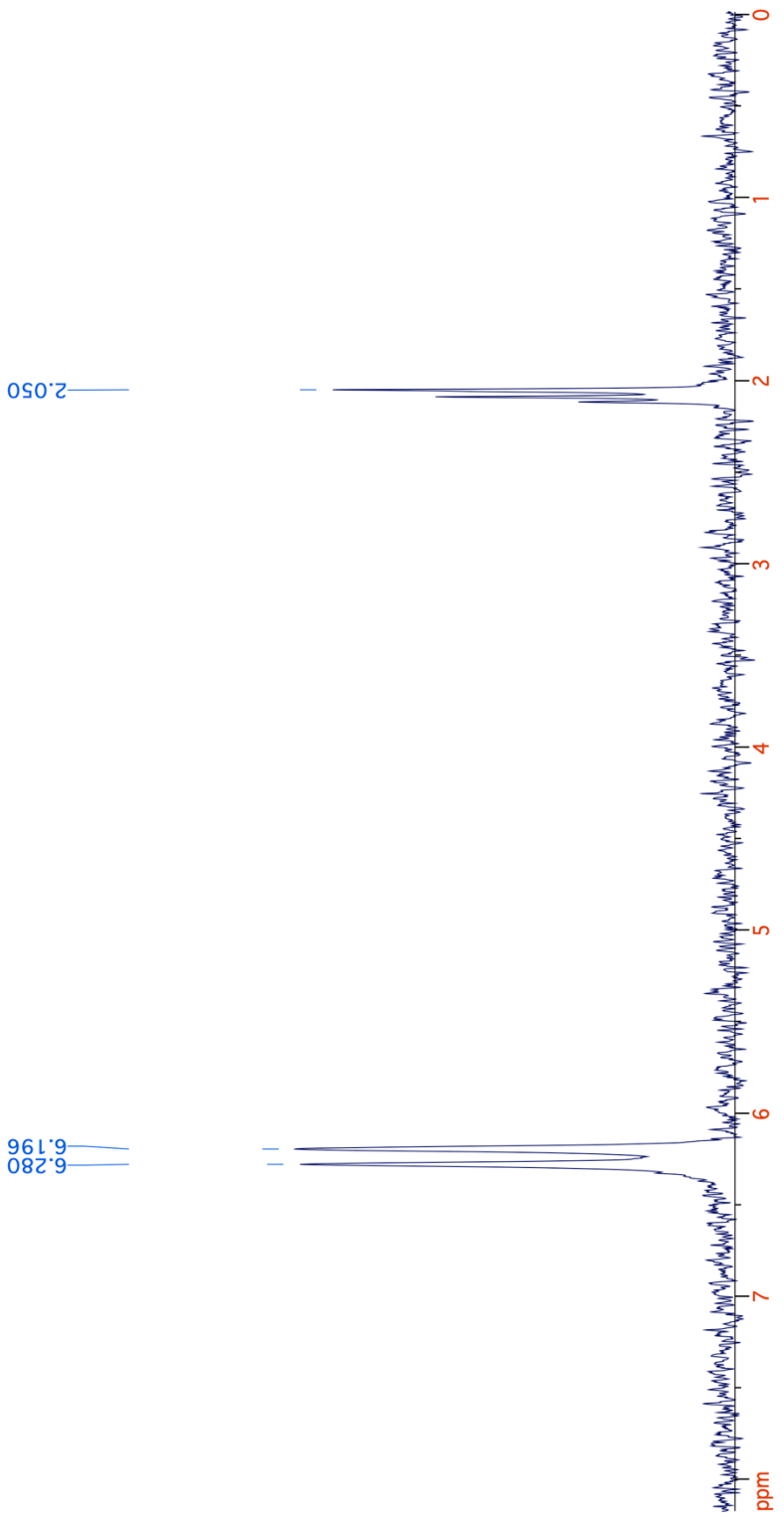


Figure 23. ^{2}H NMR spectrum (500 MHz, acetone) of crude reaction mixture of **14-*ZZZ*-*d*$_2$** (0.075 M) with CpRu(NCMe)$_3$PF$_6$ (0.038 M) to generate complex **28** and **29** in acetone.

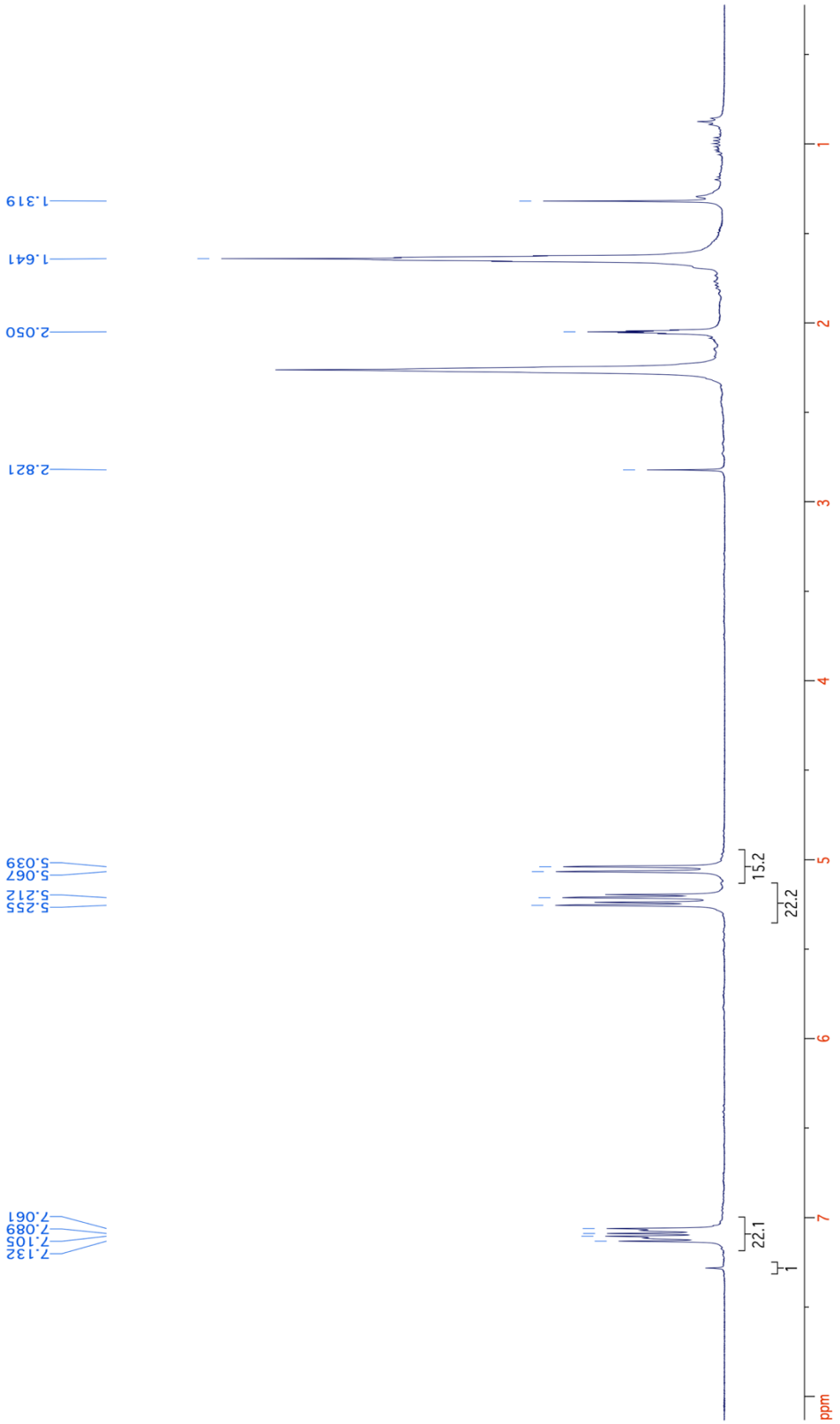


Figure 24. ^{1}H NMR spectrum (400 MHz, acetone-d_6) of triene **14** and **14-*EZE*-d_2**.

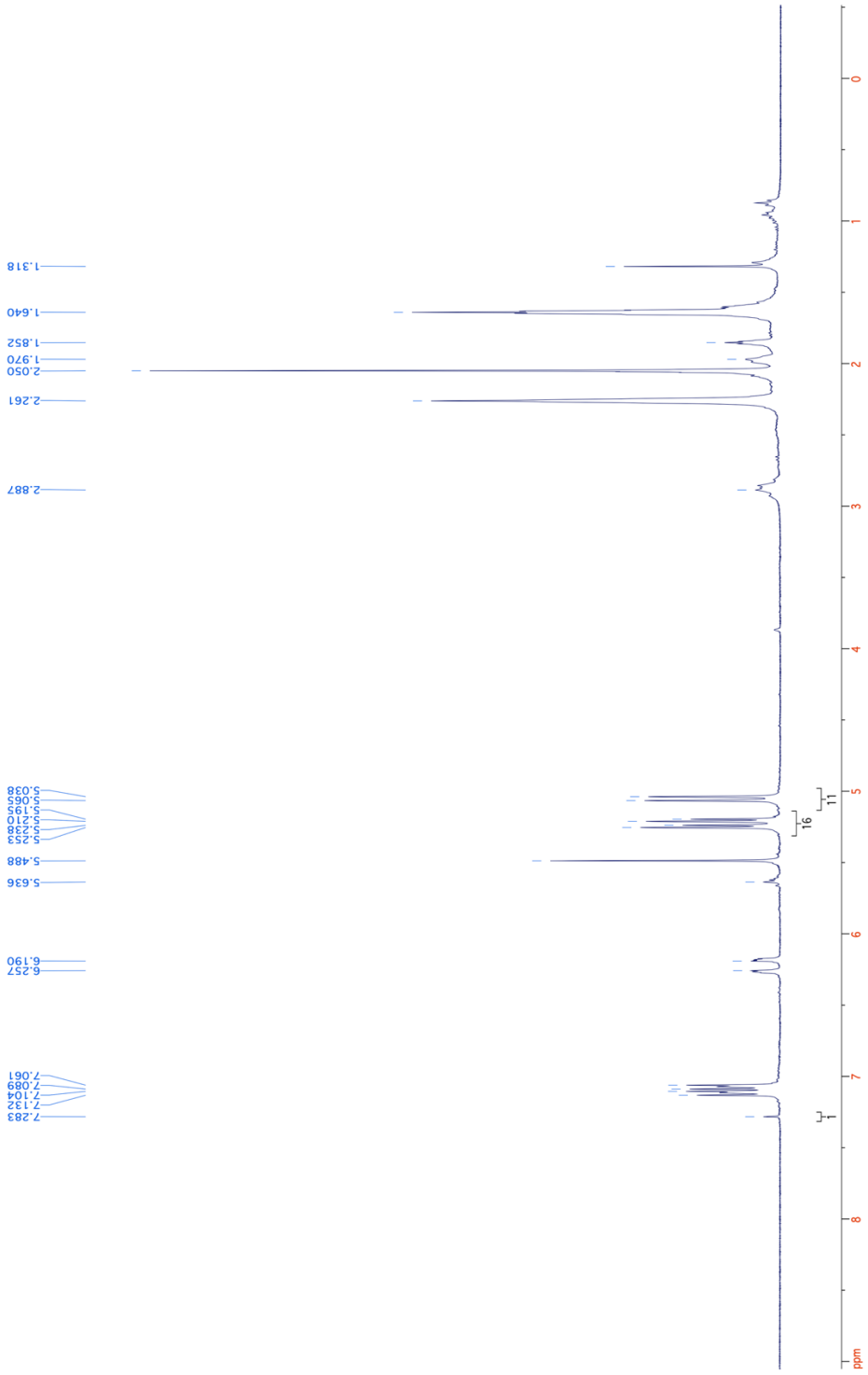


Figure 25. ^{1}H NMR spectrum (400 MHz, acetone-d_6) of crude reaction mixture of **14** (1 eq.) and **14-*EZE*-d_2** (0.8 eq.) with [CpRu(NCMe)$_3$]PF$_6$ (0.3 eq.) at ambient temperature overnight.

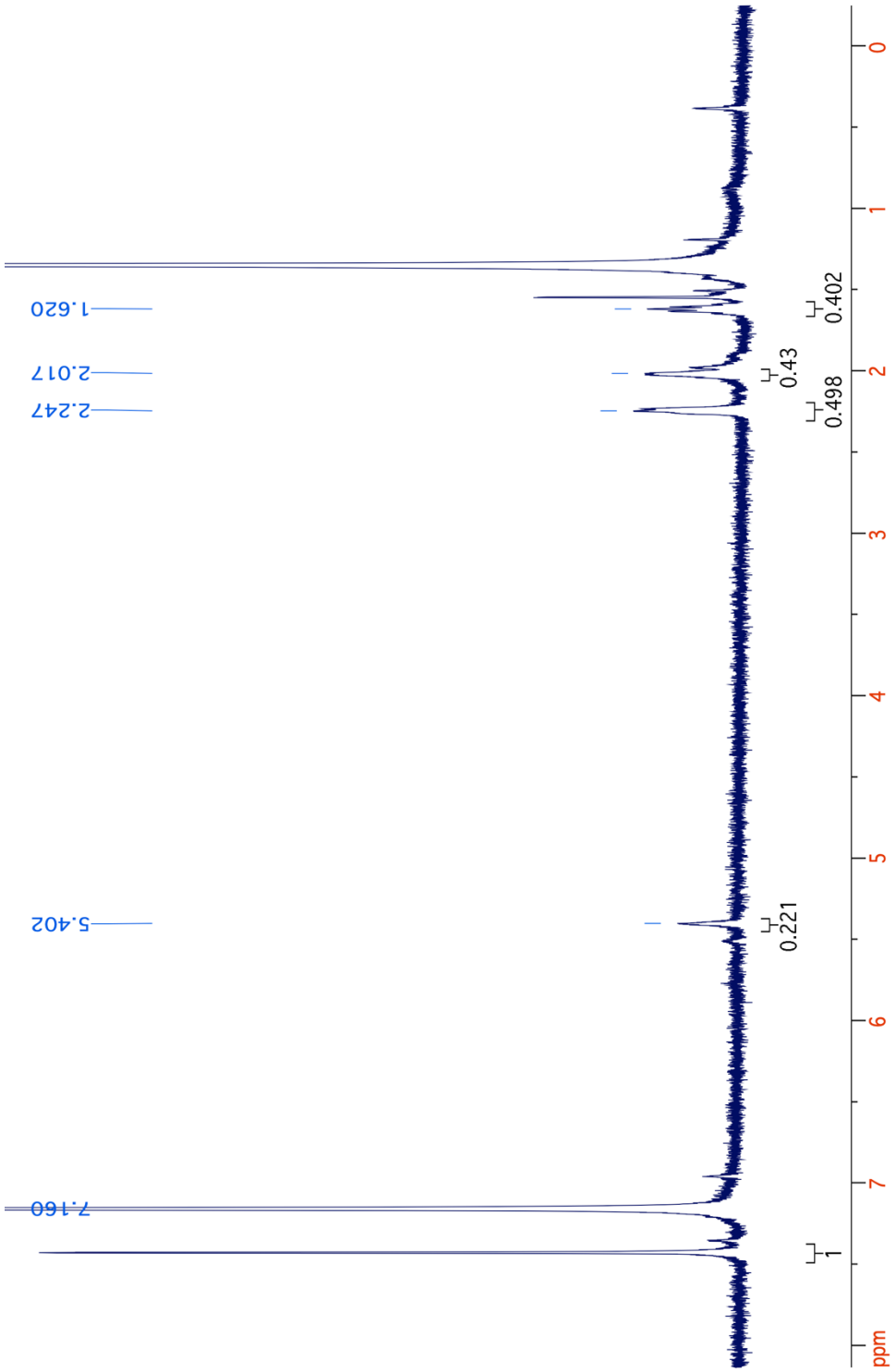


Figure 26. ^{1}H NMR (400 MHz, bezene-d_6) spectrum of crude reaction mixture of heating 1,2-divinylcyclohex-1-ene (**14**) for 650 minutes.

Figure 27. ^{1}H NMR (400 MHz, acetone-d_6) spectrum of crude reaction mixture of photolyzing 1,2-divinylcyclohex-1-ene (**14**) for 8 days.

E. References

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