Studies Towards the Acceleration of Diels -Alder Reactions using η^6-metal Arene Complex Substituents

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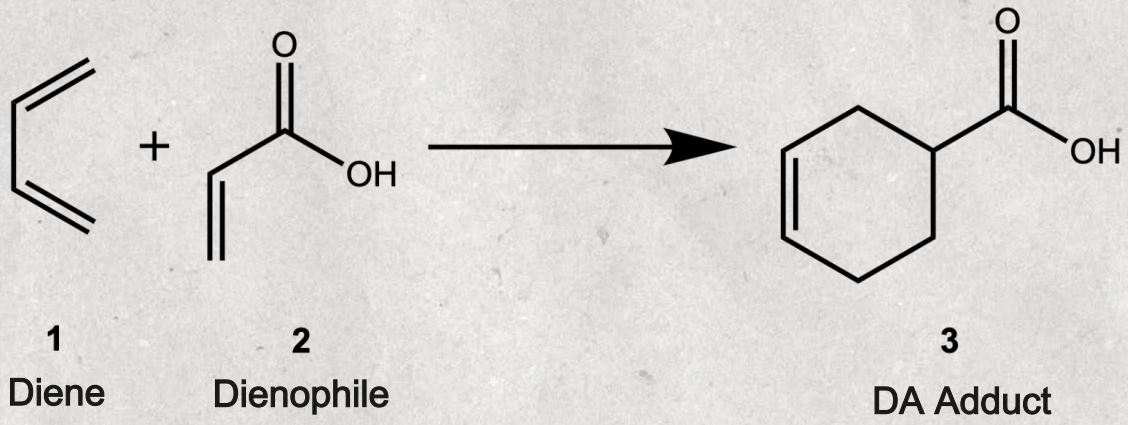
The Diels-Alder (DA) Reaction



1 Diene

2 Dienophile

3 DA Adduct

Cycloaddition reaction between conjugated diene (1) and two atom π system termed the dienophile (2)

- Product (3) is an unsaturated six-membered ring

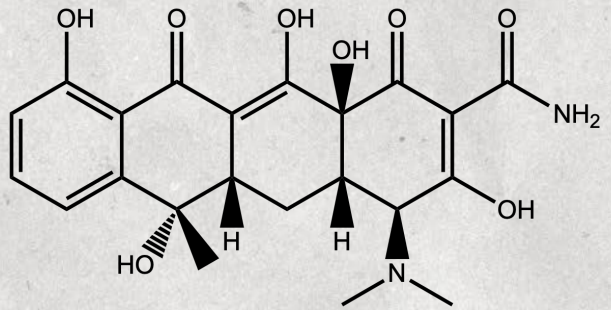
Require an electron-withdrawing group (EWG) to proceed at a reasonable rate

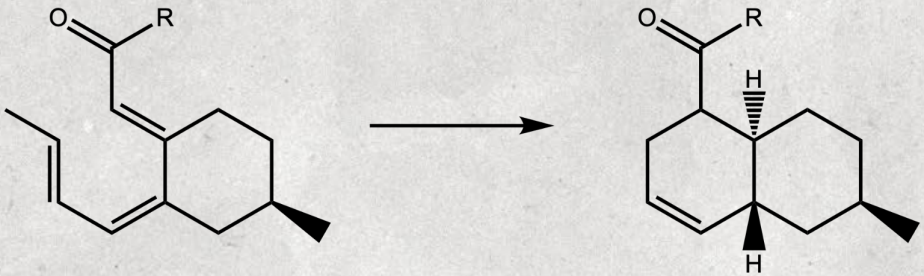
- Functional groups conjugated with π system
  - Commonly nitriles, carbonyl, and nitro groups

Importance of DA Reactions

Tetracycline Antibiotics:

- Class of Broad-Spectrum Antibiotics
  - Plague, typhoid, syphilis, anthrax, malaria

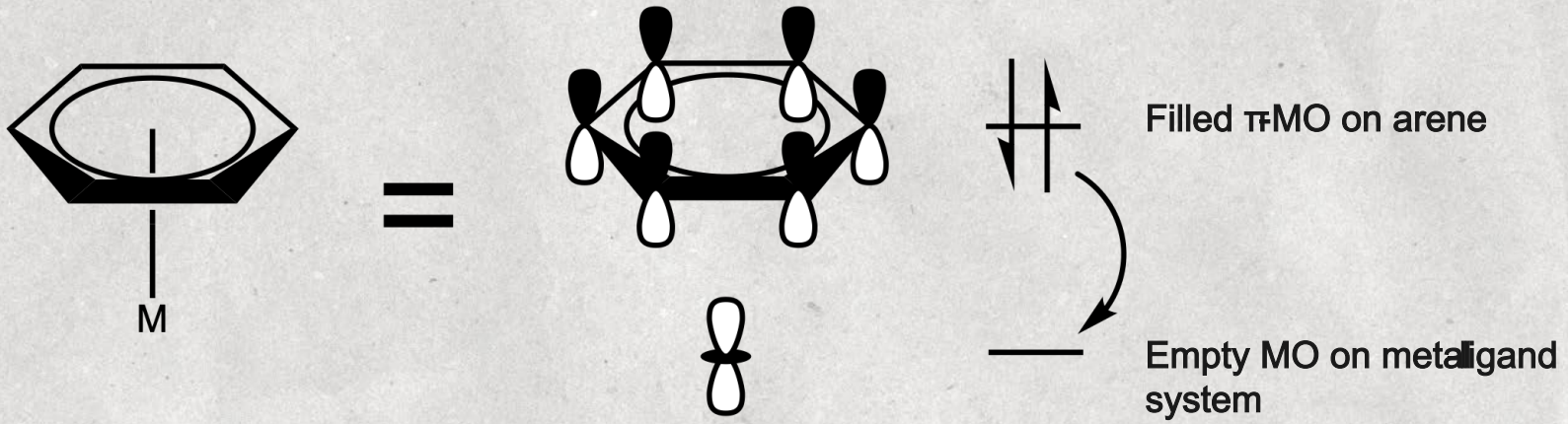




Lovastatin:

- Medication to treat high blood cholesterol
- Reduce the risk of cardiovascular disease

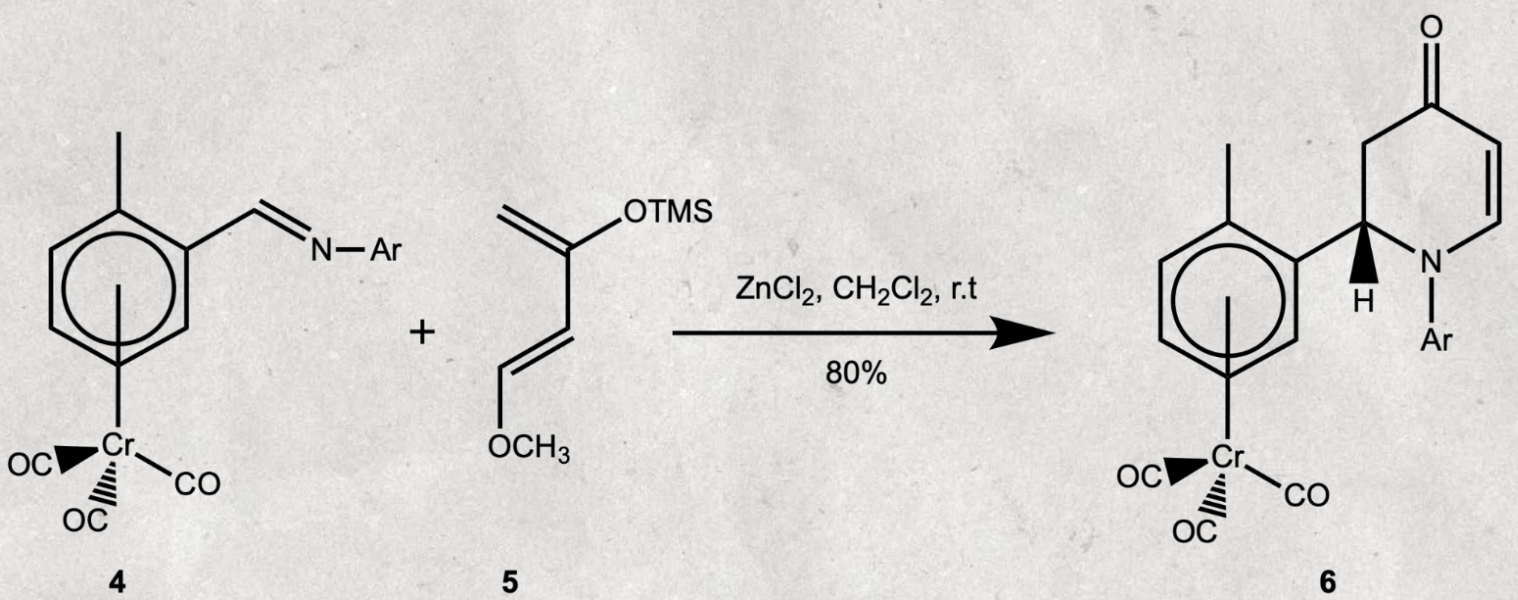
Metal-Ligands as EWGs



Metal-arene η^6 complexation occurs when a metal-ligand fragment bonds to six carbon atoms on the face of an arene

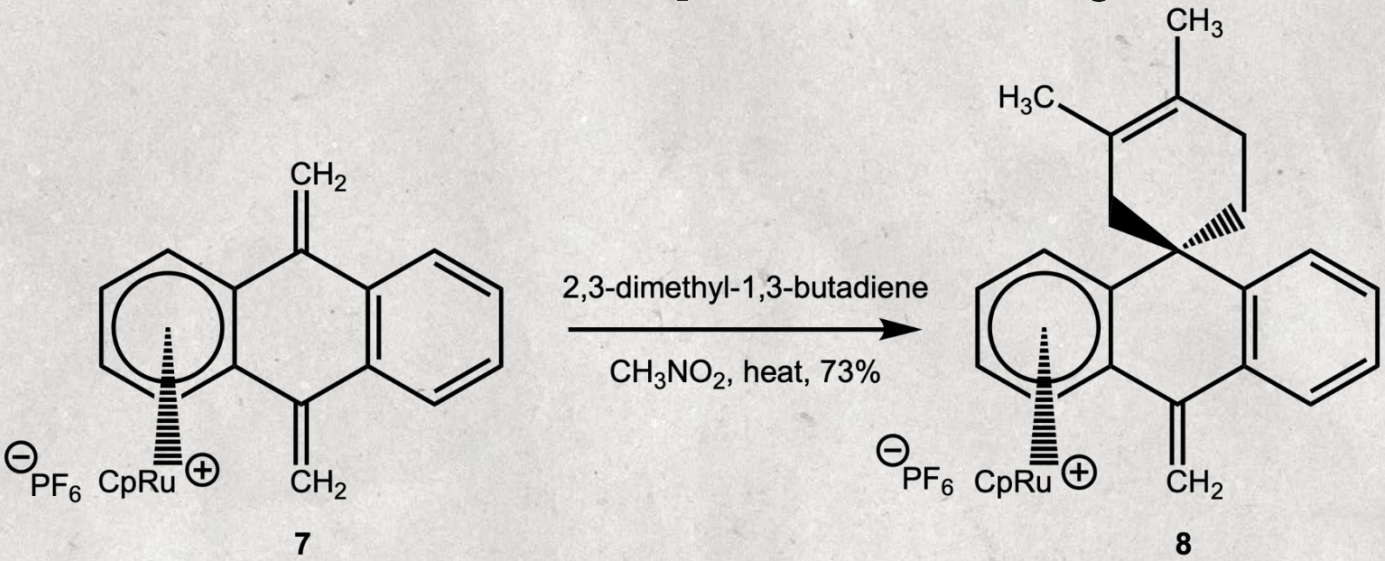
- Modification of reactivity
  - Lowering of arene reactivity associated with electrophilic aromatic substitution reactions (EAS)
- Most metal ligands are highly electron withdrawing

Chromium Catalyzed DA



4 5 6

Ruthenium Complex Catalyzed DA

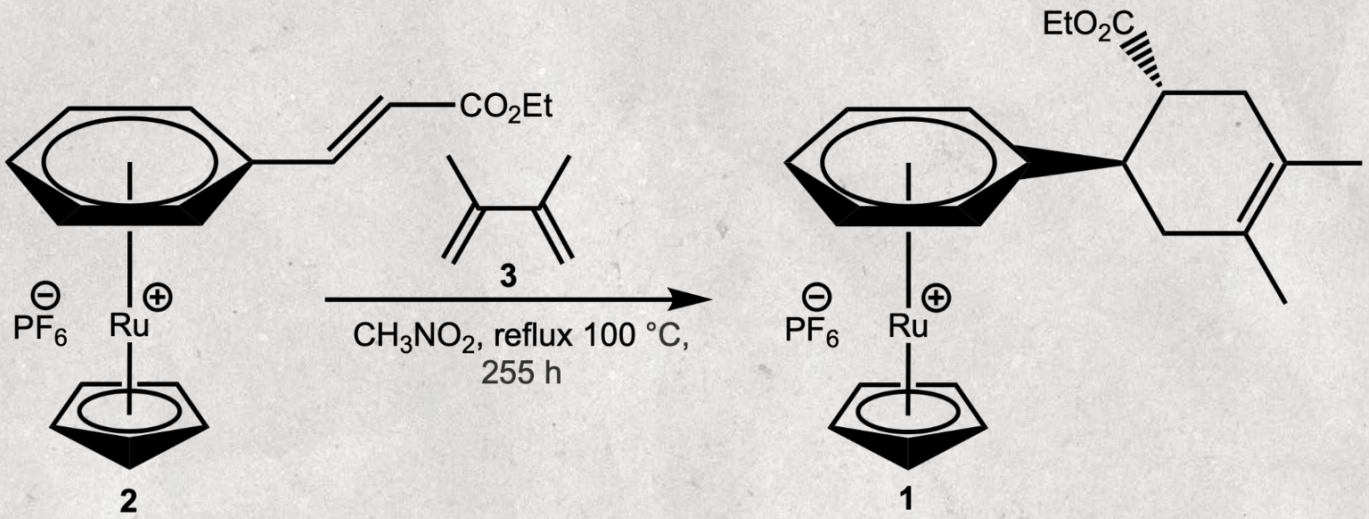


7 8

Ruthenium Advantages:

- Ru fragment is cationic compared to neutral chromium complex
  - May contribute to increased electron withdrawing characteristics
- Ru is easily recoverable
  - Cost-efficient reusable catalyst

Synthesis of DA Adduct

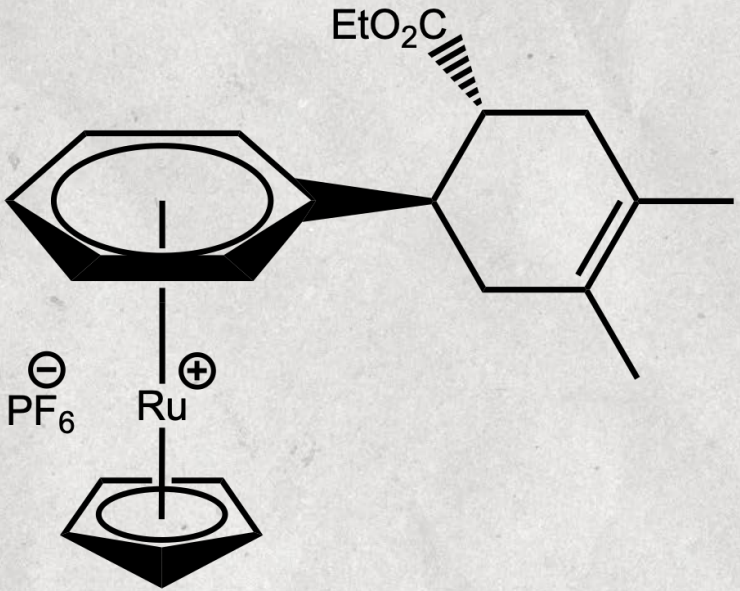


Improved synthetic procedure: "Diene Feeding" Method

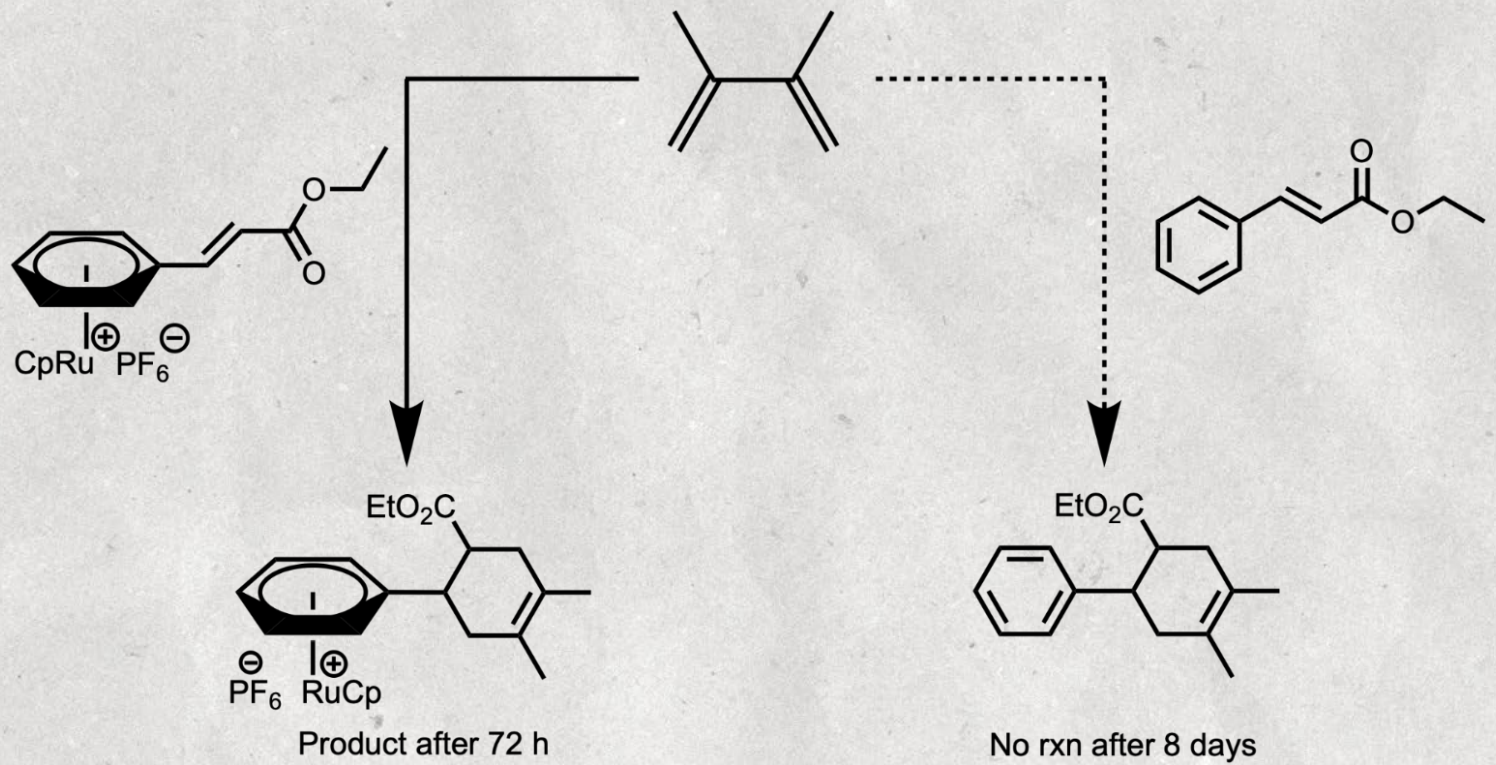
- BP of nitromethane = 100 °C
- BP of 2,3-dimethyl-1,3-butadiene (3) = 8 °C

Characterization of DA Adduct

- ^{1}H NMR
- ^{13}C NMR
- Infrared (IR)
- Purified crystals were analyzed by X-ray diffraction (XRD)
  - Not publication quality



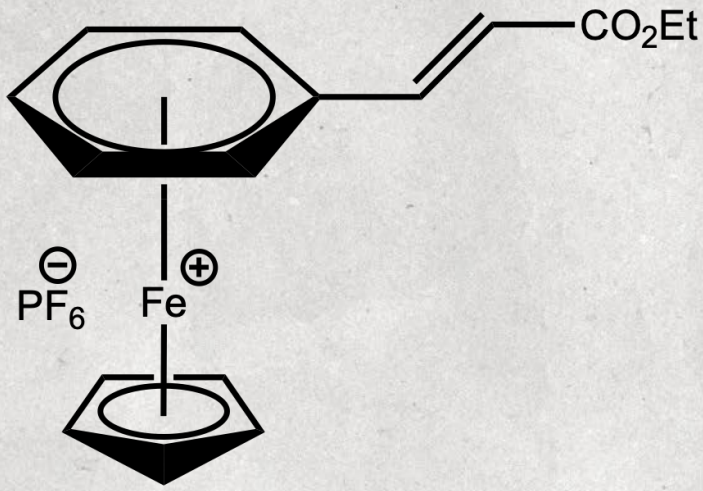
Control Study



Product after 72 h

No rxn after 8 days

Analogous Iron Complex



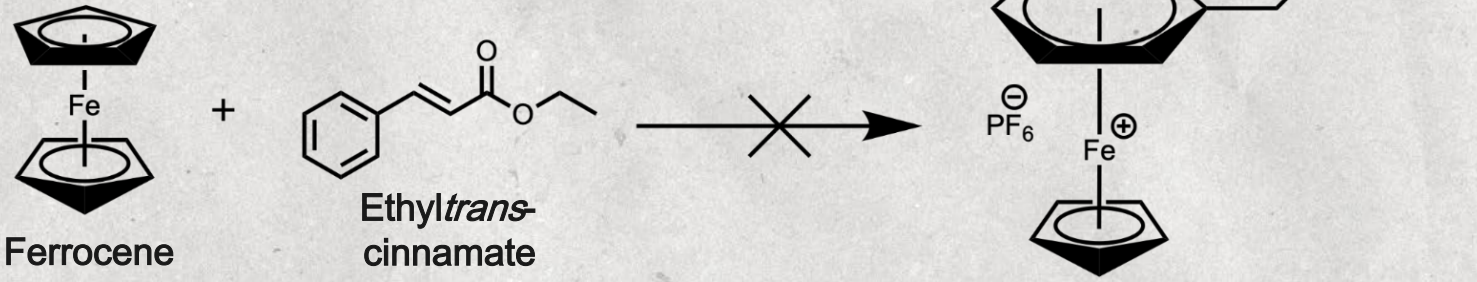
- $CpFe^+$ complexes are also known to be electron withdrawing
  - Kinetic studies reveal comparable rates to two nitro groups

Advantages:

- More cost effective than Ruthenium
- Easier removal of the $CpFe^+$ Complex after DA reaction
  - Photolytic cleavage

Previous Synthetic Attempts

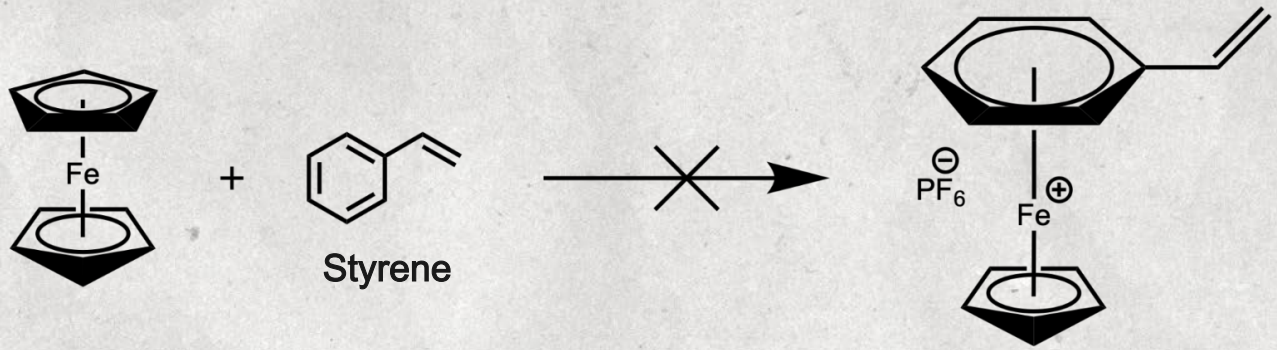
1



Ferrocene

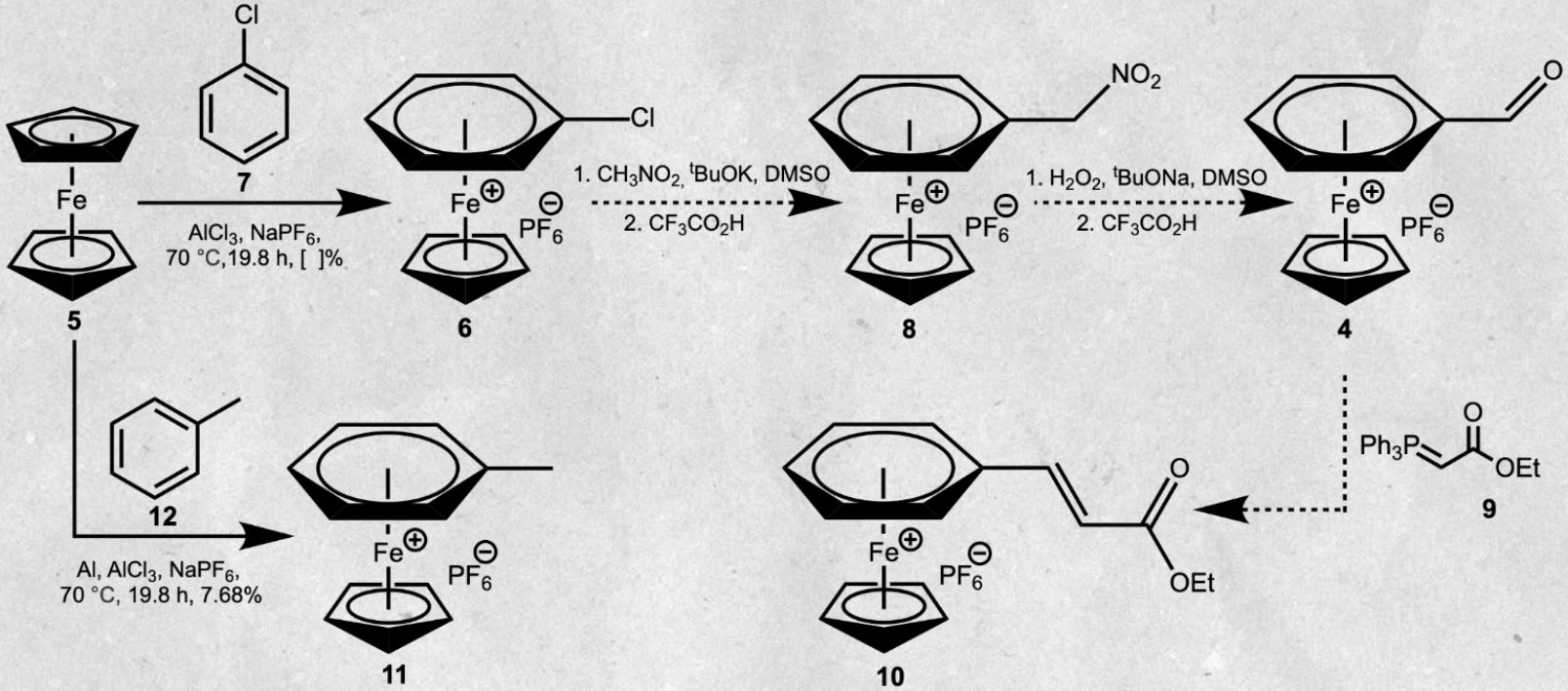
Ethyl*trans*-cinnamate

2



Styrene

New Proposed Synthesis



Future Directions

1) Synthesis of Proposed Iron Complex

2) Complete Characterization of Ru and Fe Complexes and Adducts

3) Kinetic Studies Comparing rates of Metallated Dienophiles to the Non-Metallated analogs

References

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Thanks!

Do you have any questions?

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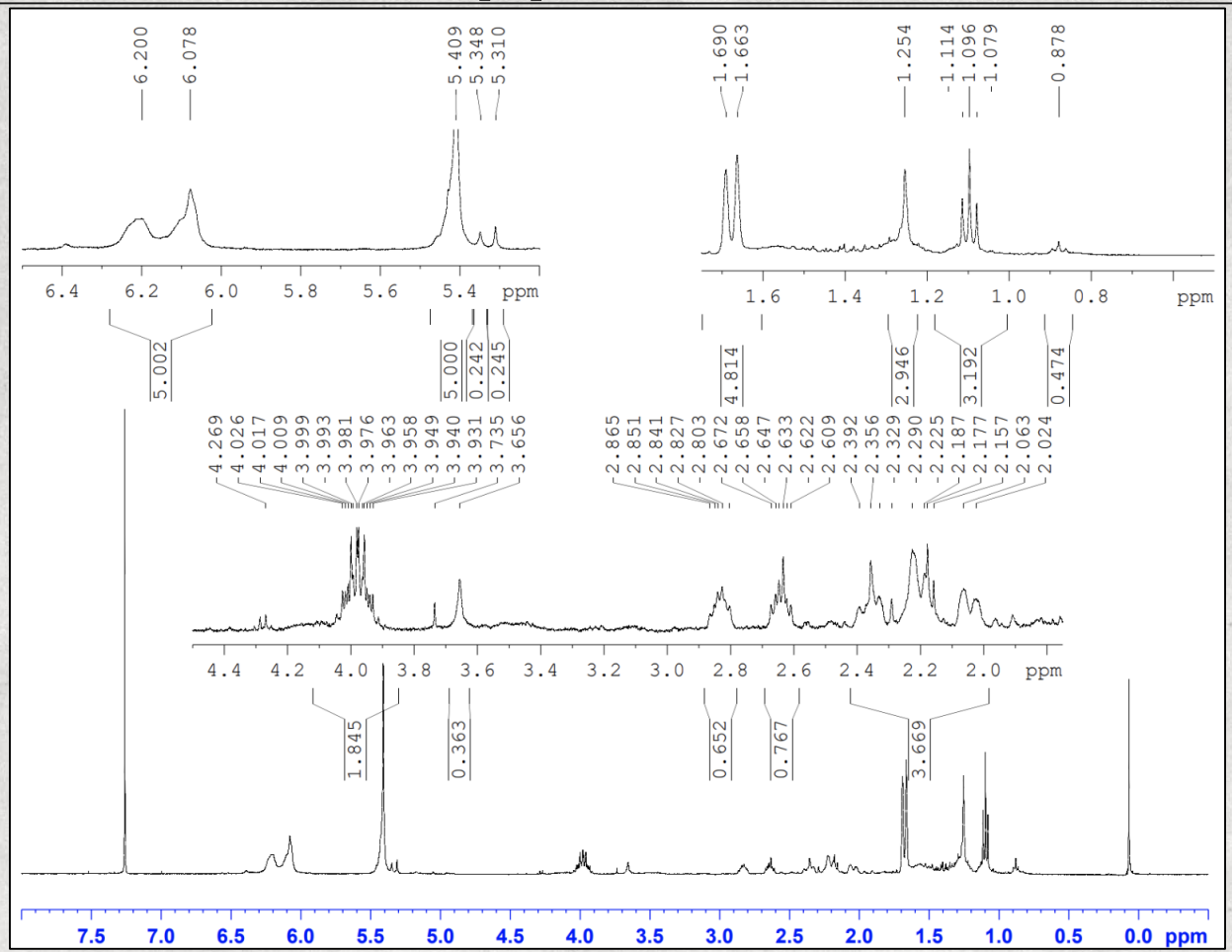
Appendix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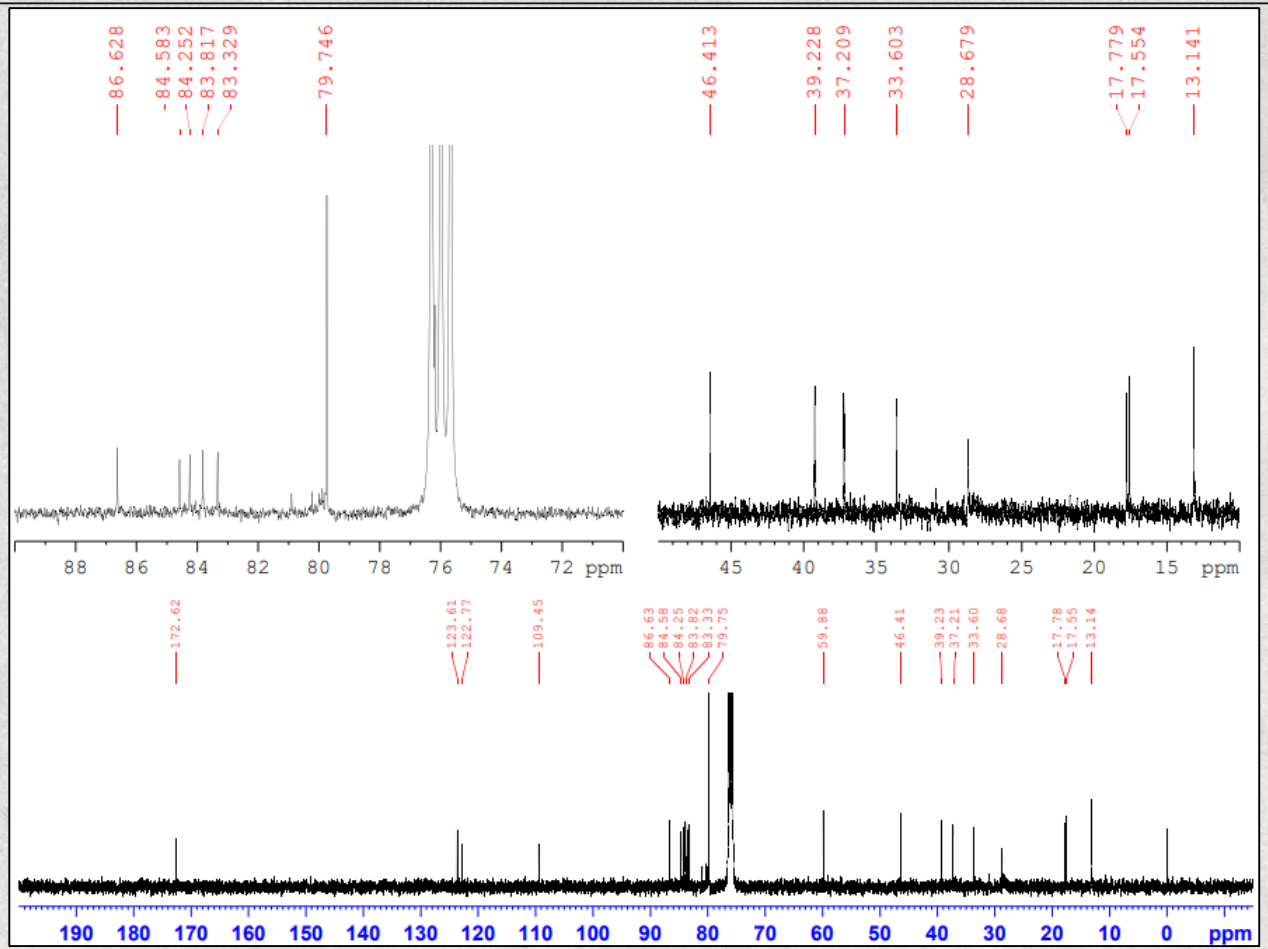
6.078
5.409
5.348
5.310
1.690
1.663
1.254
1.114
1.096
1.079
0.878
6.4 6.2 6.0 5.8 5.6 5.4 ppm
1.6 1.4 1.2 1.0 0.8 ppm
5.002
5.000
0.242
0.245
4.814
2.946
3.192
0.474
4.269
4.026
4.017
4.009
3.999
3.993
3.981
3.976
3.963
3.958
3.949
3.940
3.931
3.735
3.656
2.865
2.851
2.841
2.827
2.803
2.672
2.658
2.647
2.633
2.622
2.609
2.392
2.356
2.329
2.290
2.225
2.187
2.177
2.157
2.063
2.024
4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 ppm
1.845
0.363
0.652
0.767
3.669
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm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83.329
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46.413
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17.554
13.141
88 86 84 82 80 78 76 74 72 ppm
45 40 35 30 25 20 15 ppm
172.62
123.61
122.77
109.45
86.63
84.58
84.25
83.82
83.33
79.75
59.88
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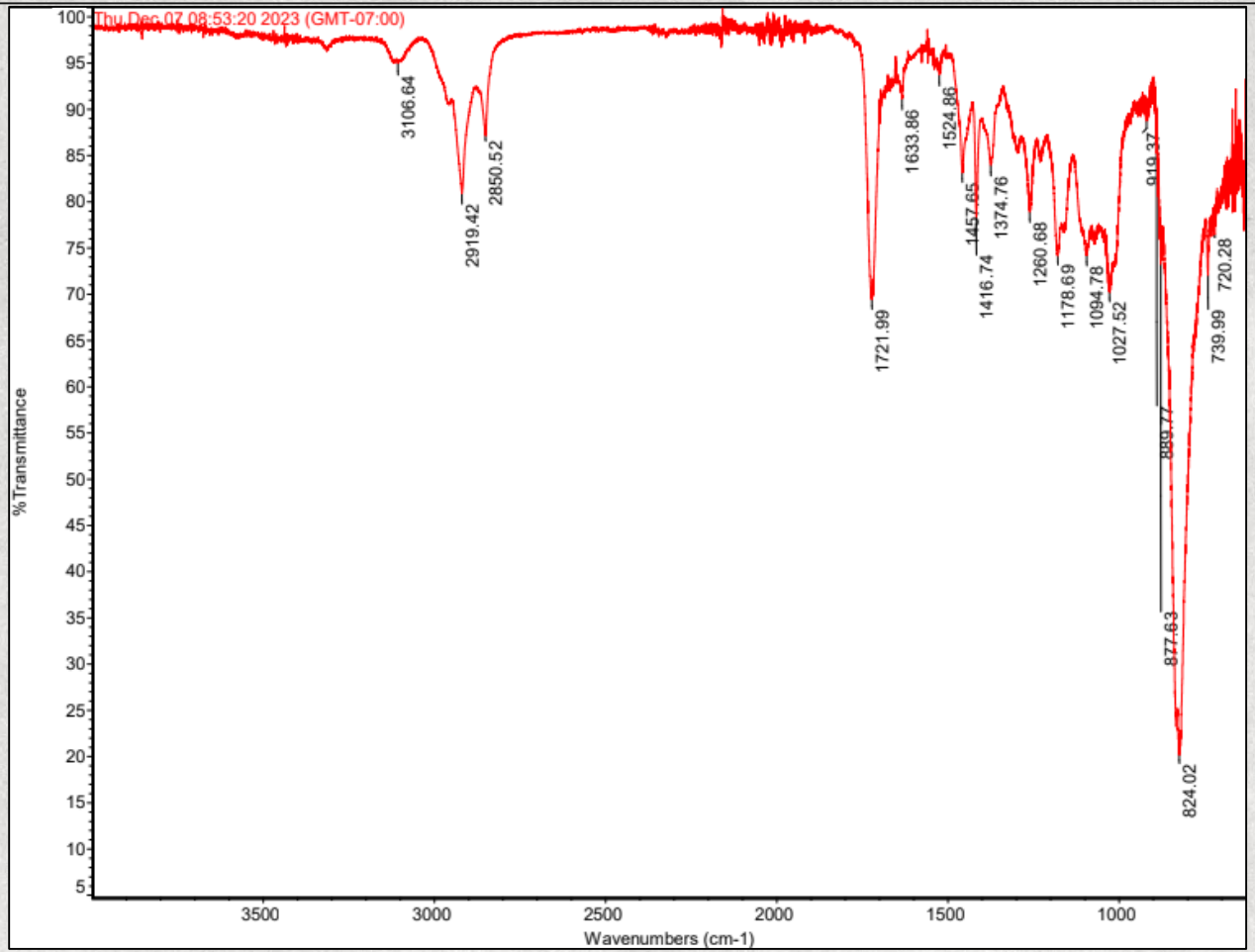
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1094.78
1027.52
877.63
824.02
739.99
720.28