

# Olefin Metathesis: Catalysts and Catalysis

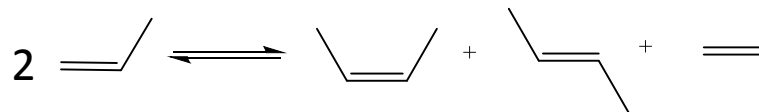
Matthew Cohan  
and Dr. Marcetta Darensbourg

# Outline

- Introduction
  - What is metathesis?
  - Why is it important?
- Reactions
  - Simple synthesis reactions
  - Catalysis for C-C formation
  - Olefin metathesis
- Historical background
  - Nobel prizes
  - Mechanisms
- Catalysts types
  - Grubbs
  - Schrock
- Industrial and Synthetic Organic Applications

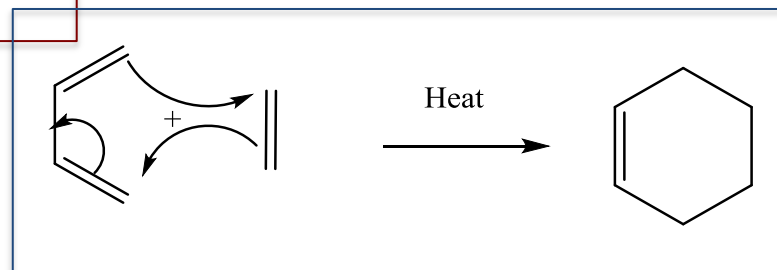
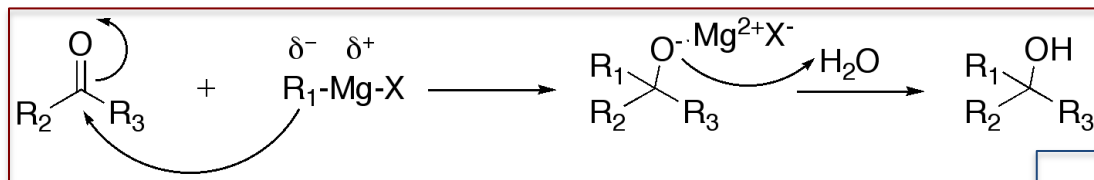
# Metathesis

- Metathesis in the general sense is the formation of a product that has exchanged bonds between starting materials.
  - $A-B + C-D \rightarrow A-D + C-B$
  - Double replacement/displacement reaction.
- Metathesis in acid-base chemistry and ion exchange is well defined and simple. However, until recently, bond formation in organic reactants is difficult without the presence of catalysts.
- In the past 30 years or so industry has used olefin metathesis to form alkenes into other alkenes through a variety of mechanisms.



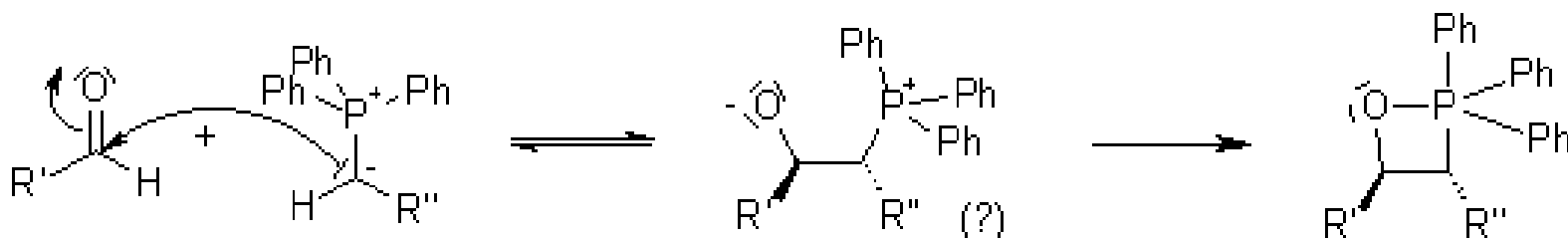
# Metathesis Reactions

- Simplest are ion exchange in salts and acid-base neutralization
  - $\text{KCl} + \text{NaF} \rightarrow \text{NaCl} + \text{KF}$
  - $\text{H}_2\text{SO}_4 + 2\text{NaOH} \rightarrow \text{Na}_2\text{SO}_4 + 2\text{H}_2\text{O}$
- More synthetically useful reactions include
  - The Grignard, Diels-Alder and Wittig reactions

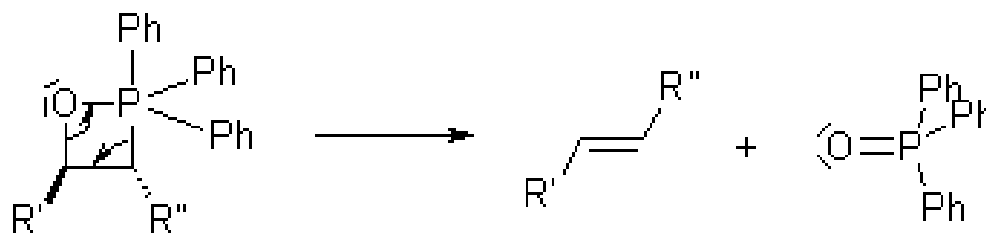


# Wittig Reaction

- Provides the same end goal of C-C bond formation but through a ring opening/closing pathway. A pathway that has similarity to catalytic olefin metathesis.



- Then the ring opening step forms the all important C=C bond.



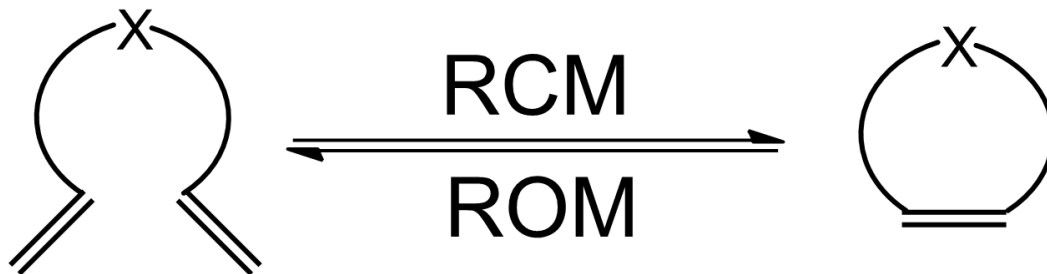
- Not Catalytic!

# Classification of Olefin Metathesis Reactions

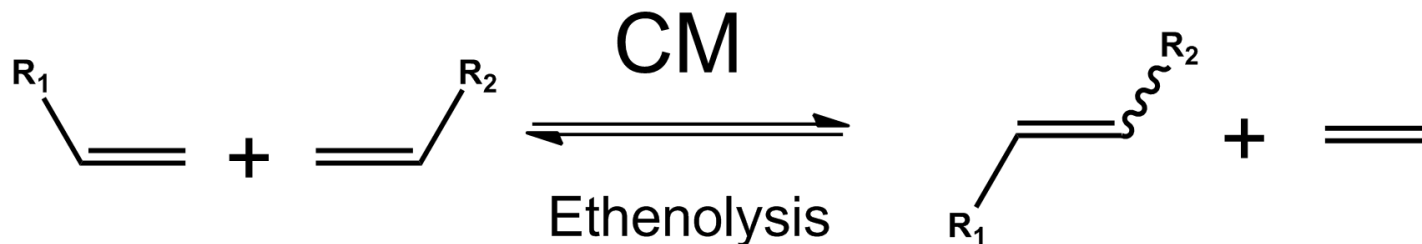
Ring **O**pening **M**etathesis **P**olymerization:



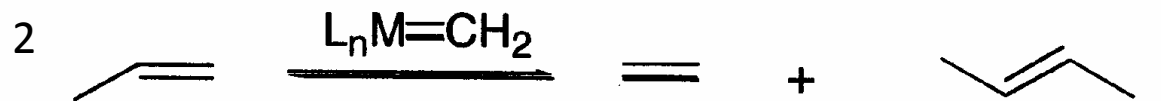
Ring **C**losing **M**etathesis; Ring **O**pening **M**etathesis:



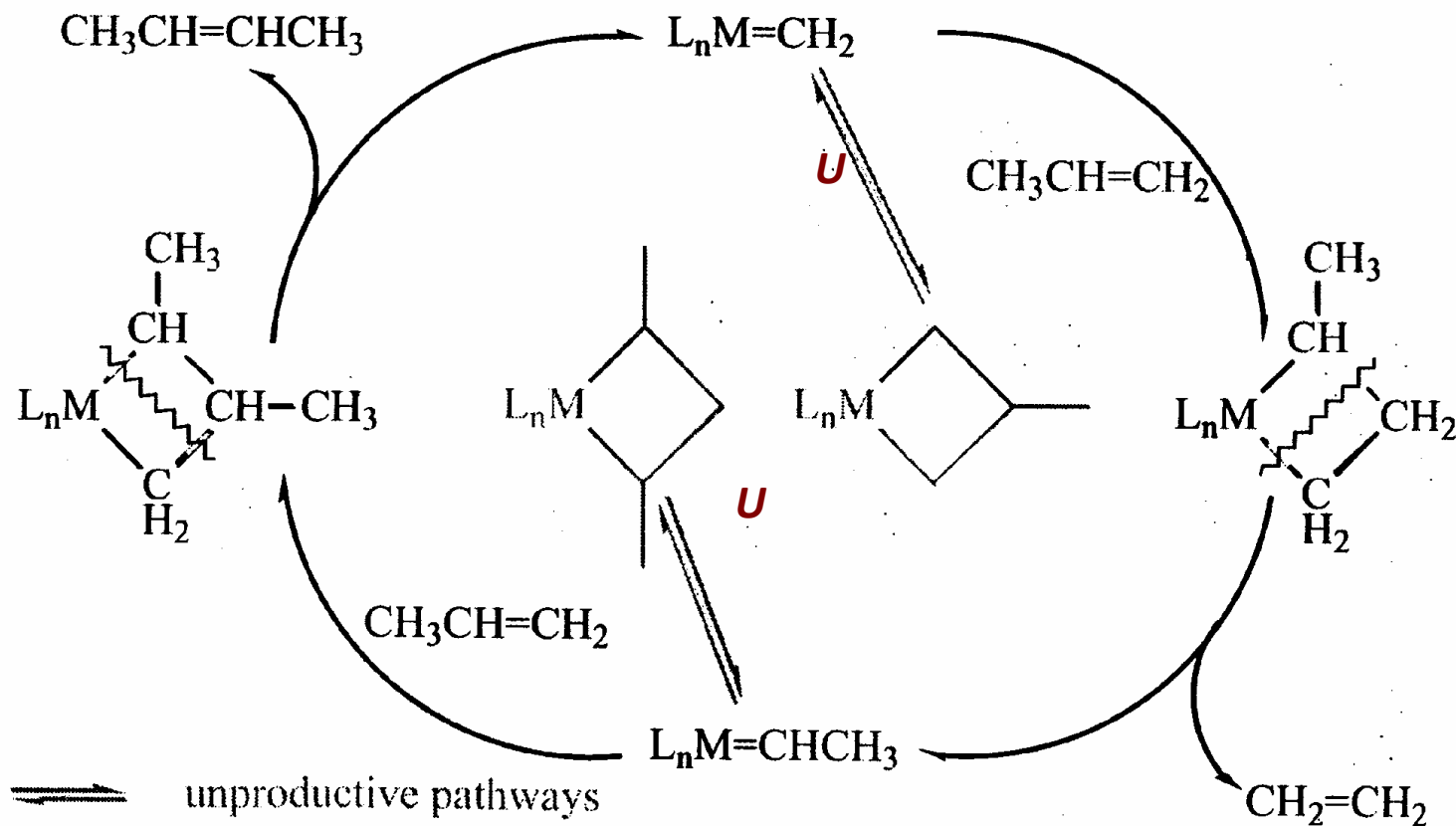
Cross **M**etathesis:



# Cross Metathesis: Midsize alkenes converted to smaller/ larger alkenes

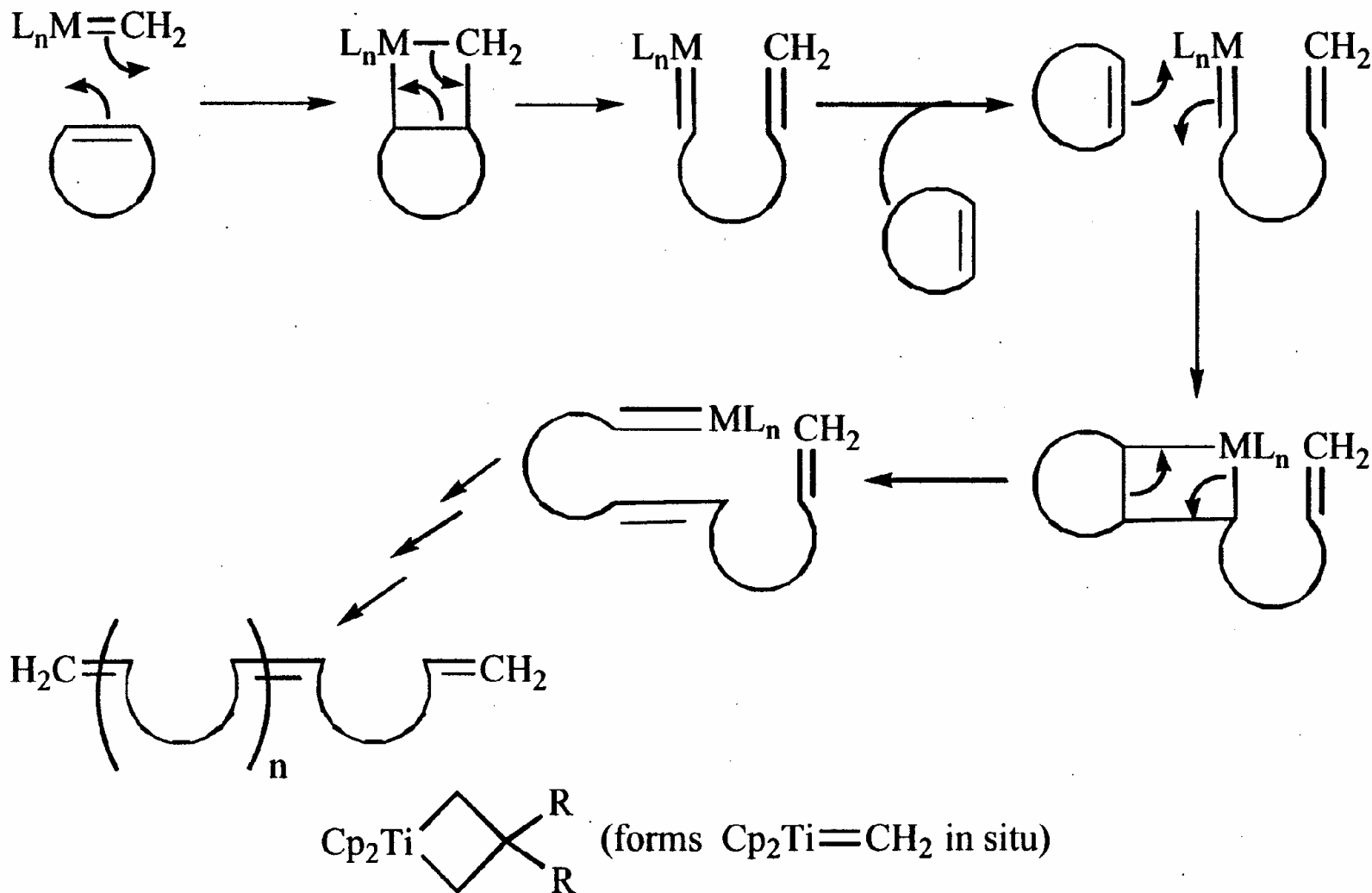


Mechanism: reversible electrocyclic addition.



# Ring Opening Metathesis Polymerization:

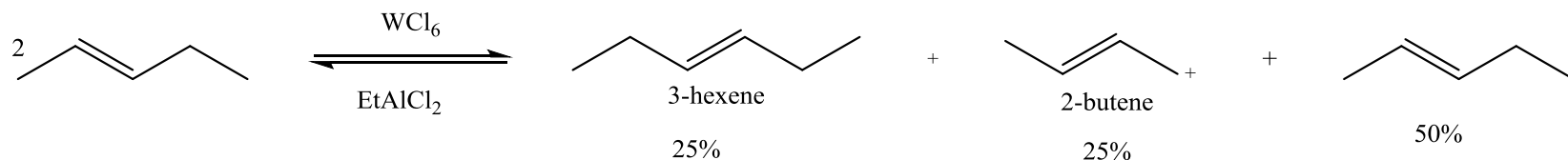
Olefin metathesis applied to cyclic olefins:





# Olefin Metathesis Catalysis: The Beginning

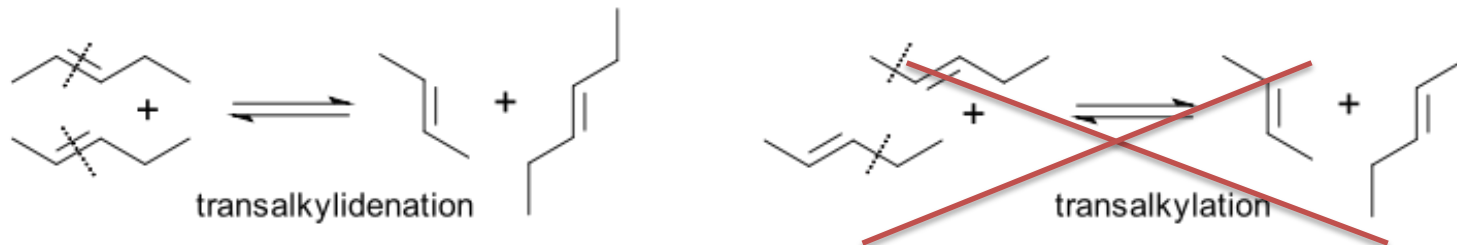
- Transition metal-chlorides in the presence of co-catalysts were the first to be studied that afforded C-C bond formation, e.g.,  $\text{CH}_3\text{CH}_2\text{AlCl}_2$  and  $\text{WCl}_6$



- Calderon proposed two mechanisms for the above: transalkylation and transalkylidenation. Experiments with deuterated alkenes indicated a transalkylidenation mechanism.
- This was the start Grubbs took to find a catalyst to perform synthetically useful reactions.

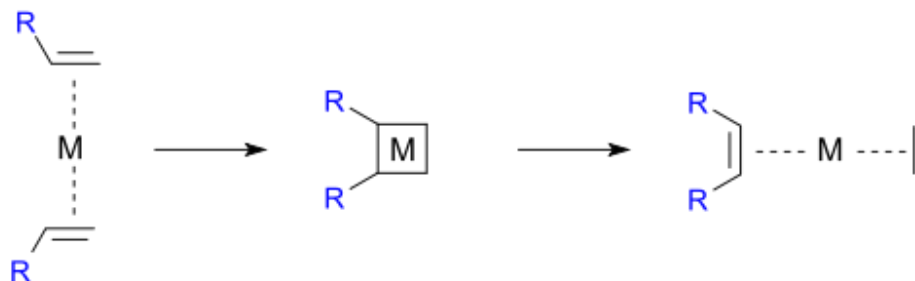
# A Bit of History for the Olefin Metathesis Reaction

Calderon: Isotope distribution studies proved olefin was split at the C=C bond:

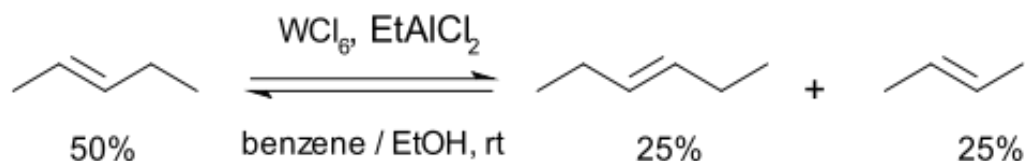


**Phillips Petroleum; 1964:** Olefin "Disproportionation" (symmetry forbidden by W-H Rules).

Catalysts:  $W(CO)_6$ ,  $Mo(CO)_6$ ,  $Mo_xO_y/Al_2O_3$



**Goodyear Tire Company:**



# Nobel Prizes

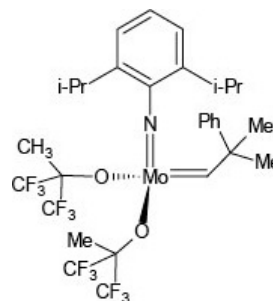
## Historical Frame of Reference

- Previously mentioned Grignard, Diels-Alder and Wittig reactions awarded in 1912, 1950 and 1979.
- Chauvin, Grubbs and Schrock were awarded in 2005 for their work in olefin metathesis.
  - Preceded by decades of research prior to 2005.
- Chauvin was the first to produce a viable mechanism for olefin metathesis.
- Schrock accidentally created first stable metal carbene catalyst at MIT.
- Grubbs gave synthetic chemists an air stable and water-soluble metal carbene.

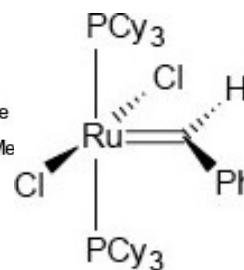
*“For the development of the metathesis method in organic synthesis.”*



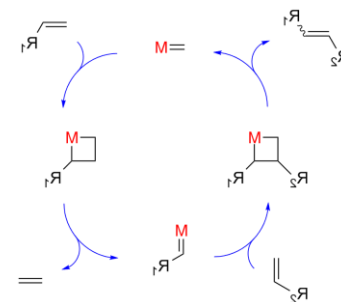
Schrock



Grubbs

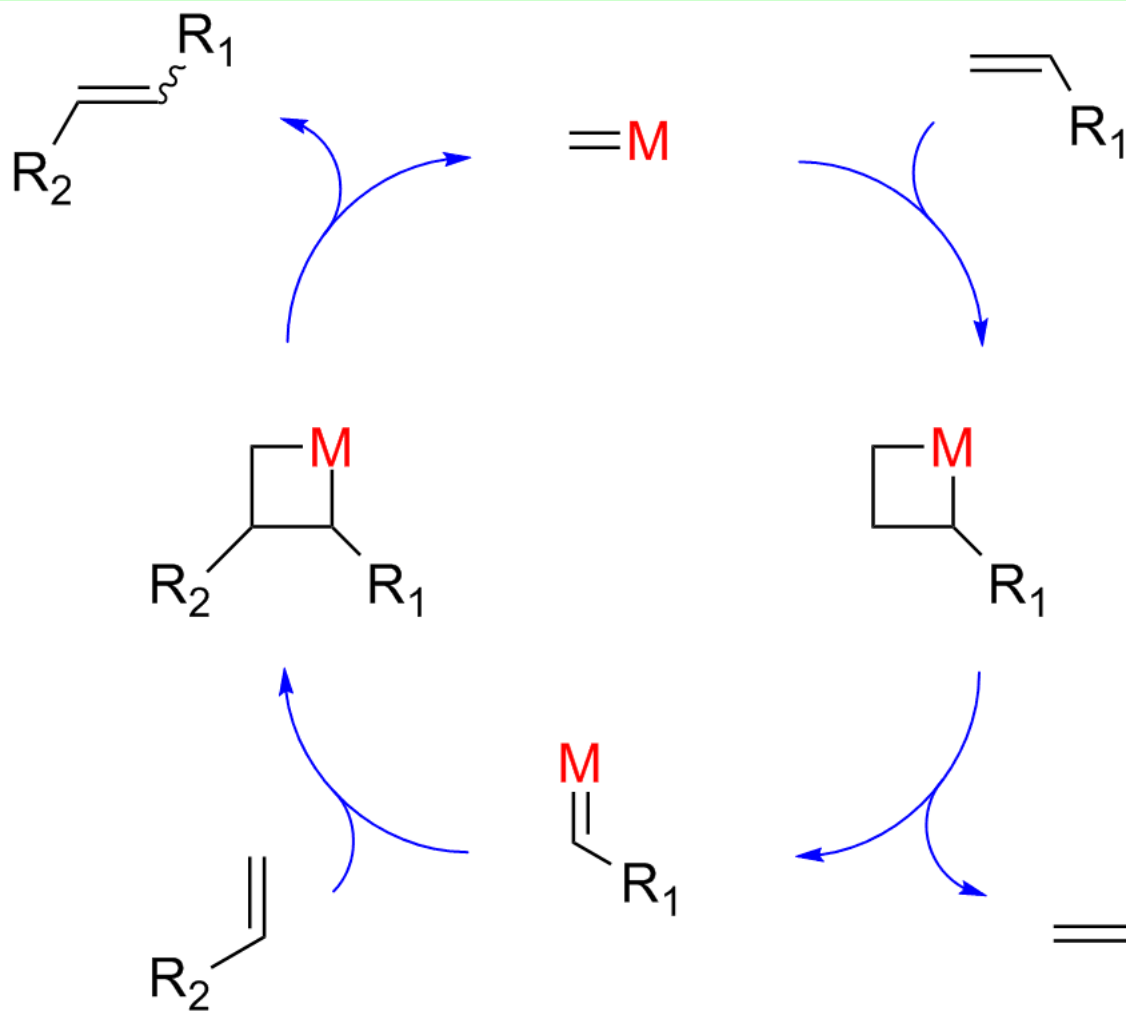


Chauvin



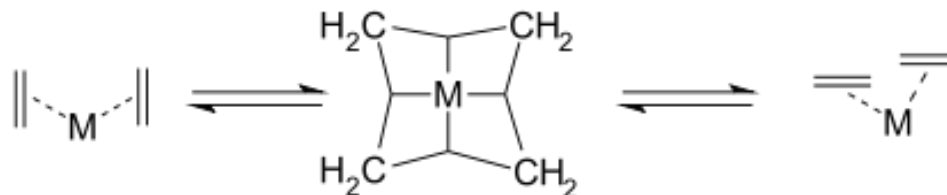
# Chauvin Mechanism 1971

Olefin Metathesis: Conversion of smaller to larger alkenes;  
Begins with a Transition Metal Carbene (alkylidene).

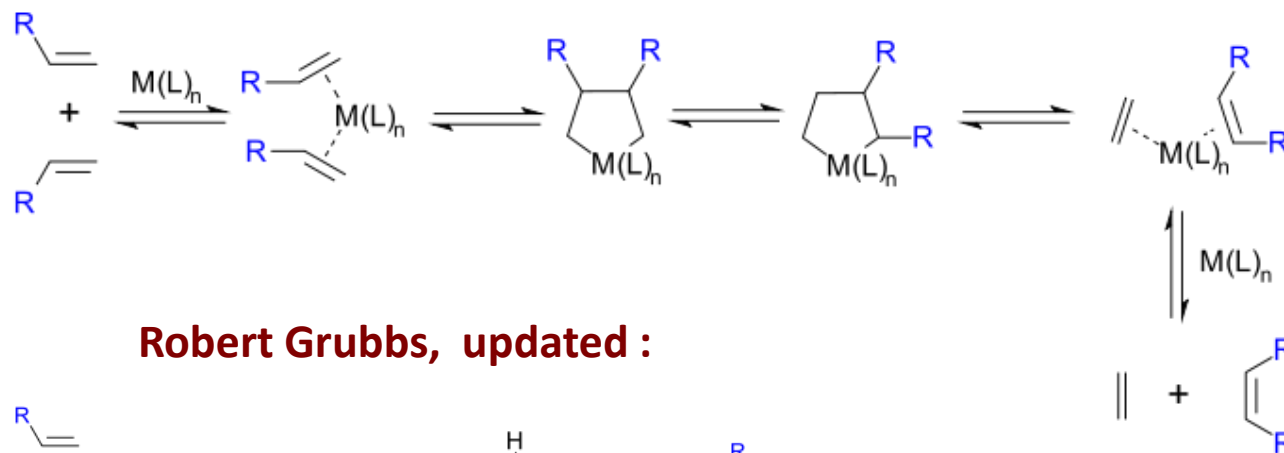


# Other Proposed Mechanisms

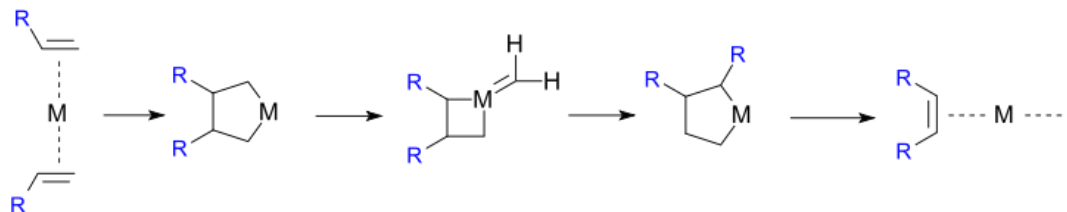
Rowland Pettit, the Cyclobutane Intermediate Possibility:



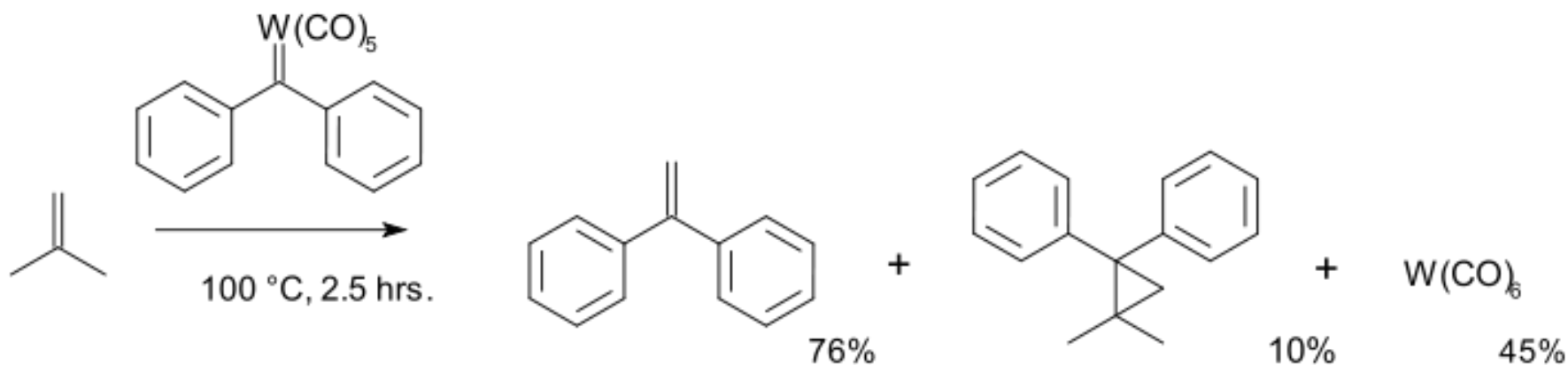
Robert Grubbs, the Metallocycle Intermediate Possibility:



Robert Grubbs, updated :

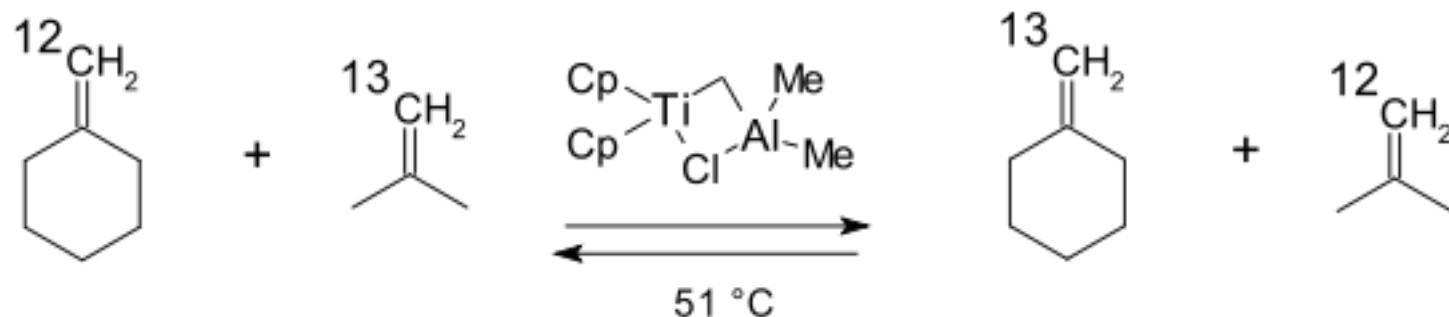


*1976: From Fischer-Type Carbene, Casey discovers valuable clues to mechanism*

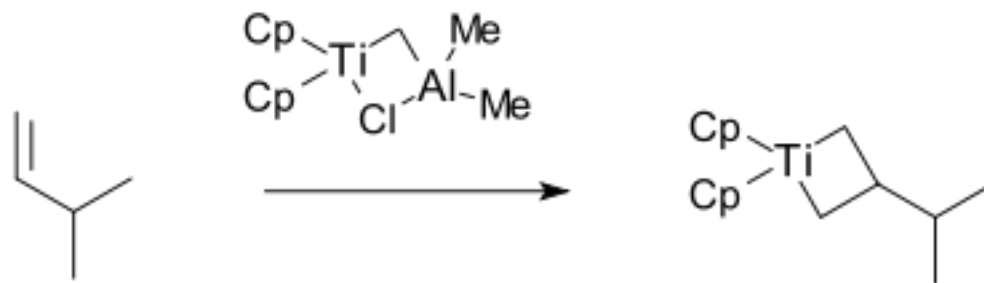


*Question to class: Synthesize the tungsten complex beginning from  $\text{W}(\text{CO})_6$  and  $\text{PhLi}$ . What else is needed?*

# Other Proposed Mechanisms: Now, getting to the truth: Fred Tebbe, 1976, the Tebbe reagent

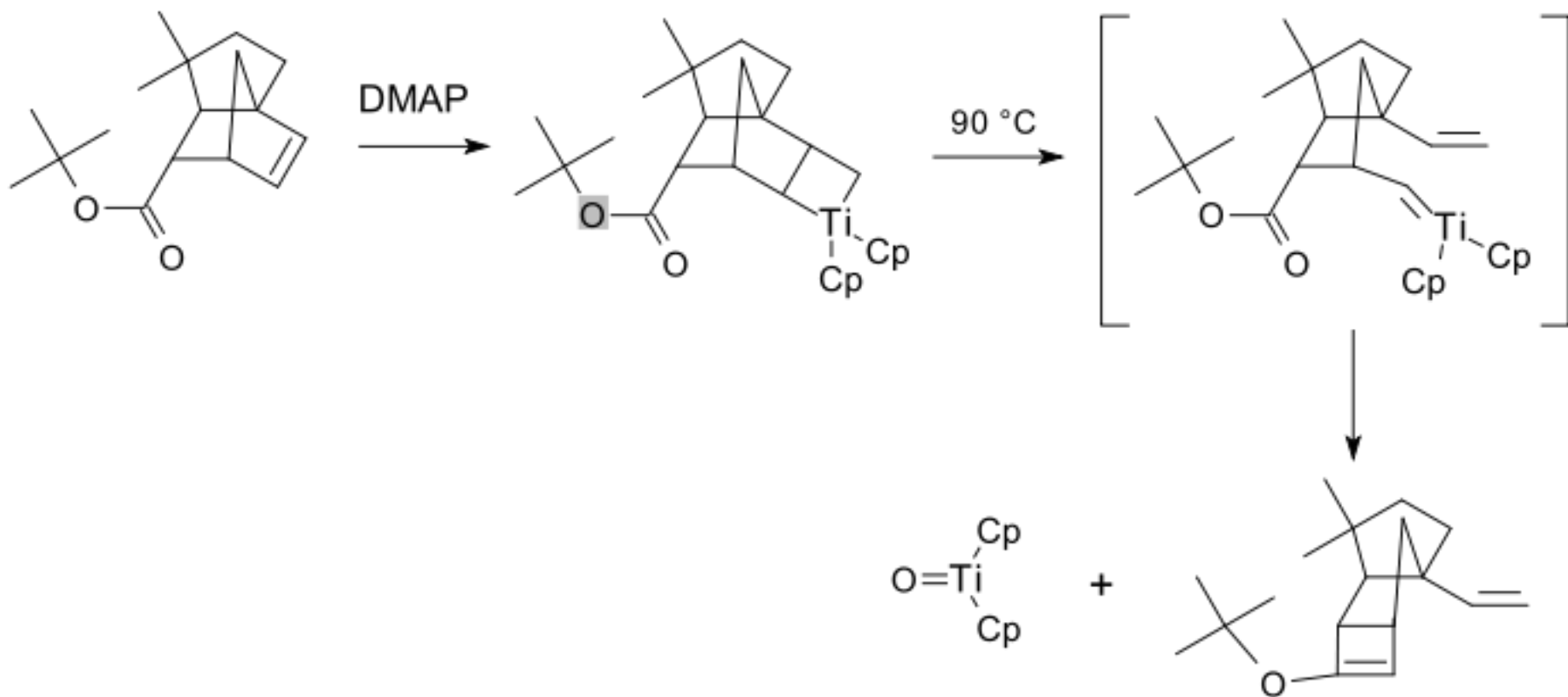


**In 1980 Grubbs uses the Tebbe Reagent and isolates:**



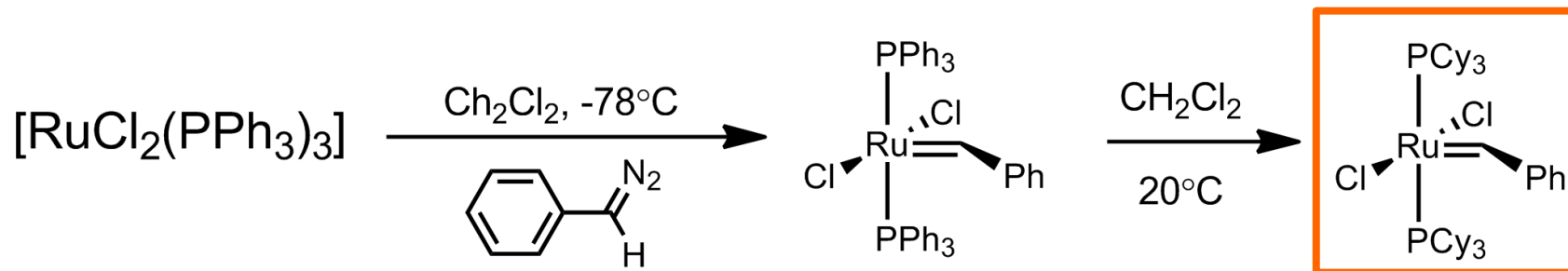
Class: Can you analyze the Tebbe Reagent? With and without the  $\text{Me}_2\text{AlCl}$ ?

# Grubbs also Uses $\text{Cp}_2\text{Ti}=\text{CH}_2$ in Natural Product Synthesis



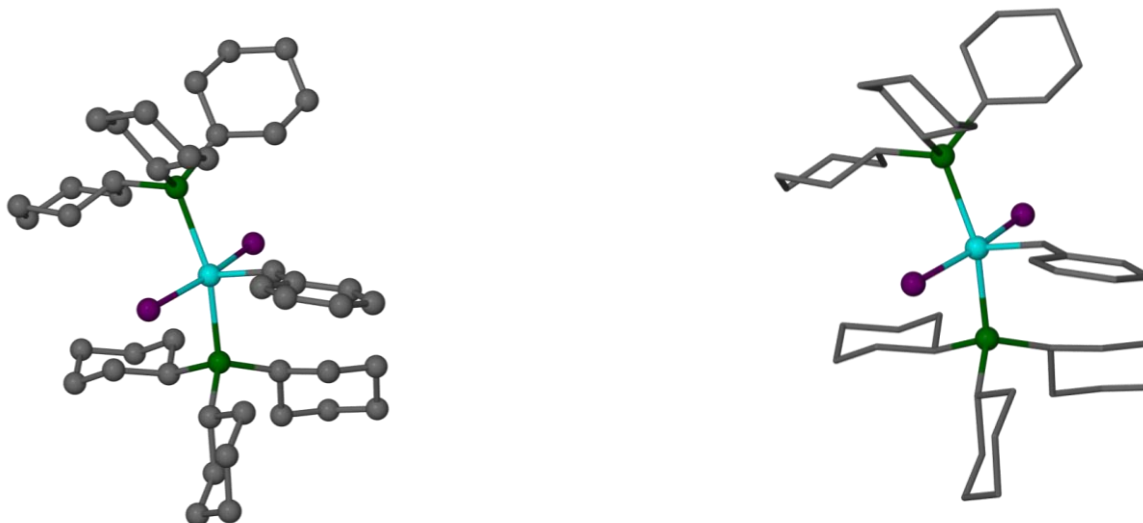


# Grubbs' First Generation O.M. Catalyst: Synthesis



## Grubbs Catalyst: Structure X-ray Diffraction Analysis of Crystals

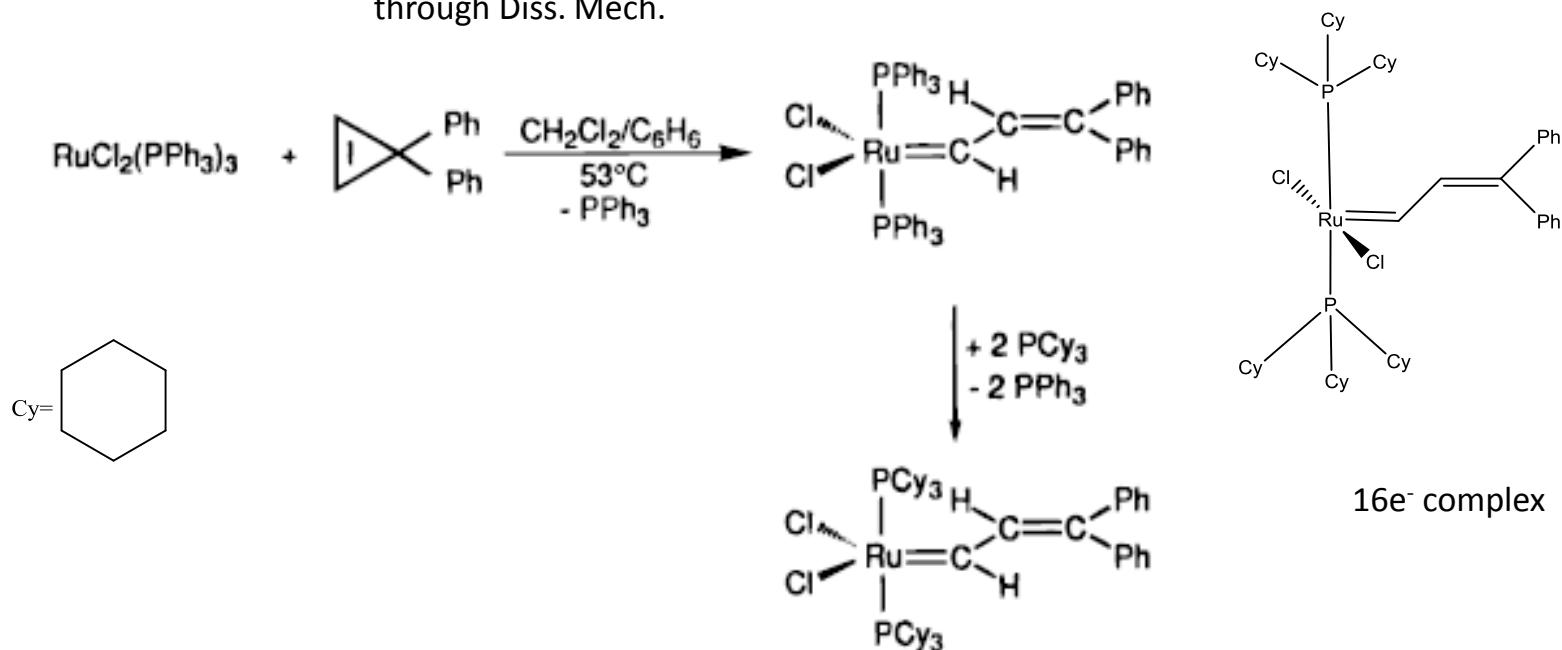
$\tau = 0.10$



Addison's tau value: trigonal bipyramid has  $\tau = 1$ ; square pyramid has  $\tau = 0.0$

# Grubbs' 1<sup>st</sup> generation Catalyst

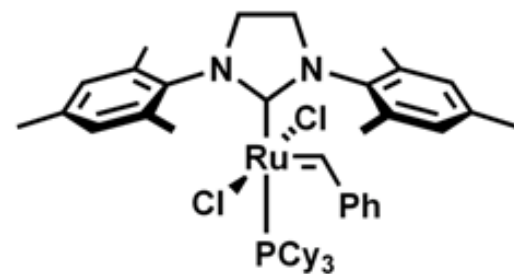
Complex first needs to  
lose  $\text{PCy}_3 \rightarrow$  proceeds  
through Diss. Mech.



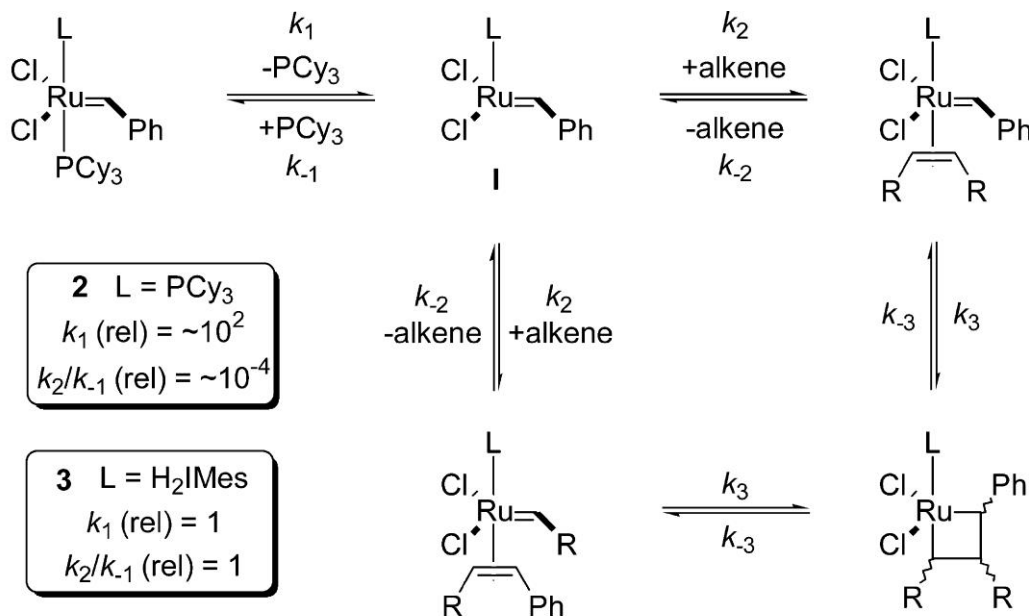
J. Am. Chem. Soc. 1996, 118,  
100-110

# Lead up to 2<sup>nd</sup> Generation Catalyst

- Let's replace  $\text{PR}_3$  ligand with a heterocyclic carbene and see what happens.
  - Increased catalytic activity, but why?



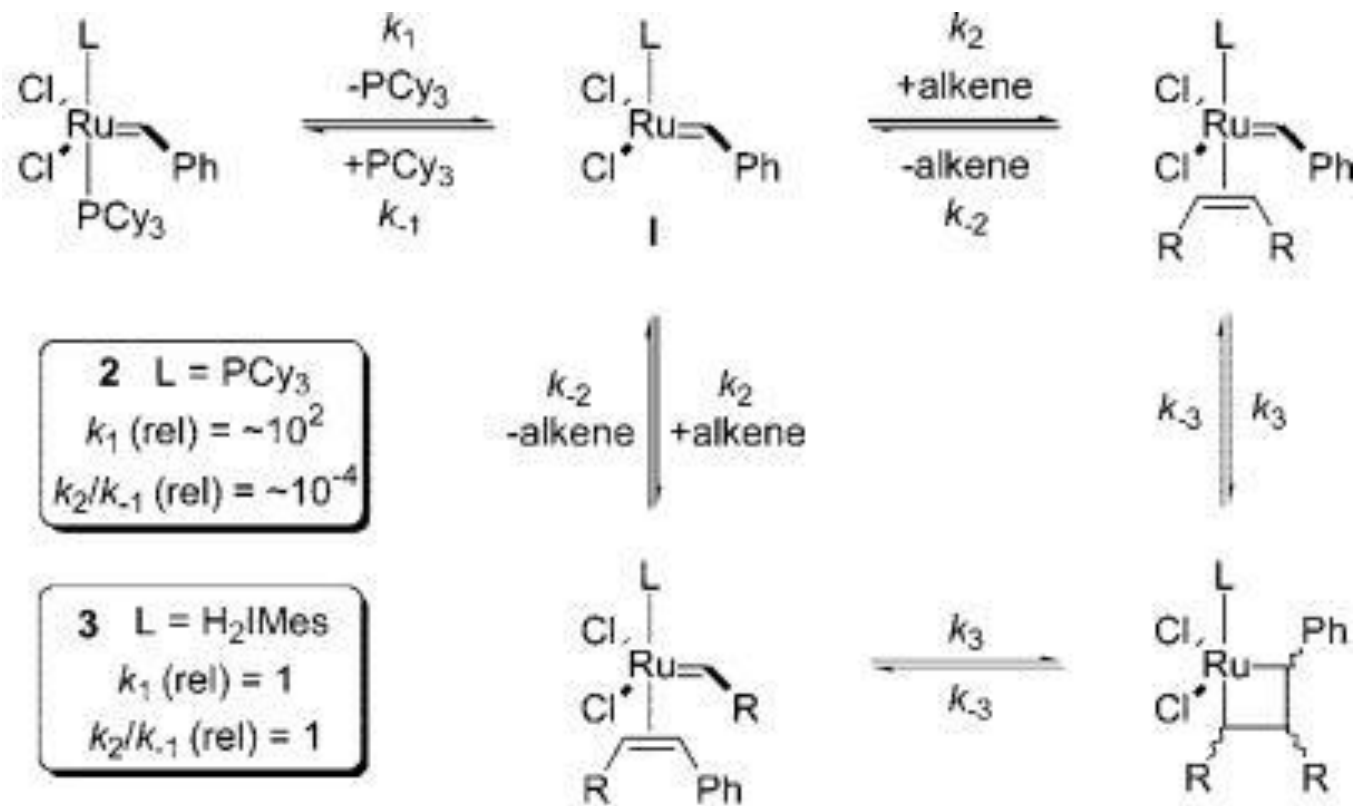
- $[\text{Ru}]$  center prefers basic olefins over rebinding  $\text{PCy}_3$



Chem. Rev. 2010, 110, 1746–1787

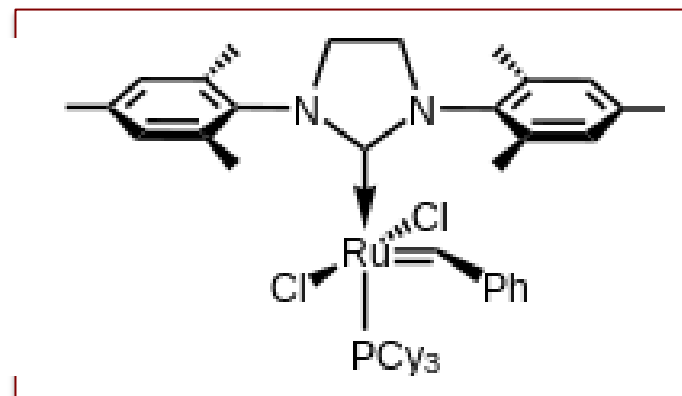
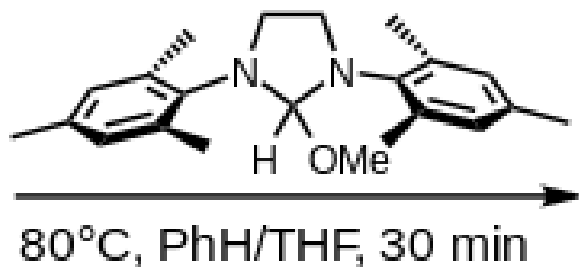
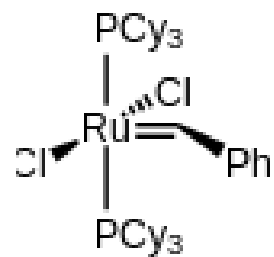


# Kinetic Comparison of Phosphines and N-heterocyclic Carbenes (NHC)

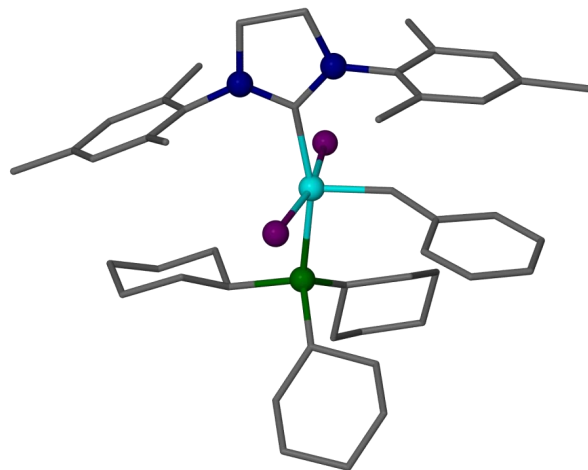


Class: What is  $k_2/k_{-1}$ ?

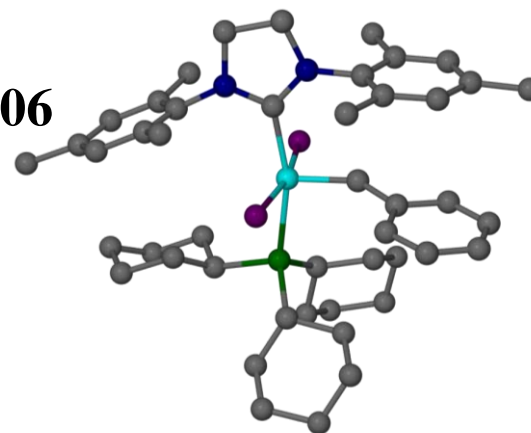
# Grubbs' Second Generation O.M. Catalyst



## Grubbs Catalyst: Structure X-ray Diffraction Analysis of Crystals

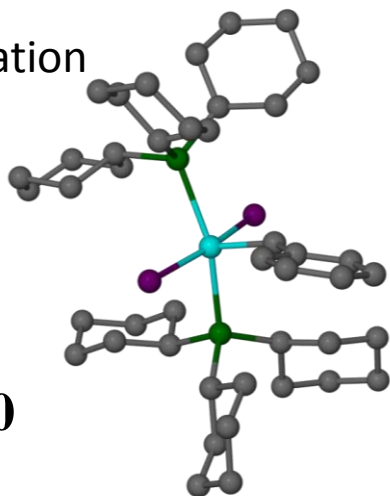


$$\tau = 0.06$$

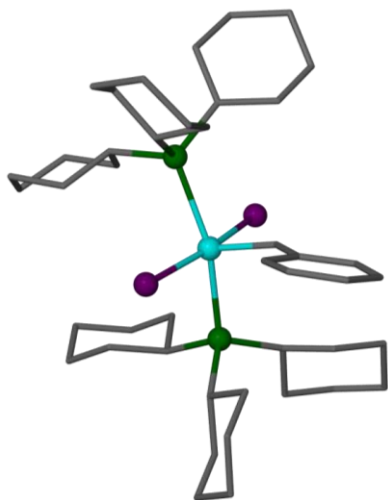


## Grubbs' Catalysts: Comparison of 1<sup>st</sup> and 2<sup>nd</sup> Generation Catalysts

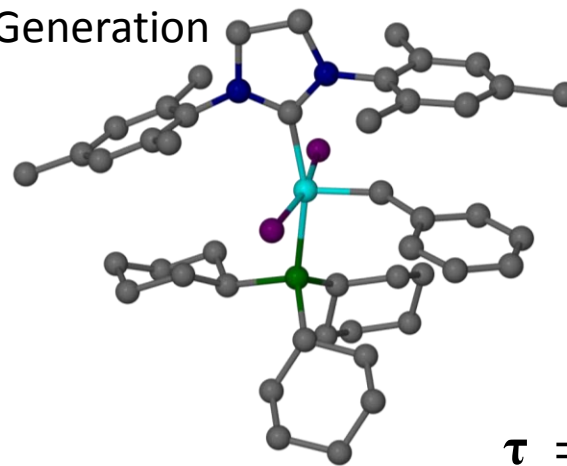
1<sup>st</sup> Generation



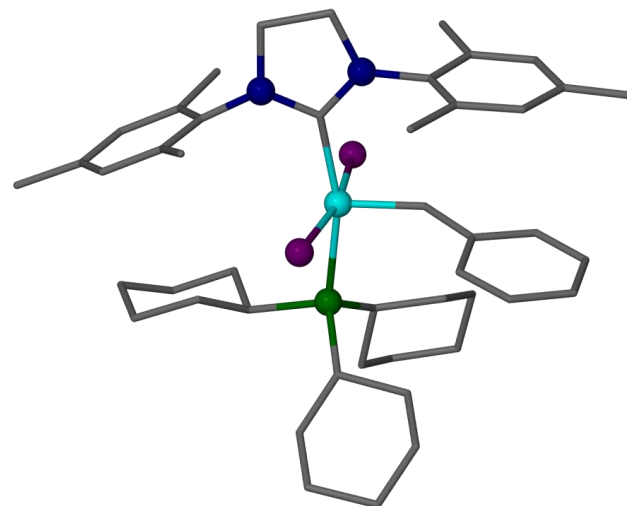
$\tau = 0.10$



2<sup>nd</sup> Generation



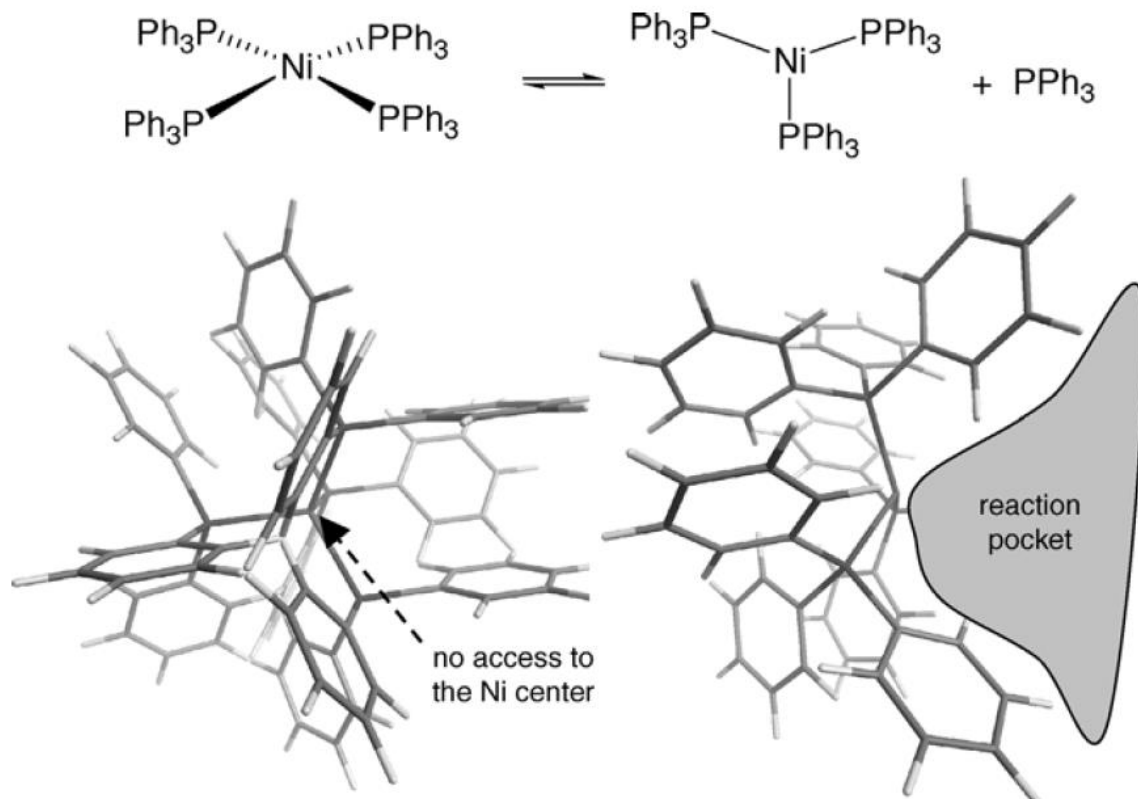
$\tau = 0.06$



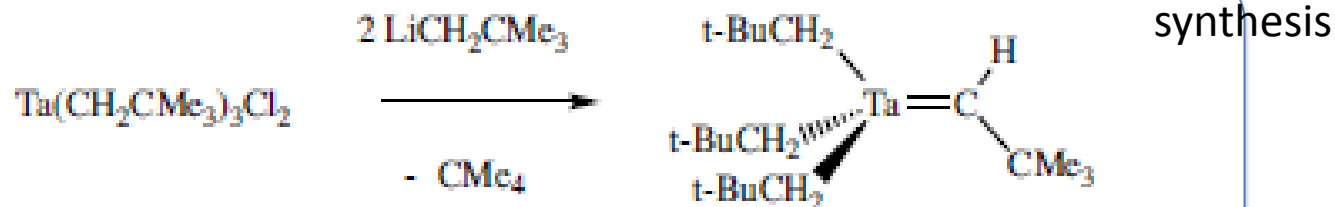
Addison's tau value: trigonal bipyramid has  $\tau = 1$ ; square pyramid has  $\tau = 0.0$

Class: What advantage do the large bulky ligands give? Protection for A reaction pocket.

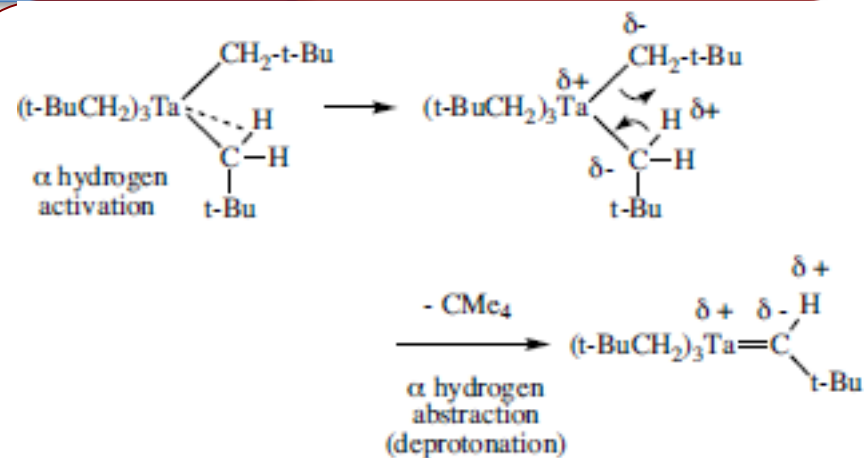
5.1 Metal Complex Catalysis in the Liquid Phase | 89



# Schrock Catalyst: The First Alkylidene



mechanism



First alkylidene structure

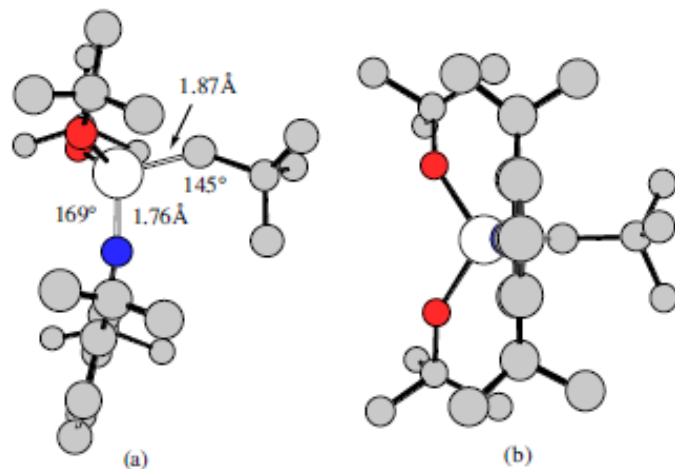
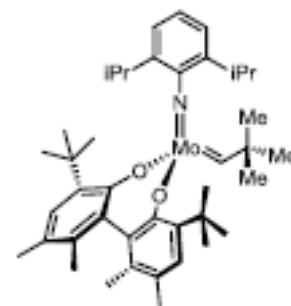
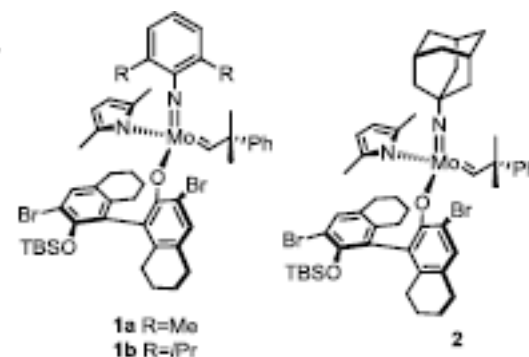
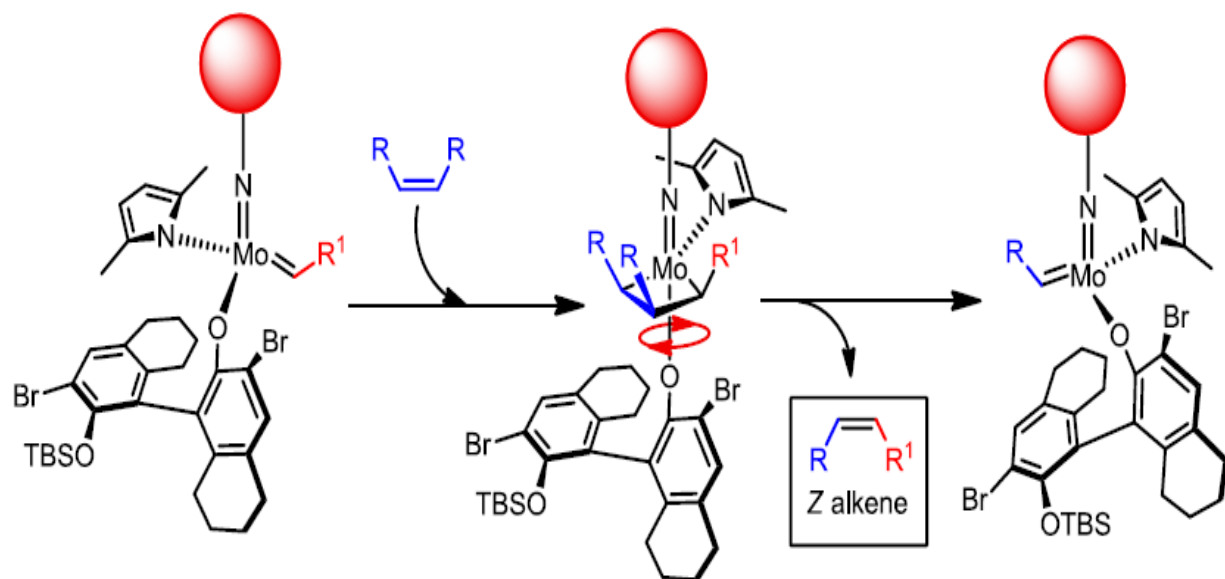


Figure 4. The structure of  $\text{W}(\text{NAr})(\text{CH-t-Bu})(\text{O-t-Bu})_2$ ; (a) top view; (b) side view.

Schrock Nobel Lecture

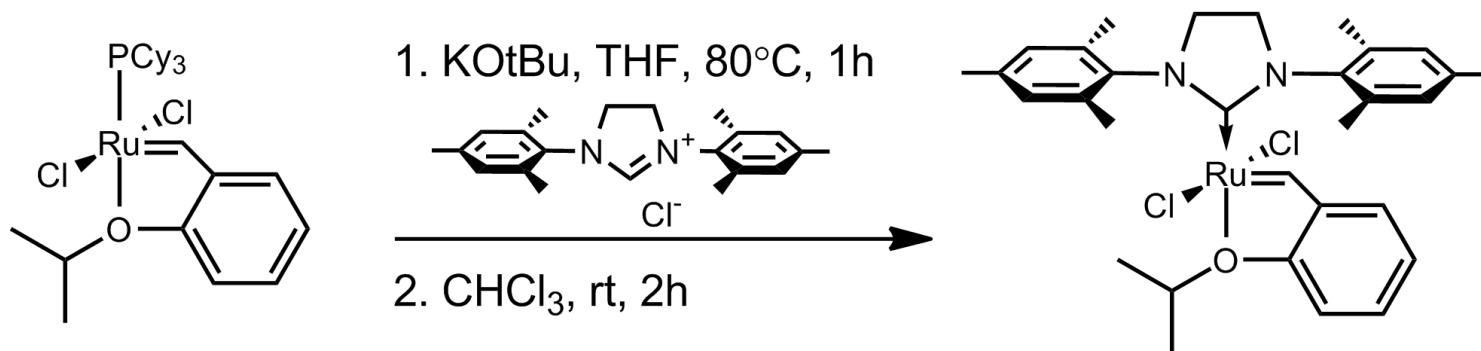
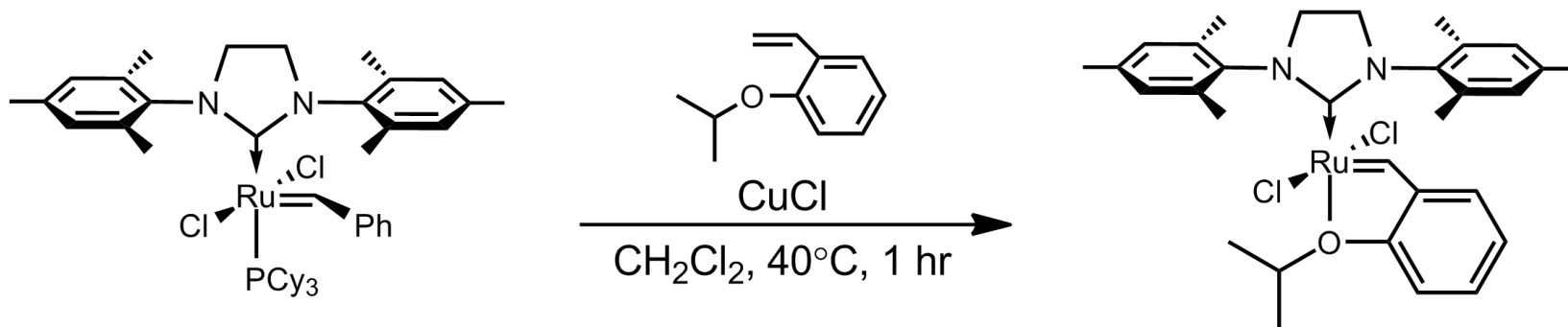


# Schrock: Mo alkylidene selectivity



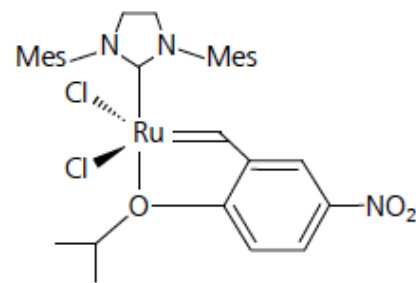
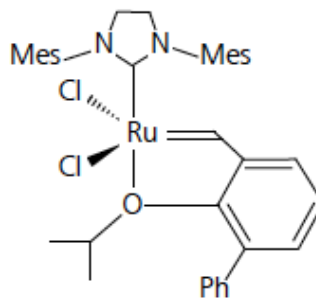
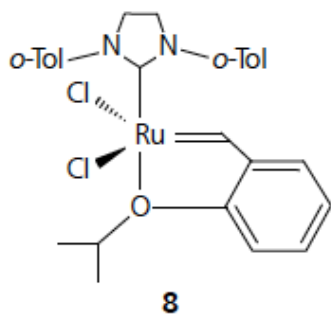
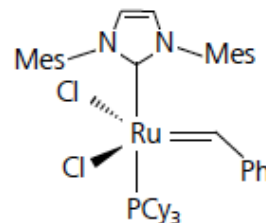
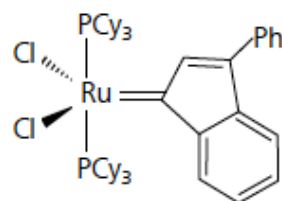
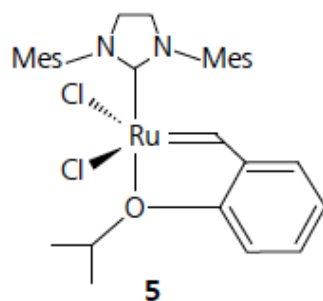
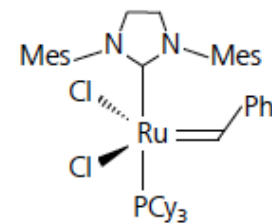
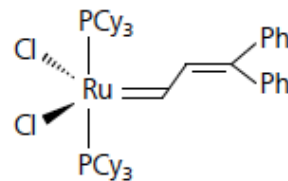
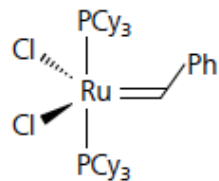
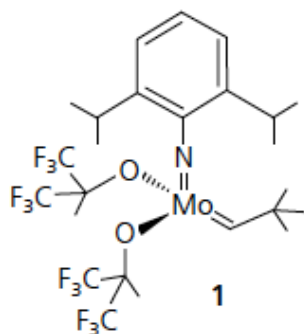
Catalyst	Time	Conv (%)	Z:E
1a	2 h	85	98:2
1b	2 h	47	>98:2
2	2 h	37	>98:2
3	2 h	<2	NA

# Hoveyda-Grubbs' O.M. Catalyst: anchored alkylidene

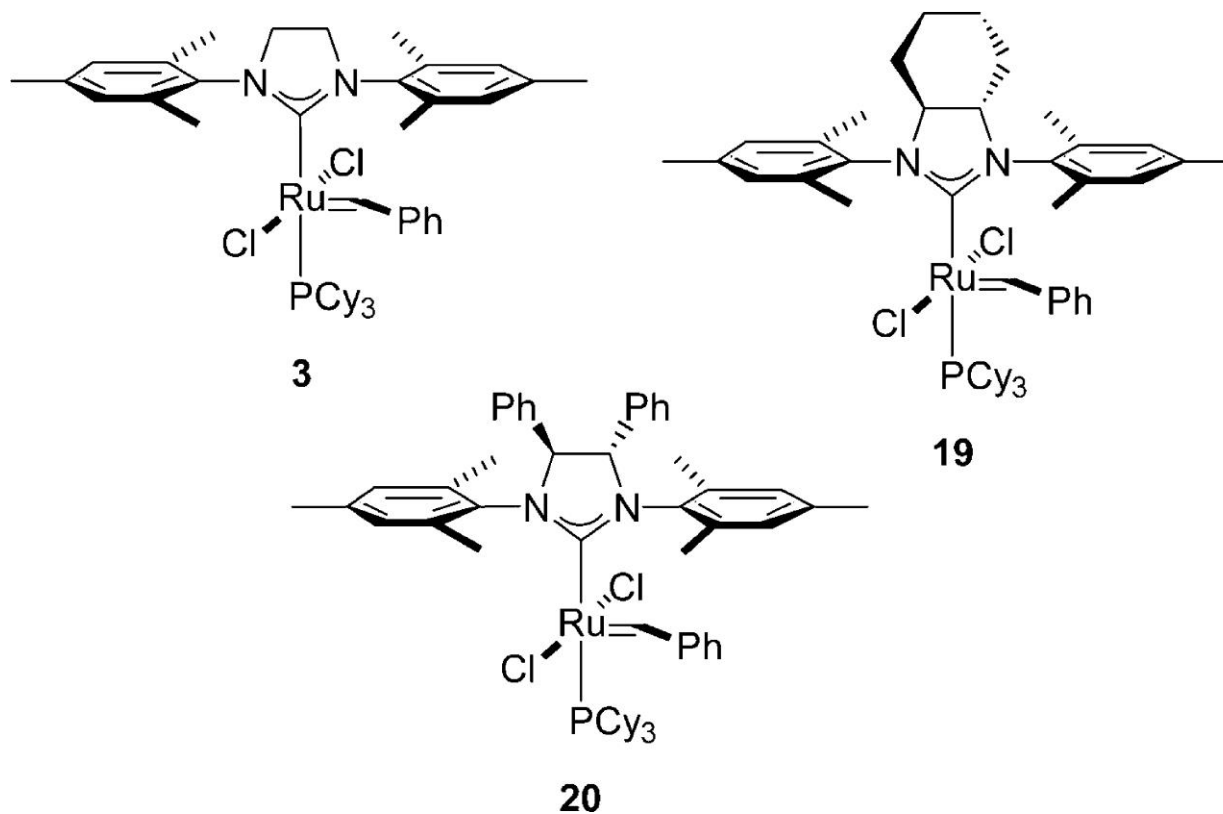


# Modifications are endless:

Some examples of metal-alkylidene metathesis catalysts:

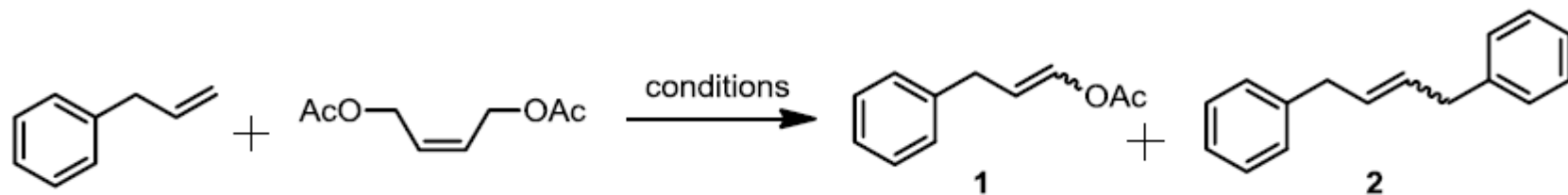


# Modifications - even more:

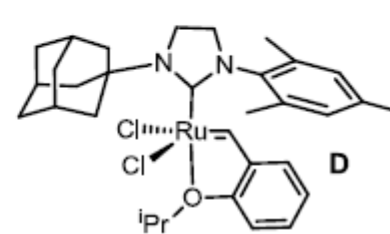
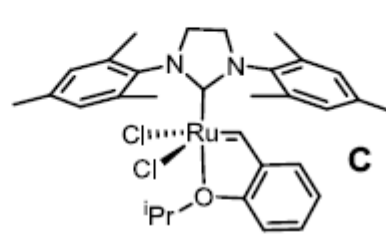
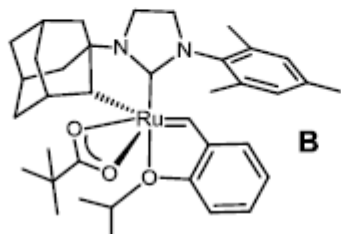
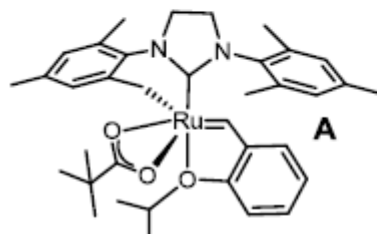


Ruthenium-based metathesis catalysts **3**, **19**, and **20**.

# Effects of [Ru] Modification



Cat	mol% cat	Solvent	Temp (°C)	Time (min)	Yield 1 (%)	Z/E 1	Yield 2 (%)	Z/E 2
A	2.5	C <sub>6</sub> H <sub>6</sub>	23	60	57	31:69	3	17:83
B	5.0	C <sub>6</sub> H <sub>6</sub>	70	120	36	88:12	26	94:6
B	5.0	THF	Reflux	240	60	81:19	31	96:4
B	5.0	THF/H <sub>2</sub> O	Reflux	240	64	86:14	29	97:3
C	2.5	C <sub>6</sub> H <sub>6</sub>	23	30	66	9:91	10	15:85
D	2.5	C <sub>6</sub> H <sub>6</sub>	23	30	<1	34:66	NA	NA



# Catalyst Comparisons

## Grubbs Catalyst(s)

- Less reactivity; greater selectivity for less bulky and or strained alkenes
- Bench stable
- Higher substrate functional group tolerance

## Schrock alkylidene

- Greater reactivity with bulky and  $e^-$  deficient alkenes
- Inert condition-stable
- Low substrate functional group tolerance

*Nobel Chemistry Prize Lectures. Grubbs' and Schrock's*

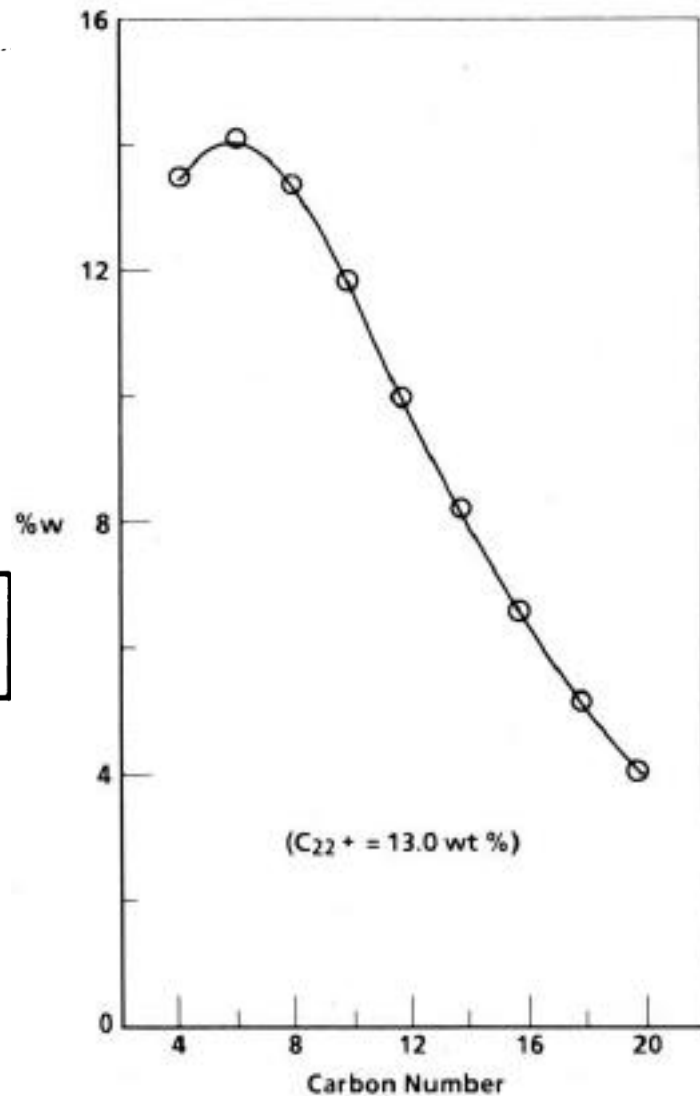
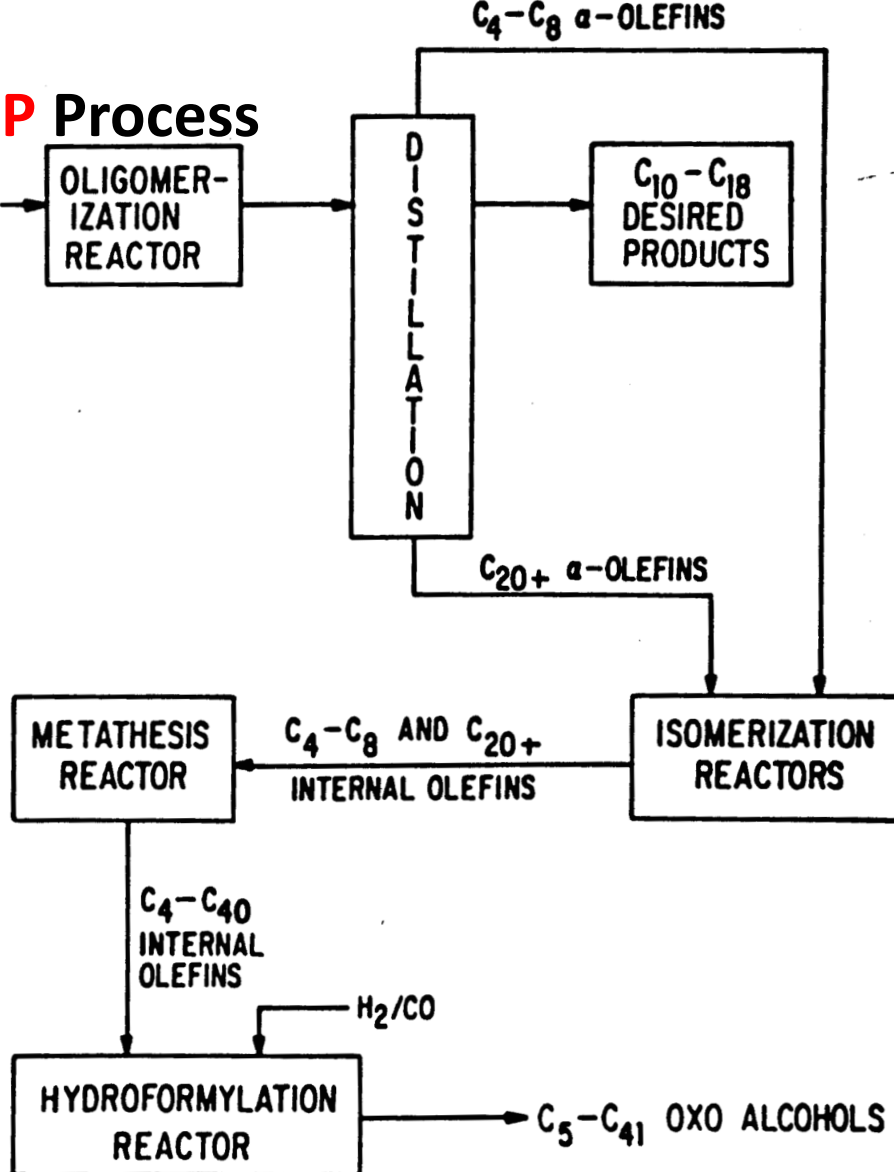
# Applications





# The SHOP Process

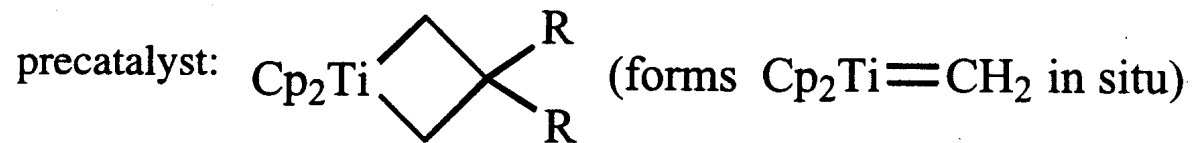
Shell  
Higher  
Olefin  
Process



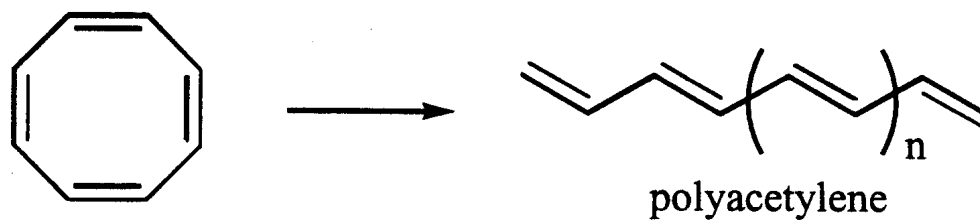
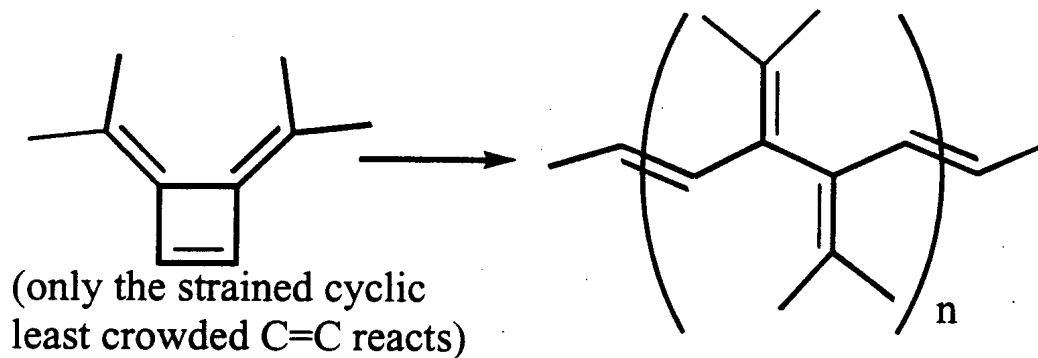
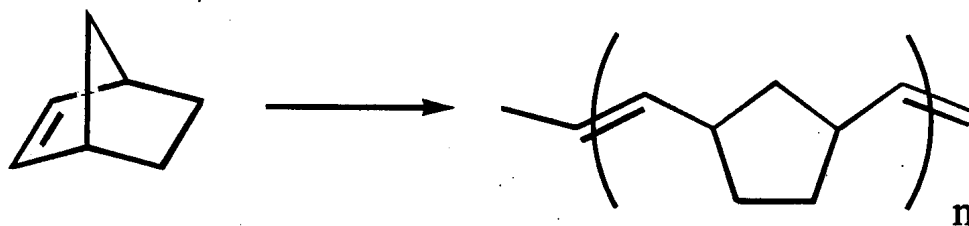
### Typical Quality of Alpha-Olefins (composition wt %)

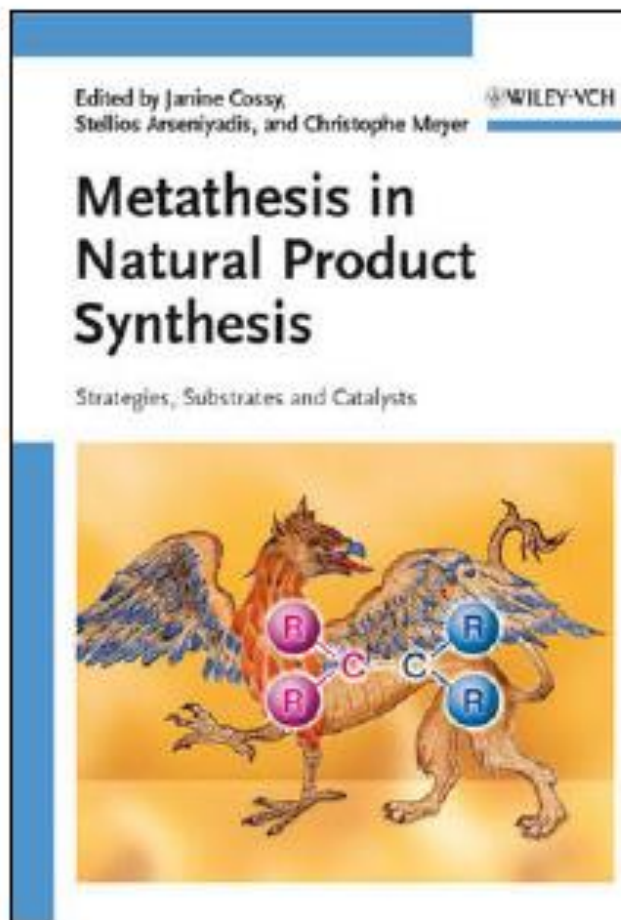
Hydrocarbon Type	Carbon Number			
	12	14	16	18
<i>n</i> -alpha-Olefins	96+	95+	95+	94+
Branched Olefins	2	3	3	4
Beta Internal Olefins	1.5	1.5	1.5	1.5
Paraffins	<0.1	<0.1	<0.1	<0.1
Conjugated Dienes	<0.1	<0.1	<0.1	<0.1
Aromatics	<0.1	<0.1	<0.1	<0.1
Total Mono-olefins	>99.5	>99.5	>99.5	>99.5

# ROMP: catalysts and substrates.



A few examples of polymers available by ROMP:

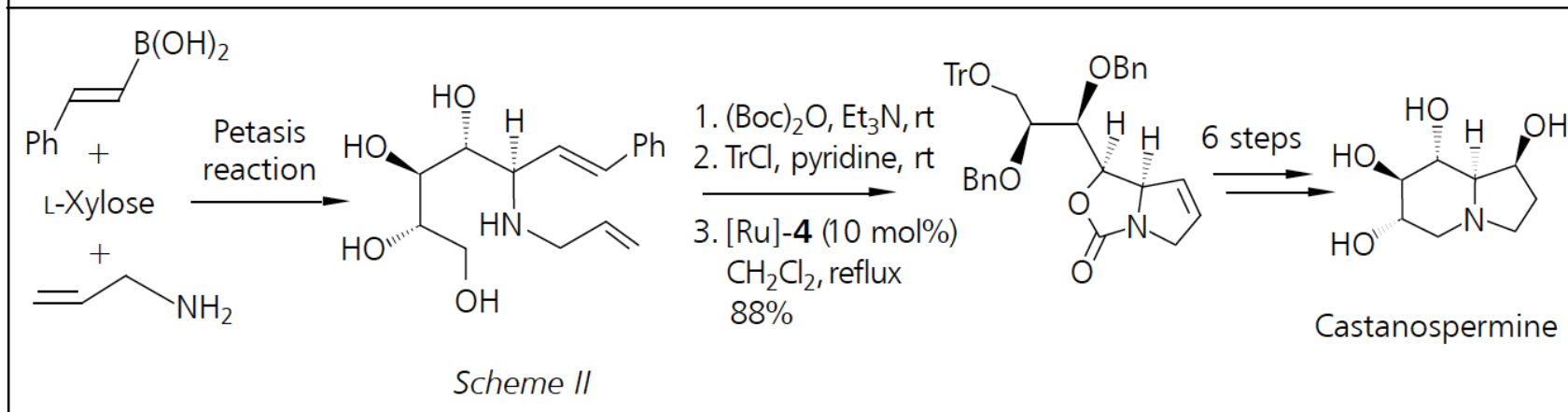
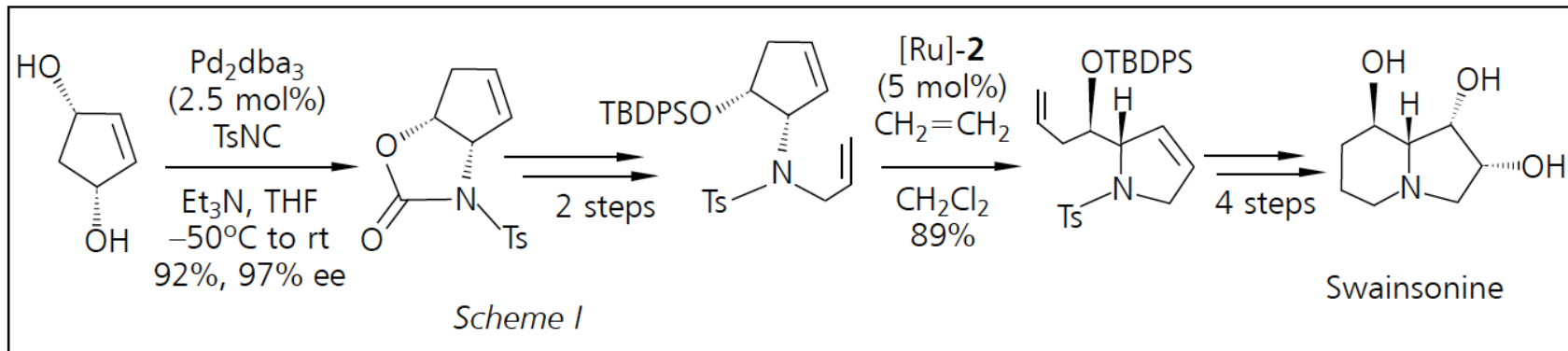




*“Metathesis in  
Natural Product  
Synthesis”*

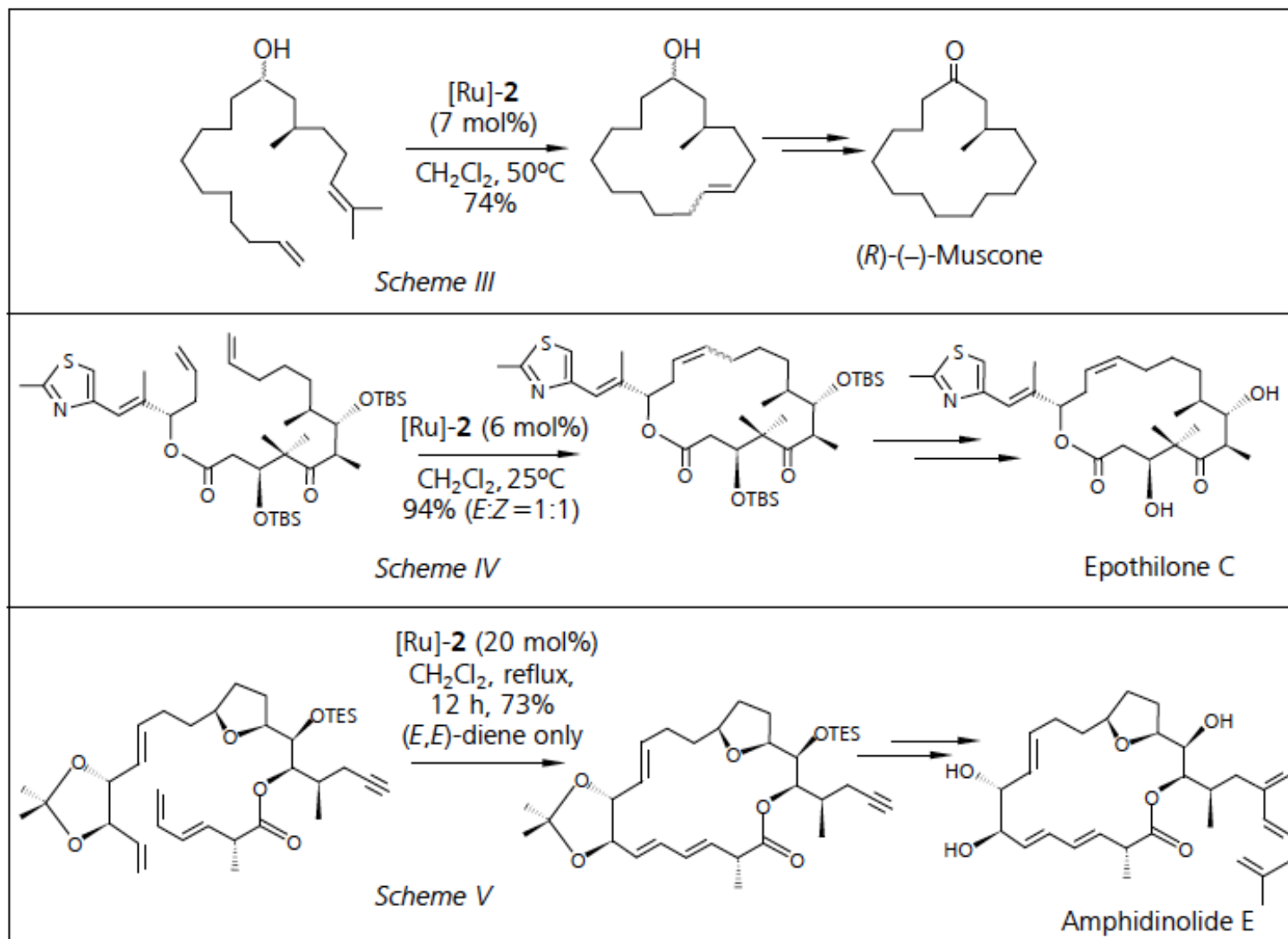
Mind Boggling Complexities!!!

# Applications of Olefin Metathesis: Natural Products Synthesis



Schemes I and II. Ruthenium-based ring-closing metathesis in synthesis of swainsonine and castanospermine

# Applications of Olefin Metathesis: Natural Products, Macrocycles



Schemes III–V. Macrocyclic access by ruthenium-based ring-closing metathesis strategy

## Applications of Olefin Metathesis: Natural Products, RCM

Some examples of natural compounds accessed by the ring-closing metathesis method:

