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# Transition metal catalyzed higher order cycloaddition

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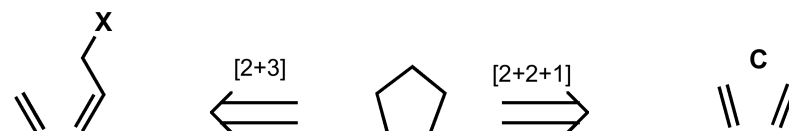
Darius D. Schwarzer  
Gaich-Group Seminar  
29.10.2012

# Overview

OVERVIEW

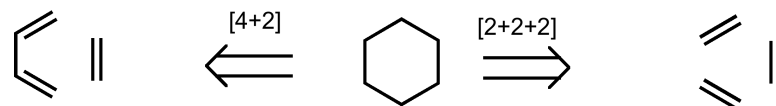
## Fivemembered ring transformation

- [3+2]
- [2+2+1]



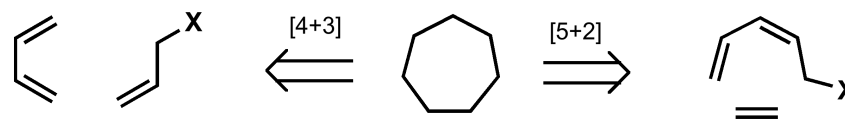
## Sixmembered ring transformation

- [2+2+2]
- [5+1]



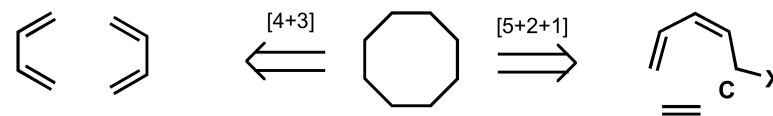
## Sevenmembered ring transformation

- [4+3]
- [5+2]
- [3+3]



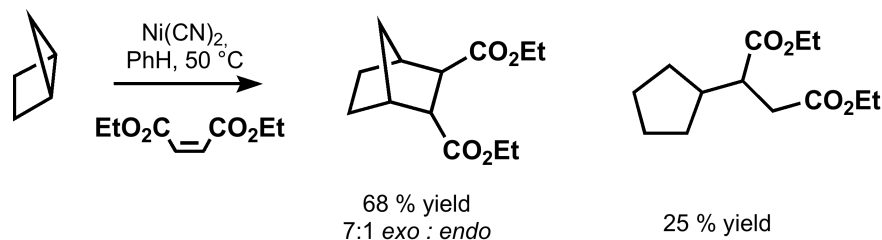
## Eightmembered ring transformation

- [4+4]
- [5+2+1]

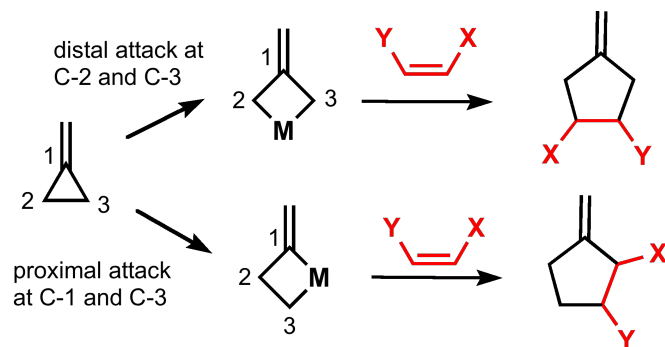
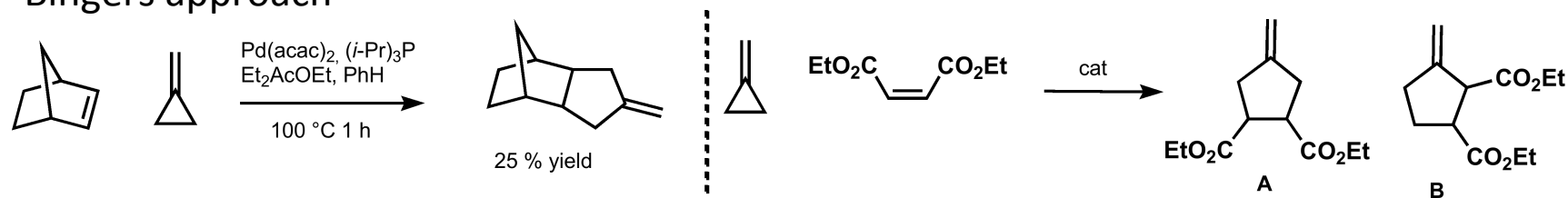


# [3+2] Cycloaddition

Noyori's transition metal catalyzed opening of strained cyclopropanes



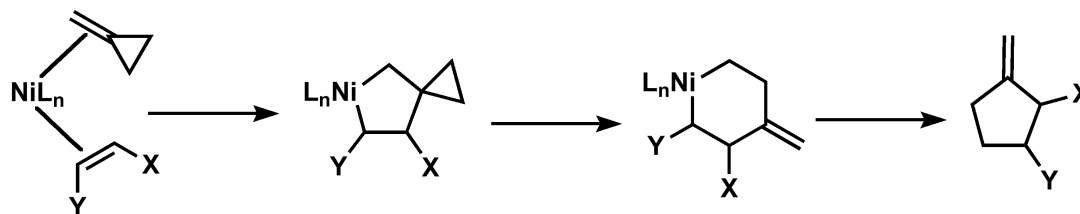
Bingers approach



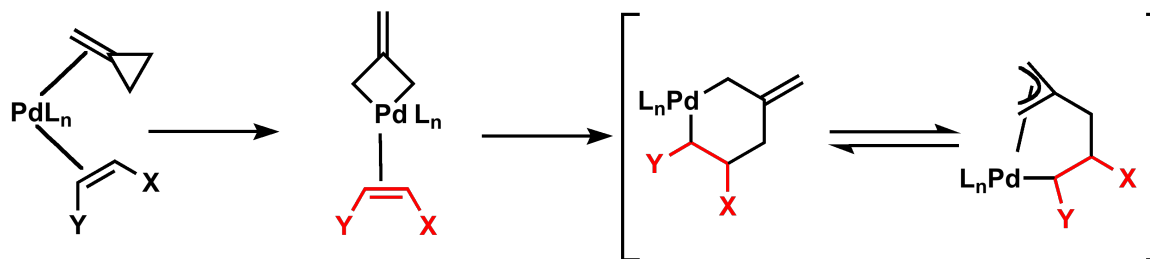
| Catalyst                                | Product |
|---|---------|
| (allyl)CpPd                             | A only  |
| Ni(COD) <sub>2</sub> , PPh <sub>3</sub> | A and B |
| Ni(COD) <sub>2</sub>                    | B only  |

# [3+2] Cycloaddition

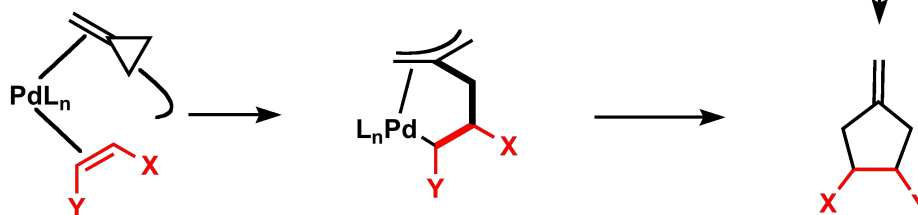
Bingers proposed mechanism for  $\text{Ni}(\text{COD})_2$  catalyzed [3+2]



Binger mechanism for Pd catalyzed [3+2]

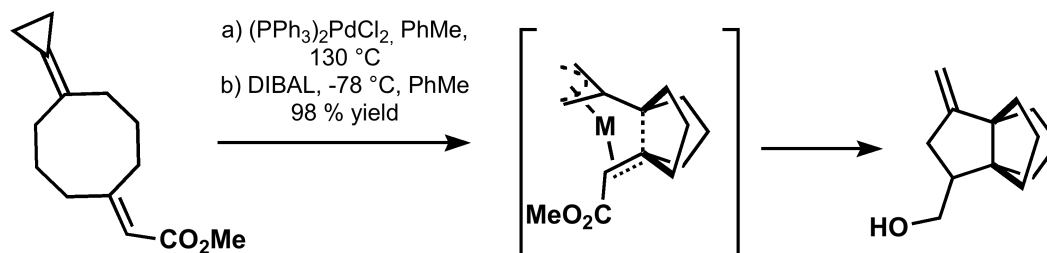
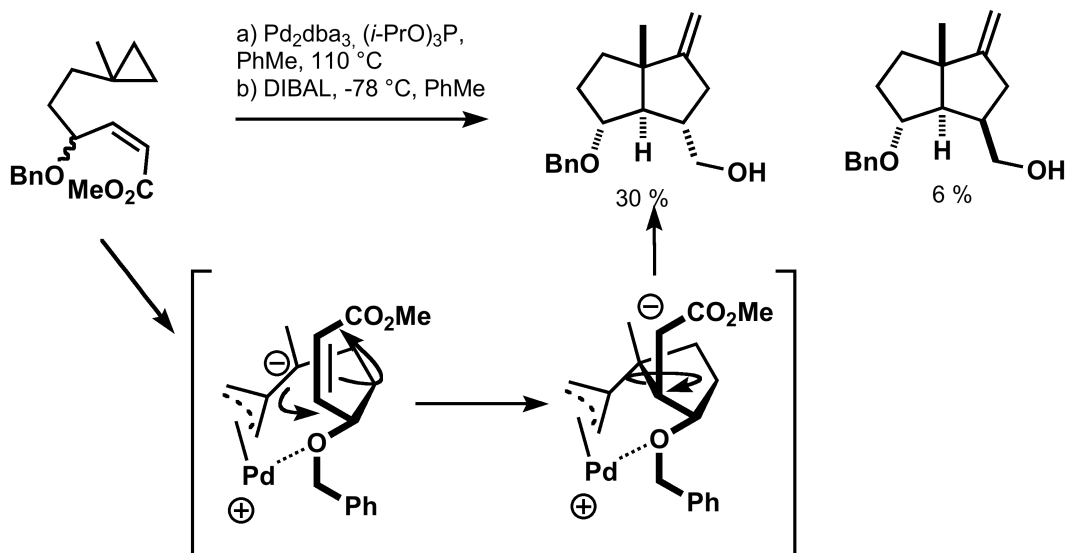


Trost's proposal



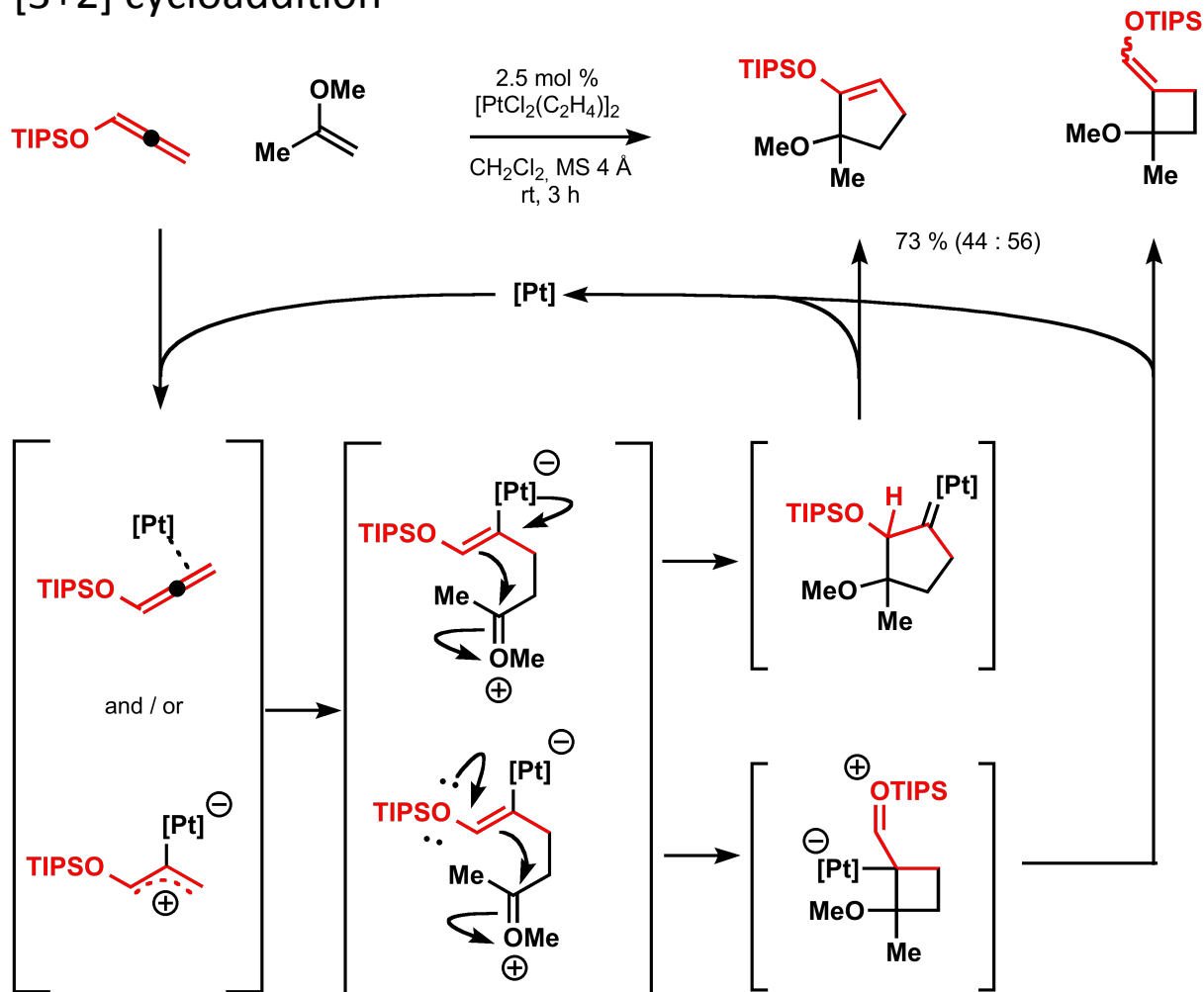
# [3+2] Cycloaddition

## Intramolecular [3+2] cycloaddition



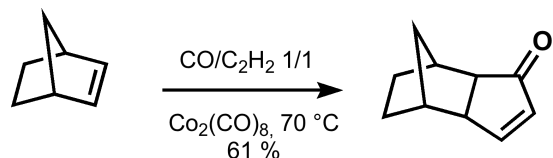
# [3+2] Cycloaddition

Pt catalyzed [3+2] cycloaddition

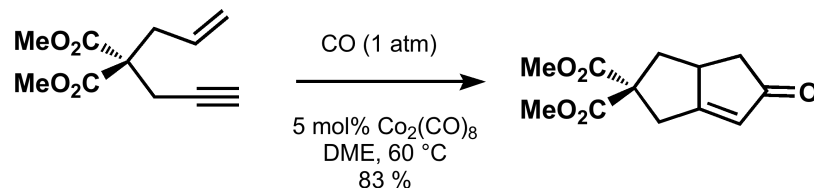


# [2+2+1] Cycloaddition

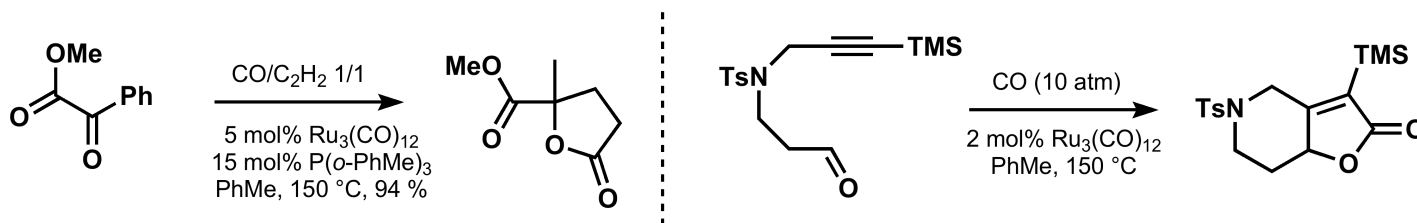
## Pauson-Khand reaction



## First catalytic Pauson Khand reaction

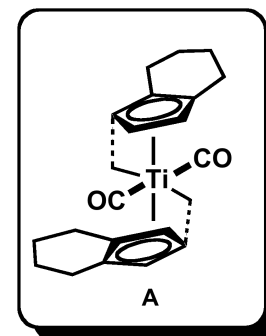
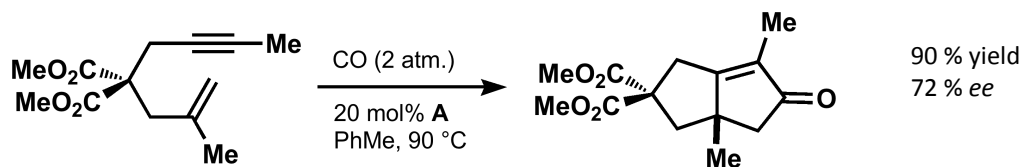
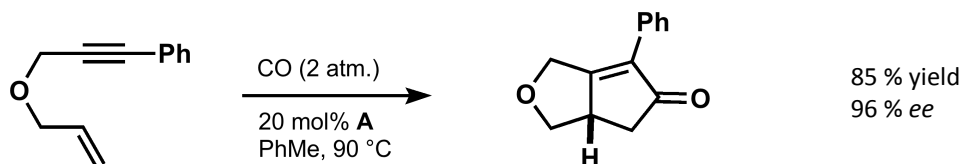


## [2+2+1] CA for synthesis of $\gamma$ -butyrolactones

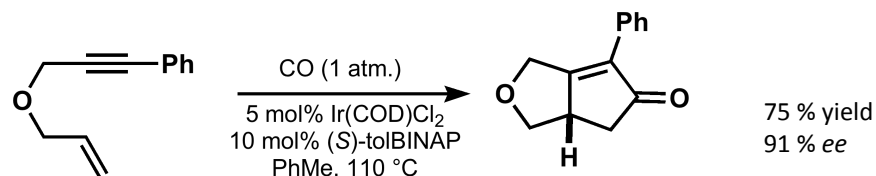
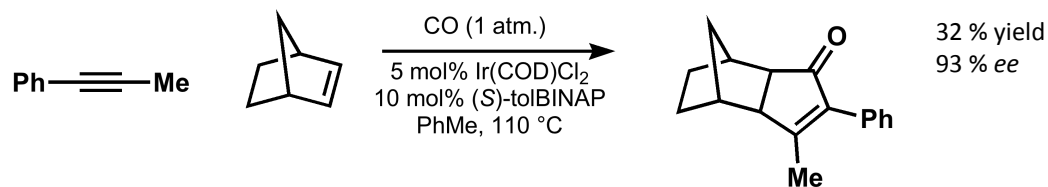


# [2+2+1] Cycloaddition

## Enantioselective catalytic Pauson Khand



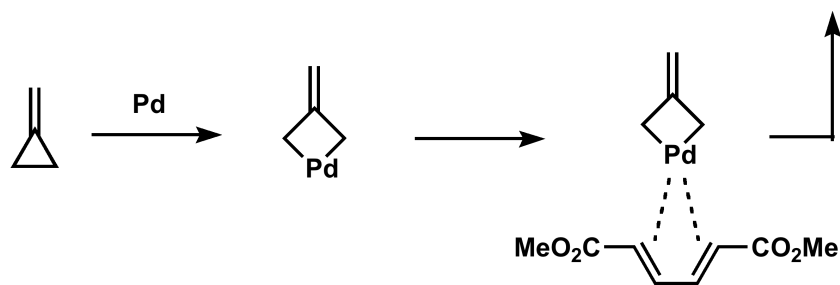
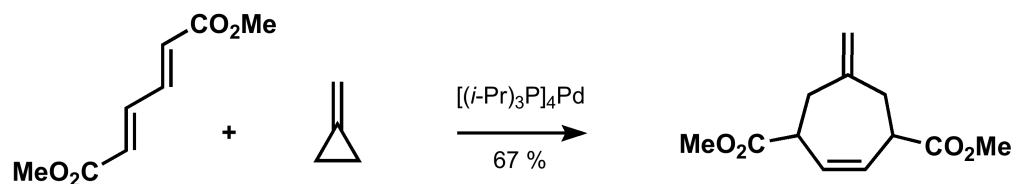
## Iridium catalyzed enantioselective Pauson Khand



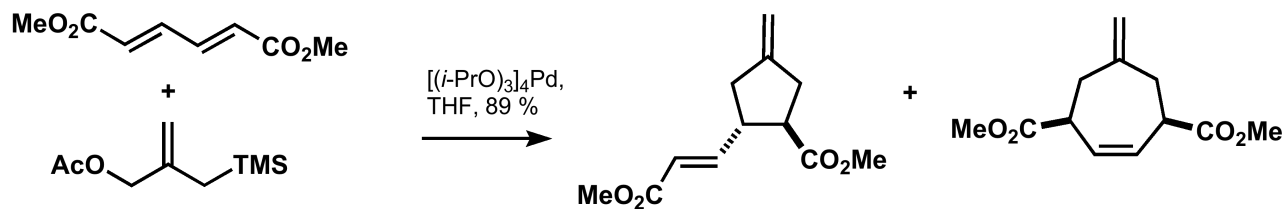


# [4+3] Cycloaddition

Cycloaddition between methylenepropane and dimethylmuconate



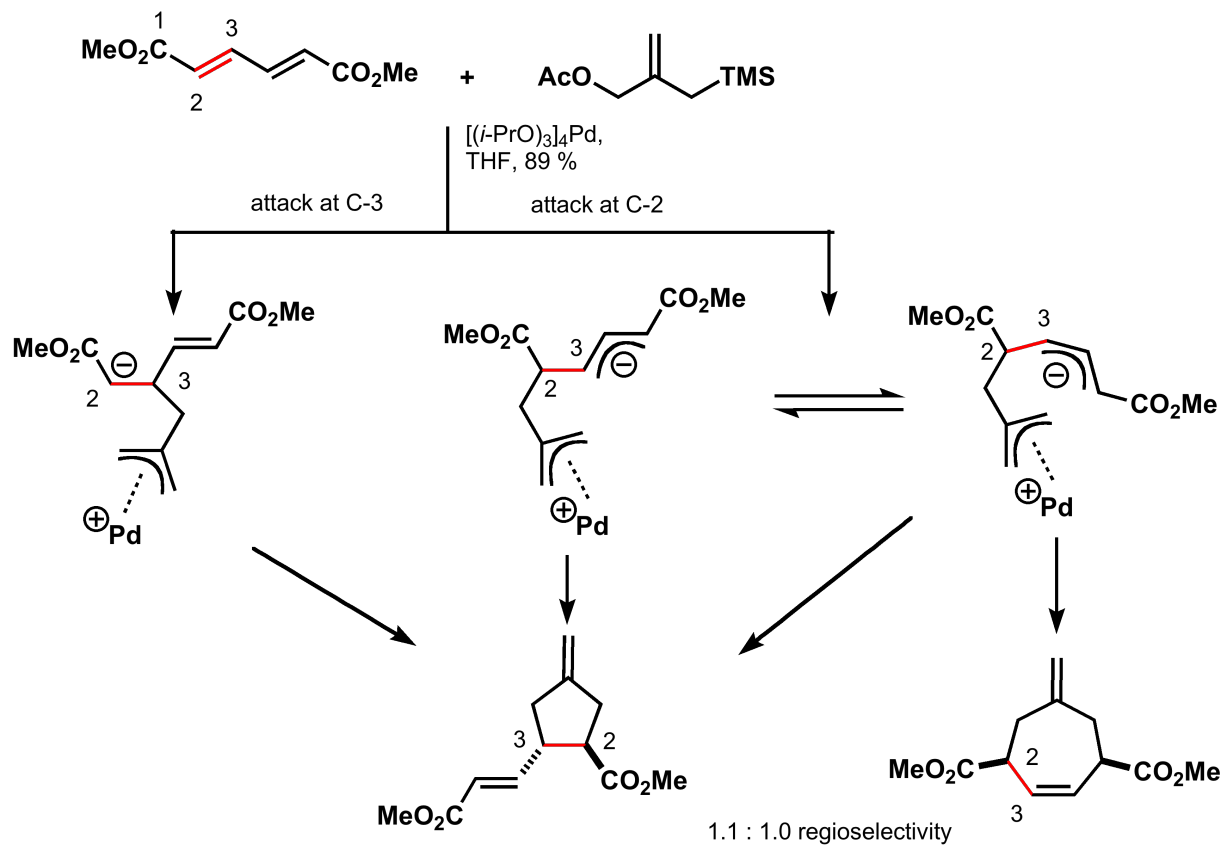
Cycloaddition between TMM and dimethylmuconate



1.1 : 1.0 regioselectivity

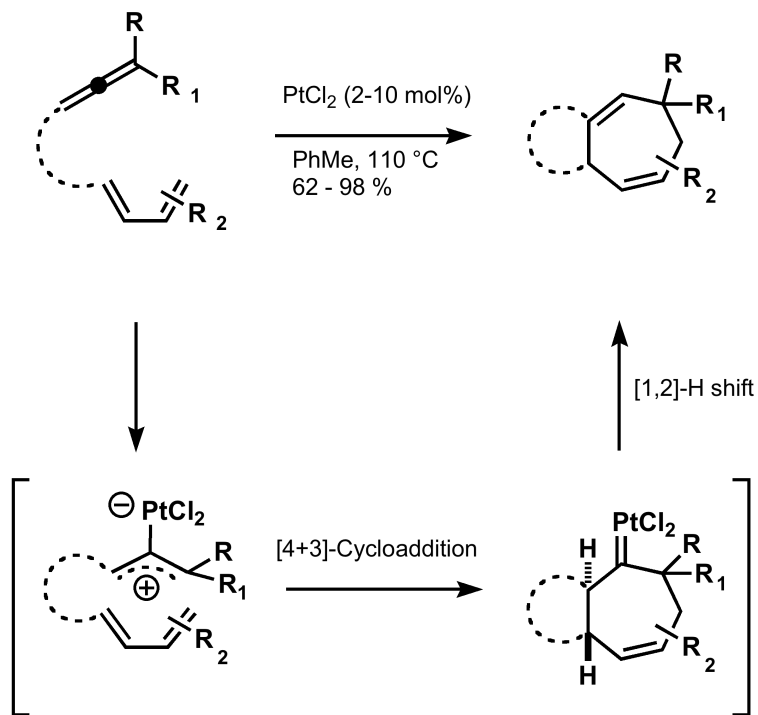
# [4+3] Cycloaddition

Two pathways for the cycloaddition

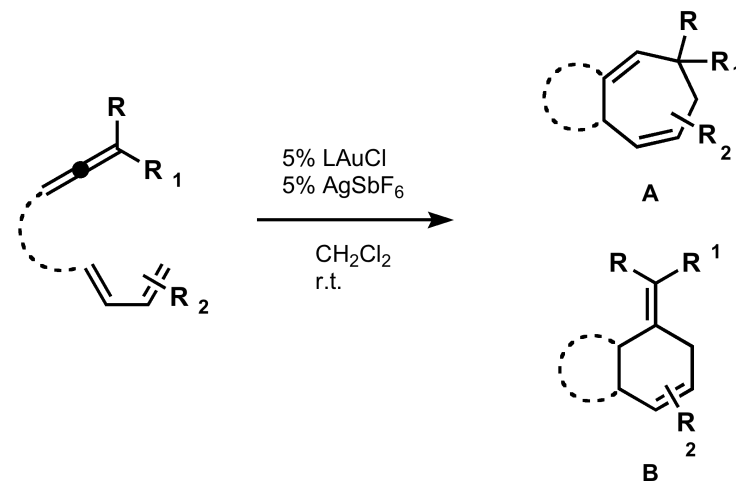


# [4+3] Cycloaddition

Pt and Au catalyzed [4+3] CA

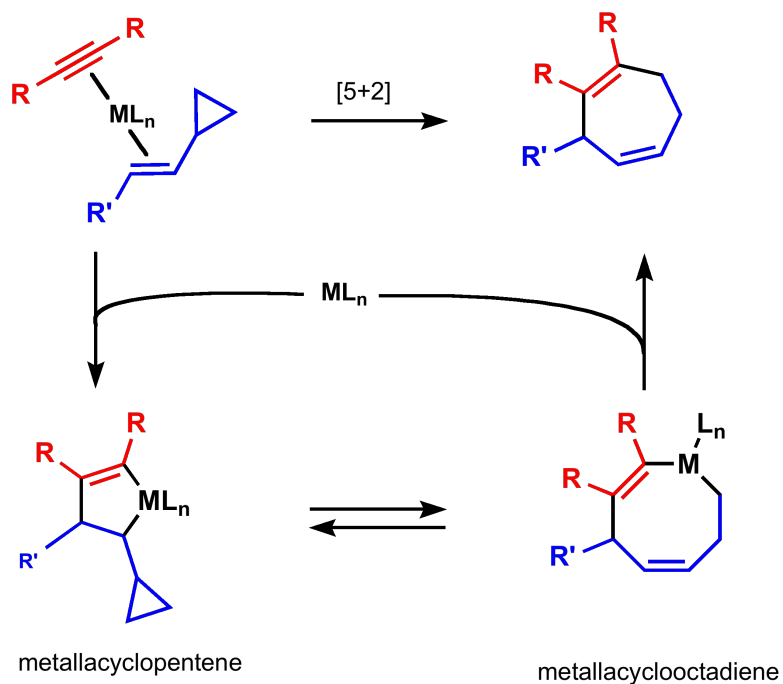
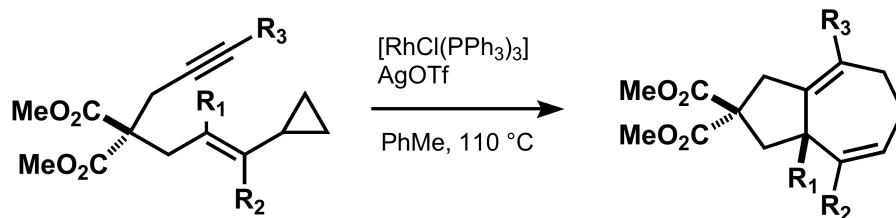


Formation of the [4+3] and [4+2] product

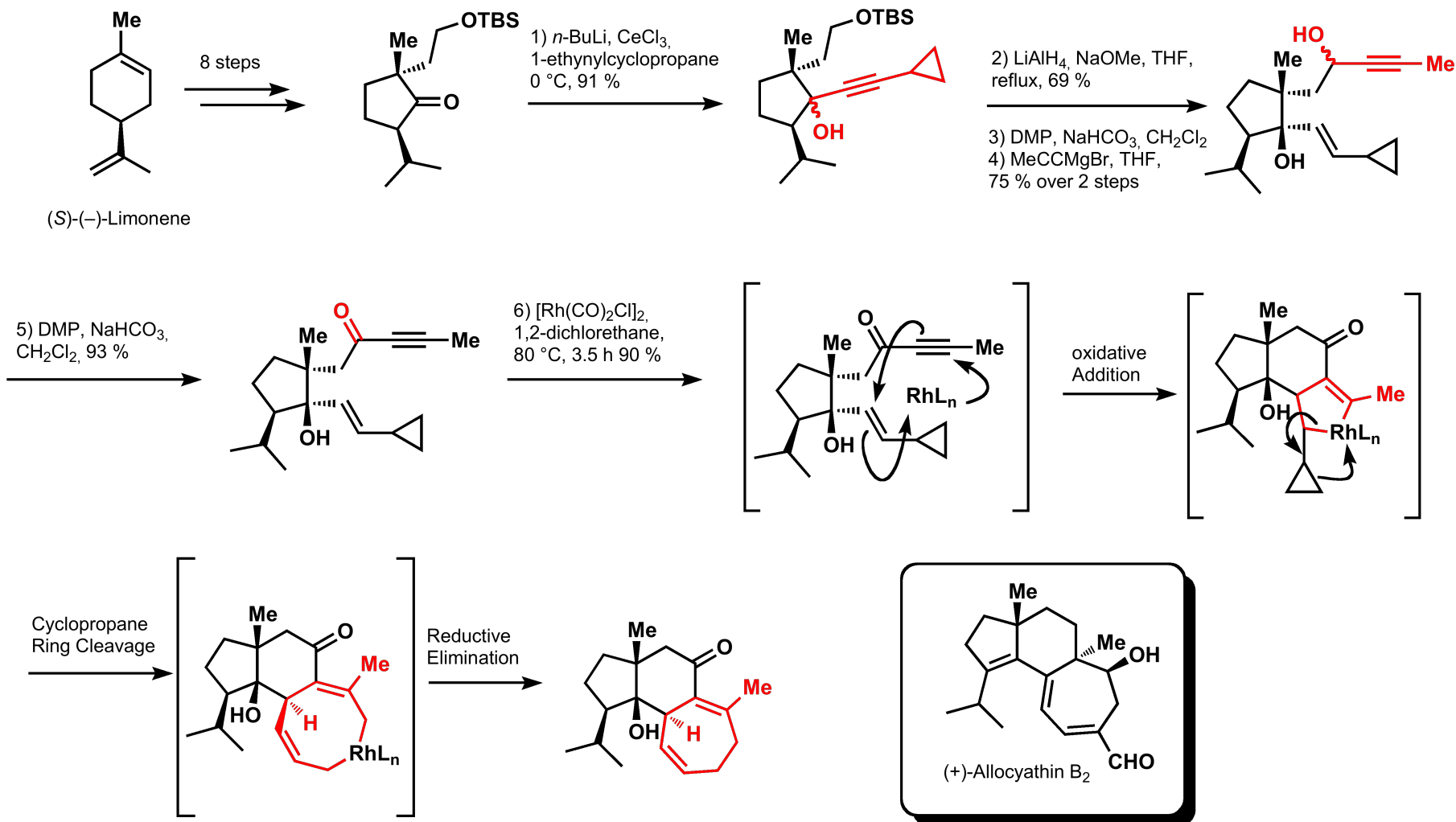


| Ligand  | Ratio A : B |
|---|-------------|
| P(OPh) <sub>3</sub>                             | 0 : 100     |
| PPh <sub>3</sub>                                | 33 : 67     |
| P( <i>t</i> -Bu) <sub>2</sub> ( <i>o</i> -biPh) | 96 : 4      |

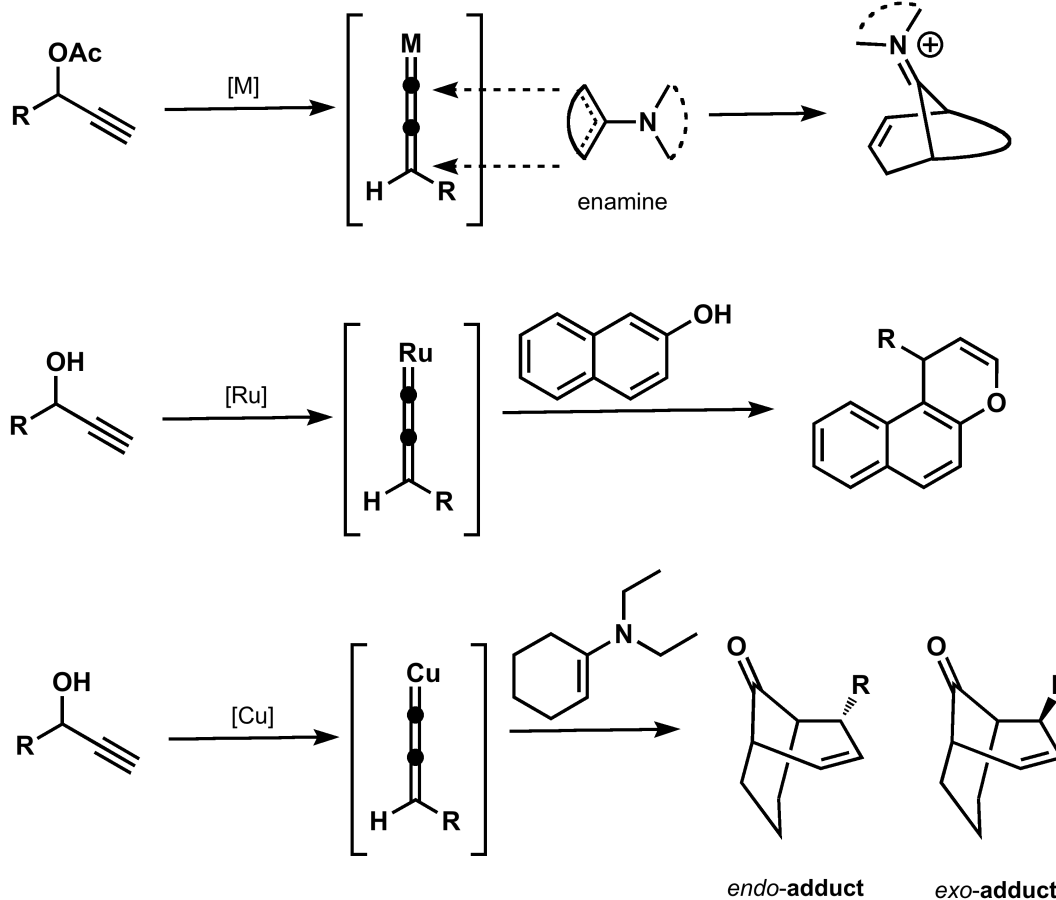
# [5+2] Cycloaddition



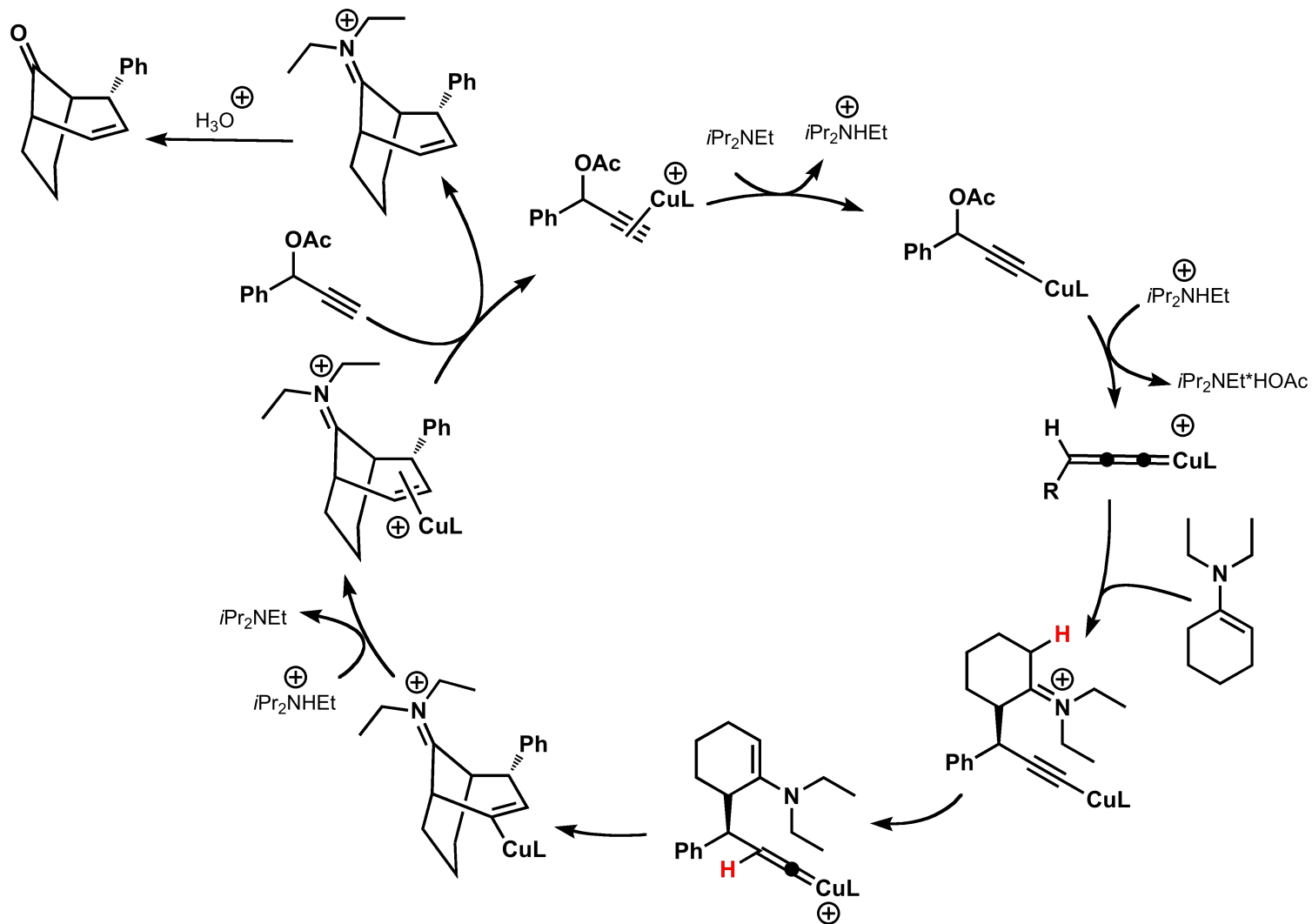
# [5+2] Cycloaddition



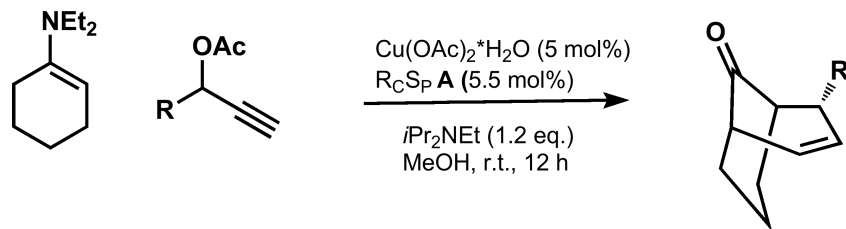
# [3+3] Cycloaddition



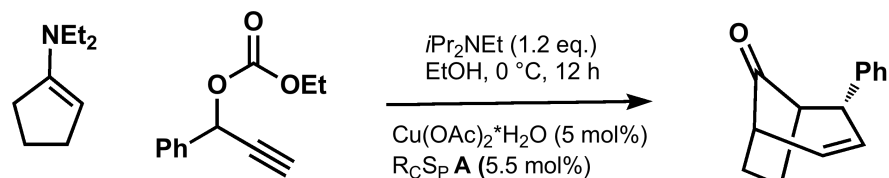
# [3+3] Cycloaddition



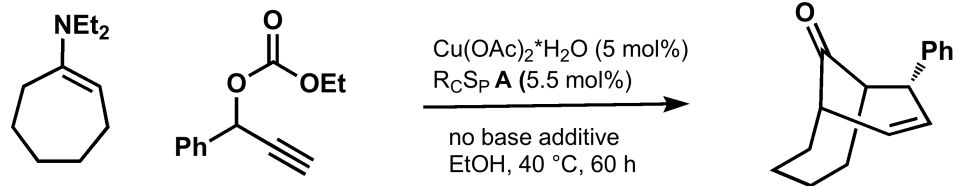
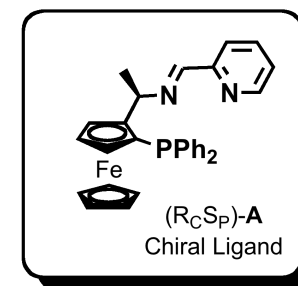
# [3+3] Cycloaddition



| R = | Yield (%) | endo/exo |
|-----|-----------|----------|
| Ph  | 86        | > 98/2   |
| Me  | 58        | > 98/2   |
| H   | 74        | -        |



endo, 50 % yield 98 % ee,  
endo/exo > 98/2

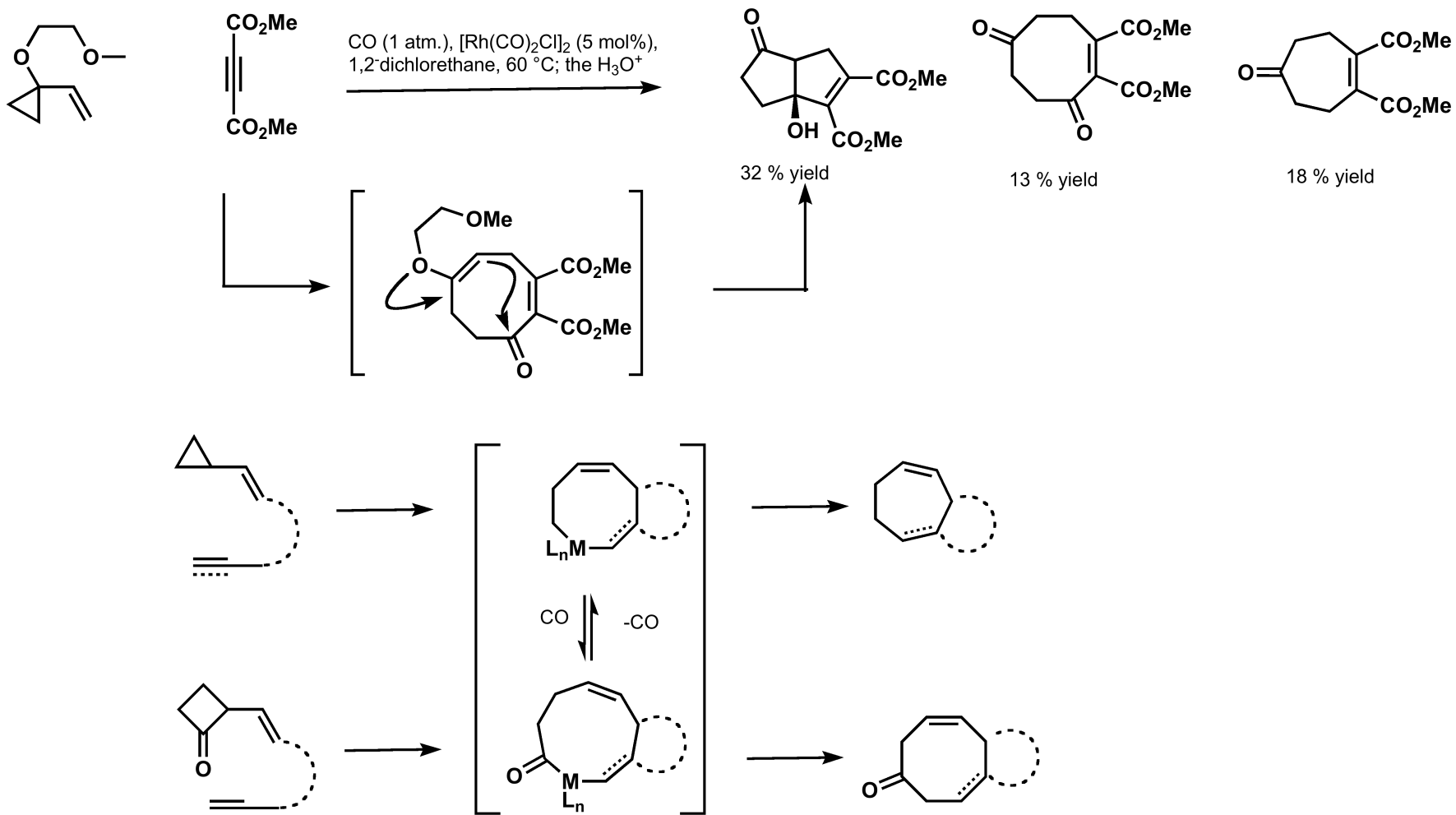


endo, 48 % yield 98 % ee,  
endo/exo > 98/2



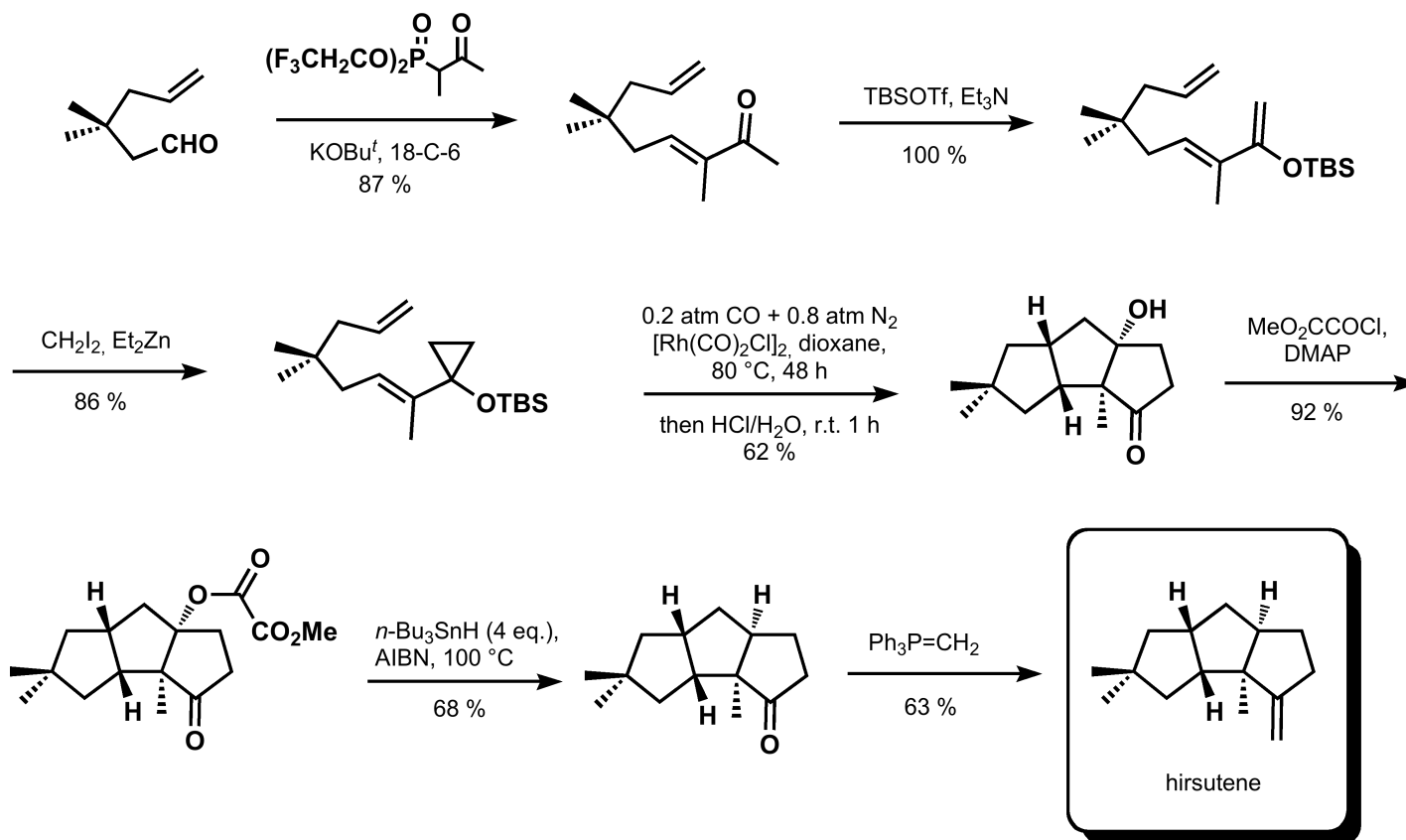
# [5+2+1] Cycloaddition

## Rhodium catalyzed [5+2+1] cycloaddition



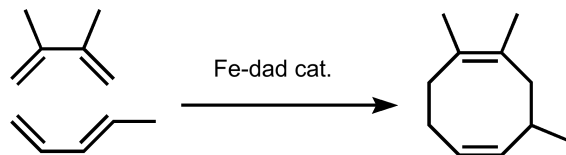
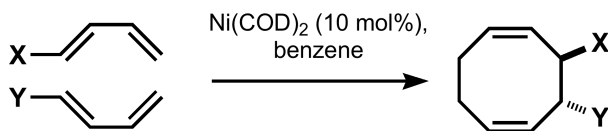
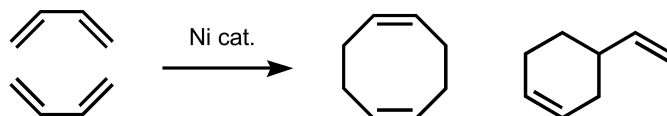
# [5+2+1] Cycloaddition

Tandem Rh(I)-Catalyzed [5+2+1] cycloaddition/Aldol in the total synthesis of Hirsutene

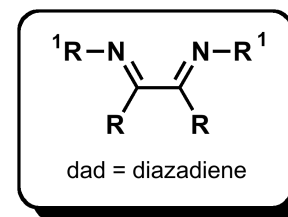


# [4+4] Cycloaddition

## Cyclodimerization reactions

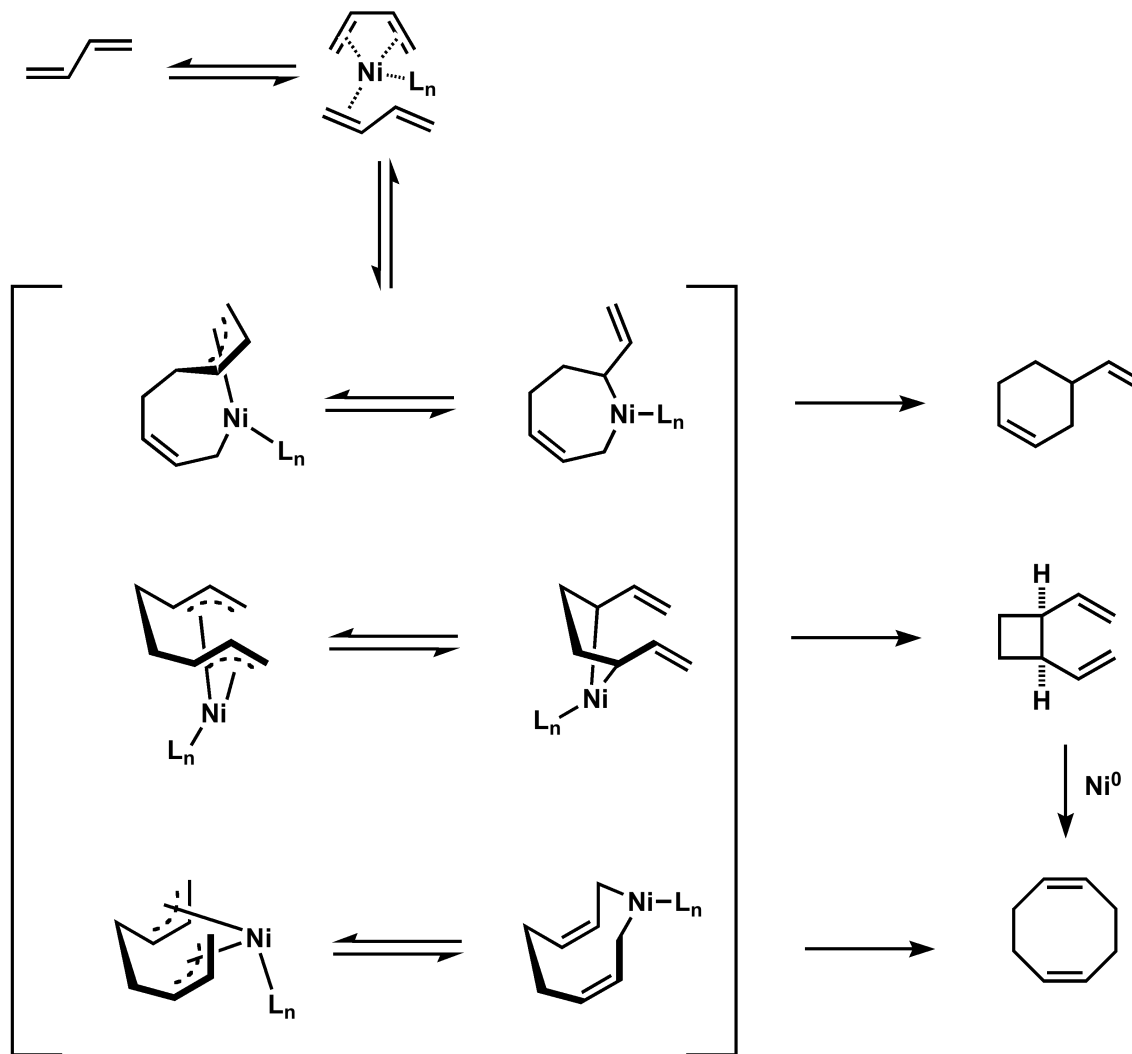


| Substituents                     | Yield % |
|----------------------------------|---------|
| X, Y = OSiMe <sub>3</sub> (18 d) | 90      |
| X, Y = CO <sub>2</sub> Me (24 h) | 70      |
| X = H, Y = CO <sub>2</sub> Me    | 30      |



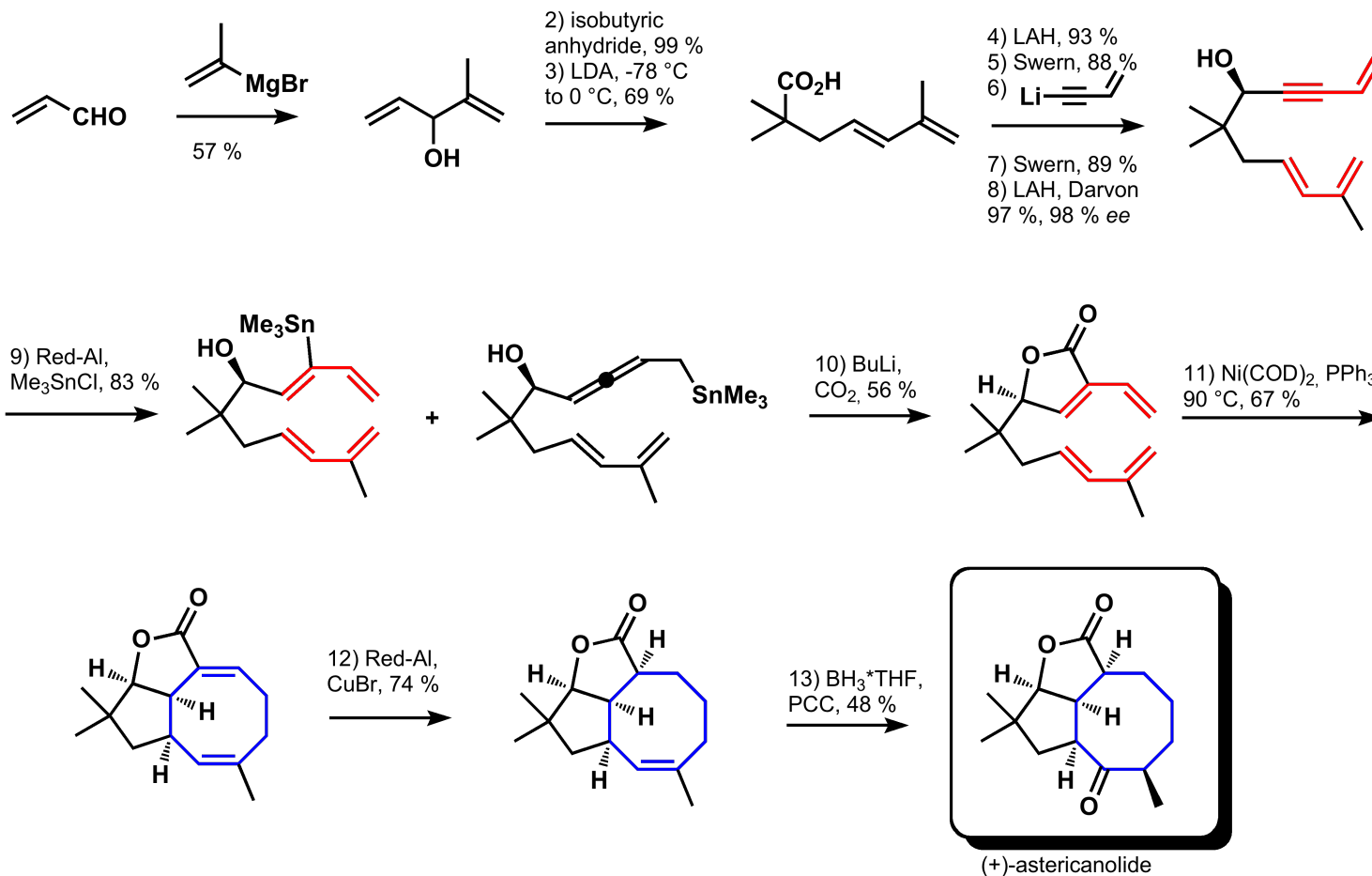
# [4+4] Cycloaddition

Mechanism for the cyclodimerization



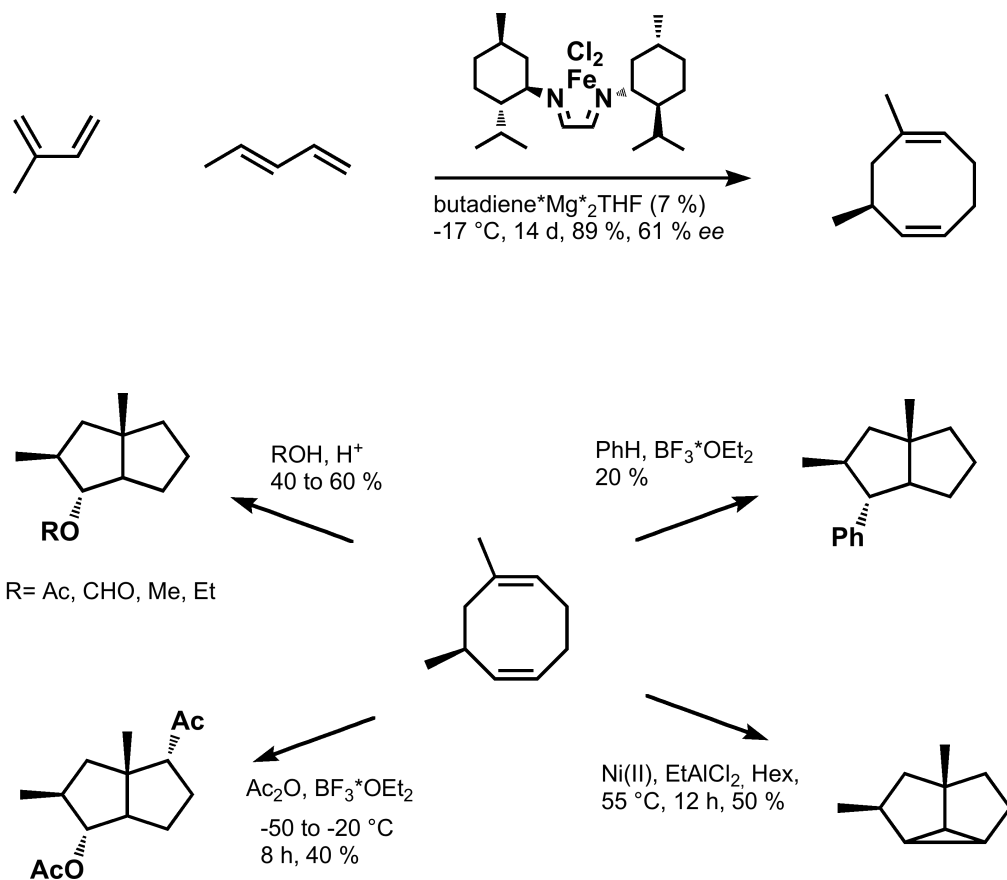
# [4+4] Cycloaddition

## Total Synthesis of (+)-Asteriscanolide



# [4+4] Cycloaddition

## Asymmetric [4+4] Cycloaddition



Thank you for your attention





