

# SOMO Activation

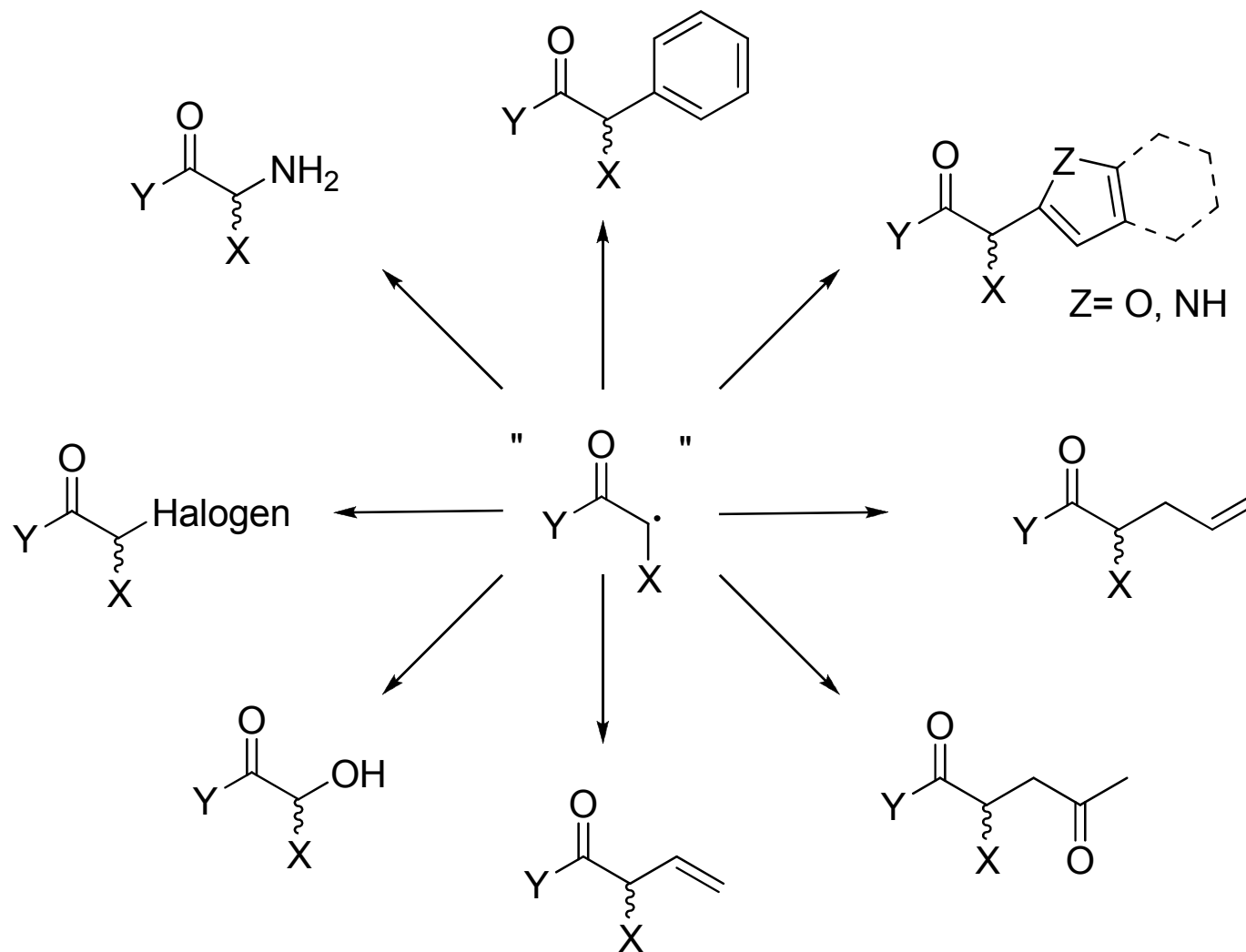
Colin Hughes

September 10 2008

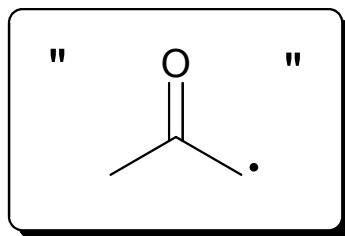
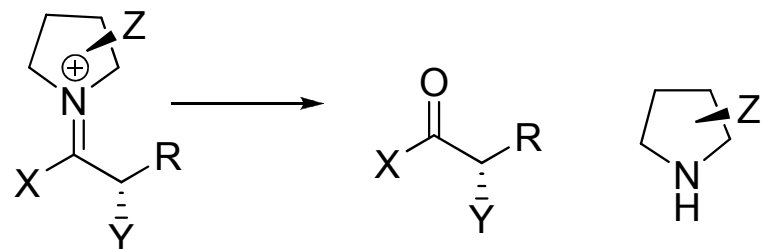
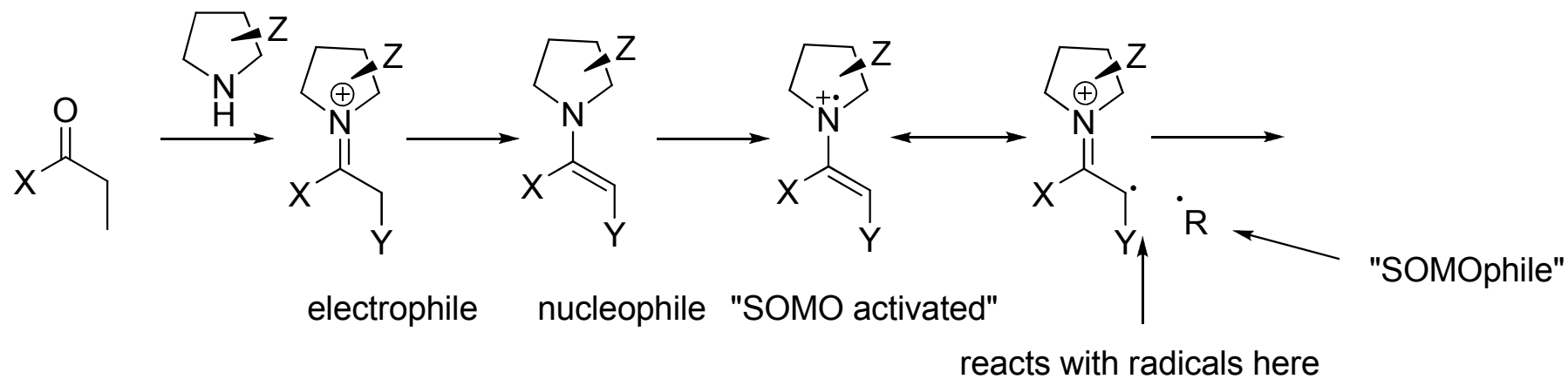
# Outline

- Brief introduction to the concept
- Overview of the different catalysts
- Requirements for SOMO to operate successfully
- Early example
- $\alpha$ - oxyamination + alternate organocatalytic method
- $\alpha$ - allylation + alternate organocatalytic method
- $\alpha$ - enolation + alternate organocatalytic method
- $\alpha$ - vinylation + alternate organocatalytic method
- Compare methods
- Side reactions
- Conclusion

# Possibilities of an $\alpha$ - Radical



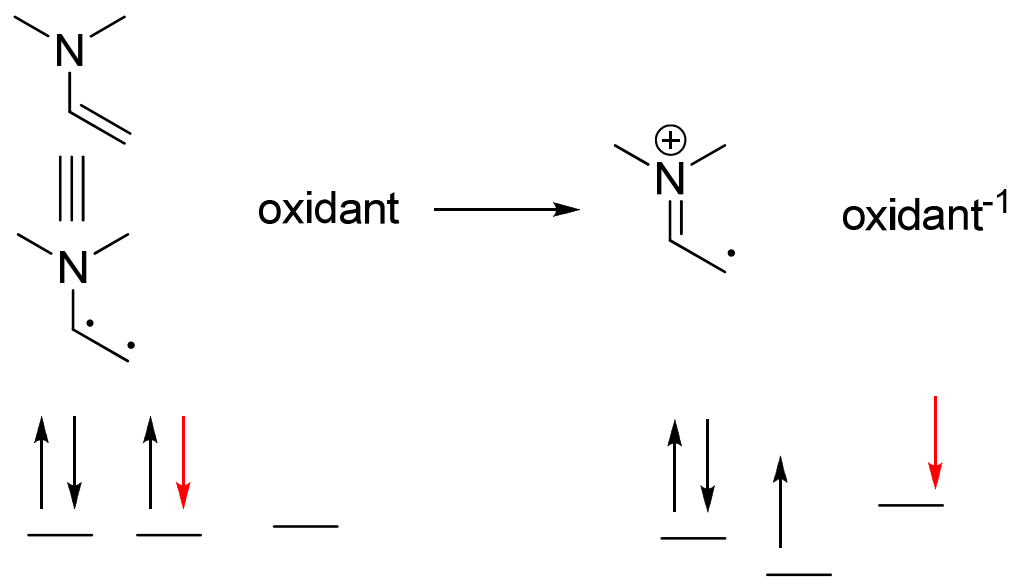
# "SOMO" Activation



# Why is SOMO activation special?

- New activation mode for asymmetric catalysis
- Once it was believed that radical reactions could not be performed with reasonable levels of enantiocontrol
- Operationally simple

# Formation of SOMO by Oxidation



Oxidant

Price

$(\text{NH}_4)_2\text{Ce}(\text{NO}_3)_6$  "CAN"

$\text{Ce}^4$

30 ¢/g

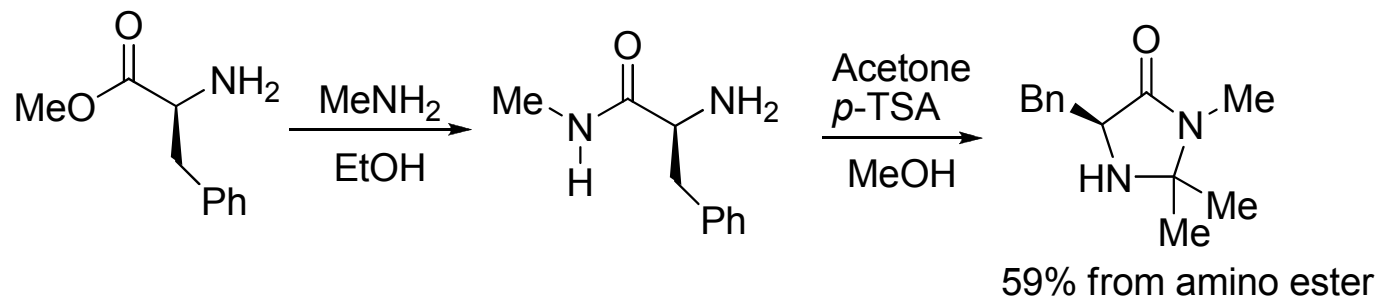
$\text{FeCl}_3$

$\text{Fe}^3$

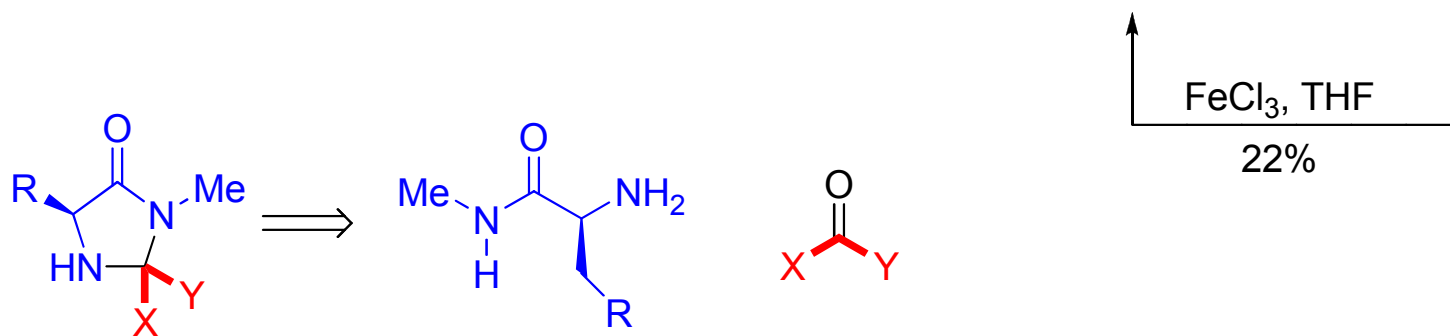
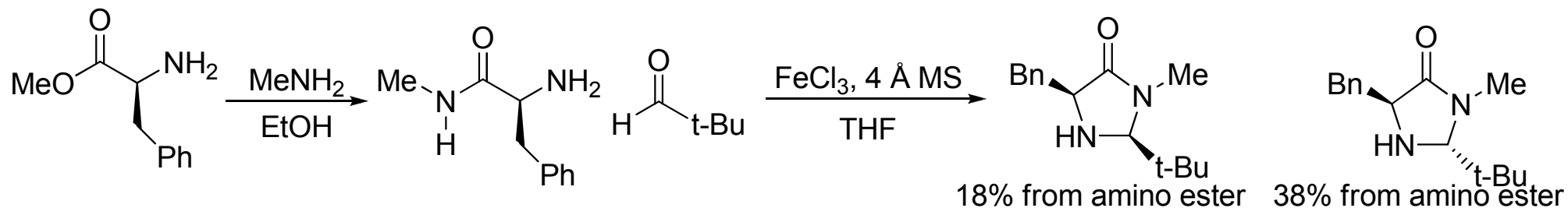
3.6 ¢/g

# Preparation of Catalyst

1<sup>st</sup> Generation



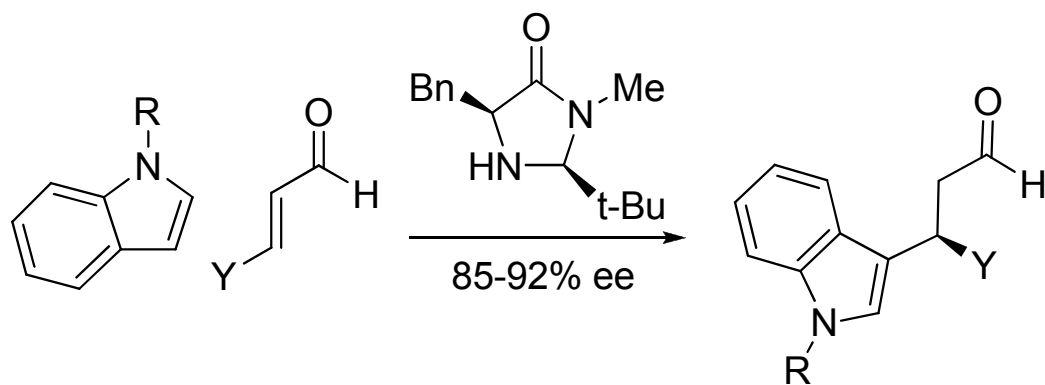
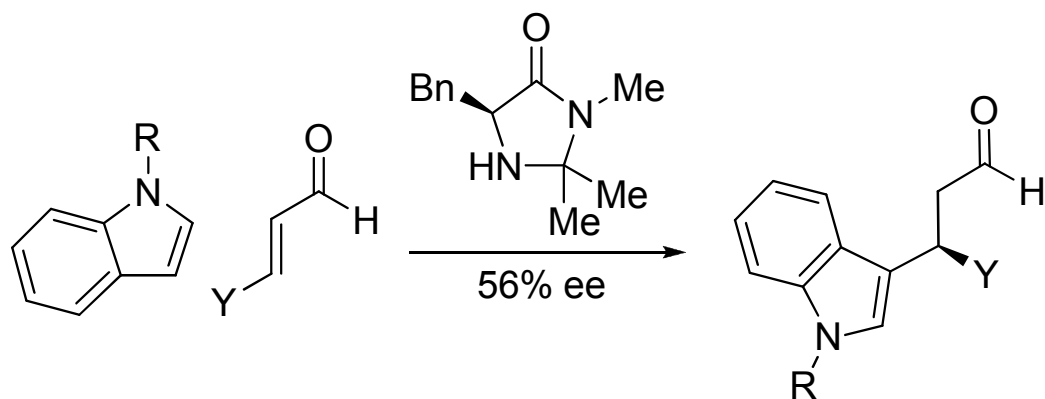
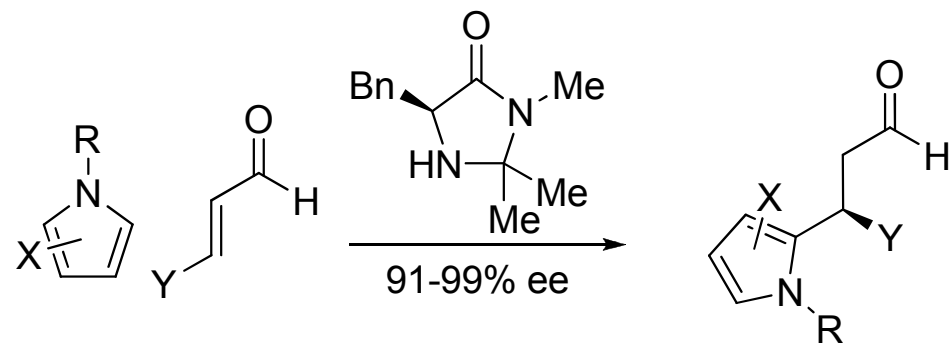
2<sup>nd</sup> Generation



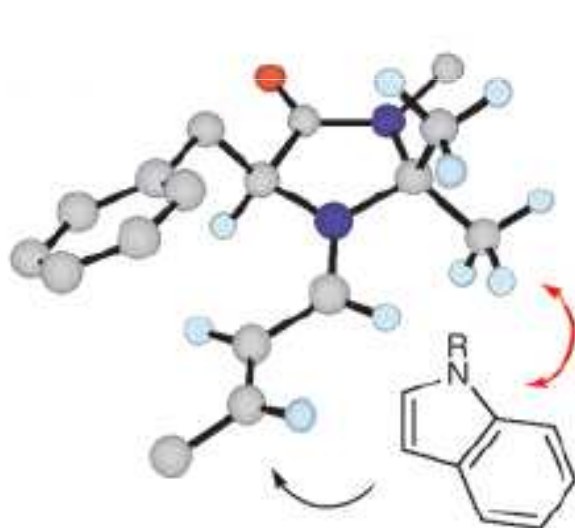
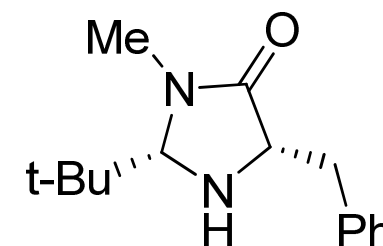
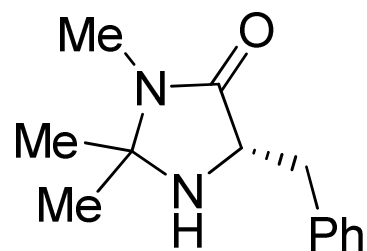
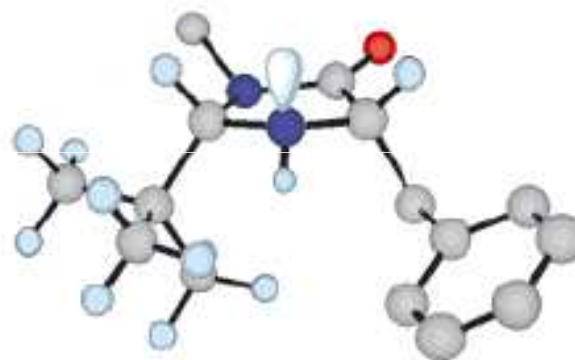
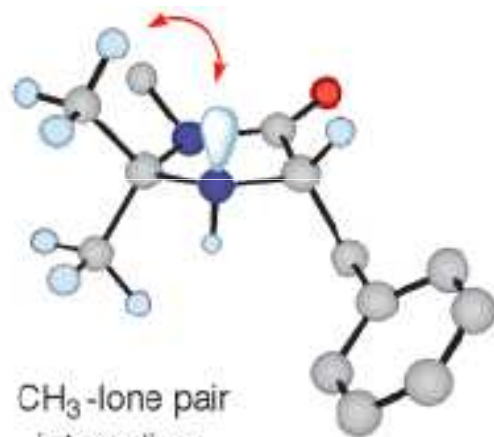
Ahrendt, K. A.; Borths, C. J.; MacMillan, D. W. C., *J. Am. Chem. Soc.*, **2000**, 122, 4243

Paras, N. A.; MacMillan, D. W. C., *J. Am. Chem. Soc.*, **2001**, 123, 4370

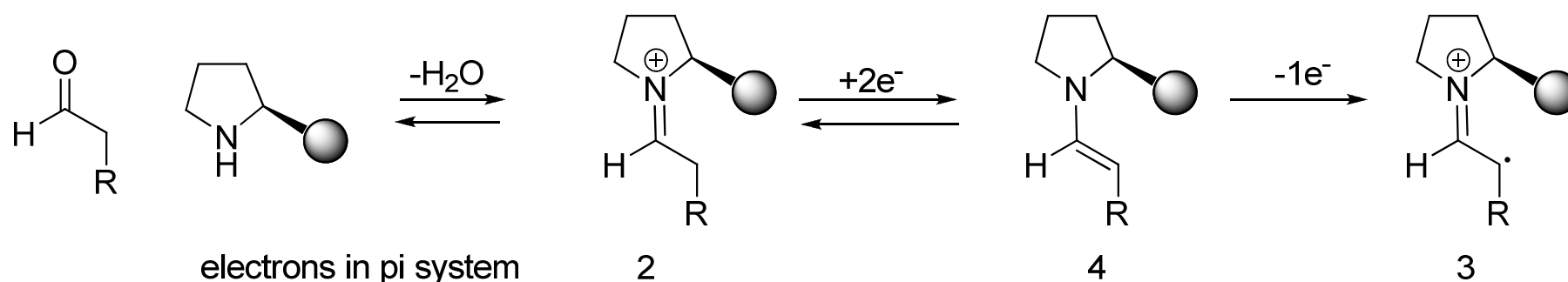
# Why Different Catalysts?



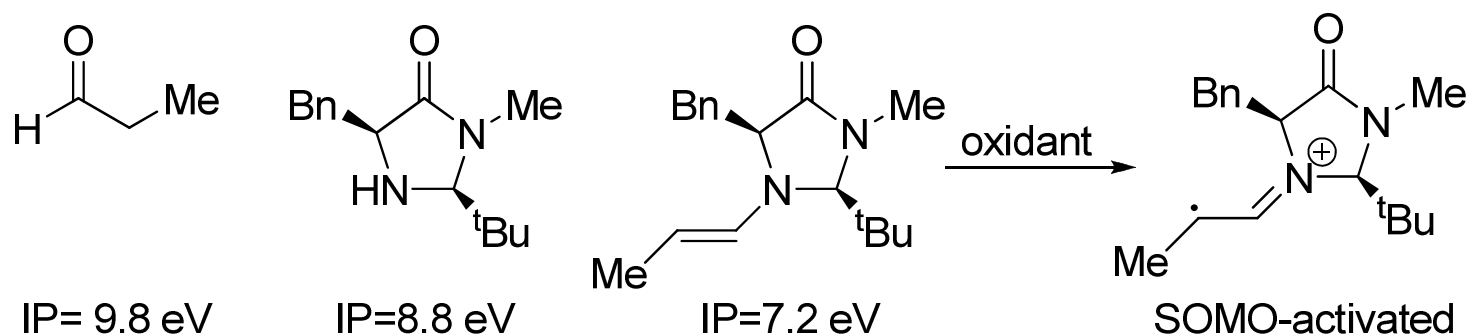
# Why Different Catalysts?

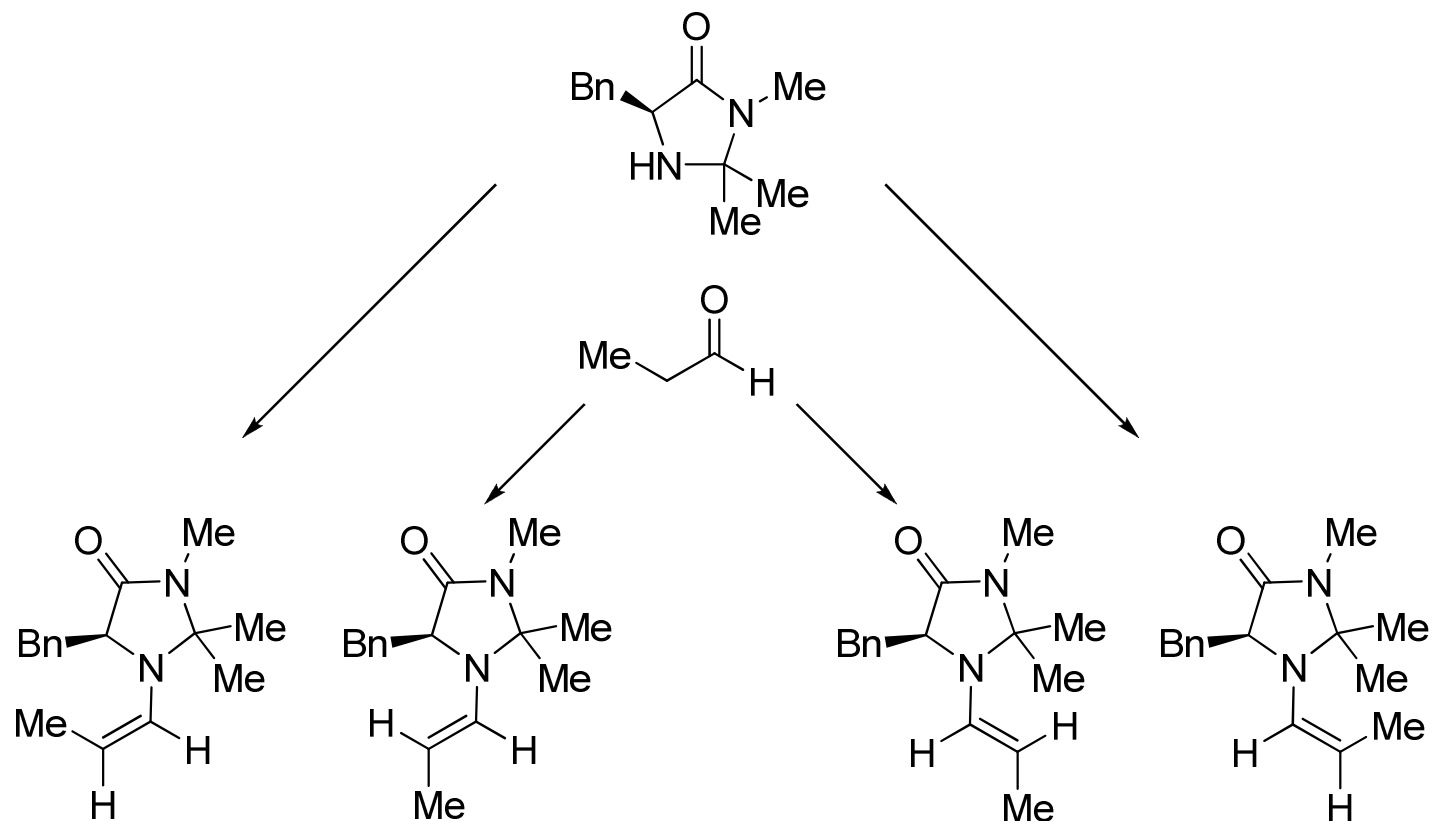


# Requirements for SOMO Activation

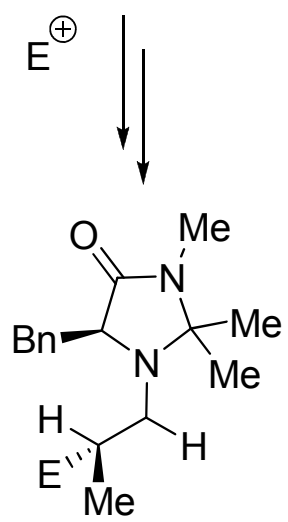


- 1) Catalyst should undergo efficient and reversible enamine formation
- 2) High levels of control of enamine geometry
- 3) Selective discrimination of olefin pi face
- 4) Enamine must undergo selective oxidation in presence of amine catalyst, aldehyde, iminium ion

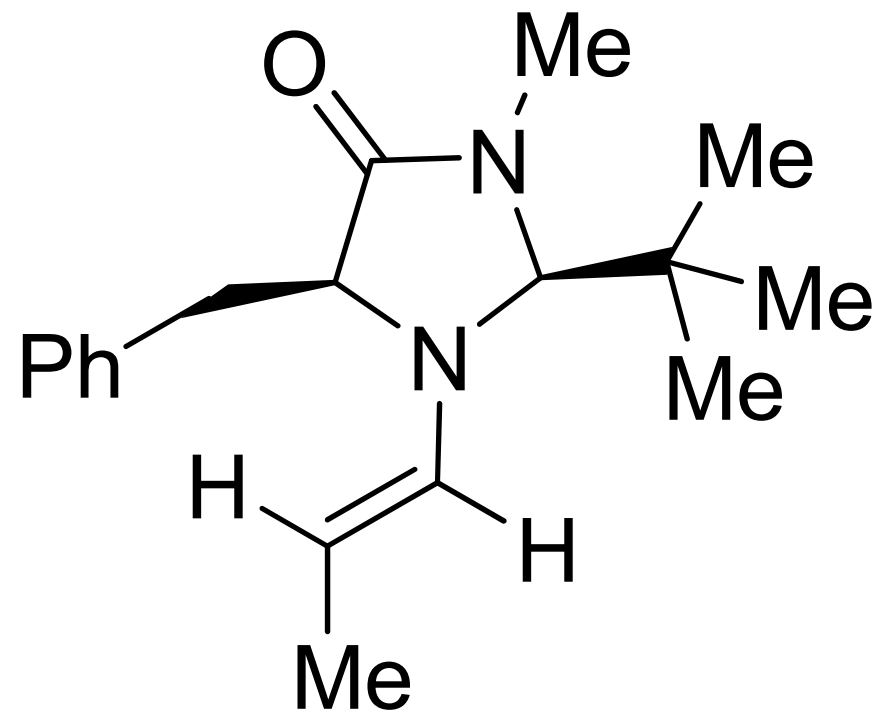
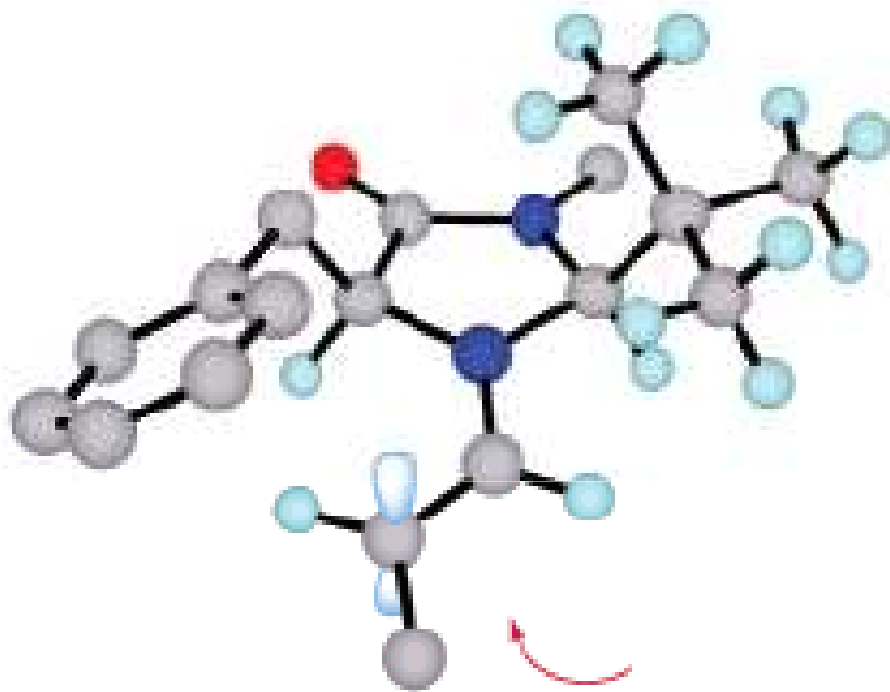




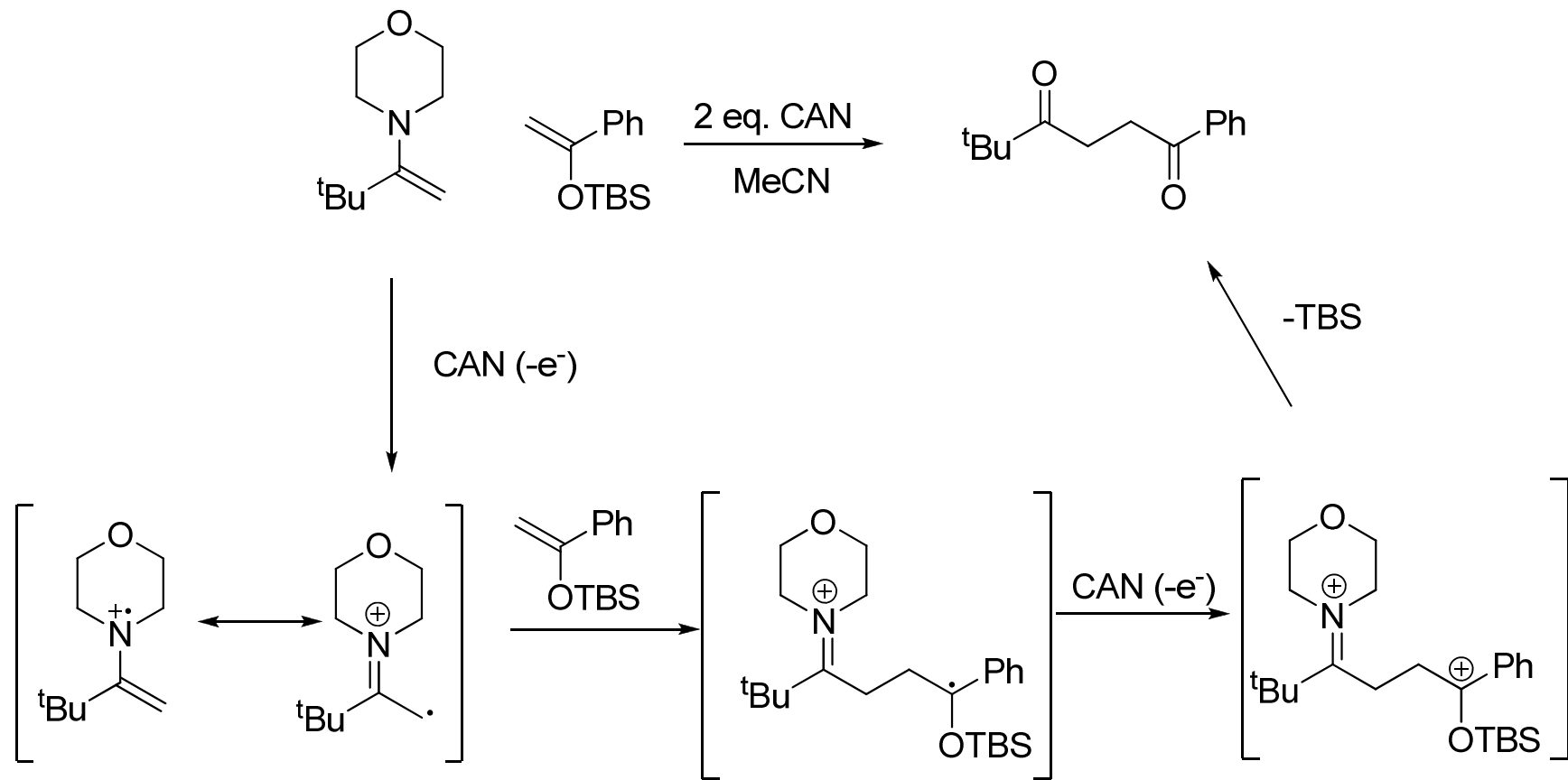
least A 1,3 strain



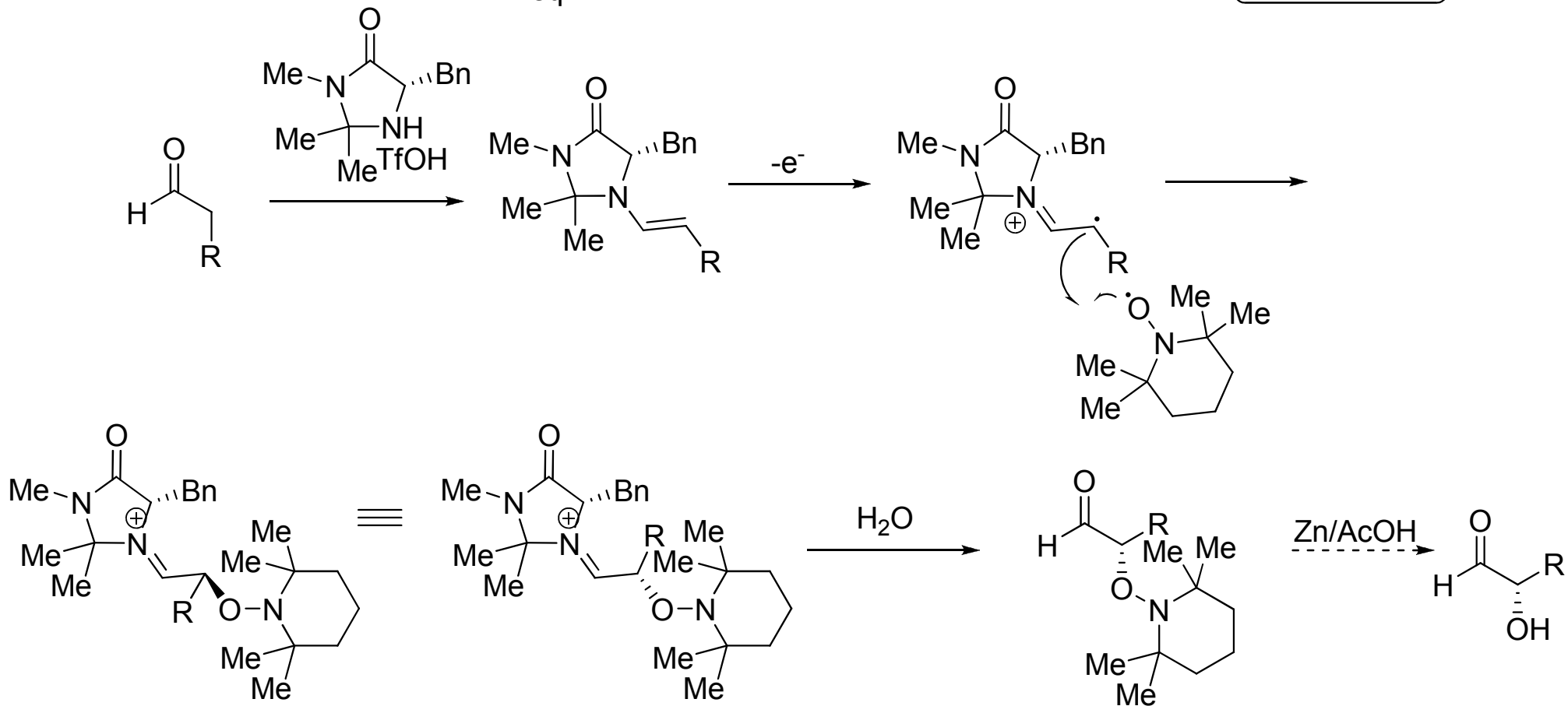
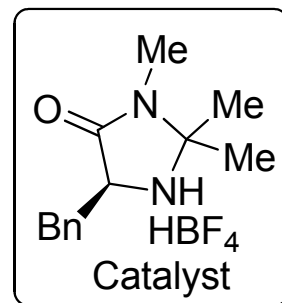
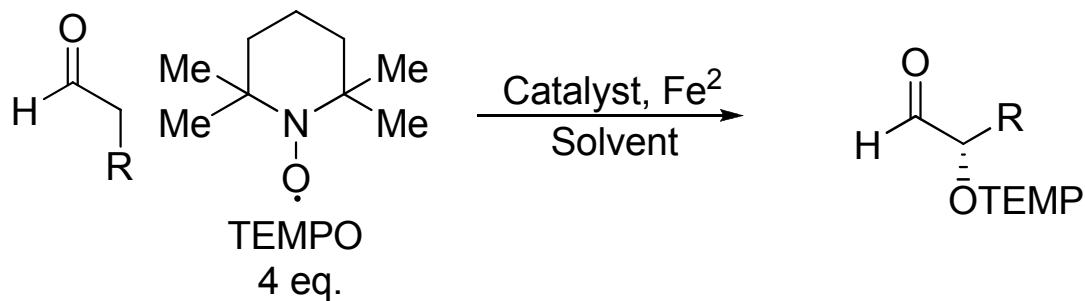
# Stereoselective Addition



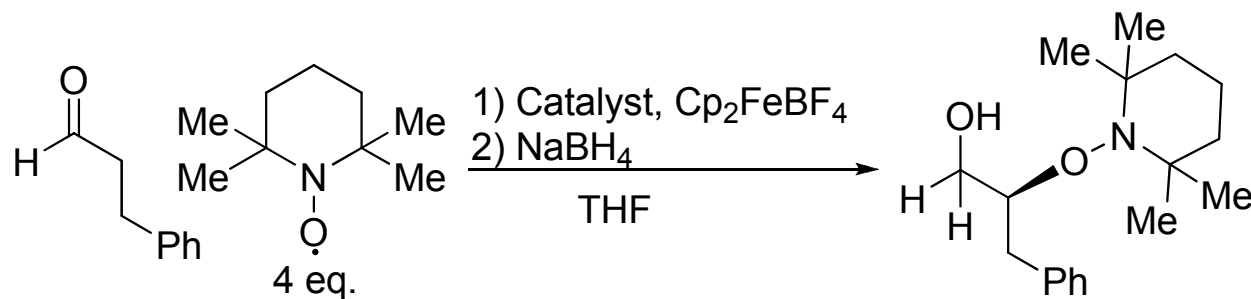
# Early Radical Cation from Enamine



# $\alpha$ -Oxyamination of Aldehydes

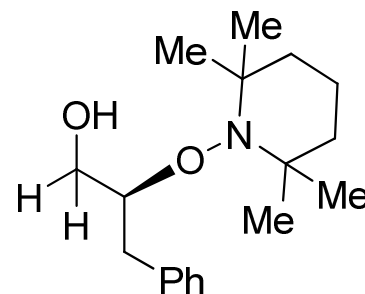
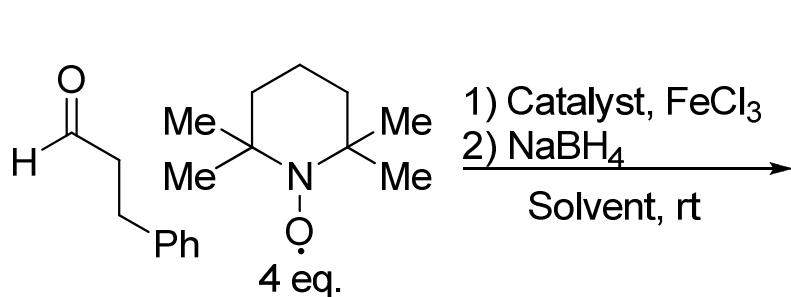


# Catalyst Screening



Catalyst	none					
mol	N/A	100%	100%	20%	20%	20%
Yield, time	<b>79%, 24h</b>	61%, 1h	63%, 1h	78%, 1h	<b>87%, 1h</b>	71%, 1h
ee	0%	0%	76%	64%	80%	-3%

# Catalyst Screening



(NH<sub>4</sub>)<sub>2</sub>Ce(NO<sub>3</sub>)<sub>6</sub> "CAN"

FeCl<sub>3</sub>

NaNO<sub>2</sub>

Price

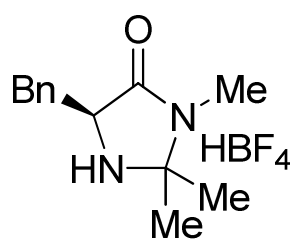
Ce<sup>4</sup>

30 €/g

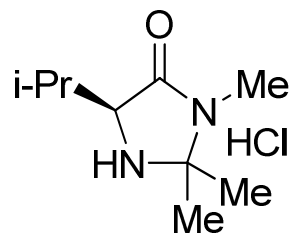
Fe<sup>3</sup>

3.6 €/g

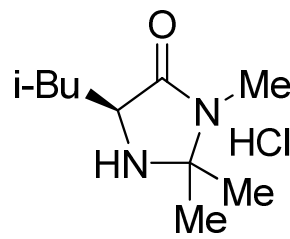
7.7 €/g



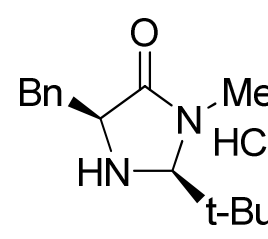
A



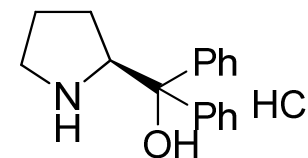
B



C



D



E

FeCl<sub>3</sub> (%)

NaNO<sub>2</sub> (%)

Catalyst

Solvent

Yield (%)

ee (%)

100

0

A

THF

4

nd

100

0

A

DMF

74

72

30

30

A

DMF

82

75

**10**

**30**

**A**

**DMF**

**83**

**72**

10

30

B

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75

5

10

30

C

DMF

64

46

10

30

D

DMF

26

0

10

30

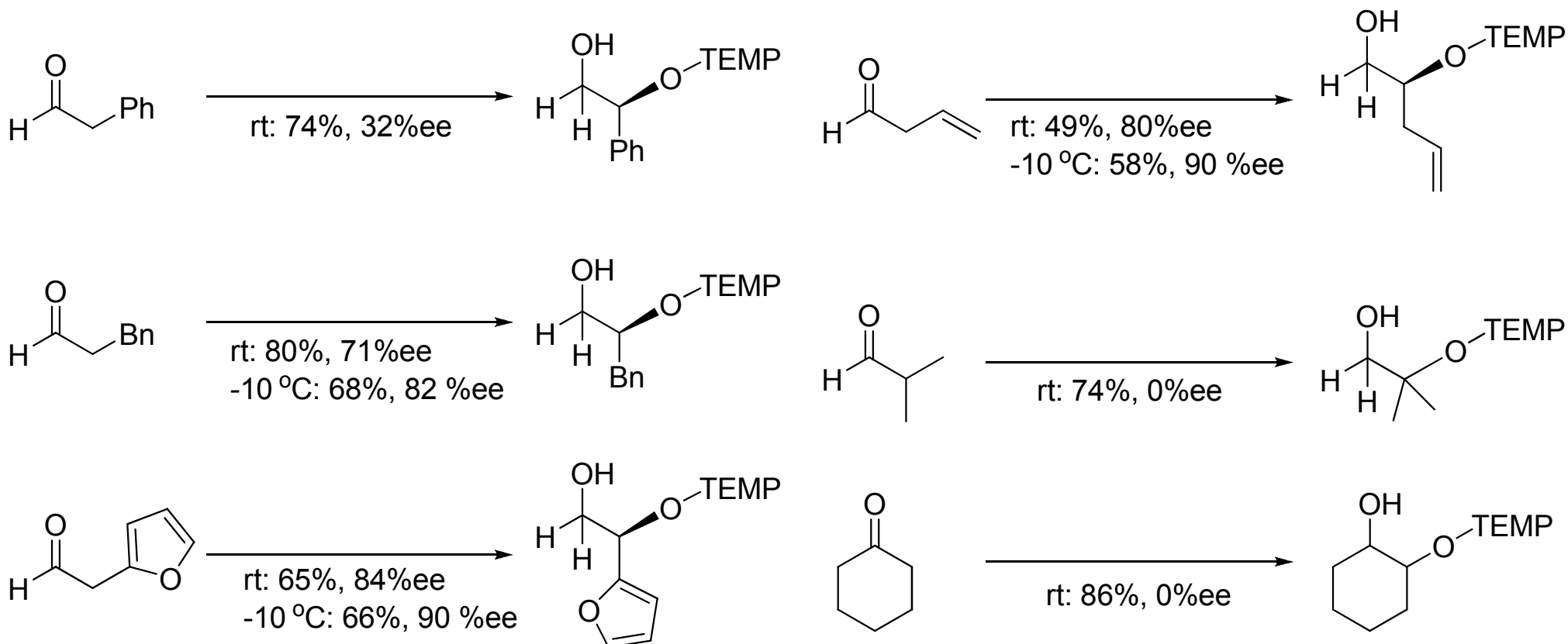
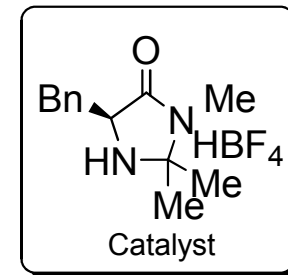
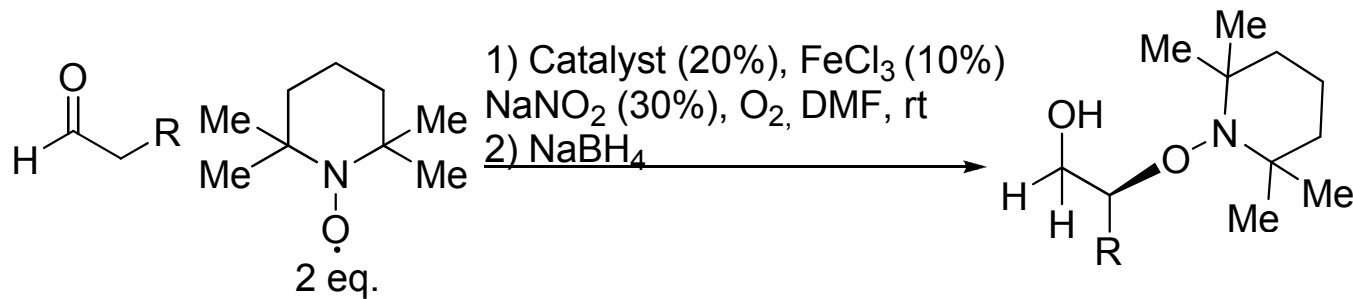
E

DMF

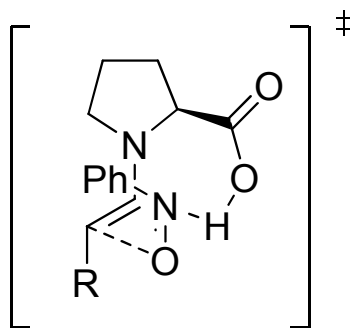
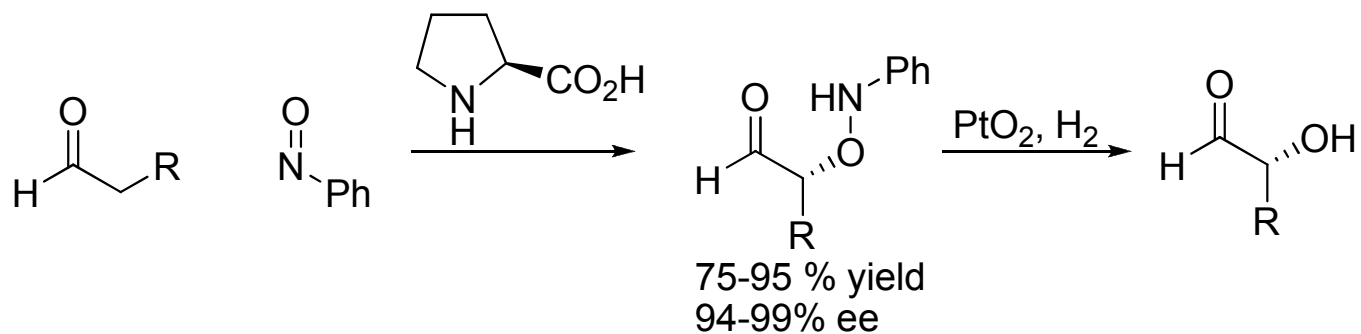
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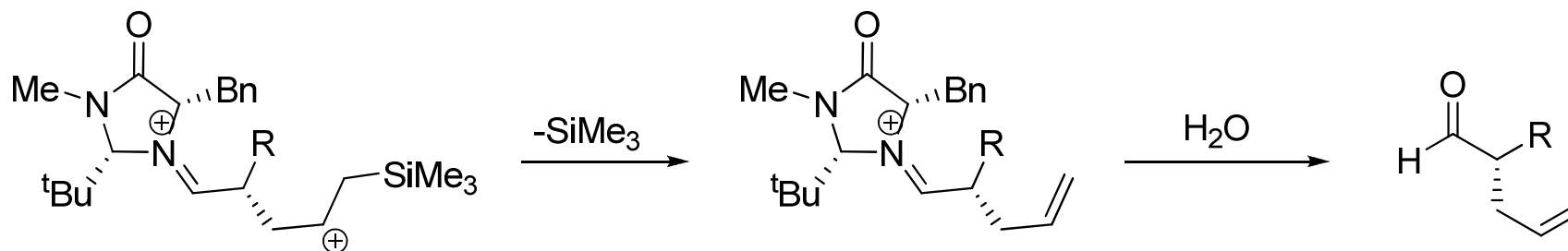
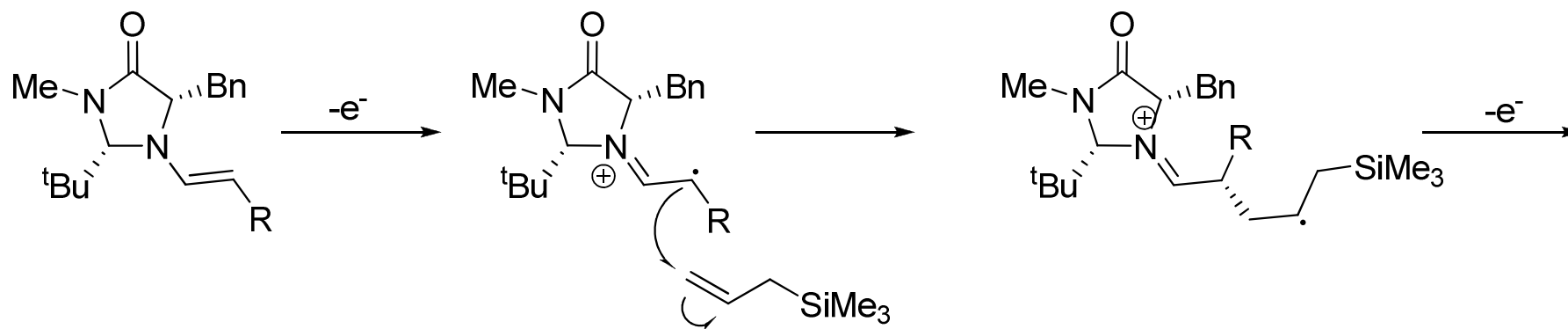
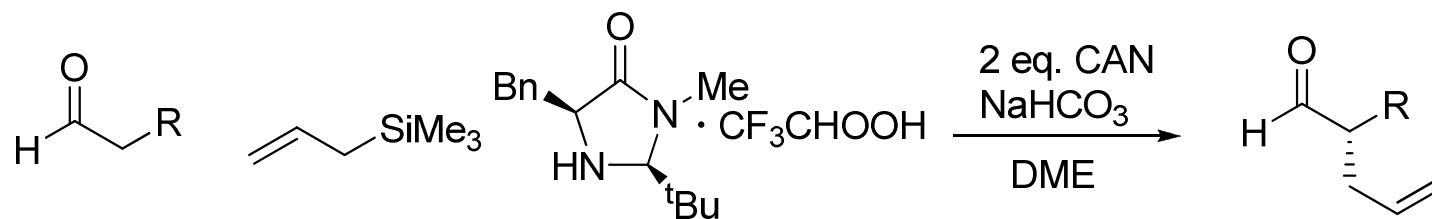
# Aldehyde Scope



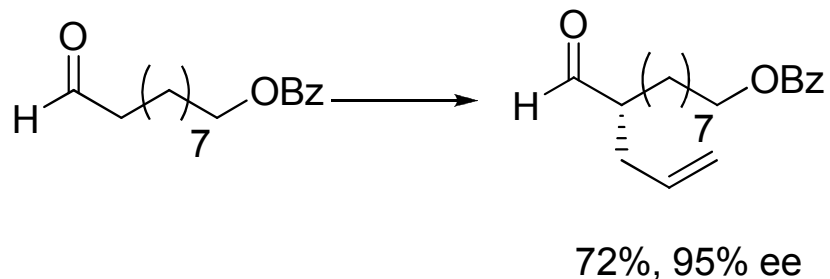
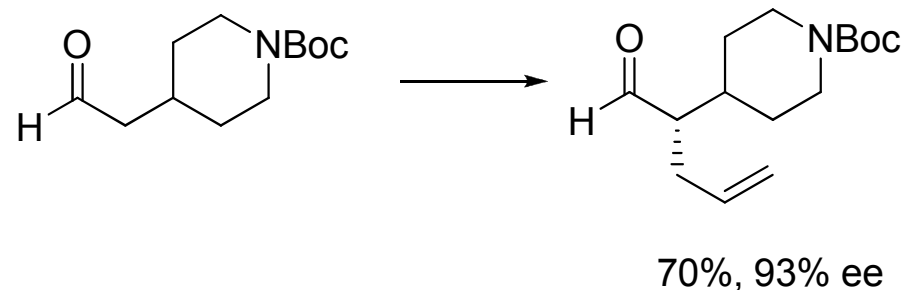
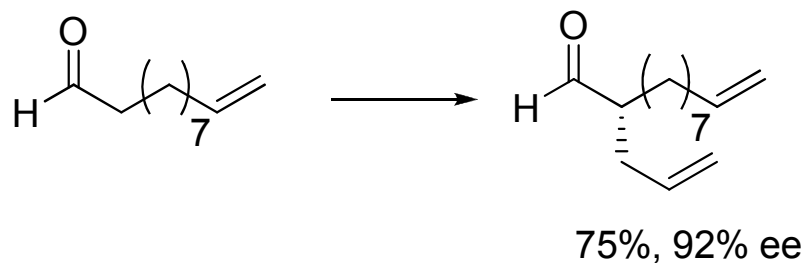
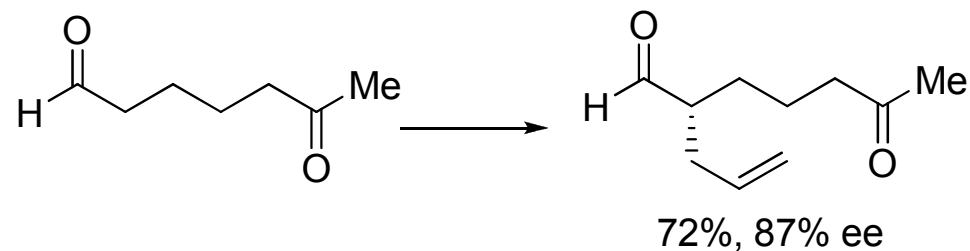
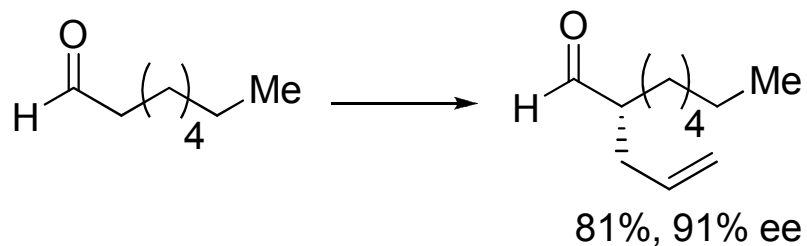
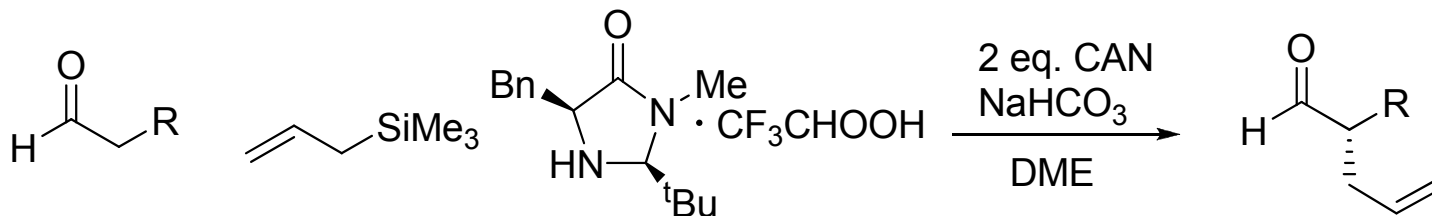
# Alternate Organocatalytic Method



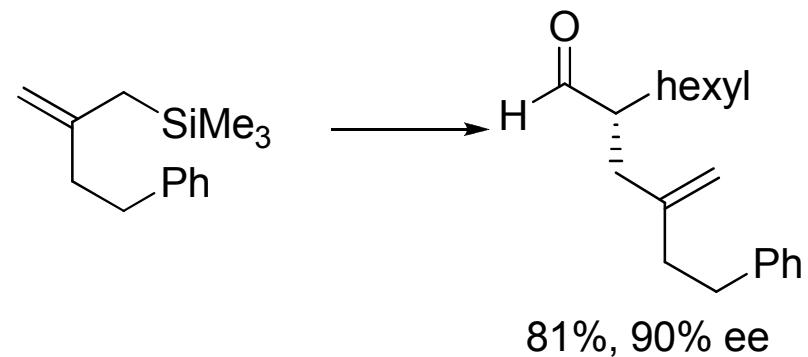
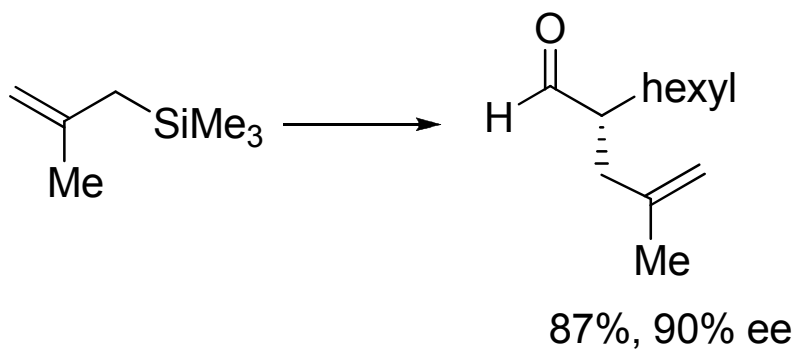
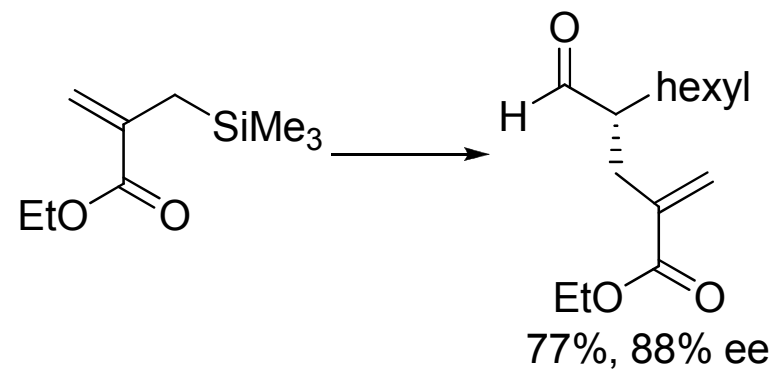
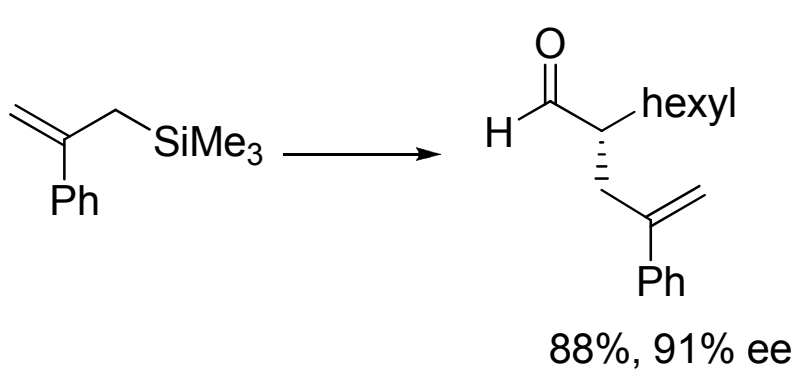
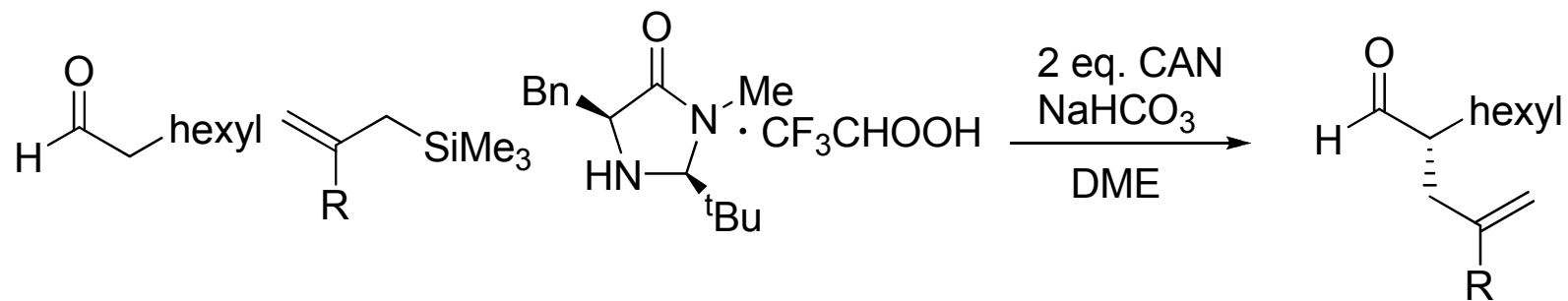
# $\alpha$ -Allylation of Aldehydes



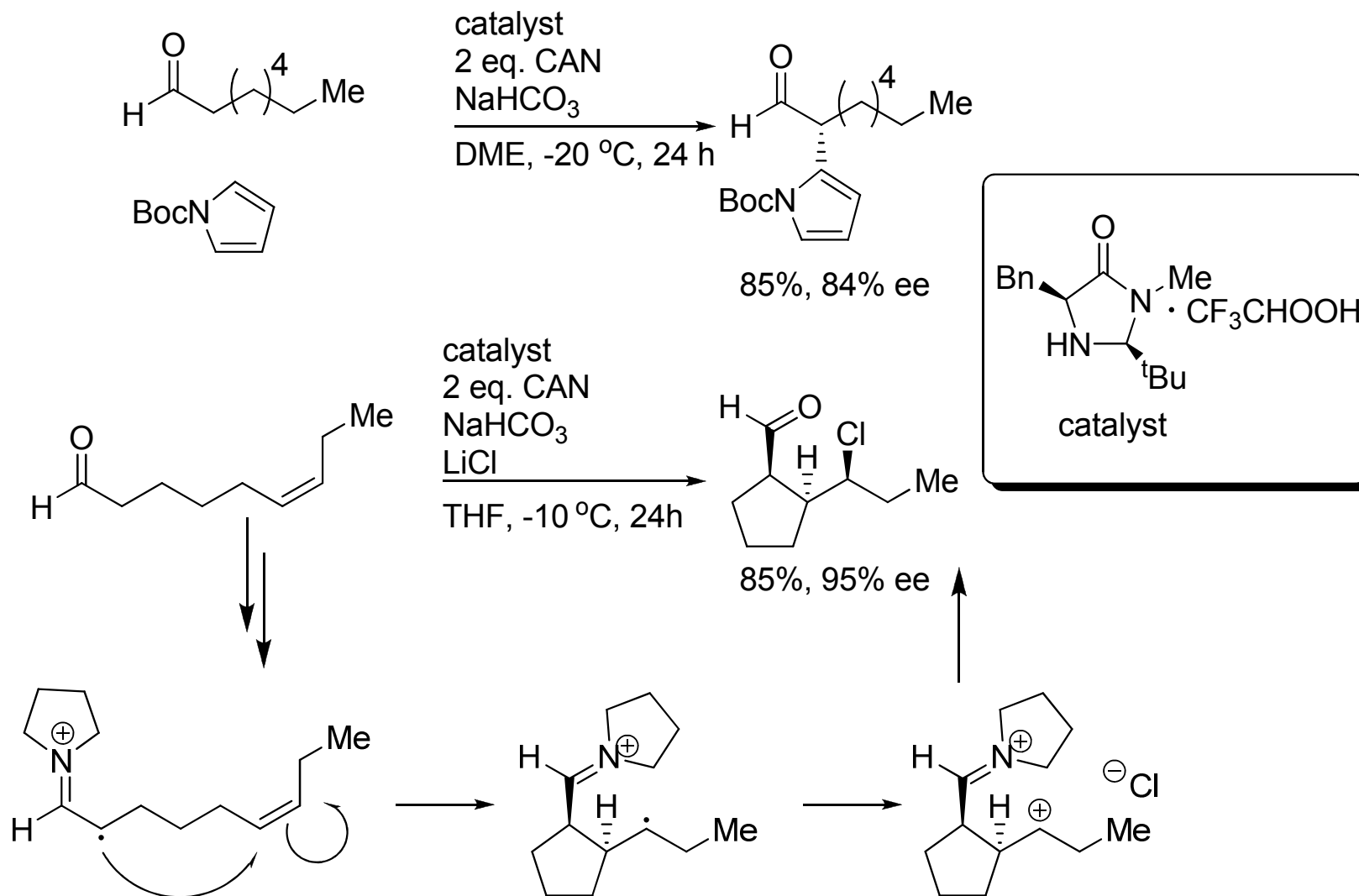
# Aldehyde Scope



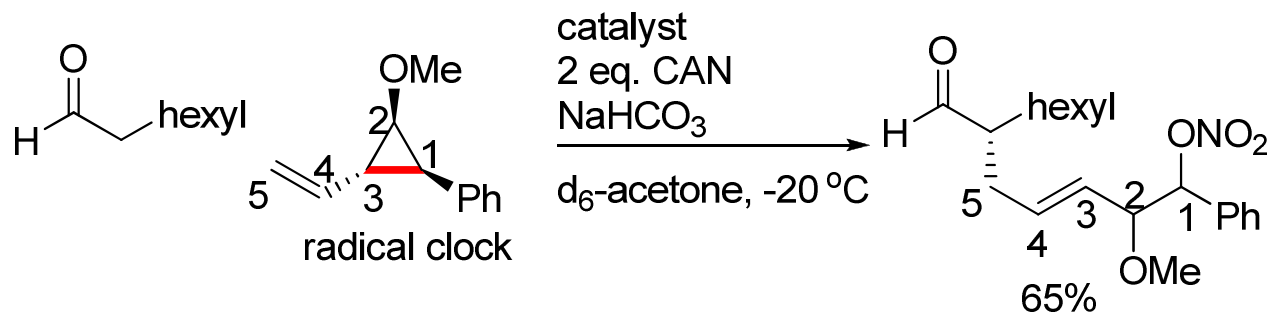
# Allyl Silane Scope



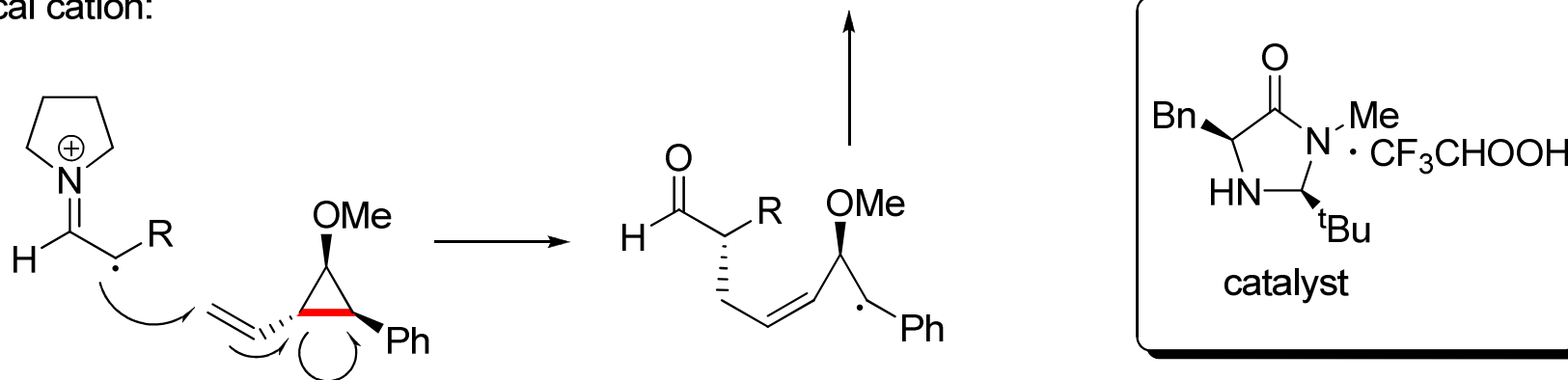
# Other Bond-Forming Events



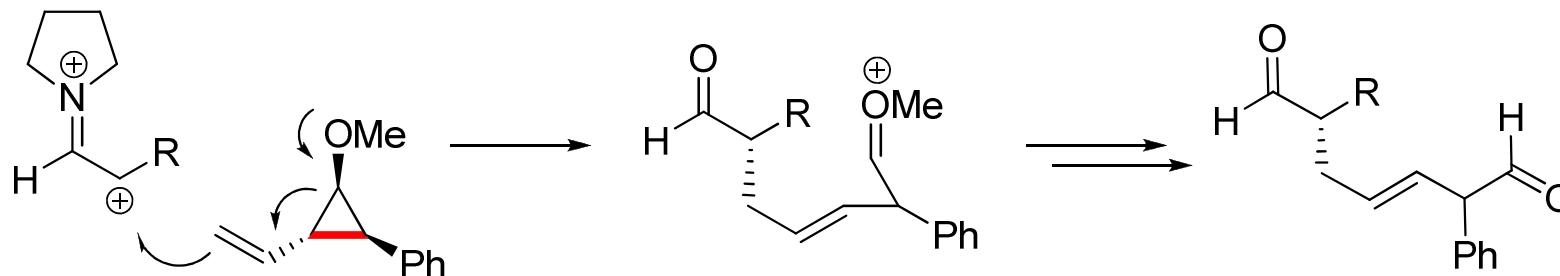
# Radical Clock



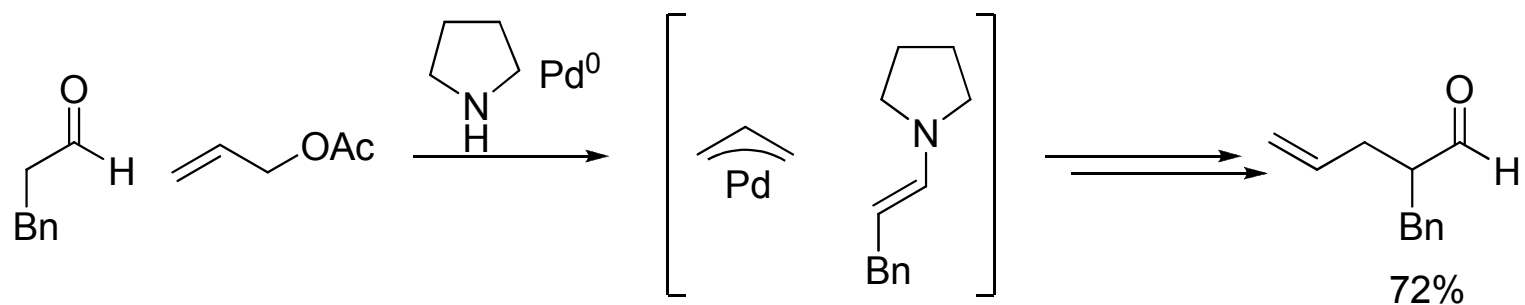
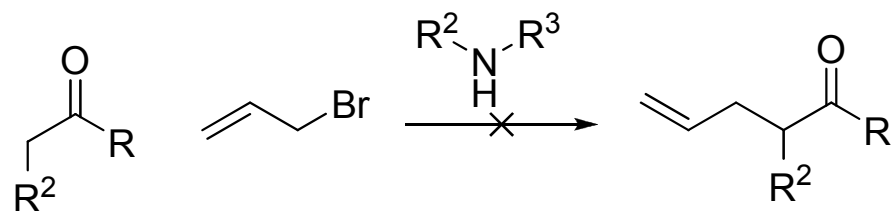
If radical cation:



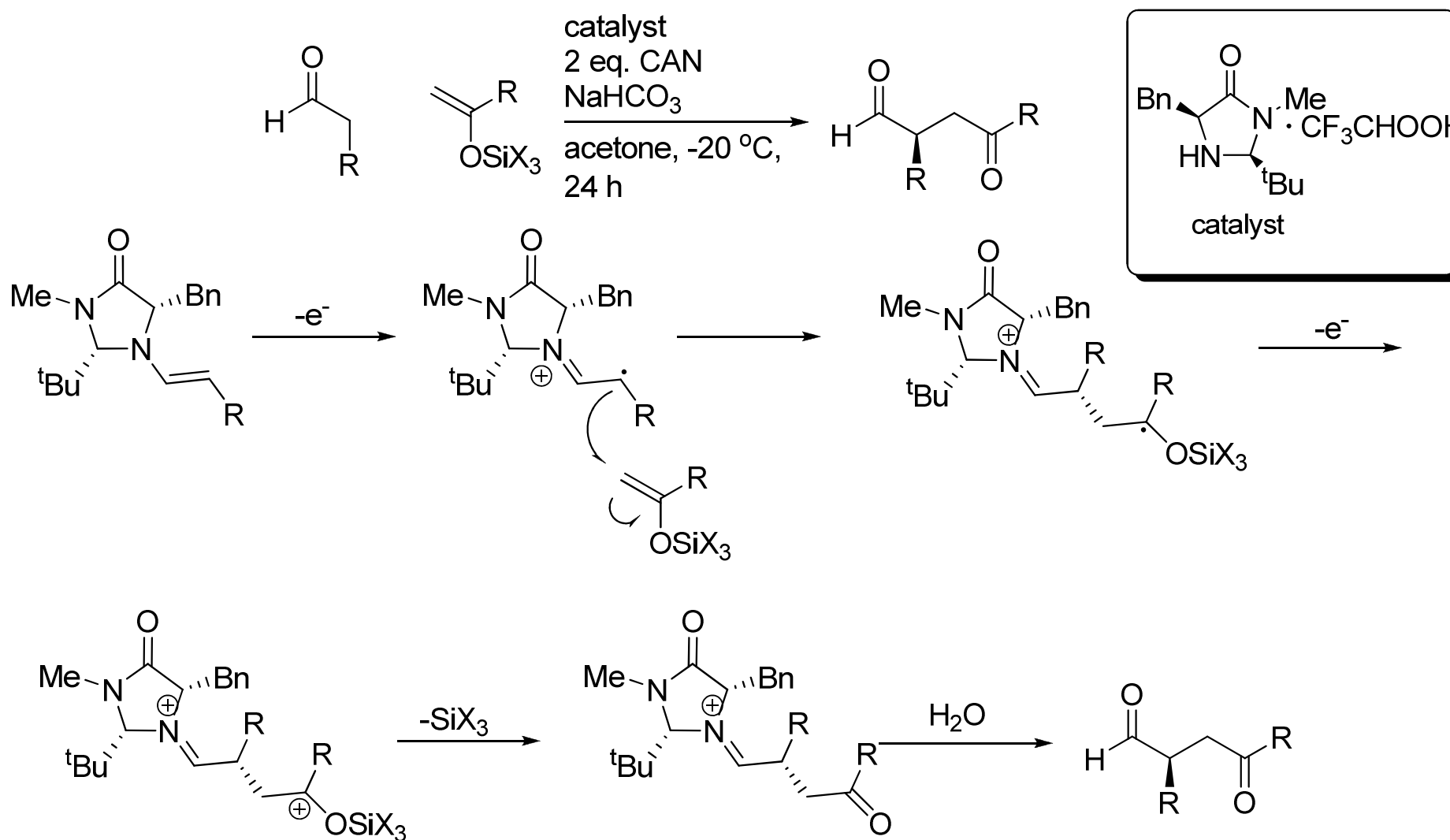
If cation:



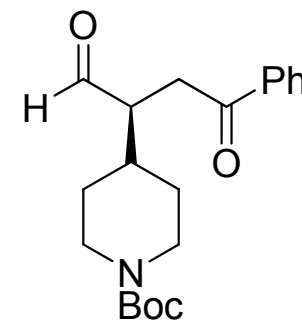
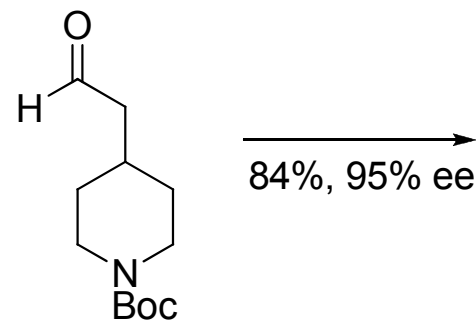
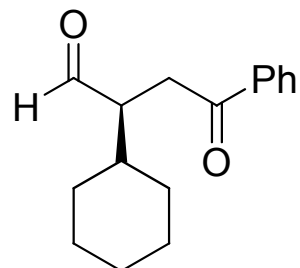
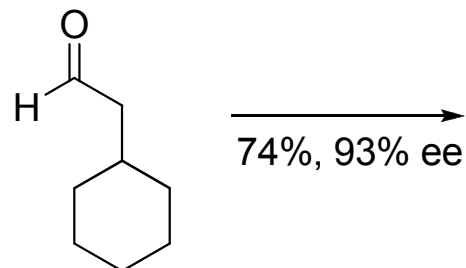
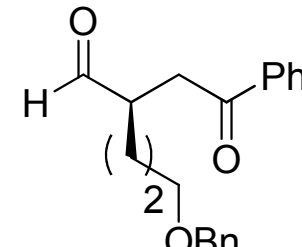
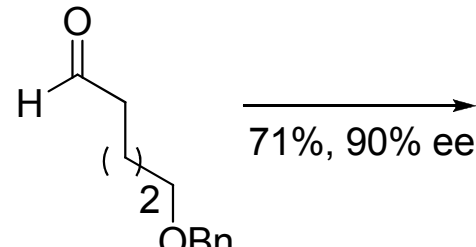
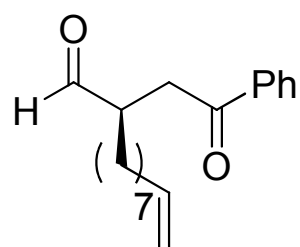
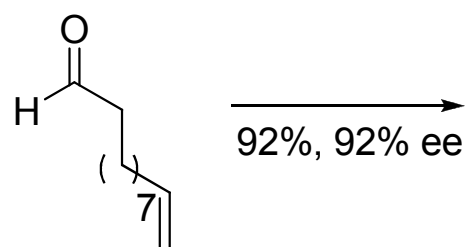
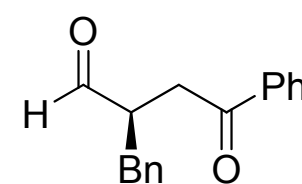
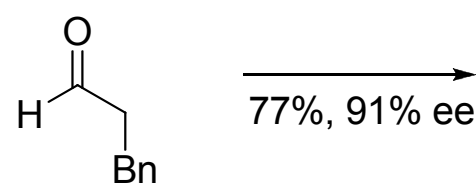
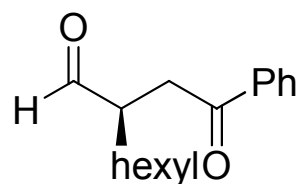
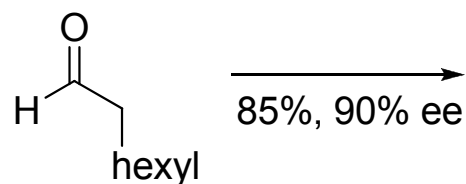
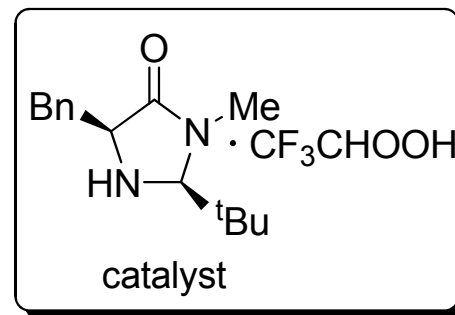
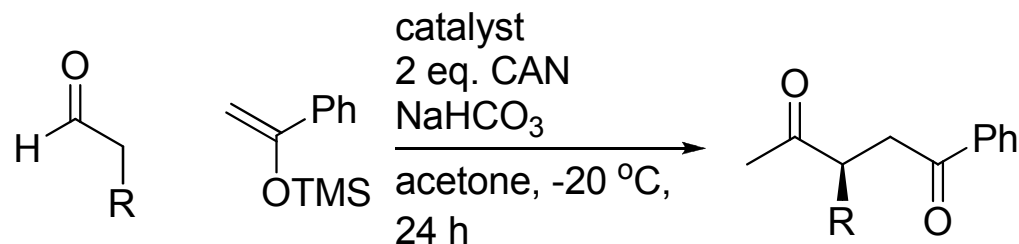
# Alternate Organocatalytic Method



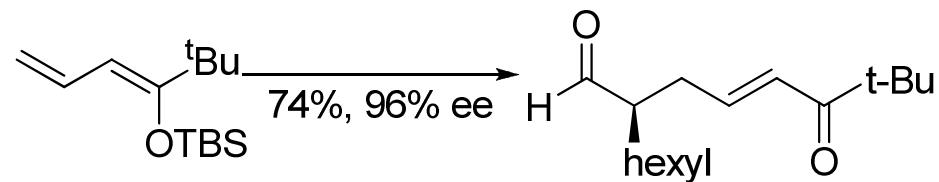
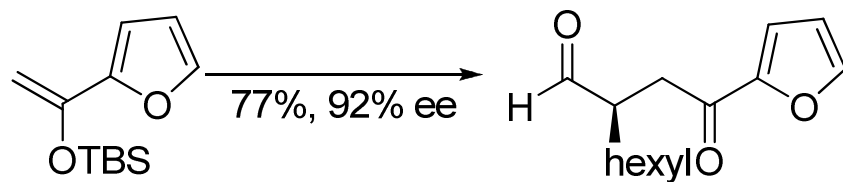
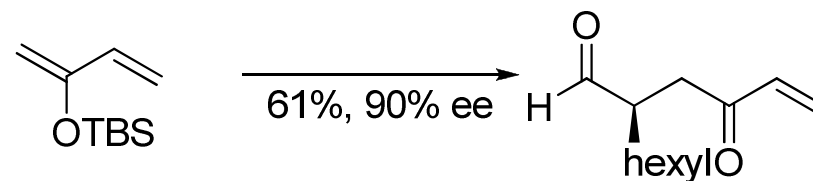
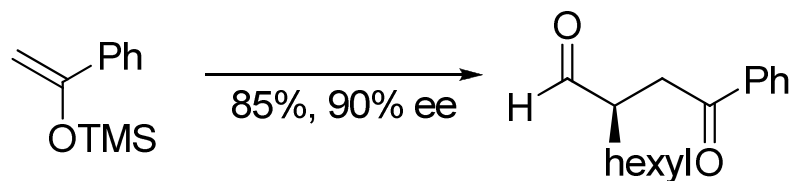
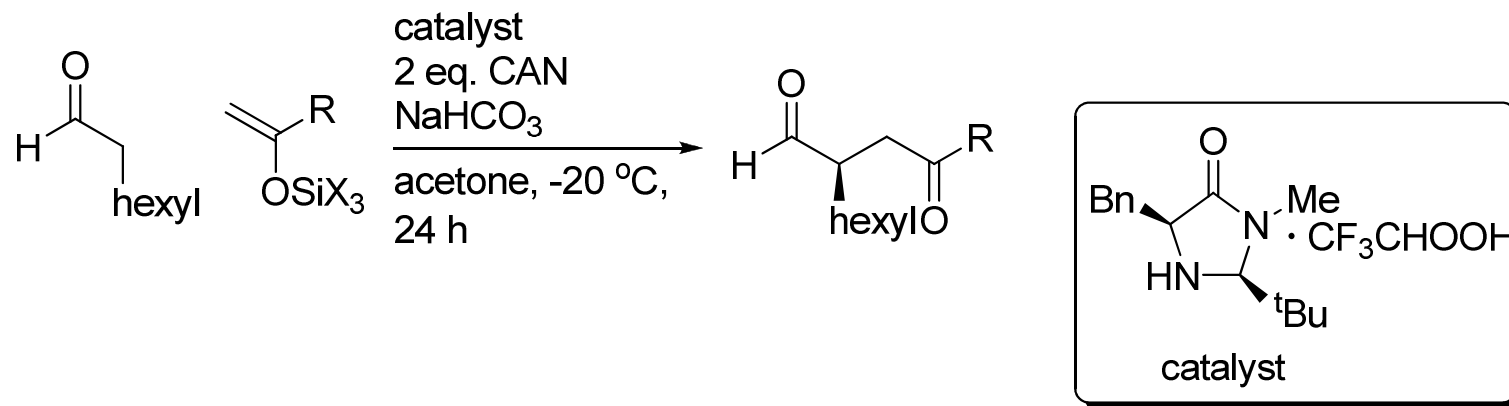
# $\alpha$ -Enolation



# Scope of Aldehyde

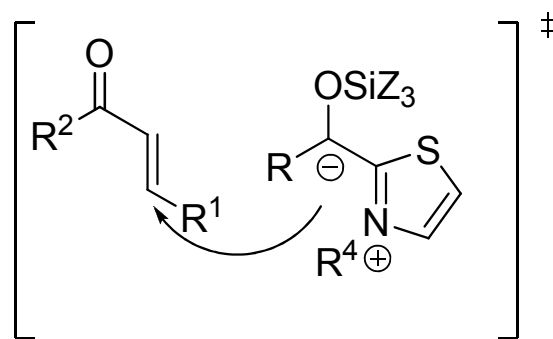
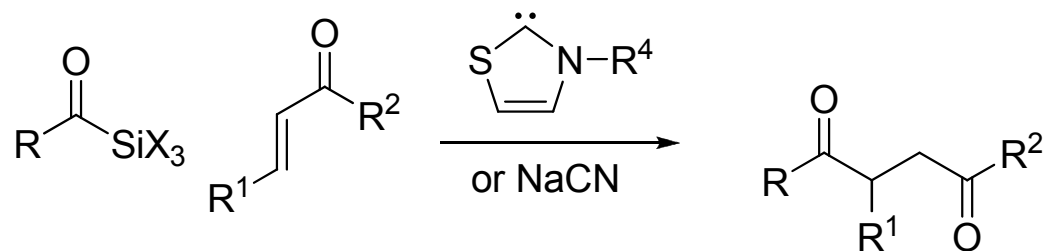


# Scope of Enolsilane

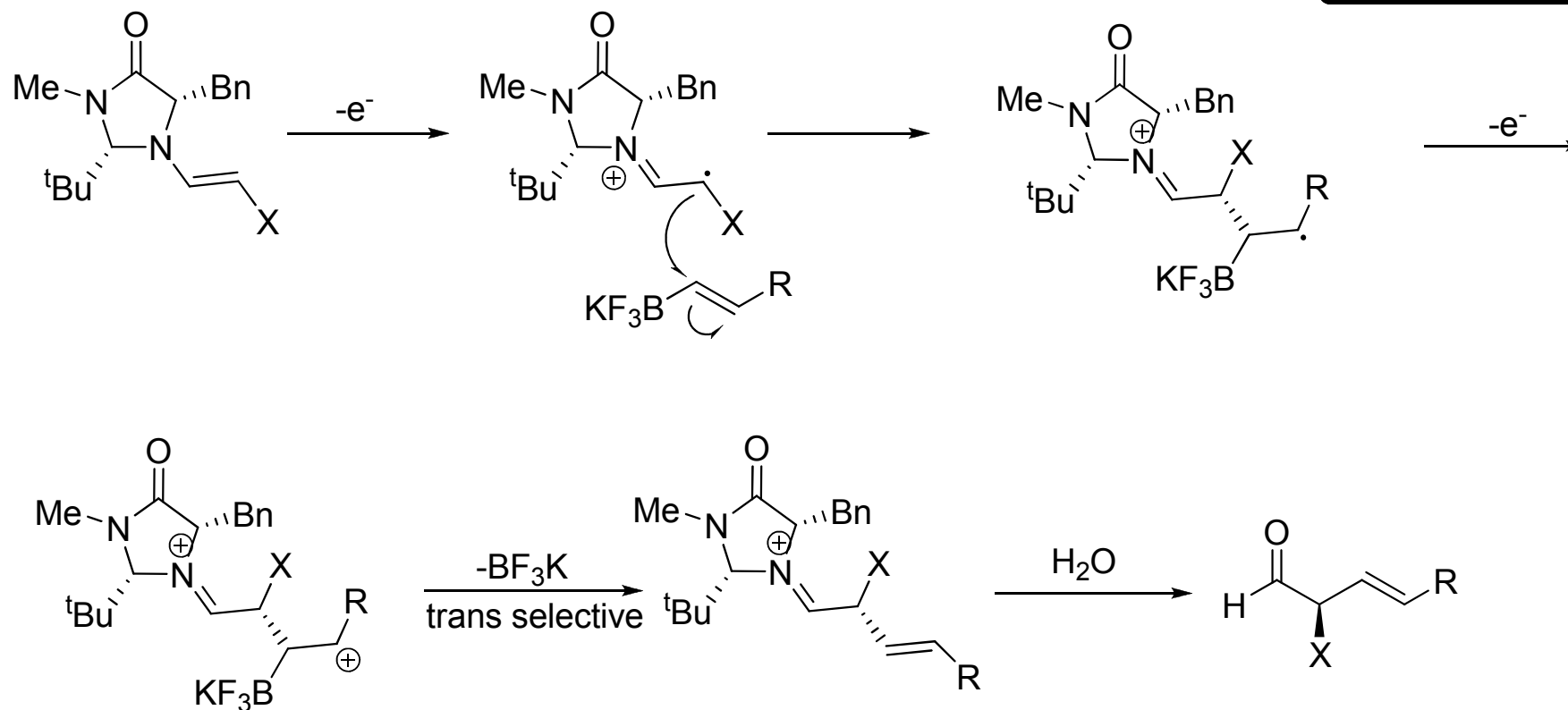
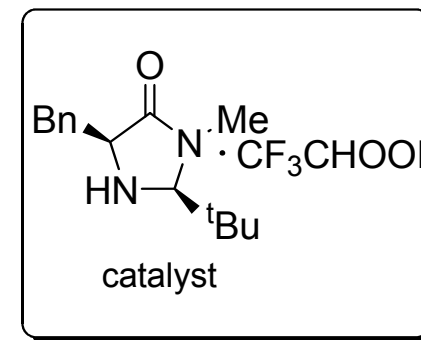
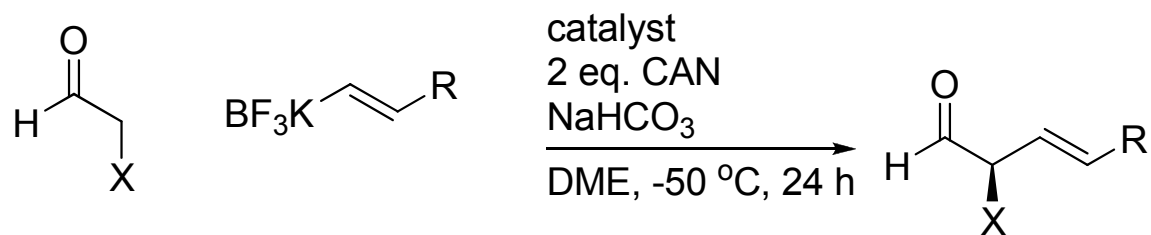




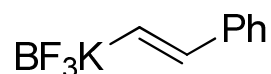
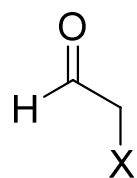
# Alternate Organocatalytic Way



# $\alpha$ -Vinylation

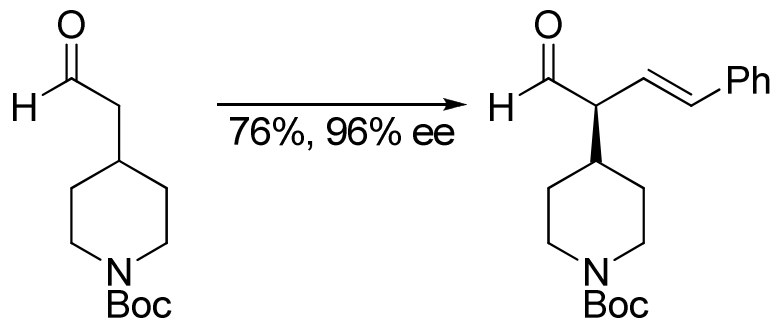
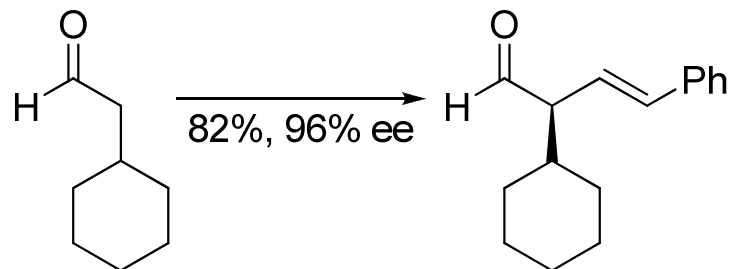
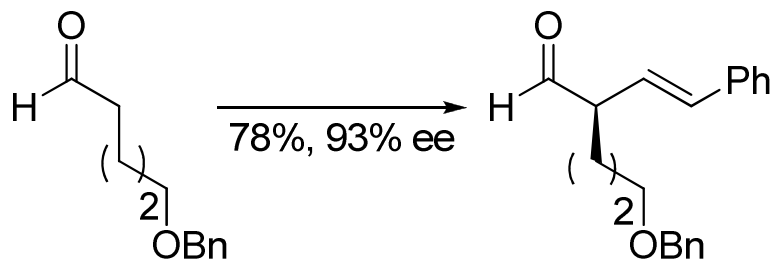
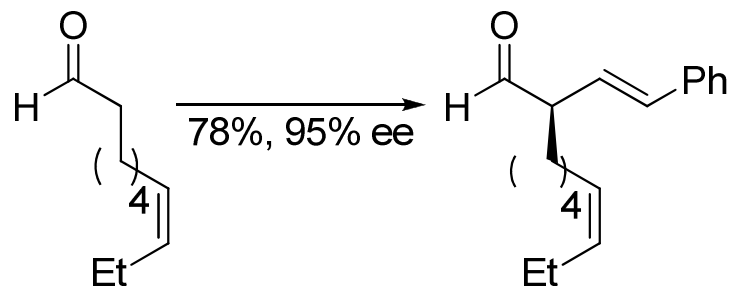
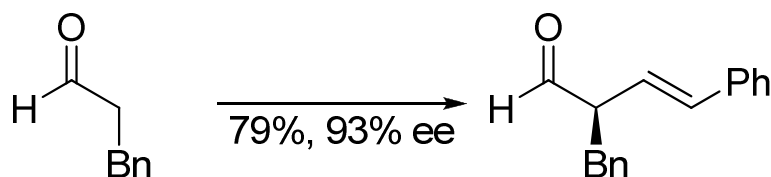
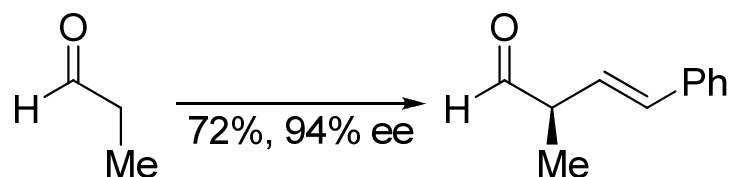
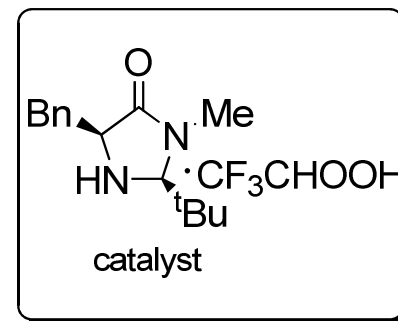
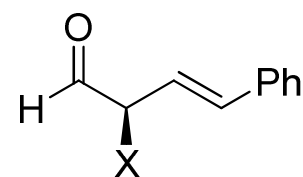


# Aldehyde Scope



catalyst  
2 eq. CAN  
NaHCO<sub>3</sub>

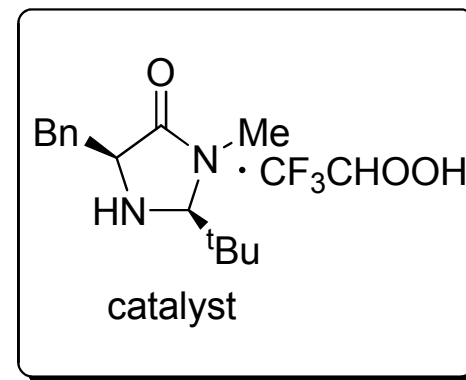
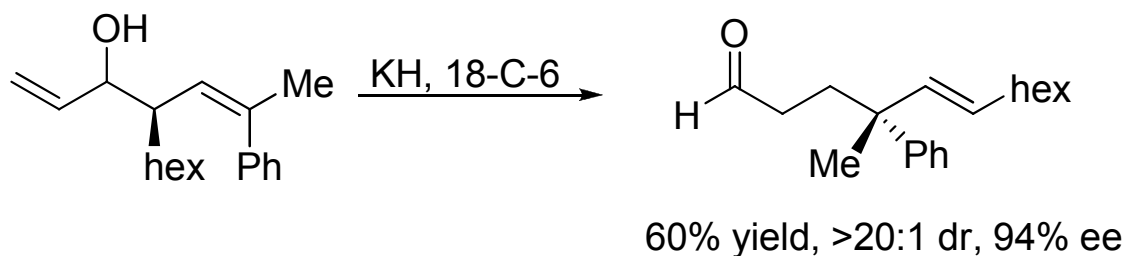
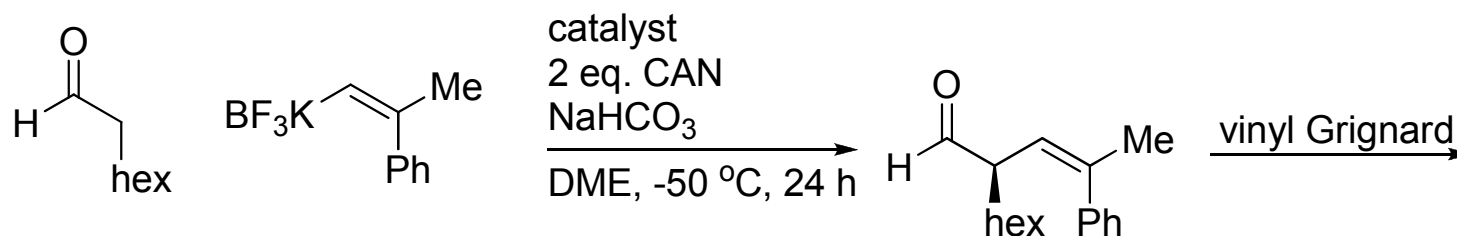
DME, -50 °C, 24 h



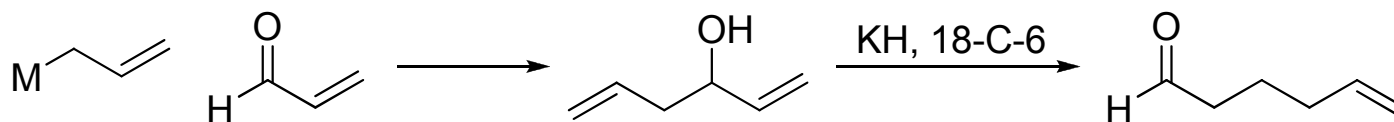
# Vinyl Trifluoroborate Scope



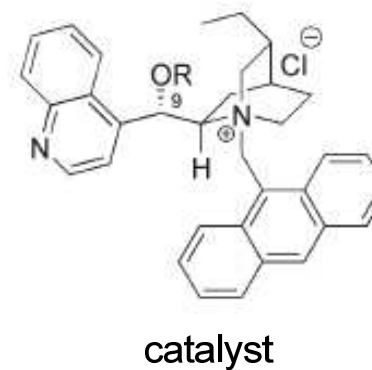
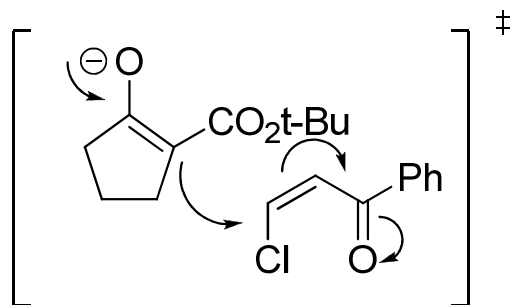
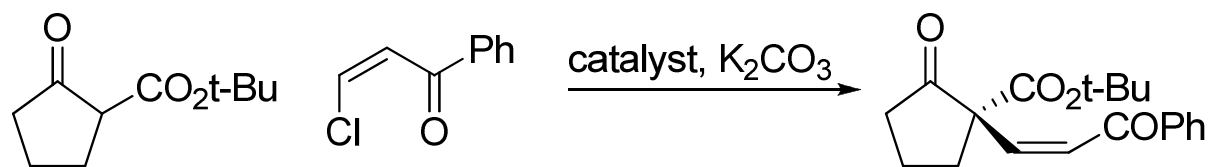
# Different Oxy-Cope Retron



Compare to:



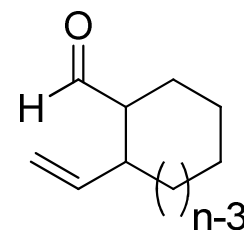
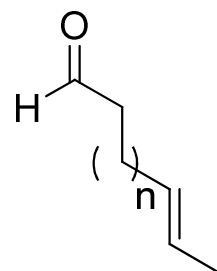
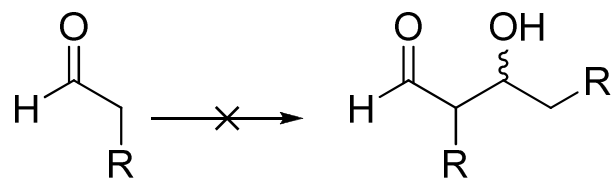
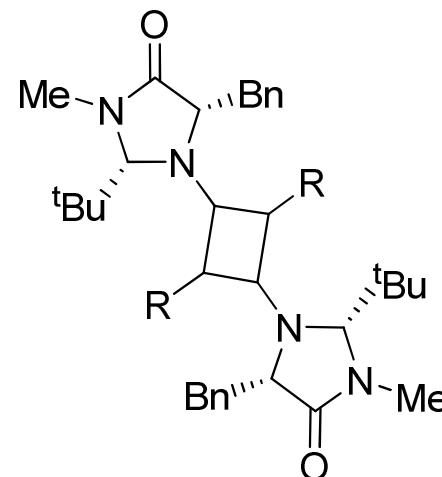
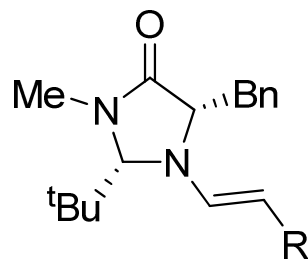
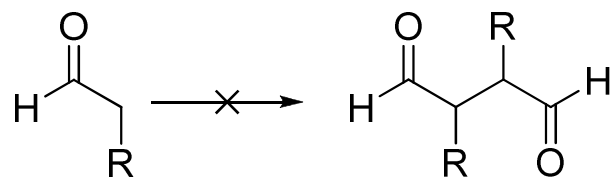
# Alternate Organocatalytic Method



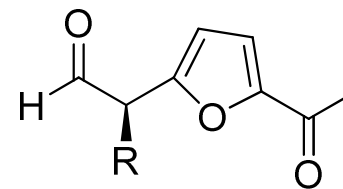
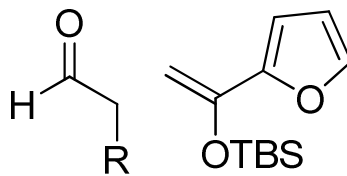
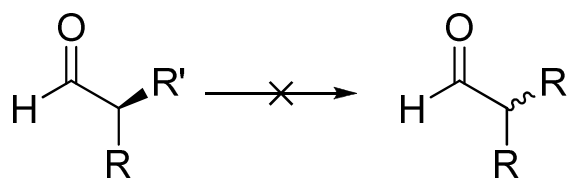
# Sibi and MacMillan

- Different oxidant ( $\text{Fe}^{\text{III}}$  Vs.  $\text{Ce}^{\text{IV}}$ )
- Sibi's at room temp, no added base
- Macmillan wider substrate scope
- Sibi reacted with persistent radicals, MacMillan used double oxidation
- Different catalysts

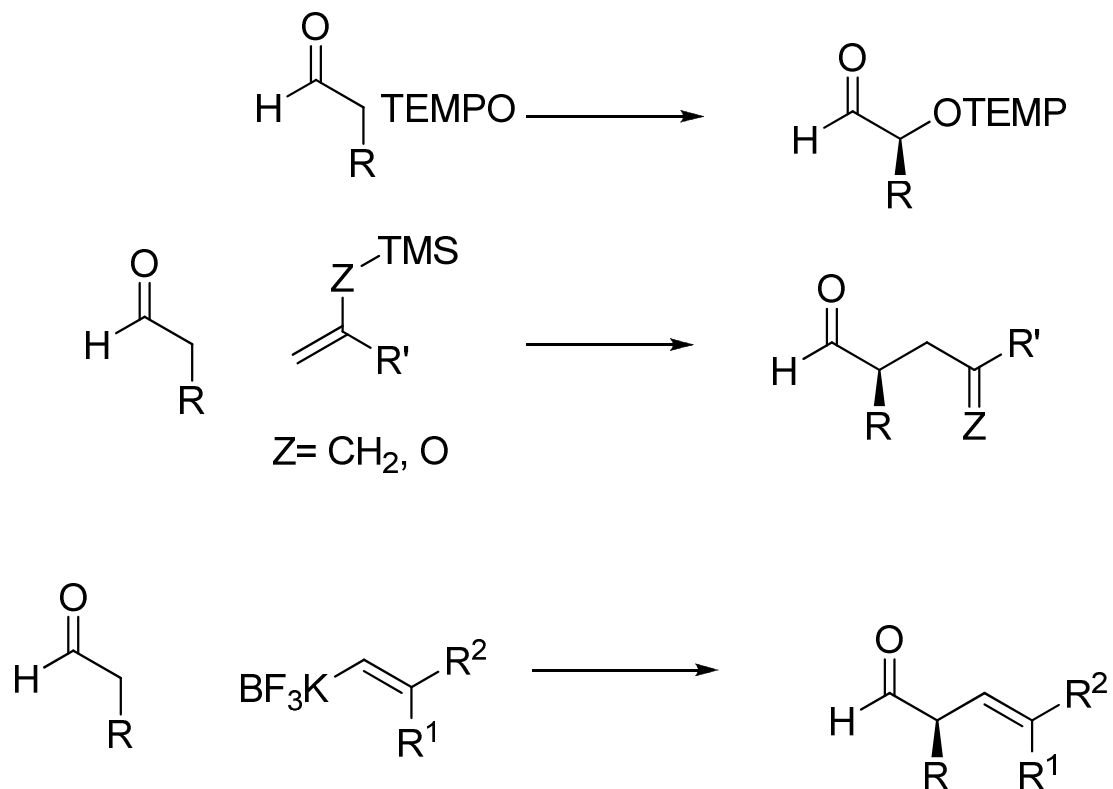
# Possible Side Products Which Nonetheless Did Not Occur



if no silylated or boron salt reagent present



# Conclusion



Mild way to make an  $\alpha$ -radical to aldehydes (ketones coming soon?)

$\alpha$ - vinylation, enolations, allylations and oxyamination proceed in good yield and ee