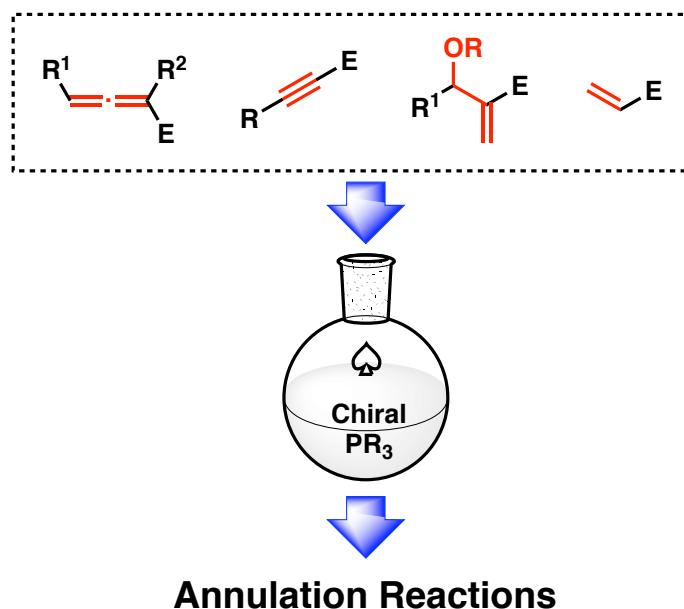


# Phosphine-catalyzed Asymmetric Cyclization



M2 HUANG Jianhao

2021.08.30

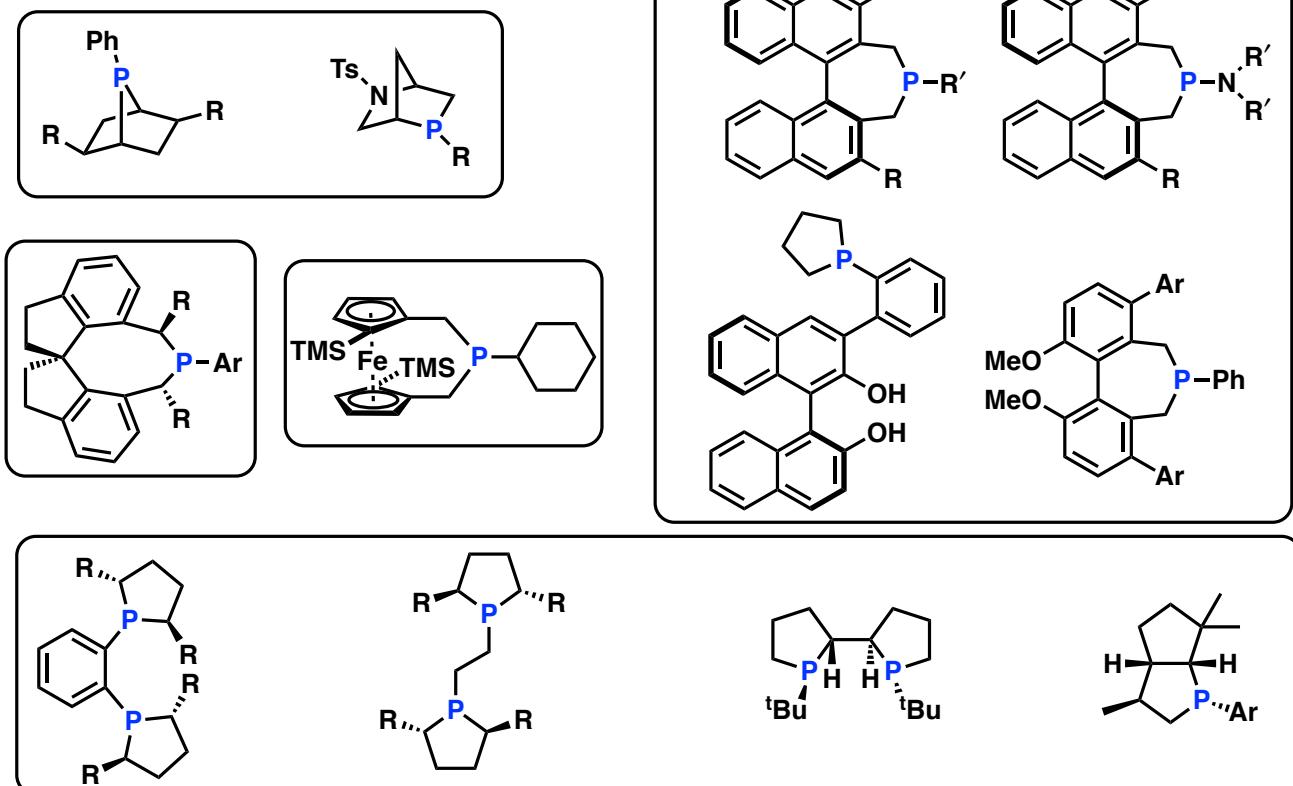
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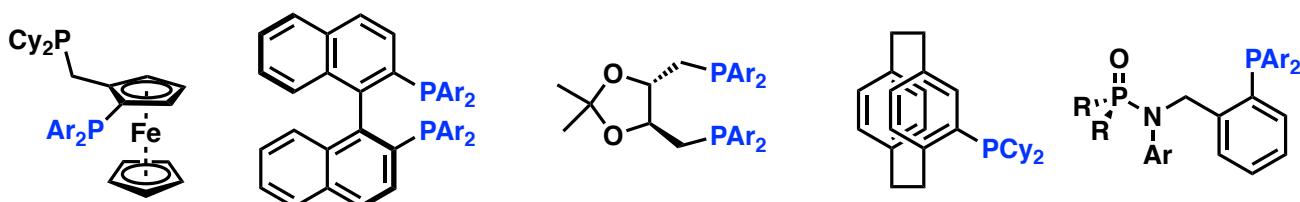
# 1. Introduction

## 1.1. Chiral Phosphine Catalysts

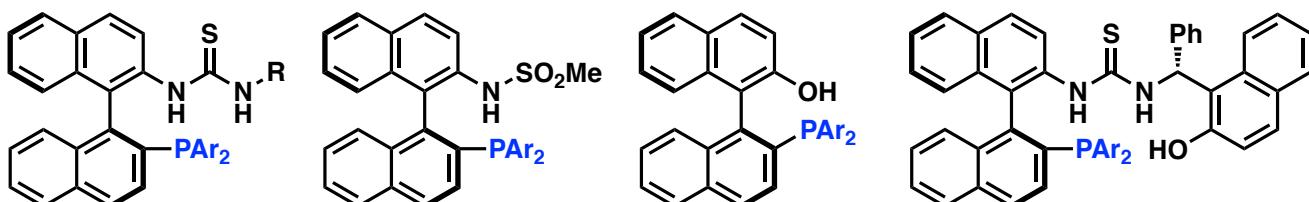
### (1) Monofunctional cyclic types



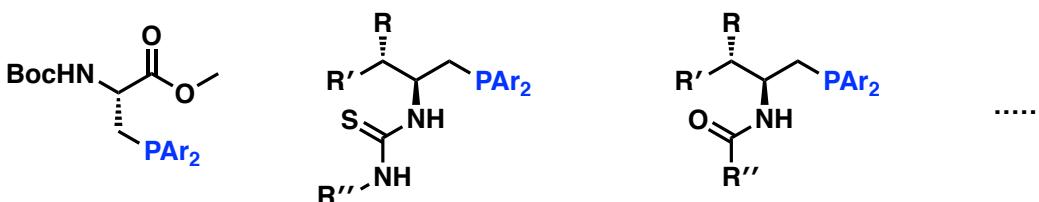
### (2) Monofunctional acyclic types



### (3) Multifunctional types derived from BINOL



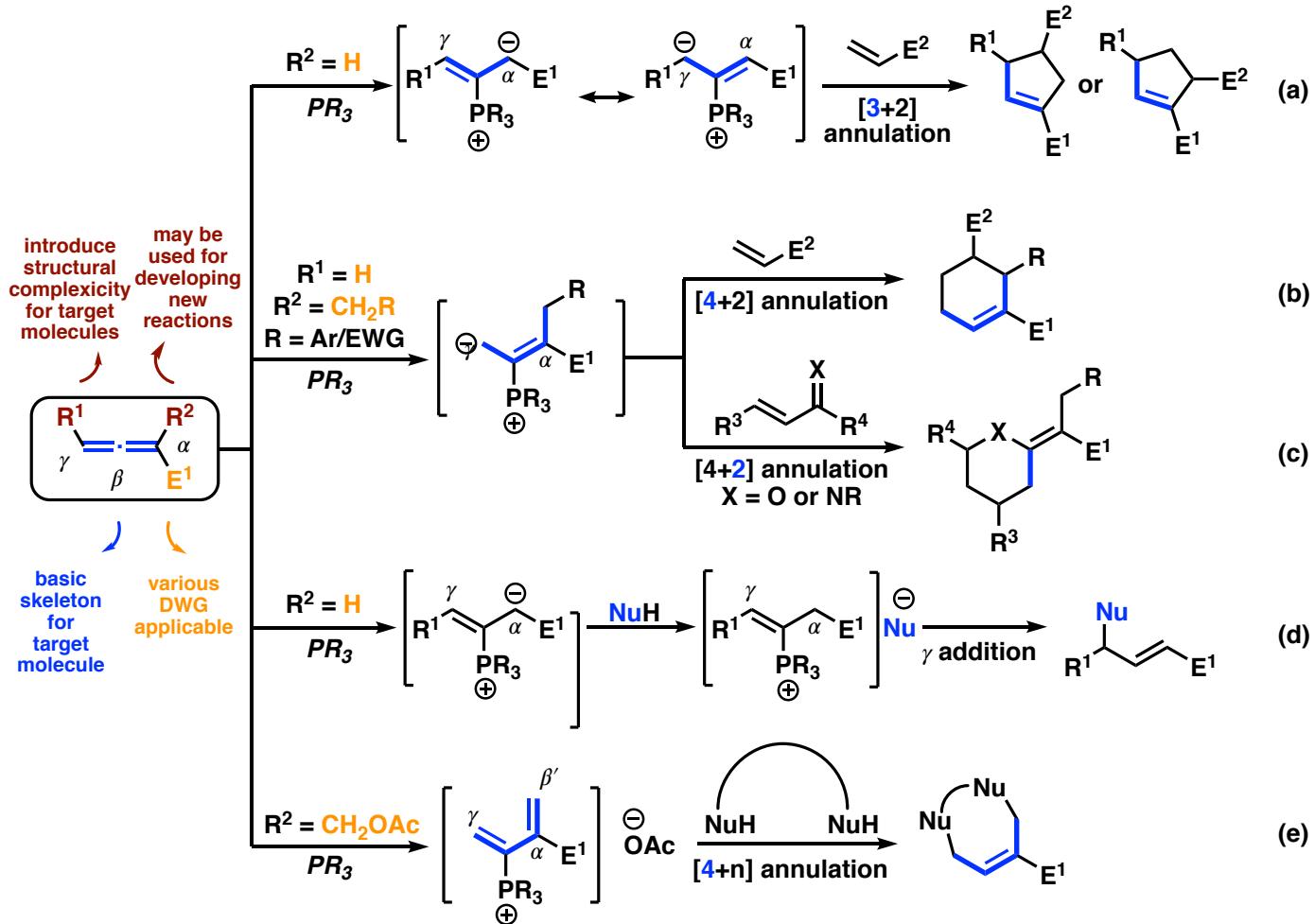
### (4) Multifunctional types derived from amino acids



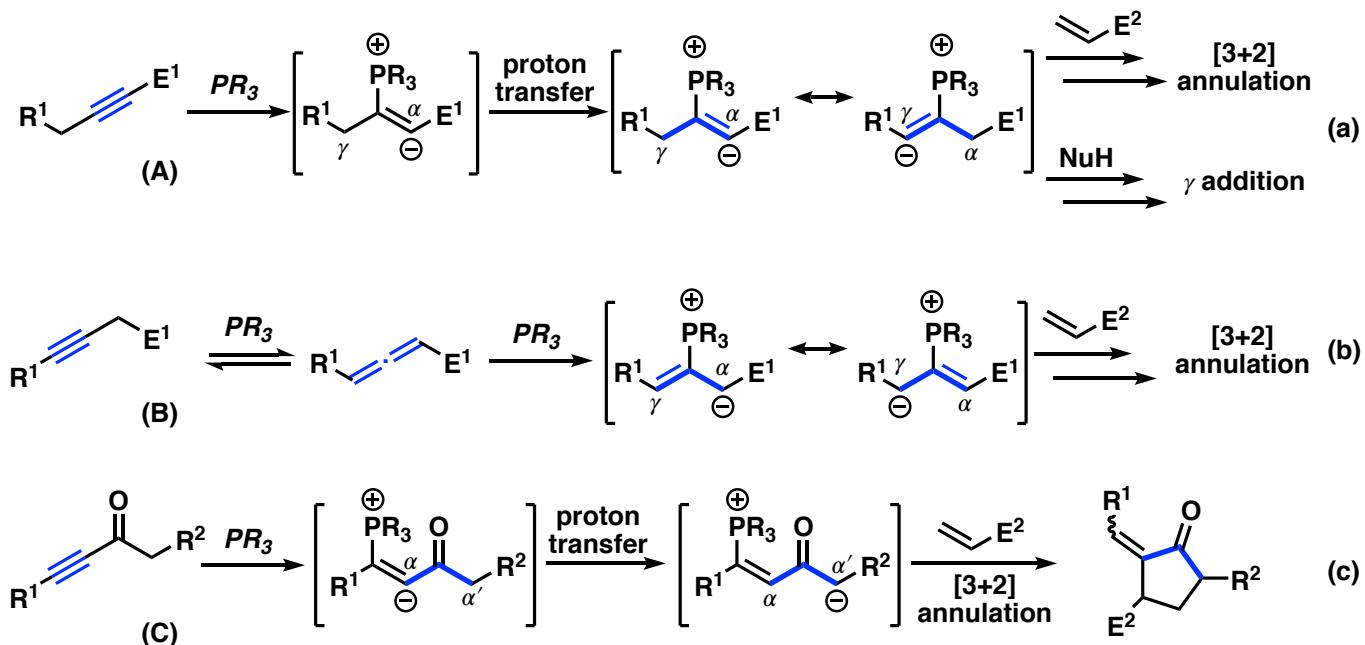
# 1. Introduction

## 1.2. Common Partners in Nucleophilic Phosphine Catalysis

### 1.2.1. Allenes in Phosphine Catalysis

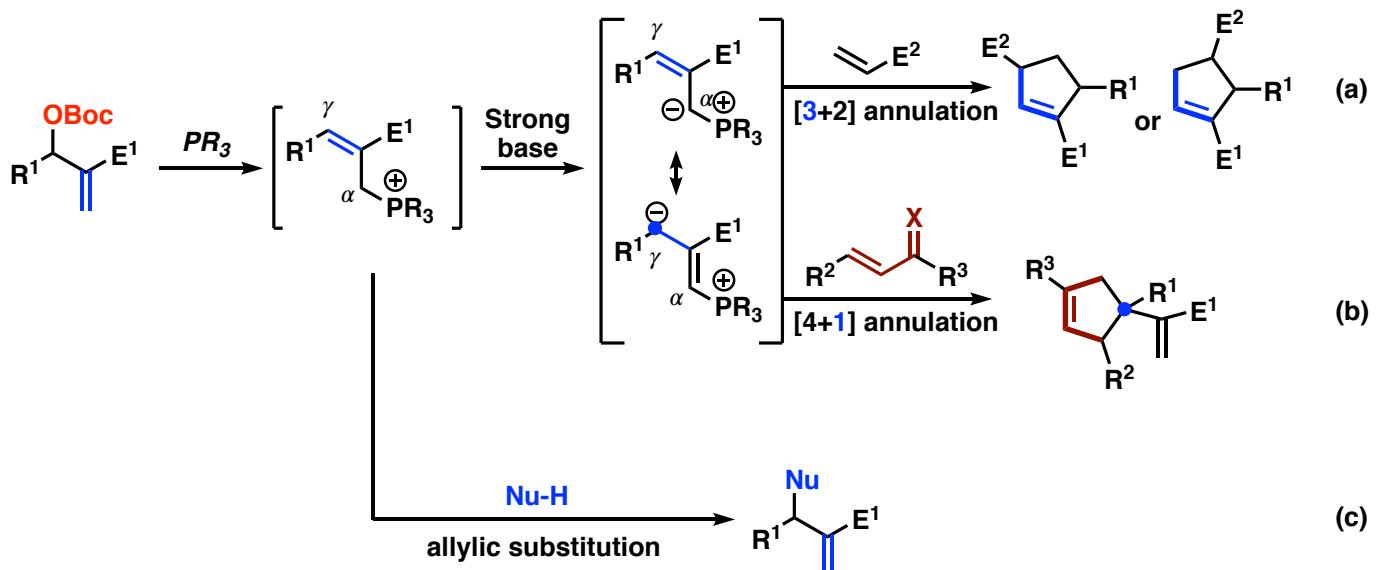


### 1.2.2. Alkynes in Phosphine Catalysis

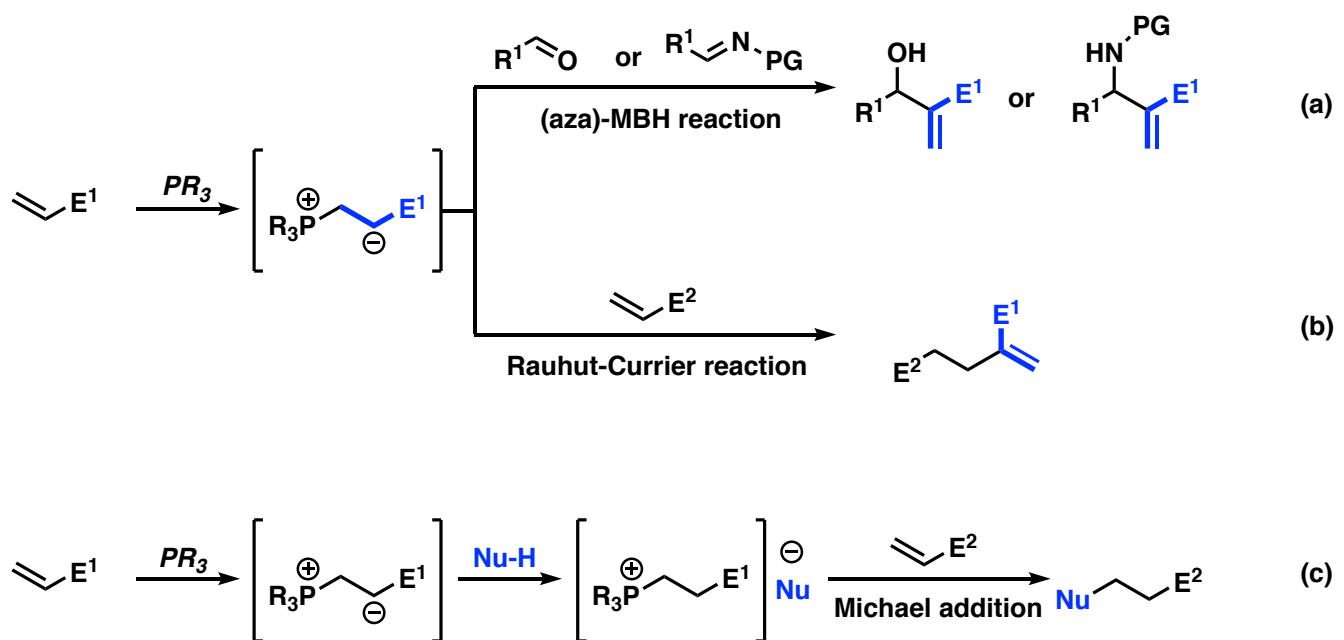


# 1. Introduction

## 1.2.3. MBH Adducts in Phosphine Catalysis



## 1.2.4. Activated Alkenes in Phosphine Catalysis

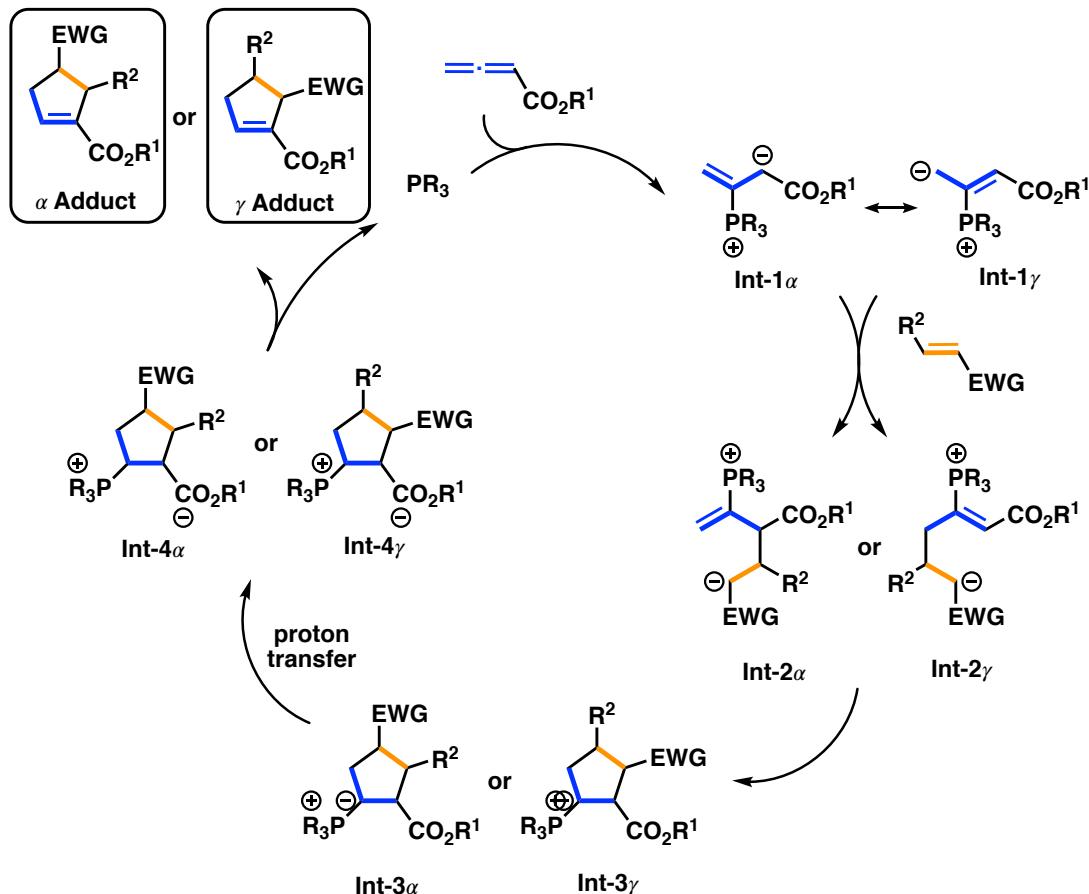


## 2. Annulation of Allenes and Alkynes

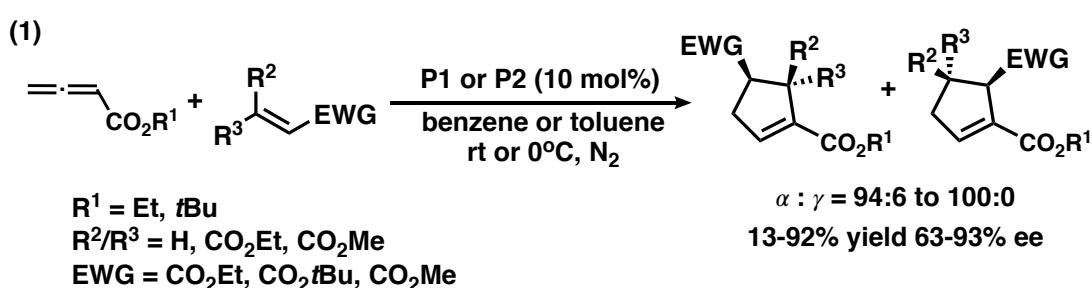
### 2.1. [3+2] Annulation of Allenolates and Alkynes

#### 2.1.1. [3+2] Annulation of Allenolates with Activated Alkenes

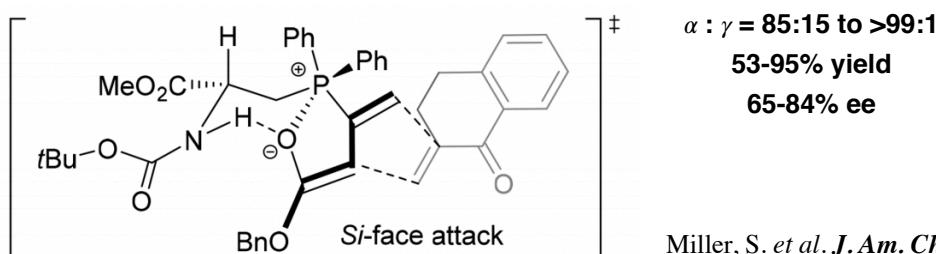
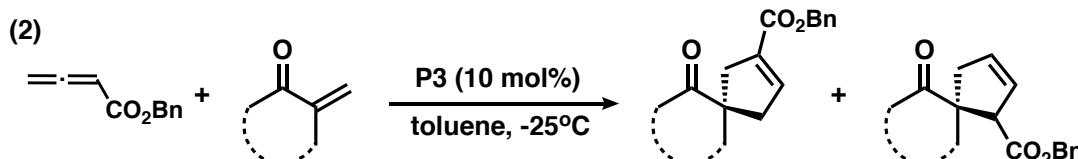
*General Mechanism:*



**Representative Reactions:**

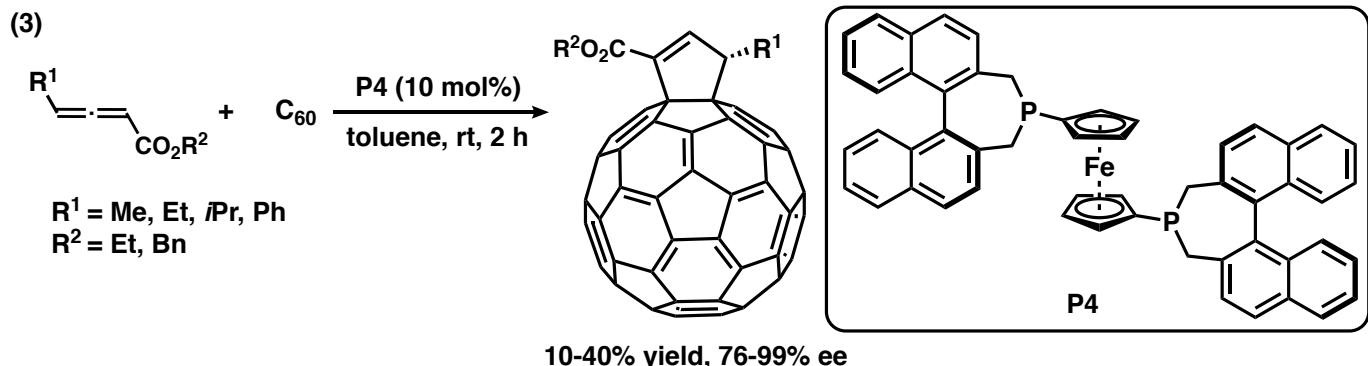


Zhang X. et al. *J. Am. Chem. Soc.* 1997, 119, 3836–3837.

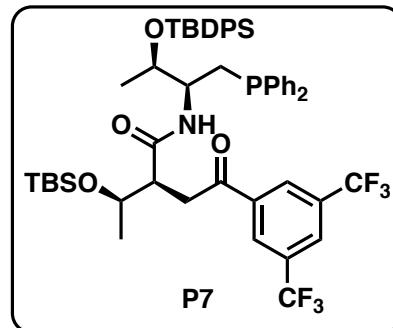
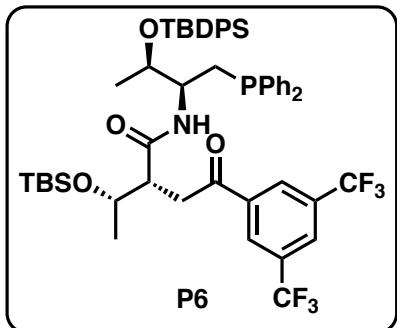
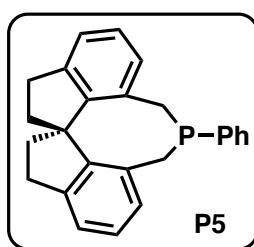
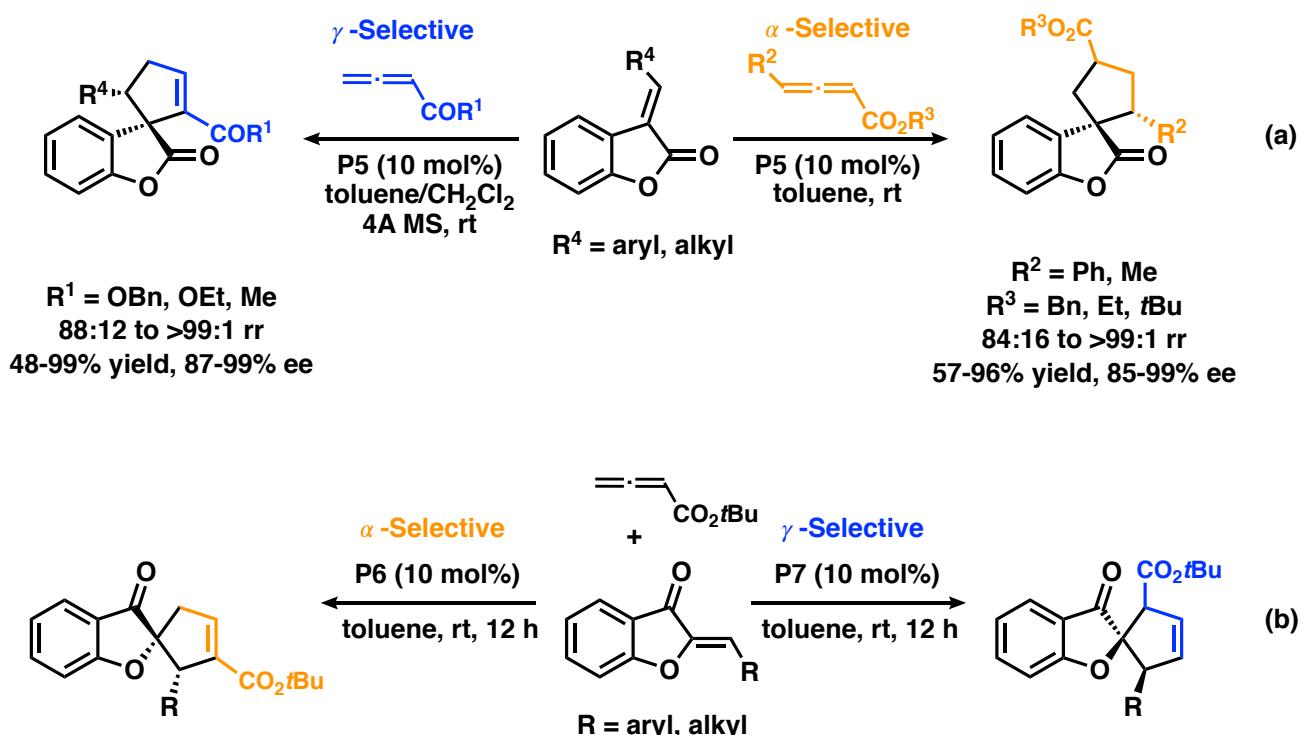


Miller, S. et al. *J. Am. Chem. Soc.* 2007, 129, 10988–10989.

## 2. Annulation of Allenes and Alkynes



Martin N. et al. *Angew. Chem., Int. Ed.* 2013, **52**, 5115–5119.

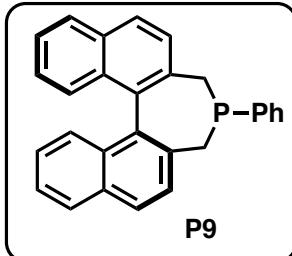
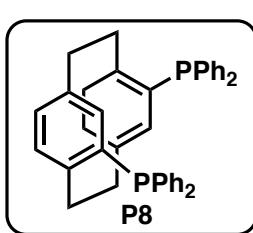
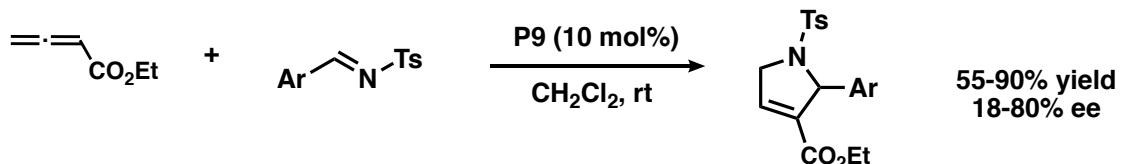
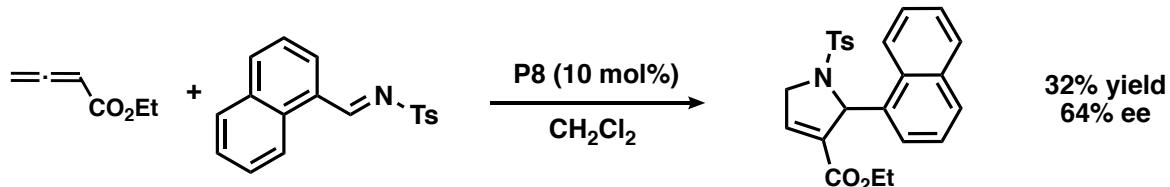


(a) Shi M. et al. *Chem. Sci.* 2015, **6**, 7319–7325.

(b) Lu Y. et al. *Chem. Sci.* 2017, **8**, 5699–5704.

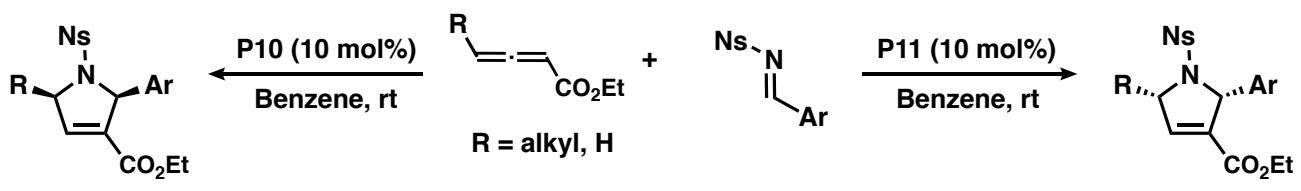
## 2. Annulation of Allenes and Alkynes

### 2.1.1. [3+2] Annulation of Allenolates with Imines

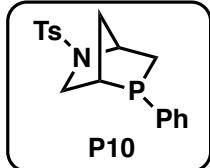


Marinetti A. et al. *Tetrahedron Lett.* 2006, 47, 2141–2145.

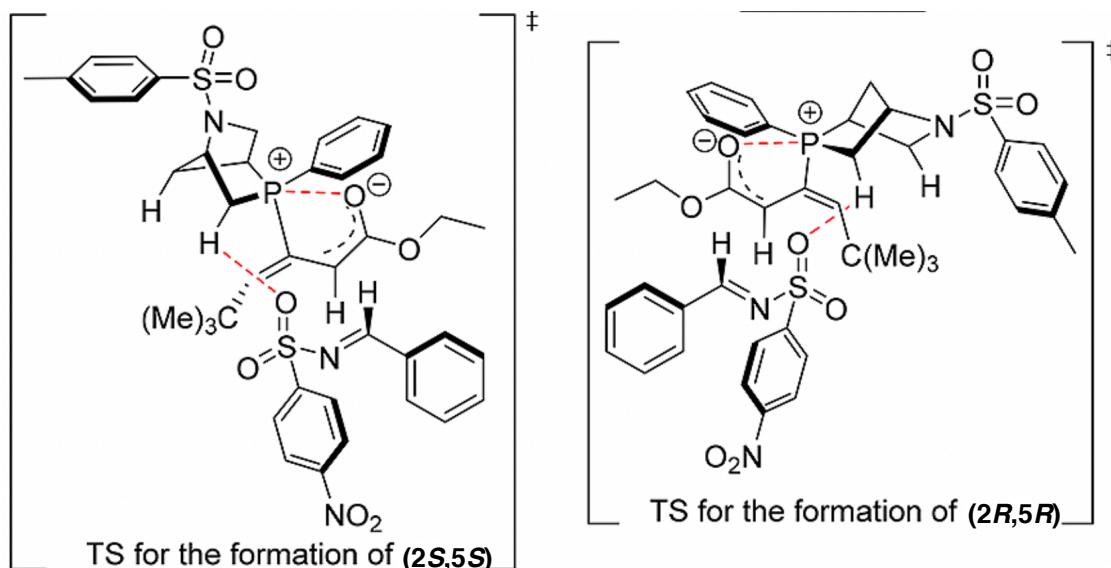
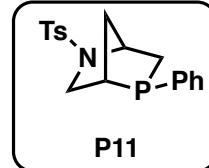
Marinetti A. et al. *Tetrahedron* 2007, 63, 11920–11927.



(2S,5S)  
76-99% yield  
56->99% ee

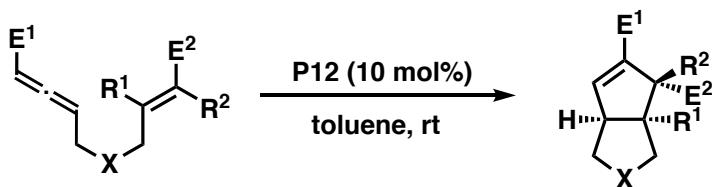


(2R,5R)  
59-94% yield  
37->99% ee



## 2. Annulation of Allenes and Alkynes

### 2.1.3. [3+2] Intramolecular Annulation of Allenes



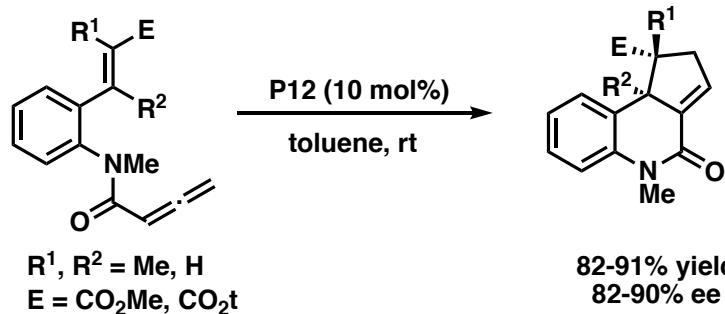
$R^1, R^2 = Me, H$

$E^1 = CO_2Me, CO_2Et, CO_2tBu$

$E^2 = C(O)SEt, C(O)NMe(OMe), CO_2Bn, CO_2Me$

$X = CH_2, NTs, C(CO_2Bn)_2$

56-94% yield, 90-98% ee



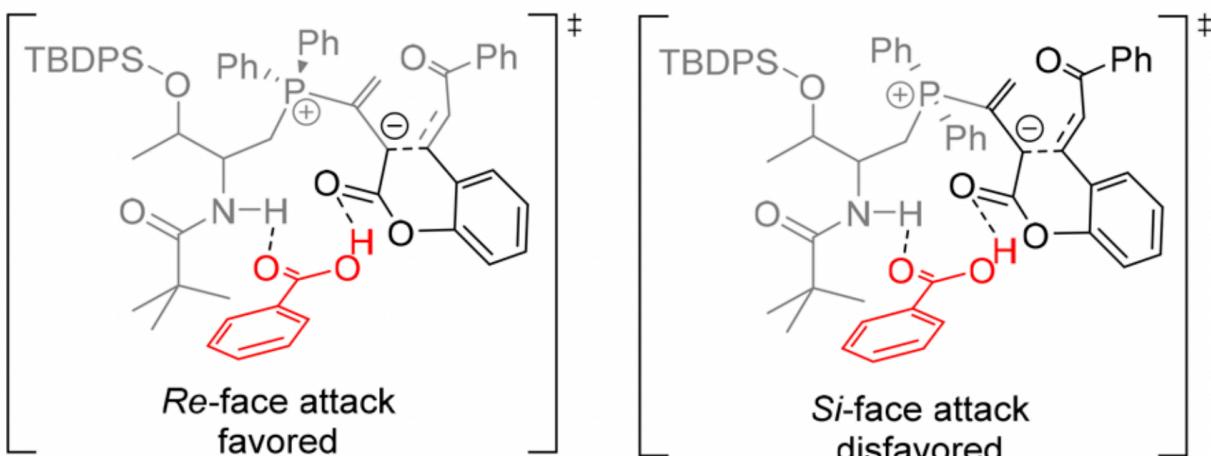
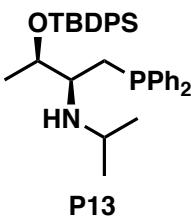
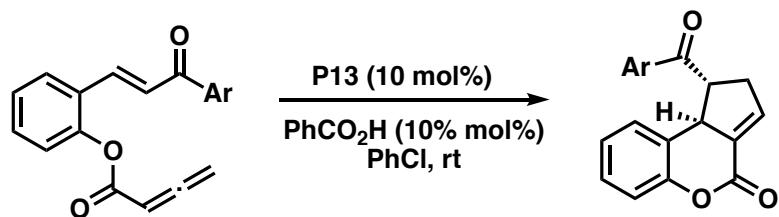
$R^1, R^2 = Me, H$

$E = CO_2Me, CO_2tBu$

82-91% yield

82-90% ee

Fu G. C. et al. *J. Am. Chem. Soc.* 2015, 137, 4587–4591.

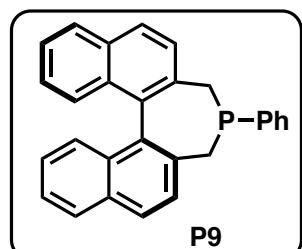
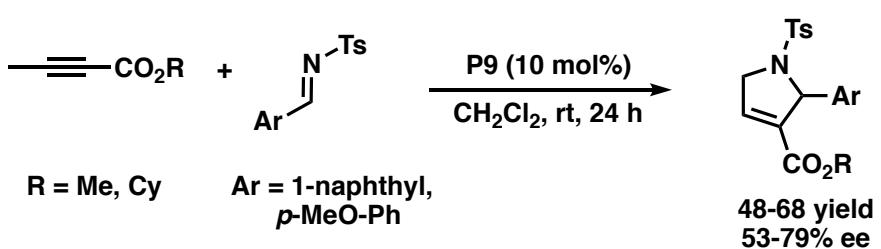
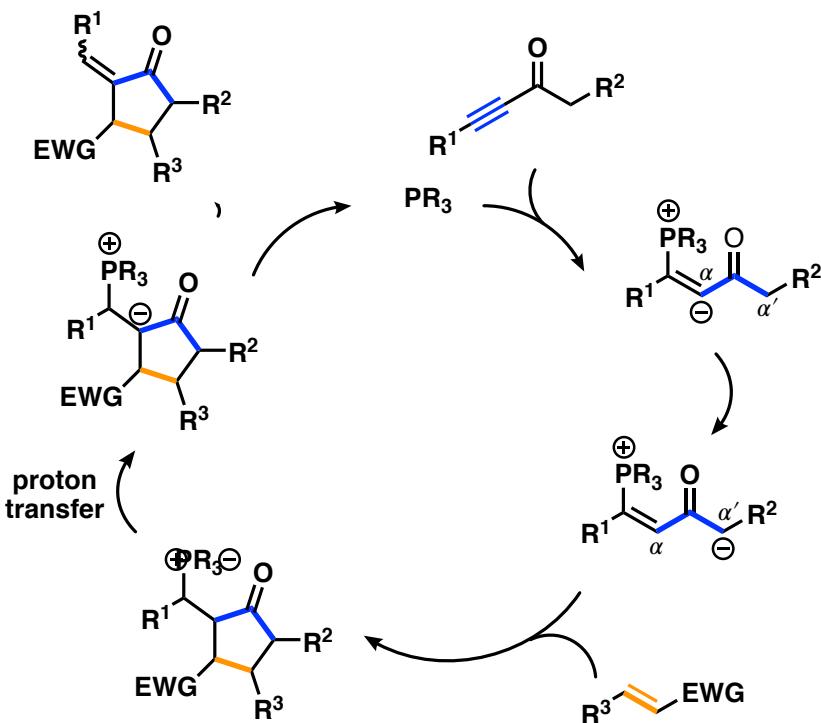
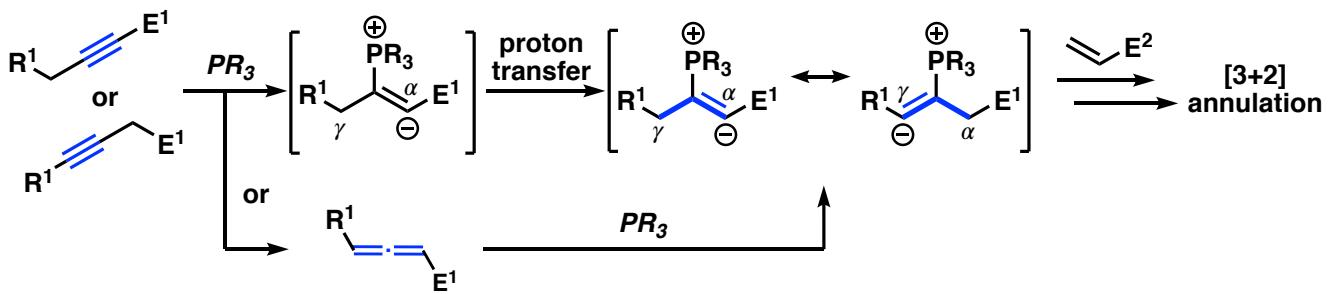


Lu Y. et al. *Chem. Sci.* 2017, 8, 5196–5200.

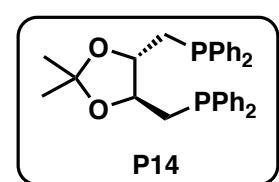
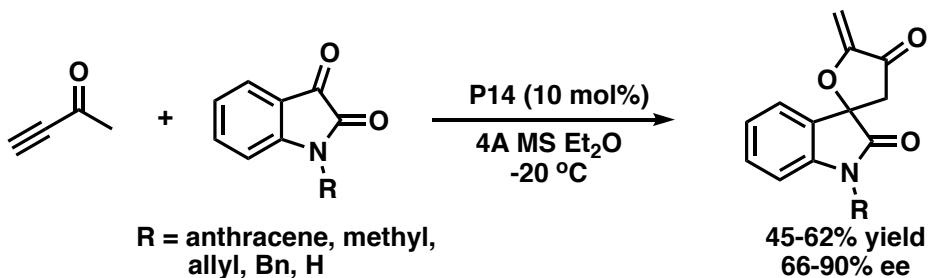
## 2. Annulation of Allenes and Alkynes

### 2.1.4. [3+2] Annulations of Alkynes

Similar reaction pattern as allenes but **lower** reactivity



Marinetti A. et al. *Eur. J. Org. Chem.* 2009, 2009, 146–151.

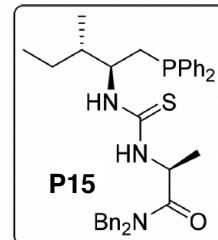
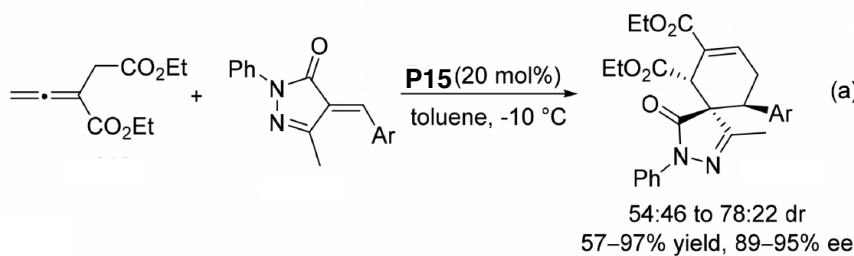
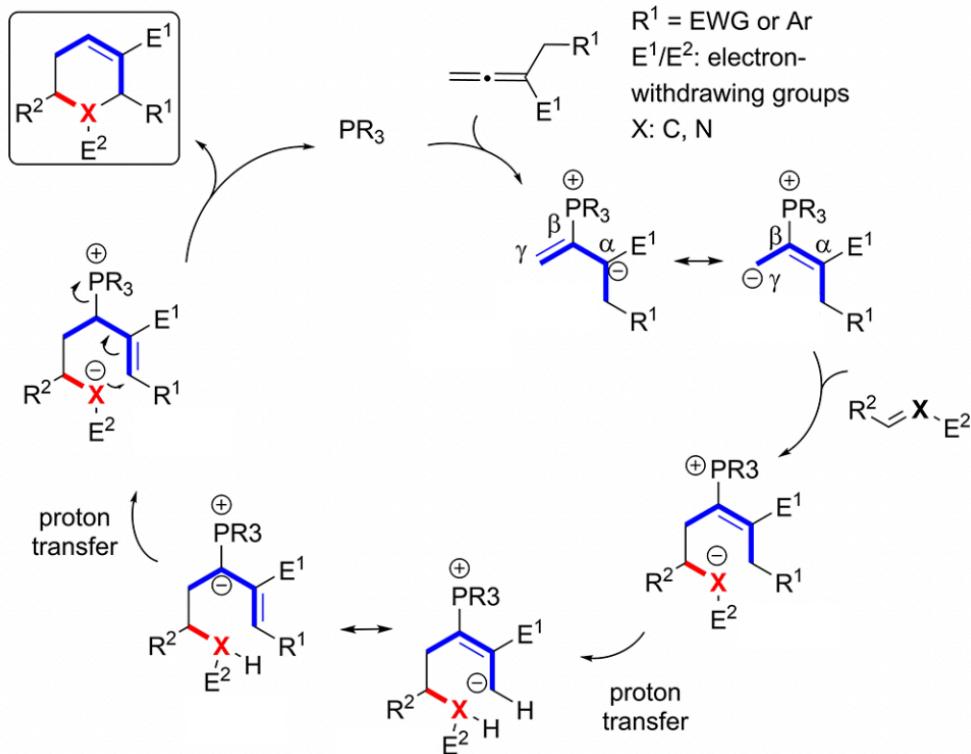


Shi M. et al. *Org. Biomol. Chem.* 2012, 10, 8048–8050.

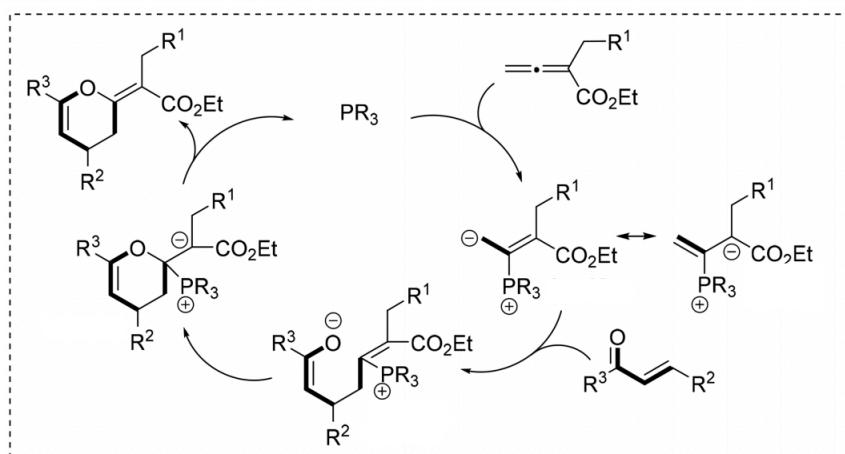
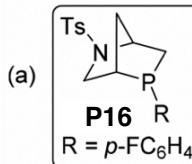
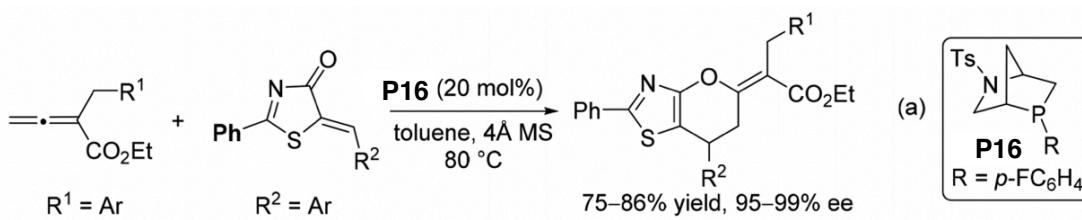
## 2. Annulation of Allenes and Alkynes

### 2.2. [4+2] Annulation of $\alpha$ -Substituted Allenoates

#### 2.2.1. [4+2] Annulation of $\alpha$ -Substituted Allenoates with Activated Alkenes



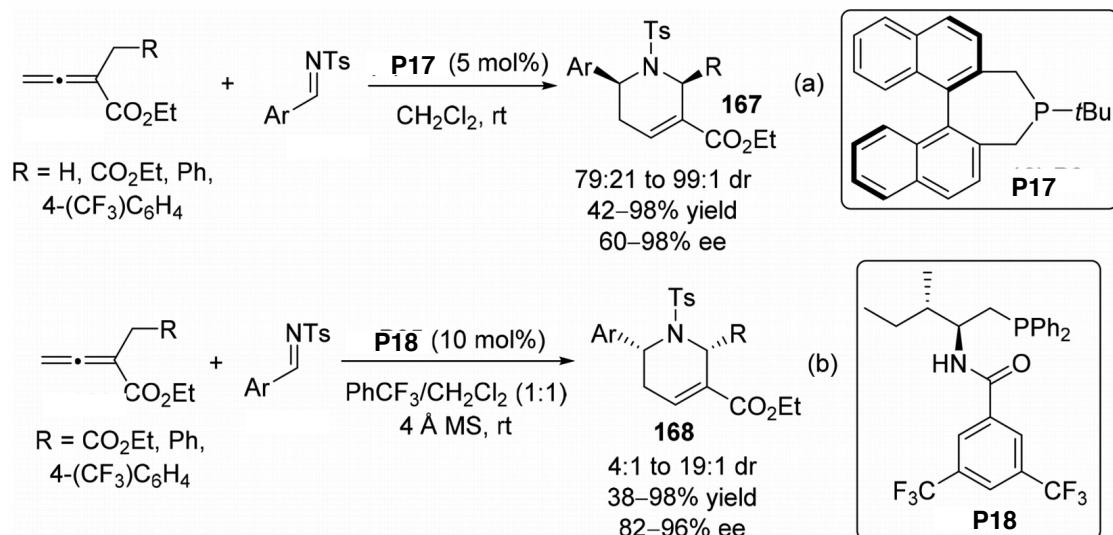
Guo H. et al. *RSC Adv.* 2015, 5, 62343–62347.



Guo H. et al. *Org. Lett.* 2016, 18, 3418–3421.

## 2. Annulation of Allenes and Alkynes

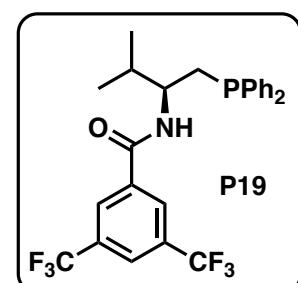
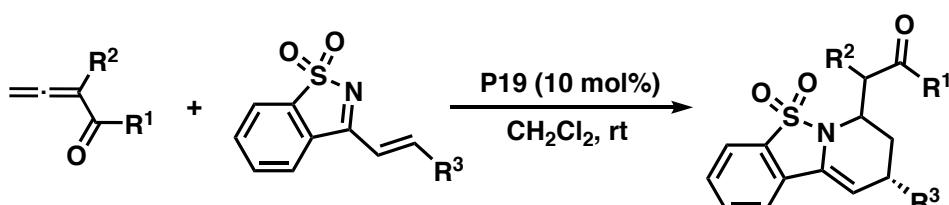
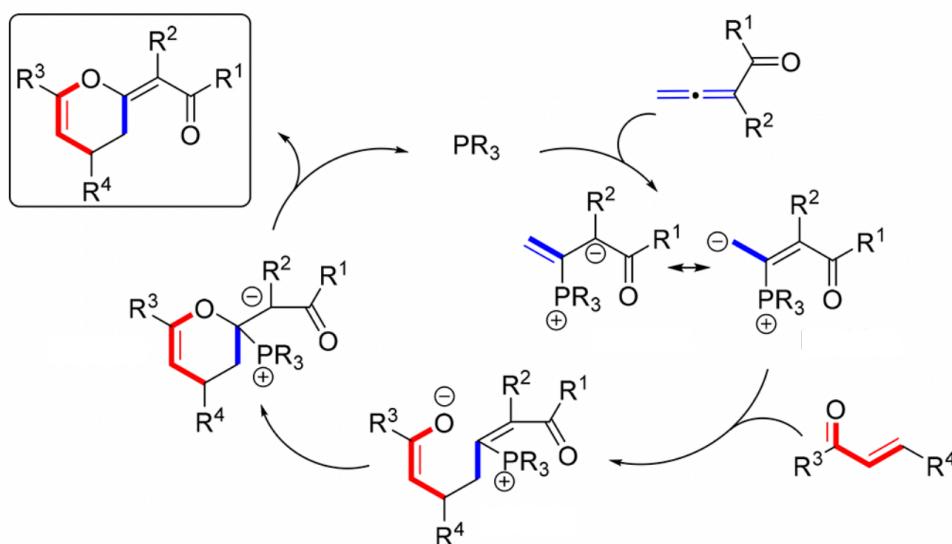
### 2.2.2. [4+2] Annulation of $\alpha$ -Substituted Allenoates with Imines



Fu G. C. et al. *J. Am. Chem. Soc.* 2005, 127, 12234–12235.

Zhao G. et al. *Chem. - Eur. J.* 2011, 17, 10562–10565.

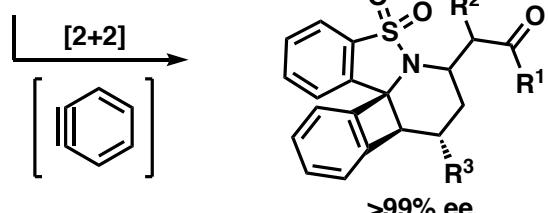
### 2.2.3. [4+2] Annulation of $\alpha$ -Substituted Allenic Ketones



$R^1$  = Me, aryl,  
heteroaryl  
 $R^2$  = Me, Bn

$R^3$  = aryl, heteroaryl, Cy

32-92 yield, 93->99% ee

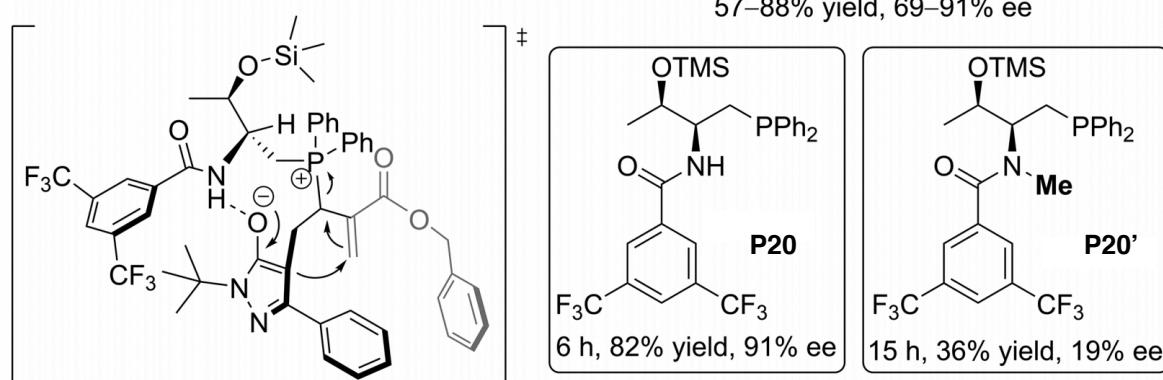
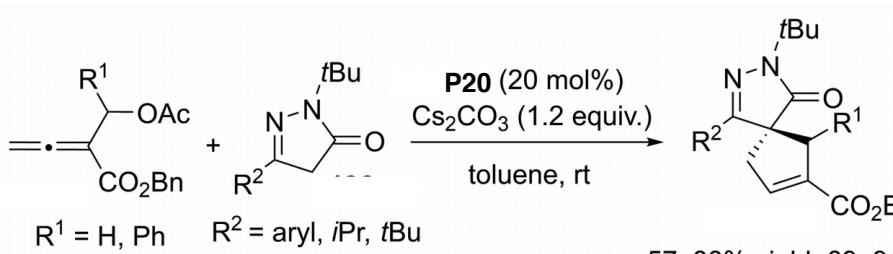
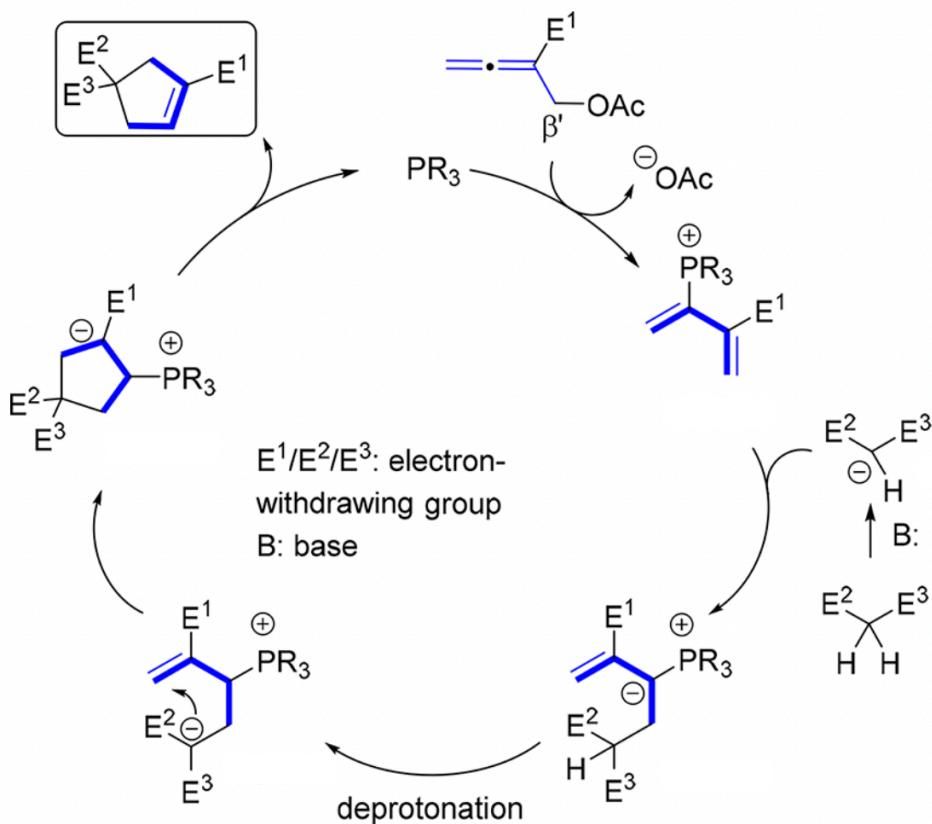


Lu Y. et al. *Org. Lett.* 2017, 19, 3111–3114.

## 2. Annulation of Allenes and Alkynes

### 2.4. Annulations of Acetate-Substituted Allenoates

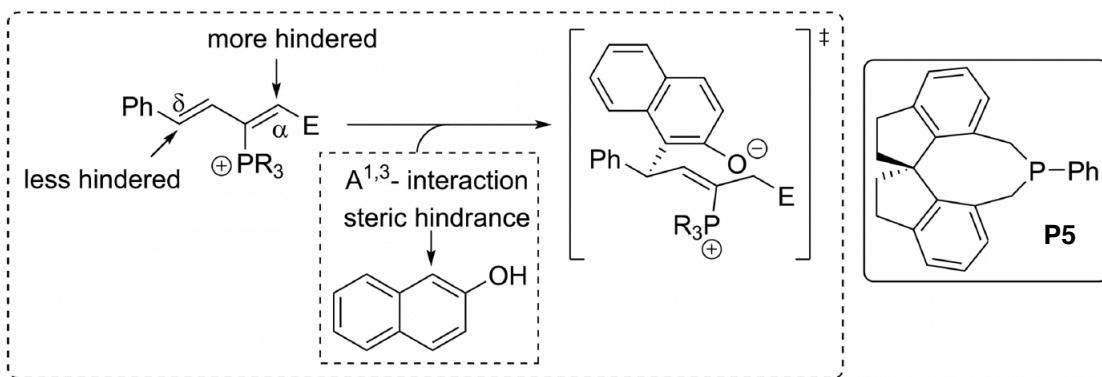
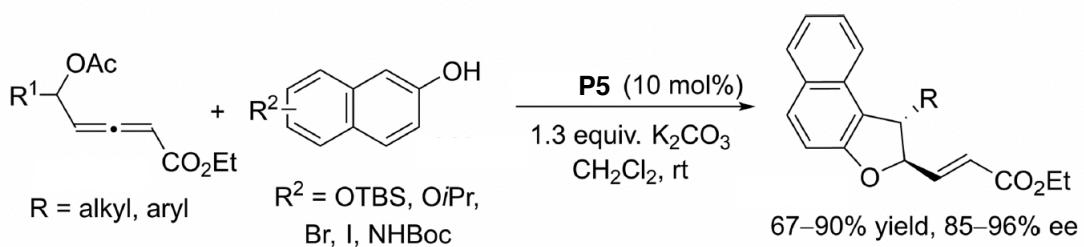
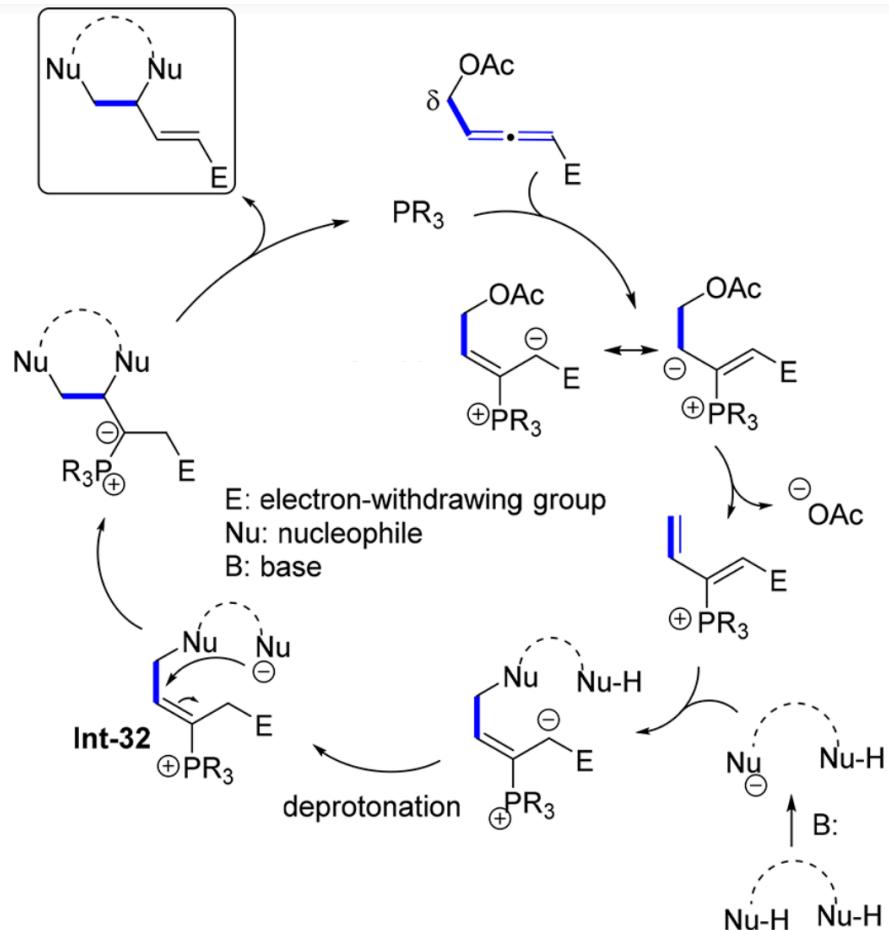
#### 2.4.1. [4+1] Annulation of $\beta'$ -Acetate-substituted Allenoates



## 2. Annulation of Allenes and Alkynes

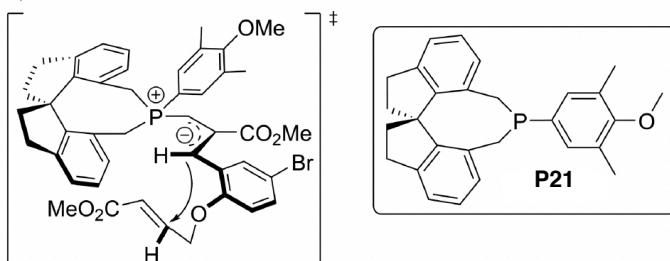
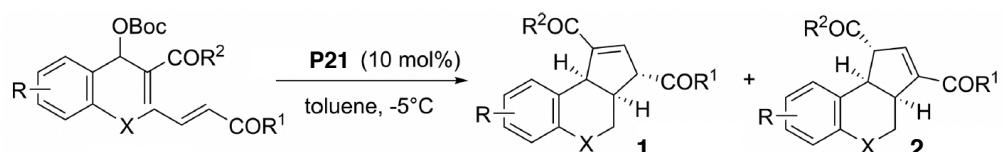
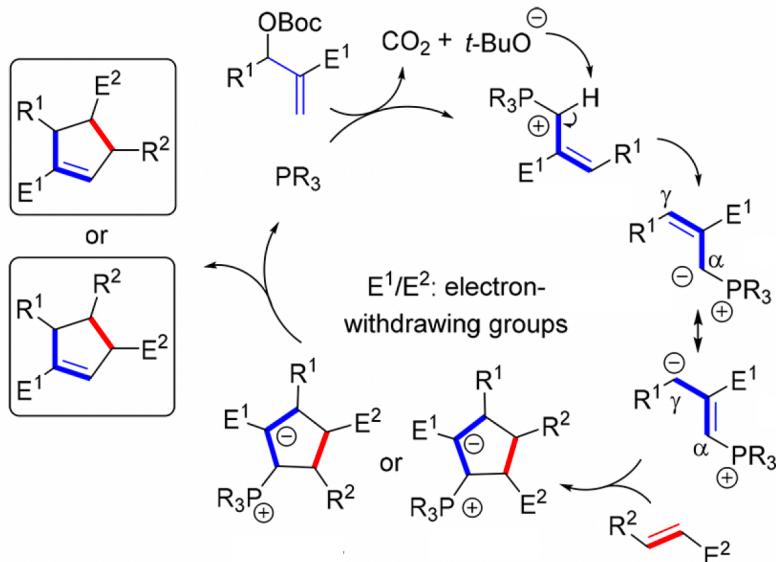
### 2.4.2. [3+2] Annulation of $\delta$ -Acetoxy-substituted Allenoates

#### [n+2] Annulation of $\delta$ -Acetoxy-substituted Allenoates & Dinucleophiles

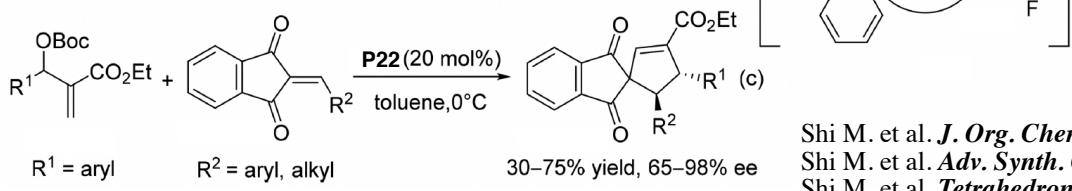
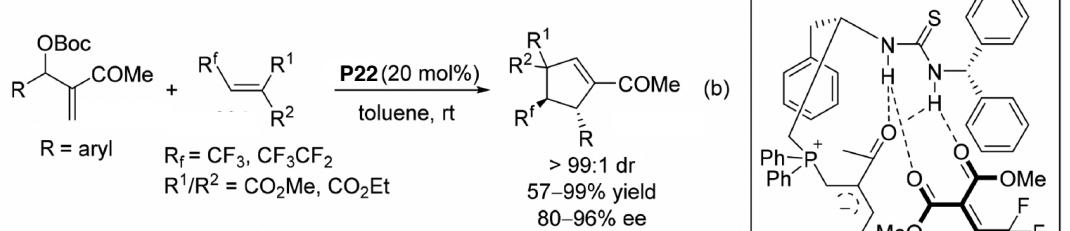
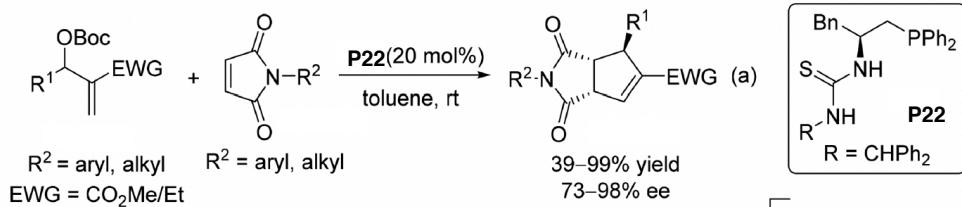


### 3. Annulation Employing the MBH adducts

#### 3.1. [3+2] Annulations



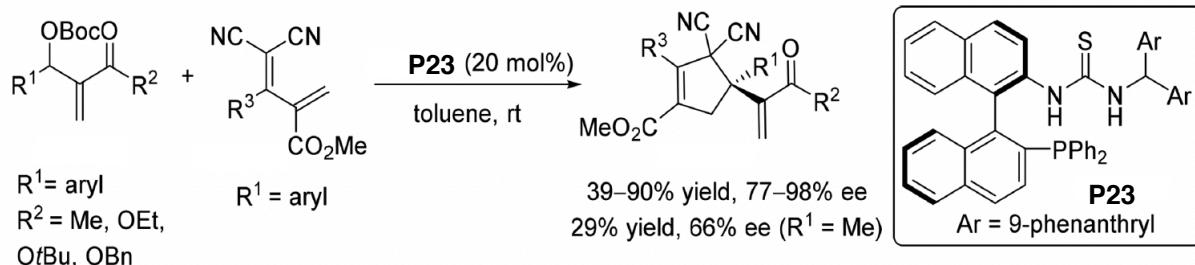
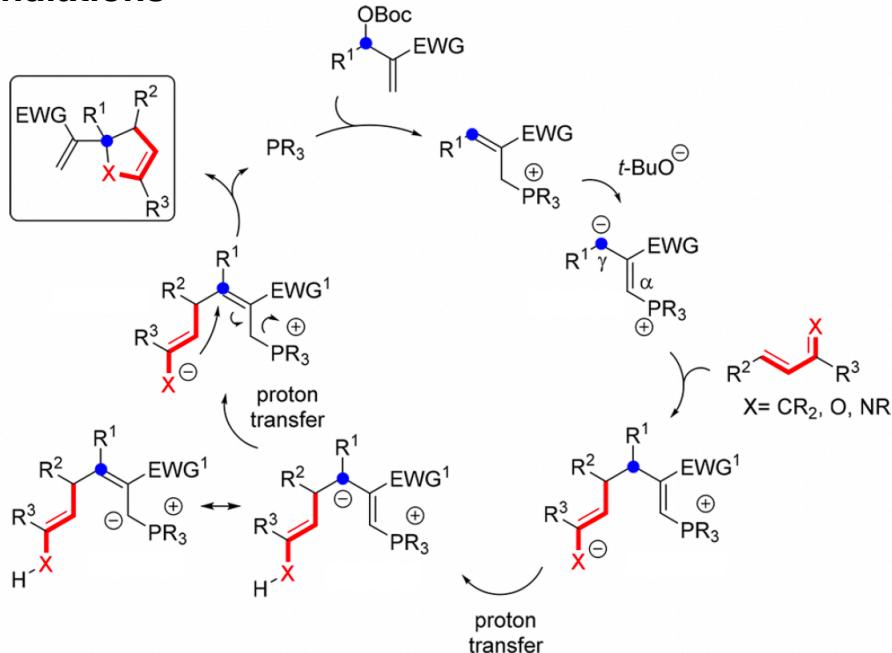
Zhou Q. L. et al. *Adv. Synth. Catal.* 2010, 352, 1914–1919.



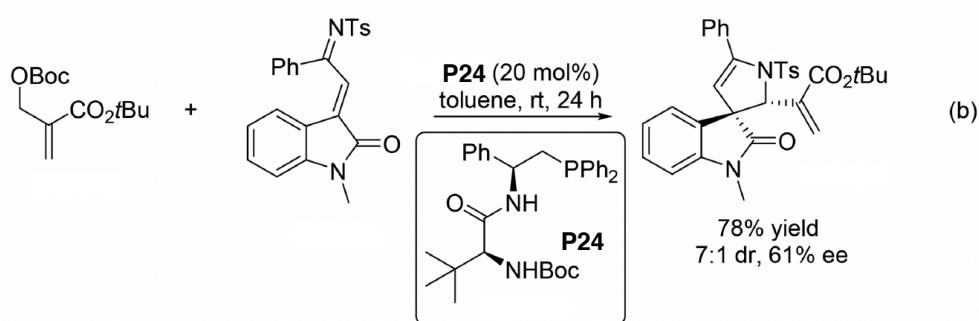
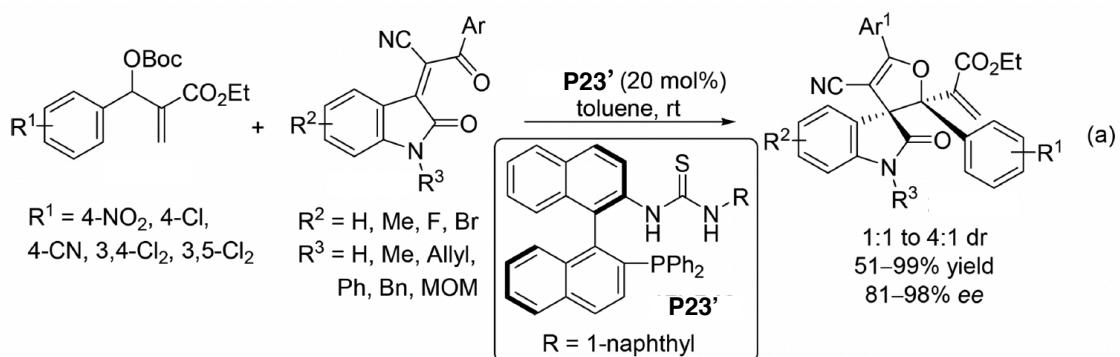
Shi M. et al. *J. Org. Chem.* 2012, 8, 1098–1104.  
 Shi M. et al. *Adv. Synth. Catal.* 2012, 354, 783–789.  
 Shi M. et al. *Tetrahedron* 2012, 68, 7911–7919.

### 3. Annulation Employing the MBH adducts

#### 3.2. [4+1] Annulations



Shi M. et al. *Chem. Commun.* 2012, **48**, 8664–8666.

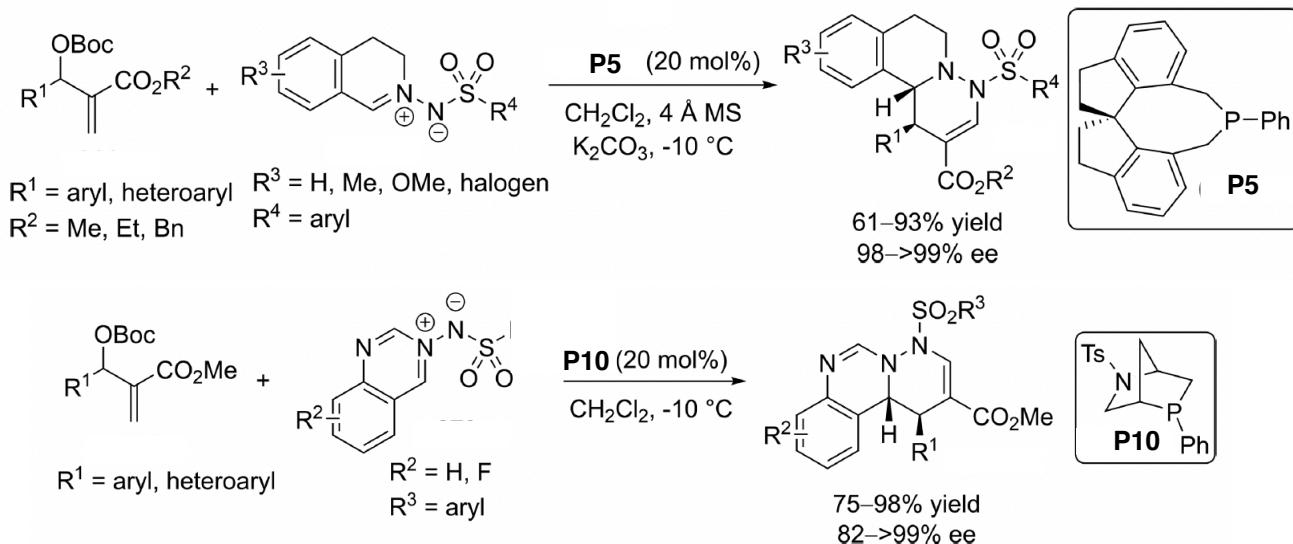


(a) Shi M. et al. *Chem. Commun.* 2014, **50**, 8912–8914.

(b) Shi M. et al. *RSC Adv.* 2015, **5**, 49657–49661.

### 3. Annulation Employing the MBH adducts

#### 3.3. [3+3] Annulations

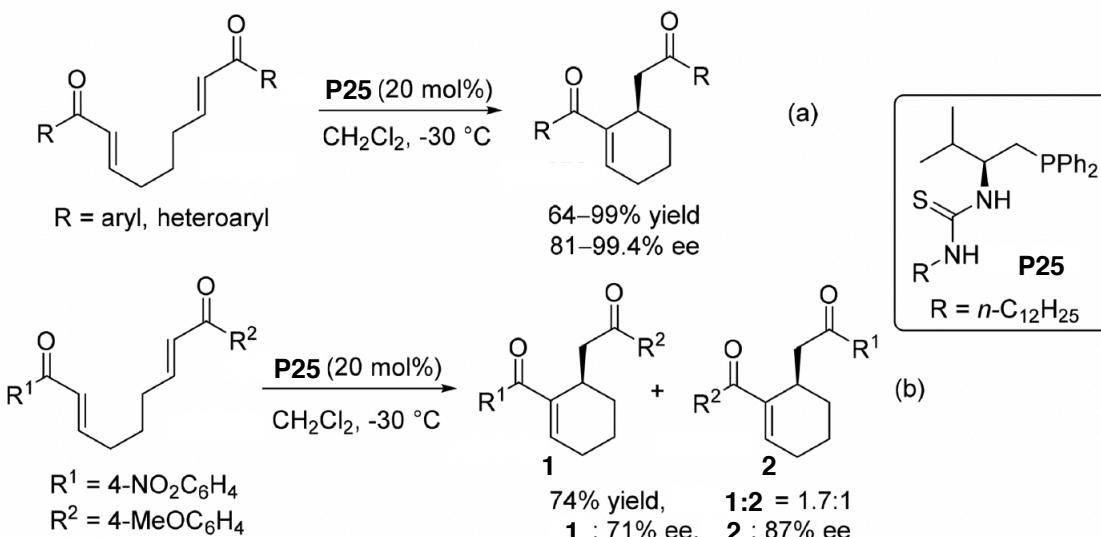
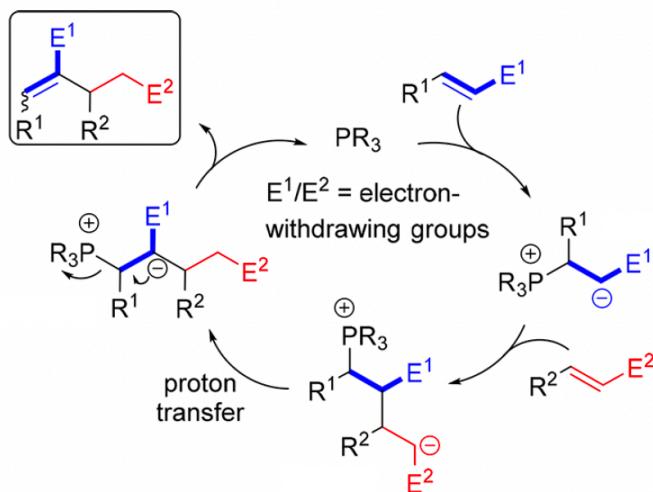


Guo H. et al. *J. Am. Chem. Soc.* 2015, 137, 4316–4319.

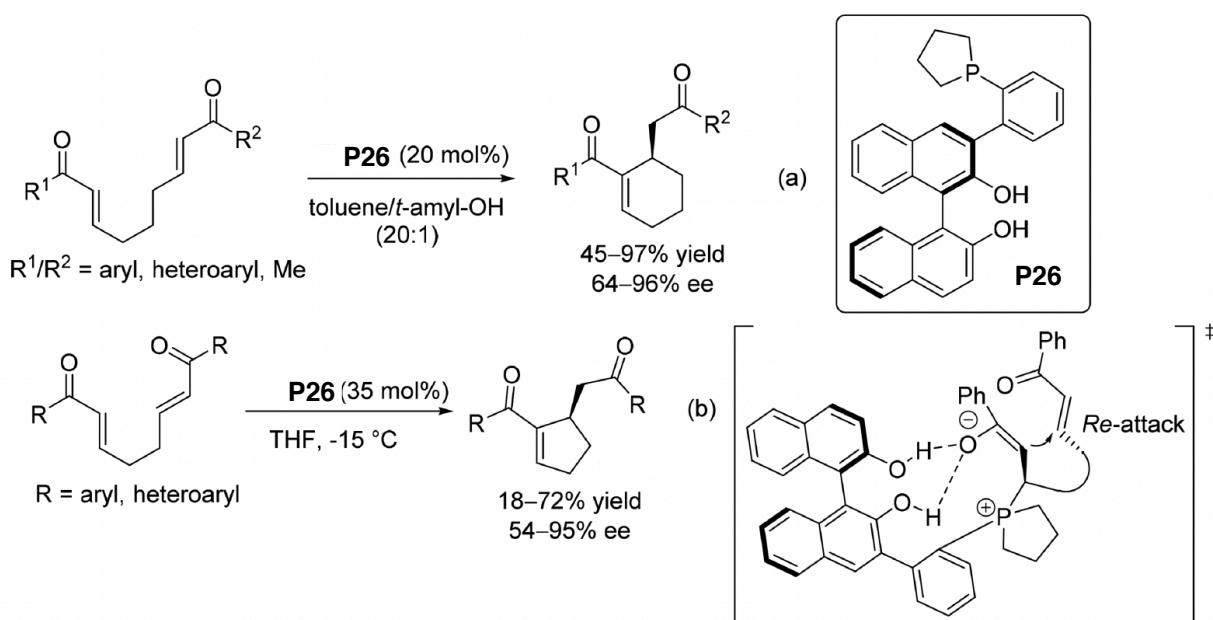
Guo H. et al. *Adv. Synth. Catal.* 2017, 359, 2316–2321.

## 4. Annulation *via* Rauhut-Currier Reactions

### 4.1. Intramolecular Rauhut-Currier Reactions

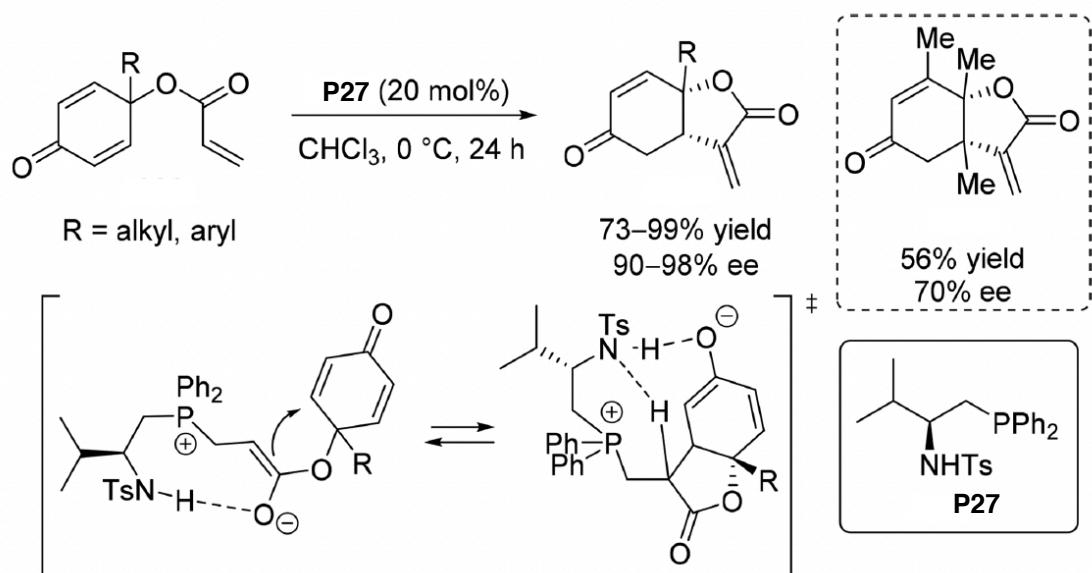


Wu X. Y. et al. *Chem. Commun.* 2011, 47, 1491–1493.  
Wu X. Y. et al. *Tetrahedron Lett.* 2015, 56, 2526–2528.

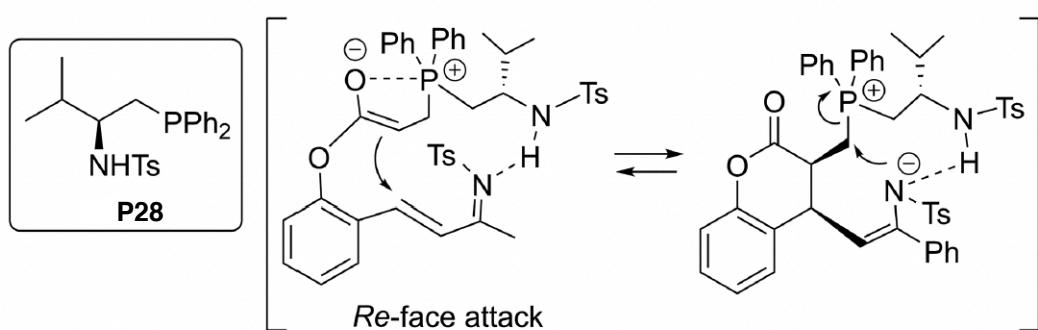
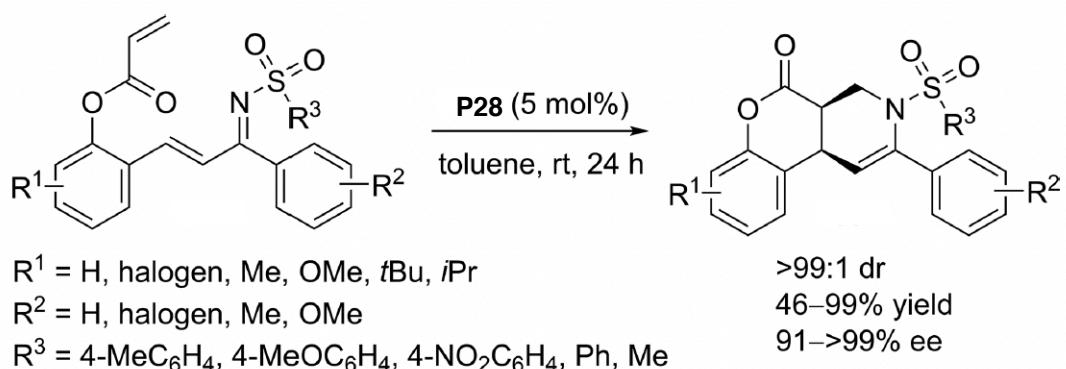


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## 4. Annulation *via* Rauhut-Currier Reactions



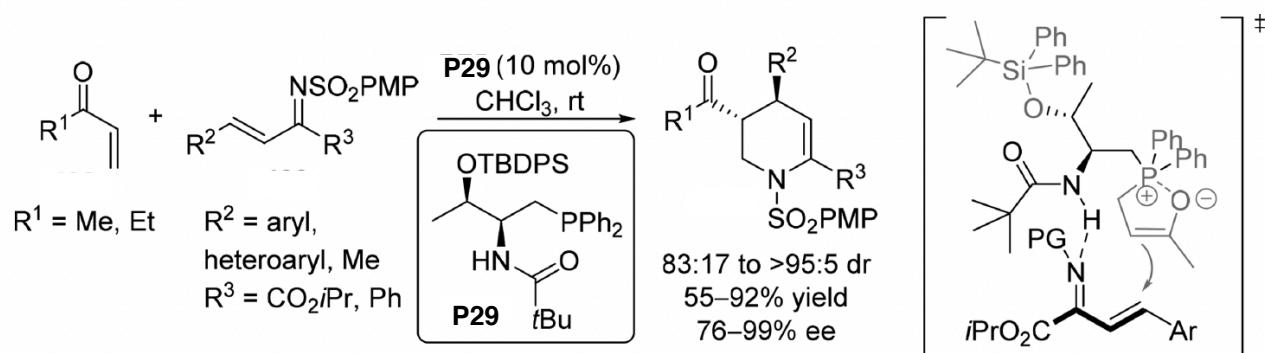
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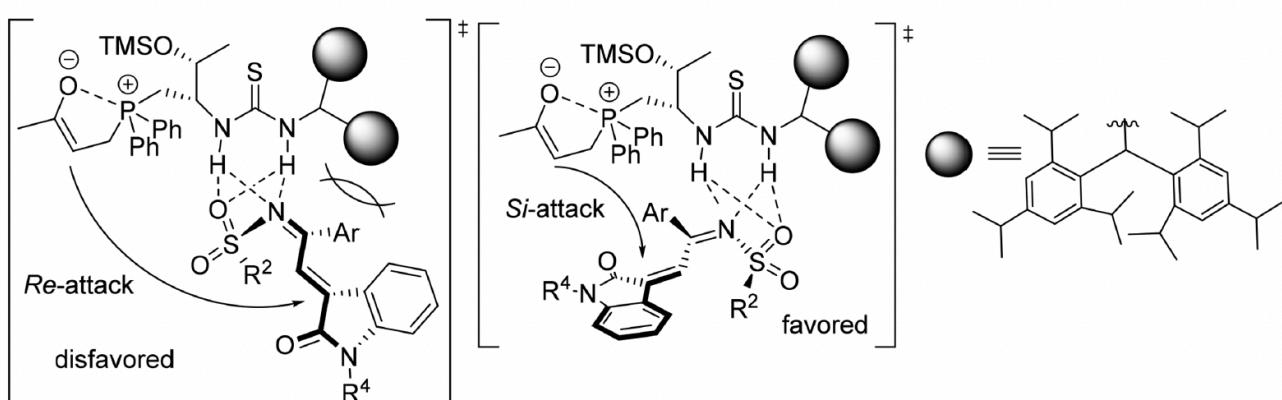
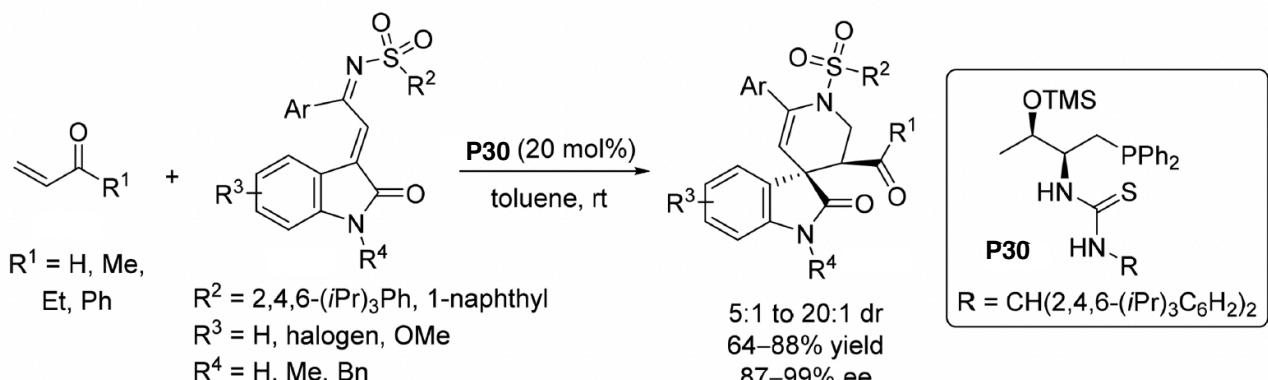
## 4. Annulation *via* Rauhut-Currier Reactions

### 4.2. Intermolecular Rauhut-Currier Reactions



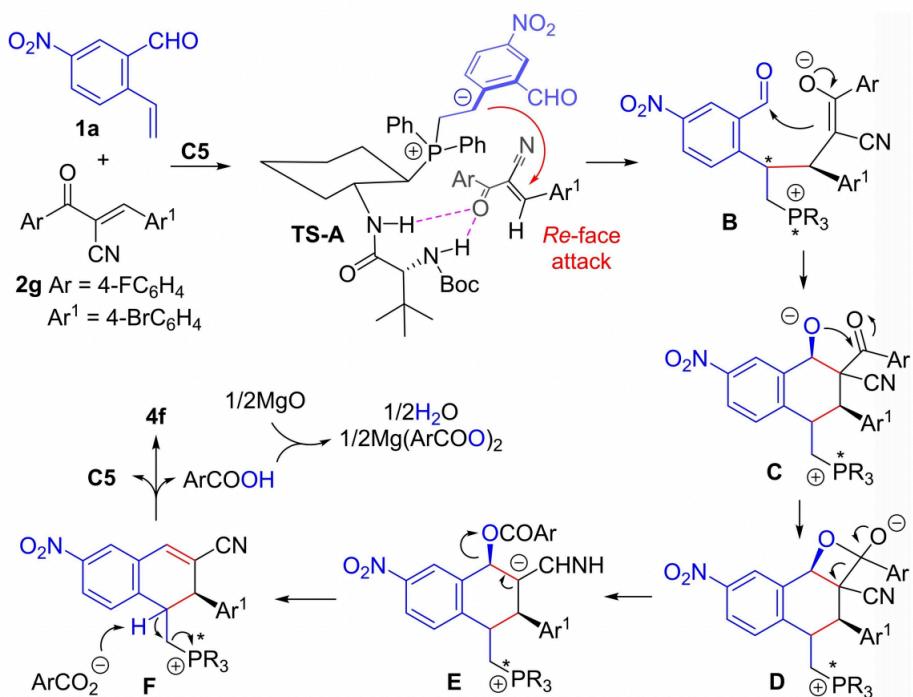
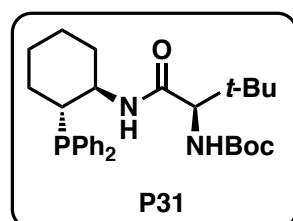
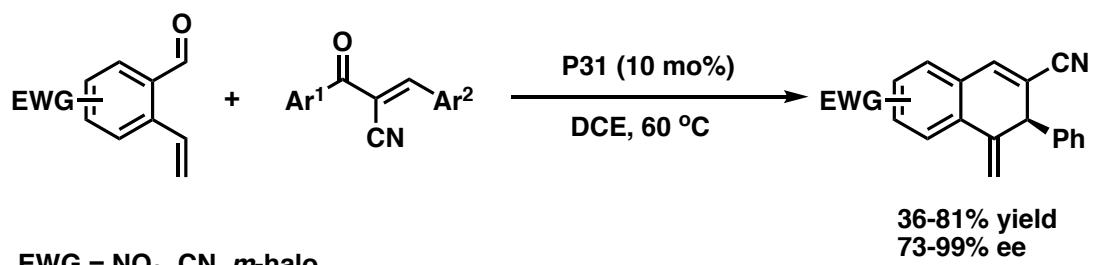
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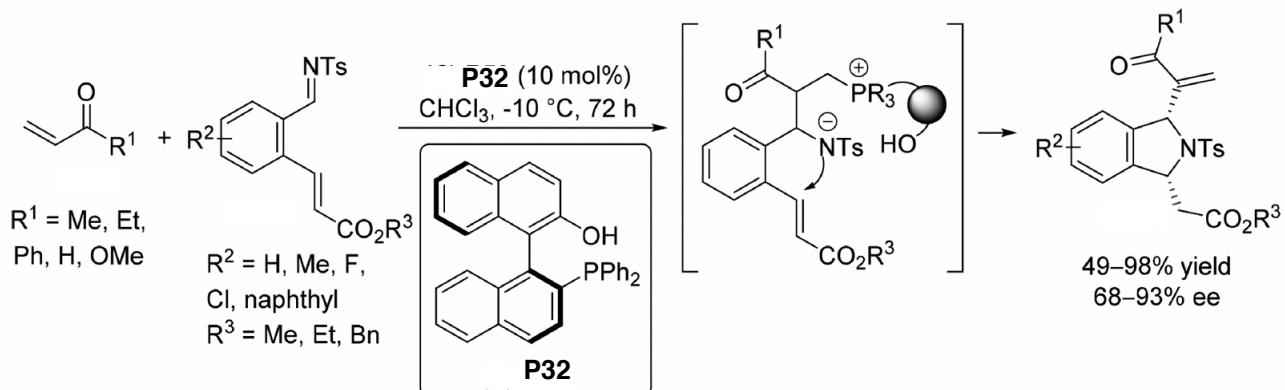
## 4. Annulation via Rauhut-Currier Reactions



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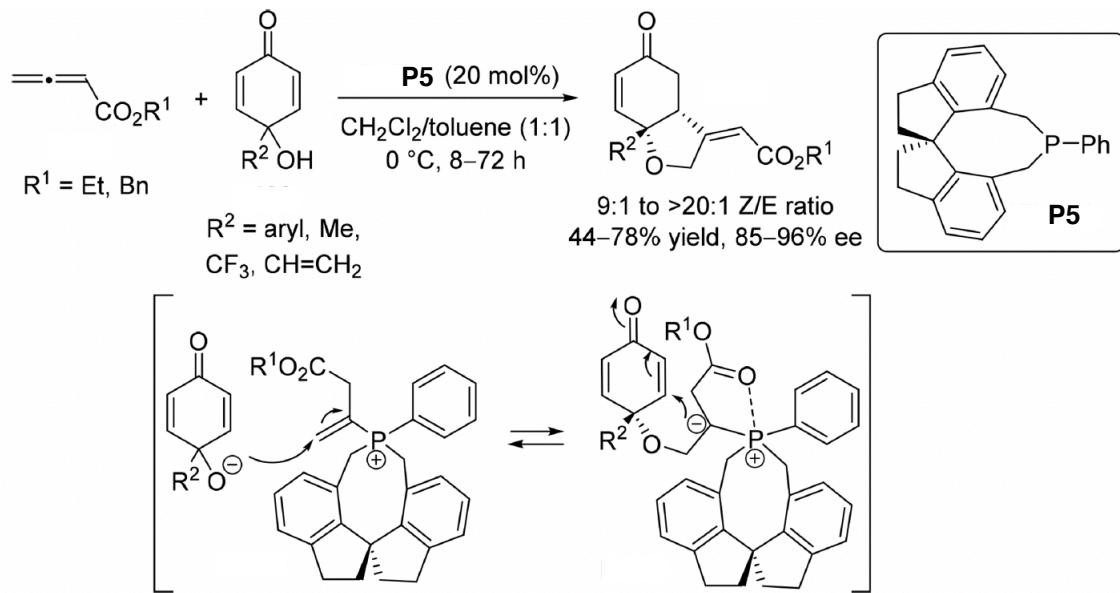
## 5. Miscellaneous Reactions

### Aza-MBH-Michael Annulation



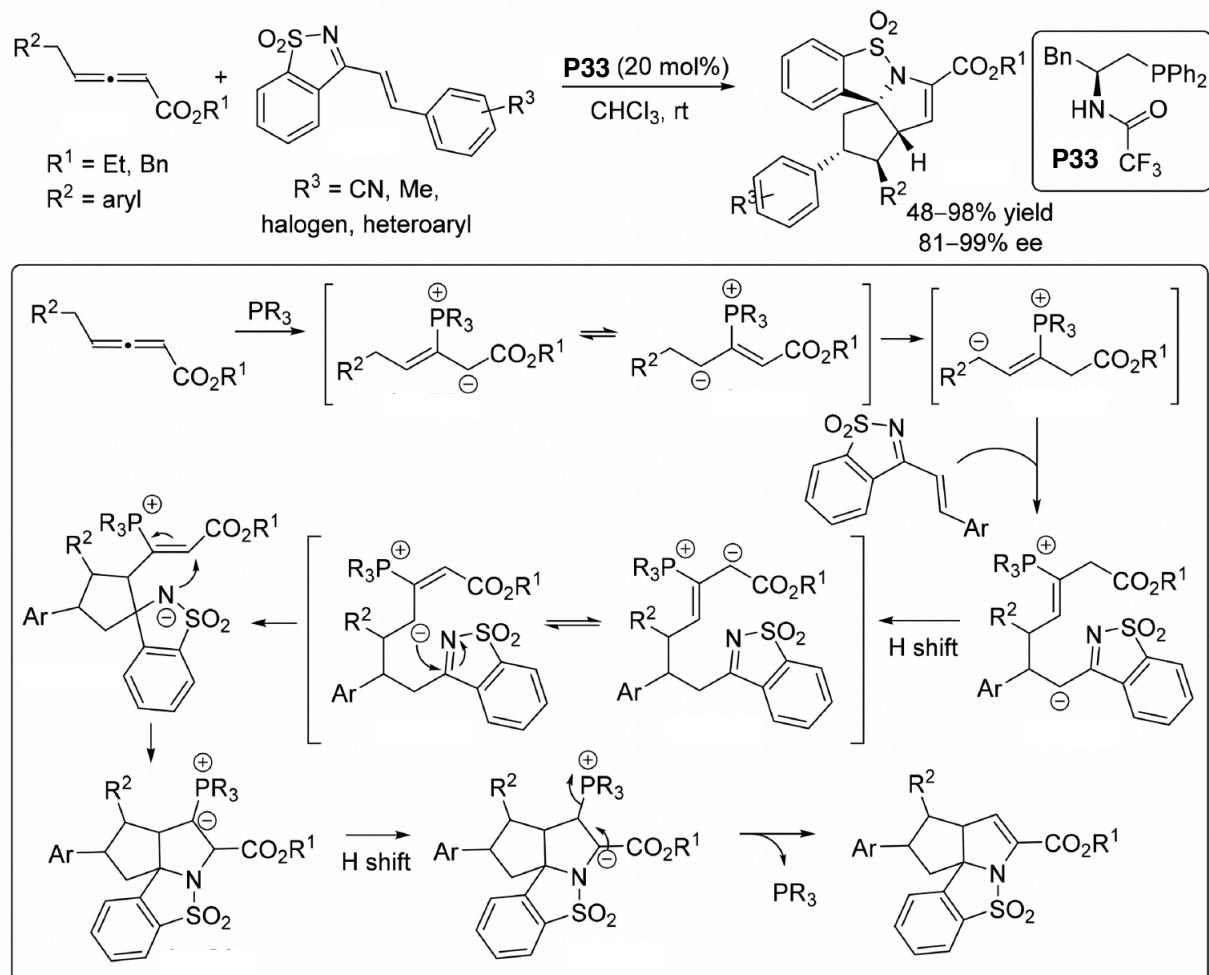
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### $\beta, \gamma$ -Umpolung Domino Reaction



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## 5. Miscellaneous Reactions



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