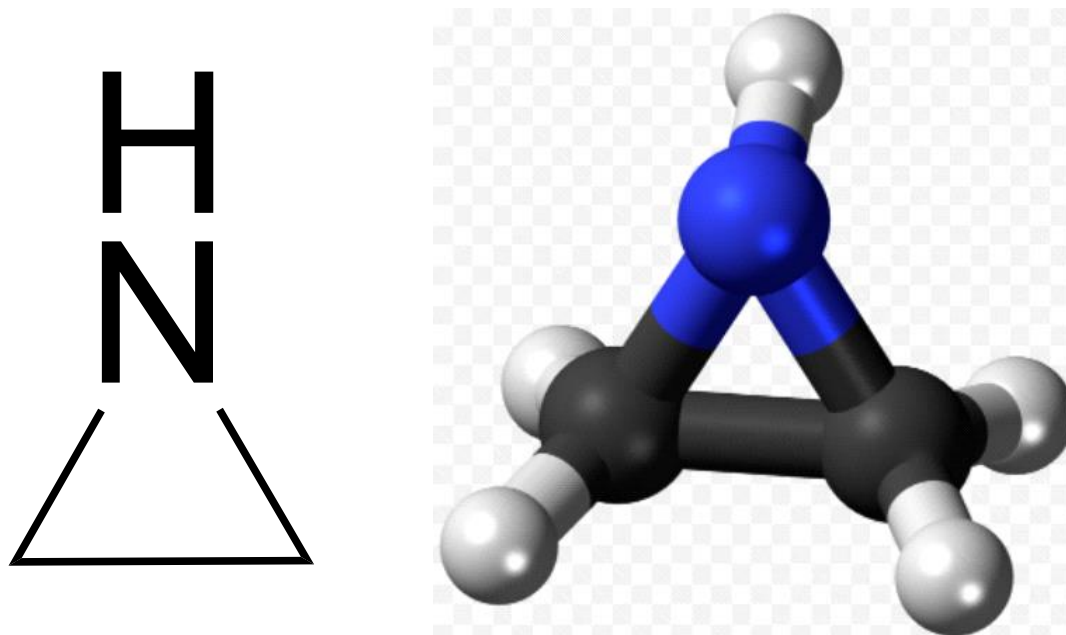


# Aziridine



Literature Review  
Presenter: Guoduan Liang

19/01/2023

# Review Outline

## 1. Introduction

## 3. Ring Opening Reactions of Aziridines

- 3.1 Ring-opening reactions with different nucleophiles
- 3.2 Rearrangement and isomerization
- 3.3 Cyclization

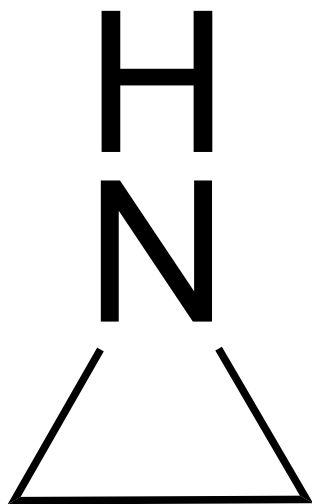
## 4. Dynamic Kinetic Resolution (DKR) of Aziridines

## 2. Aziridination-Synthesis of Aziridine

- 2.1 Aziridination with chloramine-T
- 2.2 Aziridination via nitrene transfer
- 2.3 Synthesis via intramolecular substitution
- 2.4 Synthesis from epoxides
- 2.5 Aziridination of imines

## 5. Aziridines in Natural Product Synthesis

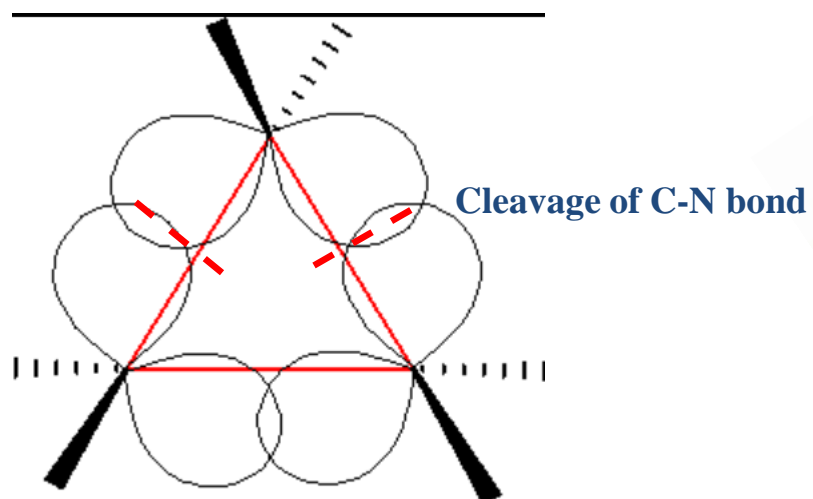
# Introduction



Three-membered heterocycles containing one nitrogen atom.

Discovered in 1888 by Siegmund Gabriel

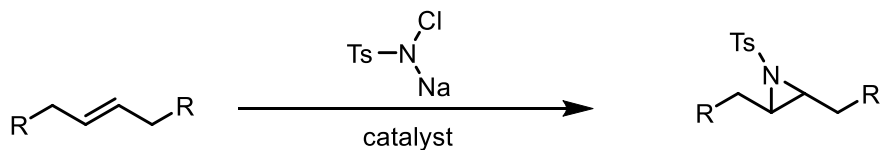
# Introduction



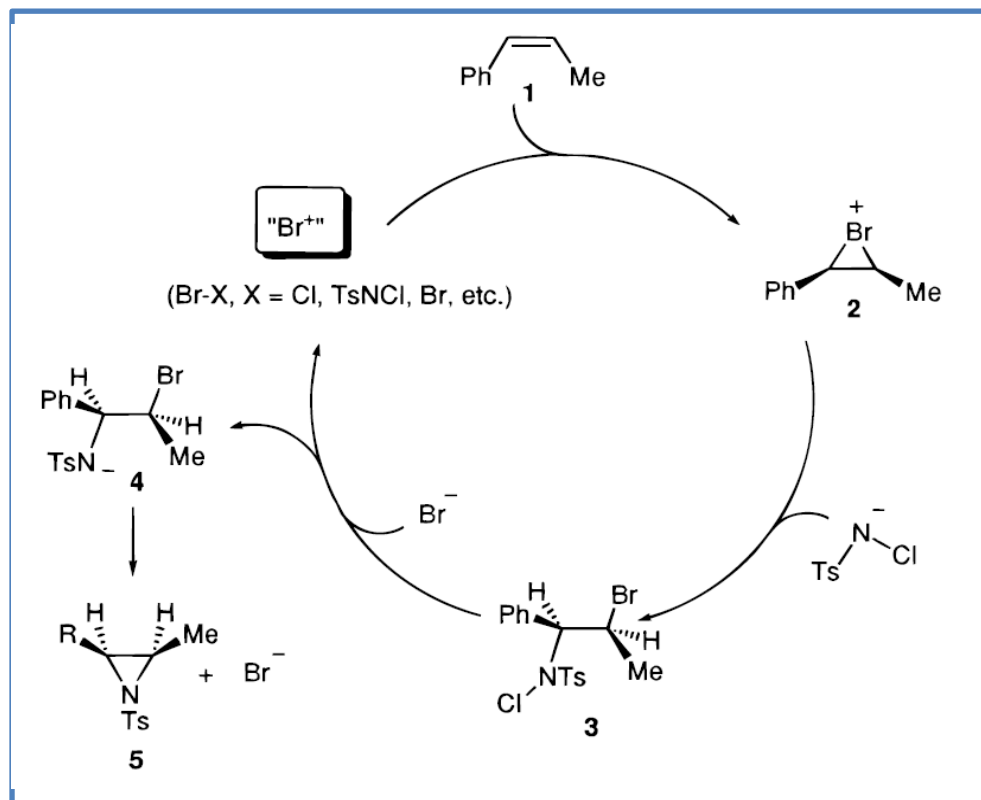
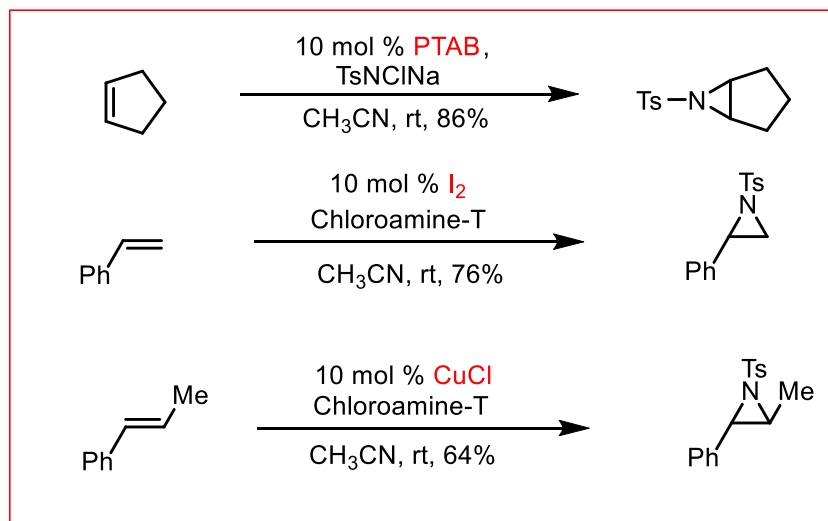
The bond angles in aziridine are approximately  $60^\circ$

## 2.1 Aziridination with chloramine-T

The most straightforward method

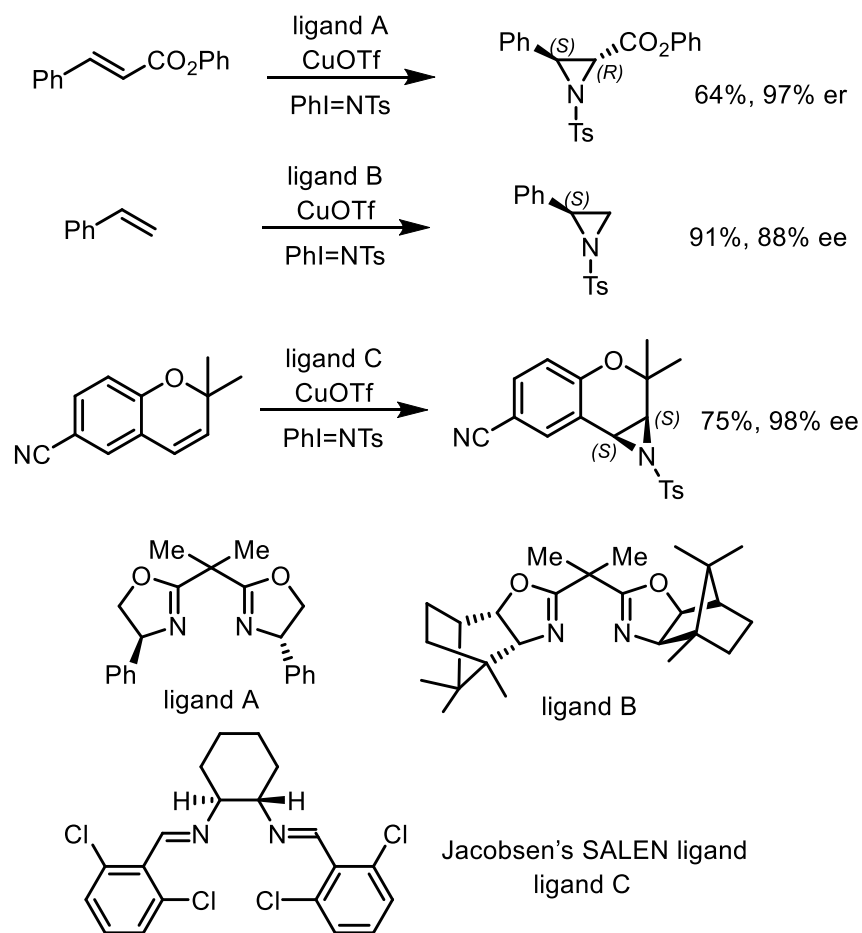
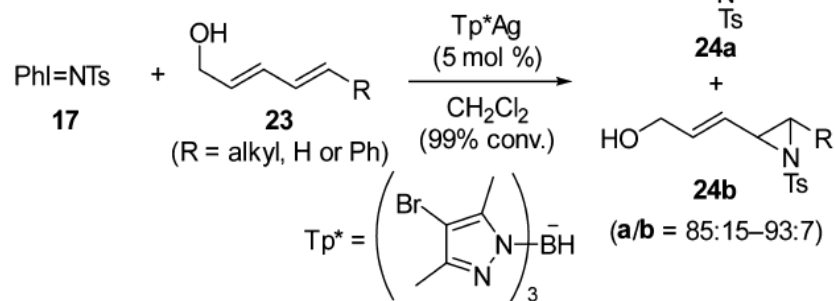
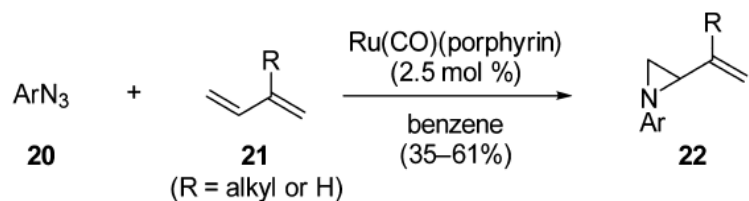
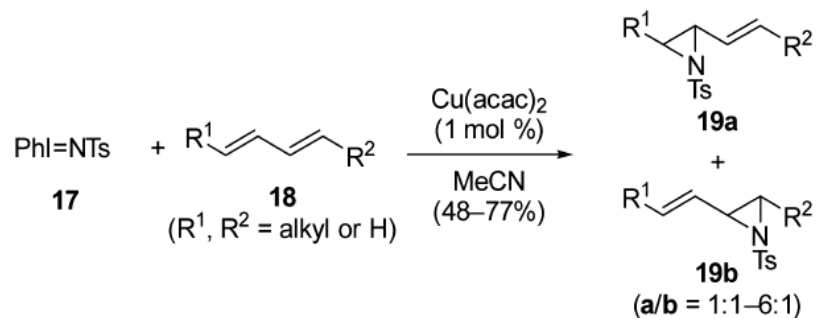


some selective examples

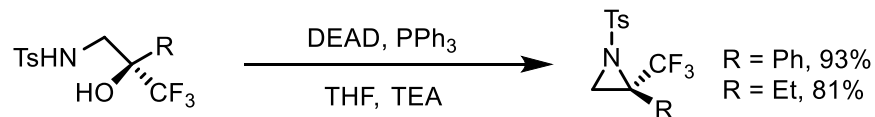
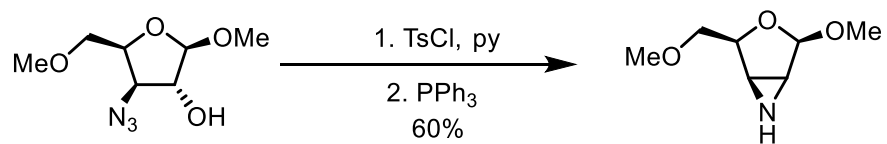
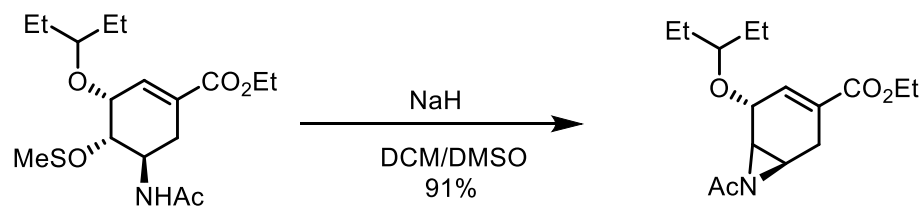
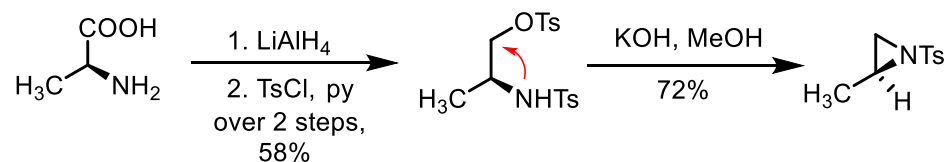


## 2.2 Aziridination via Nitrene Transfer

### Transition metal-catalyzed alkene aziridination



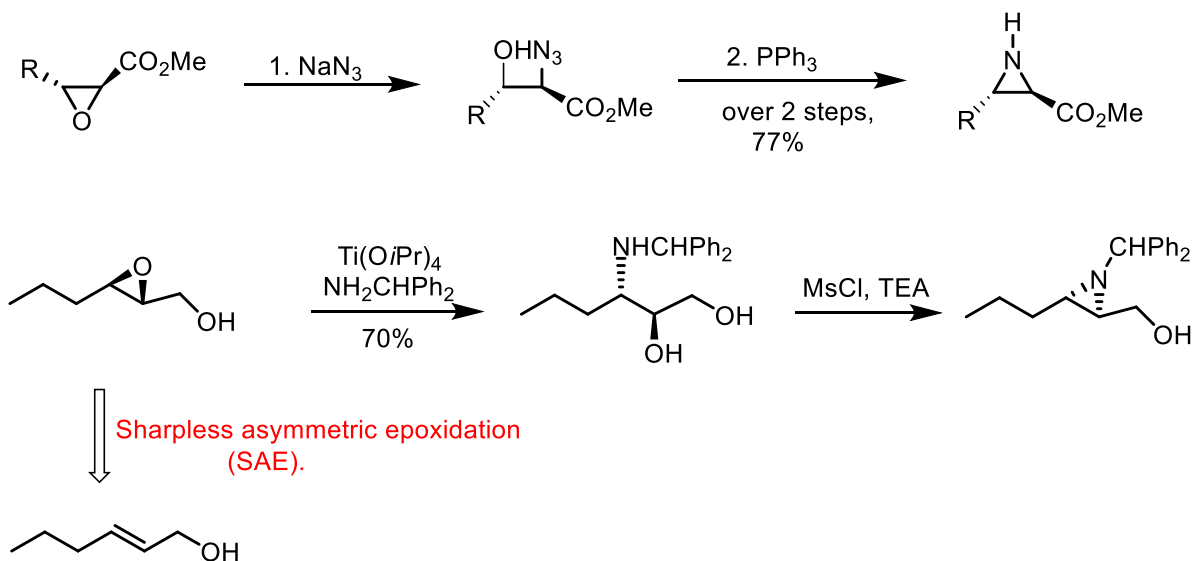
## 2.3 Aziridination via intramolecular substitution



*J. Org. Chem.* **2011**, 76, 9305–9311

*Tetrahedron: Asymmetry* **2013**, 24, 638–642.

## 2.4 Synthesis from epoxides

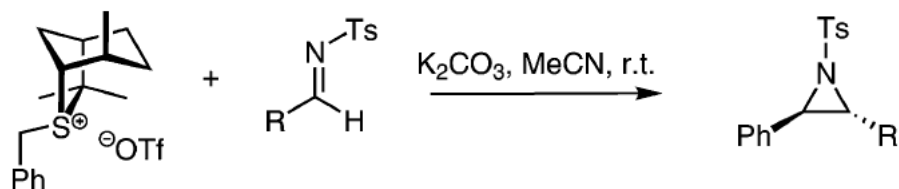


*J. Org. Chem.* **1985**, *50*, 1560–1563

*Tetrahedron Lett.* **1987**, *28*, 1211–1214

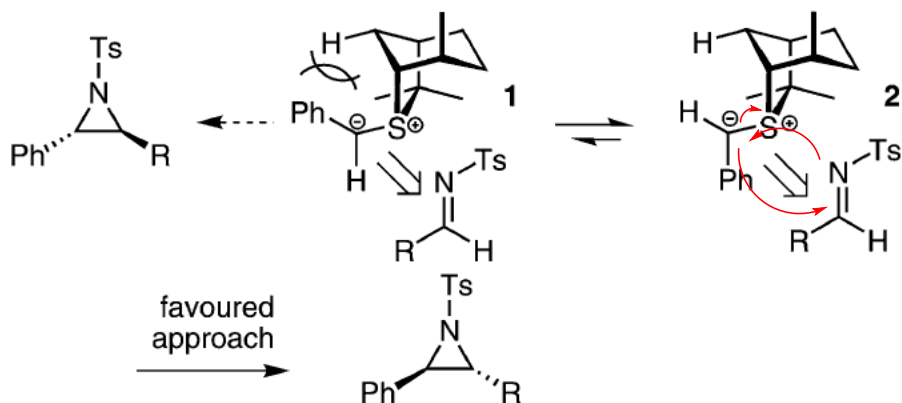
## 2.5 Aziridination of imines

### a). Ylide-mediated aziridination



R = Ph: 72%, *trans/cis* = 85:15, *ee* (*trans*) = 98%  
R = *p*-Tol: 63%, *trans/cis* = 86:14, *ee* (*trans*) = 98%  
R = *p*-ClC<sub>6</sub>H<sub>4</sub>: 65%, *trans/cis* = 75:25, *ee* (*trans*) = 98%  
R = *p*-MeOC<sub>6</sub>H<sub>4</sub>: 80%, *trans/cis* = 83:17, *ee* (*trans*) = 98%  
R = (*E*)-PhCH=CH: 78%, *trans/cis* > 99:1, *ee* (*trans*) = 96%  
R = (*E*)-TMSCH=CH: 78%, *trans/cis* = 87:13, *ee* (*trans*) = 98%  
R = *t*-Bu: 68%, *trans/cis* = 89:11, *ee* (*trans*) = 98%

rationalization of the reaction selectivity:



## 2.5 Aziridination of imines

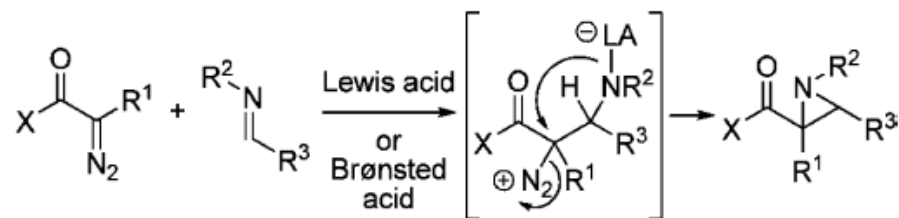
### b). Addition of metallocarbenes to imines



R<sup>1</sup> = Me, Et

R<sup>2</sup> = Boc, Cbz

R<sup>3</sup> = Ph, *o*-Tol, *m*-Tol, *p*-Tol, 2-Naph, *p*-ClC<sub>6</sub>H<sub>4</sub>,  
*p*-BrC<sub>6</sub>H<sub>4</sub>, *p*-PivOC<sub>6</sub>H<sub>4</sub>, *m*-MeOC<sub>6</sub>H<sub>4</sub>, Cy



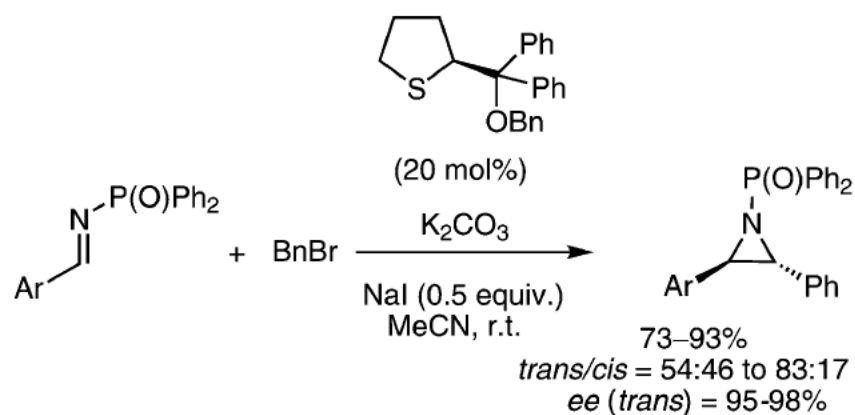
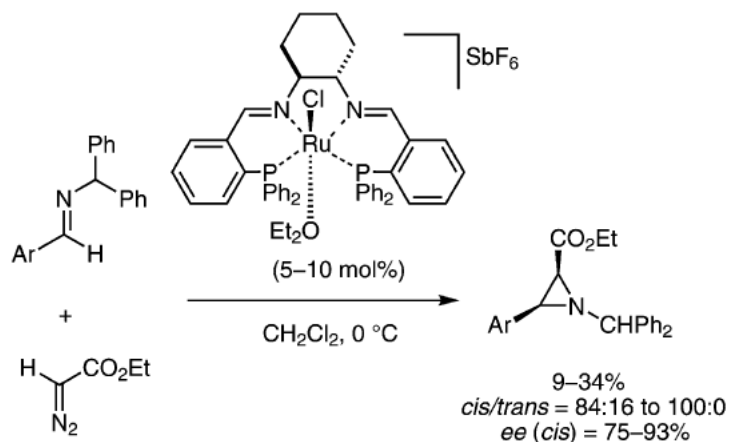
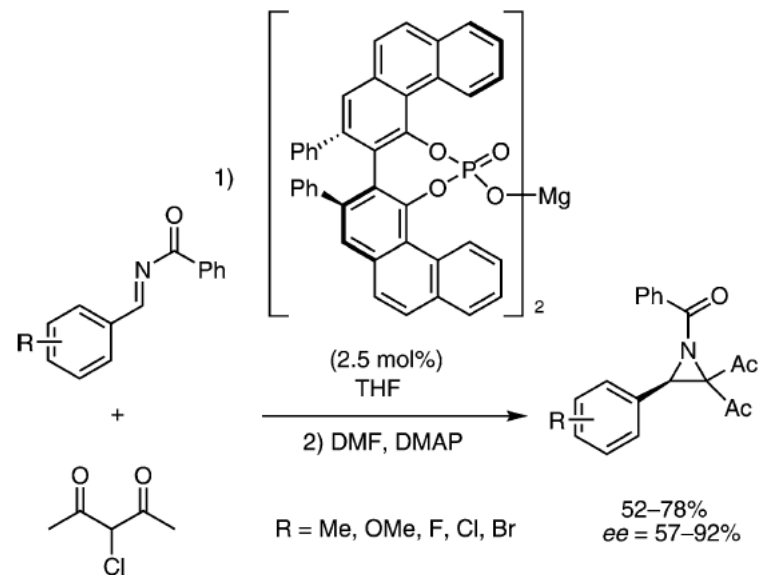
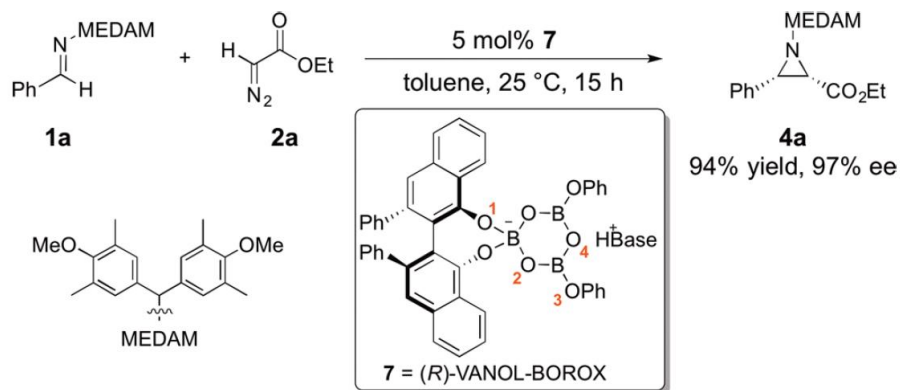
*J. Org. Chem.* **1996**, *61*, 8358–8359

*Org. Lett.* **2010**, *12*, 1668–1671



## 2.5 Aziridination of imines

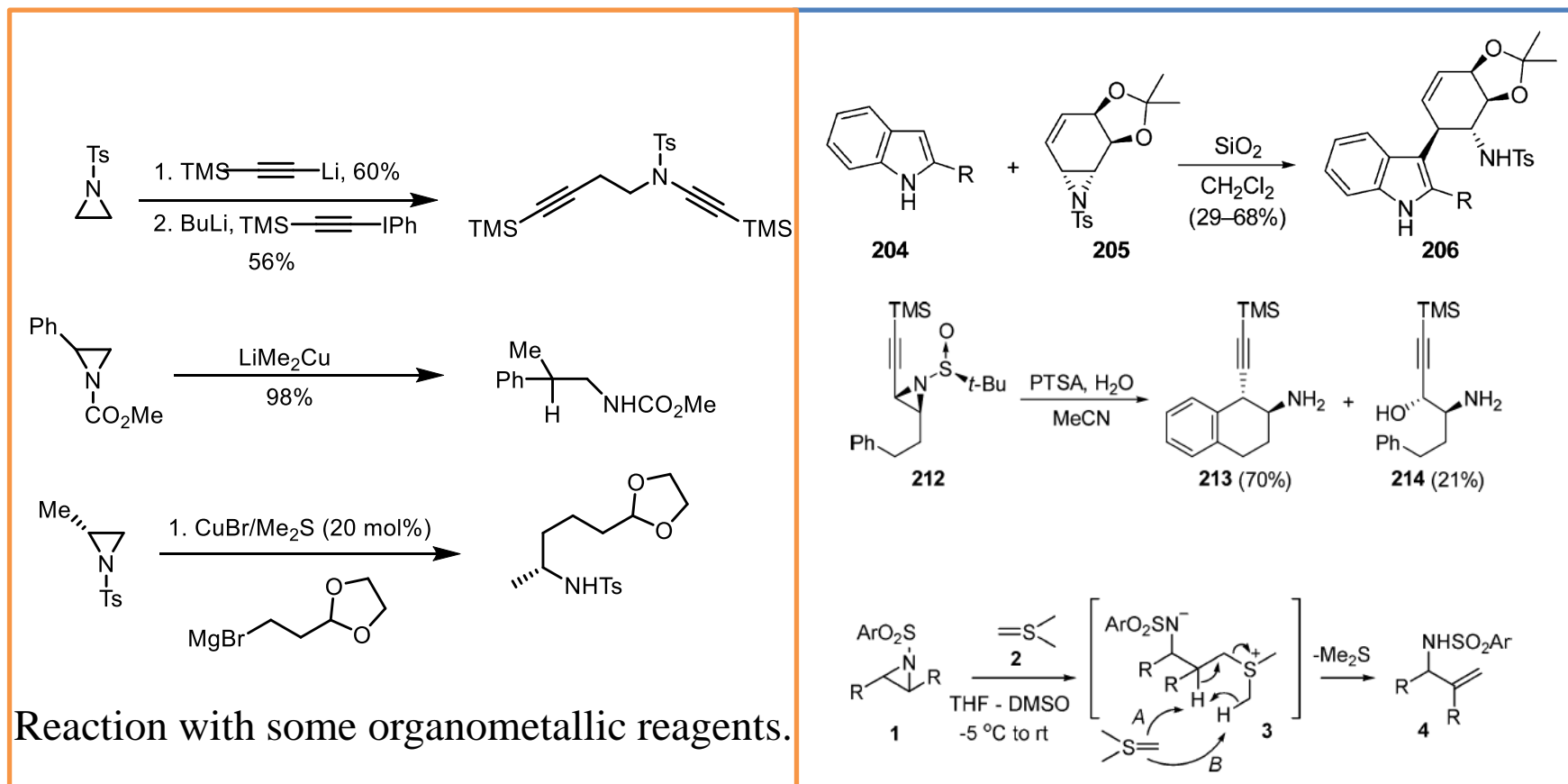
### c). Imines Aziridination based on the use of Chiral Catalysts



# 3. Ring-opening reactions of aziridines

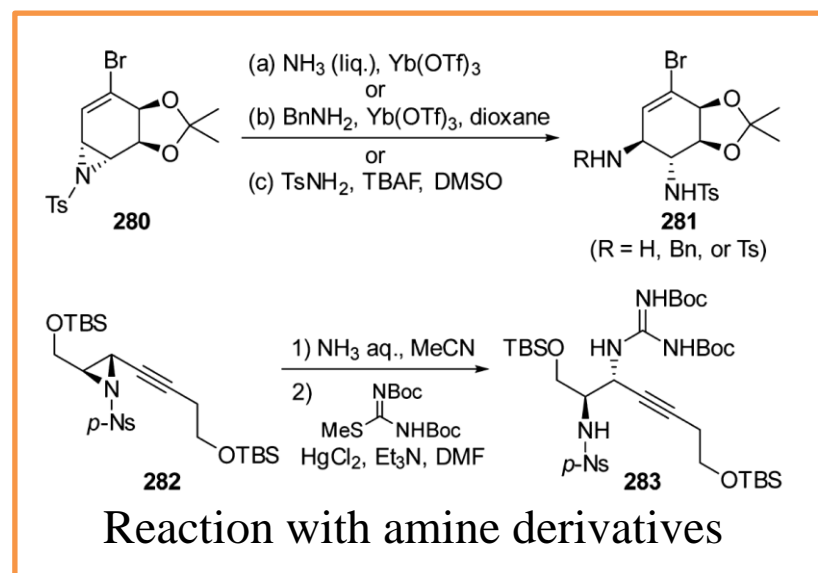
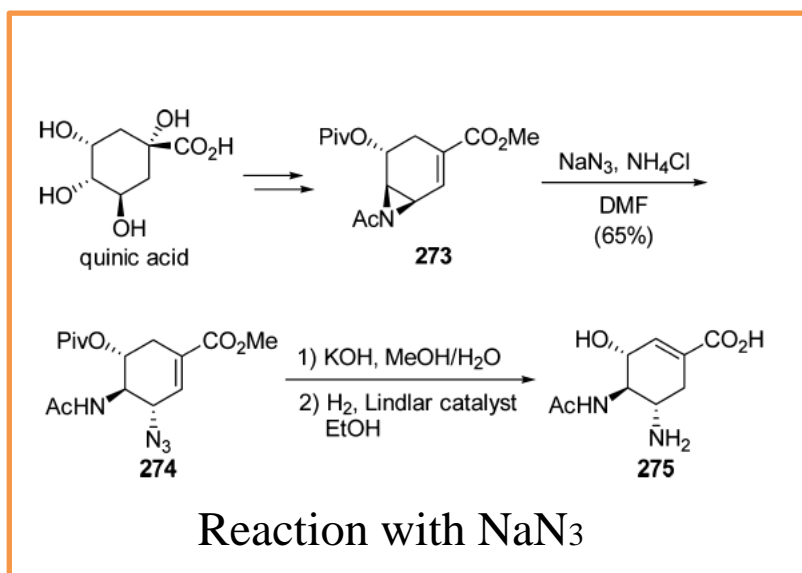
## 3.1 Ring-opening reactions with different nucleophiles-

### Carbon nucleophiles



# 3. Ring-opening reactions of aziridines

## 3.2 Ring-opening reactions with different nucleophiles- Nitrogen nucleophile

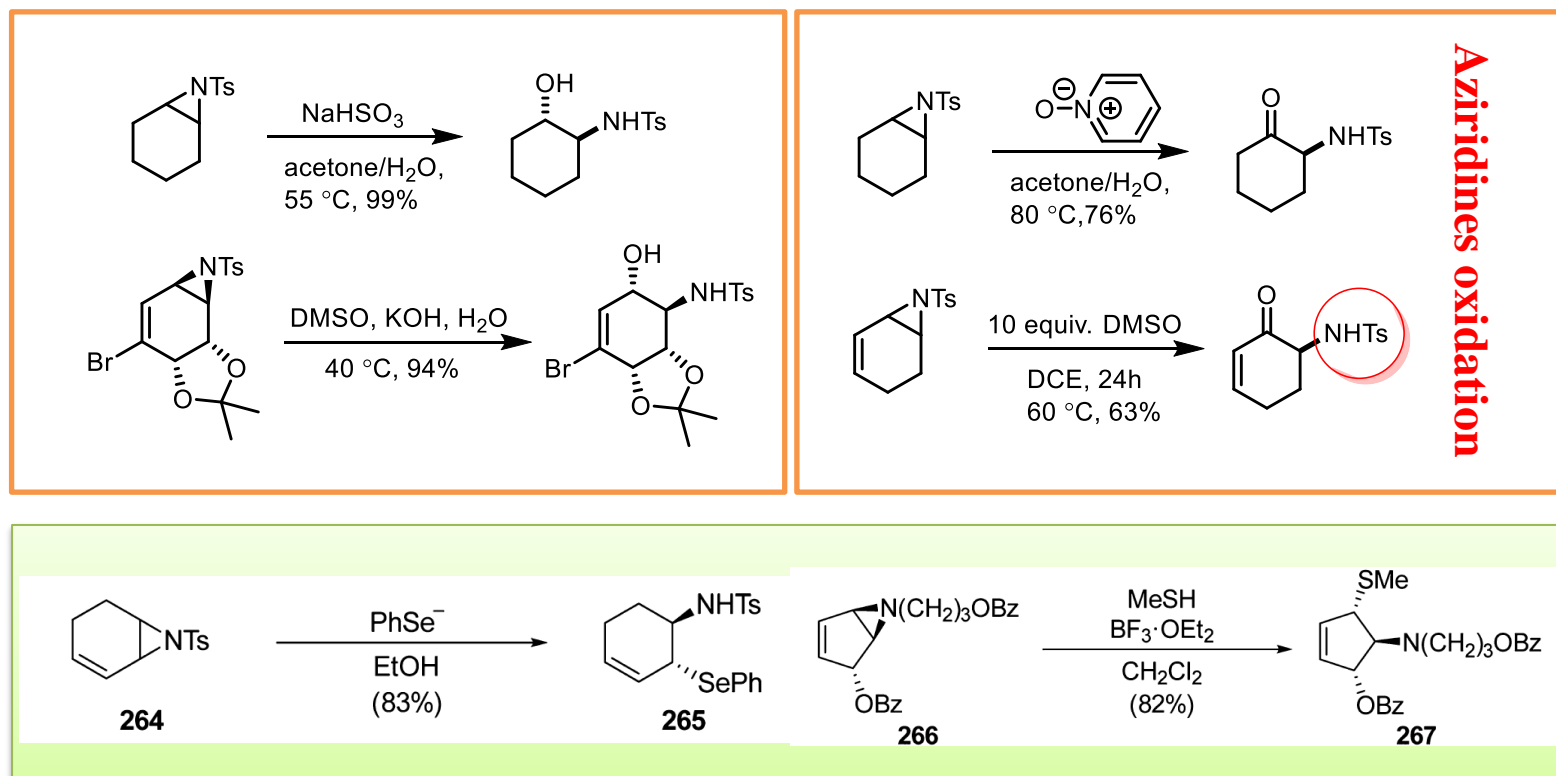


*J. Am. Chem. Soc.* **1997**, *119*, 681–690

*J. Am. Chem. Soc.* **2002**, *124*, 10416–10426

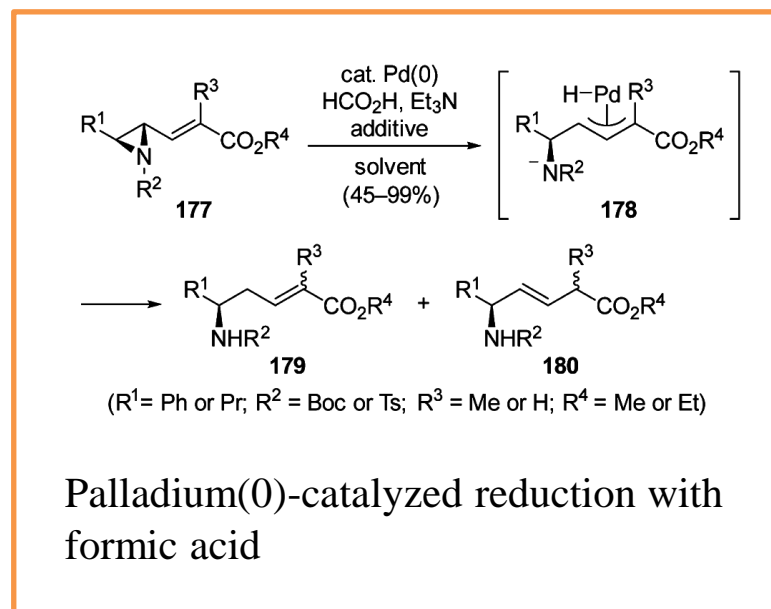
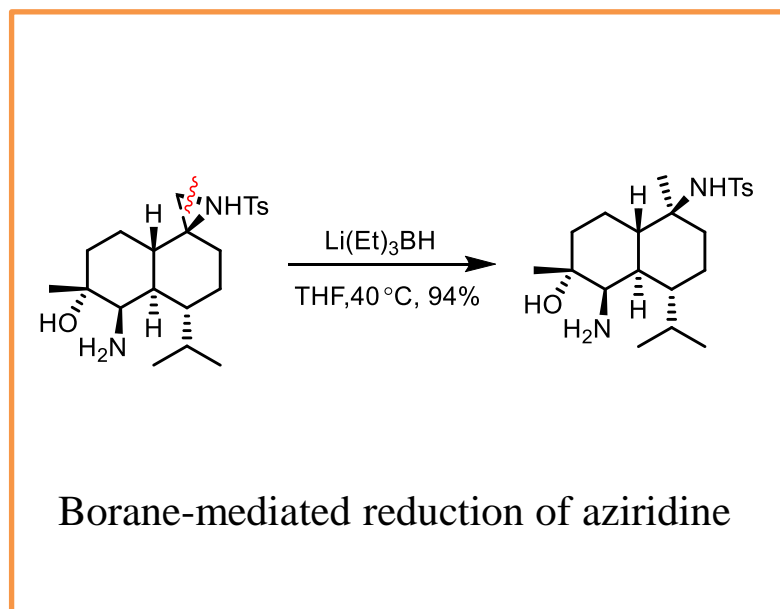
### 3. Ring-opening reactions of aziridines

#### 3.3 Ring-opening reactions with different nucleophiles- Oxygen, Sulfur and Selenium nucleophiles



### 3. Ring-opening reactions of aziridines

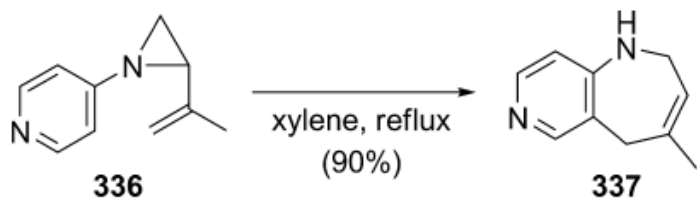
#### 3.4 Ring-opening reactions with different nucleophiles-Hydrides



### 3. Ring-opening reactions of aziridines

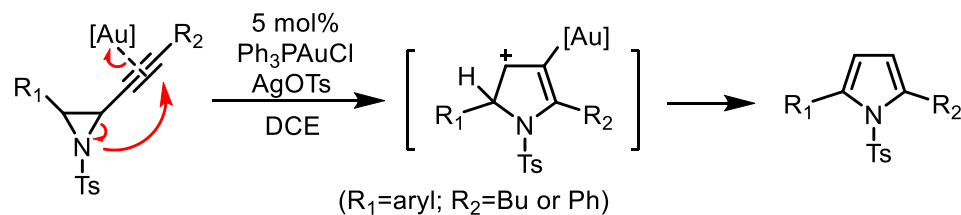
#### 3.5 Rearrangement and isomerization

##### Aza-[3,3]-Claisen Rearrangement



*Tetrahedron Lett.* **1981**, 22, 637

##### Gold Catalyzed Isomerization of Alkynyl Aziridines to Pyrroles

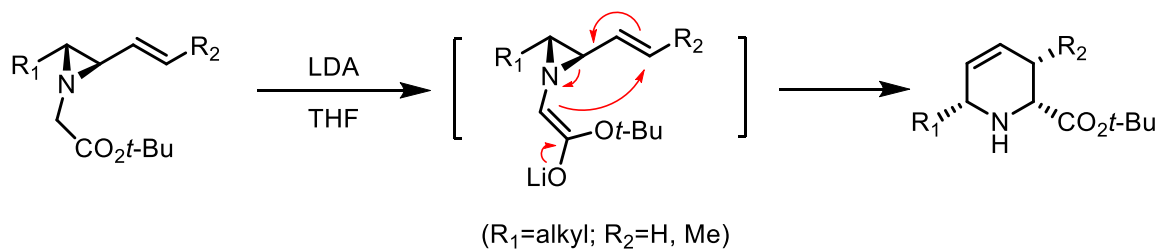


*Org. Lett.* **2009**, 11, 2293–2296

### 3. Ring-opening reactions of aziridines

#### 3.5 Rearrangement and isomerization

##### Aza-[2,3]-Wittig Rearrangement of Vinylaziridines

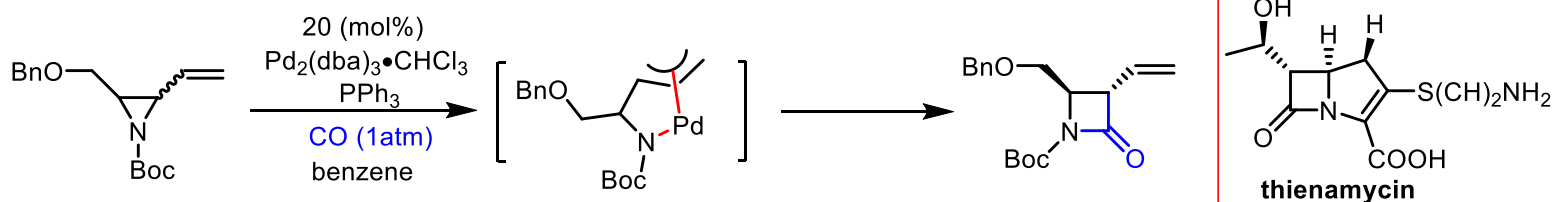


*J. Am. Chem. Soc.* **1994**, *116*, 9781–9782

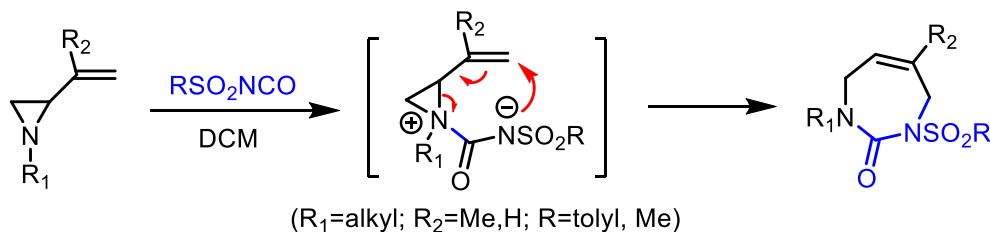
# 3. Ring-opening reactions of aziridines

## 3.6 Cycloaddition

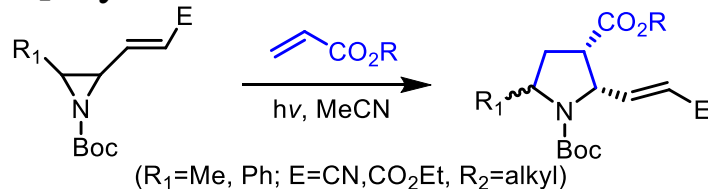
### Palladium(0)-Catalyzed Carbonylative Ring Expansion to $\beta$ -Lactams



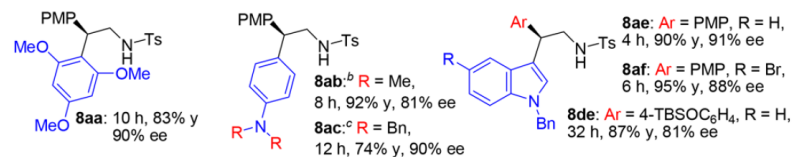
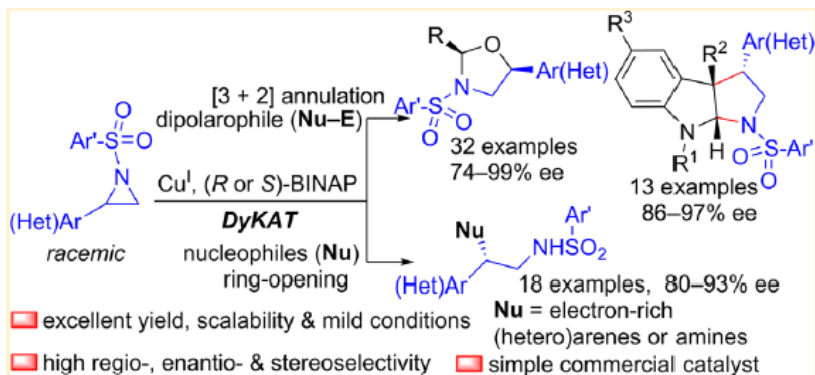
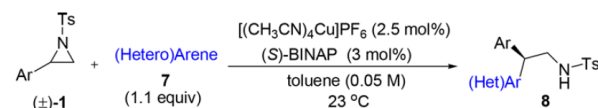
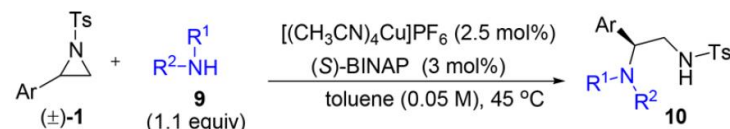
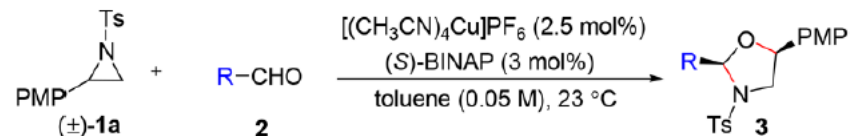
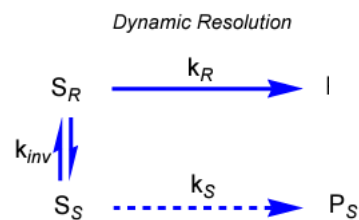
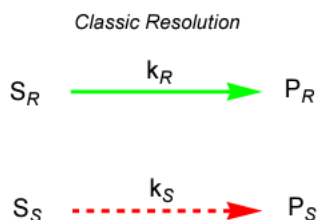
### Catalyst-Free [5 + 2] Cycloaddition with Sulfonyl Isocyanates



### Photoinduced [2 + 3] Cycloaddition with Activated Olefins

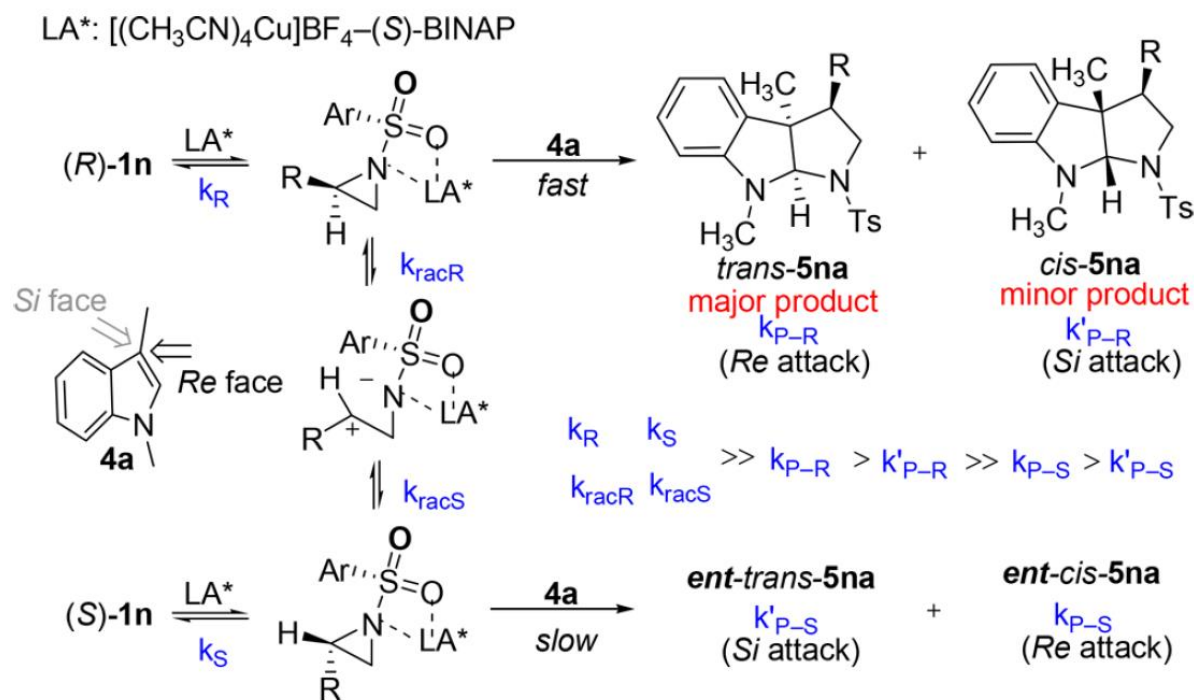


# 4. Dynamic kinetic resolution (DKR) of aziridines



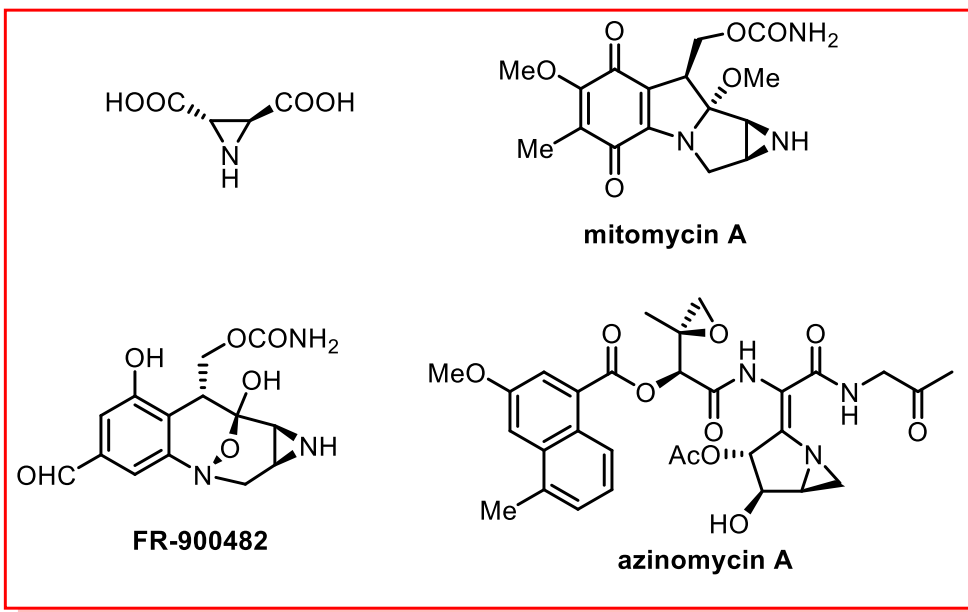
# 4. Dynamic kinetic resolution (DKR) of aziridines

## Tentative Mechanism for the [3 + 2] Annulation



## 5. Aziridines in natural product synthesis

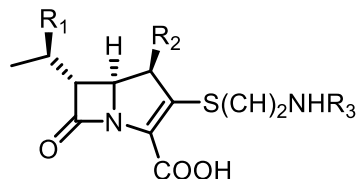
### 5.1 Some natural products containing aziridine units





# 5. Aziridines in natural product synthesis

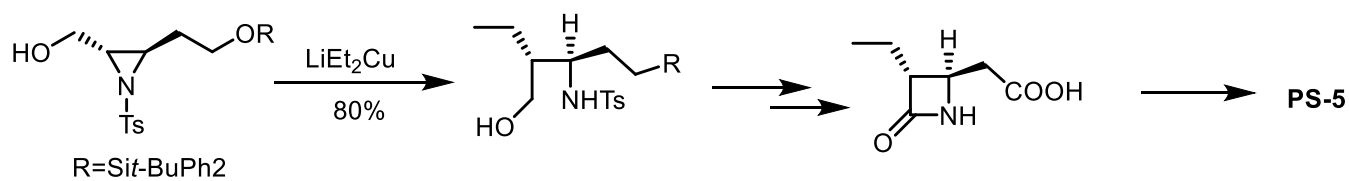
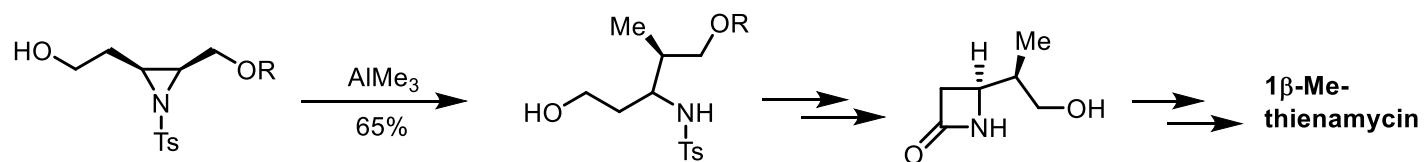
## 5.2 $\beta$ -Lactam antibiotics



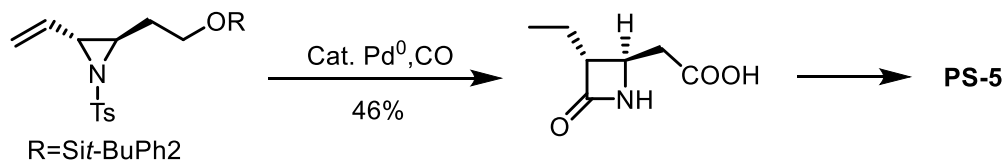
thienamycin  $R_1=OH, R_2, R_3=H$

PS-5  $R_1, R_2=H, R_3=Ac$

1 $\beta$ -Me-thienamycin  $R_1=OH, R_2=Me, R_3=H$



R=Sif-BuPh<sub>2</sub>



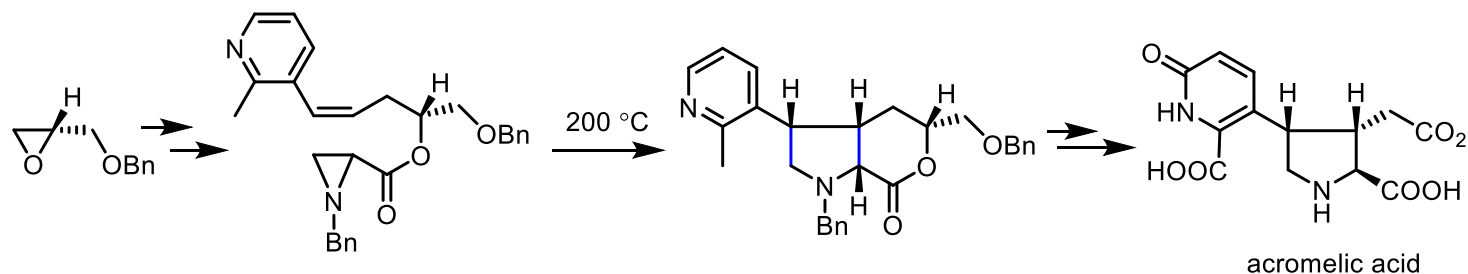
R=Sif-BuPh<sub>2</sub>

*Tetrahedron Lett.* **1987**, 28,1211.

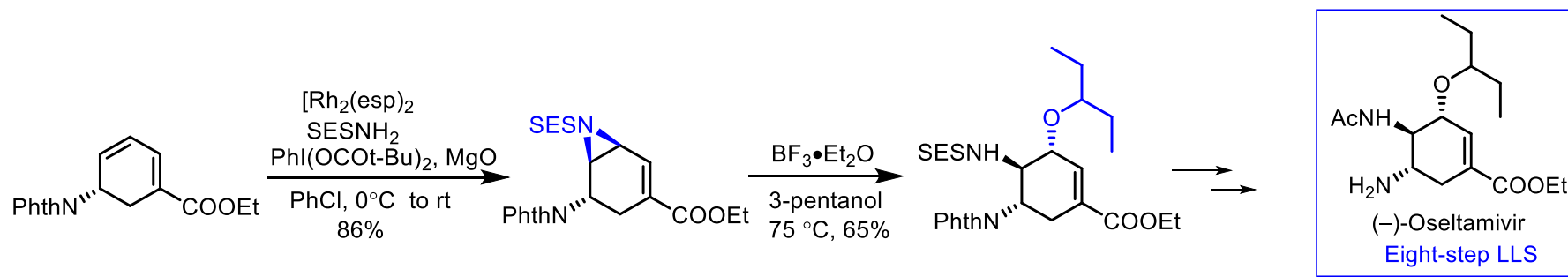
*Bioorg. Med. Chem. Lett.* **1993**, 3, 2415

# 5. Aziridines in natural product synthesis

## 5.3 Synthesis of amino acids and derivatives



## 5.4 Synthesis of (-)-Oseltamivir (Tamiflu)

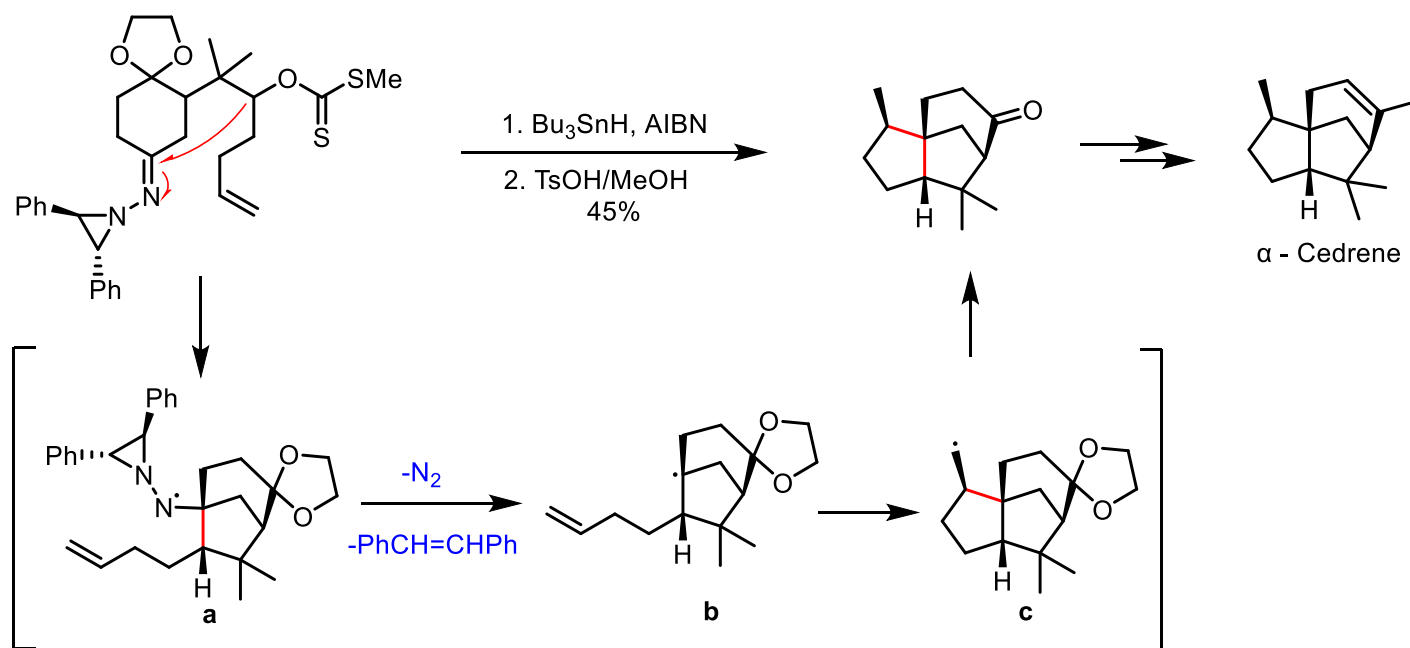


Heterocycles, **1989**, 29,1473

*Chem. Eur. J.* **2011**, 17, 3630–3643

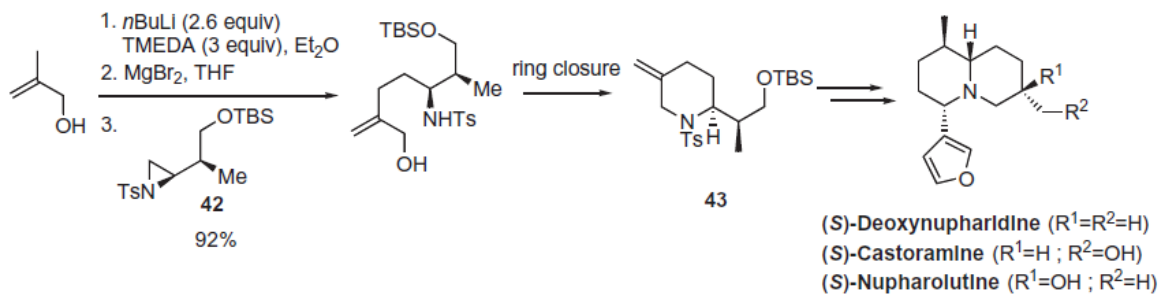
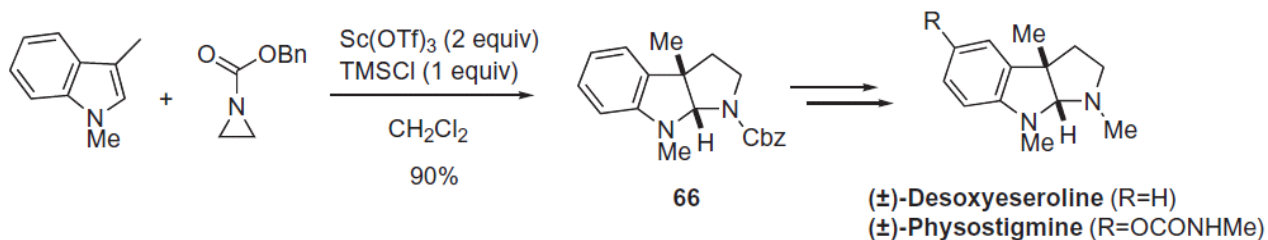
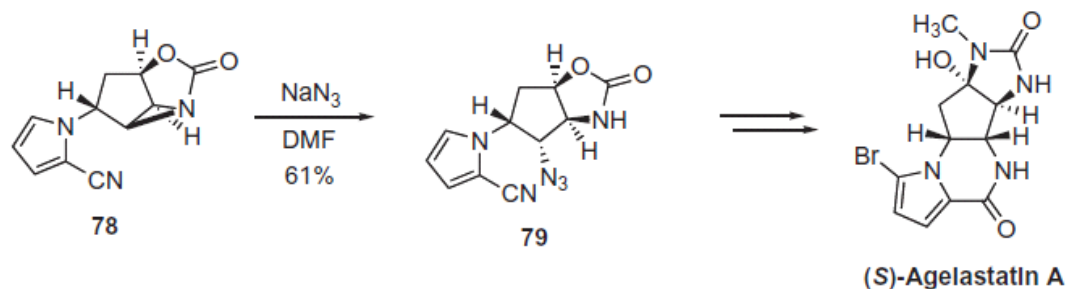
## 5. Aziridines in natural product synthesis

### 5.5 Synthesis of terpene $\alpha$ - Cedrene



# 5. Aziridines in natural product synthesis

## 5.6 Syntheses of alkaloids

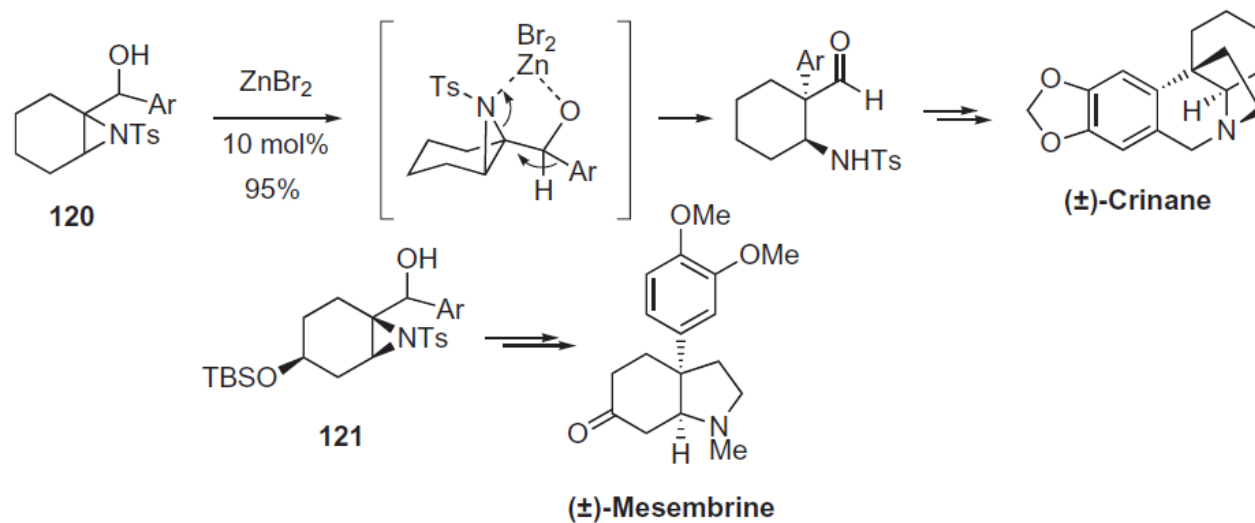


*Org. Lett.* **2008**, *10*, 5457–5460.

*J. Org. Chem.* **1984**, *49*,40; *Tetrahedron Lett.* **2006**, *47*, 331–333.

## 5. Aziridines in natural product synthesis

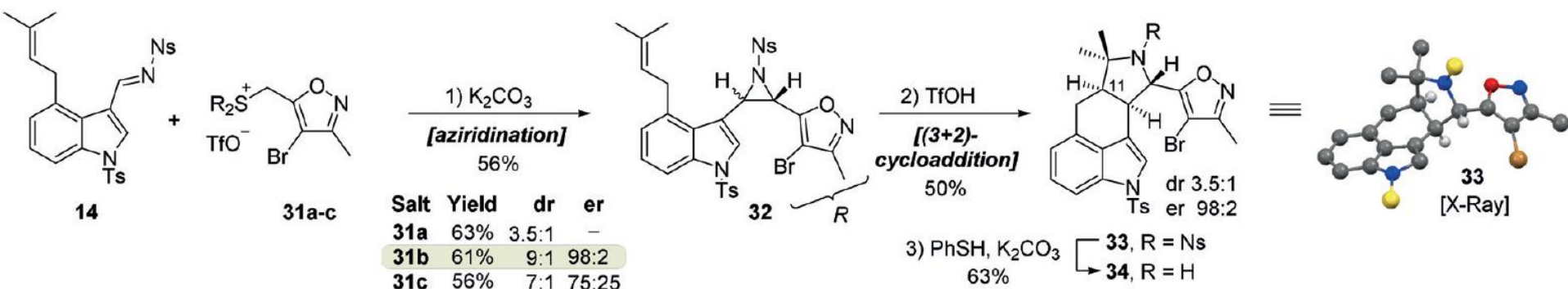
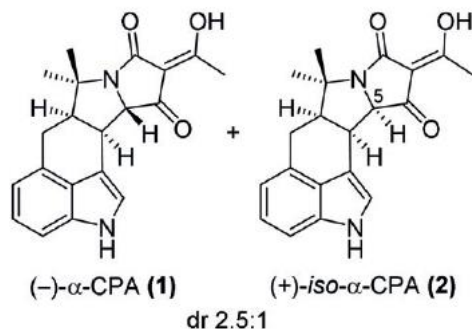
### 5.6 Syntheses of alkaloids



# 5. Aziridines in natural product synthesis

## 5.6 Syntheses of alkaloids

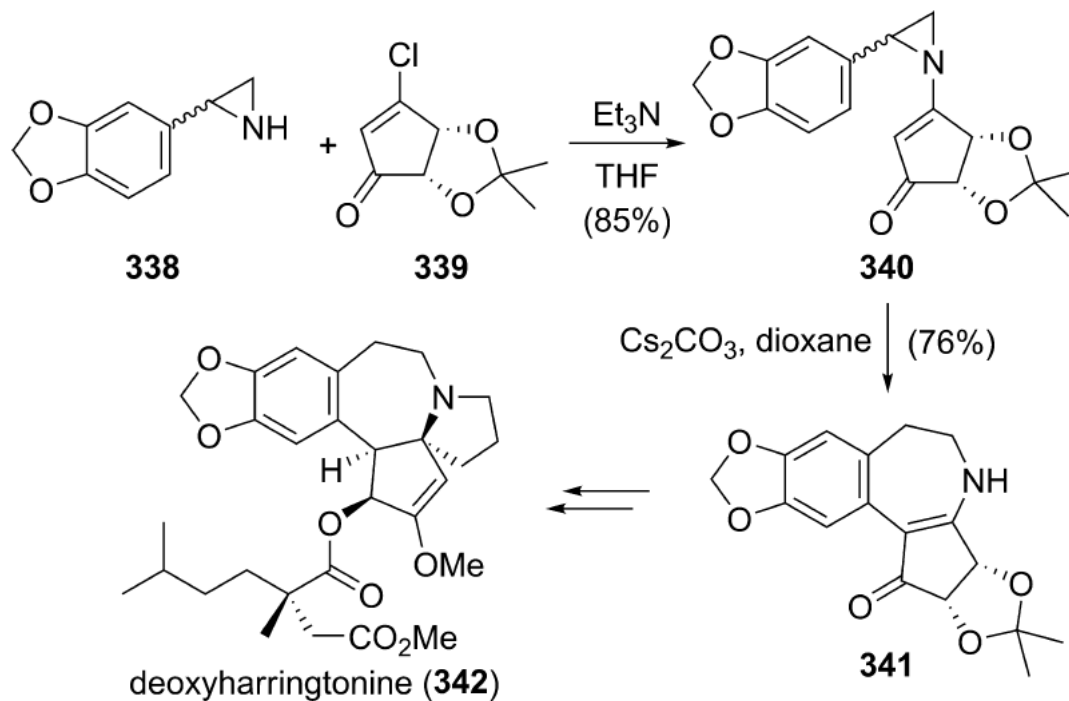
### *α*-Cyclopiazonic acid (*α*-CPA, 1)



## 5. Aziridines in natural product synthesis

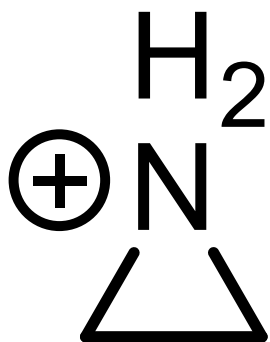
### 5.6 Syntheses of alkaloids

Total Synthesis of (-)-Deoxyharringtonine via  
[3,3]-Claisen Rearrangement of *N*-Alkenyl-2-arylaziridine

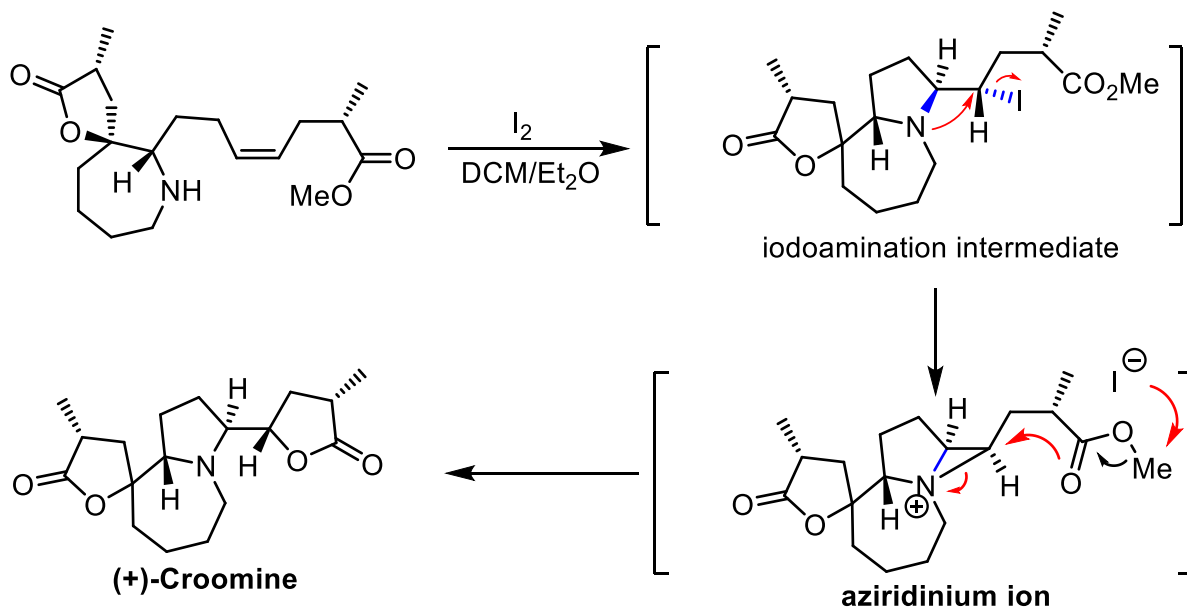


## 5. Aziridines in natural product synthesis

5.7 Synthesis of natural products involving the transformation of an **aziridinium ion** moiety

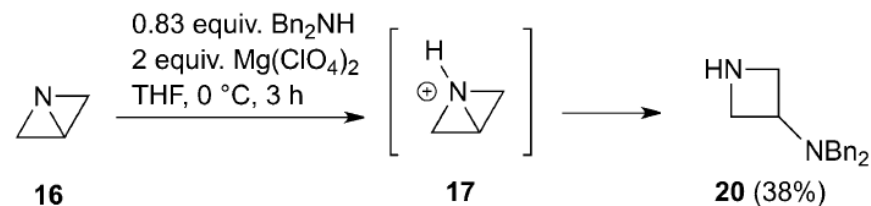
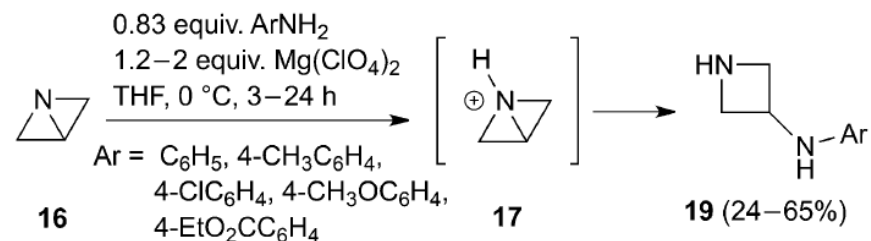
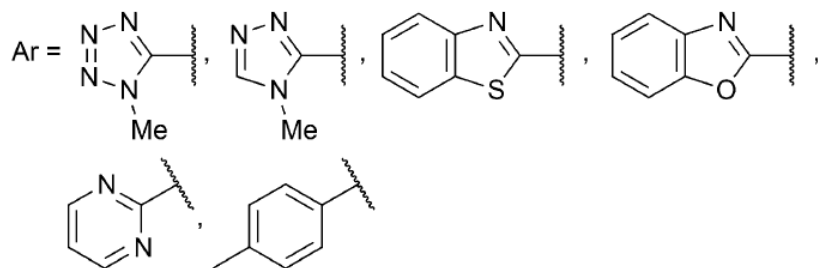
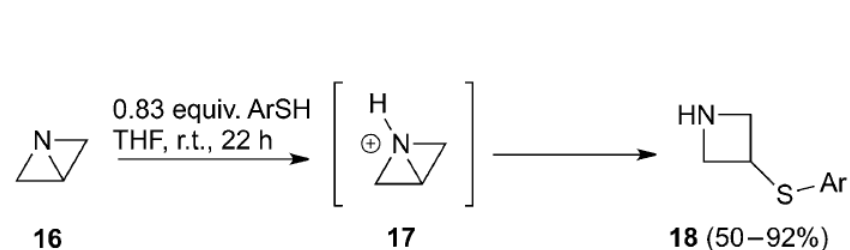


**Aziridinium** is the ionic form of the class of molecules known as aziridines



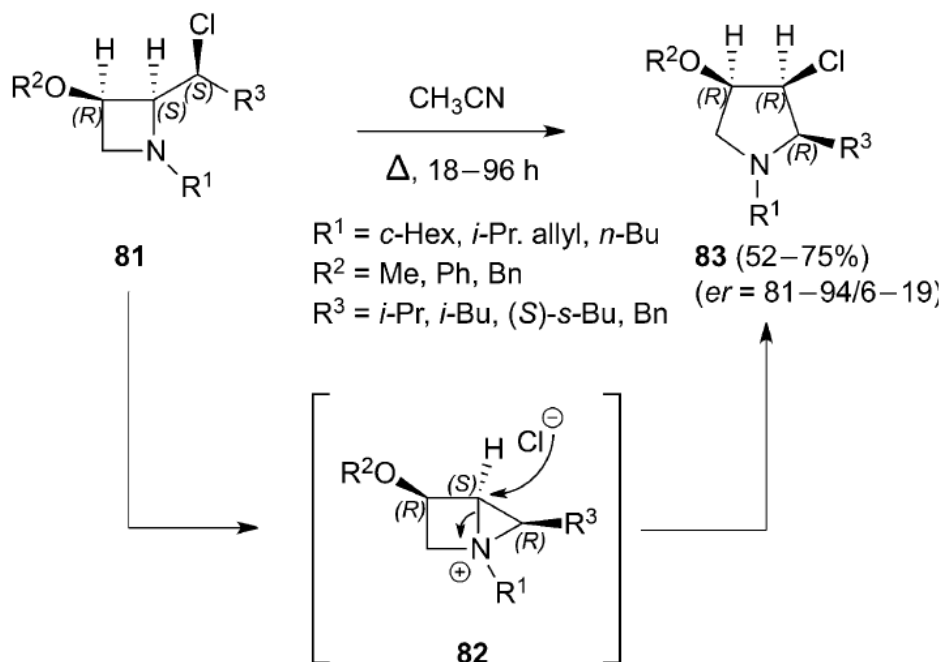
## 5. Aziridines in natural product synthesis

### 5.8 Reaction of 1-azabicyclo[1.1.0]butane with aromatic thiols and amines.

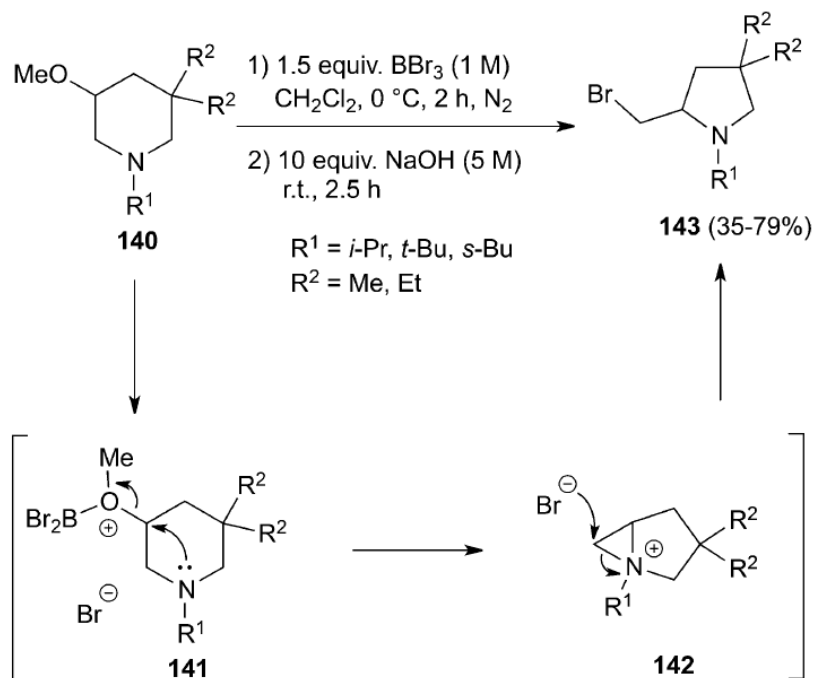


## 5. Aziridines in natural product synthesis

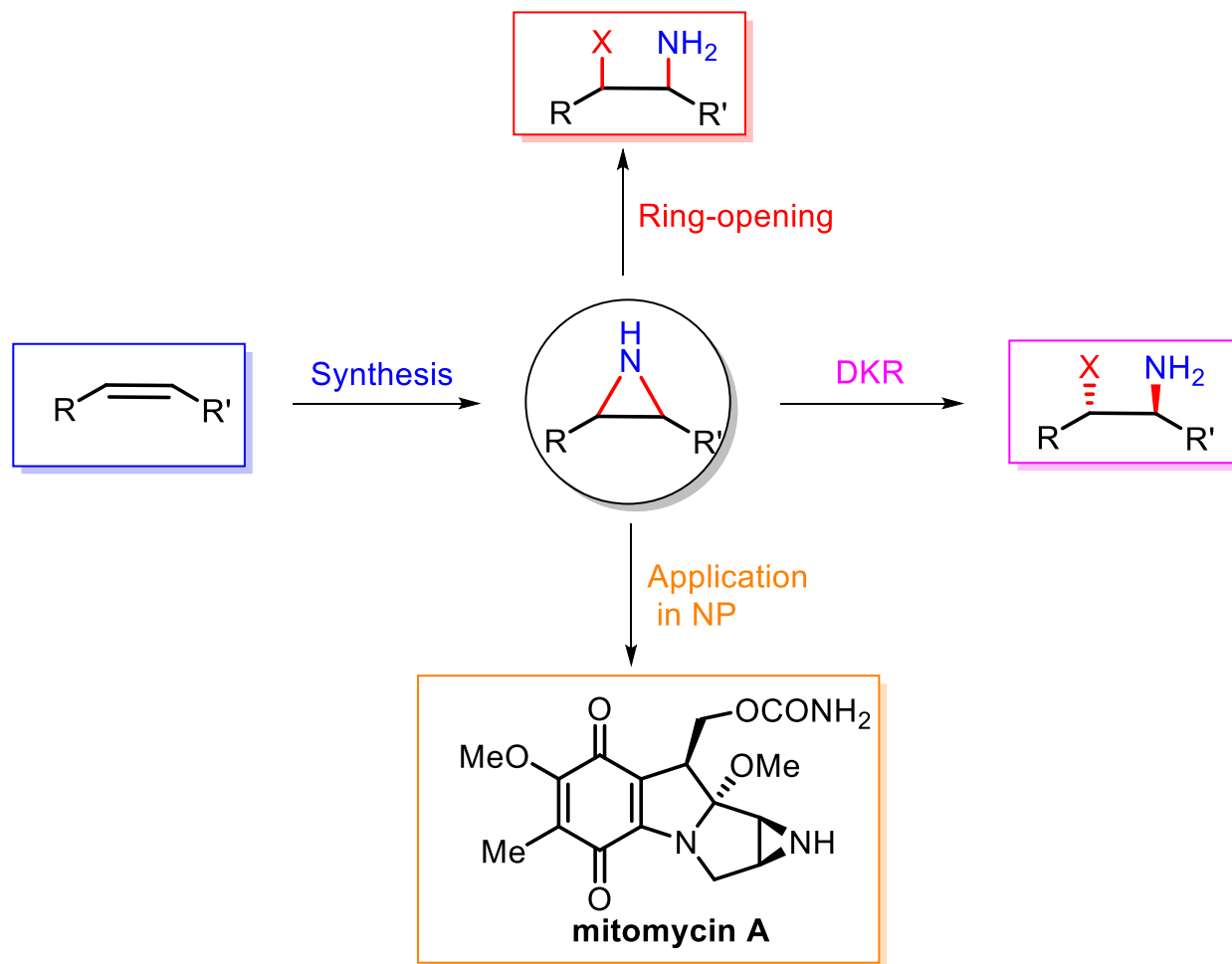
### Ring expansion of azetidines to 3-chloropyrrolidines



### Ring contraction of 3-methoxypiperidines to pyrrolidines



# Summary and conclusion



# Thank you for your attention!

