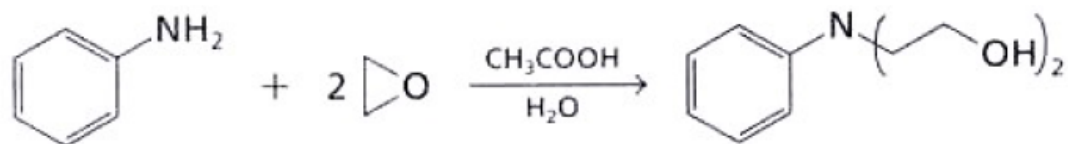
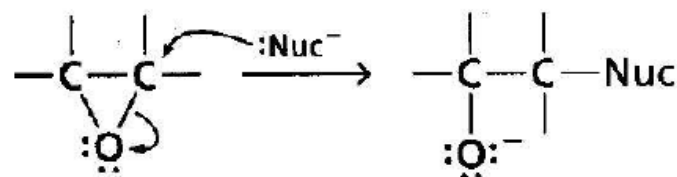


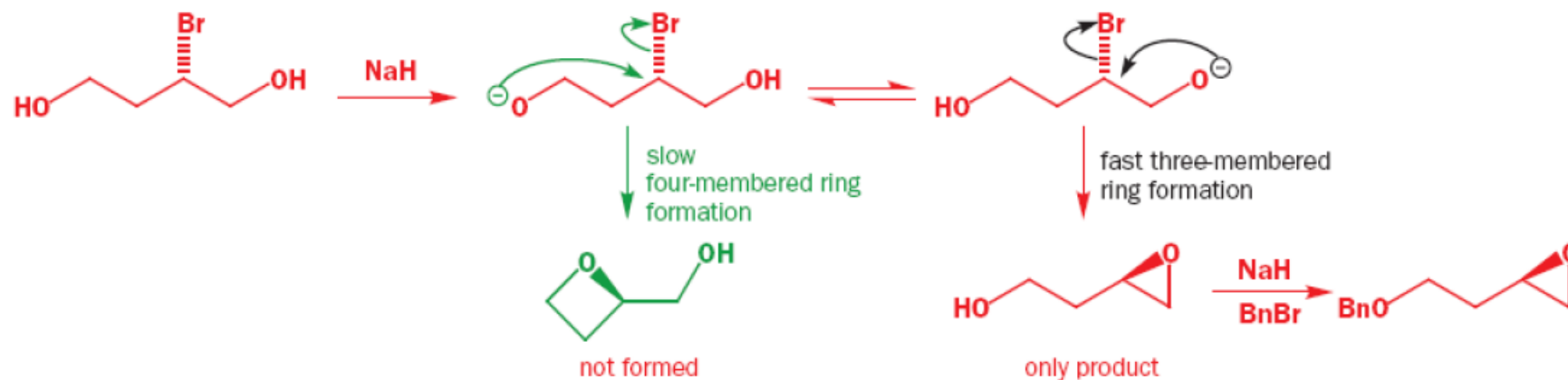
## Three-membered rings: oxiranes, aziridines and thiiranes



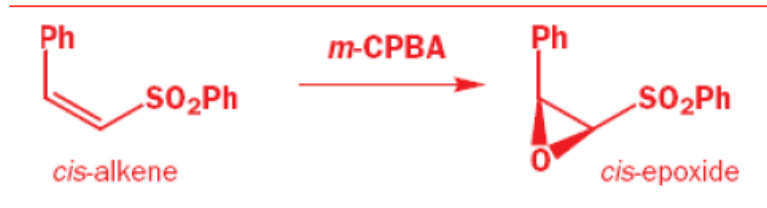
Three-membered heterocycles, owing to ring strain, react easily with nucleophiles



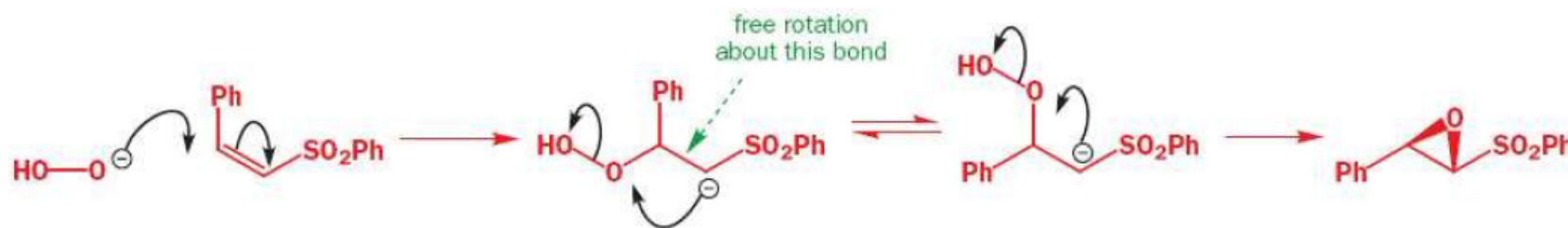
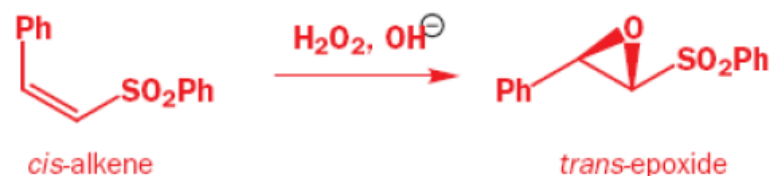
## Epoxides (oxiranes): synthesis



Electrophilic oxidation with peracids:  
concerted, stereospecific

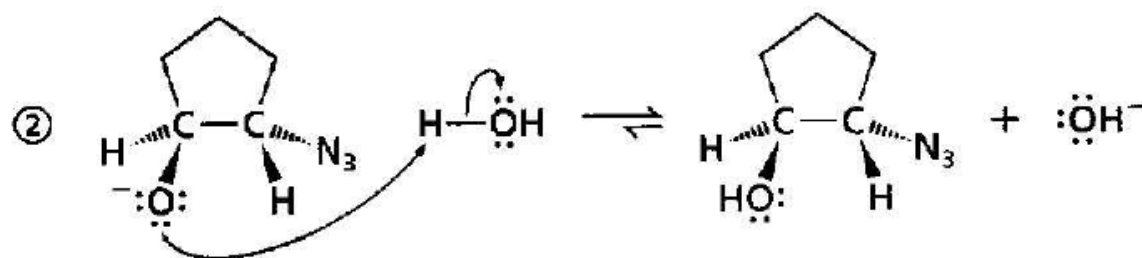
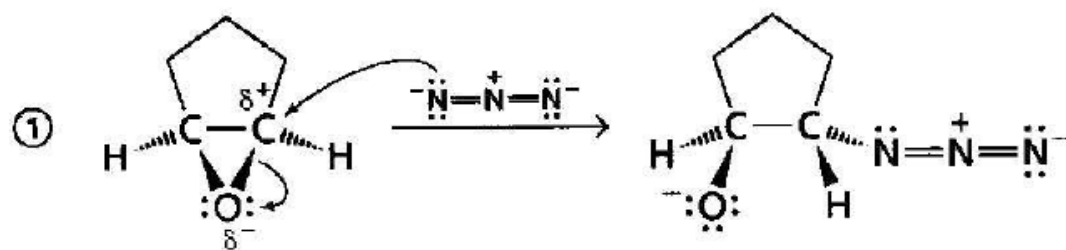
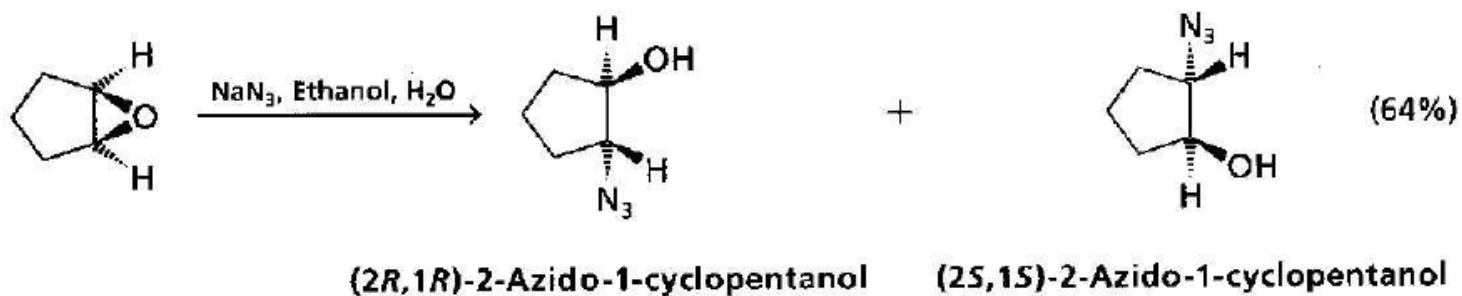


Nucleophilic oxidation with  $\text{HOO}^-$ :  
stepwise, thermodynamic control



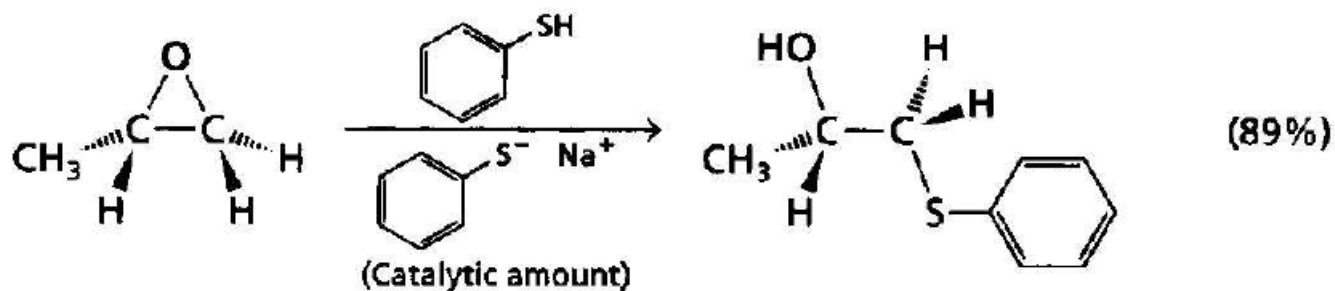
# Epoxides or oxiranes

## Stereospecific substitution reactions ( $S_N2$ )

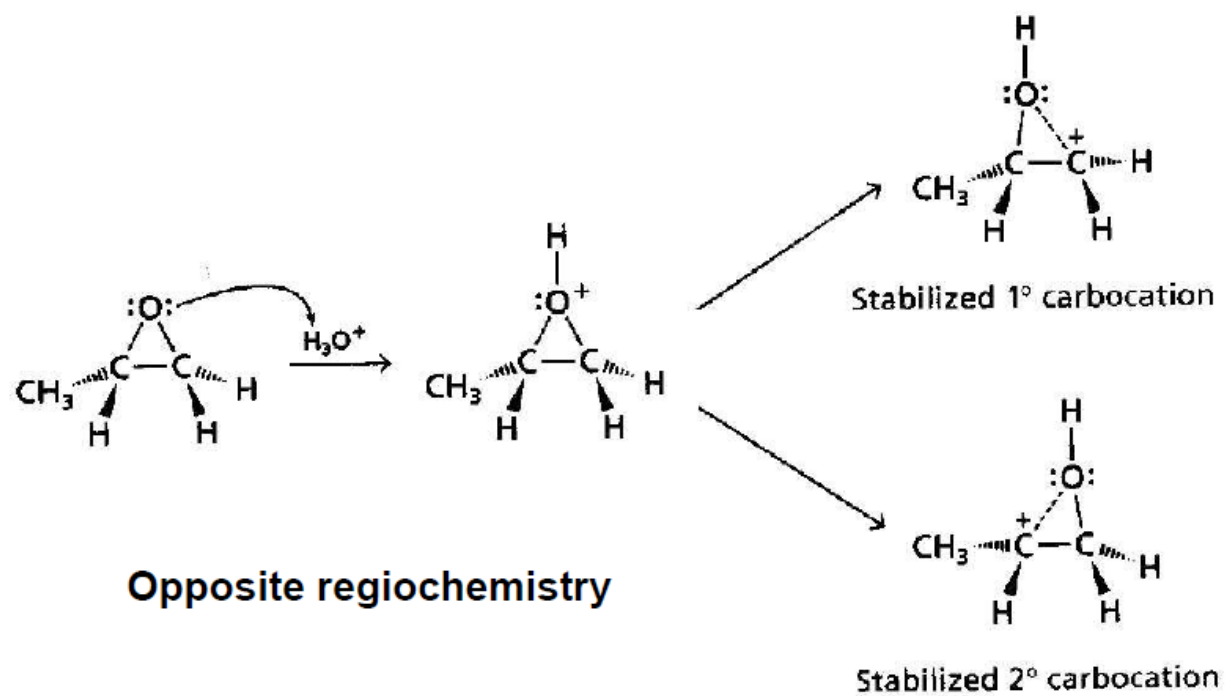
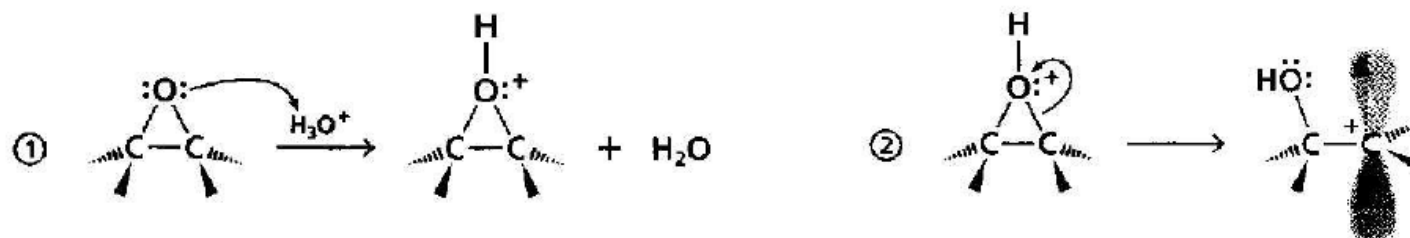


## Sostituzione nucleofila negli epossidi: regioselettività

Regiochemistry: substitution at the less substituted/less hindered position, unless acid catalysis is employed

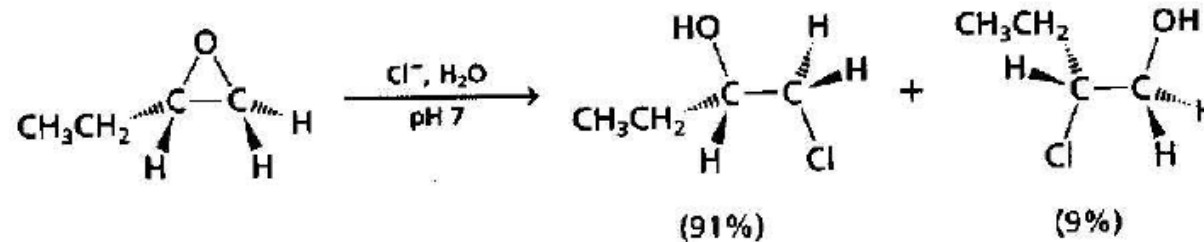


## Acid-catalyzed, nucleophilic ring opening



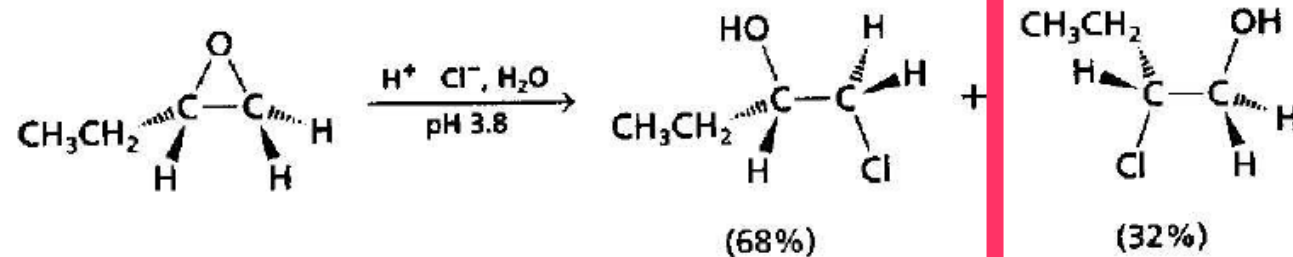
## Controllo della regiochimica della sostituzione

pH 7



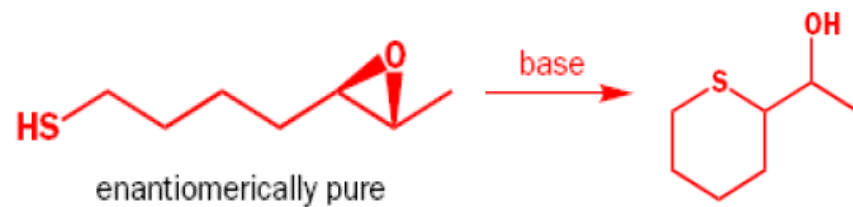
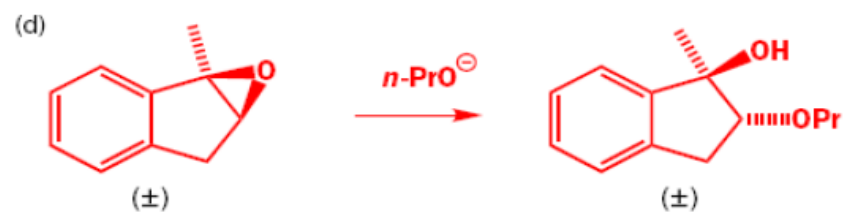
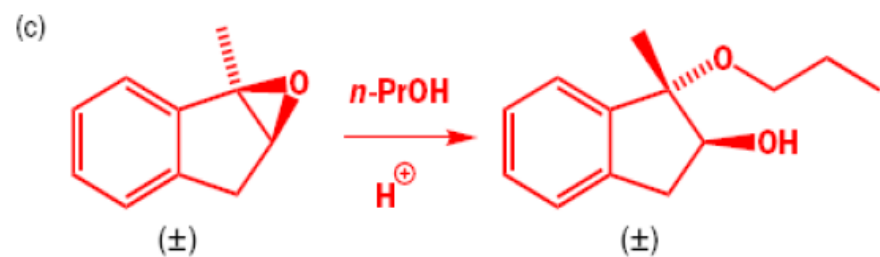
A pH 7 l'attacco avviene alla posizione meno sostituita (S<sub>N</sub>2)

pH 3.8

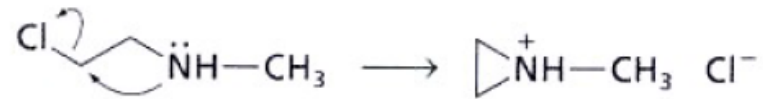


A pH 4 l'attacco avviene anche alla posizione più sostituita (via formazione del carbocatione più stabile, tipo S<sub>N</sub>1)

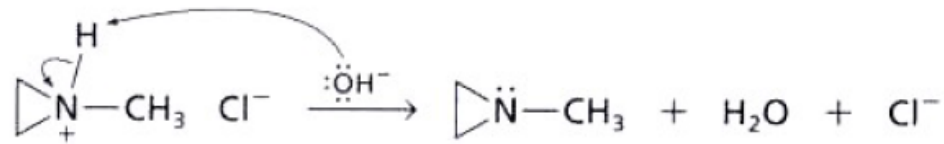
**Esercizi. Dire se queste reazioni sono  $S_N1$  o  $S_N2$  e motivare la regiochimica osservata. Indicare la stereochimica dei prodotti ottenuti.**



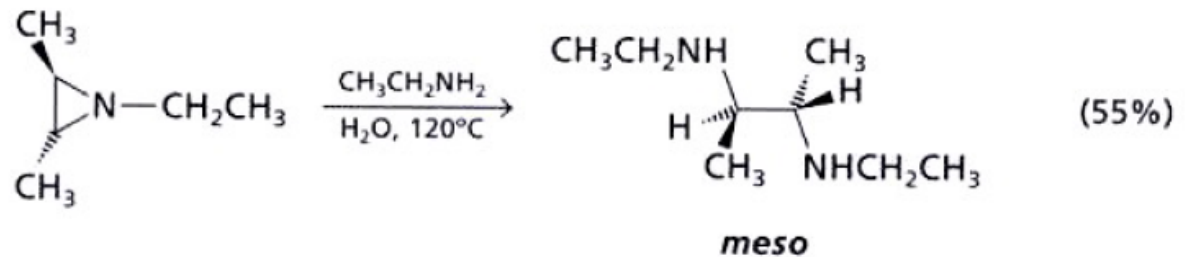
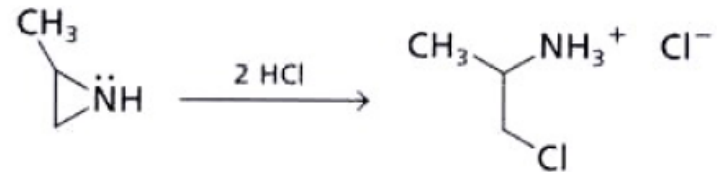
# Aziridine



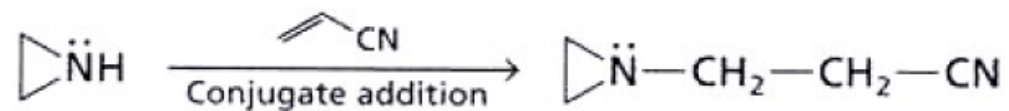
## Sintesi



L'addizione avviene in  
maniera analoga agli  
epossidi

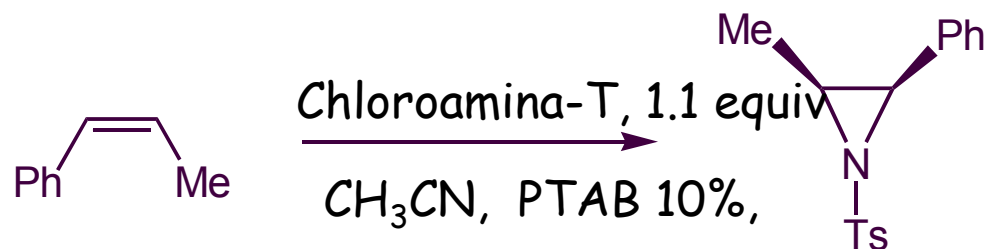


Possono fungere da  
nucleofili



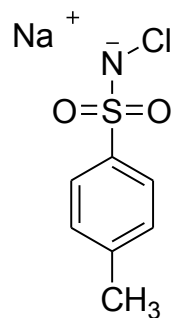


## Synthesis of aziridines

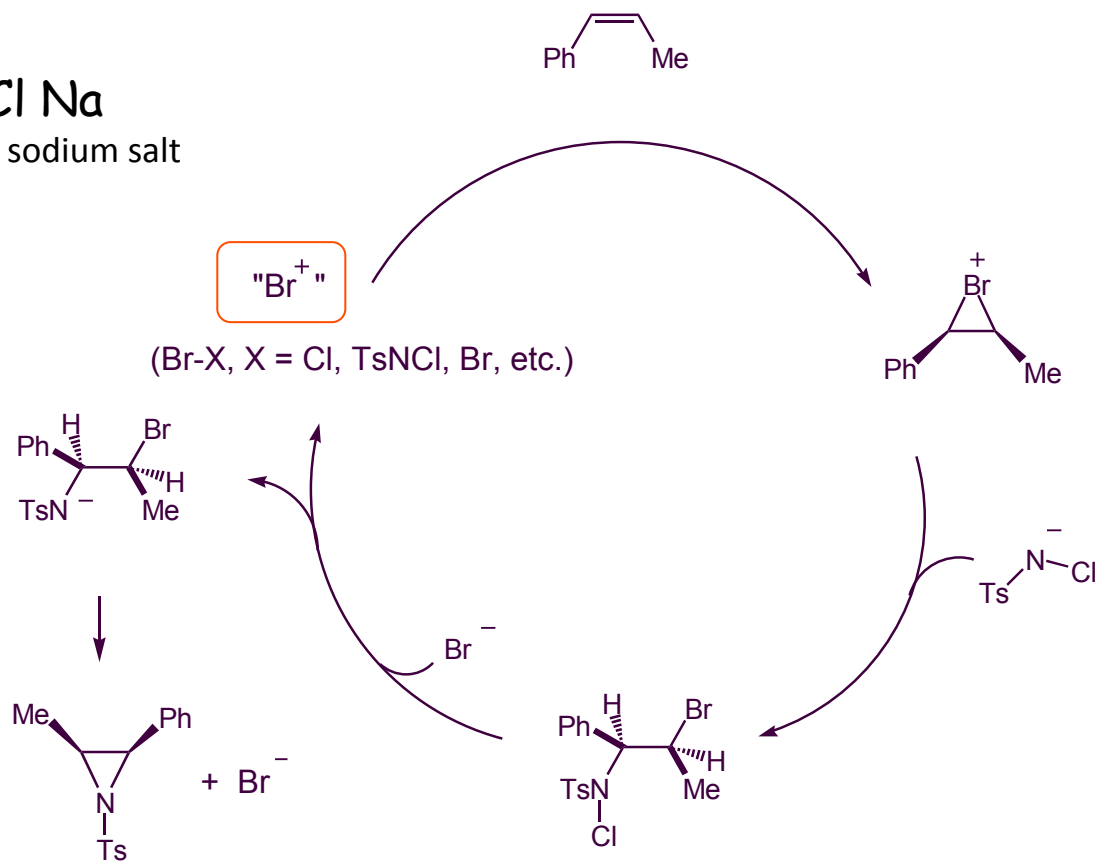


Chloroamina-T = TsNCl Na

*N*-Chloro-*p*-toluenesulfonamide sodium salt



**PhNMe<sub>3</sub><sup>+</sup>Br<sub>3</sub><sup>-</sup> (PTAB)  
come catalizzatore**



# CLICK CHEMISTRY

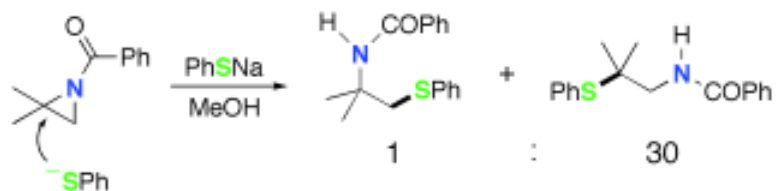
**Aziridines** are prepared by: direct aziridination of olefins  
manipulation of epoxides or amino alcohols  
haloazidation of olefins followed by reductive cyclization

**Aziridines** enable much greater product diversity than epoxides



N pyramidal

Nu attacca il carbonio meno ingombrato

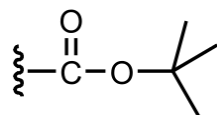
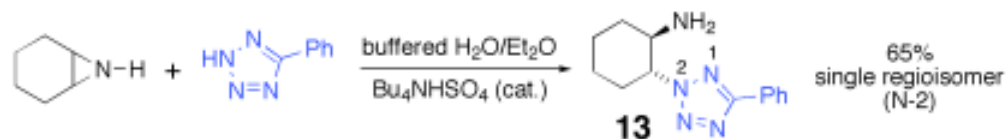
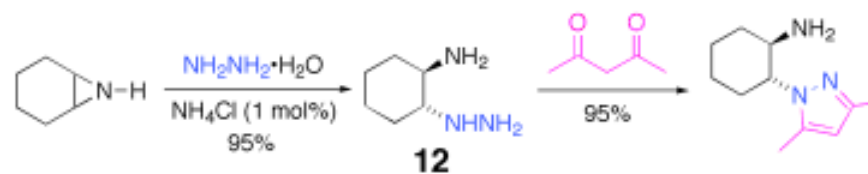
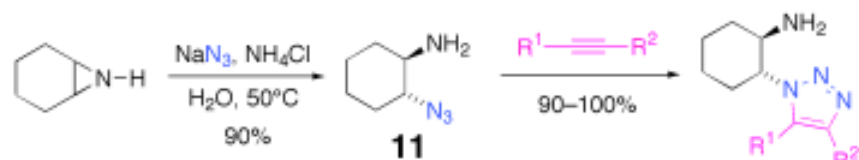
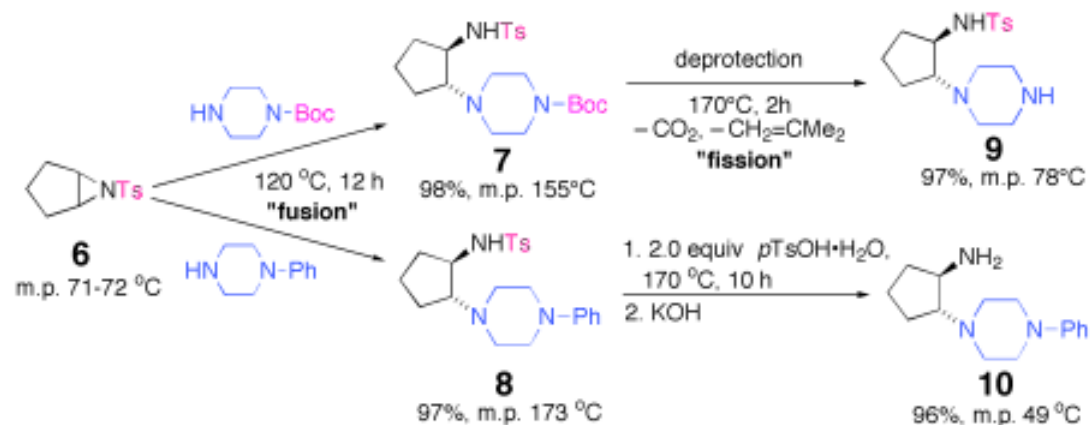


N planar

Nu attacca il carbonio piu' ingombrato

Influence of the nitrogen substituent (sulfonyl, acyl) on the regioselectivity of aziridine opening.

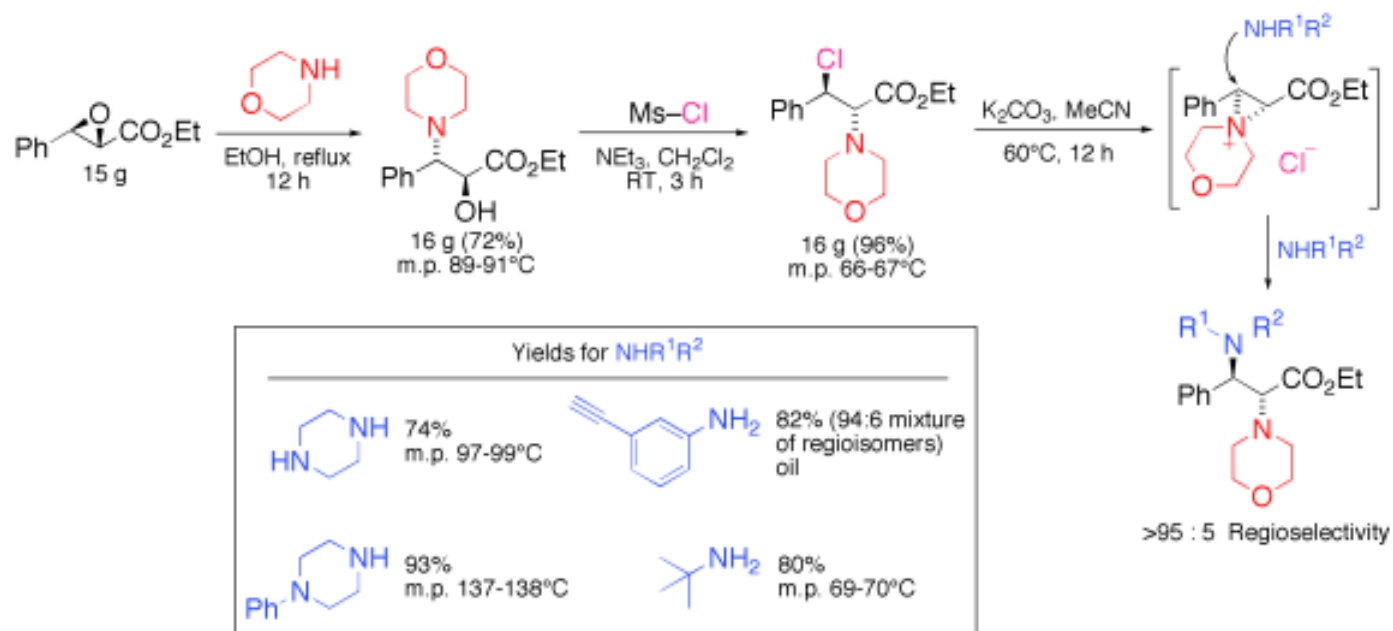
- Aziridines are stable under basic conditions
- They can be readily opened by heteroatom nucleophiles under buffered conditions in various solvent including water or neat



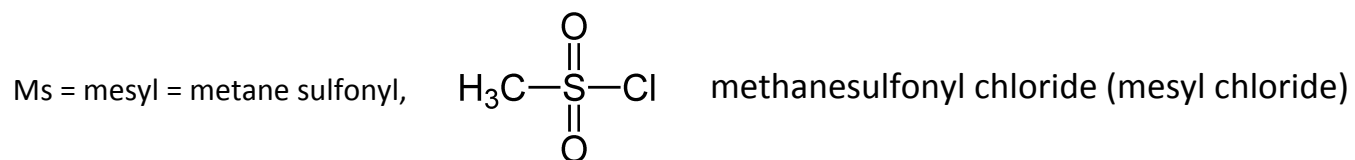
Boc = tert-butoxycarbonyl

Use of activated and nonactivated aziridines as building blocks

## Rapid generation of building blocks and combinatorial libraries



## Aziridinium intermediates in combinatorial assembly

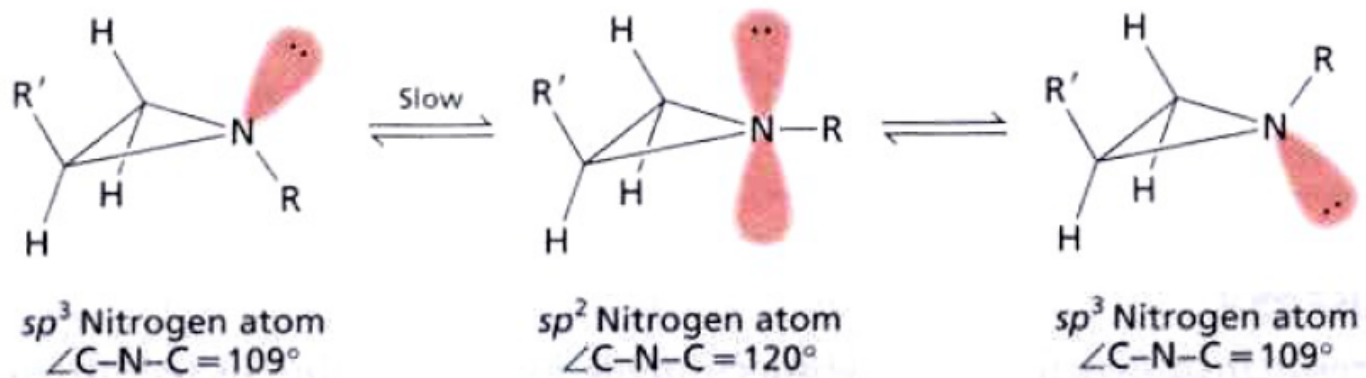


# Inversione piramidale e racemizzazione delle aziridine

Il doppietto non condiviso si trova in un MO con forte carattere s.

L'inversione è molto più lenta rispetto alle ammine acicliche

Le aziridine hanno stereoisomeri separabili

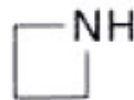


## Cicli a quattro termini: ossetani, azetidina e tietani



Oxacyclobutane

Oxetane



Azacyclobutane

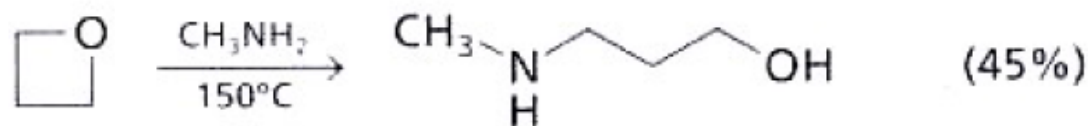
Azetidine



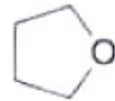
Thiacyclobutane

Thietane

Sono anch'essi in grado di reagire con nucleofili, sebbene con reattività molto inferiore.



# Cicli a 5 e 6 termini: tetraidrofurano, pirrolidina e tetraidrotiofene



Tetrahydrofuran

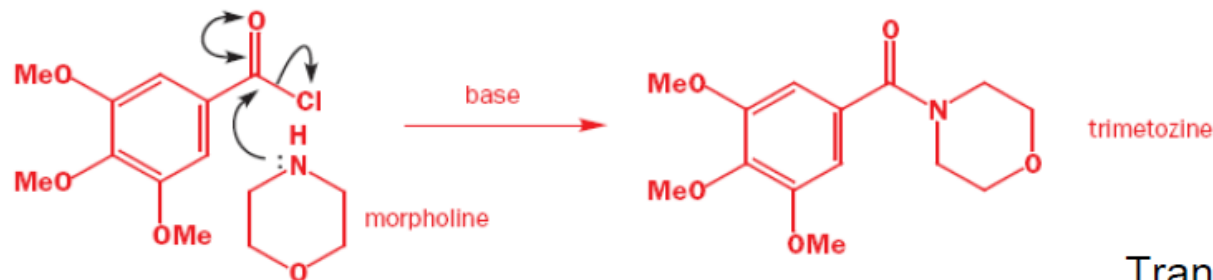
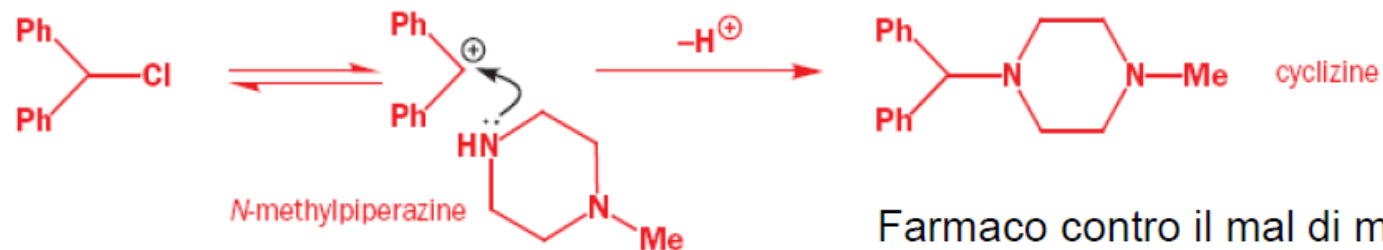


Pyrrolidine

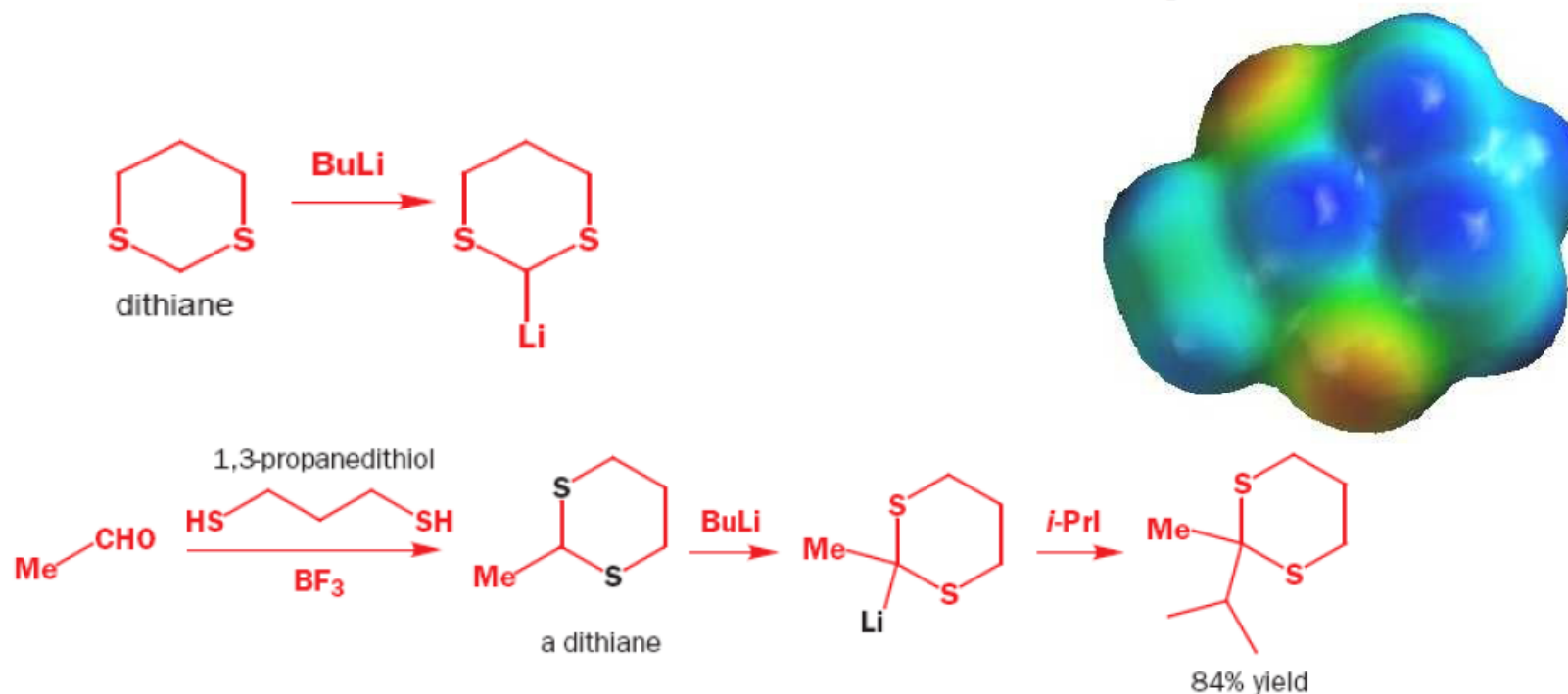


Tetrahydrothiophene

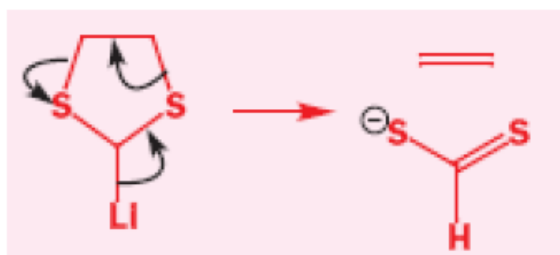
Gli anelli a 5-6 termini sono essenzialmente inerti alla sostituzione nucleofila; si comportano esattamente come gli analoghi derivati a catena aperta.



## 1,3-Ditiani da aldeidi: acil anioni equivalenti



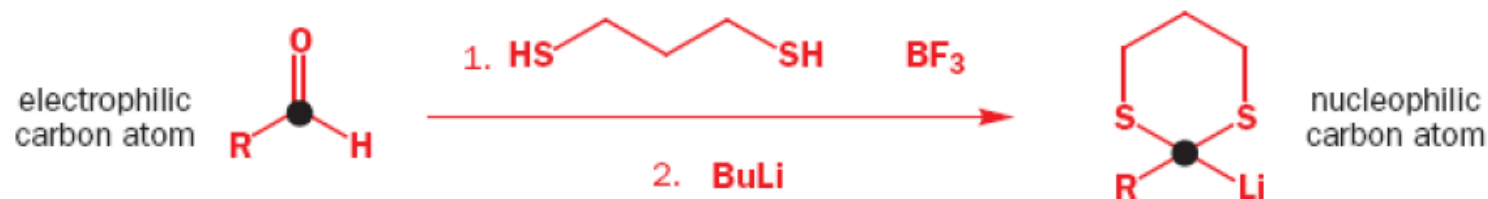
Un atomo di zolfo è in grado di stabilizzare un anione adiacente. L'anione può essere generato per semplice reazione con un alchil litio. Questi sistemi vengono definiti **acil anioni equivalenti** o acil sintoni



L'anione dell'analogo ciclo a 5 termini (1,3-ditiolano) non è stabile e si decompone

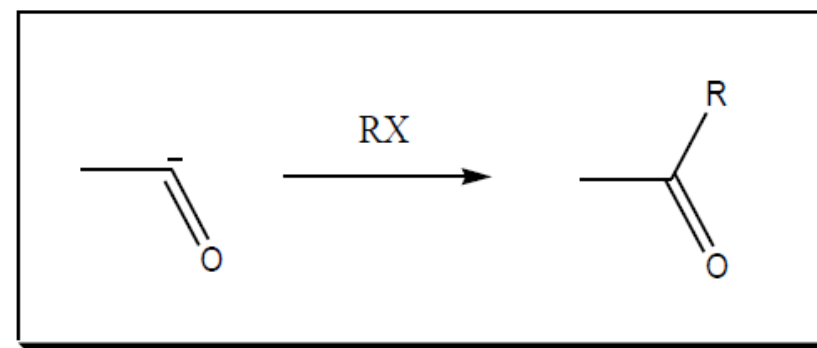
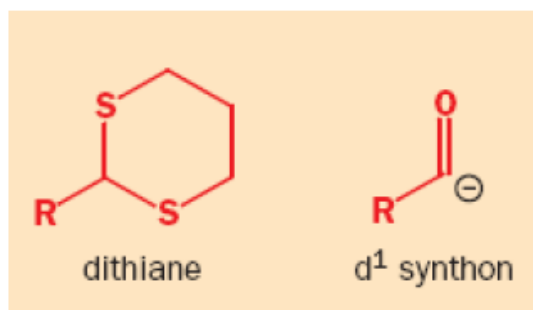


## Umpolung (inversione) della reattività



Passando da aldeide a ditiano si inverte la polarità dell'atomo di carbonio: da elettrofilo a nucleofilo

E' come se, formalmente, avesse reagito un acil anione, sistema che non esiste



## Alchilazione dei 1,3-ditiani

