

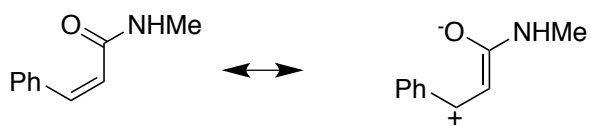
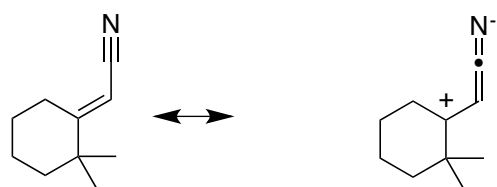
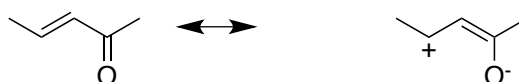
# 25 Conjugate Additions

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from chapter(s) \_\_\_\_\_ in the recommended text

## A Introduction

## B Polarization Of $\alpha,\beta$ -Unsaturated Carbonyl Compounds

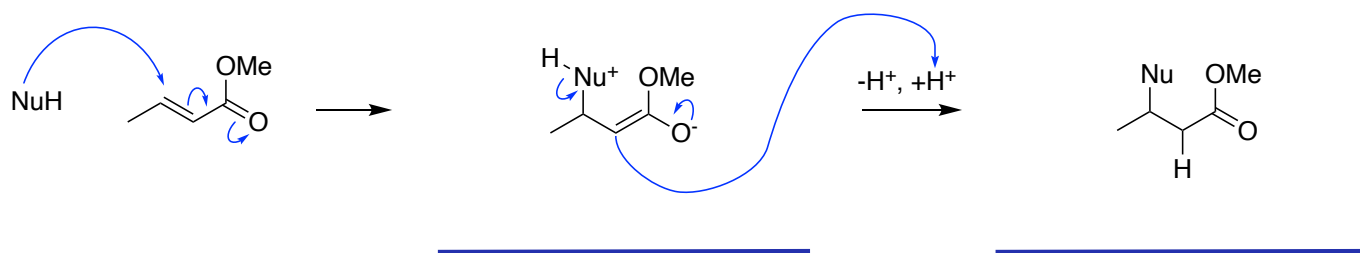
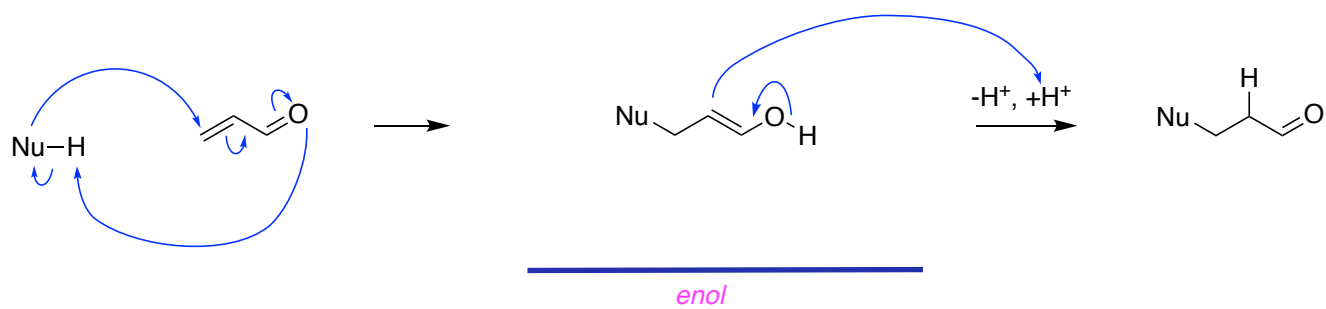
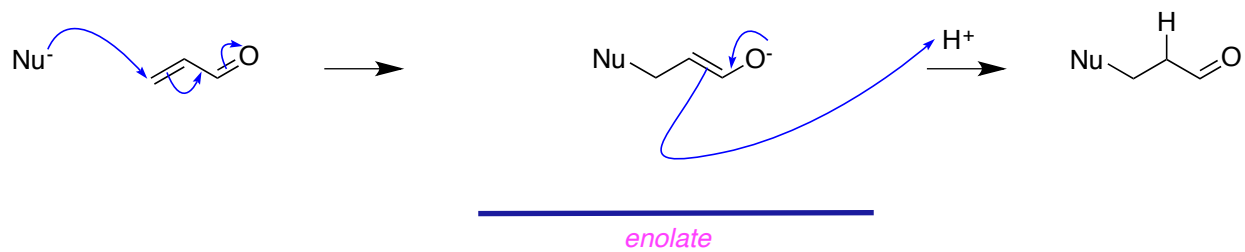


*is* always on the  $\beta$ -carbon

*LUMO*

*more / less* stable

### C Mechanism Of Conjugate Addition

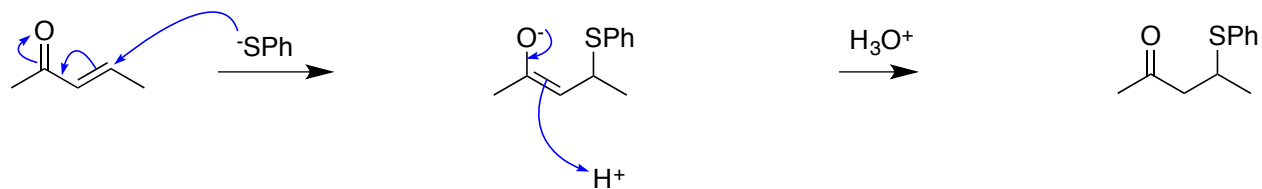


## D Examples Of Conjugate Additions

### Amines And Thiols

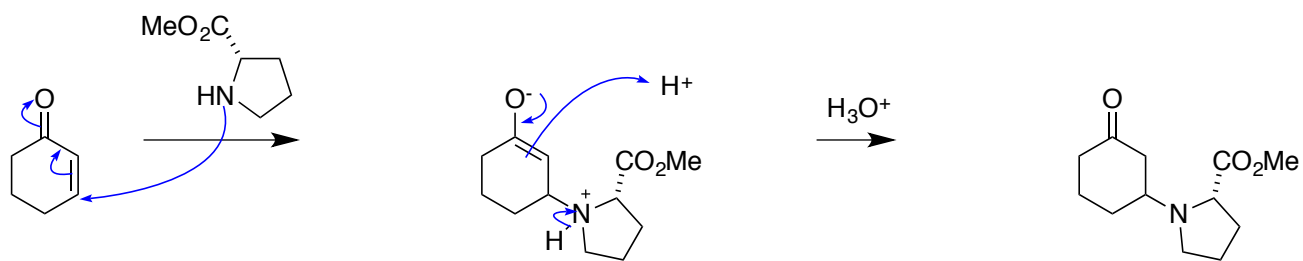
the *nucleophile* adds to the 4-position

the *proton* adds to the oxygen



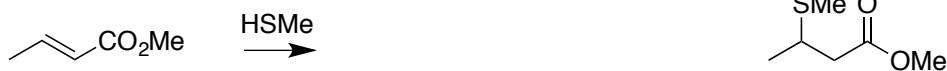
*enolate intermediate*

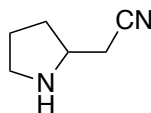
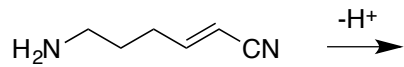
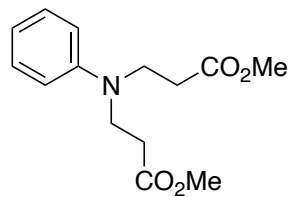
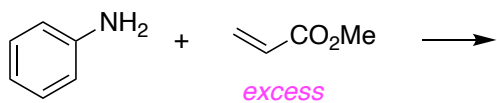
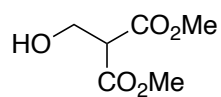
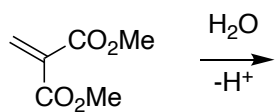
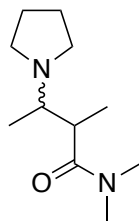
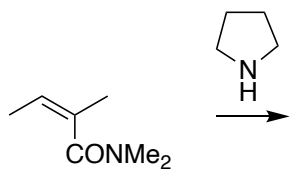
*1,4-addition product*



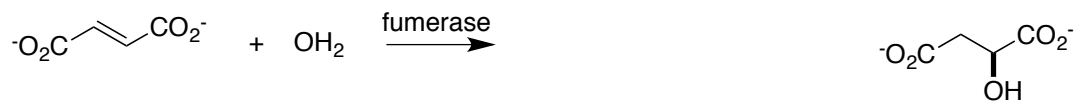
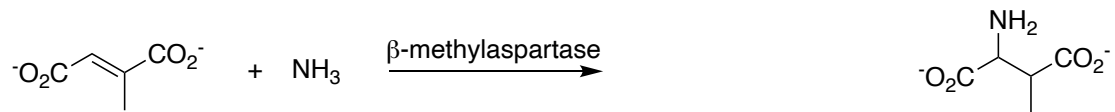
*enolate intermediate*

*1,4-addition product*

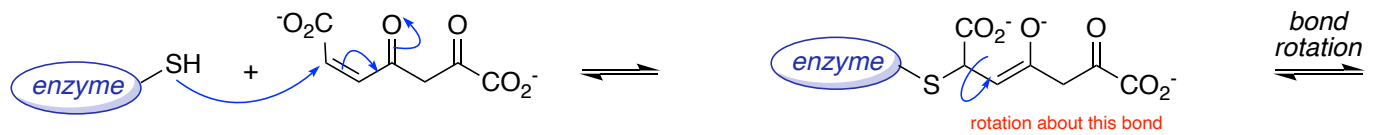




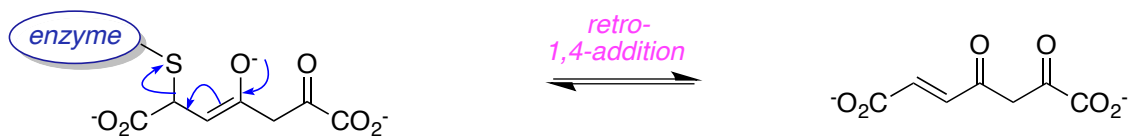
## Enzyme-mediated Conjugate Additions



*S-product*



*adduct*

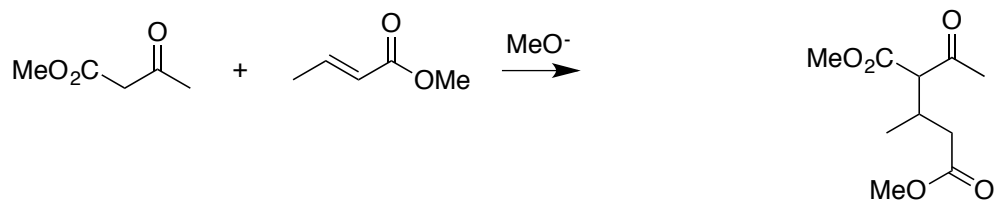
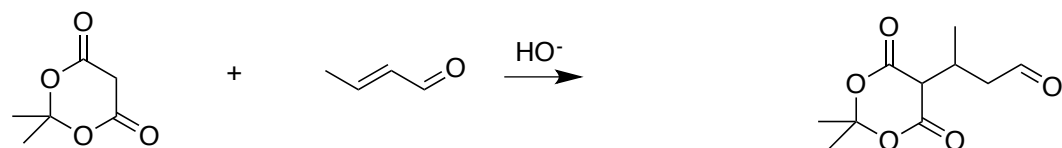
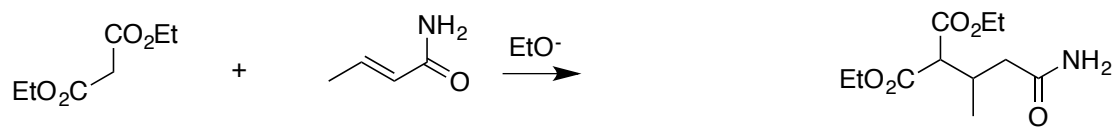


*rotamer of initial adduct*

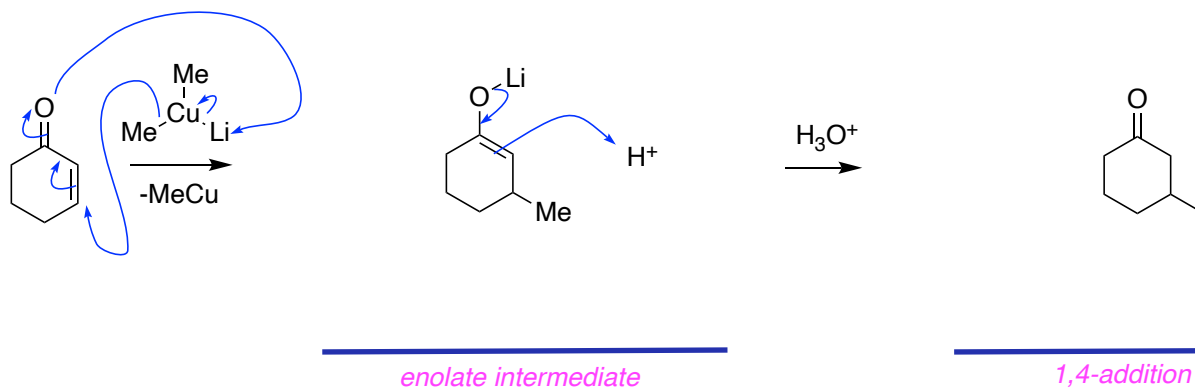
*isomerized product*

## Stabilized C-Anion Nucleophiles

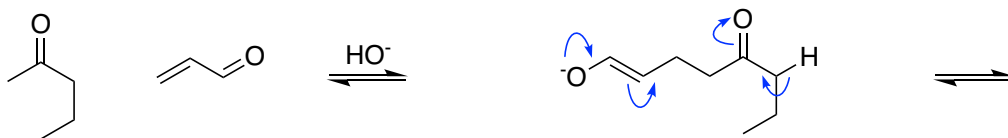
the base is required in *stoichiometric* quantities.



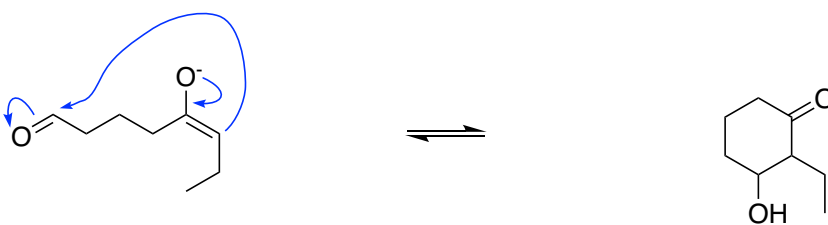
## Organometallic Agents In Laboratory Chemistry



## E Conjugate Addition Then Aldol Condensation



*conjugate addition product*



*an enolate that can cyclize easily*

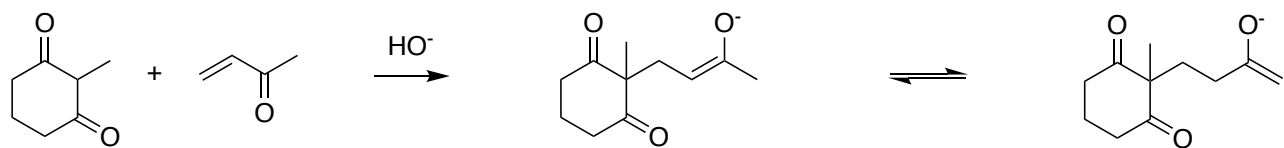
*cyclization product*



*cyclic aldol/dehydration product*



Predict the products of the following reactions.



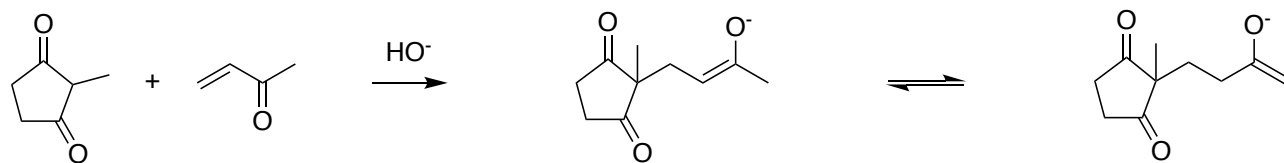
enolate from conjugate addition

terminal enolate



intramolecular cyclization product

enone



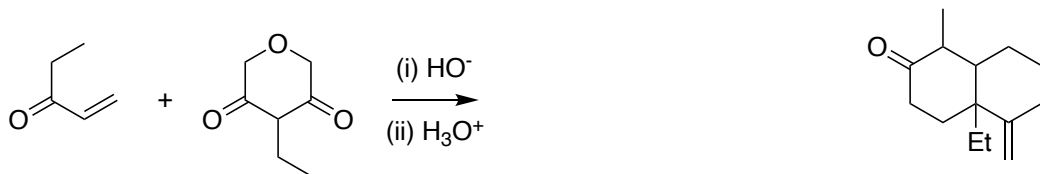
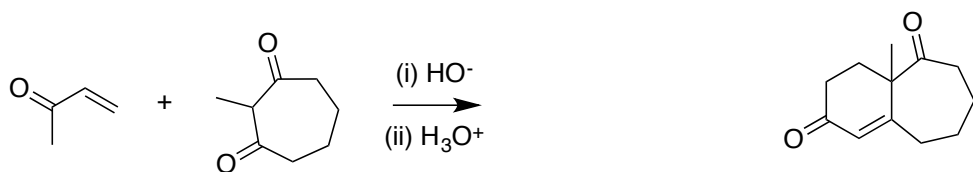
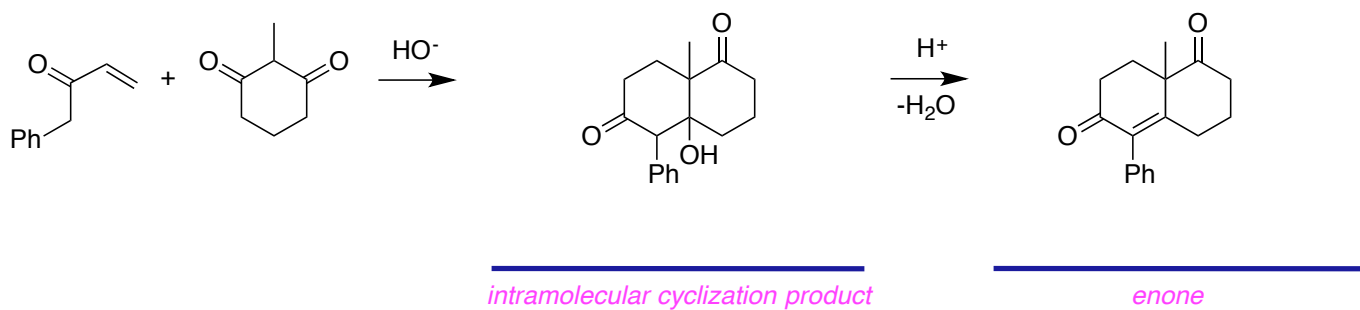
enolate from conjugate addition

terminal enolate



intramolecular cyclization product

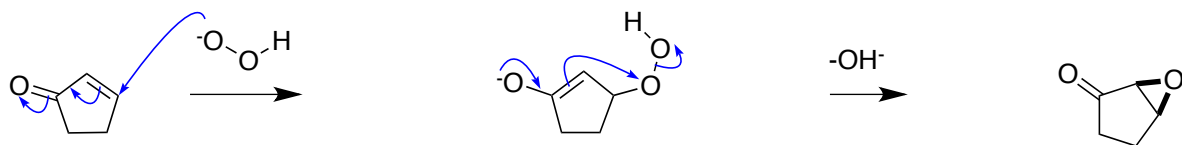
enone



## F Nucleophilic Epoxidation

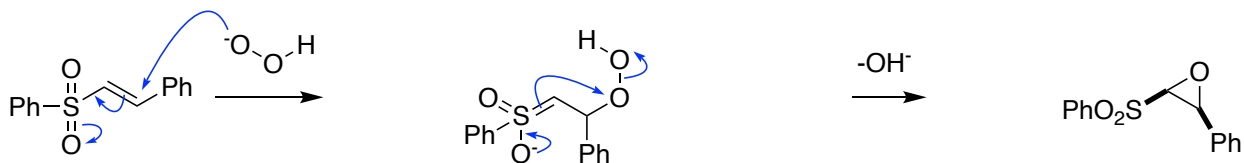
*α-effect*

*more* acidic than water



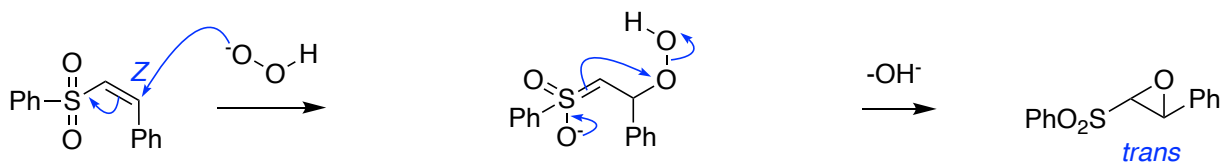
*enolate intermediate*

*epoxide*



*enolate*

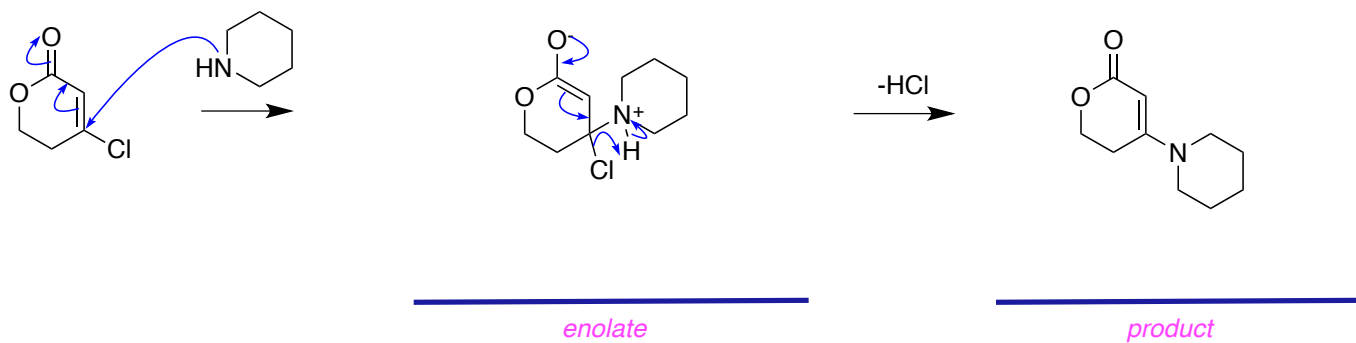
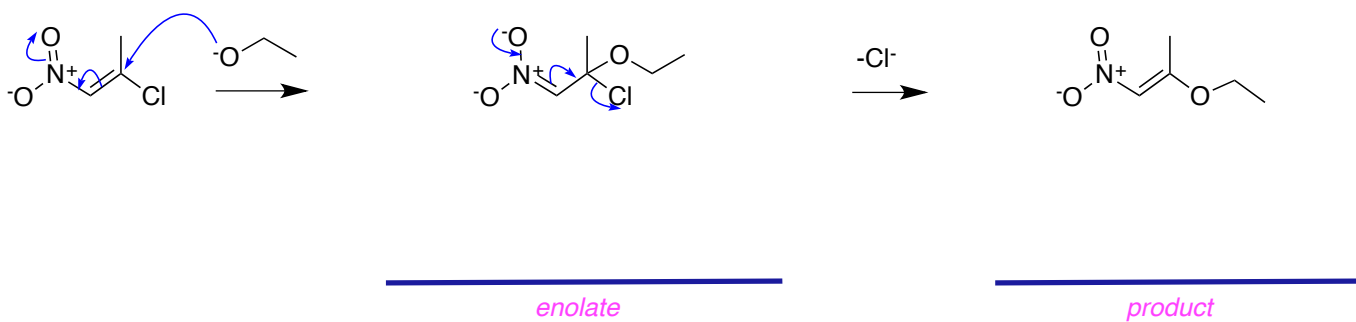
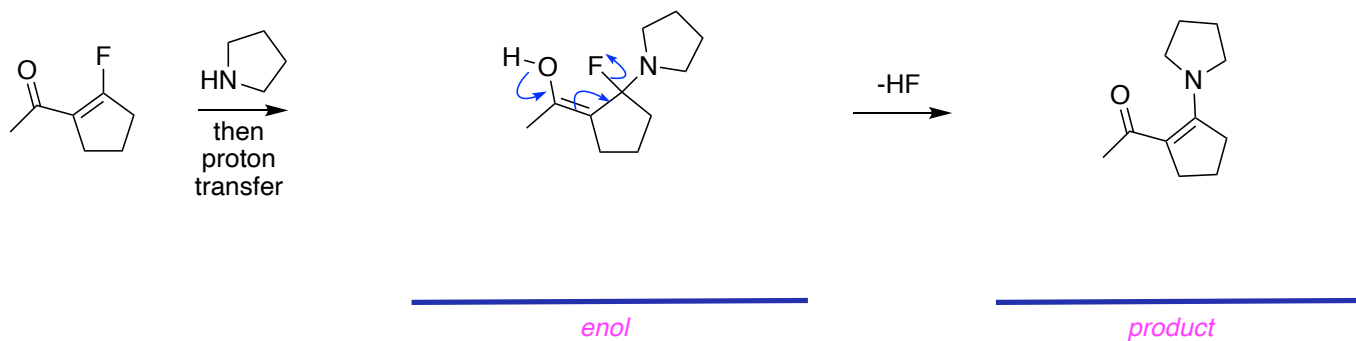
*epoxide*

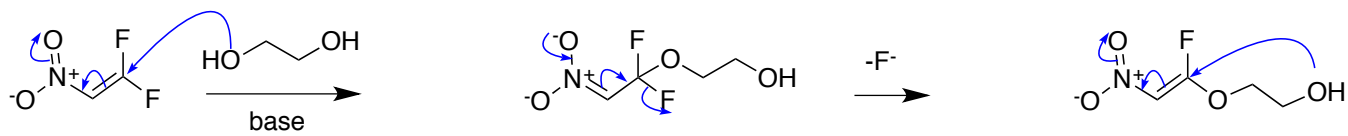


*enolate intermediate*

It *is not* possible

## G Addition Elimination Reactions





*enolate*

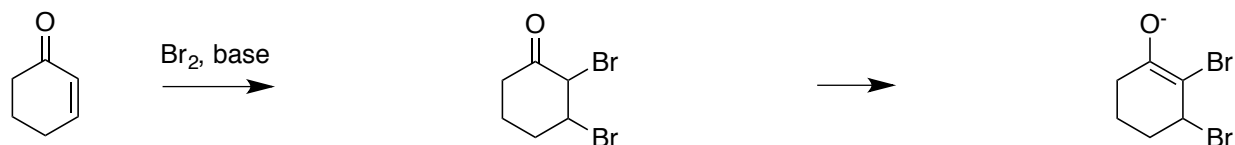
*intermediate*



*enolate*

*product*

### Formation Of $\alpha$ -Bromo Enones



*dibromide intermediate*

*enolate*



*monobrominated product*

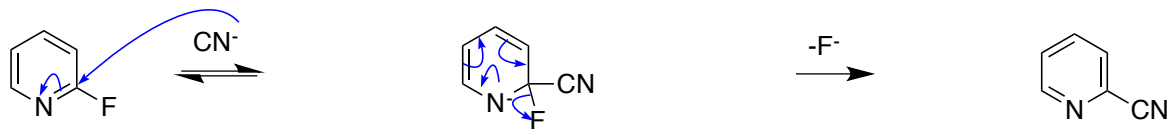
## H Nucleophilic Aromatic Substitution

$S_NAr$  processes.

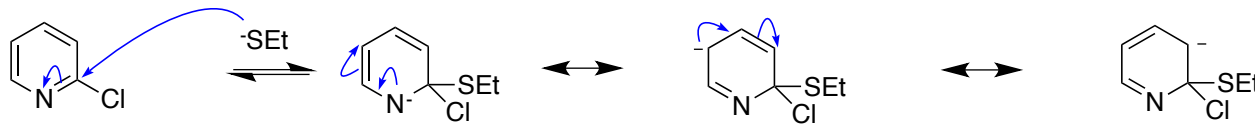
They involve *rate-limiting* addition

*anionic* intermediates

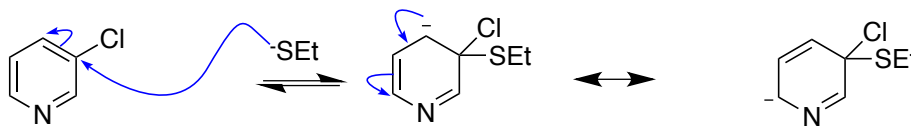
$sp^3$  hybridized C-atom.



### 2-chloropyridine



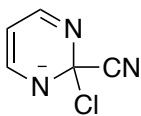
### 3-chloropyridine



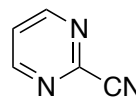
2- isomer.

Addition occurs fastest for the 2- and 4-isomers

2-chloro-1,3-pyrimidine reacted with cyanide



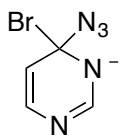
intermediate



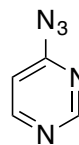
product

fast

4-bromo-1,3-pyrimidine reacted with azide



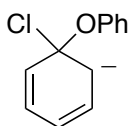
intermediate



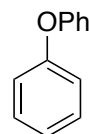
product

slow

chlorobenzene reacted with phenoxide



intermediate



product

slow