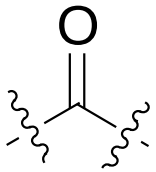
台灣大學開放式課程

有機化學乙

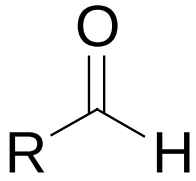
蔡蘊明　教授

Chapter 16
Aldehydes and Ketones
Nucleophilic addition to the carbonyl group

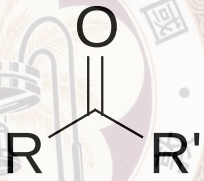
※ Nomenclature



carbonyl group (羰基)

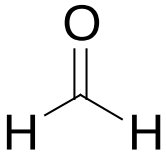


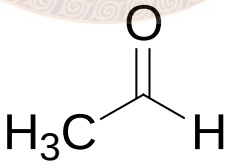
aldehyde
醛

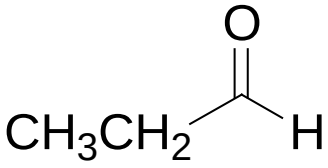


ketone
酮

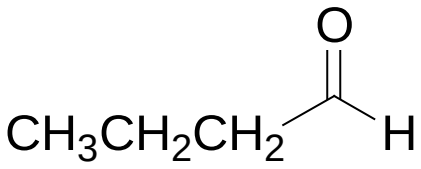
✓ Aldehydes



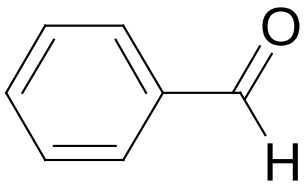




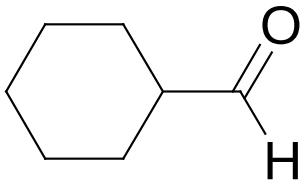
IUPAC: methanal (formaldehyde) ethanal (acetaldehyde) propanal (propionaldehyde)



(butyraldehyde)

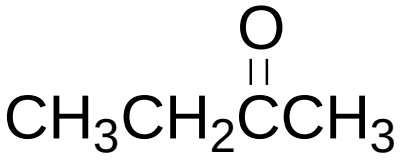


benzenecarbaldehyde
(benzaldehyde)

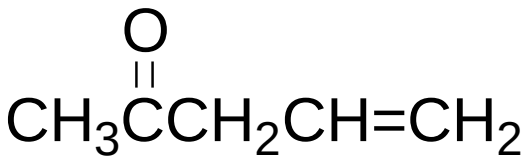


cyclohexanecarbaldehyde

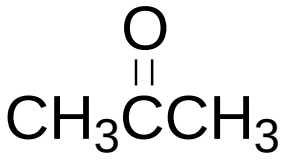
✓ Ketones



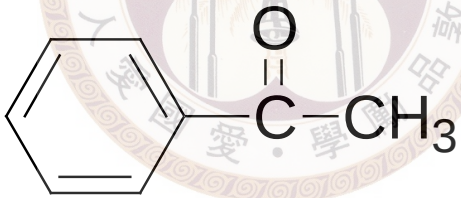
2-butanone
(ethyl methyl ketone or
methyl ethyl ketone; MEK)
bp 80 °C 常用溶劑



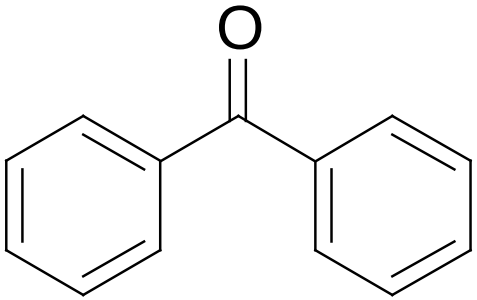
4-penten-2-one



propanone
(acetone)
bp 56 °C
常用溶劑

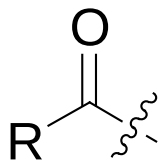


acetophenone
苯乙酮

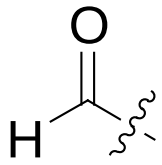


benzophenone

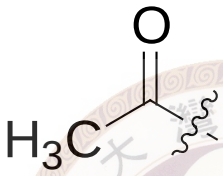
✓ As substituent



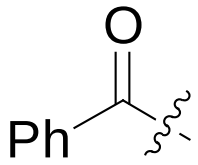
alkanoyl
(acyl)



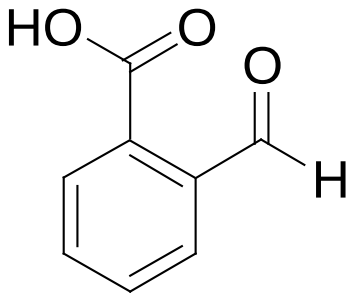
methanoyl
(formyl)



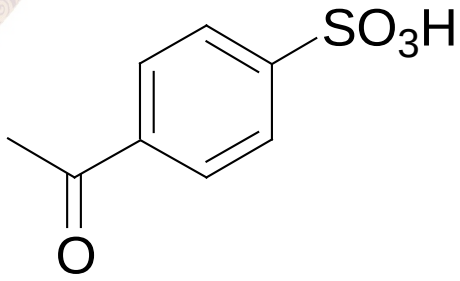
ethanoyl
(acetyl = Ac)



benzoyl = Bz



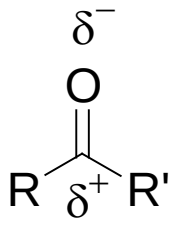
2-methanoylbenzoic acid
(*o*-formylbenzoic acid)



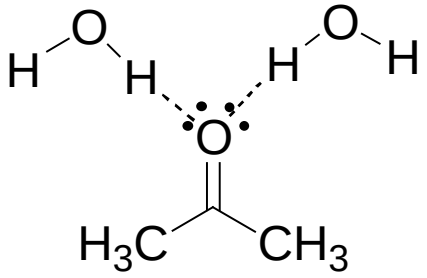
4-ethanoylbenzenesulfonic acid
(*p*-acetylbenzenesulfonic acid)

※ Physical properties

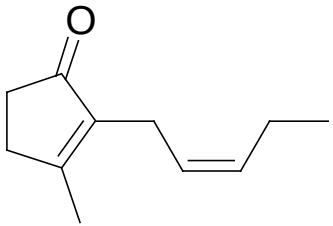
Polar



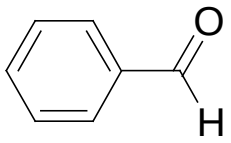
Hydrogen bonding with water
→ soluble in water when small



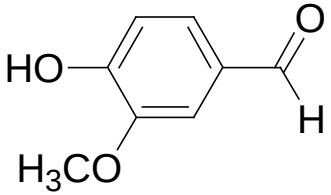
Some aldehydes and ketones have pleasant fragrances



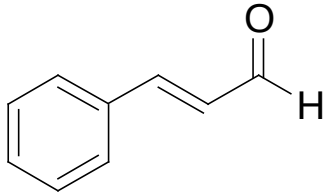
Z-jasmone
(jasmine ordor)



benzaldehyde
(almond ordor)

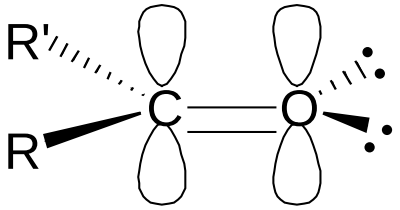


vanillin



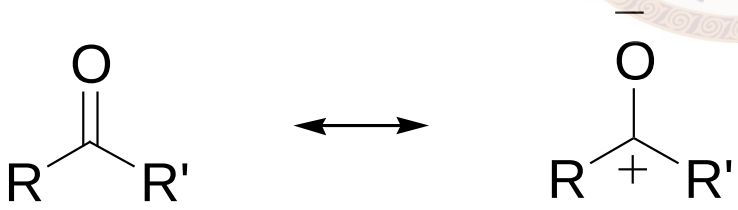
cinnamaldehyde

※ Structure



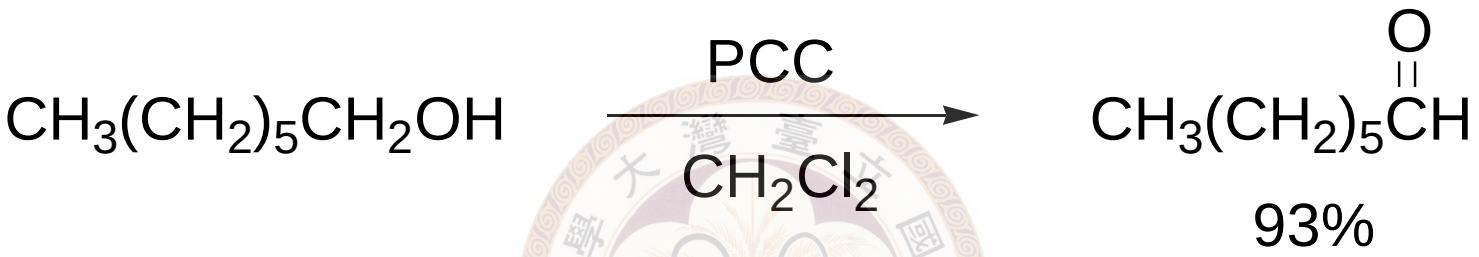
planar

π bond ~365 kJ/mol
cf. C=C ~252 kJ/mol
C–O 387 kJ/mol (in $H_3C–OCH_3$)

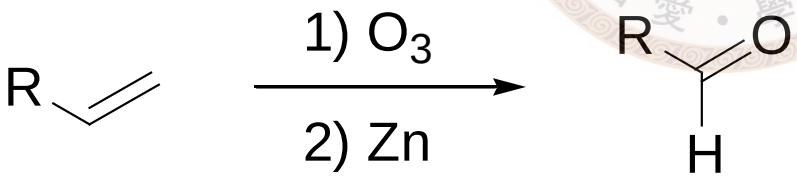


※ Preparation of aldehydes

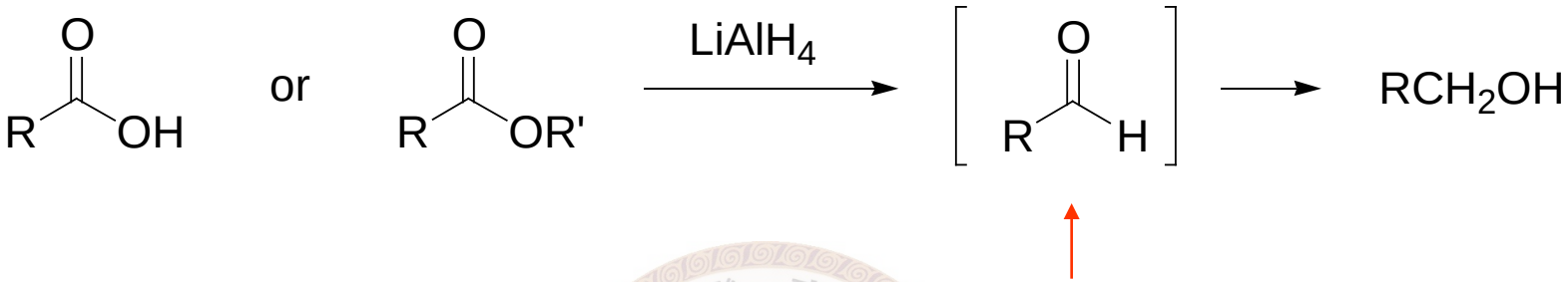
◎ Oxidation of alcohols



◎ Ozonolysis of olefin

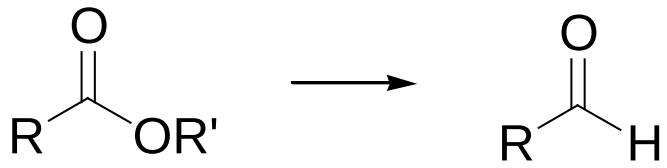


◎ Reduction of acid or derivatives

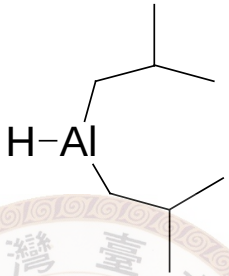


more reactive than SM

can not stop at aldehyde

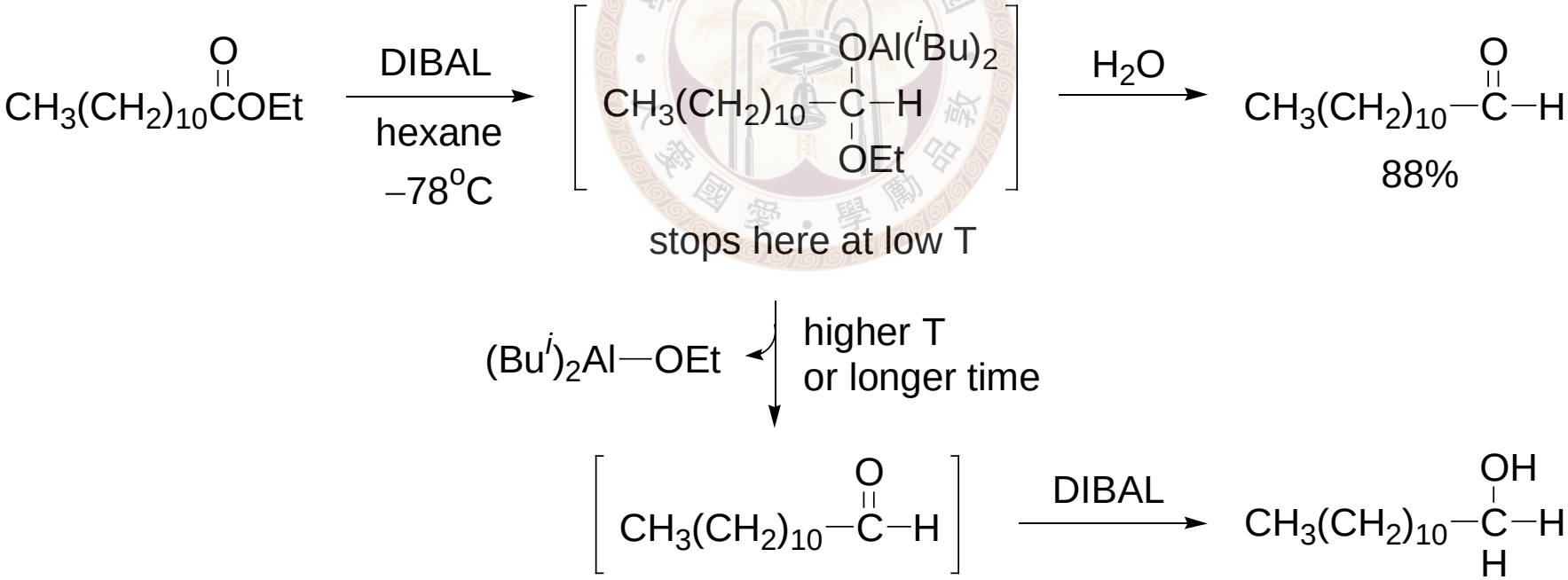
✓ 

ester

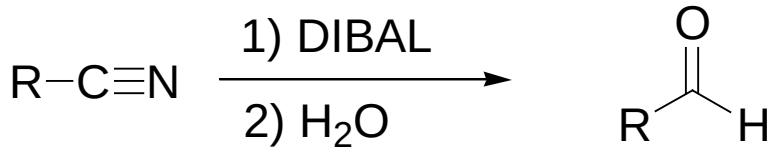
Reducing agent used: 

diisobutylaluminum hydride

簡稱：DIBAL or DIBAL-H
or DIBAH
(soluble in org. solv. at low T)

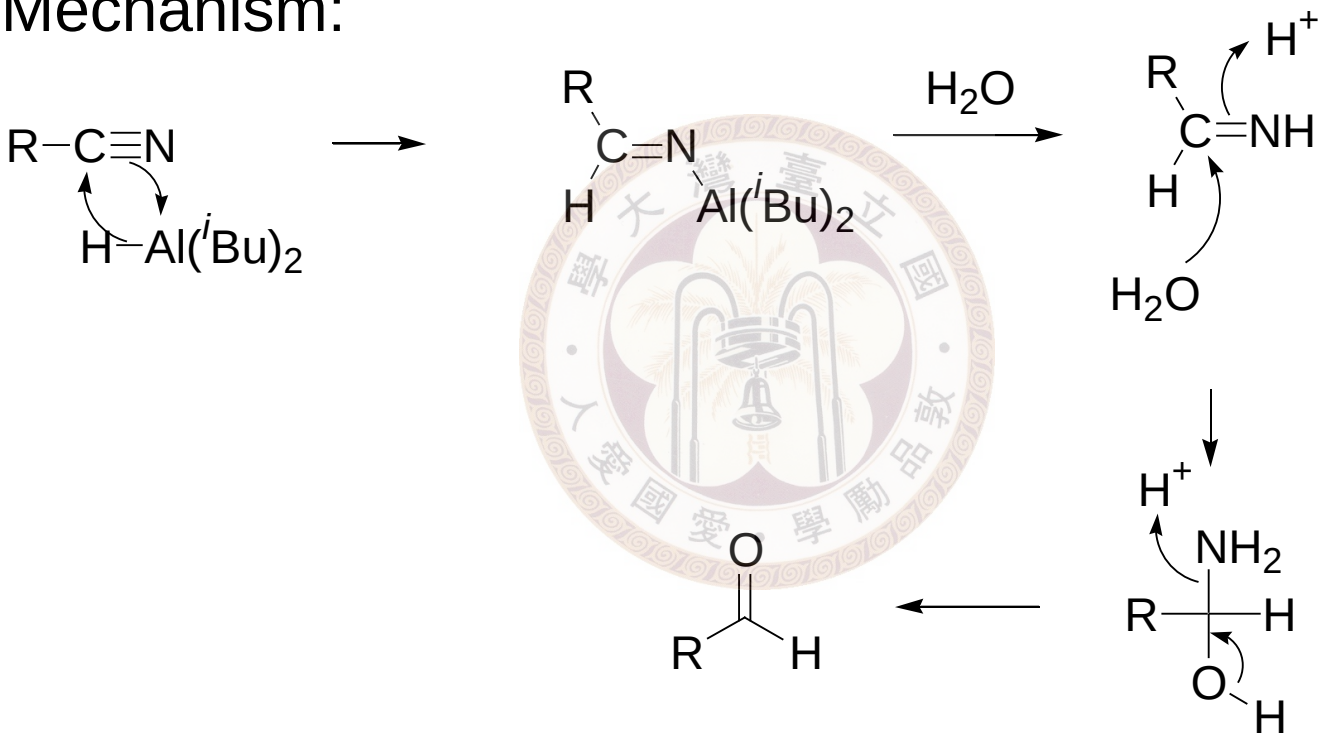


✓

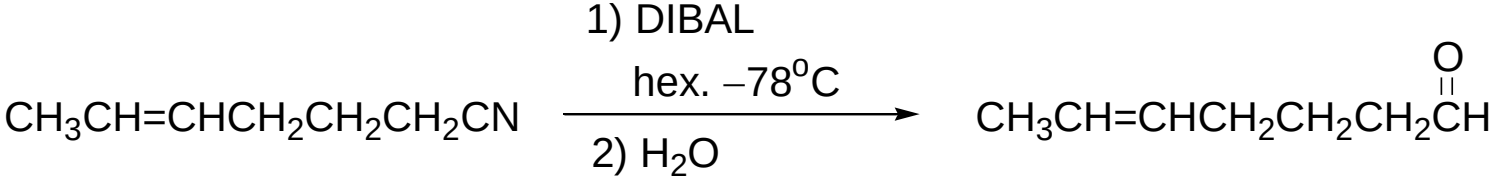


nitrile

Mechanism:

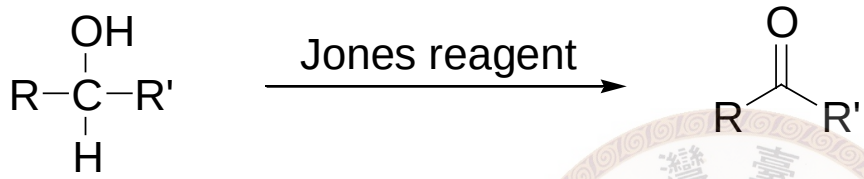


例

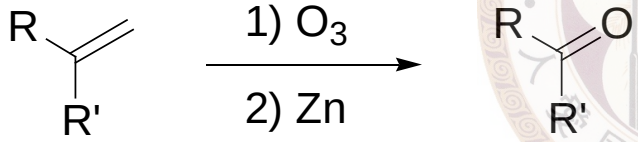


※ Preparation of ketones

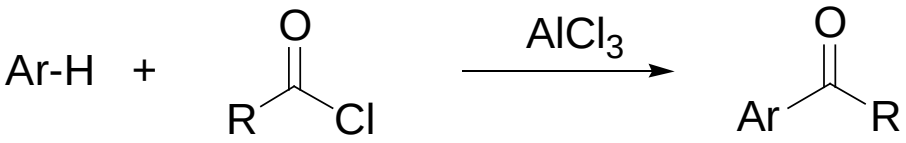
◎ Oxidation



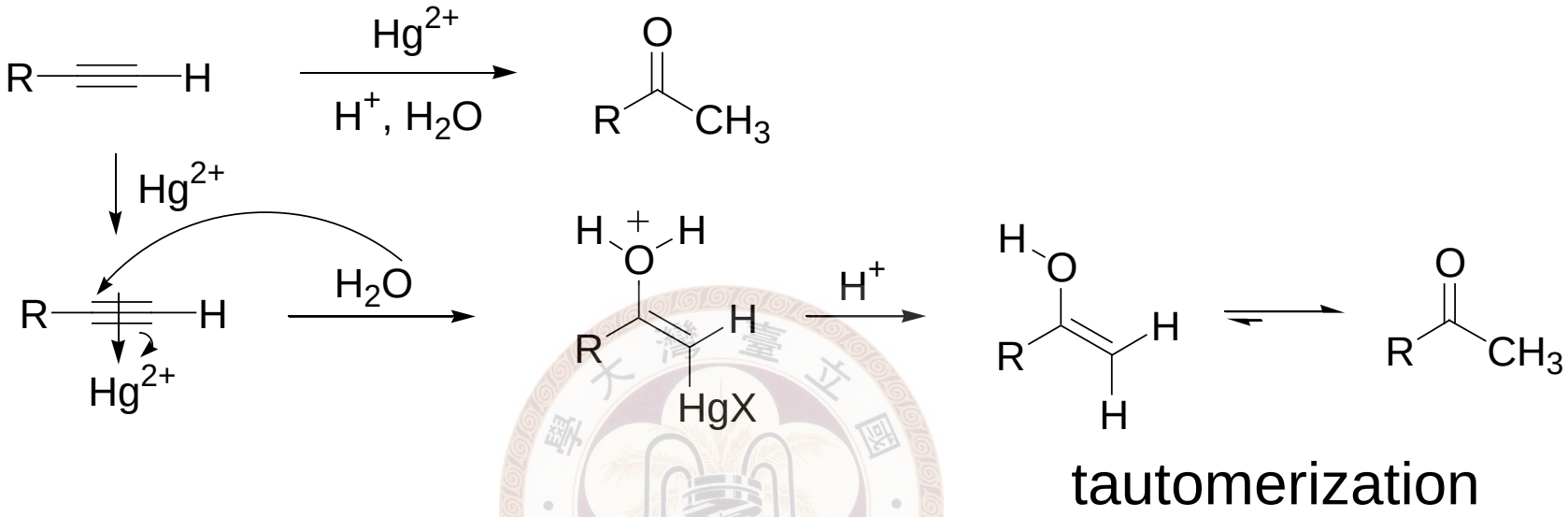
◎ Ozonolysis



◎ Friedel-Crafts acylation

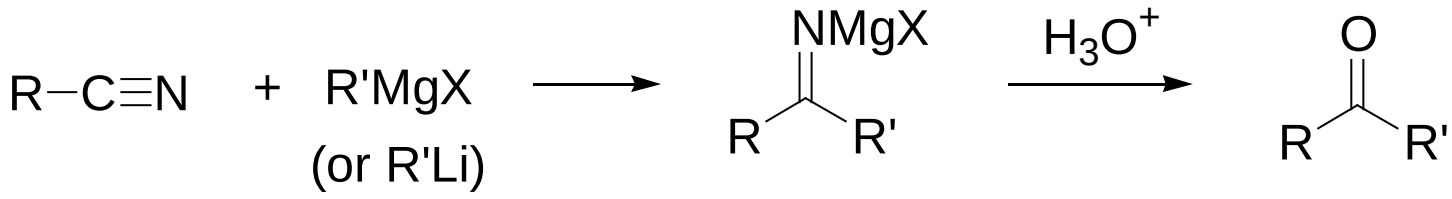


◎ Terminal acetylene → methyl ketone

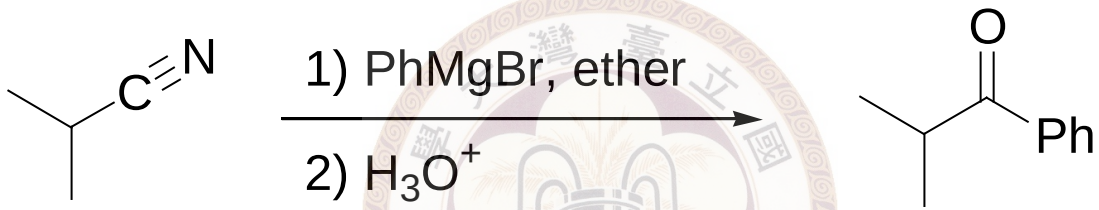


tautomerization

◎ From nitrile

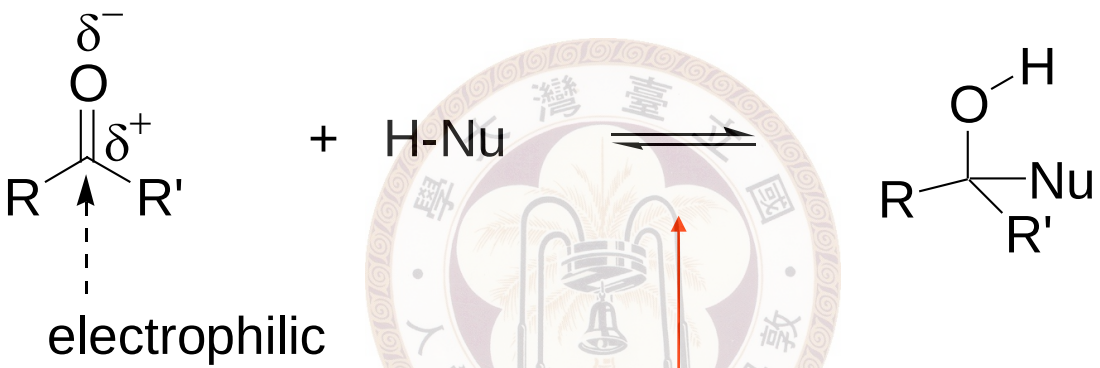


例



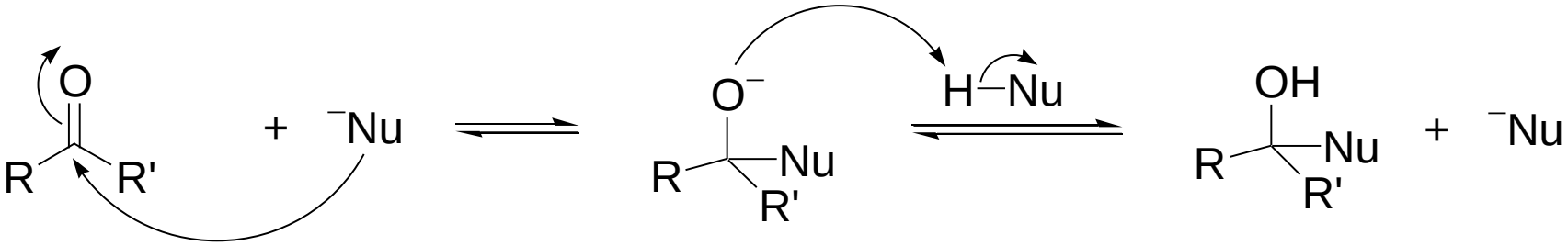
※ Reactions of aldehydes and ketones

Nucleophilic addition to the carbonyl



Reversibility depends on the nucleophile

✓ Under basic conditions

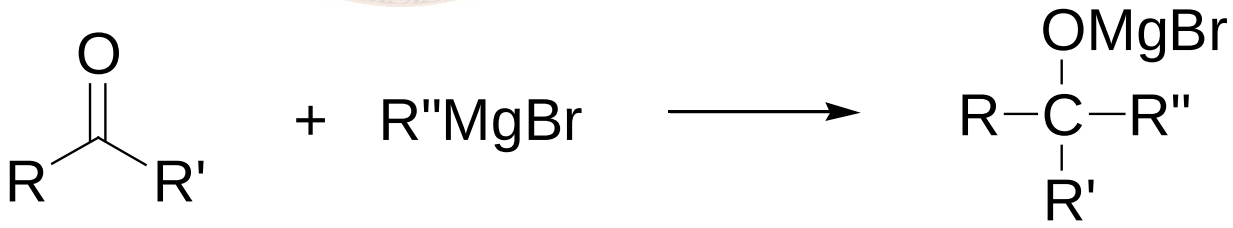


★ In general:

when the nucleophilic center is a heteroatom such as O, N, S → reversible

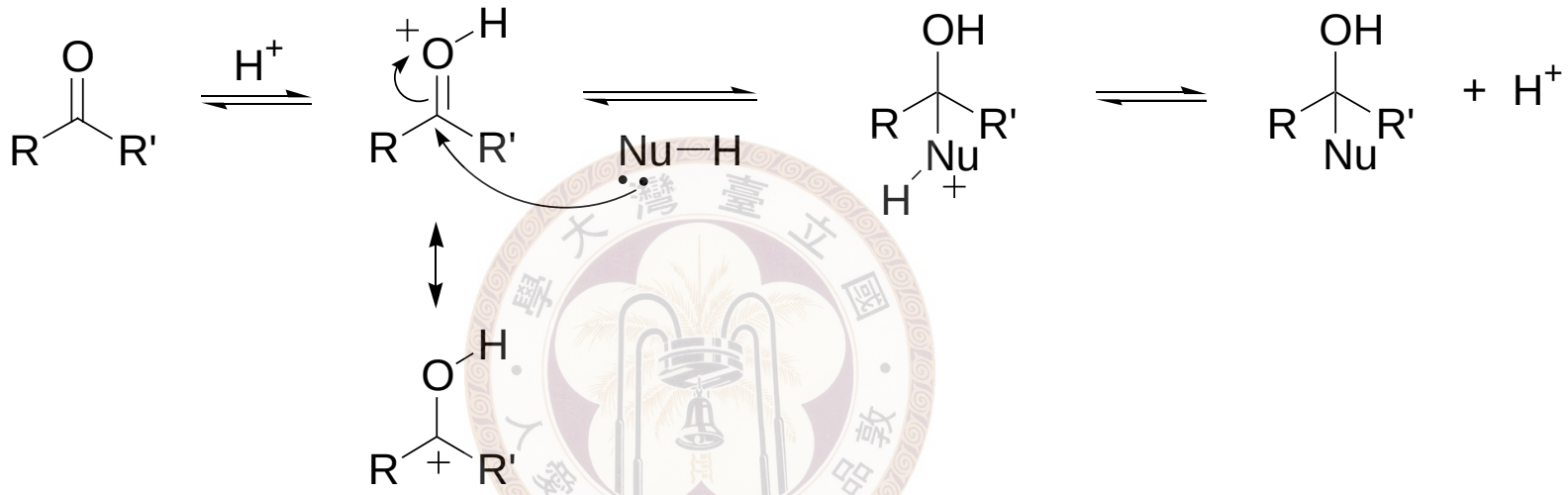
if C → irreversible (unless stabilized anion)

例



✓ Acid catalyzed

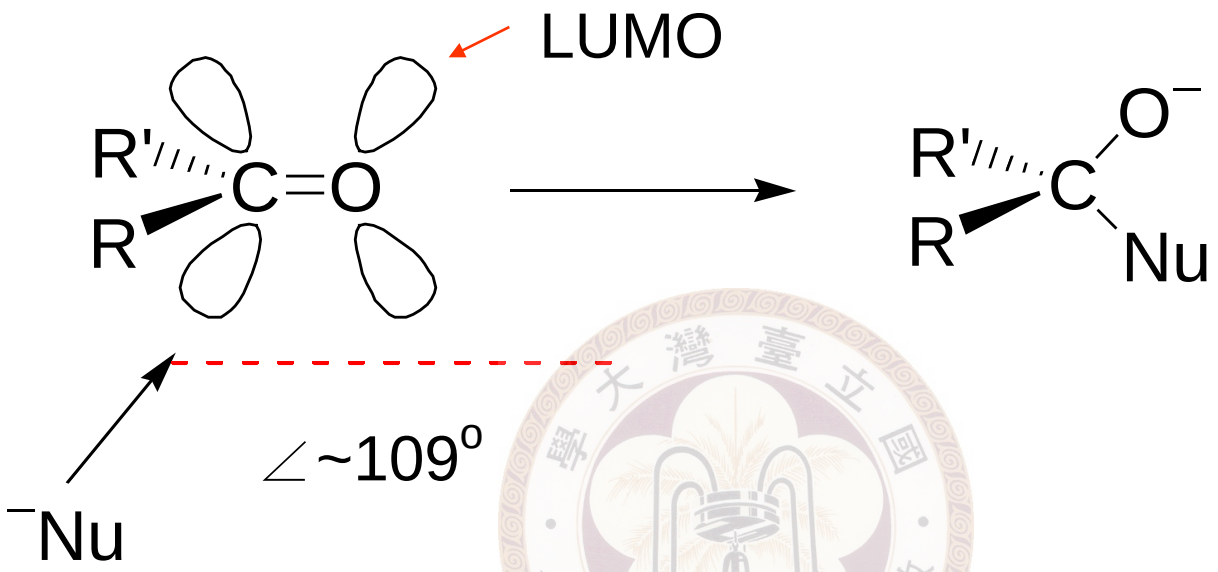
use a protic acid or a Lewis acid



an oxonium ion

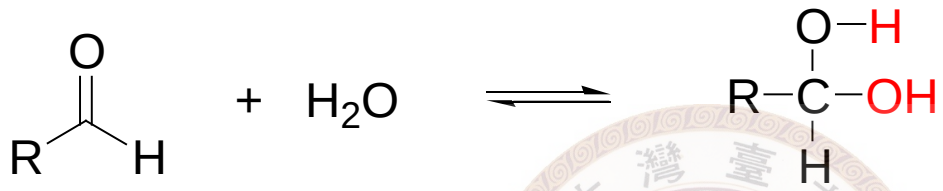
reactivity is enhanced

◎ Stereochemistry of the attack



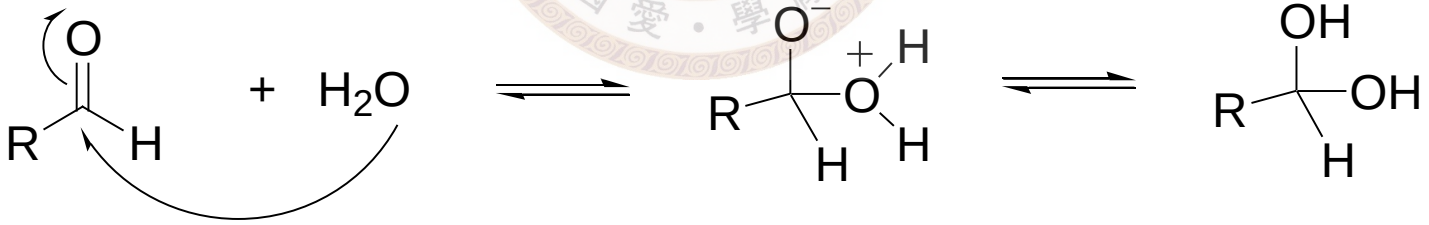
※ Oxygen nucleophile

◎ Hydrates

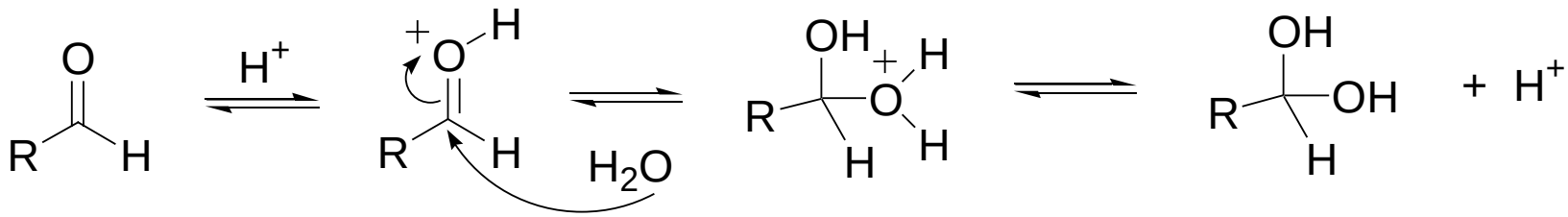


a hydrate or a *gem*-diol
(gem for geminal)

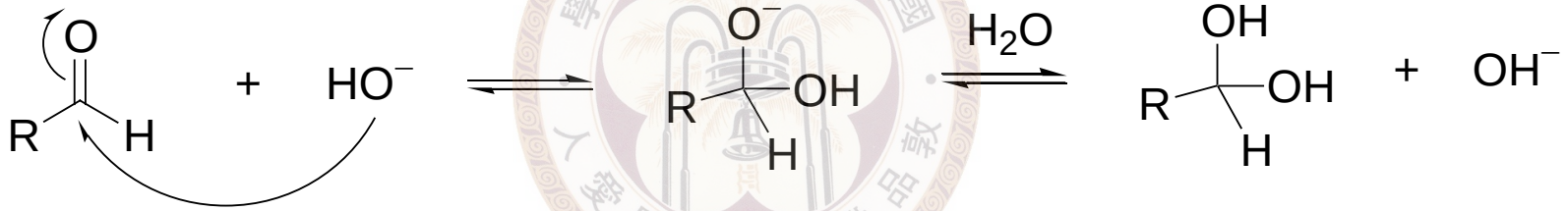
Mechanism:



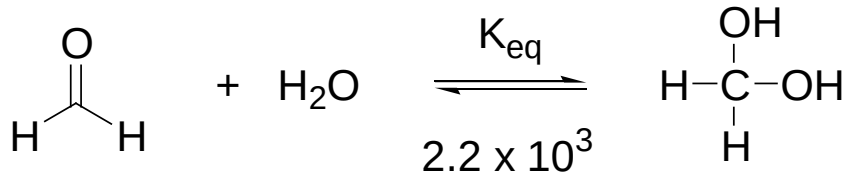
✓ Catalyzed by acid

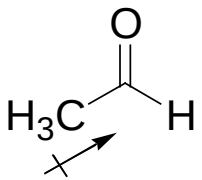


✓ Catalyzed by base



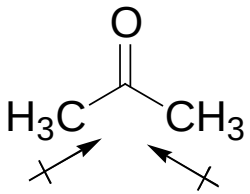
✓ The equilibrium constant



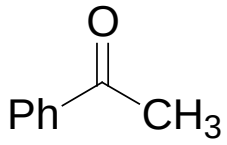


1.0

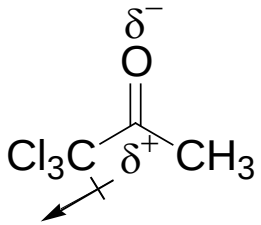
hydrates usually can not be isolated and exists only in solution



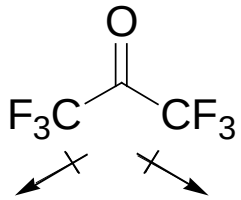
1.4×10^{-3}

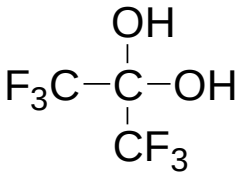


6.6×10^{-6} ⇐ stabilized by conjugation



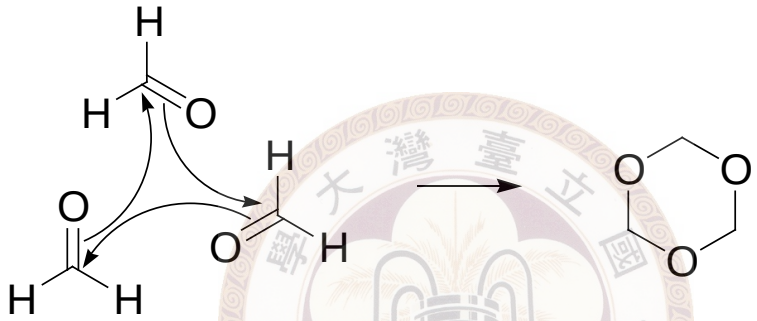
2.8×10^{4} ⇐ destabilized by EWG



⇐ exists as: 

⇐ this one is special

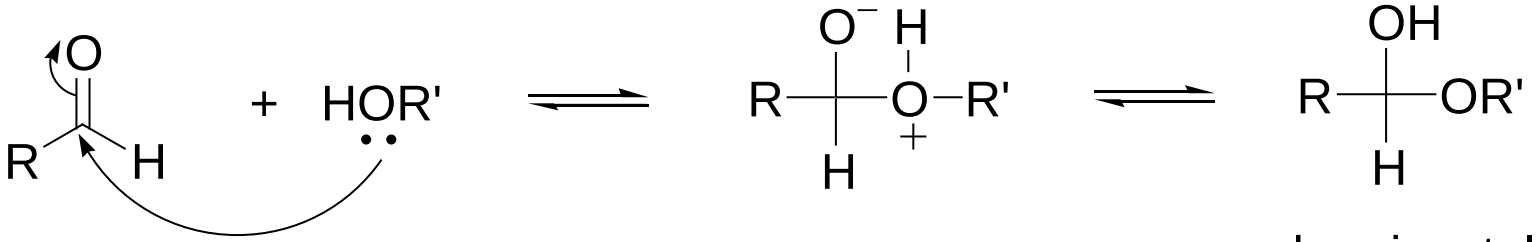
★ Kinetically aldehyde is also more reactive
due to steric effect
→ formaldehyde is extremely reactive
in fact, it forms a trimer



✓ Electronically: aldehyde is also more reactive

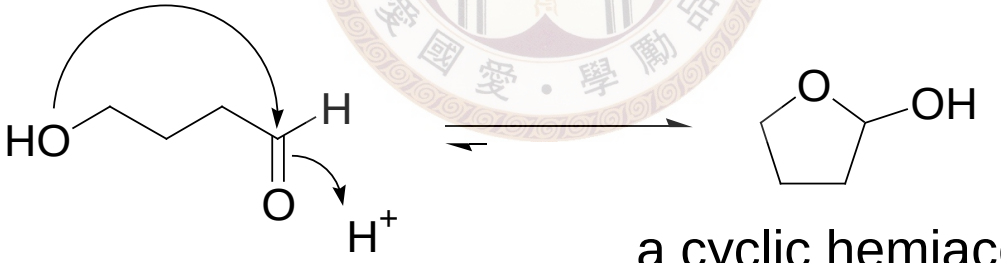
More electron donating group
attached to carbonyl
→ carbonyl carbon is less positive

◎ Hemiacetals (半縮醛)

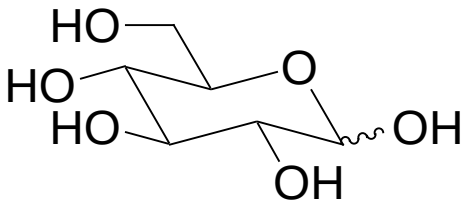


hemiacetal

- ✓ Catalyzed by acid and base
- ✓ Hemiacetals are unstable
  usually exist in solution
- ✓ Cyclic hemiacetals are more stable

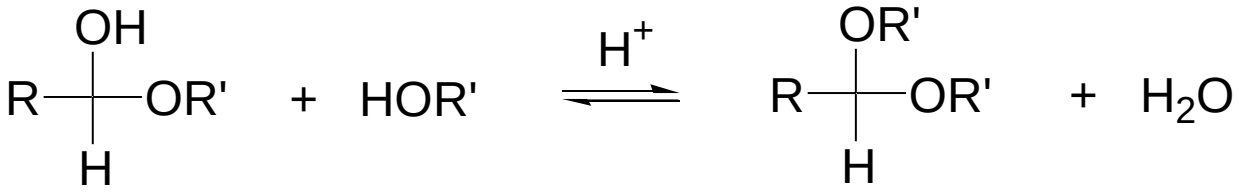


a cyclic hemiacetal



← glucose exists in this form

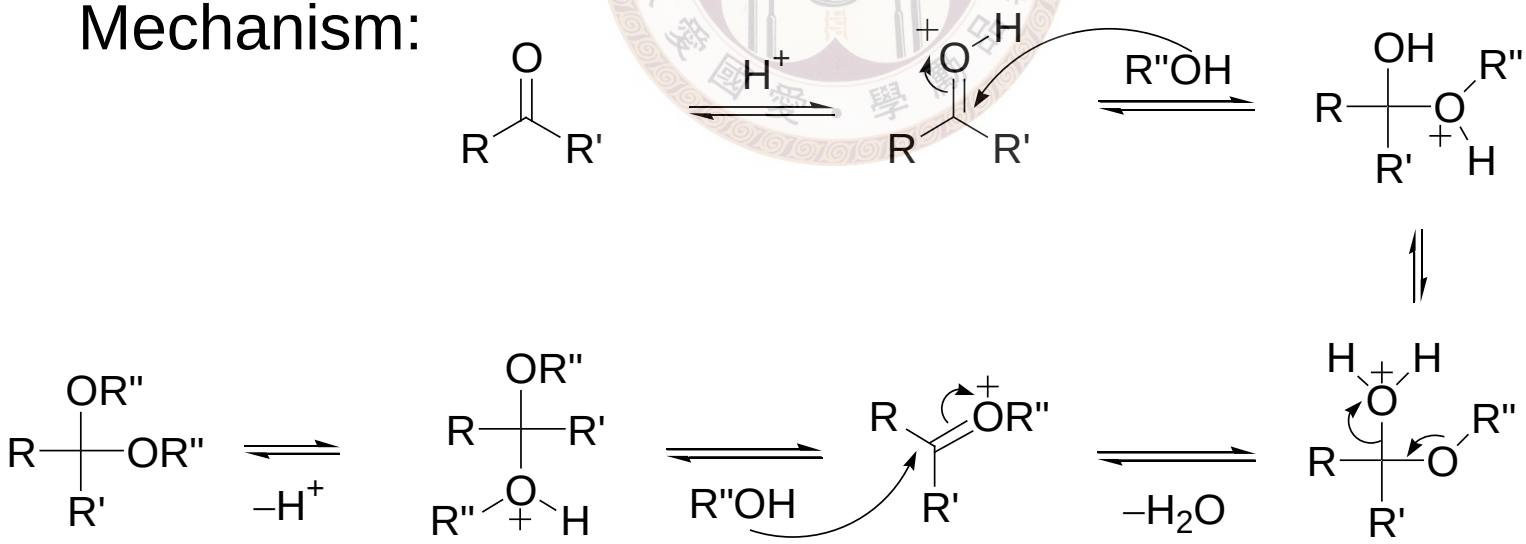
◎ Acetals (縮醛)



acetal

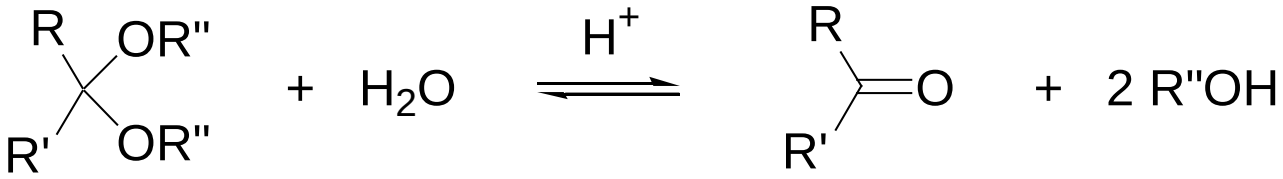
Overall:

Mechanism:



✓ Acetals are stable and isolable

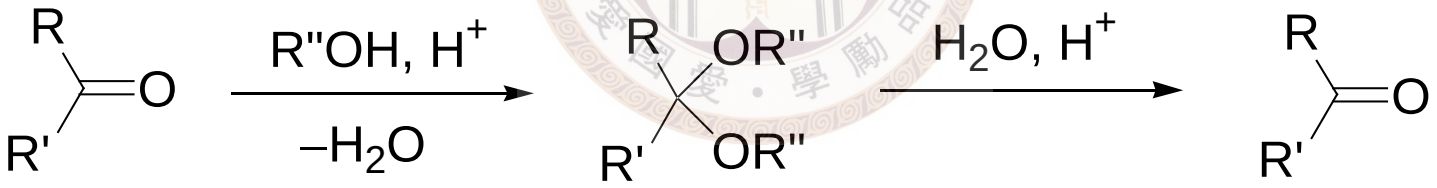
✓ Sensitive to acidic condition



also called as a hydrolysis (水解) reaction

stable under basic condition

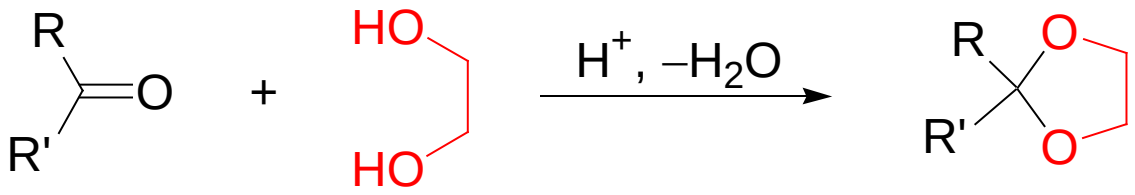
→ used as carbonyl protecting group (保護基)



protection

deprotection

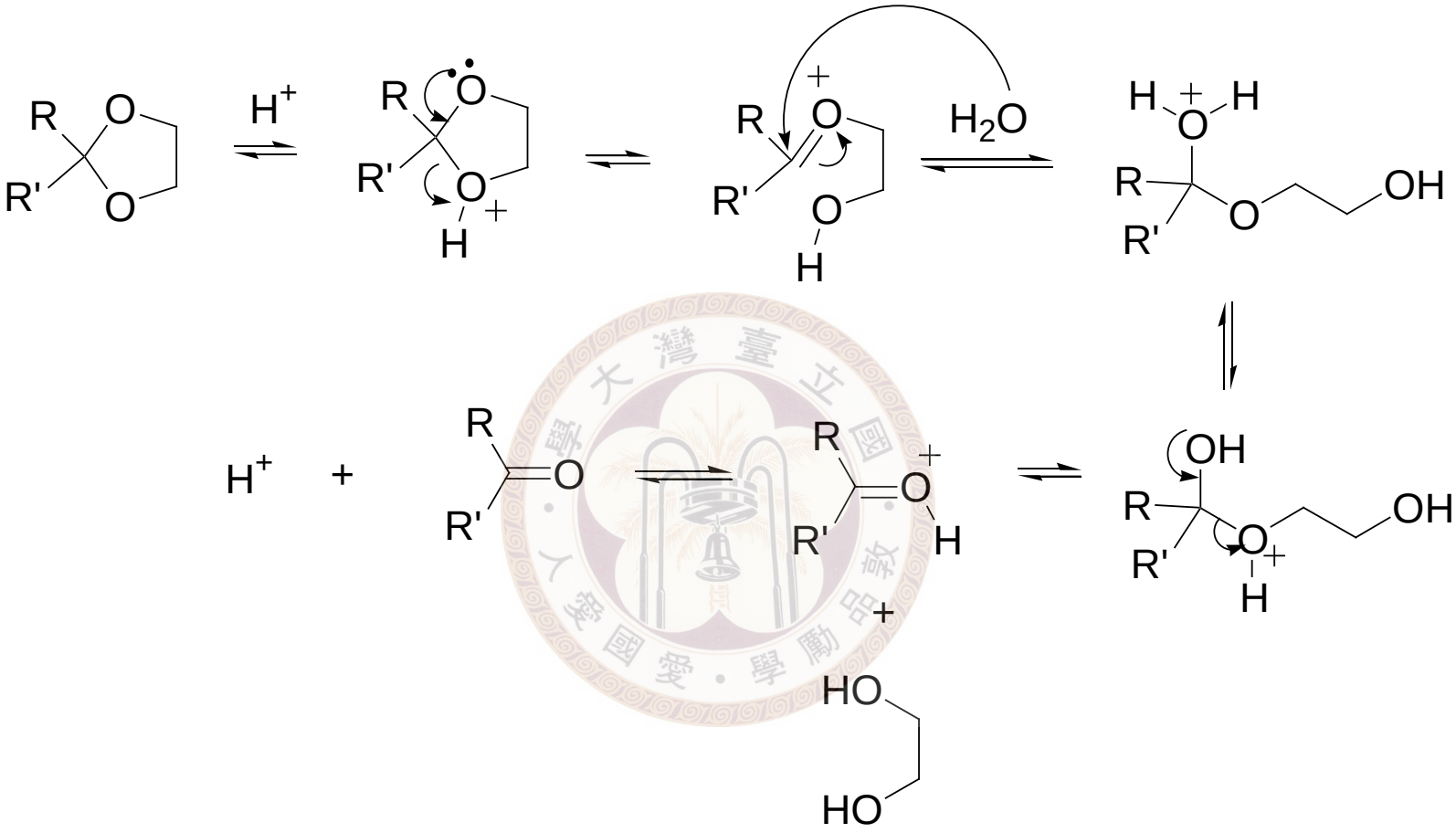
✓ Cyclic acetals are often used as protecting groups



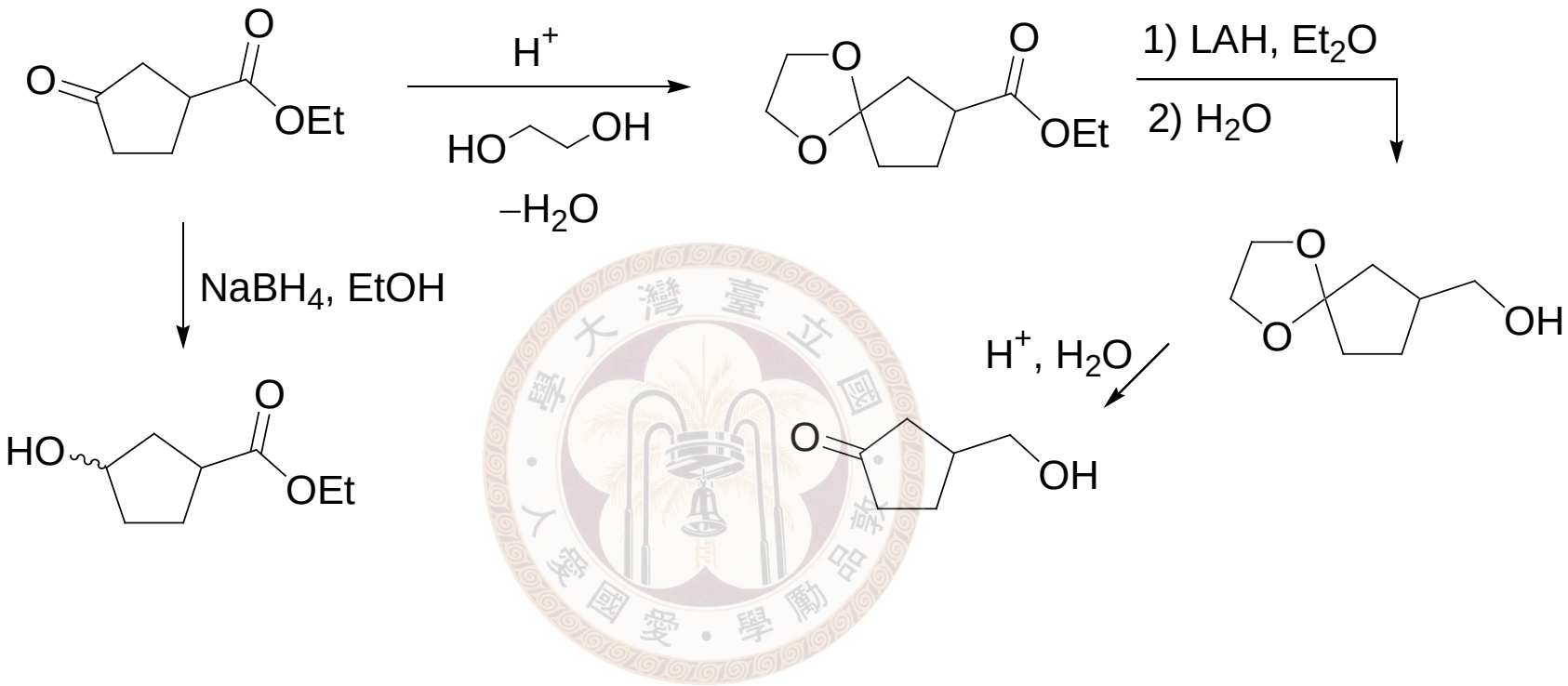
an ethylene acetal

Deprotection:

Mechanism:

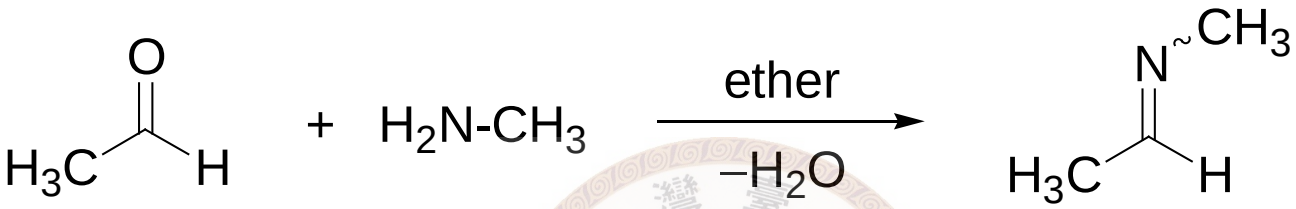


例


O
O
OEt
H+
HO
OH
–H2O
O
O
O
OEt
1) LAH, Et2O
2) H2O
NaBH4, EtOH
HO
O
OEt
H+, H2O
O
OH
O
O
OH

※ Nitrogen nucleophiles

★ Reactions with amines



an imine (亞胺)
(acetaldimine)

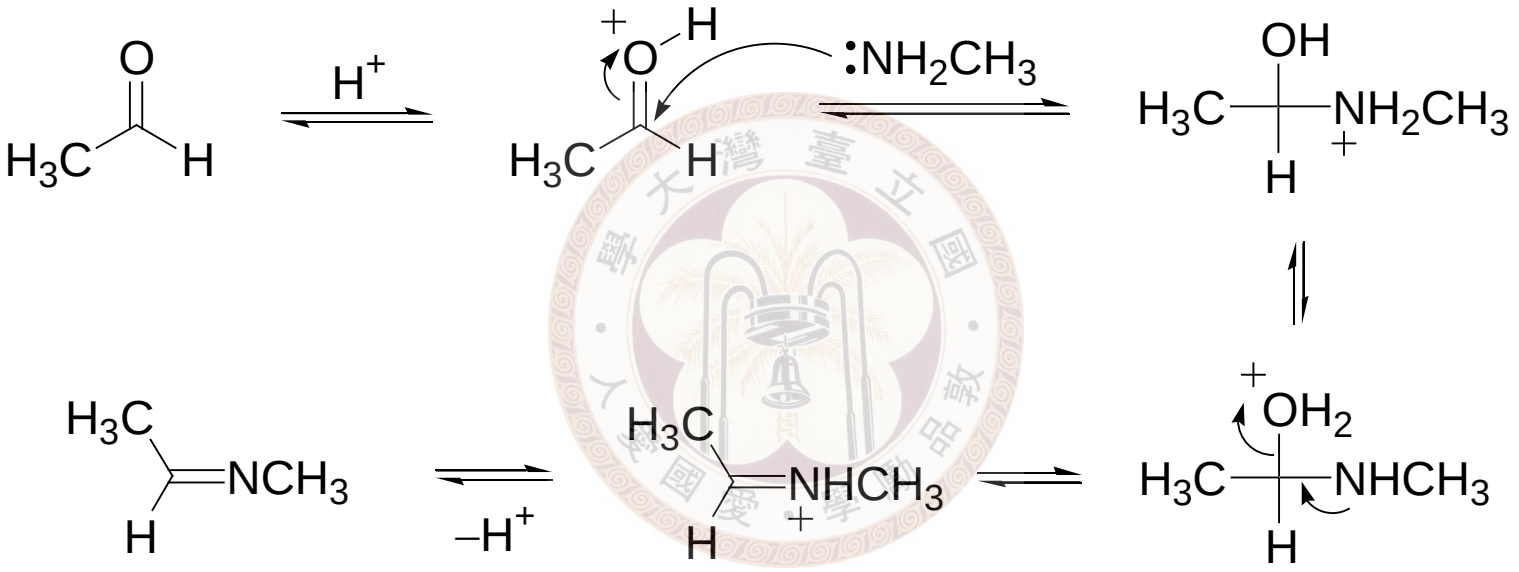
also called: Schiff base

→ hydrolyzes back very easily

Mechanism:

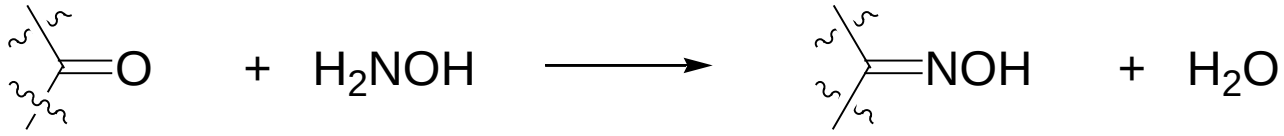
usually catalyzd by acid

best performed at pH ~3-4



an iminium ion

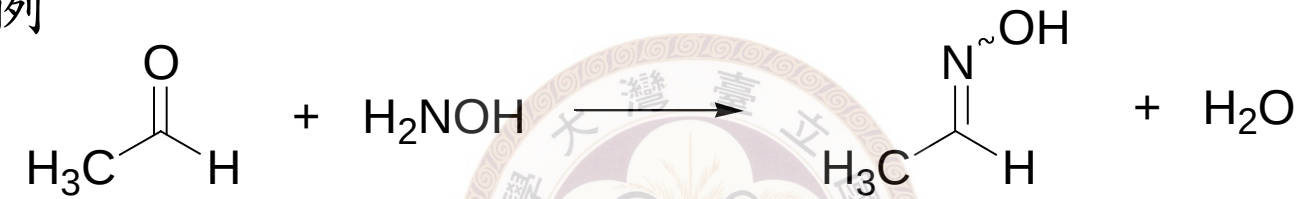
◎ Oxime and hydrazone

✓ 

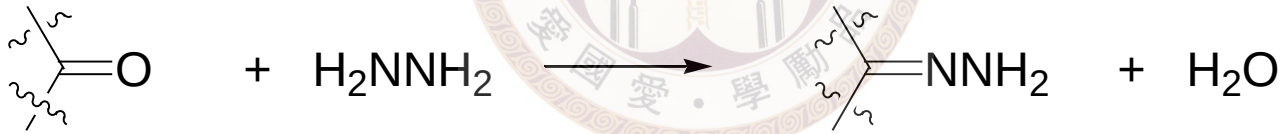
hydroxylamine

an oxime

例

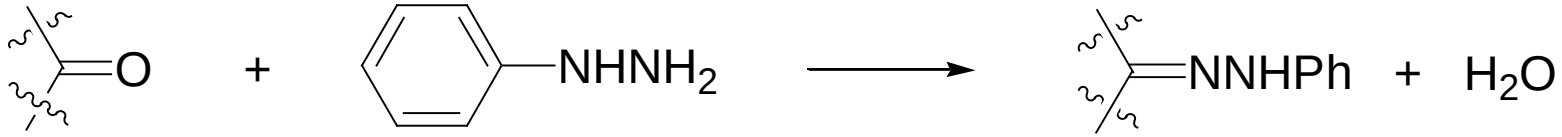


acetaldoxime

✓ 

hydrazine

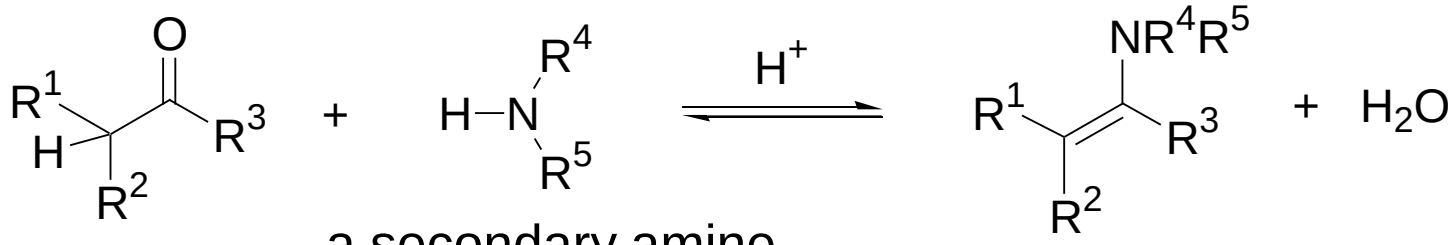
a hydrazone



phenylhydrazine

a phenylhydrazone

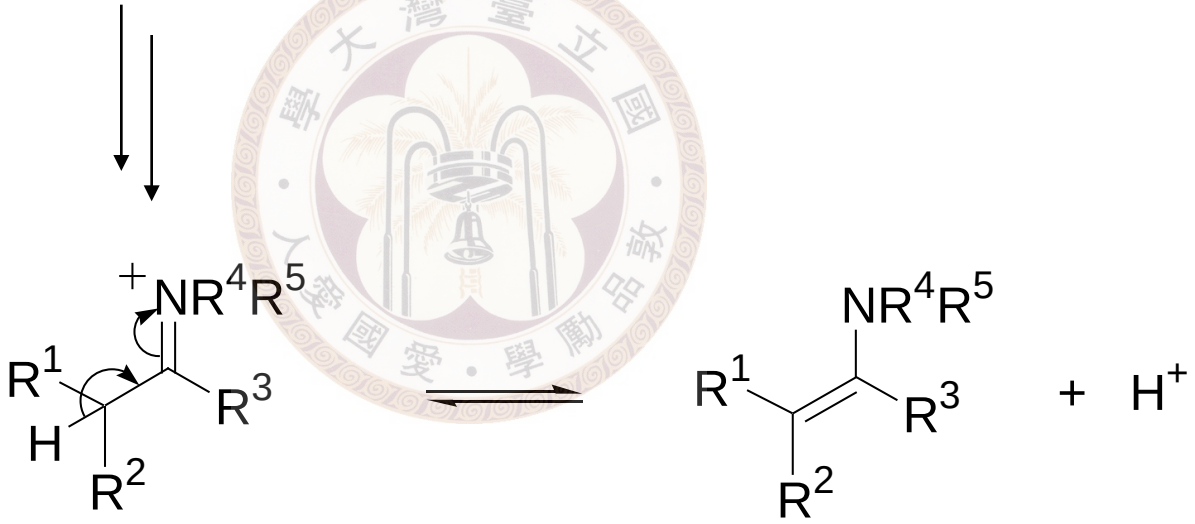
◎ Formation of enamines



a secondary amine

an enamine

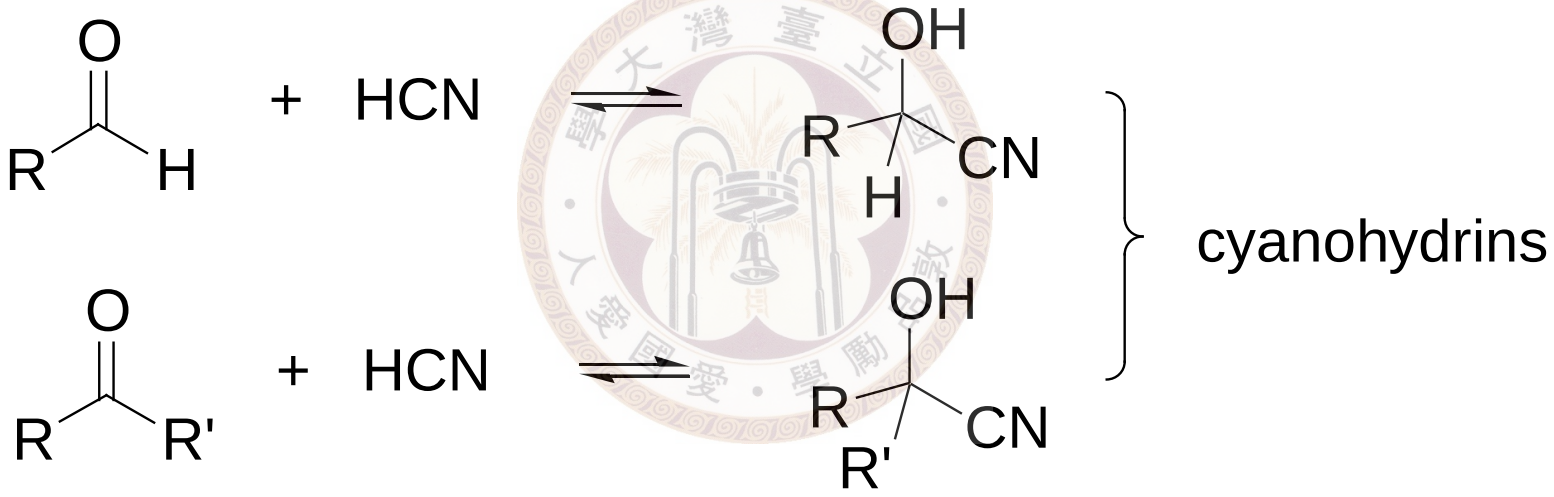
Mechanism:



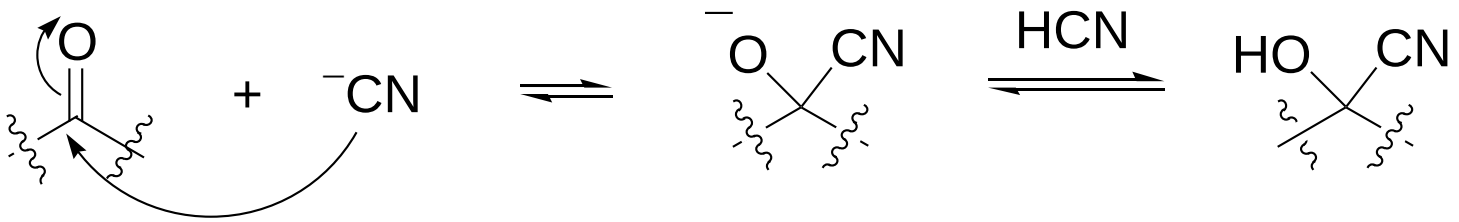
※ Carbon nucleophiles

◎ Addition of HCN

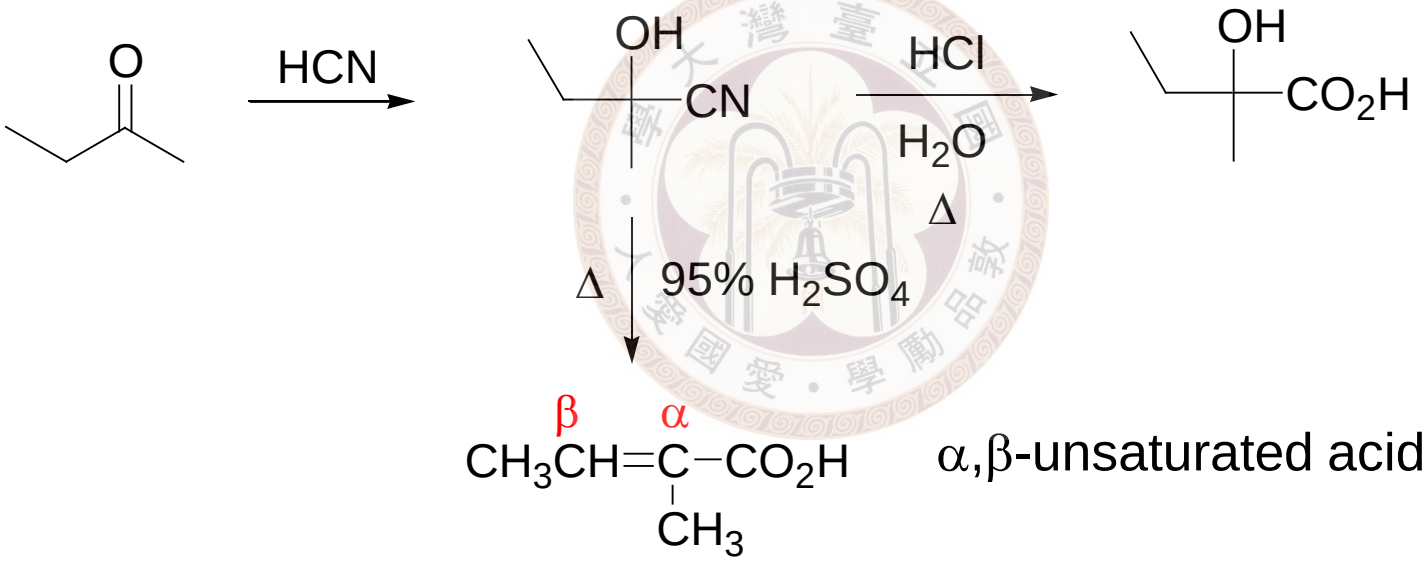
pK_a ~9

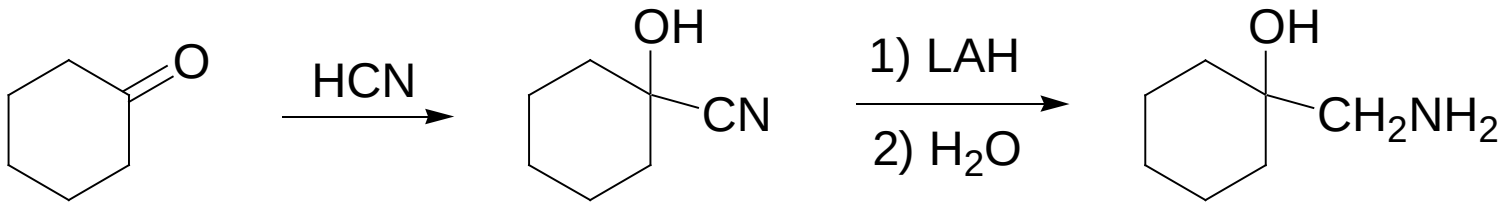


Mechanism:



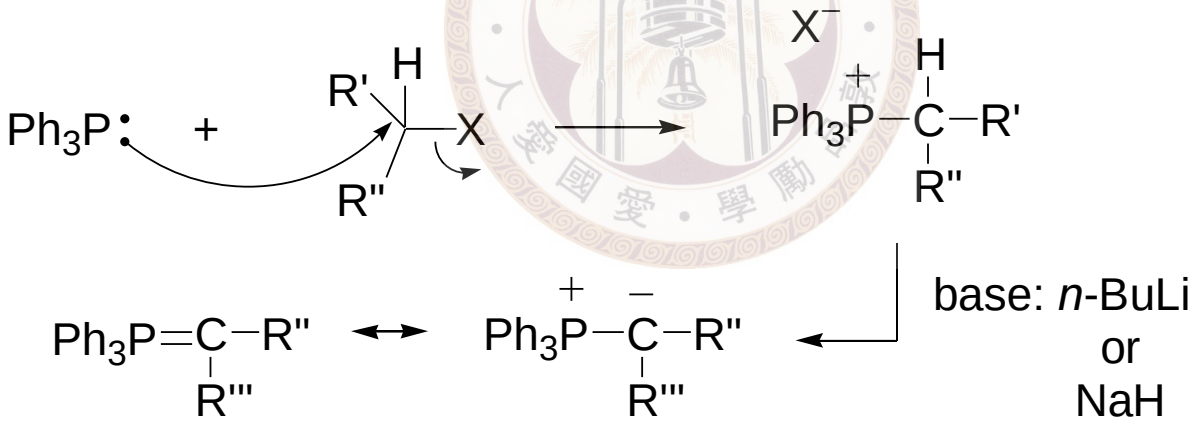
Applications:



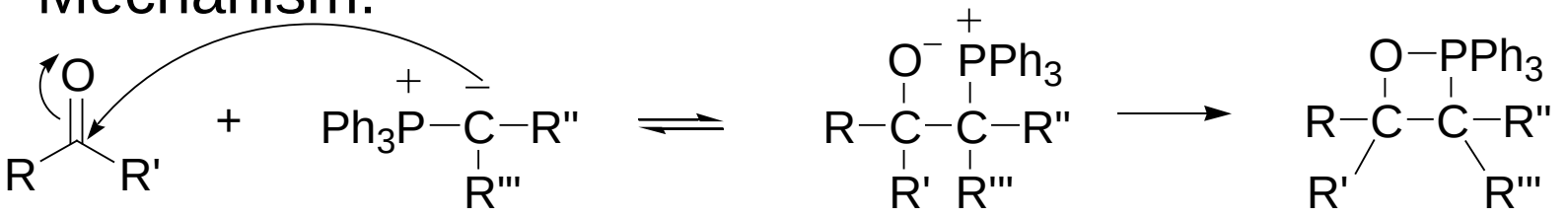


★ The Wittig reaction

✓ Preparation of the ylide



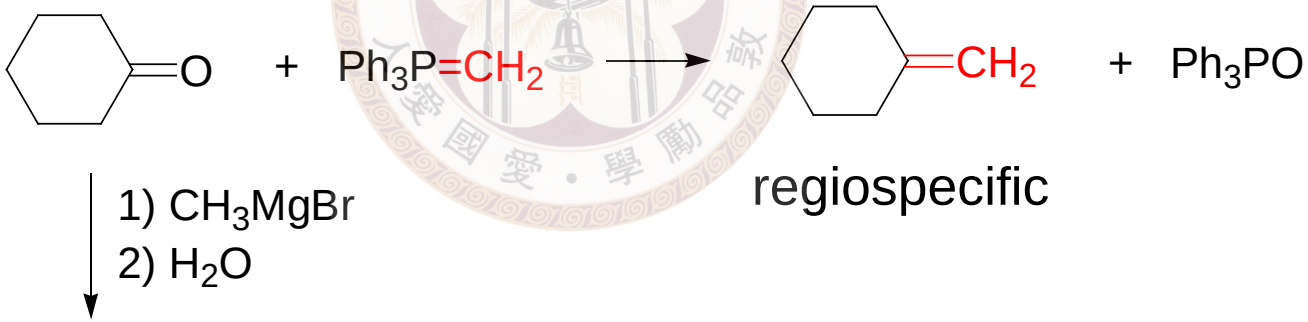
✓ Mechanism:

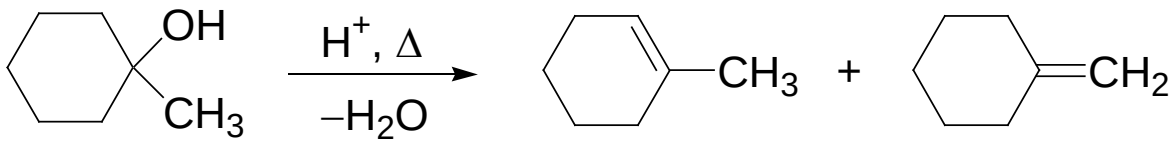


$RR'C{=}CR''R'''$ + $Ph_3P{=}O$

(*E* + *Z*)

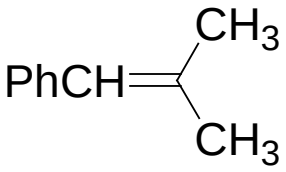
例

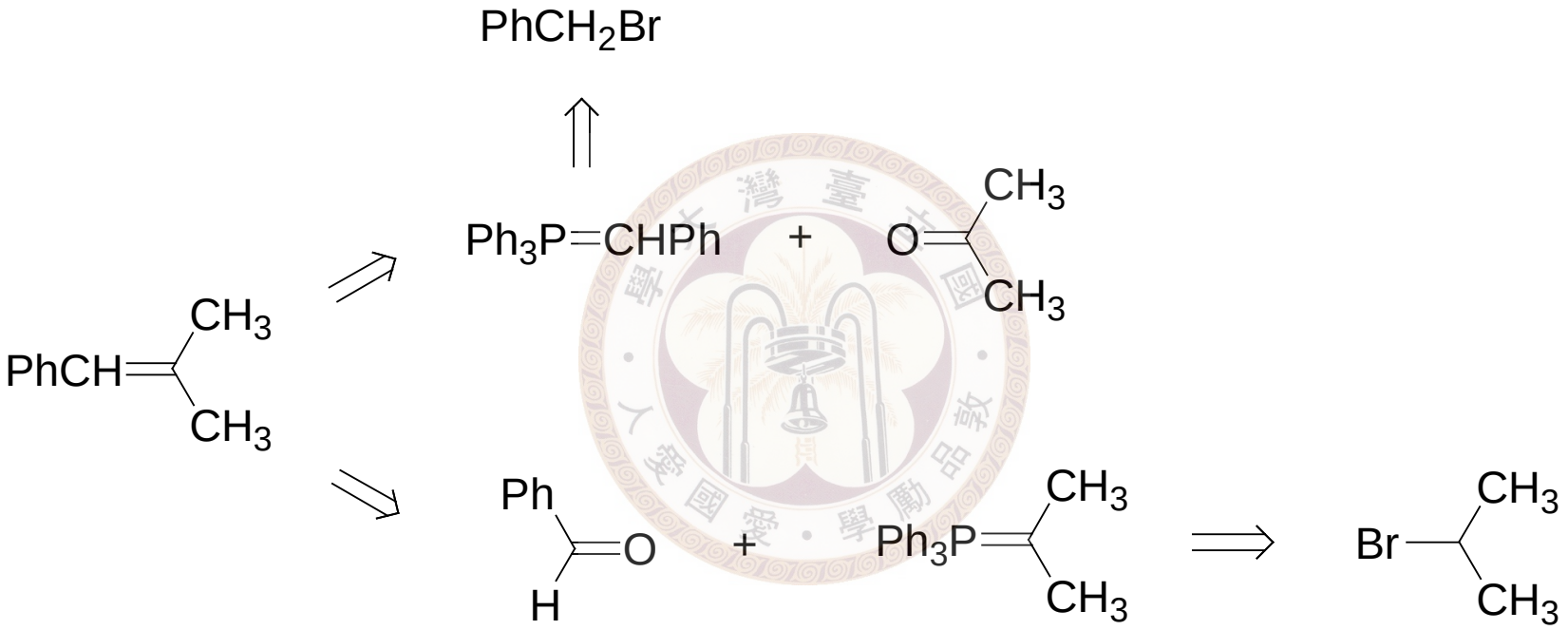




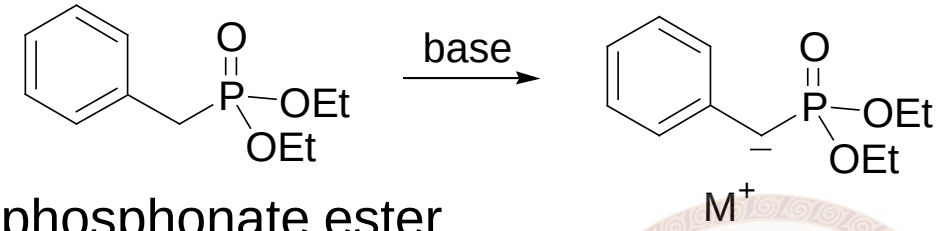
a mixture is obtained

→ non-regiospecific

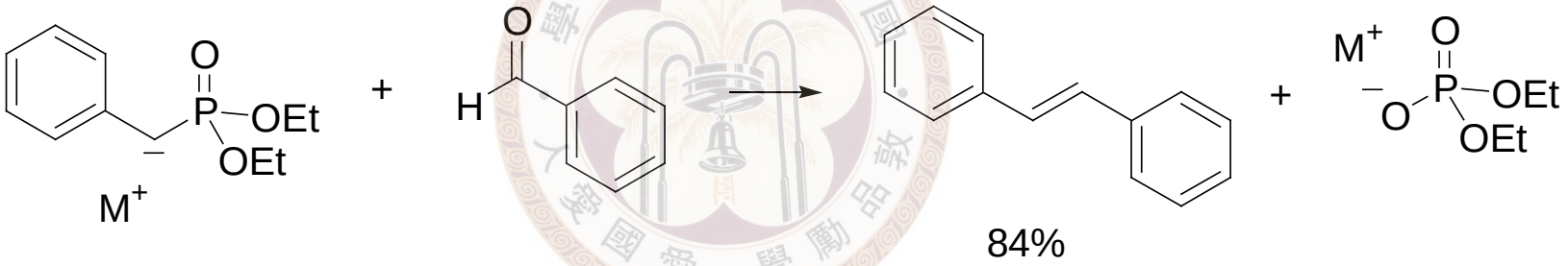
Q: How to prepare  ?



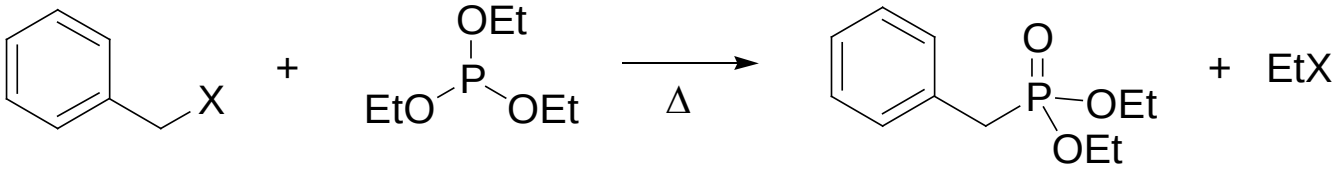
◎ The Horner-Wadsworth-Emmons modification of Wittig reaction



a phosphonate ester

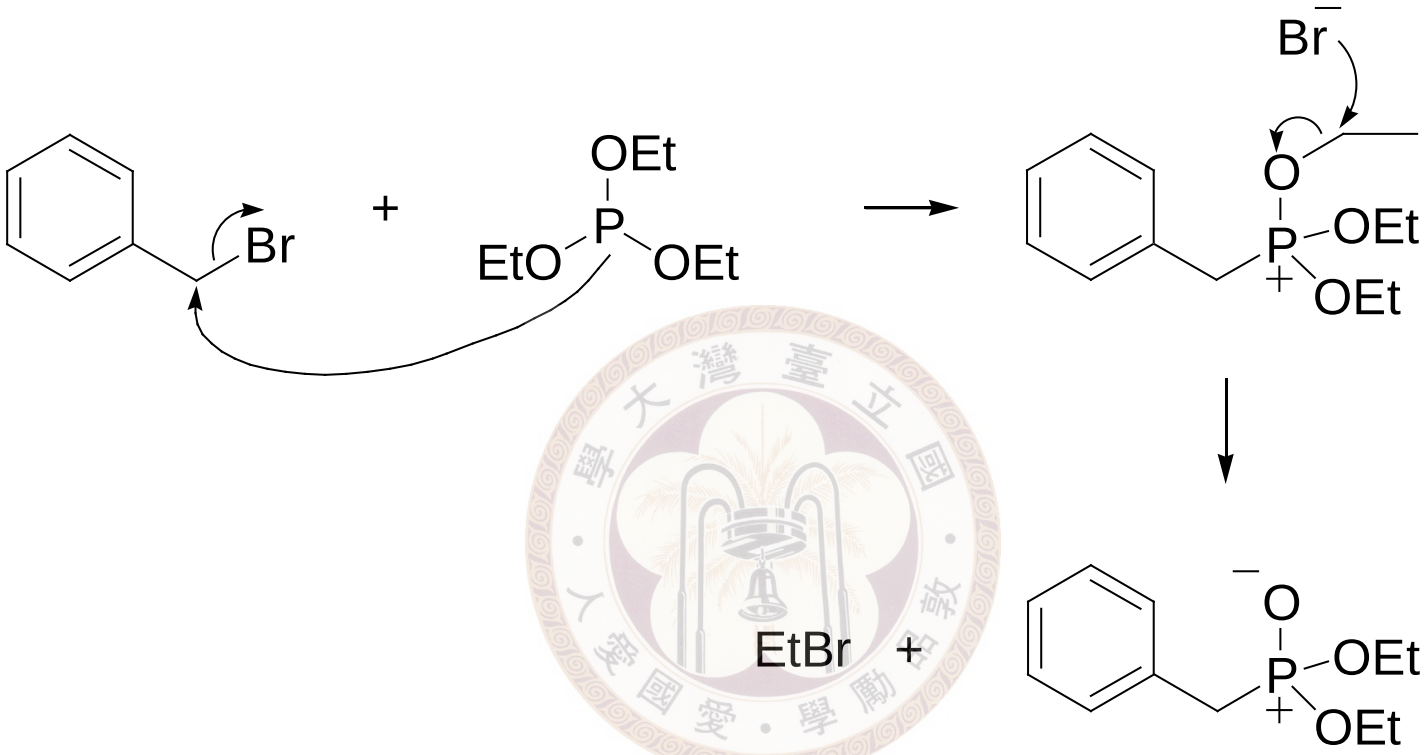


*Preparation of phosphonate ester (Arbuzov reaction):

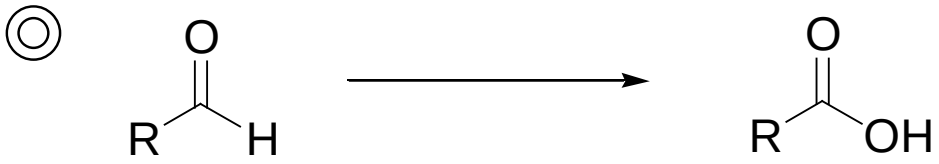


triethyl phosphite

Mechanism of Arbuzov reaction:



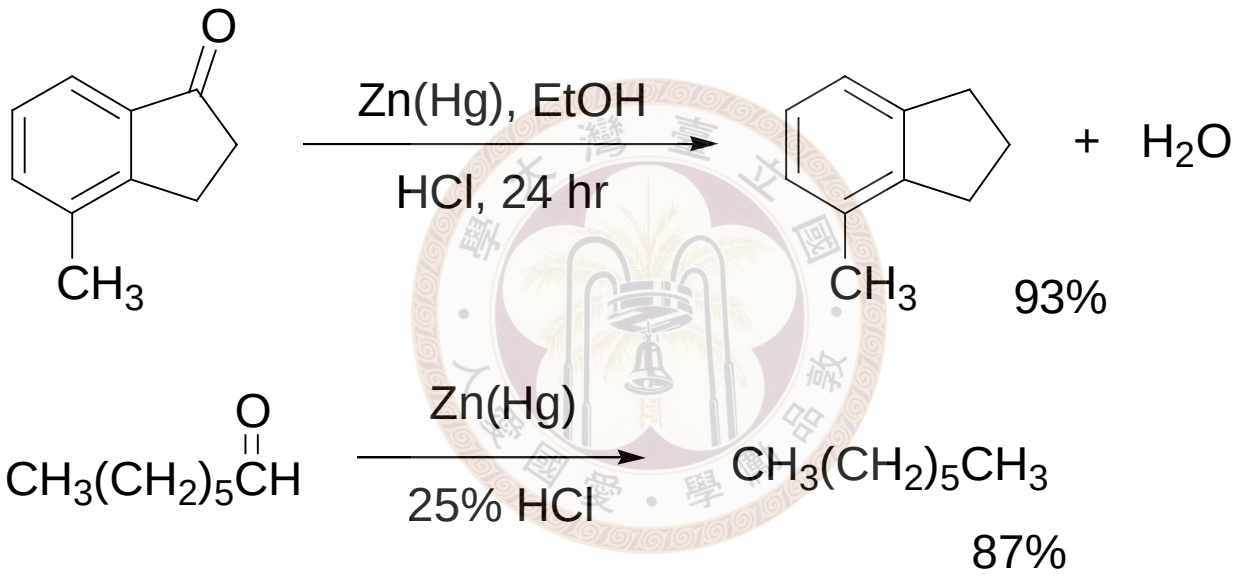
※ Oxidation



- ✓ Jones
- ✓ $KMnO_4$, OH^-; H^+
- ✓ Ag_2O, OH^-; H^+

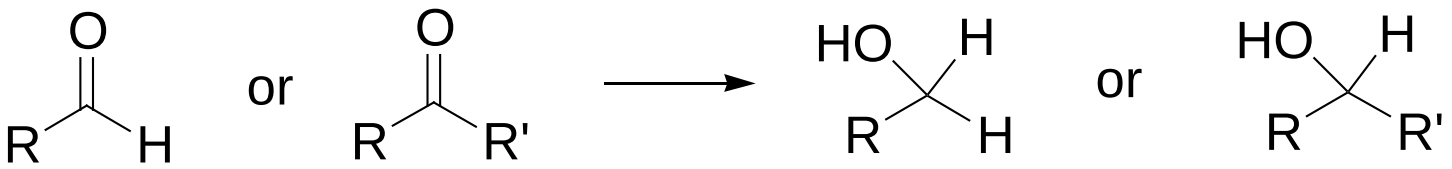
※ Reduction

◎ Clemmensen reduction



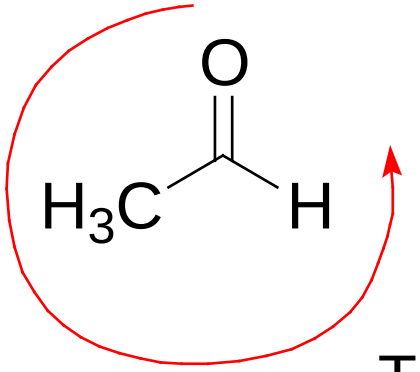
*Zinc amalgam: a solution of zinc metal in Hg

◎



- ✓ LAH
- ✓ $NaBH_4$/EtOH

※ More about prochirality



Viewing from the top face:

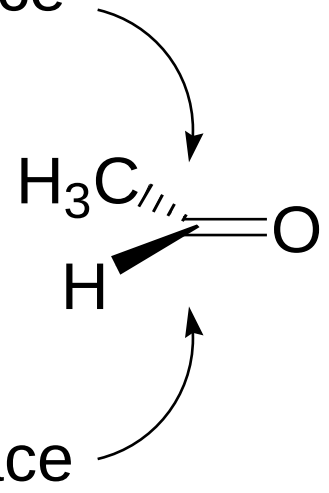
→ conuter-clockwise

→ *Si* face

The bottom face (backside of the screen):

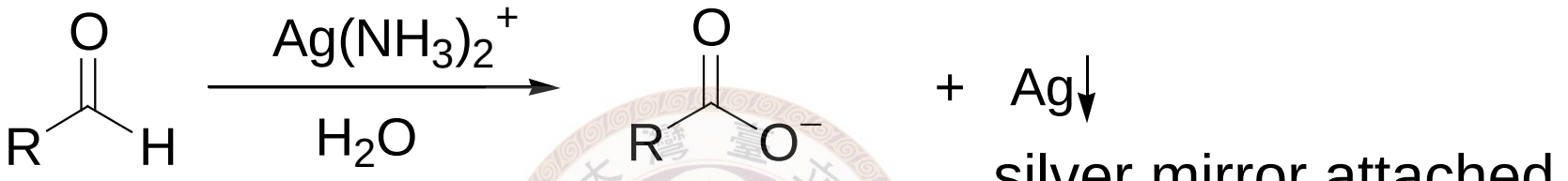
Re face

Viewing from a different angle:



※ A simple chemical test for aldehyde

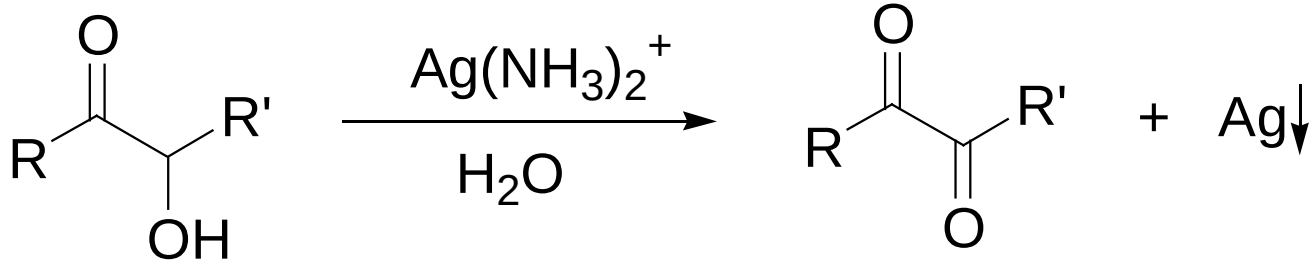
Tollen's test (silver mirror test)



silver mirror attached on test tube

negative test (no reaction)

but:



α-hydroxy ketone

※ Spectroscopy

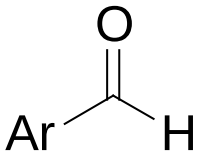
✓ IR: C=O stretching

This form has higher contribution in ketones → has more single bond character (less reactive)

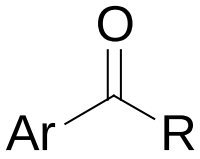
1720-1740 (~1730)

1705-1720 (~1715)

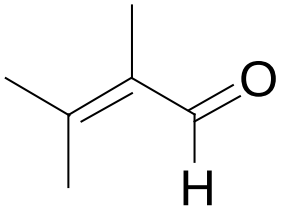
Conjugation effect:



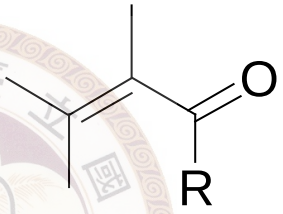
1695-1715
(~1700)



1680-1700
(~1690)

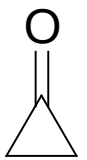


1680-1690
(~1700)

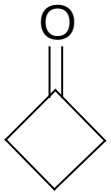


1665-1680
(~1690)

Ring size effect:

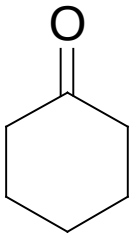


1850

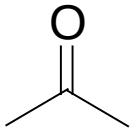


1780

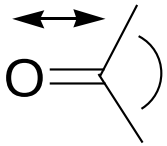
1750



1715

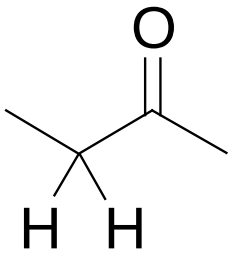


1715

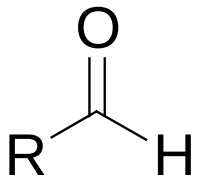


angle changes due to stretching
→ smaller angle, higher strain, higher freq.

✓ ^{1}H NMR



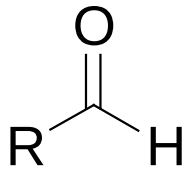
δ ~2 ppm



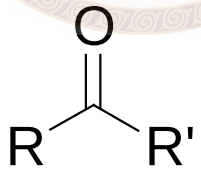
δ ~9-10 ppm

small J (~3 Hz) with α-hydrogens

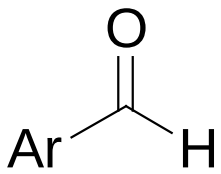
✓ ^{13}C NMR



200



210

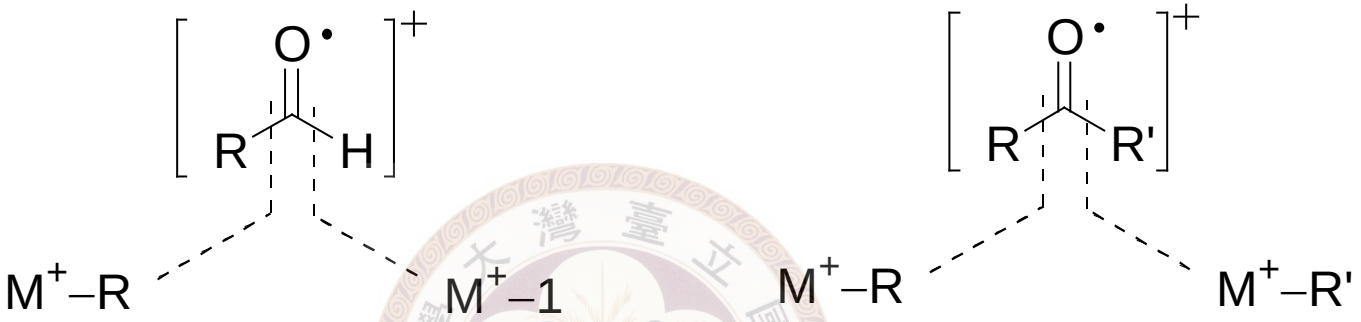


190

ketone signal is weak

✓ Mass

α-Cleavage



McLafferty rearrangement

Cleavage of α,β-bond