臺灣大學化學系
NTU Chemistry

台灣大學開放式課程

有機化學乙

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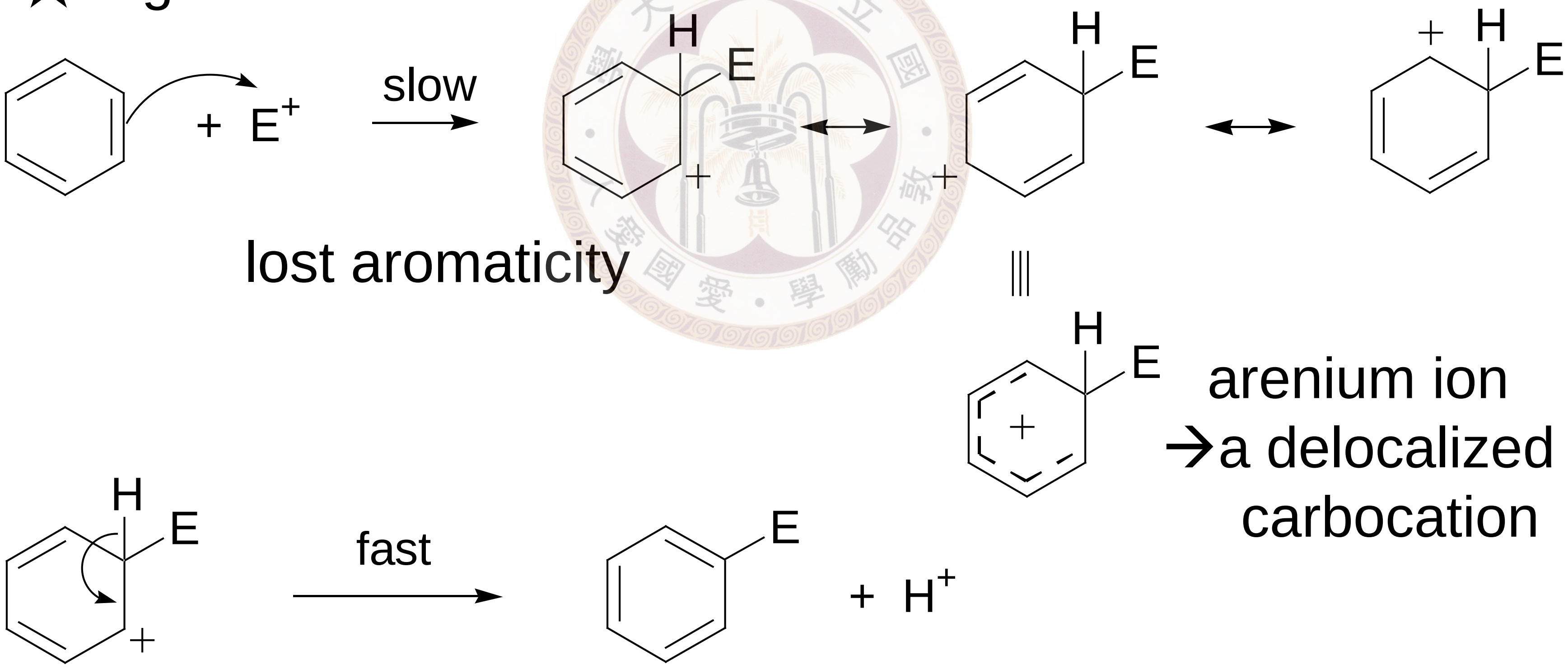
臺大開放式課程

Chapter 15
Reactions of aromatic compounds

※ Electrophilic aromatic substitution (親電性芳香族取代反應)

$$\text{Ar-H} + \text{E}^+ \rightarrow \text{Ar-E} + \text{H}^+$$

★ A general mechanism

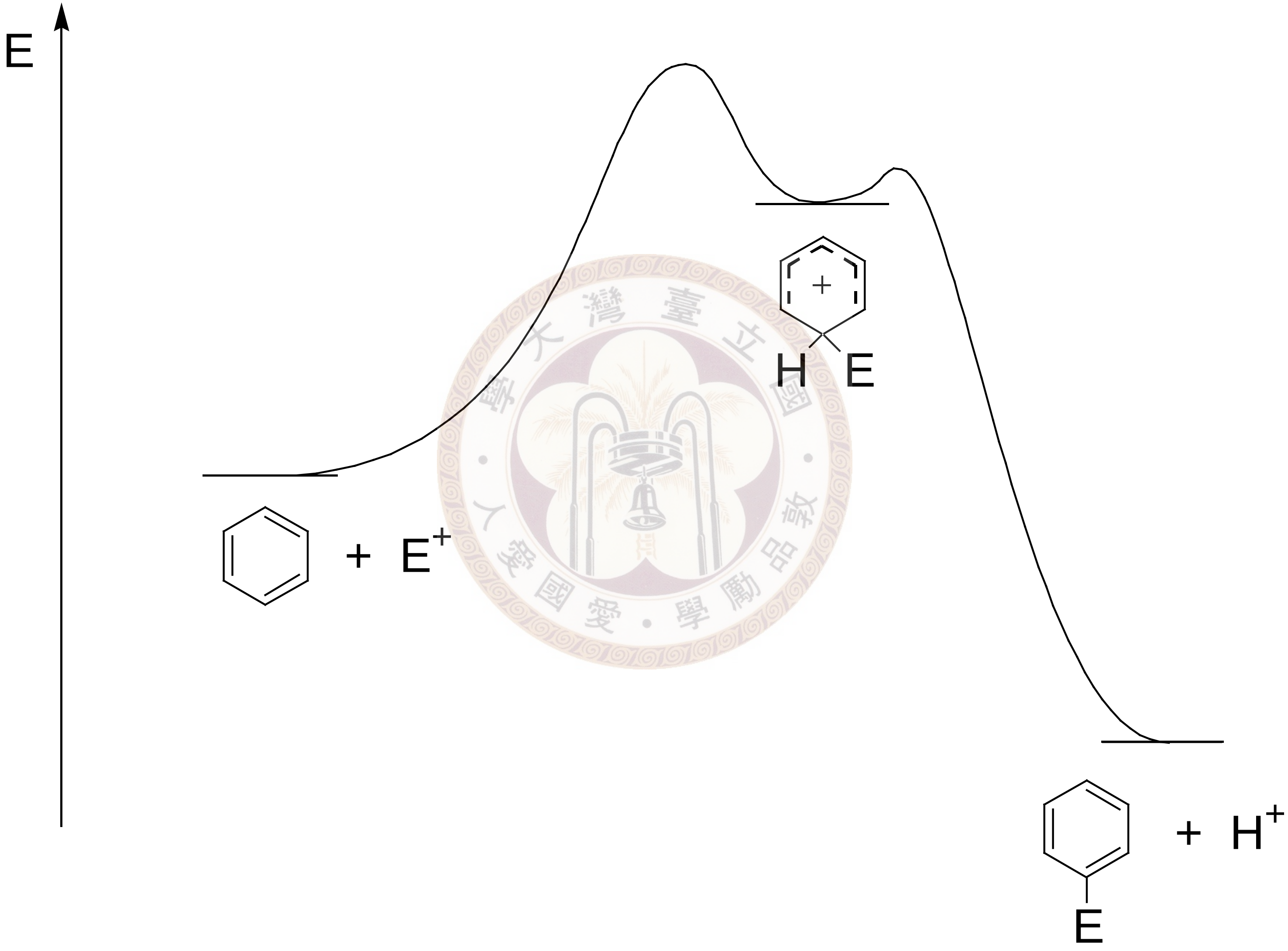


lost aromaticity

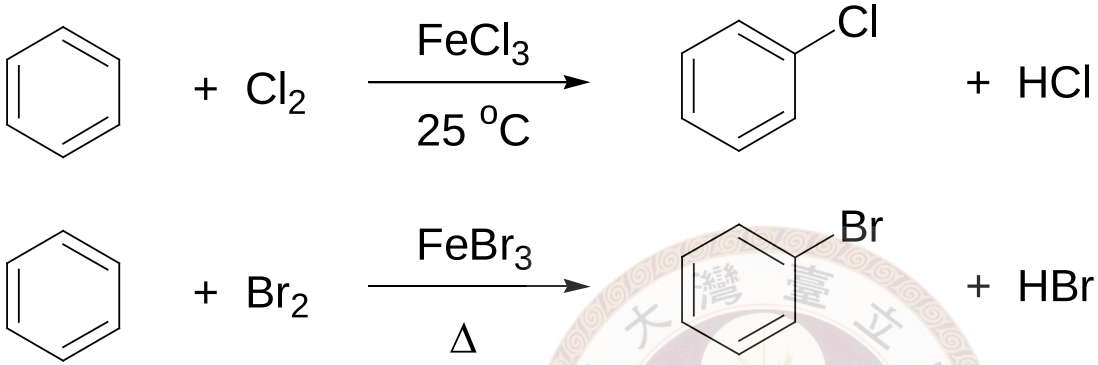
arenium ion
→a delocalized carbocation

recover aromaticity

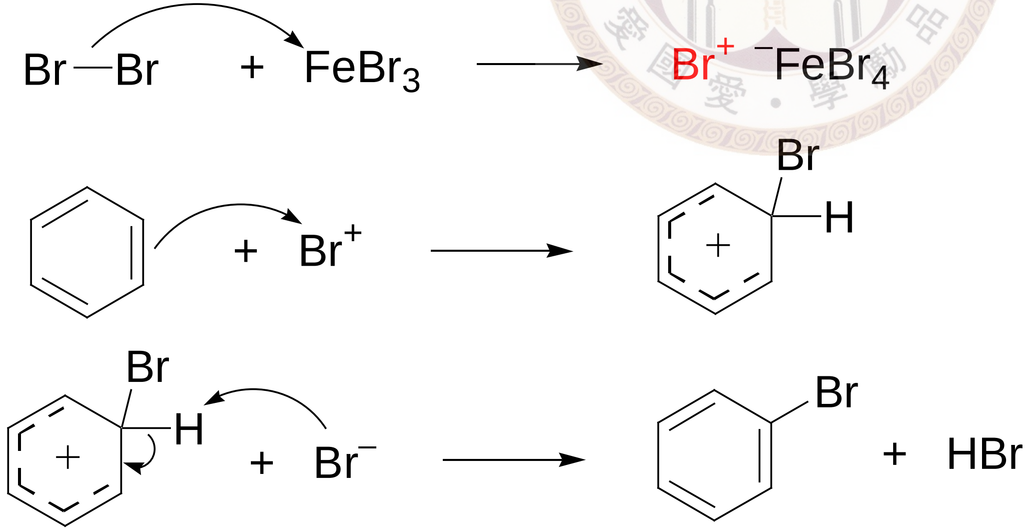
✓ Energy profile



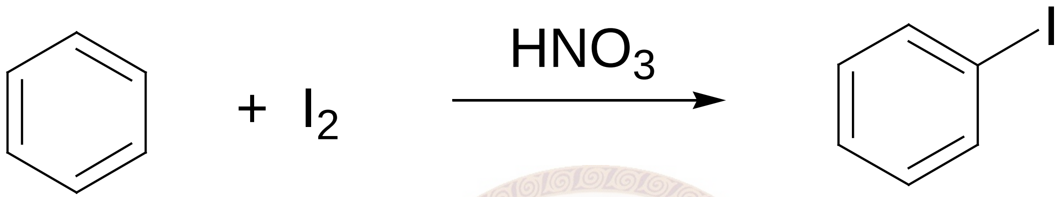
※ Halogenation



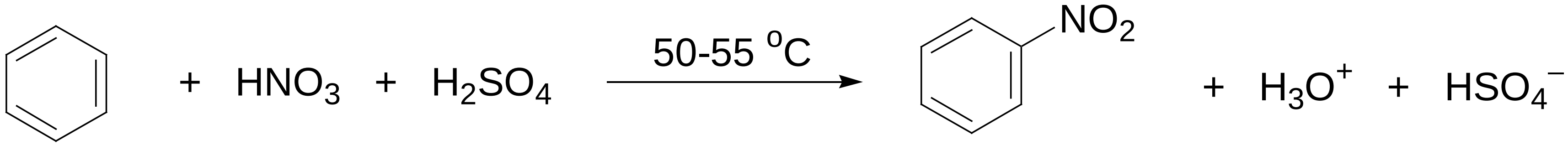
Mechanism:



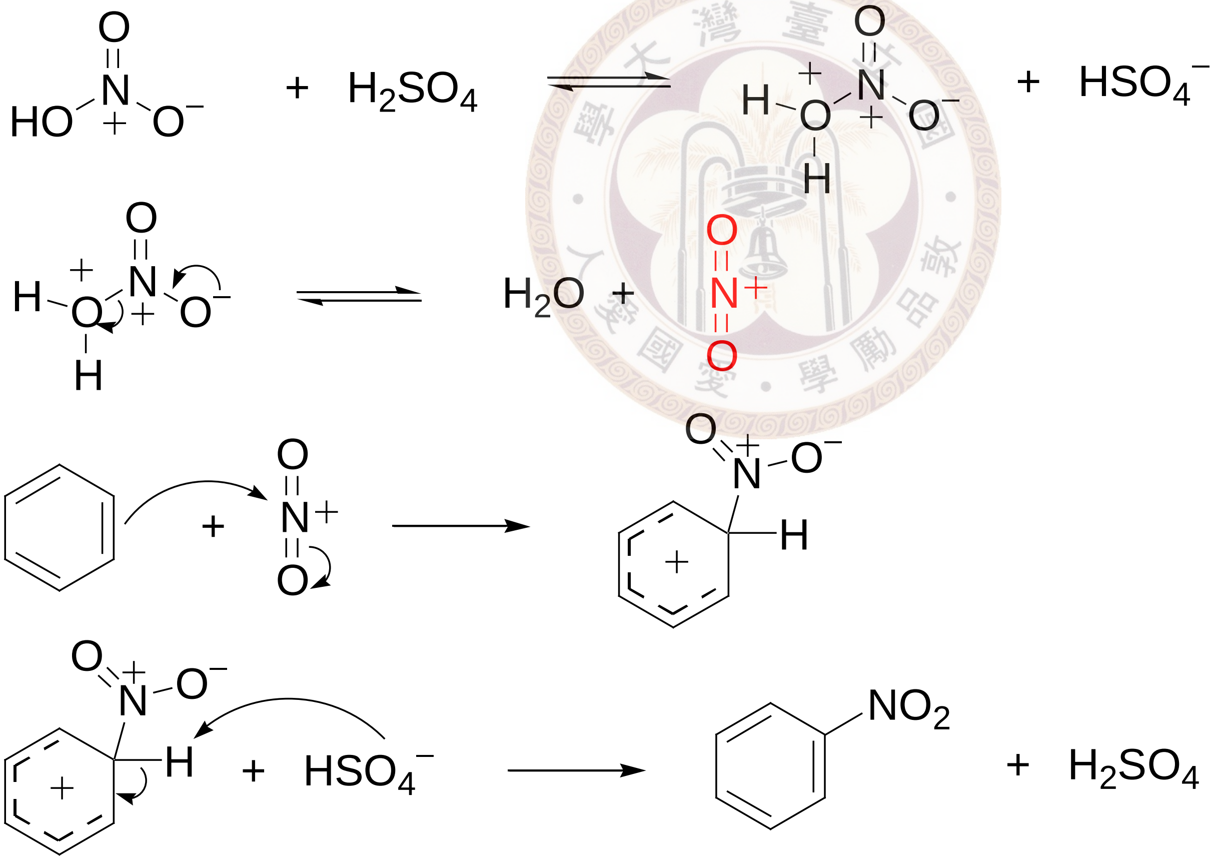
Fluorination: too reactive
Iodination: too unreactive



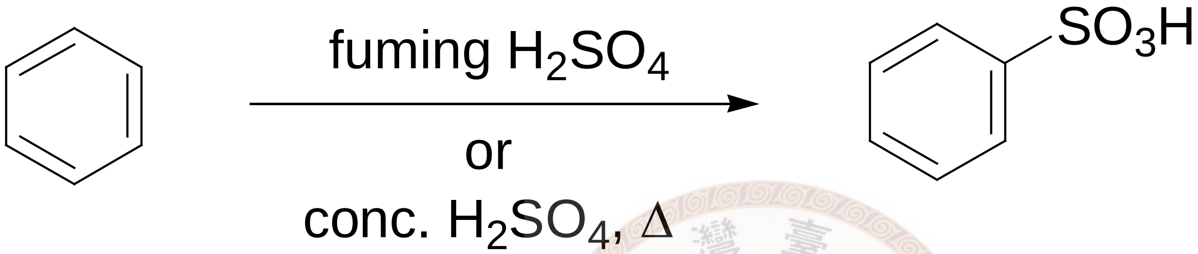
※ Nitration



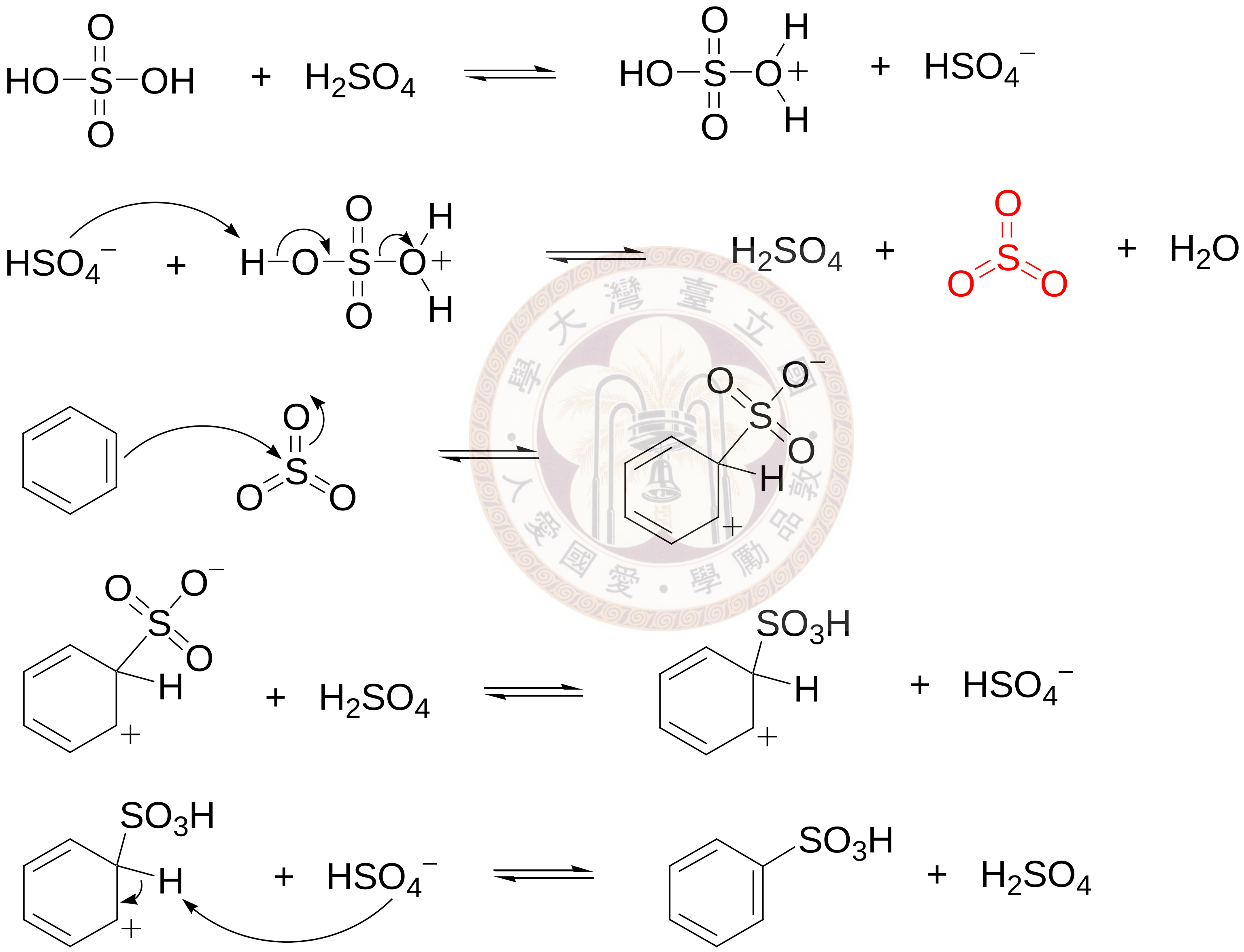
Mechanism:



※ Sulfonation



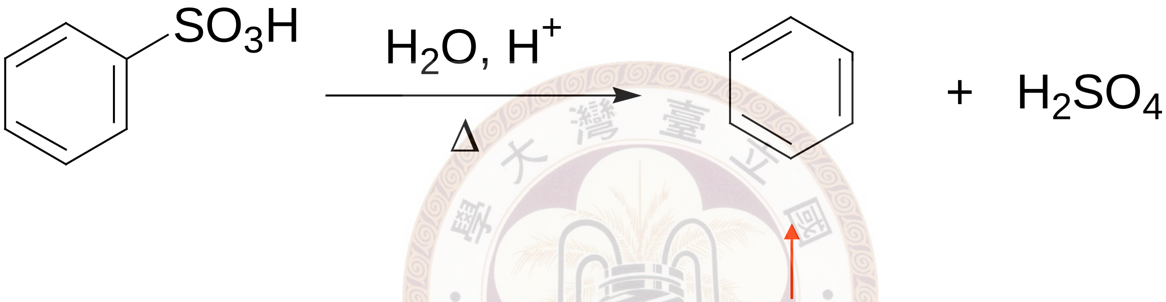
Mechanism:


HO–S(=O)(=O)–OH + H_2SO_4 ⇌ $HO–S(=O)(=O)–OH_2^+$ + HSO_4^-
HSO_4^- + $H–O–S(=O)(=O)–OH_2^+$ ⇌ H_2SO_4 + SO_3 + H_2O
+
O⁻
+
SO_3H
H
+ HSO_4^-
SO_3H + H_2SO_4

- ✓ Fuming sulfuric acid (發煙硫酸)

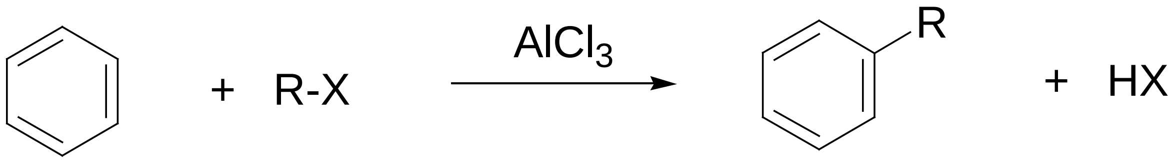
  conc. H_2SO_4 saturated with SO_3

- ✓ Sulfonation is reversible

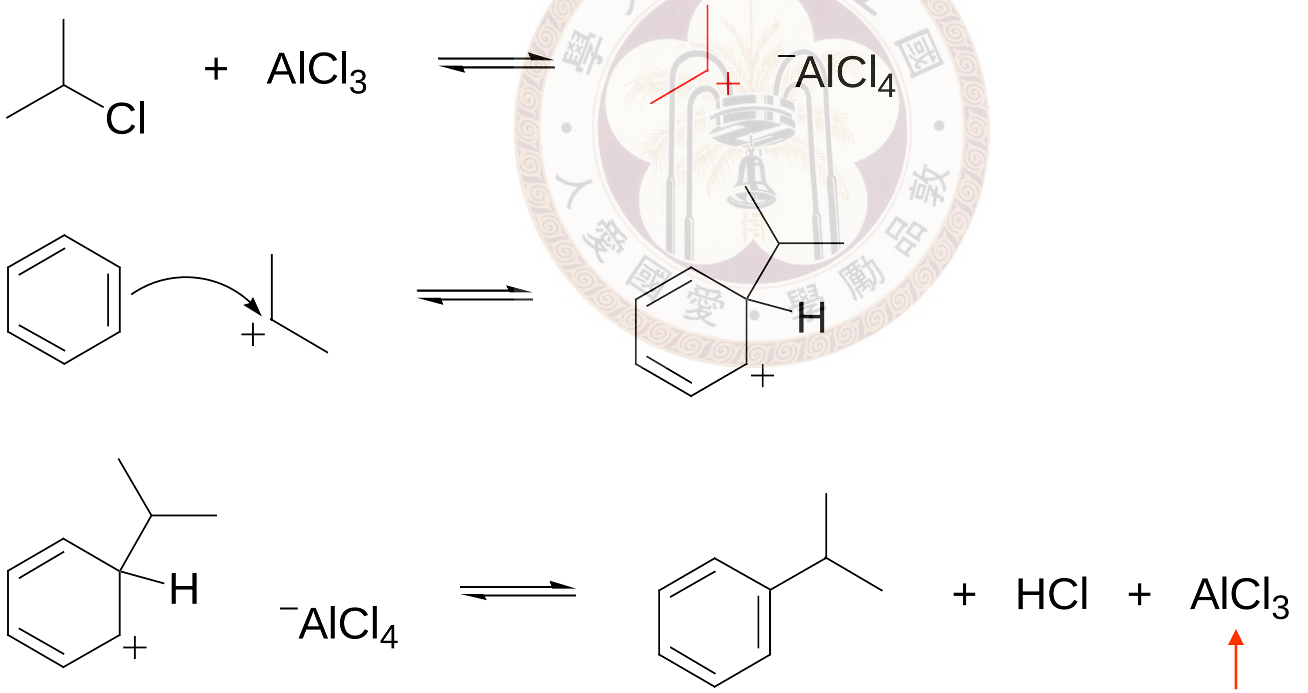


lower bp
can be removed in situ
by distillation

※ Friedel-Crafts alkylation

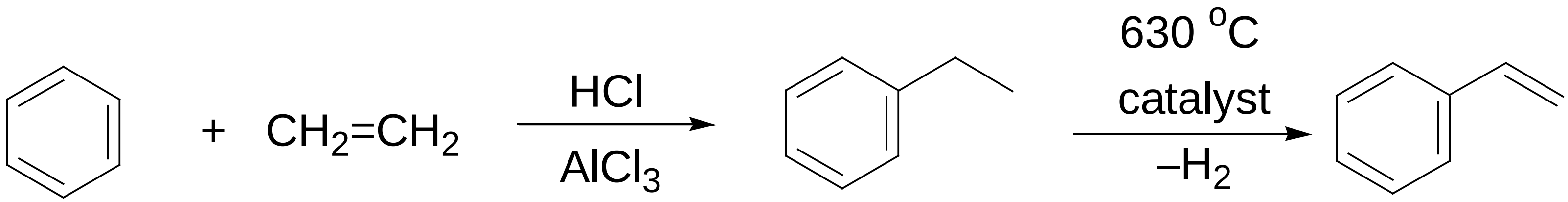


Mechanism:

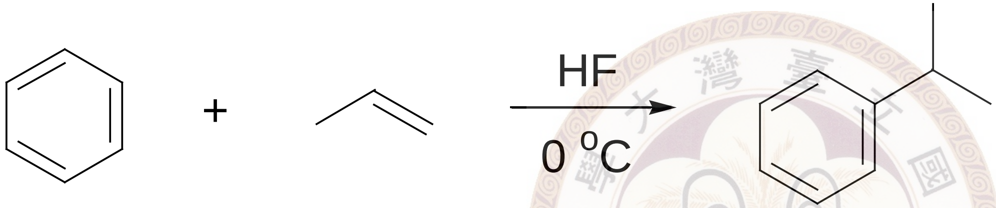


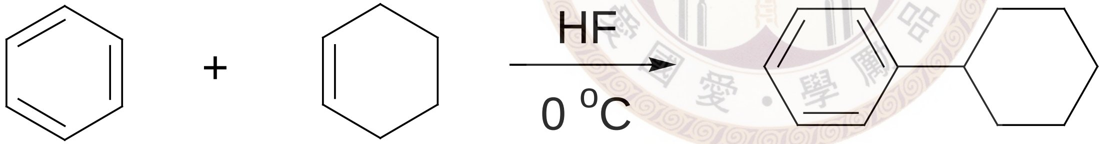
catalytic

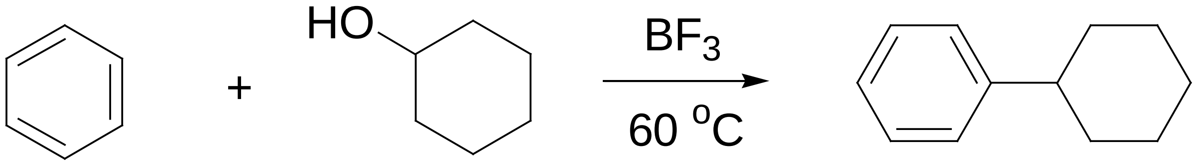
Other examples:



styrene



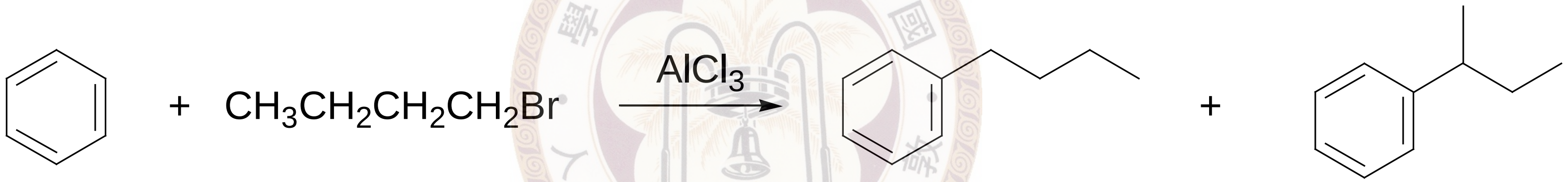




- ✓ For primary halides:
  carbocation may not be involved

$$\overset{\delta^+}{RCH_2}\text{---}Cl\text{----}\overset{\delta^-}{AlCl_3}$$

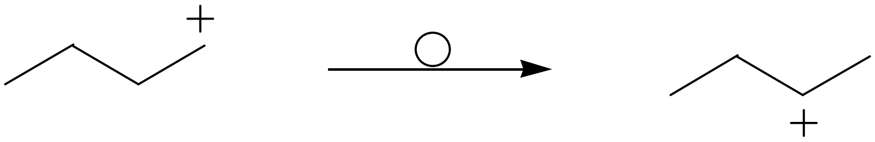
- ✓ Problems:



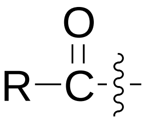
32-36%

64-68%

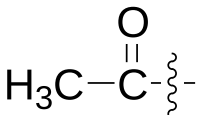
reason: due to carbocation rearrangement



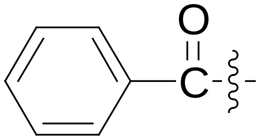
※ Friedel-Crafts acylation



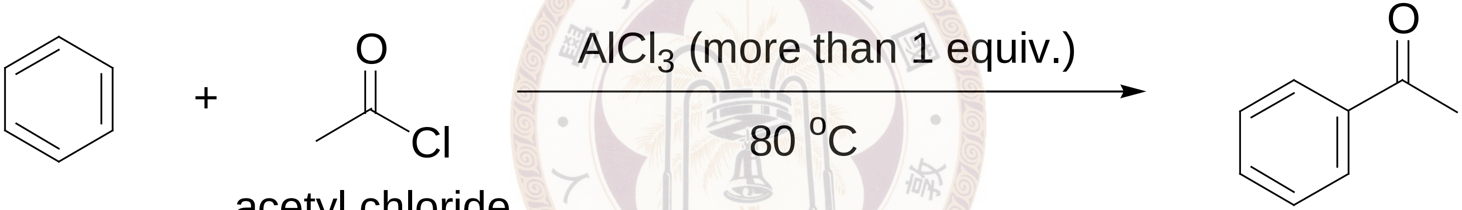
an acyl group
IUPAC: ethanoyl



acetyl (Ac)

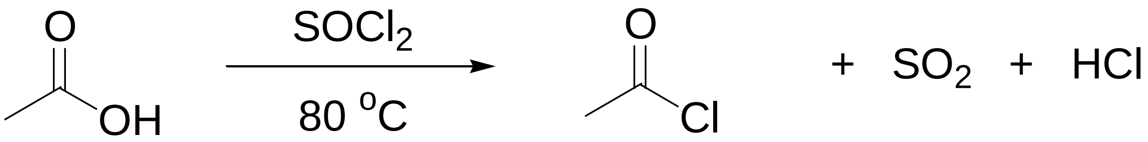


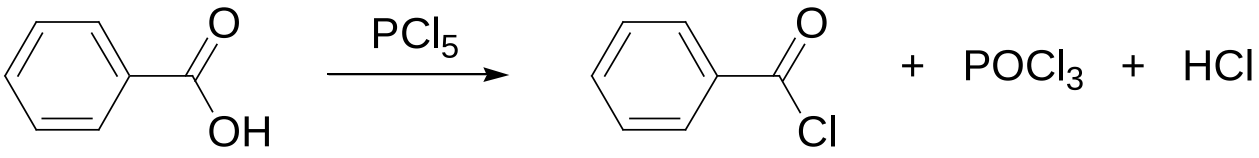
benzoyl (Bz)



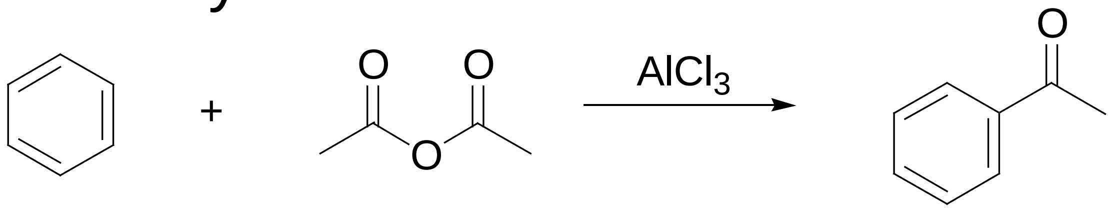
acetyl chloride

Preparation of acid chloride:

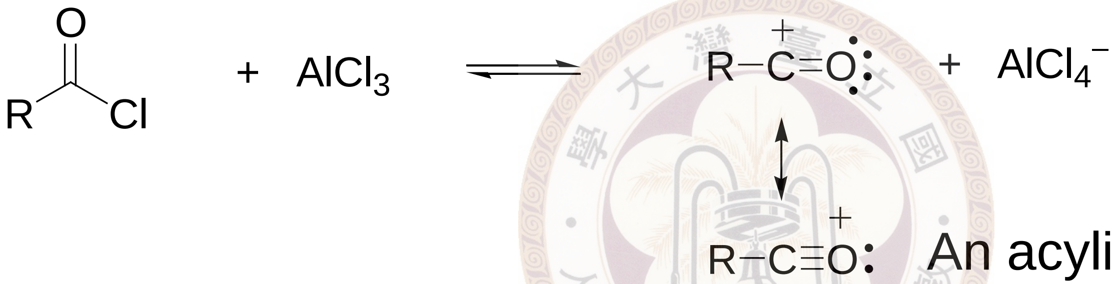




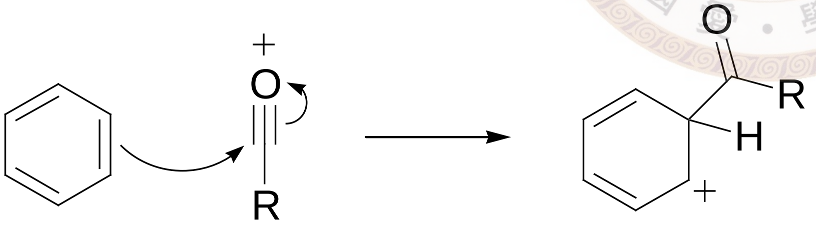
From anhydride

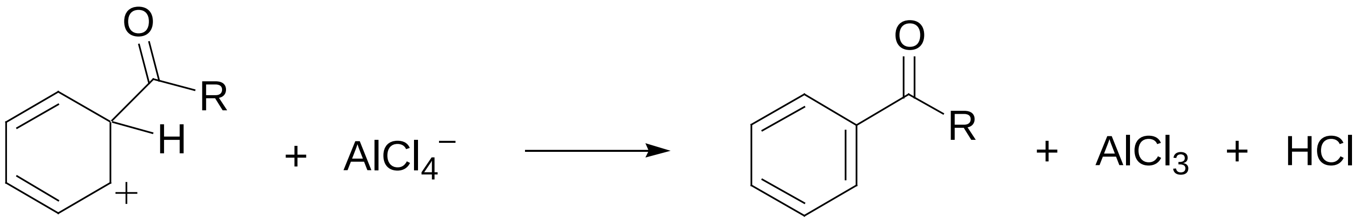


Mechanism:

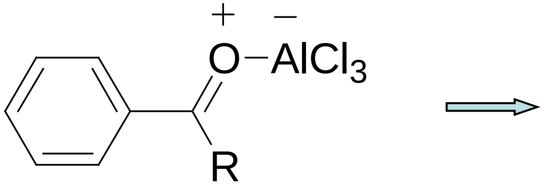


An acylium ion
very stable – does not rearrange

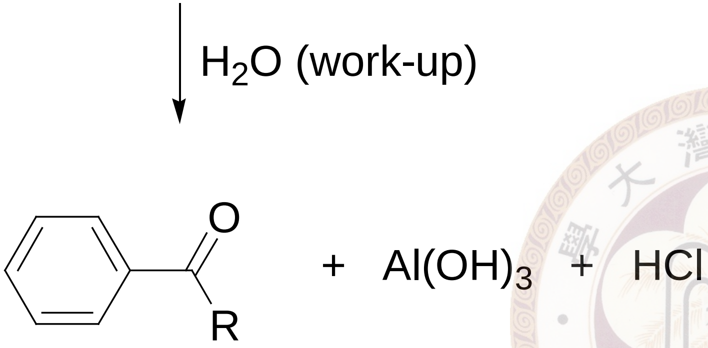




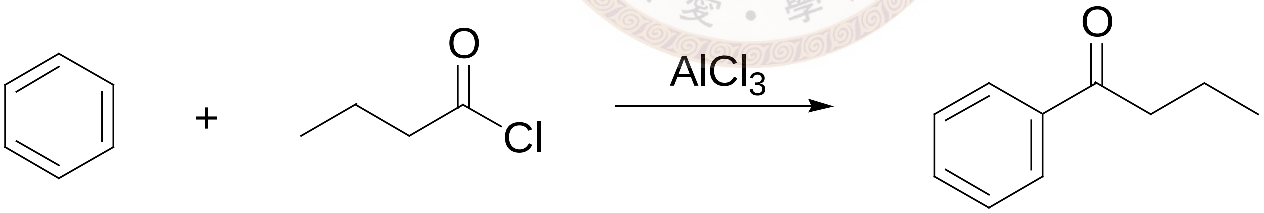
- ✓ The product will complex with $AlCl_3$

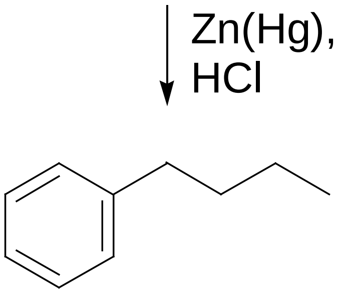


more than one equiv. of $AlCl_3$ should be used



- ✓ Compare with Friedel-Crafts alkylation

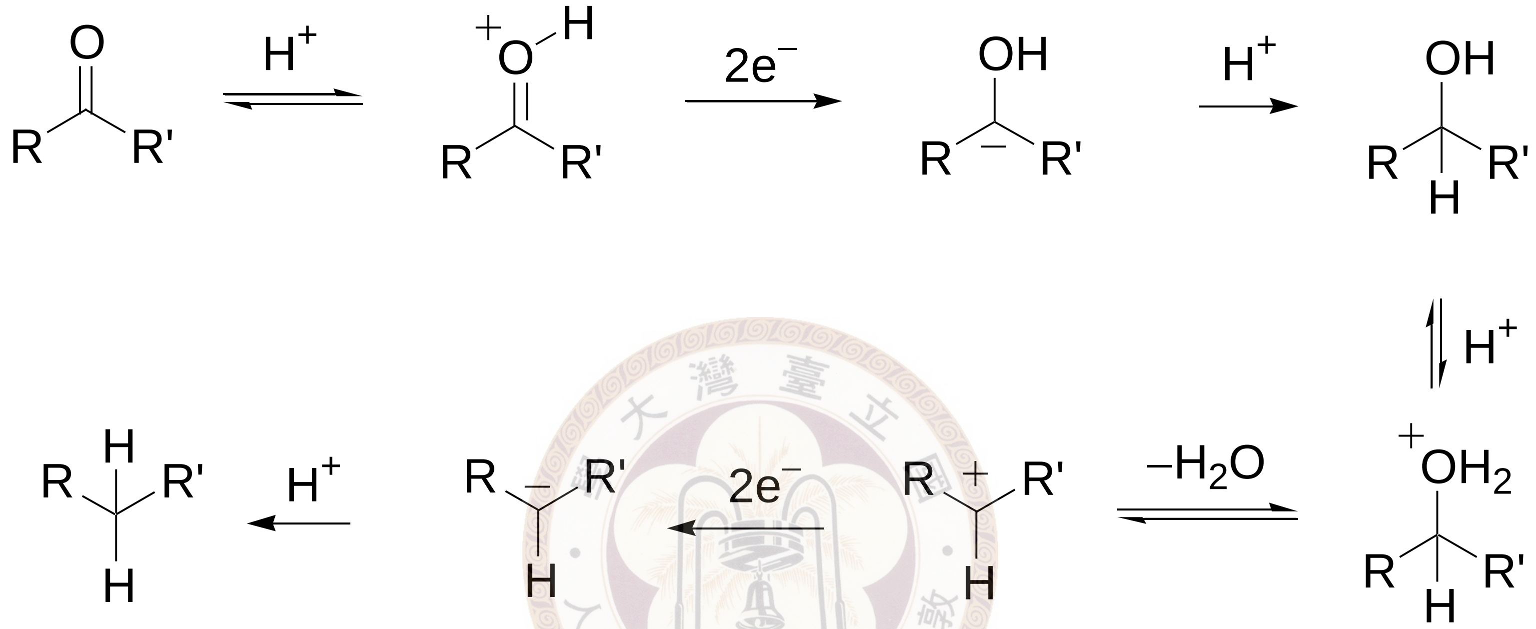




Clemmensen reduction

Solves the rearrangement problem

Mechanism of Clemmensen reduction:

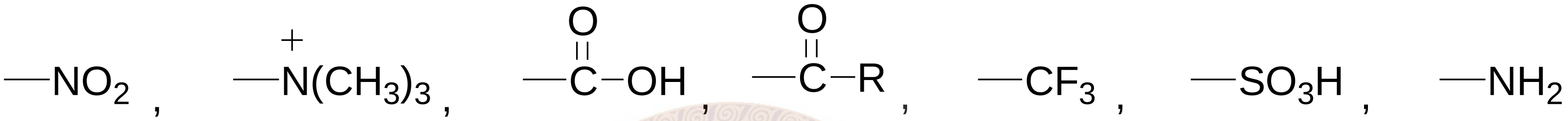


*The reason of using zinc amalgam:

to decrease the oxidative potential of zinc
so that it does not react with H^+

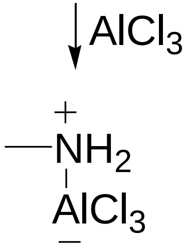
◎ Limitations of Friedel-Crafts reaction

✓ With strong EWG on benzene ring
→ no reaction



$-NO_2$, $-\overset{+}{N}(CH_3)_3$, $-\overset{O}{\overset{\|}{C}}-OH$, $-\overset{O}{\overset{\|}{C}}-R$, $-CF_3$, $-SO_3H$, $-NH_2$

(EWG: electron withdrawing group)



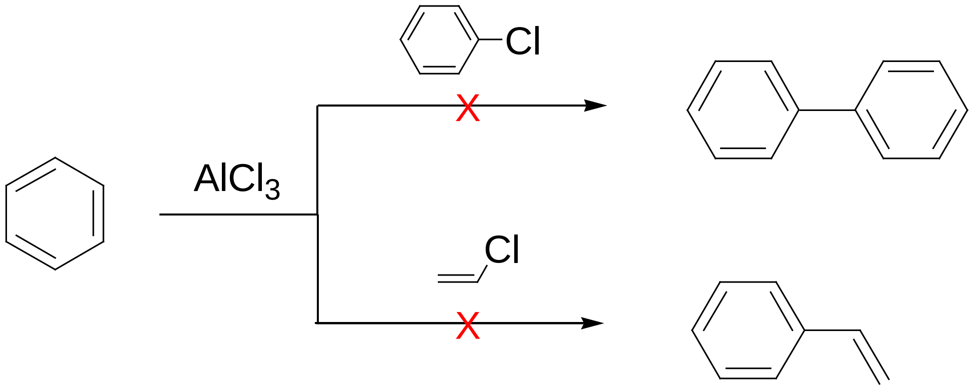
$\downarrow AlCl_3$

$-\overset{+}{N}H_2-\overset{-}{AlCl_3}$

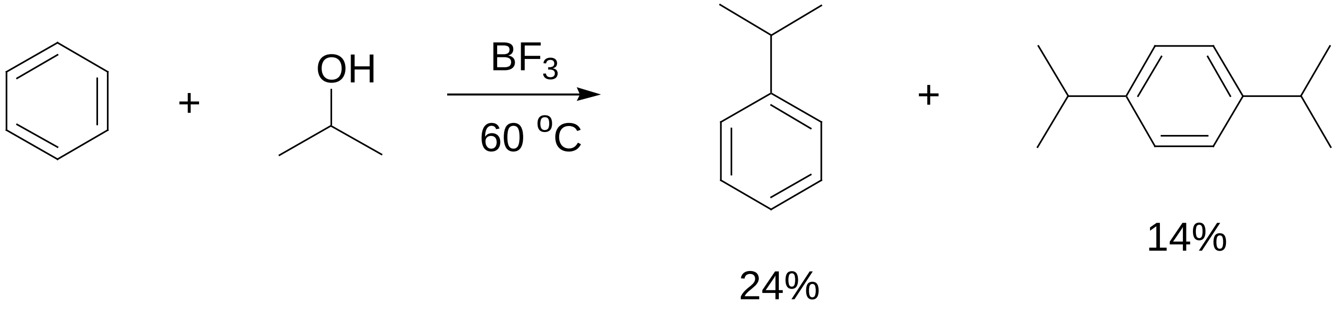
Reason:

decreases π electron density of benzene ring
→ decreases reactivity

✓ Aryl or vinyl halides do not react



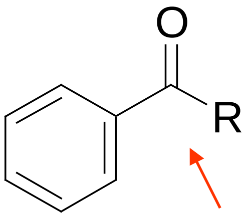
✓ Polyalkylation possible



Reason:

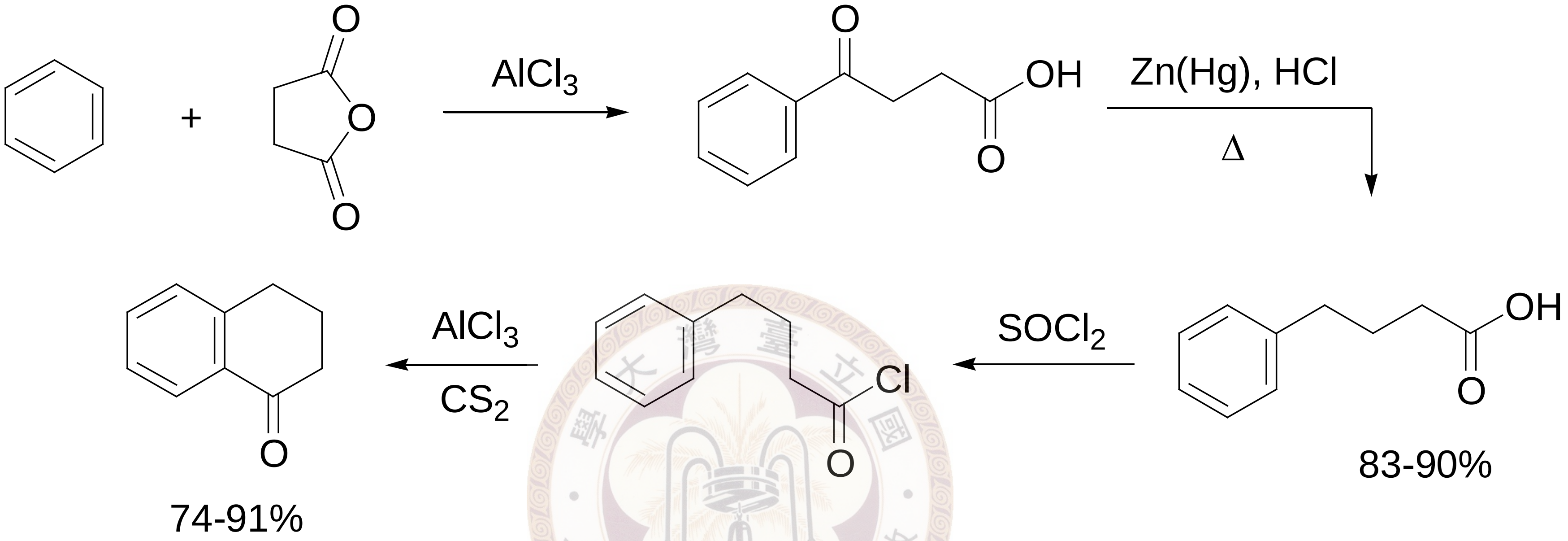
alkyl group is electron donating
→ increases π electron density of benzene ring
→ increases reactivity

Solution: acylation has no problem

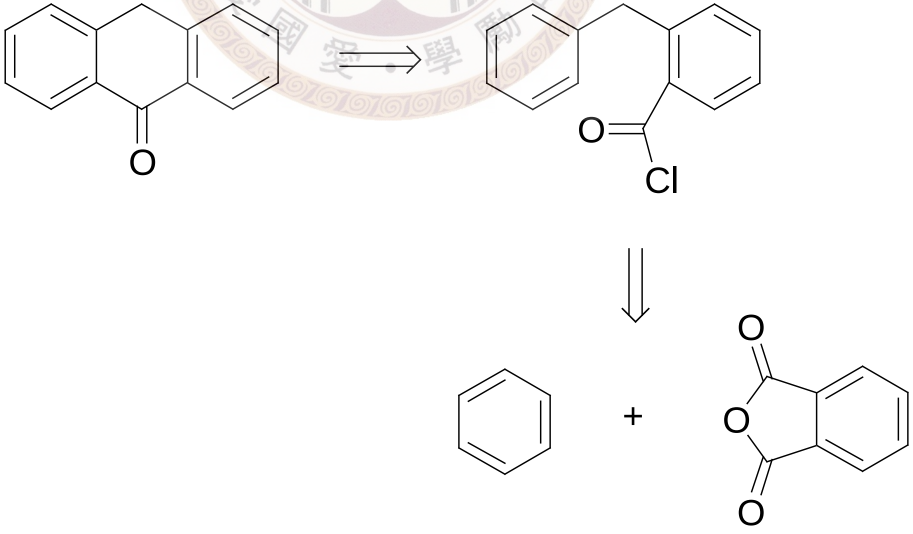


EWG
reactivity
decreases

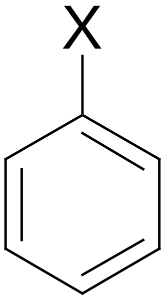
More examples



Synthesize :

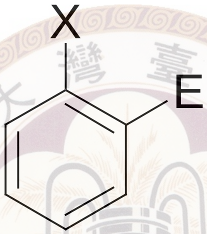


※ Effect of substituents

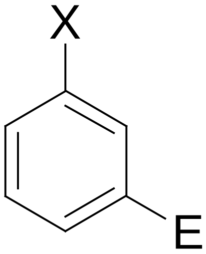


Reactivity:
more reactive or less reactive than benzene?

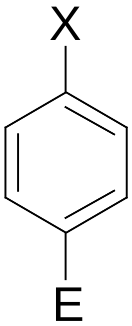
Orientation?



ortho
鄰

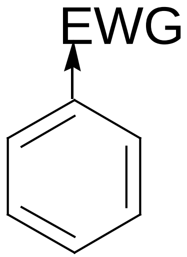


meta
間



para
對

◎ Electron withdrawing groups – deactivating groups



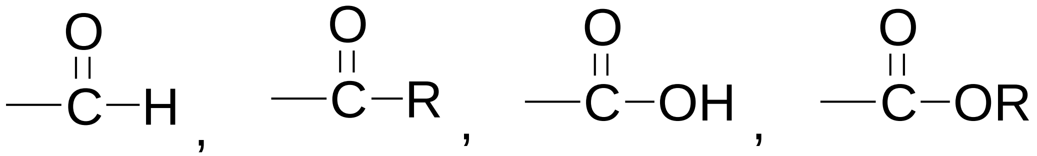
← electron poor
less reactive

Strongly deactivating:

$-NO_2$, $-\overset{+}{N}R_3$, $-CF_3$, $-CCl_3$,

Moderately deactivating:

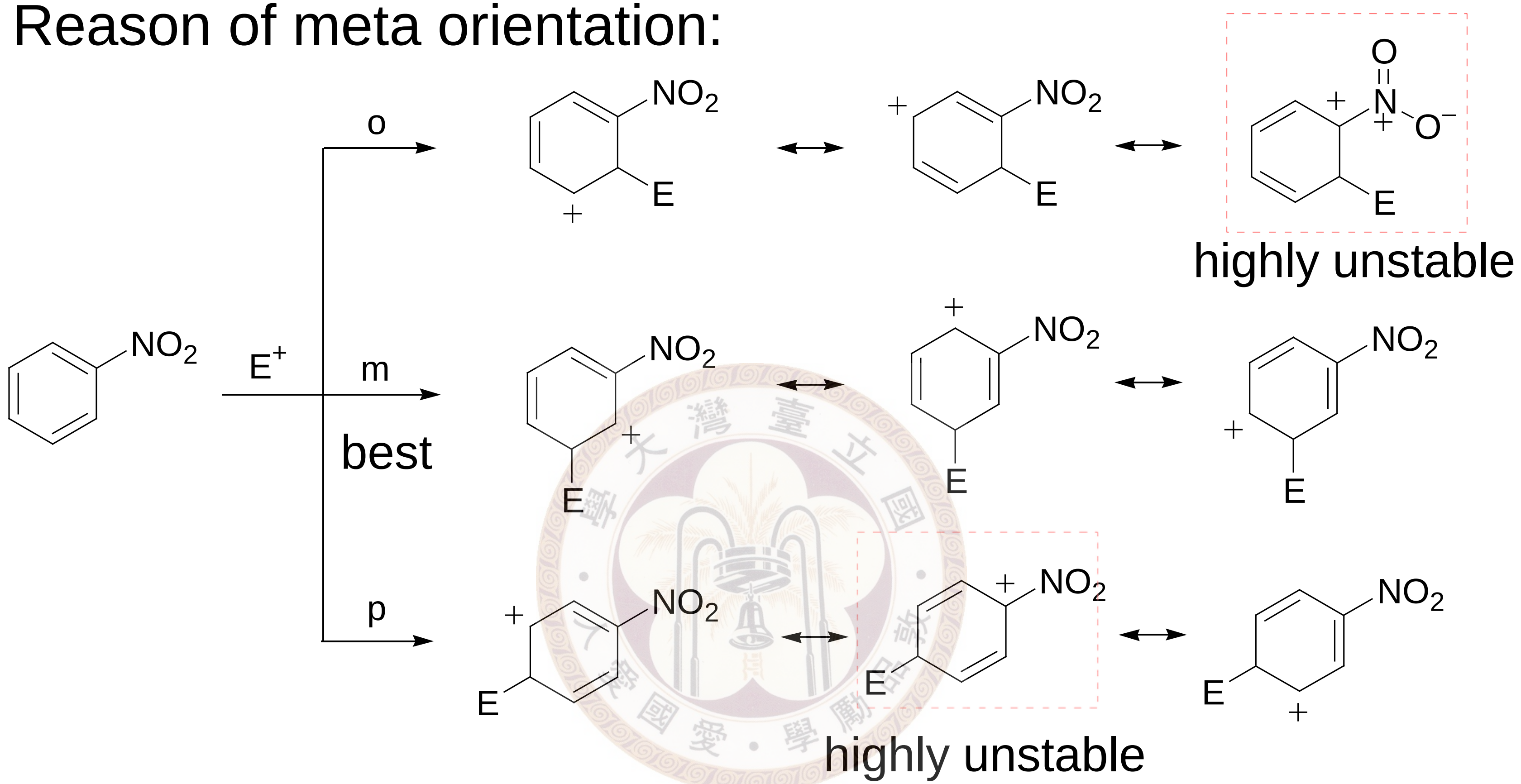
$-C\equiv N$, $-SO_3H$,

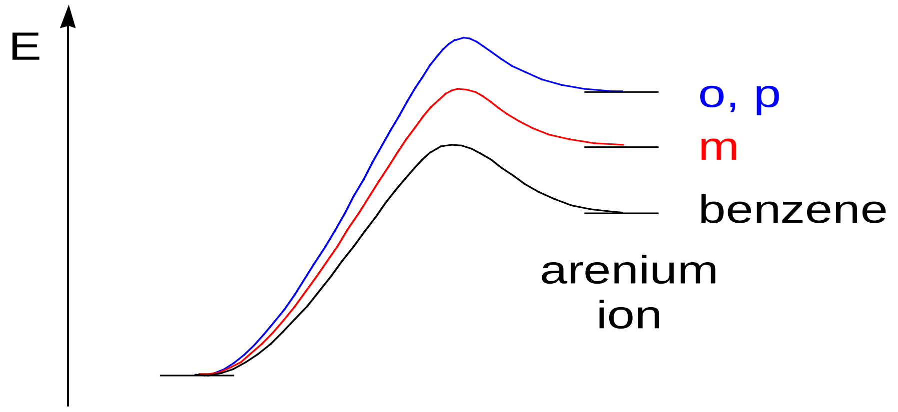


$-\overset{O}{\overset{\|}{C}}-H$, $-\overset{O}{\overset{\|}{C}}-R$, $-\overset{O}{\overset{\|}{C}}-OH$, $-\overset{O}{\overset{\|}{C}}-OR$

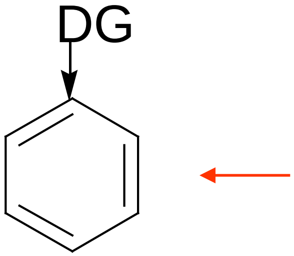
They are meta directors

Reason of meta orientation:





◎ Electron donating groups – activating groups



electron rich
more reactive

Strongly activating: $-\ddot{N}H_2$, $-\ddot{N}HR$, $-\ddot{N}R_2$

$-\underset{\cdot\cdot}{\ddot{O}}H$, $-\underset{\cdot\cdot}{\ddot{O}}\!:^{-}$

Moderately activating: $-\ddot{N}HCOCH_3$, $-\ddot{N}HCOR$,

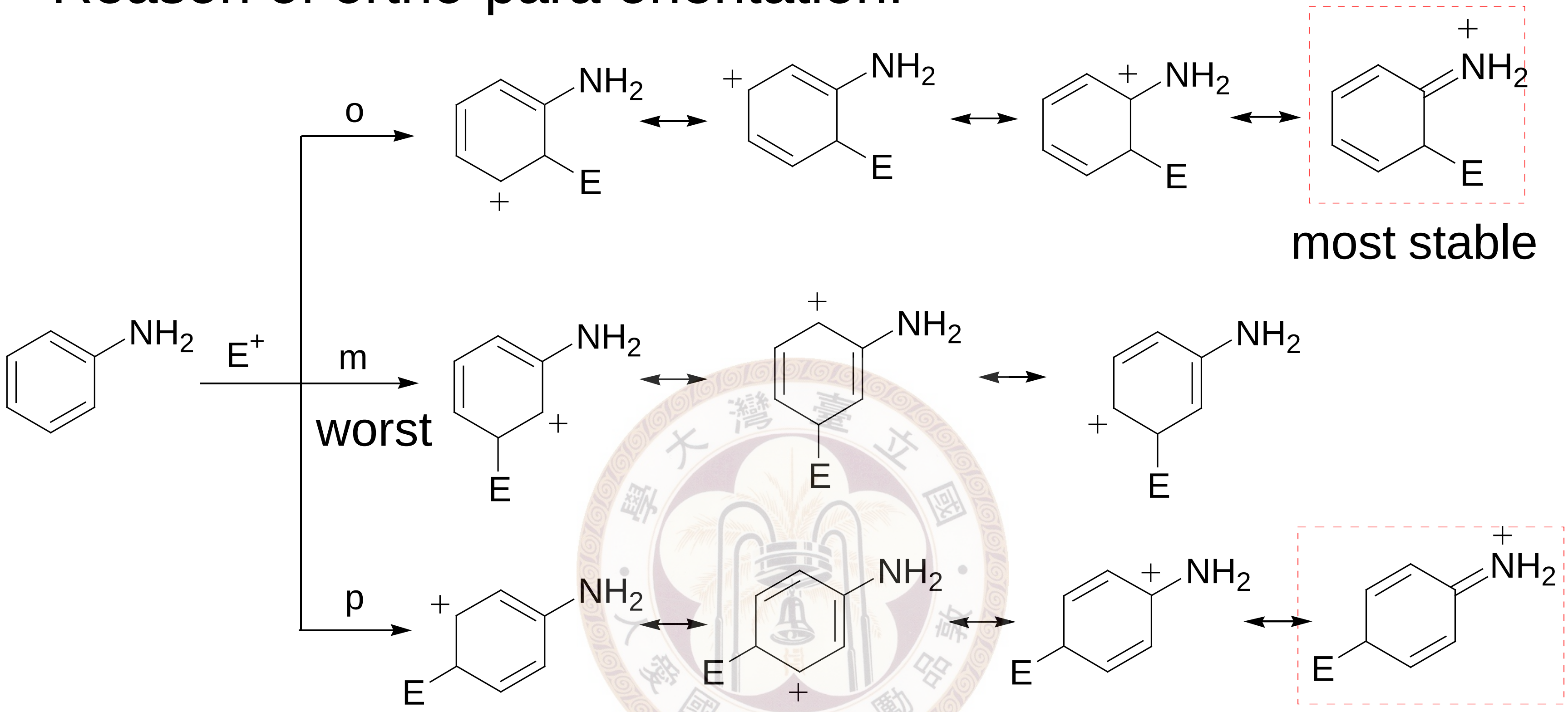
$-\ddot{O}R$

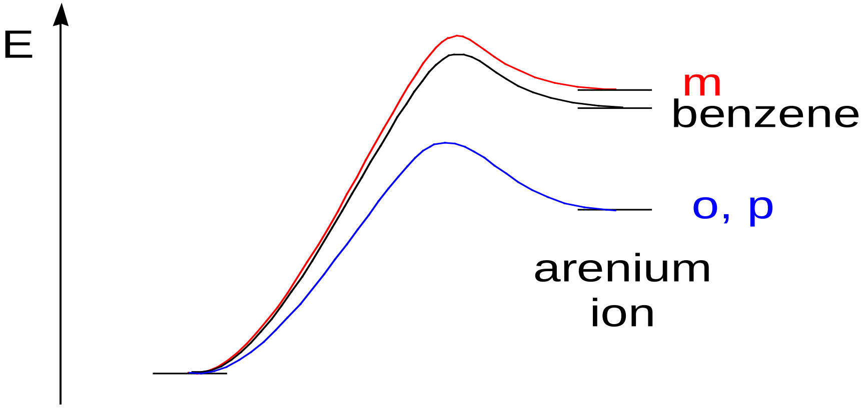
All
contain
lone pair
electrons

Weakly activating: $-R$, $-C_6H_5$

They are ortho-para directors

Reason of ortho-para orientation:





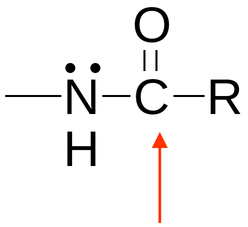
✓ Activating groups such as –NH_2 (with lone pair) are resonance donating

In fact, N and O (with high EN) are inductively withdrawing with the resonance donating effect stronger than the inductive effect

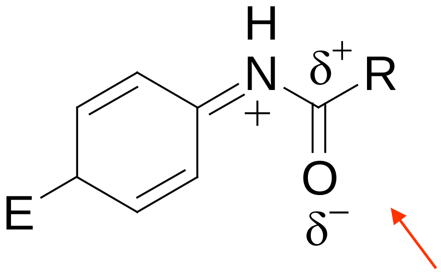
✓ Ability of resonance donating

$-NH_2, -NR_2 > -OH, -OR$

smaller EN　　larger EN

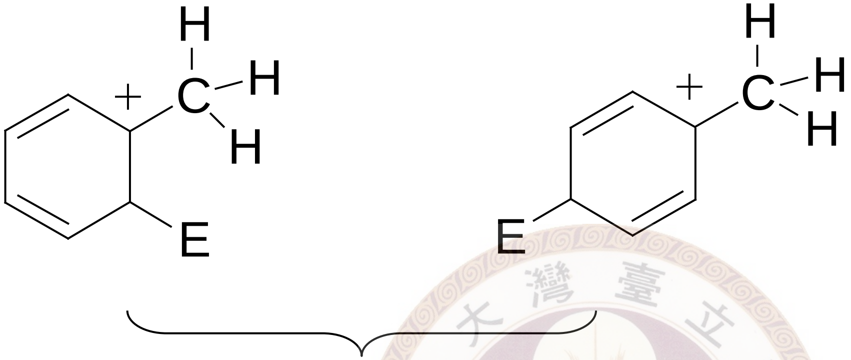


Electron withdrawing
→ decreases the resonance donating ability of N



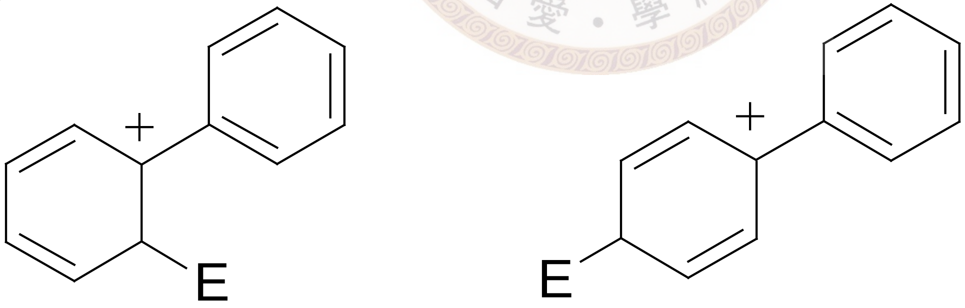
Not so good

Alkyl substituents



weakly stabilized via hyperconjugation

Phenyl



carbocation stabilized by conjugation with phenyl group

◎ F, Cl, Br, I:

weak deactivating but ortho-para director

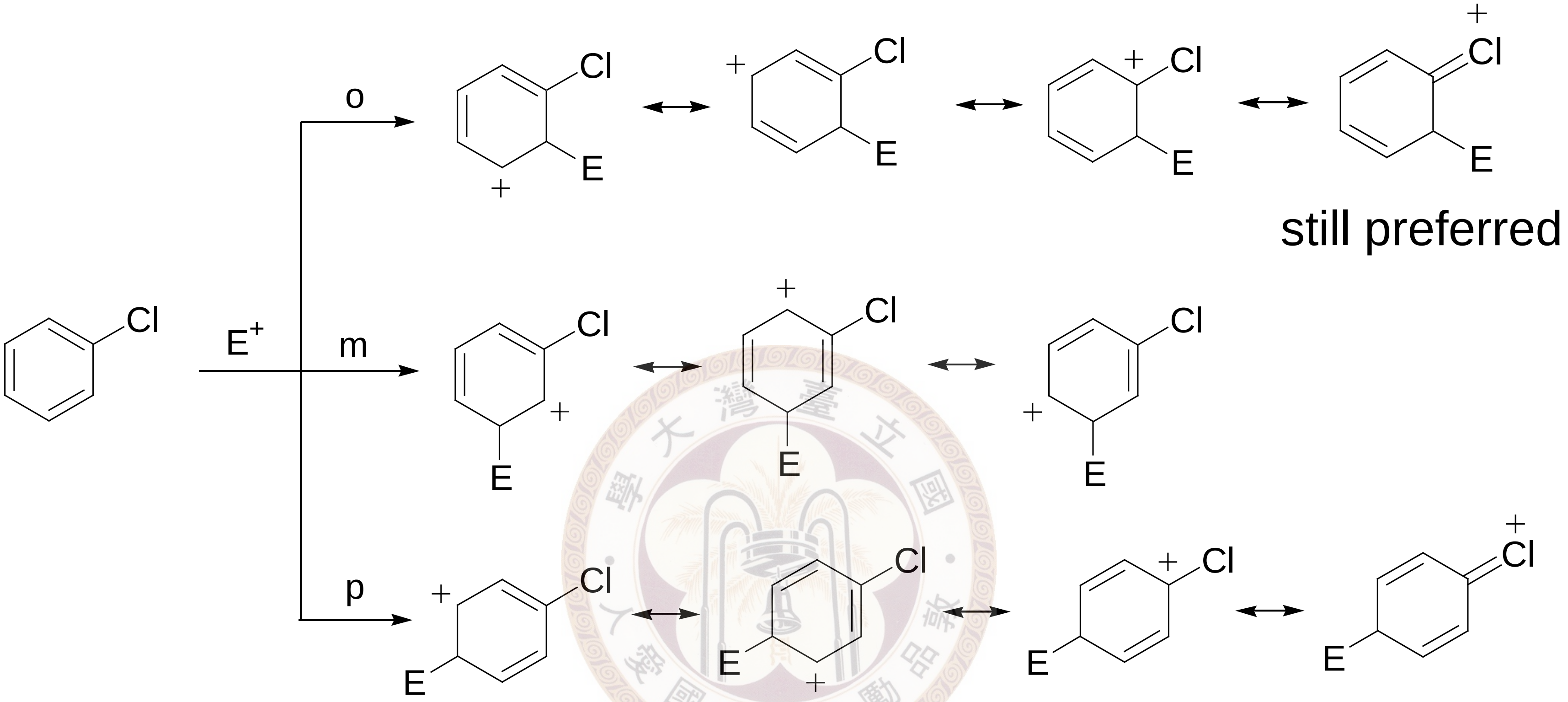
–F: very high EN
→ worse donor
→ inductive effect larger than resonance effect

–Cl
–Br
–I
} lower EN
but resonance effect is even lower

C and Cl belong to different period
→ weak π bonding (poor orbital overlap)

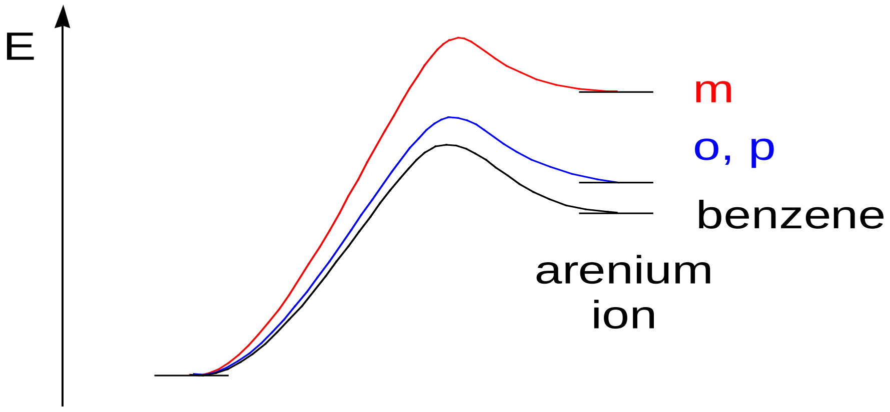
Overall: weak deactivating

Reason of ortho-para orientation:



still preferred

still preferred



◎ Summary

$–NO_2$, $–\overset{+}{N}R_4$
etc.

strong EWG
deactivating
meta director

–F, Cl, Br, I

weakly deactivating
o, p-director

$–NH_2$
–OH
etc.
with lone pair
strong DG

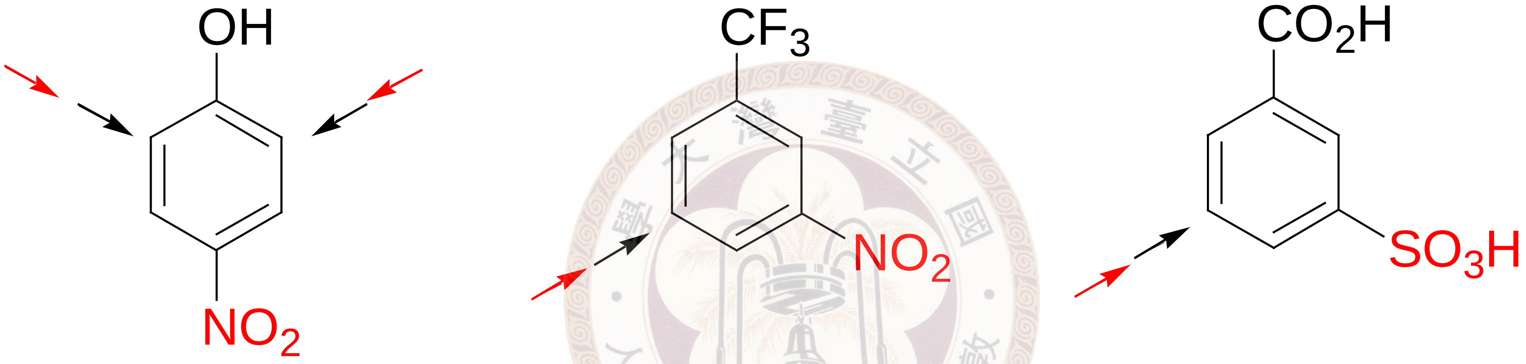
alkyl
aryl

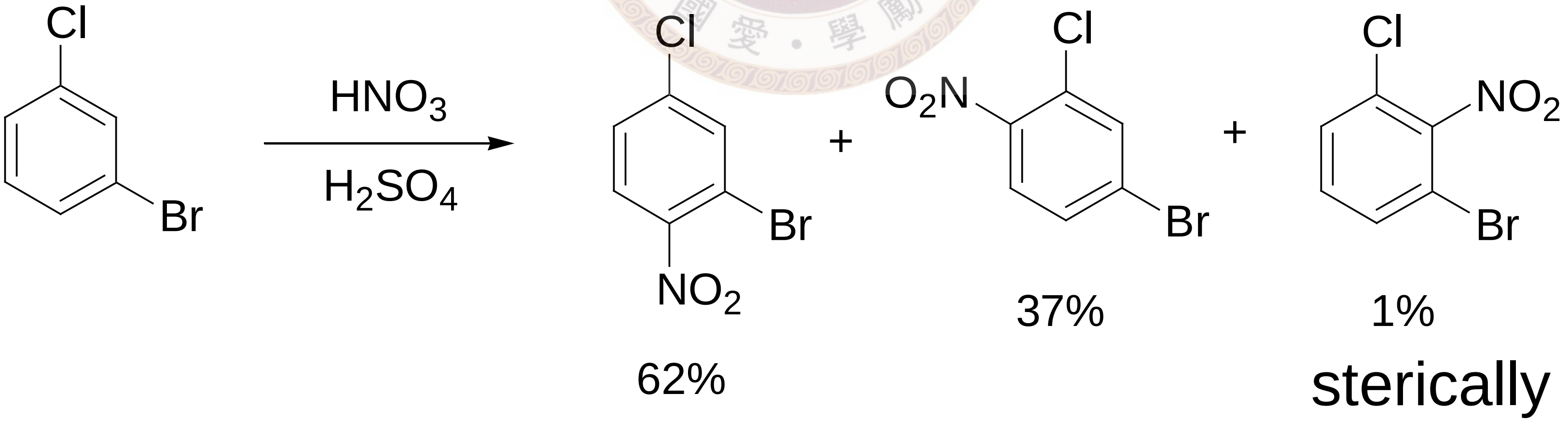
weak DG

activating
o, p-director

◎ With more than one substituents

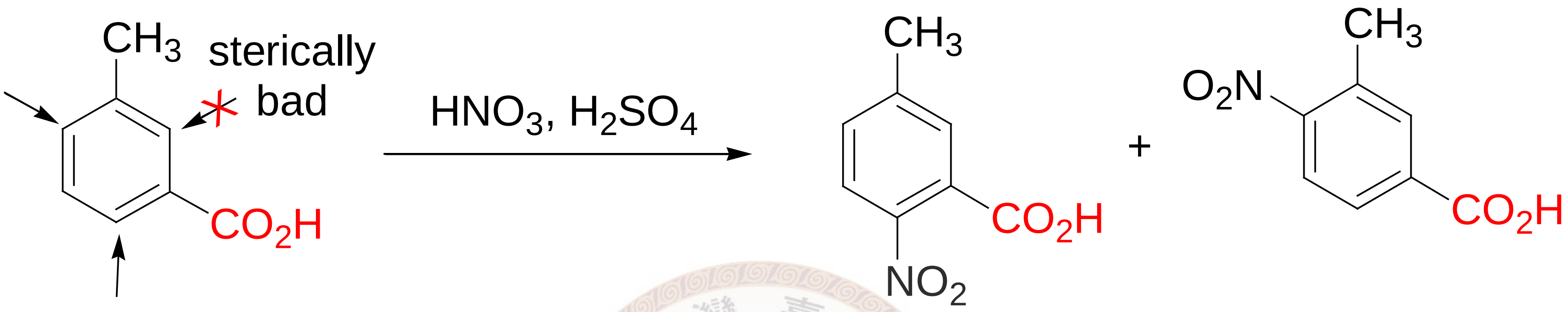
✓ Consonant: no problem





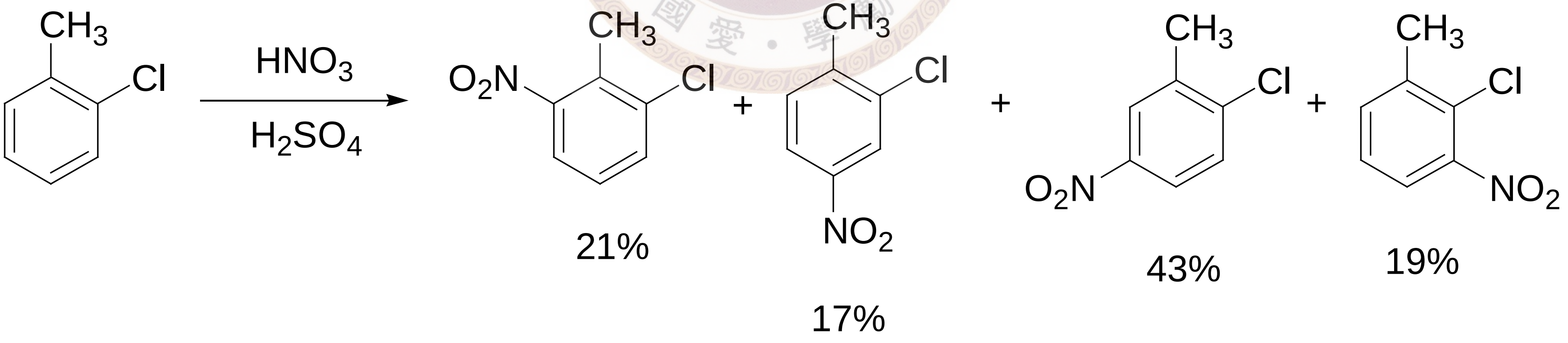
sterically unfavorable

✓ Dissonant: the stronger activating group controls



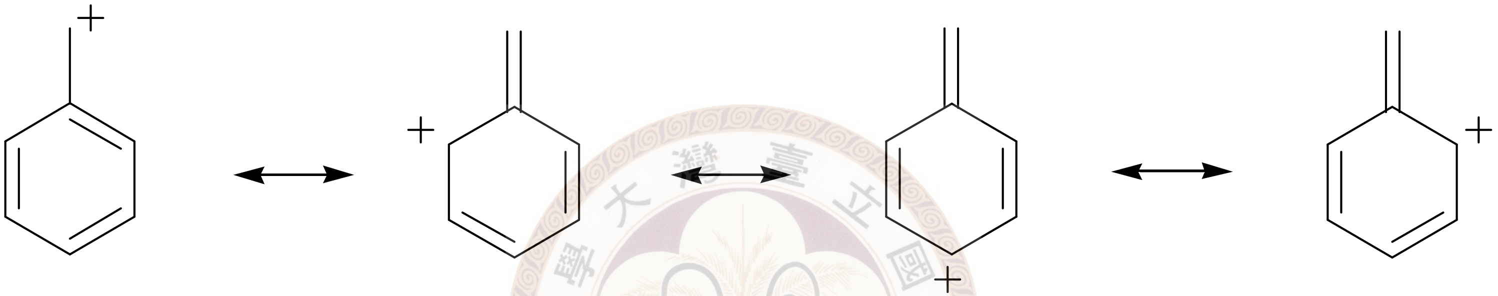
✓ Weak deactivating vs. weak activating

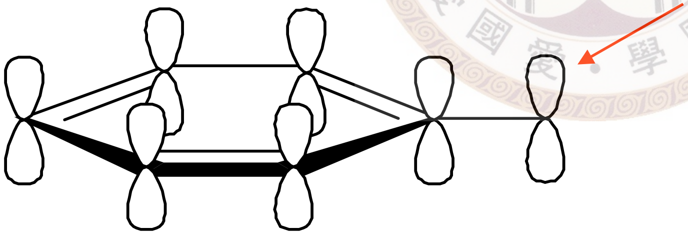
– difficult to predict



※ Reactions of the side chain of alkylbenzenes

✓ Benzylic cation: stabilized by resonance effect

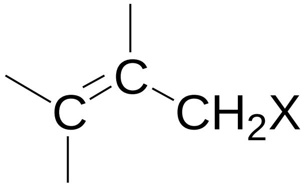




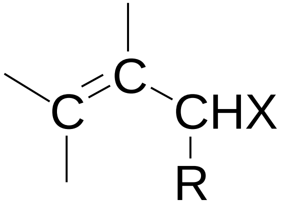
This orbital is in conjugation with the aromatic ring

✓ Benzylic radical is also stabilized for the same reason

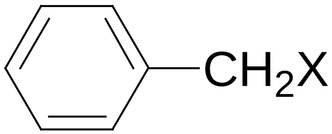
✓ For nucleophilic substitution reaction



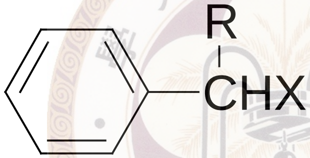
1^o allylic



2^o allylic



1^o benzylic

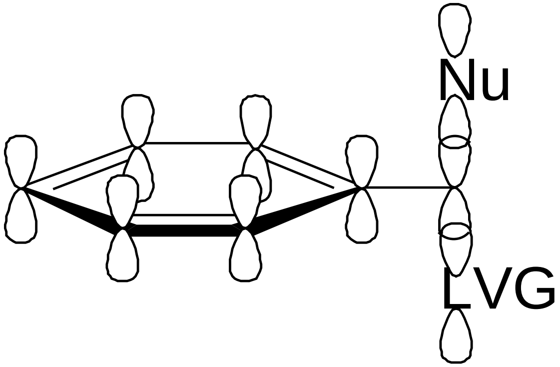


2^oenzylic

Go through S_N1 or S_N2

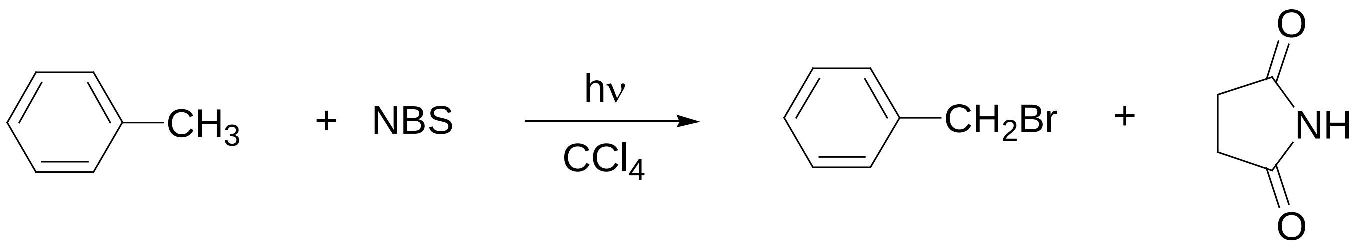
↑

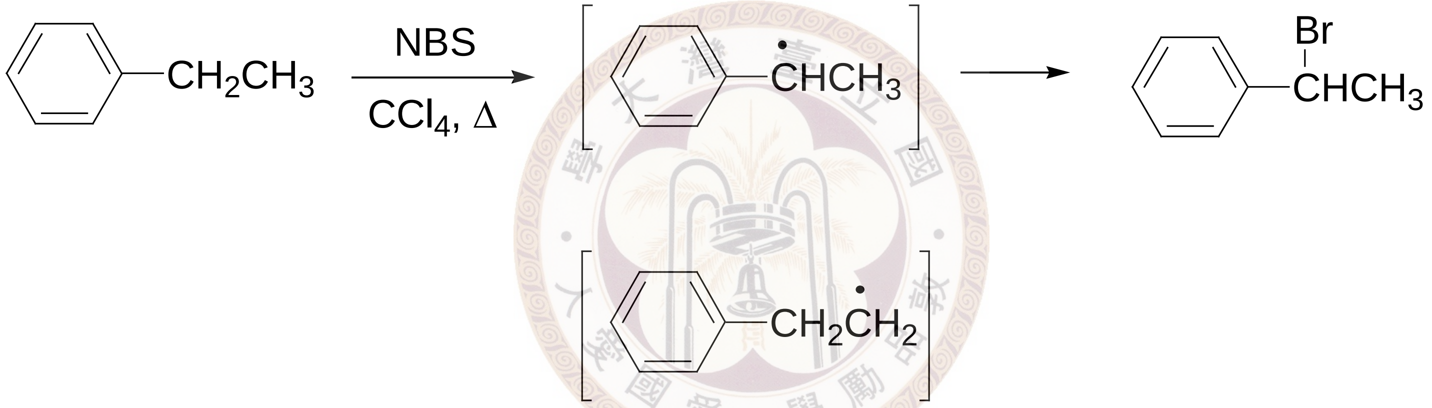
The allylic and benzylic carbocation is more stable



The transition state of S_N2 reaction is also stabilized by conjugation

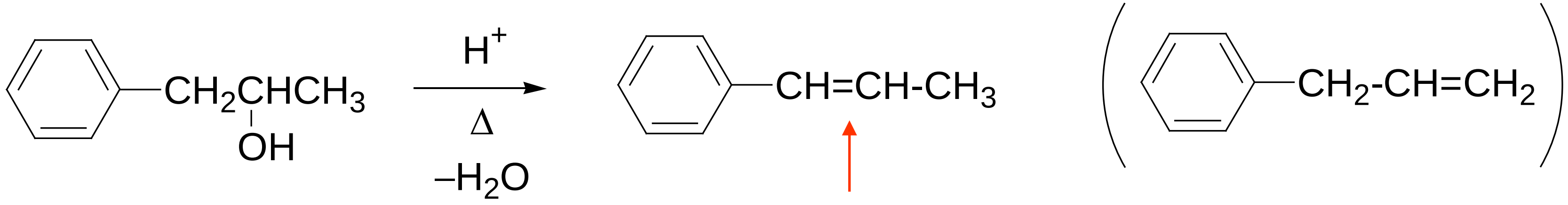
◎ Halogenation of benzylic position





less stable
not formed

◎ The effect of conjugation

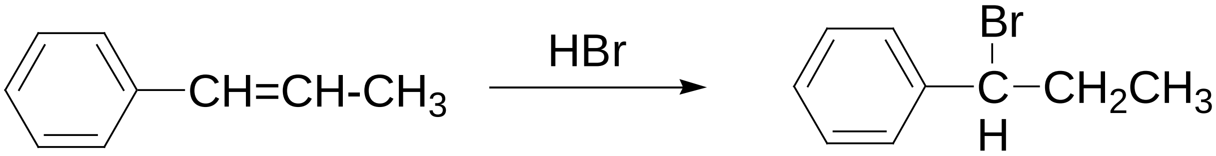


conjugated with benzene ring → more stable

not formed

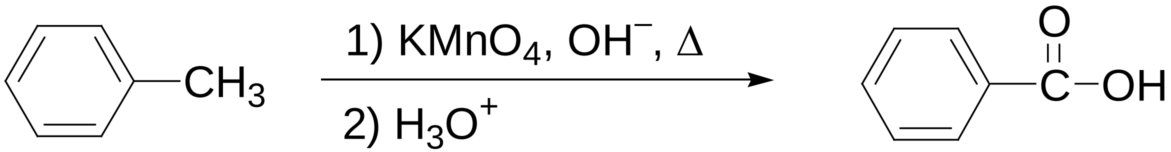
◎ Some chemistry of alkenylbenzenes

Formation of more stable radical (anti-Markovnikov's orientation)

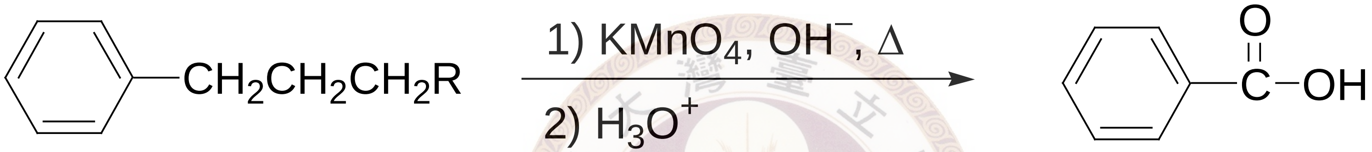


Formation of more stable carbocation (Markovnikov's orientation)

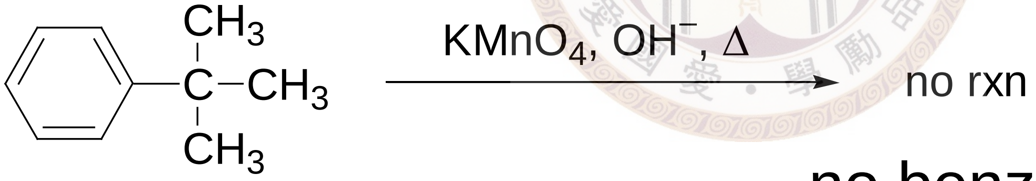
◎ Side chain oxidation



benzoic acid
~100%



Possibly go through a benzylic radical

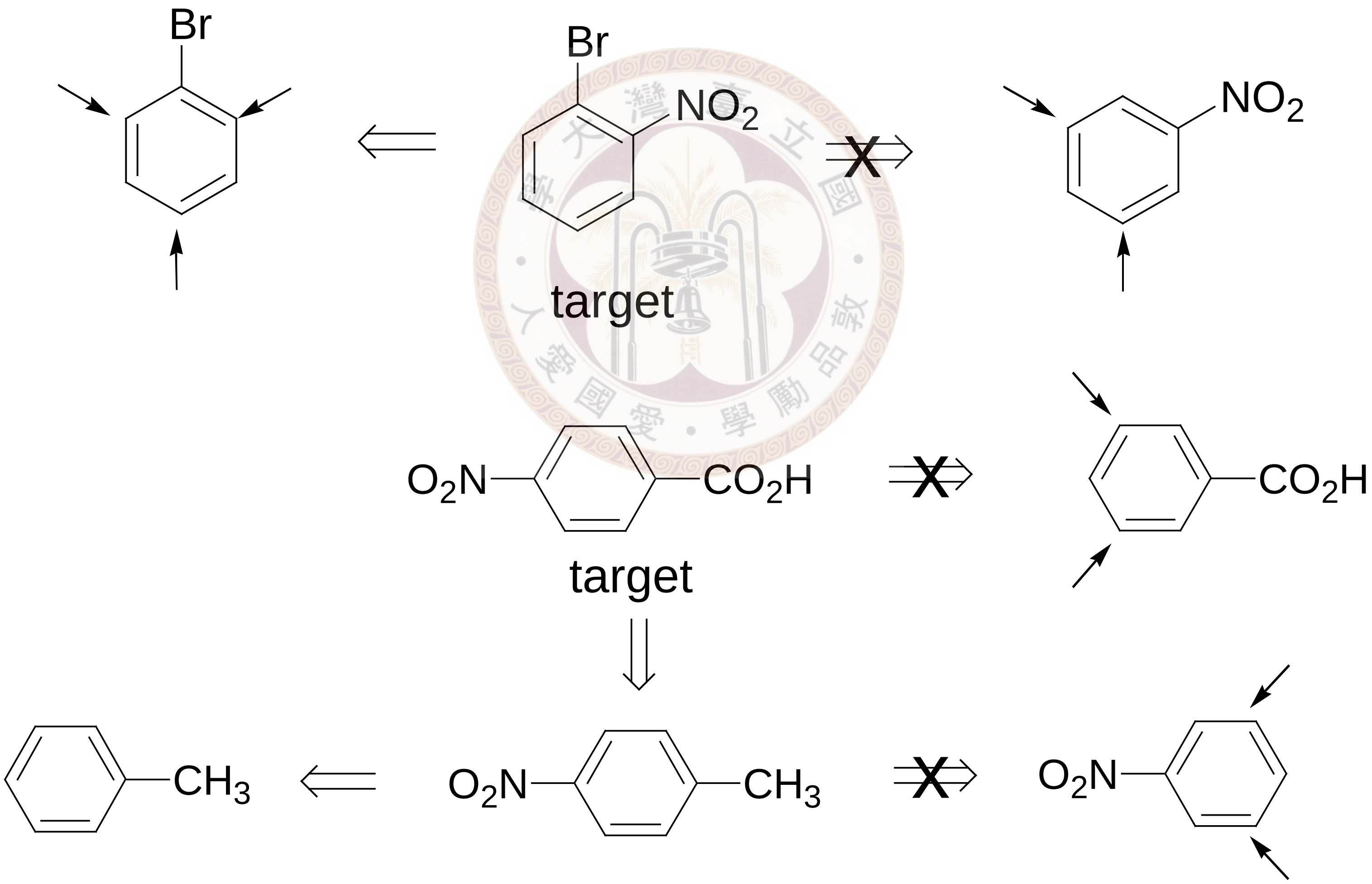


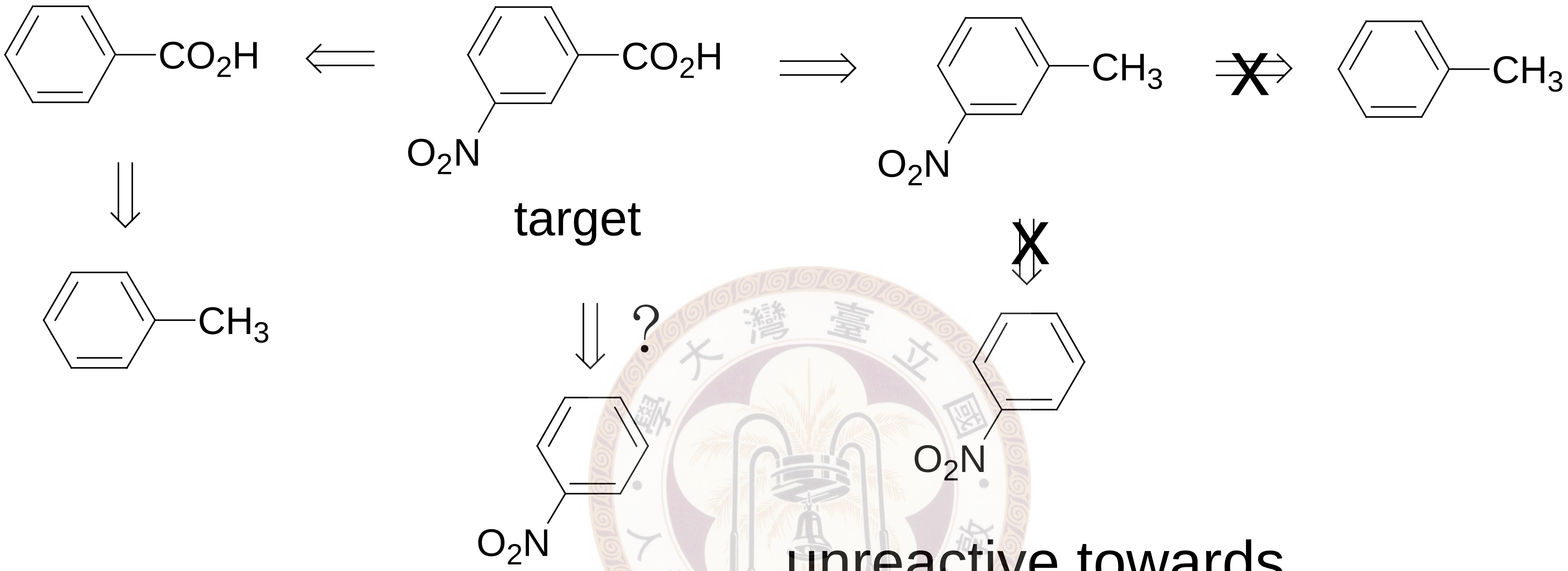
no benzylic hydrogen
→ no oxidation

※ Synthetic application

✓ Introduction of substituents

different order → different product

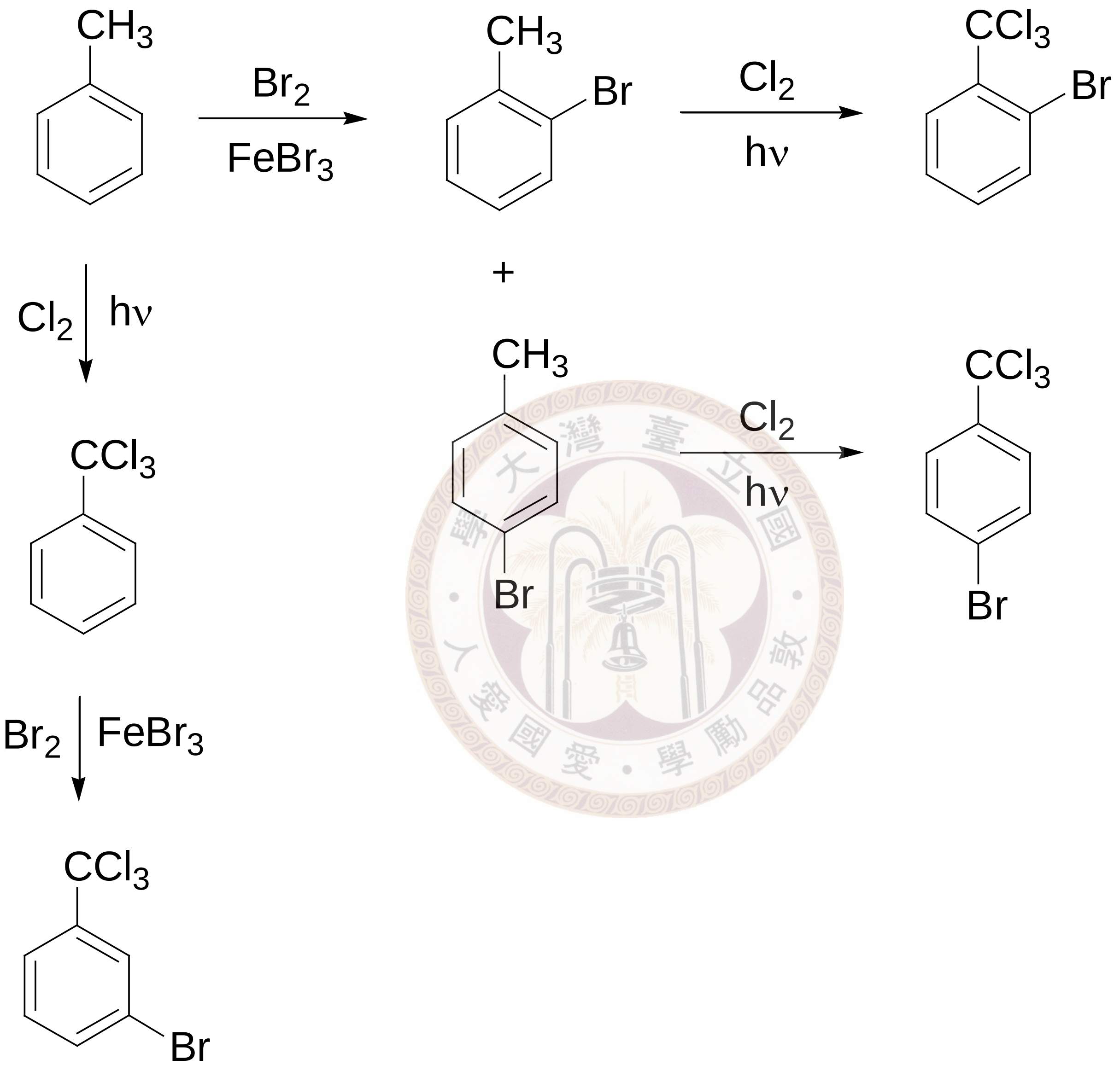




target

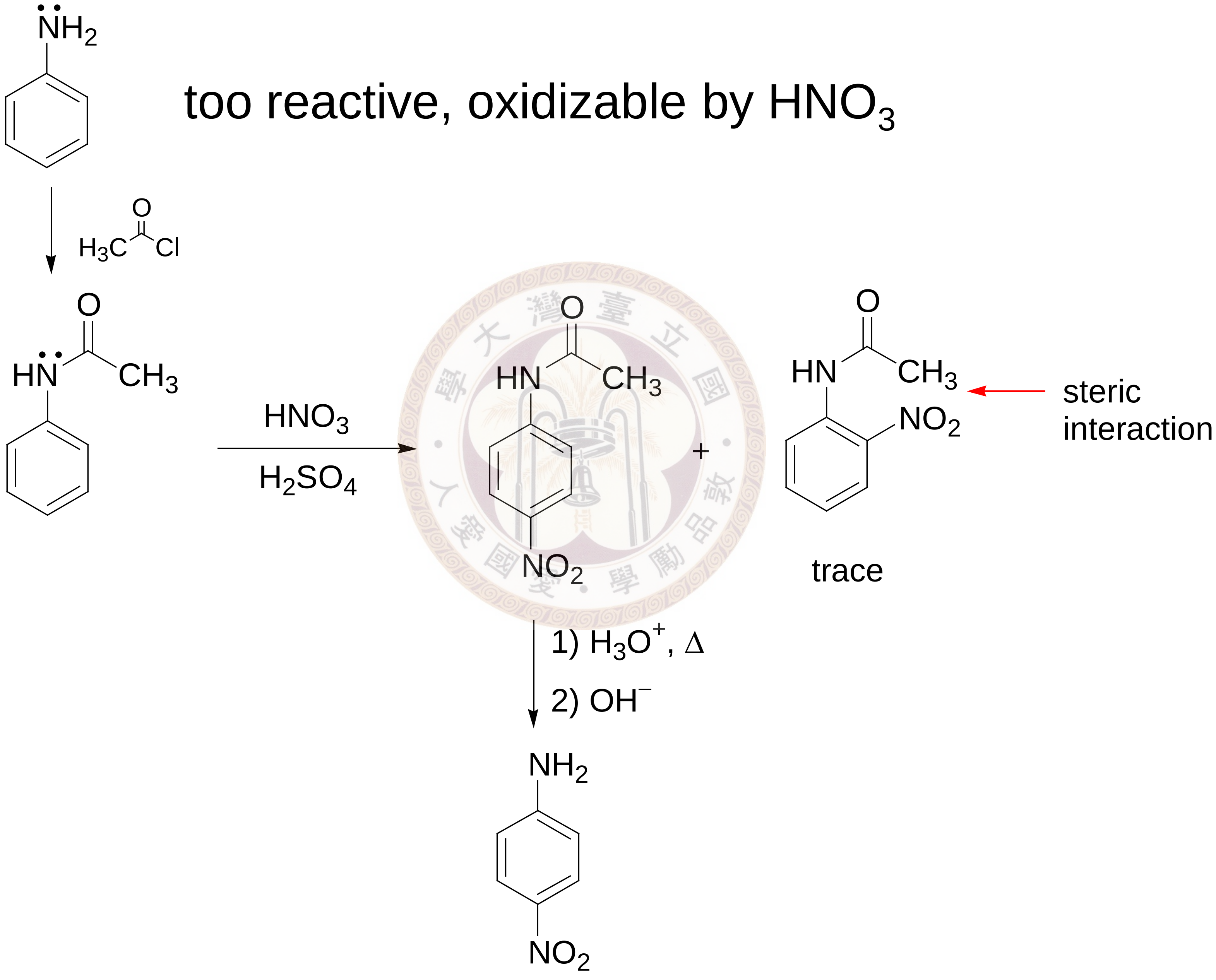
unreactive towards Friedel-Crafts alkylation

例



CH_3
Br_2
$FeBr_3$
CH_3
Br
Cl_2
hν
CCl_3
Br
+
CH_3
Br
Cl_2
hν
CCl_3
Br
Cl_2
hν
CCl_3
Br_2
$FeBr_3$
CCl_3
Br

✓ Control of reactivity



too reactive, oxidizable by HNO_3

trace

steric interaction

✓ Control of regio-selectivity