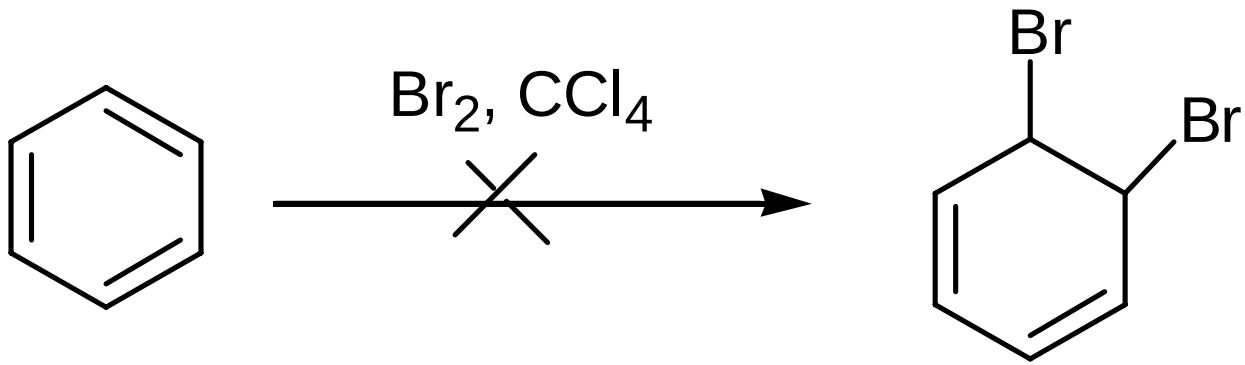
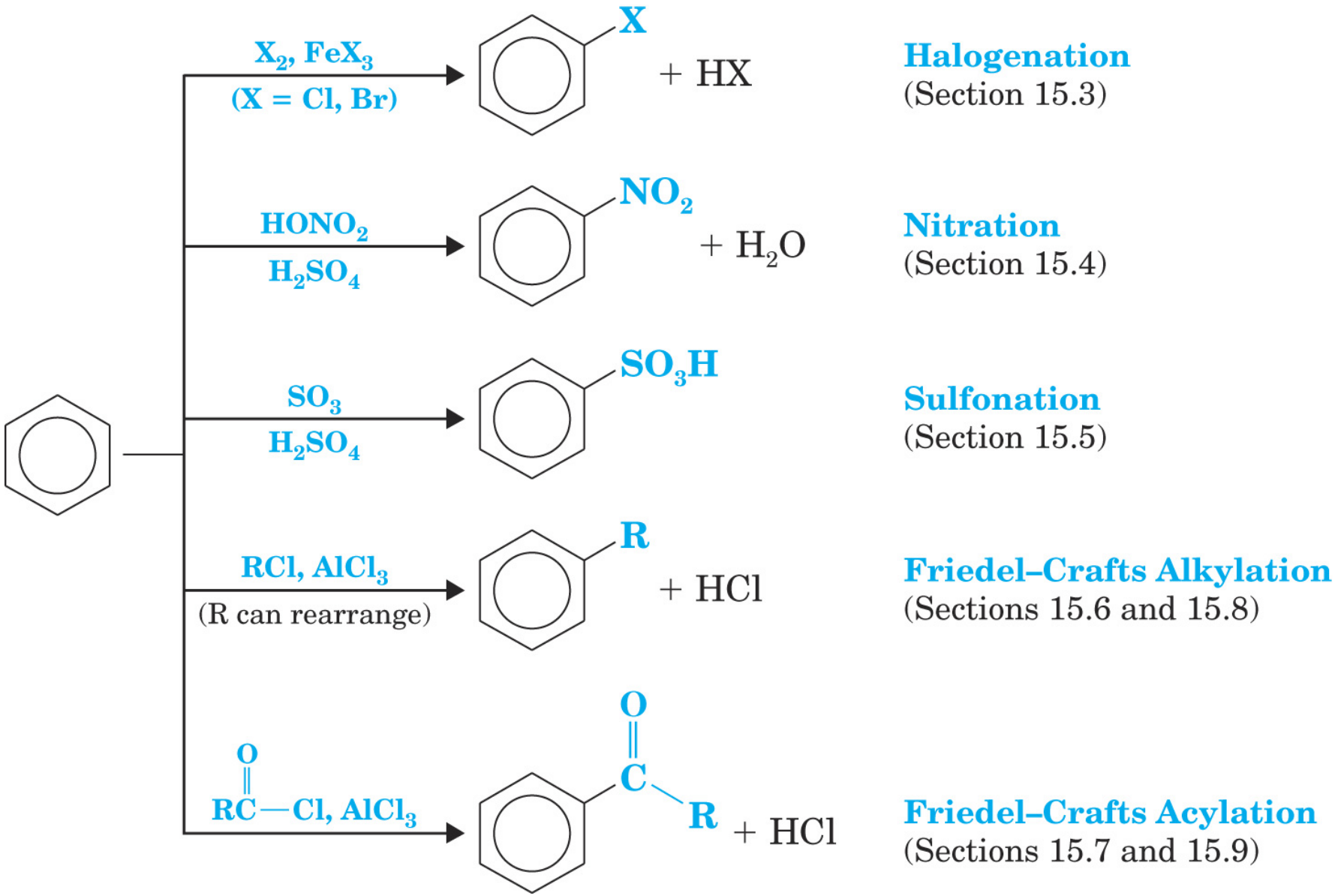
第15章 苯類化合物的有機反應

1)苯環與親電試劑（electrophile）發生的取代反應(electrophilic aromatic substitution)



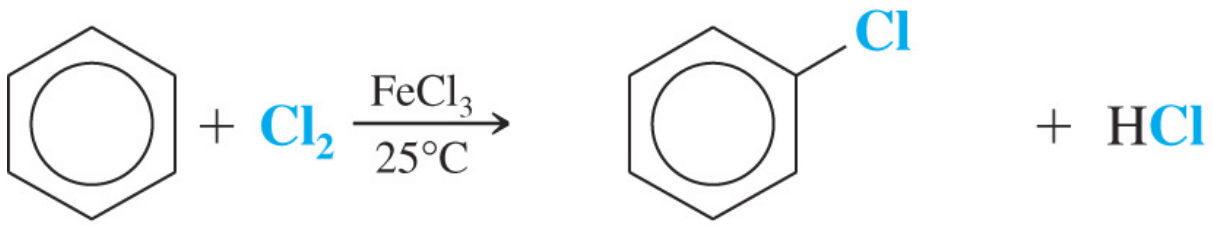
$$C_6H_6 + Br_2 \xrightarrow{FeBr_3} C_6H_5Br + HBr$$

Observed

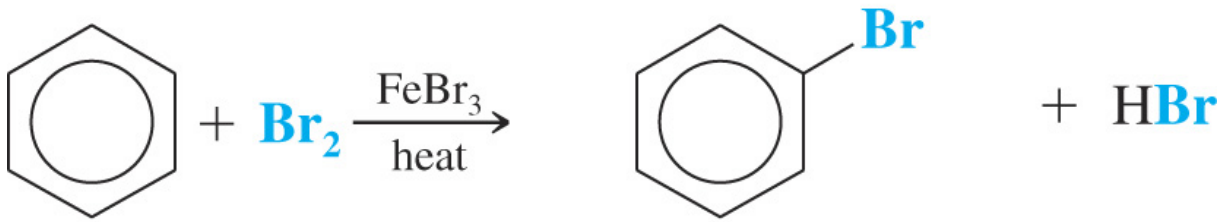

X2, FeX3
(X = Cl, Br)
X
+ HX
Halogenation
(Section 15.3)
HONO2
H2SO4
NO2
+ H2O
Nitration
(Section 15.4)
SO3
H2SO4
SO3H
Sulfonation
(Section 15.5)
RCl, AlCl3
(R can rearrange)
R
+ HCl
Friedel–Crafts Alkylation
(Sections 15.6 and 15.8)
O
RC—Cl, AlCl3
O
C
R
+ HCl
Friedel–Crafts Acylation
(Sections 15.7 and 15.9)

a) Halogenation

F_2與苯環反應相當劇烈，故通常得到多取代的產物

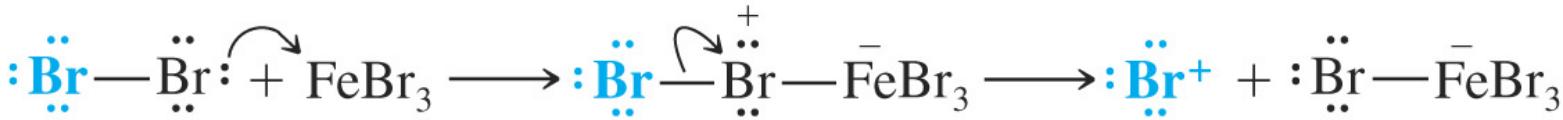


Chlorobenzene (90%)



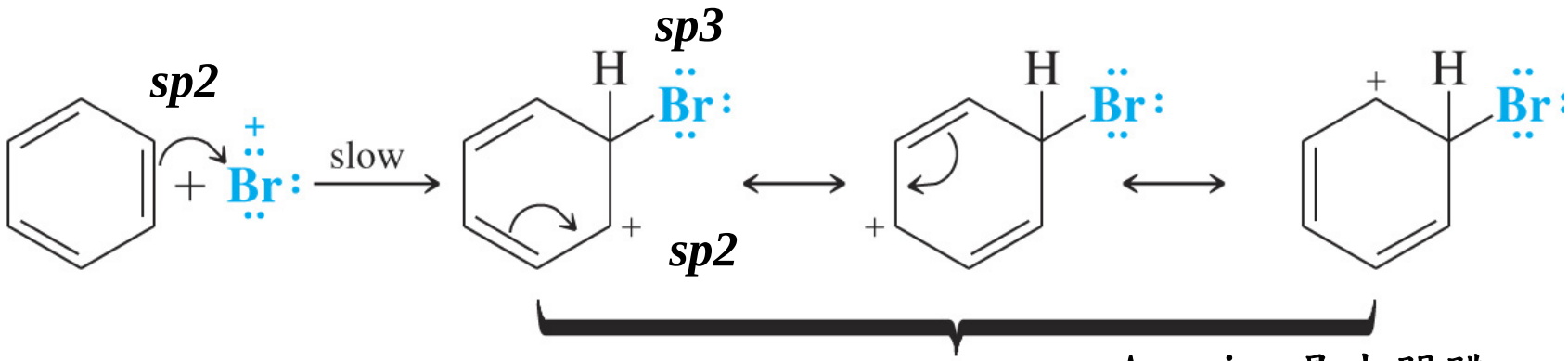
Bromobenzene (75%)

Step 1:



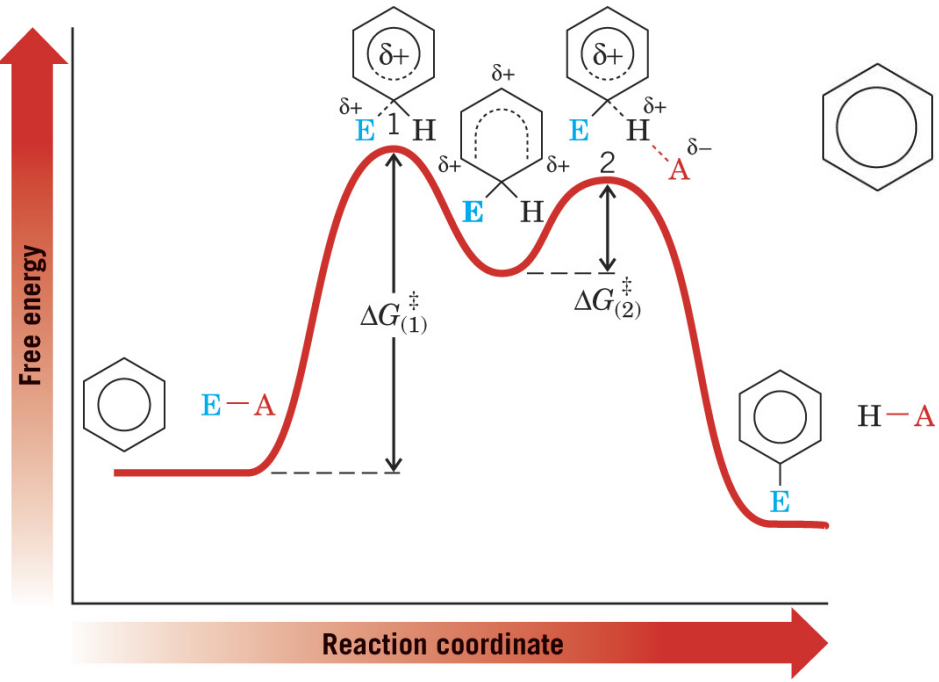
Bromine combines with $FeBr_3$ to form a complex that dissociates to form a positive bromine ion and $FeBr_4^-$.

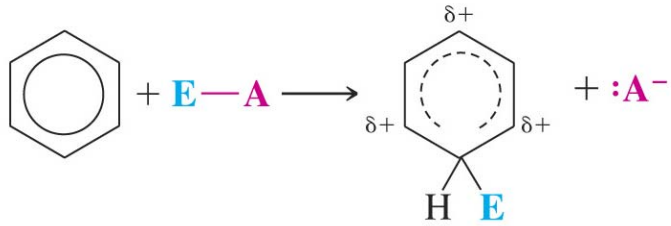
Step 2:



Arenium是中間體
(intermediate)

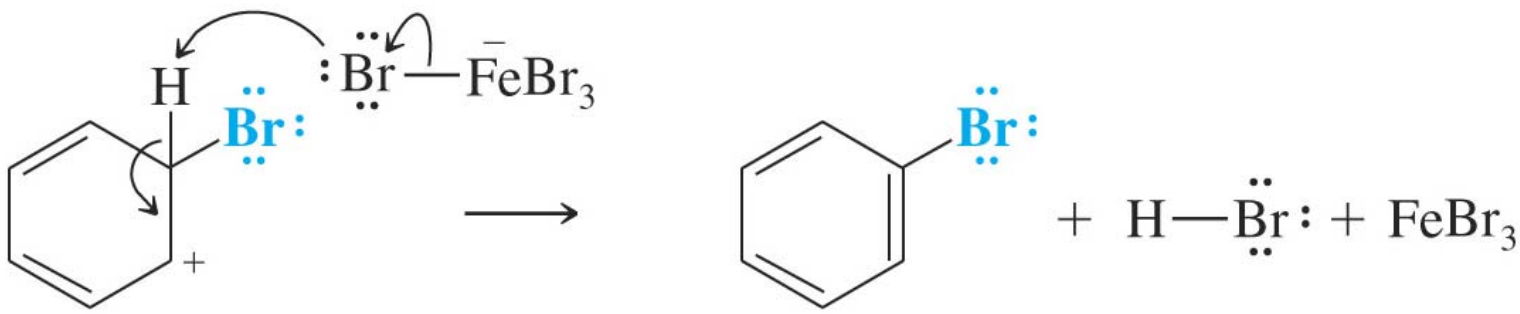
The positive bromine ion attacks benzene to form an arenium ion.





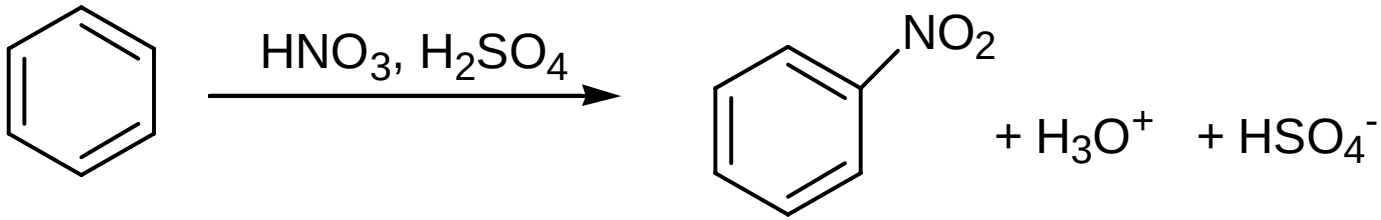
Slow, rate determining

Step 3:

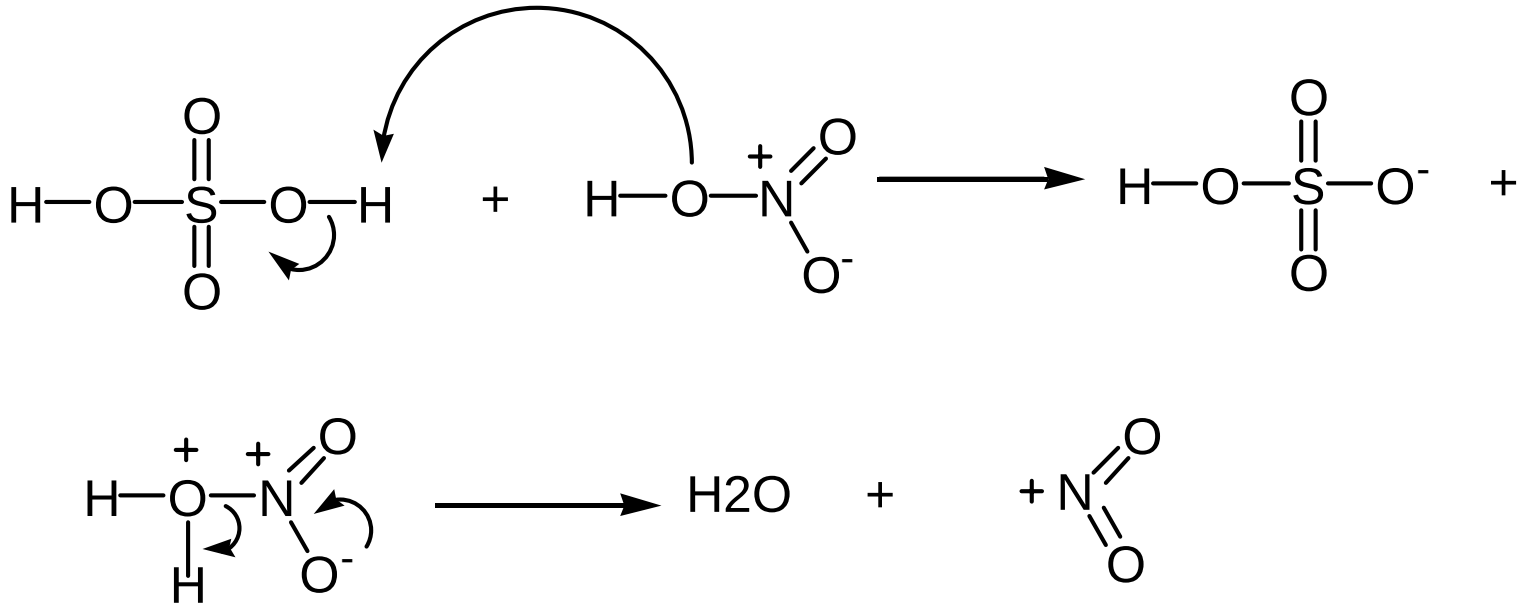


A proton is removed from the arenium ion to become bromobenzene.

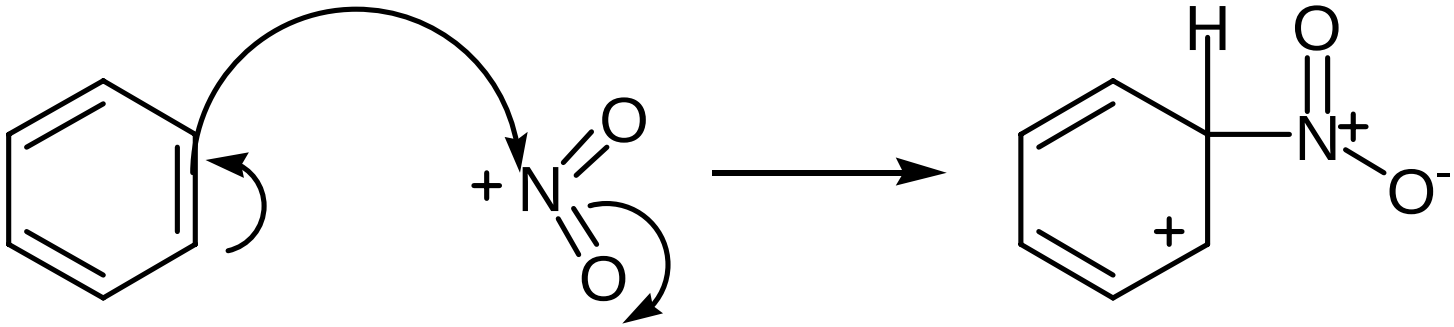
b) Nitrition:



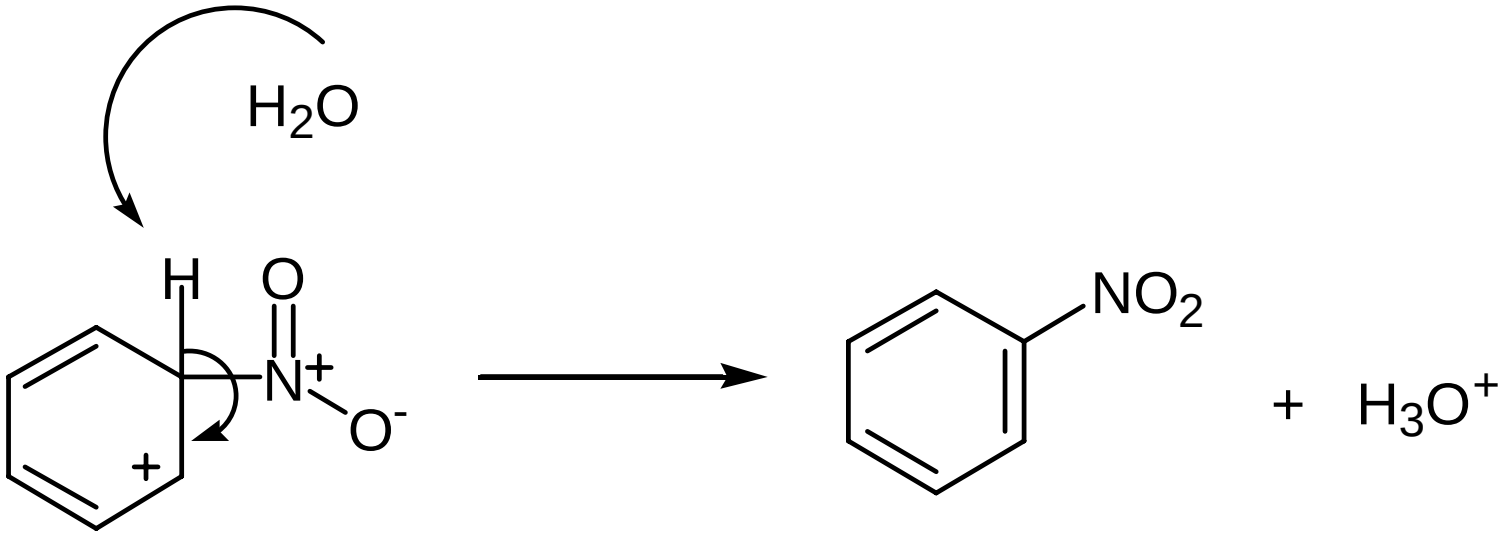
Step 1: generation of electrophile



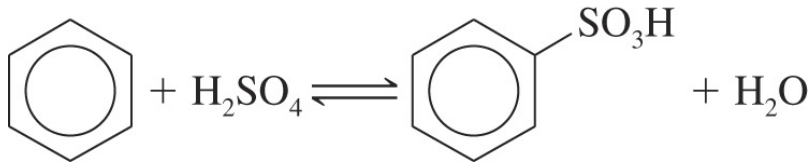
Step 2: Electrophilic addition:



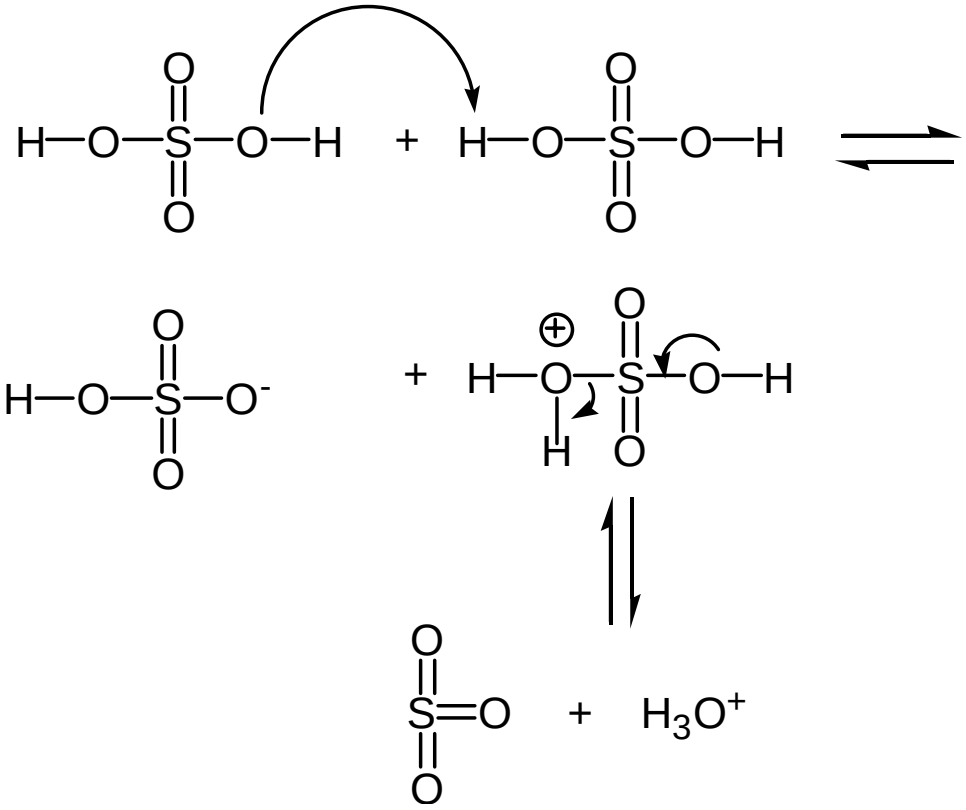
Step 3: Regeneration of aromatic system:



c) Sulfonation:



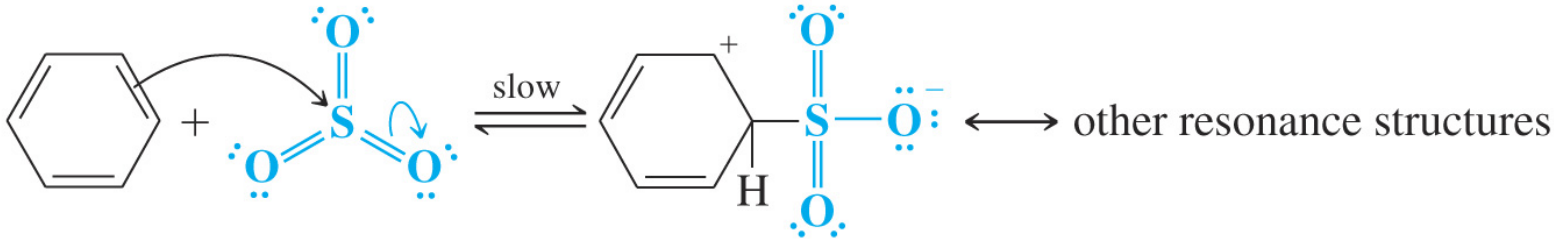
Fuming sulfuric acid



Step 1 $2\,H_2SO_4 \rightleftharpoons SO_3 + H_3O^+ + HSO_4^-$

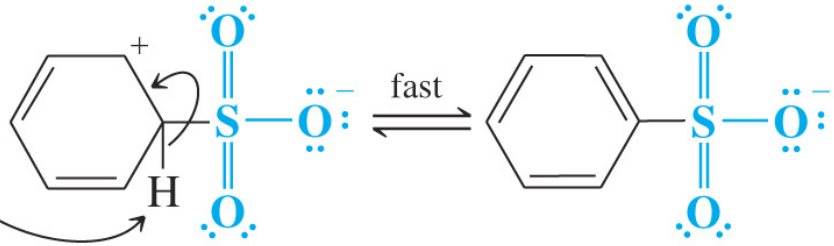
This equilibrium produces SO_3 in concentrated H_2SO_4.

Step 2



SO_3 is the actual electrophile that reacts with benzene to form an arenium ion.

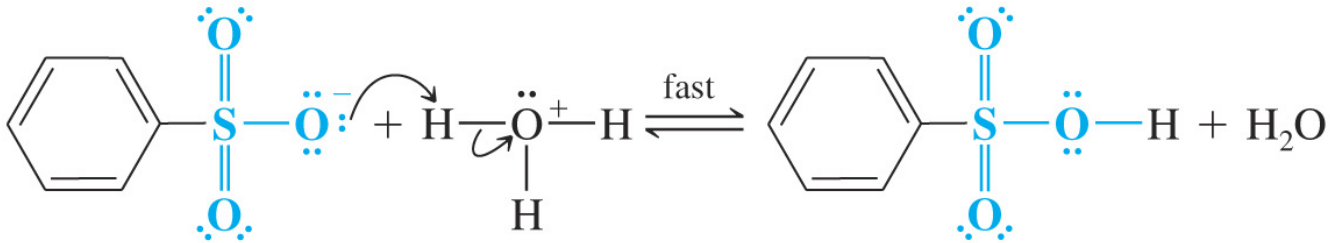
Step 3 $HSO_4^- +$



$+ H_2SO_4$

A proton is removed from the arenium ion to form the benzenesulfonate ion.

Step 4

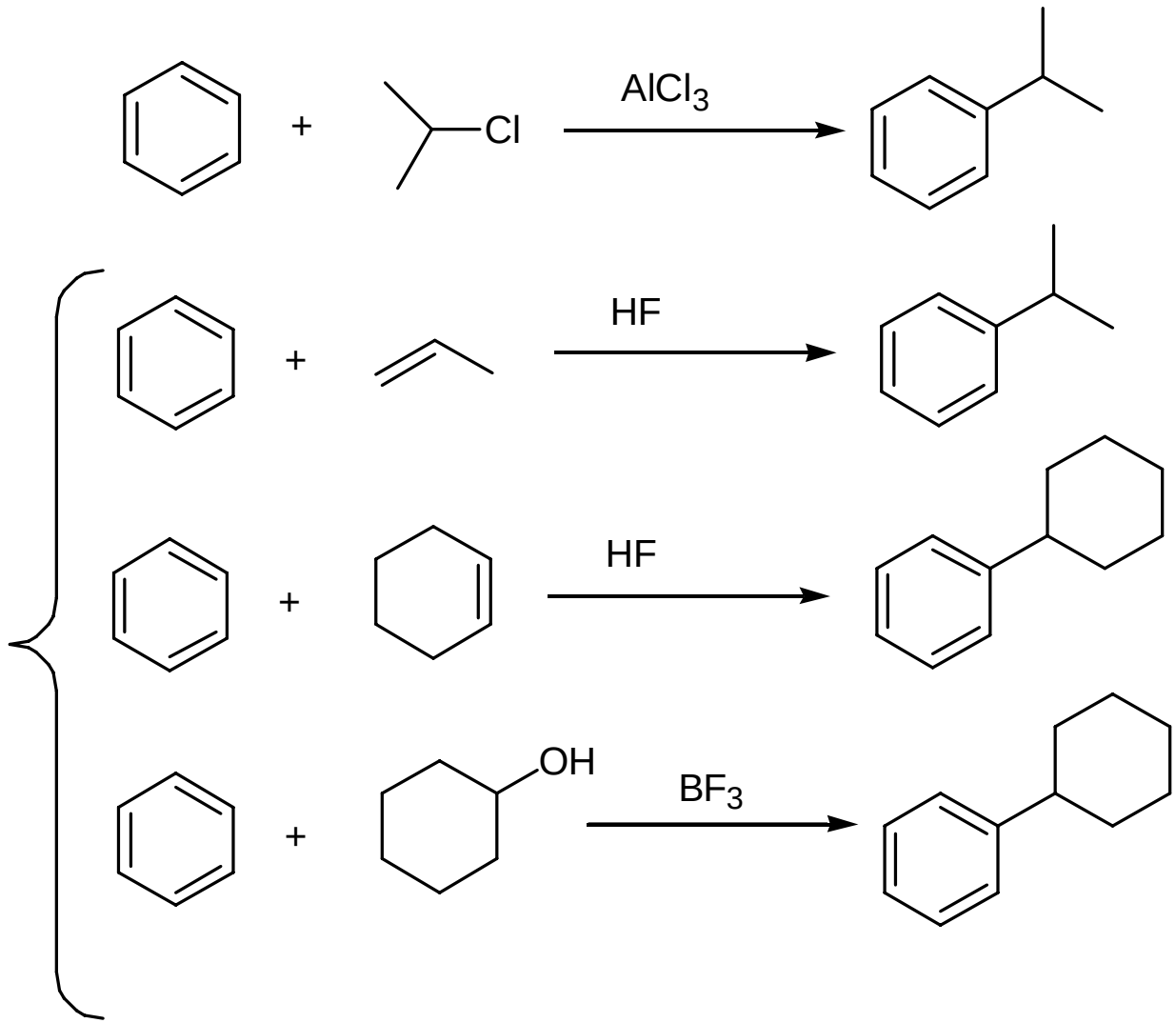


$+ H_2O$

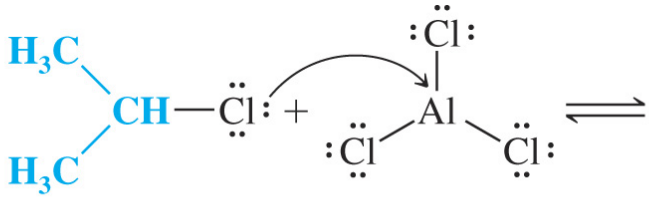
The benzenesulfonate ion accepts a proton to become benzenesulfonic acid.

d) Friedel-Craft Alkylation — 在苯環上引入烷基

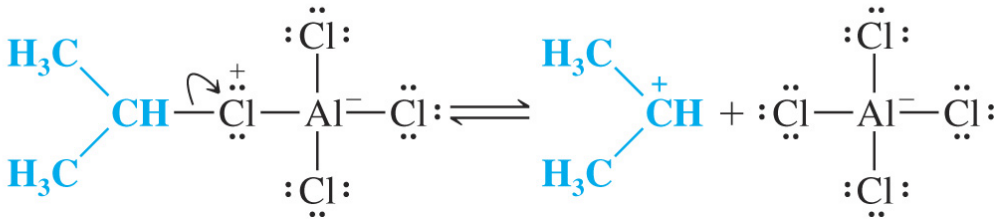
解釋反應機制



Step 1

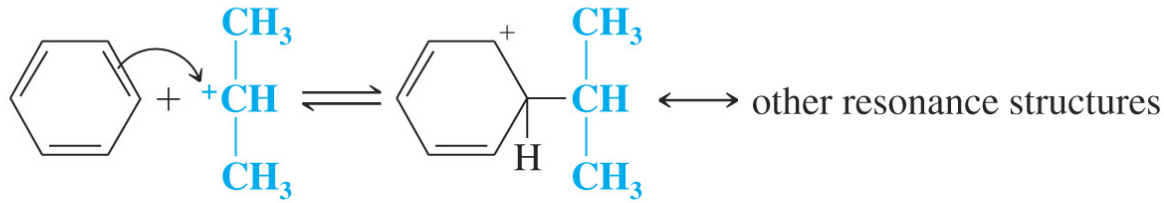


This is a Lewis acid–base reaction (see Section 3.2B).



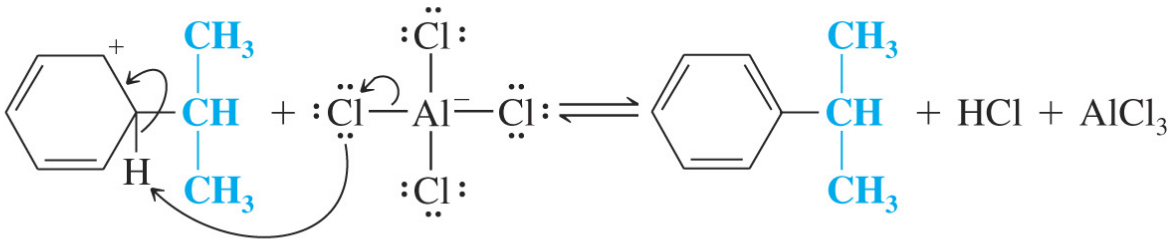
The complex dissociates to form a carbocation and $AlCl_4^-$.

Step 2



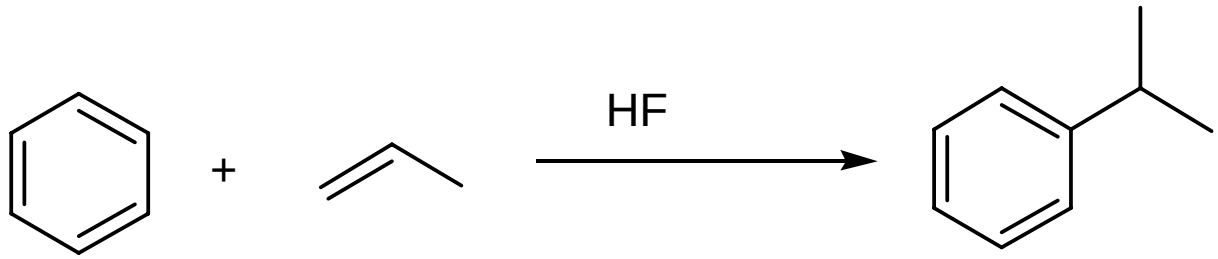
The carbocation, acting as an electrophile, reacts with benzene to produce an arenium ion.

Step 3

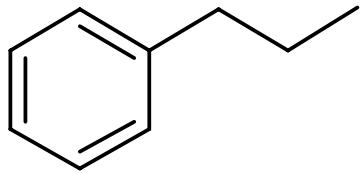


A proton is removed from the arenium ion to form isopropylbenzene. This step also regenerates the $AlCl_3$ and liberates HCl.

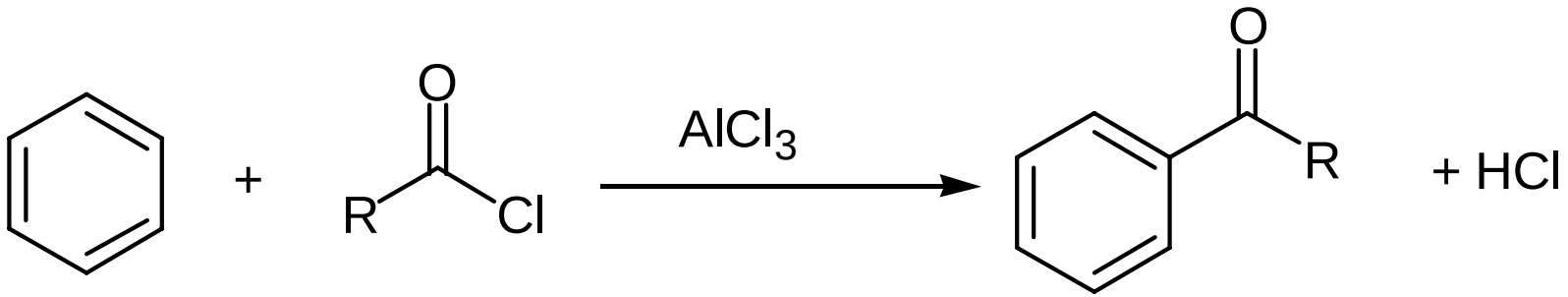
Page 673；解釋反應機制：

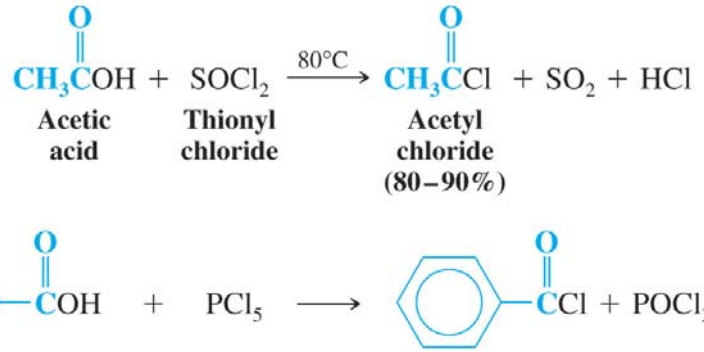


Why not

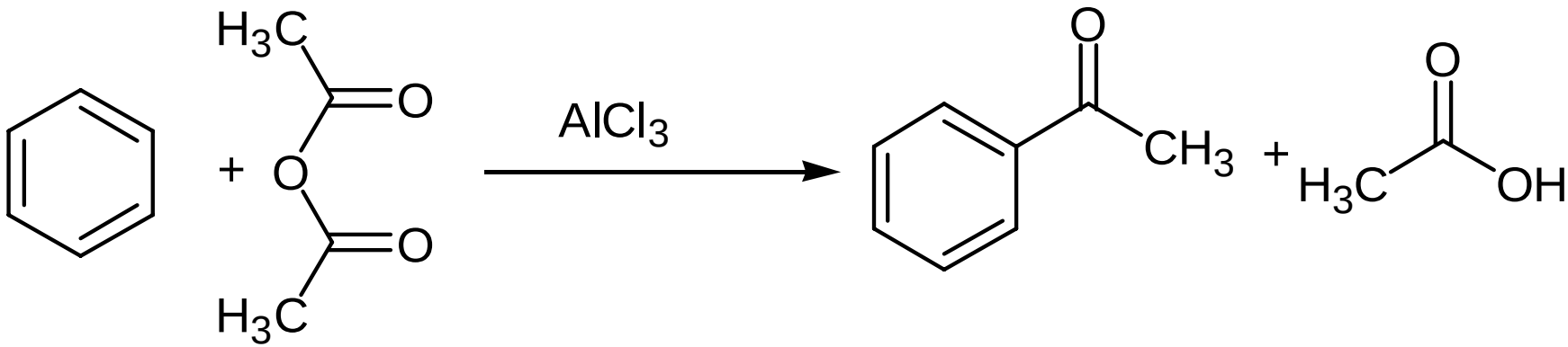


e) Friedel-Craft Acylation 反應 — 在苯環上引入酰基 (acyl group: RCO)

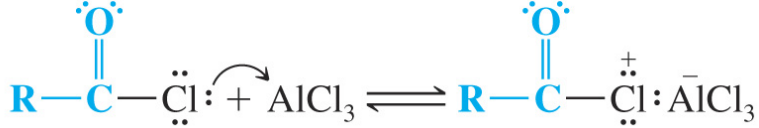




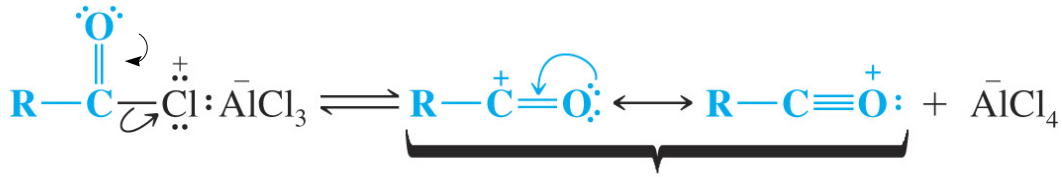
Explain the mechanism



Step 1

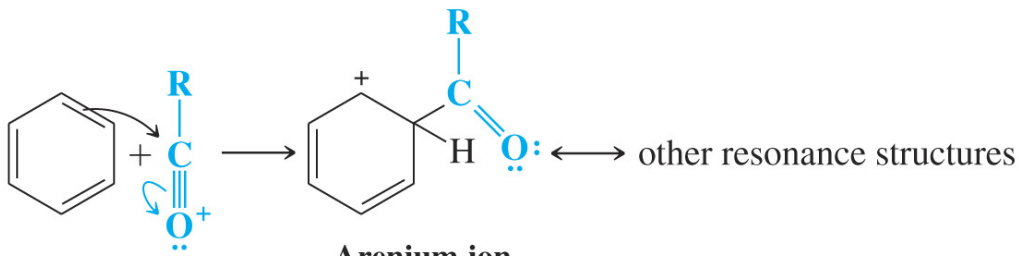


Step 2



An acylium ion

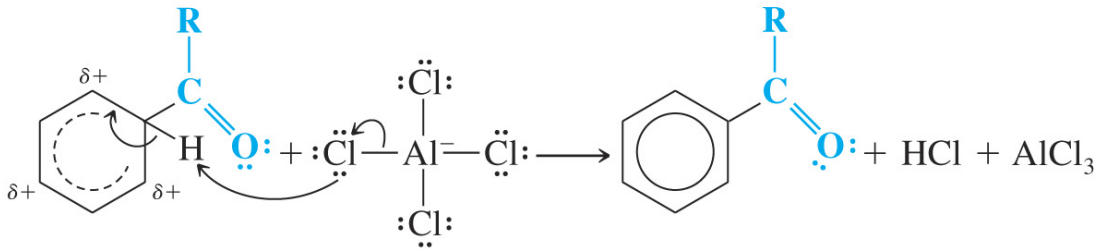
Step 3



Arenium ion

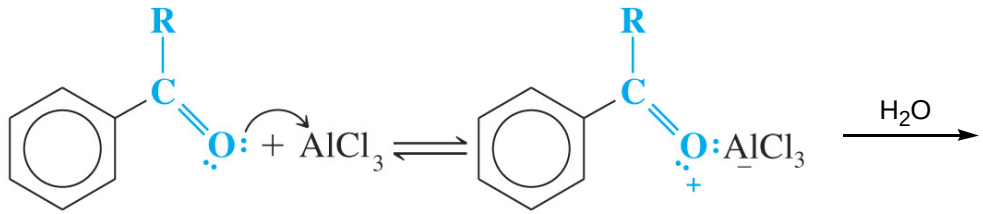
The acylium ion, acting as an electrophile, reacts with benzene to form the arenium ion.

Step 4



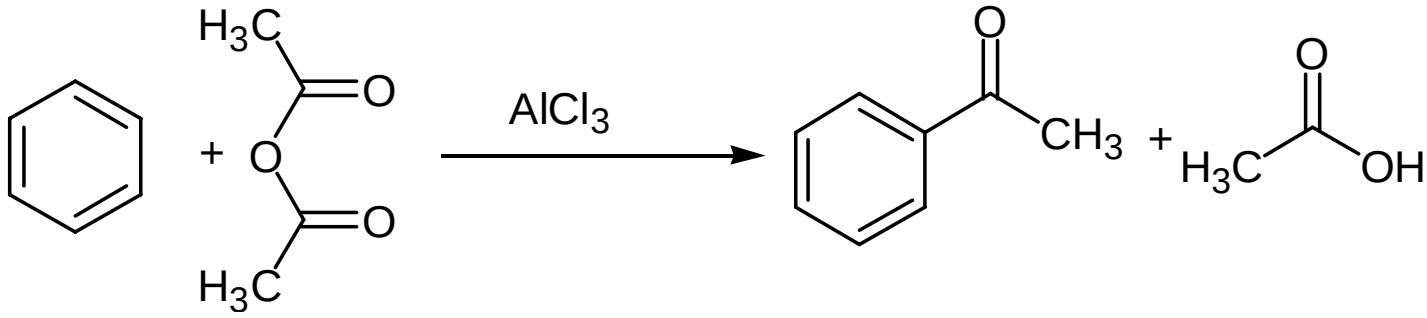
A proton is removed from the arenium ion, forming the aryl ketone.

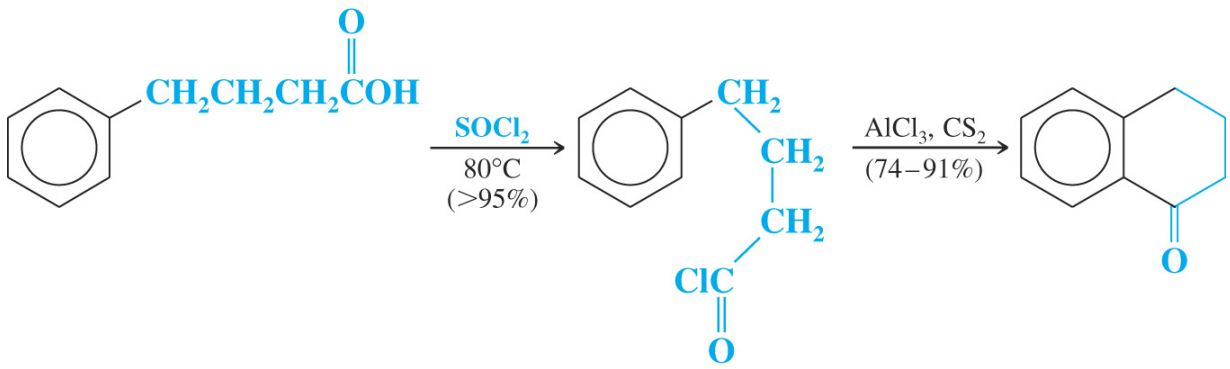
Step 5



The ketone, acting as a Lewis base, reacts with aluminum chloride (a Lewis acid) to form a complex.

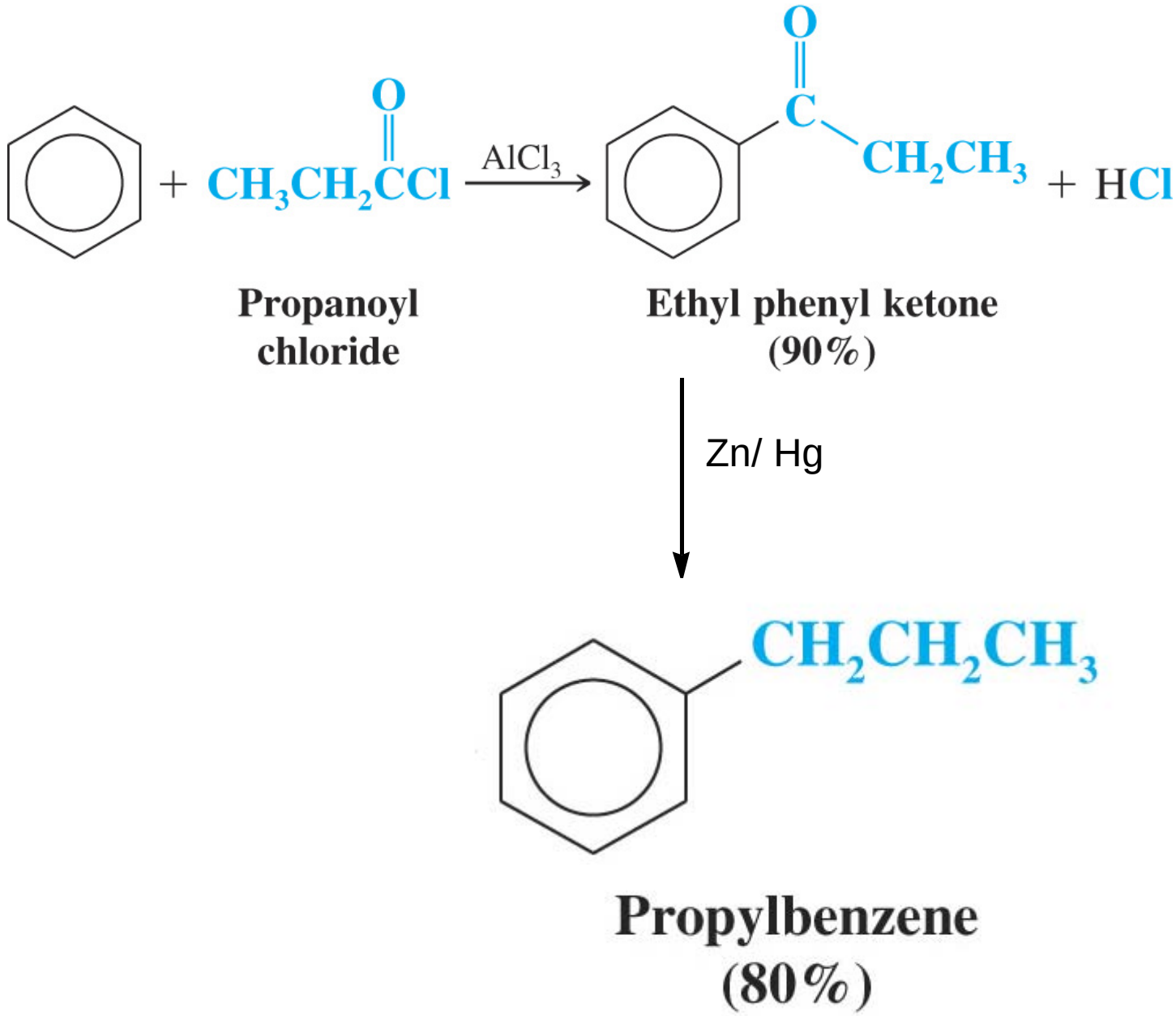
Page 675; drawing the mechanism:



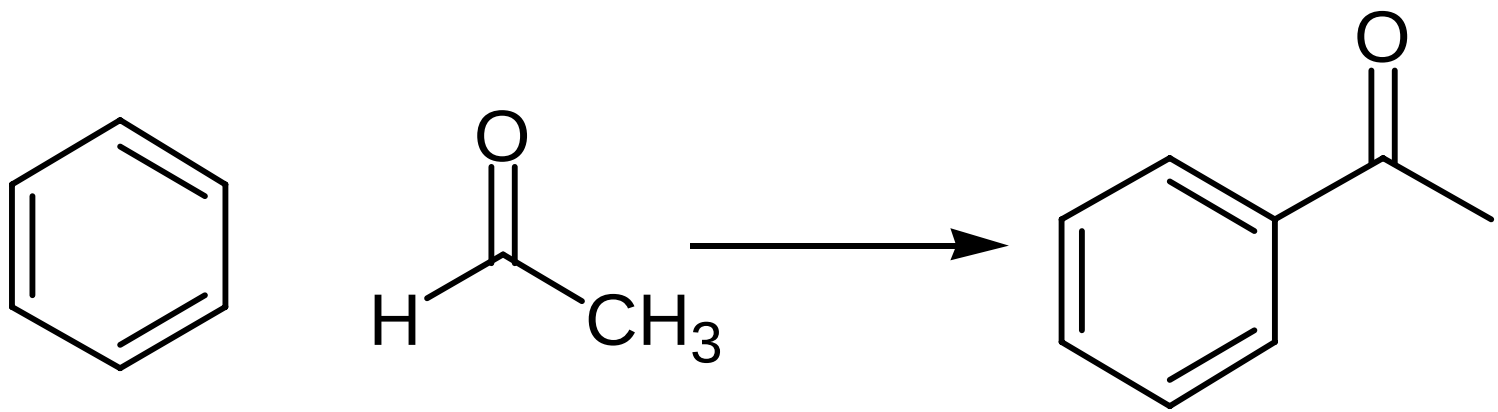


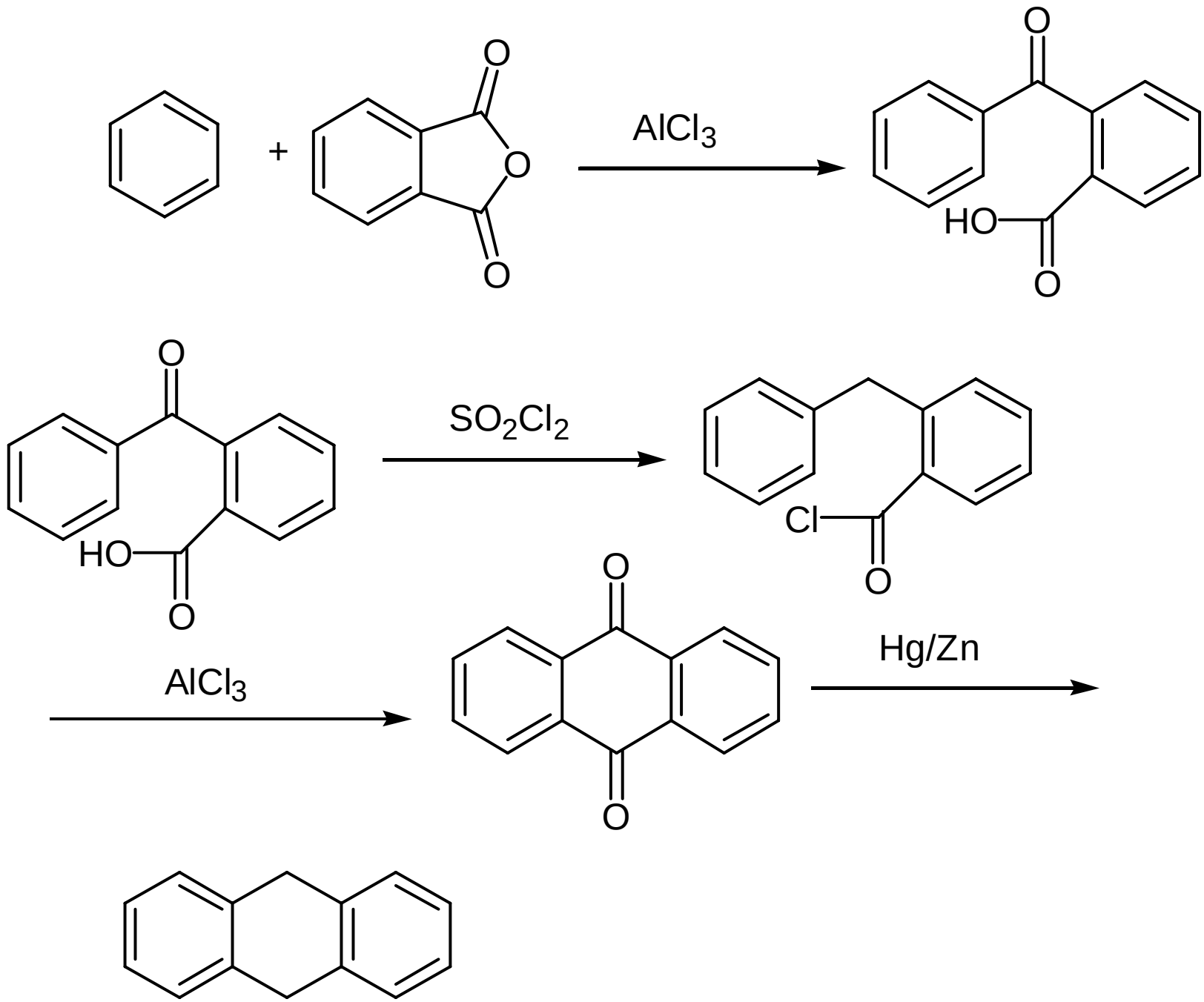
4-Phenylbutanoic acid | **4-Phenylbutanoyl chloride** | ***α*-Tetralone**

Drawing the mechanism


O
CH3CH2CCl
AlCl3
C
CH2CH3
+ HCl
Propanoyl chloride
Ethyl phenyl ketone (90%)
Zn/ Hg
CH2CH2CH3
Propylbenzene (80%)

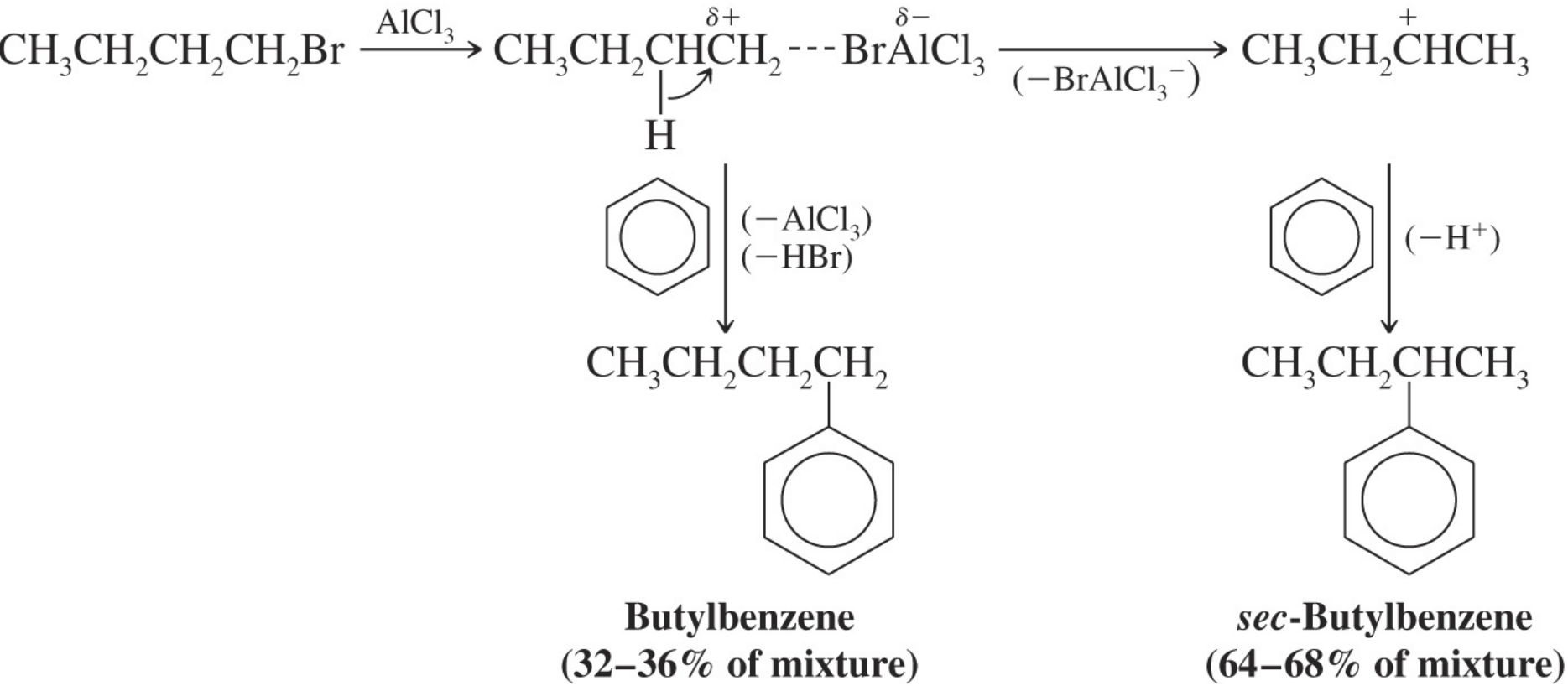
設計合成途徑



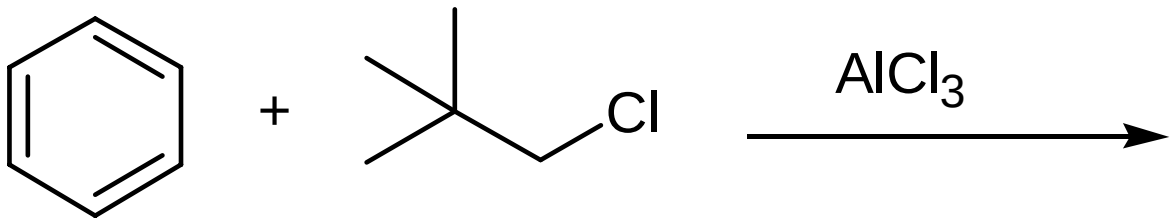

+
O
O
O
AlCl3
O
HO
O
O
HO
O
SO2Cl2
Cl
O
AlCl3
O
O
Hg/Zn

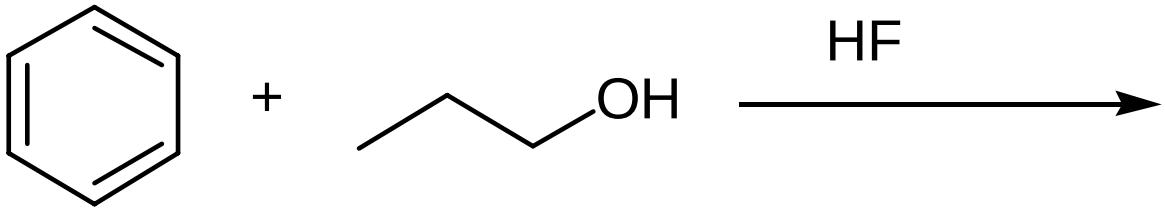
f) Friedel-Craft反應的應用所受到的限制

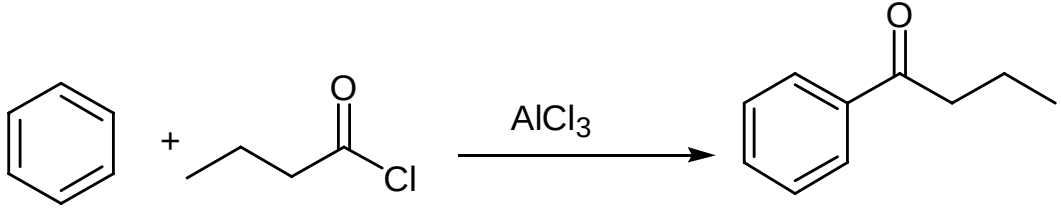
親電試劑的重排



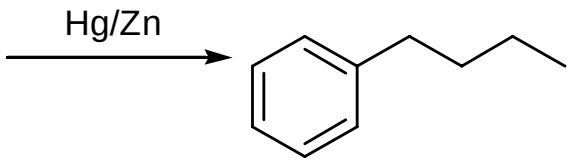
Page 677;給出主產物並解釋反應機制

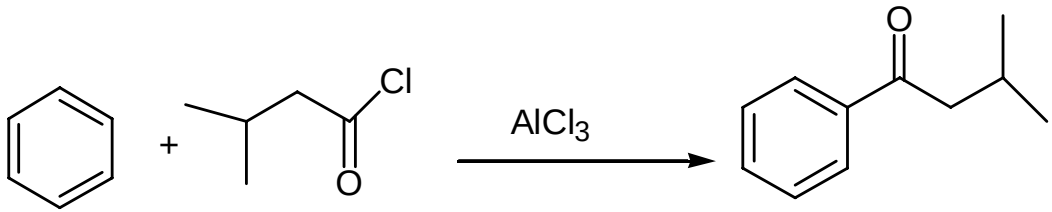


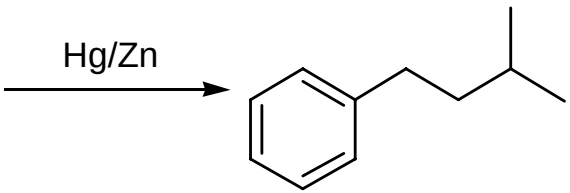


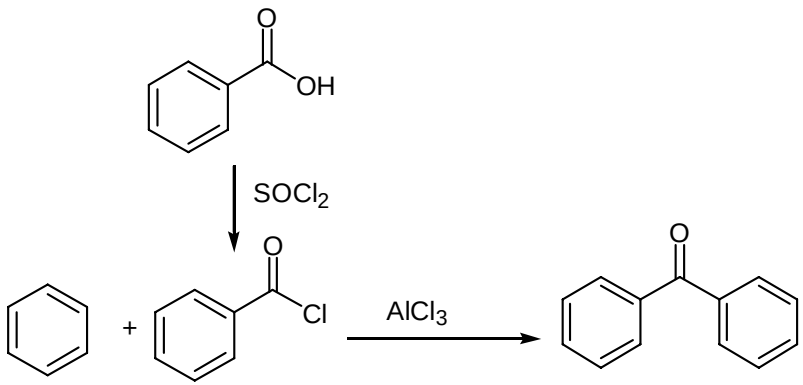


Page 677;已知起始物合成下列化合物



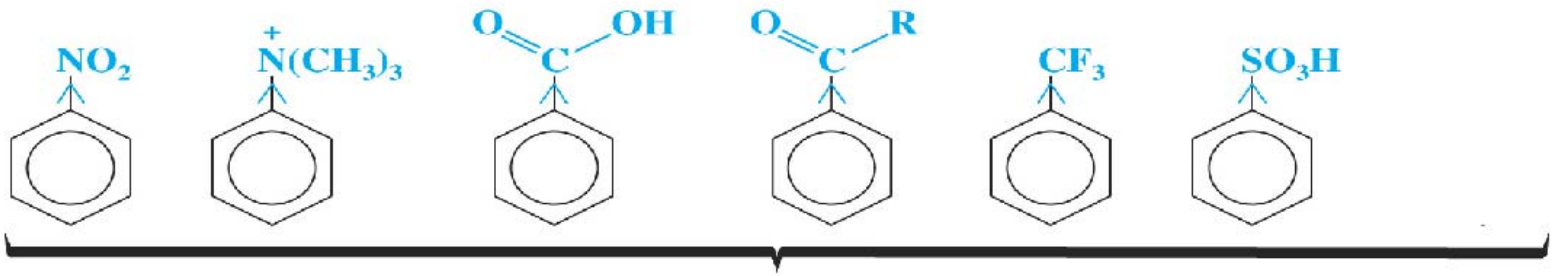






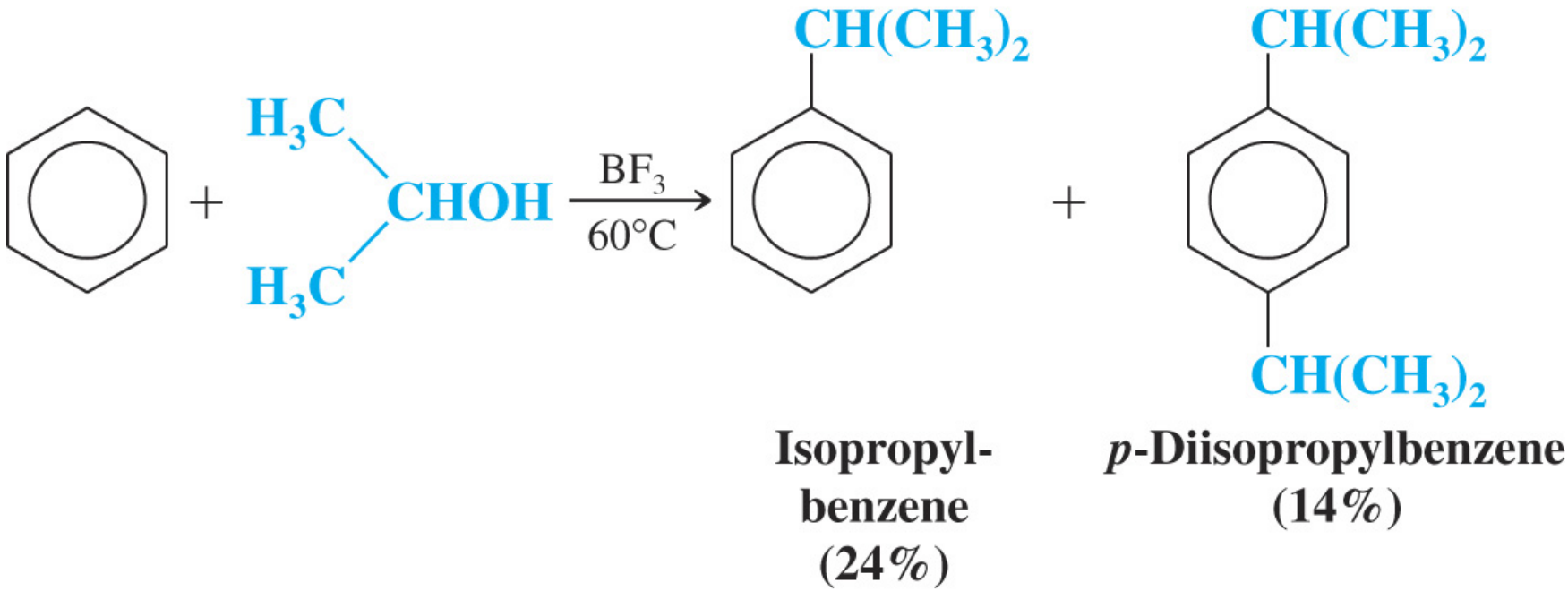
g)取代基效應:

i)當苯環上有以下取代基時，反應活性降低



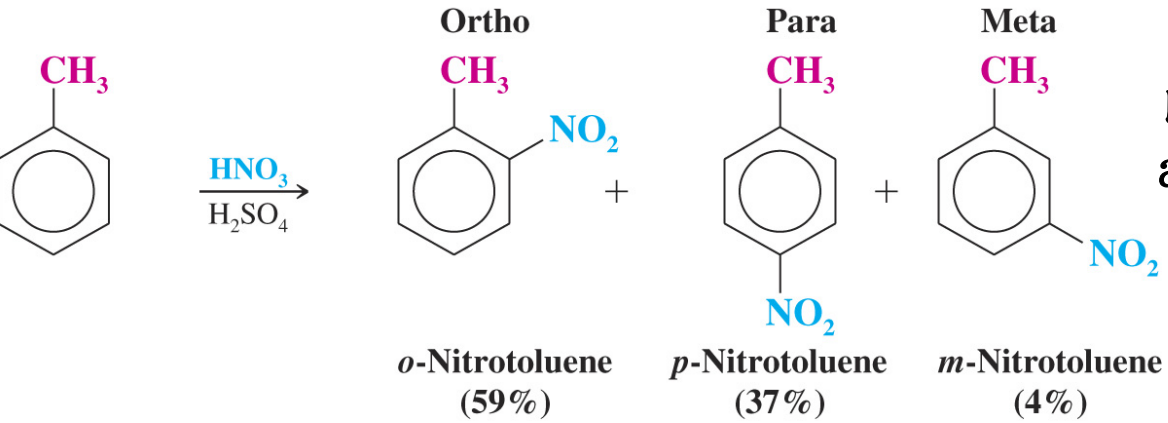
These usually give poor yields in Friedel–Crafts reactions.

ii)多重烷基化反應的發生

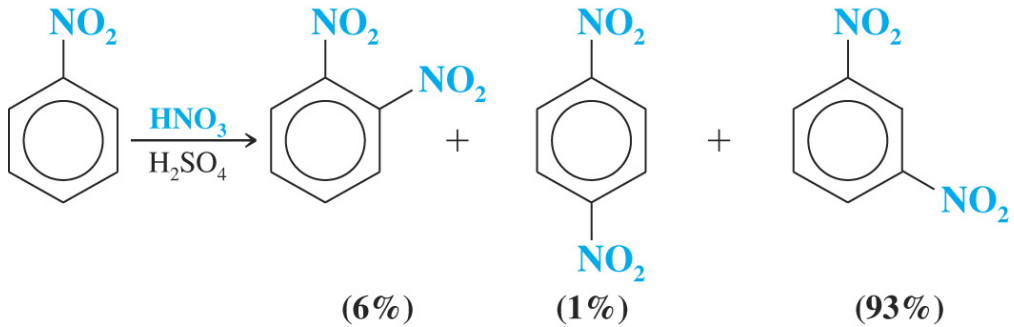


iii) Polyacylation does not occur because the acyl group deactivates the aromatic ring to further substitution

在苯類化合物的親核取代反應中，若取代基的存在使得取代苯比苯本身更為active, 則此類取代基被稱為activating groups (ortho-para directors);
反之則稱為deactivating group (meta director).



比苯的反應更容易進行, 故CH_3為activating group



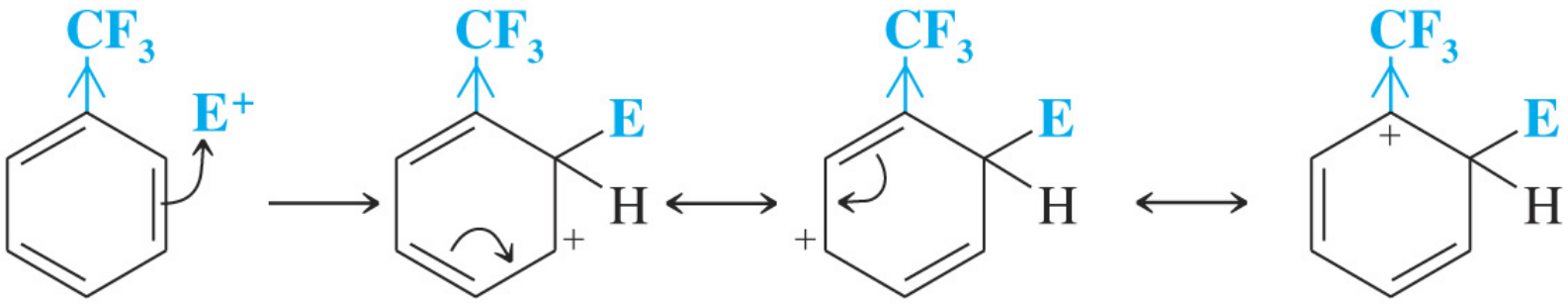
反應速度只有苯的10^{-4}, 故NO_2為deactivating group

Ortho–Para Directors	Meta Directors
Strongly Activating —$\ddot{N}H_2$, —$\ddot{N}HR$, —$\ddot{N}R_2$ —$\ddot{O}H$, —$\ddot{O}:^-$	**Moderately Deactivating** —C≡N —SO_3H —CO_2H, —CO_2R —CHO, —COR
Moderately Activating —$\ddot{N}HCOCH_3$, —$\ddot{N}HCOR$ —$\ddot{O}CH_3$, —$\ddot{O}R$	**Strongly Deactivating** —NO_2 —NR_3^+ —CF_3, —CCl_3
Weakly Activating —CH_3, —C_2H_5, —R —C_6H_5	
Weakly Deactivating —$\ddot{F}:$, —$\ddot{C}l:$, —$\ddot{B}r:$, —$\ddot{I}:$	

鹵族元素取代基(Br, Cl)為一特例；它們是deactivating group, 但可使反應發生在ortho-para位

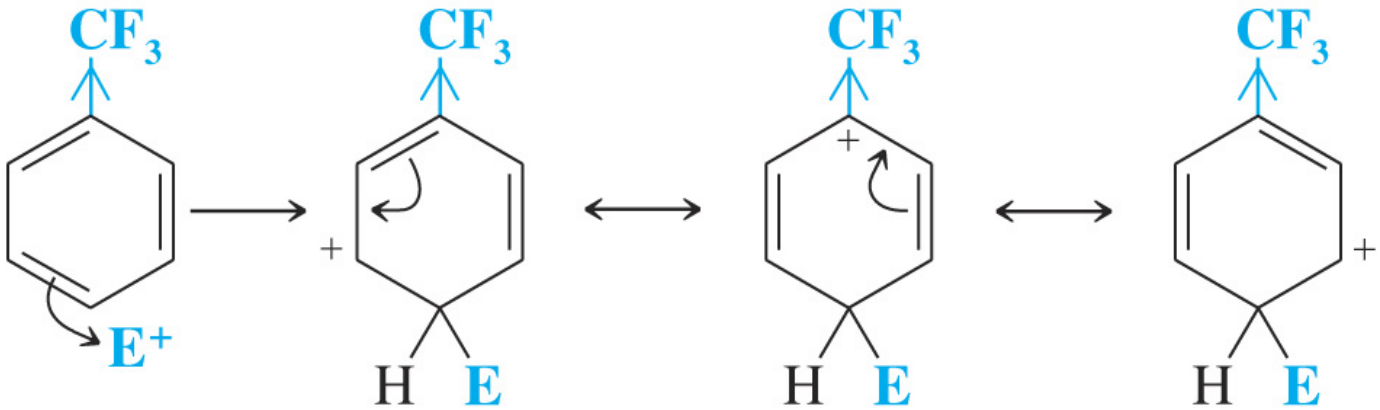
Reaction	Ortho Product (%)	Para Product (%)	Total Ortho and Para (%)	Meta Product (%)
Chlorination	39	55	94	6
Bromination	11	87	98	2
Nitration	30	70	100	
Sulfonation		100	100	

Ortho Attack



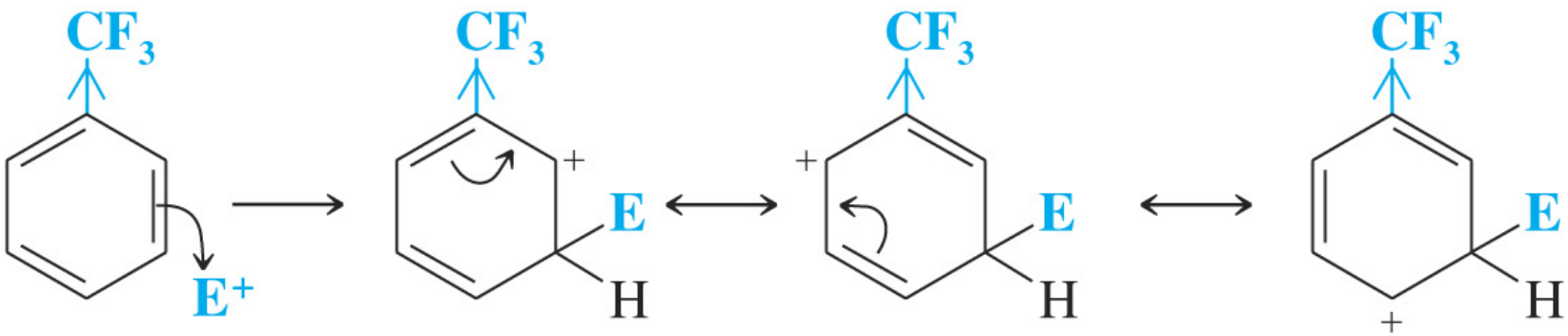
Highly unstable contributor

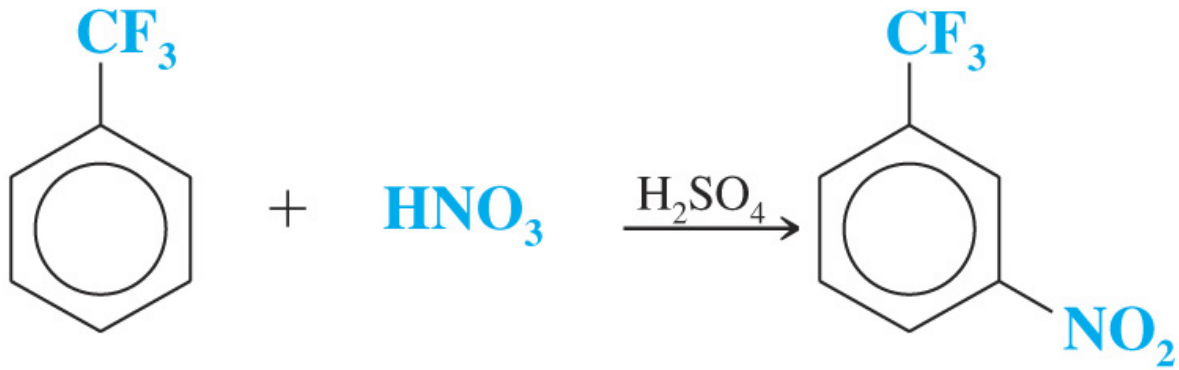
Para Attack



Highly unstable contributor

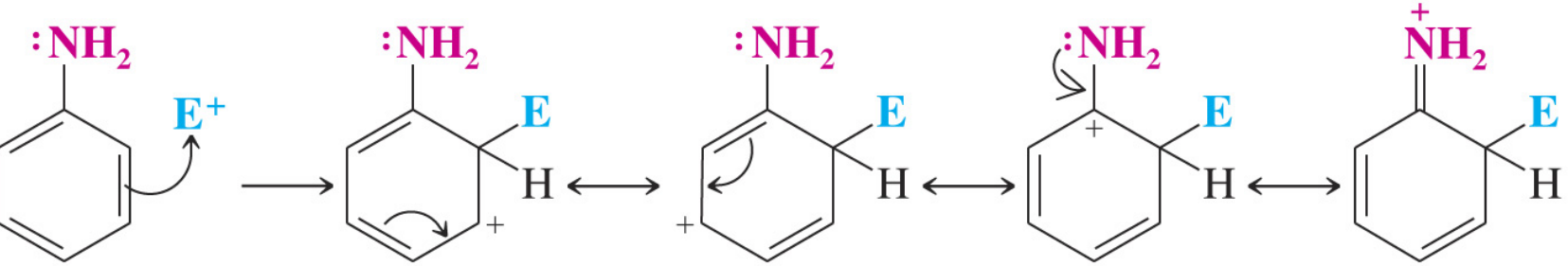
Meta Attack



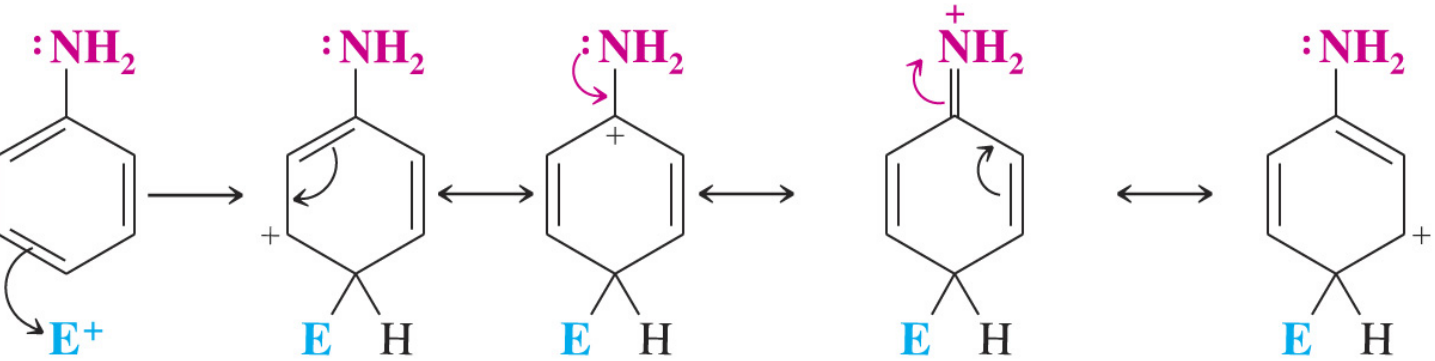


Trifluoromethylbenzene **(~100%)**

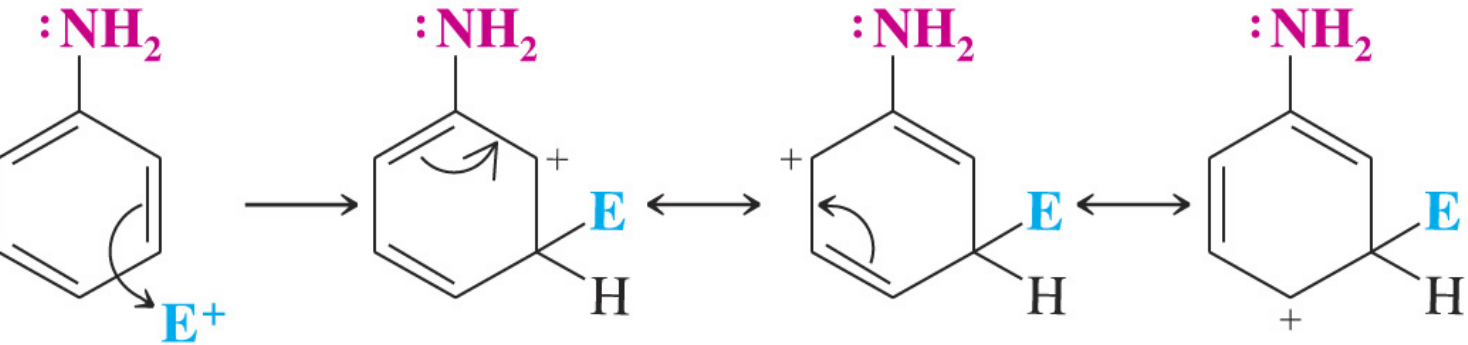
Ortho Attack



Para Attack

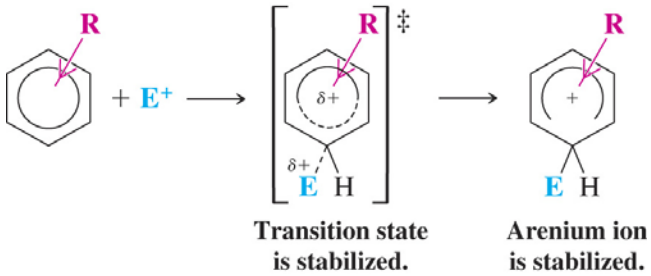


Meta Attack



Most electron donating

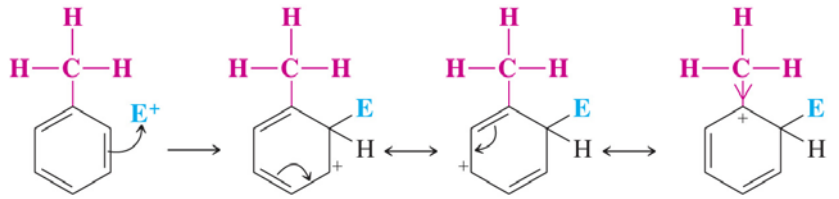
Least electron donating



Transition state is stabilized.

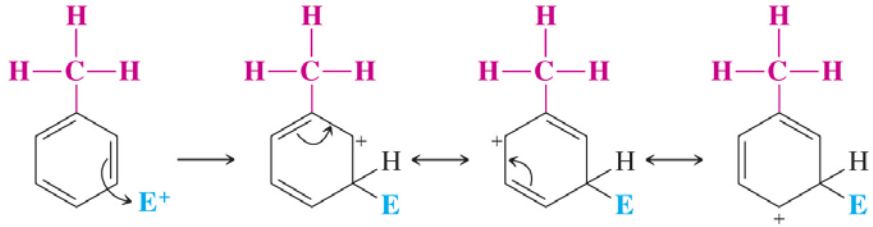
Arenium ion is stabilized.

Ortho Attack

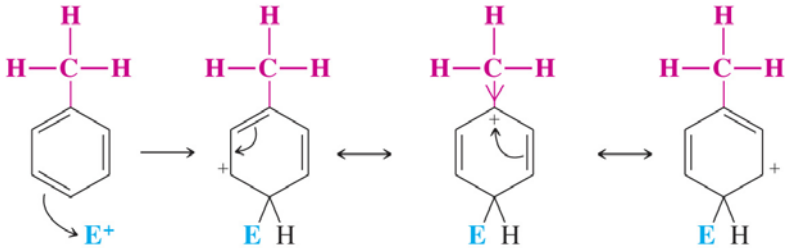


Relatively stable contributor

Meta Attack

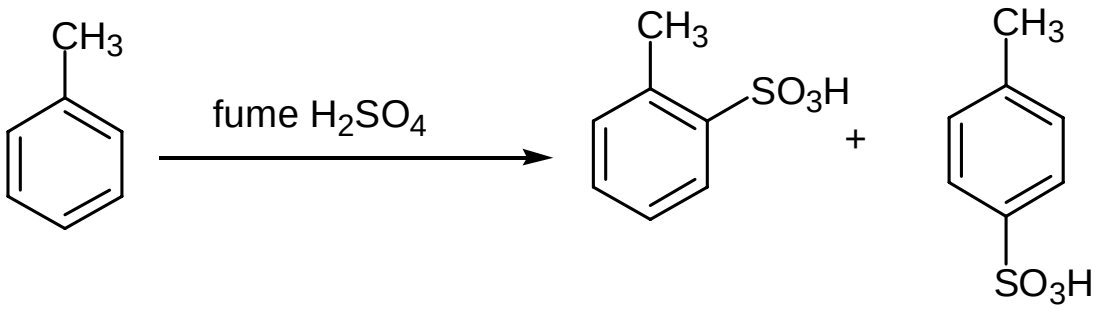


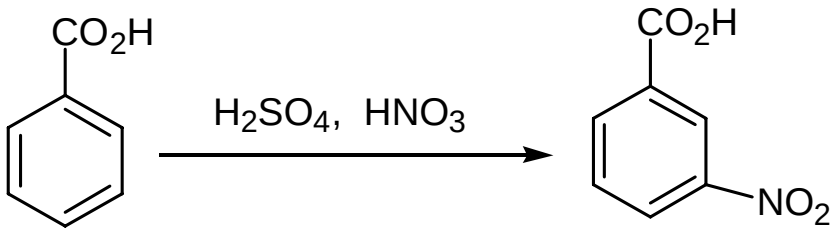
Para Attack

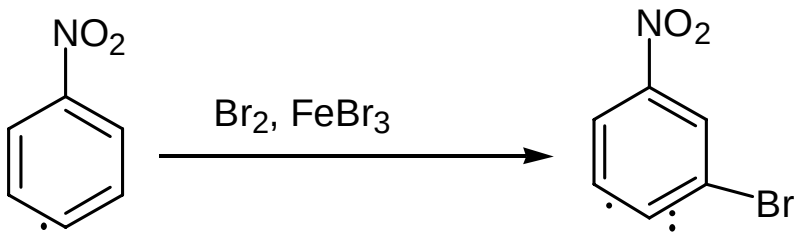


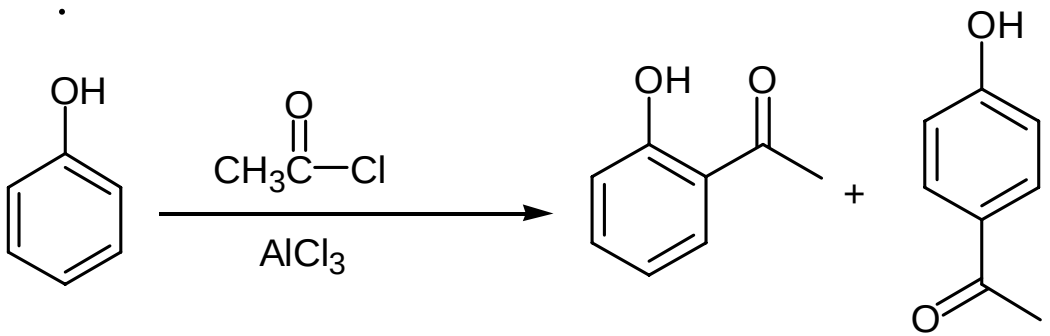
Relatively stable contributor

Page 681 exercise: Predict the major producs:





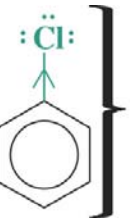




Halo groups are ortho-para directors but are also deactivating

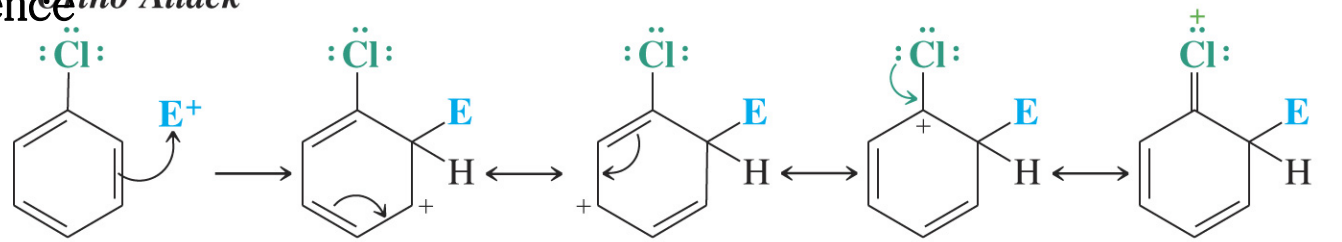
* The electron-withdrawing inductive effect of the halide is the primary influence that deactivates haloaromatic compounds toward electrophilic aromatic substitution

**The electron-donating resonance effect of the halogen's unshared electron pairs is the primary ortho-para directing influence



Inductive effect of chlorine atom deactivates ring.

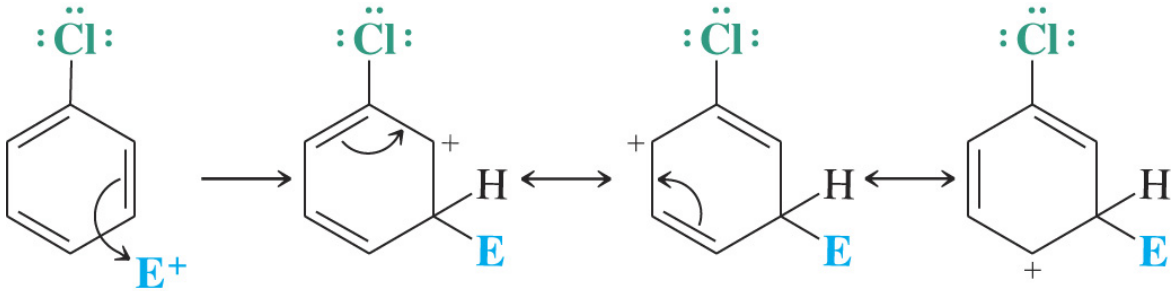
Ortho Attack



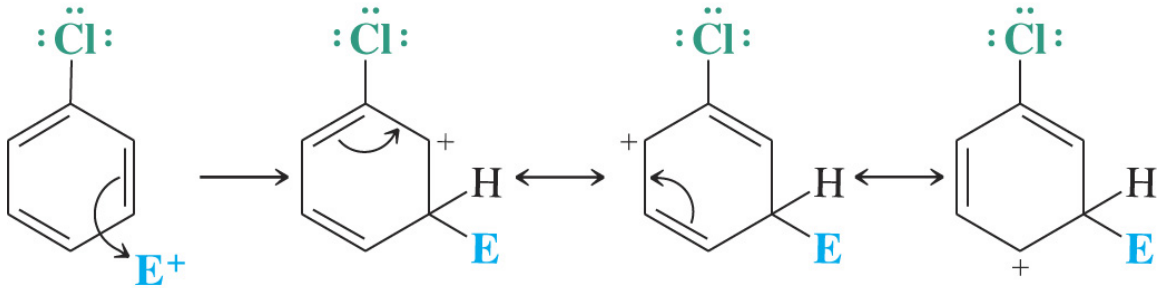
Relatively stable

ıtor

Meta attack



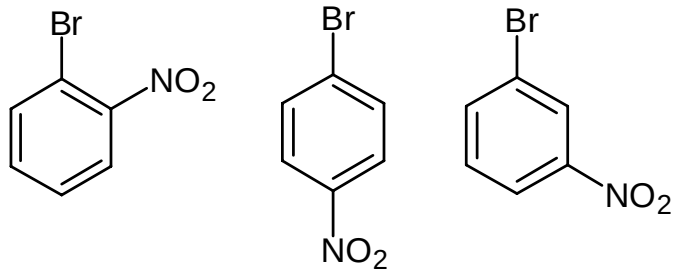
Meta attack

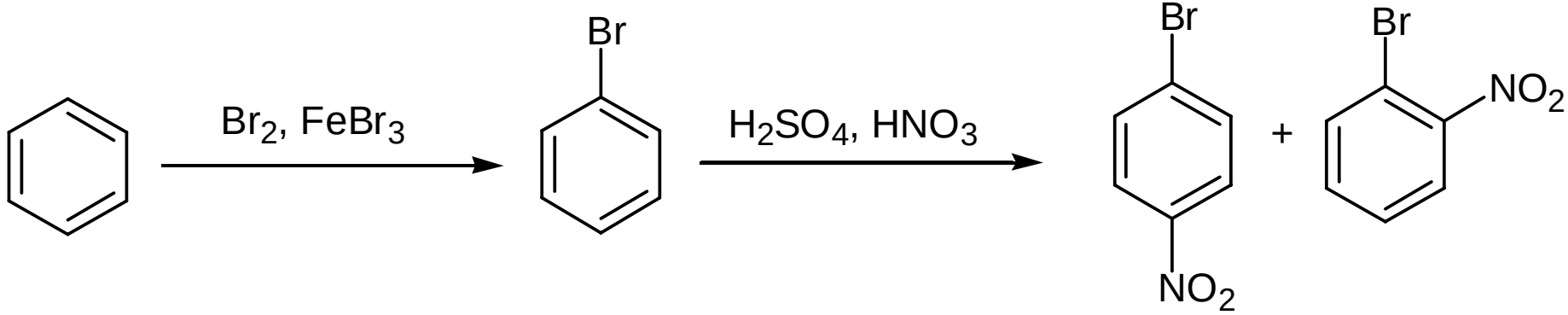


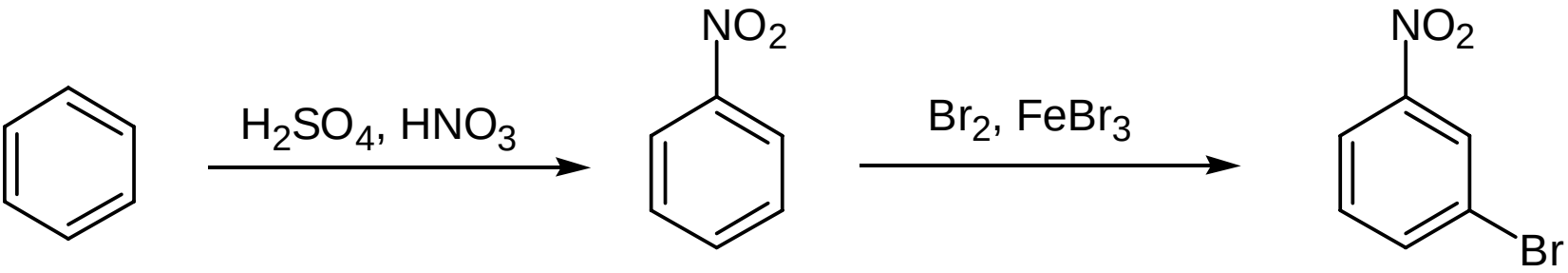
g)取代反應之應用實例 (699-703):

When designing a synthesis of substituted benzenes, the order in which the substituents are introduced is crucial

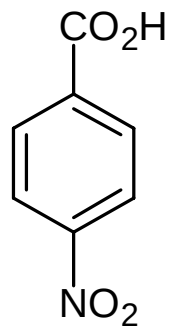
如何由苯製備下列化合物：

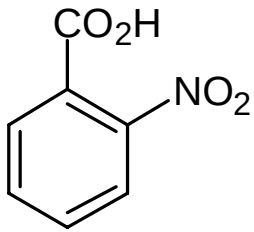


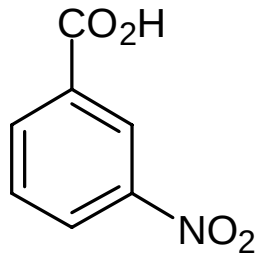


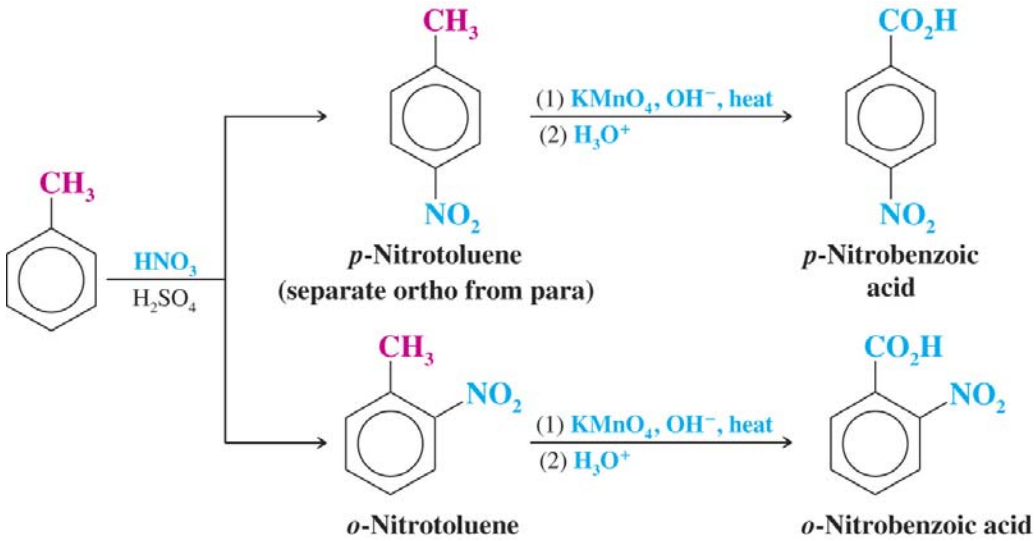


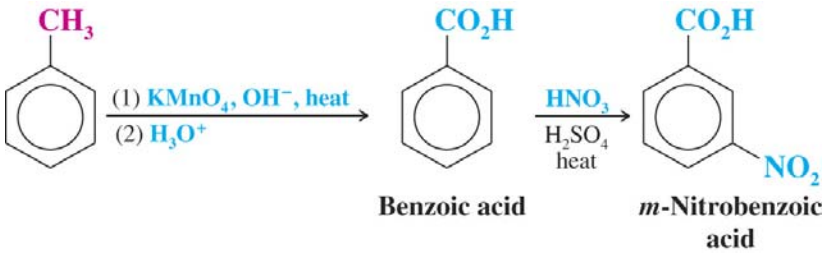
如何由甲苯製備下列化合物：



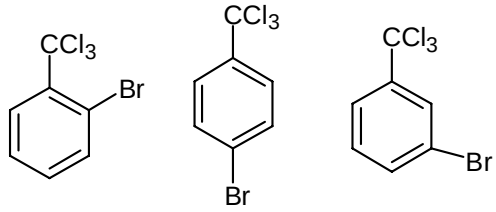


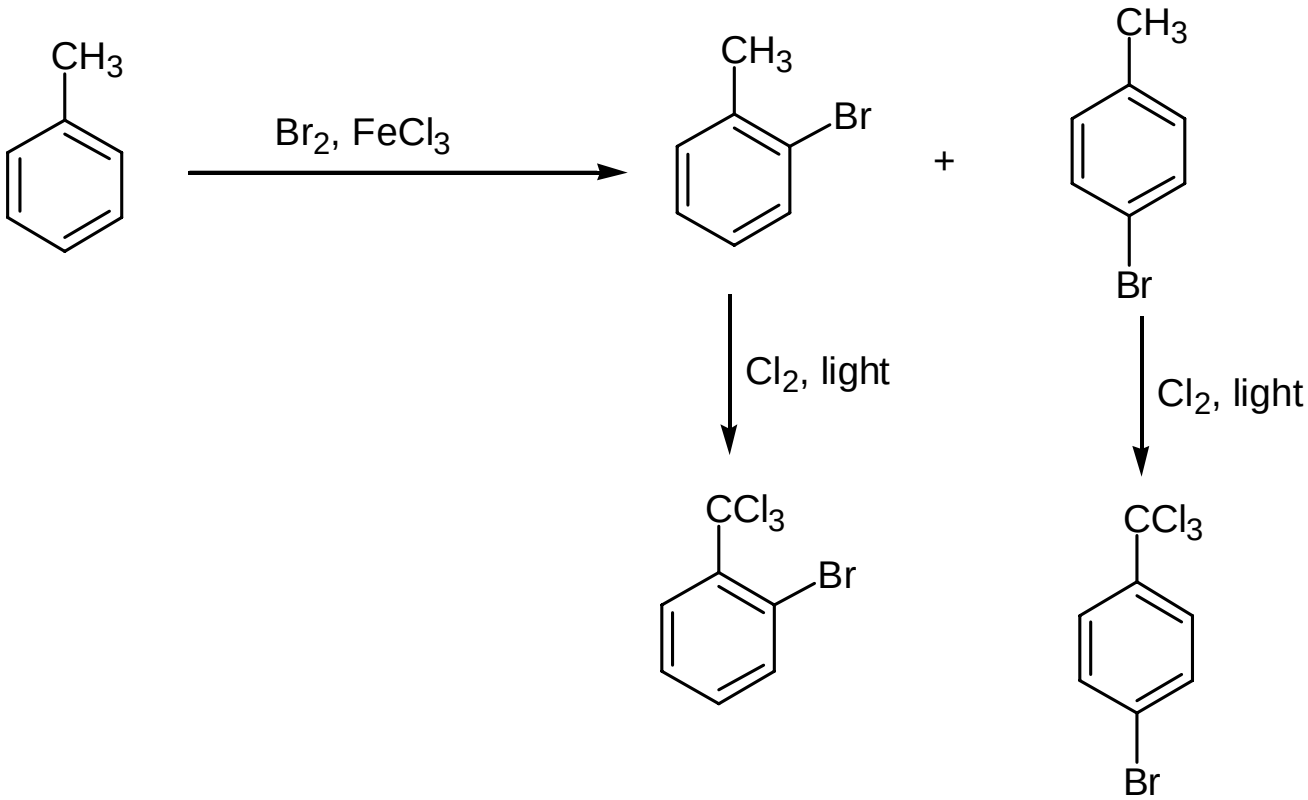


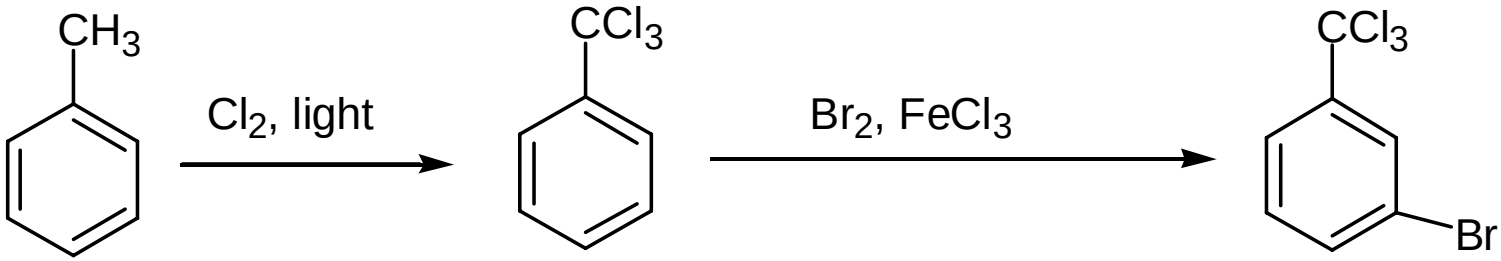


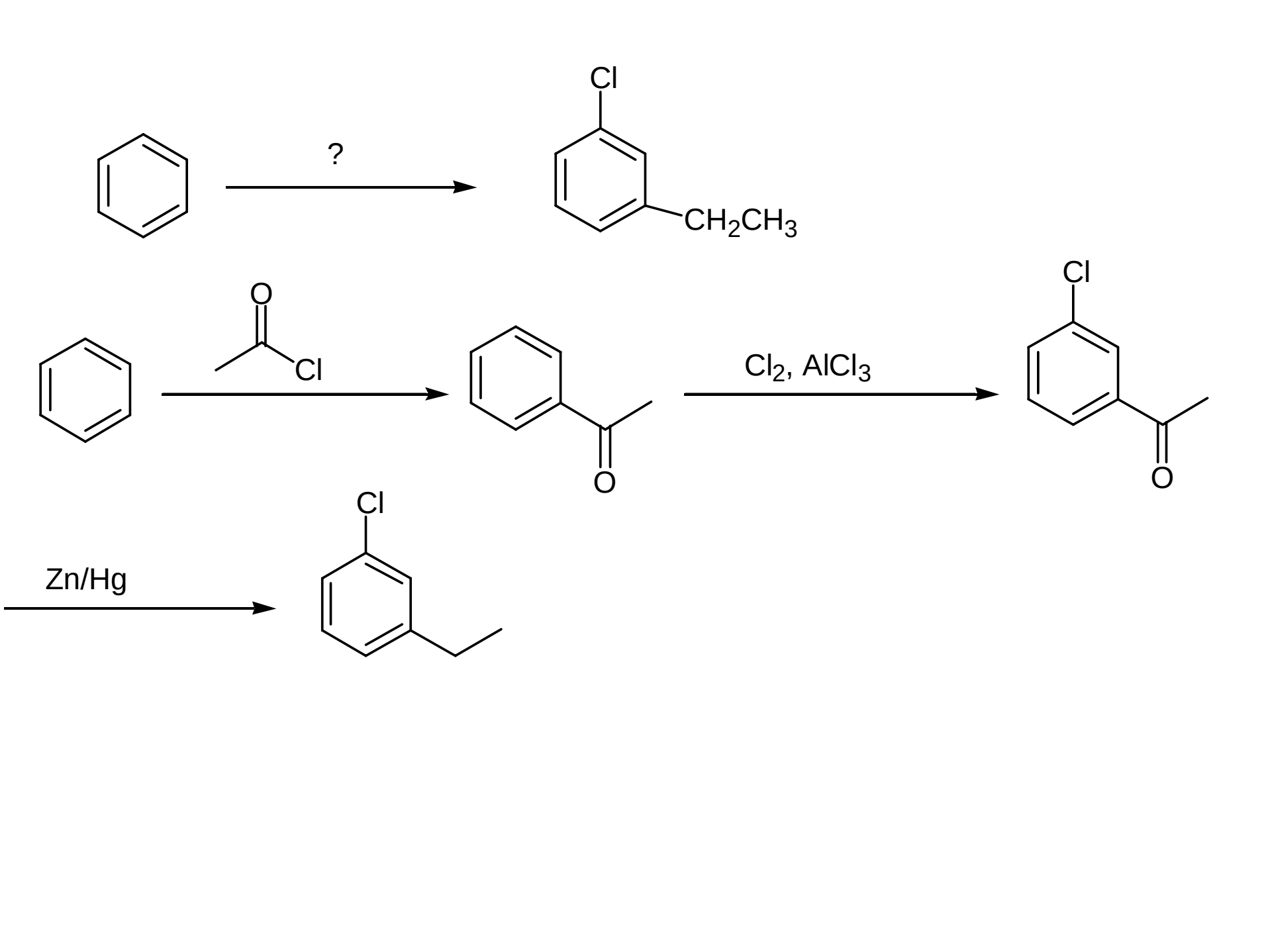


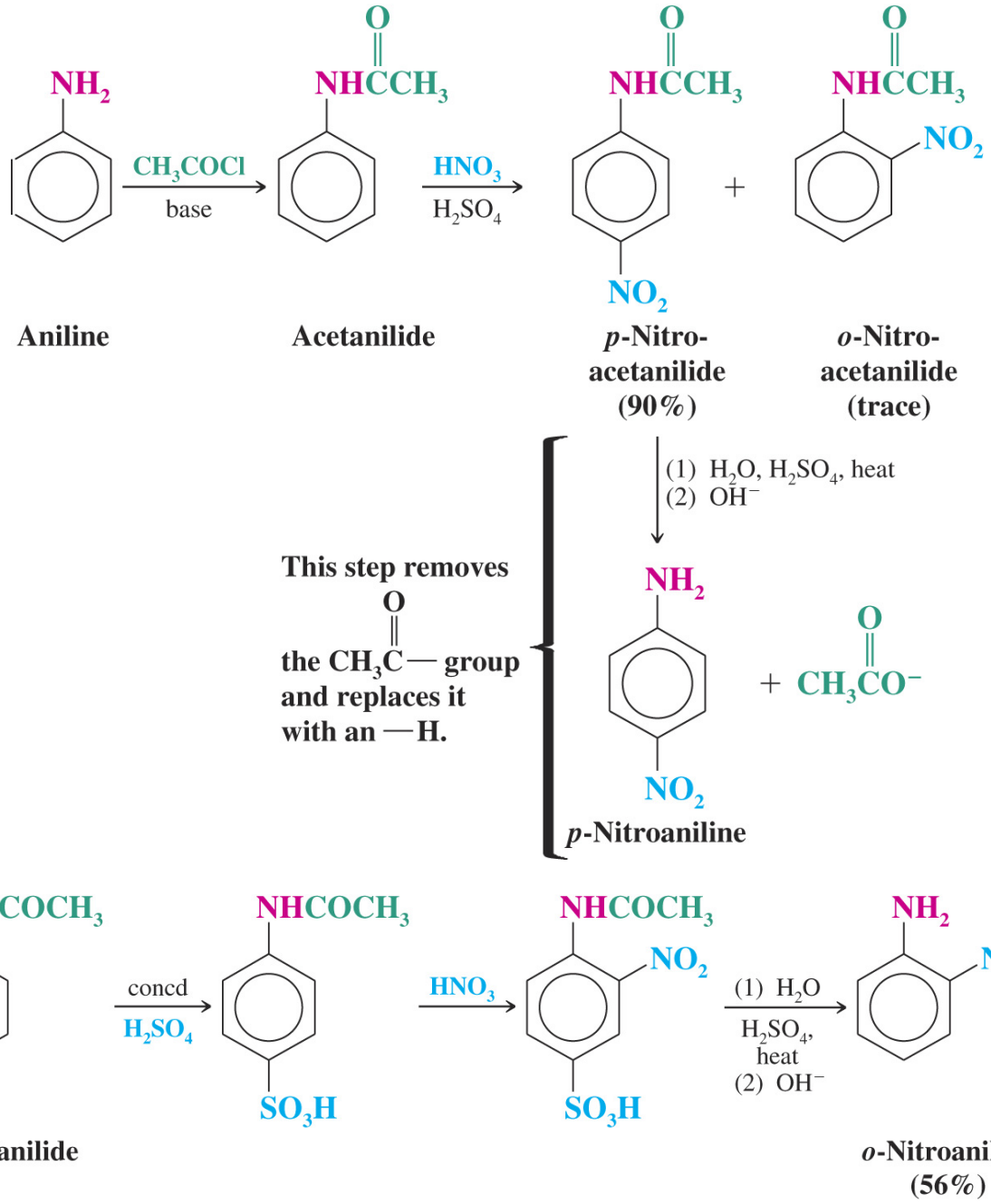
如何由甲苯製備下列化合物：







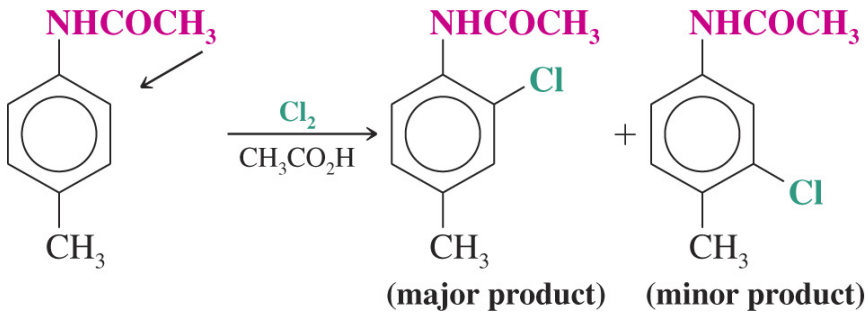

?
Cl
CH2CH3
O
Cl
O
Cl2, AlCl3
Cl
O
Zn/Hg
Cl



The concept of the protecting group

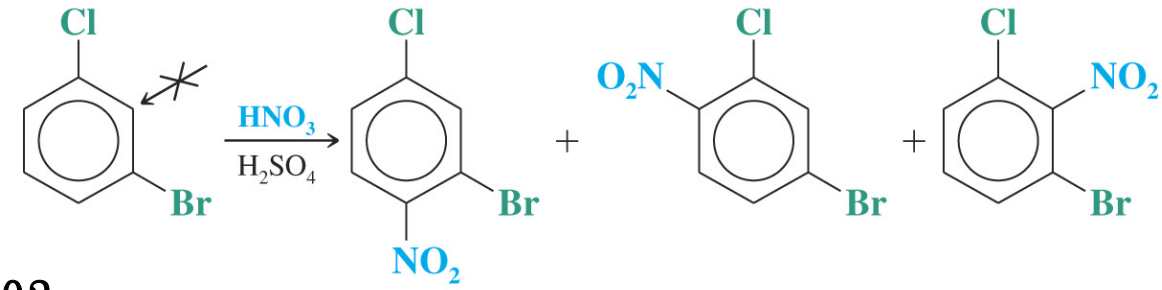
h) Orientation in disubstituted benzene:

i) When two substituents are present on the ring initially, the more powerful activating group generally determines the orientation of subsequent substitution



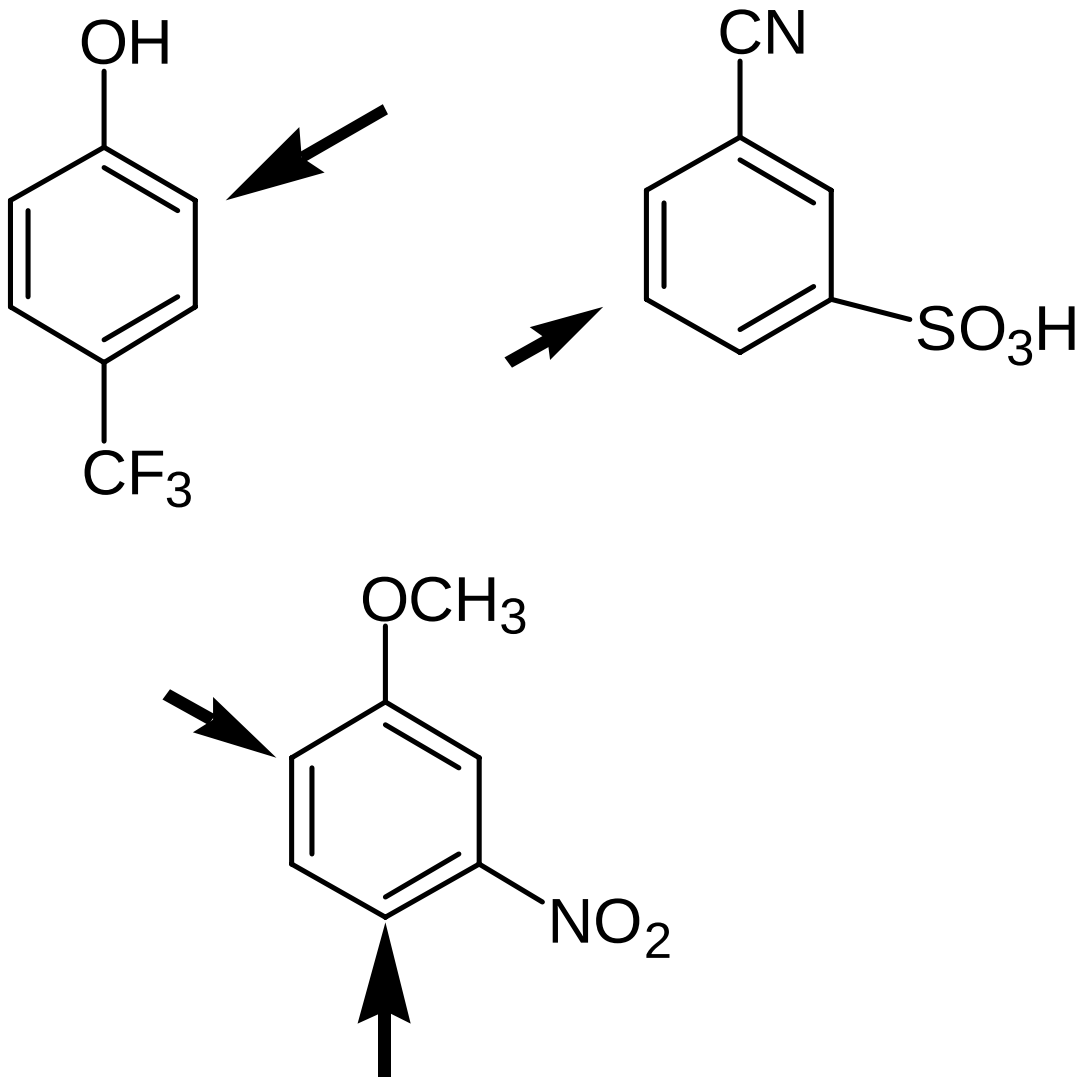
ii) Ortho-para directors determine orientation over meta directors

iii) Substitution does not occur between meta substituents due to steric hindrance

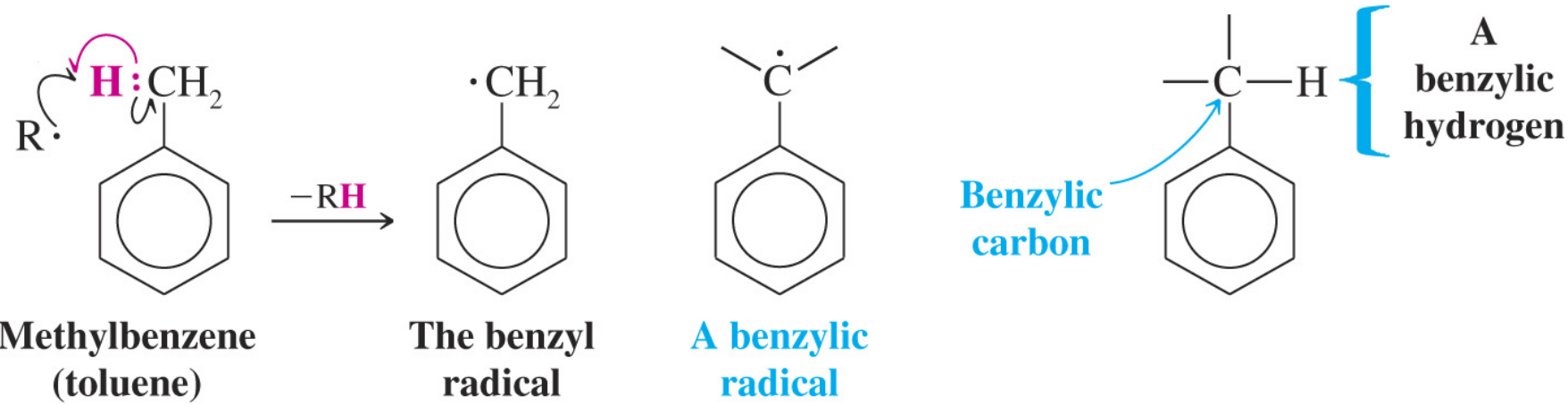


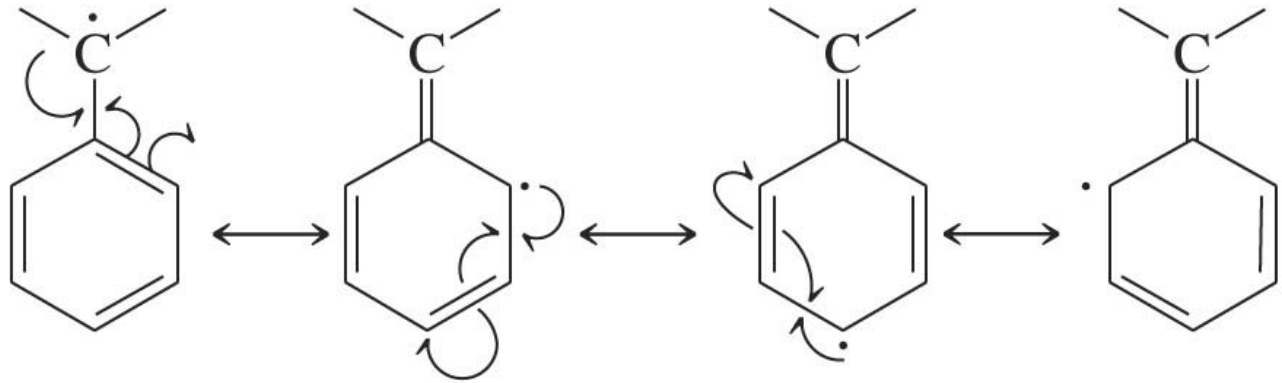
Exercise 703

Exercise on page 703

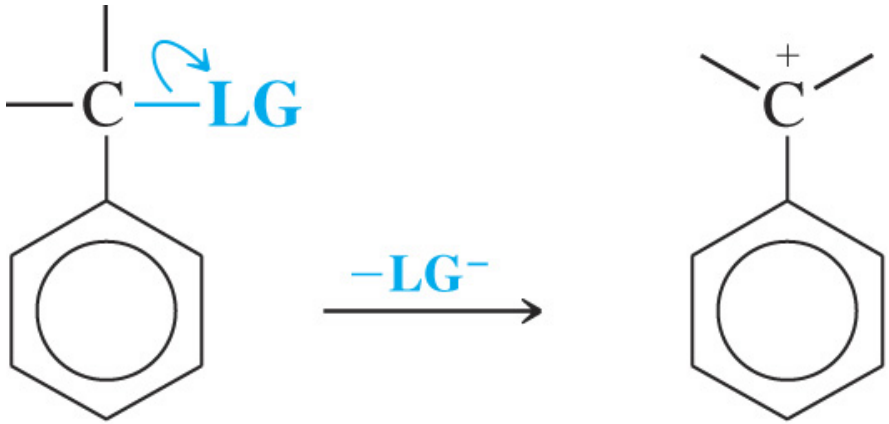


2）Benzylic 的自由基和正碳離子反應

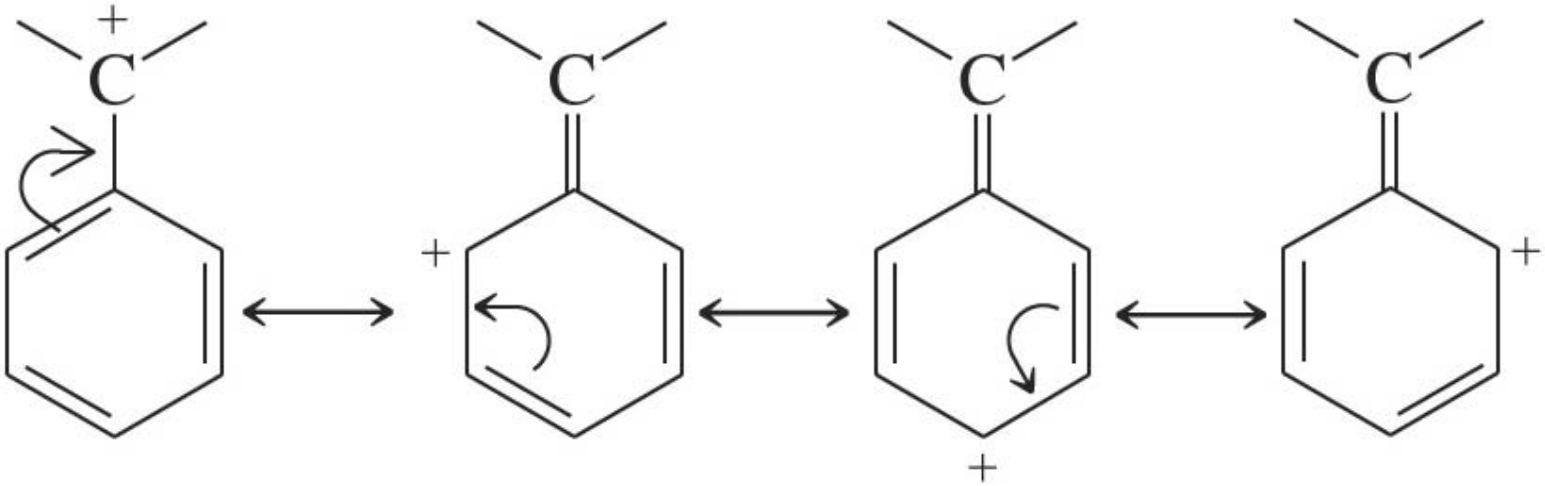




Benzylic radicals are stabilized by resonance.

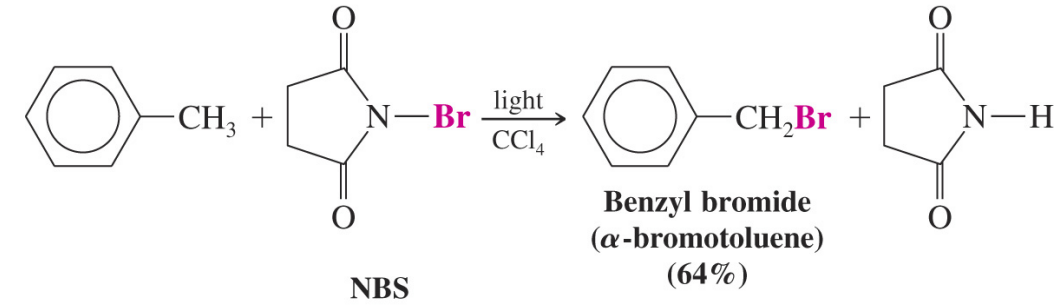


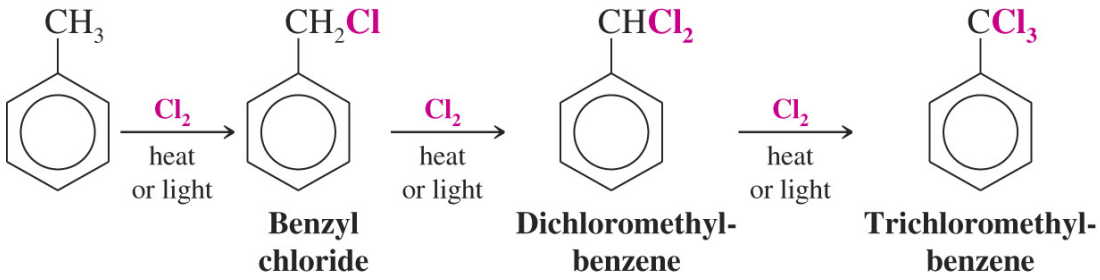
A benzylic cation



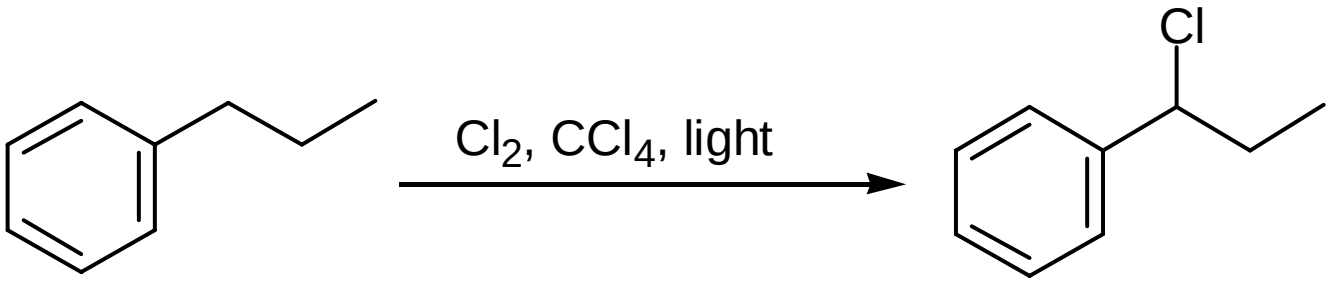
Benzylic cations are stabilized by resonance.

a)自由基反應

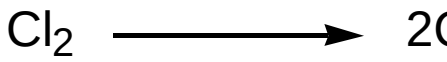


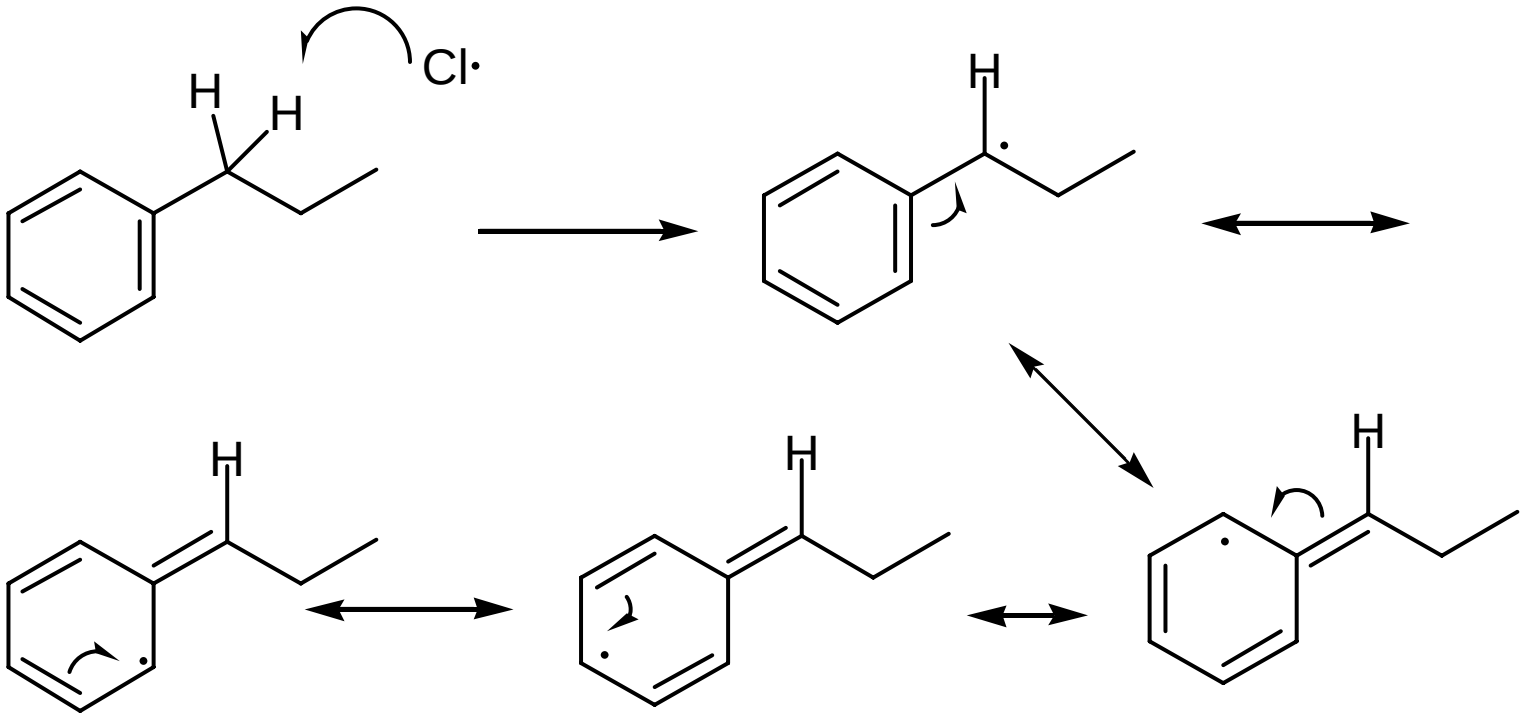


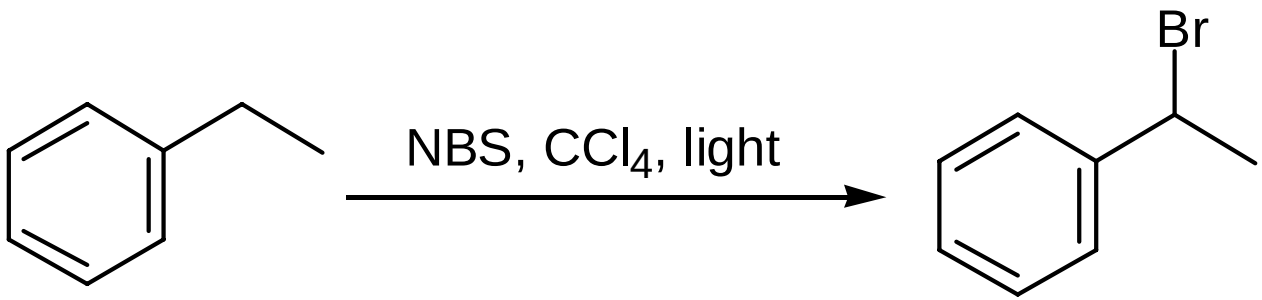
Drawing the mechanisms of the above reactions



major product



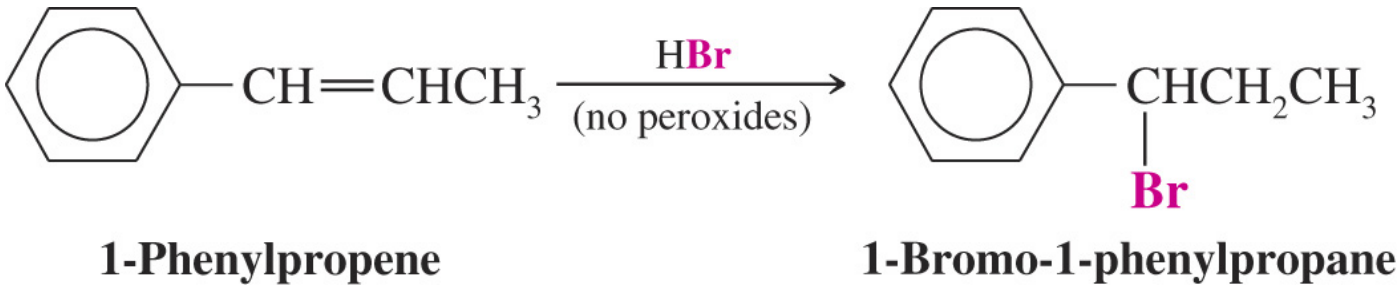




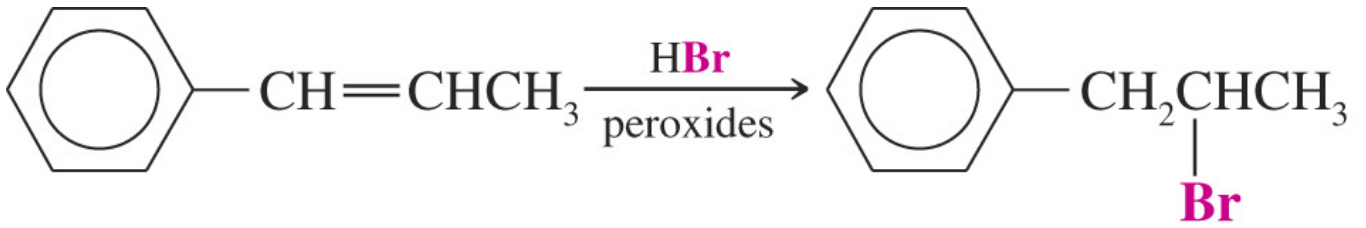
Explain

major product

b) Benzylic 的正碳離子反應

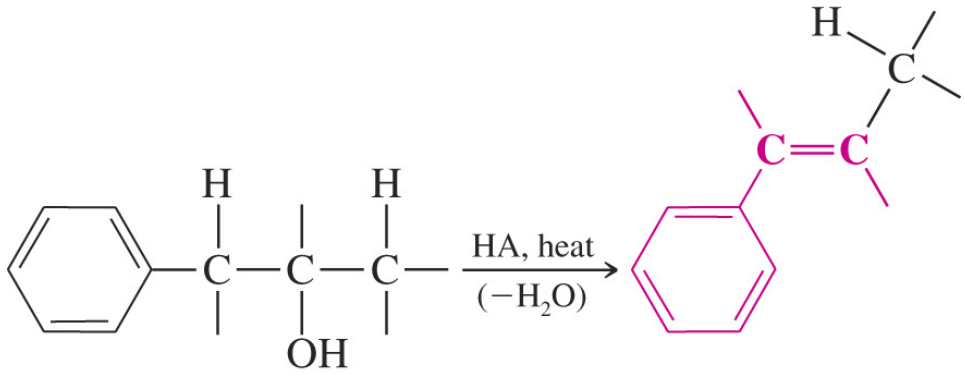


1-Phenylpropene **1-Bromo-1-phenylpropane**



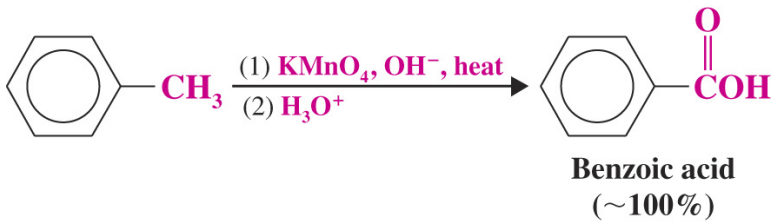
1-Phenylpropene **2-Bromo-1-phenylpropane**

3)脫水反應

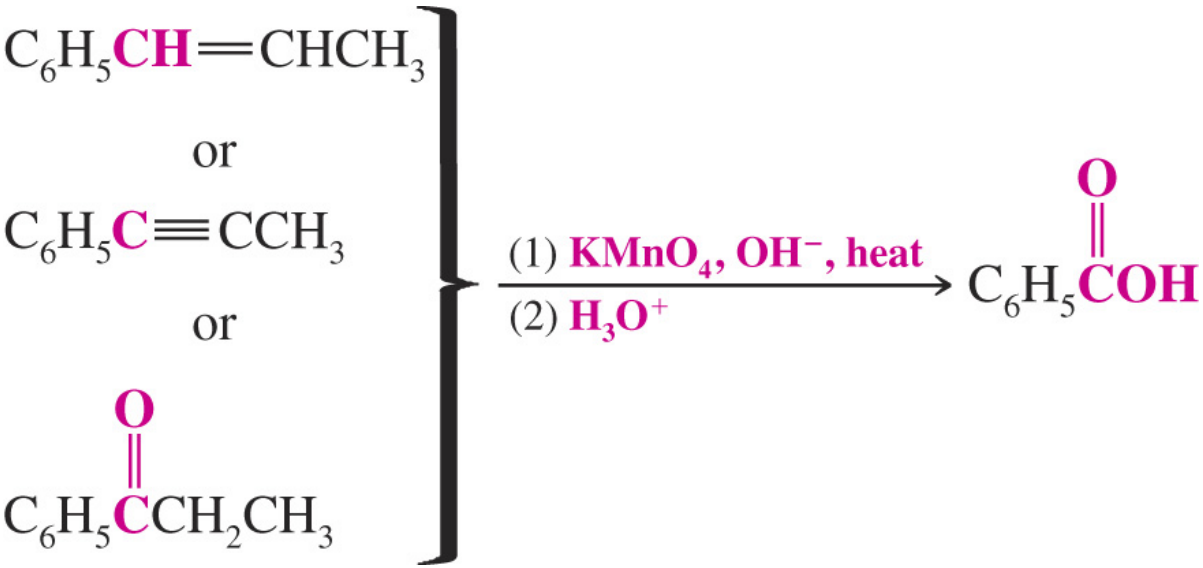


Dehydration of the alcohol below yields only the more stable conjugated alkenyl benzene

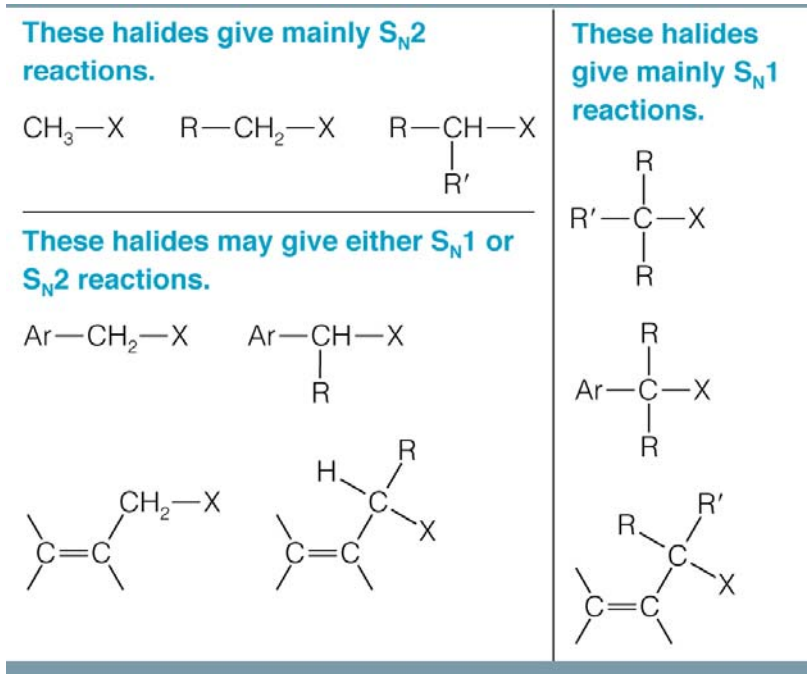
4) 氧化反應

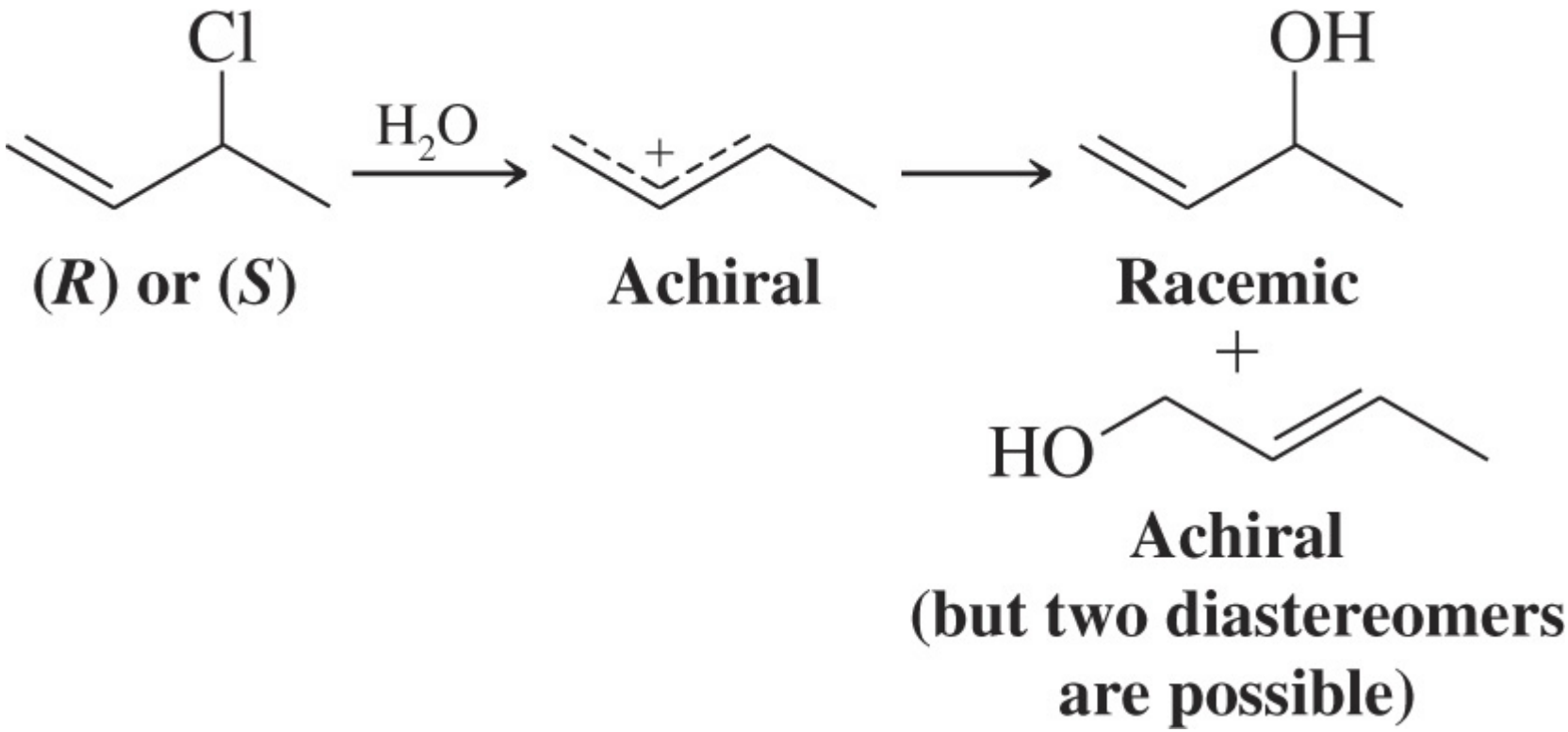


An alkylbenzene **Benzoic acid**



5)Benzylic halide 的SN2, SN1反應





(*R*) or (*S*)

Achiral

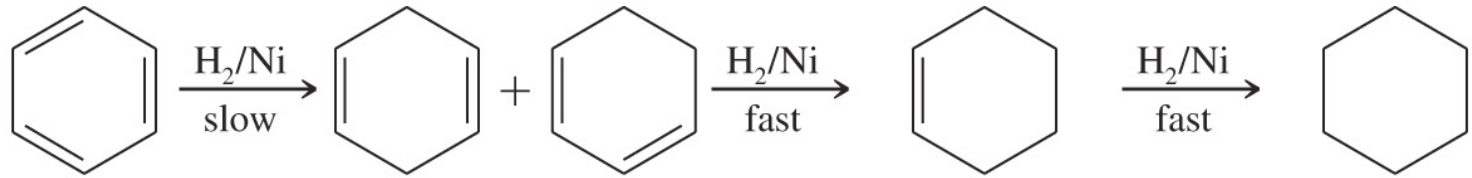
Racemic

+

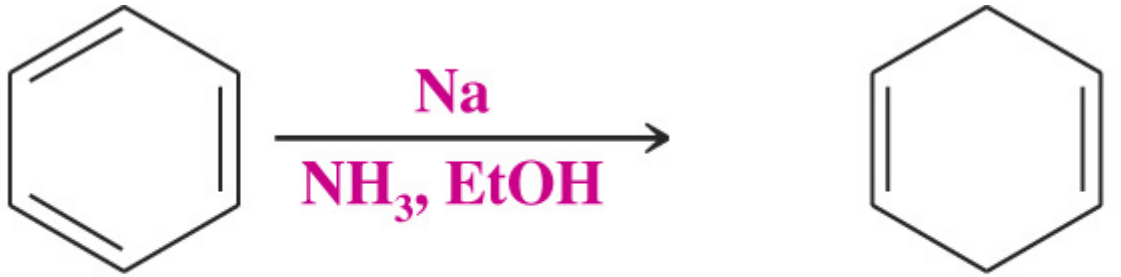
Achiral

(but two diastereomers are possible)

6）苯類化合物的還原反應



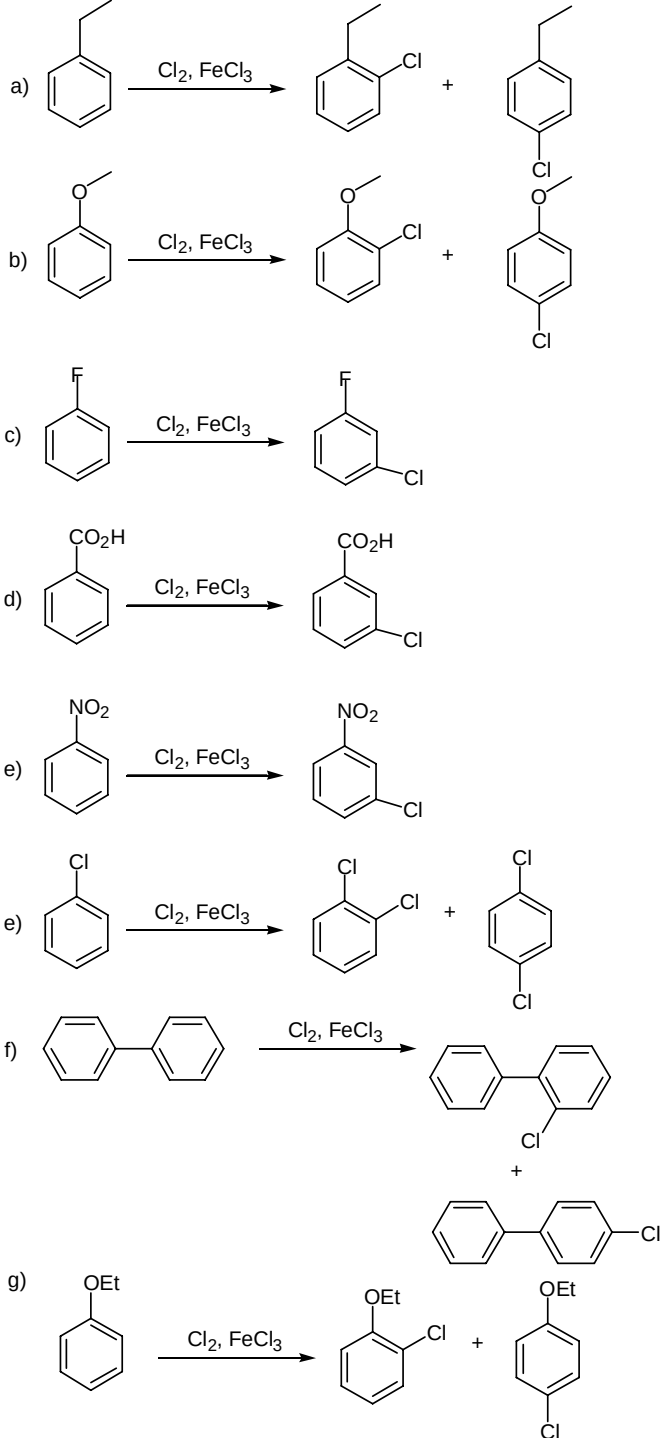
Benzene **Cyclohexadienes** **Cyclohexene** **Cyclohexane**



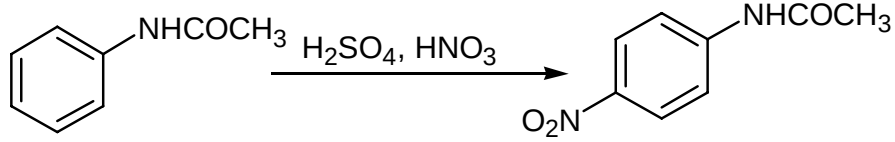
Benzene **1,4-Cyclohexadiene**

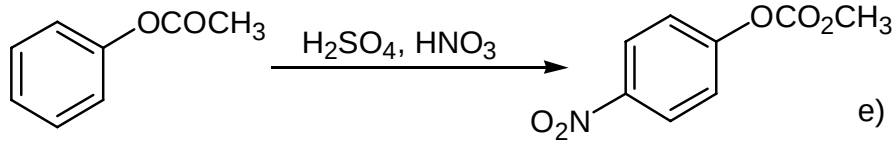
Birch reduction

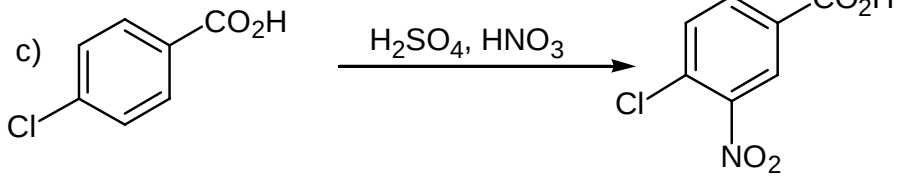
15.26: give the major product:

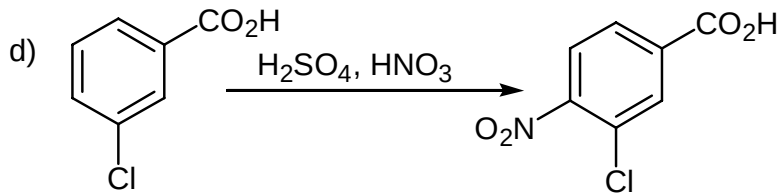


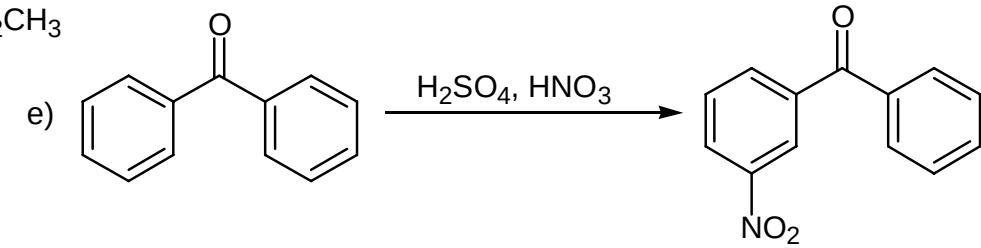
15.27: give the major product:

a) 

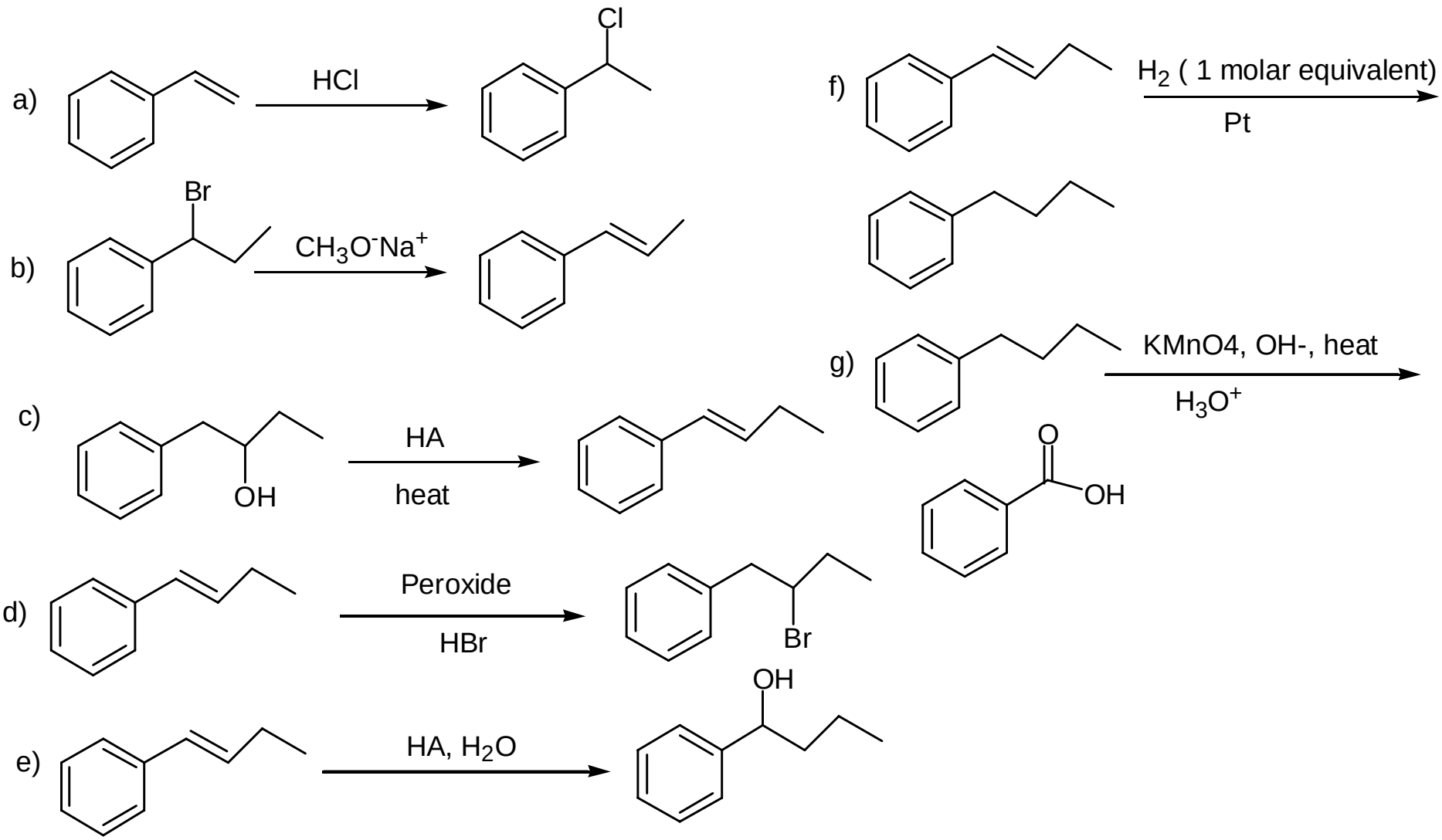
b) 

c) 

d) 

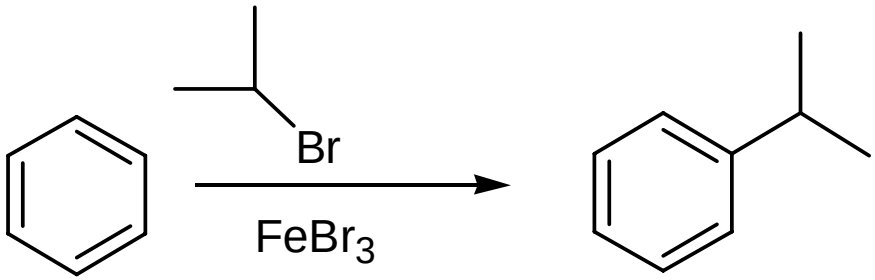
e) 

15.28: Predict the major product(s):

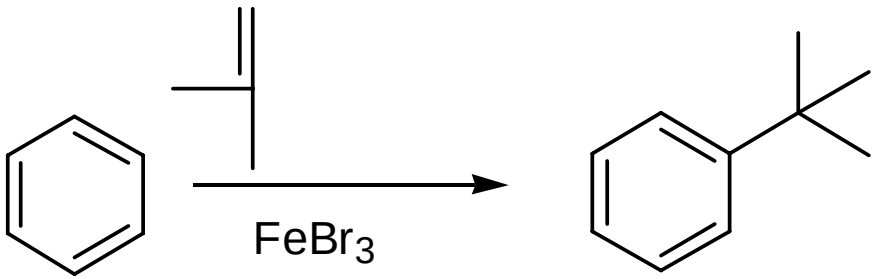

a)
HCl
Cl
b)
Br
$CH_3O^-Na^+$
c)
OH
HA
heat
d)
Peroxide
HBr
Br
e)
HA, H_2O
OH
f)
H_2 (1 molar equivalent)
Pt
g)
KMnO4, OH-, heat
H_3O^+
O
OH

15.29: From benzene, synthesize the following compounds:

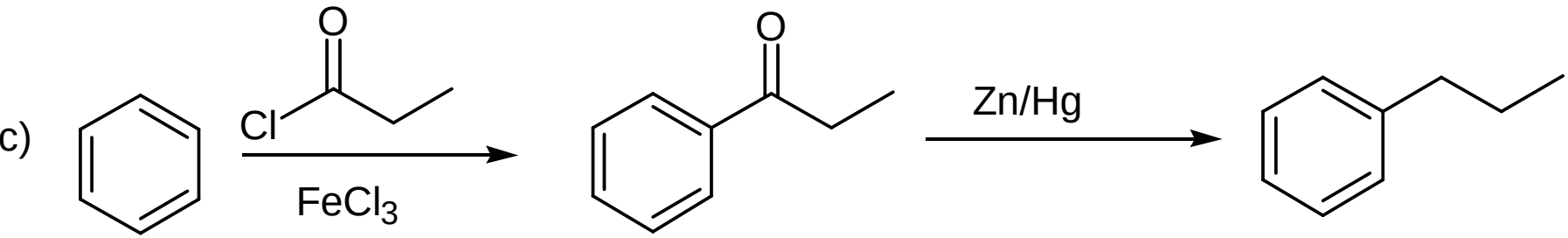
a)



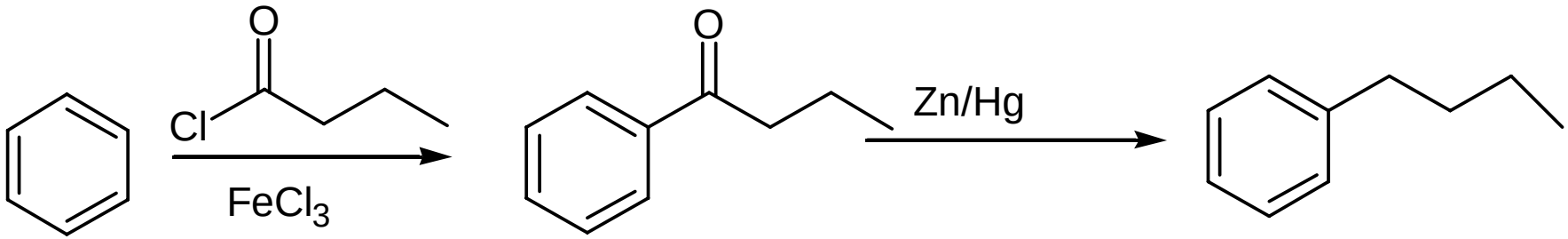
b)



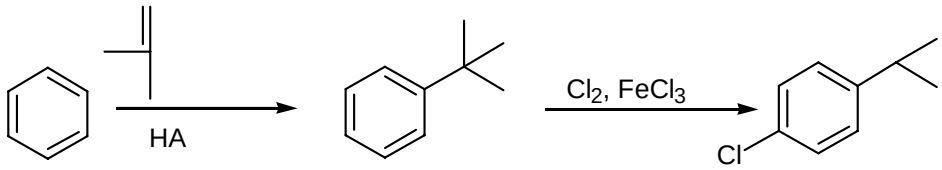
c)



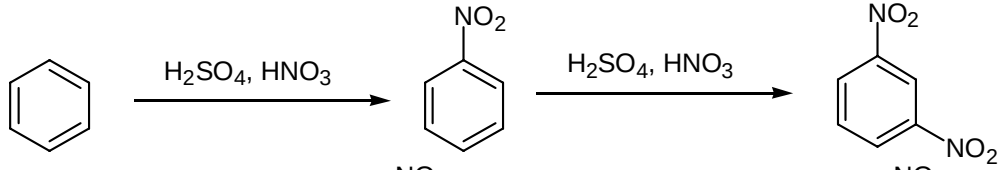
d)



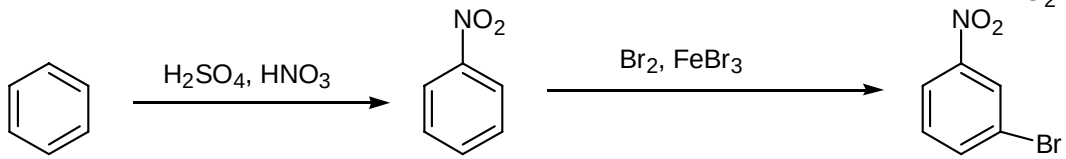
e)


HA
Cl2, FeCl3
Cl

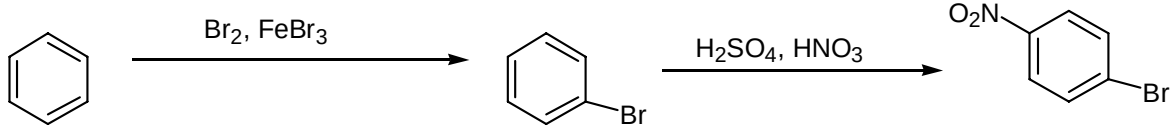
h)


H2SO4, HNO3
NO2
H2SO4, HNO3
NO2
NO2

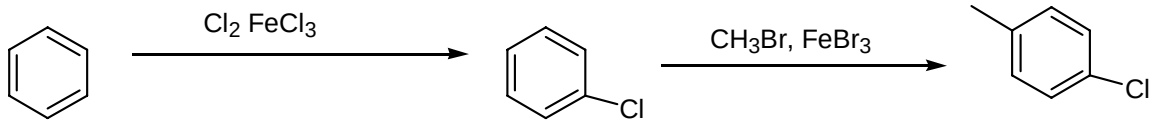
i)

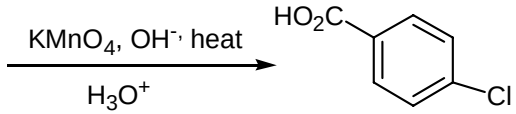

H2SO4, HNO3
NO2
Br2, FeBr3
NO2
Br

j)

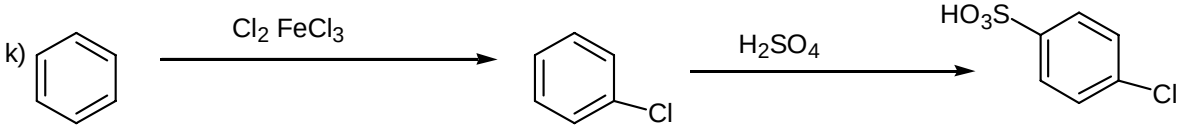

Br2, FeBr3
Br
H2SO4, HNO3
O2N
Br

j)

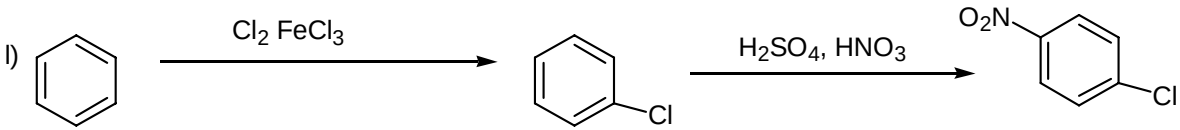

Cl2 FeCl3
Cl
CH3Br, FeBr3
Cl


KMnO4, OH-, heat
H3O+
HO2C
Cl

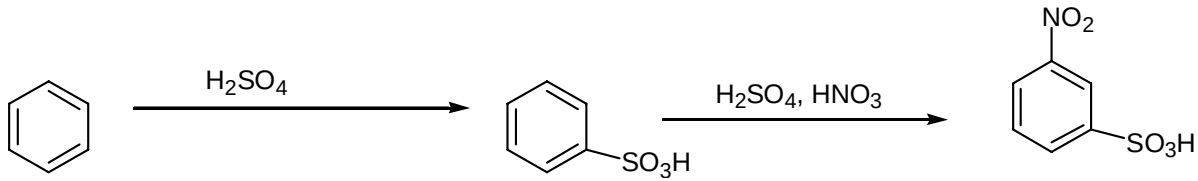
k)


Cl2 FeCl3
Cl
H2SO4
HO3S
Cl

l)


Cl2 FeCl3
Cl
H2SO4, HNO3
O2N
Cl

m)


H2SO4
SO3H
H2SO4, HNO3
NO2
SO3H