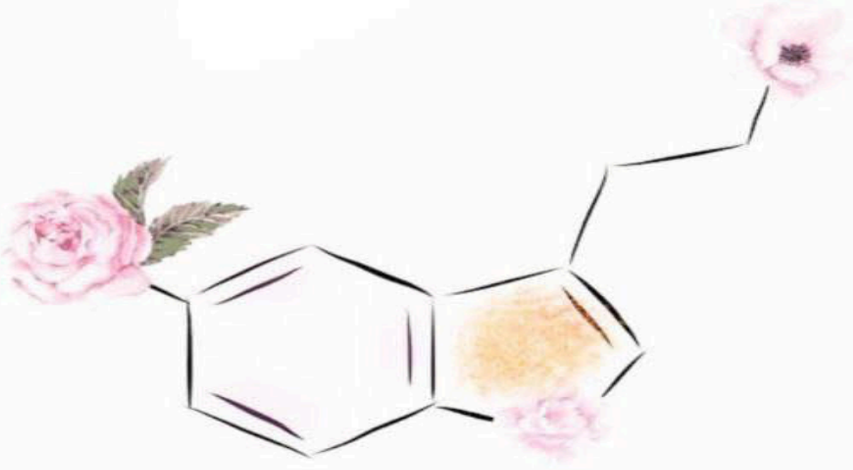
Date:
23 / 12 / 2023

لجان الدُّفعات

Soul Academy



تفريغ عضويه 1

موضوع المحاضرة: Benzene and Aromatics

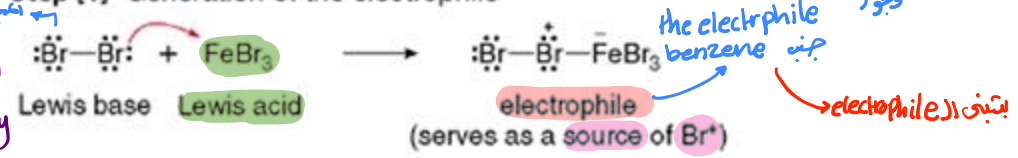
رقم المحاضرة : (٩)

إعداد الصيدلانيه : Gufran khseeb

Halogenation

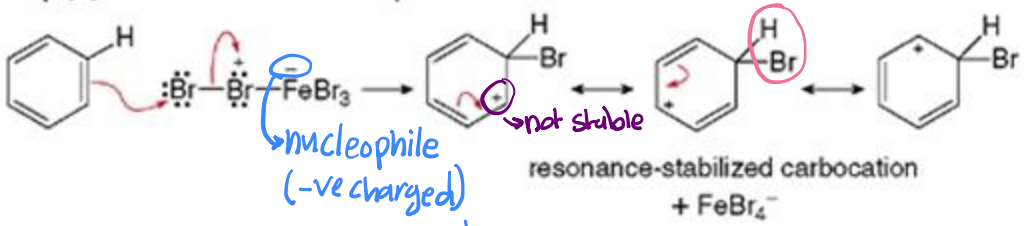
Mechanism 18.2 Bromination of Benzene

Step [1] Generation of the electrophile



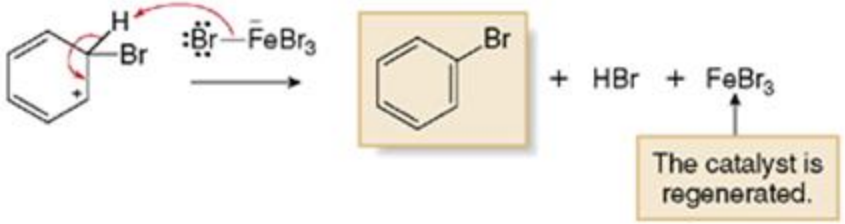
- Lewis acid–base reaction of Br_2 with $FeBr_3$ forms a species with a weakened and polarized Br–Br bond. This adduct serves as a source of Br^+ in the next step.

Step [2] Addition of the electrophile to form a carbocation



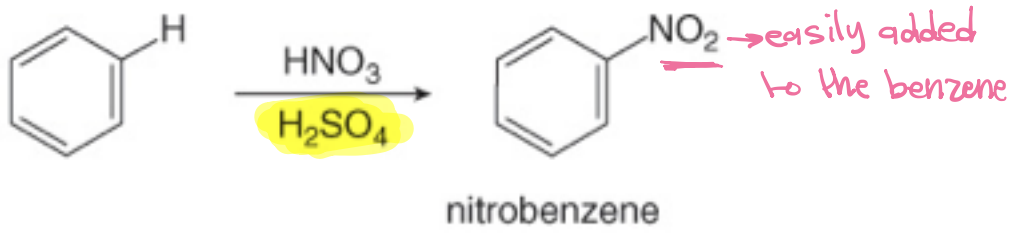
- Addition of the electrophile forms a new C–Br bond and generates a carbocation. This carbocation intermediate is resonance stabilized—**three resonance structures can be drawn.**
- The $FeBr_4^-$ also formed in this reaction is the base used in Step [3].

Step [3] Loss of a proton to re-form the aromatic ring

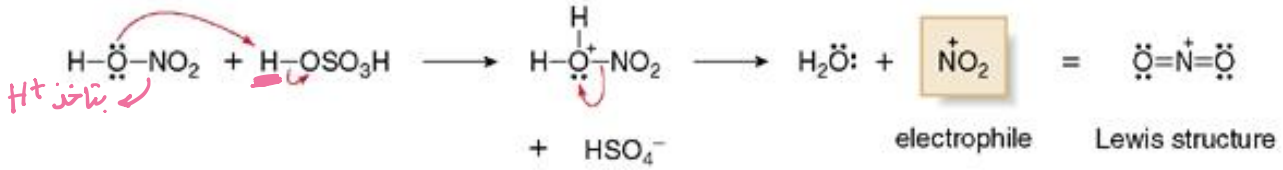


- $FeBr_4^-$ removes the proton from the carbon bearing the Br, thus re-forming the aromatic ring.
- $FeBr_3$, a catalyst, is also regenerated for another reaction cycle.

Nitration

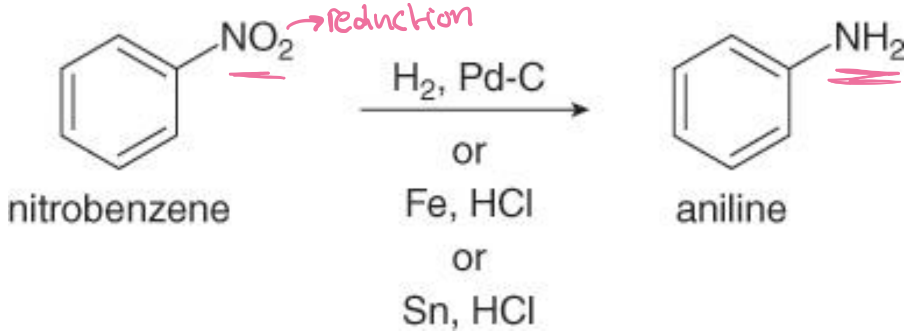


Mechanism 18.3 Formation of the Nitronium Ion ($^+NO_2$) for Nitration

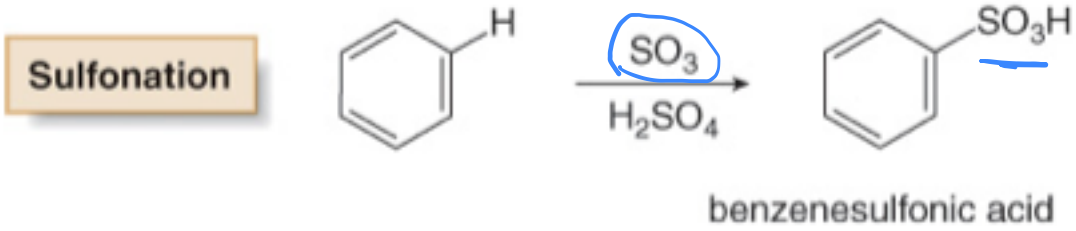


Nitro Group Reduction

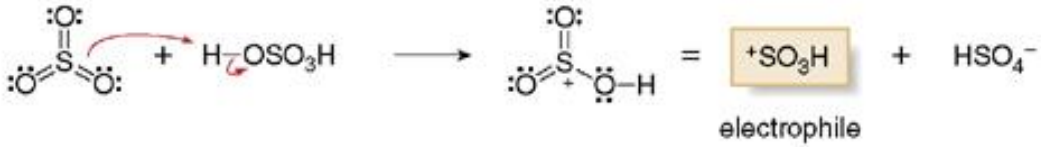
Aromatic nitro groups (NO_2) can readily be reduced to amino groups (NH_2) under a variety of conditions.



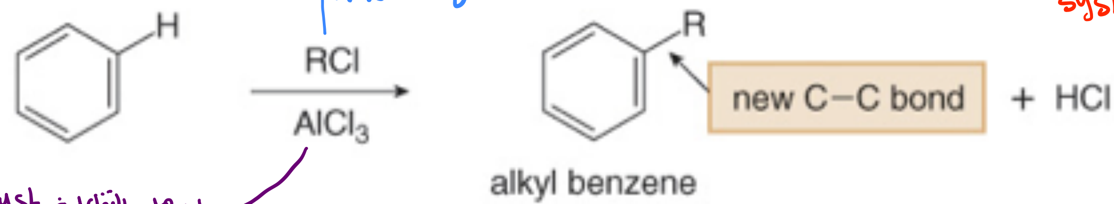
Sulfonation



Mechanism 18.4 **Formation of the Electrophile $^{+}SO_3H$ for Sulfonation**

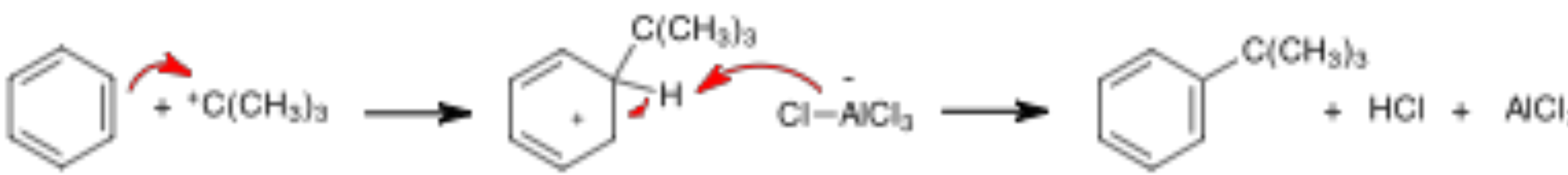


Friedel-Crafts Alkylation



creat the electrophile → then the benzene react with electrophile (at end up with alkyl/methyl---etc benzene)

$$(CH_3)_3C\text{-}Cl + AlCl_3 \longrightarrow (CH_3)_3C{-}\overset{+}{Cl}{-}\overset{-}{Al}Cl_3 \longrightarrow (CH_3)_3C^+ + AlCl_4^-$$



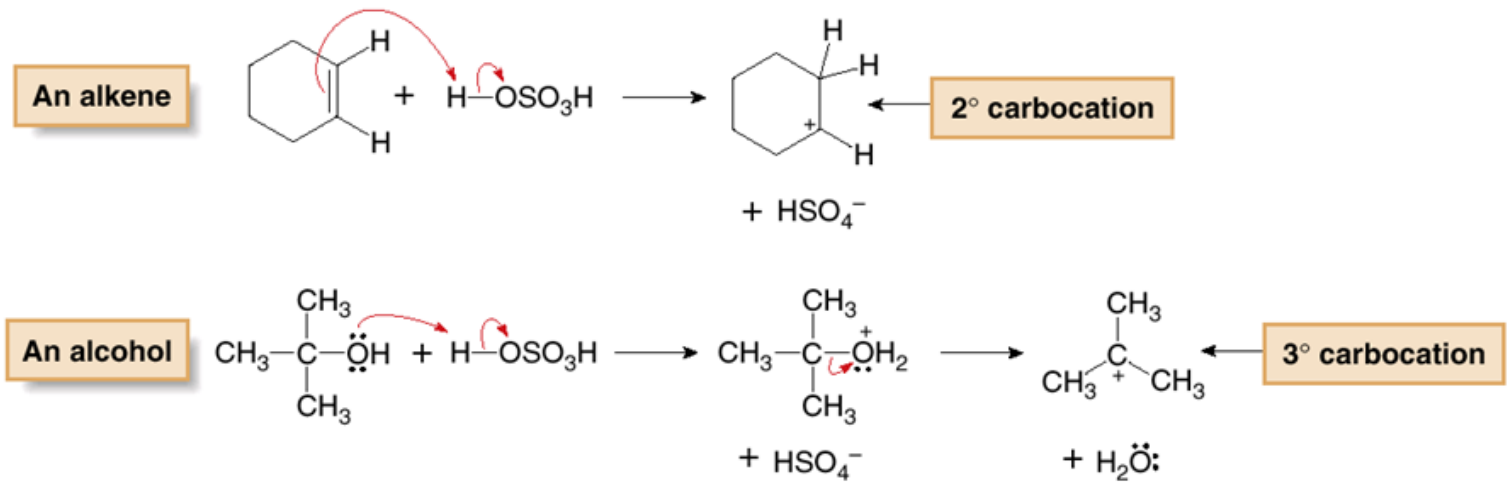
Best with 2ry and 3ry halides

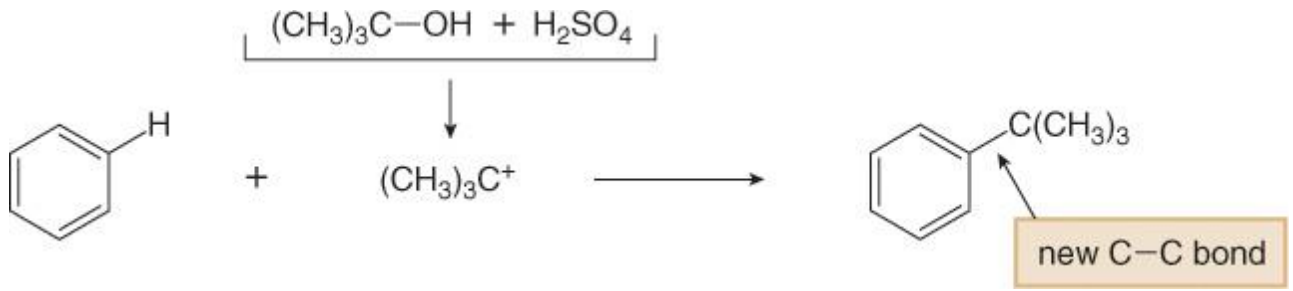
have 2 problems
→ ما بترتبط مع كل المركبات
→ ممكن تعطي اكثر من product
at chemistry
① لازم افصلهم → high cost
② الكمية اقل للمصانع (نسبة و تناسب) (not efechency)

Friedel-Crafts Alkylation

تعريف → the addition of alkyl group to benzene and it it electrophyl دعوا difficient on é add to the rich benzene ring

Other functional groups that form carbocations can also be used as starting materials.

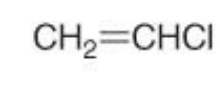




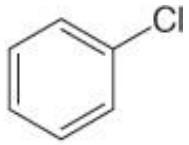
Limitations

[1] Vinyl halides and aryl halides do not react in Friedel-Crafts alkylation.

Unreactive halides in the Friedel–Crafts alkylation

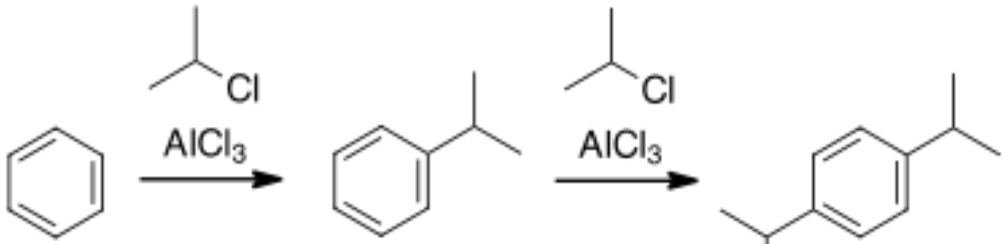


vinyl halide



aryl halide

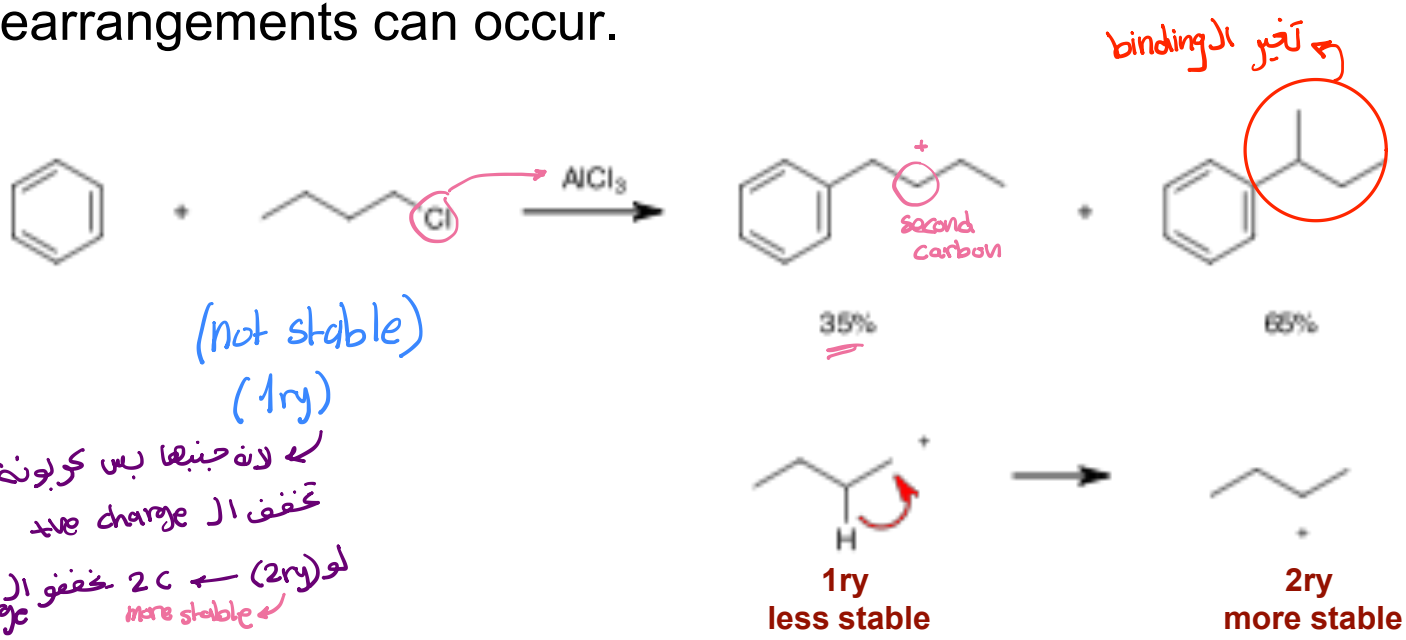
[2] Disubstituted products are obtained in F.-C. alkylations, but not in acylations.



More reactive than benzene

Limitations

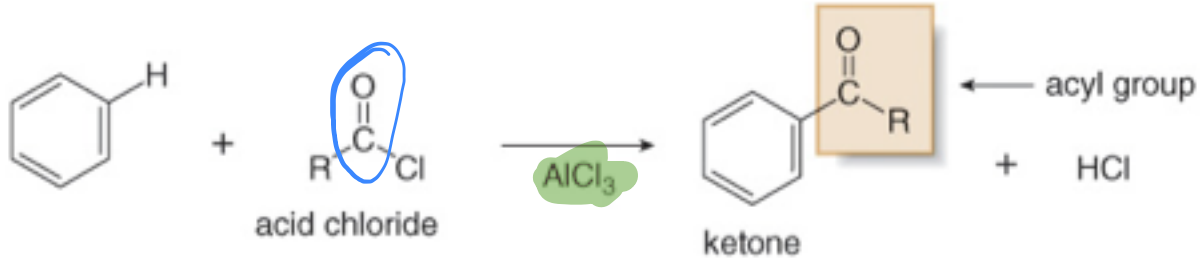
[3] Rearrangements can occur.

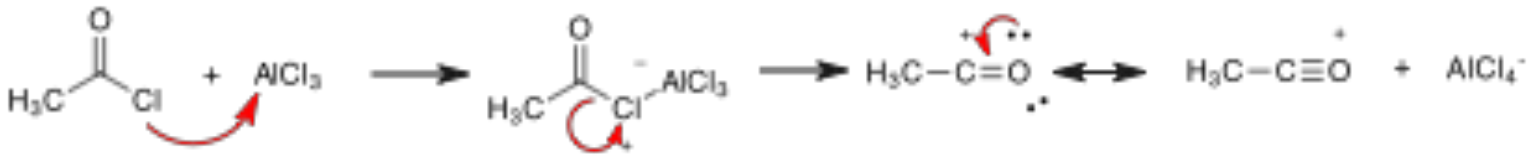


Friedel-Crafts Acylation

(the carbon group bind with acid chloride

Friedel–Crafts acylation—General reaction



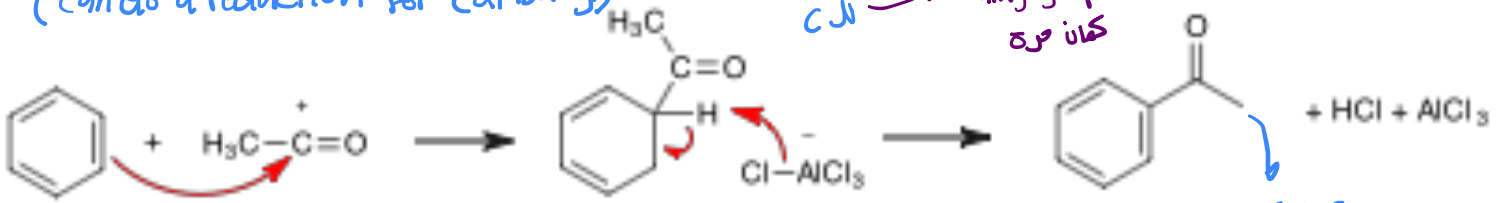


→ عدد الكربونات غير محدد

(can do a reduction for carbonyl) →

ما رجعها لل C

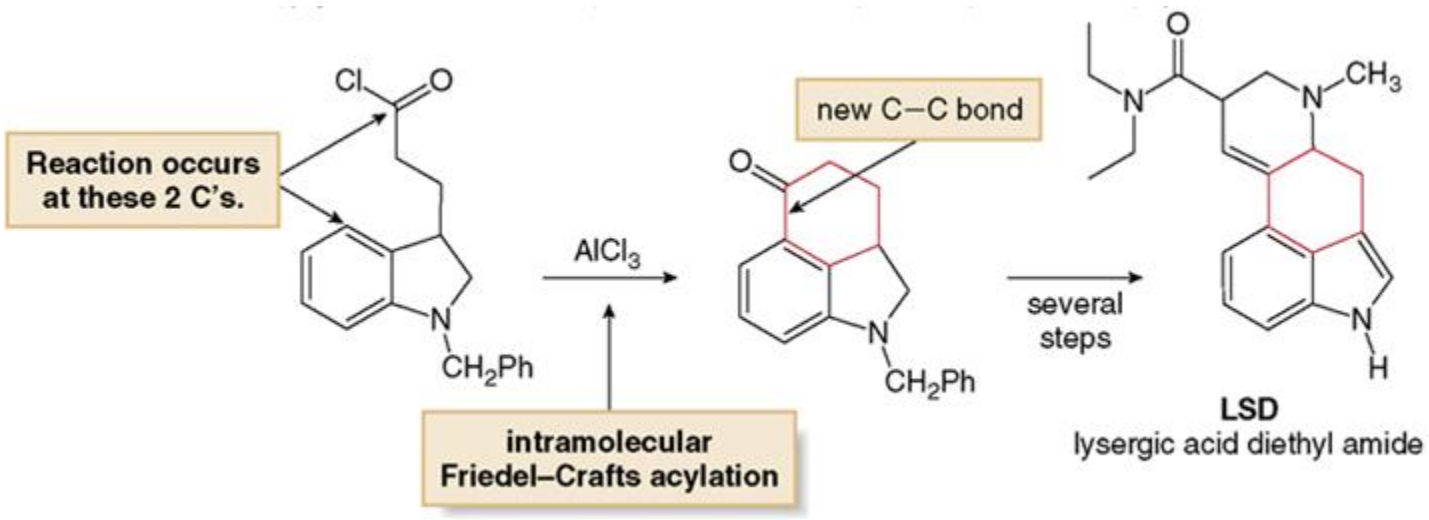
زي كأنو اخذت alkyl group كمان مرة



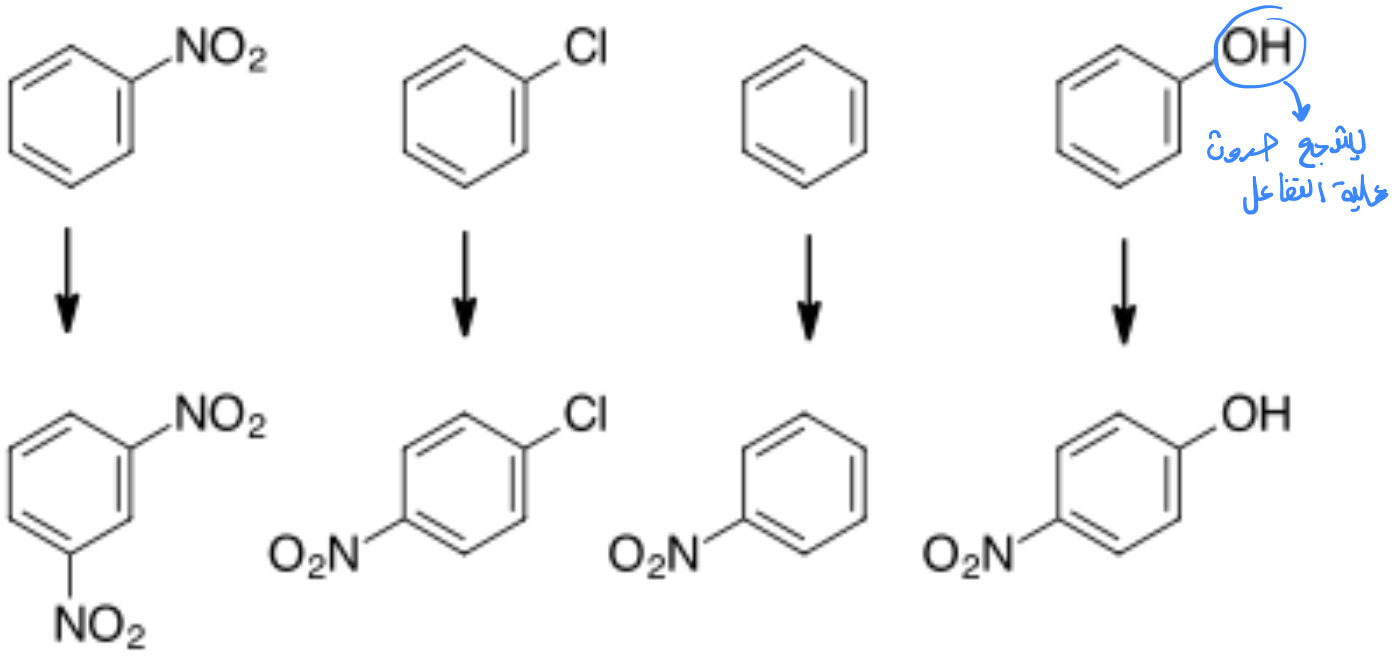
ممكن تكون سلسلة طويلة

intramolecular Friedel-Crafts reactions.

جزء من مركب مع جزء
acyclic group ← من مركب سوا



Nitration of Substituted Benzenes



Relative rates	6×10^{-8}	0.033	1	1000

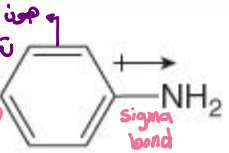
Substituents modify the electron density in the benzene ring, and this affects the course of electrophilic aromatic substitution.

Substituted Benzenes

Inductive effects (through σ bonds):

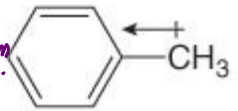
- Atoms more electronegative than carbon—including N, O, and X—pull electron density away from carbon and thus exhibit an electron-withdrawing inductive effect.
- Polarizable alkyl groups donate electron density, and thus exhibit an electron-donating inductive effect.

Electron-withdrawing inductive effect



- N is **more electronegative** than C.
- N inductively withdraws electron density.

Electron-donating inductive effect



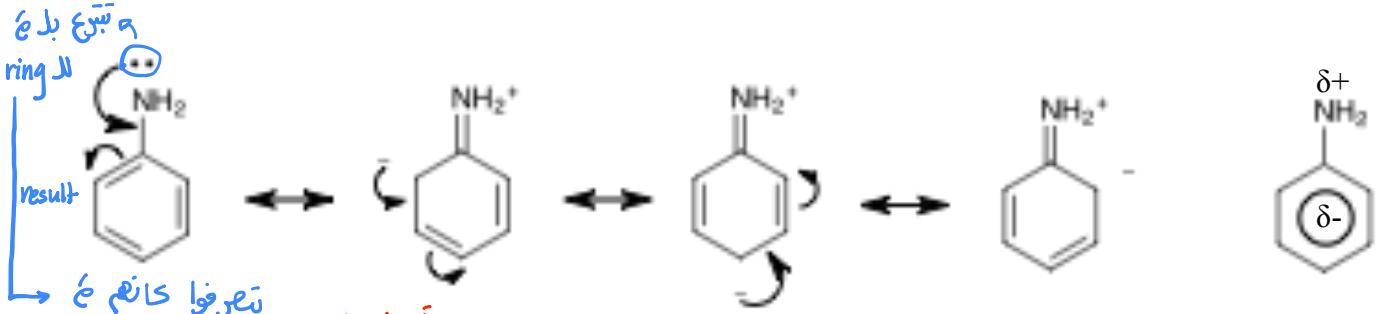
- Alkyl groups are **polarizable**, making them electron-donating groups.

- I	$-NH_3^+$	$-NH_2$,	-OH	-F	-CHO	-CN	SO_3H	$-NO_2$
	$-CF_3$	-NHR	-OR	-Cl	-COR		SO_2R	
		$-NR_2$		-Br	-COOH			
				-I	-COOR			
+ I	$-CH_3$							
	-Alkyl							
	$-SiR_3$							

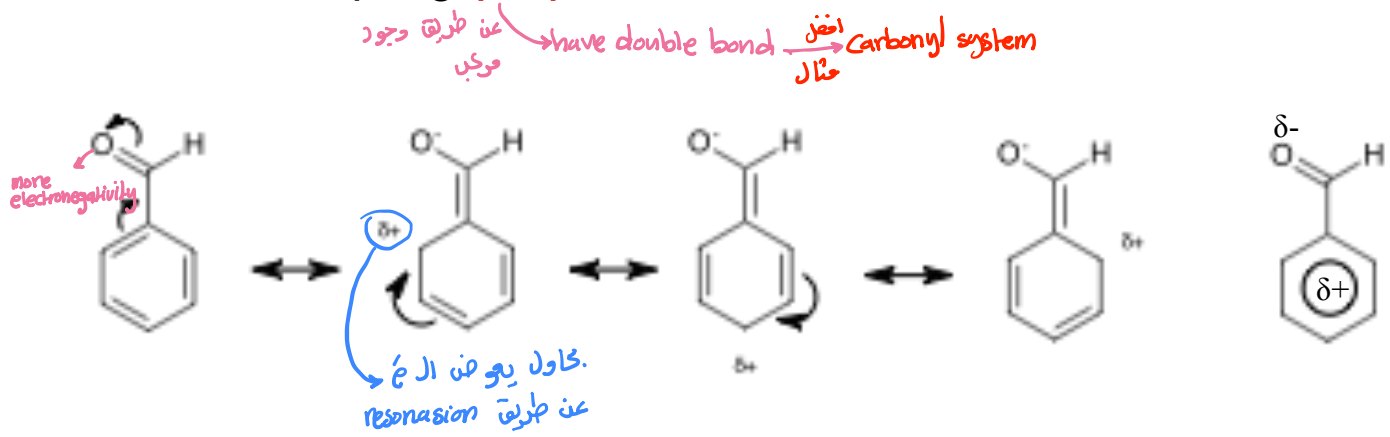
Substituted Benzenes

② **Resonance effects** (through π bonds) are only observed with substituents containing lone pairs or π bonds.

- Substituents containing lone pairs are electron donating **(+ R)**



- Substituents –Y=Z (C_6H_5-Y=Z), where Z is more electronegative than Y are electron accepting **(- R)**

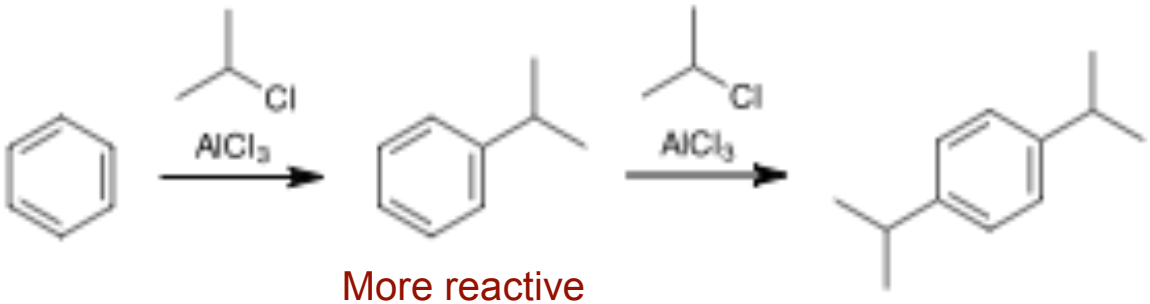


Substituted Benzenes: Activation

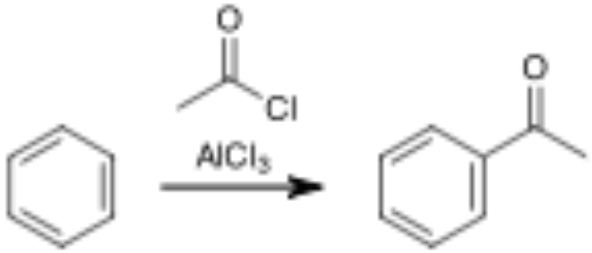
		+ R			- R			
		+R > -I		-I >+R				
- I	$-NR_3+$ CF_3	$-NH_2$, -NHR $-NR_2$	-OH -OR	-F -Cl -Br -I	-CHO -COR -COOH -COOR	CN	SO_3H SO_2R	$-NO_2$
+ I	$-CH_3$ -Alkyl $-SiR_3$							

- Substituents that increase the electron density on the ring activate the ring towards electrophiles. Substituents that decrease the electron density on the ring deactivate the ring towards electrophiles.
- To predict whether a substituted benzene is more or less electron rich than benzene itself, we must consider the net balance of both the inductive and resonance effects.

Substituted Benzenes: Activation



More reactive
than benzene



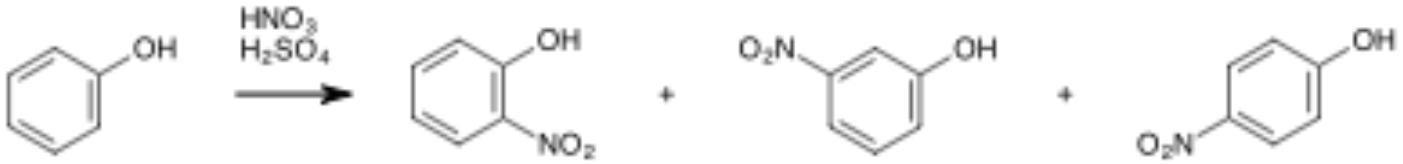
Less reactive
than benzene

Substituted Benzenes: Orientation

(substitution صعبة اجمالية)

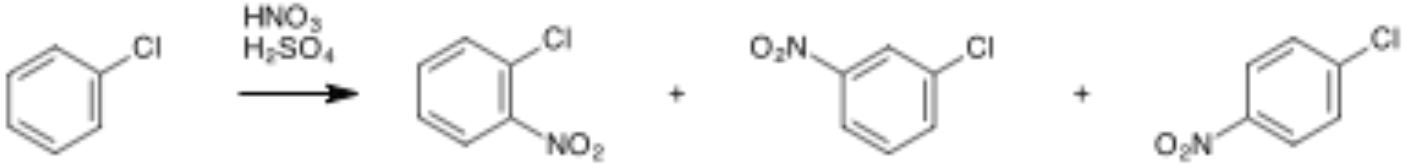
اجمالية meta دايرة لاكن نسبة حدوثها قليلة جدا

+R > -I (-OR, -NR2): activating, o- p- directing



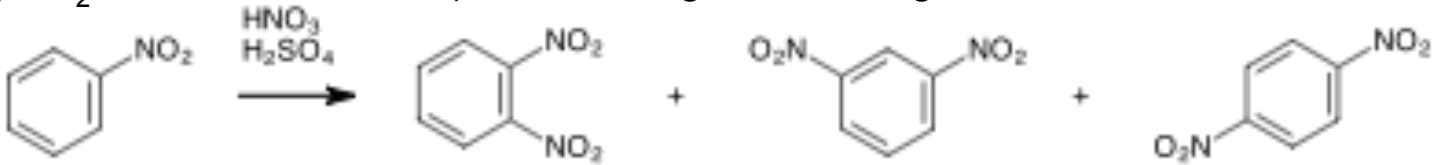
(النسب مش مهمة) 30% traces 70%

-I > +R (-F, -Cl, -Br, -I): deactivating, o- p- directing



35% traces 65%

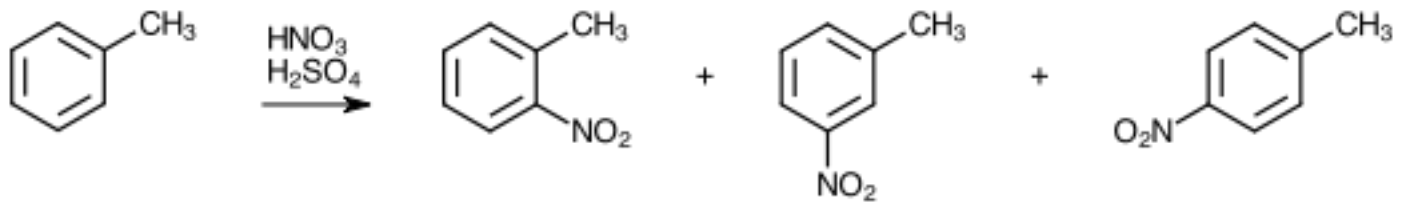
-I, -R (-NO_2, -SO3H, -CN, -COR): deactivating, m- directing.



5% 90% 5%

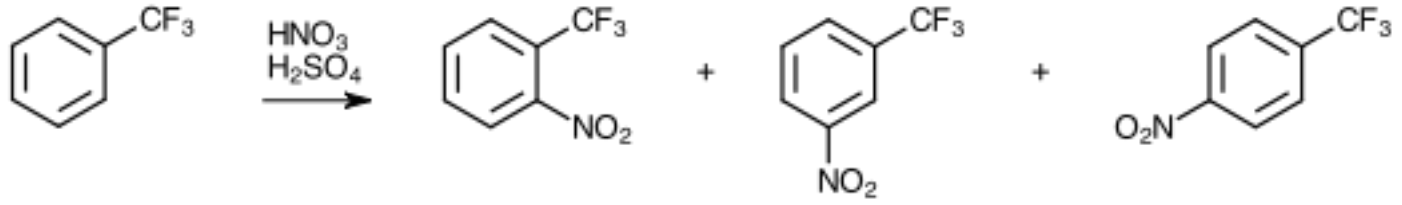
Substituted Benzenes: Orientation

+ I: activating, -o -p directing (same as + R)



58% 5% 37%

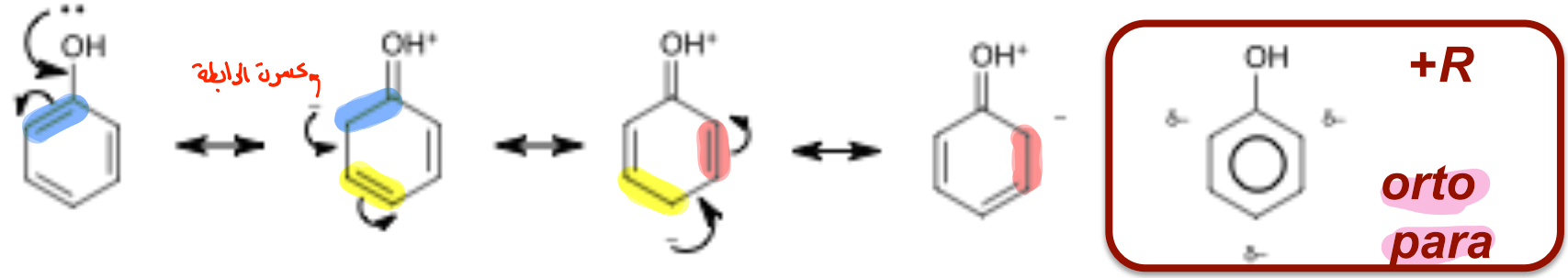
- I: deactivating, -m directing (same as - R)

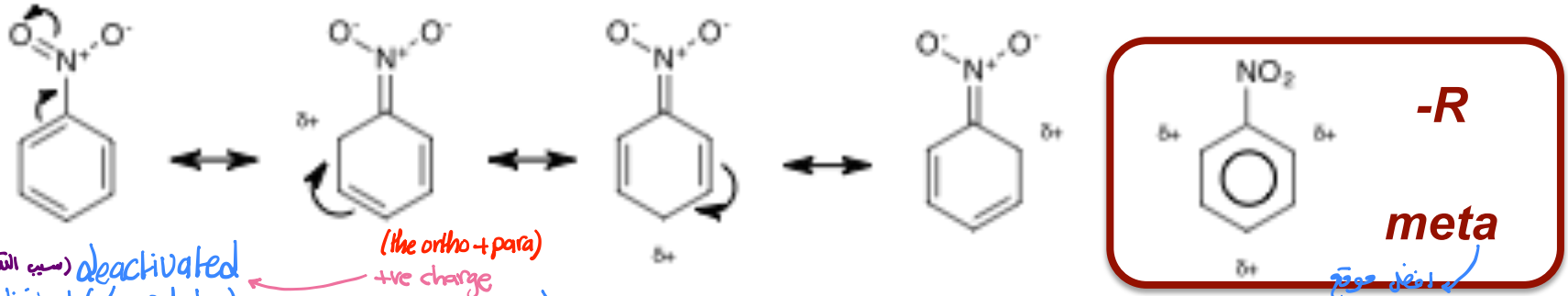


6% 91% 3%

Substituted Benzenes: Orientation

The new group is located either ortho, meta, or para to the existing substituent. The resonance effect of the first substituent determines the position of the second incoming substituent



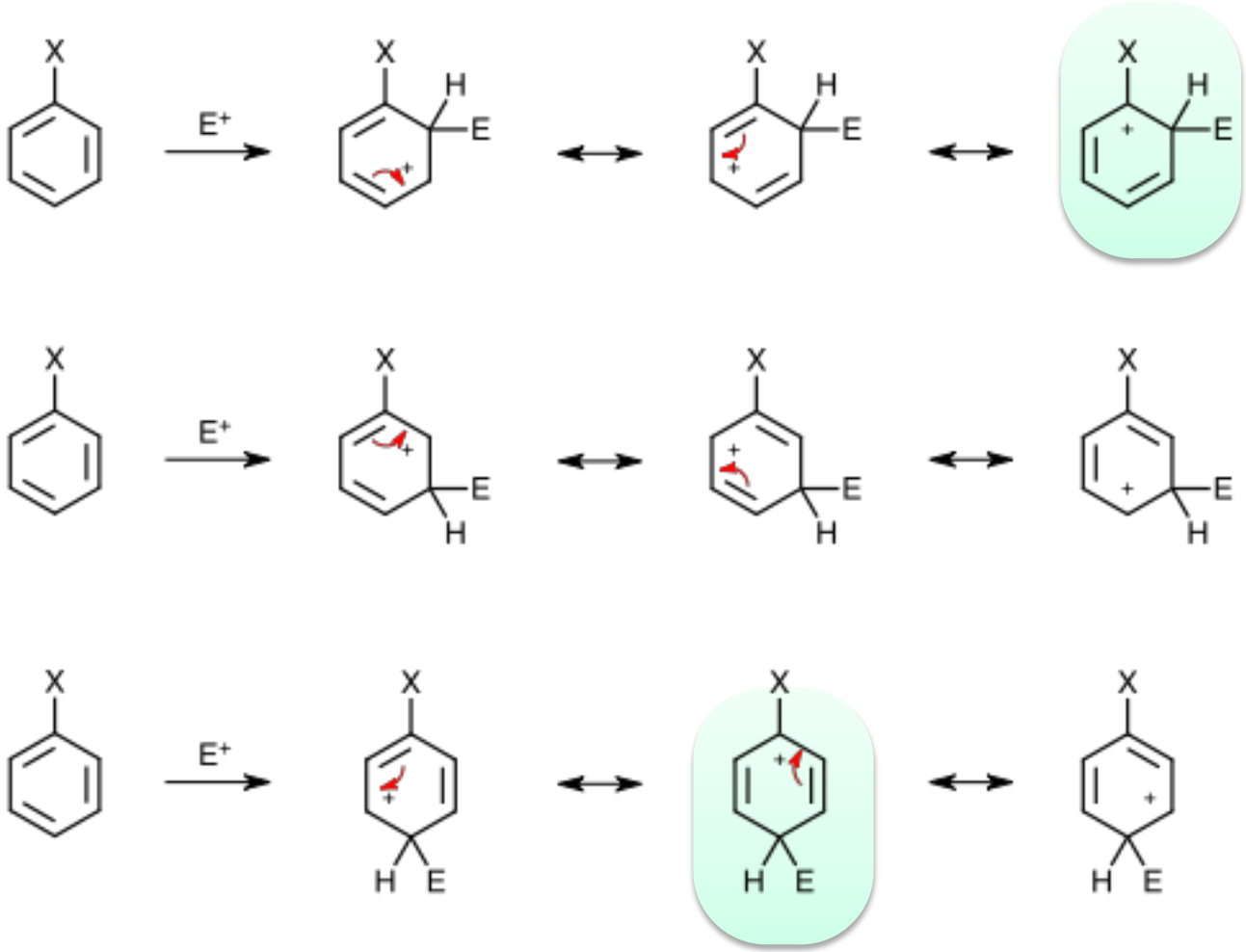


(سبب التسمية) deactivated
ما بتفاعل مع + (ما عليهم ك) electrophile

(the ortho + para)
+ve charge
(the double bond بتعادل تقوش)

Substituted Benzenes: Orientation

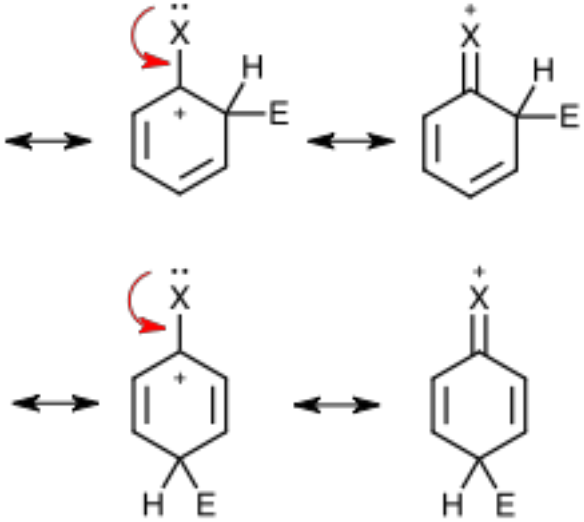
examples



Substituted Benzenes: Orientation

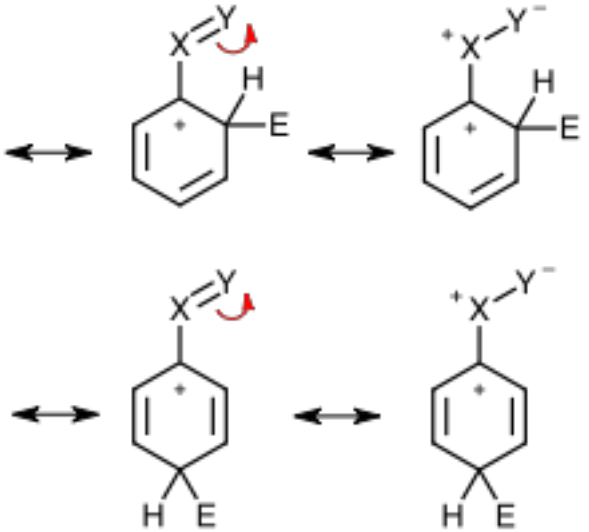
+ R

-o, -p intermediates are resonance stabilised



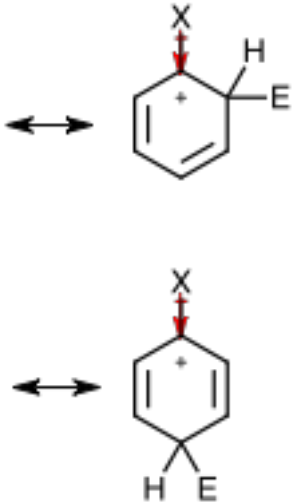
- R

-o, -p intermediates are resonance destabilised



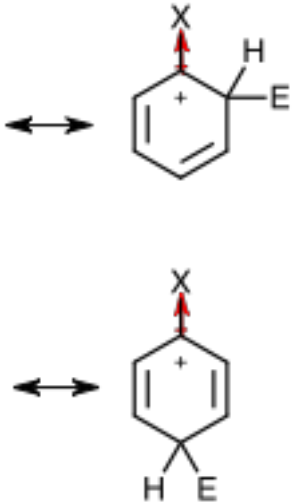
+ I

-o, -p intermediates are inductively stabilised

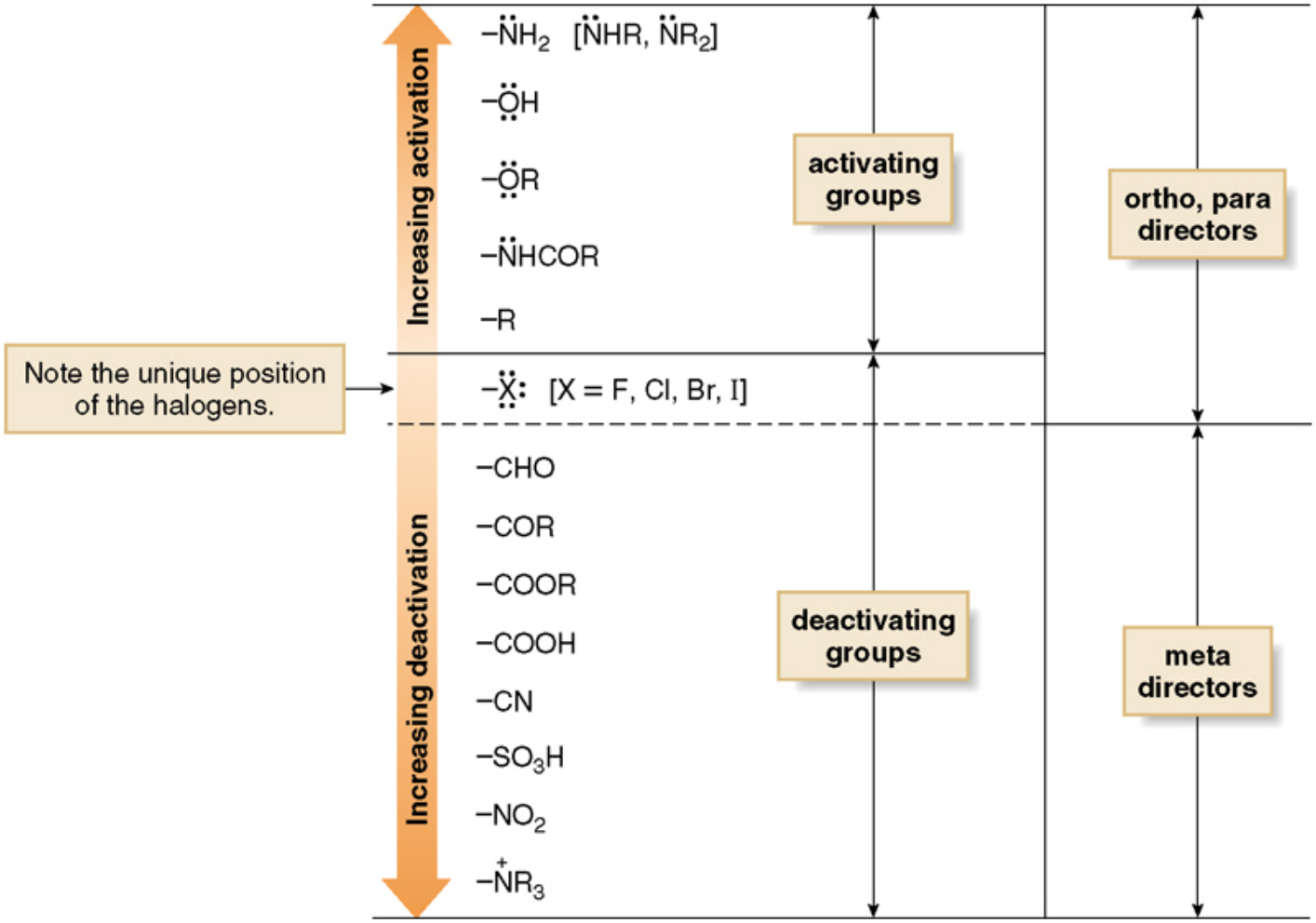


- I

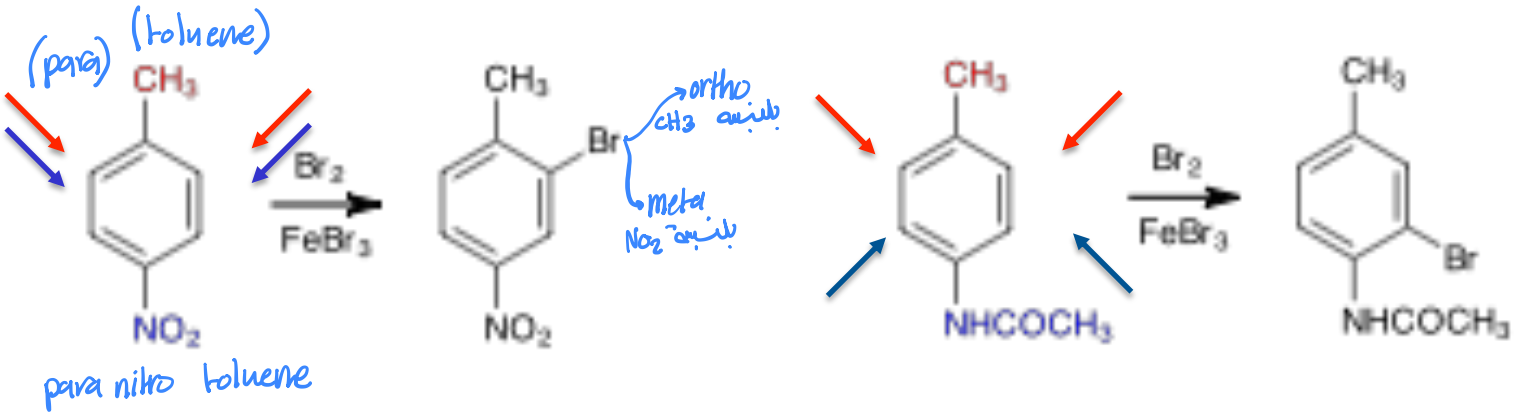
-o, -p intermediates are inductively destabilised

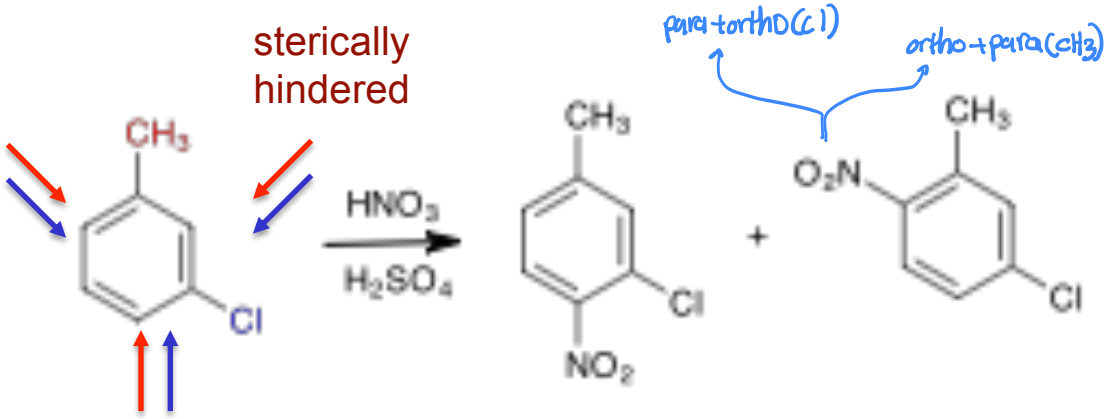


Substituent Effects. Summary

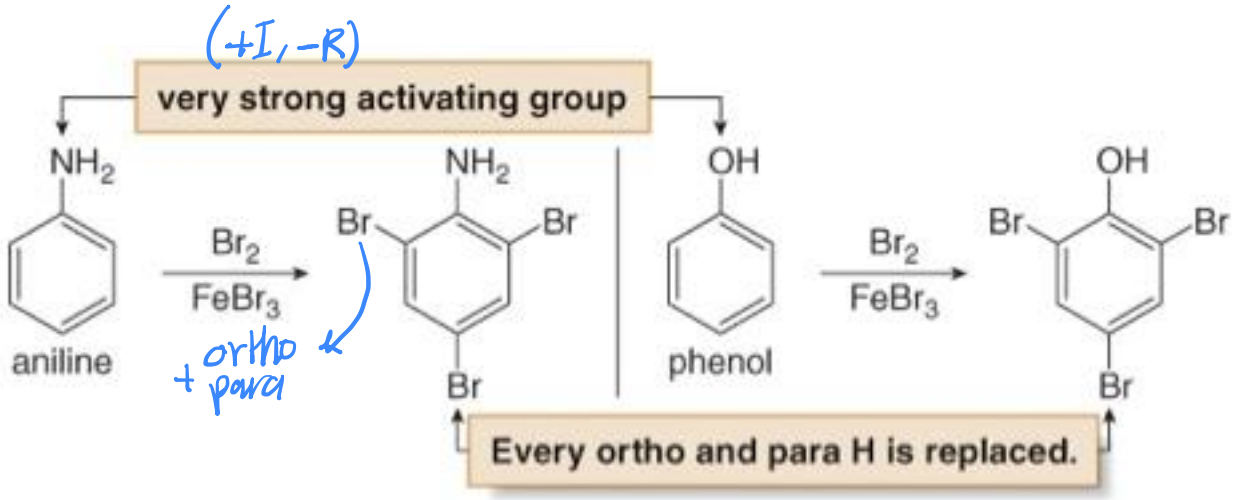


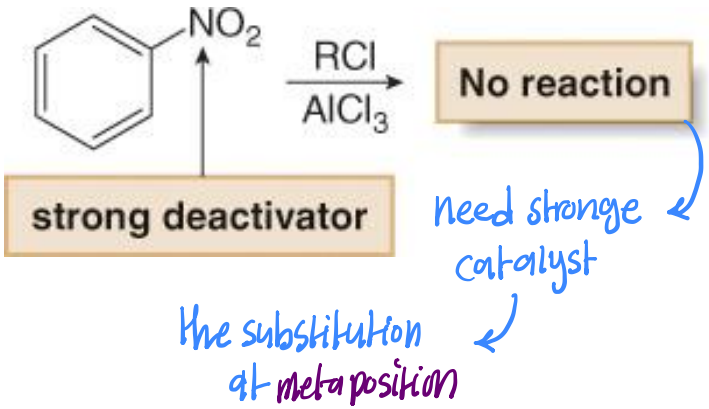
Disubstituted Benzenes



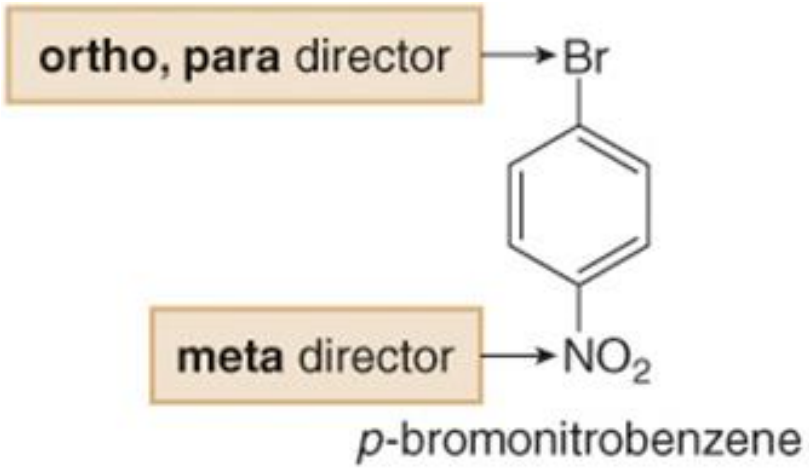


Further Examples





Synthesis of Polysubstituted Benzenes



p-bromonitrobenzene

Synthesis of Polysubstituted Benzenes

Pathway [1]: Bromination before nitration

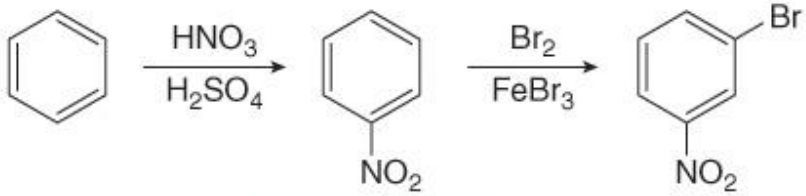
ortho, para director

para product

The ortho isomer can be separated from the mixture.

This pathway gives the desired product.

Pathway [2]: Nitration before bromination



meta director

meta isomer

This pathway does NOT form the desired product.

Reaction of Amines with Nitrous Acid

to add benzene nucleophile ← reason

use this compound for different purposes

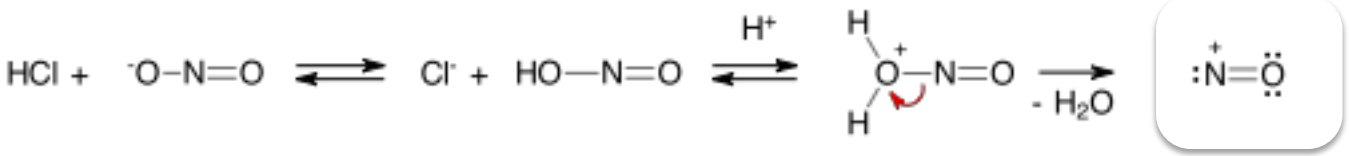
it a started material for other compounds

(nucleophile ← يتفاعل)

(الحر)

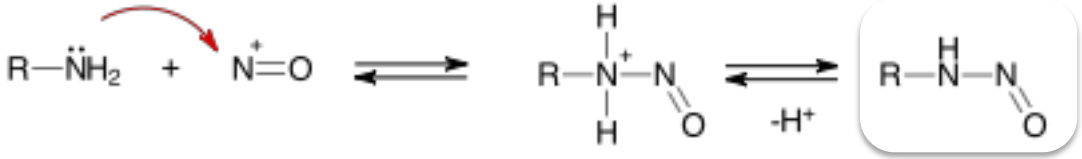
Reaction of Amines with Nitrous Acid

1. generation of the electrophile



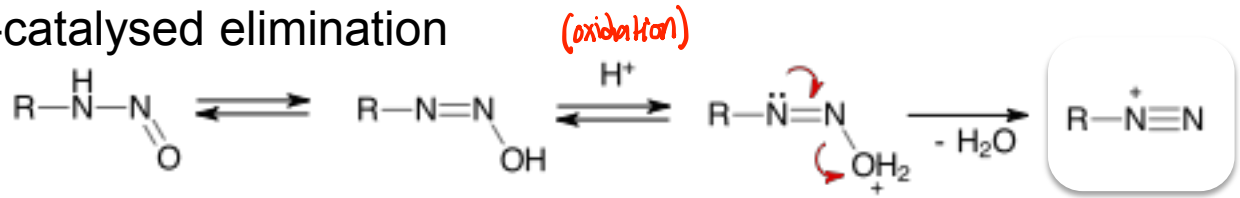
nitrosonium ion

2. nitrosation



N-nitrosamine

3. acid-catalysed elimination

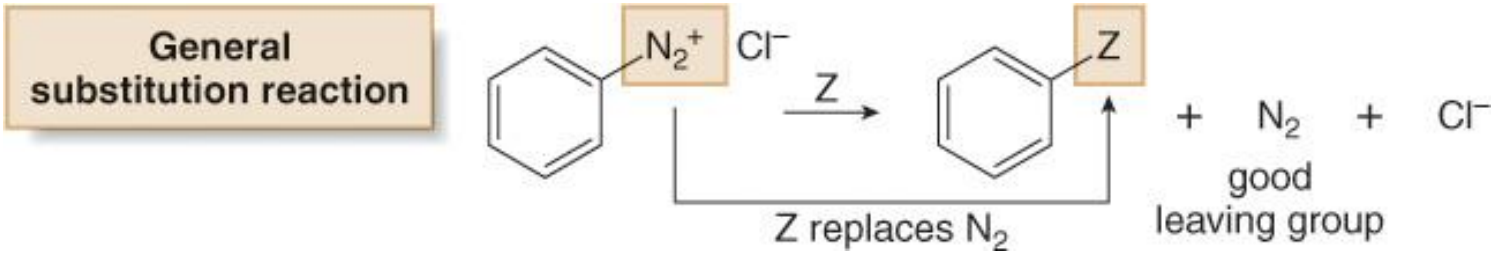


diazonium ion

ممكن استبدلو حد another nucleophile

Substitution Reactions of Aryl Diazonium Salts

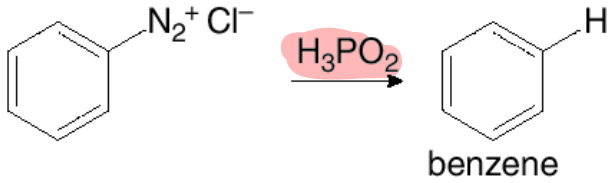
- Aryl diazonium salts react with a variety of reagents to form products in which a nucleophile Z replaces N_2, a very good leaving group.
- The mechanism of these reactions varies with the identity of Z.



for the benzene التفاعلات اللي ممكن استخدامها

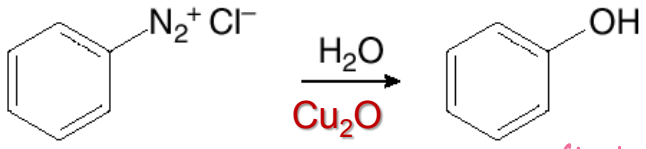
Substitution Reactions of Aryl Diazonium

Substitution by H—Synthesis of benzene



A diazonium salt reacts with hypophosphorus acid to form benzene. This reaction is useful in synthesizing compounds that have substitution patterns that are not available by other means.

Substitution by OH—Synthesis of phenols



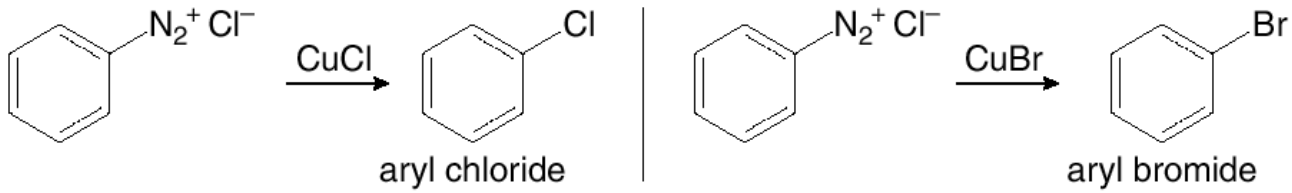
benzene → diazonium → phenol

فبستخدم هاي الطريقة

water with or مركب فيه hydroxy group ← benzene ring على طول ← ما بزبط اتفاعل

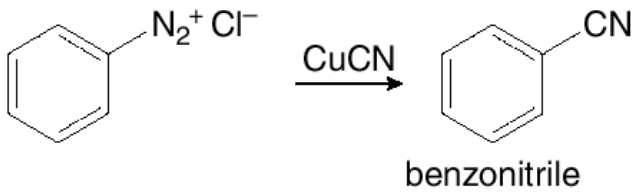
Substitution Reactions of Aryl Diazonium

Substitution by Cl or Br—Synthesis of aryl chlorides and bromides



This is called the Sandmeyer reaction. It provides an alternative to direct chlorination and bromination of the aromatic ring using Cl_2 or Br_2 and a Lewis acid catalyst.

Substitution by CN—Synthesis of benzonitriles

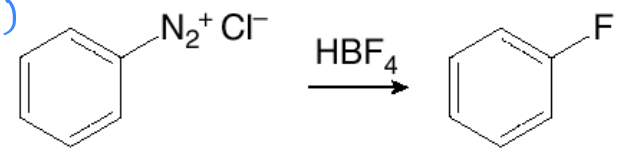


Since the cyano group can be converted into a variety of other functional groups, this reaction provides easy access to a wide variety of benzene derivatives.

Substitution Reactions of Aryl Diazonium Salts

Substitution by F—Synthesis of aryl fluorides

highly reactive (sometimes exclusive)

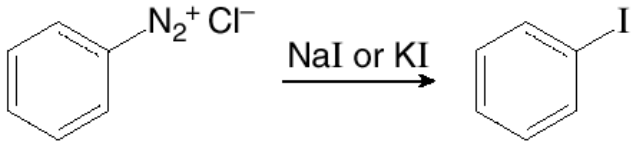


aryl fluoride

This is a useful reaction because aryl fluorides cannot be produced by direct fluorination with F_2 and a Lewis acid catalyst.

Substitution by I—Synthesis of aryl iodides

unreactive



aryl iodide

This is a useful reaction because aryl iodides cannot be produced by direct iodination with I_2 and a Lewis acid catalyst.