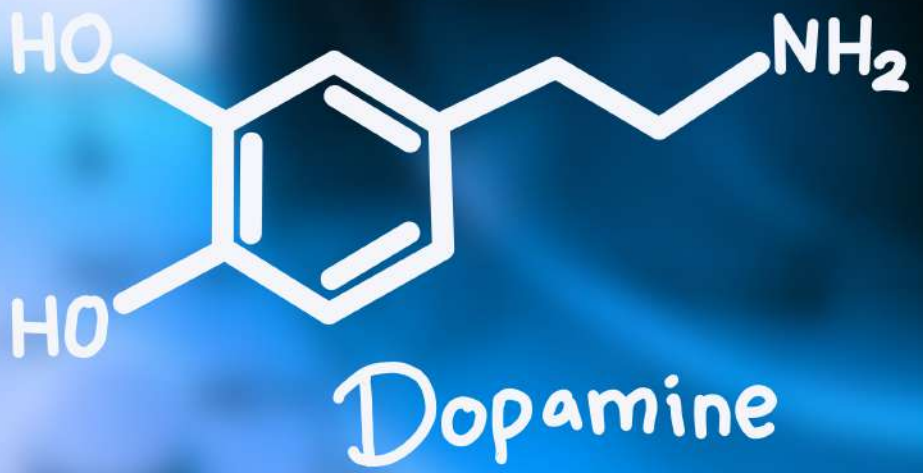
Organic 1

Subject: Benzene and Aromatic Compounds



Dopamine

لجان الدُّفعات

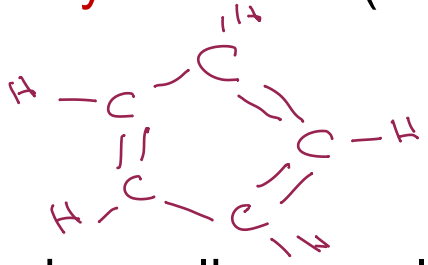
DOPAMINE ACADEMY

Benzene and Aromatic Compounds

Chapter 15
Organic Chemistry, *8th Edition*
John McMurry

Background

- Benzene (C_6H_6) is the simplest aromatic hydrocarbon (or arene).
- Four degrees of unsaturation.
- It is planar.
- All C—C bond lengths are equal.



- Whereas unsaturated hydrocarbons such as alkenes, alkynes and dienes readily undergo addition reactions, benzene does not.

Benzene (an arene)

$$C_6H_6 \xrightarrow{Br_2} \text{No reaction}$$

- Benzene reacts with bromine only in the presence of $FeBr_3$ (a Lewis acid), and the reaction is a substitution, not an addition.

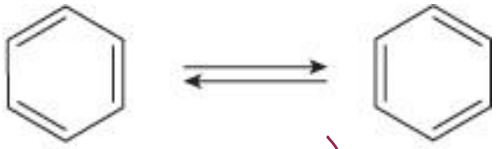
$$C_6H_6 \xrightarrow[FeBr_3]{Br_2} C_6H_5Br$$

substitution
Br replaces H

Background

- August Kekulé (1865) proposed that benzene was a rapidly equilibrating mixture of two compounds, each containing a six-membered ring with three alternating π bonds.

Kekulé description: An equilibrium

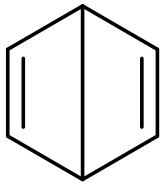


لا ينتقل
البنزين بين الشكلين

This structure implies that the C–C bonds should have **two different lengths**.

- three short bonds
- three long bonds

- All C—C bond lengths are equal!



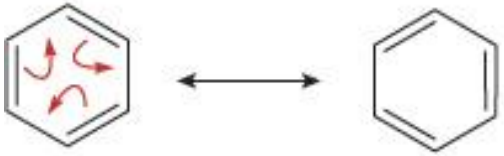
James Dewar (1967) : the Dewar benzene was prepared in 1962 but it is not stable and it converts to benzene

The Structure of Benzene: Resonance

- The true structure of benzene is a resonance hybrid of the two Lewis structures.

الشكل الحقيقي للبنزين

50%



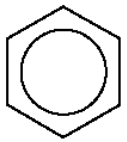
50%

The hybrid

The electrons in the π bonds are **delocalized** around the ring.

موزعين على 6 كامل الحلقة بالتساوي

Some texts draw benzene as a hexagon with an inner circle:



3 double bond

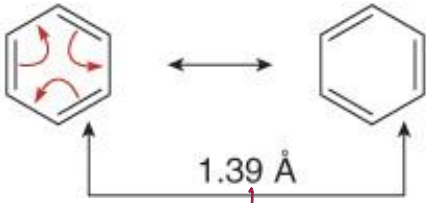
The circle represents the **six π electrons,** distributed over the six atoms of the ring.

CH_3-CH_3

1.53 Å

$CH_2=CH_2$

1.34 Å



1.39 Å

بين جذول single و double

The C–C bonds in benzene are equal and intermediate in length.

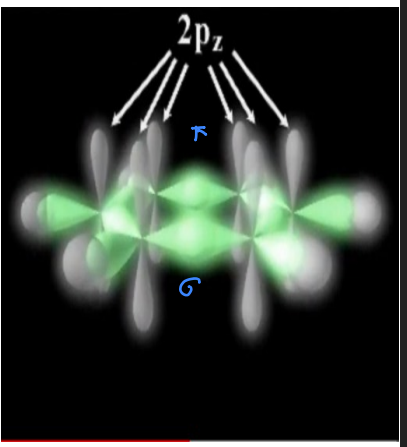
The Structure of Benzene: MO

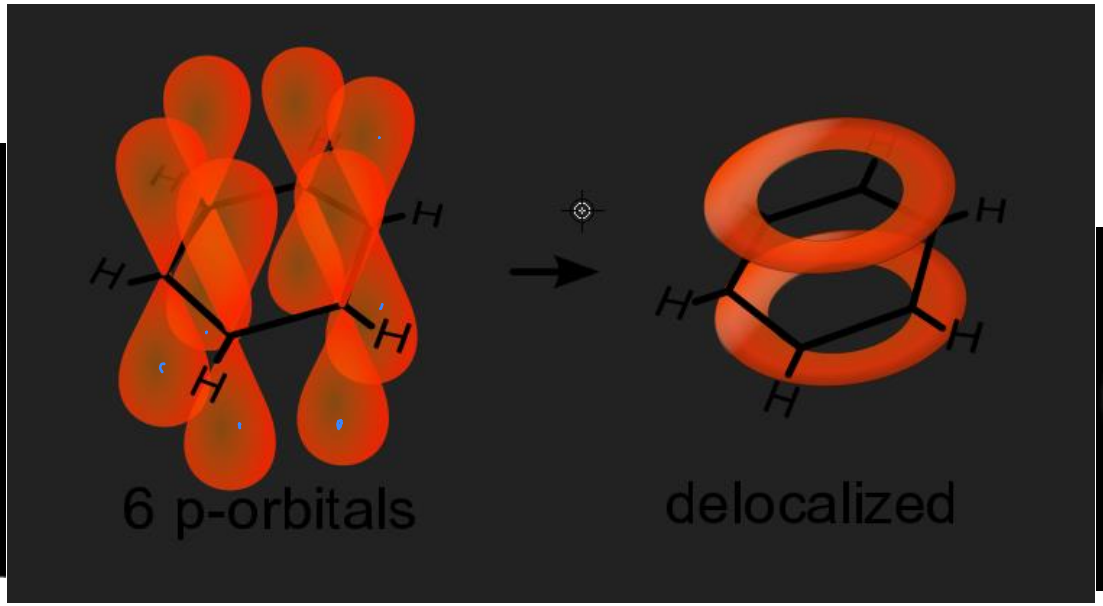
التهجين

3 sp^2

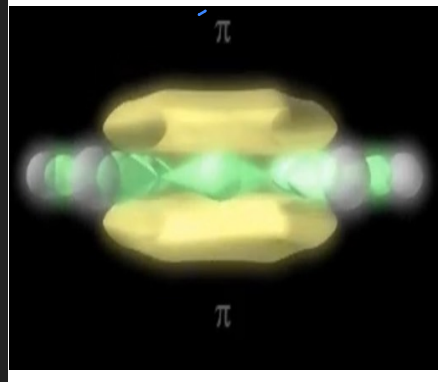
1 p

صورة إضافية

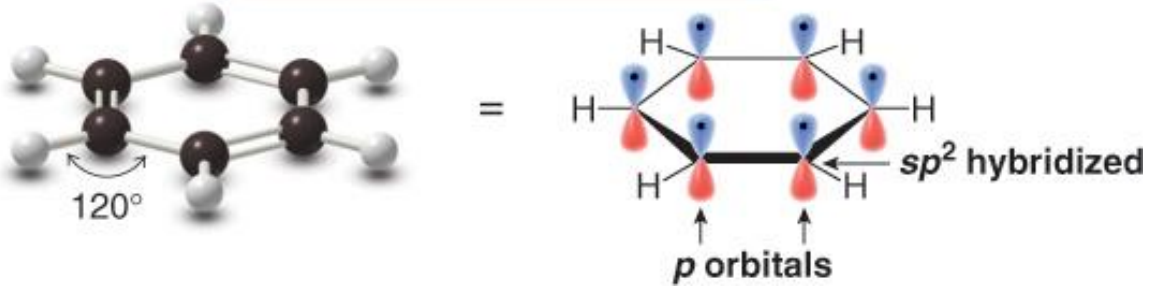




صورة إضافية



Benzene—A planar molecule



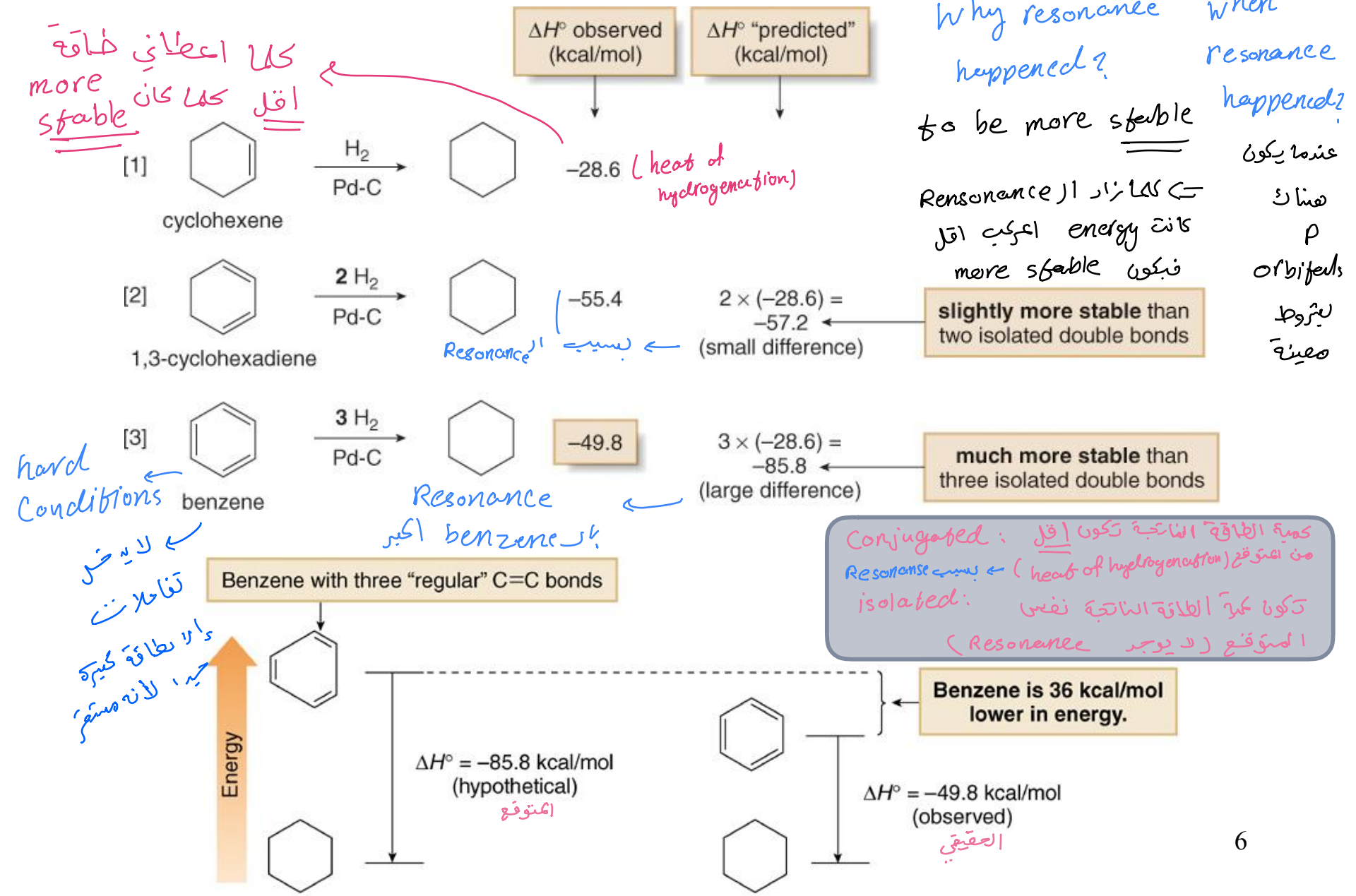
Resonance

(electron delocalization)

↓

بين مدارين pi تركب orbitals p

Aromaticity – Resonance Energy

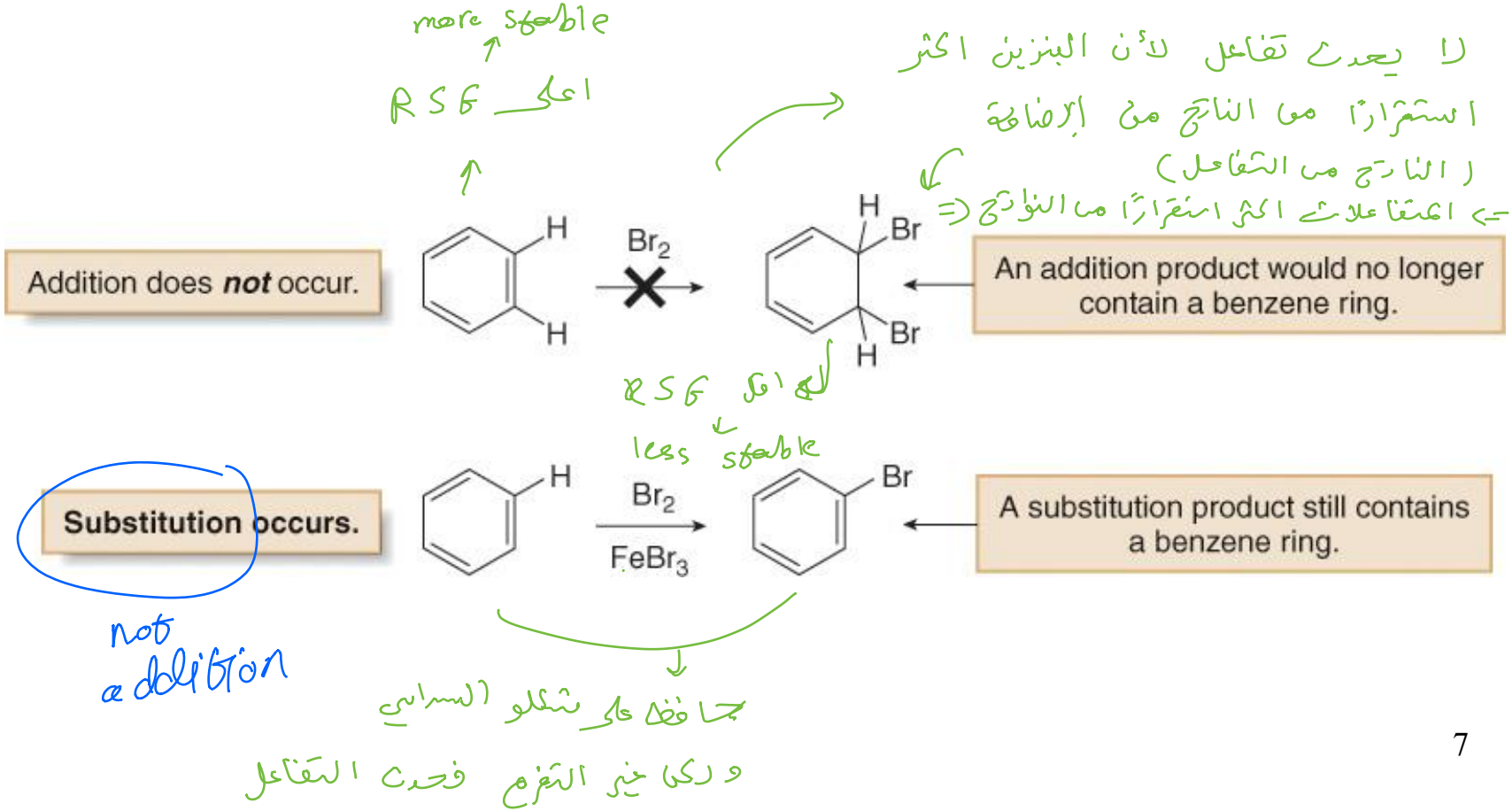


"Resonance stabilization" energy = الفرق بين كمية الطاقة المتوقعة والناتجة تسمى

Stability of Benzene - Aromaticity

كلما زاد RSE ← more stable

- Benzene does not undergo addition reactions typical of other highly unsaturated compounds, including conjugated dienes.



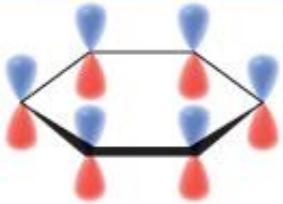
The Criteria for Aromaticity

Four structural criteria must be satisfied for a compound to be aromatic.

ملاحظة: تعتبر Cyclic 

[1] A molecule must be cyclic.

Cyclic compound

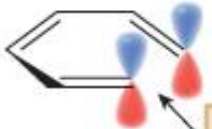


benzene

Every *p* orbital overlaps with two neighboring *p* orbitals.

aromatic

Acyclic compound



1,3,5-hexatriene

There can be no overlap between the *p* orbitals on the two terminal C's.

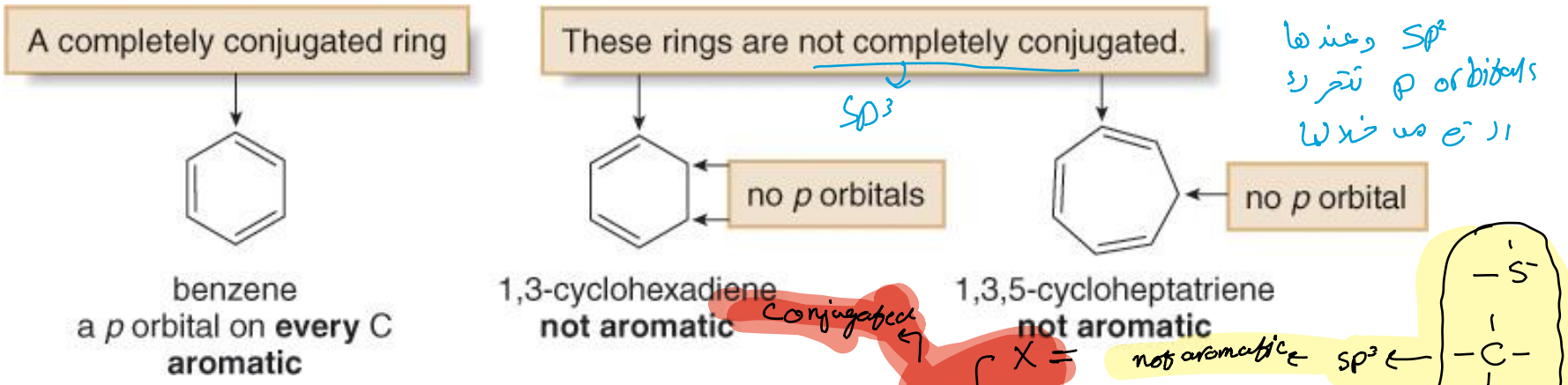
not aromatic

Resonance: movement of e- between atoms thrue p orbitals in atoms

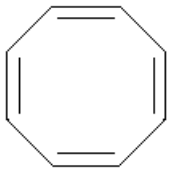
ضمن الشروط يكون فيه overlap الـ e- تتحرك من خلاله

The Criteria for Aromaticity

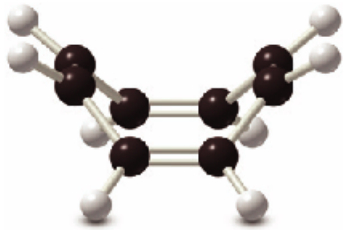
[2] A molecule must be completely conjugated (all atoms sp^2).



[3] A molecule must be planar.



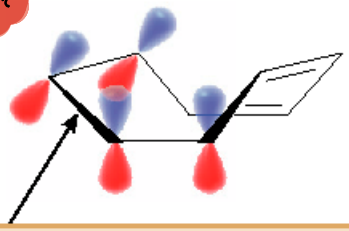
planner



cyclooctatetraene
not aromatic

a tub-shaped,
eight-membered ring

not planner



Adjacent *p* orbitals cannot overlap.
Electrons cannot delocalize.

The Criteria for Aromaticity—Hückel's Rule

[4] A molecule must satisfy Hückel's rule.

- An aromatic compound must contain $4n + 2$ π electrons (n = 0, 1, 2, and so forth).
- Cyclic, planar, and completely conjugated compounds that contain $4n$ π electrons are especially unstable, and are said to be *antiaromatic.*

$4n$ أو $4n+2$ اذا ينطبق على (Cyclic, conjugated, planar) في اعرف في حال تحقق اول 3 شروط في المركب

n = whole number ← Antiaromatic

n = whole number ← Aromatic

واذا ما انطبقت على المركب كلا الحالتين يكون non-aromatic

Benzene An aromatic compound	Cyclobutadiene An antiaromatic compound
	
$4n + 2 = 4(1) + 2 =$ 6 π electrons aromatic	$4n = 4(1) =$ 4 π electrons antiaromatic

Table 17.2 The Number of π Electrons That Satisfy Hückel's Rule

n	$4n + 2$
0	2
1	6
2	10
3	14
4, etc.	18

π

أو

0 ← زوجي ← Anti-aromatic

4, 8, 12, 16, 20 ← Antiaromatic

2, 6, 10, 14, 18 ← Aromatic

زوجي ← Aromatic

$4n + 2 = \pi$

= ↓ 2

N O S ⁻C ↓ 2

double bond X= ↓ O

أي ذرة عليها C ↓ O

π 1 p-orbital · e^-

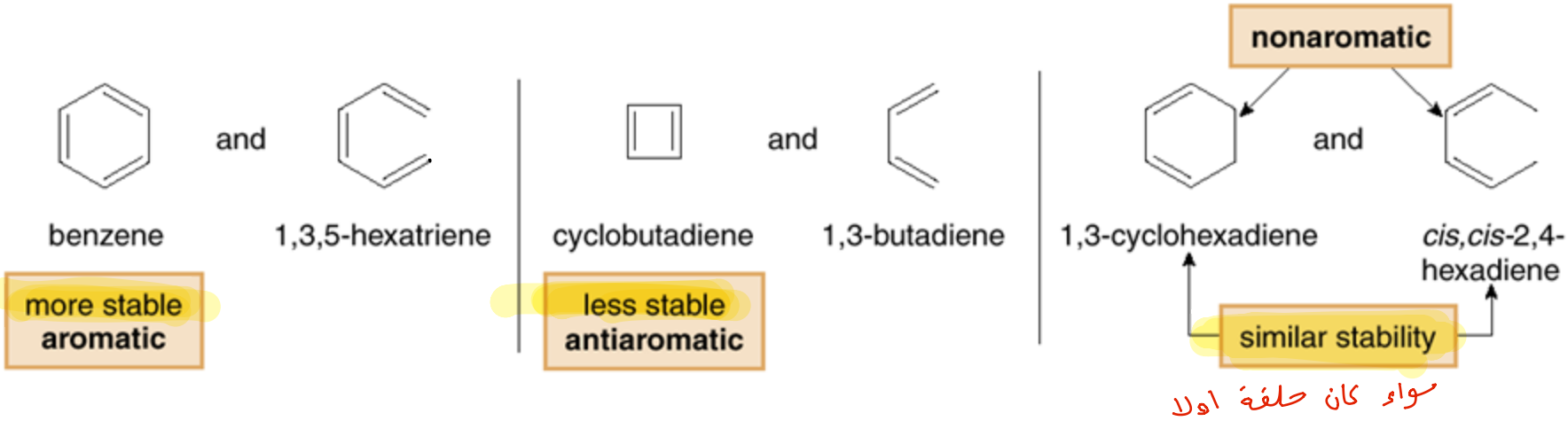
Aromatic: high stability (الأكثر طاقة)

non-Aromatic: بالنص (متوسط)

Anticaromatic: very less stability 10 (الأقل طاقة)

The Criteria for Aromaticity—Hückel's Rule

1. Aromatic—A cyclic, planar, completely conjugated compound with $4n + 2$ π electrons.
2. Antiaromatic—A cyclic, planar, completely conjugated compound with $4n$ π electrons.
3. Not aromatic (nonaromatic)—A compound that lacks one (or more) of the following requirements for aromaticity: being cyclic, planar, and completely conjugated.



Examples of Aromatic Rings

Cyclooctatetraene
8 π electrons

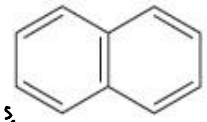
planar
antiaromatic

puckered
nonaromatic

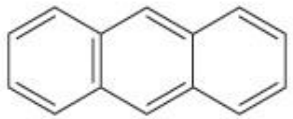
$4n+2=8$
$4n=6$
$n=\frac{3}{2}$ not whole number

poly cyclic system:

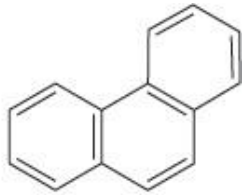
تأكد ان كل الذرات ١٠ تهجينها sp^2 في حال تحقق هذا الشرط يتم التعامل مع المركب كأنه حلقة واحدة



naphthalene
10 π electrons



anthracene
14 π electrons



phenanthrene
14 π electrons

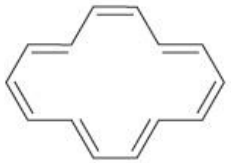
→ poly cyclic system وكلهم بنزين aromatic فبعتبرهم

(annulene لا يعتبر

في حالم يتحقق الشرط →

في حالم وجود حلقة واحدة على الأقل aromatic فالمركب aromatic

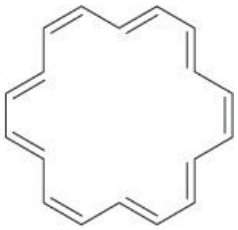
في حال وجود 8 حلقة anti + non فالمركب antiaromatic



[14]-annulene
$4n + 2 = 4(3) + 2 =$
14 π electrons
aromatic

→ 7 double bond

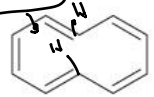
planner



[18]-annulene
$4n + 2 = 4(4) + 2 =$
18 π electrons
aromatic

[10]-Annulene fits Hückel's rule, but it's **not planar**.

لو كان المركب planner رح يتصادموا مع بعض فبغير شكله



[10]-annulene
10 π electrons
not aromatic

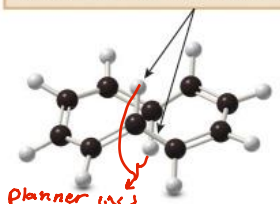
عدد ذرات الكربون في المركب

10 C
5 double bond
(not planner

not planne

=

The molecule puckers to keep these H's further away from each other.

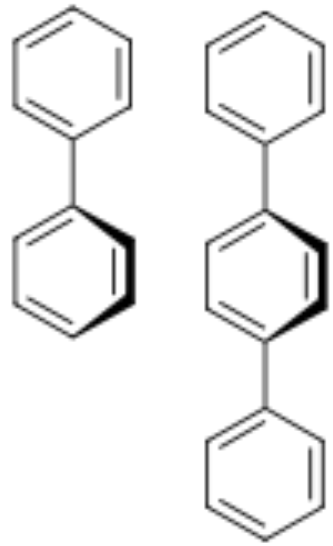


3-D representation

لأن planner كان صار في تنافر بين ال H

[12]-annulene + [16]-annulene ↗

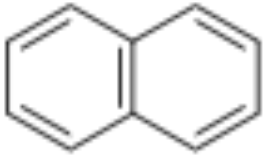
Polycyclic Aromatic Hydrocarbons



biphenyl

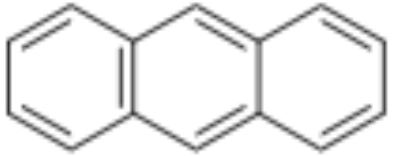
terphenyl

No interactions between rings



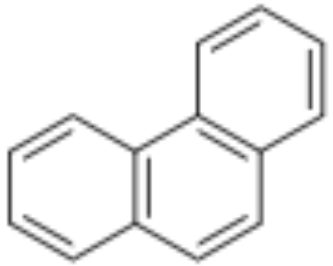
naphthalene

61 kcal/mol



anthracene

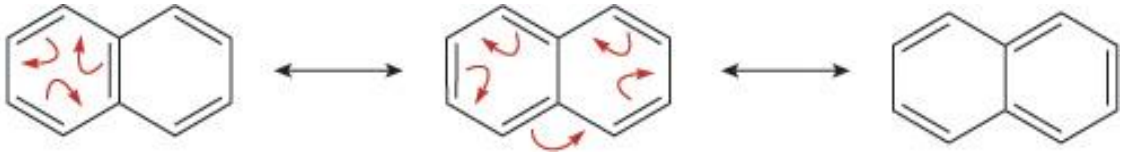
84 kcal/mol

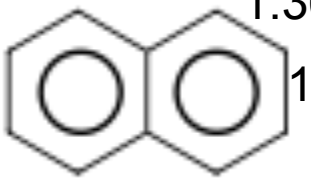


phenanthrene

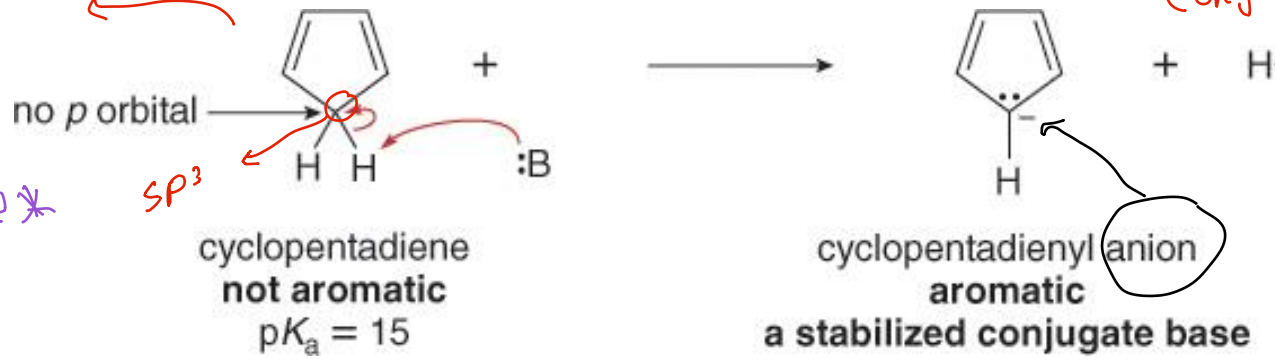
92 kcal/mol

Three resonance structures for naphthalene



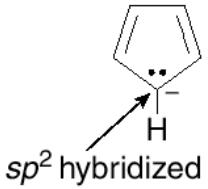


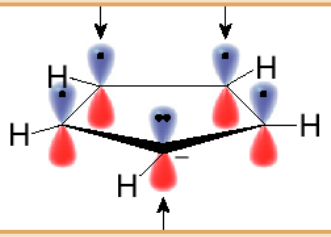
Other Aromatic Compounds



The cyclopentadienyl anion

The ring is completely conjugated with **6 π electrons**.





The lone pair resides in a *p* orbital.

- The cyclopentadienyl anion is aromatic because it is cyclic, planar, completely conjugated, and has six π electrons.

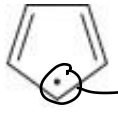
Other Aromatic Compounds

cyclopentadienyl anion
- 6 π electrons
- contains $4n + 2$ π electrons

aromatic

cyclopentadienyl cation
- 4 π electrons
- contains $4n$ π electrons

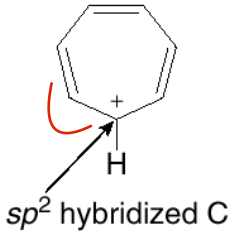
antiaromatic



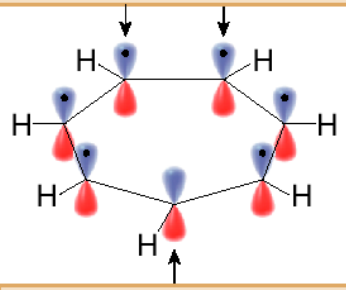
cyclopentadienyl radical
- 5 π electrons
- does not contain either $4n$ or $4n + 2$ π electrons

nonaromatic

The tropylium cation

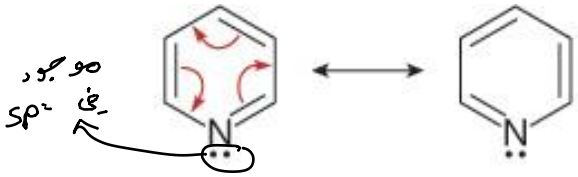


The ring is completely conjugated with **6 π electrons**.

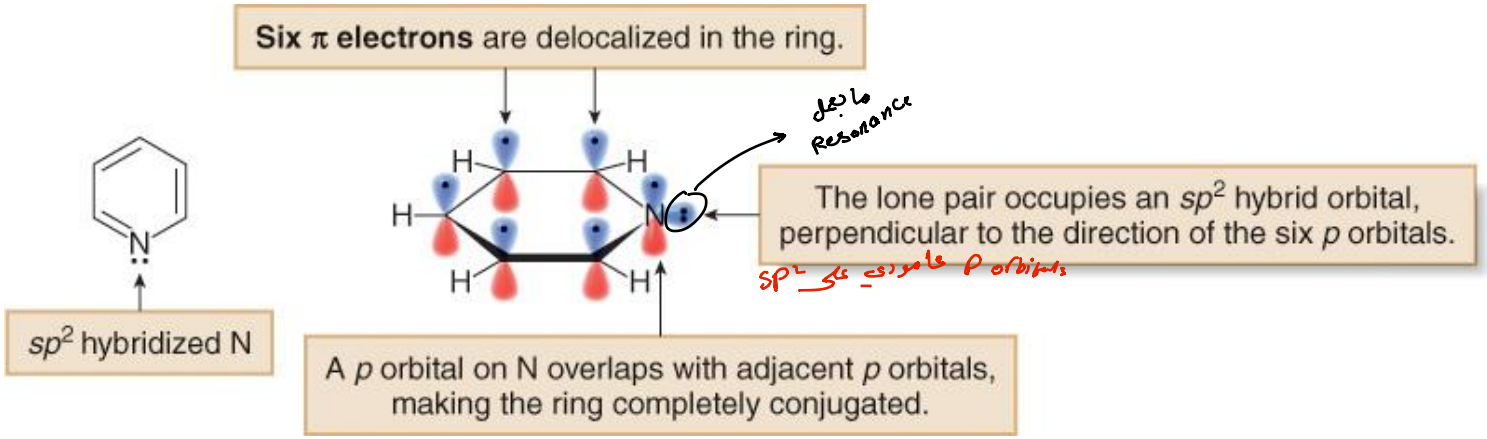


- The tropylium cation is aromatic because it is cyclic, planar, completely conjugated, and has six π electrons delocalized over the seven atoms of the ring.

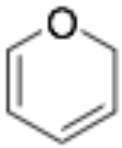
Aromatic Heterocycles



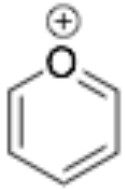
two resonance structures for pyridine
6 π electrons



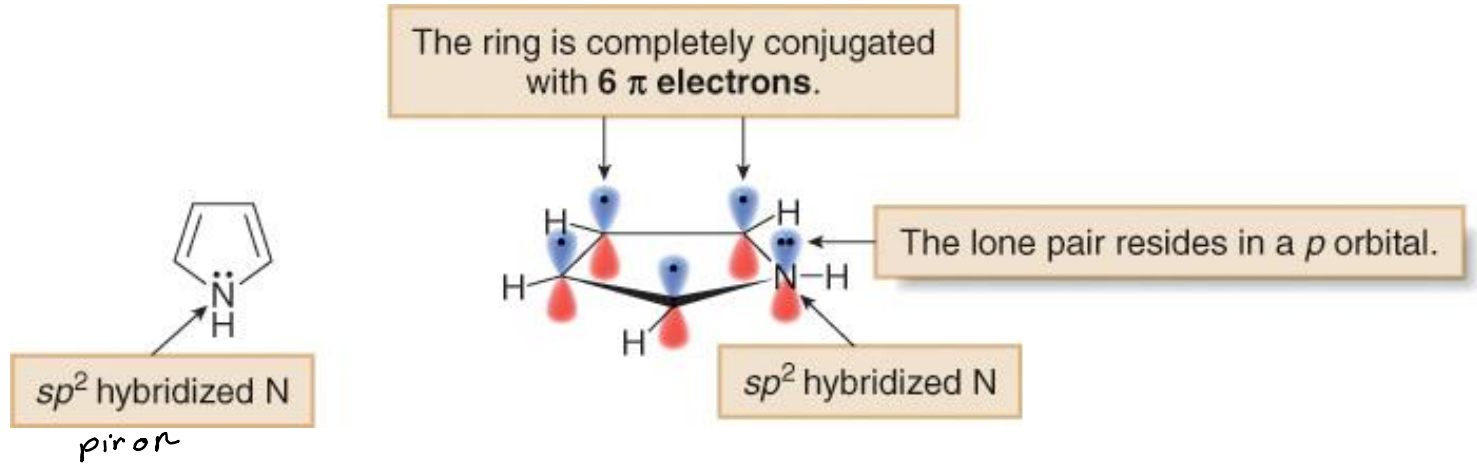
2H-pyran
4 π electrons
nonaromatic

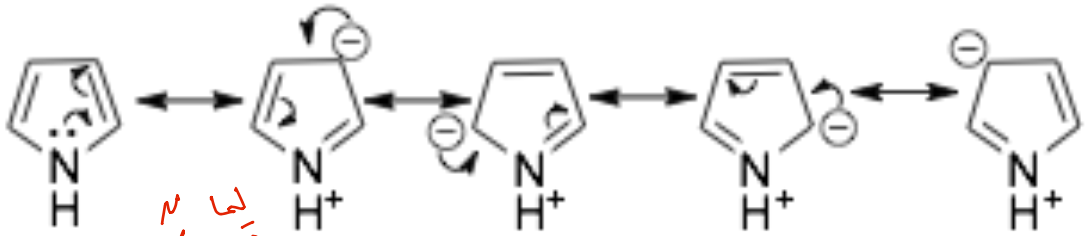


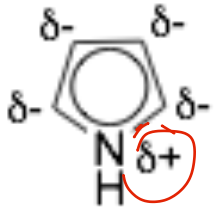
2H-pyrilium ion
6 π electrons
aromatic



Aromatic Heterocycles





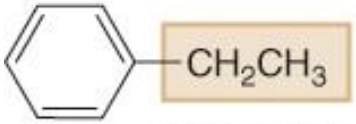


furan

thiophen

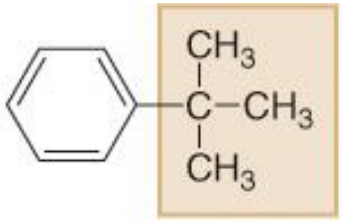
Nomenclature: 1 Substituent

Systematic:



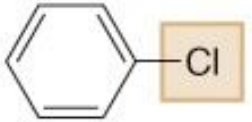
ethyl group

ethylbenzene



tert-butyl group

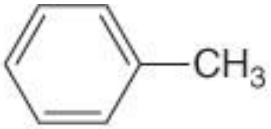
tert-butylbenzene



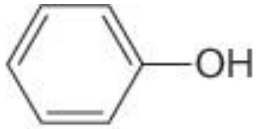
chloro group

chlorobenzene

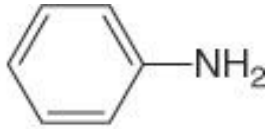
Common:



toluene
(methylbenzene)



phenol
(hydroxybenzene)

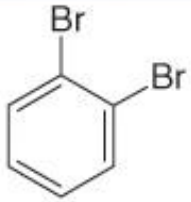


aniline
(aminobenzene)

Nomenclature: 2 Substituents

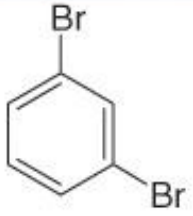
Identical:

1,2-disubstituted benzene
ortho isomer



1,2-dibromobenzene
o-dibromobenzene

1,3-disubstituted benzene
meta isomer



1,3-dibromobenzene
m-dibromobenzene

1,4-disubstituted benzene
para isomer

1,4-dibromobenzene
p-dibromobenzene

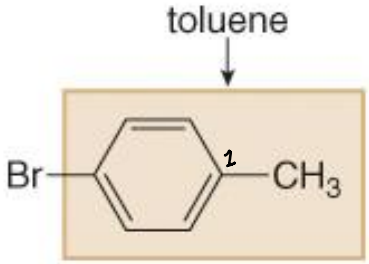
Different:

Alphabetize two different substituent names:

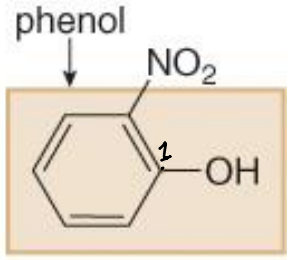
***o*-bromochloro-benzene**

***m*-fluoronitro-benzene**

Use a common root name:



***p*-bromo**toluene**

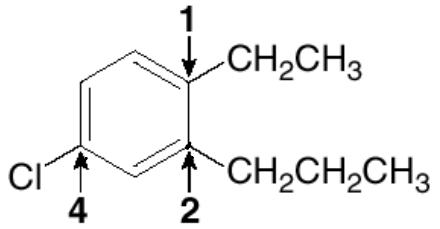


***o*-nitro**phenol**

Nomenclature: 3 or More Substituents

Examples of naming polysubstituted benzenes

[1]



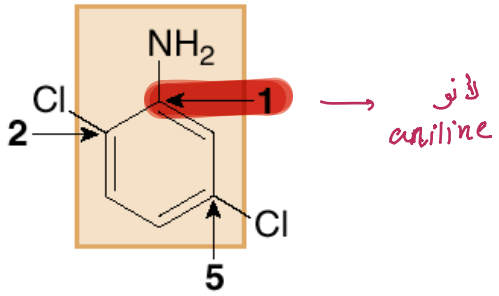
بغض النظر عن الأبجدية

تختار الطريق الي بعطي اقل رقم ممكن

- Assign the lowest set of numbers.
- Alphabetize the names of all the substituents.

4-chloro-1-ethyl-2-propylbenzene

[2]



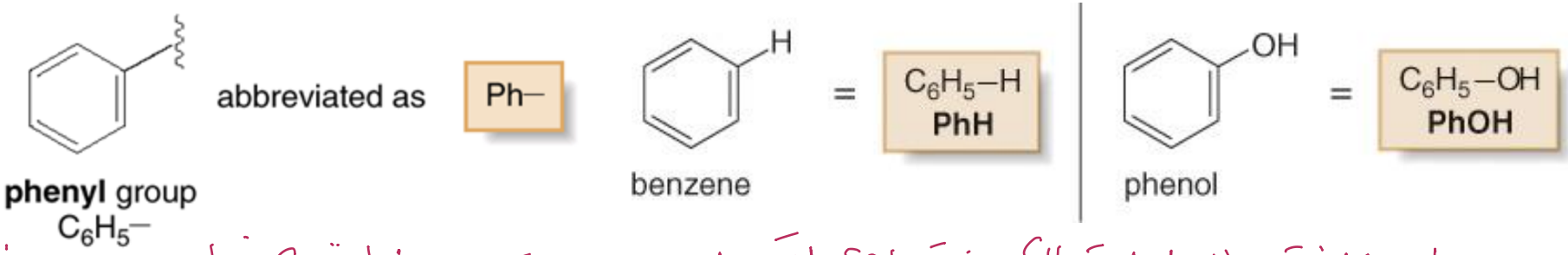
لأنو aniline

- Name the molecule as a derivative of the common root **aniline.**
- Designate the position of the NH_2 group as "1," and then assign the lowest possible set of numbers to the other substituents.

2,5-dichloroaniline

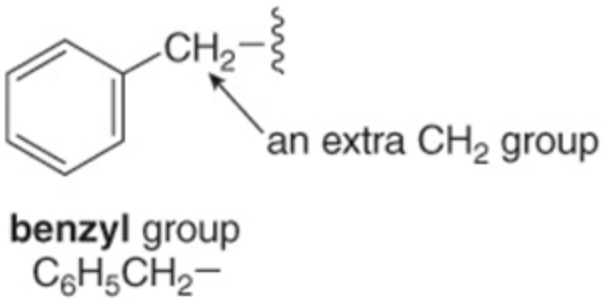
Nomenclature

- A benzene substituent is called a phenyl group, and it can be abbreviated in a structure as "Ph-".

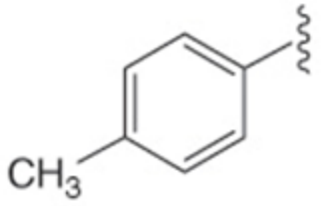


← إذا كانت السلسلة الكربونية المتصلة بالبنزين طويلة (عدد ذرات C فيها > عدد ذرات C في البنزين) يتم معاملة البنزين كمتفرع

- The benzyl group:

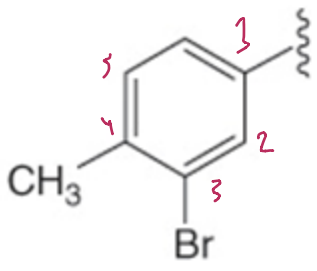


- Aryl groups:



(methyl benzil)

(toluene)



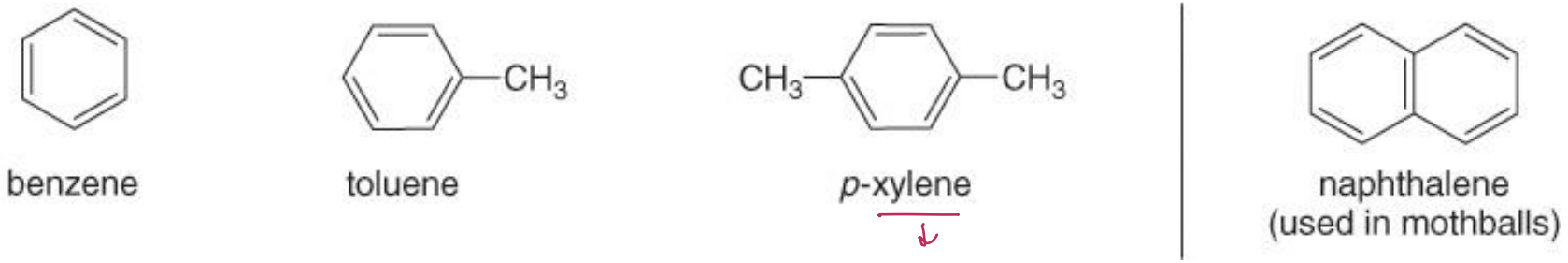
3-bromo-4-methyl phenil

Interesting Aromatic Compounds

- Benzene and toluene, are obtained from petroleum refining and are useful starting materials for synthetic polymers.
- Compounds containing two or more benzene rings that share carbon—carbon bonds are called polycyclic aromatic hydrocarbons (PAHs). Naphthalene, the simplest PAH, is the active ingredient in mothballs.

معلومة إضافية: هذه المواد مسرطنة

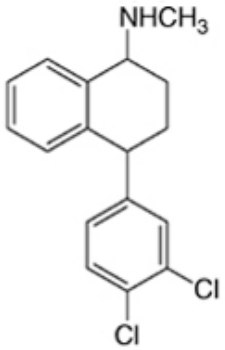
The components of the gasoline additive BTX



benzene | toluene | *p*-xylene | naphthalene (used in mothballs)

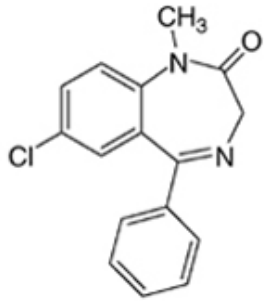
إذا بنزين وعليها مجموعتين ميثيل

Interesting Aromatic Compounds



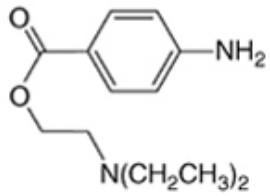
- Trade name: **Zoloft**
- Generic name: **sertraline**
- Use: a psychotherapeutic drug for depression and panic disorders

نوبات الهلع



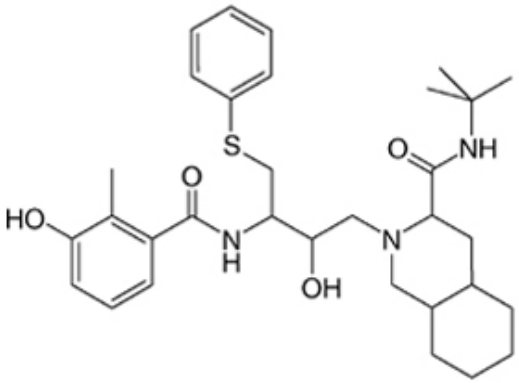
- Trade name: **Valium**
- Generic name: **diazepam**
- Use: a sedative

مخدر

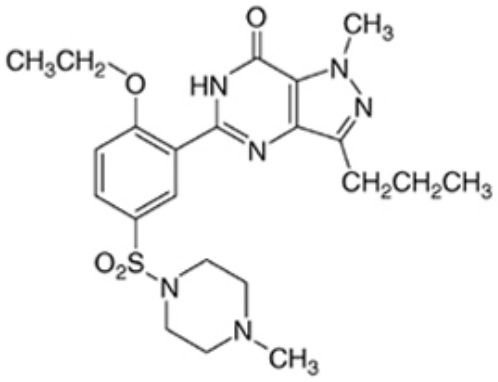


- Trade name: **Novocain**
- Generic name: **procaine**
- Use: a local anesthetic

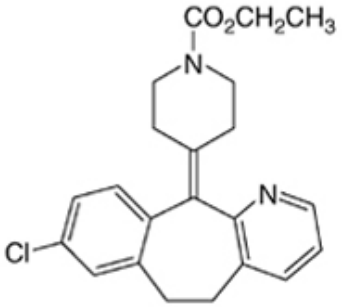
مخدر موضعي



- Trade name: **Viracept**
- Generic name: **nelfinavir**
- Use: an antiviral drug used to treat HIV



- Trade name: **Viagra**
- Generic name: **sildenafil**
- Use: a drug used to treat erectile dysfunction

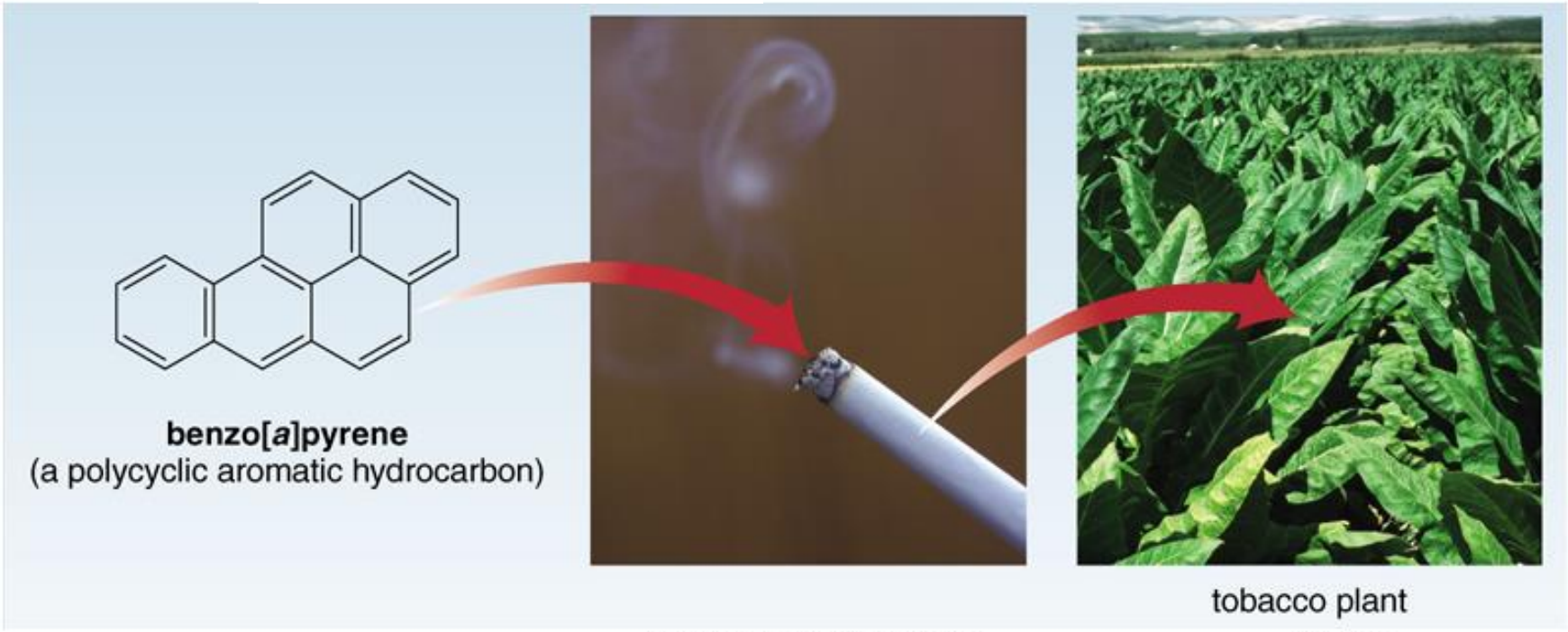


- Trade name: **Claritin**
- Generic name: **loratadine**
- Use: an antihistamine for seasonal allergies

Interesting Aromatic Compounds

- Benzo[*a*]pyrene, produced by the incomplete oxidation of organic compounds in tobacco, is found in cigarette smoke.

الإحتراق غير الكامل لدخان السجائر



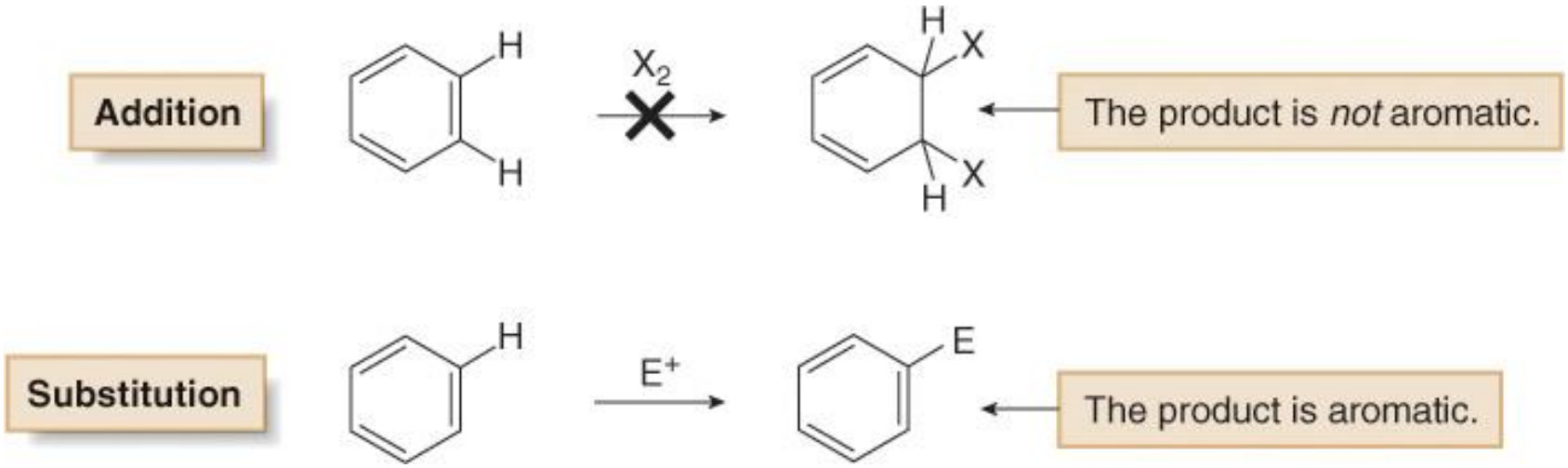
يبتلعه يستنشقه

- When ingested or inhaled, benzo[a]pyrene and other similar PAHs are oxidized to carcinogenic products.

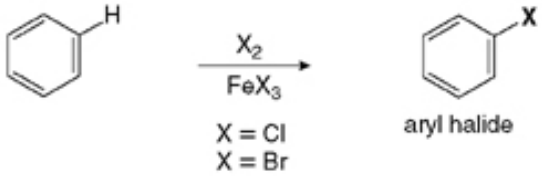
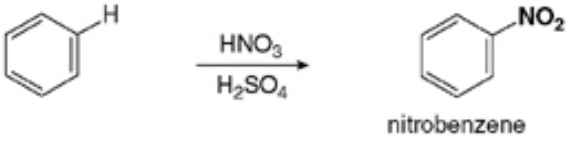
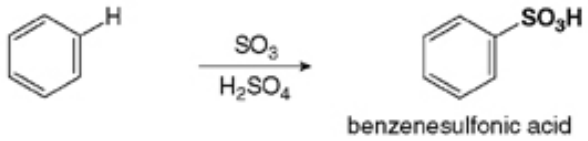
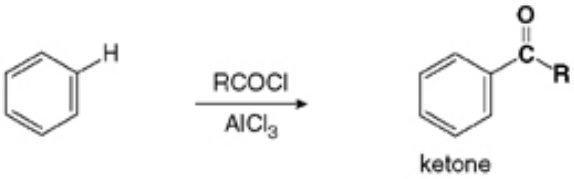
Electrophilic Aromatic Substitution

Chapter 16
Organic Chemistry, *8th Edition*
John McMurry

Introduction



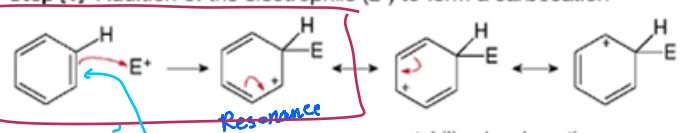
Introduction

Reaction	Electrophile
[1] Halogenation—Replacement of H by X (Cl or Br)	
	$E^+ = Cl^+$ or Br^+
[2] Nitration—Replacement of H by NO_2	
	$E^+ = \overset{+}{N}O_2$
[3] Sulfonation—Replacement of H by SO_3H	
	$E^+ = \overset{+}{S}O_3H$
[4] Friedel–Crafts alkylation—Replacement of H by R	
	$E^+ = R^+$
[5] Friedel–Crafts acylation—Replacement of H by RCO	
	$E^+ = R\overset{+}{C}O$

Mechanism

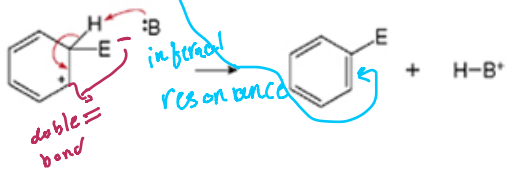
Mechanism 18.1 General Mechanism—Electrophilic Aromatic Substitution

Step [1] Addition of the electrophile (E^+) to form a carbocation

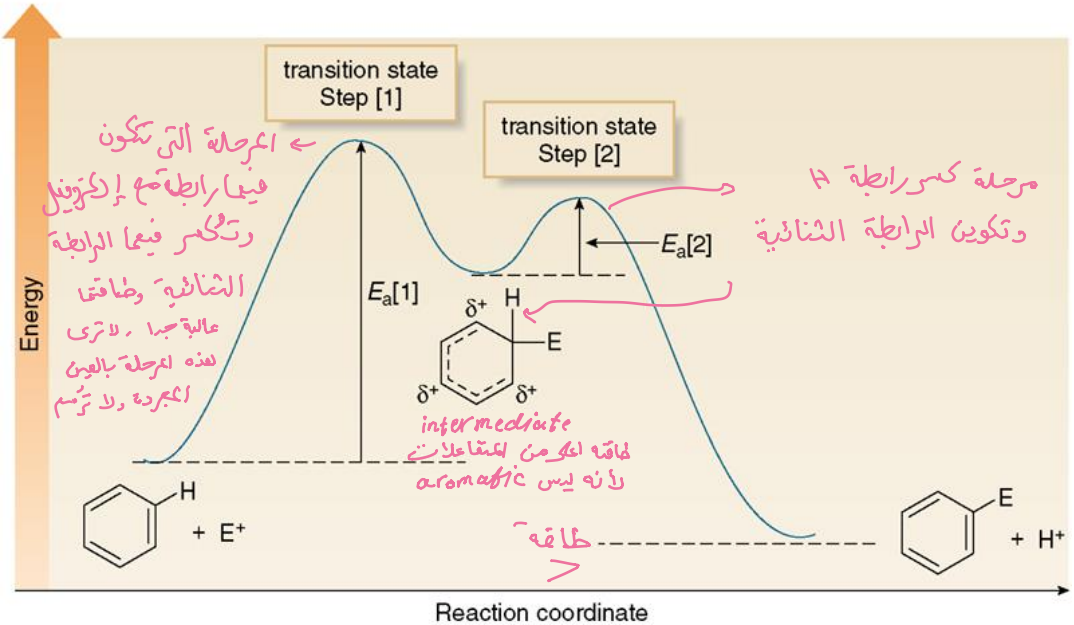


- Addition of the electrophile (E^+) forms a new C–E bond using two π electrons from the benzene ring, and generating a carbocation. This carbocation intermediate is not aromatic, but it is resonance stabilized—three resonance structures can be drawn.
- Step [1] is rate-determining because the aromaticity of the benzene ring is lost.

Step [2] Loss of a proton to re-form the aromatic ring



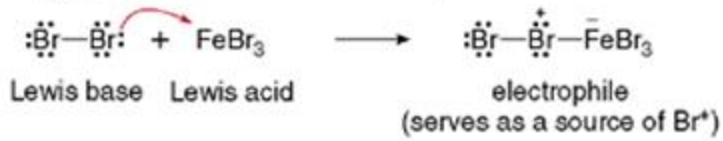
- In Step [2], a base (B:) removes the proton from the carbon bearing the electrophile, thus re-forming the aromatic ring. This step is fast because the aromaticity of the benzene ring is restored.
- Any of the three resonance structures of the carbocation intermediate can be used to draw the product. The choice of resonance structure affects how curved arrows are drawn, but not the identity of the product.



Halogenation

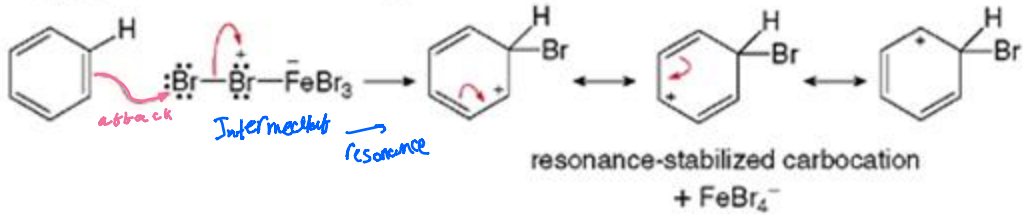
Mechanism 18.2 Bromination of Benzene

Step [1] Generation of the electrophile (تكوين إلكتروفيل)



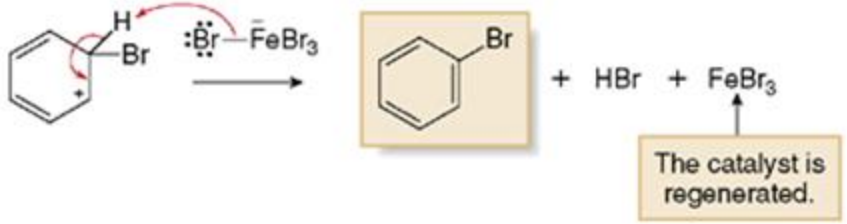
- Lewis acid–base reaction of Br_2 with $FeBr_3$ forms a species with a weakened and polarized Br – Br bond. This adduct serves as a source of Br^+ in the next step.

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



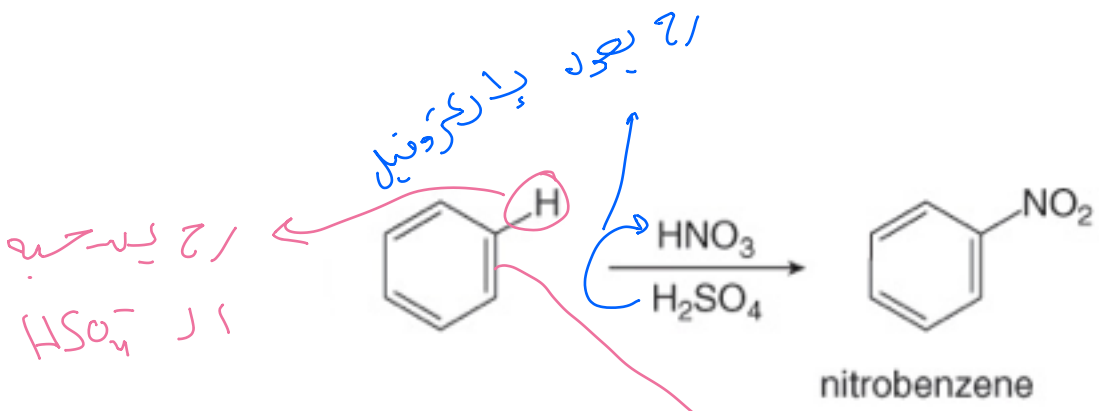
- Addition of the electrophile forms a new C – Br bond and generates a carbocation. This carbocation intermediate is resonance stabilized—**three resonance structures can be drawn.**
- The $FeBr_4^-$ also formed in this reaction is the base used in Step [3].

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



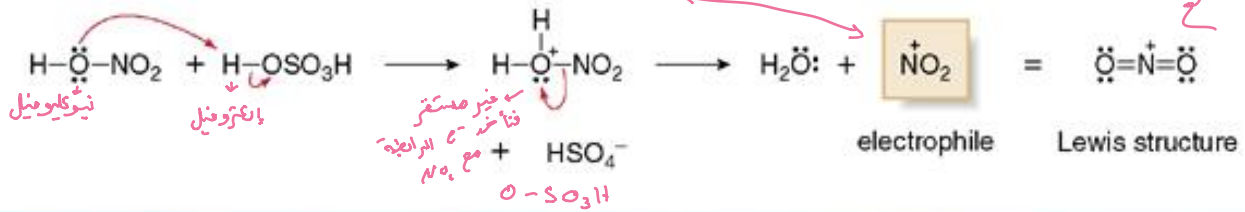
- $FeBr_4^-$ removes the proton from the carbon bearing the Br, thus re-forming the aromatic ring.
- $FeBr_3$, a catalyst, is also regenerated for another reaction cycle.

Nitration ($HNO_3 + H_2SO_4$)



attack

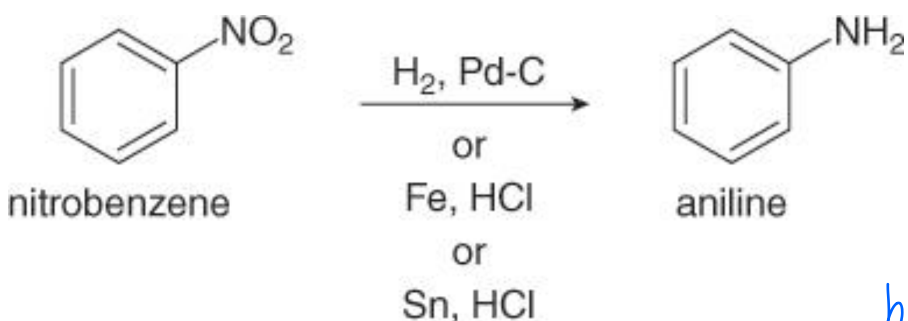
Mechanism 18.3 Formation of the Nitronium Ion ($^+NO_2$) for Nitration



H_2SO_4 أقوى من HNO_3 فيتصرف HNO_3 كقاعدة ويمنح H^+ ويتصرف H_2SO_4 كحمض ويستقبل H^+ على الرغم من كون كلاهما حمضان قويان

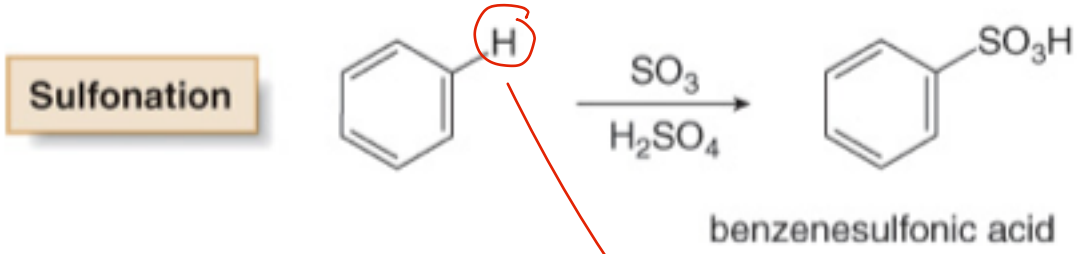
Nitro Group Reduction

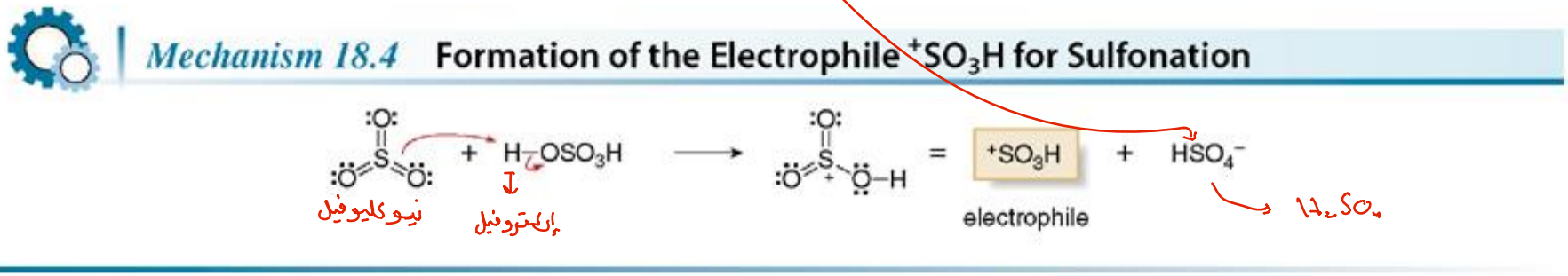
Aromatic nitro groups (NO_2) can readily be reduced to amino groups (NH_2) under a variety of conditions.



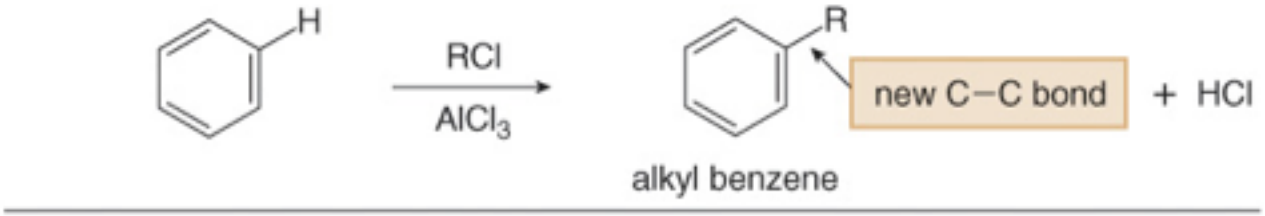
ما بزبط
اضيف مباشرة
NH_2 على benzene
لأنه الثنين نيوكليوفيل

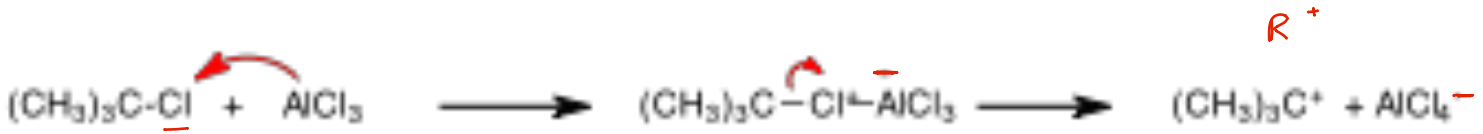
Sulfonation

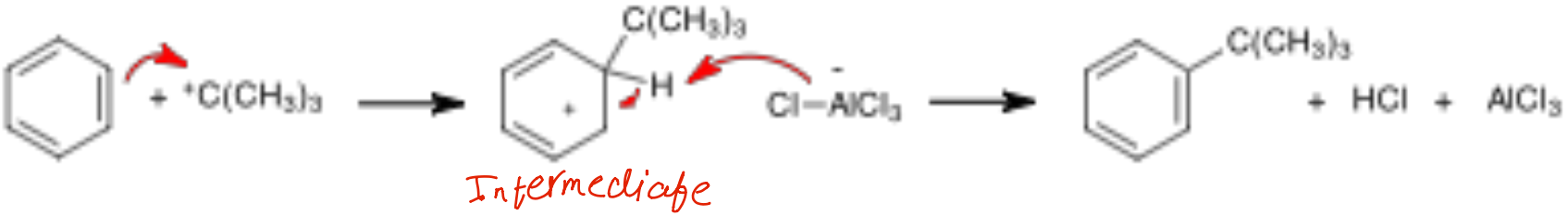




Friedel-Crafts Alkylation



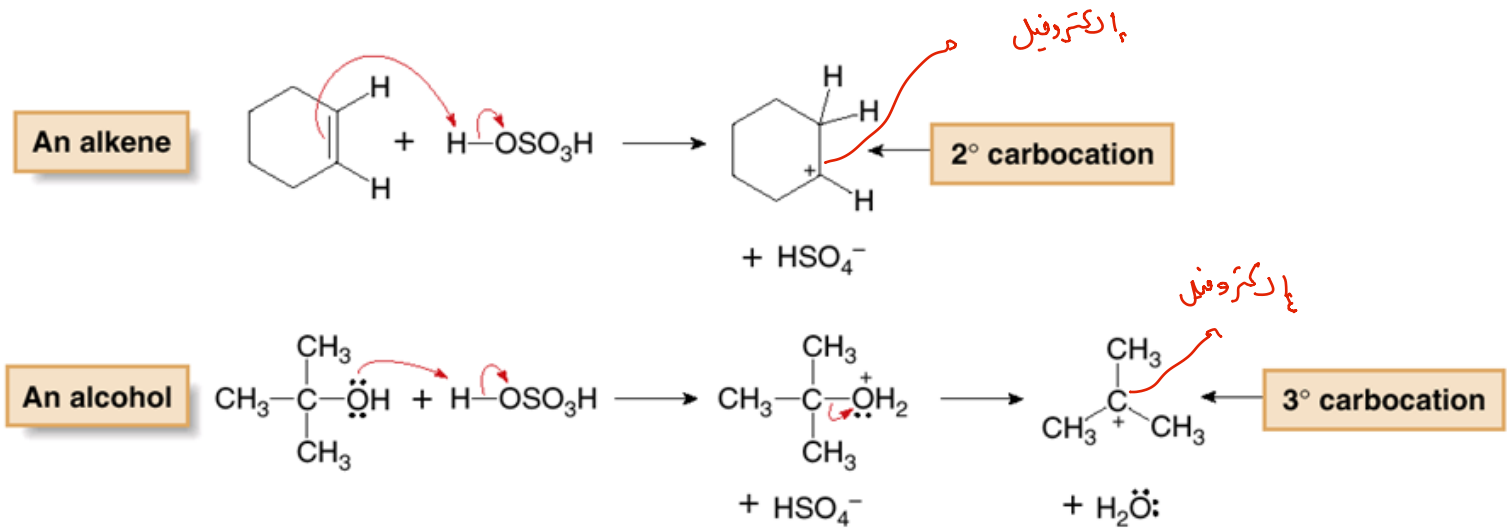


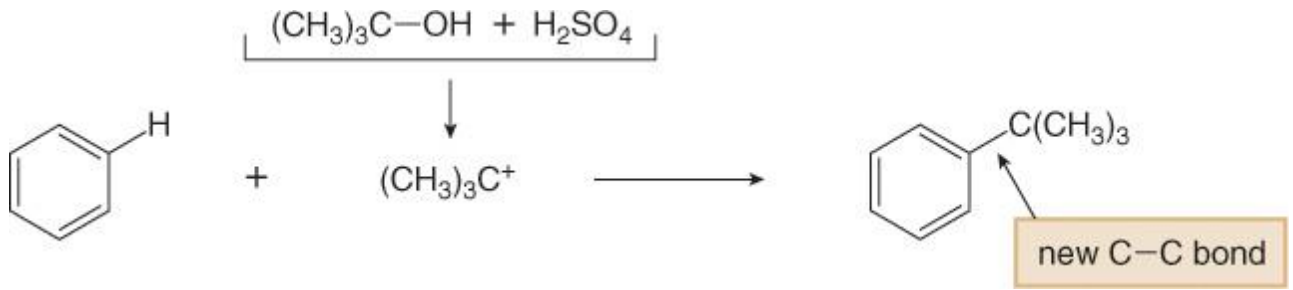


Best with 2ry and 3ry halides

Friedel-Crafts Alkylation

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.

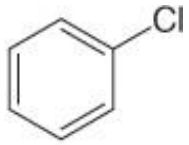
Unreactive halides in the Friedel–Crafts alkylation

highly unstable ← $CH_2=CH^+$ ← لو اخذنا ال Cl رح يصير

لا يمكن ان يتشكل في الكيمياء ←

$CH_2=CHCl$

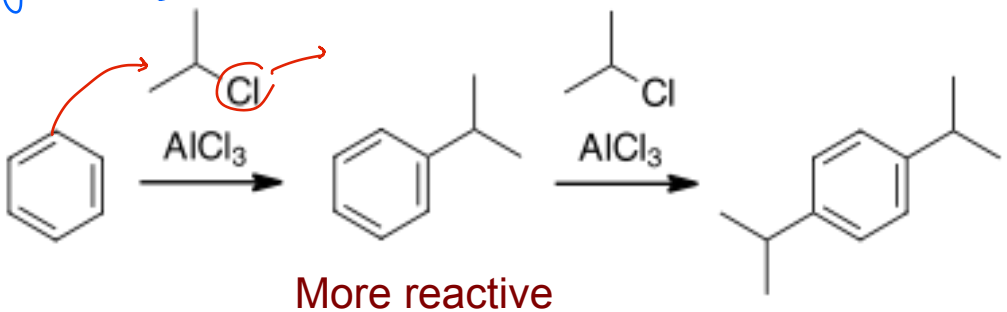
vinyl halide



aryl halide

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

بنتج الكل من مركب



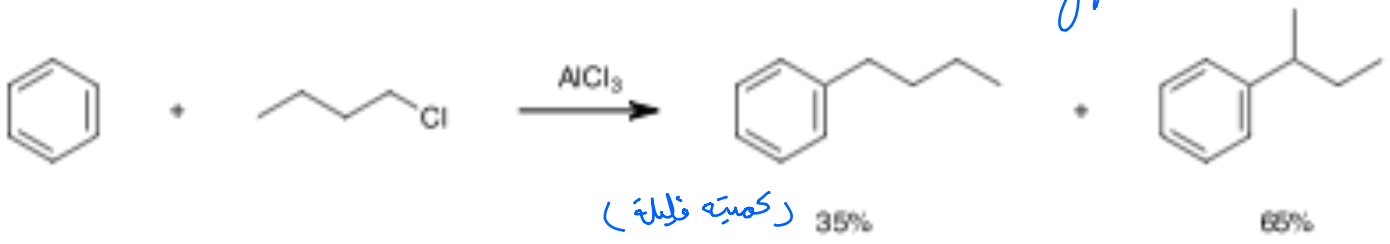
More reactive than benzene

- نواتج الـ Alkylation تفاعلها Fridel craft اسرع من البنزين
- نواتج الـ acylation ابطأ Fridel craft تفاعل من البنزين

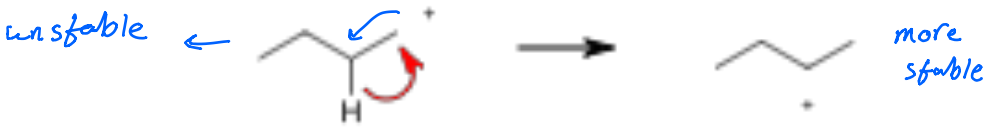
Limitations

[3] Rearrangements can occur.

2 types of product

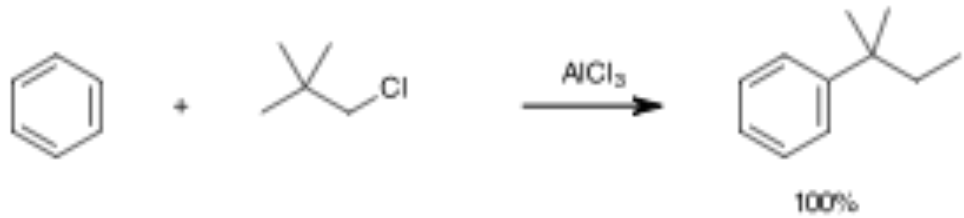


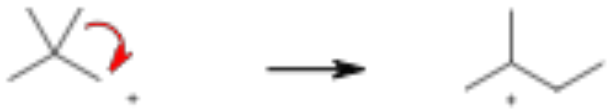
(كمية قليلة)



1ry
less stable

2ry
more stable



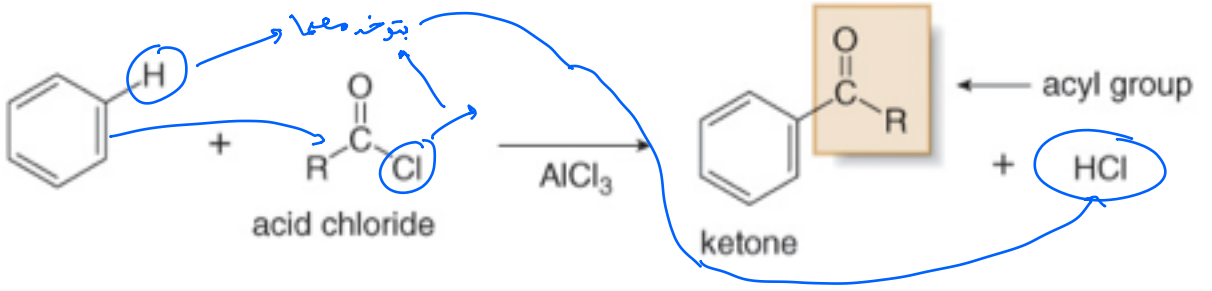


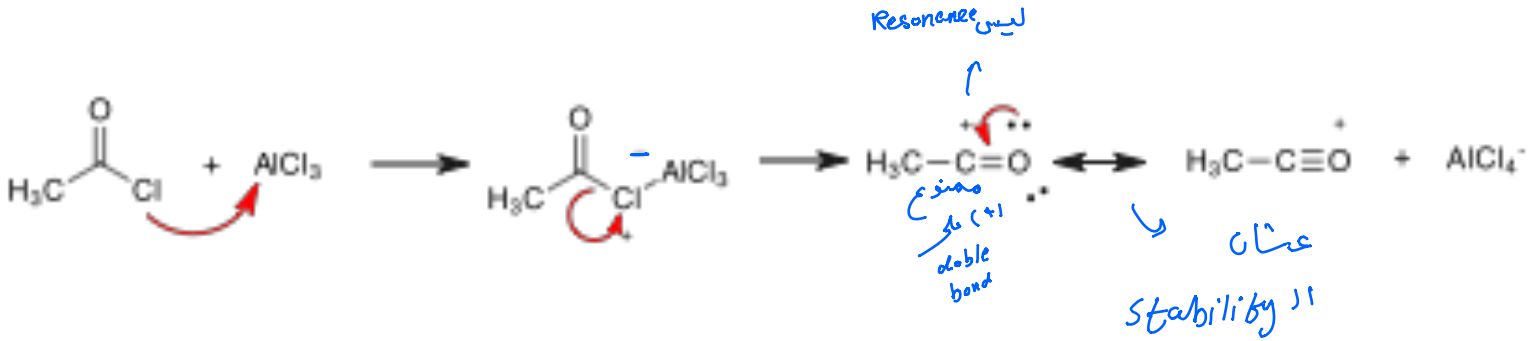
1ry
less stable

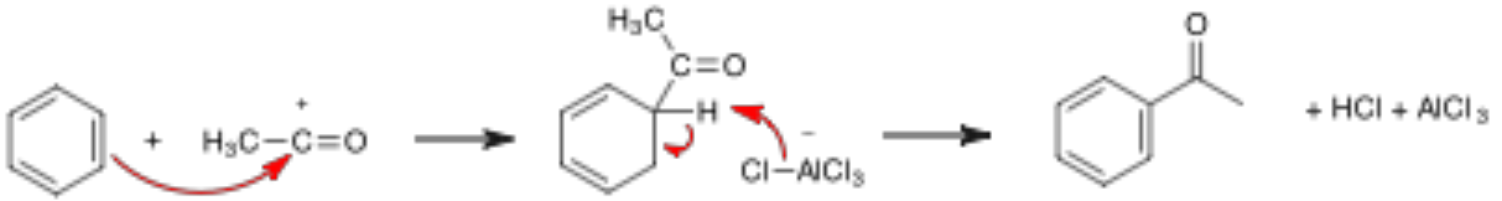
3ry
more stable

Friedel-Crafts Acylation

Friedel–Crafts acylation—General reaction

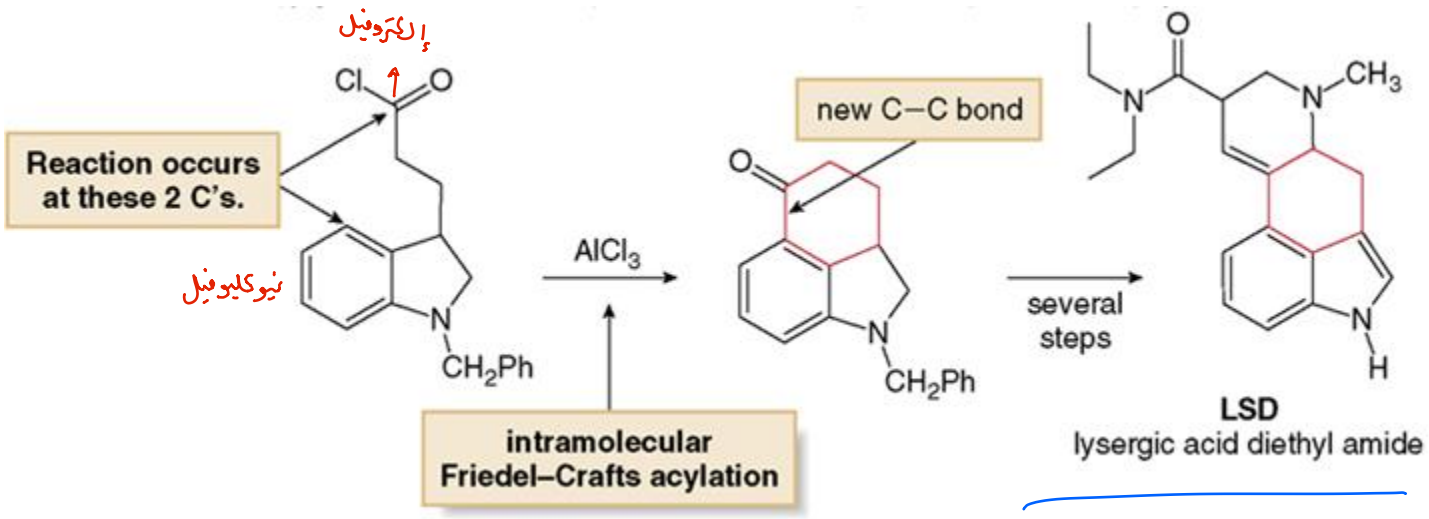




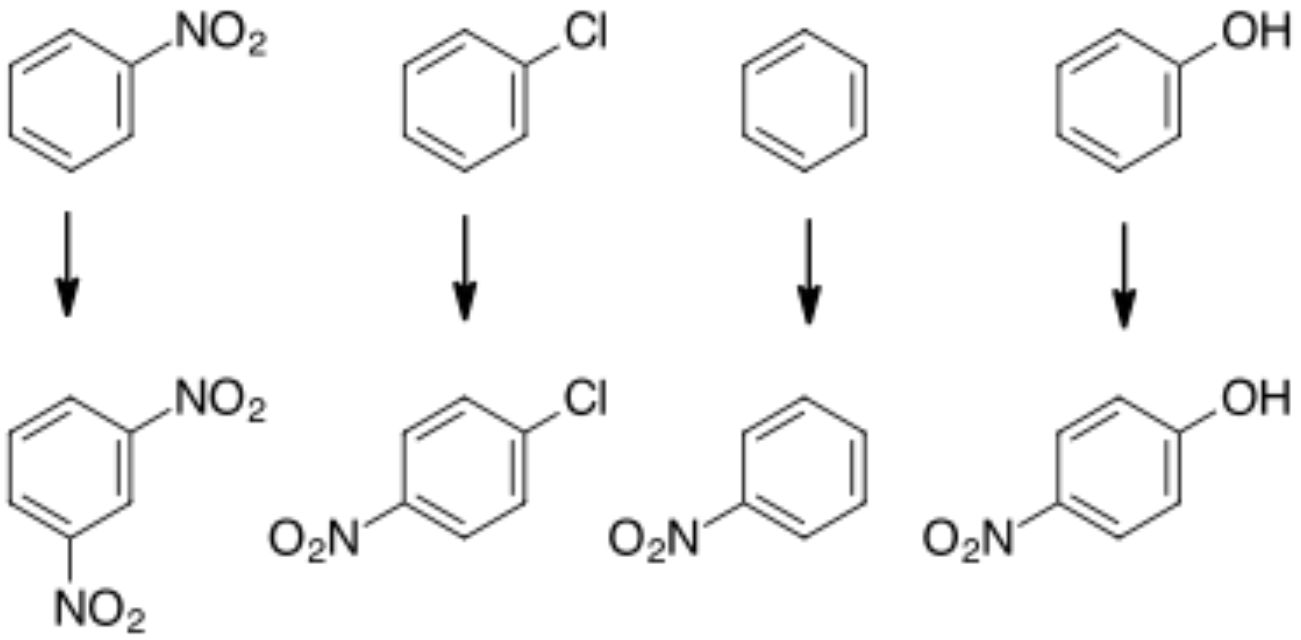


intramolecular Friedel-Crafts reactions.

بتصير العملية في المركب الواحد



Nitration of Substituted Benzenes



Relative rates	6×10^{-8}	0.033	1	1000

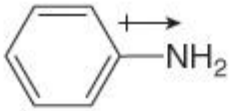
Substituents modify the electron density in the benzene ring, and this affects the course of electrophilic aromatic substitution.

Substituted Benzenes

Inductive effects (through σ bonds):

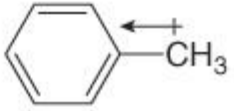
- Atoms more electronegative than carbon—including N, O, and X—pull electron density away from carbon and thus exhibit an electron-withdrawing inductive effect.
- Polarizable alkyl groups donate electron density, and thus exhibit an electron-donating inductive effect.

Electron-withdrawing inductive effect



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

Electron-donating inductive effect



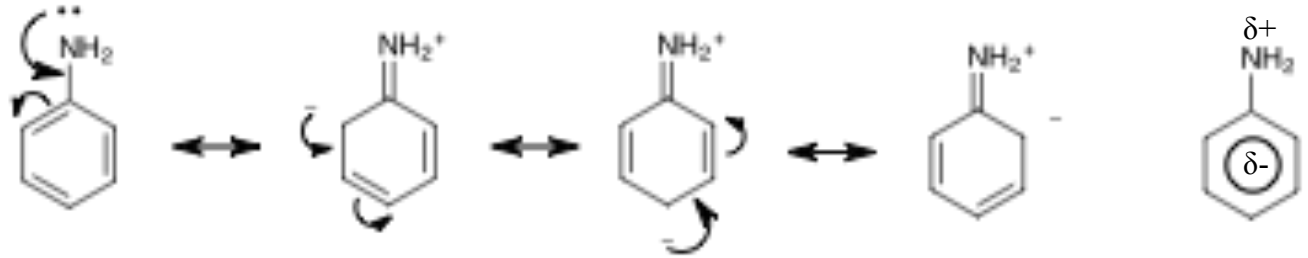
- Alkyl groups are **polarizable**, making them electron-donating groups.

- 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							
	$-SiR_3$							

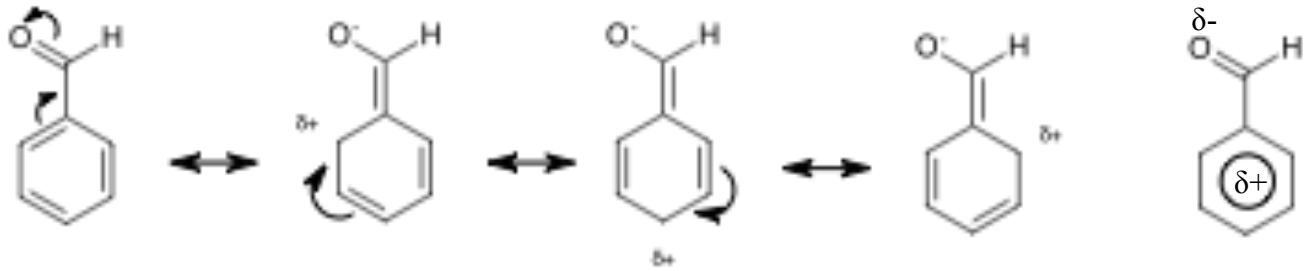
Substituted Benzenes

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)**

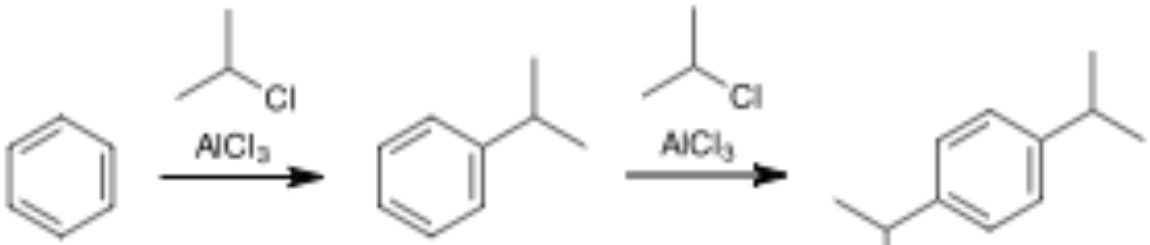


Substituted Benzenes: Activation

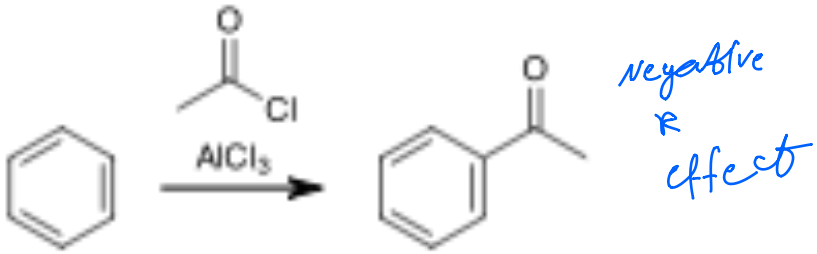
		+ R		- R
		+R > -I	-I >+R	
- I	$-NR_3^+$ CF_3 Inductive	$-NH_2$, $-OH$ $-NHR$ $-OR$ $-NR_2$	-F -Cl -Br -I	-CHO -COR -COOH -COOR CN SO_3H SO_2R $-NO_2$
+ I	$-CH_3$ -Alkyl $-SiR_3$ Inductive			

- 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



negative
R
effect

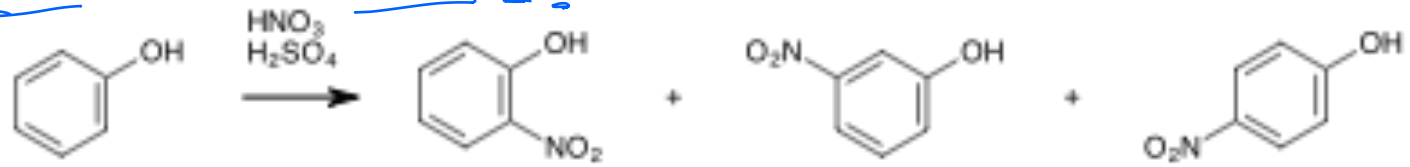
Less reactive
than benzene

Substituted Benzenes: Orientation

اسرع من البنزين

↑

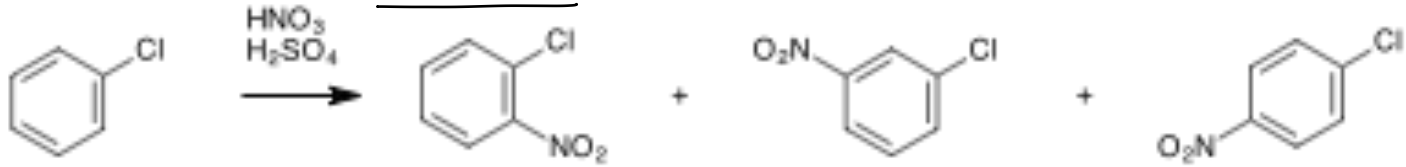
+R > -I (-OR, -NR2): activating, o- p- directing



30% traces 70%

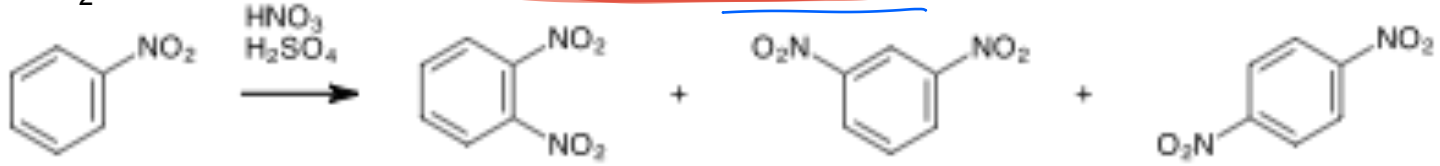
ابطأ من البنزين

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



35% traces 65%

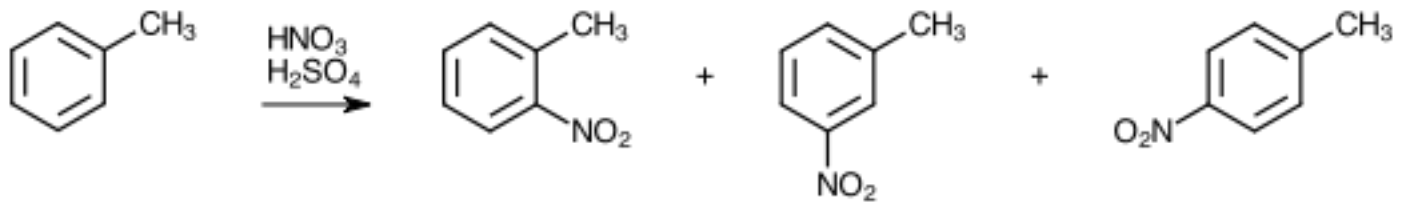
-I, -R (-NO_2, -SO3H, -CN, -COR): deactivating, m- directing.



5% 90% 5%

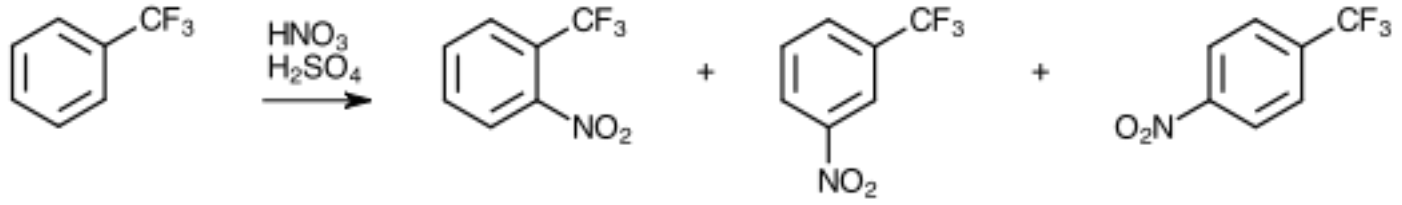
Substituted Benzenes: Orientation

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



58% 5% 37%

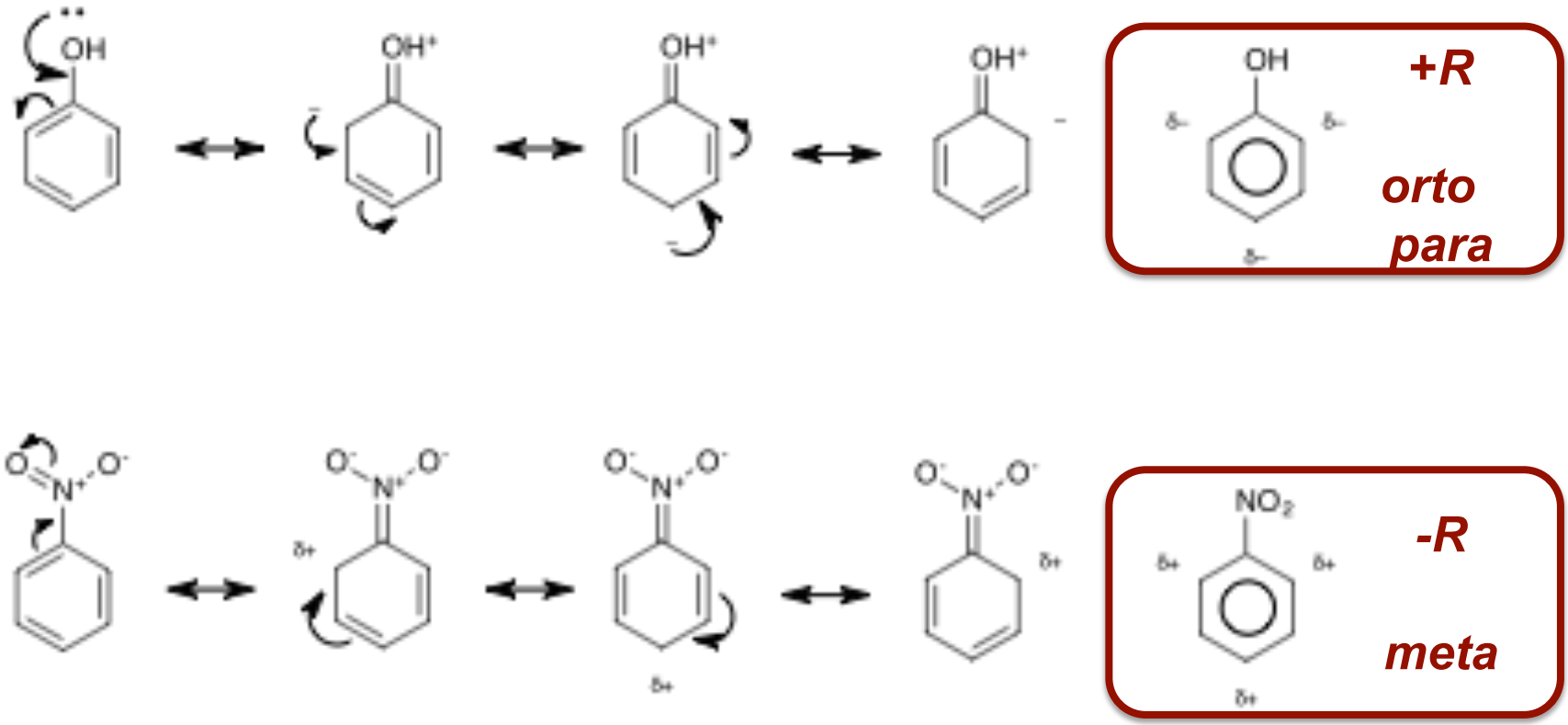
- I: deactivating, -m directing (same as - R)



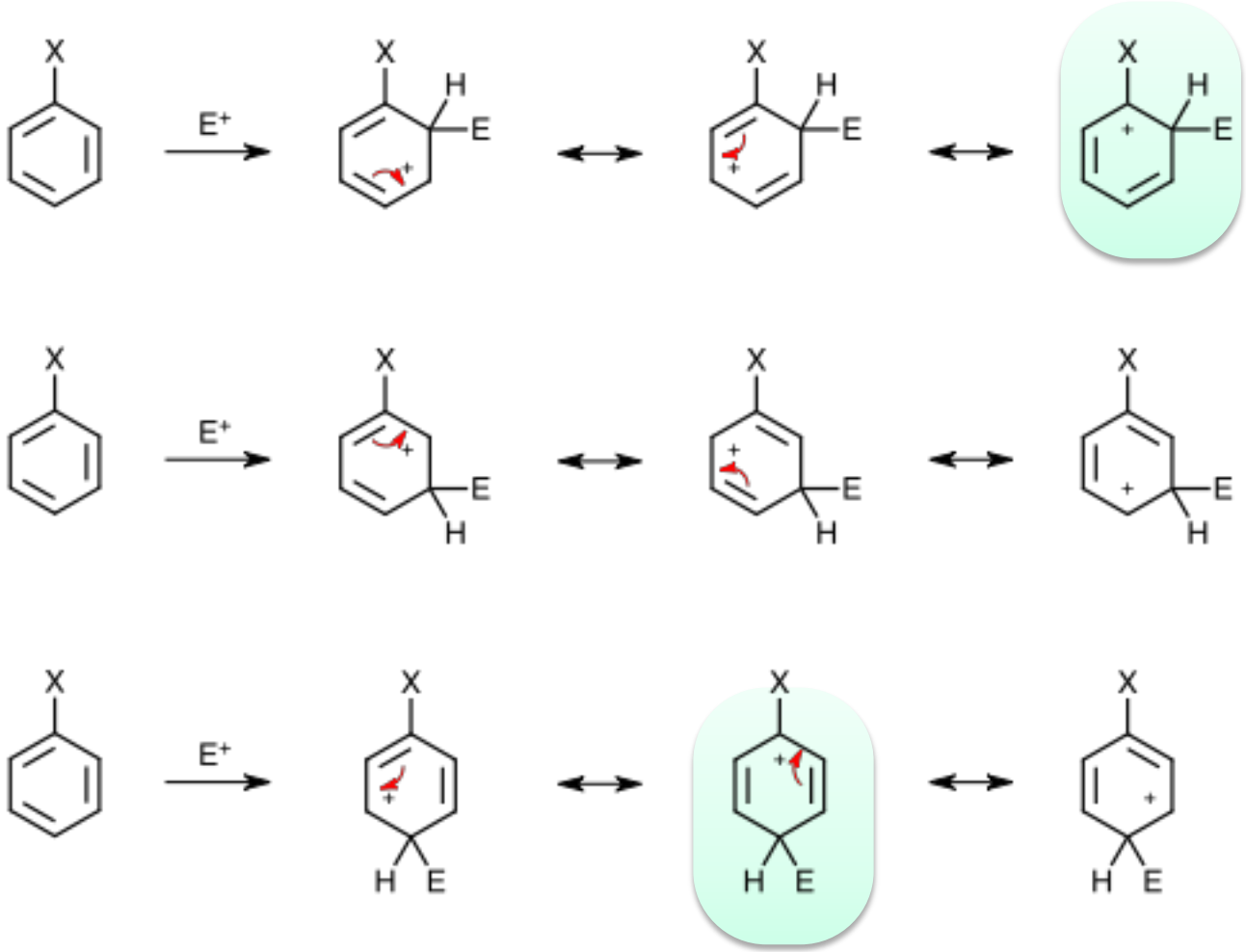
6% 91% 3%

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



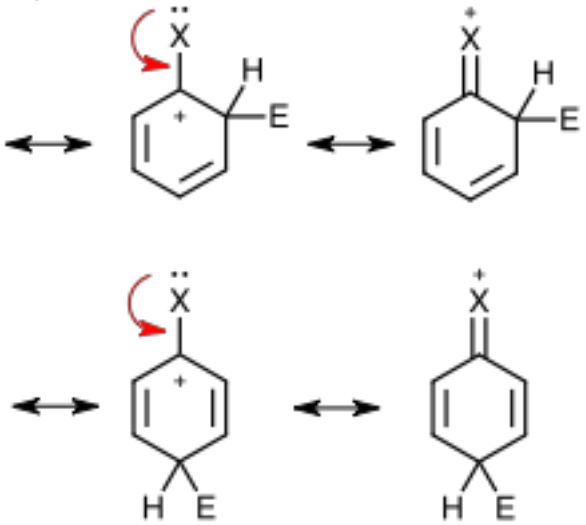
Substituted Benzenes: Orientation



Substituted Benzenes: Orientation

+ R (donating by Resonance)

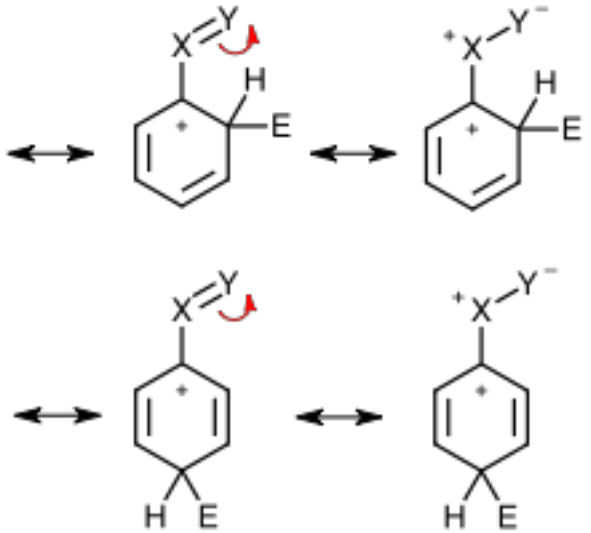
-o, -p intermediates are resonance stabilised



وجود (+) تحت X يعزز الـ Stabilisation للتوجيه

- R

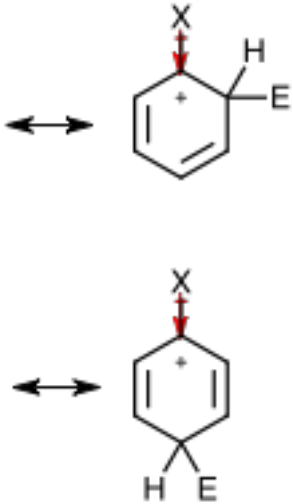
-o, -p intermediates are resonance destabilised



يتفضل

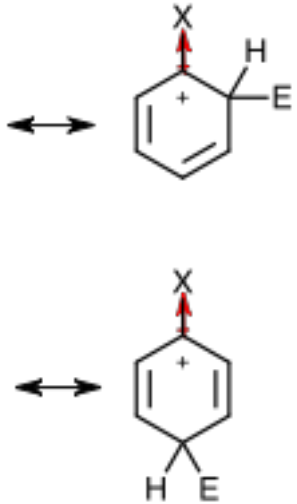
+ I (donating by inductive)

-o, -p intermediates are inductively stabilised

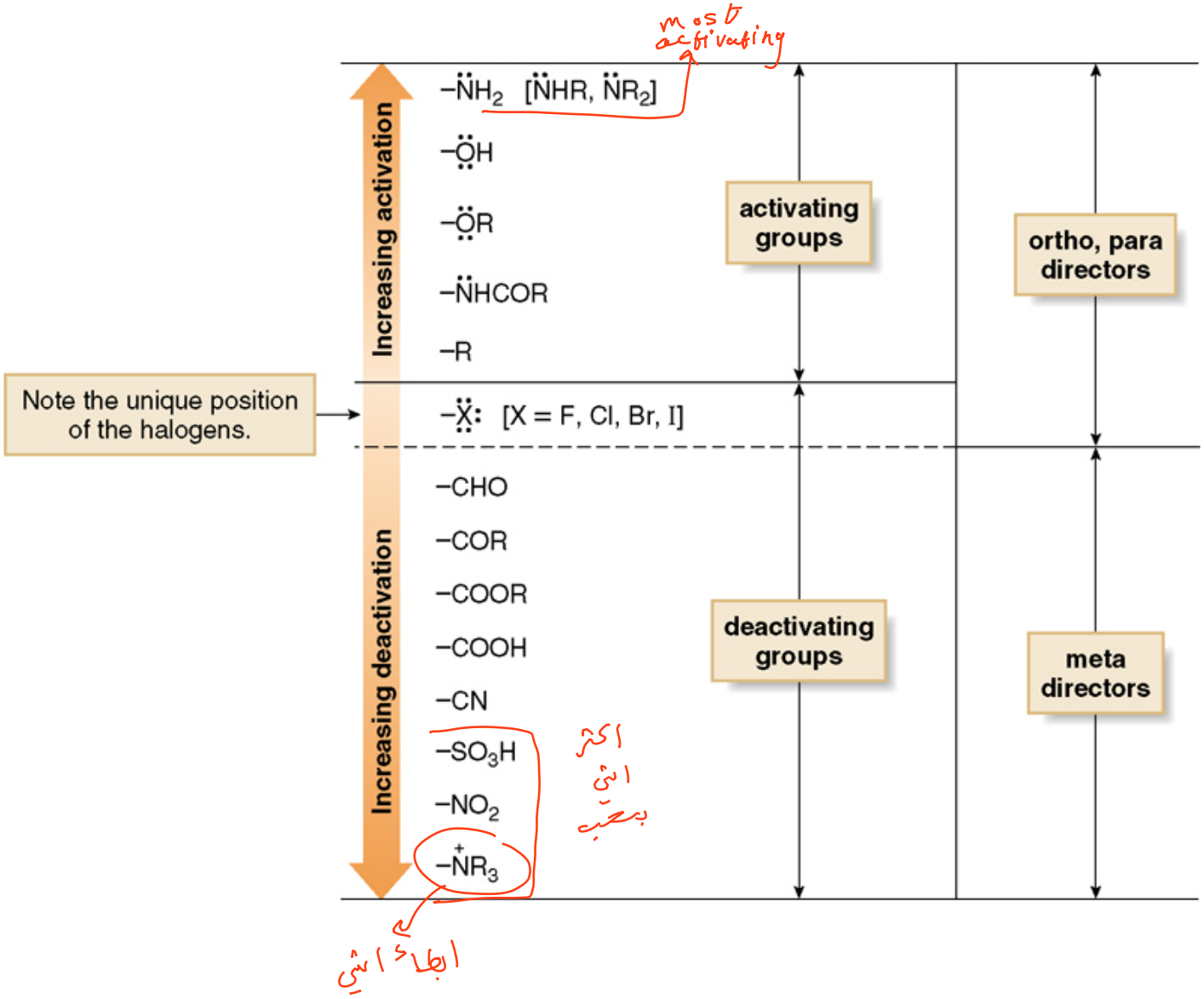


- I

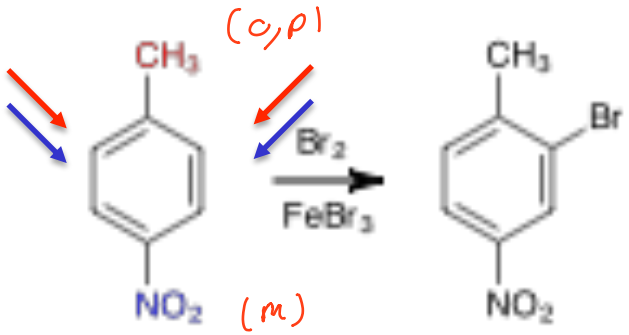
-o, -p intermediates are inductively destabilised



Substituent Effects. Summary

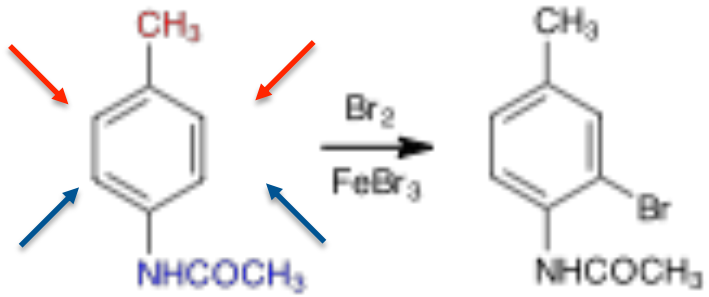


Disubstituted Benzenes



(m) (ortho)

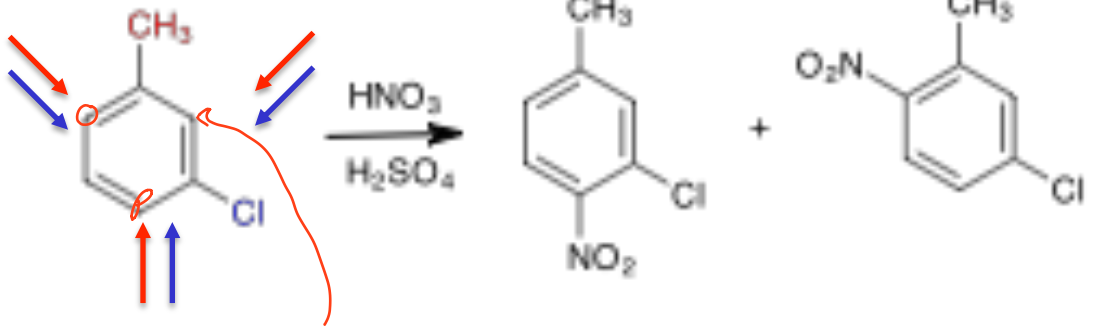
(الاثنين اشتركوا بموقع واحد فاختار)



(الأقوى هي التي تُعتمد في حال الإختلاف)

$NHCOCH_3 > CH_3$

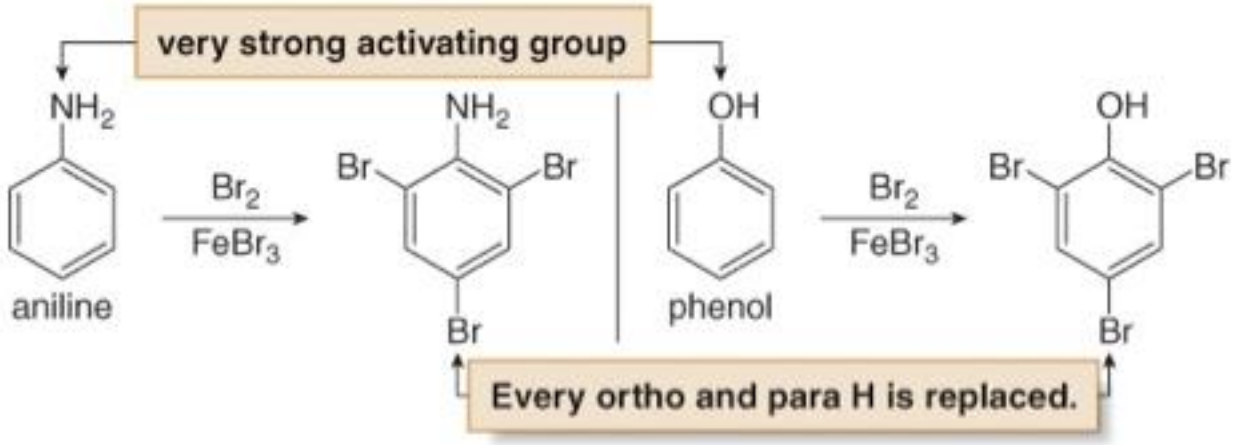
sterically hindered

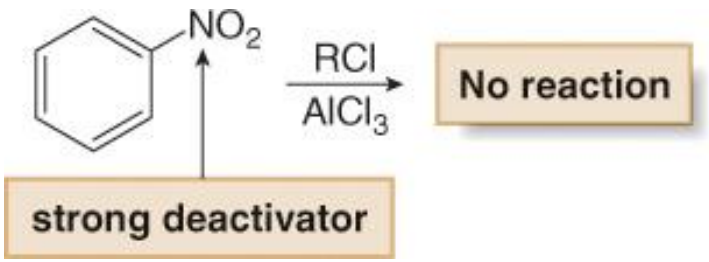


(لاتصبف اشي بين تفرعين)

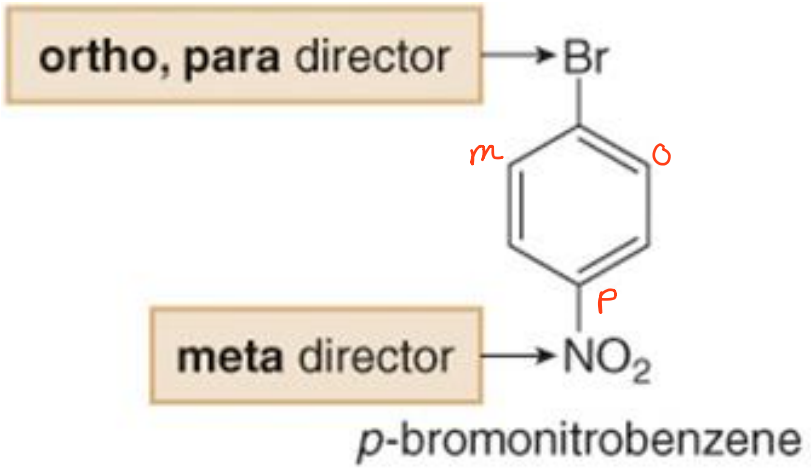
(الاثنين اشتركوا بموقعين
فاختار اعوقعين)

Further Examples





Synthesis of Polysubstituted Benzenes



p-bromonitrobenzene

لو بدي انتج

ببدأ بإضافة Br

على البنزين حتى

تكون إضافة NO_2 على

Para

Synthesis of Polysubstituted Benzenes

Pathway [1]: Bromination before nitration

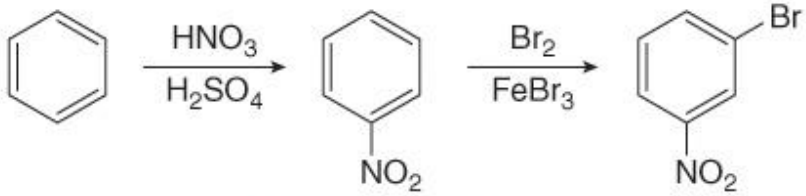
ortho, para director

para product

The ortho isomer can be separated from the mixture.

This pathway gives the desired product.

Pathway [2]: Nitration before bromination



meta director

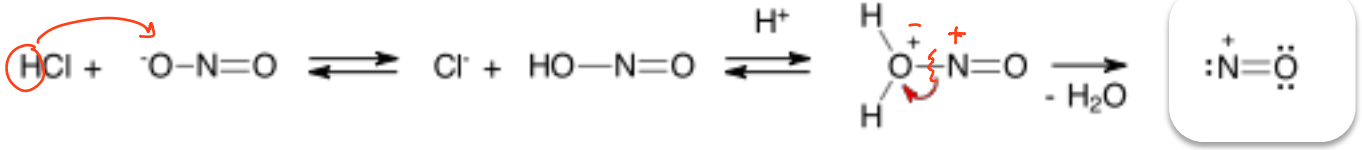
meta isomer

This pathway does NOT form the desired product.

Reaction of Amines with Nitrous Acid

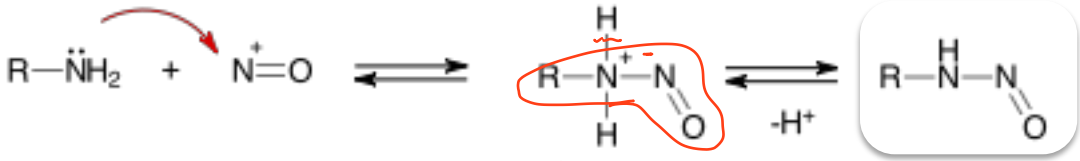
Reaction of Amines with Nitrous Acid

1. generation of the electrophile



nitrosonium ion

2. nitrosation

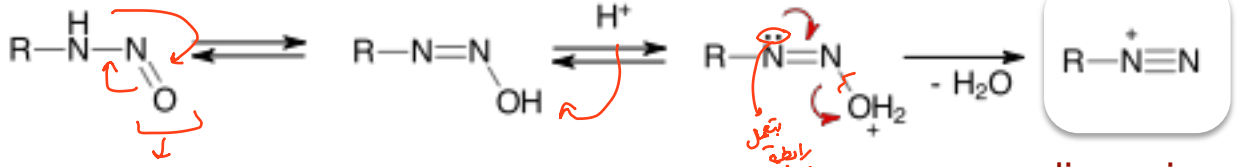


N-nitrosamine

unstable

فبتخرج H

3. acid-catalysed elimination



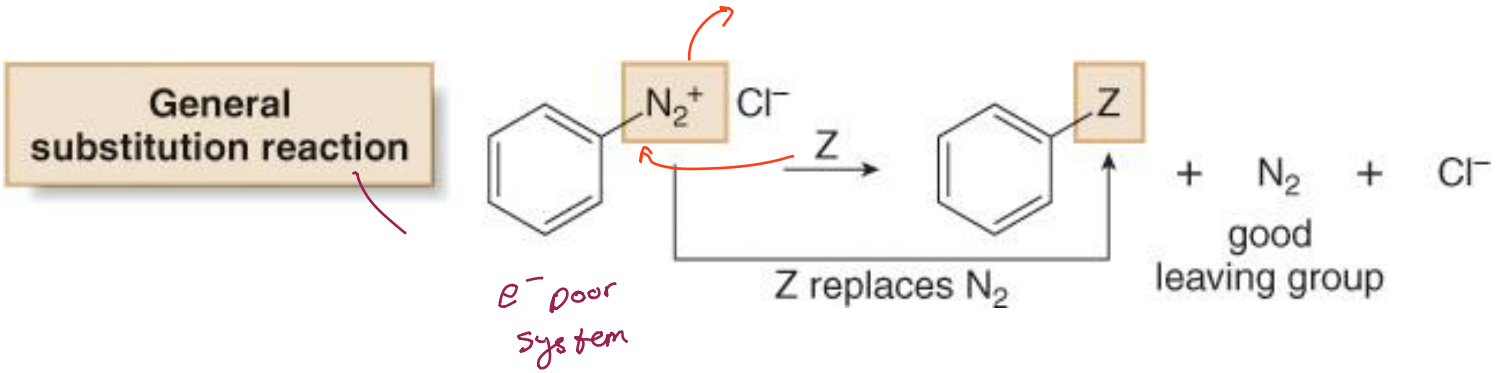
diazonium ion

العملية اسمها tautomerism

بتعمل رابطة ثنائية وبتطلع H_2O

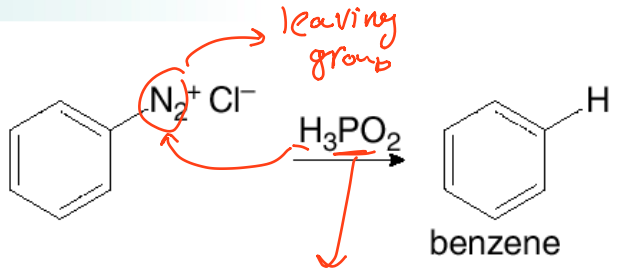
Substitution Reactions of Aryl Diazonium Salts

- 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.



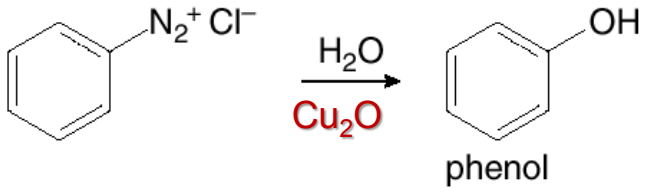
Substitution Reactions of Aryl Diazonium

Substitution by H—Synthesis of benzene



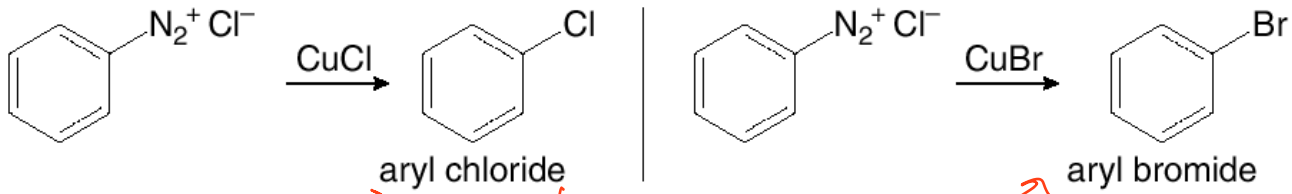
A diazonium salt reacts with hypophosphorus acid to form benzene. This reaction is useful in synthesizing compounds that have substitution patterns that are not available by other means.

Substitution by OH—Synthesis of phenols



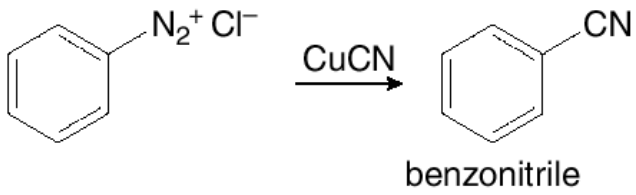
Substitution Reactions of Aryl Diazonium

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.

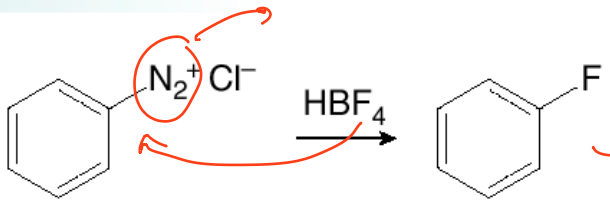
Substitution by CN—Synthesis of benzonitriles



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.

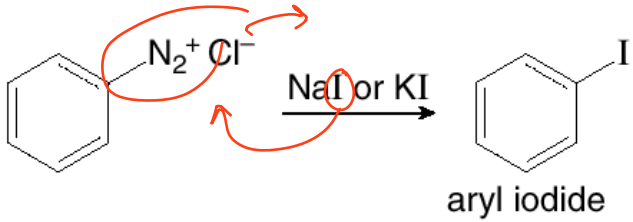
Substitution Reactions of Aryl Diazonium Salts

Substitution by F—Synthesis of aryl fluorides



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

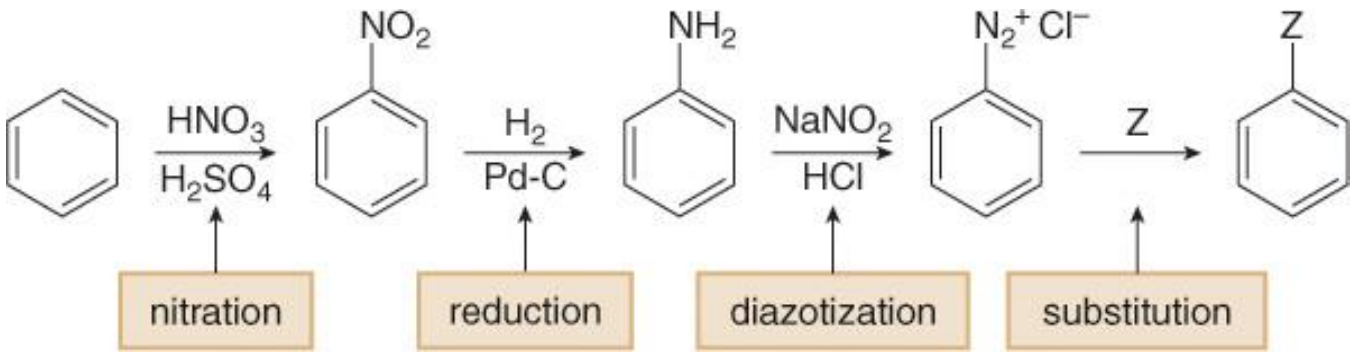
Substitution by I—Synthesis of aryl iodides



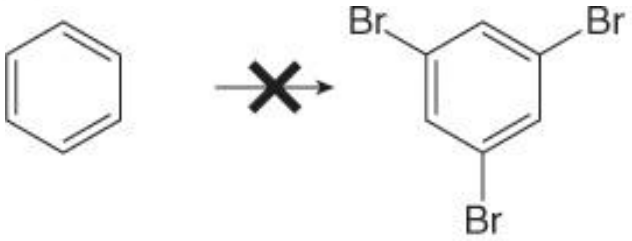
This is a useful reaction because aryl iodides cannot be produced by direct iodination with I_2 and a Lewis acid catalyst.

Substitution Reactions of Aryl Diazonium Salts

Diazonium salts provide easy access to many different benzene derivatives. Keep in mind the following four-step sequence, because it will be used to synthesize many substituted benzenes.



Substitution Reactions of Aryl Diazonium Salts



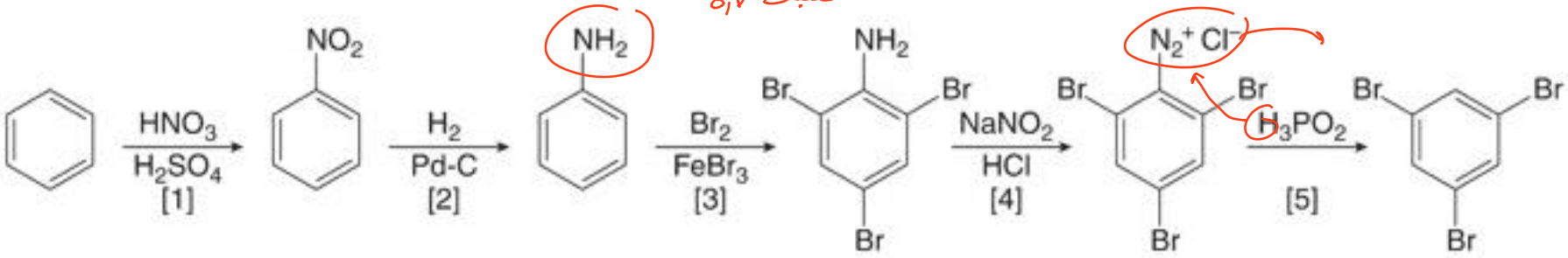
1,3,5-tribromobenzene

The Br atoms are ortho, para directors located meta to each other.

السبب

يستحيل تحضيره بأي electrophilic

very fast activating group
حقنقف o,p

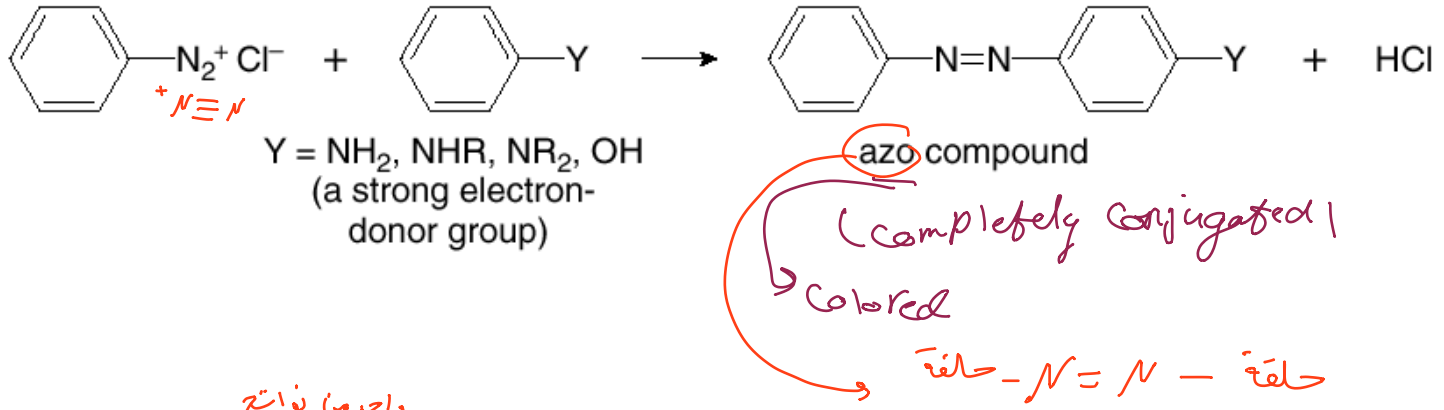


- Nitration followed by reduction forms aniline ($C_6H_5NH_2$) from benzene (Steps [1] and [2]).
- Bromination of aniline yields the tribromo derivative in Step [3].
- The NH_2 group is removed by a two-step process: diazotization with $NaNO_2$ and HCl (Step [4]), followed by substitution of the diazonium ion by H with H_3PO_2.

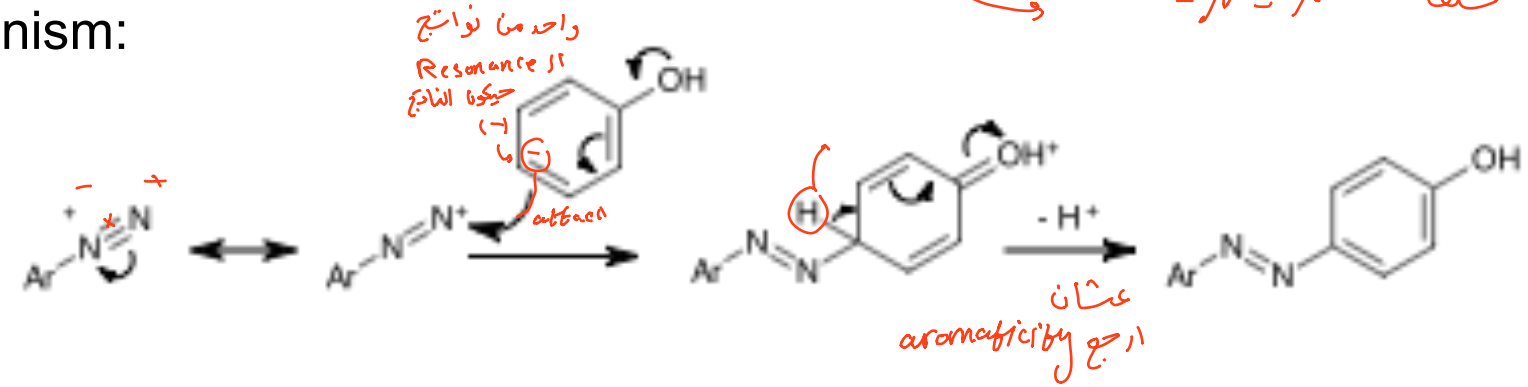
Coupling Reactions of Aryl Diazonium Salts

- When a diazonium salt is treated with an aromatic compound activated by a strong electron-donor group, a substitution reaction takes place giving an azo compound.

Azo coupling



Mechanism:

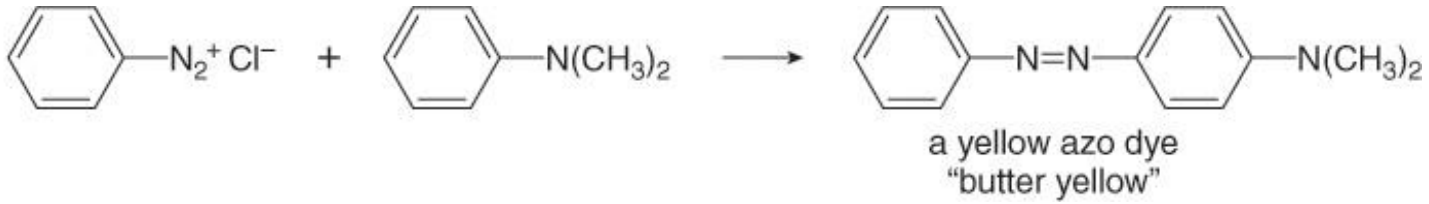


The para position is preferred for steric reasons

Azo Dyes

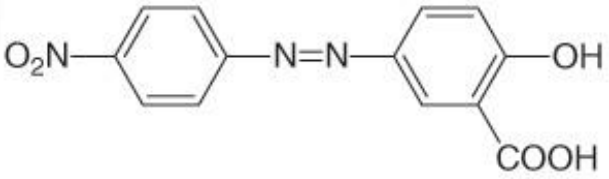
- Azo compounds are highly conjugated, rendering them colored. Many of these compounds are synthetic dyes. Butter yellow was once used to color margarine.

Example

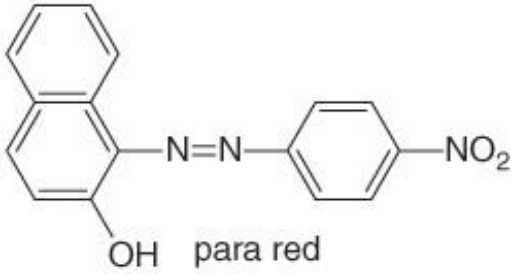


a yellow azo dye
"butter yellow"

Three azo dyes

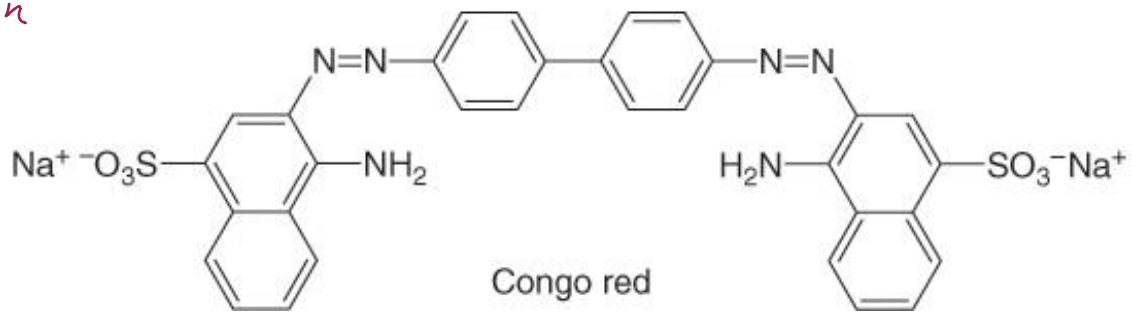


alizarine yellow R



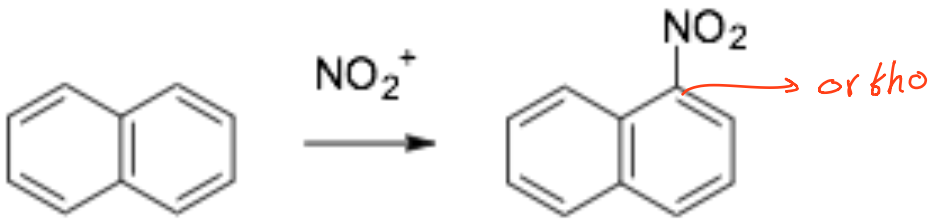
para red

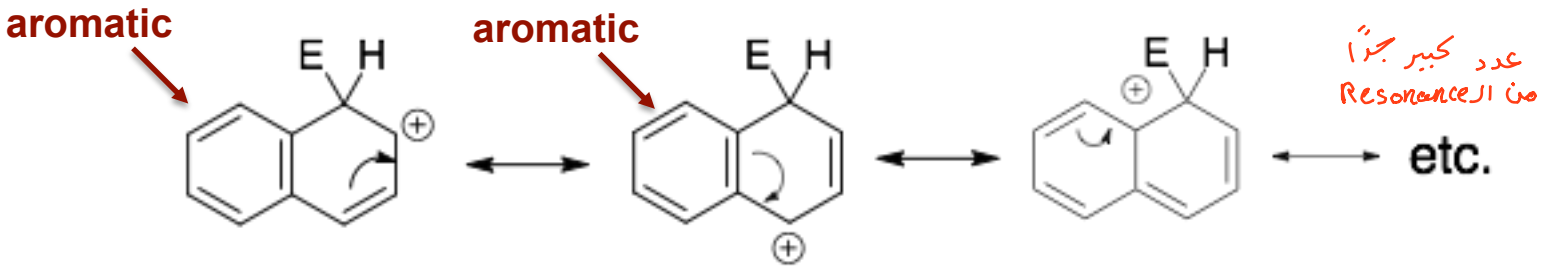
كلما زاد ال
conjugation كان
اللون أقوى

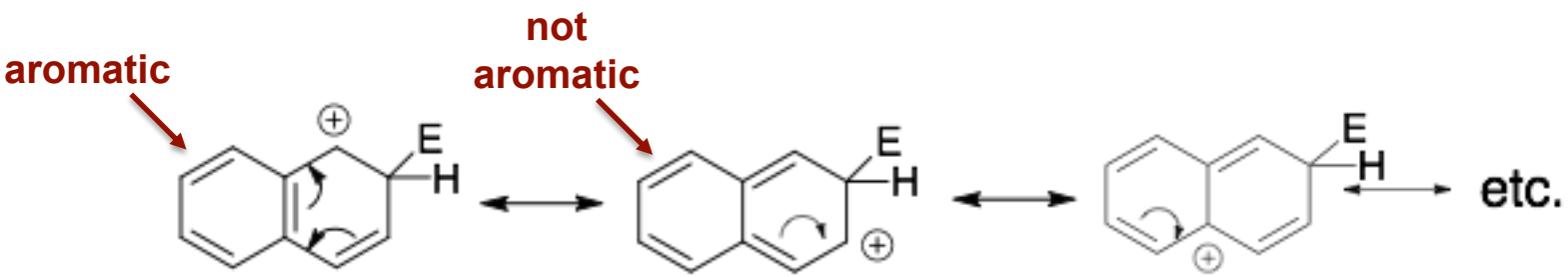


Congo red

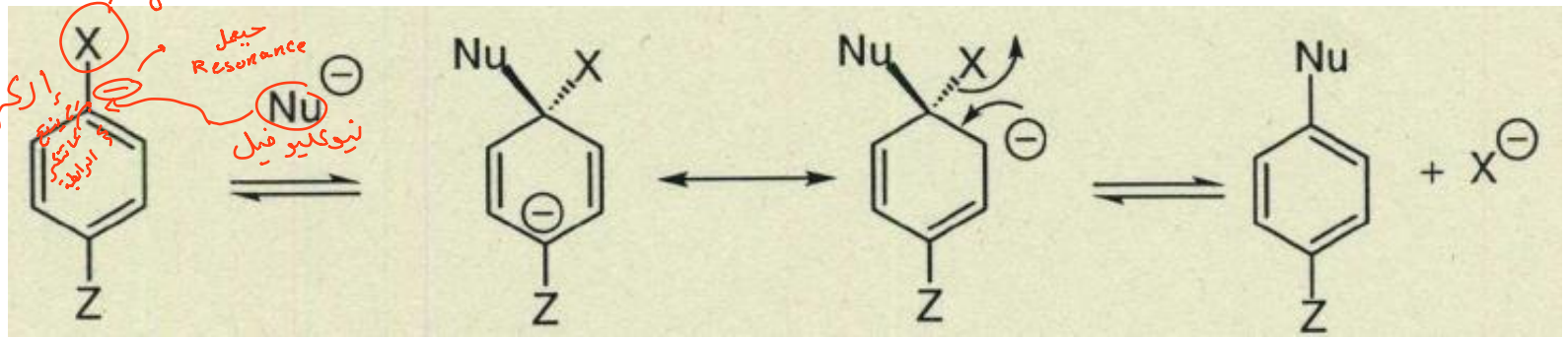
S_EAr in Polyciclic Aromatic Compounds





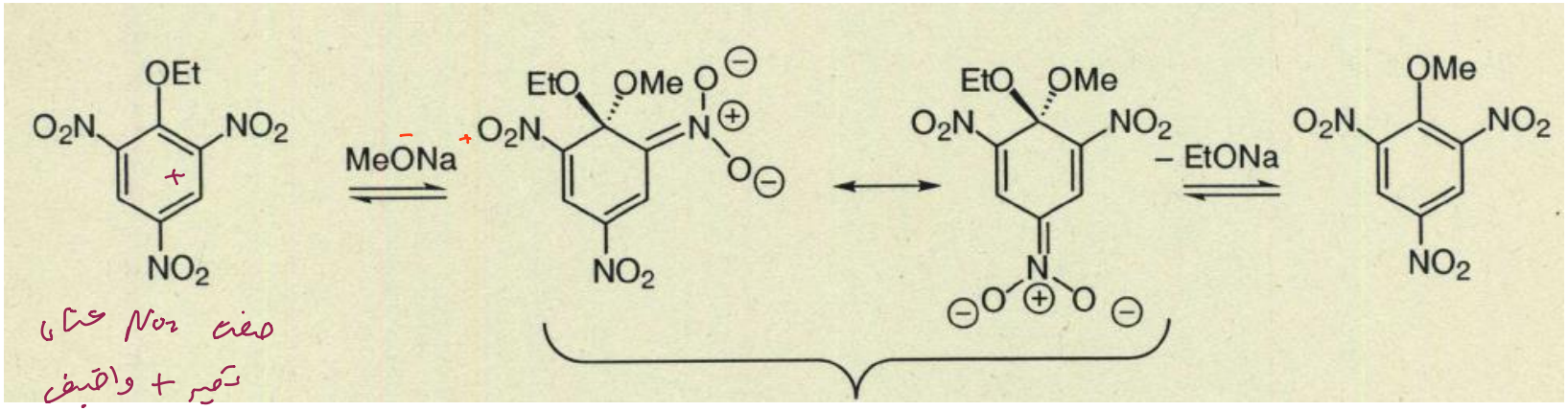


Nucleophilic Aromatic Substitutions, S_NAr



Z = Electron Accepting Substituent (sigma or π: NO_2, CN, N_2^+, SO_2R)
X = Leaving Group

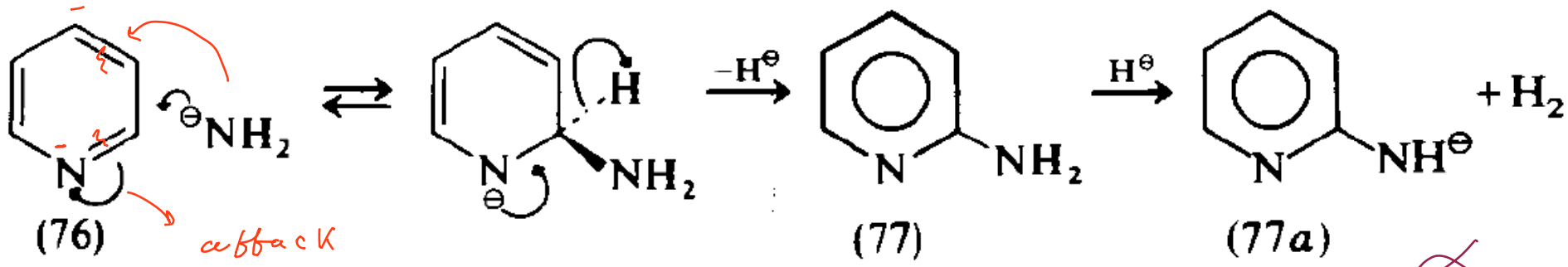
Example



Examples of S_NAr

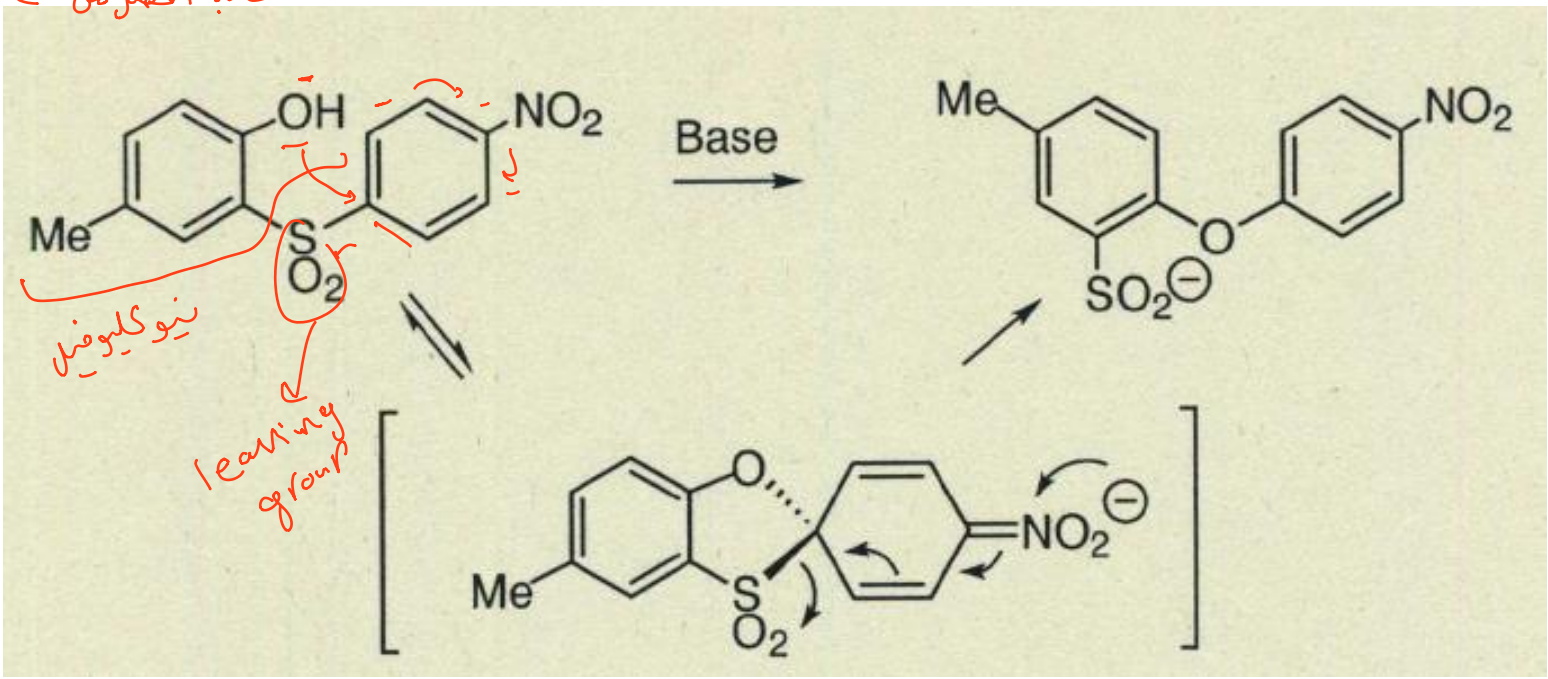
* الذرات الأقل سالبية بتحمل الشحنة الموجبة احسن
* الذرات الأكثر سالبية بتحمل الشحنة السالبة احسن

1)



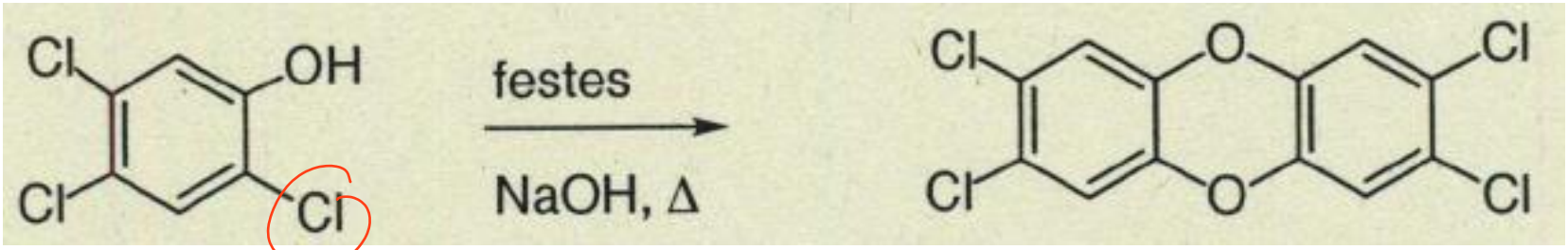
attack يصير على الرابطة مع N لأنو قدرة N عا حمل الشحنة السالبة افضل من C

2)



Examples of S_NAr

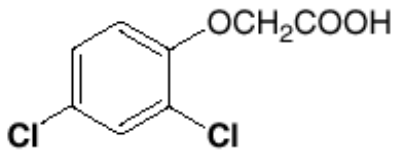
3)



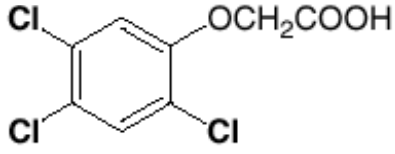
leaving

تخترق الحشرات insects سيولة

Herbicides were used extensively during the Vietnam War to defoliate dense jungle areas. The concentration of certain herbicide by-products in the soil remains high today.

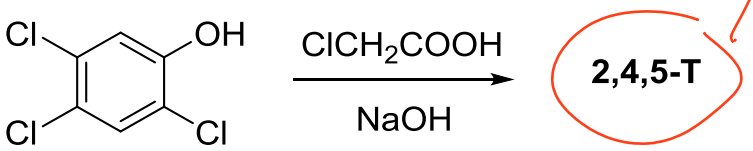


2,4-D
2,4-dichlorophenoxy-acetic acid herbicide

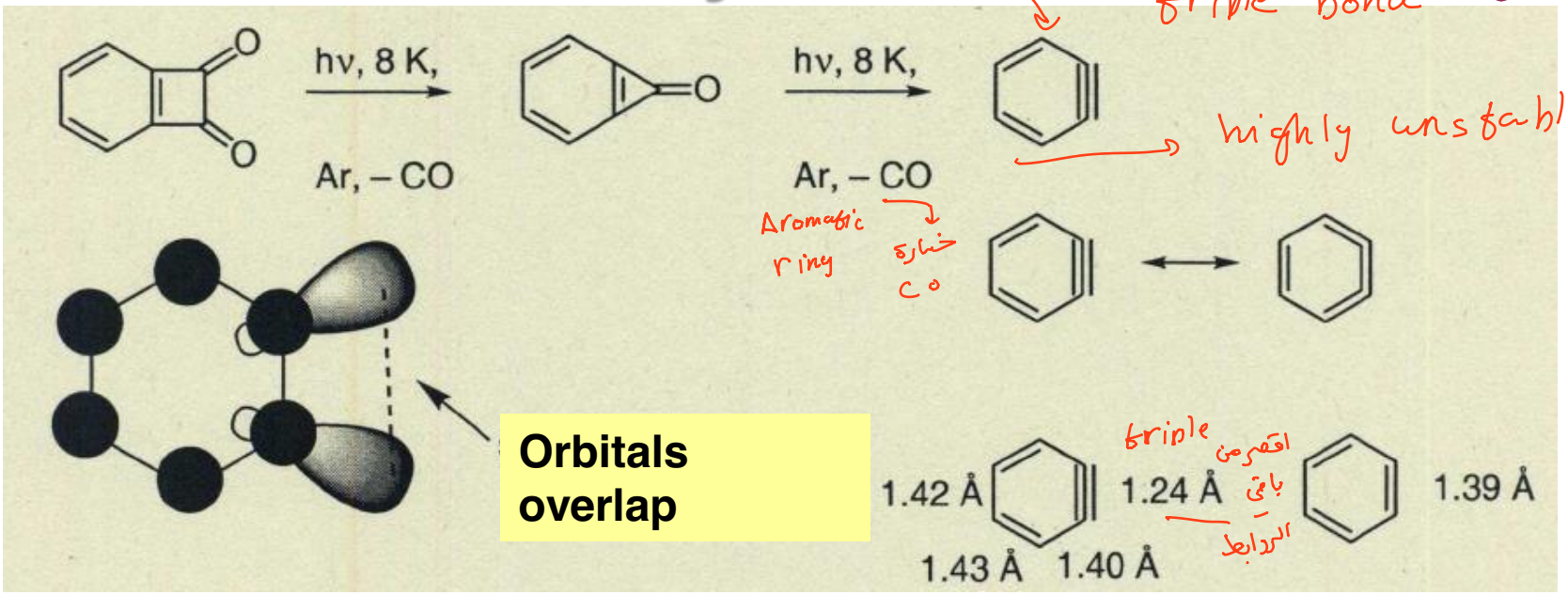


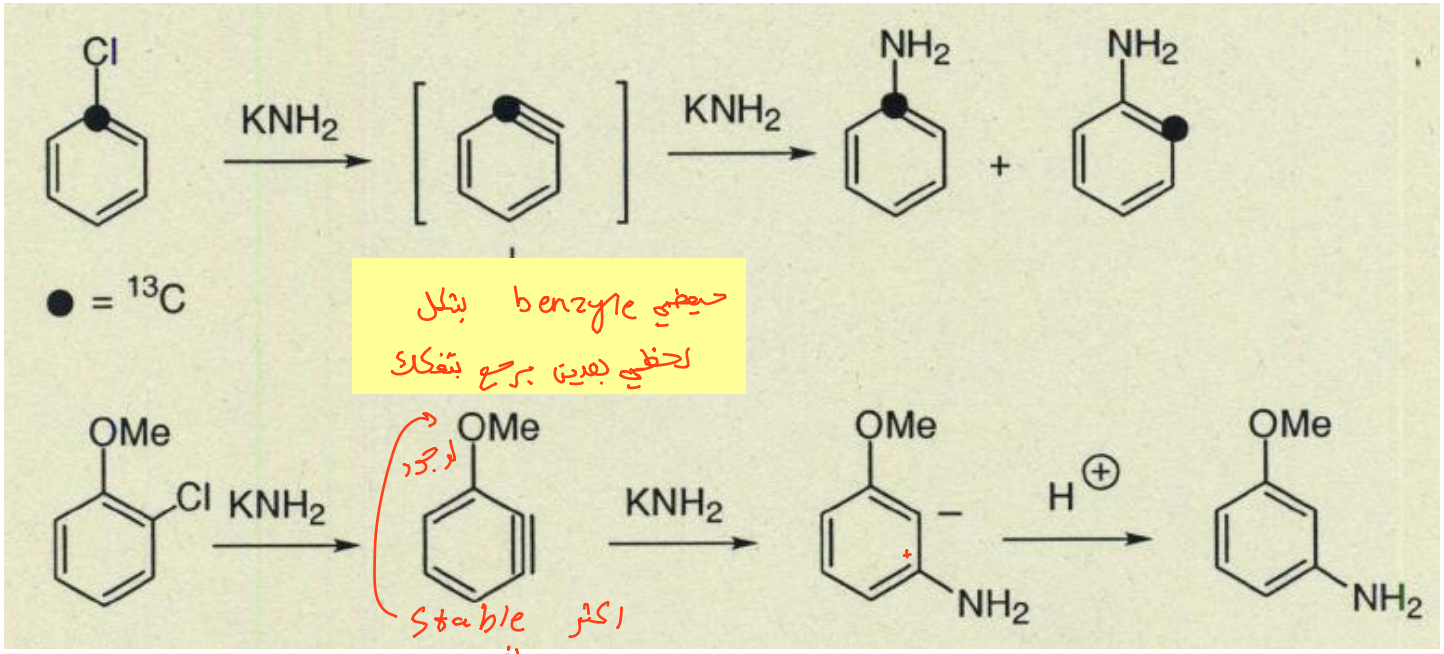
2,4,5-T
2,4,5-trichlorophenoxy-acetic acid herbicide

the active components in **Agent Orange**, a defoliant used in the Vietnam War



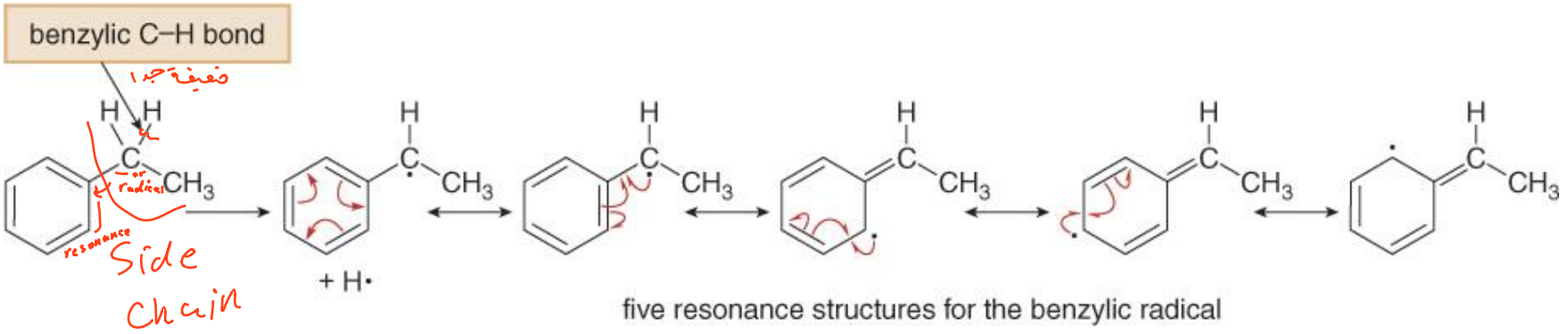
Benzyne

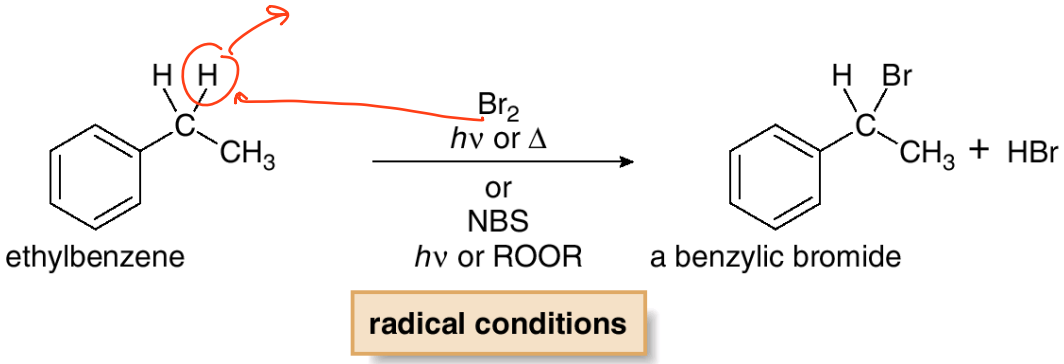

hν, 8 K,
Ar, – CO
hν, 8 K,
Ar, – CO
Aromatic ring
Orbitals overlap
1.42 Å
1.43 Å
1.40 Å
1.24 Å
1.39 Å


Cl
KNH2
KNH2
NH2
NH2
+
= 13C
OMe
Cl
KNH2
OMe
KNH2
OMe
H
NH2
NH2

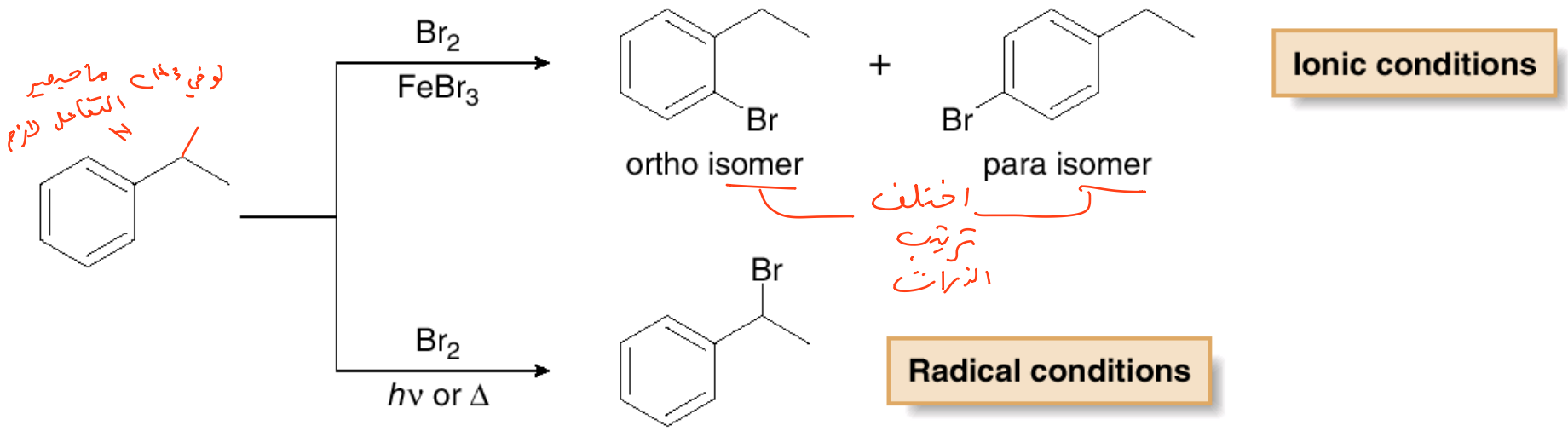
Side Chain Reactivity: Radical Halogenation

Benzylic C—H bonds are weaker than most other sp^3 hybridized C—H bonds, because homolysis forms a resonance-stabilized benzylic radical.

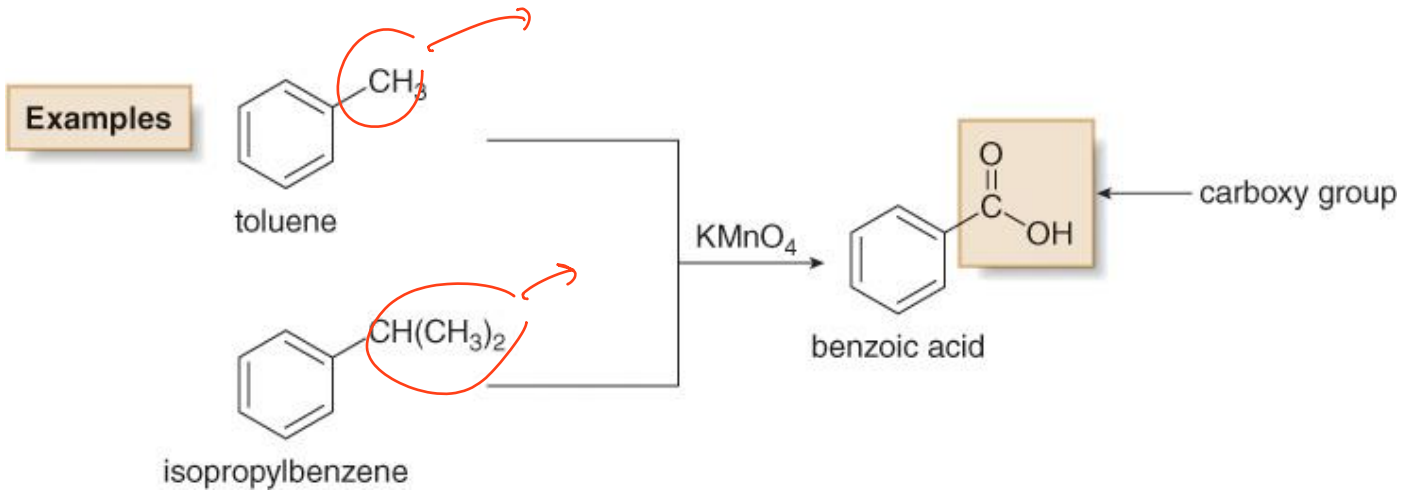


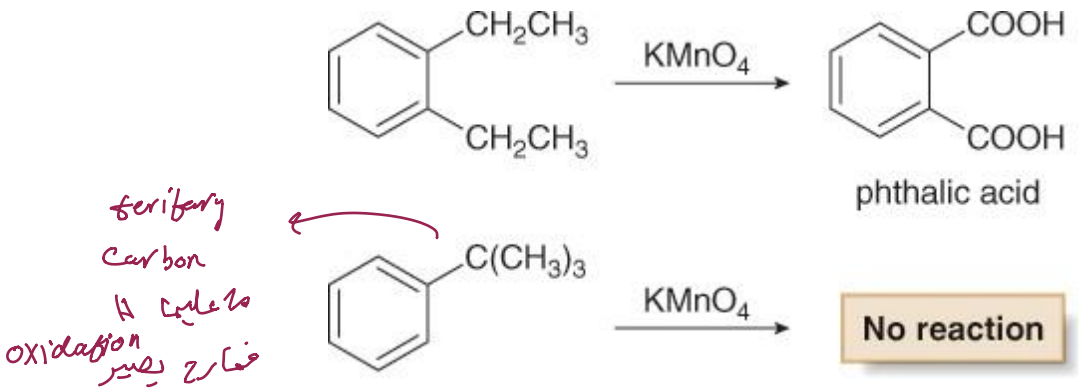


Side Chain Reactivity



Side Chain Reactivity: Oxidation





Side Chain Reactivity: Reduction