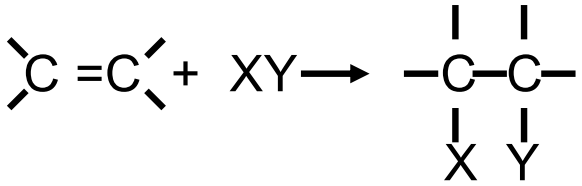
Organic Chemistry Reactions

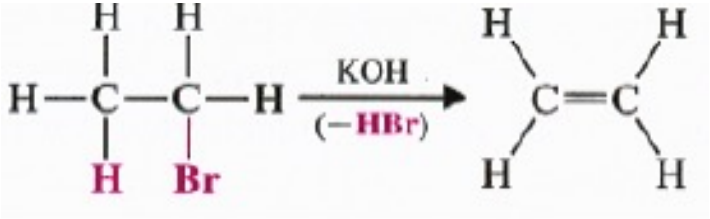
1. **Substitution**

$$CH_4 + Cl_2 + \text{energy} \longrightarrow CH_3Cl + HCl$$

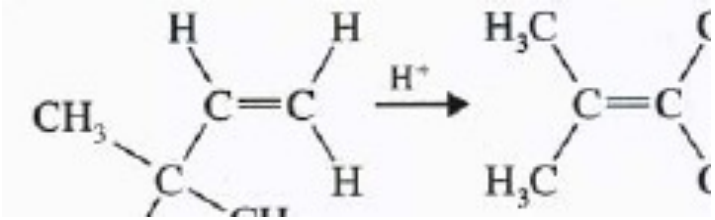
2. **Addition**



3. **Elimination**



4. **Rearrangement**



Electrophiles e Nucleophiles

Electrophiles reagents: lack electrons (Lewis acids)

Attract the substrate's lone pair

Examples:

H^+ , Cl^+, Br^+ NH_4^+, RNH_3^+

Nucleophiles reagents: have a lone pair that can be shared with substrates (Lewis bases)

Examples:

OH^- **(Arrhenius bases)**

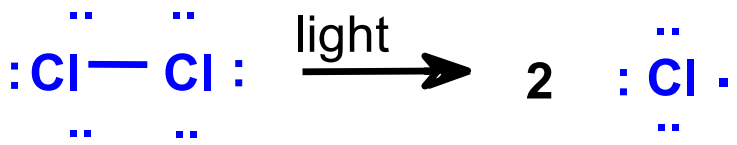
H_2O, NH_3 **(Broensted bases)**

CN^-, Cl^- Br^- , NO_3^-, NO_2^-, $CH_3CO_2^-$ **(Anions)**

Alkanes halogenation

CHAIN REACTION

1. Initiation



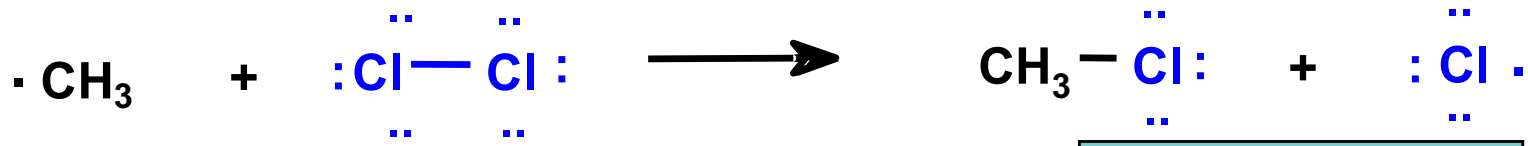
"dissociation"

PASSI RIPETUTI

2. Chain propagation

"hydrogen extraction"

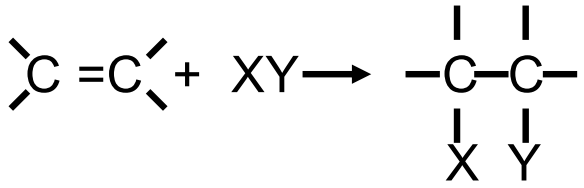
3. Chain propagation



Into step 2

ALKENES: electrophile addition

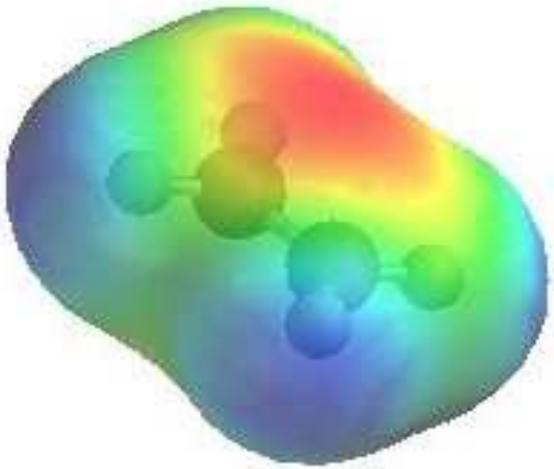
Π electrons are less tightly bound than σ ones: they are more available *for electrophilc attack*. The double bond acts as a "*source of electrons*" (Lewis base) and it can react with electrophiles (Lewis acids). The typical reaction is **electrophile addition**, of acidic compounds.



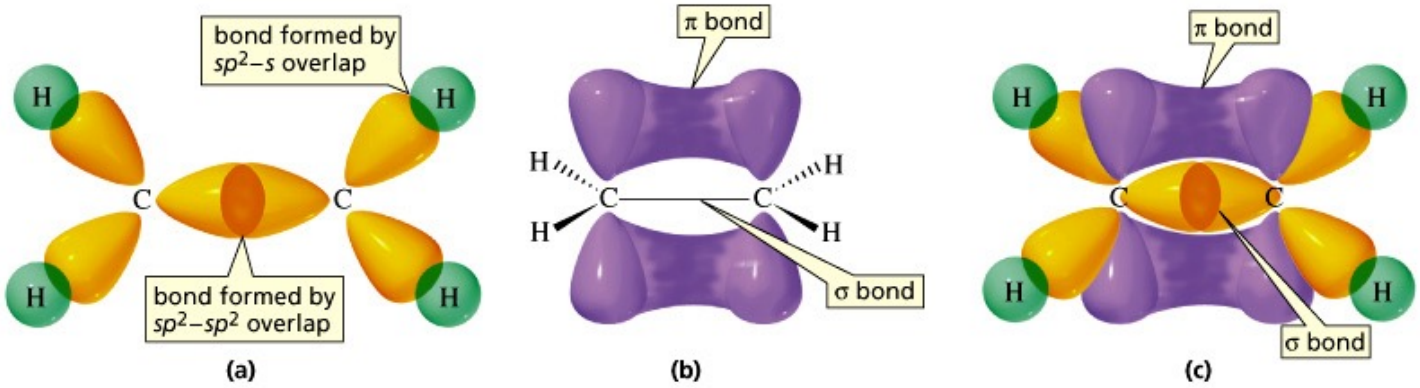
2 bonds are formed(2 σ)

2 bonds are broken(1 σ, 1π)

The double (or triple) bond is a reaction centre.



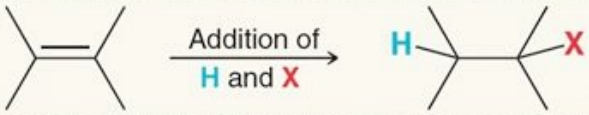
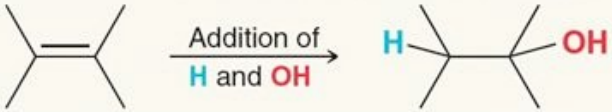
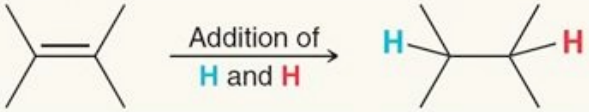
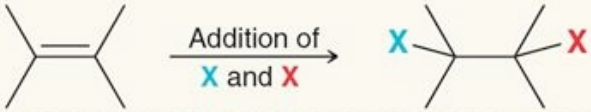
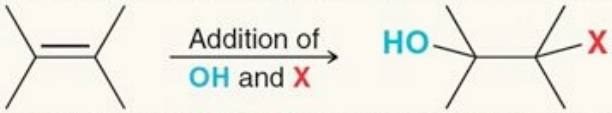
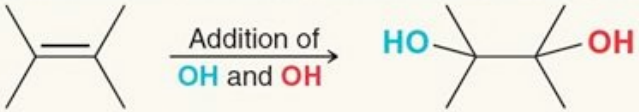
Having a high e^- density,
it tends to react.



Addition Reactions

- Addition is the opposite of elimination
- A pi bond is converted to a sigma bond

TABLE 9.1 SOME COMMON TYPES OF ADDITION REACTIONS

TYPE OF ADDITION REACTION	NAME	SECTION
	Hydrohalogenation (X=Cl, Br, or I)	9.3
	Hydration	9.6
	Hydrogenation	9.7
	Halogenation (X=Cl or Br)	9.8
	Halohydrin formation (X=Cl, Br, or I)	9.8
	Dihydroxylation	9.9, 9.10

WILEY

Water addition (hydratation)

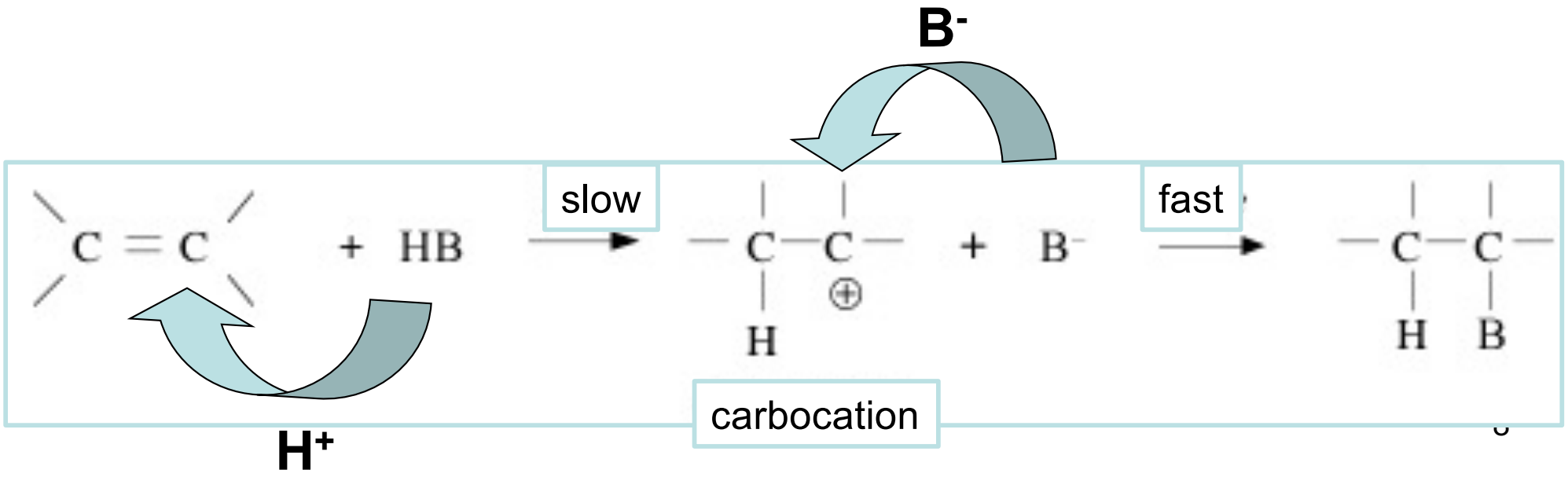
Frequent in biochemistry.

Alkenes are not reactive in pure water: its dissociation into H_3O^+ and OH^- is too weak.

In an acidic environment, alcohols are formed.

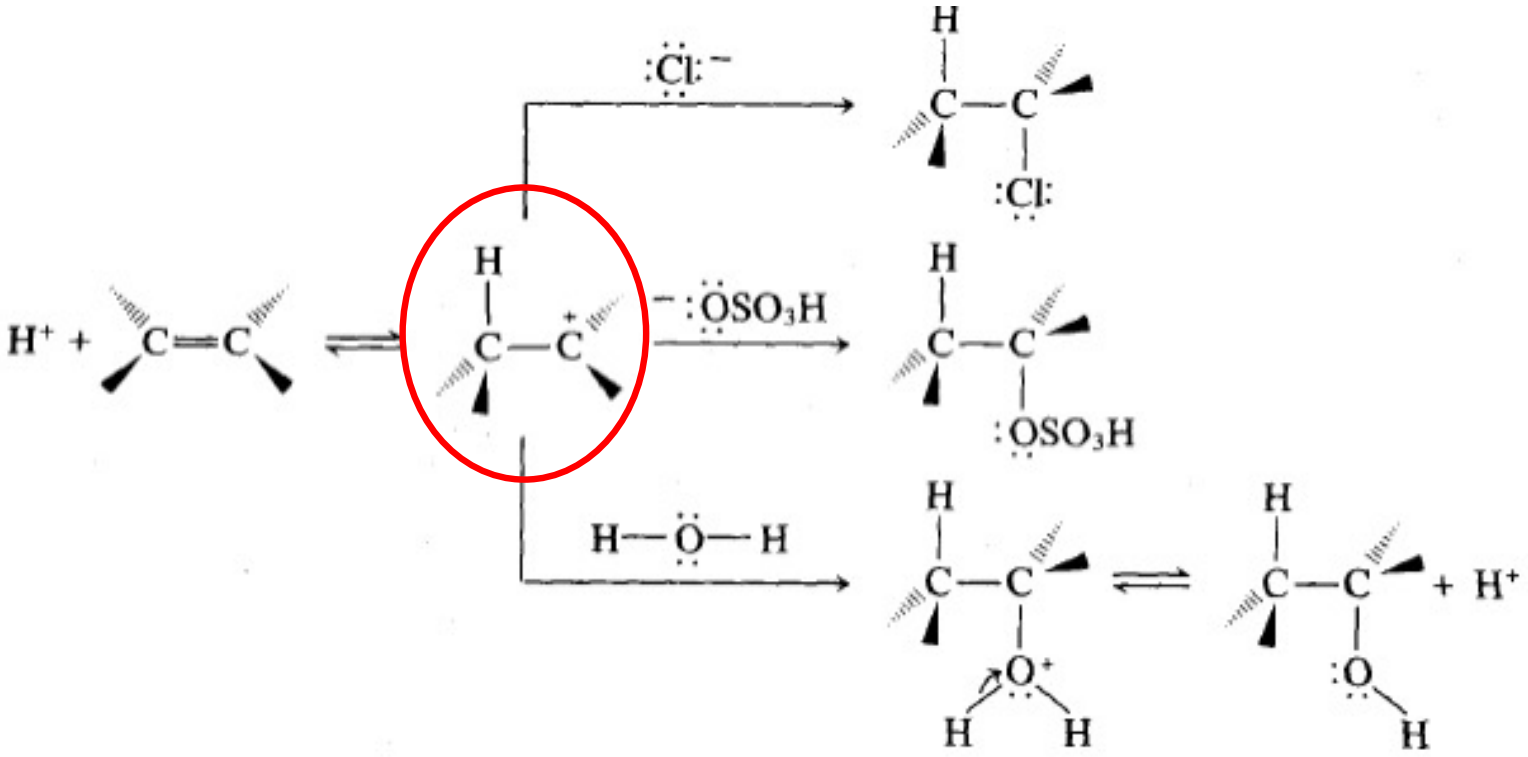
The reaction involves 2 steps, via a carbocation intermediate (C with a positive charge).

The 1st step (slow) is the true *electrophile addition* : the alkene takes in the positive part of the added compound. The H^+ acts as an electophile favouring the *carbocation* formation. In the 2nd step it binds the "negative" component, or more in general, a basic component.

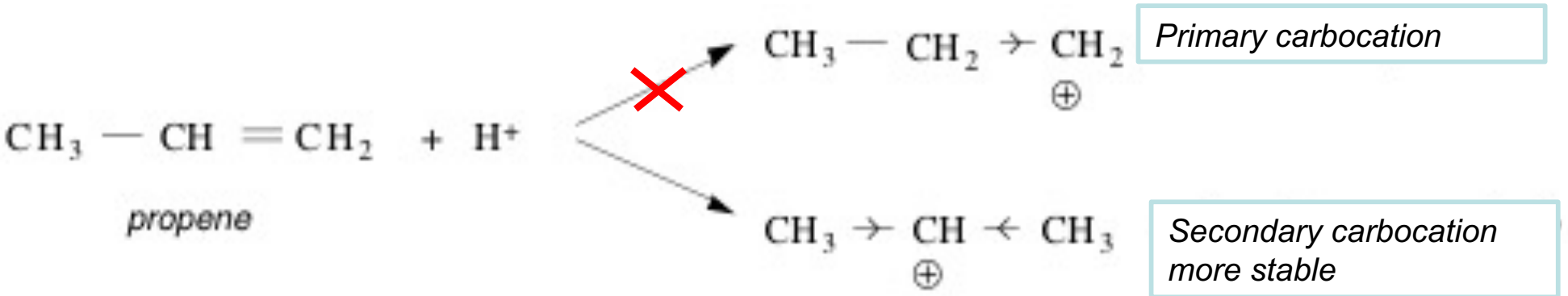


Electrophile addition reactions

- **halogen addition eg. Cl_2**
- **halogen acids addition eg. HCl**
- **water addition**

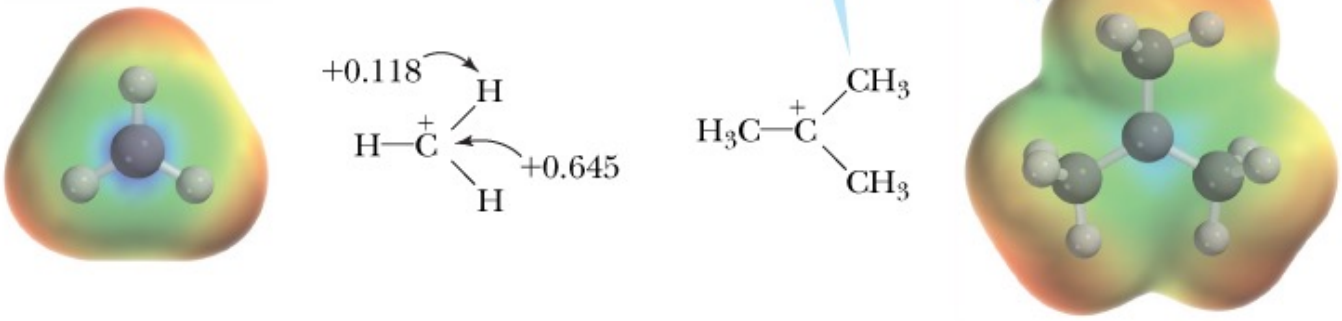


Regiospecificity of electrophilic addition



In addition to the C=C double carbon bond, the positive electrophile binds the C with the largest number of bound H atoms.

The methyl groups provide electron density to the carbocation compensating the positive charge



Inductive effect of alkylic groups

The alkyl group donates electrons, stabilizing the carbocation.

The carbocation stability is inversely proportional to the positive charge.

Modified from da Brown & Poon
Introduzione alla chimica organica

Aromatic hydrocarbons

1825: M. Faraday isolates benzene

1834: its formula is discovered C_6H_6

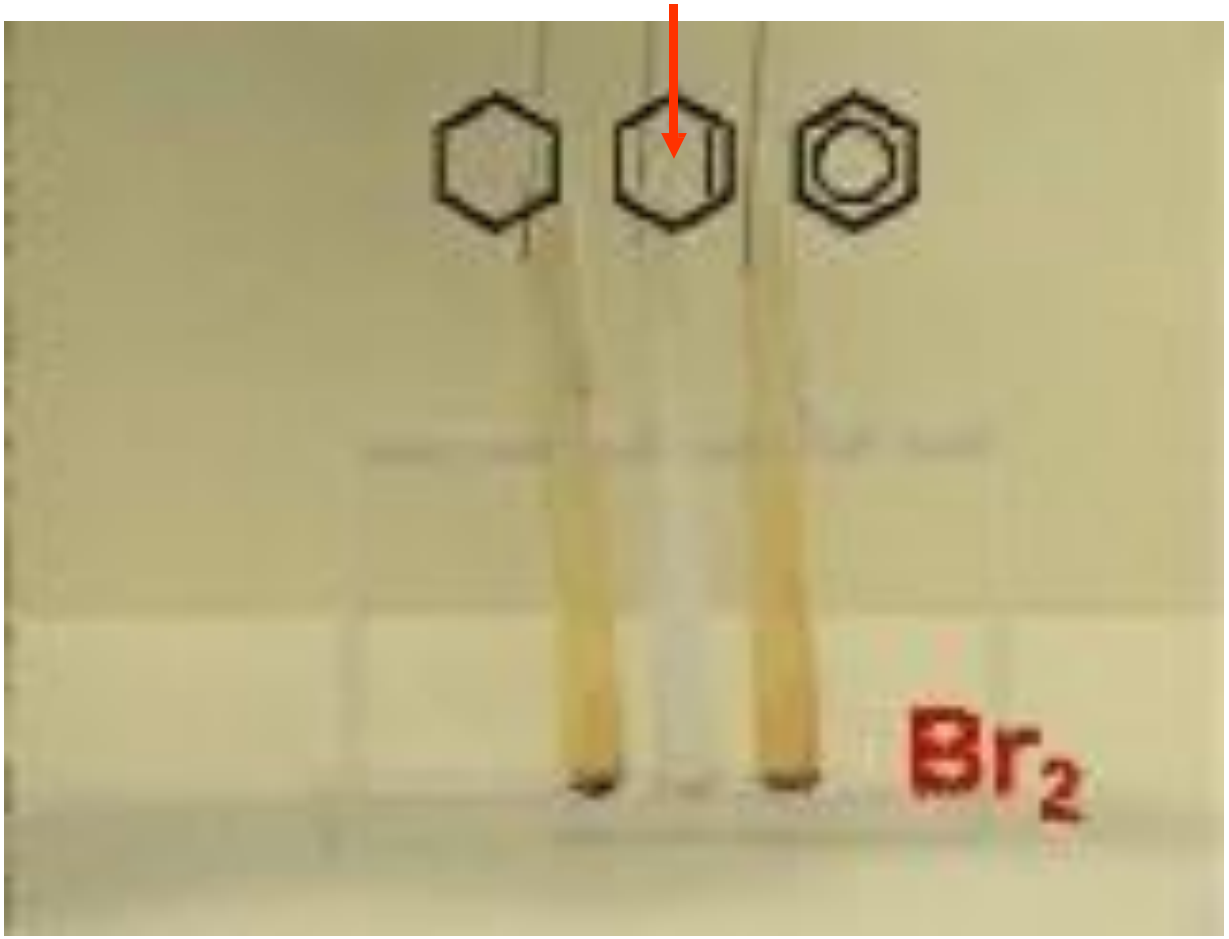
In spite of the probable high degree of insaturation (see alkenes) it is very stable.

Kekulè, Couper, Boutlerov: define a new class of compounds

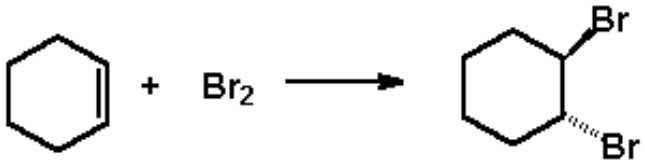
AROMATIC

- Low H/C ratio
-"Aromatic"
- Poor reactivity if compared to alkenes

This corresponds to a precise chemical nature.



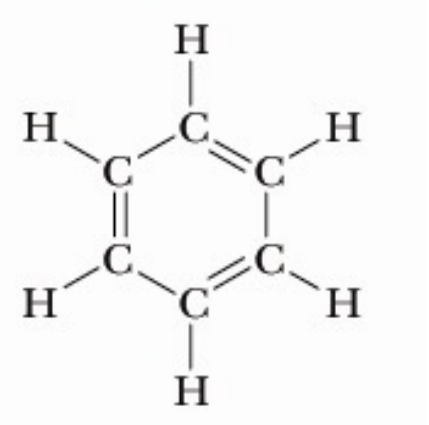
$C_6H_{10} + Br_2 \longrightarrow C_6H_{10}Br_2$

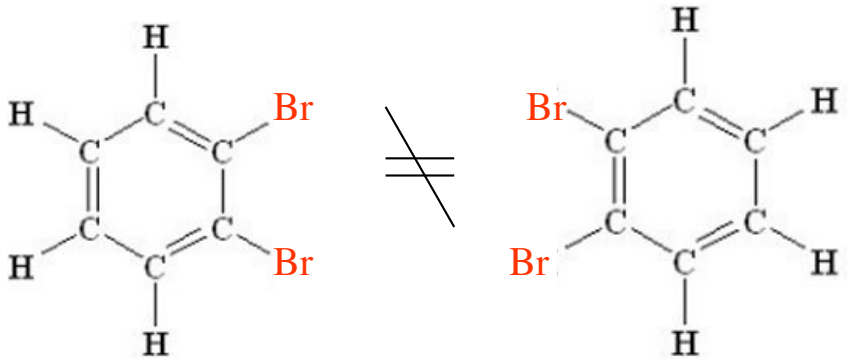


Cyclohexene (coloured) Colourless

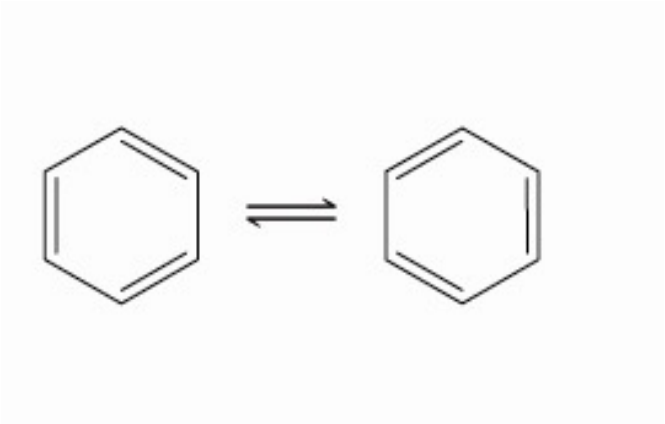
Cyclohexene reacts with bromine to give a colourless product but **cyclohexane and benzene do not**.

Kekulè structure of benzene:



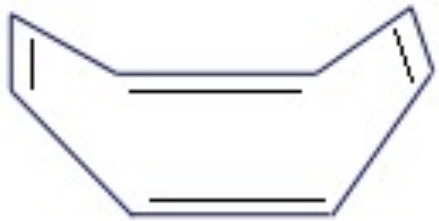


Only one
1-2 di-bromo benzene



Kekulè proposes an equilibrium.

Until 1900 the aromatic characted was ascribed to alternate double bonds.



cyclooctatetraene

R. Willstater synthesizes cyclo-octa-tetraene which is not aromatic.

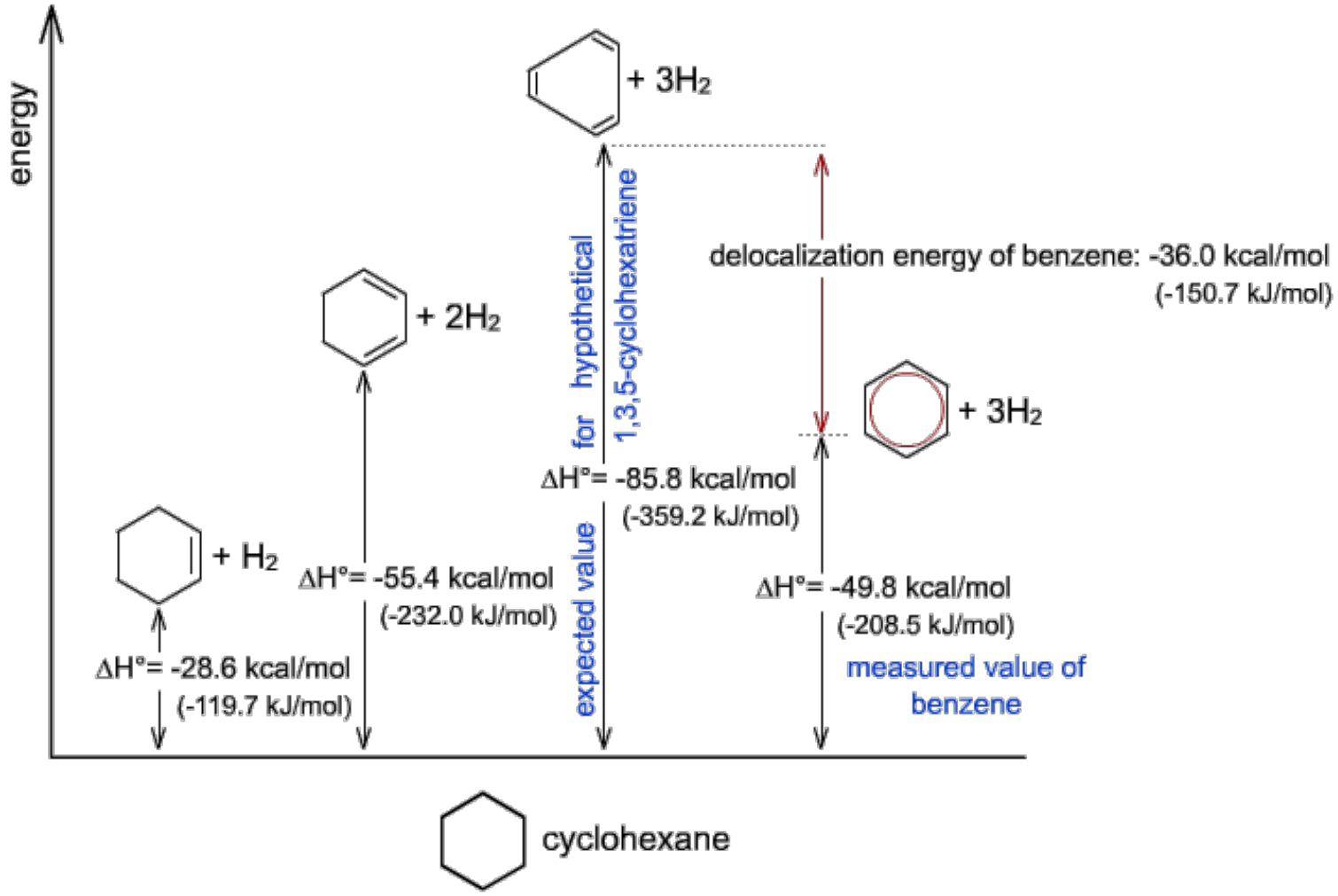
Condition for a compound to be aromatic: (4n+2) π electons

To be aromatic a compound must possess a cyclic "cloud" of 4n+2 delocalized π electrons (Hückel's rule).

Delocalization is not sufficient, but **a precise number (2, 6, 10, 14, etc.) of π electrons is required.**

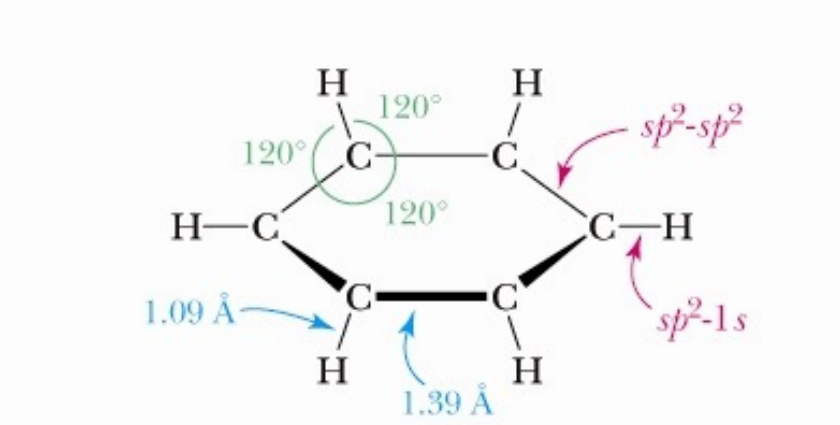
Therefore, cycol-octatetraene, having 8 π electrons can not be aromatic, as confirmed experimentally, C-C are short an long, whereas in aromatic compounds thay have the same length).

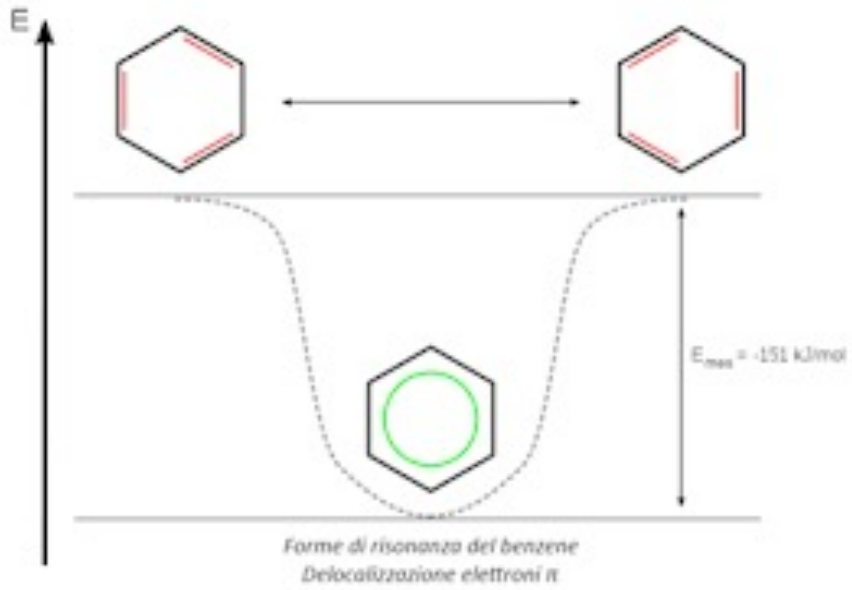
Aromatic energy

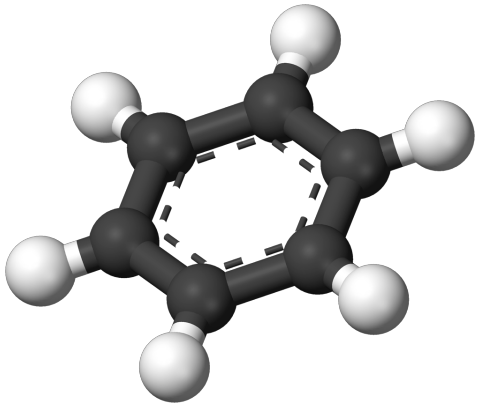


All C-C bonds in benzene are identical and they have a length and an energy intermediate between double and single bond (~1.39 Å).

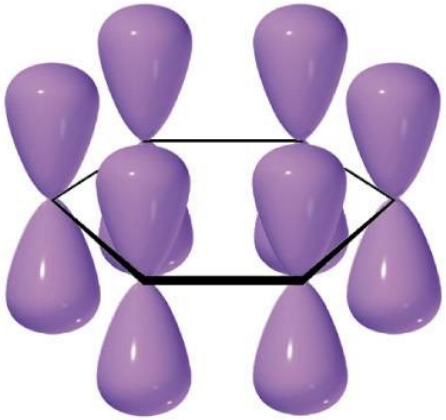
Therefore the structure is a resonance hybrid of two forma:





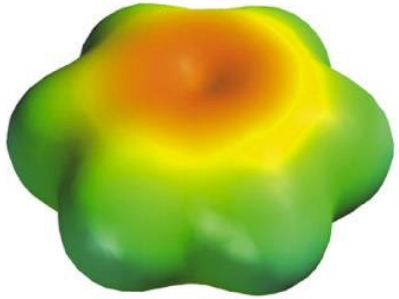


b.



c.

d.



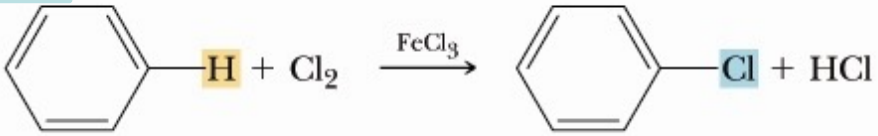
In benzene the six electron of the aromatic system are delocalized
Above and below the plane of the ring.
(aromatic sextet)

Ractions of benzene

Benzene does not yield addition reaction products but rather substitution ones, since the loss of the sextet would yield a product with energy higher than the reactant one.

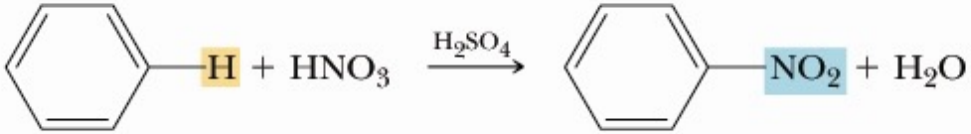
The electrophil substitues an hydrogen that leaves the ring

Halogenation



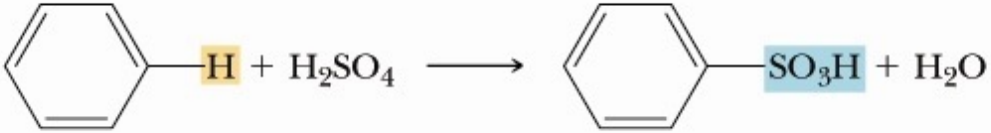
Chlorobenzene

Nitration



Nitrobenzene

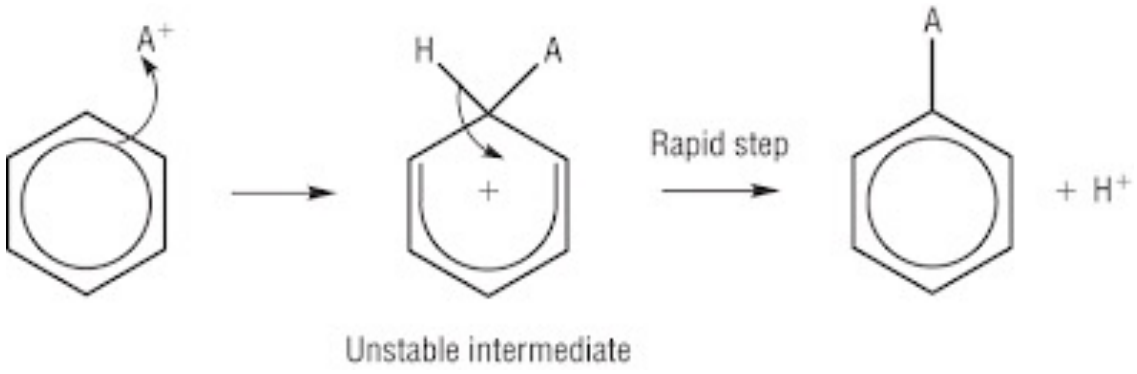
sulphonation



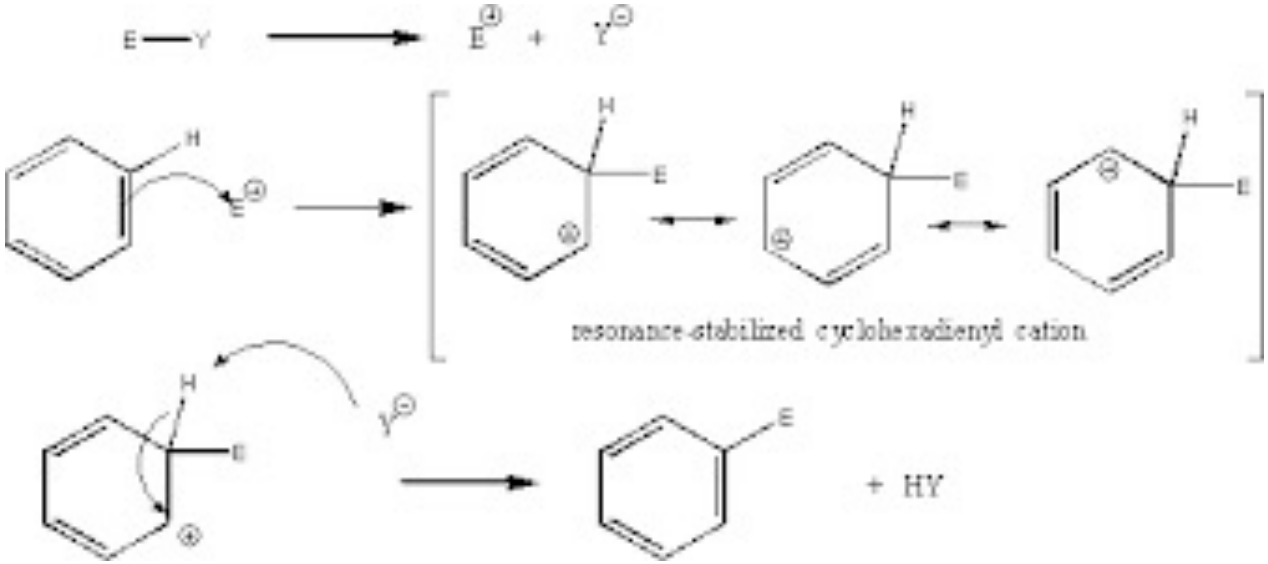
Benzensulphonic acid

Modified fromBrown & Poon
Introduzione alla chimica organica

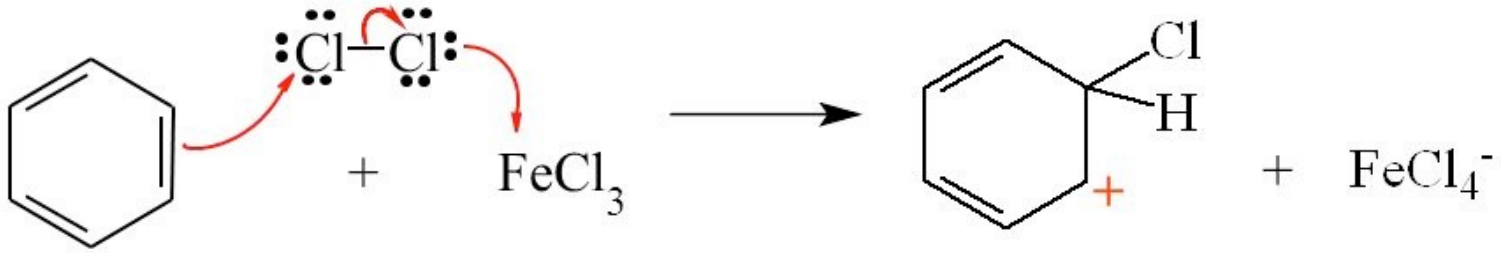
Benzene Substitution Reactions.

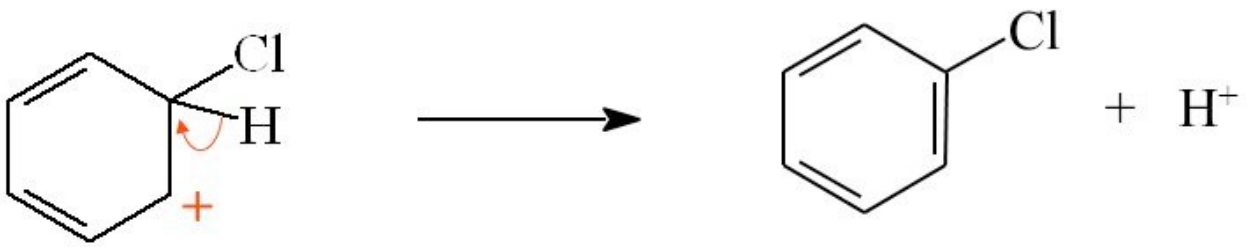


The electrophile E^+ attacks the ring
The carbocation is stabilized by resonance
The proton reacts with a base



Benzene Substitution Reactions.





$$FeCl_4^- + H^+ \longrightarrow FeCl_3 + HCl$$

Effect of substituents

The groups linked to the benzene ring influence their reactivity. They can be classified as activating and deactivating.

The activators make the derivative more reactive than benzene: they are able to "supply" electrons tothe ring (electron donors).

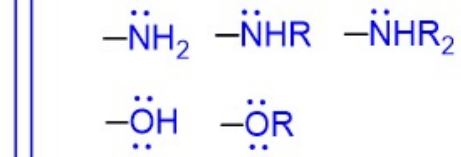
The deactivating compounds make the compound less reactive than benzene: they deplete the ring (electron attracters) of electrons.

The terms "more reactive" or "less reactive" are always referred to benzene, with respect to electrophilic replacement reactions.

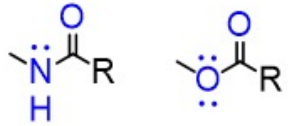
Ortho-, Para- and Meta- Directors

Activators

Strongly activating



Moderately activating



R- Alkyl groups

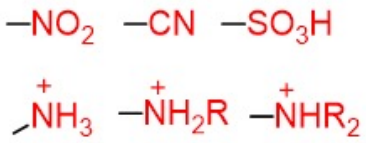
Deactivators

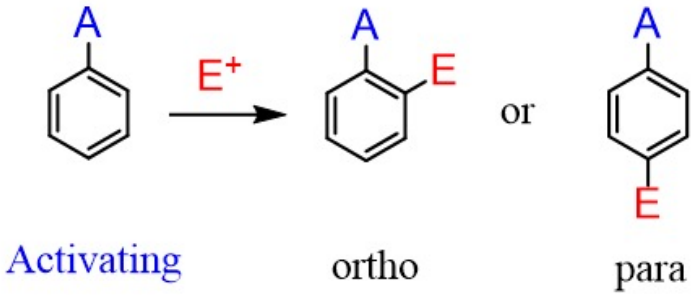
Deactivating

–F, Cl, Br, I

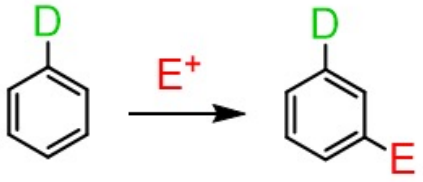
Strongly Deactivating

R = H, OH, Cl, OR



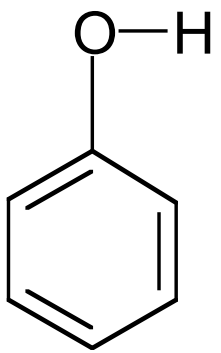


Activating ortho para

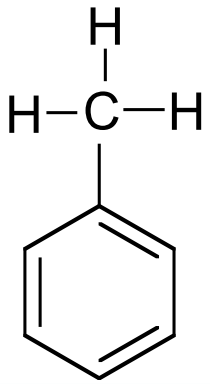


Deactivating meta

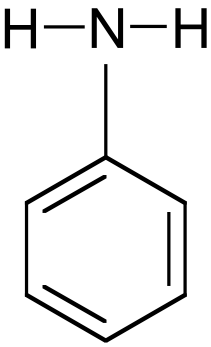
Some derivatives of benzene



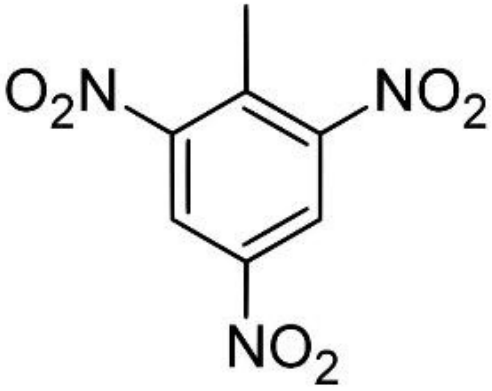
Phenol



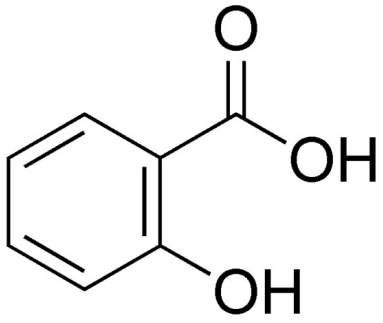
Toluene
(methylbenzene)



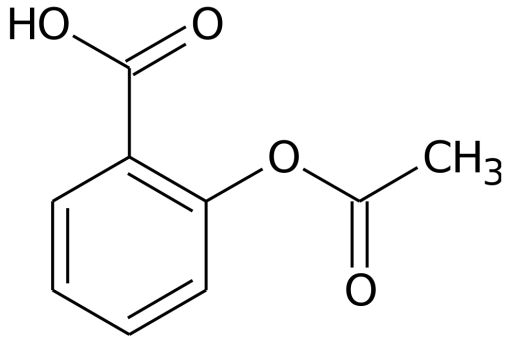
Aniline
(amminobenzene)



TNT
Tri-nitro-toluene



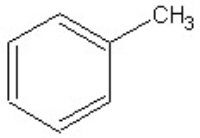
Salicylic acid



Acetylsalicylic acid
(aspirin)

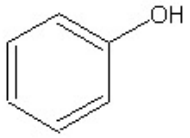
Nomenclature
Common definitions & IUPAC

methyl-benzene



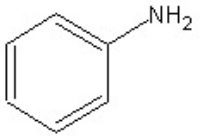
toluene

hydroxy-benzene

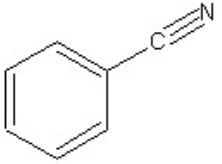


phenol

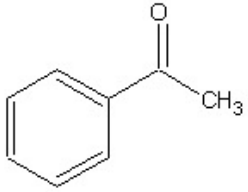
amino-benzene



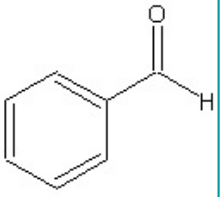
aniline



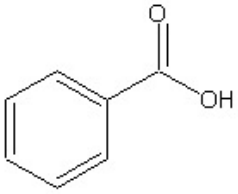
benzonitrile



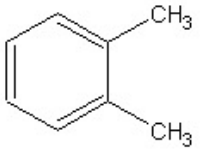
acetophenone



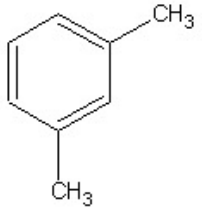
benzaldehyde



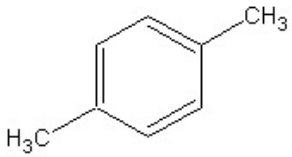
benzoic acid



o-xylene

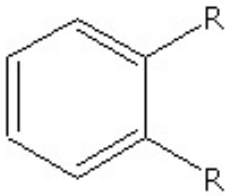


m-xylene

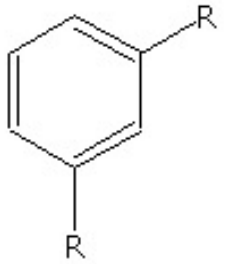


p-xylene

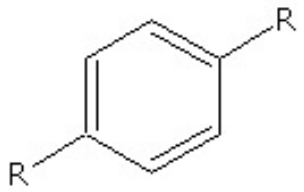
Di-substituted benzene derivatives



ortho

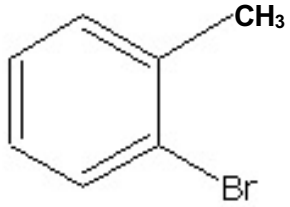


meta

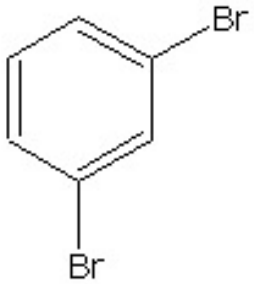


para

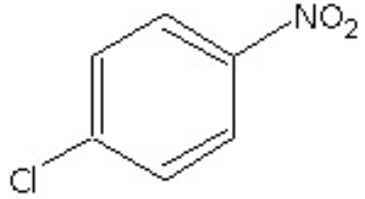
Examples:



ortho-bromotoluene

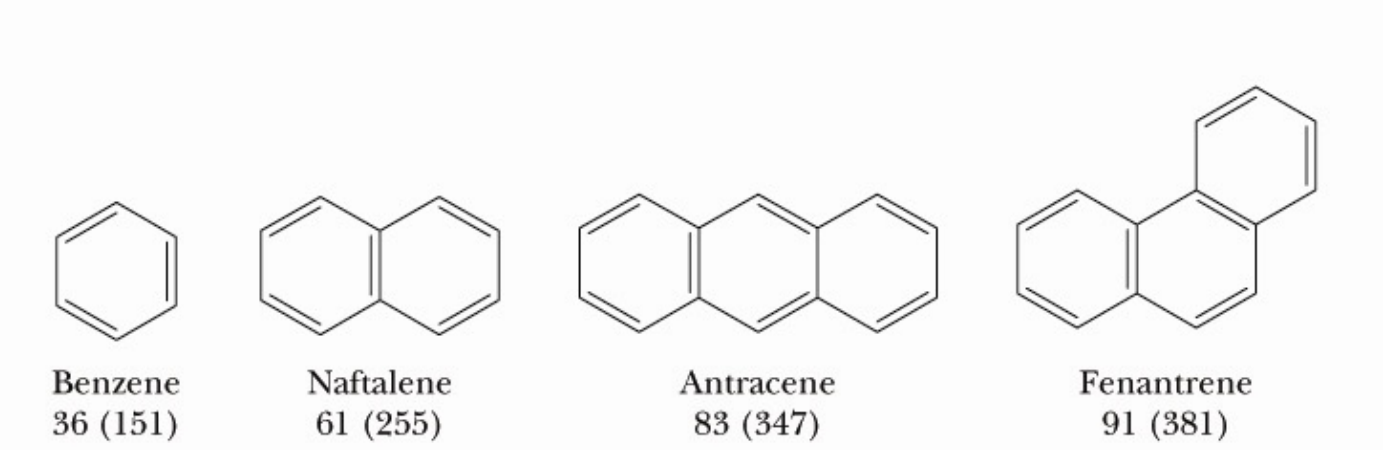


meta-dibromobenzene



para-chloronitrobenzene

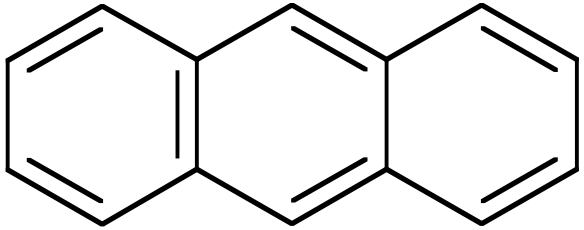
Benzene derivatives (condensed rings).



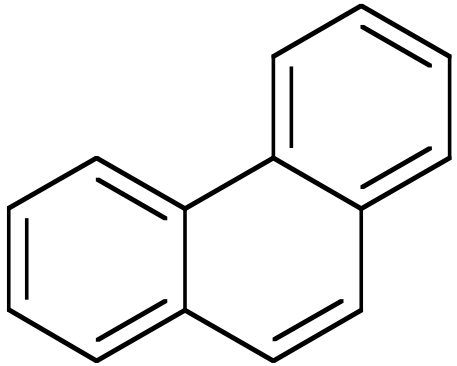
They have a planar structure and have electronic delocalization on the whole molecule.
They are produced by the combustion of oils, fuels, coal, tobacco and organic materials.
They are agents intercalating on DNA and may have mutagenic effects.

ARENES

Polycyclic derivatives of benzene



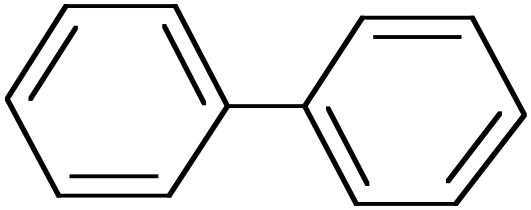
antracene



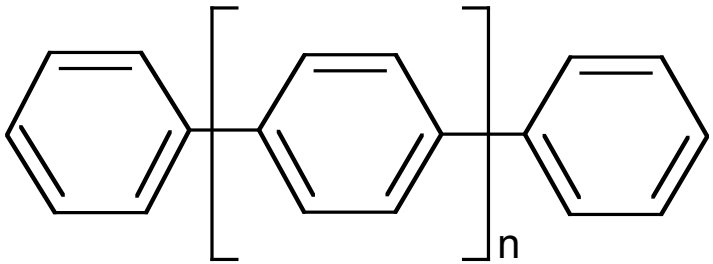
fenantrene

Rings are

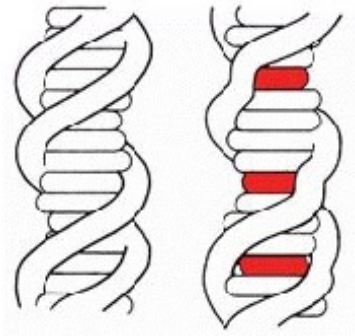
- ***condensed*** when the share C atoms
- ***linked*** when they are joind by one C atom



biphenyl

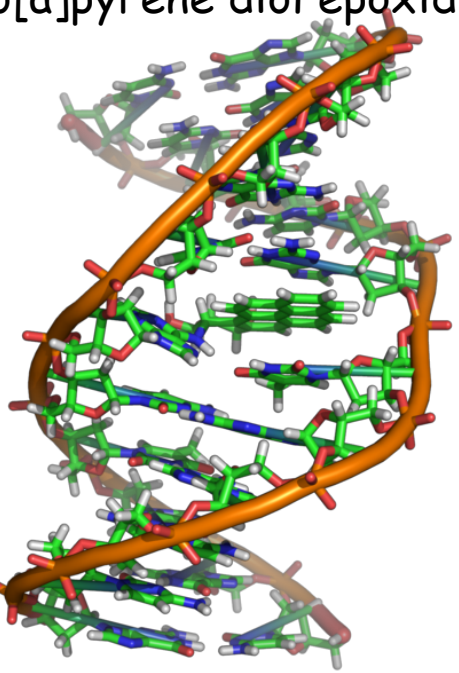


polyphenyl

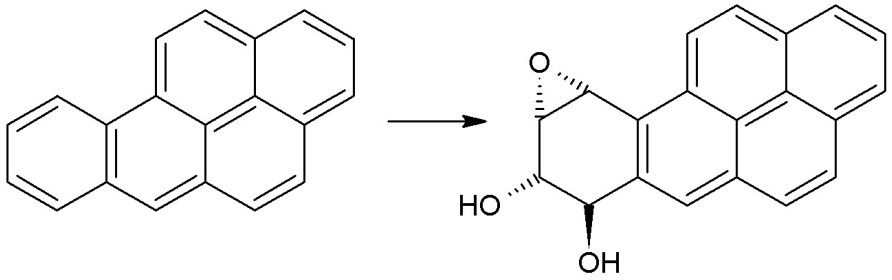


Benzopyrene carcinogenicity

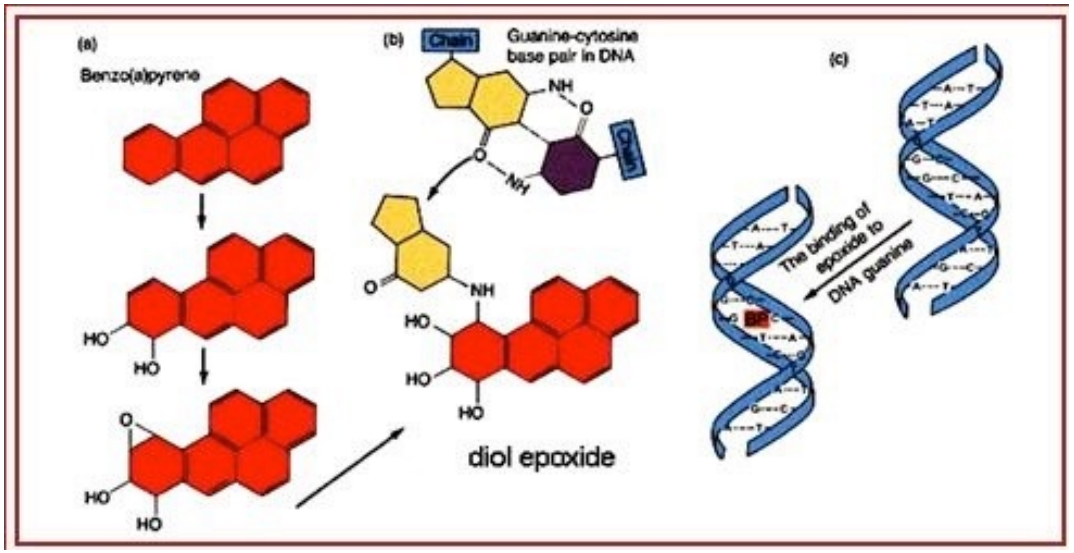
Properly speaking, benzo[a]pyrene is a procarcinogen, meaning that the mechanism of carcinogensis of benzo[a]pyrene depends on its enzymatic metabolism to the ultimate mutagen, benzo[a]pyrene diol epoxide.



This molecule intercalates in DNA covalently bonding to the nucleotide guanine, this binding distorts the DNA, inducing mutations by perturbing the double-helical structure. This disrupts the normal process of copying DNA and induces mutations, which explains the occurrence of cancer.



Benzopirene oxidation



Heterocyclic aromatic compounds

Cyclic molecules in which the Hückel rule is respected,
where in the ring there are one or more atoms different from carbon

.

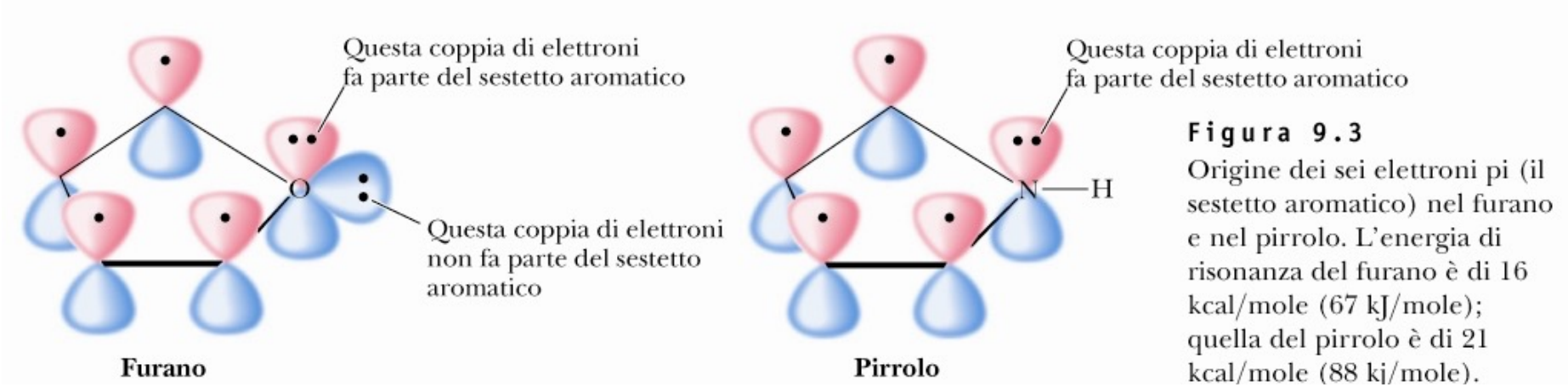
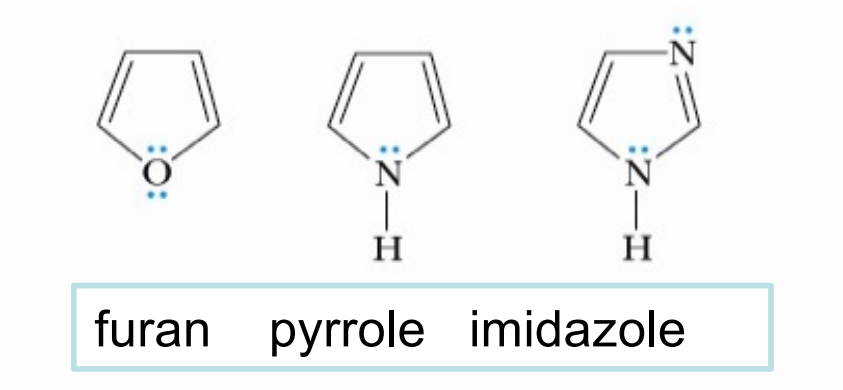
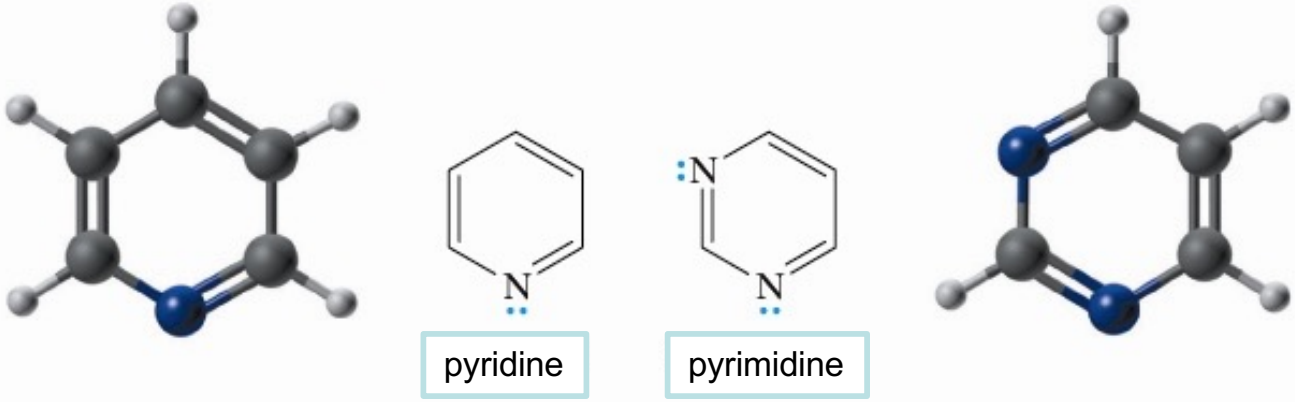


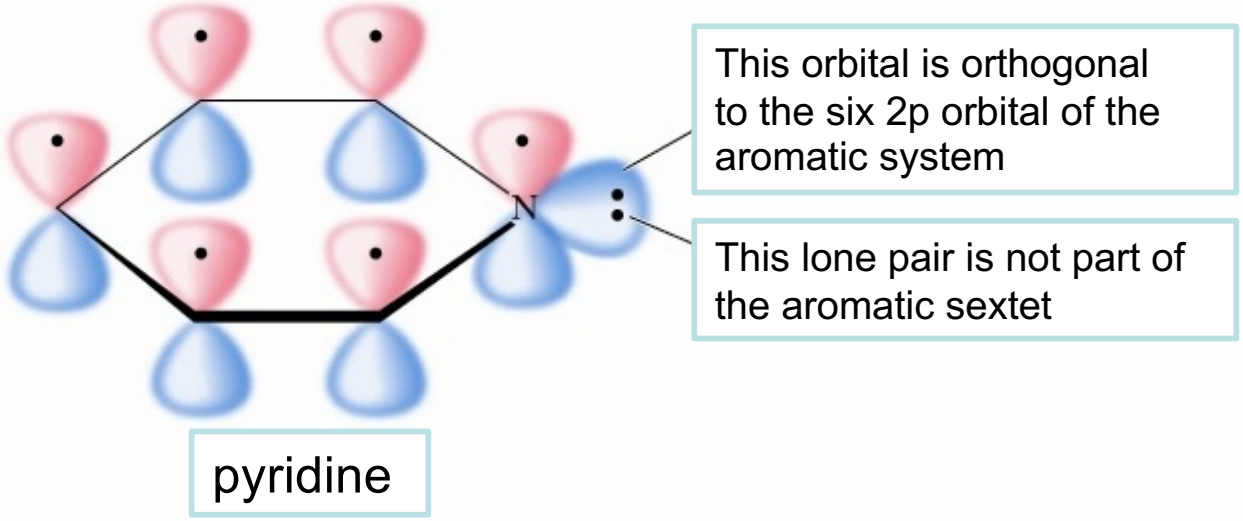
Figura 9.3
Origine dei sei elettroni pi (il sestetto aromatico) nel furano e nel pirrolo. L'energia di risonanza del furano è di 16 kcal/mole (67 kJ/mole); quella del pirrolo è di 21 kcal/mole (88 kj/mole).



If a lone pair is not part of the aromatic sextet the compound has basic properties.

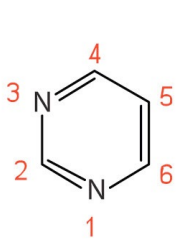
Derivatives of pyrimidine are among the aromatic nitrogenous bases that present in nucleic acids.



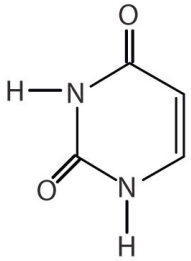


p

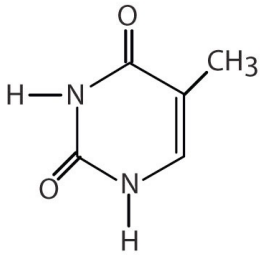
The aromatic nitrogenous bases of nucleic acids.



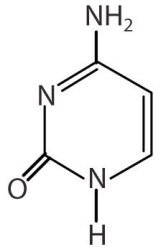
Pyrimidine



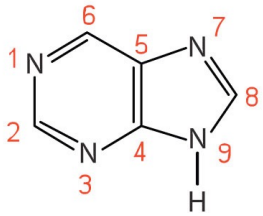
Uracil (U)
RNA only



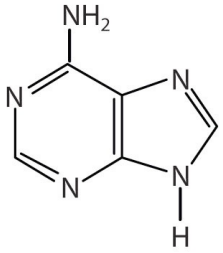
Thymine (T)
DNA only



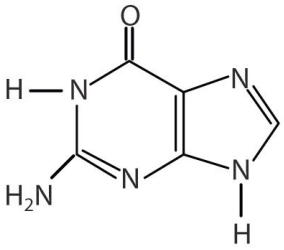
Cytosine (C)
both DNA and RNA



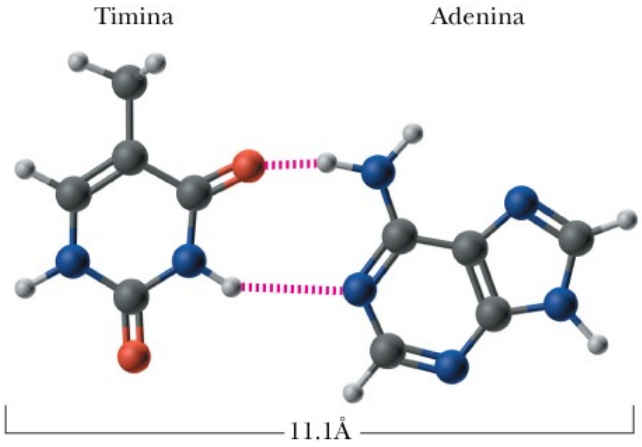
Purine



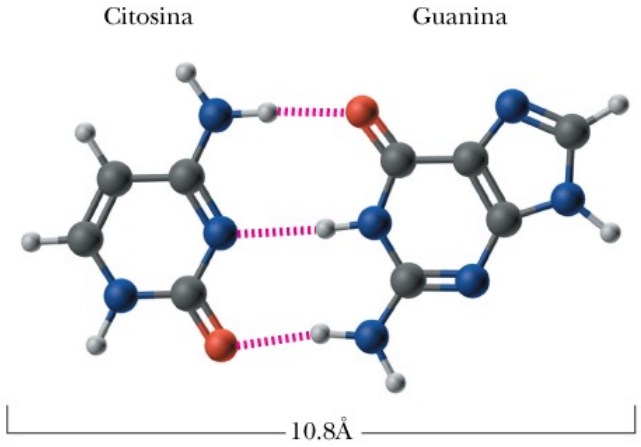
Adenine (A)



Guanine (G)

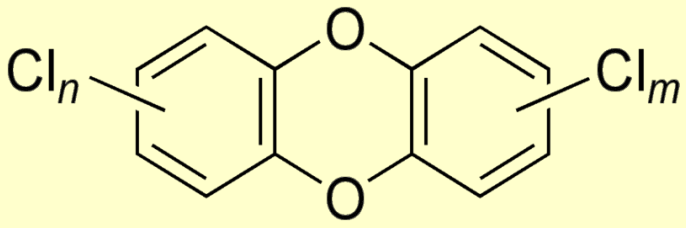


2 H-bonds



3 H-bonds

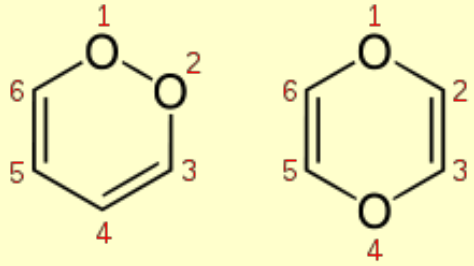
The specific pairing among the bases and the complementarity of form between purines and pyrimidines allow DNA to duplicate.



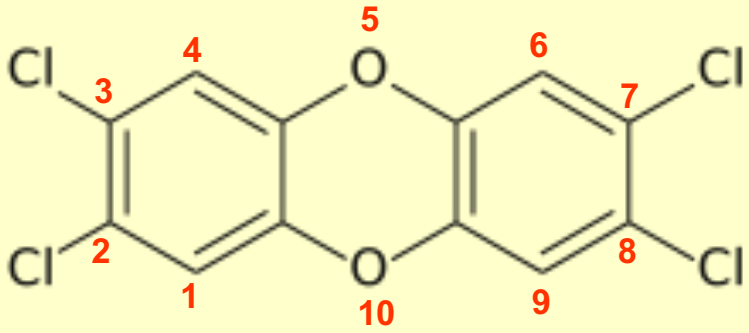
Polychlorinated dibenzodioxins

Dioxines
~200 stable compounds

toxic, when halogenated…



1,4-dioxin

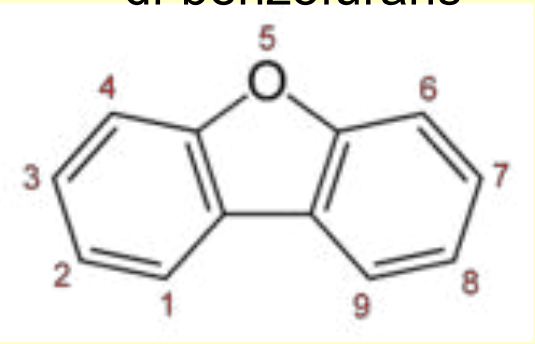


2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCCD)

barely soluble in H_2O – highly in fat (x $10^{6)}$

TCDD (in man) half life 5 – 11 years DL50 0.5 μg / Kg

di-benzofurans

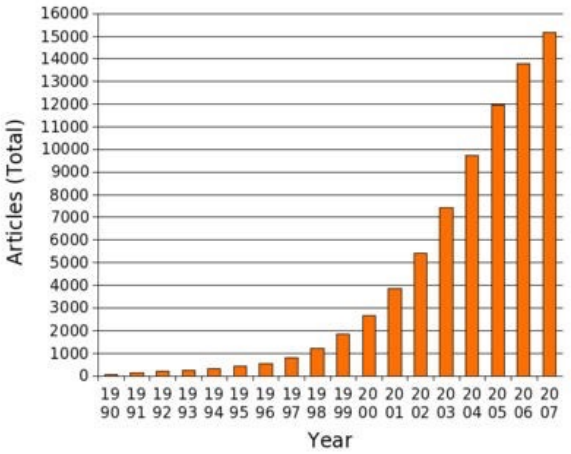


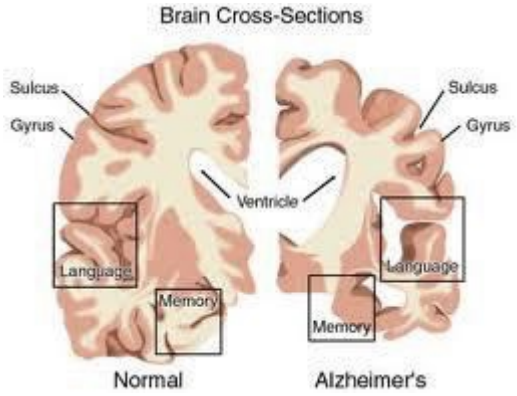
Healthy too…!!

Hypericin & Alzheimer d.

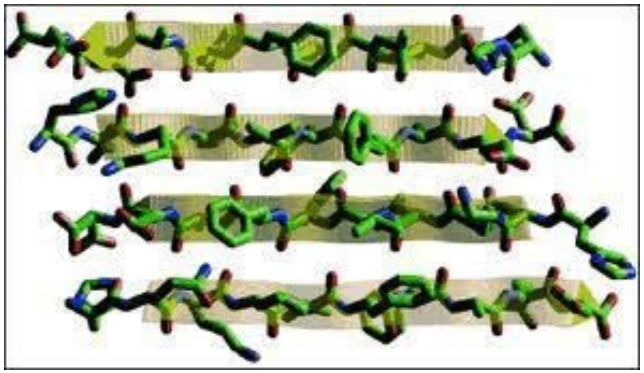
Paolo Sarti 2011
Department of Biochemistry
Sapienza

It perturbs β-amiloid polimerization processes
Read more: http://www.solaris.it/indexprima.asp?Articolo=1798#ixzz0Zgn7WMC9

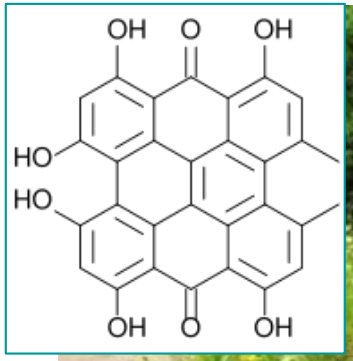


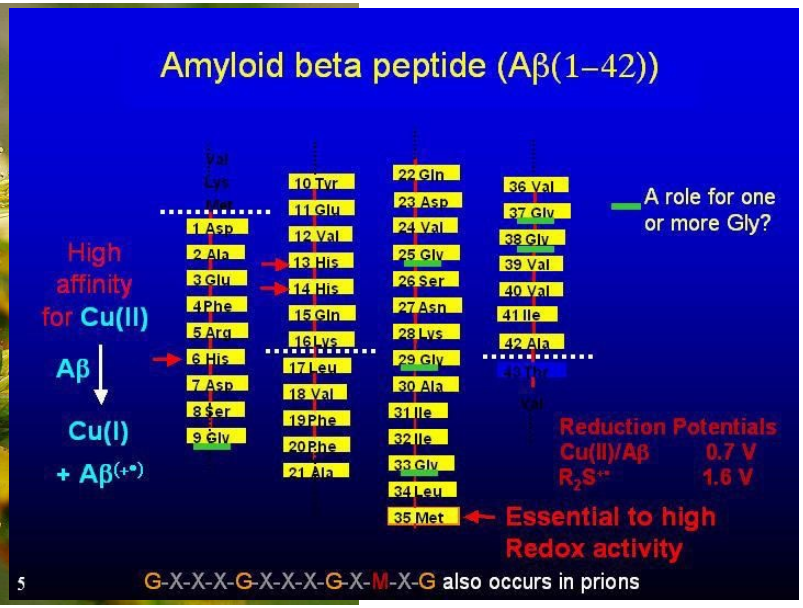


β-amiloid



hypericin





Ipericum (flower of S. Giovanni, *June 24th*)