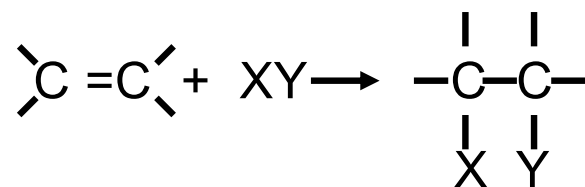


Organic Chemistry Reactions

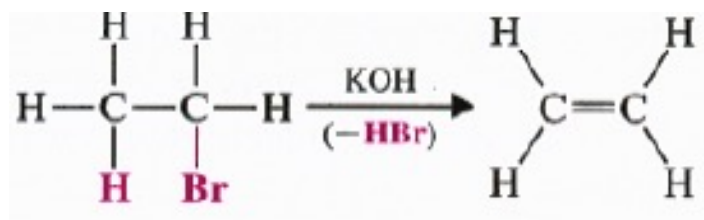
1. Substitution



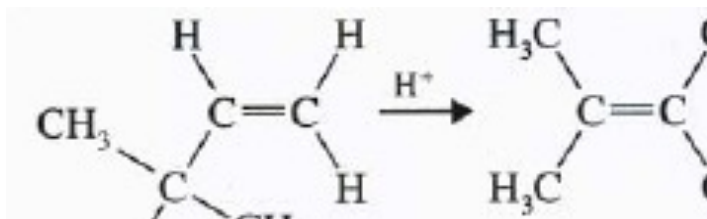
2. Addition



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:

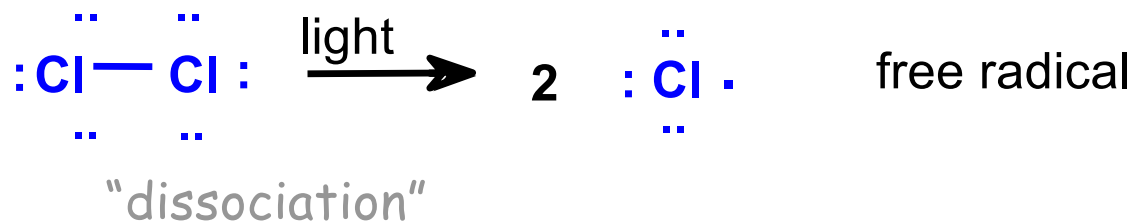
OH^- (Arrhenius bases)

H_2O , NH_3 (Broensted bases)

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

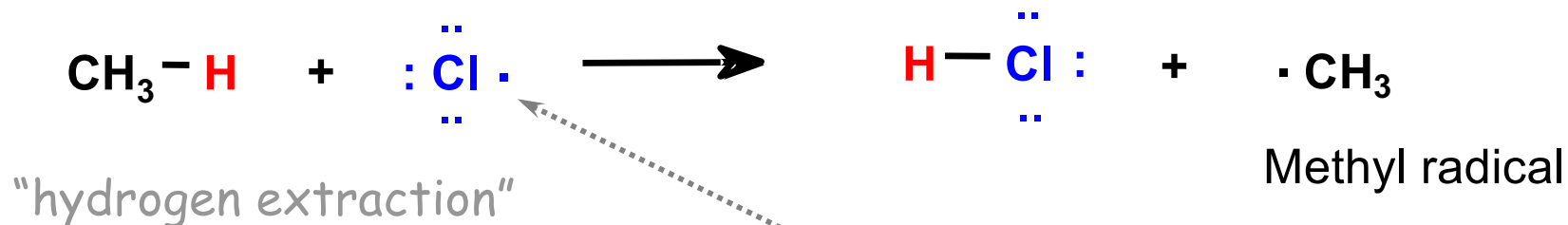
Alkanes halogenation

1. Initiation

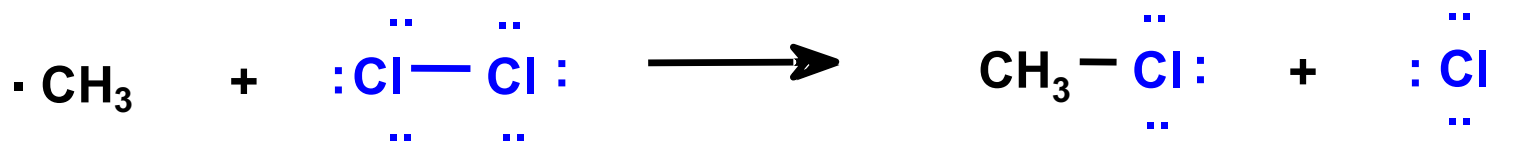


CHAIN REACTION

2. Chain propagation



3. Chain propagation



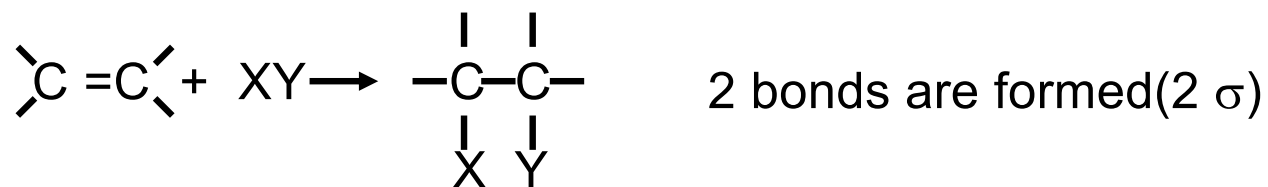
Into step 2

3

P
A
S
S
I
R
I
P
E
T
U
T
I

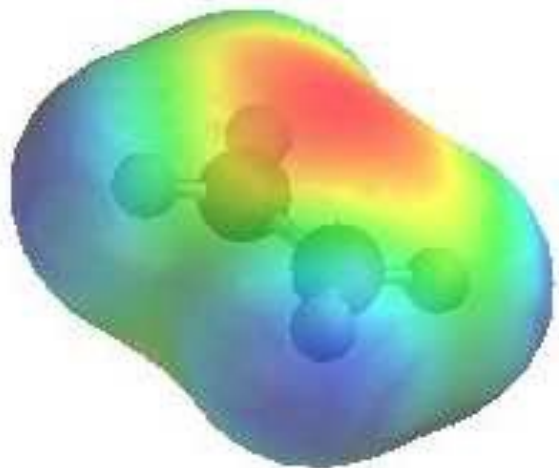
ALKENES: electrophile addition

Π electrons are less tightly bound than σ ones: they are more available for electrophilic 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.

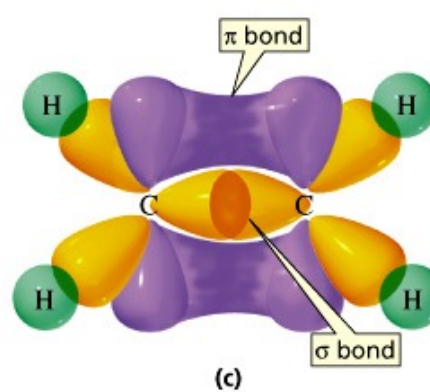
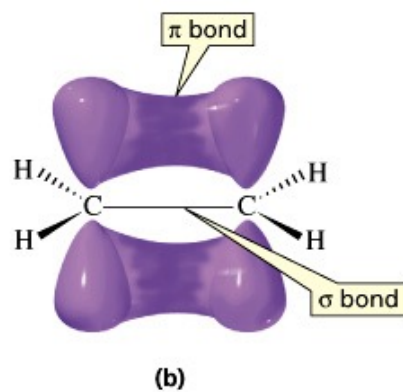
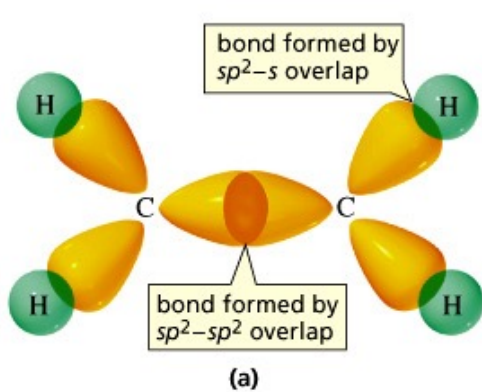


2 bonds are broken (1 σ , 1 π)

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 (hydration)

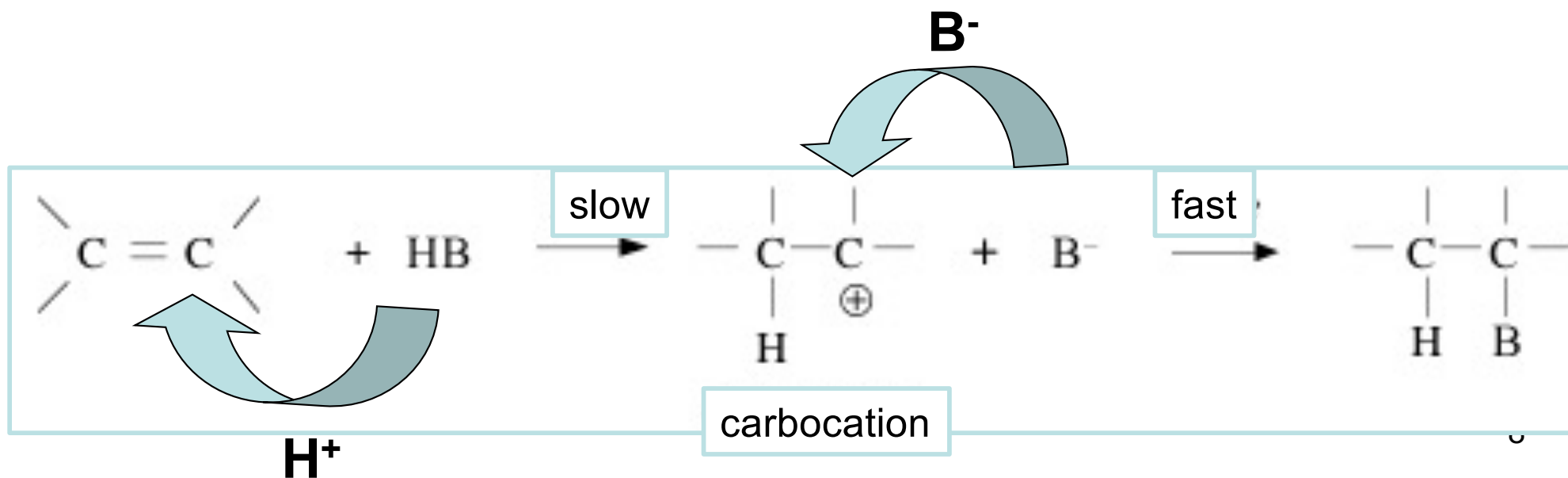
Frequent in biochemistry.

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

In an acidic environment, alcohols are formed.

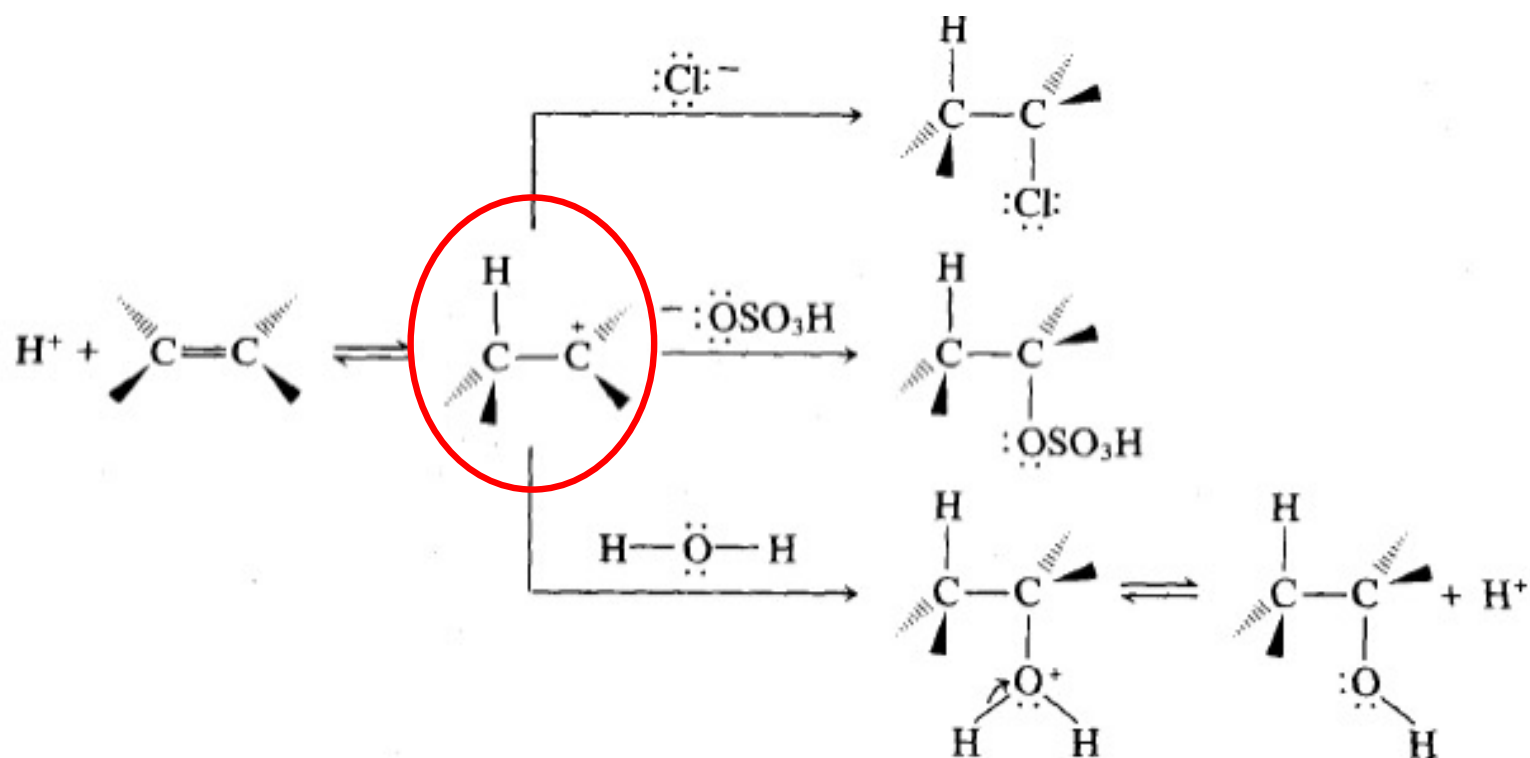
The reaction involves **2 steps**, via a **carbocation intermediate** (C with a positive charge).

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 electrophile favouring the *carbocation* formation. In the **2nd step** it binds the "negative" component, or more in general, a basic component.

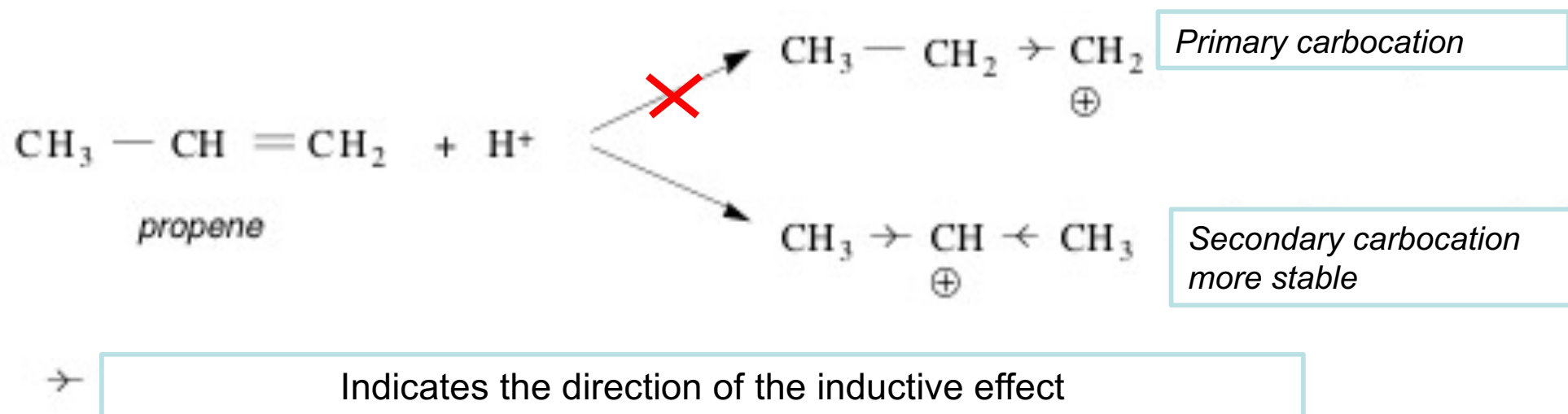


Electrophile addition reactions

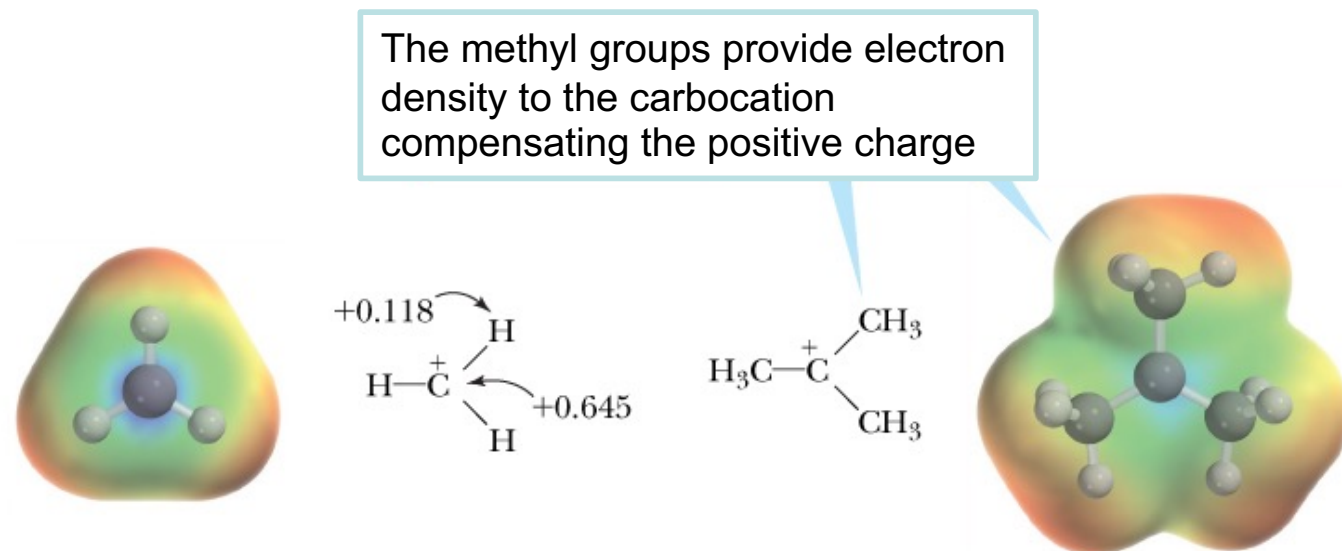
- halogen addition eg. Cl_2
- halogen acids addition eg. HCl
- water addition



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.



Inductive effect of alkylic groups

The alkyl group donates electrons, stabilizing the carbocation.

The carbocation stability is inversely proportional to the positive charge.

Aromatic hydrocarbons

1825: M. Faraday isolates benzene

1834: its formula is discovered C_6H_6

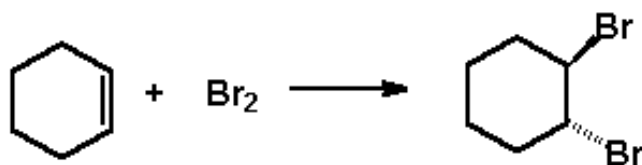
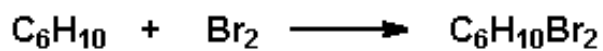
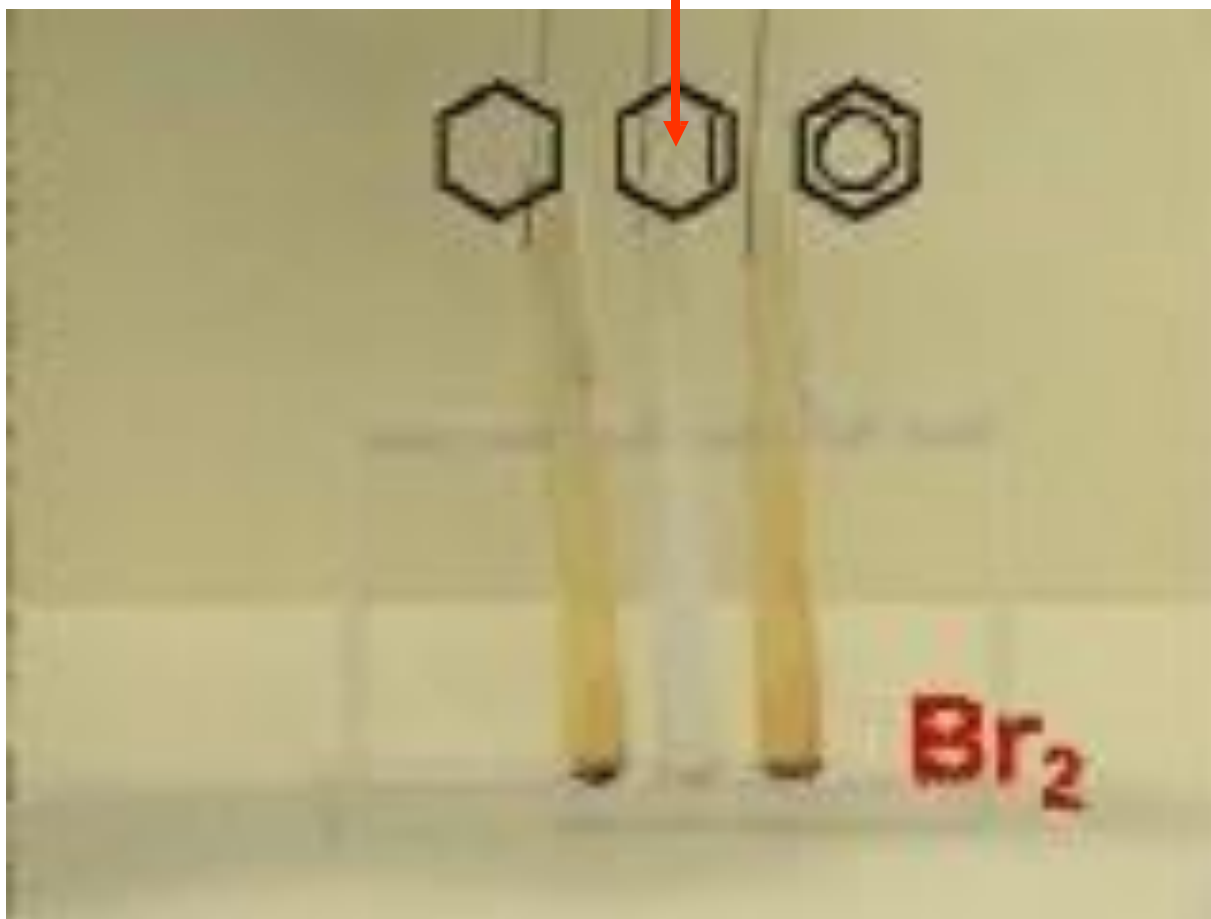
In spite of the probable high degree of insaturation (see alkenes) it is very stable.

Kekulé, 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.

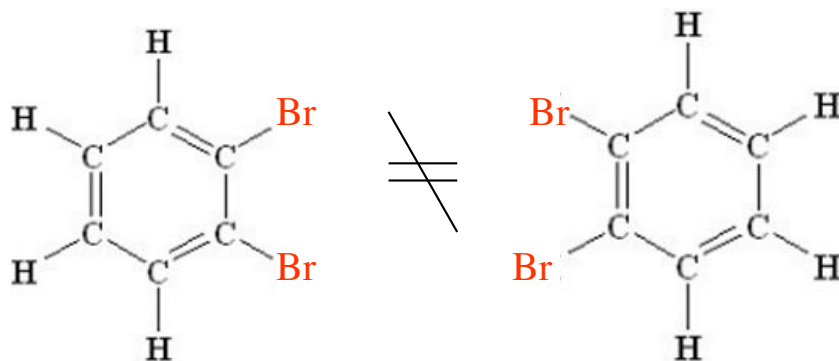
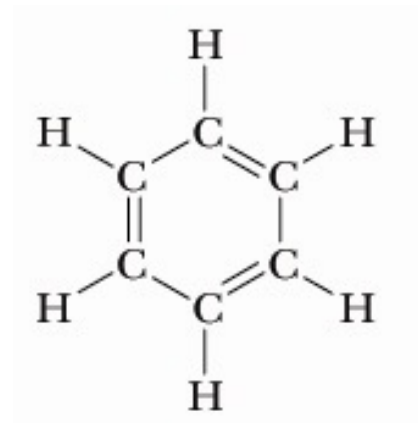


Cyclohexene (coloured)

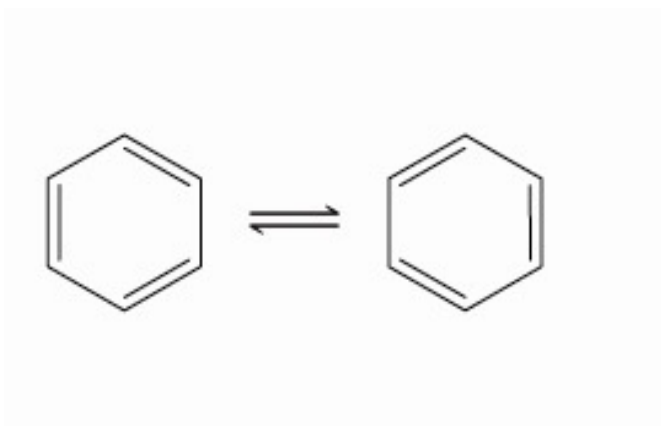
Colourless

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

Kekulé structure of benzene:



Only one
1-2 di-bromo benzene



Kekulé proposes an equilibrium.

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



cyclooctatetraene

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

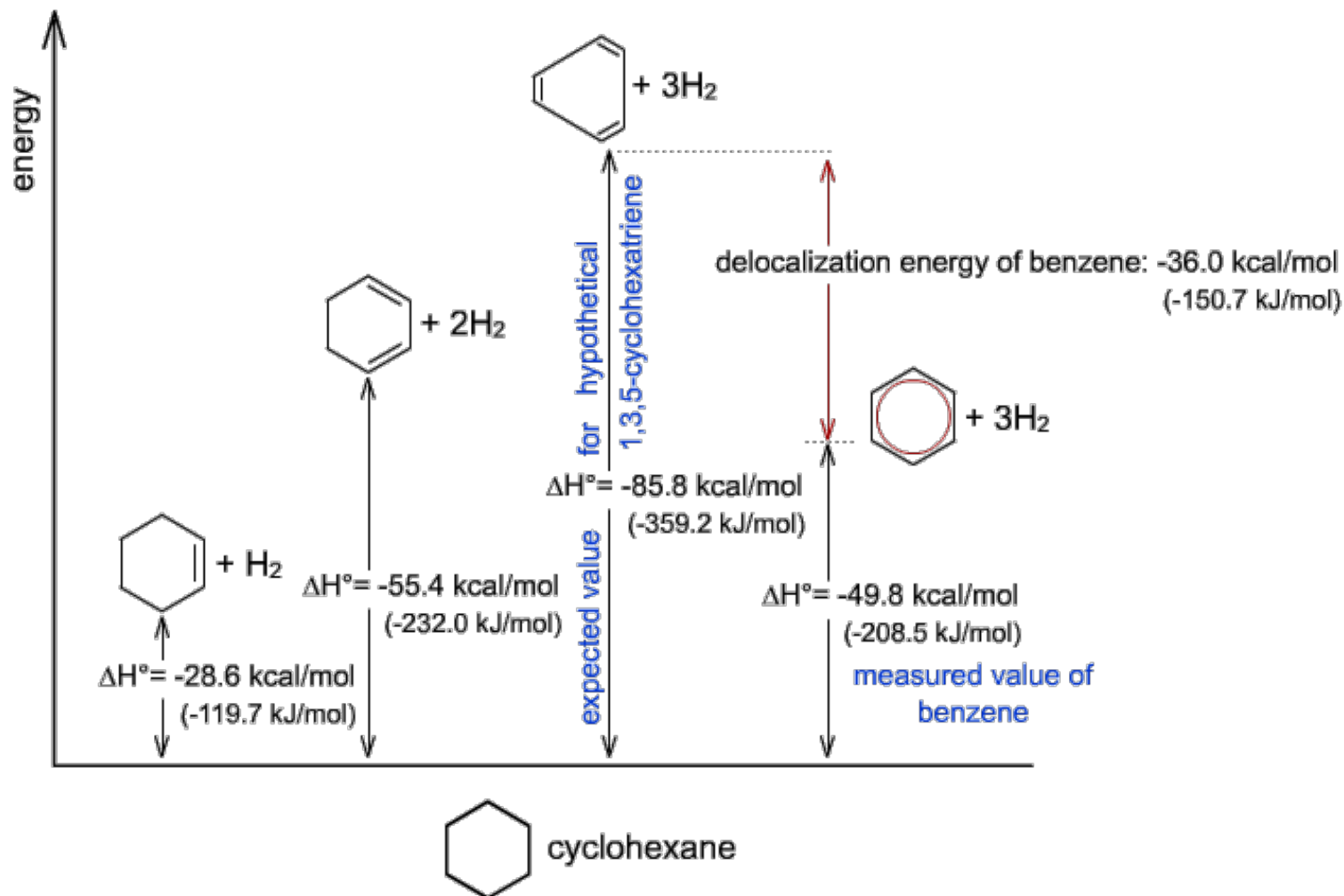
Condition for a compound to be aromatic: $(4n+2)$ π electrons

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.

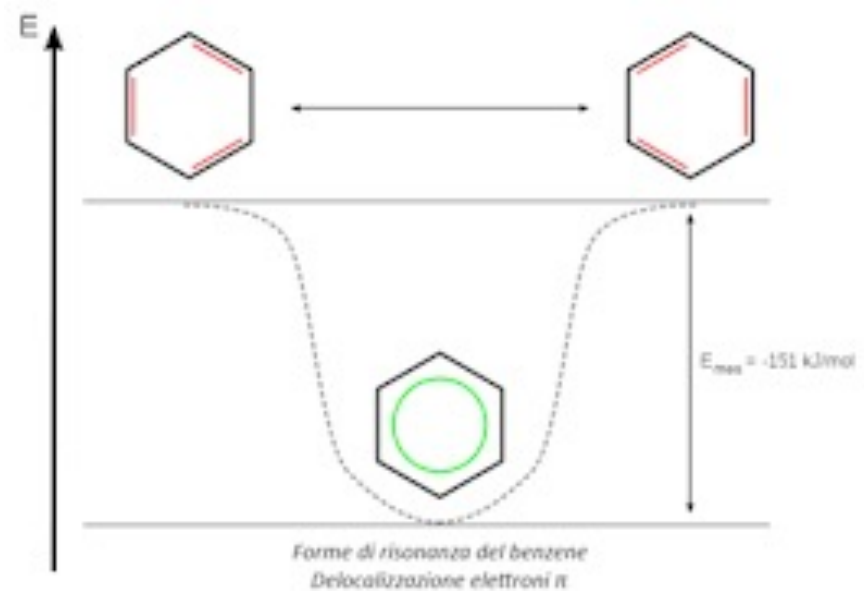
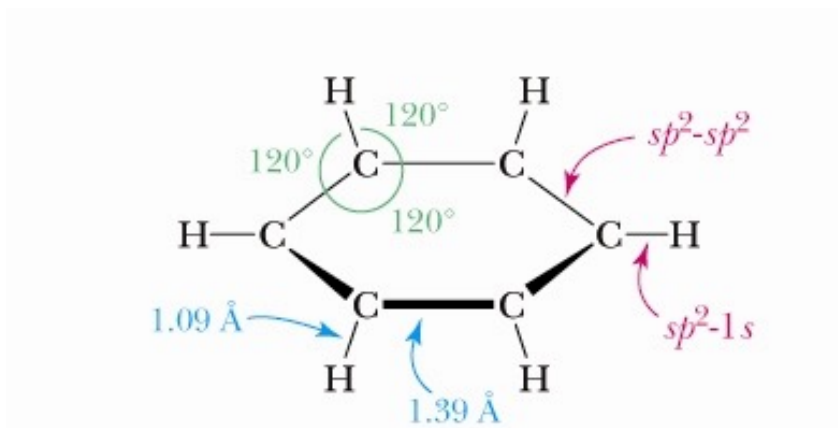
Therefore, cyclo-octatetraene, having 8 π electrons can not be aromatic, as confirmed experimentally, C-C are short and long, whereas in aromatic compounds they have the same length).

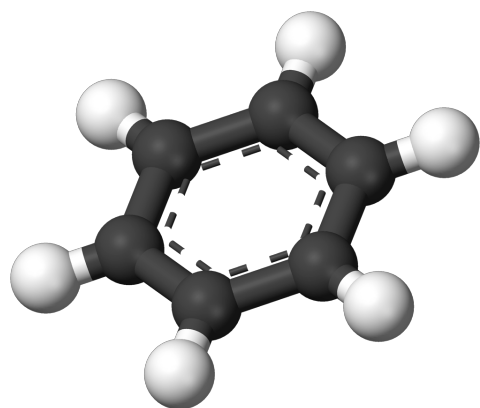
Aromatic energy



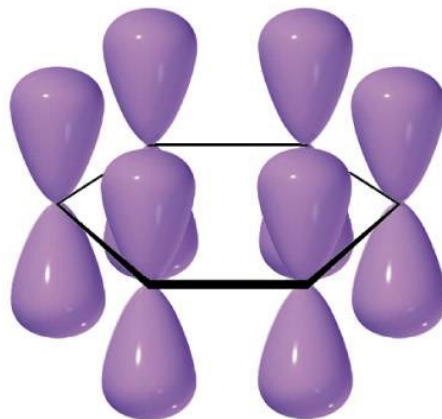
All C-C bonds in benzene are identical and they have a length and an energy intermediate between double and single bond ($\sim 1.39 \text{ \AA}$).

Therefore the structure is a resonance hybrid of two forma:





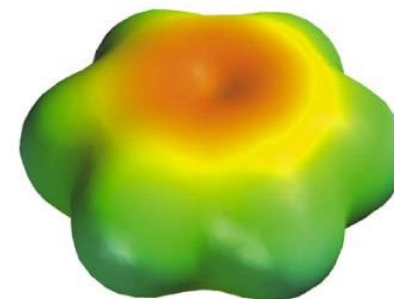
b.



c.



d.

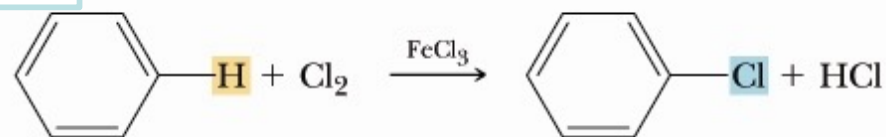


In benzene the six electron of the aromatic system are delocalized
Above and below the plane of the ring.
(aromatic sextet)

Reactions of benzene

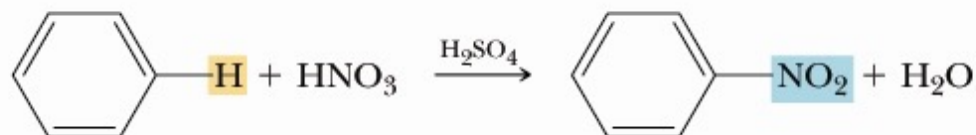
Benzene does not yield addition reaction products but rather **substitution** ones, since the loss of the sextet would yield a product with energy higher than the reactant one.

Halogenation



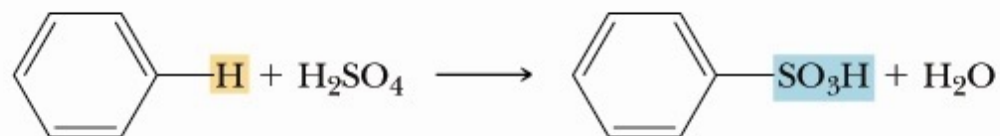
Chlorobenzene

Nitration



Nitrobenzene

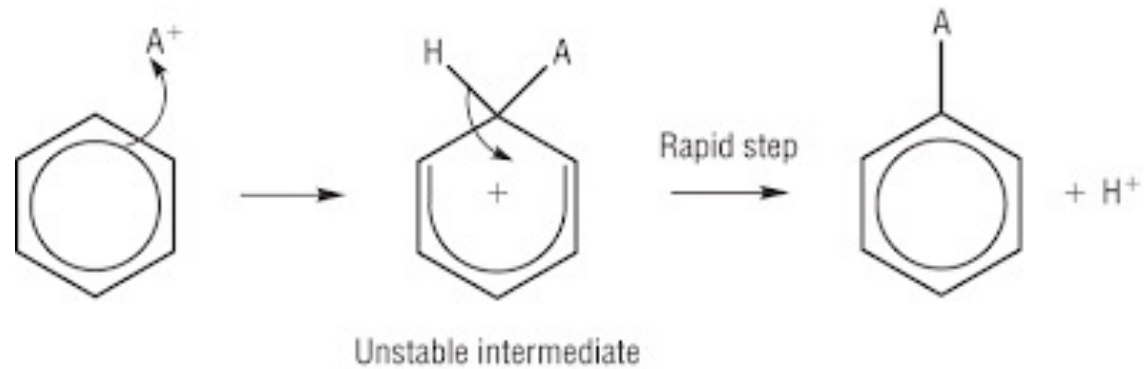
sulphonation



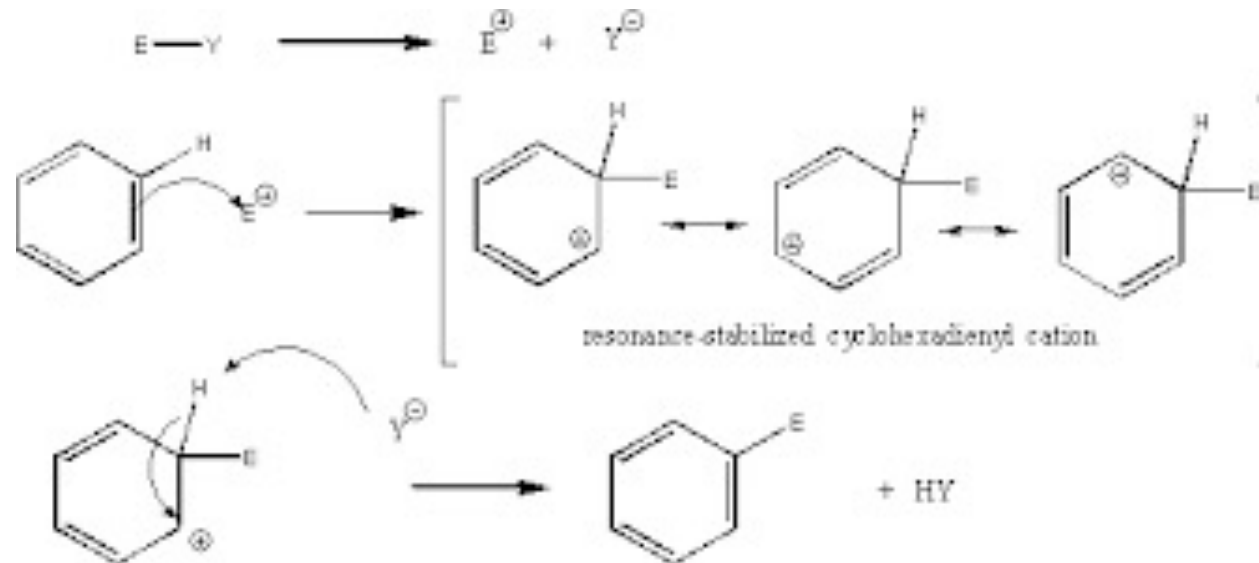
Benzenesulphonic acid

The electrophil substitutes an hydrogen that leaves the ring

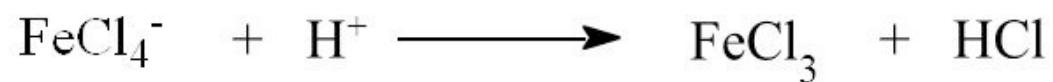
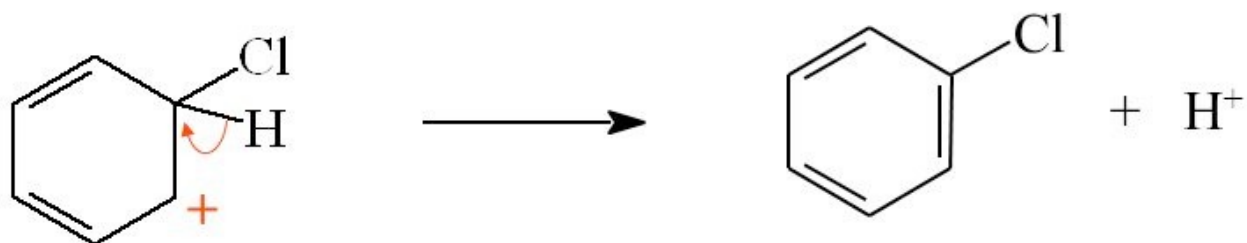
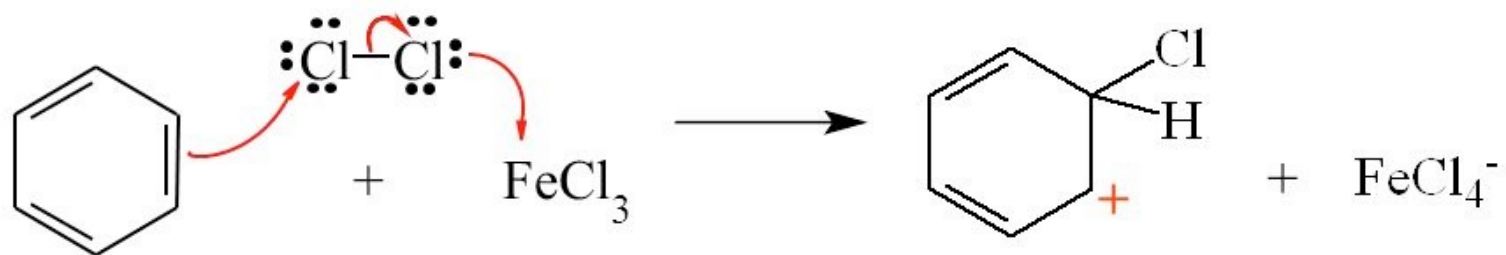
Benzene Substitution Reactions.



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



Benzene Substitution Reactions.



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 to the ring (electron donors).

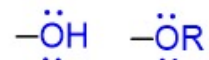
The deactivating compounds make the compound less reactive than benzene: they deplete the ring (electron attracters) of electrons.

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

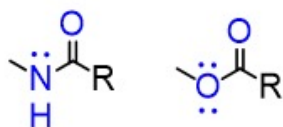
Ortho-, Para- and Meta- Directors

Activators

Strongly activating



Moderately activating



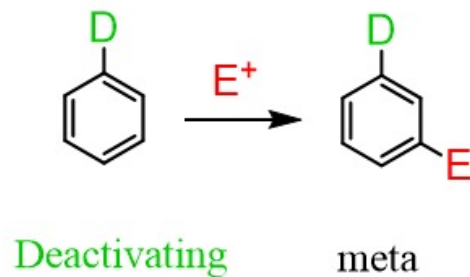
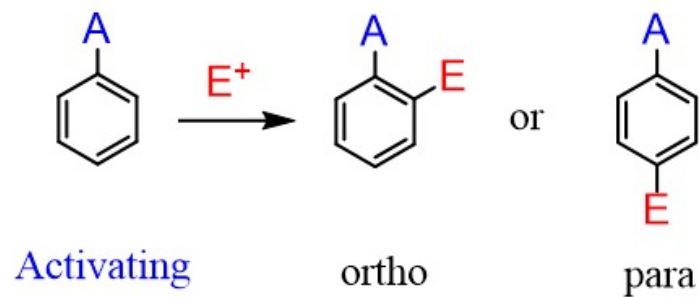
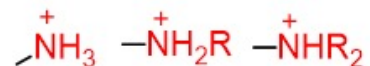
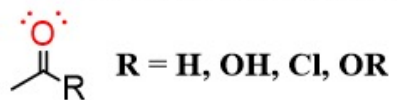
R- Alkyl groups

Deactivators

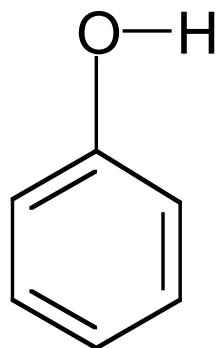
Deactivating



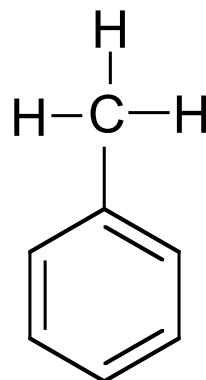
Strongly Deactivating



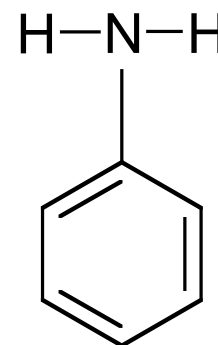
Some derivatives of benzene



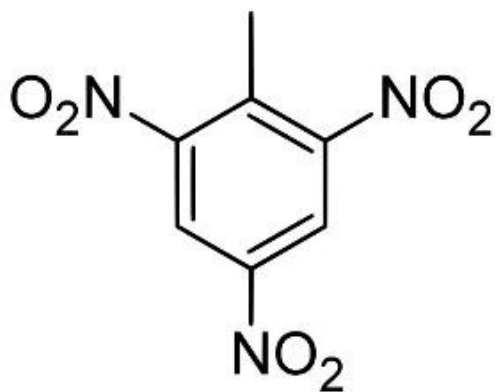
Phenol



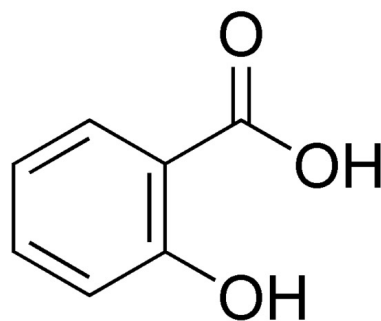
Toluene
(methylbenzene)



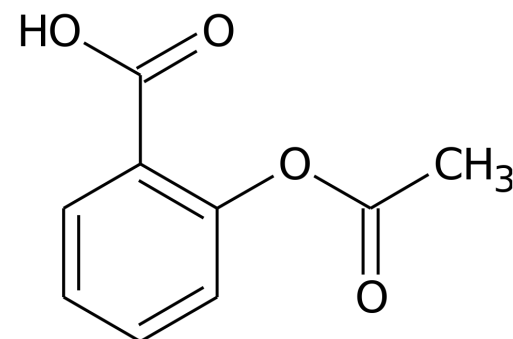
Aniline
(aminobenzene)



TNT
Tri-nitro-toluene



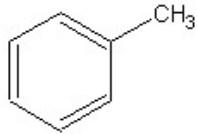
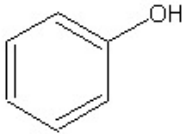
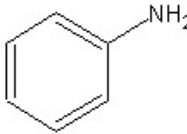
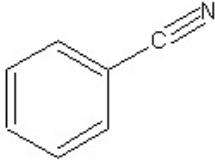
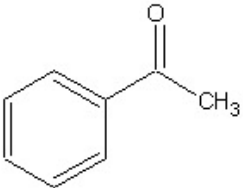
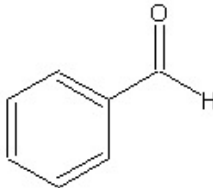
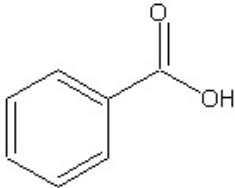
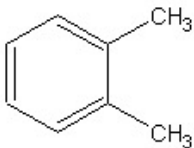
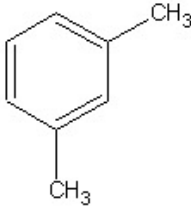
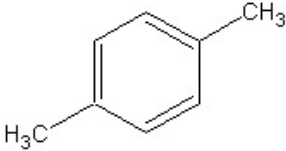
Salicylic acid



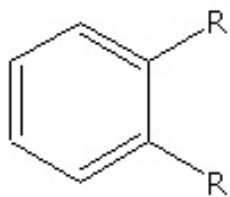
Acetylsalicylic acid
(aspirin)

Nomenclature

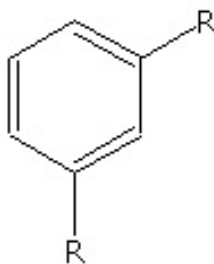
Common definitions & IUPAC

methyl-benzene	hydroxy-benzene	amino-benzene
		
toluene	phenol	aniline
		
benzonitrile	acetophenone	benzaldehyde
		
benzoic acid	<i>o</i> -xylene	<i>m</i> -xylene
		
	<i>p</i> -xylene	

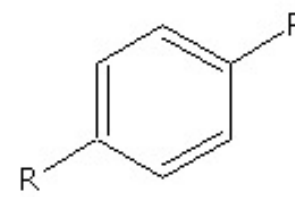
Di-substituted benzene derivatives



ortho

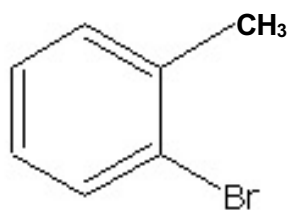


meta

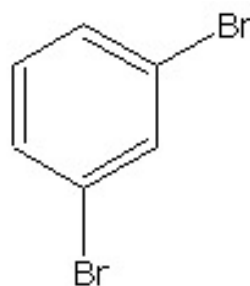


para

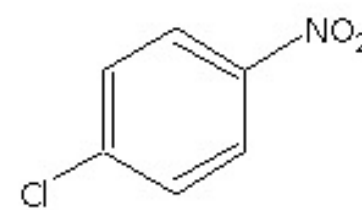
Examples:



ortho-bromotoluene

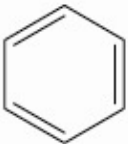
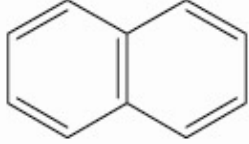
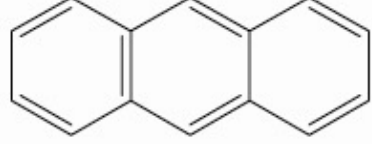
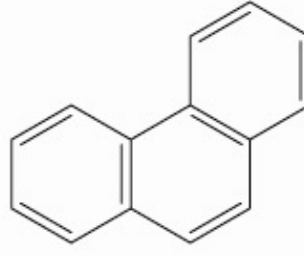


meta-dibromobenzene



para-chloronitrobenzene

Benzene derivatives (condensed rings).

Resonance energy kcal/mol (kj/mol)				
	Benzene	Naftalene	Anthracene	Fenanthrene
	36 (151)	61 (255)	83 (347)	91 (381)

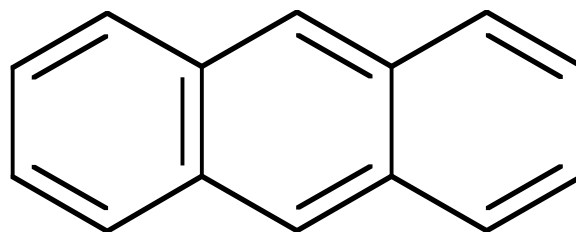
They have a planar structure and have electronic delocalization on the whole molecule.

They are produced by the combustion of oils, fuels, coal, tobacco and organic materials.

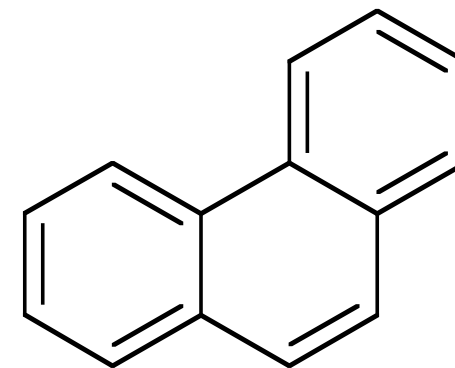
They are agents intercalating on DNA and may have mutagenic effects.

ARENES

Polycyclic derivatives of benzene



anthracene

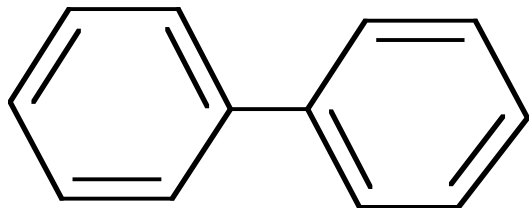


phenanthrene

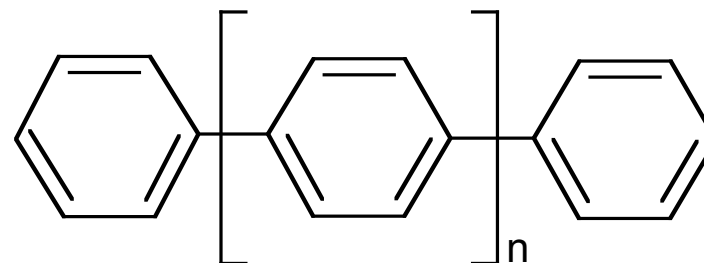
Rings are

condensed when they share C atoms

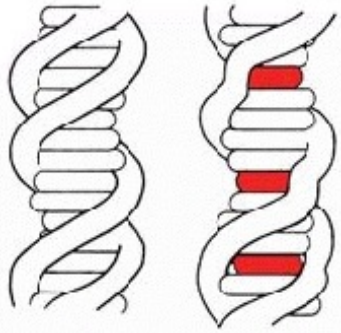
linked when they are joined by one C atom



biphenyl



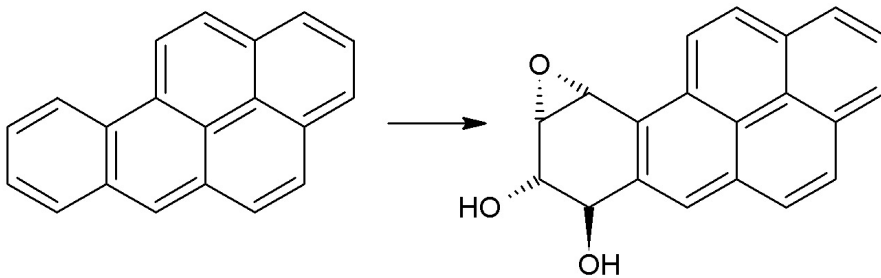
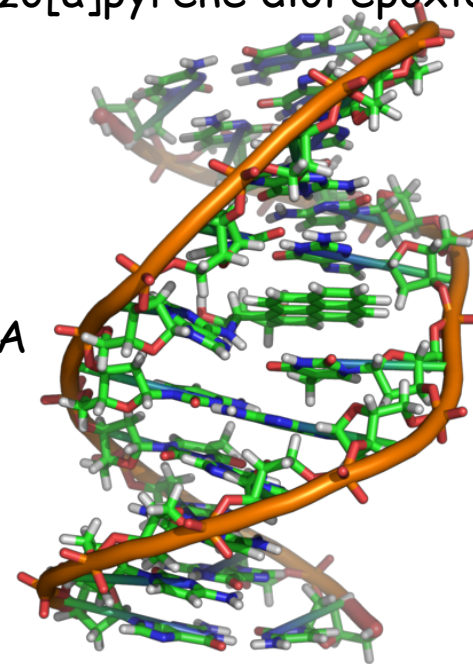
polyphenyl



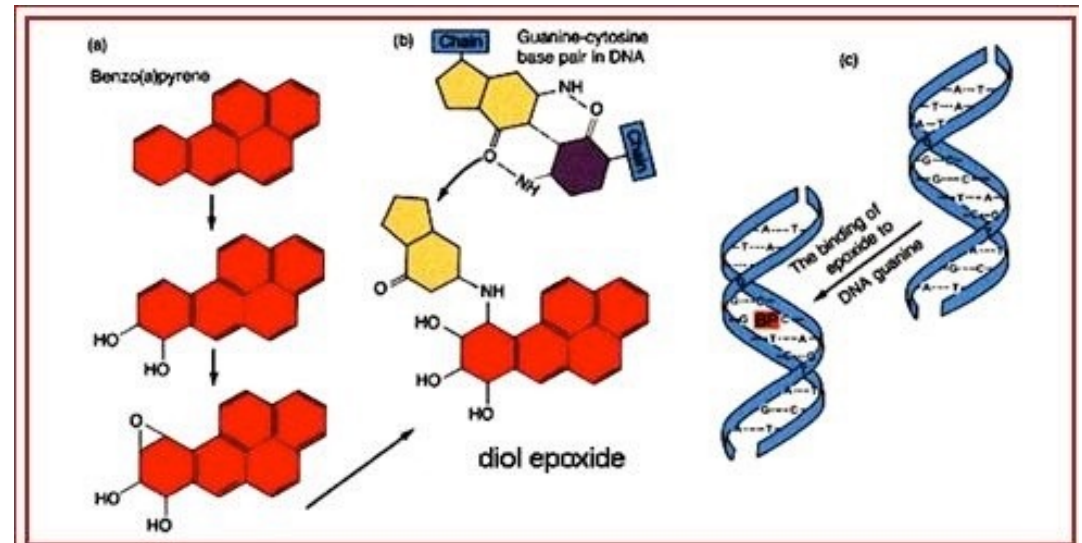
Benzopyrene carcinogenicity

Properly speaking, benzo[a]pyrene is a procarcinogen, meaning that the mechanism of carcinogenesis 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.

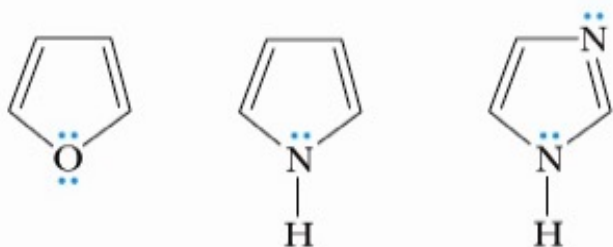
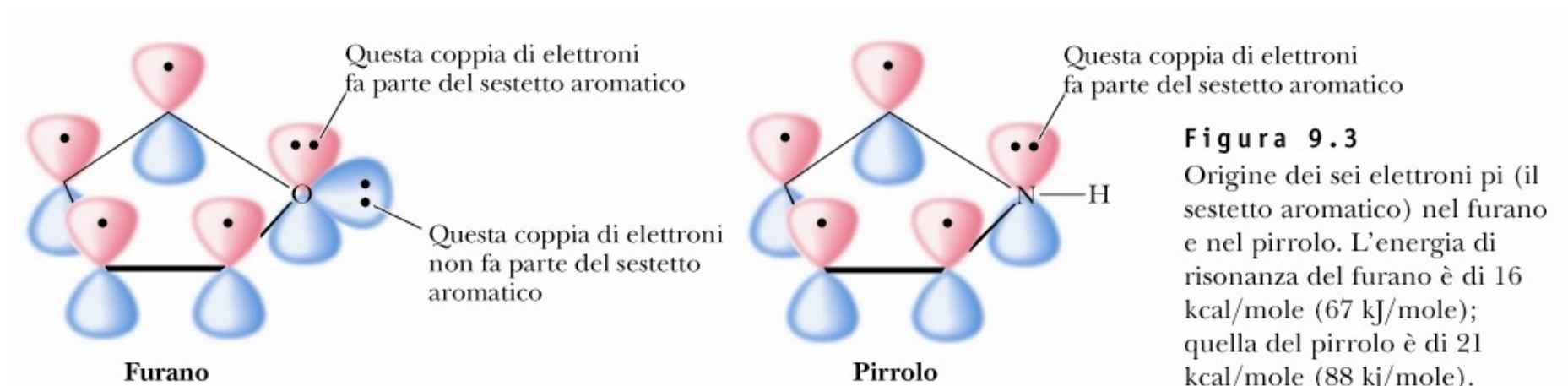


Benzopyrene oxidation



Heterocyclic aromatic compounds

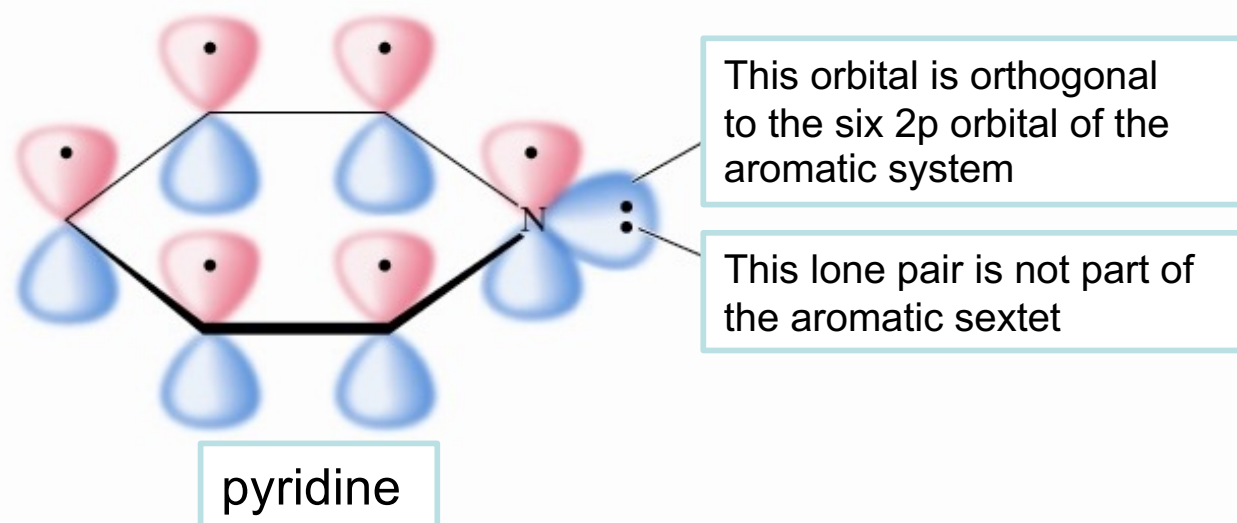
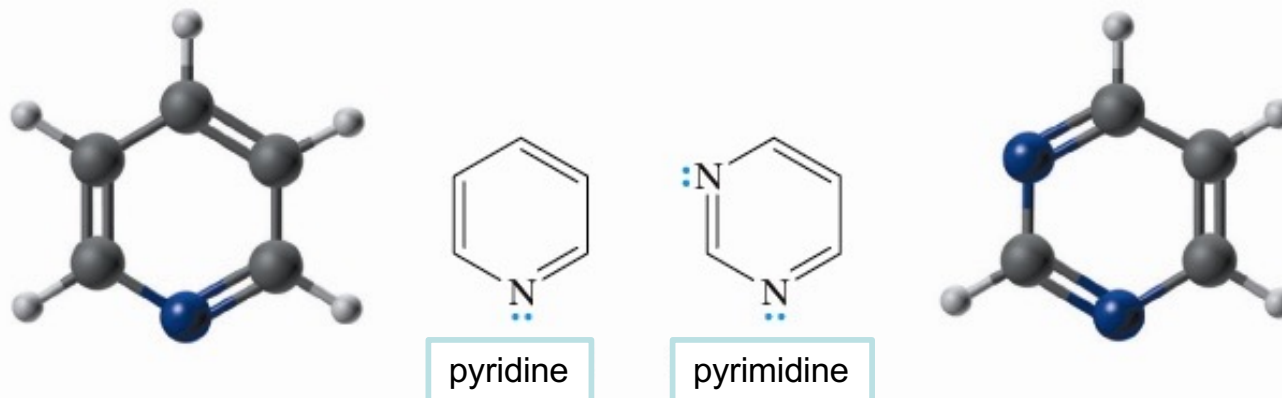
Cyclic molecules in which the Hückel rule is respected, where in the ring there are one or more atoms different from carbon



furan pyrrole imidazole

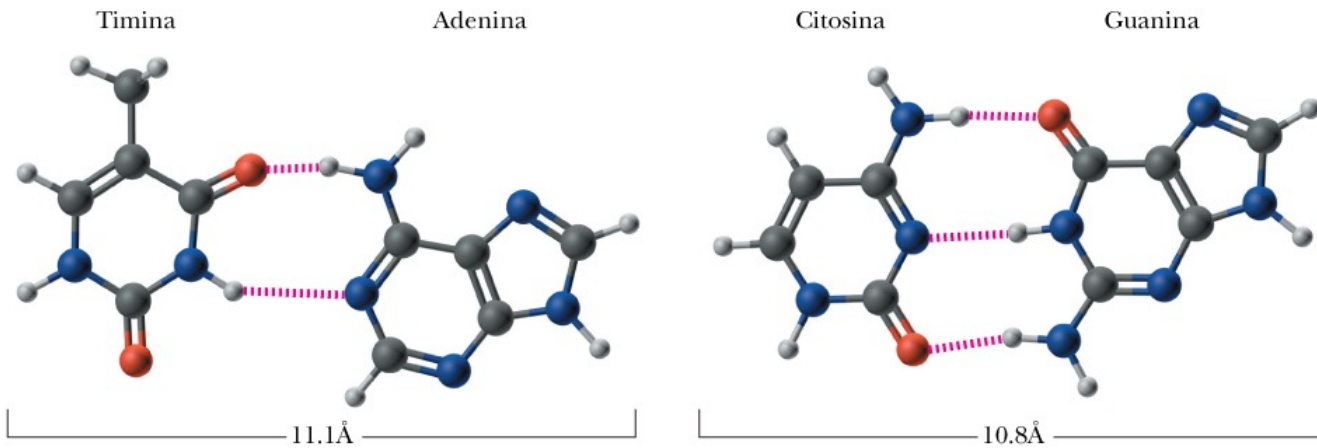
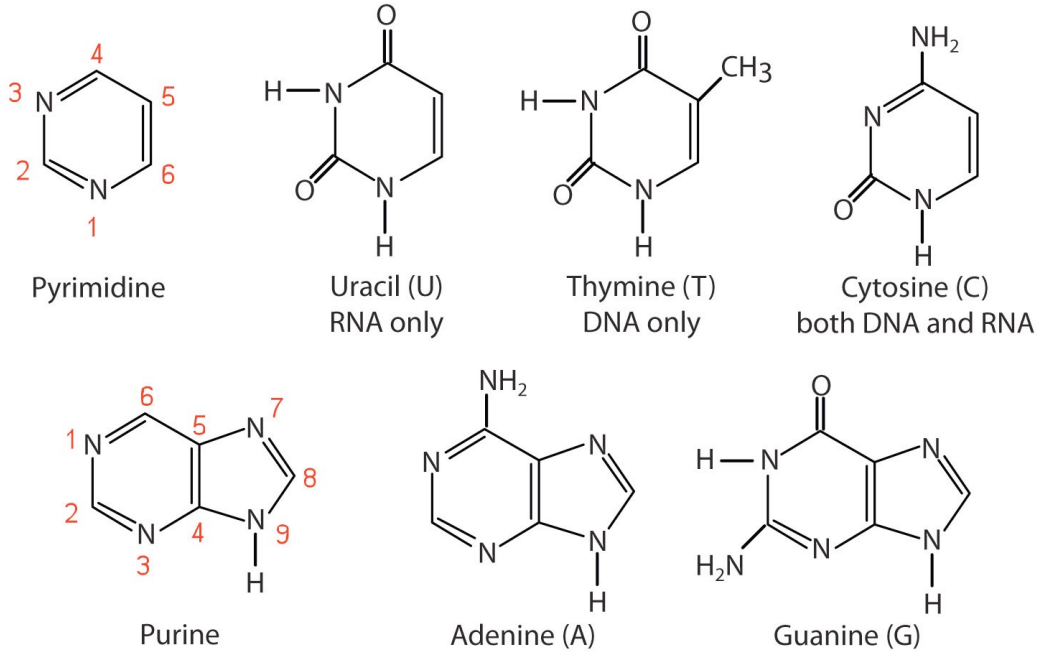
If a lone pair is not part of the aromatic sextet the compound has basic properties.

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



p

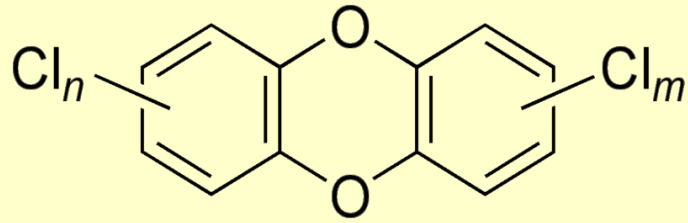
The aromatic nitrogenous bases of nucleic acids.



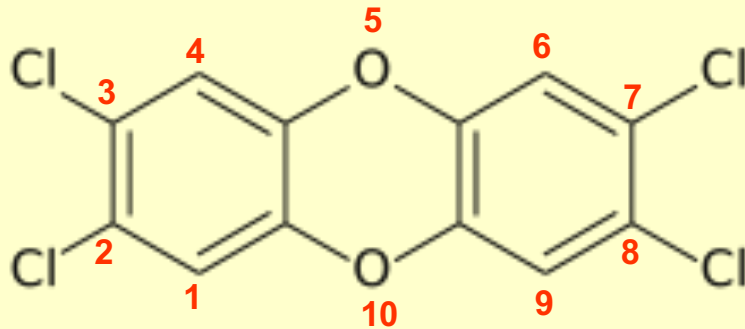
2 H-bonds

3 H-bonds

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



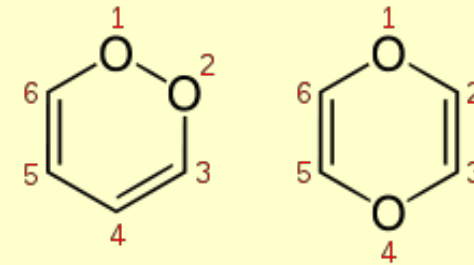
Polychlorinated dibenzodioxins



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

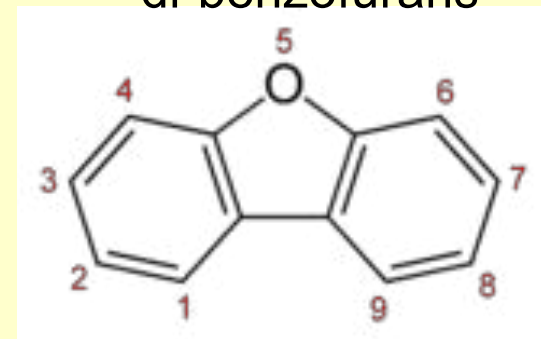
barely soluble in H₂O – highly in fat (x 10⁶)
TCDD (in man) half life 5 – 11 years DL50 0.5
μg / Kg

Dioxines
 ~200 stable compounds
 toxic, when halogenated...



1,4-dioxin

di-benzofurans



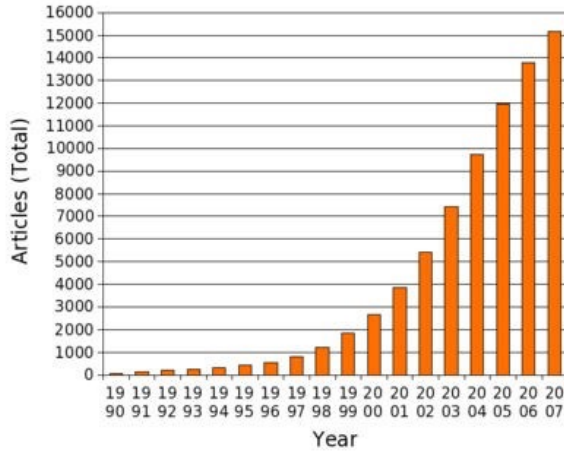
Healthy too...!!

Hypericin & Alzheimer d.

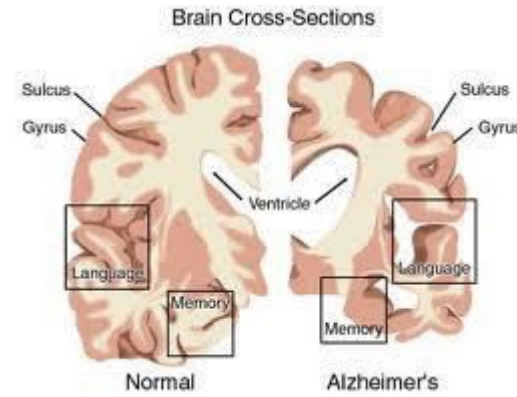
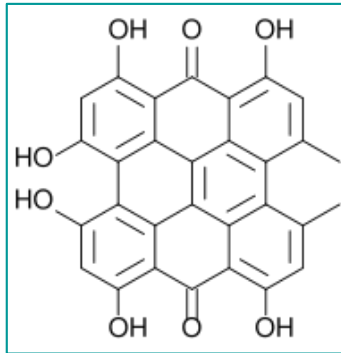
Paolo Sarti 2011
 Department of Biochemistry
 Sapienza

It perturbs β -amiloid polymerization processes

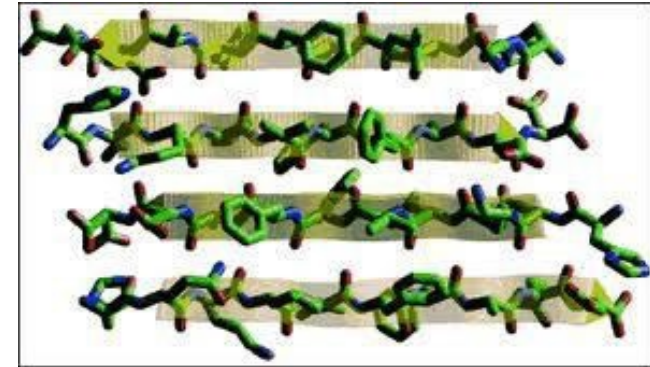
Read more: <http://www.solaris.it/indexprima.asp?Articolo=1798#ixzz0Zgn7WMC9>



hypericin



β -amiloid



Amyloid beta peptide ($A\beta(1-42)$)

High affinity for Cu(II)
 $A\beta \downarrow$
 Cu(I)
 + $A\beta^{(+)}$

1 Asp	10 Tyr	22 Gln	36 Val
2 Ala	11 Glu	23 Asp	37 Gly
3 Glu	12 Val	24 Val	38 Gly
4 Phe	13 His	25 Gly	39 Val
5 Arg	14 His	26 Ser	40 Val
6 His	15 Gln	27 Asn	41 Ile
7 Asp	16 Lys	28 Lys	42 Ala
8 Ser	17 Leu	29 Gly	
9 Glu	18 Val	30 Ala	
	19 Phe	31 Ile	
	20 Phe	32 Ile	
	21 Ala	33 Gly	
		34 Leu	
		35 Met	

Reduction Potentials
 Cu(II)/ $A\beta$ 0.7 V
 R_2S^{2-} 1.6 V

Essential to high Redox activity

A role for one or more Gly?

G-X-X-X-G-X-X-X-G-X-M-X-G also occurs in prions

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