Fonction et réaction organiques II

Fall Semester 2022

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1. Aromatic Chemistry

1.1. Aromaticity
- 1.1.1. Hückel theory
- 1.1.2. Frost-Musulin cycle
- 1.1.3. Polycyclic aromatic compounds

1.2. Electrophilic Aromatic Substitution S_EAr
- 1.2.1. General principles
- 1.2.2. Important S_EAr reactions
  - 1.2.2.1. Nitration
  - 1.2.2.2. Halogenation: bromination / chlorination
  - 1.2.2.3. Friedel-Crafts reaction
  - 1.2.2.4. Sulfonation
  - 1.2.2.5. Chlorosulfonation
  - 1.2.2.6. Deuteration by ipso-substitution
  - 1.2.2.7. Formylation
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  - 1.2.2.9. Hydroxy methylation
  - 1.2.2.10. Chloro methylation
  - 1.2.2.11. Diazo-coupling
- 1.2.3. Secondary substitution on the benzene ring
- 1.2.4. Introducing a 3rd substituent

1. Aromatic Chemistry

1.3. Quantitative substitution Effects

1.4. Reactions proceeding by arenium cations

1.5. Reversibility in S_EAr reactions

1.5.1. Reactivity of condensed aromatic substrates

1.6. Nucleophilic Aromatic Substitution S_NAr

1.7. Reactions of diazonium salts

1.8. Substitution by the aryne mechanism

1.9. Reduction of the aromatic ring

1.10. Construction of the aromatic ring: metal-catalyzed [2+2+2]-cyclization

2. Heterocycles

2.1. Nomenclature
- 2.1.1. Trivial names
- 2.1.2. The Hantsch-Widman system

2.2. Aromaticity and reactivity of heteroaromatics
- 2.2.1. Comparison between pyrrole and pyridine
- 2.2.2. Reactivity of electron rich heteroaromatics
- 2.2.3. Reactivity of electron poor heteroaromatics
- 2.2.4. The Tschitschibabin reaction

2.3. Syntheses of five-membered ring heteroaromatics
- 2.3.1. Furane syntheses
- 2.3.2. Thiophene syntheses
- 2.3.3. Pyrrole syntheses
- 2.3.4. Indole syntheses
- 2.3.5. Oxazole syntheses
- 2.3.6. Pyrazole and isoxazole syntheses
- 2.3.7. Thiazole syntheses
- 2.3.8. Imidazole syntheses

2.4. Syntheses of six- membered ring heteroaromatics
- 2.4.1. Pyridine synthesis
- 2.4.2. Quinoline synthesis
- 2.4.3. Isoquinoline synthesis

3. Diels-Alder Cycloaddition

4. 1,3-dipolar cycloaddition and concerted molecular rearrangements

4.1. 1,3-dipolar cycloadditions

- 4.1.1. Ozonolysis
- 4.1.2. Huisgen azide-alkyne cycloaddition, Click chemistry
- 4.1.3. Nitrile-oxide cycloaddition

4.2. Pericyclic reactions; concerted molecular rearrangements

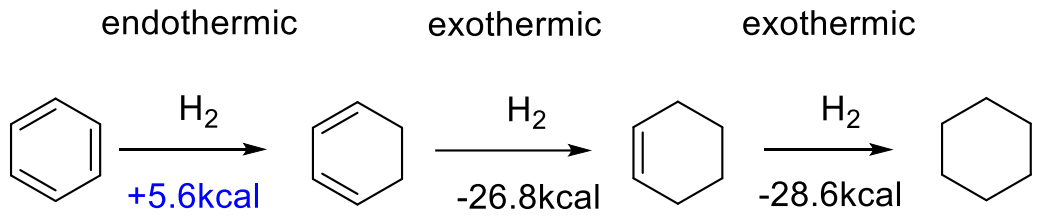
- 4.2.1. Cope rearrangement
- 4.2.2. Claisen rearrangement
- 4.2.3. Ene reactions

1.1. Aromaticity

Definition of aromaticity :

- Ancient : smelling compounds, originally coming from coal tar destillates containing aromatic compounds
- Nowadays: lower reactivity through stabilization of an unsaturated molecule.

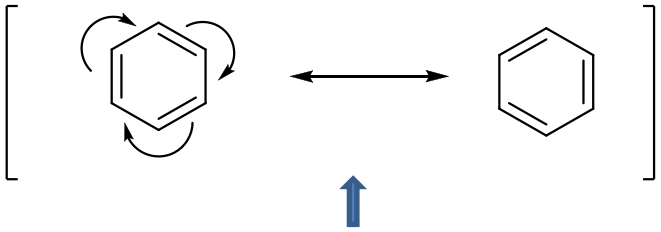
Example:



Benzene aromatic

Endothermic reaction ⟹ Contribution of aromaticity of benzene

Mesomeric structure



The ´mesomeric arrow´ does not correspond to the one in equilibrium

1.1.1. Hückel theory

Hückel theory is a simple theory to estimate if a compound is aromatic

Basic requirements:

1) Cyclic and planar
2) Atoms all sp^2-hybridized

Rules:

1) Strongly valid only for monocycles

2) The amount of π electrons

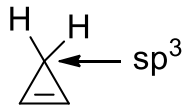
aromatic : 4n+2, n=0,1,2,3....

antiaromatic: 4n, n=1,2,3....

Anti-aromatic is the contrary of aromatic: higher reactivity than expected and/or difficult or impossible to synthesize.

1.1.1. Hückel theory

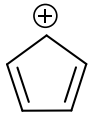
Examples:



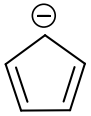
cyclopropene
n.a

cycloprop-2-en-1-ylium
2π
a

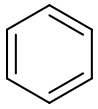
cyclobuta-1,3-diene
4π
aa



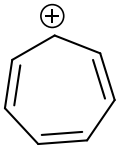
cyclopenta-2,4-dien-1-ylium
4π
aa



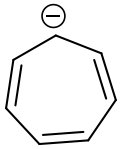
cyclopenta-2,4-dien-1-ide
6π
a



benzene
6π
a

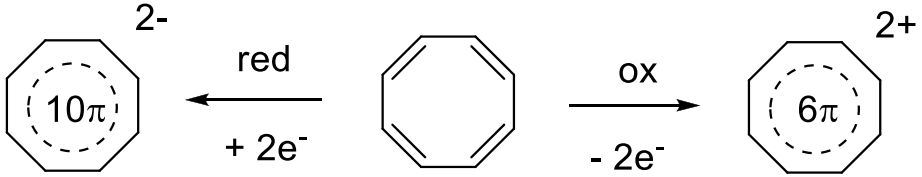


tropylium cation
6π
a



tropylium anion
8π
aa

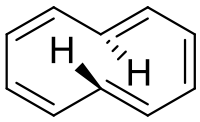
n.a=non aromatic
a=aromatic
aa=antiaromatic



10π
a

8π
aa

6π
a



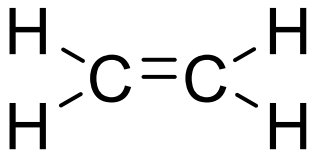
10π
twisted
sp^2
n.a.

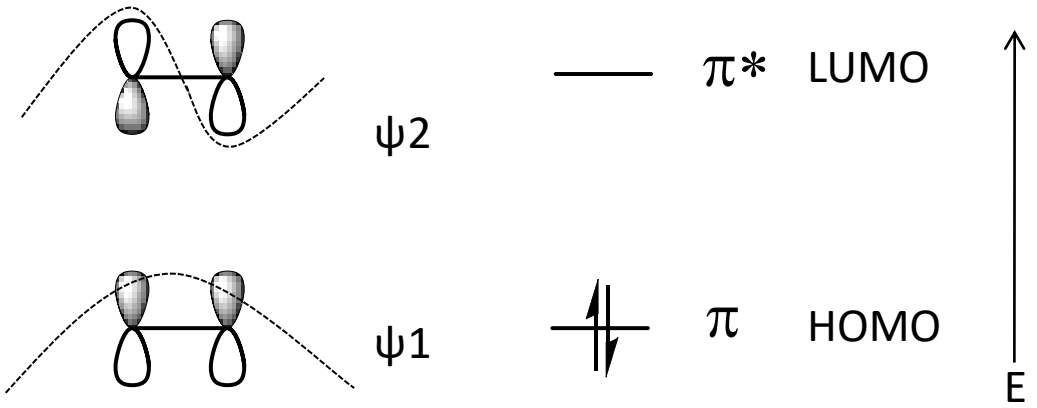
10π
planar
a

1.1.1. Hückel theory

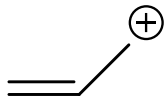
Molecular orbital (MO): scheme for unsaturated hydrocarbons

The π-system of ethene:

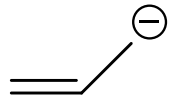




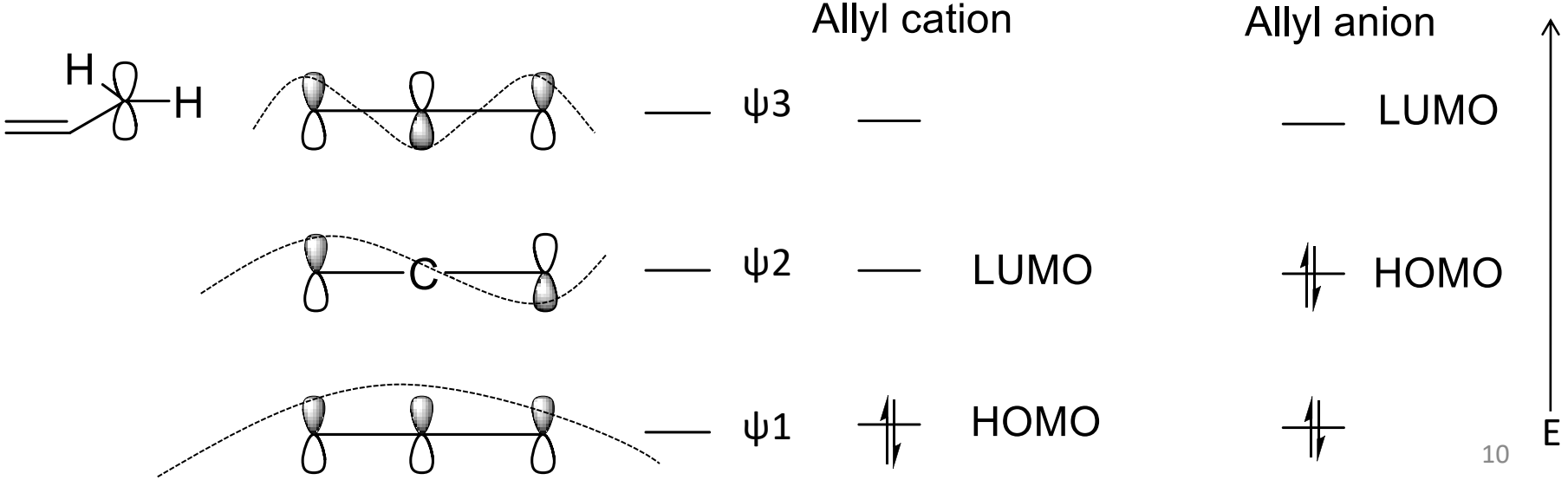
The Allyl-system



Allyl cation

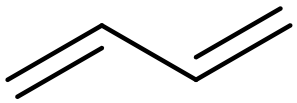


Allyl anion

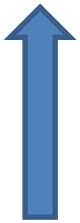


1.1.1. Hückel theory

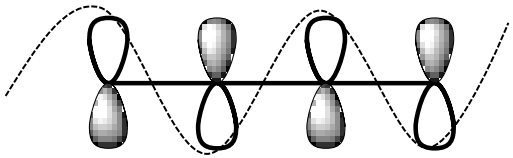
Butadiene



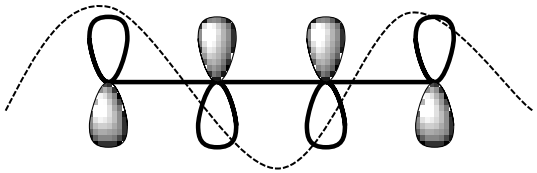
4 π-electrons



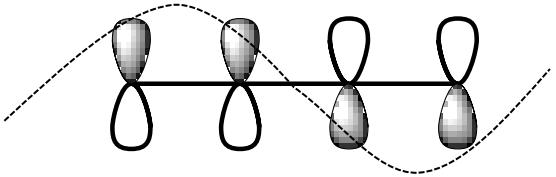
E



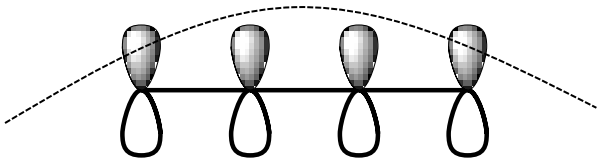
ψ4



ψ3 LUMO

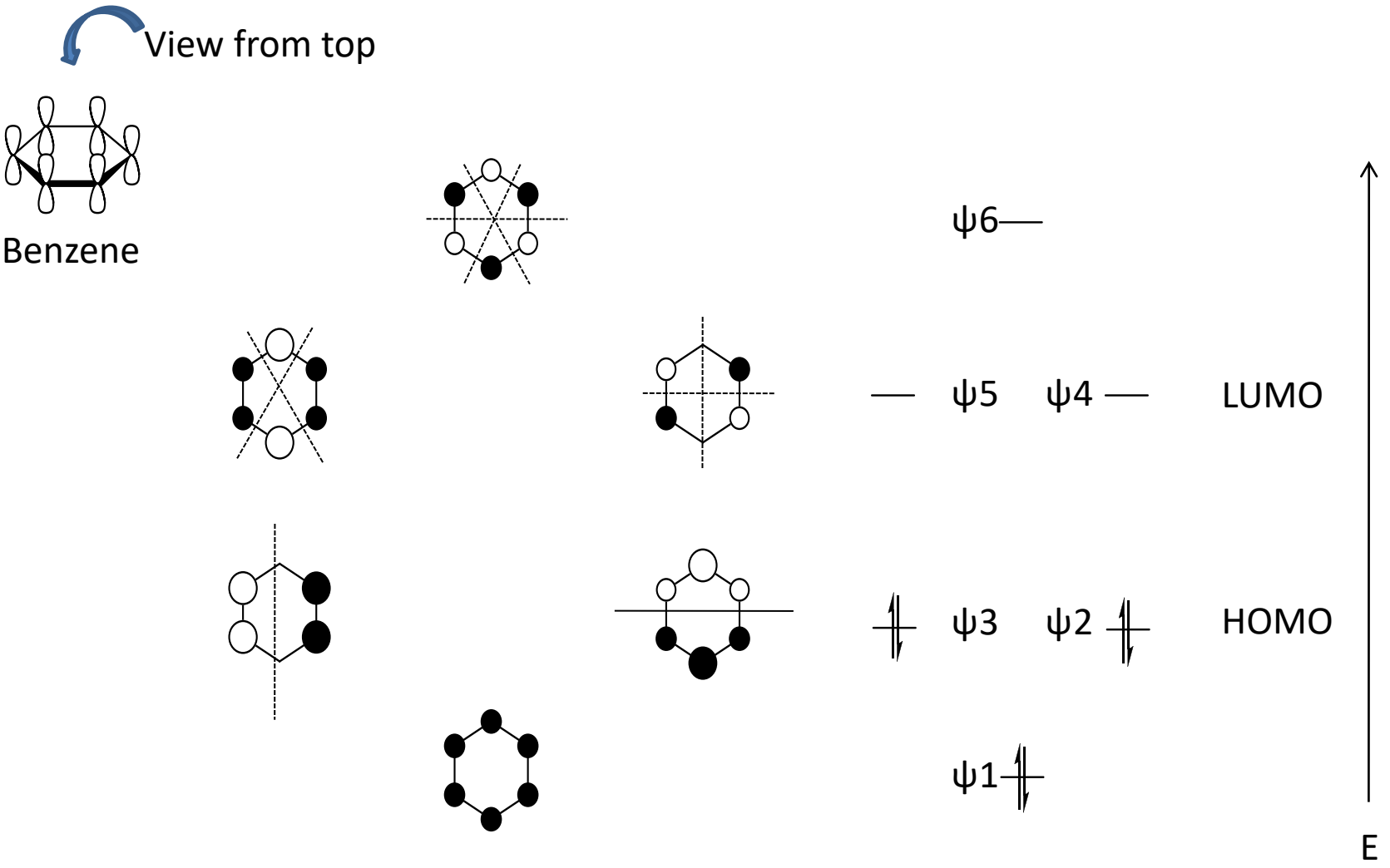


ψ2 HOMO



ψ1

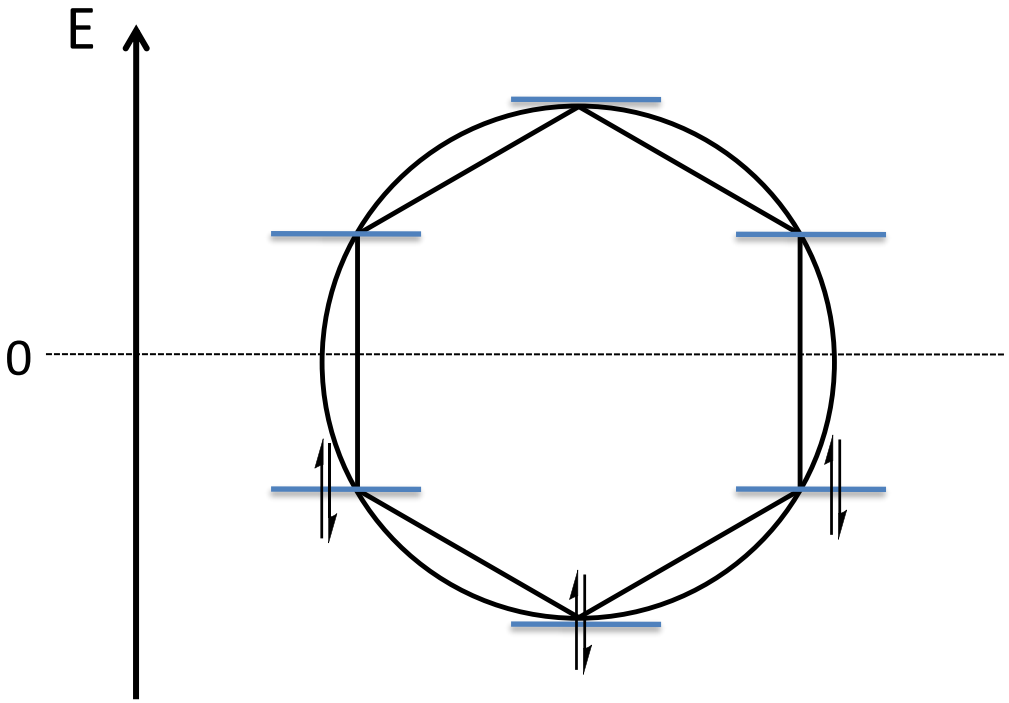
1.1.1. Hückel theory



1.1.2. Frost-Musulin cycle

It is a tool for monocyclic aromatic compounds to estimate the degree of aromaticity by relative energy of their Molecular Orbital (MO).

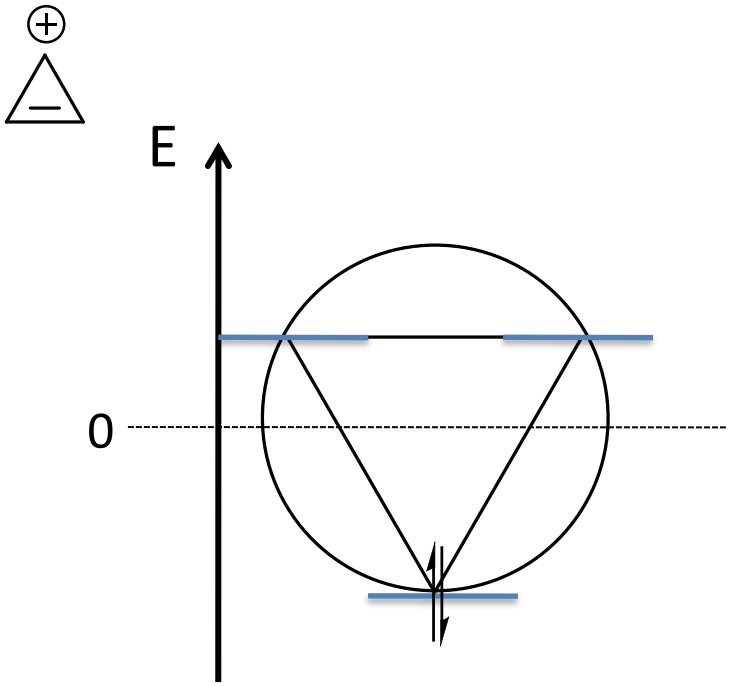
Constructed : molecule sits on an edge!



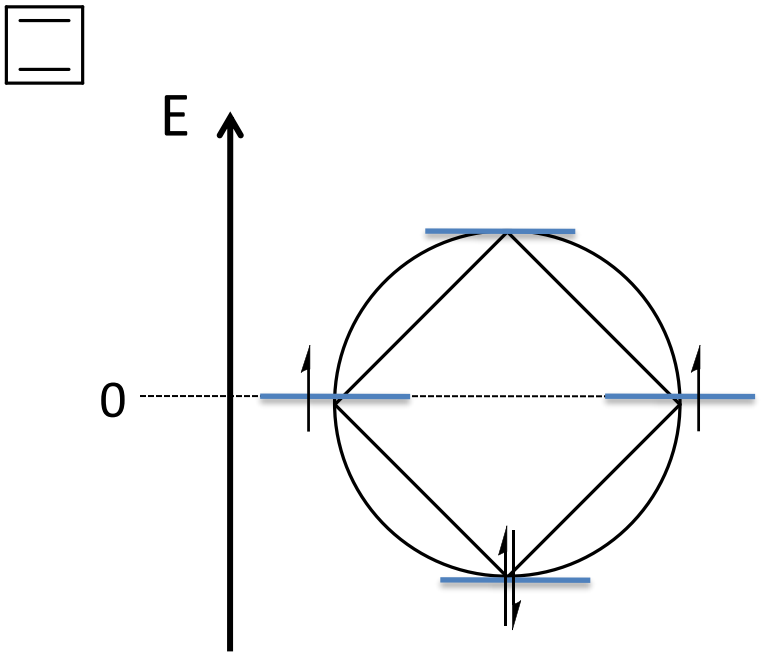
- All corners represent energy-levels
- Fill in electron from buttom
- Read out stabilization / destabilization

1.1.2. Frost-Musulin cycle

Example: Cyclopropenylium cation and cyclobutadiene



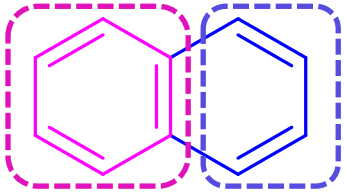
Stabilized / aromatic



4 π; biradical species
anti aromatic

1.1.3. Polycyclic aromatic compounds

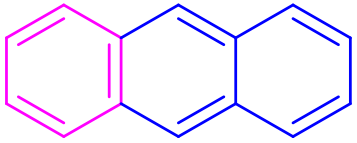
Important example:

Benzoide  Quinoide

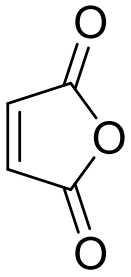
Naphthaline

Quinoide rings are more reactive than benzoide rings

Example:



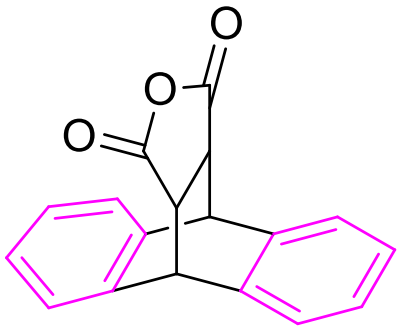
anthracene



Maleic anhydride

Diels-Alder cycloaddition

ΔT

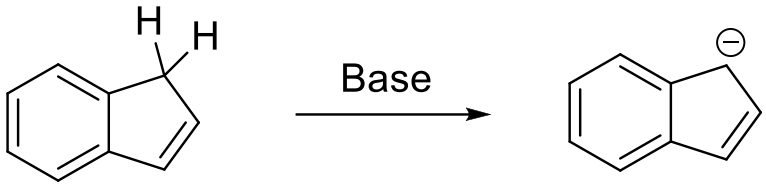


two quinoide rings
one benzoide ring
14 π - Aromatic

the product contains two benzoide rings

1.1.3. Polycyclic aromatic compounds

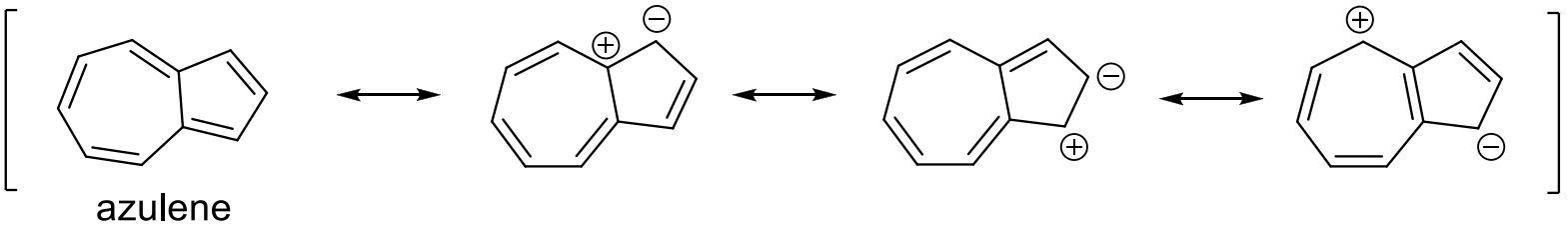
Indene - Anion



indene

10 π-aromatic

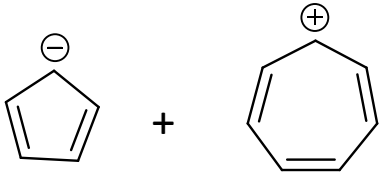
Azulene: blue color! Observation of color is due to its high dipole moment.



azulene

10 π

Color comes from charge transfer



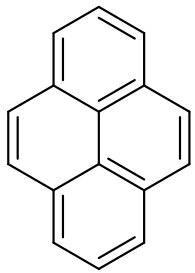
'composed' from the aromatic compounds cyclopentadienide and cycloheptatrienylium

1.1.3. Polycyclic aromatic compounds

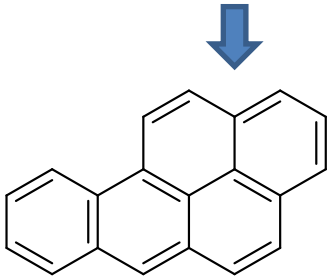
Examples:

Produced by incomplete combustion at 300-600°C from:

- coal tare
- diesel engine exhaust fumes
- cigarette
- barbecue

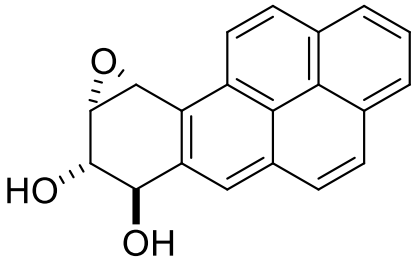


16 π
pyrene, aromatic

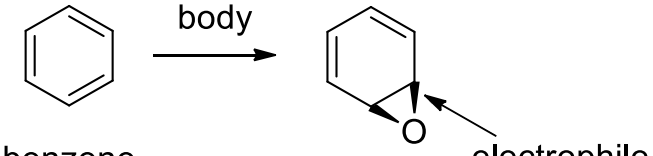


20 π
Benzo [a] pyrene
very cancerogenic
mutagenic tetratogenic

DNA intercalator

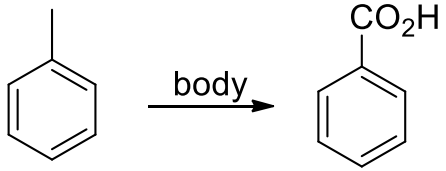


Toxicity of benzene v.s toluene



benzene

electrophile



toluene

benzoic acid
excreted