

Fonction et réaction organiques II

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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

1.2.2.8. Carboxylation

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 Hantzsch-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

3.1. Diels-Alder Cycloadditions

- 3.1.1. General reaction principle
- 3.1.2. The nature of the diene
- 3.1.3. The nature of the dienophile

3.2. Mechanism and stereochemical implications

- 3.2.1. Diene and dienophile conformation
- 3.2.2. Exo/Endo selectivity

3.3. Regioselectivity in the Diels-Alder cycloaddition

3.4. Additional examples of Diels-Alder cycloadditions

- 3.4.1. Extended polycyclic aromatics as diene component
- 3.4.2. Benzyne as dienophile
- 3.4.3. Intramolecular Diels-Alder reactions (IMDA)
- 3.4.4. Retro-Diels-Alder reaction

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

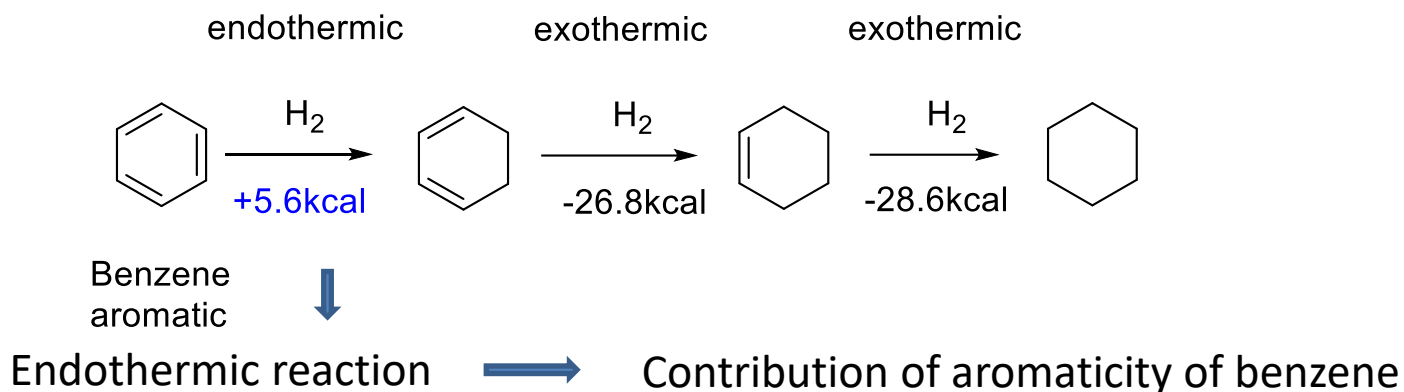
4.2.3. Ene reactions

1.1. Aromaticity

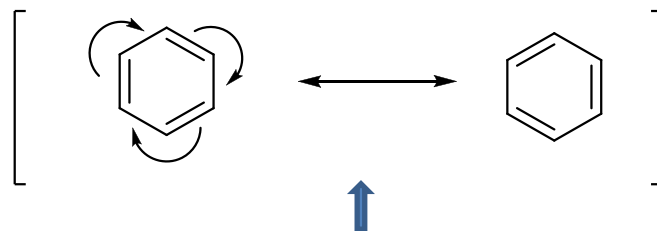
Definition of aromaticity :

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

Example:



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

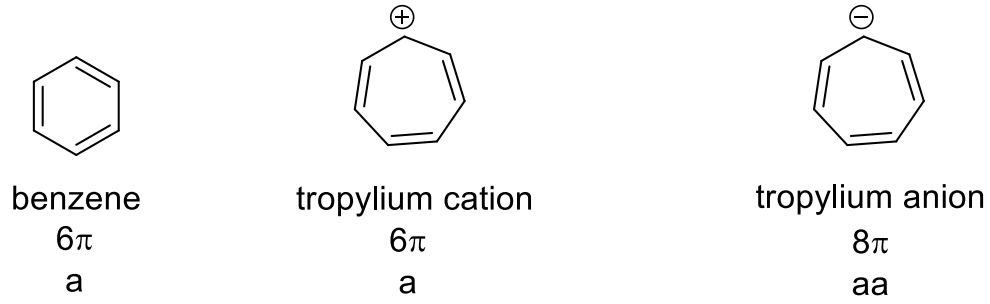
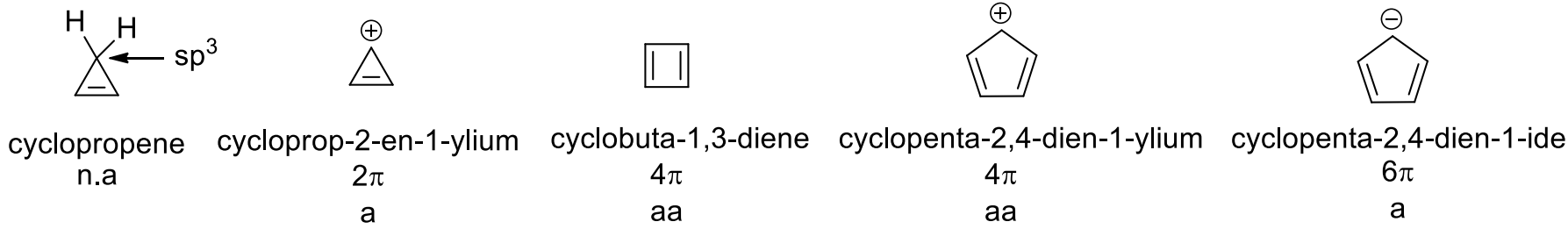
aromatic : $4n+2$, $n=0,1,2,3,\dots$

antiaromatic: $4n$, $n=1,2,3,\dots$

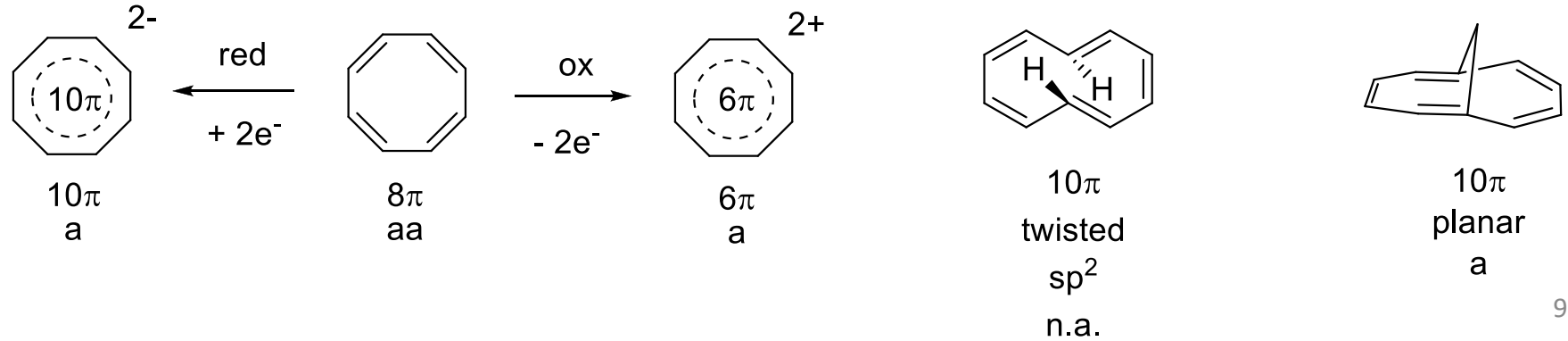
Anti-aromatic is the contrary of aromatic: higher reactivity than expected and/or difficult or impossible to synthesize.

1.1.1. Hückel theory

Examples:



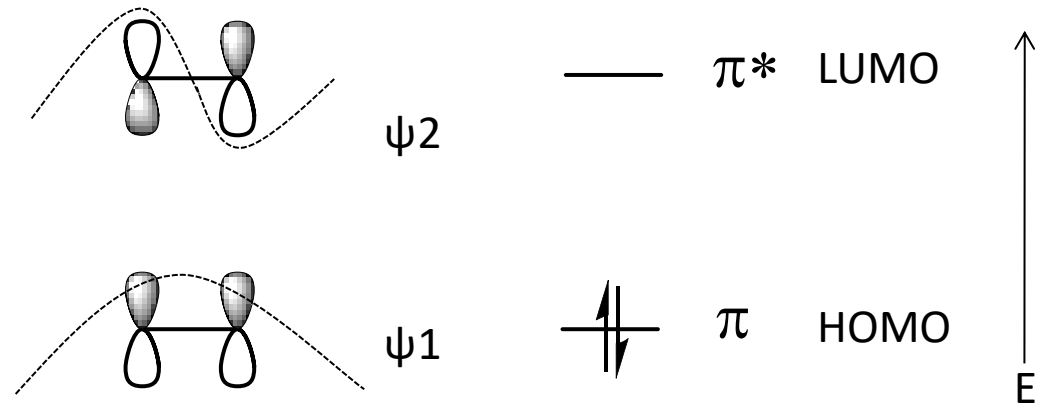
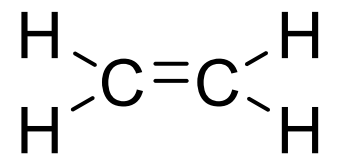
n.a=non aromatic
a=aromatic
aa=antiaromatic



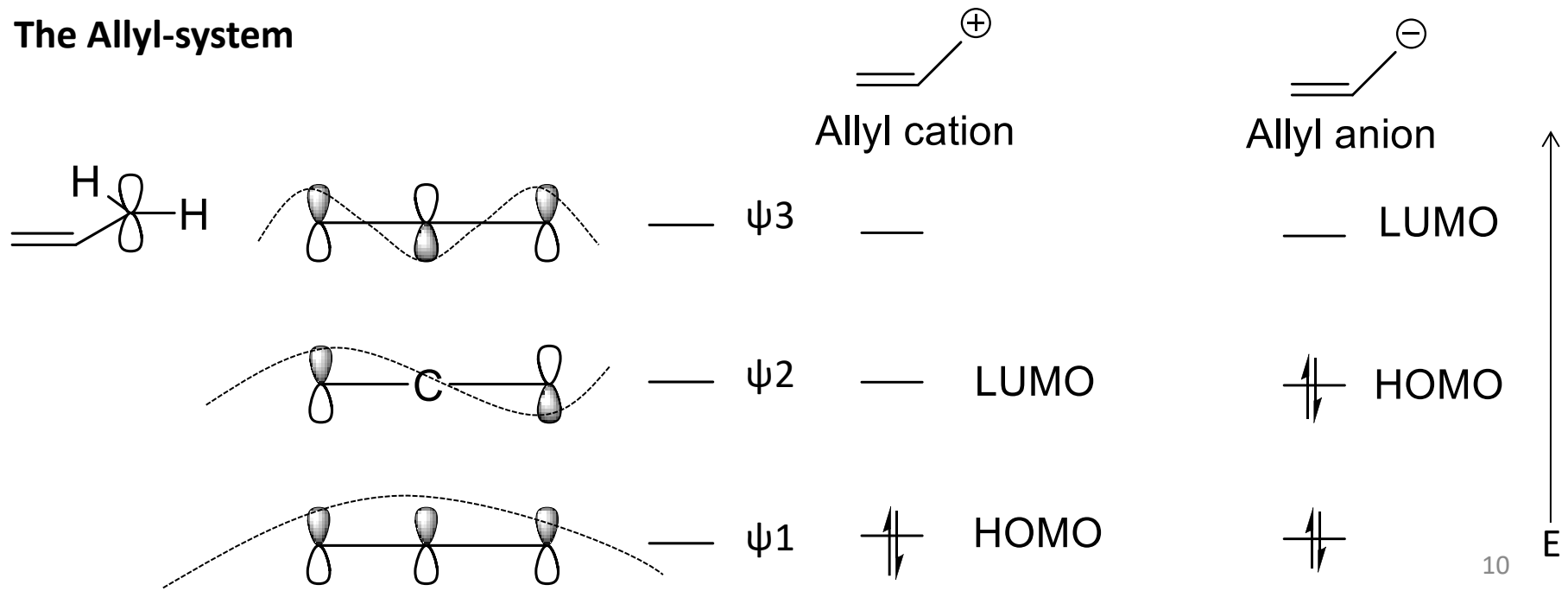
1.1.1. Hückel theory

Molecular orbital (MO): scheme for unsaturated hydrocarbons

The π -system of ethene:

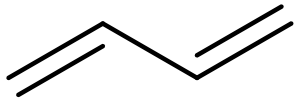


The Allyl-system

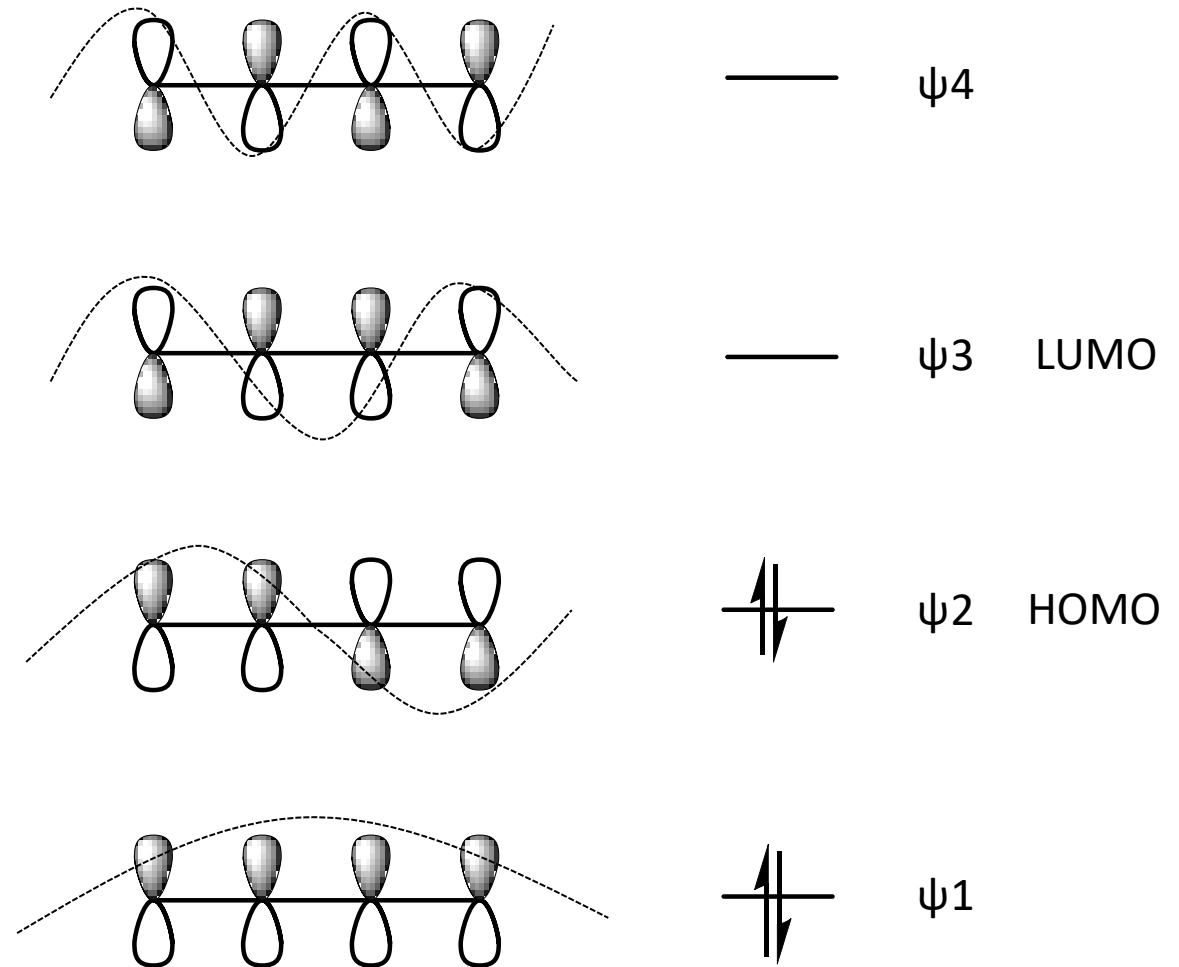
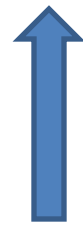


1.1.1. Hückel theory

Butadiene

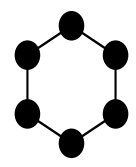
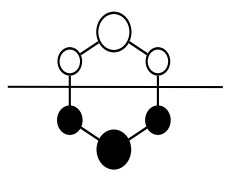
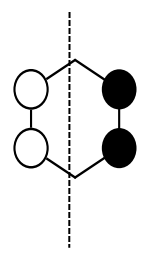
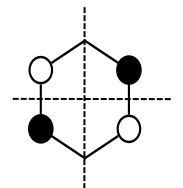
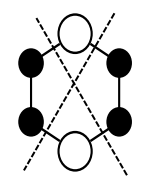
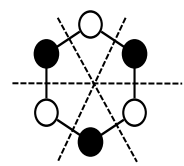
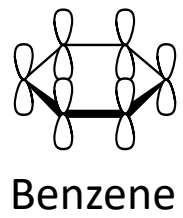


4 π -electrons



1.1.1. Hückel theory

View from top



ψ_6 —

— ψ_5 ψ_4 — LUMO

$\uparrow\downarrow$ ψ_3 ψ_2 $\uparrow\downarrow$ HOMO

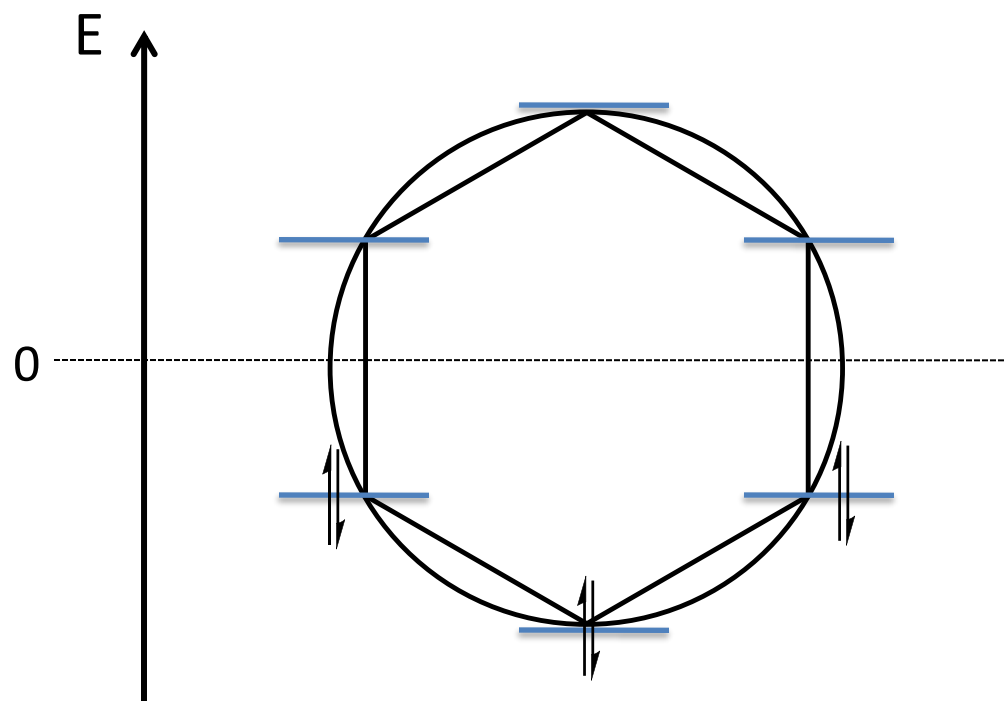
ψ_1 $\uparrow\downarrow$



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).

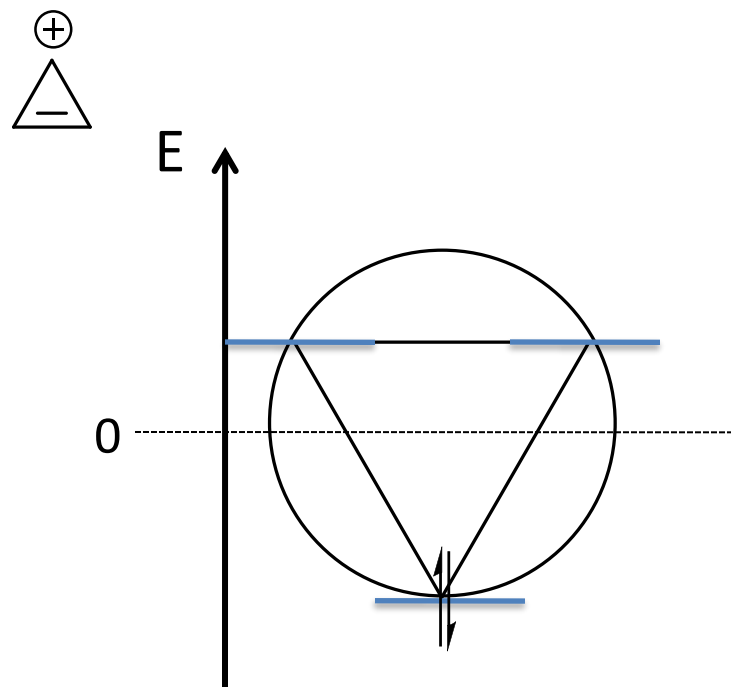
Constructed : molecule sits on an edge!



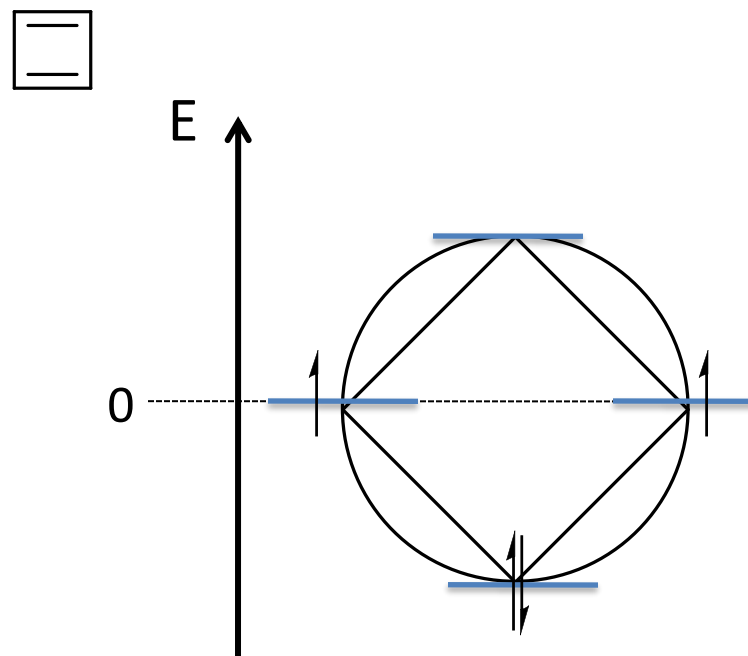
- All corners represent energy-levels
- Fill in electron from bottom
- Read out stabilization / destabilization

1.1.2. Frost-Musulin cycle

Example: Cyclopropenylum cation and cyclobutadiene



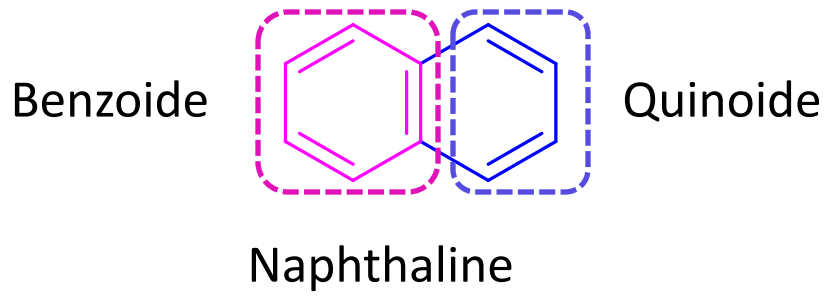
Stabilized / aromatic



4π ; biradical species
anti aromatic

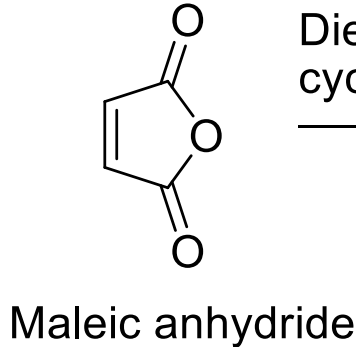
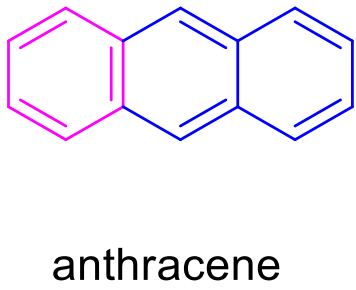
1.1.3. Polycyclic aromatic compounds

Important example:

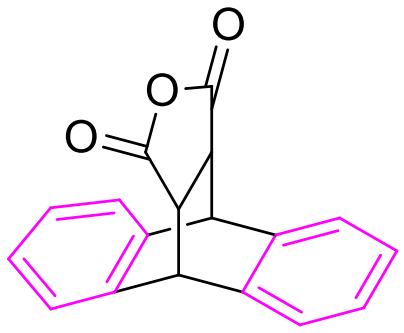


Quinoide rings are more reactive than benzoide rings

Example:



Diels-Alder cycloaddition
→
 ΔT

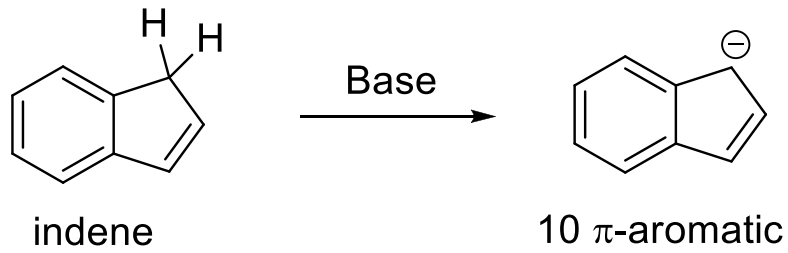


two quinoide rings
one benzoide ring
14 π - Aromatic

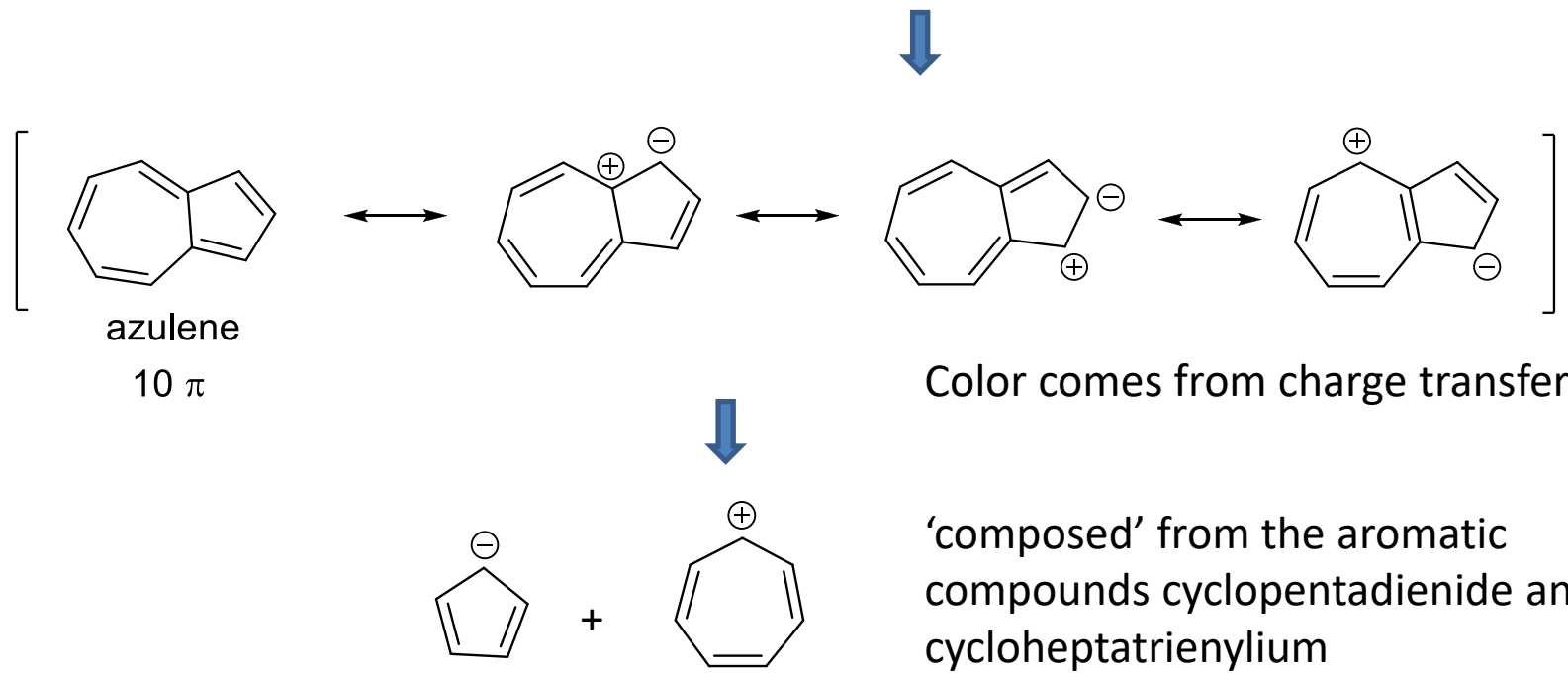
the product contains
two benzoide rings

1.1.3. Polycyclic aromatic compounds

Indene - Anion



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

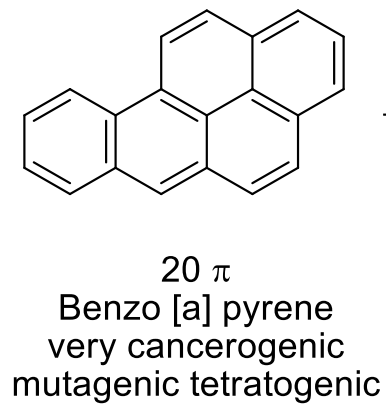
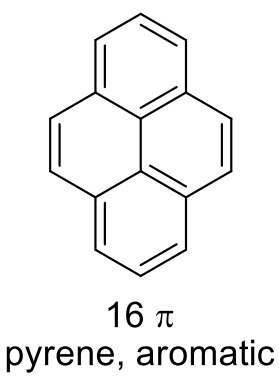


1.1.3. Polycyclic aromatic compounds

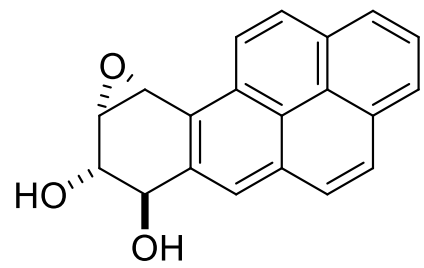
Examples:

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

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



DNA intercalator



Toxicity of benzene v.s toluene

