Chapter 4

Aromaticity

The goal of this chapter:

- Illustrating the multifaceted definition of aromaticity
- Quantifying (anti)aromaticity
- Identifying (anti)aromatic molecules

A fuzzy chemical concept

Il me faut cependant avouer que la chimie proprement dite ne m'a jamais beaucoup intéressé. Pourquoi ? Peut-être parce que des notions telles que celles de valence, de liaisons chimique etc., m'ont toujours semblées peu claires du point de vue conceptuel.

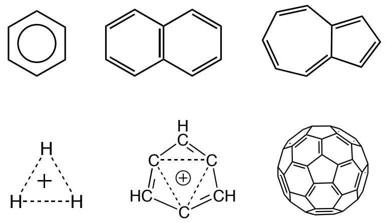
René Thom, 1983.

I have to confess that I have never been really interested in chemistry. Why? Maybe because such notions as valence, chemical bonds etc. have always seemed unclear to me from the conceptual point of view.

Gonthier, J. Steinmann, S. N.; Wodrich M. D.; Corminboeuf, C. *Chem. Soc. Rev.* **2012**, *41*, 4671.

Nature of the aromaticity concept

- **Easily to recognize (but not always)**
- **Many kinds**
- **Hard to compare**
- **Difficult to quantify**
- **Various opinions, no general agreement**
- **Interpreted differently**



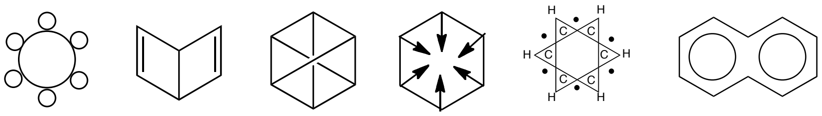
Beauty (Aromaticity) is in the eye of the beholder!

The restricted textbook definition

- Planar structure
- Conjugated π-system
- Molecule must be cyclic
- Hückel Rule: 4n+2 π electrons (n = 0, 1, 2, 3, …etc.)

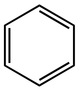
A Brief History of Benzene…

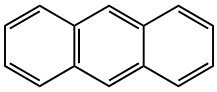
< 1825		Aromatic smell; naphthalene (crystalline)
1825	Faraday	Isolation of benzene (high C/H ratio)
1861	Loschmidt	A ring of carbon atoms suggested for benzene
1865	Kekulé	Benzene structure
1866	Erlenmeyer	Benzene: substitution more favorable than addition
1866	Erlenmeyer	Chemical formula for naphthalene
1867	Dewar/Claus	Dewar benzene/Diagonal benzene structure
1890	Armstrong	Six centric “affinities”
1897	J. J. Thompson	Discovery of electrons
1922	Crocker	“Six aromatic electrons” and heteroaromaticity
1925	Armit/Robinson	Aromatic sextet
1933	Pauling	Resonance energy
1931	Hückel	Theory of cyclic (4n+2) π electrons systems
1951	Doering	4n+2 π electron rule
1972	Clar	Clar “aromatic sextet”



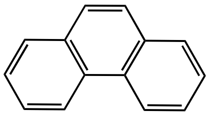
Types of aromatic systems

Planar polycyclic aromatic compounds (PAH’s) comprised of six-membered rings

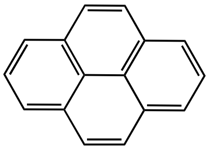




Anthracene



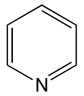
Phenanthrene



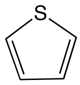
Pyrene
16 π electrons

Types of aromatic systems

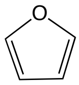
Non-benzenoid aromatic compounds (charged and neutral)



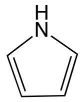
Pyridine



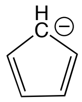
Thiophene



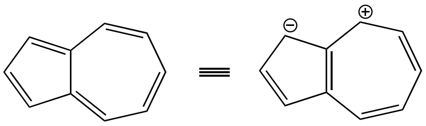
Furane



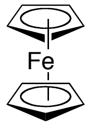
Pyrrole



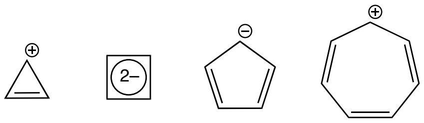
Cyclopentadienyl anion



Azulene

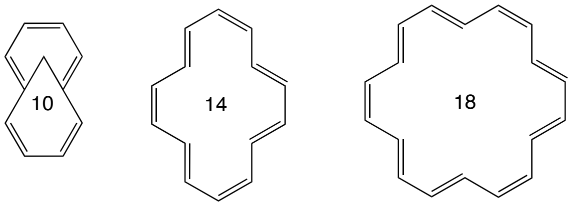


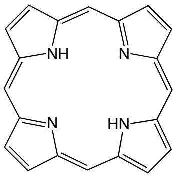
Ferrocene



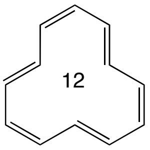
Types of aromatic systems

[n]Annulenes: 4n+2 π electrons hydrocarbon rings

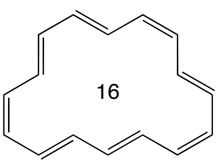




Porphyrin

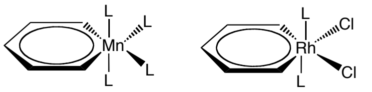


Not aromatic

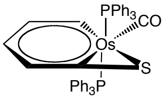


Not aromatic

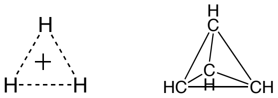
Other types of aromatic compounds



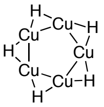
Predicted by Hoffman in 1979.



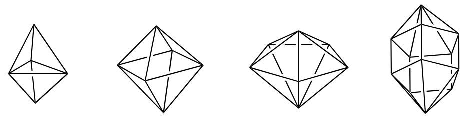
Synthesized in 1982.



H_3^+ and tetrahedrane



Transition metal clusters



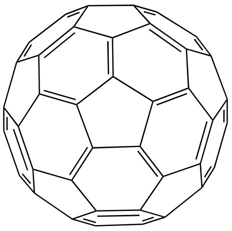
$C_2B_3H_5$

$B_6H_6^{2-}$
$C_2B_4H_6$

$B_7H_7^{2-}$
$C_2B_5H_7$

$B_{12}H_{12}^{2-}$
$C_2B_{10}H_{12}$

3D boron and carborane clusters



Fullerenes C_{60}
(superaromatic or only weakly aromatic?)

What is aromaticity?

historically
Structure criteria
Reactivity criteria
Energy criteria
Magnetic criteria

Aromaticity

aromatic smell (before 1825)

Discovery of benzene Faraday (1825)

Hight carbon ratio (before 1865)

Benzene structure Kekulé 1865

Substitution > addition Erlenmeyer (1866)

Exalted diamagnetic susceptibility Pascal (1910)

Electron sextet Armit-Robinson (1925)

4n+2 electron Hückel (1931)

Energy evalation through theromochemiscal data Kistiakowsky (1936)

Ring current theory Pauling (1936)

pi electron to contribution to magnetic susceptibilty London (1937)

Ring current effect on NMR chemical shift, Pople (1956)

Magnetic sucseptibility exaltation Dauben (1969) Flygare (1970)

Nucleus-Independent chemical shift (NICS) Schleyer (1996)

Structural aspects of aromaticity (not discussed here)

Quantum chemical evaluation of delocalization energy (2000)

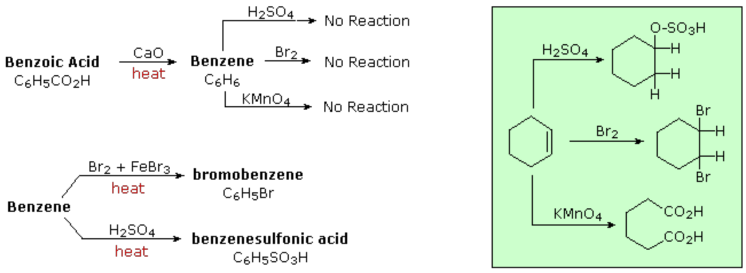
Schleyer and Jiao, *Pure Appl. Chem*. **1996**, *68*, 209-218

Main criteria

- **Structural**
  – equalized bond length tendencies
- **Energetic**
  – enhanced thermodynamic stability
- **Spectroscopic**
  – proton chemical shifts, UV, magnetic susceptibility exaltation,
- **Reactivity**
  – lower reactivity, electrophilic substitution

Aromaticity

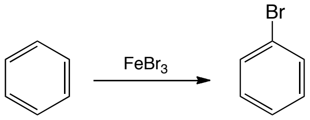
Reactivity: They are unreactive to common double bond transformation.



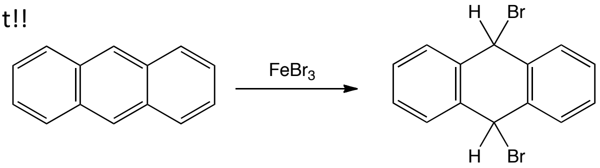
Benzene undergoes substitutions rather than addition reactions (Erlenmeyer, 1866).

Aromaticity

Reactivity: Electrophilic substitution is not always preferred



But!!



Substitution impossible
Addition easy!

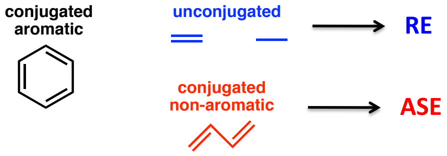
Aromaticity is a ground state property

Aromaticity: RE vs. ASE

Energetic: Aromatic compounds are unusually stable!

Resonance Energy (RE): Stabilization from π-conjugation.

Aromatic stabilization energy (ASE): extra stabilization "in excess" of the RE due to cyclic π-conjugation



conjugated aromatic

unconjugated ⟶ **RE**

conjugated non-aromatic ⟶ **ASE**

Resonance or delocalization Energy: The Pauling-Wheland definition of "resonance energy" captures all these "delocalization" effects".

$$\mathrm{RE} = E(\psi_1) - E(\Psi)$$

The quantity obtained by subtracting the actual energy of the molecule in question from that of the most stable contributing structure.

Wheland, "The Theory of Resonance", 1944, Page 52.

Aromaticity: Energetic evaluations

- **Stability: Compared to what?**

  Resonance energy (RE) vs. Aromatic Stabilization Energy (ASE)

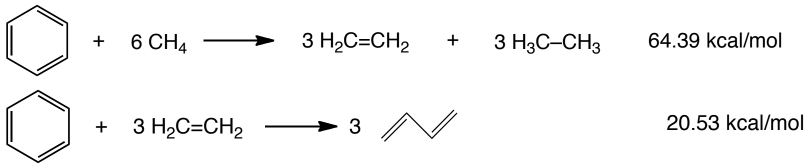
- **Balanced Chemical Equations**

  Appropriate and flawed reference compounds

Aromaticity

Energetic Aromatic compounds are unusually stable!

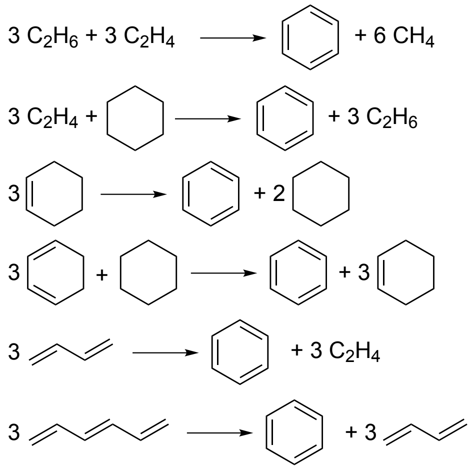
1. Literature energy estimates of aromatic stabilization energies (ASE) and resonance energies (RE) vary greatly (from 20 to 65 kcal/mol for benzene).
2. Such evaluations strongly depend on the equation used and the choice of reference molecules.
3. The ASE's and RE's of strained and more complicated systems are particularly difficult to evaluate (e.g. cyclobutadiene, biphenylene).



Aromaticity (RE and ASE)

Conventional Evaluation using a selection of reference systems: **isodesmic or homodesmotic reactions**

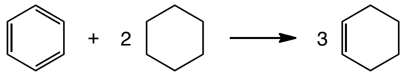
RE vs. ASE



-65.1 kcal/mol	**RE**
-48.5 kcal/mol	**RE**
-36.0 kcal/mol	**RE (historic but flawed)**
-28.8 kcal/mol	**ASE value recommended**
-20.5 kcal/mol	**ASE (from Dewar)**
-22.5 kcal/mol	**ASE**

Warning: these equations are not balanced for hyperconjugation and branching effects (as discussed earlier in this course)

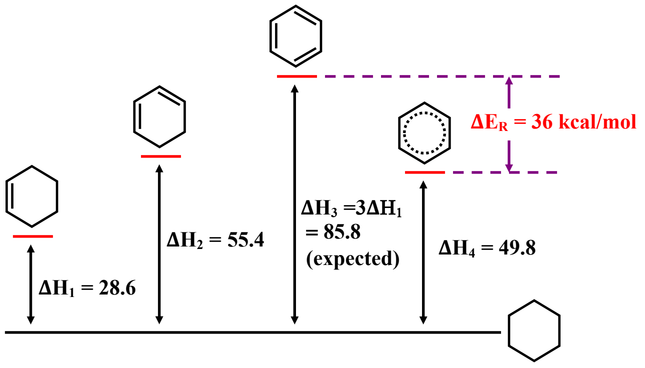
Conventional benzene Resonance energy



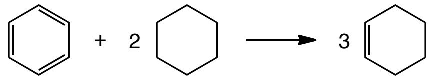
35.95 kcal/mol

(1936) Kistiakowsky's experimental determination of the stabilization of benzene:

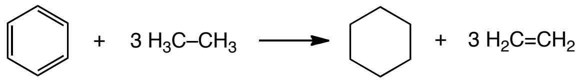
Historically important but flawed.



What is the Resonance Energy of benzene?

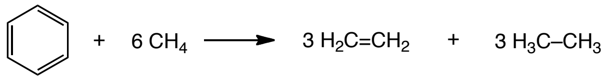


35.95 kcal/mol



48.25 kcal/mol

Isodesmic: bond separation energy (BSE)

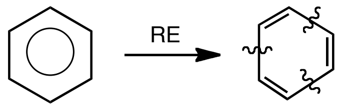


64.39 kcal/mol

GOOD!

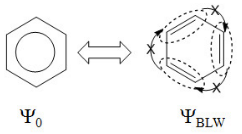
What is the Resonance Energy of benzene?

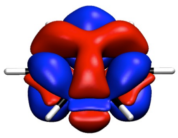
Modern and direct computational approach:
The block localized wavefunction (BLW) method



BLW computed benzene RE:
64.1 kcal/mol (B3LYP/6-311+G**)

Energy difference between benzene and
the hypothetical 1,3,5-cyclohexatriene





$$\Psi_I^{BLW} = \hat{A}\{\Phi_1\Phi_2\cdots\Phi_k\}$$

$$\Phi_i = \varphi_{i1}\alpha(1)\varphi_{i1}\beta(2)\varphi_{i2}\alpha(3)\cdots\varphi_{i\frac{n_i}{2}}\beta(n_i)$$

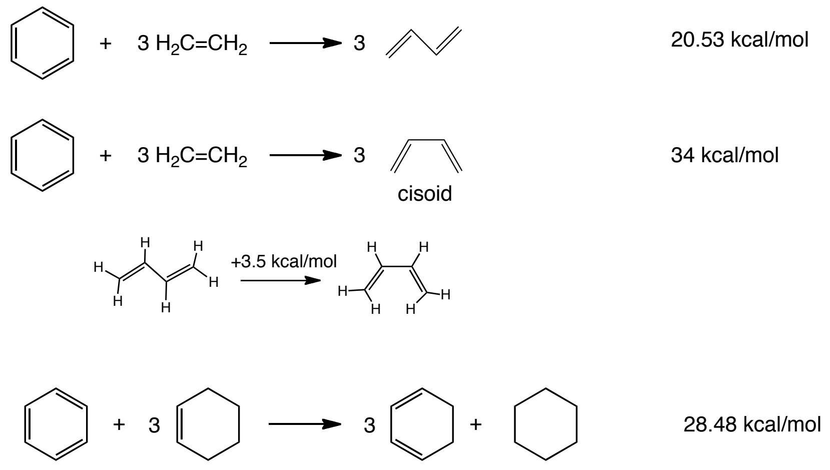
$$\varphi_{ij} = \sum_{\mu=1}^{m_i} C_{ij\mu}\chi_{i\mu}$$

$$\langle\varphi_{ij}|\varphi_{kl}\rangle = \begin{cases}\delta_{jl} & i=k\\ s_{jl}^{ik} & i\neq k\end{cases}$$

Y. Mo, S. D. Peyerimhoff, *J. Chem. Phys.* **1998**, *109*, 1687.
Y. Mo, L. Song, Y. Lin *J. Phys. Chem. A* **2007**, *111*, 8291.

What is the ASE of benzene?

Dewar resonance energy = ASE

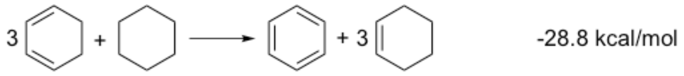


GOOD!

Aromaticity in benzene (ASE)

The ASE evaluates the “extra benzene resonance energy” relative to conjugated but non-aromatic reference molecules:

The recommended value based on chemical equations is **28.8 kcal mol^{-1}**.

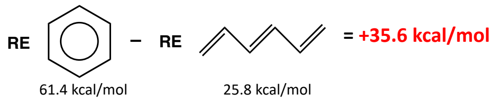


A related aromaticity probe is the **“extra cyclic resonance energy” (ECRE)** defined as the difference between the resonance energies of a cyclic conjugated compound and an acyclic polyene either with the **same number of bonds** (**ECRE1**) or with the **same number of diene conjugations (ECRE2)**.

A third alternative is the “**isomerization stabilization energy**” **(ISE)** based on the energy difference between cyclically delocalized and merely conjugated isomers.

Extra Cyclic Resonance Energy (ECRE)

ECRE1: same number of double bonds

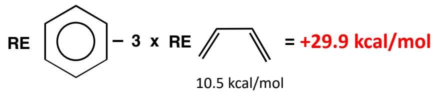

RE − **RE** = **+35.6 kcal/mol**

61.4 kcal/mol 25.8 kcal/mol

ECRE 2: same number of conjugations


RE − **3 x RE** = **+24.8 kcal/mol**

12.2 kcal/mol


RE − **3 x RE** = **+29.9 kcal/mol**

10.5 kcal/mol

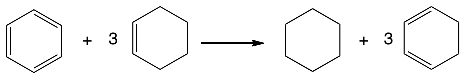
ECRE:
Energy difference between the resonance energies of a cyclic conjugated compound and its corresponding acyclic polyene

ECRE > 0 Aromatic
ECRE ≈ 0 Non-aromatic
ECRE < 0 Antiaromatic

Y. Mo, P. v. R. Schleyer *Chem. Eur. J.* **2006**, *12*, 2009–2020.

BLW: B3LYP/6-31G*

Best experimental aromatic stabilization energy (ASE) estimate for benzene

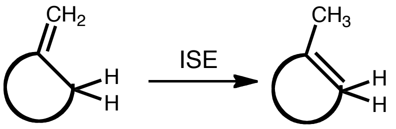


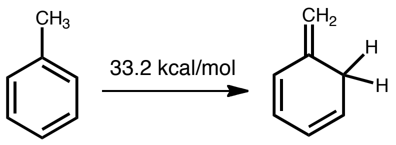
+28.8 kcal/mol (expt.)

Balanced for hyperconjugation, hybridization and protobranchings (as seen earlier in the course).

Isomerization Stabilization Energy (ISE)

ASE derived from the energy difference between a methyl derivative of the aromatic system and its non-aromatic exocyclic methylene isomer





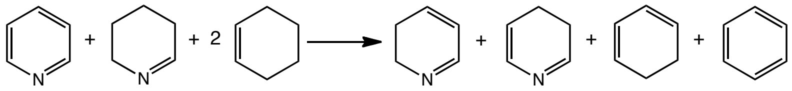
1 bond type correction (–3.6 kcal/mol)
1 syn-anti correction (+3.6 kcal/mol)

Schleyer, P. v. R.; Puhlhofer. F. *Org. Lett.* **2002**, *4*, 2873.

Mini Quiz 7

- Evaluate the RE of cyclobutadiene.
- What is its antiaromatic destabilization energy?
- What are some potential problems?
- What is the proper equation for the ASE of Pyridine?

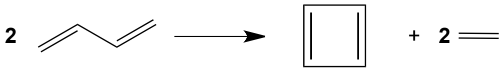
*http://cccbdb.nist.gov/ (Experimental data/ Enthalpy of formation)
(use ΔH_f = 104.2 kcal/mol for cyclobutadiene)



Antiaromaticity of D_{2h}Cyclobutadiene

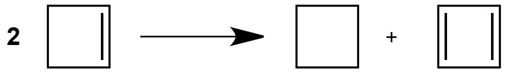
Estimating the destabilization imparted by the antiaromaticity of cyclobutadiene is more of a challenge.

- According to Hückel Theory, the π-electronic energy of CBD is twice that of ethene (*i.e.*, RE=0).
- Using the Benson conjugated increment (4*6.78 kcal mol^{-1}), CBD ($\Delta_f H^\circ$ =104 kcal mol^{-1}) is destabilized by 77. 2 kcal mol^{-1}.



ΔH° = 77.7 kcal/mol

How to incorporate the strain effects?



ΔH° = 35.7 kcal/mol

ΔH_f 37.5 6.7 104

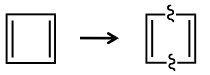
What about hyperconjugation?

Is the antiaromaticity (RE or ASE) of CBD really substantial?

Wu, J.; Mo, Y.; Evangelista, F.; Schleyer, P.v.R. *Chem. Comm.* **2012**, *48*, 8437.

ECRE2 for D_{2h} Cyclobutadiene (CBD)

CBD Resonance energy (RE)



= **+5.1** kcal/mol

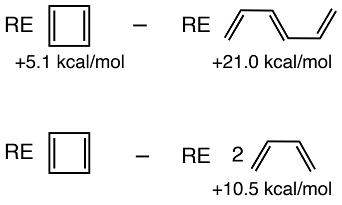
E(DFT) *Delocalized*

E(BLW) *Localized*

Antiaromatic species do NOT have negative RE's, but are net π stabilized!

Extra cyclic resonance energy

ECRE2 based on models with two conjugations



RE – RE

+5.1 kcal/mol +21.0 kcal/mol

RE – RE 2

+10.5 kcal/mol

ECRE= **–15.9** kcal/mol

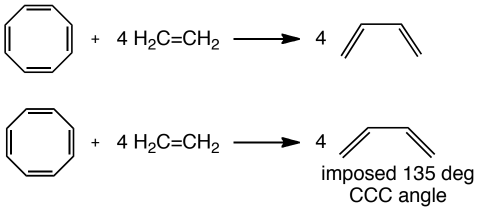
CBD is only modestly destabilized by antiaromaticity!

Flawed literature estimates –35 to –45 kcal/mol

BLW: B3LYP/6-31G*

ECRE2 for D_{4h} Cyclooctatetraene (COT)

Homodesmotic Equation
(negative aromatic stabilization energy, ASE, based on four conjugations)



+ 4 $H_2C{=}CH_2$ → 4

–14.18 kcal/mol
Flawed ASE evaluation

(too large due to the 10-11 kcal/mol D4h COT ring strain)

+ 4 $H_2C{=}CH_2$ → 4

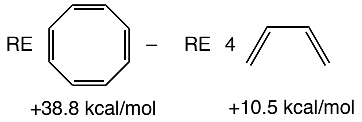
imposed 135 deg CCC angle

–3.79 kcal/mol
Better ASE evaluation

(B3LYP/6-311+G**with ZPE)

Extra cyclic resonance energy (ECRE)

ECRE2 based on models with four conjugations



RE – RE 4

+38.8 kcal/mol +10.5 kcal/mol

ECRE = **–3.2** kcal/mol

COT is very weakly destabilized by antiaromaticity!

BLW: B3LYP/6-31G*

Aromaticity: Energetic evaluations based on Hückel theory

$$E_k = \alpha + 2\beta \cos\frac{k\pi}{(n+1)}$$

$$E_k = \alpha + 2\beta \cos\frac{2k\pi}{(n)}$$

acyclic chains

k = 1, 2, 3…

cyclic systems

k = 0, ±1, ±2…*n*/2 for even *n*

n = number of atoms
E_k= energy level *k*
k = quantum number identifying the MO

Etylene: $E_1 = \alpha + \beta$

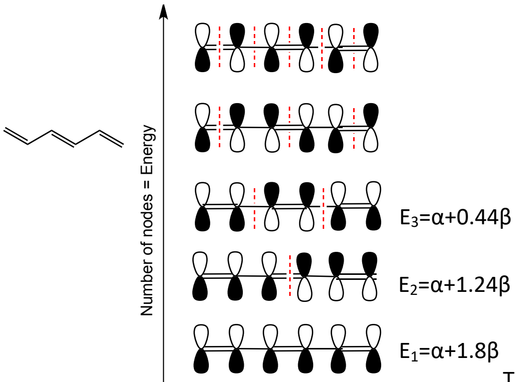
Benzene: $E_0 = \alpha + 2\beta$

$E_1 = \alpha + \beta$

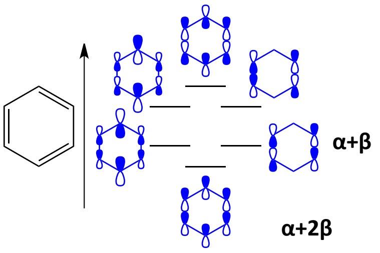
Aromaticity: Energetic evaluations based in Hückel theory

Aromatic compounds are unusually stable!

Quantum chemical demonstration using MO Theory:



4n+2 π electrons



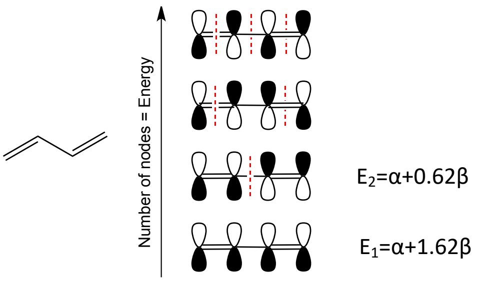
The stabilization of hexatriene bonds: 7β-6β = β

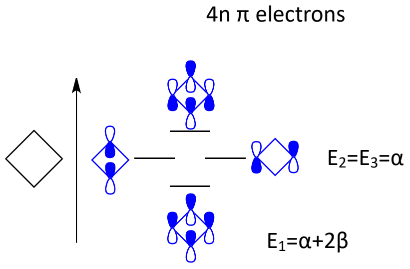
The stabilization compared to three isolated bonds: 8β- 6β = 2β

Aromaticity: Energetic evaluations based in Hückel theory

Antiaromatic compounds are unstable!

Quantum chemical demonstration using MO Theory:

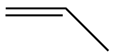
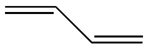
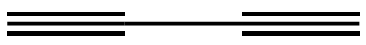
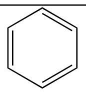




The stabilization of butadiene bonds: 4.48β-4β = 0.48β

The stabilization compared to two isolated bonds: 4β- 4β = 0

Estimate of conjugative and hyperconjugative Stabilizations

Molecule	**Conventional**	**BSE**	**BLW**
	2.5	5.7	5.4
	5.0	7.8	10.5
	3.7	14.8	9.9
	0.2	15.1	20.1
$H_3C—CH_3$	NA	NA	3.3
	36.0	64.4	64.1

Values are in kcal mol^{-1}
BSE=bond separation energy

How is Aromaticity Measured?

1. Energetic evaluations:

- Balanced chemical equations
- Modern computational methods (BLW)

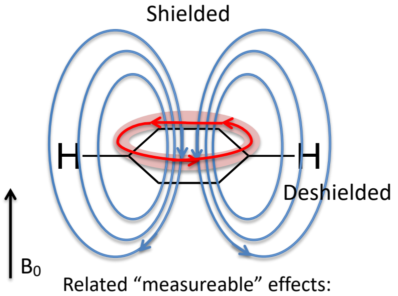
2. Magnetic evaluations:

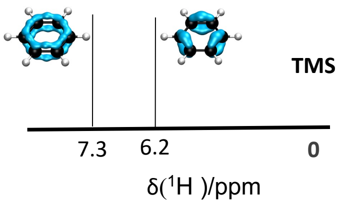
- ^{1}H NMR Chemical Shifts
- ^{7}Li NMR Chemical Shifts
- Magnetic suceptibility exaltation
- Nucleus Independent Chemical Shifts (NICS)
- ARC/ACID/Current density plots

Magnetic Aromaticity

Alternative definition: Aromatic compounds exhibits a ring current !

Pople's Ring Current Model (1956):





Related "measureable" effects:

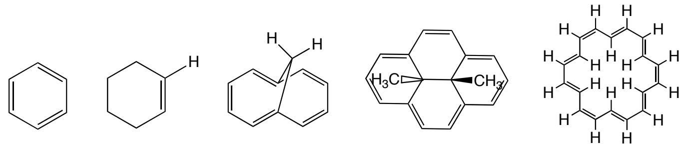
1. Downfield/upfield ^{1}H chemical shifts for H's outside/inside the ring.
2. Exalted diamagnetic susceptibility
3. Magnetic susceptibility anisotropy

Magnetic Aromaticity

- **^{1}H NMR chemical shift:** A criterion most often used experimentally.
- Due to the ring current induced by an external magnetic field, the inner protons are shifted upfield, and the outer protons are downfield-shifted.

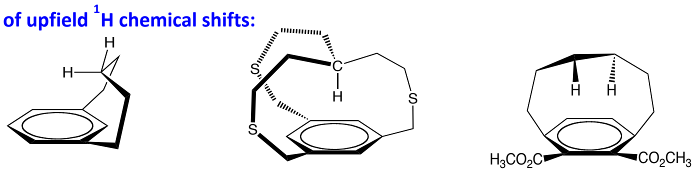
Proton NMR chemical shifts

*Olefinic: 5.6-5.8 ppm



7.3 ppm	5.6 ppm	Ring 8.14-8.67 ppm CH_3 –4.25 ppm	Ring 6.95-7.27 ppm CH_3 –0.15 ppm	Outer 9.0 ppm Inner –3.0 ppm

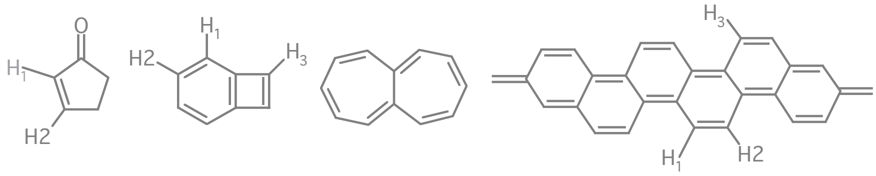
More examples of upfield ^{1}H chemical shifts:



Predicted	1.2 ppm	1.5 ppm	1.2 ppm
Observed	–0.2 ppm	–0.2 ppm	–0.4 ppm

Magnetic Aromaticity

But !!!



H_1: 6.10
H_2: 7.71
nonaromatic

H_1: 5.78
H_2: 6.26
H_3: 6.36
4-membered ring is antiaromatic

4-5
antiaromatic

H_1: 8.6
H_2: 8.1
H_3: 8.5
Nonaromatic

Magnetic Aromaticity

^{7}Li$^+$ NMR Chemical Shift

- Lithium bonding is primarily electrostatic, experimental ^{7}Li chemical shifts generally shows little variation among different compounds.
- Lithium cations, typically coordinate to the π faces of aromatic (or anti-aromatic) systems.
- This complexation results in a significant shielding (or deshielding) of the ^{7}Li NMR signal due to ring current effects.

Magnetic Aromaticity

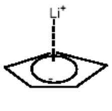
^{7}Li$^+$ NMR as an Experimental probe

(aromatic)

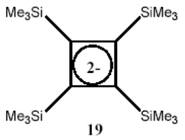
Paquette, L. A. et al, ***JACS,*** **1990**, *112*, 8776.

(Antiaromatic)

Sekiguchi et al, ***JACS***, **1991**, *113*, 7081.

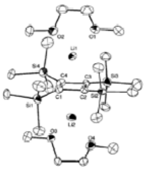


18



19

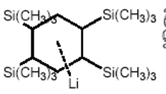
Top view
(DME is omitted)



Side view

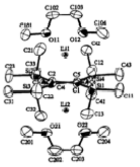
δ ^{7}LI -8.60 ppm in Et$_2$O

δ ^{7}Li -5.07 ppm in THF



20

Top view
(DME is omitted)



Side view

δ ^{7}LI 10.7 ppm in toluene

Magnetic Aromaticity

Advantages and limitations of $^{7}Li^{+}$ NMR Chemical Shift

- Experimental ^{7}Li NMR chemical shifts can be well reproduced by modern computations.
- The clear advantage of using $\delta(^{7}Li)$ as a theoretical probe lies in the possibility to provide a comparison with ^{7}Li NMR spectrum of experimental Li^{+} complexes.
- However, the number of Li^{+} complexes and therefore the utility of Li^{+} as a computational probe are rather limited.

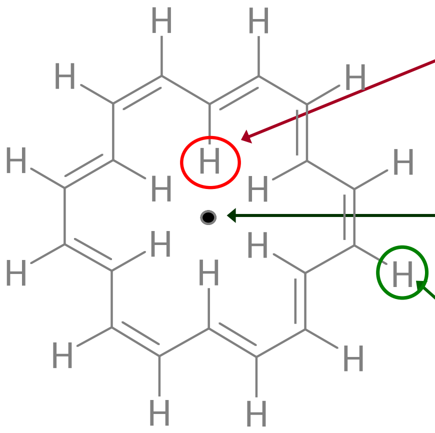
Magnetic Aromaticity

Why not use the absolute chemical shielding of a virtual nucleus to probe (the ring current effects of) aromaticity?

--Schleyer et al, *JACS*, **1996**, *118*, 6317.

Magnetic Aromaticity

NMR properties of [18]-annulenes



The six inner hydrogens resonate at δ =-3.0 ppm

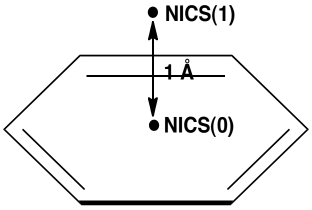
Upfield of TMS !!!

Nucleus-**I**ndependent **C**hemical **S**hifts
(-14.2 ppm**)**

The twelve outside hydrogens resonate at δ = 9.0 ppm

1996 Schleyer: Nucleus-Independent Chemical Shifts (NICS):
J. Am. Chem. Soc. 1996, *118*, 6317.

Magnetic Aromaticity



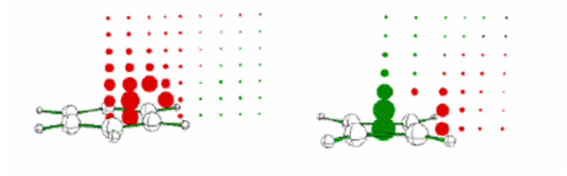
– Negative
Shielded at the ring center
diatropic ring current
(aromatic)

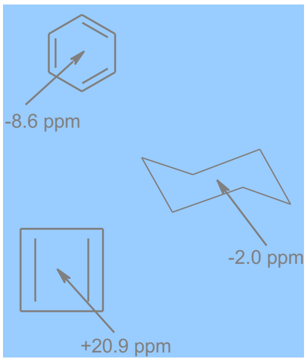
+ Positive
Deshielded at the ring center
paratropic ring current
(antiaromatic)

NICS correspond to the negative value of the magnetic shielding computed at chosen points in the vicinity of molecules. (The sign of the computed magnetic shielding is reversed to conform to the expt. NMR scale.)

Magnetic Aromaticity

Nucleus-Independent Chemical Shifts = NICS (the most used aromaticity probe).



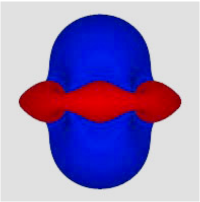


NICS are the negative of magnetic shieldings computed at non-nucleus positions Negative (diatropic, upfield); positive (paratropic, downfield)

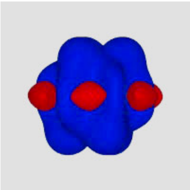
Magnetic criteria : the nucleus-independent chemical shift

Paratropic (B deshielded)
Diatropic (B shielded)

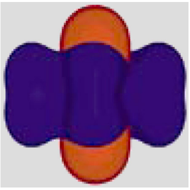
Grid of NICS points



benzene



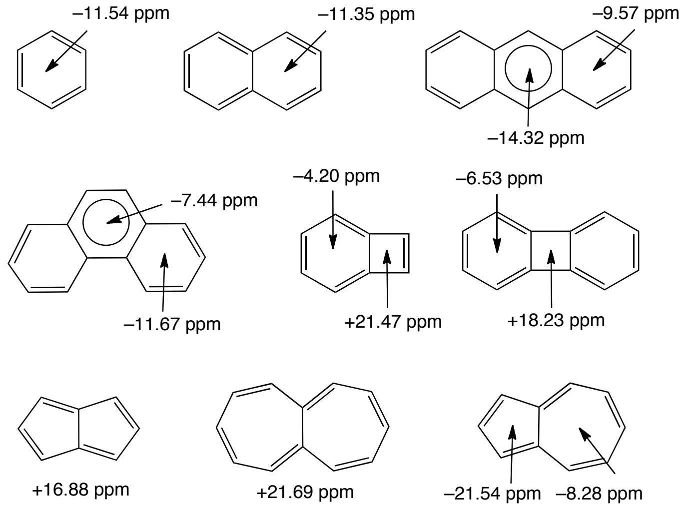
cyclohexane



cyclobutadiene

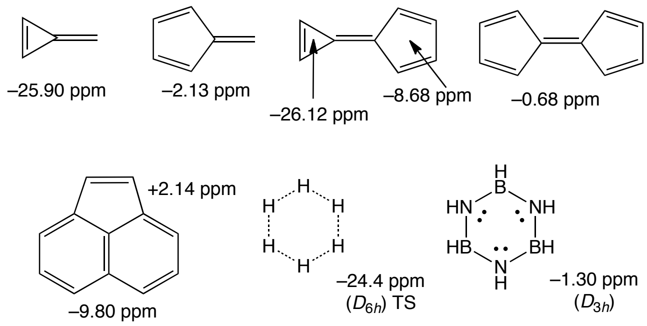
Aromatic: long-range magnetic shielding
Antiaromatic: long-range magnetic deshielding
Non-aromatic:short range magnetic response

Magnetic criteria : the nucleus-independent chemical shift

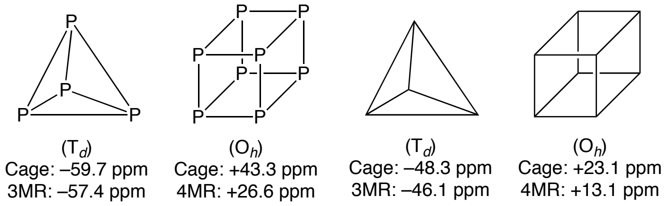


HF/6-31G*//B3LYP/6-31G*

More examples:



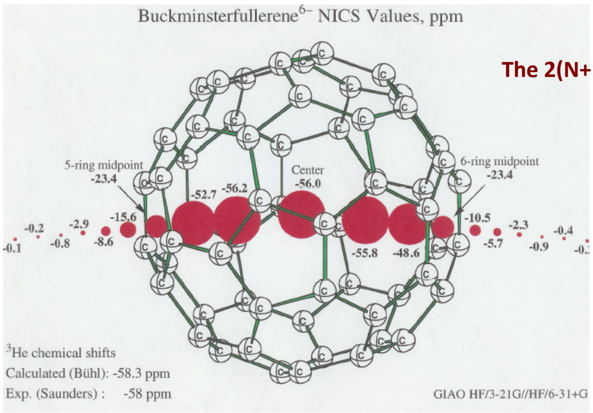
Super sigma-(anti) aromaticity



Fullerenes (Endohedral ^{3}He δ):

Cages	B3LYP/6-31G*	δ (^{3}He)
C_{60}	–2.8 ppm	–6.3 ppm
C_{60}^{6-}	–50.0 ppm	–48.7 ppm

NICS:



The $2(N+1)^2$ rule

Bühl, M.; Hirsch, A. *Chem. Rev.* 2001, *101*, 1153.

Nucleus Independent Chemical Shifts (NICS)

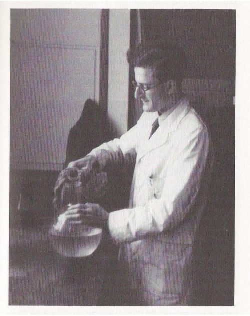
Advantages

1. Easy to compute, not level sensitive.
2. Very general (inorganic/organic rings, transition states etc.).
3. No reference needed (absolute method).
4. Proportional to “aromaticity” (does not depend on ring size).

Disadvantages

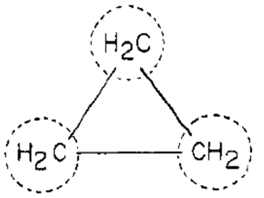
1. Not an experimentally observable.
2. The total NICS does not depend purely on the π system, but is also influenced by magnetic shieldings due to the local circulations of electrons in bonds, lone pairs, and core electrons. However, these can be minimized or removed.

σ-aromaticity

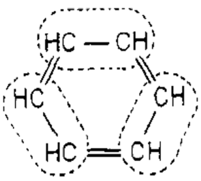


Dewar at Dyson

"Cyclopropane should be isoconjugate with benzene and hence σ-aromatic."



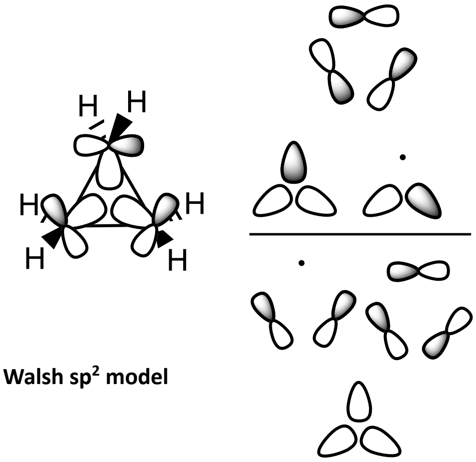
1



2

Dewar, *J. Am. Chem. Soc.* **1984**, *106*, 669

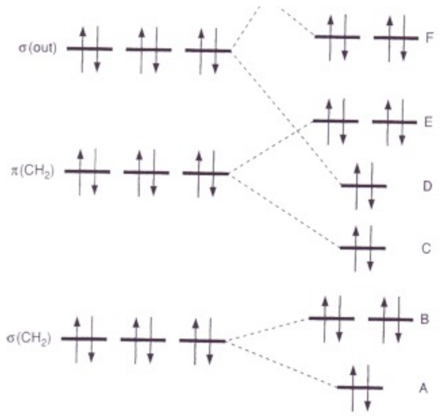
σ-aromaticity

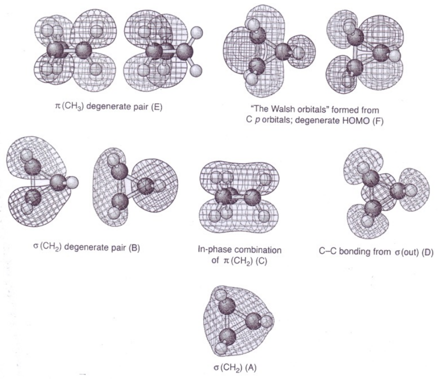


Walsh sp^2 model

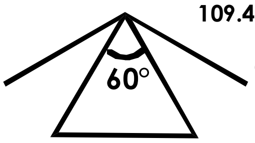
Dewar, *J. Am. Chem. Soc.* **1984**, *106*, 669

σ-aromaticity





Baeyer Stain (1885)



109.49° tetrahedral value

angle deviation

$$\begin{array}{r} 109.49^\circ \\ -\ 60^\circ \\ \hline \mathbf{49.49^\circ} \end{array}$$

ring size	angle deviation	ring strain kcal/mol
3	**49.44°**	**27.7**
4	**19.44°**	**26.8**
5	**1.49°**	**7.1**
6	**-10.56°**	**0.7**
7	**-19.13°**	**6.8**

Why is the strain in cylcopropane and cyclobutane so similar?

Dewar's original idea of "σ" aromaticity

Dewar, JACS **1984**, *106*, 669.
Cremer and Kraka, JACS, **1985**, *107*, 3800 and 3811.
Cremer and Gauss, JACS, **1986**, *108*, 7467.

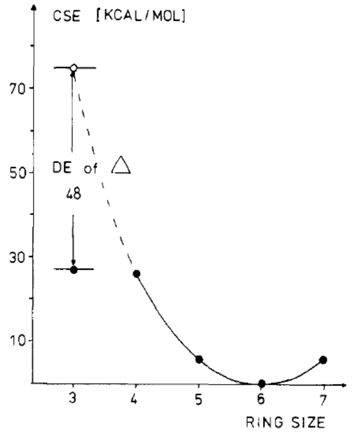
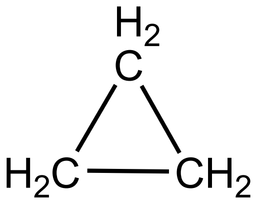


Figure 6. Dependence of conventional strain energies (CSE; ●) of cycloalkanes[41] on the size of the ring. Aromatic delocalization energy (DE) and real strain (○) of cyclopropane are given.

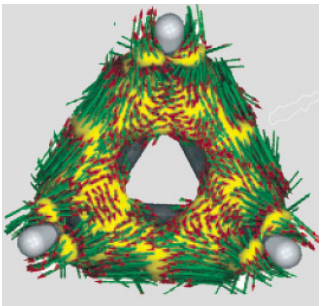


6 σ electrons
σ-aromatic

Deviation due to σ-aromaticity

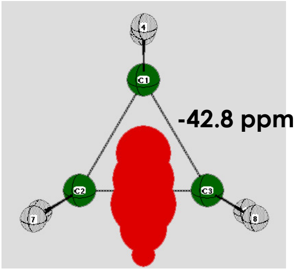
Evidence for the σ-aromaticity of cyclopropane

Diatropic current

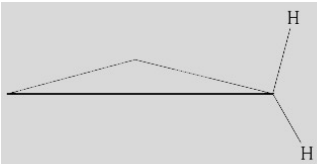


Anisotropy of Current Induced Density (ACID)
Herges *et al. Chem. Rev.* **2005**, *105*, 3758

Negative NICS



NICS
Moran, Heine, Manoharan and Schleyer *Org. Lett.* **2003**, *5*, 23.



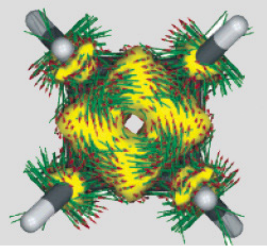
	cyclopropane	Propane (CH_2)
^{1}H δ(ppm)	0.22	1.1

The proton chemical shift appears upfield as compared to a similar acyclic molecule

Evidence for the σ-antiaromaticity of cyclobutane

- **Dewar first argued that cyclobutane should be considered as σ-antiaromaticity but predicted a small destabilization energy.**
- **The σ-antiaromaticity hypothesis is confirmed by magnetic criteria.**

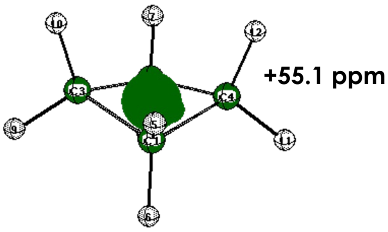
Paratropic current



ACID

Herges *et al. Chem. Rev.* **2005**, *105*, 3758.

Positive NICS$_{zz}$

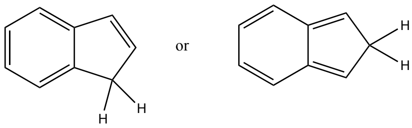


NICS

Moran, Heine, Manoharan and Schleyer *Org. Lett.* **2003**, *5*, 23.

Mini Quiz 5

1. **What is aromaticity?**
2. **Which isomer is the most stable, which is the stronger acid and why?**



3. **Identify each of the following molecules as being aromatic, antiaromatic or non-aromatic. How would you verify your prediction?**