Antiaromaticity

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Defining Antiaromaticity

• Introduced by Breslow in 1965
• Most criteria are the opposite of aromaticity
• Hückel Rule: Planar 2n \( \pi \) system
• Chemical criteria
  — High kinetic reactivity
• Energetic criteria
  — Low thermodynamic stability
    • Aromatic stabilization energy
  — Resonance energy
    • Hückel
    • Dewar
• Structural criteria:
  — Bond length Alternation (use caution)
    • HOMA
    • 2\textsuperscript{nd} order Jahn-Teller effect for singlet ground states
    • No alternation for triplet ground states
• Magnetic / NMR Criteria : Paratropic ring current
  — Nucleus independent chemical shift (NICS) > 0
  — Exaltation of magnetic susceptibility (\( \Lambda \)) > 0
  — Magnetic anisotropy
  — Various other magnetic criteria have been defined but are less commonly used

R. Breslow Chem, Eng, News, 43, 90
Origin of Aromaticity and Antiaromaticity
The Example of Cyclobutadiene

The simple (modified) Hückel approach

\[ E_{\text{loc}} = 2(\alpha + 2.0699\beta) + 2(\alpha + 0.4660\beta) = 4\alpha + 5.07\beta \]
\[ E_\pi = 4\alpha + 4\beta \]
\[ \Delta E = E_\pi - E_{\text{loc}} = -1.07\beta \]

The actual ground state

Square (D_{4h}) Triplet

Rectangular (D_{2h}) Singlet

Thermodynamic Definitions

- Low thermodynamic stability demonstrated by reference reactions esp. homoisodesmic reactions
- May be based on computational or experimental enthalpies

Ex. Hydrogen transfer from \( n \)-butane

<table>
<thead>
<tr>
<th>Hydrogen Transfer Energies, 25 °C, kcal/mol</th>
</tr>
</thead>
<tbody>
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<td>( \Delta ) ( \rightarrow ) ( \Delta )</td>
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</tbody>
</table>

ASE

\[ 3 \text{ } 3 \rightarrow \text{ } \text{ phenyl} + 3 \text{ } \text{H}_2\text{C}=\text{CH}_2 \quad (2) \]

or

\[ 3 \text{ } \text{phenyl} + \text{ cyclohexane} \rightarrow \text{ phenyl} + 3 \text{ } \text{cyclohexane} \quad (3) \]

ISE

Correction factor reduces dependence on choice of isomer

Problems: Experimental data is scarce for antiaromatic systems
Many ways to calculate
Choice of reference reactions can have large effects on the result
Separating ring strain from (anti)aromatic (de)stabilization energies is difficult

Magnetic/NMR Criteria

- Based on induced ring currents and the anisotropic NMR shielding/deshielding that they generate at or above the center of the ring or at the sides
  - Face is shielding for aromatics, deshielding for antiaromatics
  - Sides are deshielding for aromatics, shielding for antiaromatics

Experimental Methods:

**$^7\text{Li}^+$ NMR**

- Top view (DME is omitted): $\delta ^7\text{Li} = -8.60$ ppm in Et$_2$O
- Side view: $\delta ^7\text{Li} = 5.07$ ppm in THF

**$^1\text{H}$ NMR**

- Effects are modest (some studies say completely unreliable) unless the substituent is positioned inside or over the ring
  - $\delta = 5.38$
  - $\delta = 5.97$
  - $\delta = 6.47$

Drawbacks: Limited to observable Li$^+$ complexes

Exaltation of Magnetic Susceptibility

- Originally experimental method (although computation is now common)
- Compares measured (or computed) bulk magnetic susceptibility to a functional group additivity method
- Aromatics <0, antiaromatics >0
- Can be highly correlated with thermodynamics (within a series of similar compounds)
- Caveat: Magnitude depends on ring area

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**TABLE 1.** Computed bond lengths (Å) and magnetic susceptibility exaltation, Λ (ppm cgs).

<table>
<thead>
<tr>
<th>compound</th>
<th>benzene</th>
<th>borazine</th>
<th>cyclohexane</th>
<th>C5H5+(singlet)</th>
<th>C4H4+(singlet)</th>
</tr>
</thead>
<tbody>
<tr>
<td>bond length</td>
<td>1.395</td>
<td>1.431</td>
<td>1.537</td>
<td>1.355; 1.565</td>
<td>1.344; 1.565</td>
</tr>
<tr>
<td>Λ</td>
<td>-13.4</td>
<td>-1.7</td>
<td>+1.1</td>
<td>+32.6</td>
<td>+18.0</td>
</tr>
</tbody>
</table>

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NMR Criteria: Nucleus Independent Chemical Shift (NICS)

- **Computational method**
  - Includes the uncertainties associated with computation, but doesn’t require preparing highly unstable compounds.
- The chemical shift of a dummy atom is evaluated in the center of the ring (NICS(0)) or 1.0 Å above the center (NICS(1)).
- Use of a dummy atom avoids perturbing the system.
- Easily applied with reasonable computational cost, hence very popular.
- In small rings NICS(0) includes large contributions from the $\sigma$-bonds (so-called $\sigma$-aromaticity/antiaromaticity as well as simple proximity effects). NICS(1) reduces this; other schemes have been devised to partition the value into $\sigma$ and $\pi$ components.
- No dependence on ring area.

- For aromatic compounds NICS <0 (typically <-8.0 for NICS(1))
- For antiaromatic compounds NICS >0 (variable, commonly 10 -30).


*Figure 3.* The NICS grid plot of benzene and cyclobutadiene at the GIAO–B3LYP/6-311+G*/B3LYP/6-311+G* level of theory. The red and green dots denote diatropic (aromatic) and paratropic (antiaromatic) ring currents, respectively.
There is no clear agreement on which criteria are superior
Much of this is a matter of definition – There is no unambiguous definition of antiaromaticity

Cyclobutadiene

Prototypical antiaromatic molecule

Highly unstable to dimerization

Several very hindered cyclobutadienes can be crystallized

All show bond length alternation \( \Rightarrow \) singlet ground state

Triplet state (square) is very low lying (10-15 kcal/mol)

Substituted Cyclobutadienes: Preparation and Reactivity

NMR shows 2 t-butyl signals
4a and 4b: rapidly interconverting homomers at -196 °C

Observation of Cyclobutadiene 1: Ar Matrix isolation

First reports by Kranz and Chapman (independently) Photolysis at 8 K in Ar limited characterization to UV, IR

Observation of 4 IR bands (rather than 7) led to misassignment of the symmetry as $D_{4h}$ rather than $D_{2h}$

Careful reinvestigation and isotopic labeling showed one observed band was due to interaction with CO$_2$, and 4 low-intensity bands had been missed.

No ESR signals could be observed (inconsistent with a $D_{4h}$ triplet)

<table>
<thead>
<tr>
<th>Assignment</th>
<th>Calculated</th>
<th>Experimental</th>
</tr>
</thead>
<tbody>
<tr>
<td>$B_{1u}$ $\nu$(CH)</td>
<td>3299 (14.4)</td>
<td>3105 (4.2)</td>
</tr>
<tr>
<td>$B_{2u}$ $\nu$(CH)</td>
<td>3279 (6.8)</td>
<td>3073 (1.7)</td>
</tr>
<tr>
<td>$B_{1u}$ $\nu$(C=O)</td>
<td>1619 (1.0)</td>
<td>1526 (1.2)</td>
</tr>
<tr>
<td>$B_{2u}$ $\delta$i.p.(CH)</td>
<td>1293 (24.4)</td>
<td>1242 (25.1)</td>
</tr>
<tr>
<td>$B_{1u}$ $\delta$i.p.(CH)</td>
<td>1081 (0.6)</td>
<td>1028 (0.6)</td>
</tr>
<tr>
<td>$B_{2u}$ $\delta$(Ring)</td>
<td>750 (4.4)</td>
<td>719 (5.7)</td>
</tr>
<tr>
<td>$B_{3u}$ $\delta,o,o,p.$(CH)</td>
<td>560 (100)</td>
<td>569 (100)</td>
</tr>
</tbody>
</table>

Observation of Cyclobutadiene 2: Hemicarcerand Isolation

Hemicarcerand prevents dimerization
Well resolved NMR spectrum is inconsistent with a triplet ground state

Scheme 1. Thermal and photochemical transformations of α-pyron. The three frames contain reactions carried out: —— historically in solution and gas phase; —— historically in an argon matrix at 8 K; —— in the inner phase of the hemicarcerand 1, and reported here (except cyclooctatetraene formation, which occurs outside).

Current controversy: Dimethylcyclobutadiene in a Calixarene Matrix

Points of Contention

Previous studies found that the β-lactone intermediate must be irradiated <290 nm, study used 320-500 nm

Bond lengths of Me$_2$CBD$^S$ in deposited data don’t match what is shown in paper

Bond lengths of all CBD compounds are very similar when error is considered

CO$_2$ position and geometry is nearly what would be expected for the Dewar lactone

The authors stand by their data and interpretation

Comments:
Response to Comments:
Cyclopropenyl Anion

- The smallest $4n\pi$ system
- One of the first antiaromatic systems to be explored experimentally
- All data and calculations point to a ca. 5-6 kcal/mol destabilization
- Geometry is likely non-planar, consistent with the small destabilization

**Table 3. Acidity Relative to Ethene, 25 °C, kcal/mol**

<table>
<thead>
<tr>
<th>Compound</th>
<th>B3LYP</th>
<th>MP2</th>
<th>CCSD(T)</th>
<th>G2</th>
<th>obs$^32$</th>
</tr>
</thead>
<tbody>
<tr>
<td>△</td>
<td>13</td>
<td>11</td>
<td>12</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>△</td>
<td>6</td>
<td>5</td>
<td>6</td>
<td>5</td>
<td>3±2</td>
</tr>
</tbody>
</table>

Group Problem

Draw a mechanism that explains these observations.

Cyclopentadienyl Cation: A Ground State Triplet

- Triplet ground state, unlike cyclobutadiene
- Theoretical calculations predict a $D_{5h}$ symmetry (equal bond lengths)
- Calculated magnetic criteria (NICS +54, $\Lambda$ 32) support antiaromaticity of singlet state, aromaticity of the triplet state! (observed magnetic properties reflect the very strong paramagnetism of unpaired electrons which is much larger than ring current effects)

Triplet State (Anti)aromaticity

Baird argues Hückel criteria for aromaticity (and antiaromaticity) are reversed in lowest triplet states based on perturbation theory.

Thermodynamic and magnetic criteria agree relative to open-chain triplet states.

Bond lengths for aromatic triplets should also be equal.

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Planar Cyclooctatetraene Derivatives

[12]-Annulene

ISE calculations at a planar geometry place an upper limit of 9 kcal/mol of destabilization (with NICS(0) +24.5)

### Antiaromaticity in porphyrins

5 is $28 \pi$

6 is $26 \pi$

<table>
<thead>
<tr>
<th>Sample</th>
<th>Method</th>
<th>Inner N–H</th>
<th>Outer N–H</th>
<th>Inner $\beta$-H</th>
<th>Outer $\beta$-H</th>
<th>TIPS-H</th>
<th>NICS(0) (ppm)</th>
</tr>
</thead>
</table>

- **5**

- **6**


N,N-Dihydrodiazatetracene Derivatives

Net character is aromatic in all cases (no surprise)
Antiaromatic character is partially delocalized

Conclusions

- Anti-aromaticity is more challenging to define than aromaticity because molecules will adopt otherwise unfavorable geometric and electronic configurations to minimize destabilization.

- A conjugated cyclic $4n \pi$ system is required for antiaromaticity.

- Multiple criteria must be examined to determine and quantify antiaromaticity.

- In some cases e.g. $C_5H_5^+$, the energetic and magnetic criteria may not be reconcilable without a more precise definition of antiaromaticity.