Antiaromaticity

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Denmark Group Meeting

11-30-2010

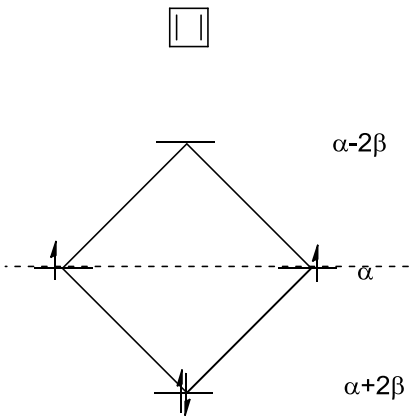
Defining Antiaromaticity

- Introduced by Breslow in 1965
- Most criteria are the opposite of aromaticity
- Hückel Rule: Planar 2n π 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
    - 2nd 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 (Λ) > 0
  - Magnetic anisotropy
  - Various other magnetic criteria have been defined but are less commonly used

R. Breslow *Chem, Eng, News*, **43**, 90
Wiberg, K. B. *Chem. Rev.* **2001,** *101,* 1317**.**
Chen, Z.; Wannere, C. S.; Corminboeuf, C.; Puchta, R.; Schleyer, P. V. R. *Chem. Rev.* **2005,** *105,* 3842.

Origin of Aromaticity and Antiaromaticity
The Example of Cyclobutadiene

The simple (modified) Hückel approach

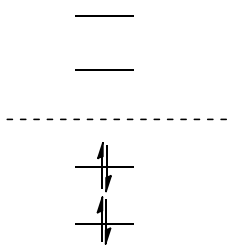


Square (D_{4h}) Triplet

$E_{loc}=2(\alpha+2.0699\beta)+2(\alpha+0.4660\beta)=4\alpha+5.07\beta$

$E_{\pi}=4\alpha+4\beta$ $\Delta E= E_{\pi}-E_{loc}=-1.07\beta$

The actual ground state



Rectangular (D_{2h}) Singlet

2nd –order Jahn-Teller distortion and electron correlation effects

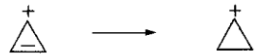
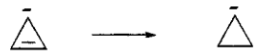
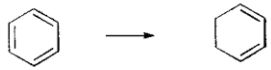
Hess, B. A.; Schaad, L. J. *J. Am. Chem. Soc.* **1971,** *93,* 305.

Thermodynamic Definitions

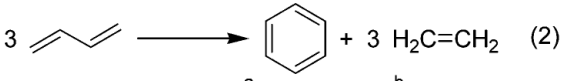
- Low thermodynamic stability demonstrated by reference reactions esp. homoisodesmic reactions
- May be based on computational or experimental enthalpies

Ex. Hydrogen transfer from *n*-butane

Hydrogen Transfer Energies, 25 °C, kcal/mol

	B3LYP	MP2	CCSD(T)	G2	obs[32]
	29	37	32	34	
	-33	-31	-31	-32	
	-39	-37	-35	-35	-49±11
	37	39	33	35	34.0±0.4

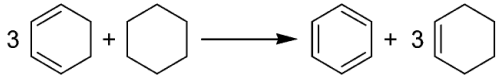
ASE



(2)

-21.5[a] (-20.6/-22.8)[b] kcal/mol (expt)

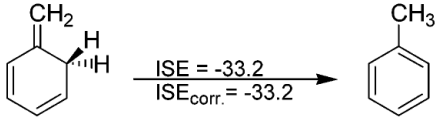
or



(3)

-30.5[a] (-28.8)[b] kcal/mol (expt)

ISE



2a (C_1) **1** (C_s)

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

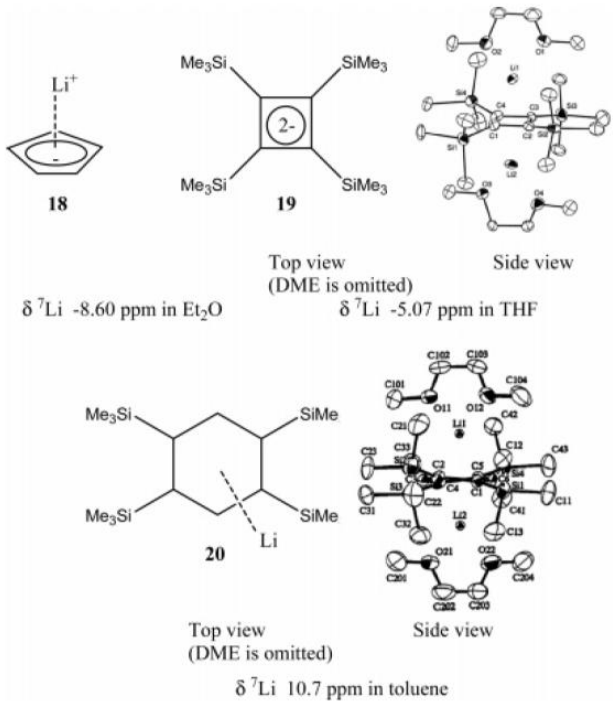
Wiberg, K. B. *Chem. Rev.* **2001,** *101,* 1317**.**
Schleyer, P. v. R.; Pühlhofer, F. *Org. Lett.* **2002***, 4*, 2873.

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

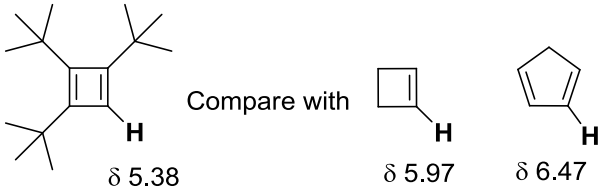
Experimental Methods:

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



Drawbacks: Limited to observable Li^{+} complexes

^{1}H NMR



Effects are modest (some studies say completely unreliable) unless the substituent is positioned inside or over the ring

Chen, Z.; Wannere, C. S.; Corminboeuf, C.; Puchta, R.; Schleyer, P. v. R. *Chem. Rev.* **2005,** *105,* 3842.

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

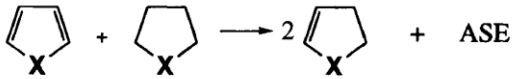
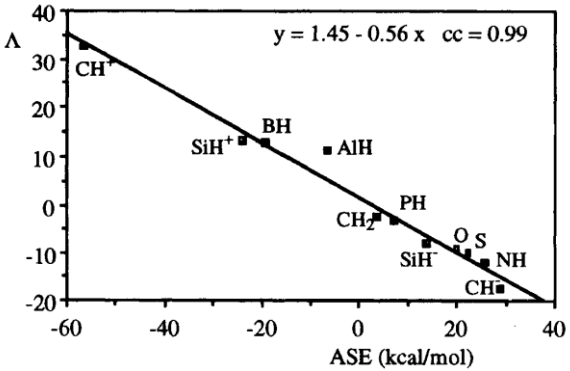


TABLE 1. Computed bond lengths (Å) and magnetic susceptibility exaltation, Λ (ppm cgs).

compound	benzene	borazine	cyclohexane	$C_5H_5^+$(singlet)	cyclobutadiene (singlet)
bond length	1.395	1.431	1.537	1.355; 1.565	1.344; 1.565
Λ	-13.4	-1.7	+1.1	+32.6	+18.0



Schleyer, P. v. R.; Jiao, H. *Pure Appl. Chem.* **1996**, *68*, 209.

NMR Critera: 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 σ-bonds (so called σ-aromaticity/antiaromaticity as well as simple proximity effects) NICS(1) reduces this, other schemes have been devised to partition the value into σ and π 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)

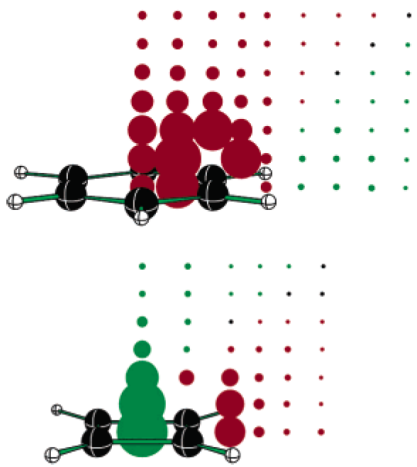
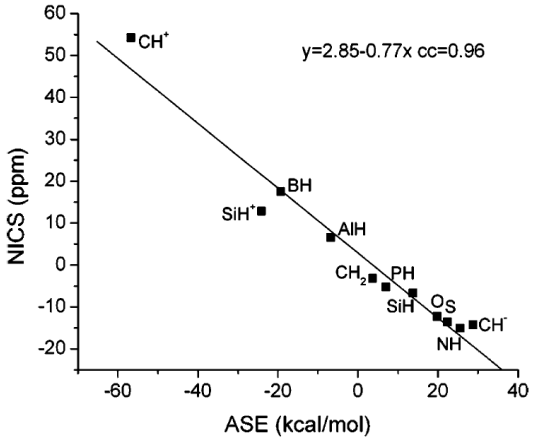


Figure 3. The NICS grid plot of benzene and cyclobutadiene at the GIAO−B3LYP/6-311+G*//B3LYP/6-311+G* level of theory. The red and green dots denote diatropic (aromatic) and paratropic (antiaromatic) ring currents, respectively.



Chen, Z.; Wannere, C. S.; Corminboeuf, C.; Puchta, R.; Schleyer, P. v. R. *Chem. Rev.* **2005,** *105,* 3842.
Schleyer, P. v. R.; Maerker, C.; Dransfeld, A.; Jiao, H.; Hommes, N. J. R. V. E. *J. Am. Chem. Soc.* ***1996****, 118*, 6317.

Criteria Compared

Table 6. The Difference between Shortest and Longest [4*n*]Annulene Bond Length (Δr), Syn−Anti Corrected[150] Isomerization Stabilization Energies (kcal/mol) Evaluated by the Schleyer−Pühlhofer Method (ISE_{Spcorr}, Scheme 2), Magnetic Susceptibility Exaltations (Λ, cgs·ppm), and Averaged Inner (δ H_{inner}) and Outer (δ H_{outer}) ^1H NMR Chemical Shifts of the Antiaromatic [4*n*]Annulenes in Planar Bond Alternating Geometries[a]

[*n*]	symm	Δr (Å)	ISE_{Spcorr}	Λ	NICS(0)	$NICS(0)_\pi$	δ H_{inner}	δ H_{Outer}
6	D_{6h}	0.000	33.2	−17.6	−8.8	−20.7		7.5
4	D_{2h}	0.243	−35.2	13.0	20.8	−0.2		5.9
8	D_{4h}	0.130	0.6	79.4	35.9	28.4		2.0
12	D_{2h}	0.174	−9.0	98.8	24.5	19.2	32.4	2.8
16	D_{2h}	0.129	−6.1	187.7	23.4	20.2	33.1	0.9
20	D_{2h}	0.110	−4.8	296.6	21.5	19.5	33.3	1.4
24	C_s	0.087	−3.1	407.3	19.3	18.1	33.0	−1.9

[a] ISE_{Spcorr} was evaluated at B3LYP/6-31G*+ ZPE (B3LYP/6-31G*) + syn−anti corrections (Scheme 2). $\Lambda = \chi_M - \chi'_M$. Magnetic susceptibilities of parent [4*n*]annulenes, χ_M, were calculated at CSGT-B3LYP/6-31+G*//B3LYP/6-31+G*; magnetic susceptibilities of nonaromatic models, χ'_M, were evaluated using increments. NICS(0), $NICS(0)_\pi$, H_{outer}, and H_{inner} were calculated at IGLO/TZ2P//B3LYP/6-31G*.

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

Chen, Z.; Wannere, C. S.; Corminboeuf, C.; Puchta, R.; Schleyer, P. v. R. *Chem. Rev.* **2005,** *105,* 3842.

Cyclobutadiene

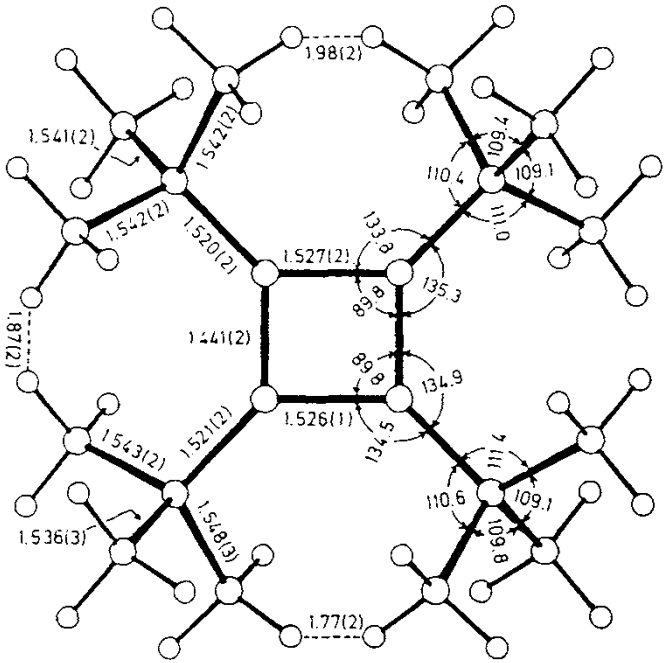
Prototypical antiaromatic molecule

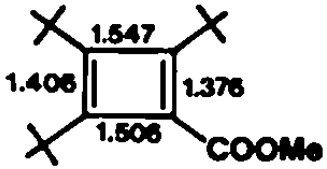
Highly unstable to dimerization

Several very hindered cyclobutadienes can be crystallized

All show bond length alternation ∴ singlet ground state

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





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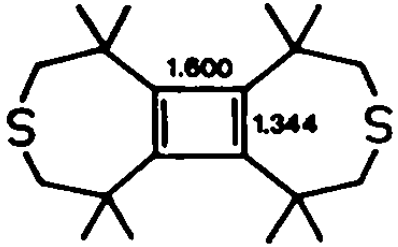
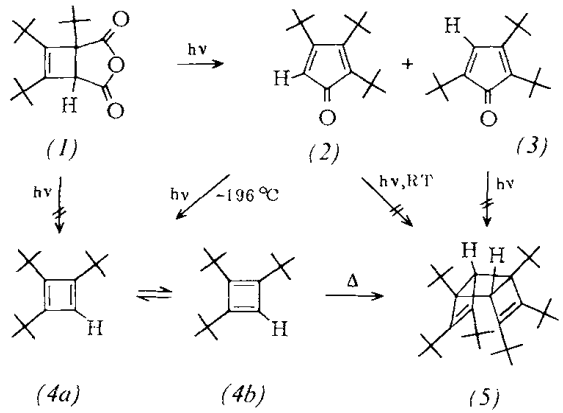
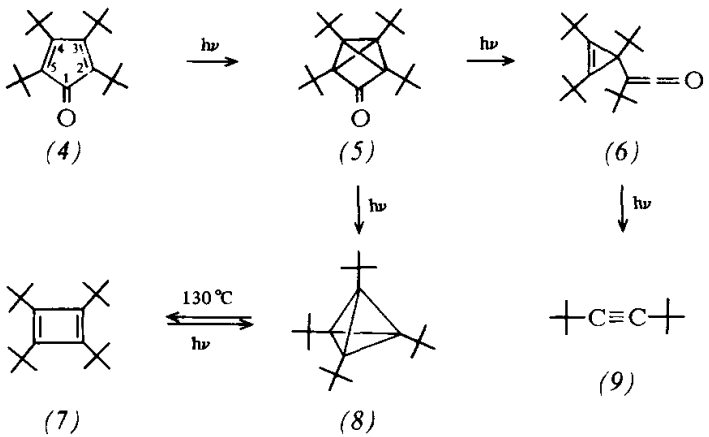


7

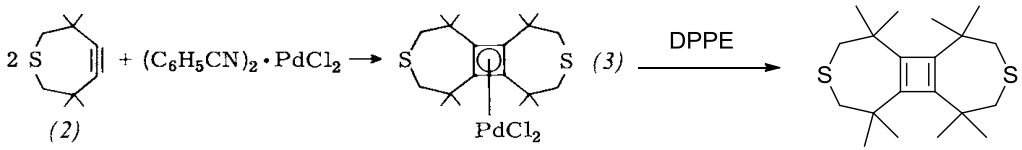
Maier, G. *Angew. Chem. Int. Ed. Engl.* **1974**, *13*, 425.
Balley, T.; Masamune, S. *Tetrahedron* **1980,** *36*, 343.

Substituted Cyclobutadienes:Preparation and Reactivity



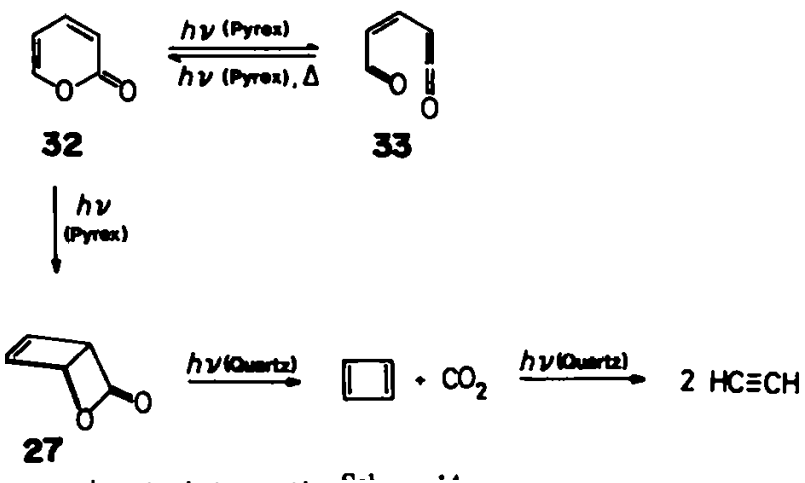


NMR shows 2 *t*-butyl signals
4a and 4b: rapidly interconverting homomers at -196 °C



Maier, G.; Alzerreca, A. *Angew. Chem.Int. ed. Engl.* **1973***, 12*, 1015.
Maier, G; Pfriem, S.; Schaefer, U.; Matusch, R. . *Angew. Chem.Int. ed. Engl.* **1978**, 17, 520.
Kimmling, H.; Krebs, A. . *Angew. Chem.Int. ed. Engl.* **1972** 932.
Irnagaringer, H; Rodewald H; . *Angew. Chem.Int. ed. Engl.* **1974** 740

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.

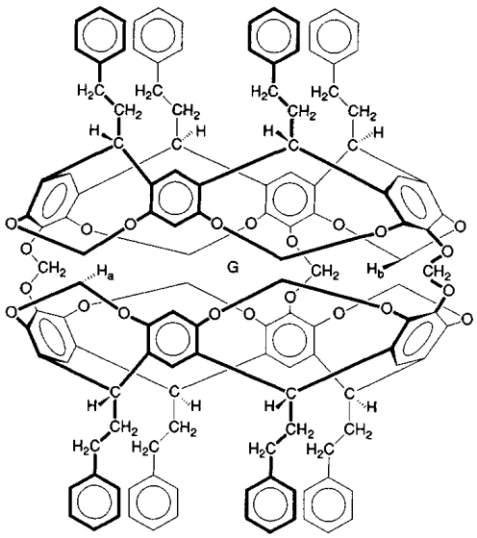
No ESR signals could be observed (inconsistent with a D_{4h} triplet)

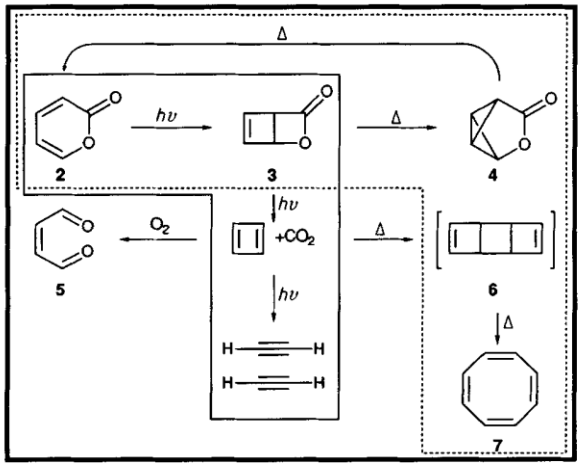
Table 2. Comparison of experimental [135] and calculated [177c] IR spectrum of D_{2h}-cyclobutadiene [cm^{-1}] (E, relative intensity).

Assignment		Calculated		Experimental	
B_{1u}	ν(CH)	3299	(14.4)	3105	(4.2)
B_{2u}	ν(CH)	3279	(6.8)	3073	(1.7)
B_{1u}	ν(C=C)	1619	(1.0)	1526	(1.2)
B_{2u}	δ*i.p.*(CH)	1293	(24.4)	1242	(25.1)
B_{1u}	δ*i.p.*(CH)	1081	(0.6)	1028	(0.6)
B_{2u}	δ(Ring)	750	(4.4)	719	(5.7)
B_{3u}	δ*o.o.p.*(CH)	560	(100)	569	(100)

Chapman, O. L.; McIntosh, C. L.; Pacansky, J. *J. Am. Chem. Soc.* **1973**, *95*, 614.
Lin, C. Y.; Krantz, a. *J. Chem. Soc., Chem. Commun.* **1972**, 1111.
Balley, T.; Masamune, S. *Tetrahedron* **1980,** *36*, 343.

Observation of Cyclobutadiene 2: Hemicarcerand Isolation





Scheme 1. Thermal and photochemical transformations of α-pyrone. 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).

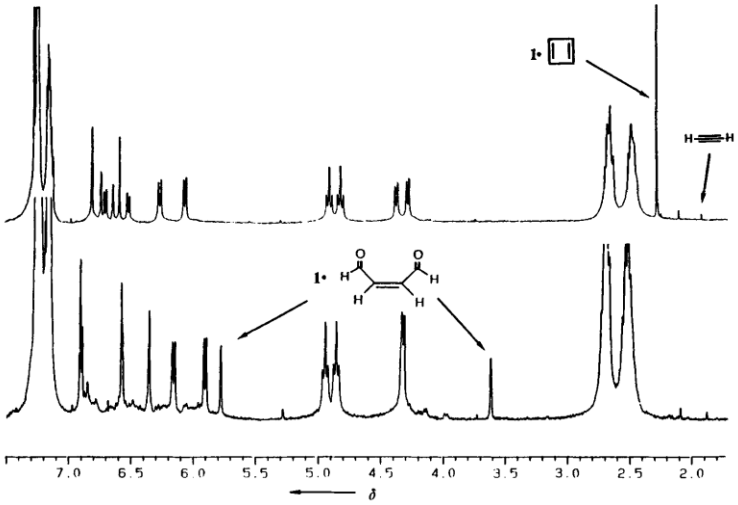


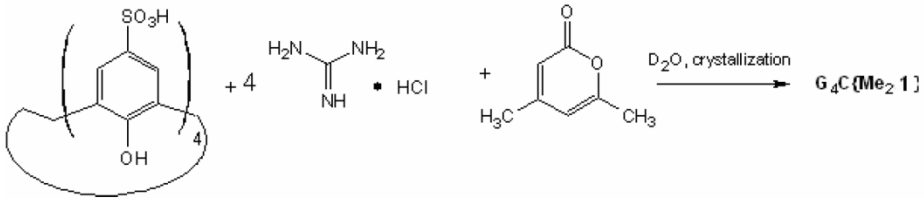
Fig. 2. ^{1}H NMR spectra (500 MHz, $CDCl_3$, 60°C) of hemicarceplexes **1** · $(CH)_4$ and **1** · (*Z*)-OHCCH=CHCHO.

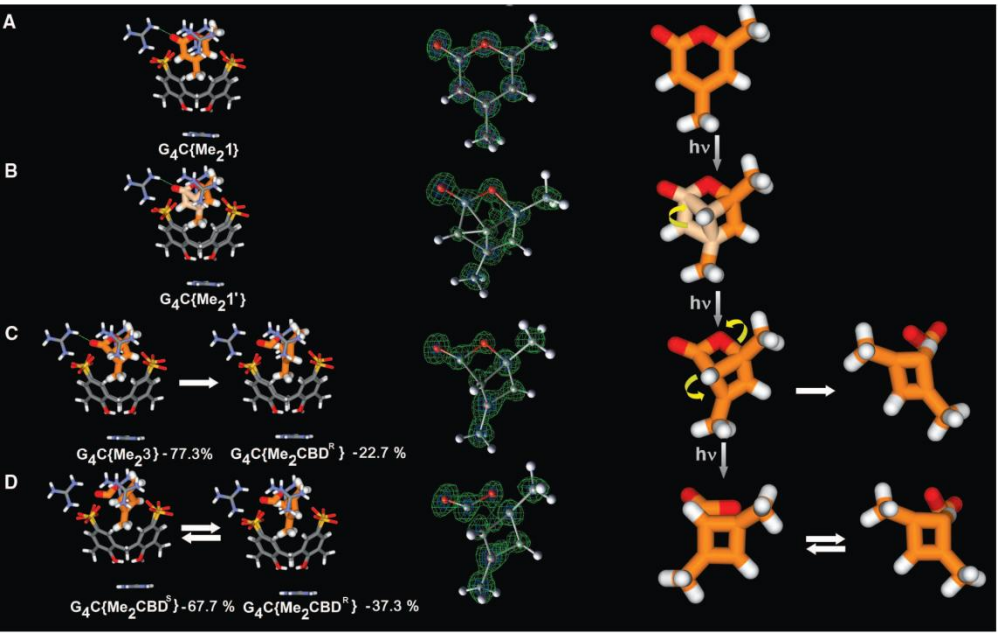
Hemicarcerand prevents dimerization

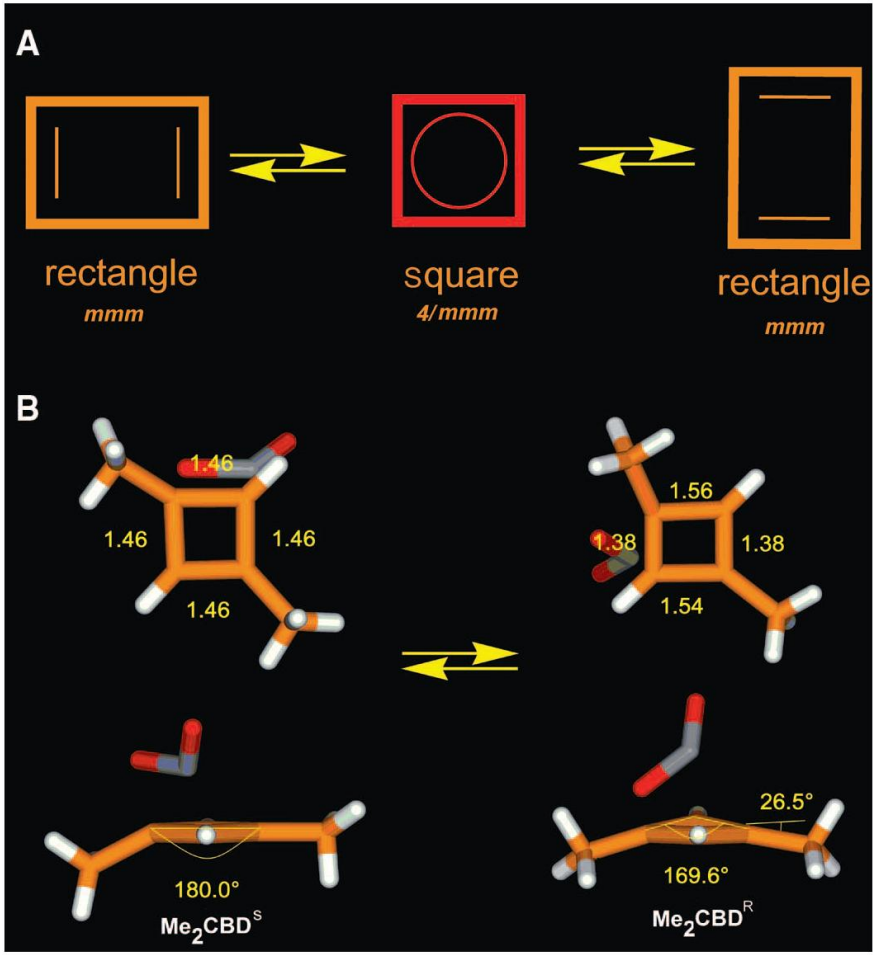
Well resolved NMR spectrum is inconsistent with a triplet ground state

Cram, D. J.; Tanner, M. E.; Thomas, R. *Angew. Chem. Int. Ed. Engl.* **1991***, 30,* 1024.

Current controversy: Dimethylcyclobutadiene in a Calixarene Matrix

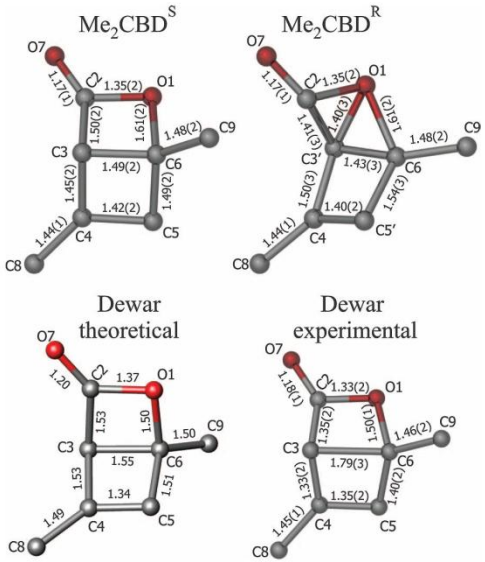


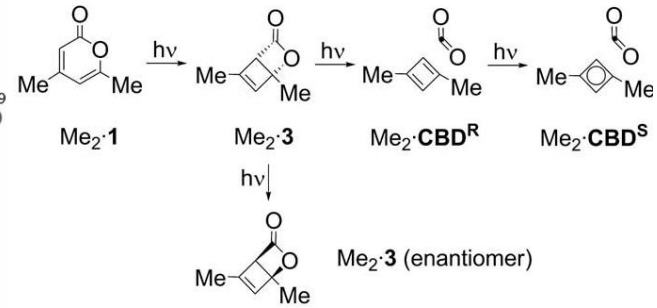




Legrand, Y.-M.; van Der Lee, A.; Barboiu, M. *Science* **2010**, *329*, 299.

Points of Contention





Scheme 1. Reaction proposed by Legrand *et al.* (1 (top) and reinterpretation presented here (bottom) The host, guanidinium-sulfonate-calixarene (G_4C) is not displayed.

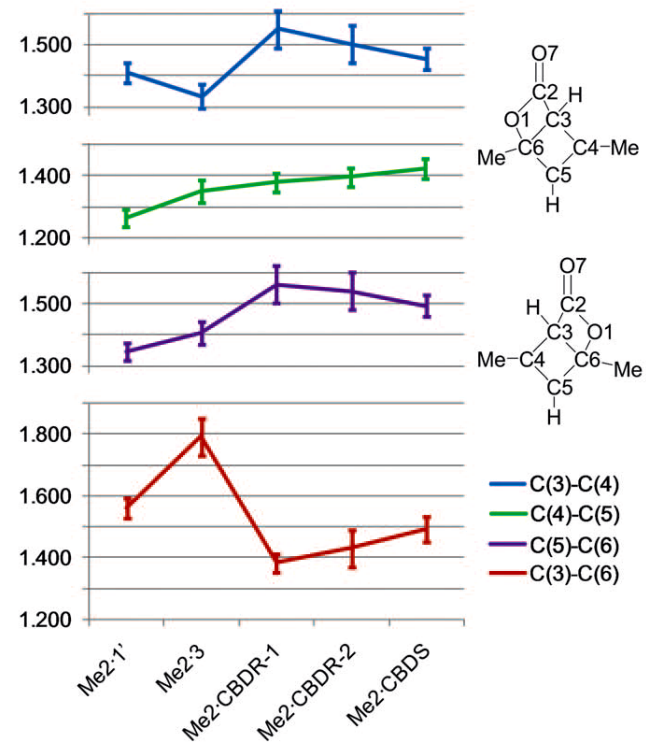


Fig. 2. Distances between endocyclic carbon atoms [data from CSD 764866 to 764868 (*1*)]. Error bars, 4 SD.

- Previous studies found that the β-lactone intermediate must be irradiated <290 nm, study used 320-500 nm
- Bond lengths of Me_2CDB^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
- CO2 position and geometry is nearly what would be expected for the Dewar lactone
- The authors stand by their data and interpretation

Comments :

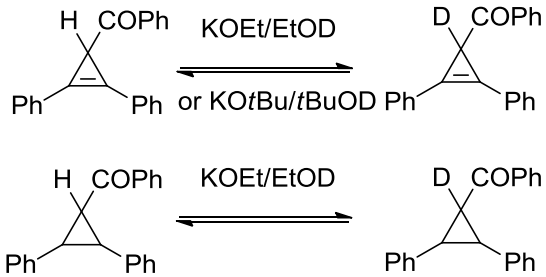
Alabugin, I. V.; Gold, B.; Shatruk, M.; Kovnir, K. *Science* **2010**, *330*, 1047.

Scheschkewitz, D. *Science* **2010**, *330,* 1047.

Response to Comments:

Legrand, Y.-M.; van der Lee, a.; Barboiu, M. *Science* **2010**, *330*, 1047.

Cyclopropenyl Anion



$k_{cyclopropyl} / k_{cyclopropenyl} \cong 6000$

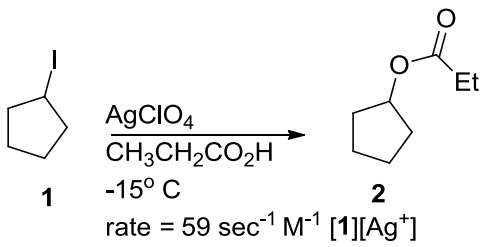
Table 3. Acidity Relative to Ethene, 25 °C, kcal/mol

Compound	B3LYP	MP2	CCSD(T)	G2	obs[32]
	13	11	12	11	
	6	5	6	5	3±2

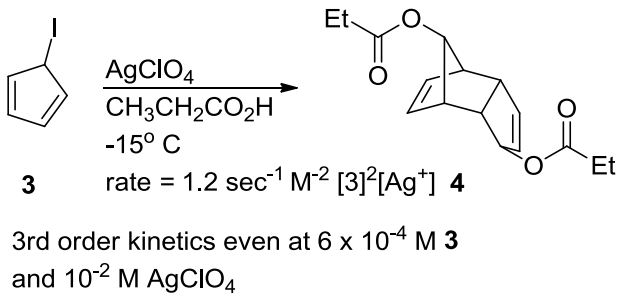
- The smallest 4n π system
- One of the first antiaromatic systems to be explored experimentally
- All data and calculations point to a ca. 5-6 kcal/mol destabilization
- Geometry is likely non-planar, consistent with the small destabilization

Breslow, R.; Brown, J.; Gajewski, J. J. *J. Am. Chem. Soc.* **1967***, 89*, 4383.
Wiberg, K. B. *Chem. Rev.* **2001,** *101,* 1317**.**

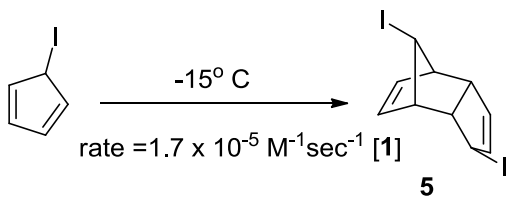
Group Problem



Draw a mechanism that explains these observations

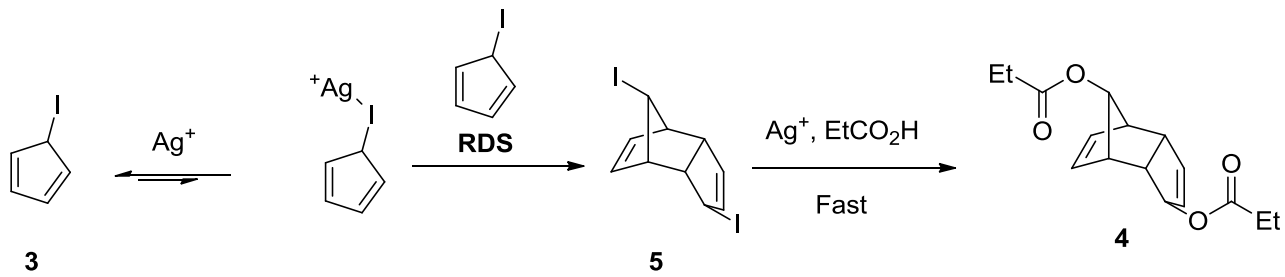


3rd order kinetics even at 6 x 10^{-4} M **3** and 10^{-2} M $AgClO_4$

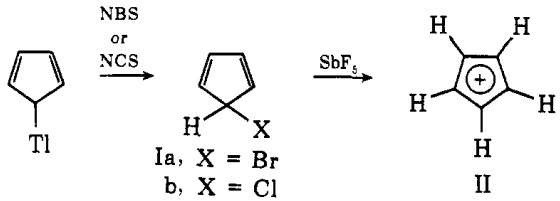


Breslow, R.; Hoffman, J. M. *J. Am. Chem. Soc.* **1972**, *94,* 2110

Solution



Cyclopentadienyl Cation: A Ground State Triplet



ASE estimated -31 kcal/mol

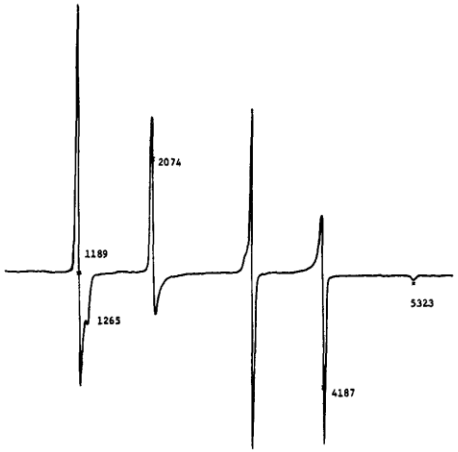
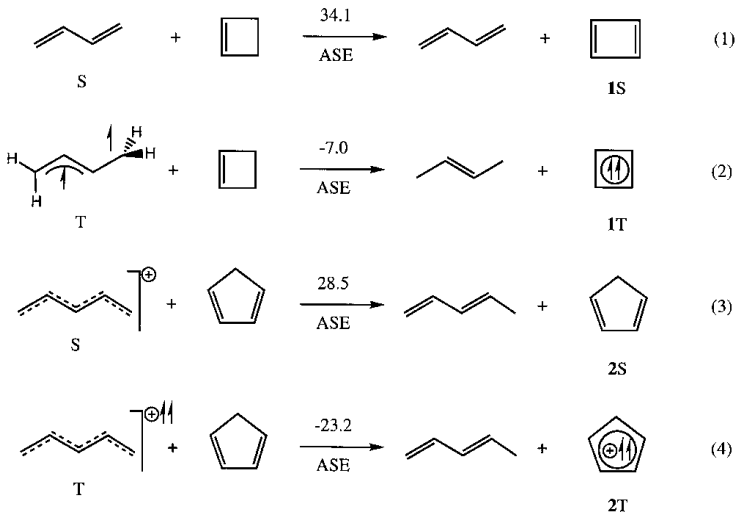


Figure 1. The epr spectrum of $C_5H_5^+$ at 78°K in a matrix of SbF_5.

- Triplet ground state, unlike cyclobutadiene
- Theoretical calculations predict a D_{5h} symmetry (equal bond lengths)
- Calculated magnetic criteria (NICS +54, Λ 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)

Saunders: M.; Berger, R.; Jaffe, A.; McBride, J. M.; O'Neill, J.; Breslow, R.; Hoffman, J. M., Jr.; Perchonock, C.; Wasserman, E.; Hutton, R. S.; Kuck, V. J. *J. Am. Chem. Soc.* **1973**, *95*, 3017.
Jiao, H.; Schleyer, P. V. R.; Mo, Y.; McAllister, M. a.; Tidwell, T. T. *J. Am. Chem. Soc.* **1997,** *119,* 7075.

Triplet State (Anti)aromaticity



Scheme 1. Aromatic stabilization energies [kcal mol^{-1}] evaluated from isogyric equations at the CCSD(T)/cc-pVDZ level of theory.

Table 2. Nucleus-independent chemical shifts (NICS), magnetic susceptibilities, and magnetic susceptibility exaltations (Λ) for singlet and triplet species calculated at the GIAO-SCF level.[a]

Compound		Point group	Electronic state	$\delta(^1H)$[b, c]	NICS[c]	Magnetic suscept.[c]	Λ[c]
C_4H_4	**1S**	D_{2h}	$^1A_{1g}$	5.9	27.6	−7.7	12.5[d]
	1T	D_{4h}	$^3A_{2g}$	7.4	−5.3	−22.8	−3.5[e]
$C_5H_5^+$	**2S**	C_{2v}	$^1A_1$	5.2	49.2	4.8	30.5[f]
	2T	D_{5h}	$^3A_1'$	8.0	−4.5	−28.4	−3.3[g]
$C_6H_6^{2+}$	**3S**	C_s	$^1A'$	7.0	11.0	−13.7	
	3T	D_{3d}	^3B_g	8.5	−1.5	−28.2	
$C_7H_7^-$	**4S**	C_2	^1A	3.1	42.9	24.7	
	4T	D_{7h}	$^3A_1'$	7.7	−11.9	−64.5	
C_8H_8	**5S**	D_{2d}	$^1A_1$	6.0	3.0	−46.2	
	5T	D_{8h}	$^3A_{2u}$	8.1	−12.4	−81.6	
TS[h]		D_{4h}	$^1A_{1g}$	3.1	30.1	4.1	60.4[i, j]
$C_9H_9^+$	**6S**	C_s	$^1A'$	1.0	9.1		
	6T[k]	C_s	$^3A'$	8.6	−9.7		
C_5H_5 radical		C_{2v}	$^2A_1$	6.5	2.6	−30.6	
benzene		D_{6h}	$^1A_{1g}$	7.8	−9.7[i]	−51.3	−13.4[i, j]

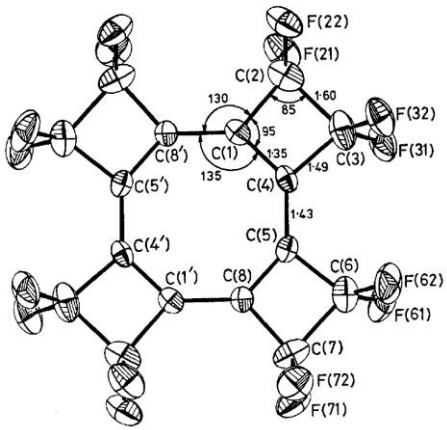
Table 1. Singlet–triplet (S→T) adiabatic transitions for $4n\pi$-electron annulenes calculated at B3LYP and CCSD(T) ab initio levels.[a]

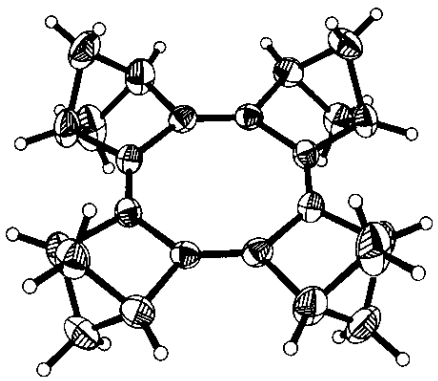
Compound	Transition	B3LYP/ 6–311+G(d,p)	CCSD(T)/cc-pVDZ// B3LYP/6–311+G(d,p)
C_4H_4	**1S**→**1T**	5.9	11.5[b]
C_4H_6	S→T	54.2	57.0
$C_5H_5^+$	**2S**→**2T**	−10.5	−7.6
$C_5H_7^+$	S→T	44.1	47.1
$C_6H_6^{2+}$	**3S**→**3T**	−2.3	0.5
$C_7H_7^-$	**4S**→**4T**	−2.6	−1.0
C_8H_8	**5S**→**5T**[c]	15.5	24.3
$C_9H_9^+$	**6S**→**6T**[d]	−1.2	–

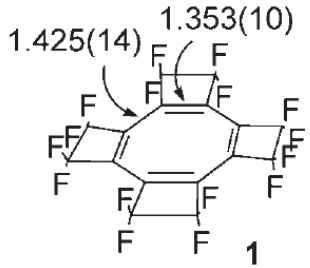
- Baird argues Hückel criteria for aromaticity (and antiaromaticity) are reversed in lowest triplet states based on perturbation theory
- Thermodynamic and magnetic criteria agree *relative to open-chain triplet states*
- Bond lengths for aromatic triplets should also be equal.

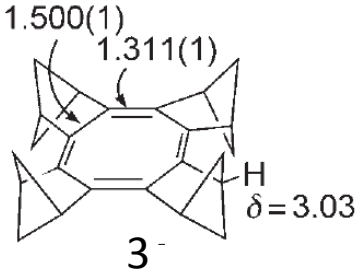
Jiao, H.; Schleyer, P. V. R.; Mo, Y.; McAllister, M. a.; Tidwell, T. T. *J. Am. Chem. Soc.* **1997,** *119,* 7075.
Baird, N. C. *J. Am. Chem. Soc.* **1972**, *94*, 4941.

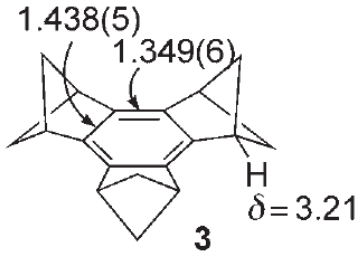
Planar Cyclooctatetraene Derivatives











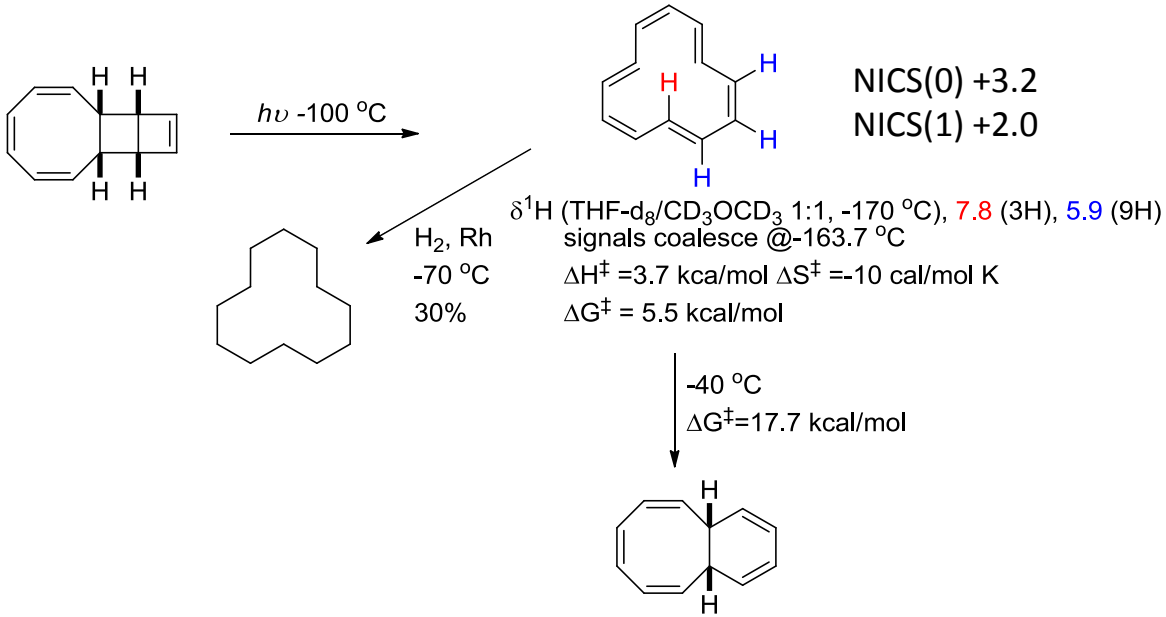
compd	ASE[b]	Λ[c]	NICS[d]
benzene	−34.1	−16.2	−9.7
2	−34.0	−8.4	−8.0
planar COT (D_{4h})	2.9	61.1	27.2
3	4.1	17.2	10.6

[a] B3LYP/6-31G* geometries were employed. [b] B3LYP/6-311+G**.[17] [c] CSGT-HF/6-31+G**.[17] [d] GIAO−HF/6-31+G**.

2

Einstein, F. W. B.; Willis, A. C. *J. Chem. Soc., Chem. Commun.* **1981***, 386*, 526.
Matsuura, A.; Komatsu, K. *J. Am. Chem. Soc.* **2001,** *123*, 1768.
Nishinaga, T.; Uto, T.; Inoue, R.; Matsuura, A.; Treitel, N.; Rabinovitz, M.; Komatsu, K. *Chem.--Eur. J.* **2008***, 14,* 2067.

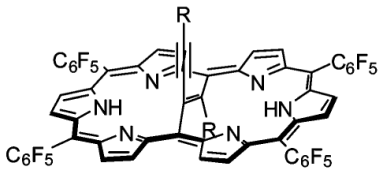
[12]-Annulene



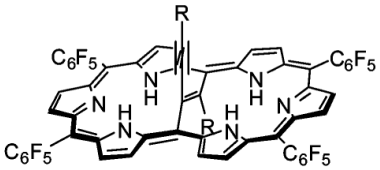
- ISE calculations at a planar geometry place an upper limit of 9 kcal/mol of destabilization (with NICS(0) +24.5)

Othe, J. F. *Tetrahedron Lett.* **1970***,* 61.
Othe, J. F.; Gilles, J. M. *Tetrahedron Lett.* **1970,** 67.
Castro, C.; Karney, W. L.; Vu, C. M. H.; Burkhardt, S. E.; Valencia, M. A. *J. Org. Chem.* **2005***, 70*, 3602.

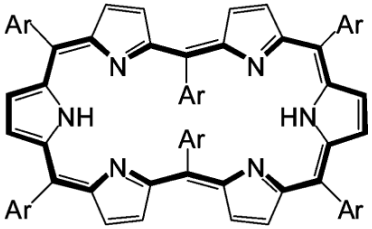
Antiaromaticity in porphyrins



5 : R = TIPS



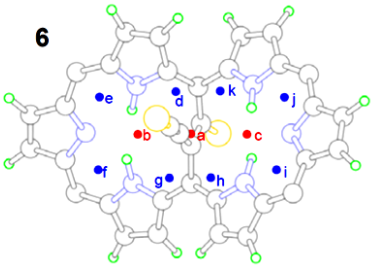
6 : R = TIPS



5 is 28 π
6 is 26 π

sample	method	chemical shift (ppm) [no. of H] inner N−H	outer N−H	inner β-H	outer β-H	TIPS-H	NICS(0) (ppm)[f]
5	exptl	−[e] [2]	–	–	8.56 [2] 8.72 [6] 9.92 [2] 10.01 [2]	−1.2 [21] −1.67 [18] −2.63 [3]	
	calcd	−1.9 [1] −2.0 [1]	–	–	8.7 to 10.6 [12]	−0.30 to −5.9 [42]	−13.8
6	exptl	26.96 [2] 27.32 [2]	–	–	3.19 to 3.74 [12]	3.26 [18] 3.46 [3] 4.34 [18] 5.33 [3]	
	calcd	34.7 to 38.9 [4]	–	–	0.74 to 2.5 [12]	2.6 to 14.2 [42]	18.7

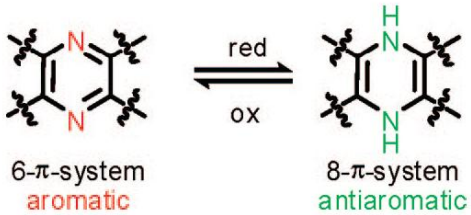
6

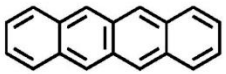


label	NICS(0) (ppm)	centroid	Bq-atom
a	18.7	36 atoms (1-36)	163Bq
b	26.9	14 atoms (1-7, 13-19)	164Bq
c	22.7	14 atoms (19-25, 31-36, C1)	165Bq
d	17.0	4 atoms (C37, C1, C2, N6)	173Bq
e	33.0	4 atoms (N6, C5, C8, N12)	166Bq
f	35.4	4 atoms (N12, C11, C14, N18)	167Bq
g	18.6	4 atoms (N18, C17, C19, C38)	168Bq
h	11.8	4 atoms (C38, C19, C20, N24)	169Bq
i	30.0	4 atoms (N24, C23, C26, N30)	170Bq
j	31.1	4 atoms (N30, C29, C32, N36)	171Bq
k	12.0	4 atoms (N36, C35, C1, C37)	172Bq

Yoon, M.-C.; Cho, S.; Suzuki, M.; Osuka, A.; Kim, D. *J. Am. Chem. Soc.* **2009**, *131*, 7360.
Shin, J.-Y.; Kim, K. S.; Yoon, M.-C.; Lim, J. M.; Yoon, Z. S.; Osuka, A.; Kim, D. *Chem. Soc. Rev.* **2010**, *39*, 2751.

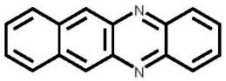
N,N-Dihydrodiazatetracene Derivatives





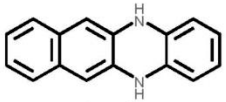
tetracene

LMO					
Remote	-1.6	-3.4	-	-	$\Sigma NICS(0)_{1zz}$ = -10.0
Local	-28.4	-39.2	-	-	$\Sigma NICS(0)_{1zz}$ = -135.2
Total	-30.0	-42.6	-	-	$\Sigma NICS(0)_{1zz}$ = -145.2
CMO					
Total	-29.6	-42.1	-	-	$\Sigma NICS(0)_{1zz}$ = -143.4



7

LMO					
Remote	-2.0	-3.8	-3.6	-2.8	$\Sigma NICS(0)_{1zz}$ = -12.2
Local	-28.0	-39.1	-38.2	-27.9	$\Sigma NICS(0)_{1zz}$ = -133.2
Total	-30.0	-42.9	-41.8	-30.4	$\Sigma NICS(0)_{1zz}$ = -145.4
CMO					
Total	-30.0	-42.5	-41.1	-30.1	$\Sigma NICS(0)_{1zz}$ = -144.0



planar **8**

LMO					
Remote	7.9	15.1	2.1	15.7	$\Sigma NICS(0)_{1zz}$ = 40.8
Local	-35.1	-29.9	27.6	-33.4	$\Sigma NICS(0)_{1zz}$ = -70.8
Total	-27.2	-14.8	29.7	-17.7	$\Sigma NICS(0)_{1zz}$ = -30.0
CMO					
Total	-26.3	-14.2	31.3	-16.7	$\Sigma NICS(0)_{1zz}$ = -25.9

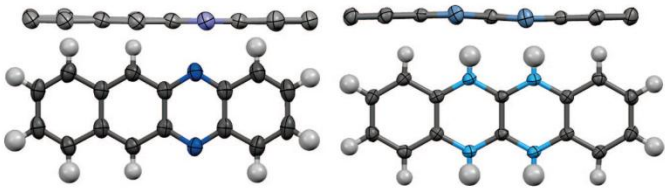


Figure 4. Molecular structures of **7** (left) and of **8** (right). The top view displays the planarity of both **7** and **8**. The four powder blue colored positions in **8** contain overall two nitrogen atoms in either the 5,12- or the 6,11-position as a consequence of the disorder of **8**, where it can take on two different orientations.

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

Miao, S.; Brombosz, S. M.; Schleyer, P. V. R.; Wu, J. I.; Barlow, S.; Marder, S. R.; Hardcastle, K. I.; Bunz, U. H. F. *J. Am. Chem. Soc.* **2008**, *130*, 7339.

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 π 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.