NEUTRAL AND ANIONIC HOMOAROMATIC COMPOUNDS

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INTRODUCTION

A SciFinder Scholar® search of the word "aromaticity" currently yields over 460,000 references, indicating that this term is a staple in the vocabulary of chemists. Despite the frequent use of the term "aromaticity" in the literature, there has been no universally accepted definition. Most definitions of aromaticity state that the molecule must be planar and have a cyclically delocalized system of $(4n+2)\pi$ electrons.[1,2] This cyclic delocalization leads to an extra thermodynamic stabilization of the aromatic molecule when compared to a localized resonance form, as well as intermediate bond lengths between single and double. Furthermore, the reactivity of aromatic compounds differs significantly from alkenes in that the former tend to undergo substitution reactions as opposed to addition reactions. Lastly, a ring current can be induced in aromatic compounds by the application of a magnetic field. Several molecules display aromatic character but do not strictly follow the definition mentioned above, leading to extensions to the definition of aromaticity. For instance, Möbius aromatics have $(4n)\pi$ electrons yet demonstrate aromatic character; spherically aromatic structures such as C_{60} are aromatic in spite of being nonplanar;[3] cyclopropane displays aromaticity in sigma orbitals rather than pi orbitals and inorganic pi complexes such as ferrocene exhibit aromaticity in three dimensions.[4] This report will review homoaromatic species which behave as aromatic molecules despite containing one or more saturated linkages.[5]

Homoaromatic structures are named according to the number of saturated linkages they contain (i.e. mono for one interruption etc.). Three types of homoaromatic interactions exist: through-space, through-bond (σ), and transannular. The best established homoaromatic molecules are cationic in nature (Scheme 1 and Figure 1), and only recently have anionic counterparts been identified as homoaromatic. A truly neutral homoaromatic compound has eluded researchers thus far. The focus of this report will be to review recent efforts towards the synthesis and characterization of neutral and anionic homoaromatic compounds.

INDICES OF AROMATICITY

Three different ways to quantify the degree of aromaticity of a compound are based on: energetic, geometric and magnetic criteria. Current research efforts are directed toward finding a single criterion to evaluate aromaticity. This is a point of contention since Schleyer and co-workers[3] claim that a one-dimensional classification method will eventually be achieved, whereas Katritzky[6] and Jug[7] claim that aromaticity is a multi-dimensional phenomenon that cannot be described by a single variable.

Energetic Criteria

One basic criterion to judge the degree of aromaticity in a molecule is to calculate the aromatic stabilization energy (ASE) associated with cyclic delocalization as compared to a non-aromatic standard. Traditionally the ASE has been calculated or measured experimentally using isodesmic, homodesmotic or hyperhomodesmotic equations. However, these methods have a serious flaw since the ASE value obtained is highly dependent on the choice of reference. Many papers have been published on the value of the ASE of the most well understood aromatic compound, benzene, and these numbers differ by up to 53.4 kcal/mol![1] Recently, Schleyer proposed a new method for calculating ASE using the isomerization stabilization energy (ISE) method.[8] This method attempts to solve the problem found in homodesmotic equations as it only involves the use of one reference molecule, which is a methyl derivative of a nonaromatic isomer of the molecule in question. It has been tested for numerous known compounds and provided accurate results. A drawback of ASE is that it is not unique to aromatic compounds as nonaromatic molecules such as CF_4 can have calculated stabilization energies of up to 38.6 kcal/mol due to anomeric effects.[2] As a result, other indices of aromaticity are needed to identify an aromatic compound.

Geometric Criteria

A typical indication of aromaticity is a large degree of bond length equalization. Therefore, there have been many attempts to find indices that reflect this phenomenon. The most highly utilized index is the Harmonic Oscillator Model for Aromaticity (HOMA).[9] This model is based on the following equation:

Equation 1. Mathematical expression for HOMA

$$\begin{aligned} \text{HOMA} &= 1 - [(\alpha/n)\sum(R_{opt}-R_i)^2] \\ &= 1 - \alpha(R_{opt}-R_{av})^2 - (\alpha/n)\sum(R_{av}-R_i)^2 \\ &= 1 - \text{EN} - \text{GEO} \end{aligned}$$

where α is an empirical constant that is fixed so that aromatic compounds (where all bonds equal R_{opt}) have HOMA = 1 and nonaromatic compounds have HOMA = 0 and R_i is the individual bond lengths. Since both the EN and GEO terms are dearomatization terms, an increase in either term decreases the degree of aromaticity. The EN term describes the difference between the mean bond length and the optimal bond length, and the GEO term reflects the degree of bond alternation. The bond lengths used in this calculation can be computed or measured experimentally. The phenomenon of bond equalization is not unique and does not unequivocally indicate aromaticity; however it can be substantiated by other criteria such as energetic or magnetic measurements.

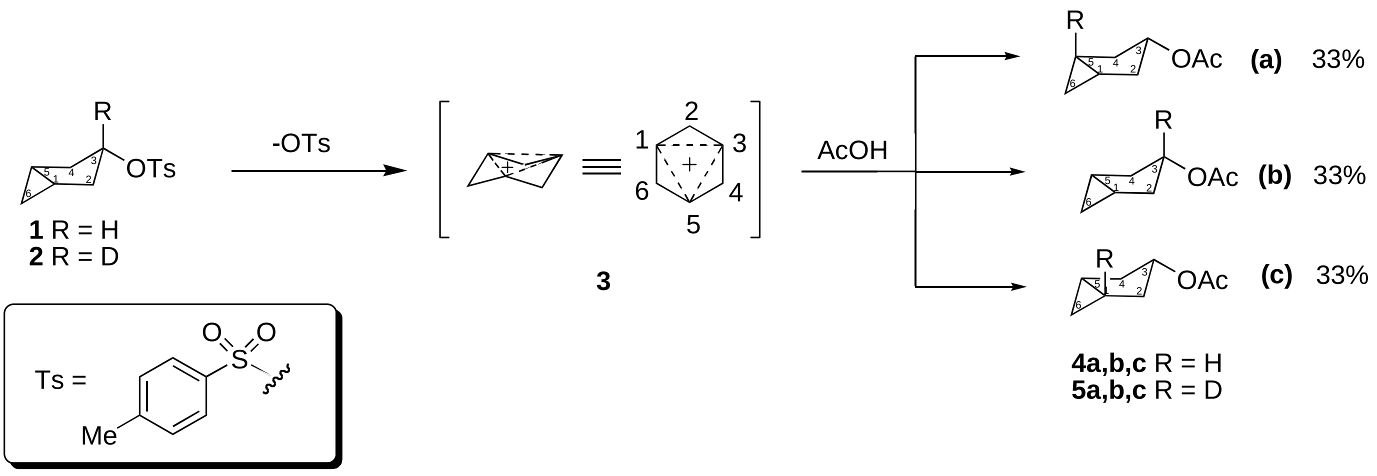
Magnetic Criteria

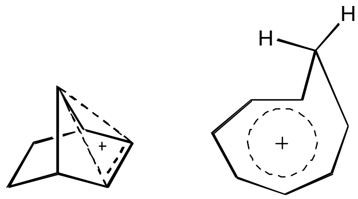
Theoretical and experimental magnetic anisotropy and diamagnetic exaltation values have also been used to characterize aromatic compounds. Traditionally the diamagnetic susceptibility exaltation[10] (Λ), which is the difference between the measured magnetic susceptibility and that computed by an additive scheme, is one of the most common magnetic indices. The more negative the value of Λ, the greater the degree of aromaticity. Λ has been said to be the only index of aromaticity that is unique to aromatic compounds; however, it is very dependent on ring size. To correct for this, Schleyer has introduced a new index called Nucleus Independent Chemical Shifts[11] (NICS) which is a computed value of the magnetic shielding experienced at 1Å above the center of the ring in question. Similar to diamagnetic susceptibility exaltation, the more negative the NICS value the greater the degree of aromaticity. The NICS value cannot be experimentally determined, and it only gives insight into local aromatic effects, but it has been shown to correlate well with HOMA and ASE. The most easily measured magnetic effect is the downfield chemical shift of protons in an NMR spectrum.[12] Once again, this phenomenon is not unique to aromatic compounds, but can be substantiated with the indices mentioned above.

ORIGINS OF HOMOAROMATICITY

The tris-homocyclopropenyl cation (**3**) was the first compound ever to be classified as homoaromatic.[5] Winstein proposed a homoaromatic structure for **3** based on evidence collected from an acetolysis experiment of **1** where the *cis* epimer reacted 35 times faster than the *trans* epimer (Scheme 1), suggesting anchimeric assistance in the solvation of the former.[13] Further evidence for the delocalized structure (**3)** was acquired from deuterium scrambling in the acetolysis of **2**, where 66% of the deuterium was found on the cyclopropane ring (postitions 1, 5) and 33% on the carbinol carbon (position 3), suggesting that positions 1, 3 and 5 were equivalent which substantiated the homoaromatic nature of **3**. Numerous modern experimental and theoretical studies have upheld Winstein's theory that **3** is homoaromatic, including a calculation that indicated that **3** is 12 kcal/mol more stable than its localized/classical structure.[14]

Scheme 1. Formation of tris-homocyclopropenyl cation





6 **7**

Figure 1. Structure of norbornen-7-yl cation (**6**) and homotropylium cation (**7**)

Since this discovery, numerous cationic compounds have been suggested to be homoaromatic. The best established, both theoretically and experimentally being the homotropylium cation[15] (**7**) and the norbornen-7-yl cation[16] (**6**).

NEUTRAL HOMOAROMATIC COMPOUNDS

Monohomoaromatics

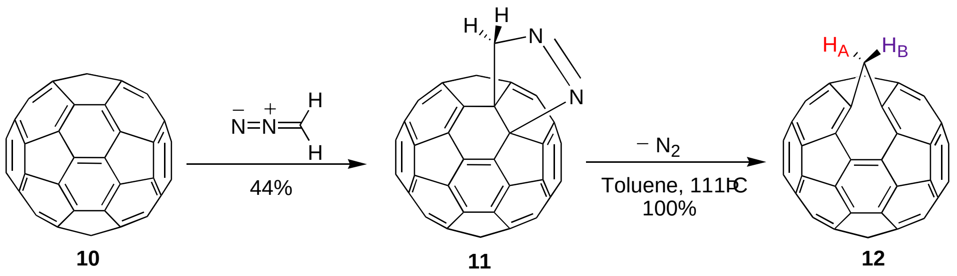
There are numerous examples in the literature such as cycloheptatriene (**8**)[17] and dihydro-1,2,4,5 tetrazine **9**[18] that were once proposed as neutral homoaromatics but have now been classified as only marginally homoaromatic using modern experimental and theoretical methods. This section will focus on the most notable candidates for neutral homoaromaticity.

8 **9**

Figure 2. Cycloheptatriene (**8**) and general structure of tetrazine (**9**)

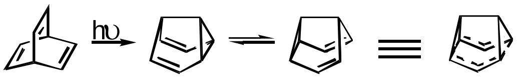
Fulleroids (for example **12**), which display transannular homoaromaticity, could also be classified as monohomoaromatic. The homoaromatic fullerenes were synthesized by a dipolar cycloaddition at the [6,6] ring junction with a diazomethane to form **11**, followed by nitrogen extrusion at high temperature, and rearrangement to the homoaromatic species **12**.[19]

Scheme 2. Formation of C_{60} fulleroid



The UV spectrum of **12** was identical to that of C_{60} itself, indicating no interruption in aromaticity; in addition **12** was characterized by ^{1}H and ^{13}C NMR and mass spectrometry. A more extensively characterized C_{70} fulleroid was prepared by Baddon and co-workers, and X-ray crystallography clearly confirmed that the methano bridge was found at the [5,6] ring junction.[20] Although these molecules display neutral homoaromatic interactions, they are not considered to be "pure" neutral homoaromatics because without this transannular through-space neutral homoaromatic interaction these molecules would still be aromatic.

Bishomoaromatics

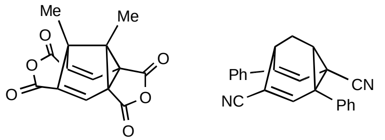


13 14 15 16

Scheme 3. Synthesis of semibullvalene from barralene

The class of compounds most likely to exhibit neutral homoaromaticity are semibullvalene and barbaralane molecules. Zimmerman and Grunewald first synthesized semibullvalene in 1966 through the photochemical isomerization of barralene (Scheme 3).[21] This molecule undergoes a rapid Cope rearrangement to the degenerate tautomer (Scheme 3). It was initially suggested that semibullvalene could have the delocalized structure **16** due to the presence of only three hydrogen resonances in a 2:4:2 ratio in the ^{1}H NMR spectrum. A variable temperature NMR study revealed no change in the hydrogen resonances down to –110 °C, but the delocalized structure was discounted due to a shoulder found in the UV spectrum, which was similar to one found in the UV spectrum of dihydrobullvalene. In 1974, Anet and co-workers were able to reach the coalescence temperature at -143°C and found the free energy of activation for the degenerate Cope rearrangement to be 5.5 kcal/mol.[22] This proved that semibullvalene is not a ground state neutral homoaromatic, but it was hypothesized that with some structural modifications it could be transformed into a neutral homoaromatic species. This problem has since been approached by either destabilizing the localized state with small ring annelations or by stabilizing the transition state by appending donor and acceptor groups at strategic positions on the semibullvalene core.

Numerous studies have shown that appending donor and acceptor groups to semibullvalene can significantly lower the free energy of activation of the degenerate Cope rearrangement. However, no examples of a ground state neutral homoaromatic species have been reported to date using this strategy. Recently Quast and co-workers, have shown that substituted semibullvalenes and barbaralanes (for example **18**) are thermochromic, meaning that a longer wavelength band is observed as temperature increases, representing the excitation of the delocalized state.[23] From the temperature dependence of this long wavelength band, one can calculate the $\Delta G^{\ddagger}$ between the localized and delocalized states. It was shown for the first time that the delocalized state of a functionalized barbaralane was stabilized by 0.72 kcal/mol relative to the localized state in dipolar and polarizable solvents such as DMPU. This was explained by the delocalized state being more polarizable than the localized state and thus more stable in polar solvents.



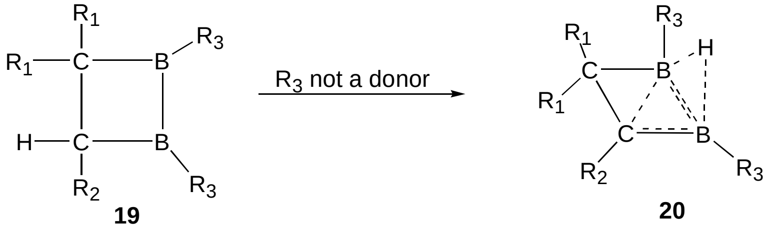
17 18

Figure 3. Annelated semibullvalene (**17**) and functionalized barbaralane(**18**)

The most promising attempt at annelation of semibullvalenes to destabilize the ground state was carried out by Williams using a target molecule that was chosen based on high-level calculations and ease of synthesis.[24] It was found that this molecule (**17**) was not a ground state neutral homoaromatic in the solid state or solution state but the free energy of activation of the degenerate Cope rearrangement had decreased to 3.3 kcal/mol. The inaccuracy of the computed results was attributed to the gas phase approximation, as Quast and co-workers have shown that solvent can have a large effect on these systems. Solvent effects should be taken into account in future calculations in order to improve the predictive power of theory. Although the annelated semibullvalene (**17**) is not homoaromatic in solution or in the solid phase, research is on-going to demonstrate its homaromatic nature in the gas phase.

1, 2-diboroetanes

Diborirane is known to have a nonclassical structure that is 50.8 kcal/mol more stable than its localized structure.[25] It was hypothesized that this phenomenon might exist in the known 1,2-diboroetanes and that they would be neutral homoaromatic compounds. The known diboroetanes have a classical structure when electron donating substituents are attached to the boron atoms, but it was predicted that electron-withdrawing substituents on boron would favor a nonclassical structure (Figure 4). When the 1,2-diboroetanes were functionalized with three different substituents on boron, the experimental chemical shifts matched up extremely well with those calculated based on a nonclassical model.[26] In addition, a crystal stucture was obtained for the triethylsilyl derivative and the geometry observed was in agreement with values calculated for the nonclassical structure. This class of molecules has been thoroughly investigated both experimentally and theoretically to establish that they are neutral homoaromatic. However, some experts contend they are not "true" neutral homoaromatics as they are electron deficient species that are isoelectronic with the homocyclopropenium cation.

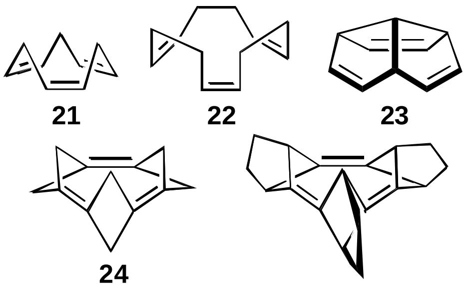


19 **20**

Figure 4. Localized and delocalized forms of 1,2-diboroetane

TRISHOMOAROMATICS

Cyclic trienes **21-23**, have been considered as potential structures that might possess homoaromatic stabilization through the interaction of the three double bonds.[27] However, upon synthesis and through numerous theoretical and experimental investigations, it was found that, at best, the stabilization gained due to delocalization was 5% that of benzene.[28] Recently, Schleyer and co-workers have suggested new targets (**24, 25**) for trishomobenzenes based on diamagnetic susceptibility exaltation, NICS and ASE calculations.[29] Although these theoretical predictions are promising, experimental evidence is needed before **24** and **25** can be confirmed as homoaromatic.



21 **22** **23**

24 **25**

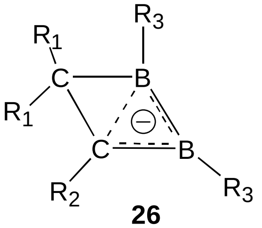
Figure 5. Potential trishomoaromatics

SELECTED CASES OF ANIONIC HOMOAROMATICITY

There are several molecules in the literature such as the bicyclo[3.2.1]octadienyl anion[30] which were thought to be examples of anionic homoaromaticity but numerous theoretical and experimental investigations found them to be only marginally homoaromatic. However, recently the 1,2-diboroetanides and the dianionic bis-diazenes, which are discussed below, have been established as examples of "true" anionic homoaromaticity.

1,2-Diboroetanides and related derivatives

1,2-Diboroetanides were prepared from their neutral nonclassical analogues by two-electron reduction with lithium metal. The resulting compound contains a three-center two-electron bond which Berndt and co-workers suggested could have homoaromatic stabilization.[31] This claim was substantiated by NMR shifts which correlated well with those predicted from a model of the nonclassical structure. In a crystal structure of one derivative a shorter C-B interaction was observed than in the classical structure. Furthermore an inversion barrier of 19.5 kcal/mol was calculated. Berndt and co-workers have synthesized numerous analogues with larger ring sizes, different bridging substituents and different core atoms such as silicon, all of which have displayed differing degrees of anionic homoaromaticity.[32, 33] In addition this concept has been applied to create an analogous bishomoaromatic[34] and trishomoaromatic[35] species.



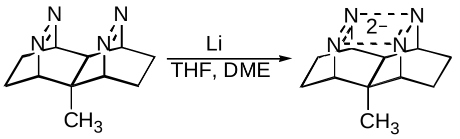
26

Figure 6. 1,2-Diboroetanide

Dianionic Bis-diazenes

Reaction of bis-diazene **27** with lithium metal produced dianion **28**.[36, 37] A large color change observed upon reduction, suggested that this dianionic bis-diazene had a four-center six-electron bond and could be an in-plane σ bishomoaromatic species. This hypothesis was confirmed through ^{1}H and ^{13}C NMR spectroscopy and X-ray crystallography, which indicated shortening of the transannular N-N distances and lengthening of the vicinal N-N bond lengths. As mentioned above, the dianionic bis-diazenes have been classified as "true" anionic homoaromatics as a result of both theoretical calculations and experimental characterization.

Scheme 4. Synthesis of anionic homoaromatic form of bis-diazene



27 **28**

CONCLUSIONS

It is difficult to devise a simple definition of aromaticity and for this reason it is also hard to constrain aromaticity to any single criterion of characterization. Potential aromatic compounds are evaluated by energetic, geometric and magnetic criteria. Numerous cationic compounds have been substantiated unequivocally as homoaromatic species and recently anionic homoaromaticity has also been proven beyond a reasonable doubt due to the discovery of the 1,2-diboroetanides and the dianionic bis-diazenes. Neutral homoaromaticity is not nearly as accepted; however the 1,2-diboroetanes have been studied extensively and all experimental and theoretical results agree that they are indeed homoaromatic. Research continues to find new semibullvalenes and barbaralanes as potential neutral homoaromatics.

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