MÖBIUS AROMATICITY: WHICH SIDE ARE YOU ON?

Reported by Philip A. Janowicz February 22, 2007

INTRODUCTION

The idea of Möbius aromaticity was first proposed by Heilbronner in 1964.[3] He postulated that a molecule could gain Möbius aromatic stabilization if the nuclear framework were twisted so the p-orbitals composing the π-system would contain an odd number of nodes. To introduce a node in the orbitals, Heilbronner theorized that a series of p-orbitals could itself be twisted by contorting the nuclear framework. The twisted p-orbitals would then form a C_2-symmetric π-system that lies on the surface of a Möbius strip (Figure 1). A Möbius strip is a one-sided, three-dimensional surface that is constructed from a rectangle by holding the first end fixed, rotating the second end 180°, and joining the two ends together (Figure 1). In normal planar annulenes like benzene, the $4n + 2$ electrons in the delocalized π-system give the molecule an overall stability associated with a closed-shell Hückel occupancy.[6] In contrast, if $4n$ electrons are present, the Hückel molecular orbital analysis results in an open-shell configuration, leading to a destabilization of the molecule relative to the same molecule without delocalization of electrons; this destabilization is also known as "anti-aromatic" character. However, if a 180° phase shift is introduced into the array, Hückel analysis predicts a closed-shell electron configuration for the $4n$ electron case with one phase change and an open-shell configuration for the $4n + 2$ case, leading to a reversal in the pattern of stabilization. Heilbronner used Hückel molecular orbital analysis (Figure 2) to calculate the π–electron energy for the twisted p-orbitals in the Möbius case and found that the energy lost from smaller orbital overlap is exactly equal to the energy gained from pairing the two electrons in non-bonding orbitals into an orbital degenerate with the lowest energy molecular orbital (α + 2β). Zimmerman provided a mnemonic for remembering the new Möbius molecular orbital system (Figure 2).[7,8]

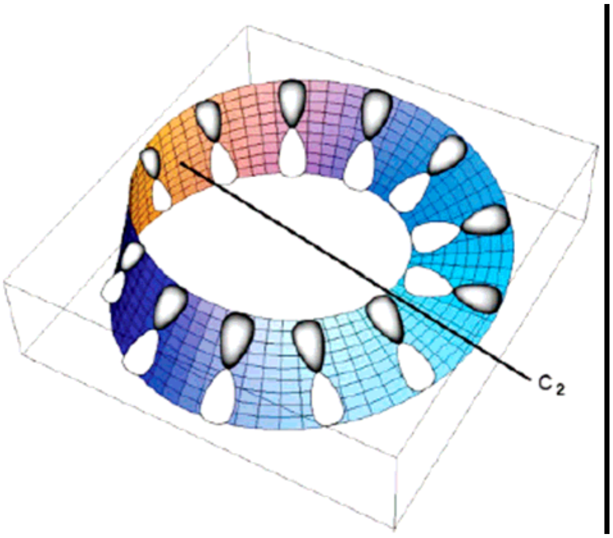


Figure 1. A theoretical Möbius strip bearing p-orbitals.[1]

One obvious challenge in preparing Möbius annulenes is the twisting of the bonds that gives rise

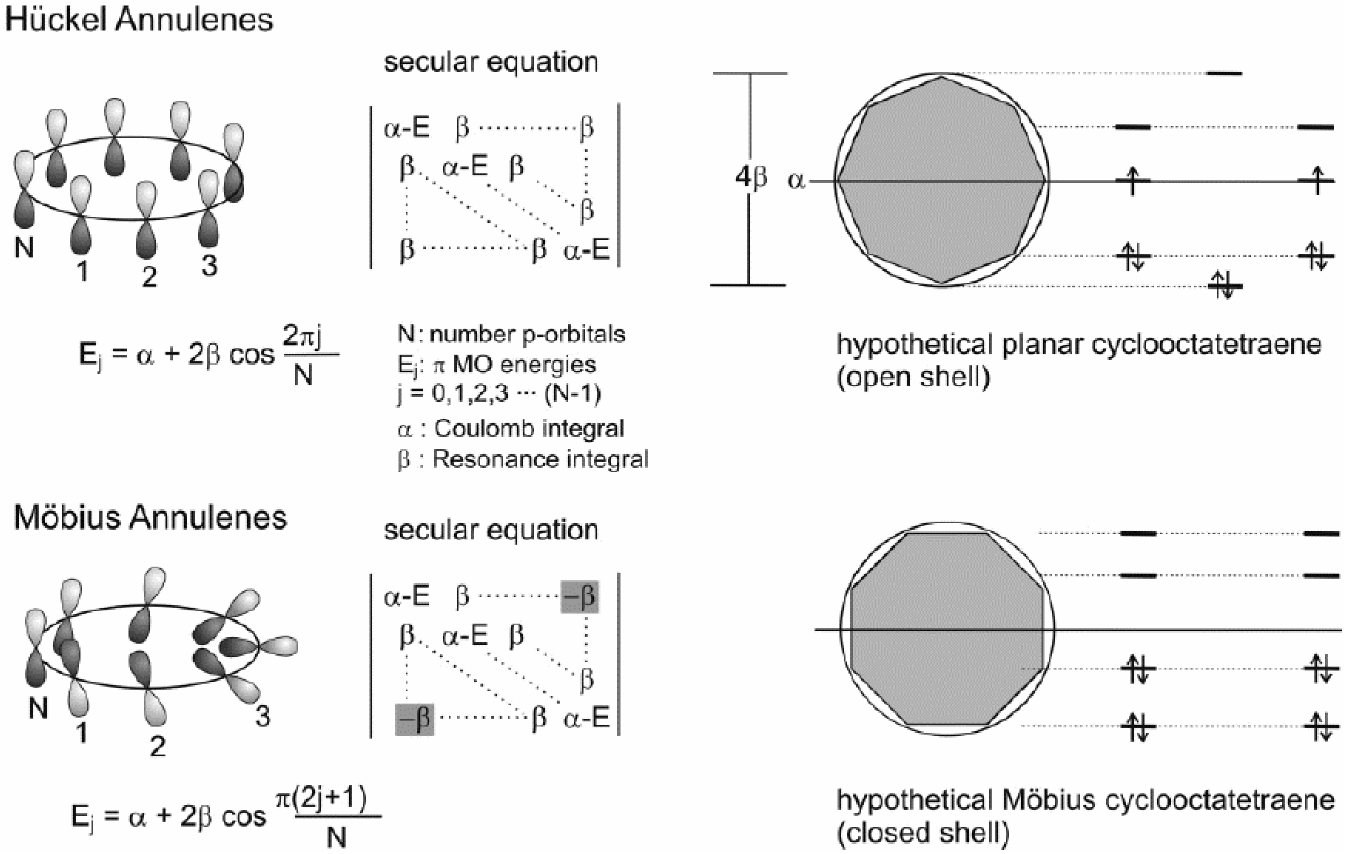


Figure 2. The Hückel molecular orbital analysis for both Hückel and Möbius annulenes. The –β in the Möbius secular determinant arises from the sign inversion of the p-orbitals and causes the change in energy levels from Hückel to Möbius annulenes.[2]

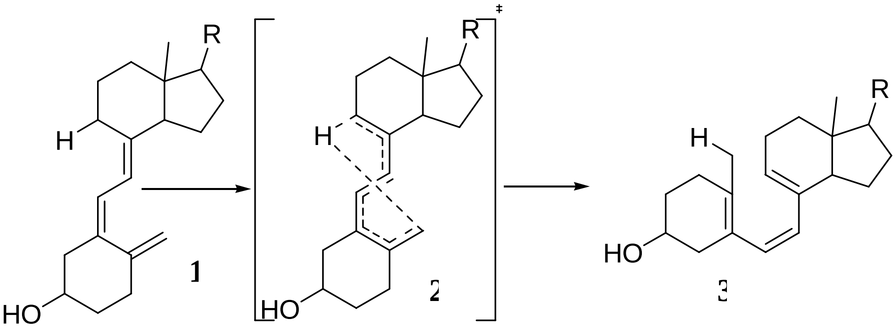
to extra energy stabilization also contorts the ring and thereby creates more ring strain than in the untwisted annulene. Heilbronner claimed that Möbius aromatic annulenes with more than 20 carbons could be twisted without adding any strain arising from bond angle contortions or from steric repulsion.[3] Although his claim proved hard to substantiate at the time, extensive research has been conducted on the subject since his initial conjecture.

MÖBIUS AROMATICITY IN TRANSITION STATES

The most immediate impact of Heilbronner's work was its application by Zimmerman to the Woodward-Hoffmann rules.[8-14] Zimmerman noted that pericyclic reactions could be mechanistically described using the idea of Möbius aromaticity. Zimmerman stated that a series of p orbitals with $4n + 2$ electrons would prefer to react in a pericyclic manner to form a Hückel aromatic ring and that a series of p orbitals with $4n$ electrons would prefer to form a Möbius aromatic ring. Zimmerman's method has a distinct advantage over the previously developed Woodward-Hoffmann rules because the Zimmerman method works for both symmetric and nonsymmetric systems. Also, no knowledge of the molecular orbitals is necessary for predicting pericyclic reactions in order to give the same results as applying the Woodward-Hoffmann rules.

The first computational study of a Möbius transition state was reported by Jiao and Schleyer in 1993.[2] They studied the [1,7] sigmatropic hydrogen shift in 1,3,5-heptatriene that, according to the Zimmerman method for pericyclic reactions, must proceed via a Möbius transition state with the hydrogen moving to the antarafacial side. A [1,7] sigmatropic shift was first postulated to occur in the rearrangement of calciferol to precalciferol (Scheme 1), but the reaction was not studied computationally until 30 years later.[15-18] Jiao and Schleyer used the Gaussian 92 program package to calculate the energy minima of the possible transition states. The calculations showed that the transition state has C_2 symmetry and that the C–C bond lengths have bond equalization similar to that of benzene (Figure 3). The computations also showed that the transition state has a diamagnetic ring current, which is one of the criteria for aromaticity.[19,20] Jiao and Schleyer used the Individual Gauge for Localized Orbitals (IGLO) method to compute the NMR chemical shifts of the transition-state hydrogens and the diamagnetic ring current.[21] They found a diamagnetic contribution of 17.1 ppm cgs (i.e., parts per million in cgs units) to the proposed Möbius transition state, a value very close to the diamagnetic contribution of benzene, 15.4 ppm cgs.[22] In addition, the values computed for the chemical shifts of hydrogen are 6.3–6.9 ppm, which is very close to 7.0 ppm for benzene. A more compelling reason is the different chemical shift values computed for the hydrogens on C^1 and C^7, which point into the ring and out of the ring. As is the case in aromatic ground states, protons on the outside of the ring experience a ring current that causes the chemical shift to move downfield, but protons on the inside of the ring experience an upfield chemical shift because of the same ring current.[19,20] The protons on C_1 and C_7 that point outside have a chemical shift of 5.4 ppm, and the protons pointing to the inside have a chemical shift of –4.7 ppm, values typical of aromatic systems.

Scheme 1. The equilibrium between calciferol (**1**) and precalciferol (**3**) proceeding through a [1,7]-sigmatropic shift with a Möbius aromatic transition state (**2**).



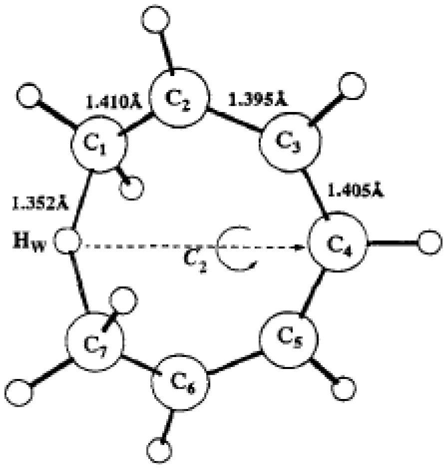
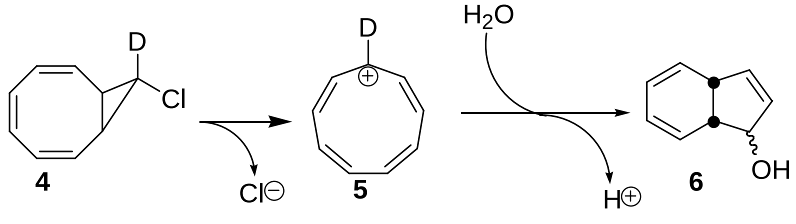


Figure 3. The RMP2(full)/6-31G* optimized [1,7] sigmatropic shift transition state.[1]

ELUCIDATION OF THE FIRST MÖBIUS AROMATIC INTERMEDIATE

Interest in chemical structures that exhibit Möbius topology was renewed in 1998 when Mauksch et al. showed computationally that the monocyclic intermediate $(CH)_9^+$ displays Möbius aromatic characteristics.[23] $(CH)_9^+$ was first proposed in 1971 as an intermediate in the solvolysis of *exo*-9-chlorobicyclo[6.1.0]nona-2,4,6-triene in aqueous acetone at 75 °C (Scheme 2).[24] Mauksch et al. used density functional theory to calculate the lowest energy conformation of the intermediate, and the C_2-symmetric helical structure shown in Figure 4 is indeed the lowest energy conformer.

Scheme 2. Reaction of deuterated **4** through the Möbius aromatic intermediate **5** to form **6**. The deuterium label in **4** was completely statistically distributed in **6**, giving evidence to a delocalized intermediate.



Like aromatic molecules, the intermediate shows small C–C bond alternation with a maximum bond-length difference (BLD) of 0.043 Å. It also has a large negative nucleus-independent chemical shift (NICS) of –13.4 (cf. NICS value for benzene = –9.7)[25] and an average ^1H NMR chemical shift of 8.5 ppm. Clearly, based on both geometric and magnetic criteria, this intermediate exhibits aromatic character.

SYNTHESIS OF THE FIRST MÖBIUS AROMATIC MOLECULE

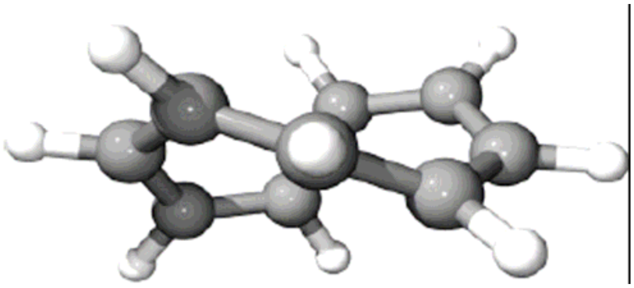


Figure 4. DFT calculation of the lowest energy conformation of the $(CH)_9^+$ intermediate.

Prior to 2003, work related to Möbius aromaticity was largely theoretical and applied mainly to transition states and intermediates as described above. However, in 2003, Ajami et al. reported the synthesis of the first neutral Möbius aromatic molecule.[26] Their strategy was to combine two components. The first component was a "normal" aromatic system in which the p orbitals are lined up perpendicular to the plane containing the bonds. The second component was a pyramidalized "in-plane" aromatic system in which the p-orbitals are all pointing in and out of the ring itself, similar to a ship's steering wheel (Figure 5). When these two aromatic systems are combined using pericyclic reactions, a Möbius aromatic system is formed (Scheme 3). Five isomers were obtained from the reactions, one of which was the predicted Möbius aromatic structure (**7**).[26] Ajami et al. confirmed the formation of **7** by NMR and X-ray crystallography and also calculated the geometric and magnetic properties of the molecule to evaluate its aromaticity. The compound was found to have a maximum C–C BLD of 0.095 Å, which is rather large for a supposedly aromatic molecule. The authors also used the

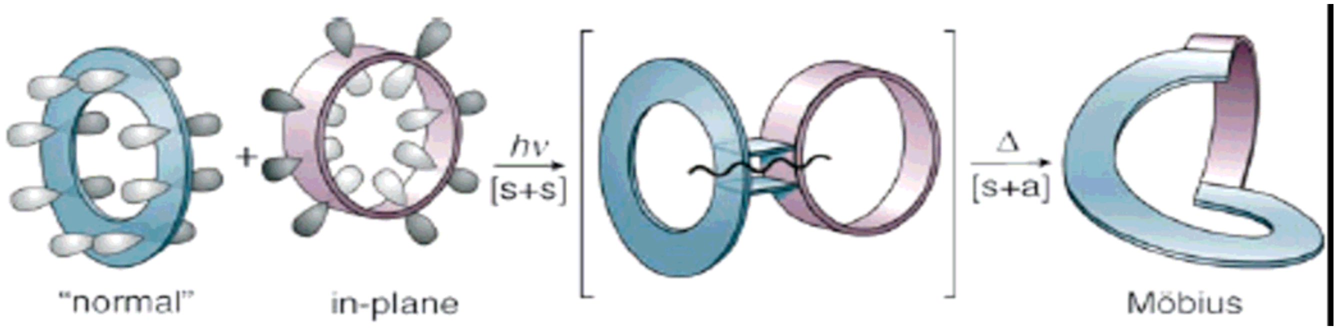
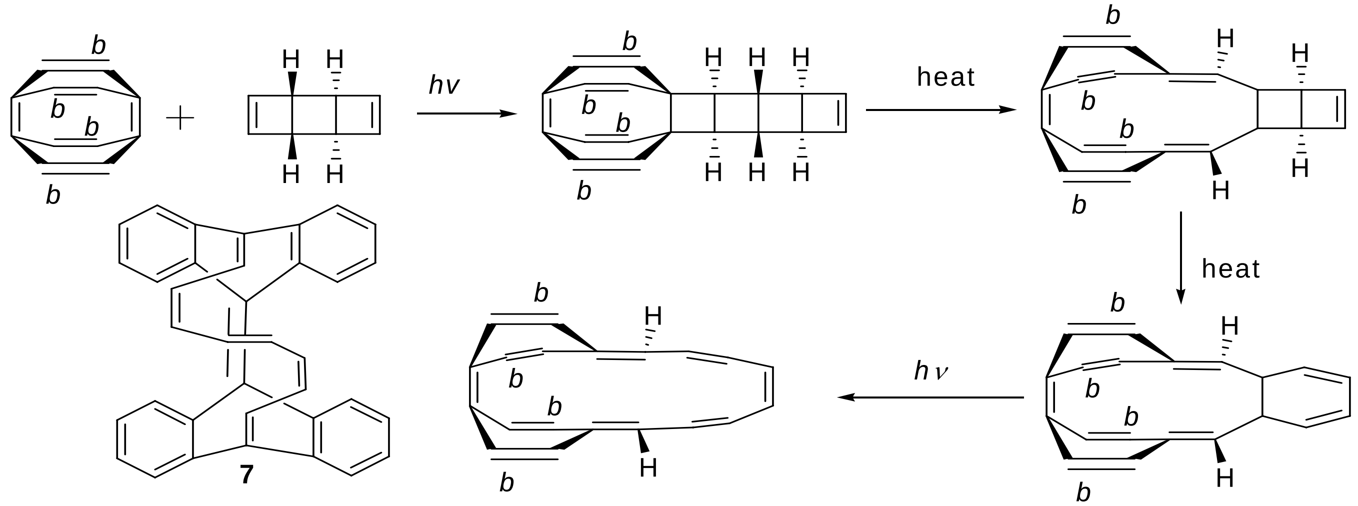


Figure 5. Strategy to stabilize the Möbius structure of annulenes.[4]

Scheme 3. The strategy for the synthesis of a [16]annulene that exhibits Möbius aromaticity. Bonds marked with a *b* are part of benzo groups which have been omitted for simplicity.[1]



indene-isoindene method (ISE_{II})[27] to estimate the stabilization from the conjugation of π bonds. A stabilization energy of 4.04 kcal mol^{-1} due to conjugation was computed for the Möbius topological [16]annulene, a value five times smaller than the ISE_{II} value for benzene. Also, a stabilization energy of –2.22 kcal mol^{-1} was computed for the Hückel topological [16]annulene with Hückel topology. The magnetic susceptibility exaltation (Λ) for **7** was computed to be –30.0 ppm cgs, a highly negative value that indicates a diamagnetic ring current present in the molecule, one of the criteria for aromaticity.[22] Based on these arguments, the authors claimed that **7** exhibits Möbius aromaticity.

DEBATE OVER THE MÖBIUS AROMATICITY OF 7

Evidence for the Nonaromaticity of 7

The seemingly extraordinary results presented by Ajami et al. were not met without scrutiny. Castro et al. extensively reviewed the methods used by Ajami et al. in 2003 and reported several errors in the computed and crystallographic data used to support the claims of aromaticity.[28] First, the geometric data was reviewed. Whereas Ajami et al. presented a maximum C–C BLD of 0.095 Å, a value which the original authors even noted was large, Castro et al. noted that this BLD was confined to the polyene bridge of **7** and that the bond lengths of the entire [16]annulene should be considered. When this correction was made, a maximum C–C BLD of 0.135 Å was computed, a larger value than had been reported. This large BLD points to localization of the π electrons and not to a delocalized aromatic structure.

Castro et al. also postulated that benzannelation of the [16]annulene destroys the aromaticity of the system. They considered the view of Clar and argued that the electrons in one aromatic ring cannot easily contribute to adjoining rings' aromaticity.[29] They concluded that the double bonds cannot contribute to the aromaticity of both the benzene rings and the polyene bridge. To test their claim, they used the harmonic oscillator measure of aromaticity (HOMA), a method of normalizing bond length differences in terms of aromaticity.[30] Ajami et al. computed a HOMA value of 0.35 for **7** (cf. HOMA value for benzene = 0.98). Castro et al. computed their own value after removing the effects of the double bonds contained in the benzo groups, and a HOMA value of –0.02 was obtained. This value is typical of nonaromatic molecules that show no delocalization.

Castro et al. then questioned the ISE_{II} data, noting that ISE_{II} methods had not been tested on any nonplanar systems before the initial use by Ajami et al. So Castro et al. applied the ISE_{II} method to the polyene bridge with the benzo groups removed, a similar approach as shown above. The data for the cyclic annulenes were exactly as had been originally computed, but the data for the acyclic models were comparable. The Möbius topological polyene bridge gave an ISE_{II} value of 4.4 kcal mol^{-1}, and the Hückel topological polyene gave an ISE_{II} value of –2.9 kcal mol^{-1}. Therefore, the difference in ISE_{II} values between the Möbius and Hückel topologies is not due to aromatic stabilization but rather to stabilization effects contained within the polyene bridge itself. Also, Castro et al. noted that the original ISE_{II} value for **7** was an uncorrected value that did not take into account s-cis/s-trans corrections that arise from the fact that s-trans dienes are more stable than s-cis dienes. Once these corrections are made to the ISE_{II} value obtained for **7**, the value drops to 0.6 kcal mol^{-1}, indicating that **7** is not stabilized by aromaticity. Castro et al. also noticed that several of the dihedral angles in **7** deviate as much as 70° from maximum p-p orbital overlap for a π bond. If p-p orbital overlap is not large enough, then the π electrons cannot delocalize around the ring, thereby making aromaticity unachievable.

The magnetic criteria for aromaticity were also examined for **7**. Castro et al. argued that the large negative value of the magnetic susceptibility exaltation (Λ) is largely due to the four benzo groups in **7** and not from the [16]annulene. To test their claim, the benzo groups were removed, and the computations were run again, this time giving a highly paramagnetic Λ value of +19.6 ppm cgs, thereby casting doubt on the claims of aromaticity in **7**. One concern with the method used to remove the benzo groups from the calculation is that the value of benzene was merely subtracted from the original value four times, once for each benzo group. Castro et al. claim that **7** is nonaromatic, yet a value of +19.6 ppm cgs points to an antiaromatic molecule. In order to compute Λ, the four benzo groups should be removed, and the computation should be repeated. Extrapolating computational data for Λ is scientifically unacceptable.

Evidence for the Aromaticity of 7

Ajami et al. responded in 2006 and restated their initial claims from 2003 that **7** does indeed exhibit characteristics of Möbius aromaticity.[5] Ajami et al. used principal component analysis (PCA) to determine statistically whether certain factors that determine aromaticity accurately predict the topology of certain [16]annulenes. PCA is a statistical tool that determines the most important factors that control the variance in the data.[31] Their analysis used six parameters: relative energy (E_{rel}), maximum deviation of dihedral angles from planarity (T_{max}), HOMA, Julg (a bond-length equalization index similar to HOMA), magnetic susceptibility exaltation, and NICS. Through the analysis, the authors concluded that [16]annulenes with Möbius topology exhibit aromatic properties such as those used in the PCA analysis.

The claims made by Ajami et al. have obvious flaws. First, PCA is a statistical tool that measures only the variables that are manually put into the system. If another criterion for aromaticity were added to the analysis, a different output would be obtained that may contradict the previous results. The users of PCA can essentially hand pick the variables that agree with the predicted results and exclude variables that dispute their data. Also, Ajami et al. state, "it is interesting to note that the relative energy [E_{rel}] does not correlate strongly with any of the aromaticity parameters. Aromaticity, evidently, does not play an important … role in stabilizing the structures."[5] The authors explicitly state that aromaticity does not stabilize the structures relative to nonaromatic molecules but then conclude that because of aromaticity, "structures with Möbius topology [like **7**] are now more stable than Hückel isomers."[5] The general conclusion is that the aromaticity parameters in the PCA correlate with either Möbius or Hückel topology but do not contribute to energetic stabilization of the structures.[5] Therefore, another reason for the stabilization of one structure over another that has nothing to do with aromaticity or delocalization must exist, yet the authors make no such conjecture.

CONCLUSION/FUTURE WORK

The first reported synthesis of a neutral [4n]annulene derivative with Möbius topology is indeed an important discovery. Although a strong argument can be made that the molecule does not exhibit Möbius aromaticity, the unchallenged fact that Möbius topology has been achieved in **7** is a novelty. The discovery of a new type of stabilization is important because molecules can be synthesized to exhibit the extra stabilization associated with Möbius aromaticity and because molecules with this stabilization are less reactive than those without. Therefore, this stabilization can be exploited and the aromaticity potentially broken to make use of the bonds and atoms that were previously less reactive because of the stabilization. The synthesis of Ajami et al. is an important stepping stone for a possible future synthesis of a molecule with Möbius topology that also exhibits unambiguous aromatic stabilization. Perhaps work on higher-order [4n]annulenes with $n > 20$ would be possible, as Heilbronner originally predicted.[3]

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