Quantifying Vertical Resonance Energy in Aromatic Systems with Natural Bond Orbitals

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Abstract

Natural bond orbitals (NBOs) provide the familiar Lewis type (2c-2e) localized description of a molecule. Interactions between nearly filled (2e) orbitals and empty (π* or σ*) anti-bonding orbitals represent delocalization in the system and creates a framework to study stereoelectronic interactions. Here we show that deleting the interactions between π and π* orbitals in aromatic systems and acquiring the energy with the NBO program provides a highly intuitive and quantitative picture of π-aromaticity that correlates with the well-established nucleus-independent chemical shift (NICS) method. This natural bond orbital resonance energy (NBO-RE) measures the vertical resonance energy (VRE) of aromatic systems without the use of an external reference structure. The NBO-RE method is applicable to the study of local aromaticity in polycyclic aromatic hydrocarbons (PAHs) and other non-planar systems.

Introduction

Since its first theoretical description using Hückel molecular orbital theory (HMO),¹ the concept of aromaticity has evolved considerably.² The most noticeable change is the variety of compounds that are now classified as aromatic. The discovery of Baird,³ Möbius,⁴ spherical,⁵ and stacked ring aromaticity⁶ represent some of the most recently studied. This conceptual evolution initially appears to be suspicious⁷ but is quite reasonable when considering the complexity of the phenomenon. Indeed, the vagueness of the concept of aromaticity has been beneficial for

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chemistry as the prospect of discovering novel aromatic structures has incentivized exploration. Advances in our understanding of electronic structure and modern synthetic methods have also led to the ability to both theorize and prepare a wide variety of novel aromatic compounds. However, as of yet there is no satisfactory way to provide a general quantifiable description of aromaticity, this is in part due to its ill-defined and somewhat elusive nature. Therefore, it is important to explore all the ways in which it manifests.

For traditional aromatic systems, Hückel’s $(4n + 2)\pi$ electrons criterion is the de facto way to identify classical aromaticity. However, this encounters difficulties when absolute measurements of aromaticity are desired. For the purposes of aromaticity quantification, certain experimental methods have been developed. Heats of hydrogenation, $^1$H NMR chemical shifts, and exaltation of diamagnetic susceptibility are amongst the most popular and widely used. These methods have numerous drawbacks, notably $^1$H NMR chemical shifts are considered unreliable for quantifying aromaticity. Though it is challenging to identify the correct computational techniques to use in the absence of experimental evidence, computational methods have largely displaced experimental methods.

Several classes of computational descriptors exist, though methods that assess magnetic properties or the extent to which electrons are delocalized are particularly common. In regards to magnetic criteria, the nucleus-independent chemical shift (NICS) descriptor has been the most widely used. In principle, it exploits the phenomenon of magnetic anisotropy that is experienced by all aromatic rings. A set of XYZ coordinates are generated for a structure containing an aromatic ring and a ghost atom is placed at some position above or in plane with the centroid. The absolute shielding is then measured at the location specified by the ghost atom, the negative of this is taken to be the NICS. There have been many types of NICS calculations with NICS(0), NICS(1), NICS(1)$_{zz}$, and NICS(0/1)$_{\pi-\pi}$ are amongst the most commonly employed. Integrated NICS (\textit{\textipa{\textint{NICS}_{\pi-\pi}}}) has also been explored but has only seen limited use. NICS methods have also been adapted for use in the T1 state. Each of these methods results in varying scales and are typically not directly comparable, though relative comparisons are possible.
While all methods have their own shortcomings, it is generally accepted that methods that place the ghost atom out of plane of the ring and consider only the out of plane component of the magnetic shielding tensor (NICS(r)zz methods) give results that better represent the effect of the \( \pi \)-system when compared against typical isotropic NICS methods (NICS(1) and NICS(0)). More refined methods have attempted to eliminate spurious effects unrelated to aromaticity.

Despite the conceptual advances and constant refinement of NICS, there are still many concerns with the methods, making their use in quantification of aromaticity difficult. For instance, it is challenging to properly assess multi-ringed systems (polycyclic aromatic hydrocarbons) due to convolutions of adjacent rings. Additionally, non-planar systems are not appropriate for the NICS method due to unclear indications for ghost atom placement.

Electron delocalization methods are more diverse and include techniques that assess the wavefunction, electron density, or the density matrix. These methods typically require more complex computational procedures, but often provide a more precise description of a particular facet of aromaticity. They have also permitted a more in-depth study of traditional or non-traditional aromatic systems, validating their pursuit. The extra-cyclic resonance energy (ECRE) approach by Mo and coworkers is notable. Additionally, a recently developed and important method is the electron distribution of delocalized bonds (EDDB) by Szczepanik et al.

Structural methods and various energetic criteria are also known. Energetic methods using isomerization of double bonds and/or homodesmotic reactions are well established. It is worth noting that energetic methods typically measure adiabatic resonance energy (ARE) since the reference structures (cyclohexene, cyclohexadiene, and a “true cyclohexatriene”, Figure 1) do not have the same geometry as benzene. This is different from the vertical resonance energy (VRE), which accounts for the difference in energy between a fully delocalized system (ie. benzene) and a structure of the same geometry with non-interacting double bonds (“bond equalized cyclohexatriene”) (Figure 1). The distinction between the two methods is important as they return different energies, with the ARE values necessarily being lower.
Figure 1: Vertical resonance energy (VRE) of benzene measures the difference between benzene (1) and an identical “cyclohexatriene” (2) system with non-interacting double bonds. Adiabatic resonance energy (ARE) measures the difference in energy between benzene and a bond length alternated cyclohexatriene (3).

Method

All geometry minimizations, frequency calculations and NMR predictions were done with either Gaussian09\textsuperscript{29} or Gaussian16\textsuperscript{30} packages. All geometries were minimized at the M06-2X/6-31+G(d,p) level except otherwise stated. DLPNO-CCSD(T) calculations were performed with Orca 4\textsuperscript{31}. LNO-CCSD(T)\textsuperscript{32} calculations were performed with MRCC\textsuperscript{33}. Frequency calculations were done with Gaussian 09/16 for all PAHs and Möbius aromatics to ensure the absence of imaginary frequencies. Natural bond orbital (NBO) and NBO-RE calculations were performed with NBO6/7\textsuperscript{34} implemented in Gaussian16 at the M06-2X/6-31+G(d,p) level. Nucleus-independent chemical shifts (NICS) calculations were performed using M062X/6-31+G(d,p) geometries with ghost atoms (Bqs) that were placed at the ring centroid either 1 Å above or directly in the plane of the ring. All molecular models were depicted with CYLview\textsuperscript{20}.\textsuperscript{35} Orbital images were generated with Jmol\textsuperscript{36} with PLOT files obtained from the NBO program.

Results and Discussion
The natural bond orbital (NBO) approach to quantifying vertical resonance energy in aromatic systems. Localized orbitals provide a unique perspective on structure and bonding and generally act as a bridge between the typically only computationally accessible delocalized molecular orbitals and the intuitive 2-center-2-electron (2c-2e) picture chemists cultivate. Many useful methods exist for localizing orbitals (e.g., block-localized wavefunctions,\(^{37}\) adaptive natural density partitioning,\(^{25c}\) etc.).\(^{38}\) Natural bond orbitals (NBOs)\(^{39}\) are amongst one of the most popular methods, especially for the consideration of stereoelectronic effects\(^{40}\) (e.g., anomeric effect, Figure 2). In the NBO method, deviations from the localized 2c-2e Lewis-picture (delocalization) are assessed by the energies of interactions between idealized mostly filled (2e\(^{-}\)) orbitals (non-bonding, \(\sigma\), or \(\pi\)) and adjacent empty orbitals (non-bonding, \(\sigma^*\), or \(\pi^*\)). The energetic of these interactions (e.g., \(n_{\text{NBO}} \rightarrow \sigma^*_{\text{NBO}}, \pi_{\text{NBO}} \rightarrow \pi^*_{\text{NBO}}, \pi_{\text{NBO}} \rightarrow \pi^*_{\text{NBO}},\) etc) are typically assessed by a second order perturbation (E2pert) approach and can provide a reasonable assessment of the strength of an interaction.\(^{41}\) Importantly, such an approach measures the isolated interaction energies between a completely filled bonding orbital and an empty non-bonding orbital without explicit consideration of other adjacent delocalizing interactions.

![Figure 2: Stereoelectronic interaction \((n_{\text{NBO}} \rightarrow \sigma^*_{\text{NBO}})\) describing the origin of the anomeric effect.](image)

Here we describe that another approach, involving deleting cross terms in the Fock NBO matrix (NBODel in the NBO6/7 programs)\(^{34}\) describing \(\pi \rightarrow \pi^*\) interactions and passing the matrix through one self consistent field (SCF) cycle to obtain the energy\(^{42}\) provides a highly intuitive assessment of a system’s relative \(\pi\)-aromaticity. For aromatic systems, this VRE approach is more desirable than a simple perturbative approach as recomputing the electronic
structure after deletion of $\pi \rightarrow \pi^*$ interactions considers the energy of a highly localized system (a bond length equalized “cyclohexatriene” that corresponds to a single Kekulé structure in the case of benzene, 2, Figure 1). Importantly, this can then be compared to the energy of the original wavefunction (fully delocalized benzene, 1, Figure 1) without use of an external reference molecule if the dominant (regardless of degeneracy) resonance structure is selected.

We show that the natural bond orbital resonance energies (NBO-RE) obtained in this manner correlate quite well with NICS$_{zz}$ measurements for monocyclic systems that include a range of benzenoids, non-benzenoids and heteroaromatics. We also show that the NBO-RE method is easily adaptable to the study of other non-Hückel aromatic systems such as polycyclic aromatic hydrocarbons (PAHs) and those that deviate from planarity (e.g., Möbius aromaticity), making it a highly valuable and general approach.

Validating The NBO-RE Approach. Using benzene as a representative case, we can see how the $\pi$-MOs corresponding to the degenerate HOMOs and the HOMO-1 (Figure 3, left) are represented by a series of $\pi_{NBO}$s (Figure 3, top right). Importantly, each such $\pi_{NBO}$ also has a corresponding $\pi^*_{NBO}$ on the same C=C fragment. The energies of interactions between all $\pi$ and adjacent (not overlapping) $\pi^*$ orbitals represents the vertical resonance energy (Figure 3, bottom right). Deleting these interactions (six in total for benzene) from the Fock NBO matrix and passing through one SCF cycle (NBODel) without changing the geometry results in an energy change of 150.5 kcal/mol (see SI for step-by-step procedure for obtaining the value for benzene).

We propose the $\pi$-electron corrected value (150.5 kcal·mol$^{-1}$/6$\pi$e$^-$ = 25.1 kcal·mol$^{-1}$/$\pi$e$^-$) to be called the natural bond orbital resonance energy (NBO-RE). In principle this method is comparable to any method that measures the vertical resonance energy (VRE) of benzene, which does not allow for localized bonds to relax (compress) to non-aromatic $\pi$-bond lengths (Figure 1). The values should not be compared to methods that measure the ARE of benzene, which typically provide values around 30 kcal/mol and require external or multiple reference molecules. Interestingly, the non-electron corrected NBO-RE measurement of benzene (150.5 kcal/mol) corresponds to the energies predicted by spectroscopic measurements (a $\pi-\pi^*$ excitation, 138 kcal/mol). Complete deletion of $\pi^*$ orbitals also yields an energy that is very similar to that
which has been previously proposed to arise from the excitation of the ground state (1A1g) to the 1B2u excited state, which is obtained from the symmetric and antisymmetric combinations of Kekulé structures.46

Figure 3: left: Degenerate HOMOs and HOMO-1 of benzene. top right: The π- and π*-NBOs of benzene. bottom right: the interactions associated with delocalization in benzene.

To establish the generality of the method, the NBO-RE was determined for a series of >100 compounds, ranging from substituted benzenoids to expanded annulenes and heterocyclic aromatics (see SI for a full list of structures). A variety of structures were chosen to ensure weakly aromatic and highly aromatic structures are well represented. The dominant resonance structure for each compound as determined by the NBO analysis was chosen as the reference. These values were then compared against their corresponding NICSzz values.47 In the test set, only molecules with one aromatic ring were permitted to ensure that multi-ring currents do not confound NICS measurements. Additionally, as the NBO-RE measurement effectively probes the resonance energy per electron (REPE), the NICS values were also normalized (per electron), which is also necessary due to the dependence of NICS on electron count.17a The vast majority of benzenoid systems fall between the 20-25 kcal·mol⁻¹/πe⁻ range, though the set contains weak and non-aromatic (4n+2)πe⁻ systems that have values as low as 11.1 kcal·mol⁻¹/πe⁻. The correlation is excellent, especially when considering the variety of the molecular structures under study (Fig 4-5).
Assessing the aromaticity of 5-membered ring (5MR) heteroaromatic compounds has typically been difficult to do reliably. However, with the use of the NICS(0)\textsubscript{\(\pi\)-zz} method, an excellent correlation with NBO-RE can be observed with a variety of heteroaromatics (see SI for a full list of structures) (Fig 5). The bulk dataset of 5MR heterocyclics was acquired from the literature.

Figure 4: Correlation between NICS(1)\textsubscript{zz}/\(\pi\)e and the NBO-RE/\(\pi\)e (\(R^2=0.8443\)) for monocyclic Hückel systems.

Figure 5: Correlation between NICS(0)\textsubscript{\(\pi\)-zz}/\(\pi\)e and the NBO-RE/\(\pi\)e (\(R^2=0.819\)) for 5MR heteroaromatics.
The remarkable correlation between NBO-RE and NICS for a wide variety of aromatic systems validates the use of NBO-RE as a measurement of vertical resonance energy of aromatic systems. The simplicity of the method is also worth emphasizing as it does not rely on external reference compounds, such as the BLW-derived extra-cyclic resonance energy (ECRE).\textsuperscript{25j}

However, despite the fact that NBO-RE measurements are consistent with aromatic trends, it is unclear where the cut-off point for aromaticity lies. Such a distinction is more important here as the NBO-RE method measures resonance energy, a value that is necessarily greater than zero. This is exemplified by the NBO-RE measurements of linear alkenes. Starting with butadiene (6.2 kcal·mol\(^{-1}\)/\(\pi e\)), the NBO-RE of polyenes increases with system length until a plateau near dodecahaexene (10.8 kcal·mol\(^{-1}\)/\(\pi e\)) (Table 1, Figure 6). However, it is clear that the resonance stabilization in large conjugated non-aromatic systems is unlikely to exceed the weakest (4n+2)\(\pi e^-\) systems shown previously.

Further probing of non-aromatic systems shows that when branched pro-aromatic systems (systems containing one or more aromatic resonance structures) are used, the NBO-RE values slightly increase past this plateau (4 and 5, Figure 7). Systems that can generate two aromatic rings exhibit the expected further increase in NBO-RE values. Close inspection of these systems also serves to emphasize the difference between E2pert energies typically used in stereoelectronic analysis and the NBO-RE deletion approach described herein. The dodecahexaene perturbation energies describing each isolated \(\pi_{\text{NBO}} \rightarrow \pi^*_{\text{NBO}}\) interactions are between 16.9-18.6 kcal/mol (unrelated to NBO-RE values) and those of the pro-aromatic structures are between 16.5-18.7 kcal/mol, suggesting a similar degree of stabilization between the two hexaenes. This is unusual given that the systems are expected to have aromatic resonance forms (Figure 7). This discrepancy and the origin of the similarities between perturbation energies is clarified when it is considered that perturbative analysis only interrogates the isolated interaction between adjacent and completely filled (2e\(^{-}\)) orbitals (\(\pi_{\text{NBO}} \rightarrow \pi^*_{\text{NBO}}\)). As aromaticity is an emergent property of \(\pi/\pi^*\) interactions, it is only possible to truly assess global delocalization effects by severing all interactions and recomputing the system.
energy (NBO-RE, Figure 7). Simply estimating the adjacent interaction energies (via E2Pert) is insufficient.

**Table 1:** NBO-RE values for linear polyenes

<table>
<thead>
<tr>
<th>number of $\pi$ electrons of linear polyenes</th>
<th>NBO-RE ($\text{kcal mol}^{-1}/\pi e^{-1}$)</th>
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<tbody>
<tr>
<td>4 (butadiene)</td>
<td>6.2</td>
</tr>
<tr>
<td>6 (hexatriene)</td>
<td>8.5</td>
</tr>
<tr>
<td>8 (octatetraene)</td>
<td>9.8</td>
</tr>
<tr>
<td>10 (decapentaene)</td>
<td>10.5</td>
</tr>
<tr>
<td>12 (dodecahexaene)</td>
<td>10.8</td>
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i. All NBO-RE values computed using M06-2X/6-31+G(d,p) and M06-2X/6-31+G(d,p) geometries

**Figure 6:** Relationship between NBO-RE and the length of a polyene ($y = -0.0821x^2 + 1.8743x + 0.08$, $R^2=0.994$).
Figure 7: Structures and NBO-RE values of pro-aromatic compounds 4-5. NBO-RE values obtained for 12 \( \pi \text{e}^- \). NICS(1)\( \text{ZZ} \) values are indicated at the center of the rings.

**Polycyclic aromatic hydrocarbons (PAHs).** The NBO-RE methodology can also be used to study polycyclic aromatic hydrocarbons (PAHs) in a highly intuitive manner.\(^\text{51}\) It is known that NICS measurements can be challenging to interpret in PAHs due to the difficulties in differentiating global and local induced currents. Representing PAHs by locating the largest number of disjoint Clar sextets (semi-isolated \( 6\pi \text{e}^- \) “islands”) has been found to be a highly reliable way to identify electronic characteristics.\(^\text{52}\) This concept has also been extended to BN\(^\text{53}\) and organometallic\(^\text{54}\) analogues of PAHs. However, it is usually only justified to identify the best Clar sextet\(^\text{52, 55}\) representation when it is unambiguous and only one possible representation exists. Furthermore, it is not possible to easily estimate the degree to which a system is aromatic by only using the Clar representations.

Triphenylene (9, Figure 8) is a model example of an unambiguous system, with the sextets localized exclusively on the lateral rings, leaving a relatively “empty” central ring. This is observed very clearly with the associated NBO-RE values (Table 2, entry 5) where the lateral rings (20.0 kcal mol\(^{-1}/\pi \text{e}^-\)) are closer to that of benzene (entry 1, 25.1 kcal mol\(^{-1}/\pi \text{e}^-\)) than is the NBO-RE of the central ring (7.9 kcal mol\(^{-1}/\pi \text{e}^-\)). Phenanthrene (8) is also an interesting case because the system prefers to adopt an electronic structure with two isolated sextets at the cost of creating an isolated double bond in the central ring. However, this penalty is easy to pay due to the
stability of two isolated sextets. NBO-RE clearly reflects this (entry 4) and the energy of the central ring (10.4 kcal mol\(^{-1}/\pi e^*\)) is much lower than that of each of the lateral rings (18.2 kcal mol\(^{-1}/\pi e^*\)). Pyrene (11) is similar to phenanthrene and contains two isolated sextets at the expense of two localized double bonds. This is evident by the NBO-RE (entry 7), where the lateral rings are highly aromatic (17.6 kcal mol\(^{-1}/\pi e^*\)) when compared to the central rings (10.4 kcal mol\(^{-1}/\pi e^*\)). It is also worth noting that the NBO-RE values of isolated sextets in PAHs are typically smaller than that of benzene, suggesting that aromaticity in the individual rings decreases due to increasing amounts of global and multi-ring circuits. This is especially clear when comparing phenanthrene, pyrene and the much larger kekulene (entry 8) where there is a decrease in the overall NBO-RE of individual sextets as the system becomes larger, despite the presence of a clear favoured Clar sextet picture. In any case, the NBO-RE depictions of these non-ambiguous PAHs is highly consistent with what is expected by the Clar heuristic. The low NBO-RE values for non-Clar sextets do not suggest anti-aromaticity, but instead simply that the specified ring contributes proportionately less to the overall aromaticity of the molecule. It is also worth noting that in larger systems, the percentage contribution of each ring somewhat decreases as the number of possible sextets increases.
Figure 8: left: Structures of commonly encountered PAHs and their migrating Clar sextets (or global circuit in the case of naphthalene). right: Expanded PAHs showing migrating sextets only in cases of degeneracy.

Table 2: The NBO-RE values of benzene (1) and the isolated rings in PAHs (6-12).

| entry | structure
<table>
<thead>
<tr>
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<tr>
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<td>Benzene (1)</td>
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<td>Naphthalene (6)</td>
</tr>
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<td>Anthracene (7)</td>
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<td>Triphenylene (10)</td>
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<tr>
<td>7</td>
<td>Pyrene (11)</td>
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<td>8</td>
<td>Kekulene (12)</td>
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<tr>
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<th>NBO-RE (kcal mol⁻¹/πe⁻¹)</th>
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<tbody>
<tr>
<td>1</td>
<td>25.1 (100%)iii</td>
</tr>
<tr>
<td>2</td>
<td>15.8 (50%)</td>
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<tr>
<td>3</td>
<td>15.6 (24%)</td>
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<td>4</td>
<td>18.2 (29%)</td>
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<tr>
<td>5</td>
<td>15.4 (24%)</td>
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<tr>
<td>6</td>
<td>15.7 (24%)</td>
</tr>
<tr>
<td>7</td>
<td>15.6 (24%)</td>
</tr>
<tr>
<td>8</td>
<td>18.2 (29%)</td>
</tr>
</tbody>
</table>

i. All NBO-RE values computed using M06-2X/6-31+G(d,p). ii. M06-2X/6-31+G(d,p) geometries. iii. Values in parentheses correspond to percent contributions of the indicated ring to the π-NBODel energy of the entire system. Note that only the contribution of one ring is measured.

Other ambiguous systems are more challenging to study with NICS or other magnetic criteria, possibly due to the presence of counter rotating currents that cause cancelling at ring junctions and the presence of multi-ring currents.\textsuperscript{56}

This is particularly clear for naphthalene (entry 2) where there is no clear Clar sextet and there exists the possibility of either an oscillating sextet or a global [10]annulene-like system. Anisotropy of the induced current density (AICD) suggests the latter, but the presence of a very short bridging bond suggests a large double bond character. This is in contrast to azulene, a 10π system whose bridging bond more approximates the bond length of a single bond.\textsuperscript{57} The situation is easily resolved with NBO-RE where it is evident that the oscillating sextet is slightly preferred.

In anthracene (7), magnetic criteria (e.g., NICS) suggests the central ring is apparently more aromatic than the lateral rings, a fact that can be attributed to the presence of multi and global ring currents rather than inherent aromaticity.\textsuperscript{56a} This corresponds to reactivity.\textsuperscript{56b} A
different picture emerges with NBO-RE where it is observed that both rings appear to be similar (< 1 kcal mol\(^{-1}\)/\(\pi e^-\) difference, entry 3).\(^{58}\) Coronene (10, entry 6) is also a difficult case that has been discussed extensively in the literature.\(^{59}\) It is an ambiguous system purported to exist as either a set of oscillating sextets (Figure 9, 10a) or two distinct inner (6\(\pi e^-\)) and outer (18\(\pi e^-\)) currents (Figure 9, 10b). NBO-RE values of the central (6\(\pi e^-\), 9.2 kcal mol\(^{-1}\)/\(\pi e^-\)), lateral (6\(\pi e^-\), 12.7 kcal mol\(^{-1}\)/\(\pi e^-\)) and peripheral (18\(\pi e^-\), 14.6 kcal mol\(^{-1}\)/\(\pi e^-\)) rings were measured. The very low value obtained for the central ring is consistent with NICS scans and STM images.\(^{59}\) The fact that the peripheral [18]annulene-like ring has a larger NBO-RE than the lateral sextets seems counterintuitive until one considers that part of the peripheral 18\(\pi e^-\) system is dependent on the diene moiety in the sextets. It is interesting to note that the absence of a favoured Clar representation seems to increase global delocalization as the 18\(\pi e^-\) clearly is a significant contributor.

Figure 9: The oscillating Clar sextet (10a) and the independent circuit (10b) models of coronene.

Möbius aromatics and other non-planar systems. The NBO-RE method is also perfectly adaptable for the study of non-planar aromatic structures, for which the NICS method is unable to provide useful information due to its dependence on ghost atom location. Möbius aromatics, which follow a 4\(n\pi e^-\) rule for aromaticity due to an inversion of p-orbital symmetry in the ring\(^4\)
have non-planar structures and provide an interesting framework for study using the NBO-RE method. The first reported structure of a Möbius aromatic was the benzenoid containing [16]annulene by Herges and coworkers (13, Figure 10).60 The aromaticity of this molecule has been a source of considerable controversy and debate.61 One key issue in the structure is the highly strained tetrasubstituted alkene (13, side view), which appears to only be minimally conjugated with the rest of the $\pi$-system. In order to isolate the effects of the Möbius ring and to assess the NBO-RE of the putative aromatic structure, the highly localizing benzenoid rings in the crystal structure geometry were removed and replaced with saturated carbon atoms or hydrogen atoms while leaving the aromatic circuit untouched (14).62 Interestingly, an NBO-RE value of 8.7 kcal mol$^{-1}$/\(\pi e^-\) is obtained, which strongly suggests that the monocyclic conjugated system is non-aromatic.

![Top view](image1)

![Side view](image2)

**Figure 10:** left: A purported Möbius aromatic [16]annulene (13). middle: (14) The isolated $\pi$-system containing the geometry of [16]annulene 13 without the localizing benzenoid rings (CCCTCTCC configuration); right: a recomputed theoretical structure of a similar Möbius [16]annulene (15, CCCTTTTT configuration).
A Möbius [16]annulene framework (15) with a similar topology to 13/14 was investigated by Schleyer et al. (Figure 10, compare side view of 14-15), who found that a B3LYP minimized geometry was aromatic with significant bond length equalization. This is consistent with the larger NBO-RE value of 15.0 kcal·mol⁻¹/πe⁻, which suggests a slight but present aromaticity, indicating that the strained tetrasubstituted alkene in 13/14 may be attenuating aromaticity. However, it is known that B3LYP has a tendency of overestimating aromaticity, suggesting that the structure may not be reasonable. Interestingly when the geometry was minimized with the M06-2X functional a more bond localized structure is obtained and the NBO-RE value drops to 13.6 kcal·mol⁻¹/πe⁻, a value consistent with weakly aromatic species.

![Figure 11: Structures of previously reported [4n] annulenes reported to have Möbius conformations. 16: [12]annulene; 17: [16]annulene; 18-19: [20]annulene.](image)

**Table 3: NBO-RE of various theoretical Möbius annulenes at various geometries.**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Möbius annulene</th>
<th>B3LYP/6-31G(d)</th>
<th>M06-2X/6-311++G(d,p)</th>
<th>ΔE [B3LYP – M06-2X] geometries using DLPNO-CCSD(T)</th>
<th>ΔE [B3LYP – M06-2X] geometries using LNO-CCSD(T)</th>
</tr>
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<tr>
<td>1</td>
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<td>15.0</td>
<td>13.6</td>
<td>6.16</td>
<td>-0.24 (-0.44)</td>
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<tr>
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<td>16</td>
<td>11.5</td>
<td>7.6</td>
<td>4.51</td>
<td>4.04 (3.91)</td>
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<tr>
<td>3</td>
<td>17</td>
<td>16.6</td>
<td>12.1</td>
<td>2.40</td>
<td>1.76 (1.36)</td>
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<td>4</td>
<td>18</td>
<td>14.6</td>
<td>11.3</td>
<td>8.70</td>
<td>4.05 (3.53)</td>
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<td>5</td>
<td>19</td>
<td>13.4</td>
<td>11.1</td>
<td>6.03</td>
<td>2.44 (2.01)</td>
</tr>
</tbody>
</table>
i. NBO-RE values computed at M06-2X/6-31+G(d,p) with the indicated geometries.

ii. Values indicate how much more stable the M06-2X/6-311++G(d,p) geometry is compared to the B3LYP/6-31G(p) geometry as computed with DLPNO-CCSD(T)/cc-pVTZ.

iii. Values indicate how much more stable the M06-2X/6-311++G(d,p) geometry is compared to the B3LYP/6-31G(p) geometry as computed with LNO-CCSD(T)/cc-pVDZ. Values are obtained using lcorthr=normal (without brackets) and lcorthr=tight (in brackets).

This finding warranted further investigation into the various Möbius [4π] annulene structures that have also been previously reported as being aromatic (Figure 11). NBO-RE values of the previously computed B3LYP/6-31G(d) geometries mostly show very weakly aromatic systems (Table 3), despite the tendency of B3LYP to enhance bond equalization. Möbius [12]annulene 16 appears to be the least stabilized (entry 2, 11.5 kcal mol⁻¹/πe⁻) and Möbius [16]annulene 17 approaches the NBO-RE values of weaker aromatics (entry 3, 16.6 kcal mol⁻¹/πe⁻). However, as previously observed with 15, minimizing the geometries with M06-2X/6-311++G(d,p) results in a significant drop in the NBO-RE values, with almost all species becoming either non-aromatic or very weakly aromatic. In order to confirm the reliability of the M06-2X geometries, their energies were recomputed with DLPNO-CCSD(T)/cc-pVTZ and compared against the corresponding recomputed energies of the B3LYP geometries. Not unexpectedly, almost all of the M06-2X recomputed geometries are lower in energy, suggesting that the M06-2X/6-311++G(d,p) geometries are more accurate, supporting the fact that these neutral conformations are only weakly aromatic at best. However, it has been recently shown that DLPNO-CCSD(T) can result in significant errors with strongly correlated systems such as Möbius aromatics.⁶⁵ Thus, the systems were recomputed with LNO-CCSD(T), which has been demonstrated to be superior.⁶⁵ The general trend remains the same for 16-19, but differs for 15.
where the two structures appear to be nearly identical in energy. Regardless, it is apparent that slight perturbations in Möbius structure energies result in large variations in NBO-RE values.

### Table 4: Summary statistics for single bond NBO-RE values of structures 15-19.

<table>
<thead>
<tr>
<th>entry</th>
<th>Möbius annulene</th>
<th>standard deviation</th>
<th>mean</th>
<th>range</th>
<th>min/max value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>15</td>
<td>0.159</td>
<td>1.504</td>
<td>0.42</td>
<td>1.26/1.68</td>
</tr>
<tr>
<td>2</td>
<td>16</td>
<td>0.616</td>
<td>0.918</td>
<td>1.34</td>
<td>0.30/1.64</td>
</tr>
<tr>
<td>3</td>
<td>17</td>
<td>0.101</td>
<td>1.597</td>
<td>0.27</td>
<td>1.46/1.73</td>
</tr>
<tr>
<td>4</td>
<td>18</td>
<td>0.214</td>
<td>1.005</td>
<td>0.58</td>
<td>0.65/1.23</td>
</tr>
<tr>
<td>5</td>
<td>19</td>
<td>0.231</td>
<td>1.028</td>
<td>0.57</td>
<td>0.70/1.27</td>
</tr>
<tr>
<td>6</td>
<td>14</td>
<td>0.324</td>
<td>0.497</td>
<td>0.89</td>
<td>0.59/1.49</td>
</tr>
</tbody>
</table>

i. Standard deviation of single bond NBO-RE values. ii. Max-min single bond NBO-RE values

In order to identify the origins of the attenuated aromaticity, \( \pi_{NBO} \rightarrow \pi_{NBO}^* \) orbital interactions corresponding to the interaction of only two adjacent double bonds was investigated for all interactions within each system. Such adjacent pair NBO-RE (ap-NBO-RE) values are measured by deleting (2) adjacent interactions and normalizing per electron as previously demonstrated (Table S4). This is then done for each pair of interactions present in the molecule. Summary statistics for each such deletions for all Möbius annulenes are given in Table 4 with raw data in the SI. The values obtained for [12]annulene 16 have a relatively large range (entry 2, 1.34 kcal·mol\(^{-1}\)/πe\(^{-}\)), standard deviation (0.616 kcal·mol\(^{-1}\)/πe\(^{-}\)), and low mean (0.918 kcal·mol\(^{-1}\)/πe\(^{-}\)). Examining the individual pairs of interactions also shows that 16 has values as low as 0.30 kcal·mol\(^{-1}\)/πe\(^{-}\). Conversely, the [16]annulenes 15 and 17 show a tighter range (0.42/0.27 kcal·mol\(^{-1}\)/πe\(^{-}\)) and standard deviation (1.59/0.101 kcal·mol\(^{-1}\)/πe\(^{-}\)), as well as a larger mean (1.504/1.597 kcal·mol\(^{-1}\)/πe\(^{-}\)). Interestingly the minima and maxima for 15/17 are relatively high at 1.26/1.53 kcal·mol\(^{-1}\)/πe\(^{-}\) and 1.68/1.73 kcal·mol\(^{-1}\)/πe\(^{-}\) for 15/17 respectively. This is contrasted with 14, which has the lowest mean and several extremely poor interactions that result in the very low
NBO-RE value. [20]annulenes 18 and 19 are in between those of the [12] and [16]annulenes, also with a reasonably large range and low minimum values. From this information it is apparent that the very poorly Möbius aromatic systems have attenuated aromaticities due to a small number of poor $\pi_{\text{NBO}} \rightarrow \pi_{\text{NBO}*}$ interactions. In the case of the [16]annulenes (15/17) no such bad actors exist, suggesting that these structures are likely near optimal for Möbius aromatic [16]annulenes. However, comparison of these adjacent pair values to benzene (4.41 kcal mol$^{-1}$/πe') also demonstrates that even nearly idealized Möbius annulenes are weakly aromatic.

Conclusion

In summary, we have shown that aromaticity can be understood and explored with the highly intuitive 2c-2e (Lewis-like) NBOs, further emphasizing their use in understanding electronic structures. By deleting adjacent $\pi_{\text{NBO}} \rightarrow \pi_{\text{NBO}*}$ interactions, the localized electronic structure can be obtained and compared against the fully delocalized system. A large dataset of aromatic and heteroaromatic structures shows a good correlation with the standard NICS$_{zz}$ methods, suggesting it is a highly general method that can be used for a wide variety of compounds. We have also shown that the method can be used for the assessment of local rings in PAHs, where it was discovered that the favourability of a Clar-like localization of aromatic subunits decreases rapidly with increasing ring size. The NBO-RE method is also easily applied to non-planar systems such as Möbius annulenes, where a preliminary investigation into their aromaticity is provided.

Associated Content
Computational methods, NBO-RE calculation procedure and data are provided in the Supporting Information document.

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**Notes**
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**References**


9. Hückels rules also require that a compound be planar and fully conjugated.


There are a significant number of potential NICS methods to choose from. In this manuscript we have elected to use NICS(1)π for the monocyclic 6-membered ring because of the relative ease with which a large dataset could be obtained. Though this method is not the most refined technique, it has been demonstrated to be quite effective in our case and there would not be much benefit in using the more computationally complex NICSπ methods. In the case of the 5-membered ring heteroaromatics, a smaller dataset of the more refined NICS(0)π was acquired from the literature. See Schleyer et al. (Org. Lett. 2006, 8, 5, 863–866) for more information.

There are six such interactions in benzene (see SI).

Vertical resonance energy (VRE) of benzene considers the difference between the energy of the fully delocalized benzene and a structure of the same geometry with isolated double bonds.


(b) The complete deletion of ππ* orbitals by the NBODel methodology results in an energy change of 127.3 kcal/mol, which is very close to the energy predicted by the Kekulé avoided crossing model (113 kcal/mol, see ref 45c). For reference, the BLW method computes an energy of 88-92 kcal/mol (see ref 45a). The origin of this value and its relationship to the Kekulé avoided crossing model are to be part of a future study. Despite this, NBO-RE was left as a deletion of ππ -> ππ* interactions due to its more intuitive nature.

There are a significant number of potential NICS methods to choose from. In this manuscript we have elected to use NICS(1)zz for the monocyclic 6-10 membered rings because of the relative ease with which a large dataset could be obtained. Though this method is not the most refined technique, it has been demonstrated to be quite effective in our case and there would not be much benefit in using the more computationally complex NICSzz methods. In the case of the 5-membered ring heteroaromatics, a smaller dataset of the more refined NICS(0)zz was acquired from the literature. See Schleyer et al. (Org. Lett. 2006, 8, 5, 863–866) for more information.


The benzenoid rings will ultimately serve to further limit conjugation due to the propensity of Clar sextets to localize in smaller rings.