Stacking Interactions

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Taking the Aromaticity out of Aromatic Interactions**

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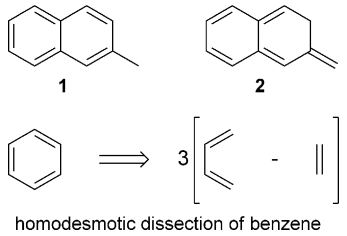
The phrase "aromatic interactions" is widely used to describe π stacking, cation–π, and anion–π interactions, among others.[1] These interactions are central to many areas of modern chemistry and molecular biology,[2] and are vital tools in the supramolecular armamentarium.[2a] The concept of aromaticity appears almost universally in definitions of these interactions, implying that they are somehow dependent on aromatic π delocalization in the interacting monomers. But does aromaticity actually enhance these interactions, or can stronger noncovalent interactions be achieved, for example, by using planar, nonaromatic polyenes?

We show below, through robust ab initio studies of model systems, that the cyclic π-electron delocalization associated with aromaticity often hinders π stacking and anion–π interactions, although it strengthens cation–π interactions. The implication is that more favorable stacking interactions can be achieved in supramolecular complexes by exploiting interactions with nonaromatic polyenes rather than aromatic systems.

In 2008, Grimme[3] showed that stacking interactions in the parallel-displaced benzene and naphthalene dimers are comparable in magnitude to the corresponding saturated cyclic systems. However, for larger acenes (i.e., anthracene and tetracene), Grimme reported enhanced stacking interactions in the aromatic dimers that are not mirrored in the saturated systems. This was attributed to long-range correlation effects.[3] The impact of aromaticity on these stacking interactions, however, was not directly addressed.

Here, we quantify the effect of aromatic π-electron delocalization on the strength of π stacking, cation–π, and anion–π interactions. We first consider the sandwich dimers of benzene with the unsubstituted rings of 2-methylnaphthalene (**1**) and 2-methylene-2,3-dihydronaphthalene (**2**; Scheme 1 and Figure 1a). Isomer **2** provides a means of quenching the aromaticity present in **1** while conserving the number of π electrons.[4] Isomers **1** and **2** can thus be used to quantify the electronic effects of aromatic π delocalization on stacking interactions.[5] SCS-MP2/TZVPP interaction energies at equilibrium separations are provided in Figure 1, and are plotted as a function of inter-monomer distance (*R*) in Figure S1 of the Supporting Information. Across the full range of distances, the stacking interaction of benzene with the nonaromatic isomer **2** is more favorable than with **1**. In other words, the nonaromatic isomer engages in stronger stacking interactions with benzene than does the aromatic isomer. This difference is not attributable to differential direct interactions[6] between benzene and the methyl/CH or methylene/CH_2 groups in **1** and **2** (see the Supporting Information), but instead results from the localization of the π system in isomer **2**.



Scheme 1. Molecular systems used to quantify the effect of aromatic π delocalization on stacking and other aromatic interactions: 2-methylnaphthalene (**1**), 2-methylene-2,3-dihydronaphthalene (**2**), and dissected benzene. In the dissected benzene, the nuclear positions are such that all interatomic distances exactly match those in benzene.

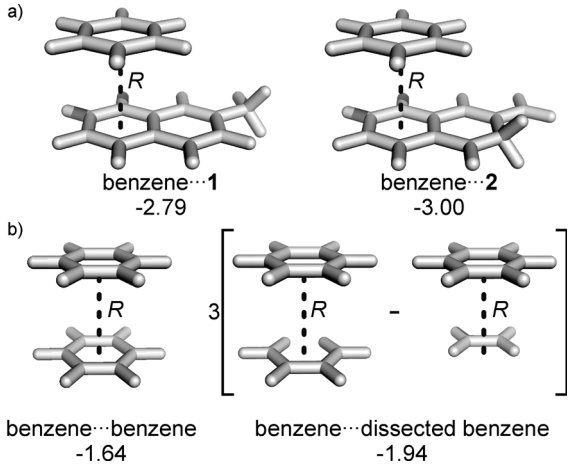


Figure 1. Sandwich dimers and interaction energies (kcal mol^{-1}) for benzene with a) 2-methylnaphthalene (**1**) and 2-methylene-2,3-dihydronaphthalene (**2**) at the SCS-MP2/TZVPP level of theory and b) benzene and dissected benzene at the CCSD(T)/AVTZ level of theory.

The homodesmotic[7] dissection of benzene depicted in Scheme 1 provides an alternative means of quantifying the effect of aromatic π delocalization on stacking interactions (Figure 1b and Table 1).[8] Comparing CCSD(T) interaction energies in the benzene sandwich dimer with the interaction between benzene and dissected benzene yields the same conclusion as above: π localization stabilizes sandwich stacking interactions by 0.31 kcal mol^{-1} at the corresponding

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Table 1: Estimated CCSD(T)/AVTZ interaction energies (kcal mol^{-1}) of benzene, Cl^-, and Na^+ with benzene and dissected benzene.[a]

	C_6H_6 (S)	C_6H_6 (P)	Cl^-	Na^+
Benzene	−1.64	−2.60	+0.86	−23.5
Dissected benzene	−1.94	−3.60[b]	−1.10	−18.2

[a] (S) = sandwich dimer; (P) = parallel-displaced dimer. [b] Interaction energy is −3.09 kcal mol^{-1} if the dissected benzene is rotated 60°.

equilibrium inter-monomer separations (3.92 and 3.84 Å for benzene and dissected benzene, respectively).

These effects are even larger for the parallel-displaced dimer.[9] In this configuration, replacing benzene with dissected benzene increases the interaction by 1.0 kcal mol^{-1}, or nearly 40% of the total interaction energy! Moreover, the magnitude of this energy difference is dependent on the regiochemistry of the localized π system (Table 1). This suggests a potential means of controlling the orientation of parallel-displaced stacking interactions in the case of localized π systems.

Cation–π and anion–π interactions are also affected by π localization. Indeed, the differences between the interaction of Na^+ or Cl^- with benzene and the dissected benzene are substantially larger than in the stacking interactions (see Figures S3 and S4 in the Supporting Information and Table 1). Intriguingly, localization of the benzene π system enhances the interaction with Cl^- to such an extent that this model system is actually bound in the gas phase, unlike benzene–Cl^-.[10] In the case of the cation–π complexes, π localization diminishes the interaction by more than 5 kcal mol^{-1}.

The enhanced stacking interaction in the sandwich dimer of benzene with dissected benzene extends over the full range of inter-monomer distances (Figure 2a). These differences are reproduced at the Hartree–Fock (HF) level of theory (gray curves), thus indicating that electron correlation effects (e.g., dispersion interactions) have little net impact. This is corroborated by SAPT2 analyses,[11,12] the results of which are plotted in Figure 2b as a function of *R*. The enhanced interaction of benzene with dissected benzene arises from a reduction in exchange repulsion, which is tempered by electrostatic effects. These electrostatic effects favor the interaction with dissected benzene for distances larger than 3.4 Å but favor benzene at closer distances. The contribution of dispersion to the difference is negligible except at small inter-monomer distances.

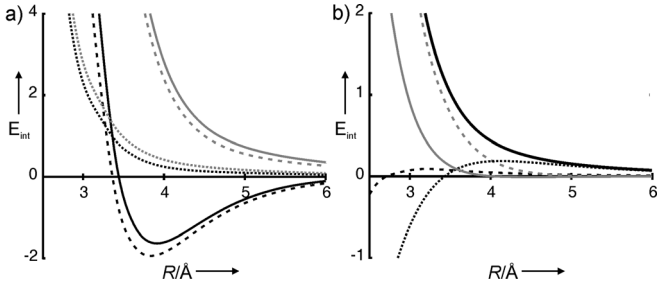

Figure 2. a) Estimated CCSD(T)/AVTZ (black lines) and HF/AVTZ (gray lines) interaction energies (E_{int}, kcal mol^{-1}) for benzene with benzene (solid lines) and dissected benzene (dashed lines), and the difference between the two (dotted lines). b) SAPT2 components [E_{SAPT2}, black solid line; E_{exch}, gray dashed line; E_{elec}, black dotted line; E_{ind}, gray solid line; E_{disp}, black dashed line] of the difference between benzene interacting with benzene and dissected benzene.

The long-range behavior of the electrostatic component can be explained based on molecular quadrupole moments. Upon π delocalization, electron density shifts towards the ring centroid (see Figure S2 in the Supporting Information), thus increasing the benzene quadrupole moment relative to the dissected case. This increased molecular quadrupole leads to more unfavorable quadrupole–quadrupole interactions in the benzene dimer compared to the dimer of benzene with dissected benzene. At close inter-monomer distances, there are larger attractive electrostatic interactions for C_6H_6 interacting with benzene compared to dissected benzene, presumably because of the enhanced charge interpenetration[13] in the delocalized system.

In complex molecular systems there will be other contributing factors, and nonaromatic compounds will not always engage in stronger stacking interactions than aromatic analogues. In particular, other electronic changes can overwhelm changes because of the π localization in the ring of interest. For example, SCS-MP2 predicts that the stacking interaction of benzene with the central ring of triphenylene is more favorable than with 2,3-dihydrotriphenylene, 2,3,6,7-tetrahydrotriphenylene, or 2,3,6,7,10,11-hexahydrotriphenylene, despite the mild aromaticity of the central ring in triphenylene that is not present in the other systems.[14]

Similarly, in larger analogues of isomers **1** and **2**, the effect of disrupting aromaticity diminishes with increasing size. The result is that the stacking interaction of benzene with methyl- and methylene-substituted tetracene, for example, only differs by 0.03 kcal mol^{-1} (see the Supporting Information). This attenuation of the effect of π localization could be a manifestation of the enhanced π–π interactions involving larger acenes reported by Grimme.[3] Despite these and other exceptions, many molecules with naturally localized π systems do exhibit enhanced stacking interactions, and should be of utility in practical applications. This includes 2,3-dimethylene-2,3-dihydronaphthalene, for which the interaction of benzene with the nonsubstituted ring is 0.34 kcal mol^{-1} more favorable than with naphthalene.

As noted previously by Grimme,[3] π–π interactions are not unique, and noncovalent interactions involving nonaromatic rings are often quite favorable. For example, the above computed interaction energies for model ethene–benzene and butadiene–benzene complexes are substantial (−0.85 and −1.50 kcal mol^{-1} for ethene and butadiene, respectively). In the latter case, the interaction energy is on par with that of the benzene sandwich dimer. Similarly, for sandwich complexes of cyclohexane with benzene, the interaction energy (−2.91 kcal mol^{-1}) is nearly 80% greater than that exhibited by the benzene sandwich dimer. This difference arises because although the dispersion interactions in the cyclohexane–benzene complex are slightly diminished compared to those in the benzene sandwich dimer, the electrostatic interactions are far more favorable (see Table S3 in the Supporting Information).

In conclusion, our main findings can be summarized as follows:

1. Monomer aromaticity is not a defining feature of "aromatic interactions", and π stacking and anion–π interactions should be more generally defined without reference to aromaticity.
2. For small cyclic polyenes, nonaromatic systems engage in stronger π stacking and anion–π interactions than analogous aromatic systems. The enhanced stacking interactions for nonaromatic polyenes stem from a reduction in exchange repulsion, not dispersion effects.
3. Noncovalent interactions of arenes with many nonaromatic cyclic systems are more attractive than similar arene–arene interactions, and sometimes exhibit a dependence on orientation. Consequently, these other types of interactions should be of utility in supramolecular applications.

Ramifications of these findings abound. For example, in supramolecular chemistry, it should be advantageous to incorporate interactions involving planar, nonaromatic polyenes to exploit the orientation dependence and enhanced stacking interactions provided by localized π systems.

Computational Methods

Interaction energies were computed via the supramolecular approach using either SCS-MP2/TZVPP[15] or an estimate of CCSD(T)/AVTZ, where AV*X*Z denotes the standard aug-cc-pV*X*Z basis of Dunning.[16] Monomer structures were fixed at B97-D/TZV(2*d*,2*p*)[17] optimized geometries in the former case, and MP2/AVTZ optimized geometries in the latter. CCSD(T)/AVTZ energies were estimated by appending a correction for basis set incompleteness (MP2/AVTZ–MP2/AVDZ) to CCSD(T)/AVDZ energies. All supramolecular interaction energies were corrected for BSSE[18] and were computed using Molpro, while B97-D geometries were optimized with Gaussian09.[19] Density fitting was used in all SCS-MP2 and B97-D computations. Only the 1s orbital was frozen on Na^+, for which the cc-pCVXZ basis sets were used. All core orbitals were frozen in the other correlated computations. SAPT2[11a] computations utilized the AVDZ′ basis set[20] and were executed using SAPT2008.[11b] For the 1D potential energy curves in Figure 2, energies were evaluated every 0.4 Å across the full range and then every 0.1 Å surrounding the energy minimum.

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