Molecular Modeling Exercises and Experiments

Quantitative Thermodynamic Descriptions of Aromaticity Ⱳ

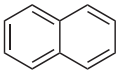## A Computational Exercise for the Organic Chemistry Laboratory

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The availability of software packages for molecular modeling and quantum mechanical calculations has led to greater use of computational models in organic chemistry courses at all levels. While very few introductory organic texts include actual problems that students must solve using computer modeling, several are accompanied by CDs or Web sites that host three-dimensional structures generated by computational means *(1)* and some offer supplements that provide excellent computational exercises *(2)*. The purpose of this article is to illustrate how students in the introductory organic chemistry course at Iona College use a particular software package, SPARTAN ES-02,[1] to study the concept of aromaticity.
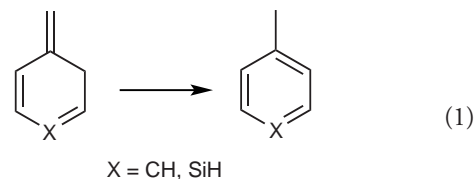
This computational exercise is designed to be part of the second-semester organic chemistry laboratory and is presented the week before an experiment on electrophilic aromatic substitutions. Students are familiar with the theory of aromaticity from the lecture part of the course and this concept is reviewed briefly in the context of the exercise prior to dis-

missal from the laboratory. The software is made available to the students outside the laboratory setting via the college's computer network[2] under a limited site license purchased from the manufacturer. Although most students have had prior experience with the software from exercises completed in the preceding semester, detailed instructions for building and manipulating the structures and making the calculations are included in the laboratory handout for the exercise.[3] The first assignment is to consider a set of four hydrocarbons and two hydrocarbon ions and determine whether each is aromatic, nonaromatic, or antiaromatic. To do so, students are instructed to provide all the information required to complete Table 1, that is, the number of π electrons, the geometry, and the resonance energy. Students obtain the number of electrons by inspection of the structures. Geometries are determined using semiempirical (AM1) calculations. The resonance energies are then calculated from the isodesmic isomerization reactions shown in Table 2. For this, ab initio computations of a single-point energy for each isomer are made at the Hartree-Fock 3-21G(*) level from the AM1 geometry. The specific isomerization reactions in Table 2 are meant to show the energetic cost of disrupting the cyclic conjugated system and are written in a student friendly fashion to directly yield a positive ΔE value for aromatic compounds. Calculations utilizing such hypothetical reactions (eq 1) have been published in the recent literature *(3)* as an example of one type of descriptor that can be used in attempting to determine the aromaticity of a particular structure.

$$X = CH, SiH \qquad (1)$$

One can see that the net change in eq 1 is the formation (for X = CH) of the benzene ring system. If this, or any analogous reaction, is highly exothermic, the given structure is considered to be aromatic. On the other hand, highly endothermic values in such a reaction would be characteristic of antiaromatic compounds, while values close to zero (arbitrarily, ±5 kcal/mol) indicate that a given structure is nonaromatic. This method is then used to evaluate three heterocyclic compounds, pyridine, thiophene, and furan. The data on these compounds are found in Tables 4 and 5 in the Supplemental Material.Ⱳ

Table 1. Aromaticity in Conjugated Cyclic Hydrocarbons and Hydrocarbon Ions

Structure	Number of π Electrons	Geometry	Resonance Energy/ (kcal/mol)	Aromaticity[a]
	6	planar	37.7	aromatic
	10	planar	25.2	aromatic
	4	planar	−45.2	antiaromatic
	8	nonplanar	0.549	nonaromatic
	6	planar	32.5	aromatic
	8	planar	−19.3	antiaromatic

[a]Compounds are considered aromatic, nonaromatic, or antiaromatic.

Some additional considerations are warranted when multiple isomers are possible. For example, in applying eq 1, either 1-methylnaphthalene (resonance energy, RE = 26.2 kcal/mol), 2-methylnaphthalene (RE = 25.2 kcal/mol) or both isomers in combination could be used to demonstrate the aromaticity of naphthalene. The 2-methyl isomer is selected here to minimize any steric bias[4] in the results. This is an attempt to concentrate student focus on aromaticity, but is hardly necessary and some instructors might even find it desirable to explore steric effects in this context. Likewise, the all cis isomer of cyclooctatetraene is used to avoid straying from the main purpose of the exercise. However, a computational exercise that explores energy differences between cis and trans cycloalkenes is available *(4)* and the study of this concept in connection with aromaticity is perhaps worthy of further investigation.

From the exercises described above, students were able to conclude the following about the nature of the compounds studied:

Aromatic: benzene ~ pyridine > cycloheptatrienyl cation > naphthalene > thiophene > furan

Nonaromatic: cyclooctatetraene

Antiaromatic: cyclobutadiene > cycloheptatrienyl anion

Students report that the total computational time and the time required to build the structures does not exceed the normal four-hour laboratory period and are generally pleased with both the results of the exercise and freedom to do it at a time of their own choosing.

Part of the student satisfaction may be due to fact that the actual computations are fast. In using SPARTAN software, geometry optimizations are reported to be generally

Table 2. Resonance Energy for Hydrocarbons and Hydrocarbon Ions

Resonance Structures	Energy of B/ au	Energy of A/ au	ΔE/ au	ΔE^a/ (kcal/mol)
	−268.173786	−268.233861	0.060075	37.7
	−419.989034	−420.029287	0.040253	25.2
	−191.660695	−191.588701	−0.071994	−45.2
	−344.618063	−344.618938	0.000875	0.549
	−306.156826	−306.208581	0.051755	32.5
	−306.360845	−306.330057	−0.030788	−19.3

NOTE: 1 au = 627.5 kcal.

slower than the calculation of single-point energies and computational time increases from semiempirical < HF 3-21G(*) < pBP/DN* < HF 6-31G* < MP2/6-31G* *(5)*. This was found to be the case in practice, although the student version of this software precludes the use of density-functional models since they are not available on SPARTAN ES-02. The geometry optimizations for Table 1 are essentially instantaneous using the AM1 model. However, as indicated by Table 3, both the AM1 and PM3 models yield energy values for eq 1 that are lower than the ab initio methods by approximately one-third. Thus, the thermodynamic calculations for Table 2 are performed using the HF 3-21G(*) model and are complete in a matter of a few seconds. Also from Table 3, it can be seen that the energy values obtained are not overly sensitive to the size of the basis set used. Since all other Hartree–Fock methods, as expected, require considerably more computer time, the HF 3-21G(*) is the most economical; that is, it is by far the fastest of the useful methods.

Finally, it should be emphasized that the methodology employed here is widely applicable and the examples used in this case are merely representative. The exercise can be easily modified to suit individual needs.

Aromaticity

Chemists in the 19th century discovered a large number of stable, naturally occurring compounds that contained the benzene ring as a unit. The fact that the benzene ring maintained its integrity over a wide range of physical and chemical processes was a mystifying development because of the general awareness in that era of the highly reactive nature of unsaturated organic compounds. The benzene ring was unsaturated, but often required forcing conditions to react and, unlike alkenes and alkynes, maintained the same degree of unsaturation after combination with electrophilic reagents. Since some of the earliest studies focused on highly fragrant compounds such as vanillin, molecules containing benzene rings were characterized "aromatic".

Table 3. Comparison of the Resonance Energy of Methylbenzene Calculated with Various Computational Models[5]

Method[a]	$-\Delta E$/(kcal/mol)
HF3-21G(*) from AM1	37.7
HF6-31G* from AM1	36.1
HF6-31G* from 3-21G(*)	34.9
pBP/DN* from AM1	38.8
pBP/DN* from 3-21G(*)	34.5
pBP/DN* from 6-31G*	34.4
MP2 6-31G* from AM1	33.5
Reference	35.2[b]
PM3 from initial	25.8
AM1 from initial	24.2

[a]Values used to determine $-\Delta E$ are single-point energies calculated with given method from indicated geometry.
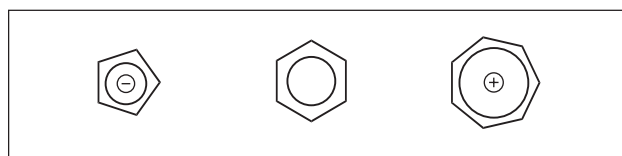[b]From ref 3.

Figure 1. Doering's triad of cyclic species that contained six π electrons and exhibited enhanced stability.

Throughout the first half of the 20th century significant effort was extended in attempting to define a general concept of aromaticity. Some niche in the structural theory was sought to rationally explain the rather remarkable properties of benzene, which in the modern era came to include unique geometric and magnetic aspects, in addition to high stability and specialized reactivity. Ultimately, Hückel successfully applied MO theory to produce the following generalization for molecules and ions, or portions of molecules and ions, that are planar, cyclic, and fully conjugated: Those containing $4n + 2$ π-orbital electrons are aromatic, while those containing $4n$ π-orbital electrons are antiaromatic. The term "antiaromatic" was used to denote those molecular systems predicted to be particularly unstable or extremely reactive. An article by Kikuchi that highlights Hückel's contribution to the development of the structural theory of benzene appeared in this *Journal (6)*. Kikuchi comments that the first actual verification of Hückel's rule occurred in 1954 with Doering's isolation of cycloheptatrienylium bromide (eq 2) as a stable, water soluble, ionic solid.

(2)
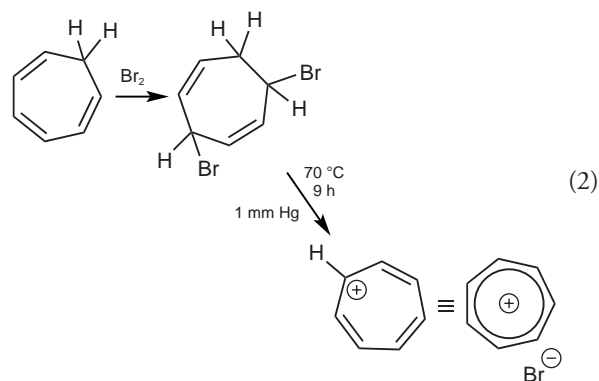
In his work Doering cited a previously known preparation of the cyclopentadienyl anion and looked upon the cycloheptatrienyl cation as the final member of a "triad", consisting of benzene and the two ions (Figure 1), that confirmed theoretical predictions of enhanced stability for cyclic species that contained six electrons *(7)*.

Subsequent experiments served to confirm the validity of Hückel's insight, which is based on the filling order of the bonding MOs. For species that exist as planar regular polygons, there is a low-energy orbital followed by a series of n degenerate orbital pairs. Hence, after filling the first orbital (2 electrons), $4n + 2$ systems retain the 4 electrons necessary to completely fill each of the n successive orbital pairs, while
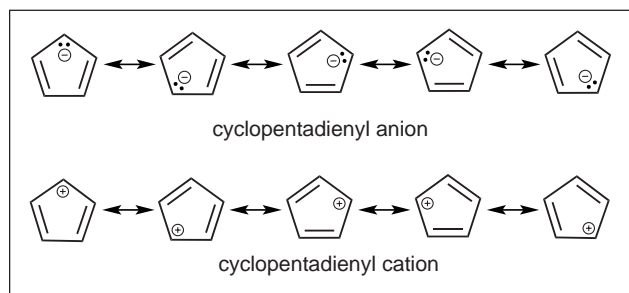
Figure 2. Canonical forms for the cyclopentadienyl cation and anion.

$4n$ systems would have just 2 electrons available for the nth orbital pair.[6] According to Hund's rule, this results in a configuration that contains a single electron in each orbital of the highest occupied pair. Preparation and analysis of the four-electron cyclopentadienyl cation is perhaps the clearest demonstration of antiaromaticity. The final transformation in the sequence, shown by eq 3, required a highly specialized apparatus cooled by liquid nitrogen just to manipulate reagents and observe the product.
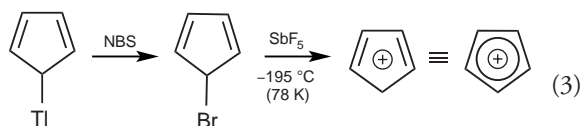
In accord with Hückel theory the compound was shown by spectroscopy to be a triplet diradical (8).

Implicit in the use of MO theory is the failure of resonance theory to provide a meaningful explanation of aromaticity. Although simple qualitative resonance theory has proved to be an invaluable device for instructors in organic chemistry, it has been noted (9) that the same number of equivalent canonical forms can be drawn for either the cyclopentadienyl cation or anion (Figure 2). Given the current state of experimental knowledge regarding these two ions, it is clear that real distinctions cannot be made solely on the basis of electron delocalization. On the other hand, Hückel MO theory predicts aromatic stability for the $4n + 2$ electron anion and antiaromaticity for the $4n$ electron cation, both of which are found experimentally.

Quite naturally the question arises as to how systematic distinctions of aromaticity can be made and whether such differences can be rendered suitable for undergraduate instruction. A recent *Journal* article (10) compared the thermodynamic, magnetic, and geometric properties of cyclooctatetraene with those of benzene to characterize the former as nonaromatic. In addition, the reactivity of cyclooctatetraene in the Diels–Alder reaction was used as a further illustration of how such distinctions can be accomplished.

However, this type of one-to-one comparison was not intended to establish any sort of quantitative scale. Moreover, direct computations of the energies of conjugated cyclic compounds using Hückel MO theory did not provide a realistic quantitative scale of aromaticity until Schaad and

Hess (11) modified the reference system in 1974 by devising additive bond-energy terms such that the reference energy for the benzene molecule, for example, was given by three times the standard energy of the ($-CH=CH-$) bond plus three times the standard energy of the ($=CH-CH=$) bond. The sum of the reference bond energies (in this case, 7.6 β)[7] was subtracted from the Hückel energy (8 β for benzene) and the authors then used the computed values divided by the number of π electrons, the so-called resonance energy per electron (REPE = 0.066 β for benzene), as a quantitative measure to be compared with the known properties of various conjugated cyclic hydrocarbons. Consequently, it is gratifying to see that the isodesmic isomerization reaction used in the exercises described above produces similar, if not somewhat improved results when applied to the same structures. These results are included in the Supplemental Material[W] as Table 6, which is essentially a recreation of the data table presented by Schaad and Hess some three decades ago.

Summary

Computations based on the isodesmic reaction shown in eq 1 proved suitable for student exercises that establish a quantitative scale of aromaticity. The computations are straightforward in the sense that they require students to obtain the energies of only two structures per measurement. The energy values must be computed using ab initio methods but are not overly sensitive to the size of the basis set used and thus, are reasonably fast. The methodology is applicable over a wide range of structures

Acknowledgments

[W]Supplemental Material

A student version of the exercise and three data tables are available in this issue of *JCE Online*.

Notes

1. Available from Wavefunction, Inc. 18401 Von Karmen Ave., Suite 370, Irvine CA 92612

2. Students use Pentium 4 based PCs at 1.7 GHz (minimum) with 512 MB of RAM operating under Windows XP.

3. A copy of this student exercise is included in the Supplemental Material.[W]

4. 2-Methylnaphthalene is more stable than 1-methylnaphthalene by 1.3 kcal/mol when the energies are computed using the HF 3-21G* method from the AM1 geometry. However, the hypothetical polyene precursor for the 2-methyl isomer shown in Table 2 is more stable than the precursor for the 1-methyl isomer by an energy value of 2.2 kcal/mol when calculated in the same fashion. The presumption here is that the energy difference in the precursors is due to steric effects from a forced s-cis conformation in the latter. Thus, the energy released by isomerization of the polyene to the aromatic 1-methylnaphthalene includes a small com-

ponent (ca. 1 kcal/mole) resulting from relief of steric strain that is not a factor in the corresponding conversion to the 2-methyl isomer.

5. Table 3 requires PC SPARTAN Pro (Wavefunction, Inc.) for computations.

6. For further discussion see ref *9*, p. 57.

7. In Hückel MO theory, the resonance integral is designated by β. In this article it serves as a relative energy indicator.

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