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Perspective

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Using Antiaromaticity To Illuminate Aromaticity during a Research Career with Undergraduates

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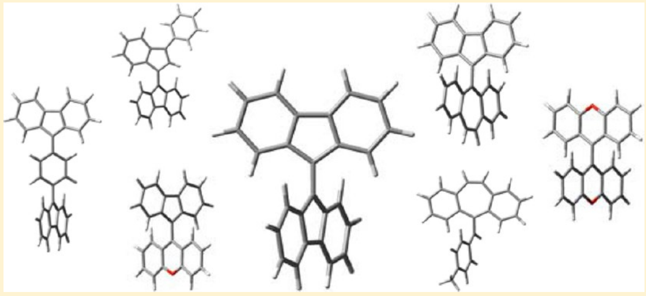
ABSTRACT: Antiaromatic species tend to be among the least well-studied and understood group in organic chemistry, primarily because their anticipated instability dissuaded most chemists from exploring their behavior. A research project that was intended to form three-dimensional aromatic dications resulted instead in a set of antiaromatic dications from oxidation of fluorenylidene derivatives. These dications can be modified in ways that help illuminate factors that affect both antiaromaticity and aromaticity. The characterization of these species, as well as antiaromatic dianions, through magnetic, energetic, and structural properties is described along with the relationships between these properties. Because this work represents contributions almost exclusively from undergraduate researchers, and because many readers of the Journal may not have a great deal of experience in this environment, I also include some thoughts about the opportunities and challenges of undergraduate research.

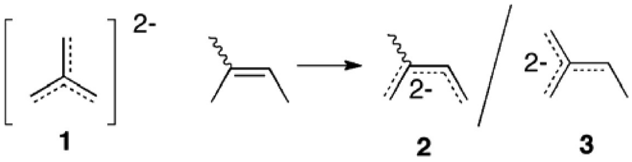


I am delighted to have the opportunity to give my perspective on two areas, antiaromaticity and undergraduate research. I began my research life looking at novel forms of aromaticity in hydrocarbon dianions, and that research has evolved to an examination of antiaromaticity in hydrocarbon dications and dianions. The ability to experimentally characterize antiaromatic species has provided greater credence to calculated measures of antiaromaticity and may provide the opportunity for a deeper understanding of aromaticity. This article also allows me an opportunity to reflect on the process of research at predominantly undergraduate institutions (PUIs) and to comment on the value, challenges, and rewards of undergraduate research and the infrastructure, both local and national, necessary to ensure its health.

■ INITIAL WORK WITH AROMATIC SPECIES

My career in aromaticity and antiaromaticity began with my graduate work with Robert Bates at the University of Arizona on delocalized dianions. I had initially started with a new project for the Bates group, the generation of delocalized radicals related to the anions being studied by the group. The plan was straightforward, the generation of the radicals in the cavity of an ESR spectrometer through initial photochemical cleavage of *tert*-butyl peroxide followed by hydrogen atom abstraction. I could not find evidence of radicals to save my soul. It was clear that I could do the classroom work but I was apparently incapable in the laboratory. I took coursework in library science but that was not the right fit for me. Finally, I developed a project looking at the use of the potentially Y-aromatic isobutylene dianion, **1**, in synthesis. I took the successful results to Professor Bates and convinced him to let me do this work for my thesis. So, a potentially aromatic species saved my professional life.[1−3]

That work served as the basis for my initial undergraduate research program, started first at Carleton College and continued at Trinity University. The isobutylene dianion, a 6π-electron species, was of interest because dilithiation of isobutylene occurred more rapidly than monolithiation,[4] with the apparent stability possibly associated with a novel form of aromaticity.[5] We examined the question by looking at dilithiation in species, such as 2-methyl-2-butene, which could form either linear- or cross-conjugated dianions, **2**/**3**. The first experiments showed initial formation of the linearly conjugated dianion **2** with isomerization with time to cross-conjugated **3**, suggesting its greater stability.[6] Subsequent studies, however, showed that the preference for the formation of cross-conjugated dianions may have been the result in part of the stabilization afforded by lithium with its ability to coordinate twice.[7−11] During my time at Carleton, I benefited greatly from mentoring by the faculty of the chemistry department, particularly Jerry Mohrig. His insistence that I write proposals early in my two-year term appointment resulted in successful applications to both PRF and Research Corporation. I am particularly grateful for the confidence that the Research Corporation demonstrated in my potential by providing me with two years of funding, even though my position at Carleton only guaranteed one summer of research, and at the time of the award, I had no certainty of a permanent position after Carleton.



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STARTING AN UNDERGRADUATE RESEARCH PROGRAM

As I reflect about my time at Carleton and the challenges of starting a successful undergraduate research program, a key element for me was the opportunity to bring expertise from my graduate work to my research program. A challenge for researchers at PUIs is the uncertainty of expertise related to their research among colleagues in the department. Beginning with a project related to graduate or postdoctoral research helps ensure that the necessary technical competency will be there. Of course, there is also the concern about intellectual ownership of the research. It must be clear to reviewers of proposals that the ideas represent the PI's own definition of a problem rather than that of the graduate supervisor.

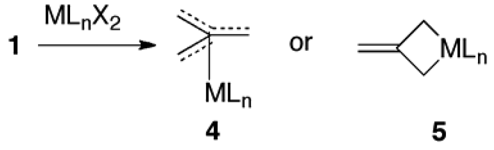
The mentoring I received at Carleton was invaluable, but sometimes the environment is not as supportive. I would encourage researchers starting their own research programs, including postdoctoral researchers, to look at the resources provided by the Council on Undergraduate Research, www.cur.org, which can offer the services of a mentor and provide guidance in developing a research program or writing proposals. The key for any faculty member considering a research program with undergraduates is to first identify research ideas worth pursuing and to consider how they can be done in the anticipated environment, in terms of infrastructure, time, and the more limited opportunity to develop expertise among students who may be involved in the project for only a semester or a summer. It is also important to select a research area that is important but not so cutting edge that the project can be "scooped" by an effort from a major research university with greater resources. However, even though research will be done by undergraduates and will progress at a slower rate, the quality of research must continue to be high. One should not underestimate the abilities of capable undergraduate students.

My research program continued to mature after I moved to Trinity for a tenure-track position. Again, I benefited from supportive colleagues with special support from the other organic chemistry professor, Ben Plummer. Ben had established a robust research program with funding from the Welch Foundation and then NSF and provided for me a model of how research with undergraduates could be productive. Mike Doyle, who joined the department in 1984, provided a model of undergraduate research on a larger scale and an expanded vision of what I could aspire to do. I found that in the early years it was most practical for me to do the "bread and butter" research that had the greatest likelihood of being successful, rather than giving those projects to my students. If I wanted to establish a fundable research program that would support students in the future, I needed to make sure that I had good papers coming out of my lab early. I presented some of these ideas at a symposium on Undergraduate Research as Chemical Education at a national ACS meeting in 1982 and subsequently published them in *J. Chem. Educ.*[12] A paper that is almost done is no different in the eyes of the outside world, and funding agencies, than a paper that is just a glimmer in a faculty member's eyes. It is challenging in science at all levels to live in three time periods, the past that one is writing up, the present with the current activities of students in lab, and the future in the context of grant proposals to write, but you put any of these aside to focus on the others at your peril.

POTENTIALLY DISRUPTIVE EVENTS: STARTING A FAMILY AND CHANGING RESEARCH DIRECTIONS

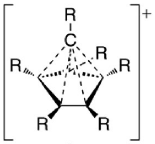
During this early period of my career, two potentially disruptive events happened. First, in 1986 my daughter was born, timed beautifully for late June, since Trinity had no maternity leave program at that time, and in 1988 my son arrived, again in the summer but in early August.[13] When I was pregnant, I needed to limit my time in the lab, so my working style had to change. I increased the size of my research group so that I could form research teams, an experienced student paired with a less experienced student. The benefits from such a model are great, and I continue to operate with it. Because I have been able to obtain sufficient funding for a large group, I am able to have students work in my lab for more than one summer and to capitalize on their expertise. I am able, and was forced, to extend the research experience to students very early in their academic career in order to fill my group. An early research experience can be invaluable for students, helping them to develop intellectually and to learn about areas of potential interest at a time when they can act on this knowledge in shaping their college career. In the research team, the experienced student, who might have been a freshman the previous summer, gets a taste of leadership as he/she is expected to train the new researchers in common techniques in lab as well as the use of *Chemical Abstracts* and the design of research presentations. I am aided in this plan by the Trinity curriculum, which has for nearly 20 years begun the organic sequence in the spring of the first year, thus providing students with the skills necessary for research in organic chemistry in the summer following their first year in college.

The second potentially disruptive event was a substantial change in the focus of my research program from cross-conjugated dianions to the use of the isobutylene dianion as a synthon in the preparation of transition metal complexes, potentially forming either trimethylene methane complex **4** or metallocyclobutane **5**. My naïve thought was that if the complex was stable, it could be characterized, while an unstable metallocyclobutane might be an olefin metathesis catalyst. While this proved to be a fundable idea, I certainly did not have the technical skills to deal with such potentially air-sensitive materials nor did I have the background to recognize a useful result if it was not really obvious. We were able to publish several papers,[14,15] but it was clear that I was not likely to be successful in this area so I returned to physical organic chemistry. My ability to move into a new area that was not particularly productive in terms of papers illustrates the relatively forgiving nature of research in the undergraduate arena. You have to demonstrate an ability to be productive in your environment, but once some capital is established, you can spend a bit of time learning a new area. You need to recognize relatively rapidly if it is not likely to be productive, but you can have a grace period in terms of funding because the costs of supporting an undergraduate research program are relatively small. I found my period of time in the world of organometallics to be really liberating in terms of the broader array of elements available to me, but this did not trump my lack of expertise.



THE ROAD TOWARD ANTIAROMATICITY

At this point in my career, I felt that I had mined the world of cross-conjugated dianions. I decided that changing to dications would keep me in the area of polyions and allow the exploration of the differences in behavior of dications compared to dianions within the same carbon framework.[16] In addition, the ability of cations to form nonclassical carbocations could allow access to another novel form of aromaticity, three-dimensional aromatic hypervalent species cations such as **6** and dications such as **7**. We began by attempting to reproduce the synthesis of **6**, R = CH_3, beginning with hexamethyl Dewar benzene but found the synthesis of the starting material to be much more sensitive in our hands than was apparent from the literature.[17] Fulvenes appeared to be more tractable so we considered access to **6** from that angle.



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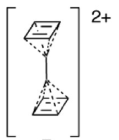

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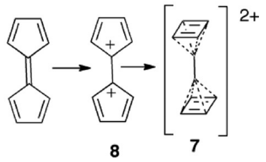
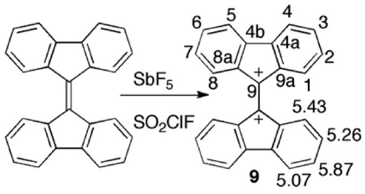


At that time, we also began to consider access to other pyramidal species by oxidation of [5.5]fulvalenes. Our plan was to form the antiaromatic bis-indenylidene dication **8** with SbF_5 in SO_2ClF assuming that it would isomerize to the three-dimensional aromatic dication **7**, a species shown to be a minimum on the potential energy surface by Moriarity.[18] Clearly, the antiaromaticity of the initial dication would be a strong incentive for the dication to isomerize to the potentially aromatic dication. Because the parent [5.5]fulvalene was susceptible to polymerization, we chose to begin with the examination of the oxidation and rearrangement of tetrabenzo[5.5]fulvalene. To our surprise and concern, the oxidation stopped with **9**, which was formally antiaromatic. But of course it could not be antiaromatic because we could characterize it. That then forced us to consider what properties typify aromatic species so that we could determine whether we did indeed have a species that was functionally antiaromatic.



There are three general categories of properties that have been used to characterize aromatic species, properties that come from the behavior of benzene.[19−21] Of greatest value to chemists is the special *stability* associated with benzene, often evaluated through aromatic stabilization energies[22] as well as kinetic stability related to the large HOMO−LUMO gap characteristic of benzene.[23,24] *Structural* properties, including planarity and lack of bond length alternation, can be evaluated through the harmonic oscillator model of aromaticity (HOMA)[25] which considers both the increase in bond length alternation (GEOmetrical contribution) and an increase in the mean bond length compared to benzene (ENergetic contribution). *Magnetic* properties are based on the existence of a ring current that, while experimentally unobservable, can be measured through the chemical shift of protons,[26,27] by evaluation of magnetic susceptibility exaltation, Λ, and anisotropy,[28−31] and through the nucleus-independent chemical shift (NICS),[32,33] which probes the magnetic environment at the center of the ring current. NICS is a calculated value that uses as the probe a dummy (ghost) atom placed 1 Å above and below the plane of the ring to avoid the effects of the σ-electrons in small rings. Recent advances have demonstrated the importance of using the tensor of the chemical shift that is perpendicular to the ring, $\mathbf{NICS(1)}_{zz}$.[33] While the ease of calculation of NICS has made it one of the most commonly used measures of aromaticity, it has not been universally accepted because there are no general experimental measures that can be used directly to validate NICS.[34]

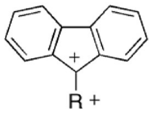
The challenge comes with the use of these properties as quantitative measures of aromaticity. That is, after all, the use we wish to make of aromaticity, to tell us not only that a proposed molecule is stable, for example, but how stable it is. If all properties described above are measuring the same phenomenon, one should see a linear relationship between them. This appeared to be untrue for aromaticity,[35−37] with some workers in the field suggesting that we should consider different types of aromaticity: "magnetic" or "classical/energetic" aromaticity.[37] Thus, it was not clear which property would most reliably evaluate the potential antiaromaticity of **9**.

As we embarked on the examination of our unusually stable antiaromatic dication, we used properties from all of these categories to determine whether our dication and related species were behaving as though they were antiaromatic. That is, would their magnetic properties be opposite in sign from those of aromatic compounds, would they be less stable than an appropriate reference compound, or would they demonstrate bond length alternation or be nonplanar? Not knowing which of these properties would be appropriate, we tried to evaluate all of them.

■ MAGNETIC PROPERTIES: ^{1}H NMR SHIFTS

Because aromatic compounds are distinguished by a diatropic shift, we looked for a paratropic ^{1}H NMR shift in our dication.[38] The proton shifts for **9** range from 5.07 to 5.87 ppm, upfield shifts from the starting material, but the magnitude of that shift is complicated by the positive charge. We examined the difference between the average shift of **9** and that of the tetraphenylethylene dication, a model that could not sustain an antiaromatic ring current, and found that **9** was 3.34 ppm upfield, a substantial paratropic shift.[39] When this comparison is done for the substituted fluorenyl monocations of Olah and Schleyer,[40] the largest difference found was 0.50 ppm, when the substituent on C-9 of the fluorenyl system was Cl. While the fluorenyl monocation had initially been considered as antiaromatic because solvolysis of fluorenyl derivatives was slower than for reference systems, suggesting destabilization of the fluorenyl cation,[41] subsequent examinations failed to find evidence of substantial antiaromaticity using either energetic or magnetic measures.[42,43] However, the substantial paratropic ^{1}H NMR shift of **9** compared to the smaller shift of the fluorenyl cation suggested that the second fluorenyl cationic system, which could be considered as a cationic substituent on C-9, resulted in the apparent increase in antiaromaticity. In essence, a positively charged substituent could increase the antiaromaticity of the fluorenyl cation by decreasing the availability of electron density in that substituent available to stabilize the fluorenyl system. This suggested that other positively charged substituents at C-9 might result in additional examples of antiaromatic fluorenyl systems, **10**, indeed indicating that altering the degree of electron density might provide a suite of antiaromatic fluorenyl cations whose antiaromaticity could be studied systematically.

We next prepared the dication of tetrabenzo[5.7]fulvalene, **11**, with ^{1}H NMR shifts of the fluorenyl system similar to those of **9**, as well as the aromatic dication of tetrabenzo[7.7]fulvalene, **12**. Comparison of the protons of **9** and **11** showed an unexpected pattern. The chemical shifts for H-3 and H-4 of **11** were more downfield than the corresponding protons of **9**, suggesting diminished antiaromaticity but the chemical shifts for H-1 and H-2 were more upfield. We proposed that the ring systems of these dications were perpendicular, resulting in the ortho protons of each ring system essentially protruding into the "center" of the ring current of the opposing ring systems. For **9** that would mean that the ortho proton on the fluorenyl system with a shift of 5.43 ppm would feel the effects of the antiaromatic ring current on the fluorenyl system and be shifted downfield while the analogous protons of **11**, 4.98 ppm, would be shifted upfield by the aromatic ring current of the tropylium cation. A second confirmation of this effect was demonstrated by the ortho protons on the tropylium system of **11** and **12**.[44]



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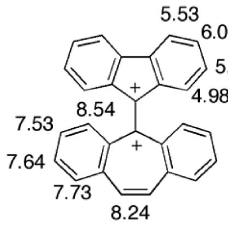

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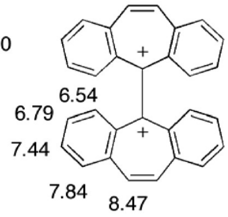

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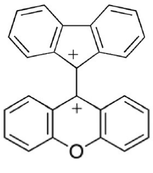
MAGNETIC MEASURES: NICS AND MAGNETIC SUSCEPTIBILITY EXALTATION

We extended the examination of the dications of fluorenylidene systems with cyclic substituents to **13**, **14**, and **15**. We were again able to vary the antiaromaticity of the fluorenyl system by varying the substituent on C-9. We could not use the sum of the ^{1}H NMR shifts to assess antiaromaticity because of the interaction of the protons on C-1 and C-2 with the opposing ring system, but the proton on C-4 showed that the order of increasing antiaromaticity was **12** < **15** < **14** < **13** < **9**.[45] I had become more proficient in computational methods as a result of a sabbatical leave spent in the laboratories of Professor Josef Michl at the University of Colorado, allowing us to include calculated measures of antiaromaticity such as NICS and magnetic susceptibility exaltation, Λ,[46] which agreed with the order from the shift of C-4.

While we had determined Λ from the calculated magnetic susceptibility of our dications and the compounds used to create the increments that form the localized reference system, it is possible to experimentally determine Λ by using a variety of approaches including the Evans method[47−50] to obtain these magnetic susceptibilities. NICS, however, has no experimental analogue, which has been a source of concern with its use, as mentioned previously. Since the method used to calculate NICS is the same as that used to calculate the ^{1}H and ^{13}C NMR shifts, a good relationship between the experimental and calculated shifts gives support to the use of NICS. That relationship was shown for these fluorenyl cations with cationic cyclic substituents.



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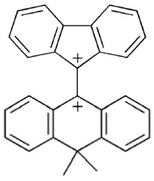

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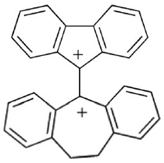

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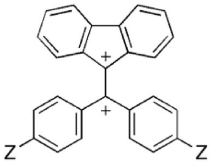
ENERGETIC MEASURES: SMALL HOMO−LUMO GAPS

We sought evidence of kinetic stability through examination of the HOMO−LUMO gap. The large HOMO−LUMO gap for aromatic species has been associated with high stability and low reactivity. Experimental evidence for this gap should be related to the lowest energy/longest wavelength transition in the electronic spectrum, and we sought that information for these dications. We used TD-DFT calculations to model the longest wavelength transition in the electronic spectrum, which was crucial because the calculations showed that the longest wavelength transition would be in the near-IR, which was inaccessible to us through instrumentation limitations. However, we were able to demonstrate that the TD-DFT calculations accurately modeled the region of the spectrum accessible to us, allowing us to draw conclusions from calculated NIR absorbance. As anticipated, there was a linear relationship between the energy of the longest wavelength transition and the HOMO−LUMO energies for the fluorenylidene dications with cyclic substituents, along with a series of aromatic mono- and dications. Those species with small HOMO−LUMO gaps were also those with an electron count consistent with antiaromaticity.

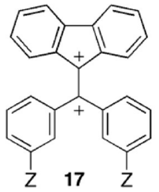
ENERGETIC MEASURES: OXIDATION POTENTIALS AND Δ$E_{\text{DICATION-NEUTRAL}}$

As described above, the ortho protons on the fluorenyl system of the dications described above are affected by the ring current of the opposing ring system. We were able to avoid this by preparing dications, without cyclic substituents, of diphenylmethyl fluorenylidenes, **16** and **17**. In the *para*-substituted system, **16**, the greatest antiaromaticity, as evaluated through the magnetic measures of ^{1}H NMR shifts and NICS, was seen when the substituent was fluorine, with the following order for all substituents: F > Cl > H ~ CH_3.[51] Our conclusion from this order is that electron-withdrawing substituents enhance antiaromaticity in these systems because they prevent donation of electron density to the fluorenyl system.



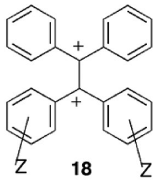
16

Z=F, Cl, H,
CH_3, OCH_3



17

Z=CF_3, Br, Cl,
F, CH_3OCH_3



18

Z=CF_3, Br, Cl,
F, CH_3OCH_3

We evaluated the stability of these dications through their electrochemical generation, reasoning that the more positive the oxidation potential, in comparison with that of a reference compound, the less stable it would be. Cyclic voltammetry in dichloromethane with microelectrodes and very fast scan rates gave cyclic voltammograms that were well-resolved for all species except *p*-CF_3. As expected, the oxidation potentials for formation of both dication and monocation radical were related to the electron-withdrawing ability of the substituents. The oxidation potentials for formation of the corresponding dications of tetrasubstitued tetraphenyl ethylenes were in general less positive, supporting the greater instability of **16**. In a subsequent paper,[52] we expanded the range of substituents to include *m*-substituted phenyl rings, **17**, and refined the tetraphenylethylene reference compounds to use only the *para*- and *meta*-substituted tetraphenylethylenes with substituents on two of the four phenyl rings, **18**. The oxidation potentials for formation of **17** were larger than for the analogously substituted **16**, suggesting their greater instability, and were larger than the oxidation potentials of the analogously substituted tetraphenyl ethylene **18**, indicating the instability expected for antiaromatic species. The NICS values confirmed the antiaromaticity of the diphenylmethylidene fluorene dications and also showed a good correlation when plotted against the oxidation potentials for formation of the dications, suggesting a linear relationship between magnetic and energetic measures of antiaromaticity.

This work was extended to the formation of dications from substituted benzylidenefluorenes **19**/**20**.[53] The relationship between calculated and experimental chemical shifts for the protons of **19**, Z = OCH_3, was good, as shown in Figure 1, which also supports the magnitude of NICS values calculated in the same way. Some researchers have concluded that the calculations of NICS for antiaromatic species give values that are abnormally large, but it is clear that the relationship of calculated and experimental chemical shift for the protons on the benzyl substituent are the same as for the fluorenyl systems, which cannot then be abnormally large.

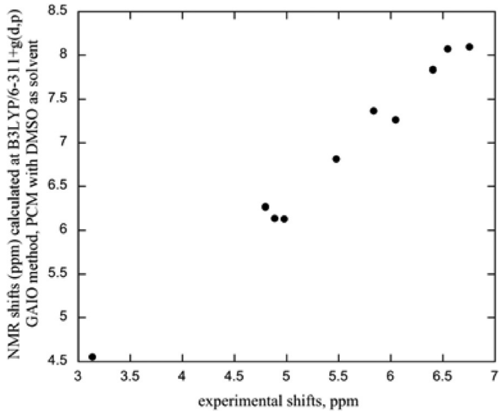
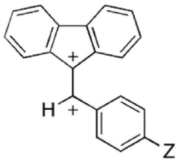
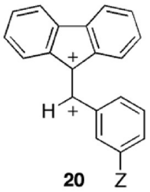


Figure 1. Plot of experimental vs calculated shifts for **19**, Z = OCH_3.



19
z=CF_3, H, F,
Cl, CH_3, OCH_3



20
Z=CF_3, H, F, Cl
CH_3, OCH_3

As would be expected, the removal of one phenyl substituent resulted in an increase in the oxidation potential needed to form the dication and resulted in an inability to observe reversible oxidation for the *meta*-substituted compounds. We again sought a relationship between experimental and calculated values, in this case between oxidation potentials, which are a measure of stability, and the calculated difference in energy between the dication and its neutral precursor, $\Delta E_{\text{dication-dianion}}$. There is a linear relationship, with r=0.960. This relationship allows us then to examine the relationship between calculated magnetic measures (NICS) and calculated energetic measures ($\Delta E_{\text{dication-dianion}}$) for all fluorenylidene dications with diphenyl methyl or benzylidene substituents, including those that could not be characterized experimentally. There is a linear relationship between magnetic and energetic measures of antiaromaticity for closely related species, but the relationship, as shown by the slope of the line, is different as the species become more diverse.

■ STRUCTURAL MEASURES: BOND LENGTH ALTERNATION

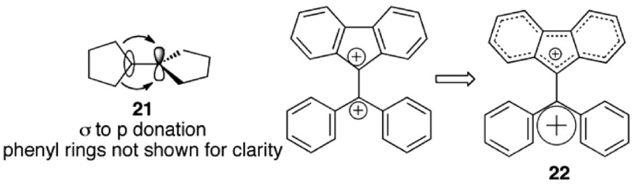
We also examined a structural measure of aromaticity, the harmonic oscillator model of aromaticity (HOMA), using the calculated geometries of **16**,[54] considering only the term reflecting bond length alternation. By that measure we saw much less variation for the variously substituted dications than was apparent through NICS values or oxidation potentials, suggesting that this was a much less sensitive probe of antiaromaticity and potentially aromaticity.

■ INTERACTION BETWEEN THE CATIONIC SUBSTITUENT ON C-9 AND THE FLUORENYL SYSTEM

It is clear that the antiaromaticity of the fluorenyl system is affected by the nature of the substituent on C-9, but the calculated geometries show that the substituent is definitely not coplanar with the fluorenyl system, in some cases perpendicular to it, so the interaction cannot be occurring through resonance.

Our initial idea for that interaction came from the observation that the ^{13}C NMR shifts of C-9 were abnormally far upfield, compared to the fluorenyl monocation, and showed much greater variation in **9**, **11**, and **13**−**15** than did the other carbon shifts.[46,55] We considered that the mode of interaction of these perpendicular systems might be due to σ-p donation, **21**, Scheme 1, a type of cross-hyperconjugation, which would allow an increase in electron density on these carbons and an upfield shift.[38]

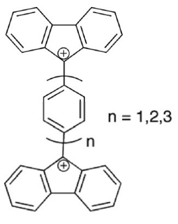
Scheme 1. Modes of Interaction between Nonplanar Systems



Having access to the optimized geometry through calculation allowed us to assess the suggestion that σ−p donation was involved in the interaction of the ring systems through a decrease in the C-9 to C-9′ bond length and an increase in the bond length for C-9′ to C-9a′ of the opposing substituent. There was a regular decrease in the C-9 to C-9′ bond length as antiaromaticity increased from **12** to **9**, but there was no corresponding increase in the bond from which electron density should be supplied, C-9′ to C-9a′, suggesting that σ−p donation was not a major factor in the interaction of the ring systems.[46] A similar effect was seen in **16** and **17**.[52]

This suggested an alternative mode of interaction in which the magnitude of the charge on the carbon directly attached to the fluorenyl system forced greater delocalization of charge in the fluorenyl system, **22**. For example, a trifluoromethyl substituent would result in the development of greater positive charge on the carbon of the diphenylmethyl substituent, resulting in greater impetus to delocalize the positive charge of the fluorenyl system into its benzene rings, causing in greater antiaromaticity with the loss of the stability of the benzene ring. This was given support by the linear relationship between the charge calculated on carbon 9 of the fluorenyl system vs the NICS values for **16** and **17**.[52]

The support for the proposal of σ−p donation was further eroded with the examination of fluorenylidene dications with spacers. To solve a potential problem of cyclization between indenyl and fluorenyl dications, vide infra, we decided to separate the systems spatially by preparing a series of dications with phenyl, alkynyl, and alkyl spacers. We began with the dications of tetrabenzo[5.5]fulvalenes **23**−**25** since they offered the greatest ease of synthesis and because we had the greatest experience with **9**. We spent some time exploring the synthesis of precursors that could give the dications by oxidation with SbF_5, but the oxidation of the precursor with an alkynyl spacer gave challenging NMR spectra, and the precursor to the dication with a phenyl spacer gave rapid oxidation upon handling. We therefore prepared diol or diether precursors from which the dication could be prepared by ionization with Magic Acid, FSO_3H/SbF_5.



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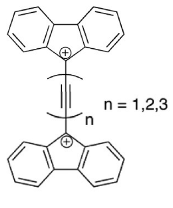

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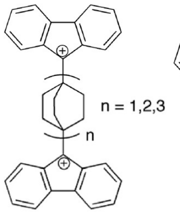
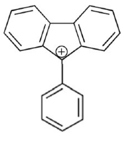


25

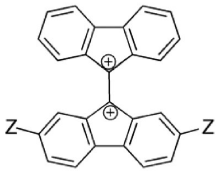


26

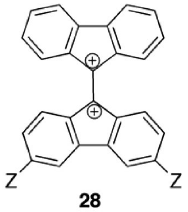
The order of antiaromaticity, based on NICS and Λ from these studies, was **23** < **24** < **9** for dications with a single spacer.[56] As might be expected, it appears that the larger spacer was able to delocalize charge more effectively than a smaller spacer, resulting in a decrease in antiaromaticity. Because the dihedral angle of the fluorenyl system with the phenyl spacer was ∼44° in the optimized geometry, it is not clear that σ−p donation was viable for that spacer. A reviewer of the first paper suggested that it would be interesting to consider the effect of distance on the antiaromaticity of dications of tetrabenzo[5.5]fulvalene. Capitalizing on that excellent suggestion,[57] we examined dications with multiple phenyl and alkynyl spacers. We also included the study of **25** to examine the effect of distance without needing to consider delocalization of the charge though a conjugated system. As always, we tried to prepare as many dications as possible to allow comparison of experimental and calculated NMR shifts to support other calculated values. The original suggestion by the reviewer, that the distance between the charges was affecting the antiaromaticity of the dications, was explored by the relationship between the NICS values and the distance between the geometric centers of the fluorenyl systems. There were linear relationships between distance and antiaromaticity but they were dependent on the system being examined. This was particularly evident when the antiaromaticity of systems with spacers of similar length (**23**, $n = 1$, compared to **24**, $n = 2$) were compared and showed that the ΣNICS values for the system with bis-alkynyl spacer were 16% greater than the ΣNICS values for the dication with a single phenyl spacer. If the mode of interaction of the fluorenyl systems was dependent upon the charge of one system forcing greater delocalization in the second, the increase in the number of phenyl or alkynyl spacers should decrease the amount of antiaromaticity because the charge was delocalized more effectively. However, bicyclo[2.2.2]octyl spacers were able to stabilize the dications almost as effectively as phenyl substituents, although the stabilization by the saturated spacers tended to fall off less rapidly than with unsaturated spacers. Of particular interest was the comparison of antiaromaticity in these dications with the antiaromaticity of the fluorenyl monocation, **26**. That monocation could be considered as representing the antiaromaticity of fluorenyl systems, such as **23** with the fluorenyl systems at infinite distance. The ΣNICS value was 56.3/fluorenyl unit for **26**; that of dications with three phenyl spacers was 60.8; that of dications with three bicyclo[2.2.2]octyl spacers was 73.2. In these dications with fluorenyl systems separated by ∼18 Å, the fluorenyl systems are able to sense each other and enhance the antiaromaticity of each other.

■ ANTIAROMATICITY IN SUBSTITUTED FLUORENYL SYSTEMS

We were interested in examining the effects of substitution directly on the fluorenyl system. The dications with substituents in the 2,7- and 3,6-positions, **27** and **28**, were prepared by oxidation of the unsaturated precursor with SbF_5/SO_2ClF. The primary conclusions from this work are that substituents in the 3,6-position are more effective at reducing the antiaromaticity in the substituted fluorenyl system than are substituents in the 2,7-position. This is surprising because resonance forms can be drawn to place a positive charge on all positions, however, only in the resonance forms with positive charge on the 1, 3, 6, and 8 positions can there be an intact benzene ring. Thus, charge is not distributed evenly by delocalization. This pattern of charge alternation is also seen in the ^{13}C NMR shifts and in the calculated charges for the carbons.[58] Complete delocalization would result in the loss of the stability of both benzene rings; thus the systems demonstrate the balance between stabilization of the positive charge through resonance vs loss of the stability of an aromatic system.



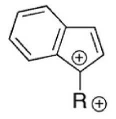
27
Z=F, Cl, CH_3



28
Z=F, Cl, CH_3

■ INDENYLIDENE DICATIONS

The NICS values showed greater antiaromaticity in the 5-membered ring in the fluorenylidene dications, but there was no way to probe this experimentally because it was impossible to put substituents on that ring. However, indenylidene systems like **29** could possess substituents on the five-membered ring, allowing a closer probe of its antiaromaticity. Our first venture in this area was the formation of dications from tribenzo[5.5]-fulvalenes with substituted phenyls in the 3′-position, **30**.[59] The dications showed the same response to substitution on the phenyl substituent as was shown by **16**−**19**; that is, the more electron-withdrawing substituents resulted in more antiaromatic dications, as evaluated through the ^1H NMR shifts of the indenyl/fluorenyl systems, through the NICS calculations, and through their magnetic susceptibility exaltation, Λ. The chemical shifts and NICS calculations also showed greater antiaromaticity in the fluorenyl system than in the indenyl system, which we attributed to the ability of the stabilizing phenyl substituent to localize charge in the five-membered ring, resulting in an indenyl system that might be characterized more as an allylic cation conjugated with a benzene ring than an indenyl cation.[60] We expanded these systems to consideration of the effect of replacing the fluorenyl cation with a tropylium cation, so that we could probe substituent effects on the indenyl system, **31**.[61] Again, the more electron-withdrawing substituent on the phenyl ring resulted in greater antiaromaticity for that dication. Comparison of **30** with **31** was most usefully done by examining the charge distribution between the indenyl and fluorenyl/tropylium systems. As would be expected, the tropylium system contained a larger fraction of the total charge of the dication than did the indenyl system, with roughly 10% more charge in the tropylium system. The fluorenyl system of **30** has less than half of the 2^+ charge when there is a phenyl substituent on the ring, supporting the stabilization afforded by a phenyl substituent, with less charge when the substituent on the phenyl substituent of the indenyl system becomes more electron-donating. This change in charge did not result in substantial differences of the antiaromaticity of the indenyl systems of **30** compared to **31**.



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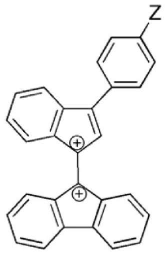
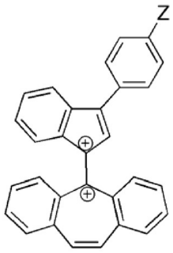


30

Z=CF_3, H, F
CH_3, OCH_3

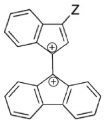


31

Z=CF_3, H, F
CH_3, OCH_3

INDENYLIDENE DICATIONS, THE USE OF SPACERS, AND THE DEVELOPMENT OF A NEW SUPERACID

The use of phenyl substituents on the indenyl systems of **30** and **31** resulted in an apparent decrease in the antiaromaticity of the indenyl system, so we were interested in replacing them with less stabilizing substituents, such as methyl, cyclopropyl, and methoxy. We were able to successfully prepare the unsaturated precursors to **32** and **33**, but attempts to oxidize the dications with SbF_5 resulted in intractable NMR spectra. Because we had previous experience with cyclization of fluorenylidene dications,[62] we considered the possibility of cyclization of the presumably less stable dication as shown for **32**. The chance that cyclization was occurring led us to consider the spacer separated fluorenylidene dications described previously.



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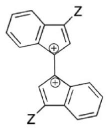
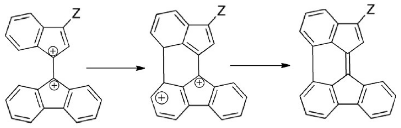


33

Z=CH_3, OCH_3, c-C_3H_5



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An excellent collaborator, Dr. Sean McClintock, suggested that the intractable NMR spectra were possibly due to overoxidation of the indenyl substrate by the SbF_5 used in our initial preparation of dications. Because SbF_5 was also present with FSO_3H in the Magic Acid we had been using for ionization to form dications and which also showed intractable NMR spectra, he looked for other "superacid" systems. We found that we had success with $FSO_3H/(CF_3CO)_2O$ where the function of the trifluoroacetic anhydride was presumably to dehydrate the FSO_3H and to remove water as it was formed during the ionization. I wondered if there was a counterion effect so a series of non-nucleophilic anions were examined. To our amazement, $FSO_3H/(CF_3CO)_2O/NaPF_6$ could be used to prepare **23** ($n = 1$) at room temperature, with the NMR spectrum still showing evidence of **23** after 8 days.[63] This relatively recent discovery is shaping our choice of new dications for examination.

DIRECT COMPARISON OF THE BEHAVIOR OF AROMATIC SYSTEMS WITH ANTIAROMATIC SYSTEMS

One of the concerns with the use of NICS values involved the way that NICS were handled for polycyclic systems. NICS are calculated for individual rings and used to evaluate the magnetic environment 1 Å above the center of the ring. It was not clear that the NICS probe was sensing only the contribution from one ring; perhaps it could also feel the influence of a second neighboring ring system. Because all of our systems were polycyclic, I needed to evaluate this concern. I felt that comparison of a global measure of aromaticity, such as the magnetic susceptibility exaltation, Λ, with the sum of NICS would highlight any contributions from neighboring ring systems because those contributions should be greatest in systems with more rings. I used the tensor of the chemical shift that was perpendicular to the plane of the ring for a probe 1 Å above that plane, $\mathbf{NICS(1)}_{zz}$ and calculated Λ with the basis set used for the NICS calculations. My initial examinations used a variety of polycyclic aromatic and antiaromatic species, including both neutral compounds, and mono- and dications. There was a very satisfactory linear relationship, $r = 0.996$.[64] At that time, I was interested in moving into an examination of antiaromatic dianions so I added a series of aromatic and antiaromatic mono- and dianions to the original set. Again there was a linear relationship but the slope was different, Figure 2a. I clearly could not use the $\mathbf{\Sigma NICS(1)}_{zz}$ to compare antiaromatic dications with dianions as I was hoping to be able to do. This paper sat on my desk for almost a year until I considered the ramifications of the fact that anions were larger than the corresponding cations. I knew that Λ was normalized by the square of the area of the ring when comparing ring systems of different sizes, so I looked at the plot of $\Lambda/\text{ring area}^2$ vs $\mathbf{\Sigma NICS(1)}_{zz}/\text{ring area}^2$ and observed a much more linear relationship, Figure 2b. Finally, to confirm that there were no hidden confounding effects, I added a series of monocyclic aromatic and antiaromatic ions and benzene. Figure 2c shows that the polycyclic and monocyclic species are responding identically. Various papers had suggested that there was a relationship between size and the magnitude of NICS; this was the first time that this relationship had been established and related to a specific factor, the area of the ring. This helps us understand that the apparent enhanced antiaromaticity of the fluorenyl system of **30** is a result of size; when normalized by the ring area, the indenyl system is actually more antiaromatic.

AROMATIC–ANTIAROMATIC CONTINUUM

Liberated by the recognition of how to handle the examination of anionic systems, we returned to one of our original precursors. Tetrabenzo[5.7]fulvalene gave upon oxidation an antiaromatic fluorenyl cation and an aromatic dibenzotropylium cation, **11**. It occurred to us that reduction would give us an aromatic fluorenyl anion and an antiaromatic dibenzocycloheptatrienyl anion, **34**. As shown in Scheme 2, we now have the perfect aromatic/antiaromatic continuum; by changing the number of electrons within a system, but not its basic carbon framework, we could move between aromaticity and antiaromaticity. The absolute values of the $\mathbf{\Sigma NICS(1)}_{zz}$ for the fluorenyl cation of **11** and the

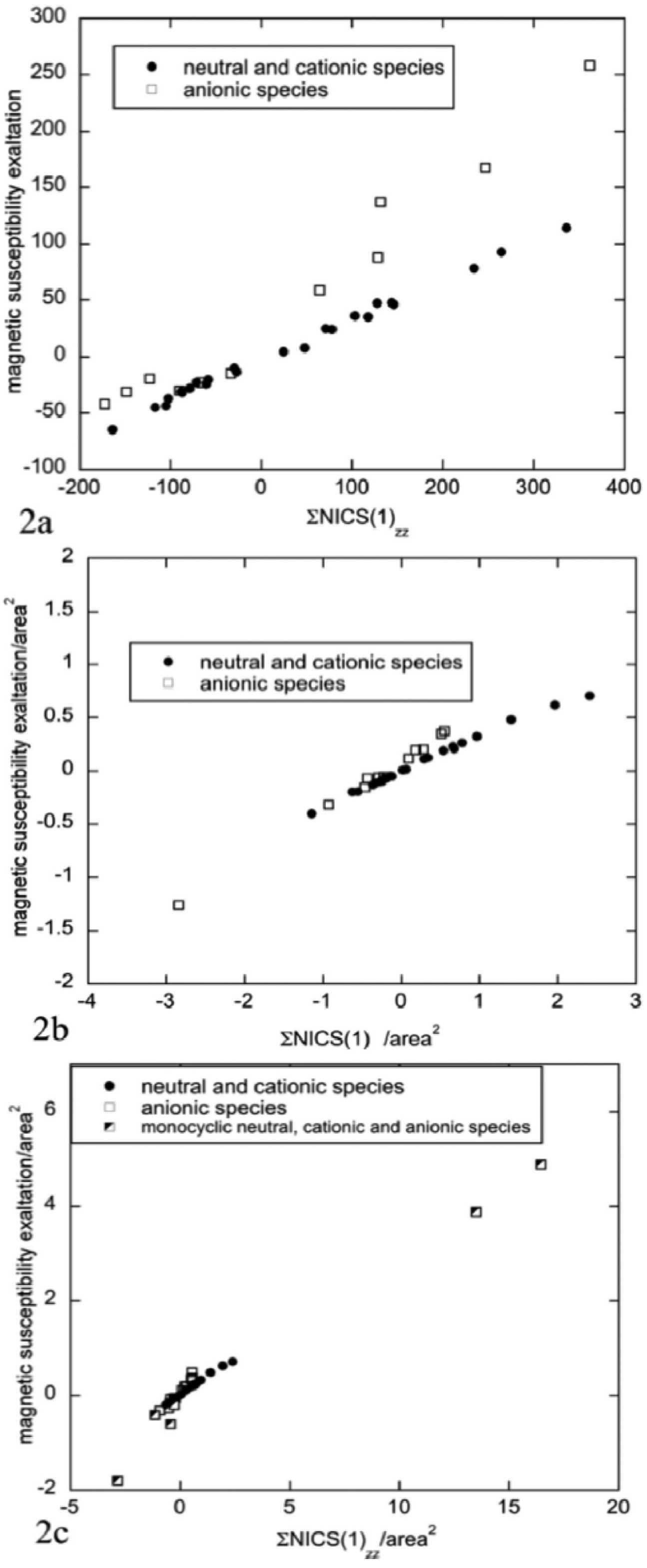
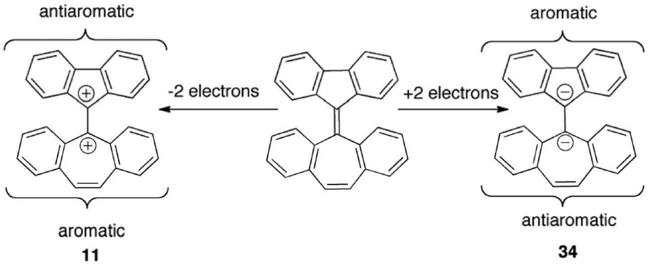


Figure 2. Λ vs $\Sigma\text{NICS}(1)_{zz}$ **2a**. Aromatic and antiaromatic di- and monocations, di- and monoanions, and neutrals, **2b**. Λ/sq area vs $\Sigma\text{NICS}(1)_{zz}$/sq area for same species, **2c**. Λ/sq area vs $\Sigma\text{NICS}(1)_{zz}$/sq area including monocyclic species.

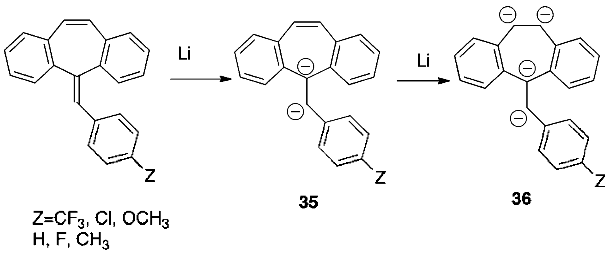
Scheme 2



fluorenyl anion of **34** showed that the antiaromaticity of the cation as measured by NICS was greater, |107.70|, than the aromaticity of the anion, |89.00|. This could be due to the charge type, but the corresponding comparison of the antiaromaticity of the dibenzocycloheptatrienide anion, |182.33|, was greater than the aromaticity of the dibenzotropylium cation, |82.52|. Thus, in these two directly comparable systems, the manifestation of antiaromaticity is larger than that of aromaticity. We were interested in examining the effect of delocalization of the electrons in each system, through an examination of the decrease in bond alternation through delocalization. We modified the fluorenyl and dibenzocycloheptatrienyl systems of the cation and anion so that there was a minimum amount of bond length alternation while maintaining the area of the optimized geometry of the dication and dianion. When the NICS were calculated for the aromatic systems, fluorenyl anion or dibenzotropylium cation, the change in the NICS values was about two units from that of the optimized geometry; however the increase in the magnitude of the $\boldsymbol{\Sigma}\textbf{NICS}(\mathbf{1})_{zz}$ for the antiaromatic fluorenyl cation was ~66 units; that for the dibenzocycloheptatrienyl anion was 161 units. The species with a lack of bond length alternation is more antiaromatic, which is certainly reasonable since antiaromatic species such as cyclobutadiene distort their bond lengths to *decrease* their antiaromaticity. Of equal interest is the observation that aromatic species are much less sensitive to changes in bond length alternation, presumably because they are already nearly delocalized. Thus, if one wants to probe effects on delocalization, an antiaromatic species is the more sensitive probe. There was also an excellent linear relationship between the experimental and calculated chemical shifts of **11** and **34**. This linear relationship between calculated and experimental measures for species that contain both antiaromatic and nonantiaromatic regions suggests that properties such as NICS that are calculated by the same method must be taken seriously.

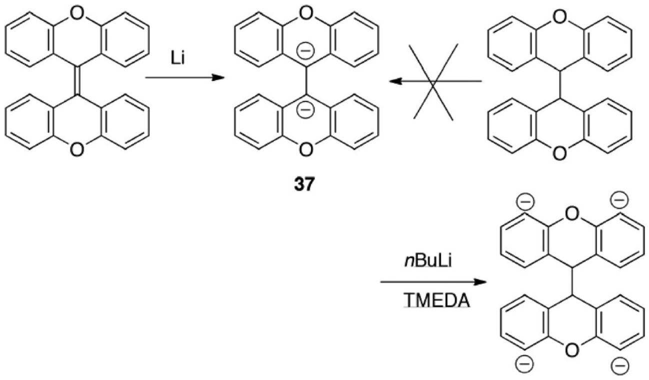
■ ANTIAROMATIC DIANIONS

The dianion of tetrabenzo[5.7]fulvalene was prepared by reduction with lithium. We then considered the examination of dianions of benzylidene dibenzocycloheptatriene, **35**, the antiaromatic anionic analogue of the dications of benzylidene fluorene, **19**/**20**. We adopted a procedure from Rabinovitz and Scott[65] which allowed us to control contact with the reducing agent that was not possible in the oxidation to form dications. We were able to monitor the formation of diamagnetic species by NMR spectroscopy; we found that the initial spectrum of starting material disappeared upon sonification within 10 min. However, although the reaction continued to change color, indicating different anionic species, nothing was visible in the NMR spectra until after an hour. Our assumption was that the species seen at that point in the spectrum was the antiaromatic dianion **35** but comparison of the calculated and experimental spectra of either the dianion or the dilithiated species did not demonstrate a linear relationship. However, the calculated spectrum of Li_4**36** showed good agreement with the experimental spectrum. The presence of Li_4**36** was supported by quench of the reaction mixture with chlorotrimethylsilane, which showed the presence of tetrasilylated product. However the quench also showed substantial amounts of the presumably dilithiated species. The inability to see the "dianion" in the NMR spectrum of the reaction mixture was rationalized by the presence of a very small HOMO−LUMO gap that resulted in the presence of diradical species. Our ability to characterize antiaromatic species by NMR in the past must have involved species with sufficiently large HOMO−LUMO gaps that the diradical character was very small. We supported this conjecture by a plot of $\boldsymbol{\Sigma}\mathbf{NICS(1)}_{zz}$/ring area^2 vs Λ/ring area^2 which demonstrated that **35** was the most antiaromatic species we have yet prepared. We have since prepared the "dianion" by deprotonation with TMEDA/*n*-butyllithium and have seen evidence for it in the quench of the reaction mixture but no signals in the ^{1}H NMR spectrum.[66]



35 **36**

We also reported the first experimental characterization of a heterocyclic antiaromatic dianion, the dianion of dixanthylidene, **37**, by reduction with lithium.[67] The NICS values for dianion **37** showed greater antiaromaticity than the monoanion, as was true for the analogous comparison of **9** with the fluorenyl monocation, but there was little difference in the reported ^{1}H NMR shifts, which might be attributed to the different solvents used. At this time, we had not explored the formation of dianions through deprotonation with *n*-butyllithium and felt that this system would be a good test case for our venture into this area because we were familiar with the spectral signature of the dianion. We anticipated that the deprotonation might not be straightforward because antiaromatic anions were difficult to form by deprotonation. However, other workers had observed that the enhanced acidity of the excited state of the substrate led to more successful formation of antiaromatic anions.[68,69] We found that deprotonation with an excess of *n*-butyllithium gave **38**, which formed the tetramethyl derivative from quench of the reaction mixture with methyl iodide, rather than the dimethyl derivative of **37**. There is precedent for ortho deprotonation of related xanthyl systems; the reason for formation of the tetra-anion without any evidence of the desired dianion comes from the equatorial geometry of the protons on the bond between the two xanthene systems which prevents the developing anion from overlapping with the *π*-system of the benzene rings.



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FUTURE OF STUDIES IN ANTIAROMATICITY

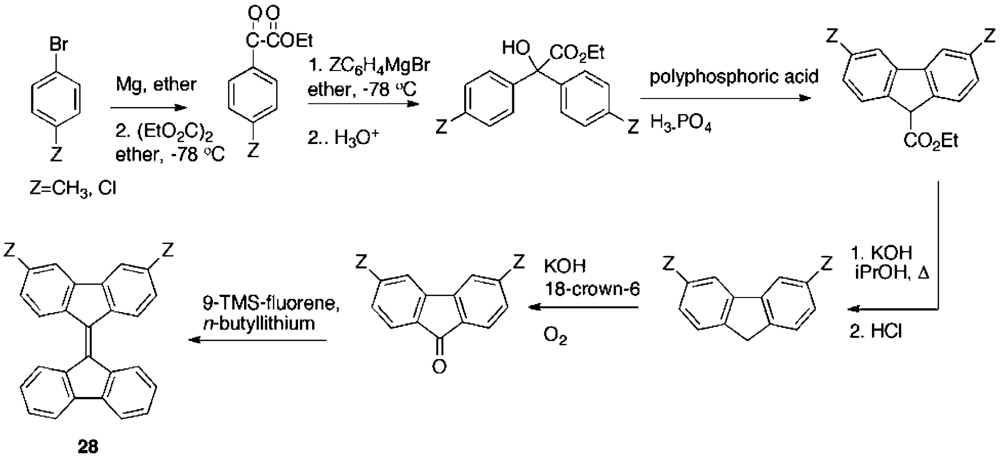
A challenge for those who study aromaticity is the tendency to stretch the concept further than appropriate to try to see some sort of aromatic behavior in all species with a Hückel number of electrons in a *π*-system. The requirement that calculated properties be supported by experimental data is the most certain way of preventing improper use of properties that may reflect aromaticity, or antiaromaticity. Lazzeretti, in a nicely presented paper,[70] argues that nonmeasurable properties cannot support a quantitative theory of aromaticity. Such properties "would not be falsifiable, which is the basic character of any scientific statement". He contends that properties of diatropicity that can be obtained experimentally, such as the out-of-plane components of magnetic susceptibility and nuclear magnetic shieldings, are more appropriate measures of aromaticity than are purely calculated measures like NICS.

If these issues exist in the study of potentially aromatic species they exist to a much greater degree in the study of antiaromatic species which, before our discovery of antiaromatic dications and dianions, had involved species so diverse as to prevent comparison of properties or had been almost exclusively studied via calculated properties. We believe that the accessibility of these antiaromatic dications and dianions offers the opportunity for a much more active study of antiaromaticity because results from calculations can more easily be compared to experimental results. For example, if the agreement between experimental and calculated chemical shifts is good, and if those shifts include protons that are not aromatic or antiaromatic, then one can reasonably conclude that NICS values calculated in the same manner and with the same basis set are reliable.

But what does the study of antiaromatic species offer us? As stated previously, antiaromatic species appear to be more sensitive to effects like delocalization than aromatic species, allowing greater insights into aromaticity *and* antiaromaticity, the opportunity to use antiaromaticity to illuminate aromaticity. That is, using antiaromatic species in which the properties are demonstrated with larger magnitude can provide a more sensitive probe of the relationship between the different measures of aromaticity. We have successfully used the linear relationship between the $\boldsymbol{\Sigma}\mathbf{NICS(1)}_{zz}$ and Λ to illuminate the importance of the ring area in the manifestation of aromaticity/antiaromaticity. We would also argue that the linear relationship between a property, Λ, that can be experimentally determined as Lazzeretti notes, also serves to support the conclusions from the NICS values. This approach should be transferrable to energetic and structural properties, in principle. We are exploring the relationship between the oxidation and reduction potentials for formation of dications and dianions, experimental measures, and the calculation of $\Delta E_{\text{di-ion-neutral}}$. Other relationships can also be examined. As has been clear from a number of our studies, the ability to demonstrate the appropriateness of a particular theoretical approach by comparison with experimental data has also allowed us to fill in the "holes" in a data set with calculated values. Thus, the relationships to be measured are less limited.

What is missing on our end, and others, is the extension of these relationships beyond a small group of compounds. Just as we demonstrated that the linear relationship between NICS and $\Delta E_{\text{dication-neutral}}$ for the dications of diphenylmethylfluorenes has a different slope from that of dications of benzylidene fluorenes,[53] chemists need to be sensitive to the issues associated with drawing conclusions beyond the group for which they were tested.

Scheme 3. Preparation of 28, R = CH_3, Cl



28

■ ROLE OF THE UNDERGRADUATE RESEARCHER IN THIS PROGRAM

Although the emphasis here has been on the antiaromatic ions, the undergraduates spent the vast majority of their time synthesizing the precursors to the ions. Only a small number of the compounds had previously been synthesized, so the work necessarily involved both synthesis and purification to analytical standards. The syntheses were normally multistep, as demonstrated by the work of one of my many excellent students, Amber Rakowitz (Schaefer), Scheme 3.

■ FACTORS THAT SUPPORT A SUCCESSFUL UNDERGRADUATE RESEARCH PROGRAM

As the expectation of scholarship increases at undergraduate institutions, it is important to discuss the infrastructure necessary to support that scholarship. Clearly, adequate resources are crucial: time, instrumentation, and materials. The Council on Undergraduate Research has a number of helpful "How To" books on issues such as starting a research program and developing an institutional research program.

■ "AWAY" SABBATICAL LEAVES

I will not repeat their excellent advice but will focus on one aspect of institutional support, the sabbatical leave program. Of particular benefit is the opportunity to spend the sabbatical at another institution full-time. It is hard to move one's family to another location, to disrupt the job of a spouse/partner, and to uproot children. I have only been able to take two "away" sabbaticals, one to the lab of Josef Michl at the University of Colorado in 1996 and one more recently to Mike Haley's lab at the University of Oregon. The opportunities to learn new techniques in a new environment and to be free of local demands can be transformative. I was able to take advantage of an NSF-Research Opportunity Award during my Colorado sabbatical that made the finances more tractable. I hope that ACS-PRF will be able to reconsider the PUI faculty sabbatical leave program in the future as their finances stabilize.

■ INVOLVEMENT WITH POSTDOCTORAL RESEARCH ASSOCIATES

A clear benefit to my research program has been the opportunity to work with postdoctoral research associates. Research in an undergraduate institution is primarily done in the summer. If the research is not completely finished by the end of the summer, it can languish until the next summer. A postdoc can pick up the loose ends of a project and move it to completion. For my initial work with super acid solutions, the preparation and characterization of dications using NMR spectroscopy required me or a postdoc because of the inherent danger of those solutions to an NMR probe if a tube broke.

There are also clear benefits to the postdoc, although I was not confident of this initially. Often, postdocs do not have a correct view of the expectations of faculty at undergraduate institutions. At Trinity University, we are able to have a cohort of postdoctoral research associates at one time, usually four to seven, supported by external funding, which allows us to create programming for them. We offer brown bag lunches on topics of value to the postdocs. Because they tend to be interested in our positions because they are considering teaching at a PUI, we talk about writing grant proposals that are appropriate to undergraduates, about the importance of identifying good science that can be done in these environments, balancing teaching and research, preparing a good applications, and what to expect in an interview. Often postdocs, even those educated at undergraduate institutions, do not have a sense of the demands on PUI faculty. In most places, there is no NMR technician or other dedicated instrumental support, and while undergraduates can be trained on the normal maintenance of the lab, changing vacuum pump oil, dealing with stills, etc., the students are with us for a relatively short time, so we are continually retraining. We include our postdocs in departmental meetings so that they can develop an understanding of curricular issues and a sense of faculty expectations beyond the anticipated ones of teaching and research. My concern in the beginning was that there would be no market for a postdoc from an undergraduate institution. However, all of my postdocs who wanted PUI faculty positions have gotten them; those who chose alternative careers found that the experience helped them better understand the academic environment. I have been blessed with reviewers of proposals who clearly understood the benefits for the training of postdocs.

■ SUSTAINABILITY OF UNDERGRADUATE RESEARCH

There are two temporal issues in the sustainability of an undergraduate research program. The first lies in the challenge in the initial years of balancing the demands of teaching and research when it is clear that learning to be a good teacher could easily consume all available time.[12] The second often occurs after obtaining tenure, when a faculty member may feel removed from

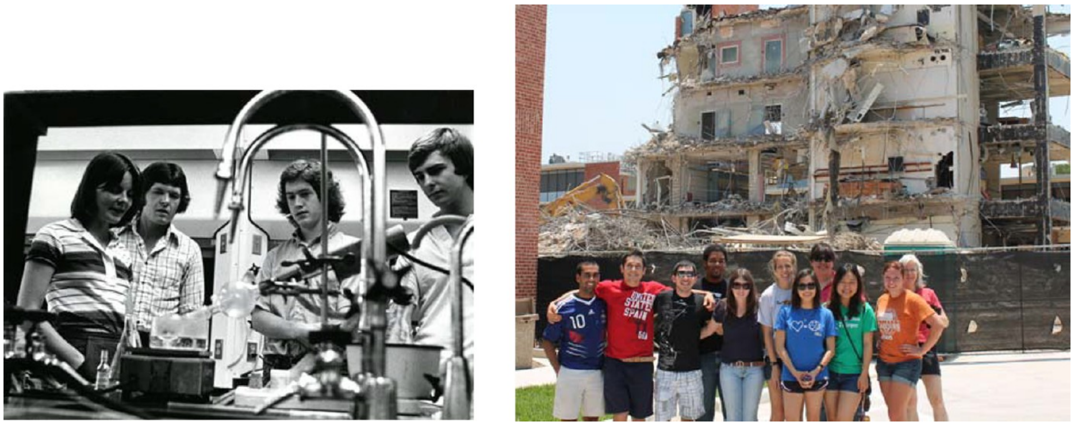


Figure 3. First Mills research group (from left, Nancy Mills, Mark Hollingsworth, Brian Hatcher, and Michael Werdick), Carleton College, 1978, and current Mills research group (from left, Remu Navaz Gangji, Marlow Taylor, Isaac Zoch, Devon Powers, Kelsey Kirkman, Margaret Hilton, Vicky Cheng, Megan Karam, Connie Hsaio, Meredith McDowell, and Nancy Mills), summer 2012, in front of the shell of the chemistry building in which the bulk of this research was done.

the strong connection with the field that was felt in graduate school. It is challenging to keep up with the literature with the demands of an undergraduate institution and the convenience of regular seminars in maintaining one's edge is not as available. Many undergraduate institutions have regular seminar programs, but they of necessity involve all disciplines of chemistry so finding insights into one's research through seminars is less direct. We grappled with these issues in a series of CUR Institutes that I organized on Mid-Career Vitality. One solution can be the establishment of a collaboration with a faculty member at a Research Intensive institution. In my case, I have only rarely published with other faculty because of my concerns about my ability to deliver samples if the request came in during the academic year and my collaborator's ability to provide me with what I needed prior to the intense summer research season. However, this model is clearly beneficial to PUI faculty. Faculty at research intensive institutions also benefit from the opportunity to enhance the broader impacts of their program. Internal collaboration, between faculty in the chemistry department or between departments, has clearly been valuable in my institution. In these times of financial constraint, it is also crucial that the support for faculty participation in professional meetings continue to be a priority for the institutions.

As has been mentioned, a big challenge for research-active PUI faculty is the relative isolation of the PUI environment in which there may be no one in the same disciplinary area, or even if there is another organic chemist, the area of expertise is almost certainly different from oneself. One solution to this that has been a benefit to me was a dispersed REU site that Dave Reingold of Juniata College spearheaded. This site is a group of six physical organic chemists from different institutions who come together with their students twice a summer, once at a national meeting in the middle of the summer and again at the end of the summer for a mini-undergraduate research symposium. A notable feature of the plan is the involvement of a faculty member from a research active institution who provides feedback to both faculty and students about their projects. The opportunity for both the graduate faculty member and the other members of the site to provide ideas for research bottlenecks is invaluable.

There are also financial issues associated in the sustainability of undergraduate research, as is true, of course, for all research. Because the pace of research with undergraduates is inherently relatively slow, there will be times when it appears that little is happening in a research lab. Funding agencies of necessity put their money in research programs that appear more productive. If an institution values undergraduate research, it must identify internal sources of funding to carry a faculty member over the inevitable "dry" periods. The funding should not be so generous as to remove from the faculty member the need to continue to publish and write grant proposals, but if an institution fails to sustain the research of a productive scholar, it risks losing the money already invested in that faculty member.

■ THE IMPORTANCE OF KNOWING YOURSELF

A successful career involves understanding yourself and the activities you find renewing. A career is a long distance race, not a sprint, and while there will be points of intense effort, knowing the activities that provide personal balance is crucial. In addition to the great pleasure I have taken in research, I also have been very fortunate to be involved in service activities and have found that for me, meaningful service is a renewing force. This began with my involvement in the Council on Undergraduate Research as a councilor and then chemistry division chair, from 1990 to 2001. The organization was small enough at that time that anyone with a good idea and the willingness to develop it did not feel the impediments often existing in a larger organization. I was able to create a mentor network in chemistry that is still active as well as to make connections with some amazing faculty, both in chemistry and in other STEM disciplines. I followed that with service on the Committee on Professional Training of the ACS and was fortunate to be able to be involved in the new guidelines for approval of chemistry departments. It was challenging and rewarding to grapple with the need for flexibility in the chemistry curriculum while also maintaining its rigor. Of course, the real pleasure was again in working with so many thoughtful, hardworking colleagues on CPT.

■ SUMMARY

I was the beneficiary of early support from the Undergraduate Research Program of NSF during the summer following my sophomore year at Grinnell College in Iowa on a project of Gene Wubbel's on the acid-catalyzed photoreduction of nitrobenzene by 2-propanol. It was during that summer of research that I began to see myself as a chemist rather than a chemistry student and to consider that a career in research might match some of my strengths and interests. For a girl from a small town in Nebraska who had never met a scientist, the experience was particularly transformative. I am grateful to have had the chance to offer similar opportunities to my many undergraduate research students (Figure 3).

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Notes

The authors declare no competing financial interest.

Biography

Nancy Mills received her BA in Chemistry and American Studies from Grinnell College and her Ph.D. in Chemistry from the University of Arizona under the direction of Professor Robert Bates in 1976. Following several years at Carleton College, she joined the faculty of Trinity University where she is currently a Murchison Professor. Her research is focused on the characterization of antiaromatic cations and anions.

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Special thanks go to the Welch Foundation (Grant No. W-794) for continuous funding since my arrival at Trinity University in 1979, providing important stability to my research program throughout my career, to the Research Corporation and ACS-PRF who provided early support for my research and who have served as the mainstay of research support for PUI research programs in chemistry, and to the National Science Foundation for support for instrumental acquisition and facilities renovation as well as for my individual research program, most recently Grant Nos. CHE-0948445 and CHE-0957839. My thanks also go to Venetia Dubose, the publications designer at Trinity University, for her excellent work in converting my thoughts about antiaromaticity to the cover art she created. I have been fortunate to work with a number of excellent postdocs during my career. Of particular help to me in the area of antiaromaticity were Ellen Burns, my Dreyfus postdoc who did much of the early work with our antiaromatic dications, Jim Malandra, who worked on the very first set and dealt with the issues when an NMR tube containing SbF_5 broke in the probe of our NMR spectrometer, Shelly Brooks Benish, from Larry Scott's group, and Bart Dahl and Sean McClintock from Mike Haley's group. Without the intellectual interaction of these folks, I would have found the process of research in an undergraduate institution more challenging. Finally, and most importantly, I need to acknowledge the work of over 200 undergraduates over the course of my career at Carleton College and then at Trinity University. My students have provided an important source of momentum for my research efforts because they kept things moving when other demands encroached on my time. They were hard-working, good company, and sometimes fearless. My career has been greatly enriched by my interactions with them.

REFERENCES

(1) Bahl, J. J.; Bates, R. B.; Beavers, W. A.; Mills, N. S. *J. Org. Chem.* **1976**, 1620−1622.

(2) Bates, R. B.; Gordon, B.; Keller, P. C.; Rund, J. V. *J. Org. Chem.* **1980**, *45*, 168−169.

(3) Bates, R. B.; Beavers, W. A.; Gordon, B.; Mills, N. S. *J. Org. Chem.* **1979**, *44*, 3800−3803.

(4) Klein, J.; Medlik, A. *J. Chem. Soc., Chem. Commun.* **1973**, 275−276.

(5) Gund, P. *J. Chem. Educ.* **1972**, *49*, 100−103.

(6) Mills, N. S.; Shapiro, J.; Hollingsworth, M. *J. Am. Chem. Soc.* **1981**, *103*, 1263−1264.

(7) Meyer, S. D.; Mills, N. S.; Runnels, J. B.; de la Torre, B.; Ruud, C. C.; Johnson, D. K. *J. Org. Chem.* **1991**, *56*, 947−952.

(8) Mills, N. S.; Rusinko, A. R. I. *J. Org. Chem.* **1986**, *51*, 2567−2571.

(9) Rusinko, A. I.; Mills, N. S. *J. Org. Chem.* **1982**, *47*, 5198−5201.

(10) Mills, N. S. *J. Am. Chem. Soc.* **1982**, *104*, 5689−5693.

(11) Schleyer, P. v. R. *Pure Appl. Chem.* **1983**, *55*, 355−362.

(12) Mills, N. S. *J. Chem. Educ.* **1984**, *61*, 513−514.

(13) My family provided an invaluable sense of perspective, as well as joy, and I am immensely glad that we did not miss this experience.

(14) Lokey, R. S.; Mills, N. S.; Rheingold, A. L. *Organometallics* **1989**, *8*, 1803−1805.

(15) Murphy-Simmons, A.-M.; Mills, N. S.; Iyer, S. R. *Inorg. Chim. Acta* **1986**, *116*, 43−46.

(16) Mills, N. S. *J. Org. Chem.* **1992**, *57*, 1899−1904.

(17) Di Maio, D. M.; Mills, N. S.; Mosser, S. M.; Gum, A. G. *Microchimica Acta* **1993**, *47*, 167−171.

(18) Moriarty, R. M.; John, L. S.; Luxon, B. A. *Tetrahedron Lett.* **1983**, *24*, 1139−1142.

(19) Minkin, V. I.; Glukhovtsev, M. N.; Simkin, B. Y. *Aromaticity and Antiaromaticity*; John Wiley and Sons: New York, 1994.

(20) Glukhovtsev, M. *J. Chem. Educ.* **1997**, *74*, 132−136.

(21) Schleyer, P. v. R.; Jiao, H. *Pure Appl. Chem.* **1996**, *68*, 209−218.

(22) Schleyer, P. v. R.; Puehlhofer, F. *Org. Lett.* **2002**, *4*, 2873−2876.

(23) Zhou, Z.; Pearson, R. G. *Tetrahedron Lett.* **1988**, *29*, 4843−4846.

(24) Zhou, Z. *Int. Rev. Phys. Chem.* **1992**, *11*, 243−261.

(25) Kruszewski, J.; Krygowski, T. M. *Tetrahedron Lett.* **1972**, 3839−3842.

(26) Mitchell, R. H. *Chem. Rev.* **2001**, *101*, 1301−1316.

(27) Gomes, J. A. N. F.; Mallion, R. B. *Chem. Rev.* **2001**, *101*, 1349−1384.

(28) Dauben, H. J. J.; Wilson, D. J.; Laity, J. L. *J. Am. Chem. Soc.* **1968**, *90*, 811−813.

(29) Gayoso, J.; Ouamerali, O. *Rev. Roum. Chim.* **1981**, *26*, 1035−1040.

(30) Schmalz, T. G.; Norris, C. L.; Flygare, W. H. *J. Am. Chem. Soc.* **1973**, *95*, 7961−7967.

(31) Flygare, W. H. *Chem. Rev.* **1974**, *74*, 643−687.

(32) Schleyer, P. v. R.; Maerker, C.; Dransfeld, A.; Jiao, H.; Hommes, N. J. v. E. *J. Am. Chem. Soc.* **1996**, *118*, 6317−6318.

(33) Fallah-Bagher-Shaidaei, H.; Wannere, C. S.; Corminboeuf, C.; Puchta, R.; Schleyer, P. v. R. *Org. Lett.* **2006**, *8*, 863−866.

(34) Chen, Z.; Wannere, C. S.; Corminboeuf, C.; Puchta, R.; Schleyer, P. v. R. *Chem. Rev.* **2005**, *105*, 3842−3888.

(35) Jug, K.; Koster, A. M. *J. Phys. Org. Chem.* **1991**, *4*, 163−169.

(36) Katritzky, A. R.; Karelson, M.; Sild, S.; Krygowski, T. M.; Jug, K. *J. Org. Chem.* **1998**, *63*, 5228−5231.

(37) Katritzky, A. R.; Barczynski, P.; Musumarra, G.; Pisano, D.; Szafran, M. *J. Am. Chem. Soc.* **1989**, *111*, 7−15.

(38) Malandra, J. L.; Mills, N. S.; Kadlecek, D. E.; Lowery, J. A. *J. Am. Chem. Soc.* **1994**, *116*, 11622−11624.

(39) Mills, N. S. *Recent Developments in Carbocation and Onium Ion Chemistry*; ACS Symposium Series; American Chemical Society: Washington, DC, 2007; pp 210−233.

(40) Olah, G. A.; Prakash, G. K. S.; Liang, G.; Westerman, P. W.; Kunde, K.; Chandrasekhar, J.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1980**, *102*, 4485−4492.

(41) Friedrich, E. C.; Taggart, D. B. *J. Org. Chem.* **1978**, *43*, 805−808.

(42) Amyes, T. L.; Richard, J. P.; Novak, M. *J. Am. Chem. Soc.* **1992**, *114*, 8032−8041.

(43) Jiao, H.; Schleyer, P. v. R.; Mo, Y.; McAllister, M. A.; Tidwell, T. T. *J. Am. Chem. Soc.* **1997**, *119*, 7075−7083.

(44) The larger bond angle of the 7-membered ring would serve to place the ortho proton on that ring further into the ring current of the opposing ring system, increasing the magnitude of that shift.

(45) Mills, N. S.; Malandra, J. L.; Burns, E. E.; Green, A.; Unruh, K. E.; Kadlecek, D. E.; Lowery, J. A. *J. Org. Chem.* **1997**, *62*, 9318−9322.

(46) Mills, N. S. *J. Org. Chem.* **2002**, *67*, 7029−7036.

(47) Homer, J.; Whitney, P. M. *Chem. Commun.* **1972**, 153−154.

(48) Evans, D. F. *J. Chem. Soc.* **1959**, 2003−2007.

(49) Schubert, E. M. *J. Chem. Educ.* **1992**, *69*, 62.

(50) Kozik, M.; Casan-Pastor, N.; Hammer, C. F.; Baker, L. C. W. *J. Am. Chem. Soc.* **1988**, *110*, 7697−7701.

(51) Mills, N. S.; Malinky, T.; Malandra, J. L.; Burns, E. E.; Crossno, P. *J. Org. Chem.* **1999**, *64*, 511−517.

(52) Mills, N. S.; Tirla, C.; Benish, M. A.; Rakowitz, A. J.; Bebell, L. M.; Hurd, C. M. M.; Bria, A. L. M. *J. Org. Chem.* **2005**, *70*, 10709−10716.

(53) Do, C.; Hatfield, J.; Patel, S.; Vasudevan, D.; Tirla, C.; Mills, N. S. *J. Org. Chem.* **2011**, *76*, 181−187.

(54) Mills, N. S.; Benish, M. M.; Ybarra, C. *J. Org. Chem.* **2002**, *67*, 2003−2012.

(55) Mills, N. S. *J. Am. Chem. Soc.* **1999**, *121*, 11690−11696.

(56) Dahl, B. J.; Mills, N. S. *J. Am. Chem. Soc.* **2008**, *130*, 10179−10186.

(57) Dahl, B. J.; Mills, N. S. *Org. Lett.* **2008**, *10*, 5605−5608.

(58) Mills, N. S.; McClintock, S. P. *Chem. Commun.* **2012**, *48*, 8099−8101.

(59) Mills, N. S.; Llagostero, K. B.; Tirla, C.; Gordon, S.; Carpenetti, D. *J. Org. Chem.* **2006**, *71*, 7940−7946.

(60) Later work showed the dependence of the magnitude of NICS on the square area of the ring, vide infra.

(61) Mills, N. S.; Cheng, F. E.; Baylan, J. M.; Tirla, C.; Hartmann, J. L.; Patel, K. C.; Dahl, B. J.; McClintock, S. P. *J. Org. Chem.* **2011**, *76*, 645−653.

(62) Mills, N. S.; Malandra, J. L.; Hensen, A.; Lowrey, J. E. *Polycycl. Arom. Compd.* **1998**, *12*, 239−247.

(63) McClintock, S. P.; Mills, N. S. *J. Org. Chem.* **2011**, *76*, 10254−10257.

(64) Mills, N. S.; Llagostera, K. B. *J. Org. Chem.* **2007**, *72*, 9163−9169.

(65) Shenhar, R.; Beust, R.; Hagen, S.; Bronstein, H. E.; Willner, I.; Scott, L. T.; Rabinovitz, M. *J. Chem. Soc., Perkin Trans. 2* **2002**, 449−454.

(66) Whitaker, K.; Cheng, V.; Thrall, A.; Kirkman, K.; Mills, N. S. Unpublished work.

(67) Black, M.; Woodford, C.; Mills, N. S. *J. Org. Chem.* **2011**, *76*, 2286−2290.

(68) Budac, D.; Wan, P. *J. Photochem. Photobiol. A* **1992**, *67*, 135−166.

(69) Wan, P.; Krogh, E.; Chak, B. *J. Am. Chem. Soc.* **1988**, *110*, 4073−4074.

(70) Lazzeretti, P. *Phys. Chem. Chem. Phys.* **2004**, *6*, 217−223.