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Aromaticity and stability of furofurans and thienothiophenes

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ABSTRACT: The topological resonance energy (TRE) calculated for a polycyclic π-system cannot always be used to predict the thermodynamic or kinetic stability of the π-system. For example, furo[3,4-*c*]furan (**1d**) and thieno[3,4-*c*]thiophene (**2d**) are aromatic with large positive TREs and large negative nucleus independent chemical shift (NICS) values at the ring centers. However, these heterobicycles are predicted to be very high in energy with very small HOMO–LUMO energy separations. These unusual properties of the heterobicycles are closely associated with the fact that classical resonance structures cannot be drawn for them. In general, the kinetic stability of a polycyclic π-system reflects not only the aromaticity of the π-system but also the kinetic stability of the polyene reference. Copyright © 2004 John Wiley & Sons, Ltd.

KEYWORDS: aromaticity; stability; nucleus-independent chemical shift; furofurans; thienothiophenes

INTRODUCTION

Quantitative relationships among the magnetic, energetic and geometric criteria of aromaticity have been noted for a variety of monocyclic heterocycles.[1,2] However, these criteria sometimes give different predictions on aromaticity when it comes to polycyclic π-systems.[3–5] This aspect of polycyclic species has been explicitly revealed by theoretical investigations carried out on the isomers of furofuran (**1a–d**) and thienothiophene (**2a–d**)[6–8] (Fig. 1, Table 1). These species are the simplest among polycyclic π-systems, being iso-π-electronic with aromatic naphthalene. For these heterobicycles, the lowest energy isomer is not always the most aromatic.

The stability orders of furofuran and thienothiophene isomers are $\mathbf{1a} \approx \mathbf{1b} > \mathbf{1c} > \mathbf{1d}$ and $\mathbf{2a} \approx \mathbf{2b} > \mathbf{2c} > \mathbf{2d}$, respectively.[6–8] The low-energy isomers **1a**, **1b**, **2a** and **2b** satisfy the topological charge stabilization (TCS) rule.[9] However, the relative aromaticities of **1a–d** and **2a–d** as predicted by their nucleus-independent chemical shift (NICS)[1,2] values show the highest-energy isomers **1d** and **2d** to be the most highly aromatic (Table 1).[6–8] Note that NICS has been used widely as a magnetic criterion for estimating the degree of aromaticity. The lowest energy isomers **1a** and **2a** proved not to have the largest aromatic or resonance stabilization. If the relative aromaticities thus determined were fully reliable, it would imply that highly aromatic molecules are not always thermodynamically very stable. This does not conform to our image of aromatic molecules.

In this paper, we critically evaluate the aromaticities of **1a–d** and **2a–d** using our graph theories of aromaticity and magnetotropicity[10–15] and establish that at least some aromatic molecules might be energetically or kinetically very unstable. We use the term 'magnetotropicity' when diatropicity and paratropicity are referred to collectively.

THEORY

Topological resonance energy (TRE) and bond resonance energy (BRE) are typical energetic quantities defined by our graph theory. TRE represents a stabilization energy due solely to cyclic π-conjugation,[10,11] which is evaluated relative to the π-binding energy of the graph-theoretically defined polyene reference. We use TRE as a standard measure of aromaticity. BRE represents the contribution of a given π-bond to the TRE.[12,13] If the smallest BRE in a π-system has a large negative value, the π-system will be kinetically very unstable with chemically reactive sites. Both TRE and BRE are given in units of $|\beta|$, where β is the standard resonance integral in Hückel theory. We assume that all five-membered rings are regular pentagons in shape. Hückel parameters employed for **1** and **2** are those determined consistently by Van-Catledge:[16] $h_O = 2.09$, $k_{C—O} = 0.66$, $h_S = 1.11$ and $k_{C—S} = 0.69$.

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A graph-theoretical variant[3–5,14,15] of the Hückel–London theory[17] is utilized to calculate the intensities of π-electron currents magnetically induced in polycyclic π-systems. According to this, a π-electron current induced in a polycyclic π system can be partitioned formally among all possible circuits in the π-system. Here a circuit stands for any cyclic path in a π-system. Let a π-system from which one or more circuits can be chosen be denoted by G. A current assigned to the ith circuit, r_i, may be called the ith circuit current. The intensity of the ith circuit current, I_i, can be expressed in the form[14,15]

$$\frac{I_i}{I_0} = 18\frac{S_i}{S_0}\prod_{m}^{r_i} k_m \sum_{j}^{\mathrm{occ}} \frac{P_{G-r_i}(X_j)}{P'_G(X_j)} \qquad (1)$$

where I_0 is the intensity of a current induced in the benzene ring; S_i and S_0 are the areas of r_i and the benzene ring, respectively; G–r_i is the subsystem of G, obtained by deleting r_i from G; $P_G(X)$ and $P_{G-r_i}(X)$ are the characteristic polynomials for G and G–r_i, respectively; k_m is the heterobond parameter for the mth π bond; m runs over all π-bonds that belong to r_i; X_j is the jth largest zero of $P_G(X)$; and j runs over all occupied π-orbitals. If there are degenerate π-orbitals, this formula must be replaced by others.[14,15] Positive and negative values for I_i signify diatropicity and paratropicity, respectively.

NICS is defined as the negative of the magnetic shielding calculated at a ring center.[1,2] Positive and negative NICS values at ring centers are associated primarily with paramagnetic and diamagnetic π-electron currents, respectively. Schleyer and many others have referred to NICS as a convenient indicator of local magnetotropicity or local aromaticity for polycyclic π-systems.[1,2,6,8]

RESULTS AND DISCUSSION

NICS values at the ring centers of furofurans (**1a–d**) and thienothiophenes (**2a–d**) are summarized graphically in Fig. 1, which are those calculated by Subramanian *et al.* at the CSGT-HF/6–31+G$**$ level of theory.[6] It is noteworthy that **1d** and **2d** exhibit the largest negative NICS values at the ring centers. On this basis, Subramanian *et al.* predicted that these isomers must be the most aromatic although they are the energetically least stable isomers.[6] As shown in Table 1, **1d** and **2d** have the smallest total π-binding energies. For these two species, large negative NICS values never represent thermodynamic stability. They do not conform to the TCS rule.[9]

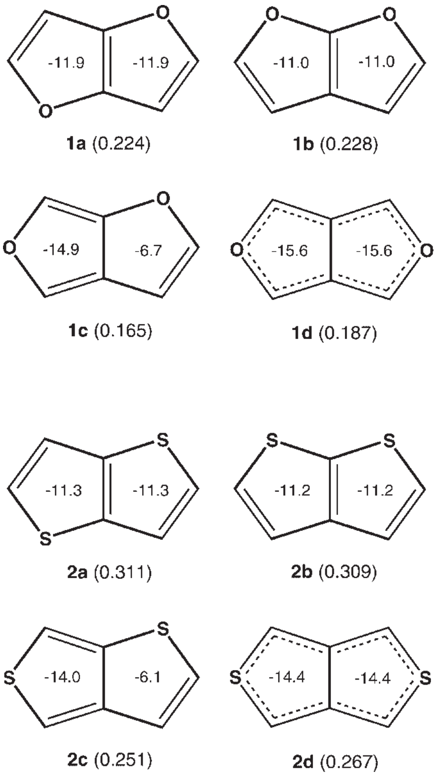

Figure 1. NICS values at ring centers for furofurans (**1a–d**) and thienothiophenes (**2a–d**), all calculated at the CSGT-HF/6–31+G$**$ level of theory.[6] Values in parentheses are the TREs in units of $|\beta|$

Current density maps for **1a–d** and **2a–d** are shown in Fig. 2, where the intensities of all π-electron currents are given in units of that induced in the benzene ring. These maps were obtained by superposing all possible circuit currents. The magnetic field is assumed to be perpendicular to the plane of this figure; counterclockwise and clockwise arrows denote diamagnetic and paramagnetic π-electron currents, respectively. Two rings of these heterobicycles are diatropic with negative NICS values at their ring centers. There is no doubt that each NICS value straightforwardly reflects the magnetotropicity of the ring concerned. Rings that sustain large diatropic currents exhibit large negative NICS values. This in turn proves that π-electron current calculations based on our simple Hückel model are fully acceptable.

Since heterobicycles **1a–d** and **2a–d** are essentially of the same size with the same number of π-electrons, the relative magnitudes of the TREs can be associated

Table 1. TREs and related quantities for furofurans and thienothiophenes (all in units of $|\beta|$)

Species	Total π-binding energy	HOMO–LUMO gap	TRE
Furo[3,2-*b*]furan (**1a**)	7.793	1.153	0.224
Furo[2,3-*b*]furan (**1b**)	7.749	1.374	0.228
Furo[3,4-*b*]furan (**1c**)	7.648	1.117	0.165
Furo[3,4-*c*]furan (**1d**)	7.077	0.356	0.187
Thieno[3,2-*b*]thiophene (**2a**)	8.223	1.283	0.311
Thieno[2,3-*b*]thiophene (**2b**)	8.199	1.547	0.309
Thieno[3,4-*b*]thiophene (**2c**)	8.076	1.134	0.251
Thieno[3,4-*c*]thiophene (**2d**)	7.690	0.568	0.267

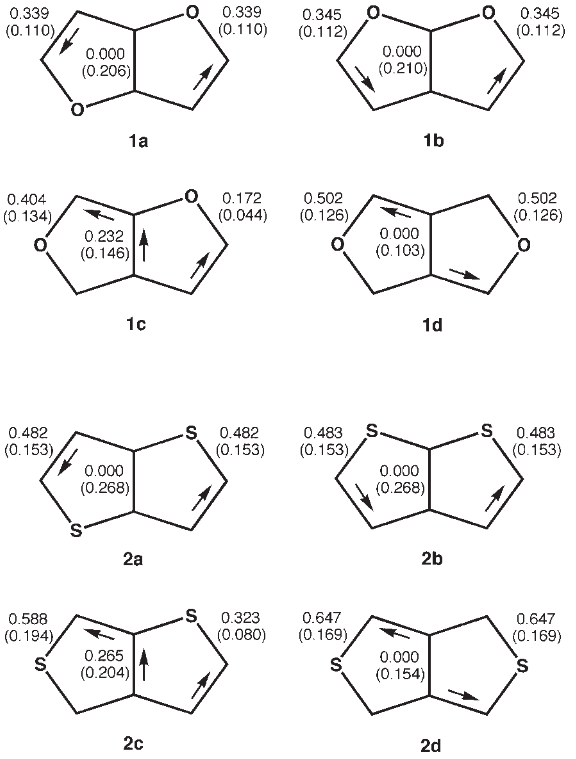

Figure 2. π-Electron currents induced in the isomers of furofuran (**1a–d**) and thienothiophene (**2a–d**), all in units of that for benzene (I_0). Values in parentheses are the BREs in units of $|\beta|$

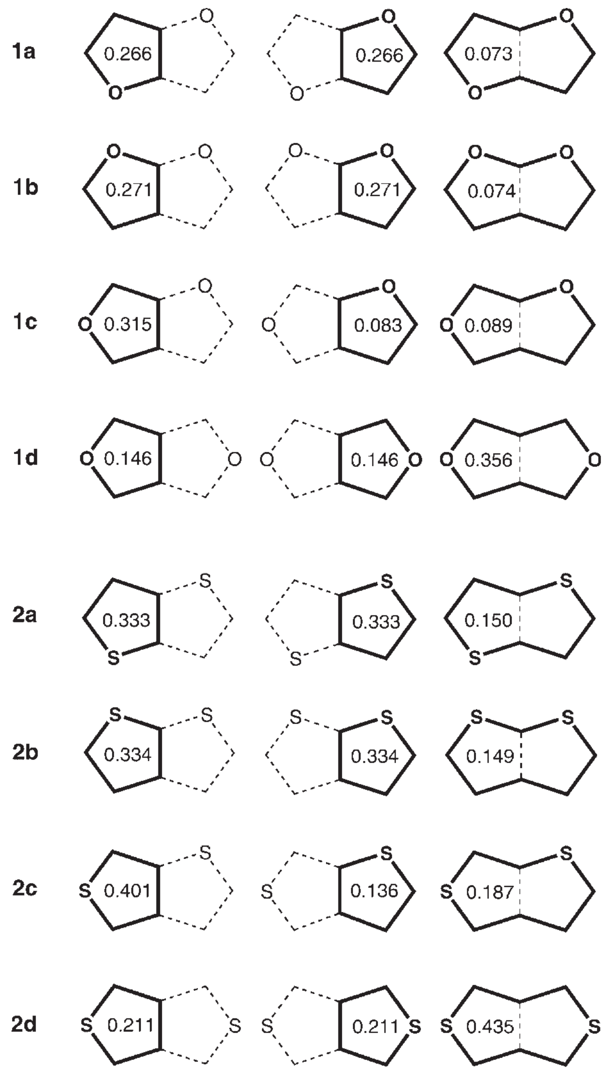

Figure 3. Circuit currents for furofurans (**1a–d**) and thienothiophenes (**2a–d**), all in units of that for benzene (I_0)

naively with the order of aromaticity. TREs for these bicyclic π-systems are given in parentheses in Fig. 1. The orders of aromaticity of furofuran and thienothiophene isomers thus determined are $\mathbf{1a} \approx \mathbf{1b} > \mathbf{1d} > \mathbf{1c}$ and $\mathbf{2a} \approx \mathbf{2b} > \mathbf{2d} > \mathbf{2c}$, respectively. These orders are somewhat different from those predicted from the NICS values ($\mathbf{1d} > \mathbf{1a} \approx \mathbf{1b} > \mathbf{1c}$ and $\mathbf{2d} > \mathbf{2a} \approx \mathbf{2b} > \mathbf{2c}$).[6,8] It is still noteworthy that **1d** and **2d** have larger TREs than **1c** and **2c**, respectively, although the former species are energetically much less stable than the latter. In this sense, **1d** and **2d** are two of the rare examples that are energetically unstable but fully aromatic.

Why does the TRE order of aromaticity differ from the NICS order? A clue to this problem is obtained by partitioning the π-electron currents among the circuits. All heterobicycles studied have three circuits: two five-membered circuits and one eight-membered circuit. Current intensities induced in the individual circuits, i.e. intensities of all circuit currents, are given in Fig. 3. All circuits sustain diamagnetic currents when **1a–d** and **2a–d** are placed in the magnetic field. In **1a**. **1b**, **2a** and **2b**, strong currents are induced in two five-membered circuits and a weaker one in the eight-membered circuit. In **1c** and **2c**, a strong current is induced in only one of the two five-membered circuits. In marked contrast, **1d** and **2d** sustain very large diatropic currents not only along the two five-membered circuits but also along the peripheral eight-membered circuit. Thus, **1d** and **2d** are different in the relative intensities of circuit currents from other isomers. Therefore, it follows that it is not always meaningful to predict the aromaticity order from the relative NICS values.

BRE is a useful measure for estimating the contribution of individual circuits to aromaticity.[12,13] If a π-bond is shared by two or more aromatic circuits, the BRE will have a large positive value. BREs for all species are added in Fig. 2. All π-bonds in the heterobicycles studied have positive BREs, which is consistent with the view that all these molecules are aromatic with positive TREs. As for **1a**, **1b**, **2a** and **2b**, the central CC bond, i.e. the bond shared by two rings, has a large BRE, which indicates that the two five-membered circuits are highly aromatic on which ca six π-electrons reside. In contrast, the central bonds in **1d** and **2d** have much smaller BREs, suggesting that the two five-membered circuits are much less aromatic. Central bonds in **1c** and **2c** are intermediate in aromatic contribution, which implies that only one of the five-membered circuits is highly aromatic. The length of the central CC bond increases along the sequences **1a** ≈ **1b** < **1c** < **1d** and **2a** ≈ **2b** < **2c** < **2d**.[7] These orders are in exact accord with those of the BRE for the central CC bonds.

A classical resonance structure is a kind of canonical structure that consists of CC double bonds and isolated divalent heteroatoms. As shown in Fig. 1, such resonance structures can be drawn for **1a–c** and **2a–c**. Aromaticity of these species can hence be interpreted in terms of conjugated circuit theory.[18,19] All circuits in **1a**, **1b**, **2a** and **2b** are a kind of conjugated circuit since a resonance structure can be drawn for the π-system obtained by deleting from the entire π-system the conjugated atoms that constitute any of the circuits. Left five-membered circuits in **1c** and **2c** are also conjugated. As predicted by Herndon and Ellzey[18] and Randić,[18,19] these circuits must contribute significantly to aromaticity and magnetotropicity. Eight-membered circuits in **1c** and **2c** are conjugated. This way of reasoning provides a qualitative explanation on the origin of aromaticity and diatropicity in polycyclic π-systems.

However, the conjugated circuit model cannot be applied to **1d** and **2d**, for which classical resonance structures cannot be drawn. A large diatropic current is induced along the eight-membered circuit although it is not a conjugated circuit. Thus, high aromaticity of these species arises both from the eight- and five-membered circuits, being supported by the structural measures of aromaticity,[6–8] such as BAI (Baird's Aromaticity Index)[20] and HOMA (Harmonic Oscillator Model of Aromaticity).[8] These two measures are closely associated with the degree of bond-length variation in a π-system. In particular, the BAI decreasing orders of aromaticity are exactly the same as determined on the basis of relative NICS values.[6,7] According to these geometric criteria the least stable positional isomers, **1d** and **2d**, should be the most aromatic. π-Electrons in such species are forced to delocalize over the entire π-system because double-bond fixation is prohibited in the non-classical π-systems.

In general, an aromatic molecule is kinetically stable with a large energy separation between the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO).[21] However, as shown in Table 1, **1d** and **2d** have very small HOMO–LUMO gaps with non-bonding HOMOs. It follows that these species must be chemically very reactive even if they are highly aromatic. Since classical resonance structures cannot be drawn for **1d** and **2d**, classical resonance structures also cannot be drawn for the polyene references. Such non-classical reference structures are supposed to be extremely reactive like non-classical acyclic polyenes. The extreme reactivity of non-classical polyene references for **1d** and **2d** could not be overcome by the TRE even if it had a large positive value.

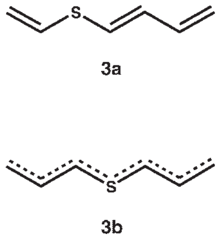

Figure 4. Two isomers of C_6H_8S (**3a** and **3b**)

In fact, the chemistry of **2a–d** is fully consistent with the above interpretation of TREs and HOMO–LUMO gaps.[22,23] Thienothiophenes **2a** and **2b**, which have the largest positive TREs and the largest HOMO–LUMO gaps, are kinetically very stable and undergo electrophilic substitution, whereas isomer **2c**, with the smallest positive TRE and a smaller HOMO–LUMO gap, is sensitive to air. Isomer **2d**, whose polyene reference must be extremely reactive, is available only as a transient or heavily substituted species.[22,23] It is much more reactive than **2a** or **2b**. No experimental studies are available for furofurans **1a–d**.

Consider, for example, two acyclic isomers of C_6H_8S (**3a**, **b**) in Fig. 4. Both have no TREs because they are acyclic in topology. It is obvious that **3b** is kinetically much more unstable than **3a** since a classical resonance structure cannot be drawn for the former species. As suggested above, even acyclic polyenes must be extremely reactive if they are non-classical species. This constitutes the reason why aromatic **2d** is extremely reactive. Likewise, **1d** must be very reactive. At least we can say that not only acyclic polyenes but also hypothetical polyene references are very diverse in chemical reactivity. Therefore, a large positive TRE is not always a good indicator of high thermodynamic or kinetic stability. Most open-shell species must be kinetically very unstable even if they have large positive TREs.

CONCLUSION

We have seen that the TREs calculated for polycyclic π-systems cannot always be associated with the thermodynamic or kinetic stability of the π-system. Heterobicycles **1d** and **2d** have large negative NICS values at all ring centers in accord with the large positive TREs. However, they must be kinetically very unstable because the non-classical polyene references are supposed to be extremely reactive. The TCS rule[9] proved to be a rule of thermodynamic stability but not that of aromaticity. We have repeatedly pointed out that NICS is not always a good indicator of aromaticity for polycyclic π-systems.[2–4] Note that all of the TREs, BREs and circuit currents, all utilized in this study, are defined exactly within the same Hückel framework so that these quantities are theoretically consistent with each other.[10–15]

Acknowledgments

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