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A Thiadiazole-Fused *N,N*-Dihydroquinoxaline: Antiaromatic but Isolable

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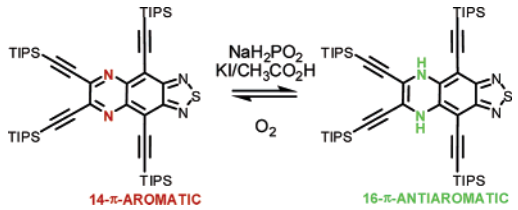
ABSTRACT



An antiaromatic–aromatic pair of peralkynylated heterocycles readily interconvert via redox reactions.

Antiaromaticity generally connotes instability, both energetic (thermodynamic) and kinetic (low persistence and high reactivity).[1] Antiaromatic compounds are often difficult to prepare and, like cyclobutadiene, have fleeting lifetimes. However, this behavior is not general for larger $4n$ π-electron systems. The tub conformation of cyclooctatetraene is preferred due to angle strain; the planar cyclically conjugated D_{4h} alternative is not destabilized appreciably.[2] Hückel molecular orbital (HMO) theory predicts that the antiaromatic vs aromatic differences between $4n$ and $4n + 2$ systems will eventually vanish for larger planar annulenes. Modern computational studies verify this expectation.[3] Some larger, planar polycyclic $4n$ π-electron systems, such as the 12π-electron dibenzocyclobutadiene (biphenylene), are readily isolable, suggesting that the energetic penalty for antiaromaticity may not be too severe, even though cyclobutadiene moieties may be involved.

Even the strong relationship of stability and persistence with aromaticity breaks down in the higher [n]acenes. Their stabilization energies, on a per-ring-carbon basis, decrease only modestly and remain nearly as large as that of benzene.[4] However, the larger acenes are not persistent environmentally, unless their reactions are blocked, for example, by attaching large silylethynyl groups in strategic positions.[5] The Clar rule[6] stating that structures with more sextet (cyclohexatriene) rings are more favorable explains why anthracene and the higher acenes undergo cycloadditions readily. Acenes have only one Clar sextet ring but are transformed by reduction of the central rings into products having two of these stabilizing features in two separated aromatic systems.

We now present an unprecedented example where neutral aromatic (**4**) and neutral antiaromatic (**5**) forms with a specific scaffold can be reversibly interchanged by reduction and oxidation. The closest analogies involve the inter-

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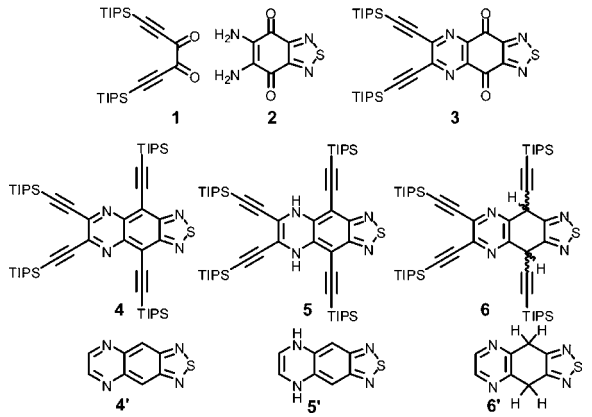
conversion of polycyclic aromatic hydrocarbons and their environmentally unstable dianions, even though in those only the numbers of π-electrons change, whereas in the pair **4/5**, two hydrogen atoms are added.[7] Although **5** may not be the most thermodynamically stable dihydro isomer, it is readily isolable and is persistent for weeks in the solid crystalline state. Air oxidation of **5** to **4** is very slow. Unlike the acenes, where reduction forms a saturated ring, the reduction of the pyrazine ring in **4** increases the number of π-electrons to the antiaromatic count. The formation and persistence of **5** are even more remarkable as a consequence.

Peralkynylated heterocycles such as **4** are critical intermediates for the construction of larger polyazaacenes. Condensation of Faust's butadione **1** with the known diamine **2** in ethanol furnished diyne **3** in 70% yield as a colorless, stable, crystalline solid (mp 78 °C).[8,9] Reaction of **3** with



the TIPS-acetylene anion, obtained through deprotonation with BuLi in THF, was followed by workup with moist ethyl ether and column filtration (hexane/ethyl acetate, 5:1). The product was immediately suspended in acetic acid and treated with an excess of an equimolar mixtue of potassium iodide and NaH_2PO_2.[10]

Instead of isolating **4**, as the expected sole product, we obtained a binary mixture separable by column chromatography using 4:1 hexanes−dichloromethane. Both products are red, crystalline, fluorescent solids. The ^{13}C NMR spectrum of the less polar, minor compound (Figure 1) is in good accord with structure **4** with four aromatic (δ = 154.8, 141.2, 140.4, 114.0) and four alkyne (110.7, 103.8, 101.5, 100.6) signals above the $CDCl_3$ peak and four signals for the two TIPS groups ranging from 11 to 19 ppm. The GIAO-computed aromatic chemical shifts agree with these assignments (see the Supporting Information). The molecular mass was confirmed by the m/z = 909 (EI) peak in the mass spectrum of **4**.

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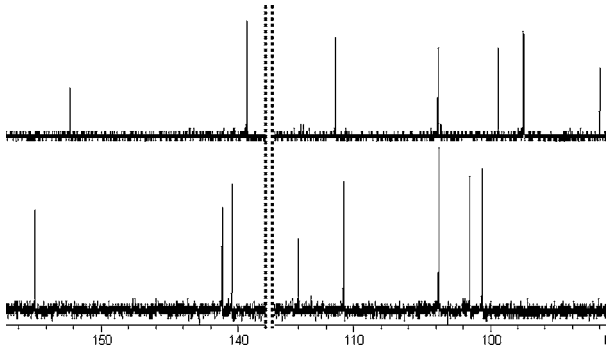

Figure 1. Top: ^{13}C NMR of **5** in $CDCl_3$. Bottom: ^{13}C NMR of **4** in $CDCl_3$. The broken double line refers to a cutout in the spectral region that ranges from 115 to 138 ppm where there are no signals visible.

The ^{13}C NMR (Figure 1, top) of the main fraction is similar to that of **4** in that it has four aromatic (δ = 152.3, 139.4, 111.4, 103.9) and four alkyne (99.5, 97.7, 97.6, 92.2) signals as well as four bands for the two TIPS groups.[11] The absorption and emission UV−visible spectra of both compounds (Figure 2) displayed similar features, but those of

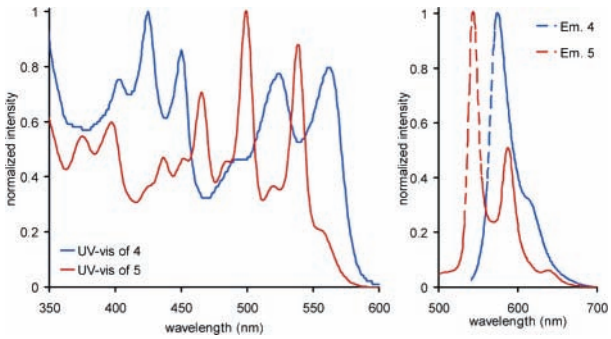

Figure 2. UV−vis and emission spectra of **4** and **5** (λ_{max} abs **4** = 562 nm; progression, 1327 cm^{-1}; λ_{max} em. **4** = 574 nm; progression, 1161 cm^{-1}; λ_{max} abs **5** = 539 nm; progression, 1479 cm^{-1}; λ_{max} em. **4** = 544 nm; progression, 1376 cm^{-1}).

the less polar component **4** are red shifted. Structure **5** for the major product is consistent with the m/z = 911 molecular ion in the mass spectrum and the N−H stretching vibration in the IR spectrum, which is eliminated by deuterium exchange in D_2O. The GIAO-computed aromatic ^{13}C NMR chemical shifts for the unsubstituted parent of **5**, **5′**, agree (see the Supporting Information). Note that **5** has an antiaromatic 16 π electron count, and according to DFT computations (PW91/6-311G**), **5′** is 7 kcal/mol less stable than its isomer, **6′**. Why is **5** formed and not **6**? The central position in **4** is shielded by the large TIPS-ethynyl group,

(11) See the Supporting Information for a careful discussion of details for the structure determination and spectral assignments of **5**.

posing a significant barrier toward reaction. Protonation of the pyrazine ring in acetic acid significantly *increases* the electrophilicity of the diazabutadiene substructure and will facilitate the formal hydride transfer from the $H_2PO_2^-$ anion[12] to form the thermodynamically less stable **5** as the kinetic product.

Compounds **4** and **5** constitute a redox-interconvertible pair; **5** is oxidized easily into **4** (93%) by DDQ, and **4** can be reduced to **5** by a heterogeneous mixture of NaH_2PO_2 and KI in acetic acid.

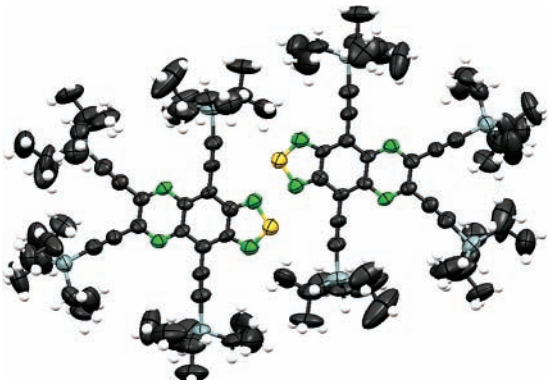

Figure 3. Single-crystal X-ray structure of **4**. The short (3.14 Å) intermolecular S−N contacts between two adjacent benzothiadiazole units of **4** are less than the sum of the van der Waals radii of sulfur and nitrogen, 3.40 Å.

The X-ray crystal structures of **4** (Figure 3) and **5** (Figure 4) corroborate our structural assignments.[13] The X-ray and

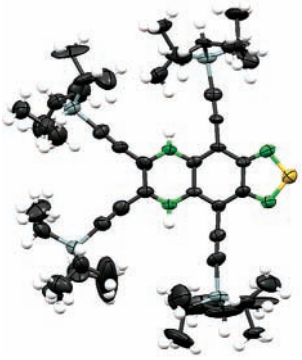

Figure 4. Single-crystal X-ray structure of **5**.

computed geometries of **4** and **5** (Figure 5) are surprisingly similar despite their aromatic and antiaromatic character. There are no dramatic differences in bond lengths. The expected aromaticity of **4** and the antiaromaticity of **5** were confirmed by detailed nucleus-independent chemical shift (NICS) computations, $NICS(0)_{\pi zz}$,[14] which evaluate the perpendicular (zz) tensor contributions of the individual

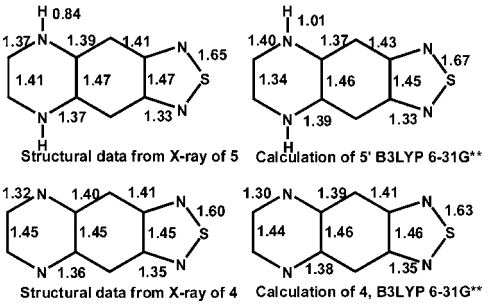

Figure 5. Comparison of X-ray and computed structures.[13] The bond lengths are in Å.

canonical (CMO) or localized (LMO) π molecular orbitals at ring centers (Figure 6). Both CMO and LMO $NICS(0)_{\pi zz}$ contributions show that **4** is quite aromatic,[15] the total values given inside all three rings are strongly diatropic (negative). Furthermore, the LMO data show that the diatropicity of each ring is due to the sum of the local contributions of each of its π electron components (given in red). Also, as shown in Figure 6, the contributions of the remote π components to the total (given in green) are small.

After reduction, the aromatic (diatropic) pyrazine ring of **4** (LMO $NICS(0)_{\pi zz}$ −26.1) becomes the antiaromatic (paratropic) dihydropyrazine ring of **5** ($NICS(0)_{\pi zz}$ +27.7). The aromaticities of the center carbocyclic and the thiadiazole rings are sharply reduced after the reduction ($NICS(0)_{\pi zz}$ −7.5 and −20.5 in **5** vs −38.6 and −41.2 in **4**, respectively). All data for the naphthalene-fused benzothiadiazole comparison model (Figure 6, bottom structure) are aromatic as expected; the introduction of the pyrazine nitrogens in **4** does not change its aromatic character. What is then responsible for the facile interconversion of the aromatic/antiaromatic pair **4**/**5**?

To evaluate this peculiar behavior, we calculated heats of hydrogenation at the B3LYP 6-311+G** level of DFT theory (with ZPE corrections)

$$\mathbf{4}' + H_2 \rightarrow \mathbf{5}'$$

$$\Delta H = -14.0 \text{ kcal/mol} \qquad (1)$$

This degree of exothermicity is remarkably large, as shown by the heats of hydrogenation of benzene and of pyrazine (computed at the same level). Both are endothermic, evidently due to the greater loss of stabilization:

$$\text{pyrazine} + H_2 \rightarrow \textit{N,N}\text{-dihydropyrazine } (D_{2h} \text{ form})$$

$$\Delta H = +14.9 \text{ kcal/mol} \qquad (2)$$

$$\text{benzene} + H_2 \rightarrow \text{1,4-dihydrobenzene } (D_{2h})$$

$$\Delta H = +11.7 \text{ kcal/mol} \qquad (3)$$

An important point here is that the 3.2 kcal/mol difference in energy between eqs 2 and 3—the "anitaromaticity penalty" is rather small.

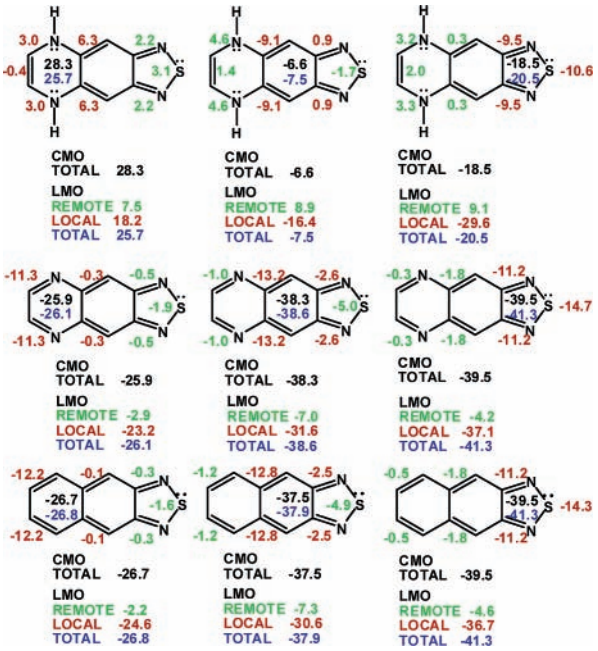

Figure 6. Comparison of CMO and LMO NICS(0)πzz data both computed at the PW91/6-311G** level using the NBO 5.0g program. "Local" refers to the π LMO contributions of individual double bonds and lone pairs (shown in red) associated with the designated ring. Note that 6 or 8 π electrons may be involved for aromatic rings, formally depending upon the localization. "Remote" refers to the remaining π contributions (shown in green). Note also that the sum of the remote (green) and local (red) LMO contributions (given in blue) matches the CMO total (given in black) closely.

As the aromaticity of **4′** (and **4**) seems to be quite normal, the exothermicity of eq 1 indicates that **5′** (and **5**) rather than being destabilized by antiaromaticity actually *is stabilized by synergistic interaction between the dihydropyrazine and the thiadiazole rings.* This stabilization, evidently arising from beneficial electron polarization, can be evaluated, e.g., by the isodesmic disproportionation reaction, eq 4, which is exothermic by 10.2 kcal/mol.

$$\text{1,4-diaza-1,4-dihydronaphthalene} + \text{benzothiadiazole} \rightarrow \mathbf{5'} + \text{benzene}$$

$$\Delta H = -10.2 \text{ kcal/mol} \qquad (4)$$

Similarly, the heat of hydrogenation of eq 1 is 11.7 kcal/mol more exothermic than that of eq 5, involving reduction of the outer ring of the naphthalene moiety:

$$\text{naphthothiadiazole} + H_2 \rightarrow \text{1,4-dihydronaphthothiadiazole}$$

$$\Delta H = -2.3 \text{ kcal/mol} \qquad (5)$$

The experimental and computational data agree that the antiaromaticity of **5** (and **5′**) is less "punishing" than might be expected. Nevertheless, **5** is neither "stable" nor "persistent". Isomer **6′** of **5′** is 7 kcal/mol lower in energy. ^{13}C NMR spectroscopy revealed that **5** converted to **4** *in the solid state* (approximately 80% after 4−6 weeks), presumably by air oxidation. The formation of **5** rather than **6** appears to be kinetically controlled. Anthony's[3] observation that bulky silylethynyl groups protect the vulnerable central positions in oligoacenes is applicable to **4**.

Although the aromaticity and antiaromaticity of the redox-interconvertible pair **4**/**5** agree with the computed magnetic properties (particularly NICS(0)$_{\pi zz}$), **5′** appears to enjoy special stabilization due to the favorable synergistic interaction between its two heterocyclic moieties.

In conclusion, we have synthesized and characterized an aromatic/antiaromatic pair (**4** and **5**)[16] of planar peralkynylated arenes (Vollhardt perimeters),[17] which are reversibly interconverted by oxidation and reduction. Aromatic **4** is persistent. Although **5** can be isolated, it reverts to **4** slowly under ambient conditions. As an overall consequence, antiaromaticity[18] does not result in a prohibitive energetic penalty generally, even in molecules as small as *N*,*N*-dihydropyrazine.

In future contributions, we will describe other systems in which pairs of aromatic and antiaromatic molecules are available[19] and interconvertible.

Acknowledgment. We thank the National Science Foundation (Grants CHE 0548423 and 0209857) for financial support.

Supporting Information Available: Experimental details and characterization of **4** and **5** and their synthetic intermediates, details concerning the computational evaluation of **4′** and **5′**, and a summary of the crystallographic data of **4** and **5** as cif files. This material is available free of charge via the Internet at http://pubs.acs.org.

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