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Lemniscular Hexaphyrins as Examples of Aromatic and Antiaromatic Double-Twist Möbius Molecules

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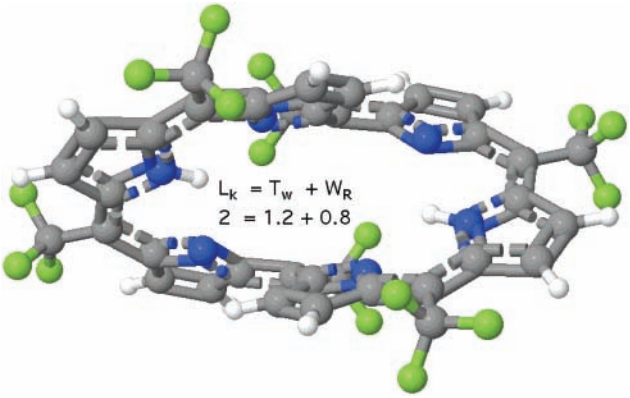
ABSTRACT



Two reported [26] and [28]hexaphyrins are analyzed via measured and computed geometries and NMR-shieldings as examples of respectively $4n + 2$ π-electron aromatic and $4n$ π-electron antiaromatic double-twist Möbius ring systems, adopting a lemniscular/figure-eight topology with linking number $L_K = 2\pi$. Values of local twist (T_W) and nonlocal writhe (W_R) derived from the relation $L_k = T_w + W_R$ appear relatively insensitive to the aromatic/antiaromatic character. The [26]hexaphyrin may adopt differing solution and solid-state conformations.

Heilbronner postulated in 1964[1] that suitably sized [4*n*]-electron annulenes might exist as singlet species by adopting a conformation in which a Möbius-like single half-twist is imparted to the basis set of 2p atomic orbitals forming the cyclically conjugated system. More recently it was proposed that this class of chiral, and potentially aromatic, molecule be extended to include double and higher order half-twisted systems,[2] and this was followed by suggestions that a (hypothetical) [14]annulene[3a] and 10-electron electrocyclic reaction[3b] and some members of a real class of molecules known as octaphyrins[4] might be examples of such double-twist Möbius systems. The most prominent candidate for a single half-twist system is the [16]annulene **1** as achieved via a rational synthesis by Herges et al.,[5] but the degree of conjugation and associated aromaticity for this molecule has proven controversial.[4,6] In the present article, it is proposed

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[1] Heilbronner, E. *Tetrahedron Lett.* **1964**, 1923−1928. DOI: 10.1016/S0040-4039(01)89474-0.

[2] Rzepa, H. S. *Chem. Rev.* **2005**, *105*, 3697−3715. DOI: 10.1021/cr030092l.

[3] (a) Rzepa, H. S. *Org. Lett.* **2005**, *7*, 4637−39. DOI: 10.1021/ol0518333. (b) Rzepa, H. S. *Chem Commun.* **2005**, 5220−22. DOI: 10.1039/b510508k.

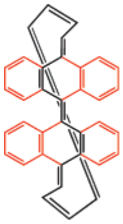
[4] Herges, R. *Chem. Rev.* **2006**, *106*, 4820−4842. DOI: 10.1021/cr0505425.

[5] Ajami, D.; Oeckler, O.; Simon, A.; Herges, R. *Nature* **2003**, *426*, 819−821. DOI: 10.1038/nature02224.

[6] Castro, C.; Zhongfang, C.; Wannere, C. S.; Jiao, H.; Karney, W. L.; Mauksch, M.; Puchta, R.; Hommes, N. J. R.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **2005**, *127*, 2425−2432. DOI: 10.1021/ja0458165.

10.1021/ol703129z CCC: $40.75

that two recently synthesized chiral hexaphyrins[7] constitute particularly well-characterized examplars of respectively antiaromatic and aromatic double half-twist Möbius molecules.



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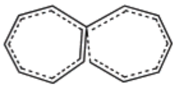

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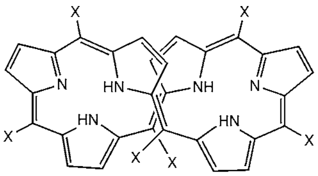
A doubly twisted "figure-eight", or lemniscular conformation of [14]annulene **2** has been calculated as being energetically accessible if suitably substituted.[3a] Such a double half-twisted moiety (more generally any system with an even number of such twists) can be shown to follow a $4n + 2$ electron rule for singlet stability and potential aromaticity.[8] Given however that two-half-twists have to be sustained by the $2p_\pi$ manifold within a relatively small ring, some explanation was needed to account for the relative stability of this conformation. We suggested[8,9] this was the result of reduction of (overlap-reducing) local twists of adjacent $p_\pi-p_\pi$ orbitals (quantified by the integrated parameter T_w) by supercoiling of the central axis of the ring into three dimensions, a process known as writhing (quantified by the nonlocal parameter W_R). Twist and writhe are formally related by L_k, the so-called linking number of the orbital basis set ribbon, via the relationship: $L_k = T_w + W_R$, where L_k is restricted to (positive or negative) integer values when expressed in units of "half-twist" (i.e., π).[9]

L_k alone determines whether a cyclic array of 2p atomic orbitals must inevitably result in a phase shift (true for odd values of L_k) or whether it has no mandatory phase shift in this basis (true for even values of L_k). According to this scheme, the singly half-twisted systems proposed first by Heilbronner, and exemplified by the [16]annulene **1** synthesized by Herges, belong to the L_k = odd category. Doubly half-twisted lemniscular systems of which **2** is an example, belong to the L_k = even category. These two types follow singlet ground state $4n$ and $4n + 2$ electron rules, respectively. For the chiral conformation of the [14]annulene, it has been shown[9] that the ribbon constructed from the 2p orbital basis set for **2** does indeed have the numerical value $L_k = 2\pi$, and that this is partitioned as $T_w = 1.11$ and $W_r = 0.89\pi$. Almost half of the undesirable (at least in terms of π-electronic conjugation) "twist" has been eliminated by conversion into "writhe" via bending of the central annulene curve into three dimensions. That such a chiral system can also be strongly aromatic was shown via a computed NICS(0) index[10] which revealed a prominent diatropic ring current. This particular conformation of [14]annulene remains hypothetical; the issue is now whether any well-characterized conjugated lemniscular molecules might be real exemplars of this type of aromaticity.

Two candidates **3** and **4** appear to deserve analysis in these terms. These are both hexaphyrins recently characterized by Osuka and co-workers.[7] Species **3** is a [28]hexaphyrin which follows a $4n$ π-electron rule, but it is easily oxidized by MnO_2 to **4**, a system following a $4n + 2$ π-electron rule. The structures of both **3** and **4** have been determined crystallographically as having "figure-eight" lemniscular conformations, and both therefore may conform to the L_k = 2 classification noted above. Whereas **4** as a $4n + 2$ system might be expected to be magnetically diatropic and chirally aromatic, the $4n$-electron **3** would be expected to be magnetically paratropic and (if L_k = 2/even) to be *antiaromatic*.



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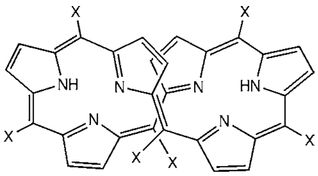

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The ^1H NMR spectrum recorded for **3** certainly bears out its antiaromaticity. The four NH protons point inward and are reported to have strongly deshielded chemical shifts (δ 14.95, 12.35 ppm) as appropriate for a paratropic ring current. The outward-facing *meso* positions are occupied not by protons but by CF_3 groups, but protons here would be expected to be shielded upfield. The crystallographic structure also supports this by evidence of prominent bond-length alternation. The two pairs of C−N lengths on the nitrogens bearing no hydrogen reveal an average Δ_r of 0.072 Å; the six pairs of C−C bond lengths centered at the *meso* positions show similar variation (Δ_r of 0.079). The four pyrrole units with NH groups partition into a pair bearing two long (~1.46) and one short (1.33−1.34) bonds; the other pair reveals local bond equality (in a manner reminiscent of the Clar sextet),[11] all of which points to the essentially localized valence structure shown as the formula for **3**.

The solid-state structure of **4** is in marked contrast, with average Δ_r of 0.021, 0.009, and 0.015 Å for the C−N, C−NH, and *meso* C−C lengths, respectively. It is clearly better represented by the mean of the valence bond form shown for **4** and its Kekulé bond-shifted isomer. The reported ^1H solution NMR is however more mysterious. The two inner-pointing NH protons are reported at 11.1 ppm, apparently also indicative of a paratropic rather than a diatropic ring current. This observation led the authors[7] to conclude

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[7] Shimizu, S.; Aratani, N.; Osuka, A. A. *Chem. Eur. J.* **2006**, *12*, 4909−4918. DOI: 10.1002/chem.200600158.

[8] (a) Fowler, P. W.; Rzepa, H. S. *Phys. Chem. Chem. Phys.* **2006**, 1775−77. DOI: 10.1039/b601655c. (b) Rzepa, H. S. *Abstracts of Papers*, 232th ACS National Meeting, San Francisco, CA, Sept. 10−14, 2006; American Chemical Society: Washington, DC, 2006; COMP-343.

[9] Rappaport, S.; Rzepa, H. S. *J. Am. Chem. Soc.*, submitted for publication.

[10] (a) Schleyer, P. v. R.; Maerker, C.; Dransfeld, A.; Jiao, H.; van Eikema, H.; Nicolaas, J. R. *J. Am. Chem. Soc.* **1996**, *118*, 6317−6318. (b) For a review, see: Chen, Z.; Wannere, C. S.; Corminboeuf, C.; Puchta, R.; Schleyer, P. v. R. *Chem. Rev.* **2005**; *105*, 3842−3888. DOI: 10.1021/cr030088+.

[11] Steiner, E.; Fowler, P. W.; Soncini, A.; Jenneskens, L. W. *Faraday Discuss.* **2007**, *135*, 309−323. DOI: 10.1039/b604769f.

that **4** was not in fact aromatic, despite its 26π-electron conjugation. The resulting contradiction between the delocalized bond lengths and this NH NMR shift was left unexplained.

To conform these various hypotheses and to ascertain whether **4** is truly aromatic or not, density functional calculations and derived values for the computed magnetic shieldings of the protons (X═H, CF_3), the bond lengths around the rings, the NICS(0) index, and selected values for L_k, T_w, and W_r were conducted. The density functional hybrid/basis set combination MPW1PW91/6-31g(d,p) was employed,[12] since this has been demonstrated to provide reasonably accurate relative magnetic shieldings at feasible computational cost for systems of this size.[13]

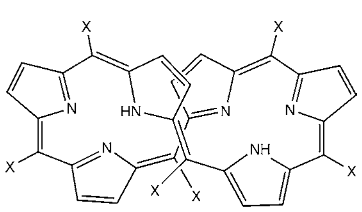
Ⓦ A web-enhanced table showing the calculated properties for compounds **3**−**7** is available.

At this theoretical level, the computed values for **3**$_{X = CF_3}$, are a NICS(0) of +4.9 ppm (Web-Enhanced Table 1) and an average Δ_r of 0.056/0.063 Å for the C−N/*meso* C−C lengths, respectively. The corresponding values for X = H are +9.7, 0.047/0.058. The ^{1}H magnetic shieldings (X = CF_3) relative to TMS were computed at the GIAO level with an applied solvation field (CPCM, solvent = dichloromethane) as 19.8 and 15.2 ppm. The observed values for the NH protons **3**$_{X = CF_3}$ (14.95, 12.35) are ∼3 to 4 ppm less than the calculated values, but they do represent room-temperature averaged shifts and not that of one specific conformer. Nevertheless, an unambiguously paratropic ring current is indicated. The computed CH shifts for the pyrrole rings ranged from 9.0 to 6.3 ppm, compared with 7.4−6.8 observed; these are within the level of accuracy supported by the GIAO method for ^{1}H shifts. The averaged values for the ^{19}F shifts differ by 1.8 ppm for the three nonequivalent pairs of trifluoromethyl substituents, compared with 2.1 ppm measured. With X = H, the computed NH shieldings show even greater downfield shifts of 22.9 and 17.9 ppm, suggesting that the *meso*-CF_3 substitution mildly attenuates the antiaromaticity of this ring system.

The 26π system **4**$_{X = CF_3}$, shows opposite behavior. The NICS(0) values (Web-Enhanced Table 1) are characteristic of aromatic, diatropic molecules.[2] Average Δ_r values of 0.004, 0.003, and 0.003 Å for the C−N, C−NH, and *meso*-C−C lengths, respectively, indicate virtually no bond length alternation and hence essentially complete aromatic delocalization.

Values for the linking number L_k and its components T_w and W_R for **4**$_{X = CF_3}$, were obtained by constructing a ribbon from the 2p atomic orbital basis set following the procedure reported previously.[9] However, this procedure was based on carbocyclic annulenes for which only one unique ribbon can be constructed; with the phyrins, passage through the five-membered pyrrole ring offers several ways of constructing a ribbon based on a single continuous 2p AO path. Analysis of the bond lengths, as set out above, suggest that a route involving all the nitrogens better represents the conjugated pathway than the alternative involving instead the C═C atoms of the pyrrole unit. Using this former path, the values obtained for **3**$_{X = H/CF_3}$, were $L_k = 2$, $T_w = 1.31/1.22(1.19)$, and $W_R = 0.69/0.78(0.81)\pi$, and for **4**$_{X = H/CF_3}$; $L_k = 2$, $T_w = 1.28/1.20(1.13)$, and $W_R = 0.72/0.80(0.87)\pi$ (values in parentheses were obtained by using crystallographic rather than computed coordinates). These values formally confirm both **3** and **4** as double half-twisted Möbius rings stabilized by conversion of a significant measure of local twist into writhe. The difference between the values of T_w and W_R for the antiaromatic and aromatic rings is surprisingly small, given that an aromatic system might have been expected to induce a much smaller twist as a means of enhancing the conjugating delocalization at the expense of greater bending-derived writhing in the σ framework. Also of interest is that the mpw1pw91/6-31g(d,p) theoretical combination appears to slightly overestimate T_w (and hence under-estimate W_R) for these systems; the ability to reproduce these values may indeed provide one selection mechanism for adopting new density functional procedures suitable for the calculation of π-delocalization and aromaticity.

The computed solution NH chemical shift for **4**$_{X = CF_3}$, (5.2 ppm) differs substantially from that measured for this system in $CDCl_3$ (11.1 ppm), and can be considered outside the expected error of the GIAO method. It is however consistent with the shielded shift expected from the inside region of a diatropic ring current. The pyrrolic CH protons (8.9−6.0) do however match with the values reported (7.9−6.0). The NMR values for **4**$_{X = H}$, are even clearer; the NH proton is predicted at the strongly shielded value of 3.8 ppm. The *meso* CH protons for **4**$_{X = H}$, are also intriguing; the pairs close to the lemniscate crossover region come between 4.9 and 5.5, while the outer four appear between 8.5 and 7.4, reminding that in a helical aromatic, the shielding/deshielding regions are not the simple cone associated with a purely planar aromatic.



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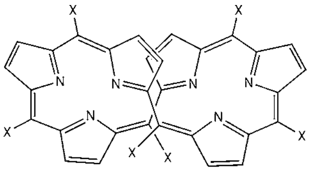
[12] Using Gaussian 03, rev. D.02: Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03*, revision D.02; Gaussian, Inc.: Wallingford, CT, 2004.

[13] (a) Rychnovsky, S. D. *Org. Lett.* **2006**, *8*, 2895−2898. DOI: 10.1021/ol0611346. (b) Braddock, D. C.; Rzepa, H. S. *J. Nat. Prod.* **2008**, in press.

A possible solution to the NH NMR shift paradox might be that the solution conformation differs from that of the crystal. Thus an alternative position for the NH pyrrole units in **4** to adopt is **5**. This is 8.3 kcal/mol less stable than **4** (free energy difference for a chloroform CPCM continuum solvation model), in part because the more stable bifurcated N···H···N hydrogen bond in **4** is replaced by a more conventional one. A small computed distortion from exact C_2 symmetry is found for **5**$_{\mathrm{X\,=\,CF_3}}$, resulting in two NH peaks predicted at 10.9 and 10.1 ppm, although this is likely to average out at room temperatures because of conformational mobility. This average value of 10.5 ppm is close to the observed value of 11.1 ppm. The remaining ring protons are predicted between 8.3 and 6.8 ppm, compared with the observed values of 7.9−6.0. An attenuated NICS(0) of −6.8 ppm and average Δ_r values of 0.042, 0.007, and 0.042 Å for the C−N, C−NH, and *meso* C−C lengths indicate that **5** is less aromatic than **2**, but clearly not yet nonaromatic, and most probably is not the same conformation/tautomer as the crystal structure. It is possible that the apparent preference for **5** in solution might be the result of explicit H-bonding with solvent molecules not included in the continuum solvent model.

Also included for completeness are the (hypothetical) systems **6** and **7**, which represent respectively the further oxidation of **4** to a 24 π-electron and formally antiaromatic system, and reduction of the antiaromatic **3** to a 30 π-electron formally aromatic system. The NICS(0) index for **6** (Web-Enhanced Table 1) indicates it as nonaromatic, with CH resonances in the region 7−4−8.3 and alternating bonds; Δ_r (*meso* C−C) = 0.099 Å. More interesting is **7**$_{\mathrm{X\,=\,CF_3}}$, which manifests as the expected aromatic system (Web-Enhanced Table 1), nonalternating bonds (Δ_r (*meso* C−C) = 0.007 Å), inner-facing NH shifts in the region 1.1−3.2 ppm, and outer facing CH shifts of 5.1−6.4 (in the crossover region) and 8.0−8.8 ppm. The calculated free energy of reduction (**3**$_{\mathrm{X\,=\,CF_3}}$ + H_2 = **7**$_{\mathrm{X\,=\,CF_3}}$) of −6.4 kcal/mol appears synthetically viable.



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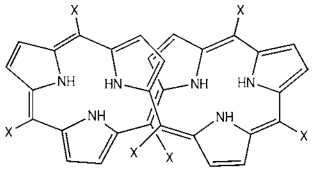

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The extensive crystallographic information available for the phyrins suggests that further tests of the type reported here may prove valuable for both analysis of these types of chirally aromatic system and the theories used to model them.

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