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The Chiro-optical Properties of a Lemniscular Octaphyrin

Henry S. Rzepa*

Department of Chemistry, Imperial College London, South Kensington Campus, Exhibition Road, London SW7 2AZ, U.K.

rzepa@imperial.ac.uk

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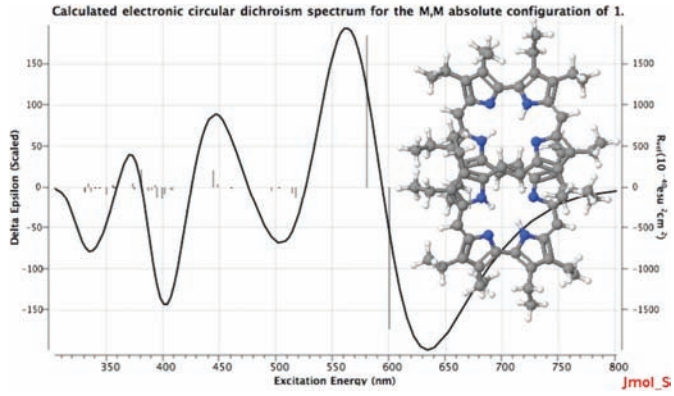
ABSTRACT



The match between the calculated TD-DFT electronic circular dichroism spectrum of the *M,M* configuration of the lemniscular [36]octaphyrin 1 and the previously reported measured spectrum suggests that the assignment of the latter to the *P,P* enantiomer requires inverting to *M,M*. The unusually large magnitude of the calculated optical rotations for these species may reflect the aromatic character of the system.

Whereas macrocyclic rings based on four pyrrole units are planar, extended cycles with between six and nine such building blocks can adopt chiral figure-eight or lemniscular motifs.[1] These crystalline and deeply colored materials have the potential for uninterrupted π-conjugation around the entire ring periphery. As such, they can be classified according to an extended version of the Hückel $4n+2$ and $4n$ π-electron rules, which incorporates the topological form of the π-electron density via a linking number *Lk*.[2] This index can be a positive or negative integer (in units of π), which adopts the specific value of $\pm 2\pi$ for lemniscular π-systems. For closed-shell singlet-state systems with such even values of *Lk*, stability and aromaticity are associated with $4n+2$ conjugated π-electrons and antiaromaticity with $4n$ electrons. The rules are inverted (aromatic $4n$/antiaromatic $4n+2$) for Möbius cycles with odd values for *Lk*. Examples ranging from hexa- to nonaphyrins,[3] which adopt a lemniscular form, and with either $4n+2$ or $4n$ π-electrons occupying the π-molecular orbital manifold have been characterized. Several have been explicitly identified[4] as having respectively aromatic or antiaromatic properties.

The key feature of the lemniscate is its intrinsic chirality, a molecule having $Lk = +2$ being the enantiomer of one with $Lk = -2$. Compound **1** (or a possible tautomer **2**) is an example of a [36]octaphyrin, and it represents the first (and to date only[5]) reported example of the successful kinetic separation of the two enantiomers and the assignment of their absolute configuration[6]

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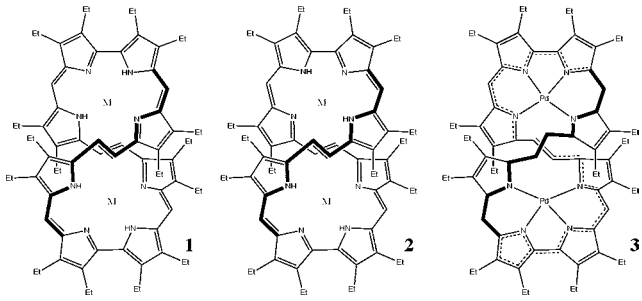
to either *P*,*P* or (as shown for **1**) *M*,*M* helicity. Not all lemniscular phyrins are configurationally stable; thus, a study of an [32]octaphyrin (4*n*, *n* = 8) using dynamic NMR techniques has revealed relatively low barriers to enantiomerization.[5]



The absolute *M*,*M* helical configuration of **1** was previously established[6] via a single-crystal anomalous X-ray scattering analysis of its Pd complex **3**. This in turn enabled assignment of the electronic circular dichroism (ECD) spectra to each enantiomer of **1**. The same article describes how the intense color of these molecules unfortunately prevented any measurement of the sign and magnitude of the optical rotation $[\alpha]_D$ of the pure enantiomers. A much studied and closely related class of molecules are the helicenes, where in fact it has been possible to measure $[\alpha]_D$ for the entire range penta- to tetradecahelicene.[7] The magnitudes and signs of the optical rotations are in the range −2000 to −8000° for this *M*-helicene series, which suggests that the value and sign of $[\alpha]_D$ (at 589 nm, the sodium D line, or at other frequency) for **1** if measurable would also be highly diagnostic of the absolute configuration.

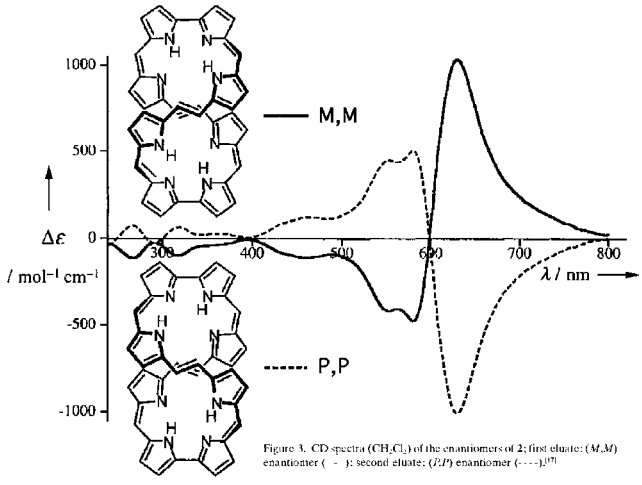


Figure 1. Experimental ECD spectrum of **1** reproduced with permission from Figure 3 of ref 6 and edited to show the *M*,*M*- and *P*,*P* assignments.

The past few years have seen the methodology for computing reliable ECD spectra[8] and $[\alpha]_D$ rotations[9] using TD-DFT methods becoming viable for molecules of this size. This now provides an opportunity to recheck the absolute configurations of **1** previously assigned to the ECD spectra of each enantiomer and to predict the anticipated optical rotations should their measurement in turn be viable. Furthermore, calculation now offers the possibility of exploring whether the chiro-optical properties are in any way dependent on the aromatic (4*n*+2) or antiaromatic (4*n*) character of the macrocycle.

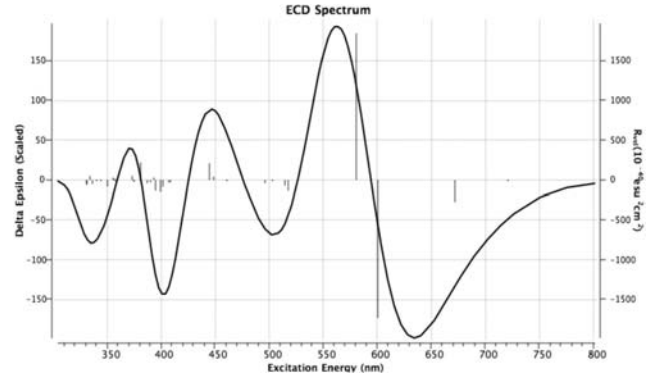


Figure 2. Calculated [B3LYP/6-31G(d,p)] ECD spectrum of *M*,*M*-**1** using TD-DFT for 40 states and SCRF(cpcm) correction for dichloromethane. Convoluted line width 0.14 eV.

The reported crystal structure **1** (deposited in the CCDC database[10] as reference code HOYPEQ) shows the four NH groups located as shown in **2**, although the published annotation of the ECD spectrum (Figure 3 of ref 6) shows an alternative tautomer **1**. It is quite possible that in solution, both tautomers coexist and equilibrate. The published[6] ECD spectrum of **1** (Figure 1) assigns a positive transition at ∼630 nm to the *M*,*M* enantiomer. The ECD spectrum of *M*,*M*-**1** was calculated using time-dependent DFT methods at the B3LYP/6-31G(d,p) level (geometries were optimized using the reported X-ray structure as the starting point where possible; use of more accurate basis sets is not yet feasible for a molecule of this size) (Figure 2). Specifying 40 initial states for the calculation together with a continuum solvation correction (CPCM) appropriate for dichloromethane resulted in a convoluted spectral envelope for *M*,*M*-**1** which is

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essentially indistinguishable from that calculated for the tautomer *M*,*M*-**2** (full details of all of the calculations are available via the Web-enhanced table). This suggests that the ECD spectrum is not sensitive to the nature of the N−H tautomers. The match with the experimental spectrum in the region 500−700 nm is excellent in terms of the energy of the transition, but the signs of the two bands at ∼570 and 630 nm match that assigned to the *P*,*P*-enantiomer in the experimental spectrum.[6]

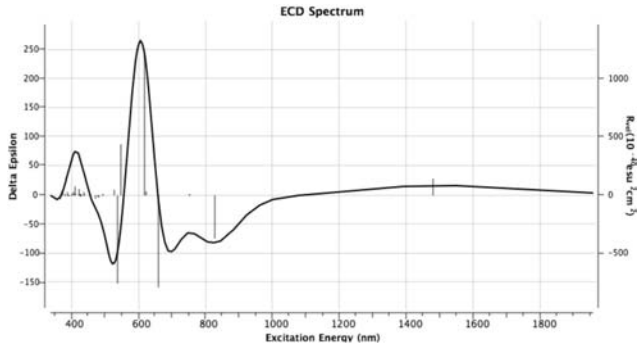


Figure 3. Calculated [B3LYP/6-31G(d,p)] ECD spectrum of **3**, using TD-DFT for 40 states and SCRF(cpcm) correction for dichloromethane. Convoluted line width 0.14 eV.

As a calibration check, the ECD spectrum of *M*-hexahelicene was computed at the same level of theory and procedure (full details of all of the calculations are available via the Web-enhanced table); both the energy and (negative) sign of the transition at ∼330−340 nm match the experimental trace well. It is also noteworthy that both **1** and hexahelicene have similar ECD features, which appear to be characteristic of the *M* (or double *M*,*M*) helix.[11]

These calculations imply that the published ECD assignments[6] may require inversion, with the first eluate from a chiral column assigned as having *M*,*M* chirality (Figure 3 of ref 6) instead being designated of *P*,*P* chirality and the second eluate now being the true *M*,*M* enantiomer. While it remains possible that the discrepancy between our calculations and the experimental spectra is due to a simple mislabeling of Figure 3 of ref 6, footnote 17 in ref 6 also restates the result implied in this caption: "a comparison of the CD spectra of all pure enantiomers showed that the sequence of elution of the optical isomers reversed after complex formation; the second eluted enantiomer of the binuclear Pd complex **3**... (...the (*M*,*M*) form) corresponded to the first eluted enantiomer of **1** and vice versa." The ECD spectrum of **3** is unfortunately not reported,[6] but its calculated form (Figure 3) does show significant differences from **1**, which may in turn be due to the atropisomerism of the *trans*-alkene in the crossover region which occurs to accommodate the Pd. Whether these perturbations might account for the transposition in assignment noted in footnote 17 of ref 6 remains unclear. It might also be that Pd complex formation from **1** involves an associated inversion of lemniscular configuration by an unknown mechanism,[5] in addition to the atropisomerism already noted.

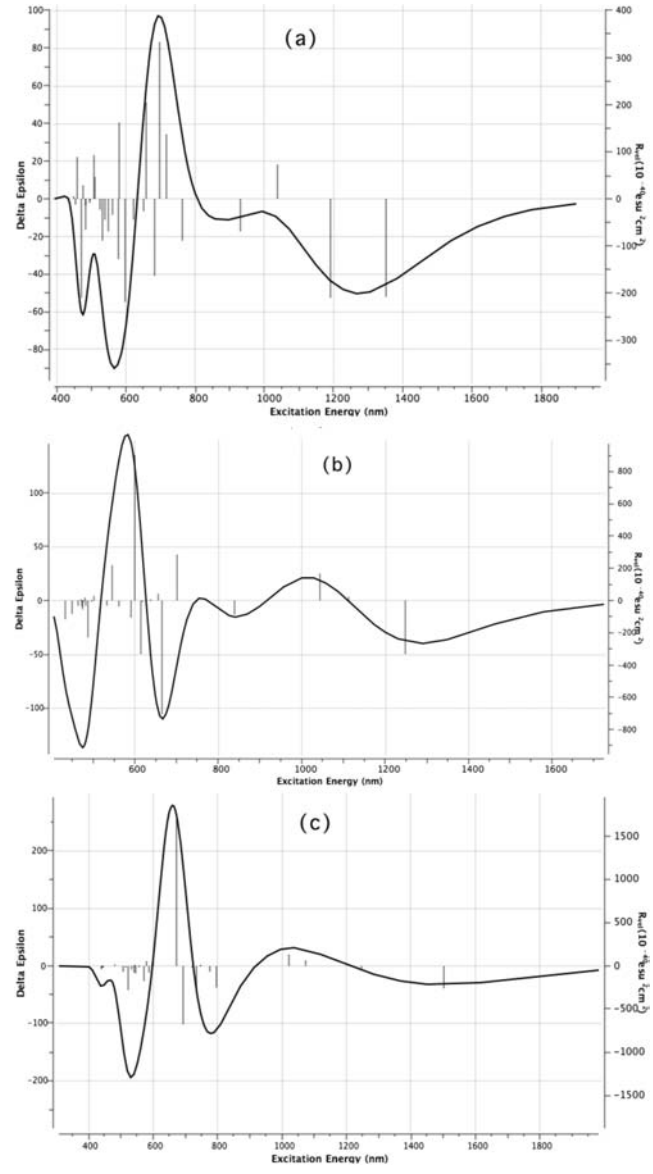
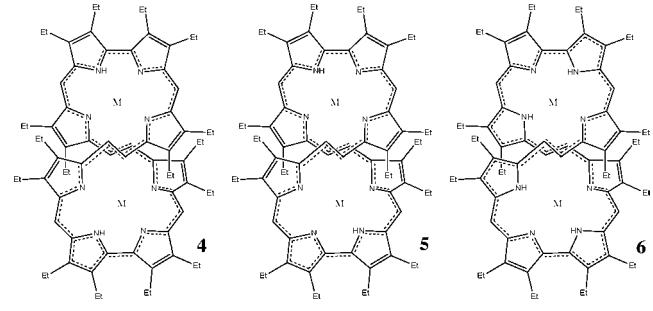


Figure 4. (a) Calculated [B3LYP/6-31G(d,p)] ECD spectrum of **4**, (b) **5** and (c) **6**, using TD-DFT for 30 states, and SCRF(cpcm) correction for dichloromethane. Convoluted line width 0.14 eV.



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Both **1** and **2** have a π-electron classification of 4n (n = 9), and are therefore antiaromatic according to the Hückel rule noted above. Whereas more flexible molecules having a 4n π-electron count such as, e.g., cyclo-octatetraene can adopt a nonaromatic and hence unconjugated tub-shaped conformation, **1** appears to be too rigid to eliminate antiaromatic character by such a mechanism. The antiaromaticity can instead manifest by relatively facile oxidation[3,4] that aromatizes the cycle by reducing the π-electron count by two from 4n to 4n+2. This can be achieved chemically by oxidizing two pyrrolic N−H groups down to the imino form **4** or its tautomer **5**. A second model, which eliminates even that small structural perturbation, would instead be a direct two-electron oxidation to a dication **6**.[12] Either operation will covert the [36]phyrin to the [34]-aromatic form, and provide additional systems whose chiro-optical properties can be predicted (Web-enhanced table) and potentially measured.

The geometries of **4**−**6** were all optimized starting from edited X-ray coordinates of **1**; these oxidized [34]π-electron aromatic phyrins exhibit less bond length alternation, at either the four *meso*-positions, or at the two four-carbon *trans*-alkene motifs at the lemniscular cross over positions, compared to the antiaromatic unoxidized form. The calculated ECD spectra also differ (Figure 4); the most prominent highest wavelength transition is a relatively intense band at ∼1300−1500 nm rather than at ∼700 nm (**1** also has a predicted transition in the same region, but of lower intensity, see the Web-enhanced table).

The value of the optical rotation ($[\alpha]_D$ at the sodium D line of 598 nm, or other frequency), if measurable, is also a potential means of assigning absolute configurations.[9] This quantity can be calculated either as a static-field approximation or from a frequency dependent formulation.[13] Solvation corrections are now recognized as also important, as is an exhaustive exploration of conformational space. The latter is fortunately less of an issue with the rigid lemniscular π-framework of **1** (although the ethyl substituents are conformationally mobile, they inflict only a small perturbation to the π-electronic transitions). The frequency dependent solution did prove problematic, the CPHF linear equations frequently failing to converge at 589 nm (the sodium D-line). Reported here therefore are the static values, but with the frequency dependent values computed instead at $[\alpha]_{880}$ (the highest wavelength available for commercial polarimeters). The computed static value of $[\alpha]_D$ for hexahelicene (−1933°) is significantly underestimated compared to the recorded value (−3640°) (and is improved only slightly with larger basis sets), whereas the calculated frequency dependent value (−4613°) overshoots by ∼27%. However, the sign in both cases is correctly predicted (Web-enhanced table).

The calculated optical rotations for the 4−π systems **1**−**2** reveals that the static $[\alpha]_D$ values (∼−3900 to −5200°) are predicted to be ∼3-fold larger than for hexahelicene; the signs are again all negative and characteristic of the *M*,*M* helix. The frequency dependent values $[\alpha]_{880}$ (∼ −4254°) are likewise exalted compared to hexahelicene at that wavelength (∼−1440°). In the case of the Pd complex **3**, the static $[\alpha]_D$ changes sign (+4950°) and $[\alpha]_{880}$ (−22806°) reveals an unusually large sensitivity to wavelength, an effect which if correct deserves further experimental study. The 4n+2−π molecules **4**−**6** show a further 2−4-fold increase in the magnitude of the rotations resulting from aromatization of **1**, resulting in exceptionally large values for this property. Thus **6** has a predicted $[\alpha]_{1000}$ of −31597°. These preliminary results imply that the optical rotations of such leminscular phyrins may be an interesting new probe of both the capacity of theory to correctly reproduce them, of aromatic or antiaromatic behavior, and if they prove measurable, providing further verification of the absolute configurations of this class of species.

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