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Heliphyrin: a ring open porphyrinoid with helical chirality†

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Heliphyrin, a new porphyrinoid with a helicene-type structure, can be produced in two steps from commercially available reagents. Three macrocycle-like structures were produced *via* a template reaction involving a benzimidazolylidene modified iminoisoindoline and divalent metal (Co, Ni, and Cu) salts. The heliphyrins are tetradentate, dianionic ligands that coordinate the central metal in a square planar configuration, while forming a helical structure around the metal due to the steric bulk of the benzimidazole units. These compounds are panchromatic chromophores, and we interrogated their electronic structures using DFT and TDDFT methods. We could also separate racemic heliphyrins into enantiomers using chiral chromatography, and axial ligation by tartaric acid induces formation of chiral species as detected by circular dichroism spectroscopy. Due to their chiral nature, these complexes may have uses in biological and sensor applications.

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Normal porphyrins and phthalocyanines are highly symmetric aromatic macrocycles which typically do not exhibit chirality. Optical activity in porphyrinoids can be induced by incorporating chiral substituents or *via* functionalization at the periphery.^{1–4} Alternatively, porphyrin assemblies have also been shown to exhibit optical activities.^{4–6} To make the core ring itself chiral, one needs to break the symmetric reflection planes that lie in and orthogonal to the macrocycle. In this report, we present a new porphyrinoid where the reflection plane symmetry is eliminated due to its open ring structure which adopts a helical structure around a central metal atom. The helicity in these porphyrinoids is similar to that seen in the well-studied helicene class of compounds,^{7–10} and so we have named this new class of porphyrin inspired chelate as the heliphyrins (Hlp). The heliphyrins can be synthesized in two steps from commercially available reagents. We have produced cobalt, nickel, and copper metalated heliphyrins, and we can separate the enantiomers by chiral chromatography.

Over the past few years, we have been exploring the reactivity of 1,3-diiminoisoindoline (DII) with organic acids that possess a sp^3 hybridized carbon atom with a $pK_a < 20$.^{11–13}

These organic acids can substitute the imine groups in DII with carbon–carbon double bonds to form ylidenes. Frequently, bis(ylidene)isoindolines are formed, but the reaction of equivalent amounts of 2-(benzimidazolyl)acetonitrile with DII produces a 1:1 adduct (compound **1**, BzIm-DII) where just one of the two imine groups on the isoindoline is replaced with a carbon–carbon double bond (Fig. 1). We have fully characterized this compound, including *via* X-ray crystallography, and BzIm-DII is a planar bidentate chelate that can be considered as a *meso* carbon variant of the semihemiporphyrine ligand. This compound also exhibits visible absorption bands that are similar to those observed in ylidene-modified isoindolines.¹³ Additionally, the structure of BzIm-DII is

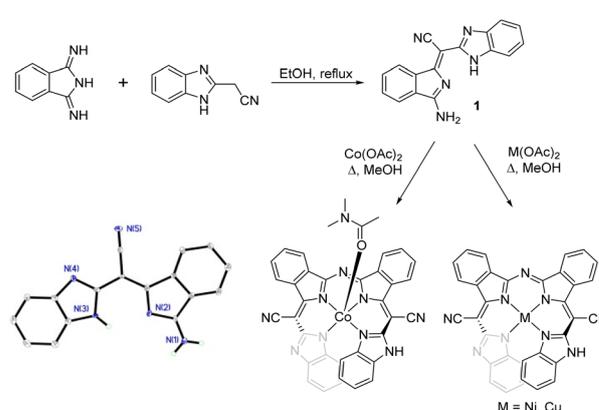


Fig. 1 The synthesis of the heliphyrins along with the structure of the precursor chelate.

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analogous to that of the pyrazole and indazole substituted DIIs which are precursors to the biliazine class of phthalocyanines analogues.^{14–16} We observe conjugation between both heterocycles in the BzIm-DII chelate as measured by the C–C bond distances about the cyano-modified sp² hybridized carbon position (~1.37 and ~1.45 Å) as well as in the UV-visible spectrum (Fig. S15†), which shows a maxima at 438 nm.

When reacted with the transition metal ions Co(II), Ni(II), and Cu(II), two equivalents of BzIm-DII template at the metal centres to form an open porphyrinoid structure. The templating reactions are shown in Fig. 1, and the structures of the resultant metal adducts (Co(Hlp))(DMF)₂, Ni(Hlp), and Cu(Hlp) are shown in Fig. 2. These compounds are sparingly soluble in most organic solvents but can be dissolved in DMF, pyridine, and DMSO. The heliphyrins have a single *meso* nitrogen atom linking the two isoindoline units, and there are two nitrile modified *meso* carbon atoms connecting the benzimidazole groups to each isoindoline. Heliphyrin acts as a tetradentate ligand, binding each metal in a distorted square planar geometry, and the ligands act as dianions with the metals in the +2 oxidation state. In the Ni and Cu complexes, the metals are four coordinate overall, but in the Co complex there is an equivalent of solvent dimethylformamide present in the axial position. The M–N bonds around the metal are nearly equivalent in length, unlike that seen in the traditional hemiporphyrin macrocycles, which exhibit asymmetric lengths about metal centres.^{17–20} In all three compounds, the M–N bond distances are relatively short as well, with all below 2.0 Å in length.

As in the biliazine porphyrinoid, the M(Hlp) macrocycles are not closed by a covalent bond. As a result, the steric bulk of the benzene ring of benzimidazoles are forced to adopt a slipped stack configuration. These open porphyrinoids thus adopt a helical configuration, as shown in the Fig. 2. Since the helicity is induced upon template reaction, the metal complexes of the heliphyrins are isolated as racemic mixtures. This can be seen in the crystal structures of the three metal complexes presented herein, as all the space groups have inversion centre symmetry. The spacing between the overlapping benzimidazole units, as measured by the distance between the 4

carbon positions, ranges between 3.4 and 3.6 Å, which also represents the rise in the helix for the single turn. Due to the limited size of the benzimidazole unit, the overlap occurs only at the 4 and 5 carbon atom positions on each terminal heterocycle. Previously, ring open hemiporphyrins have been shown to adopt helical structures, but these ligand systems do not exhibit cross conjugation as observed in the heliphyrins.^{21,22} In addition to the similarities to the helices, this helicity has parallels to the chemistry of the bilines and bilindiones.^{23–27} These open ring systems were produced as models for the metabolic byproducts of heme degradation, such as biliverdin. When coordinated to metals, the terminal carbonyls of the cleaved porphyrin ring create steric hindrance that forces the bilines and bilindiones to adopt helical configurations.

The heliphyrins are strongly absorbing chromophores, with intense absorption bands across the entire UV-visible spectrum (Fig. 3). Like many of ylidene-modified isoindolines,^{11,13,16} the precursor BzIm-DII chelate is a chromophore itself. Upon the template formation of the heliphyrins, the absorption bands extend through the visible out

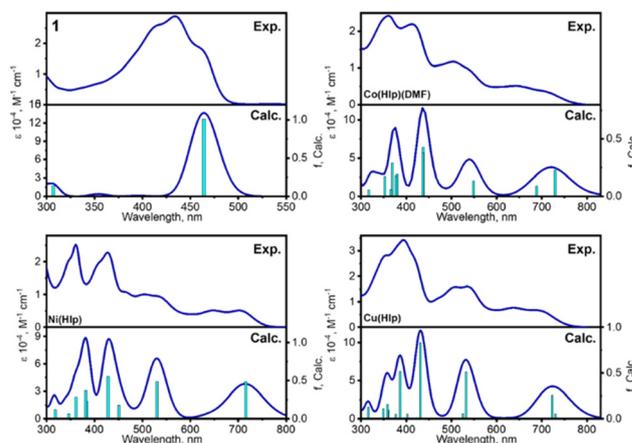


Fig. 3 Experimental (DMF) and B3LYP TDDFT-predicted spectra for 1 and M(Hlp) complexes.

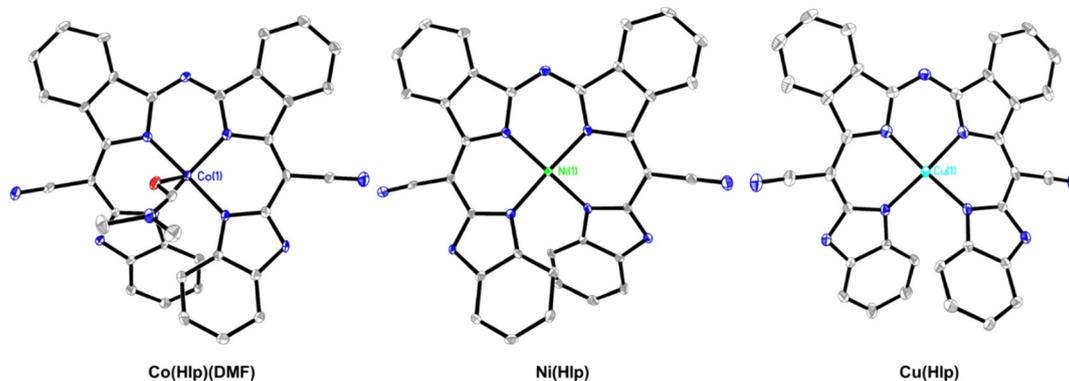


Fig. 2 The structures of cobalt, nickel, and copper heliphyrins.



to the near-IR region. In the heliphyrins, the extinction coefficients are relatively large, on the order of $10^4 \text{ M}^{-1} \text{ cm}^{-1}$, although they are not as intense as in normal porphyrins due to the lack of ring closure to form an 18 electron annulene-type aromatic ring. Notably, the bands in all the heliphyrin complexes are very broad, such that we observe continuous absorbance from $\sim 300 \text{ nm}$ to 750 nm , which includes the entire visible region. Thus, the heliphyrins are black in colour, and we can characterize this behaviour as panchromatic. In this regard, they are potentially useful for their light harvesting properties. As part of our characterization of these compounds, we investigated their cyclic voltammetry. We observed partially reductions of the ligand around -1 V as well as some metal-based redox events for the Co(Hlp) and Cu(Hlp) variants (Fig. S9–S11†).

In order to interrogate the optical properties of the biliazines, we carried out DFT and TDDFT calculations on Co(Hlp)(DMF)₂, Ni(Hlp), and Cu(Hlp). The energies of the frontier orbitals for the heliphyrin complexes and compound **1** are shown in Fig. S13 and S14† along with the structures of the HOMO and LUMO orbitals in Fig. S12.† The frontier orbitals are predominantly π in character. Additionally, the LUMOs are relatively energetically isolated from the LUMO+*n* orbitals in these complexes. The TD-DFT calculations, shown in Fig. 3, are in good agreement with the experimental data (taking into consideration the presence of vibronic 0-*n* transitions associated with all major bands in the experimental spectra). Similar vibronic satellites can be seen in other isoindoline based chromophores.^{11–14} The lowest energy band observed around 700 nm in all complexes was predicted to be dominated by the HOMO \rightarrow LUMO single-electron transition.

To isolate the different enantiomers of heliphyrin, we employed chiral chromatography. Using an HPLC equipped with a $5 \mu\text{m}$ CHIRALPAK IE (Daicel) column, we were able to separate the two enantiomers for all three products. Fig. 4 shows the separation between the two enantiomers of Ni(Hlp).

However, due to the overall lack of overlap between the benzimidazole units and from the flexibility in the metal coordination environments, we observe re-isomerization in solution relatively quickly ($<1 \text{ hour}$). However, we could drive the equilibrium toward the formation of a single enantiomer by axial ligation. Fig. 4 also shows the CD spectra of Co(Hlp)(DMF) in the presence of D- and L-tartaric acid. CD spectra of these enantiomers are clear mirror images of each other. In contrast, the Ni(Hlp) variant shows no such induction (based on CD spectroscopy data). Square planar Ni(II) complexes, unlike Co(II) analogues, do not readily bind ligands at their axial positions (see ESI† for more details) and thus the presence of the racemic mixture is still experimentally observed. We have carried out calculations on the axial induction of chirality in Co(II) complexes coordinated with one and three tartaric acids and observe good agreement with experimental data (Fig. S16†). Notably, the bilinones and bilindiones also exhibit induction of chirality by use of point modification, allosteric interactions, or solvent effects.^{25–27}

In conclusion, we have synthesized a new ring open porphyrinoid using a simple metal mediated template reaction. The chelate precursor can be readily generated from commercially available reagents. The cobalt, nickel, and copper adducts of heliphyrin exhibit a helical structure similar to that seen in the helicenes. These ligands are fully conjugated and absorb light across the UV-visible spectrum so they can be considered panchromatic in character. The template synthesis reactions of the M(Hlp) compounds produce a racemic mixture, and although enantiomers can be separated, they are only transiently stable to equilibration. However, axial binding by the chiral ligands D- or L- tartaric acid can be used to drive the equilibrium to a single enantiomer. We are continuing our work on developing new porphyrinoids with a focus on isoindoline chemistry as a starting point.

Conflicts of interest

There are no conflicts to declare.

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References

- H. Lu and N. Kobayashi, Optically Active Porphyrin and Phthalocyanine Systems, *Chem. Rev.*, 2016, **116**, 6184–6261.
- G. Travagliante, M. Gaeta, R. Purrello and A. D'Urso, Recognition and Sensing of Chiral Organic Molecules by Chiral Porphyrinoids: A Review, *Chemosensors*, 2021, **9**, 204.

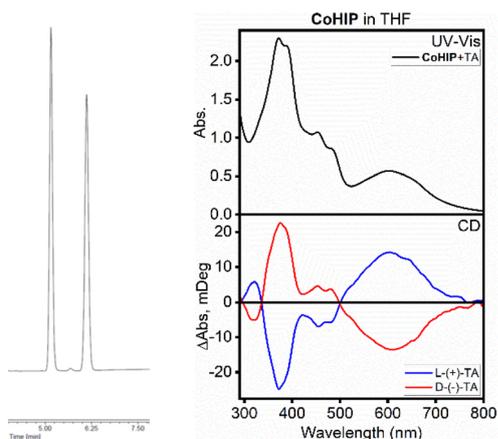


Fig. 4 Chiral HPLC separation of the two enantiomers of Ni(Hlp) (left) and the CD spectra of Co(Hlp) in THF in the presence of D and L tartaric acid.



- 3 J. T. Groves and R. S. Myers, Catalytic asymmetric Epoxidations with Chiral Iron Porphyrins, *J. Am. Chem. Soc.*, 1983, **105**, 5791–5796.
- 4 V. Borovkov, Supramolecular Chirality in Porphyrin Chemistry, *Symmetry*, 2014, **6**, 256–294.
- 5 J. Ouyang, A. Swartjes, M. Geerts, P. J. Gilissen, D. Wang, P. C. P. Teeuwen, P. Tinnemans, N. Vanthuyne, S. Chentouf, F. P. J. T. Rutjes, J. V. Naubron, J. Crassous, J. A. A. W. Elemans and R. J. M. Nolte, Absolute Configuration and Host-Guest Binding of Chiral Porphyrin-Cages by a Combined Chiroptical and Theoretical Approach, *Nat. Commun.*, 2020, **11**, 4776C.
- 6 C. Maeda, K. Ogawa, K. Sadanaga, K. Takaishi and T. Ema, Chiroptical and Catalytic Properties of Doubly Binaphthyl-Strapped Chiral Porphyrins, *Chem. Commun.*, 2019, **55**, 1064–1067.
- 7 R. H. Martin, The Helicenes, *Angew. Chem., Int. Ed. Engl.*, 1974, **13**, 649–660.
- 8 M. Gingras, One Hundred Years of Helicene Chemistry. Part 1, *Chem. Soc. Rev.*, 2013, **42**, 968–1006.
- 9 M. Gingras, G. Félix and R. Peresutti, One Hundred Years of Helicene Chemistry. Part 2, *Chem. Soc. Rev.*, 2013, **42**, 1007–1050.
- 10 G. Gingras, One Hundred Years of Helicene Chemistry. Part 3, *Chem. Soc. Rev.*, 2013, **42**, 1051–1095.
- 11 S. Gaire, B. R. Schrage, V. N. Nemykin and C. J. Ziegler, An Isoindoline Chelate with a Stretched Electronic Structure, *Dalton Trans.*, 2021, **50**, 826–829.
- 12 B. R. Schrage, C. A. Farmer, V. N. Nemykin and C. J. Ziegler, The Synthesis and Characterization of Ylideneisoindolinones, *J. Porphyrins phthalocyanines*, 2021, **25**, 1048–1054.
- 13 Y. V. Zatsikha, B. R. Schrage, J. Meyer, V. N. Nemykin and C. J. Ziegler, 1,3-Diylideneisoindolines: Synthesis, Structure, Redox, and Optical Properties, *J. Org. Chem.*, 2019, **84**, 6217–6222.
- 14 B. R. Schrage, V. N. Nemykin and C. J. Ziegler, Biliazine: A Ring Open Phthalocyanine Analog with a Meso Hydrogen Bond, *Chem. Commun.*, 2020, **56**, 6628–6631.
- 15 B. R. Schrage, V. N. Nemykin and C. J. Ziegler, Subbiliazine: A Contracted Phthalocyanine Analog, *Org. Lett.*, 2021, **23**, 1076–1080.
- 16 B. R. Schrage, V. N. Nemykin and C. J. Ziegler, BOSHPY Fluorophores: BODIPY Analogues with Single Atom Controlled Aggregation, *Org. Lett.*, 2021, **23**, 5246–5250.
- 17 D. Attanasio, I. Collamati and E. Cervone, *Inorg. Chem.*, 1983, **22**, 3281–3287.
- 18 I. Collamati, E. Cervone and R. Scoccia, Synthesis, Characterization, and Spectroscopic Studies of Some Metal Derivatives of Hemiporphyrine, *Inorg. Chim. Acta*, 1985, **98**, 11–17.
- 19 S. M. Huber, G. Mata, A. Linden and N. W. Luedtke, Synthesis and Structure of a Hydrogenated Zinc Hemiporphyrine, *Chem. Commun.*, 2013, **49**, 4280–4282.
- 20 S. Sripathongnak, A. M. Pischera, M. P. Espe, W. S. Durfee and C. J. Ziegler, Synthesis and Characterization of Lithium Hemiporphyrines, *Inorg. Chem.*, 2009, **48**, 1293–1300.
- 21 Y. Tanaka, T. Murayama, A. Muranaka, E. Imai and M. Uchiyama, Ring-Opened Hemiporphyrines: Helical Molecules Exhibiting Circularly Polarized Luminescence, *Chem. – Eur. J.*, 2020, **26**, 1768–1771.
- 22 Y. Tanaka, X. Ouyang, T. Murayama, A. Muranaka and M. Uchiyama, Formation of a Dinuclear Zinc Complex with Open-Ring Hemiporphyrine, *J. Porphyrins Phthalocyanines*, 2023, **27**, 184–189.
- 23 J. F. Bonfiglio, R. Bonnett, M. B. Hursthouse and K. M. A. Malik, Crystal Structure of the Nickel Complex of 2,3,7,8,12,13,17,18-Octaethyl-1,19(21H,24H)-Bilindione (Octaethylbilatriene-abc), *J. Chem. Soc., Chem. Commun.*, 1977, 83–84.
- 24 A. L. Bach, M. Mazzanti, B. C. Noll and M. M. Olmstead, Coordination Patterns for Biliverdin-Type Ligands. Helical and Linked Helical Units in Four-Coordinate Cobalt and Five-Coordinate Manganese(III) Complexes of Octaethylbilindione, *J. Am. Chem. Soc.*, 1994, **116**, 9114–9122.
- 25 T. Mizutani, S. Yagi, T. Morinaga, T. Nomura, T. Takagishi, S. Kitagawa and H. Ogoshi, Helical Chirality Induction by Point Chirality at Helix Terminal, *J. Am. Chem. Soc.*, 1999, **121**, 754–759.
- 26 T. Mizutani, N. Sakai, S. Yagi, T. Takagishi, S. Kitagawa and H. Ogoshi, Allosteric Chirality Amplification in Zinc Bilindione Dimer, *J. Am. Chem. Soc.*, 2000, **122**, 748–749.
- 27 S. Yagi, T. Morinaga, T. Nomura, T. Takagishi, T. Mizutani, S. Kitagawa and H. Ogoshi, Solvent Effect on Helicity Induction of Zinc Bilindione Bearing a Chiral Auxiliary at the Helix Terminal, *J. Org. Chem.*, 2001, **66**, 3848–3853.

