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Chelation-Enhanced Circular Dichroism of Tripodal Bisporphyrin Ligands

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Porphyrins are superb chromophores that offer well-defined metal binding sites rich with reaction and molecular recognition chemistry.[1] The photochemical behavior of porphyrins has played an important role in studies of artificial photosynthesis, photoreduction, photodynamic therapy, sensors, optical materials, and much more.[1,2] Circular dichroism (CD) has become a versatile tool for configurational assignment and the structural evaluation of chiral porphyrins and phthalocyanines.[3] In particular, exciton coupled circular dichroism (ECCD) has become the spectral method of choice for configurational assignment of chiral substrates containing dichroic chromophores due to its non-empirical theoretical foundation.[4] We have utilized this method and demonstrated such an approach with quinoline-derivatized chiral amino acids, primary amines, and alcohols.[5−7] Additionally, we have used ECCD to characterize redox-responsive coordination complexes of interest as optical materials.[6,7] Here we report a chiral tripodal ligand readily prepared from primary amines that contains two monosubstituted tetraphenylporphyrin (TPP) moieties and show that chelation of Cu(II) results in strong ECCD spectra with visible wavelength light.

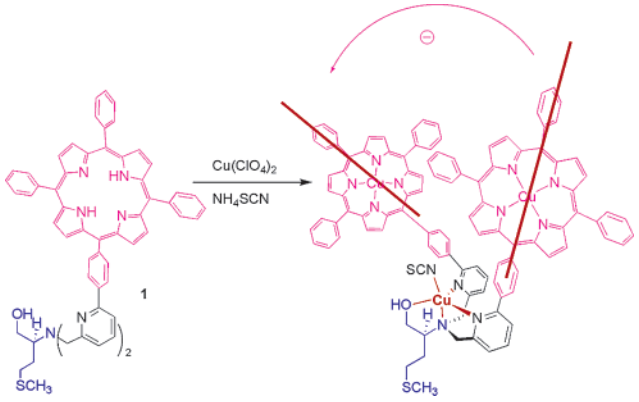
Scheme 1 shows the target ligand designed to retain the N,N,N,O coordination environment of previously characterized tripodal ligands[8] but incorporating TPP as chromophores. The ligand is conformationally mobile and adopts many conformations in solution. Complexation with Cu(II) causes the ligand to wrap around the metal, fixing the geometry of the chromophores in a preponderant conformation to position the porphyrins such that the strong Soret electronic transitions couple, giving ECCD.[9] In this case the target compound is derived from methioninol, for which analogous quinoline derivatives showed strong ECCD spectra.[8]

The synthetic approach involved the preparation of a mesylate derivative of a tetraphenylporphyrin, used to alkylate *S*-methioninol. Porphyrin **2** (4−5%) was obtained by reacting 4-boropinacolatobenzaldehyde, benzaldehyde, pyrrole, tetraphenylphosphonium chloride, and boron trifluoride-diethyl etherate, followed by the addition of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ).[10,11] Suzuki coupling of **2** with 6-bromo-2-formylpyridine (60−81%)[12] followed by reduction with sodium borohydride (53−70%)[13] and reaction with mesyl chloride gave **3** (80%).[14] Alkylation of *S*-methioninol under S_N2 conditions provided the target **1** (26%).[15]

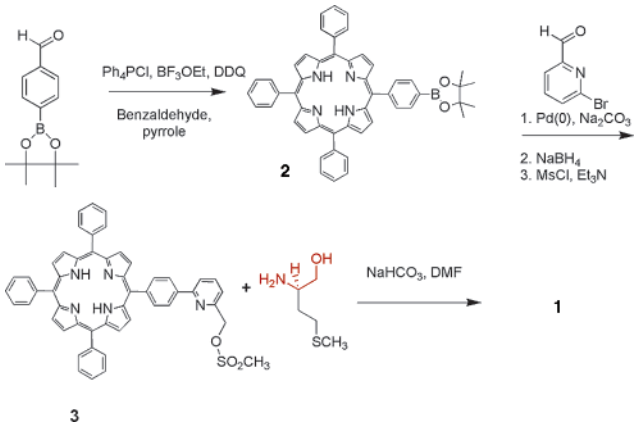
Figure 1 shows absorbance and CD spectra of **1** and its complex formed with excess Cu(II). The free ligand shows an absorbance in the Soret region very similar to that of TPP (λ_{max} 418, ϵ 500,000 M^{-1} cm^{-1} in CH_2Cl_2) with λ_{max} at 417 nm. No CD signal appears for the ligand in absence of metal. Complexes were formed by adding a solution of metal salt and NH_4SCN in methanol to a dichloromethane (DCM) solution of ligand such that the final methanol concentration was <1%.

As shown in Figure 1 (bottom), addition of 3 equiv of $Cu(ClO_4)_2$ in the presence of NH_4NCS resulted in a single absorbance maximum at 415 nm (purple line), which matches that reported for CuTPP (414 nm). In Figure 1 (top), a typical ECCD spectrum appears, with apparent splitting of 9 nm between 411 and 420 nm, as well as a metalloporphyrin characteristic peak at 538 nm (Supporting Information (SI), Figure S-1). The ECCD spectra

Scheme 1



Scheme 2



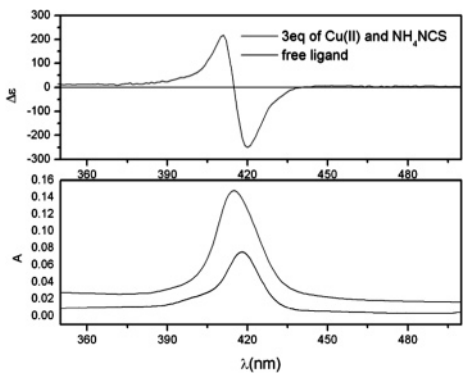


Figure 1. ECCD and UV/vis spectra of **1** with addition of $3Cu(ClO_4)_2$ + $3NH_4NCS$ (purple) in methylene chloride and <1% MeOH.

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suggest free librational motion about the porphyrin−phenyl bond involved in the linkage to the tripodal ligand site.[16] The CD amplitude is very strong, consistent with the strong electronic absorbance of the porphyrin moieties and with favorable geometry giving rise to strong coupling. The amplitude is on scale with other reported bisporphyrin systems,[17,18] but strong even compared to these. A blue-shift in the absorbance and the bisignate shape of the CD spectra indicate binding of metals at both porphyrin sites as well as the tripodal ligand site. Addition of Co(II), Ni(II), or even Ca(II) gave much weaker ECCD spectra, probably due to less optimal orientation of the porphyrin moieties. Similar weak ECCD spectra were observed with such complexes that are probably six-coordinate and therefore lack the strong twist associated with five-coordinate complexes.[19] Preliminary experiments with addition of one equivalent of Cu(II) indicated that metalation of the tripod and porphyrin sites was competitive and complex, so that it was not possible to metalate only the tripod site.

The CD spectrum of the metalated complex is consistent with the structure shown in Scheme 1 and in good agreement with data previously obtained with bisquinoline chiral ligands.[6] Crystallographic data for analogous amino alcohol compounds has established the N,N,N,O-chelation mode of the tripod binding site.[9] The negative couplet in the CD spectrum indicates a spatial orientation of the net transition dipole from the Soret bands in the porphyrins with a counterclockwise twist, corresponding to the *S* configuration of the chiral center.[17] These data suggest that configurational assignment of chiral amino alcohols and amino acids containing tetraphenylporphyrin through metal-assisted chelation is possible by ECCD. Our earlier extension of this configurational assignment protocol to primary amines should also benefit from this chromophore.[5] Thus, the porphyrin-derivatized chiral metal complexes serve as promising reporters of stereochemistry at the carbon adjacent to a primary amine. This is particularly attractive for chiral amines that contain chromophores that absorb in the UV region. These chromophores would not overlap with the porphyrin transitions, and therefore a clear spectroscopic window for stereochemical analysis is provided. If the mesyl porphyrin **3** were commercially available, the preparation of porphyrin-containing ligands could be obtained via simple one-step synthesis in respectable yields using <1 mg of chiral substrate.

The responsiveness of the complex to redox reactions was examined. Reduction of the fully metalated compound with ascorbic acid results in little change in the UV−vis spectrum but complete loss of CD signal. Addition of Cu(I)PF_6 provides a similar lack of CD signal, but exposure to air results in a spectrum similar to ligand that is fully metalated with Cu(II) (SI, Figure S-2). This differs from the previously described methioninol derivative, in which inversion of the CD spectra were observed. Several attempts failed to establish conclusively the structure of the Cu(I) complex; the Cu(I) binds weakly or induces a geometry that does not provide structural definition necessary to observe ECCD. Thus, the chiroptical properties of the compound are strongly dependent on metal ion association and oxidation state, similar to previously published on/off chiroptical switches.[20]

It is interesting to draw an analogy between the metal dependence of the CD spectra and the well-known "chelation-enhanced fluorescence" (CHEF).[21] In CHEF, metal association results in strong enhancement of spectroscopic signal. In chelation-enhanced CD, the strong enhancement is due to geometrical changes when the spectroscopic mechanism is ECCD.

This approach provides excellent CD spectral characteristics with visible light. Further work is underway to engineer improved metal binding at the tripod site, which will allow better addressing of metals to a particular site.

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Supporting Information Available: Experimental procedures. This material is available free of charge via the Internet at http://pubs.acs.org.

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