

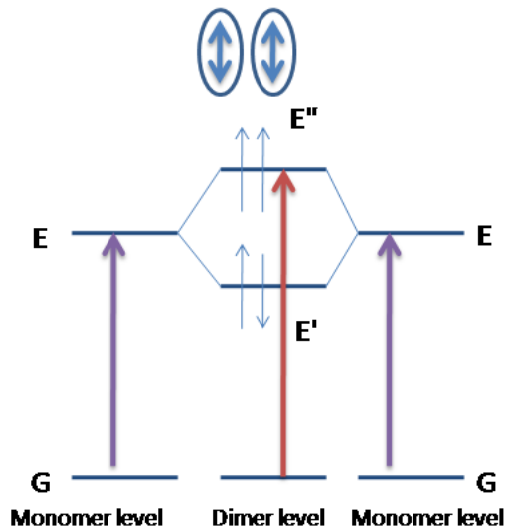
Probing Molecular Chirality Using Metallo-Bisporphyrin Hosts

Supramolecular chirogenesis is one of the most important interdisciplinary field to be looked into, because of its occurrences in many natural (DNA double helix, heme proteins, secondary α -helix structure of proteins etc.) and artificial systems. Although, chiroptical spectroscopy such as Circular Dichroism (CD) is inherently sensitive to chirality, it has not enjoyed tremendous use as a method for stereochemical determinations, mainly because the results of CD analysis are empirical. Exciton Coupled Circular Dichroism (ECCD) is a nonempirical spectroscopic method that is based on detecting the through-space exciton interaction between helically orientated independently conjugated chromophores. The relative orientation of the two chromophores in space results in a predicted sign of the couplet; *i.e.*, a clockwise orientation of two interacting chromophores yields a positive couplet and vice versa. Therefore, the challenge lies in orienting two or more chromophoric receptor groups in a chiral fashion as a direct result of the binding of a chiral compound and extrapolating the chirality of the bound compound from the ECCD spectra. Since the observed sign of the couplet is a direct consequence of the relative position of the chromophores, the assignment of chirality is nonempirical.

Porphyrimoids have been shown to be well suited for studying the processes involved in supramolecular chirality induction owing to their interesting photo-physical properties, versatile modification, great biological importance, and wide applicability. As non-covalent interactions are the key elements of supramolecular chirality, there are various external and internal factors controlling chirality induction. Our group is currently engaged investigating the various aspects of chirality induction and control for probing molecular chirality using Exciton Coupled Circular Dichroism (ECCD).

Kasha Exciton Coupling Theory

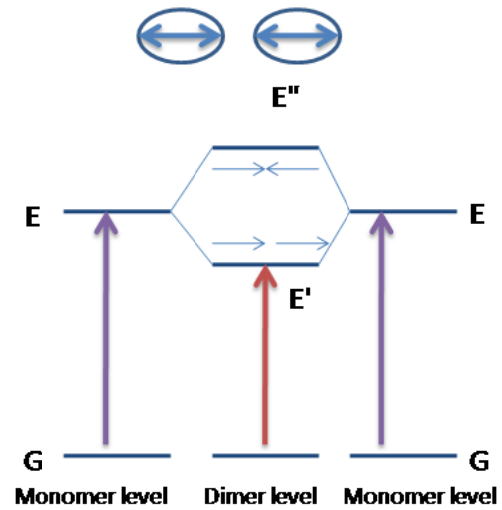
Parallel dipoles



Allowed transition to E'' level.

Blue shifting

In-line dipoles



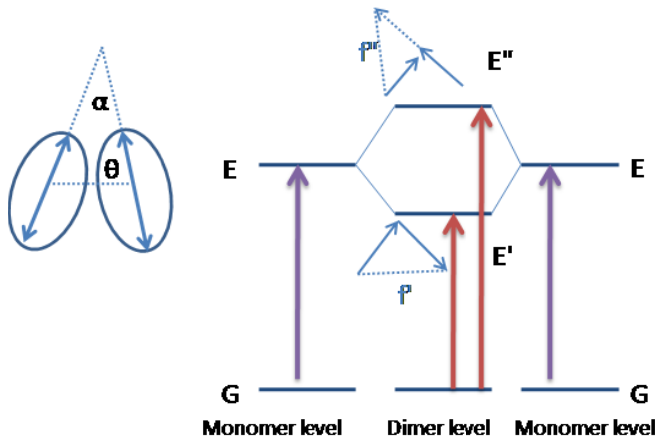
Allowed transition to E' level.

Red shifting

**Greater the transition dipole-moment, greater the splitting ($\Delta\epsilon$),
Greater the distance of two dipole-moments, lesser the splitting**

Kasha et al. Pure Appl. Chem. 1965, 11, 371.

Oblique Dipoles



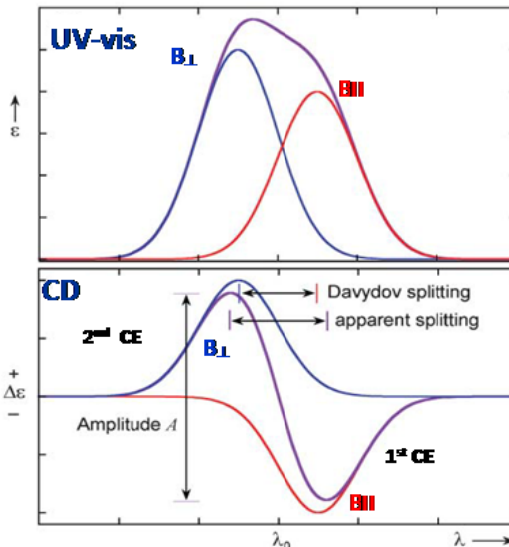
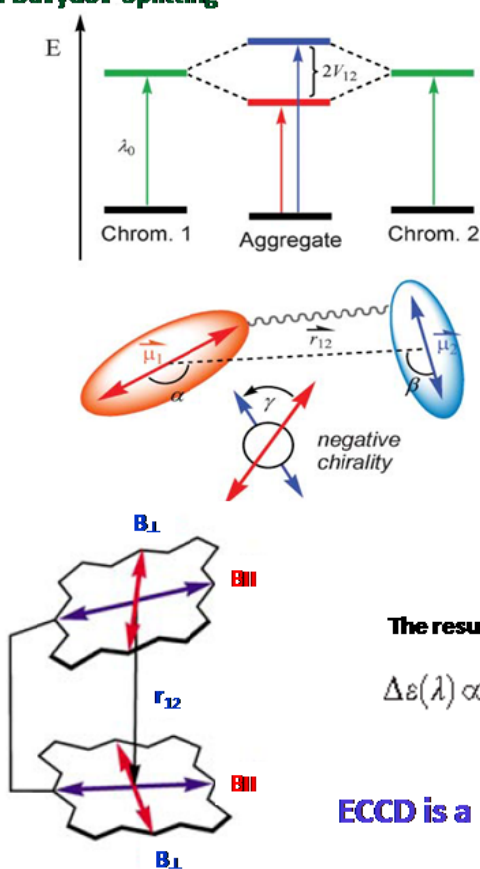
Both E' and E'' levels are allowed for transition

$$\Delta\epsilon = \frac{2IM^2}{r_{12}^3} (\cos\alpha + 3\cos^2\theta)$$

- **In-phase dipole arrangement**
lower the energy
- **Out-of-phase arrangement**
Increase the energy

Exciton Coupled Circular Dichroism (ECCD)

2V₁₂: Davydov Splitting

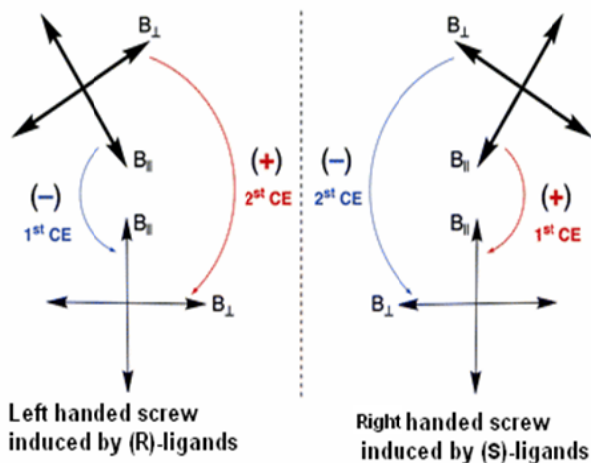


The resulting CD couplet is determined by

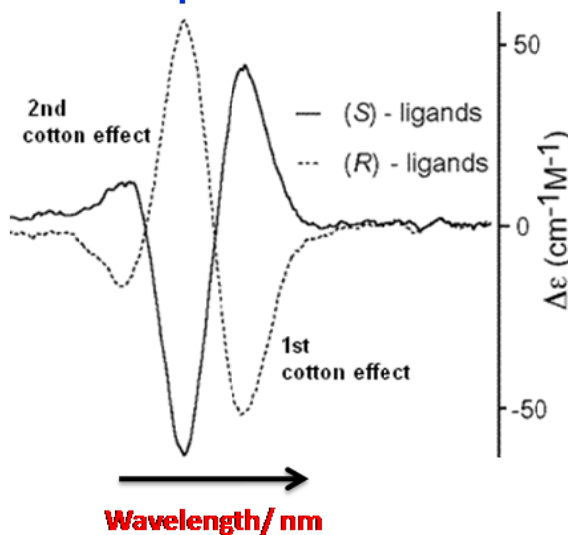
$$\Delta\varepsilon(\lambda) \propto \pm \Gamma(\lambda, \lambda_0) V_{12} \vec{r}_{12} \cdot \vec{\mu}_1 \times \vec{\mu}_2 \propto \pm \Gamma(\lambda, \lambda_0) \frac{\mu_1^2 \mu_2^2}{r_{12}^2} \Omega(\alpha, \beta, \gamma)$$

ECCD is a non-empirical spectroscopic method.

Orientation of Soret Band Transitions in Chiral Complexes

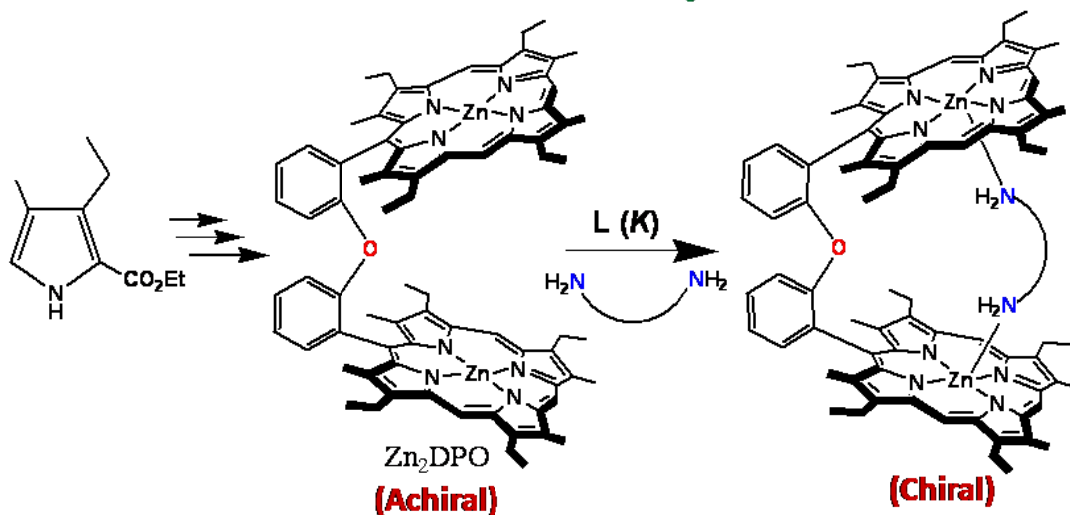


CD Spectra

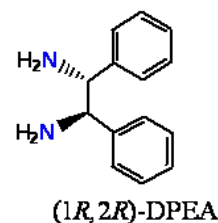
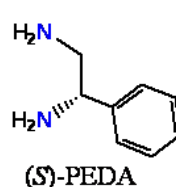
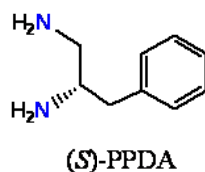
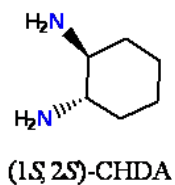
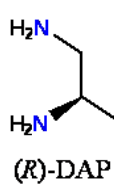


CD spectra for complex with (R)- and (S)-ligands.

Induction and Rationalization of Chirality

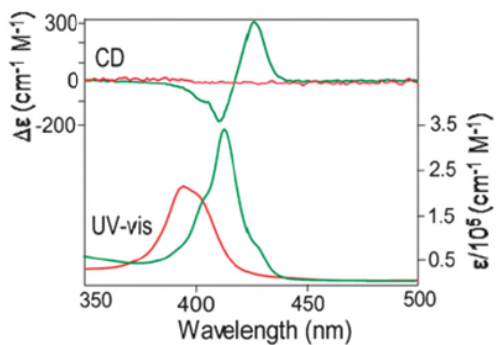
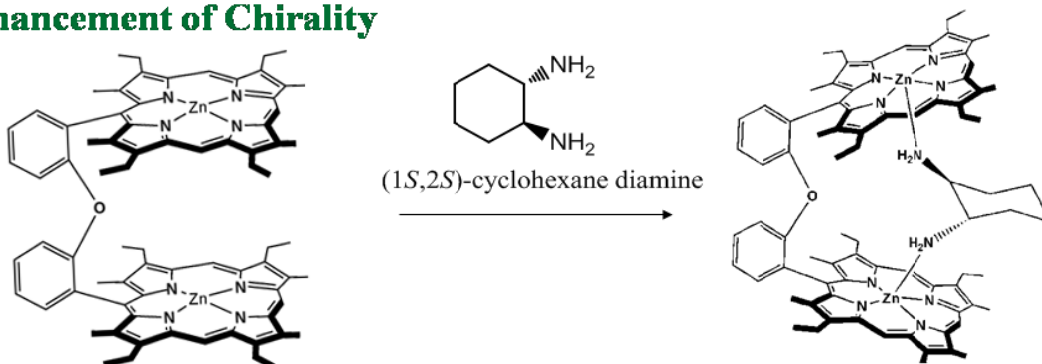


Chiral diamine ligand (L) used:



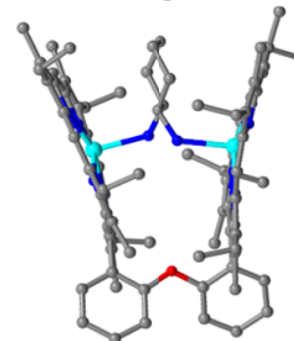
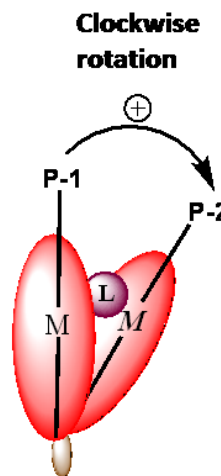
Inorg. Chem. **2014**, *53*, 49–62.

Enhancement of Chirality



$$A_{\text{obs}} = +515 \text{ cm}^{-1} \text{ M}^{-1}$$

❖ **Intense CD signal**

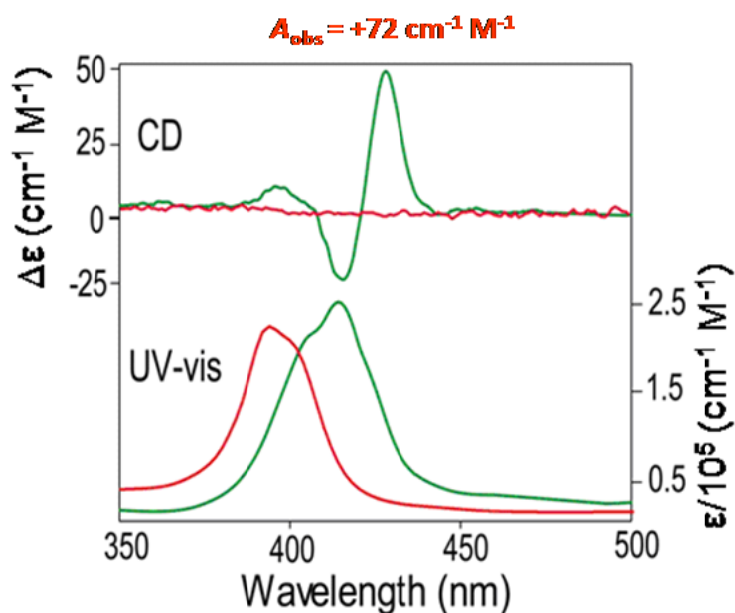
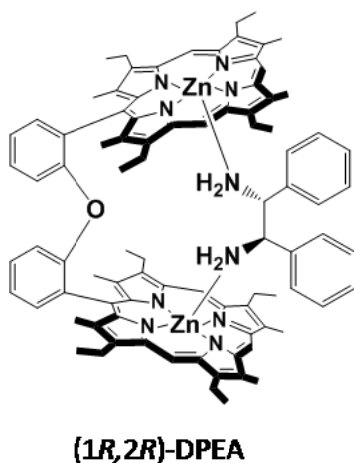


Space group: **P2₁**

Chiral Space Group

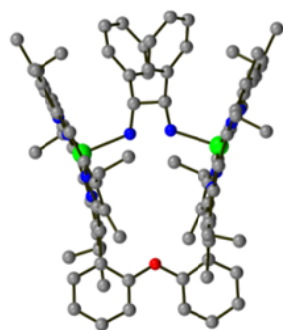
Twist angle: +30.8(5)°

Reduction of Chiral Intensity



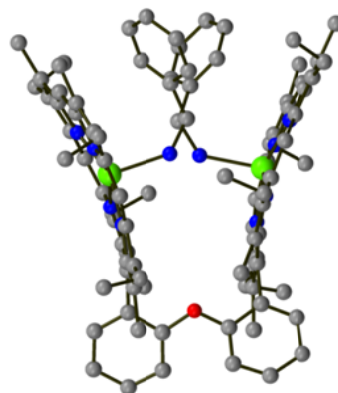
- ❖ Low CD amplitude
- ❖ Positive CD signal for (*R*)-ligand is not 'expected'

Reduction of Chiral Intensity



Space Group: *C*2 (chiral)

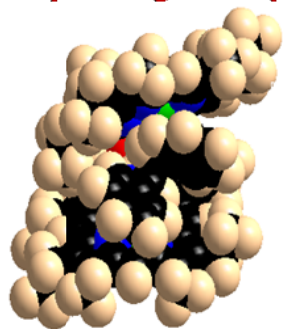
Twist angle: $+34.5(7)^\circ$



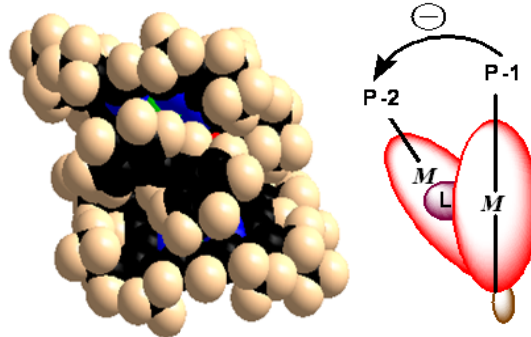
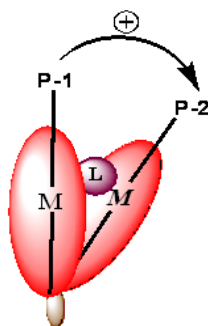
Twist angle: $-33.1(7)^\circ$



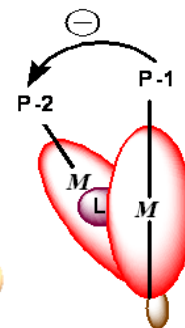
Corey-Pauling-Koltun (CPK) Molecular Model



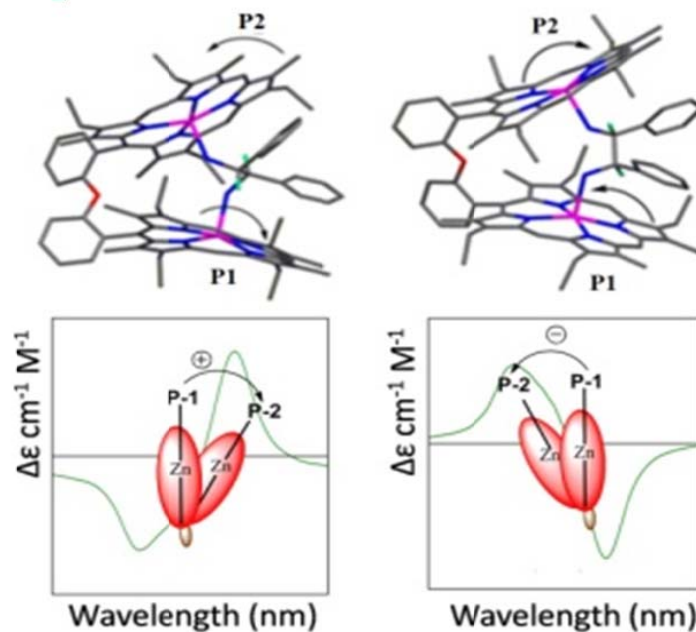
Right-handed tweezer



Left-handed tweezer

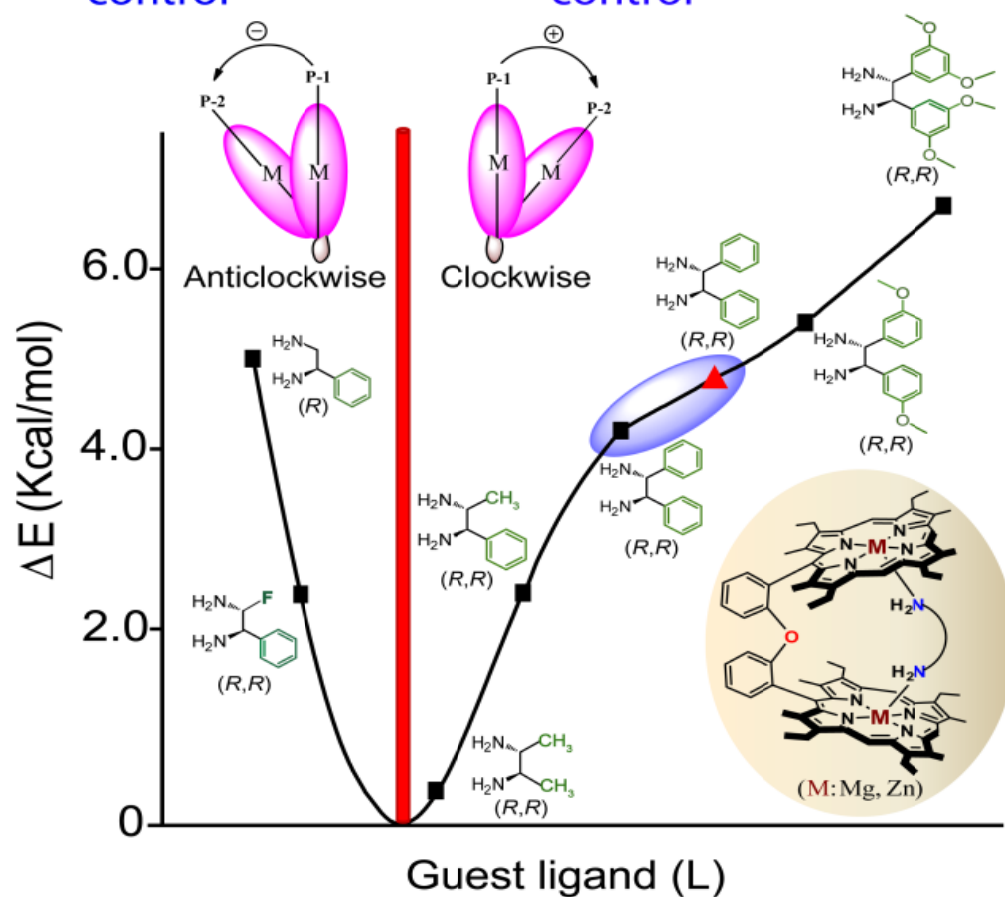


Binding Mechanism



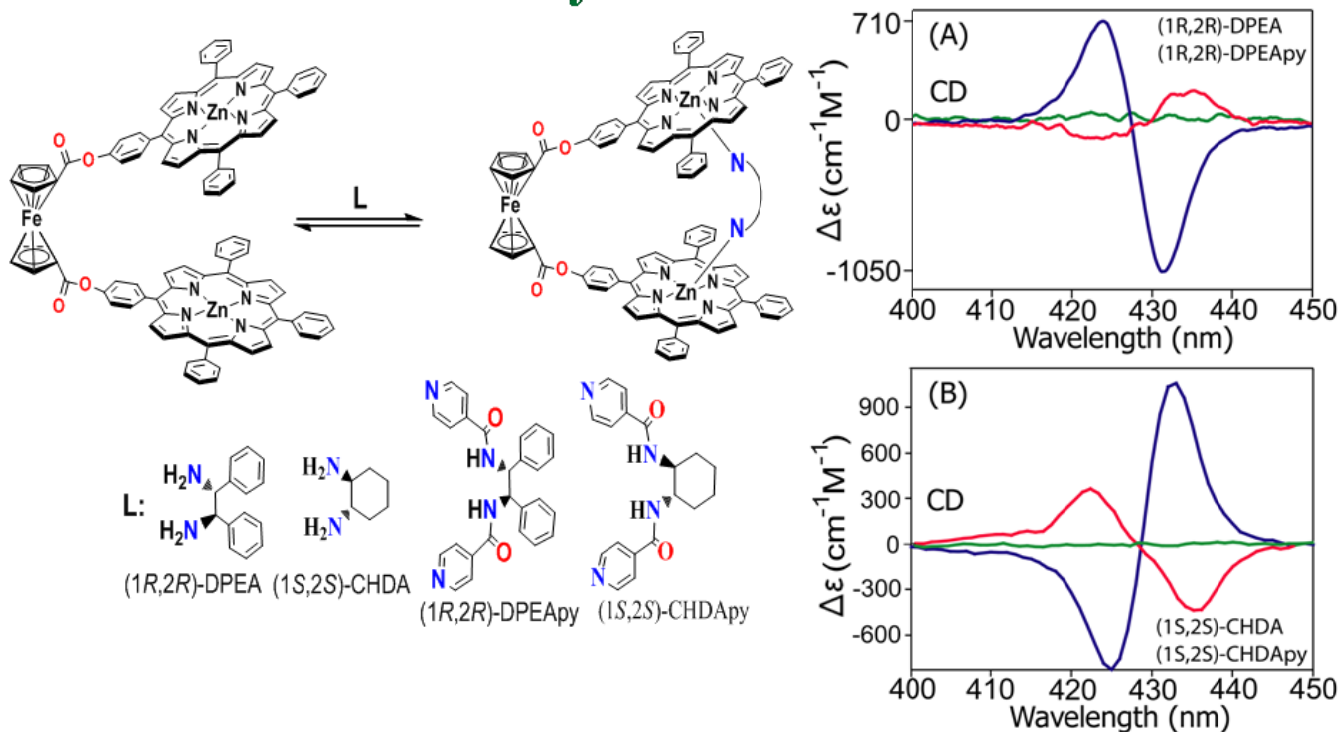
Inorg. Chem. **2014**, *53*, 49-62.

Chirality control \longleftrightarrow Steric control



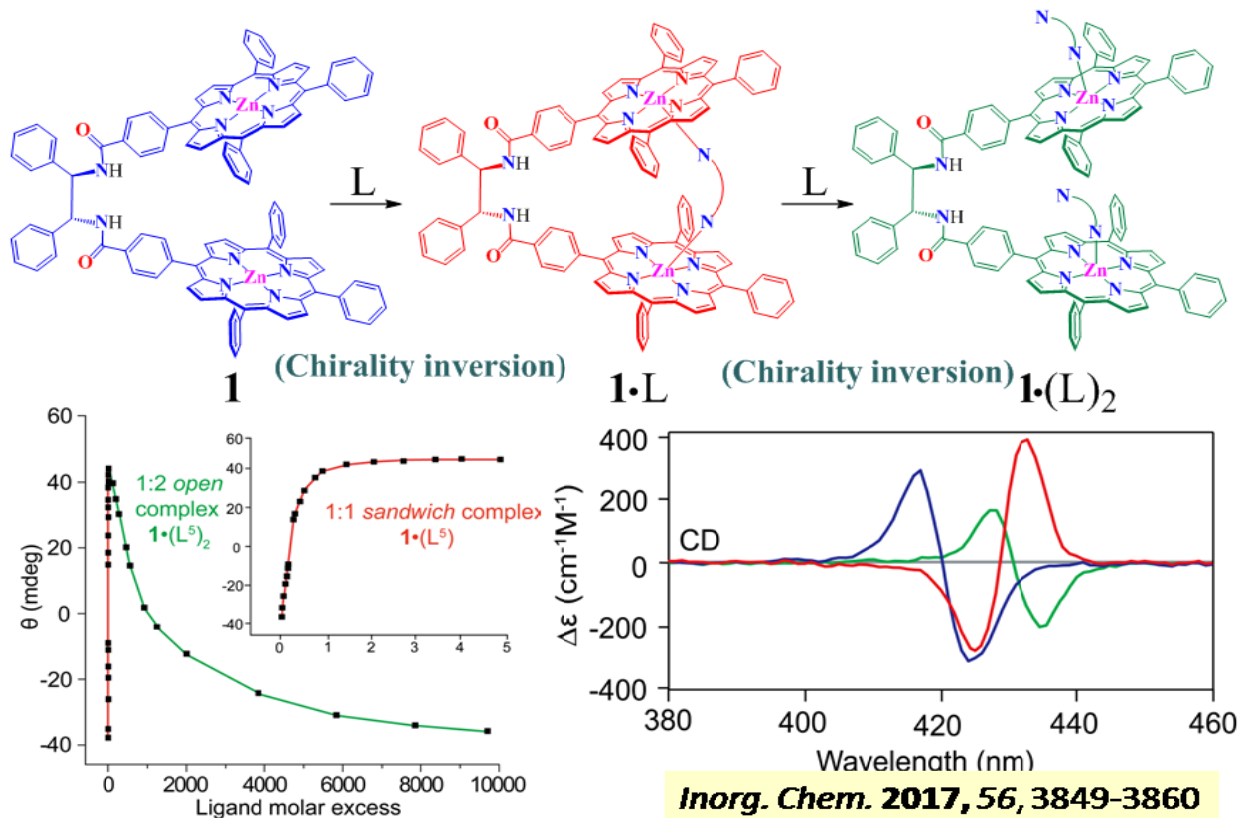
Inorg. Chem. **2016**, *55*, 13014-13026.

Enhancement of Chirality



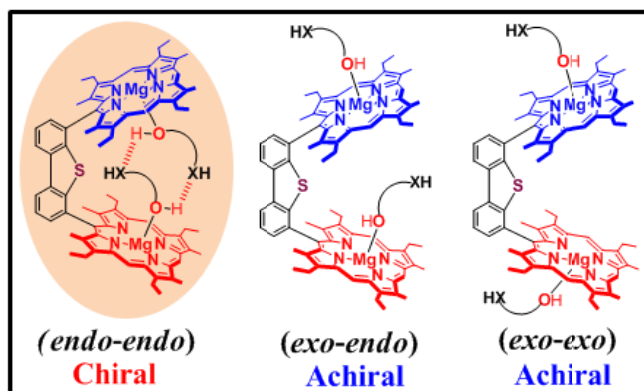
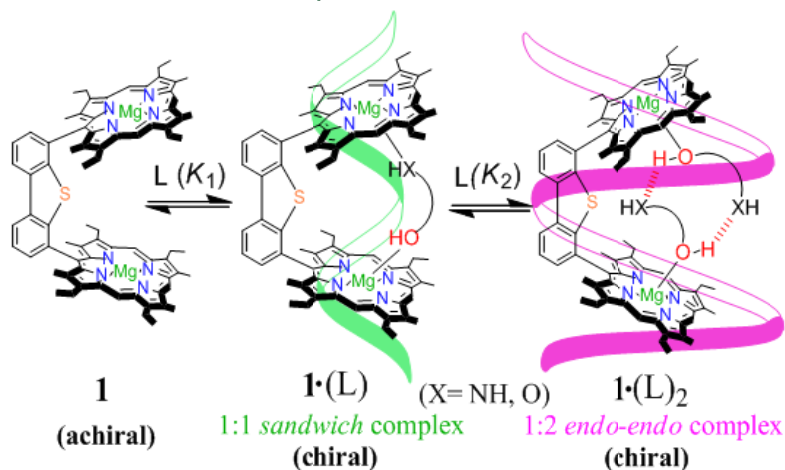
Inorg. Chem. **2014**, *53*, 2381–2395

Two-Step Inversion of Interporphyrin Helicity

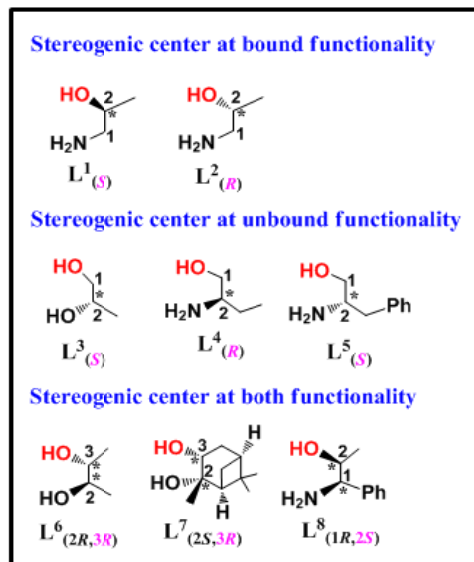


Inorg. Chem. **2017**, *56*, 3849–3860

Direct Determination of the Absolute Configuration of 1,2-Diols and Amino Alcohols

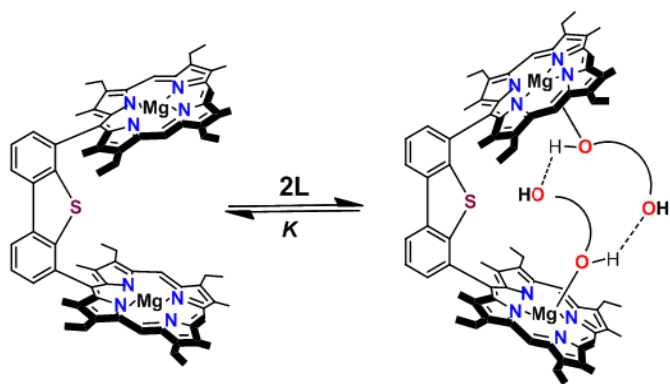


Chiral ligands used:

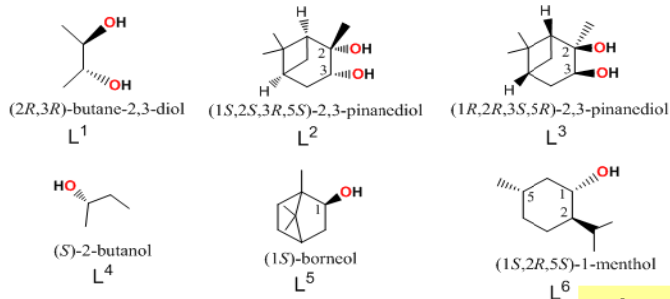


J. Org. Chem. **2016**, *81*, 5440
Chem. Commun. **2014**, *50*, 14037

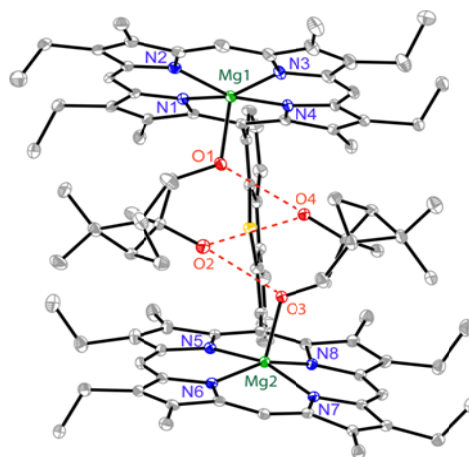
Transfer and Control of Molecular Chirality



Chiral substrate (L) used

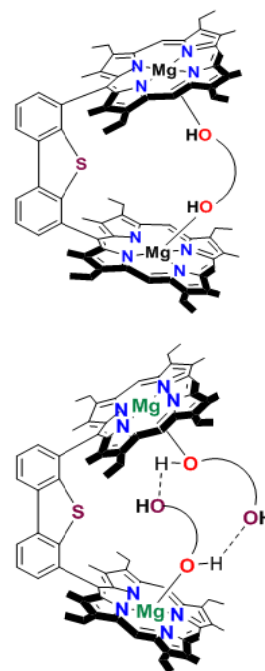
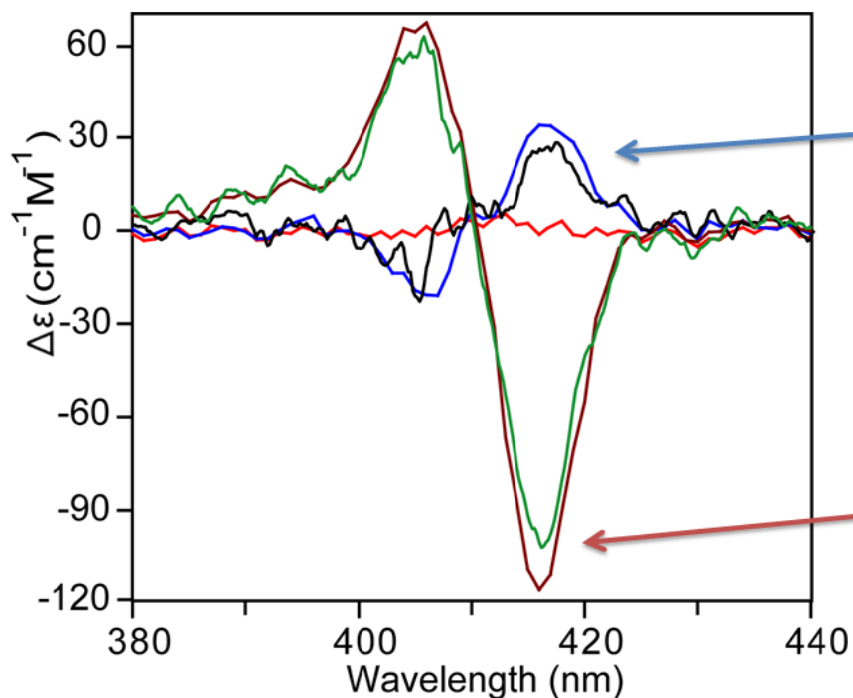


X-ray Crystal Structure



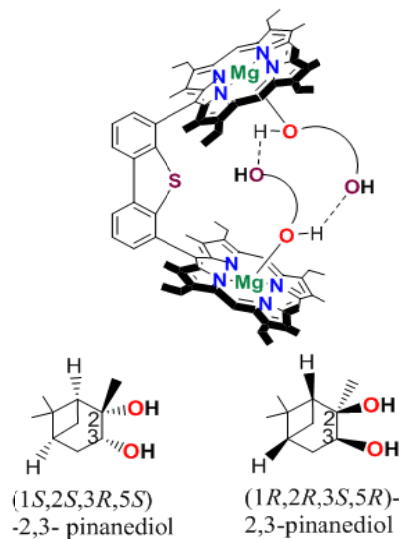
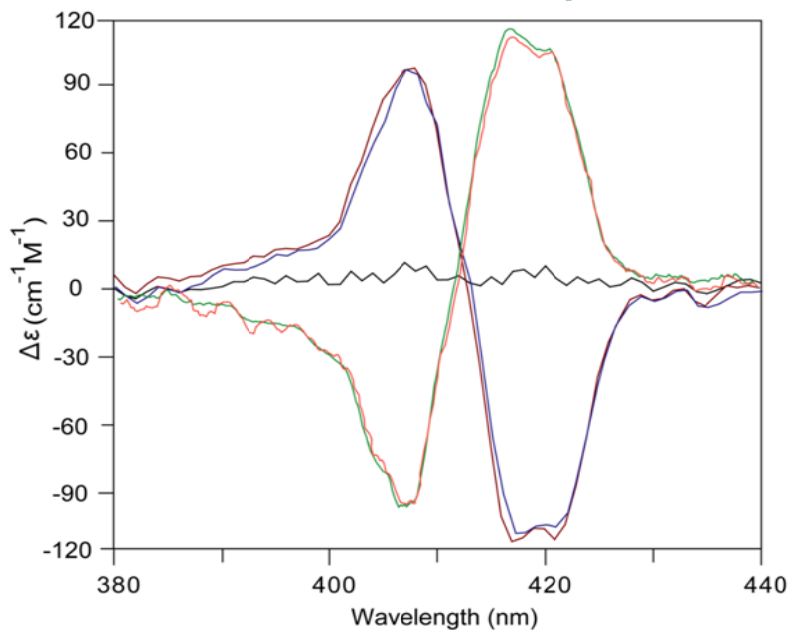
Chem. Commun. **2014**, *50*, 14037 - 14040

Observed and Calculated CD Spectra



Calculated CD spectra of **1** (red), **1•L¹** (blue), **1•(L¹)₂** (brown) and observed CD spectra of **1•L²** (black) and **1•(L²)₂** (green).

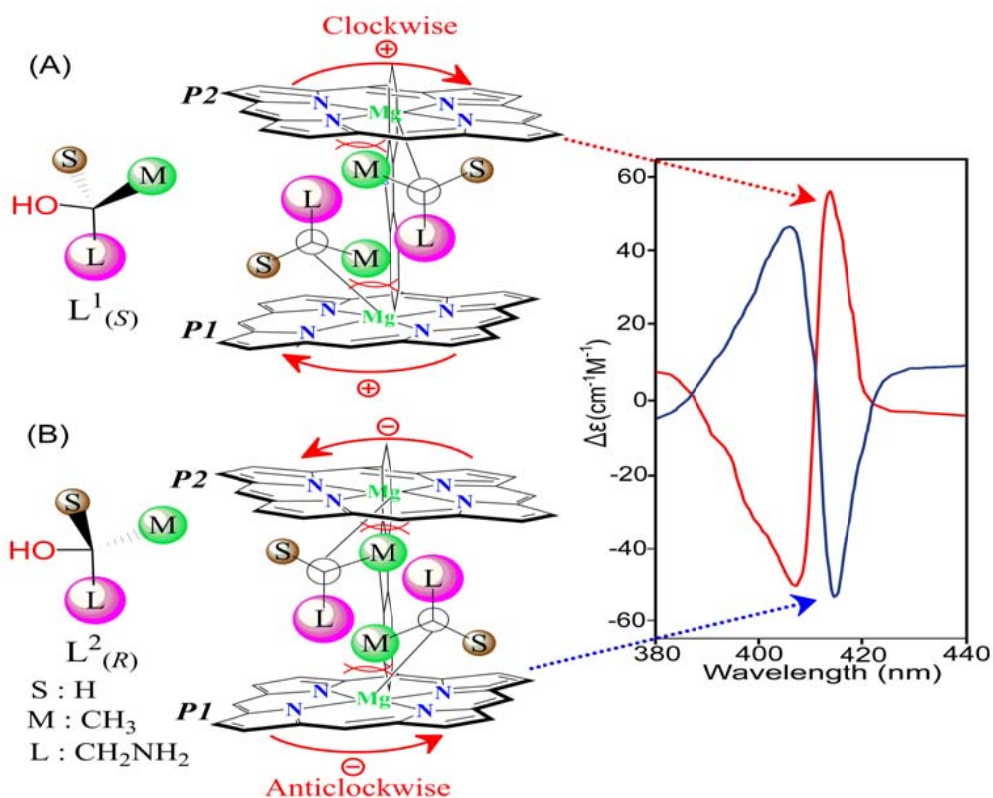
Observed and Calculated CD Spectra



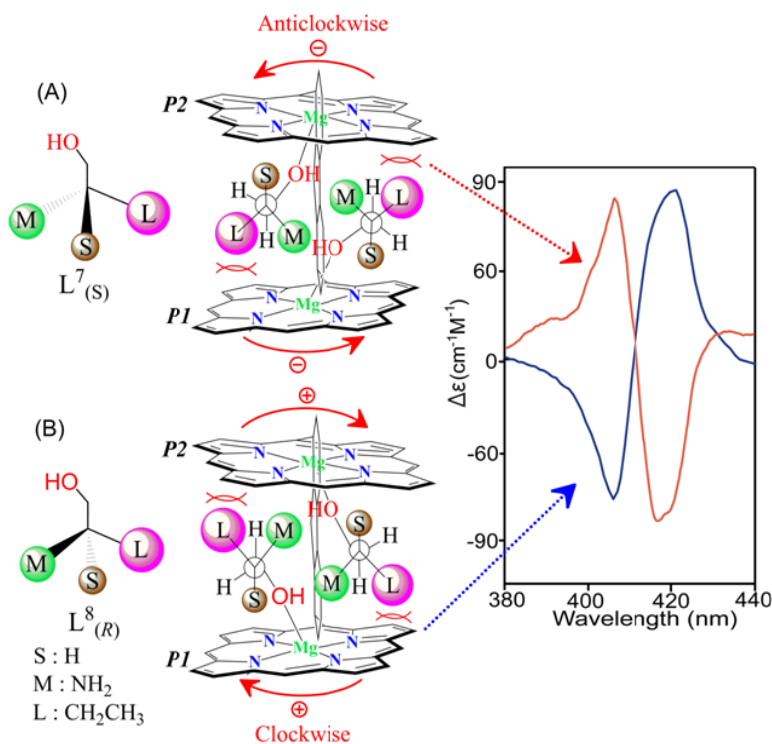
(enantiomer)

Calculated CD spectra of **1** (black), **1•(L²)₂** (brown) and **1•(L³)₂** (green) and observed CD spectra of **1•(L²)₂** (blue) and **1•(L³)₂** (red).

(S)-guest shows positive CD couplet while (R)-guest produces negative CD couplet in the 1:2 host-guest complex

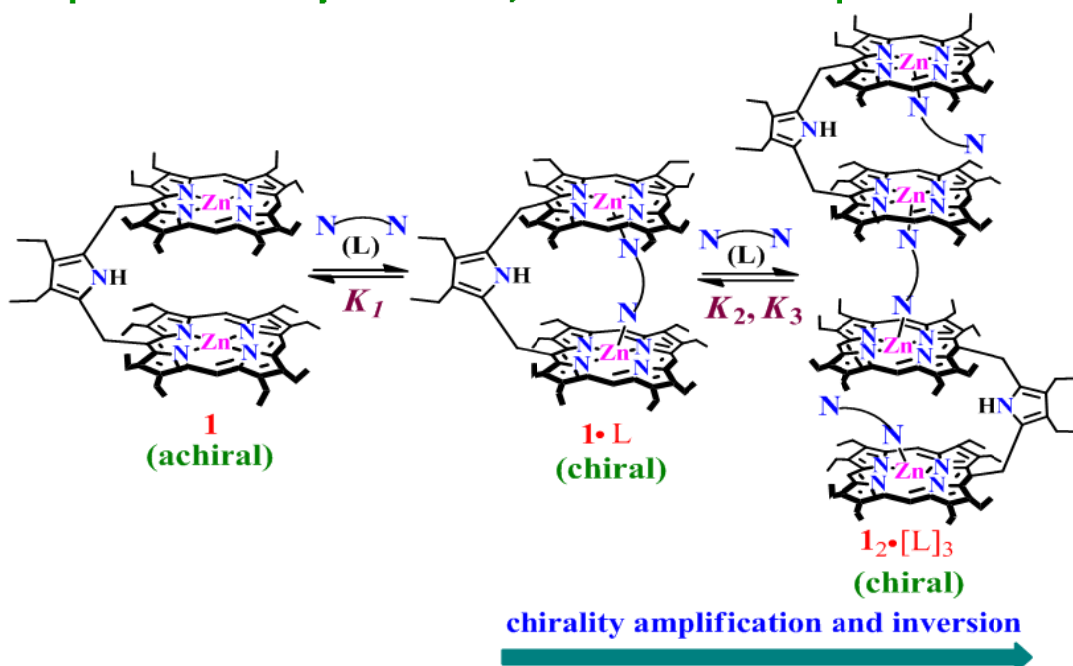


Working model for the 1:2 *endo-endo* complex correlating helicity of the interacting chromophore with the observed CD couplet of (A) $1\cdot(L^1(S))_2$ and (B) $1\cdot(L^2(R))_2$. Here stereogenic center is at the bound functionality. Peripheral substituent on the porphyrin ring has been omitted for clarity.

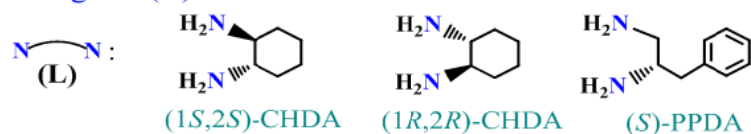


Working model for the 1:2 *endo-endo* complex correlating helicity of the interacting chromophore with the observed CD couplet of (A) $1\cdot(L^7(S))_2$ and (B) $1\cdot(L^8(R))_2$. Here stereogenic center is at the unbound functionality. Peripheral substituent on the porphyrin ring has been omitted for clarity.

Step-wise Chirality Induction, Inversion and Amplification

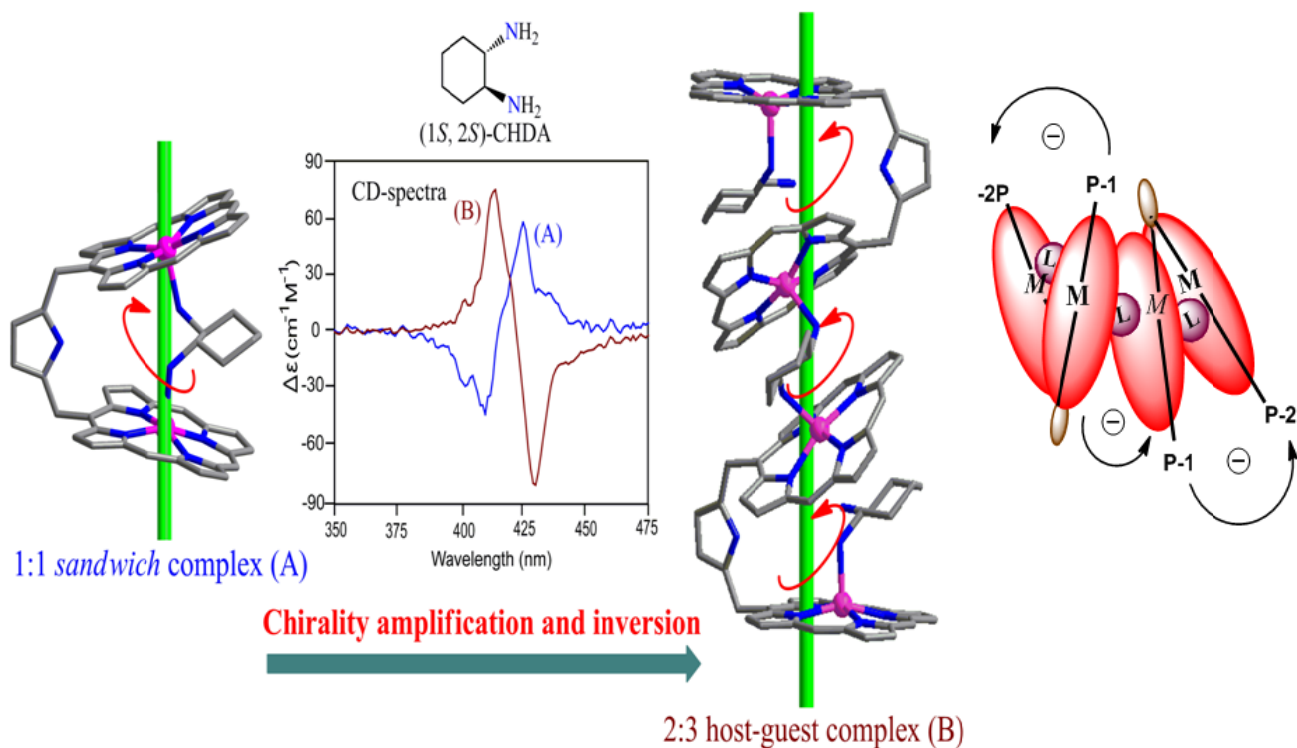


Chiral guest (L) used:

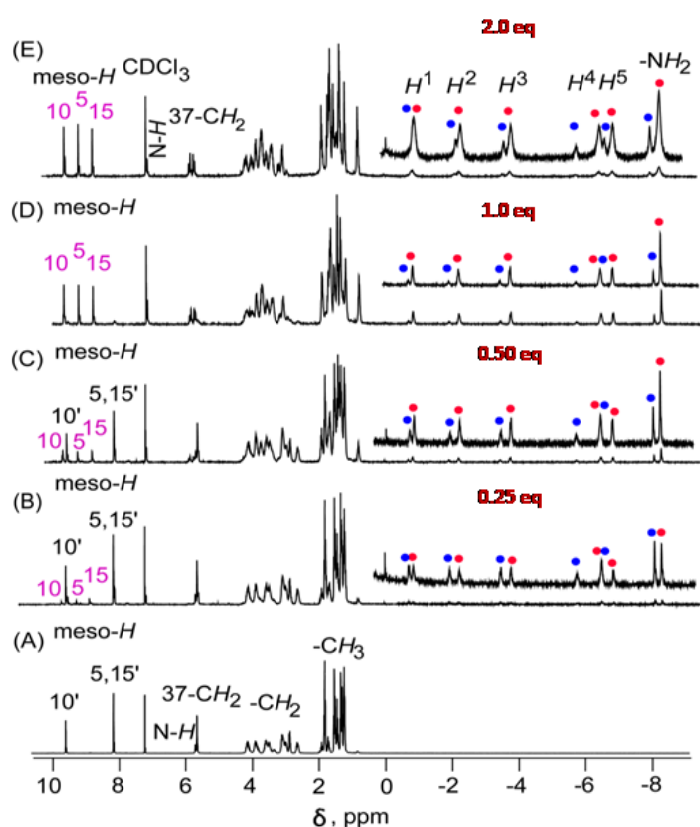


Chem. Commun. **2015**, *51*, 895-898.

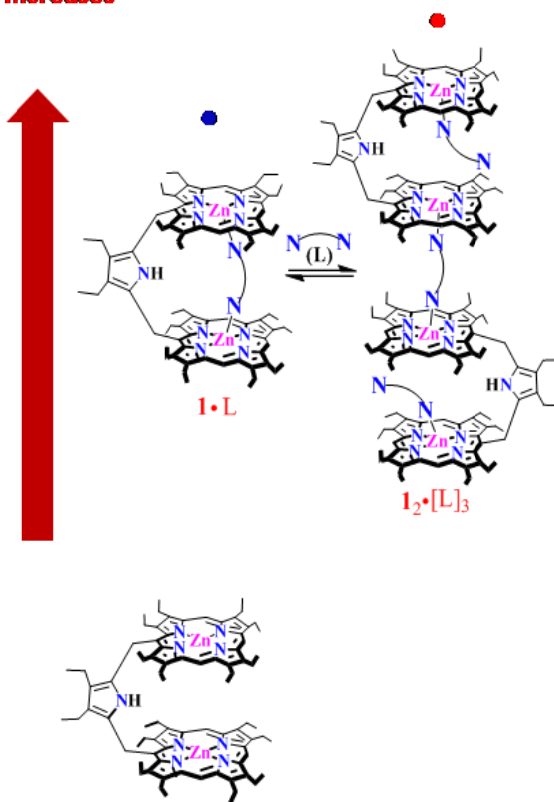
Step-wise Chirality Inversion and Amplification



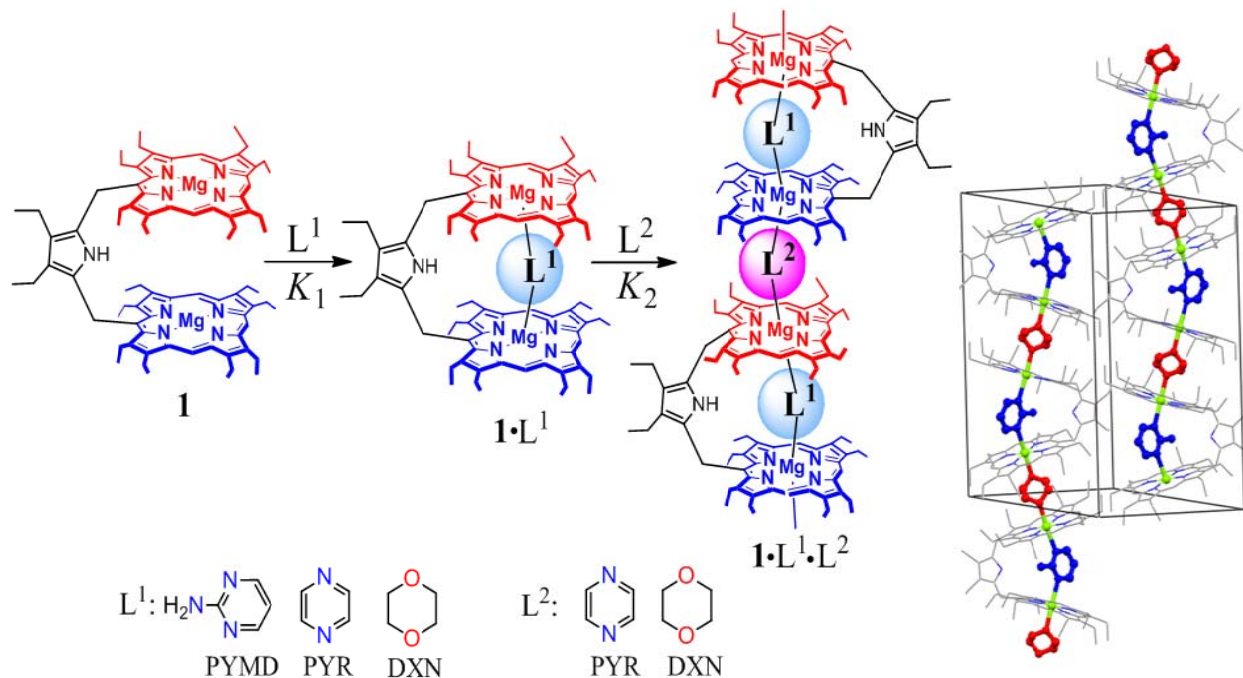
¹H NMR Titration



Oligomer formation
Increases



Metal-coordination-driven Mixed Ligand Binding



Representative Publications:

- 1. Complexation of Chiral Zinc-Porphyrin Tweezer with Achiral Diamines: Induction and Two-Step Inversion of Interporphyrin Helicity Monitored by ECD**
B. Saha, S. A. Iqbal, A. G. Petrovic, N. Berova* and S. P. Rath*
Inorg. Chem. **2017**, *56*, 3849-3860.
- 2. Induction and Rationalization of Supramolecular Chirality in the Tweezer–Diamine Complexes: Insights from Experimental and DFT Studies**
A. Dhamija, S. A. Iqbal and S. P. Rath*
Inorg. Chem. **2016**, *55*, 13014-13026.
- 3. A Nonempirical Approach for Direct Determination of the Absolute Configuration of 1,2-Diols and Amino Alcohols using Mg(II)bisporphyrin**
S. A. Iqbal, A. Dhamija, S. Brahma and S. P. Rath*
J. Org. Chem., **2016**, *81*, 5440–5449.
- 4. Step-wise Induction, Amplification and Inversion of Molecular Chirality Through the Coordination of Chiral Diamines with Zn(II)bisporphyrin**
S. A. Iqbal, S. Brahma and S. P. Rath*
Chem. Commun. **2015**, *51*, 895 - 898.
- 5. Metal-coordination-driven Mixed Ligand Binding in Supramolecular Bisporphyrin Tweezers**
Sk. A. Iqbal, A. Dhamija and S. P. Rath*
Chem. Commun. **2015**, *51*, 14107 - 14110.
- 6. Stoichiometry-controlled Supramolecular Chirality Induction in Magnesium (II) Porphyrin Dimer by Amino Alcohols: Mechanistic Insights and Effect of Ligand Bulkiness**
S. A. Iqbal, B. Saha and S. P. Rath*
J. Indian Chem. Soc. **2015**, *92*, 2001-2014. (Special issue dedicated to Prof. Animesh Chakravorty on the occasion of his 80th birthday)

7. **Transfer and Control of Molecular Chirality in the 1:2 Host-Guest Supramolecular Complex Consisting of Mg(II) bisporphyrin and Chiral Diols: Effect of H-bonding on Rationalization of Chirality**

Sk. A. Iqbal, S. Brahma and S. P. Rath*

Chem. Commun. **2014**, *50*, 14037 - 14040.

8. **Highly Enhanced Bisignate Circular Dichroism of Ferrocene-Bridged Zn(II) Bisporphyrin Tweezer with Extended Chiral Substrates due to Well-matched Host-Guest System**

S. Brahma, Sk. A. Iqbal, A. Dhamija and S. P. Rath*

Inorg. Chem. **2014**, *53*, 2381 - 2395.

9. **Synthesis, Structure, and Properties of a Series of Chiral Tweezer-Diamine Complexes Consisting of an Achiral Zinc(II) Bisporphyrin Host and Chiral Diamine Guest: Induction and Rationalization of Supramolecular Chirality**

S. Brahma, Sk. A. Iqbal and S. P. Rath*

Inorg. Chem. **2014**, *53*, 49 - 62.

10. **Induction of Supramolecular Chirality in Di-Zinc(II) Bisporphyrin via Tweezer Formation: Synthesis, Structure and Rationalization of Chirality**

S. Brahma, Sk. A. Iqbal, S. Dey and S. P. Rath*

Chem. Commun. **2012**, *48*, 4070 - 4072. (Invited article in a special thematic issue 'Porphyrins and Phthalocyanines')