

Direct Determination of Absolute Configuration of Monoalcohols by Bis(magnesium Porphyrin)

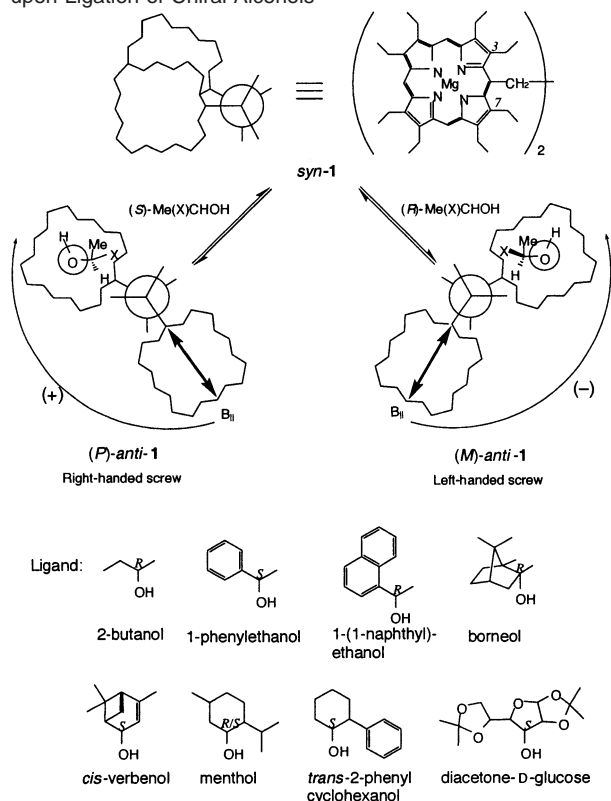
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Received April 30, 2002

Absolute configuration determination has been a challenge for the past century, but the search for better methods continues even more intensively. Recently, supramolecular chirality induction (supramolecular chirogenesis) has drawn much interest among several research groups yielding some breakthrough results.^{1–3} On the basis of the circular dichroism (CD) exciton chirality method,⁴ it is now possible to determine directly the absolute configuration of a variety of mono-^{5,6} and diamines^{1,7,8} by ligating them to the chirality sensing receptor molecules possessing chromophores with known electronic transitions.

Scheme 1. Mechanism of Chirality Induction in Bis(Mg Porphyrin) **1** upon Ligation of Chiral Alcohols^a



^a Only one inside-bound ligand is shown, and the other penta- or hexacoordinating ligands are omitted for clarity.

A prerequisite for the supramolecular chirogenesis is the sufficient binding affinity between the ligand and the receptor. Chiral alcohols, which constitute one of the major class of biologically active and natural compounds, are weakly ligated with all of the

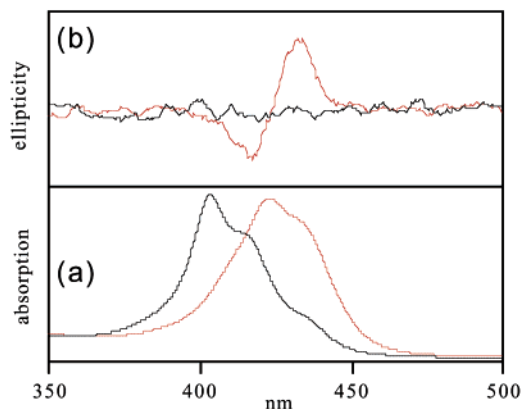


Figure 1. (a) UV-vis spectra of **1** in the absence (black) and presence (red) of (*S*)-(-)-1-phenylethanol in CH₂Cl₂ at 298 K. (b) CD spectra of **1** (black) and **1** in the presence of (*S*)-(-)-1-phenylethanol (red) in CH₂Cl₂ at 298 K.

chirality sensing receptors reported so far. The only reports about the direct determination of the absolute configuration of alcohols, without any chemical modifications, employ either very low temperatures² or require chiral alcohol as 50% cosolvent.⁹

Herein, we report the use of bis(Mg porphyrin) **1** (Scheme 1) for the direct determination of the absolute configuration of a variety of monoalcohols at millimolar concentrations and room temperature based on the CD exciton chirality method.⁴

Bis(porphyrin) **1** was obtained from its free base form by using the method developed by Lindsey et al.¹⁰ The UV-vis spectrum of **1** in dichloromethane shows one major peak with two shoulders at longer wavelengths in the B-band (Soret) region (Figure 1a). The major peak at 404 nm is assigned to the syn (face-to-face) conformer of **1**, as was the case with the syn form of the corresponding bis(Zn porphyrin) complex.¹¹ The shoulders at 416 and 435 nm are likely due to the ligand-induced partial syn-anti equilibrium.¹²

Addition of chiral alcohol into the CH₂Cl₂ solution containing **1** caused a large bathochromic shift of the Soret band, which is induced by the formation of alcohol-ligated anti-**1** absorbing at 423 and 432 nm (shoulders) (Figure 1a). This behavior is similar to the axial ligation-induced syn-anti conformational change reported for the corresponding bis(Zn porphyrin).¹¹ The CD spectrum is silent for achiral syn-**1**, whereas the bisignate CD signal at the Soret region arises upon axial ligation of the chiral alcohol, yielding anti conformation (Figure 1b). The sign of the induced Cotton effect is determined solely by the absolute configuration of the alcohol. A plausible mechanism for the generation of the CD couplet resembles that established for the bis(Zn porphyrin) sensor,^{2,5,6} where the right- or left-handed screw is created upon ligation of the (*S*)- or (*R*)-alcohol, respectively (Scheme 1). The right-handed screw formation

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Table 1. CD Spectral Data for Supramolecular Chirogenesis upon Complexation of Bis(Mg Porphyrin) **1** with Various Chiral Alcohols in Dichloromethane at 298 K^a

ligand	CD sign and peak position		total amplitude <i>A</i> ^b
	1st Cotton effect	2nd Cotton effect	
(<i>R</i>)-(-)-2-butanol	-(432 nm)	+(415 nm)	-20
(<i>S</i>)-(-)-1-phenylethanol	+(432 nm)	-(417 nm)	+31
(1 <i>S</i> ,2 <i>R</i>)-(-)-borneol	-(433 nm)	+(415 nm)	-27
(1 <i>S</i> ,2 <i>R</i> ,5 <i>S</i>)-(+)-menthol	+(429 nm)	-(405 nm)	+27
(1 <i>R</i> ,2 <i>S</i> ,5 <i>R</i>)-(-)-menthol	-(429 nm)	+(409 nm)	-27
(<i>R</i>)-(+)-1-(1-naphthyl)ethanol	-(432 nm)	+(407 nm)	-29
(1 <i>S</i> ,2 <i>R</i>)- <i>trans</i> -2-phenylcyclohexanol	+(437 nm)	-(408 nm)	+9
(1 <i>S</i> ,2 <i>S</i>)- <i>cis</i> -verbenol	+(431 nm)	-(405 nm)	+9
(3 <i>S</i>)-diacetone-D-glucose	+(432 nm)	-(401 nm)	+46

^a [**1**] = 3.1–3.9 × 10⁻⁶ M, [alcohol] = 3.0–6.0 × 10⁻³ M. ^b *A* = (Δε₁ - Δε₂) M⁻¹ cm⁻¹.

is the consequence of steric repulsion between the largest substituent (X) at the chiral center of the bound (*S*)-alcohol and the ethyl group at the 3-position of the neighboring porphyrin ring. This makes the corresponding coupled B electronic transitions optically active and gives the split CD signals.² Thus, all of the (*S*)-alcohols examined induce positive chirality. On the contrary, upon ligation of (*R*)-alcohols, the largest substituent X at the chiral center causes steric repulsion with the ethyl group at the 7-position of the neighboring porphyrin ring, leading to the left-handed screw and the negative chirality.¹³

Although the signs of the Cotton bands follow the rule found for the corresponding Zn complex, the total amplitudes of the observed CD signals do not appear to be correlated directly with the ligand bulkiness (Table 1). The amplitude of the CD signal should depend on the dihedral angles of the coupling electronic transitions present in the chiral anti screw conformation.⁶ Thus, with increasing size of the largest substituent X at the chiral center (from ethyl to phenyl and then to naphthyl), the dihedral angles between B dipoles are changed, inducing stronger Cotton effects as was the case with the corresponding Zn complex.^{6,14}

In the present cases, however, the magnitudes of the intensities of the Cotton effects are relatively low and show no systematic dependence on the ligand structure. Additionally, nonperfect UV-vis absorption maxima matching and less split B-band of Mg complex over Zn complex suggest that all allowed transitions contribute more equally in the Mg complex, resulting in very complicated CD spectra where only the lowest energy B_{||} transition, which determines the sign of the CD signal, can be effectively applied for the chirality sensor purpose. Also, Cotton effect insensitivity was observed when an extremely low concentration of chiral monoamine (10⁻⁶ M) was used as ligand, implying that the weaker binding of the alcohols (as pentacoordinating species) is not the major reason for the observed CD intensity changes which cannot be related directly to the ligand size.¹⁵ It is not clear at present whether the hexacoordinated anti species is responsible for this behavior. The possibility of ligand dependent left-hand-right-hand screw equilibrium (enantiomeric excess), as found for the M/P helicity ratio of various zinc bilinone systems,¹⁹ should not be ruled out either.

Table 1 also reveals that the second Cotton effect peak deviates over a wide range of wavelength of 401–417 nm, while the first

Cotton effect peak stays in a more constant wavelength region of 429–437 nm. Similar observations have been reported for the complexes of monomeric Mg porphyrin with chiral amino acids,²⁰ suggesting that the nature of the ligand plays a crucial role in positioning the Cotton effect peaks in Mg porphyrins.

Although the UV-vis spectral changes upon ligation follow the general behavior found in the corresponding Zn complex in the Soret region, a more close examination reveals some differences, such as a less pronounced bathochromic shift and the appearance only as a shoulder instead of the well-resolved split for the ligation-induced anti species.

Because practically no other chirality probe can sense absolute configuration of chiral alcohols of low concentrations at ambient temperature, the ability and potential of **1** as a chirality sensor are important and promising. Hence, we examined a variety of synthetic and natural monoalcohols, including α-substituted aliphatic and aromatic alkanols with one chiral center, as well as alicyclic alcohols with 2–5 chiral centers to give the consistent results. In the case of alcohols with multiple chiral centers, the absolute configuration of the carbon α to OH is always read out.

Acknowledgment. We thank Prof. T. Mizutani for valuable comments about this manuscript.

Supporting Information Available: Synthesis, UV-vis, FAB-MS, and ¹H NMR data of **1** (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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- Despite the considerable efforts, the absolutely pure ligand-free *syn*-bis-(octaethylporphyrin) could not be obtained. This is due to the fact that *syn*-**1** is extremely sensitive to even a trace quantity of ligand, causing partial *syn*-anti equilibrium.
- In the present case, the priority rules for absolute configuration assignment coincide with the substituent's bulkiness at the chiral center. However, if the substituent's bulkiness order differs from the priority rules, the signs of the CD signals are inverted.¹⁴
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JA0267270