Chiral recognition of amino acid esters by a novel oxalic amide-linked bisporphyrin

ARTICLE *in* DALTON TRANSACTIONS · MARCH 2013

Impact Factor: 4.2 · DOI: 10.1039/c3dt50380a · Source: PubMed

5 AUTHORS, INCLUDING:

Chuanjiang Hu
Soochow University (PRC)
60 PUBLICATIONS **777** CITATIONS

SEE PROFILE

Dalton Transactions

RSC Publishing

PAPER

Chiral recognition of amino acid esters by a novel oxalic amide-linked bisporphyrin†

Cite this: *Dalton Trans.*, 2013, **42**, 7651

Jiaxun Jiang,[a] Zhiqiang Feng,[a] Baozhen Liu,[a] Chuanjiang Hu*[a,b] and Yong Wang*[a]

Received 7th February 2013,
Accepted 6th March 2013

DOI: 10.1039/c3dt50380a

www.rsc.org/dalton

A novel oxalic amide-linked bisporphyrinate **1** has been designed and synthesized, which shows chiral recognition ability for amino acid ethyl esters. The structure of complex **1**·(D-Phe-OEt)(L-Phe-OEt) has been solved by X-ray crystallography. It reveals the following information: bisporphyrin unit adopts *anti*-configuration; compound **1** forms 1 : 2 complex with amino acid ethyl esters; one important hydrogen bond is formed between the coordinated nitrogen of amino acid ester and carbonyl oxygen in the amide group. The chiral recognition mechanism has been further investigated by UV-Vis spectra, ^{1}H NMR and DFT/TDDFT calculations.

Introduction

Porphyrins, especially bisporphyrins, have been intensively studied as chirality probes, sensors *etc.* in recent years.[1] Many different bisporphyrin systems have been developed by several groups. For example, Berova, Nakanishi and coworkers have designed a bisporphyrin linked by a pentanediol linker which can assign the absolute configuration of several chiral acyclic diamines or amino alcohols by the intense bisignate CD signals in the Soret band region.[2] Borovkov, Inoue and co-workers have developed a dimer of octaethylporphyrin linked through a 1,2-ethane bridge which is capable of binding N- or O-donors (amines, O-protected amino acids and alcohols) through ligand-to-metal coordination.[3] Canary's group has reported a chiral tripodal ligand that contains two monosubstituted tetraphenylporphyrin moieties and shown that chelation of Cu(II) results in strong CD spectra with visible wavelength light.[4] Borhan's group have developed a fluorinated porphyrin tweezer which can be used to determine absolute configuration for diols, amino alcohols, diamines and epoxy alcohols.[5] In these systems, it was found that the chirality of the guest was transferred to achiral porphyrin hosts, therefore leading to strong CD response in the Soret band region.

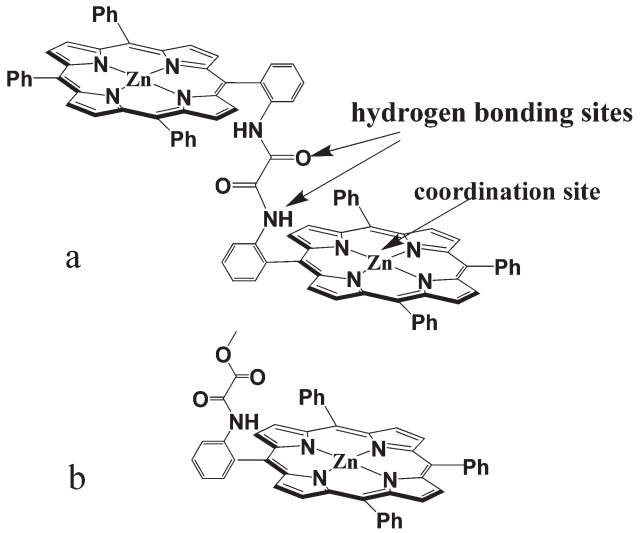
We have been working on porphyrin-related hydrogen bonds and chirality in recent years.[6] The above mentioned porphyrin-related chiral recognition arouses our interests. It is apparent that effective control of these functional systems rests upon the comprehensive understanding of the detailed operative mechanisms and the corresponding driving forces. However, such understanding is actually very limited due to the difficulty in obtaining crystals suitable for X-ray analysis; the exact structures of most host–guest bisporphyrin complexes remain unknown. So far, only few crystallographically characterized bisporphyrinate complexes have been reported.[7] So it is a great challenge to design a suitable bisporphyrin system which cannot only perform effective chiral recognition but also be easy to discover the corresponding mechanism. We realize it is very crucial to use the appropriate linkage between two porphyrin subunits. For our purpose, oxalic amide group becomes an ideal candidate for the following reasons: (1) It is a rigid group which can limit the number of conformations in these systems, and therefore facilitate crystal growth. (2) It has potential hydrogen bonding sites which can increase the interactions with the chiral guests. The designed compound **1** is shown in Scheme 1.

In the current work, we have synthesized compound **1**, studied its chiral recognition ability for five amino acid ethyl esters, and solved the crystal structure of complex **1**·(D-Phe-OEt)(L-Phe-OEt) (complex formed between compound **1** and racemic Phe-OEt; Phe-OEt = phenylalanine ethyl ester). Based on the structural data, we have further investigated the chiral recognition mechanism by UV-Vis spectra, ^{1}H NMR and DFT/TDDFT calculations.

[a]*Key Laboratory of Organic Synthesis of Jiangsu Province, College of Chemistry, Chemical Engineering and Materials Science, Soochow University, Suzhou 215123, P. R. China. E-mail: cjhu@suda.edu.cn; Fax: +86-25-65880903; Tel: +86-25-65880903*

[b]*State Key Laboratory and Coordination Chemistry Institute, Nanjing University, Nanjing 210093, P. R. China*

†Electronic supplementary information (ESI) available: Fig. S1 gives the CD spectra of a solution of compound **1** and alanine/valine ethyl esters, Fig. S2–S10 display the UV-Vis spectral changes upon titration, Fig. S11–S15 present CD titration curves, Fig. S16 shows UV-Vis spectrum of complex formed between compound **1** and L-Phe-OEt. Fig. S17 displays selected HOMO and LUMO orbital plots at the B3LYP/6-31G* level. Fig. S18–19 give the mass spectra of compound **1** and **2**. Table S1 lists selected bond distances for the calculated structure of complex **1**·(L-Phe-OEt)$_2$. Table S2 lists main experimental and calculated optical transitions. CCDC 896637. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c3dt50380a



Scheme 1 Designed porphyrins with amide functional group. (a) Compound **1**. (b) Compound **2**.

Experimental section

Material and physical methods

All reagents were obtained from commercial sources without further purification unless otherwise noted. Pyrrole was freshly distilled before use. Triethylamine (Et_3N) was distilled over potassium hydroxide. Anhydrous tetrahydrofuran (THF) was dried and redistilled over sodium benzophenone ketyl. The dichloromethane (CH_2Cl_2) used for CD measurements was spectral grade and treated with CaH_2 before use. All amino acid ethyl ester hydrochlorides used were purchased from commercial sources. The fresh distilled amino ester were prepared as reported methods.[6a,8] The zinc 5-(2-aminophenyl)-10,15,20-triphenyl-porphyrinate was synthesized according to reported methods.[9] Elemental analyses (C, H and N) were performed with an Elementar Vario EL III analytical instrument. ^{1}H NMR spectra were carried out using a Bruker AVANCE 400 spectrometer in $CDCl_3$ with tetramethylsilane (TMS) as the internal standard, Chemical shifts are expressed in ppm relative to chloroform (7.26 ppm). UV/Vis spectra were measured with a Shimadzu UV-3150 spectrometer. Mass spectra were taken with Agilent 6220 Accurate-Mass TOF LC/MS. The CD spectra were recorded on a AVIV Model 410 spectropolarimeter at 25 °C. Scanning conditions were as follows: wavelength step = 1.00 nm, bandwidth = 2 nm, response time = 0.1 s, averaging time = 0.100 seconds, settling time = 0.333 seconds.

General procedure for CD measurement

The background spectrum was then taken from 380 nm to 460 nm with a scan rate of 100 nm min^{-1} at 25 °C. Zinc bisporphyrin solution (3.37×10^{-6} M, 2.50 mL) was injected into a 1 cm quartz cuvette. Then 400 equivalents of D-(or L-) amino acid esters (leucine ethyl ester, phenylalanine ethyl ester, phenylglycine ethyl ester, alanine ethyl ester and valine ethyl ester) or α-methyl benzyl amine were added into the above solution to form the corresponding complex. The CD spectra were measured after several minutes (minimum of 4 accumulations). The resultant ECCD spectra recorded in millidegrees were normalized based on the zinc bisporphyrinate concentration.

UV-Vis, CD and ^{1}H NMR titration

UV-Vis and CD titration experiments were carried out as follows. Portions of a solution of the D-(or L-) amino acid ethyl esters in CH_2Cl_2 were added to the solution of compound **1**, compound **2** or [Zn(TPP)] (2.50 mL, TPP = dianion of tetraphenylporphyrin) in methylene dichloride in a 1 cm quartz cell, UV-Vis or CD spectra were taken after each addition.

^{1}H NMR titration experiments were done as follows. Portions of a solution of D-leucine ethyl esters in $CDCl_3$ were added to the solution of compound **1** (2.0 mg, 600 μL) in $CDCl_3$ in a 5 mm o.d. NMR tube and ^{1}H NMR spectra were taken after each addition.

Synthesis of compound 1

The reaction was carried out under anaerobic condition. Zinc 5-(2-aminophenyl)-10,15,20-triphenyl-porphyrinate (0.57 g, 0.79 mmol) was dissolved in anhydrous THF (40 mL). Et_3N (150 μL, 1.07 mmol) was added to the above solution and stirred for 15 minutes at ice bath, and then oxalyl chloride (37 μL, 0.39 mmol) was added dropwise under N_2 condition. The mixture was slowly warmed up to room temperature and monitored by TLC. After 4 h, the reaction was complete. It was filtered and the precipitate washed by methanol several times, dried under the vacuum. The red solid was obtained and purified by column chromatography (silica, CH_2Cl_2–petroleum ether = 1 : 1) (70% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (8 H, q, J 5.1), 8.78 (4 H, d, J 4.3), 8.40 (4 H, d, J 4.3), 8.32–8.20 (10 H, m), 8.10 (4 H, d, J 7.2), 8.01 (2 H, d, J 7.1), 7.76 (18 H, s), 7.35 (2 H, d, J 8.3), 7.26 (2 H, s), 7.12 (2 H, d, J 8.2). MS (ESI) m/z: 1437.32 $[M + H]^+$. Anal. Calcd for $C_{90}H_{56}N_{10}O_2Zn_2 \cdot 2H_2O$: C, 73.22; H, 4.10; N, 9.49; Found: C, 72.96; H, 4.01; N, 9.51.

Synthesis of the crystals of complex 1·(D-Phe-OEt)(L-Phe-OEt)

Compound **1** (43.2 mg, 0.03 mmol) was dissolved in 3 mL of chloroform, and 0.2 mL of racemic D,L-Phe-OEt was added by syringe. The mixture was stirred at room temperature for 3 min in Schlenk flask under anaerobic condition. Then it was cannula filtered to 8 mm × 250 mm glass tubes. Hexane was added as nonsolvent and the tube was sealed under N_2. X-ray quality crystals were obtained after three weeks.

Synthesis of compound 2

Zinc 5-(2-aminophenyl)-10,15,20-triphenylporphyrinate (0.27 g, 0.30 mmol) was dissolved in 30 mL anhydrous THF, Et_3N (100 μL, 0.72 mmol) was added to the above solution and stirred for 10 min at ice bath, and then methyl oxalyl chloride (13.8 μL, 0.15 mmol) was added dropwisely under N_2 condition. The mixture was slowly warmed up to the room temperature. After 4 h, the reaction was completely monitored by TLC. The solution was rotor evaporated to dryness under the

vacuum. The red solid was purified by silicon chromatography, eluted with (silica, CH_2Cl_2–petroleum ether = 1 : 1). Purple solid was obtained (55% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.95 (d, J = 4.1 Hz, 6H), 8.82–8.76 (m, 3H), 8.51 (s, 1H), 8.30–8.14 (m, 7H), 7.88 (t, J = 7.9 Hz, 1H), 7.82–7.70 (m, 10H), 7.61 (t, J = 7.5 Hz, 1H), 3.13 (s, 3H). MS (ESI) m/z: 778.18 $[M + H]^+$; Anal. Calcd for $C_{47}H_{31}N_5O_3Zn{\cdot}0.5CH_2Cl_2$: C, 65.18; H, 4.31; N, 7.68; Found: C, 65.61; H, 4.63; N, 7.26.

X-ray crystallography

Single crystals of complex **1**·(D-Phe-OEt)(L-Phe-OEt) were obtained by slow diffusion of hexane into chloroform solution of compound **1** and racemic mixture of D,L-phenylalanine ethyl esters. All measurements were made on a Rigaku Mercury CCD X-ray diffractometer by using graphite monochromated Mo Kα (λ = 0.071073 nm) at 223(2) K. The structure was solved by direct methods and refined on F^2 using full matrix least-squares methods with SHELXTL version 97.[10] All non-hydrogen atoms were refined anisotropically. In the asymmetric unit, the three NH hydrogen atoms (H(5), H(6A) and H(6B)) were found in difference Fourier maps, and their coordinates and isotropic temperature factors were refined, other hydrogen atoms were theoretically added and riding on their parent atoms. Complete crystallographic details, atomic coordinates, anisotropic thermal parameters, and fixed hydrogen atom coordinates are given in the cif file. The asymmetric unit contains half compound **1** molecule, one phenylalanine ethyl ester ligand molecule and badly disordered chloroform molecules. The phenylalanine ethyl ester molecule was found to be disordered over two positions, a major and a minor position. The final refinement gave the occupancy as 0.50 for the major component. While SQUEEZE[11] was used to model all disordered chloroform solvate. Electron counts within the inter porphyrin voids of 131e (corresponding to roughly 2.3 molecules of $CHCl_3$ per compound **1**). Details of the crystal parameters, data collection, and refinements are summarized in Table 1.

Table 1 Crystal data and structural refinements of **1**·(D-Phe-OEt)(L-Phe-OEt)

Chemical formula	$C_{112}H_{86}N_{12}O_6Zn_2$
Formula weight	1826.67
Wavelength (Å)	0.71073
Temperature	223(2) K
Crystal system	Triclinic
Space group	$P\bar{1}$
a (Å)	13.264(3)
b (Å)	14.531(3)
c (Å)	15.136(3)
α (°)	75.06(3)
β (°)	74.00(3)
γ (°)	85.09(3)
V(Å^3)/Z	2709.2(9)/1
Density (g cm^{-3})	1.120
Abs coeff. (mm^{-1})	0.498
F(000)	950
Data collect θ range	3.11–25.00
Index range	$-15 \le h \le 15$ $-16 \le k \le 17$ $-13 \le l \le 17$
Reflns collected	21 837
R_{int}/R_{sigma}	0.0415/0.0909
Independent reflns	7484
Data/restraints/parameters	9498/326/698
Goodness-of-fit on F^2	1.022
Final R indices [$I > 2\sigma(I)$]	R_1 = 0.0773 wR_2 = 0.2381
Final R indices for all data	R_1 = 0.0932 wR_2 = 0.2562
Residual peak/hole (e Å^{-3})	0.568/−0.669

$R_1 = \sum(||F_o| - |F_c||)/\sum|F_o|$, $wR_2 = \sum w(|F_o| - |F_c|)^2/\sum w(|F_o|^2)^2]^{1/2}$.

Computation methods

All calculations were carried out with Gaussian03 programs.[12] We employed the density functional theory (DFT) and time-dependent DFT (TDDFT) with no symmetry constraints to investigate the optimized geometries, HOMOs, and LUMOs with the three-parameter hybrid functional (B3LYP). The B3LYP calculations were carried out by 6-31G* basis set.

Results and discussion

Synthesis

Compound **1** was synthesized by the reaction of zinc 5-(2-aminophenyl)-10,15,20-triphenylporphyrinate with oxalyl chloride in anhydrous tetrahydrofuran in anaerobic condition. The reaction is efficient and lead to a yield of 70%. Electrospray-ionization (ESI) mass spectrometry revealed the ion peak at m/z = 1437.32 which corresponds to $[M + H]^+$. For comparison, compound **2** shown in Scheme 1 has also been prepared.

Circular dichroism studies of complexation

We have tested the chiral recognition ability of compound **1** for five amino acid ethyl esters. Compound **1** and enantiopure D- or L-amino acid ethyl esters were mixed in methylene dichloride, and the corresponding CD spectra were measured. For leucine, phenylalanine or phenylglycine derivatives, the spectra showed bisignate Cotton effects in the Soret region in Fig. 1. (Others are provided in ESI.†) For L-type guests, the corresponding longer-wavelength peak of the Soret band was positive and the shorter-wavelength peak was negative. On the other hand, the spectrum of the complex formed between compound **1** and D-type guests showed similar shape and intensity but with the opposite sign. For alanine and valine derivatives, CD spectra show different shapes and intensities. Instead of bisignate signals, they are more like "W" or "M" shape. Their amplitude values are much smaller. These values are listed in Table 2.

Such results suggest that the designed bisporphyrin is a good candidate as a chiral recognition host, and the signs of the induced CD reflect the absolute configuration of the chiral guests. What we are more concerned is the mechanism of such chiral recognition. It can reveal some internal factors that influence the chiral recognition process and help us to develop and extend such a system.

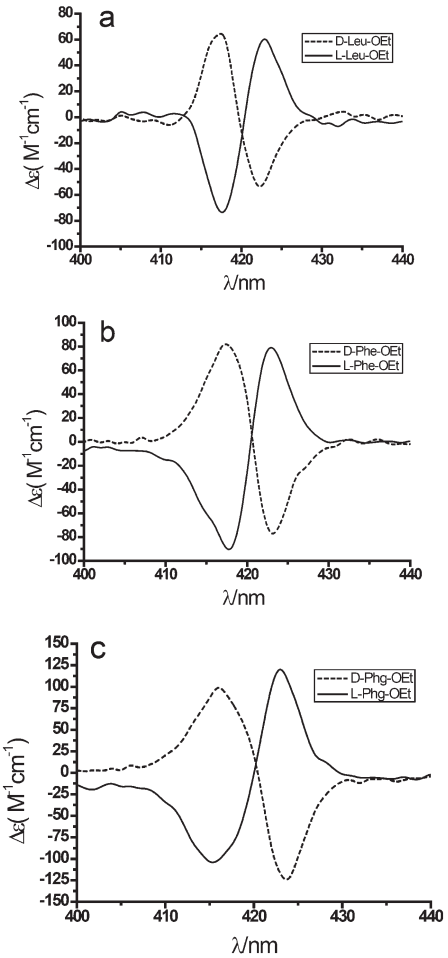


Fig. 1 Circular dichroism spectra of a solution of compound **1** (3.4×10^{-6} M) and 400 equivalents of (a) L- (solid line) and D- (dash line) leucine ethyl ester, (b) L- (solid line) and D- (dash line) phenylalanine ethyl ester and (c) L- (solid line) and D- (dash line) phenylglycine ethyl ester in methylene dichloride at 25 °C.

We noticed that there was structural similarity between subunits of our porphyrin and monomeric porphyrin system bearing two naphthol groups reported by Ogoshi and Mizutani.[13] Their proposed mechanism suggested that the induced CD was caused by the coupling between the magnetic transition dipole moment of the carbonyl group of the guest molecule and the electric transition dipole moment of the Soret band of the porphyrin host. But for our system, the sign of the corresponding CD is different from theirs for the guest with the same handness, and the intensities of induced CD are four times stronger than theirs. Thus that mechanism is not appropriate for our system. Extra evidences have been further provided by a comparison experiment with compound **2** as the host. When such monoporphyrin species was mixed with enantiopure amino acid ethyl ester, no observable signal was obtained. All of the above suggests that the induced CD is not caused by the interactions between porphyrin and carbonyl group of amino acid esters. Instead, the dominated contribution is most likely from the interactions within the bisporphyrin host. In order to figure out the possible

Table 2 Induced CD of the complexes of compound **1** with amino acid esters in methylene dichloride at 25 °C

Amino acid ethyl esters	Compound **1** [$\Delta\varepsilon$ (M^{-1} cm^{-1})]
L-Ala-OEt	+10 (422 nm)
	−42 (418 nm)
	+28 (412 nm)
D-Ala-OEt	−27 (422 nm)
	+48 (417 nm)
	−25 (412 nm)
L-Val-OEt	+15 (422 nm)
	−70 (418 nm)
	+30 (412 nm)
D-Val-OEt	−14 (422 nm)
	+64 (418 nm)
	−33 (412 nm)
L-Leu-OEt	+60 (422 nm)
	−78 (418 nm)
D-Leu-OEt	−60 (422 nm)
	+70 (418 nm)
L-Phe-OEt	+80 (422 nm)
	−90 (418 nm)
D-Phe-OEt	−80 (422 nm)
	+82 (418 nm)
L-Phg-OEt	+120 (422 nm)
	−104 (418 nm)
D-Phg-OEt	−124 (422 nm)
	+100 (418 nm)

mechanism, we did further studies on X-ray crystallography, UV-Vis spectroscopy, ^{1}H NMR and DFT/TDDFT calculations.

Crystal structure of 1·(D-Phe-OEt)(L-Phe-OEt)

One useful method that can be used to further explore the detailed mechanism is to obtain direct structural information through the X-ray crystallography for the complex formed between host and guest molecules. We have tried to obtain single crystals from the mixture of compound **1** and enantiopure phenylalanine ethyl ester, but did not get the suitable crystals. Fortunately, when we mixed compound **1** and racemic mixture of D,L-phenylalanine ethyl esters under anaerobic condition, the suitable single crystals for X-ray crystallography were obtained. To the best of our knowledge, this is the first structure of zinc porphyrinate with amino acid esters as ligands. Its structure was solved and shown in Fig. 2. It clearly reveals the following information: (i) Bisporphyrin unit adopts *anti*-configuration (two porphyrin subunits are on the two sides of the oxalic amide group). (ii) Zinc is five-coordinate; phenylalanine ethyl ester functions as a monodentate ligand and is coordinated to zinc by nitrogen atom, facing the oxalic amide side. (iii) There is one important hydrogen bond involved, which is between the coordinated nitrogen of amino acid ester and carbonyl oxygen of the amide group, the corresponding N(6)···O(1#) (symmetry operator #: $-x + 1$, $-y + 1$, $-z + 2$) distance is 3.098 Å. Obviously, it is the important stabilizing factor to cause the ligand to face the oxalic amide side. Surprisingly, there is no hydrogen bond involving amide nitrogen. Compared with monoporphyrin bearing two naphthol groups reported by Ogoshi and Mizutani,[13] the position of amide nitrogen in our case is similar to that naphthol oxygen in their system. Their results suggest there were hydrogen

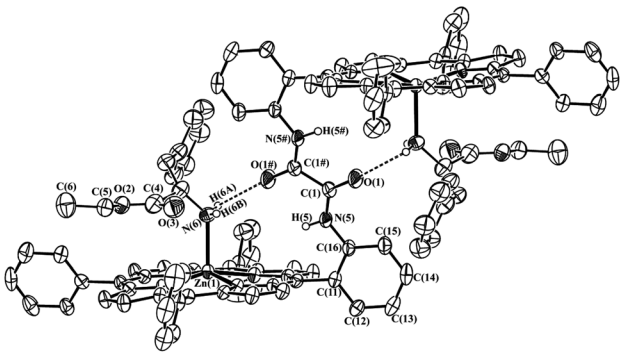


Fig. 2 ORTEP view for complex **1**·(D-Phe-OEt)(L-Phe-OEt) at 50% probability thermal ellipsoids. Except H(6A), H(6B) and H(5), other hydrogen atoms have been omitted for clarity. Selected bond parameters (distance (Å), angle (°)): Zn(1)–N(1) = 2.082 (4), Zn(1)–N(2) = 2.053(4), Zn(1)–N(3) = 2.070(4), Zn(1)–N(1) = 2.067(4), Zn(1)–N(1) = 2.173(4), N(6)···O(1#) = 3.098, N(6)–H(6B)···O(1#) = 130.27 (symmetry operator #:$-x + 1, -y + 1, -z + 2$).

bonds between naphthol oxygen of the host and carbonyl oxygen of the guest molecule, but there is no such hydrogen bonds in our case in the solid state. The possible reason is that the naphthol is a much stronger hydrogen bond donor than amide group. In the structure, there are both D and L-phenylalanine ethyl esters, so the overall molecule is centrosymmetric (achiral).

Binding constant determination by UV-Vis spectroscopic titration

The binding constants between zinc porphyrinate and amino acid ethyl esters are determined by UV-vis spectroscopic titration method. A representative example of visible spectral change of host **1** induced by the addition of phenylalanine ethyl esters is shown in Fig. 3. (Others are provide in ESI.†) Addition of phenylalanine ethyl esters to a CH_2C1_2 solution of compound **1** results in a significant change of the visible spectrum. Before the addition, the spectrum of compound **1** shows one strong Soret band at 421 nm. During the titration at low concentrations of phenylalanine ethyl esters, the electronic spectra show that the intensity of band at 421 nm decreases. An isosbestic point was observed at 426 nm. When the concentration of phenylalanine ethyl esters is over about 6.1×10^{-5} mol L^{-1}, the band at 421 nearly disappeared and an new band formed with increased intensity at 428 nm by the increasing of ligand concentration, and a new isosbestic point showed at 424 nm.

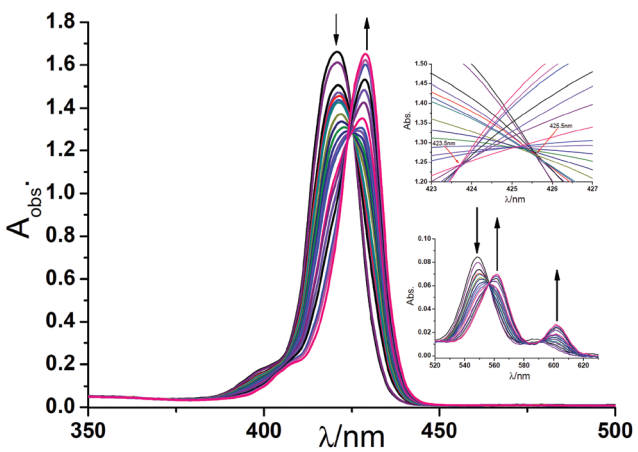


Fig. 3 UV-Visible spectral changes of compound **1** (3.0×10^{-6} M) in methylene dichloride upon addition of L-Phe-OEt as the host : guest molar ratio changes from 1 : 0 to 1 : 167.5 at 25 °C. Arrows indicate absorbance changes with increasing guest concentrations.

Based on the X-ray structure and computation results, the *trans*-conformation of bisporphyrin is more energetically favorable. CD titration curves have also been shown in Fig. S11–S15.† There is no observable change at very high concentrations of guests. It suggests no conversion between *syn*- to *trans*-conformations occurs. So the above spectroscopic changes could be interpreted as being due to the formation of 1 : 2 complexes between compound **1** and phenylalanine ethyl esters, where such complexation requires two steps. The first step is the formation of a 1 : 1 complex [eqn (1)] and the second step is the formation of a 1 : 2 complex [eqn (2)].

$$1 + \mathrm{L} \overset{K_1}{\rightleftharpoons} 1 \cdot \mathrm{L} \tag{1}$$

$$1 \cdot \mathrm{L} + \mathrm{L} \overset{K_2}{\rightleftharpoons} 1 \cdot (\mathrm{L})_2 \tag{2}$$

Two binding constants have to be considered. According to the literature's method,[14] eqn (3) can be used for the nonlinear least-square curve-fitting of the absorption spectral data for 1 : 2 complexation.

$$\Delta A_{\mathrm{obs}} = (A_1 \times K_1 \times [\mathrm{L}] + A_2 \times K_1 \times K_2 \times [\mathrm{L}]^2)/ (1 + K_1 \times [\mathrm{L}] + K_1 \times K_2 \times [\mathrm{L}]^2) \tag{3}$$

where ΔA_{obs} is absorbance changes at 421 nm, K_1 and K_2 are equilibrium constants for two steps, $A_1 = A_1' - A_0$, $A_2 = A_2' - A_0$, A_0 is the absorbances for the pure **1**; A_1' is the calculated absorbances for the pure **1**·L; A_2' is the calculated absorbances for the pure **1**·$(L)_2$.

But when both K_1 and K_2 were treated as free variable, the fitting led to large errors. So alternative method was used: we use fixed K_1 and free variable K_2 to do the fitting which gave the values in the Table 3. The fixed K_1 was obtained from the binding constants K_a between compound **2** and the corresponding amino acid ester (considering the symmetry factors of the equilibria in eqn (1), it is easy to show that $K_1 = 2K_a$).[15] While K_a was obtained from the nonlinear least-square curve-fitting of the absorption spectral data for 1 : 1 complexation by applying eqn (4)[16] in which A_0 and A_∞ are absorbances of pure zinc porphyrinate **2** and **2**·L at the corresponding wavelength respectively (Fig. 4), ΔA is absorbance changes and [L] is the concentration of guest added.

$$\Delta A = (A_0 + K_a[\mathrm{L}]A_\infty)/(1 + K_a[\mathrm{L}]) \tag{4}$$

These association constants are summarized in Table 3. K_1 range from 2.0×10^4 to 7.2×10^4, which are 4–8 times as the

Table 3 Binding constants of [Zn(TPP)], compound **1** and **2** with different amino acid ethyl esters in CH_2Cl_2 at room temperature

	[Zn(TPP)] (10^3)	**2** (10^4)	**1** (10^4)	
D-Ala-OEt	4.9(1)	1.0 (1)	K_1	2.0
			K_2	1.1(1)
L-Ala-OEt	4.9(1)	1.1 (1)	K_1	2.2
			K_2	1.0(1)
D-Leu-OEt	9.0(1)	2.4 (1)	K_1	4.8
			K_2	1.1(1)
L-Leu-OEt	7.2(3)	2.6 (1)	K_1	3.2
			K_2	1.0(1)
D-Val-OEt	7.2(2)	3.3 (1)	K_1	6.6
			K_2	1.0(1)
L-Val-OEt	8.5(2)	3.6 (1)	K_1	7.2
			K_2	1.1(1)
D-Phe-OEt	10.3(1)	3.1 (1)	K_1	6.2
			K_2	1.1(1)
L-Phe-OEt	9.2(1)	3.4 (1)	K_1	6.8
			K_2	1.2(1)
D-Phg-OEt	8.0(2)	3.1 (3)	K_1	6.2
			K_2	1.0(1)
L-Phg-OEt	7.1(1)	3.5 (3)	K_1	7.0
			K_2	1.1(1)

corresponding binding constants for [Zn(TPP)]. It suggests there are extra factors to stabilize the resulting complexes, which could be due to the hydrogen bonding interactions between the coordinated nitrogen of amino acid ester and oxygen of amide group as shown in the structure of **1**·(D-Phe-OEt)(L-Phe-OEt). As shown in Table 3, another common feature for these equilibrium constants is that: the values of K_1 and K_2 are in the same order and $K_1 > K_2$ for all cases. It suggests the binding affinity to the second ligand is a little more difficult than to the first ligand. Considering that the coordination geometry for the first and the second ligand is different when enantiopure ligands are used, such difference in binding constants is reasonable (Fig. 5).

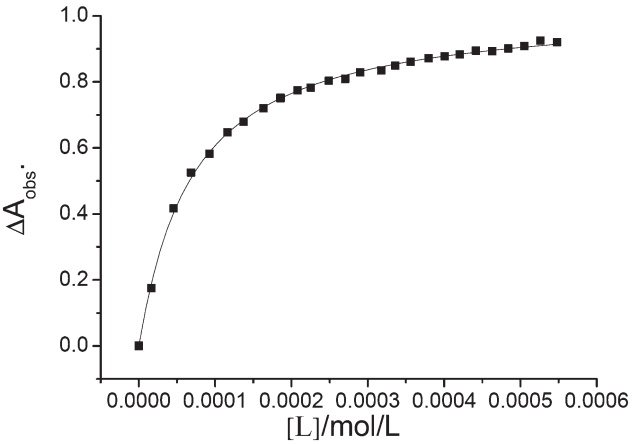


Fig. 5 Plot of ΔA_{obs} *vs.* [L] (mol L^{-1}) for titration of compound **1** by L-phenylalanine ethyl ester. The non-linear fitting gives $K_1 = 6.8 \times 10^4$ and $K_2 = 1.2(1) \times 10^4$. The correlation coefficient of R is 0.99905, where Pearson's R[17] was used to judge the fit to the data. $R = \Sigma_i(X_i - \bar{X})(y_i - \bar{y})/\sqrt{\Sigma_i(x_i - \bar{x})^2\sqrt{\Sigma_i(y_i - \bar{y})^2}}$

^{1}H NMR studies

The spectra of compound **1** in the presence of different concentrations of D-leucine ethyl ester are shown in Fig. 6. It is clearly that when amino acid ester was added, the resonance of ligand protons shows remarkable upfield shifts, it indicates the coordination of ligand to the zinc and the shielding effect of the ring current causes such shifts. Comparing with Kuroda's studies,[18] the most upfield signal at −3.36 ppm is assigned to $-NH_2$ protons of amino acid ester. Such a large upfield shift is due to the direct coordination to the zinc atom of the porphyrin.

In the absence of ligand (guest), the integration suggests there are eight protons at 8.4–8.9 ppm with 2 : 1 : 1 ratio. They are assigned to the signals of eight β-protons, which is similar to the corresponding values for *meso*-5,10,15,20-tetraphenylporphyrin.[19] The 2 : 1 : 1 ratio of β-protons is consistent with

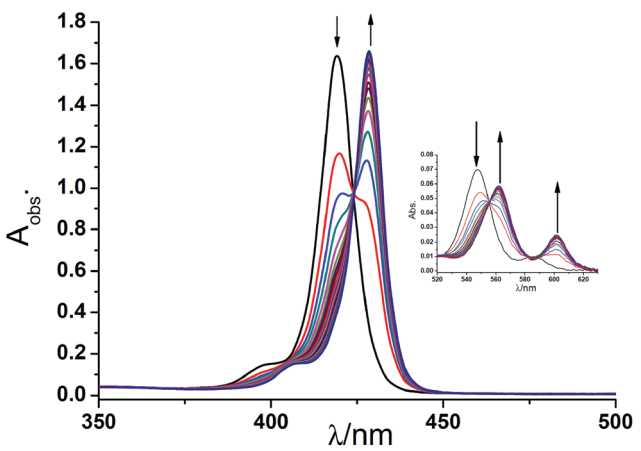


Fig. 4 UV-Visible spectral changes of compound **2** (1.9×10^{-6} M) in methylene dichloride upon addition of L-Phe-OEt as the host : guest molar ratio changes from 1 : 0 to 1 : 240 at 25 °C. Arrows indicate absorbance changes with increasing guest concentrations.

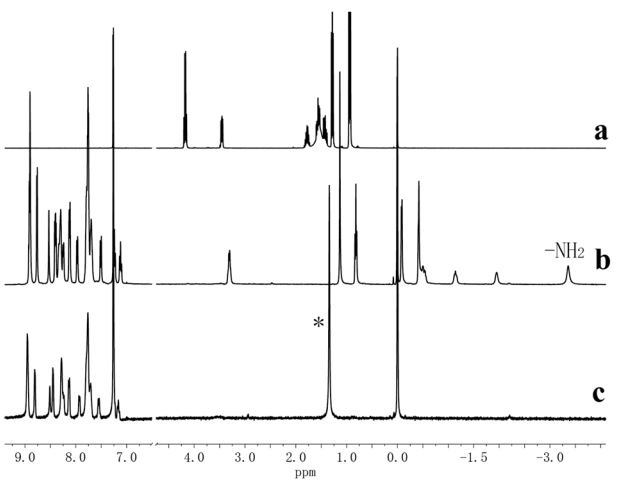


Fig. 6 ^{1}H NMR of (a) D-leucine ethyl ester. (b) The mixture of compound **1** and D-leucine ethyl ester. (c) Compound **1**.

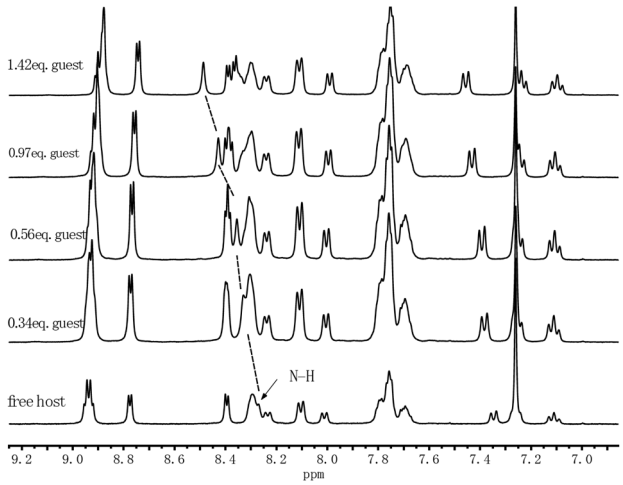


Fig. 7 ^{1}H NMR of compound **1** (host) with D-leucine ethyl ester (guest).

the C_{2h} symmetry of bisporphyrin **1**. When D_2O was added, the signal at 8.3 ppm disappeared, which indicates it is the resonance of the NH proton of amide group. As shown in Fig. 7, upon addition of ligand, the NH resonance has observable downfield shift in the aromatic region from 8.3 to 8.5 ppm. Comparing with studies reported by Kuroda *et al.*,[18] such shift is possible related to the host–guest interaction. Considering about the X-ray structure of **1**·(D-Phe-OEt)(L-Phe-OEt), it is possible due to the hydrogen bonds between the coordinated $-NH_2$ of guest and the carbonyl oxygen of amide group. But we cannot rule out the possibility of contribution from the hydrogen bonds between NH of amide group and carbonyl oxygen of guests in solution. Another feature of the ^{1}H NMR spectra is related to the β-protons. In the absence of ligand (guest), the signals of eight β-protons are symmetric. Upon addition of ligand, the signal at 8.9 ppm became less symmetric which indicates the formation of asymmetric molecule caused by the coordination of chiral molecules.

Computation studies

In the solid structure of **1**·(D-Phe-OEt)(L-Phe-OEt), there are both D and L-phenylalanine ethyl esters, the overall molecule is centrosymmetric (achiral). However, when an enantiopure guest molecule is used, an effective chirality transfer could lead to structural deformation, which can be detected by circular dichroism (CD) spectroscopy. Therefore, we need to further investigate the structure information for the complex formed between compound **1** and enantiopure chiral guest.

For those chirally arranged porphyrins, many studies use theoretical calculations to elucidate the mechanism. After the formulation of the time-dependent density functional theory (TDDFT) and its implementation into common quantum chemical programs at the B3LYP/6-31G* level, CD spectra of medium-sized systems could be calculated with a reasonable precision.[20] In order to figure out the mechanism of induced circular dichroism (ICD) in our case, we have also done DFT/TDDFT calculations for complex **1**·(L-Phe-OEt)$_2$ based on the above crystal structural data.

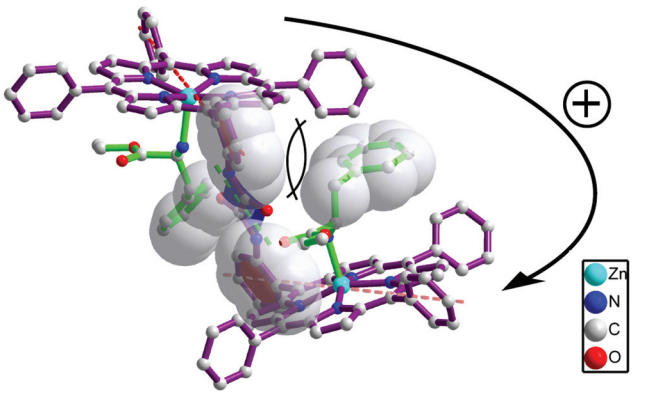


Fig. 8 DFT B3LYP/6-31G* optimized structure of complex **1**·(L-Phe-OEt)$_2$. All hydrogen atoms are omitted for clarity.

The calculated structure was shown in Fig. 8. As shown in Table S1,† the corresponding Zn–N distances and hydrogen bonds are similar to those values from the crystal structure of complex **1**·(D-Phe-OEt)(L-Phe-OEt). In this calculated structure, the ligands are only L-phenylalanine ethyl esters, and the interactions between compound **1** and the enantiopure ligands lead to the overall chiral arrangement of the complex. The relative rotation between two porphyrin subunits is clockwise. The angle between 5,15 axes of two porphyrins is 156.0°. Such rotation is most likely related to the repulsive interactions between the host and guest molecules. As shown in Fig. 8, when L-phenylalanine ethyl ester is coordinated to the bottom zinc porphyrinate, the phenyl ring of the top porphyrin forms a dihedral angle 22° with oxalic amide plane, which could be caused by the repulsion between the phenyl ring of top porphyrin and benzyl group of L-phenylalanine ester. The phenyl group of the other amino ester has different orientation, which is far from the phenyl ring of the bottom porphyrin, the phenyl ring of the bottom porphyrin forms a dihedral angle 3.7° with oxalic amide plane. It suggests two amino acid esters have different contributions to the twist of two porphyrins. It is also consistent with two different binding constants obtained from the UV-Vis titration. The overall arrangement leads to the clockwise twist between two porphyrin subunits. Based on the exciton chirality method,[21] such chiral arrangement will generally lead to positive Cotton effect. It is consistent with our experimental results. The above also suggest the CD signal is related to the size of the substituent of amino acid esters. It is confirmed by ICD amplitude values for different amino acid esters. As shown in Table 3, the ICD amplitude values are in the following order: Phg-OEt > Phe-OEt > Leu-OEt > Val-OEt > Ala-OEt, which is consistent with the bulkness of the alkyl group size of amino acid ester series. We also did comparison experiment by using α-methyl benzyl amine as a guest. When such monoamine was used, no observable signal was obtained. It suggests the ester group also play an important role in the chiral recognition process. Considering the experimental structure and calculated structure in the solid state, the ester group is "locked" between two *meso* phenyl substituents, which could contribute to the chiral

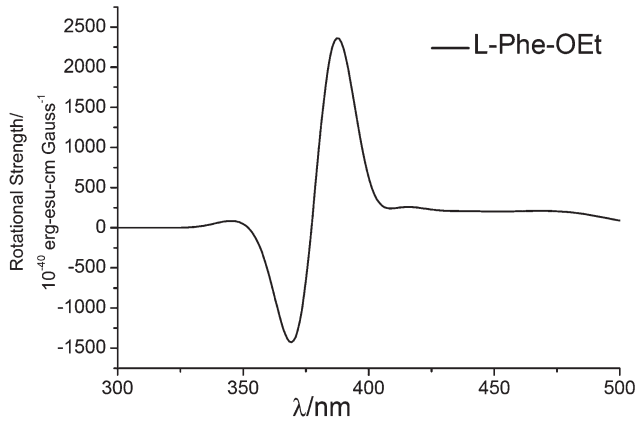


Fig. 9 Calculated CD spectrum of complex formed between compound **1** and L-Phe-OEt.

configuration. Besides this, there could be other contributions in solution, such as the hydrogen bonds between NH of amide group and carbonyl oxygen of guests.

Such structural studies suggest that in the chiral recognition process, the coordination, hydrogen bonding interactions and the repulsive interactions all contribute to the chirality transfer from the phenylalanine ester to the supramolecular system.

Based on the calculated structure, TDDFT calculations gave calculated electronic CD and UV-Vis curves as shown in Fig. 9 and Fig. S16.† The calculated CD spectrum is well in agreement with the experimental result, especially the sign and shape. Comparing with the observed CD bands, the calculated CD bands have slight blue-shift. Such case has also been reported in other DFT-based calculations.[9,20a] Moreover, TDDFT reveals more information on the corresponding optical transitions as summarized in Table S2 and Fig. S17.†

According to DFT and TDDFT calculations, the positive band experimentally found for complex **1**·(L-Phe-OEt)$_2$ around 422 nm mainly originates typical π–π* transitions due to their orbital characters of the corresponding starting and arriving states. The negative band around 416 nm is contributed by both π–π* transitions and metal-to-ligand charge-transfer. It is very clear there is no direct contribution involving phenylalanine ester, which is also consistent with comparison experiments for compound **2**. So the overall mechanism of ICD could be the following: for the zinc bisporphyrinate without ligand, the *anti*-configuration is more favorable than the *syn*-configuration, and such zinc bisporphyrinate itself is centrosymmetric (achiral). When it is mixed with enantiopure phenylalanine ethyl esters, through coordination, hydrogen bonding and repulsion interactions between host and guest molecules, two porphyrin subunits adopt chiral arrangements, the optical transitions within bisporphyrin cause the corresponding induced CD.

The above studies reveal the possible mechanism for the chiral recognition process. As we notice, for alanine and valine derivatives, CD spectra show different shapes and amplitudes. Their first two long wavelength peaks are at similar positions as leucine, phenylalanine or phenylglycine derivatives. We are not sure the exact ICD mechanism for these two guests. But considering the bulkness–amplitudes relationship for these species, one possibility is that less bulky substituent allows more flexible conformations, the presence of multiple competing CD-active conformations could contribute to "W" or "M" shape signals. Similar case has been proposed by Borhan *et al.* in their bisporphyrin system.[22]

Conclusion

We have designed and synthesized a rigid bisporphyrin with oxalic amide as the linkage. Such bisporphyrin has the chiral recognition ability for amino acid ethyl ester. The mechanism of chiral recognition has also been investigated by X-ray crystallography, UV-Vis spectra, ^{1}H NMR and DFT/TDDFT calculations. The results suggest that the combination of coordination interaction, hydrogen bonding interaction and steric repulsion lead to the chiral arrangement of bisporphyrin which can be detected by CD spectroscopy in the Soret band region. Our study suggests that the amide-linked rigid porphyrin provides a good candidate for chiral recognition study. We are developing other amide-linked bisporphyrin systems by adjusting the hydrogen bonding interactions and steric repulsions, such as those with phthalic amides as the linkage.

Acknowledgements

We thank the National Nature Science Foundation of China for financial support (no. 20971093 and 21271133) and the Priority Academic Program Development of Jiangsu Higher Education Institutions.

References

1 (*a*) G. A. Hembury, V. V. Borovkov and Y. Inoue, *Chem. Rev.*, 2008, **108**, 1; (*b*) N. Berova, G. Pescitelli, A. G. Petrovica and G. Pronic, *Chem. Commun.*, 2009, 5958; (*c*) L. Rosaria, A. Durso, A. Mammana and R. Purrello, *Chirality*, 2008, **20**, 411.

2 (*a*) X. Huang, B. H. Rickman, B. Borhan, N. Berova and K. Nakanishi, *J. Am. Chem. Soc.*, 1998, **120**, 6185; (*b*) T. Kurtàn, N. Nesnas, F. E. Koehn, Y. Li, K. Nakanishi and N. Berova, *J. Am. Chem. Soc.*, 2001, **123**, 5974.

3 (*a*) V. V. Borovkov, N. Yamamoto, J. M. Lintuluoto, T. Tanaka and Y. Inoue, *Chirality*, 2001, **13**, 329; (*b*) V. V. Borovkov, G. A. Hembury, N. Yamamoto and Y. Inoue, *J. Phys. Chem. A*, 2003, **107**, 8677; (*c*) V. V. Borovkov, G. A. Hembury and Y. Inoue, *Acc. Chem. Res.*, 2004, **37**, 449.

4 A. E. Holmes, D. Das and J. W. Canary, *J. Am. Chem. Soc.*, 2007, **129**, 1506.

5 (*a*) X. Li and B. Borhan, *J. Am. Chem. Soc.*, 2008, **130**, 16126; (*b*) X. Li, M. Tanasova, C. Vasileiou and B. Borhan, *J. Am. Chem. Soc.*, 2008, **130**, 1885.

6 (*a*) J. Yang, J. Jiang, W. Fang, X. Kai, C. Hu and Y. Yang, *J. Porphyrins Phthalocyanines*, 2011, **15**, 197; (*b*) C. Hu, C. D. Sulok, F. Paulat, N. Lehnert, A. I. Twigg, M. P. Hendrich, C. E. Schulz and W. R. Scheidt, *J. Am. Chem. Soc.*, 2010, **132**, 3737; (*c*) C. Hu, B. C. Noll, P. M. B. Piccoli, A. J. Schultz, C. E. Schulz and W. R. Scheidt, *J. Am. Chem. Soc.*, 2008, **130**, 3127.

7 (*a*) V. V. Borovkov, I. Fujii, A. Muranaka, G. A. Hembury, T. Tanaka, A. Ceulemans, N. Kobayashi and Y. Inoue, *Angew. Chem., Int. Ed.*, 2004, **43**, 5481; (*b*) S. Brahma, S. A. Ikbal, S. Dey and S. P. Rath, *Chem. Commun.*, 2012, 4070.

8 K. E. Otto, S. Hesse, T. N. Wassermann, C. A. Rice, M. A. Suhm, T. Stafforst and U. Diedesen, *Phys. Chem. Chem. Phys.*, 2011, **13**, 14119.

9 P. E. Goudriaan, X.-B. Jang and M. Kuil, *Eur. J. Org. Chem.*, 2008, 6079.

10 G. M. Sheldrick, *Acta Crystallogr., Sect. A: Fundam. Crystallogr.*, 2008, **64**, 112.

11 A. L. Spek, *J. Appl. Crystallogr.*, 2003, **36**, 7.

12 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong. C. Gonzalez and J. A. Pople, *GAUSSIAN 03 (Revision B.04)*, Gaussian, Inc., Wallingford, CT, 2003.

13 T. Mizutani, T. Ema, Y. Yoshida, Y. Kuroda and H. Ogoshi, *Inorg. Chem.*, 1993, **32**, 2072.

14 V. V. Borovkov, J. M. Lintuluoto, H. Sugeta, M. Fujiki, R. Arakawa and Y. Inoue, *J. Am. Chem. Soc.*, 2002, **124**, 2993.

15 G. Ercolani, *J. Am. Chem. Soc.*, 2003, **125**, 16097.

16 (*a*) J. V. Nardo and J. H. Dawson, *Inorg. Chim. Acta*, 1986, **123**, 9; (*b*) J. V. Nardo and J. H. Dawson, *Spectrosc. Int. J.*, 1983, **2**, 326.

17 R. E. Walpole, R. H. Meyers, S. L. Meyers and K. Ye, *Probability and Statistics for Engineers and Scientists*, Prentice Hall, Upper Saddle River, NJ, 7th edn, 2002.

18 Y. Kuroda, Y. Kato, T. Higashioji, J. Hasegawa, S. Kawanami, M. Takahashi, N. Shiraishi, K. Tanabe and H. Ogoshi, *J. Am. Chem. Soc.*, 1995, **117**, 10950.

19 M. S. Somma, C. J. Medforth, N. Y. Nelson, M. M. Olmestead, R. G. Khoury and K. M. Smith, *Chem. Commun.*, 1999, 1221.

20 (*a*) J. L. Alonso-Gomez, A. G. Petrovic, N. Harada, P. Rivera-Fuentes, N. Berova and F. Diederich, *Chem.–Eur. J.*, 2009, **15**, 8396; (*b*) Y. Wang, Y. Wang, J. Wang, Y. Liu and Y. Yang, *J. Am. Chem. Soc.*, 2009, **131**, 8839; (*c*) J. Šebek and P. Bouř, *J. Phys. Chem. A*, 2008, **112**, 2920.

21 N. Berova, K. Nakanishi and R. W. Woody, *Circular Dichroism: Principles and Applications*, Wiley-VCH, New York, 2nd edn, 2000.

22 X. Li, C. E. Burrell, R. J. Staples and B. Borhan, *J. Am. Chem. Soc.*, 2012, **134**, 9026.