Pergamon

Tetrahedron 54 (1998) 5041–5064

TETRAHEDRON

A Two-Step Chemical / Chiroptical Method for Determining Absolute Configurations of α-Hydroxy Acids

Barry H. Rickman, Stefan Matile,† Koji Nakanishi,* Nina Berova*

Department of Chemistry, Columbia University, New York, NY 10027

Received 7 January 1998; accepted 24 February 1998

Abstract: A general, chemical/chiroptical approach based on the CD exciton chirality method has been developed to determine the absolute configuration of α-hydroxy acids. This approach consists of amidation of the carboxyl group with ethanolamine followed by derivatization with the hydrophobic 10,15,20-triphenylporphyrinyl-5-benzoyl chromophore to form π,π-bisporphyrin derivatives which undergo intramolecular stacking. The sign of the observed bisignate couplet resulting from this stacking (in methylcyclohexane) is dictated by the preferred lower energy conformer and reflects the absolute configuration of the stereogenic center.

Introduction

The excition chirality method is a sensitive, nonempirical microscale approach for determining the absolute configuration of cyclic and acyclic compounds containing two or more chromophores located nearby in space.[1,2] The through space interaction between the chromophores leads to an exciton split CD curve, the relative signs and amplitudes of which depend on the absolute skewness of the electric transition moments of the interacting chromophores.[1,2] The chromophores can be preexisting within the parent molecule and/or introduced by derivatization of -OH, $-NH_2$ and other functionalities.

We recently have developed a method for assigning absolute configurations to acyclic compounds with a single stereogenic center *CXYSL, where X is -OH or $-NH_2$, Y is an acyclic chain with a terminal -OH or $-NH_2$, and S (small) and L (large) represent sterically distinct groups.[3] The method consists of attaching porphyrins to X and Y, followed by CD measurements. Strong attractive interactions between the porphyrins lead to intramolecular π,π-stacking in solution characterized by a bisignate CD curve, the sign of which is dependent on the configuration at the stereogenic center carrying the S and L groups. This protocol has been applied to acyclic compounds varying from 1,3- to 1,15-diols, diamines and amino alcohols, where S is hydrogen and L ranges from methyl to larger groups.[3]

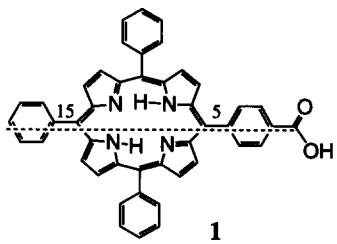
α-Hydroxy acids occur widely in nature in the free form or as esters and amides, and play central roles in biochemical metabolites, anticancer drugs, antiseptics, antibiotics, etc. Several methods have been reported for the synthesis of chiral α-hydroxy acids and derivatives.[4-7] This class of molecules has also been employed

E-mail: kn5@columbia.edu & ndb1columbia.edu Fax: 212-932-8273

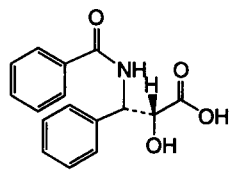
†Current address: Department of Chemistry, Georgetown University, Washington DC 20057

0040-4020/98/$19.00
PII: S0040-4020(98)00221-X

extensively in synthesis of glycols, haloesters, epoxides, and amino acids.[8-12] The absolute configuration of α-hydroxy acids have conventionally been determined with the usage of Mosher's reagent,[13] chiral shift reagents,[14] or comparisons of specific rotations with reference compounds.[15] However, more general approaches are highly desired. Recently, a CD exciton coupling method has been reported for assigning the absolute configuration of D- and L-lactic acid by introduction of 9-anthryl and 2-naphthoate chromophores.[16] In the following we describe a general microgram scale method for determining the absolute configurations of a variety of α-hydroxy acids, including **2h**, the side chain of Taxol,™ based on intramolecular π,π-stacking of porphyrins.



1



2h

Concept

The protocol utilizes the stacking properties of the hydrophobic 5-(*p*-carboxyphenyl)-10,15,20-triphenylporphyrin (TPP) **1** moiety. Porphyrins are powerful chromophores for exciton coupled CD due to the intense and sharp red-shifted Soret band at 414 nm, ε = 350,000, the known direction of the transition moment (the effective transition moment is depicted by the dashed line in **1**[18]), and the availability of both hydrophilic and hydrophobic derivatives;[17-20] a recent application has shown that two hydrophilic porphyrins interact intramoleculary even at distances of 40-50 Å.[20] According to X-ray and solution studies, the stacked formation of porphyrins adopts a cofacial arrangement with their centers offset. This geometry consists of an interplanar separation of 3.4 - 3.6 Å, and an orientation in which the nitrogen-nitrogen axes are parallel, with one porphyrin being offset relative to the other (lateral shift) by 4 Å along the nitrogen-nitrogen axis.[21-27]

This work describes a method which depends on the intramolecular stacking between two porphyrin chromophores linked to a stereogenic *CXYSL substrate, where S is hydrogen, L is a large group and, X is -OH, and Y represents the original -COOH group linked to ethanolamine through an amide bond to give the moiety -C(O)NHCH$_2$CH$_2$*OH* (**3a-3j**, Table 1); this terminal *-OH* constitutes a "1,5-diol system" with the original X or hydroxyl group. Ethanolamine was chosen as the linker based on the finding that the 1,5-diol moiety was optimal for the stacking of the two porphyrin groups. The scheme is illustrated in Figure 1 with the bisporphyrin derivative (bis-TPP) **4f** of *S*-mandelic acid (is the substrate).

The flexibility of the hydrocarbon (ethanolamine) chain enables the bis-TPP molecule to undergo intramolecular π,π-stacking where the terminal porphyrin approaches the chiral center from the less hindered side carrying the hydrogen (**I**, Figure 1). The positive dihedral angle between the effective porphyrin transition moments, polarized in the 5-15 direction[18] gives rise to a positive exciton split CD band; it is sterically unfavorable for the terminal porphyrin to stack with the α-porphyrin from the side linked to the larger substituent (**II**, Figure 1). The enantiomeric derivative, *R*-(-)-mandelic acid, **4g**, in turn, should yield a negative exciton split CD band.

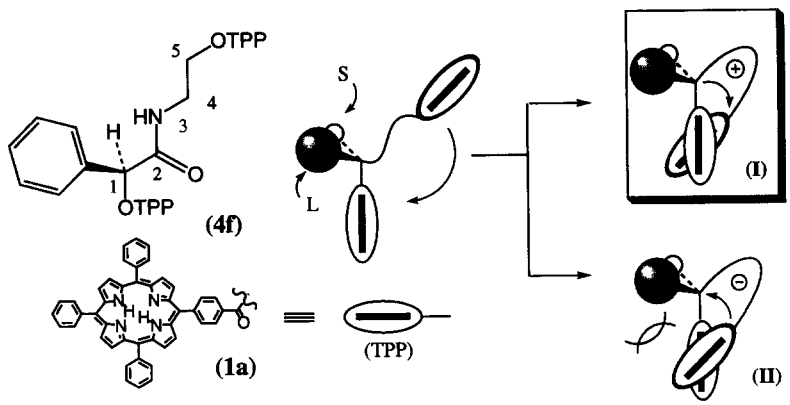


Figure 1. Assignment of the absolute configuration of a single stereogenic center by exciton coupled CD: Bisporphyrin derivative in favorable (I, positive CD couplet) and unfavorable (II, negative CD couplet) intramolecular π,π–stacked conformations, respectively; the positive or negative sign of the CD couplet depends on the chiral sense of twist between the porphyrin electric transition dipoles shown in **1** by the dashed line.[3]

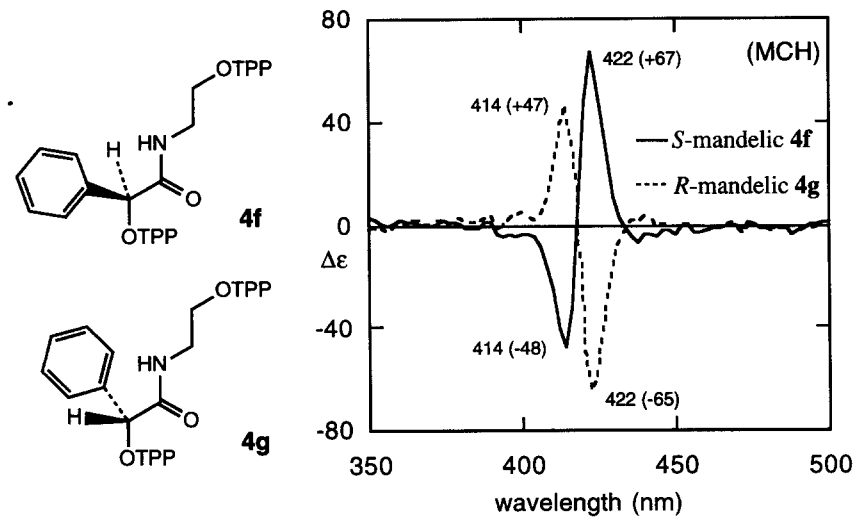


Figure 2. CD spectra of **4f** and **4g** in methylcyclohexane (MCH).

This prediction is in full agreement with the experimental data obtained for the *R*- and *S*-mandelic acid derivatives (Figure 2). Compound (**4f,** *S*-configuration) exhibits a positive couplet at 422 nm (Δε+67) / 414 nm (Δε-48), amplitude A =+115 in methylcyclohexane, while the enantiomer (**4g,** *R*-configuration) shows a negative couplet at 422 nm (Δε-65) / 414 nm (Δε+47), A = -112.

α-Hydroxy acids containing a variety of R groups at the stereogenic center were next selected to explore the applicability of this chemical/chiroptical approach for general configurational assignments (**2a-2j**, Table 1). The R groups ranged from the small methyl in L-lactic acid (**2a**, Table 1) to aliphatic and aromatic R groups with different steric bulk (**2b-2g**, Table 1) and large R groups present in the α-hydroxy sidechains of Taxol,™ bestatin[28]and amastatin[29] (**2h, 2i, 2j**, respectively, Table 1). The two step derivatization consists of coupling the amino group of ethanolamine[30] to the carboxyl group of the hydroxy acid with carbonyldiimidazole (CDI), THF at room temperature, to afford a "1,5-diol", which is then derivatized with TPP **1** in CH_2Cl_2 at rt overnight to form the bis-TPP derivative. Purification of reaction products is readily performed by silica gel column chromatography.

Results and Discussion

CD Measurements and Solvent Dependence

The CD measurements were performed in various solvents, polar, nonpolar, protic and nonprotic, to search for the most suitable solvent (see experimental). Methylcyclohexane (MCH) produced the highest amplitudes (Table 1) and, in all cases, the predicted exciton couplets. Triethylamine (TEA) consistently produced the predicted CD as well. However, while hexane, toluene, CH_2Cl_2, and $CHCl_3$ were employed they yielded either the correct sign or no CD, methanol gave no CD , most likely due to the absence of intramolecular stacking (see below).

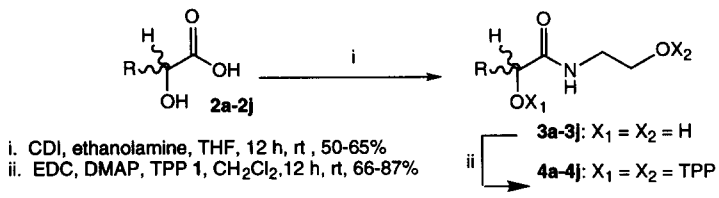
A stock solution of the bis-TPP derivative is prepared in CH_2Cl_2 rather than other solvents because of the high solubility in CH_2Cl_2 and poor solubility in solvents generally used for CD measurements, e.g., MCH, TEA, hexanes , MeOH. An aliquot of the stock solution is then added to MCH for CD measurements (see experimental).

The CD amplitude is strongly dependent on the size of the R group attached to the α-carbon. As shown in Table 1, an increase in the size of the R group results in weaker CD . The amplitude (A = +185) is strongest when R is methyl (**4a**, Table 1), and decreases by 20% and 73%, respectively, when R is cyclohexyl (**4d**, A = +138) and the bulky side chain (**4h**, A = -50). This can be rationalized by inhibition of intramolecular stacking due to steric interference. The CD amplitude for **4h** and **4i** were lower than for the other examples (**4a-4d,4j**). Thus examining α-hydroxy acids containing different aromatic or heterocyclic R groups, one should take possible interactions with the porphyrin groups into consideration. The intensity of the sharp Soret band of bis-TPP derivatives (i.e. **4a-4j**) enables one to work in the 1 μM range, i.e., ca. 1-2 μg of the bis-TPP derivative per mL of solvent for CD measurements.

Selection of Optimal Linker

Of the two groups in α-hydroxy acids, the carboxylic group cannot be readily derivatized by porphyrin **1** unless a linker is used. Moreover, even if direct derivatization with two porphyrins were possible, this would give rise to a 1,2-bis-TPP, similar to that encountered in the 1,2-bis-TPP derivative of L-serine ester ("1,2-amino alcohol"),[3] or 1*R*,2*R*-cyclohexane diol[18] where interpretation of CD data was not straightforward due to proximity of the two bulky porphyrin moieties. However, insertion of an ethanolamine linker yields a "1,5-diol system", which similar to 1,5-diamines[3] leads to facile bis-TPP derivatization and straightforward analysis of CD data.

In the studies for an optimal "C_2"-linker we employed ethanolamine, ethylene glycol and ethylenediamine and*S*-(-)-2-hydroxyisocaproic acid as the model. The ethanolamine linker yielding **4c** gave the strongest CD amplitude (A = +182) compared to the diol and diamine linker (**5a**, A = + 39, **5b**, A = +81, respectively)(Figure 3).



i. CDI, ethanolamine, THF, 12 h, rt , 50-65%
ii. EDC, DMAP, TPP 1, CH_2Cl_2,12 h, rt, 66-87%

Cmpd		R	H	1st / 2nd [λ(Δε)]	A (MCH)
4a	*(S)-*	Me	H	422 (+113) / 414 (-72)	+185
4b	*(S)-*		H	422 (+87) / 414 (-59)	+143
4c	*(S)-*		H	423 (+108) / 415 (-74)	+182
4d	*(S)-*		H	422 (+82) / 414 (-56)	+138
4e	*(S)-*	Ph	H	423 (+56) / 413 (-23)	+79
4f	*(S)-*	Ph	H	422 (+67) / 414 (-48)	+115
4g	*(R)-*	Ph	H	422 (-65) / 414 (+47)	-112
4h	*(2R, 3S)-*	Ph, NH, Ph	H	422 (-33.8) / 414 (+16.4)	-50
4i	*(2S, 3R)-*	NHBoc, Ph	H	422 (+17.2) / 414 (-17.1)	+34
4j	*(2S, 3R)-*	NHBoc	H	422 (+40.7) / 414 (-38.7)	+79

Table 1. A two step derivatization of α-hydroxy acids (**2a-2j**) into their bis-TPP derivatives (**4a-4j**) and CD (λnm/Δε and amplitudes, A) in MCH of **4a-4j**; in MeOH the CDs are weak and noncharacteristic. The signs of the bisignate couplets agree with the predicted in all cases. The R-groups in **2a-2j** and **3a-3j** correspond to the R-groups in **4a-4j**.

These results showed that ethanolamine might contribute to the conformational stability of the macrocyclic structure due to possible hydrogen bond formation (Figure 4). In the stacked conformation, the amide hydrogen in **4c** can be proximal to the carbonyls of one or both porphyrin esters to form stabilized seven-membered

hydrogen bond structures, which in turn would result in an intensified CD amplitude due to decreased flexibility stemming from the hydrogen bonds. The ethylene glycol linked **5a** cannot form hydrogen bonds, while in the ethylene diamine linked **5b** the presence of two amide bonds could lead to less flexibility making it difficult to form stable hydrogen bonds (Figure 3).

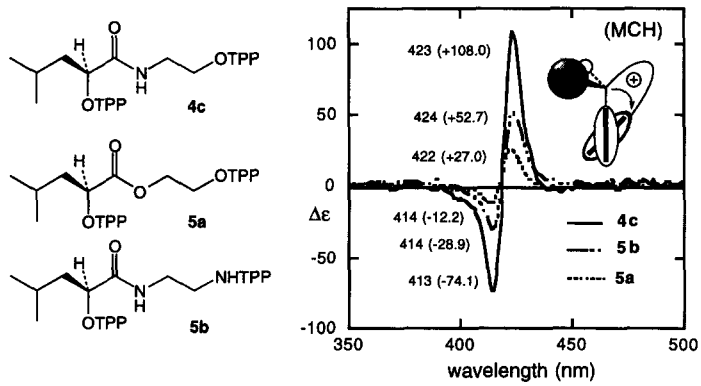


Figure 3. Bis-TPP derivatives of 2-hydroxyisocaproic acid incorporating various "C_2"-linkers: ethanolamine (**4c**), ethylene glycol (**5a**), and ethylene diamine (**5b**).

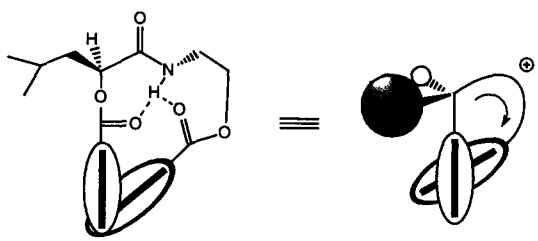


Figure 4. Hydrogen bonding of the amide with the porphyrin ester carbonyls in compound **4c**.

The presence of intramolecular hydrogen bonding in **4c** is supported by the IR data in CCl_4, c=1 mM. Thus, the ester absorptions in **4c** appear at 1724 cm^{-1} and 1709 cm^{-1} whereas in porphyrinyl methyl ester **1** it appears at the higher frequency of 1729 cm^{-1} (5 mM); in the N-H stretch region, the only absorptions are at 3313 and 3411 cm^{-1} representing the pyrrole and hydrogen-bonded N-H stretches, respectively.

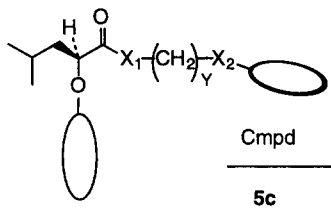
No exciton split CD was observed for compounds **4a-4j** (Table 1) when CD experiments were performed in MeOH. This could be ascribed to disruptions of the intramolecular H-bonding and porphyrin stacking shown in Fig. 4 caused by solvation of MeOH to the N-H group. Compound **5a** (Fig. 3) which lacks the amide NH bond exhibits an exciton coupled split CD curve in MeOH (A = +39.2).

S-(-)-2-Hydroxyisocaproic acid was also used as the model for selecting the linker with optimal length (Table 2).[31] No CD was observed with the 1,3-propanediol linker **5c**. In the case of amino alcohol linkers C_3 (**5d**), C_4 (**5e**), and C_5 (**5f**) (Table 2), the CD amplitudes decreased drastically with increase in chain length; **5f**

showed no CD. Besides the large amplitude of +182 exhibited by the C_2 linker as in **4c** (Fig. 3), an additional advantage for employing ethanolamine as a linker is that the amine selectively reacts with the carboxylic acid in the presence of two other hydroxyl groups, that of the hydroxy acid and the ethanolamine.

Proof of Intramolecular Stacking

Compounds containing two porphyrin groups can undergo intramolecular and/or intermolecular stacking. In this section three results which indicated that the observed exciton split intense CD curves are due to intramolecular porphyrin-porphyrin interactions are described: (i) a CD experiment with Zn and non-metalated porphyrin derivatives; (ii) CD concentration studies; and (iii) NMR studies.



Cmpd	X_1	X_2	Y	A (MCH)
5c	O	O	3	n.d.
5d	NH	O	3	+117
5e	NH	O	4	+13
5f	NH	O	6	n.d.

Table 2. Bis-TPP derivatives of 2-hydroxyisocaproic acid formed from linkers of various lengths; n.d. = non descriptive CD curve.

(i) CD studies of porphyrin derivatives with / without zinc

Consider two compounds, each having two porphyrin chromophores, i.e., A-A and B-B, and assume that the absorption maximum of A is blue shifted compared to B. When A-A and B-B are mixed in a 1:1 ratio in solution, one of two processes can occur: (a) If only intramolecular stacking were taking place, then A-A and B-B would each show two independent different CD couplets. (b) If intermolecular stacking were also present, one would observe an additional couplet, namely three different curves: A-A, B-B and A-B; the resulting spectrum will be the sum of all three curves in ratios depending on the affinity for A and B to stack (see control experiment with heterobisporphyrin **7**, Fig. 5).

Homobisporphyrin derivatives were first investigated (Fig. 5): bis-tetraphenylporphyrin (bis-TPP) **4d**, λ_{max} = 416 nm in MCH and λ_{max} = 417 in CH_2Cl_2, and bis-Zn-tetraphenylporphyrin (bis-Zn-TPP, **6**), λ_{max} = 415 nm in MCH and λ_{max} = 418 nm in CH_2Cl_2. Under these conditions the two absorptions are indistinguishable. However, it is well known that Zn in porphyrins is almost exclusively five-coordinate and that coordination with amines shifts the Soret peak to the red.[32] Thus, addition of isopropylamine to bis-Zn-TPP **6** results in a ca. 10 nm red shift; λ_{max} = 425 nm in MCH and λ_{max} = 428 nm in CH_2Cl_2[33] which is reflected in the CD spectrum of the amine complex **6a** (Fig. 5a); however, addition of i-$PrNH_2$ to bis-TPP **4d** does not change the position and amplitude of the UV and CD bands. The experimental CD upon mixing bis-TPP **4d** and bis-Zn-TPP amine complex **6a** in a 1:1 molar ratio is represented by the solid curve in Fig. 5b. The identity of this curve with the computer sum CDs of **4d** and **6a** (depicted on Figure 5a) in a 1:1 ratio shown by the dashed line proves the lack of any measurable

intermolecular stacking; if any intermolecular stacking were involved, the experimental curve would not match the summation spectrum of **4d** and **6a**. In addition, all CD measurements in this study are performed at very dilute concentrations (10^{-6}M), a factor of 10^4 below the reported intermolecular stacking concentration.[3,23,34]

The heterodimer derivative (TPP/Zn-TPP, **7**) was synthesized in order to demonstrate that zinc containing TPP (i.e. **6**) can indeed intramolecularly stack with metal-free TPP. Thus, the CD of compound **7** with TPP attached to the stereogenic center and Zn-TPP attached to the ethanolamide side chain was in agreement with that expected for intramolecular stacking: 422 nm (+30.8), a shoulder at 430 nm (+15.2), 418 nm (0), and 414 nm (-26.6) (in MCH containing 1μL $iPrNH_2$/ mL MCH).[3]

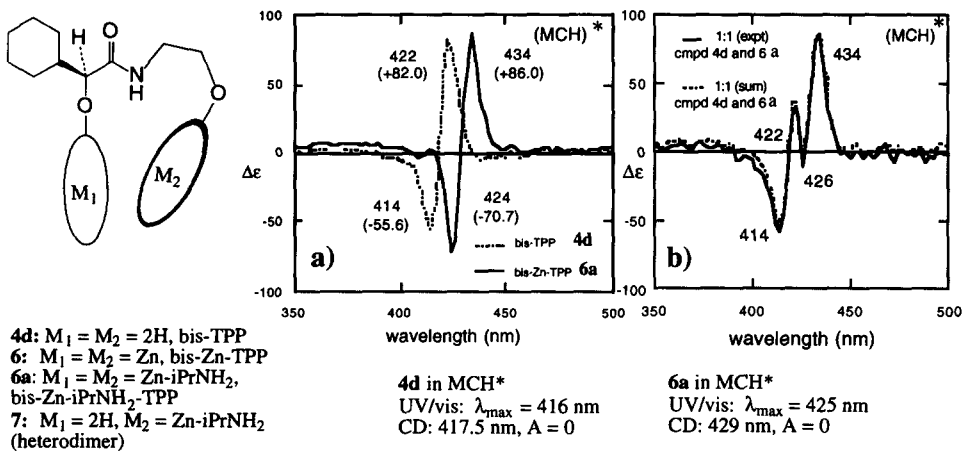


Figure 5. UV and CD spectra of hexahydromandelic acid derivatives: **a)** bis-TPP **4d** (dotted line), bis-Zn-TPP amine complex **6a** (solid line) in methylcyclohexane containing 1 μL ($iPrNH_2$)/mL MCH; **b)** 1:1 mixture of bis-TPP **4d** and bis-Zn-TPP amine complex **6a** (experimental, solid line); computer sum curve of CDs in 1:1 ratio of **4d** and **6a** in methylcyclohexane containing 1μL ($iPrNH_2$)/mL MCH (dotted line).

*The solvent MCH contains 1 μL ($iPrNH_2$) per mL MCH in all cases.

(ii) Concentration dependence

The exciton split CD curve of (-)-2-hydroxyisocaproic acid bisporphyrin derivative **4c** was subjected to concentration variation studies to differentiate between intramolecular stacking vs. intermolecular stacking, which are respectively, concentration independent and concentration dependent processes. The positive CE (A =+66) of **4c** in $CHCl_3$ was concentration independent in the range of: (a) 1.02 μM (1x), (b) 1.91 μM (1.87x), and (c) 19.1 μM (18.7x) (Figure 6).

The CD concentration study of **4c** was performed in $CHCl_3$ to make a direct comparison with the NMR stacking studies described below; no change in the CD was observed in MCH as well. In contrast, the CD of

monoporphyrin derivative **8** of the same substrate as in **4c**, but with only one porphyrin, displayed no exciton split CD in $CHCl_3$ (concentration variation 3.67 μM - 36.7 μM), MCH, TEA and CH_2Cl_2; the same was true for the two monophorphyrin derivatives of cyclohexyl compound **4d**. Furthermore, the CD of bisporphyrin derivatives **4a-4j** were also concentration independent. These results are in accord with intramolecular stacking and rule out the participation of any intermolecular stacking. An earlier study with other bisporphyrin compounds on CD concentration dependence in the 1.6 - 0.4 μM range had also shown the occurrence of intramolecular stacking.[3]

(iii) NMR studies

The presence or absence of porphyrin stacking was also monitored by the upfield or downfield NMR shifts of the porphyrin aromatic protons induced by ring current (Fig. 8).[37] The NMR of the following porphyrin derivatives of 2-hydroxyisocaproic acid were measured in $CHCl_3$ (Fig. 7) and the results were compared with the CD data.

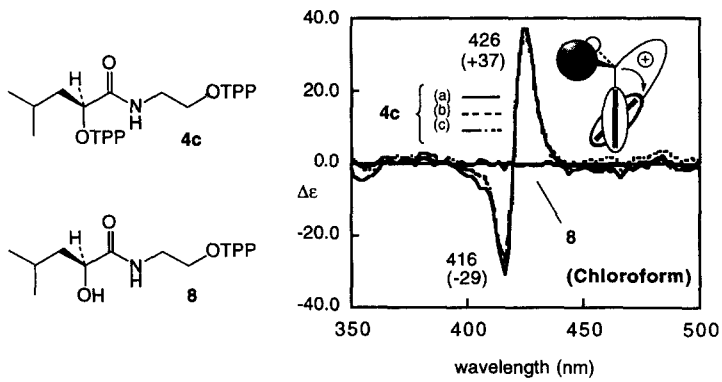


Figure 6. (i) Concentration dependence study of **4c**. All three spectra at different concentrations are displayed (a) 1.02 μM, (b) 1.91 μM, and (c) 19.1 μM (see NMR studies at 18.5 μM and 1.37 mM, Figure 7). (ii) The monomer, **8**, showing no CD spectrum (c= 5.0 μM).

(a) Monoporphyrin **8**: No intermolecular stacking was detected in the 3.67 - 36.7 mM range (by CD, Fig. 6).

(b) Bisporphyrin compound **5f** (Table 2): No CD in MCH and TEA; weak positive couplet (2.06 mM, A = +9) in $CDCl_3$.[38] NMR of a 1.5 mM solution was measured.

(c) Bisporphyrin compound **4c**: CD showed intramolecular stacking (Fig. 6) NMR of 18.5 μM and NMR of 1.37 mM solutions measured.

In Fig. 7, the ^1H NMR of unstacked compound **8** displays only one set of aromatic protons. In the ^1H NMR of bisporphyrin **5f**, compared to **8**, no anisotropic shifts are observed other than the presence of additional aromatic protons arising from the second porphyrin group, and hence no stacking is taking place. Although NMR spectra were measured at much higher concentrations, these results corroborate the CD results of Fig. 6 (for **8**) and Table 2 (for **5f**), respectively. The intramolecular stacking in **4c**, as evidenced by the positive CD couplet (A

= +66, $CHCl_3$, Fig. 6) is clearly reflected in the ^1H NMR (Fig. 7c and 7d). The aromatic signals of the meta- and para-hydrogens associated with four of the six phenyl groups shift approximately 0.2-0.3 ppm upfield to around 7.5 ppm, while the meta- and para-hydrogens of the two remaining phenyl rings at 7.75 ppm show no shift compared to monomer **8**. Upfield shifts to 7.8-7.9 ppm are observed in the ortho-protons of four of the six phenyl groups; upfield shifts are also seen with the pyrrole protons. The porphyrin protons undergoing upfield shifts suggest that they are located above the ring of the other porphyrin, while the protons showing no shift are more remote from the ring as depicted schematically in Fig. 8.

This data coincides with the NMR shifts and patterns seen in the previous NMR study by Matile et. al.[3] It should be noted that although the data shown on Figs. 7c and 7d were measured at a concentration difference of ca. 75-fold, no concentration dependence is seen, thus indicating that the stacking is intramolecular.

Although the NMR spectra were measured at concentrations >>1,000-fold than those of CD measurements

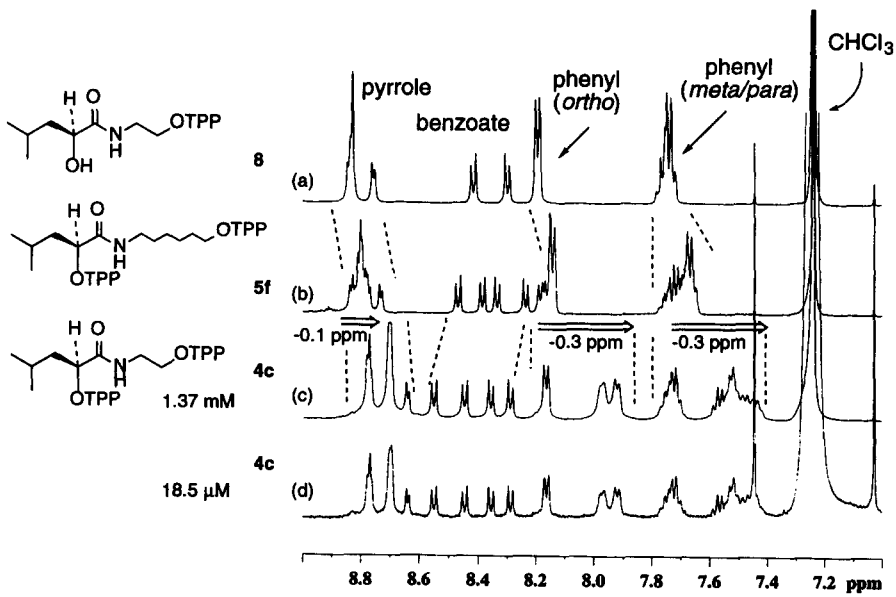


Figure 7. 500MHz ^1H NMR spectra in $CDCl_3$ of (a) 2-hydroxyisocaproic ethanolamide monoporphyrin, **8**, (b) 2-hydroxyisocaproic-1,6-hexanolamide bisporphyrin, **5f**, (c) 2-hydroxyisocaproic ethanolamide bisporphyrin, **4c**, at 1.37 mM, and (d) 2-hydroxyisocaproic ethanolamide bisporphyrin, **4c**, at 18.5 μM (see CD studies at 19.1 μM - Fig. 6).

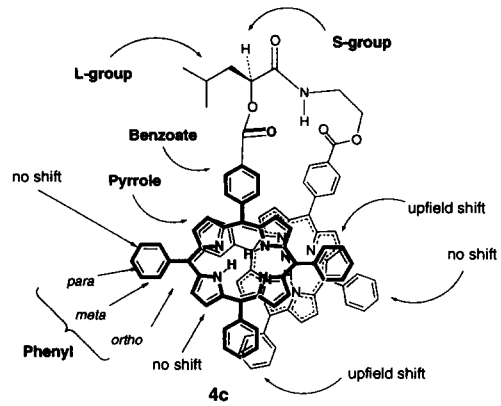


Figure 8. A proposed intramolecular stacking model of the bisporphyrin derivative **4c** derived from the ^{1}H NMR data in Fig. 7c.

(c = ca. 1.0 μM for CD, Figure 6, curve a; and c = ca. 1.4 mM for NMR, Figure 8c), the direct correlation of NMR with CD clearly indicates that there is no intermolecular interference within the concentration range of 1 μM to 1.4 mM. This experiment, as well as the Zn/non Zn CD study and the CD concentration dependence studies described above, all indicate the occurrence of intramolecular stacking.

Conclusion

This paper describes a general two-step microscale method for determining the absolute configuration of α-hydroxy acids, while the protocol described in the previous paper[3] is applicable to a variety of 1,3- to 1,5-diols, diamines, and aminoalcohols. Both cases depend on the intramolecular stacking between porphyrins attached to the stereogenic center *CXYSL: X represents -OH or -NH_2, Y represents a -COOH (present paper) or an acyclic chain with terminal -OH or -NH_2, S represents hydrogen, and L varies from methyl to large complex groups, e.g., the Taxol™ side chain.

Experimental

Reagents and starting materials were purchased from common commercial suppliers and were used as received. General procedures and synthesis of **1** are as described in the references[17,18] Reactions were followed by thin-layer chromatography (Tlc) on Merck (0.25 mm) glass-packed, precoated silica gel plates (60 F_{254}). Preparative Tlc (pTlc) were performed on the same plates as general Tlc plates. CD spectra were recorded on a JASCO J-720 spectropolarimeter and given as λ_{ext}[nm] ($\Delta\varepsilon_{ext}$[λmol^{-1}cm^{-1}]. The solutions for CD measurement of all porphyrin derivatives were prepared based on stock solutions (0.1 mmol) in CH_2Cl_2. Each time, an aliquot of this stock solution (10 μl) was added to 1 ml of the corresponding solvent to yield 10^{-6}M solutions. All intermediates and final products were characterized by ^{1}H-NMR spectroscopy (Varian VXR400 or Bruker 500) and spectra were recorded in parts per million (ppm) using residual proton solvent peaks of either $CDCl_3$ at 7.24 ppm, CD_3OD at 3.30 ppm, or DMSO at 2.56 ppm as an internal standard, with coupling constants (*J* in Hertz (Hz)). IR spectra were recorded at room temperature under a N_2 atmosphere on an Paragon 1000 Perkin Elmer FT-IR Spectrophotometer. A KBr liquid cell was used (path length 0.013 mm). MS(Cl)(NH_3) spectra were

obtained on a NERMAG R10-10 while low resolution MS(FAB) (3-nitrobenzyl alcohol matrix) spectra were obtained with a JOEL JMS-DX303 HF, ms are expressed as *m/z*. In most cases the M + H^+ or M + NH_4^+ were the strongest peaks. UV/vis spectra were recorded in methylene chloride on a Perkin-Elmer Lambda 4B spectrophotometer, and reported as λ_{max}[nm]($\Delta\varepsilon_{max}$[l $mol^{-1}cm^{-1}$]).

Hydroxyacid derivatization method.

General coupling procedures:

Method A. Hydroxyacid and ethanolamine (3a-3j): To a solution of hydroxyacid (200 μmol, 1 equivalent) in THF (2 mL) at rt was added carbonyldiimidazole (250 μmol, 1.25 equivalents). The mixture was stirred at rt for 1 h. Ethanolamine (3.17 mmol, ca. 15 equivalents) was added and the reaction mixture was stirred at rt overnight. After the removal of solvent, the residue was purified by silica gel flash chromatography (solvent systems ranged from 15:1 to 10:1 CH_2Cl_2/ MeOH).

Method B. Porphyrin coupling (4a-4j): To a solution of TPP **1** (ca. 17 μmol, 3.5 equivalents), EDC (ca. 17.4 μmol, 3.7 equivalents), and DMAP (ca. 17.4 μmol, 3.7 equivalents) in CH_2Cl_2 (1.0 mL), a solution of **3** (ca. 4.4 μmol, 1 equivalent) in CH_2Cl_2 (1.0 mL) was added. The reaction mixture was stirred at rt for 12 h. The solution was applied directly to a silica gel column (solvent systems ranged from 60:1 to 100:1 CH_2Cl_2/MeOH) with an additional purification if needed (silica gel pipette column solvent system ranging from 5:5 to 7:3 $CHCl_3$/hexanes) to yield pure bisporphyrin as a deep purple powder.

(2*S*)-[2'N-hydroxyethyl]-2-hydroxypropanamide (3a)

Prepared from L-lactic acid (19.0 mg, 0.21 mmol) according to method A to afford a 1:2 mixture of product/ imidazole as a white powder (30.6 mg, 54%). The product was used immediately to make **4a**. ^{1}H-NMR ($CDCl_3$, 400MHz) δ 1.42 (d, *J* = 6.8 Hz, 3H, C*H*$_3$CH), 3.37-3.50 (m, 2H, NHC*H*$_2$CH$_2$OH), 3.68-3.73 (m, 2H, NHCH$_2$C*H*$_2$OH), 4.24 (q, *J* = 6.8 Hz, 1H, H-C(α)), 6.26 (br s, 1H, C(O)N*H*), 7.09 (s, 2H, imidazole), 7.67 (s, 1H, imidazole); CI-MS (NH_3): *m/z* 133 (m + 1)$^+$, 151 (m + 18)$^+$.

(2*S*)-[2'N-hydroxyethyl]-2-hydroxy-3-methylbutanamide (3b)

Prepared from (*S*)-(+)-2-hydroxy-3-methylbutyric acid (21.5 mg, 0.18 mmol) according to method A to afford product as a yellow oil (19.0 mg, 65%). ^{1}H-NMR ($CDCl_3$, 400MHz) δ 0.85 (d, *J* = 6.8 Hz, 3H, C*H*$_3$ from iPr), 0.99 (d, *J* = 6.8 Hz, 3H, C*H*$_3$ from iPr), 2.11-2.18 (m, 1H, C*H*(CH$_3$)$_2$), 2.83 (br s, 1H, OH), 2.92 (br s, 1H, OH), 3.38-3.51 (m, 2H, NHC*H*$_2$CH$_2$OH), 3.69-3.73 (m, 2H, NHCH$_2$C*H*$_2$OH), 3.99 (br s, 1H, H-C(α)), 6.92 (br s, 1H, C(O)N*H*); CI-MS (NH_3): *m/z* 162 (m + 1)$^+$, 179 (m + 18)$^+$.

(2*S*)-[2'N-hydroxyethyl]-2-hydroxy-4-methylpentanamide (3c)

Prepared from (-)-2-hydroxyisocaproic acid (22.0 mg, 0.17 mmol) according to method A to afford product as a yellow oil (17.0 mg, 59%). ^{1}H-NMR ($CDCl_3$, 400MHz) δ 0.91 (d, *J* = 6.4 Hz, 3H, C*H*$_3$ from iPr), 0.93 (d, *J* = 6.4 Hz, 3H, C*H*$_3$ from iPr), 1.47-1.61 (m, 2H, C*H*$_2$iPr, 1.81 (m, 1H, C*H*(CH$_3$)$_2$), 2.98 (br s, 2H, OH),

3.30, 3.49 (2m, 2H, NHCH_2CH_2OH), 3.62-3.73 (m, 2H, NHCH_2CH_2OH), 4.10 (dd, J = 9.8 Hz, 3.5 Hz, 1H, H-C(α)), 7.19 (br s, 1H, C(O)NH); CI-MS (NH_3): m/z 176 (m + 1)$^+$, 193 (m + 18)$^+$.

(2*S*)-[2'N-hydroxyethyl]-2-hydroxy-2-cyclohexylacetamide (3d)

Prepared from (*S*)-(+)-hexahydromandeic acid (21.1 mg, 0.13 mmol) according to method A to afford product as a clear oil (13.9 mg, 52%). ^{1}H-NMR ($CDCl_3$, 400MHz) δ 1.07-1.30 (m, 4H, cyclohexane), 1.49-1.52 (m, 1H, cyclohexane), 1.64-1.83 (m, 6H, cyclohexane), 2.82 (br s, 1H, OH), 2.95 (br s, 1H, OH), 3.37-3.52 (m, 2H, NHCH_2CH_2OH), 3.67-3.75 (m, 2H, NHCH_2CH_2OH), 3.96 (br s, 1H, H-C(α)), 6.93 (br s, 1H, C(O)NH); CI-MS (NH_3): m/z 202 (m + 1)$^+$.

(2*S*)-[2'N-hydroxyethyl]-2-hydroxy-3-phenylpropanamide (3e)

Prepared from L-3-phenyllactic acid (18.3 mg, 0.11 mmol) according to method A to afford product as an off-white oil (13.9 mg, 61%). ^{1}H-NMR ($CDCl_3$, 400MHz) δ 1.99 (br s, 2H, OH), 2.91 (dd, J = 14.0 Hz, 8.1 Hz, 1H, PhCH(H)CHOH), 3.21 (dd, J = 14.0 Hz, 4.0 Hz, 1H, PhCH(H)CHOH), 3.39 (m, 2H, NHCH_2CH_2OH), 3.65 (m, 2H, NHCH_2CH_2OH), 4.33 (dd, J = 8.1 Hz, 4.0 Hz, 1H, H-C(α)), 6.85 (br s, 1H, C(O)NH), 7.23-7.34 (m, 5H, C_6H_5); CI-MS (NH_3): m/z 210 (m + 1)$^+$, 227 (m + 18)$^+$.

(2*S*)-[2'N-hydroxyethyl]-2-hydroxy-2-phenylacetamide (3f)

Prepared from (*S*)-(-)-mandelic acid (20.2 mg, 0.13 mmol) according to method A to afford product as an off-white powder (16.0 mg, 62%). ^{1}H-NMR ($CDCl_3$, 400MHz) δ 2.00 (br s, 1H, OH), 3.42 (m, 2H, NHCH_2CH_2OH), 3.69 (m, 2H, NHCH_2CH_2OH), 5.07 (s, 1H, H-C(α)), 6.69 (br s, 1H,C(O)NH), 7.36 (m, 5H, C_6H_5); CI-MS (NH_3): m/z 196 (m + 1)$^+$, 213 (m + 18)$^+$.

(2*R*)-[2'N-hydroxyethyl]-2-hydroxy-2-phenylacetamide (3g)

Prepared from (*R*)-(-)-mandelic acid (18.8 mg, 0.12 mmol) according to method A to afford product as a white powder (14.2 mg, 59%). ^{1}H-NMR ($CDCl_3$, 400MHz) δ 1.67 (br s, 1H, OH), 3.43 (m, 2H, NHCH_2CH_2OH), 3.70 (m, 2H, NHCH_2CH_2OH), 5.07 (s, 1H, H-C(α)), 6.59 (br s, 1H, C(O)NH), 7.37 (m, 5H, C_6H_5); CI-MS (NH_3): m/z 196 (m + 1)$^+$, 213 (m + 18)$^+$.

(2*R*,3*S*)-[2N'-hydroxyethyl]-3-N'-benzoyl-2-hydroxy-3-phenylpropanamide (3h)

Prepared from N-benzoyl-(2*R*,3*S*)-3-phenylisoserine (36.7 mg, 0.13 mmol) according to method A to afford product as a white powder (22.2 mg, 53%). ^{1}H-NMR (DMSO, 500MHz) δ 3.10 (m, 2H, NHCH_2CH_2OH) 3.27 (m, 2H, NHCH_2CH_2OH), 4.25 (d, J = 3.38 Hz, 1H, H-C(α)), 5.38 (dd, J = 8.63 Hz, 3.58 Hz, 1H, PhC(O)NHCH), 7.21-7.54 (m, 8H, H-Ar), 7.81 (m, 2H, H-Ar), 7.94 (t, J = 5.74, 1H, C(O)NH), 8.48 (d, J = 8.66 Hz, 1H, PhC(O)NH; CI-MS (NH_3): m/z 329 (m + 1)$^+$, 347 (m + 18)$^+$.

(2*S*,3*R*)-[2'N-hydroxyethyl]-*t*-Boc-3-amino-2-hydroxy-4-phenylbutanamide (3i)

Prepared from N-*t*-Boc-(2*S*,3*R*)-3-amino-2-hydroxy-4-methylbutyric acid (10.0 mg, 0.034 mmol) according to method A to afford product as a clear oil (5.8 mg, 50%). ^{1}H-NMR ($CHCl_3$, 500MHz) δ 1.35 (s, 9H, *Boc*NH),

3.00 (d, J = 7.53 Hz, 2H, CH_2Ph), 3.21 (m, 1H, NHCH_2CH$_2$OH) 3.62 (m, 2H, NHCH$_2$CH_2OH, 1H, NHCH_2CH$_2$OH), 4.04 (br s, 2H, BocNHCH), 4.45 (t, J = 7.9 Hz, CH$_2$OH), 4.98 (d, J = 8.8 Hz, 1H, H-C(α)), 6.65 (br s, 1H, C(O)NH), 7.20-7.30 (m, 5H, C$_6$H$_5$); CI-MS (NH_3): m/z 339 (m + 1)$^+$, 356 (m + 18)$^+$.

(2*S*,3*R*)-[2'N-hydroxyethyl]-*t*-Boc-3-amino-2-hydroxy-5-methylhexanamide (3j)

Prepared from N-*t*-Boc-(2*S*,3*R*)-3-amino-2-hydroxy-5-methylhexanoic acid (5.0 mg, 0.019 mmol) according to method A to afford product as a clear oil (3.3 mg, 57%). ^{1}H-NMR ($CHCl_3$, 500MHz) δ 0.93 (d, J = 7.3 Hz, 3H, CH_3 from iPr), 0.94 (d, J = 6.8 Hz, 3H, CH_3 from iPr), 1.39 (s, 9H, *Boc*NH, 1H from CH_2iPr under singlet), 1.65 (m, 1H, CH(CH$_3$)$_2$, 1H, CH_2iPr), 3.22 (m, 1H, NHCH_2CH$_2$OH) 3.65 (m, 2H, NHCH$_2$CH_2OH, 1H, NHCH_2CH$_2$OH), 3.91 (m, 1H, BocNHCH), 4.03 (d, J = 1.8 Hz, 1H,BocNH), 4.45 (t, J = 7.9 Hz, 1H, CH$_2$CH$_2$OH), 4.90 (d, J = 9.4 Hz, 1H, H-C(α)), 6.71 (br s, 1H, C(O)NH); CI-MS (NH_3): m/z 305 (m + 1)$^+$, 322 (m + 18)$^+$.

(2*S*)-[2'N-[(p-[10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)]-ethyl]-2-(p-[10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)-propanamide (4a)

Prepared from **3a** (1.0 mg, 7.6 μmol) according to method B to afford pure product as a deep purple powder (6.8 mg, 73%). UV/vis (CH_2Cl_2) 645 (8 800), 590 (10 800), 549 (15 800), 515 (34 100), 417 (690 000); ^{1}H-NMR ($CDCl_3$, 400MHz) δ -2.90 (s, 4H, NH of pyrrole), 1.82 (d, J = 6.6 Hz, 3H, CH_3CH), 3.92-3.99 (m, 2H, NHCH_2CH$_2$O), 4.75-4.77 (m, 2H, NHCH$_2$CH_2O), 5.75 (q, J = 6.6 Hz, 1H of H-C(α)), 7.11 (m, 1H, C(O)NH), 7.46-7.60 (m, 10 H, H-C(p,m) of phenyl), 7.71-7.75 (m, 8H, H-C(p,m) of phenyl), 7.88-7.98 (m, 8H, H-C(o) of phenyl), 8.14-8.18 (m, 4H, H-C(o) of phenyl), 8.27 (d, $J_{(o,m)}$ = 8.1 Hz, 2H of benzoate), 8.37 (d, $J_{(o,m)}$ = 8.1 Hz, 2H of benzoate), 8.45 (d, $J_{(o,m)}$ = 8.1 Hz, 2H of benzoate), 8.58 (d, $J_{(o,m)}$ = 8.1 Hz, 2H of benzoate), 8.63-8.79 (m, 16H of pyrrole); FABMS: m/z 1414 (m + H$^+$); CD (MCH): 422 (+113.2), 417 (0), 414 (-71.9); CD (CH_2Cl_2): 424 (+43.9), 419 (0), 416 (-26.7); CD (hexanes): 422 (+90.1), 416.5 (0), 414 (-51.2); CD (TEA): 422 (+67.5), 417.5 (0), 413 (-33.8).

(2*S*)-[2'N-[(p-[10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)]-ethyl]-2-(p-[10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)-3-methylbutanamide (4b)

Prepared from **3b** (0.7 mg, 4.4 μmol) according to method B to afford pure product as a deep purple powder (4.1 mg, 66%). UV/vis (CH_2Cl_2) 647 (13 600), 591 (16 800), 548 (21 300), 514 (39 300), 417 (690 000); ^{1}H-NMR ($CDCl_3$, 400MHz) δ -2.90 (s, 2H, NH of pyrrole), -2.88 (s, 2H, NH of pyrrole), 1.22 (d, J = 6.2 Hz, 3H, CH_3 from iPr), 1.24 (d, J = 6.2 Hz, 3H, CH_3 from iPr), 2.60-2.69 (m, 1H, CH(CH$_3$)$_2$), 3.87-4.02 (m, 2H, NHCH_2CH$_2$O), 4.73-4.75 (m, 2H, NHCH$_2$CH_2O), 5.56 (d, J = 4.4 Hz, 1H, H-C(α)), 6.9 ((m, 1H, C(O)NH), 7.45-7.59 (m, 10 H, H-C(p,m) of phenyl), 7.70-7.76 (m, 8H, H-C(p,m) of phenyl), 7.92-7.99 (m, 8H, H-C(o) of phenyl)), 8.16-8.17 (m, 4H, H-C(o) of phenyl), 8.28 (d, $J_{(o,m)}$ = 8.1 Hz, 2H of benzoate), 8.37 (d, $J_{(o,m)}$ = 8.1 Hz, 2H of benzoate), 8.44 (d, $J_{(o,m)}$ = 8.1 Hz, 2H of benzoate), 8.57 (d, $J_{(o,m)}$ = 8.1 Hz, 2H of benzoate), 8.65-8.79 (m, 16H of pyrrole); FABMS: m/z 1442 (m + H$^+$); CD (MCH): 422 (+113.2), 417 (0),

414 (-71.9); CD (CH_2Cl_2): 423 (+27.0), 418 (0), 415 (-13.1); CD (hexanes): 422 (+76.7), 417 (0), 414 (-50.0); CD (TEA): 422 (+61.0), 417 (0), 413 (-33.7).

(2*S*)-[2'N-[(p-[10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)]-ethyl]-2-(p-[10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)-4-methylpentanamide (4c)

Prepared from **3c** (0.26 mg, 1.84 μmol) according to method B to afford pure product as a deep purple powder (1.8 mg, 67%). UV/vis (CH_2Cl_2) 645 (11 800), 589 (14 100), 549 (19 800), 515 (36 600), 417 (690 000); ^{1}H-NMR ($CDCl_3$, 400MHz) δ -2.90 (s, 2H, NH of pyrrole), -2.89 (s, 2H, NH of pyrrole), 1.09 (d, J = 6.24 Hz, 3H, CH_3 from iPr), 1.11 (d, J = 6.28 Hz, 3H, CH_3 from iPr), 1.99-2.05 (m, 2H, iPrCH_2), 2.08-2.15 (m, 1H, CH(CH_3)$_2$), 3.91-3.96 (m, 2H, NHC$H_2$$CH_2O$), 4.72-4.74 (m, 2H, NHCH$_2$CH_2O), 5.71 (m, 1H, H-C(α)), 6.93 (m, 1H, C(O)NH), 7.44-7.58 (m, 10 H, H-C(p,m) of phenyl), 7.70-7.76 (m, 8H, H-C(p,m) of phenyl), 7.92-7.99 (m, 8H, H-C(o) of phenyl), 8.15-8.18 (m, 4H, H-C(o) of phenyl), 8.29 (d, $J_{(o,m)}$ = 8.3 Hz, 2H of benzoate), 8.36 (d, $J_{(o,m)}$ = 8.3 Hz, 2H of benzoate), 8.45 (d, $J_{(o,m)}$ = 8.3 Hz, 2H of benzoate), 8.55 (d, $J_{(o,m)}$ = 8.3 Hz, 2H of benzoate), 8.64-8.78 (m, 16H of pyrrole); IR (1 mM in CCl_4) 3411 (N-H amide), 3313 (N-H pyrrole), 1724 (ester C=O), 1709 (ester C=O), 1690 (amide C=O), 1607, 1263; FABMS: *m/z* 1456 (m + H$^+$); CD (MCH): 423 (+108.0), 418.5 (0), 415 (-74.1); CD (CH_2Cl_2): 424 (+36.5), 419 (0), 415 (-20.7); CD (hexanes): 422 (+96.6), 417 (0), 414 (-65.3); CD (TEA): 423 (+68.1), 417 (0), 413 (-39.5); CD (MeOH): n.d.; CD (toluene):
426 (+55.4), 417 (0), 413 (-39.5).

(2*S*)-[2'N-[(p-[10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)]-ethyl]-2-(p-[10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)-2-cyclohexylacetamide (4d)

Prepared from **3d** (1.5 mg, 7.4 μmol) according to method B to afford pure product as a deep purple powder (8.2 mg, 75%). UV/vis (CH_2Cl_2) 645 (8 400), 590 (10 800), 549 (16 400), 514 (35 400), 417 (690 000); ^{1}H-NMR ($CDCl_3$, 400MHz) δ -2.87 (s, 2H, NH of pyrrole), -2.86 (s, 2H, NH of pyrrole), 1.21-1.58 (m, 4H, cyclohexane), 1.71-2.18 (m, 6H, cycylohexane), 2.31 (m, 1H, cyclohexane), 3.85-4.06 (m, 2H, NHC$H_2$$CH_2O$), 4.73-4.77 (m, 2H, NHCH$_2$CH_2O), 5.56 (d, J = 4.4 Hz, 1H, H-C(α)), 6.87 (m, 1H, C(O)NH), 7.48-7.61 (m, 10H, H-C(p,m) of phenyl), 7.71-7.78 (m, 8H, H-C(p,m) of phenyl), 7.96-8.02 (m, 8H, H-C(o) of phenyl), 8.16-8.29 (m, 4H, H-C(o) of phenyl), 8.30 (d, $J_{(o,m)}$= 8.3 Hz, 2H of benzoate), 8.38 (d, $J_{(o,m)}$= 8.3 Hz, 2H of benzoate), 8.45 (d, $J_{(o,m)}$= 8.3 Hz, 2H of benzoate), 8.57 (d, $J_{(o,m)}$= 8.3 Hz, 2H of benzoate), 8.67-8.84 (m, 16 H of pyrrole); FABMS: *m/z* 1483 (m + H$^+$); CD (MCH): 422 (+82.0), 417.5 (0), 414 (-55.6); CD (CH_2Cl_2): n.d.; CD (hexanes): 422 (+62.7), 416.5 (0), 414 (-31.7); CD (TEA): 422 (+57.5), 417 (0), 413 (-25.0).

(2*S*)-[2'N-[(p-[10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)]-ethyl]-2-(p-[10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)-3-phenylpropanamide (4e)

Prepared from **3e** (0.45 mg, 2.30 μmol) according to method B to afford pure product as a deep purple powder (2.6 mg, 74%). UV/vis (CH_2Cl_2) 646 (10 400), 591 (11 700), 550 (16 300), 514 (35 400), 417 (690 000); ^{1}H-NMR ($CDCl_3$, 400MHz) δ -2.90 (s, 4H, NH of pyrrole), 3.55 (m, 2H, CH_2Ph), 3.85 (m, 2H, NHC$H_2$$CH_2O$),

4.59 (m, 2H, $NHCH_2CH_2O$), 5.89 (m, 1H, H-C(α)), 6.74 (t, J = 5.2 Hz, 1H, C(O)N*H*), 7.25-7.60 (m, 10H, H-C(p,m) of phenyl, 5 H, C_6H_5), 7.70-7.77 (m, 6H, H-C(p,m) of phenyl), 7.90-7.98 (m, 8H, H-C(o) of phenyl), 8.16-8.17 (m, 4H, H-C(o) of phenyl), 8.28 (d, $J_{(o,m)}$= 8.3 Hz, 2H of benzoate), 8.33 (d, $J_{(o,m)}$= 8.3 Hz, 2H of benzoate), 8.39 (d, $J_{(o,m)}$= 8.3 Hz, 2H of benzoate), 8.48 (d, $J_{(o,m)}$= 8.3 Hz, 2H of benzoate), 8.63-8.78 (m, 16 H of pyrrole); FABMS: *m/z* 1490 (m + H^+); CD (MCH): 436 (-10.1), 423 (+56.0), 418 (0), 413 (-23.3); (MeOH): n.d.; (TEA): 437 (-3.2), 426 (+35.6), 420 (0), 417 (-24.4); (CH_2Cl_2): 438 (-8.1), 424 (+36.6), 419 (0), 415 (-27.4); (toluene): 426 (+43.0), 420 (0), 417 (-33.5).

(2*S*)-[2'N-[(p-[10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)]-ethyl]-2-(p-[10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)-2-phenylacetamide (4f)

Prepared from **3f** (1.88 mg, 2.30 μmol) according to method B to afford pure product as a deep purple powder (12.0 mg, 83%). UV/vis (CH_2Cl_2) 645 (11 800), 590 (14 900), 550 (16 800), 515 (34 800), 417 (690 000); ^{1}H-NMR ($CDCl_3$, 400MHz) δ -2.87 (s, 2H, NH of pyrrole), -2.85 (s, 2H, NH of pyrrole), 3.89-4.04 (m, 2H, $NHCH_2CH_2O$), 4.75 (m, 2H, $NHCH_2CH_2O$), 6.61 (s, 1H, H-C(α)), 7.07 (m, 1H, C(O)N*H*), 7.41-7.77 (m, series of m, 18 H, H-C(p,m) of phenyl, 5H, H-C of mandelic phenyl), 7.95-8.07 (m, 8H, H-C(o) of phenyl), 8.17-8.20 (m, 4H, H-C(o) of phenyl), 8.28 (d, $J_{(o,m)}$ = 8.0 Hz, 2H of benzoate), 8.38 (d, $J_{(o,m)}$ = 7.8 Hz, 2H of benzoate), 8.40 (d, $J_{(o,m)}$ = 7.8 Hz, 2H of benzoate), 8.62 (d, $J_{(o,m)}$ = 8.2 Hz, 2H of benzoate), 8.71-8.82 (m, 16 H of pyrrole); FABMS: *m/z* 1476 (m + H^+); CD (MCH): 422 (+66.9), 418 (0), 414 (-47.7); (hexanes): 422 (+42.3), 417(0), 414 (-32.2); (TEA) 422 (+26.0), 418 (0), 414 (-15.6); (CH_2Cl_2): n.d.

(2*R*)-[2'N-[(p-[10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)]-ethyl]-2-(p-[10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)-2-phenylacetyamide (4g)

Prepared from **3g** (1.88 mg, 2.30 μmol) according to method B to afford pure product as a deep purple powder (12.0 mg, 84%). UV/vis (CH_2Cl_2) 645 (8 200), 590 (11 600), 550 (14 600), 515 (33 300), 417 (690 000); ^{1}H-NMR ($CDCl_3$, 400MHz) δ -2.87 (s, 2H, NH of pyrrole), -2.85 (s, 2H, NH of pyrrole), 3.89-4.03 (m, 2H, $NHCH_2CH_2O$), 4.75 (m, 2H, $NHCH_2CH_2O$), 6.60 (s, 1H, H-C(α)), 7.07 (m, 1H, C(O)N*H*), 7.41-7.77 (m, series of m, 18 H, H-C(p,m) of phenyl, 5H, H-C of mandelic phenyl), 7.94-8.06 (m, 8H, H-C(o) of phenyl), 8.16-8.19 (m, 4H, H-C(o) of phenyl), 8.28 (d, $J_{(o,m)}$ = 8.0 Hz, 2H of benzoate), 8.37 (d, 2H, $J_{(o,m)}$ = 8.0 Hz, 2H of benzoate), 8.39 (d, 2H, $J_{(o,m)}$ = 8.0 Hz, 2H of benzoate), 8.62 (d, 2H, $J_{(o,m)}$ = 8.0 Hz, 2H of benzoate), 8.71-8.82 (m, 16H of pyrrole); FABMS: *m/z* 1476 (m + H^+); CD (MCH): 422 (-65.0), 418 (0), 414 (+46.6); (hexanes): 422 (-45.9), 417(0), 414 (+30.5); (TEA) 422 (-25.6), 418 (0), 414 (+20.4); (CH_2Cl_2): n.d.

(2*R*,3*S*)-[2'N-[(p-[10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)]-ethyl]-[2-(p-[10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)]-3-N'-benzamide-3-phenylpropanamide (4h)

Prepared from **3h** (1.2 mg, 3.66 μmol) according to method B to afford product as a deep purple powder (4.5 mg, 76.4%). UV/vis (CH_2Cl_2) 643 (9 200), 589 (14 400), 549 (19 500), 515 (39 700), 417 (690 000); ^{1}H-NMR ($CHCl_3$, 500MHz) δ -2.91 (s, 2H, NH of pyrrole), -2.90 (s, 2H, NH of pyrrole), 3.79 (m, 2H, $NHCH_2CH_2O$), 4.49, 4.57 (2 m, 2H, $NHCH_2CH_2O$), 5.88 (dd, J = 8.24 Hz, 4.69 Hz, 1H, PhC(O)NHC*H*), 6.14 (d, J = 3.38 Hz, 1H, H-C(α)), 6.96 (t, J = 5.3 Hz, 1H, C(O)N*H*), 7.21-8.17 (series of m, 18 H, H-

C(p,m) of phenyl, 12H, H-C(o) of phenyl, 10 H, 2-C_6H_5), 8.24 (d, $J_{(o,m)}$= 7.99 Hz, 2H of benzoate), 8.34 (d, $J_{(o,m)}$= 8.01 Hz, 2H of benzoate), 8.40 (d, $J_{(o,m)}$= 8.01 Hz, 2H of benzoate), 8.54 (d, $J_{(o,m)}$= 8.02 Hz, 2H of benzoate), 8.62-8.78 (m, 16H of pyrrole, 1H, PhC(O)N*H*); FABMS: *m/z* 1609 (m + H^+); CD (MCH): 440 (+4.8), 422 (-33.8), 417 (0), 414 (+16.4); CD (TEA): 436 (+6.1), 422 (-37.2), 416.5 (0), 414 (+15.6); CD (toluene): 424 (39.9), 419 (0), 416 (+16.3); CD (hexanes): 438 (+6.3), 422 (-12.5), 416 (0), 412 (+6.6); CD (CH_2Cl_2): 440 (+6.3), 424 (-43.5), 417 (0), 414 (+24.9).

(2*S*,3*R*)-[2'N-[(p-[10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)]-ethyl]-[2-(p-[10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)]-t-Boc-3-amino-4-phenylbutanamide (4i)

Prepared from **3i** (1.3 mg, 3.9 μmol) according to method B to afford product as a deep purple powder (5.5 mg, 87%). UV/vis (CH_2Cl_2) 645 (10 100), 589 (13 900), 550 (19 100), 514 (39 200), 417 (690 000); ^{1}H-NMR ($CHCl_3$, 500MHz) δ -2.87 (s, 2H, NH of pyrrole), -2.86 (s, 2H, NH of pyrrole), 1.40 (s, 9H, *Boc*NH), 3.12 (m, 1H, C*H*$_2$Ph), 3.17 (m, 1H, C*H*$_2$Ph), 3.94 (m, 2H, NHC*H*$_2$CH$_2$O), 4.68 (m, 1H, BocNHC*H*), 4.75 (m, 2H, NHCH$_2$C*H*$_2$O), 5.38 (m, 1H, BocN*H*), 5.70 (1H, m, H-C(α)), 6.97 (m, 1H, C(O)N*H*), 7.20-7.38 (m, 5H, C_6H_5), 7.45-7.61 (m, 12H, H-C(p,m) of phenyl), 7.71-7.77 (m, 6H, H-C(p,m) of phenyl), 7.94-8.00 (m, 8H, H-C(o) of phenyl), 8.17-8.21 (m, 4H, H-C(o) of phenyl), 8.26-8.46 (series of m, 8H of benzoate), 8.66-8.84 (m, 16H of pyrrole); FABMS: *m/z* 1620 (M + H^+); CD (MCH): 440 (-1.68), 422 (+17.2), 418 (0), 414 (-17.1); CD (TEA): 422 (+9.3), 418 (0), 414 (-13.2); CD (toluene): 426 (+11.9), 420 (0), 416 (-13.5); CD (hexanes): n.d.; CD (CH_2Cl_2): 424 (+19.2), 419 (0), 414 (-12.2).

(2*S*,3*R*)-[2'N-[(p-[10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)]-ethyl]-[2-(p-[10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)]-*t*-Boc-3-amino-5-methylhexanamide (4j)

Prepared from **3j** (1.0 mg, 3.3 μmol) according to method B to afford product as a deep purple powder (3.2 mg, 61%). UV/vis (CH_2Cl_2) 645 (8 000), 589 (12 600), 550 (18 200), 514 (36 700), 417 (690 000); ^{1}H-NMR ($CHCl_3$, 500MHz) δ -2.87 (s, 4H, NH of pyrrole), 1.02 (d, *J* = 6.6 Hz, 3H, C*H*$_3$ from iPr), 1.04 (d, *J* = 6.5 Hz, 3H, C*H*$_3$ from iPr), 1.46 (s, 9H, *Boc*NH), 1.65 (m, 2H, C*H*$_2$iPr), 1.85 (m, 1H, C*H*(CH$_3$)$_2$), 3.93 (m, 2H, NHC*H*$_2$CH$_2$O), 4.47 (m, 1H, BocNHC*H*), 4.73 (m, 2H, NHCH$_2$C*H*$_2$O), 5.10 (d, *J* = 8.8 Hz, 1H, N*H*Boc), 5.66 (m, 1H, H-C(α)), 7.03 (m, 1H, C(O)N*H*), 7.45-7.61 (m, 12H, H-C(p,m) of phenyl), 7.71-7.82 (m, 6H, H-C(p,m) of phenyl), 7.95-7.99 (m, 8H, H-C(o) of phenyl), 8.16-8.18 (m, 4H, H-C(o) of phenyl), 8.29 (d, $J_{(o,m)}$= 7.83 Hz, 2H of benzoate), 8.37 (d, $J_{(o,m)}$= 7.66 Hz, 2H of benzoate), 8.46 (d, $J_{(o,m)}$= 7.12 Hz, 2H of benzoate), 8.57 (d, $J_{(o,m)}$= 7.92 Hz, 2H of benzoate), 8.67-8.84 (m, 16H of pyrrole); FABMS: *m/z* 1586 (M + H^+); CD (MCH): 422 (+40.7), 418 (0), 414 (-38.7); CD (TEA): 422 (+50.8), 417 (0), 414 (-34.4); CD (toluene): 426 (+31.5), 419.5 (0), 416 (-21.4); CD (hexanes): 422 (+14.0), 417 (0), 412 (-15.1); CD (CH_2Cl_2): 424 (+43.0), 419 (0), 414 (-24.0).

(2*S*)-[(p-[10',15',20'-triphenyl-5'porphyrinyl]benzoyl)-ethyl]-2-(p-[10',15',20'-triphenyl-5'porphyrinyl]benzoyl)-4-methylpentanoate (5a)

step 1, (2*S*)-[hydroxyethyl]-2-hydroxy-4-methylpentanoate: To a solution of (-)-2-hydroxyisocaproic acid (49.0 mg, 0.371 mmol) in ethylene glycol (8 mL) was added EDC (175.0 mg, 0.913 mmol) and DMAP (111.5 mg,

0.913 mmol). The solution was stirred at rt (4 days), dissolved in CH_2Cl_2 (40 mL), washed with sat. aq. NH_4Cl (2 x 20 mL), brine (2 x 20 mL), dried with Na_2SO_4, and evaporated. Product was purified by silica chromatography (MeOH/CH_2Cl_2 1:15) to afford product as an off white solid (5.4 mg, 8.2%). It was then used immediately in the next reaction; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.93 (d, J = 6.67 Hz, 3H, CH_3 from iPr), 0.94 (d, J = 6.59 Hz, 3H, CH_3 from iPr), 1.56 (m, 2H, CH_2iPr), 1.88 (m, 2H, $CH(CH_3)_2$), 2.05 (br s, 1H, OH), 2.72 (br s, 1H, OH), 3.85 (t, J = 4.62 Hz, 2H, OCH_2CH_2OH), 4.24 (t, J = 6.79 Hz, 1H, H-C(α)), 4.29 (2H, m, OCH_2CH_2OH), CI-MS (NH_3): m/z 194 (m + 18)$^+$.

step 2, final product: A solution of TPP (8.4 mg, 12.8 mmol), EDC (0.81 mg, 4.26 mmol), and DMAP (0.52 mg, 4.26 mmol) in CH_2Cl_2 (1 mL) was added to a solution of product obtained from step 1 (0.7 mg, 3.97 mmol) in CH_2Cl_2 (1 mL). The mixture was stirred for 24 h at rt, diluted with CH_2Cl_2 (20 mL), washed with a solution of sat. aq. NH_4Cl (3 x 25 mL), brine (2 x 25 mL), dried (Na_2SO_4), and evaporated to give crude product which was purified by silica chromatography (CH_2Cl_2/MeOH, 40:1) to afford product as a purple powder (1.0 mg, 16%). UV/vis (CH_2Cl_2) 644 (5 600), 589 (8 400), 548 (16 200), 514 (29 900), 418 (690 000); ^{1}H NMR ($CDCl_3$, 400MHz) δ -2.85 (s, 2H, NH from pyrrole), -2.84 (s, 2H, NH from pyrrole), 1.11 (d, J = 6.7 Hz, 6H, $CH(CH_3)_2$), 1.99-2.34 (m, 3H, $CH_2CH(CH_3)_2$), 4.75 (m, 2H, OCH_2CH_2O), 4.81 (m, 2H, OCH_2CH_2O), 5.55 (dd, 2H, J = 9.2 Hz, 4.0 Hz, H-C(α)), 7.5-7.78 (m, 18H, H-C(p,m) of phenyl), 8.04-8.20 (m, 12 H-C(o) of phenyl), 8.28, (d, $J_{(o,m)}$ = 7.9 Hz, 2H of benzoate), 8.33 (d, $J_{(o,m)}$ = 8.2 Hz, 2H of benzoate), 8.48 (d, $J_{(o,m)}$ = 7.7 Hz, 2H of benzoate), 8.50 (d, $J_{(o,m)}$ = 7.9 Hz, 2H of benzoate), 8.72-8.82 (m, 16H, pyrrole); FABMS: m/z 1457 (m + H$^+$); CD (MCH): 422(+27.0), 417 (0), 414 (-12.2); CD (CH_2Cl_2): 425 (+10.6), 418 (0), 413 (-5.33); CD (hexanes): 422 (+29.9), 416.5 (0), 412 (-13.8); CD (MeOH): 424(+36.4), 415.5 (0), 411 (-6.2); CD (TEA): 422 (+37.3), 416.5 (0), 412 (-18.4).

(2*S*)-[2'N-[(p-[10',15',20'-triphenyl-5'-porphyrinyl]benzamide]-ethyl]-2-(p-[10',15',20'-triphenyl-5'-porphyrinyl]-benzoyl)-4-methylpentanamide (5b)

step 1, N-[p-[10',15',20'-triphenyl-5'-porphyrinyl]benzamide)-N'-Boc-ethylene diamine: To a solution of TPP (10.4 mg, 15.8 μmol), EDC (3.9 mg, 20.5 μmol), amd DMAP (2.5 mg, 20.5 μmol) in CH_2Cl_2 (1.5 mL), was added N-Boc-ethylenediamine (7.6 mg, 47.4 μmol). The mixture was stirred overnight at rt and was applied directly to a silica column (50:1 CH_2Cl_2/MeOH) to yield pure product as a deep purple powder (3.4 mg, 68%); UV/vis (CH_2Cl_2) 417, 515, 548, 589, 644; ^{1}H NMR ($CDCl_3$, 400 MHz) δ - 2.80 (s, 2 H, NH of pyrrole), 1.47 (s, 9H, *Boc*NH), 3.54 (m, 2H, CH_2), 3.73 (m, 2H, CH_2), 5.10 (m, 1H, NH amide), 7.58 (m, 1H, NH amide), 7.68- 7.81 (m, 9H, H-C(p,m) of phenyl), 8.14-8.29 (m, 6H, H-C(o) of phenyl, 4H of benzamide), 8.77-8.86 (m 8H, pyrrole); CI-MS (NH_3, neg ion): m/z 800 (m).

step 2, (2*S*)-N-[p-[10',15',20'-triphenyl-5'-porphyrinyl]benzamide)-ethyl]-2-hydroxy-4-methylpentanamide: 4M HCl in dioxane (2 mL) was added to the product from step 1 (15.0 mg, 18.8 μmol). The solution was stirred at rt for 1.5 h followed by the removal of solvent. The compound was resuspended in CH_2Cl_2 (2 mL) and washed with aq sat. $NaHCO_3$ (2 X 1 mL) and then dried with Na_2SO_4. The free amine was obtained as green powder after the removal of solvent. This was used immediately for the following reaction. (-)-2-hydroxy-isocaproic acid (2.3 mg, 17.0 μmol), and CDI (2.8 mg, 17.0 μmol) were stirred in CH_2Cl_2 (1.5 mL) for 40 minutes, followed by the addition of the free amine prepared above. The mixture was stirred overnight at rt and

was applied directly to a silica column (40:1 CH_2Cl_2/MeOH) to yield pure product as a deep purple powder (3.8 mg, 28%); UV/vis (CH_2Cl_2), 417, 514, 548, 589, 644; ^1H NMR ($CDCl_3$, 400 MHz) δ -2.80 (s, 2 H, NH of pyrrole), 0.94 (d, J = 6.6 Hz, 6H, $CH(CH_3)_2$), 1.59-1.86 (m, 3H, $CH_2CH(CH_3)_2$), 3.68 (m, 2H, CH_2), 3.77 (m, 2H, CH_2), 4.21 (m, 1H, H-C(α)), 7.57 (m, 1H, NH amide), 7.70- 7.77 (m, 9H, H-C(p, m) of phenyl, 1H, NH amide under m), 8.18-8.30 (m, 6H, H-C(o) of phenyl, 4H of benzamide), 8.76-8.83 (m, 8H, pyrrole); CI-MS (NH_3): m/z 815 $(m+1)^+$.

step 3, final product: A solution of product obtained from step 2 (2.8 mg, 3.4 μmol) in CH_2Cl_2 (0.5 mL) was added to a solution of TPP (4.0 mg, 6.1μmol), EDC (1.2 mg, 6.2μmol), and DMAP (0.8 mg, 6.2 μmol) in CH_2Cl_2 (1 mL) at rt. The mixture was stirred overnight at rt and was applied directly to a silica column (40:1 CH_2Cl_2/MeOH) to yield pure product as a deep purple powder (3.4 mg, 68%). UV/vis (CH_2Cl_2) 645 (13 000), 590 (16 300), 549 (21 100), 515 (40 100), 417 (690 000); ^1H NMR ($CDCl_3$, 400 MHz) δ -2.87 (s, 2 H, NH of pyrrole), -2.85 (s, 2 H, NH of pyrrole), 1.09, (d, J = 6.22 Hz, 3H, CH_3 from iPr) 1.10 (d, J = 6.15 Hz, 3H, CH_3 from iPr), 1.97 - 2.16 (m, 3H, $CH_2CH(CH_3)_2$), 3.76-3.92 (m, 4H, $NHCH_2CH_2NH$), 5.67 (dd, 1H, J = 9.7 Hz, 3.35 Hz, H-C(α)), 7.11 (m, 1H, NH amide), 7.45 (m, 1H, NH amide), 7.54 (m, 18H, H-C(p, m) of phenyl), 8.03 (m, 12 H, H-C(o) of phenyl), 8.20 - 8.29 (2d, $J_{(o,m)}$ = 8.10 Hz, 8.06 Hz 4H of benzoate), 8.36-8.56 (2d, $J_{(o,m)}$ = 7.98 Hz, 8.06 Hz 4H of benzoate), 8.72 - 8.82 (m, 16H of pyrrole); FABMS: m/z 1453 ($m + H^+$); CD (CH_2Cl_2): 425 (+41.92), 419 (0), 415 (-14.89); CD (hexanes): 422 (+33.6), 417 (0), 414 (-24.5); CD (MCH): 424 (+52.7), 419 (0), 414 (-28.87); CD (MeOH): n.d.; CD (TEA): 423 (+85.3), 417 (0), 413 (-39.2); CD (toluene): 426 (+50.7), 420 (0), 417 (-23.8).

(2*S*)-[(p-[10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)-propyl]-2-(p-[10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)-4-methylpentanoate (5c)

step 1, (2*S*)-[hydroxypropyl]-2-hydroxy-4-methylpentanoate: To a solution of (-)-2-hydroxyisocaproic acid (124.5 mg, 0.94 mmol) in CH_2Cl_2 (40 mL) at rt was added EDC (270.9 mg, 1.41 mmol) and DMAP (172.3 mg, 1.41 mmol). After 5 minutes, 1,3-propanediol (1.75 g, 23.0 mmol) was added and the reaction mixture was stirred at room temperature for 24 h. The excess diol was decanted and the organic layer was washed with aqueous sat. NH_4Cl (3 x 40 mL), followed by aqueous sat. NaCl (2 x 40 mL), and dried with $MgSO_4$. The residue was purified by silica gel flash chromatography (20:1 CH_2Cl_2/ MeOH) to afford a cleare oil as product (11.8 mg, 7%); ^1H-NMR ($CDCl_3$, 400MHz) δ 0.91 (d, J = 3.2 Hz, 3H, CH_3 from iPr), 0.94 (d, J = 3.2 Hz, 3H, CH_3 from iPr), 1.53 (m, 1H, CH_2) 1.80-1.95 (m, 3H, CH_2, $CH(CH_3)_2$), 2.13 (br s, 2H, OH), 3.68 (t, J = 12.4 Hz, 2H, $CH_2CH_2CH_2OH$), 4.18 (m, 1H, H-C(α)) , 4.32 (t, J = 12.4 Hz, 2H, $CH_2CH_2CH_2OH$); CI-MS (NH_3): m/z 208 $(m + 18)^+$.

step 2, final product: A solution of the product obtained from step 1 (0.75 mg, 3.2 μmol) in CH_2Cl_2 (1.0 mL) was added to a solution of TPP (7.7 mg, 11.8 μmol), EDC (2.3 mg,11.8 μmol), and DMAP (1.45 mg, 11.8 μmol) in CH_2Cl_2 (0.5 mL). The reaction mixture was stirred at rt for 22 h. The solution was applied directly to a silica gel column (85:1 CH_2Cl_2/MeOH) to yield pure product as a deep purple powder (3.6 mg, 62%). UV/vis (CH_2Cl_2) 644 (4 700), 589 (6 600), 550 (10 200), 514 (24 600), 418 (690 000); ^1H-NMR ($CDCl_3$, 400MHz) δ -2.81 (s, 2H, NH of pyrrole), -2.80 (s, 2H, NH of pyrrole), 1.20 (d, J = 6.51 Hz, 3H, CH_3 from iPr), 1.30 (d, J = 6.51 Hz, 3H, CH_3 from iPr), 1.91-2.41 (4 sets of m, 5H, $CH_2CH(CH_3)_2$, $NHCH_2CH_2CH_2O$), 4.59 (t, J =

6.4 Hz, 2H, CH_2), 4.67 (m, 2H, CH_2), 5.51 (dd, 1H, J = 9.8 Hz, 4.0 Hz, H-C(α)), 7.65-7.75 (m, 18 H, H-C(p,m) of phenyl), 8.15-8.20 (m, 12H, H-C(o) of phenyl), 8.31 (m, 4H of benzoate), 8.48 (m, 4H of benzoate), 8.78-8.83 (m, 16H of pyrrole); FABMS: *m/z* 1472 ($M+H^+$); CD (CH_2Cl_2): 424 (+6.3), 419 (0), 415 (-7.0); CD (MCH): n.d.; CD (hexanes): n.d.; CD (TEA): n.d.; CD (toluene): n.d.

General procedure for 5d-5f:

step 1 (attaching aminoalcohol linker): To a solution of (-)-2-hydroxyisocaproic acid (29.7 mg, 0.23 mmol) in THF (2 mL) at rt was added carbonyldiimidazole (43.8 mg, 0.27 mmol). The mixture was stirred at rt for 1 h. The diol or aminoalcohol linker used (3.38 mmol) was added and the reaction mixture was stirred at rt for 12 h. After the removal of solvent, the residue was purified by silica gel flash chromatography (12:1 CH_2Cl_2/ MeOH) to afford product .

step 2 (forming bisporphyrin derivative): To a solution of TPP (6.4 mg, 9.7 μmol), EDC (1.9 mg, 10.1 μmol), and DMAP (1.23 mg, 10.1 μmol) in CH_2Cl_2 (1.0 mL), a solution of product obtained from step 1 (0.61 mg, 3.2 μmol) in CH_2Cl_2 (1.0 mL) was added. The reaction mixture was stirred at rt for 12 h. The solution was applied directly to a silica gel column (70:1 CH_2Cl_2/MeOH) followed by a pipette silica column (7:3 $CHCl_3$/hexanes) to yield pure product as a deep purple powder.

(2*S*)-[2'N-[(p-[10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)]-propyl]-2-(p-[10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)-4-methylpentanamide (5d)

step 1, (2*S*)-[2N'-[hydroxypropyl]]-2-hydroxy-4-methylpentanamide was prepared from (-)-2-hydroxyisocaproic acid (29.7 mg, 0.23 mmol) according to step one afforded a clear oil as product (16.1 mg, 38%). ^{1}H-NMR ($CDCl_3$, 400MHz) δ 0.93 (d, J = 6.6 Hz, 3H, CH_3 from iPr), 0.95 (d, J = 6.6 Hz, 3H, CH_3 from iPr), 1.47-1.54, 1.61-1.71 (m, 4H, $(CH_3)_2CHCH_2$, $NHCH_2CH_2CH_2OH$), 1.81 (m, 1H, $CH(CH_3)_2$), 2.60 (br s, 2H, OH), 3.43 (m, 2H, $NHCH_2CH_2OH$), 3.60 (m, 2H, $NHCH_2CH_2OH$), 4.14 (dd, J = 10 Hz, 3.1 Hz, 1H, H-C(α)), 6.89 (br s, 1H, C(O)N*H*); CI-MS (NH_3): *m/z* 190 (m + 1)$^+$, 207 (m + 18)$^+$.

step 2, final product was prepared from step 1 product (0.61 mg, 3.2 μmol) according to step 2 afforded pure product as a deep purple powder (3.0 mg, 64%). UV/vis (CH_2Cl_2) 644 (5 400), 590 (8 500), 549 (14 300), 514 (35 300), 417 (690 000); ^{1}H-NMR ($CDCl_3$, 400MHz) δ -2.83 (s, 2H, NH of pyrrole), -2.80 (s, 2H, NH of pyrrole), 1.10 (d, J = 8.64 Hz, 3H, CH_3 from iPr), 1.12 (d, J = 8.44 Hz, 3H, CH_3 from iPr), 1.99-2.23 (3 sets of m, 5H, $CH_2CH(CH_3)_2$, $NHCH_2CH_2CH_2O$-), 3.65 (m, 2H, $NHCH_2CH_2O$), 4.67 (m, 2H, $NHCH_2CH_2O$), 5.71 (dd, J = 9.3 Hz, 3.5 Hz, 1H, H-C(α)), 6.89 (t, J = 6.0 Hz, 1H, C(O)N*H*), 7.35-7.51 (m, 7 H, H-C(p,m) of phenyl), 7.63-7.77 (m, 11H, H-C(p,m) of phenyl), 8.00-8.07 (m, 4H, H-C(o) of phenyl), 8.12-8.21 (m, 8H, H-C(o) of phenyl), 8.26 (d, $J_{(o,m)}$ = 8.1 Hz, 2H of benzoate), 8.37 (d, $J_{(o,m)}$ = 8.1 Hz, 2H of benzoate), 8.44 (d, $J_{(o,m)}$ = 8.0 Hz, 2H of benzoate), 8.57 (d, $J_{(o,m)}$ = 8.1 Hz, 2H of benzoate), 8.70-8.82 (m, 16H of pyrrole); FABMS: *m/z* 1470 (m + H^+); CD (MCH): 423 (+68.4), 417 (0), 414 (-48.3); CD (CH_2Cl_2): 424 (+42.7), 419 (0), 415 (-23.8); CD (hexanes): 422 (+47.0), 416 (0), 412 (-32.6); CD (TEA): 423 (+64.1), 417.5 (0), 413 (-46.3); CD (toluene): 426 (+51.9), 420 (0), 413 (-43.3).

(2*S*)-[2'N-[(p-[10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)]-butyl]-2-(p-[10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)-4-methylpentanamide (5e)

step 1, (2*S*)-[N'-[hydroxybutyl]]-2-hydroxy-4-methylpentanamide was prepared from (-)-2-hydroxyisocaproic acid (25.9 mg, 0.20 mmol) according to step 1 to afford a clear oil as product (23.0 mg, 57%); ^{1}H-NMR ($CDCl_3$, 400MHz) δ 0.91 (d, *J* = 6.6 Hz, 3H, C*H*$_3$ from iPr), 0.93 (d, *J* = 6.6 Hz, 3H, C*H*$_3$ from iPr), 1.44-1.61 (m, 6H, NHCH$_2$C*H*$_2$C*H*$_2$CH$_2$OH, (CH$_3$)$_2$CHC*H*$_2$, 1.81 (m, 1H, (CH$_3$)$_2$C*H*), 3.26 (m, 2H, NHC*H*$_2$CH$_2$), 3.63 (t, *J* = 5.8 Hz, 2H, CH$_2$C*H*$_2$OH), 4.07 (dd, *J* = 9.9 Hz, 3.4 Hz, 1H, HC(α)), 6.89 (br s, 1H, C(O)N*H*); CI-MS (NH_3): *m/z* 204 (M+1)$^+$, 221 (M+18)$^+$.

step 2, final product was prepared from step 1 product (0.48 mg, 2.35 μmol) according to step 2 to afford pure product as a deep purple powder (3.1 mg, 89%). UV/vis (CH_2Cl_2) 645 (8 000), 589 (11 900), 549 (18 000), 514 (41 600), 417 (690 000); ^{1}H-NMR ($CDCl_3$, 500MHz) δ -2.82 (s, 2H, NH of pyrrole), -2.81 (s, 2H, NH of pyrrole), 1.09 (d, *J* = 5.9 Hz, 3H, C*H*$_3$ from iPr), 1.10 (d, *J* = 5.7 Hz, 3H, C*H*$_3$ from iPr), 1.66 (m, 1H, CH(CH$_3$)$_2$), 1.90-2.12 (3 sets of m, 6H, iPrC*H*$_2$, NHCH$_2$C*H*$_2$C*H*$_2$CH$_2$O), 3.56 (m, 2H, NHC*H*$_2$CH$_2$), 4.58 (t, *J* = 6.3 Hz, 2H, NHCH$_2$C*H*$_2$O), 5.65 (dd, *J* = 9.4 Hz, 3.5 Hz, 1H, H-C(α)), 6.39 (t, *J* = 5.9Hz, 1H, C(O)N*H*), 7.63-7.76 (m, 18 H, H-C(p,m) of phenyl), 8.11-8.20 (m, 12H, H-C(o) of phenyl), 8.29 (d, $J_{(o,m)}$ = 8.1 Hz, 2H of benzoate), 8.35 (d, $J_{(o,m)}$ = 8.1 Hz, 2H of benzoate), 8.44 (d, $J_{(o,m)}$ = 8.1 Hz, 2H of benzoate), 8.49 (d, $J_{(o,m)}$ = 8.1 Hz, 2H of benzoate), 8.74-8.82 (m, 16H of pyrrole); FABMS: *m/z* 1485 (M + 1)$^+$; CD (MCH): 426 (+4.7), 417 (0), 414 (-8.1); CD (CH_2Cl_2): 424 (+8.0), 419 (0), 416 (-8.6); CD (hexanes): 420 (+2.9), 416 (0), 412 (-4.9); CD (TEA): 423 (+10.2), 417 (0), 413 (-8.1); CD (toluene): 426 (+4.8), 420 (0), 413 (-6.6).

(2*S*)-[2'N-[(p-[10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)]-hexyl]-2-(p-[10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)-4-methylpentanamide (5f)

step 1: (2*S*)-[2'N-[hydroxyhexyl]]-2-hydroxy-4-methylpentanamide was prepared from (-)-2-hydroxyisocaproic acid (11.2 mg, 84.7 μmol) according to step 1 to afford a yellow oil as product (11.7 mg, 60%); ^{1}H-NMR ($CDCl_3$, 400MHz) δ 0.93 (d, *J* = 6.6 Hz, 3H, C*H*$_3$ of iPr), 0.94 (d, *J* = 6.7 Hz, 3H, C*H*$_3$ of iPr), 1.33-1.63 (series of m, 10H, NHCH$_2$(C*H*$_2$C*H*$_2$)$_2$CH$_2$OH, (CH$_3$)$_2$CHC*H*$_2$), 1.82 (m, 1H, (CH$_3$)$_2$C*H*), 3.25 (m, 2H, NHC*H*$_2$CH$_2$), 3.61 (t, *J* = 6.4 Hz, 2H, CH$_2$C*H*$_2$OH), 4.10 (dd, *J* = 9.9 Hz, 3.3 Hz, 1H, H-C(α)), 6.61 (br s, 1H, C(O)N*H*); CI-MS (NH_3): *m/z* 232(m + 1)$^+$, 249 (m + 18)$^+$.

step 2, final product was prepared from step 1 product (0.79 mg, 3.4 μmol) according to step 2 to afford pure product as a deep purple powder (2.0 mg, 39%) . UV/vis (CH_2Cl_2) 644 (5 400), 591 (8 200), 549 (12 100), 514 (17 500), 417 (690 000); ^{1}H-NMR ($CDCl_3$,400MHz) δ -2.83 (s, 2H, NH of pyrrole), -2.82 (s, 2H, NH of pyrrole), 1.07 (m, J = 5.2 Hz, 3H, C*H*$_3$ from iPr), 1.08 (d, *J* = 5.2 Hz, 3H, C*H*$_3$ from iPr), 1.55-1.73 (m, 10H, iPrC*H*$_2$, NHCH$_2$(C*H*$_2$C*H*$_2$)$_2$CH$_2$O), 1.96 (m, 1H, CH(CH$_3$)$_2$), 3.44 (m, 2H, NHC*H*$_2$CH$_2$O), 4.51 (t, *J* = 6.6 Hz, 2H, NHCH$_2$C*H*$_2$O), 5.62 (dd, 1H, *J* = 9.0 Hz, 3.4 Hz, H-C(α)), 6.30 (m, 1H, C(O)N*H*), 7.64-7.76 (m, 18 H, H-C(p,m) of phenyl), 8.14-8.19 (m, 12H, H-C(o) of phenyl), 8.24 (d, $J_{(o,m)}$ = 8.0 Hz, 2H of benzoate), 8.33 (d, $J_{(o,m)}$ = 8.3 Hz, 2H of benzoate), 8.39 (d, $J_{(o,m)}$ = 8.2 Hz, 2H of benzoate), 8.47 (d, $J_{(o,m)}$ = 8.3 Hz, 2H of benzoate), 8.73-8.84 (m, 16H of pyrrole); FABMS: *m/z* 1514 (M+1)$^+$; CD (MCH): n.d.; CD (CH_2Cl_2):

423 (+6.0), 420 (0), 415 (-5.4); CD (hexanes): n.d.; CD (TEA): n.d.; CD (MeOH): n.d.; CD ($CHCl_3$, very noisy): 424 (+3.9), 419 (0), 416 (-5.0).

(2*S*)-[2'N-[(p-[zinc-10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)]-ethyl]-2-(p-[zinc-10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)-2-cyclohexylacetamide (6)

To a solution of **4d**, (2*S*)-[2'N-[p-[10',15',20'-triphenyl-5'-porphyrinyl]benzoyl]-ethyl]-2-(p-[10',15',20'-triphenyl-5'porphyrinyl]benzoyl)-2-cyclohexylacetamide (8.2 mg, 5.5 μmol) in $CHCl_3$ (1.0 mL), $Zn(OAc)_2$ (10 mg, 54.5 μmol) was added. The reaction mixture was stirred at rt for 11h. The solution was applied directly to a silica gel column (100:1 CH_2Cl_2/MeOH), then a second column (toluene/EtOAc 20:1) to yield pure Zn bisporphyrin compound (6.9 mg, 78%) as a deep purple powder. UV/vis (CH_2Cl_2, neutral): 586 (4 600), 548 (41 300), 418 (782 000); UV/vis (CH_2Cl_2, 1μL i-$PrNH_2$/mL): 604 (18 600), 563 (40 500), 428 (878 600);^{1}H-NMR ($CDCl_3$, 400MHz) δ 1.23-1.93 (m, 10H, of cyclohexane), 2.23 (m, 1H, cyclohexane), 3.78-3.98 (m, 2H, NHCH_2CH_2OH), 4.67-4.72 (m, 2H, NHCH_2CH_2OH), 5.46 (d, J = 4.1 Hz, 1H, H-C(α)), 6.82 (t, J = 4.6 Hz, 1H, C(O)N*H*), 7.50-7.69 (m, 10H, H-C(p,m) of phenyl), 7.71-7.73 (m, 8H, H-C(p,m) of phenyl), 7.94-8.00 (m, 8H, H-C(o) of phenyl), 8.15 (m, 4H, H-C(o) of phenyl), 8.27 (d, $J_{(o,m)}$= 7.8 Hz, 2H of benzoate), 8.36 (d, $J_{(o,m)}$= 7.7 Hz, 2H of benzoate), 8.40 (d, $J_{(o,m)}$= 8.0 Hz, 2H of benzoate), 8.53 (d, $J_{(o,m)}$= 8.1Hz, 2H of benzoate), 8.71-8.86 (m, 16 H of pyrrole); FABMS: *m/z* 1610 ($M+H^+$); CD (MCH, c = 1.56e-6M, 1μL i-$PrNH_2$/mL MCH): 434 (+86.0), 429 (0), 424 (-70.7).

(2*S*)-[2'N-[(p-[zinc-10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)]-ethyl]-2-(p-[10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)-2-cyclohexylacetamide (7)

step 1, Zn porphyrin on 1° alcohol: (2*S*)-[2'N-[p-[zinc-10',15',20'-triphenyl-5'porphyrinyl]benzoyl)]-ethyl]-2-hydroxy-2-cyclohexylacetamide: To a solution of TPP (4.2 mg, 6.38 μmol), EDC (1.3 mg, 7.0 μmol), and DMAP (0.86 mg, 7.0 μmol) in CH_2Cl_2 (1.0 mL), a solution of **4d** (6.0 mg, 29.9 μmol) in CH_2Cl_2 (2.0 mL)was added. The reaction mixture was stirred at rt for 12 h. $Zn(OAc)_2$ (3mg, 12.1μmol) was then added. After 3 hours of stirring at rt, the solution was applied directly to a silica gel column (40:1 CH_2Cl_2/MeOH) to yield pure product (3.9 mg, 67.6%) as a magenta powder; UV/vis (CH_2Cl_2) 547 (24 300), 419 (574 000); ^{1}H-NMR ($CDCl_3$, 400MHz) δ 1.18-1.72 (m, 10H, cyclohexane), 1.92 (m, 1H, cyclohexane), 3.36 (m, 1H, H-C(α)), 3.43 (m, 2H, NHCH_2CH_2O), 4.34 (t, J = 5.2 Hz, 2H, NHCH_2CH_2O), 6.56 (t, J = 5.6 Hz, 1H, C(O)N*H*), 7.71-7.79 (m, 9H, H-C(p,m) of phenyl), 8.20-8.31 (m, 6H, H-C(o) of phenyl and 4H of benzoate), 8.83-8.96 (m, 8 H of pyrrole); CI-MS (NH_3): *m/z* 905 $(M+1)^+$, 922 $(M + 18)^+$.

step 2, 2H porphyrin on 2° alcohol: To a solution of TPP (5.0 mg, 7.6 μmol), EDC (1.56 mg, 8.17 μmol), and DMAP (1.0 mg, 8.17 μmol) in CH_2Cl_2 (2.0 mL), a solution of product obtained from step 1 (3.9 mg, 4.3 μmol) in CH_2Cl_2 (2.0 mL)was added. The reaction mixture was stirred at rt for 21 hr. The solution was applied directly to a silica gel column (50:1 CH_2Cl_2/MeOH) to yield pure product (3.9 mg, 67.6%) as a red powder; UV/vis[39] (CH_2Cl_2): 644 (2 000), 590 (7 300), 547 (24 400), 514 (17 6000), 418 (736 000); UV/vis (MCH, neutral): 644, 592, 546, 512, 415; UV/vis (i$PrNH_2$1μL/mL MCH): 646, 600, 559, 514, 427, 417; ^{1}H-NMR ($CDCl_3$, 500MHz) δ -2.87 (s, 2H, NH of pyrrole), 1.18-1.72 (m, 10H, cyclohexane), 1.92 (m, 1H, cyclohexane), 3.43 (m, 2H, NHCH_2CH_2O), 4.34 (t, J = 5.2 Hz, 2H, NHCH_2CH_2O), 5.46 (d, J = 4.43 Hz, 1H, H-C(α)), 6.81 (t, J = 5.5

Hz, 1H, C(O)N*H*), 7.47-7.64 (m, 12H, H-C(p,m) of phenyl), 7.72-7.78 (m, 6H, H-C(p,m) of phenyl), 7.99-8.05 (m, 8, H-C(o) of phenyl), 8.18-8.20 (m, 4, H-C(o) of phenyl), 8.31 (d, $J_{(o,m)}$= 8.1 Hz, 2H of benzoate), 8.39 (d, $J_{(o,m)}$= 8.1 Hz, 2H of benzoate), 8.43 (d, $J_{(o,m)}$= 8.2 Hz, 2H of benzoate), 8.57 (d, $J_{(o,m)}$= 8.0 Hz, 2H of benzoate),8.72-8.99 (m, 16 H of pyrrole); FAB-MS m/z 1546 $(M + 2)^+$; CD (MCH/neutral) 428 (+44.6), 423 (0), 418 (-27.9); CD ($iPrNH_2$ 1μL/mL MCH):[39] 430 (sh, +15.2), 422 (30.8), 418 (0), 414 (26.6).

(2*S*)-[2'N-[(p-[10',15',20'-triphenyl-5'-porphyrinyl]benzoyl)]-ethyl]-2-hydroxy-4-methylpentanamide (8)

To a solution of TPP (3.1 mg, 4.7 μmol), EDC (0.9 mg, 4.7 μmol), and DMAP (0.57 mg, 4.7 μmol) in CH_2Cl_2 (1.0 mL), a solution of **3c** (5 mg, 28.6 μmol) in CH_2Cl_2 (1.0 mL) was added. The reaction mixture was stirred at rt for 2 h. The solution was applied directly to a silica gel column (80:1 CH_2Cl_2/MeOH) to yield pure product as a deep purple powder (2.6 mg, 68%). UV/vis (CH_2Cl_2) 645 (4 600), 589 (6 700), 549 (9 200), 515 (19 700), 417 (350 000); ^{1}H-NMR ($CDCl_3$, 400MHz) δ -2.84 (s, 2H, NH of pyrrole), 0.97 (d, J = 6.5 Hz, 6H, $CH(CH_3)_2$), 1.60 (m, 2H, iPrCH_2), 1.86 (m, 1H, $CH(CH_3)_2$), 3.84 (m, 2H, $NHCH_2CH_2O$), 4.13 (m, 1H, H-C(α)), 4.62 (t, J = 4.8 Hz, 2H, $NHCH_2CH_2O$), 6.48 (m, 1H, C(O)N*H*), 7.72-7.79 (m, 9 H, H-C(p,m) of phenyl), 8.20 (d, J = 6.85 Hz, 6H, H-C(o) of phenyl), 8.30 (d, $J_{(o,m)}$ = 7.9 Hz, 2H of benzoate), 8.42 (d, $J_{(o,m)}$ = 7.9 Hz, 2H of benzoate), 8.84 (m, 8H of pyrrole); CI-MS (NH_3): *m/z* 816 $(M + 1)^+$; CD (MCH): n.d.; CD (CH_2Cl_2): n.d.; CD (TEA): n.d.

Acknowledgments. We would like to thank Xuefei Huang for helpful discussions with the zinc porphyrin experiments. This study was supported by NIH GM 34509.

References and Notes

1. Harada, N.; Nakanishi, K. *Circular Dichroic Spectroscopy - Exciton Coupling in Organic Stereochemistry*; University Science Books: Mill Valley, 1983.
2. Nakanishi, K.; Berova, N. The Exciton Chirality Method. In *Circular Dichroism, Principles and Applications;* Nakanishi, K.; Berova, N.; Woody, R. W. Eds.; VCH Publishers: New York, 1994; pp. 361.
3. Matile, S.; Berova, N.; Nakanishi, K. *Enantiomer* **1996**, *1*, 1.
4. Corey, E. J.; Link, J. O. *Tetrahedron Lett.* **1992**, *33*, 3431.
5. Koh, K.; Durst, T. *J. Org. Chem.* **1994**, *59*, 4683.
6. Kim, M.-J.; Whitesides, G. M. *J. Am. Chem. Soc.* **1988**, *110*, 2959.
7. Evans, D. A.; Morissey, M. M.; Dorrow, R. L. *J. Am. Chem. Soc.* **1985**, *107*, 4346.
8. Prelog, V.; Wilhelm, M.; Bright, D. B. *Helv. Chim. Acta* **1954**, *37*, 221.
9. Lee, J. B.; Downie, I. M. *Tetrahedron* **1967**, *23*, 359.
10. Mori, K.; Takigawa, T.; Matsuo, T. *Tetrahedron* **1979**, *35*, 933.
11. Barton, D. H. R.; Ollis, D. W. . In *Comprehensive Organic Chemistry;* Barton, D. H. R.; Ollis, D. W. Eds.; Pergamon Press: Oxford, 1979; pp. 69.
12. Hanessian, S. *Total Synthesis of Natural Products: The Chiron Approac*h. In *Total Synthesis of Natural Products: The Chiron Approach;* Hanessian, S. Ed.; Pergamon Press: New York, 1983; pp. Chapter 2.

13. Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512.
14. Corey, E. J.; Bakshi, R. K. *Tetrahedron Lett.* **1990**, *31*, 611.
15. Akiyama, T.; Nishimoto, H.; Ozaki, S. *Tetrahedron Lett.* **1991**, *32*, 1335.
16. Gimple, O.; Schreier, P.; Humpf, H.-U. *Tetrahedron: Asymmetry* **1997**, *8*, 11.
17. Matile, S.; Berova, N.; Nakanishi, K.; Novkova, S.; Philipova, I.; Blagoev, B. *J. Am. Chem. Soc.* **1995**, *117*, 7021.
18. Matile, S.; Berova, N.; Nakanishi, K.; Fleischhauer, J.; Woody, R. *J. Am. Chem. Soc.* **1996**, *118*, 5198.
19. Huang, D.; Matile, S.; Berova, N.; Nakanishi, K. *Heterocycles* **1996**, *42*, 723.
20. Matile, S.; Berova, N.; Nakanishi, K. *Chemistry and Biology* **1996**, *3*, 379.
21. Scheidt, W. R.; Lee, Y. J. *Struct. Bond.* **1987**, *64*, 24.
22. Fuhrhop, J.-H.; Demoulin, C.; Boettcher, C.; Köning, J.; Siggel, U. *J. Am. Chem. Soc.* **1992**, *114*, 4159.
23. Leighton, P.; Cowan, J. A.; Abraham, R. J.; Sanders, J. K. M. *J. Org. Chem.* **1988**, *53*, 733.
24. Hunter, C. A.; SanDers, J. K. M. *J. Am. Chem. Soc.* **1990**, *112*, 5525.
25. Hunter, C. A.; Leighton, P.; Sanders, J. K. M. *J. Chem. Soc. Perkin Trans. 1* **1989**, 547.
26. Tamiaki, H.; Suzuki, S.; Maruyama, K. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 2633.
27. Bucks, R. R.; Boxer, S. G. *J. Am. Chem. Soc.* **1982**, *104*, 340.
28. Ricci, J. S.; Bousvaros, A.; Taylor, A. *J. Org. Chem.* **1982**, *47*, 3063.
29. Rich, D. H.; Moon, B. J.; Boparai, A. S. *J. Org. Chem.* **1980**, *45*, 2288.
30. A Detailed study for choosing this linker is discussed later in this paper.
31. (*S*)-mandelic acid was also used as a model. Three different linkers were compared: ethanolamine, ethylenediamine and 1,3-propanolamine with amplitudes of +115, +24, and +77, respectively (in MCH).
32. Hunter, C. A.; Meah, M. N.; Sanders, J. K. M. *J. Am. Chem. Soc.* **1990**, *112*, 5773.
33. (a) Zn dimer in CH_2Cl_2 (λ_{max} = 418 nm, ε = 782 000); (b) the Zn dimer in CH_2Cl_2 containing 1μL/mL isopropylamine displays a red shift and increases in epsilon (λ_{max} = 428 nm, ε = 878 600) relative to the neutral Zn dimer.
34. Abraham, R. J.; Fell, S. C. M.; Pearson, H.; Smith, K. M. *Tetrahedron* **1979**, *35*, 1759.
35. Abraham, R. J.; Eivazi, F.; Pearson, H.; Smith, K. M. *J. Chem. Soc., Chem. Comm.* **1976**, 699.
36. This was a qualitative study to ensure that intramolecular stacking is possible between the Zn and 2H-porphyrins. See experimental of **7**.
37. Scheer, H.; Katz, J. J. *Porphyrins and Metalloporphyrins*; Elsevier Scientific Publishing Company: Amsterdam, 1975.
38. CD ($CHCl_3$): 424 (+3.9), 419 (0), 416 (-5.0). The other solvents, MCH, TEA, and hexanes show no CD amplitudes at all. An amplitude of (+10) is observed in CH_2Cl_2. The ^{1}H-NMR spectrum of this compound shows very little stacking interactions in $CHCl_3$.
39. The extinction coefficient was estimated by taking the average of the two known extinction coefficients for **4d** (bis-TPP) and and **6** (Zn-bis-TPP) (690 000 and 782 000, respectively). This molecule was synthesized in order to conduct a qualitative experiment. Exact values were not essential for the UV and CD analysis.