HETEROCYCLES, Vol. 61, 2003, pp. 417 - 432
Received, 6th August, 2003, Accepted, 8th October, 2003, Published online, 14th October, 2003

# SYNTHESES AND SPECTROSCOPIC PROPERTIES OF METHYLBENZOATE DERIVATIVES OF TETRABENZOPORPHYRIN, APPLICATION TO CIRCULAR DICHROISM STUDIES

**Maryline Giraud-Roux, Gloria Proni, Koji Nakanishi, * and Nina Berova***

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

Abstract – The syntheses, UV-VIS and fluorescence data of two methylbenzoate derivatives of tetrabenzoporphyrins, i.e., 5-*p*-methoxycarbonylphenyl-tetrabenzoporphyrin (TBPPh$CO_2$Me), 5-*p*-methoxycarbonylphenyl-10,15,20-triphenyltetrabenzoporphyrin (TPTBP$CO_2$Me), and their zinc and magnesium complexes are described. The latter was tested as a bis(zinc-porphyrin) host in the CD-based molecular recognition studies because of its expanded surface compared to the conventional porphyrin rings and its red shifted Soret band with a large extinction coefficient.

## INTRODUCTION

During the last few years porphyrins and metalloporphyrins have been widely used in the studies of π-π interactions, photosynthetic mimics and molecular recognition.[1] Due to their intense red shifted Soret band, their propensity to undergo π-π stacking in a stereocontrolled manner, and facile metal incorporation, porphyrins have attracted widespread attention as reporter groups for structural studies by circular dichroism (CD) spectroscopy.[2,3] The chromophore 5-(*p*-carboxyphenyl)-10,15,20-triphenylporphyrin (TPPCOOH) has been extensively employed for structural analysis and determination of chirality following three main approaches. (i): It has been used as a reporter group for absolute configurational assignments of chiral diols with a rigid skeleton by the CD exciton chirality method. The enhanced sensitivity obtained in comparison with commonly used chromophores allows observation of

exciton coupling over very large distances.[4] (ii): Hydroxyl- and amino-containing chiral compounds with acyclic flexible skeletons have been converted into their bis-derivatives of Zn-(TPPCOOH). Under conditions in which the bis-derivatives undergo stereoselective intramolecular π-π stacking, the CD couplet reveals the absolute sense of twist between the porphyrins dictated by the configuration of the chiral substrate.[5] (iii): An alternative approach requiring no porphyrin derivatization is possible for mono- and bis-functionalized chiral compounds, namely, a chiral bidentate conjugate (guest) forms a host/guest complex with a bis(Zn-porphyrin)tweezer (host). The absolute configuration of the conjugate determines the absolute sense of twist between the two porphyrins by favoring a host/guest conformation where the bulkier group lies outside the complex giving rise to an exciton CD couplet. This approach has been applied to amines,[6, 7] secondary alcohols[8] and carboxylic acids.[9]

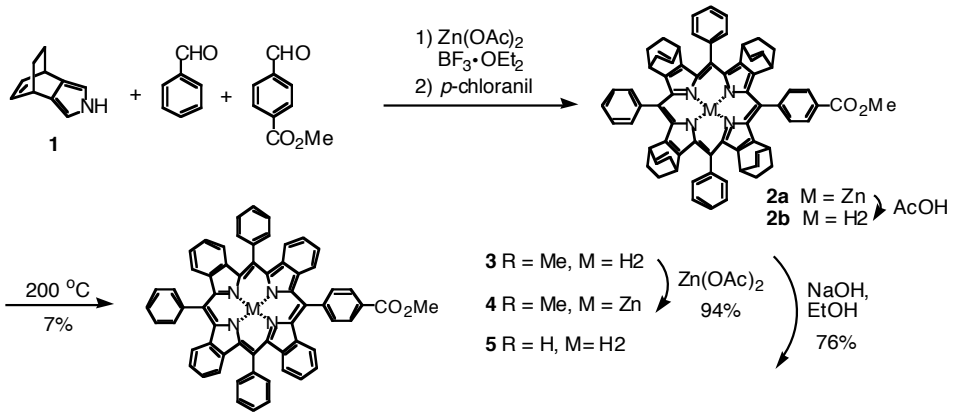
To further explore the use of porphyrins as CD reporter groups and to improve the CD sensitivity and chiral recognition, we are currently developing new porphyrin chromophores. We focused our attention on a subset of porphyrins bulkier than tetraphenylporphyrin and also on porphyrins expected to show stronger fluorescence for possible application in Fluorecence Detected Circular Dichroism (FDCD),[10] a technique with generally much higher sensitivity than conventional CD. Tetrabenzoporphyrins (TBP) appeared to be good candidates because of the expanded surface compared to porphyrin and their unique spectral properties. *Meso*-tetraphenylsubtituted TBPs (TPTBP) exhibit large extinction coefficients (*ca.* 300,000) and red-shifted Soret (*ca.* 460 nm) and Q bands.[11, 12] The metallated Zn and Mg TBP also show an intense and narrow Soret band (*ca.* 426 nm and 428 nm) in most solvents while the absorption spectrum of the free TBP (H2-TBP) is more complex.[13-15] Another attractive property of TBPs is their high fluorescence compared to tetraphenylporphyrins. Literature shows that the fluorescence quantum yield depends on the geometry of the tetrapyrrole ring and on the nature of the metal forming the complex.[16] The quantum yields of H2-TBP and Mg-TBP are 0.41 and 0.50, respectively, while that of Zn-TBP is 0.11 and lower. In order to use TBPs as CD-reporter group, the presence of a phenyl substituent bearing a carboxyl group was required for derivatization of chiral molecule of interest. In this paper, the syntheses of 5-*p*-methoxycarbonylphenyl-10,15,20-triphenyltetrabenzoporphyrin (TPTBP$CO_2$Me) and 5-*p*-methoxycarbonylphenyltetrabenzoporphyrin (TBPPh$CO_2$Me) and their spectroscopic properties are

described. We also report results using dimeric (Zn-TPTBP) chromophore as a host for absolute configuration studies of chiral compounds.

## RESULTS AND DISCUSSION

### Synthesis and spectral properties of 5-*p*-methoxycarbonylphenyl-10,15,20-triphenyltetrabenzoporphyrins and 5-*p*-methoxycarbonylphenyltetrabenzoporphyrins.

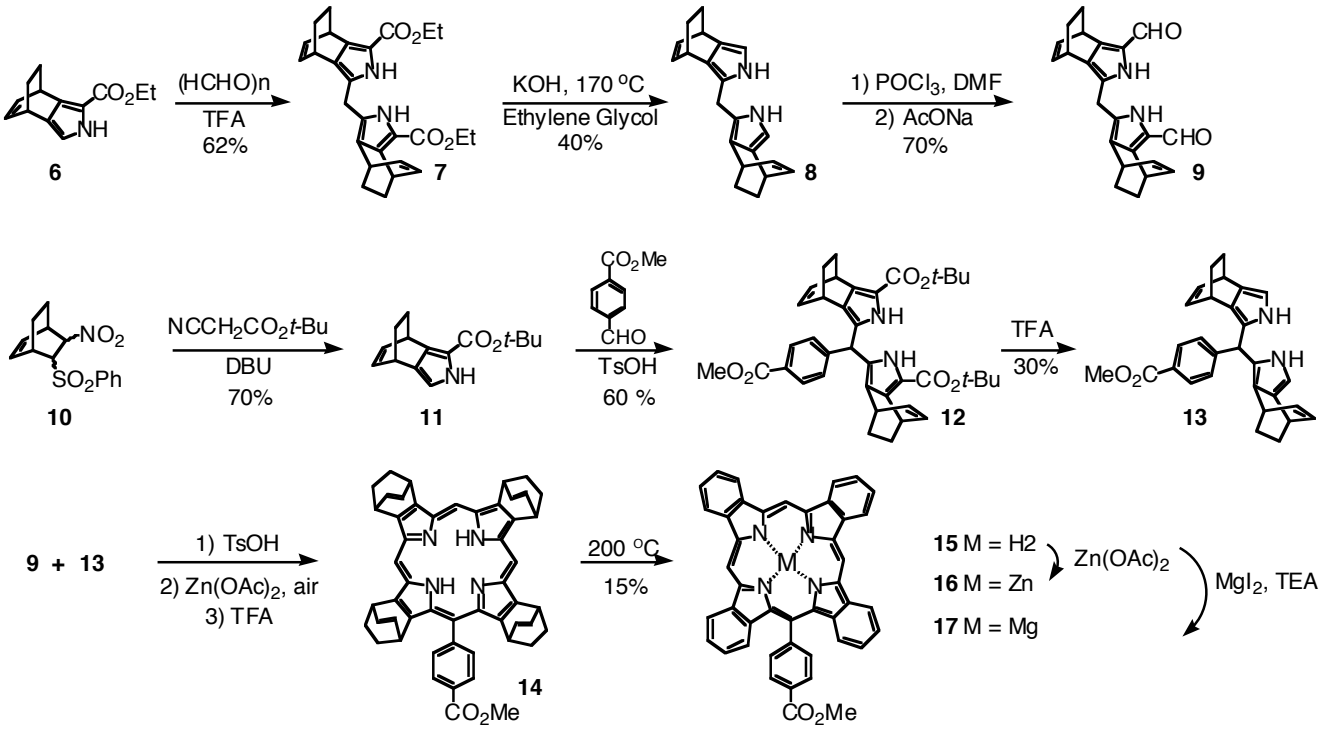
Convenient methods for the preparation of symmetrical TBPs with functional groups have recently been reported.[17-19] To prepare TPTBP$CO_2$Me **(3)**, we used a strategy described for the preparation of symmetrical TPTBP based on the thermal reaction of porphyrins fused with bicyclo [2.2.2]octadiene.[17] In our case we condensed two different aldehydes with the isoindole precursor **(1)** prepared according to the literature.[20] Mixed condensation between isoindole **(1)**, benzaldehyde and methyl 4-formylbenzoate catalysed by $BF_3$-etherate and subsequent oxidation gave a statistical mixture of zinc derivatives including **2a**. Treatment of **2a** with acetic acid to remove the zinc provided **2b** which after *retro* Diels-Alder reaction led to porphyrin **(3)** that was isolated from the mixture of compounds by chromatography with a yield of 7%. Zinc-TPTBP$CO_2$Me **(4)** was readily obtained by reaction with an excess of zinc acetate with a yield of 94%. (Scheme 1)




**Scheme 1**

Mono *meso*-phenylsubstituted TBP **(15)** was prepared by application of the "2 + 2" MacDonald methodology and using intermediates **(6)** and **(10)** as described by Ono and coworkers (Scheme 2).[17,20] Reaction of isoindole **(6)** with paraformaldehyde in the presence of trifluoroacetic acid afforded the

dicarboxylate compound **(7)**, yield 62%. Cleavage of the ester groups with KOH in ethylene glycol at 170°C, performed in the dark to avoid polymerization, gave compound **(8)** in a moderate yield. Diformylation in presence of $POCl_3$/DMF followed by hydrolysis with an aqueous solution of sodium acetate led to compound **(9)** with a yield of 70%. On the other hand, *t*-butyl 4,7-dihydro-4,7-ethanoisoindole-1-carboxylate **(11)** was prepared by treatment of **10** with *t*-butyl isocyanoacetate and DBU. Condensation between **11** and methyl 4-formylbenzoate catalyzed by toluene-*p*-sulfonic acid, under mild conditions compatible with the presence of *tert*-butyl ester groups, afforded **12**. Decarboxylation by TFA at room temperature gave the product **(13)**. Condensation between **9** and **13** with toluene-*p*-sulfonic acid followed by air oxidation in presence of zinc acetate followed by demetalation with TFA led to intermediate **(14)** that was not purified. TBPPh$CO_2$Me **(15)** was obtained by *retro* Diels-Alder reaction with a yield of 15% after purification. The zinc and the magnesium complexes **(16)** and **(17)** were easily prepared from **15** by reactions, respectively, with zinc acetate and magnesium iodide in the presence of triethylamine.




**Scheme 2**

Figure 1a shows the UV-VIS absorption spectra of porphyrins **(3)** and **(4)** in dichloromethane. Similarly to symmetrical TPTBP absortion spectra, both Soret and Q bands are red-shifted in comparison to tetraphenylporphyrin (Soret *ca*. 423 nm) and tetrabenzoporphyrin.[22] The extinction coefficients of **3** and **4**

measured in $CH_2Cl_2$ are 291,000 ($\lambda_{max}$ = 464 nm) and 305,700 ($\lambda_{max}$ = 456 nm).

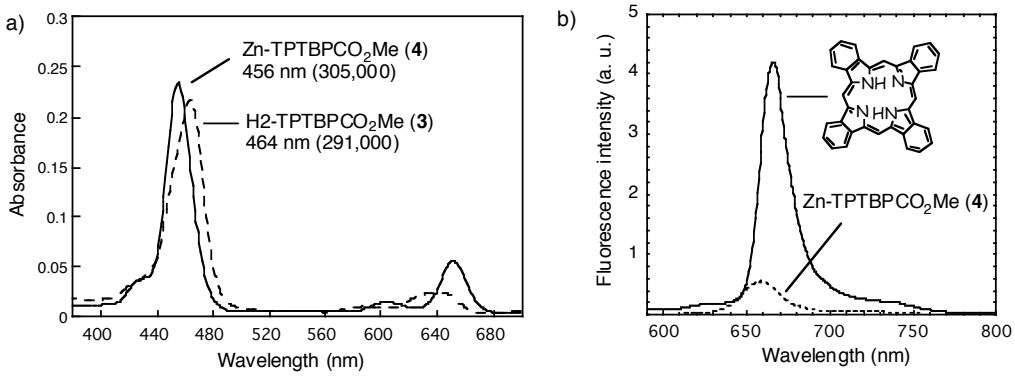



**Figure 1**. (a) Absorption spectra of $TPTBPCO_2Me$ **(3)** and **(4)** in $CH_2Cl_2$. (b) Fluorescence emission of Zn-$TPTBPCO_2Me$ **(4)** compared to H2-TBP (solutions in $CH_2Cl_2$ with an absorbance = 0.15)

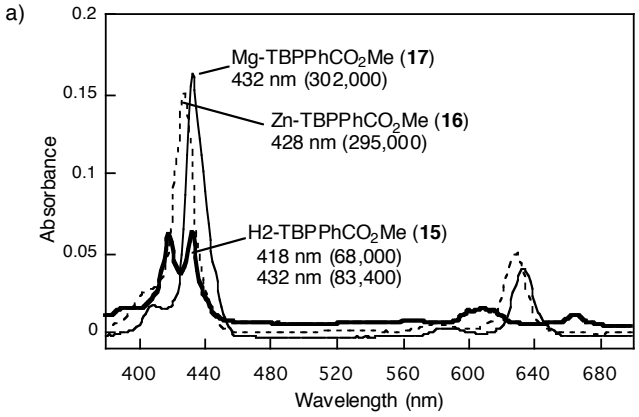
The fluorescence properties of **(4)** were also studied. The emission spectrum in dichloromethane consists of a single band with a maximum centered at 657 nm. The fluorescence spectra of a solution of **(4)** in dichloromethane and a solution of H2-TBP with similar absorbances are given in Figure 1b. Fluorescence quantum yield ($\Phi_f$) was determined using H2-TBP as reference and calculations using the following equation:[23]

$$\Phi_{f\,(S)} = \Phi_{f\,(R)} \left( \mathbf{F}_{(S)} / \mathbf{F}_{(R)} \right) \left( \mathbf{A}_{(R)} / \mathbf{A}_{(S)} \right) \left( \mathbf{n_D}_{(S)} / \mathbf{n_D}_{(R)} \right)$$

where $\Phi_{f\,(R)}$ is the quantum yield of H2-TBP in non-degassed DMF ($\Phi_{f\,(R)}$ = 0.41),[16] A is the absorbance at the excitation, F is the integrated area of the emission spectra, and n is the refractive index of the solution. The symbols S and R refer to the sample and the reference, respectively. The quantum yield calculated according to the equation is 0.06. The fact that Zn-TPTBP exhibits a low fluorescence compared to TBPs had already been briefly mentioned but no value of $\Phi_f$ was reported.[11] X-Ray data by Cheng *et al*. show that TPTBP adopts a saddle-shaped structure. This non-planarity resulting from the steric hindrance between the *meso*-phenyl substituents and the benzoporphyrin ring might be a reason for its much weaker fluorescence.[24]

Figure 2a shows the UV-VIS spectra of monophenylsubstituted TBP (**15**, **16** and **17**). Zn-$TBPPhCO_2Me$ **(16)** and Mg-$TBPPhCO_2Me$ **(17)** exhibit intense and narrow Soret band at 428 nm and 432 nm, respectively. These absorptions are slightly red shifted (2-3 nm) compared to the corresponding

symmetrical TBPs. As described for the unsubstituted H2-TBP, the absorption of H2-TBPPhCO$_2$Me **(15)** is more complex (split Soret and Q bands) and also much less intense.[13] Fluorescence emission bands for **15**, **16** and **17** are reported in Figure 2b. The quantum yields were determined as described previously for **4** using H2-TBP as reference. High fluorescence was obtained for H2-TBPPhCO$_2$Me **(15)** ($\Phi_f$ = 0.36) and Mg-TBPPhCO$_2$Me **(17)** ($\Phi_f$=0.41) while a weaker fluorescence was obtained for Zn-TBPPhCO$_2$Me **(16)**. These results are in agreement with the fact that the introduction of Mg increases the fluorescence while introduction of Zn leads to a decreases.[16] In contrast with the *meso*-tetraphenylsubstituted TPTBPCO$_2$Me **(4)**, the presence of a *meso-p*-methoxycarbonyl substituent in **15** has a negligible effect on the fluorescence.




b)

| | Fluorescence Emission | Quantum yield* |
|---|---|---|
| 16 | 630 nm | 0.18 |
| 15 | 665 nm | 0.36 |
| 17 | 633 nm | 0.41 |

* determinated using H2-TBP as reference ($\Phi_f$ = 0.41)

**Figure 2.** (a) Absorption spectra of TBPPhCO$_2$Me **(15**, **16** and **17)** in $CH_2Cl_2$. (b) Fluorescence emission and quantum yield of **15**, **16** and **17** in $CH_2Cl_2$.

**Zn-tetraphenyltetrabenzoporphyrin tweezer**

The intense and narrow absorption bands exhibited by TPTBPCO$_2$Me **(3)** and **(4)** and by TBPPhCO$_2$Me **(16)** and **(17)** suggest that these new porphyrins appear to be suited for exciton coupling interactions. In the first application, we tested the chromophore Zn-TPTBPCO$_2$Me **(4)** as a dimeric porphyrin host for absolute configurational assignments. We synthesized tweezer **(18)** by coupling 1,5-dibromopentane with 5-*p*-carboxyphenyl-10,15,20-triphenyltetrabenzoporphyrin **(5)** in presence of DBU followed by zinc insertion. Tweezer **(18)** exhibits similar UV-VIS absorption to the monomer **(4)** ($\lambda_{max}$ = 456 nm, $\varepsilon$ = 600,000 ($CH_2Cl_2$)), however with twice the intensity. We tested this new tweezer which is significantly

bulkier than the Zn-tetraphenylporphyrin (Zn-TPP) tweezer used earlier by employing several chiral substrates. These results were compared with the data of (Zn-TPP) tweezer reported earlier.[6-9] In the tweezer protocol, the chiral substrate (as depicted in Figure 3 for the carboxylic acid **(19)**) is derivatized with an achiral carrier to give a bifunctional conjugate. This conjugate forms a 1:1 host guest complex with the zinc porphyrin tweezer *via* coordination to the zinc atoms of the porphyrins P-1 and P-2. For conjugates derived by chiral carboxylic acids, the zinc in porphyrin P-1 coordinates with the terminal primary amino group while the amide carbonyl is responsible for the complexation with P-2. In the case of secondary alcohols, secondary amines and primary amines a nitrogen/zinc coordination is always responsible for the host-guest binding to P1 and P2. The two porphyrins in the complex adopt a preferred helicity dictated by the substituents (Large L, Medium M) on the basis of their conformational energy values[25] and consequently related to the chirality of the stereogenic center. An exciton coupled CD is detected, the sign of which is diagnostic of the absolute configuration of the substrate. In particular, the most stable conformer when conjugate **(20)** is sandwiched between the two TPTBPs leads to a positive helicity in which the less bulky group is sanwiched between P-1 and P-2, while the bulkier group L is pointed out and away from the P-2 porphyrin ring.

Table 1 summarizes the CD data of conjugates from **20** to **25** after complexation with Zn-TPP tweezer and Zn-TPTBP tweezer **(18)**. Data with conjugates **(20**, **21**, **22**, **24)** and Zn-TPP tweezer have previously been reported.[6-9] Conjugates **(23)** and **(25)** were prepared according to the literature procedure.[7] Thirty equivalents of conjugate was added to *ca.* 1 □M solution of porphyrin tweezers and UV/CD were measured in methylcyclohexane. The UV-VIS and CD spectra of complex **(20)** with tweezer **(18)** are shown in Figure 3. Upon binding a shift to higher wavelenghts of the zinc porphyrin Soret band occurs from 453 nm to 463 nm. Conjugate **(20)** gave the expected positive CD couplet with an amplitude more than two-fold intense than with Zn-TPP tweezer. The two groups L= Et and M= Me are distinguished on the basis of their conformational energy values that are, respectively, 1.79 and 1.65.[25] This subtle energy difference results in a better stereodifferentiation with tweezer **(18)**.

With conjugates **(21)** and **(22)**, the tweezer gave CD amplitudes comparable to those obtained with the Zn-TPP tweezer. Replacement of the isopropyl group in **22** with an ethyl group as in **23** resulted in a low

amplitude but with the right predicted sign while the results with Zn-TPP tweezer is not in agreement with the prediction based on the steric size.

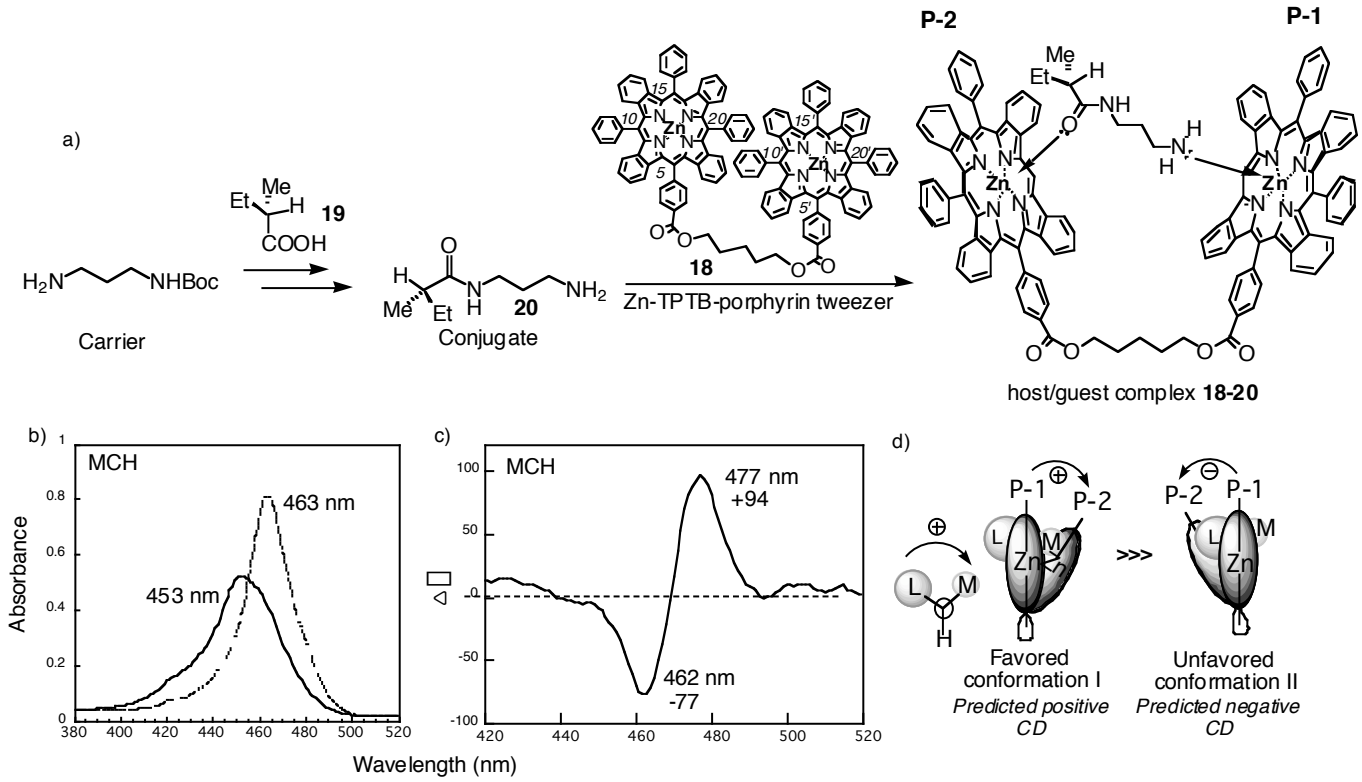



**Figure 3.** (a) Complex formation between conjugate **(20)** and Zn-TPTBP tweezer **(18)** (two phenyl groups have been ommited in the representation of the complex **(18-20)** for clarity) . (b) UV-VIS spectra of Zn-TPTBP tweezer **(18)** before complexation (solid line) and after complexation with **20** (dotted line). (c) CD spectrum of complex **(18-20)**. d) Intra porphyrin twist adopted according to the subtituent relative size.

Finally with conjugates **(24)** and **(25)** from benzyl secondary amines, tweezer **(18)** gave CD couplets with the predicted sign and good amplitude although weaker compared to Zn-TPP tweezer. These last two results may suggest that bulky aromatic groups (naphthyl in **24**) attached to the stereogenic center or in  positions (Bn in **25**) are better handled by the Zn-TPP tweezer. Further investigations of this new tweezer are currently ongoing by varying the lengths of the linker between the two porphyrins, and by exploring new carriers and screening various ligands. In summary, new benzoporphyrins TPTBPCO$_2$Me **(3/4)** and

TBPPhCO$_2$Me **(15/16/17)** have been prepared. These porphyrins exhibit intense UV-VIS absorptions and a narrow Soret band (except for TBPPhCO$_2$Me **(15)**) indicating their suitability for exciton coupled CD.

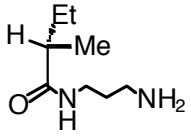
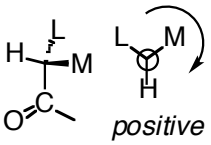
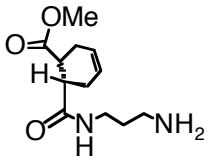
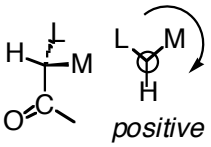
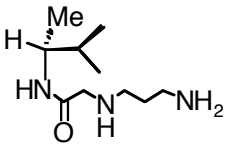
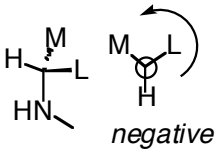
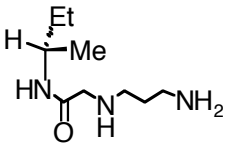
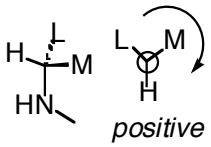
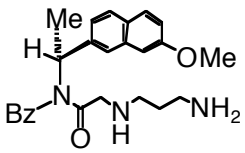
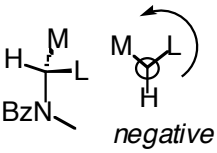
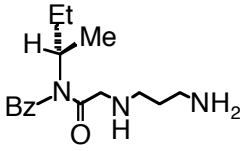
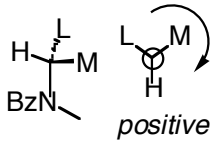
| Conjugates | CD Couplet *predicted* | **Zn-TPP Tweezer** | | **Zn-TPTBP Tweezer** | |
|---|---|---|---|---|---|
| | | □ □□ | $A_{CD}$ | □ □□ | $A_{CD}$ |
|  **20** |  *positive* | 430 nm + 40<br>421 nm - 35 | + 75 | 477 nm + 95<br>462 nm - 77 | + 172 |
|  **21** |  *positive* | 430 nm + 54<br>421 nm - 20 | + 74 | 479 nm + 30<br>463 nm - 19 | + 49 |
|  **22** |  *negative* | 433 nm - 42<br>422 nm + 38 | - 80 | 484 nm - 50<br>464 nm + 30 | - 80 |
|  **23** |  *positive* | 430 nm - 21<br>421 nm - 16 | - 37 | 482 nm + 14<br>464 nm - 10 | + 24 |
|  **24** |  *negative* | 430 nm - 503<br>421 nm + 436 | - 939 | 486 nm - 273<br>469 nm + 233 | - 506 |
|  **25** |  *positive* | 434 nm + 263<br>423 nm - 196 | + 459 | 484 nm + 145<br>468 nm - 124 | + 269 |

**Table 1.** Structure of conjugates from **20** to **25**, predicted CD couplet sign and CD data with Zn-TPP and Zn-TPTBP **18** tweezers.

Fluorescence quantum yields of monophenyl subtituted TBPs are comparable to those of TBPs and is very high for Mg-TBPPh$CO_2$Me **(17)**. For CD applications, we prepared the Zn-TPTBP tweezer and tested it for the determination of absolute configuration of several substrates. Zn-TPTBP chromophore with a larger surface did not necessarily leads to increased CD sensitivity. The use of Zn or Mg-TBPPh$CO_2$Me **(16/17)** as a tweezer for similar molecular recognition studies is under investigation. Mg-TBPPh$CO_2$Me **(17)** with an intense fluorescence appears to be a promising fluorophore for Fluorecence Detected Circular Dichroism studies.

## EXPERIMENTAL

### General

Anhydrous solvents were dried and distilled ($CH_2Cl_2$ from $CaH_2$, THF from Na/benzophenone). Other solvents used were Optima or HPLC grade. Column chromatography was performed using ICN silica gel (32-63 mesh). NMR spectra were obtained on a BRUKER DMX 300 MHz spectrometer. Chemical shifts are reported in ppm relative to TMS and coupling constants (*J*) in Hz. MS spectra were measured on a JEOLJMS-DX30. UV-VIS spectra were recorded at 25 °C on a Perkin-Elmer Lambda 40 spectrophotometer, corrected for background and reported as $\lambda_{max}$ [nm] ($\varepsilon_{max}$ [$mol^{-1}cm^{-1}$]). The CD spectra were recorded on a JASCO-80 spectrophotometer. The CD spectra were converted into $\Delta\varepsilon_{max}$ [L $mol^{-1}cm^{-1}$] / $\lambda$[nm] units.

### 5-*p*-Methoxycarbonylphenyl-10,15,20-triphenyltetrabenzoporphyrin (3)

A solution of 4,7-dihydro-4,7-ethano-*2H*-isoindole (0.470 g, 3.24 mmol), benzaldehyde (0.235 mL, 2.43 mmol), methyl-4-formylbenzoate (0.132 g, 0.81 mmol) and $Zn(OAc)_2$ (1.6 g, 8.72 mmol) in dry $CH_2Cl_2$ (470 mL) was stirred for 5 min followed by the addition of $BF_3.OEt_2$ (0.42 mL, 3.24 mmol). The resulting solution was allowed to stir in the dark for 3.5 h at rt and then *p*-chloranil (0.200 g, 0.81 mmol) was added. After 3 h the reaction was quenched with 10% $NaHCO_3$, extracted with $CH_2Cl_2$ and dried over $Na_2SO_4$. After evaporation of the solvent the residue was dissolved in glacial acetic acid (20 mL) and the solution was stirred overnight. Acetic acid was evaporated and the crude was dissolved in $CH_2Cl_2$. The organic layer was washed with 10% $NaHCO_3$ and dried over anhydrous $Na_2SO_4$. After removal of the solvent, the residue was filtered on silica ($CH_2Cl_2$/MeOH). All the fractions were collected and

evaporated. The residue was heated under vacuum at 200°C for 10 min. Purification by chromatography on silica ($CH_2Cl_2$) led to a pure green blue powder (50 mg, 7%).

UV-VIS ($CH_2Cl_2$) 464 (294,000), 588 (13,300), 640 (33,400); $^1$H NMR (300 MHz, $CDCl_3$) -1.13 (2H, s), 4.18 (3H, s), 7.10-7.30 (16H, m), 7.85-7.98 (9H, m), 8.35 (6H, d, *J*= 7.56), 8.51 (2H, d, *J*= 8.16), 8.56 (2H, d, *J*= 8.16); $^{13}$C NMR (75 MHz, $CDCl_3$) 77.5, 114.5, 116.3, 116.4, 124.8, 126.4, 129.4, 130.5, 130.9, 134.9, 135.3, 142.2, 146.9, 168.0; HRMS calcd for $C_{62}H_{40}N_4O_2$: 872.3151. Found: 873.3199 ($M^+$+H).

**Zinc-5-*p*-methoxycarbonylphenyl-10,15,20-triphenyltetrabenzoporphyrin (4)**

**3** (5 mg, 0.0057 mmol) and $Zn(OAc)_2$ (10 mg, 0.057 mmol) in dry $CH_2Cl_2$ (1 mL) were stirred overnight. The mixture was washed with water and dried over anhydrous $Na_2SO_4$. After evaporation of the solvent, the residue was purified by chromatography on silica to afford a green blue powder ($CH_2Cl_2$ / 1% TEA) (5 mg, 94%).

UV-VIS ($CH_2Cl_2$) 456 (305,000), 606 (15,250), 651 (69,100); $^1$H NMR (300 MHz, $CDCl_3$) 4.14 (3H, s), 7.15 (16H, m), 7.83-8.01 (9H, m), 8.28 (6H, d, *J*= 6.81), 8.48 (2H, d, *J*= 8.14), 8.53 (2H, d, *J*= 8.14); HRMS calcd for $C_{62}H_{38}N_4O_2Zn$: 934.2286. Found: 934.2270.

**5-*p*-Carboxyphenyl-10,15,20-triphenyltetrabenzoporphyrin (5)**

To a solution of **3** (37 mg, 0.042 mmol) in ethanol (1.5 mL) a 2N NaOH solution (2.6 mL) was added and the suspension was refluxed for 10 h. Cooled to rt, the reaction was quenched with 1N HCl until neutralization. The solution was extracted 3 times with ethyl acetate and the extract was washed with water and brine then dried over $Na_2SO_4$. Evaporation of the solvent led to **3** as a green blue powder (28 mg, 76%).

$^1$H NMR (300 MHz, $CDCl_3$) -1.10 (2H, s), 7.08-7.30 (16H, m), 7.35-8.05 (9H, m), 8.32 (6H, d, *J*= 7.10), 8.49 (2H, d, *J*= 8.16), 8.55 (2H, d, *J*= 8.16); HRMS calcd for $C_{61}H_{39}N_4O_2$: 858.2995. Found: 859.3024 ($M^+$+H).

**Diethyl-2,2'-di(4,7-dihydro-4,7-ethano-*2H*-isoindolyl)methane-9,9'-dicarboxylate (7)**

A solution of ethyl 4,7-dihydro-4,7-ethano-*2H*-isoindole-1-carboxylate (0.390 g, 1.78 mmol), paraformaldehyde (26 mg) and trifluoroacetic acid (6.2 mL) in $CHCl_3$ / MeOH (3 mL / 6 mL) was stirred for 2 days. After evaporation of the solvents, the residue was dissolved in $CH_2Cl_2$ and the organic layer was washed with a solution of 1M NaOH and dried over anhydrous $Na_2SO_4$. After removal of the solvent,

chromatography on silica ($CH_2Cl_2$ / MeOH, 50/1) gave the compound **(7)** as a pale yellow solid (0.190 mg, 62%).

$^1$H NMR (300 MHz, $CDCl_3$) 1.33-1.57 (14H, m), 3.74-4.01 (4H, m), 4.37 (2H, s), 4.30 (4H, m), 6.50 (4H, m), 9.65 (2H, s); $^{13}$C NMR (75 MHz, $CDCl_3$) 14.8, 23.5, 23.4, 26.6, 27.3, 32.8, 32.8, 34.3, 60.4, 112.8, 112.9, 125.2, 125.3, 128.5, 128.6, 135.7, 136.4, 138.0, 162.8; HRMS calcd for $C_{27}H_{30}N_2O_4$: 446.2206. Found: 446.2217.

**2,2'-Di(4,7-dihydro-4,7-ethano-*2H*-isoindolyl)methane (8)**

A stirring mixture of **7** (100 mg, 0.22 mmol) and KOH (43 mg, 0.76 mmol) in ethylene glycol (1.2 mL) was heated at 160-170 °C under argon in dark for 3.5 h. The reaction mixture was poured into water and extracted 3 times with $CH_2Cl_2$. The organic layer was washed with brine and dried over anhydrous $Na_2SO_4$. After evaporation of the solvent, crude **8** was purified by a short chromatography on silica ($CH_2Cl_2$) to afford a white solid (27 mg, 40%).

$^1$H NMR (300 MHz, $CDCl_3$) 1.47-1.56 (8H, m), 3.57 (2H, m), 3.78 (2H, m), 3.90 (2H, s), 6.25 (2H, s), 6.44-6.51 (4H, m), 7.15 (2H, s); $^{13}$C NMR (75 MHz, $CDCl_3$) 23.5, 28.0, 32.5, 33.8, 46.6, 106.8, 106.9, 119.3, 126.5, 129.91, 129.9, 136.7; HRMS calcd for $C_{21}H_{22}N_2$: 302.1783. Found: 302.1803.

**2,2'-Di(4.7-dihydro-4,7-ethano-*2H*-isoindolyl)methane-9,9'-dicarboxaldehyde (9)**

At 0°C under argon DMF (0.033 mL, 0.44 mmol) and $POCl_3$ (0.04 mL, 0.44 mmol) were stirred at rt for 15 min. A solution of **8** (60 mg, 0.2 mmol) in 1.6 mL of dry $CH_2Cl_2$ was added dropwise at 0°C. The resulting mixture was heated at 40°C for 1 h. A solution of sodium acetate (135 mg in 1.6 mL of water) was added at 0°C and then the mixture was refluxed for 1 h. The layers were separated and the aqueous layer was extracted with $CH_2Cl_2$. The extract was then washed with brine, dried over anhydrous $Na_2SO_4$ and evaporated under vacuum. Purification by chromatography on silica ($CHCl_3$/ MeOH) gave **9** as a white solid (50 mg, 70%).

$^1$H NMR (300 MHz, $CD_3OD$) 1.36-1.69 (8H, m), 3.40-3.63 (m, 2H), 4.06 (2H, s), 4.34 (2H, s), 6.47 (4H, m), 9.46 (1H, s), 9.47 (1H, s); $^{13}$C NMR (75 MHz, $CD_3OD$) 23.4, 26.8, 27.7, 32.8, 32.9, 33.3, 124.2, 129.3, 129.8, 129.9, 135.0, 136.5, 136.6, 176.5; HRMS calcd for $C_{23}H_{22}N_2O_2$: 358.1681. Found: 359.1718 ($M^+$+H).

***t*-Buyl 4,7-dihydro-4,7-ethano-*2H*-isoindole-1-carboxylate (11)**

To a stirred solution of **10** (1g, 3.4 mmol) and *t*-butyl isocyanoacetate (0.54 mL, 3.7 mmol) in dry THF (50 mL) at 0°C under argon was added DBU (1.1 mL, 7.4 mmol). After 4 h, THF was evaporated and the residue was dissolved in $CH_2Cl_2$. The organic layer was washed with $H_2O$ and extracted with $CH_2Cl_2$. The extract was dried over anhydrous $Na_2SO_4$ and the solvent evaporated. Purification by chromatography on silica gave **11** as a white solid (590 mg, 70%).

$^1$H NMR (300 MHz, $CDCl_3$) 1.61-1.67 (4H, m), 1.68 (s, 9H), 3.96 (m, 3H), 4.43 (m, 3H), 6.56-6.62 (m, 3H), 8.49 (1H, s); $^{13}$C NMR (75 MHz, $CDCl_3$) 25.6, 26.9, 29.0, 32.3, 33.0, 80.7, 112.9, 115.8, 128.1, 133.6, 136.2, 161.8; HRMS calcd for $C_{15}H_{19}NO_2$: 245.1416. Found: 245.1406.

**Bis[9-*t*-butoxycarbonyl(4,7-dihydro-4,7-ethano-*2H*-isoindolyl)](*p*-methoxycarbonylphenyl)methane (12)**

To a solution of methyl 4-formylbenzoate (97 mg, 0.59 mmol) and toluene-*p*-sulfonic acid (67.5 mg, 0.35 mmol) in dry $CH_2Cl_2$ (5 mL) and in dark was added **11** (300 mg, 1.20 mmol). After stirring for 90 min, 30 mg (0.15 mmol) of toluene-*p*-sulfonic acid was added and the solution was stirred for 30 min. The reaction was quenched with 10% $NaHCO_3$ and the aqueous layer was extracted with $CH_2Cl_2$. After removal of the solvent, chromatography on silica ($CH_2Cl_2$) gave pure **12** as a white solid (230 mg, 60%).

$^1$H NMR (300 MHz, $CDCl_3$) 1.28-1.68 (26H, m), 3.10 (2H, m), 3.85 (3H, s), 4.22 (2H, m), 5.43 (1H, d, *J*= 3.43), 6.41 (2H, m), 6.56 (2H, t, *J*= 6.9), 7.32 (2H, m), 8.02 (2H, s), 8.08 (2H, m); $^{13}$C NMR (75 MHz, $CDCl_3$) 26.7, 26.8, 28.9, 32.8, 34.1, 42.40, 52.5, 80.7, 114.8, 124.9, 128.7, 129.3, 129.5, 130.5, 136.0, 136.1, 137.5, 146.2, 161.4, 167.1; HRMS calcd for $C_{39}H_{44}N_2O_6$: 636.3199. Found: 636.3168.

**Bis(4,7-dihydro-4,7-ethano-*2H*-isoindolyl)(*p*-methoxycarbonylphenyl)methane (13)**

**12** (88 mg, 0.14 mmol) in 0.88 mL of TFA was stirred for 10 min in dark under argon. The solution was diluted with $CH_2Cl_2$ and washed with water and 10% $NaHCO_3$. The organic layer was dried over $Na_2SO_4$ and the solvent evaporated. Short chromatography on silica ($CH_2Cl_2$/TEA 1%) led to **13** as a pale yellow solid (18 mg, 30%).

$^1$H NMR (300 MHz, $CDCl_3$) 1.45-1.70 (8H, m), 3.08 (2H, m), 3.74 (2H, m), 3.89 (3H, m), 5.50 (1H, t, *J*= 5.47), 6.30 (4H, m), 6.43 (2H, m), 7.10 (2H, m), 7.25 (2H, m), 7.95 (2H, m).

**5-*p*-Methoxycarbonylphenyltetrabenzoporphyrin (15)**

**9** (12 mg, 0.033 mmol) and **13** (15 mg, 0.034 mmol) were dissolved in 30 mL of dry $CH_2Cl_2$ and toluene-

*p*-sulfonic acid (9 mg, 0.047 mmol) in 1 mL of MeOH was added. The solution was stirred overnight in dark under argon. A saturated solution of $Zn(OAc)_2$ in MeOH (2 mL) was added to the mixture and stirring was continued for 2 days. The mixture was washed with water, the solvent evaporated and the residue was dissolved in a small amount of TFA to demetalate the zinc complex. After dilution with $CH_2Cl_2$ and quenching with 10% $NaHCO_3$, the solvent was evaporated. The residue was filtered on silica ($CH_2Cl_2$/MeOH 40/1). All the fractions were collected and evaporated. The residue was heated under vacuum at 200°C for 10 min. Purification by chromatography on silica (Hex/EtOAc 8/2) led to a pure green blue powder (3 mg, 15%).

UV-VIS ($CH_2Cl_2$) 418 (68,000), 432 (83,400), 566, 608, 664; $^1$H NMR (300 MHz, $CDCl_3$) 4.12 (3H, s), 7.26 (16H, m) 8.35 (2H, d, *J*= 8.11), 8.73 (2H, d, *J*= 8.11), 9.45 (3H, s); HRMS calcd for $C_{44}H_{28}N_4O_2$: 644.2212. Found: 645.2250 ($M^+$+H).

**Zinc-5-*p*-methoxycarbonylphenyltetrabenzoporphyrin (16)**

3 mg (0.005 mmol) of **15** was stirred overnight in presence of an excess of $Zn(OAc)_2$ in dry $CH_2Cl_2$ (0.25 mL). Filtration on silica ($CH_2Cl_2$/TEA 1%) led to **16** as a green blue powder (3 mg, 93%).

HRMS calcd for $C_{44}H_{26}N_4O_2Zn$: 706.1347. Found: 706.1324.

**Magnesium-5-*p*-methoxycarbonylphenyltetrabenzoporphyrin (17)**

3 mg (0.005 mmol) of **15** was stirred overnight in presence of $MgI_2$ (21 mg, 0.075 mmol), triethylamine (9 μL) in dry $CH_2Cl_2$ (0.25 mL). Filtration on silica ($CH_2Cl_2$/TEA 1%) led to **17** as a green blue powder (2.5 mg, 75%).

HRMS calcd for $C_{44}H_{26}MgN_4O_2$: 666.1906. Found: 666.1906.

**Zn-TPTBP tweezer (18)**

A solution of **5** (5 mg, 0.006 mmol), 1,5-dibromopentane (1 mg, 0.004 mmol) and DBU (1.7 mg, 0.011 mmol) in toluene (1 mL) was refluxed. After 24 h a solution of **5** (6 mg, 0.007 mmol) and DBU (1.5 mg 0.016 mmol) in 1 mL of toluene was then added and the mixture was refluxed again for 24 h. The reaction was quenched with water and extracted with ethyl acetate. The organic layer was dried over $Na_2SO_4$ and the solvents evaporated. The crude was purified by chromatography on silica (Hex/EtOAc 8/2). The residue was stirred in $CH_2Cl_2$ in presence of an excess of $Zn(OAc)_2$ for 4 h. Purification by chromatography on silica (Hex/EtOAc 9/1) led to **18** as a green blue powder (40%, 3 mg).

UV-VIS ($CH_2Cl_2$) 456 (600,000), 606 (37800), 651 (148000); $^1$H NMR (300 MHz, $CDCl_3$) 1.48 (2H, m), 1.90 (4H, m), 4.67 (4H, t, *J*= 6.25), 7.05-7.30 (32H, m), 7.75-7.90 (18H, m), 7.75-7.90 (18H, m), 8.13 (12, m), 8.37 (4H, d, *J*=7.10), 8.57 (4H, d, *J*=7.10); MALDI observed 1914.3691

**General procedure for host/guest complexes preparation and for CD measurements**.

In a typical experiment, a 1 μM tweezer **(18)** solution was prepared by the addition of a 10 μM aliquot of tweezer (0.1 mM in anhydrous $CH_2Cl_2$) to a 1 mL of MCH. The exact concentration of the diluted tweezer was determined by UV-VIS from the ε value. The free amine solution of the conjugate was prepared by adding 0.5 mL of MeOH and solid $Na_2CO_3$ to the corresponding amine TFA salt. The solvent was evaporated under a stream of argon followed by placement under high vacuum for 20 min. Anhydrous $CH_2Cl_2$ was added to yield the free amine solution of the conjugate (3 mM). An aliquot from this solution (10 μM) was added to the solution 1 μM of tweezer. The UV-VIS and CD spectra were recorded according to the general procedure.

**ACKNOWLEDGEMENTS**

This research was supported by NIH Grant 34509 and 065716-01 (GP). We are grateful to Prof. Noboru Ono, Ehime University, for suggestions and Dr S. Jockusch, Columbia University, for help in fluorescence measurements.

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