A Versatile and Convenient Method for the Functionalization of Porphyrins

Amandine Didier,[a] Lydie Michaudet,[a] David Ricard,[a] Valérie Baveux-Chambenoît,[a] Philippe Richard,[a] and Bernard Boitrel*[a]

Dedicated to the memory of Dr. Michel Momenteau

Keywords: Porphyrins / Oxidoreductases / Heme proteins / Enzyme models / Cations

The condensation of 3-(chloromethyl)benzoyl chloride with different atropisomers of *meso*-(tetra-*o*-aminophenyl)porphyrin (TAPP), followed by the reaction of a series of nucleophilic reagents leads, among others, to precursors of biomimetic models of heme proteins such as cytochrome *c* oxidase (C*c*O). This synthesis can also be applied as an efficient two-step reaction to obtain highly functionalized porphyrin derivatives potentially useful for cation binding.

Introduction

An exciting prospect in the domain of biomimetic chemistry is represented by the design and the development of structural and, if possible, functional models, often reproducing a complex biological reactivity. A timely example is illustrated by the Fe_{a3}-Cu_B cytochrome *c* oxidase (C*c*O) active site. Indeed, this enzyme, essential for life on Earth, reduces dioxygen to water without generating toxic reactive intermediates, accepting four electrons produced by the metabolic cycles and conserving the released energy for the synthesis of ATP.[1−3] Although the coordination sphere of the so-called Cu_B is now well established as consisting of three histidine residues[4,5] and despite the increasing number of very pertinent synthetic analogues,[6−14] some intermediates of the catalytic cycle still remain controversial. In particular, the peroxo-level stage is thought to be either a μ-peroxo complex between the two metal centres (Fe_{a3} and Cu_B) or a hydroperoxo adduct bound to heme a_3. The latter hypothesis is sustained by the recent 1.9 Å resolution structure of the mammalian enzyme in its reduced form.[15] We have reported the synthesis[16] and the electrocatalytic studies of tris-(2-aminoethylamine) (tren) capped porphyrins and quinolinoyl-picket porphyrins.[17]

Surprisingly, and in contrast with the bimetallic approach, the iron-only complexes — without an intramolecular fifth ligand — were shown to be more efficient and selective catalysts than the iron-copper ones.[18] However, it seems important to verify that this behaviour can be applied to the iron-only complexes of imidazolyl-picket porphyrins as this crucial information has never been studied.[11,13] Herein, we report a general and easy preparation of several types of binucleating systems in only two steps, starting from different "U-shaped" acceptors, themselves obtained by acylation of three isomers[19] of TAPP. This methodology, initially designed to graft onto a porphyrin the same motif used for targeting potential C*c*O models, was serendipitously shown to be particularly adapted to the preparation of different cation-binding superstructures. Our synthesis can be regarded as a generalisation of Chang's ligand-appended reaction[20] or as the pendant of Collman's congruent Michael addition[21] with a "conformationally restrained" linker.

Results and Discussion

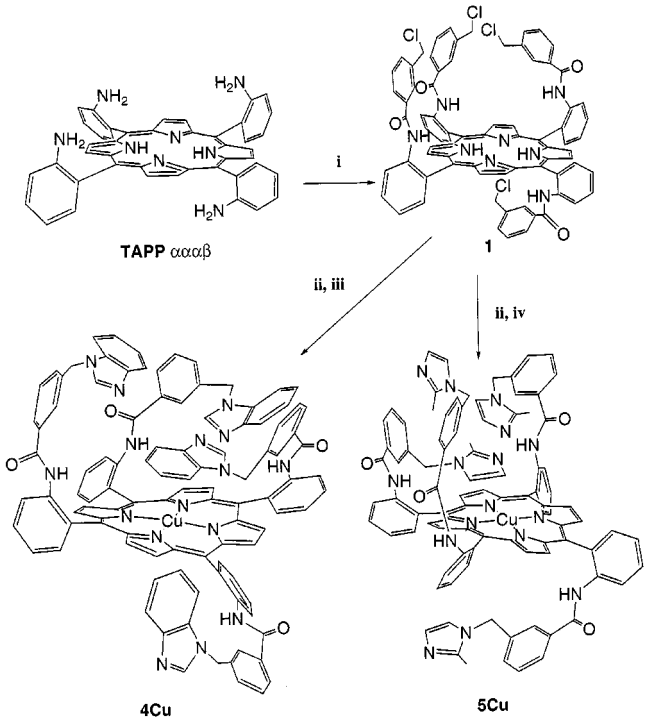
With this aim, we developed a new general strategy by which different types of potential catalysts can be obtained at will by reaction of different nucleophilic reagents susceptible to be grafted onto a porphyrin. In order to be efficient, our new strategy has to fulfil three basic requirements: a) The facility and the rapidity of the synthesis vs. several elegant, but multi-step and tedious synthetic pathways including protection-deprotection procedures previously reported;[22,23] b) For different purposes, we wanted this method to be applicable to all atropisomers of TAPP, and our report details its application on three of them; c) Finally, it might be interesting to be able to enforce the structure tethered with the porphyrin toward the centre of the cavity by conformational control. This type of spatial control has already been described for porphyrins with pickets built with Kemp's triacid.[24,25] Unfortunately, the reaction conditions to achieve this coupling cannot be applied to either isomer of TAPP because of its possible atropisomerization. On the other hand, 3-(chloromethyl)benzoic acid, owing to its *meta* benzyl linkage, has been shown to enforce the coordination of an imidazole to a heme.[20]

Thus, the benzyl chloride picket porphyrins **1**, **2** and **3** are obtained in high yield (90%) by reaction of 3-(chloromethyl)benzoyl chloride with the atropisomers αααβ, αααα and ααββ of TAPP, respectively. Scheme 1 summarises different examples particularly useful for C*c*O modelling by probing the absolute necessity of: (i) an intramolecular fifth

[a] L. S. E. O. − UMR-CNRS 5632, Université de Bourgogne, 6, boulevard Gabriel, 21000 Dijon, France
Fax: (internat.) + 33-3/80396098
E-mail: bboitrel@satie.u-bourgogne.fr

  1434−193X/01/0510−1917 $ 17.50+.50/0

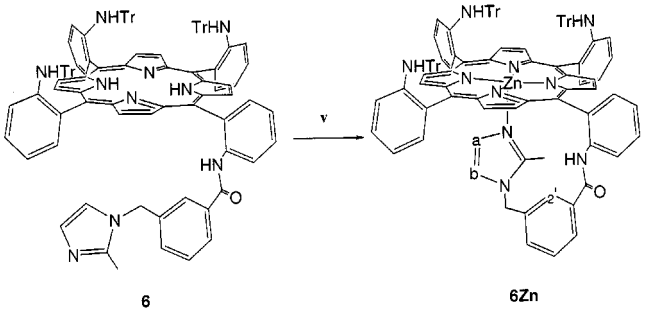
ligand on the porphyrin, and (ii) a copper atom held above the iron to obtain a selective reduction of dioxygen to water. Indeed, this is the first example of such a straightforward functionalization on the ααaβ atropisomer of TAPP to graft both a coordination site for copper(I) and an intramolecular nitrogen base on each side of a porphyrin.



Scheme 1. Synthesis of different potential C*c*O models, starting from the ααaβ atropisomer of TAPP: i) 3-(chloromethyl)benzoyl chloride/THF/NEt_3/0 °C; ii) $Cu(OAc)_2$/NaOAc/CH_3OH/$CHCl_3$/ room temp.; iii) BIm/THF/NEt_3/50 °C; iv) 2-MeIm/THF/NEt_3/ 50 °C

For C*c*O models, the use of imidazole is obvious for building the copper coordination sphere as well as for stabilizing the iron, but it generates two important problems. Firstly, grafting imidazole on **1** would lead, after iron insertion, to an iron complex in which two imidazoles would be strongly coordinated to the iron centre. To circumvent this problem, we have employed 2-methylimidazole (2-MeIm) as it is well-known that the formation of the six-coordinate iron complex is definitely forbidden with such a nitrogen base.[26] Secondly, if the free-base **1** is used, the resulting porphyrin decomposes very rapidly due to the reaction of singlet dioxygen with imidazole derivatives.[27,28] To avoid these photosensitised oxygenation reactions, in the particular case described in Scheme 1, the condensation of the imidazole derivatives was carried out only on **1Cu** and not on **1**. We chose to insert copper into the porphyrin as a paramagnetic metal because square-planar copper(II) porphyrins, without any axial ligand, are easier to purify than their iron counterparts. Obviously, in our future studies of these potential C*c*O models, iron(II) will replace copper(II) in the porphyrin and, eventually, copper(I) will be coordinated by the three distal imidazole derivatives. In the case of **4Cu**, four benzimidazole (BIm) molecules have been attached to the porphyrin. With this particular model, we plan to avoid any eventual intermolecular reaction owing to the size of benzimidazole in comparison with imidazole. A previous work concerning 2-methylbenzimidazolyl-picket porphyrins (known as pincer-porphyrins) has already been reported by Reed et al.,[29] but at that time only two coordinating groups had been attached to the porphyrin.

Furthermore, to appreciate the structural conformation in solution of the pickets in the porphyrin analogue of **5Cu** with a coordinating metal such as iron, we have synthesised the ligand **6** (Scheme 2) and its zinc complex **6Zn**.[30] The free-base porphyrin **6** was obtained in three steps starting from the αααα atropisomer of TAPP tri-protected by the trityl group. The remaining amino group of this porphyrin was isomerised on the other face of the macrocycle. Thus, the reaction of one equivalent of 3-(chloromethyl)benzoyl chloride led to a single "U-shaped" picket porphyrin, onto which a 2-MeIm molecule was grafted. The incorporation of zinc was achieved by the usual methods.



Scheme 2. Coordination of the tailed nitrogen base of **6Zn** by incorporation of zinc in **6**: v) $Zn(OAc)_2$/NaOAc/CH_3OH/$CHCl_3$/50 °C; (Tr = trityl)

By comparing the chemical shifts of the different protons of the free base **6** (Table 1) with the corresponding chemical shifts of ethyl-3-[(2-methylimidazol-1-yl)methyl]benzoate (**7**) (the free picket as its ethyl ester), we can verify the effect of the anisotropic ring current of the porphyrin. It is apparent that both protons H_{im} are upfield-shifted by 0.6 and 1 ppm, a shielding which seems to indicate that the 2-MeIm is actually oriented as drawn in Scheme 2; otherwise the two chemical shifts would differ by a greater amount.

Table 1. Variation of the chemical shifts (300 K) due to the coordination of the tailed nitrogen base in **6Zn**

	7	**6** (δ_1)	**6Zn** (δ_2)	$\Delta\delta = \delta_2 - \delta_1$
H_{im}	6.96	6.32	1.51 (H_a)	−4.8
H_{im}	6.85	5.84	5.05 (H_b)	−0.8
CH_2(Bn)	5.10	4.15	3.95	−0.2
Me	2.33	1.70	−1.50	−3.2
H_2'	7.83	6.61	5.32	−1.3

The variation of chemical shift Δδ between the zinc complex **6Zn** and its free-base **6** is a direct probe of the coor-

dination of the picket. For this type of movement through space, the most influential factor is the proximity to the ring current, so it is not surprising to observe such a difference of Δδ between the two protons of the coordinated imidazole (their chemical shifts are almost the same in **7**). In the case of the zinc complex **6Zn**, we can assign with assurance H_a to the most upfield-shifted signal (Δδ = −4.8) and H_b to the least-shifted one (Δδ = −0.8). The variation of chemical shift for the benzylic protons CH_2 between **7** and the porphyrins **6** or **6Zn** is worth noting. Indeed, it is almost the same (δ = 0.95 and 1.15) for the free-base and its zinc complex, leading to a Δδ = −0.2. This observation means that without any driving force, such as the coordination of the picket to a metal, the benzylic methylene group is preoriented toward the inner cage, thus favouring an effective "U-shaped" geometry of the picket.

Finally, the proton H_2' (Scheme 2) deserves to be discussed as, in light of its position, it should be very sensitive to the slightest conformational change of the picket. Moreover, it represents an effective probe as the expected signature for such a proton is an apparent triplet with a *J* value of 1.7 Hz[31] and it is therefore easy to locate in the NMR spectrum. The significant Δδ = −1.3 for H_2' may appear to be inconsistent with the negligible Δδ value of the benzylic methylene group. However, in the free base, if we consider that the two aromatic rings of the picket, conjugated through the amide bond, are not coplanar (Figure 1) as generally reported,[24,25] the aromatic cycle of the picket is not perpendicular to the porphyrin plane but somehow in a flattened position and offset from the centre of the porphyrin. The coordination of the nitrogen base should therefore induce the movement of this aromatic ring in a perpendicular position as the 2-MeIm is directly attached to the benzyl group. This phenomenon could explain the value of Δδ = −1.3 for H_2' even though the displacement of the benzylic residue is insignificant.

The same two-step strategy can be applied to the αααα atropisomer of TAPP targeting, among others, new compounds with a suitable coordination sphere for cations such as lanthanides. We have recently shown that, surprisingly, porphyrins bearing ethyl ester pickets can stabilise a metal such as bismuth(III) in a dimer.[34] It would be of prime importance to investigate if a comparable monomeric structure is possible. In this respect, the two strapped porphyrins **8** and **9** (Scheme 3) are suitable as the strap(s) should avoid an eventual intermolecular interaction, while delivering one or several ester group(s) close to the metal coordination site.

The preparation of the αααα "U-shaped" acceptor **2** is achieved in the same manner as for the αααβ atropisomer. In the second step of the synthesis, the nucleophilic reagent is not a nitrogen base but the anion of diethyl malonate. Depending on the reaction conditions, a very interesting reactivity is observed leading to the two strapped porphyrins **8** and **9** in high yield. Furthermore, if 20 equivalents of diethyl malonate are used, the bis-strapped porphyrin **8** is the major compound, obtained in 80% yield. If a very large excess (1000 equivalents) of diethyl malonate is employed, the single-strapped porphyrin **9** is favoured (74%).[35] Under our reaction conditions, we were not able to obtain the porphyrin resulting from the expected addition of one diethyl

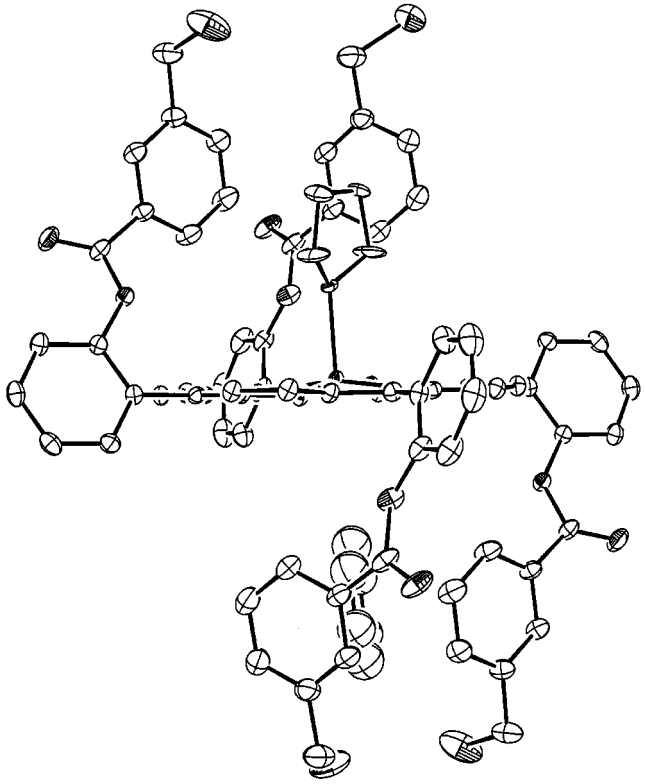
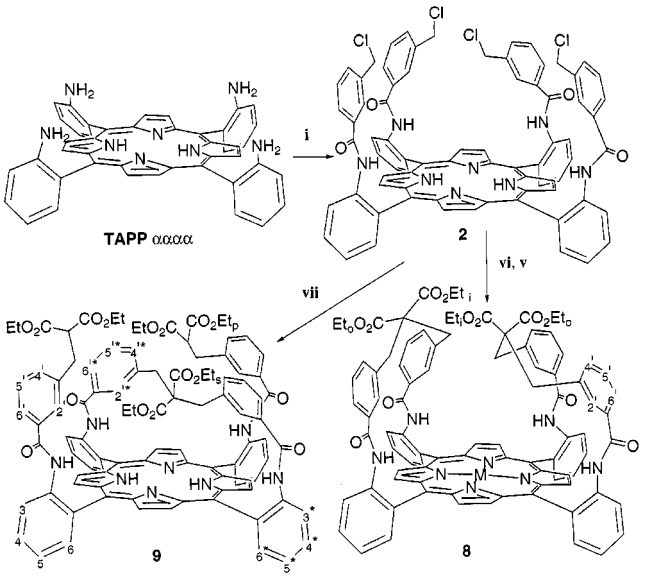


Figure 1. ORTEP view of the solid-state structure of the Zn ααββ "U-shaped" acceptor **3Zn**; for the sake of clarity, the two toluene solvate molecules and the hydrogen atoms are omitted



Scheme 3. Two different possibilities for the use of the αααα atropisomer of TAPP: i) 3-(chloromethyl)benzoyl chloride/THF/NEt_3/0 °C; v) $Zn(OAc)_2$/NaOAc/CH_3OH/$CHCl_3$/50 °C; vi) $CH_2(CO_2Et)_2$ (20 equiv.)/THF/NaOEt/room temp.; vii) $CH_2(CO_2Et)_2$ (1000 equiv.)/THF/NaOEt/room temp.; the subscripted letters i, o, s and p of the ethyl groups stand for in, out, strap and picket

malonate on each picket; this result can be explained by a severe steric hindrance due to the U-shape of the picket. However, the formation of the unique strap of **9** indicates that the two pickets in the meso positions 5 and 15[36] are spatially close enough to allow a single carbon atom to react with both of them, clearly confirming the conformation of the "U-shaped" picket. Again, ^{1}H NMR spectroscopy is a valuable method to determine the orientation of these two different types of strap. For example, the observation of two different groups of signals for the ethyl ester residues shows that the representation of the porphyrin **8** in Scheme 3 is quite realistic. These two different groups of protons are labelled "i" and "o" for "in" and "out". The chemical shifts of these protons are δ = 1.09/3.98 (Et_o) and δ = 0.64/3.53 (Et_i)[37] indicating that these two ethyl groups are orientated inside the cavity whereas the others are directed outside. The variation of chemical shift of 1 ppm for the benzylic methylene group between **8** (δ = 2.28) and the "U-shaped" acceptor **2** (δ = 3.22)[38] demonstrates that the formation of the straps in **8** does not affect the spatial arrangement of the linker. Additionally, as a result of the different magnetic environment, this methylene group appears as an AB system (J = 13.8 Hz) in **8** (Figure 2) instead of a singlet in **2**.

In the case of porphyrin **9** with a strap linked across the macrocycle, we can differentiate the signals due to the protons of the strap from those of the pickets. Obviously, the protons of the strap are the most upfield shifted ones with chemical shifts of δ = −0.6, 0.95 and 1.63 for the CH_3, the CH_2 of the ester group and the benzylic CH_2, respectively. The protons of the pickets in **9** present chemical shifts quite similar to those observed for the strap of **8** with the exception of the proton H_2'. Indeed, in **9**, H_2' appears at δ = 7.55 instead of δ = 6.52 in **2** (Figure 3). This clearly demonstrates that the two pickets in **9**, in comparison with the pickets of **2**, are forced away from the centre of the porphyrin by the strap across the macrocycle. On the other hand, the H_2' chemical shift is the same in both compounds **2** and **8**, indicating that the formation of the straps between two adjacent *meso* positions does not induce significant conformational change in the linker. Moreover, the variation of chemical shift of −1.7 for H_2'* is consistent with a linkage above the ring current of the porphyrin.

Finally, it is plausible that in the αααα "U-shaped" acceptor **2** as well as the bis-strapped porphyrin **8**, the pickets (or the straps) are not as bent over the porphyrin as they should be, because of an eventual and mutual steric hindrance. A pertinent way to probe this hypothesis consists in synthesising the analogous molecules in the ααββ series. Thus, both the "U-shaped" acceptor **3** and the bis-strapped porphyrin **10** have been prepared under the same conditions as in Scheme 3. Obviously, in this particular geometry for **3** and **10**, we have only two pickets and one strap per side (Scheme 4). The X-ray structure of **3Zn** is reported in Figure 1. The fifth coordination site of the zinc is occupied by a THF molecule [ΔN4 = 0.243(2) Å, <Zn−N> = 2.036(5) Å and Zn−O(THF) = 2.196(4) Å]. The most important fact concerns the effective conformation of the pickets in the solid state. Indeed, one can observe that the aromatic ring of the picket can adopt two different conformations with either the proton H_2' inside or outside the cavity. But it is worth noting that, whatever the conformation is, the benzylic methylene group is oriented towards the centre of the cage built by the four pickets. Nevertheless, the fact that the two aromatic rings of the same picket are not coplanar is observable in the solid state. This angle is not the same for each picket and is found to be 42.0(2)° or 60.4(2)°. In solution, a first comparison between the protons H_2' and CH_2(Bn) of **2** and **3** (Table 2) indicates that no significant difference in the chemical shifts are observed (δ = 6.52/3.22 vs. 6.55/3.52, respectively). Therefore, the conformation of the picket seems to be roughly the same in both "U-shaped" acceptors. On the other hand, by comparing the two bis-strapped porphyrins **8** and **10** (obtained from **2** and **3,** respectively) and considering **8** as a reference, an important upfield-shift is observed for most of the protons of the straps: H_2', CH_2(Bn) and also the two different ethyl groups (Figures 2 and 4). For example, H_2' and CH_2(Bn) (as an AB system) are shielded by almost 1 ppm. The same value can be calculated concerning the ethyl group directed towards the centre of the porphyrin (CH_2i and CH_3i). For

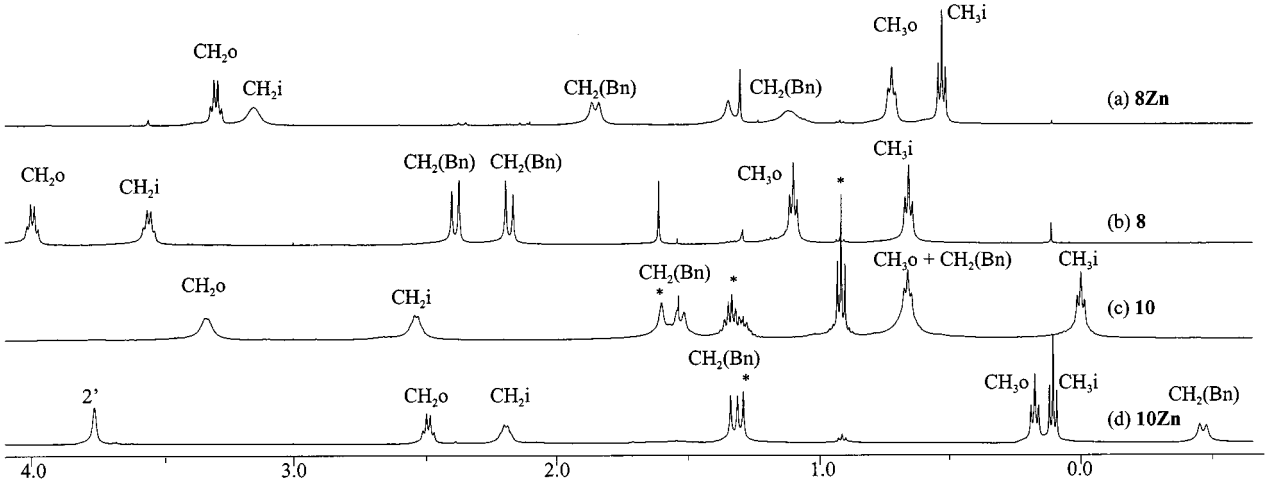


Figure 2. Aliphatic domain of the ^{1}H NMR spectra (300 K) of: (a) **8Zn**, (b) **8**, (c) **10** and (d) **10Zn**; * = impurities

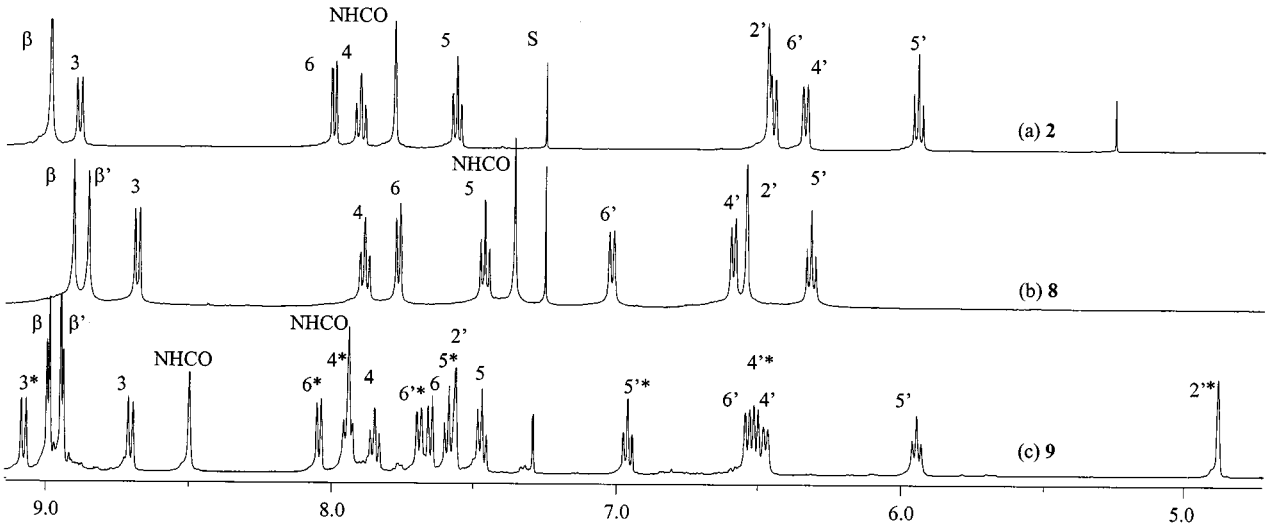
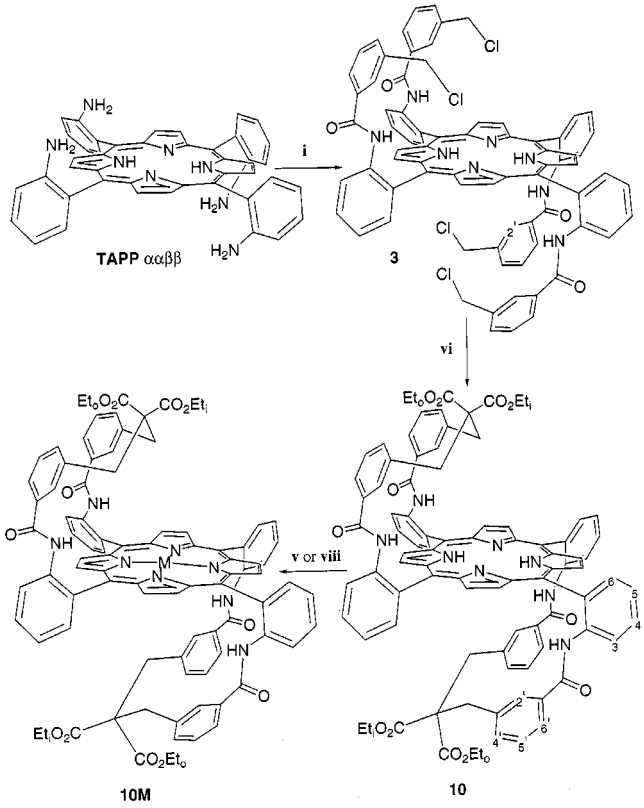


Figure 3. Aromatic region of the ^{1}H NMR spectra (300 K) of: (a) **2**, (b) **8**, (c) **9**



Scheme 4. Synthesis of a bis-strapped cation-binding porphyrin starting from the αααβ atropisomer of TAPP: i) 3-(chloromethyl)-benzoyl chloride/THF/NEt_3/0 °C; v) M = Zn: $Zn(OAc)_2$/NaOAc/$CH_3OH/CHCl_3$/50 °C; vi) $CH_2(CO_2Et)_2$ (20 equiv.)/THF/NaOEt/room temp.; viii) M =Ni: $Ni(OAc)_2$/pyridine/110 °C

CH_2i, the shift is equal to 1 ppm (δ = 3.53 to δ = 2.53) and for CH_3i, it is of 0.62 ppm (δ = 0.64 to δ = 0.01). From these observations, we can logically deduce that the straps of **10** are more bent over the porphyrin than they are in **8**. This phenomenon can be explained by a reciprocal hindrance of the two straps, on the same side in **8**, which is suppressed in **10** as each strap is linked on one side of the porphyrin. As the chemical shifts observed for **10** and **10Ni** are not significantly different, the same deduction can be reached by comparing **8** with **10Ni**, in which nickel(II) is known to remain square planar without any axial ligand.

Table 2. Selected ^{1}H NMR spectroscopic data (300 K) for the compounds synthesised from the αααα and ααββ atropisomers

	2	**3**	**8**	**8Zn**	**10**	**10Zn**	**10Ni**
H_2'	6.52	6.55	6.59	5.63	4.97	3.76	4.84
CH_2(Bn)	3.22	3.52	2.38/2.18	1.84/1.10	1.53/0.66	1.31/−0.47	1.68/0.98
CH_2o	X	X	3.98	3.29	3.33	2.48	3.39
CH_2i	X	X	3.53	3.14	2.53	2.19	2.83
CH_3o	X	X	1.09	0.72	0.66	0.17	0.69
CH_3i	X	X	0.64	0.52	0.01	0.10	0.14

Furthermore, zinc(II), which is most of the time five-coordinate in a porphyrin, by completing its coordination sphere with an oxygen-donor ligand was also inserted in **8** and **10**. The comparison between each free-base porphyrin and its zinc(II) complex is very instructive. As pointed out above, the complexes **10** and **10Ni** exhibit the same chemical shifts for the protons of their straps, whereas most of the signals of **10Zn** experience an upfield shift of about 1 ppm in comparison with the free base. This observation is also valid for **8**: for example, H_2', shielded by 1.2 ppm in the comparison **10/10Zn**, is shifted by 1.0 ppm in the comparison **8/8Zn**. This result is easily extended to the other protons CH_2(Bn), CH_2i and CH_2o, although CH_3i and CH_3o are less influenced. The most plausible explanation consistent with these observations, is the coordination of an oxygen atom from an ethoxycarbonyl group on the zinc. This phenomenon has already been observed for other strapped[39] and picket porphyrins either with the same metal or bismuth(III)[34] in the porphyrin.

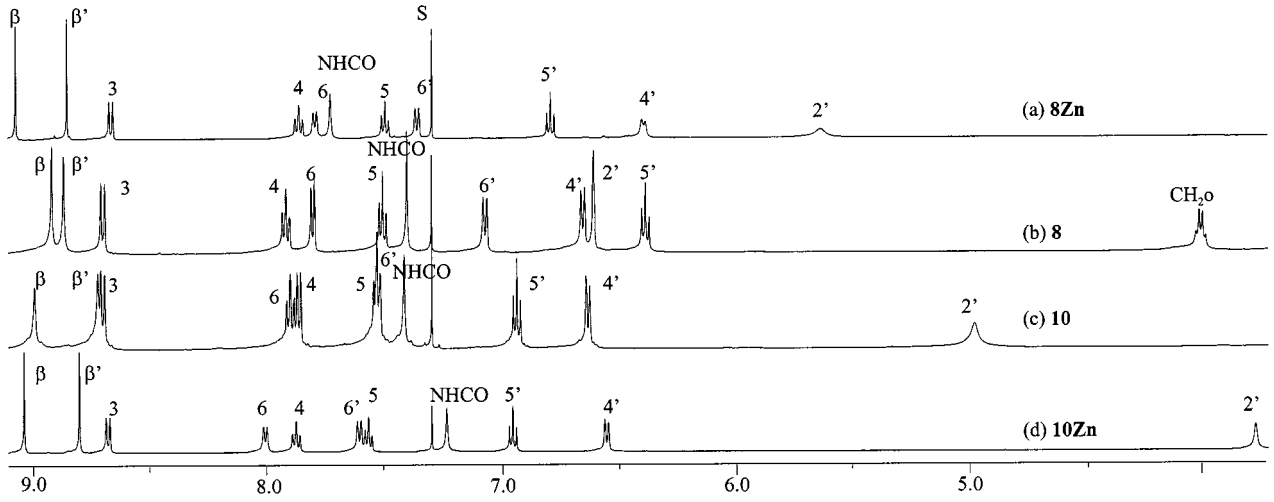


Figure 4. Aromatic region of the ^{1}H NMR spectra (300 K) of: (a) **8Zn**, (b) **8**, (c) **10** and (d) **10Zn**

Conclusion

We have described three significant examples of the possibility offered by the congruent reaction of different nucleophilic reagents on porphyrins bearing "U-shaped" pickets obtained by the simple condensation of a specific acyl chloride on TAPP. The two steps of this new strategy are both convenient reactions and should be applicable to a wide range of compounds. Moreover, we have shown that these reactions lead to very interesting new porphyrins, whatever the TAPP atropisomer employed. Work is in progress to apply this methodology to the preparation of other superstructures such as chiral catalysts and NO synthase models.

Experimental Section

General: ^{1}H (500.13 MHz) NMR spectra were recorded on a Bruker Avance DRX 500 spectrometer and referenced to the residual proton solvents. Mass spectra were performed on an MS/MS ZABSpec TOF spectrometer at the University of Rennes I (C.R.M.P.O.). UV/Visible spectra were recorded on a Varian Cary 1E and a Bruker IFS 66 spectrometers. All solvents (ACS for analysis) were purchased from Carlo Erba. THF was distilled from potassium metal whereas methanol was distilled from magnesium turns. CH_2Cl_2 was used as received. Triethylamine was distilled from over CaH_2. The starting materials were generally used as received (Acros, Aldrich) without any further purification. All reactions were performed under an argon atmosphere and monitored by TLC (silica, CH_2Cl_2/CH_3OH). Column flash chromatography was performed on silica gel (Merck TLC-Kieselgel 60 H, 15 μm). Elemental analyses were obtained on an EA 1108 Fisons Instruments.

α-5,10,15,β-20-Tetrakis{2-[(3-chloromethyl)benzoylamido]phenyl}-porphyrin (1): A 250 mL three neck round bottom flask equipped with a stir bar was charged with ααα**β**-TAPP (1 mmol, 674 mg), dry THF (100 mL), and Et_3N (16 mmol, 2.22 mL). After cooling in an ice bath, 3-(chloromethyl)benzoyl chloride (5 mmol, 0.71 mL) dissolved in 10 mL of dry THF was injected dropwise. The reaction mixture was allowed to stir for three hours at 0 °C. THF was finally removed under vacuum. The resulting powder was dissolved in CH_2Cl_2 and directly loaded onto a silica gel chromatography column. The expected compound, eluted with 1% CH_3OH/CH_2Cl_2, was obtained in 88% yield (1.154 g). − ^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ = 9.00 (s, 4 H), 8.99 (s, 4 H), 8.87 (d, *J* = 8.5 Hz, 2 H), 8.86 (d, *J* = 7.5 Hz, 2 H), 8.14 (d, *J* = 7.5 Hz, 1 H), 8.11 (d, *J* = 7.5 Hz, 2 H), 7.98 (d, *J* = 7.5 Hz, 2 H), 7.93 (m, 4 H), 7.86 (s, 1 H), 7.64−7.57 (m, 7 H), 7.50 (s, 1 H), 6.85 (d, *J* = 7.0 Hz, 1 H), 6.83 (t, *J* = 1.5 Hz, 1 H), 6.65 (d, *J* = 8.0 Hz, 4 H), 6.56−6.51 (m, 2 H), 6.44 (t, *J* = 7.5 Hz, 2 H), 6.40 (s, 1 H), 6.32 (s, 2 H), 6.05 (t, *J* = 8.0 Hz, 1 H), 3.60 (s, 2 H), 3.53 (s, 2 H), 3.26 (d, *J* = 12.5 Hz, 2 H), 3.20 (d, *J* = 12.5 Hz, 2 H), −2.49 (s, 2 H). − HR-MS (LSI-MS): *m/z* ($C_{76}H_{54}Cl_4N_8NaO_4$ [M + Na]$^+$): calcd. 1305.2920; found 1305.2912. − $C_{76}H_{54}Cl_4N_8O_4$ (1285.1): calcd. C 71.03, H 4.24, N 8.72; found C 70.88, H 4.14, N 8.54. − UV/Vis (CH_2Cl_2): λ nm (10^{-3}·ε, M^{-1} cm^{-1}) = 422 (243.4), 515 (14.3), 548 (3.7), 589 (4.3), 645 (1.9).

(α-5,10,15,β-20-Tetrakis{2-[(3-chloromethyl)benzoylamido]phenyl}-porphyrin)copper(II) (1Cu): Porphyrin **1** (150 mg, 1.16 mmol) was dissolved in $CH_3OH/CHCl_3$, and an excess of $Cu(OAc)_2$ and sodium acetate was added at room temperature. The mixture was stirred for 2 hours. The solvents were removed under vacuum and the residue redissolved in $CHCl_3$, filtered and dried again. The expected compound was purified by flash chromatography on a silica gel column and eluted with 2% CH_3OH/CH_2Cl_2 (yield = 90%, 141 mg). − HR-MS (LSI-MS): *m/z* ($C_{76}H_{52}Cl_4N_8NaO_4Cu$ [M + Na]$^+$): calcd. 1366.2059; found 1366.2060. − $C_{76}H_{52}Cl_4CuN_8O_4$·CH_3OH·H_2O (1396.7): calcd. C 66.22, H 4.19, N 8.02; found C 66.31, H 3.86, N 7.67. − UV/Vis (CH_2Cl_2): λ nm (10^{-3}·ε, M^{-1} cm^{-1}) = 418 (389.1), 540 (20.1), 621 (1.7).

α-5,10,15,20-Tetrakis{2-[(3-chloromethyl)benzoylamido]phenyl}-porphyrin (2): The procedure described above for **1** was used with the αααα atropisomer of TAPP (200 mg), and the desired compound was eluted with CH_2Cl_2 (yield = 90%, 300 mg). − ^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ = 8.99 (s, 8 H), 8.89 (d, *J* = 8.0 Hz, 4 H), 8.21 (d, *J* = 7.5 Hz, 4 H), 7.93 (t, *J* = 8.0 Hz, 4 H), 7.80 (s, 4 H), 7.59 (t, *J* = 7.5 Hz, 4 H), 6.52 (t, 4 H, H_2', *J* = 1.5 Hz), 6.50 (d, *J* = 8.0 Hz, 4 H), 6.39 (d, *J* = 8.0 Hz, 4 H), 6.00 (t, *J* = 7.5 Hz,

4 H), 3.22 (s, 8 H), −2.48 (d, 2 H). − HR-MS (LSI-MS): *m/z* ($C_{76}H_{54}Cl_4N_8NaO_4$ [M + Na]$^+$): calcd. 1305.2920; found 1305.2909. − $C_{76}H_{54}Cl_4N_8O_4$ (1285.1): calcd. C 71.03, H 4.24, N 8.72; found C 70.89, H 4.11, N 8.83. − UV/Vis (CH_2Cl_2): λ nm (10^{-3}·ε, M^{-1} cm^{-1}) = 422 (247.8), 515 (13.4), 548 (3.6), 589 (4.1), 645 (1.7).

α-5,10,β-15,20-Tetrakis{2-[(3-chloromethyl)benzoylamido]phenyl}-porphyrin (3): The procedure described above for **1** was used on the ααββ atropisomer of TAPP (220 mg), and the desired compound was eluted with CH_2Cl_2 (yield = 86%, 360 mg). − ^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ = 9.00 (s, 4 H), 8.99 (s, 4 H), 8.90 (d, *J* = 8.3 Hz, 4 H), 8.07 (d, *J* = 7.3 Hz, 4 H), 7.93 (t, *J* = 8.3 Hz, 4 H), 7.66 (s, 4 H), 7.61 (t, *J* = 7.5 Hz, 4 H), 6.74 (d, *J* = 7.5 Hz, 4 H), 6.55 (s, 4 H, H_2'), 6.52 (d, *J* = 8.3 Hz, 4 H), 6.39 (t, *J* = 7.7 Hz, 4 H), 3.55 (d, *J* = 12.1 Hz, 4 H), 3.52 (d, *J* = 12.1 Hz, 4 H), −2.52 (s, 2 H). − HR-MS (LSI-MS): *m/z* ($C_{76}H_{54}Cl_4N_8NaO_4$ [M + Na]$^+$): calcd. 1305.2920; found 1305.2899. − $C_{76}H_{54}Cl_4N_8O_4$ (1285.1): calcd. C 71.03, H 4.24, N 8.72; found C 70.62, H 4.19, N 8.94. − UV/Vis (CH_2Cl_2): λ nm (10^{-3}·ε, M^{-1} cm^{-1}) = 422 (363.8), 515 (20.6), 549 (5.1), 589 (6.2), 646 (2.6).

(α-5,10,β-15,20-Tetrakis{2-[(3-chloromethyl)benzoylamido]phenyl}-porphyrin)zinc(II) (3Zn): Porphyrin **3** (100 mg) was dissolved in 30 mL of 2% $CH_3OH/CHCl_3$ and an excess of $Zn(OAc)_2$ and sodium acetate were added. The mixture was stirred and refluxed during 1 hour. The solvents were removed under vacuum and the residue was redissolved in CH_2Cl_2, filtered, and dried again. Chromatography on a silica gel column yielded the final compound after elution with CH_2Cl_2 (yield 98%, 103 mg). − ^{1}H NMR (500 MHz, $CDCl_3$, 323 K): δ = 9.04 (s, 4 H), 8.99 (s, 4 H), 8.77 (d, *J* = 7.9 Hz, 4 H), 8.09 (d, *J* = 7.6 Hz, 4 H), 7.89 (t, *J* = 7.9 Hz, 4 H), 7.64 (s, 4 H), 7.59 (t, *J* = 7.6 Hz, 4 H), 6.59 (d, *J* = 7.5 Hz, 4 H), 6.37 (d, *J* = 7.5 Hz, 4 H), 6.27 (t, *J* = 7.5 Hz, 4 H), 6.19 (s, 4 H, H_2'), 3.41 (d, *J* = 11.9 Hz, 4 H), 3.30 (d, *J* = 11.9 Hz, 4 H). − MS (FAB): *m/z* = 1345.3 [M + H]$^+$. − $C_{76}H_{52}Cl_4N_8O_4Zn·3H_2O$ (1402.5): calcd. C 65.08, H 4.17, N 7.99; found C 65.17, H 4.23, N 8.14. − UV/Vis (CH_2Cl_2): λ nm (10^{-3}·ε, M^{-1} cm^{-1}) = 427 (295.4), 554 (14.5), 593 (2.2).

α-5,10,15,β-20-Tetrakis(2-{[(3-(benzimidazol-1-yl)methyl]benzoylamido}phenyl)porphyrin (4): MS (MALDI-TOF): *m/z* = 1612.14 [M + H]$^+$.

[α-5,10,15,β-20-Tetrakis(2-{[3-(benzimidazol-1-yl)methyl]benzoylamido}phenyl)porphyrin]copper(II) (4Cu): αααβ U-Shaped copper(II) acceptor **1Cu** (130 mg, 0.1 mmol) was dissolved in 50 mL of freshly distilled THF with benzimidazole (91 mg, 0.77 mmol) and a catalytic amount of NaI. The solution was heated overnight at 50 °C. After evaporation of the solvent to dryness, the mixture was chromatographed on a silica gel column and the major porphyrin eluted with 3% $CH_3OH/CHCl_3$ (yield = 30%, 48 mg). − HR-MS (LSI-MS): *m/z* ($C_{104}H_{72}CuN_{16}NaO_4$ [M + Na]$^+$): calcd. 1694.5116; found 1694.5117. − $C_{104}H_{72}CuN_{16}O_4·CH_2Cl_2·CHCl_3$ (1877.6): calcd. C 68.19, H 4.09, N 12.19; found C 67.80, H 4.03, N 11.94. − UV/Vis (CH_2Cl_2): λ nm (10^{-3}·ε, M^{-1} cm^{-1}) = 428 (165.4), 551 (14.8), 591 (2.3).

α-5,10,15,β-20-Tetrakis(2-{[3-(imidazol-1-yl)methyl]benzoylamido}-phenyl)porphyrin (5): MS (MALDI-TOF): *m/z* = 1467.02 [M + H]$^+$.

[α-5,10,15,β-20-Tetrakis(2-{[3-(imidazol-1-yl)methyl]benzoylamido}phenyl)porphyrin]copper(II) (5Cu): The preceding procedure was used with 2-MeIm (yield = 50%, 57 mg). − HR-MS (LSI-MS): *m/z* ($C_{88}H_{67}CuN_{14}O_4$ [M − MeIm]$^+$): calcd. 1446.4766; found 1446.4775. − MS (FAB): *m/z* = 1527.0 [M]$^+$. − $C_{94}H_{80}CuN_{16}O_6·2CH_3OH$ (1593.3): calcd. C 70.86, H 5.06, N 14.07; found C 70.57, H 4.92, N 14.12. − UV/Vis (CH_2Cl_2): λ nm (10^{-3}·ε, M^{-1} cm^{-1}) = 428 (279.9), 551 (13.7), 589 (2.2).

α-5,10,15-Tris(2-triphenylmethylaminophenyl)-β-20-(2-{[3-(imidazol-1-yl)methyl]benzoylamido}phenyl)porphyrin (6): In a 500 mL three neck round bottom flask equipped with a stir bar, 500 mg of TAPP αααα (0.74 mmol) was dissolved in dry THF (90 mL) and Et_3N (0.88 mmol, 1.22 mL). Triphenylmethyl bromide (813 mg, 0.25 mmol) dissolved in 30 mL of dry THF was slowly added over one hour. After stirring for five hours at 0 °C under argon, the solvent was finally removed under vacuum. The resulting powder was dissolved in a 40% toluene/hexane solution and loaded onto a silica gel chromatography column prepared with a mixture of 30% toluene/hexane. Elution with 50% toluene/hexane led to the α-5,10,15-tris-{2-triphenylmethylaminophenyl}:α-20-{2-aminophenyl}porphyrin in 39% yield (400 mg): ^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ = 9.09 (d, *J* = 4.7 Hz, 2 H), 9.04 (d, *J* = 4.7 Hz, 2 H), 8.99 (m, 3 H), 8.89 (d, *J* = 4.7 Hz, 2 H), 8.00 (d, J_o = 7.3 Hz, J_m = 1.5 Hz, 1 H), 7.68 (t, J_o = 7.8 Hz, J_m = 1.5 Hz, 1 H), 7.64 (d, J_o = 7.3 Hz, J_m = 1.6 Hz, 1 H), 7.43 (d, J_o = 7.3 Hz, J_m = 1.5 Hz, 2 H), 7.27−7.20 (m, 15 H), 7.12 (m, 7 H), 7.03−6.91 (m, 22 H), 6.84−6.74 (m, 8 H), 6.80−6.75 (m, 3 H), 5.51 (s, 2 H), 5.21 (s, 1 H), 3.69 (s, 2 H), −2.59 (s, 2 H).

The following step consisted in the atropisomerization of the aminophenyl group[40] which led, after chromatography on a silica gel column, to the expected porphyrin in 60% yield (240 mg), eluted with 80% toluene/hexane.

α-5,10,15-Tris(2-triphenylmethylaminophenyl)-β-20-(2-aminophenyl)porphyrin: ^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ = 9.02 (d, *J* = 4.5 Hz, 2 H), 8.99 (d, *J* = 4.5 Hz, 2 H), 8.96 (d, *J* = 4.5 Hz, 2 H), 8.88 (d, *J* = 4.5 Hz, 2 H), 7.94 (d, J_o = 7.5 Hz, J_m = 1.0 Hz, 1 H), 7.67 (t, J_o = 7.8 Hz, J_m = 1.5 Hz, 1 H), 7.57 (d, J_o = 7.5 Hz, J_m = 1.5 Hz, 1 H), 7.43 (d, J_o = 7.0 Hz, J_m = 1.0 Hz, 2 H), 7.25 (m, 4 H), 7.19 (m, 12 H), 7.10 (m, 7 H), 7.00−6.96 (m, 21 H), 6.84 (m, 3 H), 6.80−6.75 (m, 9 H), 5.42 (s, 2 H), 5.25 (s, 1 H), 3.65 (s, 2 H), −2.61 (s, 2 H).

The procedure described for the synthesis of **1** was then used to obtain the picket porphyrin "U-Shaped" acceptor (yield 90%, 239 mg).

α-5,10,15-Tris(2-triphenylmethylaminophenyl)-β-20-{2-[(3-chloromethyl)benzoylamido]phenyl}porphyrin: ^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ = 9.09 (d, *J* = 4.5 Hz, 2 H), 9.00 (d, *J* = 4.5 Hz, 2 H), 8.99 (m, 1 H), 8.97 (d, *J* = 4.5 Hz, 2 H), 8.91 (d, *J* = 4.5 Hz, 2 H), 8.15 (d, J_o = 7.5 Hz, J_m = 1.0 Hz, 1 H), 7.97 (t, J_o = 8.5 Hz, J_m = 1.5 Hz, 1 H), 7.84 (s, 1 H), 7.66 (t, J_o = 7.5 Hz, J_m = 1.0 Hz, 1 H), 7.60 (d, J_o = 7.5 Hz, J_m = 1.5 Hz, 1 H), 7.39 (d, J_o = 7.5 Hz, J_m = 1.0 Hz, 2 H), 7.26 (t, J_o = 8.5 Hz, J_m = 1.5 Hz, 2 H), 7.20 (m, 12 H), 7.11 (m, 6 H), 7.02−6.88 (m, 22 H), 6.86 (m, 4 H), 6.84−6.72 (m, 10 H), 6.49 (t, *J* = 7.5 Hz, 1 H), 6.38 (d, *J* = 8.0 Hz, 1 H), 5.40 (s, 2 H), 5.21 (s, 1 H), 3.75 (s, 2 H), −2.56 (s, 2 H).

Finally, grafting of 2-MeIm was performed with an excess of nitrogen base and a catalytic amount of NaI added to 230 mg (1.48 mmol) of the acceptor dissolved in 60 mL of toluene/ethanol (1:1) at 55 °C, in the dark and under argon. The reaction was allowed to proceed for 12 hours, then the mixture was evaporated to dryness. The residue was poured onto a silica gel column and the desired product **6**, collected under argon, was eluted with 0.5% $CH_3OH/CHCl_3$ and stored in a glove box (yield = 70%, 165 mg). ^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ = 9.10 (d, *J* = 4.5 Hz, 2 H), 8.99 (d, *J* = 7.0 Hz, 2 H), 8.98 (d, *J* = 3.5 Hz, 2 H), 8.97 (d, *J* = 4.5 Hz, 2 H), 8.94 (d, *J* = 4.5 Hz, 2 H), 8.15 (d, J_o = 7.5 Hz,

J_m = 1.5 Hz, 1 H), 7.98 (t, J = 8.0 Hz, 1 H), 7.82 (s, 1 H), 7.67 (t, J = 7.5 Hz, 1 H), 7.57 (d, J_o = 7.0 Hz, J_m = 1.5 Hz, 1 H), 7.32 (d, J_o = 7.5 Hz, J_m = 1.5 Hz, 2 H), 7.29 (s, 1 H), 7.26 (t, J_o = 8.0 Hz, J_m = 1.5 Hz, 2 H), 7.19 (m, 13 H), 7.10 (d, J = 8.0 Hz, 6 H), 7.00−6.92 (m, 19 H), 6.88 (t, J_o = 7.5 Hz, J_m = 1.0 Hz, 2 H), 6.84 (d, J = 7.0 Hz, 1 H), 6.80 (d, J = 8.5 Hz, 2 H), 6.79−6.72 (m, 4 H), 6.61 (s, 1 H, H_2'), 6.44 (d, J = 5.0 Hz, 2 H), 6.36−6.33 (m, 2 H), 6.32 (d, J = 1.5 Hz, 1 H), 5.84 (d, J = 1.5 Hz, 1 H), 5.39 (s, 2 H), 5.16 (s, 1 H), 4.15 (s, 2 H), 1.70 (s, 3 H), −2.55 (s, 2 H). − MS (FAB): m/z = 1600.3 $[M]^+$.

[α-5,10,15-Tris(2-triphenylmethylaminophenyl)-β-20-(2-{[3-(imidazol-1-yl)methyl]benzoylamido}phenyl)porphyrin]zinc(II) (6Zn): In a glove box, **6** was dissolved in methanol and an excess of $Zn(OAc)_2$ and sodium acetate was added. The mixture was stirred and refluxed for 10 hours. After evaporation to dryness, the residue was suspended in CH_2Cl_2, filtered, and the solvent removed under vacuum. Chromatography on a silica gel column yielded the final compound **6Zn** eluted with $CHCl_3$. − ^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ = 9.24 (d, J = 8.5 Hz, 1 H), 9.01 (d, J = 4.0 Hz, 2 H), 8.99 (d, J = 4.5 Hz, 2 H), 8.93 (d, J = 4.5 Hz, 2 H), 8.78 (d, J = 4.5 Hz, 2 H), 8.04 (d, J_o = 7.5 Hz, J_m = 1.5 Hz, 1 H), 7.98 (d, J = 8.0 Hz, 1 H), 7.87 (t, J_o = 8.0 Hz, J_m = 1.5 Hz, 2 H), 7.57−7.46 (m, 4 H), 7.39−7.19 (m, 10 H), 7.18−7.01 (m, 16 H), 6.97−6.83 (m, 19 H), 6.82−6.67 (m, 14 H), 5.32 (t, J = 1.5 Hz, 1 H, H_2'), 5.05 (d, J = 1.6 Hz, 1 H), 3.95 (s, 2 H), 1.51 (d, J = 1.6 Hz, 1 H), −1.50 (s, 3 H). − MS (FAB): m/z = 1661.7 $[M + H]^+$.

Ethyl 3-[(2-Methylimidazol-1-yl)methyl]benzoate (7): 3-(Chloromethyl)benzoyl chloride (100 μL, 0.7 mmol) was injected into 10 mL of degassed ethanol over the space of one hour. After evaporation of the solvent to dryness, a brown oil was obtained. − ^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ = 8.04 (t, J_m = 1.5 Hz, 1 H), 7.97 (d, J_o = 8.0 Hz, J_m = 1.5 Hz, 1 H), 7.54 (d, J_o = 8.0 Hz, J_m = 1.5 Hz, 1 H), 7.39 (t, J = 7.5 Hz, 1 H), 4.58 (s, 2 H), 4.36 (q, J = 7.0 Hz, 2 H), 1.37 (t, J = 7.0 Hz, 3 H). This ester was then added to 2-MeIm (57.4 mg, 0.7 mmol) in 5 mL of DMF under reflux and stirred for 4 hours. The solvent was removed under vacuum and the resulting mixture was chromatographed on a silica gel column with $CHCl_3$ as eluent to give **7** as an yellow oil. − ^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ = 7.98 (d, J = 8.0 Hz, 1 H), 7.83 (s, 1 H, H_2'), 7.41 (t, J = 8.0 Hz, 1 H), 7.18 (d, J_o = 8.0 Hz, J_m = 0.5 Hz, 1 H), 6.96 (s, 1 H), 6.85 (s, 1 H), 5.10 (s, 2 H), 4.36 (q, J = 7.5 Hz, 2 H), 2.33 (s, 3 H), 1.39 (t, J = 7.5 Hz, 3 H).

α-5,10,α-15,20-Bis(2,2′-{3,3′-[2,2-(diethoxycarbonyl)propane-1,3-diyl]dibenzoylamido}diphenyl)porphyrin (8): A 50 mL three neck round bottom flask equipped with a stir bar was charged with sodium (0.8 mmol, 18 mg) in 3 mL of EtOH. After 30 min., diethyl malonate (0.8 mmol, 118 μL) was added and the mixture was stirred for 1 hour. The porphyrin **2** (0.04 mmol, 50 mg) was dissolved in 10 mL of dry THF and slowly added to the reaction mixture. After 24 hours, the solvent was removed and the residue was chromatographed on a silica gel column eluting with 0.5% CH_3OH/CH_2Cl_2. Compound **8** was obtained in 80% yield (45 mg). − ^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ = 8.92 (s, 4 H), 8.86 (s, 4 H), 8.69 (d, J = 8.4 Hz, 4 H), 7.91 (t, J_o = 7.8 Hz, J_m = 1.3 Hz, 4 H), 7.80 (d, J_o = 7.5 Hz, J_m = 1.2 Hz, 4 H), 7.48 (t, J = 7.5 Hz, 4 H), 7.40 (s, 4 H), 7.07 (d, J = 7.9 Hz, 4 H), 6.65 (d, J = 7.5 Hz, 4 H), 6.59 (s, 4 H, H_2'), 6.39 (t, J = 7.7 Hz, 4 H), 3.98 [q, J = 7.0 Hz, 4 H, -$(CH_2)_o$$CH_3$], 3.53 [q, J = 7.1 H, 4 H, -$(CH_2)_i$$CH_3$], 2.38 (d, J = 13.8 Hz, 4 H), 2.18 (d, J = 13.8 Hz, 4 H), 1.09 [t, J = 6.9 Hz, 6 H, -$CH_2(CH_3)_o$], 0.64 [t, J = 7.1 Hz, 6 H, -$CH_2(CH_3)_i$], −2.95 (s, 2 H). − HR-MS (LSI-MS): m/z ($C_{90}H_{74}N_8NaO_{12}$ $[M + Na]^+$): calcd. 1481.5335; found 1481.5324. − $C_{90}H_{74}N_8O_{12}$·CH_2Cl_2 (1544.5): calcd. C 70.76, H 4.96, N 7.25; found C 70.68, H 5.06, N 6.92. − UV/Vis (CH_2Cl_2): λ nm (10^{-3}·ε, M^{-1} cm^{-1}) = 419 (448.7), 512 (24.6), 544 (4.9), 586 (7.6), 642 (1.9).

[α-5,10,α-15,20-Bis(2,2′-{3,3′-[2,2-(diethoxycarbonyl)propane-1,3-diyl]dibenzoylamido}diphenyl)porphyrin]zinc(II) (8Zn): Porphyrin **8** (20 mg) was dissolved in $CHCl_3$ containing 2,6 lutidine (0.2 mL). The mixture was stirred and refluxed for 1 hour. After evaporation, the crude product was chromatographed on a silica gel column with CH_2Cl_2 to give **8Zn** in 85% yield (23 mg). − ^{1}H NMR (500 MHz, $CDCl_3$, 323 K): δ = 9.07 (s, 4 H), 8.84 (s, 4 H), 8.65 (d, J = 8.3 Hz, 4 H), 7.85 (t, J_o = 7.8 Hz, J_m = 1.3 Hz, 4 H), 7.78 (d, J = 7.7 Hz, 4 H), 7.72 (s, 4 H), 7.48 (t, J_o = 7.7 Hz, J_m = 1.0 Hz, 4 H), 7.35 (d, J = 7.8 Hz, 4 H), 6.78 (t, J = 7.7 Hz, 4 H), 6.38 (d, J = 7.4 Hz, 4 H), 5.63 (large s, 4 H, H_2'), 3.29 [q, J = 7.1 Hz, 4 H, -$(CH_2)_o$$CH_3$], 3.14 [q, J = 6.1 Hz, 4 H, -$(CH_2)_i$$CH_3$], 1.84 (d, J = 13.0 Hz, 4 H), 1.10 (d, J = 13.0 Hz, 4 H), 0.72 [t, J = 7.1 Hz, 6 H, -$CH_2(CH_3)_o$], 0.52 [t, J = 6.8 Hz, 6 H, -$CH_2(CH_3)_i$]. − MS (MALDI-TOF): m/z = 1520.3 $[M]^+$. − $C_{90}H_{72}N_8O_{12}Zn$·$2H_2O$ (1559.0): calcd. C 69.34, H 4.91, N 7.19; found C 69.01, H 5.09, N 6.78. − UV/Vis (CH_2Cl_2): λ nm (10^{-3}·ε, M^{-1} cm^{-1}) = 425 (549.7), 516 (5.8), 554 (27.8), 590 (3.8).

α-5,15-(2,2′-{3,3′-[2,2′-(Diethoxycarbonyl)propane-1,3-diyl]dibenzoylamido}diphenyl)-α-10,20-bis(2,2′-{3,3′-[1,1′-(diethoxycarbonyl)ethane-2-yl]benzoylamido}phenyl)porphyrin (9): The procedure described above for **8** was used. Sodium (0.89 g, 40 mmol) and diethyl malonate (5.9 mL, 40 mmol) were dissolved in 30 mL of EtOH and the porphyrin **2** (50 mg, 0.04 mmol), dissolved in 10 mL of THF, was added. After 24 hours, the solvent was removed and the residue was chromatographed on a silica gel column, eluting with 5% pentane/CH_2Cl_2. Compound **9** was obtained in 74% yield (46 mg). − ^{1}H NMR (500 MHz, $CDCl_3$, 320 K): δ = 9.08 (d, J = 8.4 Hz, 2 H), 9.06 (d, J = 4.7 Hz, 4 H), 8.95 (d, J = 4.7 Hz, 4 H), 8.71 (d, J = 8.4 Hz, 2 H), 8.56 (s, 2 H), 8.04 (d, J_o = 6.9 Hz, J_m = 1.1 Hz, 2 H), 7.94 (large t, J = 6.6 Hz, 4 H), 7.85 (t, J_o = 8.2 Hz, J_m = 1.3 Hz, 2 H), 7.69 (d, J = 7.7 Hz, 2 H), 7.65 (d, J_o = 7.7 Hz, J_m = 1.3 Hz, 2 H), 7.59 (t, J = 7.2 Hz, 2 H), 7.55 (s, 2 H, $H_{2'}$), 7.47 (t, J = 7.5 Hz, 2 H), 6.97 (t, J = 7.7 Hz, 2 H), 6.50 (d, J = 7.8 Hz, 4 H), 6.44 (d, J = 5.7 Hz, 2 H), 5.88 (t, J = 7.4 Hz, 2 H), 4.84 (s, 2 H, H_2'*), 4.09 [m, 8 H, -$(CH_2)_p$-CH_3], 3.38 (t, J = 7.6 Hz, 2 H, -CH_2CH-), 2.81 (d, J = 7.6 Hz, 4 H, -CH_2CH-), 1.63 (s, 4 H, -CH_2-), 1.17 [t, J = 7.2 Hz, 12 H, -$CH_2(CH_3)_p$], 0.95 [large s, 4 H, -$(CH_2)_s$-CH_3], −0.60 [large s, 6 H, -CH_2-$(CH_3)_s$], −2.25 (s, 2 H). − MS (MALDI-TOF): m/z = 1619.3 $[M]^+$. − $C_{97}H_{86}N_8O_{16}$·H_2O (1637.8): calcd. C 71.14, H 4.42, N 6.84; found C 69.92, H 4.25, N 6.63. − UV/Vis (CH_2Cl_2): λ nm (10^{-3}·ε, M^{-1} cm^{-1}) = 422 (283.5), 516 (19.8), 550 (5.4), 590 (5.9), 647 (2.2).

α-5,10,β-15,20-Bis(2,2′-{3,3′-[2,2-(diethoxycarbonyl)propane-1,3-diyl]dibenzoylamido}diphenyl)porphyrin (10): The procedure described for **8** was used. Sodium (190 mg, 40 mmol) and diethyl malonate (1.3 mL, 40 mmol) were dissolved in 20 mL of EtOH and the porphyrin **3** (35 mg, 0.04 mmol), dissolved in 10 mL of CH_2Cl_2, was added. After 2 hours, the solvent was removed and the residue was chromatographed on a silica gel column, eluting with CH_2Cl_2. Compound **10** was obtained in 75% yield (44 mg). − ^{1}H NMR (500 MHz, $CDCl_3$, 323 K): δ = 8.98 (s, 4 H), 8.70 (d, J_o = 8.4 Hz, J_m = 1.0 Hz, 4 H), 8.69 (s, 4 H), 7.89 (d, J_o = 8.4 Hz, J_m = 1.6 Hz, 4 H), 7.87 (t, J_o = 7.3 Hz, J_m = 1.0 Hz, 4 H), 7.55 (t, J_o = 7.3 Hz J_m = 1.6 Hz, 4 H), 7.51 (t, J_o = 7.6 Hz, J_m = 1.2 Hz, 4 H), 7.42 (s, 4 H), 6.93 (t, J = 7.6 Hz, 4 H), 6.61 (d, J = 7.6 Hz, 4 H), 4.84 (s, 4 H, H_2'), 3.29 [q, J = 7.0 Hz, 4 H, -$(CH_2)_o$$CH_3$], 2.53 [q, J = 7.0 Hz, 4 H, -$(CH_2)_i$$CH_3$], 1.44 (d, J = 13.5 Hz, 4 H), 0.63 [t, J = 7.0 Hz, 6 H, -$CH_2(CH_3)_o$], 0.57 (d, J = 13.5 Hz, 4 H), 0.01 [t, J =

7.0 Hz, 6 H, -$CH_2(CH_3)_i$], −2.16 (s, 2 H). − MS (FAB): *m/z* = 1458.6 $[M]^+$. − $C_{90}H_{74}N_8O_{12}$ (1459.6162): calcd. C 74.06, H 5.11, N 7.68; found C 74.25, H 5.35, N 7.30. − UV/Vis (CH_2Cl_2): λ nm (10^{-3}·ε, M^{-1} cm^{-1}) = 422 (433.5), 516 (17.4), 550 (4.8), 590 (5.6), 647 (1.4).

[α-5,10,β-15,20-Bis(2,2′-{3,3′-[2,2-(diethoxycarbonyl)propane-1,3-diyl]dibenzoylamido}diphenyl)porphyrin]nickel(II) (10Ni): Porphyrin **10** (45 mg) was dissolved in 15 mL of pyridine and an excess of $Ni(OAc)_2$ was added. The mixture was stirred and refluxed for 48 hours. The solvent was removed under vacuum and the residue was redissolved in CH_2Cl_2, filtered, and dried again. Chromatography on a silica gel column yielded the final compound **10Ni** after elution with 2% CH_3OH/CH_2Cl_2 (yield 20%, 9 mg). − ^1H NMR (500 MHz, $CDCl_3$, 323 K): δ = 8.85 (s, 4 H), 8.70 (d, J_o = 8.1 Hz, J_m = 0.9 Hz, 4 H), 8.65 (s, 4 H), 7.82 (t, J_o = 8.1, J_m = 1.2 Hz, 4 H), 7.77 (d, J_o = 7.6 Hz, J_m = 1.2 Hz, 4 H), 7.59 (t, J_o = 7.7 Hz, J_m = 1.4 Hz, 4 H), 7.47 (t, J_o = 7.6 Hz, J_m = 0.9 Hz, 4 H), 7.34 (s, 4 H), 6.96 (t, *J* = 7.6 Hz, 4 H), 6.67 (d, *J* = 7.6 Hz, 4 H), 4.85 (s, 4 H, H_2'), 3.41 [q, *J* = 7.1 Hz, 4 H, -$(CH_2)_oCH_3$], 2.81 [q, *J* = 7.1 Hz, 4 H, -$(CH_2)_iCH_3$], 1.66 (d, *J* = 13.7 Hz, 4 H), 1.01 (d, *J* = 13.7 Hz, 4 H), 0.70 [t, *J* = 7.1 Hz, 6 H, -$CH_2(CH_3)_o$], 0.16 [t, *J* = 7.1 Hz, 6 H, -$CH_2(CH_3)_i$]. − MS (MALDI-TOF): *m/z* = 1514.71 $[M]^+$. − $C_{90}H_{72}N_8NiO_{12}$·H_2O (1534.3): calcd. C 70.45, H 4.86, N 7.30; found C 70.54, H 5.21, N 7.06. − UV/Vis (CH_2Cl_2): λ nm (10^{-3}·ε, M^{-1} cm^{-1}) = 415 (242.5), 527 (19.5), 558 (6.7).

[α-5,10:β-15,20-Bis[2,2′-{3,3′-[2,2-(diethoxycarbonyl)propane-1,3-diyl]dibenzoylamido}diphenyl)porphyrin]zinc(II) (10Zn): Porphyrin **10** (45 mg) was dissolved in 15 mL of $CH_3OH/CHCl_3$ and an excess of $Zn(OAc)_2$ and sodium acetate were added. The mixture was stirred and refluxed during 1 hour. Solvents were removed under vacuum and the residue was redissolved in CH_2Cl_2, filtered, and dried again. Chromatography on a silica gel column gave the final compound **10Zn** after elution with 2% CH_3OH/CH_2Cl_2 (yield 98%, 45 mg). − ^1H NMR (500 MHz, $CDCl_3$, 323 K): δ = 9.03 (s, 4 H), 8.79 (s, 4 H), 8.69 (d, J_o = 8.3 Hz, J_m = 0.9 Hz, 4 H), 7.99 (d, J_o = 7.5 Hz, J_m = 1.2 Hz, 4 H), 7.86 (t, J_o = 8.1 Hz, J_m = 1.5 Hz, 4 H), 7.62 (t, J_o = 8.1 Hz, J_m = 1.6 Hz, 4 H), 7.55 (t, J_o = 7.6 Hz, J_m = 1.2 Hz, 4 H), 7.26 (s, 4 H), 6.94 (t, *J* = 7.7 Hz, 4 H), 6.54 (t, J_o = 7.7 Hz, J_m = 1.3 Hz, 4 H), 3.82 (s, 4 H, H_2'), 2.46 [q, *J* = 7.2 Hz, 4 H, -$(CH_2)_oCH_3$], 2.27 [q, *J* = 7.2 Hz, 4 H, -$(CH_2)_iCH_3$], 1.31 (d, *J* = 13.0 Hz, 4 H), 0.21 [t, *J* = 7.1 Hz, 6 H, -$CH_2(CH_3)_o$], 0.11 [t, *J* = 7.1 Hz, 6 H, -$CH_2(CH_3)_i$], −0.40 (d, *J* = 13.0 Hz, 4 H). − MS (MALDI-TOF): *m/z* = 1522.01 $[M + H]^+$. − $C_{90}H_{72}N_8O_{12}Zn$·$2H_2O$ (1559.0): calcd. C 69.34, H 4.91, N 7.19; found C 69.09, H 4.90, N 7.43. − UV/Vis (CH_2Cl_2): λ nm (10^{-3}·ε, M^{-1} cm^{-1}) = 429 (391.2), 556 (20.9), 595 (3.0).

X-ray Crystallographic Study of 3Zn:[41] $(C_{80}H_{60}Cl_4N_8O_5Zn)$·$2(C_7H_8)$·$C_6H_6$; *M* = 1682.91. Enraf−Nonius Kappa-CCD diffractometer, Mo-K_α radiation (λ = 0.71073 Å), *T* = 110 K; triclinic, $P\bar{1}$, *a* = 13.3350(6), *b* = 13.6190(4), *c* = 13.8300(6) Å, α = 69.213(2), β = 66.947(2), γ = 83.917(3)°, *V* = 2159.06(15), *Z* = 1, D_x = 1.294 g cm^{-3}, μ = 0.467 mm^{-1}. The structure was solved by direct methods and subsequent difference Fourier analysis.[42] Due to the weak diffracting power of the crystal, the refinement was performed on the 6866 observed reflections with [$I > 3\sigma(I)$] among the 9679 reflections collected. The porphyrin is located on the inversion centre and the zinc atom with the axial ligand (THF), disordered over both faces of the macrocycle, was refined with a multiplicity *m* = 0.5. One benzene solvate molecule located at the opposite face with respect to the axial ligand was isotropically refined and its multiplicity converged to the value *m* = 0.5. One chlorine atom was disordered and refined with multiplicities m_1 = 0.6462 and $m_2 = 1 - m_1$. One toluene solvate molecule was also found to be disordered over two positions and refined with final multiplicities m_3 = 0.7224 and $m_4 = 1 - m_3$. A final refinement on F^2 with 6866 observed intensities and 525 parameters converged at $wR(F^2)$ = 0.209 and $R(F)$ = 0.077.

[1] B. G. Malmström, *Chem. Rev.* **1990**, *90*, 1247−1260.
[2] M. X. Calhoun, J. W. Thomas, R. B. Gennis, *TIBS* **1994**, 325−330.
[3] R. B. Gennis, S. Ferguson-Miller, *Science* **1995**, *269*, 1063−1064.
[4] T. Tsukihara, H. Aoyama, E. Yamashita, T. Tomizaki, H. Yamaguchi, K. Shinzawa-Itoh, R. Nakashima, R. Yaono, S. Yoshikawa, *Science* **1995**, *269*, 1069−1074.
[5] S. Iwata, C. Ostermeier, B. Ludwig, H. Michel, *Nature* **1995**, *376*, 660−669.
[6] K. D. Karlin, A. Nanthakumar, S. Fox, N. N. Murthy, N. Ravi, B. H. Huynh, R. D. Orosz, E. P. Day, *J. Am. Chem. Soc.* **1994**, *116*, 4753−4763.
[7] M. J. Scott, S. C. Lee, R. H. Holm, *Inorg. Chem.* **1994**, *33*, 4651−4662.
[8] J. P. Collman, P. C. Herrmann, B. Boitrel, X. M. Zhang, T. A. Eberspacher, L. Fu, J. L. Wang, D. L. Rousseau, E. R. Williams, *J. Am. Chem. Soc.* **1994**, *116*, 9783−9784.
[9] T. Sasaki, Y. Naruta, *Chem. Lett.* **1995**, 663−664.
[10] F. Tani, Y. Matsumoto, Y. Tachi, T. Sasaki, Y. Naruta, *Chem. Commun.* **1998**, 1731−1732.
[11] J. O. Baeg, R. H. Holm, *Chem. Commun.* **1998**, 571−572.
[12] J. P. Collman, L. Fu, P. C. Herrmann, Z. Wang, M. Rapta, M. Bröring, R. Schwenninger, B. Boitrel, *Angew. Chem. Int. Ed.* **1998**, *37*, 3397−3400.
[13] J. P. Collman, M. Rapta, M. Bröring, L. Raptova, R. Schwenninger, B. Boitrel, L. Fu, M. L′Her, *J. Am. Chem. Soc.* **1999**, *121*, 1387−1388.
[14] M.-A. Kopf, K. D. Karlin, *Inorg. Chem.* **1999**, *38*, 4922−4923.
[15] S. Yoshikawa, K. ShinzawaItoh, R. Nakashima, R. Yaono, E. Yamashita, N. Inoue, M. Yao, M. J. Fei, C. P. Libeu, T. Mizushima, H. Yamaguchi, T. Tomizaki, T. Tsukihara, *Science* **1998**, *280*, 1723−1729.
[16] B. Andrioletti, B. Boitrel, R. Guilard, *J. Org. Chem.* **1998**, *63*, 1312−1314.
[17] D. Ricard, A. Didier, M. L′Her, B. Boitrel, *ChemBioChem.* **2001**, *2*, 144−148.
[18] D. Ricard, B. Andrioletti, M. L′Her, B. Boitrel, *Chem. Commun.* **1999**, 1523−1524.
[19] J. P. Collman, R. R. Gagne, C. A. Reed, T. R. Halbert, G. Lang, W. T. Robinson, *J. Am. Chem. Soc.* **1975**, *97*, 1427−1439. The rotation of the aminophenyl group leads to four atropisomers, stable in solution at room temperature. They have been named αααα for the isomer with the four amino groups on the same side of the porphyrin, ααaβ for the isomer with three amino groups on one side and the fourth one on the other side, ααββ when the porphyrin bears two contiguous amino groups on one face with the two others on the other face. Finally, the amino groups of the isomer αβαβ are alternatively on one side and on the other one. They are cited above by decreasing polarity, with their statistical abundance in brackets: αααα (12.5%), ααaβ (50%), ααββ (25%), αβαβ (12.5%). The abundance of the atropisomer αααα is raised up to 70% according to ref.[40].
[20] R. Young, C. K. Chang, *J. Am. Chem. Soc.* **1985**, *107*, 898−909.
[21] J. P. Collman, X. Zhang, P. C. Herrmann, E. S. Uffelman, B. Boitrel, A. Straumanis, J. I. Brauman, *J. Am. Chem. Soc.* **1994**, *116*, 2681−2682.
[22] J. P. Collman, M. Bröring, L. Fu, M. Rapta, R. Schwenninger, A. Straumanis, *J. Org. Chem.* **1998**, *63*, 8082−8083.
[23] J. P. Collman, M. Bröring, L. Fu, M. Rapta, R. Schwenninger, *J. Org. Chem.* **1998**, *63*, 8084−8085.
[24] C. K. Chang, Y. Liang, G. Aviles, *J. Am. Chem. Soc.* **1995**, *117*, 4191−4192.
[25] Ò H. Aissaoui, R. Bachmann, A. Schweiger, W.-D. Woggon, *Angew. Chem. Int. Ed.* **1998**, *37*, 2998−3002.
[26] J. P. Collman, C. A. Reed, *J. Am. Chem. Soc.* **1973**, *95*, 2048−2049.

[27] H. H. Wasserman, K. Stiller, M. B. Floyd, *Tetrahedron Lett.* **1968**, *29*, 3277−3280.
[28] M. Kaplan, *Chem. Tech.* **1971**, 621−626.
[29] N. G. Larsen, P. D. W. Boyd, S. J. Rodgers, G. E. Wuenschell, C. A. Koch, S. Rasmussen, J. R. Tate, B. S. Erler, C. A. Reed, *J. Am. Chem. Soc.* **1986**, *108*, 6950−6960.
[30] In this particular case in which the porphyrin bears only one imidazole, the decomposition of the porphyrin was slow enough to allow the ^{1}H NMR characterisation of both the free-base and the diamagnetic zinc complex.
[31] In most of these compounds, a gaussian transformation has to be performed to observe the *meta* coupling constant for this proton which otherwise appears as a large singlet.
[32] M. P. Du Plessis, T. A. Modro, L.R. Nassimbeni, *J. Crystallogr. Spectrosc. Res.* **1983**, *13*, 179−189.
[33] W. W. Adams, A. V. Fratini, D. R. Wiff, *Acta. Crystallogr., Sect. B* **1978**, *34*, 954−956.
[34] L. Michaudet, P. Richard, B. Boitrel, *Chem. Commun.* **2000**, 1589−1590.
[35] The same reaction has been tested with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as a nonnucleophilic base but, in our hands, this procedure was not reproducible.
[36] In the case of TAPP, the four aniline aromatic rings are connected to the carbon atoms in the *meso* positions numbered 5, 10, 15, 20.
[37] The chemical shifts of diethyl malonate $(CH_3-CH_2-OOC)_2CH_2$ are: δ = 1.23 (t, 6 H), 3.51 (q, 4 H), 2.18 (s, 2 H).
[38] The same difference is found between benzyl chloride (δ = 4.5) and diethylbenzyl malonate (δ = 3.6).
[39] To be published: the coordination of the zinc atom in a chiral bis-strapped porphyrin by the oxygen atom of an amide bond has been observed both in the solid state and in solution.
[40] J. Lindsey, *J. Org. Chem.* **1980**, *45*, 5215.
[41] Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-154271 Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].
[42] SHELX-97 − Programs for Crystal Structure Analysis (Release 97−2). G. M. Sheldrick, Institüt für Anorganische Chemie der Universität, Tammanstrasse 4, D-3400 Göttingen, Germany, **1998**.

Received October 4, 2000
[O00517]