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Novel crowned-porphyrin ligands. Synthesis and conformational studies

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Abstract—Three new macromolecules—a cryptand, a bis-macrocycle, and a tris-macrocycle—have been synthesized as chelating ligands for cation binding. They result from the surprisingly simple reaction of various bis-functionalized *meso*-aryl porphyrins with a diaza-crown ether coupled one to each other through either one or several urea linkage(s). Indeed, the latter induces some additional rigidity in comparison with the usual amide linkage found in such macromolecules. Various strategies are reported to optimize the yield of the reaction towards the formation of a cofacial singly-linked crown-porphyrin, which is the most promising ligand to stabilize large cations such as bismuth(III) as the angle between the two macrocycles can vary.

1. Introduction

In our on-going research program dedicated to the coordination of various cations of medical interests, we have been studying for almost a decade different types of macromolecular architectures.[1] Among these cations, one can cite gadolinium, yttrium, bismuth, or europium. The first one is obviously known to be efficient in the design of new imaging agents[2] where the last one is commonly employed for the preparation of luminescent molecules.[3] The second and third elements are either already clinically used in β-radiotherapy[4] or evaluated for α-radiotherapy,[5] respectively. An example of these chelating molecules is the cofacial cyclam-strapped porphyrins, which have proved to be efficient for the coordination of two transition metals as iron and cobalt.[6] However, such edifices are likely too rigid to be efficient chelators of larger cations such as gadolinium, europium or bismuth. Indeed, neither the former nor the latter are stabilized in single-crowned[7] or bis-crowned porphyrins,[8] respectively. In the first case, we have explained this non coordination of gadolinium presumably because of a *para*-pyridyl residue on two *meso* positions of the porphyrin, which can directly interact with the lanthanide cation, a competitive interaction to the metallation process. In the second example, the bis-crowned porphyrin was not flexible enough to be distorted and hence to allow the entry of the bismuth cation inside the cavity. However, as these three elements exhibit different radii,[9] our goal was to design a rigid but still flexible family of molecules, which could adapt its size to the desired cation.[10] This is the reason why we have investigated the synthesis of singly-linked crown porphyrins.

2. Results and discussion

The reaction of 1,4,10,13-tetraoxa-7,16-diaza-cyclooctadecane (Kryptofix-2,2 or diaza-18-crown-6 ether) on a 5,15-*o*-diamido picket porphyrin or on a 5,15-*o*-diaminophenyl porphyrin usually leads to the formation of a macromolecule in which the two different macrocycles appear to be in a cofacial geometry as in macrotricycle **1**.[11] Indeed, in the latter, the diaza-crown ether being bis-linked on the porphyrin, cannot escape from its apical position, as it can in compound **2**. However, when the bonds between the two

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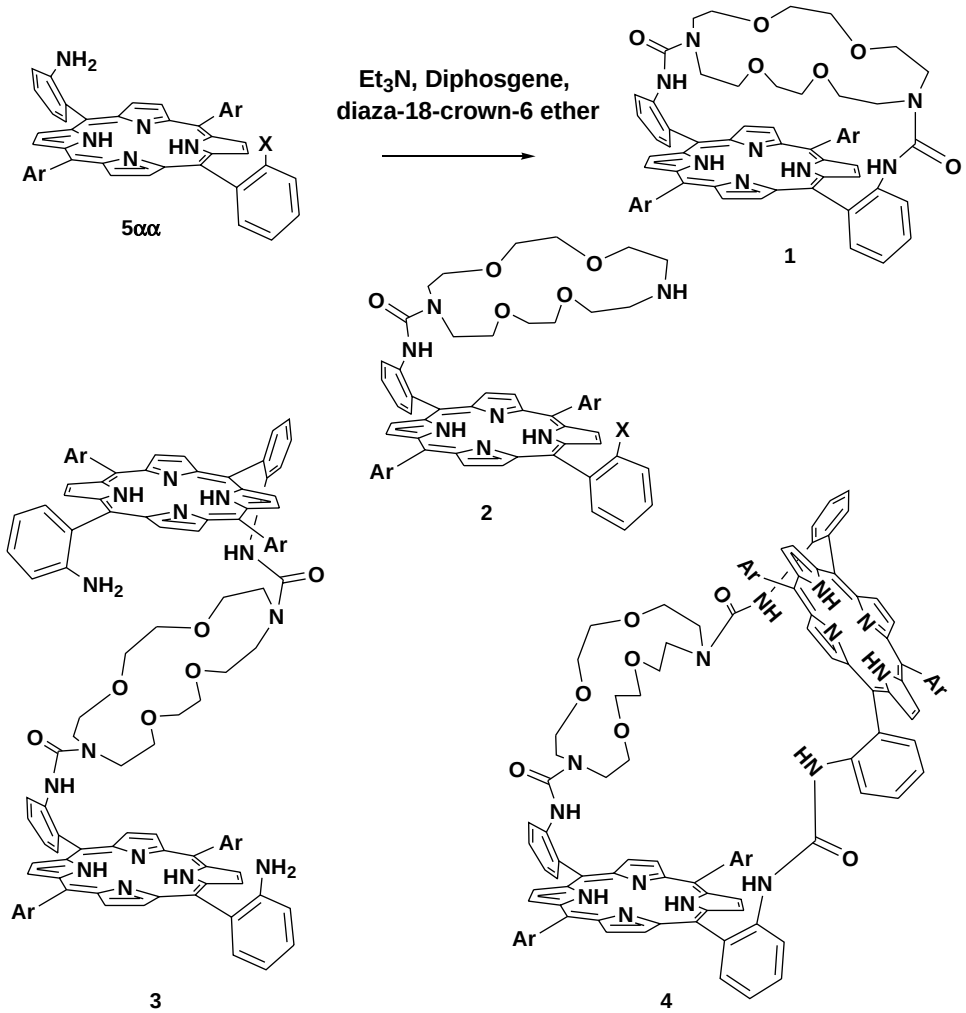
macrocyles are very short as in the case of a urea bond,[12] we noticed that the system was not sufficiently flexible to coordinate metal cations bulkier than zinc for instance. To obtain flexible systems, we required the crown-ether motif to be able—more or less—to move away from the porphyrin according to the cation to stabilize, hence the target molecule **2**. Such a compound should exist as two different isomers (*endo* and *exo*) but owing to the urea bond, the cofacial geometry is expected to be favored. Moreover, if one considers that the crown-ether is attached by the *meso* positions 5 and 15, it is obvious that the steric hindrance induced by the two other *meso* positions, namely 10 and 20 can influence the approach of the cage by the cation and also the position of the strapped crown-ether. Accordingly, we studied various aromatic groups (Scheme 1) such as 2,4,6-trimethylphenyl (mesityl, compounds labeled **a**) or 3,5-dimethoxyphenyl (compounds labeled **b**). Indeed, in the case of the dimesityl porphyrin, the two *ortho* positions of the aromatic rings in the positions 10 and 20 being substituted by a methyl group, the crown ether is expected to be less mobile than in the other series with methoxy groups in *meta* positions. This detail will be discussed vide infra. Actually, by choosing the experimental conditions, we could optimize the reaction towards the preparation of **1** or **2**, concomitantly with the synthesis of the tris-macrocycle **3** and the macrotetracycle **4**. Obviously, to avoid unambiguously the synthesis of the macrotricyclic crown-porphyrin **1**, the unique procedure would consist in protecting one amino function of both the porphyrin and the crown-ether. But in regard with the facility of the synthetic path of Scheme 1, we preferred to vary the experimental procedure (method B vs method A, see Section 4.2) to obtain compound **2**. Additionally, in the mesityl series **a**, we have also investigated an alternative procedure that consists in working with a singly reduced porphyrin such as **5aNO$_2$**. In literature, this type of selectivity has already been achieved either by reducing[13] only one nitro group of a 2,6-dinitro-*meso*phenyl group or by acylating only one amino function after reduction of the two nitro functions.[14] Theoretically, in a typical synthesis, **1** should be the single product of the reaction but is also the less attractive. Practically, the three other compounds exhibit more sophisticated structures. For instance, in compound **2**, two structural criterions have to be considered. The first deals with the 'face-to-face' spatial arrangement of the two macrocycles. As already mentioned, the urea bond itself should maintain this cofacial geometry. Moreover, this is verified by proton NMR spectroscopy, since we can carry



Scheme 1. General synthesis of crowned porphyrins from an α-5,15-bis-(2-amino-phenyl)porphyrin or from an α-5-(2-amino-phenyl)-α-15-(2-nitro-phenyl)porphyrin. Compounds are labelled as follow: series **a**: Ar=2,4,6-trimethyl-phenyl, series **b**: Ar=3,5-dimethoxy-phenyl. When X=NO_2, NO_2 is added at the end of the name. Note that two methods can be used for this reaction.

out a reliable comparison with compound **1** for which we know precisely the conformation. For instance, in **1b**, the fingerprint of the crown-ether is composed of 3 singlets integrating for 8 protons each at 2.56, 1.94 and 0.49 ppm. In the case of **2b**, the NMR signature becomes 6 broad singlets of 4 protons in the range 2.68–1.43 ppm. In the latter compound, signals upfield shifted as in compound **1b** do not exist anymore, which testifies well to the larger distance —at least for some protons— of the crown-ether to the cone of anisotropy of the porphyrin. However, it is difficult to investigate if the crown-ether motif is still above the porphyrin or presumably slightly off-centered. In the 2,4,6-trimethyl-phenyl series **a**, a similar conclusion is drawn with signals at 2.60, 2.07 and 1.56 ppm for **1a** and signals between 2.88 and 1.97 ppm for **2aNO$_2$**.

But the most intriguing observation resulting from the comparison of the various NMR data consists in the signature of the crown-ether obtained in the case of the bis-porphyrin compound **3b**. Indeed, one can easily conceive various spatial arrangements in solution for this type of compound (Fig. 1). The most probable is depicted in representation (c1) with no specific conformation of the crown-ether moiety and the two porphyrin units most distant one from the other. Yet, this conformation is not consistent at all with the chemical shifts of the protons from the crown-ether, which resonate as broad singlets of 8 protons each at 1.82, 1.13, and −0.46 ppm. Theses chemical shifts show that all the protons of the crown-ether in **3b** are more shielded than they are in **1b**. More particularly, 8 of them are more upfield-shifted of 1 ppm (−0.46 ppm) relatively to the 8 most shielded protons in **1b** (0.49 ppm). This observation implies that **3b** has to exist in a conformation in which the crown-ether motif undergoes the additive effect of the two porphyrin rings. Such possible conformations are represented in (c2) and (c3) (Fig. 1). However, the conformation (c2) is difficult to explain as there is no argument to justify a 'curved' conformation of the crown-ether. Conversely, in conformation (c3), the fact that the crown-ether is pinched between the two porphyrins could be induced by the urea linkage itself, as in compound **2b** in which a relaxed face-to-face conformation is observed. Hence, we propose this 'Z-shape' structure in solution for compound **3b**.

Finally, the fourth isolated compound is the macrotetracycle **4b**. Although related somehow to the coreceptor molecules reported by Lehn and co-workers,[15] **4b** is different as the two porphyrin units are not expected to be cofacial. Indeed, in this compound, the two porphyrinic units are attached via a urea linkage, which act as a hinge, and the angle between the two porphyrins is actually imposed by the crown-ether, which acts as a spacer. The chemical shifts of the protons from the crown-ether are 3.80, 2.15, and 0.89 ppm. In light of the structure of **4b**, these chemical shifts are expected as they are more down-field shifted than in **2b**, one of them being almost the same (0.89 ppm in **4b** vs 0.49 ppm in **2b**). According to these data, it can be predicted that the angle between the porphyrin(s) and the crown-ether is larger in **4b** than it is in **2b**. But obviously, **4b** should be more flexible than **2b**.

As already mentioned, to optimise the formation of compounds **2** relatively to compounds **1**, we have employed two different approaches. The first one that we have described consists in modifying the experimental procedure. For instance, when method B (see Section 4) is applied instead of method A, the yield of isolated compound **2b** rises up from 5 to 48% yield, mostly at the expense of compounds **1b** and **3b**, the yield of compound **4b** increasing from 3 to 11%. Actually, these two experimental procedures differ mainly by the fact that in method B, both reagents, the activated porphyrin and the crown-ether are added together. The second approach, increasing the yield of **2a** consists in

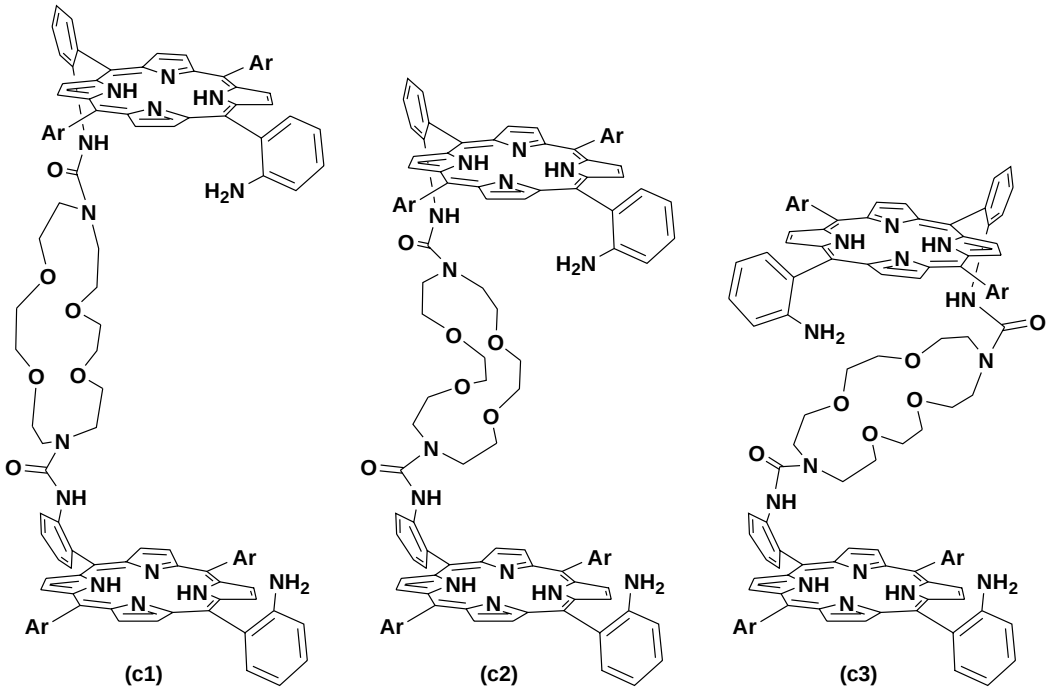
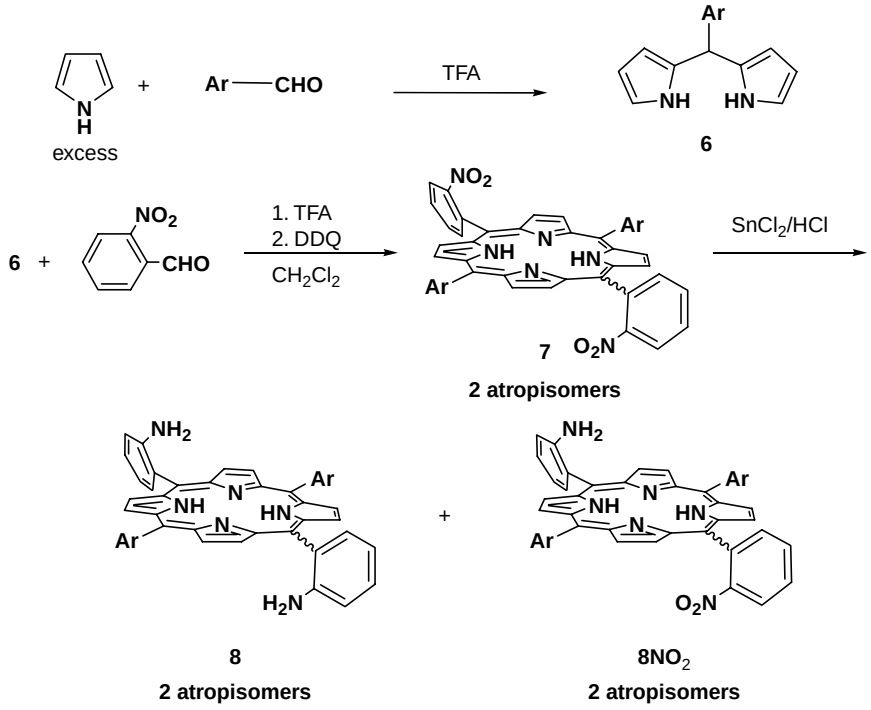


Figure 1. Various possible conformations (c1–c3) of tris-macrocycle **3**.



Scheme 2. Synthesis of the two porphyrinic building-blocks. For compounds labelling, use convention of Scheme 1. When Ar=2,4,6-trimethyl-phenyl, the reduction step leading to **8** was performed at 0 °C.

inhibiting the reactivity of one of the anilines of the porphyrin. Therefore, we have performed a partial reduction of the nitro groups of **7a** to obtain **8aNO$_2$** (Scheme 2), and then, after a separation of the two atropisomers, obtained the **5aNO$_2$**$\alpha\alpha$ atropisomer (Scheme 1). Hence, following the same procedure applied for the diamino counterparts, it is obvious that the formation of either **1a** or **4a** becomes impossible, thereby controlling the reaction towards the exclusive formation of **2a** and **3a**. However, when the reaction was performed with **5aNO$_2$**$\alpha\alpha$, it should be noted that compound **3a** was not obtained either, or only as negligible traces. This observation demonstrates that working with a mono-nitro mono-amino tetraaryl porphyrin represents an efficient alternative for the almost exclusive synthesis of bis-macrocycles **2**.

Incidentally, in compounds **2**, if one considers that the 2-amino (or nitro) aryl groups are on the 5 and 15 *meso* positions, the substitution of the two other *meso* aryl groups may have some influence on the conformation of the compound. For example, in the mesityl series (compounds **a**), it could be probed if the two methyl groups in *ortho* position generate a steric hindrance with the crown-ether or not. Again, this is confirmed by comparing the proton NMR data of **2a** with **2b**. For instance, the chemical shifts of the protons from the crown-ether in **2a** are slightly larger than their analogues in **2b** but the difference is not really significant. Therefore, we can assume that the conformation is not strongly affected by the nature of the two *meso* aryl groups in positions 10 and 20. Additionally, it should be pointed out that any possible distortion of the porphyrin could influence the geometry of the various compounds. Actually, consideration of the X-ray structure of **7a**$\alpha\alpha$, that could be determined (Fig. 2), reveals that there is indeed a slight distortion of the porphyrin cycle, presumably due to the steric hindrance of the two *ortho* positions (Fig. 2b). According to the distances of atoms from the mean porphyrin plane, the distortion may be chiefly described in terms of a saddled conformation, in view of the alternate

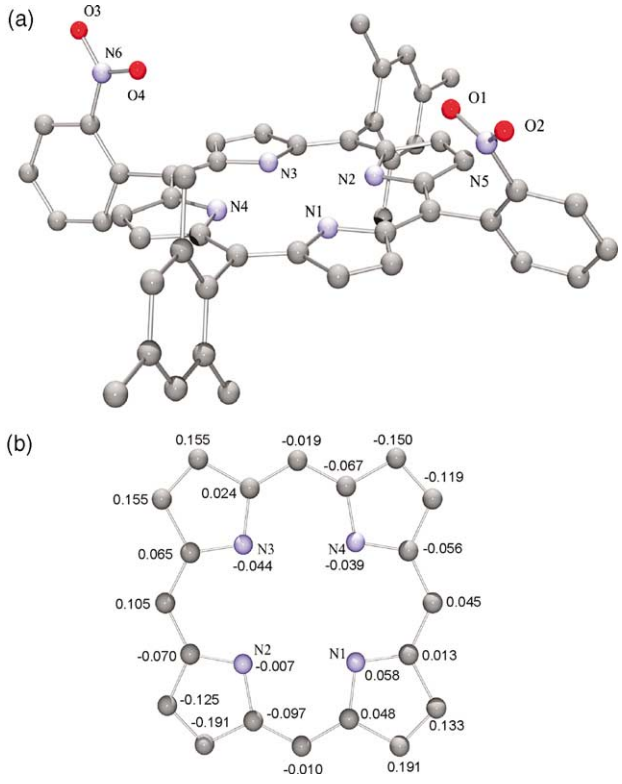


Figure 2. Ball and stick representation of the X-ray structure of the atropisomer $\alpha\alpha$ of **7a**; (a) perspective view, (b) apical view with distances in Å of each atom to the mean plane of the porphyrin.

tilting of adjacent pyrrolic units and *meso* carbons. However, the distortion is not purely saddled as it also exhibits some ruffling, since the Cα–N–N–Cα torsion angles between two diametrically opposed pyrroles are equal to 2.41 and 8.61°.

3. Conclusion

According to two different approaches, we have shown that with a simple and unique reaction, we can synthesize four macromolecules, all of them incorporating at least one porphyrin unit as well as one crown-ether moiety. Whereas one of the two described methods allows the preponderant formation of both the bis-macrocycle and the macrotetracycle, an alternative approach is also proposed to optimize the synthesis of the bis-macrocycle versus the macrotetracycle. Among these four ligands, three of them should exhibit very different properties towards the binding of various cations from groups 13 and 15 or lanthanides. These three macromolecules differ both by the shape and the size of the cavity resulting from the assembly of several macrocycles either by one or two link(s). Coordination studies of these novel bis-macrocycle, tris-macrocycle, and macrotetracycle will be reported elsewhere.

4. Experimental

4.1. General considerations

^{1}H (500.13, 300.13 MHz) NMR spectra were recorded on Bruker Avance spectrometers and referenced to the residual protonated solvent. Mass spectra were performed on a MS/MS ZABSpec TOF spectrometer at the University of Rennes I (C.R.M.P.O.). UV–vis spectra were recorded on a Varian Cary 1E and an Uvikon XL spectrometers. Infrared spectra were recorded on Bruker IFS 66 and 28 spectrometers. All solvents (ACS for analysis) were purchased from Carlo Erba. THF was distilled from potassium metal whereas methanol was distilled from magnesium turnings. CH_2Cl_2 was used as received. Triethylamine was distilled from 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/MeOH). Column flash chromatography was performed on silica gel (Merck TLC-Kieselgel 60H, 15 μm). Elemental analyses were obtained on an EA 1108 Fisons Instruments.

4.2. General synthetic paths

The two following procedures were performed to graft a crown ether on the porphyrin: method A optimises the yield of **1b** and method B, the yield of **2b**.

Method A. In a two neck round bottom flask equipped with a stir bar and a gas inlet, **5bαα** (120 mg, 0.16 mmol) was charged with dry THF (10 mL) and Et_3N (0.1 mL). The mixture was cooled to 0 °C then, diphosgene (9.6 μL, 79 μmol) was added. After 1 h, diaza-18-crown-6 ether (46 mg, 0.18 mmol) in 10 mL of dry CH_2Cl_2 was added dropwise over 30 min and the mixture was stirred for an additional 1 h. The solvent was removed under vacuum and the residue was purified by silica gel chromatography. The compound **4b** was eluted with CH_2Cl_2 and obtained in 3% yield (9 mg), compound **3b** was eluted with 0.2% methanol/CH_2Cl_2 and obtained in 15% yield (22 mg), compound **1b** was eluted with 0.8% methanol/ CH_2Cl_2 and obtained in 55% yield (97 mg) and compound **2b** was eluted with 2% methanol/CH_2Cl_2 and obtained in 5% yield (8.4 mg).

Method B. In a two neck round bottom flask equipped with a stir bar and a gas inlet, **5bαα** (120 mg, 0.16 mmol) was charged with dry THF (10 mL) and Et_3N (0.1 mL). The reaction mixture was cooled to 0 °C then diphosgene (7.2 μL, 59 μmol) was added. After 1 h, the resulting reaction mixture of activated porphyrin was charged in a 10 mL syringe as well as a solution of diaza-18-crown-6 ether (46 mg, 0.18 mmol) in dichloromethane (10 mL). These two solutions were added dropwise over 2 h with a syringe pump to a solution of THF (400 mL) and NEt_3 (0.1 mL). The mixture was stirred for an additional 1 h. The solvent was removed under vacuum and the residue was purified by chromatography column. Compound **4b** was eluted with CH_2Cl_2 and obtained in 11% yield (33 mg), compound **3b** was eluted with 0.2% methanol/CH_2Cl_2 and obtained in 13% yield (19 mg), compound **1b** was eluted with 0.8% methanol/CH_2Cl_2 and obtained in 20% yield (35 mg), and compound **2b** was eluted with 2% methanol/ CH_2Cl_2 and obtained in 46% yield (77 mg). As far as concern the series of **a** derivatives, the yields are identical via method A or B with those of series **b**.

4.2.1. 1,4,10,13-Tetraoxa-7,16-diaza-cyclooctadecane-7,16-dicarboxylic acid {2,2′-[10,20-bis-(2,4,6-trimethylphenyl)-porphyrin-α-5,15-diyl]-diphenyl}-diamide 1a. ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=8.82$ (d, $J=4.5$ Hz, 4H, βpyr), 8.69 (d, $J=4.5$ Hz, 4H, βpyr), 8.60 (d, $J=7$ Hz, 2H, aro), 8.04 (d, $J=7.5$ Hz, 2H, aro), 7.73 (t, $J=7.5$ Hz, 2H, aro), 7.52 (t, $J_1=7$ Hz, 2H, aro), 7.37 (s, 2H, aro), 7.24 (s, 2H, aro), 5.96 (s, 2H, NHCO), 2.65 (s, 6H, –CH_3), 2.60 (s, 8H, –CH_2–), 2.11 (s, 6H, –CH_3), 2.07 (s, 8H, –CH_2–), 1.64 (s, 6H, –CH_3), 1.56 (s, 8H, –CH_2–), −2.23 (s, 2H, NHpyr). ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=157.0$, 141.5, 140.1, 138.9, 138.3, 138.1, 133.9, 130.3, 129.7, 128.4, 128.2, 120.8, 120.0, 118.6, 114.0, 69.2, 50.3, 30.1, 22.1, 22.0, 21.8. HRMS (ES^+) Calcd for $C_{64}H_{66}N_8O_6Na$ $(M+Na)^+$ 1065.5003. Found, 1065.5006. UV–vis (CH_2Cl_2) λ nm ($10^{-3}\varepsilon$, $dm^3\,mol^{-1}\,cm^{-1}$): 420 (329.3), 516 (23.6), 550 (7.4), 591 (7.2), 647 (3.9).

4.2.2. 1,4,10,13-Tetraoxa-7,16-diaza-cyclooctadecane-7,16-dicarboxylic acid {2,2′-[10,20-bis-(3,5-dimethoxyphenyl)-porphyrin-α-5,15-diyl]-diphenyl}-diamide 1b. ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=8.98$ (d, $J=4.5$ Hz, 4H, βpyr), 8.88 (d, $J=4.5$ Hz, 4H, βpyr), 8.54 (dd, $J_1=7.5$ Hz, $J_2=1.5$ Hz, 2H, aro), 7.96 (d, $J=8$ Hz, 2H, aro), 7.80 (td, $J_1=8$ Hz, $J_2=1$ Hz, 2H, aro), 7.60 (td, $J_1=7.5$ Hz, $J_2=$ 1 Hz, 2H, aro), 7.53 (s, 2H, aro), 7.15 (s, 2H, aro), 6.92 (t, $J=2$ Hz, 2H, aro), 5.80 (s, 2H, NHCO), 4.12 (s, 6H, –OCH_3), 3.92 (s, 6H, –OCH_3), 2.56 (s, 8H, –CH_2–), 1.94 (s, 8H, –CH_2–), 0.49 (br s, 8H, –CH_2–), −2.51 (s, 2H, NHpyr). ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=159.1$, 156.5, 155.4, 148.6, 147.5, 146.4, 142.2, 140.9, 133.5, 131.3, 129.4, 122.2, 121.7, 114.3, 113.8, 99.9, 69.3, 55.6, 49.7. HRMS

(ES$^+$) Calcd for $C_{62}H_{62}N_8O_{10}Na$ $(M+Na)^+$ 1101.4486. Found, 1101.4495. UV–vis (CH_2Cl_2) λ nm ($10^{-3}\varepsilon$, $dm^3\,mol^{-1}\,cm^{-1}$): 418 (301.3), 516 (17.1), 551 (5.5), 589 (5.4), 646 (2.6).

4.2.3. 1,4,10,13-Tetraoxa-7,16-diaza-cyclooctadecane-7-carboxylic acid {2-[α-15-(2-nitro-phenyl)-10,20-bis-(2,4,6-trimethyl-phenyl)-porphyrin-α-5-yl]-phenyl}-amide 2aNO_2. A mixture of porphyrin **5aNO_2**αα (31 mg, 41 μmol), triethylamine (11 μL, 82μmol) and carbonic acid ditrichloromethyl ester (triphosgene) (4 mg, 13.6 μmol) in dry CH_2Cl_2 (20 mL) was stirred for 1 h under argon at room temperature. This mixture was added dropwise, over 2 h with a syringe pump to a solution of diaza-18-crown-6 ether (11 mg, 41 μmol) in dry CH_2Cl_2 (10 mL). The mixture was stirred for an additional 1 h. The solvent was removed under vacuum and the residue was purified by chromatography column. The desired compound **2aNO_2** was eluted with 1% methanol/CH_2Cl_2 and obtained in 88% yield (38 mg). ^{1}H NMR (500 MHz, $CDCl_3$): δ=8.83 (d, J=4.5 Hz, 2H, βpyr), 8.69–8.62 (m, 4H, βpyr and 1H, aro), 8.59 (d, J=4.5 Hz, 2H, βpyr), 8.43 (dd, J_1=8 Hz, J_2=1.5 Hz, 1H, aro), 8.23 (dd, J_1=7 Hz, J_2=1.5 Hz, 1H, aro), 7.99–7.92 (m, 3H, aro), 7.74 (td, J_1=8 Hz, J_2=1.5 Hz, 1H, aro), 7.69 (s, 1H, NHCO), 7.34 (td, J_1=7.5 Hz, J_2=1 Hz, 1H, aro), 7.30 (s, 2H, aro), 7.28 (s, 2H, aro), 5.00 (br s, 1H, NH), 2.88 (br s, 4H, –CH_2–), 2.63 (s, 6H, –CH_3), 2.38 (br s, 12H, –CH_2–), 1.97 (br s, 8H, –CH_2–), 1.85 (s, 6H, –CH_3), 1.82 (s, 6H, –CH_3), −2.51 (s, 2H, NHpyr). ^{13}C NMR (125 MHz, $CDCl_3$): δ=157.3, 152.2, 141.6, 139.7, 139.2, 138.5, 138.2, 137.4, 136.6, 135.5, 131.5, 130.1, 129.9, 129.8, 128.4, 128.3, 124.3, 120.8, 119.4, 119.2, 116.0, 114.0, 71.5, 69.8, 68.7, 49.1, 47.0, 22.2, 22.0, 21.9. HRMS (ES$^+$) Calcd for $C_{63}H_{67}N_8O_7$ $(M+H)^+$ 1047.5132. Found, 1047.5131. UV–vis (CH_2Cl_2) λ nm ($10^{-3}\varepsilon$, $dm^3\,mol^{-1}\,cm^{-1}$): 420 (261.8), 516 (15.6), 549 (5.4), 592 (4.9), 648 (2.6).

4.2.4. 1,4,10,13-Tetraoxa-7,16-diaza-cyclooctadecane-7-carboxylic acid {2-[α-15-(2-amino-phenyl)-10,20-bis-(3,5-dimethoxy-phenyl)-porphyrin-α-5-yl]-phenyl}-amide 2b. ^{1}H NMR (500 MHz, $CDCl_3$): δ=9.06 (d, J=4.5 Hz, 2H, βpyr), 9.04 (d, J=4.5 Hz, 2H, βpyr), 8.98 (d, J=5 Hz, 2H, βpyr), 8.93 (d, J=5 Hz, 2H, βpyr), 8.59 (d, J=9 Hz, 1H, aro), 7.99 (d, J=7.5 Hz, 1H, aro), 7.87 (d, J=7.5 Hz, 1H, aro), 7.78 (t, J=6.5 Hz, 1H, aro), 7.64 (t, J=7.5 Hz, 1H, aro), 7.38 (m, 5H, aro), 7.19 (m, 3H, aro and NHCO), 6.93 (t, J=2.5 Hz, 2H, aro), 4.03 (s, 6H, –OCH_3), 4.01 (s, 1H, NH), 3.97 (s, 6H, –OCH_3), 2.68 (br s, 4H, –CH_2–), 2.52 (br s, 4H, –CH_2–), 2.36 (br s, 4H, –CH_2–), 1.96 (br s, 4H, –CH_2–), 1.61 (br s, 4H, –CH_2–), 1.43 (br s, 4H, –CH_2–), −2.75 (s, 2H, NHpyr). ^{13}C NMR (125 MHz, $CDCl_3$): δ=159.1, 150.2, 140.6, 134.9, 131.6, 129.7, 121.0, 119.8, 117.7, 114.6, 113.7, 111.5, 99.9, 95.9, 70.3, 68.4, 64.1, 55.6, 48.5, 46.6. HRMS (ES$^+$) Calcd for $C_{61}H_{65}N_8O_9$ $(M+H)^+$ 1053.4874. Found, 1053.4867. UV–vis (CH_2Cl_2) λ nm ($10^{-3}\varepsilon$, $dm^3\,mol^{-1}\,cm^{-1}$): 419 (215.3), 512 (14.7), 548 (4.3), 588 (4.4), 646 (2.3).

4.2.5. 1,4,10,13-Tetraoxa-7,16-diaza-cyclooctadecane-7,16-dicarboxylic acid bis-{2-[α-15-(2-amino-phenyl)-10,20-bis-(2,4,6-trimethyl-phenyl)-porphyrin-α-5-yl]-phenyl}-diamide 3a. ^{1}H NMR (500 MHz, $CDCl_3$): δ=8.76 (d, J=4.5 Hz, 4H, βpyr), 8.59 (d, J=4.5 Hz, 8H, βpyr), 8.51 (d, J=4.5 Hz, 4H, βpyr), 8.34 (d, J=8 Hz, 2H, aro), 7.86 (d, J=7.5 Hz, 2H, aro), 7.77 (d, J=7.5 Hz, 2H, aro), 7.63 (t, J=8 Hz, 2H, aro), 7.57 (t, J=7.5 Hz, 2H, aro), 7.27 (m, 2H, aro), 7.24 (s, 4H, aro), 7.19 (s, 4H, aro), 7.14–7.08 (m, 4H, aro), 6.88 (s, 2H, NHCO), 3.60 (br s, 4H, NH_2), 2.62 (s, 12H, –CH_3), 1.76 (s, 12H, –CH_3), 1.58 (s, 8H, –CH_2–), 1.38 (m, 8H, –CH_2–), 1.29 (s, 12H, –CH_3), −1.02 (br s, 8H, –CH_2–), −2.80 (s, 4H, NHpyr). ^{13}C NMR (125 MHz, $CDCl_3$): δ=158.1, 153.5, 145.3, 139.0, 138.7, 138.2, 136.9, 136.6, 135.2, 130.5, 129.7, 128.4, 124.1, 120.8, 119.7, 119.3, 116.2, 114.0, 71.5, 69.8, 68.8, 50.7, 46.8, 22.5, 22.1, 21.7. HRMS (ES$^+$) Calcd for $C_{114}H_{111}N_{14}O_6$ $(M+H)^+$ 1771.8811. Found, 1771.8813. UV–vis (CH_2Cl_2) λ nm ($10^{-3}\varepsilon$, $dm^3\,mol^{-1}\,cm^{-1}$): 418 (512.3), 515 (40.3), 547 (19.8), 592 (19.1), 647 (12.5).

4.2.6. 1,4,10,13-Tetraoxa-7,16-diaza-cyclooctadecane-7,16-dicarboxylic acid bis-{2-[α-15-(2-amino-phenyl)-10,20-bis-(3,5-dimethoxy-phenyl)-porphyrin-α-5-yl]-phenyl}-diamide 3b. ^{1}H NMR (500 MHz, $CDCl_3$): δ=8.87 (d, J=4.8 Hz, 4H, βpyr), 8.82 (d, J=4.8 Hz, 4H, βpyr), 8.79 (d, J=4.8 Hz, 4H, βpyr), 8.65 (d, J=4.8 Hz, 4H, βpyr), 8.38 (d, J=8.1 Hz, 2H, aro), 7.85 (d, J=7.2 Hz, 2H, aro), 7.79 (d, J=7.2 Hz, 2H, aro), 7.68 (t, J=7 Hz, 2H, aro), 7.62 (t, J=7.8 Hz, 2H, aro), 7.26 (m, 6H, aro), 7.17 (m, 6H, aro), 7.08 (d, J=7.8 Hz, 2H, aro), 6.87 (br s, 4H, aro), 6.78 (br s, 2H, NHCO), 3.93 (s, 12H, –OCH_3), 3.90 (s, 12H, –OCH_3), 3.53 (br s, 4H, NH_2), 1.82 (br s, 8H, –CH_2–), 1.13 (br s, 8H, –CH_2–), −0.46 (br s, 8H, –CH_2–), −2.93 (s, 4H, NHpyr). ^{13}C NMR (125 MHz, $CDCl_3$): δ=158.8, 146.8, 140.5, 134.9, 130.7, 129.9, 120.7, 119.3, 117.5, 114.3, 113.7, 99.9, 68.4, 67.5, 55.6, 48.9. HRMS (ES$^+$) Calcd for $C_{110}H_{102}N_{14}O_{14}Na$ $(M+Na)^+$ 1865.7598. Found, 1865.7577. UV–vis (CH_2Cl_2) λ nm ($10^{-3}\varepsilon$, $dm^3\,mol^{-1}\,cm^{-1}$): 418 (523.5), 514 (33.4), 549 (9.6), 589 (10.2), 645 (4.7).

4.2.7. 1,3-Bis-{2-[1,4,10,13-tetraoxa-7,16-diaza-cyclooctadecane-7,16-dicarboxylic acid bis-{2-[2-{10,20-bis-(3,5-dimethoxy-phenyl)}-α-15-phenyl]-amide}-porphyrin-α-5,5′-diyl]-diphenyl}-urea 4b. ^{1}H NMR (500 MHz, $CDCl_3$): δ=8.73 (d, J=4.2 Hz, 4H, βpyr), 8.67 (d, J=5.1 Hz, 4H, βpyr), 8.65 (d, J=5.1 Hz, 4H, βpyr), 8.60 (d, J=4.2 Hz, 4H, βpyr), 8.51 (d, J=8.2 Hz, 2H, aro), 8.43 (d, J=8.2 Hz, 2H, aro), 7.84 (t, J=8.4 Hz, 2H, aro), 7.71 (m, 4H, aro), 7.61 (d, J=7.5 Hz, 2H, aro), 7.40 (t, J=7.5 Hz, 2H, aro), 7.30 (t, J=7.5 Hz, 2H, aro), 7.16 (s, 4H, aro), 6.98 (s, 4H, aro), 6.81 (s, 4H, aro), 6.77 (s, 2H, NHCO), 5.69 (s, 2H, NHCO), 3.87 (s, 12H, –OCH_3), 3.78 (s, 12H, –OCH_3), 3.80 (br s, 8H, –CH_2–), 2.15 (br s, 8H, –CH_2–), 0.89 (br s, 8H, –CH_2–), −3.25 (s, 2H, NHpyr). ^{13}C NMR (125 MHz, $CDCl_3$): δ=158.9, 140.0, 139.3, 129.6, 129.2, 128.1, 127.5, 126.2, 125.4, 124.6, 121.2, 115.2, 105.5, 55.8, 52.8, 29.7. HRMS (ES$^+$) Calcd for $C_{111}H_{100}N_{14}O_{15}Na$ $(M+Na)^+$ 1891.7390. Found, 1891.7372. UV–vis (CH_2Cl_2) λ nm ($10^{-3}\varepsilon$, $dm^3\,mol^{-1}\,cm^{-1}$): 422 (435.5), 515 (24.4), 550 (8.7), 589 (8.8), 646 (4.7).

4.2.8. α-5,15-Bis-(2-aminophenyl)-10,20-bis-(2,4,6-trimethyl-phenyl)-porphyrin 5aαα and α-5-β-15-(2-aminophenyl)-10,20-bis-(2,4,6-trimethyl-phenyl)-porphyrin 5aαβ. The two atropisomers of **7a** (200 mg, 0.25 mmol) were dissolved in CH_2Cl_2 (50 mL) in a 250 mL round flask.

$SnCl_2 \cdot 2H_2O$ (0.95 g, 5 mmol) and concentrated hydrochloric acid (50 mL) were added and the resulting green mixture was stirred for 12 h at room temperature; then cautiously neutralized at 0 °C with concentrated aqueous ammonia. CH_2Cl_2 (100 mL) was added and the organic layer was washed with aqueous $NaHCO_3$ (3×100 mL) and brine (2×100 mL). The organic layer was dried ($MgSO_4$), concentrated and the residue was chromatographed on a silica gel column. The **5a**αβ atropisomer was eluted with CH_2Cl_2 and obtained in 62% yield (114 mg) where **5a**αα atropisomer was eluted with 0.5% ethanol/CH_2Cl_2 and obtained in 34% yield (61 mg). **5a**αα. ^{1}H NMR (500 MHz, $CDCl_3$): δ=8.84 (d, J=5 Hz, 4H, βpyr), 8.69 (d, J=5 Hz, 4H, βpyr), 7.92 (dd, J_1=7.2 Hz, J_2=1.5 Hz, 2H, aro), 7.59 (td, J_1=8 Hz, J_2=1.5 Hz, 2H, aro), 7.28 (s, 2H, aro), 7.27 (s, 2H, aro), 7.17 (td, J_1=7.5 Hz, J_2=1.5 Hz, 2H, aro), 7.11 (dd, J_1=7.2 Hz, J_2=1.5 Hz, 2H, aro), 3.54 (s, 4H, NH_2), 2.63 (s, 6H, –CH_3), 1.88 (s, 6H, –CH_3), 1.80 (s, 6H, –CH_3), −2.58 (s, 2H, NHpyr). ^{13}C NMR (125 MHz, $CDCl_3$): δ= 147.3, 139.7, 138.5, 138.1, 135.2, 131.7, 130.9, 130.0, 128.3, 127.4, 118.7, 117.9, 115.7, 115.5, 22.1, 22.0, 21.9. HRMS (ES^+) Calcd for $C_{50}H_{45}N_6Na$ $(M+Na)^+$ 751.3525. Found, 751.3518. UV–vis (CH_2Cl_2) λ nm ($10^{-3}\varepsilon$, $dm^3\ mol^{-1}\ cm^{-1}$): 418 (362.7), 514 (22.4), 550 (6.7), 588 (6.8), 649 (3.4). **5a**αβ. ^{1}H NMR (500 MHz, $CDCl_3$): δ= 8.84 (d, J=5 Hz, 4H, βpyr), 8.69 (d, J=5 Hz, 4H, βpyr), 7.85 (dd, J_1=7.5 Hz, J_2=1.5 Hz, 2H, aro), 7.59 (td, J_1= 8.2 Hz, J_2=1.5 Hz, 2H, aro), 7.28 (s, 4H, aro), 7.15 (t, J= 7.5 Hz, 2H, aro), 7.12 (d, J=8.2 Hz, 2H, aro), 3.60 (s, 4H, NH_2), 2.63 (s, 6H, –CH_3), 1.84 (s, 12H, –CH_3), −2.58 (s, 2H, NHpyr). ^{13}C NMR (125 MHz, $CDCl_3$): δ=147.2, 139.8, 138.2, 135.2, 131.5, 130.7, 130.0, 128.2, 118.6, 117.8, 115.6, 115.5, 22.1, 21.9. HRMS (ES^+) Calcd for $C_{50}H_{45}N_6Na$ $(M+Na)^+$ 751.3525. Found, 751.3518. UV–vis (CH_2Cl_2) λ nm ($10^{-3}\varepsilon$, $dm^3\ mol^{-1}\ cm^{-1}$): 418 (362.7), 514 (22.4), 550 (6.7), 588 (6.8), 649 (3.4).

4.2.9. α-5-(2-Aminophenyl)-α-15-(2-nitrophenyl)-10,20-bis-(2,4,6-trimethyl-phenyl)-porphyrin 5aNO_2αα. To a solution of porphyrin **7a**αα (110 mg, 0.14 mmol) in CH_2Cl_2 (280 mL) was added concentrated hydrochloric acid (0.55 mL, 5.6 mmol). This was followed by addition of $SnCl_2 \cdot 2H_2O$ (0.16 g, 0.84 mmol), and the reaction mixture was stirred at 0 °C and monitored by TLC. After stirring for 9 h, concentrated aqueous ammonia (3 mL), was added to the reaction mixture, and then the mixture was washed with aqueous $NaHCO_3$ (3×100 mL) and brine (2×100 mL). The organic layer was dried ($MgSO_4$), concentrated and the residue was chromatographed on a silica gel column. Compound **5aNO_2**αα was eluted with CH_2Cl_2 and obtained in 65% yield (69 mg). ^{1}H NMR (500 MHz, $CDCl_3$): δ= 8.87 (d, J=5 Hz, 2H, βpyr), 8.72 (d, J=5 Hz, 2H, βpyr), 8.70 (d, J=4.5 Hz, 2H, βpyr), 8.60 (d, J=4.5 Hz, 2H, βpyr), 8.46 (d, J=8 Hz, 1H, aro), 8.27 (d, J=7 Hz, 1H, aro), 7.95 (m, 2H, aro), 7.91 (d, J=7.5 Hz, 1H, aro), 7.61 (t, J=7.5 Hz, 1H, aro), 7.31 (s, 2H, aro), 7.29 (s, 2H, aro), 7.18 (t, J=7.5 Hz, 1H, aro), 7.13 (d, J=7.5 Hz, 1H, aro), 3.61 (s, 2H, NH_2), 2.64 (s, 6H, –CH_3), 1.91 (s, 6H, –CH_3), 1.83 (s, 6H, –CH_3), −2.52 (s, 2H, NHpyr). ^{13}C NMR (125 MHz, $CDCl_3$): δ=152.0, 147.1, 139.8, 138.4, 138.2, 137.4, 137.0, 135.0, 131.7, 131.2, 131.1, 130.3, 130.2, 128.3, 128.1, 127.0, 124.9, 124.5, 119.1, 117.8, 116.0, 115.5, 114.0, 22.2, 22.0, 21.9. HRMS (ES^+) Calcd for $C_{50}H_{43}N_6O_2$ $(M+H)^+$ 759.3447. Found, 759.3446. UV–vis (CH_2Cl_2) λ nm ($10^{-3}\varepsilon$, $dm^3\ mol^{-1}\ cm^{-1}$): 419 (343.8), 515 (24.0), 549 (7.7), 591 (7.5), 647 (3.6).

4.2.10. α-5-(2-Aminophenyl)-β-15-(2-nitrophenyl)-10,20-bis-(2,4,6-trimethyl-phenyl)-porphyrin 5aNO_2αβ. To a solution of porphyrin **7a**αβ (287 mg, 0.36 mmol) in $CHCl_3$ (680 mL) was added concentrated hydrochloric acid (1.43 mL, 14.4 mmol). This was followed by addition of $SnCl_2 \cdot 2H_2O$ (410 mg, 2.16 mmol), and the reaction mixture was stirred was stirred at 0 °C and monitored by TLC. After stirring for 4 h, concentrated aqueous ammonia (7 mL), was added to the reaction mixture, and then the mixture was washed with aqueous $NaHCO_3$ (3×100 mL) and brine (2× 100 mL). The organic layer was dried ($MgSO_4$), concentrated and the residue was chromatographed on a silica gel column. Compound **5aNO_2**αβ was eluted with CH_2Cl_2/ hexane 6:4 and obtained in 21% yield (57 mg). ^{1}H NMR (500 MHz, $CDCl_3$): δ=8.84 (d, J=5 Hz, 2H, βpyr), 8.69 (m, 4H, βpyr), 8.59 (d, J=4.5 Hz, 2H, βpyr), 8.47 (dd, J_1= 8 Hz, J_2=1 Hz, 1H, aro), 8.21 (dd, J_1=7.5 Hz, J_2=1.5 Hz, 1H, aro), 7.98–7.91 (m, 2H, aro), 7.89 (dd, J_1=7.5 Hz, J_2= 1 Hz, 1H, aro), 7.60 (td, J_1=8 Hz, J_2=1 Hz, 1H, aro), 7.28 (s, 2H, aro), 7.27 (s, 2H, aro), 7.17 (t, J=7.5 Hz, 1H, aro), 7.12 (d, J=8 Hz, 1H, aro), 3.60 (s, 2H, NH_2), 2.63 (s, 6H, –CH_3), 1.85 (s, 12H, –CH_3), −2.54 (s, 2H, NHpyr). ^{13}C NMR (125 MHz, $CDCl_3$): δ=152.0, 147.1, 139.2, 138.3, 138.1, 137.4, 137.0, 135.2, 131.7, 131.1, 130.9, 130.2, 130.1, 130.0, 128.3, 128.1, 127.4, 124.4, 119.1, 118.0, 116.0, 115.6, 114.0, 22.1, 21.9. HRMS (ES^+) Calcd for $C_{50}H_{43}N_6O_2$ $(M+H)^+$ 759.3447. Found, 759.3446. UV–vis (CH_2Cl_2) λ nm ($10^{-3}\varepsilon$, $dm^3\ mol^{-1}\ cm^{-1}$): 419 (343.8), 515 (24.0), 549 (7.7), 591 (7.5), 647 (3.6).

4.2.11. α-5,15-Bis-(2-aminophenyl)-10,20-bis-(3,5-dimethoxy-phenyl)-porphyrin 5bαα and α-5-β-15-bis-(2-aminophenyl)-10,20-bis-(3,5-dimethoxy-phenyl)-porphyrin 5bαβ. In a 250 mL beaker, the two atropisomers of **7b** (1 g, 1.2 mmol) were dissolved in concentrated hydrochloric acid (100 mL) at room temperature and $SnCl_2 \cdot 2H_2O$ (2.17 g, 9.6 mmol) was added. The resulting green mixture was stirred for 2 days, then cautiously neutralized at 0 °C with aqueous potassium hydroxide. Ethyl acetate (100 mL) was added and the mixture stirred for 1 h. The ethyl acetate layer was separated and the aqueous layer extracted several times with ethyl acetate. The organic layer was concentrated and the residue was chromatographed on a silica gel column. The **5b**αβ atropisomer was eluted with CH_2Cl_2 and obtained in 38% yield (348 mg), where the **5b**αα atropisomer was eluted with 0.4% methanol/CH_2Cl_2 and obtained in 40% yield (367 mg). **5b**αα. ^{1}H NMR (500 MHz, $CDCl_3$): δ= 8.97 (d, J=4.5 Hz, 4H, βpyr), 8.91 (d, J=4.5 Hz, 4H, βpyr), 7.91 (dd, J_1=7.5 Hz, J_2=1.5 Hz, 2H, aro), 7.63 (td, J_1=8 Hz, J_2=1.5 Hz, 2H, aro), 7.40 (d, J=2.5 Hz, 4H, aro), 7.20 (t, J=7.5 Hz, 2H, aro), 7.14 (d, J=8 Hz, 2H, aro), 6.91 (t, J=2 Hz, 2H, aro), 3.97 (s, 12H, –OCH_3), 3.53 (s, 4H, NH_2), −2.73 (s, 2H, NHpyr). ^{13}C NMR (125 MHz, $CDCl_3$): δ=164.7, 150.1, 140.9, 139.2, 137.5, 135.6, 133.2, 130.7, 128.6, 126.6, 123.9, 123.1, 122.2, 121.9. HRMS (ES^+) Calcd for $C_{48}H_{40}N_6O_4Na$ $(M+Na)^+$ 787.3008. Found, 787.2982. UV–vis (CH_2Cl_2) λ nm ($10^{-3}\varepsilon$, $dm^3\ mol^{-1}\ cm^{-1}$): 420 (337.6), 514 (21.9), 549

(5.2), 588 (5.9), 646 (2.3). **5bαβ**. ^{1}H NMR (500 MHz, $CDCl_3$): δ=8.97 (d, J=4.5 Hz, 4H, βpyr), 8.91 (d, J=4.5 Hz, 4H, βpyr), 7.88 (dd, J_1=7.5 Hz, J_2=1.5 Hz, 2H, aro), 7.64 (td, J_1=8 Hz, J_2=1.5 Hz, 2H, aro), 7.41 (d, J=2.5 Hz, 4H, aro), 7.20 (t, J=7.5 Hz, 2H, aro), 7.15 (d, J=8 Hz, 2H, aro), 6.92 (t, J=2 Hz, 2H, aro), 3.98 (s, 12H, –OCH_3), 3.58 (s, 4H, NH_2), −2.72 (s, 2H, NHpyr). ^{13}C NMR (125 MHz, $CDCl_3$): δ=164.2, 149.7, 140.9, 139.1, 137.5, 135.6, 133.3, 130.5, 128.6, 126.6, 123.9, 123.0, 122.2, 121.7. HRMS (ES^+) Calcd for $C_{48}H_{40}N_6O_4Na$ $(M+Na)^+$ 787.3008. Found, 787.2982. UV–vis (CH_2Cl_2) λ nm ($10^{-3}\varepsilon$, dm^3 mol^{-1} cm^{-1}): 420 (337.6), 514 (21.9), 549 (5.2), 588 (5.9), 646 (2.3).

4.2.12. 2-[(1*H*-Pyrrol-2-yl)-(2,4,6-trimethyl-phenyl)-methyl]-1*H*-pyrrole 6a. A solution of 2,4,6-trimethyl-benzaldehyde (2.65 mL, 18 mmol) and pyrrole (50 mL, 720 mmol) was degassed by argon bubbling for 15 min. Trifluoroacetic acid (138 μL, 1.8 mmol) was then added and the solution was stirred under argon at room temperature for an additional hour and then quenched with triethylamine (0.4 mL). The mixture was diluted with toluene (150 mL) then washed with brine (2×100 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure and then the unreacted pyrrole was removed by vacuum distillation at room temperature. The residue was dissolved in CH_2Cl_2 and filtered through a short pad of silica using CH_2Cl_2 as the eluent. Evaporation of the solvent under reduced pressure resulted in a brown solid. This solid was washed with cyclohexane and then with hexane, giving a pale yellow solid, which was collected by filtration (1.85 g). Yield: 70%. ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.95 (br s, 2H, NHpyr), 6.87 (s, 2H, Ar), 6.67 (br s, 2H, pyr), 6.18 (m, 2H, pyr), 6.02 (br s, 2H, pyr), 5.93 (s, 1H, *meso*), 2.27 (s, 3H, –CH_3), 2.06 (s, 6H, –CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ=138.0, 137.0, 135.0, 131.7, 130.8, 116.6, 109.1, 106.9, 38.8, 21.2, 21.0. HRMS (ES^+) Calcd for $C_{18}H_{20}N_2$ $(M^{\cdot})^+$ 264.1626. Found, 264.1615.

4.2.13. 2-[(1*H*-Pyrrol-2-yl)-(3,5-dimethoxy-phenyl)-methyl]-1*H*-pyrrole 6b. A solution of 3,5-dimethoxy-benzaldehyde (3 g, 18 mmol) and pyrrole (50 mL, 720 mmol) was degassed by argon bubbling for 15 mL, then trifluoroacetic acid (138 μL, 1.8 mmol) was added. After 1 h, the reaction mixture was neutralized with Et_3N (0.44 mL, 3.2 mmol). The unreacted pyrrole was removed by vacuum distillation and the mixture was diluted with toluene and washed with aqueous 10% NaCl (2×100 mL). The organic phase was dried with $MgSO_4$, filtered and the solvent removed under vacuum. Finally, the residue was chromatographed on a silica gel column and eluted with (hexane/ethyl acetate/triethylamine; 80:20:1). The expected compound was recrystallized with (hexane/ethyl acetate; 98:2) at 0 °C, washed with hexane (100 mL), and obtained in 71% yield (3.6 g). ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.94 (br s, 2H, NHpyr), 6.71 (q, J=4.5 Hz, 2H, pyr), 6.41–6.38 (m, 3H, Ar), 6.18 (q, J=3.1 Hz, 2H, pyr), 5.98 (br s, 2H, pyr), 5.43 (s, 1H, *meso*), 3.76 (s, 6H, –OCH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ=118.8, 108.1, 105.7, 109.3, 108.0, 45.2, 55.5. HRMS (ES^+) Calcd for $C_{17}H_{18}N_2O_2$ $(M^{\cdot})^+$ 282.1368. Found, 282.1371.

4.2.14. α-5,15-Bis-(2-nitro-phenyl)-10,20-bis-(2,4,6-trimethyl-phenyl)-porphyrin 7aαα and α-5-β-15-(2-nitro-phenyl)-10,20-bis-(2,4,6-trimethyl-phenyl)-porphyrin 7aαβ. A solution of **6a** (2 g, 7.6 mmol) and 2-nitro-benzaldehyde (1.15 g, 7.6 mmol) in CH_2Cl_2 (780 mL) was degassed by argon bubbling for 15 mL, and then trifluoroacetic acid (1.11 mL, 14.5 mmol) was added. The solution was stirred for 30 mL at room temperature, then, DDQ (1.9 g, 8.4 mmol) was added and the mixture was stirred for an additional 1 h. The reaction mixture was poured onto a pad of alumina and eluted with CH_2Cl_2 until the eluting solution was pale brown. Removal of the solvent under reduced pressure gave **7a** (2 atropisomers: αα and αβ) in 20% yield (220 mg). The mixture of the two atropisomers was chromatographed on a silica gel column. The **7a**αβ atropisomer was eluted with CH_2Cl_2/hexane 1:1 and obtained in 13% yield (143 mg), where **7a**ααα atropisomer was eluted with CH_2Cl_2/hexane 3:2 and obtained in 7% yield (77 mg). **7aααα**. ^{1}H NMR (500 MHz, $CDCl_3$): δ=8.67 (d, J=4.5 Hz, 4H, βpyr), 8.58 (d, J=4.5 Hz, 4H, βpyr), 8.47 (dd, J_1=8 Hz, J_2=1.5 Hz, 2H, aro), 8.21 (dd, J_1=7.5 Hz, J_2=1.5 Hz, 2H, aro), 7.97 (td, J_1=8 Hz, J_2=1.5 Hz, 2H, aro), 7.92 (td, J_1=7.5 Hz, J_2=1.5 Hz, 2H, aro), 7.29 (s, 2H, aro), 7.26 (s, 2H, aro), 2.62 (s, 6H, –CH_3), 1.87 (s, 6H, –CH_3), 1.82 (s, 6H, –CH_3), −2.50 (s, 2H, NHpyr). ^{13}C NMR (125 MHz, $CDCl_3$): δ=152.0, 140.2, 139.5, 138.4, 138.3, 137.4, 136.9, 131.3, 131.0, 130.5, 129.9, 128.4, 128.0, 124.5, 119.5, 114.4, 22.3, 22.0, 21.8. HRMS (ES^+) Calcd for $C_{50}H_{41}N_6O_4$ $(M+H)^+$ 789.3189. Found, 789.3164. UV–vis (CH_2Cl_2) λ nm ($10^{-3}\varepsilon$, dm^3 mol^{-1} cm^{-1}): 419 (333.6), 516 (18.7), 550 (6.1), 592 (5.7), 649 (2.9). **7a**αβ. ^{1}H NMR (500 MHz, $CDCl_3$): δ=8.65 (d, J=4.5 Hz, 4H, βpyr), 8.57 (d, J=4.5 Hz, 4H, βpyr), 8.46 (dd, J_1=8 Hz, J_2=1.5 Hz, 2H, aro), 8.23 (dd, J_1=7.5 Hz, J_2=1.5 Hz, 2H, aro), 7.95 (td, J_1=8 Hz, J_2=1.5 Hz, 2H, aro), 7.94 (td, J_1=7.5 Hz, J_2=1.5 Hz, 2H, aro), 7.26 (s, 4H, aro), 2.61 (s, 6H, –CH_3), 1.83 (s, 12H, –CH_3), −2.52 (s, 2H, NHpyr). ^{13}C NMR (125 MHz, $CDCl_3$): δ=152.0, 139.8, 138.4, 138.2, 137.4, 136.9, 131.4, 130.8, 130.4, 129.9, 128.2, 124.6, 119.0, 114.1, 22.1, 21.9. HRMS (ES^+) Calcd for $C_{50}H_{41}N_6O_4$ $(M+H)^+$ 789.3189. Found, 789.3164. UV–vis (CH_2Cl_2) λ nm ($10^{-3}\varepsilon$, dm^3 mol^{-1} cm^{-1}): 419 (333.6), 516 (18.7), 550 (6.1), 592 (5.7), 649 (2.9).

4.2.15. 5,15-Bis-(2-nitrophenyl)-10,20-bis-(3,5-dimethoxy-phenyl)-porphyrin 7b. A solution of **6b** (3 g, 10.6 mmol) and 2-nitro-benzaldehyde (1.6 g, 10.6 mmol) in dry CH_2Cl_2 (1.1 L) was degassed by argon bubbling for 15 mL, then trifluoroacetic acid (787 μL, 10.6 mmol) was added. The solution was stirred for 12 h at room temperature, then, DDQ (2.4 mg, 10.6 mmol) was added and the mixture was stirred for an additional 1 h, and neutralized with Et_3N (440 mL, 10.6 μmol). The solvent was removed under vacuum, and the expected compound was recrystallized with a minimum of CH_2Cl_2 at 0 °C, and finally washed with CH_2Cl_2 (500 mL) and methanol (500 mL). Compound **7b** (2 atropisomers: αα and ββ) was obtained in 30% yield (1.3 g). HRMS (ES^+) Calcd for $C_{48}H_{37}N_6O_8$ $(M+H)^+$ 825.2672. Found, 825.2660.

4.2.16. X-ray crystallographic studies. 7aαα: crystal data: formula $C_{50}H_{40}N_6O_4 \cdot C_6H_{14}$, $M_w = 875.05$, monoclinic, space group $P2_1/n$, $a = 14.054(7)$ Å, $b = 11.269(6)$ Å, $c = 28.422(9)$ Å, $\beta = 91.72(3)°$, $V = 4499(4)$ Å^3, $Z = 4$, $D_c = 1.292$ g cm^{-3}, $\mu = 0.082$ mm^{-1}. Diffraction data were collected at room temperature in difficult conditions, since the material did not diffract strongly and only low-angle reflections could be measured. Nevertheless, the structure determination could be unambiguously performed and it was considered to be sufficiently detailed to the limited purpose of the present study. All operations were performed with a Nonius-Bruker MACH3 diffractometer, using graphite-monochromated Mo Kα radiation ($\lambda = 0.71073$ Å). The structure was solved by direct methods[16] and refined[17] on F_o^2 values, isotropically for the porphyrin ring atoms and anisotropically for the most peripheral atoms of the attached groups. Phenyl rings were treated as rigid groups with idealized geometry. Hydrogens were in calculated positions, riding, with temperature factors linked to those of the respective carrier atoms. There is a disordered hexane solvate molecule, which was modeled as two fractions with complementary population parameters. Hydrogen atoms were not added to the hexane carbon atoms backbones, since this was not found to yield improvements. The final values of the agreement factors are $R1$ 0.095 (on the 1370 observed reflections, having $I > 2\sigma I$) and 0.295 (on all of the measured 3916 reflections); $wR2$ 0.243 (observed) and 0.327 (all); GoF 1.026. Crystallographic data (excluding structure factors) for the structure in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 277156. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: 144 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2006.01.029. Complete NMR spectra (1D and 2D) of new compounds described in this work.

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