Synthesis of *meso*-substituted cationic porphyrins as potential photodynamic agents

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Dedicated to Professor Roberto A. Rossi and Professor Edmundo Rúveda

Abstract

Novel *meso*-substituted cationic porphyrins have been synthesized as potential photodynamic agents. 5,10-bis(4-Acetamidophenyl)-15,20-bis(4-methylphenyl)porphyrin **1** was prepared using a modification of the Alder-Longo procedure. However, two different approaches were compared in the synthesis of 5-(4-trifluorophenyl)-10,15,20-tris(4-acetamidophenyl)porphyrin **2**. One involved a condensation of binary mixture of aldehydes and pyrrole under equilibrium conditions and the other a binary mixture of aldehydes and *meso*-(4-acetamidophenyl)dipyrromethane **3**. The last synthetic pathway was advantageous mainly for an easier reaction work up and a higher yield. Both amido porphyrin **1** and **2** were hydrolyzed in basic media and treated with methyl iodide to form 5,10-di(4-methylphenyl)-15,20-di(4-trimethylammonium phenyl)porphyrin iodide **4** and 5-(4-trifluorophenyl)-10,15,20-tris(4-trimethyl ammoniumphenyl)porphyrin iodide **5**, respectively. Porphyrin **5** bears a highly lipophilic trifluoromethyl group, which increases the amphiphilic character of the structure. On the other hand, the photodynamic properties of porphyrin **5** were changed forming metal complex with Pd(II), porphyrin **6**. Absorption and fluorescence spectroscopic studies of these porphyrins were compared in different solvents. These amphiphilic cationic porphyrins are promising photosensitizers with potential applications in bacteria inactivation by photodynamic therapy.

Keywords: Cationic porphyrin, dipyrromethane, amphiphilic structure, palladium

Introduction

Tetrapyrrolic macrocycles occupy a central place in bioorganic chemistry.[1] *Meso*-substituted porphyrins have recently found specific biomedical applications, particularly in the field of

detection and treatment of neoplastic tissues.[2,3] Photodynamic therapy (PDT) consists of the administration of a photosensitizer, which is selectively retained by the neoplastic tissue. The subsequent irradiation with visible light in the presence of oxygen specifically inactivates tumor cells.[4,5] Adequate photosensitizers are deemed to have a high absorption coefficient in the visible region of the spectrum and have a triplet excited state, with a long lifetime, to efficiently produce $O_2(^1\Delta_g)$.[6]

Cationic porphyrins have several interesting features, which make these compounds attractive photosensitizers for a variety of biological systems.[7-11] These porphyrins are able to interact with DNA bases, inducing DNA lesions upon photoactivation.[12,13] Recently, cationic porphyrins have also shown important applications as sensitizers to photoinduce direct inactivation of multidrug resistant microorganisms.[14] Gram-positive bacteria are susceptible to the photodynamic effect produced by neutral and anionic sensitizers. Gram-negative bacteria have only been inactivated in these conditions in the presence of an agent, which stimulates the membrane translocation of the porphyrins.[15] However, studies with cationic porphyrin derivatives have been shown to photoinduce direct inactivation of Gram-negative bacteria without the presence of an additional permeabilization agent.[16-18]

The combination of hydrophobic and hydrophilic substituents in the sensitizer structure results in an intramolecular polarity axis, which can facilitate membrane penetration and produces a better accumulation in subcellular compartments, enhancing the effective photosensitization.[19,20] This sensitizer architecture required the formation of asymmetrically *meso*-substituted porphyrins. These porphyrins containing two different types of *meso*-substituents (A and B) can be prepared by a binary mixed aldehyde and pyrrole condensation.[21,22] This approach is statistical in nature and usually six porphyrins are formed, which involve AABB- and AB$_3$-porphyrin patterns.[23] However, the isolation of the desired porphyrin requires slow and careful chromatography for purification, the yield is very poor and obtaining pure porphyrin is not always possible. A convenient approach for the synthesis of *meso*-substituted *trans*-porphyrins (ABAB-porphyrins) has been developed from the condensation of dipyrromethane with an aldehyde in a MacDonald-type 2+2 condensation.[24,25] Also, condensation of a dipyrromethane with a binary mixture of aldehydes was used to obtain *meso*-substituted porphyrins bearing three identical substituents, B and one different A (AB$_3$-porphyrins).[26,27] In these cases, the structure A bears a functional group, which can be used to link the porphyrin with other molecules, while B was used to change the macrocycle properties.

This paper reports the synthesis of novel asymmetrically *meso*-substituted cationic porphyrins with AABB- and AB$_3$-porphyrin symmetry pattern, 5,10-bis(4-methylphenyl)-15,20-bis(4-trimethylammoniumphenyl)porphyrin iodide **4** and 5-(4-trifluorophenyl)-10,15,20-tris(4-trimethylammoniumphenyl) porphyrin iodide **5**. Thus, 5,10-bis(4-acetamidophenyl)-15,20-bis(4-methylphenyl)porphyrin **1** was prepared from a binary mixture of aldehyde and pyrrole using a modification of the Alder-Longo procedure. On the other hand, two synthetic methods were compared in the formation of 5-(4-trifluorophenyl)-10,15,20-tris(4-acetamidophenyl)porphyrin **2**, which is a precursor of **5**. These approaches involve the

condensation of a binary mixture of aldehyde and, either pyrrole or dipyrromethane derivative, catalyzed by acid. Tricationic porphyrin **5** contains a trifluoromethyl group. The influence of the trifluoromethyl group in biologically active molecules is often associated with the increased lipophilicity that this substituent imparts.[28-30] Also, fluorine porphyrin derivatives are suitable candidates for application in diagnosis and therapy of cancer.[31,32] The positive charges were incorporated at the peripheral position to increase the amphiphilic character of the structure. The photodynamic properties of porphyrin **5** were changed by forming a metal complex with Pd(II) **6**.[33] The coordination of tetrapyrrilic macrocycles with palladium produces an increase in the triplet state production, which improves the photodynamic activity of these sensitisers.[33,34,35]

## Results and Discussion

Synthesis

5,10-bis(4-Acetamidophenyl)-15,20-bis(4-methylphenyl)porphyrin **1** was synthesized from a binary mixture of aldehydes and pyrrole using a modification of the Alder-Longo method as showed in Scheme 1.[36]
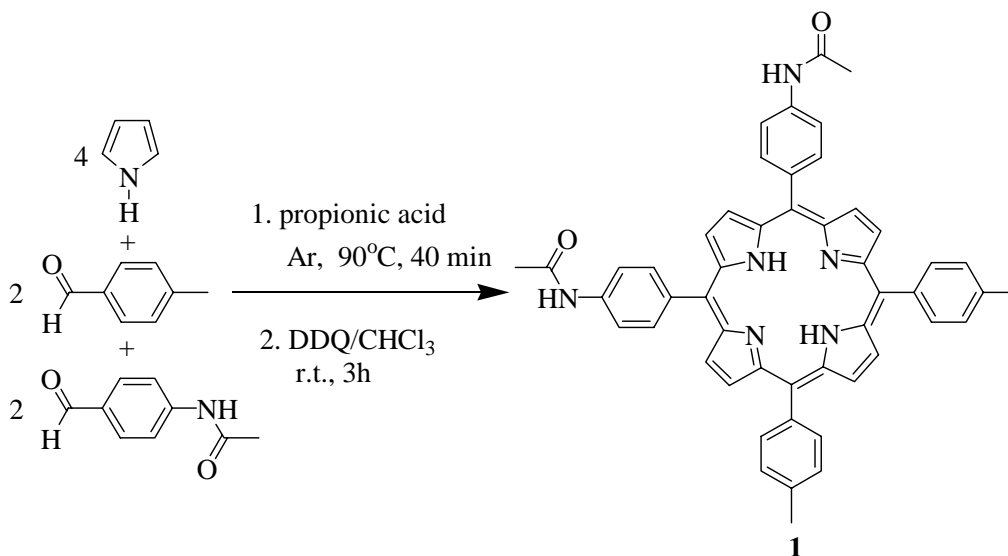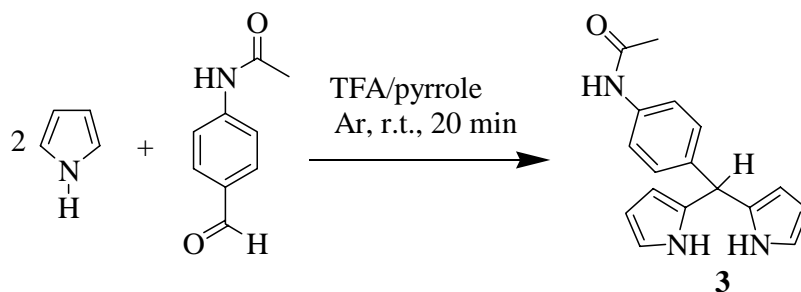

Scheme 1

To obtain the AABB-porphyrin **1**, 4-acetamidobenzaldehyde, 4-methylbenzaldehyde and pyrrole (2:2:4 molar ratio) were heated in propionic acid at 90 ºC for 40 min. The reaction work up difficult because of problems in removing propionic acid and some tar. The mixture was then oxidized with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ). The isolation requires a slow and careful chromatographic separation and the yield was very poor (1.4 %).

5-(4-Trifluoromethylphenyl)-10,15,20-tris(4-acetamidophenyl) porphyrin **2** was synthesized by two different methods. In one case, the AB$_3$-porphyrin **2** was obtained by a condensation of a binary mixture of aldehydes and pyrrole catalyzed by trifluoroacetic acid, TFA, at room temperature (Scheme 2). After treatment with DDQ, the mixture produced porphyrin **2**, which was separated by column chromatographic with a yield of 3.6 %.
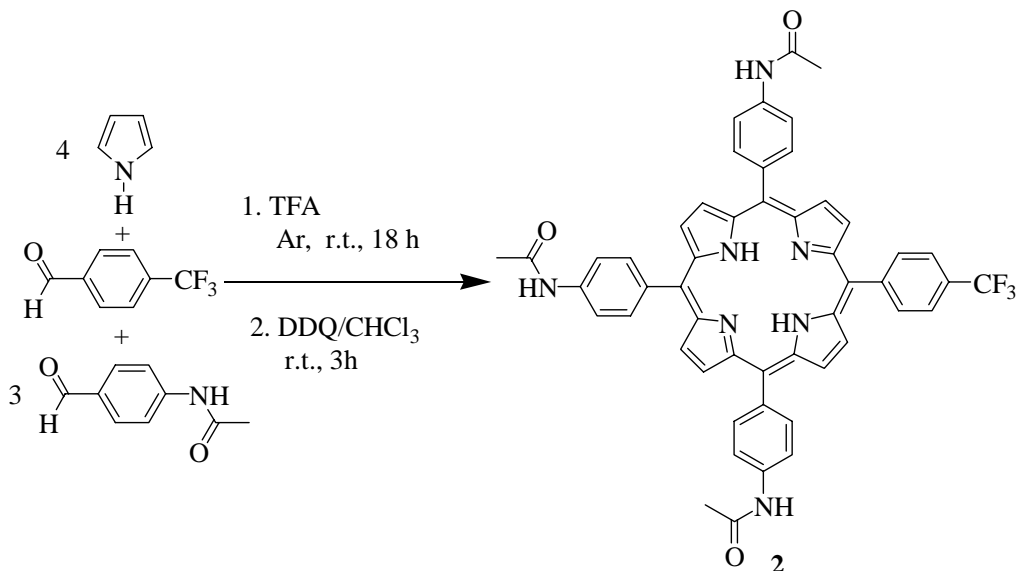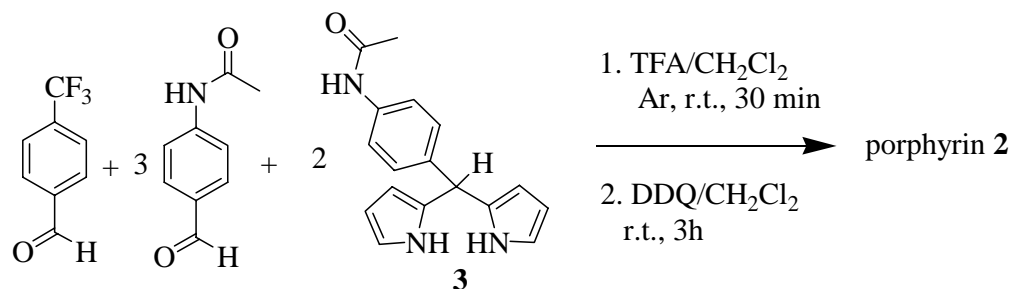

Scheme 2

The alternative method to synthesize porphyrin **2** involved two steps: 1) formation of *meso*-(4-acetamidophenyl)dipyrromethane **3** (Scheme 3) and 2) condensation of dipyrromethane **3** with the appropriate benzaldehyde mixture (Scheme 4). Thus, dipyrromethane **3** was obtained from the condensation of 4-acetamidobenzaldehyde with a large excess of pyrrole (1:38 aldehyde/pyrrole mol ratio) catalyzed by TFA (Scheme 3). The reaction mixture was stirred for 20 min at room temperature resulting in the complete disappearance of aldehyde. In these reaction conditions, pyrrole serves as the reactant in excess and as the solvent for the reaction, giving direct formation of dipyrromethane. The brown crude solution was washed with dilute aqueous NaOH. The dipyrromethane **3** was isolated (70 %) by flash chromatography on silica gel in a mildly basic medium, using ethyl acetate/triethylamine (100:1) as eluent. Under this condition, triethylamine prevents decomposition of the dipyrromethane on silica column, which is slightly acidic. Dipyrromethane **3** is stable in the purified form upon storage at 0°C in nitrogen atmosphere and absence of light. Then, dipyrromethane **3** was condensed with 4-acetamidobenzaldehyde and 4-trifluoromethylbenzaldehyde [2:0.9:1.1 mol ratio, respectively] under catalysis by TFA and at room temperature to form a mixture of porphyrins. The reaction was catalyzed by TFA at room temperature. After oxidation with DDQ, the desired amido porphyrin **2** (15 %) was separated by flash chromatography.
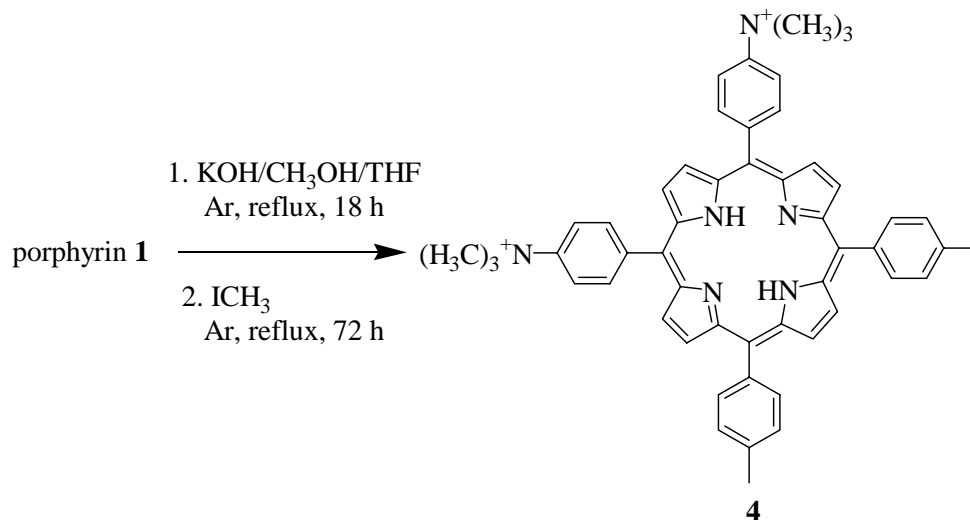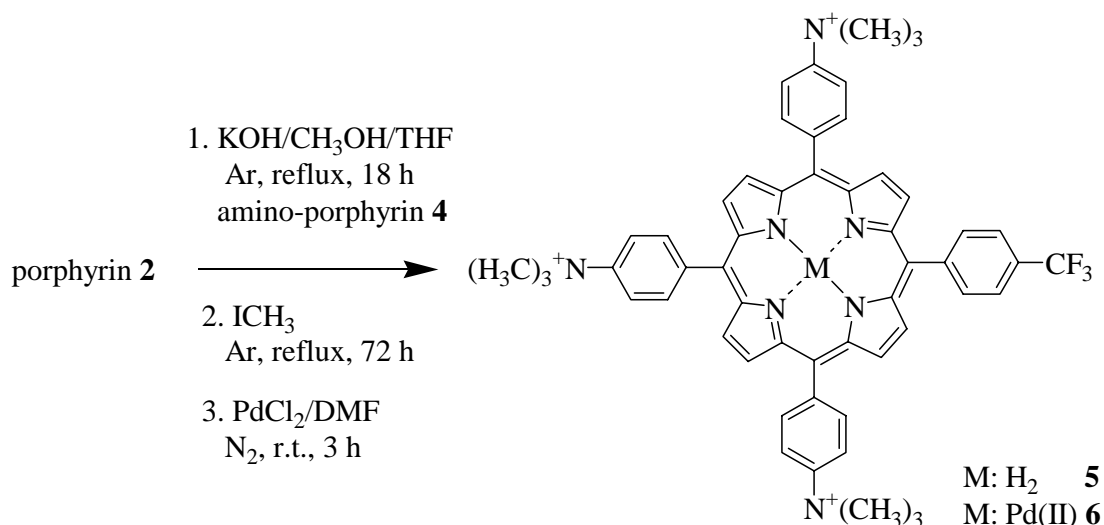
Scheme 3

Scheme 4

Both amido porphyrins, **1** and **2**, were hydrolyzed in basic medium to afford the corresponding 5,10-bis(4-aminophenyl)-15,20-bis(4-methylphenyl)porphyrin and 5-(4-trifluoromethylphenyl)-10,15,20-tris(4-aminophenyl)porphyrin with 77 % and 74 % yields, respectively (Scheme 5 and 6). Treatment of amino porphyrins with methyl iodide afforded 5,10-bis(4-methylphenyl)-15,20-bis(4-trimethylammoniumphenyl)porphyrin iodide **4** (Scheme 5) and 5-(4-trifluorophenyl)-10,15,20-tris(4-trimethylammoniumphenyl)porphyrin iodide **5** (Scheme 6) with 93 % and 95 % yields, respectively.

The treatment of porphyrin **5** with $PdCl_2$ in DMF produces the metallo complex Pd(II) porphyrin **6** (93 %) (Scheme 6).

1. KOH/CH$_3$OH/THF
   Ar, reflux, 18 h

porphyrin **1** $\longrightarrow$

2. ICH$_3$
   Ar, reflux, 72 h

Scheme 5

1. KOH/CH$_3$OH/THF
   Ar, reflux, 18 h
   amino-porphyrin **4**

porphyrin **2** $\longrightarrow$

2. ICH$_3$
   Ar, reflux, 72 h

3. PdCl$_2$/DMF
   N$_2$, r.t., 3 h

M: H$_2$ **5**
M: Pd(II) **6**

Scheme 6

Porphyrin properties and spectroscopic studies

Porphyrin **4** bears two 4-methylphenyl groups and two cationic 4-trimethylammoniumphenyl groups with a AABB-porphyrin symmetry, while porphyrin **5** contains one 4-trifluoromethylphenyl group and three 4-trimethylammoniumphenyl groups. To evaluate the effect produced by this distribution of different polarity groups upon the intramolecular polarity, the dipole moments of the porphyrins were estimated. The semi-empirical method for molecular modeling (AM1) was used in structure geometry optimization calculations. Values of 39.7 D and 39.9 D were found for **4** and **5**, respectively. These values are approximately 10 times higher that of the corresponding porphyrin models substituted by amino and methyl groups. As expected,

the presence of cationic groups in the periphery of porphyrins considerably enhances the dipole moment with respect to the non-charged structure. In particular, for porphyrin **5**, a trifluoromethyl group produces an increase from 25.4 D to 39.9 D with respect to a methyl group.

The absorption spectrum of porphyrins **4**, **5** and **6** in methanol show the typical Soret and Q-bands characteristic of free-base porphyrin derivatives and their metal-complex (Figure 1A).[37] The spectra of porphyrins were also recorded in different solvents. The absorption maxima are summarized in Table 1. The solvatochromic effect on the location of Soret absorption band shows a slight blue shift upon solubilization in methanol.
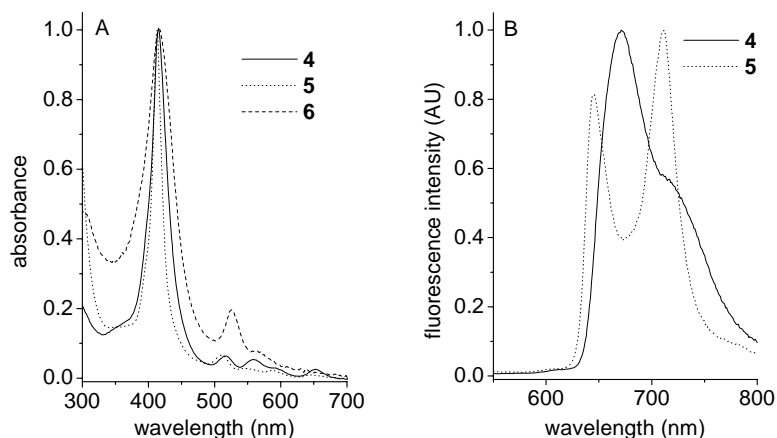

Figure 1. Absorption spectra (A) and fluorescence emission spectra (B) of porphyrin **4** (solid line), **5** (dotted line) and **6** (dashed line) in methanol, λ_{exc}=515 nm.

Table 1. Absorption and fluorescence emission data for porphyrin 4 in different solvents

Solvent	Absorption λ_{max} (nm)					Emission λ_{max} (nm)		
			porphyrin **4**					
DCM	420	520	563	593	654	670	726	
DMSO	419	519	567	591	655	657	715	
Methanol	415	516	558	591	652	669	-	
			porphyrin **5**					
DCM	418	514	551	588	649	658	712	
DMSO	418	513	549	589	647	649	712	
Methanol	413	511	547	587	646	647	711	
			porphyrin **6**					
DCM	420	528		568		-	-	
DMSO	418	529		574		-	-	
Methanol	416	526		566		-	-	

The steady-state fluorescence emission spectra of porphyrins **4** and **5** in methanol are shown in Figure 1B. No emission from the Pd(II) porphyrin **6** was detected. Two bands are characteristic for porphyrin derivatives and they have been assigned to Q(0-0) and Q(0-1) transitions. Also, a small Stokes shift is expected for tetraphenylporphyrin derivatives indicating that the spectroscopic energy is nearly identical to the relaxed energy of the singlet state.[38]

Conclusions

Two different approaches were compared in the synthesis of 5-(4-trifluorophenyl)-10,15,20-tris(4-acetamidophenyl)porphyrin **2**. One involved a condensation of binary mixture of aldehydes and pyrrole and the other a binary mixture of aldehydes and *meso*-(4-acetamidophenyl)dipyrromethane **3** catalyzed by acid. The last synthetic pathway was advantageous mainly for a relatively simpler reaction work up and higher yield (~4 times) than the reaction in the presence of pyrrole. However, this approach can not be used to synthesize AABB-porphyrin patterns, such as **1**. Thus, porphyrin **1** was obtained by the first method with a low yield. Both amido porphyrin **1** and **2** were hydrolyzed in basic media and treated with methyl iodide to form dicationic **4** and tricationic **5** porphyrin derivatives, respectively. Porphyrin **5** bears a highly lipophilic trifluoromethyl group, which increases the amphiphilic character of the structure. On the other hand, the photodynamic properties of porphyrin **5** were changed by forming metal complex with Pd(II), porphyrin **6**. These amphiphilic cationic porphyrins offer a promising molecular architecture for photosensitizer agents with potential applications in bacteria inactivation by photodynamic treatment. Studies of photosensitization *in vitro*, using Gram-negative bacteria *Escherichia coli*, are presently in progress in our laboratory.

Experimental Section

General Procedures. UV-visible and fluorescence spectra were recorded on a Shimadzu UV-2401PC spectrometer and on a Spex FluoroMax fluorometer, respectively. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on a Bruker ARX 300 multinuclear spectrometer at 300 MHz. Mass Spectra were taken with a Varian Matt 312 operating in EI mode at 70 eV. Silica gel (230-400 mesh, Merk) was used for column chromatography. Alumina neutral (150 mesh, Aldrich) was employed. Silica gel thin-layer chromatography (TLC) plates 250 microns from Aldrich (Milwaukee, WI, USA) were used. All the chemicals from Aldrich were used without further purification. Solvents (GR grade) from Merck were distilled. Semiempirical molecular orbital calculations (AM1) were carried out using HyperChem software.

5,10-bis(4-Acetamidophenyl)-15,20-bis(4-methylphenyl)porphyrin (1). A solution of 4-methylbenzaldehyde (3.42 g, 21 mmol) and 4-acetamidobenzaldehyde (2.52 g, 21 mmol) in propionic acid (150 mL) was stirred at 90 °C and pyrrole (3.0 mL, 42 mmol) was slowly added. The resulting mixture was heated to reflux for 40 min. The mixture was poured into of water (500 mL), containing of NaCl (20 g). The precipitated material was collected by vacuum filtration and dried under vacuum at 100 ºC for 48 hours to remove propionic acid. The resulting material was dissolved in chloroform/methanol (5%) and filtered through a short column of alumina (5 cm). This procedure was repeated using silica gel. The solvents were removed under reduced pressure and the residue treated with DDQ (2.27 g, 10 mmol) in 200 mL of chloroform for 3 hours. The solvent was evaporated and the residue was pulverized to a fine powder. Slow chromatographic column (silica gel, chloroform/methanol gradient) afforded porphyrin **1** (purple solid, 111 mg, 1.4 %) as second moving band. TLC analysis (dichloromethane/methanol 5%) R_f 0.35. ^{1}HNMR (CDCl$_3$, TMS) δ [ppm] -2.78 (brs, 2H, pyrrole N-H), 2.34 (s, 6H, COCH$_3$), 2.70 (s, 6H, Ar-CH$_3$), 7.56 (d, 4H, J=7.9Hz, 5,10-Ar 3,5-H), 7.46 (brs, 2H, NHCO), 7.87 (d, 4H, J=8.0 Hz, 15,20-Ar 3,5-H), 8.10 (d, 4H, J=7.9Hz, 5,10-Ar 2,6-H), 8.17 (d, 4H, J=8.0 Hz, 15,20-Ar 2,6-H), 8.75 (s, 2H, β-pyrrole), 8.80 (d, 2H, J= 4.9 Hz, β-pyrrole), 8.86 (d, 2H, J= 4.9 Hz, β-pyrrole), 8.90 (s, 2H, β-pyrrole). MS m/z 756 (M$^+$) (756.3213 calculated for C$_{50}$H$_{40}$N$_6$O$_2$). Anal. calcd. C 79.34, H 5.33, N 11.10; found C 79.27, H 5.38, N 11.06.

***meso*-(4-Acetamidophenyl)dipyrromethane (3).** A solution of 4-acetamicobenzaldehyde (2.45 g, 15 mmol) and pyrrole (40.0 mL, 576 mmol) was degassed by bubbling with argon for 15 min. Then trifluoroacetic acid (210 μL, 2.7 mmol) was added. The solution was stirred for 20 min at room temperature, at which point no starting aldehyde was shown by TLC analysis (ethyl acetate/triethylamine 100:1). The mixture was treated with aqueous NaOH (0.1 M, 50 mL) and extracted with dichloromethane (2 x 50 mL). The solvent was removed under reduced pressure. The unreacted pyrrole was removed by vacuum distillation at room temperature. The product was purified by flash chromatography (silica gel, cyclohexane/ethyl acetate/triethylamine, 60:40:1 and then ethyl acetate/triethylamine 100:1) to give dipyrromethane **3** (2.92 g 70 %). TLC (silica gel) Rf (ethyl acetate/triethylamine 100:1) = 0.17. ^{1}HNMR (DMSO-d$_6$, TMS) δ [ppm] 2.20 (s, 3H, COCH$_3$), 5.47 (s, 1H, *meso*-H), 5.83 (m, 2H, pyrrole-H), 6.08 (q, 2H, pyrrole-H), 6.78 (d, 2H, pyrrole-H), 7.26 (d, 2H, J = 8.6 Hz, Ar 2,6-H), 7.64 (d, 2H, J = 8.6 Hz, Ar 3,4-H), 10.05 (s, brs, 1H, HNCO), 10.69 (s, brs, 2H, pyrrole NH). MS [m/z] 279 (M$^+$) (279.1372 calculated for C$_{17}$H$_{17}$N$_3$O). Anal. calcd. C 73.10, H 6.13, N 15.04; found C 73.23, H 6.20, N 15.01.

5-(4-Trifluoromethylphenyl)-10,15,20-tris(4-acetamidophenyl)porphyrin (2). A solution of 4-acetamidobenzaldehyde (757 mg, 4.64 mmol), 4-trifluorobenzaldehyde (985 mg, 5.66 mmol) and *meso*-(4-acetamidophenyl)dipyrrometane **3** (2.87 g, 10.27 mmol) in dichloromethane (1 L) was purged with argon for 15 min. Then TFA (1.40 mL, 3.5 mmol) was slowly added. The solution was stirred for 30 min at room temperature. Then, DDQ (6.80 g, 30.0 mmol) was added and the mixture was stirred for an additional 1.5 h at reflux. The solvent was removed under reduced pressure and flash column chromatography (silica gel, dichloromethane/methanol 8%

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gradient to 12 %) yielded the pure selected porphyrin **2** (purple solid, 610 mg, 15 %) as the second porphyrin band. TLC analysis (dichloromethane/methanol 7 %) R_f 0.37. ^{1}HNMR (CDCl$_3$, TMS) δ [ppm] -2.88 (brs, 2H, pyrrole N-H), 2.30 (s, 9H, COCH$_3$), 7.45 (brs, 3H, NHCO), 7.84 (d, 6H, J=8.1 Hz, 10,15,20-Ar 3,5-H), 7.93-7.98 (m, 4H, 5-Ar), 8.09 (d, 6H, J=8.1 Hz, 10,15,20-Ar 2,6-H); 8.69 (d, 2H, J=4.8 Hz, β-pyrrole), 8.79-8.83 (m, 6H, β-pyrrole). MS m/z 853 (M$^+$) (853.2988 calculated for C$_{51}$H$_{38}$F$_3$N$_7$O$_3$). Anal. calcd. C 71.74, H 4.49, N 11.48; found C 71.66, H 4.55, N 11.39.

Also, porphyrin **2** was synthesized from a mixture of 4-acetamidobenzaldehyde (130.5 mg, 0.80 mmol), 4-trifluorobenzaldehyde (46.4 mg, 0.27 mmol) and pyrrol (74 μL,1.07 mmol) in 50 mL of dichloromethane. After purging the solution with argon for 15 min, TFA (950 μL, 12.33 mmol) was slowly added to the mixture that was magnetically stirred over night at room temperature. Then the mixture was treated with DDQ (100mg, 0.44mmol) for 3 h. The solvent was removed and porphyrin **2** (8 mg, 3.5 %) was isolated by column chromatography (silica gel, dichloromethane/methanol 8% gradient to 12 %).

5,10-Bis(4-methylphenyl)-15,20-bis(4-trimethylammoniumphenyl)porphyrin iodide (4). Amido porphyrin **1** (60 mg, 0.079 mmol) was dissolved in 30 mL of THF/methanol (1:1, 30 mL) and aqueous KOH (50 % w/v, 30 mL) was added. The reaction mixture was stirred under a nitrogen atmosphere for 18 h at reflux. Then, the mixture was diluted with dichloromethane (100 mL) and washed with aqueous sodium carbonate (0.1 M, 50 mL). The organic solvent was evaporated under reduced pressure. Flash column chromatography (silica gel, dichloromethane/methanol 3 %) afforded 5,10-bis(4-aminophenyl)-15,20-bis(4-trifluoromethylphenyl)porphyrin (purple solid, 41 mg, 77 %). TLC analysis (dichloromethane/methanol 5%) R_f 0.66. MS m/z 672 (M$^+$) (672.3001 calculated for C$_{46}$H$_{36}$N$_6$). The crude amino-porphyrin (30 mg, 0.045 mmol) was refluxed in 4 mL of methyl iodide under argon atmosphere for 72 h. The solvent was removed under reduced pressure and the solid, after washing with diethyl ether, yielded porphyrin **4** (42 mg, 93 %). ^{1}HNMR (DMSO-d$_6$, TMS) δ [ppm] -2.92 (brs, 2H, pyrrole N-H), 2.71 (s, 9H, -CH$_3$), 3.90 (s, 18H, N-CH$_3$), 7.14 (d, 4H, J=8.4 Hz, 15,20-Ar 3,5-H), 7.62 (d, 4H, J=8.0 Hz, 5,10-Ar 3,5-H), 8.00 (d, 4H, J=8.4 Hz, 15,20-Ar 2,6-H), 8.07 (d, 4H, J=8.0 Hz, 5,10-Ar 2,6-H), 8.74 (s, 2H, β-pyrrole), 8.82 (d, 2H, J= 4.9 Hz, β-pyrrole), 8.87 (d, 2H, J= 4.9 Hz, β-pyrrole), 8.92 (s, 2H, β-pyrrole). MS m/z 758 (M$^+$-2I) (758.4097 calculated for C$_{52}$H$_{50}$N$_6$). Anal. calc. C 61.67, H 4.98, N 8.30; found C 61.58, H 4.90, N 8.38. Absorption spectrum λ$_{max}$ (methanol) [nm] (ε,dm3mol-1cm-1) 415 (164 000), 516 (8 900), 558 (4 700) 652 (4 200).

5-(4-Trifluoromethylphenyl)-10,15,20-tris(4-trimethylammoniumphenyl)porphyrin iodide (5). To a solution of amido-porphyrin **2** (100 mg, 0.117 mmol) in THF/methanol (1:1, 40 mL) was added aqueous KOH (50 % w/v, 40 mL). The reaction mixture was stirred under an argon atmosphere for 18 h at reflux. Then, the mixture was diluted with dichloromethane (100 mL) and washed with aqueous sodium carbonate (0.1 M, 50 mL). The organic solvent was evaporated under reduced pressure. Flash chromatography column (silica gel, dichloromethane/methanol/triethylamine 98.5:1.5:1) afforded 5-(4-trifluoromethylphenyl)-

10,15,20-tris(4-aminophenyl)porphyrin (purple solid, 63 mg, 74 %). TLC analysis (dichloromethane/methanol/triethylamine 98.5:1.5:1) R_f 0.63. MS m/z 727 (M$^+$) (727.2671 calculated for $C_{45}H_{32}F_3N_7$). The crude amino-porphyrin (50 mg, 0.069 mmol) was refluxed in methyl iodide (4 mL) under argon atmosphere for 72 h. The solvent was removed under reduced pressure and the solid washed with *n*-heptane to yield porphyrin **5** (81 mg, 95 %). ^{1}HNMR (DMSO-d$_6$, TMS) δ [ppm] -2.93 (brs, 2H, pyrrole N-H), 3.94 (s, 27H, N-CH$_3$), 7.17 (d, 6H, J=8.1 Hz, 10,15,20-Ar 3,5-H), 7.92-7.98 (m, 4H, 5-Ar), 8.03 (d, 6H, J=8.1 Hz, 10,15,20-Ar 2,6-H), 8,83 (d, 2H, J=4.8 Hz, β-pyrrole), 8.70-8.98 (m, 6H, β-pyrrole). MS m/z 856 (M$^+$-3I) (856.4315 calculated for $C_{54}H_{53}F_3N_7$). Anal. calc. C 52.40, H 4.32, N 7.92; found C 52.48, H 4.27, N 7.96. Absorption spectrum λ$_{max}$ (methanol) [nm] (ε,dm^{3}mol^{-1}cm^{-1}) 413 (170 000), 511 (11 100), 547 (4 700) 587 (3 700) 646 (3 000)

Palladium 5-(4-trifluoromethylphenyl)-10,15,20-tris(4-trimethylammoniumphenyl) porphyrin iodide (6). To a solution of porphyrin **5** (10 mg, 0.008 mmol) in DMF (5 mL) was added palladium(II) chloride (10 mg, 0.056 mmol). The mixture was stirred for 5 h at reflux in atmosphere of argon. The solvent was removed under vacuum, the solid was redissolved in dichloromethane, filtered and dried to yield porphyrin **6** (dark purple solid, 10 mg, 93 %). MS m/z 960 (M$^+$-3I) (960.3193 calculated for $C_{54}H_{51}F_3N_7Pd$). Anal. calc. C 48.32, H 3.83, N 7.31; found C 48.23, H 3.91, N 7.25. Absorption spectrum λ$_{max}$ (methanol) [nm] (ε,dm^{3}mol^{-1}cm^{-1}) 416 (168 000), 526 (19 000), 566 (3 800).

Acknowledgments

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