Supplemental information for:

**Design of porphyrin-based ligands for the assembly of**

\[d\text{-block metal:calcium}] bimetallic centers

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Contribution of the

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1 Experimental procedures

1.1 Materials and methods

Dipyrrylmethane was prepared according to a previously published procedure.\[1\] 2-nitrobenzaldehyde, trifluoroacetic acid (TFA), 1,2-dicyano-4,5-dichloroquinone (DDQ), tin chloride (SnCl\(_2\)), zinc acetate dihydrate (ZnOAc.2H\(_2\)O), N-bromosuccinimide (NBS), potassium phosphate tribasique (K\(_3\)P\(_2\)O\(_4\)), sodium tetraphenyldiborate (NaBPh\(_4\)), 2-(1H-Benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU), p-toluenesulfonic acid (p-TSA), methyl-2-formylbenzoate, citric acid, and boron trifluoride etherate (BF\(_3\).Et\(_2\)O) complex were purchased from Alfa-Aesar. Triethylamine (TEA), chloroacetyl chloride (ClCH\(_2\)COCl), tetrahydrofuran (THF) stabilized with BHT, dimethylformamide (DMF), benzene, 4,13-diaza-18-crown-6, 4-aza-18-crown-6, and benzaldehyde were obtained from Acros Organics. Methyl-2-carboxyphenylboronic acid was purchased from Aldrich. Palladium(0) tetrakis-triphenylphosphine (Pd(PPh\(_3\))\(_4\)) and zinc(0) powder ~ 40 mesh were obtained from Strem Chemicals. Hydrochloric acid (HCl, 37% aqueous solution), ammonium hydroxide (28 % aqueous solution), glacial acetic acid (AcOH), Sodium bicarbonate (NaHCO\(_3\)), sodium sulfate (Na\(_2\)SO\(_4\)), potassium carbonate (K\(_2\)CO\(_3\)), potassium hydroxide (KOH), pyridine, and ethylene glycol were obtained from JT-Baker. Chloroform (CHCl\(_3\)) stabilized with ethanol, toluene, dichloromethane stabilized with amylene (CH\(_2\)Cl\(_2\)), hexanes, methanol (MeOH), acetone, ethyl acetate (EtOAc) were obtained from BDH and absolute ethanol from Decon labs. All the reagents were purchased with ACS grade quality or higher, and were used without further purification for synthesis purposes. Solvents were distilled prior to use. Dichloromethane, hexane and ethyl acetate were distilled over calcium chloride. Dioxane and THF were distilled over sodium and were stored under Argon (Ar). Analytical thin layer chromatography (TLC) was conducted on glass-coated silica gel 60 F254 plates obtained from EMD-Millipore. Column chromatography were conducted on silica gel (SiO\(_2\), 43–60 μm) provided by Silicycle. Unless specified, the 43–60 μm silica gel was used as stationary phase for the columns as well as the adsorption support for dry loading. Celite® 545 was purchased from EMD-Millipore.

Mass spectrometry was conducted on an Voyager DE STR MALDI-TOF spectrometer from Applied Biosystems using tertiophene or trans-2-[3-(4-tert-Butylphenyl)-2-methyl-2-propenylidene]malononitrile (DCTB) as ionization matrix. High res SM was conducted on a JEOL LCmate mass spectrometer using ESI ionization mode. \(^{1}\)H NMR were conducted on Varian spectrometers operating at 400 or 500 MHz in the appropriate deuterated solvents. Residual solvent peaks or TMS were used to calibrate the chemical shifts. UV–Visible spectroscopy was performed using a Shimadzu UV-2550 UV–Visible spectrophotometer.
1.2 Preparation of ligands 1a and 1b

Scheme 1. Synthetic scheme for ligands 1a and 1b. a) TFA (trifluoroacetic acid), CHCl₃, Ar (argon), RT (room temperature); b) DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone), CHCl₃, RT; c) SnCl₂, HCl, Ar, 65°C; d) SiO₂, Toluene, Ar, 90°C; e) ClCH₂COCl, K₂CO₃, CH₂Cl₂, Ar, O°C - RT; f) Zn(OAc)₂ (zinc(II) acetate), DMF (dimethylformamide), 45°C; g) NBS (N-bromosuccinimide), pyridine, CHCl₃, Ar, 0°C; h) TFA, CH₂Cl₂, RT; i) EtOH (ethanol), Ar, 70°C; j) Pd(PPh₃)₄, K₃PO₄, dioxane, Ar, 80°C ; k) KOH, MeOH (methanol), THF, H₂O, Ar, 45°C; l) NaBPh₄, pyridine-toluene 1-4, Ar, 90°C.

**General synthetic strategy**

In brief, the 5,15-bis(2-nitrophenyl)porphyrin (7) was obtained as a mixture of two atropisomers by direct condensation of dipyrrylmethane[2] and 2-nitrobenzaldehyde under acid catalysis. The nitro groups were subsequently reduced to amines using tin(II) chloride in acidic conditions. Thermal treatment of the resulting mixture in the presence of silica, according to the protocol described by Lindsey[3], yielded the desired α,α-atropisomer (6) as the major product. After isolation, 6 was acylated with chloroacetyl chloride at low temperature and the resulting derivative (5) was brominated with N-bromosuccinimide. Treatment of the mono-bromo macrocycle (4) with 4,13-diaza-18-crown-6 in refluxing ethanol gave the capped porphyrin (3) in good yield. The latter was engaged in a palladium-catalyzed Suzuki coupling with 2-(carboxymethyl)phenylboronic acid to yield the methyl-ester form of ligands: 1a-OMe and 1b-OMe. The ratio of 1a-OMe/1b-OMe was estimated to be 1/8 by ¹H-NMR spectroscopy (see section 2.1). The two atropisomers 1a and 1b could only be separated after the hydrolysis of the esters. The final ligands 1a and 1b were stable at room temperature, showing no detectable interconversion in solution over days. However, at elevated temperatures (>80 °C) the atropisomers underwent dynamic exchange and rapidly re-equilibrated into the initial 1a/1b ratio of 1/8. The final proportion of 1a in the mixture could be increased by annealing either pure 1b or the initial mixture of both 1a and 1b atropisomers in the presence of sodium tetraphenylborate in a pyridine-toluene (1-4) mixture. Under these conditions the ratio of the atropisomers equilibrated at roughly
1a/1b ~ 1/2 and thus permitted isolation of the desired conformer 1a in higher quantity (cf. SI section 2.2).

**Synthesis of 5,15-bis-(2-nitrophenyl)porphyrin 7**

In a two-neck 1L round bottom flask, 2-nitrobenzaldehyde (552 mg, 3.65 mmol) was dissolved in chloroform (720 mL), the solution was sparged with nitrogen for 15 minutes and dipyrrylmethane (600 mg, 3.65 mmol) was added. The mixture was further sparged with nitrogen for 15 minutes and trifluoroacetic acid (2.4 mL, 3.55 g, 31 mmol) was added. The solution was sparged with nitrogen for another 5 minutes, then it was stirred in the dark, under a nitrogen atmosphere, for 1 hour at room temperature. 1,2-dicyano-4,5-dichloro-1,4-benzoquinone (3.0 g, 13.2 mmol) was added and the mixture was stirred at room temperature for 1 hour. Triethylamine (4 mL) was added and the mixture was extracted with water (3 x 400 mL). The organic layer was collected, dried over sodium sulfate, filtered and the solvent was evaporated under reduced pressure. The crude product was purified on column chromatography (SiO$_2$, CH$_2$Cl$_2$-hexanes 7-3) to yield the desired 5,15-bis-(2-nitrophenyl) porphyrin as a mixture of two atropisomers (376.6 mg, 0.68 mmol, 37 %). The $^1$H-NMR spectrum of the obtained porphyrins mixture was in good agreement with the previously reported data.[4]

$^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 10.28 (s, 2H), 9.36 (d, $J = 4.7$ Hz, 4H), 8.84 (d, $J = 4.6$ Hz, 4H), 8.55 – 8.40 (m, 2H), 8.35 – 8.22 (m, 2H), 8.09 – 7.90 (m, 4H), -3.10 (s, 2H).

**Synthesis of 5,15-bis(2-aminophenyl)porphyrin 6**

In a 100 mL round bottom flask, 5,15-bis-(2-nitrophenyl)porphyrin 7 (340 mg, 0.62 mmol) was dissolved in concentrated hydrochloric acid (37% aqueous solution, 30 ml), tin(II) chloride dihydrate (1.04 g, 4.62 mmol) was added and the mixture was stirred at room temperature for 3 hours. It was treated with a concentrated aqueous ammonium hydroxide solution until the pH was stabilized at 7. The aqueous layer was extracted with a CH$_2$Cl$_2$-EtOAc 4-1 mixture (2 x 200 mL). The combined organic layers were dried over Na$_2$SO$_4$, filtered and the solvent was evaporated. The crude material was purified by column chromatography (SiO$_2$) with the following elution gradient: CH$_2$Cl$_2$-hexane (8-2) – CH$_2$Cl$_2$-CH$_2$Cl$_2$-1% acetone. The 5,15-bis(2-aminophenyl)porphyrin was obtained as two bands, the first eluted with pure CH$_2$Cl$_2$ corresponded to the $\alpha\beta$ isomer (151.4 mg, 0.31 mmol, 50%), the second band eluted with the use of CH$_2$Cl$_2$-1% acetone corresponded to the desired $\alpha\alpha$ isomer (140.3 mg, 0.29 mmol, 47%). The $^1$H-NMR spectra of the prepared porphyrins were in good agreement with the previously reported data.[5]

$\alpha\beta$-5,15-bis-(2-aminophenyl)porphyrin

$^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 10.27 (s, 2H), 9.38 (d, $J = 4.6$ Hz, 4H), 9.10 (d, $J = 4.6$ Hz, 4H), 7.90 (dd, $J = 7.4$, 1.6 Hz, 2H), 7.72 – 7.56 (m, 2H), 7.25 – 7.10 (m, 4H), 3.58 (s, 2H), -3.13 (s, 2H).

$\alpha\alpha$-5,15-bis-(2-aminophenyl)porphyrin

$^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 10.27 (brs, 2H), 9.37 (d, $J = 4.6$, 4H), 9.10 (d, $J = 4.6$ Hz, 4H), 7.95 (dd, $J = 7.4$, 1.6 Hz, 1H), 7.90 (dd, $J = 7.4$, 1.6 Hz, 2H), 7.66 – 7.60 (m, 2H), 7.24 – 7.18 (m, 2H), 7.16 – 7.12 (m, 2H), 3.57 (s, 2H), 3.52 (s, 2H), -3.13 (s, 2H).
**Isomerization of αβ-5,15-bis-(2-aminophenyl)porphyrin**

A two-neck 250 mL round bottom flask equipped with a dean stark condenser was charged with silica (12 g) and toluene (70 mL). The silica slurry was refluxed under Ar for 2 hours and 25 mL of a mixture of toluene and water was collected in the dean-stark apparatus. The temperature was reduced to 80 °C and the αβ-5,15-bis-(2-aminophenyl) porphyrin was added (270 mg, 0.55 mg). The slurry was stirred at 80 °C, under Ar, for 10h. The mixture was cooled down to room temperature and filtered on a silica short plug (SiO$_2$, CH$_2$Cl$_2$). The remaining αβ-5,15-bis-(2-aminophenyl)porphyrin was eluted with CH$_2$Cl$_2$ (53 mg, 0.11 mmol, 20%). The desired αα-5,15-bis-(2-aminophenyl)porphyrin was then eluted with CH$_2$Cl$_2$-1% acetone (199 mg, 0.41 mmol, 74%). The $^1$H-NMR spectra of the isomerized porphyrin perfectly matched the spectra of the as-prepared porphyrins.

**Synthesis of αα-5,15-bis-(2-(2-chloroacetyl)aminophenyl)porphyrin 5**

In a 100 mL round bottom flask, αα-5,15-bis-(2-aminophenyl) porphyrin 6 (365 mg, 0.74 mmol) was dissolved in chloroform (60 mL). Potassium carbonate (0.92 g, 8.7 mmol) was added to the solution and the mixture was cooled to 0 °C under nitrogen. Chloroacetyl chloride (0.32 mL, 460 mg, 4.1 mmol) was added and the mixture was further stirred at 0 °C for 10 minutes. The reaction mixture was warmed up to room temperature then quenched with the slow addition of water (30 mL). The organic layer was collected and further washed with 5% NaHCO$_3$ solution (1 x 50 mL), saturated ammonium chloride solution (1 x 50 mL) and water (1 x 50 mL). The organic layer was collected, dried over Na$_2$SO$_4$, filtered and the solvent was evaporated. The crude material was filtered over a silica short plug (SiO$_2$, CH$_2$Cl$_2$-1% acetone) to yield the desired product as a bright purple crystalline solid (474 mg, 0.73 mmol, 99%).

$^1$H-NMR (400 MHz, CDCl$_3$) δ 10.34 (s, 2H), 9.42 (d, $J$ = 4.6 Hz, 4H), 8.98 (d, $J$ = 4.6 Hz, 4H), 8.74 (d, $J$ = 7.5 Hz, 2H), 8.16 (s, 2H), 8.09 (dd, $J$ = 7.5, 1.6 Hz, 2H), 7.90 (ddd, $J$ = 8.7, 7.7, 1.6 Hz, 2H), 7.62 (td, $J$ = 7.5, 1.2 Hz, 2H), 3.42 (s, 4H), -3.09 (s, 2H).

**Synthesis of αα-5,15-bis-(2-(2-chloroacetyl)aminophenyl)-10-bromoporphyrin 4**

**a) zinc insertion**

αα-5,15-bis-(2-(2-chloroacetyl)aminophenyl)porphyrin 5 (302 mg, 0.47 mmol) was dissolved in tetrahydrofuran and zinc acetate (3.01 g, 13.7 mmol) was added. The mixture was stirred at 30 °C for 30 minutes after which TLC analysis (SiO$_2$, CH$_2$Cl$_2$-0.5% acetone) indicated complete metallation of the porphyrin. The porphyrin was precipitated in water (200 mL) and the solid was recovered by filtration. The solid was thoroughly washed with water (200 mL), dissolved in CH$_2$Cl$_2$-THF 5-1 (200 mL) and the organic layer was further extracted with water (3 x 100 mL). The organic layer was recovered, dried over Na$_2$SO$_4$, filtered and the solvent was evaporated under reduced pressure. The obtained compound was used in the following step without further purification (333 mg, 0.47 mmol, 100 %).

**b) bromation**

The metallated porphyrin (333 mg, 0.47 mmol) was dissolved in chloroform (150 mL) containing 1% v/v of pyridine. The solution was cooled to 0 °C and N-bromosuccinimide (75 mg, 0.42 mmol) was added. The reaction mixture was stirred at 0 °C for 15 minutes before being quenched by the addition of acetone (20 mL). The mixture was washed with water (3 x 100 mL), the organic layer was collected, dried
over Na$_2$SO$_4$, filtered, and the solvent was evaporated under reduced pressure. The crude solid was partly dissolved in CH$_2$Cl$_2$ (100 mL), trifluoroacetic acid (15 mL) was added and the mixture was stirred at room temperature for 15 minutes. The mixture was extracted with water (2 x 100 mL), diluted sodium hydroxide solution (1% aqueous, 2 x 50 mL) and water (1 x 100 mL). The organic layer was collected, dried over Na$_2$SO$_4$, filtered and the solvent was evaporated under reduced pressure. Column chromatography (SiO$_2$, CH$_2$Cl$_2$-0.5% acetone) yielded three major fractions in the following order:

**αα-5,15-bis-(2-(2-chloroacethyl)aminophenyl)-10,20-dibromoporphyrin** (72.6 mg, 90 μmol, 19%)

$^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 9.54 (d, $J = 4.9$ Hz, 4H), 8.68 (d, $J = 4.9$ Hz, 4H), 8.62 (dd, $J = 8.5$, 1.1 Hz, 2H), 7.96 – 7.88 (m, 4H), 7.84 – 7.77 (m, 2H), 7.55 – 7.49 (m, 2H), 3.36 (s, 4H), -2.70 (s, 2H).

MS (MALDI-TOF, positive) calcd for C$_{36}$H$_{24}$Br$_2$Cl$_2$N$_6$O$_2$ [M$^+$] m/z (100%) 799.97, found m/z (100%) 800.03.

**αα-5,15-bis-(2-(2-chloroacethyl)aminophenyl)-10-bromoporphyrin** (219.9 mg, 0.30 mmol, 64%)

$^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 10.17 (s, 1H), 9.73 (d, $J = 4.8$ Hz, 2H), 9.29 (d, $J = 4.7$ Hz, 2H), 8.88 – 8.84 (m, 4H), 8.70 (d, $J = 8.4$ Hz, 1H), 8.06 (brs, 2H), 8.05 – 7.95 (m, 4H), 7.92 – 7.86 (m, 2H), 7.59 (td, $J = 7.5$, 1.2 Hz, 2H), 3.41 (s, 4H), -2.94 (s, 2H).

MS (MALDI-TOF, positive) calcd for C$_{35}$H$_{25}$BrCl$_2$N$_6$O$_2$ [M$^+$] m/z (100%) 722.06, found m/z (100%) 722.04.

**αα-5,15-bis-(2-(2-chloroacethyl)aminophenyl)porphyrin** (24.1 mg, 80 μmol, 17%); $^1$H NMR spectrum matched the spectrum of the as-prepared compound.

**Synthesis of strapped porphyrin 3**

A two-neck 1L round bottom flask equipped with a reflux condenser was charged with αα-5,15-bis-(2-(2-chloroacethyl)aminophenyl)-10-bromoporphyrin 4 (185 mg, 0.26 mmol), 4,13-diaza-18-crown-6 (400 mg, 1.52 mmol) and absolute ethanol (650 mL). After sparging the suspension with argon for 20 minutes it was gently refluxed at 60 °C under argon. The progression of the reaction was followed by TLC (SiO$_2$, CH$_2$Cl$_2$-5% acetone). After 4 days of gentle reflux no more starting material remained. The solvent was evaporated under reduced pressure and the crude solid was dissolved in dichloromethane (300 mL). The mixture was extracted with water (2 x 200 mL) dried over Na$_2$SO$_4$ filtered and the solvent was evaporated. Column chromatography (SiO$_2$, elution gradient: CH$_2$Cl$_2$-15% acetone to CH$_2$Cl$_2$-20% acetone) was conducted and the desired strapped porphyrin was obtained as the second eluted compound. Recrystallization from CH$_2$Cl$_2$-hexanes yielded porphyrin 3 as bright purple crystals (210.7 mg, 0.23 mmol, 88%).

$^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 10.18 (s, 1H), 9.74 (d, $J = 4.8$ Hz, 2H), 9.29 (d, $J = 4.6$ Hz, 2H), 8.99 (s, 2H), 8.96 – 8.91 (m, 4H), 8.83 – 8.69 (m, 2H), 7.98 (dd, $J = 7.5$, 1.5 Hz, 2H), 7.91 – 7.84 (m, 2H), 7.62 – 7.45 (m, 2H), 2.81 – 2.43 (m, 4H), 2.13 (brs, 2H), 1.65 (brs, 2H), 1.46 (brs, 12H), 0.86 (brs, 2H), 0.25 (brs, 6H), -2.84 (s, 2H).

MS (MALDI-TOF, positive) calcd for C$_{48}$H$_{49}$Br$_2$N$_8$O$_6$ [M$^+$] m/z (100%) 914.29, found m/z (100%) 914.47.
**Synthesis of strapped porphyrins 1a-OMe and 1b-OMe**

*Synthesis of the methyl ester porphyrins (mixtures of atropisomers)*

An oven-dried 3-neck 100 mL round bottom flask equipped with a reflux condenser was charged with porphyrin 3 (90 mg, 98.5 μmol), methyl-2-carboxyphenylboronic acid (90 mg, 0.5 mmol), finely grounded anhydrous potassium phosphate tribasic (232 mg, 0.87 mmol) and freshly distilled dioxane (50 mL). The slurry was sparged with argon for 30 min and palladium(0) tetrakis-triphenylphosphine was added. The mixture was stirred at 85 – 90 °C under argon; the progression of the reaction was followed by TLC analysis (SiO₂, CH₂Cl₂-15% acetone). After 4h no starting materials remained, the reaction mixture was cooled down to room temperature and the solvent was evaporated. The crude solid was dissolved in dichloromethane, and the mixture was extracted with saturated aqueous ammonium chloride solution (2 x 50 mL), and water (1 x 50 mL). The organic phase was collected, dried over Na₂SO₄, filtered and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography (SiO₂, elution gradient: CH₂Cl₂-10% acetone to CH₂Cl₂-20% acetone); the desired strapped-porphyrin was eluted as a mixture of atropisomers (second band collected). Recrystallization from CH₂Cl₂-hexanes yielded compound 1-OMe (mixture of atropisomers) as bright purple crystals (64.5 mg, 67 μmol, 68%).

*Note:* due to the small relative quantity of the cis atropisomer in the initial mixture (3a/3b ~ 1/9) and due to the partial overlap the signals of the two atropisomers, the following ¹H NMR signals are characteristic for the major trans atropisomer.

¹H-NMR (400 MHz, CDCl₃) δ 10.19 (s, 1H), 9.33 (d, J = 4.7 Hz, 2H), 9.02 (s, 2H), 8.98 (d, J = 4.6 Hz, 2H), 8.82 (d, J = 4.8 Hz, 2H), 8.69 (d, J = 4.8 Hz, 3H), 8.43 – 8.34 (m, 1H), 8.34 – 8.24 (m, 1H), 8.06 (dd, J = 7.6, 1.5 Hz, 2H), 7.99 – 7.88 (m, 2H), 7.88 – 7.80 (m, 2H), 7.58 – 7.53 (m, 2H), 2.80 (s, 3H), 2.62 (s, 4H), 1.54 (s, 15H), 0.48 (s, 6H), -2.73 (s, 2H).

MS (MALDI-TOF, positive) calcd for C₅₆H₅₆N₈O₈ [M⁺] m/z(100%) 968.42, found m/z(100%) 968.61.

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**Saponification of the methyl ester and isolation of atropisomers 1a and 1b**

In a 25 mL round bottom flask, porphyrin 2 was dissolved in tetrahydrofuran (3 mL), and a solution of potassium hydroxide (2 M in ethanol-water 8-2, 5 mL) was added. The mixture was stirred at room temperature and the evolution of the reaction was followed by TLC analysis (SiO₂, CH₂Cl₂-20% acetone). After 4 hours all the starting material was converted. The mixture was diluted with CH₂Cl₂ (25 mL) and the organic phase was extracted with an aqueous citric acid solution (5 % m/v, 1 x 25 mL) and water (2 x 25 mL). The organic layer was collected, dried over Na₂SO₄, filtered and the solvent was evaporated under reduced pressure. The crude solid was purified by column chromatography (SiO₂, CH₂Cl₂-20 % acetone). Two bands were collected, the first (major) was assigned to the trans-atropisomer (1b), the second was assigned to the cis-atropisomer (1a). Recrystallization for CH₂Cl₂-hexanes yielded the desired porphyrins as bright purple crystals.

1b (19.3 mg, 20.2 μmol, 93%).
$^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 10.14 (s, 1H), 9.28 (d, $J = 4.7$ Hz, 2H), 8.97 – 8.92 (m, 3H), 8.78 (d, $J = 4.8$ Hz, 2H), 8.69 – 8.57 (m, 4H), 8.28 (m, 2H), 7.99 (d, $J = 7.4$ Hz, 2H), 7.90 –7.80 (m, 4H), 7.54 – 7.49 (m, 2H), 2.58 (s, 4H), 2.04 – 0.4 (br.m, 24H), -2.86 (s, 2H).

MS (MALDI-TOF, positive) calcd for C$_{55}$H$_{54}$N$_8$O$_8$ [M$^+$] m/z(100%) 954.41, found m/z(100%) 954.52.

HRMS (ESI-TOF, positive) calcd for C$_{55}$H$_{55}$N$_8$O$_8$ [M + H$^+$] m/z(100%) 955.4143, found m/z(100%) 955.4181.

$^1$H-NMR (500 MHz, CDCl$_3$) $\delta$ 10.21 (s, 1H), 9.41 (s, 2H), 9.33 (d, $J = 4.6$ Hz, 2H), 8.95 (d, $J = 4.6$ Hz, 2H), 8.85 (d, $J = 4.7$ Hz, 2H), 8.77 (d, $J = 8.0$ Hz, 2H), 8.75 (d, $J = 4.7$ Hz, 2H), 8.50 (d, $J = 8.0$ Hz, 1H), 7.97 (d, $J = 8.0$ Hz, 2H), 7.96 – 7.89 (m, 2H), 7.86 – 7.84 (m, 2H), 7.79 – 7.77 (m, 1H), 7.53 – 7.51 (m, 2H), 3.23 – 3.04 (m, 2H), 2.89 – 2.85 (m, 2H), 2.81 (d, $J = 17.4$ Hz, 2H), 2.80 – 2.74 (m, 2H), 2.68 – 2.64 (m, 2H), 2.55 (d, $J = 17.4$ Hz, 2H), 1.37 – 1.32 (m, 4H), 1.28 – 1.21 (m, 2H), 0.86 – 0.76 (m, 2H), 0.70 – 0.65 (m, 2H), 0.63 – 0.58 (m, 2H), -0.21 – 0.17 (m, 2H), -0.92 – -0.87 (m, 2H), -2.82 (s, 2H).

MS (MALDI-TOF, positive) calcd for C$_{55}$H$_{54}$N$_8$O$_8$ [M$^+$] m/z(100%) 954.41, found m/z(100%) 954.44.

HRMS (ESI-TOF, positive) calcd for C$_{55}$H$_{55}$N$_8$O$_8$ [M + H$^+$] m/z(100%) 955.4143, found m/z(100%) 955.4152.

Note: the saponification step can be executed directly after the Suzuki coupling reaction, purification of the methyl ester precursor mixture (porphyrin 2). Residual palladium and boronic acid impurities can be conveniently removed by a short plug filtration (SiO$_2$, CH$_2$Cl$_2$-25% acetone) before saponification. During the final column chromatography purification conducted after saponification (SiO$_2$, CH$_2$Cl$_2$-20 % acetone) a first band eluted rapidly and could be attributed the product resulting for the debromination of the starting material. No decrease in the isolated yields of compounds 1a and 1b was otherwise noticed.

**Isomerization of 1b**

In a 50 mL three-neck round bottom flask, equipped with a reflux condenser, the porphyrin atropisomer 1b (50 mg, 52.3 μmol) and sodium tetraphenylborate (100 mg, 0.29 mmol) were dissolved in a mixture of toluene-20% pyridine (10 mL). The mixture was purged with argon (vacuum-argon cycles, 3 times) and gently refluxed at 100 – 105 °C for 4 hours under argon. The mixture was cooled down to room temperature and the solvent was evaporated. The residue was purified on a column chromatography (SiO$_2$, CH$_2$Cl$_2$-acetone 1-1) to yield, after recrystallization from CH$_2$Cl$_2$-hexanes, 1b atropisomer (32 mg, 33.5 μmol, 64%, first band eluted) and 1a atropisomer (17 mg, 17.8 μmol, 34%).

Note: under similar conditions and treatment but in the absence of sodium tetraphenylborate the yields obtained after column chromatography and recrystallization were: 1b (42 mg, 44 μmol, 85%) and 1a (6 mg, 6.3 μmol, 12 %). In all cases the $^1$H NMR, and MS of ligands 1a and 1b recovered after the described annealing processes were similar to the spectra obtained for the products isolated directly after saponification of the ester precursors. The compounds were therefore used without distinction for the physico-chemical studies reported in this work.
1.3 Preparation of the precursor 12

Scheme 2. Synthetic scheme for the functionalized precursor 12. a) ethylene glycol, benzene, p-toluene sulfonic acid, Ar, reflux 12 h (Dean-Stark), Ar; b) KOH, THF, MeOH, H₂O, 5h; c) 2-(1H-Benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU), DMF, RT, N₂.

**Synthesis of methyl-2-carboxyphenyldioxolane 14**

A two-neck 250 mL round bottom flask equipped with a Dean-Stark condenser was charged with methyl-2-formylbenzoate (4.0 g, 24.4 mmol), ethylene glycol (1.75 mL, 1.94 g, 31.3 mmol) and benzene (100 mL). The mixture was sparged with argon for 15 minutes and p-toluene sulfonic acid (0.137 g, 0.80 mmol) was added. The reaction mixture refluxed, under argon, for 12 hours. During this time the water/benzene mixture that was collected in the Dean-Stark condenser was discarded every 4 hours. The solution was cooled down to room temperature and the organic phase was extracted with 5% aqueous NaHCO₃ solution (3 x 100 mL). The organic layer was collected, dried over Na₂SO₄, filtered and the solvent was evaporated under reduced pressure. The crude oil was purified by filtration over a silica short plug (SiO₂, CH₂Cl₂) to yield the desired compound as a pale yellow oil (3.74 g, 18 mmol, 74%).

¹H-NMR (400 MHz, CDCl₃) δ 7.87 (dd, J = 7.8, 1.4 Hz, 1H), 7.76 (dd, J = 7.8, 1.4 Hz, 1H), 7.54 (td, J = 7.6, 1.4 Hz, 1H), 7.41 (td, J = 7.6, 1.4 Hz, 1H), 6.60 (s, 1H), 4.06 (s, 4H), 3.92 (s, 3H).

**Saponification of the methyl-2-carboxyphenyldioxolane 13**

In a 100 mL round bottom flask, methyl-2-carboxyphenyldioxolane 14 (1.69 g, 8.12 mmol) was dissolved in tetrahydrofuran (5 mL). Potassium hydroxide (0.48 g, 8.6 mmol) dissolved in a methanolic solution (8-2 methanol-water mixture, 5 mL) was added and the mixture was stirred at room temperature for 5h, after which no starting material remained according to TLC analysis (SiO₂, CH₂Cl₂). The solvent was evaporated under reduced pressure and the crude solid was dried via azeotropic distillation with toluene, to yield a white solid (1.91 g, quant.). The compound was immediately used in the following step without further purification.

**Synthesis of 2-N,N-bis(2-methoxyacetonyl)amidophenyldioxolane 12**

The potassium salt of the 2-carboxyphenyldioxolane 13 (2.33 g, 10 mmol) was suspended in dry dimethylformamide (30 mL). 2-(1H-Benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU) (4 g, 10.5 mmol) was added portion-wise (4 x 1g) over 5 minutes and the mixture was stirred
until all the solid dissolved (15 minutes). *N,N*-bis-(2-metoxyacethyl)amine (2 g, 12.4 mmol) was added and the mixture was stirred for 10 hours at room temperature, under nitrogen. The mixture was poured into water (100 mL) and the aqueous phase was extracted with diethyl ether until only traces of the desired product remained in the aqueous phase (4 x 100 mL). The combined organic layers were dried over Na$_2$SO$_4$, filtered and the solvent was evaporated under reduced pressure. Column chromatography (SiO$_2$, CH$_2$Cl$_2$-1% acetone) yielded the desired product (third band) as a thick oil (2.15 g, 6.37 mmol, 64%).

$^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 7.63 (dd, $J = 7.7$, 1.4 Hz, 1H), 7.44 (td, $J = 7.5$, 1.5 Hz, 1H), 7.39 (td, $J = 7.5$, 1.5 Hz, 1H), 7.30 – 7.27 (m, 1H), 5.90 (s, 1H), 4.85 – 4.45 (br s, 2H), 4.30 – 3.95 (br m, 6H), 3.78 (s, 3H), 3.68 (s, 3H).

1.4 Preparation of ligands 2a and 2b

Scheme 3. Synthetic scheme for ligand 2a. The same synthetic strategy was followed to prepare ligand 2b, starting from the atropisomer 11b (for which the nitro group and diester substituents are facing towards the two opposite sides of the porphyrin macrocycle). a) BF$_3$.Et$_2$O, CH$_3$Cl, Ar, RT; b) DDQ, CHCl$_3$, RT; c) Zn(OAc)$_2$, CHCl$_3$, MeOH, RT; d) Zn, AcOH (acetic acid), CH$_2$Cl$_2$, THF, Ar, RT; e) CICH$_2$COCl, K$_2$CO$_3$, CH$_2$Cl$_2$, Ar, O°C - RT; f) EtOH, Ar, 70°C; g) NaOH, MeOH, H$_2$O, Ar, RT.

General synthetic strategy

The precursor porphyrin (11) was obtained as a mixture of two atropisomers from the statistical acid-catalyzed condensation of dipyrromethane with 2-nitrobenzaldehyde and the acetal derivative of dimethyl 2,2'-[2-formylbenzamido]diacetate. Each atropisomer of the desired mixed-porphyrin, 11a and 11b, could be isolated in its pure form after column chromatography. Importantly, only relatively slow rates of interconversion between the two atropisomers were observed above 60°C. The latter could thus be engaged in further reactions in their pure forms and were not subjected to significant re-equilibration during the subsequent synthetic steps. Reduction of the nitro functionality was conducted using zinc(0) in the presence of acetic acid at room temperature. Next, the amino-porphyrin 10a (or 10b) was acylated with chloroacetyl chloride at low temperature, followed by treatment of the resulting derivative 9a (or 9b) with 4-aza-18-crown-6 in gently refluxing methanol. Finally, saponification of the diester led to the desired ligands 2a (or 2b).
**Synthesis of 5-(2-nitrophenyl)-15-(2-N,N-(bis-2-methoxyacetyl)amidophenyl)porphyrins 11a and 11b**

The atropisomers 11a and 11b were more easily separated as their zinc complexes. Therefore, we first isolated the two isomers as a mixture of the free base porphyrins and subsequently metallated macrocycles before separation.

*a) Condensation of the porphyrin macrocycle*

A 4 L three-neck flask was charged with 2-nitrobenzaldehyde (0.964 g, 6.4 mmol), 2-N,N-bis(2-methoxyacetonyl)amidophenylidioxolane 12 (2.15 g, 6.4 mmol), chloroform (2.4 L), and the mixture was sparged with argon under vigorous stirring for 45 minutes. Dipyrrylmethane (1.865 g, 12.8 mmol) was added and the solution was further sparged with argon for 15 minutes. Boron trifluoride diethyl ether complex (380 μL, 429 mg, 3 mmol) dissolved in deoxygenated chloroform (5 mL) was added and the mixture was stirred under argon for 4 hours. 2,3-dichloro-4,6-dicyano-1,4-benzoquinone (6 g, 26.4 mmol) was added and the mixture was stirred at room temperature for 2 hours. Triethylamine (1 mL) was added and the organic phase was extracted with 5% aqueous NaHCO₃ solution (3 x 1.5 L). The organic layer was collected, dried over Na₂SO₄, filtered and the solvent was evaporated under reduced pressure. The crude mixture was purified by column chromatography (SiO₂, elution gradient: CH₂Cl₂-1% acetone to CH₂Cl₂-4% acetone). The desired porphyrin was collected as a mixture of the two thermally stable atropisomers 11a and 11b (third band eluted; 433.3 mg, 0.62 mmol, 9.7%).

³H-NMR was poorly informative due to the overlapping signals of the two atropisomers which resulted in a complex pattern of signals over the entire range of the spectra.

**MS (MALDI-TOF, positive)** calcd for C₃₉H₃₀N₆O₇ [M⁺] m/z(100%) 694.22, found m/z(100%) 694.09.

*b) Metallation of 5-(2-nitrophenyl)-15-(2-N,N-(bis-2-methoxyacetyl)amidophenyl)porphyrin and isolation of the pure atropisomers 11a and 11b*

The mixture of the two atropisomers (433.3 mg, 0.62 mmol) and zinc acetate dihydrate (2.5 g, 11.5 mmol) were suspended in a chloroform-methanol 1-3 mixture (70 mL). The slurry was stirred for 10 h at room temperature and TLC analysis (SiO₂, CHCl₃-EtOAc 8-2) confirmed the full metallation of the porphyrins. The solvent was evaporated and the crude residue taken in chloroform-5% methanol (200 mL). The organic layer was washed with water (3 x 200 mL), collected, dried over Na₂SO₄, filtered and the solvent was evaporated under reduced pressure. Column chromatography (SiO₂, Toluene-EtOAc 8-2), followed by recrystallization from CH₂Cl₂-hexanes, yielded the two atropisomers in their pure form.

Note: due to the higher solubility of the material in chlorinated solvents the crude was loaded on the column using CHCl₃-EtOAc 7-3; the column was subsequently run with the solvents mixture indicated above.

αα'-5-(2-nitrophenyl)-15-(2-N,N-(bis-2-methoxyacetyl)amidophenyl)-zinc-porphyrin (197.2 mg, 0.26 mmol, 42%) was obtained as the first major band (11a).
1H-NMR (400 MHz, CDCl₃) δ 10.23 (br. s, 2H), 9.47 – 9.30 (m, 4H), 9.10 (br. s, 2H), 8.90 (d, J = 4.5 Hz, 2H), 8.71 (d, J = 7.5 Hz, 1H), 8.47 – 8.38 (m, 2H), 8.06 – 7.94 (m, 3H), 7.84 (td, J = 7.7, 1.3 Hz, 1H), 7.63 (dd, J = 7.7, 1.4 Hz, 1H), 3.67 (br. s, 1H), 3.38 – 3.10 (br. s, 3H + 1H), 2.20 (br. s, 1H), 1.95 (br. s, 2H), 1.03 (s, 3H).

MS (MALDI-TOF, positive) calcd for C₁₃₉H₂₈N₆O₇Zn [M⁺] m/z(100%) 756.13, found m/z(100%) 756.49.

αβ'-5-(2-nitrophenyl)-15-(2-N,N-(bis-2-methoxyacetyl)amidophenyl)-zinc-porphyrin (234.6 mg, 0.31 mmol, 50%) was obtained as the second major band (11b).

MS (MALDI-TOF, positive) calcd for C₁₃₉H₂₈N₆O₇Zn [M⁺] m/z(100%) 756.13, found m/z(100%) 756.49.

Synthesis of αα'-5-(2-aminophenyl)-15-(2-N,N-(bis-2-methoxyacetyl)amidophenyl)-zinc-porphyrin 10a

In a two-neck 25 mL flask equipped with a 10 mL addition funnel, αα'-5-(2-nitrophenyl)-15-(2-N,N-(bis-2-methoxyacetyl)amidophenyl)-zinc-porphyrin 11a (21 mg, 28 μmol) was dissolved in a mixture of tetrahydrofuran-dichloromethane 1:1 (8 mL). Zinc powder (50 mg) was added and a solution of 10% glacial acetic acid in dichloromethane (4 mL) was added dropwise over 20 minutes, while stirring vigorously the suspension at room temperature. After complete addition, TLC analysis (SiO₂, CH₂Cl₂-10% EtOAc) indicated the remaining presence of unreacted nitro porphyrin; additional zinc powder (50 mg) was added and the mixture further stirred for another 30 minutes at room temperature. After that time, TLC analysis still indicated the presence of unreacted starting material. Another 50 mg of zinc powder was added and the mixture further stirred at room temperature for 30 minutes, after what TLC analysis showed that only traces amount of staring material was left. The zinc powder was filtered off and the mixture diluted to 100 mL with dichloromethane. It was washed with a 5% aqueous NaHCO₃ solution (100 mL) and water (100 mL). The organic layer was collected, dried over Na₂SO₄, filtered and the solvent was evaporated under reduced pressure. Column chromatography (SiO₂, elution gradient: CH₂Cl₂-EtOAc 8-2 to CH₂Cl₂-EtOAc 4-2) yielded the desired compound 10a (16 mg, 22 μmol, 79%) as a deep purple solid (third eluted compound).

1H-NMR (400 MHz, CDCl₃-MeOD 4-1) δ 10.21 (s, 2H), 9.38 (d, J = 4.4 Hz, 2H), 9.35 (d, J = 4.4 Hz, 2H), 9.11 (d, J = 4.5 Hz, 2H), 8.97 (br. s, 2H), 8.30 – 8.24 (m, 1H), 7.94 (dd, J = 7.4, 1.6 Hz, 1H), 7.93 – 7.83 (m, 2H), 7.64 (td, J = 7.8, 1.6 Hz, 1H), 7.28 – 7.16 (m, 2H), 4.23 (s, 2H), 3.27 – 3.24 (br. s, 3H + 2H), 2.77 (s, 3H).

Note: due to the presence of deuterated methanol the labile protons form the amino groups are not observed.

MS (MALDI-TOF, positive) calcd for C₁₃₉H₃₀N₆O₅Zn [M⁺] m/z(100%) 736.16, found m/z(100%) 726.49.

Synthesis of αβ'-5-(2-aminophenyl)-15-(2-N,N-(bis-2-methoxyacetyl)amidophenyl)-zinc-porphyrin 10b

αβ'-5-(2-aminophenyl)-15-(2-N,N-(bis-2-methoxyacetyl)amidophenyl)-zinc-porphyrin was prepared following the same procedure as described for αα'-5-(2-aminophenyl)-15-(2-N,N-(bis-2-methoxyacetyl)amidophenyl)-zinc-porphyrin, using the following reactants and solvent quantities: αα'-
5-(2-nitrophenyl)-15-(2-N,N-(bis-2-methoxyacetyl)amidophenyl)-zinc-porphyrin 11b (65 mg, 87 μmol), tetrahydrofuran-dichloromethane 1:1 (20 mL), 10% glacial acetic acid in dichloromethane (10 mL), zinc powder (4 x 50 mg). Column chromatography (SiO$_2$, elution gradient: CH$_2$Cl$_2$-EtOAc 8-2 to CH$_2$Cl$_2$-EtOAc 4-2) yielded the desired compound 10b (44 mg, 61 μmol, 70%) as a deep purple solid (third eluted compound).

$^1$H-NMR (400 MHz, CDCl$_3$) δ 10.21 (s, 2H), 9.38 – 9.35 (m, 4H), 9.04 (br s, 2H), 9.02 (d, $J$ = 4.5 Hz, 2H), 8.50 – 8.40 (m, 1H), 7.94 – 7.83 (m, 2H), 7.80 (d, $J$ = 7.5 Hz, 1H), 7.77 – 7.71 (m, 1H), 7.57 (td, $J$ = 7.8, 1.5 Hz, 1H), 7.16 (td, $J$ = 7.5, 1.1 Hz, 1H), 6.91 (d, $J$ = 8.1 Hz, 1H), 4.06 (br. s, 1H), 3.24 (s, 2 + 1H), 3.16 (s, 3H), 3.05 (br. s, 1H), 2.90 (br s, 1H), 1.89 (s, 3H).

MS (MALDI-TOF, positive) calcd for C$_{39}$H$_{30}$N$_6$O$_5$Zn [M$^+$] m/z (100%) 726.16, found m/z (100%) 726.49.

**Synthesis of αα’-5-(2-(2-chloroacetyl)aminophenyl)-15-(2-N,N-(bis-2-methoxyacetyl)amidophenyl)-zinc-porphyrin 9a**

A 50 mL round bottom flask, was charged with αα’-5-(2-aminophenyl)-15-(2-N,N-(bis-2-methoxyacetyl)amidophenyl)-zinc-porphyrin 10a (40 mg, 55 μmol), potassium carbonate (36.4 mg, 0.28 mmol) and dichloromethane (10 mL). The mixture was cooled down to 0 °C under argon and 2-chloroacetyl chloride (8.6 μL, 12.2 mg, 11 μmol) was added. The mixture was stirred under argon at 0 °C. The evolution of the reaction was followed by TLC analysis (SiO$_2$, CH$_2$Cl$_2$-1% EtOAc). After 1 hour no staring material remained. The mixture was diluted to 100 mL with dichloromethane and the organic phase was washed with a 5% NaHCO$_3$ aqueous solution (1 x 100 mL) and water (1x 100 mL). The organic layer was collected, dried over Na$_2$SO$_4$, filtered and the solvent was evaporated under reduced pressure. Column chromatography (SiO$_2$, CH$_2$Cl$_2$-7% EtOAc) followed by recrystallization form CH$_2$Cl$_2$-hexannes, yielded the desired compound 9a as deep purple crystals (second eluted compound, 40.6 mg, 51 μmol, 92%).

$^1$H-NMR (400 MHz, CDCl$_3$) δ 10.28 (s, 2H), 9.42 – 9.37 (m, 4H), 9.06 (br s, 2H), 9.01 (d, $J$ = 4.5 Hz, 2H), 8.72 (d, $J$ = 8.3 Hz, 1H), 8.42 – 8.34 (m, 1H), 8.23 (s, 1H), 8.19 (dd, $J$ = 7.5, 1.5 Hz, 1H), 7.94 – 7.83 (m, 3H), 7.81 – 7.74 (m, 1H), 7.66 – 7.58 (m, 1H), 4.13 (br s, 1H), 3.74 (br. s, 1H), 3.33 (s, 2H), 3.25 –3.05 (br. s, 3H + 2H), 2.24 (s, 3H).

MS (MALDI-TOF, positive) calcd for C$_{31}$H$_{41}$ClN$_6$O$_6$Zn [M$^+$] m/z (100%) 802.13, found m/z(100%) 802.43.

**Synthesis of αβ’-5-(2-(2-chloroacetyl)aminophenyl)-15-(2-N,N-(bis-2-methoxyacetyl)amidophenyl)-zinc-porphyrin 9b**

αβ’-5-(2-(2-chloroacetyl)aminophenyl)-15-(2-N,N-(bis-2-methoxyacetyl)amidophenyl)-zinc-porphyrin 9b was prepared following the same procedure as described for αα’-5-(2-(2-chloroacetyl)aminophenyl)-15-(2-N,N-(bis-2-methoxyacetyl)amidophenyl)-zinc-porphyrin 9a with the following reactants and solvent quantities: αα’-5-(2-aminophenyl)-15-(2-N,N-(bis-2-methoxyacetyl)amidophenyl)-zinc-porphyrin 10b (32 mg, 44 μmol), potassium carbonate (29 mg, 0.22 mmol), chloroacetyl chloride (6.9 μL, 9.7 mg, 88 μmol), dichloromethane (10 mL). Purification was conducted using column chromatography (SiO$_2$, elution gradient: CH$_2$Cl$_2$-5% EtOAc to CH$_2$Cl$_2$-10% EtOAc)
followed by recrystallization from CH$_2$Cl$_2$-hexanes to yield the desired product 9b as deep purple crystals (30.8 mg, 40 μmol, 91%).

$^1$H-NMR (400 MHz, CDCl$_3$) δ 10.29 (s, 2H), 9.46 – 9.38 (m, 4H), 9.09 (d, J = 4.5 Hz, 2H), 8.99 (d, J = 4.5 Hz, 2H), 8.76 (d, J = 8.4 Hz, 1H), 8.47 (dd, J = 7.0, 1.5 Hz, 1H), 8.16 (s, 1H), 8.07 (dd, J = 7.5, 1.6 Hz, 1H), 7.92 (td, J = 7.5, 1.7 Hz, 1H), 7.90 – 7.82 (m, 2H), 7.78 – 7.70 (m, 1H), 7.59 (td, J = 7.5, 1.3 Hz, 1H), 4.20 – 2.60 (m, 9H), 1.90 (s, 3H).

Between 3.6 and 4.3 ppm a complex pattern is observed with a very broad baseline signal overalling two well defined singlet centered at 3.34 and 3.17 ppm respectively. We can attribute the broad signal to the two slowly exchanging CH$_2$COOMe arms, the singlet centered at 3.34 ppm to the protons of the CH$_2$Cl and the singlet centered at 3.17 ppm to one of the COOC$_3$H$_7$ groups. The theoretical total integration should be 9 protons; we observed 8.6 on the normalized spectra which is explained by the broadening of the signal associated to the two CH$_2$COOMe groups.

MS (MALDI-TOF, positive) calcd for C$_{31}$H$_{41}$ClN$_6$O$_6$Zn [M$^+$] $m/z$(100%) 802.13, found $m/z$(100%) 802.44.

Synthesis of porphyrin 8a

A three-neck 50 mL round bottom flask equipped with a reflux condenser was charged with porphyrin 9a (60 mg, 75 μmol), 4-aza-18-crown-6 (90 mg, 0.34 mmol) and methanol (20 mL). The mixture was sparged with argon for 15 minutes and stirred at 60 °C, under argon for 60 hours. The mixture was cooled down to room temperature, and the solvent was evaporated. Column chromatography purification (SiO$_2$, elution gradient CH$_2$Cl$_2$-1% MeOH to CH$_2$Cl$_2$-7% MeOH) followed by recrystallization from CH$_2$Cl$_2$-hexanes yielded the desired product 8a (42.3 mg, 41 μmol, 55%, third eluted compound) as deep purple crystals.

$^1$H-NMR (500 MHz, CDCl$_3$) δ 10.20 (s, 2H), 9.34 (d, J = 4.4 Hz, 2H), 9.31 (d, J = 4.4 Hz, 2H), 9.26 (s, 1H), 8.98 (d, J = 4.4 Hz, 2H), 8.87 (br. s, 2H), 8.70 (d, J = 8.3 Hz, 1H), 7.95 – 7.87 (m, 2H), 7.86 – 7.82 (m, 2H), 7.77 (d, J = 7.6 Hz, 1H), 7.66 (td, J = 7.5, 1.5 Hz, 1H), 7.50 (td, J = 7.5, 1.3 Hz, 1H), 4.67 (s, 2H), 3.74 (s + br s, 3 + 2H), 3.33 (s, 3H), 2.64 (s, 2H), 2.50 – 2.29 (m, 8H), 1.88 (s, 4H), 1.22 (m, 4H), 1.01 (m, 4H).

Note: the signal of 4 protons are not visible (crown ether CH$_3$), due to the overlapping signal of the water at 1.38 ppm.

$^1$H-NMR (500 MHz, DMSO-$_d_6$) δ 10.33 (s, 2H), 9.48 (d, J = 4.4 Hz, 2H), 9.43 (d, J = 4.4 Hz, 2H), 9.32 (s, 1H), 8.84 – 8.81 (m, J = 4.4, 2.7 Hz, 4H), 8.75 (dd, J = 8.4, 1.3 Hz, 1H), 8.04 (dd, J = 7.6, 1.3 Hz, 1H), 7.95 (td, J = 7.7, 1.2 Hz, 1H), 7.90 (dd, J = 7.4, 1.6 Hz, 1H), 7.88 – 7.80 (m, 2H), 7.76 (dd, J = 8.0, 1.4 Hz, 1H), 7.52 (td, J = 7.5, 1.3 Hz, 1H), 4.47 (s, 2H), 3.52 (s, 3H), 3.45 (s, 2H), 2.94 – 2.77 (m, 4H), 2.66 (s, 3H), 2.58 (s, 2H), 2.53 – 2.48 (m, 4H), 1.78 (br. s, 4H), 1.40 (br. s, 4H), 0.92 – 0.83 (m, 4H), 0.70 (br. s, 4H).

Note: the signal of 4 protons are not distinguished (crown ether CH$_3$) due to the overlapping of the residual DMSO signal at 2.50 ppm.

MS (MALDI-TOF, positive) calcd for C$_{53}$H$_{55}$N$_7$O$_{11}$Zn [M$^+$] $m/z$(100%) 1029.33, found $m/z$(100%) 1029.66.

Partial thermal re-equilibration of the αα’ atropisomer during the synthesis led to the isolation of atropisomer 8b (6 mg, 5.8 μmol, 8%, second eluted compound) in addition to 8a.
Synthesis of porphyrin 8b

Porphyrin 8b was obtained following the same procedure described for 8a with the following reagent and solvent quantities: porphyrin 9b (50 mg, 62 μmol), 4-aza-18-crown-6 (80 mg, 0.30 mmol) and methanol (20 mL). Purification was conducted using column chromatography (SiO₂, elution gradient CH₂Cl₂-1% MeOH to CH₂Cl₂-4% MeOH) followed by recrystallization from CH₂Cl₂-hexanes. Only limited thermal re-equilibration of the starting αβ’ atropisomer occurred during the reaction and yield to the isolation of traces of 8a (1 mg, 0.97 μmol, 2% (third product eluted) in addition to the desired porphyrin 8b (41 mg, 40 μmol, 65%, second product eluted).

¹H-NMR (500 MHz, CDCl₃) δ 10.18 (s, 2H), 9.82 (s, 1H), 9.33 (br. s, 2H), 9.32 (d, J = 4.4 Hz, 2H), 9.09 (br. s, 2H), 9.13 (dd, J = 8.6, 1.2 Hz, 1H), 8.94 (d, J = 4.3 Hz, 2H), 8.41 – 8.37 (m, 1H), 7.91 – 7.85 (m, 2H), 7.85 – 7.78 (m, 2H), 7.70 (dd, J = 7.4, 1.6 Hz, 1H), 7.39 (td, J = 7.4, 1.3 Hz, 1H), 4.05 (br. s, 1H), 3.29 (br. s, 1H), 3.01 (br. s, 2H), 2.66 (s, 3H), 2.63 (s, 2H), 2.06 (br. s, 8H), 1.60 (s, 3H), 1.47 (m, 4H), 1.29 – 1.05 (m, 12H).

¹H-NMR (500 MHz, DMSO-d₆) δ 10.32 (s, 2H), 9.45 (d, J = 4.4 Hz, 2H), 9.41 (d, J = 4.4 Hz, 2H), 8.94 (s, 1H), 8.81 – 8.75 (m, 3H), 8.74 (d, J = 4.4 Hz, 2H), 8.01 (dd, J = 7.4, 1.6 Hz, 1H), 7.95 – 7.91 (m, 2H), 7.86 – 7.79 (m, J = 13.4, 2H), 7.72 (dd, J = 8.2, 1.4 Hz, 1H), 7.53 (td, J = 7.5, 1.3 Hz, 1H), 4.43 (s, 2H), 3.48 (s, 2H), 2.64 (s, 3H), 2.48 – 2.43 (m, 4H), 2.40 (s, 2H), 2.21 – 2.02 (m, 4H), 1.59 – 1.41 (m, 4H), 0.66 (q, J = 6.7, 5.8 Hz, 8H), 0.04 – 0.02 (m, 4H).

Note: The signal of 4 protons (crown ether CH₂) is partly overlapping the residual DMSO signal

MS (MALDI-TOF, positive) calcd for C₅₃H₅₅N₇O₁₁Zn [M⁺] m/z(100%) 1029.33, found m/z(100%) 1029.67.

Synthesis of porphyrin 2a

Porphyrin 8a (6.4 mg, 6.2 μmol) was dissolved in 2 mL of a 0.1 M NaOH solution (MeOH-20% H₂O). The solution was stirred at room temperature for 4 hours. TLC analysis (SiO₂, EtOAc-CH₂Cl₂-MeOH, 6-6-1) showed that all the starting material was converted. The solvent was evaporated and the crude residue was purified by column chromatography (SiO₂, elution gradient: ACN-12% H₂O to ACN-15% H₂O). The desired compound was collected as the second (main) band. Recrystallization from CH₂Cl₂-0.1%MeOH / hexanes to yield the desired porphyrin 2a as a purple powder (5.3 mg, 5.3 μmol, 86%).

¹H-NMR (400 MHz, DMSO-d₄) δ 18.48 (s, 2H), 10.36 (s, 2H), 9.49 (d, J = 4.5 Hz, 2H), 9.46 (d, J = 4.4 Hz, 2H), 9.30 (s, 1H), 8.87 (d, J = 4.4 Hz, 2H), 8.82 – 8.76 (m, 3H), 8.04 – 7.95 (m, 1H), 7.92 – 7.82 (m, 2H), 7.81 – 7.75 (m, 2H), 7.55 – 7.49 (m, 1H), 2.79 (s, 2H), 2.69 – 2.63 (m, 4H), 2.55 (s, 2H), 2.17 – 2.11 (m, 4H), 1.27 (br. s, 4H), 1.18 (br. s, 4H), 0.90 – 0.78 (m, 4H), 0.49 – 0.40 (m, 4H).

MS (MALDI-TOF, positive) calcd for C₅₃H₅₁N₇O₁₁Zn [M + K⁺] m/z(100%) 1040.26, found m/z(100%) 1040.43.

Note: the protons associated to the methylene groups of the diacid moieties do not lead to the observation of well defined peaks in the ¹H-NMR spectrum; instead a very broad signal could be observed in the baseline between 3.65 – 3.20 ppm.
**Synthesis of porphyrin 2b**

Porphyrin 2b was obtained following the same procedure described for 2a with the following reagent and solvent quantities: porphyrin 8b (9 mg, 8.7 μmol), 0.11 M NaOH in MeOH-20% H2O (2.5 mL). An additional 1 mL of THF was required to fully dissolve the material. Hydrolysis was complete after 4 hours as observed by TLC analysis (SiO2, EtOAc-CH2Cl2-MeOH, 6-6-1). Column chromatography purification (SiO2 ACN-12% H2O, followed by recrystallization from CH2Cl2-0.1%MeOH / hexanes yielded the desired porphyrin 2b as a purple powder (7.9 mg, 7.9 μmol, 94%).

**1H-NMR (400 MHz, DMSO-d6)** δ 18.40 (s, 2H), 10.35 (s, 2H), 9.48 (d, J = 4.5 Hz, 2H), 9.45 (d, J = 4.5 Hz, 2H), 8.93 (s, 1H), 8.84 (d, J = 4.4 Hz, 2H), 8.81 – 8.73 (m, 3H), 8.04 (d, J = 7.4 Hz, 1H), 8.01 (d, J = 7.4 Hz, 1H), 7.94 – 7.79 (m, 3H), 7.74 (d, J = 7.6 Hz, 1H), 7.56 (t, J = 7.5 Hz, 1H), 3.81 (br. s, 2H), 2.67 (s, 2H), 2.55 – 2.50 (m, 4H), 2.42 (s, 2H), 2.21 – 2.11 (m, 4H), 1.60 – 1.50 (m, 4H), 0.80 – 0.72 (m, 4H), 0.72 – 0.65 (m, 4H), 0.11 – 0.02 (d, J = 5.8 Hz, 4H).

**MS (MALDI-TOF, positive)** calcd for C51H51KN7O11Zn [M + K+] m/z(100%) 1040.26, found m/z(100%) 1040.41.

**1.5 Preparation of ligands R1 and R2**

![Scheme 4](image)

**Scheme 4.** Synthetic scheme for ligand R2. a) TFA, CHCl3, Ar, RT; b) DDQ, CHCl3, RT; c) Zn(OAc)2, CH2Cl2, MeOH, RT; d) Zn, AcOH, CH2Cl2, THF, Ar, RT; e) TFA, CH2Cl2, RT; f) ClCH2COCl, K2CO3, CH2Cl2, Ar, O°C – RT; g) Zn(OAc)2, DMF, 45°C; h) EtOH, Ar, 78°C.

**Synthesis of 5-phenyl-15-(2-nitrophenyl)porphyrin 17**

A two-neck 1 L round bottom flask was charged with benzaldehyde (140 mg, 1.37 mmol), 2-nitrobenzaldehyde (207 mg, 1.37 mmol) and chloroform (500 mL). The mixture was sparged with argon
for 30 minutes and dipyrrylmethane (450 mg, 2.74 mmol) was added. The mixture was further sparged
with argon for 10 minutes and trifluoroacetic acid (0.8 mL, 534 mg, 4.7 mmol) was added. The mixture
was stirred under argon, at room temperature, for 1 hour and 2,3-dichloro-5,6-dicyao-1,4-benzoquinone
(2 g, 8.8 mmol) was added. The mixture was further stirred at room temperature for 1 hour. The reaction
mixture was quenched with the addition of triethylamine (1 mL) and washed with a 5% aqueous NaHCO₃
solution (3 x 200 mL) and water (1 x 100 mL). The organic layer was collected, dried over Na₂SO₄, filtered
and the solvent was evaporated under reduced pressure. The crude residue was filtered through a silica
short plug (SiO₂, CH₂Cl₂); fractions were collected until no porphyrin eluted; the solvent was evaporated
under reduced pressure, and the resulting porphyrin mixture was further purified by column
chromatography (SiO₂, CH₂Cl₂-hexanes 1-1) to yield the desired 5-phenyl-15-(2-nitrophenyl)porphyrin
17 (second product eluted) as purple crystals after recrystallization for CH₂Cl₂-hexanes (148 mg, 0.29
mmol, 21%).

¹H-NMR (400 MHz, Chloroform-d) δ 10.31 (s, 2H), 9.38 (d, J = 4.6 Hz, 4H), 9.07 (d, J = 4.6 Hz, 2H), 8.87 (d,
J = 4.6 Hz, 2H), 8.56 – 8.41 (m, 1H), 8.35 – 8.28 (m, 1H), 8.28 – 8.19 (m, 1H), 8.09 – 7.91 (m, 2H), 7.88 –
7.76 (m, 3H), -3.10 (s, 2H).

MS (MALDI-TOF, positive) calcd for C₃₂H₂₁N₅O₂ [M⁺] m/z(100%) 507.17, found m/z(100%) 507.31.

Synthesis of 5-phenyl-15-(2-aminophenyl)porphyrin 16

Metallation:

In a 100 mL round bottom flask, 5-phenyl-15-(2-nitrophenyl)porphyrin 17 (45 mg, 89 μmol) was dissolved
in CH₂Cl₂-MeOH 2-1 (40 mL); zinc acetate dihydrate (250 mg, 1.1 mmol) was added and the mixture was
stirred at room temperature for 10 hours. The mixture was washed with water (3 x 50 mL), the organic
layer was collected, dried over Na₂SO₄, filtered and the solvent was evaporated. The resulting material
was used without further purification in the following step.

Reduction of the nitro group:

A 25 mL three-neck flask equipped with a 10 mL addition funnel was charged with the zinc porphyrin,
zinc powder (50 mg, 0.74 mmol) and a mixture of CH₂Cl₂-THF 1-1 (10 mL). The slurry was sparged with
argon for 5 minutes before a solution of 10% acetic acid in CH₂Cl₂ (7 mL) was added dropwise over a
period of 30 minutes. After the end of the addition the mixture was further stirred at room temperature
under argon. The progression of the reaction was followed by TLC analysis (SiO₂, CH₂Cl₂), when no
starting material remained (~ 45 minutes stirring at room temperature) the remaining zinc powder was
removed by filtration and the mixture was diluted to 50 mL with CH₂Cl₂. The organic phase was extracted
with a 5% aqueous NaHCO₃ solution (2 x 100 mL), and water (1 x 100 mL). The organic layer was
collected, dried over Na₂SO₄, filtered and the solvent was evaporated under reduced pressure.

Demetallation:

Due to the poor solubility of the resulting material the crude zinc-5-phenyl-15-(2-aminophenyl)porphyrin
was demetallated before purification. The crude product obtained from the precedent step was partly
solubilized in CH₂Cl₂ (20 mL) and trifluoroacetic acid (0.5 mL) was added. The mixture was stirred at room
temperature for 5 minutes, transferred into a separatory funnel and washed with water (1 x 50 mL), 5%
aqueous NaHCO₃ solution (2 x 50 mL) and again water (1 x 50 mL). The organic layer was collected, dried over Na₂SO₄, filtered and the solvent was evaporated. Column chromatography (SiO₂, CH₂Cl₂-10% hexanes) followed by recrystallization from CH₂Cl₂-1% MeOH/hexanes yielded the desired 5-phenyl-15-(2-aminophenyl)porphyrin (third compound eluted) as bright purple needles (36.6 mg, 77 μmol, 86%).

³¹H-NMR (400 MHz, Chloroform-d) δ 10.30 (s, 2H), 9.39 (d, J = 4.6, 4H), 9.10 (d, J = 4.6 Hz, 2H), 9.08 (d, J = 4.6 Hz, 2H), 8.34 – 8.27 (m, 1H), 8.27 – 8.20 (m, 1H), 7.93 (dd, J = 7.4, 1.5 Hz, 1H), 7.85 – 7.76 (m, 3H), 7.64 (td, J = 7.8, 1.6 Hz, 1H), 7.22 (td, J = 7.2, 1.5 Hz, 1H), 3.58 (s, 2H), -3.12 (s, 2H).

MS (MALDI-TOF, positive) calcd for C₃₂H₂₃N₅ [M⁺] m/z (100%) 477.20, found m/z (100%) 477.40.

Synthesis of 5-phenyl-15-(2-(2-chloroacethylaminophenyl))porphyrin zinc(II) complex 15

In a 50 mL round bottom flask, 5-phenyl-15-(2-aminophenyl)porphyrin (33 mg, 70.3 μmol) was dissolved in CH₂Cl₂ (10 mL). Potassium carbonate (120 mg, 87 mmol) was added and the slurry was sparged with argon for 5 minutes. The mixture was cooled to 0 °C under argon and 2-chloroacetyl chloride (9.8 μL, 13.9 mg, 0.12 mmol) was added. The mixture was stirred at 0 °C, under argon, for 5 minutes then allowed to warm up to room temperature. The progression of the reaction was followed by TLC analysis (SiO₂, CH₂Cl₂). After 30 minutes no starting material remained, the reaction mixture was diluted to 50 mL with CH₂Cl₂, and was transferred to a separatory funnel. It was washed with 5% aqueous NaHCO₃ (2 x 50 mL) and water (1 x 50 mL) the organic layer was collected, dried over Na₂SO₄, filtered and the solvent was evaporated under reduced pressure. The crude residue was filtered through a silica short plug (SiO₂, CH₂Cl₂) the eluted product was recrystallized from CH₂Cl₂-hexanes to yield the desired 5-phenyl-15-(2-(2-chloroacethyl)aminophenyl)porphyrin as deep purple crystals (37 mg, 67 μmol, 95 %). This compound was metallated before further characterization.

Metallation:

The porphyrin (37 mg, 67 μmol) was dissolved in DMF (10 mL) and zinc acetate (44 mg, 0.2 mmol) was added. The mixture was stirred at 45 °C for 1 hour after which time no starting material remained according to TLC analysis (SiO₂, CH₂Cl₂-1% MeOH). The mixture was poured into 100 mL of water and the solid filtered. It was further washed with water (100 mL) then dissolved in CH₂Cl₂-1% MeOH (50 mL). The solution was extracted with water (3 x 50 mL), dried over Na₂SO₄, filtered and the solvent was evaporated. The crude solid was filtered over a silica short plug (SiO₂, CH₂Cl₂-1% MeOH) CH₂Cl₂ 1% MeOH-hexanes to yield the desired porphyrin as bright purple crystals (38 mg, 62 μmol, 92 %).

³¹H-NMR (500 MHz, Chloroform-d) δ 10.35 (s, 2H), 9.48 – 9.44 (m, 4H), 9.16 (d, J = 4.4 Hz, 2H), 9.02 (d, J = 4.4 Hz, 2H), 8.67 (dd, J = 8.5, 1.2 Hz, 1H), 8.30 – 8.26 (m, 1H), 8.26 – 8.20 (m, 1H), 8.13 (dd, J = 7.5, 1.6 Hz, 1H), 8.12 (br. s, 1H), 7.87 (ddd, J = 8.7, 7.7, 1.6 Hz, 1H), 7.85 – 7.74 (m, 3H), 7.61 (td, J = 7.5, 1.3 Hz, 1H), 3.27 (s, 2H).

MS (MALDI-TOF, positive) calcd for C₃₄H₂₂Cl₂N₅OZn [M⁺] m/z (100%) 615.08, found m/z (100%) 615.38.
Synthesis of R2

A three-neck 50 mL round bottom flask equipped with a reflux condenser was charged with 5-phenyl-15-(2-(2-chloroacethyl)aminophenyl)porphyrin (37 mg, 67 μmol), 4-aza-18-crown-6 (106 mg, 0.40 mmol) and ethanol (20 mL). The mixture was sparged with argon for 10 minutes and then stirred under argon, under vigorous reflux. The progression of the reaction was followed by analytical TLC (SiO\(_2\), CH\(_2\)Cl\(_2\)-10% acetone). After 48 hours only trace amount of starting material remained, the reaction mixture was cooled down to room temperature and the solvent evaporated under reduced pressure. The crude residue was dissolved in CH\(_2\)Cl\(_2\) (50 mL) and extracted with water (3 x 100 mL). The organic layer was collected, dried over Na\(_2\)SO\(_4\), filtered and the solvent was evaporated under reduced pressure. Column chromatography (SiO\(_2\), eluting gradient: CH\(_2\)Cl\(_2\)-10% acetone to CH\(_2\)Cl\(_2\)-30% acetone 0.5% triethylamine). The compound was obtained in several fraction of increasing polarity. \(^1\)H NMR analysis indicated the presence of increasing amounts of triethylammonoium salts in the fractions. The combined fractions were treated with 0.5% aqueous citric acid solution (1 x 100 mL), EDTA aqueous solution (pH 9) (1 x 100 mL) and water (2 x 100 mL). The organic layer was collected dried over Na\(_2\)SO\(_4\), filtered and the solvent was evaporated. Recrystallization from CH\(_2\)Cl\(_2\)-hexanes yielded the desired compound as small violet needles (55 mg, 65 μmol, 97%).

\(^1\)H-NMR (500 MHz, DMSO-\(d_6\)) \(\delta\) 10.40 (s, 2H), 9.51 (dd, \(J = 4.4, 4.0\) Hz, 2H), 9.02 – 8.88 (m, 3H), 8.86 – 8.76 (m, 3H), 8.35 – 8.25 (m, 1H), 8.16 – 8.10 (m, 1H), 8.06 (dd, \(J = 7.4, 1.5\) Hz, 1H), 7.92 – 7.82 (m, 4H), 7.56 (td, \(J = 7.5, 1.3\) Hz, 1H), 2.48 – 2.44 (m, 4H), 2.43 (s, 2H), 2.19 – 2.06 (m, 4H), 1.58 – 1.48 (m, 4H), 0.76 – 0.70 (m, 4H), 0.68 (t, \(J = 5.9\) Hz, 4H), 0.05 (t, \(J = 5.8\) Hz, 4H).

MS (MALDI-TOF, positive) calcd for C\(_{46}\)H\(_{46}\)N\(_6\)O\(_6\)Zn [M\(^+\)] \(m/z\) (100%) 842.28, found \(m/z\) (100%) 842.62.

HRMS (ESI-TOF, positive) calcd for C\(_{46}\)H\(_{47}\)N\(_6\)O\(_6\)Zn [M + H\(^+\)] \(m/z\) (100%) 843.2849, found \(m/z\) (100%) 843.3881.

Synthesis of R1

In a 25 mL round bottom flask, porphyrin 11a (15 mg, 19.8 μmol) was dissolved in tetrahydrofuran-20 % methanol mixture (5 mL) and the solution was sparged with argon for 15 minutes. Aqueous potassium hydroxide (1 M solution in MeOH-H\(_2\)O 1-1, 1 mL) was added and the mixture was stirred at room temperature under argon. The progression of the reaction was followed by TLC analysis (SiO\(_2\), EtOAc-Acetone-H\(_2\)O 10-9-1); after 1 hour at room temperature the hydrolysis was complete. The reaction mixture was poured into saturated aqueous NH\(_4\)Cl solution (50 mL) and the aqueous layer was extracted with EtOAc-10% MeOH, until most of the porphyrin was recovered (5 x 25 mL). The combined organic layer was died over Na\(_2\)SO\(_4\) filtered and the solvent was evaporated to yield the desired R1 as a purple powder (7.8 mg, 10.7 μmol, 54%).

Note due to the high water-solubility of the target compound and the small quantity of the starting material used losses during the work up of the reaction explain the low yield of material isolated after saponification. The compound was particularly insoluble in most organic solvent and required the addition of a base to reach an acceptable concentration for \(^1\)H-NMR studies.
$^1$H-NMR (400 MHz, Methanol-$d_4$ - 5% Pyridine-$d_5$) δ 10.20 (s, 2H), 9.38 (d, $J = 4.5$ Hz, 4H), 8.98 (d, $J = 4.4$ Hz, 2H), 8.89 (d, $J = 4.4$ Hz, 2H), 8.50 (d, $J = 8.6$ Hz, 1H), 8.35 – 8.28 (m, 1H), 8.28 – 8.21 (m, 1H), 8.13 – 8.03 (m, 2H), 7.98 (d, $J = 7.3$ Hz, 1H), 7.96 – 7.84 (m, 2H), 2.95 (s, 2H).

Note: the signals of the CH$_2$ – carboxylic acids are missing probably due to slow exchange. The acidic protons are not expected to be observed in these conditions.

$^1$H-NMR (500 MHz, DMSO-$d_6$ - 5% Pyridine-$d_5$) δ 10.31 (s, 2H), 9.48 (d, $J = 4.4$ Hz, 2H), 9.44 (d, $J = 4.4$ Hz, 2H), 8.85 (d, $J = 4.4$ Hz, 2H), 8.82 (d, $J = 4.4$ Hz, 2H), 8.55 – 8.50 (m, 1H), 8.45 – 8.38 (m, 1H), 8.19 (d, $J = 7.4$, 1H), 8.18 – 8.12 (m, 2H), 7.92 (td, $J = 7.8$, 1.3 Hz, 1H), 7.86 (td, $J = 7.5$, 1.5 Hz, 1H), 7.82 – 7.76 (m, 1H), 3.99 (br. s, 2H), 2.79 (s, 2H).
2 $^1$H NMR analysis

2.1 Determination of the ratio of 1a-OMe/1b-OMe

Figure S1. Selected area of the 1HNMR spectra of the mixture of the atropisomers 1a-OMe and 1b-OMe obtained directly after the Suzuki coupling reaction. The arrow indicates the signals corresponding to the minor isomer (1a-OMe). A ratio of 1/8 was estimated from the integration of the meso-signals of porphyrin rings (left most signals). Spectra recorded in CDCl$_3$, at 295 K, on a 400 MHz spectrometer.
2.2 Comparison of the $^1$H NMR spectra of 1a isolated after hydrolysis of 1a-OMe/1b-OMe mixture and of 1a obtained after thermal equilibration of 1b in presence of NaBPh$_4$

A) Figure S2. Qualitative comparison of the $^1$H NMR spectra of ligand 1a obtained after hydrolysis and purification of the methyl ester precursors mixture (1a-OMe and 1b-OMe 1/8 mixture, top), and of the product obtained after annealing 1b in pyridine at 90 °C in the presence of sodium tetraphenylborate (bottom). Spectra recorded in CDCl$_3$, at 295 K, on a 400 MHz spectrometer. Note the perfect matching between the spectra. Aromatic region (A) and aliphatic region (B).
2.3 Assignments of the conformations of ligands 1a and 1b

As shown in the following the $^1$H-NMR spectra of ligands 1a and 1b in deuterated chloroform (CDCl$_3$) are distinct, both in the aromatic and the aliphatic regions (see Figures S4 and S5). The most striking differences are observed for the signals associated with the crown ether moieties (HCr) and with the protons of the methylene groups (CH$_2$/CH$_2'$) which link the crown ether to the porphyrin macrocycle. In the case of ligand 1a the signals associated with the crown ether substituent form a well resolved series of peaks spread over a large range of chemical shifts (between -1 ppm and 4 ppm). The signals of the methylene bridges appear as two doublets centered at 2.6 ppm and 2.8 ppm. In contrast, for 1b the signals of the crown ether moiety form a broad massif that extends over a narrower range of chemical shifts (from ca. 0 ppm to 2 ppm) and presents only two major features, centered at 1.6 ppm and 1.4 ppm. Moreover, the signals associated with the methylene bridges appear as a sharp singlet centered at 2.6 ppm. These observations led us to the assignment of 1b to the trans atropisomer and 1a to the cis atropisomer. For the latter, the orientation of the carboxylic acid towards the crown ether strap permits the development of an internal hydrogen bond and locks the structure into a well-defined conformation. On the contrary, in the case of the trans atropisomer, the orientation of the carboxylic acid towards the opposite face of the porphyrin does not permit stabilization of any specific conformation of the strap and thus results in the observation of a much less resolved set of signals. The formation of an internal hydrogen bond in 1a is supported by the observation that the addition of deuterated methanol (MeOD) leads to the partial loss of the strongly unsymmetrical signal pattern observed in pure CDCl$_3$ and to the coalescence of the strap signals into broad massifs reminiscent of the signals observed for 1b (cf. section 2.4).

Assignment of the $^1$H NMR signals for 1a

![Scheme 5. Schematic representation of 1a and protons numbering](image)

$^1$H NMR (500 MHz, Chloroform-d) δ 10.21 (s, 1H, Hm), 9.41 (s, 2H, NH), 9.33 (d, J = 4.6 Hz, 2H, Ha), 8.95 (d, J = 4.6 Hz, 2H, Hb), 8.85 (d, J = 4.7 Hz, 2H, Hc), 8.77 (d, J = 8.0 Hz, 2H, ar4), 8.75 (d, J = 4.7 Hz, 2H, Hd), 8.50 (d, J = 8.0 Hz, 1H, ar5), 7.97 (d, J = 8.0 Hz, 2H, ar1), 7.96 – 7.89 (m, 2H, ar6,8), 7.86 – 7.84 (m, 2H, ar3), 7.79 – 7.77 (m, 1H, ar7), 7.53 – 7.51 (m, 2H, ar2), 3.23 – 3.04 (m, 2H, HCr), 2.89 – 2.85 (m, 2H, HCr), 2.81 (d, J = 17.4 Hz, 2H, CH2), 2.80 – 2.74 (m, 2H, HCr), 2.68 – 2.64 (m, 2H, HCr), 2.55 (d, J = 17.4 Hz, 2H, CH2), 1.37 – 1.32 (m, 4H, HCr), 1.28 – 1.21 (m, 2H, HCr), 0.86 – 0.76 (m, 2H, HCr), 0.70 – 0.65 (m, 2H, HCr), 0.63 – 0.58 (m, 2H, HCr), -0.21 – 0.17 (m, 2H, HCr), -0.92 – -0.87 (m, 2H, HCr), -2.82 (s, 2H, NHPor).
Note: the aromatic protons could be assigned using the careful analysis of COSY and ROESY spectra; chemical exchange and weak NOE signals impeded the full attribution of the aliphatic signals (crown-ether).

Figure S3. Principal Nuclear Overhauser Effect (NOE) contacts observed for ligand 1a (aromatic region).

Assignment of $^1$H NMR signals for 1b

Scheme 6. Schematic representation of 1a and protons numbering

$^1$H NMR (400 MHz, Chloroform-d$_2$) $\delta$ 10.14 (s, 1H, Hm), 9.28 (d, $J = 4.7$ Hz, 2H, Ha), 8.97 – 8.92 (m, 3H, Hb, NH), 8.78 (d, $J = 4.8$ Hz, 2H, Hc), 8.69 – 8.57 (m, 4H. Hd, ar4), 8.28 (m, 2H, ar5, ar8), 7.99 (d, $J = 7.4$ Hz, 2H, ar1), 7.90 – 7.80 (m, 4H, ar6, ar7, ar3), 7.54 – 7.49 (m, 2H, ar2), 2.58 (s, 4H, CH2), 2.04 – 0.4 (br.m, 24H, HCr), -2.86 (s, 2H, NHPor).

-due to the overlapping signals the full attribution of the aromatic protons could not be conducted; the attribution is proposed based on the analysis of the spectra of 1a and assuming minor shifting of the aromatic peaks between the two atropisomers-
Figure S4. Comparison of the aromatic protons signals of the ligands 1a (top) and 1b (bottom) in CDCl₃, at 295 K. ¹H NMR spectra recorded on a 400 MHz spectrometer. Due to the overlapping signals the full attribution of the aromatic protons of the spectra of 1b could not be conducted; the attribution is proposed based on the analysis of the spectra of 1a, assuming minor shifting of the signals. Differences in the spectra are however evident.
Figure S5. Comparison of the aliphatic protons signals of ligands 1a (top) and 1b (bottom) in CDCl$_3$, at 295 K. $^1$H NMR spectra recorded on a 400 MHz spectrometer. Due to the broadness of the crown ether signals only weak NOE contacts could be observed in the ROESY spectra. The analysis was further complicated by chemical exchange between the crown ether signals and thus, did not permit the unambiguous assignment of all crown ether signals in the case of 1a. However the presence of a well-defined set of signals as compared to the wide massif observed for 1b points towards a much slower dynamical exchange of the crown ether protons, ie. a more rigid structure of 1a in solution.
2.4 Effect of the addition of MeOD on the $^1$H NMR spectra of 1a

**Figure S6.** Comparison the $^1$H NMR spectra (aliphatic region) of ligand 1a recorded in the presence (top) or absence (bottom) of MeOD, in CDCl$_3$, at 295 K. Spectra recorded on a 400 MHz spectrometer. Signals belonging to the crown ether moiety are indicated with orange arrows. Note the coalescence of the individual signals of the crown ether into broad massifs upon addition of methanol.
2.5 Assignments of the conformations of ligands 2a and 2b

The assignments of the conformations of ligands 2a and 2b were supported by a careful analysis of their respective $^1$H-NMR spectra in deuterated dimethylsulfoxide (DMSO-$d_6$). As shown in the following, both the aromatic and the aliphatic regions of the spectra exhibit distinct patterns for the two ligands (Figures S17 and S18). More specifically, in the aliphatic region, the signals of the crown ether (HCr1-HCr6) are generally shifted more up-field for 2b than for 2a, suggesting a stronger influence of the ring-current of the porphyrin macrocycle, i.e., a generally closer proximity of the crown ether to the porphyrin plane for 2b than for 2a. In the absence of notable differences observed for the signals of the protons of the carboxylic acids functionalities of 2a and 2b (Figure S17), the differences noticed for the chemical shifts of the protons belonging to the crown ether moiety can be simply attributed to the steric effects associated with the orientation of the substituents with respect to each other; we thus can attribute 2b to the trans atropisomer and 2a to the cis atropisomer. To further support this attribution, we note the presence of an identical pattern for the crown ether signals in the $^1$H-NMR spectrum of 2b and that of the reference ligand R2. The latter does not bear the carboxylic acid functionalities and thus the crown ether moiety experiences minimal steric crowding as expected for the trans-atropisomer (cf. section 2.6). Furthermore, the observation of a clear nuclear Overhauser effect (NOE) indicating contacts between the crown ether and the opposite phenyl substituent in the case of 2b (Figure S16), as well as weak NOE effects indicating contacts between the crown ether substituent and a methyl group of the dicarboxylic acid substituent in the case of ligand 2a (Figure S10), confirm our assignments.

Assignment of the $^1$H NMR spectrum of 2a

\[ \text{Scheme 7. Schematic representation of 2a and protons numbering.} \]

$^1$H NMR (500 MHz, DMSO-$d_6$ 1% Pyridine-$d_5$) δ 18.1 (br s, 2H, COOH) 10.31 (s, 2H, Hm), 9.46 (d, J = 4.4 Hz, 2H, Hb), 9.43 (d, J = 4.4 Hz, 2H, Hc), 9.18 (s, 1H, NH), 8.86 (d, J = 4.4 Hz, 2H, Hd), 8.79 (d, J = 4.5 Hz, 2H, Ha), 8.66 (d, J = 8.4 Hz, 1H, ar4), 8.02 (d, J = 7.4 Hz, 1H, ar8), 7.95 (d, J = 7.4, 1H, ar1), 7.92 – 7.86 (m, 1H, ar6), 7.87 –7.83 (m, 1H, ar3), 7.83 – 7.77 (m, 1H, ar7), 7.76 (d, J = 7.8 Hz, 1H, ar5), 7.56 – 7.52 (m, 1H, ar2), 2.83 (br s, 4H, HCr6), 2.73 (br s, 2H, CH2b/b’), 2.48 (s, 2H, CH2a), 2.40 (br s, 4H, HCr5), 1.66 (br s, 4H, HCr4), 1.52 (br s, 4H, HCr3), 1.02 (br s, 4H, HCr1), 0.88 (br s, 4H, HCr2)
The spectra were recorded in DMSO-d$_6$ containing 1% of deuterated pyridine, with presaturation of the water signal at 1 db. The addition of pyridine permits to reach a higher concentration of the ligand, which was required for ROESY experiments. The presence of pyridine lead to noticeable shifts of the proton signal of the ligands (see below) due to coordination to the zinc. It led to a better resolved spectra (slightly less overlapping signals). See below for the comparison of the spectra of 2a in presence or absence of pyridine. Importantly the assignment obtained in the presence of pyridine could be used to assign the spectra of 2a in pure DMSO as well.

**Note:** the signature of 2 CH$_2$ protons associated with the carboxylic arms (CH$_2$b/b’) are not visible on the spectra, as mentioned in the experimental part, these signals associated with these protons experience important broadening effects probably to restricted structural relaxation of the system.

**Figure S7.** Shifting of the aromatic signals of the $^1$HNMR spectrum of ligand 2a upon addition of pyridine.

**Figure S8.** Shifting of the aliphatic signals of the $^1$HNMR spectrum of ligand 2a upon addition of pyridine.
Figure S9. Principal NOE contacts observed in the aromatic region of the \textsuperscript{1}HNMR spectrum of ligand 2a, recorded in DMSO-\textsubscript{d}6 – 1% pyridine-\textsubscript{d}5.

Figure S10. Principal NOE contacts observed in the aliphatic region the \textsuperscript{1}HNMR spectrum of ligand 2a, recorded in DMSO-\textsubscript{d}6 – 1% pyridine-\textsubscript{d}5.

Note the weak NOE contacts observed between CH2b’ (carboxylic acid arms) and HCr4/3 (crown ether substituent) confirming the attribution of this atropisomer to the cis-isomer (purple circles).
Figure S11. Aliphatic-aromatic NOE contacts observed in the $^1$HNMR spectrum of ligand 2a, recorded in DMSO-d$_6$ – 1% pyridine-d$_5$. 
Assignment of the $^1$H NMR spectrum of 2b

![Scheme 8. Schematic representation of 2b and protons numbering.](image)

$^1$H NMR (500 MHz, DMSO-$d_6$) $\delta$ 18.3 (br s, 2H, COOH), 10.34 (s, 2H, Hm), 9.47 (d, $J = 4.4$ Hz, 2H, Hb), 9.44 (d, $J = 4.4$ Hz, 2H, Hc), 8.92 (s, 1H, NH), 8.84 (d, $J = 4.4$ Hz, 2H, Hd), 8.78 – 8.75 (m, 1H, ar4), 8.76 (d, $J = 4.6$ Hz, 2H, Ha), 8.04 (dd, $J = 7.5$, 1.6 Hz, 1H, ar1), 8.00 (d, $J = 7.4$ Hz, 1H, ar8), 7.90 – 7.87 (m, 1H, ar6), 7.87 – 7.84 (m, 1H, ar3), 7.83 – 7.80 (m, 1H, ar7), 7.73 (d, $J = 7.8$ Hz, 1H, ar5), 7.57 – 7.53 (m, 1H, ar2), 3.80 (br s, 2H, CH2b/CH2b'), 2.66 (s, 2H, CH2b/CH2b'), 2.52 – 2.50 (m, 4H, HCr6), 2.41 (s, 2H, CH2a), 2.18 – 2.16 (b, 4H, HCr5), 1.56 – 1.55 (m, 4H, HCr4), 0.75 (br s, 4H, HCr3), 0.69 (br s, 4H, HCr1), 0.07 (br s, 4H, HCr2).

The spectra were recorded in DMSO-$d_6$ containing 1% of deuterated pyridine, with presaturation of the water signal at 1 db. The addition of pyridine permits to reach a higher concentration for the ligand, which was beneficial for ROESY experiments. At the concentration used, the presence of pyridine did not lead to major shifts in the $^1$H NMR spectrum (see below).

**Note:** the signature of 2 CH$_2$ protons associated with the carboxylic arms (CH$_2$b/b') are not visible on the spectra, as mentioned in the experimental part, these signals associated with these protons experience important broadening effects probably to restricted structural relaxation of the system.
Figure S12. Comparison between the aromatic region of the $^1$HNMR spectrum of ligand 2b in presence (top) or absence (bottom) of pyridine-$d_5$ in DMSO-$d_6$.

Figure S13. Comparison between the aliphatic region of the $^1$HNMR spectrum of ligand 2b in presence (top) or absence (bottom) of pyridine-$d_5$ in DMSO-$d_6$. 
Figure S14. Principal NOE contacts observed in the aromatic region of the $^1$HNMR spectrum of ligand 2b.

Figure S15. Principal NOE contacts observed in the aliphatic region of the $^1$HNMR spectrum of ligand 2b.
Figure S16. Aliphatic-aromatic NOE contacts observed in the $^1$HNMR spectrum of ligand 2b.
Comparison between the $^1$H NMR spectra of compounds 2a and 2b in DMSO-d$_6$

Figure S17. Comparison between the aromatic regions of the $^1$H NMR spectra of ligands 2a (top) and 2b (bottom) in DMSO-d$_6$, at 295 K. Spectra recorded on a 500 MHz spectrometer.
Figure S18. Comparison between the aliphatic regions of the $^1$H NMR spectra of ligands 2a (top) and 2b (bottom) in DMSO-$d_6$, at 295 K. Spectra recorded on a 500 MHz spectrometer.
2.6 $^1$H NMR spectra of 2a, 2b, and R2 in DMSO-d$_6$

**Figure S19.** Selected area of the $^1$H NMR spectra of ligands 2a (top) and 2b (middle) and R2 (bottom) in DMSO-d$_6$, at 295 K. Spectra recorded on a 500 MHz spectrometer. The attribution of the crown ether signals is proposed based on the analysis of 2D $^1$HNMR GCOSY and ROESY spectra of the ligands. Note the close matching between the chemical shifting of the signals of the crown ether substituents of ligand 2b and R2.
2.7 Titration of ligand 1a with Ca\(^{2+}\)

Spectra recorded for 2 mM solutions of the ligands in DMSO-\(d_6\) - 5% pyridine-\(d_5\) at 298 K. Bottom spectra: free ligand (2 mM), subsequent spectra recorded after the addition of 1 to 50 equivalents of CaCl\(_2\). Note the slight broadening and shifting of the signals at high calcium concentration but generally minor effect of the salts at low concentration. The starred signals correspond to protons belonging to the pyridine.

Aromatic region

**Figure S20.** Evolution of the aromatic signals of the \(^1\)H NMR spectra of 1a upon addition of Ca\(^{2+}\).

**Figure S21.** Evolution of the aliphatic signals of the \(^1\)H NMR spectra of 1a upon addition of Ca\(^{2+}\).
2.8 Titration of ligand 2a with Ca^{2+}

Figure S22. Effect of the addition of Ca^{2+} on the ^1H NMR spectra of 2a. Spectra recorded for 2 mM solutions of the ligand in MeOD - 5% diisopropylamine (DIPEA) at 298 K. Top spectra: free ligand (2 mM), subsequent spectra recorded after the addition of 0.1 to 20 equivalents of CaCl_{2}. Note the gradual broadening and shifting of the signals upon addition of calcium. The aliphatic area is not shown for simplicity. The attribution of the signals was done with the help of GCOSY and ROESY correlations obtained for the free ligand. The starred massif of peaks correspond to the overlay of ar3, ar5 and ar7 signals (see above for numbering of the signals).
2.9 Titration of ligand 2b with Ca\(^{2+}\)

Figure S23. Effect of the addition of Ca\(^{2+}\) on the \(^1\text{H}\) NMR spectra of 2b. Spectra recorded for 2 mM solutions of the ligand in MeOD - 5% diisopropylamine (DIPEA) at 298 K. Top spectra: free ligand (2 mM), subsequent spectra recorded after the addition of 0.1 to 20 equivalents of CaCl\(_2\). Note the rapid broadening of the signals upon addition of calcium and refining of the spectra at high calcium concentration. The aliphatic area is not shown for simplicity. The attribution of the signals was done with the help of GCOSY and ROESY correlations obtained for the free ligand. The starred massif of peaks correspond to the overlay of ar3, ar6 and ar7 signals (see above for numbering of the signals).
2.10 $^1$H COSY spectrum of 2a in the presence of excess Ca$^{2+}$

Figure S24. GCOSY correlation spectrum of 2a in the presence of 5 equivalents of Ca$^{2+}$. Selected region of the GCOSY spectra of a solution of ligand 2a (2 mM) in MeOD–5% DIPEA, in the presence of 5 equivalents of CaCl$_2$ (A). The clear J-J coupling pattern observed points towards the presence of a well-defined species in solution. Protons belonging to the same spin systems are indicated by the same color. Consecutive protons of each spin system are indicated by following indices.
2.11 $^1$H NMR spectra of $[2a{\subset}Ca^{2+}]$ complexes: effect of the concentration

Figure S25. Selected region of the $^1$H NMR spectra of a 2 mM solution of $2a$ in MeOD-5% DIPEA in absence (top) or presence of 5 equivalents of CaCl$_2$ (bottom). The middle spectrum was obtained from dilute solution of $2a$ (0.125 mM) in MeOD-5% DIPEA, in the presence of 1 equivalent of CaCl$_2$. Note the sharpness of the signals at lower concentration suggesting no or limited oligomerization of the ligand in these conditions. The presence of two well-defined meso signals and, corresponding sets of beta and aromatic protons, suggests the presence of two major species in slow equilibrium in these conditions. The shifting of all signals as compared to the free ligand (see arrow) suggests the presence complexed $[2a{\subset}Ca]$ species only in these conditions. The two sets of signals are thus tentatively attributed to two distinct modes of calcium binding by the ligand. Using the integration of the meso signals, the ratio between the two forms of complexed $[2a{\subset}Ca]$ species is estimated to be $[2a{\subset}Ca]/[2a{\subset}Ca'] \sim 2/3$. Further studies are required to fully characterize the two possible mode of calcium complexation within the ligands.
3 Fluorescence anisotropy decay analysis

3.1 General:

Time resolved fluorescence anisotropy measurements were performed with a time-correlated single photon counting (TC-SPC) system. The excitation source was a fiber supercontinuum laser based on a passive mode-locked fiber laser and a high-nonlinearity photonic crystal fiber supercontinuum generator (Fianium SC450). The laser provides 6 ps pulses at a repetition rate variable between 0.1 and 40 MHz. The laser output was sent through an Acousto-Optical Tunable Filter (Fianium AOTF) to obtain excitation pulses at the desired wavelength. Fluorescence emission was collected at 90° and detected using a double-grating monochromator (Jobin-Yvon, Gemini-180) and a microchannel plate photomultiplier tube (Hamamatsu R3809U-50). The polarization of the emission was horizontal or vertical relative to that of the excitation. Data acquisition was done using a single photon counting card (Becker-Hickl, SPC-830). The IRF had a FWHM of ~50 ps, measured from the scattering of sample at the excitation wavelength. The data was globally fitted as a sum of exponential decays including IRF deconvolution using locally written software (ASUFIT) developed in a MATLAB environment (Mathworks Inc.).

Time resolved fluorescence anisotropy were calculated as described elsewhere \[6\]. Setting a polarizer to obtain vertical polarization of the incident light, the fluorescence time resolved was recorded with a vertical or horizontal polarizer in front of the detector. Same procedure was realized with horizontal polarization of incident light. The anisotropy decay was calculated from the following equation \[4b\]:

\[
I(t) = \frac{I_H(t) - G \times I_V(t)}{I_H(t) + 2G \times I_V(t)}
\]

Equation S1

where \(I_H\) (or \(I_V\)) is the fluorescence decay when the excitation light is vertically polarized and only the vertical (or horizontal) polarization component of the emission light is detected, respectively. The \(G\) factor is defined by \(I_H(t)/I_V(t)\) which is equal to the ration of the sensitivities of the detection system for vertical and horizontal polarizations. It was determined for each set of measurements and was 1.04 ± 0.01 in our experimental setup.

The obtained anisotropy decay were then fitted using build-in Origin 8.5 fitting equation for single or multi-exponential decays using the following equation:

\[
r(t) = \sum_{i=1}^{l} r_i(0) \times \exp\left(\frac{-t}{\theta_i}\right)
\]

Equation S2

Rotational correlation times \(\theta\) and the anisotropy at time zero \(r_0\) were determined. The time of Brownian rotation of a molecule, \(\theta\), gives information on the hydrodynamic radius (R) by the Stokes–Einstein–Debye relation \[7\]:

\[
\theta^{-1} = \frac{6kT}{(8\pi\eta R^3)}
\]

Equation S3
where $k$ is the Boltzmann constant, $T$ the absolute temperature, and $\eta$ the viscosity. On the other hand, $r_o$ is related to the relative orientation of the excited- and fundamental state dipole moments of the particles.

### 3.2 Fluorescence anisotropy decay of the free ligand 2a

![Graph](image)

**Figure S26.** Fluorescence anisotropy decay of a 2 mM solution of ligand 2a in MeOH-5% DIPEA, observed at 298 K, in the absence of Ca$^{2+}$. The sample was excited at 590 nm and the emission was collected at 680 nm. Experimental data (open squares) and fitting curves (red lines). The parameters obtained from the fitting procedure are reported on the graph. A single-exponential decay was best describing the evolution of the fluorescence anisotropy decay.

* Fixed value.

**Figure S27.** Fluorescence anisotropy decays of 2 mM and 0.1 mM solutions of ligand 2a in MeOH-5% DIPEA, observed at 298 K in the absence of CaCl$_2$ (left and right panel, respectively). The samples were excited at 590 nm and the emission was collected at 680 nm. The fits were obtained using a fixed lifetime value of 370 ps. Experimental data (open squares) and fitting curves (red lines). The parameters obtained from the fitting procedure are reported on the graphs. A single-exponential decay was best describing the evolution of the fluorescence anisotropy decay in each case.
3.3 Fluorescence anisotropy decay of the free ligand 2b

**Figure S28.** Fluorescence anisotropy decays of a 2 mM solution of ligand 2b in MeOH-5% DIPEA, observed at 298 K, in the absence of CaCl$_2$. The sample was excited at 590 nm and the emission was collected at 680 nm. Experimental data (open squares) and fitting curves (red lines). The parameters obtained from the fitting procedure are reported on the graph. A single-exponential decay was best describing the evolution of the fluorescence anisotropy decay.

3.4 Fluorescence anisotropy decays of ligand 2a in the presence of Ca$^{2+}$

**0 to 0.1 equivalents**

**Figure S29.** Fluorescence anisotropy decays of a 2 mM solution of ligand 2a in MeOH-5% DIPEA, observed at 298 K, in the presence of 0 and 0.1 equivalents of CaCl$_2$ (left and right panel, respectively). The sample was excited at 590 nm and the emission was collected at 680 nm. Experimental data (open squares) and fitting curves (red lines). The parameters obtained from the fitting procedure are reported on the graphs. A single-exponential decay was the best fitting describing the evolution of the fluorescence anisotropy decay in each case.
**0.2 to 0.4 equivalents**

Figure S30. Fluorescence anisotropy decays of a 2 mM solution of ligand 2a in MeOH-5% DIPEA, observed at 298 K, in presence of 0.2 and 0.4 equivalents of CaCl₂ (left and right panel, respectively). Experimental data (open squares) and fitting curves (red lines). The sample was excited at 590 nm and the emission was collected at 680 nm. The parameters obtained from the fitting procedure are reported on the graphs. A single-exponential decay was the best fitting describing the evolution of the fluorescence anisotropy decay in each case.

**1 to 5 equivalents**

Figure S31. Fluorescence anisotropy decays of a 2 mM solution of ligand 2a in MeOH-5% DIPEA, observed at 298 K, in presence of 1 and 5 equivalents of CaCl₂ (left and right panel, respectively). The sample was excited at 590 nm and the emission was collected at 680 nm. Experimental data (open squares) and fitting curves (red lines). The parameters obtained from the fitting procedure are reported on the graphs. A bi-exponential decay was the best fitting describing the evolution of the fluorescence anisotropy decay in each case. The shortest component was fixed to 370 ps to account for the presence of monomeric porphyrin species in solution (see main text).
0 to 1 equivalents in diluted conditions

Figure S32. Fluorescence anisotropy decays of a 0.1 mM solution of ligand 2a in MeOH-5% DIPEA, observed at 298 K, in presence of 0 and 1 equivalents of CaCl₂ (left and right panels respectively). The sample was excited at 590 nm and the emission was collected at 680 nm. Experimental data (open squares) and fitting curves (red lines). The parameters obtained from the fitting procedure are reported on the graphs. A single-exponential decay was the best fitting describing the evolution of the fluorescence anisotropy decay in each case. A life-time of 370 ps described accurately each decay (see main text, footnote §).
3.5 Fluorescence anisotropy decays of ligand 2b in the presence of Ca$^{2+}$

1 to 20 equivalents

* Fixed value.

Figure S33. Fluorescence anisotropy decays of a 2m M solution of ligand 2b in MeOH-5% DIPEA, observed at 298 K, in presence of 1 and 20 equivalents of CaCl$_2$ (left and right panel, respectively). The sample was excited at 590 nm and the emission was collected at 680 nm. Experimental data (open squares) and fitting curves (red lines). The parameters obtained from the fitting procedure are reported on the graphs. A tri-exponential decay was best describing the evolution of the fluorescence anisotropy decay in each case. Top panels: one component was fixed to 480 ps to account for the presence of monomeric porphyrin species in solution (see main text). Bottom panels: fitting obtained while letting all the parameters freely floating. Note the good agreement between the values of the components observed by constraining one component to 480 ps and by letting all the components floating during the fitting process.
4 Uv-visible spectroscopy

4.1 General

UV–Visible spectroscopy was performed using a Shimadzu UV-2550 UV–Visible spectrophotometer, using quartz cuvettes with an optical path of 1 cm. The solvents used were of spectroscopic grade and used as received. During the titrations the concentration of the porphyrin ligands was kept constant by the addition of concentrated CaCl$_2$ aliquots containing the ligand in the appropriate concentration. During the titration, the cell was kept in its original position, without removing it from the cell holder. The concentrated calcium aliquots were added with the use of glass micro-syringe and the solution mechanically stirred to permit complete equilibration of the systems before measurement were taken. All the titrations were conducted in a mixture of methanol containing 5 % (v/v) of diisopropylethylamine, at 298 K. The spectral resolution of the spectrophotometer was set-up to 0.1 nm; standard deviation on the wavelength values is ± 0.1nm (manufacturer specifications).

The association constants were estimated using a global fitting procedure using the build-in equation solving module of Origin 8.5.

In all cases we suppose the establishment of a 1:1 equilibrium in solution during the titration (see main text):

\[ [L] + [Ca] \leftrightarrow [L\subset Ca] \]  \hspace{1cm} \text{Equation S4}

From this assumption and we can derive the classical expression to fit the evolution of the spectra at any given wavelength:

\[
Abs([Ca]_T) = A_i - A_f \times \frac{[L]_0 - [Ca]_T}{[L]_0 - [Ca]_T - \frac{1}{K_a}} + \sqrt{\left([Ca]_T - [L]_0 + \frac{1}{K_a}\right)^2 + 4 \times \frac{[L]_0}{K_a}} + A_f \]  \hspace{1cm} \text{Equation S5}

where \( Abs([Ca]_T) \) is the experimentally measured absorbance after adding the desired calcium concentration, \([Ca]_T\), the total concentration of calcium added, \(A_i\) the initial absorbance of the porphyrin solution at the wavelength considered, \(A_f\) the final absorbance of the porphyrin solution at the wavelength considered, \([L]_0\) the total concentration of the porphyrin ligand, and \(K_a\) the association constant of the equilibrium considered, with:

\[
K_a = \frac{[L \subset Ca]}{[L][Ca]} \]  \hspace{1cm} \text{Equation S6}

Where \([L \subset Ca]\) represents the concentration of the complexed species in solution, \([Ca]\), the concentration of the remaining free calcium in solution and \([L]\) the concentration of the remaining free ligand in solution.
4.2 Titration of ligand 2a with Ca$^{2+}$

High concentration

**Figure S34.** Evolution of the UV-Visible absorption spectra of 2a upon addition of CaCl$_2$. Solution of 2a at 5 µM in MeOH-5% DPEA. Addition of 0 to 100 equivalents of Ca$^{2+}$. Full range spectra (A), details of the Soret band (B) and of the Q bands evolution (C) upon addition of 0 to 100 eq of Ca$^{2+}$. 
**Low concentration**

**Figure S35.** Evolution of the UV-Visible absorption spectrum of ligand 2a (1 μM) upon the addition of 0 to 4.5 equivalents of CaCl$_2$; between 0 (black line) and 4 equivalents of CaCl$_2$ (blue line), every step correspond to the addition of 0.2 equivalents of CaCl$_2$. General evolution (A), detailed view (B) note the presence of a clear isobestic point. To determine the association constant $K_a$ of the equilibrium, the evolution of the absorption of 2a (1 μM) upon titration with 0 to 4.5 equivalents of CaCl$_2$ was followed at 412.3 nm (black circles) and 412.8 nm (red circles). The graph (C) shows the mean values of the absorbance obtained from 2 distinct measurements; the respective standard deviation are indicated by the vertical bars. Using Equation S4 and applying a global fitting procedure permitted to estimate $K_a$. 

$$K_a = 2.4 \pm 0.2 \times 10^6 \text{M}^{-1}$$

$$R^2 = 0.9999$$
4.3 Titration of ligand R1 with Ca\(^{2+}\)

**Figure S36.** Evolution of the UV-Visible absorption spectrum of R1 (2.5 μM) over time after the addition of 15 equivalents of Calcium. Spectra taken directly after the addition of calcium (black) then after five (blue), ten (grey), twenty (green) and sixty minutes (purple). Note the gradual decrease and broadening of the absorption spectra over time. The evolution of the spectra over time is most likely due to the calcium-induced aggregation of the ligand.
4.4 Titration of ligand R2 with $\text{Ca}^{2+}$

Figure S37. Evolution of the UV-Visible absorption spectra of R2 (2.5 $\mu$M) upon addition of CaCl$_2$. Addition of 0 (black line) to 180 eq of CaCl$_2$ (blue line). Soret band (A), details of the spectra highlighting the presence of an isobestic point (B). To determine the association constant $K_a$ of the equilibrium, the absorption of R2 (2.5 $\mu$M) upon titration with 0 to 180 equivalents of CaCl$_2$ was followed at 411.0 nm (black squares) and 411.3 nm (red squares) (C). The association constant was estimated using a global fitting procedure and Equation S4. We suppose the establishment of a 1:1 equilibrium in solution during the titration (see main text).
4.5 Titration of ligand 8b with Ca$^{2+}$

**Figure S38.** Evolution of the UV-Visible absorption spectra of 8a (2.5 μM) upon addition of CaCl$_2$. Addition of 0 (black line) to 250 eq of CaCl$_2$ (blue line). Soret band (A), details of the spectra highlighting the presence of an isobestic point (B). To determine the association constant $K_a$ of the equilibrium, the absorption of R2 (2.5 μM) upon titration with the addition of 0 to 250 equivalents of CaCl$_2$ followed at 411.9 nm (black squares) and 411.8 nm (red squares). (C). The association constant was estimated using a global fitting procedure and Equation S4. We suppose the establishment of a 1:1 equilibrium in solution during the titration (see main text).
**5 $^1$H NMR spectra**

5.1 $^1$H NMR spectra of 5,15-bis-(2-nitrophenyl)porphyrin mixture in CDCl$_3$

Residual signals: residual CHCl$_3$ (7.26 ppm); residual H$_2$O (1.54); adventitious aliphatic grease (1.25, 0.88)
5.2 $^1$H NMR spectra of αβ-5,15-bis-(2-aminophenyl)porphyrin in CDCl$_3$

Residual signals: residual CHCl$_3$ (7.26 ppm); residual H$_2$O (1.52)
5.3 $^1$H NMR spectra of αα-5,15-bis-(2-aminophenyl)porphyrin in CDCl$_3$

Residual signals: residual CHCl$_3$ (7.26 ppm); residual H$_2$O (1.51)
5.4 $^1$H NMR spectra of αα-5,15-bis-(2-(2-chloroacetyl)aminophenyl)porphyrin in CDCl$_3$

Residual signals: residual CHCl$_3$(7.26 ppm); residual acetone (2.17 ppm); residual H$_2$O (1.52)
5.5 $^1$H NMR spectra of αα-5,15-bis-(2-(2-chloroacethyl)aminophenyl)-10-bromoporphyrin 4 in CDCl$_3$

Residual signals: residual CHCl$_3$ (7.26 ppm); residual CH$_2$Cl$_2$ (5.30 ppm); residual acetone (2.17 ppm); residual H$_2$O (1.51); adventitious aliphatic grease (1.25, 0.88); residual silicon grease (0.09 ppm)
5.6 $^1$H NMR spectra of strapped porphyrin 3 in CDCl$_3$

Residual signals: residual CHCl$_3$ (7.26 ppm); residual CH$_2$Cl$_2$ (5.31 ppm); residual H$_2$O (1.59)
5.7 $^1$H NMR spectra of the mixture of strapped porphyrins 1a-OMe and 1b-OMe in CDCl$_3$

Residual signals: residual CHCl$_3$ (7.26 ppm); residual CH$_2$Cl$_2$ (5.29 ppm); residual acetone (2.16 ppm); residual H$_2$O (1.54); adventitious aliphatic grease (1.25, 0.88); residual silicon grease (0.09 ppm)
5.8 $^1$H NMR spectra of atropisomer 1a-OH in CDCl$_3$

Residual signals: residual CHCl$_3$ (7.26 ppm); residual CH$_2$Cl$_2$ (5.29 ppm); residual H$_2$O (1.54); adventitious aliphatic grease (1.25, 0.88); residual silicon grease (0.09 ppm)
5.9 $^1$H NMR spectra of methyl-2-carboxyphenyldioxolane 14 in CDCl$_3$

Residual signals: residual CHCl$_3$ (7.26 ppm); residual H$_2$O (1.54)
5.10 $^1$H NMR spectra of 2-N,N-bis(2-methoxyacetonyl)amidophenylidioxolane 12 in CDCl$_3$

Residual signals: residual CHCl$_3$ (7.26 ppm); residual acetone (2.17 ppm); residual H$_2$O (1.56); adventitious aliphatic grease (1.25, 0.88)
5.11 $^1$H NMR spectra of $\alpha\alpha'$-5-(2-nitrophenyl)-15-(2-N,N-(bis-2-methoxyacetyl)amidophenyl)porphyrins 11a in CDCl$_3$.

Residual signals: residual CHCl$_3$ (7.26 ppm); residual CH$_2$Cl$_2$ (5.29 ppm); residual acetone (2.16 ppm)
5.12 $^1$H NMR spectra of αα′-5-(2-aminophenyl)-15-(2-N,N-(bis-2-methoxyacetyl)amidophenyl)-zinc-porphyrin 10a in CDCl$_3$-MeOD 4-1

Residual signals: residual CHCl$_3$ (7.36 ppm); residual CH$_2$Cl$_2$ (5.3 ppm); residual H$_2$O (3.69 ppm); residual MeOH (3.37 ppm); adventitious aliphatic grease (1.25, 0.88)
5.13 $^1$H NMR spectra of $\alpha \beta'$-5-(2-aminophenyl)-15-(2-N,N-(bis-2-methoxyacetyl)amidophenyl)-zinc-porphyrin 10b in CDCl$_3$

Residual signals: residual CHCl$_3$ (7.26 ppm); residual CH$_2$Cl$_2$ (5.29 ppm); adventitious aliphatic grease (1.25, 0.88)
5.14 $^1$H NMR spectra of $\alpha\alpha'$-5-(2-(2-chloroactyl)aminophenyl)-15-(2-N,N-(bis-2-methoxyacethyl)amidophenyl)-zinc-porphyrin 9a in CDCl$_3$

Residual signals: residual CHCl$_3$ (7.26 ppm); residual CH$_2$Cl$_2$ (5.30 ppm); residual acetone (2.17 ppm); adventitious aliphatic grease (1.25, 0.88)
5.15 $^1$H NMR spectra of $\alpha\beta'$-5-(2-(2-chloroactyl)aminophenyl)-15-(2-N,N-(bis-2-methoxyacetyl)amidophenyl)-zinc-porphyrin 9b in CDCl$_3$

Residual signals: residual CHCl$_3$ (7.26 ppm); residual CH$_2$Cl$_2$ (5.31 ppm); residual H$_2$O (1.41 ppm); adventitious aliphatic grease (1.25, 0.88)
Residual signals: residual CHCl$_3$ (7.26 ppm); residual CH$_2$Cl$_2$ (5.29 ppm); residual H$_2$O (1.41 ppm); adventitious aliphatic grease (1.25, 0.88)
Residual signals: residual H$_2$O (3.30 ppm); residual DMSO (2.50 ppm); adventitious aliphatic grease (1.25, 0.88)
5.18 $^1$H NMR spectra of porphyrin 8b in CDCl$_3$

Residual signals: residual CHCl$_3$ (7.26 ppm); residual CH$_2$Cl$_2$ (5.32 ppm); adventitious aliphatic grease (1.25, 0.88)
5.19 $^1$H NMR spectra of porphyrin 8b in DMSO-$d_6$

Residual signals: residual CH$_2$Cl$_2$ (5.75 ppm); residual H$_2$O (3.30 ppm); residual DMSO (2.48 ppm)
5.20 $^1$H NMR spectra of porphyrin 2a in DMSO-d$_6$

Residual signals: residual H$_2$O (3.30 ppm); residual DMSO (2.48 ppm)
Residual signals: residual H$_2$O (3.32 ppm); residual DMSO (2.48 ppm); adventitious aliphatic grease (1.25, 0.88)
5.22 $^1$H NMR spectra of 5-phenyl-15-(2-nitrophenyl)porphyrin 17 in CDCl$_3$

Residual signals: residual CHCl$_3$ (7.26 ppm); residual H$_2$O (1.53 ppm)
Residual signals: residual CHCl₃ (7.26 ppm); residual H₂O (1.53 ppm); adventitious aliphatic grease (1.25, 0.88)
5.24 $^1$H NMR spectra of 5-phenyl-15-(2-(2-chloroacethylaminophenyl))porphyrin zinc(II) complex 15 in CDCl$_3$

Residual signals: residual CHCl$_3$ (7.26 ppm); residual H$_2$O (1.50 ppm); adventitious aliphatic grease (1.25, 0.88)
5.25 $^1$H NMR spectra of R2 in DMSO-$d_6$

Residual signals: residual CH$_2$Cl$_2$ (5.75 ppm); residual H$_2$O (3.31 ppm); residual DMSO (2.48 ppm)
5.26 $^1$H NMR spectra of R1 in MeOD-5% Pyridine-d$_5$

Residual signals: residual pyridine (8.53, 7.83, and 7.41 ppm); residual H$_2$O (4.90 ppm); residual MeOH (3.33 ppm)
Residual signals: residual pyridine (8.56, 7.79, and 7.38 ppm); residual H$_2$O (3.34 ppm); residual DMSO (2.51 ppm)
6 References


