Synthesis and characterization of trans-di-(4-pyridyl)porphyrin dimers

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ABSTRACT: Preparation and characterization of a small library of symmetric trans-di(4-pyridyl)porphyrin dimers, obtained by either Glaser-Hay or Sonogashira coupling reactions from appropriately prepared trans-di-4-pyridylporphyrin precursors, is presented. The porphyrin dimers are differentiated by a phenyl-alkynyl bridge of increasing length at one meso position, while for all the derivatives the two remaining opposite meso positions are tailored with a phenyl moiety bearing a short polyether chain. Coordination of the four pyridyl groups towards appropriate metal fragments may be exploited to construct tubular hollow structures, with varied internal sizes, depending on the choice of the porphyrin dimer component.

KEYWORDS: trans-di-(4-pyridyl)porphyrin, porphyrin dimers, synthesis, metal-mediated self-assembling.

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INTRODUCTION

Pyridylporphyrins are essential elements in the modern molecular tool-box of the supramolecular chemist. They combine the peculiar structural, optical and redox properties of porphyrins with the ability to act as rigid, flat multitopic donors in the formation of metal-organic complexes [1]. Within the field of the metal-mediated directional bonding approach [2], these features along with the properties of several transition metal ions (e.g. Pd(II), Pt(II), Ru(II), Rh(II), Re(I)) has led to a variety of coordination adducts. These species can have many different topologies (such as rhomboids, squares, rectangles, triangles) and interesting potential applications in the fields of optoelectronic, catalysis, molecular recognition, etc [3].

In this context, we have recently started to investigate the interaction of pyridylporphyrin based metallacycles with phospholipid membranes and, in particular, their ability to modify the membrane permeability forming large self-assembled channels [4]. Following the approach developed in the group of J. T. Hupp [5], we prepared 4+4 Re(I)-porphyrin metallacycles starting from Re(CO)Br and trans-A2B2 di-4-pyridylporphyrins bearing, in the two meso positions, different types of aromatic substituents [6]. When peripheral carboxylic acid functionalized porphyrins were used, the resulting metallacycle showed a very interesting ionophoric activity that was attributed to its ability to assemble dimeric structures long enough to span the entire phospholipid bilayer, thus forming a trans-membrane nanopore [7]. These results encouraged us to further develop our porphyrin ligands, and the new molecules were designed to be able to form unmolecular tubular structures long enough to span a double-layer of a phospholipid membrane. Our target was to synthesize dimeric trans-di-4-pyridylporphyrins (Figure 1), which would ideally bind to 90° metal fragments in a 1:2 ratio thus forming 4+8 parallelepiped-shaped hollow structures with two hydrophilic ends (see also Figure 7). While dimeric porphyrin molecules are well known [8], examples of dimeric trans-di-4-pyridylporphyrins are very few as well as are the studies on their metal-mediated self-assembling behavior [9]. In this paper we report the synthesis of dimers 1a-1c, their characterization and some preliminary experiments on their coordination abilities towards Re(I) and Pd(II) 90° metal fragments.

RESULTS AND DISCUSSION

Synthesis of the trans-di-4-pyridylporphyrin dimers

The structures of the target trans-di-4-pyridylporphyrin dimers are shown in Figure 1. They are symmetric dimers in which two trans-di-4-pyridylporphyrins are connected at the meso position with a phenyl-alkynyl bridge of increasing length. This kind of linking bridge has been chosen in order to ensure rigidity and linearity to the whole molecule, thus avoiding bent conformations. It also granted rather simple synthetic pathways through standard Glaser-Hay or Sonogashira coupling reactions. Moreover, for a better solubility in polar solvents and membrane compatibility, the dimers have been functionalized on the two opposite meso positions with phenyl rings bearing a short polyether chain. In the linear conformation, the overall length of dimers 1a-c, estimated from molecular modelling and excluding the polyether chains, is about 36, 38, and 43 Å, respectively, sufficient in each case to span a phospholipid bilayer, which is about 40 Å thick.

The key intermediates in the synthesis of the tetra-pyridylporphyrin dimers are 5,15-bis-(4-pyridyl)-10-(4-ethynylphenyl)-20-(4-[2-(2-methoxyethoxy)ethoxy]ethoxy)phenyl)porphyrin (2a), and 5,15-bis-(4-pyridyl)-10-(4-iodophenyl)-20-(4-[2-(2-methoxyethoxy)ethoxy]ethoxy)phenyl)porphyrin (3a) (Figure 2).
Porphyrrins 2a and 3a are A₂BC trans meso-substituted derivatives, which can be conveniently obtained by a modification of the Lindsey’s approach [10], in which the 5-(4-pyridyl)dipyrromethane is reacted with half an equivalent of two different aldehydes (Scheme 1). This is a statistical approach, leading to the A₂BC porphyrin together with the two symmetric trans products (A₂B₂ and A₂C₂). Notably, if the two aldehydes have comparable reactivity the desired A₂BC isomers are obtained, in predominant yield. In the case of the synthesis of 2a 5-(4-pyridyl)dipyrromethane was reacted with 4-[(trimethylsilyl)ethynyl]benzaldehyde and 4-[2-(2-methoxyethoxy)ethoxy]ethoxy]benzaldehyde (Scheme 1) in a molar ratio 1:0.5:0.5. The latter aldehyde, commercially available but exceedingly expensive, was in turn obtained by a standard Mitsunobu reaction between 4-hydroxybenzaldehyde and triethyleneglycolmonomethylether. The macrocyclization reaction was performed in CH₂Cl₂ at 0 °C and under Ar atmosphere using TFA as the acidic catalyst. After oxidation with DDQ in air, the crude product was neutralized and treated with tetrabutylammonium fluoride (TBAF) to remove the silyl protecting groups. Repeated purification steps by silica chromatography and crystallization from CHCl₃/MeOH afforded the three porphyrins in 12 % (2a), 7% (2b) and 3% (2c) yield. Starting from 4-iodobenzaldehyde, and following a similar scheme of reactions, porphyrins 3a,b and 2c were obtained in 17%, 8%, and 5% yield, respectively. All the porphyrins were fully characterized by ¹H- and 13C-NMR, ESI-MS, IR, UV-Vis and emission spectroscopies (see also Fig. S1-S10 and Fig. S25-S26 of the Supplemental Material).

Porphyrrins 2a and 3a were then used for the preparation of dimers 1. Dimer 1b was obtained in good yield via Glaser-Hay homocoupling of 2a (Scheme 2). The reaction proceeds smoothly at room temperature in the presence of CuCl, tetramethylethylenediamine (TMEDA) and under a positive pressure of oxygen giving, after column chromatography purification, the desired product in good yield.

Dimers 1a and 1c were likewise obtained by Sonogashira coupling between 2a and 3a and between 3a and 1,4-diethynylbenzene, respectively (Scheme 3). The copper-free variation of the Sonogashira coupling reaction was used in order to avoid possible undesired porphyrin-metallation side products. The coupling proceeds in the presence of Pd(PPh₃)₄ and a large excess of TEA in a THF/DMF mixture, under Ar atmosphere and under microwave irradiation for 1 hour, at 120 °C. After purification, dimers 1a and 1c were obtained in 24% and 62% yield, respectively.

Characterization of the trans-di-4-pyridylporphyrin dimers

All the porphyrin dimers were fully characterized by ESI-MS, ¹H- and 13C-NMR, IR, UV-Vis and emission spectroscopies, with the mass spectra unambiguously identifying the nature of each product. The ¹H-NMR spectra (assigned by 2D H-H and H-C NMR experiments, see also Supplemental Material) of the three porphyrin dimers closely resemble that of the reference monomer porphyrin 2a, reflecting the symmetry of the molecules. In particular, the upfield and the midfield regions of the reference porphyrin and the dimers, comprising the resonances of the NH core protons and of polyether chains, respectively, are practically superimposable (see Fig. S17 in the Supplemental Material). Small but significant differences are however observed in the downfield region of the spectra (Figure 3).

With respect to 2a, the pattern of the β-pyrrolic protons (β-H, Figure 3) in the dimers is, in general, more resolved and the proton resonances of the phenyl ring bearing the ethynyl substituents (H₂- and H₄-Ph, Figure 3) are downfield shifted, to different extents depending on the dimer. As expected, due to the long distance from the linkers, the peaks corresponding to the pyridyl protons (H₆- and H₈- Py) and to the phenyl rings bearing the polyether chain (H₁- and H₂-Ph) are, on the contrary, essentially unchanged. A spectroscopic signature of dimer 1c is the singlet at ca. 7.75 ppm. which can be ascribed to the protons of the central phenyl ring of the linker (H₅-Ph, Figure 3), lying on the center of symmetry of the molecule. Similarly to the ¹H-NMR analysis, the 13C-NMR spectra of the various dimers are also very similar to that of porphyrin 2a, except for the number and position of the ethynyl carbon signals, together with the
presence, for dimer 1c, of two peaks around 135 ppm, assigned to the phenyl carbons of the linker (see Fig. S18 of the Supplemental Material).

To better characterize the dimers, their diffusion coefficients were determined using \(^1\)H-DOSY NMR experiments. Figure 4 shows the \(^1\)H-DOSY spectra for dimer 1a and, for comparison, porphyrin 2c. Similar 2D-maps were also obtained for dimers 1b and 1c and are reported in the Supplemental Material.

Inspection of the 2D-map of Figure 4 shows that all the signals of the two molecules, except the solvent and water residues, are aligned along one single value of diffusion coefficient indicating the presence in solution of a single species with a well-defined dimension. Moreover, the porphyrin monomer has a higher diffusion coefficient than the dimer, in agreement with the latter species having a bigger size. The diffusion coefficients for all these species together with their hydrodynamic diameters obtained from the Stokes-Einstein equation, while not being meaningful in terms of absolute values, are consistent with the expected increased dimension going from monomer 2a to dimers 1 (see Table 1 in the Supplemental Material).

Finally, the absorption and emission spectroscopic features of the three dimers were investigated. Figure 5 reports the UV-vis spectra of the dimers (1 \(\mu\)M in DCM) in comparison with porphyrin 2a (2 \(\mu\)M in DCM). The Soret band for the dimers is only slightly red-shifted (2-3 nm) with respect to the one of 2a, while the position of the Q-bands is almost unaffected. The intensity of the absorption bands changes substantially among the series. Dimer 1b, which is the exact double of the porphyrin monomer, has practically the same molar absorptivity of 2a, while the intensity of the Soret and of the Q-bands decreases on going from 1a to 1c. Clearly the substitution with two phenyl ring in 1a and the presence of the central phenyl in 1c has a negative effect on the conjugation between the ethynyl group and the porphyrin aromatic macrocycle, resulting in a lower molar absorptivity.

Figure 6 reports the emission spectra of the dimers 1 (1 \(\mu\)M) and of porphyrin 2a (2 \(\mu\)M) recorded in DCM with the excitation wavelength fixed at 420 nm. All the spectra are almost superimposable, both in terms of intensity and position of the emission bands, as might be expected.

**Preliminary studies for the preparation of 4+8 \(\text{trans-di-4-pyridylporphyrin metallacyclic assemblies}\)**

Preliminary investigations towards the preparation of 4+8 \(\text{trans-di-4-pyridylporphyrin metallacyclic assemblies}\) with a parallelepiped shape were performed using dimer 1b in combination with two different 90° metal fragments. Despite the rotational freedom of the two macrocycles around the phenyl-alkynyl linker, we envisaged the possibility of a thermodynamic self-sorting process, leading to the successful obtainment of metallacyclic assemblies as unique products (Figure 7).

We first investigated the use of the [Pd(dppp)(OTf)] metal complex (dppp = 1,3-bis(diphenylphosphino)propane, OTf = trifluorosulphonate), which is known to readily form soluble 4+4 metallacycles with \(\text{trans-di-4-pyridylporphyrins}\) [11]. The solubility in both polar and apolar organic solvents is normally ascribed both to the positive charge of the metal complex, due to the loss of the two triflate anions upon coordination of two pyridyl groups, and to the out-of-plane phenyl substituents of the dppp ancillary ligand disfavoring possible aggregation of the resulting assemblies. Also, the two phosphorus atoms of the ancillary dppp ligand are a useful tag for \(^{31}\)P-NMR investigations. However, simply mixing dimer 1b with two equivalents of [Pd(dppp)(OTf)] in CDCl\(_3\) directly in the NMR tube afforded very complex \(^1\)H- and \(^{31}\)P-NMR spectra suggesting the presence of several species, possibly in dynamic equilibrium. Heating and/or increasing of the building blocks concentrations, did not change or simplify the overall pattern of the NMR spectra.

A second preliminary attempt to prepare metallacyclic parallelepiped assemblies was made using [Re(CO)\(_3\)Br] as metal fragment. Compared to Pd(II), Re(I) is known to form kinetically and thermodynamically more stable bonds with
pyridyl ligands, leading to the formation of stable discrete cyclic structures. The chemistry of the \([\text{Re}(\text{CO})_3\text{X}]\) (X = Cl\(^{-}\) or Br\(^{-}\)) complex in the formation of stable 4+4 metallaclycles with trans-di-4-pyridylporphyrins has been pioneered by J.T. Hupp \[5, 12\]. The strong labilizing effect of CO serves to activate two (and only two) cis-carbonyls for substitution, presumably first by solvent molecules (e.g. tetrahydrofuran) and then by pyridyl ligands. The reaction is slow and can take up to 2 days for completion under refluxing conditions. We therefore reacted 1b and \([\text{Re}(\text{CO})_3\text{Br}]\) in a mixture of THF and toluene under reflux, until the porphyrin starting material was fully consumed. Work-up of the reaction afforded a solid which was scarcely soluble in a variety of solvents. The \(^1\text{H}-\text{NMR}\) spectra of this solid in pyridine-\(d_5\) were difficult to interpret, although a DOSY experiment suggested the presence of a single species in solution (Figure S20 of the Supplemental Material) \[13\]. Once again, variation of the temperature did not lead to any simplification of the NMR spectrum, which would be expected if a highly symmetrical assembly had formed. Most likely, the very low solubility of reagents and intermediates hampers the instauration of a fast thermodynamic equilibrium, that should lead to the desired metallaclycic product, and consequently the porphyrin dimer gets consumed in the formation of undesired oligomeric coordination open-species. The difficulty to identifying a single 4+8 supramolecular adduct with a di-4-pyridylporphyrin dimer and a Re(I) complex when the porphyrin dimer bears a triphenyl bridge has been also reported by Hupp et al. and was attributed to unacceptably slow conversion of “wrong” kinetic intermediate products \[9b\].

**EXPERIMENTAL**

**General**

All commercially available reagents were purchased from Aldrich, Fluka and Strem Chemicals and used without purification unless otherwise mentioned. Solvents were purchased from Aldrich, VWR, Fluka and Riedel, and deuterated solvents from Cambridge Isotope Laboratories and Aldrich. Analytical thin layer chromatography (TLC) was carried out on Merck aluminium backed silica gel plates (thickness 0.25 mm). Flash column chromatography (FCC) was carried out on Merck silica gel 60 (230–400 Mesh).

NMR spectra were recorded on a Varian 500 MHz spectrometer (operating at 500 MHz for \(^1\text{H}\) and at 125 MHz for \(^{13}\text{C}\)). Chemical shifts are reported as parts per million (ppm) relative to the solvent residual signal as internal reference. [CDCl\(_3\)]; \(\delta\text{H}, \text{ppm} 7.27; \delta\text{C}, \text{ppm} 77.36; \text{CD}_{3}\text{OD}; \delta\text{H}, \text{ppm} 3.31; \delta\text{C}, \text{ppm} 49.00; \text{pyridine-}d_5; \delta\text{H}, \text{ppm} 8.74; \delta\text{C}, \text{ppm} 150.30].

IR spectra were recorded on a Perkin Elmer System 2000 NIR spectrophotometer with the KBr pellet technique and only major peaks are reported. UV-Vis spectra were recorded on a Perkin Elmer Lambda 35 spectrophotometer. Fluorescence emission spectra were recorded on a Varian Cary Eclipse spectrofluorimeter. Electrospray ionization mass spectra (ESI-MS) were performed on a Perkin Elmer APII at 5600 eV.

1,4-diethynylbenzene was purchased from Aldrich. 5-(4-Pyridyl)dipyrromethane \[14\], \([\text{ReBr}(\text{CO})_5]\) \[15\] and \([\text{Pd}(\text{dppp})(\text{OTf})_2]\) \[16\] were prepared as reported previously.

Abbreviations used in the text: AcOEt = ethyl acetate; DCM = dichloromethane; PE = petroleum ether; Py = pyridine; TBAF = tetra-n-butylammonium fluoride; THF = tetrahydrofuran; n-Hx = n-hexane; DMF = dimethylformamide; TEA = triethylamine; TFA = trifluoroacetic acid; DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone; DIAD = diisopropylazodicarboxylate; dppp = 1,3-bis-(diphenylphosphino)propene; TMEDA = tetramethylethylendiamine; TMSA = trimethylsilylacetylene; dba = tris-dibenzyldeneacetone; tol = tolyl; MS = molecular sieves; \(\mu\)Wave = microwave; TLC = thin layer chromatography; FCC = flash column chromatography; CC = column chromatography.
Synthesis of A_{3}BC porphyrins 2a-2c and 3a-3c

4-[2-(2-Methoxyethoxy)ethoxy]ethoxy]benzaldehyde (TegPhCHO) \[\text{8c}\]

Triphenylphosphine (5.5 g, 21.0 mmol) was dissolved in 70 mL of anhydrous THF under Ar atmosphere and the solution was cooled to 0 °C. DIAD (2.0 mL, d = 1.420 g/mL, 14.0 mmol) was then added dropwise. The solution became pale yellow and a fine white precipitate was formed. Then a solution of triethylenglycolmonomethylether (THF solution, 2.20 mL, d = 1.048 g/mL, 14.0 mmol) and of p-hydroxybenzaldehyde (1.71 g, 14.0 mmol) in anhydrous THF was added dropwise. The reaction mixture was stirred under inert atmosphere for 4 hours at room temperature. The reaction mixture was stirred for further 2 hours. The crude mixture was directly washed three times with a saturated solution of NaHCO₃ and with no more inert atmosphere, DDQ (885 mg, 3.90 mmol) was added and the reaction was let to reach 0 °C with an ice bath. Then TFA (5.99 mL, d = 1.535 g/mL, 80.6 mmol) was added dropwise and the reaction kept under stirring for 1.5 hours. The reaction mixture was let to reach room temperature and with no more inert atmosphere, DDQ (885 mg, 3.90 mmol) was added and the reaction was stirred for further 2 hours. The crude mixture was directly washed three times with a saturated solution of NaHCO₃ and once with water. The organic phase was dried over Na₂SO₄, filtered, and the solvent was removed under vacuum. The crude mixture was further purified by another CC on silica gel (CHCl₃/THF from 100/0 to 97/3 v/v). Fractions containing the three porphyrins were purified by another CC on silica gel (CHCl₃/MeOH from 100/0 to 98/2). Each product was then obtained as a violet solid by precipitation from CHCl₃/MeOH. Yield: 2a 12%, 2b 7%, 2c 3%. Total porphyrins yield 22.0%.

5,15-Bis-(4-pyridyl)-10-(4-ethynylphenyl)-20-(4-[2-(2-methoxyethoxy)ethoxy]ethoxy]phenyl)porphyrin (2a):

R_f = 0.53 (SiO₂, CHCl₃/MeOH 97/3 v/v). ¹H-NMR (500 MHz; CDCl₃): δ_{H} ppm 9.04 (4H, d, J = 5.6 Hz, H₂-Py), 8.94 (2H, d, J = 4.7 Hz, β-H), 8.88 (2H, d, J = 4.7 Hz, β-H), 8.82 (4H, m, β-H), 8.17 (6H, s, H₆-Py and H₂-Py), 8.10 (2H, d, J = 8.5 Hz, H₁-Ph), 7.91 (2H, d, J = 8.0 Hz, H₁-Ph), 7.32 (2H, d, J = 8.5 Hz, H₂-Ph), 4.44 (2H, m, PhOCH₂CH₂O), 4.07 (2H, m, OCH₂CH₂O), 3.89 (2H, m, OCH₂CH₂O), 3.80 (2H, m, OCH₂CH₂O), 3.75 (2H, m, OCH₂CH₂O), 3.62 (2H, m, OCH₂CH₂O), 3.43 (3H, s, OCH₃), 3.33 (1H, s, CCH), −2.84 (2H, br, NH). ¹³C-NMR (125 MHz; CDCl₃): δ_C ppm 159.0, 150.3, 148.5, 142.4, 135.7, 134.6, 134.2, 129.5, 122.1, 121.3, 119.7, 117.3, 113.2, 83.6, 78.7, 72.1, 71.1, 70.9, 70.8, 70.0, 67.9, 59.2. MS (ESI): m/z 803, 825, 841 (calcd. for [C₅H₄₂N₆O₄ + H]^+) 803.33, [C₅H₄₂N₆O₄ + Na]^+ 825.31, [C₅H₄₂N₆O₄ + K]^+ 841.29. UV-vis (CHCl₃): λ_{max} nm (relative intensity, %) 419 (100), 515 (4.7), 549 (2.3), 590 (1.6), 649 (1.5). Fluorescence Emission (CH₂Cl₂, λ_{exc} 420 nm): λ_{em} nm 652, 718. IR (KBr): ν, cm⁻¹ 2923, 2853, 1637, 1384, 1281, 1248, 1109, 801.

Porphyrins 2a-2c

The reaction was conducted under Ar atmosphere and in the dark. 5-(4-Pyridyl)dipyrromethane (580 mg, MW = 223.27, 2.60 mmol) and 4-[2-(trimethylsilyl)ethynyl]benzaldehyde (263 mg, MW = 202.32, 1.30 mmol) were dissolved in anhydrous DCM (270 mL). A solution of TegPhCHO (349 mg, MW = 268.306, 1.30 mmol) in 30 mL of anhydrous DCM was added and the mixture was cooled to 0 °C. DIAD (2.0 mL, d = 1.420 g/mL, 14.0 mmol) was added dropwise and the reaction kept under stirring for 1.5 hours. The reaction mixture was let to reach room temperature and with no more inert atmosphere, DDQ (885 mg, 3.90 mmol) was added and the reaction was stirred for further 2 hours. The crude mixture was directly washed three times with a saturated solution of NaHCO₃ and once with water. The organic phase was dried over Na₂SO₄, filtered, and the solvent was removed under vacuum. The crude mixture was further purified by another CC on silica gel (CHCl₃/MeOH from 100/0 to 97/3 v/v). Fractions containing the three porphyrins were further purified by another CC on silica gel (CHCl₃/MeOH from 100/0 to 98/2). Each product was then obtained as a violet solid by precipitation from CHCl₃/MeOH. Yield: 2a 12%, 2b 7%, 2c 3%. Total porphyrins yield 22.0%.
5.15-Bis-(4-pyridyl)-10,20-bis-(4-ethynylphenyl)porphyrin (2b): $R_f = 0.47$ (SiO$_2$, CHCl$_3$/MeOH 97/3 v/v). $^1$H-NMR (500 MHz; CDCl$_3$): $\delta_{H}$, ppm: 9.05 (4H, d, $J = 5.5$ Hz, H$_5$-Py), 8.89 (4H, d, $J = 4.7$ Hz, $\beta$-H), 8.83 (4H, d, $J = 4.6$ Hz, $\beta$-H), 8.18 (8H, os, H$_5$-Py and H$_r$-Ph), 7.91 (4H, d, $J = 8.0$ Hz, H$_5$-Ph), 3.34 (2H, s, CCH), $-2.86$ (2H, br, NH). $^{13}$C-NMR (125 MHz; CDCl$_3$): $\delta_{C}$, ppm: 150.2, 148.5, 142.3, 134.57, 130.8, 129.5, 122.2, 120.1, 117.5, 83.6, 78.7, 77.1. MS (ESI): $m/z$ 665.2 (calcd. for [C$_{42}$H$_{39}$N$_1$O$_1$ + H]$^+$ 665.24). UV-vis (CH$_2$Cl$_2$): $\lambda_{max}$, nm (relative intensity, %) 418 (100), 514 (4.8), 549 (2.0), 589 (1.6), 645 (1.0). Fluorescence Emission (CH$_2$Cl$_2$): $\lambda_{exc}$ 420 nm; $\lambda_{em}$ nm 650, 716. IR (KBr): $\nu$, cm$^{-1}$ 2924, 2854, 1514, 962, 800, 728.

5.15-Bis-(4-pyridyl)-10,20-bis-[4-[2-(2-methoxyethoxy)ethoxy]ethoxy]phenyl] porphyrin (2c): $R_f = 0.46$ (SiO$_2$, CHCl$_3$/MeOH 95/5 v/v). $^1$H-NMR (500 MHz; CDCl$_3$): $\delta_{H}$, ppm: 9.04 (4H, dd, $J = 6.0$, 1.5 Hz, H$_5$-Py), 8.92 (4H, d, $J = 4.5$ Hz, $\beta$-H), 8.80 (4H, d, $J = 5.0$ Hz, $\beta$-H), 8.17 (4H, dd, $J = 6.0$, 2.0 Hz, H$_5$-Py), 8.1 (4H, d, $J = 8.5$ Hz, H$_5$-Ph), 7.32 (4H, d, $J = 8.5$ Hz, H$_5$-Ph), 4.44 (4H, m, PhOC$_2$H$_2$O), 4.07 (4H, m, OCH$_2$CH$_2$O), 3.89 (4H, m, OCH$_2$CH$_2$O), 3.80 (4H, m, OCH$_2$CH$_2$O), 3.75 (4H, m, OCH$_2$CH$_2$O), 3.62 (4H, m, OCH$_2$CH$_2$OCH$_3$), 3.42 (6H, s, OCH$_3$), $-2.83$ (2H, br, NH). $^{13}$C-NMR (125 MHz, CDCl$_3$): $\delta_{C}$, ppm: 159.0, 150.4, 148.4, 134.5, 134.3, 129.5, 126.6, 122.4, 120.8, 120.3, 117.0, 113.1, 111.7, 72.1, 71.1, 70.9, 70.8, 70.0, 67.9, 59.2. MS (ESI): $m/z$ 963 (calcd. for [C$_{42}$H$_{39}$N$_1$O$_1$ + Na]$^+$ 963.40). UV-vis (CH$_2$Cl$_2$): $\lambda_{max}$, nm (relative intensity, %) 419 (100), 516 (5.2), 550 (3.0), 592 (1.9), 651 (2.7). Fluorescence Emission (CH$_2$Cl$_2$): $\lambda_{exc}$ 426 nm; $\lambda_{em}$ nm 655, 719. IR (KBr): $\nu$, cm$^{-1}$ 3078, 2922, 2860, 1637, 1593, 1449, 1404, 1384, 1351, 1286, 1246, 1175, 1108, 967, 788, 737.

Porphyrians 3a-3b

The reaction was conducted under Ar atmosphere and in the dark. 5-(4-Pyridyl)dipyrromethane (594 mg, MW = 223.27, 2.66 mmol) and 4-iodobenzaldehyde (309 mg, MW = 232.02, 1.33 mmol) were dissolved in anhydrous DCM (270 mL). A solution of TegPhCHO (381 mg, MW = 268.306, 1.33 mmol) in 30 mL of anhydrous DCM was added and the mixture was cooled to 0°C with an ice bath. Then TFA (6.12 mL, $d = 1.535$ g/mL, 82.5 mmol) was added dropwise and the reaction was kept under stirring for 1.5 hours. The reaction mixture was let to reach room temperature and with no more inert atmosphere DDQ (1.21 g, 5.32 mmol) was added and the reaction was stirred for further 2 hours. The crude mixture was directly washed three times with a saturated solution of NaHCO$_3$ and once with water. The organic phase was dried over Na$_2$SO$_4$ and the solvent was removed under reduced pressure. The residue was purified by CC on silica gel (CHCl$_3$/EtOH from 100/0 to 97/3 v/v). The fractions containing the three porphyrians were further purified by another CC on silica gel (CHCl$_3$/EtOH from 100/0 to 98/2). Each product was then obtained as a violet solid by precipitation from CHCl$_3$/MeOH. Yield: 3a 17%, 3b 8.0%, 2c 5%. Total porphyrians yield 30%.

5.15-Bis-(4-pyridyl)-10-(4-iodophenyl)-20-[4-[2-(2-methoxyethoxy)ethoxy]ethoxy]phenyl] porphyrin (3a): $R_f = 0.49$ (SiO$_2$, CHCl$_3$/MeOH 97/3 v/v). $^1$H-NMR (500 MHz; CDCl$_3$): $\delta_{H}$, ppm: 9.06 (4H, d, $J = 5.5$ Hz, H$_5$-Py), 8.95 (2H, d, $J = 5.0$ Hz, $\beta$-H), 8.89 (2H, d, $J = 4.5$ Hz, $\beta$-H), 8.82 (4H, m, $\beta$-H), 8.18 (4H, d, $J = 5.5$ Hz, H$_5$-Py), 8.12 (4H, s, H$_1$-Ph and H$_r$-Ph), 7.95 (4H, d, $J = 8.0$ Hz, H$_5$-Ph), 7.33 (4H, d, $J = 9.0$ Hz, H$_5$-Ph), 4.45 (2H, m, PhOC$_2$H$_2$O), 4.08 (2H, m, OCH$_2$CH$_2$O), 3.90 (2H, m, OCH$_2$CH$_2$O), 3.81 (2H, m, OCH$_2$CH$_2$O), 3.76 (2H, m, OCH$_2$CH$_2$O), 3.64 (2H, m, OCH$_2$CH$_2$OCH$_3$), 3.44 (3H, s, OCH$_3$), $-2.85$ (2H, br, NH). $^{13}$C-NMR (125 MHz; CDCl$_3$): $\delta_{C}$, ppm: 158.9, 150.2, 148.3, 141.3, 136.1, 136.0, 135.6, 134.1, 129.4, 121.2, 119.1, 117.1, 113.0, 94.4, 72.0, 71.0, 70.8, 70.7, 70.0, 67.8, 59.2. MS (ESI): $m/z$ 905, 927 (calcd. for [C$_{49}$H$_{41}$N$_2$O$_1$ + H]$^+$ 905.23, [C$_{49}$H$_{41}$N$_2$O$_1$ + Na]$^+$ 927.21). UV-vis spectrum (CH$_2$Cl$_2$): $\lambda_{max}$, nm (relative intensity, %) 419 (100), 515 (4.8), 550 (2.2), 591 (1.5), 651 (1.8). Fluorescence Emission (CH$_2$Cl$_2$): $\lambda_{exc}$ 420 nm; $\lambda_{em}$ nm 655, 717. IR (KBr): $\nu$, cm$^{-1}$ 2922, 2853, 1636, 1593, 1472, 1384, 1283, 1248, 1105, 968, 799, 732.
5,15-Bis-(4-pyridyl)-10,20-bis-(4-iodophenyl)porphyrin (3b) [17]: Rf = 0.67 (SiO2, CHCl3/MeOH 97/3 v/v). 1H-NMR (500 MHz; CDCl3): δH, ppm 9.07 (4H, dd, J = 5.5, 1.5 Hz, H2-Py), 8.90 (4H, d, J = 4.5 Hz, β-H), 8.84 (4H, d, J = 5.0 Hz, β-H), 8.17 (4H, dd, J = 6.0, 2.0 Hz, H4-Py), 8.13 (4H, d, J = 8.0 Hz, H2-Phl), 7.95 (4H, d, J = 8.0 Hz, H2-Ph), −2.89 (2H, br, NH). 13C-NMR (125 MHz; CDCl3): δC, ppm 150.0, 148.3, 141.1, 136.1, 136.0, 129.3, 119.5, 117.3, 94.5. MS (ESI): m/z 869 (calcd. for [C26H32I2N6 + H]+ 869.04). UV-vis (CH2Cl2): λmax, nm (relative intensity, %) 418 (100), 514 (4.3), 548 (1.5), 590 (1.1), 650 (1.0). Fluorescence Emission (CH2Cl2, λexc 420 nm): λem, nm 656, 716. IR (KBr): ν, cm⁻¹ 2921, 1637, 1591, 14783, 1384, 967, 796, 783, 725.

Synthesis of porphyrin dimers 1a-c

**Dimer 1a**

Anhydrous THF, anhydrous DMF and TEA were degassed for 1 hour with Ar. A solution of 2a (21 mg, MW = 802.9, 0.026 mmol) in 1 mL of anhydrous THF was prepared and kept under Ar atmosphere. Porphyrin 3a (21.7 mg, MW = 904.79, 0.024 mmol) was placed in the microwave reactor vessel under inert atmosphere. Then DMF (1.2 mL) and TEA (0.8 mL) were added and the mixture was degassed for 15 minutes with Ar. Lastly, keeping the vessel under inert atmosphere, Pd(PPh3)4 (1.4 mg, MW = 1154.56, 0.0012 mmol) was added and the mixture was degassed for further 15 minutes. Keeping the vessel under Ar, the solution of 2a was added. The reaction was stirred for 1 hour at 120°C under microwave irradiation (ramping time = 10 min, P = 300 W). The crude mixture was passed through a very short Celite® 521 pad washing with CHCl3/MeOH 9/1. The organic solvent was then extracted twice with distilled water to remove the DMF, dried with Na2SO4 and finally the solvent was removed under reduced pressure. Purification of the crude by CC (CHCl3/MeOH from 98/2 to 97:3 v/v) afforded a purple solid. Yield 9.1 mg (24%). Rf = 0.43 (SiO2, CHCl3/MeOH 95/5 v/v). 1H-NMR (500 MHz; CDCl3): δH, ppm 9.08 (8H, d, J = 5.5 Hz, H2-Py), 9.00 (4H, d, J = 4.5 Hz, β-H), 8.97 (4H, d, J = 4.5 Hz, β-H), 8.89 (4H, d, J = 5.0 Hz, β-H), 8.84 (4H, d, J = 5.0 Hz, β-H), 8.31 (4H, d, J = 8.0 Hz, H4-Ph), 8.21 (8H, dd, J = 6.0, 3.0 Hz, H6-Py), 8.14 − 8.11 (8H, ov, H2-Ph and H3-Ph), 7.35 (4H, d, J = 8.5 Hz, H2-Ph), 4.46 (4H, m, PhOCH2CH2O), 4.09 (4H, m, OCH2CH2O), 3.91 (4H, m, OCH2CH2O), 3.82 (4H, m, OCH2CH2O), 3.77 (4H, m, OCH2CH2O), 3.65 (4H, m, OCH2CH2O), 3.44 (6H, s, OCH3), −2.80 (4H, br, NH). 13C-NMR (125 MHz; CDCl3): δC, ppm 159.3, 150.6, 148.7, 142.4, 135.9, 135.0, 134.4, 130.6, 130.1, 129.8, 123.4, 121.5, 120.1, 117.5, 113.4, 91.0, 72.4, 71.3, 71.2, 70.3, 68.1, 59.5. MS (ESI): m/z 1577 (calcd. for [C26H32I2N6O2 − H]+ 1577.63). UV-vis (CH2Cl2): λmax, nm (relative intensity, %) 423 (100), 516 (5.2), 551 (2.5), 591 (1.2), 649 (0.9). Fluorescence Emission (CH2Cl2, λexc 420 nm): λem, nm 654, 718. IR (KBr): ν, cm⁻¹ 2919, 1853, 2361, 1719, 1637, 1592, 1473, 1384, 1282, 1247, 1106, 1072, 968, 800, 732.

**Dimer 1b**

CuCl (5.3 mg, 0.0054 mmol) was inserted in a round bottom flask and TMEDA (24.0 μL, d = 0.78, 0.162 mmol) was added under stirring. Then 1.0 mL of anhydrous DCM and activated molecular sieves (4Å, ~380 mg) were added in sequence. Lastly a solution of 2a (87 mg, MW = 802.9, 0.108 mmol) in 3.5 mL of anhydrous DCM was added and the reaction was stirred for 16 hours, at room temperature, under air pressure. The reaction was quenched with 3 mL of H2O, then the organic layer was washed three times with water, dried over Na2SO4 and filtered. The solvent was removed under reduced pressure and the crude was purified by CC (silica gel, CHCl3/EtOH from 99/1 to 95/5 v/v) giving a purple solid. Yield 66 mg (76%). Rf = 0.30 (SiO2, CHCl3/MeOH 98/2 v/v). 1H-NMR (500 MHz; CDCl3): δH, ppm 9.07 (8H, d, J = 5.4 Hz, H2-Py), 8.95 (4H, d, J = 5.1 Hz, β-H), 8.93 (d, J = 4.8 Hz, β-H), 8.86 (4H, d, J = 4.5 Hz, β-H), 8.82 (4H, d, J = 4.4 Hz, β-H), 8.25 (4H, d, J = 8.1 Hz, H2-Ph), 8.18 (8H, d, J = 5.6 Hz, H6-Py), 8.11 (4H, d, J = 8.4 Hz, H2-Ph), 8.04 (4H, d, J = 8.1 Hz, H1-Ph), 7.33 (4H, d, J = 8.6 Hz, H2-Ph), 4.46 (4H, m, PhOCH2CH2O), 4.07
(4H, m, OCH₂CH₂O), 3.90 (4H, m, OCH₂CH₂O), 3.81 (4H, m, OCH₂CH₂O), 3.76 (4H, m, OCH₂CH₂O), 3.63 (4H, m, OCH₂CH₂O), 3.43 (6H, s, OCH₃), −2.82 (4H, br, NH). ¹³C-NMR (125 MHz; CDCl₃): δC, ppm 159.3, 150.5, 148.7, 143.3, 135.9, 135.0, 134.4, 131.4, 129.7, 125.7, 121.9, 121.6, 119.7, 117.6, 113.4, 82.4, 75.7, 72.4, 71.3, 71.1, 71.0, 70.3, 68.1, 59.5. MS (ESI): m/z 1603, 1626 (calcd. for [C₁₀₂H₅₂N₁₂O₄⁺ + H]⁺ 1603.64, [C₁₀₂H₅₂N₁₂O₄Na⁺]⁺ 1626.63). UV-vis (CH₂Cl₂): λmax, nm (relative intensity, %) 423 (100), 516 (5.7), 551 (3.5), 591 (2.1), 649 (1.8). Fluorescence Emission (CH₂Cl₂, λexc 420 nm): λem, nm 655, 718. IR (KBr): ν, cm⁻¹ 2921, 2853, 2361, 1717, 1636, 1592, 1384, 1284, 1247, 1108, 799.

Dimer 1c

A solution of 1,4-diethylnylbenzene (2.1 mg, 0.016 mmol) in 1 mL of anhydrous THF was prepared and kept under Ar atmosphere. The vessel was degassed and the mixture was degassed for another 15 minutes with Ar. Lastly, keeping the vessel under inert atmosphere, Pd(PPh₃)₄ (4 mg, 0.0035 mmol) was added and the mixture was degassed for further 15 minutes. Keeping the vessel under Ar, the solution of 1,4-diethylnylbenzene was added. The reaction was stirred for 1 hour at 120°C under microwave irradiation (ramping time = 10 min, P = 300 W). The crude mixture was passed through a very short Celite® 521 pad washing with CHCl₃. The organic solvent was extracted three times with distilled water to remove DMF. The organic phase was dried with Na₂SO₄, filtered and the solvent was removed under reduced pressure. The residue was purified by two CC (CHCl₃:EtOH from 100/0 to 97/3 v/v) to give dark purple solid. Yield 16 mg (62%). Rf = 0.36 (CHCl₃/MeOH 97/3 v/v). ¹H-NMR (500 MHz; CDCl₃): δH, ppm 9.07 (8H, d, J = 4.0 Hz, H₂-Py), 8.96 – 8.94 (8H, ov, β-H), 8.86 (4H, d, J = 4.5 Hz, H₂-Py), 8.83 (4H, d, J = 5.0 Hz, β-H), 8.25 (4H, d, J = 7.5 Hz, H₂-Ph), 8.19 (8H, d, J = 5.0 Hz, H₃-Py), 8.12 (4H, d, J = 8.5 Hz, H₁-Ph), 8.00 (4H, d, J = 7.5 Hz, H₃-Ph), 7.77 (4H, s, H₂-Ph), 7.34 (4H, d, J = 8.5 Hz, H₂-Ph), 4.46 (4H, m, PhOCH₂CH₂O), 4.09 (4H, m, OCH₂CH₂O), 3.90 (4H, m, OCH₂CH₂O), 3.81 (4H, m, OCH₂CH₂O), 3.76 (4H, m, OCH₂CH₂O), 3.64 (4H, m, OCH₂CH₂O), 3.44 (6H, s, OCH₃), −2.81 (4H, br, NH). ¹³C-NMR (125 MHz; CDCl₃): δC, ppm 159.3, 150.6, 148.7, 142.4, 135.9, 135.0, 134.5, 132.7, 132.2, 130.5, 129.8, 121.5, 120.1, 117.5, 113.4, 110.4, 91.6, 72.4, 71.3, 71.1, 71.0, 70.3, 69.1, 59.5. MS (ESI): m/z 1680 (calcd. for [C₁₀₂H₅₀N₁₂O₄⁺ + H]⁺ 1679.67). UV-vis (CH₂Cl₂): λmax, nm (relative intensity, %) 421 (100), 516 (5.2), 551 (3.0), 591 (1.7), 650 (1.8). Fluorescence Emission (CH₂Cl₂, λexc 420 nm): λem, nm 655, 719. IR (KBr): ν, cm⁻¹ 2923, 2853, 1639, 1593, 1247, 1108, 800, 732.

Supplemental Material

¹H-NMR and ¹³C-NMR spectra of porphyrins 2a-c and 3a,b and of dimers 1a-c. ¹H-DOSY experiments. UV-vis and fluorescence emission spectra of porphyrins 2a-c and 3a,b.

CONCLUSION

In conclusion, a small library comprising three different porphyrin dimers was successfully prepared via either Glaser-Hay or Sonogashira coupling. The various systems, together with their monomer precursors, were fully characterized by NMR techniques and their UV-vis and fluorescent properties were assessed as well. Although not very successful, the preliminary experiments for the formation of metallacyclic assemblies with a parallelepiped shape gave us good insights on the complexity of this ambitious project. From this standpoint, different metal complexes will be tried as alternatives 90° metal fragments in order to overcome the major issues encountered in this report.
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REFERENCES


13. Given the inert nature of the Re–nitrogen bond at room temperature, we exclude that pyridine-d5 is competing with the already formed Re–nitrogen bonds, even though at least a partial competition cannot be excluded for prolonged exposure times.


FIGURES AND SCHEMES CAPTIONS

Fig. 1. Structures of the trans-di-(4-pyridyl)porphyrin dimers prepared in this work.

Fig. 2. Structures of the trans-di-(4-pyridyl)porphyrin monomers prepared in this work.

Scheme 1. Synthetic route to porphyrins 2a-c.

Scheme 2. Synthesis of dimer 1b.

Scheme 3. Synthesis of dimers 1a and 1c.

Fig. 3. Expansion of the downfield region of the $^1$H-NMR spectrum (CDCl$_3$) of the reference monomer porphyrin 2a, and of the dimers 1a-1c; the asterisk in the spectrum of 1b indicates a chloroform satellite.

Fig. 4. $^1$H-DOSY (500 MHz; CDCl$_3$, 298 K) of porphyrin 2c, and of the dimer 1a. The 1D trace of 1a is also shown.

Fig. 5. UV-vis spectra (CH$_2$Cl$_2$) of the reference porphyrin 2a (2 µM), and of the dimers 1a-1c (1 µM): $\lambda_{max}$, nm 419 (2a), 423 (1a), 423 (1b), 421 (1c).

Fig. 6. Fluorescence emission spectra (CH$_2$Cl$_2$, $\lambda_{exc} = 420$ nm) of the reference porphyrin 2a (2 µM), and of the dimers 1a-1c (1 µM): $\lambda_{em}$, nm 652, 718 (2a); 654, 718 (1a); 655, 718 (1b); 655, 719 (1c).

Fig. 7. Schematic depiction of the intended metallacyclic assemblies with a parallelepiped shape, in which four dimers 1b are coordinated via the peripheral pyridyl groups to eight 90° metal fragments.
Fig. 1.
Fig. 2.

2a: \( R_1 = -C\equiv C-H \); \( R_2 = (OCH_2CH_2)_3OCH_3 \)
2b: \( R_1 = R_2 = -C\equiv C-H \)
2c: \( R_1 = R_2 = (OCH_2CH_2)_3OCH_3 \)

3a: \( R_1 = I \); \( R_2 = (OCH_2CH_2)_3OCH_3 \)
3b: \( R_1 = R_2 = I \)
Scheme 1.
Scheme 2.
Scheme 3.

2a + 3a → Pd(PPh)₄, Et₃N, DMF, THF, μWave 120 °C, 1h

3a + 3a → Pd(PPh)₄, Et₃N, DMF/THF, μWave 120 °C, 1h

1a (24%)
Fig. 3.
Fig. 4.
Fig. 5.
Fig. 6.
Fig. 7.

Legend:

- porphyrin donor
- metal complex
A small library of symmetric trans-di-(4-pyridyl)porphyrin dimers have been prepared. The porphyrin dimers are differentiated by a phenyl-alkynyl bridge of increasing length at one meso position, while for all the derivatives the two remaining opposite meso positions are tailored with a phenyl moiety bearing a short polyether chain.