Inorganic Chemistry
COMMUNICATION
pubs.acs.org/IC

Synthesis of New Metalloporphyrin Triads: Efficient and Versatile Tripod Optical Sensor for the Detection of Amines[†]

Sara M. A. Pinto, Mirtha A. O. Lourenço, Mário J. F. Calvete, Artur R. Abreu, Mário T. S. Rosado, Hugh D. Burrows,* and Mariette M. Pereira*

Departamento de Química, Universidade de Coimbra, Coimbra, Portugal

S *Supporting Information*

ABSTRACT: Zinc and manganese complexes of porphyrin triads have been synthesized and are shown to be efficient as highly sensitive and selective tripod optical sensors for amines at the picomolar level.

Dendron-type materials are of current interest for a multitude of applications.[1−5] Their unique structural features can be tailored and controlled; the size and shape of the molecule and the orientation of the functional groups, arising from their three-dimensional architecture, can be designed for specific applications.[6]

Multiporphyrin arrays have also been the focus of considerable attention, resulting, in particular, from possibilities of incorporating multiple functionalities,[7,8] designed specifically for advanced applications, including molecular optoelectronic gates,[9] molecular photonic wires,[10] optical switches,[11] and light-harvesting arrays.[5] Because dendritic architectures allow for maximum interactions between the chromophores, the construction of branched multiporphyrin structures seems to provide an efficient and alternative approach for the synthesis of porphyrin triads,[12] which will maximize these interactions by taking advantage of the synergy between the individual porphyrin constituents.

We report a straightforward methodology for the preparation of a tripodal porphyrin system, linked through the branched triol tris(hydroxymethyl)ethane, an interesting starting material for the design of hyperbranched dendritic compounds.[13] Combining a strongly interacting system with a highly conjugated structure, whose electronic distribution, in either central or radial porphyrin sites,[14] changes after interaction with a toxic analyte (e.g., amines) are expected to allow sensing of low concentrations of these chemicals. Amine detection is of particular importance[15] because both aliphatic and aromatic amines can induce toxicological responses at low concentrations.[16] Aliphatic amines are found in many wastewater effluents from industry, agriculture, pharmaceuticals, and food processing,[17] and their easy detection is valuable in environmental and industrial monitoring, food quality control, etc.[18]

The synthesis of compound **3** was accomplished via the nucleophilic substitution reaction of tris(triflate) ether (**2**)[19] with 5-(3-hydroxyphenyl)-10,15,20-triphenylporphyrin (**1**),[20] using Cs_2CO_3 as the base and dimethylformamide (DMF) as the solvent and gave the triad **3** in 42% yield (Scheme 1). Metalation of the porphyrin cavity was achieved by reflux with an excess of $Zn^{II}OAc_2$ or $Mn^{II}OAc_2$ during approximately 5 h. After appropriate workup, the corresponding metalloporphyrin triads **3a** and **3b** were obtained in 79% and 74% yield, respectively. Characterization of the systems was achieved using MS, NMR, and UV−vis.[21]

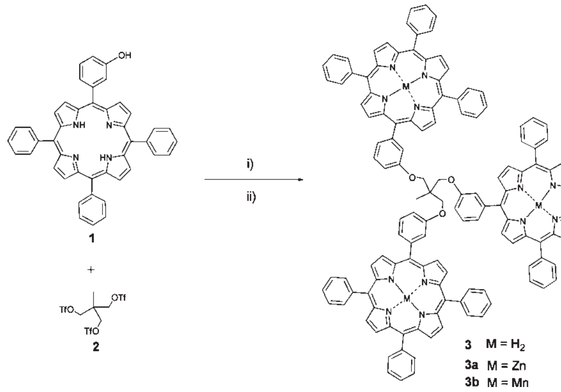
Full geometry optimization computational studies were carried out for several possible conformers of compound **3**, using the semiempirical PM6 Hamiltonian[22] available in MOPAC2009.[23] This focused on a relatively large number of conformers with different spatial organization levels, ranging from C_3-symmetry conformers in syn and anti configurations with M orientation[24] to unsymmetrical (C_1), termed nonorganized forms. We found that the differences in the heats of formation between the lowest-energy conformers found for each of the C_3- and C_1-symmetry forms are relatively small, ca. 1 kcal/mol, showing that there is not a large stability difference between them (Figure 1 and Supporting Information, SI).

We have looked at the effect on the UV−vis spectra, recorded in tetrahydrofuran (THF), of various structurally different amines to test the synergic effect of the zinc(II) triad complex **3a** as an optical sensor. Picomolar quantities of amines, with open aliphatic chain (primary, secondary, and tertiary), secondary cyclic (piperidine), tertiary cyclic (1,4-diazabicyclo[2.2.2]octane, DABCO), and aromatic (pyridine) structures, were successively added. The addition of amines leads, in most cases, to a 6 nm bathochromic shift, except in the cases of pyridine (3 nm) and triethylamine, where no change was observed. For example, with piperidine, it was observed that the change in the zinc(II) complex (as the triad) in UV−vis spectra started after the addition of 13 pmol of piperidine to a solution containing 9.3×10^{-7} mol of the zinc(II) triad (Figure SI1 in the SI); with dimethylamine and methylamine, a similar shift was observed after the addition of 2 nmol and 20 pmol, respectively, while DABCO required the addition of 100 pmol. In contrast, with triethylamine no change was observed. These UV−vis spectral changes were accompanied by similar modifications in the NMR spectra (Figure 2) and were consistent with changes in the electron density in the porphyrin ring caused by amine binding to the metal ion. However, it is worth noting that only a gradually shifting single set of peaks is observed for the β protons of the triad. This indicates that the three porphyrin moieties are equivalent on the NMR time scale, indicating fast ligand exchange.

The actual dynamic binding equilibrium appears to be complex and may involve more than one species (Figure SI3 in the SI).

Received: April 8, 2011
Published: August 05, 2011

Scheme 1. Synthesis of the Triads 3, 3a, and 3b[a]



[a] Reagents and conditions: (i) for **3**, Cs_2CO_3, DMF, RT, 48 h; (ii) for **3a** (M = Zn): $Zn(OAc)_2$, DME, 70 °C, 5 h (1:8 porphyrin/salt); for **3b** (M = Mn): $Mn(OAc)_2$, DME, 70 °C, 5 h (1:10 porphyrin/salt).

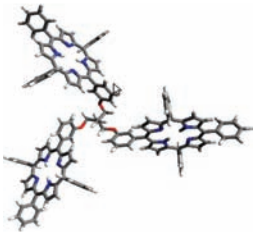


Figure 1. PM6 calculation for a C_3 syn M-oriented lowest-energy conformer (blue, gray, red, and white represent nitrogen, carbon, oxygen, and hydrogen, respectively).

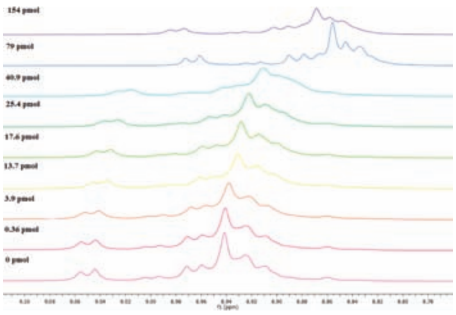


Figure 2. Chemical shift variation (^1H NMR) from the porphyrinic β protons of the zinc(II) porphyrin triad **3a**, resulting from titration with piperidine [initial quantity of zinc(II) triad = 9.3×10^{-7} mol; the solvent was THF].

A binding constant was calculated for piperidine using UV−vis data and gave a value of $K_{assoc} = 9.8 \times 10^4\ M^{-1}$ (λ = 401 nm). However, $10^5\ M^{-1}$ values for K_{assoc} seem to be the limit for NMR titration experiments[25] and therefore no binding constant was calculated in this case.

We have also carried out a UV−vis study on the effect of amine with the corresponding manganese(III) porphyrin acetate triad to test its potential in sensing applications. This shows the typical 474 nm absorption band of manganese(III) porphyrins, while no signal was seen in the NMR spectrum, suggesting the species is paramagnetic, in agreement with this oxidation state.[26] As with the zinc(II) complex, successive additions of amine lead to alterations in the UV−vis spectra, in all cases, except with pyridine and triethylamine. However, the spectral changes were much more pronounced than those with the zinc(II) complex, with a 35 nm hypsochromic shift of the B-band maximum, upon addition of methylamine, whose progress can be seen in Figure 3.

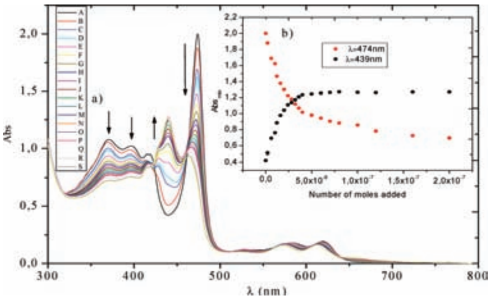


Figure 3. UV−vis titration of **3b** with methylamine, recorded in THF. Number of moles of amine added ($\times 10^{-8}$ mol): A, 0; B, 0.2; C, 0.6; D, 1; E, 1.2; F, 1.6; G, 2; H, 2.4; I, 2.8; J, 3.2; K, 3.6; L, 4; M, 5; N, 6; O, 7; P, 8; Q, 9.6; R, 10; S, 12. (b) Graphical response upon amine addition at λ = 439 and 474 nm (initial number of moles of the manganese(III) triad = 4.7×10^{-7} mol).

Similar behavior was observed with the other amines tested, but with differences in the sensitivity. The detection limit proved to be the lowest (highest sensitivity) for the case of methylamine, where 2 nmol was necessary to induce a minimal spectral change in a solution containing 4.7×10^{-7} mol of the manganese(III) triad. The association constant with methylamine, determined from UV−vis spectra, gave a value of $K_{assoc} = 7.71 \times 10^4\ M^{-1}$ (λ = 474 nm).

To confirm the synergic effect of the manganese(III) triad, we tested the manganese tetraphenylporphyrin (Mn^{III}TPP acetate) and found that the sensing effect comes purely from the triad system because only small changes in the spectrum of Mn^{III}TPP were observed upon the incremental addition of methylamine (λ = 474 nm, $K_{assoc} = 4.5 \times 10^1\ M^{-1}$). With both ions (Zn and Mn), chosen as representative transition-metal ions (having di- and trivalent oxidation states), no significant changes were observed upon the addition of amines to the corresponding monomeric zinc or manganese tetraphenylporphyrins, while marked spectral changes were seen with the triads, confirming the synergic effect of the dendritic architectural structure, which allows for excellent interaction between the chromophores and really establishes our intended *pièce de résistance*. In addition, differences were observed in both the wavelength shifts and sensitivity with the type of amine studied, which implies selectivity for these systems. The two triads can readily be combined in a colorimetric sensor array,[27] to combine high sensitivity with selectivity for amine detection.

In conclusion, zinc(II) and manganese(III) triads have been synthesized and are effective as selective high-sensitivity sensors for amines. With the reported triads, the dendron-type architecture leads to a synergic effect, as shown by an ca. 170-fold increase in binding, confirming amplification of the interactions between the porphyrin counterparts and between them and the bound substrates. These types of materials are likely to be important in sensing not only these types of amines but also other analytes. Work on this is currently underway.

In addition, the straightforward methodology used is currently being extended to more complex hyperbranched dendritic systems, with advanced materials applications.

■ ASSOCIATED CONTENT

Supporting Information. UV–vis spectra, titration results, and conformer analysis. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: mmpereira@qui.uc.pt (M.M.P.), burrows@ci.uc.pt (H.D.B.). Tel: +351239854474. Fax: +351239827703.

■ ACKNOWLEDGMENT

The authors thank the FCT and QREN/FEDER (COMPETE-Programa Operacional Factores de Competitividade) and PTDC/QUI-QUI/112913/2009 for funding. S.M.A.P. thanks the FCT for Ph.D. grant SFRH/BD/47022/2008.

■ DEDICATION

[†]Dedicated to Prof. Dr. Dr. h. c. Michael Hanack, on the occasion of his 80th birthday

■ REFERENCES

(1) Maes, W.; Dehaen, W. *Eur. J. Org. Chem.* **2009**, 4719.

(2) Li, W.-S.; Aida, T. *Chem. Rev.* **2009**, *109*, 6047.

(3) Caminade, A. M.; Hameau, A.; Majoral, J. P. *Chem.—Eur. J.* **2009**, *15*, 9270.

(4) Carlmark, A.; Hawker, C.; Hult, A.; Malkoch, M. *Chem. Soc. Rev.* **2009**, *38*, 352.

(5) D'Ambruso, G. D.; McGrath, D. V. *Adv. Polym. Sci.* **2008**, *214*, 87.

(6) Mongin, O.; Papamicael, C.; Hoyler, N.; Gossauer, A. *J. Org. Chem.* **1998**, *63*, 5568.

(7) Harvey, P. D. *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic Press/Elsevier: New York, 2003; Vol. 18, Chapter 113.

(8) Pereira, A. M. V. M.; Soares, A. R. M.; Calvete, M. J. F.; de la Torre, G. *J. Porphyrin Phthalocyanines* **2009**, *13*, 419.

(9) Ambroise, A.; Wagner, R. W.; Rao, P. D.; Riggs, J. A.; Hascoat, P. J.; Diers, R.; Seth, J.; Lammi, R. K.; Bocian, D. F.; Holten, D.; Lindsey, J. S. *Chem. Mater.* **2001**, *13*, 1023.

(10) Jurow, M.; Schuckman, A. E.; Batteas, J. D.; Drain, C. M. *Coord. Chem. Rev.* **2010**, *254*, 2297.

(11) O'Neil, M. P.; Niemczyk, M. P.; Svec, W. A.; Gosztola, D.; Gaines, G. L., III; Wasielewski, M. R. *Science* **1992**, *257*, 63.

(12) Takai, A.; Chkounda, M.; Eggenspiller, A.; Gros, C. P.; Lachkar, M.; Barbe, J.-M.; Fukuzumi, S. *J. Am. Chem. Soc.* **2010**, *132*, 4477.

(13) Hecht, S.; Emrick, T.; Fréchet, J. M. J. *Chem. Commun.* **2000**, 313.

(14) Dunbar, A. D. F.; Brittle, S.; Richardson, T. H.; Hutchinson, J.; Hunter, C. A. *J. Phys. Chem. B* **2010**, *114*, 11697.

(15) Mizutani, T.; Wada, K.; Kitagawa, S. *J. Org. Chem.* **2000**, *65*, 6097.

(16) DeBorba, B. M.; Rohrer, J. S. *J. Chromatogr. A* **2007**, *1155*, 22.

(17) Gong, W.-L.; Sears, K. J.; Alleman, J. E.; Blatchley, E. R., III *Environ. Toxicol. Chem.* **2004**, *23*, 239.

(18) Shakila, R. J.; Vijayalakshmi, K.; Jeyasekaran, G. *Food Chem.* **2003**, *82*, 347.

(19) Synthesis of Tris(triflate) Ether 1,3-Bis[[(trifluoromethyl)-sulfonyl]oxy]-2-[(trifluoromethyl)sulfonyl]oxy]-2-methylpropane (**2**): In a 100 mL round-bottomed flask containing a solution of 2-(hydroxymethyl)-2-methylpropane-1,3-diol (0.5 g, 4.2×10^{-3} mol) in dry CH_2Cl_2 (15 mL) at 0 °C was sequentially added 5 mL of dry triethylamine and triflic anhydride (3.5 mL, 2.0×10^{-2} mol). The reaction was left for 12 h at room temperature in a N_2 environment. The solvent was then evaporated, and silica gel column chromatography was used with CH_2Cl_2 as the eluent to purify the compound (1.6 g, 74%). HRMS (ESI-TOF): m/z_{calcd} 538.9163, m/z_{found} 538.9157 ($[M + Na]^+$). ^1H NMR (250 MHz, $CDCl_3$): δ 3.40 (s, 6H, $C\underline{H}_2$), 0.95 (s, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$): δ 118.5, 72.8, 34.1, 18.1.

(20) Gonsalves, A. M. A. R.; Varejão, J. M. T. B.; Pereira, M. M. *J. Heterocycl. Chem.* **1991**, *28*, 635.

(21) (a) Synthesis of the Triad 1,3-bis[5-(3-hydroxyphenyl)-10,15,20-triphenylporphyrin]-2-[5-(3-hydroxyphenyl)-10,15,20-triphenylporphyrin]-2-methylpropane (**3**): 5-(3-Hydroxyphenyl)-10,15,20-triphenylporphyrin (0.100 g, 0.158 mmol, 1 equiv) and Cs_2CO_3 (0.3 g, 0.948 mmol, 6 equiv) were dissolved in 2 mL of DMF. The mixture was stirred for 0.5 h at room temperature, and then **2** (0.02 g, 0.036 mmol, $^1/_4$ equiv) was added dropwise. The mixture was then allowed to stand for 48 h at room temperature. The crude material was extracted with CH_2Cl_2/H_2O (five times), and the organic phase was dried with sodium sulfate and evaporated. For purification, silica gel column chromatography was used with CH_2Cl_2 as the eluent. The trimer was recrystallized from CH_2Cl_2/*n*-hexane (42 mg, 42%). HRMS (ESI-TOF): m/z_{calcd} 978.3864, m/z_{found} 979.3937 ($[M]^{2+)}$. ^1H NMR (300 MHz, $CDCl_3$): δ 8.82–8.69 (m, 24H, β-H), 8.23–8.02 (m, 18H, *o*-H, 10,15,20-Ph), 7.83 (s, 3H, *o*-H, 5-Ph), 7.77–7.52 (m, 27H, *m,p*-H 10,15,20-Ph), 7.50–7.49 (m, 6H, *o,m*-5-Ph), 7.34–7.33 (*m*, 3H, *p*-H, 5-Ph), 4.41 (s, 6H, $-CH_2$), -2.82 (s, 6H, $-NH$). UV–vis (THF): 420 ($\varepsilon = 6.99 \times 10^5$ mol^{-1} dm^3 cm^{-1}), 514 ($\varepsilon = 3.06 \times 10^4$ mol^{-1} dm^3 cm^{-1}), 549 ($\varepsilon = 1.42 \times 10^4$ mol^{-1} dm^3 cm^{-1}), 591 ($\varepsilon = 8.72 \times 10^3$ mol^{-1} dm^3 cm^{-1}), 647 ($\varepsilon = 6.34 \times 10^3$ mol^{-1} dm^3 cm^{-1}), 549 ($\varepsilon = 1.42 \times 10^4$ mol^{-1} dm^3 cm^{-1}), ($\varepsilon = 1.16 \times 10^3$ mol^{-1} dm^3 cm^{-1}). (b) General Procedure for the Preparation of zinc and manganese complexes **3a** and **3b**: The porphyrin triad **3** (0.100 g, 1 equiv) was dissolved in dimethoxyethane (DME), and an excess of the salt was added [for the zinc complex, zinc acetate (eight times) was used, and for the manganese complex, manganese acetate (10 times) was used]. The mixture was allowed to stand for 5 h at 70 °C (for zinc) and 80 °C (for manganese) and controlled by UV–vis. The crude material was extracted with CH_2Cl_2/water several times and dried with Na_2SO_4. The crude material was purified using silica gel column chromatography with CH_2Cl_2 as the eluent. **3a**: 82 mg, 79%. HRMS (MALDI-TOF): m/z_{calcd} 2149.5093; m/z_{found} 2149.4940 ($[M + H]^{+)}$. ^1H NMR (300 MHz, $CDCl_3$): δ 8.82–8.69 (m, 24H, β-H), 8.23–8.02 (m, 18H, *o*-H, 10,15,20-Ph), 7.83 (s, 3H, *o*-H, 5-Ph), 7.77–7.52 (m, 27H, *m,p*-H, 10,15,20-Ph), 7.50–7.49 (m, 6H, *o,m*-5-Ph), 7.34–7.33 (*m*, 3H, *p*-H, 5-Ph), 4.41 (s, 6H, $-CH_2$). UV–vis (THF): 424 ($\varepsilon = 2.57 \times 10^5$ mol^{-1} dm^3 cm^{-1}), 555 ($\varepsilon = 1.13 \times 10^4$ mol^{-1} dm^3 cm^{-1}), 595 ($\varepsilon = 4 \times 10^3$ mol^{-1} dm^3 cm^{-1}). **3b**: 72 mg, 74%. HRMS (MALDI-TOF): m/z_{calcd} 2259.1510, m/z_{found} 2259.1440 ($[M + Na]^+$). UV–vis (THF): 474 ($\varepsilon = 1.11 \times 10^4$ mol^{-1} dm^3 cm^{-1}), 583 ($\varepsilon = 1.05 \times 10^3$ mol^{-1} dm^3 cm^{-1}), 619 ($\varepsilon = 1.16 \times 10^3$ mol^{-1} dm^3 cm^{-1}).

(22) Stewart, J. J. P. *J. Mol. Model.* **2007**, *13*, 1173.

(23) Web link http://openmopac.net/.

(24) Reetz, M. T.; Guo, H.; Ma, J.-A.; Goddard, R.; Mynott, R. J. *J. Am. Chem. Soc.* **2009**, *131*, 4136.

(25) Thordarson, P. *Chem. Soc. Rev.* **2011**, *40*, 1305.

(26) Chylarecka, D.; Kim, T. K.; Tarafder, K.; Müller, K.; Gödel, K.; Czekaj, I.; Wäckerlin, C.; Cinchetti, M.; Ali, Md. E.; Piamonteze, C.; Schmitt, F.; Wüstenberg, J.-P.; Ziegler, C.; Nolting, F.; Aeschlimann, M.; Oppeneer, P. M.; Ballav, N.; Jung, T. A. *J. Phys. Chem. C* **2011**, *115*, 1295.

(27) Feng, L. A.; Musto, C. J.; Kemling, J. W.; Lim, S. H.; Zhong, W.; Suslick, K. S. *Anal. Chem.* **2010**, *82*, 9433.