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Novel porphyrinic peptides with assigned sequence of metallated chromophores, a further step towards redox switches

Nicolas Aubert, Vincent Troiani, Maurice Gross and Nathalie Solladié*

Laboratoire d'Electrochimie et de Chimie Physique du Corps Solide, Université Louis Pasteur et CNRS, 4 rue Blaise Pascal, 67000 Strasbourg, France

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Abstract—This paper reports the synthesis and the characterization of peptides encompassing an assigned sequence of chromophores. The obtained pentaporphyrin is expected to be a good candidate for the elaboration of redox switches.

The processing of information at the molecular level, and the controlled elaboration of nano-materials such as photonic or electronic wires capable of excited-state energy transfer or electron-transfer processes are nowadays attracting growing interest.[1] In particular considerable efforts are dedicated to the elaboration of molecular switches through the development of new bi-functional compounds able to properly generate or inhibit a signal in a controlled manner.[2] Such a signal may be, for instance, the emission of an electromagnetic wave by pigment molecules such as porphyrins, which thus appear as good candidates for the elaboration of photonic logical gates. In such wires, directing the excited-state energy transmission towards a non-luminescent bi-functional switch site and gating the energy transfer process towards this component of the molecule will allow the emission to be switched on/off in a controlled manner. In this spirit, we have recently synthesized the pentapeptide represented on Fig. 1. The peptidic backbone allowed the elaboration of this pen-

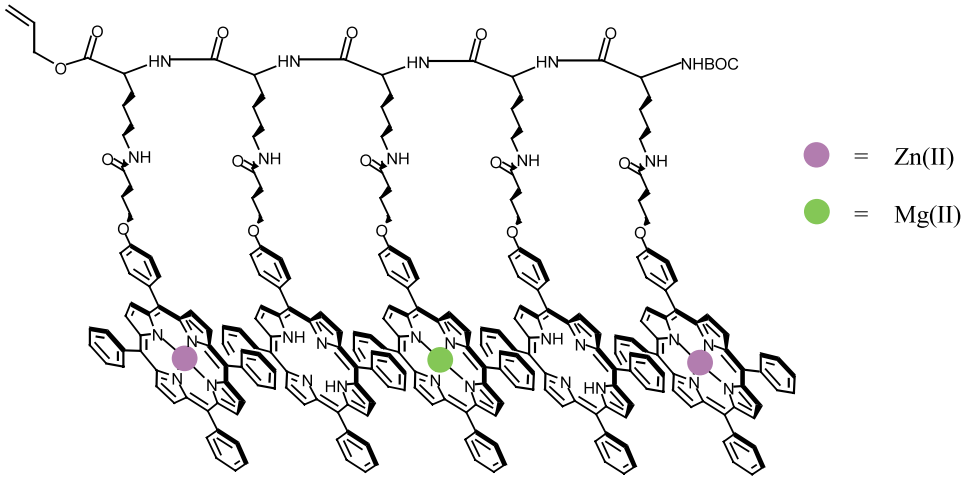

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Figure 1. The pentapeptide **1** was obtained by oligomerization of a lysine derivative functionalized by various porphyrins, either metallated or not. Substituents on the tetraphenylporphyrins are omitted here for clarity.

* Corresponding author. Fax: 33 3 90 24 14 31; e-mail: nsolladie@chimie.u-strasbg.fr

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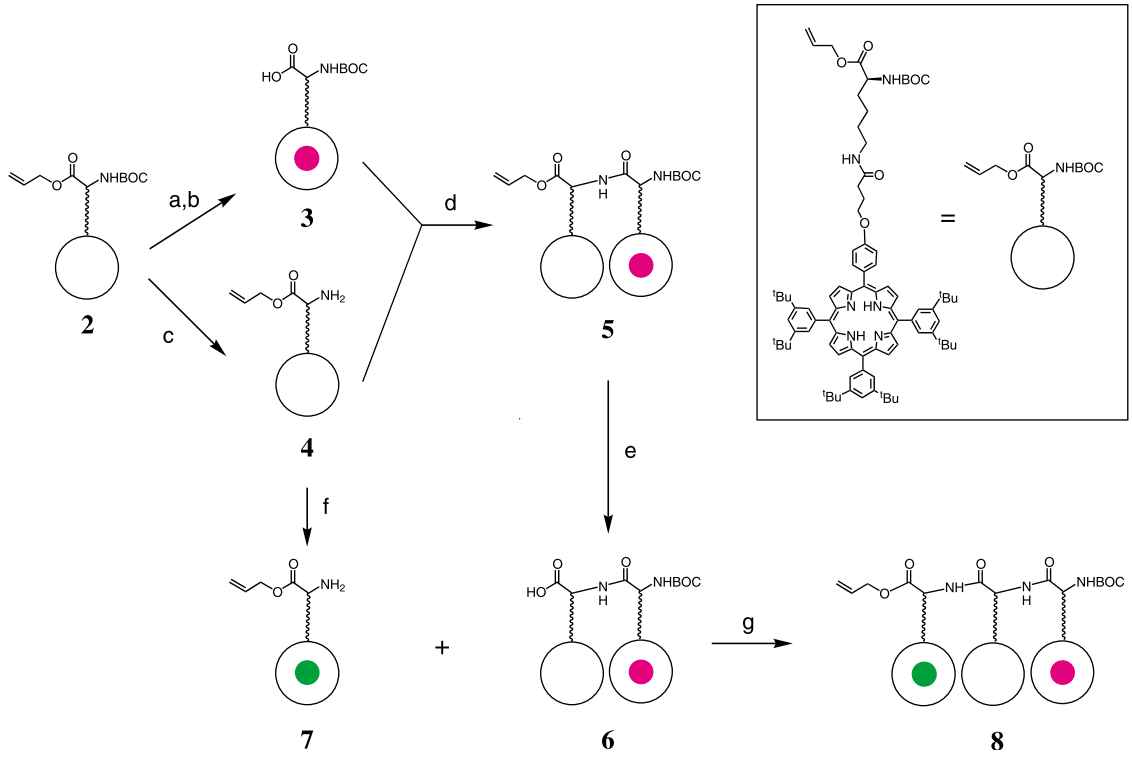
taporphyrin with an assigned sequence of chromophores (**1**), through the synthesis of a peptide built according to a pre-determined sequence of amino-acids holding porphyrin-functionalized lateral chain.[3]

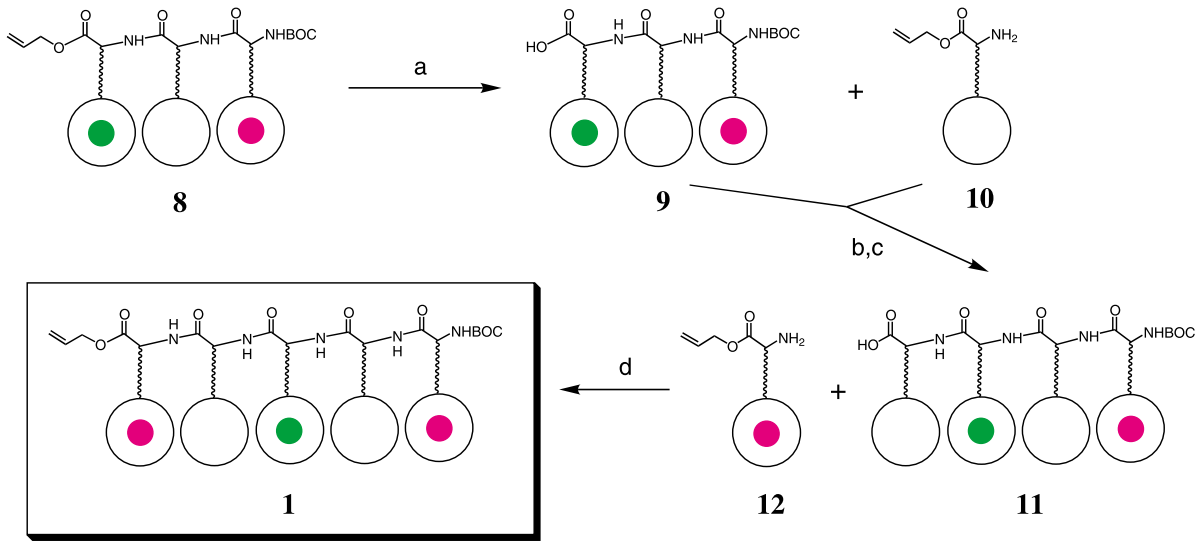
Since the physico-chemical properties of a molecule depends on its structure among other features, a peptide with a symmetrical environment of metallated porphyrins around a unique Mg(II) core chromophore has been chosen, so as to combine both antenna effect and bi-functionality of the central Mg(II) porphyrin. Indeed, a Mg(II) porphyrin in its oxidized non-luminescent form has a first singlet excited state which lies lower than the first singlet excited state of a free-base porphyrin, and is therefore a perfect switching site candidate. We thus expect that the photonic energy collected on both ends of the pentapeptide **1** by the two Zn(II) porphyrins will be transferred towards the central oxidized Mg(II) chromophore. Hence, energy transfer from the free-base porphyrins to the Mg(II) core chromophore should be inhibited or permitted depending on the oxidation state of the latter. Such a control of the energy transfer path via electrochemical control of the redox state of the Mg(II) porphyrin should allow an on/off switching of the luminescence of the compound.

The preparation of the multi-porphyrinic peptide **1** is depicted in Schemes 1 and 2. It is based on the oligomerization of a porphyrin functionalized lysine derivative bearing either a free-base (**2**)[3] or a metallated chromophore. To preclude any demetallation of the porphyrins during the course of the acidic cleavage of the BOC protecting group, the peptide growth was realized at the C-terminus. After metallation of the free-base porphyrin of the lysine derivative **2** with zinc acetate in refluxing chloroform, compound **3** was obtained by selective deprotection of the carboxylic acid under basic conditions with an overall yield of 91% (Scheme 1).[4] Meanwhile, cleavage of the BOC protecting group of **2** in a 1 M dichloromethane solution of trimethylsilylchloride and phenol at room temperature for 6 h 30 min gave compound **4** in 91% yield.[5] A peptidic coupling reaction was then realized between the latter free primary amine (**4**) and the carboxylic acid **3** in dichloromethane in the presence of *N*,*N*′-dicyclohexylcarbodiimide (DCC) and 1-hydroxybenzotriazole (HOBT) for one night at room temperature.[6] Dimer **5**, bearing the free-base porphyrin at the C-terminus, was obtained in 80% yield.

After having quantitatively cleaved the allyl ester of **5** in a 4/1 mixture of dimethylacetamide/piperidine in the presence of a catalytic amount of tetrakistriphenylphosphine palladium(0) at room temperature for 6 h, an amino-acid bearing a Mg(II) porphyrin (**7**) was coupled at the C-end of the dipeptide under similar conditions as those used for the synthesis of dimer **5**. It is worth noting that the Mg(II) cation was introduced into the porphyrinic ring after deprotection of the amino group. Indeed, a Mg(II) porphyrin is acid sensitive[7] and this cation is too labile to survive the acidic conditions required for the cleavage of the BOC group. The tripeptide **8** was thus obtained in 85% yield.



Scheme 1. (a) $Zn(OAc)_2{\cdot}2H_2O$, $CHCl_3$, reflux, 3 h, 92%. (b) $Pd(PPh_3)_4$, piperidine/DMA 1/5, rt, 3 h, 99%. (c) Me_3SiCl, PhOH, CH_2Cl_2, rt, 6 h 30 min, 91%. (d) DCC, HOBT, CH_2Cl_2, rt, overnight, 80%. (e) $Pd(PPh_3)_4$, piperidine/DMA 1/5, rt, 6 h, 99%. (f) MgI_2, $NEt(^iPr)_2$, CH_2Cl_2, rt, 45 min, 71%. (g) DCC, HOBT, CH_2Cl_2, rt, overnight, 85%. The pink dots stand for Zn(II) cations and the green dots for Mg(II) cations.



Scheme 2. (a) Na_2CO_3, THF/H_2O, reflux, 7 days. (b) DCC, HOBT, CH_2Cl_2, rt, overnight, 45%. (c) Na_2CO_3, THF/H_2O, reflux, 7 days, 90%. (d) DCC, HOBT, CH_2Cl_2, rt, overnight, 64%. The pink dots stand for Zn(II) cations and the green dots for Mg(II) cations.

The preparation of pentamer **1** was then realized by following a similar synthetic strategy based on the C-end oligomerization of other amino-acids. However, cleavage of the allyl ester of trimer **8** required harsher basic conditions. Indeed, deprotection of the carboxylic acid was performed in a mixture THF/H_2O, in the presence of sodium carbonate under reflux for 7 days. We believe this may be due to the presence of the Mg(II) porphyrin, since no particular difficulty was encountered for the cleavage of the allyl ester of the free-base tetramer[3] and octamer.[8] Besides, the tendency of the Mg(II) porphyrin to accept axial ligands such as carboxylates probably explains the unusually low yield observed for the peptidic coupling of the deprotected trimer **9** with the free-amine **10**.[7] Even though similar reaction conditions were used for the synthesis of both the heterodipetide **5** or higher oligomers in the free-base family,[3] the desired tetramer was obtained in only 45% yield. Pentapeptide **1** was finally obtained in 64% yield by realizing one more peptidic coupling between the carboxylic acid **11** and the free-amine **12**. The recovery of a better yield was ascribed to the larger distance which exists between the free carboxylic function and the Mg(II) porphyrin in **11** when compared to compound **9**. Pentapeptide **1** was purified by column chromatography on silica gel (CH_2Cl_2 containing 0.1% of NEt_3 was used as eluent to avoid demetallation of the Mg(II) porphyrin), and by gel permeation chromatography (GPC) in toluene. Compound **1** was characterized by FAB mass spectrometry (6124.4, $[M]^+$, calcd 6125.5), ^1H NMR and UV–vis spectroscopy (Fig. 2).

The comparison of the absorption spectrum of pentapeptide **1** with the sum of the absorption spectra of

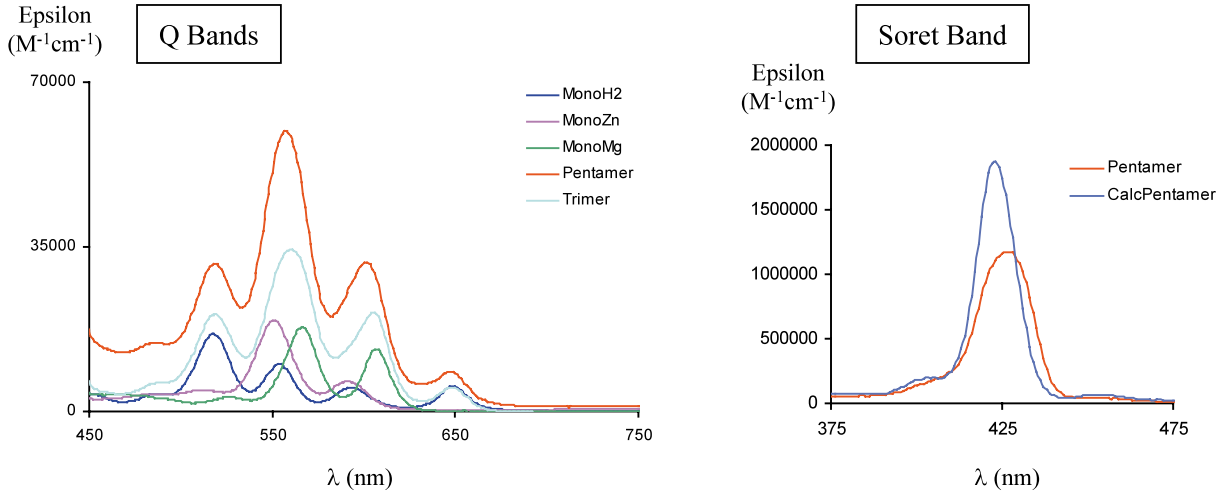


Figure 2. *Q bands:* UV–vis spectra of the three monomers (free-base, Mg(II) and Zn(II)), trimer **8** and pentamer **1**. *Soret band:* comparison of the absorption spectrum of pentamer **1** (red) with the sum of the absorption spectra of two Zn(II) monomers, two free-base monomers and one Mg(II) monomer (blue).

the components shows, as expected, a close match of the spectra in the Q band region. However, the latter comparison highlights a 5 nm broadening of the Soret band (Fig. 2), which documents the existence of some interaction between the porphyrins. The chromophores probably adopt a more or less parallel conformation allowing them to come in close proximity: if this orientation was absent, these porphyrins, which are held together by a non-conjugated peptidic backbone, would be unable to exhibit any electronic coupling. Such interactions are expected to favor energy transfers along the pentapeptide by decreasing as much as possible the inter-chromophore distances. We therefore have confidence in the potential redox switching capabilities of pentapeptide **1**. Gating studies on this peptide, as well as the determination of its physico-chemical properties, are currently under way.

The use of a new porphyrin functionalized amino-acid for the elaboration of peptides bearing an assigned sequence of chromophores is documented here through the synthesis and characterization of a pentaporphyrin. This polyporphyrin is expected to be a good candidate as a redox switching device. We anticipate that in such a device, the energy transfer process will be selectively gated by one-electron alteration of the redox state of the Mg(II) core porphyrin, thus enabling an electrochemical control of the luminescence.

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References

1. (a) Nakano, A.; Osuka, A.; Yamazaki, T.; Nishimura, Y.; Akimoto, S.; Yamazaki, I.; Itaya, A.; Murakami, M.; Miyasaka, H. *Chem. Eur. J.* **2001**, *7*, 3134–3151; (b) Ambroise, A.; Wagner, R. W.; Rao, P. D.; Riggs, J. A.; Hascoat, P.; Diers, J. R.; Seth, J.; Lammi, R. K.; Bocian, D. F.; Holten, D.; Lindsey, J. S. *Chem. Mater.* **2001**, *13*, 1023–1034; (c) Nakano, A.; Yamazaki, T.; Nishimura, Y.; Yamazaki, I.; Osuka, A. *Chem. Eur. J.* **2000**, *6*, 3254–3271; (d) Wagner, R. W.; Lindsey, J. S. *J. Am. Chem. Soc.* **1994**, *116*, 9759–9760; (e) Anderson, H. L. *Inorg. Chem.* **1994**, *33*, 972–981.
2. (a) De Silva, A. P.; Gunaratne, H. Q. N.; Gunnlaugsson, T.; Huxley, A. J. M.; McCoy, C. P.; Rademacher, J. T.; Rice, T. E. *Chem. Rev.* **1997**, *97*, 1515–1566; (b) Asakawa, M.; Ashton, P. R.; Balzani, V.; Credi, A.; Hamers, C.; Mattersteig, G.; Montalti, M.; Shipway, A. N.; Spencer, N.; Stoddart, J. F.; Tolley, M. S.; Venturi, M.; White, A. J. P.; Williams, D. J. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 333–337; (c) Armaroli, N.; Eckert, J.-F.; Nierengarten, J.-F. *Chem. Commun.* **2000**, 2105–2106; (d) Wagner, R. W.; Lindsey, J. S.; Seth, J.; Palaniappan, V.; Bocian, D. F. *J. Am. Chem. Soc.* **1996**, *118*, 3996–3997; (e) Lammi, R. K.; Ambroise, A.; Wagner, R. W.; Diers, J. R.; Bocian, D. F.; Holten, D.; Lindsey, J. S. *Chem. Phys. Lett.* **2001**, *341*, 35–44; (f) Lammi, R. K.; Wagner, R. W.; Ambroise, A.; Diers, J. R.; Bocian, D. F.; Holten, D.; Lindsey, J. S. *J. Phys. Chem. B* **2001**, *105*, 5341–5352; (g) Plenio, H.; Aberle, C. *Chem. Eur. J.* **2001**, *7*, 4438–4446; (h) Tomohiro, Y.; Satake, A.; Kobuke, Y. *J. Org. Chem.* **2001**, *66*, 8442–8446; (i) Akasaka, T.; Otsuki, J.; Araki, K. *Chem. Eur. J.* **2002**, *8*, 130–136; (j) Lomoth, R.; Häupl, T.; Johansson, O.; Hammarström, L. *Chem. Eur. J.* **2002**, *8*, 102–110.
3. Solladié, N.; Hamel, A.; Gross, M. *Tetrahedron Lett.* **2000**, *41*, 6075–6078.
4. Stanley, M. S. *J. Org. Chem.* **1992**, *57*, 6421–6430.
5. Kaiser, E., Sr.; Tam, J. P.; Kubiak, T. M.; Merrifield, R. B. *Tetrahedron Lett.* **1988**, *29*, 303–306.
6. (a) Dandliker, P. J.; Diederich, F.; Gross, M.; Knobler, C. B.; Louati, A.; Sanford, E. M. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1739–1742; (b) Lindsey, J. S.; Prathapan, S.; Johnson, T. E.; Wagner, R. W. *Tetrahedron* **1994**, *50*, 8941–8968; (c) Kunz, H.; März, J. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1375–1377.
7. (a) Sanders, J. K. M.; Bampos, N.; Clyde-Watson, Z.; Darling, S. L.; Hawley, J. C.; Kim, H. J.; Mak, C. C.; Webb, S. J. In *The Porphyrin Handbook*; Kadish, K. M.; Smith, K. M.; Guilard, R., Eds.; Academic Press: San Diego, CA, 2000; Vol. 3, p. 5; (b) Lindsey, J. S.; Woodford, J. N. *Inorg. Chem.* **1995**, *34*, 1063–1069; (c) O'Shea, D. F.; Miller, M. A.; Matsueda, H.; Lindsey, J. S. *Inorg. Chem.* **1996**, *35*, 7325–7338.
8. Unpublished results.