New and Efficient Synthesis of Oligomeric Porphyrins *via* Stepwise Nucleophilic Substitution of Aminoporphyrins to Cyanuric Chloride

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Porphyrin oligomers ($\mathbf{P_n}$, n = 2, 3, 4, 5) were prepared by the nucleophilic substitution of amino porphyrin monomers to cyanuric chloride. In this method, two different porphyrins can be joined stepwise to 1,3,5-triazine ring in one-pot by choosing appropriate reaction temperatures. The reaction proceeded under relatively mild conditions (K_2CO_3 as a base, 61 °C) and in good yields (ca. 80%).

In biological systems, aggregation of several prosthetic groups and their coupled activity are ubiquitous strategy to construct catalytic reaction centers. A number of tetrapyrrole dimers and oligomers have been synthesized to construct artificial models for understanding these catalytic reactions.[1] Recently, these oligomeric tetrapyrroles are drawing much interest in terms of molecular engineering, as a promising method to invent a new functional system on molecular level. However, synthesis of such porphyrin oligomers usually requires long and tedious work. During last decade, convenient ways to synthesize such porphyrin assemblies have been sought for.[1d] We now report a new strategy to synthesize porphyrin oligomers, which are connected by 1,3,5-triazine rings (Figure 1).

The synthetic route of oligomeric porphyrins is shown in Scheme 1. The starting mono- and diaminoporphyrin (**1a** and **1b**) were prepared from bis(3-hexyl-4-methyl-2-pyrrolyl)methane and corresponding aldehyde in good yield (**1b**: 75% in 2 steps) under the conditions previously reported by others.[1c] Hexyl groups were introduced to enhance the solubility of oligomeric porphyrins in conventional organic solvents.

Substitution of cyanuric chloride by monoaminoporphyrin **1a** gave dimeric porphyrin $\mathbf{P_2}$ (Scheme 1). This reaction can be stopped at the monosubstitution stage by choosing reaction temperature.[2,3] The monosubstitution of cyanuric chloride by the aminoporphyrin rapidly occurred at around 0 °C. The second substitution, however, was very slow at room temperature, and it required higher temperature (61 °C).

Porphyrin dimer $\mathbf{P_2}$ was synthesized quantitatively by refluxing the THF solution of cyanuric chloride and aminoporphyrin (2.1 equiv.) with K_2CO_3. After purification by flash chromatography (silica gel, $CHCl_3$-EtOH-Et_3N) and recrystallization (from CH_2Cl_2-EtOH), $\mathbf{P_2}$ (R'=H) was obtained in 94% yield.[4] The *N*-trityl dimer ($\mathbf{P_2}$, R'=$NHCPh_3$) was synthesized from the corresponding protected monomer **1b**[5] in a similar manner (95%).[4] The dimer was further used for the synthesis of the corresponding porphyrin tetramer. After deprotection of the amino groups in $\mathbf{P_2}$ with HCl, the free amino dimer was again brought to the reaction with cyanuric chloride (2.0 equiv.) at lower temperature to give the resulting substitution product at the terminal amino groups. Without its isolation, the intermediate was mixed with aminoporphyrin **1a** (2.0 equiv. to $\mathbf{P_2}$) in THF. The mixture was heated with the base under reflux for 4 days to give the porphyrin tetramer $\mathbf{P_4}$[4] in a good yield (95% based on $\mathbf{P_2}$).

Porphyrin trimer $\mathbf{P_3}$ was synthesized from monomeric diaminoporphyrin **1c** and monoaminoporphyrin **1a** in a similar manner (85%).[4] From protected porphyrin trimer $\mathbf{P_3}$ (R'=$NHCPh_3$), we obtained the corresponding pentamer $\mathbf{P_5}$ in 45% isolated yield, by repeating deprotection and stepwise substitution as in the tetramer synthesis described above.[4]

The triazine-linked porphyrins demonstrated in this paper have several advantages over other ones reported previously. First, our method is remarkably economical in utilizing porphyrins. Each substitution step hardly gives any by-products arising from porphyrins. Starting aminoporphyrins can also be obtained in good yields from dipyrrolylmethane. Second, the coupling reactions can be controlled simply by the applied reaction temperature. By stepwise connection of porphyrin to the linker molecule, overall coupling reaction can be achieved in one pot. Third, porphyrins of various arrangement can be obtained by this synthetic method. In some preceding oligomer synthesis through one-step coupling methods,[1c-e] the resultant products were obtained as a mixture of several species, and the isolation of desired products was difficult.

Furthermore, each 1,3,5-triazine ring in these oligomeric porphyrins has a remaining chloride, which also can be substituted by various nucleophiles at higher temperature to introduce functional groups to the porphyrin oligomers. Using NH_4OH[6] or aminotriethylsilane,[7] amino groups were smoothly introduced at 110 °C in a good yield (ca. 90% for $\mathbf{P_4}$). Resultant 1,3,5-triaminotriazine (melamine) derivative is known as a good device for hydrogen-bonded molecular assemblies.[8]

We are currently working on the applications of these compounds.

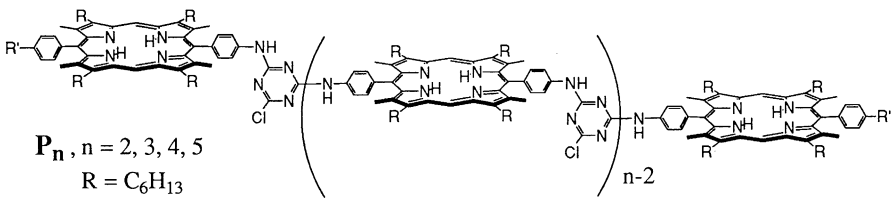
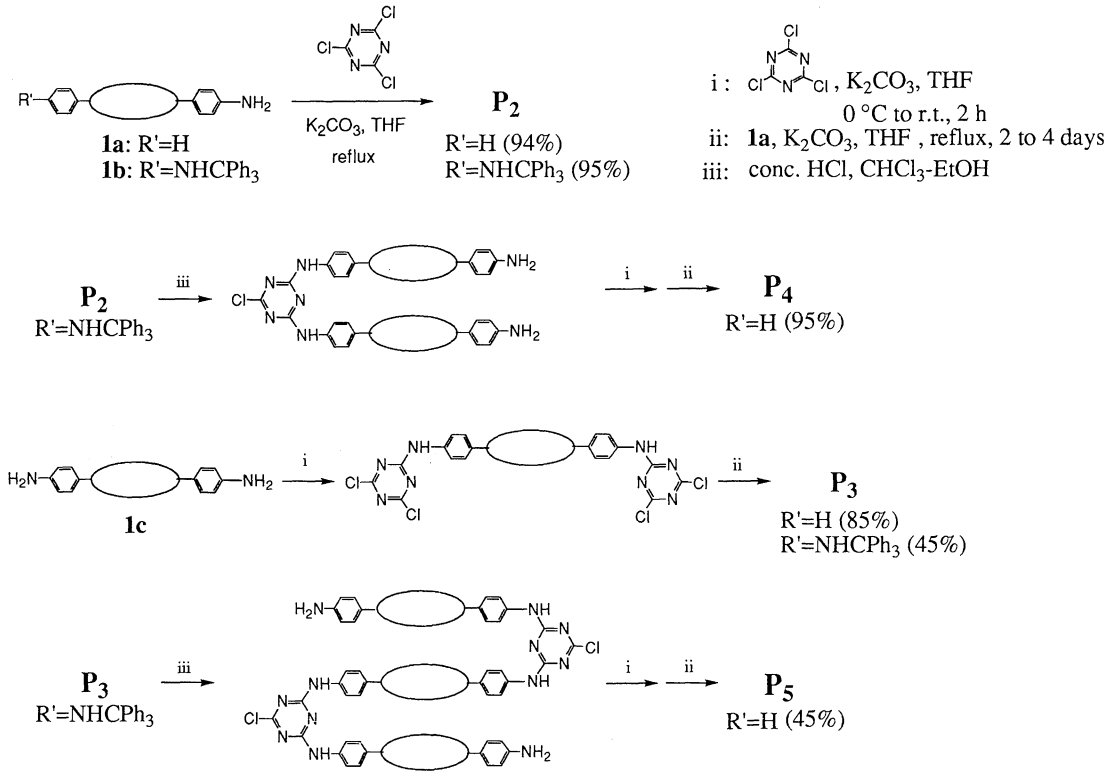


Figure 1. 1,3,5-Triazine-linked porphyrin oligomers.



Scheme 1.

References and Notes

1 a) G. M. Dubowchik and A. D. Hamilton, *J. Chem. Soc., Chem. Commun.*, **1987**, 293. b) J. Davila, A. Harriman, and L. R. Milgrom, *Chem. Phys. Lett.*, **136**, 427 (1987). c) T. Nagata, A. Osuka, and K. Maruyama, *J. Am. Chem. Soc.* , **112**, 3054 (1990). d) S. Prathapan, T. E. Johnson, and J. S. Lindsey, *J. Am. Chem. Soc.*, **115**, 7519 (1993) and references sited therein. e) H. L. Anderson, A. Bashall, K. Henrick, M. Mcpartlin, and J. K. M. Sanders, *Angew. Chem., Int. Ed. Engl.*, **33**, 429 (1994).

2 J. M. E. Quirke, In "Comprehensive Heterocyclic Chemistry," ed by A. R. Katritzky and C. W. Rees, Pergamon Press, New York (1984), Vol. 3, Part 2B, p. 457.

3 J. T. Turston, J. R. Dudley, D. W. Kaiser, I. Hechenbleikner, F. C. Schaefer, and D. Holm-Hansen, *J. Am. Chem. Soc.*, **73**, 2981 (1951).

4 All the compounds obtained were characterized by ^{1}H-NMR, mass, and UV-vis spectra. Selected spectroscopic data of **P$_2$-P$_5$** :

P$_2$ (R'=H): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.24-9.90 (4 H, meso-H), 8.10 (12 H, Ph), 7.73 (6 H, Ph), 3.98-3.54 (16 H, CH_2 of hexyl group), 2.58 (12 H, Me), 2.46 (12 H, Me), 2.26-1.86, 1.72-1.62. 1.54-1.22, 0.89 (24 H, CH_2 of hexyl group), –2.5 (4 H, pyr NH); MS (FAB) *m/z* 1947 $(M + H)^+$; UV-vis (THF) λ_{max} 416, 507, 545, and 579 nm.

P$_3$ (R'=H): ^{1}H NMR ($CDCl_3$) δ 10.3-9.8 (6 H, meso-H), 7.9 (16 H, Ph), 7.8-7.6 (10 H, Ph), 4.2-3.2 (28 H, CH_2 of hexyl group + NH), 2.7-2.4 (36 H, Me), 2.2-1.8 (24 H, CH_2 of hexyl group), 1.8-1.5 (24 H, CH_2 of hexyl group), 1.5-1.0 (48 H, CH_2 of hexyl group), 1.0-0.7 (36 H, CH_2 of hexyl group), –2.2- –2.6 (6 H, pyr NH); MS (FAB) *m/z* 2848 $(M + H)^+$; UV-vis (CH_2Cl_2) λ_{max} 410, 508, 541, 574, and 626 nm.

P$_4$ (R'=H): ^{1}H NMR ($CDCl_3$) δ 10.3-9.7 (8 H, meso-H), 8.2-7.8 (24 H, Ph), 7.8-7.5 (12 H, Ph), 4.3-3.3 (38 H, NH + CH_2 of hexyl group), 2.8-2.2 (48 H, Me), 2.3-1.8 (32 H, CH_2 of hexyl group), 1.8-1.4 (32 H, CH_2 of hexyl group), –2.1- –2.8 (8 H, pyr NH); MS (FAB) *m/z* 3845 $(M + H)^+$; UV-vis (CH_2Cl_2) λ_{max} 410, 508, 541, 575, 626, and 653 nm.

P$_5$ (R'=H): ^{1}H NMR ($CDCl_3$) δ 10.3-9.7 (10 H, meso-H), 8.2-7.8 (32 H, Ph), 7.8-7.4 (10 H, Ph), 4.1-3.3 (40 H, CH_2 of hexyl group), 2.7-2.3 (60 H, Me), 2.3-2.0 (40 H, CH_2 of hexyl group), 2.0-1.5 (40 H, CH_2 of hexyl group), 1.5-0.4 (140 H, CH_2 of hexyl group), –2.1- –2.8 (br, 10 H, pyr NH); MS (FAB) *m/z* 4843 $(M + H)^+$; UV-vis (CH_2Cl_2) λ_{max} 410, 508, 541, 575, 626, and 656 nm.

5 Monomer **1b** was easily obtained from diaminoporphyrin **1c** and tritylbromide (1.0 equiv.) in 50% yield.

6 C. T. Seto, J. P. Mathias, and G. M. Whitesides, *J. Am. Chem. Soc.*, **115**, 1321 (1993).

7 D. L. Bailey, L. H. Sommer, and F. C. Whitmore, *J. Am. Chem. Soc.*, **70**, 435 (1948).

8 As a review, J. C. McDonald, G. M. Whitesides, *Chem. Rev.*, **94**, 2383 (1994).