Templating Giants

DOI: 10.1002/anie.201103984

Vernier Templating of Nanoscopic Porphyrin Rings**

Arjan W. Kleij*

macrocycles · nanorings · porphyrins ·
supramolecular chemistry · Vernier templating

In nature, DNA replication constitutes a well-known template-assisted process, in which each individual strand of the original DNA serves as a template[1] for production of the complementary strand. Templation is now widely recognized as a means to selectively connect different components with each other, thereby increasing molecular complexity and function.[2] However, upon increasing the dimensions of the synthetic target, larger and more complex template molecules are required. Such sophisticated templates[3] are, however, not always (easily) available, and thus the selective preparation of architectures beyond the nanosize becomes incredibly challenging. An elegant solution for this problem is the use of Vernier complexes; this approach makes use of the difference in the number of binding sites in the templating agent and the molecular building blocks that are programmed to be coupled. In Vernier complexes, the number of binding sites is the lowest common multiple between the host (that needs to be coupled) and guest (template) system, and thus smaller and simpler template molecules may selectively give access to relatively large structures (Figure 1) using relative little synthetic input. Although Vernier templating has all the characteristics of a powerful tool for the creation of molecular complexity, surprisingly only a few synthetic examples have been reported to date.[4,5]

A recent contribution from Anderson and co-workers[6] now elegantly describes the use of Vernier templating for the preparation of a very large π-conjugated macrocycle (i.e., a nanoring), which is difficult to prepare using conventional approaches. As building block, a linear tetrameric Zn^{II} porphyrin (**1**) complex with two terminal acetylene functions was considered, and a hexapyridyl template **4** was applied to produce the [3+2] Vernier complex (Scheme 1). The key binding motif is the Zn–pyridine coordination pattern (a well-established and popular supramolecular interaction)[7] that is dynamic, thus allowing equilibration to the Vernier assembly. Hereafter, the linear tetrameric Zn^{II} porphyrin can be oxidatively coupled under Pd/Cu catalysis to give the 12-site macrocycle/template in 39 % yield. The other products in this

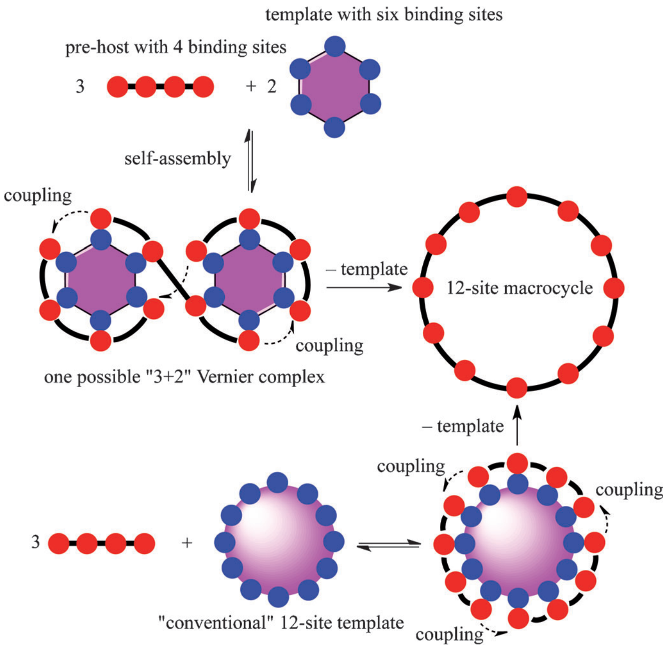
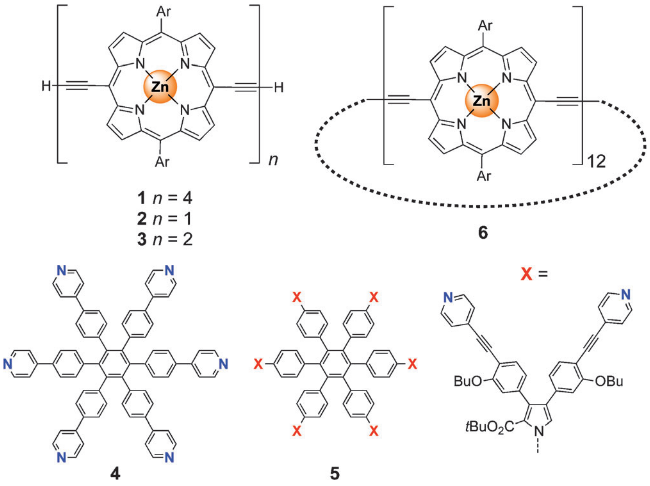


Figure 1. The principle of Vernier templation and the formation of a 12-site macrocycle using a 6-site template (Vernier approach) and a classical approach with the 12-site template.



Scheme 1. The porphyrin building blocks **1–3** and template molecules **4–5** used by Anderson. A schematic picture of the 12-site macrocycle **6** is presented at the top right.

---

[*] Prof. Dr. A. W. Kleij
Institute of Chemical Research of Catalonia (ICIQ)
Av. Països Catalans 16, 43007 Tarragona (Spain)
and
Catalan Institute for Research and Advanced Studies (ICREA)
Pg. Lluís Companys 23, 08010 Barcelona (Spain)
E-mail: akleij@iciq.es
Homepage: http://www.iciq.es

[**] ICIQ, ICREA, Consolider Ingenio 2010 (project CSD2006-0003) and the Spanish Ministry of Science and Innovation (MICINN, CTQ2008-02050) are thanked for financial support.

reaction are insoluble components and are connected with polymeric structures. Such structures are feasible as a result of "mistakes" that may arise from (partial) decomplexation of one of the terminal Zn^{II} porphyrins from the template, and coupling to a partner associated with another Vernier complex. The template molecule is easily removed by excess addition of a competitive ligand (pyridine), and the free 12-site macrocycle **6** (Scheme 1) was thoroughly characterized by various spectroscopic (MS, NMR), small angle X-ray scattering (SAXS), and scanning tunneling microscopy (STM) analyses. In particular STM provided a unique way to visualize these nanorings at the single-molecule level.

Upon using a 12-site template **5** (i.e., a "classical" approach, Scheme 1) having twelve pyridine donor fragments, a similar yield (35%) of the 12-site macrocycle **6** could be obtained. The main disadvantage of the application of this larger template derivative **5** is obviously that it requires a lengthy, ten step synthesis that is low in yield, whereas the 6-site template **4** is available in only two synthetic steps. The fact that in the absence of any template only linear polymers are observed demonstrates the essential role of the templating agent in the formation of the macrocyclic product. Another key feature is the use of sufficiently large porphyrin building blocks. Whereas the tetranuclear Zn(porhyrin) system **1** (Scheme 1) results in formation of appreciable amounts of the 12-site macrocycle in the templated process using the 6-site template **4**, under comparable experimental conditions, the use of mono-nuclear **2** and dinuclear Zn^{II} porphyrin analogue **3** preferentially leads to a cyclic hexamer and only trace amounts of the 12-site macrocycle **6** could then be detected. This may point to some cooperative phenomenon[8] upon binding of the tetranuclear porphyrin system to the 6-site template, and thus a specific directing effect is achieved when a Vernier complex is formed.

For the templating system it is clear that synthetically accessible, smaller compounds may have a dramatic effect on the synthetic efficiency of large, nanoscopic materials. However, in the case of the porphyrin building blocks this accessibility is more delicate, since their preparation can require a number of steps and column purification. This prerequisite limits, to some extent, the application potential of this type of synthon despite the clear illustration of its bright perspective in materials science.[9] Future directions in this field can and perhaps should also focus on other, readily available building blocks that can be used in this template-driven process based on coordination chemistry. A good example in this context is the salen scaffold that has proven to be an excellent supramolecular building block.[10] It would also be interesting to see if the approach is extendable to template processes with more than two components (in the present case, one building block and a template) by a clever combination of complementary (supramolecular) functions, and to processes that make use of other efficient synthetic conversions including Huisgen 1,3-dipolar cycloaddition ("click") chemistry and olefin metathesis.[11]

The work from the Anderson group nicely shows that templated oxidative coupling is an excellent strategy towards monodisperse π-conjugated macromolecules: its nanosize dimensions should be a function of the length of the linear building motif and Vernier complexes of various stoichiometries can be foreseen. In order to increase the success of Vernier templation (yield, selectivity), a deeper understanding and further fine-tuning of the supramolecular assembly process is desirable. For now, the tremendous potential of Vernier templation has been well illustrated by Anderson and co-workers, and a bright future can be predicted for this elegant strategy toward nanoscopic materials with exciting new (photophysical) properties.[9] Undoubtedly, this approach will find its way to the toolbox of researchers working in various important areas of (materials) chemistry.

Received: June 10, 2011

---

[1] For the use of DNA as template in organic synthesis, see: X. Li, D. R. Liu, *Angew. Chem.* **2004**, *116*, 4956–4979; *Angew. Chem. Int. Ed.* **2004**, *43*, 4848–4870.

[2] a) F. Diederich, P. J. Stang, *Templated Organic Synthesis*, VCH-Wiley, Weinheim, **1999**; b) S. Anderson, H. L. Anderson, J. K. M. Sanders, *Acc. Chem. Res.* **1993**, *26*, 469–475; c) N. V. Gerbeleu, V. B. Arion, J. Burgess, *Template Synthesis of Macrocyclic Compounds*, Wiley-VCH, Weinheim, **1994**; d) Q. Zhang, W. Wang, J. Goebl, Y. Yin, *Nano Today* **2009**, *4*, 494–507; e) J. D. Crowley, S. M. Goldup, A.-L. Lee, D. A. Leigh, R. T. McBurney, *Chem. Soc. Rev.* **2009**, *38*, 1530–1541; f) M. S. Vickers, P. D. Beer, *Chem. Soc. Rev.* **2007**, *36*, 211–225; g) M. Hoffmann, C. J. Wilson, B. Odell, H. L. Anderson, *Angew. Chem.* **2007**, *119*, 3183–3186; *Angew. Chem. Int. Ed.* **2007**, *46*, 3122–3125.

[3] Z. J. Gartner, B. N. Tse, R. Grubina, J. B. Doyon, T. M. Snyder, D. R. Liu, *Science* **2004**, *305*, 1601–1605.

[4] T. R. Kelly, R. L. Xie, C. K. Weinreb, T. A. Bregant, *Tetrahedron Lett.* **1998**, *39*, 3675–3678.

[5] C. A. Hunter, S. Thomas, *J. Am. Chem. Soc.* **2006**, *128*, 8975–8979.

[6] M. C. O'Sullivan, J. K. Sprafke, D. V. Kondratuk, C. Rinfray, T. D. W. Claridge, A. Saywell, M. O. Blunt, J. N. O'Shea, P. H. Beton, M. Malfois, H. L. Anderson, *Nature* **2011**, *469*, 72–75.

[7] For a few recent examples, see: a) A. M. Kluwer, R. Kapre, F. Hartl, M. Lutz, A. L. Spek, A. M. Brouwer, P. W. N. M. van Leeuwen, J. N. H. Reek, *Proc. Natl. Acad. Sci. USA* **2009**, *106*, 10460–10465; b) M. L. Merlau, M. del Pilar Mejia, S. T. Nguyen, J. T. Hupp, *Angew. Chem.* **2001**, *113*, 4369–4372; *Angew. Chem. Int. Ed.* **2001**, *40*, 4239–4242; c) C. A. Hunter, C. M. R. Low, M. J. Packer, S. E. Spey, J. G. Vinter, M. O. Vysotsky, C. Zonta, *Angew. Chem.* **2001**, *113*, 2750–2754; *Angew. Chem. Int. Ed.* **2001**, *40*, 2678–2682.

[8] For details on cooperative phenomena, see: a) C. A. Hunter, H. L. Anderson, *Angew. Chem.* **2009**, *121*, 7624–7636; *Angew. Chem. Int. Ed.* **2009**, *48*, 7488–7499; b) G. Ercolani, L. Schiaffino, *Angew. Chem.* **2011**, *123*, 1800–1807; *Angew. Chem. Int. Ed.* **2011**, *50*, 1762–1768; c) A. Mulder, J. Huskens, D. N. Reinhoudt, *Org. Biomol. Chem.* **2004**, *2*, 3409–3424.

[9] a) Y. Nakamura, N. Aratani, A. Osuka, *Chem. Soc. Rev.* **2007**, *36*, 831–845; b) M.-H. Chang, M. Hoffmann, H. L. Anderson, L. M. Herz, *J. Am. Chem. Soc.* **2008**, *130*, 10171–10178.

[10] A. W. Kleij, *Chem. Eur. J.* **2008**, *14*, 10520–10529.

[11] A. V. Chuchuryukin, H. P. Dijkstra, B. M. J. M. Suijkerbuijk, R. J. M. Klein Gebbink, G. P. M. van Klink, A. M. Mills, A. L. Spek, G. van Koten, *Angew. Chem.* **2003**, *115*, 238–240; *Angew. Chem. Int. Ed.* **2003**, *42*, 228–230.