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Macrocycles Hot Paper

International Edition: DOI: 10.1002/anie.201804787
German Edition: DOI: 10.1002/ange.201804787

Shadow Mask Templates for Site-Selective Metal Exchange in Magnesium Porphyrin Nanorings

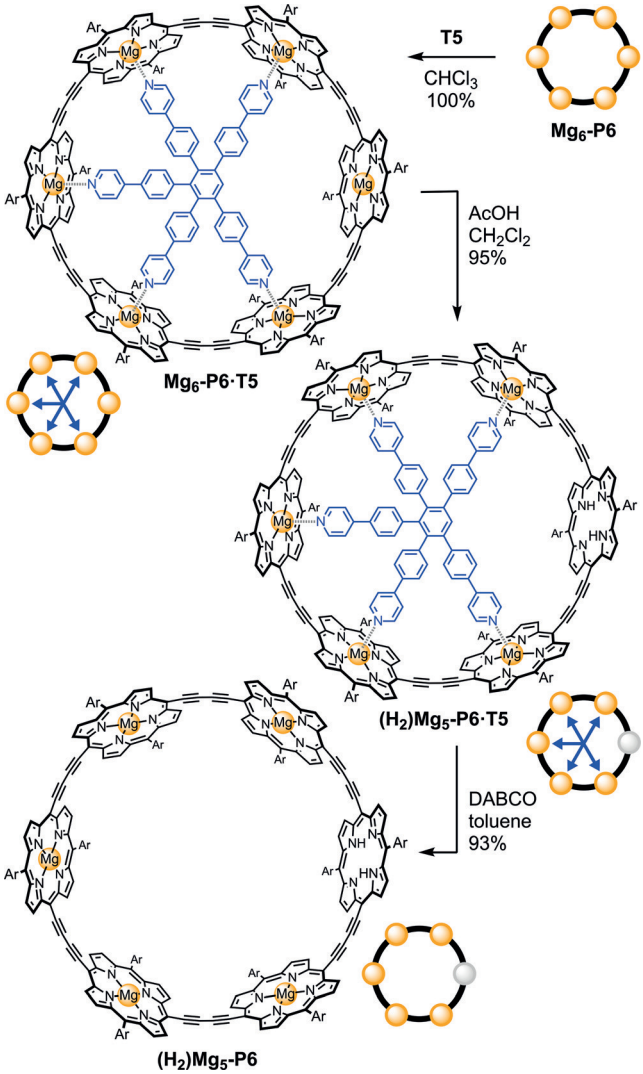
*Pernille S. Bols and Harry L. Anderson**

Dedicated to Professor Jeremy Sanders on the occasion of his 70th birthday

Abstract: *Molecular templates can be used in many different ways to control the outcome of chemical reactions. Herein, we present a new type of template-directed synthesis. We show that templates can be used as shadow masks: The shape of the template becomes imprinted on the product because reactions only occur at sites not masked by the template. We demonstrate this effect by using oligopyridine templates to dictate the sites of demetalation when a magnesium porphyrin nanoring is treated with acid. Magnesium centers that are coordinated to the template are protected whereas uncoordinated magnesium centers are removed. After site-selective demetalation, the template can be removed, and other cations, such as zinc(II) and copper(II), can be inserted into the free-base porphyrin centers. This strategy provides a simple route to a wide range of heterometalated porphyrin arrays.*

Stencils and shadow masks have been used to create patterns for about 60000 years,[1] and this strategy has been widely exploited in top-down nanofabrication.[2] Herein, we demonstrate the same effect on a molecular scale, through the use of "shadow mask templates". Busch defined a chemical template as a species that organizes an assembly of atoms with respect to one or more geometric loci to achieve a particular linking of atoms.[3] A template provides instructions for the formation of a single product from a substrate or substrates that otherwise have the potential to assemble and react in a variety of ways.[4] Recently, many new types of template-directed syntheses have been developed, providing routes to previously inaccessible molecular architectures.[5–7] There are previous reports on the use of molecules as shadow masks,[8] but to the best of our knowledge, this is the first time that this principle has been used to create precisely defined molecular structures.

The work presented here developed from a simple observation: Treatment of the magnesium complex of a butadiyne-linked six-porphyrin nanoring, **Mg_6-P6**, with acetic acid in dichloromethane resulted in rapid removal of the magnesium cations from all six porphyrin centers whereas the complex of this nanoring with a hexapyridyl template, **Mg_6-P6·T6**, was not demetalated under these conditions. We concluded that the template masks the magnesium ions from acid. To test this hypothesis, we inserted a five-legged template **T5**[7] into a magnesium porphyrin nanoring and submitted it to the demetalation conditions. As expected, the uncoordinated magnesium porphyrin was cleanly demetalated whereas the template-coordinated magnesium cations remained in place (Scheme 1). Analysis of the crude reaction mixtures by ^{1}H NMR spectroscopy and MALDI-TOF mass



Scheme 1. The template masking method applied to the synthesis of **$(H_2)Mg_5$-P6** using the template **T5**. Ar = 3,5-bis(trihexylsilyl)phenyl.

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Supporting information and the ORCID identification number(s) for the author(s) of this article can be found under: https://doi.org/10.1002/anie.201804787.

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spectrometry showed that the site-selective demetalation of **Mg_6-P6·T5** to **$(H_2)Mg_5$-P6·T5** is a quantitative reaction with no detectable traces of over-demetalated side products. The template was displaced from **$(H_2)Mg_5$-P6·T5** by treatment with a large excess of DABCO, and **$(H_2)Mg_5$-P6** was isolated in 88% yield from **Mg_6-P6**.[6,7,9]

To test the scope of this template effect, we investigated whether it could be applied to four-legged templates by comparing three ligands with pyridine coordination sites in different positions (**T4a**, **T4b**, and **T4c**; Figure 1).[10,11] In each case, the complex of the template with the magnesium nanoring **Mg_6-P6** was treated with 10% acetic acid in dichloromethane. All three reactions gave clean, site-selective demetalation, and the products were obtained in high yields without the need for chromatographic purification (Scheme 2). The identities of the final compounds were confirmed by ^{1}H NMR and MALDI-TOF MS analysis. The NH protons in the free-base porphyrins give distinctive proton resonances at chemical shifts of $\delta = -1.0$ to -1.3 ppm, and the exact chemical shift is characteristic of each isomer.

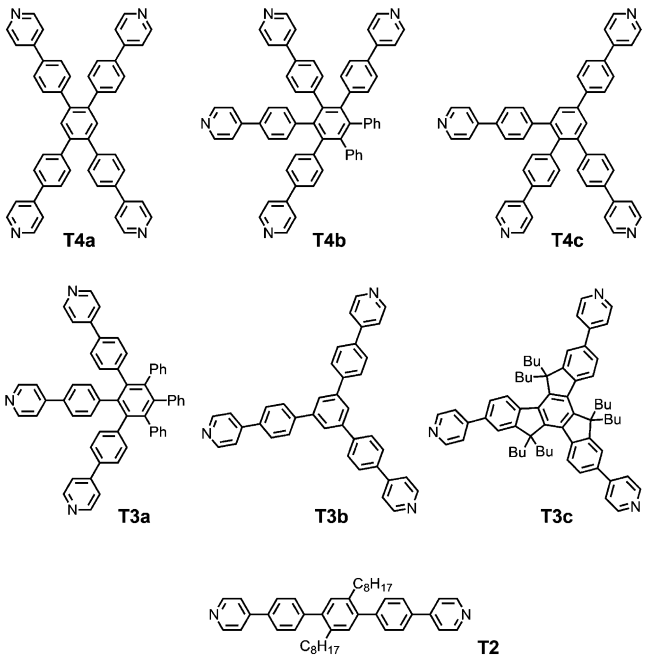
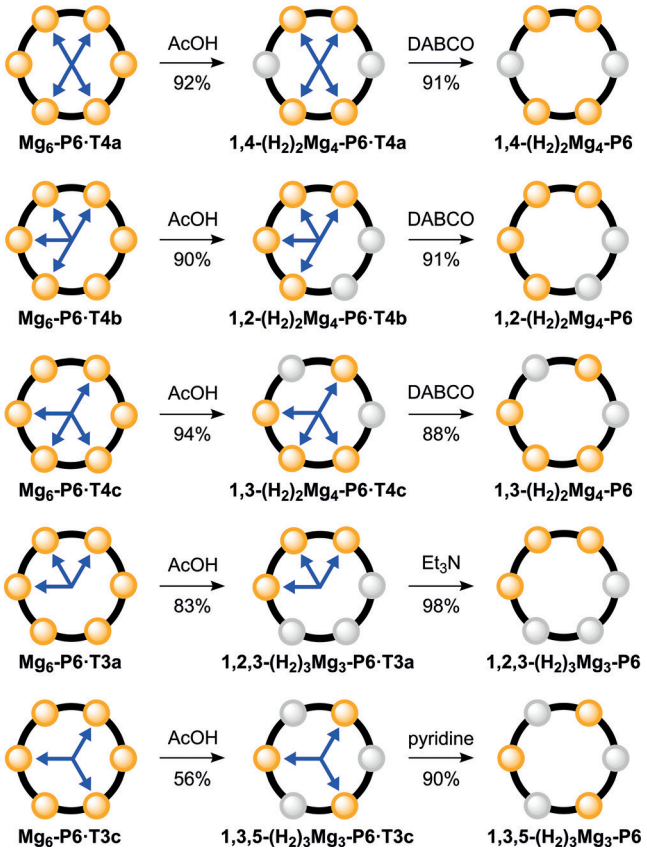


Figure 1. Structures of the oligopyridine ligands tested as masking templates. (**T3b** and **T2** were found not to be effective as masking templates.)

Next, we tested three-legged templates, starting with the 1,2,3-isomer **T3a** (Figure 1).[11] Treatment of **Mg_6-P6** with one equivalent of **T3a** followed by acetic acid addition resulted in site-selective demetalation to form **1,2,3-$(H_2)Mg_3$-P6·T3a**, together with about 7% of the fully demetalated ring **$(H_2)_6$-P6**. This fully demetalated nanoring is easily separated from **1,2,3-$(H_2)Mg_3$-P6·T3a** by chromatography on silica gel. The formation of **$(H_2)_6$-P6** as a side product during the reaction of **Mg_6-P6·T3a** with acetic acid reflects the weaker association constant of this tridentate template compared with **T6**, **T5**, and **T4a**–**T4c**.[11]



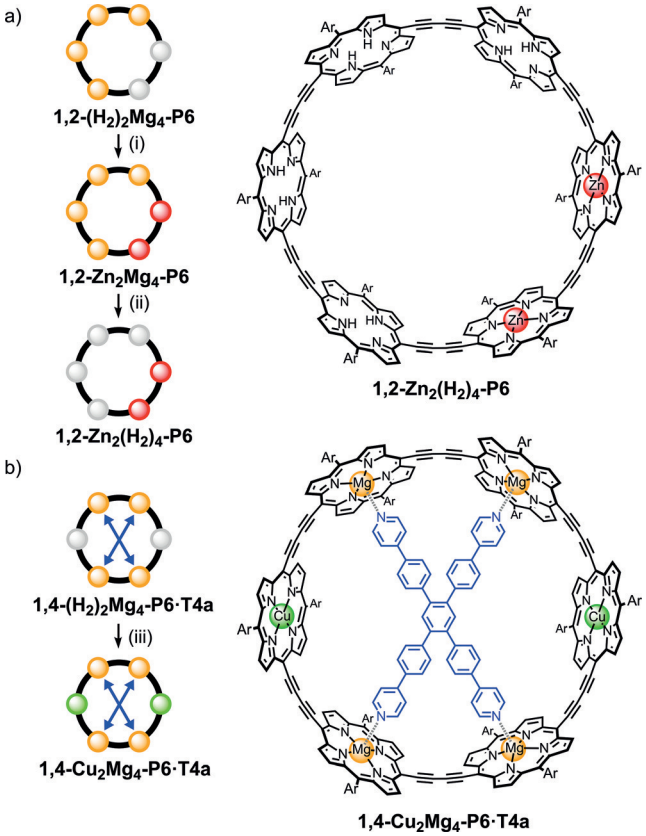
Scheme 2. The template masking method applied to the synthesis of five heterometalated rings from **Mg_6-P6**.

Disappointingly, treatment of **Mg_6-P6** with the symmetric three-legged template **T3b**[12] (1:1 molar ratio) followed by acetic acid addition did not result in site-selective demetalation. The main products were unreacted starting material and the fully demetalated ring **$(H_2)_6$-P6**. ^{1}H NMR titrations revealed the reason for this result: When one equivalent of **T3b** is added to **Mg_6-P6**, the main product is the 1:2 complex **Mg_6-P6·(T3b)$_2$**, together with a small amount of the 1:1 complex **Mg_6-P6·T3b** and some uncomplexed **Mg_6-P6** nanorings. It appears that the formation of the 1:2 complex with **T3b** is too favorable, making this ligand ineffective as a masking template. To solve this problem, we designed a three-legged template with bulky groups to prevent the stacking, **T3c**, which is based on a truxene core.[13] Template **T3c** has a similar coordination geometry to **T3b**, but the bulky *n*-butyl chains in the truxene were expected to hinder stacking. ^{1}H NMR spectroscopy showed that addition of **T3c** to the nanoring only led to formation of a 1:1 complex, **Mg_6-P6·T3c**. Addition of acetic acid to this complex resulted in site-selective demetalation, together with formation of the fully demetalated nanoring **$(H_2)_6$-P6**. ^{1}H NMR analysis of the crude reaction mixture (see the Supporting Information, Figure S2) showed that the reaction mixture consisted of 83% **1,3,5-$(H_2)_3Mg_3$-P6·T3c** and 17% **$(H_2)_6$-P6**. These two products were readily separated by chromatography on silica gel. The weaker binding resulting from the presence of only three pyridine coordination sites makes **T3c** less effective than

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T4a–**T4c** as a masking template, but the bulk of the truxene effectively prevents the formation of the 1:2 complex. The two-legged template **T2** (Figure 1) binds too weakly to control the demetalation process; treatment of the complex of **Mg_6-P6** and **T2** with acetic acid gave only the fully demetalated ring **$(H_2)_6$-P6**.

Magnesium porphyrins are readily demetalated by acid, but they do not easily undergo transmetalation when treated with other metal salts,[14] which makes it possible to use shadow mask templates to achieve site-selective transmetalation. For example, treatment of **1,2-$(H_2)_2Mg_4$-P6** with zinc(II) acetate resulted in clean insertion of zinc(II) at the two free-base positions to give **1,2-Zn_2Mg_4-P6**; the remaining magnesium centers can then be demetalated selectively with acetic acid to yield **1,2-$Zn_2(H_2)_4$-P6** (Scheme 3a).[15] This



Scheme 3. Synthesis of heterometalated rings. a) Synthesis of a di-zinc(II) porphyrin ring. Reagents and conditions: i) $Zn(OAc)_2$, 2 h, 20 °C, 75% yield; ii) 50% AcOH in CH_2Cl_2, 30 min, 20 °C, 69% yield. b) Synthesis of a di-copper(II) porphyrin ring. Reagents and conditions: iii) CuOAc, air, 1 h, 60 °C, 87% yield. Ar = 3,5-bis(trihexylsilyl)-phenyl.

compound is useful for testing the cooperativity of ligand binding inside nanorings.[11] We also prepared a heterometalated nanoring containing two paramagnetic copper(II) ions opposite to each other (**1,4-Cu_2Mg_4-P6·T4a**; Scheme 3b). In this reaction, the **T4a** template was left in place during the insertion of copper(II) into the two free-base centers of **1,4-$(H_2)Mg_4$-P6·T4a**. We removed **T4a** and inserted **T6** to obtain **1,4-Cu_2Mg_4-P6·T6** (see the Supporting Information), which is a valuable compound for investigating quantum interference through long-range exchange coupling.[16] Many metal cations can be inserted into porphyrins under mild conditions,[17] so the magnesium/free-base nanorings reported here should be useful intermediates for preparing diverse heterometalated systems.

In summary, we have demonstrated that oligopyridine ligands can be used as shadow mask templates for the site-selective demetalation of magnesium porphyrin nanorings. Selective demetalation is quantitative with five- and four-legged templates, and it provides useful selectivity with three-legged templates when the binding of more than one template unit can be prevented; however, it does not work with two-legged templates. This new template effect provides a simple synthetic route to functional heterometalated porphyrin arrays.

Acknowledgements

We thank the ERC (grant 320969), the EPSRC, and the John Templeton Foundation for support, Dr. Huawei Jiang, Dr. Jonathan Cremers, Michael Jirasek, and Isabell Grübner for providing samples of starting materials, and the EPSRC National Mass Spectrometry Service at Swansea University and Dr. Renée Haver for mass spectrometry.

Conflict of interest

The authors declare no conflict of interest.

Keywords: macrocycles · magnesium · masking · porphyrin oligomers · template-directed synthesis

How to cite: *Angew. Chem. Int. Ed.* **2018**, *57*, 7874–7877
Angew. Chem. **2018**, *130*, 8000–8003

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Manuscript received: April 24, 2018
Accepted manuscript online: May 9, 2018
Version of record online: May 24, 2018

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