

Template-Directed Synthesis of Supramolecular Heterometallated Nanorings



Pernille Sørensen Bols

Hertford College

University of Oxford

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Abstract

This thesis presents the synthesis, characterization and study of a range of heterometallated porphyrin nanorings. These studies revealed some fascinating electronic and supramolecular properties.

Chapter 1 summarizes some of the work done in the Anderson group on porphyrin nanostructures and reviews the literature regarding template-directed synthesis.

Chapter 2 describes the discovery of the novel technique “shadow mask templates”. We show that oligopyridine ligands can be used to dictate the sites of demetallation 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 demetallation, the template can be removed, and other cations, such as zinc(II), copper(II), and silver(II) can be inserted into the free-base porphyrin centers. This strategy provides a simple route to a wide range of heterometallated porphyrin arrays.

Chapter 3 describes the investigation of quantum interference phenomena in bis-copper and bis-silver six-porphyrin nanorings by EPR spectroscopy via measurement of the exchange coupling between the paramagnetic centers. Using orientationally selective DEER and RIDME, we investigate how various factors affect the exchange coupling between two spin centers in a porphyrin nanoring.

Chapter 4 describes the thermodynamic and kinetic investigation of complexes where two oligopyridine templates stack on top of each other inside porphyrin nanorings. Using UV/vis/NIR titrations and kinetic ^1H NMR experiments, it was found that in a 12-porphyrin nanoring where there is space for the templates to bend, there is high positive allosteric cooperativity. In a 6-porphyrin nanoring where the templates are more constrained, there is negative cooperativity. In the case of the negatively cooperative systems, there is a high kinetic barrier for exchange of templates and reaching equilibrium can take up to several weeks.

Chapter 5 describes how stacked templates can be used in a novel type of Vernier template-directed synthesis because they fit a favorable conformation of the targeted complex and does not require the complex to twist. This turns out to be a significant advantage when synthesizing complexes with sterically bulky solubilizing groups, and is the most efficient method to prepare a 12-porphyrin nanoring with THS-solubilizing groups.

Supplement to Statement of Authorship

In Chapter 3, the CW and pulsed EPR experiments were designed and carried out by Dr Alice M. Bowen (CAESR, Oxford). She also performed the simulations and analyses and drew the main conclusions from the EPR experiments. The DFT calculations of exchange couplings were performed by Dr Qingqing Wu under the supervision of Prof. Colin Lambert (Lancaster University).

In Chapter 4 and 5, **T6e** was designed and synthesized by Dr Michel Rickhaus and Dr Henrik Gottfredsen, **T3N** was designed and synthesized by Dr Lara Tejerina, and the molecular modelling was performed by Dr Michael Jirasêk and Kristina Eriksen.

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List of publications

- 1) P. S. Bols, M. Rickhaus, L. Tejerina, H. Gotfredsen, K. Eriksen, M. Jirasek, H. L. Anderson, 'Allosteric Cooperativity and Template-Directed Synthesis with Stacked Ligands in Porphyrin Nanorings' *J. Am. Chem. Soc.* **2020**, just accepted.
- 2) P. S. Bols, H. L. Anderson, 'Template-Directed Synthesis of Molecular Nanorings and Cages' *Acc. Chem. Res.* **2018**, 51, 2083-2092.
- 3) P. S. Bols, H. L. Anderson, 'Shadow Mask Templates for Site-Selective Metal Exchange in Magnesium Porphyrin Nanorings' *Angew. Chem. Int. Ed.* **2018**, 57, 7874-7877.

List of Abbreviations

Ac	Acetate
Ar	Aryl
AWG	arbitrary waveform generator
B3LYP	Becke, 3-parameter, Lee-Yang-Parr
CPDIPS	Cyanopropyldiisopropylsilane
CPDMS	Cyanopropyldimethylsilane
CW	Continuous wave
d	doublet
DABCO	1,4-diazabicyclo[2.2.2]octane dba dibenzylideneacetone
DEER	Double Electron-Electron Resonance
DFT	Density Functional Theory
DIPA	Diisopropylamine
DOSY	Diffusion ordered spectroscopy
dppf	Bis(diphenylphosphino)ferrocene
DNA	Deoxyribonucleic acid
EPR	Electron Paramagnetic Resonance
ESEEM	Electron Spin Echo Envelope Modulation
ESI	Electrospray
Et	Ethyl
EXSY	Exchange spectroscopy
THF	Tetrahydrofuran
GPC	Gel Permeation Chromatography

HRMS	High resolution mass spectroscopy
m	multiplet
MALDI	Matrix-Assisted Laser Desorption/Ionisation
Me	Methyl
MS	Mass spectrometry
NMR	Nuclear Magnetic Resonance
Ph	Phenyl
RIDME	Relaxation induced dipolar modulation enhancement
s	singlet
SEC	Size Exclusion Chromatography
STM	Scanning Tunneling Microscope
t	triplet
TBAF	Tetra-n-butylammonium fluoride
<i>t</i> -Bu	<i>tert</i> -Butyl
THS	Trihexylsilane
TLC	Thin Layer Chromatography
ToF	Time of flight
UV-vis-NIR	Ultra-violet, visible and near infra-red

Introduction

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Most of this chapter was published in:

Template-Directed Synthesis of Molecular Nanorings and Cages

P. S. Bols, H. L. Anderson, *Acc. Chem. Res.* **2018**, *51*, 2083-2092.

1.1 Porphyrins

Porphyrins are essential building blocks in numerous biological systems. Plants use magnesium porphyrins in the pigment chlorophyll to harvest solar energy, and mammals use iron porphyrins in hemoglobin to transport oxygen around the body. Besides being biologically relevant, porphyrins attract interest because of their aromaticity and synthetic tractability which has made it possible to create gigantic π -conjugated macrocycles and cages. Finally, porphyrins can act as ligands for nearly every metal in the periodic table.¹

Porphyrins are a family of compounds consisting of four pyrrole units connected by methine bridges. Porphin is the simplest example of a porphyrin in which all substituents in the periphery of the macrocycle are hydrogen atoms.² The structure and the standard labelling of positions of a porphyrin is shown in Figure 1.1.

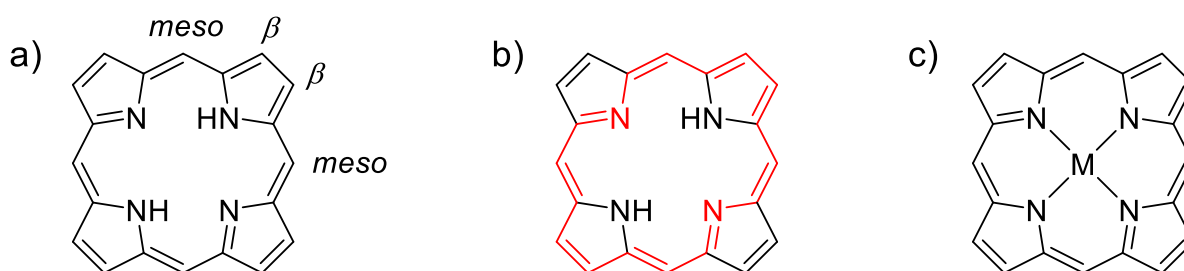


Figure 1.1. a) Structure of the free-base porphin with the *meso*- and β -positions indicated, b) the bonds shown in red indicate one of the conjugated 18 π -electron pathways responsible for aromaticity in porphyrins, and c) the general structure of a metalloporphyrin.

The molecular backbone of a porphyrin contains 22 delocalized π -electrons of which 18 form a conjugated pathway (Figure 1.1b). Following Hückel's rule, porphyrins are therefore aromatic. The aromaticity is observed in the ^1H NMR spectrum, where the two inner N-H protons are heavily shielded with chemical shifts ranging from -1 to -4 ppm, and the external protons are deshielded with chemical shifts from 8 to 11 ppm.

The center of the porphyrin contains four nitrogen atoms which make them excellent ligands for a wide range of metals (Figure 1.1c). Metal centers can be used to introduce functionality to the porphyrin,^{3,4} or they can act as a handle for the synthesis of supramolecular structures through axial ligand coordination.^{5,6}

The ability of metalloporphyrins to coordinate axial ligands varies with different metals and oxidation states. For example, the d^8 systems of palladium(II) and platinum(II) porphyrins show negligible affinity for axial ligands.⁷ Nickel(II) porphyrins, which are also d^8 , also generally have low affinity for axial coordination.⁸ If axial coordination is forced upon them, for example by molecular design, they change their spin-state.⁹ In copper(II) porphyrins, which are d^9 systems, there is strong ligand binding in the equatorial plane due to a single vacancy in the $3d_{x^2-y^2}$ orbital. Bonding in the porphyrin plane is further enhanced by hybridization of the 4s and the $3d_{z^2}$ orbitals which leads to a build-up of electron density along the z-axis, which is the cause of the low binding affinity of copper(II) porphyrins towards axial ligands.¹⁰

When the d-shell is full, as in zinc(II), the driving force for bonding in the equatorial plane is reduced, as is the 4s/ $3d_{z^2}$ hybridization, and axial ligands bind more strongly.¹¹ Zinc(II) porphyrins generally coordinate one axial nitrogen-based ligand with association constants ranging from 10^3 to 10^4 M^{-1} .¹² However, zinc(II) porphyrins with two axial ligands are never observed in solution unless it is forced by molecular design.¹³

1.2 Template directed synthesis

The word ‘template’ is used in many different ways. In this thesis, it is thought of as the wooden frames that builders use to hold stone blocks in place while they are cemented together to form an arch (Figure 1.2). The template defines the shape of the arch, but it is not an integral part of the final structure.

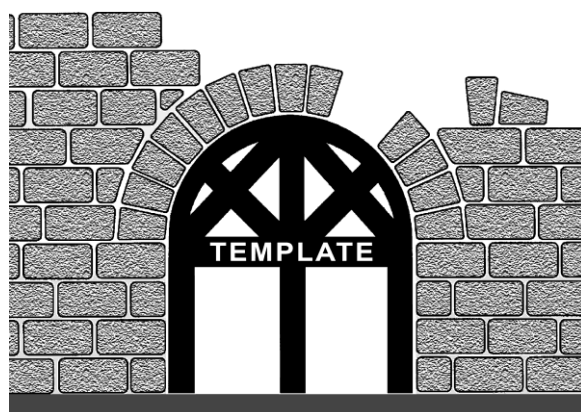


Figure 1.2. A template is used to hold stones in place while they are cemented together to form an arch; it is then removed from the final structure.

Busch provided a formal definition,

*“A chemical template organizes an assembly of atoms, with respect to one or more geometric loci, in order to achieve a particular linking of atoms.”*¹⁴

which was refined by Sanders:

*“The template provides instructions for the formation of a single product from a substrate or substrates which otherwise have the potential to assemble and react in a variety of ways.”*¹⁵

In most cases, templates are not catalysts and a stoichiometric amount of template is required to form the product. However, at least in principle, the template can be removed from the product, which means that the template must connect to the substrate or substrates *via* temporary bonding interactions. These temporary interactions are often metal-ligand coordination bonds, but they can also be H-bonds, van der Waals interactions, or cleavable covalent bonds.

The first chemical templates were metal cations, and metal cation templates continue to be used to create spectacular new architectures, such as rotaxanes, catenanes and knots.¹⁶⁻¹⁹ Metal cation templates are typically used with building blocks that are amine or ether ligands. In the template-directed synthesis of porphyrin arrays, the roles are reversed: the metal cation is part of the porphyrin building block and the template is a multi-dentate amine ligand.^{6,15,20-24} Anions also find increasing use as templates, *via* H-bonding interactions.^{25,26} For example, Kobayashi and coworkers prepared a cyclo[10]pyrrole using croconate ($C_5O_5^{2-}$) as a template,²⁷ while the use of sulfate as a smaller template resulted in formation of the cyclo[8]pyrrole. Leigh's synthesis of a pentafoil knot uses both cationic and anionic templates (Fe^{2+} and Cl^-).¹⁸ Neutral H-bond acceptors, such as bis-*N*-oxides, have also been used in the synthesis of capsules.²⁸ Van der Waals interactions and aromatic stacking forces are less directional than metal-ligand bonds or H-bonds, which makes it difficult to predict how they will operate, but there are many cases where these softer interactions give rise to strong template effects.^{29,30} On the other hand, covalent bonds provide a predictable connection to the template, and ester links have been used to achieve the template-directed synthesis of large macrocycles, rotaxanes and catenanes.³¹⁻³⁴

Most examples of template-directed synthesis are under kinetic control: the template accelerates formation of the desired covalent architecture and the reaction is irreversible. If the reaction is reversible and under thermodynamic control, the template may favor formation of a specific product by binding it selectively and shifting the equilibrium toward this species. The product can then be made kinetically stable by changing the conditions, so that the template can be removed without re-establishing the equilibrium. This field of dynamic combinatorial chemistry, which was pioneered by Sanders and Lehn during the 1990s,^{35,36} is particularly open to serendipity. In a dynamic combinatorial library, simple building blocks are mixed together so that they can couple reversibly to form many possible species. Adding a template to this library can result in the selective amplification of an unexpected product. For example, acetylcholine was found to template the formation of a hydrazone-linked catenane, and this amazing result was neither designed nor anticipated.³⁷

Control of molecular topology has been an important area of template-directed synthesis ever since Sauvage discovered that metal cations can direct the formation of catenanes in 1983.^{19,38} In these systems, the metal template is 'passive': it dictates the topology of the coupling but it does not accelerate the coupling reaction. In 2006, Leigh and coworkers developed the concept of 'active metal templates'.^{39,40} These reactions use metal complexes of macrocyclic ligands in which the metal promotes coupling of two components to form a covalent thread through the cavity of the macrocycle. This strategy is 'traceless' in the sense that the newly formed thread does not need a recognition site for the metal, and in some cases the template can be used in sub-stoichiometric amounts.

Self-replicators are a fascinating class of templates.^{41,42} In the simplest case, a self-replicator is a template for construction of another copy of itself. Alternatively, a self-replicator may be a template for a complementary structure, which in turn is a template for the original molecule, as in DNA replication. The challenge is to avoid the formation of stable template-template complexes, so as to achieve autocatalytic turnover and exponential growth. Designing an efficient self-replicator is more difficult than designing an effective template.

1.3 Template directed synthesis of porphyrin nanorings, -tubes and -cages

1.3.1 Introduction

The combination of metalloporphyrin building blocks and oligopyridine templates is a fruitful area for exploring new strategies for template-directed synthesis, because the template effect is directional and modular: one pyridine binding site coordinates to one metalloporphyrin center. This controllable directionality allows large porphyrin arrays to be created with high selectivity.^{6,15,20-24} As described in Section 1.1, the affinity for axial ligands and thus the template effect can be tuned by changing the metal in the porphyrin. These large conjugated porphyrin arrays are fascinating model systems for studying the delocalization of charge^{43,44} and electronic excitation,^{45,46} and for mimicking photosynthetic light harvesting systems.

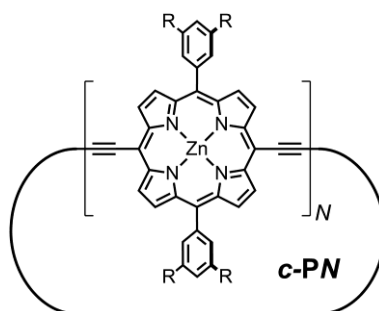


Figure 1.3. General structure of a porphyrin nanoring **c-PN**, (*c* denotes *cyclic*, *P*: porphyrin, *N*: number of porphyrins; *N* = 5–50; the solubilizing group is *R* = *t*-Bu, OC₈H₁₇ or Si(C₆H₁₃)₃). The corresponding linear oligomers are designated **l-PN**, where *l* denotes *linear*.

1.3.2 Classical template-directed macrocyclization

The first breakthrough in the synthesis of fully π -conjugated cyclic porphyrin arrays was the template-directed synthesis of a π -conjugated cyclic porphyrin octamer, **c-P8**.⁴⁷ This was soon followed by a cyclic hexamer, **c-P6** (Figure 1.4),^{48,49} which became the archetype for a family of nanorings. The rigid **T6** template is almost the ideal size and shape for the cavity of **c-P6**; crystallographic studies indicate that it is 2.5% too small.⁴⁹ It is effective as a template for forming **c-P6** via the palladium-catalyzed oxidative homo-coupling of two linear porphyrin trimers, or three linear dimers, or six units of porphyrin monomer. The crystal structure of **c-P6·T6** shows that the molecule has a regular cylindrical π -system.⁴⁹ This **c-P6·T6** complex is amazingly stable; it has a formation constant of about 10^{36} M^{-1} , due to the cooperative effect of

six metal-template interactions with an effective molarity of about 300 M.⁵⁰ However, the **T6** template can be removed from the complex by displacement with a large excess of a competing ligand such as quinuclidine or DABCO (1,4-diazabicyclo[2.2.2]octane), or by treating **c-P6·T6** with acid to remove the zinc atoms, to give the free-base nanoring, which can then be remetallated with zinc or another metal cation.

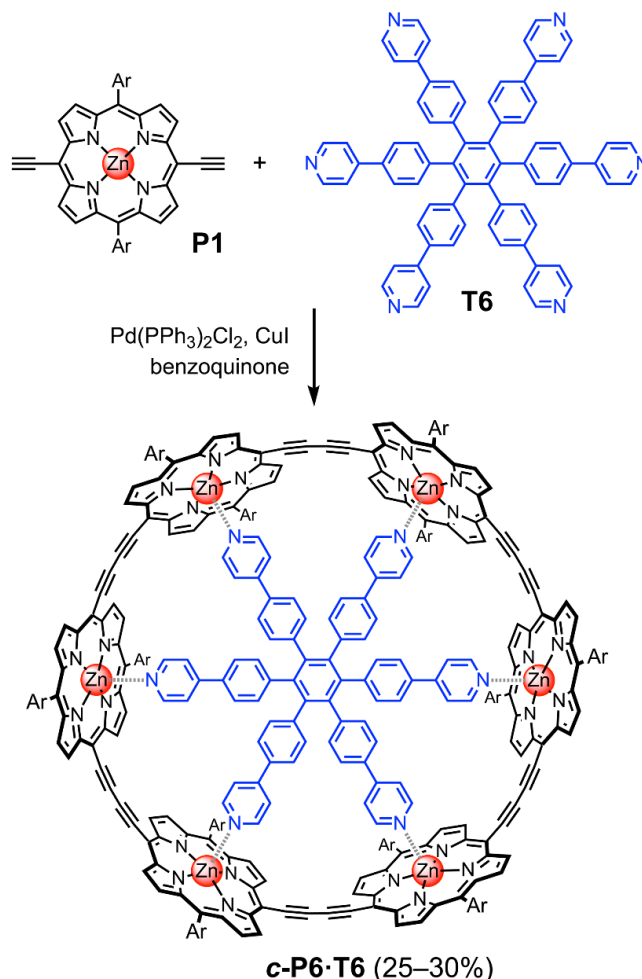


Figure 1.4. Template-directed synthesis of **c-P6**.^{48,49}

It might be imagined that the template-directed synthesis of **c-P6** shown in Figure 1.4 involves the initial formation of a complex in which six porphyrin monomers bind to the **T6** template, followed by intramolecular coupling. However, this is unlikely to be the correct mechanism, because the strength of the zinc-nitrogen interaction under the reaction conditions is too weak to form a significant amount of the (**P1**)₆·**T6** complex. Linear oligomers probably form by coupling of monomers that are not bound to the template; then they bind the template and couple further to form nanorings.

The use of **T6** to synthesize **c-P6** suggests that the template needs to be extremely rigid and to have a close geometrical match to the cavity of the target nanoring, however subsequent work showed that flexible or poorly matching templates can be almost as effective. For example, a flexible **T7** template based on β -cyclodextrin was used to prepare **c-P7**,⁵¹ and a **T5** template based on corannulene was used to synthesize **c-P5** even though the centroid-nitrogen distance of this template is calculated to be 11% too small for the cavity (Figure 1.5).⁵² The largest template used in this type of reaction is **T12**, which yielded the 12-porphyrin ring **c-P12** by bringing together three equivalents of a linear porphyrin tetramer (Figure 1.5).⁵³ Nearly all of the porphyrin oligomers discussed here are linked with butadiyne bridges, but recently a six-porphyrin nanoring with single-acetylene links, **c-P6'**, was prepared using Sonogashira coupling and template **T6'** (which is 7% too large for the cavity of **c-P6'**).⁵⁴

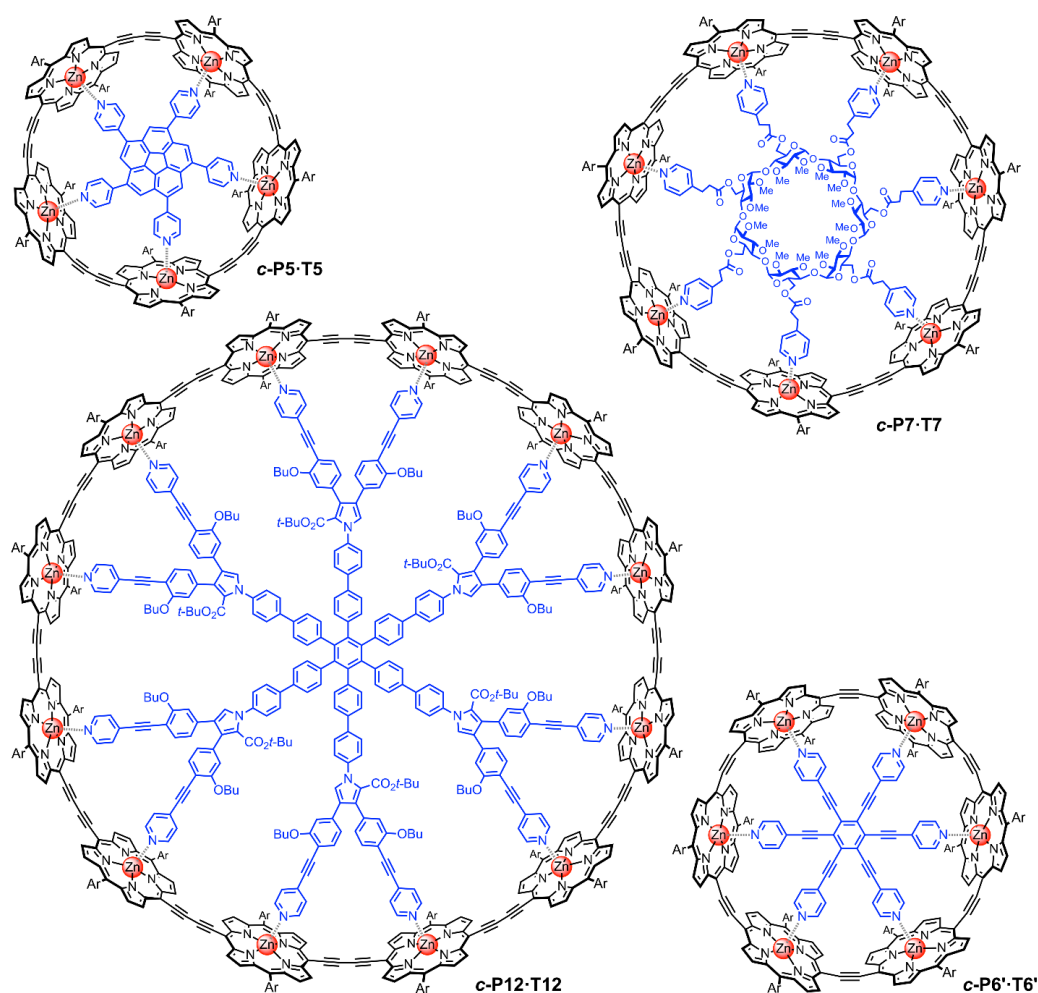


Figure 1.5. Structures of nanoring-template complexes from classical template-directed synthesis.⁵¹⁻⁵⁴

1.3.3 Vernier templates

In the classical 1:1 template-directed reactions discussed above, a single template molecule defines the size of the product, and the product has the same number of binding sites as the template. The limitation of this strategy is that large macrocycles require large templates, which are difficult to synthesize. One solution is to use a Vernier complex.

Vernier complexes are formed when a host with x binding sites binds a guest with y binding sites, where x is not a multiple of y . The Vernier complex has z binding sites, where z is the lowest common multiple of x and y . The formation of a Vernier complex between components with different numbers of binding sites provides a way to amplify the molecular length-scale, generating precisely defined assemblies (Figure 1.6a). The name ‘Vernier complex’ comes from the French mathematician Pierre Vernier (1580–1637), who applied this mismatch principle in measuring devices. The formation of supramolecular Vernier complexes was first suggested by Lindsey⁵⁵ by analogy with models for the self-assembly of collagen proteins,⁵⁶ but few examples have been investigated experimentally. The principle has been applied to prepare double-strand⁵⁷ and triple-strand⁵⁸ non-covalent Vernier assemblies and dynamic covalent molecular ladders.⁵⁹ Synthetic DNA nanostructures have also been created as Vernier complexes.^{60,61} It turns out that the formation of Vernier complexes is a powerful strategy for the template-directed synthesis of large porphyrin macrocycles.⁵³ The idea (illustrated in Figure 1.6b) is based on the realization that Vernier complexes do not need to be linear. A template with six binding sites, **T6**, binds to a building block with four binding sites, **I-P4**, to form a Vernier complex **(I-P4)₃·(T6)₂**, which probably consists of two isomers. The **I-P4** units can then be coupled together covalently, to give a figure-of-eight complex, **c-P12·(T6)₂** in 39% isolated yield (Figure 1.7). Displacement of the template with pyridine gives the free macrocycle **c-P12**. The figure-of-eight geometry of **c-P12·(T6)₂** was deduced by NMR spectroscopy⁵³ and confirmed by X-ray crystallography.⁶²

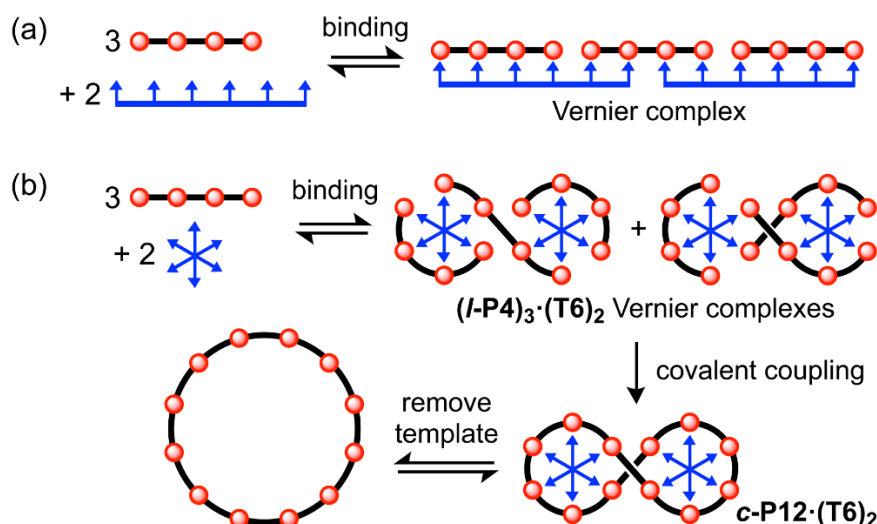


Figure 1.6. Cartoons showing the concept of Vernier templating.⁵³ (a) Formation of a molecular 3:2 Vernier complex. (b) Vernier templating: the use of Vernier complex formation to direct the formation of a 12-site macrocycle (**c-P12**) using a 6-site template (**T6**).

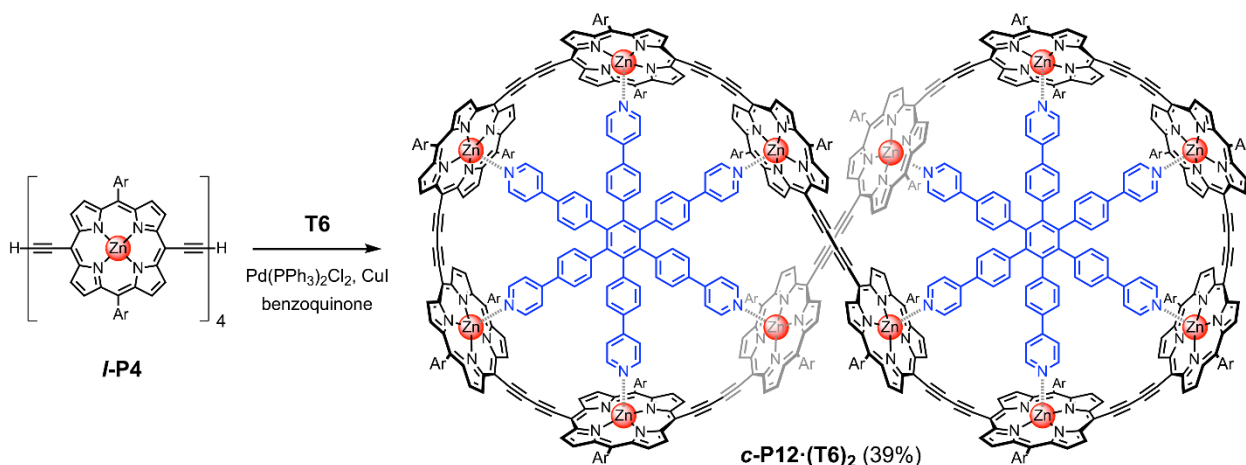


Figure 1.7. Vernier templated synthesis of **c-P12**.^{53,62} The isolated yield of **c-P12**·(**T6**)₂ is 39% for the case with Ar = 3,5-di-*tert*-butylphenyl.

Vernier templating has been used to prepare a range of large nanorings, including **c-P24** (both from **I-P6** with **T8** and from **I-P8** with **T6**),⁶³ **c-P30** (from **I-P10** with **T6**) and **c-P40** (from **I-P10** with **T8**).⁶⁴ All these large nanorings were characterized by STM imaging on a gold surface with sufficient resolution to count the individual porphyrin units around the ring. For example Figure 1.8 shows images of **c-P24**.^{63,65} The Vernier templated synthesis of these large nanorings is less selective than that of **c-P12**, but all the different cyclic oligomers can be separated by recycling gel permeation chromatography, including products such as **c-P50**,

which is the largest monodisperse covalent synthetic macrocycle yet reported. It is interesting that **c-P50** is not formed by coupling **I-P10** in the absence of a template, but it is formed in 5–10% yield by running the reaction in the presence of either **T6** or **T8**.⁶⁴

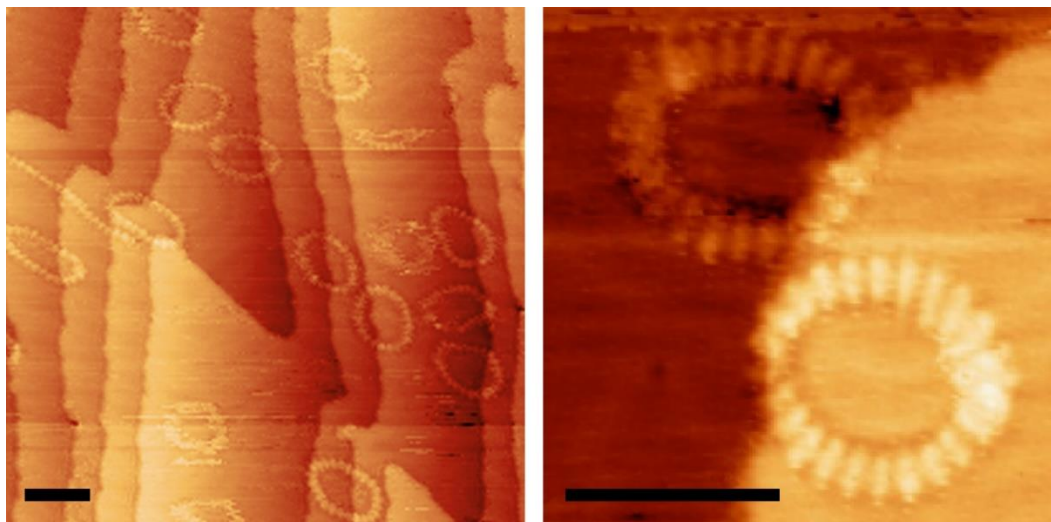


Figure 1.8. STM images of **c-P24** molecules on a gold surface. In both cases, the compound was deposited by electrospray from a solution in methanol/toluene containing 5% pyridine to prevent aggregation (scale bar 10 nm; structure shown in Figure 1.3 with R = OC₈H₁₇).^{63,65}

The Vernier principle can also be applied to synthesize linear porphyrin oligomers. Linear Vernier templating has some similarities with DNA replication, and it opens up the possibility of coupling along both strands of the Vernier complex, so that there is no longer a distinction between the ‘template’ and the ‘building block’. This strategy has been demonstrated as ‘*mutual Vernier templating*’ in the synthesis of linear porphyrin dodecamers (Figure 1.9).⁶⁶ In this design, a *meso*-4-pyridyl group was used to bind a nickel porphyrin strand to a zinc porphyrin strand. The nickel centers do not have significant affinity for pyridine ligands, and the presence of the nickel was used to block accidental insertion of copper during the Glaser coupling reaction. The product duplex has reactive free alkyne terminals, which makes it necessary to limit the extent of the coupling reaction to avoid polymerization.

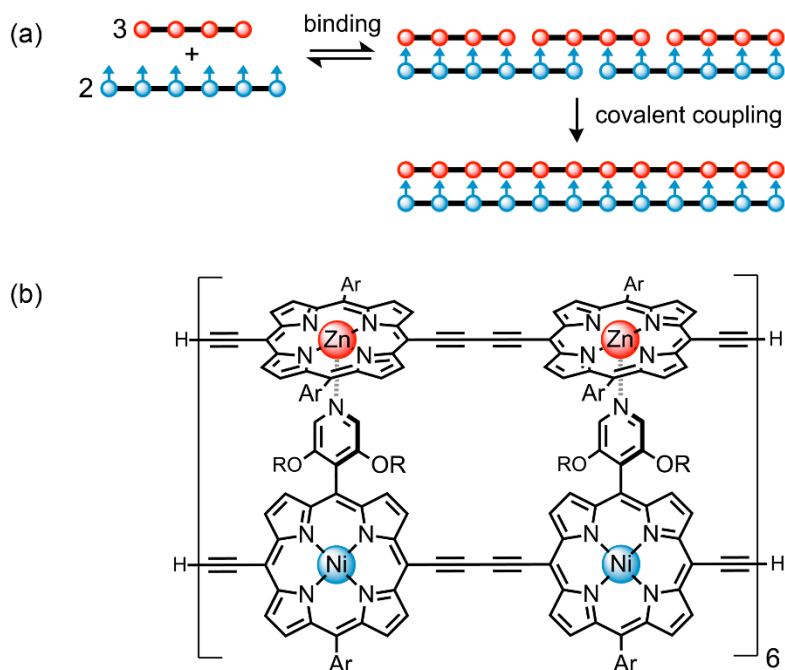


Figure 1.9. Mutual Vernier templating: both strands couple and there is no distinction between the ‘template’ and the ‘substrate’. (a) Cartoon of the reaction; (b) structure of the product duplex. $R = C_{12}H_{25}$; $Ar = 3,5\text{-bis(trihexylsilyl)phenyl}$.⁶⁶

1.3.4 Caterpillar track templates

A mismatch between the number of binding sites on a host and guest does not always lead to a Vernier complex — it can also give complexes with vacant coordination sites. For example, when **T6** is added to **c-P10** the product is a 2:1 complex, **c-P10·(T6)₂**. Similarly, addition of **T6** to **c-P8** forms **c-P8·(T6)₂** (Figure 1.10).⁶⁷ ¹H NMR exchange spectroscopy experiments (EXSY) show that these complexes are dynamic in solution and that the two template units rotate in a correlated way, like the caterpillar tracks of a bulldozer. This correlated motion resembles that in a molecular gear, except that in caterpillar track complexes the rotation of the two template “wheels” is conrotatory, whereas in a gear the motion is disrotatory. If some of the pyridine sites on the template are deleted, similar “caterpillar track” complexes can be formed which have no vacant coordination sites and which are not dynamic. The formation of these complexes can be exploited for template-directed synthesis; for example, coupling the linear porphyrin dimer **I-P2** in the presence of **T4** or **T5** gives **c-P8** or **c-P10**, respectively (Figure 1.11).⁶⁷ This strategy was used recently to prepare a 8-porphyrin nanoring with single-acetylene links.⁵⁴ The two main advantages of caterpillar templating, compared with classical

1:1 templating, are that smaller templates are easier to synthesize and that the size and shape of the template do not need to be so well matched to the cavity of the target structure. The synthesis of **c-P50** from **I-P10** using **T6** or **T8** as templates, mentioned above, probably involves intermediates similar to caterpillar track complexes.

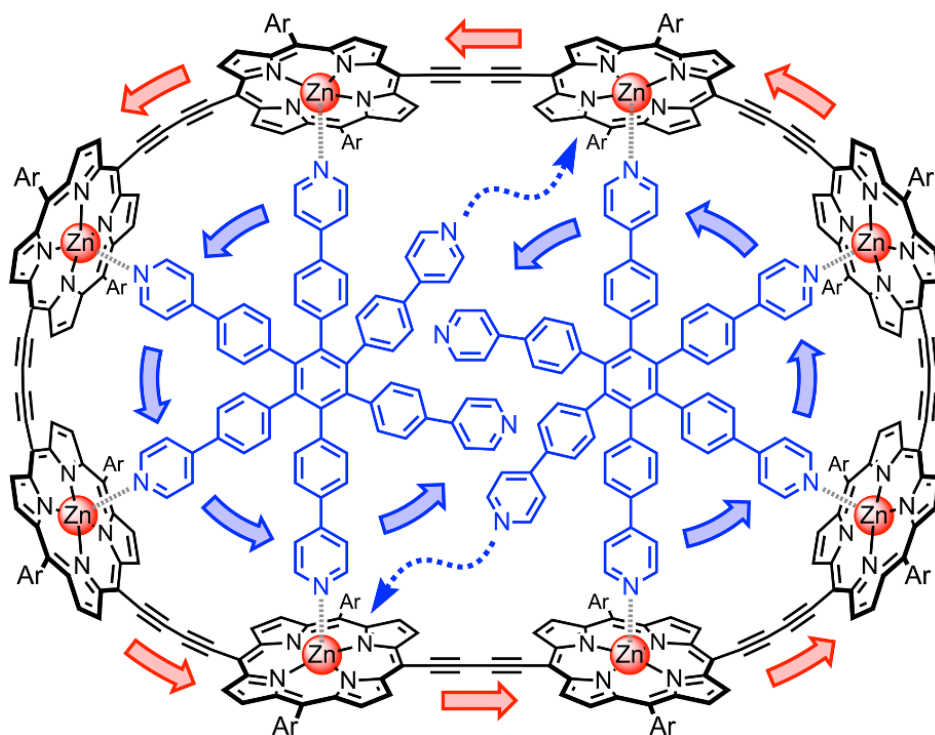


Figure 1.10. Caterpillar track motion in **c-P8·(T6)₂**, as revealed by ¹H NMR EXSY experiments.⁶⁷ The red and blue arrows show the directions of motion of the porphyrin and template units, respectively, and the dashed arrows indicate how ligand sites coordinate to zinc centers during rotation.

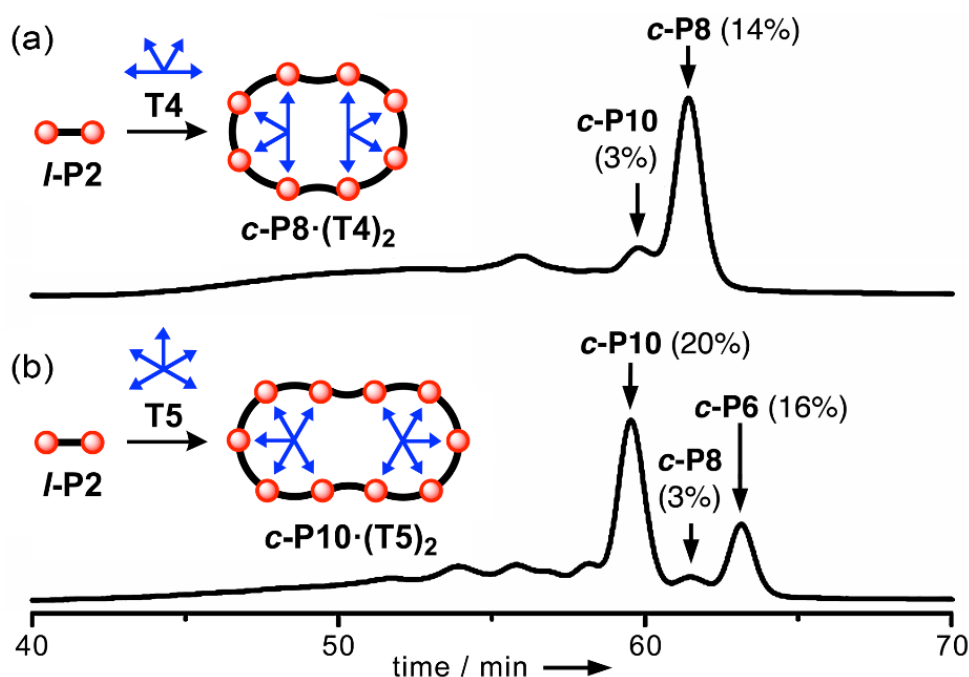


Figure 1.11. Caterpillar track templating. Cartoons showing coupling of a porphyrin dimer (*I*-P2) in the presence of templates (a) T4 and (b) T5, together with analytical GPC traces of the crude reaction mixtures from these three reactions.⁶⁷

1.3.5 Russian doll templating

Hierarchical ring-in-ring assemblies suggest that larger and larger molecules might be created by building shells out from a central core, such that each shell acts as a template for the next. This idea was explored by investigating a Russian doll complex consisting of an aluminum *c*-P6 held inside zinc *c*-P12 by six bis-imidazole-carboxylate ligands (Figure 1.12).⁶⁸ Aluminum is used for the inside ring because it coordinates two axial ligands rather than one. The complex of aluminum *c*-P6 and the bis-imidazole-carboxylate ligands is an effective template for directing the formation of the outer *c*-P12 ring from linear tetramer *I*-P4. However, it would not be simple to extend this approach to even larger structures.

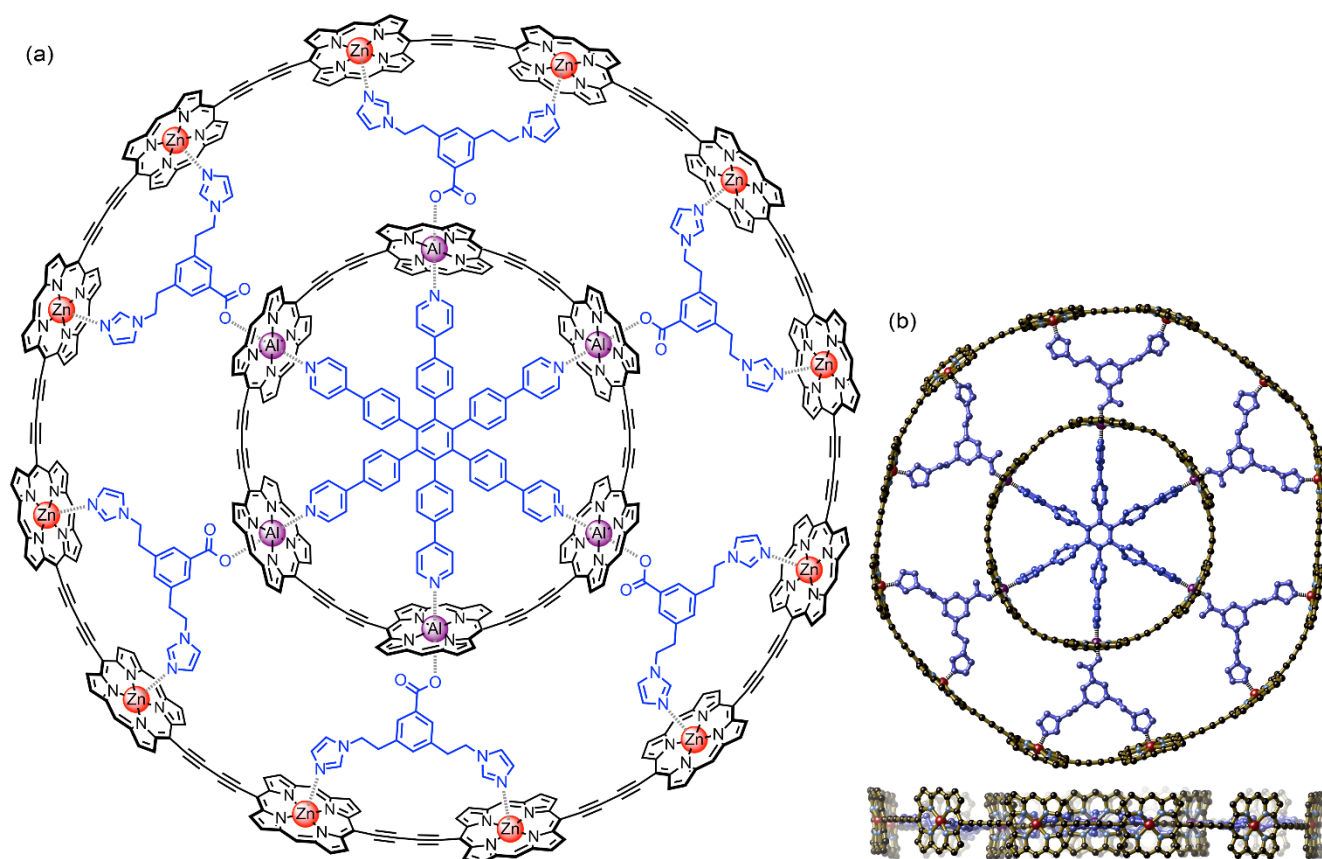


Figure 1.12. Structure of the Russian doll complex.⁶⁸ (a) Chemical structure (with *meso*-aryl side groups omitted for clarity). (b) Two orthogonal views of the calculated structure. (MM+ force field, HyperChem; *meso*-aryl side groups were not included in the calculations; hydrogen atoms omitted for clarity.)

1.3.6 Tubes and balls

The discussion above (Sections 1.3.2–1.3.5) focused on using templates to create topologically flat cyclic porphyrin oligomers. Similar strategies can also be used to create three-dimensional tubes and cages, by starting from slightly more elaborate building blocks, as illustrated by the architectures in Figure 1.13.^{13,69,70} All three of these structures were synthesized using the same **T6** template (introduced in Figure 1.4). Two units of **T6** were used to direct the synthesis of the 12-porphyrin nanotube (Figure 1.13a)⁶⁹ and the 11-porphyrin spiro-structure (Figure 1.13b).¹³ The 14-porphyrin ball (Figure 1.13c)⁷⁰ was prepared by first using the **T6** template to convert two porphyrin trimers into a cyclic hexamer, then coupling four equivalents of a linear dimer to this 6-porphyrin nanoring, then using two equivalents of a **T4** template to create an

orthogonal 10-porphyrin nanoring; finally both the **T6** and **T4** templates were removed by treatment with excess pyridine (Figure 1.14).

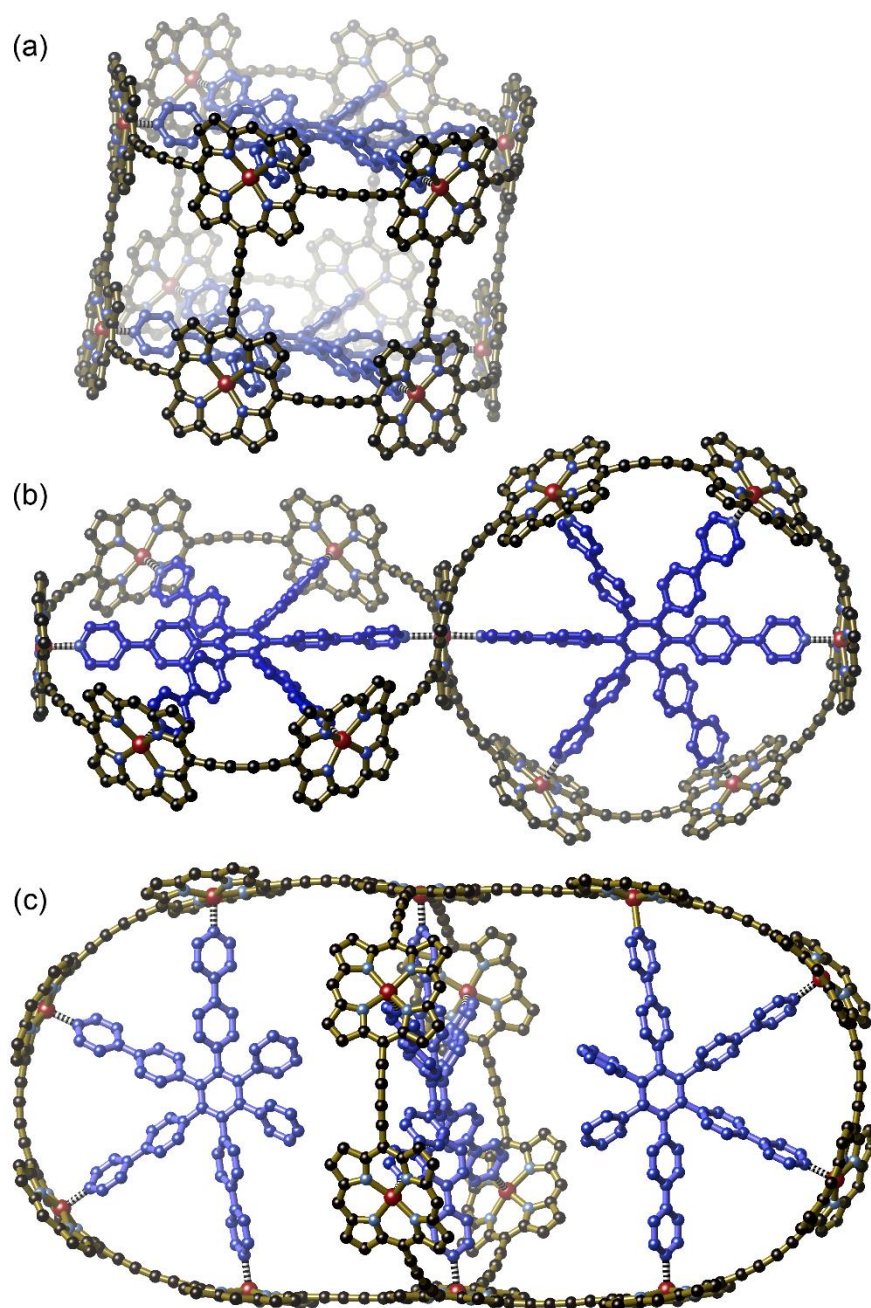


Figure 1.13. Calculated geometries of (a) a 12-porphyrin nanotube bound to two **T6** templates,⁶⁹ (b) an 11-porphyrin spiro-structure bound to two **T6** templates,¹³ and (c) a 14-porphyrin nanoball bound to a **T6** template and two **T4** templates.⁷⁰

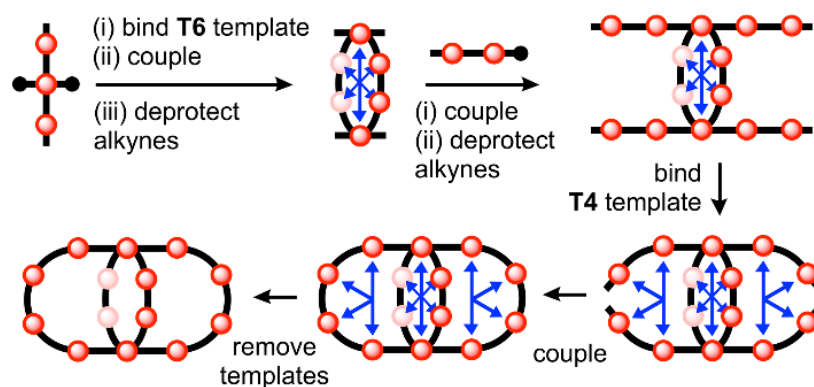


Figure 1.14. A simplified representation of the template-directed synthesis of a 14-porphyrin nanoball.⁷⁰ (Red spheres represent zinc porphyrin units; black lines and circles represent acetylene bridges and protecting groups, respectively; see ref 70 for detailed molecular structures and reagents.)

1.4 Prospective

This thesis sets out to develop new strategies for template directed synthesis of metallocporphyrin nanorings. Chapter 2 describes the discovery of the novel technique *shadow mask templates*, which can remove metal centers selectively at specific positions in the nanorings, so new metals can be inserted. This is a way of functionalizing the nanorings after macrocyclization so they can be used to study for example electron delocalization and quantum interference. In Chapter 3, these heterometallated nanorings are used to study quantum interference effects using pulsed EPR techniques.

During the work with shadow mask templates, it was discovered that oligopyridine templates can stack inside the nanorings. Chapter 4 describes the investigation of this stacking behavior and find that there is high positive allosteric cooperativity between two six-legged templates in a 12-porphyrin nanoring. It is also found that there is negative cooperativity between two three-legged templates in a six-porphyrin nanoring and that equilibration to the thermodynamically favored product happens very slowly over weeks to months at room temperature. Chapter 5 describes how the stacking templates can be used in synthesis to make large porphyrin nanorings.

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

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

P. S. Bols, H. L. Anderson, *Angew. Chem. Int. Ed.* **2018**, 57, 7874-7877.

2.1 Abstract

Molecular templates can be used in many ways to control the outcome of chemical reactions. Here 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 reaction only occurs at sites not masked by the template. We demonstrate this effect by using oligopyridine templates to dictate the sites of demetallation 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 demetallation, 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 heterometallated porphyrin arrays.

2.2 Introduction

Stencils and shadow masks have been used to create patterns since at about 60,000 years ago¹ and this strategy is widely exploited in top-down nanofabrication.² Here 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, in order to achieve a particular linking of atoms.³ A template provides instructions for the formation of a single product from a substrate or substrates which otherwise have the potential to assemble and react in a variety of ways.⁴ Recently, many new types of template-directed synthesis have been invented, providing routes to previously inaccessible molecular architectures.⁵⁻⁷ There are previous reports of the use of molecules as shadow masks,⁸ but to the best of our knowledge, this is the first time this principle has been used to create precisely defined molecular structures.

2.3 Shadow mask templates

2.3.1 Selective demetallation in magnesium porphyrin nanorings

The work presented here grew from a simple observation: treatment of the magnesium complex of a butadiyne-linked six-porphyrin nanoring, **Mg₆-c-P6**, with acetic acid in dichloromethane results in rapid removal of the magnesium cations from all six porphyrin centers, whereas the complex of this nanoring with a hexapyridyl template, **Mg₆-c-P6·T6**, is not demetallated 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 demetallation conditions. As expected, the uncoordinated magnesium porphyrin is cleanly demetallated, whereas the template-coordinated magnesium cations remain in place (Figure 2.1). Analysis of crude reaction mixtures by ¹H NMR spectroscopy and MALDI-ToF mass spectrometry shows that site-selective demetallation of **Mg₆-c-P6·T5** to **(H₂)Mg₅-c-P6·T5** is a quantitative reaction with no detectable trace of over-demetallated by-products. The template is displaced from **(H₂)Mg₅-c-P6·T5** by treatment with a large excess of DABCO, and **(H₂)Mg₅-c-P6** was isolated in 88% yield from **Mg₆-c-P6**.^{6,7,9}

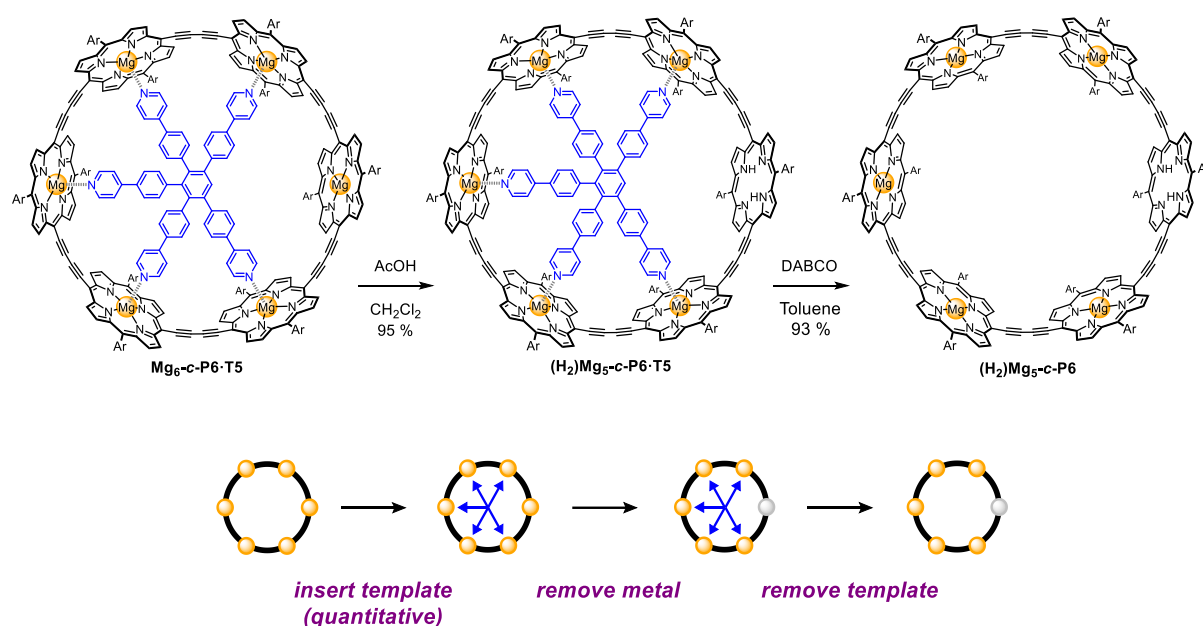


Figure 2.1. The template masking method applied to synthesize **(H₂)Mg₅-c-P6** using the template **T5**. Ar = 3,5-bis(trihexylsilyl)phenyl.

2.3.2 Scope of the reaction

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 2.2).^{10,11} In each case, the complex of the template with magnesium nanoring **Mg₆-c-P6** was treated with 10% acetic acid in dichloromethane by volume. All three reactions give clean site-selective demetallation, and the products are obtained in high yield without need for chromatographic purification (Scheme 2.1). The identities of the final compounds were confirmed by ¹H NMR and MALDI-ToF MS analysis.

The NH protons in the free-base porphyrins give distinctive proton resonances at chemical shifts of -1.0 to -1.3 ppm, and the exact chemical shift is characteristic of each isomer.

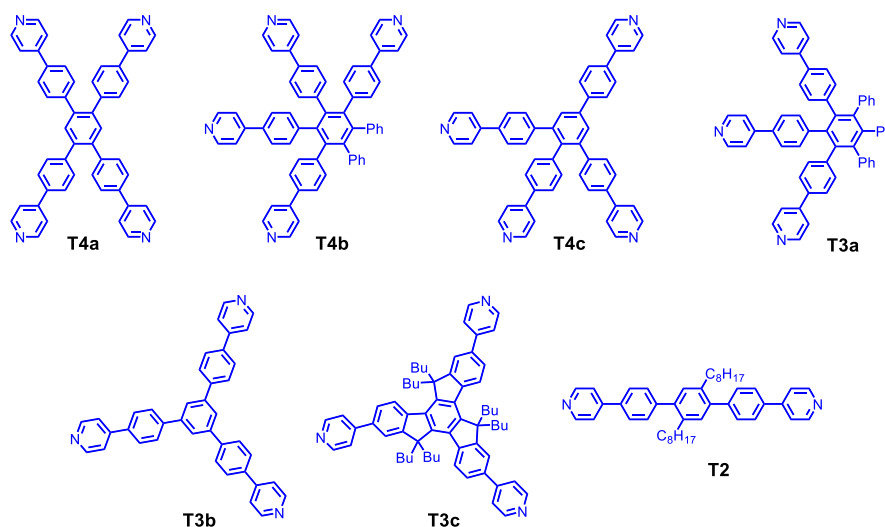
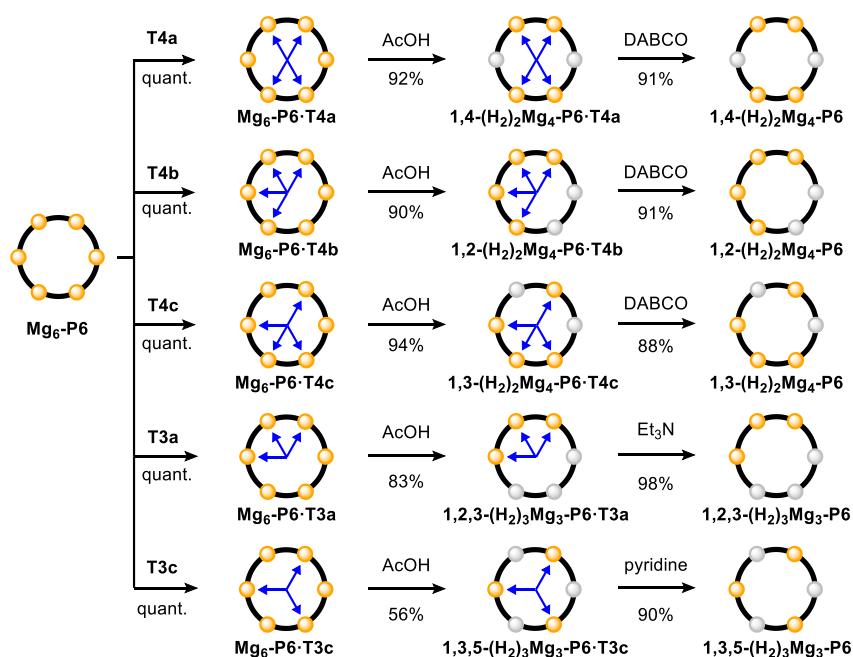


Figure 2.2. Structures of the oligopyridine ligands tested as masking templates. (T3b and T2 were found not to be effective as masking templates.)

Next, we tested three-legged templates, starting with the 1,2,3-isomer **T3a** (Figure 2.2).¹¹ Treatment of **Mg₆-c-P6** with one equivalent of **T3a** followed by acetic acid results in site-selective demetallation to form **1,2,3-(H₂)Mg₃-c-P6·T3a**, together with about 7% of the fully demetallated ring **(H₂)₆-c-P6**. This fully demetallated nanoring is easily separated from **1,2,3-(H₂)Mg₃-c-P6·T3a** by chromatography on silica. The formation of **(H₂)₆-c-P6** as a byproduct during the reaction of **Mg₆-c-P6·T3a** with acetic acid reflects the weaker association constant of this tridentate template compared with **T6**, **T5** and **T4a-c**.¹¹

Disappointingly, treatment of **Mg₆-c-P6** with the symmetric three-legged template **T3b**¹² (1:1 mole ratio) followed by acetic acid does not result in site-selective demetallation. The main products are unreacted starting material and fully demetallated ring **(H₂)₆-c-P6**. ¹H NMR titrations revealed the reason for this result: when one equivalent of **T3b** is added to **Mg₆-c-P6**, the main product is the 1:2 complex **Mg₆-c-P6·(T3b)₂**, together with a small amount of the 1:1 complex **Mg₆-c-P6·T3b**, and some template-free **Mg₆-P6** nanoring. It appears that formation of the 1:2 complex with **T3b** is too favorable, making this ligand ineffective as a masking template. Later, we discovered that the predominant formation of 1:2 product is a kinetic effect, and that equilibration to the more thermodynamically favored 1:1 product happens very slowly over weeks/months. Spectra and further investigation can be found in Chapter 4.

In order to solve this problem for the use of shadow mask templates, we designed a three-legged template with bulky groups to prevent the stacking, **T3c**, based on a truxene core.¹³ A similar tripyridyl truxene has been reported for use in organic thin-film solar cells.¹⁴ Template **T3c** has a similar coordination geometry to **T3b**, but the bulky *n*-butyl chains in the truxene are expected to hinder stacking. ¹H NMR spectroscopy shows that addition of **T3c** to the nanoring only leads to formation of a 1:1 complex, **Mg₆-P6·T3c**. Addition of acetic acid to this complex results in site-selective demetallation, together with formation the fully demetallated nanoring (**H₂**)₆-**P6**. ¹H NMR analysis of the crude reaction mixture (Figure 2.3) shows that it consists of 83% **1,3,5-(H₂)₃Mg₃-P6·T3c** and 17% (**H₂**)₆-**P6**. These two products are readily separated by chromatography on silica. The weaker binding resulting from the presence of only three pyridine coordination sites makes **T3c** less effective than **T4a–c** as a masking template, but the bulk of the truxene effectively blocks formation of the 1:2 complex. The two-legged template **T2** (Figure 2.2) binds too weakly to control the demetallation process; treatment of the complex of **Mg₆-P6** and **T2** with acetic acid gives only the fully demetallated ring (**H₂**)₆-**P6**.



Scheme 2.1. The template masking method applied to synthesize five heterometallated rings from **Mg₆-c-P6**.

2.3.3 Analysis of the synthesis of $1,3,5-(\text{H}_2)_3\text{Mg}_3\text{-c-P6}\cdot\text{T3c}$

Figure 2.3a shows the ^1H NMR spectrum of the crude reaction mixture from the synthesis of $1,3,5-(\text{H}_2)_3\text{Mg}_3\text{-c-P6}\cdot\text{T3c}$. Figure 2.3b shows a zoom on the beta pyrrole region and the -0.9 to -1.4 region. The peaks highlighted in red stem from $(\text{H}_2)_6\text{-c-P6}$, and the black peaks stem from the desired product, $1,3,5-(\text{H}_2)_3\text{Mg}_3\text{-c-P6}\cdot\text{T3c}$. The ratio between the two compounds calculated from the ratio between the integrals is 83% $1,3,5-(\text{H}_2)_3\text{Mg}_3\text{-c-P6}\cdot\text{T3c}$ and 17% $(\text{H}_2)_6\text{-c-P6}$.

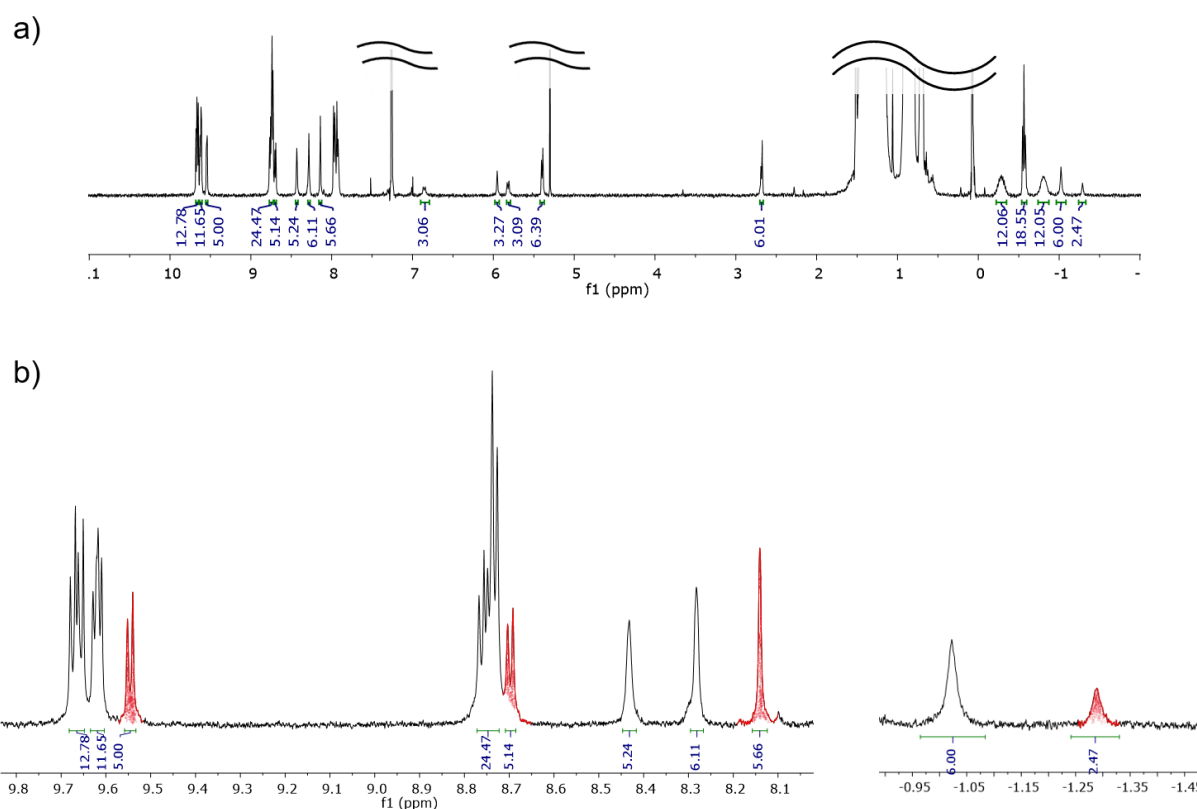


Figure 2.3. a) Full ^1H NMR spectrum (400 MHz, CDCl_3 , 298 K) of the crude reaction mixture from the synthesis of $1,3,5-(\text{H}_2)_3\text{Mg}_3\text{-c-P6}\cdot\text{T3c}$. b) Zoom of the same spectrum. Red peaks belong to the fully demetallated nanoring $(\text{H}_2)_6\text{-c-P6}$. Black peaks belong to the product with three demetallated porphyrins and three template-coordinated magnesium porphyrins $1,3,5-(\text{H}_2)_3\text{Mg}_3\text{-c-P6}\cdot\text{T3c}$. The integrals of the peaks are used to calculate the proportion of each compound in the mixture as 83% desired product and 17% fully demetallated ring.

2.4 Inserting zinc, copper and silver

Many metal cations can be inserted into porphyrins under mild conditions,¹⁵ so the magnesium/free-base nanorings reported here should be useful intermediates for preparing many other diverse heterometallated systems.

Magnesium porphyrins are readily demetallated by acid, but they do not easily undergo transmetalation when treated with other metal salts,¹⁶ which makes it possible to use shadow mask templates to achieve site-selective transmetalation.

For example, treatment of **1,2-(H₂)₂Mg₄-c-P6** with zinc(II) acetate results in clean insertion of zinc(II) at the two free-base positions to give **1,2-Zn₂Mg₄-c-P6**; the remaining magnesium centers can then be demetallated selectively with acetic acid to yield **1,2-Zn₂(H₂)₄-c-P6** (Scheme 3a).¹⁷ This compound is useful for testing the cooperativity of ligand binding inside nanorings.¹¹

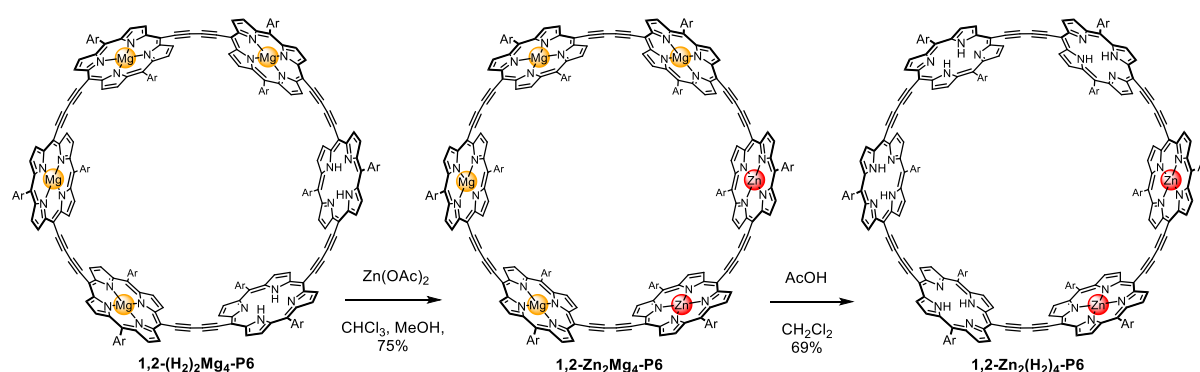
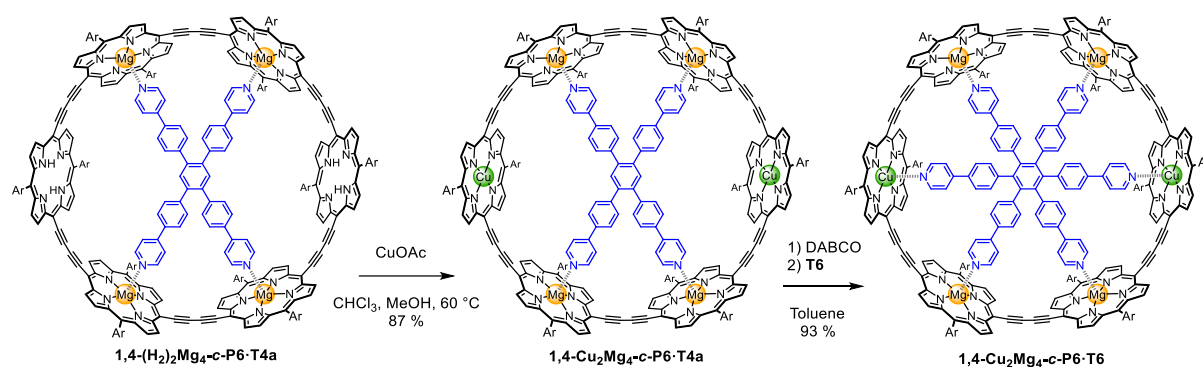


Figure 2.2. Synthesis of a bis-zinc(II) porphyrin nanoring using shadow mask templates. Ar = 3,5-bis(trihexylsilyl)phenyl.

We have also prepared a heterometallated nanoring containing two paramagnetic copper(II) ions opposite each other (**1,4-Cu₂Mg₄-c-P6·T4a** Scheme 2.3). In this reaction, the **T4a** template was left in place during insertion of copper(II) into the two free-base centers of **1,4-(H₂)Mg₄-c-P6·T4a**. We removed **T4a** and inserted **T6** to obtain **1,4-Cu₂Mg₄-c-P6·T6**, which is a valuable compound for investigating quantum interference through long-range exchange coupling, as will be explained in more detail in Chapter 3.¹⁸

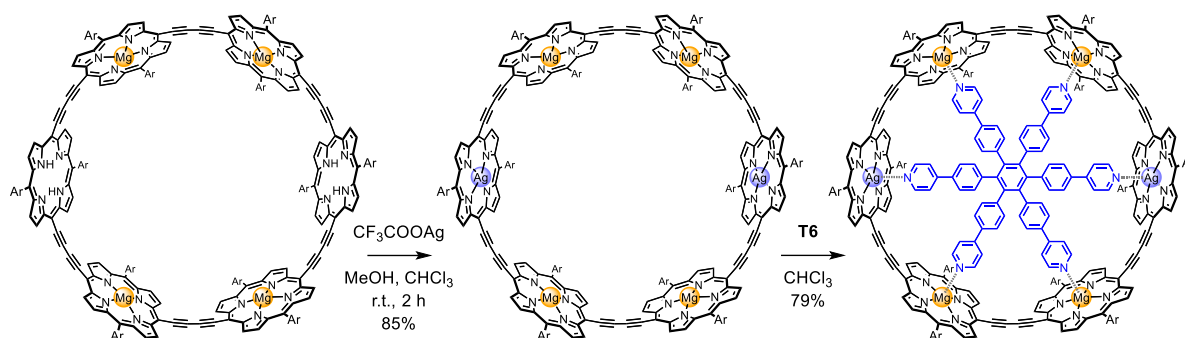


Scheme 2.3. Synthesis of a bis-copper(II) porphyrin nanoring using shadow mask templates.

Ar = 3,5-bis(trihexylsilyl)phenyl.

In addition to the copper(II) systems, we were interested to see if other paramagnetic metals could be inserted into the nanorings. We found that silver can be readily inserted into the heterometallated porphyrin nanorings, and we prepared a bis-silver(II) magnesium nanoring and inserted **T6** (Scheme 2.4). In this reaction, silver is added as silver(I) and gets oxidized to silver(II) when it inserts into the porphyrin, which is the standard practice for making silver porphyrin compounds. It is an interesting reaction that requires two equivalents of silver(I). As the large silver(I) ion (1.16 Å) is squeezed into the rigid porphyrin, its oxidation potential is lowered so the second equivalent of silver(I) is strong enough to oxidize it. Hence, you get a disproportionation reaction forming silver(0) and we indeed observed a silver mirror on the flask used for this reaction.¹⁹

In the copper-insertion in Scheme 2.3 we also used copper(I) to insert copper(II), however the discovery of this reaction was unintended as the addition of CuOAc was a mistake, and to our knowledge copper(I) has not previously been used to make copper(II) porphyrins. This could be due to a similar disproportionation reaction as described above; however, we think it is more likely that in this case, copper(I) is just spontaneously oxidized to copper(II) as the reaction was exposed to air.



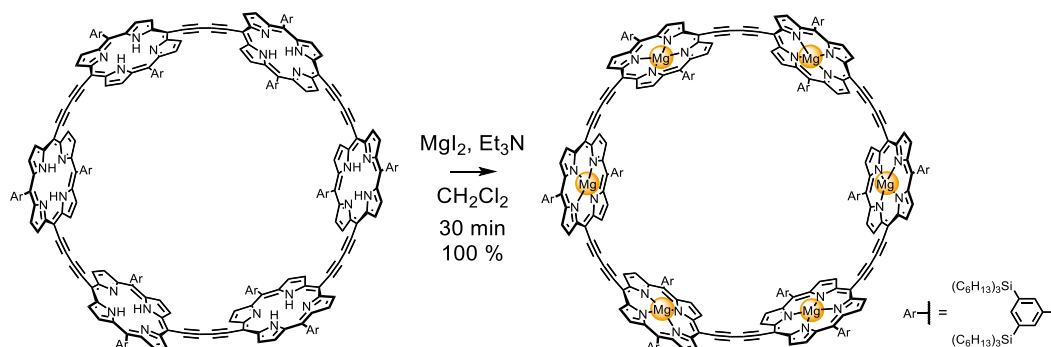
Scheme 2.4. Synthesis of bis-silver(II) magnesium nanoring using shadow mask templates. $\text{Ar} = 3,5\text{-bis(trihexylsilyl)phenyl}$.

2.5 Conclusion

In summary, we have demonstrated that oligopyridine ligands can be used as shadow mask templates to achieve site-selective demetallation of magnesium porphyrin nanorings. Selective demetallation is quantitative with five- and four-legged templates, and it provides useful selectivity with three-legged templates if 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 heterometallated porphyrin arrays.

2.6 Synthetic procedures

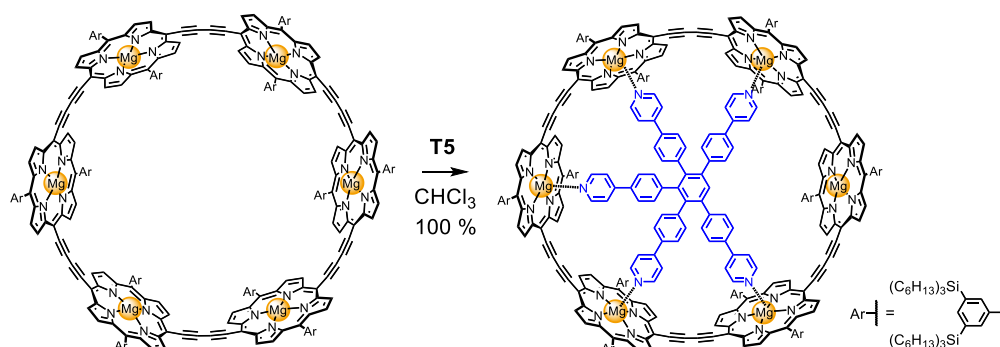
Mg₆-c-P6



Metalation with magnesium(II) was carried out using reaction conditions developed by Lindsey and Woodford.²⁰ **(H₂)6-c-P6** (30 mg, 3.1 μ mol), magnesium iodide (102 mg, 366 μ mol) and triethylamine (0.050 mL, 360 μ mol) were dissolved in anhydrous CH₂Cl₂ (5 mL) and stirred at room temperature under argon. The reaction was followed with UV. After 30 min, the reaction had reached completion. The solution was washed with water (3 $\times$ 2 mL) and the solvent was removed in vacuum.

Yield: 30.4 mg, 100%. **¹H NMR** (400 MHz, CDCl₃) δ 9.57 (d, J = 4.5 Hz, 24H), 8.71 (d, J = 4.5 Hz, 24H), 8.15 (s, 24H), 7.94 (s, 12H), 1.44 (m, 144H), 1.28 (m, 432H), 0.87 (m, 144H), 0.81 (m, 216H). **MS (MALDI-TOF):** m/z 9966 (M^+ , C₆₄₈H₁₀₂₀Mg₆N₂₄Si₂₄ requires 9967). **UV-VIS:** λ_{max} (CHCl₃) nm (log(ϵ)): 478 (5.73), 800 (5.52).

Mg₆-c-P6·T5

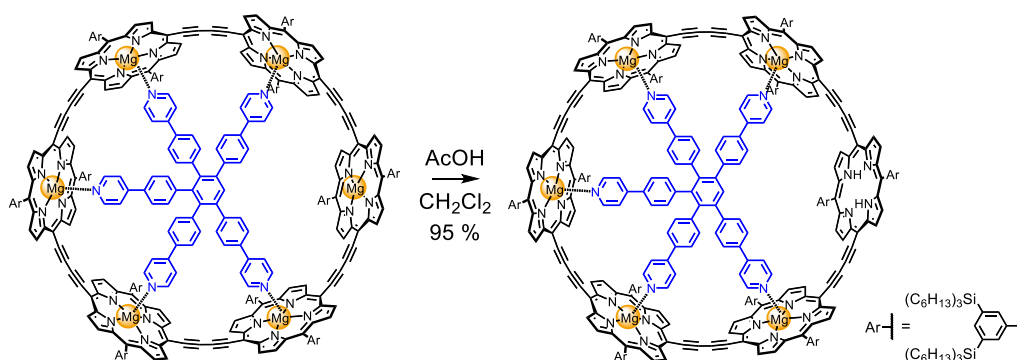


Mg₆-c-P6 (3.0 mg, 0.30 μ mol) and **T5** (1.4 mg, 1.5 μ mol) were mixed and dissolved in CHCl₃ (1.0 mL). The solution was stirred at room temperature for 15 min, after which the solvent was

evaporated. The solid was dissolved in petrol ether : CH₂Cl₂ : Et₃N (79:20:1), and passed through a silica plug eluting with the same solvent mixture. The resulting solution was concentrated and dried in vacuum.

Yield: 3.2 mg, 100%. **¹H NMR:** (400 MHz, CDCl₃) δ 9.59 (m, 4H), 9.54(m, 20H), 8.72 (m, 24H), 8.30 (m, 12H), 7.97 (m, 24H), 6.42 (s, 1H), 5.82 (d, *J* = 8.6 Hz, 4H), 5.69 (d, *J* = 8.4 Hz, 4H), 5.49 (m, 12H), 5.11 (d, *J* = 5.7 Hz, 4H), 5.01 (d, *J* = 6.0 Hz, 4H), 4.94 (d, *J* = 4.7 Hz, 2H), 2.51 (d, *J* = 5.7 Hz, 4H), 2.36 (d, *J* = 6.0 Hz, 4H), 2.32 (d, *J* = 4.7 Hz, 2H), 1.46 (m, 144H), 1.30 (m, 432H), 0.85 (m, 342H), 0.68 (m, 18H). **UV-VIS:** λ_{max} (CHCl₃) nm (log(ε)): 483 (5.68), 781 (5.51), 818 (5.60), 861 (5.49).

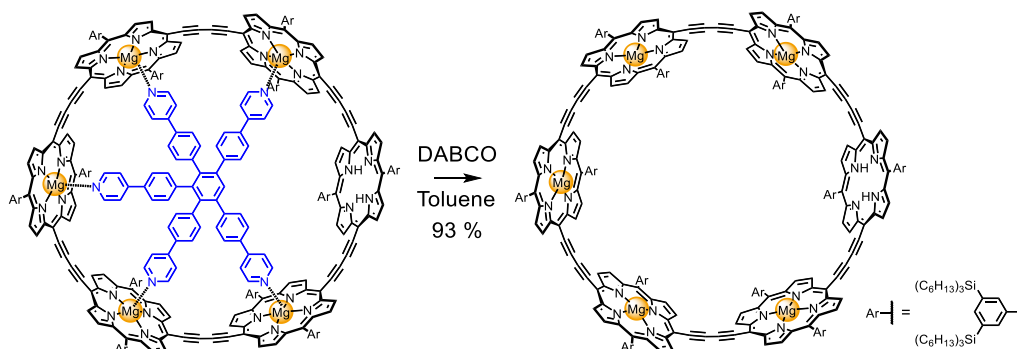
(H₂)Mg₅-c-P6·T5



Mg₆-c-P6·T5 (5.4 mg, 0.5 μmol) was dissolved in CH₂Cl₂ (1.0 mL) and glacial acetic acid (0.10 mL) was added. The solution was stirred at room temperature and the reaction was followed by MALDI TOF MS analysis. After 1 h, the reaction was complete. The solution was washed with water (3 × 2 mL) and then run through an alumina pipette plug (CH₂Cl₂). The solvent was evaporated.

Yield: 5.1 mg, 95%. **¹H NMR:** (500 MHz, CDCl₃) δ 9.58 (d, *J* = 4.3 Hz, 4H), 9.55 (d, *J* = 4.3 Hz, 8H), 9.52 (m, 12H), 8.73 (m, 20H), 8.67 (d, *J* = 4.6 Hz, 4H), 8.39 (s, 2H), 8.33 (m, 8H), 8.30 (s, 2H), 7.99 (m, 10H), 7.96 (m, 12H), 7.86 (s, 2H), 6.44 (s, 1H), 5.85 (d, *J* = 8.7 Hz, 4H), 5.71 (d, *J* = 8.7 Hz, 4H), 5.47 (m, 12H), 5.12 (d, *J* = 6.6 Hz, 4H), 5.01 (d, *J* = 6.6 Hz, 4H), 4.94 (d, *J* = 6.6 Hz, 2H), 2.49 (d, *J* = 6.6 Hz, 4H), 2.35 (d, *J* = 6.6 Hz, 4H), 2.32 (d, *J* = 6.6 Hz, 2H), 1.46 (m, 144H), 1.30 (m, 432H), 0.91 (m, 252H), 0.79 (m, 108), -1.09 (s, 2H). **MS (MALDI-TOF):** *m/z* 10789 (M⁺, C₇₀₉H₁₀₆₃Mg₅N₂₉Si₂₄ requires 10789). **UV-VIS:** λ_{max} (CHCl₃) nm (log(ε)): 481 (5.68), 615 (4.65), 781 (5.49), 817 (5.58), 858 (5.47).

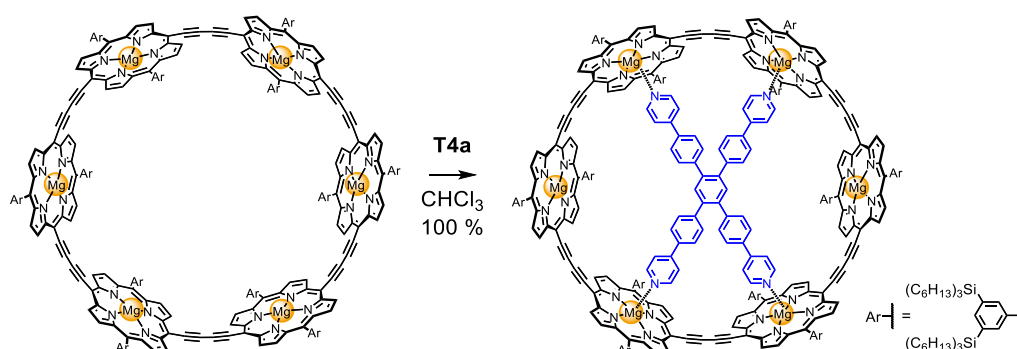
(H₂)Mg₅-c-P6



Freshly recrystallized 1,4-diazabicyclo[2.2.2]octane (15 g) was dissolved in toluene (56 mL) to achieve a 2.5 M solution. A SEC column (2.4 cm diameter, 32 cm length, Bio-Beads S-X1) was loaded with the solution. **(H₂)Mg₅-c-P6·T5** (5.1 mg) was dissolved in toluene (1 mL) and eluted through the SEC column with toluene. The obtained solution was washed with water (3 × 3 mL) and the solvent was removed in vacuum. After the first SEC column, the product mixture still contained templated ring, so the procedure was repeated one more time to obtain the pure product.

Yield: 4.4 mg, 93%. **¹H NMR:** (500 MHz, CDCl₃) δ 9.57 (m, 24H), 8.71 (m, 24H), 8.12 (m, 24H), 7.96 (s, 2H), 7.93 (s, 10H), 1.43 (m, 144H), 1.24 (m, 432H), 0.81 (m, 360H), -1.17 (s, 2H). **MS (MALDI-TOF):** *m/z* 9944 (M⁺, C₆₄₈H₁₀₂₂Mg₅N₂₄Si₂₄ requires 9945). **UV-VIS:** λ_{max} (CHCl₃) nm (log(ε)): 478 (5.70), 613 (4.65), 797 (5.49).

Mg₆-c-P6·T4a

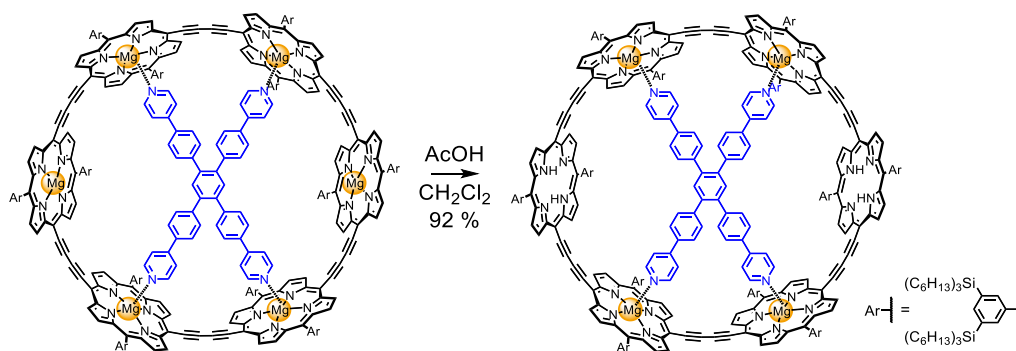


Mg₆-c-P6 (5.0 mg, 0.50 μmol) and **T4a** (1.0 mg, 1.5 μmol) was mixed and dissolved in CHCl₃ (1.0 mL). The solution was stirred at room temperature for 15 min, after which the solvent was evaporated. The solid was dissolved in petrol ether : CH₂Cl₂ : Et₃N (79 : 20 : 1), and passed

through a silica plug washing with the same solvent mixture. The resulting solution was concentrated and dried in vacuum.

Yield: 5.3 mg, 100%. **^1H NMR** (400 MHz, CDCl_3) δ 9.60 (d, J = 4.4 Hz, 8H), 9.58 (d, J = 4.4 Hz, 8H), 9.54 (d, J = 4.5 Hz, 8H), 8.75 (d, J = 4.4 Hz, 8H), 8.73 (d, J = 4.4 Hz, 8H), 8.69 (d, J = 4.5 Hz, 8H), 8.36 (s, 8H), 8.19 (s, 4H), 8.07 (s, 4H), 7.98 (s, 8H), 7.96 (s, 8H), 7.94 (s, 4H), 6.31 (s, 2H), 5.84 (d, J = 8.5 Hz, 8H), 5.77 (d, J = 8.5 Hz, 8H), 5.18 (d, J = 6.5 Hz, 8H), 2.52 (d, J = 6.5 Hz, 8H), 1.25 (m, 576H), 0.91 (m, 252H), 0.77 (t, J = 7.0 Hz, 72H), 0.65 (t, J = 6.9 Hz, 36H). **UV-VIS:** λ_{max} (CHCl_3) nm (log(ϵ)): 482 (5.71), 777 (5.50), 813 (5.60), 854 (5.50).

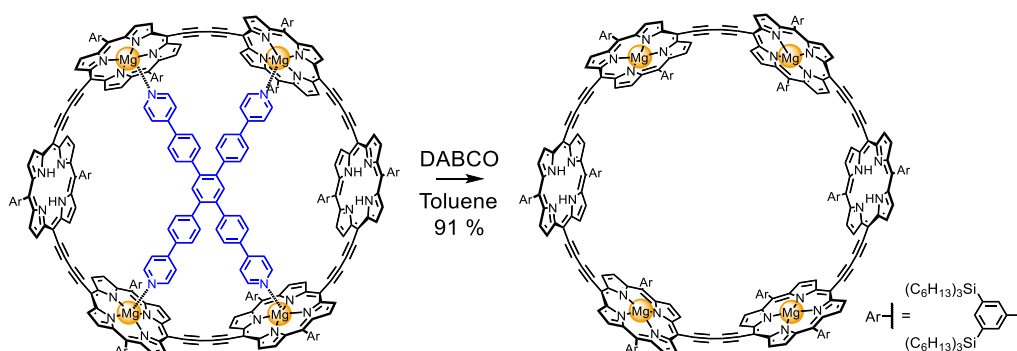
1,4-(H_2) $_2\text{Mg}_4\text{-c-P6-T4a}$



Mg₆-c-P6-T4a (5.2 mg, 0.49 μmol) was dissolved in CH_2Cl_2 (1.0 mL) and glacial acetic acid (0.10 mL) was added. The solution was stirred at room temperature and followed with TLC. After 1 h, the solution was washed with water (3×2 mL) and then run through an alumina pipette plug (CH_2Cl_2). The solvent was removed in vacuum.

Yield: 4.8 mg, 92%. **^1H NMR:** (400 MHz, CDCl_3) δ 9.58 (m, 16H), 9.49 (d, J = 4.6 Hz, 8H), 8.76 (d, J = 4.3 Hz, 8H), 8.74 (d, J = 4.3 Hz, 8H), 8.65 (d, J = 4.6 Hz, 8H), 8.35 (app. s, 12H), 7.99 (s, 8H), 7.96 (app. s, 12H), 7.88 (s, 4H), 6.35 (s, 2H), 5.87 (d, J = 8.5 Hz, 8H), 5.76 (d, J = 8.5 Hz, 8H), 5.18 (d, J = 6.4 Hz, 8H), 2.49 (d, J = 6.4 Hz, 8H), 1.44 (m, 144H), 1.30 (m, 432H), 0.89 (m, 252), 0.77 (t, J = 7.0 Hz, 72H), 0.72 (t, J = 6.8 Hz, 36H), -1.19 (s, 4H). **MS (MALDI-TOF):** m/z 10613 (M^+ , $\text{C}_{698}\text{H}_{1058}\text{Mg}_4\text{N}_{28}\text{Si}_{24}$ requires 10614). **UV-VIS:** λ_{max} (CHCl_3) nm (log(ϵ)): 478 (5.79), 689 (4.93), 779 (5.53), 815 (5.65), 854 (5.59).

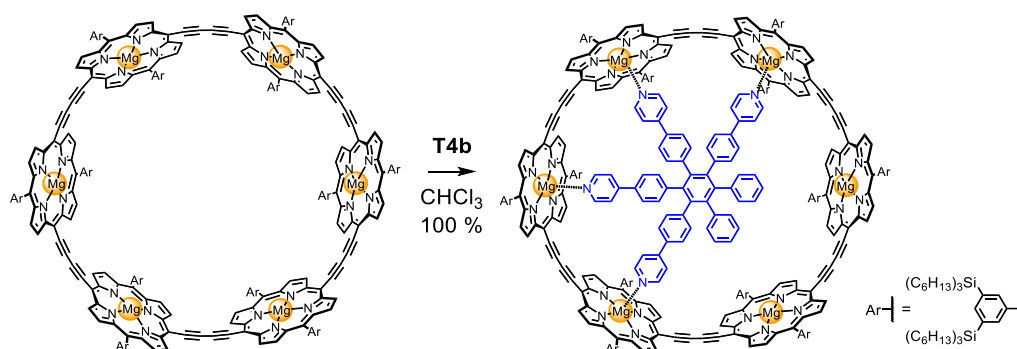
1,4-(H₂)₂Mg₄-c-P6



Freshly recrystallized 1,4-diazabicyclo[2.2.2]octane (15 g) was dissolved in toluene (56 mL) to achieve a 2.5 M solution. A SEC column (2.4 cm diameter, 32 cm length, Bio-Beads S-X1) was loaded with the solution. **1,4-(H₂)₂Mg₄-c-P6·T4a** (4.8 mg, 0.46 μmol) was dissolved in toluene (1 mL) and eluted through the SEC column with toluene. The obtained solution was washed with water (3 × 3 mL) and the solvent was removed in vacuum.

Yield: 4.1 mg, 91%. **¹H NMR:** (700 MHz, CDCl₃) δ 9.56 (m, 16H), 9.54 (d, *J* = 4.4 Hz, 8H), 8.71 (m, 16H), 8.68 (d, *J* = 4.4 Hz, 8H), 8.14 (m, 24H), 7.96 (s, 4H), 7.93 (s, 8H), 1.38 (m, 144H), 1.24 (m, 432H), 0.82 (m, 360H), −1.16 (s, 4H). **MS (MALDI-TOF):** *m/z* 9921 (*M*⁺, C₆₄₈H₁₀₂₄Mg₄N₂₄Si₂₄ requires 9923). **UV-VIS:** λ_{max} (CHCl₃) nm (log(ε)): 470 (5.72), 684 (4.93), 796 (5.49).

Mg₆-c-P6·T4b

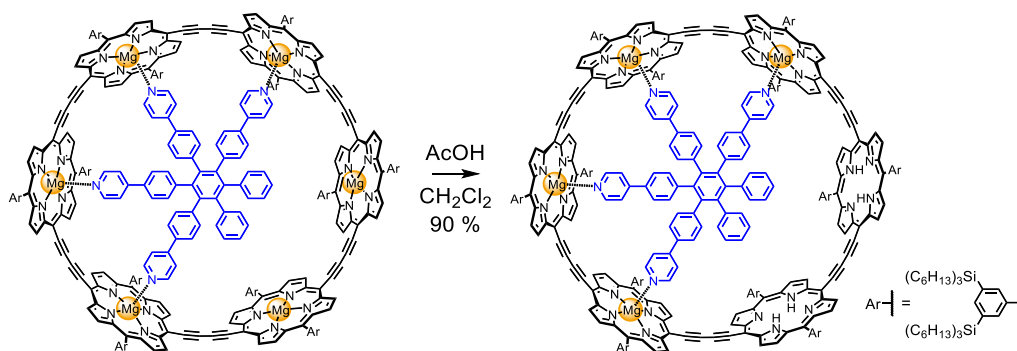


Mg₆-c-P6 (4.0 mg, 0.40 μmol) and **T4b** (1.0 mg, 1.5 μmol) was mixed and dissolved in CHCl₃ (1.0 mL). The solution was stirred at room temperature for 15 min, after which the solvent was evaporated. The solid was dissolved in petrol ether : CH₂Cl₂ : Et₃N (79 : 20 : 1), and passed

through a silica plug eluting with the same solvent mixture. The resulting solution was concentrated and dried in vacuum to give the product as a brown solid.

Yield: 4.3 mg, 100%. **^1H NMR:** (400 MHz, CDCl_3) δ 9.53 (m, 24H), 8.71 (m, 24H), 8.31 (m, 8H), 8.15 (m, 4H), 7.99 (m, 24H), 5.49 (m, 8H), 5.40 (m, 8H), 5.34 (m, 4H), 5.22 (m, 4H), 4.98 (d, $J = 6.5$ Hz, 4H), 4.95 (d, $J = 6.5$ Hz, 4H), 2.36 (d, $J = 6.5$ Hz, 4H), 2.31 (d, $J = 6.5$ Hz, 4H), 1.30 (m, 576H), 0.89 (m, 360H). **MS (MALDI-TOF):** m/z 10811 (M^+ , $\text{C}_{710}\text{H}_{1062}\text{Mg}_6\text{N}_{28}\text{Si}_{24}$ requires 10810). **UV-VIS:** λ_{max} (CHCl_3) nm ($\log(\epsilon)$): 482 (5.71), 780 (5.52), 817 (5.59), 859 (5.46).

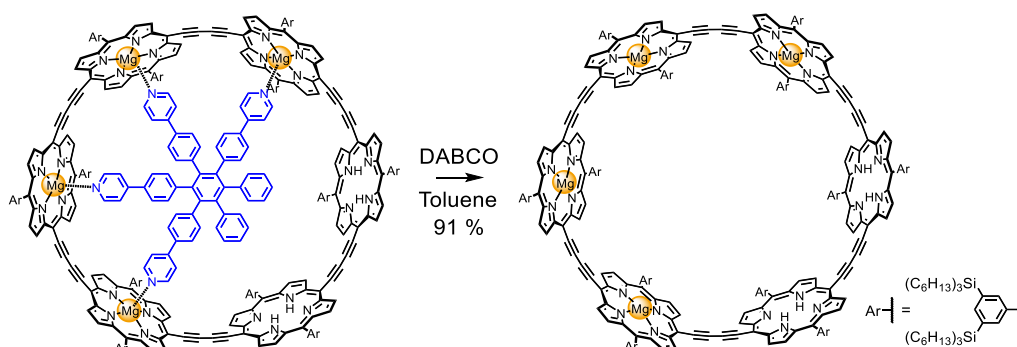
1,2-(H_2) $_2\text{Mg}_4\text{-c-P6-T4b}$



Mg₆-c-P6-T4b (4.3 mg, 0.40 μmol) was dissolved in CH_2Cl_2 (1.0 mL) and glacial acetic acid (0.10 mL) was added. The solution was stirred at room temperature and followed with TLC. After 1 h, the solution was washed with water (3×2 mL) and then run through an alumina pipette plug (CH_2Cl_2). The solvent was removed in vacuum.

Yield: 3.9 mg, 90%. **^1H NMR:** (500 MHz, CDCl_3) δ 9.53 (m, 24H), 8.73 (d, $J = 4.4$ Hz, 4H), 8.71 (m, 16H), 8.67 (d, $J = 4.4$ Hz, 4H), 8.41 (s, 4H), 8.30 (s, 8H), 8.00 (s, 8H), 7.97 (s, 4H), 7.96 (s, 8H), 7.87 (s, 4H), 5.51 (m, 8H), 5.39 (m, 12H), 5.30 (m, 4H), 5.04 (m, 2H), 5.00 (d, $J = 6.6$ Hz, 4H), 4.94 (d, $J = 6.6$ Hz, 4H), 2.34 (d, $J = 6.6$ Hz, 4H), 2.30 (d, $J = 6.6$ Hz, 4H), 1.46 (m, 144H), 1.35 (m, 432H), 0.91 (m, 252H), 0.80 (m, 108H), -1.13 (s, 4H). **MS (MALDI-TOF):** m/z 10766 (M^+ , $\text{C}_{710}\text{H}_{1066}\text{Mg}_4\text{N}_{28}\text{Si}_{24}$ requires 10766). **UV-VIS:** λ_{max} (CHCl_3) nm ($\log(\epsilon)$): 484 (5.79), 668 (4.85), 782 (5.59), 817 (5.68), 857 (5.56).

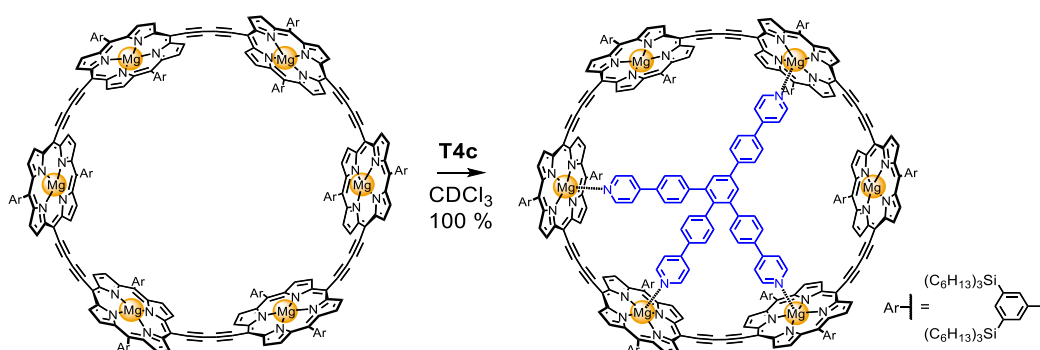
1,2-(H₂)₂Mg₄-c-P6



Freshly recrystallized 1,4-diazabicyclo[2.2.2]octane (15 g) was dissolved in toluene (56 mL) to achieve a 2.5 M solution. A SEC column (2.4 cm diameter, 32 cm length, Bio-Beads S-X1) was loaded with the solution. **1,2-(H₂)₂Mg₄-c-P6·T4b** (5.4 mg, 0.50 μmol) was dissolved in toluene (1 mL) and eluted through the SEC column with toluene. The obtained solution was washed with water (3 × 3 mL) and the solvent was removed in vacuum.

Yield: 4.5 mg, 91%. **¹H NMR:** (500 MHz, CDCl₃) δ 9.57 (m, 20H), 9.53 (d, *J* = 4.7 Hz, 4H), 8.71 (m, 24H), 8.13 (m, 24H), 7.95 (s, 4H), 7.93 (s, 8H), 1.41 (m, 144H), 1.23 (m, 432H), 0.87 (m, 144H), 0.81 (m, 216H), -1.22 (s, 4H). **MS (MALDI-TOF):** *m/z* 9924 (M⁺, C₆₄₈H₁₀₂₄Mg₄N₂₄Si₂₄ requires 9923). **UV-VIS:** λ_{max} (CHCl₃) nm (log(ε)): 476 (5.73), 664 (4.84), 795 (5.53).

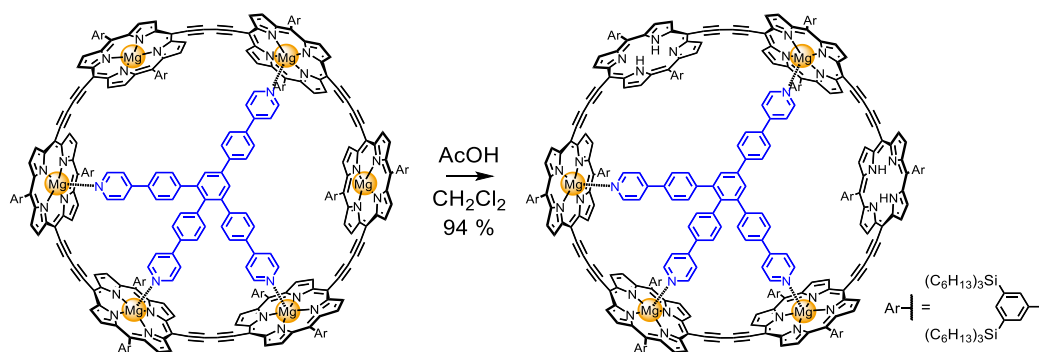
Mg₆-c-P6·T4c



Mg₆-c-P6 (2.5 mg, 0.25 μmol) and **T4c** (0.17 mg, 0.25 μmol) was mixed in CDCl₃ (0.6 mL). ¹H NMR confirmed quantitative insertion of the template.

^1H NMR: ^1H NMR (400 MHz, CDCl_3) δ 9.62 (d, J = 4.4 Hz, 4H), 9.59 (d, J = 4.2 Hz, 8H), 9.56 (m, 12H), 8.73 (m, 24H), 8.34 (m, 8H), 8.21 (s, 4H), 8.09 (s, 4H), 8.00 (s, 2H), 7.98 (s, 4H), 7.96 (m, 14H), 6.49 (s, 2H), 6.43 (d, J = 8.5 Hz, 2H), 5.98 (d, J = 8.5 Hz, 2H), 5.79 (d, J = 8.4 Hz, 4H), 5.70 (d, J = 8.4 Hz, 4H), 5.52 (d, J = 8.4 Hz, 2H), 5.47 (d, J = 8.4 Hz, 2H), 5.30 (d, J = 5.4 Hz, 2H), 5.12 (d, J = 6.5 Hz, 4H), 5.06 (d, J = 6.4 Hz, 2H), 2.65 (d, J = 5.4 Hz, 2H), 2.50 (d, J = 6.5 Hz, 4H), 2.39 (d, J = 5.4 Hz, 2H), 1.46 (m, 144H), 1.32 (m, 432H), 0.84 (m, 324H), 0.65 (t, J = 7.0 Hz, 36H).

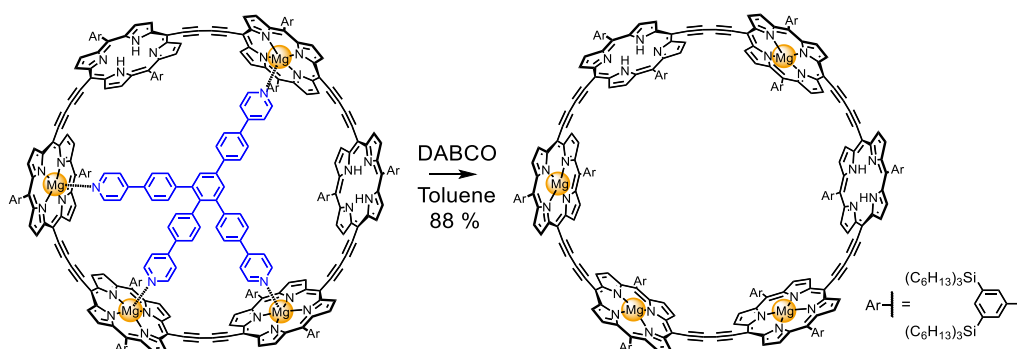
1,3-(H_2) $_2\text{Mg}_4\text{-c-P6-T4c}$



Mg₆-c-P6-T4c (2.7 mg, 0.25 μmol) was dissolved in CH_2Cl_2 (1.0 mL) and glacial acetic acid (0.10 mL) was added. The solution was stirred at room temperature and followed with TLC. After 1 h, the solution was washed with water (3×2 mL) and then run through an alumina pipette plug (CH_2Cl_2). The solvent was removed in vacuum.

Yield: 2.5 mg, 94%. **^1H NMR:** (500 MHz, CDCl_3) δ 9.62 (d, J = 4.3 Hz, 4H), 9.58 (d, J = 4.3 Hz, 4H), 9.55 (m, 12H), 9.51 (d, J = 4.6 Hz, 4H), 8.75 (m, 12H), 8.72 (d, J = 4.3 Hz, 4H), 8.68 (d, J = 4.6 Hz, 4H), 8.66 (d, J = 4.6 Hz, 4H), 8.37 (s, 4H), 8.35 (s, 2H), 8.33 (s, 4H), 8.31 (s, 2H), 8.00 (s, 6H), 7.98 (s, 2H), 7.96 (10H), 7.95 (s, 2H), 7.89 (s, 4H), 6.52 (s, 2H), 6.47 (d, J = 8.7 Hz, 2H), 6.00 (d, J = 8.7 Hz, 2H), 5.82 (d, J = 8.6 Hz, 4H), 5.70 (d, J = 8.6 Hz, 4H), 5.51 (d, J = 8.7 Hz, 2H), 5.46 (d, J = 8.7 Hz, 2H), 5.31 (d, J = 6.6 Hz, 2H), 5.13 (d, J = 6.6 Hz, 4H), 5.05 (d, J = 6.6 Hz, 2H), 2.60 (d, J = 6.6 Hz, 2H), 2.48 (d, J = 6.6 Hz, 4H), 2.36 (d, J = 6.6 Hz, 2H), 1.44 (m, 144H), 1.29 (m, 432H), 0.91 (m, 252H), 0.77 (m, 108H), -1.14 (s, 4H). **MS (MALDI-TOF):** m/z 10609 (M^+ , $\text{C}_{698}\text{H}_{1058}\text{Mg}_4\text{N}_{28}\text{Si}_{24}$ requires 10614). **UV-VIS:** λ_{max} (CHCl_3) nm ($\log(\epsilon)$): 477 (5.77), 815 (5.50), 855 (5.46).

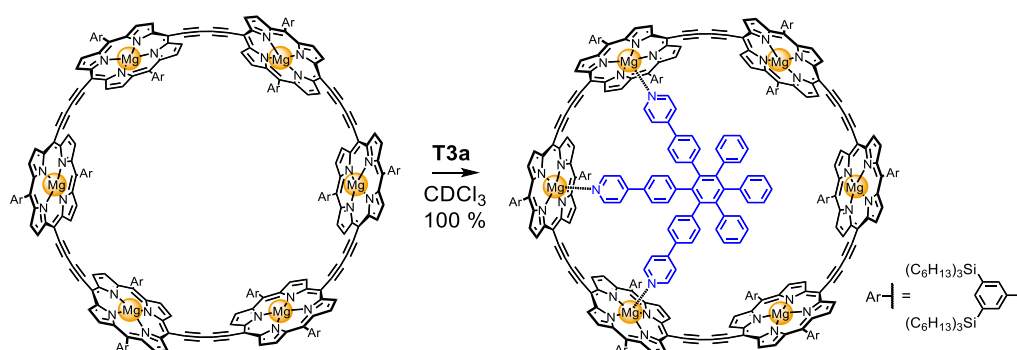
1,3-(H₂)₂Mg₄-c-P6



Freshly recrystallized 1,4-diazabicyclo[2.2.2]octane (10 g) was dissolved in toluene (38 mL) to achieve a 2.5 M solution. A SEC column (2.4 cm diameter, 32 cm length, Bio-Beads S-X1) was loaded with the solution. **1,3-(H₂)₂Mg₄-c-P6·T4c** (2.5 mg, 0.24 μmol) was dissolved in toluene (1 mL) and eluted through the SEC column with toluene. The obtained solution was washed with water (3 × 3 mL) and the solvent was removed in vacuum.

Yield: 2.1 mg, 88%. **¹H NMR:** (500 MHz, CDCl₃) δ 9.58 (m, 16H), 9.54 (d, *J* = 4.6 Hz, 8H), 8.72 (m, 16H), 8.68 (d, *J* = 4.6 Hz, 8H), 8.14 (s, 24H), 7.95 (s, 4H), 7.93 (s, 8H), 1.30 (m, 576H), 0.86 (m, 144H), 0.79 (m, 216H), -1.18 (m, 4H). **MS (MALDI-TOF):** *m/z* 9920 (M⁺, C₆₄₈H₁₀₂₄Mg₄N₂₄Si₂₄ requires 9923). **UV-VIS:** λ_{max} (CHCl₃) nm (log(ε)): 473 (5.83), 796 (5.61).

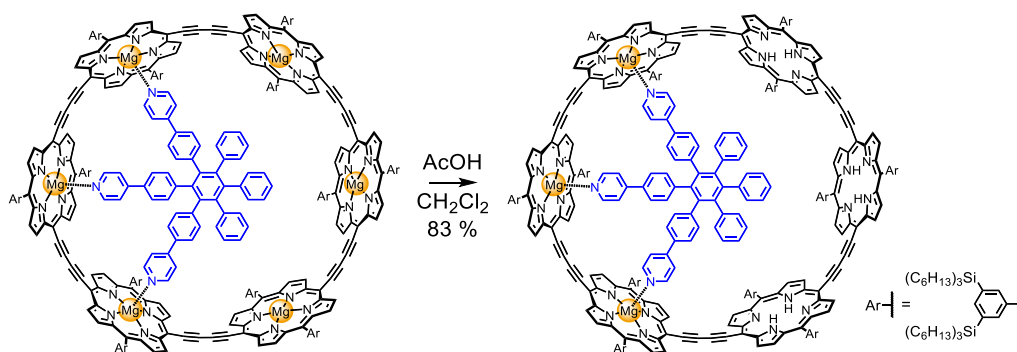
Mg₆-c-P6·T3a



Mg₆-c-P6 (5.0 mg, 0.50 μmol) and **T3a** (0.40 mg, 0.50 μmol) was mixed in CDCl₃ (0.60 mL). ¹H NMR confirmed quantitative insertion of the template.

^1H NMR: (400 MHz, CDCl_3) δ 9.53 (m, 24H), 8.71 (m, 24H), 8.31 (m, 12H), 7.96 (m, 24H), 5.39 (m, 27H), 4.99 (d, J = 6.6 Hz, 4H), 4.95 (d, J = 6.2 Hz, 2H), 2.34 (d, J = 5.4 Hz, 4H), 2.30 (d, J = 5.7 Hz, 2H), 1.26 (m, 576H), 0.91 (m, 360H). **UV-VIS:** λ_{max} (CHCl_3) nm ($\log(\epsilon)$): 482 (5.59), 777 (5.38), 813 (5.47), 854 (5.34).

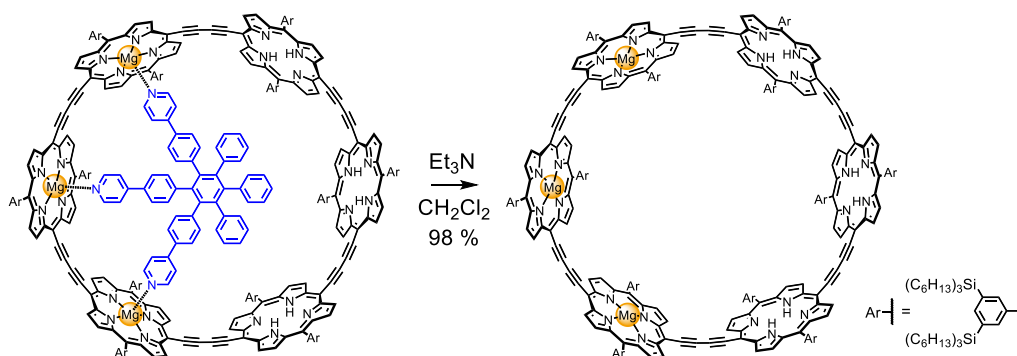
1,2,3-(H₂)₃Mg₃-c-P6-T3a



Mg₆-c-P6-T3a (5.4 mg, 0.50 μmol) was dissolved in CH_2Cl_2 (3.0 mL) and glacial acetic acid (0.30 mL) was added. The solution was stirred at room temperature and followed with TLC. After 1 h, the solution was washed with water (3×2 mL) and then run through an alumina pipette plug (CH_2Cl_2). The solvent was evaporated. The product was purified by flash column chromatography on silica (CH_2Cl_2 /petrol ether, 20:80).

Yield: 4.4 mg, 83%. **^1H NMR:** (500 MHz, CDCl_3) δ 9.53 (m, 24H), 8.70 (m, 24H), 8.41 (s, 4H), 8.38 (s, 2H), 8.30 (s, 6H), 8.00 (s, 6H), 7.96 (m, 12H), 7.89 (s, 2H), 7.86 (s, 4H), 5.50 (m, 6H), 5.45 (d, J = 8.2 Hz, 2H), 5.41 (m, 12H), 5.30 (m, 4H), 5.13 (t, J = 7.0 Hz, 1H), 5.03 (d, J = 7.2 Hz, 2H), 5.00 (d, J = 6.9 Hz, 4H), 4.95 (d, J = 6.6 Hz, 2H), 2.33 (d, J = 6.9 Hz, 4H), 2.30 (d, J = 6.6 Hz, 2H), 1.44 (m, 144H), 1.31 (m, 432H), 0.89 (m, 360H), -1.13 (s, 4H), -1.24 (s, 2H). **MS (MALDI-TOF):** m/z 10665 (M^+ , $\text{C}_{705}\text{H}_{1065}\text{Mg}_3\text{N}_{27}\text{Si}_{24}$ requires 10666). **UV-VIS:** λ_{max} (CHCl_3) nm ($\log(\epsilon)$): 480 (5.82), 776 (5.62), 807 (5.67).

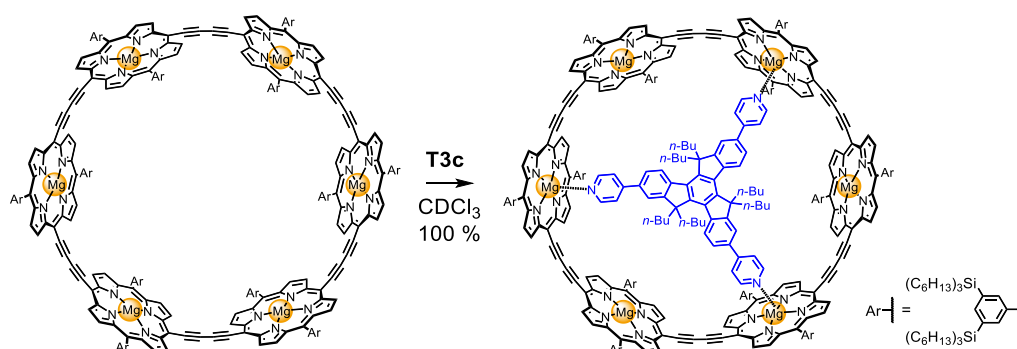
1,2,3-(H₂)₃Mg₃-c-P6



1,2,3-(H₂)₃Mg₃-c-P6·T3a (4.0 mg, 0.38 μmol) was dissolved in CH₂Cl₂/petrol ether 20:80 (1 mL). Three silica pipette plugs were prepared with 0.10 mL triethylamine each. The porphyrin solution was passed through the three plugs eluting through with CH₂Cl₂/petrol ether 20:80 solution.

Yield: 3.7 mg, 98%. **¹H NMR:** (400 MHz, CDCl₃) δ 9.55 (m, 24), 8.69 (m, 24H), 8.14 (m, 24H), 7.96 (s, 6H), 7.93 (s, 6H), 1.26 (m, 576H), 0.81 (m, 360H), −1.23 (s, 4H), −1.29 (s, 2H). **MS (MALDI-TOF):** *m/z* 9899 (*M*⁺, C₆₄₈H₁₀₂₆Mg₃N₂₄Si₂₄ requires 9900). **UV-VIS:** λ_{max} (CHCl₃) nm (log(ε)): 468 (5.66), 789 (5.41).

Mg₆-c-P6·T3c

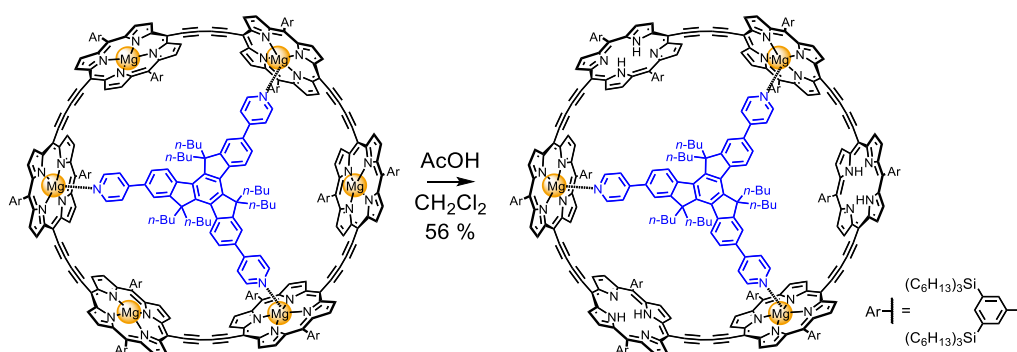


Mg₆-c-P6 (5.0 mg, 0.50 μmol) and **T3c** (0.50 mg, 0.50 μmol) was mixed in CDCl₃ (0.60 mL). ¹H NMR confirmed quantitative insertion of the template.

¹H NMR: (500 MHz, CDCl₃) δ 9.66 (m, 24H), 8.77 (m, 12H), 8.74 (d, *J* = 4.3 Hz, 6H), 8.72 (d, *J* = 4.3 Hz, 6H), 8.30 (s, 12H), 8.09 (s, 6H), 7.96 (s, 6H), 7.94 (s, 6H), 7.93 (s, 6H), 6.80 (d, *J* = 7.5 Hz, 3H), 5.93 (s, 3H), 5.78 (d, *J* = 7.5 Hz, 3H), 5.37 (d, *J* = 6.3 Hz, 6H), 2.71 (d, *J* = 6.3

Hz, 6H), 1.26 (m, 600H), 0.88 (m, 252), 0.71 (t, $J = 7.0$ Hz, 54H), 0.64 (t, $J = 7.2$ Hz, 54H), -0.30 (m, 12H), -0.59 (t, $J = 4.3$ Hz, 18H), -0.83 (m, 12H).

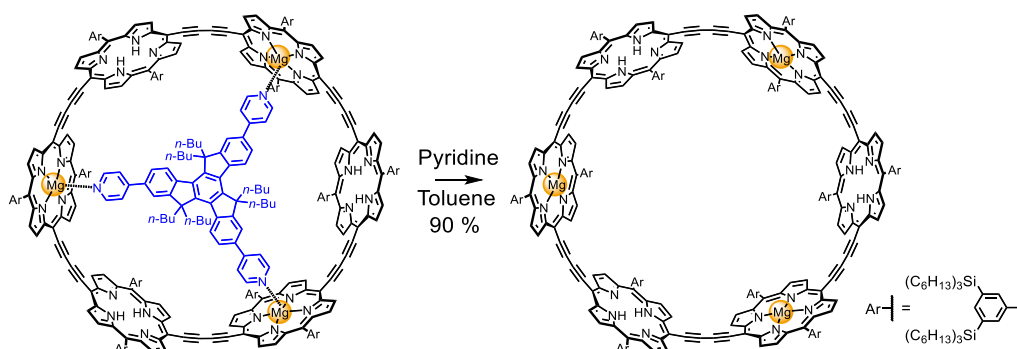
1,3,5-(H₂)₃Mg₃-c-P6·T3c



Mg₆-c-P6·T3c (5.5 mg, 0.50 μmol) was dissolved in CH_2Cl_2 (2.0 mL) and glacial acetic acid (0.20 mL) was added. The solution was stirred at room temperature and followed with TLC. After 1 h, the solution was washed with water (3×2 mL) and then run through an alumina pipette plug (CH_2Cl_2). The solvent was evaporated. The product was purified by flash column chromatography on silica (CH_2Cl_2 /petrol ether, 20:80).

Yield: 3.0 mg, 56%. **¹H NMR:** (500 MHz, CDCl_3) δ 9.67 (d, $J = 4.4$ Hz, 6H), 9.65 (d, $J = 4.4$ Hz, 6H), 9.62 (m, 12H), 8.74 (m, 24H), 8.43 (s, 6H), 8.28 (s, 6H), 7.97 (s, 6H), 7.96 (s, 6H), 7.93 (s, 6H), 7.92 (s, 6H), 6.85 (d, $J = 8.3$ Hz, 3H), 5.95 (s, 3H), 5.81 (d, $J = 8.3$ Hz, 3H), 5.39 (d, $J = 6.7$ Hz, 6H), 2.67 (d, $J = 6.7$ Hz, 6H), 1.43 (m, 144H), 1.30 (m, 456H), 0.89 (m, 252H), 0.70 (m, 108H), -0.28 (m, 12H), -0.57 (t, $J = 7.2$ Hz, 18H), -0.81 (m, 12H), -1.03 (s, 6H). **MS (MALDI-TOF):** m/z 10805 (M^+ , $\text{C}_{714}\text{H}_{1101}\text{Mg}_3\text{N}_{27}\text{Si}_{24}$ requires 10811) **UV-VIS:** λ_{max} (CHCl_3) nm (log(ϵ)): 475 (5.95), 772 (5.63), 806 (5.80), 844 (5.73).

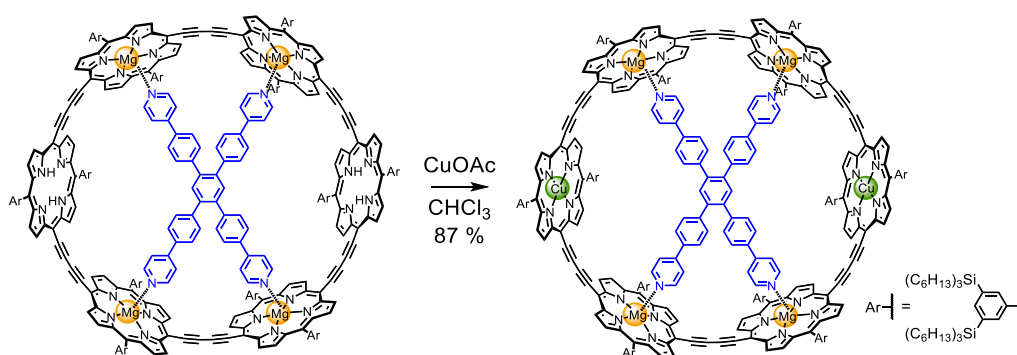
1,3,5-(H₂)₃Mg₃-c-P6



A SEC column (2.4 cm diameter, 32 cm length) was loaded with a solution of 50% pyridine in toluene (50 mL). **1,3,5-(H₂)₃Mg₃-c-P6·T3c** (3.0 mg, 0.28 μ mol) was dissolved in toluene (1 mL) and eluted through the SEC column with toluene. The solvent was removed in vacuum. The compound was run through a short silica column with petrol ether/CH₂Cl₂ 80:20 to remove the remaining pyridine.

Yield: 2.5 mg, 90%. **¹H NMR:** (500 MHz, CDCl₃) δ 9.57 (d, J = 4.2 Hz, 12H), 9.55 (d, J = 4.6 Hz, 12H), 8.72 (d, J = 4.2 Hz, 12H), 8.68 (d, J = 4.6 Hz, 12H), 8.14 (s, 12H), 8.12 (s, 12H), 7.96 (s, 12H), 7.93 (s, 12H), 1.42 (m, 144H), 1.24 (m, 432H), 0.86 (m, 144H), 0.80 (m, 216H), -1.18 (s, 6H). **MS (MALDI-TOF):** m/z 9899 (M^+ , C₆₄₈H₁₀₂₆Mg₃N₂₄Si₂₄ requires 9900). **UV-VIS:** λ_{max} (CHCl₃) nm (log(ϵ)): 468 (5.31), 793 (5.05).

1,4-Cu₂Mg₄-c-P6·T4a

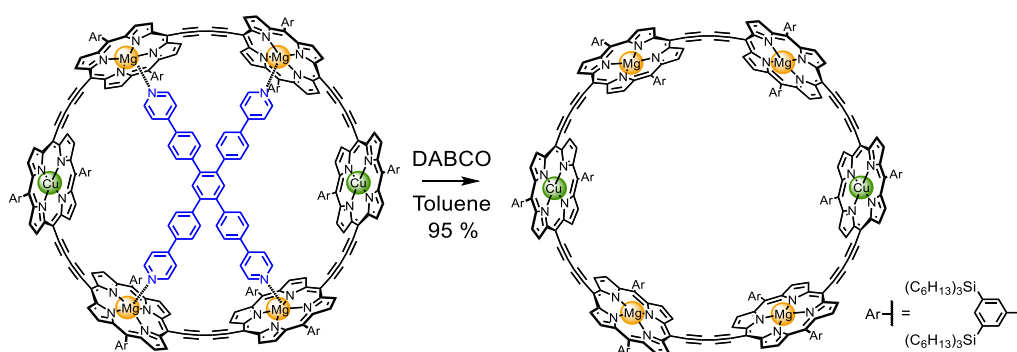


1,4-(H₂)₂Mg₄-c-P6·T4a (10 mg, 0.95 μ mol) and CuOAc (19 mg, 0.15 mmol) was dissolved in CHCl₃ (5.0 mL) and stirred at 60 °C open to air. After 1 h, the mixture was allowed to reach room temperature and washed with water (2 $\times$ 5 mL). The solvent was removed in vacuum, and the mixture was run through a silica plug with petrol ether/CH₂Cl₂ 80:20. The solvent was removed in vacuum.

Yield: 8.9 mg, 87%. **¹H NMR:** (400 MHz, CDCl₃) δ 9.60 (bs, 8H), 9.46 (vbs, 8H), 8.75 (bs, 16H), 8.37 (bs, 8H), 7.95 (bs, 20H), 6.60 (bs, 2H), 6.06 (bs, 8H), 5.93 (bs, 8H), 5.29 (bs, 8H), 2.53 (bs, 8H), 1.29 (m, 576H), 0.89 (m, 360H). Because of the paramagnetic copper(II) atoms, the signals from the copper porphyrins are so broadened that they are not seen, apart from one of the protons on the aryl solubilizing group. One of the β -protons on the magnesium porphyrins that is closest to the copper porphyrin is very broadened. **MS (MALDI-TOF):** m/z

10737 (M^+ , $C_{698}H_{1054}Cu_2Mg_4N_{28}Si_{24}$ requires 10737). **UV-VIS:** λ_{max} ($CHCl_3$) nm ($\log(\epsilon)$): 480 (5.69), 758 (5.44), 796 (5.50), 840 (5.51).

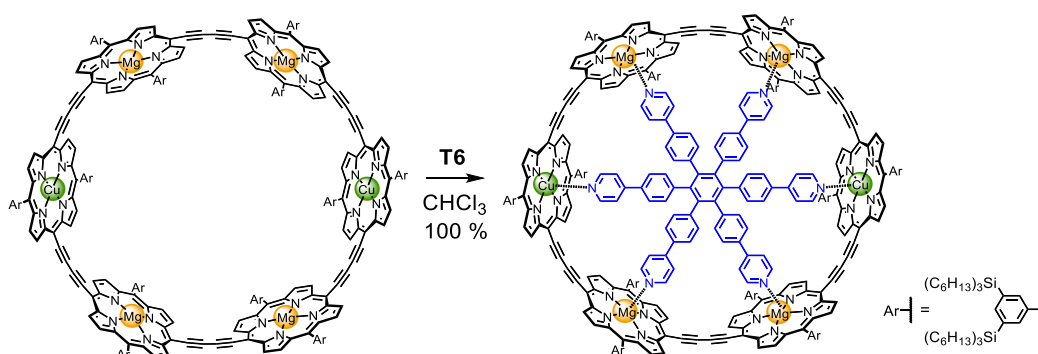
1,4- Cu_2Mg_4 -c-P6



Freshly recrystallized 1,4-diazabicyclo[2.2.2]octane (6.6 g) was dissolved in toluene (33 mL) to achieve a 1.8 M solution. A SEC column (2.4 cm diameter, 32 cm length, Bio-Beads S-X1) was loaded with the solution. **1,4- Cu_2Mg_4 -c-P6·T4a** (4.5 mg, 0.41 μ mol) was dissolved in toluene (1 mL) and eluted through the SEC column with toluene. The obtained solution was washed with water (3×3 mL) and the solvent was removed in vacuum.

Yield: 3.9 mg, 95%. **1H NMR:** (400 MHz, $CDCl_3$) δ 9.62 (bs, 8H), 9.45 (vbs, 8H), 8.73 (bs, 16H), 8.12 (bs, 16H), 7.93 (bs, 12H), 1.26 (m, 576H), 0.81 (m, 360H). Because of the paramagnetic copper(II) atoms, the signals from the copper porphyrins are so broadened that they are not seen, apart from one of the protons on the aryl solubilizing group. One of the β -protons on the magnesium porphyrins that is closest to the copper porphyrin is very broadened. **MS (MALDI-TOF):** m/z 10048 (M^+ , $C_{648}H_{1020}Cu_2Mg_4N_{24}Si_{24}$ requires 10046). **UV-VIS:** λ_{max} ($CHCl_3$) nm ($\log(\epsilon)$): 476 (5.71), 778 (5.46).

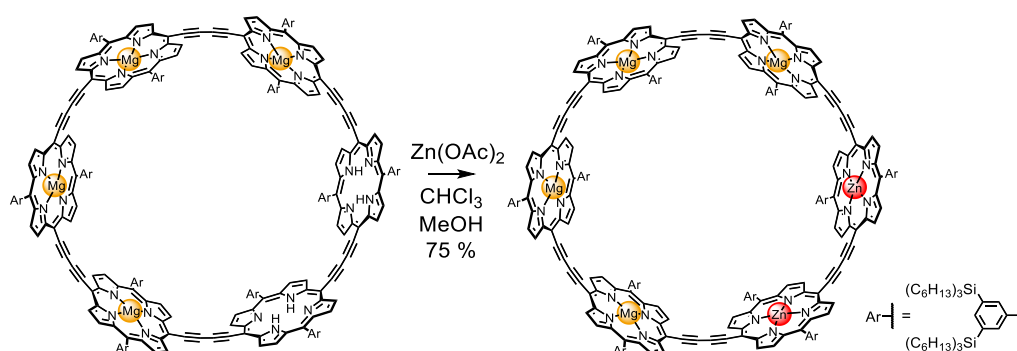
1,4- Cu_2Mg_4 -c-P6·T6



1,4-Cu₂Mg₄-c-P6 (3.7 mg, 0.37 μ mol) and **T6** (1.0 mg, 1.0 μ mol) was mixed and dissolved in CHCl₃ (1.0 mL). The solution was stirred at room temperature for 15 min, after which the solvent was evaporated. The solid was dissolved in petrol ether : CH₂Cl₂ : Et₃N (79 : 20 : 1) and passed through a silica plug eluting with the same solvent mixture. The resulting solution was concentrated and dried in vacuum.

Yield: 4.1 mg, 100%. **¹H NMR:** (400 MHz, CDCl₃) δ 9.57 (bs, 8H), 9.42 (vbs, 8H), 8.72 (bs, 16H), 8.29 (bs, 8H), 8.00 (bs, 8H), 7.95 (bs, 12H), 5.76 (bs, 8H), 5.61 (bs, 8H), 5.11 (bs, 8H), 2.44 (bs, 8H), 1.29 (m, 576H), 0.89 (m, 360H). Because of the paramagnetic copper(II) atoms, the signals from the copper porphyrins are so broadened that they are not seen, apart from one of the protons on the aryl solubilizing group. The signals from the two legs of the template that are coordinating to the copper porphyrins are also broadened into the baseline. One of the β -protons on the magnesium porphyrins that is closest to the copper porphyrin is very broadened. **MS (MALDI-TOF):** m/z 11043 (M^+ , C₇₂₀H₁₀₆₈Cu₂Mg₄N₃₀Si₂₄ requires 11043). **UV-VIS:** λ_{max} (CHCl₃) nm (log(ϵ)): 482 (5.70), 767 (5.49), 804 (5.58), 847 (5.52).

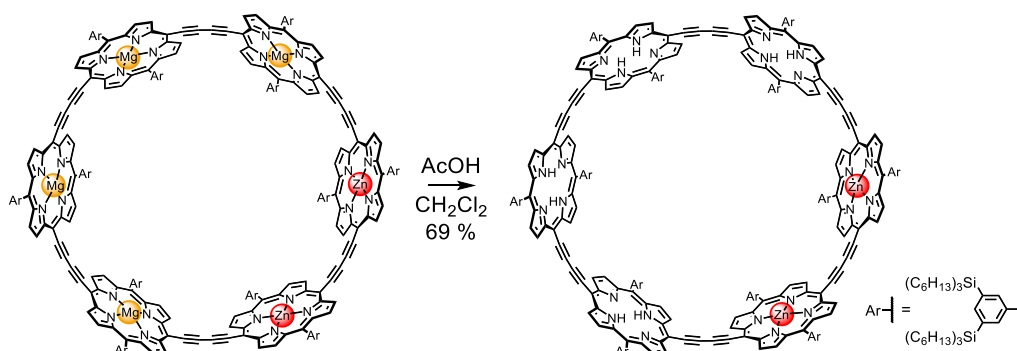
1,2-Zn₂Mg₄-c-P6



1,2-(H₂)₂Mg₄-c-P6 (13 mg, 1.3 μ mol) was dissolved in CHCl₃ (10 mL). Zn(OAc)₂·2H₂O (30 mg, 0.14 mmol) was dissolved in MeOH (0.30 mL) and added to the porphyrin solution. The mixture was stirred at room temperature for 2 h. The reaction was stopped by washing with water (2 $\times$ 5mL) and running through a silica plug with pure toluene.

Yield: 9.9 mg, 75%. **¹H NMR:** (400 MHz, CDCl₃) δ 9.59 (m, 24H), 8.75 (d, J = 4.5 Hz, 8H), 8.71 (d, J = 4.5 Hz, 16H), 8.15 (s, 16H), 8.13 (s, 8H), 7.94 (s, 12H), 1.43 (m, 144H), 1.26 (m, 432H), 0.86 (m, 144H), 0.80 (m, 216H).

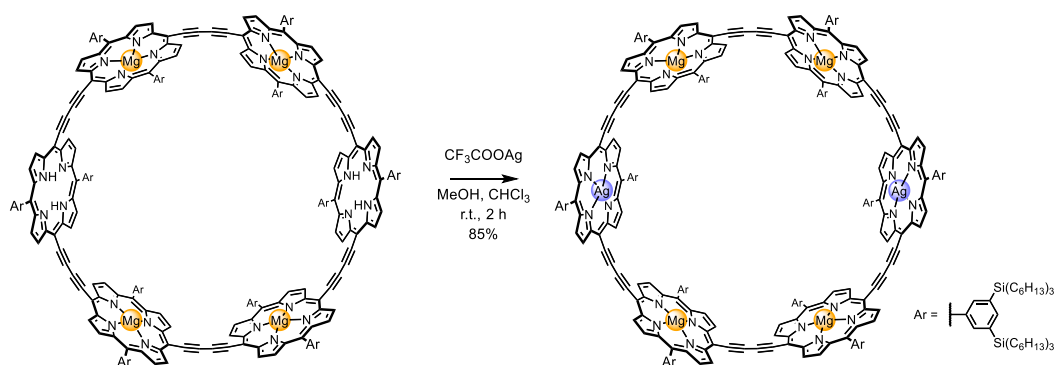
1,2-Zn₂(H₂)₄-c-P6



1,2-Zn₂Mg₄-c-P6 (9.9 mg, 0.99 μmol) was dissolved in CH_2Cl_2 (2.0 mL) and glacial acetic acid (2.0 mL) was added. The solution was stirred at room temperature. After 20 min, the solution was washed with water (3×2 mL) and then run through an alumina pipette plug (CH_2Cl_2). The solvent was evaporated.

Yield: 6.8 mg, 69%. **¹H NMR:** (400 MHz, CDCl_3) δ 9.66 (m, 8H), 9.56 (m, 16H), 8.80 (d, $J = 4.5$ Hz, 8H), 8.70 (d, $J = 4.6$ Hz, 16H), 8.15 (s, 24H), 7.96 (s, 12H), 1.43 (m, 144H), 1.31 (m, 144H), 1.24 (m, 288H), 0.87 (m, 144H), 0.81 (m, 216H), -1.27 (s, 4H), -1.30 (s, 4H). **MS (MALDI-TOF):** m/z 9959 (M^+ , $\text{C}_{648}\text{H}_{1028}\text{N}_{24}\text{Si}_{24}\text{Zn}_2$ requires 9960). **UV-VIS:** λ_{max} (CHCl_3) nm ($\log(\epsilon)$): 473 (5.85), 670 (5.24), 777 (5.61).

1,4-Ag₂Mg₄-c-P6

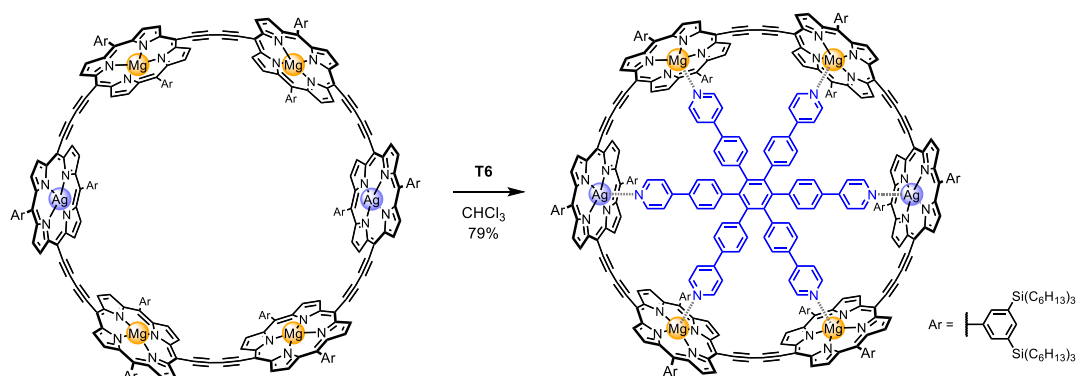


1,4-(H₂)₂Mg₄-c-P6 (0.85 mg, 0.086 μmol) was dissolved in CHCl_3 (1.0 mL). Silver trifluoroacetate (0.15 mg, 0.69 μmol) was dissolved in MeOH (0.20 mL) and added to the porphyrin solution. The reaction was stirred at 25 $^\circ\text{C}$ and monitored by UV-vis. After 2 h no further changes were observed in the UV-vis spectrum. MeOH (2 mL), CHCl_3 (2 mL), and demineralized water (10 mL) were added, and the phases were separated. The aqueous phase

was extracted with CHCl_3 (2×2 mL) and the combined organic phases were washed with demineralized water (2×10 mL) and dried over MgSO_4 . The solvents were removed in vacuum.

Yield: 0.74 mg, 85%. **^1H NMR:** (500 MHz, CDCl_3) δ 9.59 (bs), 8.72 (bs), 8.15 (bs), 7.93 (bs), 1.21 (m). Because of the paramagnetic silver(II) atoms, all the signals in the spectrum are so broadened that the shape and integrals cannot be used for much interpretation. However, the porphyrin signals can be observed in the expected positions. **UV-VIS:** λ_{max} (CHCl_3) nm ($\log(\epsilon)$): 470 (5.70), 788 (5.42).

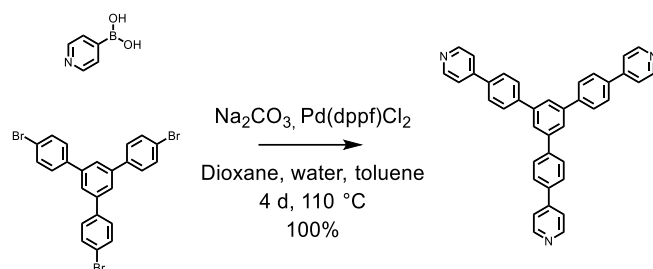
1,4- $\text{Ag}_2\text{Mg}_4\text{-c-P6}\cdot\text{T6}$



1,4- $\text{Ag}_2\text{Mg}_4\text{-c-P6}$ (0.37 mg, 0.037 mmol) and **T6** (1.0 mg, 1.0 mmol) was dissolved in CHCl_3 and then filtered through a silica pipette plug (CHCl_3).

Yield: 0.32 mg, 79%. **^1H NMR:** (500 MHz, CDCl_3) δ 9.54 (bs), 8.71 (bs), 8.33 (bs), 7.99 (bs), 7.95 (bs), 5.63 (bs), 5.51 (bs), 5.02 (bs), 2.37 (bs), 1.25 (m). Because of the paramagnetic silver(II) atoms, all the signals in the spectrum are so broadened that the shape and integrals cannot be used for much interpretation. However, the porphyrin signals can be observed in the expected positions. **MS (MALDI-TOF):** m/z 11131 (M^+ , $\text{C}_{720}\text{H}_{1068}\text{Ag}_2\text{Mg}_4\text{N}_{30}\text{Si}_{24}$ requires 11131). **UV-VIS:** λ_{max} (CHCl_3) nm ($\log(\epsilon)$): 461 (5.77), 767 (5.52), 804 (5.61), 843 (5.56).

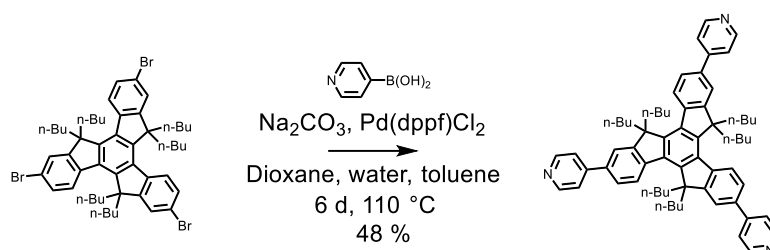
T3b



Fujita et al. prepared this compound by via Stille coupling,²¹ but we chose to prepare it via Suzuki coupling, to avoid the use of toxic organotin intermediates. The reaction conditions used here were developed by Kowitz and Wegner.²² Na_2CO_3 (236 mg, 2.23 mmol) was dissolved in water (2.5 mL). 1,3,5-Tris(4-bromophenyl)benzene (136 mg, 0.25 mmol), 4-pyridineboronic acid (336 mg, 2.98 mmol) and $\text{Pd}(\text{dppf})\text{Cl}_2 \cdot \text{CH}_2\text{Cl}_2$ (20.5 mg, 817 mmol) were suspended in dioxane (10 mL) and toluene (5 mL). The Na_2CO_3 solution was added and the mixture was degassed by three freeze-pump-thaw cycles. The final mixture was stirred under argon at 110°C (reflux) for 4 d. When the reaction was finished (monitored by TLC), the solution was allowed to reach room temperature and CHCl_3 (30 mL) and water (10 mL) was added. The layers were separated, and the water phase was extracted with CHCl_3 (3×10 mL). The combined organic phase was washed with water (20 mL) and brine (20 mL) and dried over sodium sulfate. The solvent was removed in vacuum and the pure product was obtained after flash column chromatography on silica ($\text{CH}_2\text{Cl}_2:\text{MeOH}:\text{Et}_3\text{N} = 100:2:0.5$) followed by trituration with methanol. Characterization was in agreement with previously reported results.^[11]

Yield: 134 mg, 100%. **^1H NMR:** (400 MHz, CDCl_3) δ 8.70 (d, $J = 5.4$ Hz, 6H), 7.91 (s, 3H), 7.85 (d, $J = 8.2$ Hz, 6H), 7.81 (d, $J = 8.2$ Hz, 6H), 7.58 (d, $J = 5.4$ Hz, 6H). **^{13}C NMR:** (101 MHz, CDCl_3) δ 150.56, 147.80, 141.94, 141.72, 137.68, 128.22, 127.73, 125.57, 121.65. **HRMS (ESI):** m/z 538.2275 (MH^+ , $\text{C}_{39}\text{H}_{27}\text{N}_3$ requires 538.2277).

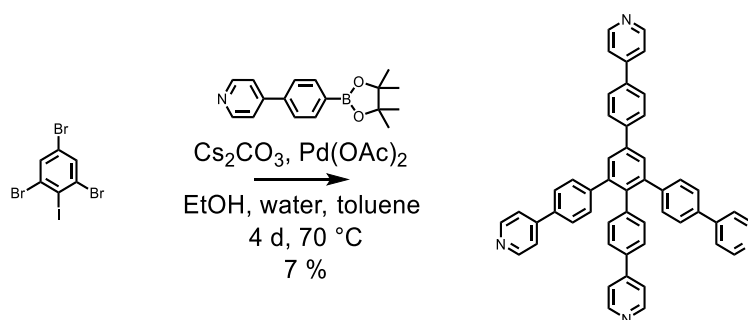
T3c



Na_2CO_3 (83.4 mg, 0.786 mmol) was dissolved in water (0.50 mL). Tribromotruxene, prepared according to literature procedures²³) (40 mg, 43.6 μmol), 4-pyridine boronic acid (64.4 mg, 0.524 mmol) and $\text{Pd(dppf)Cl}_2 \cdot \text{CH}_2\text{Cl}_2$ (7.2 mg, 8.7 μmol) was dissolved in a mixture of dioxane (2.0 mL) and toluene (1.0 mL). The two solutions were combined and degassed with three freeze-pump-thaw cycles. The solution was stirred under argon at 110 °C (reflux) for 6 d. After completion (measured with TLC) the solvents were removed and the solids were dissolved in CHCl_3 (40 mL) and water (40 mL). The layers were separated, and the aqueous phase was extracted with CHCl_3 (3×20 mL). The combined organic phase was washed with water (2×20 mL) and dried with sodium sulfate. The solvents were evaporated. The product was isolated with silica column chromatography in pure Ethyl acetate followed by a SEC column in CHCl_3 (Bio-Beads S-X3).

Yield: 19 mg, 48%. **$^1\text{H NMR}$:** (400 MHz, CDCl_3) δ 8.73 (d, $J = 6.1$ Hz, 3H), 8.50 (d, $J = 8.7$ Hz, 3H), 7.77 (m, 6H), 7.68 (d, $J = 6.1$ Hz, 3H), 3.04 (m, 6H), 2.21 (m, 6H), 0.94 (m, 12H), 0.52 (m, 30H). **$^{13}\text{C NMR}$:** (126 MHz, CDCl_3) δ 154.71, 150.51, 148.35, 146.39, 141.29, 138.15, 136.36, 125.44, 125.37, 121.68, 120.68, 56.09, 36.91, 26.73, 22.98, 13.97. **HRMS (ESI):** m/z 910.6036 (MH^+ , $\text{C}_{66}\text{H}_{75}\text{N}_3$ requires 910.6034).

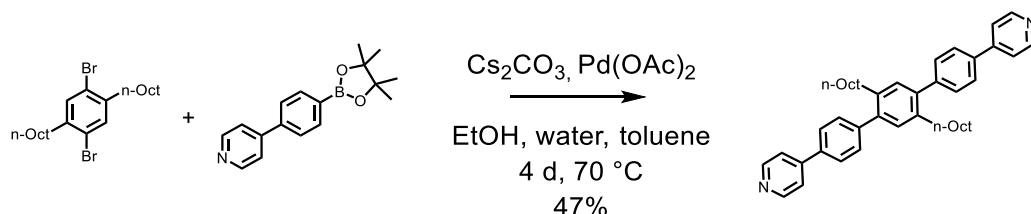
T4c



Cs₂CO₃ (358 mg, 1.1 mmol) was dissolved in water (0.5 mL). To the solution was added 1-iodo-2,4,6-tribromobenzene (49 mg, 0.11 mmol), (4-(4-pyridinyl)phenyl)boronic acid pinacol ester (250 mg, 0.89 mmol), Pd(OAc)₂ (5 mg, 0.022 mmol), toluene (2.5 mL) and ethanol (0.5 mL). The mixture was degassed by three freeze-pump-thaw cycles. The reaction was stirred under argon at 70 °C for 4 d. After completion, water (10 mL) and CHCl₃ (20 mL) was added, and the layers were separated. The aqueous phase was extracted with CHCl₃ (2 × 10 mL), and the combined organic phase was washed with water (2 × 10 mL). The organic phase was dried with sodium sulfate and the solvents were evaporated. The compound was isolated with flash column chromatography (CH₂Cl₂:MeOH:Et₃N, 97.5:2:0.5) followed by a SEC column (Bio-Beads S-X3).

Yield: 5 mg, 7%. **¹H NMR:** (500 MHz, CDCl₃) δ 8.70 (d, *J* = 5.9 Hz, 2H), 8.63 (d, *J* = 5.9 Hz, 4H), 8.59 (d, *J* = 5.8 Hz, 2H), 7.86 (d, *J* = 8.3 Hz, 2H), 7.81 (s, 2H), 7.79 (d, *J* = 8.3 Hz, 2H), 7.58 (d, *J* = 5.9 Hz, 2H), 7.52 (d, *J* = 8.3 Hz, 4H), 7.48 (d, *J* = 5.9 Hz, 4H), 7.43 (d, *J* = 5.8 Hz, 2H), 7.39 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.3 Hz, 4H), 7.09 (d, *J* = 8.3 Hz, 2H). **HRMS (ESI):** *m/z* 691.2855 (MH⁺, C₅₀H₃₄N₄ requires 691.2856).

T2



Cs₂CO₃ (326 mg, 1 mmol) was dissolved in water (0.5 mL). To the solution was added 1,4-dibromo-2,5-dioctylbenzene (46 mg, 0.1 mmol), (4-(4-pyridinyl)phenyl)boronic acid pinacol ester (112.5 mg, 0.4 mmol), Pd(OAc)₂ (4.5 mg, 0.02 mmol), toluene (2.5 mL) and ethanol (0.5 mL). The mixture was degassed by three freeze-pump-thaw cycles. The reaction was stirred under argon at 70 °C for 4 d. After completion, water (10 mL) and CHCl₃ (20 mL) was added, and the layers were separated. The aqueous phase was extracted with CHCl₃ (2 × 10 mL), and the combined organic phase was washed with water (2 × 10 mL). The organic phase was dried with magnesium sulfate and the solvents were evaporated. The compound was isolated with flash column chromatography on silica (CH₂Cl₂:MeOH:Et₃N = 98.5:1:0.5 → 97.5:2:0.5).

Yield: 28.7 mg, 47%. **¹H NMR:** (400 MHz, CDCl₃) δ 8.69 (d, *J* = 6.1 Hz, 2H), 7.72 (d, *J* = 8.2 Hz, 2H), 7.59 (d, *J* = 6.1 Hz, 2H), 7.50 (d, *J* = 8.2 Hz, 2H), 7.19 (s, 2H), 2.62 (m, 4H), 1.52 (m, 4H), 1.18 (m, 20H), 0.83 (t, *J* = 6.9 Hz, 6H). **¹³C NMR:** (101 MHz, CDCl₃) δ 150.46, 148.14, 142.99, 140.38, 137.79, 136.61, 131.06, 130.24, 126.81, 121.66, 32.76, 31.97, 31.59, 29.64, 29.39, 29.28, 22.77, 14.22. **HRMS (ESI):** *m/z* 609.4198 (MH⁺, C₄₄H₅₂N₂ requires 609.4203).

2.7 ^1H NMR, ^{13}C NMR and MALDI of new compounds

Mg₆-P6

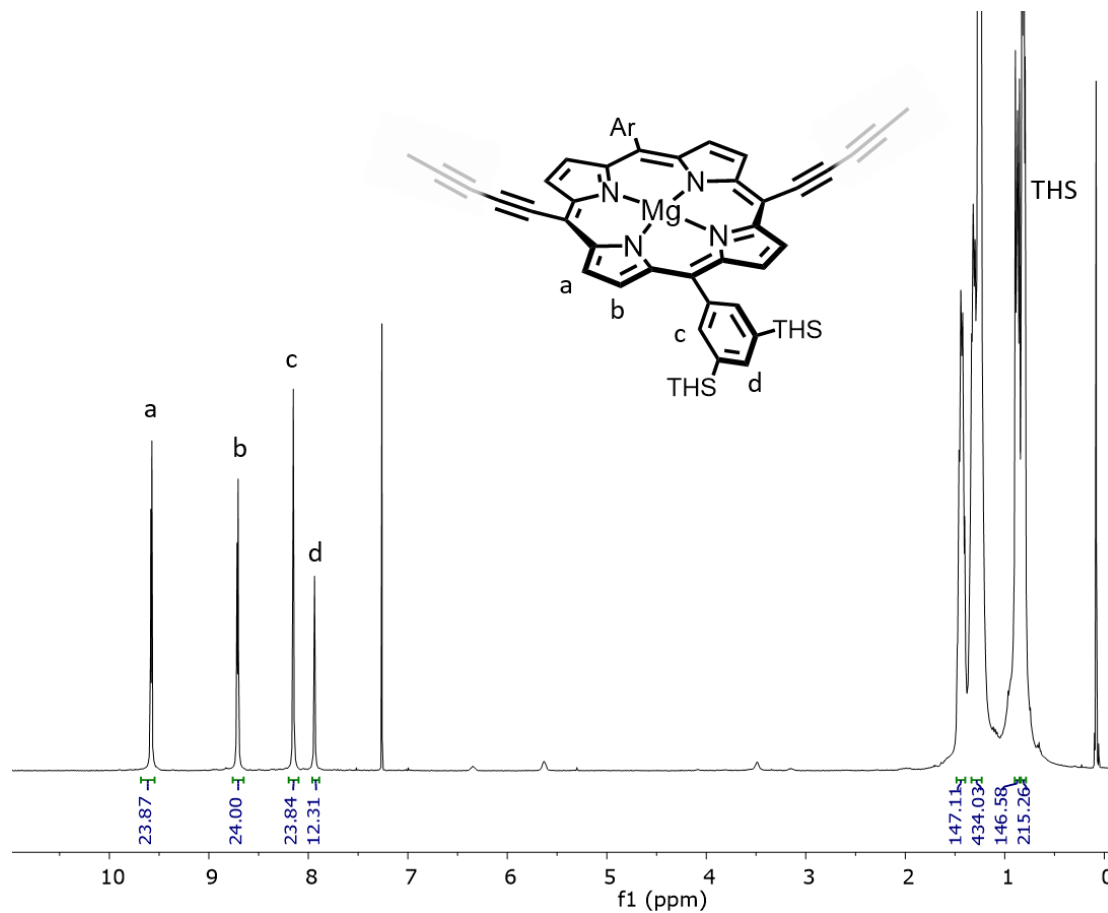


Figure 2.4. The ^1H NMR spectrum of **Mg₆-P6** (400 MHz, CDCl_3 , 298 K).

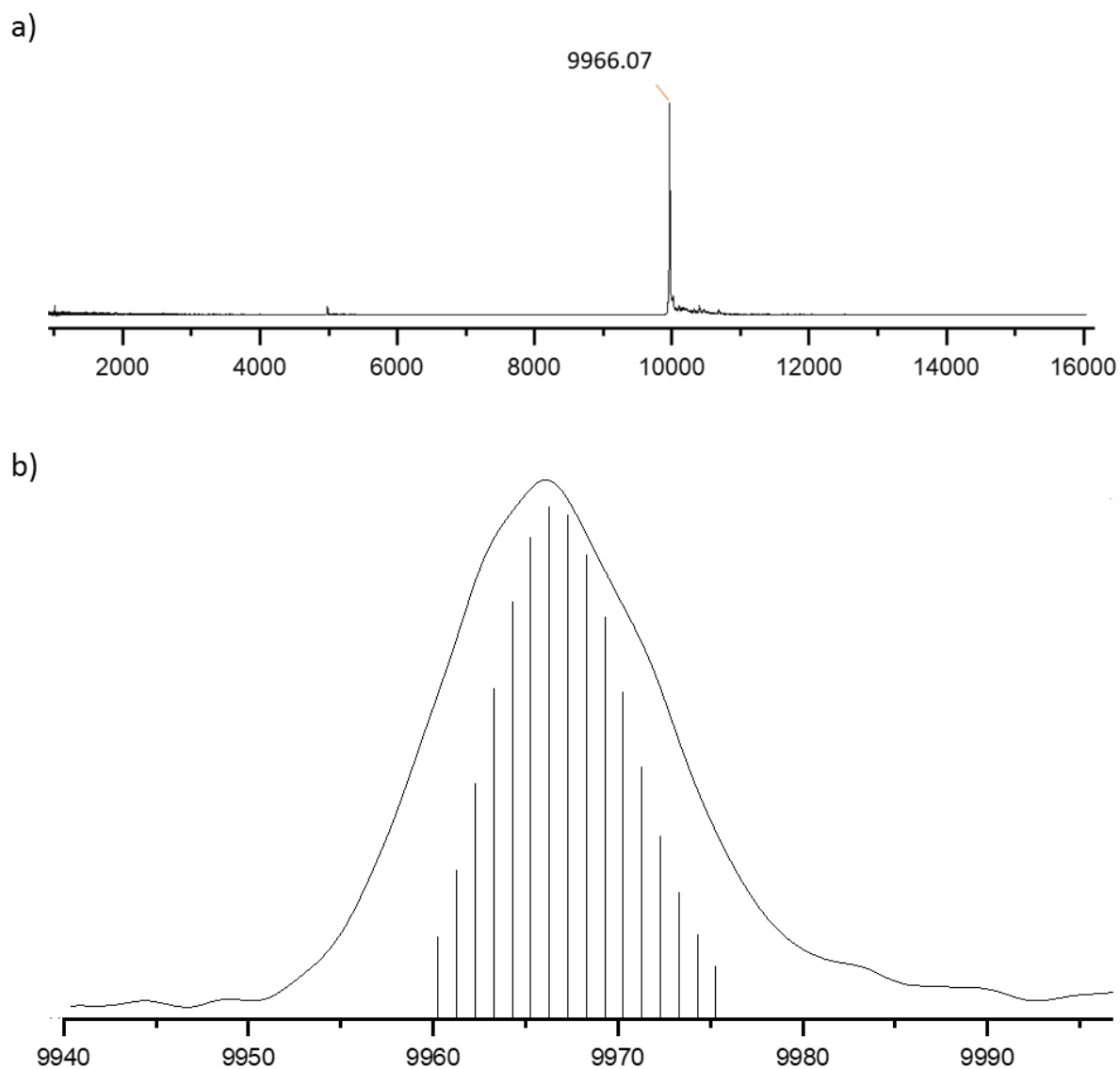


Figure 2.5. a) The MALDI-MS spectrum of **Mg₆-P6**, matrix: DCTB. M^+ , $C_{648}H_{1020}Mg_6N_{24}Si_{24}$ requires 9967. b) Zoom of the MALDI-MS spectrum of **Mg₆-P6** overlaid with the predicted isotope pattern.

Mg₆-P6·T5

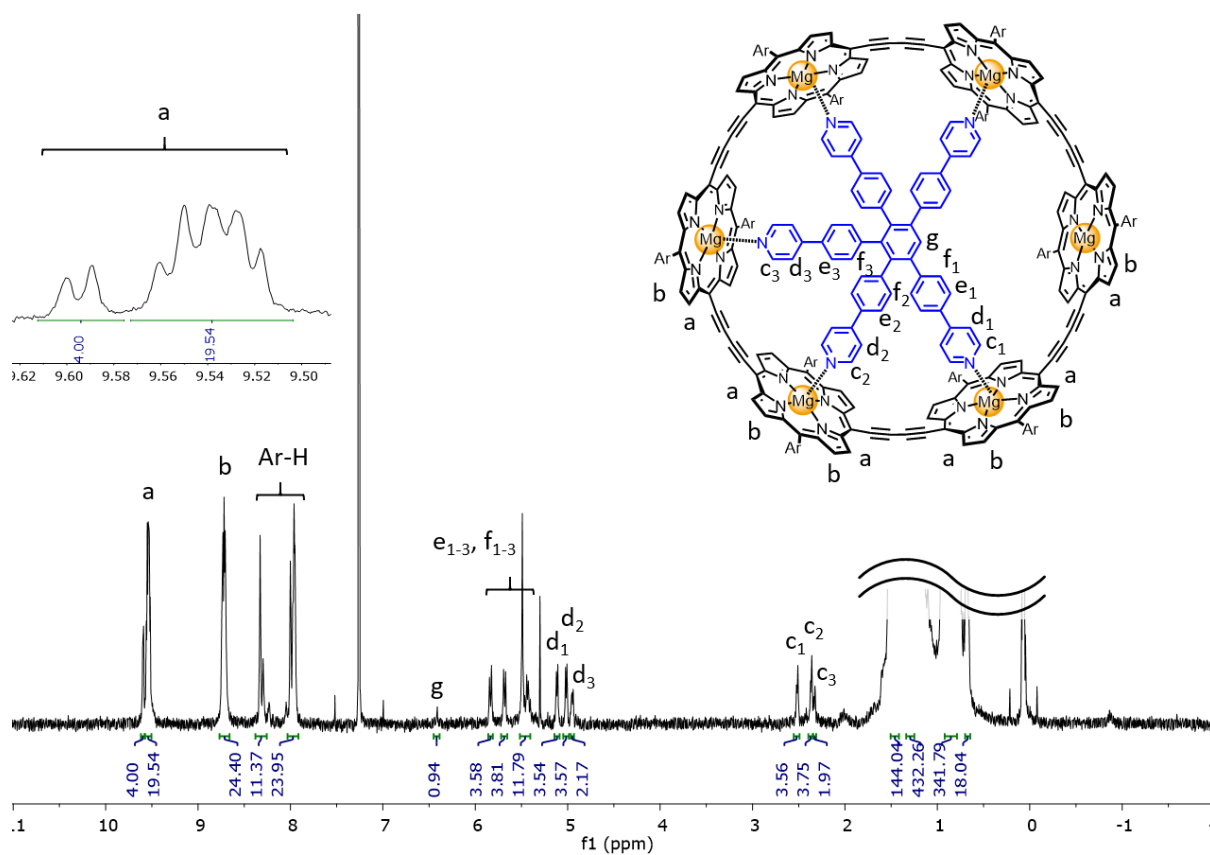


Figure 2.6. The ¹H NMR spectrum of Mg₆-P6·T5 (400 MHz, CDCl₃, 298 K).

(H₂)Mg₅-P6·T5

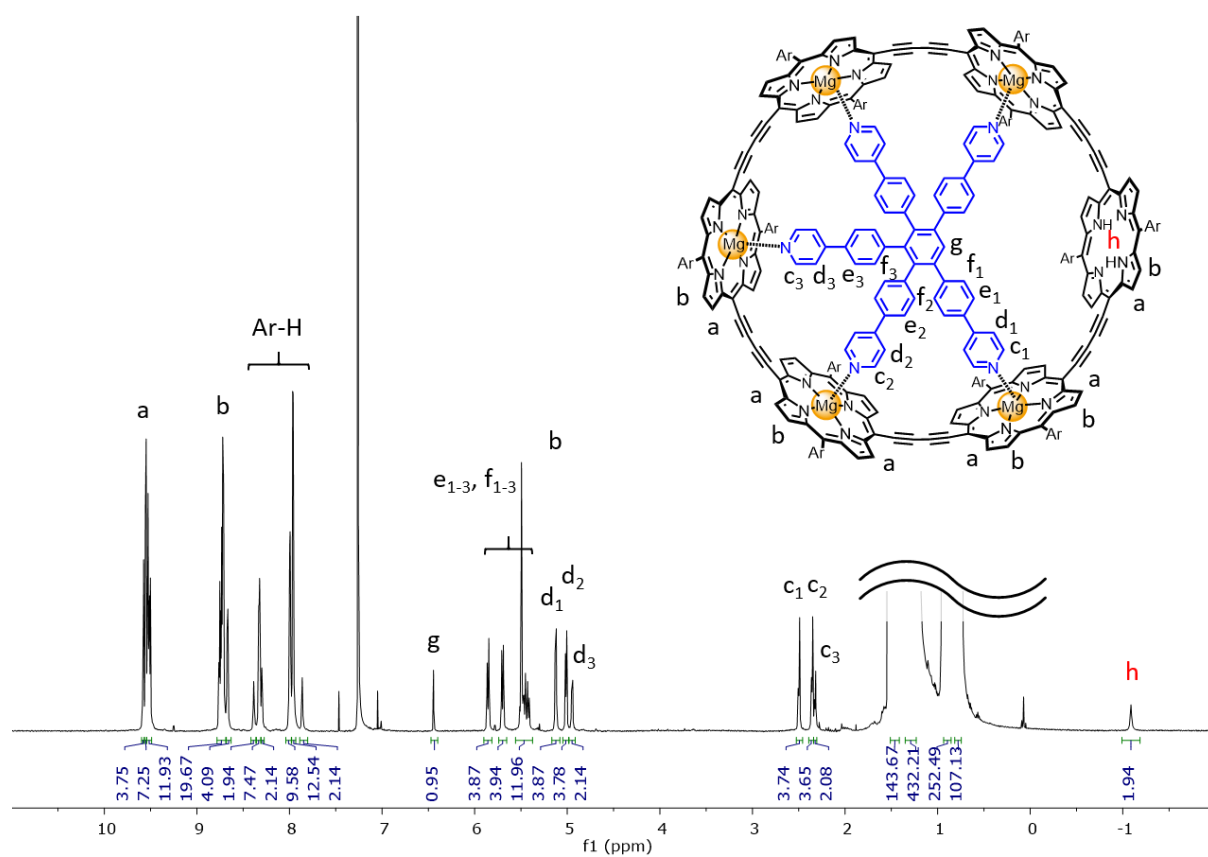


Figure 2.7. The ¹H NMR spectrum of (H₂)Mg₅-P6·T5 (500 MHz, CDCl₃, 298 K).

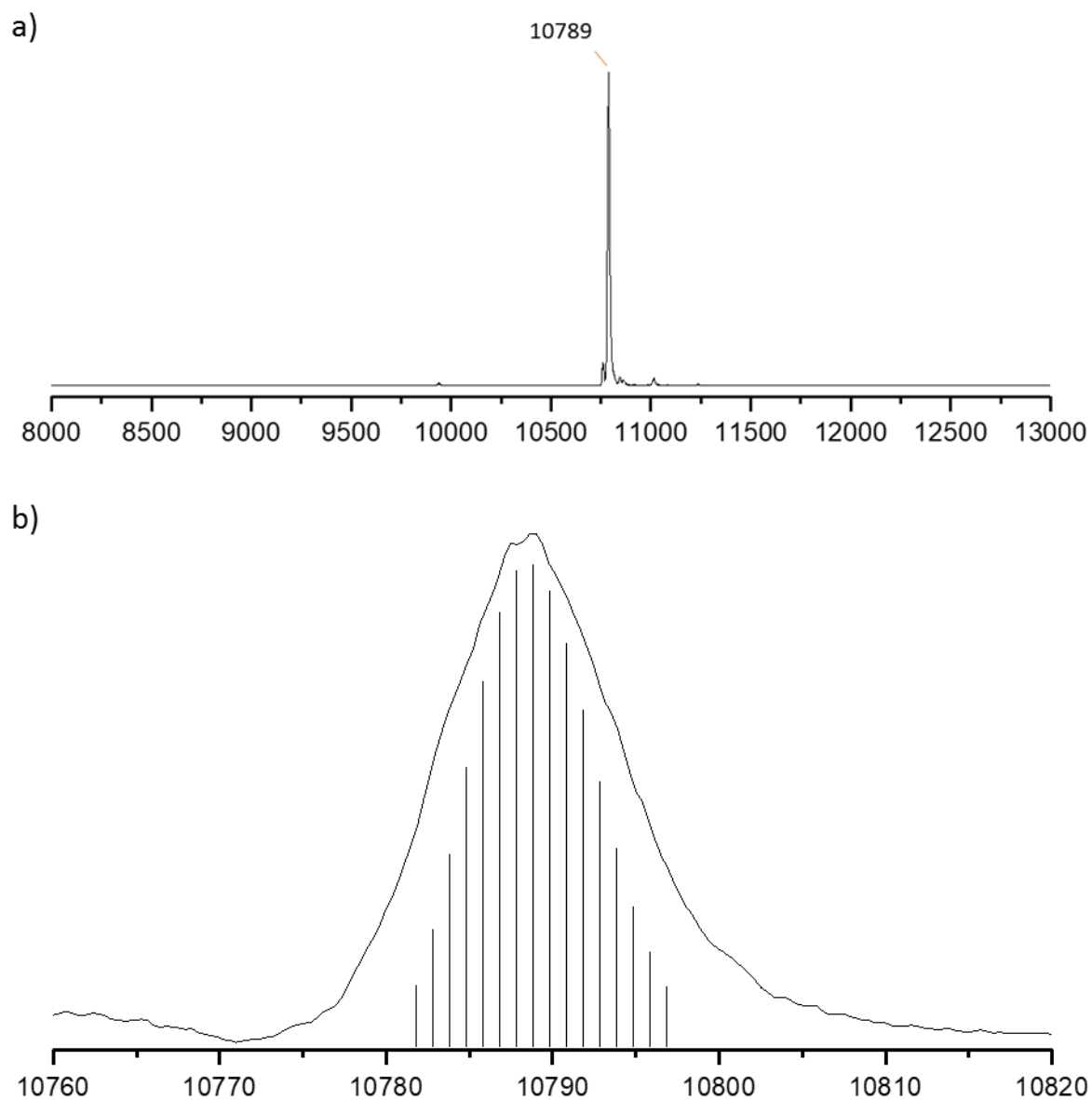


Figure 2.8. a) The MALDI-MS spectrum of $(\text{H}_2)\text{Mg}_5\text{-P6-T5}$, matrix: dithranol. M^+ , $\text{C}_{709}\text{H}_{1063}\text{Mg}_5\text{N}_{29}\text{Si}_{24}$ requires 10789. b) Zoom of the MALDI-MS spectrum of $(\text{H}_2)\text{Mg}_5\text{-P6-T5}$ overlaid with the predicted isotope pattern.

(H₂)Mg₅-P6

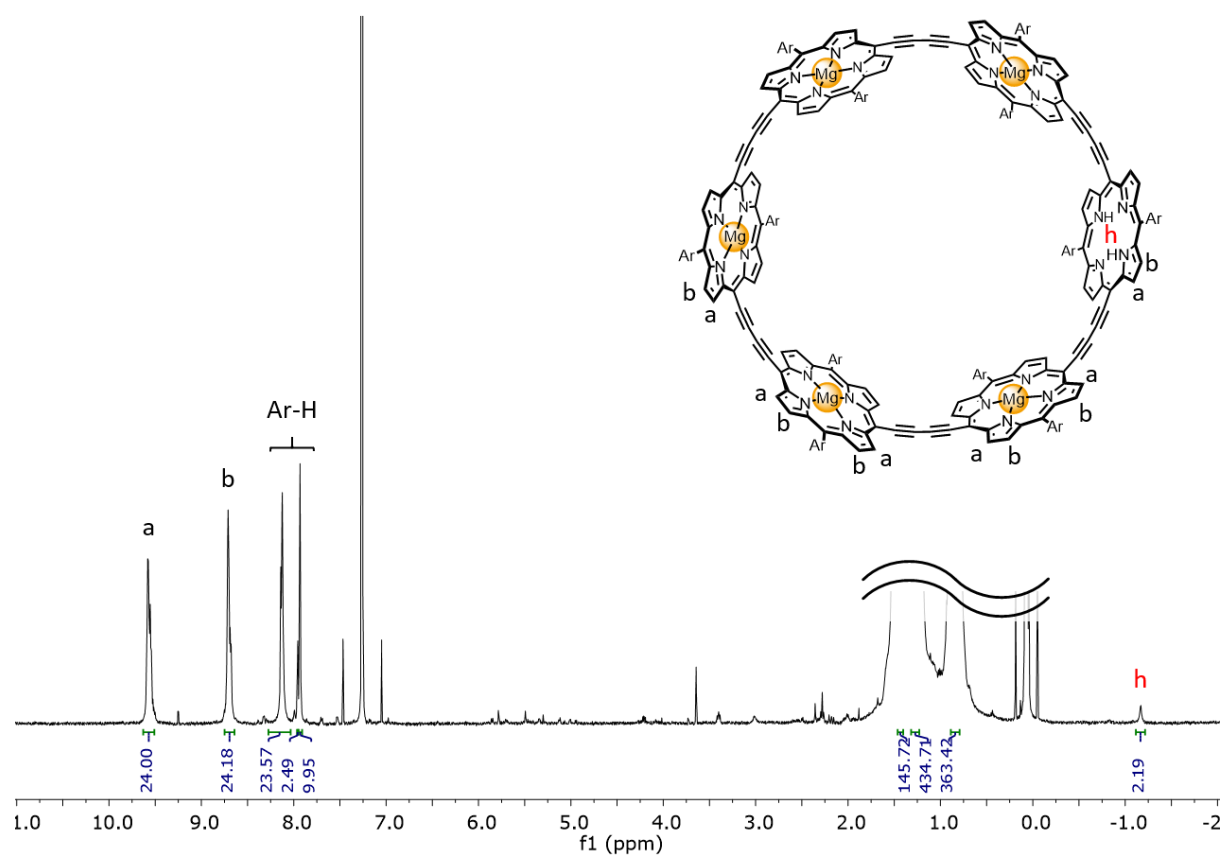


Figure 2.9. The ¹H NMR spectrum of (H₂)Mg₅-P6 (500 MHz, CDCl₃, 298 K).

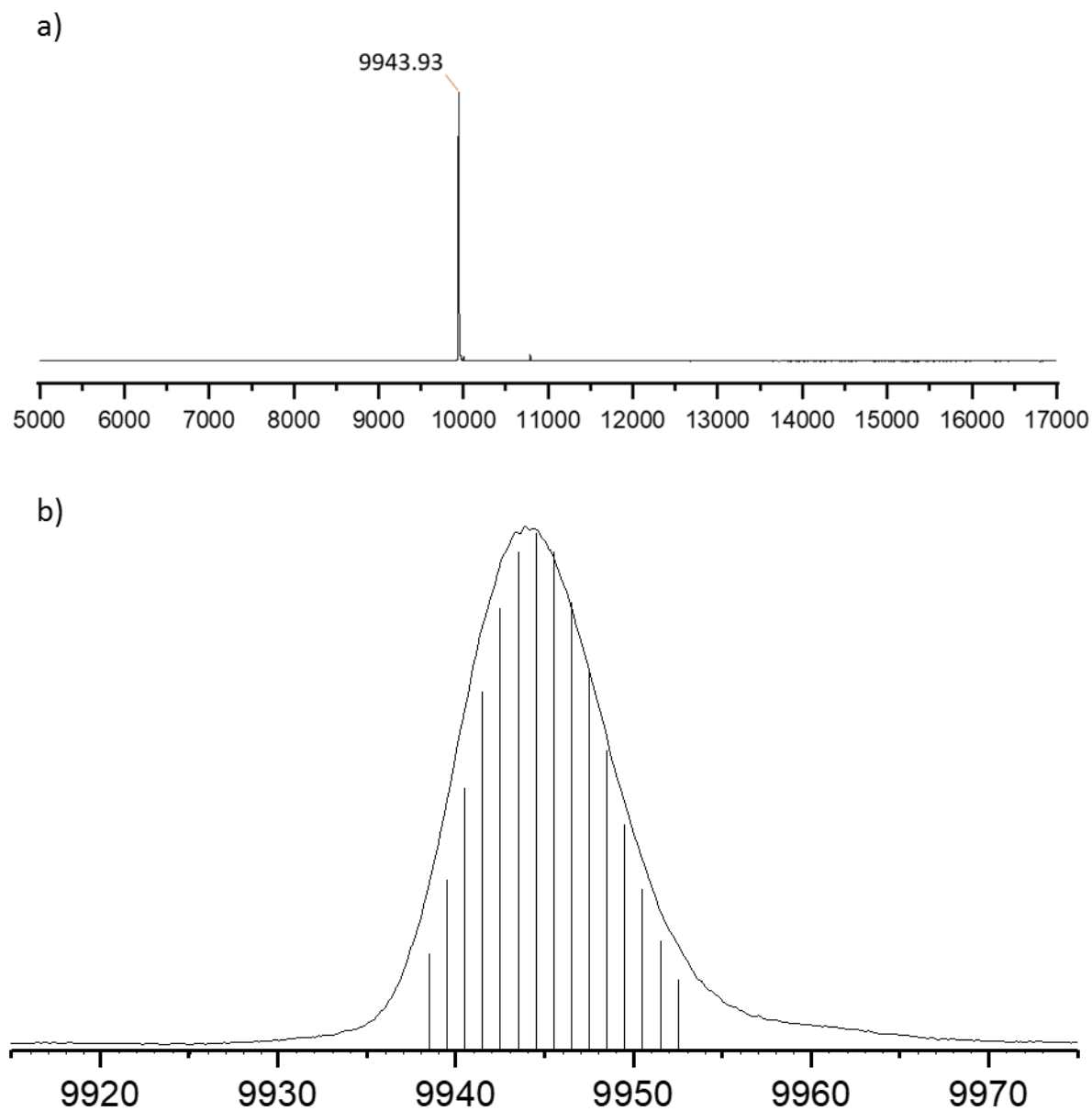


Figure 2.10. a) The MALDI-MS spectrum of **(H₂)Mg₅-P6**, matrix: dithranol. M⁺, C₆₄₈H₁₀₂₂Mg₅N₂₄Si₂₄ requires 9945. b) Zoom of the MALDI-MS spectrum of **(H₂)Mg₅-P6** overlaid with the predicted isotope pattern.

Mg₆-P6·T4a

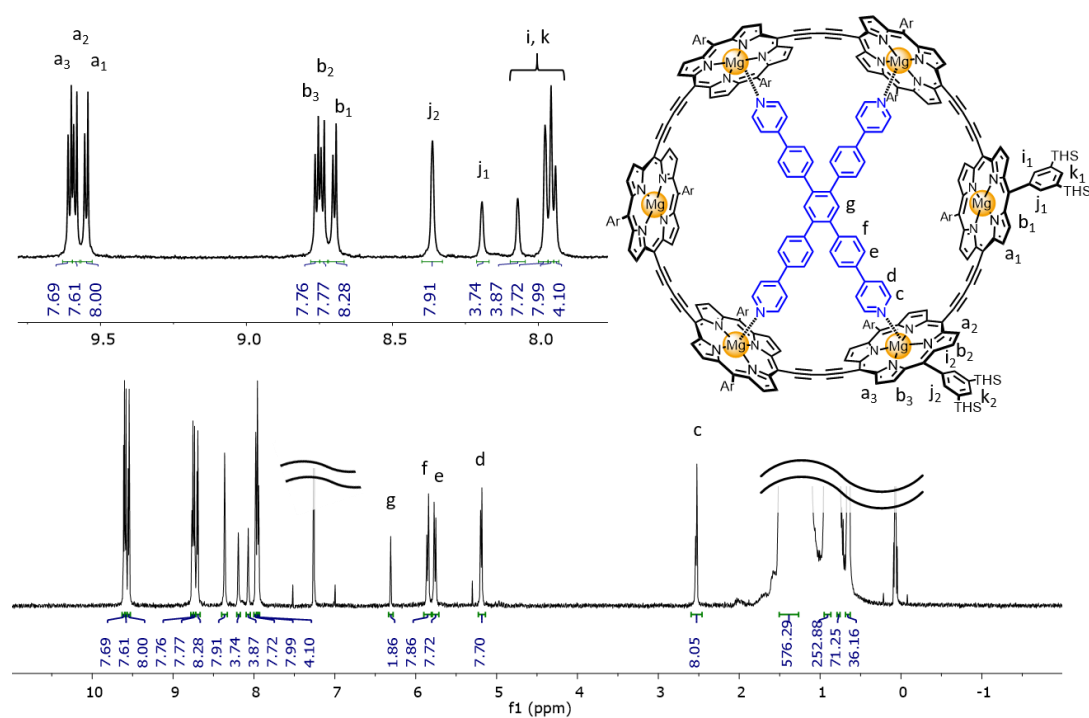


Figure 2.11. The ¹H NMR spectrum of Mg₆-P6·T4a (400 MHz, CDCl₃, 298 K).

1,4-(H₂)₂Mg₄-P6·T4a

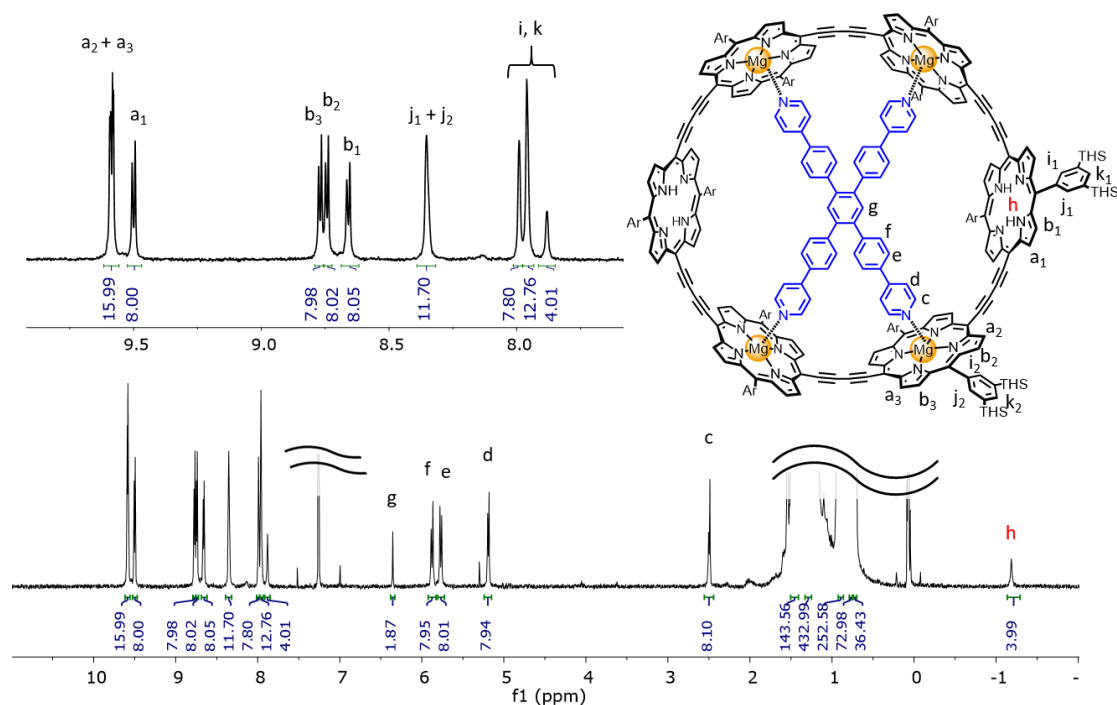


Figure 2.12. The ¹H NMR spectrum of 1,4-(H₂)₂Mg₄-P6·T4a (400 MHz, CDCl₃, 298 K).

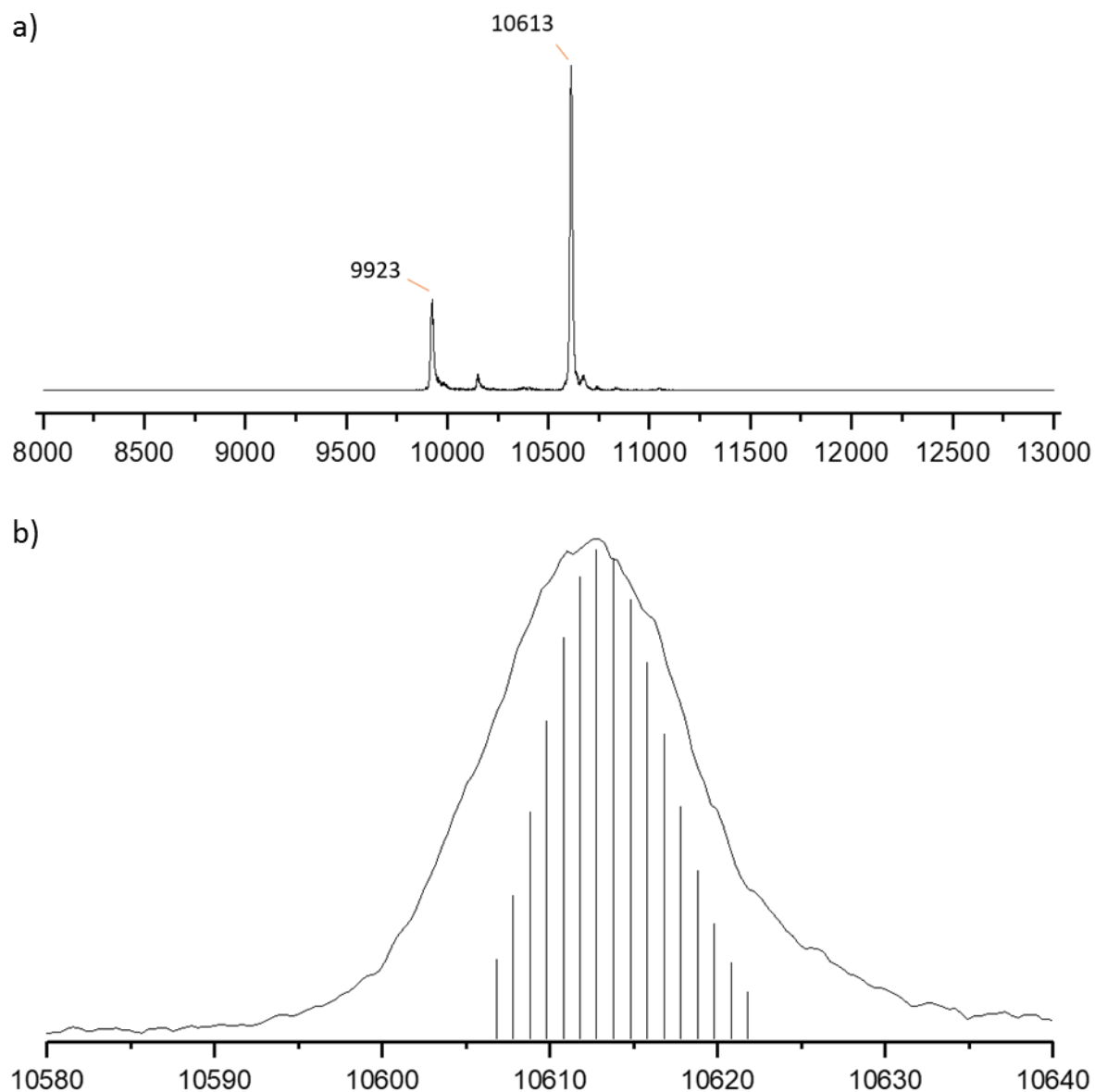


Figure 2.13. a) The MALDI-MS spectrum of **1,4-(H₂)₂Mg₄-P6-T4a**, matrix: dithranol. M⁺, C₆₉₈H₁₀₅₈Mg₄N₂₈Si₂₄ requires 10614, 9923 without template. b) Zoom of the MALDI-MS spectrum of **1,4-(H₂)₂Mg₄-P6-T4a** overlaid with the predicted isotope pattern.

1,4-(H₂)₂Mg₄-P6

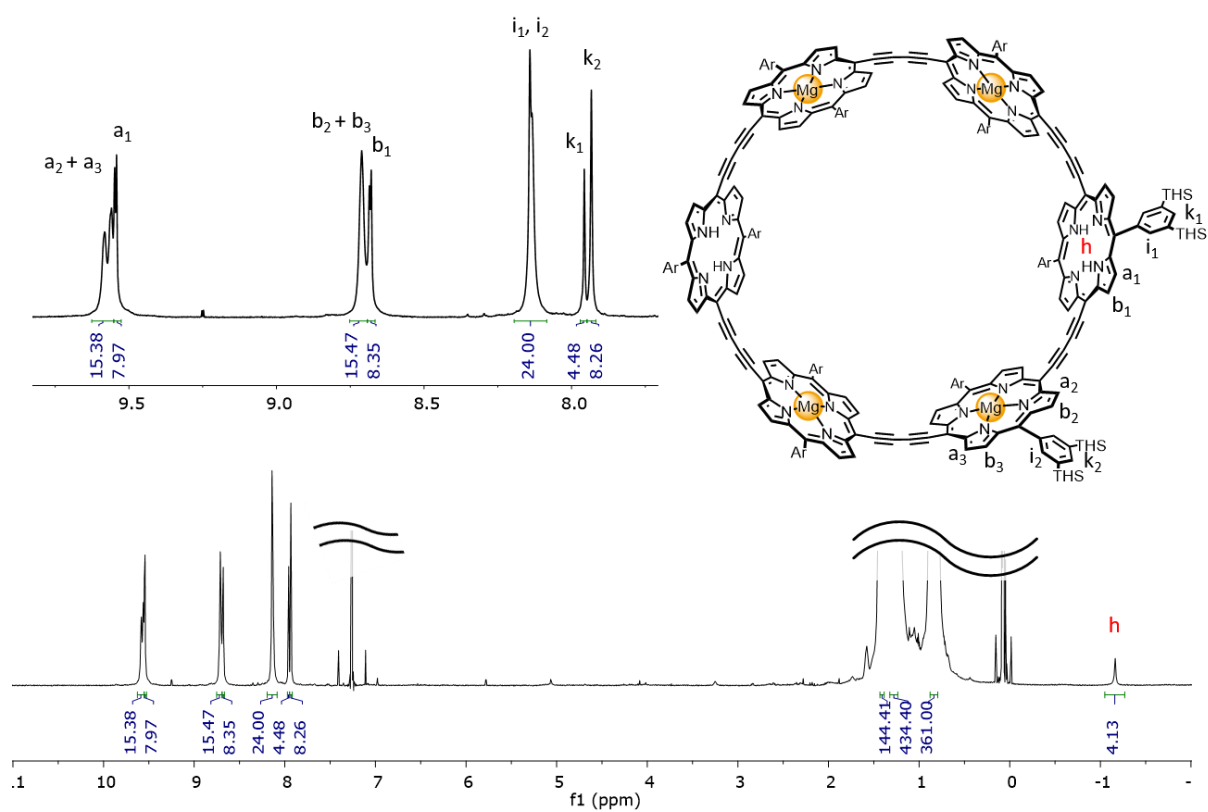


Figure 2.14. The ¹H NMR spectrum of 1,4-(H₂)₂Mg₄-P6 (700 MHz, CDCl₃, 298 K).

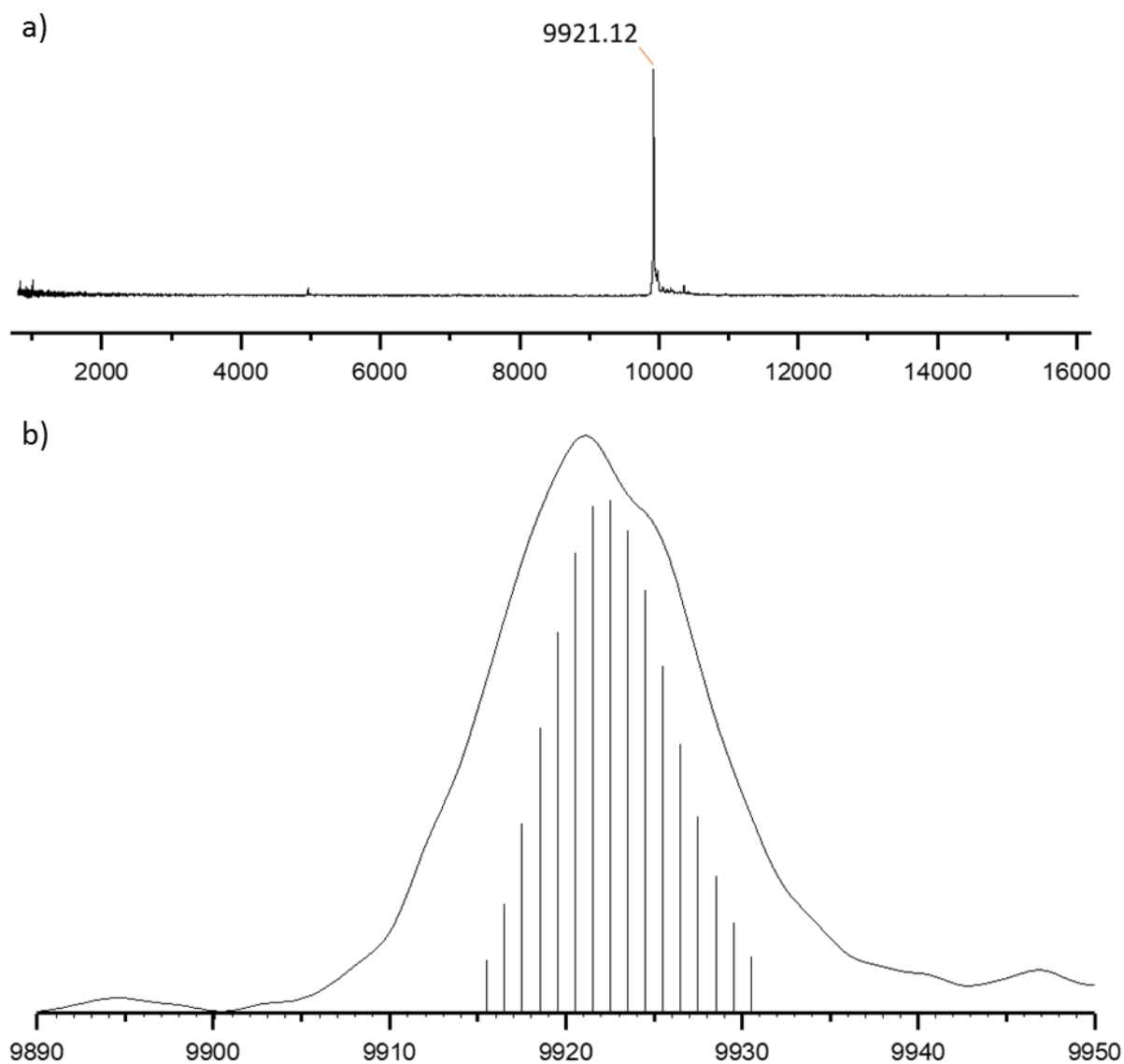


Figure 2.15. a) The MALDI-MS spectrum of **1,4-(H₂)₂Mg₄-P6**, matrix: DCTB. M⁺, C₆₄₈H₁₀₂₄Mg₄N₂₄Si₂₄ requires 9923. b) Zoom of the MALDI-MS spectrum of **1,4-(H₂)₂Mg₄-P6** overlaid with the predicted isotope pattern.

Mg₆-P6·T4b

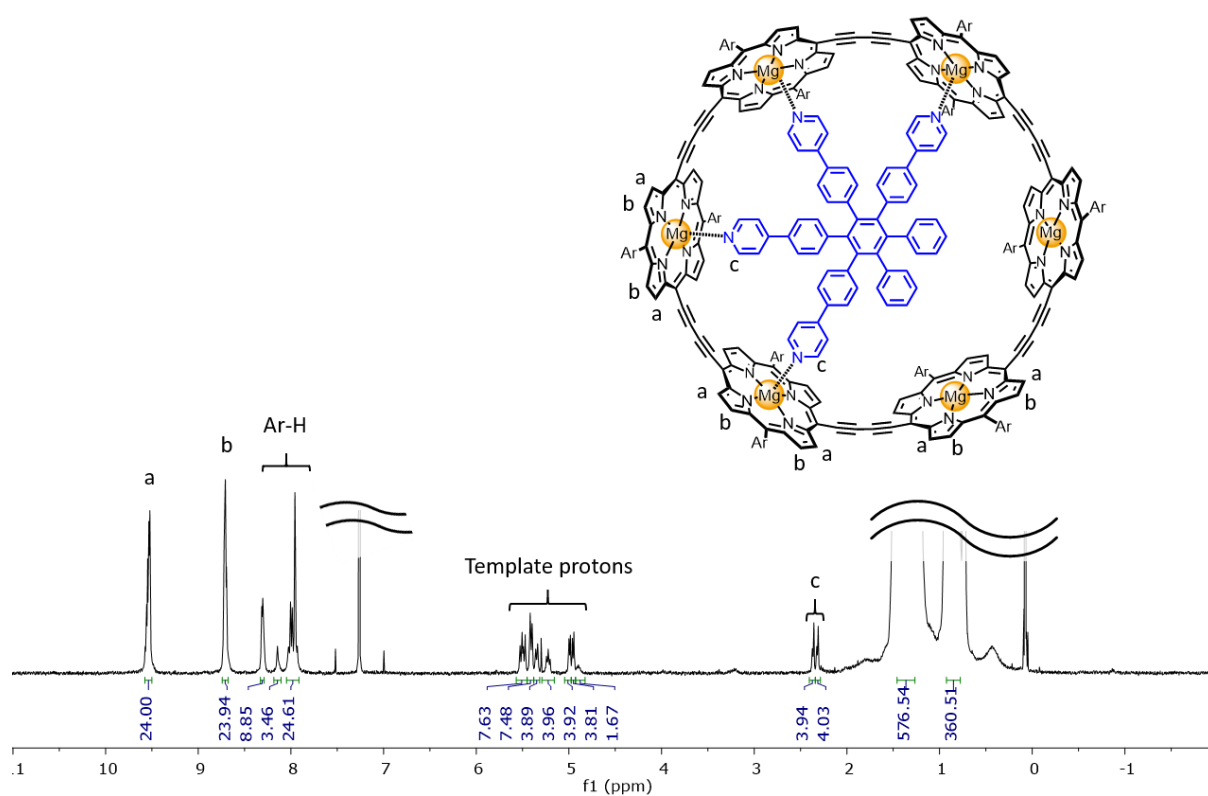


Figure 2.16. The ¹H NMR spectrum of **Mg₆-P6·T4b** (400 MHz, CDCl₃, 298 K).

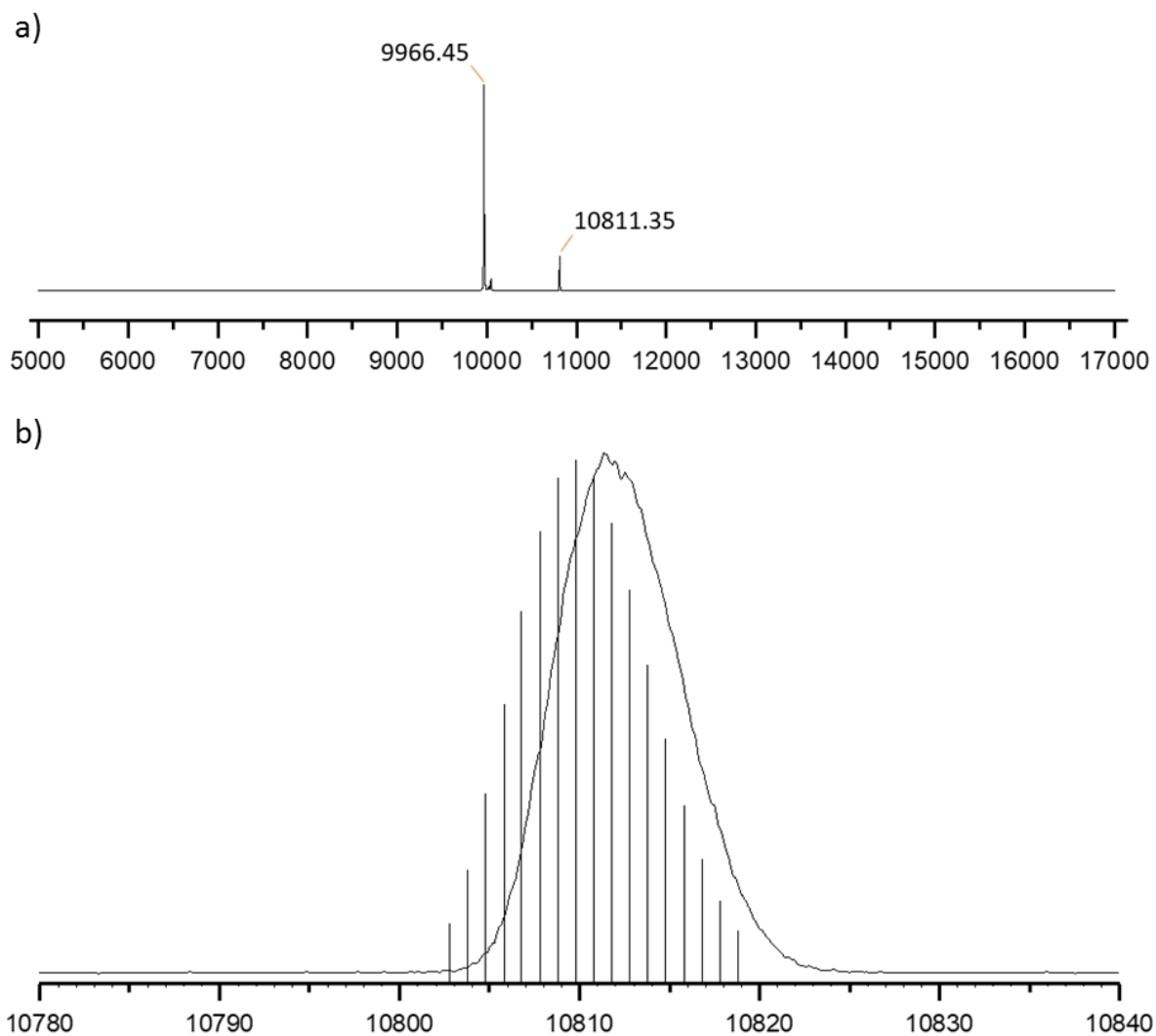


Figure 2.17. a) The MALDI-MS spectrum of **Mg₆-P6-T4b**, matrix: dithranol. M^+ , $C_{710}H_{1062}Mg_6N_{28}Si_{24}$ requires 10810, 9967 without template. b) Zoom of the MALDI-MS spectrum of **Mg₆-P6-T4b** overlaid with the predicted isotope pattern.

1,2-(H₂)₂Mg₄-P6·T4b

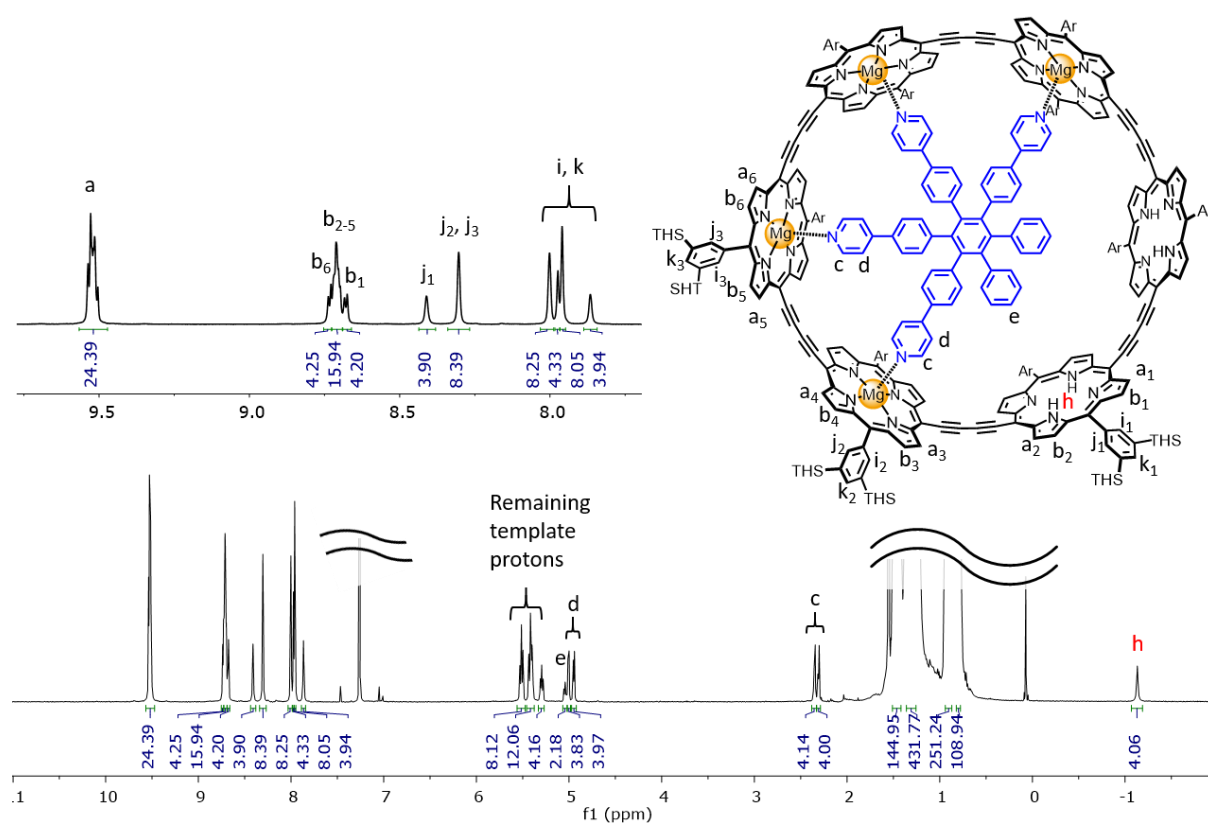


Figure 2.18. The ¹H NMR spectrum of 1,2-(H₂)₂Mg₄-P6·T4b (500 MHz, CDCl₃, 298 K).

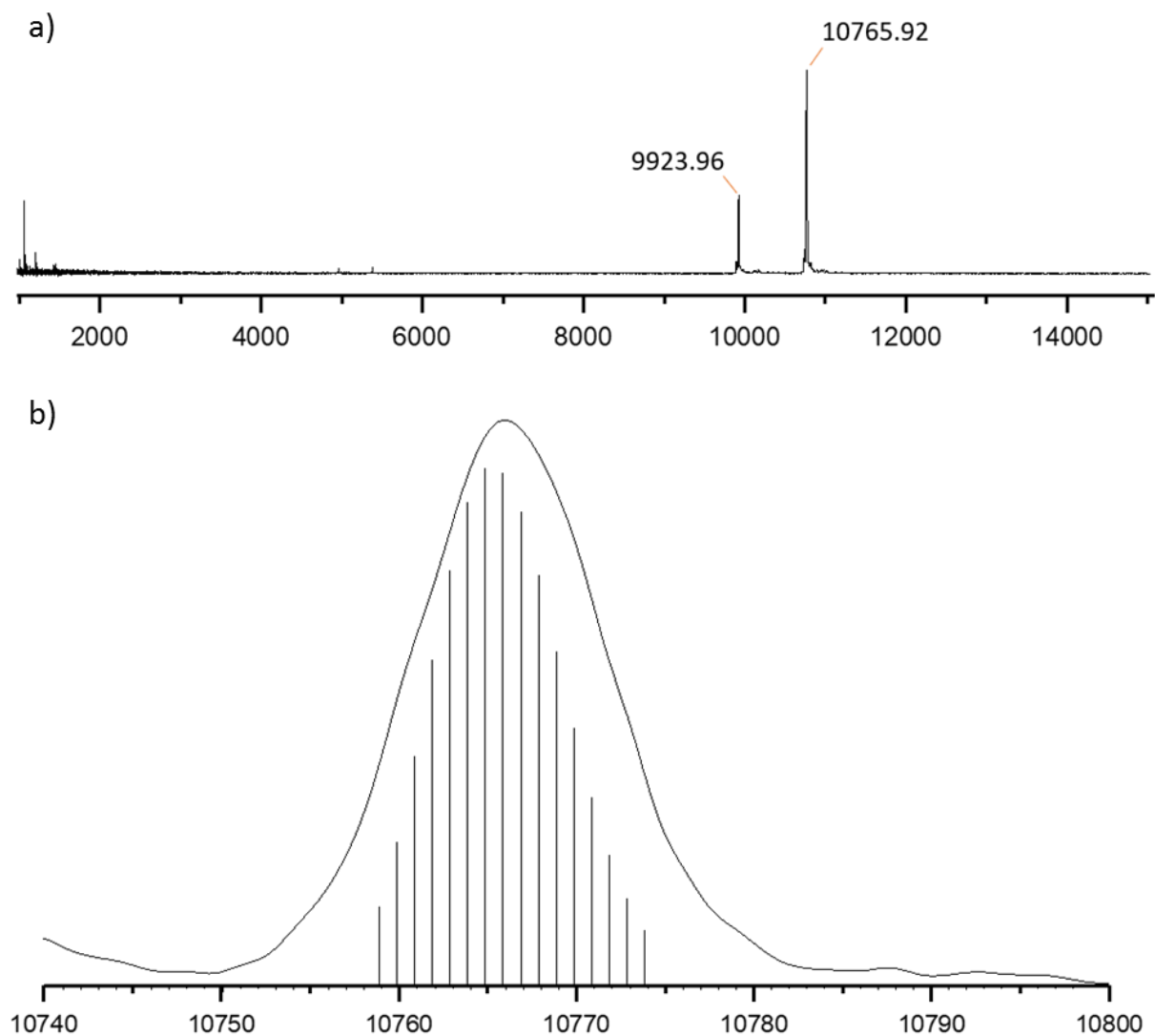


Figure 2.19. a) The MALDI-MS spectrum of **1,2-(H₂)₂Mg₄-P6-T4b**, matrix: DCTB. M⁺, C₇₁₀H₁₀₆₆Mg₄N₂₈Si₂₄ requires 10766, 9923 without template. b) Zoom of the MALDI-MS spectrum of **1,2-(H₂)₂Mg₄-P6-T4b** overlaid with the predicted isotope pattern.

$1,2-(\text{H}_2)_2\text{Mg}_4\text{-P6}$

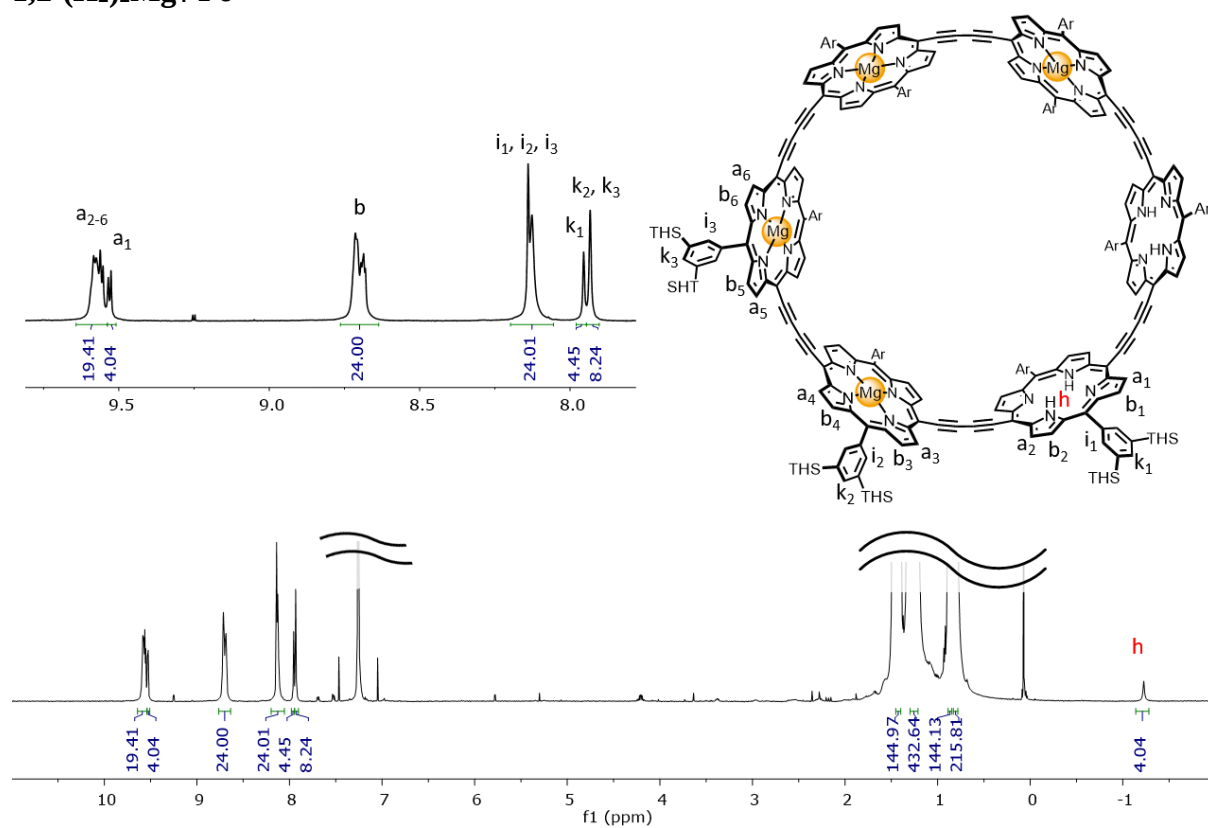


Figure 2.20. The ^1H NMR spectrum of $1,2-(\text{H}_2)_2\text{Mg}_4\text{-P6}$ (500 MHz, CDCl_3 , 298 K).

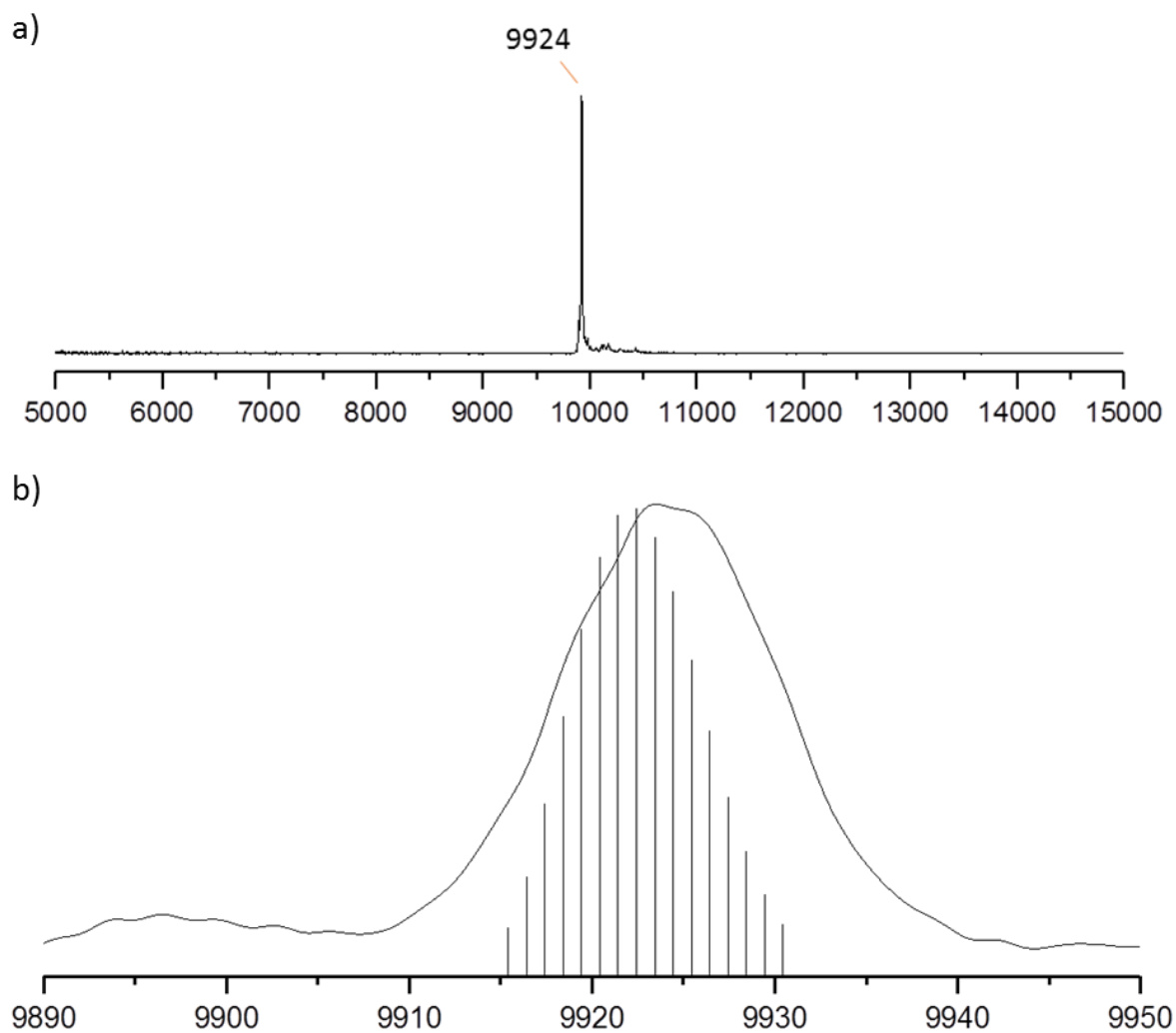


Figure 2.21. a) The MALDI-MS spectrum of **1,2-(H₂)₂Mg₄-P6**, matrix: DCTB. M⁺, C₆₄₈H₁₀₂₄Mg₄N₂₄Si₂₄ requires 9923. b) Zoom of the MALDI-MS spectrum of **1,2-(H₂)₂Mg₄-P6** overlaid with the predicted isotope pattern.

Figure 1 displays the ^1H and ^{13}C NMR spectra of compound **1**. The top panel shows the ^1H NMR spectrum (400 MHz, CDCl_3) with peaks labeled a, b, and Ar-H. The bottom panel shows the ^{13}C NMR spectrum (100 MHz, CDCl_3) with peaks labeled a through k. The chemical structure of compound **1** is shown on the right, a macrocyclic complex with three Mg-N₄ ligands and a central phenyl ring.

1,3-(H₂)₂Mg₄-P6·T4c

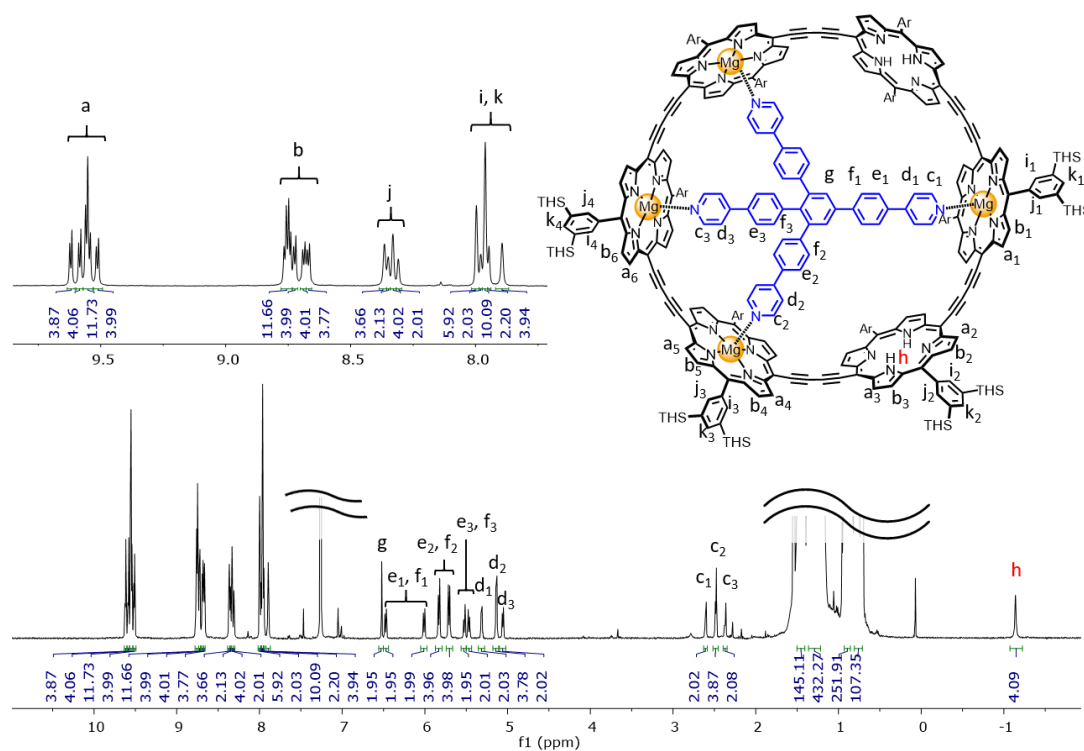


Figure 2.23. The ^1H NMR spectrum of **1,3-(H₂)₂Mg₄-P6·T4c** (500 MHz, CDCl₃, 298 K).

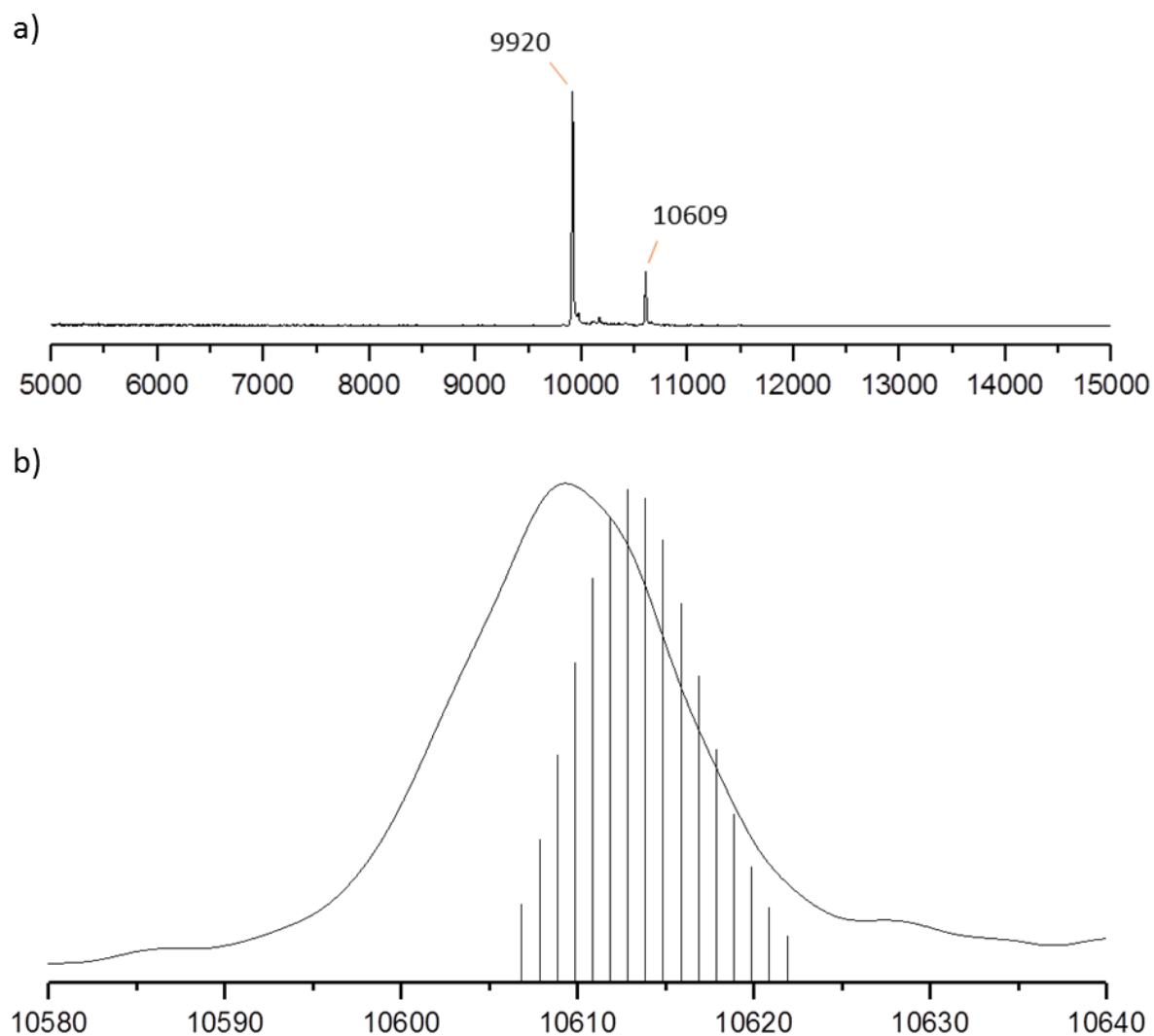


Figure 2.24. a) The MALDI-MS spectrum of **1,3-(H₂)₂Mg₄-P6-T4c**, matrix: DCTB. M⁺, C₆₉₈H₁₀₅₈Mg₄N₂₈Si₂₄ requires 10614, 9923 without template. b) Zoom of the MALDI-MS spectrum of **1,3-(H₂)₂Mg₄-P6-T4c** overlaid with the predicted isotope pattern.

1,3-(H₂)₂Mg₄-P6

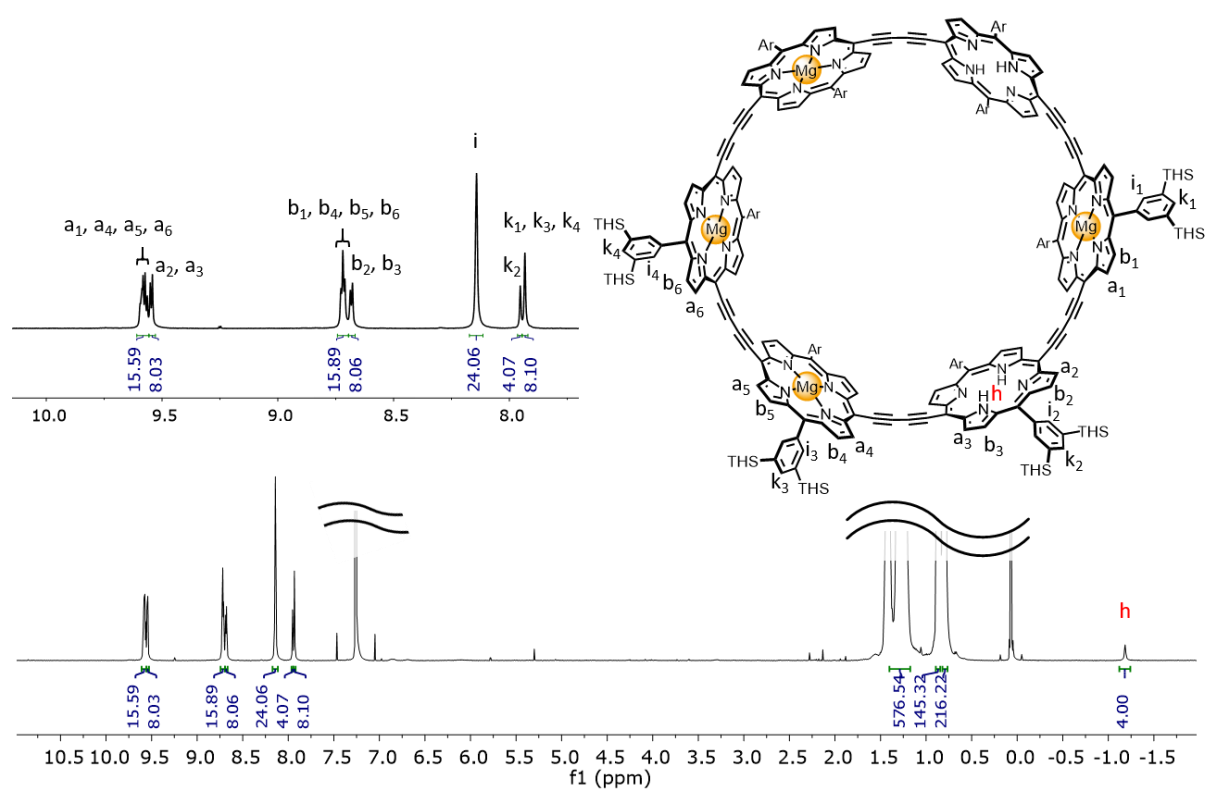


Figure 2.25. The ¹H NMR spectrum of 1,3-(H₂)₂Mg₄-P6 (500 MHz, CDCl₃, 298 K).

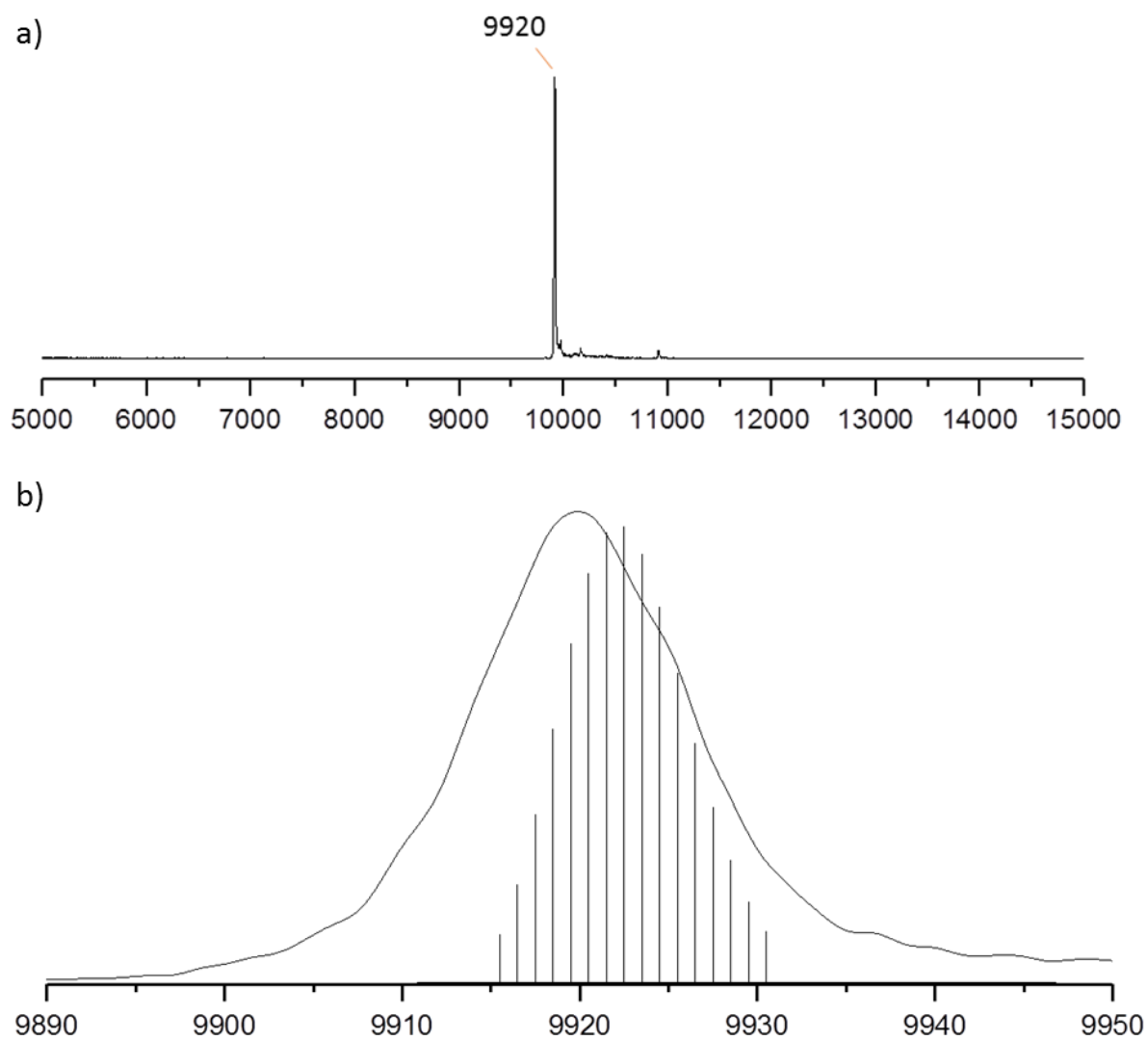


Figure 2.26. a) The MALDI-MS spectrum of **1,3-(H₂)₂Mg₄-P6**, matrix: DCTB. M⁺, C₆₄₈H₁₀₂₄Mg₄N₂₄Si₂₄ requires 9923. b) Zoom of the MALDI-MS spectrum of **1,3-(H₂)₂Mg₄-P6** overlaid with the predicted isotope pattern.

Mg₆-P6·T3

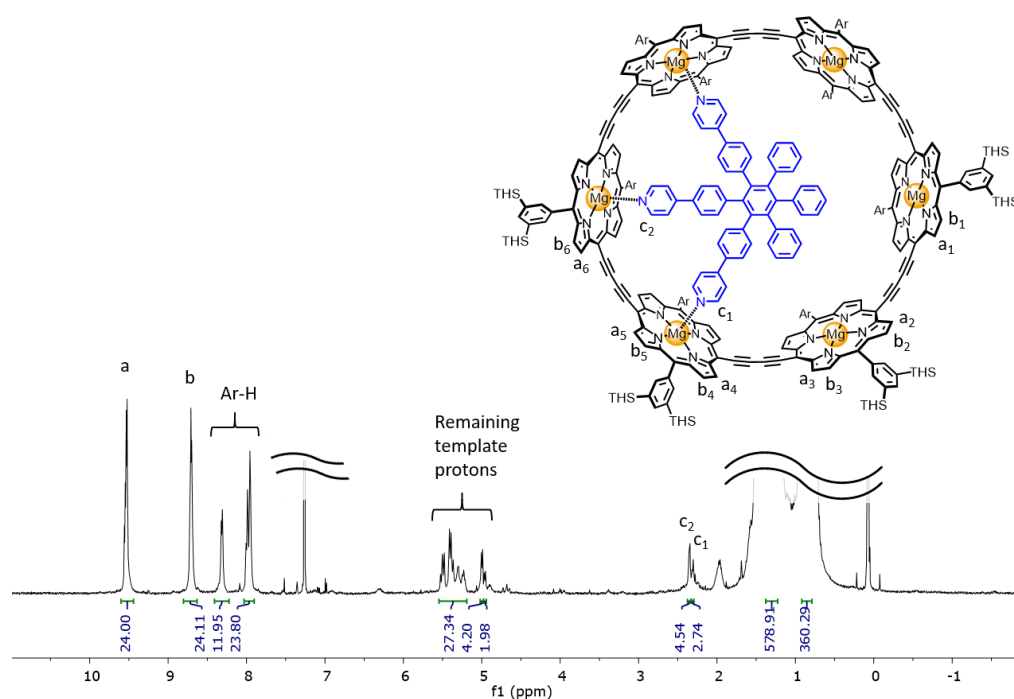


Figure 2.27. The ¹H NMR spectrum of **Mg₆-P6·T3a** (400 MHz, CDCl₃, 298 K).

1,2,3-(H₂)₃Mg₃-P6·T3a

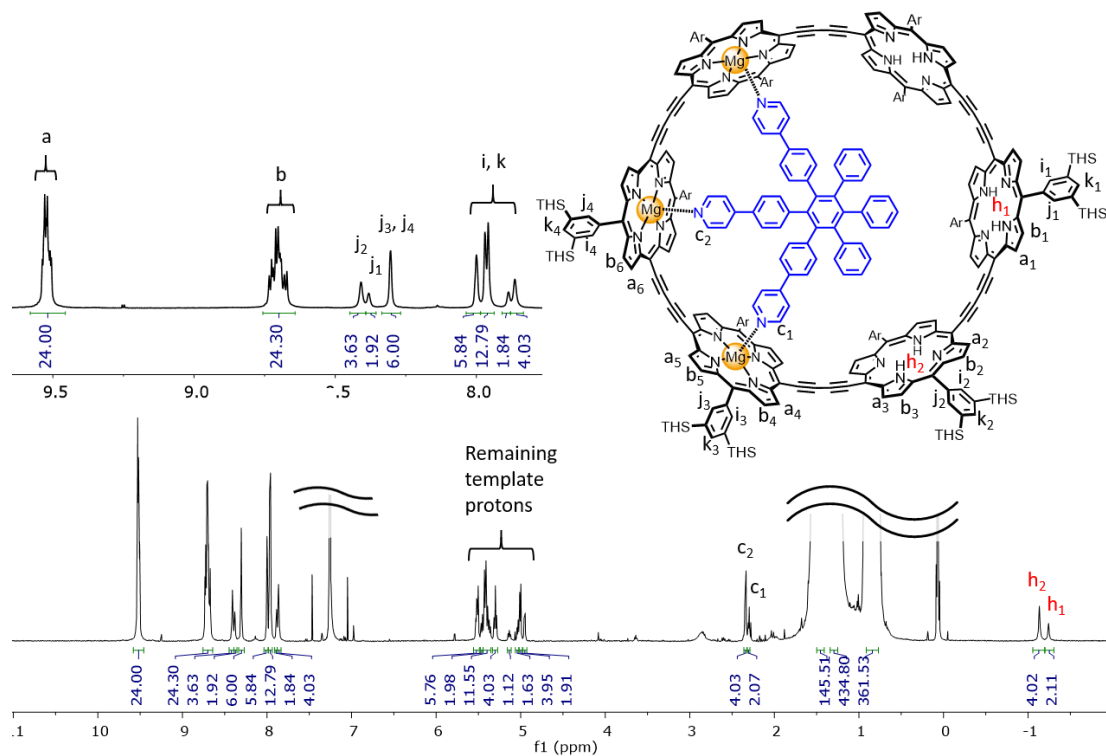


Figure 2.28. The ¹H NMR spectrum of **1,2,3-(H₂)₃Mg₃-P6·T3a** (500 MHz, CDCl₃, 298 K).

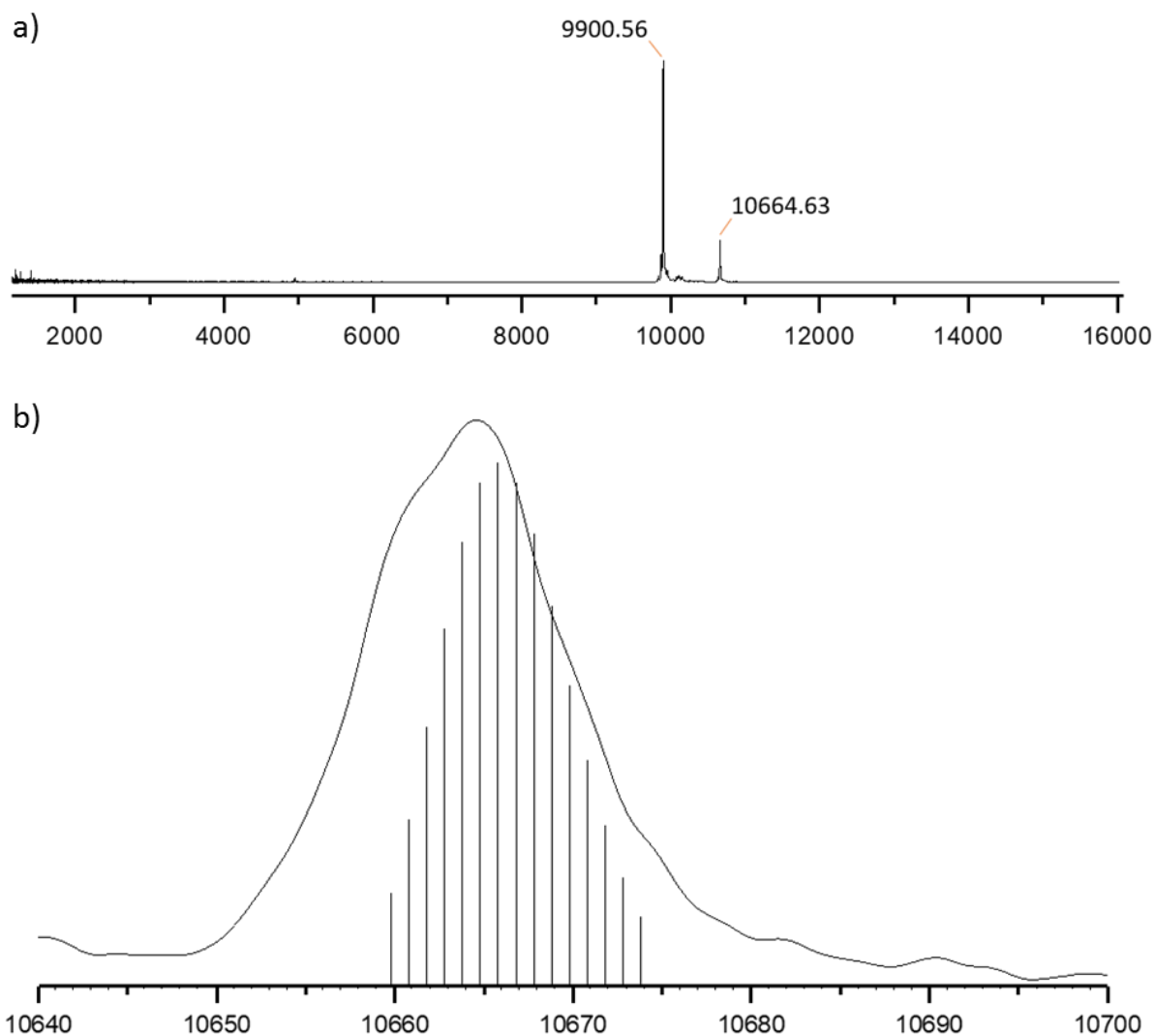


Figure 2.29. a) The MALDI-MS spectrum of **1,2,3-(H₂)₃Mg₃-P6-T3a**, matrix: DCTB. M⁺, C₇₀₅H₁₀₆₅Mg₃N₂₇Si₂₄ requires 10666, 9900 without template. b) Zoom of the MALDI-MS spectrum of **1,2,3-(H₂)₃Mg₃-P6-T3a** overlaid with the predicted isotope pattern.

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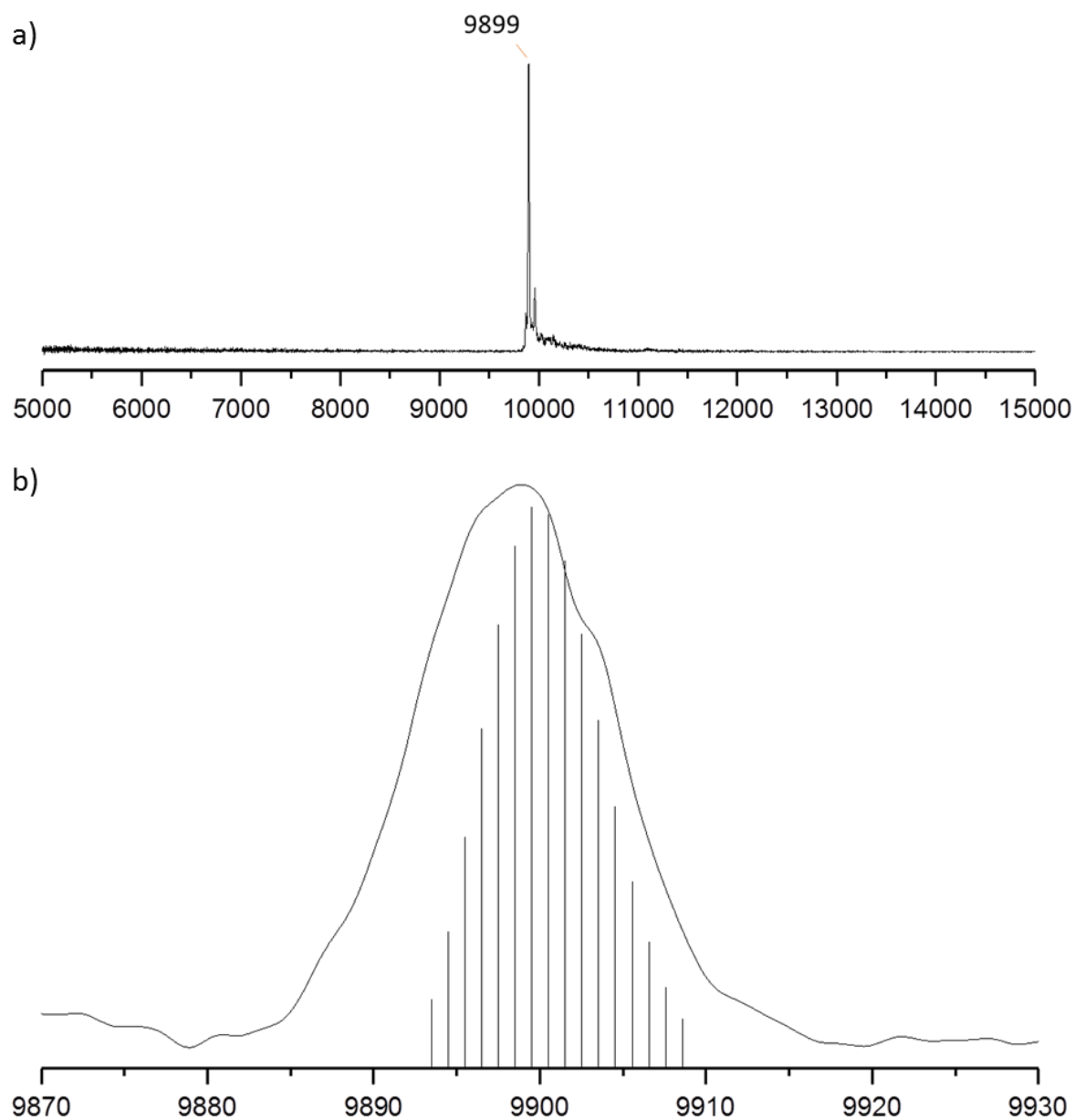


Figure 2.31. a) The MALDI-MS spectrum of **1,2,3-(H₂)₃Mg₃-P6**, matrix: DCTB. M⁺, C₆₄₈H₁₀₂₆Mg₃N₂₄Si₂₄ requires 9900. b) Zoom of the MALDI-MS spectrum of **1,2,3-(H₂)₃Mg₃-P6** overlaid with the predicted isotope pattern.

Mg₆-P6·T3b

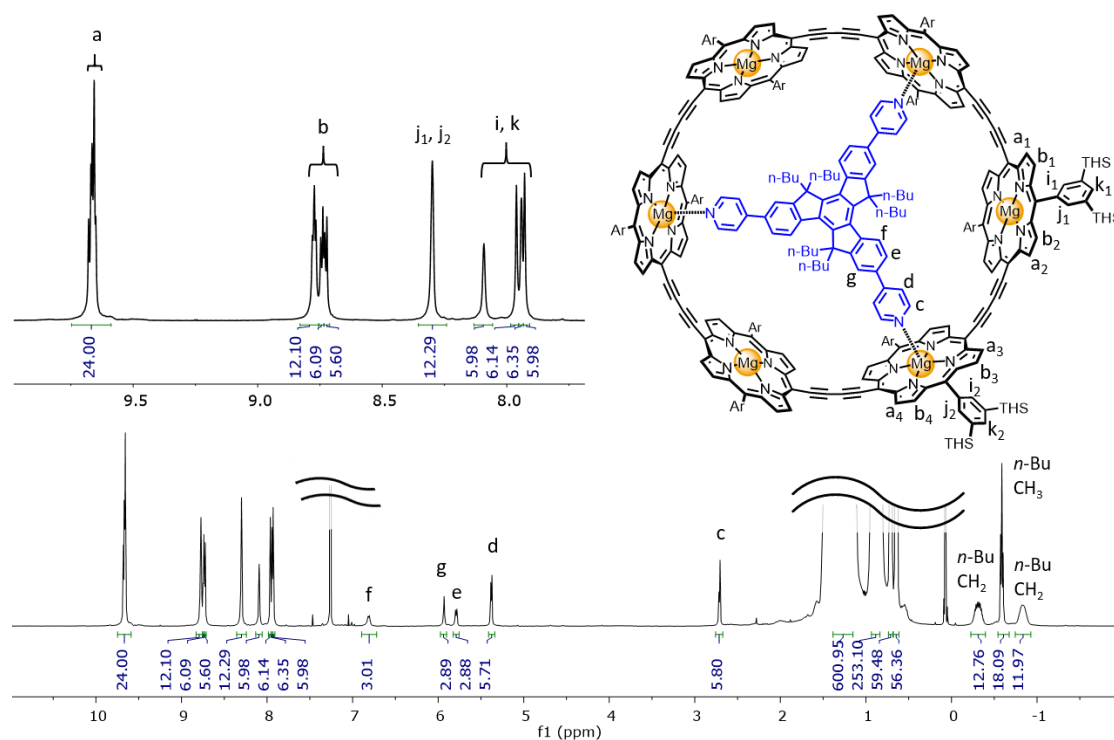


Figure 2.32. The ¹H NMR spectrum of **Mg₆-P6·T3c** (500 MHz, CDCl₃, 298 K).

1,3,5-(H₂)₃Mg₃-P6·T3c

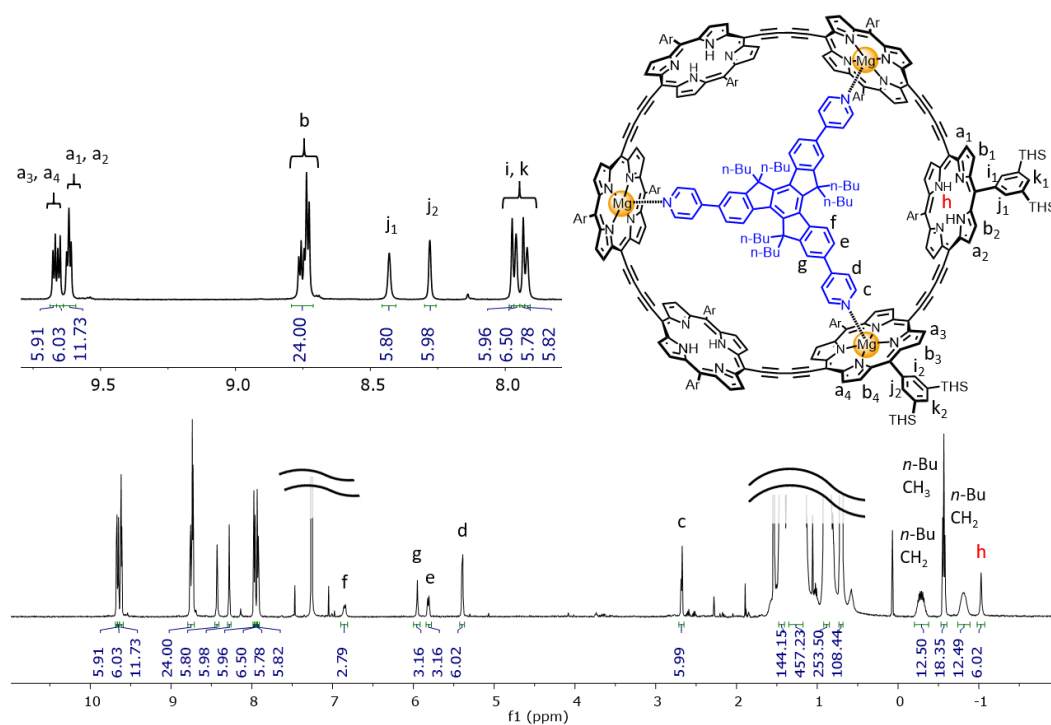


Figure 2.33. The ¹H NMR spectrum of **1,3,5-(H₂)₃Mg₃-P6·T3c** (500 MHz, CDCl₃, 298 K).

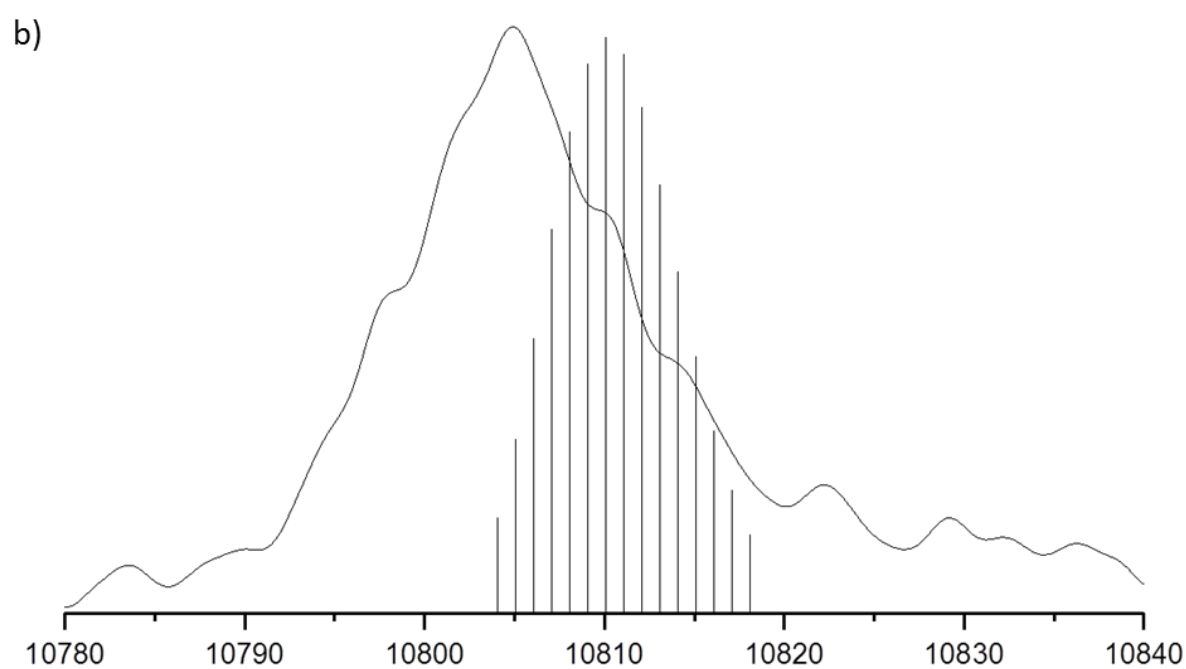
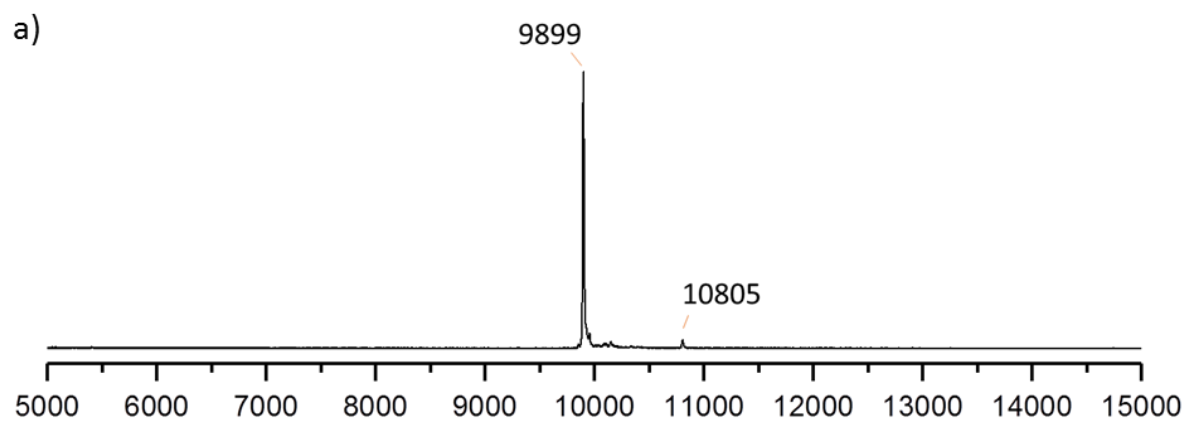


Figure 2.34. a) The MALDI-MS spectrum of **1,3,5-(H₂)₃Mg₃-P6-T3b**, matrix: DCTB. M⁺, C₇₁₄H₁₁₀₁Mg₃N₂₇Si₂₄ requires 10811, 9900 without template. b) Zoom of the MALDI-MS spectrum of **1,3,5-(H₂)₃Mg₃-P6-T3b** overlaid with the predicted isotope pattern.

1,3,5-(H₂)₃Mg₃-P6

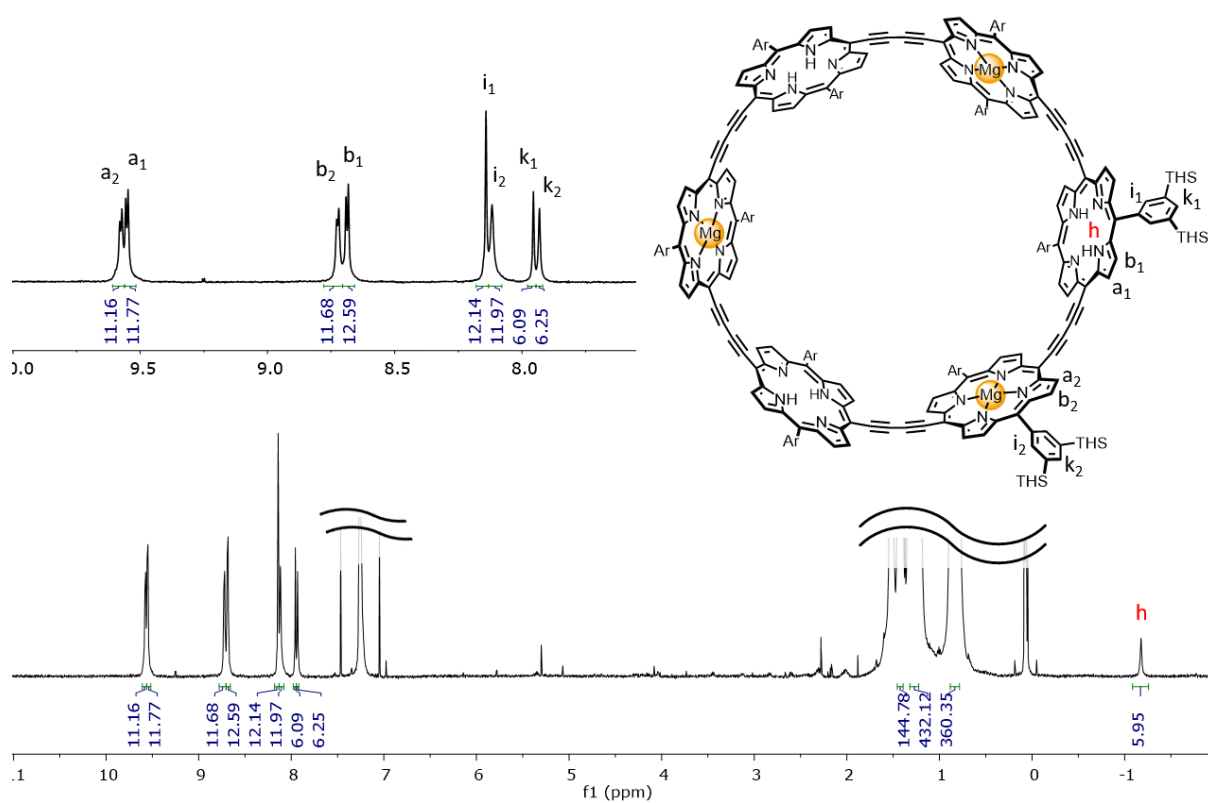


Figure 2.35. The ¹H NMR spectrum of **1,3,5-(H₂)₃Mg₃-P6** (500 MHz, CDCl₃, 298 K).

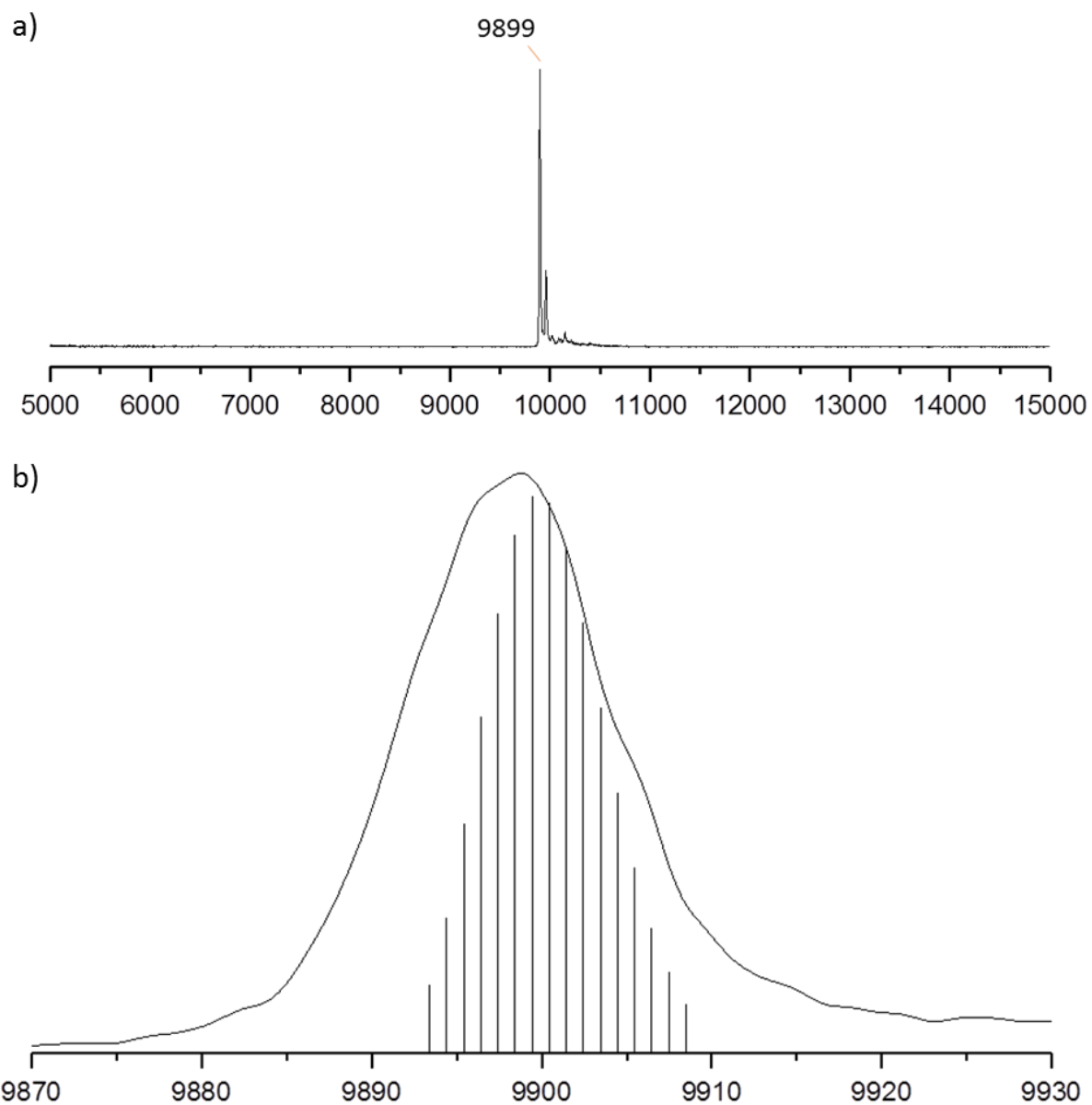


Figure 2.36. a) The MALDI-MS spectrum of **1,3,5-(H₂)₃Mg₃-P6**, matrix: DCTB. M⁺, C₆₄₈H₁₀₂₆Mg₃N₂₄Si₂₄ requires 9900. b) Zoom of the MALDI-MS spectrum of **1,3,5-(H₂)₃Mg₃-P6** overlaid with the predicted isotope pattern. Matrix: DCTB. M⁺, C₆₄₈H₁₀₂₆Mg₃N₂₄Si₂₄ requires 9900.

1,4-Cu₂Mg₄-P6·T4a

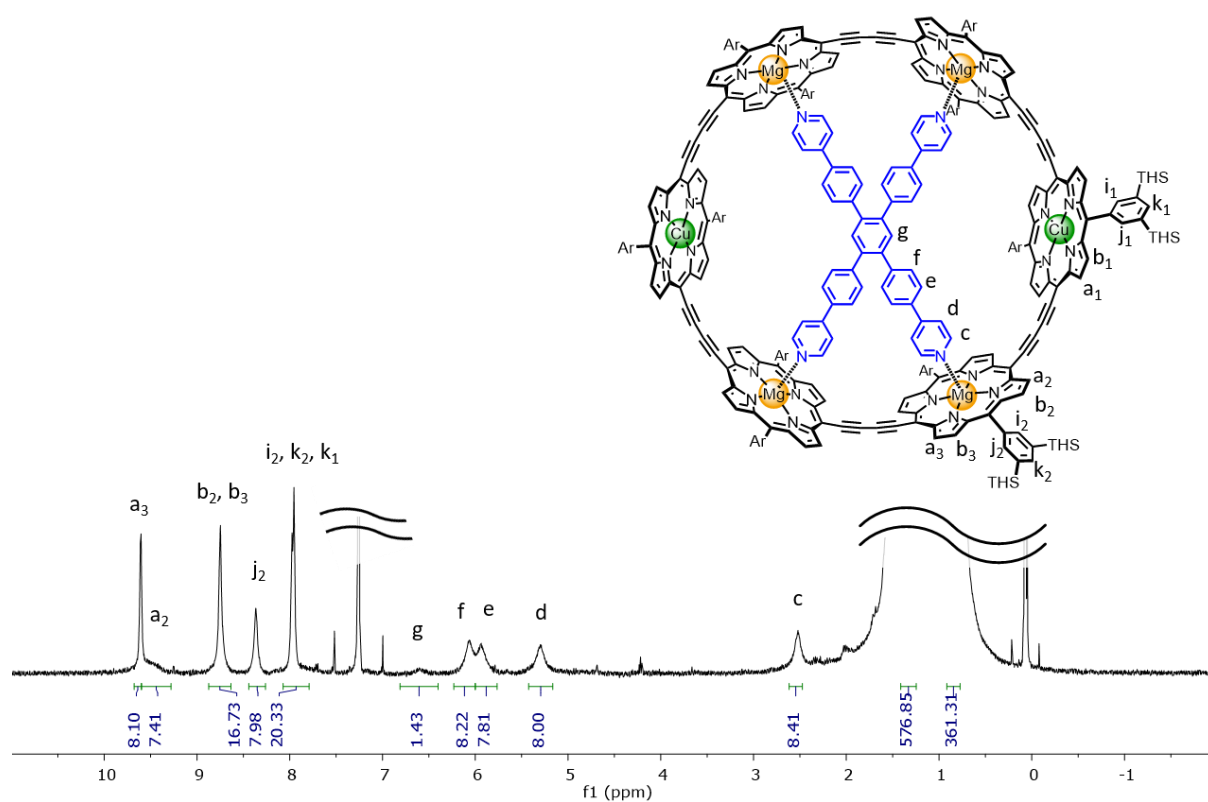


Figure 2.37. The ¹H NMR spectrum of **1,4-Cu₂Mg₄-P6·T4a** (400 MHz, CDCl₃, 298 K).

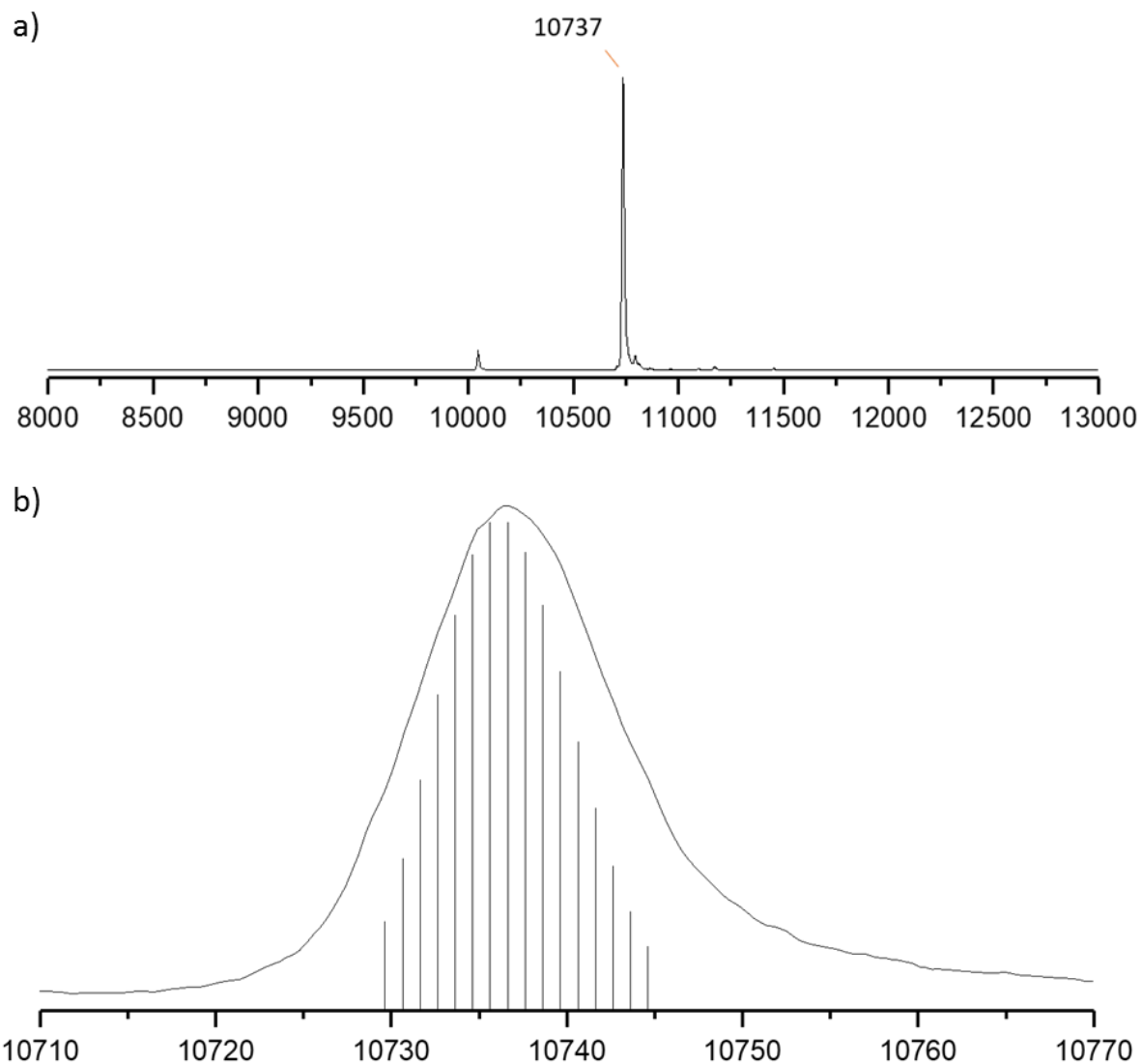


Figure 2.38. a) The MALDI-MS spectrum of **1,4-Cu₂Mg₄-P₆-T₄a**, matrix: dithranol. M^+ , $C_{698}H_{1054}Cu_2Mg_4N_{28}Si_{24}$ requires 10737. b) Zoom of the MALDI-MS spectrum of **1,4-Cu₂Mg₄-P₆-T₄a** overlaid with the predicted isotope pattern.

1,4-Cu₂Mg₄-P6

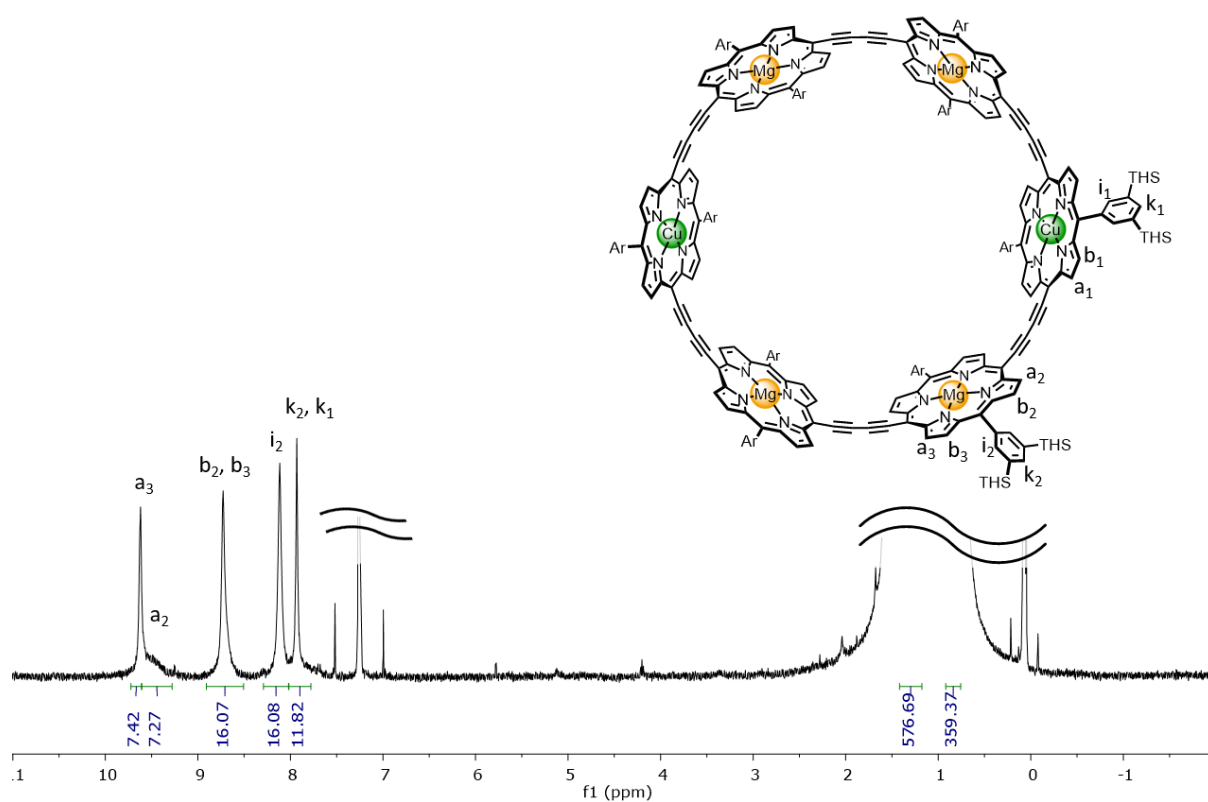


Figure 2.39. The ¹H NMR spectrum of 1,4-Cu₂Mg₄-P6 (400 MHz, CDCl₃, 298 K).

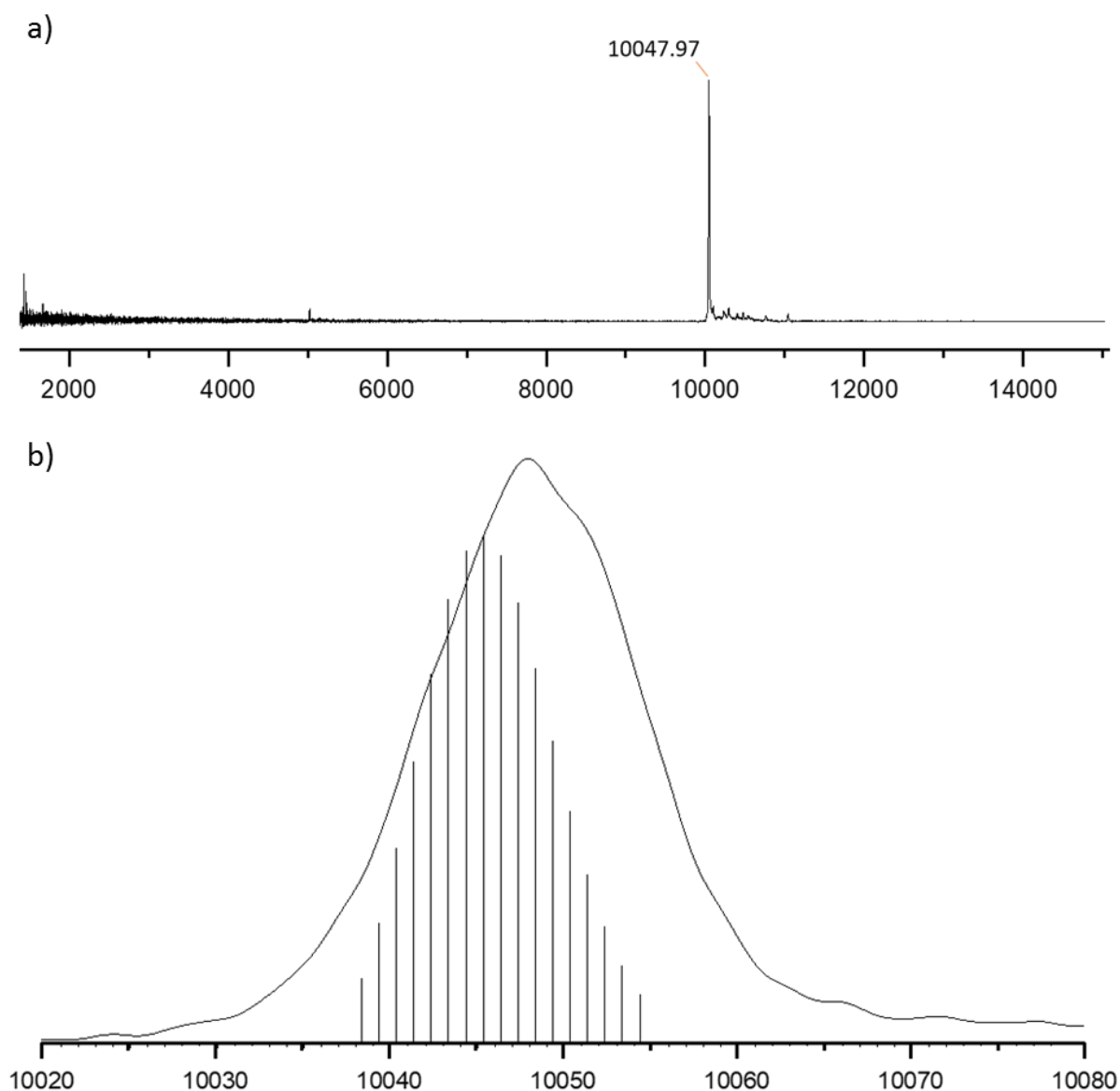


Figure 2.40. a) The MALDI-MS spectrum of **1,4-Cu₂Mg₄-P6**, matrix: DCTB. M^+ , $C_{648}H_{1020}Cu_2Mg_4N_{24}Si_{24}$ requires 10046. b) Zoom of the MALDI-MS spectrum of **1,4-Cu₂Mg₄-P6** overlaid with the predicted isotope pattern.

1,4-Cu₂Mg₄-P6·T6

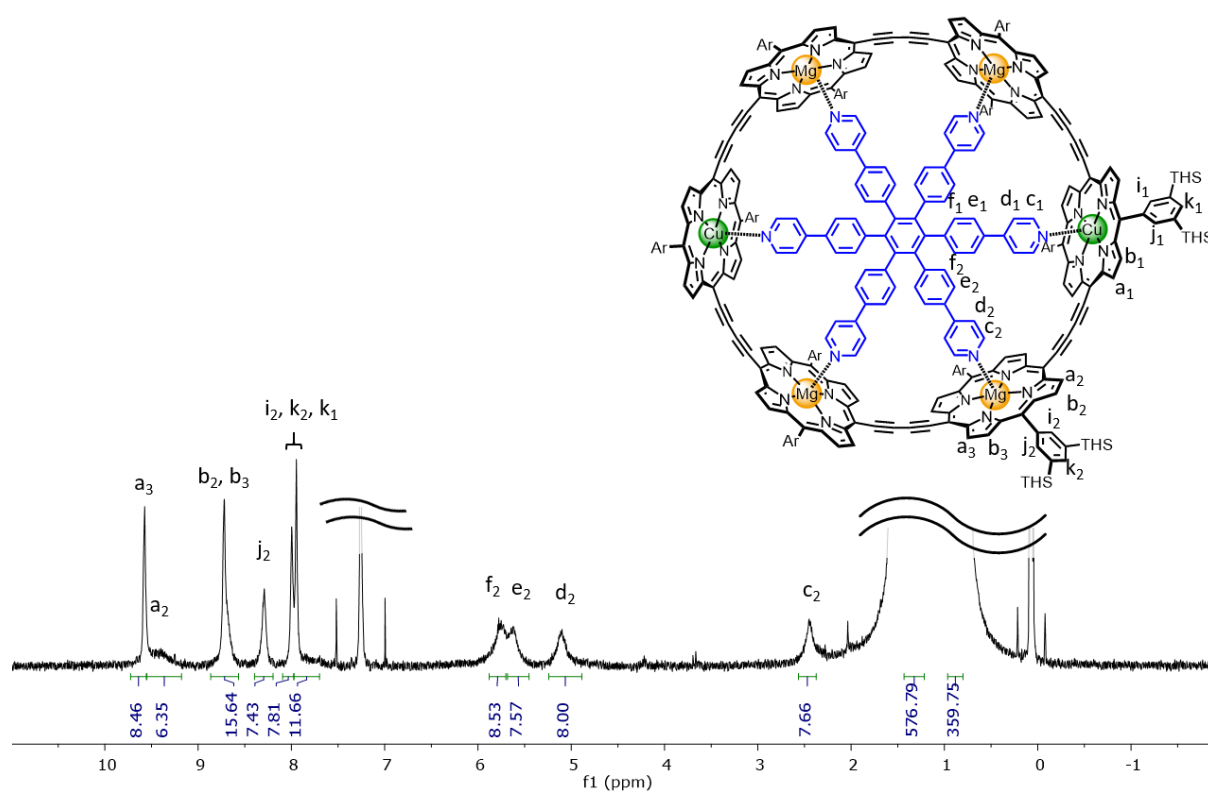


Figure 2.41. The ¹H NMR spectrum of 1,4-Cu₂Mg₄-P6·T6 (400 MHz, CDCl₃, 298 K).

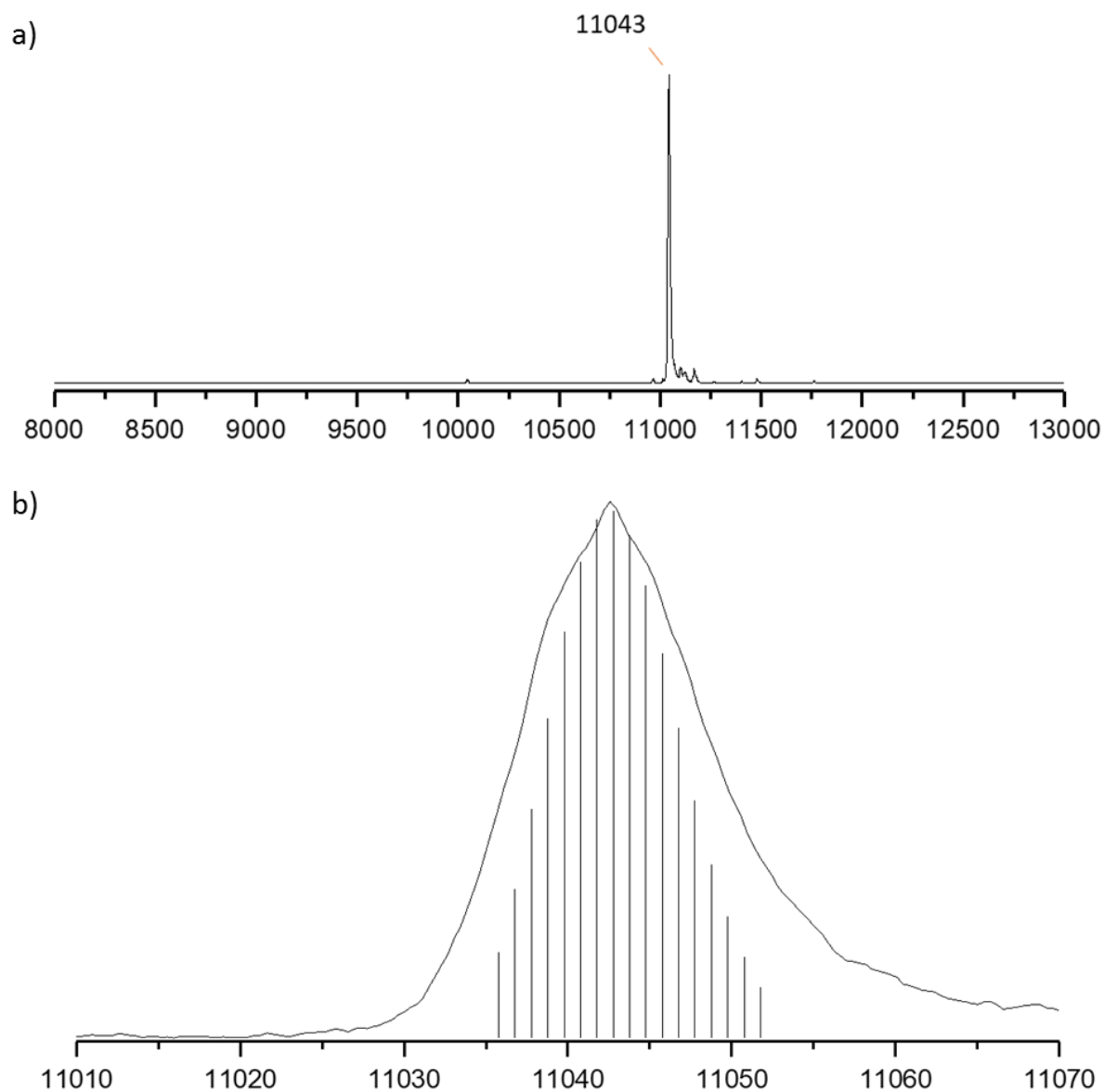


Figure 2.42. a) The MALDI-MS spectrum of **1,4-Cu₂Mg₄-P₆·T₆**, matrix: dithranol. M^+ , $C_{720}H_{1068}Cu_2Mg_4N_{30}Si_{24}$ requires 11043. b) Zoom of the MALDI-MS spectrum of **1,4-Cu₂Mg₄-P₆·T₆** overlaid with the predicted isotope pattern.

1,2-Zn₂Mg₄-P6

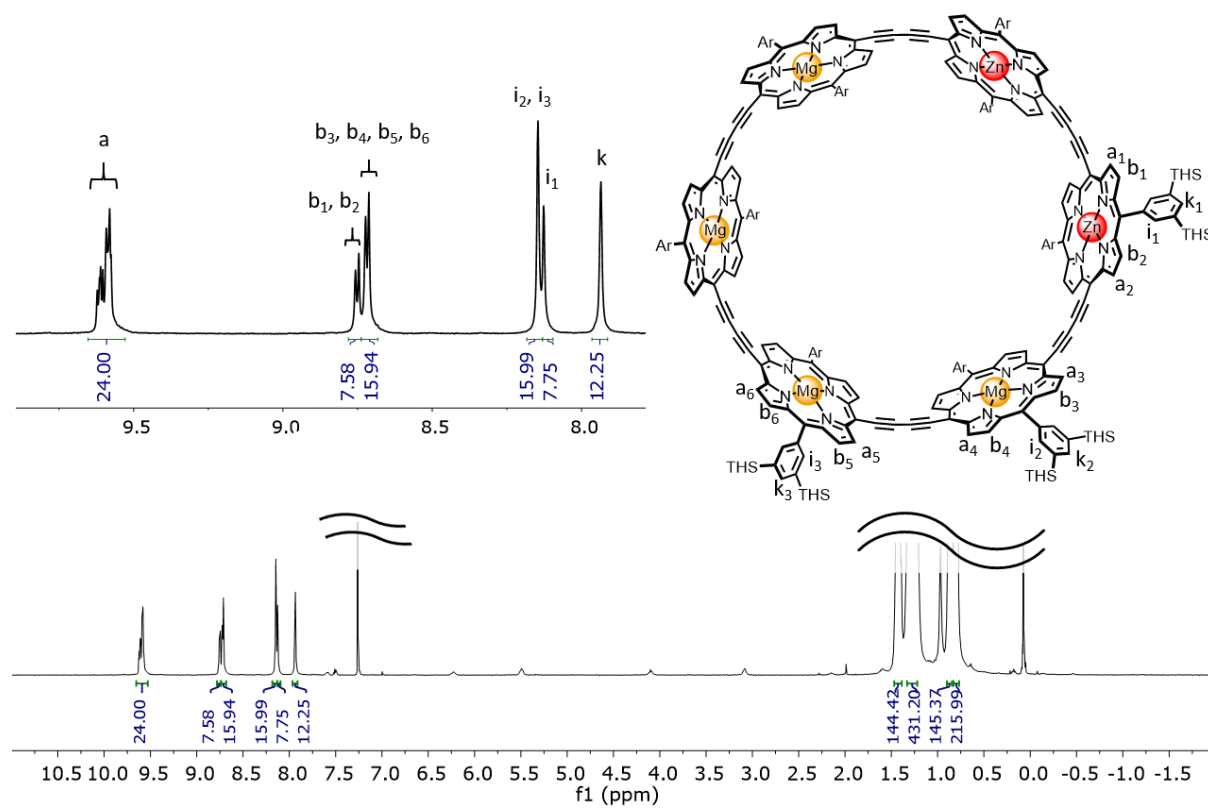


Figure 2.43. The ¹H NMR spectrum of **1,2-Zn₂Mg₄-P6** (400 MHz, CDCl₃, 298 K).

$1,2\text{-Zn}_2(\text{H}_2)_4\text{-P6}$

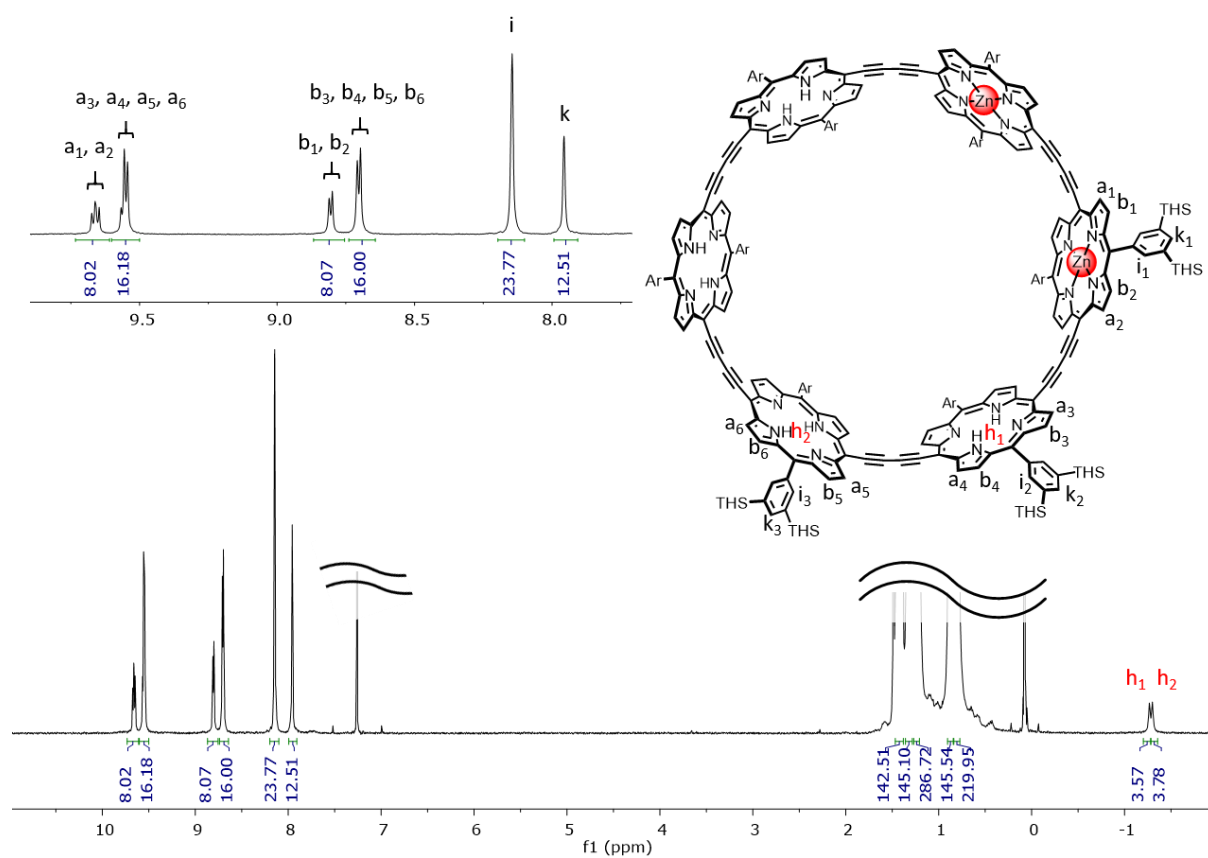


Figure 2.44. The ^1H NMR spectrum of $1,2\text{-Zn}_2(\text{H}_2)_4\text{-P6}$ (400 MHz, CDCl_3 , 298 K).

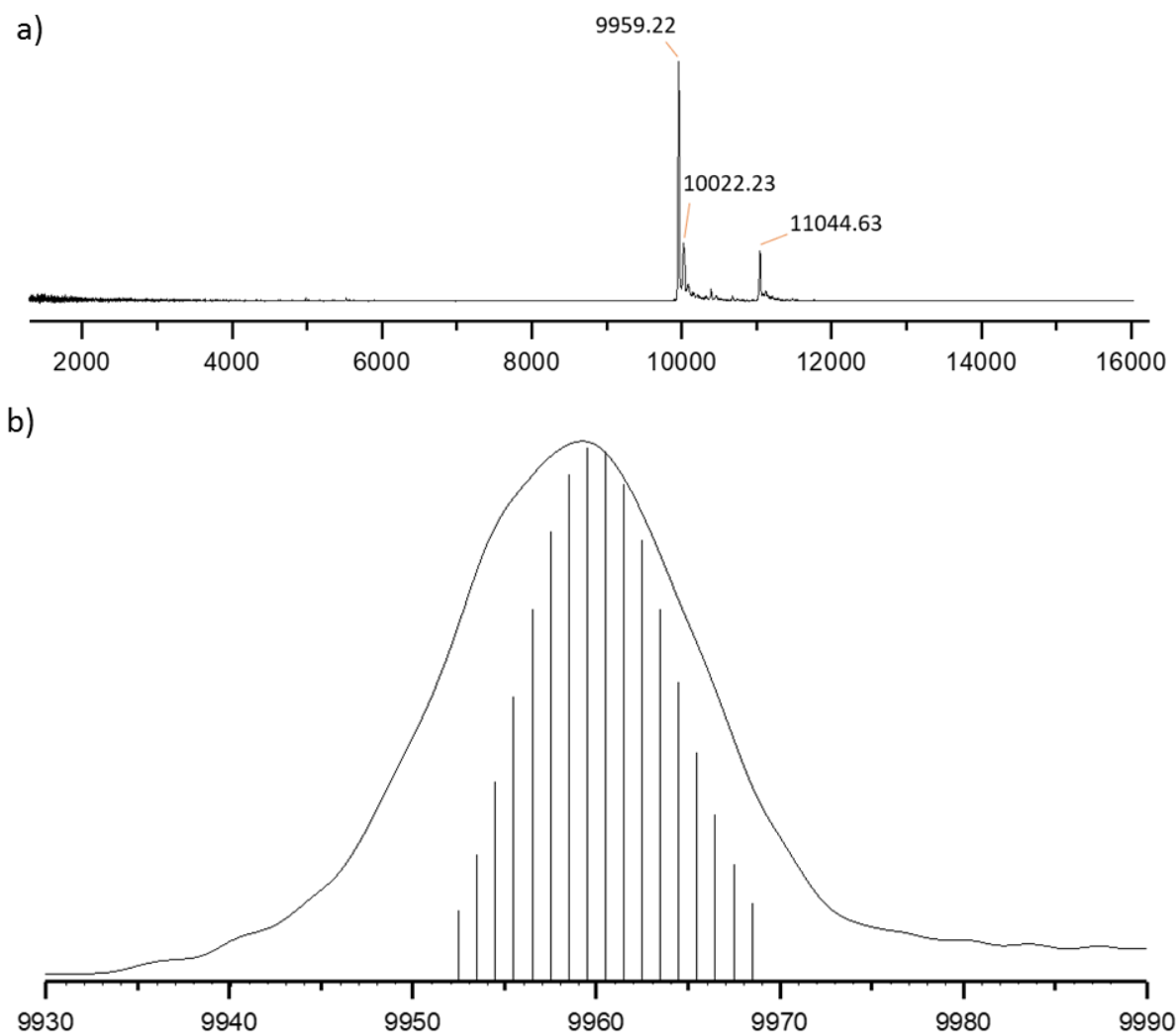


Figure 2.45. a) The MALDI-MS spectrum of **1,2-Zn₂(H₂)₄-P6**, matrix: DCTB. M⁺, C₆₄₈H₁₀₂₈N₂₄Si₂₄Zn₂ requires 9960. b) Zoom of the MALDI-MS spectrum of **1,2-Zn₂(H₂)₄-P6** overlaid with the predicted isotope pattern.

1,4-Ag₂Mg₄-P6

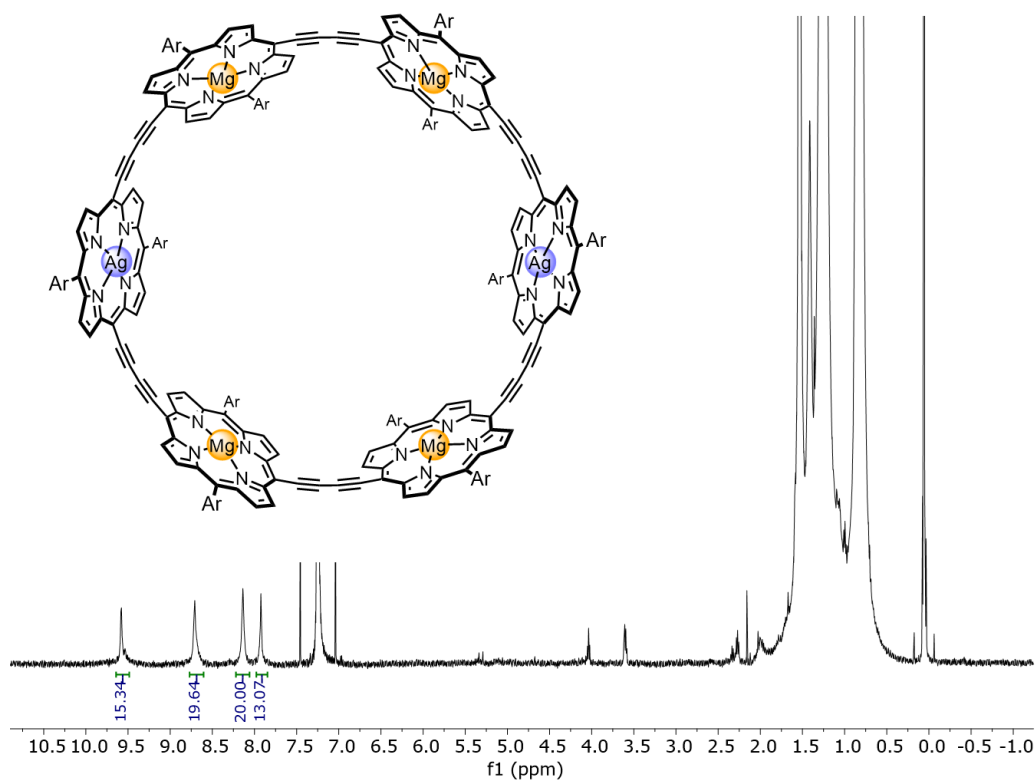


Figure 2.46. The ¹H NMR spectrum of **1,4-Ag₂Mg₄-P6** (500 MHz, CDCl₃, 298 K).

1,4-Ag₂Mg₄-P6·T6

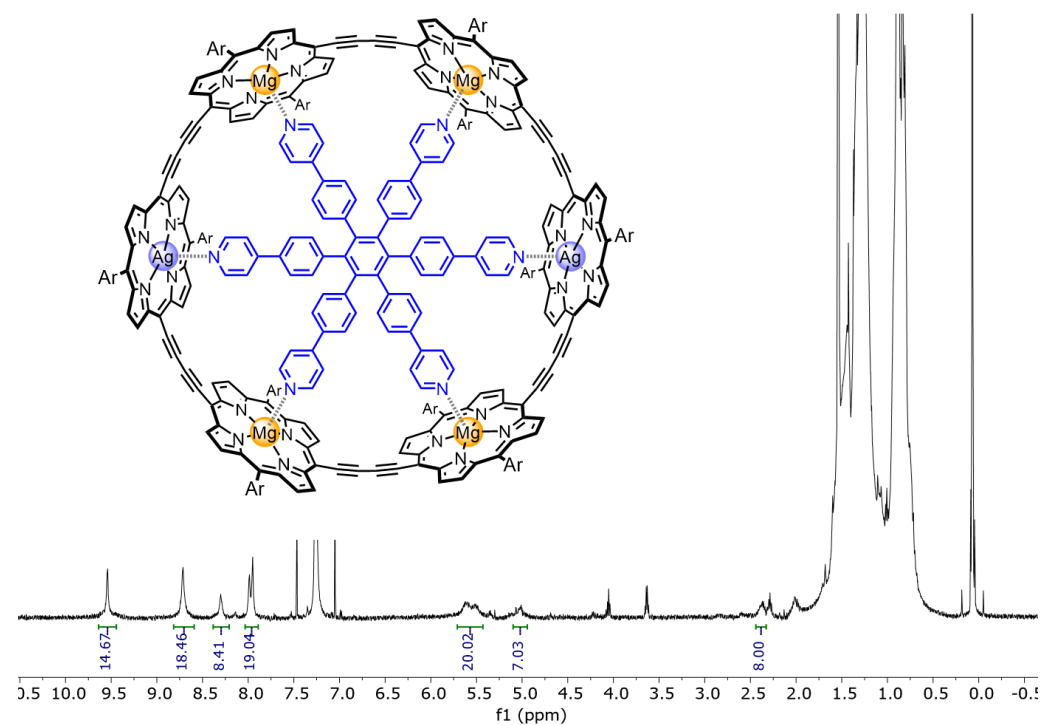


Figure 2.47. The ¹H NMR spectrum of **1,4-Ag₂Mg₄-P6·T6** (500 MHz, CDCl₃, 298 K).

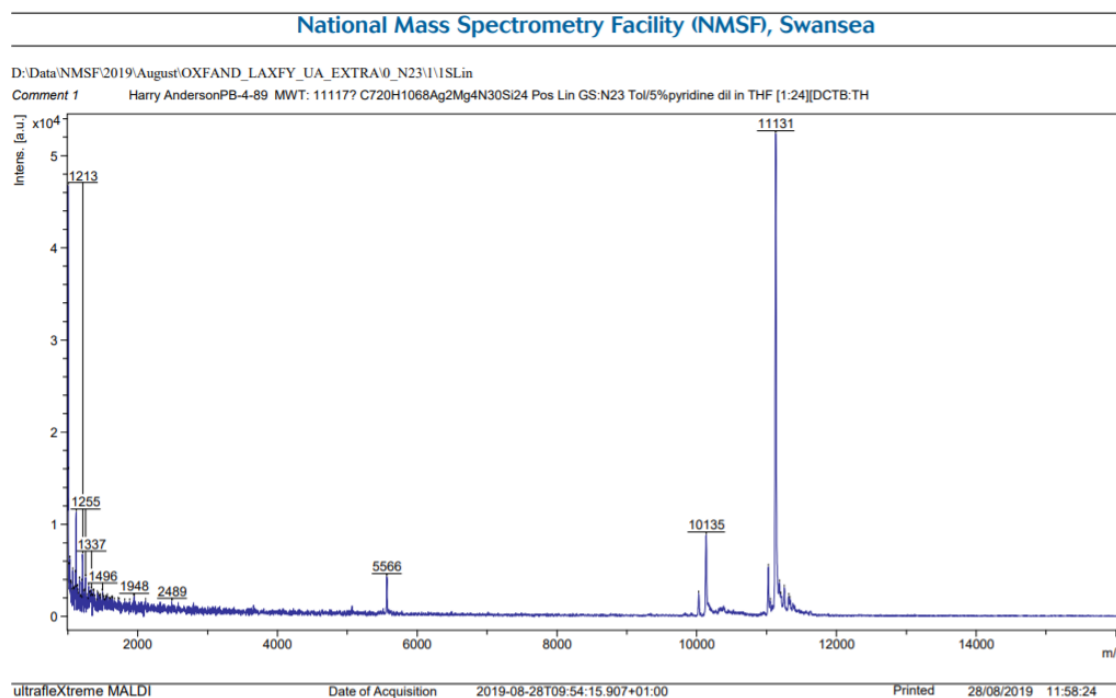


Figure 2.48. a) The MALDI-MS spectrum of **1,4-Ag₂Mg₄-P6·T6**, matrix: DCTB. M⁺, C₇₂₀H₁₀₆₈Ag₂Mg₄N₃₀Si₂₄ requires 11131.

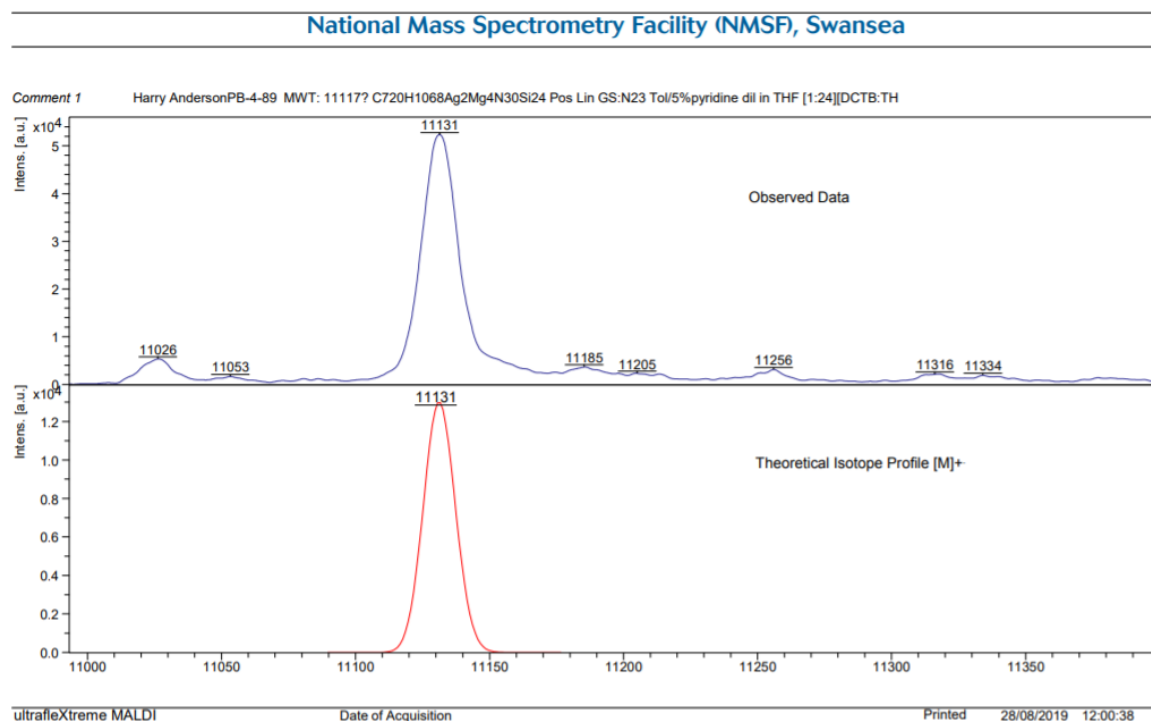


Figure 2.49. Zoom of the MALDI-MS spectrum of **1,4-Ag₂Mg₄-P6·T6** compared with the predicted isotope profile.

T3c

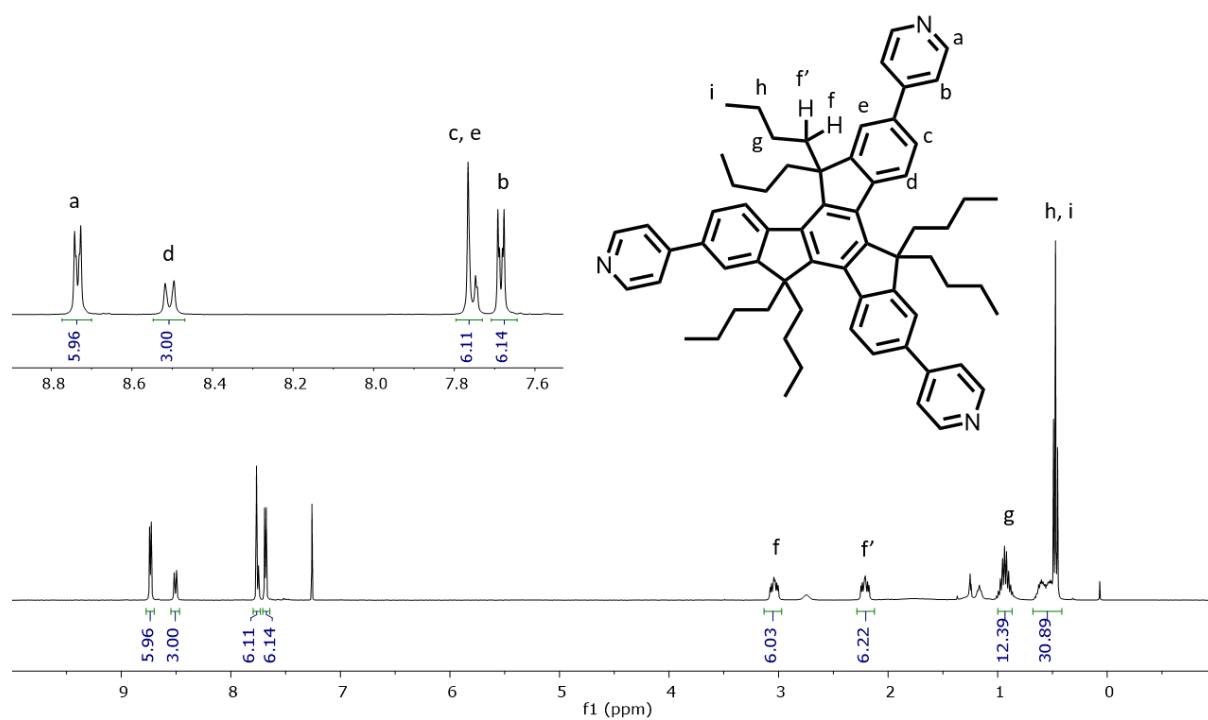


Figure 2.50. The ^1H NMR spectrum of **T3c** (400 MHz, CDCl_3 , 298 K).

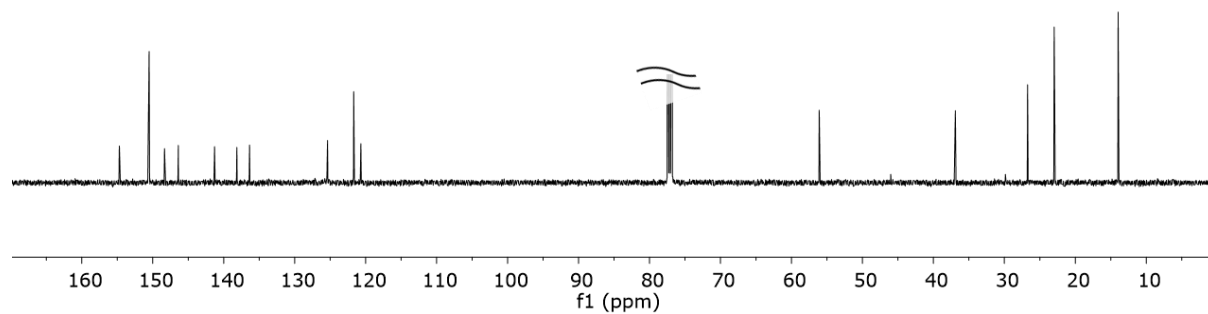


Figure 2.51. The ^{13}C NMR spectrum of **T3c** (126 MHz, CDCl_3 , 298 K).

T2

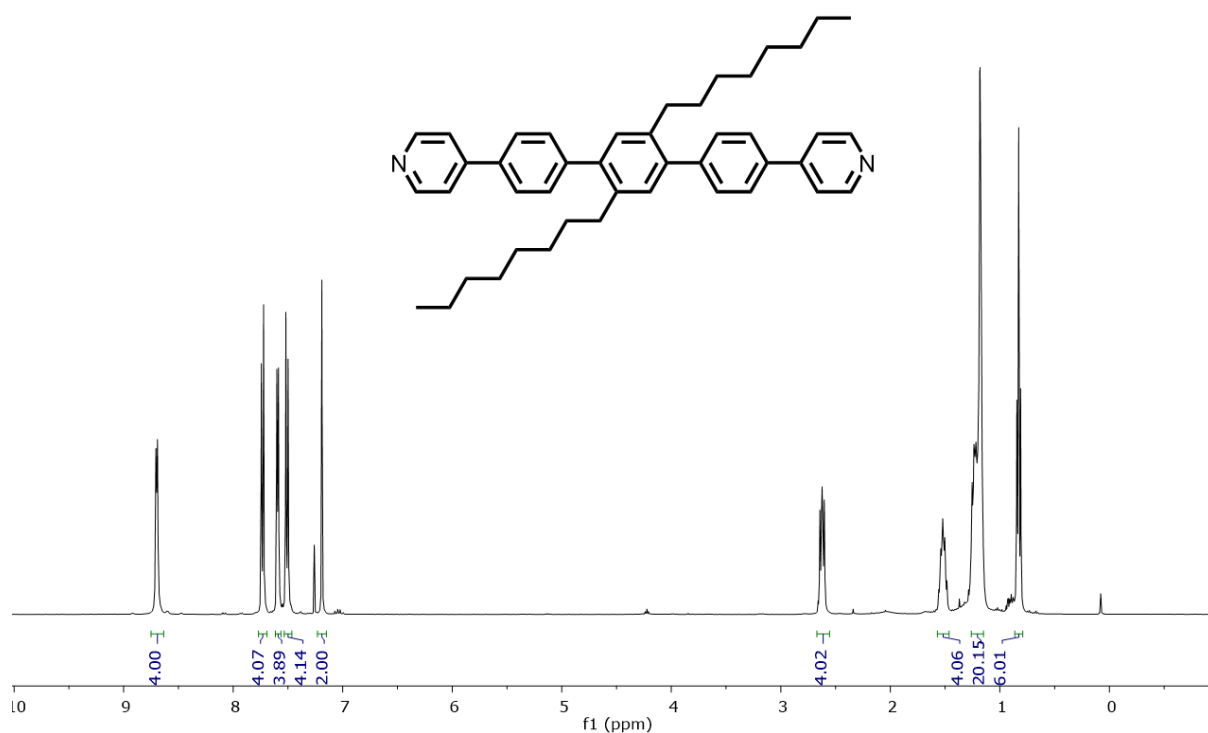


Figure 2.52. The ¹H NMR spectrum of **T2** (400 MHz, CDCl₃, 298 K).

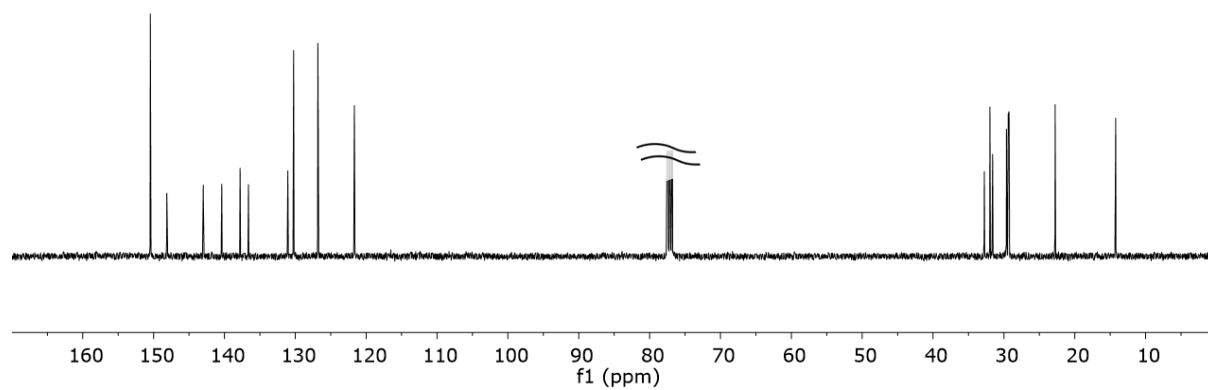


Figure 2.53. The ¹³C NMR spectrum of **T2** (101 MHz, CDCl₃, 298 K).

T3b

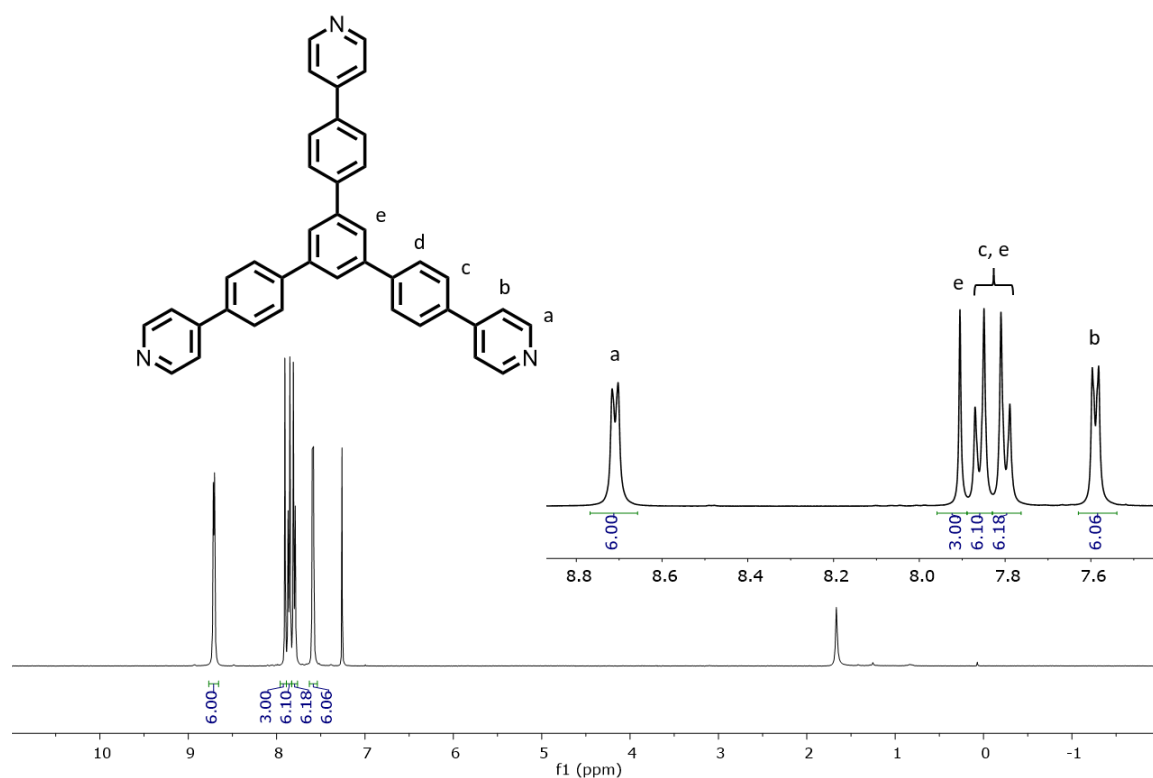


Figure 2.54. The ^1H NMR spectrum of **T3b** (400 MHz, CDCl_3 , 298 K).

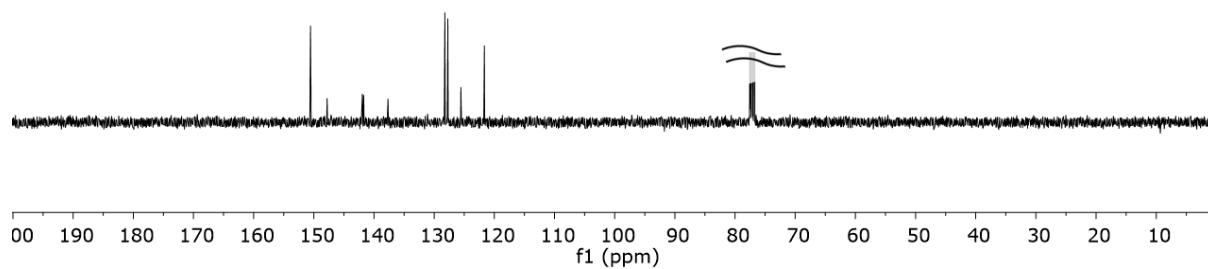


Figure 2.55. The ^{13}C NMR spectrum of **T3b** (101 MHz, CDCl_3 , 298 K).

T4c

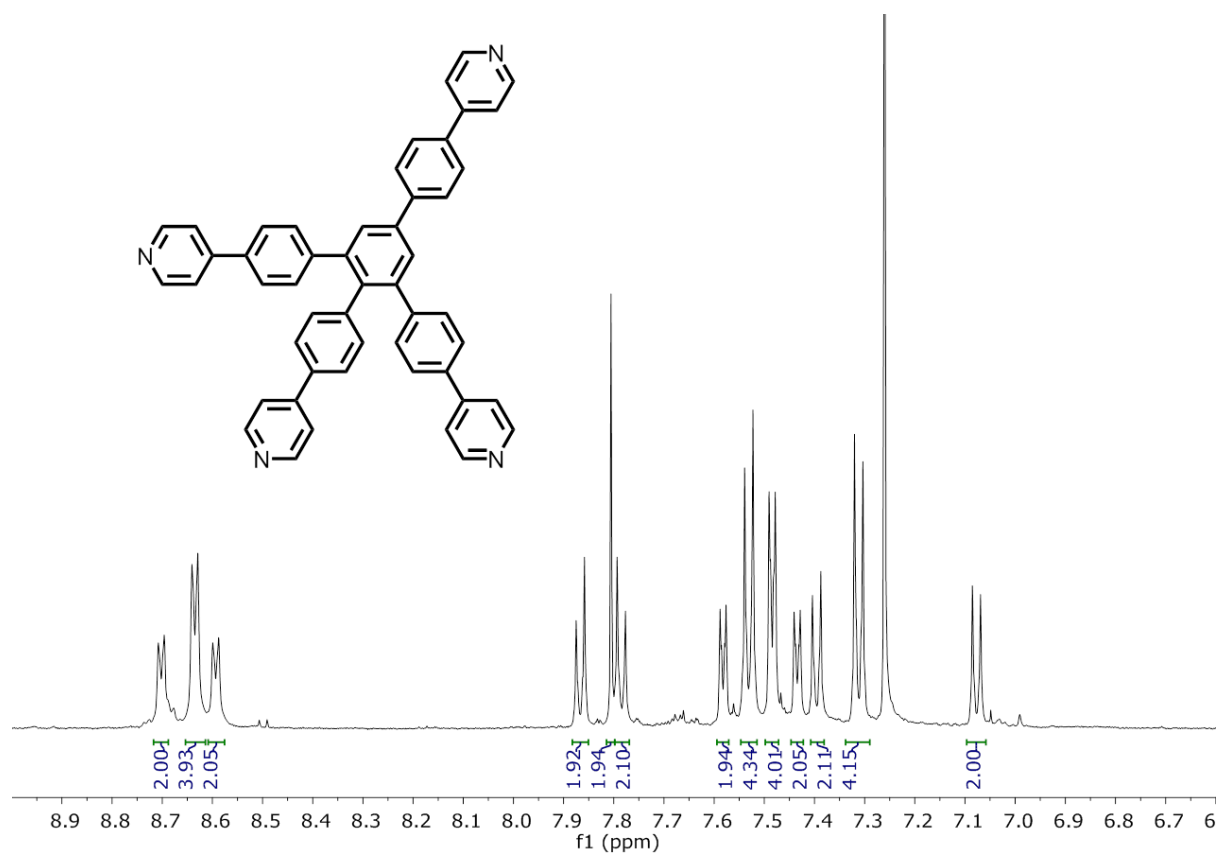


Figure 2.56. The ^1H NMR spectrum of **T4c** (400 MHz, CDCl_3 , 298 K).

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3

Quantum interference in porphyrin nanorings

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3.1 Abstract

The exchange interaction, J , between two spin centers is a convenient measure of through bond electronic communication. Here, we investigate quantum interference phenomena in bis-copper and bis-silver six-porphyrin nanorings by electron paramagnetic resonance spectroscopy via measurement of the exchange coupling between the paramagnetic centers. Using orientationally selective DEER and RIDME, we investigate how various factors affect the exchange coupling between two spin centers in a porphyrin nanoring. All the CW and pulsed EPR experiments were designed and carried out by Dr Alice M. Bowen. Dr Bowen also performed the simulations and analyses and drew the main conclusions from the EPR experiments. Dr Bowen kindly taught me about the theory behind the design of each experiment, let me run some of the experiments myself under her supervision, and helped me with writing this chapter. Together we determined which compounds to synthesize and study.

3.2 Introduction

3.2.1 Quantum interference

When electrons tunnel between two electrodes through a molecule with two parallel pathways, the wavefunctions can be in-phase or out-of-phase with each other leading to constructive or destructive quantum interference. It has been suggested that these effects contribute towards the efficiency of electron transfer in biological systems, often over distances of several nanometers.¹⁻³ In molecular electronics a key goal is to find molecules that facilitate efficient charge transport over long distances, but this is difficult as conductivity decreases dramatically the longer the wires.⁴ Quantum interference could be a tool to making highly conductive wires, effective insulators or sensitive transistors.^{5,6} The simplest test for quantum interference is to compare transmission between two points, A and B, through two identical channels in parallel, each of conductance G_1 , with that through just one isolated channel as shown in Figure 3.1. A classical system is expected to yield $G_{AB} = 2G_1$, while a quantum coherent system should give a total conductance of $G_{AB} = 4G_1$.^{7,8}

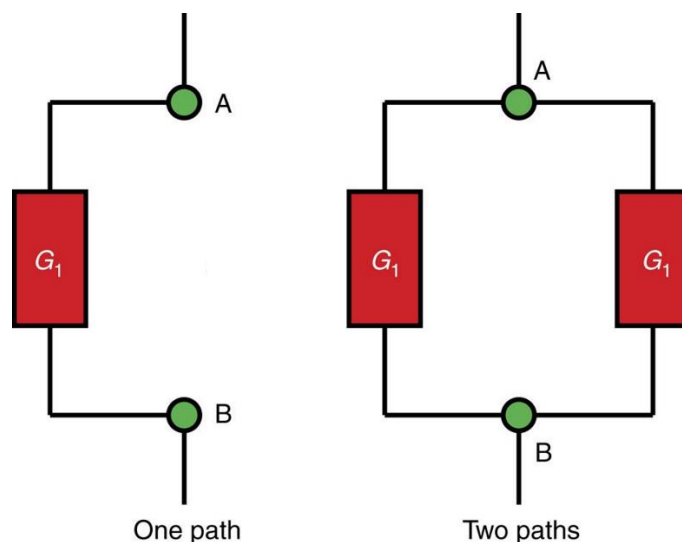


Figure 3.1. Schematic illustration of transmission through one or two pathways between points A and B.⁹

Gourdon and co-workers calculated the metal-metal coupling (V_{ab}) in the three isomers of diferrocenylbenzene using Hush's equations and found that the values are much higher for the *ortho* and *para* isomers than for the *meta* isomer. The weak interaction in the *meta* isomer was ultimately traced to destructive quantum interference effects through a cancellation of the contributions of the two electron transfer paths.¹⁰ More recently, destructive quantum interference was used to suppress coherent transmission across a molecular junction via the σ -bonds of a bicyclic silane.¹¹

Constructive quantum interference has been tested experimentally for charge transport through single molecules. STM break-junction measurements on a thioether-linked cyclophane with a pathlength of 0.7 nm gave the result $G_{AB} \approx 2.8 G_1$, providing evidence for quantum interference.¹² In another study it was demonstrated that a two-pathway α -graphyne had a conductance 40 times higher than the equivalent one-pathway system when positioned in an STM break junction. This could be attributed to constructive quantum interference but separating interference effects from effects of conformational rigidity and aromaticity in the system is not a trivial task.¹³

Despite these advances, it is still very hard to measure and confirm quantum interference in conductance of single molecules, partly because there are big uncertainties associated with the measuring techniques. In large molecules it is even more challenging because the signal

transmission is too weak to be measured with high accuracy. A solution to this problem is to use electron paramagnetic resonance (EPR) spectroscopy where the coupling between electronic spin centers can be measured with high accuracy and the exchange coupling J is closely related to the transmission G . This principle has been used to measure constructive quantum interference in a bis-copper porphyrin nanoring over a remarkably long distance of 3.9 nm (Figure 3.2).⁹

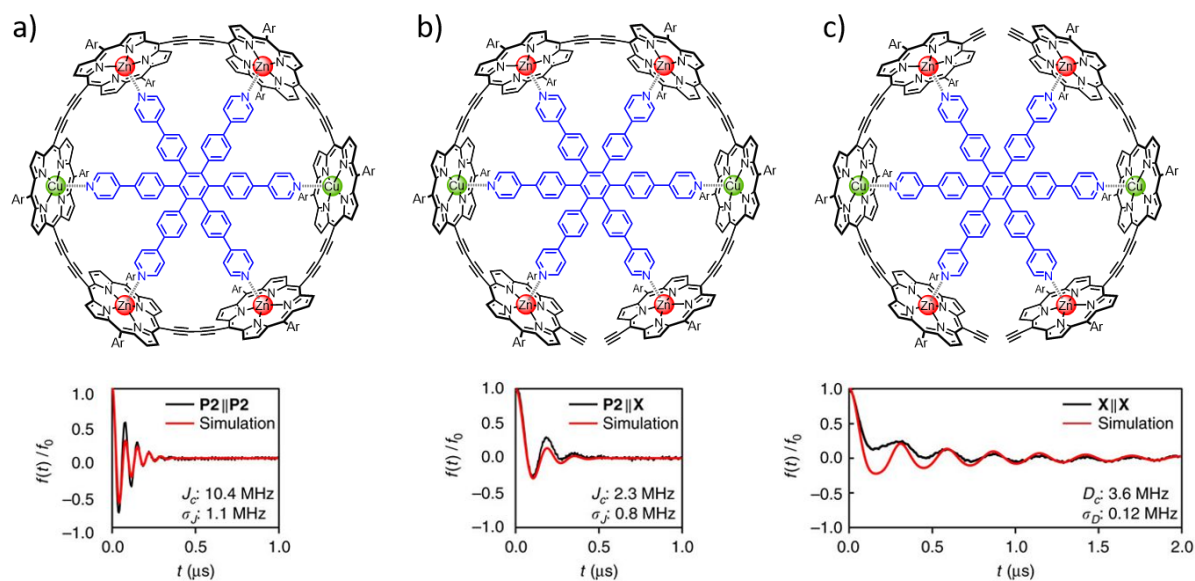


Figure 3.2. The three systems investigated in reference 9: a) the symmetric bis-copper porphyrin nanoring showing constructive quantum interference, b) the linear hexamer reference compound for measuring the coupling through one pathway, and c) the reference compound without any covalent connection between the copper centers, used to measure the dipolar coupling selectively.⁹

3.2.2 Electron paramagnetic resonance (EPR)

EPR is a technique that probes the interactions of electron spins with an external magnetic field and their couplings to other electron and nuclear spins. Pulsed and continuous wave EPR methods can be used to investigate the spin dynamics and electronic structure of a wide range of paramagnetic systems, including organic radicals, triplet states, and metal ions.¹⁴⁻¹⁶

Double electron-electron resonance (DEER) and relaxation induced dipolar modulation enhancement (RIDME) are pulsed EPR techniques used to measure the strength of the coupling between two electron spins.¹⁷⁻¹⁹ This coupling can consist of a through-space dipolar

contribution, D , and a through-bond exchange contribution, J . The dipolar coupling D can be used to give a measure of the relative spatial arrangement of the two electronic spin centers. This is used in structural studies of large biomolecules. The exchange coupling, J , provides information about the coupling through bonds which is determined by electron delocalization and orbital overlap. If the dipolar coupling D can be predicted using suitable reference systems or models, or alternatively silenced by fast tumbling or rotation of the molecules, the exchange coupling J can be quantified.

If pulsed EPR is performed on a frozen solution, the molecules within the sample will be fixed in different orientations with respect to the external magnetic field. When this is combined with the g -tensor and/or hyperfine anisotropy present in many spin active transition metals, this gives rise to the fact that electronic environments in molecules with different orientations have slightly different excitation energies, which means that the experiments can be performed with orientational selectivity.²⁰ This technique combined with the afore mentioned DEER and RIDME experiments, has been utilized in this work to determine with high certainty the relative signs of the dipolar coupling, D , and the exchange coupling, J , interactions.

For the molecules described in this chapter, there is no a-priori knowledge on the relative signs of D and J . Therefore, both positive and negative values of J , with respect to a positive D , have been simulated throughout this study.

3.3 Project aim

Building on the exciting discovery that there was constructive quantum interference over 3.9 nm in a bis-copper(II) porphyrin nanoring,⁹ this chapter will aim to use EPR to further investigate the nature of interference effects in these systems. We will look at different factors that may affect the coupling such as varying the spin-active metal and varying the chemical structure of the connecting pathways. With shadow mask templates and selective demetallation described in Chapter 2, these structures are now readily accessible in high yields. Figure 3.3 shows all the different compounds investigated in this chapter.

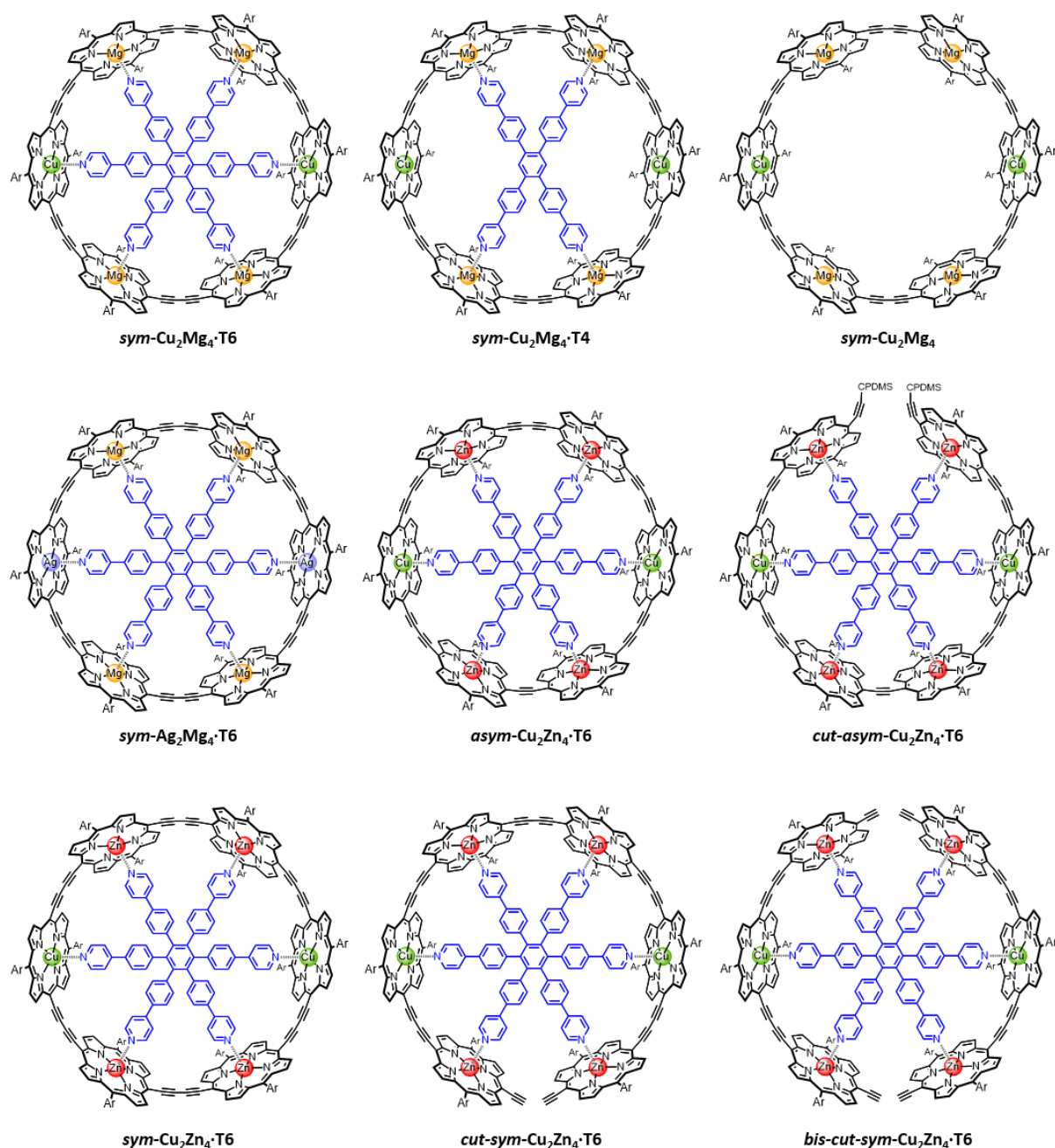


Figure 3.3. Schematic diagrams for all the systems investigated this chapter. In order to make it easier to understand, the nomenclature from Chapter 2 has been changed to put focus on symmetry and metals. ***sym*-Cu₂Zn₄·T6**, ***cut-sym*-Cu₂Zn₄·T6**, and ***bis-cut-sym*-Cu₂Zn₄·T6**, were prepared by Dr Jonathan Cremers.⁹ ‘*sym*’ refers to the nanorings where both connections have butadiyne linkers – or the equivalent broken system. ‘*asym*’ refers to the nanorings where one side has a butadiyne linker and one side has a single acetylene linker – or the equivalent broken system.

3.4 Experimental preparations and procedures for EPR experiments

Unless stated otherwise, all samples were prepared as 0.2 mM solutions in deuterated toluene and were degassed by two freeze-pump-thaw cycles. The solutions were then transferred to 1.6 mm diameter quartz Q-band EPR tubes and flash frozen with liquid nitrogen for the measurements.

CW EPR measurements at X-band (9.5 GHz microwave frequency, 0.35 T magnetic field) were carried out by Dr Alice M. Bowen at CAESR in Oxford. The spectra were recorded on Bruker EMXMicro spectrometer fitted with an Oxford Instruments E900 gas flow cryostat and an ITC temperature controller, which enabled the temperature to be maintained at 100 K. The 1.6 mm Q-band tube was placed in a 4 mm diameter quartz tube. The K- and Q-band CW measurements were carried out by Dr Alice M. Bowen using the EPSRC National Service for Electron Paramagnetic Resonance Spectroscopy at The University of Manchester, as CAESR has no K-band facility and the Q-band spectrometer was under repair.

Pulsed EPR measurements were carried out by Dr Alice M. Bowen at Q-band on a Bruker Elexys E580 spectrometer equipped with a Q-band-D2 resonator. The temperature was maintained at 15 K using a CF935 Oxford Instruments helium flow cryostat. All pulses were formed using an arbitrary waveform generator (AWG). The 4-pulse DEER sequence²¹ was used with all detection pulses having length 16 ns and the pulse having length 12 ns. The pump and detection frequencies were separated by 100 MHz. An 8-step τ -averaging cycle and a 16-step phase cycle was used to cancel unwanted echos and ESEEM (Electron Spin Echo Envelope Modulation). The 5-pulse RIDME sequence²² was used with the $\pi/2$ and π pulses having lengths 4 ns and 8 ns respectively. An 8-step phase cycle and two 8-step τ -averaging cycles were used to remove unwanted echoes and ESEEM.

In order to quantify the sign and size of the exchange coupling, J , it is necessary to know the value of the dipolar coupling D . The size and distribution in D were found by generating a geometric model of the system based on the X-ray crystal structure and fitting the model to the experimental data for double cut system. This provided a very similar result to the distribution in D as found by Richert et al.⁹ for the reference compound in reference 12 (Figure 3.2), since they have the same geometry.

Dr Alice M. Bowen performed all the simulations and analyses of the EPR experiments. The CW spectra were simulated using the MATLAB toolbox EasySpin²³ and the simulations of exchange couplings were performed using a home-written MATLAB based simulation program written as part of this work by Dr Alice Bowen and based on the algorithm for orientation dependent DEER simulations published here.²⁴

3.5 Effect of the spin-inactive metal

The first thing investigated was the effect of having magnesium porphyrins as the parallel pathways instead of zinc porphyrins as in the original study. To determine this effect, we compared **sym-Cu₂Mg₄·T6** with the previously published **sym-Cu₂Zn₄·T6**.⁹

The use of magnesium in place of zinc in the ring facilitates the use of *shadow mask templates* described in Chapter 2. Neither magnesium nor zinc is spin active in the 2+ oxidation state and will therefore not contribute to the EPR spectrum directly.

The echo detected field sweep of the template-bound nanoring **sym-Cu₂Mg₄·T6** is shown in Figure 3.4. Within this spectrum the field positions at the far right correspond to molecules oriented with the xy-plane of the *g*-tensor aligning parallel to the external field, and the field positions at the far left correspond to the molecules oriented where the z-axis of the *g*-tensor is parallel with the external field. The four features on the left of the Cu(II) EPR spectrum in Figure 3.4. are due to the hyperfine coupling of the unpaired electron to the copper nucleus which has $I = 3/2$. This hyperfine coupling is stronger (larger) in the z-orientation than in the xy-plane, and thus it is not resolved at the right of the spectrum. In both Cu(II) and Ag(II) porphyrins the z-axis of the *g*-tensor is perpendicular to the plane of the porphyrin. In order to analyze the orientation selective dipolar EPR experiments it is necessary to record the dipolar EPR experiments exciting different orientation populations of molecules as cleanly as possible. However, for the z-position, the EPR signal is of low intensity when the pulses excite at the far left of the spectrum. Therefore, it was necessary to compromise and instead experiments were performed at the field positions indicated as A, B, and C in Figure 3.4.

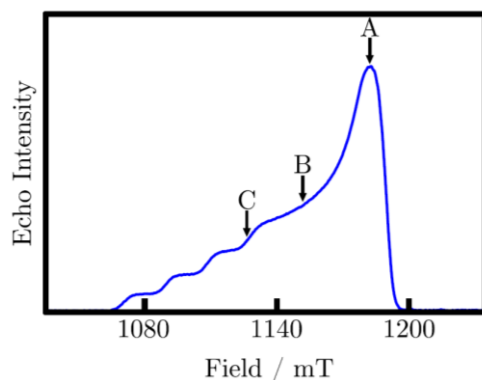


Figure 3.4. The echo detected field sweep of ***sym*-Cu₂Mg₄·T6**.

DEER and RIDME traces of ***sym*-Cu₂Mg₄·T6** are shown in Figure 3.5 together with the simulated traces for a positive and a negative J -value respectively.

It is possible to generate reasonable fits with both positive and negative values of J for DEER and RIDME traces taken at position A. For this reason, RIDME traces were recorded at lower field positions to determine the sign of the exchange coupling. While the amplitudes of the oscillations are not well simulated for the RIDME data, simulations at lower field positions are worse for negative values of J than for positive. Additionally, looking at the average value of J used in each of the fits, the averages and spreads of the positive values of J are more closely clustered. As it is expected that the value and spread in J should not be dependent on the orientation, it can be concluded that J is positive in ***sym*-Cu₂Mg₄·T6** as it was in ***sym*-Cu₂Zn₄·T6**. This means that the coupling between the Cu^{II} centers is antiferromagnetic. Furthermore, the exchange coupling in ***sym*-Cu₂Mg₄·T6** ($J \approx 11.0$ MHz) is found to be slightly larger than that in ***sym*-Cu₂Zn₄·T6** ($J \approx 10.4$ MHz) by both DEER and RIDME techniques at all field positions analyzed.

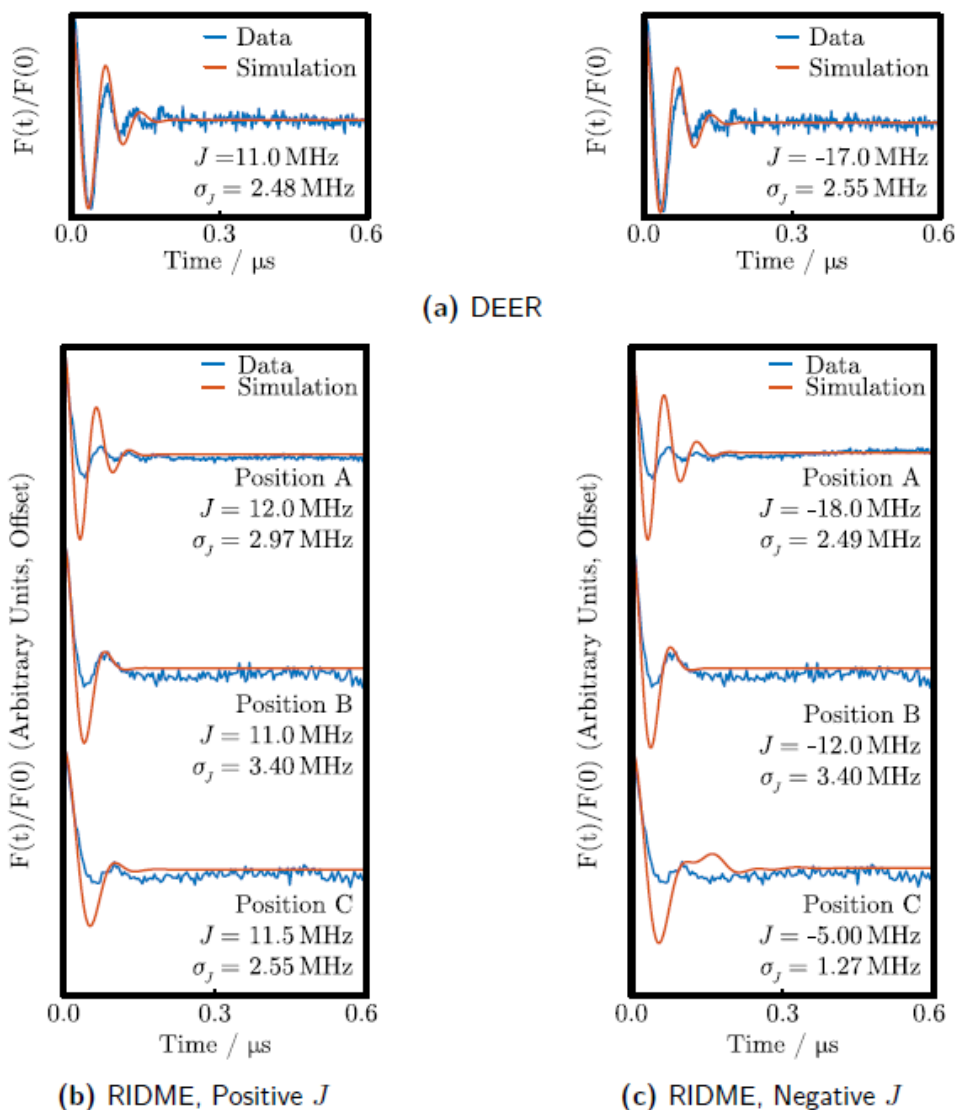


Figure 3.5. (a) The DEER trace of **sym-Cu₂Mg₄·T6** fitted with positive and negative J . (b) and (c) depict RIDME traces taken on **sym-Cu₂Mg₄·T6** fitted with positive and negative J respectively, at field positions A, B and C.

One potential explanation for this increase in J when going from **sym-Cu₂Zn₄·T6** to **sym-Cu₂Mg₄·T6** could be that changing the metals causes a change in the molecular geometry of the bridging porphyrins. Another explanation could be that the increase in J is due to electronic effects. This could suggest that the magnesium-porphyrin bond has more ionic character than the zinc-porphyrin bond, resulting in more electron density in the porphyrin ring when the central ion is magnesium than when it is zinc. As such, there might be more electron density along the exchange coupling pathways in **sym-Cu₂Mg₄·T6** compared to **sym-Cu₂Zn₄·T6**, which could be the cause of the observed increase in J .

3.6 Effect of structural rigidity

Having the **T6** template coordinated in the nanoring fixes the porphyrins and the π -systems that connect them in a specific rigid conformation. This is observed by UV-vis spectroscopy, where coordination of the template sharpens and gives significant fine structure to the UV-vis absorption spectrum. We wanted to explore how dependent the measurable quantum interference effects are on this conformational rigidity. To do this, we measured DEER and RIDME on **sym-Cu₂Mg₄·T6**, **sym-Cu₂Mg₄·T4a**, and **sym-Cu₂Mg₄**. The traces from field position A are shown in Figure 3.6.

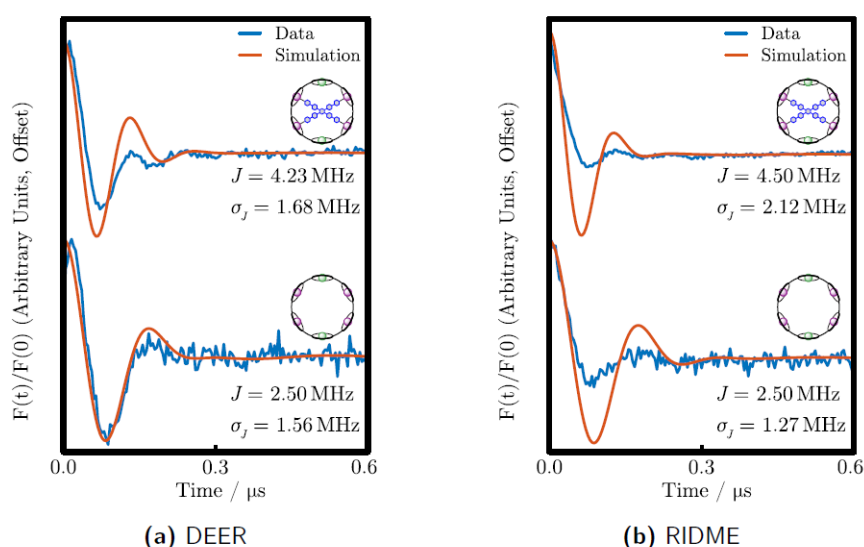


Figure 3.6. (a) DEER traces and (b) RIDME traces of **sym-Cu₂Mg₄·T4a** and **sym-Cu₂Mg₄** taken at position A and fitted with positive J .

These simulations used the same distribution in positions and orientations of the copper centers and thus the same model for calculating the dipolar contributions. Under these conditions, the simulated exchange coupling distributions for these systems show that the magnitude of J is dependent on molecular flexibility. By DEER, the J values are: 4.2 MHz for **1,4-Cu₂Mg₄-c-P6·T4a** and 2.5 MHz for **1,4-Cu₂Mg₄-c-P6**, compared with 11.0 MHz for **1,4-Cu₂Mg₄-c-P6·T6**. The magnitude of J is roughly halving when changing from **T6** to **T4a**, and then almost halved again upon complete removal of the template.

As a first approximation, we assumed that the distance and orientational distribution between the two copper centers is not significantly changed by the presence or type of template used.

The equilibrium distance between the copper porphyrins is predicted by DFT to be 2.54 nm, 2.64 nm, and 2.67 nm for **T6**, **T4a**, and template-free systems, respectively. When converting this to a purely dipolar frequency this gives values of 3.34 MHz, 2.97 MHz and 2.87 MHz, when orientation selection is ignored but considering the perpendicular g -value of the copper. As the changes in these values of the dipolar component are very small compared to the changes in the values of J found for the three systems we can conclude that the changes observed in the DEER experimental traces cannot purely be a result of changes in the dipolar coupling but must be a result of changes in the exchange coupling efficiency.

In butadiyne-linked porphyrin oligomers, there is effectively free rotation around the linker (the barrier to rotation has been determined to be 1 kcal mol⁻¹).²⁵ In the absence of a template binding to a metal center of a porphyrin in the ring, it is expected that the porphyrin will exhibit greater rotational freedom about the ring axis. Resulting in a larger relative orientation distribution of the two copper porphyrins relative to one another. This will lead to a larger spread in the dipolar frequencies contributing to the trace and may cause a dampening of the observed oscillations. The exact degree to which this dampening effect will occur depends on the flexibility of the system which is difficult to predict and thus it is difficult to disentangle this effect from the changes in the size and distribution of J also observed. It may be possible to investigate this further using neural networks such as DEERnet to deconvolute the effect of the increased orientational distributions from the changes in the exchange interaction.²⁶

Despite the uncertainties in modelling the data and thus in the precise values and spreads of the exchange coupling extracted, it can clearly be seen that the trend is: as the porphyrin rings gain more rotational freedom, the DEER and RIDME data show a decrease in the magnitude of the exchange coupling. One explanation for this is that as the rings rotate, π -bonding between the porphyrins and the butadiyne linkers is disrupted. This would increase the ‘resistance’ of the exchange coupling pathways, and lead to the decrease in exchange coupling observed. This confirms previous findings,²⁷ where DFT was used to predict the effect of rotation around a butadiyne linker on the exchange coupling between two copper porphyrins.

3.7 Comparison of silver(II) and copper(II) porphyrin nanorings

3.7.1 Motivation

After having investigated the effect of linker-metals and structural rigidity, we went on to study the effect of changing the spin-active metals in the nanoring. In copper(II) porphyrins, the spin-active electron is located in the $3d_{x^2-y^2}$ orbital, which is in the plane of the porphyrin, whereas in silver(II) porphyrins, the electron is located in the $4d_{x^2-y^2}$ which has the same symmetry but is different in other ways. An EPR study comparing copper(II) and silver(II) porphyrins showed that the hyperfine coupling to the nitrogen atoms in the porphyrin ring increases by about 40% compared to that found in the copper(II) porphyrin.²⁸ This is presumably a result of an increased delocalization of the spin density away from the metal. This study also included an interesting analysis of the mixing of the σ and π character of the unpaired spin on the nitrogen atoms and it was calculated that the π spin density was 20% of the σ spin-density for copper(II) and 10% of the σ spin density for silver(II). The unpaired electron on silver(II) thus has less π -character than the electron on copper(II), so the spin should mix less with the porphyrin π -system. With these two contradicting effects, it was not possible to predict whether the J -coupling will be stronger or weaker in the silver-system compared to the corresponding copper-system. As such, we can use a porphyrin nanoring with two silver(II) atoms to investigate which effect is stronger when we compare it to the equivalent copper(II) system.

In Chapter 2 it was described how shadow mask templates was used to synthesize the bis-silver porphyrin nanoring **sym-Ag₂Mg₄T6**, and this section will describe the EPR studies that were done on these systems.

3.7.2 Field sweep

The field sweep of **sym-Ag₂Mg₄T6** is shown in Figure 3.7. As in the field sweep of the copper systems (Figure 3.4), the field positions at the far right correspond to the silver porphyrin moieties oriented with the xy -plane of the silver g -tensor parallel to the external field (xy -position), and the position at the far left corresponds to the silver porphyrin moieties oriented with the z -axis of the silver g -tensor parallel to the external field (z -position). We investigated DEER traces recorded at five positions across the spectrum to get a wide picture for the analysis.

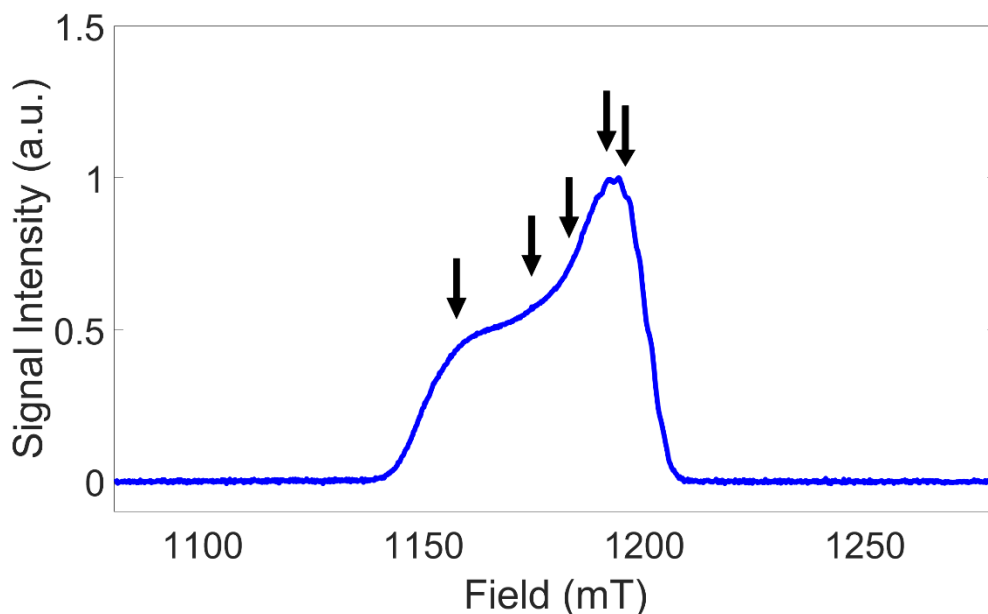


Figure 3.7. The echo detected field sweep at the detection frequencies used for the DEER traces recorded for ***sym-Ag₂Mg₄T6***, the five arrows represent the detection fields used in the DEER experiments displayed in Figure 3.10.

3.7.3 Continuous wave spectra

In order to confirm the presence of silver(II) in the system, continuous wave (CW) EPR was performed. This is also necessary in order to determine the g -factor needed to correct for the distribution of D when fitting the DEER data. The CW spectra of ***sym-Ag₂Mg₄T6*** are shown in Figure 3.8 for X-band, K-band and Q-band. The parameters gained from fitting these spectra were used in the modeling and fitting of the DEER data.

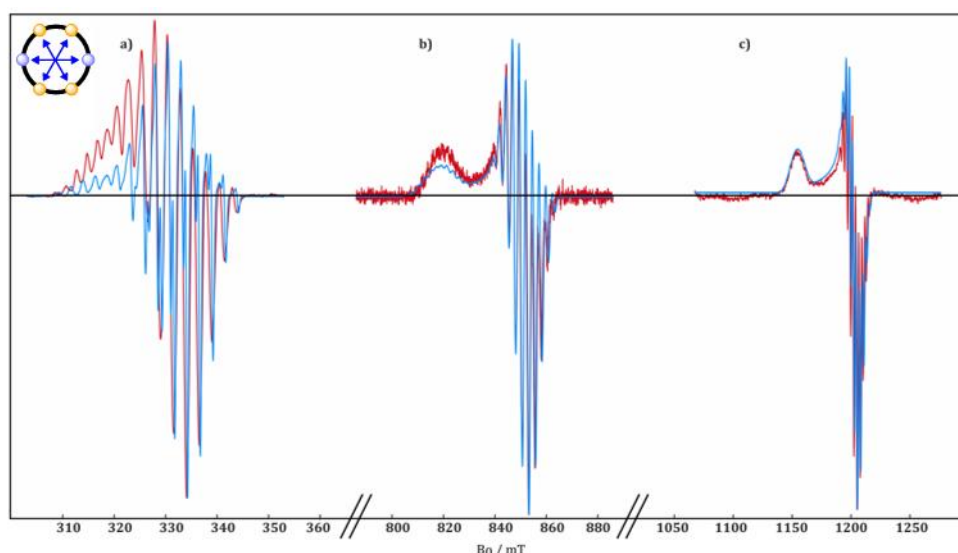


Figure 3.8. Continuous wave EPR spectra (red line) and simulated fit (blue line) for **sym-Ag₂Mg₄·T6**, measured at (a) X-band, (9.5 MHz) (b) K-band (24 MHz) and (c) Q-band (34 MHz)

3.7.4 Iterative procedure for analysis

The analysis previously carried out by Richert et al. on **sym-Cu₂Zn₄·T6** utilized a Gaussian distribution in both D and J .⁹ However, there is no physical constraint for J to be distributed in this way. Additionally the fitting procedure used by Richert et al. did not consider any orientation dependence of the dipolar contribution to the measured traces – this lead to an initial uncertainty in the relative signs of J and D , although the relative signs of these two parameters was determined in the original work by comparison of the goodness of fit for the two possible regimes. However, this assignment of signs, and the relative size and spread in J determined by the fit meant that three parameters were being determined from a fit to a single trace which could result in local minima in the fitting regime. Therefore, we adopted a new iterative procedure developed by Dr Alice M. Bowen based upon ideas developed by Marko et al.²⁹ for fitting distributions of distances and orientations (D) to orientation dependent DEER traces. Here we used this methodology to analyze the orientationally selective DEER data using multiple traces. A fixed distribution in the orientation and distance between centers derived from a model of the molecular system was used such that fitting a distribution of J , enabled the relative signs of D and J to be found and the distribution in J not to be confined to a Gaussian distribution.

The iterative procedure was tested on the known system **sym-Cu₂Zn₄·T6**, and the results are shown in Figure 3.9, where it can clearly be seen that using a positive value of J provides a better fit to the data set. While the distribution in J found from this procedure is not Gaussian in form it is possible to fit a normal Gaussian to the distribution to provide characteristic values of average J value and spread, σ_J . By fitting a normal Gaussian distribution, the average value of J in the positive fit was found to be 8.4 MHz with a broader distribution of 3.0 MHz in the iterative procedure, compared to 10.4 MHz and 1.1 MHz in the original work.⁹ The Gaussian describing the fit with negative J , has an average value of -9.8 MHz with a distribution of 5.2 MHz. The differences are likely a result of including the orientational dependence of D in the fitting procedure, and the fact that the distribution found by the new procedure is by design not gaussian. This new procedure was used to analyze the DEER data in the remainder of this chapter.

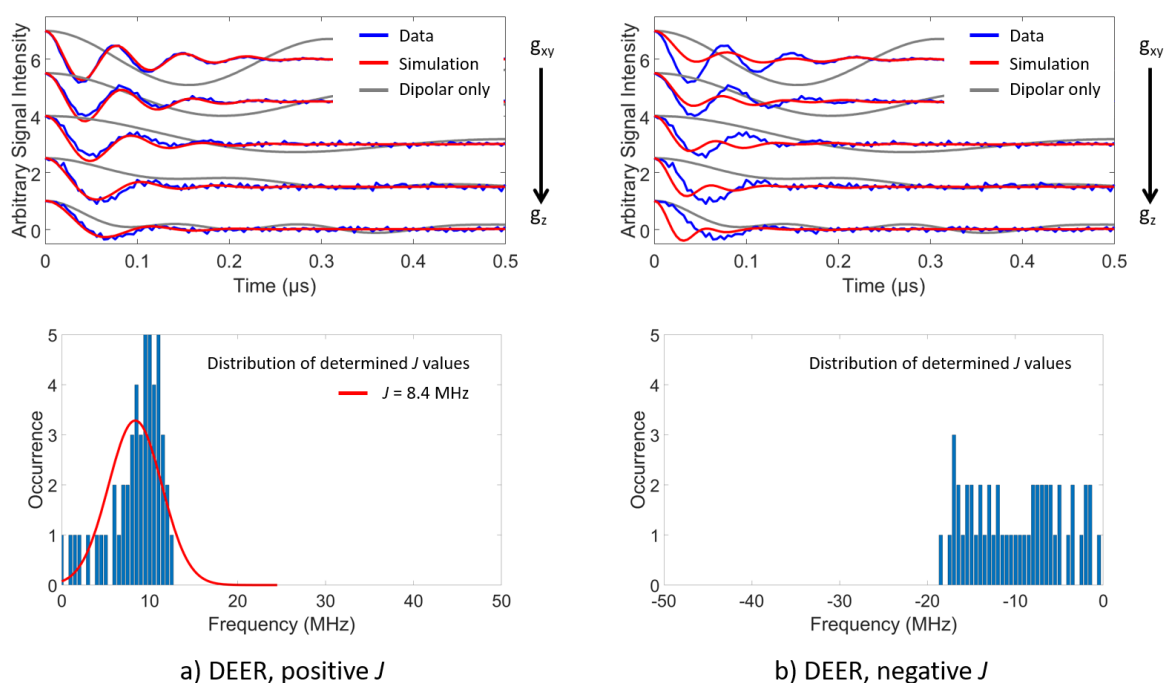


Figure 3.9. The DEER traces of **sym-Cu₂Zn₄·T6** at different field positions fitted with positive and negative J using the iterative approach. The histograms show the values of J used to generate the simulations shown in red. Fitting a normal Gaussian distribution to the positive results for J yields; $J = 8.4$ MHz, $\sigma_J = 3$ MHz. Fitting a normal Gaussian distribution to the negative results for J yields; $J = -9.8$ MHz, $\sigma_J = 5.2$ MHz. The fit using positive values of J provides a better fit to the experimental data.

3.7.5 Results and analysis of DEER measurements

The DEER traces for **sym-Ag₂Mg₄·T6** at different field positions are shown in Figure 3.10 fitted to a positive and negative J respectively. It is observed, that there is a very large spread in the values of J compared to both **sym-Cu₂Mg₄·T6** and **sym-Cu₂Zn₄·T6**. This could mean that there is more flexibility in the system which would disturb the conjugated π -system and cause many different J -values to be observed. However, it is seen that J is positive, which is particularly clear when looking at the fit to the DEER traces in the z-positions. The mean value of J when all the values in the histogram are taken into account was found to be 16.4 MHz with a spread of 11.5 MHz, which is significantly larger than the value found for **sym-Cu₂Mg₄·T6** using the same method (average of 9.2 MHz with a spread of 4.1 MHz). The best fit for negative J is significantly worse and a Gaussian fitted to the distribution generated is characterized by a mean value of -18.4 MHz and a spread of 9.9 MHz. It is nice to note that while the mean values and spreads found between the fitting procedure using a Gaussian distribution in J and using a free distribution in J are slightly different, the trend between **sym-Cu₂Mg₄·T6** and **sym-Cu₂Zn₄·T6** is preserved in that the magnesium system has a slightly higher average value of J with a larger spread.

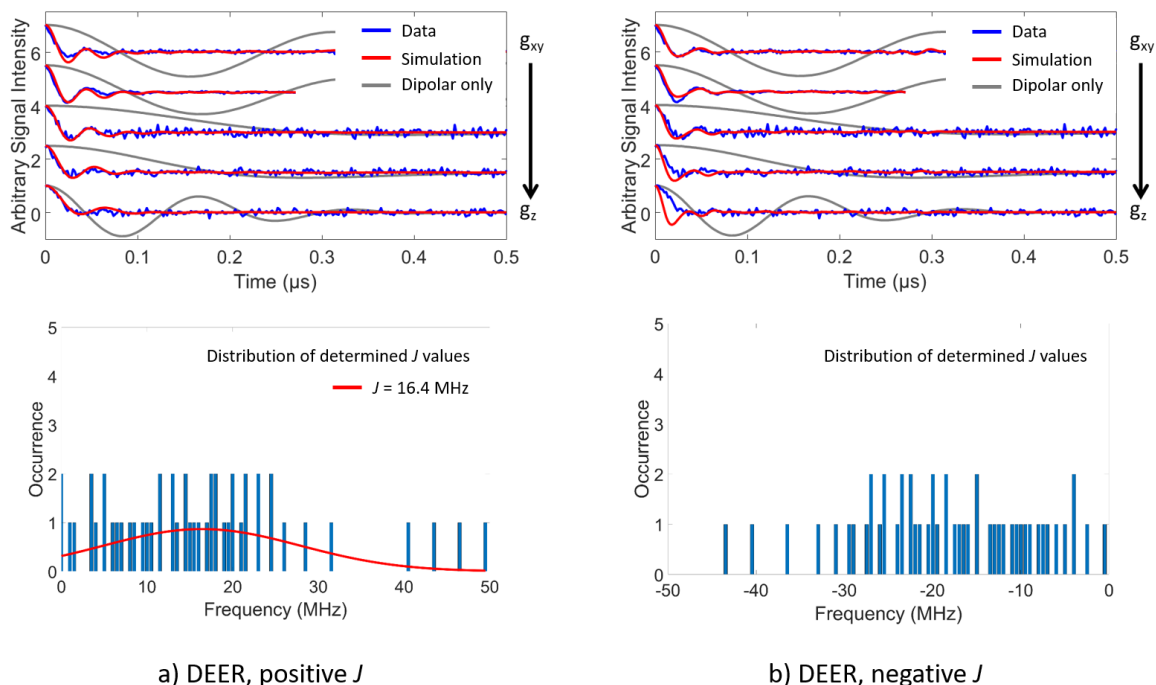


Figure 3.10. The DEER traces of **sym-Ag₂Mg₄·T6** at different field positions fitted with positive and negative J using the iterative approach. The histograms show the values of J .

Fitting a normal Gaussian distribution to the positive results for J yields; $J = 16.4$ MHz, $\sigma_J = 11.5$ MHz. Fitting a normal Gaussian distribution to the negative results for J yields; $J = -18.4$ MHz, $\sigma_J = 9.9$ MHz. The fit using positive values of J provides a better fit to the experimental data.

3.8 An asymmetric nanoring for destructive quantum interference

3.8.1 Motivation

Finally, we were interested to see whether changing the structure of the nanoring to create two inequivalent pathways would result in destructive quantum interference. This idea originated from a preliminary and unpublished computational study performed in the Colin Lambert group (Lancaster University, UK) on charge transport in porphyrin nanorings with two anchor groups and different types of pathways. According to the calculations, there would be a significant cancellation of charge transport in an asymmetric porphyrin nanoring where one of the pathways is shorter than the other one by one acetylene (Figure 3.11). This was interpreted as destructive quantum interference.

While conductance and electron spin coupling are not the same, they both involve electron tunneling and transmission is closely related to the exchange coupling J . Therefore, we hypothesized that the bis-copper(II) porphyrin nanoring with one single acetylene bridge in one of the pathways (Figure 3.11) would show destructive quantum interference in the exchange coupling J between the two copper(II) atoms in a pulse EPR experiment. Figure 3.11 also shows a singly cut model compound, which would be helpful in understanding the interference effects, in comparison to the single cut compound with all double acetylene linkers used in the original study.

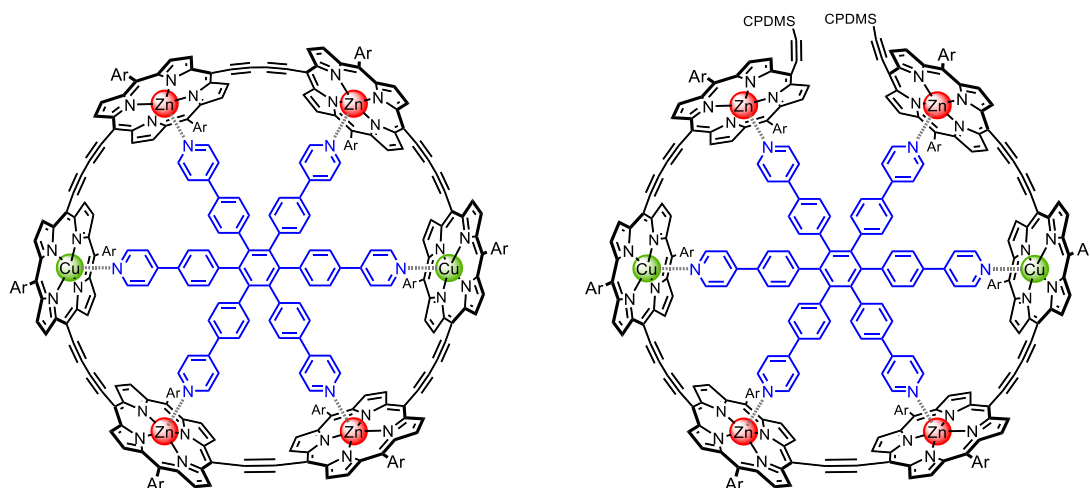


Figure 3.11. The asymmetric bis-copper(II) nanoring which we predict to show destructive quantum interference in a pulse EPR experiment, and the equivalent linear hexamer wrapped around **T6**, which we would predict to behave very similarly to the hexamer shown in Figure 3.2.

The study of pulse EPR couplings in this asymmetric bis-copper nanoring is advantageous because we expect it to have similar geometry to the symmetric bis-copper nanoring. This expectation is based on DFT calculations³⁰ on the equivalent symmetric and asymmetric nanorings where all the metals are zinc (Figure 3.12).

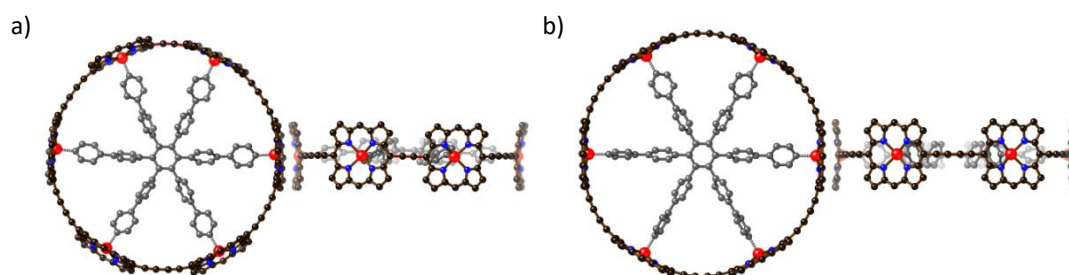


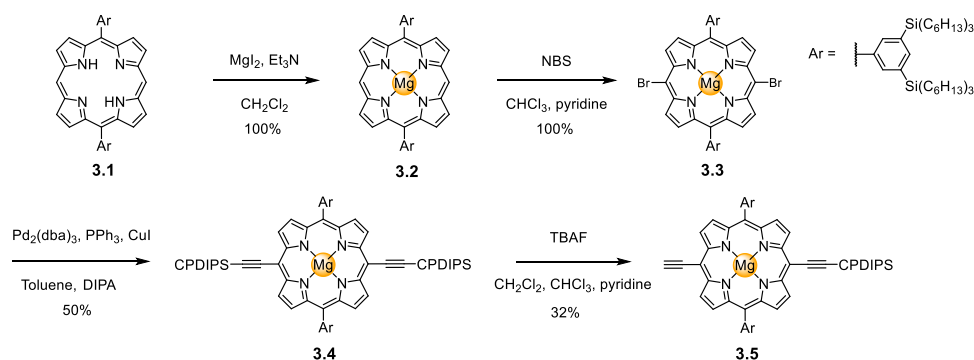
Figure 3.12. Calculated geometries of a) the asymmetric *asym*-**Zn₆•T6** and b) the symmetric *sym*-**Zn₆•T6**. Both are displayed from the top and from the side.

3.8.2 Synthesis of an asymmetric nanoring for pulsed EPR

The synthetic route follows closely the strategy developed for the synthesis of the equivalent nanoring with only zinc porphyrins.³⁰ The difference is introduction of magnesium centers that are substituted for copper after the ring-formation. The strength of introducing the copper

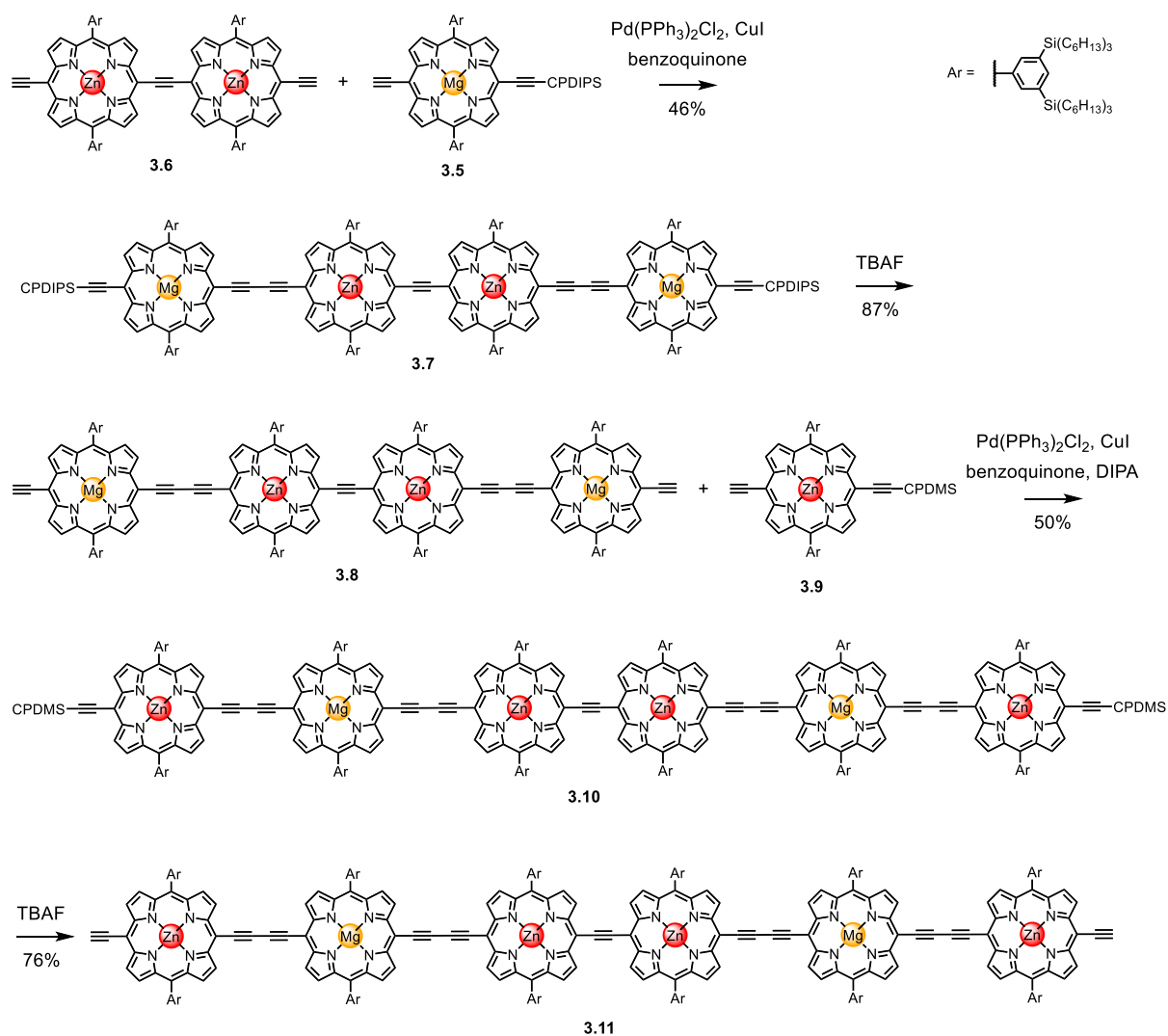
atoms late in the synthesis is that while copper coordinates weakly to the oligopyridine template and would cause low yields in the macrocyclisation,³¹ magnesium coordinates strongly and gives similar yields to zinc. Because magnesium porphyrins can be selectively demetallated in the presence of zinc porphyrins, as described in Chapter 2, the magnesium centers can conveniently be substituted for copper after the ring is formed.

The magnesium porphyrin monomer **3.2** was synthesized using magnesium iodide and triethylamine at room temperature as reported by Lindsey and Woodford.³² Bromination, substitution with CPDIPS-acetylene, and mono-deprotection of the acetylene was achieved using the same conditions as reported for the zinc-porphyrin equivalents to give the mono-deprotected magnesium monomer **3.5**.³³ (Scheme 3.1).



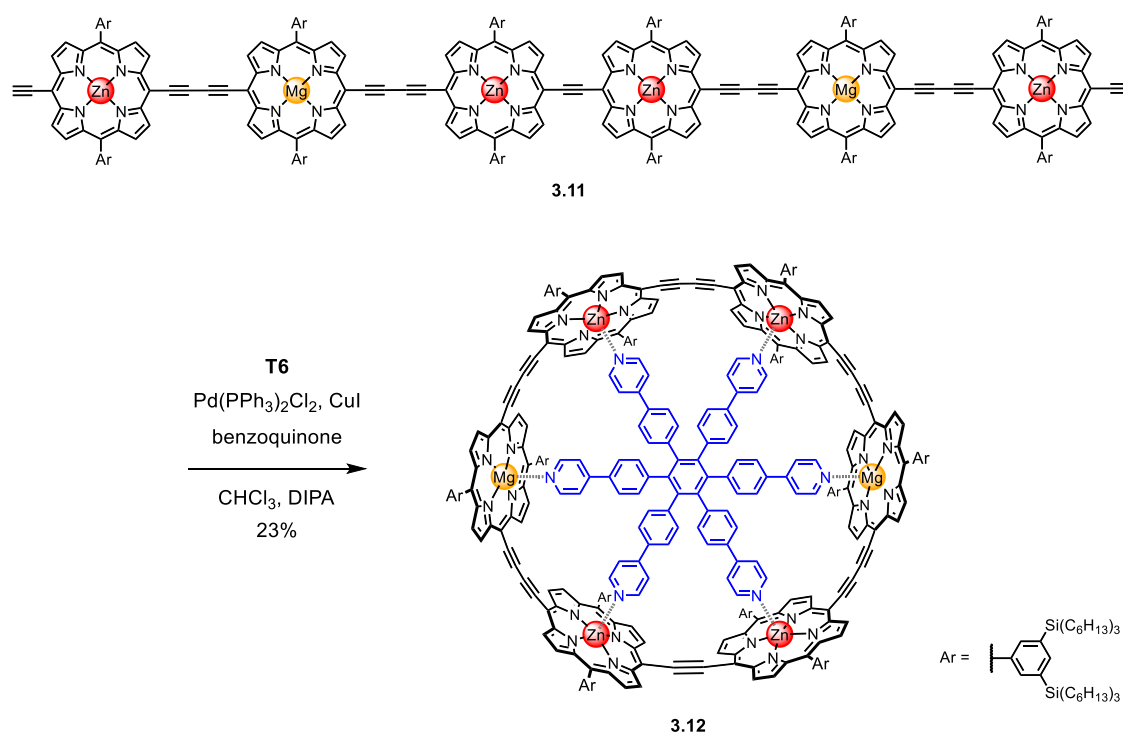
Scheme 3.1. Synthesis of the mono-deprotected magnesium porphyrin monomer.

Next, the single acetylene porphyrin dimer **3.6** was synthesized and fully deprotected according to literature procedures.³⁰ Then it was coupled with the mono-deprotected magnesium porphyrin monomer **3.5** to give the bis-magnesium-bis-zinc tetramer **3.7**. The acetylenes of the tetramer were deprotected to give **3.8** and it was reacted with a mono-deprotected CPDMS zinc porphyrin monomer **3.9** which was prepared according to literature procedures.³⁰ This gave the bis-magnesium-bis-zinc hexamer **3.10**. The acetylenes were deprotected to give **3.11** (Scheme 3.2).



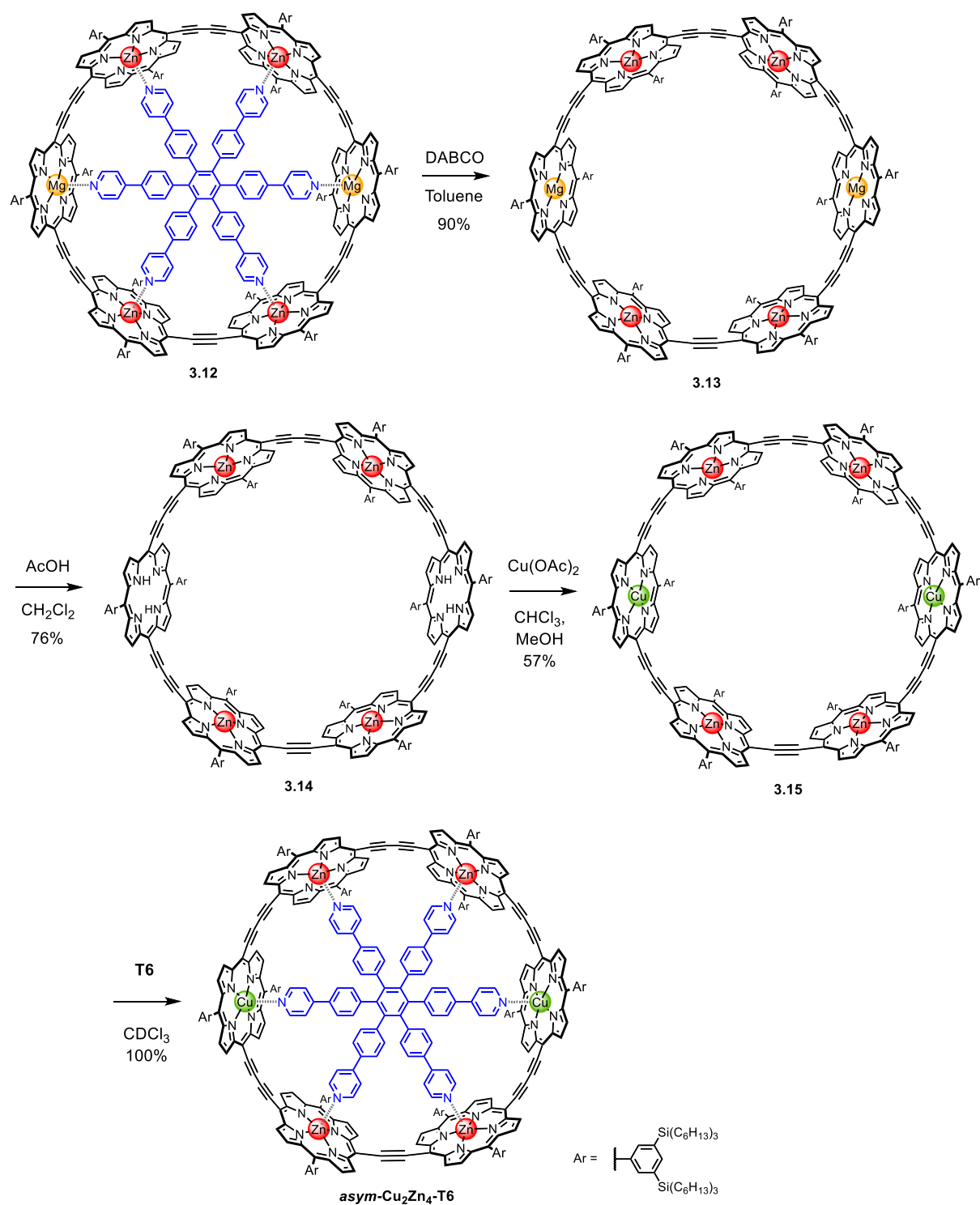
Scheme 3.2. Synthesis of the single acetylene bis-magnesium linear porphyrin hexamer.

Hexamer **3.11** was then submitted to ring formation conditions using **T6** as a template to give the *bis*-magnesium-*tetra*-zinc ring **3.12** (Scheme 3.3).



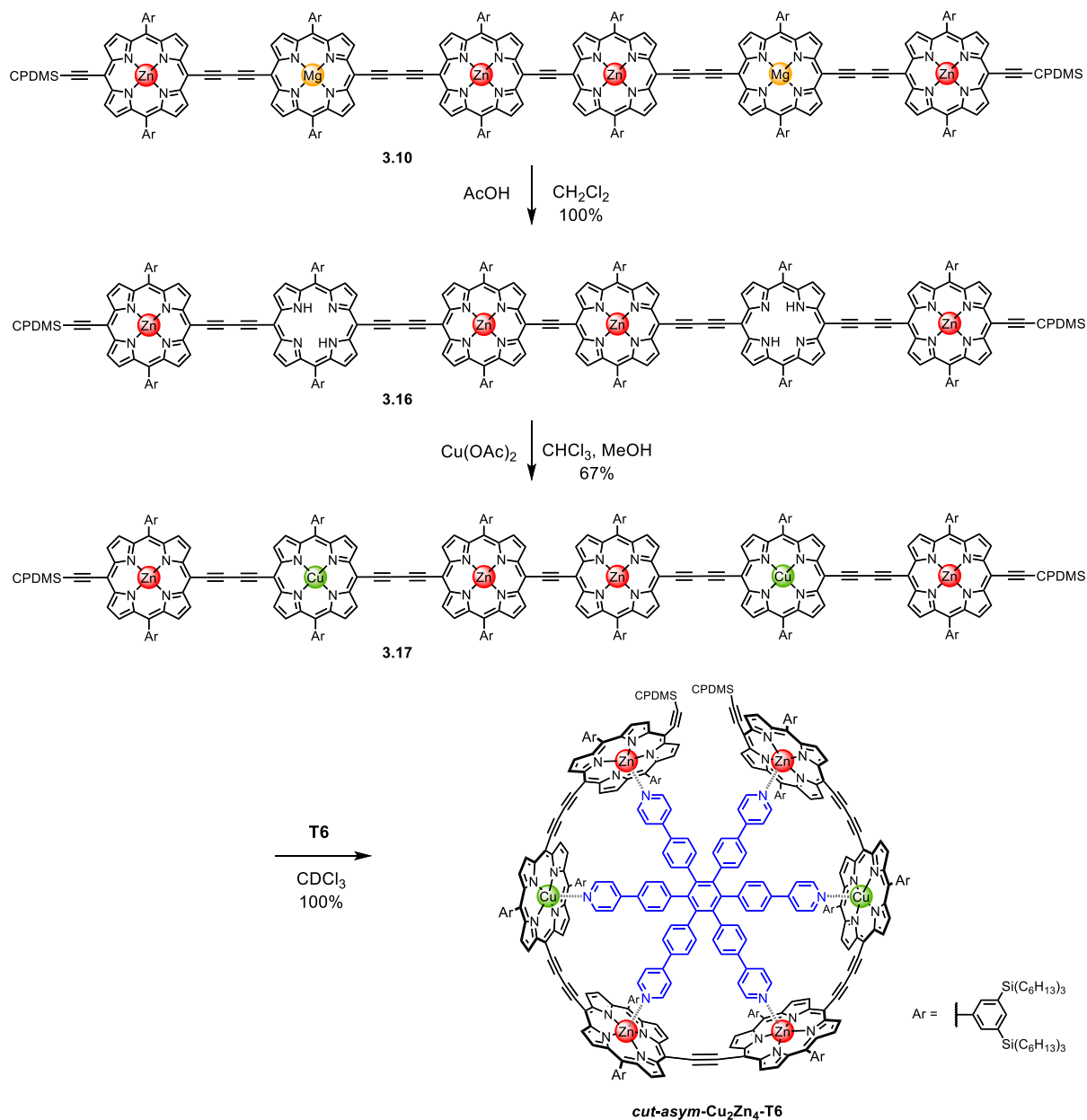
Scheme 3.3. Synthesis of the asymmetric bis-magnesium porphyrin nanoring **3.12**.

Then **T6** was removed using a size exclusion column loaded with the competing ligand DABCO, and afterwards the resulting **3.13** was treated with acetic acid to remove the magnesium atoms selectively to give **3.14**. Then copper was inserted from copper(II) acetate in a mixture of chloroform and methanol at 60 °C to give **3.15**. Finally, the template **T6** was inserted into the nanoring to achieve the structural rigidity which was found in Section 3.6 to be necessary for observing quantum interference effects (Scheme 3.3). This gave the final compound *asym*-Cu₂Zn₄·**T6**.



Scheme 3.4. Synthesis of the asymmetric bis-copper porphyrin nanoring **asym-Cu₂Zn₄·T6**.

A linear hexamer-**T6** complex was synthesized as a reference compound for the analysis, and the synthesis route is outlined in Scheme 3.5. The *bis*-magnesium-*tetra*-zinc hexamer **3.10** was treated with acetic acid to remove the magnesium atoms. Then copper was inserted into the free-base porphyrins to give the hexamer **3.17**. This hexamer was then mixed with one equivalent **T6** to give the template-bound complex *cut-asym*- $\text{Cu}_2\text{Zn}_4\cdot\text{T6}$.



Scheme 3.5. Synthesis of the reference compound *cut-asym*- $\text{Cu}_2\text{Zn}_4\cdot\text{T6}$.

3.8.3 Results and analysis of DEER measurements

The data from the DEER experiment on ***asym*-Cu₂Zn₄·T6** are shown as the blue traces in Figure 3.15. By comparison to data measured on the corresponding symmetrical ring ***sym*-Cu₂Zn₄·T6** (Figure 3.9), it is seen that in the DEER trace recorded on the *xy*-position there is very little measurable oscillation. However, at lower fields an oscillation emerges, which is most clearly seen in the far *z*-position. The traces were analyzed using the iterative procedure described in Section 3.7.4, and the results are shown in Figure 3.13. Here it is observed that a negative value of J gives a significantly better fit compared to a positive value of J . The negative J frequencies center around a value of $J = -4.4$ MHz with a spread of 3.7 MHz.

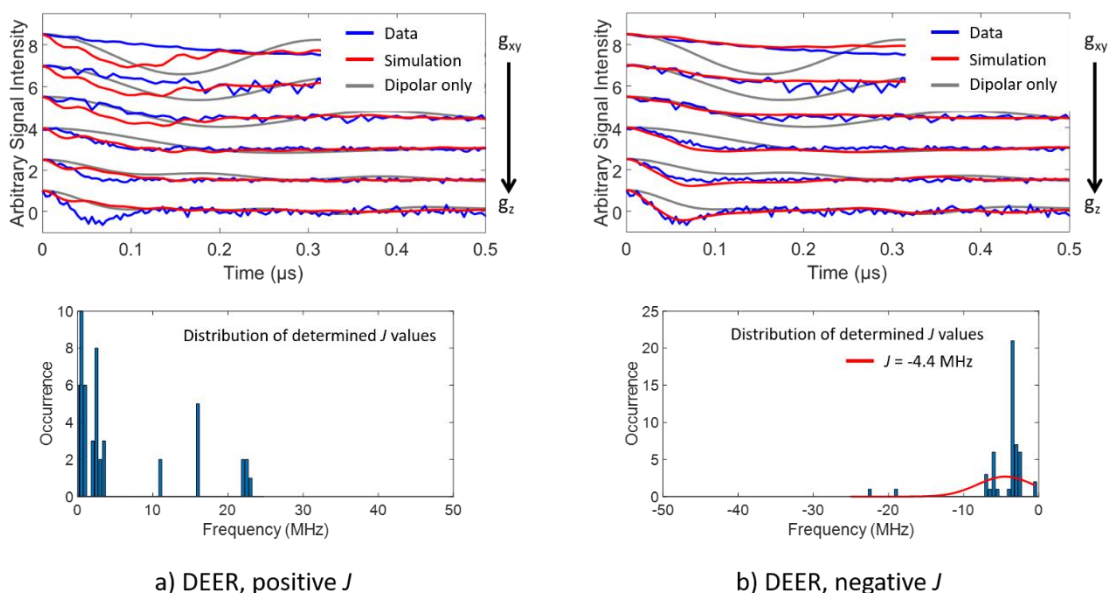


Figure 3.13. The DEER traces of ***asym*-Cu₂Zn₄·T6** at different field positions fitted with positive and negative J using the iterative approach. The histograms show the values of J . Fitting a normal Gaussian distribution to the positive results for J yields; $J = 5.4$ MHz, $\sigma_J = 7.5$ MHz. Fitting a normal Gaussian distribution to the negative results for J yields; $J = -4.4$ MHz, $\sigma_J = 3.7$ MHz. Negative values of J provide a better fit to the data recorded.

The fact that J changes sign from positive in the symmetric rings to negative in this asymmetric ring is very interesting. It means that the spin ground state is ferromagnetic rather than antiferromagnetic. To test whether this is an inherent consequence of the newly introduced single acetylene or the asymmetry in the ring, we measured DEER on the one-pathway control system ***cut-asym*-Cu₂Zn₄·T6**. These results were compared to the asymmetric ring

asym-Cu₂Zn₄·T6 and to newly recorded data on the control system from the work of Richert et al. with all butadiyne linkages.⁹ The DEER traces for **cut-asym-Cu₂Zn₄·T6** are shown in Figure 3.14, and the newly recorded orientation selective DEER results and analysis measured on the all butadiyne system are given in Figure 3.15.

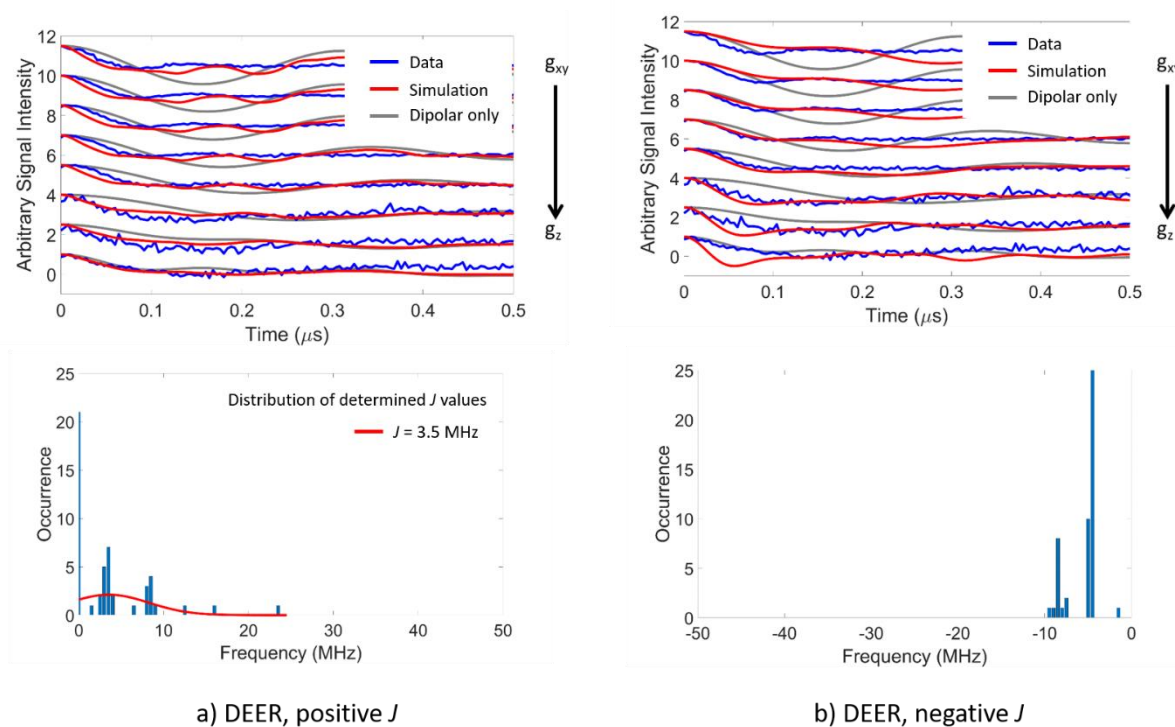


Figure 3.14. The DEER traces of **cut-asym-Cu₂Zn₄·T6** at different field positions fitted with positive J using the iterative approach. The histograms show the values of J . Fitting a normal Gaussian distribution to the positive results for J yields; $J = 3.5$ MHz, $\sigma_J = 4.7$ MHz. Fitting a normal Gaussian distribution to the negative results for J yields; $J = -5.6$ MHz, $\sigma_J = 1.8$ MHz. It can clearly be seen that positive values of J provide a better fit to the experimental data.

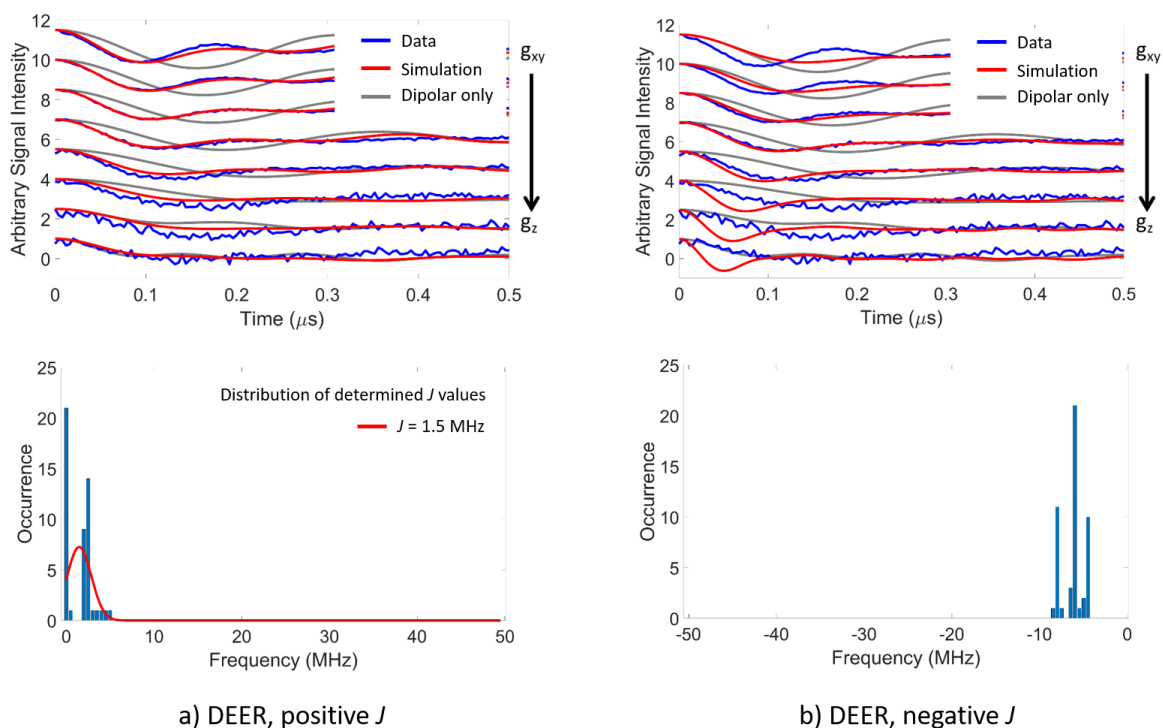


Figure 3.15. The DEER traces of **cut-sym-Cu₂Zn₄·T6** at different field positions fitted with positive J using the iterative approach. The histograms show the values of J . Fitting a normal Gaussian distribution to the positive results for J yields; $J = 1.5$ MHz, $\sigma_J = 1.4$ MHz. Fitting a normal Gaussian distribution to the negative results for J yields; $J = -6.2$ MHz, $\sigma_J = 1.2$ MHz. It can clearly be seen that positive values of J provide a better fit to the experimental data.

From this analysis, the reference compound **cut-asym-Cu₂Zn₄·T6** with a single acetylene was found to have a J -value of 3.5 MHz with a spread of 4.7 MHz. In comparison, the reference compound with butadiyne investigated by Richert et al., was found to have a J -value of 2.3 MHz in the original analysis with a spread of 0.8 MHz.⁹ Analysis considering the orientation dependence of the dipolar interaction (Figure 3.15) gave an average value of 1.5 MHz with a spread of 1.4 MHz. Differences between the value found originally and that found in the new analysis methodology are likely a result of the fact that the distribution found in J from the orientation selective analysis is not Gaussian. The results for these two systems show that shortening the pathway between the two metal centers by one acetylene increases the strength of the coupling significantly. This change is likely to be due to the shorter pathway leading to a greater degree of delocalization of the two coupled electrons throughout the pathway.

More importantly, the sign of J is the same and positive in the two reference compounds. To summarize, we observe a positive value of J for the systems where there is only one pathway and it must be assumed that there can be no interference. We observe an increased positive value of J in all the systems where there are two rigid, identical pathways. However, for the nanoring with two non-identical pathways **asym-Cu₂Zn₄-T6**, we observe a relatively small, negative value of J .

The trend in these results was confirmed by DFT (as detailed in Section 3.12), the results of which are shown in Table 3.1. These confirm that the relative sign of J switches upon the exchange of a butadiyne linker with a single acetylene in the asymmetric ring. The calculations also show the increase in J on shortening the pathway in the single cut system. However, the discrepancy of the exact magnitudes of the exchange coupling reflects the inherent difficulties of using DFT to calculate energy differences on the scale of 10^{-6} Hartrees as required in this method. This confirms the primary role of DEER measurements in determining exchange couplings on this scale.

The changes observed experimentally can be attributed to several factors including changing the geometry and the extent and shape of the π -conjugation pathway. Deconvolution of these factors to determine the driving forces in the inversion of the sign of J upon introducing asymmetry, and the increase in J upon shortening the length of the π system, would require a more detailed theoretical treatment which is outside the scope of this work.

Table 3.1. J coupling constants, in MHz, as determined by the DFT calculations (B3LYP/6-31G*) in MHz. The signs are reversed in the calculated results because a different Hamiltonian is used in the calculations compared to in the school of magnetic resonance. Details on the calculations can be found in Section 3.12.

	Method 1	Method 2	Experimental value (spread)
<i>sym</i>-Cu₂Zn₄·T6	−16.6	−6.4	8.3 (± 3)
<i>asym</i>-Cu₂Zn₄·T6	5	6	−4.4 (± 3.7)
<i>cut-sym</i>-Cu₂Zn₄·T6	N/A	N/A	1.5 (± 1.4)
<i>cut-asym</i>-Cu₂Zn₄·T6	−3	N/A	3.5 (± 4.7)

Calculation using method (2) on the single acetylene hexamer ***cut-asym*-Cu₂Zn₄·T6** was not completed during the time frame of this work due to the significant computation time required for each system. The calculations were carried out by Dr Qingqing Wu (University of Lancaster, UK).

3.9 Conclusion

Understanding the electronic communication in porphyrin oligomers is critical to their exploitation as molecular nanowires.³⁴ This chapter has shown the strength of using orientational selectivity when examining exchange couplings by EPR spectroscopy and particularly for determining the relative signs of D and J .

It was found that the exchange coupling in ***sym*-Cu₂Mg₄·T6** is slightly larger, and has a larger spread, than in the previously published ***sym*-Cu₂Zn₄·T6**, raising the possibility of being able to ‘tune’ the electronic properties of molecular nanowires. Reduction in the rigidity of the ***sym*-Cu₂Mg₄·T6** ring by changing and removing the template was observed to decrease the exchange coupling significantly. This implies that rigidity is important to the magnitude of the exchange interaction.

Furthermore, it was shown that varying the spin active nuclei present in the bis-metal nanoring has a big effect on the nature of the exchange coupling. In comparing ***sym*-Cu₂Mg₄·T6** and ***sym*-Ag₂Mg₄·T6**, it was shown that the distribution of J was significantly broadened by having Ag(II) as the spin active nuclei, and that the average magnitude of J is significantly larger. However, the large distribution in J leads to significant uncertainty in the exact size of J .

Finally, it was demonstrated that changing the symmetry of the exchange coupling pathways in the bis-copper nanorings has a large effect on the nature of the exchange coupling. Upon the introduction of asymmetry by replacing a butadiyne linker in **sym-Cu₂Zn₄·T6** with an acetylene linker in **asym-Cu₂Zn₄·T6**, it was shown that the sign of J switched relative to D . This implies there is a switch from antiferromagnetic to ferromagnetic exchange coupling upon the change to an asymmetric coupling pathway. This leads to the conclusion that in **asym-Cu₂Zn₄·T6**, the singlet spin state is lower in energy than the triplet state. It was also shown that the exchange coupling of the linear hexamer reference compound **cut-asym-Cu₂Zn₄·T6** was stronger than in the equivalent compound with butadiynes, and that it was still positive.

This leaves the asymmetric nanoring **asym-Cu₂Zn₄·T6** as the only compound we have investigated that has a negative exchange coupling. Whether this peculiar change of sign is because of destructive quantum interference or something else will require more detailed theoretical investigation. However, if there were no quantum interference, then we would expect the exchange coupling in the asymmetric nanoring to be very similar to the one measured for the symmetric ring **sym-Cu₂Zn₄·T6**, but slightly larger in magnitude, as a consequence of the stronger electronic coupling through an ethyne unit compared with a butadiyne.

3.10 Future work

The analysis shown in this chapter on the bis-metal nanorings requires some further confirmation via DFT calculations. Completion of the calculations on the linear hexamer **cut-asym-Cu₂Zn₄·T6** using Method(2) is required. This will allow for additional detail about the nature of the exchange coupling upon shortening the coupling pathway.

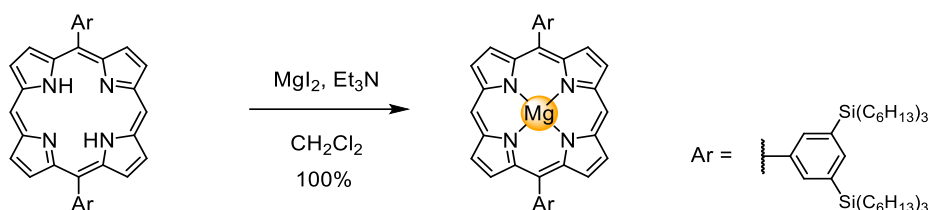
Because we suspected that having magnesium as the spin-inactive metal in the ring was partly responsible for the large spread in J observed for **sym-Ag₂Mg₄·T6**, I synthesized a zinc equivalent of this compound **sym-Ag₂Zn₄·T6**, for which we have obtained preliminary DEER data and characterization. I have not included that compound in this chapter because it needs to be resynthesized in order to get better characterization data, and our laboratory was suddenly closed due to extraordinary circumstances (COVID-19 pandemic, 2020). However, the preliminary DEER data for **sym-Ag₂Zn₄·T6** that we measured, looked very similar to

sym-Ag₂Mg₄·T6, so we no longer think that magnesium is responsible for the large spread, rather it is probably silver.

In order to test for quantum interference in the silver-systems, it is necessary to synthesize and measure a reference compound with only one pathway. We have plans to synthesize ***cut-sym-Ag₂Zn₄·T6*** and gather DEER data from it to observe the difference in having one or two pathways when silver is the spin-active metal.

3.11 Synthetic experimental procedures

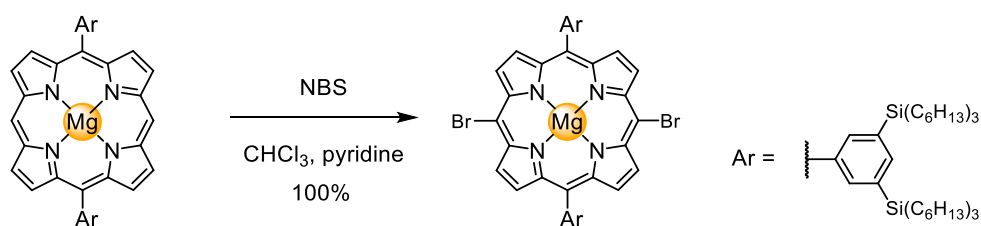
3.2



Free-base THS-porphyrin **3.1** (2.34 g, 1.47 mmol), triethyl amine (2.0 mL, 14.3 mmol), and magnesium iodide (4.1 g, 14.7 mmol) were dissolved in CH_2Cl_2 (20.0 mL) and stirred at 25 °C. The reaction was monitored with UV-vis and after 40 min it had reached completion. The solution was concentrated to 5 mL and petrol ether (20 mL) and pyridine (0.2 mL) was added. The resulting solution was filtered through a short silica plug to give **3.2** (2.52 g, 100%) as a purple oil.

^1H NMR: (400 MHz, CDCl_3) δ 10.26 (s, 2H), 9.36 (d, $J = 4.35$ Hz, 4H), 9.07 (d, $J = 4.35$ Hz, 4H), 8.33 (s, 4H), 7.98 (s, 2H), 1.51 (m, 24H), 1.36 (m, 24H), 1.30 (m, 48H), 0.94 (m, 24H), 0.87 (m, 36H).

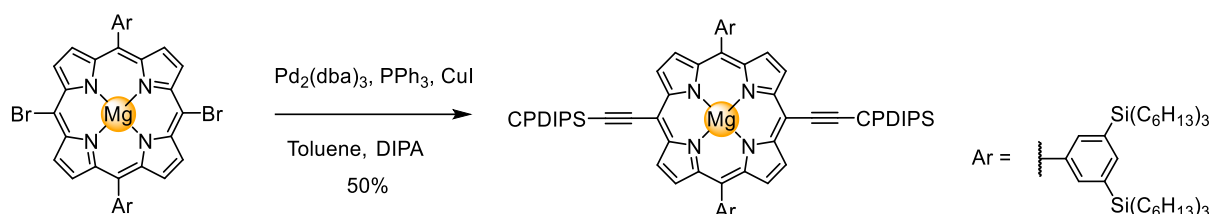
3.3



3.2 (2.49 g, 1.47 mmol) was dissolved in CHCl_3 (200 mL) and pyridine (1.0 mL) and cooled to 0 °C. Freshly recrystallized *N*-bromosuccinimide (0.53 g, 2.97 mmol) was added. The solution was stirred at 0 °C for 15 min and then it was allowed to reach 25 °C by removing the ice bath. After 30 min, the reaction was quenched by adding acetone (1.5 mL). The solvent was removed, and the residue was stirred in petrol ether for 10 min to make all the product go in solution. The solution was filtered, and the solvent removed to give **3.3** (2.71 g, 100%) as a purple oil.

¹H NMR: (400 MHz, CDCl₃) δ 9.64 (d, *J* = 4.60 Hz, 4H), 8.85 (d, *J* = 4.60 Hz, 4H), 8.21 (s, 4H), 7.98 (s, 2H), 1.48 (m, 24H), 1.37 (m, 24H), 1.30 (m, 48H), 0.92 (m, 24H), 0.87 (m, 36H).

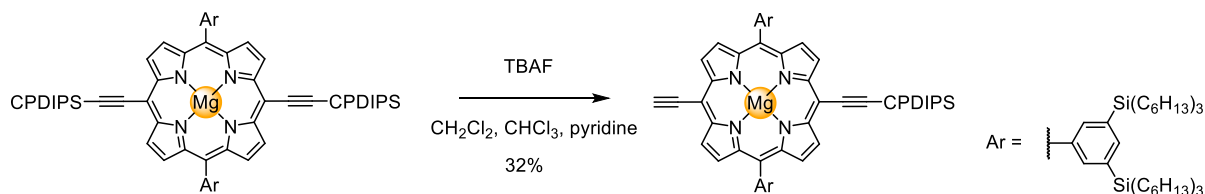
3.4



3.3 (2.61 g, 1.47 mmol), Pd₂(dba)₃ (147 mg, 0.16 mmol), triphenylphosphine (118.0 mg, 0.45 mmol), and CuI (91 mg, 0.48 mmol) were mixed and put under high vacuum for 1 h. Dry toluene (100 mL) was added and the solution was submitted to three freeze-pump-thaw cycles. CPDIPS acetylene (1.1 g, 5.22 mmol) was dissolved in freshly distilled DIPA (95.0 mL) and degassed by bubbling with N₂. The DIPA solution was added to the toluene solution and the mix was stirred at 50 °C for 2 h. The reaction was stopped by filtering through a short silica plug (CHCl₃ 1% pyridine). The product was purified by flash column chromatography, (one column with petrol ether:CH₂Cl₂ 2:1 to 3:2, and one column with toluene 1% pyridine). The pure **3.4** (1.50 g, 50%) is a green oil.

¹H NMR: (400 MHz, CDCl₃) δ 9.61 (d, *J* = 4.47 Hz, 4H), 8.82 (d, *J* = 4.47 Hz, 4H), 8.22 (s, 4H), 7.97 (s, 2H), 2.54 (t, *J* = 6.78 Hz, 4H), 2.18 (m, 4H), 1.37 (m, 108H), 1.15 (m, 4H), 0.93 (m, 24H), 0.86 (m, 36H).

3.5

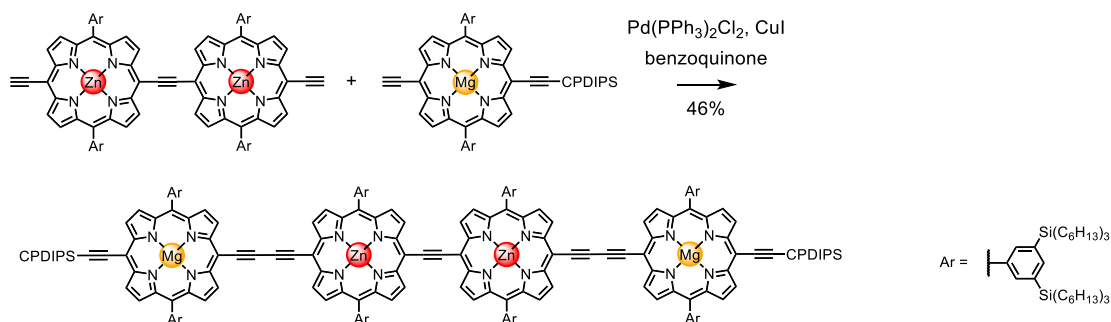


3.4 (1.50 g, 0.74 mmol) was dissolved in a mixture of CH₂Cl₂ (50 mL), chloroform (50 mL), and pyridine (10 mL) and cooled in an ice-water bath. TBAF (0.59 mL 1 M in THF, 0.59 mmol) was added and the reaction was followed by TLC (PE:CH₂Cl₂ 2:1). After 40 min more TBAF was added (0.20 mL, 0.2 mmol), and after an additional 55 min a third portion of TBAF (0.39

mL, 0.39 mmol) was added. The reaction was stopped after a total of 2 h by filtering through silica (CH_2Cl_2 , 1% pyridine). The product was purified by flash column chromatography on silica (petrol ether/chloroform 1% pyridine 20:1 to 1:1 providing the double deprotected product (383.5 mg, 23%) and the desired product **3.5** (435.5 mg, 32%).

^1H NMR: (400 MHz, CDCl_3) δ 9.65 (d, J = 4.52 Hz, 2H), 9.63 (d, J = 4.48 Hz, 2H), 8.86 (d, J = 4.48 Hz, 2H), 8.84 (d, J = 4.52 Hz, 2H), 8.25 (d, J = 0.97 Hz, 4H), 7.98 (t, J = 0.97 Hz, 2H), 4.15 (s, 1H), 2.54 (t, J = 6.90 Hz, 2H), 2.20 (m, 2H), 1.38 (m, 102H), 1.15 (m, 2H), 0.92 (m, 24H), 0.88 (m, 36H).

3.7

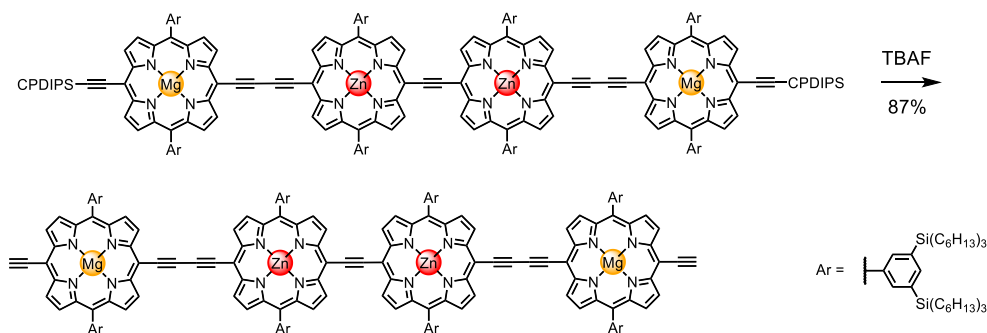


Deprotected dimer **3.6** (47.0 mg, 0.0138 mmol) and mono-deprotected magnesium monomer **3.5** (200.0 mg, 0.11 mmol) were dissolved in dry toluene (13.0 mL). $\text{Pd(PPh}_3)_2\text{Cl}_2$ (5.0 mg, 7 μmol), CuI (13.5 mg, 0.07 mmol), and 1,4-benzoquinone (30.0 mg, 0.28 mmol) were dissolved in a mixture of dry toluene (13.0 mL) and dry $i\text{-Pr}_2\text{NH}$ (2.5 mL) and this catalyst solution was added to the porphyrin solution. The reaction was stirred at room temperature overnight. After complete consumption of Mg-monomer monitored by TLC (PE: CH_2Cl_2 2:1), the mixture was passed through a plug (SiO_2 ; CHCl_3 + 1% pyridine). The solvents were removed, and the residue was purified by SEC (toluene + 1% pyridine) and further purified by recycling gel permeation chromatography (GPC, toluene + 1% pyridine) to afford **3.7** (44.9 mg, 46%) as a yellow-brown solid.

^1H NMR: (400 MHz, CDCl_3) δ 10.32 (d, J = 4.5 Hz, 4H), 9.89 (d, J = 4.5 Hz, 4H), 9.88 (d, J = 4.5 Hz, 4H), 9.63 (d, J = 4.5 Hz, 4H), 9.01 (d, J = 4.5 Hz, 4H), 8.94 (d, J = 4.5 Hz, 4H), 8.93 (d, J = 4.5 Hz, 4H), 8.86 (d, J = 4.5 Hz, 4H), 8.34 (s, 8H), 8.28 (s, 8H), 8.02 (s, 4H), 8.01 (s, 4H), 2.56 (t, J = 6.9 Hz, 4H), 2.22 (s, 4H), 1.52 (m, 96H), 1.40 (m, 96H), 1.33 (m, 192H), 1.15

(m, 32H), 0.96 (96H), 0.89 (t, $J = 7.0$ Hz, 72H), 0.82 (t, $J = 7.0$ Hz, 72H). **MALDI-ToF:** m/z 7067 (calculated for $[C_{450}H_{720}Mg_2N_{18}Si_{18}Zn_2]^+$: 7067). **UV-vis-NIR:** (CHCl₃) λ_{max} (log ϵ) 458 (5.74), 796 (5.28).

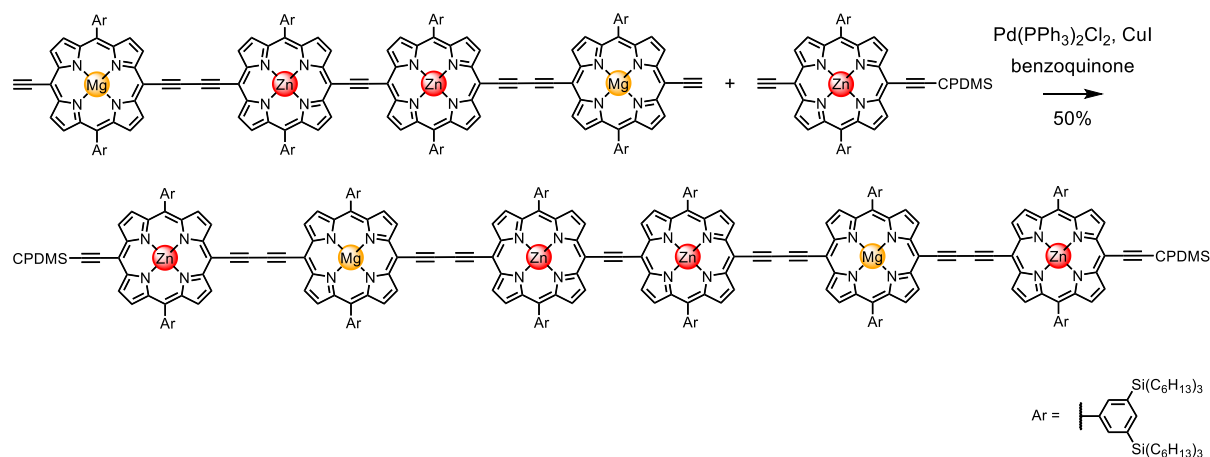
3.8



3.7 (44.9 mg, 6.4 μmol) was dissolved in CH₂Cl₂ (5 mL) and pyridine (0.05 mL). TBAF (1.0 M in THF, 0.20 mL, 0.20 mmol) was added and the reaction was stirred for 30 min at room temperature before the mixture was passed through a plug (SiO₂; CH₂Cl₂ + 1% pyridine). The solvents were removed to afford **3.8** (37.3 mg, 87%) as a brown solid.

¹H NMR: (400 MHz, CDCl₃) δ 10.38 (d, $J = 4.6$ Hz, 4H), 9.99 (d, $J = 4.6$ Hz, 4H), 9.93 (d, $J = 4.5$ Hz, 4H), 9.69 (d, $J = 4.5$ Hz, 4H), 9.10 (d, $J = 4.6$ Hz, 4H), 9.04 (d, $J = 4.6$ Hz, 4H), 8.99 (d, $J = 4.5$ Hz, 4H), 8.89 (d, $J = 4.5$ Hz, 4H), 8.40 (s, 8H), 8.33 (s, 8H), 8.07 (s, 4H), 8.04 (s, 4H), 4.21 (s, 2H), 1.54 (m, 96H), 1.41 (m, 96H), 1.34 (m, 192H), 0.98 (m, 96H), 0.91 (m, 72H), 0.85 (t, $J = 7.0$ Hz, 72H). **UV-vis-NIR:** (CHCl₃) λ_{max} (log ϵ) 455 (5.68), 795 (5.12).

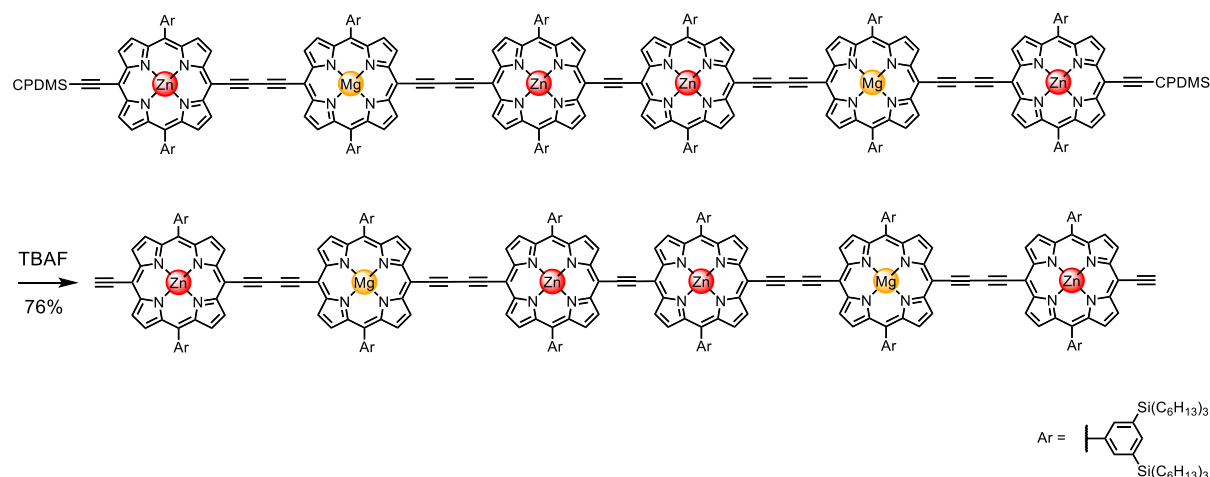
3.10



3.8 (37.0 mg, 5.5 μmol) and zinc monomer **3.9** (151 mg, 82.8 μmol) were dissolved in dry toluene (15 mL). $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (8.4 mg, 12 μmol), CuI (23 mg, 0.12 mmol), and 1,4-benzoquinone (92 mg, 0.85 mmol) were dissolved in a mixture of dry toluene (15 mL) and dry *i*-Pr₂NH (2 mL). The porphyrin solution was added to the catalyst solution. The mixture was stirred at room temperature overnight. Upon consumption of Zn-monomer (monitored by TLC) the mixture was filtered through a plug (SiO_2 ; CHCl_3 + 1% pyridine). The solvents were removed, and the residue was purified by SEC (toluene + 1% pyridine) and further purified by recycling GPC (toluene + 1% pyridine) to afford **3.10** (28.5 mg, 50%) as a brown solid.

¹H NMR: (400 MHz, CDCl_3) δ 10.34 (d, J = 4.5 Hz, 4H), 9.91 (m, 16H), 9.61 (d, J = 4.5 Hz, 4H), 9.03 (d, J = 4.5 Hz, 4H), 8.97 (m, 16H), 8.87 (d, J = 4.5 Hz, 4H), 8.36 (s, 16H), 8.28 (s, 8H), 8.04 (s, 8H), 8.02 (s, 4H), 2.58 (t, J = 6.9 Hz, 4H), 2.16 (m, 4H), 1.53 (m, 144H), 1.35 (m, 432H), 1.12 (m, 4), 0.98 (m, 144H), 0.91 (m, 144H), 0.84 (m, 72H), 0.62 (s, 12H). **MALDI-ToF:** m/z 10359 (calculated for $[\text{C}_{658}\text{H}_{1044}\text{Mg}_2\text{N}_{26}\text{Si}_{26}\text{Zn}_4]^+$: 10359). **UV-vis-NIR:** (CHCl_3) λ_{max} (log ϵ): 457 (5.96), 803 (5.47).

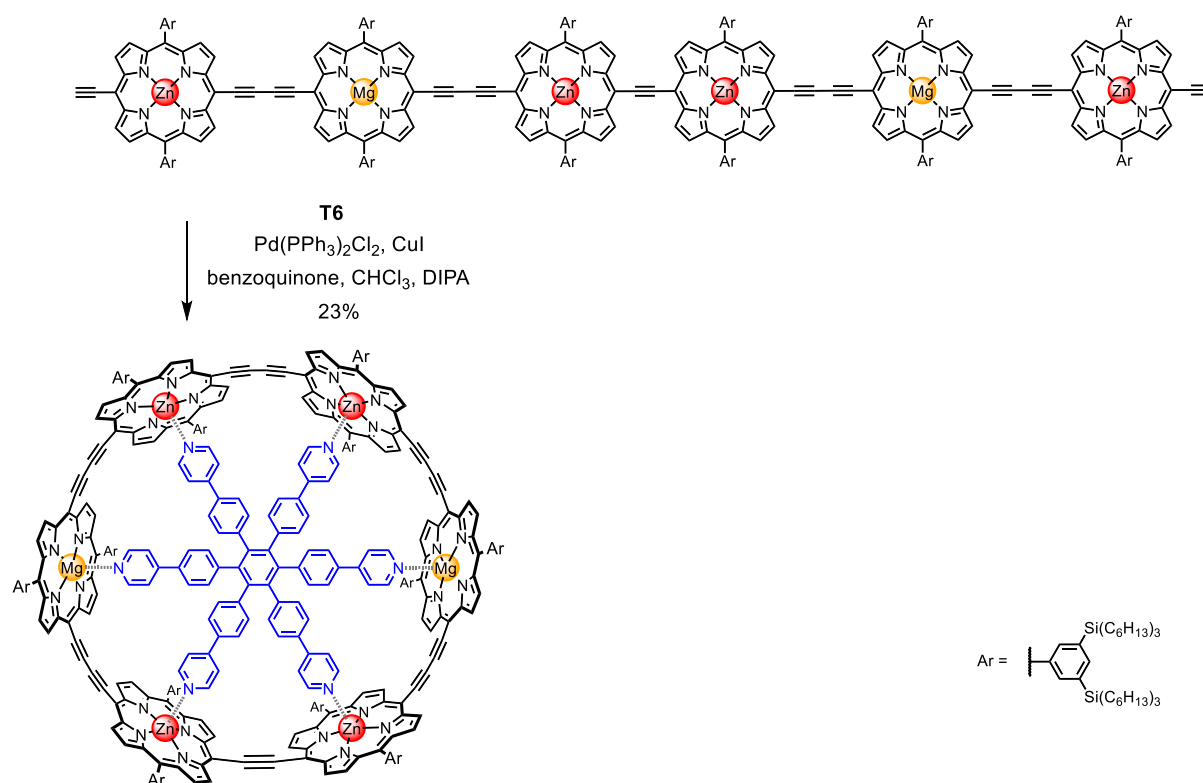
3.11



3.10 (20.0 mg, 1.9 μmol) was dissolved in CH_2Cl_2 (2.0 mL) and pyridine (0.05 mL). TBAF (1.0 M in THF, 26 μL , 26 μmol) was added. The reaction mixture was stirred for 25 min at room temperature before it was passed through a plug (SiO_2 ; $\text{PE}_{40-60}/\text{CH}_2\text{Cl}_2$ 3:1 + 1% pyridine). The solvents were removed in vacuum to afford **3.11** (14.9 mg, 76%) as a brown solid.

^1H NMR: (500 MHz, CDCl_3) δ 10.33 (d, J = 4.4 Hz, 4H), 9.90 (m, 16H), 9.67 (d, J = 4.5 Hz, 4H), 9.01 (d, J = 4.3 Hz, 4H), 8.95 (m, 16H), 8.87 (d, J = 4.4 Hz, 4H), 8.35 (s, 8H), 8.34 (s, 8H), 8.28 (s, 8H), 8.03 (s, 8H), 8.01 (s, 4H), 4.18 (s, 2H), 1.52 (m, 144H), 1.40 (m, 144H), 1.32 (m, 288), 0.96 (m, 144H), 0.89 (m, 144H), 0.83 (m, 72H). **MALDI-ToF:** m/z 10112 (calculated for $[\text{C}_{646}\text{H}_{1022}\text{Mg}_2\text{N}_{24}\text{Si}_{24}\text{Zn}_4]^+$: 10109). **UV-vis-NIR:** (CHCl_3) λ_{max} (log ϵ): 457 (5.72), 803 (5.26).

3.12

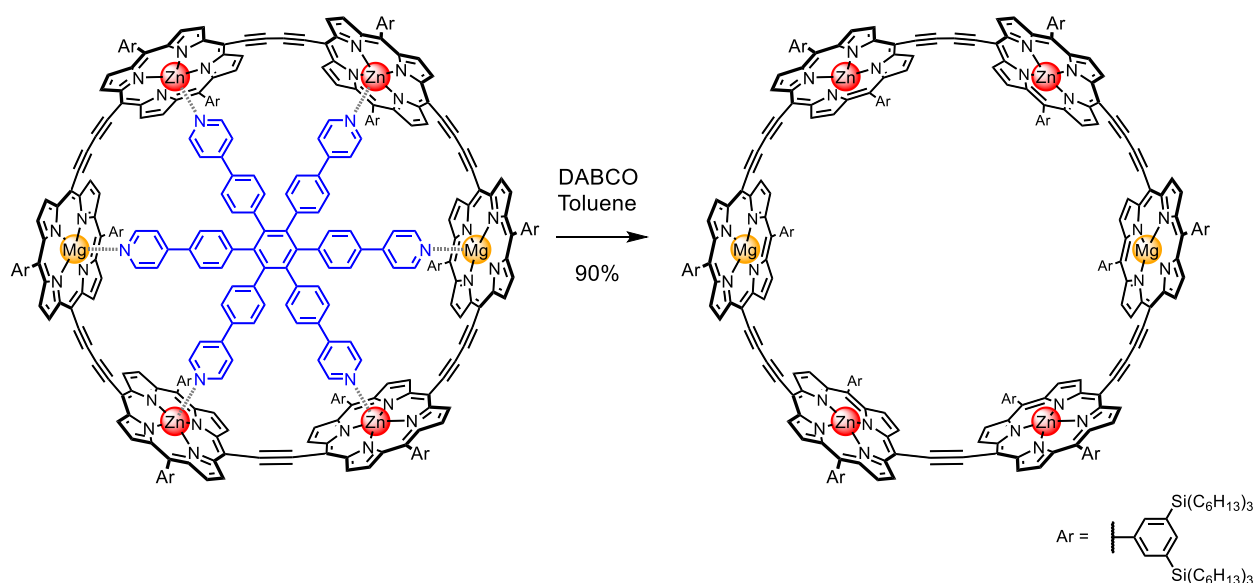


3.11 (14.0 mg, 1.38 μmol) and **T6** (2.5 mg, 2.5 μmol) were dissolved in dry CHCl_3 (10 mL). Pd(PPh₃)₂Cl₂ (6.9 mg, 10 μmol), CuI (9.1 mg, 42.5 μmol) and 1,4-benzoquinone (22.8 mg, 0.4 mmol) were dissolved in dry CHCl_3 (10 mL) and dry $i\text{-Pr}_2\text{NH}$ (0.125 mL) and added to the porphyrin solution. The reaction was stirred at r.t. overnight. The mixture was passed through a plug (SiO_2 ; CHCl_3 + 1% pyridine). The solvents were removed, and the residue was purified by SEC (toluene + 1% pyridine) and further purified by recycling GPC (toluene + 1% pyridine) to afford **3.12** (3.6 mg, 23%) as a red-brown solid.

^1H NMR: (500 MHz, CDCl_3 + 1% pyridine- d_5) δ 10.01 (d, J = 4.1 Hz, 4H), 9.43 (m, 8H), 9.37 (m, 12H), 8.78 (d, J = 4.2 Hz, 4H), 8.65 (m, 8H), 8.62 (m, 8H), 8.58 (d, J = 4.4 Hz, 4H), 8.30

(s, 4H), 8.28 (s, 4H), 8.21 (s, 4H), 7.93 (m, 24H), 5.46 (d, $J = 8.6$ Hz, 4H), 5.38 (d, $J = 8.6$ Hz, 4H), 5.32 (d, $J = 8.5$ Hz, 4H), 5.26 (d, $J = 8.5$ Hz, 4H), 5.21 (d, $J = 8.7$ Hz, 4H), 5.13 (d, $J = 8.6$ Hz, 4H), 4.79 (d, $J = 6.6$ Hz, 4H), 4.66 (d, $J = 6.6$ Hz, 4H), 4.60 (d, $J = 6.5$ Hz, 4H), 2.06 (d, $J = 6.5$ Hz, 4H), 1.96 (d, $J = 6.5$ Hz, 4H), 1.62 (d, $J = 6.0$ Hz, 4H), 1.44 (m, 144H), 1.28 (m, 432H), 0.89 (m, 180H), 0.80 (t, $J = 7.0$ Hz, 36H), 0.76 (t, $J = 6.9$ Hz, 36H), 0.73 (t, $J = 7.0$ Hz, 36H). **MALDI-ToF:** m/z 11102 (calculated for $[C_{718}H_{1068}Mg_2N_{30}Si_{24}Zn_4]^+$: 11105). **UV-vis-NIR:** (CHCl₃) λ_{max} (log ϵ) 441 (5.42), 504 (5.64), 795 (5.35), 836 (5.46), 879 (5.39).

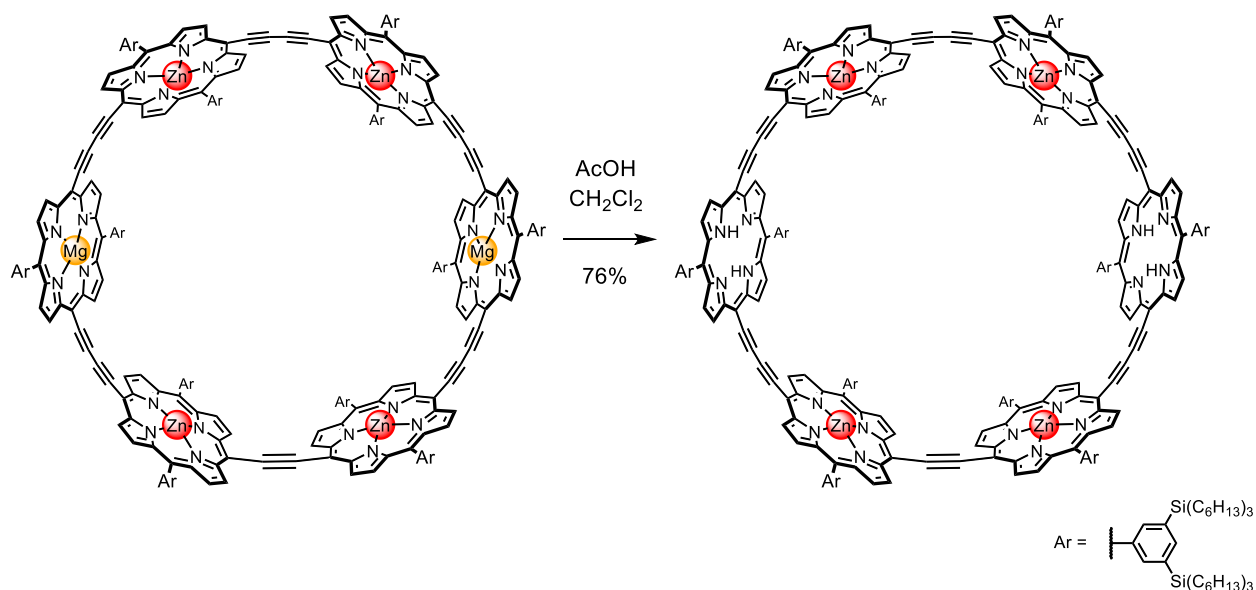
3.13



Freshly recrystallized 1,4-diazabicyclo[2.2.2]octane (10 g) was dissolved in toluene (50 mL) to achieve a 200 mg/mL solution. A SEC column (2.4 cm diameter, 32 cm length, Bio-Beads S-X1) was loaded with the solution. **3.12** (3.6 mg, 0.32 μ mol) was dissolved in toluene (1 mL) and eluted through the SEC column with toluene. The obtained solution was washed with water (3×3 mL) and the solvent was removed in vacuum. The product was dissolved in CHCl₃ and filtered through a silica pipette plug. The solvent was removed to give **3.13**.

Yield: 2.9 mg, 90%. **¹H NMR:** (500 MHz, CDCl₃) δ 10.07 (d, $J = 4.4$ Hz, 4H), 9.63 (m, 12H), 9.56 (d, $J = 4.4$ Hz, 4H), 8.84 (d, $J = 4.4$ Hz, 4H), 8.77 (m, 12H), 8.70 (m, 8H), 8.14 (s, 8H), 8.13 (s, 8H), 8.13 (s, 8H), 7.94 (m, 8H), 7.93 (s, 4H), 1.42 (m, 144H), 1.26 (m, 432H), 0.85 (m, 144H), 0.78 (m, 144H), 0.73 (t, $J = 6.9$ Hz, 72H). **MALDI-ToF:** m/z 10108 (calculated for $[C_{646}H_{1020}Mg_2N_{24}Si_{24}Zn_4]^+$: 10107). **UV-vis-NIR:** (CHCl₃) λ_{max} (log ϵ) 497 (5.38), 795 (5.09).

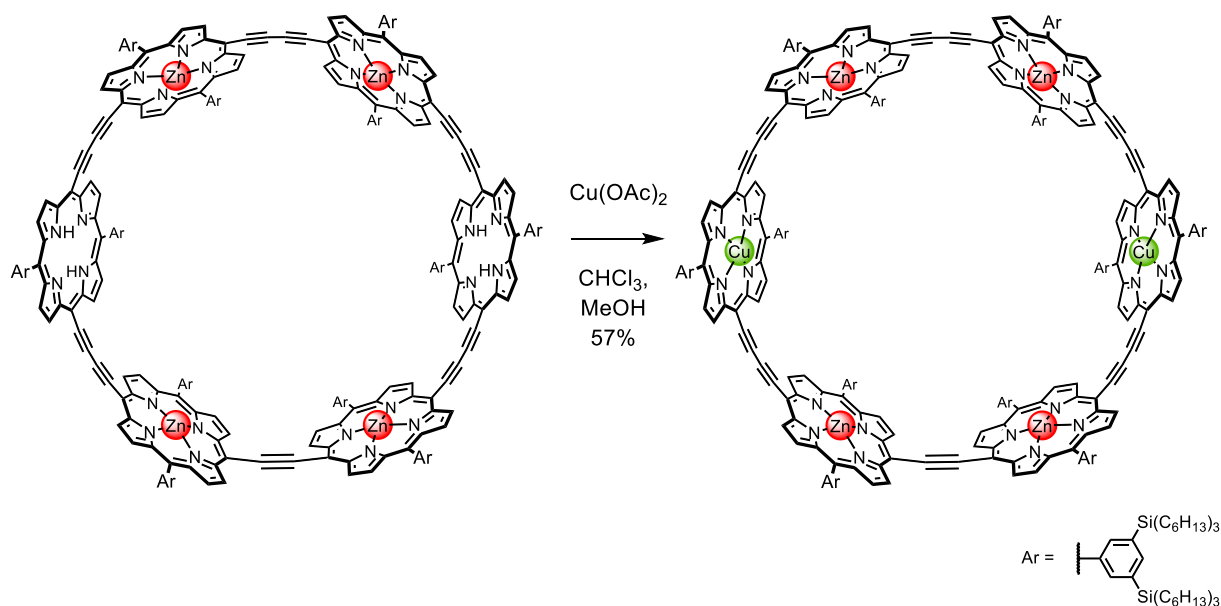
3.14



3.13 (2.9 mg, 0.29 μmol) was dissolved in CH₂Cl₂ (0.8 mL) and glacial acetic acid (0.2 mL) was added. The solution was stirred at room temperature. After 35 min, the solution was washed with water (3×2 mL) and then run through an alumina pipette plug (CH₂Cl₂). The solvent was evaporated to give **3.14**.

Yield: 2.2 mg, 76%. **¹H NMR:** (500 MHz, CDCl₃) δ 10.08 (d, $J = 4.4$ Hz, 4H), 9.63 (d, $J = 4.4$ Hz, 4H), 9.61 (d, $J = 4.5$ Hz, 8H), 9.52 (d, $J = 4.4$ Hz, 8H), 8.85 (d, $J = 4.4$ Hz, 4H), 8.77 (m, 12H), 8.67 (d, $J = 4.5$ Hz, 8H), 8.13 (m, 24H), 7.94 (s, 12H), 1.41 (m, 144H), 1.25 (m, 432H), 0.85 (m, 144H), 0.79 (m, 144H), 0.73 (m, 72H), -1.23 (s, 4H). **MS (MALDI-TOF):** m/z 10063 (M^+ , C₆₄₆H₁₀₂₄N₂₄Si₂₄Zn₄ requires 10062). **UV-VIS:** λ_{max} (CHCl₃) nm (log(ϵ)): 494 (5.67), 790 (5.39).

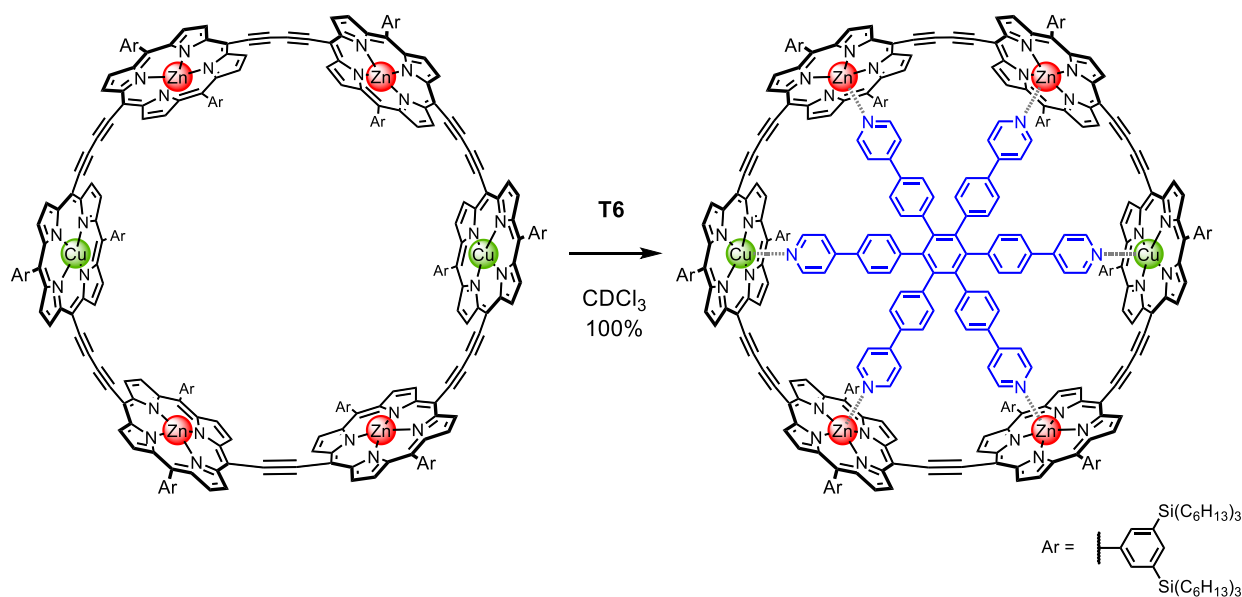
3.15



3.14 (2.2 mg, 0.22 μmol) and $\text{Cu(OAc)}_2 \cdot \text{H}_2\text{O}$ (4 mg, 20 μmol) was dissolved in CHCl_3 (1.0 mL) and methanol (0.1 mL) and stirred at 60 $^\circ\text{C}$. After 1 h, the mixture was allowed to reach room temperature and washed with water (2×5 mL). The solvent was removed in vacuum, and the mixture was run through a silica plug with petrol ether/ CH_2Cl_2 80:20. The solvent was removed in vacuum to give **3.15**.

Yield: 1.3 mg, 57%. **^1H NMR:** (500 MHz, CDCl_3) δ 10.10 (m, 4H), 9.56 (m, 10H), 8.78 (m, 16H), 8.13 (m, 16H), 7.94 (m, 12H), 1.41 (m, 144H), 1.26 (m, 432H), 0.84 (m, 360H). **MS (MALDI-TOF):** m/z 10186 (M^+ , $\text{C}_{646}\text{H}_{1020}\text{Cu}_2\text{N}_{24}\text{Si}_{24}\text{Zn}_4$ requires 10185).

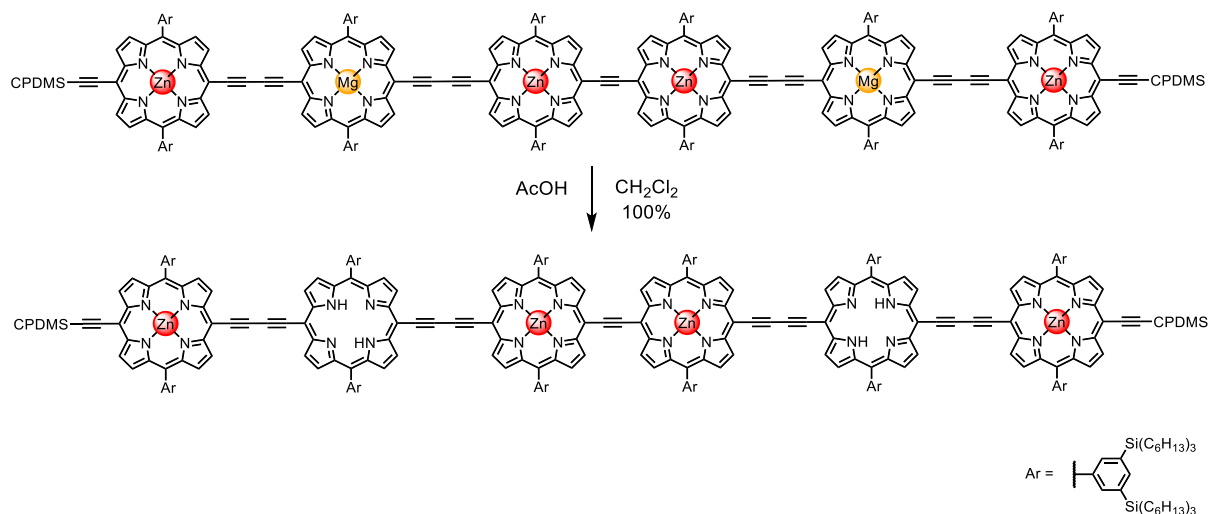
asym-Cu₂Zn₄·T6



3.15 (0.64 mg, 0.063 μmol) and **T6** (0.095 mg, 0.095 μmol) was dissolved in CDCl₃ (0.6 mL). ¹H NMR confirmed complete formation of complex. The solution was passed through a silica pipette plug (CDCl₃) and the resulting solution was concentrated and dried in vacuum to give **asym-Cu₂Zn₄·T6**.

Yield: 0.70 mg, 100%. **¹H NMR:** (500 MHz, CDCl₃) δ 10.05 (bs, 4H), 9.35 (m, 12H), 8.78 (app. s, 4H), 8.64 (m, 12H), 8.28 (m, 8H), 7.93 (m, 20H), 5.78 (bs, 8H), 5.53 (bs, 8H), 5.36 (bs, 4H), 4.96 (bs, 2H), 4.84 (bs, 2H), 1.99 (bs, 8H), 1.52-0.69 (m, THS protons). **MALDI-ToF:** m/z 11179 (M^+ , C₇₁₈H₁₀₆₈Cu₂N₃₀Si₂₄Zn₄ requires 11182). **UV-VIS:** λ_{max} (CHCl₃) nm (log(ϵ)): 440 (5.45), 503 (5.73), 779 (5.34), 821 (5.45), 863 (5.42), 952 (4.62).

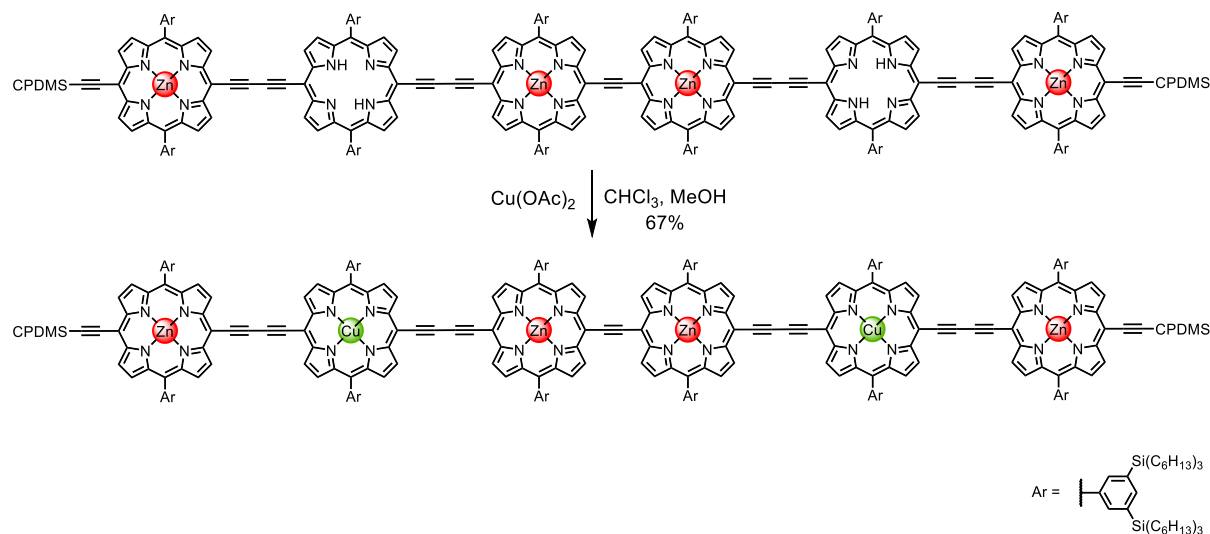
3.16



3.10 (5.0 mg, 0.48 μmol) was dissolved in CH_2Cl_2 (1.6 mL) and glacial acetic acid (0.4 mL) was added. The solution was stirred at room temperature. After 50 min, the solution was washed with water (3×2 mL) and then run through an alumina pipette plug (CH_2Cl_2). The solvent was evaporated to give **3.16**.

Yield: 5.38 mg, 100%. **^1H NMR:** (500 MHz, CDCl_3) δ 10.38 (d, $J = 4.5$ Hz, 4H), 9.98 (d, $J = 4.5$ Hz, 4H), 9.96 (d, $J = 4.5$ Hz, 4H), 9.89 (d, $J = 4.6$ Hz, 4H), 9.87 (d, $J = 4.6$ Hz, 4H), 9.68 (d, $J = 4.5$ Hz, 4H), 9.11 (d, $J = 4.5$ Hz, 4H), 9.05 (d, $J = 4.5$ Hz, 4H), 9.03 (d, $J = 4.5$ Hz, 4H), 8.94 (m, 12H), 8.39 (s, 8H), 8.37 (s, 8H), 8.31 (s, 8H), 8.06 (s, 8H), 8.04 (s, 4H), 2.58 (t, $J = 6.9$ Hz, 4H), 2.16 (m, 4H), 1.52 (m, 144H), 1.40 (m, 144H), 1.33 (m, 288H), 0.97 (m, 144H), 0.90 (m, 144H), 0.84 (t, $J = 7.0$ Hz, 4H). **MS (MALDI-TOF):** m/z 10316 (M^+ , $\text{C}_{658}\text{H}_{1048}\text{N}_{26}\text{Si}_{26}\text{Zn}_4$ requires 10315). **UV-VIS:** λ_{max} (CHCl_3) nm ($\log(\epsilon)$): 456 (5.78), 803 (5.32).

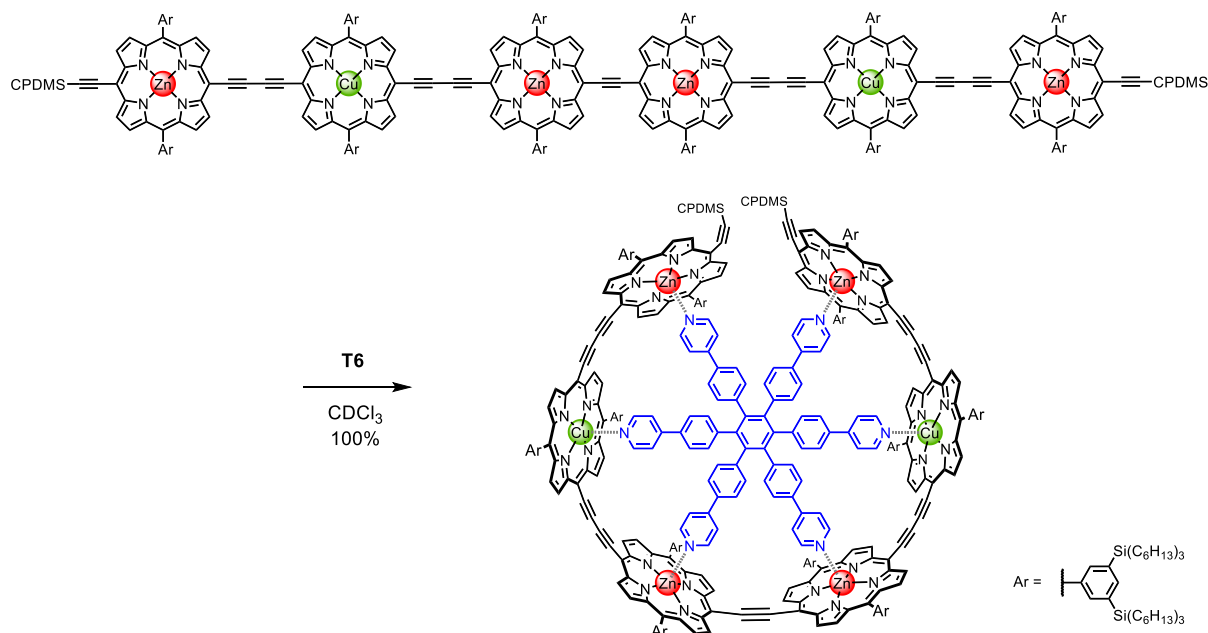
3.17



3.16 (2.7 mg, 0.26 μmol) and $\text{Cu(OAc)}_2 \cdot \text{H}_2\text{O}$ (5.0 mg, 25 μmol) was dissolved in CHCl_3 (1.5 mL) and methanol (0.15 mL) and stirred at 60 $^\circ\text{C}$. After 1 h, the mixture was allowed to reach room temperature and washed with water (2×5 mL). The solvent was removed in vacuum, and the mixture was run through a silica plug with petrol ether/ CH_2Cl_2 80:20. The solvent was removed in vacuum to give **3.17**.

Yield: 1.84 mg, 67%. **$^1\text{H NMR}$:** (500 MHz, CDCl_3) δ 10.35 (m, 4H), 9.84 (bs, 6H), 9.65 (d, $J = 4.4$ Hz, 4H), 9.07 (bs, 4H), 8.95 (m, 12H), 8.35 (s, 8H), 8.27 (s, 8H), 8.01 (m, 12H), 2.56 (t, $J = 6.9$ Hz, 4H), 2.15 (m, 4H), 1.31 (m, 576H), 0.88 (m, 360H). **MS (MALDI-TOF):** m/z 10438 (M^+ , $\text{C}_{658}\text{H}_{1044}\text{Cu}_2\text{N}_{26}\text{Si}_{26}\text{Zn}_4$ requires 10438). **UV-VIS:** λ_{max} (CHCl_3) nm ($\log(\epsilon)$): 457 (5.75), 788 (5.28).

cut-asym-Cu₂Zn₄·T6



3.17 (0.92 mg, 0.088 μmol) and **T6** (0.088 mg, 0.088 μmol) was dissolved in CDCl₃ (0.6 mL). ¹H NMR confirmed complete formation of complex, and the resulting solution was concentrated and dried in vacuum.

Yield: 0.70 mg, 100%. **¹H NMR:** (400 MHz, CDCl₃) δ 10.19 (m, 4H), 9.50 (m, 8H), 8.76 (m, 14H), 8.16 (m, 14H), 7.95 (m, 10H), 6.46-2.38 (template protons and CPDMS protons), 1.25 (m, 592H), 0.88 (m, 360H). **UV-VIS:** λ_{max} (CHCl₃) nm (log(ϵ)): 496 (5.71), 767 (5.36), 910 (5.15).

3.12 DFT calculations

The values of J measured in this work are at the limit of what can be calculated by DFT, although J -couplings of a similar magnitude have been calculated before, and the trends were consistent with experimental results.³⁵

In our case, DFT was able to reproduce the sign of J for all systems including the change in the asymmetric ring. However, our calculations were inconclusive as to the magnitude of the increase, reflecting the inherent difficulties of using DFT to calculate such small energy differences.

We calculated J by comparing the energies of triplet and broken symmetry (singlet) wavefunctions, using Yamaguchi's formula (Equation 3.1).^{36,37}

$$J = \frac{E_{BS} - E_T}{\langle S^2 \rangle_T - \langle S^2 \rangle_{BS}} \quad (3.1)$$

where E_{BS} is the energy of the broken symmetry (singlet) state, E_T is the energy of the triplet state, and $\langle S^2 \rangle_{BS}$ and $\langle S^2 \rangle_T$ are expectation values of S^2 for the broken symmetry and triplet states respectively.

Two methods were used from an initial converged triplet geometry and wavefunction to generate the singlet solution: Method (1): a broken symmetry guess at the triplet geometry was converged; Method (2): a further geometry optimization in the broken symmetry state was performed. The results of both calculations are summarized in Table 3.1.

In all structures, the solubilizing meso-aryl groups were truncated to -H. All calculations used the B3LYP/6-31G* functional/basis set combination in Gaussian09/D.01. Since the DFT calculations make use of the following Hamiltonian

$$\hat{H}_J = -2J\hat{S}_A\hat{S}_B \quad (3.2)$$

a negative J -value indicates antiferromagnetic coupling ($E_{BS} < E_T$), in agreement with the experimental data and simulations.

3.13 ^1H NMR and MALDI-ToF of new compounds

3.7

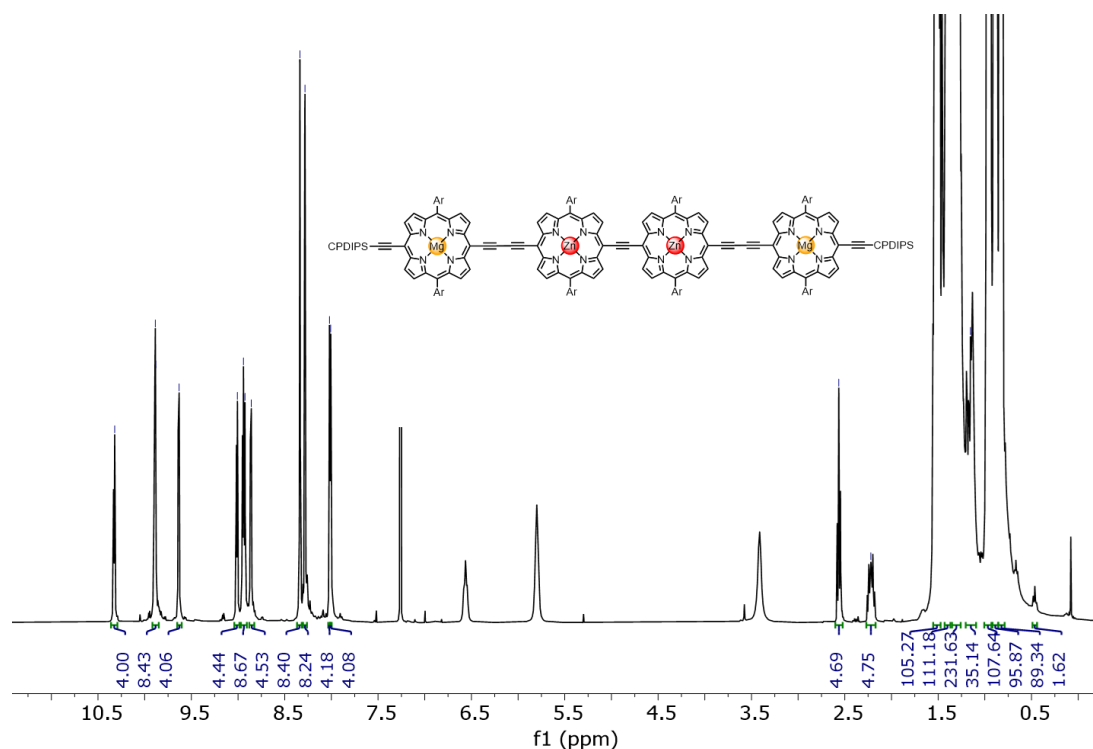


Figure 3.16. The ^1H NMR spectrum of **3.7** (400 MHz, CDCl_3 , 298 K).

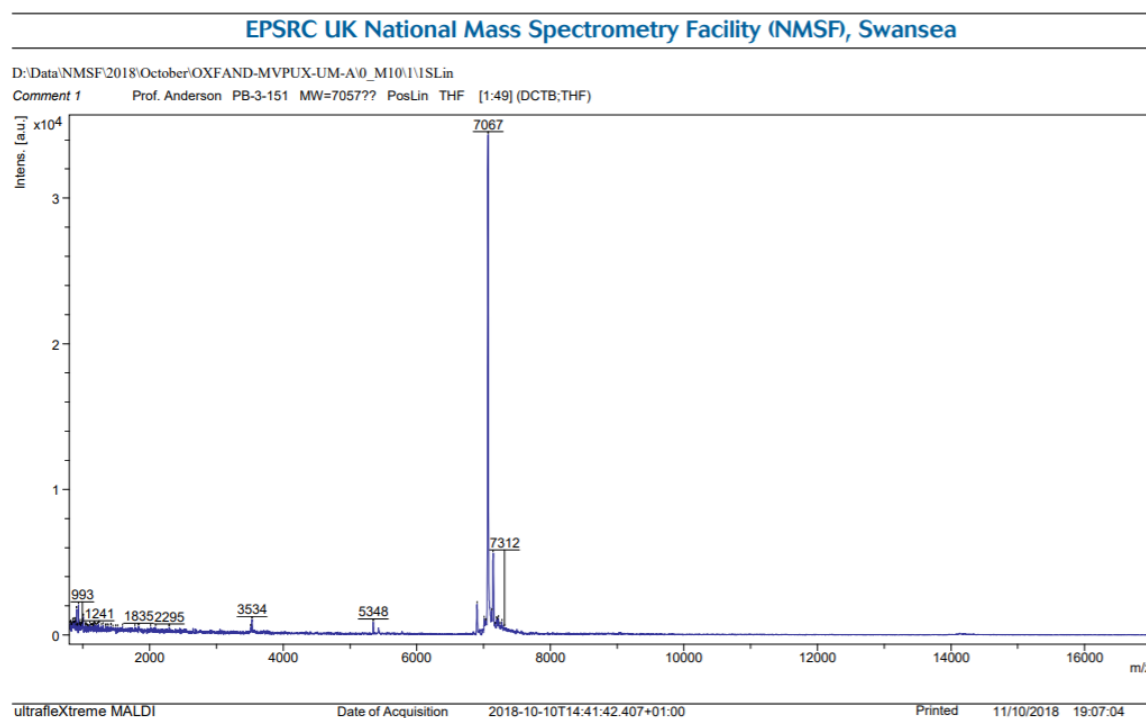


Figure 3.17. The MALDI-MS spectrum of **3.7**, matrix: DCTB. M^+ , $\text{C}_{450}\text{H}_{720}\text{Mg}_2\text{N}_{18}\text{Si}_{18}\text{Zn}_2$ requires 7067.

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Comment 1 Prof. Anderson PB-3-151 MW=7057?? PosLin THF [1:49] (DCTB;THF)

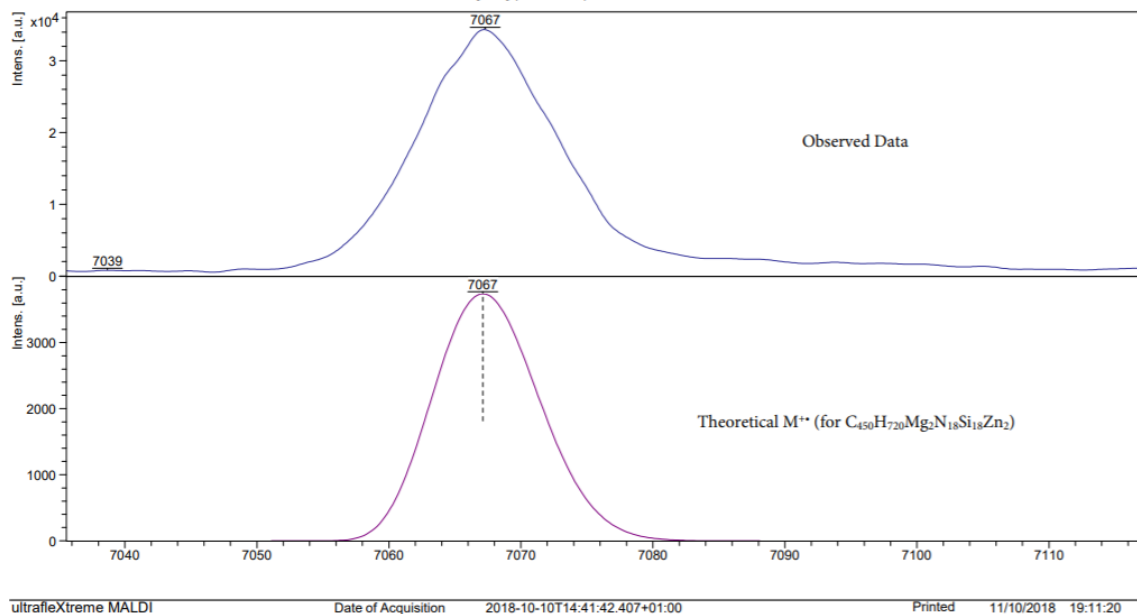


Figure 3.18. Zoom of the MALDI-MS spectrum of **3.7** compared with the predicted isotope profile.

3.8

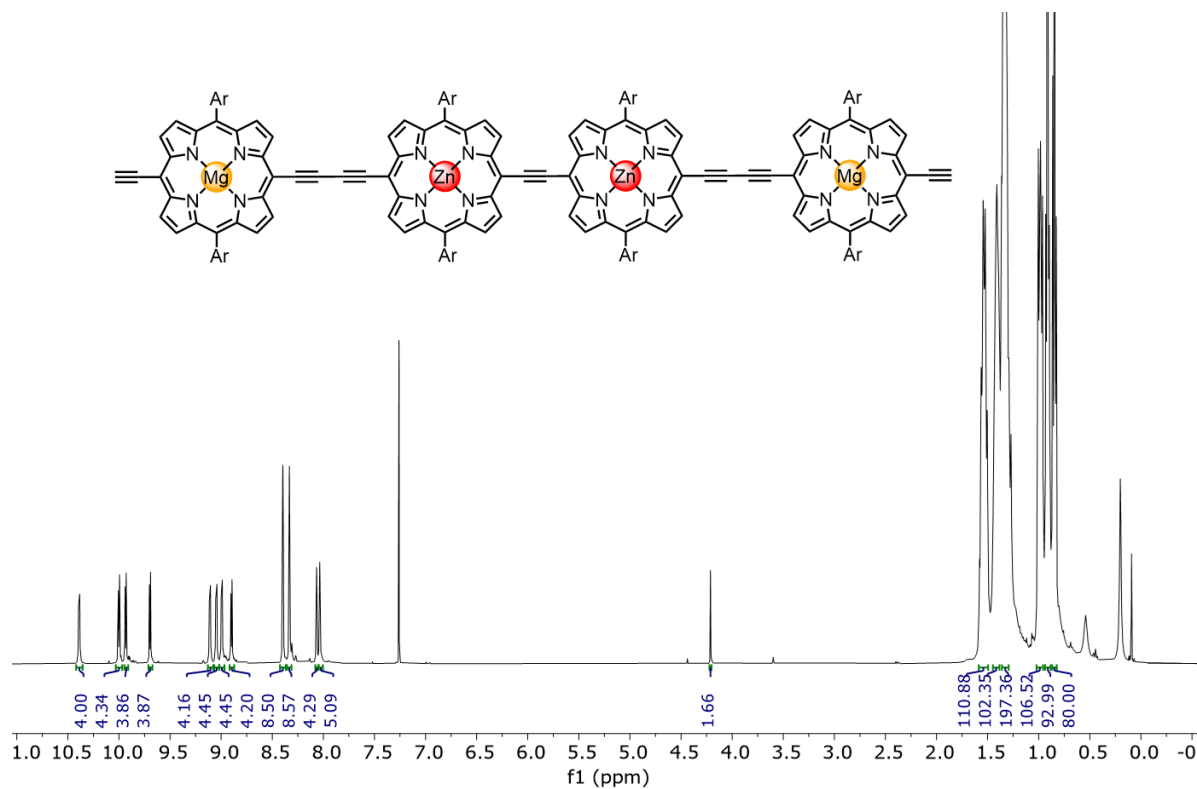


Figure 3.19. The ¹H NMR spectrum of **3.8** (400 MHz, CDCl₃, 298 K).

3.10

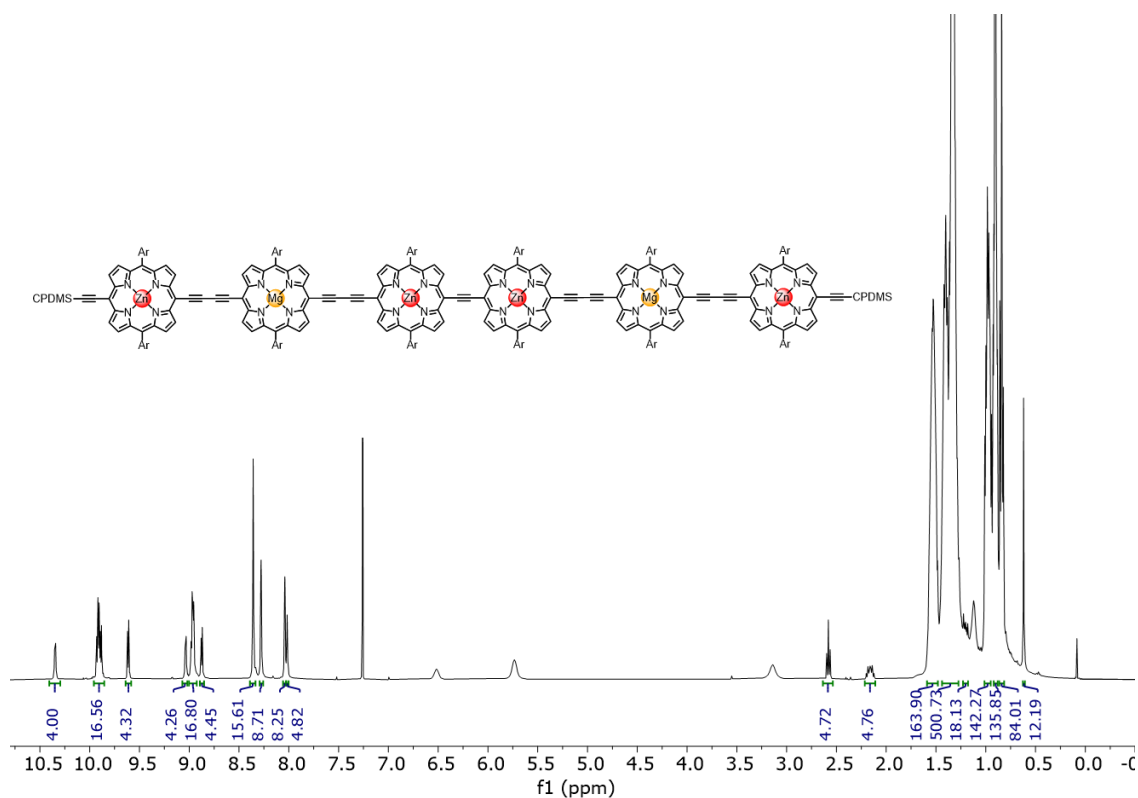


Figure 3.20. The ^1H NMR spectrum of **3.10** (400 MHz, CDCl_3 , 298 K).

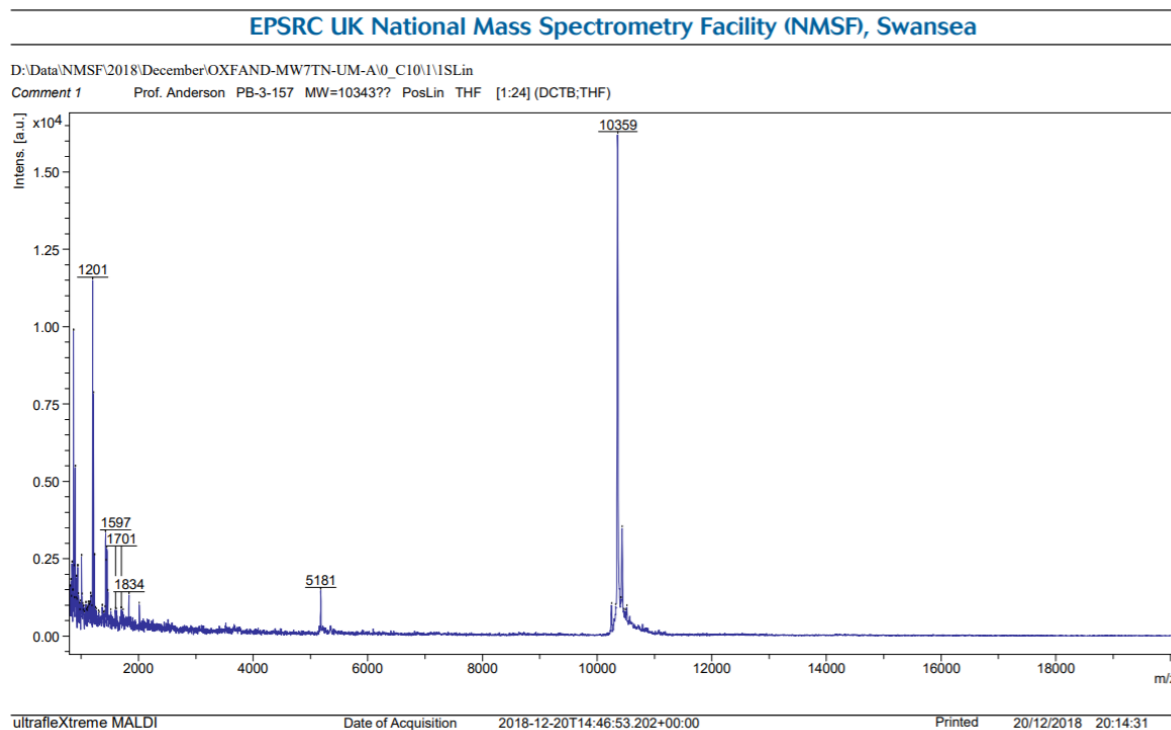


Figure 3.21. The MALDI-MS spectrum of **3.10**, matrix: DCTB. M^+ , $\text{C}_{658}\text{H}_{1044}\text{Mg}_2\text{N}_{26}\text{Si}_{26}\text{Zn}_4$ requires 10359.

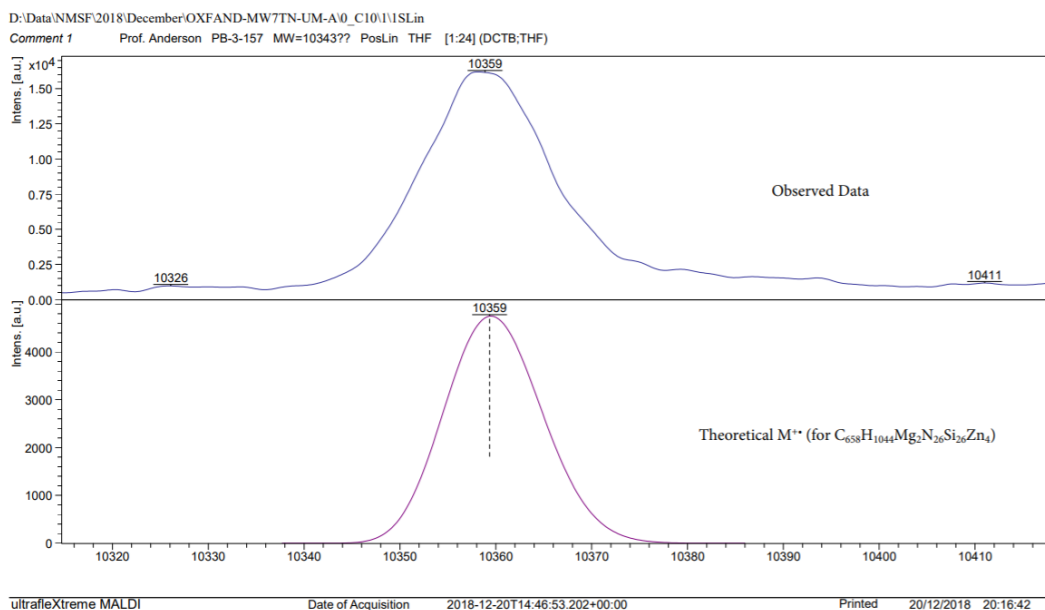


Figure 3.22. Zoom of the MALDI-MS spectrum of **3.10** compared with the predicted isotope profile.

3.11

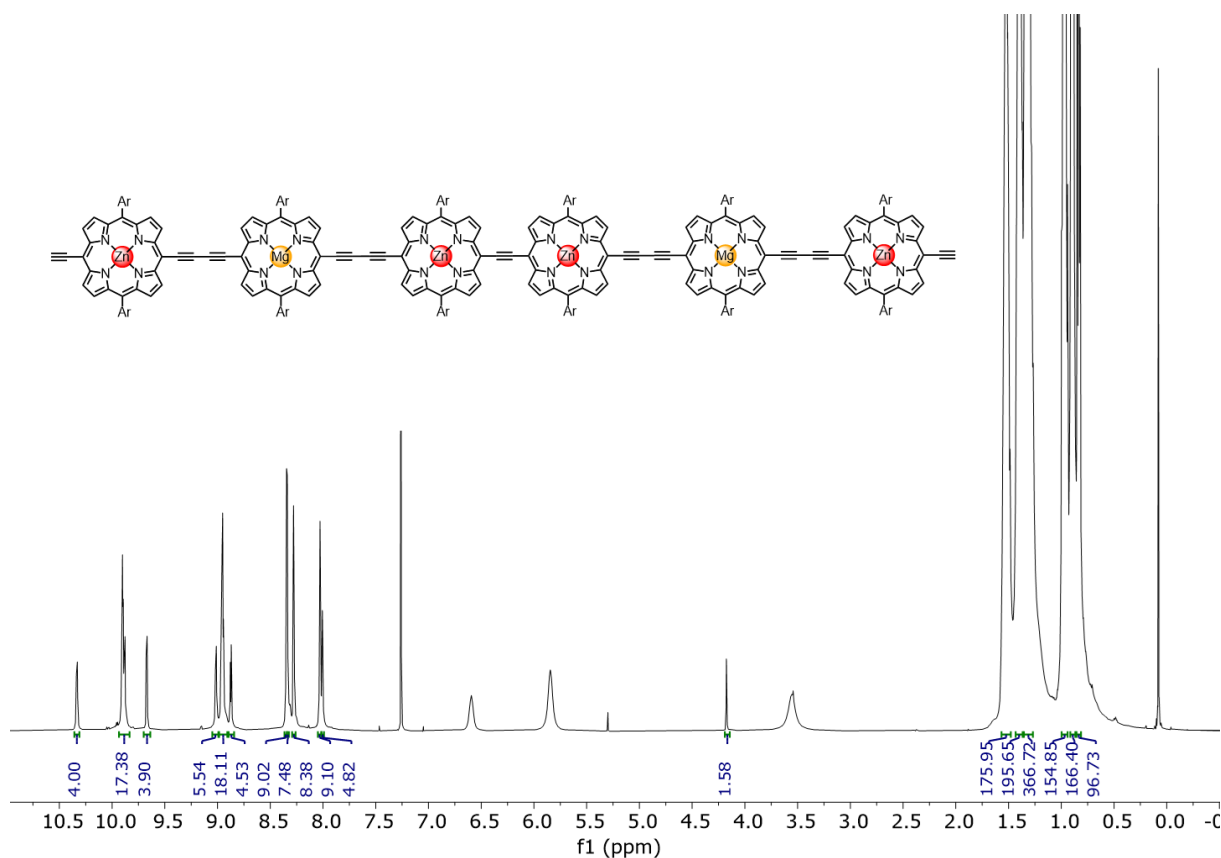


Figure 3.23. The 1H NMR spectrum of **3.11** (400 MHz, $CDCl_3$, 298 K).

3.12

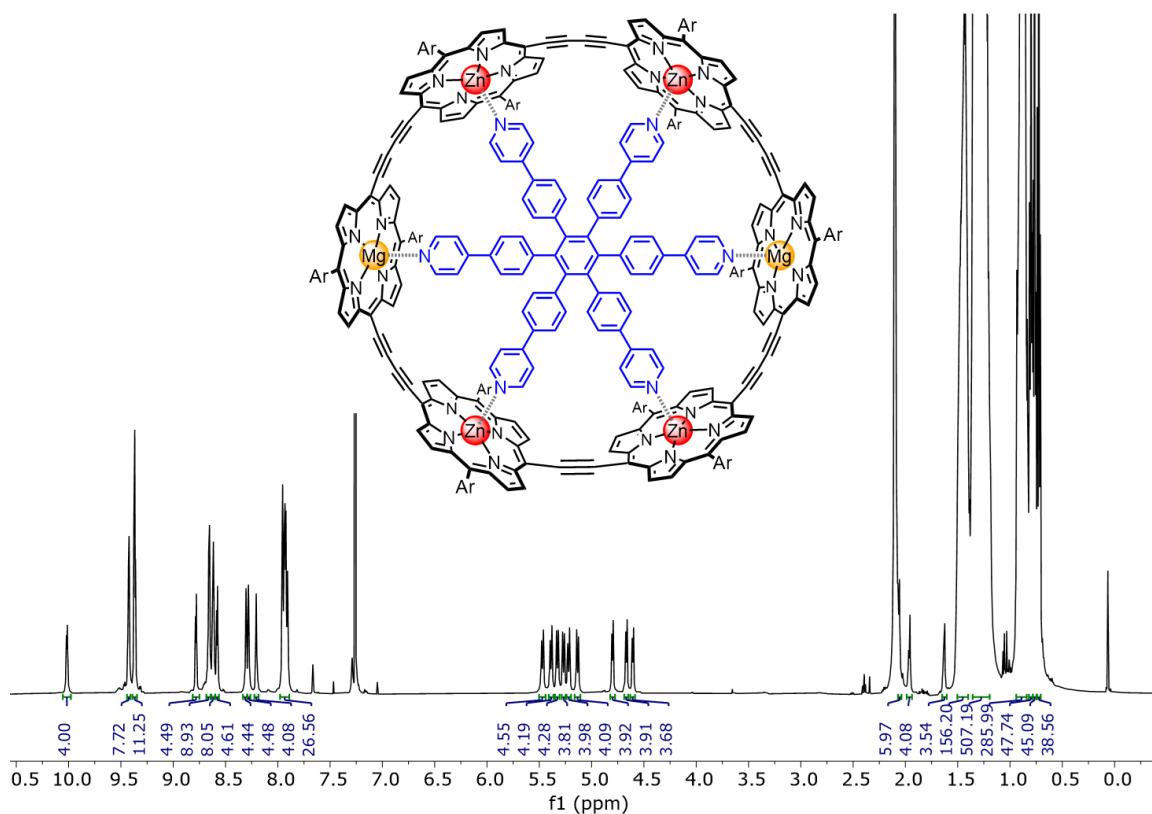


Figure 3.24. The ^1H NMR spectrum of **3.12** (500 MHz, CDCl_3 , 298 K).

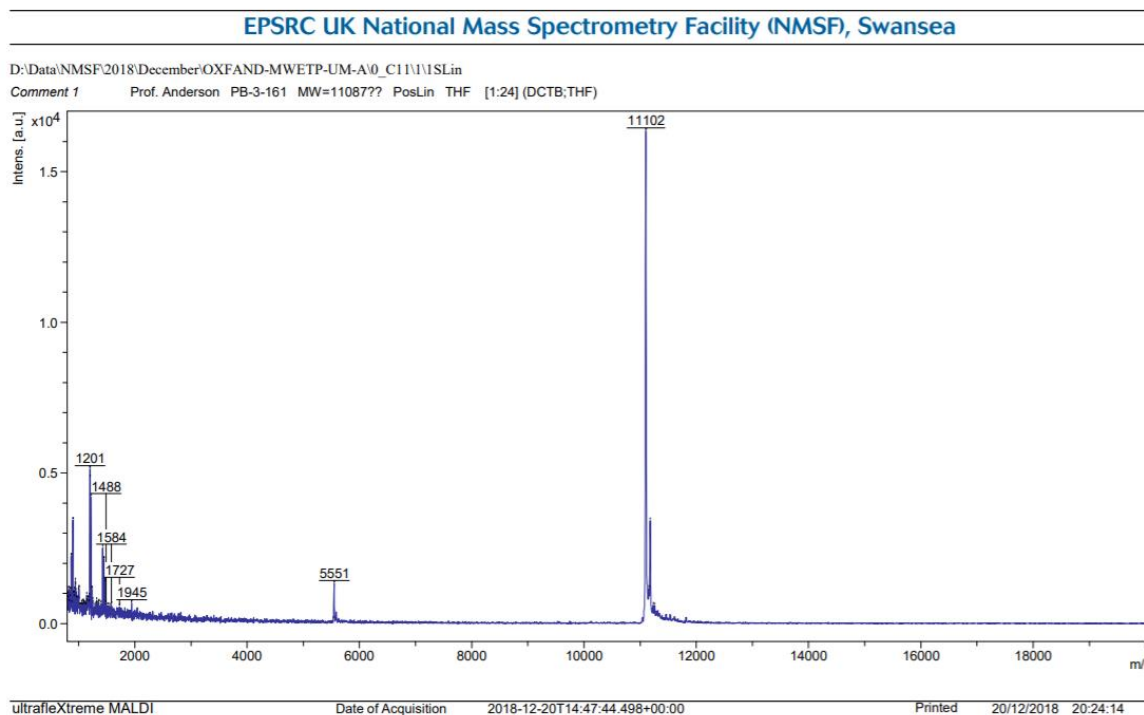


Figure 3.25. The MALDI-MS spectrum of **3.12**, matrix: DCTB. M^+ , $\text{C}_{718}\text{H}_{1068}\text{Mg}_2\text{N}_{30}\text{Si}_{24}\text{Zn}_4$ requires 11105.

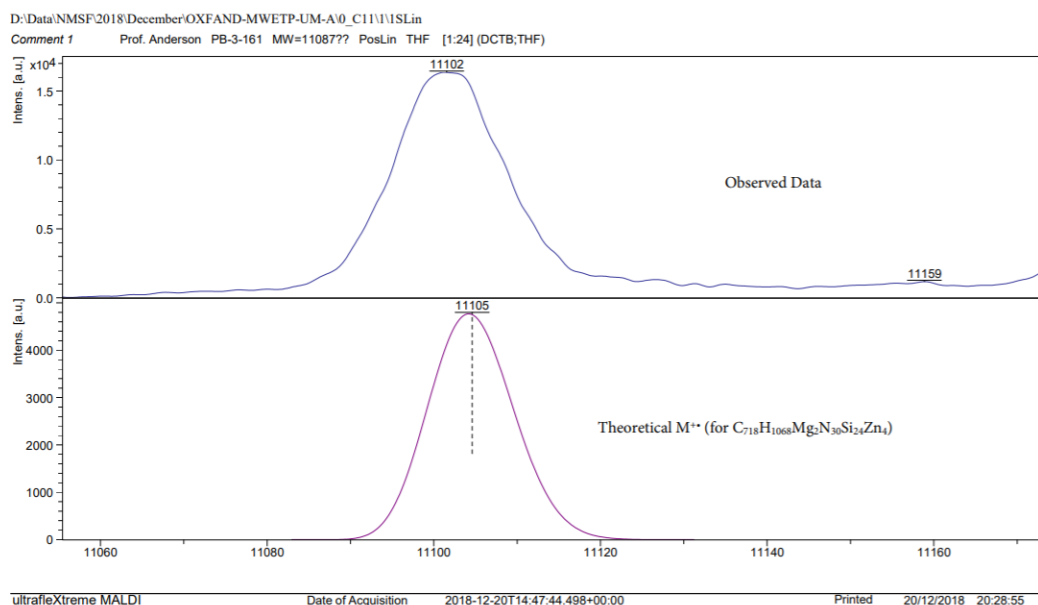


Figure 3.26. Zoom of the MALDI-MS spectrum of **3.12** compared with the predicted isotope profile.

3.13

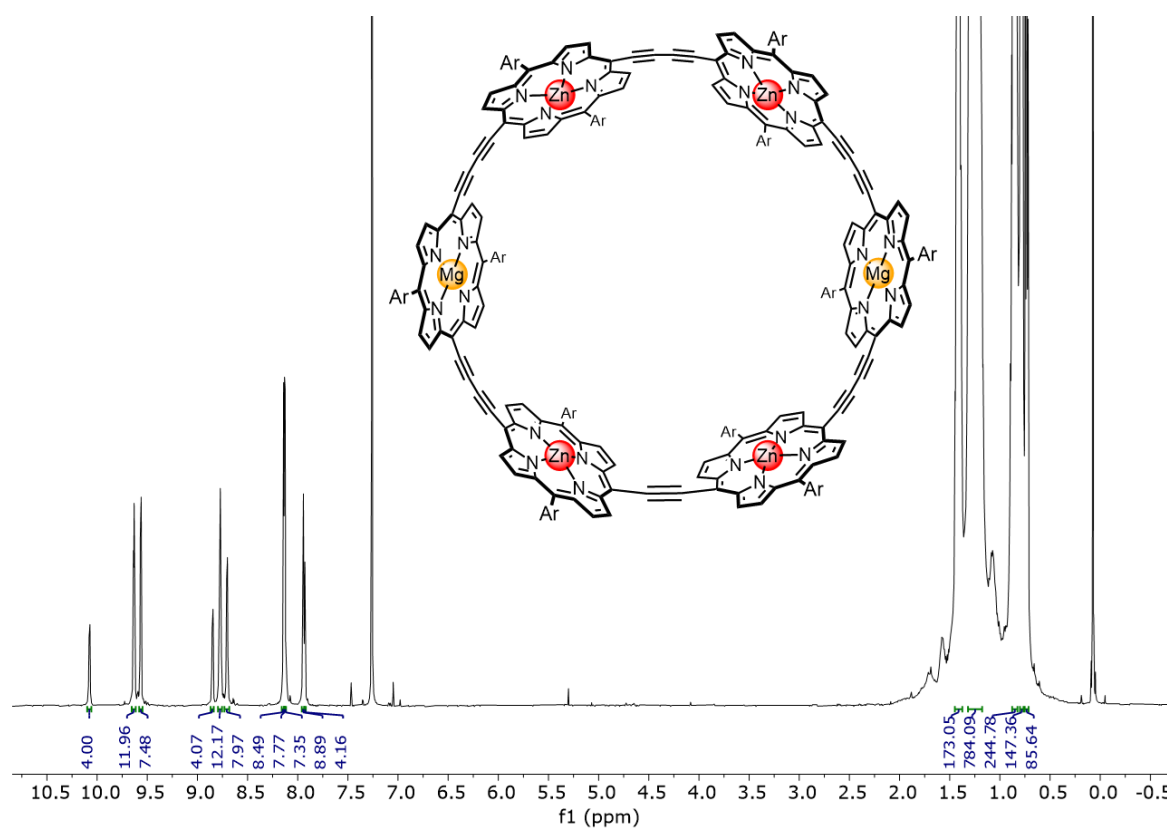


Figure 3.27. The 1H NMR spectrum of **3.13** (500 MHz, $CDCl_3$, 298 K).

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Comment 1 Prof. Anderson PB-3-169 MW=10091?? PosLin THF [1:49] (DCTB;THF)

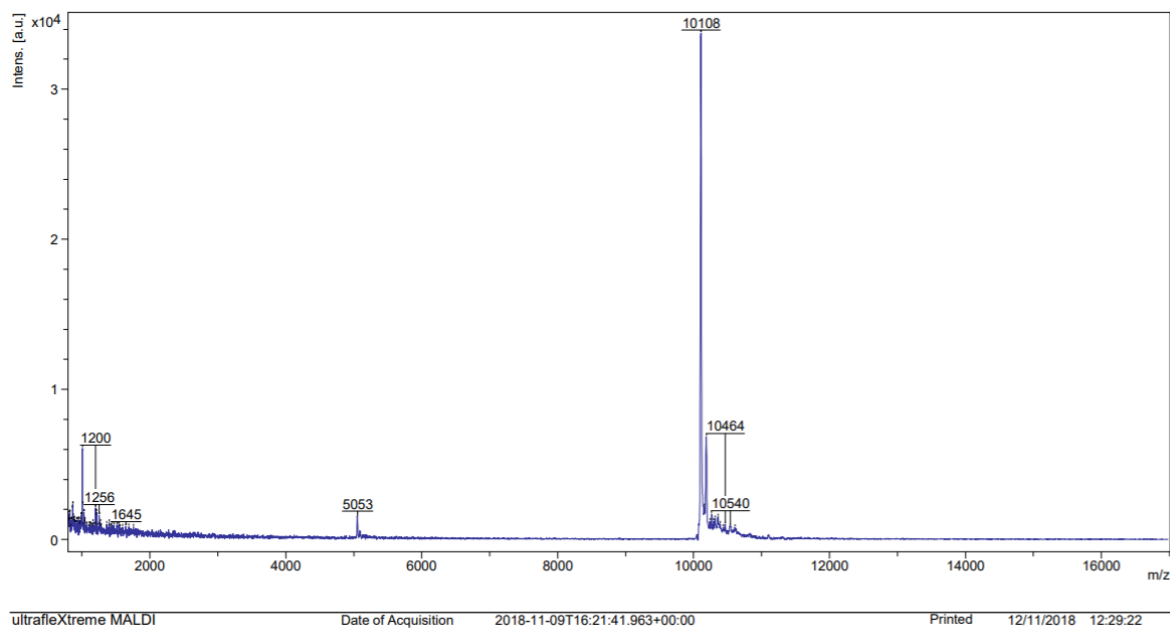


Figure 3.28. The MALDI-MS spectrum of **3.13**, matrix: DCTB. M^+ , $C_{646}H_{1020}Mg_2N_{24}Si_{24}Zn_4$ requires 10107.

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Comment 1 Prof. Anderson PB-3-169 MW=10091?? PosLin THF [1:49] (DCTB;THF)

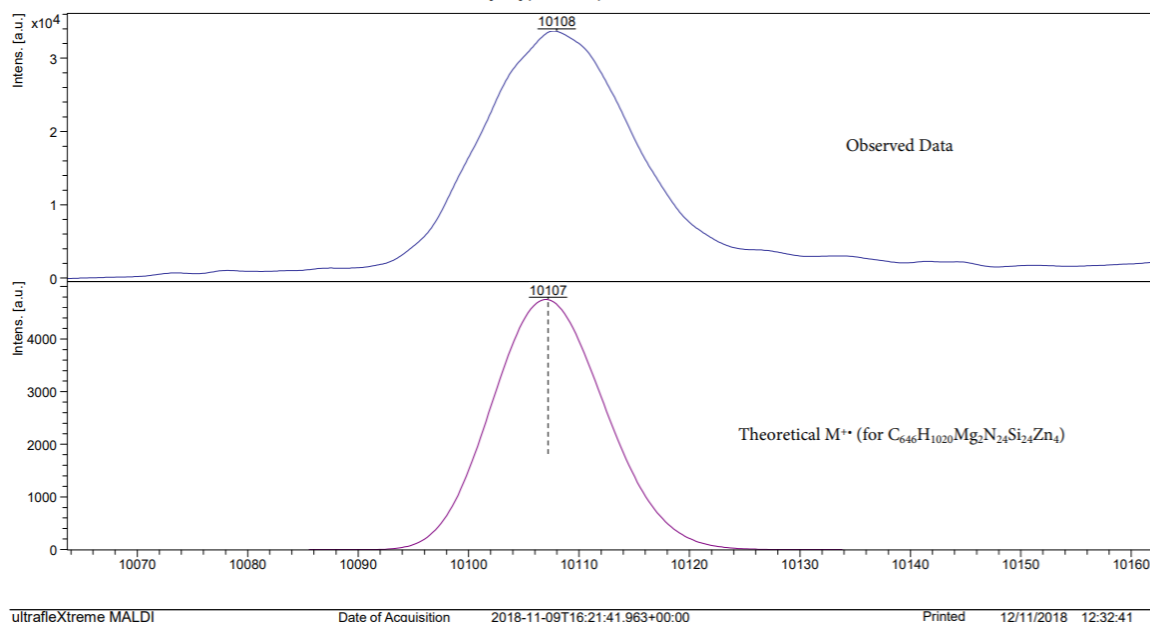


Figure 3.29. Zoom of the MALDI-MS spectrum of **3.13** compared with the predicted isotope profile.

3.14

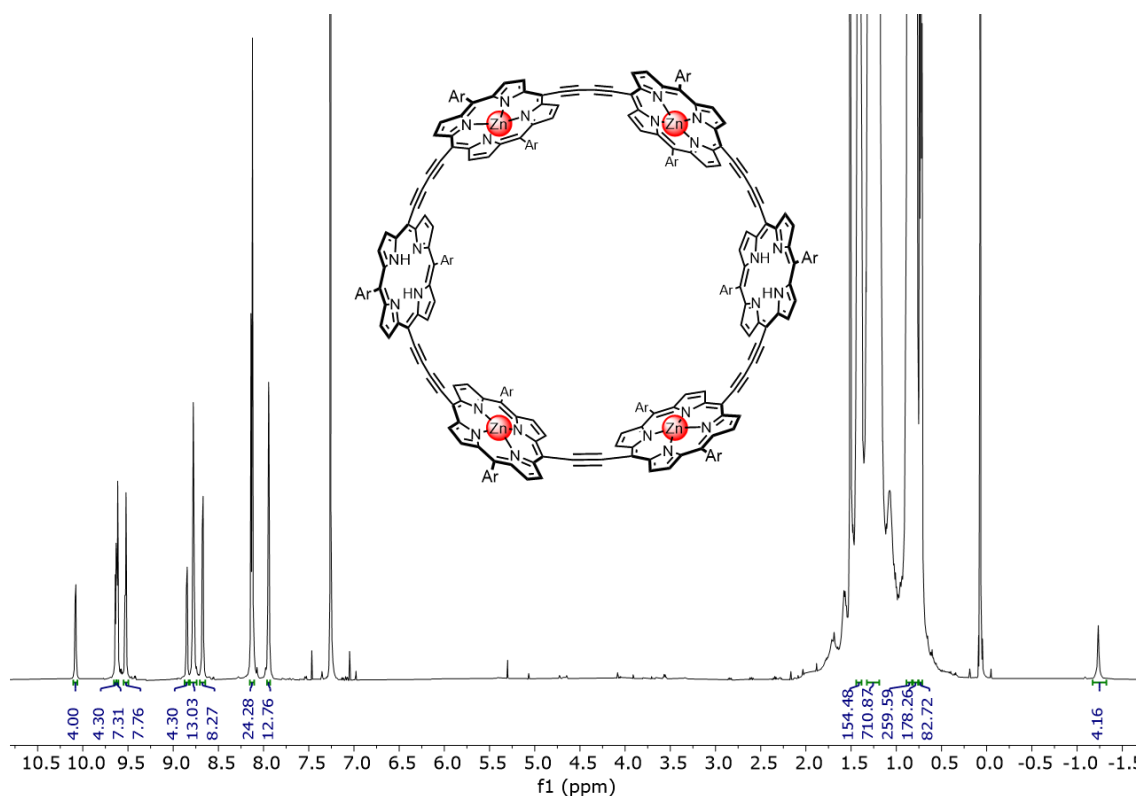


Figure 3.30. The ^1H NMR spectrum of **3.14** (500 MHz, CDCl_3 , 298 K).

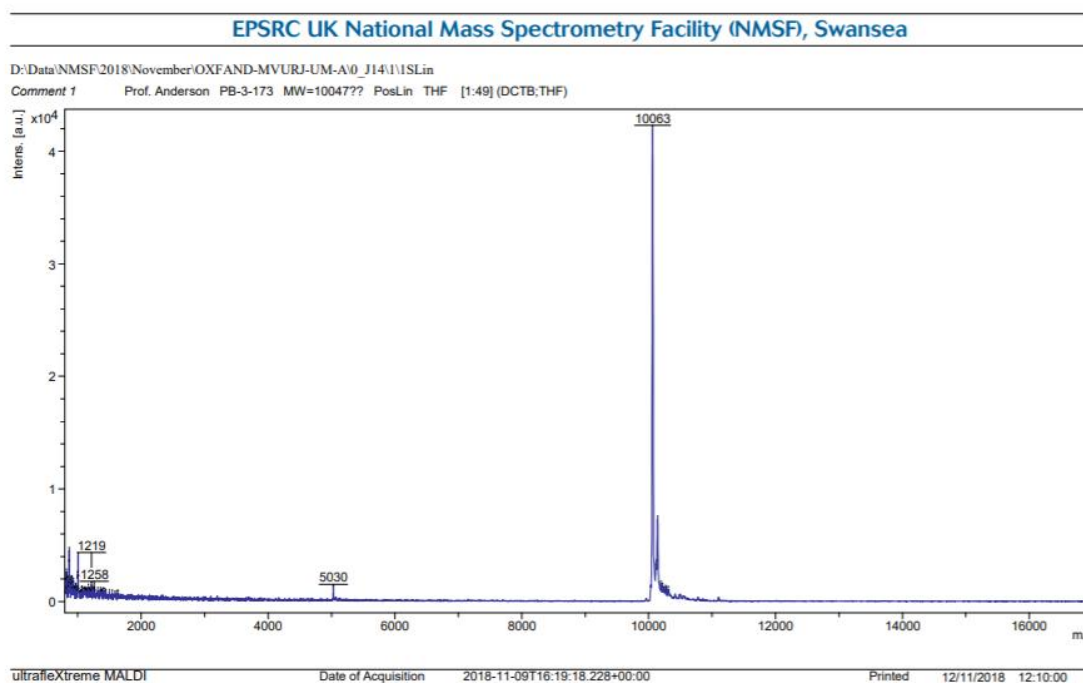


Figure 3.31. The MALDI-MS spectrum of **3.14**, matrix: DCTB. M^+ , $\text{C}_{646}\text{H}_{1024}\text{N}_{24}\text{Si}_{24}\text{Zn}_4$ requires 10062.

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Comment 1 Prof. Anderson PB-3-173 MW=10047?? PosLin THF [1.49] (DCTB;THF)

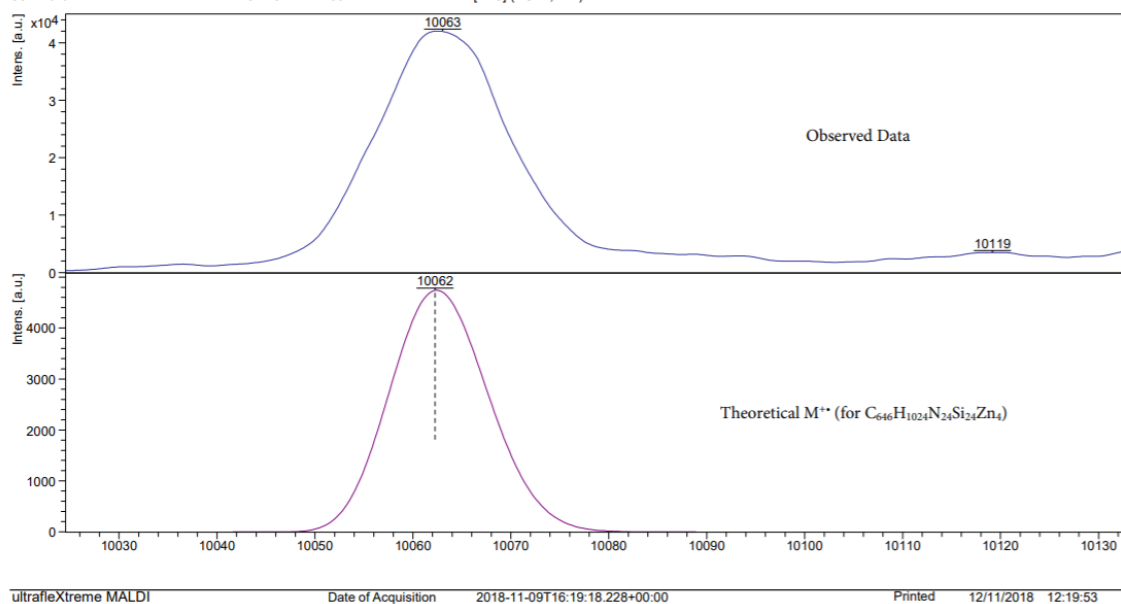


Figure 3.32. Zoom of the MALDI-MS spectrum of **3.14** compared with the predicted isotope profile.

3.15

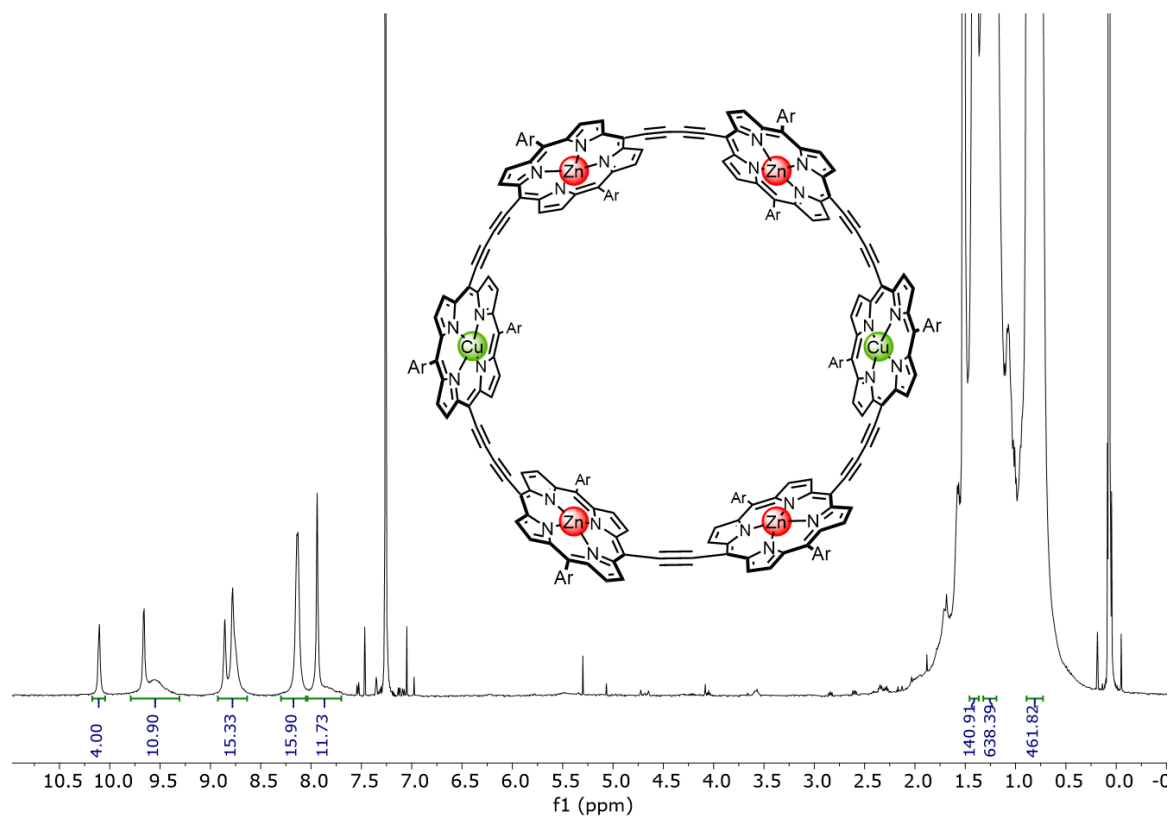


Figure 3.33. The ¹H NMR spectrum of **3.15** (500 MHz, CDCl₃, 298 K).

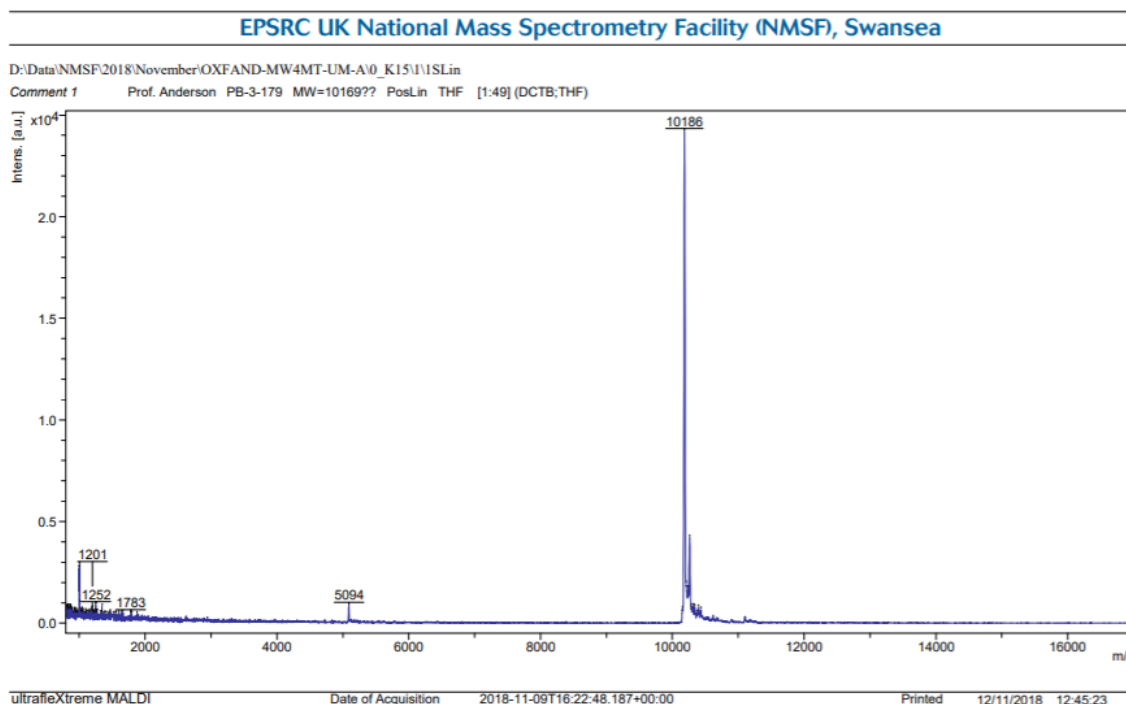


Figure 3.34. The MALDI-MS spectrum of **3.15**, matrix: DCTB. M^+ , $C_{646}H_{1020}Cu_2N_{24}Si_{24}Zn_4$ requires 10185.

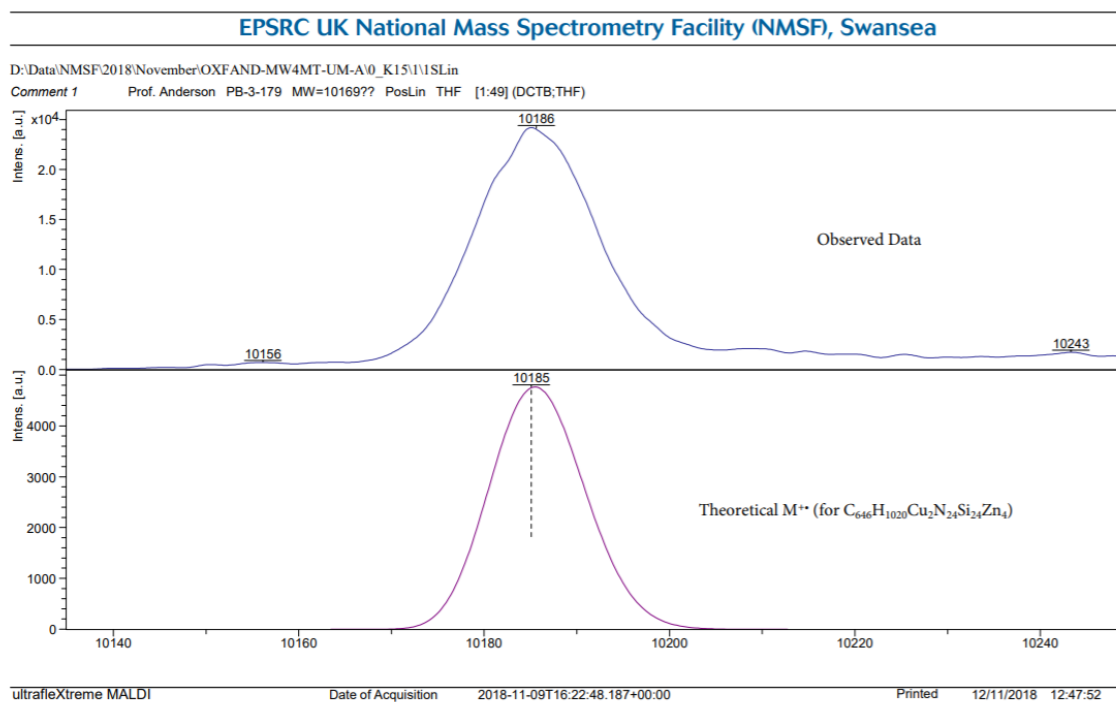


Figure 3.35. Zoom of the MALDI-MS spectrum of **3.15** compared with the predicted isotope profile.

asym-Cu₂Zn₄·T6

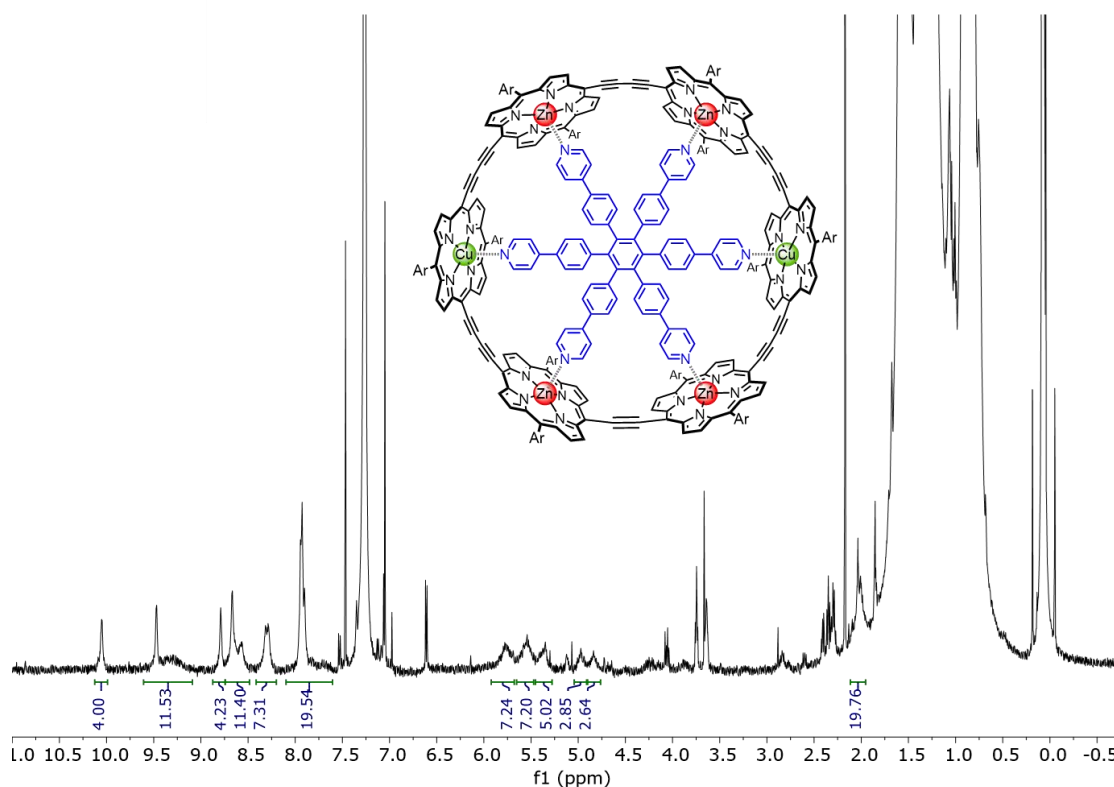


Figure 3.36. The ¹H NMR spectrum of *asym*-Cu₂Zn₄·T6 (500 MHz, CDCl₃, 298 K).

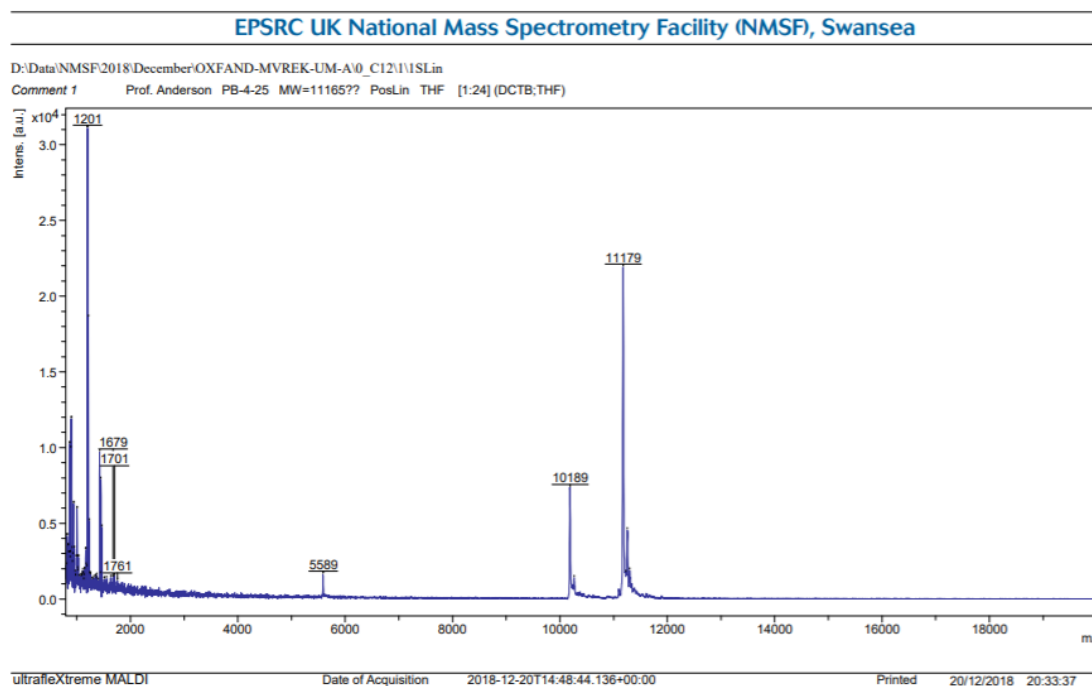


Figure 3.37. The MALDI-MS spectrum of *asym*-Cu₂Zn₄·T6, matrix: DCTB. M⁺, C₇₁₈H₁₀₆₈Cu₂N₃₀Si₂₄Zn₄ requires 11182.

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Comment 1 Prof. Anderson PB-4-25 MW=11165?? PosLin THF [1:24] (DCTB,THF)

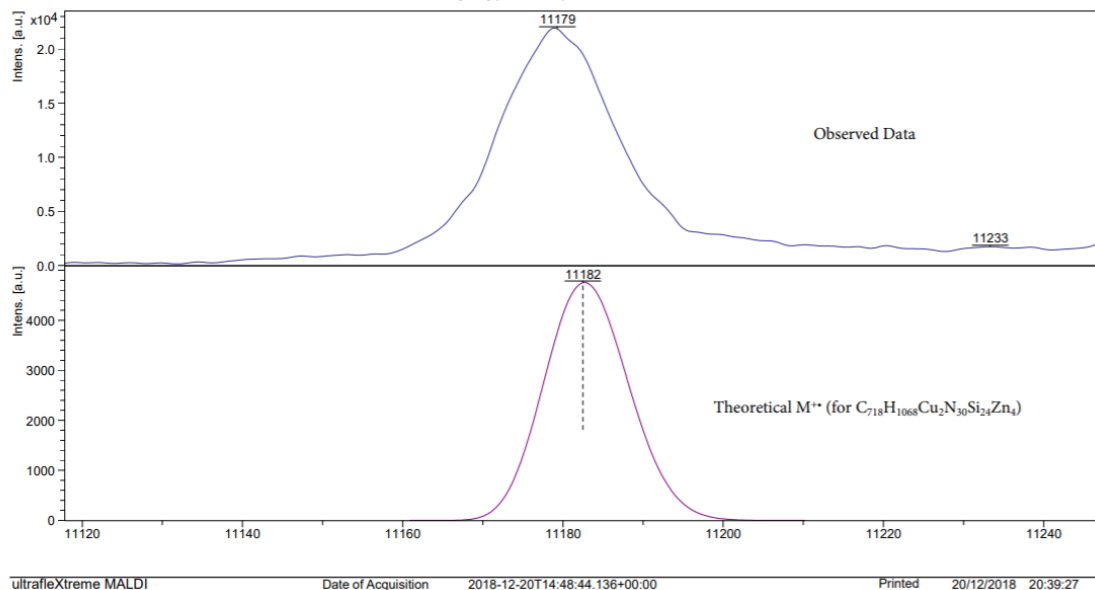


Figure 3.38. Zoom of the MALDI-MS spectrum of *asym*- $Cu_2Zn_4 \cdot T6$ compared with the predicted isotope profile.

3.16

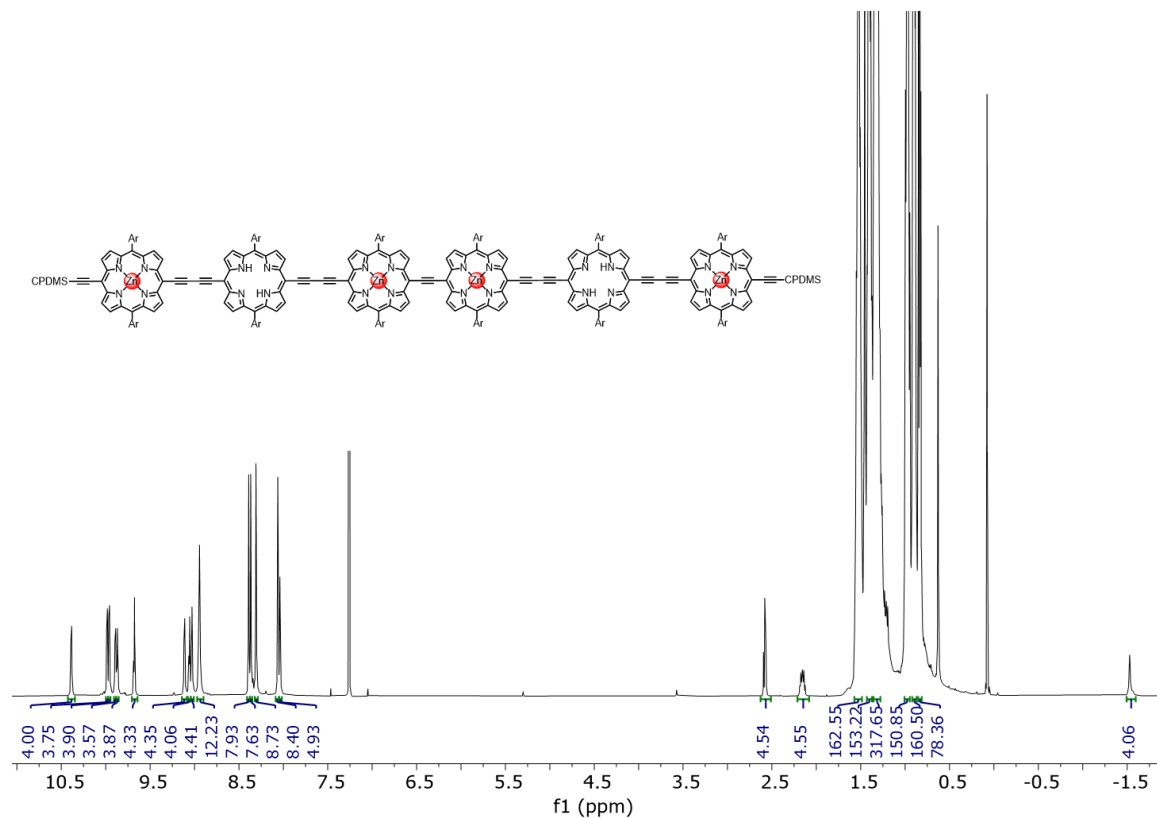
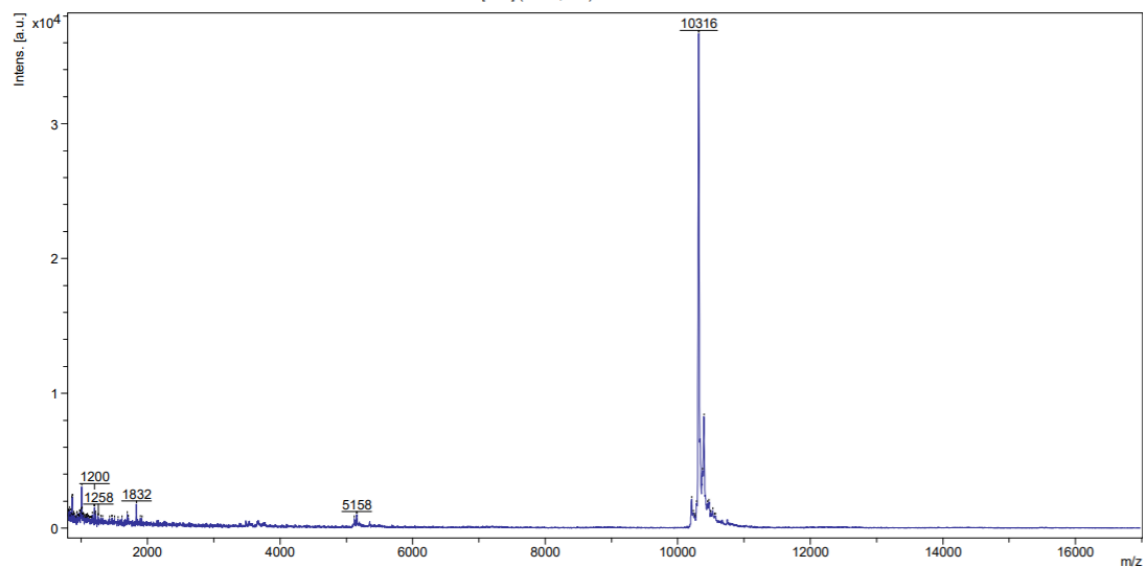


Figure 3.39. The 1H NMR spectrum of **3.16** (500 MHz, $CDCl_3$, 298 K).

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Comment 1 Prof. Anderson PB-3-171 MW=10299?? PosLin THF [1:49] (DCTB;THF)



ultrafleXtreme MALDI

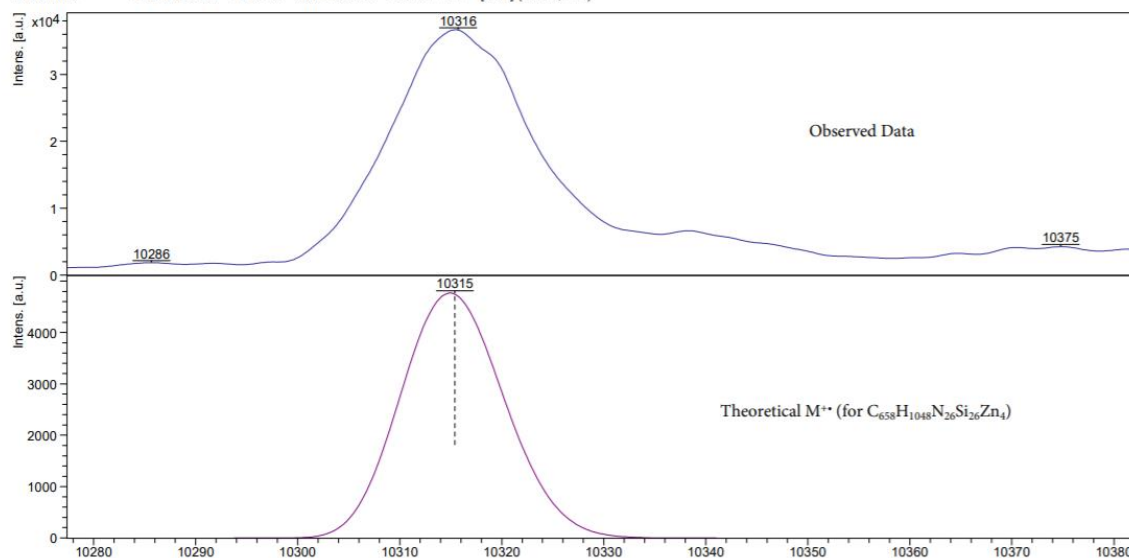
Date of Acquisition 2018-11-09T16:20:16.291+00:00

Printed 12/11/2018 12:23:07

Figure 3.40. The MALDI-MS spectrum of **3.16**, matrix: DCTB. M^+ , $C_{658}H_{1048}N_{26}Si_{26}Zn_4$ requires 10315.

D:\Data\NMSF\2018\November\OXFAND-MW3XJ-UM-A\0_J15\1\1SLin

Comment 1 Prof. Anderson PB-3-171 MW=10299?? PosLin THF [1:49] (DCTB;THF)



ultrafleXtreme MALDI

Date of Acquisition 2018-11-09T16:20:16.291+00:00

Printed 12/11/2018 12:27:07

Figure 3.41. Zoom of the MALDI-MS spectrum of **3.16** compared with the predicted isotope profile.

3.17

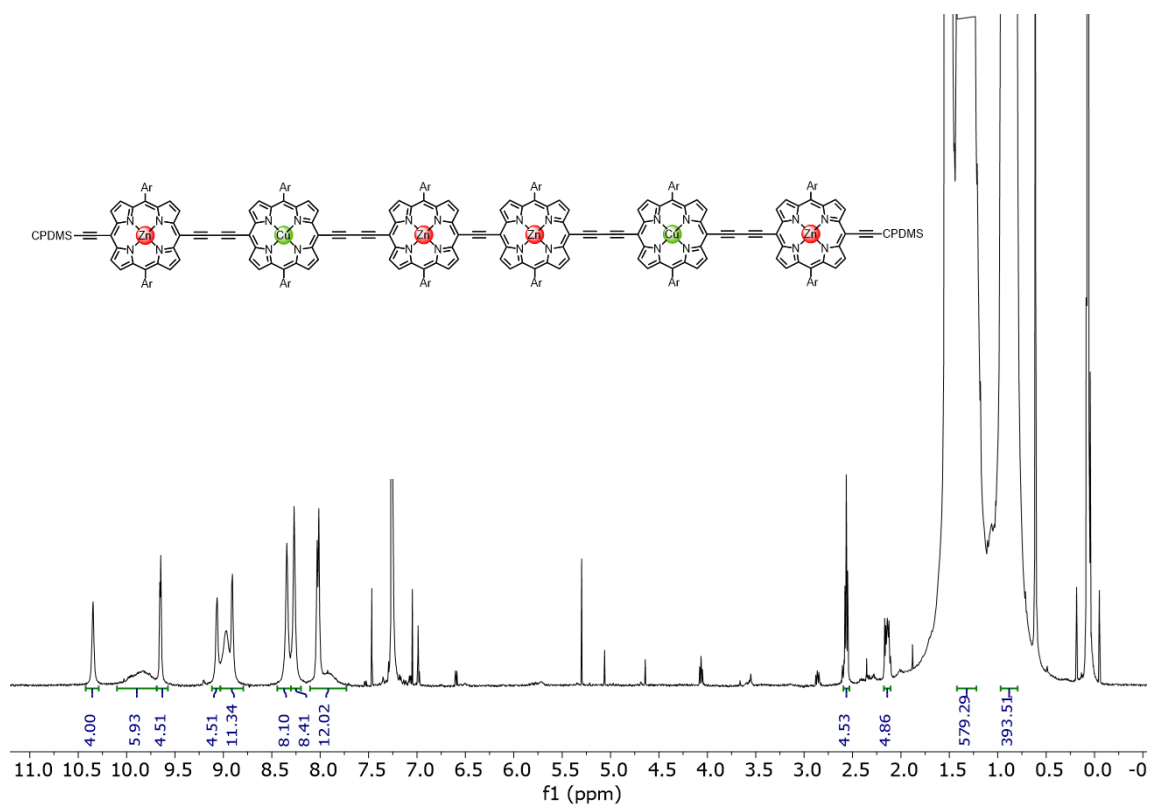


Figure 3.42. The ¹H NMR spectrum of **3.17** (500 MHz, CDCl₃, 298 K).

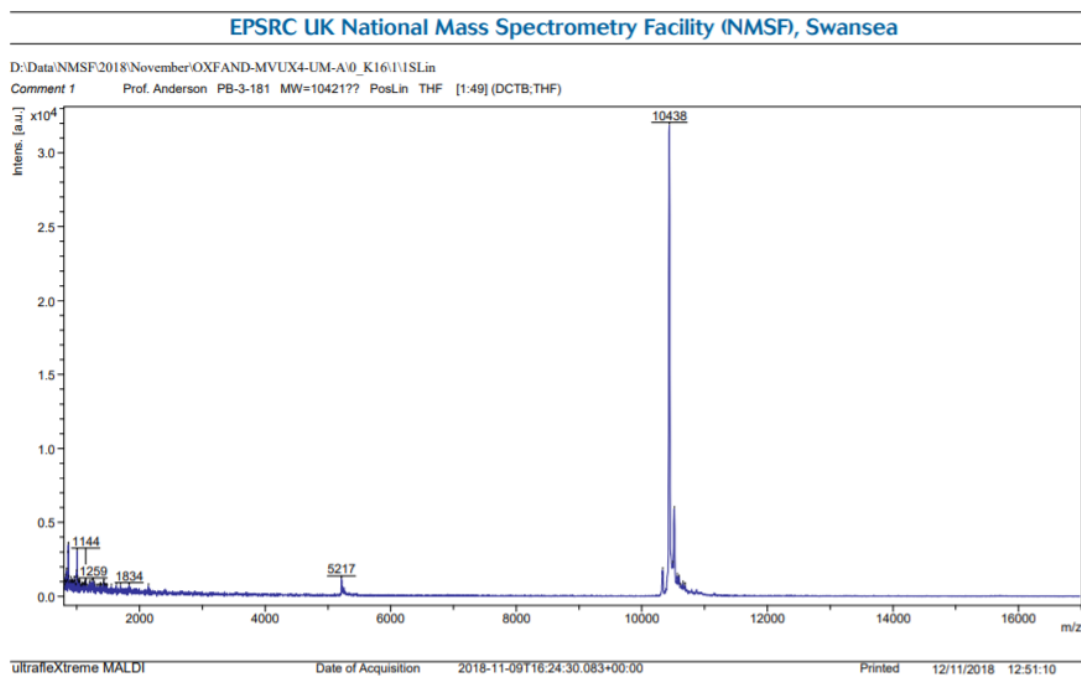


Figure 3.43. The MALDI-MS spectrum of **3.17**, matrix: DCTB. M⁺, C₆₅₈H₁₀₄₄Cu₂N₂₆Si₂₆Zn₄ requires 10438.

cut-asym-Cu₂Zn₄·T6

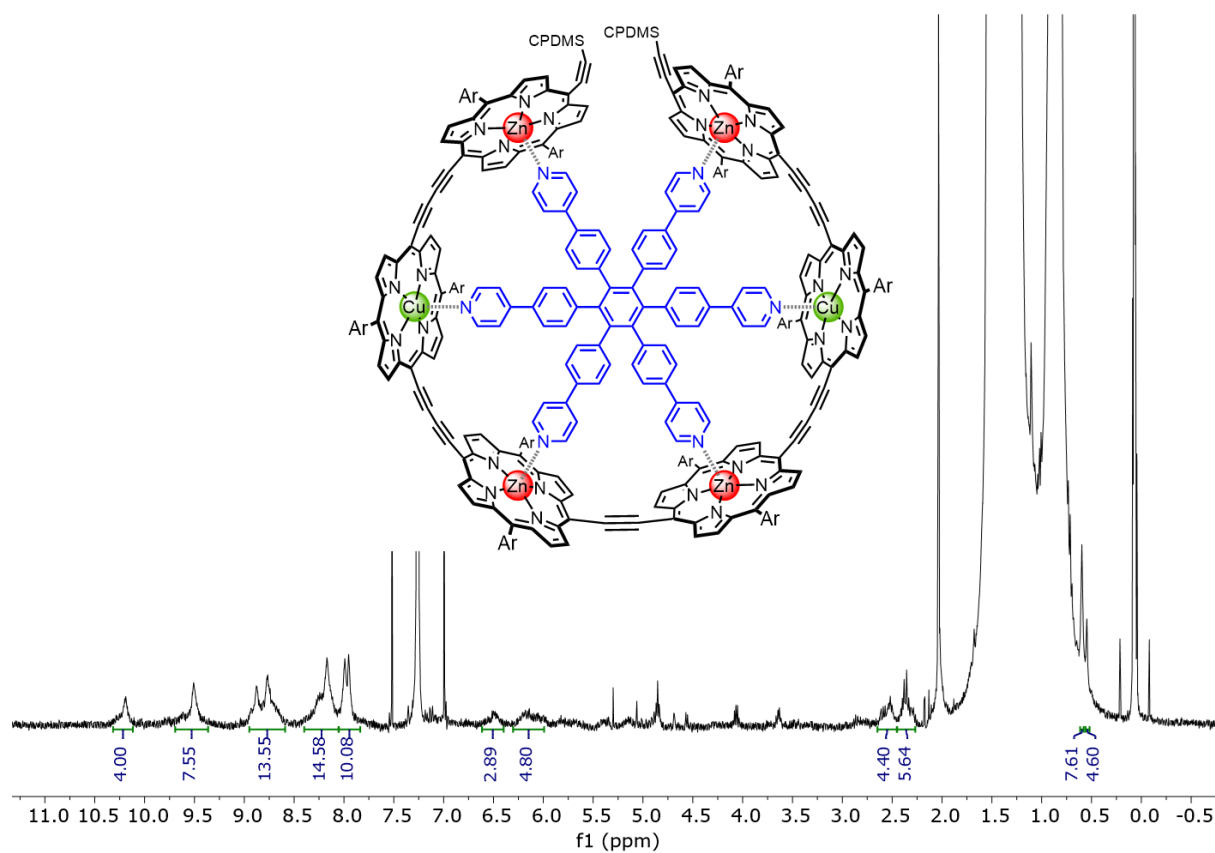


Figure 3.45. The ^1H NMR spectrum of *cut-asym-Cu₂Zn₄T6* (500 MHz, CDCl_3 , 298 K).

3.14 References

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Allosteric Cooperativity and Template-Directed Synthesis with Stacked Ligands in Porphyrin Nanorings

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4.1 Abstract

Cooperative binding processes are common in Nature and are important for regulating many enzymes and receptors. Allosteric cooperativity is a subcategory where the binding of one ligand changes the affinity for subsequent binding events. This chapter describes the thermodynamic and kinetic investigation of complexes where two oligopyridine templates stack on top of each other inside porphyrin nanorings. Using UV/vis/NIR titrations and kinetic ^1H NMR experiments, it was found that in a 12-porphyrin nanoring where there is space for the templates to bend, there is high positive allosteric cooperativity. On the other hand, in a 6-porphyrin nanoring where the templates are more constrained, there is negative cooperativity. Interestingly, in the case of the negatively cooperative systems, there is a high kinetic barrier for exchange of templates and reaching equilibrium can take up to several weeks. The details of these kinetics are investigated.

4.2 Introduction

Allosteric cooperativity, a natural biological phenomenon¹ used to either upregulate or downregulate biological activity, can act as a valuable tool in molecular and materials design.² Allosteric cooperativity can be either positive or negative, and positive cooperativity appears to be more prevalent in Nature. Less common are examples of negative cooperativity, but the decrease in affinity for successive ligands can make these systems amenable to structural studies of naturally occurring ligand-bound intermediates and, hence, allow a detailed understanding of the allosteric mechanism.³

Allosteric systems are classified as homotropic or heterotropic. Homotropic systems coordinate several identical ligands, whereas heterotropic systems coordinate different types of ligands.⁴ In the study of artificial allosteric systems, the positive homotropic type is particularly hard to achieve, but its ability to amplify weak chemical signals and properties has proven very useful in supramolecular chemistry for making sensitive chemosensors for pH fluctuations,⁵ fluoride anions,⁶ oligosaccharides,⁷ dicarboxylic acids,⁸ and fullerenes.⁹ Strong positive allosteric cooperativity has also been used in catalysis,¹⁰ for selective removal and amplified delivery of anticancer drugs,¹¹ to facilitate accurate control of switching in a molecular machine,¹² and to induce rigidity in a large macrocycle.¹³ The mechanism of allosteric cooperativity in supramolecular systems have been studied using EPR,¹⁴ NMR,¹⁵ UV-vis and fluorescence spectroscopy.¹⁶

In Chapter 2, it was described how two molecules of the template **T3** can stack and thus both bind inside the hexaporphyrin nanoring **c-P6** (Figure 4.1b).¹⁷ In this chapter the thermodynamic and kinetic details of this stacking behavior are investigated. Through mechanistic analysis of the binding process, we discovered that it occurs through an unusual kinetic effect whereby the **c-P6·(T3)₂** complex is formed initially; in the presence of free **c-P6**. This mixture slowly equilibrates to the thermodynamically favored **c-P6·T3** complex. The kinetic control in self-assembly of synthetic host-guest systems is quite a rarity, but some examples have been reported.¹⁸ Another three-legged template **T3N** was also synthesized for comparison, and this template shows the same stacking behavior as **T3**. The **T3N** ligand was selected for investigation because its *s*-triphenyltriazine core was anticipated to be flatter than the 1,3,5-triphenylbenzene core of **T3**,¹⁹ which should allow two **T3N** ligands to stack more easily inside **c-P6**. Finally, it was discovered that the stacking behavior can be used to create highly cooperative supramolecular systems. It was found, that the new, elongated six-legged template **T6e** which can stack inside the 12-porphyrin nanoring **c-P12** (Figure 4.1a)²⁰ with a very high²¹ cooperativity factor. In Chapter 5 it will be shown how this strong allosteric cooperativity can be used in synthesis.

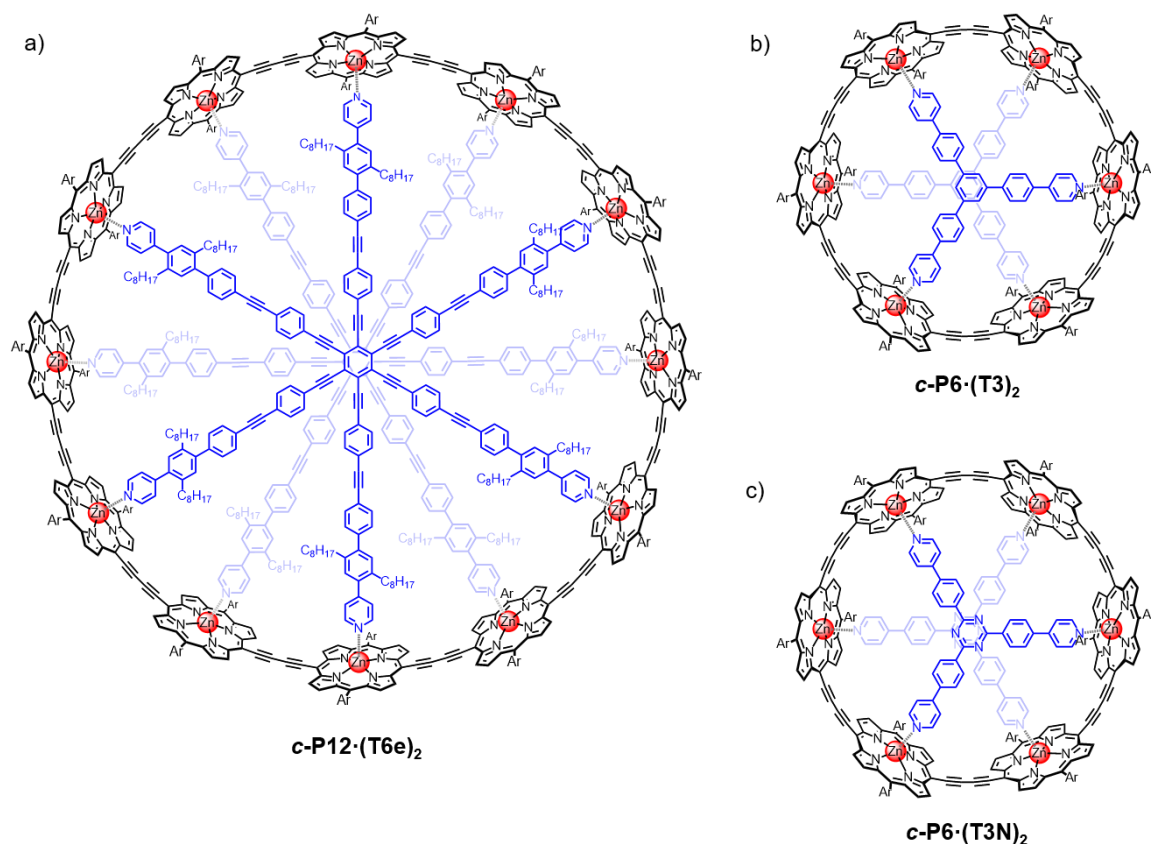


Figure 4.1. a) **c-P12·(T6e)₂**, b) **c-P6·(T3)₂** and c) **c-P6·(T3N)₂**.

4.3 Molecular modelling

Geometry optimizations were performed by Dr Michael Jirasek and Kristina Eriksen. The optimizations of the complexes and templates were simplified by replacing aryl and octyl solubilizing groups with hydrogen atoms. Geometries were optimized using Gaussian16/A.03²² and either DFT (B3LYP/3-21G functional/basis set, used for **c-P6**·(**T3**)₂, **c-P6**·(**TN3**)₂, **T3** and **TN3**) or semiempirical PM6 method (used for **c-P12**·(**T6e**)₂ and **T6e**). DFT optimized geometries were confirmed as local minima by performing frequency calculation which showed no imaginary frequencies.

Two local minima with a difference in 4 kJ/mol was found for the complex **c-P12**·(**T6e**)₂, and in both of these, **c-P12** is flat in the plane of the zinc atoms. In the geometry with the lowest energy, one of the **T6e** molecules is flat within the plane, and the other **T6e** molecule is bending into a dome-shape. The other geometry is symmetric and both **T6e** molecules are bent. The fact that these two geometries are so close in energy suggests that there is high flexibility in bowl-to-bowl inversion, as confirmed by the *D*₁₂ symmetric NMR spectra. Figure 4.2a shows the symmetric optimized geometry.

Contrary to **c-P12**, the smaller nanoring **c-P6** does not provide space for sufficient bending of the template to place nitrogen atoms in a plane and the **c-P6**·(**T3**)₂ and **c-P6**·(**T3N**)₂ complexes have to twist into saddle-shapes to facilitate the Zn–N interaction (Figure 4.2b and c). In addition, the **T3** and **T3N** templates have to bend to fit in the ring, and they have to do so more than **T6e** because the ring is smaller.

The doming of each template can be quantified from the average angle between the center of the complex and the zinc atom over the pyridine carbon *para* to the nitrogen (averaged over every pyridine of the complex) This deformation angle is as follows: **c-P6**·(**T3**)₂: 12.8°, **c-P6**·(**T3N**)₂: 12.0°, and **c-P12**·(**T6e**)₂: 5.8°. As expected, the doming of **T6e** is half of **T3** and **T3N** because the porphyrin ring is twice as big.

The average separation between the central stacked benzene units in **c-P6**·(**T3**)₂ (4.05 Å) is significantly longer than the core stacking distance in **c-P6**·(**TN3**)₂ (3.51 Å) and **c-P12**·(**T6e**)₂ (3.56 Å). This suggests a stabilizing π - π interaction in the **c-P6**·(**TN3**)₂ and **c-P12**·(**T6e**)₂ complexes. In the **c-P6**·(**T3**)₂ complex, the phenylene rings of the **T3** molecules twist in a propeller shape. It is organized such that one of the hydrogens of one phenylene ring points

directly to the middle of the π -system of another phenylene ring on the other **T3** molecule with approximately 3.0 Å distance on average. This way, they make a close stacking and have six favorable H- π interactions, even though the central core units do not seem to have much π - π stabilization.

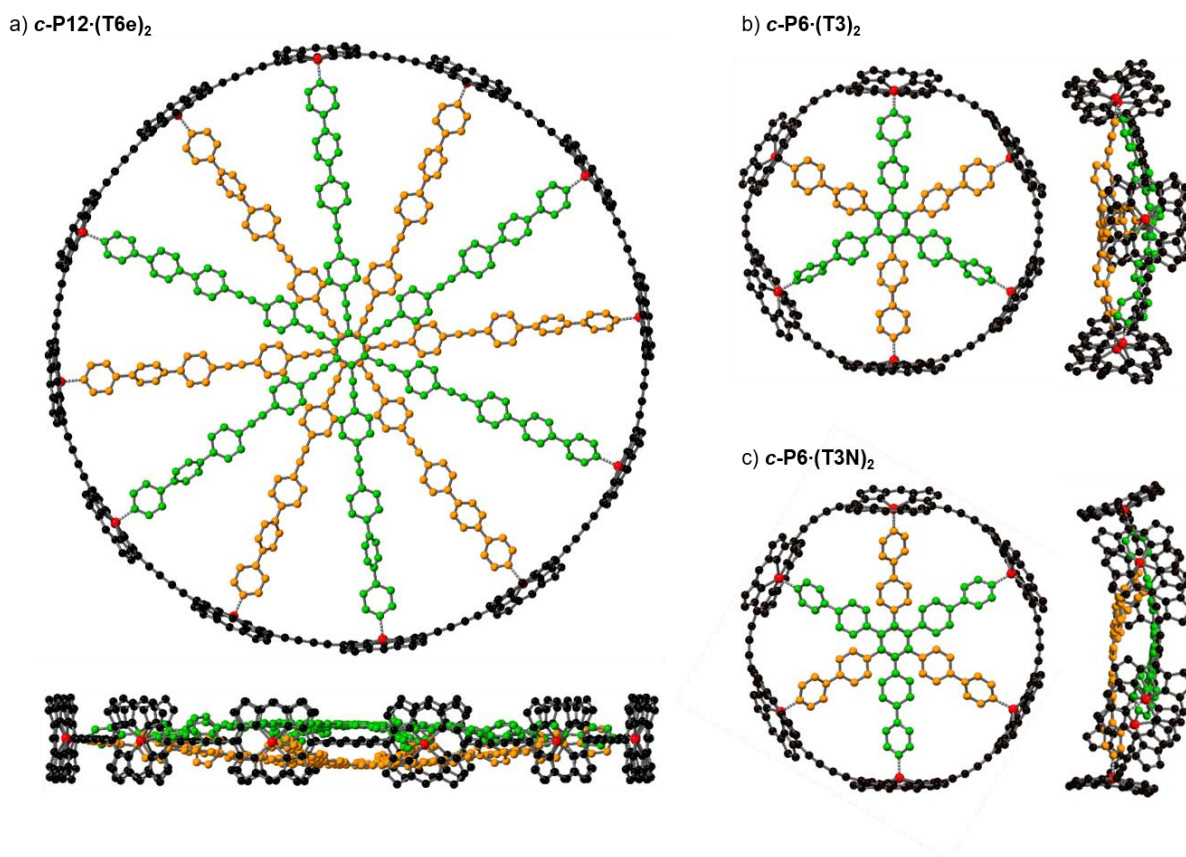
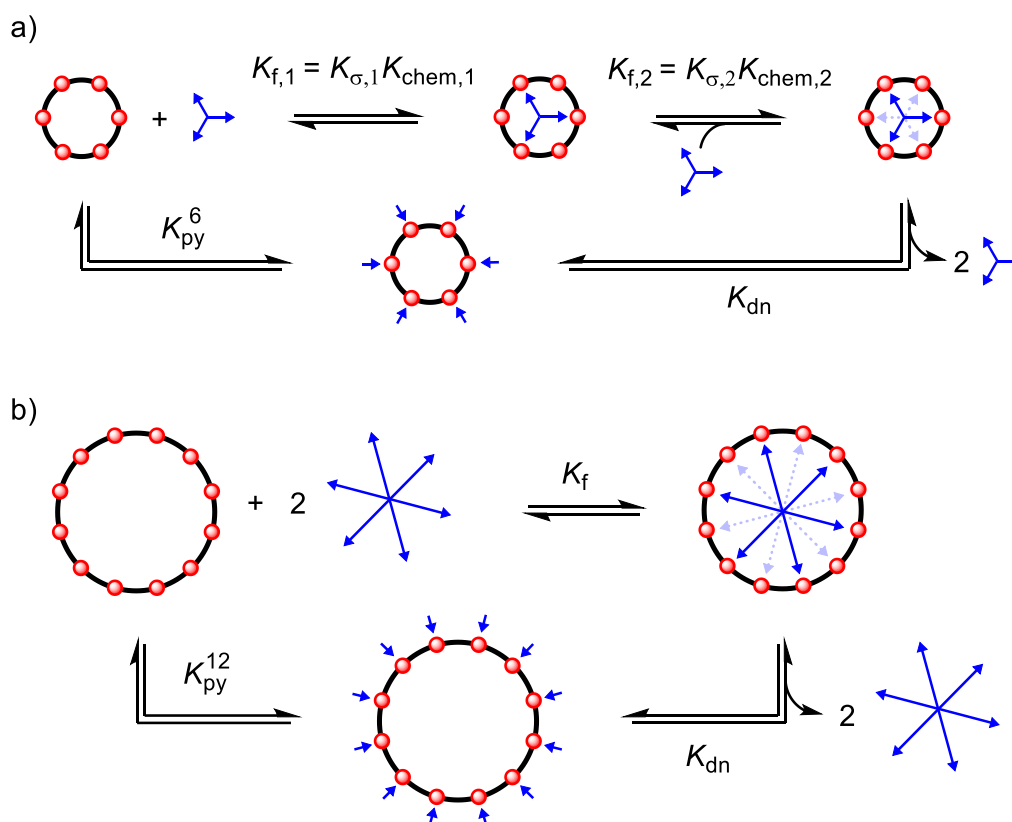


Figure 4.2. a) Optimized geometry of **c-P12·(T6e)₂** using the semi empirical method PM6. b) and c) DFT optimized geometries of **c-P6·(T3)₂** and **c-P6·(T3N)₂** respectively using B3LYP/3-21G functional/basis set. Two orthogonal views of each complex; aryl and octyl solubilizing groups were replaced by hydrogen atoms for the optimization.

4.4 UV/vis/NIR titrations

To understand the binding between template and ring, we turned to UV-vis-NIR titrations. We expected that the coordination of the two templates; **T3** or **T3N** to **c-P6**, and **T6e** to **c-P12**; must occur in two steps each with their own formation constants, $K_{f,1}$ and $K_{f,2}$. However, if $K_{f,2}$ is higher than $K_{f,1}$, it may appear as if both templates coordinate at the same time because the 1:1 complex never builds up to high concentrations (Scheme 4.1). Additionally, to quantify the

cooperativity in the system, correcting for statistical factors is required which is conveniently done by dividing the determined K_f with the statistical equilibrium constant K_σ to get K_{chem} .



Scheme 4.1. Definition of formation constants and denaturation constants.

Thus, to begin our studies, we first prepared each complex in Figure 4.1. Given the very high binding constants between oligopyridine ligands and porphyrin oligomers, it is necessary to perform denaturation titrations to determine K_f indirectly via the denaturation constant K_{dn} . Accordingly, after forming each complex, a large excess of pyridine was titrated into solutions of the 1:2 complexes (ca. 10^{-6} M in CDCl_3 filtered over basic alumina or toluene at 298 K), to displace the multidentate ligands. The changes were measured by UV-vis-NIR spectroscopy (Figure 4.3).

The denaturation titrations of **c-P12**·(**T6e**)₂ (Figure 4.3 and Section 4.7.4.2) are isosbestic. This is an indication of a two-state equilibrium going directly from **c-P12**·(**T6e**)₂ to **c-P12**·(**py**)₁₂ where the concentration of the 1:1 complex **c-P12**·(**T6e**)(**py**)₆ is always so small that it is never observed. The exception would be if the spectrum of **c-P12**·(**T6e**)(**py**)₆ were a linear combination of the spectra of **c-P12**·(**T6e**)₂ to **c-P12**·(**py**)₁₂. There is no reason for this to be

the case as they are different molecules, and the likelihood that it would be a linear combination by accident is small. It is also observed that the spectra change is dramatic going from **c-P12·(T6e)**₂ with a very sharp peak at 890 nm to **c-P12·(py)**₁₂ with a broad peak at 820 nm. This indicates that **c-P12·(T6e)**₂ adopts a significantly more rigid conformation compared to **c-P12·(py)**₁₂. The denaturation titrations of **c-P6·(T3)**₂ and **c-P6·(T3N)**₂ (Figure 4.3, Figure 4.4, and Section 4.7.4.2) are not isosbestic. This is particularly clear in Figure 4.4 at 790 and 820 nm. In addition to that, the spectra are biphasic, which is best seen at 800 nm where the absorption first increases and then decreases. These two observations both mean that there are more than two complexes with different spectra in the equilibrium. The spectra with templates have shaper peaks than the spectra with pyridine, meaning that the templates rigidify the ring. However, the change is much smaller than in the case of **c-P12·(T6e)**₂, meaning that the templates affect the conformation of **c-P12** more dramatically than **c-P6**.

The isosbestic titrations were analyzed by fitting to the appropriate binding isotherm, and the non-isosbestic titration data were analyzed via non-linear regression using a global analysis multiple regression to model the entire spectrum simultaneously (ReactLab Equilibria software by Jplus Consulting). ReactLab Equilibria allows us to determine the binding constants directly (expressed as $\log(K_f)$) and the spectra of the species involved in the equilibrium processes. The absorption spectra in the window 650-950 nm was used for equilibria involving **c-P6**.

Our analysis assumes that the denaturation process of each template is a two-state equilibrium, (i.e. that intermediate partially denaturated species such as **c-P6·(T3)**₂(py) do not build up to high concentrations). This assumption is supported by the isosbestic nature of the **c-P12·(T6e)**₂ titrations (Figure 4.3) and by the good fits of this simple model of all the titrations to the experimental isotherms. With this method, the denaturation constant K_{dn} is found, and K_f can be calculated using Equation 4.1.²³

$$K_f = \frac{K_{py}^n}{K_{dn}} \quad (4.1)$$

Where n is the number of binding sites in the porphyrin nanoring (6 or 12) and K_{py} is the binding constant of one pyridine to one porphyrin unit (see Section 4.7.4.1; $K_{py} = 8.4 \times 10^3 \text{ M}^{-1}$ in CDCl₃ at 298 K).

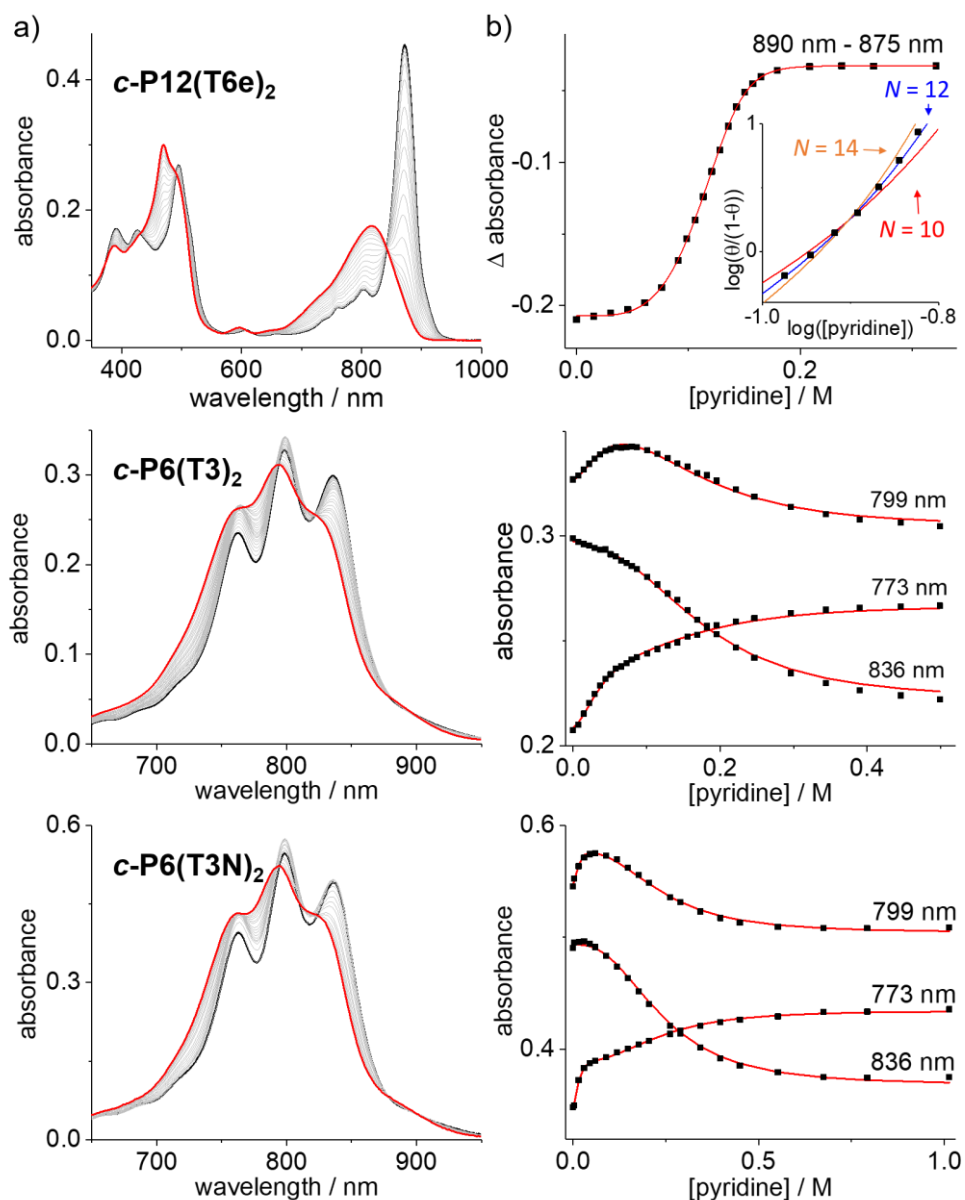


Figure 4.3. UV/vis/NIR denaturation titrations of stacked template complexes (all in CDCl_3 at 298 K). a) The spectra with the complexes in thick black lines and the end spectra (of the pyridine-saturated rings) in red, b) the experimental (black squares) and calculated (red lines) binding isotherms (insert: Hill plot with simulated curves for 10, 12 and 14 binding sites). $[c\text{-P12}] = 0.25 \mu\text{M}$, $[c\text{-P6}]_{\text{T3}} = 0.79 \mu\text{M}$, $[c\text{-P6}]_{\text{T3N}} = 1.3 \mu\text{M}$.

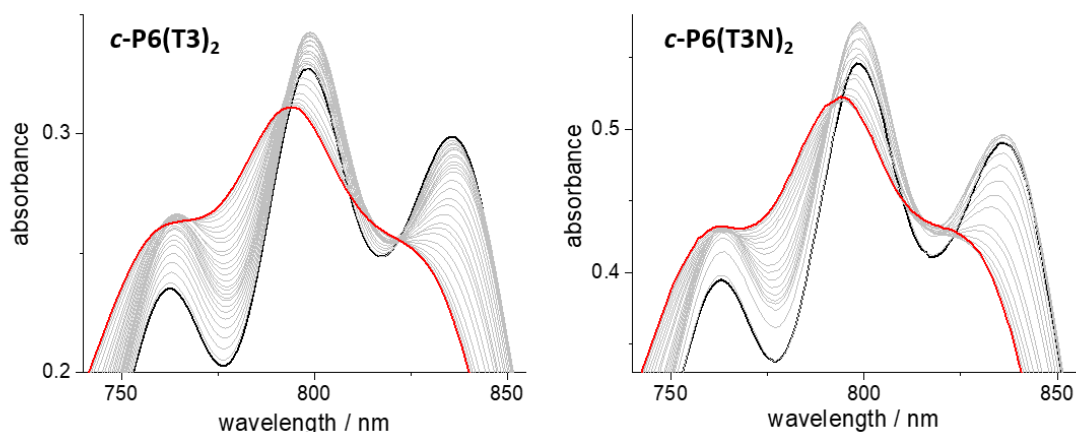


Figure 4.4. Zoom-in of the UV/vis/NIR denaturation titrations of **c-P6•(T3)₂** and **c-P6•(T3N)₂** showed in Figure 4.3, showing the biphasic and non-isosbestic nature of these titrations. The spectra with the complexes are shown in thick black lines and the end spectra (of the pyridine-saturated rings) in red.

The **c-P12•(T6e)₂** titration data were analyzed using a simple all-or-nothing model described by Equation 4.2.

$$K_{\text{dn}} = \frac{[\text{c-P12(py)}_{12}] \cdot [\text{T6e}]^2}{[\text{c-P12(T6e)}_2] \cdot [\text{py}]^{12}} \quad (4.2)$$

Figure 4.3 shows the data fit to the simulated curve for the all-or-nothing denaturation (additional titrations in Section 4.7.4.2). The data fit the model well, so we conclude that the cooperativity of the two **T6e** templates is so high, that the denaturation is effectively all-or-nothing. The values of K_f are summarized in Table 4.1. The errors are reported as the propagated sample standard deviation based on two repetitions. The Hill-plot (insert in Figure 4.3b) shows that the Hill coefficient increases with N and that the best fit is obtained with $N = 12$. The observed Hill coefficient ($n_H = 5.9$) is relatively large compared with hemoglobin ($n_H \approx 3$),²⁴ and general allosteric host molecules ($n_H = 2 - 8.4$).²⁵

The denaturation titrations of **c-P6•(T3)₂** and **c-P6•(T3N)₂** (Figure 4.3 and Section 4.7.4.2) were fitted to a two-step binding model defined in Equations 4.3 and 4.4, using ReactLab Equilibria.

$$K_{\text{dn},2} = \frac{[\text{c-P6(T3)(py)}_3] \cdot [\text{T3}]}{[\text{c-P6(T3)}_2] \cdot [\text{py}]^3} \quad (4.3)$$

$$K_{\text{dn},1} = \frac{[\text{c-P6(py)}_6] \cdot [\text{T3}]}{[\text{c-P6(T3)(py)}_3] \cdot [\text{py}]^3} \quad (4.4)$$

Figure 4.3 shows the data fit to the simulated curves for the two-step denaturation, and the determined K_f values are summarized in Table 4.1. The errors are reported as the propagated sample standard deviation based on two repetitions.

Table 4.1. K_f and α for stacked complexes in CDCl_3 and toluene

complex	solvent	$\log K_f$	α
c-P12·(T6e)₂	CDCl_3	$49.09 \pm 0.33^*$	$> 40^*$
	Toluene	$50.65 \pm 0.41^*$	$> 40^*$
c-P6·(T3)₂	CDCl_3	$\log K_{f,1} = 15.44 \pm 0.09$	0.038 ± 0.011
		$\log K_{f,2} = 13.72 \pm 0.09$	
	Toluene	$\log K_{f,1} = 16.50 \pm 0.11$	$(4.9 \pm 1.7) \times 10^{-4}$
		$\log K_{f,2} = 12.89 \pm 0.11$	
c-P6·(T3N)₂	CDCl_3	$\log K_{f,1} = 16.17 \pm 0.09$	$(1.0 \pm 0.30) \times 10^{-3}$
		$\log K_{f,2} = 12.88 \pm 0.09$	
	Toluene	$\log K_{f,1} = 16.55 \pm 0.09$	$(1.0 \pm 0.36) \times 10^{-4}$
		$\log K_{f,2} = 12.25 \pm 0.11$	

*For **c-P12·(T6e)₂** only one all-or-nothing K_f was measured, and α was calculated based on the uncertainty of the experiment (see main text and Section 4.7.4.3).

In addition to the UV-vis titrations, ^1H NMR experiments were performed to confirm the equilibrium constants. We mixed 1:1 solutions of template and nanoring and let them reach equilibrium by adding a small amount of pyridine and letting the solution stand at 298 K until no further changes were observed. The final spectra can be seen in Figure 4.5. It is worth noticing that the porphyrin signals from **c-P12·(T6e)₂** are doubled compared to **c-P12** because **c-P12·(T6e)₂** no longer has a horizontal symmetry plane and has D_{6d} symmetry where **c-P12** has D_{12h} symmetry.

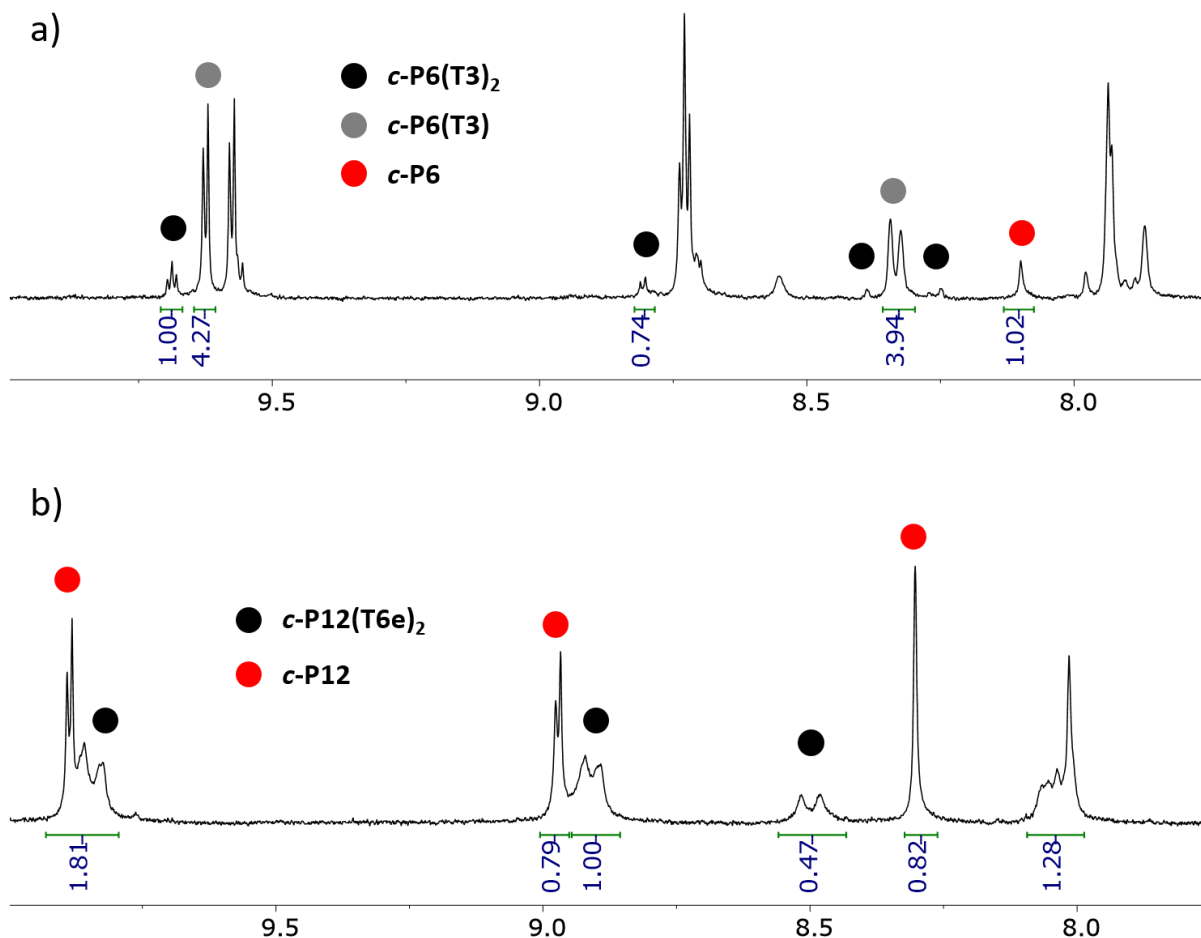


Figure 4.5. ^1H NMR (500 MHz) spectra of 1:1 mole ratios of a) *c*-P6 and T3, and b) *c*-P12 and T6e after they have reached equilibrium. CDCl_3 with a trace amount of pyridine- d_5 , 500 MHz, 298 K.

The spectrum of *c*-P12 and T6e shows that there is no visible trace of the 1:1 complex *c*-P12·T6e, which is in agreement with the very high cooperativity factor found by UV/vis/NIR. The spectrum of *c*-P6 and T3 shows a mixture of *c*-P6·(T3)₂, *c*-P6·T3 and *c*-P6. As the integrals in the spectrum corresponds to the relative concentration, the equilibrium constant can be calculated directly. We estimate a 10% error in the integration of the peaks in the ^1H NMR spectra and propagate that error to the final value.

$$K_{\text{eq,NMR}} = \frac{[\textit{c}\text{-P6}(\text{T3})]^2}{[\textit{c}\text{-P6}(\text{T3})_2] \cdot [\textit{c}\text{-P6}]} = \frac{\left(\frac{3.94}{12} \pm 0.1 \cdot \frac{3.94}{12}\right)^2}{\left(\frac{1}{24} \pm 0.1 \cdot \frac{1}{24}\right) \cdot \left(\frac{1.02}{24} \pm 0.1 \cdot \frac{1.02}{24}\right)} = 62.1 \pm 15.2 \quad (4.5)$$

This equilibrium constant can also be found as the ratio between $K_{\text{f},1}$ and $K_{\text{f},2}$, and if we use the values found by UV/vis/NIR, we get the same value for the equilibrium constant within the

error margin. This confirms the value of the formation constants determined by UV-Vis titrations.

$$K_{\text{eq,UV}} = \frac{K_{f,1}}{K_{f,2}} = \frac{10^{15.44} \pm 10^{0.09}}{10^{13.72} \pm 10^{0.09}} = 52.5 \pm 1.2 \cdot 10^{-12} \quad (4.6)$$

The cooperativity factor α is a measure of the cooperativity in a system and can be calculated as the ratio between the statistically corrected binding constants $K_{\text{chem},2}$ and $K_{\text{chem},1}$ (Scheme 4.1 and Equation 4.7). These are determined as the measured K_f values divided by their statistical factor K_σ .

$$\alpha = \frac{K_{\text{chem},2}}{K_{\text{chem},1}} = \frac{K_{f,2}}{K_{f,1}} \cdot \frac{K_{\sigma,1}}{K_{\sigma,2}} \quad (4.7)$$

If $\alpha = 1$, there is no cooperativity. If $\alpha > 1$, there is positive cooperativity and if $\alpha < 1$, there is negative cooperativity.

Table 4.2. Calculated statistical equilibrium constants (K_σ).*

equilibrium	K_σ
c-P6 → c-P6·T3	96
c-P6·T3 → c-P6·(T3)₂	48
c-P12 → c-P12·T6e	1536
c-P12·T6e → c-P12·(T6e)₂	768

* see Section 4.7.3 for calculations of statistical factors.

The calculated values of α for **c-P6·(T3)₂** and **c-P6·(T3N)₂** are shown in Table 4.1, and the calculated speciation curves are shown in Figure 4.6.

In order to estimate the cooperativity factor α for **c-P12·(T6e)₂**, we assumed a scenario where the denaturation is only almost all-or-nothing and 10% of **c-P12·(T6e)(py)₆** is in fact formed in the middle of the titration. 10% was chosen because it seems reasonable that 10% **c-P12·(T6e)(py)₆** could be present while the titration would still look isosbestic and fit the model. This assumption is supported by the ¹H NMR experiment described above and shown in Figure 4.5, where it is seen that at equilibrium it is not possible to observe any 1:1 complex by ¹H NMR. With this 10% assumption, it was calculated that α must be higher than 40 in order

for the data to fit this model so well (see Section 4.7.4.3). The values of K_f and α are summarized in Table 1.

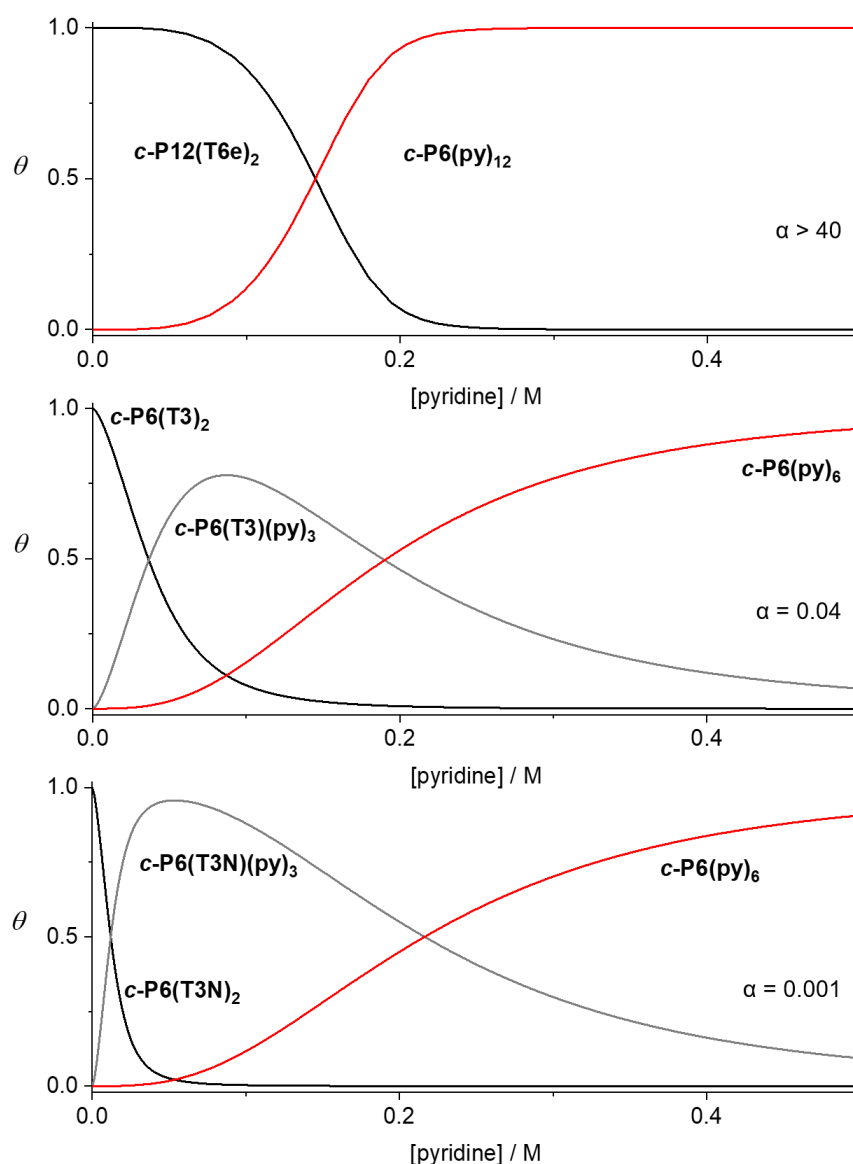


Figure 4.6. Normalized calculated speciation curves calculated with $c = 1 \mu\text{M}$. θ is the molar ratio of the total amount of porphyrin nanoring.

The values of α and the speciation curves show a clear picture of the cooperativity in these systems. The two **T6e** templates in **c-P12·(T6e)₂** show strong positive allosteric cooperativity, ($\alpha > 40$) and the intermediate 1:1 complex cannot be observed in the experiment. In CDCl_3 , **T3** and **T3N** in **c-P6** both show negative cooperativity with α -values of 0.04 and 0.001 respectively. This difference in magnitude of negative cooperativity is confirmed by the fact that the 1:1 complex **c-P6·T3N** can be isolated in CDCl_3 , whereas **c-P6·T3** cannot. In toluene,

the overall trend is the same, but the binding is stronger. Interestingly however, the cooperativity is smaller, and in toluene **c-P6**·**T3** can be isolated as a pure species.

4.5 Kinetics

When **c-P6** and **T3** are mixed in a one-to-one ratio, the initial solution consists of a mixture of **c-P6**·(**T3**)₂, **c-P6**·**T3** and **c-P6**.¹⁷ The ratio of each component is dependent of the way the compounds are mixed. If **T3** is added with no stirring the result is mostly **c-P6**·(**T3**)₂ and **c-P6**, whereas if **T3** is added dropwise under vigorous stirring, the mixture is statistical (Figure 4.7). The fact that the well mixed solution had a statistical distribution of products, despite the difference in binding constants for the first and second template, suggests that the distribution of products is not determined by thermodynamic stabilities. Rather, it seems the kinetic barriers for coordination of the template to both **c-P6** and **c-P6**·**T3** are either identical or very small so that the coordination events would be diffusion-controlled.

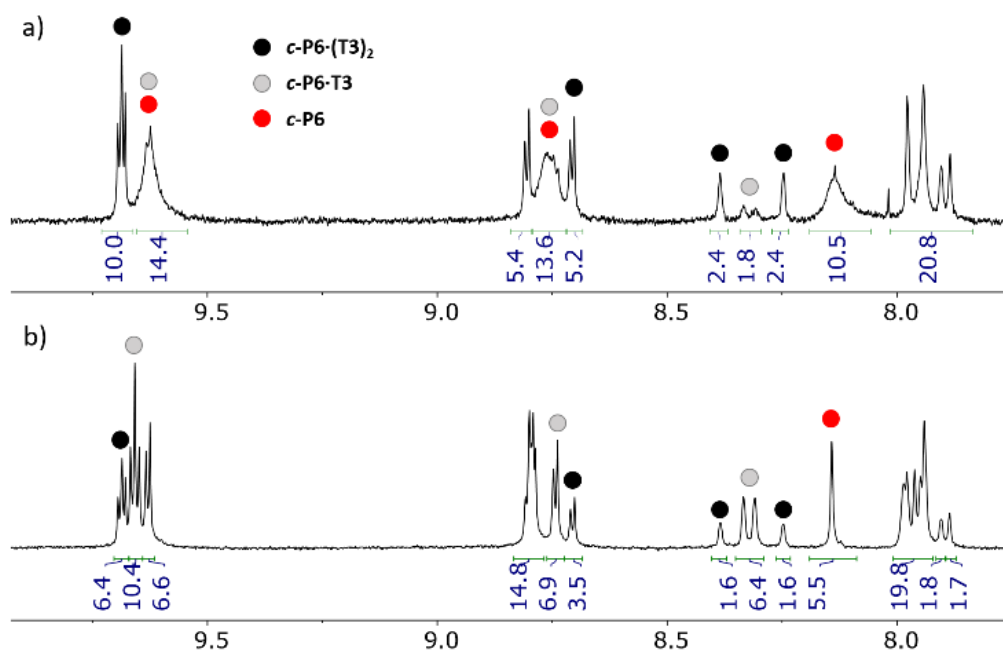


Figure 4.7. ¹H NMR (500 MHz) spectra of 1:1 mixtures of **c-P6** and **T3**, mixed under different conditions. a) **T3** was added without stirring, b) **T3** was added in a dilute solution under vigorous stirring. CDCl₃, 298 K, spectra recorded approximately 15 minutes after mixing.

Once formed, the products are kinetically trapped with equilibrium occurring over 1-2 months. To investigate this further, we monitored the concentrations of **c-P6**·(**T3**)₂, **c-P6**·**T3** and **c-P6**

over time by ^1H NMR in an experiment where $\text{c-P6}\cdot(\text{T3})_2$ was mixed with c-P6 CDCl_3 at 298 K (Figure 4.8a). Each of the three compounds have distinctive signals in the ^1H NMR spectrum and the concentration of each species is found by integrating the peaks. Figure 4.8b shows the concentration of each species over time.

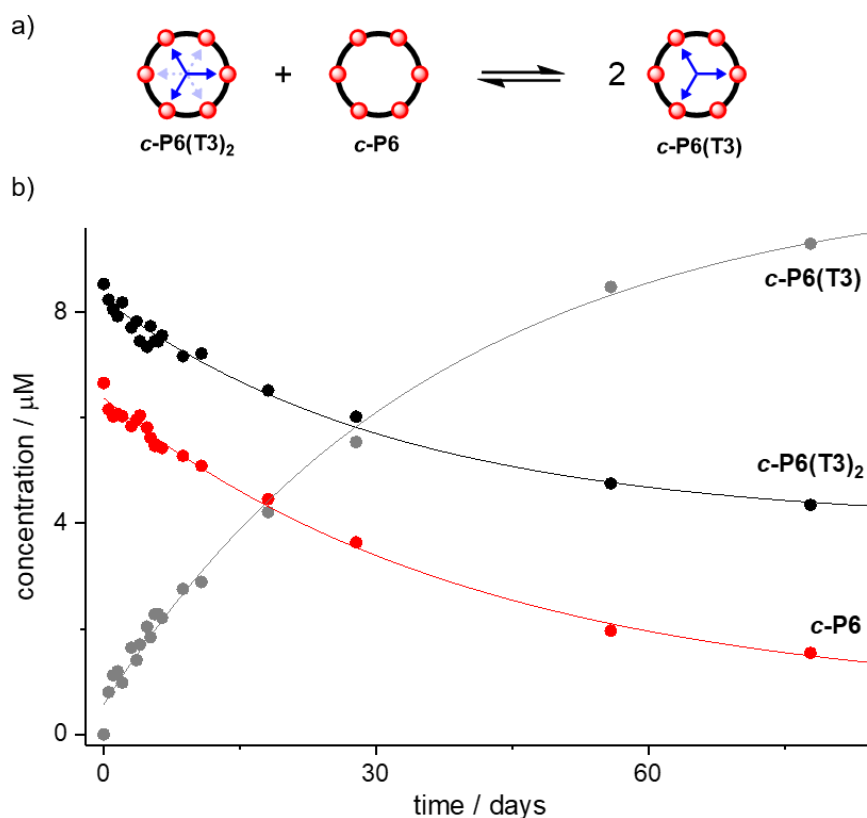
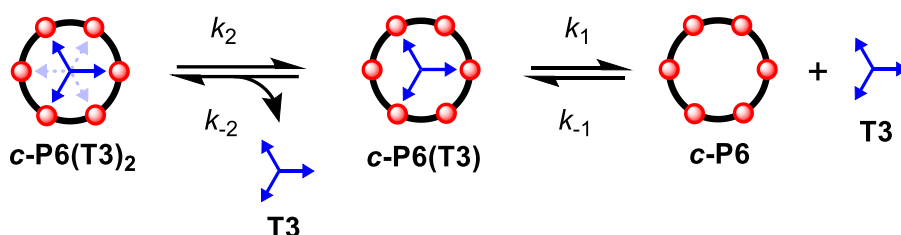


Figure 4.8. a) Scheme illustrating the equilibrium where $\text{c-P6}\cdot(\text{T3})_2$ and c-P6 form $\text{c-P6}\cdot\text{T3}$, and b) kinetic data from the experiment. Concentrations, $\text{c-P6}\cdot(\text{T3})_2$ (black), $\text{c-P6}\cdot\text{T3}$ (grey), and c-P6 (red), were determined from the integrals in the ^1H NMR spectra of the mixture. The data points are fit to simple exponential decays for illustration ($y = y_0 + P_0 \cdot \exp(-x \cdot k)$), with k being 3.54×10^{-7} , 3.13×10^{-7} , and 2.83×10^{-7} for $\text{c-P6}\cdot(\text{T3})_2$, $\text{c-P6}\cdot\text{T3}$, and c-P6 respectively.

In order to determine the rate of the reaction, the data points in Figure 4.8 was fit to simple exponential decays, and the rate constants were given by the fit as 3.54×10^{-7} , 3.13×10^{-7} , and 2.83×10^{-7} for $\text{c-P6}\cdot(\text{T3})_2$, $\text{c-P6}\cdot\text{T3}$, and c-P6 respectively. This assumes that the rate of the reaction is first order with respect to each of the concentrations. This very simple analysis results in good fits as can be seen in the figure.

In order to investigate the kinetics in more detail, an initial rate analysis was performed on this reaction with different conditions. For this analysis we measured the concentration of $c\text{-P6}\cdot(\text{T3})_2$, and we decided that the initial part of the reaction that we were going to analyze was when 15% of $c\text{-P6}\cdot(\text{T3})_2$ had been consumed. First, we varied the concentrations of $c\text{-P6}$ with respect to $c\text{-P6}\cdot(\text{T3})_2$, we found that the initial rate of the consumption of $c\text{-P6}\cdot(\text{T3})_2$ is independent of the concentration of $c\text{-P6}$ (see Section 4.7.5). This means that the initial step of the mechanism of exchange is unimolecular, and must be a spontaneous elimination of a T3 molecule. Based on this, we propose a mechanism as illustrated in Scheme 4.2.



Scheme 4.2. Proposed mechanism of exchange between $c\text{-P6}\cdot(\text{T3})_2$, $c\text{-P6}\cdot\text{T3}$ and $c\text{-P6}$ with rate constants.

With the initial rate equation being:

$$\frac{d[c\text{-P6}(\text{T3})_2]}{dt} = -k_2[c\text{-P6}(\text{T3})_2] \quad (4.8)$$

By fitting the initial data, k_2 was found to be $2.74 \times 10^{-7} \text{ s}^{-1}$ at 298 K in CDCl_3 . Since we have determined $K_{f,2}$, we can calculate k_{-2} using Equation 4.9:

$$k_{-2} = K_{f,2} \cdot k_2 = 1.44 \cdot 10^7 \text{ M}^{-1}\text{s}^{-1} \quad (4.9)$$

at 298 K in CDCl_3 . This value is very high, and we wanted to compare it to the diffusion-controlled rate of the reaction to determine if the initial statistical distribution of products shown in Figure 4.7 is caused by thermodynamics or just diffusion. In order to calculate the diffusion-controlled limit for the rate, the diffusion coefficient D was calculated using the Stokes-Einstein equation.²⁶

$$D = \frac{k_B T}{6\pi \eta r} \quad (4.10)$$

Where k_B is Boltzmann's constant, T is the absolute temperature, η is the dynamic viscosity and r is the radius of the particle. Equation 4.10 assumes that the molecule is a spherical particle.

$$D = \frac{1.38 \cdot 10^{-23} \frac{\text{J}}{\text{K}} \cdot 298.15 \text{ K}}{6 \cdot \pi \cdot 0.536 \text{ mPas} \cdot 1.2 \text{ nm}} = 3.39 \cdot 10^{-10} \text{ m}^2\text{s}^{-1} \quad (4.11)$$

The diffusion coefficients of similar molecules have been measured using ^1H DOSY NMR; for **c-P12_t-Bu**, $D = (2.29 \pm 0.03) \cdot 10^{-10} \text{ m}^2\text{s}^{-1}$, and for a special version of **c-P6_t-Bu** with bulky substituents, $D = (3.11 \pm 0.12) \cdot 10^{-10} \text{ m}^2\text{s}^{-1}$. Both were measured in CD_2Cl_2 at 298 K at 500 MHz with $\Delta = 100 \text{ ms}$, $\delta = 4 \text{ ms}$ and $g = 0.96\text{--}41 \text{ G cm}^{-1}$.²⁷ In another study, ^1H DOSY NMR was used to investigate **c-P12_{THS}** and found $D = (1.50 \pm 0.03) \cdot 10^{-10} \text{ m}^2\text{s}^{-1}$. This was in toluene- d_8 at 298 K measured at 500 MHz with $\Delta = 100 \text{ ms}$, $\delta = 4 \text{ ms}$ and $g = 0.96\text{--}41 \text{ G cm}^{-1}$.²⁸ These values are of a similar order of magnitude as the calculated D and confirms the result.

Then, the diffusion limited rate constant was calculated using Equation 4.12.²⁹

$$k_{\text{diff}} = 4\pi D_{\text{sum}} R_0 N_A \quad (4.12)$$

Where R_0 is the distance at which the particles can react, and D_{sum} is the sum of the diffusion coefficients for the two reacting species. With the known values the diffusion limited rate constant was calculated in Equation 4.13.

$$k_{\text{diff}} = 4\pi \cdot 2 \cdot 3.39 \cdot 10^{-10} \text{ m}^2\text{s}^{-1} \cdot 2.4 \text{ nm} \cdot 6.02 \cdot 10^{23} \text{ mol}^{-1} = 1.23 \cdot 10^{10} \text{ M}^{-1}\text{s}^{-1} \quad (4.13)$$

Since k_{-2} in Equation 4.9 is two orders of magnitude smaller than the diffusion limit, the initial statistical distribution of products observed when **c-P6** and **T3** are mixed (Figure 4.7) must mean that the kinetic barriers for **T3** coordinating to **c-P6·T3** or **c-P6** are identical. In other words, the rate constants k_{-2} and k_{-1} are identical. Now we can calculate k_1 using our determined value for $K_{f,1}$:

$$k_1 = \frac{k_{-1}}{K_{f,1}} = 5.23 \cdot 10^{-9} \text{ s}^{-1} \quad (4.14)$$

Zinc porphyrins only coordinate one axial ligand, and two axial ligands have only been observed in a system where it is geometrically constrained.³⁰ Because of this, pyridine can act as a catalyst for the exchange of ligands between porphyrins, by being a competing ligand.

By conducting experiments with varying concentrations of pyridine, it was found that the initial rate was roughly first order to the concentration of pyridine and that the first rate constant, $k_{py,2}$, is $4.61 \times 10^{-2} \text{ M}^{-1}\text{s}^{-1}$ assuming an initial rate equation as in Equation 4.15.

$$\frac{d[\mathbf{c-P6(T3)_2}]}{dt} = -k_{2,py}[\mathbf{c-P6(T3)_2}][py]^x \quad (4.15)$$

The rate dependence on pyridine is probably more complicated, as the rate equation is likely to consist of contributions from a mechanism proceeding without pyridine and mechanisms that are first, second and third order with respect to pyridine. The magnitude of the contributions from each type of mechanism is likely to be dependent on the concentration of pyridine, so varying the concentration might shift the contributions.

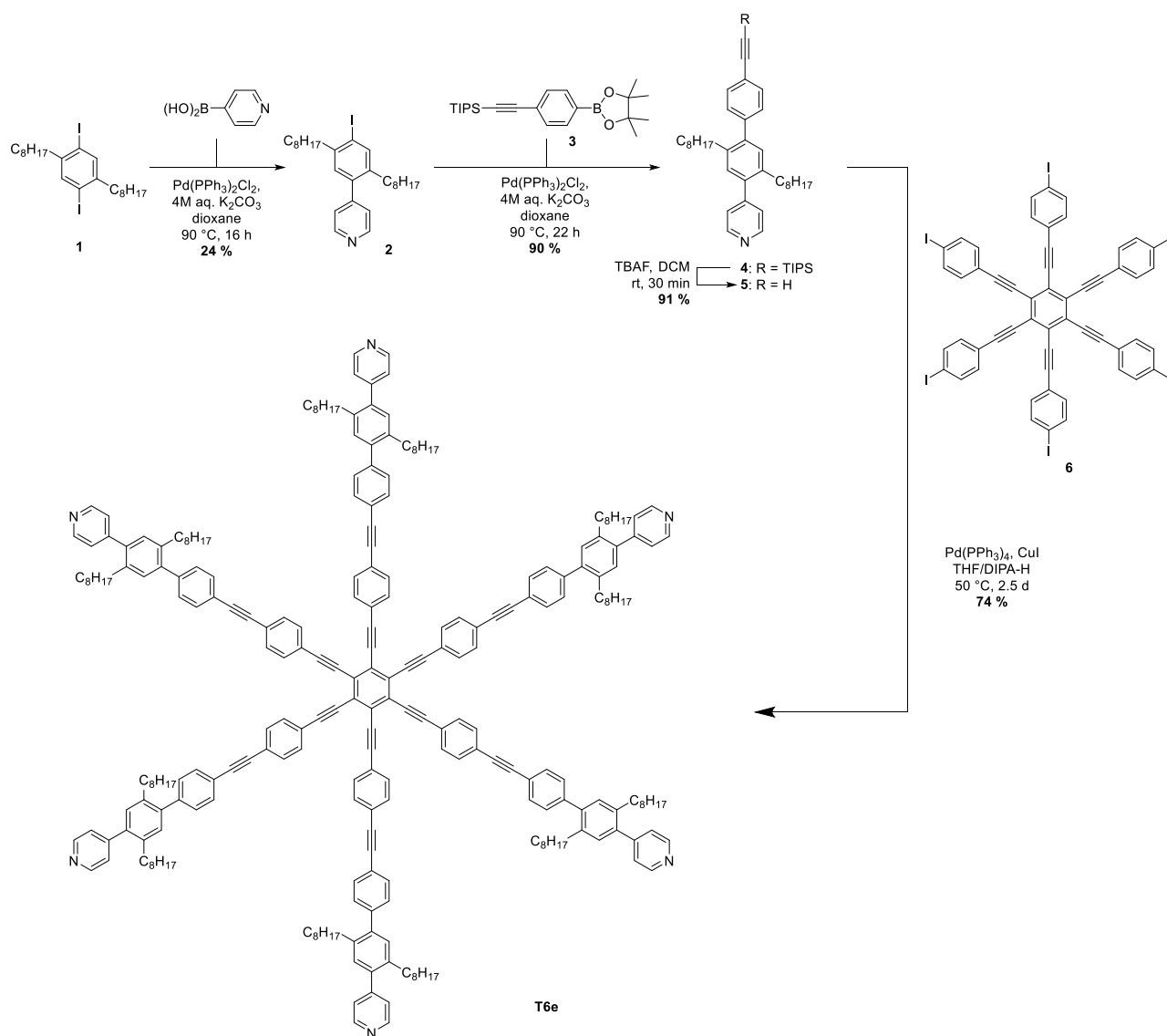
4.6 Conclusion

We have demonstrated that the stacked complexes $\mathbf{c-P6 \cdot (T3)_2}$ and $\mathbf{c-P6 \cdot (T3N)_2}$ show negative cooperativity, and that the stacked complex $\mathbf{c-P12 \cdot (T6e)_2}$ showed extremely high positive cooperativity. The fact that the cooperativity in $\mathbf{c-P12 \cdot (T6e)_2}$ is so strong might seem surprising because the two templates have to bend to fit inside the nanoring and fight sterically repulsive forces. However, upon closer inspection it becomes evident that when the first template binds, the ring must adopt a flat and rigid conformation, and the unbound porphyrins will be rotating less freely around the butadiyne bridges. Thus, the complex is locked in a conformation that is favorable for binding another template. We also investigated the kinetics of the exchange of oligopyridine templates between porphyrin nanorings and showed that thermodynamically unfavored complexes can be trapped kinetically for weeks if the binding constants are sufficiently high.

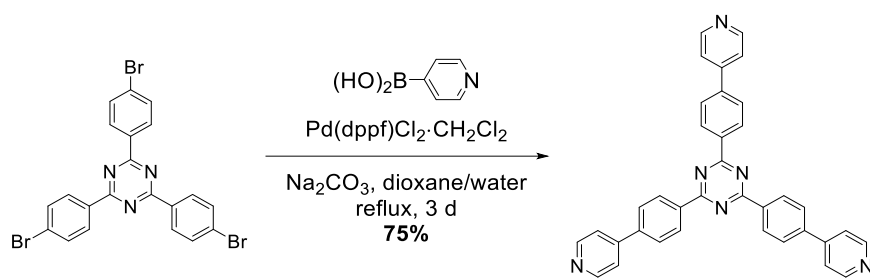
4.7 Experimental procedures and technical details

4.7.1 Synthesis of T6e and T3N

T6e was synthesized by Dr Henrik Gottfredsen and Dr Michel Rickhaus, and **T3N** was synthesized by Dr Lara Tejerina. They kindly donated their compounds for use in this study. Scheme 4.3 and 4.4 shows an overview of the synthesis routes for both compounds.



Scheme 4.3: Synthesis scheme for **T6e**.



Scheme 4.4: Synthesis scheme for **T3N**.

4.7.2 Fitting UV-vis-NIR titrations

4.7.2.1 Estimation of Formation Constants

The formation constants of the templates **T3** and **T3N** with **c-P6**, and **T6e** with **c-P12** were determined by UV-vis-NIR denaturation titrations with a large excess of the competing ligand pyridine.³¹ From the denaturation constant (K_{dn}) and the binding constant of pyridine to a single porphyrin site (K_{py}), the formation constant (K_f) can be calculated using Equation 4.16.

$$K_f = \frac{K_{py}^N}{K_{dn}} \quad (4.16)$$

where N is the number of pyridine binding sites involved.²³

Titration of **c-P6** with pyridine has shown that the binding constant of pyridine to each porphyrin site is the same as that of the porphyrin monomer.³² In other words, the porphyrins in the ring interact with pyridine as if they were not connected to each other. The binding constant of pyridine to the porphyrin monomer was found by reference titrations.

The reference titrations and the denaturation titrations of **c-P12·(T6e)₂** were analyzed using Origin. The denaturation titrations of **c-P6·(T3)₂** and **c-P6·(T3N)₂** were analyzed using the global analysis software ReactLab™ Equilibria, a multivariate data analysis program which allows the determination of binding constants in complex multistep equilibria using the whole set of wavelengths.

For the analysis of the denaturation titrations, the binding of the pyridine units and the consequent knock-out of template was simplified to happen in one step. Hence, for the denaturation of a complex with two templates, the model assumes that there are only three colored species in solution at any given time in the titration: the complex with two templates, the complex with one template and all other binding sites saturated with pyridine, and the compound with all porphyrin units bound to pyridine.

CDCl₃ was filtered through a plug of basic alumina before use to remove traces of acid and water. All titrations were performed on porphyrins with THS-solubilizing groups.

4.7.2.2 Equation for modelling the 1:1 binding of porphyrin to pyridine

The reference titration, which is the formation of a 1:1 complex between the porphyrin monomer (**P1**) and pyridine (py), was fitted to a simple 1:1 binding isotherm shown in Equation 4.17.³³

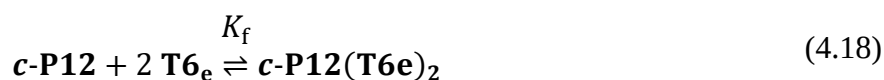
$$\frac{A - A_0}{A_f - A_0} = \frac{(K_f([\mathbf{P1}]_0 + [\text{py}]_0) + 1) - \sqrt{(K_f([\mathbf{P1}]_0 + [\text{py}]_0) + 1)^2 - 4K_f^2[\mathbf{P1}]_0[\text{py}]_0}}{2K_f[\mathbf{P1}]_0} \quad (4.17)$$

where A is absorption, A_0 is the initial absorption, A_f is the final asymptote of the titration curve, K_f is the formation constant, $[\mathbf{P1}]_0$ is the total concentration of porphyrin, and $[\text{py}]_0$ is the total concentration of pyridine.

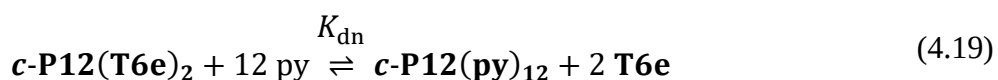
4.7.2.3 Equation for modelling the ‘all-or-nothing’ denaturation of a 1:2 complex with two identical ligands

The denaturation titration of the complex **c-P12**·(**T6e**)₂ was found to have many isosbestic points, which suggests that there are only two colored species in solution. If there are only two colored species in solution, the denaturation must be ‘all-or-nothing’ meaning that **c-P12**·(**T6e**)₂ goes directly to **c-P12**·(**py**)₁₂ without formation of any significant amount of 1:1 complex **c-P12**·**T6e**·(**py**)₆.

The function for fitting the data with this model is derived in this section. We consider the formation constant K_f of **c-P12**·(**T6e**)₂:



As described in Section 4.7.2.1, we find K_f by performing a competition experiment with pyridine. When an excess of pyridine is added to a solution of the complex, the templates are replaced with the denaturation constant K_{dn} :



$$K_{dn} = \frac{[\mathbf{c-P12(py)_{12}}] \cdot [\mathbf{T6e}]^2}{[\mathbf{c-P12(T6e)_2}] \cdot [\text{py}]^{12}} \quad (4.20)$$

Rearrangement gives:

$$0 = K_{\text{dn}} \cdot [\text{c-P12}(\text{T6e})_2] \cdot [\text{py}]^{12} - [\text{c-P12}(\text{py})_{12}] \cdot [\text{T6e}]^2 \quad (4.21)$$

The concentration of **T6e** and **c-P12·(T6e)₂** can be expressed using **c-P12·(py)₂**.

$$[\text{T6e}] = 2 \cdot [\text{c-P12}(\text{py})_{12}] \quad (4.22)$$

$$[\text{c-P12}(\text{T6e})_2] = [\text{c-P12}]_0 - [\text{c-P12}(\text{py})_{12}] \quad (4.23)$$

Inserting these into the function for K_{dn} gives:

$$0 = K_{\text{dn}} \cdot ([\text{c-P12}]_0 - [\text{c-P12}(\text{py})_{12}]) \cdot [\text{py}]^{12} - [\text{c-P12}(\text{py})_{12}] \cdot (2 \cdot [\text{c-P12}(\text{py})_{12}])^2 \quad (4.24)$$

$$0 = K_{\text{dn}} \cdot [\text{py}]^{12} \cdot [\text{c-P12}]_0 - K_{\text{dn}} \cdot [\text{py}]^{12} \cdot [\text{c-P12}(\text{py})_{12}] - 4 \cdot [\text{c-P12}(\text{py})_{12}]^3 \quad (4.25)$$

$$0 = -4 \cdot [\text{c-P12}(\text{py})_{12}]^3 - K_{\text{dn}} \cdot [\text{py}]^{12} \cdot [\text{c-P12}(\text{py})_{12}] + K_{\text{dn}} \cdot [\text{py}]^{12} \cdot [\text{c-P12}]_0 \quad (4.26)$$

This is a quadratic equation which has three roots. When solving it, it turns out that two of the roots are complex numbers, so we continue with the solution which is a real number. In this expression, $K = K_{\text{dn}}$ and $n = \text{number of porphyrins}$.

$$[\text{c-P12}(\text{py})_{12}] = \frac{1}{2} \left(\frac{\sqrt[3]{\sqrt{3} \cdot \sqrt{K_{\text{dn}}^3 \cdot [\text{py}]^{3n} + 27 \cdot K_{\text{dn}}^2 \cdot [\text{c-P12}]_0^2 \cdot [\text{py}]^{2n} + 9 \cdot K_{\text{dn}} \cdot [\text{c-P12}]_0 \cdot [\text{py}]^n}}}{3^{\frac{2}{3}}} - \frac{K_{\text{dn}} \cdot [\text{py}]^n}{\sqrt[3]{3} \cdot \sqrt[3]{\sqrt{3} \cdot \sqrt{K_{\text{dn}}^3 \cdot [\text{py}]^{3n} + 27 \cdot K_{\text{dn}}^2 \cdot [\text{c-P12}]_0^2 \cdot [\text{py}]^{2n} + 9 \cdot K_{\text{dn}} \cdot [\text{c-P12}]_0 \cdot [\text{py}]^n}}} \right) \quad (4.27)$$

In order to normalize the function, we divide by the total concentration of porphyrin nanoring on both sides of the equation.

$$\begin{aligned}
& \frac{[\mathbf{c-P12(py)}]_{12}}{[\mathbf{c-P12}]_0} \\
&= \frac{1}{2[\mathbf{c-P12}]_0} \left(\frac{\sqrt[3]{\sqrt{3} \cdot \sqrt{K_{dn}^3 \cdot [py]^{3n} + 27 \cdot K_{dn}^2 \cdot [\mathbf{c-P12}]_0^2 \cdot [py]^{2n} + 9 \cdot K_{dn} \cdot [\mathbf{c-P12}]_0 \cdot [py]^n}}}{3^{\frac{2}{3}}} \right. \\
&\quad \left. - \frac{K_{dn} \cdot [py]^n}{\sqrt[3]{3} \cdot \sqrt[3]{\sqrt{3} \cdot \sqrt{K_{dn}^3 \cdot [py]^{3n} + 27 \cdot K_{dn}^2 \cdot [\mathbf{c-P12}]_0^2 \cdot [py]^{2n} + 9 \cdot K_{dn} \cdot [\mathbf{c-P12}]_0 \cdot [py]^n}}} \right) \quad (4.28)
\end{aligned}$$

At the initial state of the titration, all porphyrin species are bound. At a specific wavelength, the absorption A_0 can be calculated as:

$$A_0 = \varepsilon_{\mathbf{c-P12(T6e)}_2} \cdot [\mathbf{c-P12}]_0 \cdot l \quad (4.29)$$

Where $\varepsilon_{\mathbf{c-P12(T6e)}_2}$ is the molar absorption coefficient of $\mathbf{c-P12(T6e)}_2$ at a specific wavelength and l is the path length of the cuvette.

At the final stage of the titration, the templates are replaced, and all porphyrin species are bound to pyridine. At a specific wavelength, the absorption A_f can be calculated as:

$$A_f = \varepsilon_{\mathbf{c-P12(py)}_{12}} \cdot [\mathbf{c-P12}]_0 \cdot l \quad (4.30)$$

The absorption A at any given moment in the titration can be calculated as:

$$A = \varepsilon_{\mathbf{c-P12(T6e)}_2} \cdot [\mathbf{c-P12(T6e)}_2] \cdot l + \varepsilon_{\mathbf{c-P12(py)}_{12}} \cdot [\mathbf{c-P12(py)}]_{12} \cdot l \quad (4.31)$$

$$A = \varepsilon_{\mathbf{c-P12(T6e)}_2} \cdot ([\mathbf{c-P12}]_0 - [\mathbf{c-P12(py)}]_{12}) \cdot l + \varepsilon_{\mathbf{c-P12(py)}_{12}} \cdot [\mathbf{c-P12(py)}]_{12} \cdot l \quad (4.32)$$

Substituting the equations for A_0 and A_f into this equation gives after rearrangements:

$$\frac{A - A_0}{A_f - A_0} = \frac{[\mathbf{c-P12(py)}]_{12}}{[\mathbf{c-P12}]_0} \quad (4.33)$$

Since we found the expression for $\frac{[\mathbf{c-P12(py)}_{12}]}{[\mathbf{c-P12}]_0}$ already, we now substitute that into this equation:

$$\begin{aligned} & \frac{A - A_0}{A_f - A_0} \\ &= \frac{1}{2 \cdot [\mathbf{c-P12}]_0} \left(\frac{\sqrt[3]{\sqrt{3} \cdot \sqrt{K_{\text{dn}}^3 \cdot [\text{py}]^{3n} + 27 \cdot K_{\text{dn}}^2 \cdot [\mathbf{c-P12}]_0^2 \cdot [\text{py}]^{2n} + 9 \cdot K_{\text{dn}} \cdot [\mathbf{c-P12}]_0 \cdot [\text{py}]^n}}}{3^{\frac{2}{3}}} \right. \\ & \quad \left. - \frac{K_{\text{dn}} \cdot [\text{py}]^n}{\sqrt[3]{3} \cdot \sqrt[3]{\sqrt{3} \cdot \sqrt{K_{\text{dn}}^3 \cdot [\text{py}]^{3n} + 27 \cdot K_{\text{dn}}^2 \cdot [\mathbf{c-P12}]_0^2 \cdot [\text{py}]^{2n} + 9 \cdot K_{\text{dn}} \cdot [\mathbf{c-P12}]_0 \cdot [\text{py}]^n}}} \right) \end{aligned} \quad (4.34)$$

Throughout the titration, pyridine is in large excess, so we approximate that the concentration of free pyridine in solution is equal to the total concentration of pyridine.

$$[\text{py}] = [\text{py}]_0 \quad (4.35)$$

When we fit titration data in Origin, it is A that we are fitting on the y-axis. Therefore, we rearrange the expression so it can be typed into the program directly:

$$\begin{aligned} & A \\ &= \frac{(A_f - A_0)}{2 \cdot [\mathbf{c-P12}]_0} \left(\frac{\sqrt[3]{\sqrt{3} \cdot \sqrt{K_{\text{dn}}^3 \cdot [\text{py}]^{3n} + 27 \cdot K_{\text{dn}}^2 \cdot [\mathbf{c-P12}]_0^2 \cdot [\text{py}]^{2n} + 9 \cdot K_{\text{dn}} \cdot [\mathbf{c-P12}]_0 \cdot [\text{py}]^n}}}{3^{\frac{2}{3}}} \right. \\ & \quad \left. - \frac{K_{\text{dn}} \cdot [\text{py}]^n}{\sqrt[3]{3} \cdot \sqrt[3]{\sqrt{3} \cdot \sqrt{K_{\text{dn}}^3 \cdot [\text{py}]^{3n} + 27 \cdot K_{\text{dn}}^2 \cdot [\mathbf{c-P12}]_0^2 \cdot [\text{py}]^{2n} + 9 \cdot K_{\text{dn}} \cdot [\mathbf{c-P12}]_0 \cdot [\text{py}]^n}}} \right) + A_0 \end{aligned} \quad (4.36)$$

4.7.2.4 Using ReactLab Equilibria to determine equilibrium constants

The multiple step denaturation titrations were analyzed via non-linear regression using a global analysis multiple regression to model the entire spectra simultaneously (ReactLab EQUILIBRIA software by Jplus Consulting). This allowed us to determine both the binding constants directly (expressed as $\log(K_f)$) and the spectra of the species involved in the equilibrium processes.

Figure 4.9 shows an example of the analysis performed with ReactLab Equilibria, in this case for titration **c-P6·(T3N)₂** in toluene run 1. In this analysis, M is **c-P6**, T is **T3N** and P is pyridine. We enter into the program the binding constants for three pyridine units binding to MT ($(K_{py})^3$, as described in Section 4.7.2.1 and found in Section 4.7.4.1) and the binding constant for six pyridine units binding to M ($(K_{py})^6$) in order to define the species MTP3 and MP6. Then, we define the steps we want to find binding constants for: M+T→MT (K_{f1}) and MT+T→MT2 (K_{f2}). The binding constants we know, the ones with pyridine are locked (here called FALSE) and the ones we want to find are allowed to vary (called TRUE). This model does not include stepwise binding of pyridine to form e.g. MP5 or MP4. The exclusion of this is valid because the binding of template to the porphyrin nanoring is extremely strong, so whenever the concentration of pyridine is high enough to knock out the template, it is also high enough to completely saturate the free porphyrin binding sites with pyridine. Hence, unbound porphyrin units are never present in the titration, and effectively we go directly from MT2→MTP3→MP6.

Reactants	Reaction Type	Products	Label	Parameters $\log K/\beta$	$\pm$	Fit p
MT+3P	=	MTP3		12.34		FALSE
M+6P	=	MP6		24.68		FALSE
M+T	=	MT		16.49	0.002	TRUE
MT+T	=	MT2		12.19	0.025	TRUE

Figure 4.9. Part of the interface in ReactLab Equilibria showing the model used for the analysis. The titration of **c-P6·(T3N)₂** in toluene run 1 is used as example.

However, in order to find the binding constants, we need to define all the species involved in our model (Figure 4.10): P and T which are non-absorbing in the titration, M and MT which are effectively never present as we just discussed, and then MT2, MTP3, and MP6. The spectra

of the defined species can be fixed to a known spectrum or be allowed to vary. In this case, the spectra of MP6, M, and MT were fixed, while MT2 and MTP3 were allowed to vary freely.

Species	P	M	T	MTP3	MP6	MT	MT2
Spectrum	non-abs	known	non-abs	colored	known	known	colored

Figure 4.10: Part of the interface in ReactLab Equilibria showing the defined species used for the analysis. The titration of **c-P6·(T3N)₂** in toluene run 1 is used as example.

For all titration analyzed with ReactLab, the results are presented as the determined formation constants, the programs prediction of the three spectra MT2, MTP3 and MP6, and a plot of data points with the binding isotherm at three characteristic wavelengths.

4.7.3 Calculation of statistical factors

To understand the stability constants of different complexes, it is useful to factor out statistical contributions. A measured equilibrium constant K_{eq} can be factorized into its statistical component K_{σ} and its statistically corrected value K_{chem} according to the following equation:



$$K_{\text{eq}} = \frac{Q_C^y Q_D^z}{Q_A^w Q_B^x} = \frac{\sigma_A^w \sigma_B^x}{\sigma_C^y \sigma_D^z} \cdot \frac{Q'_C{}^y Q'_D{}^z}{Q'_A{}^w Q'_B{}^x} = K_{\sigma} \cdot K_{\text{chem}} \quad (4.38)$$

where for each species i , Q_i is the partition coefficient, Q'_i is the statistically corrected partition coefficient, and σ_i is the symmetry number.^{18, 34-36}

Values of K_{σ} were calculated using Benson's symmetry number method.^{18,34} The symmetry number (σ) of each species is the product of its external symmetry number, σ_{ext} , (calculated from the point group of the molecule) and its internal symmetry number, σ_{int} , (calculated from the number of degenerate internal rotors). The values of σ for all the complexes involved are shown in Table 4.3. The external symmetry number is defined as the number of different but indistinguishable atomic arrangements that can be obtained by rotating a given molecule as a whole as a rigid object. The internal symmetry number is defined as the number of different but indistinguishable atomic arrangements that can be obtained by internal rotations around single bonds.

Table 4.3. Internal, external and total symmetry numbers for each component.*

compounds	point group	σ_{int}	σ_{ext}	σ
pyridine	C_{2v}	1	2	2
T3, T3N	D_{3h}	1	6	6
T6e	D_{6h}	1	12	12
c-P6, c-P6·py₆, c-P12·T6e, c-P12·T6e·py₆	D_{6h}	2 ⁶	12	768
c-P12, c-P12·py₁₂	D_{12h}	2 ¹²	24	98304
c-P6·T3, c-P6·T3N, c-P6·T3·py₃, c-P6·T3N·py₃	D_{3h}	2 ³	6	48
c-P6·(T3)₂, c-P6·(T3N)₂	D_{3d}	1	6	6
c-P12·(T6e)₂	D_{6d}	1	12	12

* Note that when counting internal rotations and calculating σ_{int} , we do not include rotors that are unaffected by the binding process, such as the *para*-phenylene links in **T3**, because if a rotor is unaffected by the binding process it has no influence on K_{σ} .

In order to factor out statistical contributions we have calculated the statistical factors (K_{σ}) for all the species involved in the break-up titrations. Figure 4.10 shows the analysis of the break-up of **c-P6·(T3)₂** and **c-P6·(T3N)₂**, which are the same, and Figure 4.11 shows the analysis of the break-up of **c-P12·(T6e)₂**. In these figures, the equilibria are drawn with regular reaction arrows to show the direction of the equilibrium constants. K_{σ} and K_{chem} were only calculated for the formation constants, and the statistically corrected formation constants were then inserted in the equations for the denaturation constants following the equation for denaturation:

$$K_f = \frac{K_{py}^n}{K_{dn}} \quad (4.39)$$

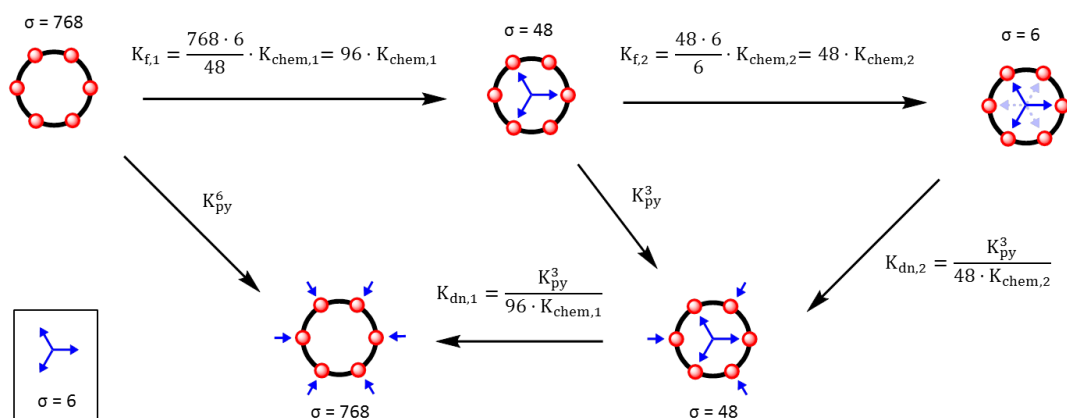


Figure 4.11. Statistical factors involved in the stepwise formation and denaturation of $c\text{-P6}\cdot(\text{T3})_2$ and $c\text{-P6}\cdot(\text{T3N})_2$.

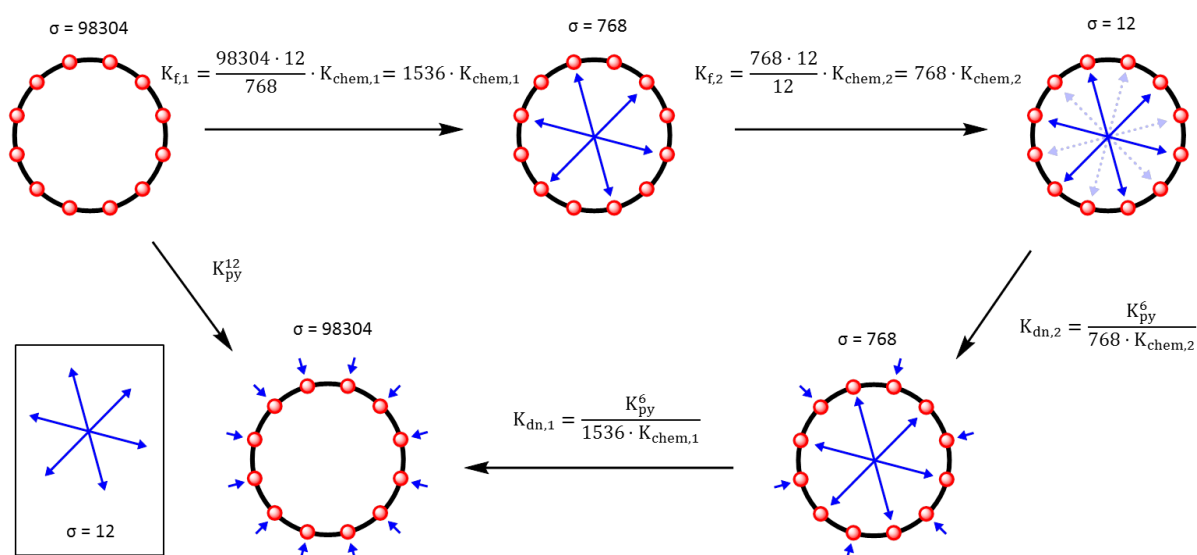


Figure 4.12. Statistical factors involved in the stepwise formation and denaturation of $c\text{-P12}\cdot(\text{T6e})_2$.

4.7.4 Titrations

4.7.4.1 Reference titrations

Reference titrations were performed to determine the binding constant K_{py} of pyridine to a porphyrin monomer in pure $CDCl_3$. The titrations were performed on a monomer (**P1**) shown in Figure 4.13. For the binding constant in toluene, the previously found value of $(1.3 \pm 0.1) \times 10^4 \text{ M}^{-1}$ was used.³⁷

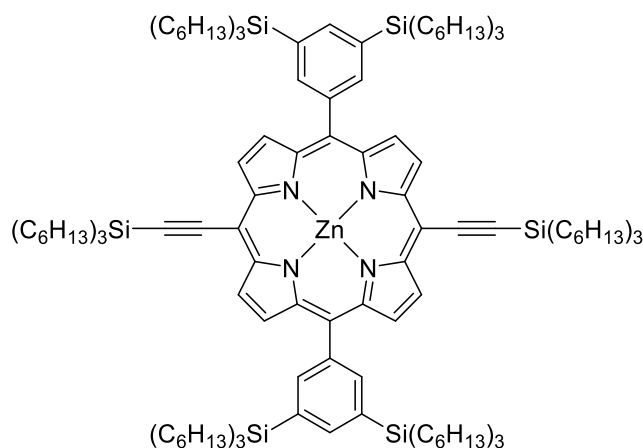


Figure 4.13: The porphyrin monomer **P1** used for reference titrations.

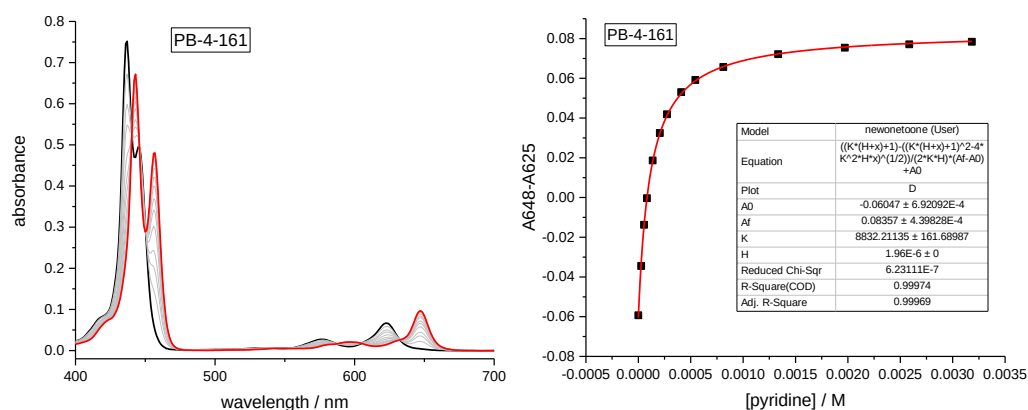


Figure 4.14. UV-vis-NIR titration of pyridine and **P1** (run 1, $CDCl_3$, 298 K, $[P1] = 1.96 \mu\text{M}$, $K_{py} = 8800 \text{ M}^{-1}$)

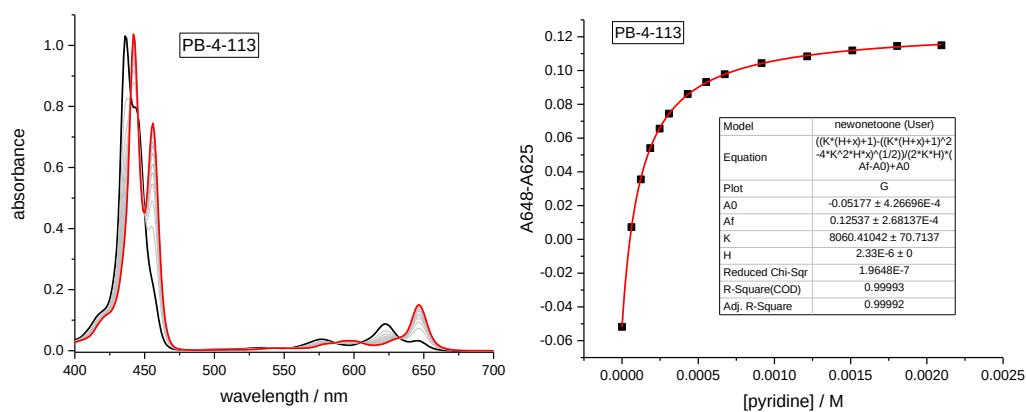


Figure 4.15. UV-vis-NIR titration of pyridine and **P1** (run 2, CDCl_3 , 298 K, $[\text{P1}] = 2.33 \mu\text{M}$, $K_{\text{py}} = 8100 \text{ M}^{-1}$)

The mean value of K_{py} in CDCl_3 was calculated to be $(8.4 \pm 0.5) \times 10^3 \text{ M}^{-1}$. Errors are reported as the sample standard deviation.

4.7.4.2 Denaturation titrations

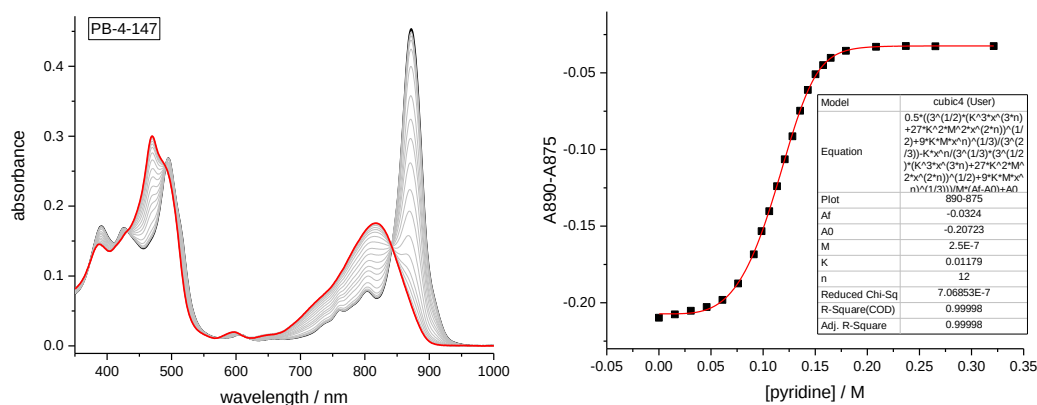


Figure 4.16. UV-vis-NIR titration of pyridine and *c*-P12·(T6e)₂ illustrating the removal of the two T6e templates. (run 1, CDCl₃, 298 K, [*c*-P12·(T6e)₂] = 0.25 μM, $K_{dn} = 0.0118 \text{ M}^{-10}$). The fitted binding isotherm is compared to the experimental data points at A890 nm - A875 nm. PB-4-147.

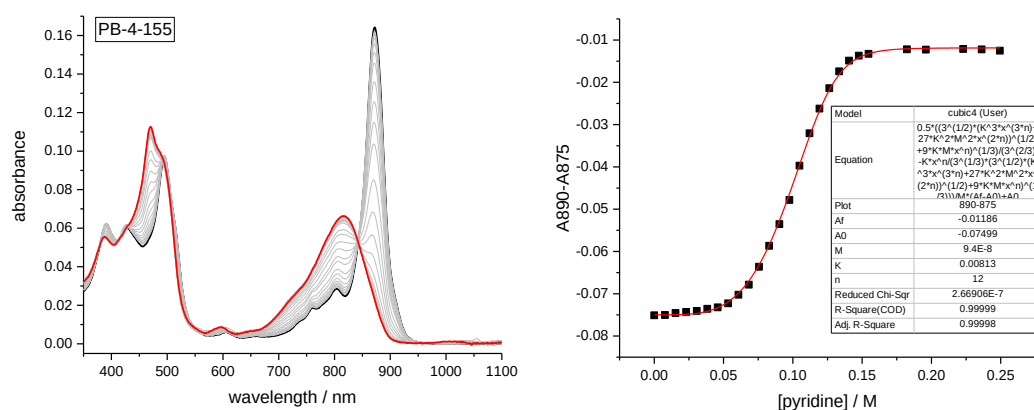


Figure 4.17. UV-vis-NIR titration of pyridine and *c*-P12·(T6e)₂ illustrating the removal of the two T6e templates. (run 2, CDCl₃, 298 K, [*c*-P12·(T6e)₂] = 0.094 μM, $K_{dn} = 0.00813 \text{ M}^{-10}$). The fitted binding isotherm is compared to the experimental data points at A890 nm - A875 nm. PB-4-155.

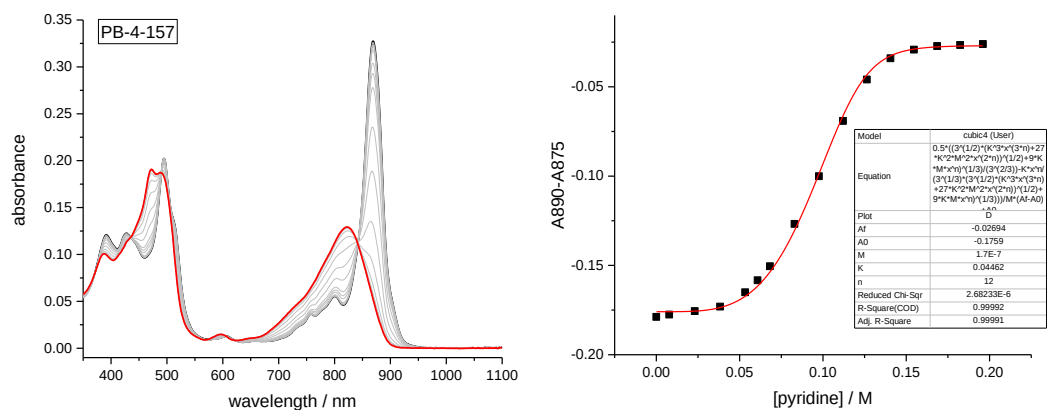


Figure 4.18. UV-vis-NIR titration of pyridine and **c-P12-(T6e)₂** illustrating the removal of the two **T6e** templates. (run 1, toluene, 298 K, [**c-P12-(T6e)₂**] = 0.17 μ M, K_{dn} = 0.0446 M⁻¹⁰). The fitted binding isotherm is compared to the experimental data points at A890 nm - A875 nm. PB-4-157.

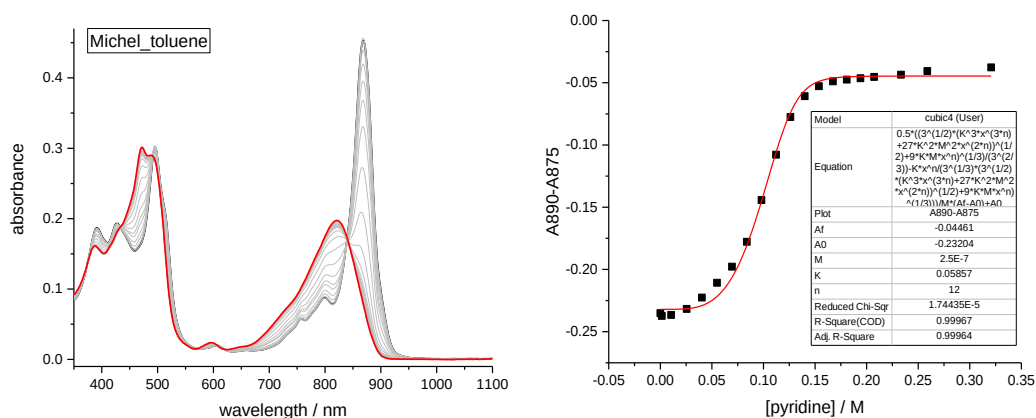


Figure 4.19. UV-vis-NIR titration of pyridine and **c-P12-(T6e)₂** illustrating the removal of the two **T6e** templates. (run 2, toluene, 298 K, [**c-P12-(T6e)₂**] = 0.25 μ M, K_{dn} = 0.0586 M⁻¹⁰). The fitted binding isotherm is compared to the experimental data points at A890 nm - A875 nm. Michel_000.

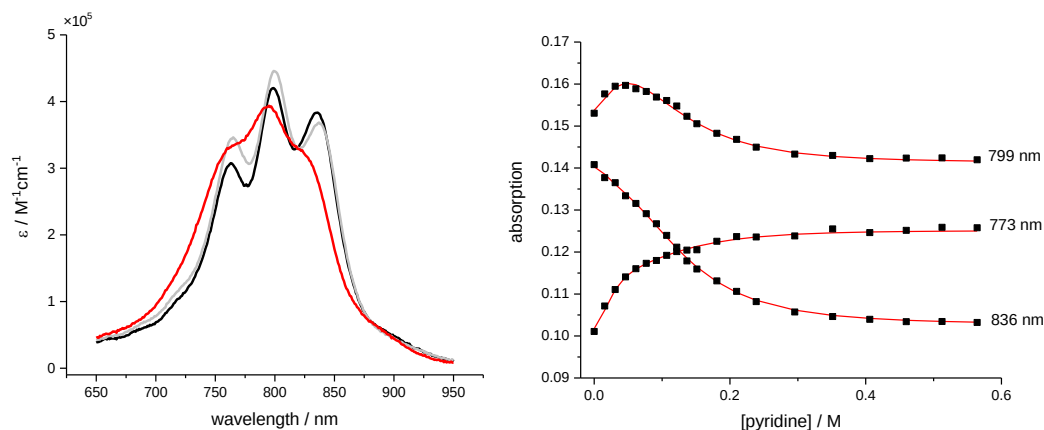


Figure 4.20. UV-vis-NIR-NIR titration of pyridine and **c-P6·(T3)₂** illustrating the removal of the two **T3** templates. (run 1, CDCl₃, 298 K, [**c-P6·(T3)₂**] = 0.37 μM, $K_{f,1} = 2.75 \times 10^{15} \text{ M}^{-1}$ $K_{f,2} = 4.90 \times 10^{13} \text{ M}^{-1}$). The fitted binding isotherm is compared to the experimental data points at characteristic wavelengths, and the fitted spectra of the three species in solution are shown: **c-P6·(T3)₂** in black, **c-P6·T3** in grey and **c-P6** in red. PB-4-111.

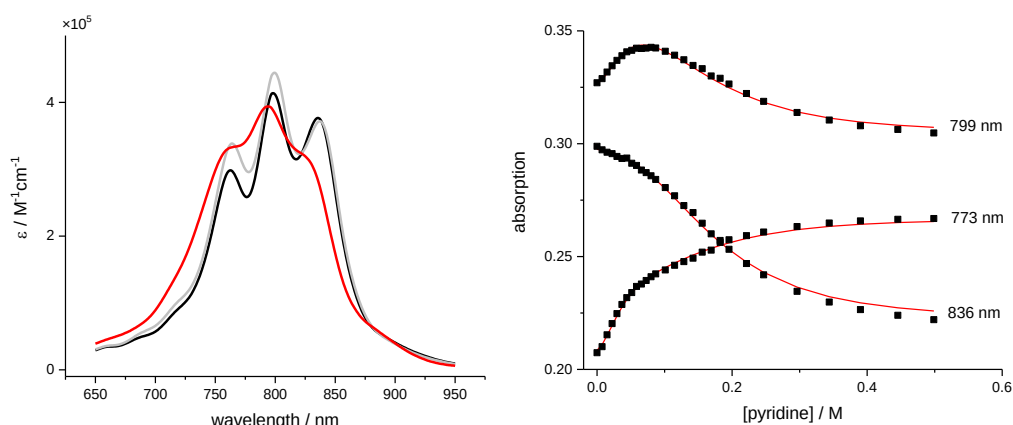


Figure 4.21. UV-vis-NIR-NIR titration of pyridine and **c-P6·(T3)₂** illustrating the removal of the two **T3** templates. (run 2, CDCl₃, 298 K, [**c-P6·(T3)₂**] = 0.79 μM, $K_{f,1} = 2.75 \times 10^{15} \text{ M}^{-1}$ $K_{f,2} = 5.62 \times 10^{13} \text{ M}^{-1}$). The fitted binding isotherm is compared to the experimental data points at characteristic wavelengths, and the fitted spectra of the three species in solution are shown: **c-P6·(T3)₂** in black, **c-P6·T3** in grey and **c-P6** in red. PB-5-49.

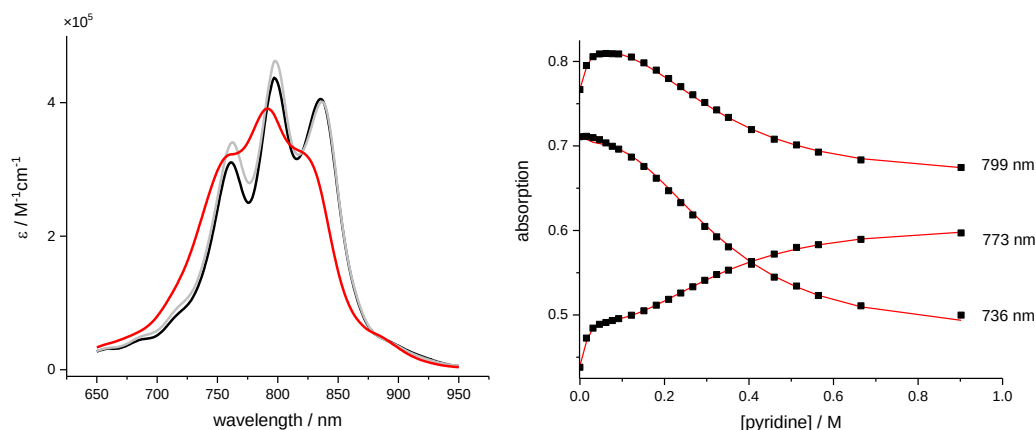


Figure 4.22. UV-vis-NIR titration of pyridine and **c-P6·(T3)₂** illustrating the removal of the two **T3** templates. (run 1, toluene, 298 K, [**c-P6·(T3)₂**] = 1.76 μM, $K_{f,1} = 2.88 \times 10^{16} \text{ M}^{-1}$ $K_{f,2} = 6.92 \times 10^{12} \text{ M}^{-1}$). The fitted binding isotherm is compared to the experimental data points at characteristic wavelengths, and the fitted spectra of the three species in solution are shown: **c-P6·(T3)₂** in black, **c-P6·T3** in grey and **c-P6** in red. PB-4-63.

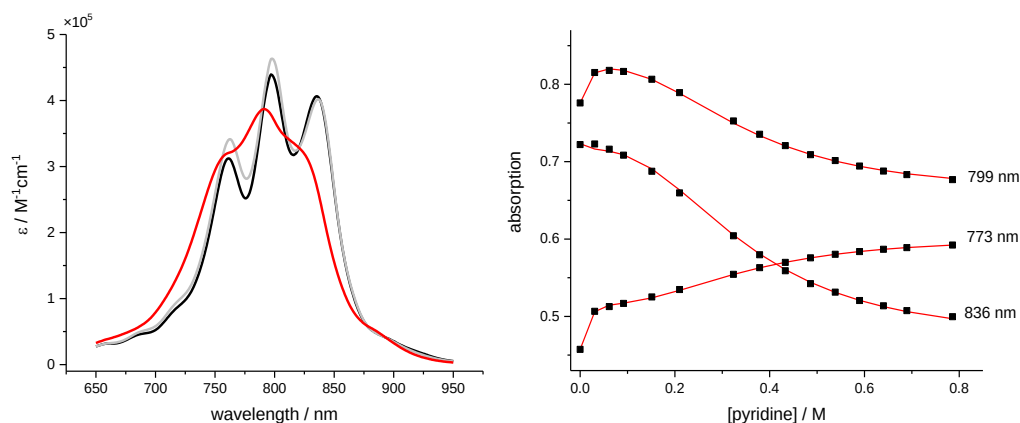


Figure 4.23. UV-vis-NIR titration of pyridine and **c-P6·(T3)₂** illustrating the removal of the two **T3** templates. (run 2, toluene, 298 K, [**c-P6·(T3)₂**] = 1.78 μM, $K_{f,1} = 3.47 \times 10^{16} \text{ M}^{-1}$ $K_{f,2} = 8.51 \times 10^{12} \text{ M}^{-1}$). The fitted binding isotherm is compared to the experimental data points at characteristic wavelengths, and the fitted spectra of the three species in solution are shown: **c-P6·(T3)₂** in black, **c-P6·T3** in grey and **c-P6** in red. PB-4-57.

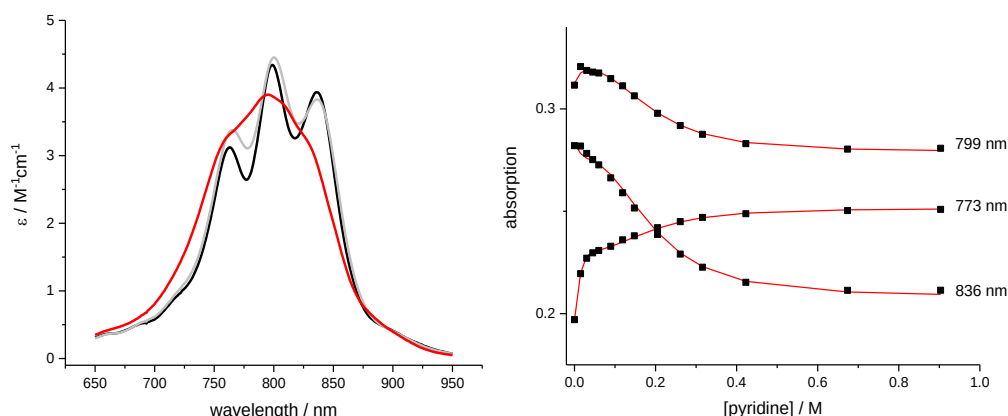


Figure 4.24. UV-vis-NIR titration of pyridine and **c-P6·(T3N)₂** illustrating the removal of the two **T3N** templates. (run 1, CDCl₃, 298 K, [**c-P6·(T3N)₂**] = 0.72 μM, $K_{f,1} = 1.45 \times 10^{16} \text{ M}^{-1}$ $K_{f,2} = 7.08 \times 10^{12} \text{ M}^{-1}$). The fitted binding isotherm is compared to the experimental data points at characteristic wavelengths, and the fitted spectra of the three species in solution are shown: **c-P6·(T3N)₂** in black, **c-P6·T3N** in grey and **c-P6** in red. PB-4-141.

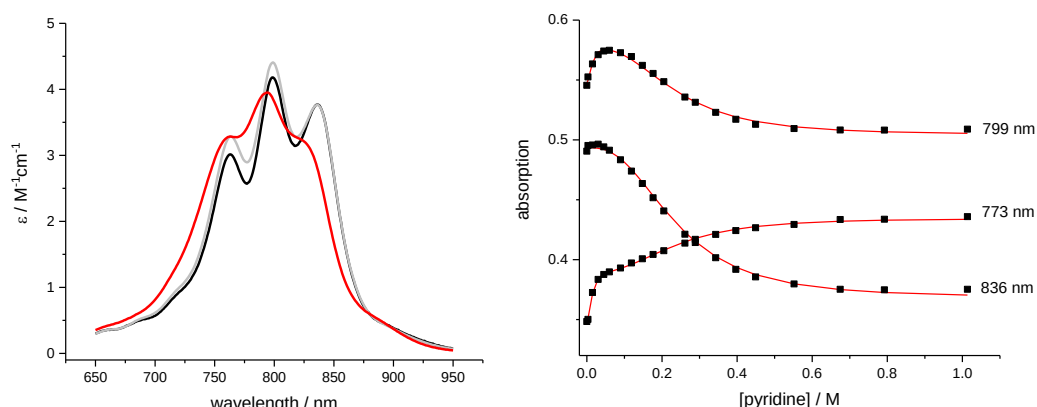


Figure 4.25. UV-vis-NIR titration of pyridine and **c-P6·(T3N)₂** illustrating the removal of the two **T3N** templates. (run 2, CDCl₃, 298 K, [**c-P6·(T3N)₂**] = 1.31 μM, $K_{f,1} = 1.48 \times 10^{16} \text{ M}^{-1}$ $K_{f,2} = 7.94 \times 10^{12} \text{ M}^{-1}$). The fitted binding isotherm is compared to the experimental data points at characteristic wavelengths, and the fitted spectra of the three species in solution are shown: **c-P6·(T3N)₂** in black, **c-P6·T3N** in grey and **c-P6** in red. PB-4-135.

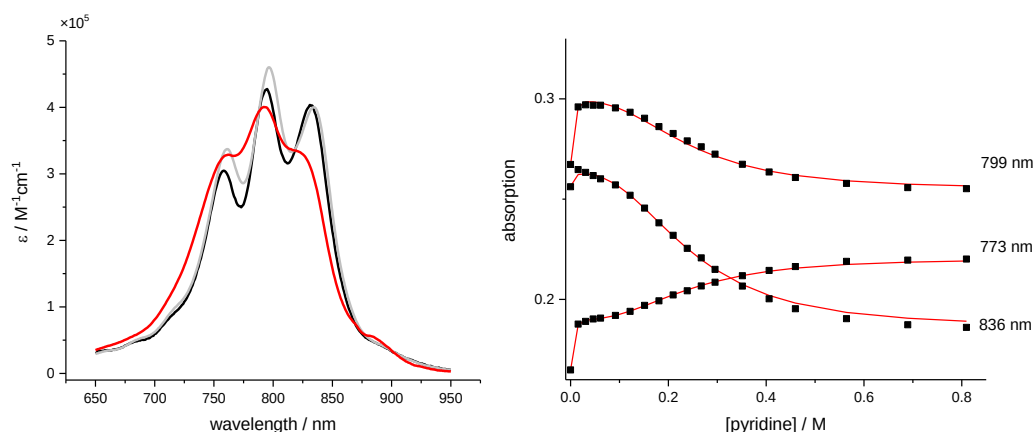


Figure 4.26. UV-vis-NIR titration of pyridine and $c\text{-P6}\cdot(\text{T3N})_2$ illustrating the removal of the two T3N templates. (run 1, toluene, 298 K, $[c\text{-P6}\cdot(\text{T3N})_2] = 0.66 \mu\text{M}$, $K_{f,1} = 3.09 \times 10^{16} \text{ M}^{-1}$, $K_{f,2} = 1.55 \times 10^{12} \text{ M}^{-1}$). The fitted binding isotherm is compared to the experimental data points at characteristic wavelengths, and the fitted spectra of the three species in solution are shown: $c\text{-P6}\cdot(\text{T3N})_2$ in black, $c\text{-P6}\cdot\text{T3N}$ in grey and $c\text{-P6}$ in red. PB-4-139.

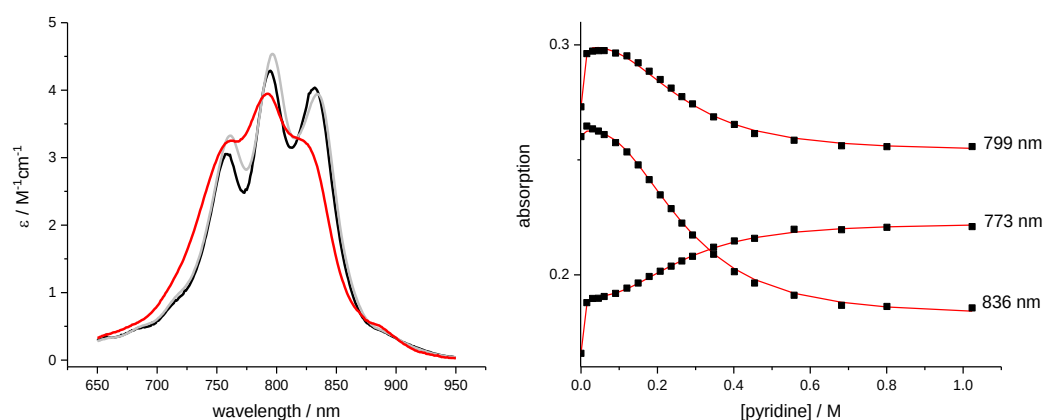


Figure 4.27. UV-vis-NIR titration of pyridine and $c\text{-P6}\cdot(\text{T3N})_2$ illustrating the removal of the two T3N templates. (run 2, toluene, 298 K, $[c\text{-P6}\cdot(\text{T3N})_2] = 0.67 \mu\text{M}$, $K_{f,1} = 4.07 \times 10^{16} \text{ M}^{-1}$, $K_{f,2} = 2.04 \times 10^{12} \text{ M}^{-1}$). The fitted binding isotherm is compared to the experimental data points at characteristic wavelengths, and the fitted spectra of the three species in solution are shown: $c\text{-P6}\cdot(\text{T3N})_2$ in black, $c\text{-P6}\cdot\text{T3N}$ in grey and $c\text{-P6}$ in red. PB-4-137.

Tables 4.4 and 4.5 show the measured K_{dn} values and calculated K_{f} values and cooperativity factors for **c-P12·(T6e)₂** titrations respectively. Tables 4.6 and 4.7 show the measured K_{f} values and the calculated statistically corrected values and cooperativity factors for **c-P6·(T3)₂** and **c-P6·(T3N)₂** titrations. The errors were determined by propagating the errors from the K_{py} values used and the sample standard deviation of K_{dn} . When ReactLab Equilibria was used to analyze the data, the value of $\log K_{\text{f}}$ is given directly. K_{f} is based on K_{py} , and the errors come from K_{py} .

Table 4.4. Summary of denaturation constants for **c-P12·(T6e)₂**

complex	solvent	K_{dn} run 1 M^{-10}	K_{dn} run 2 M^{-10}	K_{dn} M^{-10}
c-P12·(T6e)₂	CDCl_3	0.0118	0.00813	0.0131 ± 0.003
c-P12·(T6e)₂	Toluene	0.0446	0.0586	0.0516 ± 0.010

Table 4.5. Formation constants and cooperativity factor for **c-P12·(T6e)₂**

complex	solvent	$\log K_{\text{f}}$	$\log K_{\text{chem}}$	α
c-P12·(T6e)₂	CDCl_3	49.09 ± 0.33	43.02 ± 0.33	> 40 *
c-P12·(T6e)₂	Toluene	50.65 ± 0.41	44.58 ± 0.40	> 40 *

*the minimum value of α has been estimated, see Section 4.7.4.3.

Table 4.6. Summary of formation constants and cooperativity factor for **c-P6•(T3)₂** and **c-P6•(T3N)₂**

complex	solvent	log $K_{f,1}$ run 1	log $K_{f,1}$ run 2	log $K_{f,2}$ run 1	log $K_{f,2}$ run 2	log $K_{f,1}$	log $K_{f,2}$
c-P6•(T3)₂	CDCl ₃	15.44 ± 0.09	15.44 ± 0.09	13.69 ± 0.09	13.75 ± 0.09	15.44 ± 0.09	13.72 ± 0.09
	Toluene	16.46 ± 0.11	16.54 ± 0.11	12.84 ± 0.11	12.93 ± 0.11	16.50 ± 0.11	12.89 ± 0.11
c-P6•(T3N)₂	CDCl ₃	16.16 ± 0.09	16.17 ± 0.09	12.85 ± 0.09	12.90 ± 0.09	16.17 ± 0.09	12.88 ± 0.09
	Toluene	16.49 ± 0.11	16.61 ± 0.11	12.19 ± 0.11	12.31 ± 0.11	16.55 ± 0.11	12.25 ± 0.11

Table 4.7. Statistically corrected formation constants and cooperativity factor for **c-P6•(T3)₂** and **c-P6•(T3N)₂**

complex	solvent	log $K_{chem,1}$	log $K_{chem,2}$	α
c-P6•(T3)₂	CDCl ₃	13.46 ± 0.09	12.04 ± 0.09	$(3.83 \pm 1.10) \times 10^{-2}$
	Toluene	14.52 ± 0.11	11.21 ± 0.11	$(4.86 \pm 1.73) \times 10^{-4}$
c-P6•(T3N)₂	CDCl ₃	14.18 ± 0.09	11.19 ± 0.09	$(1.03 \pm 0.30) \times 10^{-3}$
	Toluene	14.57 ± 0.11	10.57 ± 0.11	$(1.00 \pm 0.36) \times 10^{-4}$

4.7.4.3 Estimation of cooperativity factor for $c\text{-P12} \cdot (\text{T6e})_2$

The ‘all-or-nothing’ knock-out model used to fit the titration data for the denaturation of $c\text{-P12} \cdot (\text{T6e})_2$ gives an ‘all-or-nothing’ value of K_{dn} . The fact that the data fit this model tells us that there is strong cooperativity, but we cannot say what the cooperativity factor (α) is because it is too high – meaning we cannot separate K_{dn1} and K_{dn2} . What we can do however, is estimate the smallest value of α that would still allow the data to be perceived as ‘all-or-nothing’.

K_{dn} , which we have determined, is the product of K_{dn1} and K_{dn2} .

$$K_{\text{dn}} = K_{\text{dn1}} \cdot K_{\text{dn2}} \quad (4.40)$$

$$K_{\text{dn}} = \frac{[c\text{-P12}(\text{py})_{12}] \cdot [\text{T6e}]^2}{[c\text{-P12}(\text{T6e})_2] \cdot [\text{py}]^{12}} \quad (4.41)$$

K_{dn1} and K_{dn2} are defined as:

$$K_{\text{dn1}} = \frac{[c\text{-P12}(\text{py})_{12}] \cdot [\text{T6e}]}{[c\text{-P12}(\text{T6e})(\text{py})_6] \cdot [\text{py}]^6} \quad (4.42)$$

$$K_{\text{dn2}} = \frac{[c\text{-P12}(\text{T6e})(\text{py})_6] \cdot [\text{T6e}]}{[c\text{-P12}(\text{T6e})_2] \cdot [\text{py}]^6} \quad (4.43)$$

If we divide K_{dn2} by K_{dn1} we get:

$$\frac{K_{\text{dn2}}}{K_{\text{dn1}}} = \frac{[c\text{-P12}(\text{T6e})(\text{py})_6] \cdot [\text{T6e}] \cdot [c\text{-P12}(\text{T6e})(\text{py})_6] \cdot [\text{py}]^6}{[c\text{-P12}(\text{T6e})_2] \cdot [\text{py}]^6 \cdot [c\text{-P12}(\text{py})_{12}] \cdot [\text{T6e}]} \quad (4.44)$$

$$\frac{K_{\text{dn2}}}{K_{\text{dn1}}} = \frac{[c\text{-P12}(\text{T6e})(\text{py})_6]^2}{[c\text{-P12}(\text{T6e})_2] \cdot [c\text{-P12}(\text{py})_{12}]} = \frac{K_{\text{f,1}}}{K_{\text{f,2}}} = \frac{2}{\alpha} \quad (4.45)$$

This ratio will be the same at any point in the titration.

The knock-out of **T6e** will never actually be ‘all-or-nothing’. The ‘all-or-nothing’ model is an approximation that can be used if the concentration of the intermediate 1:1 complex **c-P12·T6e·py₆** is always so small that it is not detected within the experimental error. Now we estimate that if there were 10% **c-P12·T6e·py₆** present in the middle of the titration (so it is not completely all-or-nothing), it would not be detected because the amount would be too small and the data would give the impression of being ‘all-or-nothing’ and give a good fit to the ‘all-or-nothing’ knock-out model.

If the knock-out is to any degree stepwise, the point in the denaturation when the concentration of intermediate would be highest would be the middle, when half of the template molecules are replaced. If we allow for the 10% 1:1 complex to be present without being detected, the ratio of complexes at the middle point of the titration will be: 45% **c-P12·(T6e)₂**, 10% **c-P12·(T6e)·(py)₆** and 45% **c-P12·(py)₁₂**. We then insert into the expression for the ratio of K_{dn2} and K_{dn1} :

$$\frac{2}{\alpha} = \frac{0.10^2}{0.45 \cdot 0.45} = 4.94 \cdot 10^{-2} \quad (4.46)$$

$$\alpha = 40.5 \quad (4.47)$$

This is then the minimum possible value of α for **c-P12·(T6e)₂**.

4.7.5 Kinetics of the exchange of T3 between nanorings

4.7.5.1 Experimental details

Exchange in CDCl₃

Two stock solutions were made: 5.29×10^{-5} M **c-P6**·(**T3**)₂ in CDCl₃, and 3.80×10^{-5} M **c-P6** in CDCl₃. These concentrations were determined using UV-Vis absorption and the extinction coefficients found in Section 4.7.4.

Experiment A: 100 μ L **c-P6**·(**T3**)₂ in CDCl₃, 100 μ L **c-P6** in CDCl₃ and 400 μ L CDCl₃ was mixed in an NMR tube making the total concentration of porphyrin nanoring 1.52×10^{-5} M. Experiment B: 100 μ L **c-P6**·(**T3**)₂ in CDCl₃, 200 μ L **c-P6** in CDCl₃ and 300 μ L CDCl₃ was mixed in an NMR tube making the total concentration of porphyrin nanoring 2.15×10^{-5} M. The tubes were sealed with an NMR cap with aluminum foil and parafilm to prevent solvent evaporation. The tubes were kept in darkness at 298 K, and ¹H NMR spectra were recorded over time.

Figure 4.28 shows the consumption of **c-P6**·(**T3**)₂ in each of the two experiments, and Figures 4.29 and 4.30 show some of the NMR spectra used in the analysis.

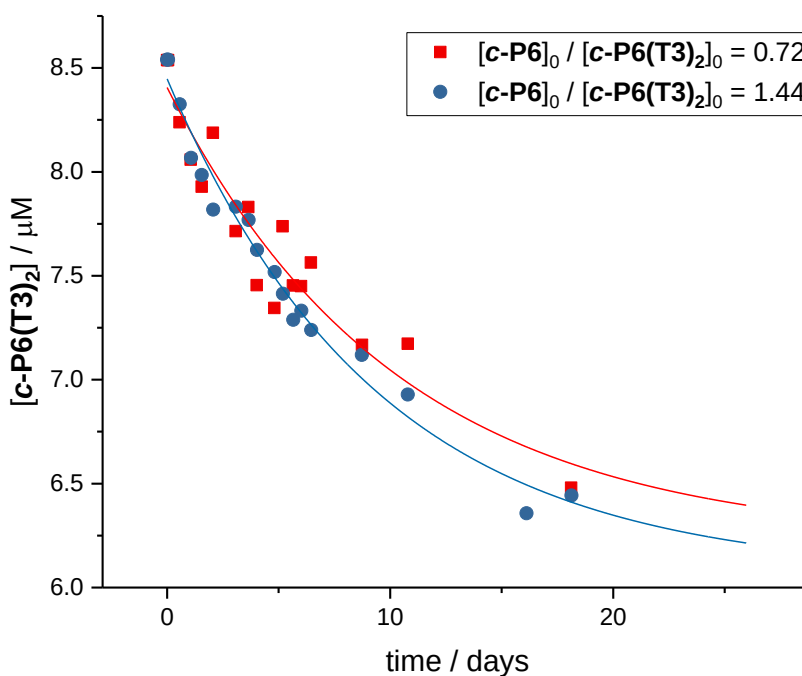


Figure 4.28. Concentration of $c\text{-P6}\cdot(\text{T3})_2$ over time in experiment A (red) and B (blue). The data points are fit to simple exponential decays for illustration ($y = y_0 + P_0 \cdot \exp(-x \cdot k)$). $k = 1.13 \times 10^{-6}$ and 1.23×10^{-6} for experiment A and experiment B respectively.

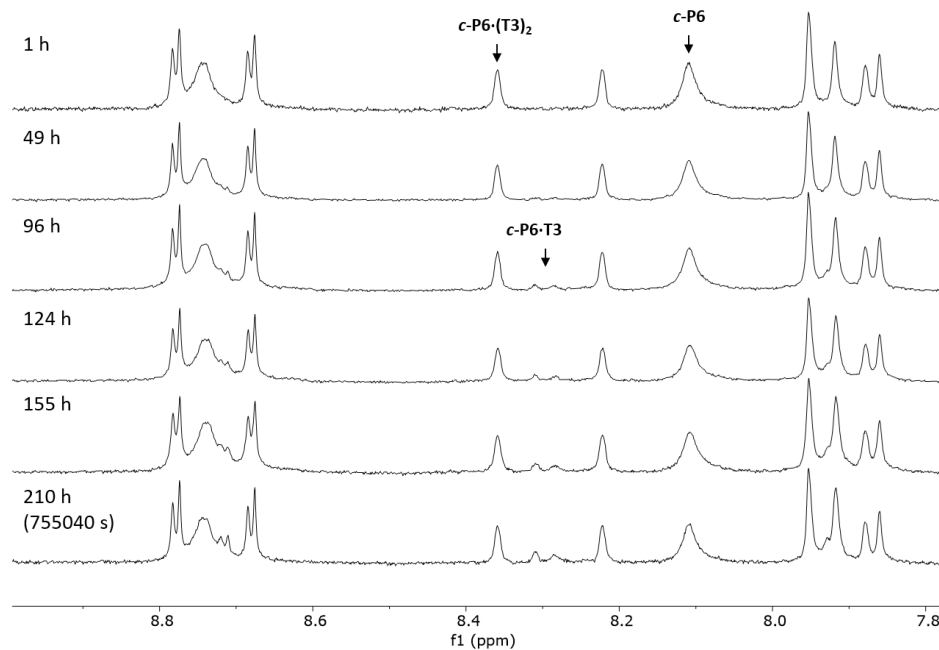


Figure 4.29. Selected ^1H NMR (500 MHz) spectra over time of experiment A. Indicated are three signals which are specific to the three components in the solution. It is these signal that are integrated and used in the analysis. CDCl_3 , 298 K.

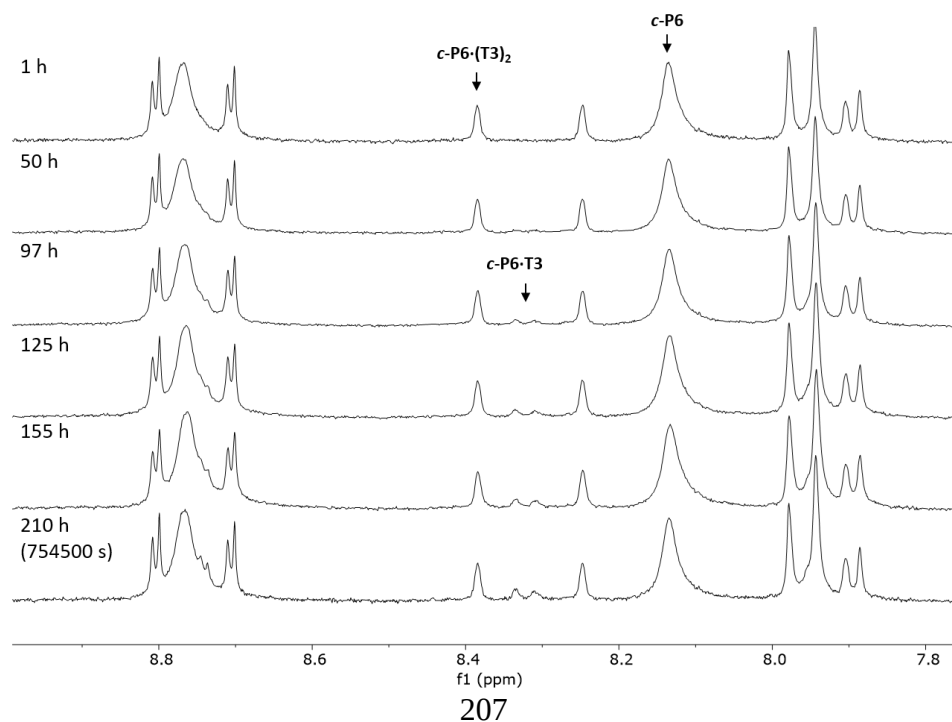


Figure 4.30. Selected ^1H NMR (500 MHz) spectra over time of experiment B. Indicated are three signals which are specific to the three components in the solution. It is these signal that are integrated and used in the analysis. CDCl_3 , 298 K.

Exchange in CDCl_3 catalyzed by pyridine

The stock solutions of **c-P6·(T3)₂** and **c-P6** from before were used again. Stock solutions with pyridine- d_5 in CDCl_3 were prepared: ‘Stock 1’: 5 μL pyridine- d_5 was mixed with 1000 μL CDCl_3 . ‘Stock 2’: 5 μL ‘Stock 1’ was mixed with 1000 μL CDCl_3 . ‘Stock 3’: 10 μL ‘Stock 1’ was mixed with 1000 μL CDCl_3 .

Experiment C: 100 μL **c-P6·(T3)₂** in CDCl_3 , 100 μL **c-P6** in CDCl_3 and 400 μL ‘Stock 2’ was mixed in an NMR tube making the total concentration of porphyrin nanoring 1.52×10^{-5} M and the total concentration of pyridine- d_5 0.20 mM.

Experiment D: 100 μL **c-P6·(T3)₂** in CDCl_3 , 100 μL **c-P6** in CDCl_3 and 400 μL ‘Stock 3’ was mixed in an NMR tube making the total concentration of porphyrin nanoring 1.52×10^{-5} M and the total concentration of pyridine- d_5 0.41 mM.

The tubes were sealed with an NMR cap with aluminum foil and parafilm to prevent solvent evaporation. The tubes were kept in darkness at room temperature, and ^1H NMR spectra were recorded over time.

Figure 4.31 shows the consumption of **c-P6·(T3)₂** in each of the two experiments, and Figure 4.32 and 4.33 shows some of the NMR spectra used in the analysis.

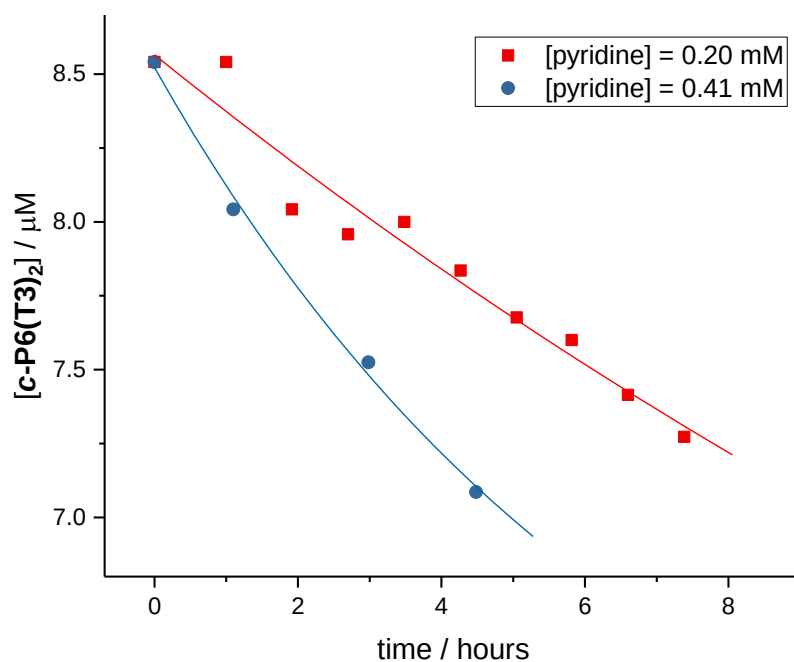


Figure 4.31. Concentration of *c*-P6·(T3)₂ over time in experiment C (red) and D (blue). The data points are fit to simple exponential decays for illustration ($y = y_0 + P_0 \cdot \exp(-x \cdot k)$). $k = 1.08 \times 10^{-5}$ and 3.99×10^{-5} for experiment C and experiment D respectively.

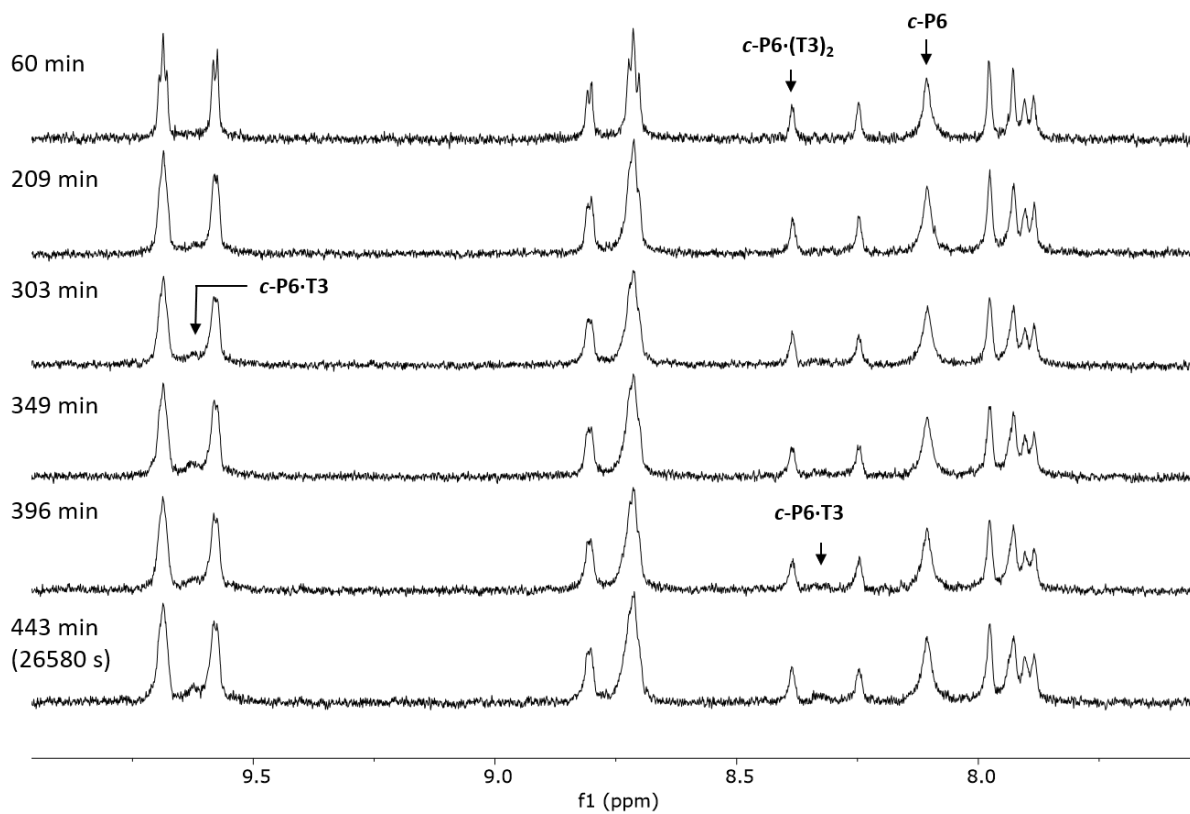


Figure 4.32. Selected ^1H NMR (400 MHz) spectra over time of experiment C. Indicated are four signals which are specific to the three components in the solution. It is these signal that are integrated and used in the analysis. For determining the concentration of **c-P6·T3**, an average of the two indicated signals were used in an attempt to make the result more reliable. CDCl_3 , 298 K.

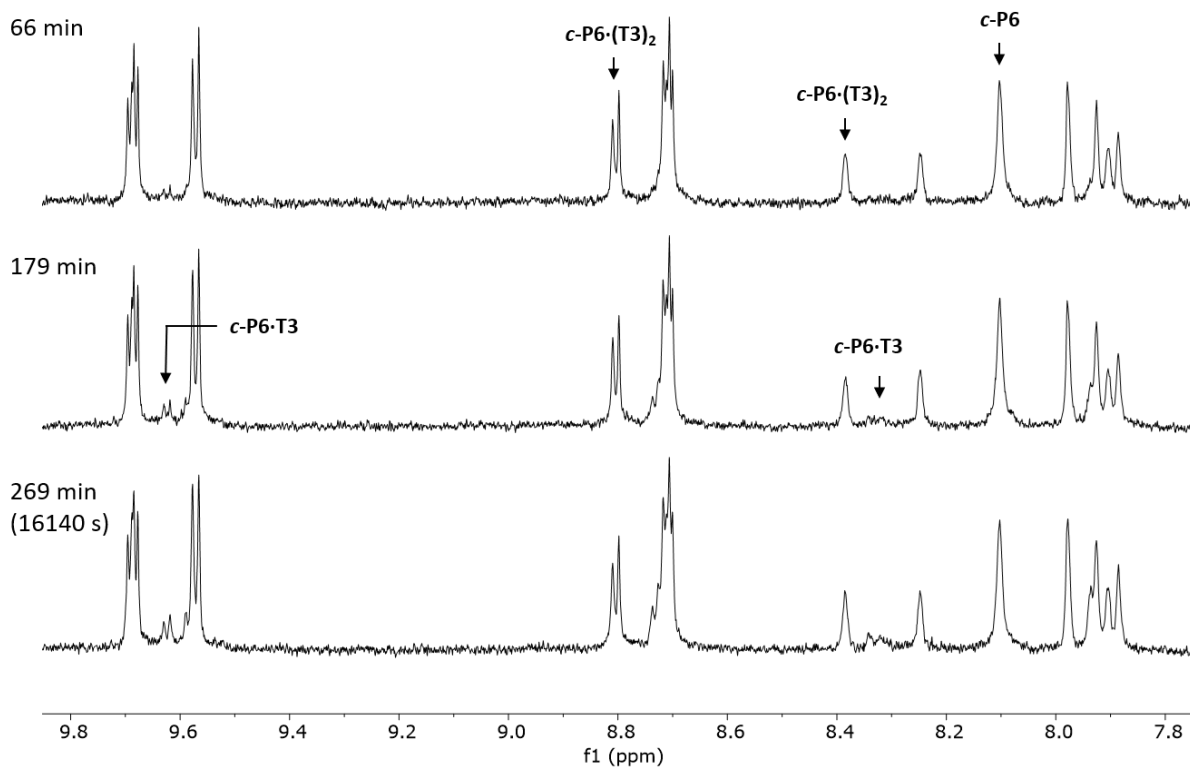
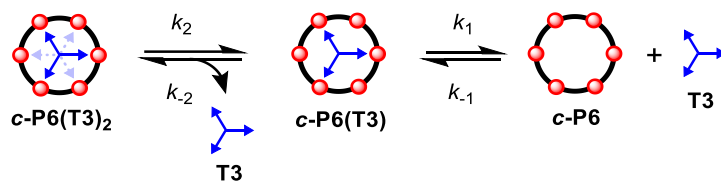


Figure 4.33. Selected ^1H NMR (400 MHz) spectra over time of experiment D. Indicated are five signals which are specific to the three components in the solution. It is these signal that are integrated and used in the analysis. For determining the concentration of **c-P6·T3**, an average of the two indicated signals were used in an attempt to make the result more reliable. CDCl_3 , 298 K.

4.7.5.2 Initial rate analysis

We propose a mechanism for the exchange:



Scheme 4.5. Proposed mechanism of exchange between $c\text{-P6}(\text{T3})_2$, $c\text{-P6}(\text{T3})$ and $c\text{-P6}$ with rate constants.

The rate equation for the change in concentration of $c\text{-P6}(\text{T3})_2$ according to the proposed mechanism is:

$$\frac{d[c\text{-P6}(\text{T3})_2]}{dt} = -k_2[c\text{-P6}(\text{T3})_2] + k_{-2}[c\text{-P6}(\text{T3})][\text{T3}] \quad (4.48)$$

At the very beginning of the experiment, the solution almost only contains $c\text{-P6}(\text{T3})_2$ and $c\text{-P6}$. The term $k_{-2}[c\text{-P6}(\text{T3})][\text{T3}]$ is going to be very small because there is a large excess of $c\text{-P6}$ present, which will react with any formed T3 . Therefore, the initial reaction kinetics are pseudo first order, and the initial rate equation is simplified to:

$$\frac{d[c\text{-P6}(\text{T3})_2]}{dt} = -k_2[c\text{-P6}(\text{T3})_2] \quad (4.49)$$

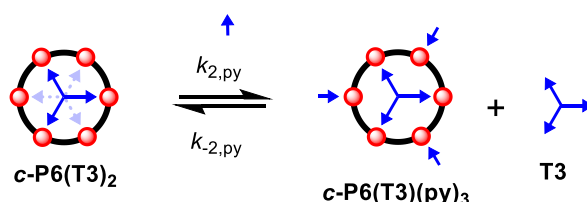
For the rough estimate of an initial rate, the first few data points were used.

Table 4.8. Initial rate analysis of **T3** exchange.

	A	B
$[c\text{-P6}\cdot(\text{T3})_2]_{\text{initial}}$	$8.54 \times 10^{-6} \text{ M}$	$8.54 \times 10^{-6} \text{ M}$
$[c\text{-P6}\cdot(\text{T3})_2]_{\text{final}}$	$7.17 \times 10^{-6} \text{ M}$	$7.12 \times 10^{-6} \text{ M}$
change in $[c\text{-P6}\cdot(\text{T3})_2]$	$-1.37 \times 10^{-6} \text{ M}$	$-1.42 \times 10^{-6} \text{ M}$
change in time	755040 s	754500 s
initial rate	$-1.81 \times 10^{-12} \text{ M/s}$	$-1.88 \times 10^{-12} \text{ M/s}$

Since the initial rate for experiment B is not double that of A, but they are in fact effectively the same, it can be concluded that the concentration of **c-P6** is not rate determining in the initial stage of the experiment. This supports the proposed mechanism where the rate determining step is unimolecular.

To test the effect of having pyridine present to catalyze the exchange, we conducted two more experiments with pyridine in two different concentrations. Again, we limit our analysis to the first few data points, where there is a large excess of **c-P6** and **T3** in solution, so there is no reaction between **c-P6** and **T3**, and the rate is determined by $k_{2,\text{py}}$.



Scheme 4.6. Initial pyridine-catalyzed consumption of **c-P6**·(**T3**)₂.

Using the same assumptions as described above, the initial rate equation for the pyridine catalyzed reaction is proposed to look like this:

$$\frac{d[c\text{-P6}(\text{T3})_2]}{dt} = -k_{2,\text{py}}[c\text{-P6}(\text{T3})_2][\text{py}]^x \quad (4.50)$$

Table 4.9. Initial rate analysis of pyridine catalyzed **T3** exchange.

	C ([py] = 0.2 mM)	D ([py] = 0.4 mM)
$[c\text{-P6}\cdot(\text{T3})_2]_{\text{initial}}$	$8.54 \times 10^{-6} \text{ M}$	$8.54 \times 10^{-6} \text{ M}$
$[c\text{-P6}\cdot(\text{T3})_2]_{\text{final}}$	$7.27 \times 10^{-6} \text{ M}$	$7.09 \times 10^{-6} \text{ M}$
change in $[c\text{-P6}\cdot(\text{T3})_2]$	$-1.27 \times 10^{-6} \text{ M}$	$-1.45 \times 10^{-6} \text{ M}$
change in time	26580 s	16140 s
initial rate	$-4.78 \times 10^{-11} \text{ M/s}$	$-8.98 \times 10^{-11} \text{ M/s}$

The initial rate for the experiment with 0.4 mM pyridine is 1.9 times higher than for the experiment with 0.2 mM pyridine. From this, it looks like the reaction is first order with respect to the concentration of pyridine.

4.7.5.3 Determining rate constants

While the initial rate can give insight into reaction mechanisms and which rate law to use, we calculate the rate constants using all the data points.

To find k_2 , we integrate Equation 4.49, remembering that because $[c\text{-P6}\cdot(\text{T3})_2]$ does not go to 0 M, we have to include a term for $[c\text{-P6}\cdot(\text{T3})_2]_{\infty}$.³⁸

$$[c\text{-P6}(\text{T3})_2] - [c\text{-P6}(\text{T3})_2]_{\infty} = ([c\text{-P6}(\text{T3})_2]_0 - [c\text{-P6}(\text{T3})_2]_{\infty})e^{-k_2 t} \quad (4.51)$$

$[c\text{-P6}\cdot(\text{T3})_2]_{\infty}$ is the concentration at equilibrium and was calculated to be $2.78 \times 10^{-6} \text{ M}$ using K_{eq} determined in Section 4.7.4.4. To find k_2 , we fit the data from experiment A to Equation 4.51 (Figure 4.34).

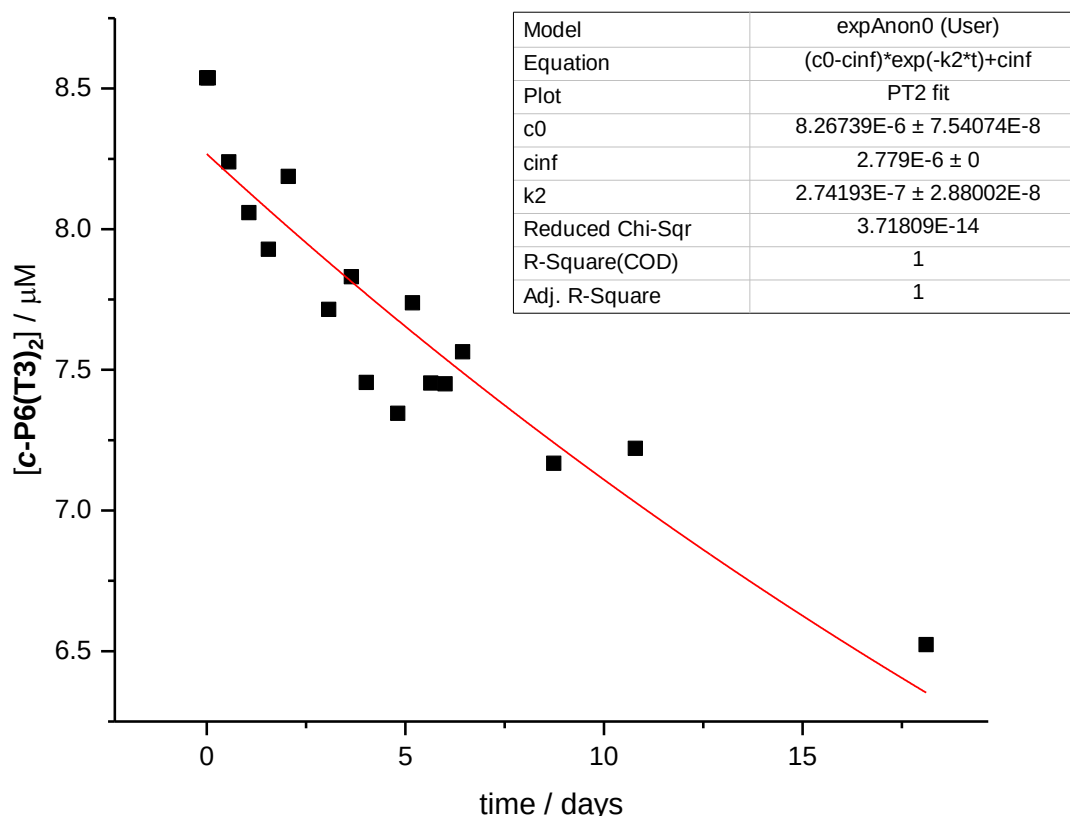


Figure 4.34. Plot of $[c\text{-P6}(\text{T3})_2]$ over time for experiment A in the beginning of the reaction.

k_2 is given by the fit to be $2.74 \times 10^{-7} \text{ s}^{-1}$. Since we have determined $K_{f,2}$ (Section 4.7.4.2) we can calculate k_{-2} using equation 4.52:

$$K_{f,2} = \frac{k_{-2}}{k_2} \quad (4.52)$$

$$k_{-2} = K_{f,2} \cdot k_2 = 5.25 \cdot 10^{13} \text{ M}^{-1} \cdot 2.74 \cdot 10^{-7} \text{ s}^{-1} = 1.44 \cdot 10^7 \text{ M}^{-1}\text{s}^{-1} \quad (4.53)$$

We found in Section 4.5 that the diffusion-controlled rate of the reaction k_{diff} is $1.23 \times 10^{10} \text{ M}^{-1}\text{s}^{-1}$. Since k_2 is three orders of magnitude lower than that, we can conclude that the reaction is not diffusion controlled, and that the statistical initial distribution of products observed when **c-P6** is mixed with **T3** under stirring is caused by k_2 and k_1 being identical.

$$k_{-1} = k_{-2} = 1.44 \cdot 10^7 \text{ M}^{-1}\text{s}^{-1} \quad (4.54)$$

Now we calculate k_1 using $K_{f,1}$.

$$k_1 = \frac{k_{-1}}{K_{f,1}} = 5.23 \cdot 10^{-9} \text{ s}^{-1} \quad (4.55)$$

Next we look at the pyridine catalyzed rate equation.

$$\frac{d[\mathbf{c-P6(T3)_2}]}{dt} = -k_{2,\text{py}}[\mathbf{c-P6(T3)_2}][\text{py}]^x \quad (4.56)$$

From the initial rate analysis, we learned that the initial rate is first order with respect to pyridine, meaning that $x = 1$.

Each time two molecules of $\mathbf{c-P6(T3)}$ are formed, one molecule of $\mathbf{c-P6}$ is consumed. This means that the number of porphyrin units available for pyridine coordination is preserved throughout the entire experiment and:

$$[\text{py}] = [\text{py}]_0 \quad (4.57)$$

Meaning pyridine is a catalyst and the reaction is pseudo first order, so we can write the rate equation as:

$$\frac{d[\mathbf{c-P6(T3)_2}]}{dt} = -k'_{2,\text{py}}[\mathbf{c-P6(T3)_2}] \quad (4.58)$$

where

$$k'_{2,\text{py}} = k_{2,\text{py}}[\text{py}]_0 \quad (4.59)$$

We integrate Equation 4.58:

$$[\mathbf{c-P6(T3)_2}] - [\mathbf{c-P6(T3)_2}]_\infty = ([\mathbf{c-P6(T3)_2}]_0 - [\mathbf{c-P6(T3)_2}]_\infty)e^{-k'_{2,\text{py}}t} \quad (4.60)$$

and fit the data from experiment C to Equation 4.60 (Figure 4.35).

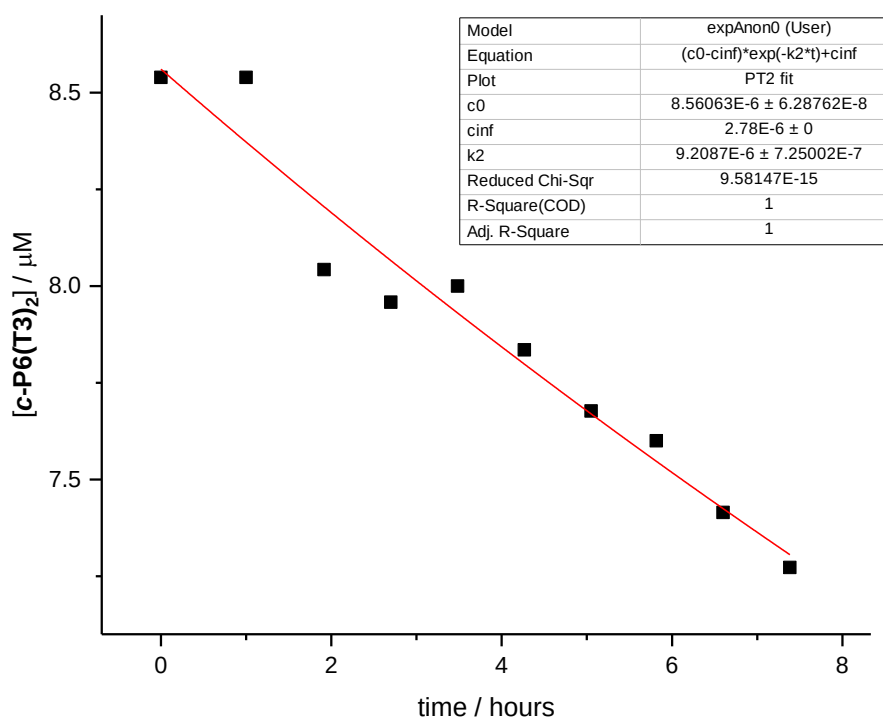


Figure 4.35. Plot of $[c\text{-P6(T3)}_2]$ over time for experiment C in the beginning of the reaction.

We calculate $k_{2,\text{py}}$.

$$k_{2,\text{py}} = \frac{k'_{2,\text{py}}}{[\text{py}]_0} = \frac{9.21 \cdot 10^{-6} \text{s}^{-1}}{0.2 \text{ mM}} = 4.61 \cdot 10^{-2} \text{ M}^{-1} \text{s}^{-1} \quad (4.61)$$

The rate dependence on pyridine is probably more complicated, as the rate equation is likely to consist of contributions from a mechanism proceeding without pyridine and mechanisms that are first, second and third order with respect to pyridine. The magnitude of the contributions from each type of mechanism is likely to be dependent on the concentration of pyridine, so varying the concentration might shift the contributions. A further analysis was therefore not attempted.

4.7.6 Molecular modelling

Model geometries of studied nanorings and templates were simplified by replacing aryl and octyl solubilizing groups with hydrogen atoms. Geometries were optimized using Gaussian16/A.03²² and either DFT (B3LYP/3-21G functional/basis set, used for **c-P6·(T3)**₂, **c-P6·(TN3)**₂, **T3** and **TN3**) or semiempirical PM6 method (used for **c-P12·(T6e)**₂ and **T6e**). Optimized geometries were confirmed as local minima by performing frequency calculation which showed no imaginary frequencies, with exception of **T6e**, for which frequency calculation revealed two imaginary frequencies of -1.6 and -0.9 cm^{-1} , to which is attributed no significance.

Template molecules are essentially flat, with subtle zig-zag alternation in phenylene-phenylene backbone. The exact geometry of optimized **T3** template possess C_1 symmetry, however, very close to the D_3 (According to symmetrising algorithm implemented in GaussView 5.0 with ‘loose’ tolerance). The radius of **T3**, assumed as distance from center of gravity to nitrogen atoms, is 10.04 Å. The exact geometry of optimized **TN3** template possess C_1 symmetry, however, very close to the C_3 . The radius of **TN3** is 9.93 Å. The exact geometry of **T6e** possess C_1 symmetry, but its star-shape implies closeness to C_6/D_6 . The diameter, measured as longest N–N distance is 47.38 Å, and thus the radius of **T6e** is 23.69 Å.

The optimized complex **c-P12·(T6e)**₂ is flat, if viewed through the Zn atom positions which deviate from plane maximally by ± 0.1 Å. One template molecule is essentially within the nanoring plane with the second template stacked on top of it in a bowl shape to maintain the coordination of pyridyl functions to zincs. Centres of the templates are stacked apart by 3.6 Å, in agreement with expected typical distance for π - π stacking.³⁹ The Zn—N distance for nanoring-template interaction is 2.11 Å for all 12 sites, which agrees with interaction distance observed in crystal structures (2.15 ± 0.02 Å).⁴⁰

Contrary to **c-P12** templated complex, the smaller nanoring **c-P6** does not provide space sufficient for bending of the template to place nitrogen atoms in a plane. Therefore, the steric requirement for template stacking is projected partly to nanoring and the **c-P6·(T3)**₂ and **c-P6·(TN3)**₂ complexes adopt saddle shapes. This distortion can be quantified by fitting the surface function $z = f(x,y)$ to core atoms positions (butadiyne and to it connected *meso* carbon

atoms and zinc porphyrin centers). For **c-P6·(T3)₂**, positions of these core atoms can be well fitted with function: $z = -0.6401 + 0.01699 \cdot x^2 - 0.009104 \cdot y^2$, (where x, y, z are coordinates of core atoms in Å of structure re-oriented to have allow best fit) with fit quality $R^2 = 0.97$.

Centres of the **T3** templates are stacked apart at distance of 4.0 Å. Saddle geometry of **c-P6·(TN3)₂** is slightly diagonally twisted relative to **c-P6·(T3)₂**. Positions of core atoms can be well fitted with function: as $z = -1.923 + 0.02447 \cdot x^2 - 0.007992 \cdot x \cdot y$, with $R^2 = 0.97$.

Centres of the **TN3** templates are stacked apart at distance of 3.52 Å.

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Synthesis of porphyrin nanorings using stacked templates

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Allosteric Cooperativity and Template-Directed Synthesis with Stacked Ligands in Porphyrin Nanorings

P. S. Bols, M. Rickhaus, L. Tejerina, H. Gotfredsen, K. Eriksen, M. Jirasek, H. L. Anderson, *J. Am. Chem. Soc.* **2020**, just accepted.

5.1 Abstract

Template-directed synthesis is widely used in chemistry to access precisely defined structures. Synthesizing the template for the reaction, however, can sometimes be the most challenging part of the process. The Vernier approach, in which several smaller less complicated templates cooperate in the synthesis, is therefore extremely useful. We have discovered a new type of Vernier template-directed synthesis where two templates form a stack that fits a favorable conformation of the targeted complex and does therefore not require the complex to twist. This turns out to be a significant advantage when synthesizing complexes with sterically bulky solubilizing groups, and is the most efficient method to prepare a 12-porphyrin nanoring with THS-solubilizing groups. The macrocyclization works well with the positively cooperative template **T6e**, but it does not work with the templates **T3** and **T3N**, which display negative allosteric cooperativity.

5.2 Introduction

While allosteric cooperativity can be used to modulate the activity of complex molecular receptors, the synthesis of such structures presents its own challenge. Template-directed synthesis is a powerful tool in this regard, because it allows highly complex architectures to be accessed from relatively simple building blocks.¹ Achieving increasingly sophisticated structures, however, is often accompanied by complicated template synthesis. As a solution, it was shown that a Vernier complex can be used, in which several small, simple oligopyridine templates bind porphyrin oligomers to ultimately create nanorings of unprecedented size.² Importantly this method is versatile, and the conditions can be altered to provide the desired ring size by varying the equivalents of porphyrins to templates. This type of Vernier templating relies on the porphyrin oligomers to form figure-of-eight shapes, which can be problematic when large solubilizing groups are required, and these twisted geometries result in significant steric clashing. Potent solubilizing groups have proven crucial for preventing aggregation and decomposition in groundbreaking studies of global aromaticity,³ quantum interference,⁴ and energy transfer⁵ in large oligomeric systems that mimic those found in Nature.

Chapter 2 describes how it was discovered that two molecules of the D_{3h} symmetrical tripyridine template **T3** can stack and thus both bind inside the hexaporphyrin nanoring **c-P6** (Figure 4.1b).⁶ In Chapter 4 this stacking behavior is investigated thermodynamically and kinetically, and it was found that it can also be applied to a hexapyridine template **T6e** that

stacks inside **c-P12**⁷ (Figure 4.1a) with a high⁸ cooperativity factor. We became curious whether this could be leveraged to access nanorings with large solubilizing groups.

5.3 Experimental design and analysis

Having demonstrated the high allosteric cooperativity in the stacked template complexes, we next explored the feasibility of leveraging this cooperativity to prepare macrocyclic structures. As proof of concept, we opted to employ the palladium-catalyzed oxidative coupling of the linear zinc-porphyrin dimers **I-P2** in the presence of **T3** and **T3N** and compared it to **T6**, for which the synthesis of **c-P6** is known to be very high-yielding.⁹ We also investigated the coupling of a linear zinc-porphyrin tetramer **I-P4** in the presence of elongated **T6e** and compared it to the coupling in the presence of the **T6**, for which isolated yields of **c-P12** have been published.¹⁰ These concepts are outlined in Figure 5.1.

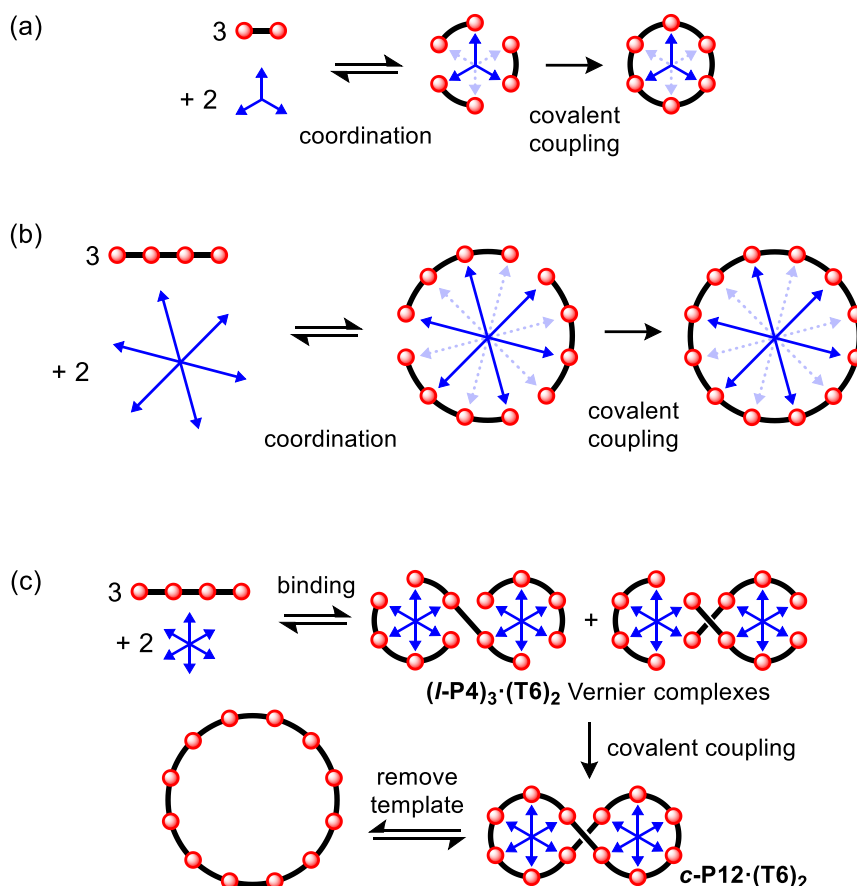


Figure 5.1. (a) and (b) synthesis of **c-P6** and **c-P12** using a stacked template approach, (c) synthesis of **c-P12** using a classical Vernier approach.

In order to determine the effectiveness with different types of solubilizing groups, we investigated the coupling with porphyrins with *t*-Bu side chains and THS side chains (Figure 5.2).

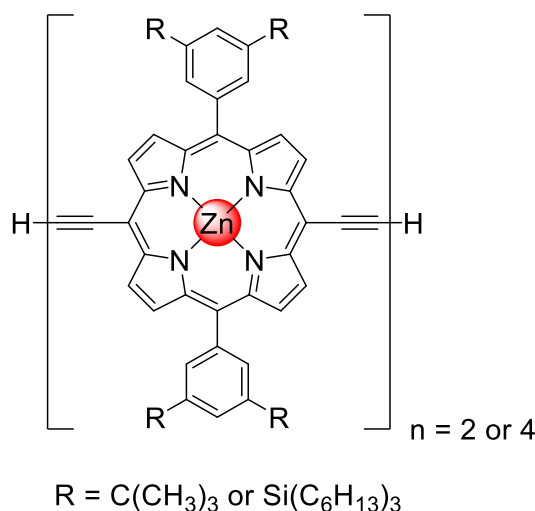


Figure 5.2. Chemical structure of the linear oligomers used in the synthesis: ***I-P2***_{*t*-Bu}, ***I-P2***_{THS}, ***I-P4***_{*t*-Bu}, and ***I-P4***_{THS}.

The linear and cyclic products of the cooperative syntheses were identified from their retention time, using a calibration scale based on the retention times of known products (see Section 5.6.1). Additionally, for the synthesis with ***I-P4***_{THS} and **T6e** (Figure 5.4a), the products were also isolated and identified with MALDI-ToF.

The analytical yields were determined through deconvolution of the GPC traces, using absorption as a quantitative measure. At 466 nm, ***I-P2*** and ***c-P6***·**T6** have the same molar absorption coefficient per porphyrin unit, and at 470 nm ***I-P4***, ***c-P8***, and ***c-P12*** have the same molar absorption coefficient per porphyrin unit (see Figure 5.8). For each GPC run of a product mixture, a reference run was measured where starting material was injected in the same amount as used in the reaction. The analytical yields were then calculated as the integral of the product peak as a percentage of the integral of the starting material external standard (see Section 5.6.2.2 for details).

5.4 Results of synthesis with stacked templates

Figure 5.3 shows the results from the couplings of ***I-P2*** in the presence of **T3**, **T3N** and **T6** respectively. The coupling of ***I-P2***_{THS} in the presence of both **T3** and **T3N** seem to be almost unaffected by the presence of the templates. The product distribution is very similar to the

distribution without any template (see Section 5.6.2.2). In the presence of **T6** however, the formation of **c-P6_{THS}** is extremely efficient (76%). The story is the same with **I-P2_{t-Bu}**. Both **T3** and **T3N** give almost exclusively long linear oligomers whereas **T6** gives a very clean reaction and a great yield of **c-P6_{t-Bu}** (63%).

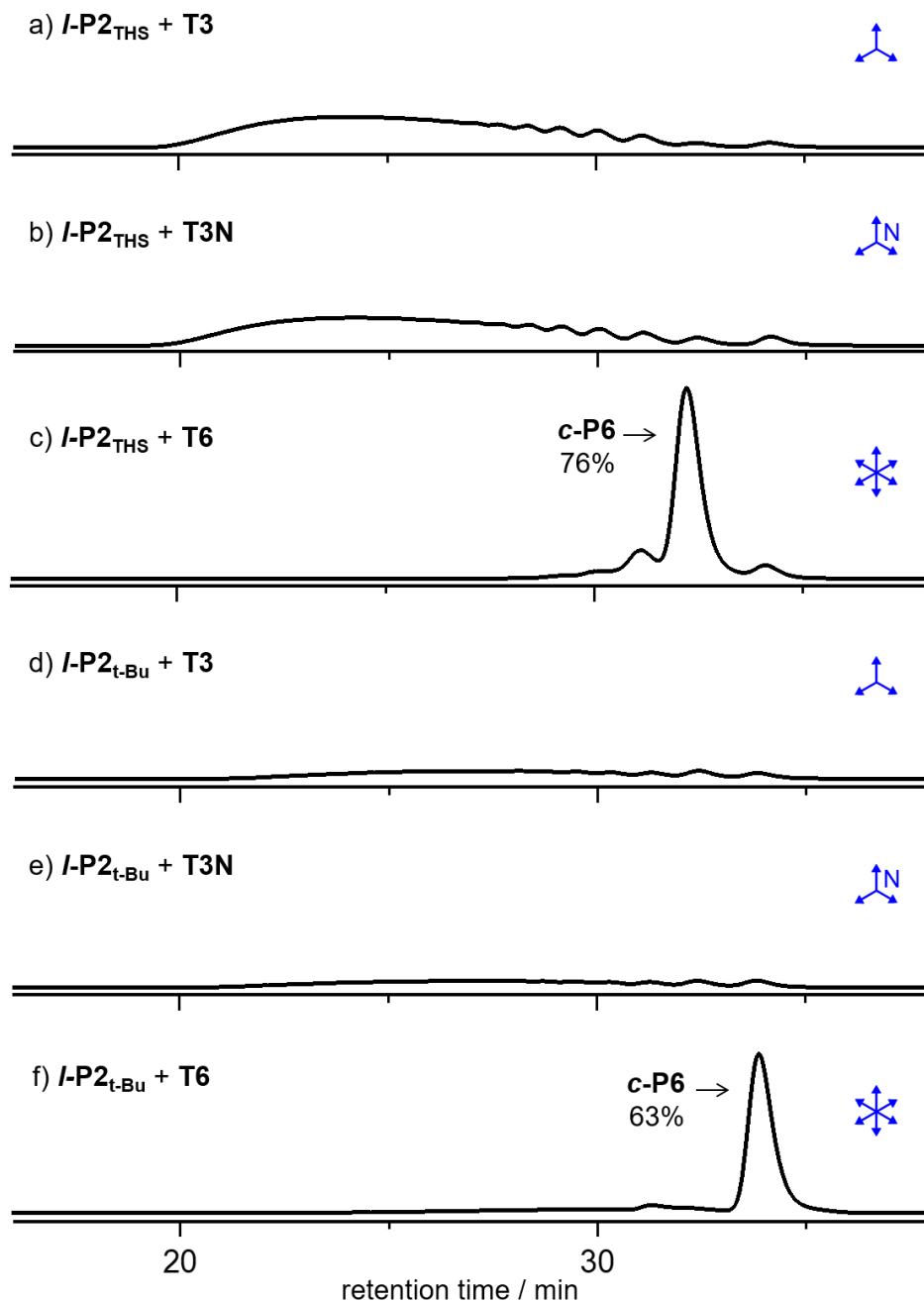


Figure 5.3. Analytical GPC traces from stacked-template reactions with porphyrin dimer with THS and *t*-Bu sidechains. The GPC traces were measured using two JIAGEL-H columns in series (3H-A then 4H-A), with THF:1% pyridine eluent and a 1 mL/min flow rate. Detection at 466 nm.

With the highly cooperative **T6e** template, the picture is completely different. Figure 5.4 shows the results from the couplings of **I-P4** in the presence of **T6e** and **T6** respectively. The coupling of **I-P4**_{THS} in the presence of **T6e** gave a high yield of **c-P12**_{THS} (30%). Other products included **c-P20**_{THS}, which was identified by MALDI-ToF. For comparison, the same experiment with **T6** gave predominantly **c-P8**_{THS} (34%) and a lower yield of **c-P12**_{THS} (18%) which is in agreement with the published isolated yield of **c-P12**_{THS} of 14%.⁵

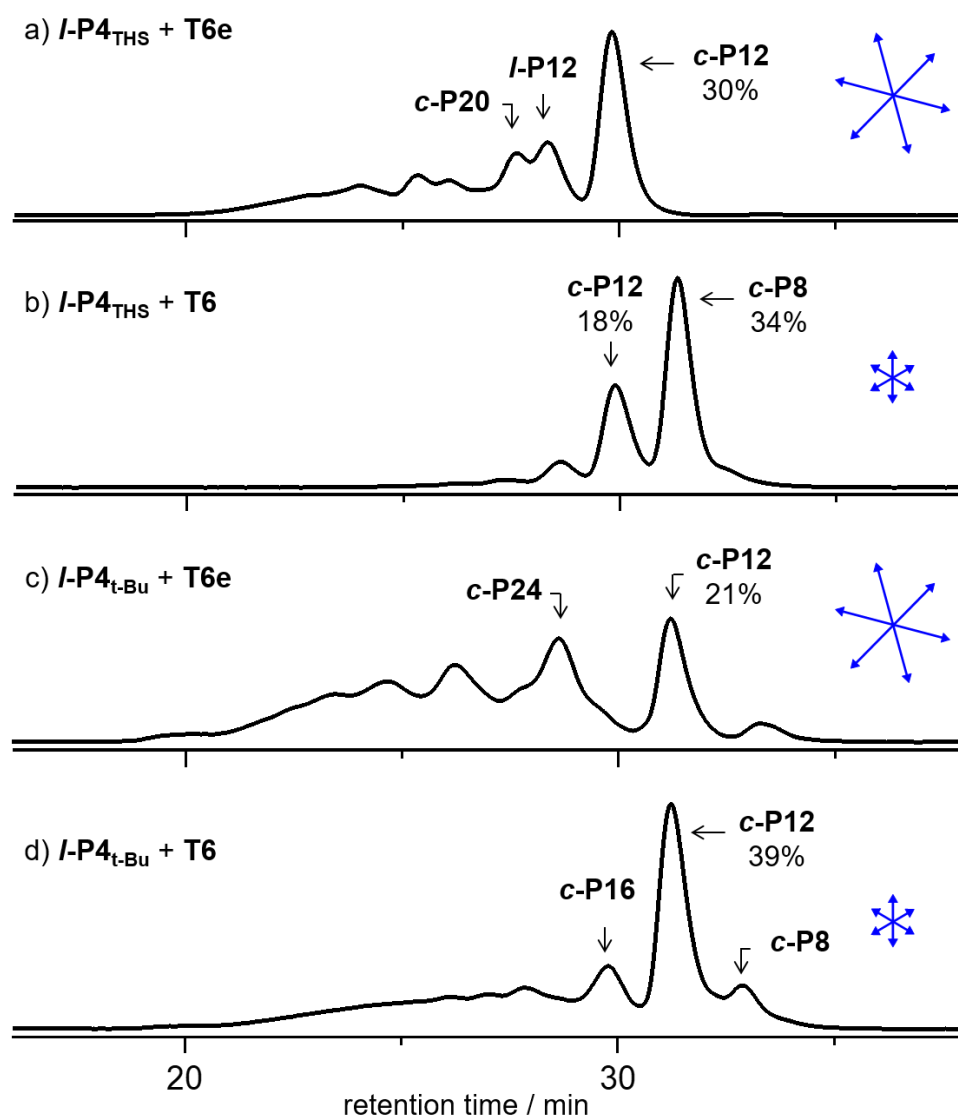


Figure 5.4. Analytical GPC traces from stacked-template reactions with porphyrin tetramer with THS and *t*-Bu sidechains. The GPC traces were measured using two JIAGEL-H columns in series (3H-A then 4H-A), with THF:1 % pyridine eluent and a 1 mL/min flow rate. Detection at 470 nm.

Coupling of ***I*-P4_{*t*-Bu}** in the presence of **T6e** gave ***c*-P12_{*t*-Bu}** in lower, though still good, yield (21%), but interestingly, a significant amount of ***c*-P24_{*t*-Bu}** was detected, evidence of a large double Vernier complex formation. For comparison, the same coupling in the presence of **T6**, gave ***c*-P12_{*t*-Bu}** in a very high yield (39%), as published,^{2a} but no detectable amount of ***c*-P24_{*t*-Bu}**.

Comparison of the results from the reactions with ***I*-P4_{THS}** and ***I*-P4_{*t*-Bu}** respectively, highlights the ease with which *t*-Bu oligomers form twisted Vernier complexes (***c*-P12·(T6)₂** and ***c*-P24·(T6e)₄**) compared to the THS oligomers that prefer to form caterpillar-track complexes (***c*-P8·(T6)₂** and ***c*-P20·(T6e)₄**). The formation of these complexes has not been confirmed, but for illustration they are shown in Figure 5.5.

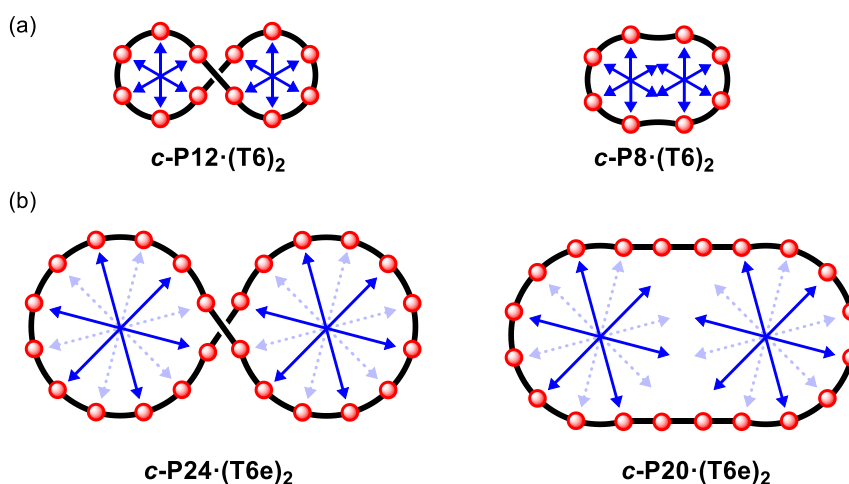


Figure 5.5. (a) Twisted Vernier complex ***c*-P12·(T6)₂** and caterpillar-track complex ***c*-P8·(T6)₂**. (b) proposed structures of twisted Vernier complex ***c*-P24·(T6e)₄** and caterpillar-track complex ***c*-P20·(T6e)₄**.

This effect can be understood by looking at the crystal structure of ***c*-P12_{*t*-Bu}·(T6)₂** (Figure 5.5).^{2b} The crossing point of the two loops is very crowded and the *tert*-butyl groups are very close (3.17-3.32 Å) to the planes of the porphyrins. Since THS groups are much larger than *tert*-butyl groups, this figure-of-eight shape is less favored when using THS. Hence, because of the bulkiness of the THS-sidechains of ***I*-P4_{THS}**, **T6e** is a better choice for forming ***c*-P12_{THS}** compared to **T6**.

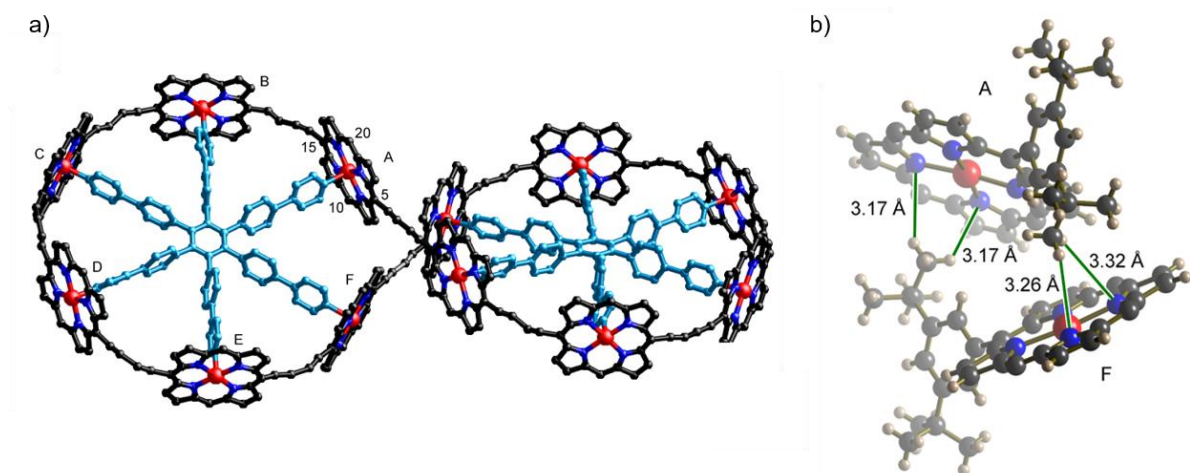


Figure 5.6. (a) Single crystal X-ray structure of *c*-P12_{*t*}-Bu•(T6)₂, and (b) zoom-in on the point where the loops cross, showing the proximity of the *tert*-butyl groups and the porphyrin planes.^{2b}

The dramatic difference between using **T3** and **T3N** or **T6e** in the Vernier synthesis is in alignment with our predictions based on the allosteric cooperativity of binding. The **T6e** template which shows strong positive cooperativity when stacking in porphyrin complexes is also highly efficient at directing the formation of nanorings where this stacking can be used (*c*-P12, *c*-P20_{THS} and *c*-P24_{*t*}-Bu). However, the **T3** and **T3N** templates that display strongly negative cooperativity when stacking, also does not seem to stack in the synthesis and hence do not lead to any ring-formation.

Table 5.1. Analytical yields for stacked template directed synthesis of porphyrin nanorings

oligomer	template	analytical yields
<i>l</i> -P4 _{THS}	T6e	<i>c</i> -P12 _{THS} : 30%
<i>l</i> -P4 _{THS}	T6	<i>c</i> -P8 _{THS} : 34%, <i>c</i> -P12 _{THS} : 18%
<i>l</i> -P4 _{<i>t</i>-Bu}	T6e	<i>c</i> -P12 _{<i>t</i>-Bu} : 21%
<i>l</i> -P4 _{<i>t</i>-Bu}	T6	<i>c</i> -P12 _{<i>t</i>-Bu} : 39%
<i>l</i> -P2 _{THS}	T3	-
<i>l</i> -P2 _{THS}	T3N	-
<i>l</i> -P2 _{THS}	T6	<i>c</i> -P6 _{THS} : 76%
<i>l</i> -P2 _{<i>t</i>-Bu}	T3	-
<i>l</i> -P2 _{<i>t</i>-Bu}	T3N	-
<i>l</i> -P2 _{<i>t</i>-Bu}	T6	<i>c</i> -P6 _{<i>t</i>-Bu} : 63%

5.5 Conclusion

We have demonstrated that large supramolecular complexes can be synthesized in high yields and with good selectivity via a Vernier stacking approach, which requires less complicated templates compared to a classical template directed synthesis. We have also shown that the magnitude of the cooperativity in the system can be used to predict the effectiveness of this strategy. The strong cooperativity in **c-P12**·(**T6e**)₂ might seem surprising because the two templates have to bend to fit inside the nanoring and fight steric repulsive forces. However, upon closer inspection it becomes evident that when the first template binds, the ring must adopt a flat and rigid conformation, and the unbound porphyrins will be rotating less freely around the butadiyne bridges. Thus, the complex is locked in a conformation that is favorable for binding another template. Our work demonstrates the strength of using allosteric cooperativity in the design of supramolecular systems in order to get better selectivity. The factors that usually limits supramolecular chemists: statistics, sterics and low yields, can be combatted through incorporating allosteric cooperativity and ligands preorganizing binding sites for subsequent ligands.

5.6 Experimental procedures and technical details

5.6.1 Analytical GPC calibration curves

A GPC column separates molecules depending on volume, but the sizes of two molecules of the same molecular weight can be very different. However, if all the molecules tested have similar chemistry and it can be assumed that the molecular volume is increasing linearly with molecular weight, then a calibration plot of $\log(M)$ versus retention time t_R will produce a straight line. This is empirical, and it will only work well in the intermediate range of the GPC column (not too close to the upper limit where everything is eluted).

We measured the retention times of a range of cyclic and linear porphyrin oligomers with *tert*-butyl and THS sidechains and used the data to make four calibration curves shown in Figure 5.7.

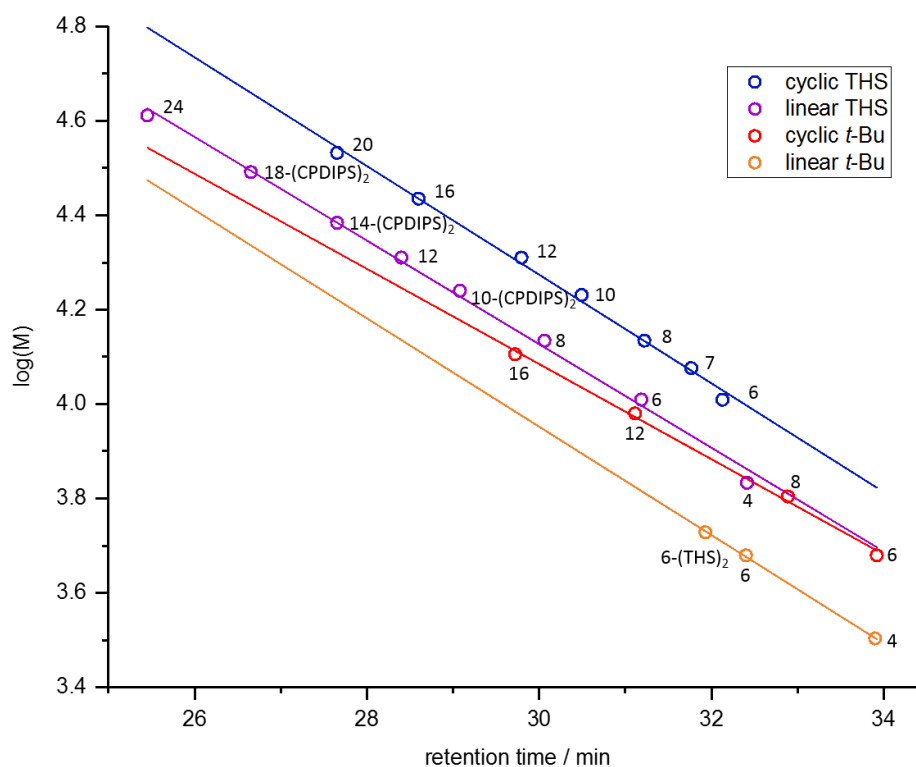


Figure 5.7. Analytical GPC retention times for THS and *t*-Bu porphyrin oligomers. The GPC retention times were measured using two JIAGEL-H columns in series (3H-A then 4H-A), with THF:1% pyridine eluent and a 1 mL/min flow rate. The plot shows $\log(M)$ versus retention

time, and the lines show linear regression fits for each group of compounds: $\log(M) = at_R + b$, where t_R is retention time.

Table 5.2. Measured retention times used to make Figure 5.7.

Cyclic THS			Linear THS		
compound	retention time / min	log(M)	compound	retention time / min	log(M)
c-P6	32.13	4.01	l-P4	32.41	3.83
c-P7	31.77	4.08	l-P6	31.19	4.01
c-P8	31.22	4.13	l-P8	30.06	4.13
c-P10	30.49	4.23	l-P10-(CPDIPS)₂	29.08	4.24
c-P12	29.79	4.31	l-P12	27.65	4.38
c-P16	28.60	4.44	l-P14-(CPDIPS)₂	26.65	4.49
c-P20	27.65	4.53	l-P18-(CPDIPS)₂	25.45	4.61
			l-P24	28.40	4.31
Cyclic t-Bu			Linear t-Bu		
compound	retention time / min	log(M)	compound	retention time / min	log(M)
c-P6	33.92	3.68	l-P4	33.90	3.50
c-P8	32.89	3.80	l-P6	32.40	3.68
c-P12	31.11	3.98	l-P6-(THS)₂	31.93	3.73
c-P16	29.72	4.11			

5.6.2 Experimental procedures for and analysis of stacked Vernier template directed synthesis

5.6.2.1 Experimental procedures

c-P12 formation run 1

Stock solutions were prepared for all reagents: **I-P4_{THS}** (9.00 mg, 1.32 μ mol) was dissolved in chloroform (2.0 mL). **I-P4_{t-Bu}** (2.96 mg, 0.929 μ mol) was dissolved in chloroform (4.0 mL) and pyridine (200 μ L). **T6e** (10.3 mg, 2.91 μ mol) was dissolved in chloroform (4.0 mL). **T6** (2.06 mg, 2.07 μ mol) was dissolved in chloroform (2.0 mL). This gave stock solutions with the concentrations:

[**I-P4_{THS}**] = 0.660 mM.

[**I-P4_{t-Bu}**] = 0.221 mM.

[**T6e**] = 0.728 mM.

[**T6**] = 1.03 mM.

Then, four reactions were set up:

- A) **I-P4_{THS}** (121 μ L, 0.080 μ mol) and **T6e** (110 μ L, 0.080 μ mol) was dissolved in chloroform (1.0 mL), concentrated to dryness, and dried in vacuum. CDCl₃ (370 μ L) and DIPA (5 μ L, 35.7 μ mol) was added and everything went in solution.
- B) **I-P4_{THS}** (121 μ L, 0.080 μ mol) and **T6** (78 μ L, 0.080 μ mol) was dissolved in chloroform (1.0 mL), concentrated to dryness, and dried in vacuum. CDCl₃ (370 μ L) and DIPA (5 μ L, 35.7 μ mol) was added and everything went in solution.
- C) **I-P4_{t-Bu}** (362 μ L, 0.080 μ mol) and **T6e** (110 μ L, 0.080 μ mol) was dissolved in chloroform (1.0 mL), concentrated to dryness, and dried in vacuum. CDCl₃ (370 μ L) and DIPA (5 μ L, 35.7 μ mol) was added and everything went in solution.
- D) **I-P4_{t-Bu}** (362 μ L, 0.080 μ mol) and **T6** (78 μ L, 0.080 μ mol) was dissolved in chloroform (1.0 mL), concentrated to dryness, and dried in vacuum. CDCl₃ (370 μ L) and DIPA (5 μ L, 35.7 μ mol) was added and everything went in solution.

A catalyst stock solution was then prepared: Pd(PPh₃)₂Cl₂ (1.73 mg, 2.46 μmol), CuI (2.56 mg, 13.4 μmol), benzoquinone (4.34 mg, 40.1 μmol), DIPA (400 μL, 2.85 mmol) and CDCl₃ (2100 μL) was mixed and stirred for 10 minutes until everything was dissolved.

To each reaction, A-D, 125 μL of catalyst stock solution was added, which means each reaction gets: Pd(PPh₃)₂Cl₂ (86.5 μg, 0.123 μmol), CuI (128 μg, 0.670 μmol), benzoquinone (217 μg, 2.01 μmol), DIPA (20 μL, 143 μmol) and CDCl₃ (105 μL).

All reactions A-D were stirred at room temperature. After 24 hours, a portion of THF 1% pyridine (5.0 mL) was added to each of the reactions. The solutions were each filtered through a syringe filter (0.45 μm) to remove larger particles and then 50 μL of each solution were injected onto an analytical GPC column.

In order to find the conversion between integral in the spectrum and actual concentration, ***I-P4_{THS}*** (121 μL, 0.080 μmol) and ***I-P4_{t-Bu}*** (362 μL, 0.080 μmol) were each dissolved in THF 1% pyridine (5.0 mL) and filtered through syringe filters, before 50 μL of each solution were injected onto the analytical GPC column.

c-P12 formation run 2

Stock solutions were prepared for all reagents: ***I-P4_{THS}*** (13.4 mg, 1.97 μmol) was dissolved in chloroform (1.0 mL). ***I-P4_{t-Bu}*** (3.45 mg, 1.08 μmol) was dissolved in chloroform (2.0 mL) and pyridine (200 μL). **T6e** (2.66 mg, 0.750 μmol) was dissolved in chloroform (1.0 mL). This gave stock solutions with the concentrations:

[***I-P4_{THS}***] = 1.96 mM.

[***I-P4_{t-Bu}***] = 0.492 mM.

[**T6e**] = 0.750 mM.

[**T6**] = 1.03 mM (the stock solution from **c-P12** formation run 1 was used).

Then, four reactions were set up:

- A) ***I-P4*_{THS}** (163 μ L, 0.32 μ mol) and **T6e** (421 μ L, 0.32 μ mol) was dissolved in chloroform (1.0 mL), concentrated to dryness, and dried in vacuum. CDCl_3 (1480 μ L) and DIPA (20 μ L, 0.14 mmol) was added and everything went in solution.
- B) ***I-P4*_{THS}** (163 μ L, 0.32 μ mol) and **T6** (310 μ L, 0.32 μ mol) was dissolved in chloroform (1.0 mL), concentrated to dryness, and dried in vacuum. CDCl_3 (1480 μ L) and DIPA (20 μ L, 0.14 mmol) was added and everything went in solution.
- C) ***I-P4*_{t-Bu}** (650 μ L, 0.32 μ mol) and **T6e** (421 μ L, 0.32 μ mol) was dissolved in chloroform (1.0 mL), concentrated to dryness, and dried in vacuum. CDCl_3 (1480 μ L) and DIPA (20 μ L, 0.14 mmol) was added and everything went in solution.
- D) ***I-P4*_{t-Bu}** (650 μ L, 0.32 μ mol) and **T6** (310 μ L, 0.32 μ mol) was dissolved in chloroform (1.0 mL), concentrated to dryness, and dried in vacuum. CDCl_3 (1480 μ L) and DIPA (20 μ L, 0.14 mmol) was added and everything went in solution.

A catalyst stock solution was then prepared: $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (2.80 mg, 3.99 μ mol), CuI (3.21 mg, 16.9 μ mol), benzoquinone (4.95 mg, 45.8 μ mol), DIPA (400 μ L, 2.85 mmol) and CDCl_3 (2100 μ L) was mixed and stirred for 10 minutes until everything was dissolved.

To each reaction, A-D, 500 μ L of catalyst stock solution was added.

All reactions A-D were stirred at room temperature. After 24 hours, 100 μ L was taken from each reaction mixture and run over a plug of basic alumina (CHCl_3 : PE : pyridine = 20:70:10). Reaction mixture C was also filtered through a silica plug with the same solvent mixture. Then all solvent was removed, and the reaction mixtures were dissolved in 1.5 mL THF 1% pyridine. The solutions were each filtered through a syringe filter (0.45 μ m) to remove larger particles and then 50 μ L of each solution were injected onto an analytical GPC column.

In order to find the conversion between integral in the spectrum and actual concentration, ***I-P4*_{THS}** (10 μ L, 19.6 nmol) and ***I-P4*_{t-Bu}** (20 μ L, 9.84 nmol) were each dissolved in THF 1% pyridine (1500 μ L) and filtered through syringe filters, before 50 μ L of each solution were injected onto the analytical GPC column.

Another method of calibration was tried to test how reliable the method is. Stock solutions were made of **c-P12**_{THS} (3.86×10^{-6} M), **c-P12**_{t-Bu} (3.03×10^{-6} M) and **c-P8**_{THS} (2.01×10^{-6} M). 50 μ L was injected onto the GPC from each stock solution to get external standards. The

yields measured with these standards were very similar to the ones measured using ***l*-P4** as standards. ***l*-P4** was chosen as the best option because there is less risk of experimental weighing error if the same stock solution is used for both experiment and calibration.

c-P6 formation run 1

Stock solutions were prepared for all reagents: ***l*-P2_{THS}** (5.8 mg, 1.7 μ mol) was dissolved in chloroform (2.0 mL). ***l*-P2_{t-Bu}** (6.4 mg, 4.0 μ mol) was dissolved in chloroform (4.0 mL) and pyridine (200 μ L). **T3** (4.76 mg, 8.85 μ mol) was dissolved in chloroform (5.0 mL). **T3N** (4.31 mg, 7.97 μ mol) was dissolved in chloroform (5.0 mL). This gave stock solutions with the concentrations:

[***l*-P2_{THS}**] = 0.851 mM.

[***l*-P2_{t-Bu}**] = 0.958 mM.

[**T3**] = 1.78 mM.

[**T3N**] = 1.60 mM.

[**T6**] = 1.03 mM (the stock solution from **c-P12** formation run 1 was used).

Then, six reactions were set up:

- A) ***l*-P2_{THS}** (188 μ L, 0.16 μ mol) and **T3** (90 μ L, 0.16 μ mol) was dissolved in chloroform (1.0 mL), concentrated to dryness, and dried in vacuum. CDCl₃ (740 μ L) and DIPA (10 μ L, 71.3 μ mol) was added and everything went in solution.
- B) ***l*-P2_{THS}** (188 μ L, 0.16 μ mol) and **T3N** (100 μ L, 0.16 μ mol) was dissolved in chloroform (1.0 mL), concentrated to dryness, and dried in vacuum. CDCl₃ (740 μ L) and DIPA (10 μ L, 71.3 μ mol) was added and everything went in solution.
- C) ***l*-P2_{THS}** (188 μ L, 0.16 μ mol) and **T6** (78 μ L, 0.080 μ mol) was dissolved in chloroform (1.0 mL), concentrated to dryness, and dried in vacuum. CDCl₃ (740 μ L) and DIPA (10 μ L, 71.3 μ mol) was added and everything went in solution.
- D) ***l*-P2_{t-Bu}** (167 μ L, 0.16 μ mol) and **T3** (90 μ L, 0.16 μ mol) was dissolved in chloroform (1.0 mL), concentrated to dryness, and dried in vacuum. CDCl₃ (740 μ L) and DIPA (10 μ L, 71.3 μ mol) was added and everything went in solution.
- E) ***l*-P2_{t-Bu}** (167 μ L, 0.080 μ mol) and **T3N** (100 μ L, 0.16 μ mol) was dissolved in chloroform (1.0 mL), concentrated to dryness, and dried in vacuum. CDCl₃ (740 μ L) and DIPA (10 μ L, 71.3 μ mol) was added and everything went in solution.

F) ***I-P2_{t-Bu}*** (167 μ L, 0.080 μ mol) and **T6** (78 μ L, 0.080 μ mol) was dissolved in chloroform (1.0 mL), concentrated to dryness, and dried in vacuum. CDCl_3 (740 μ L) and DIPA (10 μ L, 71.3 μ mol) was added and everything went in solution.

A catalyst stock solution was then prepared: $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (1.45 mg, 2.07 μ mol), CuI (2.78 mg, 14.6 μ mol), benzoquinone (3.12 mg, 28.9 μ mol), DIPA (400 μ L, 2.85 mmol) and CDCl_3 (2100 μ L) was mixed and stirred for 10 minutes until everything was dissolved.

To each reaction, A-F, 250 μ L of catalyst stock solution was added, which means each reaction gets: $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (145 μ g, 0.207 μ mol), CuI (278 μ g, 1.46 μ mol), benzoquinone (312 μ g, 2.89 μ mol), DIPA (40 μ L, 285 μ mol) and CDCl_3 (210 μ L).

All reactions A-F were stirred at room temperature. After 24 hours, another catalyst stock solution was prepared, and 250 μ L ($\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (145 μ g, 0.207 μ mol), CuI (278 μ g, 1.46 μ mol), benzoquinone (312 μ g, 2.89 μ mol), DIPA (40 μ L, 285 μ mol) and CDCl_3 (210 μ L)) was added to each reaction along with 600 μ L CDCl_3 (in an attempt to dissolve precipitate). After an additional 48 hours, a portion of 100 μ L was taken from each reaction and mixed with 200 μ L THF 1% pyridine. The solutions were each filtered through syringe filters (0.45 μ m) to remove larger particles and then 99 μ L of each solution were injected onto an analytical GPC column.

In order to find the conversion between integral in the spectrum and actual concentration, ***I-P2_{THS}*** (18.8 μ L, 0.016 μ mol) and ***I-P2_{t-Bu}*** (16.7 μ L, 0.016 μ mol) were each dissolved in THF 1% pyridine (2.0 mL) and filtered through syringe filters, before 99 μ L of each solution were injected onto the analytical GPC column.

Control experiment

Stock solutions from **c-P12** formation run 1 and **c-P6** formation run 1 were used.

[***I-P2_{THS}***] = 0.851 mM.

[***I-P2_{t-Bu}***] = 0.958 mM.

[***I-P4_{THS}***] = 0.660 mM.

[***I-P4_{t-Bu}***] = 0.221 mM.

Then, four reactions were set up:

- A) ***I-P2*_{THS}** (24 μ L, 20 nmol) was concentrated to dryness. Then CDCl_3 with 1.4% DIPA (94 μ L) was added and everything went in solution.
- B) ***I-P4*_{THS}** (30 μ L, 20 nmol) was concentrated to dryness. Then CDCl_3 with 1.4% DIPA (94 μ L) was added and everything went in solution.
- C) ***I-P2*_{t-Bu}** (21 μ L, 20 nmol) was concentrated to dryness. Then CDCl_3 with 1.4% DIPA (94 μ L) was added and everything went in solution.
- D) ***I-P4*_{t-Bu}** (90 μ L, 20 nmol) was concentrated to dryness. Then CDCl_3 with 1.4% DIPA (94 μ L) was added and everything went in solution.

A catalyst stock solution was then prepared: $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (1.40 mg, 1.99 μ mol), CuI (2.64 mg, 13.9 μ mol), benzoquinone (3.58 mg, 33.1 μ mol), DIPA (400 μ L, 2.85 mmol) and CDCl_3 (2100 μ L) was mixed and stirred for 10 minutes until everything was dissolved.

To each reaction, A-D, 31 μ L of catalyst stock solution was added, which means each reaction gets: $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (17 μ g, 25 nmol), CuI (33 μ g, 172 μ mol), benzoquinone (44 μ g, 410 nmol), DIPA (5 μ L, 35 μ mol) and CDCl_3 (26 μ L).

All reactions A-D were stirred at room temperature. After 68 hours, the reactions were stopped by adding 2.0 mL THF 1% pyridine to each of the solutions. The solutions were each filtered through syringe filters (0.45 μ m) to remove larger particles and then 99 μ L of each solution were injected onto an analytical GPC column.

In order to find the conversion between integral in the spectrum and actual concentration, ***I-P2*_{THS}** (12 μ L μ mol), ***I-P2*_{t-Bu}** (11 μ L), ***I-P4*_{THS}** (15 μ L) and ***I-P4*_{t-Bu}** (35 μ L) were each dissolved in THF 1% pyridine (1.0 mL) and filtered through syringe filters, before 50 μ L of each solution were injected onto the analytical GPC column.

5.6.2.2 Data analysis

Figure 5.8 shows part of the UV-vis absorption spectra of selected *tert*-butyl oligomers reported as molar extinction coefficient per porphyrin unit. At 466 nm, the absorbance of ***l*-P2** and ***c*-P6·T6** is the same, and at 470 nm the absorbance of ***l*-P4** and ***c*-P12** is the same.

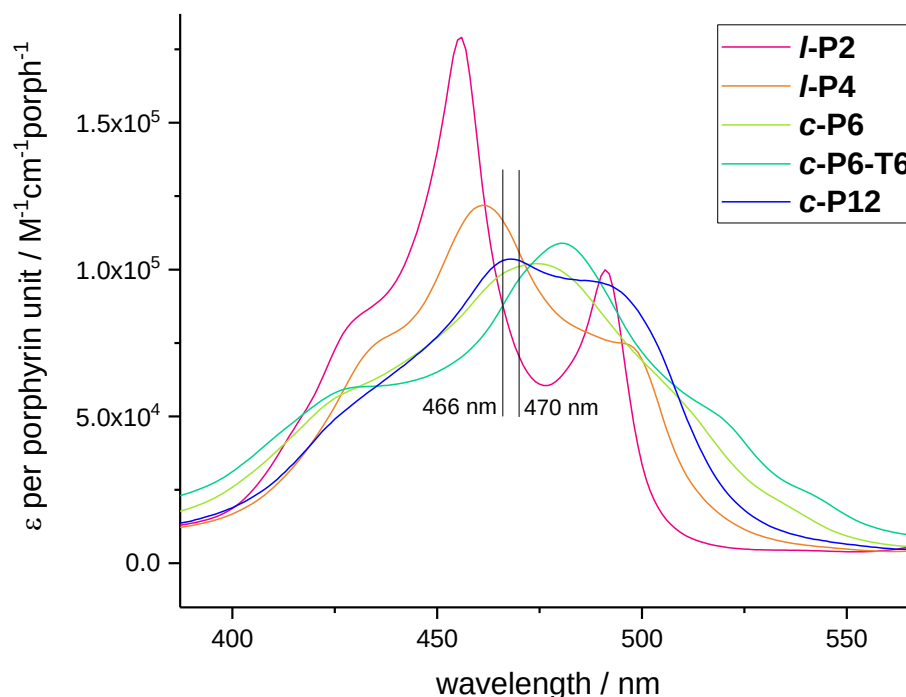


Figure 5.8. UV-vis spectra of *tert*-butyl linear and cyclic oligomers reported as the molar extinction coefficient per porphyrin unit. THF 1% pyridine, 298 K.

The peaks in the UV-vis absorption traces obtained from the analytical GPC of the reaction mixtures were fitted and integrated, and the analytical yield was determined as the percentage of the integral of the corresponding amount of injected starting material (***l*-P2** or ***l*-P4**). For reactions starting with ***l*-P2** we used the absorption at 466 nm, and for reactions starting with ***l*-P4** we used 470 nm. The calibration curve in Figure 5.7 was used to determine the identity of the elution peaks.

Figure 5.3 and 5.4 show the result of this analysis for ***c*-P12** formation run 1 and ***c*-P6** formation run 1, and Figure 5.9 shows the result from the control reaction, giving only polymers. Figure 5.10 shows the traces from ***c*-P12** formation run 2, which is very similar to ***c*-P12** formation

run 1 and shows similar yields. The main difference is that the reaction mixtures from **c-P12** formation run 2 were filtered through basic alumina, which has removed a large part of the longer oligomers and potentially some belonging the integrated signals. Especially **I-P4_{t-Bu}** + **T6e** was filtered through an additional silica plug, which means that the yield might not be directly comparable to the other traces. The yields in the figure are determined using the starting material **I-P4** as external standard, using the same stock solutions as were used for the experiments. The yields in brackets are determined using solutions with known concentrations of the specific products as external standards. The method of using **I-P4** as standard was found to be the most reliable and has the advantage of being able to determine the yields of higher oligomers as well.

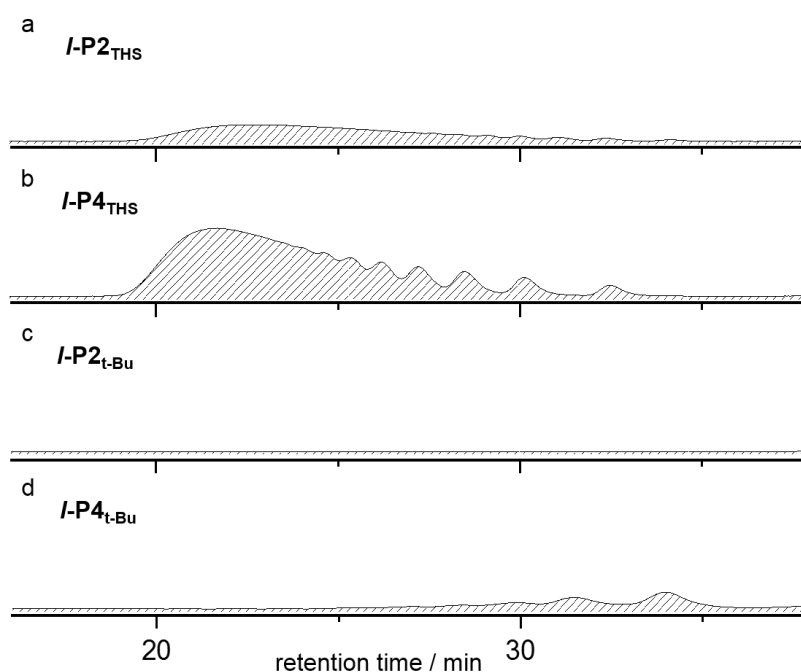


Figure 5.9. Analytical GPC traces for Control reaction, coupling of porphyrin oligomers without any template present. The GPC traces were measured using two JIAGEL-H columns in series (3H-A then 4H-A), with THF:1 % pyridine eluent and a 1 mL/min flow rate. Traces a and c show detection at 466 nm, and traces b and d show detection at 470 nm.

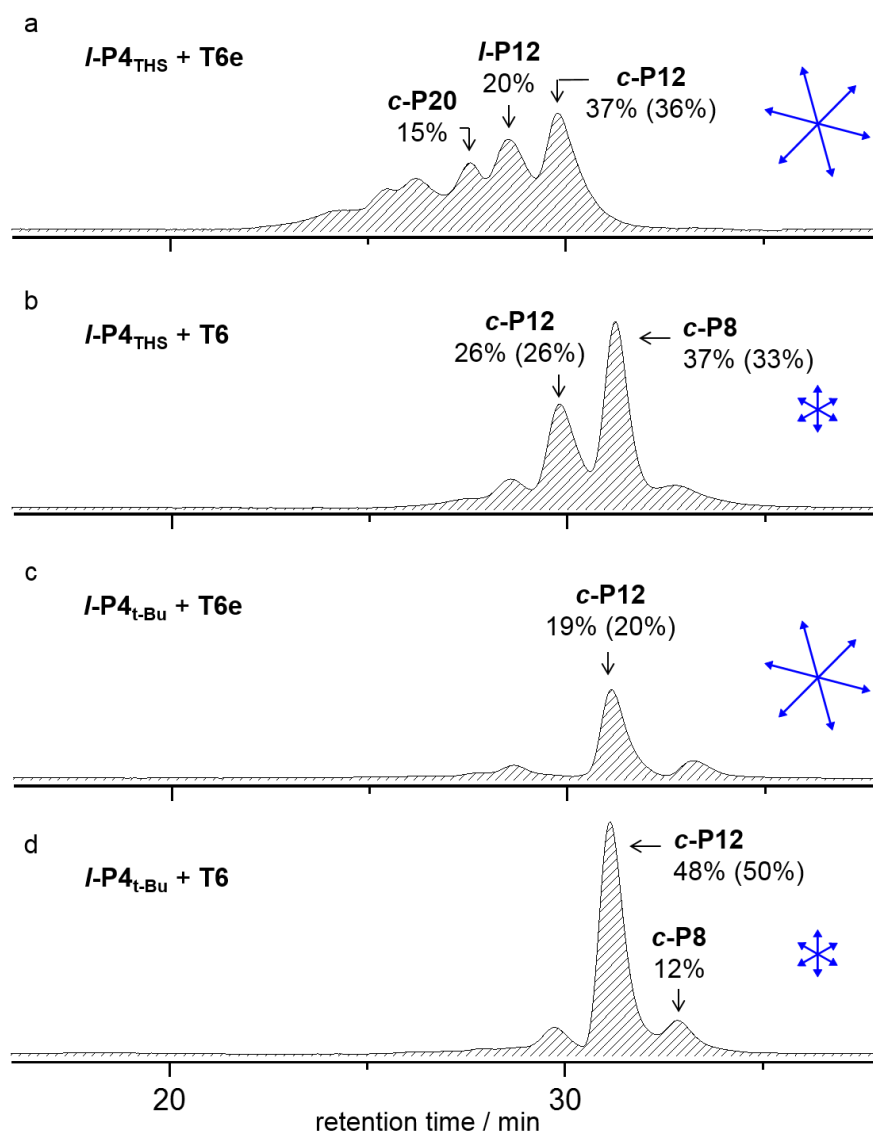


Figure 5.10. Analytical GPC traces for **c-P12** formation run 2, coupling of **I-P4** in the presence of **T6** and **T6e** respectively. The GPC traces were measured using two JIAGEL-H columns in series (3H-A then 4H-A), with THF:1 % pyridine eluent and a 1 mL/min flow rate. All traces show detection at 470 nm. The yields in brackets are determined using solutions with known concentrations of the specific products as external standards.

Table 5.3. Analytical yields from stacked template directed synthesis control experiment and repetition

experiment	start oligomer	side chain	template	yields
c-P12 formation run 2	<i>l</i>-P4	THS	T6e	c-P12: 37% (36%)* <i>l</i>-P12: 20% c-P20: 15%
	<i>l</i>-P4	THS	T6	c-P8: 37% (33%)* c-P12: 26% (26%)*
	<i>l</i>-P4	t-Bu	T6e	c-P12: 20% (21%)*
	<i>l</i>-P4	t-Bu	T6	c-P8: 12% c-P12: 48% (50%)*
control	<i>l</i>-P2	THS	-	-
	<i>l</i>-P4	THS	-	-
	<i>l</i>-P2	t-Bu	-	-
	<i>l</i>-P4	t-Bu	-	-

*analytical yields in brackets are calculated using a solution of the product as an external standard as opposed to using the starting material as an external standard (see text).

5.7 References

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