Multi-component porphyrin self-assembly

Helmich, F.A.

DOI:
10.6100/IR723515

Published: 01/01/2012

Document Version
Publisher’s PDF, also known as Version of Record (includes final page, issue and volume numbers)

Please check the document version of this publication:

• A submitted manuscript is the author’s version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher’s website.
• The final author version and the galley proof are versions of the publication after peer review.
• The final published version features the final layout of the paper including the volume, issue and page numbers.

Link to publication

Citation for published version (APA):

General rights
Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

• Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
• You may not further distribute the material or use it for any profit-making activity or commercial gain
• You may freely distribute the URL identifying the publication in the public portal

Take down policy
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.
Multi-Component Porphyrin Self-Assembly

PROEFSCHRIFT

ter verkrijging van de graad van doctor aan de Technische Universiteit Eindhoven, op gezag van de rector magnificus, prof.dr.ir. C.J. van Duijn, voor een commissie aangewezen door het College voor Promoties in het openbaar te verdedigen op dinsdag 7 februari 2012 om 14.00 uur

door

Floris Anton Helmich

geboren te Eindhoven
Dit proefschrift is goedgekeurd door de promotor:

prof.dr. E.W. Meijer

Copromotor:
dr. A.P.H.J. Schenning

Cover design: Karin Emsbroek
Printing: Gildeprint Drukkerijen, Enschede

A catalogue record is available from the Eindhoven University of Technology Library


This work has been financially supported by the Council of Chemical Sciences of the Netherlands Organization for Scientific Research (NWO-CW)
To my parents
# Table of contents

## Chapter 1
*Multi-component porphyrin self-assembly*

1.1 Introduction .......................... 1
1.2 Supramolecular polymerizations ...... 2
1.3 Supramolecular organization of porphyrins in one-component assemblies 4
1.4 Two-component supramolecular donor-acceptor constructs 8
1.5 Assessment of cooperativity in multi-component systems 11
1.6 Responsive porphyrin-based assemblies 13
1.7 Aim and outline of the thesis 19
1.8 References .......................... 23

## Chapter 2
*One-component metallo-porphyrin self-assembly*

2.1 Introduction .......................... 29
2.2 Molecular design and synthesis ...... 30
2.3 Self-assembly of S-Zn in dilute solution 32
2.4 The effect of center metal and stereocenter on the porphyrin self-assembly 33
2.5 Conclusion .......................... 41
2.6 Experimental ........................ 45
2.7 References .......................... 50

## Chapter 3
*Two-component Zn-porphyrin self-assembly with pyridine*

3.1 Introduction .......................... 53
3.2 Pyridine titration to S-Zn-Me ........ 55
3.3 Pyridine titration to S-Zn .......... 55
3.4 Modeling the pyridine-induced depolymerization of the porphyrin stacks 56
3.5 Dilution-induced self-assembly ...... 56
3.6 Microfluidic separation of porphyrin stacks and dimers complexes 58
3.7 Conclusion .......................... 62
3.8 Experimental ........................ 62
3.9 References .......................... 68

## Chapter 4
*Photo-regulation of the Zn-porphyrin self-assembly in a two-component system*

4.1 Introduction .......................... 71
4.2 Design of the system ................. 71
4.3 Synthesis, characterization and complexation of phenylazopyridines 72
4.4 Change of the binding constant upon photoirradiation 79
4.5 Modeling the photo-induced porphyrin aggregation 80
4.6 Photo-regulation of the cooperative self-assembly 80
4.7 Conclusion .......................... 87
4.8 Experimental ........................ 87
4.9 References .......................... 92
Chapter 5
Two-component Zn-porphyrin self-assembly with DABCO

5.1 Introduction
5.2 DABCO titration to S-Zn-Me
5.3 Modeling the S-Zn system in the presence of DABCO
5.4 DABCO titration to S-Zn
5.5 Preliminary chain-stopping experiments with manganese porphyrins
5.6 Conclusion
5.7 Experimental
5.8 References

Chapter 6
Chiral amplification in porphyrin assemblies: a mixing study

6.1 Introduction
6.2 Chiral amplification of Zn-porphyrins at room temperature
6.3 Chiral amplification of mixed-metal porphyrins at room temperature
6.4 Diluted-Majority-Rules: between Sergeant-and-Soldiers and Majority-Rules
6.5 Conclusion
6.6 Experimental
6.7 References

Chapter 7
Chiral amplification in porphyrin assemblies: a dynamic study

7.1 Introduction
7.2 Chiral memory via chiral amplification and selective depolymerization
7.3 Selective depolymerization in a Majority-Rules system
7.4 Selective depolymerization in a Diluted-Majority-Rules system
7.5 Conclusion
7.6 Experimental
7.7 References

Chapter 8
Towards porphyrin-based polymeric systems

8.1 Introduction
8.2 Synthesis of non-symmetrical porphyrins
8.3 Porphyrin-based telechelics
8.4 Porphyrin-based single chain nanoparticles
8.5 Conclusion and outlook
8.6 Experimental
8.7 References

Summary
Curriculum Vitae
List of publications
Acknowledgements


1

**Multi-component porphyrin self-assembly**

**Abstract.** In this chapter, an overview is presented on porphyrins that are utilized in molecular self-assembly. Firstly, strategies are highlighted, in which supramolecular interactions are used to make well-defined, one-component porphyrin assemblies. Secondly, given the unique optical properties of this chromophore, the creation of functional assemblies containing multiple components is discussed. A special focus is maintained on essential aspects in (multi-component) self-assembly, such as the thermodynamic parameters, molecular recognition and the self-assembly mechanism. Additionally, stimuli-responsiveness and the role of chirality will be discussed, which serves as a distinctive probe for the supramolecular dynamics. This chapter ends with the aim of the research described in this thesis and a short outline.
1.1 Introduction

Nature provides fascinating examples of functional self-assembled systems like the light-harvesting photosynthetic unit. Its efficiency to transfer the absorbed solar excitation to the energy trap inside the reaction center is fully governed by the mutual organization of chromophores, where structural optimization has been determined by evolution.\(^{1}\) For supramolecular chemists, chlorosomes inside green phototrophic bacteria form an inspiring class of photosynthetic antenna complexes, in which tens-of-thousands bacteriochlorophylls are positioned and connected solely by non-covalent interactions. These large aggregates serve as conceptual archetypes for artificial model systems, which are particularly interesting regarding the demand of sustainable energy. Accordingly, bacteriochlorophylls and semi-synthetic mimics based on chlorin pigments have been studied in order to elucidate the chlorosome structure and the relationship between molecular structure and aggregate properties.\(^{2}\) For the majority of these studies, the formation of rod-shaped assemblies is attributed to highly specified intermolecular metal coordination- and hydrogen bonds (Figure 1.1).\(^{3}\)

![Figure 1.1](image)

**Figure 1.1.** Supramolecular interactions between bacteriochlorophyll c (1) moieties that are involved in the formation of chlorosomes: coordination bond between the 3\(^1\)-hydroxyl group and the magnesium atom, a hydrogen bond between the coordinated 3\(^1\)-hydroxyl and 13\(^3\)-carbonyl groups and \(\pi-\pi\)-interactions between the macrocycles.\(^{3b}\)

Apart from semi-synthetic approaches with chlorin pigments, fully synthetic porphyrins have also been employed as artificial light-harvesting systems.\(^{4}\) Balaban demonstrated the tunability of the porphyrin ultraviolet-visible (UV-vis) absorbance spectrum by the substitution pattern onto the macrocycle, which affected the aggregation behavior. Herein, circular dichroism (CD) spectra indicated that the helical bias of the aggregates was controlled by the chiral separation of a racemic porphyrin solution in heptane.\(^{5}\) These types of studies also reveal that the opto-electronic properties strongly depend on the design, arrangement, and number of chromophores in the assembly. Despite the impressive
accomplishments of covalently organized porphyrin mimics, the supramolecular approach clearly reveals its versatility and tunability; highly applicable features for interesting bottom-up strategies to develop functional, nanometer-sized devices that already emerged in the field of supramolecular electronics. Considering their adaptability and optical/catalytic properties, porphyrins are highly applicable building blocks for functional assemblies. Besides their light-harvesting properties, porphyrins fulfill other vital roles in natural complexes. For instance, iron-porphyrins (hemes) serve as active sites in the oxidation reactions of endogenous chemicals for metabolic purposes in Cytochrome P540 enzymes. Furthermore, the transport of oxygen from the lungs to the tissue is fully governed by its binding with hemoglobin in red blood cells. Here, the quaternary structure of the hemoglobin tetramer is different in the (de/oxygenated state, giving rise to a cooperative effect in its oxygen binding.

Due to the presence of multiple interacting components in a dynamic assembly, these natural systems are inherently complex, which requires in-depth analyses in multi-component self-assembly. Here, a step-wise approach allows for a level of understanding in order to rationally design or mimic these functional systems. This chapter reviews the formation of (non-)discrete porphyrin-based assemblies using the directionality of supramolecular interactions. In addition, supramolecular strategies are highlighted that have provided important insights into porphyrin self-assembly by demonstrating the effects of cooperativity and molecular recognition. This chapter puts less emphasis on specific functions that arise in multi-component assemblies.

1.2 Supramolecular polymerizations

On the basis of complex molecular systems observed in Nature, synthetic supramolecular polymers have been investigated thoroughly, which resulted into an appreciable level of understanding of one-component self-assembling systems. For supramolecular polymers, the monomers are entirely held together by non-covalent interactions, such as hydrogen bonds, metal-ligand coordination and \( \pi-\pi \) interactions. These interactions are typically weak, directional, reversible and highly sensitive to thermodynamic parameters such as temperature and concentration. As a result, supramolecular materials are stimuli-responsive and dynamic in nature, which is attributed to a wide versatility of self-assembled structures. Structural control herein strongly depends on the monomer design and the thermodynamic state, which is determined by external stimuli. Additionally, the mechanism by which monomers form supramolecular polymers is a crucial aspect.

Analogous to the classification of covalent polymerization mechanisms, two general mechanisms can be distinguished for supramolecular polymers. Here, isodesmic \textit{versus} cooperative self-assembly yields strikingly different molar distributions over monomers and
aggregates (Figure 1.2). In case of isodesmic self-assembly, the successive addition of ditopic monomer to the growing chain leads to a constant decrease in free energy. As a result, the monomer affinity for the end of the polymer is independent of chain length; hence the polymerization process can be described by a single equilibrium constant \( (K_0) \). On the other hand, in case of cooperative self-assembly, the growth of the polymer chain occurs in multiple stages with a different enthalpy release per monomer. In the first stage, monomers self-assemble in an isodesmic fashion until a critical nucleus size \( 'n' \) after which the polymer grows by the same mechanism yet at a higher enthalpy release per monomer. In the cooperative mechanism, these ‘nucleation-’ and ‘elongation-stages’ can be described by equilibrium constants \( K_n \) and \( K_e \), respectively and the degree of cooperativity \( (\sigma) \) can be defined as the ratio \( K_n / K_e \), which is smaller than unity for a cooperative process. In case of a dimeric nucleus \( (n = 2) \), the \( K_2-K \) model can be employed to deduce the equilibrium constants for nucleation \( (K_n) \) and elongation \( (K) \) from concentration-dependent measurements. Van der Schoot developed a temperature-dependent model for cooperative supramolecular polymerizations, in which nucleation is described by the activation of a monomer \( (K_n) \) and successive elongation is achieved by the temperature-independent enthalpy \( (\Delta H) \) and the concentration-dependent elongation temperature \( (T_e) \). Recently, our group described a modular approach to interconvert temperature- and concentration-dependent data.

![Diagram](image)

**Figure 1.2.** A: Schematic representation of the isodesmic and cooperative self-assembly mechanism. B: Simulation of the molecular weight distribution as a function of the degree of polymerization for the isodesmic \( (K_0 = 1\times10^7 \text{ M}^{-1}) \) and cooperative \( (K_2 = 1\times10^2 \text{ M}^{-1}, K = 1\times10^9 \text{ M}^{-1}; \sigma = 10^{-5}) \) mechanism at a concentration of 1.0\times10^{-5} \text{ M}.

Conceptually, cooperativity arises from the interplay of multiple interactions, so that the system as a whole behaves differently from expectations based on the properties of the individual interactions acting in isolation. For supramolecular polymerizations, electronic, structural and hydrophobic effects are responsible for the additional affinity of the monomer to be added once the nucleus is formed. In case of a highly cooperative system \( (\sigma << 1) \), the
Multi-component porphyrin self-assembly

rise in affinity is large; resulting into “all-or-nothing” behavior, which can be characterized by a critical point such as a critical temperature or concentration. In the model consideration, this phenomenon is reflected by the non-equivalency of $K_e$ and $K$, which causes a strong bimodal distribution of monomers and aggregates (Figure 1.2B). Characteristically for cooperative processes, the equilibrium concentration of aggregates starts increasing only after reaching a critical concentration at which the equilibrium concentration of monomers does not increase anymore upon increasing the total concentration. Furthermore, above the critical monomer concentration, a sharp increase to high molecular weight polymers is observed. Both the sharpness of this transition and the size of the aggregate are significantly enhanced when compared to the isodesmic mechanism.

1.3 Supramolecular organization of porphyrins in one-component assemblies

After the general outline on supramolecular polymers and the mechanisms by which they are formed, we discuss in this section examples of self-assembling porphyrins in one-component systems. This overview focuses on the formation of porphyrin-based aggregates, in which the directionality of π-π, hydrogen-bonding and metal-ligand interactions are programmed as such to direct the self-assembly into (non-)discrete structures. Upon the aggregation of porphyrins, strong exciton coupling exists, which is reflected by a shift of the Soret band in the UV-vis absorbance spectrum. Here, the UV-vis spectra can be explained in terms of the displacement of the chromophore, where cofacial stacking (H-type aggregation) leads to a hypsochromic- (or blue-) shift, whereas a parallel arrangement (J-type aggregation) causes a bathochromic- (or red-) shift of the Soret band in the UV-vis spectrum (Figure 1.3).

Throughout this thesis, we will refer to these aggregation modes.

![Figure 1.3](image)

**Figure 1.3.** Arrangement of porphyrin monomers in aggregates, in which the transition dipole moments (arrows) have three possible orientations regarding their angles ($\alpha$ and $\beta$) with the axis through the porphyrin centers: face-to-face ($\alpha = \beta = 90^\circ$, blue-shift), head-to-tail ($\alpha = \beta = 45^\circ$, red shift) and edge-to-edge ($\alpha = 0^\circ; \beta = 90^\circ$, band splitting).
1.3.1 Porphyrin self-assembly directed by π-π interactions

The self-assembly of covalent donor-acceptor constructs based on Zn-porphyrins with four perylene bisimides (PBI) was studied by Wasielewski. These systems take advantage of the tendency of PBIs to form H-type aggregates having cofacial orientations via inter-molecular π-π interactions. By their symmetrical substitution pattern, the porphyrins stack in a cofacial fashion as shown by the combination of absorbance studies, small angle X-ray (SAXS) data and force field calculations. The type of self-assembled structure was highly dependent on the bay substitutions onto the PBI’s; having two 3,5-di-t-butylphenoxy groups on the 1-7 position of the perylene forms 2-dimensional aggregates, whereas without bay substitutions forms 1-dimensional aggregates (Figure 1.4). The latter aggregate type was found to be highly monodisperse with only five stacked units on top each other as confirmed by mass spectrometry and gel permeation chromatography (GPC). Considering the size and dispersity of the aggregate, its self-assembly mechanism does not match with isodesmic nor cooperative behavior. The authors believed that the balance between the overall steric repulsion of the alkyl tails and the stabilizing effect of the π-π interactions limits the aggregate size to five subunits, which suggests an anti-cooperative mechanism. The fact that the aggregates could be characterized by GPC reveals that they are extremely stable. In addition, no aggregate disruption was observed when dissolved in pyridine, even though it strongly bound to the Zn-porphyrin center. This suggested that the self-assembly process is driven primarily by the π-π interactions between the PBI moieties. Unlike pyridine, the addition of chloroform resulted into the disruption of the aggregates. In addition, absorbance studies revealed only weak exciton coupling between porphyrins compared to the strong effect for the PBI’s. Additional force field calculations revealed π-π distances of 3.4 Å between the PBI’s and 4.4 Å between the porphyrins.

![Figure 1.4](image-url) Molecular structure of symetrically substituted porphyrins with different perylene moieties and their calculated aggregate structures for 2 (left) and 3 (right).

---

6
1.3.2 Porphyrin self-assembly directed by hydrogen bonding

The symmetric topology of π–π interactions in the previous example resulted in the formation of discrete cofacially arranged porphyrin (H-type) aggregates. By the non-symmetric patterning of hydrogen bonding moieties, the formation of sheet-type assemblies is preferred. Here, upon functionalizing the 10,15-meso-positions of the porphyrin ring, discrete tetramers can be obtained as shown for ditopic, homocomplementary 2-ureido-4-pyrimidinone-('UPy')-substituted porphyrins (Figure 1.5).24 The non-symmetric approach towards 4 relied on the selective nitration and subsequent reduction of tetraphenylporphyrin (TPP), which was conducted prior to the coupling of the activated UPy-isocytosines. Tetramer formation was evidenced by diffusion ordered spectroscopy (DOSY-NMR) that showed a concentration-indecency of the diffusion constant up to a critical concentration. At higher concentrations, the diffusion coefficient lowered due to the polymerization of 4 rather than its cycle formation.25 Interestingly, tetramer formation was further supported by the covalent fixation of 5, in which olefin metathesis was performed on the double bonds using Grubbs catalyst. The cross-linked tetramers were analyzed by GPC, which revealed a mass corresponding to the DOSY experiment. The group of Drain studied a similar system, in which two 3,5-diacetamido-pyridinyl moieties were attached to the porphyrin core.26 Rather than the selective nitration of TPP, the porphyrins were synthesized by the Adler condensation reaction, in which a mixture of two different aldehydes was reacted with pyrrole. Out of the six possible reaction products, rotamer 6 was obtained after reaction optimization and column chromatography (Figure 1.5). The self-assembly of 6 was studied by 1H-NMR, which revealed dramatic differences between linear and closed-square tetramers, indicating a strong cooperative effect for the closed structure. Remarkably, the coassembly of 6 with uracil-substituted 7 enhanced tetramer formation significantly; compared to the homo-complementary self-assembly of 6, the hetero-complementary process afforded a more than 2 orders of magnitude stronger binding.27

![Figure 1.5](image)

**Figure 1.5.** Molecular structures of non-symmetrical porphyrins 4,24 5,24 626 and 727 containing hydrogen bonding moieties at the 10,15-meso-position that form tetrameric assemblies.
The group of Nolte reported on the self-assembly of porphyrin-functionalized benzene-1,3,5-tricarboxamide (BTA) trimers, which possess a 3-fold symmetric substitution of amide linkages around the benzene core to three non-symmetrical porphyrins. By physical dewetting techniques, discotic 8 self-assembles into 1-dimensional stacks that formed highly ordered line patterns on the surface (Figure 1.6).\textsuperscript{28} Dropcasting and evaporation of a small chloroform droplet on mica at low concentrations of 8 resulted in columnar stacks with line heights corresponding to the diameter of the discotic and narrow spatial distributions between the lines. Remarkably, upon dropcasting larger droplets, the line heights increased due to bundling of columnar stacks, yet the periodicity between the lines remained present. Solution studies on chiral derivative 9 revealed a critical aggregation concentration in chloroform, while in hexane disassembly could not be observed by concentration-dependent UV-vis studies.\textsuperscript{29} The broadening and shifting of the Soret band in UV-vis revealed the presence of cofacial aggregates, which were helical as evidenced by strong CD effects. An isosbestic point in UV-vis (i.e. a constant optical density at a certain wavelength that usually represents a two-state equilibrium) was found by temperature-dependent studies, which suggest the transition between two well-defined species and light scattering studies showed the presence of single columns with high aspect ratios. All experimental results corroborated a cooperative self-assembly mechanism. Noteworthy, different aggregation behavior was found in cyclohexane, which indicates the delicate interplay of hydrogen bonding and $\pi-\pi$ interactions on the self-assembly of the discotics.

![Molecular structure of symmetrically substituted benzene-1,3,5-tricarboxamides with achiral (8)\textsuperscript{28} and chiral (9)\textsuperscript{29} porphyrins and the schematic representation of the H-type aggregation of 9 and the formation of line patterns observed in AFM.](image)

**Figure 1.6.** Molecular structure of symmetrically substituted benzene-1,3,5-tricarboxamides with achiral (8)\textsuperscript{28} and chiral (9)\textsuperscript{29} porphyrins and the schematic representation of the H-type aggregation of 9 and the formation of line patterns observed in AFM.

The group of Shinkai investigated porphyrin-based organogelators with symmetrically substituted porphyrins having phenoxyacetamide linkers to solubilizing chains (Figure 1.7). Gelation tests revealed that 10 (bearing the amide groups at the 4-position of the *meso*-phenyl
Multi-component porphyrin self-assembly

groups) is a by far a better gelator than 11 (bearing its amides at the 3-position). In addition, the thermal stability revealed that octane gels of 10 are considerably more stable than 11. Absorbance studies showed that gelation of 10 is the cause of H-type aggregation, while J-type aggregates were found for 11. From the crystal structure of 10 it was evident that \( \pi-\pi \) stacking between the adjacent porphyrins occurs in a single column and that one porphyrin in a column is connected with two porphyrins in the neighboring column. In this configuration, stable columnar superstructures were formed since all phenoxycetamide groups were used to construct a 1-dimensional hydrogen bonding array, as evidenced by a highly ordered infrared spectrum. In order to fabricate conductive polymers with an enhanced stability, a similar strategy was performed as conducted by Nishide. In this case, covalent fixation of the self-assembled stacks was achieved by photopolymerization of diacetylene moieties on the periphery of porphyrin 12 (Figure 1.7). With respect to 10, porphyrin 12 showed similar aggregation and gelation properties and upon photoirradiation of its decalin gel, straight fiber structures were observed by AFM. This observation strongly supported the nature of this templated polymerization by a programmed bottom-up approach using self-assembly and subsequent in situ photopolymerization.

![Molecular structures of symmetrically phenoxyacetamide-substituted porphyrin 10,11 and 12 investigated by Shinkai and symmetrically substituted porphyrins having oligo(\( \mu \)-phenylene vinylenes) with trans-vinylene- (13) and amide linkages (14) studied by our group.]

The effect \( \pi-\pi \) interactions in comparison with hydrogen bond-assisted self-assembly was studied in our group with a similar donor-acceptor construct as shown by Wasielewski. Yet in this case, a porphyrin acceptor was symmetrically appended with four oligo(\( \mu \)-phenylene vinylene) (OPV) donors and the effect of trans-vinylene (13) versus amide linkages (14) between the chromophores was investigated (Figure 1.7). A strong effect on the supramolecular arrangement was found; in methylcyclohexane, 13 forms J-type and 14 stacks into H-type aggregates as shown by a red-shift and a blue-shift relative to their monomer
absorbance, respectively. The OPV moieties were decorated with (S)-2-methylbutoxy groups, which transferred their chiral information to the porphyrin core as shown by an upcoming CD effect in the porphyrin absorbance region upon aggregation. By studying temperature- and concentration-dependent CD spectroscopy, a higher anisotropy factor (g-value) was found for 14 and aggregates of 14 were more stable than aggregates of 13. The considerable improvement in supramolecular stability was attributed to the formation of intermolecular hydrogen bonds between the amides of adjacent, cofacially arranged porphyrins, which was corroborated with infrared spectroscopy. This drastic effect of the hydrogen bond assistance in 14 could underlie a different self-assembly mechanism, which was not considered at the time. Likely, the additional supramolecular interaction contributes to cooperative self-assembly for 14. Remarkable behavior was found for zinc-derivatives of 13 and 14 (13-Zn and 14-Zn, respectively), which caused the full disappearance of the CD effect for 13-Zn and a 5-fold reduction of the CD intensity for 14-Zn. No significant change was observed in the UV-vis spectrum of the former, yet in the latter, the original band decreased concomitantly with the appearance of a new (red-shifted) band. The resulting band splitting of 14-Zn was obviously related with the decrease of the CD effect and indicated a slipped stacking morphology. Further investigations into this strong metalation effect were not performed. Interestingly, mixing studies of the porphyrins with their zinc-derivatives revealed the cascade energy transfer process OPV → Free-base porphyrin → Zn-porphyrins. Judged from the donor luminescence, the efficiency of the 14/14-Zn system was higher than for the 13/13-Zn co-assembly, which was attributed to the higher g-value.

1.3.3 Porphyrin self-assembly directed by metal-ligand association

As demonstrated by the previous examples, porphyrins can easily be provided with different metal centers, which opens a wide variety of applications in the field of catalysis, tuning optical properties, light-harvesting and self-assembly by metal-ligand coordination. In the latter, one-component self-assembly is achieved by the ditopic character of an electrophilic metal center inside the porphyrin, which has a nucleophilic coordinative group substituted to the core. This leads to the formation of linear coordination oligomers/polymers and cycles, in which the topology of the metal coordination controls the self-assembled structure. In case of mono-pyridyl-functionalized Zn-porphyrins, the free lone pair of the nitrogen atom favors a perpendicular coordination regarding the porphyrin plane. As a result distinctive assembly structures arise for 235, 336 and 4-pyridyl37 substituted porphyrins.

The group of Kobuke studied a variety of meso-imidazolyl-substituted porphyrins, which were programmed to form assemblies upon the formation of metal-ligand and/or hydrogen bonds. In chloroform, bis(imidazolyl)-porphyrin 15 forms cofacial aggregates by 2-fold
intermolecular hydrogen bonds between the pre-organized imidazole moieties (Figure 1.9A).\textsuperscript{38} Similarly as observed for 13/14-Zn (vide supra), zinc insertion caused an additional metal-ligand interaction that significantly affected the chromophore orientation of 15 as evidenced by UV-vis spectroscopy.\textsuperscript{39} Elegantly, the hydrogen bonding interactions between the porphyrins were destabilized by the addition of methanol, by which the ditopic nature of the molecule was affected. Due to this constraint, \textsuperscript{1}H-NMR measurements revealed the formation of dimeric structures that were similar to 2-pyridyl-substituted porphyrins.\textsuperscript{35} The disruption of the hydrogen bonding network resulted in sharpening of the peaks and the resulting spectrum was identical to bis(N-methylated-imidazolyl)Zn-porphyrin containing methyl groups instead of protons on both imidazole moieties.\textsuperscript{40}

**Figure 1.9.** A: Formation of different cofacial aggregates of bis(imidazolyl)-porphyrin 15 by selective control over hydrogen bonding and metal-ligand coordination.\textsuperscript{38,39} B: Closed ring-shaped aggregate of bis(imidazolyl)-Zn-porphyrin 16 with a 1.3-phenylene spacer between the porphyrins.\textsuperscript{42}

These bis(imidazolyl)-Zn-porphyrins possess a 1:2-stoichiometry of metal and ligand, respectively and given the five-fold coordination of the zinc center, these molecules only form closed dimers when hydrogen bonding is omitted.\textsuperscript{39,41} By their covalent connection at the meso-position, bis(imidazolyl)-Zn-porphyrin dimers have a 1:1-stoichiometry that allows for an extended coordination structure. By connection of two mono(imidazolyl)-Zn-porphyrins at the meso-position with a 1.3-phenylene spacer, the 120° spatial orientation of building block 16 was programmed to form a discrete ring structure upon metal-ligand association six monomer (Figure 1.9B).\textsuperscript{42} Rather than the 1.3-phenylene spacer, direct meso-connection resulted in a homo-ditopic monomer (17-Zn/Zn) that formed a giant Zn-porphyrin array upon intermolecular self-coordination (vide infra).\textsuperscript{43} GPC analyses in chloroform revealed the presence of arrays comprising up to 400 units while a large Soret band splitting was observed due to the slipped, cofacial arrangement of the porphyrins. In the next section we discuss the functional chain-stopping of these extended coordinated arrays.
1.4 Two-component supramolecular donor–acceptor constructs

In the previous section, we discussed the one-component self-assembly of porphyrins, in which the directionality of π–π interactions, hydrogen- and metal-ligand bonds were used to create assemblies with predefined structures. The formation of discrete structures was either achieved by anti-cooperativity of a self-assembled system having a unidirectional topology of π–π-interactions or by a closed topology of hydrogen- and coordination bonds. In any other case, non-discrete, 1-dimensional aggregates are obtained that are the result of the supramolecular polymerization of ditopic monomers. The next step towards more complex systems comprising of functional assemblies relies on multi-component self-assembly. In this section, we highlight supramolecular strategies to position different porphyrins in a single (non-)discrete aggregate.

1.4.1 Non-discrete systems

As mentioned in the introduction of this chapter, the mutual organization of different chromophores is highly important regarding the performance of functional assemblies. In order to achieve a satisfactory level of control over position and stoichiometry, self-assembly strategies should comprehend selectivity; either via molecular recognition or the proper choice of binding motifs/strengths of moieties added to the system. In the cascade energy transfer process between 13 \(\rightarrow\) 13-Zn (or 14 \(\rightarrow\) 14-Zn), the non-discrete nature of the 1-dimensional assembly precluded the controlled positioning of donor and acceptors, for instance at the end of the stack or in an alternating fashion. The interaction between fullerenes and aromatic surfaces allows highly selective inclusion complexes of porphyrin donors and fullerene acceptors as shown by porphyrin tweezers. Our group reported on an artificial light-harvesting system in a non-discrete linear assembly by the consecutive energy- and electron transfer between OPV-appended porphyrins and Ce in water.

Kobuke and coworkers reported on several functional chain-stopping strategies of giant supramolecular porphyrin arrays based on homoditopic meso-meso-linked bis(imidazolyl)-Zn-porphyrin 17-Zn/Zn (Figure 1.10A). These porphyrin arrays were amendable to further synthetic elaboration by exchange coordination with monotopic moieties; thereby introducing specific donor/acceptor groups at the molecular terminals of a highly polarized π-electronic system. Stoichiometric metalation of 17-FB/FB using 1.5 equivalents of zinc acetate resulted in oligomers with monotopic 17-FB/Zn terminals. After preparative-scale GPC, each oligomer was separated, which featured unique nonlinear optical properties attributed to the free-base acceptor. Besides free-base terminals, zinc-terminals were investigated by the chain-stopping of 17-Zn/Zn with monotopic 18. Another elegant example is disclosed by the chain-stopping with monotopic imidazolyl manganese(III)porphyrin 19. This strategy relied on the appropriate association constant of 19 with the terminals of the 17-
**Zn/Zn** coordination polymer, which was investigated with a model study containing mixtures of 19 and 20. In case homo-dimerization of 20 would be equally strong as hetero-dimerization between 19 and 20, the antenna array cannot survive upon the addition of 19. On the other hand, if homo-dimerization of 19 would be stronger than hetero-dimerization, chain-stopping would not be very efficient. In the ideal case, homo-dimerization of 20 is strongest; followed by hetero-dimerization of 19 and 20; followed by homo-dimerization of 19. Homo-complexation of the zinc-derivative was investigated by UV-vis competition titration of N-methylimidazole to dimers of 20, from which a binding constant of $3 \times 10^{11} \text{ M}^{-1}$ was estimated. No dimer formation was observed for 19 at concentrations up to $10^{-5} \text{ M}$, hence an association constant of $1 \times 10^{3} \text{ M}^{-1}$ was estimated, which is considerably lower. Hetero-complexation was quantified by fluorescence competition titration of 19 to dimers of 20 at $1 \times 10^{5} \text{ M}^{-1}$, thereby satisfying the appropriate binding conditions for chain-stopping. Since the reduction potential of 19 was found to be low enough to accept electrons from the exited Zn-porphyrins, this chain-stopping could lead to a light-harvesting antenna-acceptor composite. A large slope in the Stern-Volmer plot revealed highly efficient quenching upon addition of 19 to self-assembled 17-Zn/Zn, while the length of the polymer gradually decreases as shown by GPC analysis and simulations based on a model comprising 19 and 20 (Figure 1.10B).

**Figure 1.10.** A: Molecular structures of *meso*-fused, bis(imidazolyl)-porphyrin dimer 17 and imidazolyl-Zn/Mn-porphyrin 18 and 20. B: Schematic representation of the formation of a light-harvesting antenna-acceptor composite by heterocomplementary coordination between ditopic 17-Zn/Zn and monotopic 19.
1.4.2 Discrete systems

Besides the chain-stopping of linear assemblies, light-harvesting properties were discovered for discrete supramolecular assemblies based on bis(imidazolyl)-Zn-porphyrins trimers containing two 1,3-phenylene spacers. Similarly as found for bis(imidazolyl)-Zn-porphyrins dimer 16,42 the trimers form cyclic oligomers, while preserving a high quantum yield suitable for light-harvesting properties. Upon the cyclization of three units of 21, three non-coordinated Zn-porphyrins remained available to complex tripodal48 and tetrapodal49 pyridine-guests with high association constants (Figure 1.11A). By the substitution of one of the tetrapodal arms with an appropriate acceptor moiety, well-defined donor-acceptor constructs were prepared.48 For instance, guest 22 contains three arms for complexation of cyclized 21 and one arm to accept energy via the bis(phenylethynyl)Zn-porphyrin moiety and accept electrons via the fulleropyrrolidine moiety.48b Spectroscopic studies revealed the three-point coordination of 22 and its energy transfer from the cyclic antenna porphyrins to porphyrin energy acceptor followed by its photoinduced electron transfer to produce charge-separated species.

![Figure 1.11. A: Schematic representation of the artificial light-harvesting complex of bis(imidazolyl)-Zn-porphyrin trimers 21 and porphyrin/fullerene-functionalized tetrapodal ligand 22.48b B: Schematic representation of a porphyrin-based supramolecular hydrogenase mimic 23.49](image)

The previous example highlights the discrete nature of supramolecular donor-acceptor constructs and its importance to rationally design efficient complexes. In the field of porphyrin-based supramolecular catalysis, this aspect has been utilized to increase stability and substrate selectivity of a manganese-porphyrin epoxidation catalyst.50 Hupp and coworkers encapsulated the manganese-porphyrin in a supramolecular cavity based on Zn-porphyrins, in which catalyst deactivation by oxo-dimerization (Mn-O-Mn) was suppressed. Furthermore, the supramolecular protection cage could complex additional ligands, which affected the selectivity for different vinylene substrates prior to their epoxidation, thereby creating an artificial enzyme.51,50 Considering the level of control over chromophore
Multi-component porphyrin self-assembly

organization and the achievements in supramolecular light-harvesting- and catalytic systems, the next step in functional, multi-component self-assembly of porphyrins directs to their merge into artificial photocatalytic units. A recent example by the group of Reek discloses a porphyrin-based supramolecular hydrogenase mimic that is able to produce hydrogen using light as an energy source.\textsuperscript{52} Bis(thiolate)-bridged diiron clusters were complexed \emph{via} pyridyl-functionalized phosphine ligands with Zn-porphyrins (Figure 1.11B), which (1) stabilized the diiron cluster by sterically preventing the formation of inactive, dimeric [FeFe]-species and (2) transfer electrons to the diiron core upon their photoadsorption. The photocatalytic activity of a number of different systems was evaluated using diisopropylethylammonium acetate as a proton source and sacrificial electron donor. Remarkably, only the non-symmetric, hetero-porphyrin diiron complex 23 showed catalytic activity by exhibiting 5 turnovers based on the amount of hydrogen gas collected.

1.5 Assessment of cooperativity in multi-component systems

As shown by the previous examples, discrete assemblies feature host-guest properties that offer the possibility to introduce or exchange new components with relative ease, thereby featuring functional properties. Generally, these molecular recognition properties are explained by high binding affinities due to cooperative effects emerging from an induced fit of a guest molecule inside a host.\textsuperscript{48,50} In addition, the self-assembly of host-structures also proceeds \emph{via} a specific mechanism (\textit{vide supra}),\textsuperscript{12} which usually encompass cooperativity due to chelate effects upon closing structures.\textsuperscript{18} Regarding the role of cooperativity in multi-component porphyrin self-assembly, pioneering work has been performed by the groups of Anderson, Hunter and Sanders by investigating the interaction between multi-porphyrin building blocks and multivalent ligands. Bidentate ligands such as DABCO (1,4-diaza[2,2,2]bicyclooctane) can coordinate two metalloporphyrins at a highly specified distance and mutual orientation. These ligands have been employed to connect calixarene-porphyrin cages,\textsuperscript{53} naphthalene diimide-porphyrin diads,\textsuperscript{54} porphyrin tweezers,\textsuperscript{55} cyclic porphyrin dimers,\textsuperscript{56} porphyrin trimers highly similar to 8\textsuperscript{57} and conjugated porphyrin strands.\textsuperscript{58}

1.5.1 Ladder structures

Anderson investigated the formation of ladder complexes by the bridging of meso-connected Zn-porphyrin strands with DABCO ligands (Figure 1.12A).\textsuperscript{58a} In a comparison study between monomer 24a and dimer 24b, the \pi-\pi-directed self-assembly of both building blocks was investigated in absence of ligand. For both species, weaker binding was observed for their free-base derivatives and the stronger binding of 24b compared to 24a was explained
by a chelation effect. Isosbestic points were observed in a concentration-dependent UV-vis experiment, while a sigmoidal relationship was found between the concentration and fraction of aggregated material, which could be fitted by a single binding constant \( K_{agg} \). The observed isosbesticity strongly suggests cooperative behavior, while the sigmoidal trend is typical for isodesmic self-assembly. Remarkably,\textsuperscript{59} this combination clearly indicated the formation discrete dimeric structures. The \(^1\)H-NMR titration of DABCO to 24\textsubscript{i} showed sharp peaks at sub-stoichiometric amounts of DABCO indicative for the discrete \((24)_{2}\)-(DABCO)\textsubscript{2} ladder complex. Excessive amounts of DABCO resulted in the breaking of the ladder, which was evaluated by plotting the chemical shift of the single observed \textit{meso}-proton signal against the amount of DABCO. In fast exchange between \((24)_{2}\)-(DABCO)\textsubscript{2} and \((24)_{2}\)-(DABCO), the dissociation constant (\( K_d \)) was fitted. The simple 1:1 association constant (microscopic binding constant \( K_i \)) between DABCO and 24\textsubscript{i} was obtained from a dilute UV-vis titration experiment with DABCO. Having determined binding constants \( K_{agg}, K_d \) and \( K_i \) from different experiment, they were linked in a thermodynamic cycle in order to calculate \( K_i \) and \( K_d \) (Figure 1.12B); both too strong binding constants to measure the direct formation of the \((24)_{2}\)-(DABCO)\textsubscript{2} ladder complex. In a follow-up study,\textsuperscript{58} the length dependency of \textit{meso}-butadiyne-linked Zn-porphyrin oligomers on the ladder formation was investigated (Figure 1.12C). In order to prevent self-assembly of the strands in absence of DABCO, oligomers 25\textsubscript{n} (with \( N = 1-6 \)) were substituted with \textit{meso}-3,5-di(t-butyl)phenyle units. For 25\textsubscript{i} with DABCO, this additional \textit{meso}-crowding significantly affected the coordination of the second nitrogen to form the \((25)_{2}\)-(DABCO) sandwich complex as well. Relative to 24\textsubscript{i}, the negative cooperativity herein clearly revealed that the second coordination is less favorable than the first. No cooperative effects were found in case of the titration of monodentate base QND (quinuclidine) to oligomer series 25\textsubscript{n-6}. \(^1\)H-NMR studies revealed that ladder formation is an all-or-nothing process, in which no other complex is observed than the unbound oligomer and is ladder structure. Even at “UV-vis concentrations”, isosbestic spectra were found throughout the whole DABCO titration \textit{(i.e. formation and breaking of the ladder complex)} of oligomers 25\textsubscript{1-6}. However, under these conditions the formation of two-rung ladders of 25\textsubscript{i} did not reach completion, as reflected by a regime of non-isosbesticity between its formation and disassembly. These results clearly indicated that cooperativity increases with ladder length resulting in high ladder stabilities. In order to break-up 50\% of hexameric ladders, 1200 equivalents of DABCO were necessary compared to only 2.9 equivalents for two-rung ladders. Accordingly, the corresponding breaking curves become more sigmoidal as the ladders become longer.
Multi-component porphyrin self-assembly

Figure 1.12. A: Molecular structures of meso-butadiyne-linked Zn-porphyrin oligomers studied by Anderson.58 B: Thermodynamic model of 24 with DABCO to relate ladder formation with individually determined association constants.56a C: Schematic representation of the ladder structure (25)$_2$(DABCO)$_3$.58b

1.5.2 Vernier assemblies

When DABCO was added to a 1:1 mixture of 26 and 26l, the only observable complexes were the two homo-ladders (25)$_2$(DABCO)$_2$ and (25)$_2$(DABCO)$_3$. Unlike the formation of Vernier complexes, the two different strands narcissistically self-sorted, which was attributed to the cooperativity of the system.60 Vernier assemblies actually arise when two different types of molecules containing a different number (n and m) of mutually complementary binding sites (separated by the same distance) interact with each other to form an assembly of length (n x m).61 A cooperative interaction is involved when the binding sites come into register, which leads to a significant increase in stability. This mechanism was successfully applied by Hunter who mixed-in η$^6$-coordinating Sn-porphyrin-dimers 26 with η$^6$-coordinating Zn-porphyrin-trimers 27. Thermodynamic modeling corroborated with fluorescence titration data and GPC indicated the formation of the 3:4 triple stranded Vernier assemblies with a length of 6 porphyrins (Figure 1.13A). Another impressive example is disclosed by Anderson and coworkers who prepared a covalent 12-porphyrin nano-ring, which is the largest π-conjugated macrocycle ever synthesized.62 By a novel Vernier templating approach, cyclic pyridine hexamer 28 was introduced to the desilylated analog of 25s (25$l'$) which formed a
bicyclic Vernier complex of 12 porphyrins (Figure 1.13B). After complex formation, Pd-catalyzed oxidative coupling yielded the covalent nano-ring, which was liberated from the template by the addition of excessive amounts of pyridine.

![Diagram A](image1.png)

![Diagram B](image2.png)

**Figure 1.13.** A: 3:4 triple stranded Vernier complex of Sn-porphyrin dimer 26 and Zn porphyrin trimer 27.61 B: bicyclic Vernier complex of Zn-porphyrin tetramer 25t and pyridine hexamer 28.62

### 1.6 Responsive porphyrin-based assemblies

After the assessment of porphyrin-based multi-component self-assembly and how cooperativity assists in this process, we now focus on the responsiveness of these dynamic assemblies. For supramolecular-based stimuli responsive materials,63a specific non-covalent interactions are addressed by selective stimuli such as temperature, concentration and solvent. In the latter, we already observed the selective breakage of hydrogen bonds by the addition of methanol in order to switch from an extended porphyrin stack to a porphyrin dimer.39 Besides these standard tools to control solution-based self-assembly processes, phototriggering is highly interesting since the stimulus can be applied remotely from a closed system without the need to introduce/exchange new molecules.63b

#### 1.6.1 Photoresponsive systems

Photochromic functional materials based on azo-molecules64 and diarylethenes65 have been investigated thoroughly, however research in the field of photoresponsive axial ligands is quite rare. Herges and coworkers recently reported on the photoswitching of the magnetic properties of phenylazopyridine-functionalized Ni-porphyrin 29 in acetonitrile (Figure 1.14A).66a In this fully reversible process, irradiation with 435 nm light caused the trans→cis isomerization, thereby sterically allowing pyridine coordination of Ni2+ into a square
pyramidal complex, which is paramagnetic. Heating-up of the complex or subsequent irradiation with 500 nm light caused the cis$\rightarrow$trans isomerization and the breakage of the pyridine-Ni$^{2+}$ bond into a square-planar, diamagnetic complex. The same principle was recently presented in a two-component system, which was inspired by pioneering work by the groups of Otsuki and Inoue. In a system comprising of Zn-porphyrins and phenylazopyridines, the fluorescence modulation of the porphyrins was investigated by the photochromism of the ligand. In its trans-form (low-energy state), 3-phenylazopyridine coordinates to the Zn-porphyrin without significant steric hindrance in contrast to the coordination of (high-energy state) cis-isomers (Figure 1.14B). In a systematic study, 2- and 3-phenylazopyridine ligands having different electron-donating/accepting groups on the 4-position were investigated. In case of 3-phenylazopyridines, stronger binding was observed for both the cis- and the trans-isomer of ligands having electron-donating groups. A combination study of UV-vis and 1H-NMR revealed the photostationary state of both the cis- and the trans-isomer; herein, PSS$^{\text{cis}}$ and PSS$^{\text{trans}}$ represent the molar fractions of cis- and trans-isomer upon irradiation with UV (trans$\rightarrow$cis) and visible (cis$\rightarrow$trans) light, respectively. After determination of the binding constants for both isomers ($K^{\text{cis}} < K^{\text{trans}}$), the switching efficiency was estimated. Porphyrin emission spectra were acquired at both PSS$^{\text{cis}}$ and PSS$^{\text{trans}}$, which revealed stronger quenching for the latter state due to energy transfer from the Zn-porphyrin to the ligand.

Figure 1.14. A: Schematic representation of phenylazopyridine-functionalized Ni-porphyrin 29 and its switching between the diamagnetic and paramagnetic state. B: 3-phenylazopyridine ligand 30 and its (de)complexation upon photoirradiation.

1.6.2 Chiral-responsive systems

As observed by the examples in this chapter, the dynamic properties of supramolecular systems afford the controlled formation of superstructures, which possess functional properties in some cases. Considering the wide variety of non-covalent interactions and the versatility of aggregate structures exhibited by porphyrins, the step towards new stimuli-responsive materials is to correlate functionality with dynamic properties of supramolecular systems, which has received little attention in literature so far. In multi-component systems,
the underlying reaction kinetics of coupled equilibria determine the dynamic properties of the system; in general, the macroscopic behavior strongly depends on the dynamics and therefore they are important regarding any application. Supramolecular chirality can be used as a probe to study the dynamic properties exhibited by a system, which will be discussed in the remainings of this section.

Helical supramolecular motifs are of great interest for the understanding of the origins of homochirality of biopolymers and the development of systems with chiroptical applications.  

Herein, the transfer, amplification and storage of chirality in supramolecular architectures is of great interest.  For these purposes, chiral porphyrin systems have been developed in organic and aqueous media. Most examples disclose the transfer of helical information from a chiral component to an achiral porphyrin assembly and, unlike other self-assembling chromophores, the number of examples on porphyrins with stereogenic centers is quite scarce. In this field, the group of Shinkai developed a series of sugar-appended porphyrins in order to template the formation of helical silicates and the group of Amabilino recently reported on the effect of the number of stereogenic centers on the self-assembly of porphyrin discotics.

Aida and coworkers investigated the transfer of chiral information from R/S-mandelic acid to fully substituted porphyrins that adopt highly non-planar conformations due to steric repulsions among the neighboring substituents. In its saddle conformation, 31 is highly basic and thermal “up-and-down” inversion of the pyrrole units cause the formation of a racemate (Figure 1.15A). The introduction of two S-mandelic acid molecules induces the formation of four hydrogen bonds between the inner-pyrrole nitrogen and the carboxylic acid moieties. This diastereoisomeric complex showed a CD effect, which was a mirror-image from the spectrum acquired from the porphyrin complex with R-mandelic acid. Upon exchange with (achiral) acetates, the CD effect remained presence indicating an increase of enantiomeric excess (ee), thus a chiral memory effect. The effect could be erased by neutralization of the complex by the addition of a base or by photoirradiation. Upon substitution of 31 with four pyridyl groups, Pt(II)-induced self-assembly of 32 resulted in the formation of aggregates with tunable helicity (Figure 1.15B). By the complexation of S/R-mandelic acid, significantly stronger molar ellipticities were acquired for the porphyrins in the aggregated state compared to the monomeric state. Unlike the monomeric state, a strong Majority-Rules effect was observed for the aggregates, in which ee-values larger than 40% R/S-mandelic acid resulted in a homochiral system. Remarkably, after simultaneous replacement of mandelic acid and breakage of the aggregate with excessive amounts of acetic acid and DPPP-ligand, respectively, the memory system still possessed the Majority-Rules trend. By these experiments, chiral amplification was performed via the aggregated state to the monomeric level, which showed a highly conformational inertness.
Figure 1.15. Molecular structure of fully substituted, saddle shaped porphyrins 31 and 32 investigated by Aida. A: Chiral memory effect on the monomeric level upon mandelic acid complexation/decomplexation of 31.73 B: Schematic representation of the Pt-induced aggregation of 32 and the Majority-Rules effect on the supramolecular and monomeric level before and after breakage of the complex, respectively.74

Besides chiral porphyrin systems in organic solutions, similar memory studies have been performed by several groups on water-soluble porphyrin systems containing achiral cationic/anionic TPPs. The group of Ribó studied the chiroptical response of achiral porphyrin aggregates under flow conditions76 and Yashima reported on the chiral induction of poly(phenylacetylenes) by chiral binaphthol moieties and their transcription to anionic porphyrins that memorized their helicity.77 In these examples, the porphyrin aggregates possess remarkably slow conformational dynamics, which have also been investigated by Purello and coworkers (Figure 1.16A).78 In absence of chiral molecules, cationic/anionic porphyrin diads form achiral J-aggregates in water,79 while three-component, chiral assemblies were obtained in presence of poly-L/D-glucamates80 and L/D-phenylalanines.81 In the former, preformed binary complexes were prepared with between cationic Cu-porphyrin 33 and L-poly-glutamate, which was evidenced by a small CD effect. The excessive addition of D-poly-glutamate changed the CD spectrum to its mirror image, indicating that the complex was “kinetically labile”. By the addition of anionic porphyrin 34, the molar ellipticities significantly increased indicating the formation of the ternary complex, which was corroborated with drastic changes in the porphyrin absorption and luminescence. Ternary complexes turned out to be “kinetically stable”; no inversion of the CD spectrum was observed by the addition of opposite poly-glutamate enantiomers and the disruption of
the polymeric template by raising the pH to ~12 did not affect the porphyrin CD spectrum either. Besides chiral templating of a polymer matrix, D/L-phenylanilines were used to prepare chiral assemblies.\textsuperscript{81} Chiral transformation only occurred by heating and cooling the ternary mixture of 33, 34 and phenylaniline. After template removal by ultrafiltration, the imprinted porphyrin aggregates retained the memory of the mold. Remarkably however, the step-wise addition of (achiral) 33 and 34 to extremely low concentrations of imprinted assemblies caused an increase in the CD spectrum. In a modest concentration domain, this enantio-specific self-replication showed a linear trend between the CD intensity and porphyrin concentration. In a follow-up study, the conformational dynamics were put to the test by a pH-switchable supramolecular complex, which comprised of 34 and ionizable, cationic porphyrin 35 containing pyridine groups (Figure 1.16B).\textsuperscript{82} Self-assembly and disassembly of the complex was performed by the addition of acid and base, respectively. Similarly as performed before,\textsuperscript{81} chiral induction and memory by the respective addition and ultrafiltration of the phenylaniline template resulted in homochiral aggregates. By “switching off” aggregation by deprotonation of the peripheral pyridyl moieties of 35 resulted in the disappearance of the CD effect, while lowering the pH caused the full restoration of the optical activity. Full switching was performed up to 10 consecutive cycles and its reversibility turned out to be dependent on the time the porphyrins we exposed under basic conditions. Also in this case, chiral seeds directed the enantiospecific reassembly process, however after long exposure to basic conditions, lowering the pH resulted in a non-chiral reassembly process indicating the full breakage of the seeds.

Figure 1.16. A: Molecular structures of cationic/anionic porphyrins 33 and 34 and ionizable porphyrin 35 studied by Purrello\textsuperscript{78,82} B: Switching of the supramolecular chiral memory of co-assemblies of 34 and 35 by pH via chiral seeds (route b) and the loss of memory by the full breakage of seeds upon long exposure under basic conditions (route a).\textsuperscript{82}
1.7 Aim and outline of the thesis

As discussed in this chapter, porphyrins are extremely versatile building blocks in molecular self-assembly. A wide variety of directional interactions can be programmed in the porphyrin monomer giving rise to different supramolecular motifs. Embracing the optical properties of the porphyrin chromophore, an outstanding level of probing is achieved in order to understand the self-assembly process. Given the functional properties arising from porphyrin systems discussed in the previous section, multi-component self-assembly becomes inherently more important but also complex.\(^3\) One may imagine how the introduction of additional supramolecular interactions affects a dynamic system, having coupled equilibria between non-covalently linked building blocks, which have been assembled according to a certain mechanism. Hence, in order to rationally design and control functional assemblies, multi-component self-assembly requires in-depth analyses, which encompasses thermodynamic modeling, cooperativity, supramolecular dynamics and proper characterization. From the previous examples, these analytical aspects have been partially considered and it seems that non-discrete supramolecular systems have received little attention herein.

Rather than the description of functional properties, the focus in this thesis is on insights into multi-component self-assembly of porphyrin monomers into non-discrete helical architectures. By the employment of modeling tools, the thermodynamic aspects of different interacting moieties via different, orthogonal supramolecular interactions are highlighted. In these analyses, the role of cooperativity is closely examined, which should lead to a mechanistic description offering the possibility to predict the behavior of multi-component systems. Next to this so-called “systems chemistry approach”,\(^4\) the expression of chirality from the monomer to the supramolecular level will be investigated by chiral amplification studies,\(^5\) which have not been considered for porphyrin assemblies so far. Given the remarkable chiral memory effects described in the last section, the dynamic properties of mixed porphyrin assemblies will be investigated. In general, both disciplines should contribute to more insights into multi-component self-assembly; in particular, (1) the tunability of aggregate size/structure and (2) the positional control and the degree of mixing between different chromophores in an aggregate. Regarding 1, stimuli-responsive properties will be explored by metal-ligand coordination studies of Zn-porphyrins, while regarding 2, chiral amplification and chain-stopping of porphyrin aggregates will be investigated. For both disciplines, a special focus is maintained on the dynamic behavior of mixed systems. Lastly, on the basis of discrete porphyrin-based assemblies, their functional combination of structural, optical, dynamic and stimuli-responsive properties is conveyed to non-discrete assemblies that resemble many biological systems.
Chapter 2 describes development of a library containing amide-functionalized porphyrins with different metal centers and stereochemistries. All porphyrins self-assemble in a highly cooperative fashion and their thermodynamic parameters are obtained after fitting temperature-dependent spectroscopy data. In Chapter 3, the addition of pyridine to the self-assembly of Zn-porphyrins is investigated by titration studies, which reveals that pyridine depolymerizes the stacks into supramolecular dimers. The proposed depolymerization mechanism is corroborated with thermodynamic modeling studies that reveal a dilution-induced self-assembly of the porphyrins. Furthermore, microfluidic separation studies are used to separate stacks from dimers that are kinetically labile. In Chapter 4, a photoswitchable phenylazopyridine ligands is developed, which is tested on a monomer compound in order to obtain its thermodynamic properties. By implementation of these parameters in a modified thermodynamic model, it is simulated and experimentally verified that Zn-porphyrin stacks can be reversibly assembled/disassembled with light via the photochromic axial ligand. In Chapter 5, a thermodynamic analysis on the bidentate DABCO ligand is performed, which shows the formation of an alternating supramolecular block copolymer with Zn-porphyrins. Titration studies reveal its formation and its high stability towards DABCO, unlike its stability towards Mn-porphyrin chain-stoppers. Chapter 6 continues on multi-porphyrin systems, in which mixing between chiral and achiral porphyrins with different center metals is investigated by chiral amplification experiments. According to the Sergeant-and-Soldiers principle, a chiral porphyrin Sergeant efficiently mixes with achiral Soldiers in the same helical aggregate and strongly biases its handedness. However, when two opposite enantiomers are mixed in a Majority Rules experiment, no chiral amplification is observed at all due to their narcissistic self sorting into conglomerate-like structures. The connection between these distinctive mixing properties is investigated with the Diluted-Majority-Rules principle, which shows that chromophore mixing can be controlled by the supramolecular chirality. In Chapter 7, the dynamic properties of the differently mixed states are investigated by the selective depolymerization of Zn-porphyrins from Zn/Cu-mixed systems. Slow depolymerization rates are observed for the mixed systems, while the self-sorted system depolymerized instantly. A stable and tunable chiral memory effect is found upon the slow depolymerization of a Zn-Sergeant from a mixed aggregate containing Cu-Soldier as well. This thesis ends with an outlook-chapter on porphyrin-functionalized polymers and proposed research directions in the field of new stimuli-responsive materials and catalytic systems. Herein, successful desymmetrization of the porphyrin building block allows for the formation of porphyrin-based dumbbell-shaped molecules and single-chain polymeric nanoparticles.
1.8 References


25. The transition from square tetramers to extended polymers is explained by a concentration effect in an operative ring-chain equilibrium. This self-assembly mechanism was not discussed in Section 1.2.
41. Zn-porphyrins generally accept one axial ligand. The binding of a second ligand is extremely weak and only at high (bulk) concentrations this is observed: Shukla, A. D.; Dave, P. C.; Suress, E.; Das, A.; Dastidar, P., *Journal of the Chemical Society-Dalton Transactions* **2000**, *4459-4463*.
Multi-component porphyrin self-assembly


70. Borovkov, V. V.; Inoue, Y. In *Supramolecular Chirality*; **2006**, 265, 89-146.


One-component metallo-porphyrin self-assembly

Abstract. A library of metallo-porphyrin derivatives was developed and the effect of metal center, amide linker and solubilizing chains on the self-assembly was investigated. In polar solvents, all porphyrin derivatives are molecularly dissolved and in methylcyclohexane they form helical, cofacial, H-type aggregates upon the formation of intermolecular hydrogen bonds and π-π interactions. For all derivatives, a highly cooperative self-assembly mechanism was deduced from temperature- and concentration-dependent UV-vis and CD spectroscopy measurements. Unlike zinc(II)- and copper(II)-porphyrins that form extended aggregates, manganese(III)-porphyrins form hydrogen bonded dimers only due to the presence of an anion. No aggregation was observed for porphyrins having N-methylated tertiary amides that cannot donate in hydrogen bonding. CD measurements revealed the effect of the side chain chirality on the supramolecular chirality. The self-assembly properties of the (S)-chiral zinc-porphyrin derivative were fully analyzed by usage of multiple characterization techniques and thermodynamic modeling assessments of the spectroscopy data.

Part of this work has been published:
2.1 Introduction

The self-assembly of organic molecules offers an attractive bottom-up approach to create nano-meter sized objects. By using functional building blocks such as porphyrins, supramolecular assemblies become highly interesting for numerous applications in the fields of sensing,\(^1\) catalysis\(^2\) and light-harvesting.\(^3\) Regarding the development of functional supramolecular materials and mimicking natural systems, it is important to understand self-assembly processes in detail and the ability to control them; particularly the control over the arrangement and number of molecules in an aggregate. A crucial basis herein is a comprehensive thermodynamic description of the self-assembly process, which encompasses binding constants and the self-assembly mechanism. Remarkably, the number of examples dealing with these types of analyses is rare, while the control over porphyrin-based assemblies has been widely investigated by changing the thermodynamic state \(e.g.\) by changing concentration, temperature and solvent.\(^4\)

For other self-assembling chromophores than porphyrins, thermodynamic modeling analyses have been exploited by different research groups in order to understand their one-component self-assembly.\(^5\) Herein, our group reported on the cooperative self-assembly of oligo(\(\chi\)-phenylene-vinylene) molecules, in which for the first time, the temperature-dependent data were analyzed with a nucleation-growth model.\(^6\) In a multi-component environment, similar thermodynamic assessments were conducted for instance in the controlling of the stacks length by chain-stopping.\(^3a,7\) In this field, our group reported on the isodesmic self-assembly of homo-ditopic ureido-pyrimidinones and their chain-stopping by monotopic moieties, which were fully corroborated by modeling studies.\(^8\) Recently, we performed a similar analysis on a cooperative system based on benzene-1,3,5-tricarboxamides (BTA’s).\(^9\) Over the years, the cooperative nature of BTA-based assemblies has been fully investigated and applied in other multi-component studies such as chiral amplification.\(^10\)

Considering the insights we have acquired into the aggregation behavior of ditopic molecules into 1-dimensional helical assemblies and the modeling aspects for cooperative self-assembly and chiral amplification, we would like to apply this knowledge to other building blocks that are more versatile. For instance, self-assembling monomers that permit a higher level of complexity by molecular design and, perhaps, possess functional properties. Hence, a new amide-functionalized porphyrin discotic is introduced to a well-established class of self-assembling dyes. In this chapter, the construction of a metallo-porphyrin library is discussed, in which a variety of building blocks is created by plain synthetic modifications only. The influence of different metals, side chains and amide linkers on the self-assembly process in methylcyclohexane (MCH) is investigated. Furthermore, by the input of temperature-dependent circular dichroism (CD) and ultraviolet-visible (UV-vis) spectroscopy data in a self-assembly model, the mechanism and thermodynamic parameters

30
are deduced that will be used throughout this thesis. Finally, model simulations are performed on the S-Zn system and its self-assembly properties are fully analyzed with a variety of characterization techniques.

2.2 Molecular design and synthesis

For the porphyrin design, the focus is on the formation of 1-dimensional helical aggregates in a similar fashion as for BTAs. Thus in order to achieve a hydrogen bond assisted self-assembly process, the tetraphenylporphyrin core is symmetrically functionalyzed with amides. Similar functionalization patterns on porphyrins provided 1-dimensional aggregates in apolar solvents, yet by the decoration of amides the porphyrins form cofacial H-type aggregates upon the formation of four intermolecular hydrogen bonds. The presence of the phenyl spacers between the porphyrin meso-positions and the amides significantly reduce π-π-interactions due to their out-of-plane rotation. In order to solubilize the porphyrins in apolar solvents that stabilize hydrogen bonds at spectroscopic concentrations, the porphyrins are decorated with trialkoxy “gallic” wedges that have been used in a wide variety of self-assembling systems. In the current configuration (Scheme 2.1), the amide is sandwiched between two phenyl rings.

Scheme 2.1. Synthetic scheme for the construction of the porphyrin library with porphyrins having different metal centers (‘M’; Zn/Cu/Mn-metal or FB free-base), side chains (‘R’; R/A/S-chirality) and amide-linkage (‘R’; H or Me methyl).
All porphyrin derivatives are synthesized from commercially available meso-tetraakis-(4-carboxyphenyl)porphyrin (TCPP) and trialkoxy aniline wedges with branched chiral or achiral side chains (Scheme 2.1). After amidation (I), the free-base porphyrins are purified by column chromatography. Prior to metalation, the purity is confirmed by $^1$H-NMR spectroscopy and after metal insertion (2) and a subsequent silica filtration, the product is purified by preparative-scale recycling gel permeation chromatography (rGPC). The porphyrins are lyophilized from benzene in order to obtain a fluffy powder, which has a purple color for the free-base porphyrin, purple/red in case of Zn-, red for Cu- and a dark-green color for Mn-porphyrins. Unlike diamagnetic Zn(II), the paramagnetism of Cu(II)- and Mn(III)-ions inside the porphyrins preclude their NMR characterization; hence we rely on mass spectrometry and UV-vis spectroscopy in order to check purity after metalation. Upon the insertion of zinc, the $^1$H-NMR signal of the inner β-pyrrolic protons at -2.77 ppm disappears, while the resonance of the outer β-pyrrolic protons shifts 0.09 ppm downfield. The N-methyl substitution of S-Zn-Me shows an upfield shift for all proton resonances and the difference between inner and outer alkoxy protons ‘e’ disappears, while the difference in chemical shift between protons ‘b’ and ‘c’ increases (Figure 2.1, Scheme 2.1).

![Figure 2.1. $^1$H-NMR spectra of S-Zn-Me (upper panel), S-Zn (middle panel) and S-FB (lower panel) in CDCl₃ (peak labels refer to the structure in Scheme 2.1).](image)

2.3 Self-assembly of S-Zn in dilute solution

In this section, the responsiveness of the self-assembly to solvent, concentration and temperature is investigated with S-Zn, which is the compound used in the upcoming chapter. At room temperature (RT), the porphyrins are highly soluble in chloroform and in this solvent the porphyrins are molecularly dissolved as evidenced by the sharp peaks in the $^1$H-NMR spectrum (Figure 2.1). In the UV-vis spectrum, this reference state shows a typical sharp Soret band at $\lambda_{\text{max}} \sim 422$ nm in chloroform, while a CD-silent spectrum is acquired
(Figure 2.2A/B). Relative to chloroform, the broadening and 30 nm blue-shift of the Soret absorbance to $\lambda_{\text{max}} \sim 390$ nm in MCH reveals the cofacial arrangement of the porphyrins in an H-type aggregate. In the CD spectrum, an intense bisignated Cotton effect ($\Delta \varepsilon_{\text{max}} \sim -2.9 \times 10^3$ L/mol·cm) is observed that indicates that the porphyrins are helically arranged, in which the helical direction is biased by the stereocenters in the side chain (Figure 2.2B, vide infra). Solution-based infrared spectroscopy shows a 28 cm$^{-1}$ shift to lower wavenumbers of the carbonyl stretch (Figure 2.2C), which corroborates the formation intermolecular hydrogen bonds in the aggregate. In the absence of solvent and side chains, force field calculations reveal a minimized energy structure of cofacially arranged porphyrins having intermolecular hydrogen bonds arranged in a helical fashion and the out-of-plane rotation of the phenyl groups (Figure 2.2D).

Figure 2.2. Solvent-dependency on the self assembled structure of S-Zn at RT by UV-vis (A) and CD (B) spectroscopy at $2.0 \times 10^{-5}$ M and IR (C) at $5 \times 10^{-5}$ M. D: minimized energy representation.

The spectroscopic data reveal the hydrogen bond assistance in the self-assembly process of S-Zn. Another control herein is the spectroscopic analysis of S-Zn-Me that lacks the hydrogen bond donation. When dissolved at spectroscopic concentrations in MCH, a sharp Soret absorbance band is observed at $\lambda_{\text{max}} \sim 420$ nm, which does not change upon heating
the solution to 90 °C (Figure 2.3A). Concomitantly with the absence of any CD activity and the spectral similarities with S-Zn in CHCl₃, S-Zn-Me is molecularly dissolved in MCH. Even at millimolar concentrations in D14-MCH, sharp peaks are observed in the ¹H-NMR spectrum for S-Zn-Me (Figure 2.3B). However, the peak broadening observed for neighboring protons ‘c’ and ‘f’ may be explained by coalescence due to rotational constraints, yet the addition of 5% chloroform or heating-up the solution yields the same ¹H-NMR spectrum acquired in chloroform (Figure 2.1). From a diffusion-ordered spectroscopy (DOSY) experiment, a diffusion constant of 2.2×10⁻¹⁰ m²·s⁻¹ is estimated, which directs to hydrodynamic radii in the order of 1.5 nm under these conditions (Figure 2.3B). This result is in line with the molecular dynamics calculations for S-Zn-Me in the gas phase, in which a spherical object with a radius of ~1.2 nm is estimated. Unlike the spectrum of S-Zn-Me, no peaks (except for the aliphatic region) are observed for S-Zn due to peak broadening, which suggests aggregation.¹⁶

Figure 2.3. A: UV-vis spectrum of S-Zn-Me in MCH (3.5×10⁻⁵ M) at 20 and 90 °C. B: DOSY-NMR spectrum of S-Zn-Me in D14-MCH (1.0×10⁻³ M) at 25 °C.

As evidenced from the spectroscopic studies, the hydrogen bonds connect the porphyrin monomers in the aggregate, which is further investigated by a series of concentration- and temperature-dependent UV-vis and CD studies in MCH. Throughout the concentration domain set by the solubility of S-Zn and the detection limit of the spectrophotometers (4×10⁻⁴ ~ 1×10⁻⁷ M, respectively), Beer’s Law holds when the aggregate Soret band at 390 nm is considered, which also reveals a CD effect that scales linearly with the concentration. This indicates that the aggregates are highly stable, which is further investigated by temperature-dependent studies. At a concentration of 1.0×10⁻⁶ M the porphyrin assemblies are disrupted by heating as evidenced by the red-shifted Soret band at λ_max ~ 419 nm and the disappearance of the CD response (Figure 2.4A/B). To ensure that the self-assembly process is monitored under thermodynamic control, a cooling rate of 30 °C·h⁻¹ is applied, which does not show hysteresis when compared to the subsequent heating run. Upon cooling a 1.0×10⁻⁶ M
solution, an isosbestic point is observed in the UV-vis spectrum at 405 nm, which is in between the transition from 419 to 390 nm; concomitantly, a reappearance of the CD effect is observed. Considering the spectral similarities in MCH of S-Zn at high temperatures with respect to S-Zn-Me at RT (Figure 2.3A) or S-Zn in chloroform (Figure 2.2A), this transition clearly reveals a two-state equilibrium between monomers and aggregates. These features are indicative for a cooperative self-assembly process, which is further examined with cooling curves. By probing the CD intensity at 392 nm, a non-sigmoidal cooling curve is obtained with a sharp transition at \( T_e = 54 \, ^\circ\text{C} \) (Figure 2.4C). An identical cooling curve is obtained by probing the UV-vis absorbance at \( \lambda_{\text{max}} \sim 390 \, \text{nm} \) (Figure 2.8B). The shape of the cooling curve is highly confirmative for a cooperative self-assembly process.\(^{17}\) The critical transition temperature \( T_e \) separates the nucleation and elongation regime; at temperatures lower than \( T_e = 54 \, ^\circ\text{C} \), monomers can readily add to the nuclei to form elongated structures. Characteristically for self-assembled systems, a shift of \( T_e \) to lower temperatures is observed upon dilution of the system (Figure 2.4C).

**Figure 2.4.** Temperature-dependent UV-vis (A) and CD (B) spectra of S-Zn at 1.0×10^{-6} \, \text{M} in MCH. C: Concentration-dependent cooling curves recorded at 392 nm by CD spectroscopy at 30 \, ^\circ\text{C} \cdot \text{h}^{-1} (\phi_n^C \, \text{represents the fraction of aggregated molecules determined after dividing the CD effect at a given temperature by the CD effect at 20 \, ^\circ\text{C} \, \text{at} \, \lambda_{\text{max}}). \text{D: Zoom-in of the nucleation regime of the cooling curve at 1.0} \times 10^{-6} \, \text{M S-Zn in MCH and the curve fits for both regimes.}
The cooling curves are analyzed by a fitting procedure using a temperature-dependent nucleation-elongation model developed by Van der Schoot\textsuperscript{6,18} in which the (concentration-dependent) elongation temperature $T_e$, the (temperature-independent) elongation enthalpy $h_e$ and the activation constant $K_o$ can be estimated directly.\textsuperscript{17} The zoom-in of the cooling curve at 1.0×10^{-6} M shows both fits of the data in the nucleation and elongation regime (Figure 2.4D). From the fit on the nucleation regime, an activation constant of $K_o = 5\times10^{-5}$ is estimated, while an enthalpy of $h_e = -130$ kJ·mol\textsuperscript{-1} is fitted from the elongation regime (Table 2.1). Both nucleation and elongation regimes fit well at to an elongation temperature of $T_e = 327.4$ K (Table 2.1).

The spectroscopic data clearly reveal that a cooperative self-assembly mechanism is operative. In order to investigate its effects on the aggregate size and molecular weight distribution, model simulations are performed. With the current set of thermodynamic parameters obtained from temperature-dependent measurements, it is possible to obtain a concentration-dependent description for the cooperative self-assembly by a $K_2$-K model.\textsuperscript{19,20} Although this model is limited to describe a cooperative process with dimeric nuclei only, it has the advantage that it can be solved analytically, which allows one to simulate cooperative polymerizations with relative ease. From a single cooling experiment at 1.0×10^{-6} M, the Van ‘t Hoff plot can be constructed from the fitted values for $h_e = -130$ kJ·mol\textsuperscript{-1} and $T_e = 54.3$ °C. Its extrapolation to RT reveals the free-monomer concentration ($C^* = 7\times10^{-8}$ M), which equals the reciprocal equilibrium constant for elongation $K_e$ at RT ($C^* = K_e^{-1}$).\textsuperscript{20} The equilibrium constant for nucleation $K_2$ is obtained with the cooperativity parameter $\sigma$, which equals $K_o$, thus $K_2 = K_o\times K$.\textsuperscript{19}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure.png}
\caption{Model simulations at $K_2 = 685$ M\textsuperscript{-1}, $K = 1.37\times10^7$ M\textsuperscript{-1}, $\sigma = K_o = 5.0\times10^{-5}$ for the (A) normalized molecular weight distribution versus the degree of polymerization at 1.0×10^{-6} and 4.0×10^{-5} M and (B) concentration of free/aggregated monomers and the number-concentration of aggregates versus the total concentration.}
\end{figure}
At a concentration of 1.0×10⁻⁶ M, the simulation shows a bimodal molecular weight distribution of monomers and long aggregates with an average length of 500 monomers (Figure 2.5A). The critical monomer concentration at RT is ~7×10⁻⁴ M, which remains constant upon increasing the total concentration (Figure 2.5B), thus the concentration of aggregated monomers grows linearly with the total concentration from C* onwards. As a consequence, ~93% of the monomers are aggregated at 1.0×10⁻⁶ M, which is also shown by integration of the molecular weight distribution when plotted on a linear scale. At higher concentrations such as 4.0×10⁻⁵ M the stack length and fraction of aggregated monomers increase to 3300 and >99%, respectively. Noteworthy, due to the considerable stack length the number of aggregates is fairly low; hence, only at millimolar concentrations the amount of aggregates equals the amount of monomers (Figure 2.5B).

Table 2.1. Thermodynamic parameters for the self-assembly of S/A-Zn/Cu in MCH estimated after fitting temperature-dependent spectroscopy data.

<table>
<thead>
<tr>
<th>Porphyrin</th>
<th>Concentration [M]</th>
<th>Tc [K]</th>
<th>h [kJ·mol⁻¹]</th>
<th>Kc [-]</th>
</tr>
</thead>
<tbody>
<tr>
<td>S-Znᵃ</td>
<td>5.0×10⁻⁵</td>
<td>341.5</td>
<td>-132</td>
<td>9×10⁻⁵</td>
</tr>
<tr>
<td>S-Znᵇ</td>
<td>1.0×10⁻⁵</td>
<td>338.9</td>
<td>-118</td>
<td>7×10⁻⁵</td>
</tr>
<tr>
<td>S-Znᶜ</td>
<td>5.0×10⁻⁶</td>
<td>336.2</td>
<td>-132</td>
<td>8×10⁻⁵</td>
</tr>
<tr>
<td>S-Znᵈ</td>
<td>1.0×10⁻⁶</td>
<td>327.4</td>
<td>-130</td>
<td>5×10⁻⁵</td>
</tr>
<tr>
<td>S-Znᵉ</td>
<td>5.0×10⁻⁷</td>
<td>325.3</td>
<td>-135</td>
<td>3×10⁻⁵</td>
</tr>
<tr>
<td>S-Cuᵃ</td>
<td>1.0×10⁻⁶</td>
<td>325.7</td>
<td>-155</td>
<td>6×10⁻⁵</td>
</tr>
<tr>
<td>A-Cuᶜ</td>
<td>1.0×10⁻⁶</td>
<td>338.6</td>
<td>-138</td>
<td>3×10⁻⁵</td>
</tr>
</tbody>
</table>

ᵃ: Self-assembly probed by CD spectroscopy
ᵇ: Cooling studies on A-Zn not performed due to different aggregate formation (Figure 2.8D).
ᶜ: Self-assembly probed by UV-vis spectroscopy

2.3.1 Aggregation properties of S-Zn in MCH

Based on spectroscopic measurements, the model analyses reveal the formation of long stacks due to the cooperative nature of the hydrogen bond-assisted self-assembly process. In addition, the resulting high fraction of aggregated monomers should determine the overall morphology when solution-based samples are being characterized. In the solid state, the formation of stacks is evidenced by atomic force microscopy (AFM) measurements on highly-ordered pyrolytic graphite (HOPG). The samples are prepared by casting a drop of a 5×10⁻⁶ M stock solution of S-Zn in MCH on a freshly cleaved HOPG surface at RT. The solvent is slowly evaporated under a MCH-vapor atmosphere and the sample is dried under
Chapter 2

vacuum for 2 h. The AFM-height image at low magnifications shows micrometer-long curled fibrillar nanostructures, in which multiple, edge-on porphyrin fibers are bundled-up (Figure 2.6A). At high magnifications, the high-resolution phase image shows a periodical striping inside the cluster, which reveals that individual porphyrin stacks are aligned next to each other (Figure 2.6B). Unfortunately, the helicity of the fibers is not visible, probably due to the softness of the material and the embedding of the stereo-center inside the alkyl chains. A typical height of ~3 nm is observed for all clusters on the surface (Figure 2.6C), which is in line with the radius estimated from the DOSY-experiment of **S-Zn-Me** (Figure 2.3B) and thus corroborates the side-on/lateral adjacent orientation of the fibers. Remarkably, a highly ordered pattern is observed underneath the clusters, which is only observable in high-resolution phase micrographs (Figure 2.6 B/D). The height analysis from the surface to the pattern shows a step of ~0.4 nm after which the periodicity is preserved. Likely, these patterns originate from monomers having a flat-on orientation regarding the surface.21

Solutions of **S-Zn** are highly viscous (*vide infra*), which indicates the formation of self-assembled structures. The aggregation of **S-Zn** in solution is probed with static and multi-angle dynamic light scattering measurements. At a concentration of 6.6×10⁻⁵ M, a linear relation with a slope of -1 is found for the normalized static intensity versus the angle q (Figure 2.6A), which is indicative for rod-like structures22a and continues in the small-angle X-ray scattering (SAXS) regime at higher q-values (Figure 2.9D, *vide infra*). In addition, the Holtzer plot (product of the normalized intensity times q against q; Figure 2.6A, inset) shows a plateau for q > 0.015 nm⁻¹ that corroborates the presence of rods in solution. From the Koyama form factor for a rigid rod, a contour length of ~250 nm is fitted. Except for the static intensity, no other concentration effects are found between 6.6×10⁻⁵ M and 3.3×10⁻⁴ M that indicates a semi-dilute regime, in which aggregate bundling does not occur, however, the stacks still interact with each other. Polarized dynamic light scattering measurements show a single relaxation rate for both angles (Figure 2.7B). Using the theory of Pecora for rigid rods, a persistence length of ~120 nm is estimated after fitting the time correlation function,22b while a contour length of ~230 nm is estimated from the q-dependence on the intensity, which is in line with the measurement in static mode. The contour lengths are in the same ballpark as the stack lengths deduced from the model simulation; at 4×10⁻⁵ M, an average stack length of ~3300 monomers is estimated, which results in ~1000 nm by assuming a typical spacing of 3.5 Å between the π-conjugated discotics. No faster relaxation rates are observed that can be attributed to rotational diffusion coefficients, which preclude the determination of the dilute regime, in which the stacks are free from any interactions. Still, a translational diffusion coefficient of ~8×10⁻¹² m²/s⁻¹ is estimated from the dynamic measurements.
Figure 2.6. AFM micrographs of S-Zn deposited from MCH (5×10⁻⁶ M) on HOPG. A: Height image (5 × 5 μm). B: High-resolution phase image (150 × 150 nm). C: High-resolution height image (400 × 400 nm) with section analysis of the cluster. D: High-resolution phase image (200 × 200 nm) with section analysis of the underlying pattern.

Considering the dipolar effect of the hydrogen bonds and the seemingly related cooperativity of the S-Zn self-assembly, the stacks are expected to be highly polarizable. Furthermore, the anisotropy of the diamagnetic susceptibility of aggregating aromatic moieties increases with their stack size; eventually, the magnetic energy overcomes the thermal energy, which allows the alignment of stacks in a magnetic field.²³ In the aggregated state, the stacks are oriented in the same direction, hence anisotropic polarizability in the magnetic field will result in anisotropy on the refractive index. Unlike a porphyrin sample in
chloroform, a 3.3×10⁻⁴ M solution in MCH shows a retardation of the birefringence when placed in the magnetic field. A typical birefringence curve shows a sigmoidal trend with the applied magnetic field. This curve, however, only reveals the onset and this quadratic behavior is non-specific in order to deduce the aggregate size; it only shows a moderate alignment of the porphyrin stacks.²³b The alignment-ability of the stacks is further investigated under flow in a Couette cell. When the stacks are aligned by a viscous flow, the difference in absorption of light polarized parallel and perpendicular to the flow direction is quantified by the linear dichroic (LD) effect.²⁴ At a revolution rate of 2000 rpm, a 5×10⁻⁵ M solution shows a strong LD effect, while no spectral response is observed in absence of a Couette flow. The negative LD effect at 390 nm confirms the perpendicular orientation of the porphyrin faces in the flow, which is consistent with the cofacial arrangement inside the aggregates. Positive LD effects have been observed for porphyrin J-aggregates in water.²⁵

![Graphs and diagrams](image_url)

**Figure 2.7.** A: Normalized static light scattering intensity versus \( q \) with form factor for rigid rods of 100 nm and a polydispersity of 1.5 (inset: Holtzer plot with the same form factor) of a sample of S-Zn in MCH (6.6×10⁻⁵ M). B: Normalized correlation functions in dynamic light scattering for the same sample at \( q = 0.03244 \) nm⁻¹ and \( q = 0.00869 \) nm⁻¹ (green laser (532 nm) at 150° and 30°, respectively) with both distributions of the relaxation times and the fit at 120 nm. C: Magnetic field induced alignment of S-Zn at 3.3×10⁻⁴ M in chloroform and MCH. D: LD spectra in the presence and absence of Couette flow of a 5.0×10⁻⁵ M solution of S-Zn in MCH.
2.4 The effect of center metal and stereocenter on the porphyrin self-assembly

The combination of characterization techniques in solution and bulk state strongly indicate the formation of 1-dimensional porphyrin stacks in solution. Considering the similarity of molecular design amongst the library members (Scheme 2.1), similar aggregation properties are expected. By means of temperature-dependent UV-vis and CD studies in MCH, the effect of center metal and side chain chirality is investigated and compared to S-Zn. The aggregation properties of S-Mn are discussed in a separate sub-section.

The effect of center metal is investigated with S-Cu, which shows the same H-type aggregate in MCH at $\lambda_{max} \sim 390$ nm (Figure 2.8C) and a similar CD effect in its Soret absorption (Figure 2.8A). The spectroscopic difference between S-Zn and S-Cu is only found in the zero-crossings of the CD effect that are red-shifted by $\sim 1$ nm and the fluorescence; Zn-porphyrins are highly fluorescent relative to Cu-porphyrins that are fully quenched (see Section 6.3). Similar to S-Zn the cooling curves probed by CD and UV-vis spectroscopy are identical and the latter reveals the same non-sigmoidal trend as found for the cooling curve of S-Zn (Figure 2.8B). However, these cooling curves reveal a different elongation temperature (Table 2.1), which is higher for S-Zn ($T_c = 327.4$ K) than S-Cu ($T_c = 325.7$ K). This indicates that a higher temperature is required to fully depolymerize aggregates of S-Zn relative to aggregates of S-Cu, which could indicate that the latter aggregates are slightly less stable.

As observed for S-Zn and S-Cu, H-type aggregate formation is evidenced by a strong CD effect in the Soret absorbance at $\lambda_{max} \sim 390$ nm. Considering the dependency of the aggregation level on the CD activity observed, this supramolecular chirality describes the aggregation of chiral building blocks into a preferred helical direction.26 As a consequence, the self-assembly properties of R/S-Zn are identical, yet relative to S-Zn, the R-Zn enantiomers bias the helical direction in the opposite fashion as evidenced by a mirror-image CD spectrum (Figure 2.8A) and a mirror-image cooling curve when probed by CD (Figure 6.3A). In case of achiral porphyrins, the lack of stereocenters precludes aggregation into a preferred helical direction. This results in an equal amount of left- and right-handed helices, which reveals a CD-silent spectrum for aggregates of A-Zn and A-Cu (Figure 2.8A). Despite the lack of a chiral probe, the self-assembly of achiral porphyrins can be followed by UV-vis spectroscopy.

By monitoring the absorbance at $\lambda_{max} \sim 390$ nm while cooling a $1.0 \times 10^{-6}$ M A-Cu sample from the molecularly dissolved state at 90 $^\circ$C to 20 $^\circ$C, a non-sigmoidal trend is observed that looks similar to the cooling curves of S-Zn and S-Cu (Figure 2.8B). After normalization and fitting of the cooling curve, a considerably higher $T_c$ is found when compared to both chiral porphyrins at the same concentration. Relative to S-Cu, the elongation temperature of A-Cu is 13 $^\circ$C higher, while the enthalpy release and the activation constant remain in the same order (Table 2.1). It is likely that the difference in $T_c$ for chiral and achiral porphyrin has a
molecular origin relating to the chirality of the side chain. The increased stability for helical assemblies based on achiral compounds has also been observed for BTA’s with three solubilizing side chains. Here it was hypothesized that the relatively small difference between the T’s of chiral and achiral BTA’s was attributed to steric effects caused by the branching of the side chains. With twelve branched side chains on the porphyrins, the considerable difference in aggregate stability between S-Cu and A-Cu may be explained by this effect. Another hypothesis relates to the rotation angle between consecutive discs, in which the optimal geometry set by the amides is frustrated by the stereocenters. Compared to achiral bipyridine diamine-derived C₃-discotics, a higher rotation angle was found for the chiral derivative in the liquid crystalline phase.

![CD spectra of S-Cu, R/S-Zn and A-Cu/Zn at 1.0×10⁻⁶ M in MCH at RT. B: Cooling curves of A-Cu, S-Zn and S-Cu recorded at 390 nm by UV-vis spectroscopy at 30 °C·h⁻¹ (‘ϕₙ’ represents the fraction of aggregated molecules determined from the absorbance at λ_max by dividing the absorbance at a given temperature by the absorbance at 20 °C). C: UV-vis spectra of A-Cu aggregates (1.0×10⁻⁶ M, RT) prepared by chloroform injection, fast and slow cooling and the spectrum of S-Cu prepared by dissolution at RT. D: UV-vis spectra of A-Zn aggregates (1.0×10⁻⁶ M, RT) prepared by chloroform injection, fast and slow cooling.](image-url)
When dissolved in MCH and after heating/cooling under thermodynamic equilibrium, all porphyrins derivatives reveal identical aggregation properties with an absorbance spectrum at ~390 nm and the presence of a CD effect for chiral porphyrins. For chiral porphyrins, no drastic effect on the self-assembly is observed by the type of metal center, however, this consistency is not observed for achiral porphyrins. Remarkably, A-Zn shows two, highly distinctive aggregate types in MCH; next to the Soret absorbance at 390 nm (type A), a red-shifted aggregate with \( \lambda_{\text{max}} \sim 416 \) nm is found (type B) (Figure 2.8D). In case of type A, high viscosity solutions are acquired while for type B, considerably lower viscosities are measured. On the other hand, the distribution between both aggregate types can be easily controlled by the preparation method. Type A aggregates are formed by injections of concentrated chloroform solutions of A-Zn in MCH or by rapidly cooling hot MCH solutions. Type B aggregation is promoted by slowly cooling the solutions from the molecularly dissolved state (Figure 2.8D). It seems evident that type B aggregates are thermodynamically more stable than type A aggregates, however, no aggregate interconversion is observed at RT upon ageing. This polymorphism\(^{28}\) is not observed for A-Cu (Figure 2.8C), hence it seems to be related to the zinc ion that easily accepts Lewis bases compared to copper ions.\(^{29}\) In the formation of type B aggregates, it is feasible that additional amide-zinc interactions are involved that give rise to more J-type character,\(^{40}\) yet this has not been confirmed by spectroscopic measurements.

### 2.4.1 Self-assembly of S-Mn

In the comparison between zinc and copper ions, relatively small differences are found for chiral porphyrins, while a strong metalation effect causes polymorphism for achiral porphyrin aggregates. These metallo porphyrins exhibit considerably different self-assembly properties than manganese porphyrins, which is the cause of the presence of an anion. When dissolved in chloroform, the infrared spectrum of S-Mn shows an identical carbonyl stretching frequency at 1674 cm\(^{-1}\) as S-Zn indicative for a molecularly dissolved state (Figure 2.9A). In this solvent, a completely different UV-vis spectrum is acquired with \( \lambda_{\text{max}} \sim 479 \) nm (Figure 2.9B), which reveals that the manganese ion is in its third oxidation state.\(^{30}\) Therefore, the Mn(III)-ion strongly holds an additional anion in order to neutralize S-Mn,\(^{30}\) which has drastic effects on its self-assembly behavior. Considering the molecular design with an anion that sterically blocks the cofacial positioning of a second porphyrin to its face that holds it,\(^{30}\) S-Mn seems to be a monotopic moiety that forms closed dimers upon the formation of hydrogen bonds. The infrared spectrum in MCH shows two vibrations for S-Mn in the carbonyl stretching region at 1653 cm\(^{-1}\) and 1679 cm\(^{-1}\), which indicates that only one set of carbonyls is involved in intermolecular hydrogen bonding. No shift is observed in the UV-vis spectrum in MCH; only a broadening of the Soret band to molar absorptivities
approximating half the values in chloroform at $\lambda_{\text{max}}$. Heating a $2.0 \times 10^{-4}$ M S-Mn solution in MCH to 90 °C does not seem to drastically affect the absorbance spectrum indicating that the hydrogen bonds are stable at this relatively high concentration. Corroborating with dimer formation, the sample shows a small CD effect ($\Delta$$$$\varepsilon$$_{\text{max}} \sim +13$ L/mol·cm), which disappears at 330 K (Figure 2.9C).

**Figure 2.9.** A: IR spectra of S-Mn in CHCl$_3$ and MCH at RT. B: UV-vis spectra of S-Mn (2.0$\times10^{-4}$ M) in CHCl$_3$ and MCH at 20 and 90 °C. C: Corresponding CD spectra (inset: Cooling curve in MCH at 487 nm and 30 °C·h$^{-1}$). D: SAXS scatter plot of S-Zn and S-Mn at 4.0$\times10^{-4}$ M in MCH with the cylindrical fits (inset: Solution viscosities of S-Zn and S-Mn at 2.0$\times10^{-5}$ M and 20 °C compared to pure MCH).

Due to the presence of the manganese(III)-metal, S-Mn is an ionic compound that has only one porphyrin face available for hydrogen bonding. As a consequence, this monotopic compound should form supramolecular dimers upon the formation of hydrogen bonds and it should be an ideal chain stopper; Mn(III)-porphyrins are not fluorescent and known to be energy acceptors for functional chain-stopping.\textsuperscript{3a} Macroscopically, the formation of small discrete assemblies is evidenced by excellent solubility in MCH (> 2$\times10^{-3}$ M) and low viscosity solutions. At a concentration of 2.0$\times10^{-5}$ M, a solution of S-Zn has a viscosity of 0.764 cP, while a solution of S-Mn has a viscosity of 0.707 cP (Figure 2.9D, inset), which
One-component metallo-porphyrin self-assembly

nearly equals the viscosity of pure MCH (0.706 cP) at 20 °C. The effect of the center metal on the size of the supramolecular object is further analyzed by small angle X-ray scattering (SAXS). The data for S-Zn shows a broad regime, in which the scattering intensity scales with \( q^{-1} \) indicating the formation of cylindrical objects (Figure 2.9D). Herewith, it lines up appropriately with the static data acquired at lower \( q \)-values (Figure 2.7A). Therefore, the deviation at lower \( q \)-values is likely related due to improper masking of the incoming beam, which is observed for both scatter plots. Since the aggregate size is out of the SAXS-regime, a cylinder length of 200 nm is set in the fitting procedure and a radius is accurately fitted from the high \( q \)-range at 1.46 nm, which is in line with the DOSY-experiments of S-Zn-Me (Figure 2.3B) and the AFM height analyses (Figure 2.6C). Even in the SAXS-regime, the S-Mn data clearly lack the \( q^{-1} \)-regime; the leveling off at lower \( q \)-values to \( q^0 \) indicates the formation of low-aspect ratio species. After fitting the data with the same cylindrical form factor,\(^3\) a radius of 1.32 nm and length of 4.1 nm is estimated.

2.5 Conclusion

A new library of porphyrin-based supramolecular monomers has been developed and the self-assembly properties have been investigated. The porphyrins form cofacial H-type aggregates upon the formation of four intermolecular hydrogen bonds, which are stabilized in MCH. The self-assembly mechanism of S-Zn has been deduced by concentration- and temperature dependent studies that reveal a highly cooperative mechanism. By fitting the cooling curves with a temperature-dependent nucleation-elongation model, the thermodynamic parameters have been determined, which were utilized to perform simulations based on a concentration-dependent model. The simulations showed a bimodal distribution of monomers and highly elongated aggregates in solution. Due to the cooperative self-assembly, a low free-monomer concentration was estimated and even a lower number-concentration of aggregates.

The formation of S-Zn aggregates was evidenced by AFM studies that revealed the presence of fibers comprising of laterally joined porphyrin stacks. In solution, cylindrical objects have been corroborated with static/dynamic light scattering and SAXS measurements. The alignment-ability by Couette flow and the magnetic field confirmed the formation of elongated structures in solution.

The center metal inside chiral porphyrins revealed a small effect on the critical temperature at which the porphyrins are fully depolymerized \( (T_c) \), in which a higher aggregate stability was deduced for S-Zn than for S-Cu. On assemblies based on achiral porphyrins, the effect of center metal was more drastic. Unlike A-Cu, another aggregate type was found next to the cofacial H-type aggregate type for A-Zn, which could be eliminated by the preparation method. Due to the presence of an additional anion, a strong effect of center metal was
deduced for Mn(III)-porphyrin S-Mn. While S-Zn and S-Cu form elongated structures, S-Mn forms supramolecular dimers as evidenced by IR-studies, SAXS and viscosity measurements.

The comparison between A-Cu and S-Cu revealed a considerable increase in $T_c$ for the achiral monomer, which is probably related to the branched side chains. On the other hand, the comparison between S-Zn and R-Zn only showed a difference in the helical direction of the aggregate as evidenced by a mirror-image CD effect, while aggregates of A-Zn were CD-silent.

### 2.6 Experimental

#### Materials and methods

Unless specifically mentioned, reagents and solvents were obtained from commercial suppliers and used without further purification. All solvents were of AR quality and the chloroform and DMF used for synthesis was dried over 4Å molsieves. Deuterated chloroform and MCH for H-NMR analyses was provided with TMS as a 0 ppm reference. The methylcyclohexane and chloroform used in all spectroscopic experiments was spectroscopic grade.

The lyophilized porphyrin powder was weighted on a microbalance in an aluminum weighing boat, which was transferred to a volumetric flask with MCH (typically; 1.51 mg in 25.00 mL for 2.0×10⁻⁵ M S-Zn). The porphyrin was dissolved by sonication without heat for 15 min and the solutions were subsequently aged at RT over covered in aluminum foil. Samples for A-Zn were prepared by chloroform injections (typically, 50 μL of a 2.01×10⁻⁴ M CHCl₃ solution was injected in 10.00 mL flask containing MCH for a 1.0×10⁻⁶ M sample with 0.5 v% CHCl₃).

#### Instrumentation

NMR spectra were recorded on a Varian 400 MHz instrument and all chemical shifts are reported in parts per million. The DOSY-experiment was performed by Paul Schlebos in the laboratory of prof. R. J. M. Nolte (Netherlands). MALDI-TOF mass spectra (MALDI-TOF MS) were recorded in reflector mode on a PerSeptive Biosystems Voyager-DE PRO. Column chromatography was performed on a Biotage SP1 using SNAP KP-sil columns and solvent gradients. Preparative-scale recycling GPC in HPLC-grade CHCl₃ was performed at a flow rate of 3.0 mL·min⁻¹ using 2 columns filled with 10 μm gel particles with 150 (JAI-2H) and 300 Å (JAI-2.5H) pore sizes. Circular dichroism (CD) spectra were measured using a Jasco J-815 CD spectrometer, with temperature controlled by a PTC-348WI Peltier system. Ultraviolet-visible (UV-vis) absorbance spectra were recorded on a Jasco V-650 UV-vis spectrometer with a Jasco ETCT-762 temperature controller. Infrared (IR) spectra were acquired on a Perkin Elmer Spectrum One spectrometer using 2 mm NaCl cells.

AFM measurements were performed by Motonori Banno in the laboratory of prof. E. Yashima (Japan). Under ambient conditions using a Veeco Multimode and Dimension Icon (with a Nanoscope III control unit) AFM operating in the tapping-mode regime. Light scattering measurements were performed on an ALV-5000 with a Nd:Yag-laser ($\lambda = 532$ nm) in a
vertical polarization experiment in the laboratory of prof. G. Fytas (Crete) by Antje Larsen. The sample bath temperature was controlled and kept stable throughout the experiment at 20 °C. The laser intensity was kept very low (~1 mW) in order to minimize thermal lensing. Interference filters (Owis-Staufen Interference filters 532 ± 1 nm) were used to remove scattered light of unwanted wavelengths. Measurement times for the dynamic light scattering studies ranged from 1000-4000 s as the scattered intensity decreased slightly with time. The solutions were filtered with a 5 μm PTFE filter into a dust-free NMR tube, which was centrifuged at 3500 rpm for 15 min and rested for 30 min before measuring. The magnetic field-induced birefringence was measured by dr. Jeroen Gielens in the laboratory of prof. J. C. Maan (Netherlands) using a standard modulation technique.33 Polarized light and its interaction with modulating devices (HINDS International, Hillsboro) using a HeNe laser (632.8nm, 1mW output, Melles-Griot) as a source of monochromatic light. The sample was contained in a 5 mm optical cell with a water-based temperature controller maintaining a temperature of 20 ± 0.1 °C. The magnetic-field induced birefringence was measured by slowly sweeping the magnetic field between 0 and 20 T with a Bitter magnet. The small birefringence of the pure solvent caused by the experimental setup was used as a background.

Flow linear dichroism was measured by dr. Cameron Lee at RT using a Jasco J-715 spectro-polarimeter and a micro-volume Couette cell as described by Rogers and coworkers.24

Viscosities of S-Zn and S-Mn in MCH were measured with a Schott 538 10 micro-Ubbelohde viscometer. Solutions were passed through a 5 μm PTFE filter before measurement. Flow times were measured automatically using a Schott AVS 350 measuring stand. The viscometer temperature was held constant at 20.0 °C using a Schott CT 1650 thermostat.

The Small-Angle X-Ray Scattering (SAXS) measurements were performed at the cSAXS - X12SA beamline at PSI in Villigen by Martijn Gillisen. SAXS images were recorded using a 2D Pilatus 2M detector with 172×172 μm² pixel size. A sample-to-detector distance of 2.17 m was used together with an X-ray photon wavelength of 1.0 Å. The observed q range was 5×10⁻² nm⁻¹ ≤ q ≤ 6.7 nm⁻¹. The 2D images were radially averaged in order to obtain the intensity I(q) vs q profiles. The liquid samples were held in 2 mm quartz capillaries. Standard data reduction procedures, i.e. subtraction of the empty capillary and solvent contribution, were applied.

Force field calculations were performed by dr. Takashi Hirose carried out in Maestro® ver. 9.0211. Optimization method: PRCG, force field: OPLS-2005 in gas phase (ϵ = 1.0).

The simulations on the Kx-K model were performed by dr. Takashi Hirose carried out in Matlab®.

**Wedge synthesis**

As described in Scheme 2.1, the porphyrins are prepared by an amidation reaction between TCPP and aniline wedges. The synthesis of achiral aniline wedge 1 (Scheme 2.2), (S)-chiral aniline wedge 2 and its N-methylated analog 3 (Scheme 2.3) is discussed in this part.
**Scheme 2.2.** Synthetic scheme for “achiral wedge” 1.

### 3.4.5-Triocetylxyloxyaniline wedge 1. (Scheme 2.2)

(a) A solution of 1,2,3-trihydroxybenzene (5.0 g, 39.6 mmol), 1-octylbromide (27 g, 140 mmol) K$_2$CO$_3$ (44.5 g, 320 mmol) and tetrabutylammonium bromide (TBAB phase transfer catalyst, 1.29 g, 4 mmol) in MIBK (200 mL) was refluxed, at 140 °C under N$_2$ atmosphere overnight. The reaction mixture was cooled to RT, diluted with ether (500 mL) and the salts were extracted with water (2 × 300 mL) and brine (300 mL). The organic phase was washed with brine (200 mL), dried with Na$_2$SO$_4$, filtered and concentrated under vacuum. A brown oil was obtained, which was purified by column chromatography (Biotage®; 25%→75% over 10 cv’s (SNAP 350 g) DCM/Heptane) and a transparent oil was obtained. Yield: 13.7 g (74%).

(b) Silica gel (1.5 g) was suspended in DCM (15 mL) and HNO$_3$ (29 mmol, 65%, 2 mL) was added while vigorously stirring. A solution of 1,2,3-tri-octyloxybenzene (2 g, 4.3 mmol) was added and the reaction mixture was stirred at RT for 15 minutes, in which the initial transparent solution turned deep red. The silica gel was removed by filtration and washed with DCM. Since higher yields were observed by running small-scale reactions, the reaction was repeated several times up to a total amount of 8 g 1,2,3-tri-octyloxybenzene. The combined filtrates were neutralized with 1 M NaOH (120 mL solution and after the addition of brine (200 mL), the product was extracted with DCM (200 mL). After washing with water (100 mL) and brine (200 mL), the organic layer was dried with Na$_2$SO$_4$, filtered and concentrated under vacuum. A dark-brown oils was purified column chromatography (Biotage®; 5%→25% over 8 cv’s (SNAP 100 g) EtOAc/Heptane) in order to obtain a light-yellow. Yield 4.74 g (54%).

(c) The 3,4,5-trioctyloxynitrobenzene (4.5 g, 8.9 mmol) was dissolved in EtOAc (20 mL) and saturated with Ar by flushing for 15 min. Pd/C (10%, 80 mg) was added and the mixture was shaken in a Parr apparatus under hydrogen atmosphere at 70 psi overnight. The catalyst was removed by filtration and the solvent was evaporated in order to obtain a viscous light-yellow oil in quantitative yield, which did not require further purification. 1H-NMR (CDCl3): δ = 0.88 (t, 9H, CH3), 1.26-1.85 (m, 36H, CH2), 3.48 (br. S, 2H, NH2), 3.82-3.94 (m, 6H, OCH2), 5.92 (s, 2H, ArH). MALDI-TOF MS: [M]+ calcd. for C30H55NO3: 477.41, found 477.5 D.
One-component metallo-porphyrin self-assembly

\[ \text{HO} \rightarrow \text{Pd/C} \rightarrow \text{H}_2 \rightarrow \text{HO} \]

\[ a \rightarrow \text{TsCl} \rightarrow \text{TMA-HCl/TEA} \rightarrow \text{DCM, 0 °C} \]

**Scheme 2.3.** Synthetic scheme for “chiral wedge” 2 and 3.

- **3,4,5-Tri[(S)-3,7-dimethyloctyloxy]aniline wedge 2.** The chiral aniline wedge was synthesized in a similar way, yet the chiral side chain was converted into the tosylate prior to its Williamson ether synthesis with methyl-3,4,5-tri hydroxybenzoate. The synthetic procedures for both S- and R-enantiomers is identical, hence only the synthesis of the S-enantiomer of 2 discussed (Scheme 2.3).

  (a) (S)-(−)-β-citronellol (Takasago, ee < -99.6%) (20 g, 128 mmol) was dissolved in EtOH (100 mL) and saturated with Ar by flushing for 15 min. Pd/C (10%, 100 mg) was added and the mixture was shaken in a Parr apparatus under hydrogen atmosphere at 70 psi overnight. The catalyst was removed by filtration and the solvent was evaporated and a transparent oil was obtained in quantitative yield.

  (b) Di-hydro-(S)-(−)-β-citronellol (20 g, 126 mmol), triethylamine (25.5 g, 250 mmol) and trimethylammonium hydrochloride (1.81 g, 19 mmol) were dissolved in 50 mL DCM and cooled to 0 °C. At this temperature, a solution of 4-toluenesulfonyl chloride (27.6 g, 145 mmol) in 50 mL was added dropwise. The solution was allowed to reach RT overnight. Water (25 mL) was added, the layers were separated and the organic layer was washed with water (100 mL) and brine (200 mL). The organic layer was dried with Na2SO4, filtered and concentrated under vacuum. The product was purified over a silica plug with DCM. Yield 33 g (84%).
Di-hydro-(S)-(+) -β-citronellyl-tosylate (5.9 g, 19 mmol), methyl gallate (1.07 g, 5.8 mmol), K$_2$CO$_3$ (8.3 g, 60 mmol) and TBAB (0.64 g, 2 mmol) were suspended in 20 mL acetone and refluxed under N$_2$ overnight. The reaction was poured into 150 mL water and extracted with diethyl ether (3 x 20 mL). The collected ether layers were washed with water (100 mL), brine (100 mL) and dried with Na$_2$SO$_4$. The solution was evaporated and the brown oil was purified by column chromatography (Biotage®; 25%→75% over 10 cv’s (SNAP 50 g) DCM/Heptane) in order to obtain a light-yellow oil. Yield: 3.2 g (91%).

Methyl-3,4,5-tri[(S)-3,7-dimethyloctyloxy]benzoate (3.2 g, 5.3 mmol) was refluxed with NaOH (5 g, 120 mmol) in 20 mL ethanol for 8 h. After saponification, ethanol was removed in vacuo and the residue was partitioned between water and DCM. The organic layer was collected and neutralized with 1 M HCl (1 x 50 mL) and washed with water (2 x 50 mL) and brine (1 x 50 mL) and subsequently dried with Na$_2$SO$_4$. The solvent was evaporated and the light-yellow oil was dried under high vacuum. Yield: 2.9 g (93%).

A solution of ethyl chloroformate (0.8 mL, 8.4 mmol) in THF (10 mL) was added dropwise to a solution of 3,4,5-tri[(S)-3,7-dimethyloctyloxy]benzoic acid (2.9 g, 4.9 mmol) and triethylamine (1.2 mL, 8.4 mmol) in THF (30 mL) at 0°C. The solution was stirred for 45 min at 0°C and the 3,4,5-tri[(S)-3,7-dimethyloctyloxy]benzoic acid chloride was not isolated. To the solution at 0°C, a solution of sodium azide (2.60 g, 40 mmol) in water (10 mL) was added. The mixture was allowed to reach RT where the solution was stirred for 2 h. Water (100 mL) and diethyl ether (20 mL) were added and the layers were separated. The water layer was extracted again with diethyl ether (2 x 50 mL) and the combined organic layers were subsequently dried with Na$_2$SO$_4$, filtered and evaporated to dryness. The obtained acyl-azide derivative was purified by column chromatography (Biotage®; 25%→50% over 8 cv’s (SNAP 50 g) DCM/Heptane) and a light-yellow oil was obtained. Yield 2.1 g (64%).

The acyl-azide (2.1 g, 3.4 mmol) was dissolved in dry dioxane (25 mL) and heated under reflux for 30 min. After reflux, the solution was cooled to 70°C and added over a period of 1 h to a solution of tetrabutylammonium hydroxide (40 wt% in water, 4.0 mL) in dioxane (100 mL) at 90°C via a cannula. The solution was stirred for 15 min at 90°C, allowed to cool to RT and evaporated to dryness. The obtained residue was partitioned between water (100 mL) and diethyl ether (100 mL) and the layers were separated. The water layer was extracted with diethyl ether (100 mL) and the combined organic layers were washed with brine (150 mL), dried over Na$_2$SO$_4$, filtered and evaporated to dryness. The light-yellow oil was purified by column chromatography (Biotage®; 10%→40% over 8 cv’s (SNAP 50 g) EtOAc/Heptane). Yield: 1.55 g (81%). $^1$H-NMR (400 MHz, CDCl$_3$): δ = 0.86 (d, 18H, J = 6.6 Hz, CH(CH$_3$)$_2$), 0.91 (d, 3H, CH$_3$), 0.92 (d, 6H, CHCH$_3$), 1.08-1.39 (m, 18H), 1.44-1.61 (m, 6H), 1.62-1.74 (m, 3H), 1.75-1.87 (m, 3H), 3.45 (br. s, 2H, NH$_2$), 3.86 (m, 2H, OCH$_2$), 3.95 (m, 4H, OCH$_2$), 5.82 (s, 2H, ArH). $^{13}$C-NMR (100 MHz, CDCl$_3$): δ = 19.7, 19.7, 22.7, 22.8, 24.9, 28.9, 28.1, 29.9, 29.9, 36.5, 37.5, 37.5, 37.7, 39.4, 39.5, 67.4, 71.9, 95.0, 131.7, 141.3, 153.9. MALDI-TOF MS: [M]+ calcd. for C$_{35}$H$_{68}$NO$_2$: 561.51; found 561.5 D.

These reactions were also performed on (R)-(+) -β-citronellol (Aldrich, ee > 98%) for the R-enantiomer of 2.
\textbullet \textbf{3,4,5-Tri[(S)-3,7-dimethyloctyloxy]-N-methyl-aniline wedge 3.} (Scheme 2.3)

(i-ii) 2 (2.0 g, 3.6 mmol) was dissolved with formic acid (1.4 mL, 37 mmol) in EtOH (20 mL) and refluxed overnight. After cooling to RT, NaBH₄ (2 g, 53 mmol) was gradually added to the formamide solution, which was stirred for 6 h. The reaction was cooled to 0 °C and carefully quenched with water. The mixture was concentrated \textit{in vacuo} and the residue was partitioned between water (100 mL) and DCM (50 mL). The organic layer was washed with water (50 mL), brine (50 mL) and dried with Na₂SO₄. After solvent evaporation, the light-yellow oil was purified by column chromatography (Biotage®; 25%→75% over 8 cv’s (SNAP 50 g) Chloroform/Heptane). Yield: 1.6 g (78%). \(^1\)H-NMR (400 MHz, CDCl₃): δ = 0.87 (d, 18H, J = 6.6 Hz, CH(CH₃)₂), 0.90 – 0.97 (m, 9H, CHCH₃), 1.04-1.40 (m, 18H), 1.43-1.93 (m, 12H), 2.79 (s, 3H, N-CH₃), 3.81-4.04 (m, 6H, OCH₂), 5.82 (s, 2H, ArH). \(^1\)C-NMR (100 MHz, CDCl₃): δ = 19.6, 22.6, 24.7, 28.0, 29.8, 31.2, 36.5, 37.4, 39.4, 67.3, 71.8, 91.9, 130.5, 145.7, 153.8. MALDI-TOF MS: [M]⁺ calcd. for C₁₆H₂₄NO: 575.53; found 575.75 D.

\section*{Porphyrin synthesis}

\textbullet \textbf{General procedure for A-FB / S-FB / R-FB.} (Scheme 2.1, (1))

Meso-tetraakis(4-carboxyphenyl)porphyrin (TCPP, 200 mg, 0.25 mmol, TCI Europe), wedge 1 (602 mg, 1.26 mmol) or 2 (708 mg, 1.26 mmol), \textit{N,N}-Disopropylethylamine (DIPEA, 348 µL, 2 mmol) and benzotriazole-1-yl-oxy-trispyrrolyldinophosphonium hexafluorophosphate (PyBOP, 780 mg, 1.5 mmol) were dissolved in DMF (10 mL) and stirred with the protection from light for 24 h at 40 °C. After reaction, the red mixture was charged in a separation funnel and 1 M HCl (20 mL) (product turned green) and diethyl ether (50 mL) was added, in which the product was extracted. The organic layer was washed with 1 M NaOH (20 mL) (product turned red) and brine (75 mL) and dried with Na₂SO₄. After filtration, the solvent was removed \textit{in vacuo} and purified by column chromatography (Biotage®; 0%→100% over 8 cv’s (SNAP 50 g) MixA/MixB; MixA = 4/4/1 (Heptane/Chloroform/Ethyl acetate) and MixB = 1/1 (Heptane/Chloroform)). Generally obtained yields: 450-550 mg (~70%).

The free-base derivatives were fully analyzed before the metalation reactions with Zn/Cu/Mn-acetate.

\textbf{A-FB:} \(^1\)H-NMR (400 MHz, CDCl₃): δ -2.79 (s, 2H, NH), 0.90 (br s, 36H, CH₂CH₃), 1.1-2.0 (m, 144H), 3.9-4.1 (m, 24H, CH₂O), 7.10 (s, 8H, ArH), 8.13 (s, 4H, NH), 8.18 (d, J = 8 Hz, 8H, ArH), 8.22 (d, J = 8 Hz, 8H, ArH), 8.78 (s, 8H, β-pyrrolic protons). MALDI-TOF MS: [M]⁺ calcd. for C₁₆H₂₄NO₃S 2627.84, found 2627.97 D.

\textbf{S-FB / R-FB:} \(^1\)H-NMR (400 MHz, CDCl₃): δ -2.77 (s, 2H, NH), 0.85-0.90 (br d, 72H, CH(CH₃)₂), 0.95-1.00 (br d, 36H, CH₂CH₃), 1.1-2.0 (m, 120H), 3.9-4.2 (m, 24H, CH₂O), 7.10 (s, 8H, ArH), 8.04 (s, 4H, NH), 8.27 (d, J = 8 Hz, 8H, ArH), 8.35 (d, J = 8 Hz, 8H, ArH), 8.86 (s, 8H, β-pyrrolic protons). \(^1\)C-NMR (100 MHz, CDCl₃): δ 19.8, 22.8, 22.9, 24.9, 28.2, 29.9, 30.0, 36.6, 37.6, 37.7, 39.5, 39.6, 67.7, 72.0, 99.5, 119.4, 125.6, 133.7, 134.9, 135.0, 135.5, 145.7, 153.6, 165.7. MALDI-TOF MS: [M]⁺ calcd. for C₁₆H₂₄NO₃S 2964.21, found 2964.66 D.
Chapter 2

- General procedure for Zn-insertion (A-Zn / S-Zn / R-Zn). (Scheme 2.1, (2))

Anhydrous Zn(OAc)_2: (500 mg, 2.73 mmol) was suspended with a solution of A-FB / S-FB / R-FB (~500 mg, -0.19 / -0.17 mmol) in DCM (15 mL) and stirred overnight with the protection from light. After the insertion of zinc, the suspension was filtered and the filtrate was evaporated to dryness. The product was purified by column chromatography (Biotage®; MixA (SNAP 50 g); MixA = 4/4/1 (Heptane/Chloroform/Ethyl acetate)) and further purified by rGPC. Successful insertion was evidenced by the disappearance of 4 Q-bands and the appearance of 2 Q-bands in UV-vis.

A-Zn: ^1^H-NMR (400 MHz, CDCl_3): No inner pyrrolic NH observed at δ < 0 ppm after Zn-insertion, δ = 0.90 (br s, 36H, CH₂CH₃), 1.2-1.6 (m, 120H), 1.7-1.9 (m, 24H, CH₂CH₂O), 3.99 (t, J = 6 Hz, 8H, CH₃O), 4.06 (t, J = 6 Hz, 8H, CH₂O), 7.06 (s, 8H, ArH), 8.04 (s, 4H, NH), 8.24 (d, J = 8 Hz, 8H, ArH), 8.34 (d, J = 8 Hz, 8H, ArH), 8.95 (s, 8H, β-pyrrolic protons). ^1^C-NMR (100 MHz, CDCl₃): δ 14.3, 22.8, 22.9, 26.3, 26.3, 29.5, 29.6, 29.7, 30.5, 32.0, 32.1, 69.4, 73.7, 99.5, 120.3, 125.4, 132.3, 133.6, 134.4, 134.8, 135.4, 146.4, 150.0, 153.5, 156.7. MALDI-TOF MS: [M]^+ calcd. for C₁₃₆H₂₆₅N₉O₆Zn 2689.75, found: 2689.67 D.

S-Zn / R-Zn: ^1^H-NMR (400 MHz, CDCl₃): No inner pyrrolic NH observed at δ < 0 ppm after Zn-insertion, δ = 0.78-0.91 (m, 72H, CH(CH₃)₂), 0.92-1.01 (m, 36H, CHCH₃), 1.12-2.04 (m, 120H, alkyl protons), 3.96-4.16 (m, 24H, CH₂O), 7.08 (s, 8H, ArH), 8.05 (s, 4H, NH), 8.25 (d, J = 8 Hz, 8H, ArH), 8.35 (d, J = 8 Hz, 8H, ArH), 8.96 (s, 8H, β-pyrrolic protons). ^1^C-NMR (100 MHz, CDCl₃): δ = 19.8, 22.8, 22.9, 24.9, 28.1, 29.9, 30.0, 36.6, 37.5, 37.7, 39.4, 39.5, 67.6, 72.0, 99.5, 120.2, 125.4, 132.2, 133.7, 134.3, 134.8, 135.4, 146.5, 150.0, 153.5, 165.8. MALDI-TOF MS: [M]^+ calcd. for C₁₃₆H₂₆₅N₉O₆Zn: 3026.13; found: 3026.04 D.

- General procedure for Cu-insertion (A-Cu / S-Cu). (Scheme 2.1, (2))

Anhydrous Cu(OAc)₂: (500 mg, 2.75 mmol) was suspended with a solution of A-FB / S-FB (~500 mg, -0.19 / -0.17 mmol) in chloroform (15 mL) and refluxed overnight with the protection from light. After the insertion of copper, the suspension was filtered and the filtrate was evaporated to dryness. The product was purified by column chromatography (Biotage®; MixA (SNAP 50 g); MixA = 4/4/1 (Heptane/Chloroform/Ethyl acetate)) and further purified by rGPC. Successful insertion was evidenced by the disappearance of 4 Q-bands and the appearance of 2 Q-bands in UV-vis. The paramagnetism of the Cu(II)porphyrins precluded NMR characterization.

A-Cu: MALDI-TOF MS: [M]^+ calcd. for C₁₃₆H₂₆₅N₉O₆Cu 2688.76, found 2688.72 D.

S-Cu: MALDI-TOF MS: [M]^+ calcd. for C₁₃₆H₂₆₅N₉O₆Cu: 3025.14, found 3024.83 D.

- General procedure for Mn-insertion (S-Mn). (Scheme 2.1, (2))

Anhydrous Mn(OAc)₂: (500 mg, 2.89 mmol) was suspended with a solution of S-FB (~500 mg, -0.17 mmol) in chloroform (10 mL) with MeOH (5 mL) and refluxed overnight with the protection from light. The green suspension was filtered and the filtrate was evaporated to dryness. The product was purified by column chromatography (Biotage®; 10%→50% over 10 cv’s (SNAP 50 g) EtOAc/Chloroform) and further purified by rGPC. Successful insertion was evidenced by the disappearance of 4 Q-bands and the appearance of 2 Q-bands in UV-vis. The paramagnetism of the Mn(III)porphyrins precluded NMR characterization.

S-Mn: MALDI-TOF MS: [M]^+ calcd. for C₁₃₆H₂₆₅N₉O₆Mn: 3017.30, found 3018.23 D.
Synthesis of S-Zn-Me. (Scheme 2.1)
TCPP (250 mg, 0.32 mmol) was suspended in 40 mL dry CHCl₃ in a flamed flask. Oxaly chloride (850 μL, 9.9 mmol) was added to the porphyrin suspension via a syringe, followed by five drops of dry DMF. After stirring overnight under a nitrogen atmosphere with protection from light, the solvent was evaporated under a stream of nitrogen and the green residue was freed of volatile compounds by vacuum pump evaporation for 2 h. The dried green residue (TCPP-acid chloride) was redissolved in dry CHCl₃ (30 mL) and to this solution a CHCl₃ solution (30 mL) containing 3 (920 mg, 1.6 mmol) and DIPEA (550 μL, 3.2 mmol) was added slowly. The reaction was stirred for 24 h under a nitrogen atmosphere with protection from light. The reaction mixture was diluted with CHCl₃ (60 mL) and sequentially washed with 10% citric acid (3 × 15 mL), 1 M NaOH (2 × 15 mL), and brine (60 mL). The organic phase was dried with Na₂SO₄, filtered and evaporated. The purple solid was dissolved in DCM (15 mL) and suspended with anhydrous Zn(OAc)₂ (500 mg, 2.3 mmol) and stirred overnight at RT with the protection from light. After zinc-insertion, the solution was filtered and purified by column chromatography (Biotage®; 0%→50% over 8 cv’s (SNAP 50 g) MixA/MixB; MixA = 4/4/1 (Heptane/Chloroform/Ethyl acetate) and MixB = 1/1 (Heptane/Chloroform)). After the column, the product was further purified by preparative-scale recycling gel permeation chromatography. Yield: 520 mg (53%). ¹H-NMR (400 MHz, CDCl₃): No inner pyrrole NH observed at δ < 0 ppm after Zn-insertion, δ 0.67-0.81 (m, 72H, CH(CH₃)₂), 0.81-0.92 (m, 36H, CHCH₃), 0.99-1.94 (m, 120H), 3.66 (s, 12H, NCH₃), 3.91-4.06 (m, 24H, CH₂O), 6.51 (s, 8H, ArH), 7.75 (d, J = 8 Hz, 8H, ArH), 8.02 (d, J = 8 Hz, 8H, ArH), 8.63 (s, 8H, β-pyrryl protons). ¹³C-NMR (100 MHz, CDCl₃): δ 14.1, 19.5, 22.5-22.7, 24.7, 27.9, 29.7, 31.9, 36.3, 37.3, 37.5, 39.1, 39.3, 67.7, 71.8, 106.0, 119.3, 126.9, 134.0, 135.6, 137.1, 140.0, 143.3, 153.4, 170.4. MALDI-TOF MS: [M]+ calcd. for C₃₈H₅ₐN₆O₆Zn: 3085.9; found 3085.15 D.

2.7 References


14. Unlike for BTA’s, the direct coupling of one solubilizing chain in order to make the amide did not provide sufficient solubility of the porphyrins in MCH. Therefore it was decided to use trialkoxy-aniline wedges.


One-component metallo-porphyrin self-assembly

30. S-Mn is prepared form S-FB and manganese(II)acetate, in which the manganese metal oxidizes to Mn(III). The presence of an ionic compound is clearly observed with thin layer chromatography (TLC). Here the ionic species have considerably lower RF-values than the free-base, Zn or Cu derivative. The nature of the anion could not be discovered as attempted with MALDI-TOF MS in positive and negative mode.
Two-component Zn-porphyrin self-assembly with pyridine

Abstract. The self-assembly of chiral Zn-porphyrins was studied in the presence of the monotopic axial ligand pyridine. Upon the addition of pyridine, the hydrogen bonded porphyrin stacks readily depolymerized into hydrogen bonded, pyridine capped porphyrin dimers in a bimodal fashion. A depolymerization mechanism was proposed and the resulting thermodynamic model was fitted to the pyridine titration data. Model simulations were used to construct a phase diagram, which described the competition between hydrogen bonding and metal-ligand coordination. Examination of the phase diagram revealed a dilution-induced self-assembly of the porphyrin stacks, which was experimentally verified. Kinetic studies revealed a slow dilution-induced self-assembly process, which was further investigated in a microfluidic diffusion cell. This microfluidic setup was used to estimate diffusion constants of the stacks and dimers in the absence and presence of pyridine, respectively. Subsequently, at a critical amount of pyridine, a mixture of stacks and dimers was separated on the microfluidic chip. Directly probing the separation process in line showed different distributions between stacks and dimers than probing of the collected samples, which was attributed to the slow supramolecular dynamics of the dilution-induced self-assembly process.

Part of this work has been published:
3.1 Introduction

In one-component systems, the control over supramolecular polymerizations of ditopic monomers is confined by the ability to tune the stability of the non-covalent interactions. Especially if only one particular interaction remains dominant in the self-assembly process, the aggregate size can be controlled by the solvent, temperature and concentration as we found for 1-dimensional porphyrin aggregates described in chapter 2. The responsiveness to these parameters strongly depends on the self-assembly mechanism, however, deviation from this behavior could occur when the self-assembly process is controlled by other stimuli, such as the introduction of multiple components. In this field, the length of 1-dimensional assemblies can be controlled by the employment of templates\textsuperscript{1} or by using chain-stoppers\textsuperscript{2}. In the latter, most examples disclose the addition of monotopic moieties that address the same supramolecular interaction in order to reduce the length of a non-discrete aggregate. In an isodesmic system, our group reported on the successful chain-stopping of a homo-ditopic, ureido-pyrimidinone-(UPy)-based polymer using monotopic UPy-derivatives that strongly reduced the solution viscosity\textsuperscript{2a}. In a cooperative system, Boutelier and coworkers presented the introduction of a chain-stopper to a system based on bis-urea derivatives, in which alkylation of one of the urea-nitrogen atoms was sufficient to create a monotopic moiety that could only accept hydrogen bonds\textsuperscript{2b}. A similar approach was conducted by our group based on benzene-1,3,5-tricarboxamides (BTA’s), which also led to the controlled decrease of the degree of polymerization upon the addition of an N-alkylated BTA-derivative\textsuperscript{2c}.

For highly discrete systems however, the closed topology of supramolecular interactions causes a different response upon the addition of monotopic moieties. For instance, the addition of pyridine led to the disruption of discrete porphyrin-based assemblies\textsuperscript{3} or the liberation of porphyrin arrays from templates\textsuperscript{4}. For intramolecular hydrogen bonded systems, similar experiments are performed with proteins that unfold upon the addition of denaturant\textsuperscript{5}. Apparently, the types of supramolecular interactions being addressed and the role of cooperativity are important factors in the interaction between monotopic and ditopic species. Rather than addressing the parent supramolecular interaction, \textit{i.e.} hydrogen bonding in the porphyrin system \textit{e.g.} by the addition of an \textit{N}-methylated porphyrin derivative (\textit{S-Zn-Me}) to stacks of \textit{S-Zn} (Scheme 2.1), we investigate the addition of a monotopic moiety that addresses an orthogonal interaction with respect to the ditopic main component. Hence, in this chapter we focus on the self-assembly of \textit{S-Zn} in the presence of pyridine, which forms stable metal-ligand coordination complexes while the porphyrin self-assembly is driven by cooperative intermolecular hydrogen bonding. The competition between both processes is studied by titration experiments and thermodynamic modeling studies that are based on a hypothesized mechanism that explains the pyridine interaction with the porphyrins.
3.2 Pyridine titration to S-Zn-Me

In the monomeric state, the complexation of pyridine to Zn-porphyrins leads to a red-shift in UV-vis, which allows determining the binding constant. For instance, in chloroform the titration of pyridine to monomers of S-Zn results in a constant of $1.2 \times 10^4$ M$^{-1}$ at room temperature (RT) after fitting the 1:1 binding isotherm. The same binding constant is obtained for the complexation of S-Zn-Me, which indicates that the Lewis acidity of the zinc ion remains identical despite the different meso-substitution. In methylcyclohexane (MCH), S-Zn-Me is molecularly dissolved as evidenced by its Soret absorption at $\lambda_{\text{max}} \sim 420$ nm and the addition of pyridine leads to an isosbestic transition at 424.8 nm to a new Soret band at $\lambda_{\text{max}} \sim 430$ nm originating from the S-Zn-Me:pyridine (1:1) complex (Figure 3.1A). After simultaneous curve fitting the binding isotherms of the monomer and the monomer complex, a binding constant of $K_c = 5.1 \times 10^4$ M$^{-1}$ is estimated (Figure 3.1B). The five-time higher association in MCH is related to its lower dielectric constant (2.02 D) relative to chloroform (4.81 D).

![Figure 3.1](image)

**Figure 3.1.** A: Pyridine titration to S-Zn-Me at 2.0 $\times$ 10$^{-6}$ M (RT) between 0 and 5000 excess in UV-vis. B: Titration curves at 420 (monomer) and 430 nm (monomer complex) with the corresponding simultaneous curve fit at $K_c = 5.1 \times 10^4$ M$^{-1}$.

3.3 Pyridine titration to S-Zn

After studying the complexation of pyridine with S-Zn-Me in the absence of hydrogen bonding and the elucidation of the one-component self-assembly of S-Zn in MCH (Chapter 2), the addition of pyridine to aggregates of S-Zn is studied by UV-vis and CD measurements in MCH. At a concentration of 2.0 $\times$ 10$^{-5}$ M in MCH at RT, monomers of S-Zn form extended, 1-dimensional aggregates in a cooperative fashion. The cofacial arrangement of the porphyrin chromophores is evidenced by their blue-shifted absorbance at $\lambda_{\text{max}} \sim 390$ nm. The preferred helical arrangement of the porphyrins, biased by twelve stereocenters, is evidenced by a strong bisignate Cotton effect in the CD spectrum, which has an opposite sign in case of R-Zn.
Two transitions are observed upon the addition of pyridine to S-Zn. The first transition between a molar excess of 0 and 75 pyridine, the Soret band at $\lambda_{\text{max}} \sim 390$ nm disappears while a new, red-shifted and split band appears at 418 and 427 nm (Figure 3.2A). This absorbance band reveals and exciton splitting energy of 500 cm$^{-1}$, which indicates an edge-to-edge, slipped cofacial arrangement. Since this band splitting has been observed earlier for dimeric porphyrin-pyridine adducts, the observed Soret band could indicate the formation of a hydrogen bonded, pyridine capped dimer. These dimer complexes are highly similar to S-Mn, in which the additional anion of the Mn(III)-ion sterically blocks one porphyrin face for hydrogen bonding (see Section 2.4.1). Analogously, the $\eta^5$-complexation of pyridine sterically blocks one porphyrin face for hydrogen bonding, while dimerization of S-Zn:pyridine (1:1) monomer complexes via hydrogen bonding allows for the formation of closed dimers. Along with the disappearance of the aggregate Soret band at $\lambda_{\text{max}} \sim 390$ nm, the CD intensity decreases, while a weak CD effect appears in the absorption regime of the dimer complexes (Figure 3.2B). The zoom-in of the CD spectra recorded at molar pyridine excesses higher than 100 show a similar CD effect (at $\Delta E_{\text{max}} \sim +25$ L/mol-cm, Figure 3.2D) as dimers of S-Mn (Figure 2.9C). Similarly as found in the pyridine titration to S-Zn-Me, the transition from S-Zn H-type aggregates ($\lambda_{\text{max}} \sim 390$ nm) of pyridine dimer complexes ($\lambda_{\text{max}} \sim 427$ nm) is accompanied by an isosbestic point (Figure 3.2A). This point at 407.2 nm is indicative for a two-stage transition between extended aggregates and dimers; both possessing the stable hydrogen bonding motif and they are spectroscopically discrete. Remarkably, once the dimer spectrum is formed at a molar pyridine excess of 75, the subsequent spectra at higher pyridine excesses remain similar (Figure 3.2C); at >10000 molar pyridine excess, the split Soret band gradually converts into a single, narrow band at 430 nm that is CD-silent (Figure 3.2D). This band is identical shape and position to a monomeric pyridine complex (Figure 3.1A). Apparently, the first transition (stacks $\rightarrow$ dimer complexes) is extremely sharp when compared to the second transition (dimer complexes $\rightarrow$ monomer complexes). The latter clearly reveals the considerable stability of the dimer complexes and their dissociation into monomer complexes is most likely related to the addition of a second pyridine ligand, which binds considerably weaker. This proposal is strengthened by the addition of similar quantities pyridine to free-base porphyrin S-FB in MCH, which does not affect its H-type aggregation indicating that the ability to form hydrogen bonds is preserved in the MCH/pyridine-mixture.
Figure 3.2. Pyridine titration to S-Zn at 2.0×10⁻⁵ M (RT) between 0 and 100 molar excess (transition from stacks to dimer complexes) in UV-vis (A) and CD (B) and between 100 and 80000 molar excess (transition from dimer- to monomer complexes) in UV-vis (C) and CD (D).

The first transition in the titration probed by UV-vis and CD spectroscopy suggests that axial ligation is responsible for depolymerization of the porphyrin stacks in a highly responsive fashion. Macroscopically, this is observed by the dissolution of S-Zn in MCH, which gets considerably facilitated in presence of pyridine. Yet in order to further investigate this coupled system, the titration experiment is repeated at a higher concentration that allows probing the depolymerization process with multiple analytical techniques. At a concentration of 3.3×10⁻⁴ M the porphyrin aggregates align in the magnetic field. However, upon the addition of pyridine the birefringence curve flattens indicating the lack of alignment, which is likely due to depolymerization (Figure 3.3A). At a molar excess of >30, no anisotropy of the refractive index is found at high magnetic field strengths. A similar sharp drop is observed for the solution viscosity; at a 30 excess of pyridine, the solution viscosity nearly equals the viscosity of pure MCH. Furthermore, the UV-vis and CD titration curves probed at 390 nm show exactly the same, non-sigmoidal trend (Figure 3.3B). Interestingly, a molar pyridine excess of 75 is necessary to depolymerize the stacks at 2.0×10⁻⁵ M, while at 3.3×10⁻⁴ M, only an excess of 30 is required (vide infra).
Figure 3.3. A: Pyridine titration curve at [S-Zn] = 3.3×10^{-4} M probed by magnetic field alignment. B: The first transition of the pyridine titration curve at [S-Zn] = 3.3×10^{-4} M probed by UV-vis/CD spectroscopy at 390 nm, magnetic field alignment-ability after determining the slope of the birefringence versus B^2 and the solution viscosity. C: IR-spectra of S-Zn in MCH without ('stacks') and with ('pyridine dimer complexes') pyridine at RT. D: Dynamic light scattering plot at a q-value of 0.00869 nm^{-1} for S-Zn at 6.6×10^{-5} M in presence of pyridine (inset: AFM phase image (1.1 × 1.1 μm) after dropcasting a solution of S-Zn at 2.0×10^{-5} M with a molar pyridine excess of 100).

After the first transition, the infrared spectrum of the depolymerized solution shows two vibrations in the carbonyl stretching region at 1646 cm^{-1} and 1680 cm^{-1} (Figure 3.3C), which is highly similar to S-Mn in MCH (Figure 2.9A). These two resonances indicate that one set of the carbonyls at lower wavenumbers is involved in intermolecular hydrogen bonding, while the other set at higher wavenumbers cannot participate due to steric blockage of the pyridine ligand. The lack of elongated objects in presence of pyridine probed by magnetic field alignment and viscosity is also confirmed by dynamic light scattering and atomic force microscopy (AFM) measurements. Relative to solutions of S-Zn without pyridine, low dynamic light scattering intensities are measured in presence of pyridine. The dynamic
measurements show two distinctive relaxations at high and low diffusivities indicative for a fast and a slow process, respectively (Figure 3.3D). The latter process observed is likely due to the presence of trace amounts of dust inside the sample; a diffusion coefficient of ~6×10⁻¹³ m²·s⁻¹ is fitted from the two-exponential decay. This diffusion constant is one order of magnitude lower than observed for S-Zn stacks at similar concentrations (~8×10⁻¹³ m²·s⁻¹, Chapter 2), which were also not evidenced by UV-vis measurements. The fast process at low q-values indicates the presence of small objects, which are likely pyridine-capped porphyrin dimers. A diffusion coefficient of 1.3×10⁻¹⁰ m²·s⁻¹ is fitted from the autocorrelation function. After dropcasting a 2.0×10⁻⁵ M S-Zn MCH solution with a 100 excess of pyridine, no fibrillar structures are observed in the Atomic Force Microscope (AFM) image (Figure 3.3D, inset), which corroborates the pyridine-induced depolymerization of porphyrin stacks.

3.4 Modeling the pyridine-induced depolymerization of the porphyrin stacks

The pyridine titration curves probed by different analytical techniques show an identical, sharp and non-sigmoidal transition from stacks to hydrogen-bonded, pyridine-capped dimers (Figure 3.3B). The shape of this transition is highly similar to the cooling curve of pure S-Zn (Figure 2.4C), which possesses a non-sigmoidal trend attributed to its cooperative self-assembly. Together with isosbesticity found in the pyridine titration curve (Figure 3.2A), it is likely that cooperative effects underlie the pyridine-induced depolymerization of the porphyrin stacks.⁷ In addition, a considerable difference in the critical amount of pyridine is found in order to fully depolymerize the stacks at different concentrations (vide supra); only a pyridine molar excess of 30 is necessary to depolymerize S-Zn stacks at 3.3×10⁻⁴ M, while approximately twice this excessive amount is required to depolymerize stacks at 2.0×10⁻⁵ M. In order to explain these observations, we closely investigate the “stack → dimer transition” by a UV-vis titration spanning the whole transition in detail. Now, a concentration of 1.2×10⁻⁵ M, the pyridine titration is repeated and the absorbance at 390 and 427 nm is probed, thereby monitoring the amount of stacks and dimer complexes, respectively (Figure 3.4A). The formation/disappearance of both species proceeds along the same cooperative trend; between a molar excess of 10 and 100 pyridine, the porphyrin assemblies fully interconvert from stacks into dimer complexes. In line with the previous titrations performed at higher concentrations, a higher pyridine excess of 100 is necessary to depolymerize stacks at 1.2×10⁻⁵ M. In order to interpret the shape of the titration curves observed, a thermodynamic modeling strategy is performed, in which a mechanism is proposed that describes the depolymerization of porphyrin stacks into dimer complexes. Subsequently, by fitting the pyridine titration curves using experimentally determined molar absorptivities and equilibrium constants for porphyrin aggregates and porphyrin-pyridine adducts, the proposed mechanism is systematically being ruled based on the quality of the fits obtained.¹¹
Based on the titration curves in Figure 3.4A, the best fits are obtained for a model that includes (1) cooperative self-assembly of S-Zn, (2) the formation of one-to-one adducts between S-Zn monomers and pyridine and (3) the dimerization of these adducts (Figure 3.4B).

**Figure 3.4.** A: Pyridine titration curves probed at the aggregate band (390 nm) and complexed dimer band (427) performed at [S-Zn] = 1.2×10⁻⁵ M at RT. B: Thermodynamic model in which aggregates, monomers, monomer complexes and dimer complexes are connected by equilibrium constants.

Albeit the thermodynamic model does not provide any mechanistic insights into the depolymerization process, it seems that these four species are necessary in order to explain this process. Considering the extremely low free-monomer concentration expected for this system (~7×10⁻⁸ M, see Section 2.3), it is remarkable that monomers figure into the equilibrium at all. However, a statistic argument can be derived from the thermodynamic analysis of the cooperative self-assembly of S-Zn. Here, the “number concentration” of aggregate end-groups is significantly lower than the concentration of monomers; 92% of the porphyrin faces is provided by monomers at 10⁻⁵ M (Figure 2.5B). A chemical argument for the monomer assistance in the depolymerization relates to the affinity difference of the axial ligand towards metal ions inside porphyrin monomers and aggregates. Here, enhanced π-π interactions present in aggregates reduce the Lewis acidity of the zinc-ion.¹³

With absorbance data as output of the model, simultaneous nonlinear curve-fitting is performed on the pyridine titration data of the aggregate and the pyridine-complexed dimer
Two-component Zn-porphyrin self-assembly with pyridine

at 390 and 427 nm, respectively (Figure 3.4A). In the full model, the absorbance at a given wavelength is determined by twelve parameters; four equilibrium constants ($K_d$, $K_c$, $K_e$ and $K_a$) and four extinction coefficients ($E_{stack}$, $E_{monomer}$, $E_{monomer-complex}$ and $E_{dimer-complex}$), both at 390 and 427 nm. To avoid the necessity to fit all parameters from one dataset, most of the parameters are determined from separate experiments. The equilibrium constants describing the cooperative self-assembly of S-Zn ($K_c$ and $K$) are derived from fitting the cooling curve of S-Zn at 1.0×10⁻⁶ M with the temperature-dependent nucleation-elongation model and the subsequent transformation of $K_d$ and $h_e$ to concentration-dependent $K_c$ and $K$ (see Section 2.3). The binding constant of pyridine to the porphyrin monomer $K_e$ is taken from the binding of pyridine with S-Zn-Me (Figure 3.1). These two processes also provided the extinction coefficients for the stack, monomer and monomer complex, thus the only parameters left for fitting are the dimerization constant ($K_d$) and the extinction coefficient of the pyridine-complexed dimer. After fitting the pyridine titration data of S-Zn at 1.2×10⁻⁵ M at 390 and 427 nm (Figure 3.4A), a dimerization constant of $K_d = 1.1×10^9\text{M}^{-1}$ is obtained, which approximates the value for the elongation constant ($K$). Considering these binding strengths, the outcome of the fit reveals that that both hydrogen bonded states (stacks and dimers) are the most abundant species in solution, which is evidenced by the isosbestic point in the titration experiment.

3.5 Dilution-induced self-assembly

Having determined all parameters for the depolymerization model, simulations allow for predictions how the system responds to thermodynamic changes, e.g. changes in porphyrin or pyridine concentration. In addition, the model can be easily adapted by changing binding constants or even the degree of cooperativity ($\sigma$). These alterations drastically affect the distribution of the porphyrins over the four different states, which is easily visualized in a phase diagram. By simulating the porphyrin distribution over stacks, monomers, pyridine monomer- and dimer-complexes at each possible concentration of porphyrin and pyridine, the phase diagram reveals the locations of the transitions when pyridine is added to the system or when the porphyrin concentration is raised (Figure 3.5A). The first transition of the pyridine titration becomes sharper when the porphyrin concentration is increased (Figure 3.5B); consequently, the coexistence line between stacks and dimers shows that the critical pyridine excess necessary to fully depolymerize porphyrin stacks drops (Figure 3.5B, inset). Furthermore, lines with a slope of 1 can be drawn inside the phase diagram that represent the dilution (or concentration) of the system at a fixed pyridine to porphyrin ratio. Remarkably, within a specific concentration regime such a line reveals a transition from dimers to aggregates when the system gets diluted. At a fixed pyridine to porphyrin ratio of 40, a strong effect on the distribution of S-Zn over the four components is observed when the total concentration is changed (Figure 3.5C). At high concentrations (C > 1.8×10⁻⁵ M), dimer
complexes are the most abundant species in solution together with a small fraction of monomer complexes. Upon dilution of the system from 1.8×10⁻⁵ M onwards, the fraction of complexed monomers remains constant, while the amount of complexed dimers reduces in favor of the formation of aggregates. This dilution-induced self-assembly remains operative until a concentration of 1.2×10⁻⁶ M, at which both hydrogen bonded states (stacks and dimer complexes) are no longer the most stable species. Further dilution leads to the breakage of hydrogen bonds inside the aggregates until a concentration of 6.9×10⁻⁸ M at which hydrogen bonds are no longer stabilized. In this concentration domain, the fraction of free monomers increases and at concentrations lower than 6.9×10⁻⁸ M, S-Zn monomers not interact with themselves while their affinity towards pyridine gradually drops.

**Figure 3.5.** A: Phase diagram constructed from the depolymerization model (Kₑ = 685 M⁻¹, K = 1.37×10⁷ M⁻¹, Kₚ = 5.1×10⁴ M⁻¹, Kₛ = 1.1×10⁶ M⁻¹, the dotted lines guide the eye to indicate the phase boundaries). B: Model simulation taken from the phase diagram describing the pyridine-induced “stack → dimer transition” at different porphyrin concentrations (inset: critical pyridine excess necessary to depolymerize all stacks (θ = 0) versus the porphyrin concentration). C: Model simulation taken from the phase diagram at a fixed pyridine to porphyrin ratio of 40 showing the distribution of the porphyrins over the four species as a function of total concentration. D: Dilution-induced self-assembly of S-Zn at a fixed pyridine excess of 40 probed over three orders of magnitude in concentration at RT.
The simulation clearly reveals that within the concentration domain of $1.8 \times 10^{-5}$ and $1.2 \times 10^{-6}$ M, the depolymerized state becomes unfavorable while aggregation is enhanced by adding solvent to the system. In order to verify this re-entrant phase transition, a dilution experiments is performed at a fixed pyridine-to-porphyrin ratio of 40. At a concentration of $2.3 \times 10^{-4}$ M (with $9.2 \times 10^{-3}$ M pyridine), the split Soret band at 427 nm has fully developed and after the 10-fold dilution, its intensity is lowered while the aggregate Soret band becomes gradually visible at 390 nm (Figure 3.5D). At this concentration ($2.3 \times 10^{-5}$ M S-Zn with $9.2 \times 10^{-4}$ M pyridine), the onset of the dimer-stacks transition is reached (Figure 3.5C), hence the subsequent addition of solvent leads to a strong response in stack/dimer distribution. Indeed, another 10-fold dilution to a concentration of $2.3 \times 10^{-6}$ M S-Zn (with $9.2 \times 10^{-5}$ M pyridine) leads to a drastic change in molar distribution, in which the porphyrin stacks are the most abundant species (> 80%). Noteworthy, the spectra in Figure 3.5D are stable several hours after the addition of MCH, indicating that the time-scale related to the dilution-induced self-assembly process is extremely slow (vide infra). As predicted by the simulation, the dilution-induced self-assembly process causes an almost full transition from the dimer complex state to the aggregated state over two orders of magnitude in system concentration. Within this concentration window ($2.3 \times 10^{-4}$ - $2.3 \times 10^{-6}$ M), the hydrogen bonds remain sufficiently stable as evidenced by the isosbestic point in the dilution experiment (Figure 3.5D).

The simulation and its experimental validation point out the design rules in order to achieve a strong response upon dilution. Firstly, dilution should start from a high porphyrin concentration that allows for a wide concentration window in which hydrogen bonds remain stable; hence a considerable amount of solvent can be added to the system, thereby “enforcing the stimulus”. Furthermore it is favorable that at high concentrations a smaller pyridine excess is necessary in order to fully depolymerize stacks since transition is becomes sharper (vide supra). Secondly, the dilution process should start right at the onset of the sharp transition, which represents the critical amount of pyridine (Figure 3.5B, inset). Considering the enhanced solubility of dimer complexes relative to porphyrin stacks, a full transition between dimers and stacks is envisioned upon dilution. In the next chapter, we utilize these design constraints for a photo-responsive ligand.

### 3.6 Microfluidic separation of porphyrin stacks and dimer complexes

As shown by the phase diagram, the distribution over the four different species strongly depends on the concentration porphyrin, pyridine and the total concentration of the system. At high porphyrin concentrations, the system is ruled by the abundance of stacks and dimers that interconvert into each other upon the addition of pyridine or dilution. Considering the size difference between stacks and dimers and their slow interconversion observed in the dilution-induced self-assembly process (vide supra), it is highly interesting to explore the
possibility to control their distribution by supramolecular separation. Similar experiments have been performed by gel permeation chromatography (GPC) to estimate the size of supramolecular aggregates and to purify discrete assemblies from supramolecular monomers.\textsuperscript{3,4} The success of those experiments relied on reduced supramolecular dynamics that preclude the re-establishment of thermodynamic equilibrium in the timescale of the measurement.\textsuperscript{15} Furthermore, the apparent\textsuperscript{16} cooperativity ascribed to the discrete nature of these assemblies significantly enhanced their stability when diluted on the GPC column. In order to properly swell gel particles for size exclusion, the required solvent polarity does not comply with the formation of hydrogen bonds. In this section, a diffusion-based separation process in a microfluidic H-cell is explored, in which the stack-dimer distribution is controlled by means of diffusive mass transfer.

\textit{3.6.1 Microfluidic setup}

A microfluidic H-cell was first introduced by Yager and coworkers as a new tool to separate small molecules from cells.\textsuperscript{17a} This H-shaped devise was further developed as a new immunoassay to detect molecules at nanomolar concentrations in blood.\textsuperscript{17b} The H-cell consists of two inlets that allow two fluids to be pumped alongside each other in a laminar fashion, after which the fluids are separated and exit via two outlets. The two flows are in contact for a well-defined time determined by the applied flow rate and the reactor volume. If one of the two streams contains an analyte, a concentration gradient over the liquid-liquid interface drives its mass transfer. Considering the confinement of fluids in microchannels, viscous forces prevail relative to inertial forces, which results in a laminar flow characterized by low Reynolds numbers.\textsuperscript{18} In the laminar flow regime, mass transfer only occurs by diffusion, which allows the determination of diffusion constants in this setup. In the experimental setup developed for porphyrin system, an equi-volumetric flow rate of MCH is maintained over both the inlets and outlets, by using well-calibrated syringe pumps and flow regulators, respectively (Figure 3.6A). As a result, the contact time of the laminar interface between both flows equals the diffusion time (\(t_{\text{diffusion}}\)), which is determined by the applied flow rate. At the exit, in-line UV-vis detection provides quantitative and qualitative analysis of the diffused species. By combining these features, the H-cell is used as a tool to estimate diffusion coefficients of porphyrin stacks and pyridine-complexed dimers. Furthermore, a mixture of stacks and dimers is separated in the H-cell, thereby creating a controlled out-of-equilibrium situation.
Figure 3.6. A: Schematic representation of the microfluidic H-cell, in which two 110 µm channels with a depth of 50 µm merge and split (FM = flow meter, FR = flow regulator; flow regulator is placed in the residual stream and in-line UV-vis measurements are performed in the extraction stream. B: In-line UV-vis spectra of S-Zn-Me (injected at 2.0×10^{-5} M) acquired at different flow rates in the extraction stream. C: Diffusion profiles for S-Zn-Me, S-Zn stacks and S-Zn:pyridine (1:1) dimers at λ_{max} ~ 420, 390 and 427 nm, respectively, with the corresponding fits and simulation at D_{DOSY} = 2.2×10^{-10} m^2 s^{-1} (Normalized diffusion = C_{diff} / 1.0×10^{-5} M). D: In-line UV-vis spectra of S-Zn stacks (injected at 2.0×10^{-5} M) acquired at different flow rates in the extraction stream. E: In-line UV-vis spectra of S-Zn dimers (injected at 2.0×10^{-5} M with a molar pyridine excess of 250) acquired at different flow rates in the extraction stream.

3.6.2 Estimation of diffusion coefficients

In order to validate the experimental setup, a diffusion experiment is performed on S-Zn-Me, which does not form stacks in MCH. At a concentration of 2.0×10^{-5} M in MCH, S-Zn-Me
is eluted against pure MCH at flow rates between 0.50 and 0.05 µL·s⁻¹ (0.35 < τ_{diffusion} < 3.52 s, respectively) and the steady-state UV-vis spectra are recorded with a photo diode array (PDA) in the extraction stream (Figure 3.6B). After calibration of the PDA between 0 and 1.0×10⁻⁵ M, the absorbance at λ_{max} ~ 420 nm is normalized to the spectrum of **S-Zn-Me** at 1.0×10⁻⁵ M (concentration at infinite diffusion time τ_{inf}) and subsequently plotted against the diffusion time (Figure 3.6C). The obtained diffusion profile is subsequently fitted to a one-dimension-unsteady-state diffusion model from which a diffusion coefficient of 3.2×10⁻¹⁰ m²·s⁻¹ is estimated, which closely resembles the value obtained in the diffusion ordered spectroscopy (DOSY) experiment of **S-Zn-Me** in D14-MCH (2.2×10⁻¹⁰ m²·s⁻¹, Figure 2.3B).

After validation of the experimental setup, identical diffusion studies on pure stacks and pure dimers of **S-Zn** are performed at 2.0×10⁻⁵ M. Similarly as performed for **S-Zn-Me**, a solution of **S-Zn** is eluted against MCH at different flow rates and the steady-state PDA spectra qualitatively show that only a small amount of material has diffused over (Figure 3.6D). Furthermore, next to the aggregate Soret band at 390 nm, the _in-line_ spectra reveal an absorbance at 420 nm, which indicates the presence of monomers. Perhaps, this is related to the enhanced diffusion of monomers relative to stacks or the dilution-induced disassembly of stacks when diffused into the extraction stream. From the normalized optical densities at λ_{max} ~ 390 nm and the corresponding diffusion times, a diffusion coefficient of 7.8×10⁻¹² m²·s⁻¹ is fitted from the diffusion profile. This value corresponds to the translational diffusion coefficient determined from dynamic light scattering measurements, which was estimated at ~8×10⁻¹² m²·s⁻¹ (see Section 2.3). While a pyridine excess of 75 is necessary to depolymerize the stacks into pyridine-capped dimers (_vid. supra_), the determination of the diffusion constant of dimers is performed at a pyridine excess of 250; this composition is remotely located from the transition in order to avoid dilution-induced self-assembly. The PDA spectra of the dimers show the enhanced mass transfer relative to **S-Zn** stacks (Figure 3.6E). After construction of the diffusion profile based on the absorbance at 427 nm, it can be observed that the profile approaches the curve of **S-Zn-Me** while it is highly distinctive relative to **S-Zn** without pyridine. A diffusion coefficient of 2.7×10⁻¹⁰ m²·s⁻¹ is fitted from the diffusion profile, while a value of 1.3×10⁻¹⁰ m²·s⁻¹ is fitted from the autocorrelation function in dynamic light scattering (Figure 3.3D).

### 3.6.3 Microfluidic separation of dimers and stacks

Despite the fact that the porphyrins are held together solely by supramolecular interactions, the different diffusion behavior of stacks and dimers is obviously related to their aggregate size. As a next step herein, the microfluidic setup is exploited to separate a mixture of the two at a concentration of 2.0×10⁻⁵ M. At a pyridine excess of 40, the molar distribution of **S-Zn** monomers over stacks and dimers is 31/69 at thermodynamic
equilibrium, as determined from the Soret band intensity ratio of 0.54 at 390 and 427 nm, respectively (Figure 3.2A). This initial mixture is eluted against MCH at a flow rate of 0.10 \( \mu \text{L}\cdot\text{s}^{-1} \) (\( \tau_{\text{diffusion}} = 1.76 \) s) and the steady state in-line PDA spectra are acquired of both the extraction and residual stream (Figure 3.7A). Compared to the initial mixture, the latter spectrum shows a drop in dimer absorbance, while the stack absorbance remains similar. As a result, the stack/dimer-ratio increases to 36/64, whereas the extraction stream reveals that predominantly dimers have diffused over; a stack/dimer-ratio of 16/84 is estimated from the spectrum.

**Figure 3.6.** In-line (A) and off-line (B) UV-vis spectra of S-Zn at 2.0\( \times \)10^{-5} M with 8\( \times \)10^{-4} M pyridine of the initial solution (‘IN’), Residual- and Extraction stream recorded at \( \tau_{\text{det}} \sim 20 \) s and \( \sim 3 \) h after separation, respectively. C: Kinetic profile of the dilution-induced self-assembly upon 2-fold dilution of the initial solution probed by CD (left axis at 390 nm) and UV-vis (right axis at 390 and 427 nm).

Based on their different mass transport, in-line UV-vis detection reveals that the bimodal distribution between stacks and dimers can be moderately controlled by this microfluidic technique. However, the diffusion process comprehends more components that are involved in the system; free pyridine and (pyridine-complexed) monomers also diffuse over at
relatively high rates, thereby pushing the system out-of-equilibrium. In order to obtain more insights into the dynamics for re-establishment of the thermodynamic equilibrium, the in-line UV-vis spectra are compared with the spectra acquired after sample collection. Considering the volume of the PDA flow cell including its tubing to the exit of the H-cell (~2 μL), a detection time of ~20 s is estimated at a flow rate of 0.10 μL·s⁻¹. On the other hand, the time required to obtain ~1 mL solution for UV-vis characterization is ~3 h. Directly after separation, the in-line spectra seem to reveal the sole diffusion process of dimers to the other stream. However after sample collection, highly distinctive spectra are observed that cannot be explained by mass transport only (Figure 3.6B). Compared to the in-line spectra, both the residual and extraction stream show an increased stack/dimer-ratio of 58/42 and 47/53, respectively. Since the separation is performed on a sample that is halfway the sharp transition from stacks to dimers, the system is extremely responsive in the dilution-induced self-assembly process, which explains the increased stack/dimer ratio in both streams. In the residual stream, the significant enhancement of stack formation is mainly due to the diffusion of pyridine and pyridine-complexed monomers that source dimerization. Despite the pyridine enrichment in the extraction stream, the modest enhancement of stacks can be explained by the dilution-induced self-assembly effect, which operates strongly at high dilutions.

Both short and long timescale analyses can be rationalized on a basis of mass transport and thermodynamic equilibria. In order to investigate how the supramolecular dynamics span these distinctive timescales, a 2-fold dilution experiment on the initial mixture is performed. This experiment moderately resembles the microfluidic separation; both represent a 2-fold dilution process albeit the microfluidic dilution is not conducted in a homogeneous fashion compared to the regular dilution experiment. In this kinetic measurement, the dilution-induced self-assembly leads to the formation of stacks, which can exclusively be probed by CD spectroscopy at 390 nm while the stack/dimer-ratio can be probed by UV-vis at 390 and 427 nm. Directly after injecting an equi-volumetric amount of MCH to the initial mixture, the kinetic profiles clearly reveal the redistribution over stacks and dimers; approximately 4 hours after dilution the new thermodynamically stable state is reached (Figure 3.6C). This comparison shows that the supramolecular dynamics for re-establishing thermodynamic equilibrium is relatively slow. The out-of-equilibrium state probed in-line gradually reached thermodynamic equilibrium while collecting the off-line samples of the extraction and residual streams. Therefore, with reference to detection, this difference clearly indicates the relevance of probing when the thermodynamic state is rapidly changed, especially in multi-component systems.¹⁹ For another supramolecular process, this feature has also been recognized in the 1:1 complexation of Zn-porphyrin and pyridine in a microfluidic mixer.²¹
3.7 Conclusion

The hydrogen bond-assisted and cooperative self-assembly of S-Zn was studied in the presence of pyridine, which competes in the hydrogen bonding process by its complexation with zinc(II)-ions inside the porphyrin. Upon the addition of pyridine, porphyrin H-type aggregates depolymerize upon the formation of pyridine-capped, hydrogen-bonded porphyrin dimers as evidenced by multiple analytical techniques. As a result of cooperativity, the depolymerization is driven via free monomers, while a bimodal distribution between stacks and dimers is featured by a sharp, non-sigmoidal transition. A proposed depolymerization mechanism was validated by fitting spectroscopy data to the corresponding thermodynamic model. After implementation of the thermodynamic parameters obtained from different experiments, the behavior of this coupled system could be fully simulated. Within a specified concentration window of porphyrin and pyridine, model predictions revealed that the addition of solvent would lead to a transition from dimer-complexes to H-type aggregates. Dilution experiments revealed this dilution-induced self-assembly, which is unusual for supramolecular polymers, yet it arises in a multi-component system featuring coupled equilibria.

Slow kinetics was deduced for the aggregate interconversion from dimer complexes to stacks upon dilution. This meta-stability was used to control the bimodal distribution of porphyrin stacks and dimer complexes by a non-thermodynamic pathway based on microfluidic separation. In a newly developed approach, diffusive mass transport in a microfluidic H-cell allowed for the estimation of the diffusion constants coefficients of stacks and dimers, which were validated by dynamic light scattering measurements. In the middle of the transition between stacks and dimer complexes, a mixture of these bimodally distributed species was separated. Directly probing after the separation process in line showed a considerably different distribution between stacks and dimers than probing of the collected samples, which was attributed to the slow supramolecular dynamics of the dilution-induced self-assembly process. These studies revealed that this microfluidic technique is highly appropriate to estimate aggregate sizes and to prepare meta-stable intermediates in a controlled fashion.

3.8 Experimental

Materials and methods
The porphyrin aggregates were prepared in the same way as described in the experimental section of Chapter 2. Pyridine titrations were performed by adding a large excess of pyridine using a microsyringe to a porphyrin solution at a known concentration in MCH of spectroscopic grade. This solution was subsequently added to a porphyrin solution at the same concentration. The samples for the titration were aged overnight prior to their measurements under thermodynamic equilibrium.
Chapter 3

Instrumentation

Circular dichroism (CD), ultraviolet-visible (UV-vis), infrared (IR), atomic force microscopy (AFM), viscosity, magnetic field alignment and dynamic light scattering measurements were performed in the same way as described in the experimental section of Chapter 2.

The AFM measurement was performed by dr. Philippe Leclère using a Veeco Multimode and Dimension Icon (with a Nanoscope V control unit).

For the microfluidic setup, stainless steel syringes (KDS, 2.5 ml with 1/16” Swagelok) were placed on a syringe pump (neMESYS starter and double module, 14.1 gearing). Via a 3-way HPLC switching valve (Rheodyne 7030), both stainless steel syringes were filled by 5 mL glass syringes (Fortuna optima with Luer lock) in one position and connected to the microfluidic chip in the other position. Via fused silica tubing (Upchurch Scientific, 360 µm OD / 150 µm ID), the valve and microfluidic chip holder (Mictronit LOAC 4515-FS) were connected using NanoPort assemblies (Upchurch Scientific, flat bottom assembly F123-H with N-123-03). The microfluidic H-cell (Mictronit B.V.) was custom made out of borosilicate glass by wet-etching techniques (50 µm deep channels, 110 µm in/outlet diameter, 220 µm diameter × 32 mm length reaction zone with 6° merging angle). At the outlet, the extraction-side was connected via a Nanoport assembly to a photo diode array (PDA) UV-vis detector (Shimadzu SPD-M20A with Semi-micro optical flow cell) and subsequently connected to a mass flow meter (Bronkhorst High-Tech B.V., µ-FLOW L01 series (L01-RZ*D-99-K-80S) with 10/32 UNF female connections) with fittights (Upchurch Scientific, F120). The residual-side was connected via a Nanoport assembly to a mass flow meter with controller (Bronkhorst High-Tech B.V., µ-FLOW L01 series (L01V02-RZ*D-99-K-80S) with 10/32 UNF female connections). After the flow meter/regulator instruments, standard Teflon HPLC tubing (Upchurch Scientific, 1/16” OD / 200 µm ID) was used to fill-up sample vials in a gas-tight configuration. The microfluidic cell holder was placed under an optical microscope in order to detect dust at the end of the reactor zone. The syringe pump, PDA and flow meter/regulators were controlled by their commercial software on a PC. The calibration of the syringe pumps, mass flow meters and the PDA is described elsewhere.21

Thermodynamic modeling

A multiple equilibrium modeling study was performed by Marko Nieuwenhuizen using MATLAB® (R2010a, version 7.10.0.499, win 32). In the model, five different species were considered: free porphyrin monomers [A], porphyrin stacks [Agg], pyridine ligands [B], porphyrin-pyridine 1:1 monomer complexes [AB] and porphyrin-pyridine 2:2 dimer complexes [(AB)2]. The total concentration of porphyrin [A0] and pyridine [B0] were described according to Equations 3.1 and 3.2.

\[
[A] = [A] + [Agg] + [AB] + 2 \cdot ([AB]_2) 
\]  

\[
[B] = [B] + [AB] + 2 \cdot ([AB]_2) 
\]  

The K≥K model (Equation 3.3) was applied to express the cooperative polymerization of porphyrin stacks. Herein, σ represents the degree of cooperativity (K≥ / K) with dimerization constant (K) and elongation constant (K).

\[
[Agg] = \sum_{i=1}^{i} \sigma K^{-1} (K[A])^i 
\]  

Equations 3.1-3.3, including the equilibrium constants for complexation (K≤) and dimerization of porphyrin-pyridine adducts (K≥) give Equations 3.4-3.7.
Two-component Zn-porphyrin self-assembly with pyridine

\[ F(1) = [1 + \alpha + \beta(1 + 2K_b\beta[A])] - [A_0] = 0 \]  
(3.4)

\[ F(2) = [B] + \beta\alpha[A](1 + 2K_b\beta[A]) - [B_0] = 0 \]  
(3.5)

\[ \alpha = \sigma \{ (1 - K[A])^2 - 1 \} \]  
(3.6)

\[ \beta = K_c [B] \]  
(3.7)

**Diffusion studies**

For the diffusion studies, 2.0×10^{-5} M porphyrin solutions (S-Zn-Me and S-Zn stacks and dimers) were pumped to one entrance of the H-cell and at equi-volumetric flow rates MCH was pumped to the other entrance. Because of the hydrodynamic resistance caused by the PDA in the extraction stream and viscosity difference between both streams, a non-symmetrical split at the exit of the H-cell was observed. In order to achieve a symmetrical split at the outlets, the flow meter in the residual stream (at lower flow resistance) was equipped with a proportional-integral-derivative (PID) controlled valve. With its tunable orifice, the valve automatically regulated the pressure drop in order to achieve an equi-volumetric outflow relative to the flow meter in the extraction stream. This PID-type of control caused fluctuations, which disappeared to an acceptable level after approximately 5 minutes. Soon after reaching this steady-state condition, constant UV–vis signals were recorded by the PDA detector, which were subsequently used to determine the amount of diffused material.

Quantification was performed by correlating the recorded spectrum to the calibration curve at \( \lambda_{\text{max}} \). The corresponding concentration (C_{eq}) was divided by 1.0×10^{-5} M, which is the concentration of the fully mixed system at infinitely long diffusion time. This normalized value was plotted against the diffusion time (t_{\text{diffusion}}), and the obtained diffusion profile was fitted with a 1-dimensional unsteady-state diffusion model (Equation 3.8). After solving the Fourier series, the expansion was used to fit the diffusion profile with fitting parameters \( C_{in} = 2.0\times10^{-5} \) M, \( t_{\text{diffusion}} = V_{\text{reactor}} / \text{flow rate} \), L = 110 \mu m and D = diffusion coefficient [m^2 s^{-1}].

\[
\frac{dC}{dz} = D \cdot \frac{d^2 C}{dz^2} = 2 \cdot \frac{C_{\text{diffusion}}}{C_{\text{in}}} = 2 \cdot \left( \sum_{n=0}^{\infty} \frac{1}{2} - \frac{\exp \left( -\left( n + \frac{1}{2} \right)^2 \cdot \frac{t_{\text{diffusion}} \cdot D \cdot \pi^2}{L^2} \right)}{\left( n + \frac{1}{2} \right)^2 \cdot \pi^2} \right)
\]  
(3.8)

### 3.9 References


9. As evidenced by the temperature-dependent self-assembly of S-Zn (Figure 2.4A) and its pyridine titration at RT (Figure 3.2A), the shape and $\chi_{\text{max}}$ of the aggregate Soret band does not change once the aggregate is formed. Despite the aggregate size changes upon the addition of pyridine, the molar absorptivity spectrum remains the same.


76
4

**Photo-regulation of the Zn-porphyrin self-assembly in a two-component system**

**Abstract.** The self-assembly of chiral Zn-porphyrins was studied in the presence of a newly developed phenylazopyridine ligand in order to photo-regulate the supramolecular (de)polymerization. A library was prepared containing different phenylazopyridine ligands with different side-groups having specific steric and electronic properties regarding their photo-induced complexation with Zn-porphyrins. One ligand was selected for elaborate studies. In the absence of porphyrin, the photoisomerization properties were investigated by UV-vis and $^1$H-NMR measurements. Subsequently, the complexation properties were investigated in absence of hydrogen bonding by UV-vis titrations with a Zn-porphyrin monomer model compound. The photostationary states and binding constants for both isomeric forms were introduced in a modified thermodynamic model that was used to assess by simulations which experimental parameters significantly influenced the photo-switchability of the supramolecular (de)polymerization. With the obtained set of thermodynamic parameters, the optimized conditions were deduced by simulations in order to photo-regulate the cooperative self-assembly of chiral Zn-porphyrins. The simulations were verified by photo-switching experiments that revealed a reversible photo-induced (de)polymerization of the porphyrin stacks between 1 and 81%. Spectroscopy measurements were corroborated with a change in solution viscosity.
4.1 Introduction

One of the challenging goals for supramolecular chemists is the control of molecular self-assembly under ambient conditions by external inputs such as electricity, pH, redox potential and light.\(^1\) Control over self-assembly by using light as a stimulus is advantageous, because photochemical reactions occur rapidly allowing for a fast response. Furthermore, this mild energy source is readily available and it can be accurately applied to isolated systems in terms of radiation frequency and intensity. These properties have already been fully exploited on photochromic dyes and molecular switches, such as azo-benzenes that show unique isomerization properties upon their photo-irradiation. This conformational change at the molecular level resulted in numerous interesting phenomena, such as macroscopic movement,\(^2\) sol-gel transitions,\(^3\) shuttling of cyclodextrins over rotaxanes,\(^4\) and self-erasable molecular inks.\(^5\) In the field of self-assembly, the conformational difference between \textit{cis}- and \textit{trans}-azo moieties also resulted in different hydrogen bonding topologies; sufficiently for the formation of discrete rosette structures,\(^6\) non-discrete hydrogen-bonding networks\(^7\) and host-guest-type of assemblies.\(^8\) In the latter, A similar approach, based on photo-switching between a supramolecular polymer and a dimer was performed by Harada and co-workers who employed the host-guest properties of a stilbene-bridged bis(\(\beta\)-cyclodextrine) and a hydrophobic, ditopic adamantyl guest in water. Similar to azo-benzene moieties, diarylethene derivatives undergo a conformational change upon their photo-induced cyclization. This resulted in the enantiospecific self-assembly of diarylethene building blocks\(^9\) and the formation of elongated hydrogen bonded structures\(^10\) due to the different binding affinity for complementary hydrogen bonding.\(^11\) Unlike non-reversible photo-triggers for self-assembly,\(^12\) these molecular switches are highly reversible without fatiguiness, which makes them interesting candidates for other dynamic processes such as complexation reactions.

The complexation of metallo-porphyrins with axial ligands is an intriguing strategy to change the optoelectronic properties of these chromophores. Inoue and co-workers studied the photo-induced complexation of stilbazole moieties with different metallo-porphyrins using absorbance spectroscopy.\(^13\) Recently, photoswitchable ligands based on azo-benzenes have successfully been employed to photo-regulate the energy transfer from the Zn-porphyrin donor to a 3-phenylazopyridine acceptor.\(^14\) Upon the \textit{cis} \(\rightarrow\) \textit{trans} isomerization of the axial ligand, its binding constant decreases due to the reduced steric hindrance between the ligand and the porphyrin face, thereby complexing the Zn-porphyrin monomer causing quenching of the fluorescence. The same photo-regulation process was investigated by the group of Herges, in which complexation of a photochromic ligand caused a change of coordination number and consequently the spin state of nickel ions inside porphyrin monomers.\(^15\)
Considering the applicability of molecular switches in self-assembly and axial ligation of porphyrin monomers, we would like to explore the combination of these processes. In the previous chapter, we described the pyridine-induced depolymerization of porphyrin aggregates into dimer complexes and the dilution-induced self-assembly, which were successfully modeled and experimentally verified. By means of photo-control of a phenylazopyridine ligand, we present in this chapter its capability to control the self-assembly of the main component. In this chapter, a library of phenylazopyridines is developed for the purpose to switch on/off the cooperative self-assembly of chiral Zn-porphyrin S-Zn. In the development, a special focus is maintained on the steric and electronic interactions of the ligand regarding its complexation of an N-methylated Zn-porphyrin monomer model compound (S-Zn-Me). Reference experiments with S-Zn-Me are conducted and their thermodynamic parameters are introduced in a modified thermodynamic model described in Chapter 3. Model simulations are performed and the photo-switch-ability of the system is experimentally verified. It should be noted that most of the experimental work described in this chapter is performed by Dr. Takashi Hirose.

4.2 Design of the system

As described in Chapter 3, the addition of an axial ligand leads to steric blockage of one porphyrin face to form hydrogen bonds. Since the ability remains to form hydrogen bonds on the other face, pyridine-capped hydrogen-bonded porphyrin dimers are formed. In the present design, 3-phenylazopyridine derivatives are utilized to span the sharp transition between porphyrin H-type aggregates and dimer complexes. Especially at high porphyrin concentrations, this transition is characterized by a relatively small pyridine-window, hence the photo-induced alternation of the binding constant could affect degree of polymerization of the H-type aggregates. When the ligand is isomerized from the trans-form into the cis-form, the coordinated state with the porphyrin metal center becomes unstable due to steric hindrance of the bulky groups attached on the azo-group (this process is represented in Figure 1.14B). The dissociation of the metal-ligand bond results in the release of porphyrin monomers, which can subsequently stack in H-type aggregates. Vice-versa, when the ligand is isomerized from the cis-form into the trans-form, the coordinated state becomes sterically allowed, which leads to depolymerization of the stacks upon the formation of dimer complexes. The switching is performed in a closed system; hence the switch-ability of the system solely depends on the difference in binding constant of the cis- and trans-isomers and their photostationary states. These two parameters determine the window-width of the “pyridine-stimulus”, which strongly determines its effect on the difference in the fraction of aggregated porphyrins. As schematically depicted in Figure 4.1, cooperativity strongly influences the responsivity of the system when the window is relatively small.
Figure 4.1. Schematic representation of the window set by the difference in binding constant and photostationary state and its effect on the degree of polymerization for an isodesmic- (σ = 1) and a cooperative system (σ = 5×10⁻⁵).

4.3 Synthesis, characterization and complexation of phenylazopyridines

The most important constraints regarding the molecular design of the phenylazopyridine are related to the binding and switching of the axial ligand, which have been fully investigated by the group of Otsuki.¹³ Electron donation at the para-position of the pyridine moiety strongly enhances its Lewis basicity, hence its binding towards Zn-porphyrins is stronger. Furthermore, bulky substituents onto the azo-bonds enhance steric interactions leading to an improved switch-ability. A phenylazopyridine derivative is employed, which has a phenyl group on the 4-position and a phenyl-azo moiety on the 3-position of pyridine. The electronic and steric effects are systematically investigated by different substituents onto the para-phenyl ring and phenyl-azo ring, respectively. A corresponding library has been synthesized, in which the azo-bond is formed by the coupling of an aniline moiety to a nitroso counterpart, which is prepared from its corresponding aniline (Scheme 4.1). This strategy allows for library with members having an increased bulkiness onto the phenyl-azo moiety (AZO-1/2/3) and members having an increased electron donation capability onto the pyridine-nitrogen (AZO-5/6/7). The synthesis of AZO-1-7 will be published elsewhere.¹⁶ AZO-4 is used in the photo-regulation of the self-assembly of S-Zn (vide infra).
Photo-regulation of the Zn-porphyrin self-assembly in a two-component system

![Reaction Scheme](image)

Scheme 4.1. Phenylazopyridine library of ligands with increasing bulkiness (AZO-1 through AZO-3) and with increasing electron donation on the pyridine nitrogen (AZO-5 through AZO-7). AZO-4 is used in the photo-regulation of the self-assembly of S-Zn.16

For all phenylazopyridines, the trans-isomer is most stable, which is directly obtained after dissolution of the compound or by heating. Upon irradiation with ultraviolet light, isomerization occurs until the photostationary state (PSS\textsubscript{cis}) is obtained, which represents the molar fraction of cis-isomers in solution that is determined by a combination study of UV-vis and 1H-NMR spectroscopy (see Section 4.3.2). Upon irradiation with visible light, the isomerization process is reversed until PSS\textsubscript{trans} is obtained; which represents the molar ratio of trans-isomers. Photo-induced isomerization does usually not result in a 100% switching capacity, which is attributed to spectral overlap of cis- and trans-isomers and a restriction when the ligand is bound to the porphyrin. The performance of the ligand not only depends on the conversion ratio (molar ratio of cis/trans isomers), but also on the difference in binding strength between the cis- and trans-isomer (K\textsubscript{c,cis} and K\textsubscript{c,trans}), which is determined by UV-vis titration of trans-isomers and subsequent photo-induced isomerization, respectively (see Section 4.4). Besides the switch-ability, the thermal stability of the higher-energy cis-state is important, which depends on the Gibbs energy of activation (ΔG\textsuperscript{f}) and is determined by time-dependent UV-vis studies at different temperatures.

4.3.1 Investigation of steric and electronic interactions

Phenylazopyridines AZO-1 through AZO-3 feature an increasing bulkiness attributed to t-butyl groups appended onto the phenyl-azo moiety, while the para-phenyl substituent onto the pyridine ring is kept the same (Scheme 4.1). The substitution does not affect the conversion ratios of the compounds significantly, however, thermal stability studies reveal that ΔG\textsuperscript{f} increases with bulkiness (Table 4.1). As a result, the half-lifetime of the cis-isomer increases from 53 h to 71 h to 215 h for AZO-1/2/3, respectively. Titration of the azo-compounds to S-Zn-Me shows the weakest binding for trans-AZO-3 (K\textsubscript{c,trans}) having two t-
butyl groups on both meta-positions of the phenyl-azo moieties indicating that steric interactions are present even in the trans-state of the ligand. Upon switching the ligand to PSS\textsubscript{cis}, a 2.5-fold smaller binding constant for the cis-isomer (K\textsubscript{cis}) is obtained after full-spectral fitting (\textit{vide infra}). DFT calculations show the largest difference in total energy (\(\Delta E\)) between both isomers for AZO-3, which also shows the largest difference in bond length between the pyridine-nitrogen and TPP-zinc atoms (\(\Delta r_{Zn-N}\)) (Table 4.1). This steric evaluation indicates that the introduction of bulky substituents at the meta-positions have a prominent effect on the switch-ability, unlike the positioning at the para-position of the phenyl-azo moiety.

Electronic effects on the binding constant are investigated with AZO-5/6/7 having an increased level of electron donation in the pyridine ring. In this series the trityl moiety onto the less-effective para-position of the phenyl-azo moiety is kept constant (Scheme 4.1). All compounds show good photochromic properties in MCH as shown by the considerably different UV-vis spectra of both photostationary states. Titration experiments with S-Zn-Me show an increase of \(K_{\text{cis}}\) from 32000 M\(^{-1}\) to 53000 M\(^{-1}\) to 77000 M\(^{-1}\) for AZO-5/6/7, respectively (Table 4.1). Despite the control over the binding constant and good photochromic properties, this series could only induce small changes in the porphyrin Soret band upon irradiation of the ligand to PSS\textsubscript{cis}. This suggests that \(K_{\text{trans}}\) and \(K_{\text{cis}}\) are similar, which may be expected considering the location of the bulky part and that the magnitude of the binding constant is not a critical factor in the photo-induced alteration of the binding constant.

Table 4.1. Thermodynamic data for the different phenylazopyridine ligands

<table>
<thead>
<tr>
<th>Ligand</th>
<th>Conv. ratio [mol%](^{a})</th>
<th>(\Delta G^{b}) [kJ\textperiodcentered mol(^{-1})]</th>
<th>(\tau_{\text{h}}^{c}) [h]</th>
<th>(K_{\text{trans}}^{d}) [M(^{-1})]</th>
<th>(K_{\text{cis}}^{e}) [M(^{-1})]</th>
<th>(\Delta E) [kJ\textperiodcentered mol(^{-1})]</th>
<th>(\Delta r_{Zn-N}) [Å]</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZO-1</td>
<td>90</td>
<td>88</td>
<td>104.3</td>
<td>53.3</td>
<td>55\texttimes 10(^3)</td>
<td>n.d.</td>
<td>59.0</td>
</tr>
<tr>
<td>AZO-2</td>
<td>n.d.</td>
<td>n.d.</td>
<td>104.9</td>
<td>70.9</td>
<td>57\texttimes 10(^3)</td>
<td>n.d.</td>
<td>59.7</td>
</tr>
<tr>
<td>AZO-3</td>
<td>88</td>
<td>93</td>
<td>107.6</td>
<td>215.5</td>
<td>38\texttimes 10(^3)</td>
<td>15\texttimes 10(^3)</td>
<td>60.5</td>
</tr>
<tr>
<td>AZO-4</td>
<td>97</td>
<td>95</td>
<td>105.3</td>
<td>83.1</td>
<td>36\texttimes 10(^3)</td>
<td>81\texttimes 10(^2)</td>
<td>67.2</td>
</tr>
<tr>
<td>AZO-5</td>
<td>n.d.</td>
<td>n.d.</td>
<td>n.d.</td>
<td>n.d.</td>
<td>32\texttimes 10(^3)</td>
<td>n.d.</td>
<td>n.d.</td>
</tr>
<tr>
<td>AZO-6</td>
<td>n.d.</td>
<td>n.d.</td>
<td>n.d.</td>
<td>n.d.</td>
<td>53\texttimes 10(^3)</td>
<td>n.d.</td>
<td>63.6</td>
</tr>
<tr>
<td>AZO-7</td>
<td>n.d.</td>
<td>n.d.</td>
<td>n.d.</td>
<td>n.d.</td>
<td>77\texttimes 10(^3)</td>
<td>n.d.</td>
<td>n.d.</td>
</tr>
</tbody>
</table>

\(^{a}\): Determined by a combination studies of \(^{1}\)H-NMR and UV-vis

\(^{b}\): Gibbs energy of activation at 25 °C determined by the Eyring plot.

\(^{c}\): Half-life time at 25 °C determined by fitting the first order rate constant at that temperature.

\(^{d}\): Determined by titration of the pure trans-ligand to S-Zn-Me

\(^{e}\): Determined by spectral fitting at PSS\textsubscript{cis} at ~50% conversion of the titration."
4.3.2 Evaluation of AZO-4

The steric and electronic investigations direct towards an appropriate design of the phenylazopyridine ligand. Considering the switch-ability of the binding constant, the meta-patterning of bulky substituents at both positions of the phenyl-azo moiety significantly enhance this process. On the other hand, the enhancement of steric hindrance precludes the successful synthesis of the ligand. DFT calculations reveal a high energy difference in the complexation of the two isomers of AZO-4, which is attributed to steric interaction of two mesityl groups (Scheme 4.1). In this sub-section, we focus on AZO-4 by performing a combination study of UV-vis and ¹H-NMR spectroscopy (all other ligands have been examined according to the same methodology).

The photoisomerization properties of AZO-4 are investigated in MCH at a concentration of 2.5×10⁻⁵ M at RT. The trans-AZO-4 shows a characteristic π-π’ absorption band at 330 nm and a weak n-π’ absorption at 470 nm. Upon irradiation with 360 nm light, the π-π’ band drastically decreases while another n-π’ band appears at 442 nm. After irradiation for ~30 min, the absorbance spectrum remains the same indicating that PSS<sub>cis</sub> is reached (Figure 4.2A). Successive irradiation with 420 nm light shows the reversal of the process; the band at 442 nm decreases while the absorbance at 330 nm increases (Figure 4.2B). After irradiation with visible light for ~30 min, PSS<sub>trans</sub> is reached and this spectrum nearly represents the initial trans-AZO-4 state, which indicates that PSS<sub>trans</sub> approximates 100% (Figure 4.2C). The generation of the cis-AZO-4 state is monitored by ¹H-NMR in D14-MCH. At a concentration of 5.0×10⁻⁴ M, the ¹H-NMR spectrum of trans-AZO-4 significantly changes upon irradiation with 360 nm light; new resonances appear for all protons and the most prominent upfield shifts are observed from the phenyl protons at the 2-position of pyridine and the ortho-protons of the phenyl-azo moiety (Figure 4.2D). After irradiation for 30 min, the non-overlapping peaks are integrated and normalized to the spectrum of pure trans-AZO-4 and after averaging-out all signals, a cis/trans ratio of 56.4/43.6 is calculated from the ¹H-NMR spectrum. Immediately after the NMR experiment, the solution is diluted 20 times with MCH and a UV-vis spectrum at 2.5×10⁻⁵ M is acquired. Under the assumption that the conversion ratio remains the same upon dilution within the timescale of the experiment (vide infra), this spectrum is used together with the spectrum of trans-AZO-4 to construct the absorbance spectrum of cis-AZO-4 (Figure 4.2C). The constructed spectrum nearly overlaps with the spectrum recorded at PSS<sub>cis</sub> indicating that this value approximates 100% as well. The values for PSS<sub>cis</sub> and PSS<sub>trans</sub> are estimated at 95 and 97%, respectively, after fitting the spectra recorded for AZO-4 after successive irradiation with 360 and 420 nm light.
**Figure 4.2.** A: UV-vis spectra of the trans $\rightarrow$ PSS$_{cis}$ isomerization of AZO-4 in MCH (2.5×10$^{-5}$ M) by irradiation with 360 nm light. B: UV-vis spectra of the PSS$_{cis}$ $\rightarrow$ PSS$_{trans}$ isomerization by irradiation with 420 nm light. C: UV-vis spectra of AZO-4 at PSS$_{cis}$ and PSS$_{trans}$ compared with the spectra for pure trans-AZO-4 and cis-AZO-4. D: $^1$H-NMR spectra of AZO-4 in D14-MCH (5×10$^{-4}$ M) before (upper) and after (lower) irradiation with 360 nm light.

The thermal stability of cis-AZO-4 is investigated by monitoring the spectral changes over time when a solution at PSS$_{cis}$ is aged at 25, 50, 70 and 90 °C. When probed at 360 nm, the normalized thermal fading curves show a first order process (Figure 4.3A), from which the rate constants are fitted. When divided by the temperature, its natural logarithm is plotted against the reciprocal temperature yielding a straight line (Eyring plot, Figure 4.3B) from which the enthalpy ($\Delta H^\ddagger = 88.4$ kJ·mol$^{-1}$), entropy ($\Delta S^\ddagger = -56.8$ J·mol$^{-1}$) and the Gibbs free energy ($\Delta G^\ddagger = 105.3$ kJ·mol$^{-1}$ at 25 °C) of activation is calculated. From the fitted reaction rate constant at 25 °C, a half-lifetime of 83 h is obtained (Table 4.1). The sufficient thermal stability allowed for the accurate construction of the UV-vis spectrum of cis-AZO-4 (*vide supra*) and it is highly applicable for switching experiments with S-Zn having relatively slow supramolecular dynamics.
Photo-regulation of the Zn-porphyrin self-assembly in a two-component system

Figure 4.3. A: Thermal fading curves probed starting at PSScis of AZO-4 at 25, 50, 70 and 90 °C. B: Temperature dependence of the thermal fading rate by the Eyring plot.

4.4 Change of the binding constant upon photoirradiation

The binding constant of trans-AZO-4 is determined by a titration experiment with S-Zn-Me in MCH at 1.75×10−5 M. Similarly as observed in the pyridine titration of S-Zn-Me (see Section 3.2), the titration of trans-AZO-4 shows an isosbestic transition at 425.0 nm between free porphyrin monomers (λmax ~ 420 nm) and S-Zn-Me:trans-AZO-4 (1:1) complexes at λmax ~ 430 nm (Figure 4.4A). The UV-vis spectra clearly show the lack of spectral overlap of the ligand (200~380 nm) and the porphyrin (390~450 nm); still, in order to accurately determine the binding constant, the absorbance of the ligand is included in the fitting procedure. After simultaneous curve fitting of the binding isotherms of the monomer and the monomer complex, a binding constant of $K_{c,trans} = 3.6\times10^4 \text{ M}^{-1}$ is estimated (Figure 4.4B).

The binding constant of cis-AZO-4 is obtained by a successive photo-irradiation experiment of a solution containing a 2.9 molar excess of trans-AZO-4. Upon irradiation with 360 nm light, the absorbance at 330 nm decreases indicative for the trans → PSScis isomerization of the ligand. Concomitantly with the spectral change of the ligand, the porphyrin Soret band at 430 nm decreases, while the band at 420 increases (Figure 4.4C). These spectral changes indicate that the binding constant of cis-AZO-4 is smaller than $K_{c,trans} = 3.6\times10^4 \text{ M}^{-1}$ and that the isomerization process leads to the generation of free S-Zn-Me monomers. After irradiation with 360 nm light, PSScis is reached, which has lowered by ~20% probably. This may be caused by spectral overlap with the porphyrin or a reduced switchability when the ligand is complexed. The process is reversible; upon irradiation with 420 nm light, PSStrans is reached, which nearly represents the initial spectrum at 100% trans. The exact values for both photostationary states and the binding constant for cis-AZO-4 ($K_{c,ci}$) are estimated by a full-spectrum fitting procedure. Under the assumption that the spectrum of the ligand remains identical in its (de)complexed state and that the absorbance for the porphyrin complex is identical when complexed with either the cis- or the trans-isomer of the ligand, the molar absorptivities of S-Zn-Me, S-Zn-Me:AZO-4 (1:1), trans-AZO-4 and cis-
AZO-4 are used to assign fraction of cis-AZO-4 bound to S-Zn-Me (Figure 4.4D). From the full-spectrum fit, the binding constant of cis-AZO-4 is estimated at $K_{cis} = 8.1 \times 10^3$ M$^{-1}$ (Figure 4.4E); hence, a 4.4-fold reduction of the binding constant is achieved by the isomerization process.

**Figure 4.4.** A: trans-AZO-4 titration to S-Zn-Me at $1.75 \times 10^{-5}$ M (RT) between 0 and 50 excess in UV-vis. B: Titration curves at 420 (monomer) and 430 nm (monomer complex) with the corresponding simultaneous curve fit at $K_{trans} = 3.6 \times 10^4$ M$^{-1}$. C: UV-vis spectra of S-Zn-Me with a 2.9 excess AZO-4 at 100% trans, PSS$^{cis}$ (after irradiation with 360 nm light) and PSS$^{trans}$ (after irradiation with 420 nm light). D: Molar absorptivity spectra of trans-AZO-4, cis-AZO-4, S-Zn-Me and S-Zn-Me:AZO-4 (1:1) in MCH. E: Full-spectrum fitting of the sample at 2.9 excess AZO-4 at PSS$^{cis}$ to determine PSS$^{cis}$ and $K_{cis}$. 86
4.5 Modeling the photo-induced porphyrin aggregation

After the assessment of the thermodynamic parameters for the binding of the ligand in its two isomeric forms, the pyridine depolymerization model introduced in Section 3.4 is modified. As schematically depicted in Figure 4.5A, the model contains two different ligands that can complex free monomers, which can subsequently dimerize. In the model consideration, the dimerization constant does not depend on the ligand type, which may comply since this step is driven by hydrogen bonds only. Using the dimerization constant for pyridine-capped monomers \( K_d = 1.1 \times 10^6 \text{ M}^{-1} \) and the equilibrium constants for nucleation \( (K_2 = 685 \text{ M}^{-1}) \) and elongation \( (K = 1.37 \times 10^7 \text{ M}^{-1}) \) for the cooperative self-assembly of \( \text{S-Zn} \), model simulations are performed to investigate which factor enhances the photo-switchability of the system. In this survey, the fraction of aggregated porphyrin monomers \( (\phi) \) is plotted against the logarithm of molar excess ligand, which lowers due to the pyridined induced depolymerization of the stacks (Figure 4.5B). This transition between stacks and dimer complexes depends on the binding strength of the ligand; at a fixed porphyrin concentration, only a small amount of strong-binding ligand is necessary, while a considerable amount of weak-binding ligand is necessary to fully depolymerize the stacks \( (\phi = 0) \). The switch-ability of the system can be depicted by the difference of these amounts, which strongly depends on the ratio of binding constants \( (\gamma) \). In the present case, \( K_{c, \text{trans}} = 3.6 \times 10^4 \text{ M}^{-1} \) and \( K_{c, \text{cis}} = 8.1 \times 10^3 \text{ M}^{-1} \) \( (\gamma = 4.4) \), which requires an excess of \( \sim 40 \) and \( \sim 180 \) for \textit{trans- AZO-4} and \textit{cis-AZO-4}, respectively to achieve \( \phi = 0 \) at \( [\text{S-Zn}] = 4.0 \times 10^{-5} \text{ M} \) (Figure 4.5B). On the logarithmic scale, the considerable spread of the critical amounts of both ligand isomers at \( \phi = 0 \) is not observed when the porphyrin concentration is increased or when the binding constants for both isomers is increased by the same factor; they only show a translation of the window towards lower molar excesses, while the crucial window-width remains similar.

A
Figure 4.5.  A: Thermodynamic model in which aggregates, monomers, monomer complexes and dimer complexes are connected by equilibrium constants. Two different monomer complexes are envisioned; having a strong binding ($K_{c,trans}$) trans-phenylazopyridine ligand and a weak binding ($K_{c,cis}$) cis-isomer, which can be interconverted with light. The dimerization constant $K_d$ is assumed to be identical for the formation of the hetero-dimer and two possible homo-dimers. B: Simulation for the fraction of aggregated $S-Zn$ (φ) versus the molar excess ligand at different conversion ratios based on the model depicted in A ($K_r = 685$ M$^{-1}$, $K = 1.37 \times 10^7$ M$^{-1}$, $K_{c,trans} = 3.6 \times 10^4$ M$^{-1}$ and $K_{c,cis} = 8.1 \times 10^3$ M$^{-1}$, $K_d = 1.1 \times 10^6$ M$^{-1}$ and [S-Zn] = 4.0$ \times 10^{-5}$ M). The vertical line represents the switch-ability at an excess of 40. C: Normalized molecular weight distribution versus the degree of polymerization of the stacks at a fixed ligand excess of 40 at different conversion ratios.

In the simulation, the binding isotherms of $K_{c,trans}$ and $K_{c,cis}$ limit the switching domain and the depolymerization curves within this domain represent the conversion ratio of the ligand; e.g. at a conversion ratio of 40%, 40% of the ligands complex with $K_{c,cis}$ and 60% with $K_{c,trans}$. The boundaries of the domain are approached by high photostationary states, hence the switch-ability of the system is easily visualized by the vertical translation at a fixed ligand to porphyrin excess from low (100% trans-AZO-4) to high (100% cis-AZO-4) conversion ratios (Figure 4.5B). At a porphyrin of $4.0 \times 10^{-5}$ M, critical molar excess of 40 AZO-4 is necessary to depolymerize all porphyrin stacks (φ = 0). Using the calculated 4.4-fold binding constant change and the corresponding photostationary states of the ligand, the simulation shows a drastic effect on φ (Figure 4.5B). Upon irradiation to PSS$^{cis} = 95 \%$, 90% of the porphyrin monomers are aggregated in stacks (φ = 0.90), while at PSS$^{trans} = 97 \%$, only 2% of the monomers form aggregates (φ = 0.02). Consequently, this transition is accompanied by a difference in aggregate size; the solution at PSS$^{trans}$ contains a low amount of short stacks, whereas the solution at PSS$^{cis}$ contains aggregates in high abundance with an average length of 3100 monomers (Figure 4.5C). This high-contrast switching of the porphyrin aggregation may account for macroscopic differences, such as the solution viscosity.
4.6 Photo-regulation of the cooperative self-assembly

The simulations demonstrate that, within a specific concentration regime, a considerable response of the porphyrin stacking is achieved upon photo-irradiation of the ligands. This behavior is experimentally verified by a titration experiment of trans-AZO-4 to S-Zn at a concentration of 4.0×10⁻⁵ M and the subsequent irradiation of a sample at the critical excess of trans-AZO-4 at which φ = 0. In the titration experiment, the addition of trans-AZO-4 leads to an isosbestic point of the UV-vis spectra, indicative for the transition between stacks (λmax ~ 390 nm) and dimer complexes (λmax ~ 428 nm) (Figure 4.6A). Herein, the latter band has fully developed after addition of a ~51 molar excess of trans-AZO-4 at which all stacks are depolymerized. In the CD spectra, depolymerization is monitored by the disappearance of the Cotton effect at 392 nm, while a weak CD effect (Δεmax ~ +30 L/mol·cm) appears in the dimer absorption region (Figure 4.6B). The titration curve probed by the CD intensity at 392 nm shows that a molar excess of ~51 is necessary to fully depolymerize the stacks, whereas the simulation at Ktrans = 3.6×10⁴ M⁻¹ shows that only a critical amount of 40 is required (Figure 4.5B).

Considering the sensitivity of the system characterized by the highly cooperative self-assembly, this difference could be related to relatively small experimental deviations, slow supramolecular dynamics or fluctuations of temperature. In order to investigate the latter, the same samples of the titration are measured at 20 and 30 °C. Remarkably, a lower critical ligand amount to fully depolymerize the stacks is observed when the temperature is raised; the trend-line of the titrations shows a reduction from 61 at 20 °C to a ligand excess of 47 at 30 °C (Figure 4.6C). This indicates that the cooperative self-assembly of porphyrin stacks, characterized by Kα and K is more sensitive to temperature than the metal-ligand interaction characterized by Ktrans. It is observed that the temperature effect on the acquired CD intensity is only marginal between RT and 30 °C (Δεmax ~ −3420 and −3300 L/mol·cm, respectively, Figure 2.4C) when compared to the difference in critical ligand excess (51 and 47, respectively). Considering the reduced amount of ligand at 30 °C, a stronger response in CD activity is expected when photoirradiation is performed at this temperature. In addition, by taking into account the inability to reach high photostationary states in presence of porphyrin (vide supra), it is decided to investigate the switch-ability of a sample containing a molar excess of 54.
Figure 4.6. A: *trans-AZO-4* titration to S-Zn at 4.0×10⁻⁵ M (RT) between 0 and 100 excess (transition from stacks to dimer complexes) in UV-vis (A) and CD (B). C: Corresponding titration curve probed by CD at 392 nm at RT, 20 and 30 °C with the simulation (K₂ = 685 M⁻¹, K = 1.37×10⁷ M⁻¹, Kₐ,trans = 3.6×10⁴ M⁻¹, Kₐ = 1.1×10⁶ M⁻¹ and [S-Zn] = 4.0×10⁻⁵ M).

The photo-regulation experiment is performed at a concentration of 4.0×10⁻⁵ M S-Zn in presence of a 54 excess of *AZO-4* at 30 °C. Before irradiation, no CD effect is observed in the aggregate Soret band region, indicative for the full depolymerization of the stacks (ϕ = 0), while the CD effect of the dimers at ~428 nm is visible (Figure 4.7B). Upon irradiation at 360 nm for 6 min, *cis-AZO-4* is formed as evidenced by decrease of absorbance at 330 nm (Figure 4.7A). From the ligand absorbance regime it is estimated that PSScis approximates 94%, which equals the PSScis in absence of porphyrin (Figure 4.2C). With a delay of ~30 min, a reduction in the Soret band of the complex at 430 is observed, while the intensity of the aggregate Soret band at 390 nm increases (Figure 4.7A). Concomitantly with that reappearance, the CD effect at 392 nm increases to an intensity corresponding to 81% (Δεmax ~ 2680 L/mol-cm) of the value of S-Zn at the same concentration in absence of any ligand (Δεmax ~ 3300 L/mol-cm), Figure 4.7B). Successive irradiation with 420 nm light showed the reversal of the process with a similar time delay owing to the relatively slow supramolecular dynamics. At PSStrans, only 1% magnitude of the CD signal at 392 nm remained, hence this photoisomerization process could control the fraction of the porphyrin stacks in the range of 1 to 81%.
Photo-regulation of the Zn-porphyrin self-assembly in a two-component system

**Figure 4.7.** UV-vis (A) and CD (B) spectra of S-Zn at 4.0×10⁻⁵ M and 30 °C in absence of ligand and in presence of a 54 molar excess **trans-AZO-4** before irradiation, at PSScis and PSStrans. C: Viscosity change of S-Zn at 4.0×10⁻⁵ M and 30 °C triggered by the addition of a 54 molar excess **trans-AZO-4** and after its irradiation to PSScis and PSStrans and after heating the solution.

As evidenced by the spectroscopic measurements, the considerable change in the photo-induced polymerization of fibrous aggregates should influence macroscopic properties such as the solution viscosity. For this experiment, it is decided to use a sample at an identical porphyrin concentration of 4.0×10⁻⁵ M, however with a molar excess of 47 **trans-AZO-4**. As shown by the titration experiment (Figure 4.6) and the model simulation (Figure 4.5B), this composition allows for switching between higher values of φ, which are envisioned to cause a larger difference in solution viscosity. The reference solution of S-Zn in MCH has a viscosity of 0.685 cP at 30 °C; 10% higher than the solvent. After the addition of **trans-AZO-4**, the viscosity lowers to 0.637 cP, which is nearly identical to pure MCH. After UV irradiation and subsequent annealing at 30 °C, the viscosity increases to 0.704 cP at PSScis, while successive irradiation with visible light causes a decrease to 0.643 cP. The switching from PSStrans to pure **trans** by heating and cooling shows a slight decrease towards an identical value corresponding to the initial state (Figure 4.7C). Noteworthy, this reversible switching process is accompanied by a color change of the solution.

91
4.7 Conclusion

By combination of the pyridine-induced depolymerization of Zn-porphyrin aggregates and alternation of the binding constant upon photo-isomerization of phenylazopyridine ligands, a photo-responsive self-assembling system was developed, in which aggregation is controlled by an auxiliary. Molecular design supported by DFT studies resulted in a mesityl-functionalized phenylazopyridine ligand with appropriate steric and electronic properties for the photo-induced (de)complexation of the Zn-porphyrin. This compound showed photostationary states close to 100% for both isomers as evidenced by a combination study of UV-vis and 1H-NMR. Titration of the trans-isomer to a monomer model and subsequent irradiation experiments revealed a reduction of the binding constant by a factor 4.4 upon isomerization from the cis- to the trans-photostationary state. The binding constants for both isomers and their photostationary states were introduced in a multi-component thermodynamic model. Model simulations revealed that the photo-switch-ability of the supramolecular (de)polymerization of porphyrin stacks is strongly determined by the ratio of binding constants of both isomers and high photostationary states. These parameters determined the window-width that allowed for the switching of the fraction of stacked monomers between 2% and 90%.

The titration of the ligand to the self-assembling Zn-porphyrin revealed a higher necessary critical ligand excess to fully depolymerize the porphyrin stacks than predicted by the model. A strong temperature-effect was found in the titration of the axial ligand, which may rationalize this difference. Remarkably, a significantly lower critical ligand excess was found at elevated temperatures, while the effect within the same temperature window on the measured CD-intensity was relatively small. Based on the CD intensity at 30 °C, the switching experiment performed at fixed ligand to porphyrin ratio showed that fraction of stacked monomers could be switched between 1% and 81%. This photo-switch-ability was corroborated with viscosity measurements that showed a relative viscosity difference of 10% only by photo-irradiation of the auxiliary.

4.8 Experimental

Materials and methods
The AZO-compounds were provided by dr. Takashi Hirose and the synthesis will be published elsewhere.16 The porphyrin aggregates were prepared in the same way as described in the experimental section of Chapter 2. Phenylazopyridine titrations were performed in the same way as described in the experimental section of Chapter 3. Irradiation experiments were performed by holding and tumbling a cuvet in front of a monochromatic light source. After irradiation for a specific time, the homogeneous solutions were measured by UV-vis to determine the conversion ratio. DFT calculations for the optimized geometries of the ligand with Zn-TPP were performed at the B3LYP/6-31g(d) level in combination with the LANL2DZ basis set with pseudopotentials for the zinc atom.
**Instrumentation**

Circular dichroism (CD), ultraviolet-visible (UV-vis) and viscosity measurements were performed in the same way as described in the experimental section of Chapter 2. Photoirradiation was carried out using a 150 W Xe lamp (Ushio UXL-159) on a Jasco FP-6500 spectrophotometer. Monochromatic light of 360 and 420 nm were isolated through a built-in monochromator using 5 or 20 nm slits.

**Thermodynamic modeling**

A multiple equilibrium modeling study was performed using MATLAB® (R2010a, version 7.10.0.499, win 32). In the model, nine different species were considered: free porphyrin monomers [A], porphyrin stacks [Agg], two isomers of the pyridine ligand [B] and [B], two porphyrin-ligand 1:1 monomer complexes [AB] and [AB] and three porphyrin-pyridine 2:2 dimer complexes [(AB)2], [(AB)24] and [(AB)26]. The total concentrations of porphyrin [A0] and phenylazopyridine [B0] were described according to Equations 4.1 and 4.2.

\[ [A_0] = [A] + [Agg] + [AB] + 2 \cdot [(AB)_{2a}] + [(AB)_{2d}] + [(AB)_{2c}] \]  
(4.1)

\[ [B_0] = [B] + [AB] + 2 \cdot [(AB)_{2b}] + [(AB)_{2e}] \]  
(4.2)

The K-model (Equation 3.3) was applied to express the cooperative polymerization of porphyrin stacks. Herein, \( \sigma \) represents the degree of cooperativity \( (K_2 / K) \) with dimerization constant \( (K_2) \) and elongation constant \( (K) \).

\[ [Agg] = \sum_i \sigma K^{-i}(K[A])^i \]  
(4.3)

Equations 4.1-4.3, including the equilibrium constants for complexation (\( K_0 \)) and dimerization of porphyrin-pyridine adducts (\( K_2 \)) give Equations 4.4-4.7.

\[ F(1) = [1 + \alpha + \beta(1 + 2K_2\beta[A])] - [A_0] = 0 \]  
(4.4)

\[ F(2) = [B] + [AB] + \beta[A](1 + 2K_2\beta[A]) - [B_0] = 0 \]  
(4.5)

\[ \alpha = \sigma(1 - K[A])^{-2} - 1 \]  
(4.6)

\[ \beta = K_{cis}([B] + [B]) \]  
(4.7)

The conversion ratio of the ligand was characterized according to Equations 4.8 and 4.9. In the latter, \( x \) is defined as the conversion ratio of the cis-isomer.

\[ F(3) = x[B_0] - (1 - x)[B_0] = 0 \]  
(4.8)

\[ x = [B_0]/([B_0] + [B_0]) \]  
(4.9)

The system is fully described by Equations 4.4, 4.5 and 4.8, which were numerically solved by a quasi-Newton method by constructing a Jacobian matrix (3.10). Herein, [A], [B] and [B] were determined with fixed [A0] and [B0] and x, so that \( F(1) = F(2) = F(3) = 0 \).

\[ J = \left[ \begin{array}{ccc} \frac{\partial F(1)}{\partial [A]} & \frac{\partial F(1)}{\partial [B]} & \frac{\partial F(1)}{\partial [B]} \\ \frac{\partial F(2)}{\partial [A]} & \frac{\partial F(2)}{\partial [B]} & \frac{\partial F(2)}{\partial [B]} \\ \frac{\partial F(3)}{\partial [A]} & \frac{\partial F(3)}{\partial [B]} & \frac{\partial F(3)}{\partial [B]} \end{array} \right] \]  
(4.10)
4.9 References

16. The synthesis of the azo-ligands was performed by dr. Takashi Hirose and reported in the Supporting information for Hirose, T; Helmich, F.; Meijer, E. W., “Photo-control of Cooperative Porphyrin Aggregation with Photoresponsive Phenylazopyridine Ligands”, manuscript in preparation.
17. In a plain 1:1 binding process, weaker binding is observed at elevated temperatures. The opposite trend is observed for the multi-component system, in which at smaller excess of ligand is necessary at elevated temperatures. For a system that shows dilution-induced self-assembly, it is feasible that this is related to heating-induced self-assembly process.
Two-component Zn-porphyrin self-assembly with DABCO

Abstract. The self-assembly of chiral Zn-porphyrins was studied in the presence of the bidentate axial ligand DABCO (1,4-diazabicyclo[2.2.2]octane). In a reference experiment, the complexation process of DABCO was studied with an N-methylated Zn-porphyrin monomer model compound. This revealed that coordination of the second nitrogen of DABCO a Zn-porphyrin monomer less favorable than the first, indicating negative cooperativity for sandwich formation. These binding properties were introduced in thermodynamic model describing the interaction between ditopic, hydrogen bonded Zn-porphyrins and the bidentate DABCO ligand. In the model, a depolymerization mechanism was proposed in which porphyrin stacks depolymerized upon the addition of DABCO and that alternating supramolecular block copolymers were formed that comprised of DABCO units and hydrogen bonded, Zn-porphyrin dimers. The validation experiments, in which DABCO was titrated to hydrogen bonded Zn-porphyrin aggregates, confirmed the formation of the copolymer. Surprisingly, the elongated complex was more stable towards excessive amounts of DABCO than anticipated by the model simulation. Modular assessments revealed that this stability was provided by positive cooperativity for sandwich formation, which was not observed in the reference experiment. Unlike its stability towards excessive amounts of Lewis base, preliminary chain-stopping experiments demonstrated that the alternating copolymer readily depolymerized upon the addition of monotopic Mn(III)-porphyrins, which revealed energy transfer upon chain-stopping.
5.1 Introduction

The axial ligation of metalloporphyrins is a widely applied approach to organize porphyrins in supramolecular architectures.\textsuperscript{1} In this field, numerous strategies have been reported on one-component systems, in which ditopic metalloporphyrins having donating groups self-assemble by metal-ligand coordinative bonds. In multi-component systems, the assembly of monotopic metalloporphyrins is usually achieved by multivalent axial ligands, such as bipyridines,\textsuperscript{2} pyridine-tri/tetrapods,\textsuperscript{3} pyridine hexamers\textsuperscript{4} and DABCO (1,4-diazabicyclo[2.2.2]octane).\textsuperscript{5} The DABCO ligand has been widely applied to form discrete assemblies and due to its high basicity and bidentate nature, it forms stable sandwich complexes with Zn-porphyrins. Anderson and co-workers discovered the remarkable stability of ladder complexes comprising of conjugated porphyrin strands and DABCO ligands.\textsuperscript{6} As the length of the strand increases, a higher degree of chelate cooperativity was deduced for its ladder formation. Here, the less favorable coordination of the second nitrogen of DABCO to form the sandwich complex with Zn-porphyrin monomers was characteristic for negative cooperativity, while positive cooperativity was found for meso-connected Zn-porphyrin oligomers and other ladder-based complexes.\textsuperscript{6-8} These phenomena have been thoroughly investigated, yet, the examples focused on systems having metal-ligand interactions only.

A complexation study of bidentate ligands in conjunction with hydrogen bonded Zn-porphyrin moieties was performed by the group of Shinkai, who reported on the gelation properties of symmetrically meso-substituted Zn-porphyrins having peripheral urea groups and solubilizing dodecyl chains (Figure 5.1).\textsuperscript{6} In benzene, the porphyrins form J-type precipitates upon hydrogen bonding between the urea moieties. The porphyrins were able to gelate the solvent only in presence of bidentate ligands such as piperazine and DABCO. The piperazine titration revealed the lowest critical gel concentration (CGC) at a 2:1-stoichiometry of porphyrin and ligand, respectively. At this composition, 1-dimensional H-type aggregates were observed by electron microscopy, while a large band-splitting (~1270 cm\textsuperscript{-1}) was observed in the absorbance spectrum. Corroborated with infrared studies, a supramolecular organization in the gel state was proposed, in which hydrogen-bonded porphyrin dimers were connected by piperazine ligands. At higher excesses of ligand, the UV-vis spectrum gradually changed into a single Soret band, while the infrared spectrum remained unchanged. At the 2:1 composition using DABCO as a bridging ligand, the porphyrins formed a 2-dimensional structure, which was attributed to the orderly interdigitation of hydrogen bonding patterns afforded by the rigid DABCO spacer. In absence of hydrogen bonding, minimized-energy structures of sandwich complexes revealed a highly symmetric structure with more rigidity for the DABCO ligand relative to piperazine.
Two-component Zn-porphyrin self-assembly with DABCO

![Schematic representations of the hypothesized aggregation modes of the meso-urea-substituted Zn-porphyrin studied in absence of piperazine (left), its 2:1 (center) and 1:1 (right) aggregates.]

Albeit this system was investigated in the gel-state, it closely resembles the self-assembly of S-Zn, in which the presence of a monotopic pyridine derivative causes the depolymerization of porphyrin stacks into pyridine-complexed, hydrogen bonded porphyrin dimers (Chapter 3/4). Now, with the propensity to form an elongated structure with S-Zn and DABCO, we would like to study the interaction between these two bidentate moieties using the same approach described in Chapter 3/4. Here, we couple the thermodynamic properties of (1) the DABCO complexation Zn-porphyrins in absence of hydrogen bonding and (2) the cooperative hydrogen bond-assisted self-assembly of the Zn-porphyrins in a thermodynamic model. Based on these individually obtained experiments, we simulate and experimentally verify the behavior of the system. We start the investigations by titration experiments of DABCO to N-methylated porphyrin derivative S-Zn-Me and study the formation of sandwich complexes.

5.2 DABCO titration to S-Zn-Me

The formation of 2:1 sandwich complexes comprising of Zn-porphyrins and DABCO has widely been studied by different groups. In order to deduce the thermodynamic properties of this process, a step-wise approach is required (Figure 5.2A); even at millimolar concentrations, strong binding and the simultaneous formation 2:1 and 1:1 complexes preclude the determination of the individual association events. Hence, a non-isobestic point is observed in the UV-vis spectra upon the addition of DABCO to S-Zn-Me at a concentration of 2.85×10⁻⁶ M (Figure 5.2B). Between the transition from the Soret band of free S-Zn-Me (420 nm) to the 1:1 complex at 430 nm, the sandwich complex is clearly visible at a molar excess of 0.35, which shows a Soret band at λ_max ~ 425 nm. According to the thermodynamic cycle (Figure 5.2A), the formation of the sandwich complex can be
determined indirectly by two independent pathways. Firstly, the exclusive formation of the 1:1 complex is conducted by UV-vis titration of DABCO to S-Zn-Me at low concentrations, at which sandwich formation is absent. Secondly, the breakage of the sandwich complex (stable at high concentrations) is conducted by an ¹H-NMR titration, in which the addition of DABCO leads to the formation of the 1:1 complex.

The UV-vis titration is conducted at a concentration of 1.0×10⁻⁷ M S-Zn-Me, which reveals the direct formation of the 1:1 complex as evidenced by an isosbestic point at 425 nm (Figure 5.2C). After simultaneous curve fitting the binding isotherms at 420 and 430 nm, a binding constant of $K_c = 3.08 \times 10^6$ M⁻¹ is estimated (Figure 5.2D), which is two orders of magnitude higher than pyridine (see Section 3.2). The ¹H-NMR titration is performed at a porphyrin concentration of 5.0×10⁻⁴ M in D14-MCH. At sub-stoichiometric amounts of DABCO (< 0.5 excess), free S-Zn-Me and the 2:1 sandwich complex are observed in slow exchange. The formation of the sandwich complex is accompanied by shifting and broadening of the peaks (Figure 5.2E) and the appearance of the DABCO signal at -5.2 ppm. The gallic proton (proton ‘d’ in Scheme 2.1) shifts 0.18 ppm downfield upon the formation of the sandwich complex, which is highly abundant at a 0.5 excess of DABCO. The breakage of the sandwich complex occurs in fast exchange on the ¹H-NMR timescale as evidenced by a single proton resonance of both the 1:1 and 2:1 complexes and the disappearance of the DABCO signals at negative chemical shifts (Figure 5.2E). In fast exchange, the chemical shift of the gallic proton shifts 0.08 ppm upfield and it is observed that the 1:1 complex is formed at already low molar excesses of DABCO (Figure 5.2F). This demonstrates that the sandwich structure is fairly labile towards DABCO and that sandwich formation occurs with negative cooperativity ($\alpha < 1$) indicating that coordination of the second nitrogen of DABCO is less favorable than the first. In accordance with Anderson, the cooperativity factor is determined by fitting the chemical shifts of S-Zn-Me in the DABCO titration, which is estimated at $\alpha \approx 0.3$ (Figure 5.2F). According to the thermodynamic cycle, the binding strength for the formation of the sandwich from the 1:1 complex is estimated at $K_c = 2.3\times10^5$ M⁻¹ (Figure 5.2A).
Figure 5.2. A: Thermodynamic cycle of the species involved in the equilibria of binding DABCO to S-Zn-Me. The overall binding constant $K_\alpha$ can be estimated by the stepwise constants $K_s$ and $K_c$. The former is obtained by UV-vis titration and the latter by $^1$H-NMR, in which $K_s = \frac{1}{4} \alpha \cdot K_c$ and $\alpha$ is the ligand cooperativity. B: DABCO titration to S-Zn-Me at 2.85×10$^{-6}$ M between 0 and 115 molar excess in UV-vis. C: Similar titration experiment performed at 1.00×10$^{-2}$ M S-Zn-Me. D: Titration curves at 420 (monomer) and 430 nm (1:1 DABCO:S-Zn-Me complex) with the corresponding simultaneous fits at $K_c = 3.08 \times 10^6$ M$^{-1}$. E: $^1$H-NMR titration of DABCO to S-Zn-Me at 5.00×10$^{-4}$ M in D14-MCH. F: Chemical shift of the gallic proton (proton $d$ in Scheme 2.1) upon the addition of DABCO and the corresponding curve fit at $\alpha = 0.3$. 

99
5.3 Modeling the S-Zn system in the presence of DABCO

Under the assumption that the hydrogen bond-assisted self-assembly of chiral Zn-porphyrin stacks and axial ligation of Zn-porphyrins remain two orthogonal processes, the initial depolymerization model developed in Chapter 3 is modified by implementing the ditopic nature of the DABCO ligand. The modular assessment of this system is particularly interesting since a high degree of cooperativity is found for the hydrogen bonding process while negative cooperativity has been deduced for the formation of sandwich complexes (vide supra). Compared to the pyridine-induced depolymerization model, the current model has been extended by dimerization events of sandwich complexes besides regular 1:1 monomer complexes, which are both characterized by $K_d$. Furthermore, the formation of sandwich complexes has been implemented as characterized by $K_s$, which is lower than complexation constant $K_d$ due to the negative cooperativity (Figure 5.3).

![Thermodynamic model of S-Zn in presence of DABCO](image)

**Figure 5.3.** Thermodynamic model of S-Zn in presence of DABCO, in which porphyrin aggregates (characterized by $K_s$ and $K_d$) depolymerize upon complexation with the ditopic ligand (characterized by $K_s$ and $K_d$). By the formation of hydrogen bonded dimers with S-Zn:DABCO 1:1 ($K_d$ in diagonal direction) and 2:1 complexes ($K_d$ in horizontal direction) and the formation of sandwich complexes ($K_s$ in vertical direction), aggregates are formed in a stepwise fashion with different length $n$ and different end-groups (S-Zn$_{2n-2}$:DABCO$_n$/S-Zn$_{2n-1}$:DABCO$_n$/S-Zn$_{2n}$:DABCO$_n$).
In the modular consideration, the stepwise formation of alternating copolymers is described by $K_s$ and $K_i$ only. Consequently, a population of copolymers arises in a stepwise fashion with different chain lengths depending on the number of DABCO molecules $n$ in the aggregate and different chain ends. For the latter, polymers with either two DABCO or two S-Zn terminals are envisioned or an aggregate with one porphyrin and one DABCO terminal. Apart from sandwich complexes and DABCO-complexed porphyrin dimers, the different copolymers for $n \geq 2$ are designated being one aggregate type, which is selectively probed by UV-vis and CD spectroscopy (vide infra). In the model it is assumed that dimerization events only occur with monomer complexes and that the dimerization constant does not depend on the nature of the ligand or the type of adduct attached onto the polymer chain; therefore, each consecutive addition is described by the dimerization constant $K_d = 1.1 \times 10^6 \text{ M}^{-1}$ estimated from the pyridine model in Chapter 3. The cooperative self-assembly for S-Zn is described by the equilibrium constants for nucleation ($K_2 = 685 \text{ M}^{-3}$) and elongation ($K = 1.37 \times 10^7 \text{ M}^{-1}$). Monomers are removed from the porphyrin stacks by the formation of 1:1 monomer complexes ($K_i = 3.08 \times 10^6 \text{ M}^{-1}$) and 2:1 sandwich complexes ($K_s = 2.3 \times 10^5 \text{ M}^{-1}$). Having determined the thermodynamic parameters necessary to describe the proposed mechanism by which DABCO and S-Zn interact, simulations are performed at each possible concentration of porphyrin and DABCO to determine the porphyrin distribution over six different aggregate types; porphyrin stacks, monomers, 1:1 monomer- and dimer complexes, 2:1 sandwich complexes and copolymers for $n \geq 2$.

![Graph A: Phase diagram of the S-Zn-DABCO system](image)

![Graph B: Horizontal section out of the phase diagram](image)

**Figure 5.4.** A: Phase diagram of the S-Zn-DABCO system depicted in Figure 5.3 with the dimensionless concentrations of porphyrin and DABCO at the vertical and horizontal axis, respectively ($K_2 = 685 \text{ M}^{-1}$, $K = 1.37 \times 10^7 \text{ M}^{-1}$, $K_i = 3.08 \times 10^6 \text{ M}^{-1}$, $K_s = 2.3 \times 10^5 \text{ M}^{-1}$, $K_d = 1.1 \times 10^6 \text{ M}^{-1}$, *the dotted lines guide the eye to indicate the phase boundaries*). B: Horizontal section out of the phase diagram at [S-Zn] = 2.0 \times 10^{-5} \text{ M} representing the porphyrin fraction over stacks, monomers, 1:1 monomer- and dimer complexes, 2:1 sandwich complexes and copolymers for $n \geq 2$. 

101
The resulting phase diagram (Figure 5.4A) reveals the cooperative self-assembly of S-Zn in the absence of DABCO (y-axis, left) and the formation of 1:1 monomer complexes at low porphyrin concentrations at which hydrogen bonds are not being formed (x-axis, bottom). In this regime, 2:1 sandwich complexes are not formed either, which is attributed to its negative cooperativity at $\alpha \approx 0.3$. At high porphyrin concentrations, the addition of DABCO leads to the formation of the alternating copolymer. However this occurs in a small regime only; upon the addition of DABCO, the copolymer readily depolymerizes into 1:1 dimer complexes. At a porphyrin concentration of 2.0×10^{-5} M, the section of the phase diagram represents the DABCO titration curve that shows the depolymerization of porphyrin stacks and the simultaneous formation of 1:1 dimer complexes and alternating copolymers (Figure 5.4B). The DABCO-induced depolymerization of the latter aggregate type, causes a sharp point in the titration curve corresponding to a maximum porphyrin fraction of 45%. Throughout the DABCO titration, the abundance of sandwich complexes remains extremely low due to its unfavorable formation and high reactivity towards hydrogen bonded dimers.

5.4 DABCO titration to S-Zn

After simulating the binding behavior of the bidentate ligand, a DABCO titration is performed at a concentration of 2.0×10^{-5} M S-Zn in MCH. Directly after the addition of the ligand, the absorbance of the Soret band and the CD effect at ~390 nm have reduced indicative for the depolymerization of porphyrin aggregates; a molar excess of ~5 is necessary to fully depolymerize the porphyrin stacks. Concomitantly, a red-shifted and splitted Soret band at $\lambda_{\text{max}} \sim 425$ nm is observed that is formed via an isosbestic point at 405 nm (Figure 5.5A), which is highly similar to the depolymerization process with (phenylazo)pyridines (Figure 3.2A/4.6A). The corresponding CD spectra of these adducts are considerably more intense ($\Delta \varepsilon_{\text{max}} \sim +790$ L/mol·cm, Figure 5.5B) than observed for the (phenylazo)pyridine dimer complexes (Figure 3.2B/4.6B), which suggest the formation of an ordered helical aggregate that could be elongated due to the ditopic nature of DABCO. Much to our surprise, the observed CD intensity for these adducts increases even further over time, indicating that the spectra in Figure 5.5A/B are not recorded at thermodynamic equilibrium. Apparently, unlike for complexes of (phenylazo)pyridines, the DABCO system requires ~24 h in order to achieve thermodynamic equilibrium as evidenced by time-dependent spectroscopy studies (data not shown).
Figure 5.5. UV-vis (A) and CD (B) spectra of the DABCO titration to S-Zn at 2.0×10⁻⁵ M between 0 and 10 excess DABCO. The ‘kinetic’ spectra are measured ±30 minutes after prepararion. C/D: Same spectra after ageing and reaching thermodynamic equilibrium. E: Titration curve probed by the maximum Cotton effect for the H-type aggregate at ~390 nm and the alternating copolymer at ~428 nm, and probed by the solution viscosity of the samples at thermodynamic equilibrium. “1” refers to the formation of the alternating copolymer and “2” refers to its DABCO-induced disruption. F: AFM phase image (5 × 5 μm) after dropcasting a S-Zn:DABCO (1:1)₈ solution on HOPG.
After ageing for 24 h at room temperature, considerably different spectra are recorded from the same samples. In the absorbance data, the isosbestic point observed for the “kinetic titration spectra” has fully disappeared. Now, at thermodynamic equilibrium, the absorbance band originating from the adducts shows a broad, split Soret band with a band-splitting of $\sim$1225 cm$^{-1}$, which is highly similar to the observations of Shinkai and co-workers (Figure 5.5C). Furthermore, the CD intensity of the adducts has increased up to $\Delta \varepsilon_{\text{max}} \sim +1290$ L/mol-cm after ageing (Figure 5.5D). By monitoring the CD effects at thermodynamic equilibrium of the aggregate at $\sim$390 nm and the maximum Cotton effect for the adduct at $\sim$428 nm, it is observed that a molar DABCO excess of only 0.5 is necessary to fully depolymerize the porphyrin stacks (Figure 5.5E). Given the strong CD effect and the thermodynamic instability of sandwich complexes (see Section 5.2), the 2:1 stoichiometry arising from this critical DABCO excess at 0.5 strongly suggests the formation of the alternating copolymer. DABCO-complexed, hydrogen bonded Zn-porphyrin dimers are not likely to be formed in this process, since they possess a 1:1 stoichiometry. Remarkably, the CD effect remains present even at higher excesses of DABCO causing a plateau in the titration curve, which suggests that the alternating copolymer remains intact despite the excess Lewis base. This observation is contrast with the simulation that shows the thermodynamic instability of the alternating copolymers towards excessive amounts of DABCO; their DABCO-induced depolymerization results in the formation of 1:1 DABCO dimer complexes (Figure 5.4B, schematic depiction in Figure 5.7). The titration curve shows a sharp drop in solution viscosity to $\sim$20% of its original value concomitantly with the full disappearance of the CD effect at 390 nm, while a mild reduction is observed in the plateau region of the alternating copolymer in which $\sim$10% of the original solution viscosity remains at a DABCO molar excess of 10 (Figure 5.5E). At a 1:1 composition of S-Zn and DABCO, the AFM phase image shows the presence of fibrillar nanostructures after casting a drop on freshly cleaved HOPG (Figure 5.5F), which strongly suggests the formation of elongated structures.

The remarkable stability of the alternating copolymer is further investigated by a similar titration experiment that reaches to higher DABCO excesses than initially pointed out by the simulation. The excessive addition of DABCO leads to the disappearance of the split Soret band and its Cotton effect at 425 nm, while a single Soret band at 428 nm appears that shows only little CD activity (Figure 5.6A). At a $\sim$1000 molar excess of DABCO, the spectra are similar to depolymerized S-Zn in presence of quinuclidine (QND), which is the monotopic analog of DABCO (Figure 5.6B). In this titration, performed at the same porphyrin concentration of 2.0$\times$10$^{-5}$ M, a QND excess of $\sim$4 is necessary to fully depolymerize the stacks. This amount is considerably lower than for pyridine (a critical pyridine excess of 40 is required at this porphyrin concentration, see Section 3.3) due to its stronger Lewis basicity.
Figure 5.6. A: UV-vis (upper panel) and CD (lower panel) spectra of the DABCO titration to S-Zn at 2.0×10^{-5} M between 0 and 1000 excess DABCO after ageing. B: UV-vis (upper panel) and CD (lower panel) spectra of the QND titration to S-Zn at 2.0×10^{-5} M. C: CD titration curves recorded at 2.0×10^{-5} and 3.3×10^{-6} M for the H-type aggregate at ~390 nm and the alternating copolymer at ~428 nm and the curve fit at α = 493. D: IR-spectra at 1.0×10^{-4} M of S-Zn without ligand (‘stacks’) and with a critical amount of DABCO (‘alternating copolymer’) and QND (‘dimer complex’).

5.4.1 Discussion on the copolymer stability

Supported by the quinuclidine reference experiment, the titration at high molar excesses of DABCO reveals stability of the alternating copolymers that has not been encountered by the simulation. In order to investigate the observed difference, we use the thermodynamic model to investigate which thermodynamic parameter accounts for the stability; strengthened by this modular investigation, we hypothesize if the outcome could figure into the molecular picture represented in the system. In this approach, we refrain from altering the mechanism by which DABCO and S-Zn interact. While preserving the same type of binding events, we merely tune the thermodynamic parameters we expect to significantly affect the stability.
Resultantly, we observed that the cooperativity for sandwich formation ($\alpha$) significantly enhances the stability of the alternating copolymer towards excessive amounts of DABCO. The titration data fit moderately to a value for $\alpha \approx 493$, which indicates that the binding constant for sandwich formation has increased to $K_c = 3.8 \times 10^8$ M$^{-1}$ in the alternating copolymer (Figure 5.6C). Considering the magnitude of this binding strength, it may not represent a chemically related event such as a metal-ligand coordination bond, albeit it also fits the data acquired at a porphyrin concentration of $3.3 \times 10^{-6}$ M with the same quality of the fit.$^9$ Without modifying the mechanism depicted in Figure 5.3, the outcome of the current model shows that the enhanced stability of the alternating copolymer could be related to a level of cooperativity. Similarly as observed by Anderson,$^{50}$ negative cooperativity was found for the sandwich formation of porphyrin monomers, while a high degree of cooperativity was found for the formation of ladder structures out of porphyrin strands. This enhanced stability was contributed to intramolecular processes that were characterized by effective molarities up to $10^6$ M$^{-1}$. While this type of chelate cooperativity is difficult to envision for the current system, an allosteric effect due to the formation of a supramolecular helix may account for the observed stability. Likely, this is the cause of the hydrogen bonding array that reaches over the axial ligand, in which two neighboring hydrogen-bonded porphyrin dimers interlock the DABCO moiety with this dipolar interaction.

At a critical amount of QND to fully depolymerize the stacks at $1 \times 10^{-4}$ M, the infrared spectrum (Figure 5.6D) is highly similar to the spectrum of S-Mn (Figure 2.9A) and S-Zn:pyridine (1:1) dimer complexes (Figure 3.3C). Interestingly, the spectrum recorded at the same porphyrin concentration with a critical amount of DABCO is significantly different from the dimer spectra; the carbonyl stretching regime has shifted to lower wavenumbers and the spectrum is fairly similar to the hydrogen-bonded stacks of S-Zn (Figure 5.6D). The spectral comparison demonstrates the additional hydrogen bonding interactions, which were also observed by Nolte and coworkers in the DABCO-induced dimerization of monocavity-appended Zn-porphyrin hosts.$^{11}$ Here, in the absence of hydrogen bonding, sandwich complexation was characterized by $\alpha \approx 0.05$, while the decoration with hydroxy groups caused a significant increase to $\alpha \approx 17$. The additional interactive elements provided a 340-fold enhancement in dimerization, which is still less than the $\sim 1640$-fold enhancement in the current system. According to the fit of the titration data, the increase from $\alpha \approx 0.3$ (sandwich complex formation of S-Zn-Me, \textit{vide supra}) to $\alpha \approx 493$ appears to be beneficial for the stability of the alternating copolymers. Considering the over-prediction of the model at substoichiometric quantities of DABCO in the depolymerization of H-type aggregates (0 – 0.5 molar excess, Figure 5.6C), the assignment of two values for $\alpha$, \textit{e.g.} ‘$\alpha_{\text{nucleation}}$’ for monomer sandwich formation and ‘$\alpha_{\text{elongation}}$’ polymer sandwich formation, may enhance the representation of the data. Here, low values for $\alpha_{\text{nucleation}}$ in the initial state suppress the monomer consumption \textit{via} sandwich formations, thereby making the transition of the
depolymerization of H-type aggregates less sharp. On the other hand, higher values for $\alpha_{\text{elongation}}$ contribute to the aggregate stability in the later stage of the DABCO titration. Albeit this modular assessment could result into an appropriate data representation, the mismatch between modeling and experimental results could be the cause of other, perhaps unforeseen, effects. For instance, the origin of the cooperativity could be related to electronic effects arising from the DABCO ligand, in which the Lewis basicity increases upon the formation of hydrogen bonded dimers.

5.5 Preliminary chain-stopping experiments with manganese porphyrins

As evidenced by UV-vis/CD spectroscopy, viscometry and AFM, the addition of DABCO leads to the formation of stable, alternating block copolymers comprising of hydrogen bonded S-Zn:DABCO (2:1) sandwich complexes. This aggregate type is remotely similar to coordination polymers developed by the group Kobuke, in which ditopic (bis)-imidazolyl-Zn-porphyrin dimers form an elongated structure upon intermolecular metal-ligand complexation.\textsuperscript{12a} The addition of monotopic imidazolyl-Mn-porphyrin monomers caused the functional chain-stopping of the polymer (Figure 1.10B).\textsuperscript{12b} In this case, however, the S-Zn:DABCO copolymer is entirely held together by hydrogen- and metal-ligand bonds in an alternating fashion. For the chain-stopping of this aggregate type by metal-ligand association (Figure 5.7), a monotopic moiety is selected that cannot participate in hydrogen bonding (1), it accepts one axial ligand only (2) and it is spectroscopically distinguishable from the S-Zn:DABCO system (3). For these requirements, S-Mn-Me is employed that is molecularly dissolved in MCH and it is known as an efficient energy/electron acceptor that quenches the fluorescence of Zn-porphyrins.\textsuperscript{12b} At an equilibrated mixture of S-Zn and DABCO (1:1), both present at 2.0×10^{-5} M, S-Mn-Me is titrated to the alternating copolymer.\textsuperscript{8}

![Figure 5.7](image-url)  
**Figure 5.7.** Schematic depiction of the formation of the supramolecular alternating copolymer and its chain-stopping upon the addition of excess DABCO (Lewis base) or S-Mn-Me (Lewis acid). The terms ‘strong’ and ‘weak’ refer to the apparently observed response of the system.
In the absence of chain-stoppers, the UV-vis spectrum shows the splitted Soret band (Figure 5.8A), a strong Cotton effect is acquired (Figure 5.8B) and the sample reveals a typical porphyrin luminescence spectrum at $\lambda_{\text{em,max}} = 610$ nm (Figure 5.8C). The addition S-Mn-Me is clearly monitored by its wide absorbance throughout the spectral domain and its Soret band at $\lambda_{\text{max}} = 474$ nm. Interestingly, the splitted Soret band originating from the alternating copolymer readily converts into the single Soret band at 429 nm after addition of small amounts of chain-stopper (‘1’, Figure 5.8A). After reaching a maximum absorbance at a molar excess of 0.28 S-Mn-Me, this single Soret band lowers in intensity probably due to peak broadening (‘2’, Figure 5.8A). The strong responsiveness of the system towards the chain-stopper is also observed in the CD spectra that reveal a strong reduction of the Cotton effect. A molar excess of $>0.46$ S-Mn-Me is necessary to obtain a CD silent signal, unlike the molar excess of 1000 for DABCO (Figure 5.7, *vide supra*). The remarkable difference between excessive additions of DABCO and S-Mn-Me is difficult to assess, especially since the binding affinity for Mn-porphyrins towards Lewis bases is considerably lower than Zn-porphyrins.\textsuperscript{12b} The seemingly strong interaction of the chain-stopper with the Zn-porphyrin aggregate leads to the quenching of its fluorescence (Figure 5.8C).

**Figure 5.8.** UV-vis (A), CD (B) and PL (C) spectra of the titration of S-Mn-Me to the S-Zn:DABCO (1:1) system at 2.0×10^{-5} M.
These preliminary chain-stopping experiments reveal the quenching of the fluorescence upon addition of the chain-stopper, while it shortens the aggregate as evidenced by the UV-vis and CD spectra. The strong response of the system is however difficult to explain since the alternating copolymer was found to be highly stable towards excess Lewis base (Figure 5.7). In addition, it is difficult to understand that donor luminescence is still observed for samples that are CD-silent. Obviously, this three-component system featuring (multiple levels of) cooperativity requires more investigations. Hence, we will study multi-porphyrin systems in the presence of Lewis bases in the upcoming chapters.

5.6 Conclusion

The cooperative self-assembly of chiral S-Zn has been studied in the presence of the bidentate ligand DABCO. In the absence of hydrogen bonding, the coordination of the second nitrogen of DABCO to S-Zn-Me into the sandwich complex was less favorable that the first complexation step, which was characterized by negative cooperativity at $\alpha = 0.3$. The resulting thermodynamic parameters were introduced in a thermodynamic model, in which they were coupled to the hydrogen bond-assisted cooperative self-assembly of S-Zn. Model simulations revealed the formation of alternating block copolymers comprising of hydrogen bonded S-Zn:DABCO (2:1) sandwich complexes upon the DABCO-induced depolymerization of S-Zn stacks. As predicted by the model, combination studies of viscosity, AFM, UV-vis and CD spectroscopy evidenced the slow formation of elongated structures upon the titration of DABCO to aggregates of S-Zn at thermodynamic equilibrium. A remarkable stability towards large DABCO excesses was found for the alternating copolymer, which was not encountered by the model simulation. The stability was investigated by a modular approach, in which curve-fitting was performed on DABCO titration data that described the full breakage of the alternating copolymer at large amounts of DABCO. These titration data fitted moderately when sandwich complexation was described by positive cooperativity. This modular assessment allowed for a tentative explanation, in which another level of cooperativity arises that describes an enhanced affinity for sandwich formation inside the alternating copolymer.

The disruption of the alternating copolymer was also studied by preliminary chain-stopping experiments monotopic Mn(III)-porphyrins. Upon the addition of S-Mn-Me, depolymerization of the alternating copolymer was evidenced by the disappearance of the CD effect and quenching of the fluorescence. Relative to excessive additions of DABCO in the two-component system, a remarkably strong response was observed in the three-component system.

109
5.7 Experimental

Materials and methods

The porphyrin aggregates were prepared in the same way as described in the experimental section of Chapter 2. DABCO and S-Mn-Me titrations were performed in the same way as described in the experimental section of Chapter 3. DABCO was used as received.

Instrumentation

Circular dichroism (CD), ultraviolet-visible (UV-vis) and viscosity measurements were performed in the same way as described in the experimental section of Chapter 2.

Emission spectra were recorded on a JASCO FP6500 with the solutions in a 1 × 10 mm cuvet. Monochromic light of 440 nm through a 10 nm slit was used to excite the solution, while the emission spectra were recorded after interference of an emission slit width of 20 nm.

Atomic Force Microscopy (AFM) measurements were performed by Dr. Philippe Leclère under the experimental conditions described in Chapter 3.

Synthesis of S-Mn-Me

Anhydrous Mn(OAc): (500 mg, 2.89 mmol) was suspended with a solution of S-FB-Me (see Chapter 2, −500 mg, −0.17 mmol) in chloroform (10 mL) with MeOH (5 mL) and refluxed overnight with the protection from light. The green suspension was filtered and the filtrate was evaporated to dryness.

The product was purified by column chromatography (Biotage; 10%→50% over 10 cv’s (SNAP 50 g) EtOAc/Chloroform) and further purified by preparative-scale recycling gel-permeation chromatography. MALDI-TOF MS: [M]+ calcd. for C₁₉₀H₂₈₈N₄O₁₈Mn: 3075.20, found 3076.53 D.

Thermodynamic modeling

A multiple equilibrium modeling study was performed by dr. Takashi Hirose using MATLAB® (R2010a, version 7.10.0.499, win 32). In the model, seven different species were considered: free porphyrin monomers [A], porphyrin stacks [Agg], DABCO ligands [B], porphyrin:DABCO 1:1 monomer complexes [C], porphyrin:DABCO 2:2 dimer complexes [C]₄, porphyrin:DABCO sandwich complexes [D] and a series of stacked sandwich complexes with n DABCO units [D]ₙ, [CD]ₙ, and [CₙD]ₙ. The total concentrations of porphyrin [A]₀ and DABCO [B]₀ were described according to Equations 5.1 and 5.2.

\[
[A]₀ = \frac{\sigma[A]}{(1 - K[A])^2} + \frac{2[D] + 2Kₐ[C][D](1 + Kₐ[C])}{(1 - Kₐ[D])^2} + \frac{Kₐ[C][D](1 + 2Kₐ[C])}{1 - Kₐ[D]} + (1 - \sigma)[A] + [C] + 2Kₐ[C]^2 \tag{5.1}
\]

\[
[B]₀ = \frac{[D] + Kₐ[C][D](1 + Kₐ[C])}{(1 - Kₐ[D])^2} + \frac{Kₐ[C][D](1 + 2Kₐ[C])}{1 - Kₐ[D]} + [B] + [C] + 2Kₐ[C]^2 \tag{5.2}
\]

Herein, \(\sigma\) represents the degree of cooperativity (\(Kₐ / K\)) with dimerization constant (\(Kₐ\)) and elongation constant (\(K\)). The concentration of the porphyrin:DABCO 1:1 monomer complexes [C] and sandwich complex [D] is given by Equations 5.3 and 5.4.
Two-component Zn-porphyrin self-assembly with DABCO

\[ [C] = 2K_c[A][B] \]  \hspace{1cm} (5.3)

\[ [D] = \frac{aK_c^2[A]^2[B]}{2} \]  \hspace{1cm} (5.4)

The mass balances are rearranged into Equations 5.5 and 5.6 with so that the Jacobian matrix can be constructed (5.11).

\[ F(1) = \sigma[A][D] + 2K_cABC(1 + K_cB) + K_cABC(1 + K_cB)(1 - K_cC) + AD[(1 - \alpha)[A] + B + 2K_cB^2 - [B]_b] \]  \hspace{1cm} (5.5)

\[ F(2) = C + K_cBC(1 + K_cB) + K_cBC(1 + K_cB)(1 - K_cC) + D([B] + B + 2K_cB^2 - [B]_b) \]  \hspace{1cm} (5.6)

Herein, A, B, C and D are represented by Equations 5.7-5.10.

\[ A = (1 - K[A])^2 \]  \hspace{1cm} (5.7)

\[ B = K_c[A][B] \]  \hspace{1cm} (5.8)

\[ C = \frac{aK_c^2[A]^2[B]}{4} \]  \hspace{1cm} (5.9)

\[ D = (1 - K_cC)^2 \]  \hspace{1cm} (5.10)

\[ J = \begin{bmatrix}
\frac{\partial}{\partial[A]} F(1) & \frac{\partial}{\partial[B]} F(1) \\
\frac{\partial}{\partial[A]} F(2) & \frac{\partial}{\partial[B]} F(2)
\end{bmatrix} \]  \hspace{1cm} (5.11)

\(^1\)H-NMR titration

The NMR titration experiment and the data analysis were performed by Marko Nieuwenhuizen. At a concentration of \(5.0 \times 10^{-4} \text{ M S-Zn-Me} \) in D14-MCH (600 \( \mu \text{l} \)), a mixture of DABCO (5.0 \times 10^{-3} \text{ M}) and S-Zn-Me (5.0 \times 10^{-4} \text{ M}) in D14-MCH was added by a syringe and the samples were equilibrated for 15 min prior to each measurement. Relative to TMS, the chemical shift of the gallic proton was recorded and plotted against the molar excess of DABCO. The titration curve was fitted in MATLAB to the model reported by Anderson.\(^{30}\)

5.8 References


Chapter 5


8. Considering the plateau in the DABCO titration curve from a molar excess of 0.5 onwards samples for AFM and the titration of S-Mn-Me is prepared at a molar excess of 1. At this composition, the highest Cotton effect is acquired and the absence of S-Zn H-type aggregates is ensured.

9. The titration data at lower concentration reveals a more gradual transition, which is attributed to dilution-induced self-assembly, which is implemented in the model.


Chiral amplification in porphyrin assemblies: a mixing study

Abstract. The mixing behavior of different porphyrin monomers was investigated by probing the supramolecular chirality of the mixed assemblies. Herein, chiral amplification experiments revealed the subtle role of the structural (mis)match between different porphyrin monomers. According to the Sergeant-and-Soldiers principle, it was shown that a chiral porphyrin Sergeant efficiently mixes with achiral Soldiers in the same helical aggregate and strongly biases its handedness. However, when two porphyrin enantiomers were mixed in a Majority-Rules experiment, no chiral amplification was observed at all, which was due to their narcissistic self-sorting into conglomerate-like aggregates. Mixed-metal chiral amplification experiments between copper- and zinc-porphyrins showed the same distinction in their mixing behavior, which was further supported by fluorescence measurements. The mixing between two enantiomers in the same stack only occurred in a Diluted-Majority-Rules experiment, in which enantiomeric mixtures of Sergeants were diluted with achiral Soldiers. The different outcomes of these chiral amplification phenomena were verified by modeling studies that revealed high mismatch penalties, which were ascribed to the high stereocenter loading of twelve methyl groups onto the monomers. In the Majority-Rules experiments, the formation of conglomerates allowed for the induction of the supramolecular chirality by the selective depolymerization of one helical aggregate type. For mixed metal conglomerates this was achieved by the selectivity of Lewis bases towards Zn- and Cu-porphyrins, while for conglomerates of the Zn-porphyrin enantiomers, this was achieved by chiral recognition of a chiral Mn(III)-porphyrin chain-stopper.

Part of this work has been published:
6.1 Introduction

In the previous chapters, we have studied the multi-component self-assembly of Zn-porphyrin monomers in the presence of competing axial ligands. These responsive systems provided insights into the thermodynamic distribution of different aggregate types of the same building block. A higher level of complexity arises when multiple building blocks are considered. Especially for non-discrete systems it is relatively difficult to control the organization of different chromophores, which is a highly important aspect in the bottom-up strategy for functional devices. In the previous chapter, the introduction of monotopic Mn-porphyrins to a non-discrete alternating copolymer allowed for selective positioning at the end of the aggregate. However, the positional control over multiple ditopic building blocks is less straightforward. The self-sorting of molecules provides valuable insights into this positional control. In synthetic self-assembled systems, self-sorting behavior is often the result of the directionality of non-covalent interactions combined with steric constraints as shown for discrete rotaxane, triangular and dendritic structures. High-fidelity behavior could also be achieved by enantiomeric self-recognition, in which the expression of chiral information leads to narcissistic self-sorting. Interestingly, the supramolecular chirality of aggregates containing different chromophoric building blocks can be exploited as a novel tool to control their mutual organization.

Different approaches have been exploited in order to control the helicity of racemic superstructures; for instance by the employment of chiral auxiliaries, enantioselective physical stimuli, and chiral amplification. In the latter approach, Sergeant-and-Soldiers experiments show that by mixing-in a chiral Sergeant with achiral Soldier monomers, the handedness of helical aggregates containing predominantly achiral Soldiers is biased by the chiral Sergeant. This results in a strong non-linear chiroptical response, which is also observed in many Majority-Rules and Diluted-Majority-Rules experiments. In these experiments, the helicity of an aggregate comprising of two opposite enantiomers is dominated by the enantiomer in excess ($\varphi$), and in case of the Diluted-Majority-Rules, achiral Soldiers are added to the system as well. The non-linear response of the optical activity in these chiral amplification experiments is caused by the subtle interplay of secondary interactions inside the supramolecular polymer. An enantiomeric imbalance introduced by one of the monomers is sufficient to transfer the chiral information to the supramolecular level; provided that both monomers are assembled in the same supramolecular polymer, which we refer to the term “coaggregation”. For self-assembly of discotic molecules, the strength of these secondary interactions depends on the location, number, and type of stereogenic centers in the chiral monomer. Over the years, our group has studied these effects in detail, for instance by using different alkyl substituted, C-symmetrical benzene-1,3,5-tricarboxamides (BTAs). In chiral amplification studies, predictive models have been
developed and employed to deduce the interplay of secondary interactions in terms of two different energy penalties paid when different monomers are coaggregated.\textsuperscript{15} Herein, the helix reversal penalty (HRP) describes the energy penalty of a helix reversal in the aggregate, whereas the mismatch penalty (MMP) is related to the incorporation of a chiral monomer in a helical aggregate of its unpreferred helicity.

In this chapter, these energy penalties are deduced from Sergeant-and-Soldiers and Majority-Rules experiments, in which porphyrins having different metals and different stereochemistries are mixed. The porphyrin library contains members with s-chiral (‘S’), r-chiral (‘R’) and achiral (‘A’) solubilizing chains at the periphery and zinc (‘Zn’) or copper (‘Cu’) metal ions in the core (Scheme 6.1). The different metal centers allow for fluorescence quenching studies and selective depolymerizations (see Section 7.2), while the methylene groups attached to the stereocenters bias the helical direction of the aggregate as evidenced by strong CD effects in the aggregate Soret absorbance (see Section 2.3/2.4). Firstly, we discuss the chiral amplification of Zn-porphyrins where we describe the Sergeant-and-Soldiers experiments between R/S-Zn and A-Zn, after which we perform Majority-Rules experiments with both porphyrin enantiomers.

![Scheme 6.1. Chiral/achiral amide-functionalized tetraphenyl-zinc/copper-porphyrins used in this study.](image)

### 6.2 Chiral amplification of Zn-porphyrins at room temperature

As shown in Chapter 2, all porphyrin monomers show the same aggregate type when prepared by injection of a concentrated chloroform solution in methylcyclohexane (MCH). For all chiral amplification experiments, aggregates are prepared by rapid injection of a 2.01×10^{-4} M mixed monomer solution in chloroform (25 μL) in 5.00 mL MCH that results in a porphyrin concentration of 1.0×10^{-6} M at 0.5 v% chloroform. This procedure results into structured H-type aggregates with a λ\textsubscript{max} at ~390 nm in the UV-vis spectrum, which represents the presence of extended cofacial aggregates. Furthermore, this preparation method affords thermodynamically stable coaggregates in a remarkably quicker and more efficient way than mixing-in pre-aggregated porphyrins in MCH, which is attributed to slow supramolecular dynamics (see Section 7.2).
Since chiral Sergeant monomers of S-Zn and achiral Soldier monomers of A-Zn form the same H-type aggregate when prepared by chloroform injection, the UV-vis spectra of their mixtures at a total constant concentration of $1.0 \times 10^{-6}$ M remain similar (Figure 6.1A). However, upon increasing the fraction of S-Zn, the CD intensity increases non-linearly with the composition; going from a CD silent state of pure A-Zn\textsuperscript{16} to a saturated, CD active state at $\sim 10\%$ S-Zn showing a negative Cotton effect at $\lambda_{\text{max}} \sim 391$ nm (Figure 6.1B). This indicates that the Sergeant comonomer transfers its own chirality to achiral A-Zn comonomers yielding a helical aggregate with a single handedness. Mirror-image CD spectra are acquired for the Sergeant-and-Soldiers experiment between R-Zn and A-Zn, which shows a positive Cotton effect at $\lambda_{\text{max}} \sim 391$ nm (Figure 6.1C). At a given composition, the Cotton effect at 391 nm is normalized to the maximum Cotton effect at $\sim 10\%$ Sergeant and this net helicity is subsequently plotted against the fraction Sergeant, which shows mirror-image behavior of R-Zn with A-Zn and S-Zn with A-Zn (Figure 6.1D). Both Sergeant-and-Soldiers experiments are simultaneously fitted with a modified model developed by van der Schoot.\textsuperscript{15a} The least-square fit on the experimental data in Figure 6.2D yields two dimensionless energy penalties; $\sigma$ and $\omega$ that represent the HRP and MMP, respectively via $\sigma = \exp[-2 \text{HRP}/RT]$ and $\omega = \exp[-\text{MMP}/RT]$. The contour plot of the sum of squared residuals reveals which set of HRP and MMP provides an accurate fit on the Sergeant-and-Soldiers data; hence we can determine a HRP of $\sim 14$ kJ mol$^{-1}$ quite accurately albeit an accurate determination of the MMP is difficult because of the wide spread in the plot for this penalty (Figure 6.1E). The minimum of the contour plot of the sum of squared residuals is found at 16.6 and 0.2 kJ mol$^{-1}$ for the HRP and MMP, respectively (Table 6.1). Similar values for the HRP have been deduced for stacks of BTAs.\textsuperscript{15a} In accordance with these chiral amplification experiments, the high value for the HRP in the porphyrin system is attributed to the 4-fold hydrogen bonding motif that causes a high energy barrier to overcome a helix reversal in the aggregate.
Figure 6.1. UV-vis (A) and CD (B) spectra of the S-Zn:A-Zn Sergeant-and-Soldiers experiment, in which each spectrum represents a specific mole fraction S-Zn at a total porphyrin concentration of $1.0 \times 10^{-6}$ M in MCH. C: CD spectra of the Sergeant-and-Soldiers between R-Zn and A-Zn. D: The net helicity as a function of the fraction Sergeants R-Zn and S-Zn for both experiments with an overlay of the data at $\sigma = 1.41 \times 10^{-4}$ and $\omega = 0.135$ (10.8 and 4.9 kJ·mol$^{-1}$) for the HRP and MMP, respectively. E: Contour plot of the sum of squared residuals obtained from fitting both R/S-Zn:A-Zn Sergeant-and-Soldiers data with the minimum at which the dotted lines cross ($\sigma = 1.3 \times 10^{-6}$ and $\omega = 0.9$).
In order to obtain a more accurate determination of the MMP, Majority-Rules experiments are performed between **R-Zn** and **S-Zn**. Similarly to the mixing with achiral porphyrins, no significant changes are observed in the UV-vis spectrum upon changing the ratio between both enantiomers (Figure 6.2A). Figure 6.2B shows the CD spectra of different enantiomeric mixtures at 1.0×10⁻⁶ M; going from pure **R-Zn** (ee = 100%), through **R-Zn:S-Zn** (1:1) (ee = 0%) to pure **S-Zn** (ee = −100%). By normalizing the Cotton effects at λmax ~ 392 nm, the net helicity versus the ee is constructed, which shows almost a linear trend (Figure 6.2C). Apart from the net helicity originating from the enantiomerically pure samples, the linear relationship indicates that chiral amplification is absent,⁴ which is in contrast to what has been observed for BTAs¹⁵a and other supramolecular polymers.¹⁷ In the case of chiral amplification, saturated CD effects are observed at ee values far below 100% indicative of a homochiral supramolecular system containing enantiomeric mixtures. The data are fitted with the Majority-Rules model⁴b and from a similar contour plot a wide spread in the HRP is found (Figure 6.2D), which makes an accurate estimation of this penalty difficult. The MMP on the other hand can be accurately determined at ~4 kJ·mol⁻¹, while the overall minimum of the contour plot is found at 5.6 and 3.4 kJ·mol⁻¹ for the HRP and MMP, respectively (Table 6.1).

Similarly as shown for BTAs,¹⁵a we can obtain a single value for both energy penalties by considering the contour plots of both Sergeant-and-Soldiers (Figure 6.1E) and Majority-Rules (6.2D) experiments. This overall minimum is estimated at 10.8 and 4.9 kJ·mol⁻¹ for the HRP and MMP, respectively. The simulation corresponding to these energy penalties overlays both chiral amplification data sets very well (Figure 6.1D and Figure 6.2C, Table 6.1). These values are quite close to each other and reveal considerable energy penalties for both the HRP and MMP, indicating that it is highly unfavorable to both reverse a stack from one handedness to the other and to incorporate a chiral monomer in a stack of its opposite chirality. In these analyses, both energy penalties seem to be related to structural aspects of the monomer; strong hydrogen bonding in the former¹⁵a and a high structural mismatch originating from twelve methyl groups in the latter. As a consequence, the likelihood of that opposite enantiomers coaggregate would be significantly reduced when both energy penalties are high in this system; ultimately leading to narcissistic self-sorting into conglomerates comprising stacks with **R-Zn** or **S-Zn** only.
Figure 6.2. UV-vis (A) and CD (B) spectra of the R-Zn:S-Zn Majority-Rules, in which each spectrum represents a specific enantiomeric excess (ee) at a total porphyrin concentration of 1.0×10^{-6} M in MCH. C: The net helicity as a function of ee with an overlay of the data at σ = 1.41×10^{-4} and ω = 0.135 (10.8 and 4.9 kJ·mol^{-1}) for the HRP and MMP, respectively. D: Contour plot of the sum of squared residuals obtained from fitting the R-Zn:S-Zn Majority-Rules data with the minimum at which the dotted lines cross (σ = 1.0×10^{-2} and ω = 0.25).

The extent of self-sorting herein is tested by the investigation of cooling curves performed at a total concentration of 1.0×10^{-6} M on solutions of pure R-Zn (ee = 100%), S-Zn (ee = -100%) and at a 1:1 mixture of these enantiomers at ee = 0%. Considering the small plateau observed in the Majority-Rules plot at high ee-values (Figure 6.2C), we expect the strongest tendency of S-Zn and R-Zn to self-sort ee = 0%. Figure 6.3A shows the CD intensity at 392 nm upon cooling a solution of R-Zn (ee = 100%) and S-Zn (ee = -100%) from the molecularly dissolved state at 65 °C to 20 °C at 30 °C/h, which reveals non-sigmoidal cooling curves indicative for their highly cooperative self-assembly (see Section 2.3). The cooling curves for pure R-Zn and S-Zn are exact mirror images; both have a sharp transition at T_c = 54.2 °C and saturate at 79 and ~78 mdeg, respectively. After converting the CD data to the dimensionless net helicity, both datasets are simultaneously fitted with a temperature-dependent nucleation-elongation model\textsuperscript{18} from which an enthalpy release of 130 kJ·mol^{-1} is estimated. In the hypothesis of the
formation of supramolecular conglomerates of R-Zn and S-Zn, no coaggregation of opposite enantiomers takes place, which implies an orthogonal self-assembly process upon cooling the mixture at \( ee = 0 \% \). When cooling this 1:1 mixture of R-Zn and S-Zn at 1.0\times10^{-6} \text{ M} no CD activity is observed due to equal abundance of both enantiomers, yet when probing the self-assembly process by UV-vis at \( \lambda_{\text{max}} \sim 390 \text{ nm} \), a similar, non-sigmoidal trend is observed with \( T_c = 49.8 \, ^\circ\text{C} \) (Figure 6.3A).\(^{19}\) By using Van’t Hoff relation, in which we correlate the total concentration to \( T_c \) at a fixed enthalpy value of 130 \text{ kJ}\cdot\text{mol}^{-1}, we obtain a porphyrin concentration of 5.0\times10^{-7} \text{ M} that matches the \( T_c \) of the 1:1 mixture; exactly half the concentration of the enantiomerically pure systems (see experimental section). This temperature analysis clearly indicates that both porphyrin enantiomers prefer the formation of their own stack with their own handedness, which is caused by the high structural mismatch. With this finding, we exceed an upper-boundary for the mismatch penalty in chiral amplification, which is in contrast with the lower-boundary we observed earlier for chiral deuterium-substituted BTAs that do not show a Majority-Rules effect due to the lack of helical bias induced by the isotope.\(^{14a}\)

**Table 6.1.** Overview of the helix reversal penalty (HRP) and the mismatch penalty (MMP) after fitting the different chiral amplification experimental data.

<table>
<thead>
<tr>
<th>Experiment (Figure)</th>
<th>Porphyrin mixture</th>
<th>HRP [\text{kJ}\cdot\text{mol}^{-1}]^c</th>
<th>MMP [\text{kJ}\cdot\text{mol}^{-1}]^c</th>
</tr>
</thead>
<tbody>
<tr>
<td>SS(^a) (6.1)</td>
<td>R/S-Zn:A-Zn</td>
<td>16.6</td>
<td>0.2</td>
</tr>
<tr>
<td>MR(^b) (6.2)</td>
<td>R-Zn:S-Zn</td>
<td>5.6</td>
<td>3.4</td>
</tr>
<tr>
<td>Average(^c) (6.1D/6.2C)</td>
<td>R/S/A-Zn</td>
<td>10.8</td>
<td>4.9</td>
</tr>
<tr>
<td>SS(^a) (6.5A/B)</td>
<td>S-Cu:A-Zn</td>
<td>14.3</td>
<td>0.7</td>
</tr>
<tr>
<td>SS(^a) (6.5C/D)</td>
<td>S-Zn:A-Cu</td>
<td>19.4</td>
<td>0.1</td>
</tr>
<tr>
<td>MR(^b) (6.6)</td>
<td>R-Zn:S-Cu</td>
<td>15.4</td>
<td>11.2</td>
</tr>
<tr>
<td>dMR(^d) (6.9)</td>
<td>R-Zn:S-Cu:A-Cu</td>
<td>9.5</td>
<td>2.6</td>
</tr>
</tbody>
</table>

\(^a\): SS, Sergeant-and-Soldiers  
\(^b\): MR, Majority-Rules  
\(^c\): For the contour plots in Figure 6.1E and 6.2D, the sum of squared residuals was normalized, added to each other and divided by 2. The resulting plot shows a similar narrow region as in Figure 6.1E, but the minimum is found at lower \( \omega \)-values due to the influence of Figure 6.2D. The absolute minimum is found at \( \sigma = 1.4\times10^{-4} \) and \( \omega = 0.14 \) and the corresponding fit is shown in both amplification phenomena in Figure 6.1D and 6.2C.  
\(^d\): dMR, Diluted-Majority-Rules  
\(^c\): The values for HRP/MMP are obtained from the minimum of the contour plots. While these values provide the best fits on the amplification curves, multiple combinations of HRP/MMP also provide satisfactory data representations as designated by the contour plots.
Chiral amplification in porphyrin assemblies: a mixing study

Figure 6.3. A: Cooling curves performed from the molecularly dissolved state at 65 to 20 °C at 30 °C/h in MCH at 1.0×10⁻⁶ M for pure R-Zn and S-Zn enantiomers probed by CD at 392 nm (left axis) and the enantiomeric (1:1) mixture at ee = 0% probed by UV-vis at 390 nm (right axis). B: UV-vis (upper panel) and CD (lower panel) spectra of R-Zn:S-Zn (1:1) at 4.0×10⁻⁵ M upon titration of S-Mn at different pseudo-enantiomeric excesses (‘ee’).²⁰

The strong structural mismatch between opposite enantiomers precludes their coaggregation, indicating that the confinement of space inside the aggregate is insufficient for the formation hydrogen bonds on both sides of the porphyrin faces. The formation of conglomerates is beneficial for enantiospecific interactions that affect one aggregate type only that, for instance, allows for the induction of supramolecular chirality at ee = 0. Considering the structural intrusion of opposite enantiomers inside the stacks, it is hypothesized that a level of steric hindrance is also operative at the end of the stack, yet to a minor extend. In this investigation, S-Mn is introduced as a third component that selectively interacts with the end of the stacks due its monotopic properties (see Section 2.4.1). At a total porphyrin concentration of 4.0×10⁻⁵ M, an equal amount of S-Zn and R-Zn (both at 2.0×10⁻⁵ M; ee = 0) is dissolved in MCH giving rise to a CD-silent spectrum (Figure 6.3B, lower panel). The addition of S-Mn is evidenced by a decrease in luminescence of the solutions (data not shown) and its absorbance over the whole spectral range with the Soret band at λmax ~ 474 nm (Figure 6.3B, upper panel). Interestingly, the changes in the absorbance spectra are accompanied by an upcoming Cotton effect that corresponds to R-Zn, which shows a positive CD effect at λmax (Figure 6.1C). This indicates that the chain-stopper has an increased affinity for the S-Zn conglomerate relative to the R-Zn conglomerate (Figure 6.4, left). Here, enantiospecific chain-stopping leads to the enhanced depolymerization of the conglomerate of the same chirality; hence its enhanced reduction of the CD intensity leads to the appearance of the CD spectrum of the other conglomerate. Under the applied conditions, a maximum Cotton effect is achieved by the addition of 0.5 molar excess S-Mn (2.0×10⁻⁵ M), which corresponds to a “pseudo-enantiomeric excess” (‘ee’) of -33%.²⁰ By crude comparison, this CD effect of +30
mdeg (optical pathway \(l\) = 1 mm at \(6.0 \times 10^{-5}\) M) can be extrapolated to +5 mdeg at \(l = 10\) mm and \(1.0 \times 10^{-6}\) M, while a CD-effect of approximately -25 mdeg is expected for the Majority-Rules at \(ee = -33\%\) under the latter conditions (Figure 6.2B/C); approximately 20\% of the opposite Majority-Rules effect is observed. On the other hand, by similar extrapolation (+79 mdeg, \(l = 10\) mm at \(1.0 \times 10^{-6}\) M, Figure 6.2B) stacks of pure \(R\text{-Zn}\) give rise to a Cotton effect of +158 mdeg at \(l = 1\) mm and \(2.0 \times 10^{-5}\) M; interestingly, the observed +30 mdeg also corresponds to an effect ~20\%, which could be a measure for its selectivity. Apparently, only by the exchange of the metal ion form Zn(II) to Mn(III), the role of the enantiomer in excess changes; going from a Majority-Rules effect to a “pseudo-Minority-Rules” effect in which the supramolecular chirality of the enantiomer in minority remains stable.

![Figure 6.4](image)

**Figure 6.4.** Schematic representation of the selective chain-stopping of the \(S\text{-Zn}\) conglomerate by the addition of \(S\text{-Mn}\) to \(R\text{-Zn}:S\text{-Zn}\) (1:1) (left) and the selective depolymerization of \(R\text{-Zn}\) by the addition of quinuclidine to \(R\text{-Zn}:S\text{-Cu}\) (1:1) (right, see Section 6.3.2).25

### 6.3 Chiral amplification of mixed-metal porphyrins at room temperature

In the present library, Cu-porphyrins are non-emissive whereas Zn-porphyrins are highly emissive, albeit their fluorescence is partially quenched upon aggregation.21 Still, the remaining aggregate fluorescence is more than sufficient for quenching studies with Cu-porphyrins that act as an energy trap when the two metal porphyrins are coaggregated,22 thereby monitoring the mixing of porphyrins with fluorescence. In the upcoming mixed-metal Sergeant-and-Soldiers and Majority-Rules experiments, the amplification of chirality is compared with the quenching of the fluorescence, which is determined by normalizing the emission intensity of the mixture to the emission of the pure Zn-porphyrin donor at \(\lambda_{em,max} \sim 604\) nm.
6.3.1 Mixed-metal Sergeant-and-Soldiers

The coaggregation of \textbf{S-Cu} and \textbf{A-Zn} is investigated by the Sergeant-and-Soldiers principle, in which chiral amplification and energy transfer are studied simultaneously. After preparation of mixtures with different feed ratios of \textbf{S-Cu} and \textbf{A-Zn} by chloroform injection at a total porphyrin concentration of 1.0×10^{-6} M, the UV-vis and CD spectra are acquired. While the absorbance spectra remain identical upon increasing the fraction of \textbf{S-Cu} Sergeant, strong chiral amplification is observed in the CD spectra (Figure 6.5A, \textit{upper panel}). Modeling of these data results in a HRP of 14.3 kJ mol^{-1} and a MMP of 0.7 kJ mol^{-1} (Figure 6.5B, Table 6.1), which is in line with the energy penalties deduced for the \textbf{S-Zn} and \textbf{A-Zn} system. A similar trend is observed for the quenching of the fluorescence of \textbf{A-Zn} upon addition of non-emissive \textbf{S-Cu} that acts as an energy trap in the coaggregate (Figure 6.5A, \textit{lower panel}, 6.5B).\textsuperscript{22} Notably, both processes seem to follow the same non-linear trend as shown at the composition of 10\% \textbf{S-Cu}, where both the Cotton effect has saturated and the non-linear quenching behavior ceases (Figure 6.5B). Similar mixing properties between chiral Sergeant and achiral Soldier porphyrins is observed for the reversed \textbf{S-Zn:A-Cu} system. Upon increasing the fraction of \textbf{S-Zn}, the upcoming CD effect of the \textbf{A-Cu} backbone reveals a slightly stronger chiral amplification (HRP = 19.4 kJ mol^{-1}, MMP = 0.10 kJ mol^{-1}, Figure 6.5C, \textit{upper panel}, 6.5D, Table 6.1).\textsuperscript{19} Considering the high fraction of non-emissive \textbf{A-Cu} in this experiment (80-100\%), the aggregate fluorescence is fully quenched for all mixtures as shown by luminescence spectra (Figure 6.5C, \textit{lower panel}).

The mixed-metal Sergeant-and-Soldiers experiments are highly similar to the same experiments performed on the homo-zinc system (\textit{vide supra}). It should be noted that the expression of the chiral amplification behavior in terms of the MMP and HRP, as outlined in Table 6.1, relies on a delicate combination for both energy penalties. Here, the wide spread of minima in the contour plots of squared residuals affords a good fit of the data at multiple sets of MMP and HRP. Still, the similarity between all Sergeant-and-Soldiers experiments reveals that the nature of the center metal ion does not strongly affect chiral amplification.
Figure 6.5. A: CD (upper panel) and PL (lower panel) spectra of the mixed-metal Sergeant-and-Soldiers between S-Cu and A-Zn at 1.0×10⁻⁶ M. B: Net helicity (left axis) and fluorescence quenching (right axis) of the experiment with the curve fit on the net helicity at 14.3 and 0.7 kJ·mol⁻¹ for the HRP and MMP, respectively. C: CD (upper panel) and PL (lower panel, same slit settings as in A) spectra of the mixed-metal Sergeant-and-Soldiers between S-Zn and A-Cu at 1.0×10⁻⁶ M. D: Net helicity (left axis) and fluorescence quenching (right axis) of the experiment with the curve fit on the net helicity at 19.4 and 0.1 kJ·mol⁻¹ for the HRP and MMP, respectively.

6.3.2 Mixed-metal Majority-Rules

Since a marginal metal-dependency is found for the chiral amplification behavior and that aggregate fluorescence can be used as a probe to investigate porphyrin coaggregation, we investigate the mixed-metal Majority-Rules experiment between R-Zn and S-Cu. Analogously to the Majority-Rules between R-Zn and S-Zn, samples are prepared in MCH by injection of monomer mixtures containing R-Zn and S-Cu at different ‘ee’ in chloroform at 1.0×10⁻⁶ M.²⁰ Since enantiomeric mixtures with the copper analogue of the S-Zn enantiomer are prepared, spectral differences in the UV-vis and CD spectra between S-Cu and S-Zn are observed. As a result, R-Zn and S-Cu are not exactly mirror images and the ‘ee’ = 0% sample
does not reveal a completely CD silent spectrum (Figure 6.6A, upper panel). Still, when the CD intensity at 392 nm is used to construct net helicity versus ‘ee’, a straight line is obtained (Figure 6.6B). This linear relationship is even more pronounced than for the homo-metal analog of the Majority-Rules, which is also expressed by the energy penalties obtained after fitting the data; 15.4 and 11.2 kJ mol⁻¹ for the HRP and MMP, respectively (Table 6.1). These chiral amplification data, in particular the high value for the MMP, clearly indicates that coaggregation between enantiomers is highly unfavorable, which can also be observed in the fluorescence response. As constructed from the emission spectra (Figure 6.6A, lower panel), only a weak deviation from linearity in the aggregate fluorescence is observed, which indicates that quenching occurs only to a small extent. This is probably caused by (monomeric) Cu-porphyrin energy acceptors that approach the Zn-porphyrin stacks within the Föster distance. Quenching due to face-to-face stacking at the Zn-Cu-porphyrin heterojunction would significantly enhance fluorescence quenching as we observe for the mixed-metal Sergeant-and-Soldiers (Figure 6.5B). In this Majority-Rules experiment, only ~20% quenching is observed at 10% S-Cu (‘ee’ = 80), which is significantly less than the ~80% observed in the former experiment. This excludes a significant contribution to the quenching due to cofacial stacking.

![Figure 6.6](image)

**Figure 6.6.** A: CD (upper panel) and PL (lower panel) spectra of the mixed-metal Majority-Rules between R-Zn and S-Cu at 1.0×10⁻⁶ M. B: Net helicity (left axis) and fluorescence quenching (right axis) of the experiment with the curve fit on the net helicity at 15.4 and 11.2 kJ mol⁻¹ for the HRP and MMP, respectively.²⁰

The mixed-metal Majority-Rules experiment reveals the similar mixing properties as found for the homo-zinc system. Therefore, a similar Tₑ is performed at ‘ee’ = 0% in order to evidence the formation of conglomerates of R-Zn and S-Cu, in which we can take advantage of the stability difference of these two pseudo-enantiomers (see Figure 2.8B, Table 2.1). The cooling curves show that R-Zn is more stable than S-Cu as evidenced by their difference in Tₑ at 53.7 and 51.6 °C, respectively (Figure 6.7A).²³ Analogously to the Tₑ analysis for R/S-Zn,
the enthalpy release for the pure enantiomers is obtained after fitting both cooling curves, while we probe the cooling of the **R-Zn:S-Cu** (1:1) mixture with CD at 392 nm. When cooling this mixture at ‘ee’ = 0% and 1.0×10⁻⁶ M, a positive CD response is observed at 49.6 °C; corresponding to the aggregation of **R-Zn**. Upon further cooling, the growth in optical activity ceases due to the aggregation of **S-Cu**, which starts at 47.0 °C. In their Van ‘t Hoff analyses, both transition temperatures correspond to the predicted T/s at 5×10⁻⁶ M for **R-Zn** and **S-Cu**, respectively (see experimental section). At lower temperatures, a nearly CD-silent state is obtained again due to the equal abundance of both aggregates with opposite helicity.

**Figure 6.7.** A: Cooling curves performed from the molecularly dissolved state at 65 to 20 °C at 30 °C/h in MCH at 1.0×10⁻⁶ M for pure **R-Zn** and **S-Cu** enantiomers and the pseudo-enantiomeric (1:1) mixture at ‘ee’ = 0% probed by CD at 392 nm. B: CD spectra of **R-Zn:S-Cu** (1:1) at 1.0×10⁻⁶ M before and after the addition of quinuclidine (1.0×10⁻² M).²⁰

Similarly as shown in the previous section, we can take advantage of the formation of conglomerates by the induction of supramolecular chirality using molecular recognition elements. While it has been shown that **S-Mn** acts as an enantiospecific chain-stopper for the chiral induction of the enantiomer in minority (vide supra), we now investigate the selective depolymerization of **R-Zn** in a 1:1 mixture of **R-Zn** and **S-Cu** (Figure 6.4, right). Driven by the considerable affinity difference between Zn- and Cu-porphyrins towards Lewis bases (see Section 7.2),²⁴ quinuclidine (QND) is employed as a third compound to selectively depolymerize the Zn-porphyrin enantiomer. Before the addition of QND, the sample at ‘ee’ = 0% shows a CD effect due to the spectral difference and stability between aggregates of **R-Zn** and **S-Cu** (Figure 6.7B). After the addition of a 10000 molar excess of QND (1.0×10⁻² M), the CD spectrum considerable changes; going from a positive Cotton effect of +10 mdeg to a negative Cotton effect of -40 mdeg at λ_{max}. In the next chapter, we further investigate this responsivity by (time-dependent) UV-vis and CD studies.
6.4 Diluted-Majority-Rules: *between* Sergeant-and-Soldiers and Majority Rules

The chiral amplification experiments between mixed-metal porphyrins reveal the same features of porphyrin coaggregation as observed for the Zn-porphyrins; under the applied conditions, coaggregation of achiral and chiral porphyrins is feasible, unlike the coaggregation of opposite enantiomers (Figure 6.8). For the latter, the formation of conglomerates allows for the induction of supramolecular chirality by enantiospecific recognition and molecular recognition. Considering the ease of helical induction of Sergeant comonomers to the achiral backbone and the high energy barrier caused by the structural mismatch between the opposite enantiomers, we would like to investigate the possibility if the opposite enantiomers coaggregate in a stack that contains achiral Soldiers as well (Figure 6.8).

![Figure 6.8. Schematic representation of the distinctive coaggregated states in Sergeant-and-Soldiers and Majority-Rules mixtures and the intermediate state for Diluted-Majority-Rules.](image)

In order to investigate this possibility, we use the Diluted-Majority-Rules principle,\textsuperscript{15a,11c,11d} in which enantiomeric mixtures of R-Zn and S-Cu Sergeants are ‘diluted’ with A-Cu Soldiers. The samples are prepared by chloroform injections of R-Zn/S-Cu/A-Cu monomer mixtures in MCH to a porphyrin concentration of 1.0×10^{-6} M. Figure 6.9A shows the Sergeant-and-Soldiers representation of this experiment with the CD effect at λ_{max} ~ 390 nm *versus* the fraction Sergeant, which represents *pseudo*-enantiomeric mixtures of R-Zn and S-Cu at ‘ee’ = 25, 50 and 75%.\textsuperscript{20} The ‘ee’ = 100% series herein represents the Sergeant-and-Soldiers of R-Zn and A-Cu, which is considered as the mirror image of S-Zn and A-Cu (‘ee’ = −100%).\textsuperscript{20} Similar to the Sergeant-and-Soldiers principle, the Diluted-Majority-Rules experiments show non-linear amplification curves towards positive CD values originating from the majority of R-Zn, in which higher ‘ee’ values result in higher CD effects. The data at 100% Sergeant represents the Majority-Rules experiment between R-Zn and S-Cu, which shows considerably lower CD effects at this wavelength. This difference is related to sharpness of the absorbance bands in the CD spectrum and the difference in CD spectra between amplified, achiral porphyrin aggregates and intrinsically chiral aggregates. Moreover, the intensity of the Cotton effect appears to be dependent on the degree of
coaggregation; despite opposite enantiomers experience high MMP’s, they participate in the aggregate by coupling their transition dipole moments in the unfavorable helical sense, thereby enhancing the CD effect. Compared to the Sergeant-and-Soldiers experiment at ‘ee’ = 100%, it can also be observed that a higher fraction of Sergeant is necessary in order to obtain a fully homochiral system when the ‘ee’ is lowered. From the amplification curves in Figure 6.9A it remains difficult to estimate whether coaggregation between both enantiomers takes place, however, when these Diluted-Majority-Rules data are represented in a Majority-Rules plot, an obvious deviation from linearity is observed. This representation in Figure 6.9B shows the linear response between the net helicity and ‘ee’ at 0% A-Cu; corresponding to the (‘non-diluted’) Majority-Rules experiment between R-Zn and S-Cu (Figure 6.6B). The net helicity for the highly diluted samples, e.g. at 80% A-Cu, is obtained from the CD effects at 20% Sergeant in Figure 6.9A. When these values at 25, 50 and 75% ‘ee’ are normalized to the Sergeant-and-Soldiers at 100% ‘ee’, the obtained net helicity shows a positive deviation from linearity.

![Figure 6.9](image)

**Figure 6.9.** A: Diluted-Majority-Rules of R-Zn + S-Cu and A-Cu at 1.0×10⁻⁶ M in MCH at RT. (A) CD effect at 390 nm versus the fraction [R-Zn + S-Cu] Sergeant for ‘ee’ values of 25, 50 and 75%. The 100% ‘ee’ dataset equals the Sergeant-and-Soldiers experiment of R-Zn and A-Cu, which is considered as the mirror image of S-Zn and A-Cu (Figure 6.5C/D) and the boxed data points at 100% Sergeant equal the Majority-Rules experiment of R-Zn and S-Cu at 390 nm (Figure 6.6A/B). (B) The same experiment represented as the net helicity versus ‘ee’ with the corresponding fits on the non-diluted (HRP = 15.4 and MMP = 11.2 kJ·mol⁻¹) and 80% diluted state (HRP = 9.5 and MMP = 2.6 kJ·mol⁻¹).

This qualitative piece of evidence for chiral amplification is identical to the trend observed for most Majority-Rules systems indicating that both enantiomers coaggregate in one stack (Figure 6.9). Despite the limited data points, this non-linearity is fitted at a HRP of 9.5 kJ·mol⁻¹ and a MMP of 2.6 kJ·mol⁻¹ (Table 6.1). As expected, the HRP remains high since it refers to a similar H-type aggregate with strong hydrogen bonds that penalize a helix
reversal. However, the MMP has considerably been reduced upon ‘dilution’ with Soldiers, which suggests that the structural mismatch between the opposite enantiomers is suppressed by the structural intrusion of achiral comonomers; hence resulting in a coaggregate containing A-Cu, R-Zn and S-Cu. The high-contrast behavior of chromophore mixing in Sergeant-and-Soldiers and Majority-Rules experiments seems to be connected by the Diluted-Majority-Rules principle. In the next chapter, we investigate the dynamic aspects of these chiral amplification phenomena.

### 6.5 Conclusion

The coaggregation behavior of porphyrins with different metals and side chains was investigated by chiral amplification. Chiral amplification behavior does not depend on the metal center inside the porphyrin, however, strong effects have been observed for the chirality of the side chain. Efficient coaggregation was observed between achiral and chiral porphyrins, as evidenced by a strong Sergeant-and-Soldiers effect. On the other hand, no chiral amplification was observed in the Majority-Rules experiment. The distinctive behavior in chiral amplification was quantified by modeling studies that revealed a combination of high helix reversal and high mismatch penalties; in the order of 10 and 5 kJ·mol⁻¹, respectively. For mixed-metal Sergeant-and-Soldiers and Majority-Rules studies, the same trends in chiral amplification are observed by fluorescence quenching between Zn and Cu-porphyrins. As evidenced by the chiral amplification phenomena, we achieved highly distinctive mixed states within the porphyrin assemblies by only subtle peripheral changes in the monomer. Within the same library, the limits of coaggregation were further explored by a Diluted-Majority-Rules experiment, which indicated that both enantiomers share the same aggregate when achiral comonomers are added to the system. For the purpose of constructing functional, multi-component nano-architectures, we envision it is highly interesting to explore these chiral amplification phenomena since they could provide additional tools to control stoichiometry and the place of the components at specified locations in the assembly.

In the Majority-Rules system, the formation of conglomerates was used as a property to induce supramolecular chirality. The addition of S-Mn to R-Zn:S-Zn lead to the enhanced selectivity to depolymerize the S-Zn conglomerate, indicating that the mismatch penalty is operative at the end of the stacks. The addition of quinuclidine to R-Zn:S-Cu leads to the selective depolymerization of the R-Zn conglomerate, indicative for the difference in sensitivity between Zn- and Cu-ions towards Lewis bases.
6.6 Experimental

Materials and methods
The porphyrin aggregates were prepared by chloroform injection as described in Section 6.2. The procedure for the removal of R-Zn with quinuclidine is described in the experimental section of Chapter 7. The titration of S-Mn to R-Zn:S-Zn (1:1) at 4.0×10⁻⁵ M was performed in the same way as described in the experimental section of Chapter 3.

Instrumentation
Circular dichroism (CD), ultraviolet-visible (UV-vis) were performed in the same way as described in the experimental section of Chapter 2. Emission spectra were recorded on a JASCO FP6500 with the solutions in a 1 × 1 cm cuvet. Monochromatic light of 405 nm through a 10 nm slit was used to excite the solution, while the emission spectra were recorded after interference of an emission slit width of 20 nm.

Cooling curves
We used the Van ‘t Hoff relation to determine the \( T_c \) at half the concentration via \( \Delta [\ln(C)] \cdot R = \Delta H \cdot \Delta [1/T_c] \) with gas constant \( R \) and the enthalpy release \( \Delta H \), which is obtained from the fit on the elongation part of the cooling curve (see Section 2.3 and 2.4). The Van ‘t Hoff analysis for R-Zn:S-Zn (1:1) is shown in Table 6.2. Accordingly, the \( T_c \) at ‘half the concentration’ should be 323.05 K and the \( T_c \) found after fitting the UV-vis cooling curve (Figure 6.3A) is 322.95 K.

**Table 6.2.** Van ‘t Hoff analysis for the pure ee = +/− 100 system at 1.0×10⁻⁶ M designated “i” and mixed system at ee = 0 and 5.0×10⁻⁷ M designated “ii”:

<table>
<thead>
<tr>
<th>( C^i )</th>
<th>1.0×10⁻⁶</th>
<th>( \ln(C^i) )</th>
<th>( \Delta [\ln(C)] )</th>
<th>( \Delta [\ln(C)] \cdot R = \Delta H \cdot \Delta [1/T_c] )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( C^i )</td>
<td>5.0×10⁻⁷</td>
<td>( \ln(C^i) )</td>
<td>( \Delta [\ln(C)] )</td>
<td>( \Delta [1/T_c] )</td>
</tr>
<tr>
<td>( \Delta H )</td>
<td>139×10³</td>
<td>( \Delta [\ln(C)] \cdot R = \Delta H \cdot \Delta [1/T_c] )</td>
<td></td>
<td></td>
</tr>
<tr>
<td>( T_c^i ) (found.)</td>
<td>327.44</td>
<td>1/ ( T_c^i ) (found.)</td>
<td>3.054×10⁻³</td>
<td>( \Delta [1/T_c] )</td>
</tr>
<tr>
<td>( T_c^j ) (calc.)</td>
<td>323.05</td>
<td>1/ ( T_c^j ) (calc.)</td>
<td>3.096×10⁻³</td>
<td>( 4.1462×10⁻⁵ )</td>
</tr>
<tr>
<td>( T_c^j ) (found.)</td>
<td>322.95</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

In a similar way for R-Zn:S-Cu (1:1), we calculate a \( T_c \) of 320.40 K for S-Cu and 322.66 K for R-Zn at 5.0×10⁻⁷ M. These values correspond to the \( T_c \)’s found for the ‘ee’ = 0 cooling curve (Figure 6.6A); 320.15 K and 322.75 K for S-Cu and R-Zn, respectively.

130
6.7 References


16. The CD spectra of achiral **A-Zn** and **A-Cu** shows a small CD effect, which is most likely due to enantiomeric impurities.


19. As described in Section 2.3, the same cooling curves are obtained when probing the cooling curve of **S-Zn** by CD or UV-vis.

20. For convenience, we refer to the term “pseudo-enantiomeric excess” (ee’) since the opposite enantiomers are differentiated by the center metal-ion only. However, the compounds are different species having different self-assembly properties (see Section 2.4).


23. The difference in $T_s$ for **R-Zn** in Figure 6.3A and 6.4A is caused by a concentration effect as evidenced by a lower absorption for the latter at $\lambda_{\text{max}}$.


25. The schematic representation shows the formation of QND-monomer complexes. Considering the low concentration of receptive **R-Zn** and the considerable concentration of QND, monomer complexes with two axial ligands are formed rather than dimer complexes (see Section 7.2).

26. Considering the mirror-image behavior in chiral amplification of **R/S-Zn** with **A-Zn** (Figure 6.1D), we assume the same behavior for the amplification of **A-Cu**.
Chiral amplification in porphyrin assemblies: a dynamic study

Abstract. The dynamic properties of mixed-metal porphyrin assemblies were investigated by the selective extraction of Zn-porphyrin co-monomers from aggregates. It was shown that axial ligation of Zn-porphyrins with quinuclidine resulted into their depolymerization while Cu-porphyrins remained unaffected. The extraction process proceeded at different time scales depending on the mixed state, which was controlled by the side-chain chirality as shown in the previous chapter. Herein, slow extraction kinetics were found for the mixed Sergeant-and-Soldiers and Diluted-Majority-Rules systems, while an instant extraction process was deduced for the self-sorted Majority-Rules system. By simultaneously monitoring the supramolecular chirality during extraction, a chiral memory effect was observed for both systems that showed slow extraction kinetics. For the Sergeant-and-Soldiers system, the remaining supramolecular backbone comprised of achiral monomers only, which gave rise to a long-lasting chiral memory with slow, entropy-driven atropisomerization. The stability of the chiral memory was analyzed by time- and temperature-dependent CD studies; for the latter, the memory could be erased and partially restored upon heating and cooling, respectively. In case of the Diluted-Majority-Rules experiment, the remaining supramolecular backbone comprised of a mixture of achiral and chiral monomers. When chiral Cu-porphyrins remained aggregated in their unpreferred helicity, a short chiral memory was found with enthalpy-driven atropisomerization.

Part of this work has been published:

7.1 Introduction

The dynamic properties arising from supramolecular systems provide important insights necessary for the rational design of stimuli-responsive materials. However, supramolecular dynamics feature multiple simultaneous processes, which (unlike a unique thermodynamic assessment) does not permit a singular allocation that marks the dynamic property of a certain system. In the previous chapters, the interaction of S-Zn with Lewis bases revealed relatively slow kinetics for the interconversion between multiple aggregate types. While the addition of a large excess of Lewis base caused rapid depolymerization for porphyrin stacks, the dilution-induced self-assembly at critical pyridine quantities was remarkably slower, hence this kinetic stability allowed for the microfluidic separation of stacks and pyridine-capped dimers (Chapter 3). Similar kinetic behavior was observed for the supramolecular response after photoisomerization of the phenylazopyridine ligand (Chapter 4) and the slow formation of the alternating copolymer with DABCO (Chapter 5). For all multi-component self-assembly processes, a single mechanism was hypothesized, in which the depolymerization of the stacks was driven by free monomers that detached from the aggregate terminals. Although the proposed model matched the thermodynamic behavior in any case, the aforementioned kinetic properties do not particularly strengthen this mechanism. In this chapter, we investigate the selective depolymerization of Zn-porphyrins from mixed Zn/Cu-porphyrin systems upon the addition of quinuclidine (QND), in which the depolymerization rate is related to the degree of mixing of different metal porphyrins.

Another perspective in supramolecular dynamics relates to memory effects, which usually embodies the lack of conformational changes within an assembly. Chiral memory is particularly interesting since it allows for the formation of a homo-chiral assembly comprising of achiral building blocks that contain an enantiospecific imprint.\(^1\) A few examples of such systems are known in which chiral auxiliaries are employed to bias the chirality of racemic covalent polymers,\(^2\) discrete supramolecular systems,\(^3\) and porphyrin-based aggregates.\(^4\) Even more remarkable examples disclose the combination of storage and amplification of supramolecular chirality as shown for porphyrins\(^5\) and calixarene-based rosettes.\(^6\) These approaches are based on a temporary diastereomeric relationship in which the conformational inertness of the kinetically trapped chiral architecture is sufficient to overcome the removal or substitution of the auxiliary. The inspiration drawn from these examples triggers the investigation to explore chiral memory at the supramolecular level by the selective depolymerization of porphyrin aggregates. The current system has advantageous properties for this approach considering the ease of biasing at the preferred helical direction with a chiral Sergeant co-monomer and the selectivity by which QND depolymerizes Zn-porphyrins relative to Cu-porphyrins (see Section 6.3.2, vide infra). Besides the examination of the depolymerization rate of the Zn-porphyrins, we investigate the
supramolecular response by simultaneously probing the chirality of the remaining assemblies.

7.2 Chiral memory via chiral amplification and selective depolymerization

The Sergeant-and-Soldiers experiment between S-Zn and A-Cu described in Section 6.3.1 reveals a strong chiral amplification, in which the S-Zn Sergeant transfers and amplifies its own chirality to the A-Cu Soldiers. At a composition of 10% S-Zn and a total porphyrin concentration of 1.0×10^{-6} M, this yields helical aggregates with a single handedness as evidenced by a saturated Cotton effect. Furthermore, the fluorescence of the S-Zn:A-Cu (1:9) coaggregate is fully quenched due to the high abundance of non-emissive Cu-porphyrins that are well-mixed among the Zn-porphyrins. These coaggregates are prepared by chloroform injections of pre-mixed monomer solution in methylocyclohexane (MCH), which affords thermodynamically stable assemblies in a remarkably quick and efficient way. Here, a chloroform mixture of 2.01×10^{-5} M S-Zn and 1.81×10^{-4} M A-Cu (total 2.01×10^{-4} M at 1:9, respectively) is prepared and 25 μL of the co-monomer solution is injected in 5.00 mL MCH to 1.0×10^{-6} M at 0.5 v% chloroform. The formation of the homo-chiral aggregate is evidenced by a time-dependent CD measurement at λ_{max} ~ 391 nm (Figure 7.1A). The kinetic profile reveals the instantaneous formation of the coaggregate and that the helicity reaches steady state ~10 min after injection. This trend is considerably different than the preparation of the coaggregate by mixing-in pre-aggregated porphyrins in MCH. In this method, 300 μL 1.0×10^{-6} M S-Zn is added to a cuvet containing 2.70 mL 1.0×10^{-6} M A-Cu. The onset in the kinetic profile originates from non-mixed S-Zn, however after ~100 min, mixing with the A-Cu backbone starts and chiral amplification becomes operative (Figure 7.1A). This comparison demonstrates the slow exchange between porphyrin monomers when aggregated, which is a different dynamic process than the interconversion between different aggregate types (vide supra), yet their time scales are within the same ballpark.
Figure 7.1. A: Kinetic profile for the preparation of the S-Zn:A-Cu (1:9) coaggregate at 1.0×10⁻⁶ M by rapid injection and the monomer exchange between pre-aggregated porphyrins. The g-value is the anisotropy factor, which is calculated via $g = \Delta \varepsilon / \varepsilon = CD$-effect (mdeg) / (32980 × OD) at $\lambda_{\text{max}} \sim 391$ nm. B: UV-vis spectra for control experiments of A-Cu at 9.0×10⁻⁷ M (upper panel) and S-Zn at 1.0×10⁻⁷ M (lower panel) before and after the addition of 1×10⁻² M quinuclidine.

The difference in sensitivity towards Lewis bases between Zn- and Cu-porphyrins allows for the induction of the supramolecular chirality of the R-Zn:S-Cu (1:1) Majority-Rules system (see Section 6.3.2). In two upcoming control experiments, this selectivity is analyzed for the S-Zn:A-Cu (1:9) coaggregate at 1.0×10⁻⁶ M; we add 1×10⁻² M QND to isolated A-Cu at 9×10⁻⁷ M (90% of 1.0×10⁻⁶ M) and S-Zn at 1.0×10⁻⁷ M (10% of 1.0×10⁻⁶ M) (Figure 7.1B, upper and lower panel, respectively). No changes in the UV-vis spectra are found in the former, indicating that QND does not affect A-Cu aggregates, while a strong effect is found in the latter. At a concentration of 1.0×10⁻⁷ M the S-Zn monomer are partly hydrogen bonded in H-aggregates as evidenced by the absorbance next to the aggregate Soret band at 390 nm. After the addition of QND, an instantaneous response is observed and a sharp, red-shifted Soret band at $\lambda_{\text{max}} \sim 431$ in acquired. This UV-vis spectrum is identical to the spectrum of S-Zn at high pyridine excesses (Figure 3.2C) and pyridine complexes of S-Zn-Me (Figure 3.1A) that are characteristic for monomer complexes. Clearly, under these conditions QND caps free Zn-porphyrin monomers that are involved in the aggregate-monomer equilibrium, which shifts upon the removal of monomers. Considering the low porphyrin concentration, the binding strength of QND and its high abundance, monomer complexes are formed having two QND ligands. Hence, by this depolymerization process, Zn-porphyrins are selectively extracted and fully removed from the self-assembling system.

Having performed the control experiments for selective depolymerization, we investigate the selective removal of S-Zn from the homo-chiral S-Zn:A-Cu (1:9) system. By adding a 10000 molar excess of QND to the coaggregates at 1.0×10⁻⁶ M, the extraction of S-Zn is pushed to completion. After ageing overnight, this causes a ~10% drop in the aggregate Soret
band at 390 nm while the band at \( \lambda_{\text{max}} \approx 431 \text{ nm} \) appears originating from the S-Zn:QND monomer complex (Figure 7.2A). By using the S-Zn:QND reference spectrum (Figure 7.1B, lower panel), we estimate by spectral fitting that at least 95% of S-Zn has been extracted from the coaggregates after treatment with QND. This indicates that the remaining aggregate contains no more than 0.5 mol% Sergeant. The selective removal is also supported by an increase of the fluorescence of S-Zn:QND, revealing the liberation of S-Zn from the coaggregate (Figure 7.2B). Remarkably, only a 15% reduction of the CD-intensity is observed after treatment with QND (Figure 7.2C). This is slightly more than expected for the \( \sim 10\% \) decrease of the aggregate Soret band, but significantly less than the CD-response expected from the highest estimate of remaining S-Zn in the aggregate. By considering the g-values for the Sergeant-and-Soldiers experiment between S-Zn and A-Cu, the reduction of the CD intensity is estimated to be \( >75\% \) when 0.5 mol% S-Zn remains coaggregated. The lack of response of the supramolecular chirality is indicative for a chiral memory effect.

**Figure 7.2.** UV-vis (A), excitation (B) and CD (C) spectra before and after extraction with QND. D: Kinetic profile for the extraction of S-Zn from the coaggregates: the formation of the S-Zn:QND complex as probed by UV-vis at \( \lambda_{\text{max}} \approx 431 \text{ (left axis)} \) and the chirality of the remaining aggregate as probed by CD at \( \lambda_{\text{max}} \approx 391 \text{ nm (right axis)} \). In all panels: [S-Zn:A-Cu (1:9)] = 1.0\times10^{-6} \text{ M with 10000 QND excess in MCH at RT.}
Chapter 7

The spectral differences before and after treatment with QND indicates that the rate of racemization in the remaining A-Cu aggregates is slower than the rate of removal of S-Zn from the coaggregates. This is clearly demonstrated by the kinetic profiles, in which the extraction kinetics (based on the time-dependent absorbance of the S-Zn:QND monomer complex) are simultaneously monitored with the supramolecular chirality of the remaining aggregate (Figure 7.2D). At a receptive Zn-porphyrin concentration of \(1.0 \times 10^{-7}\) M, it requires \(~15\ h\) to remove all coaggregated S-Zn monomers and convert them into S-Zn:QND complexes. This is significantly slower than the instantaneous depolymerization of S-Zn under the same conditions in absence of A-Cu (Figure 7.1B, lower panel). Remarkably, the atropisomerization of the A-Cu backbone is even slower than the removal of the S-Zn, as evidenced by its optical activity after removal of the Sergeant. Time-dependent UV-vis spectra show no changes in intensity and intensity ratio between the aggregate Soret band and the S-Zn:QND band (Figure 7.3A, upper panel). The corresponding CD spectra show the retention of chirality, while the shape and position of the CD curves changes (Figure 7.3A, lower panel). This indicates that the supramolecular chiral memory remains stable over months.

![Figure 7.3](image)

**Figure 7.3.** A: Time-dependent UV-vis (upper panel) and CD (lower panel) spectra of the memory system at RT. B: Temperature-dependent CD measurements at 391 nm for heating and cooling the “memorized” solutions at 6 °C/h below (20→60 heating and 60→20 cooling) and above (20→80 heating and 80→20 cooling) \(T_c\).

The lack of conformational dynamics is similar to the chiral memory effect observed for chiral porphyrin aggregates in water.\(^4\) Here, Purrello and co-workers investigated the successful restoration of the chiral memory by the disassembly and re-assembly of the complex by pH-switching.\(^10\) Analogously, the remarkable inertness at RT prompts us to investigate the possibility of releasing and restoring the chiral memory by a series of heating and cooling experiments on the solutions of imprinted chiral stacks containing A-Cu. Firstly, heating and cooling of S-Zn:A-Cu (1:9) coaggregates in the absence of QND results in a
complete loss of optical activity above the elongation temperature ($T_e$). Subsequently slow cooling from the molecularly dissolved state above $T_e$ results in a full recovery of the optical activity due to the chiral amplification by S-Zn.\textsuperscript{11} Secondly, in the presence of QND and after removal of the S-Zn from the coaggregate, the CD-effect is lost again upon heating the solution above $T_e \sim 68$ °C. But now upon slow cooling to RT no recovery of the CD-effect is observed because of the erasure of chiral memory and the absence of any chiral porphyrin in the self-assembled stack. Finally, when heating to and subsequent cooling from 60 °C ($T < T_e$), at which only a fraction of A-Cu is aggregated, a partial recovery of the chiral memory is observed (Figure 7.3B).\textsuperscript{12} At this relative high temperature of 60 °C, the conformational inertness of the remaining “A-Cu seeds” is sufficient to maintain their imprinted chirality, which allows enantiospecific self-assembly of A-Cu upon cooling (Figure 7.4).

![Figure 7.4](image_url)

**Figure 7.4.** Schematic representation of the selective depolymerization of S-Zn with chirality retention in the A-Cu backbone and its temperature-induced switching of the chiral memory.

### 7.3 Selective depolymerization in a Majority-Rules system

The mixed-metal Majority-Rules experiment between R-Zn and S-Cu described in Section 6.3.2 reveals the lack of chiral amplification due to their narcissistic self-sorting into conglomerates. This allowed for the selective removal of Zn-conglomerate upon the addition of QND. At the composition R-Zn:S-Cu (1:1, ‘ee’ = 0%, 1.0×10\textsuperscript{-6} M), a CD-silent is observed at 392 nm due to equal abundance of R-Zn stacks and S-Cu stacks in solution. When we add QND to this system with 5.0×10\textsuperscript{-7} M receptive R-Zn, we observe instant depolymerization. As shown in Figure 7.5A, ~1 min after the addition of 1×10\textsuperscript{-2} M QND, the absorption band of the R-Zn:QND band at 431 nm has fully developed. Similarly fast kinetics has been observed in the depolymerization of S-Zn in presence of large molar excesses of QND and pyridine (vide supra). Concomitantly with the instant depolymerization of R-Zn stacks, a chiral response is observed; going from a CD-silent state at ‘ee’ = 0% to a CD active state at ‘ee’ = −100% originating from S-Cu stacks at 5.0×10\textsuperscript{-7} M. The simultaneous response of CD and UV reveals the absence of a chiral memory effect and it supports the self-sorted character of the R-Zn:S-Cu system.
Figure 7.5  A: Kinetic profiles of the extraction of R-Zn from R-Zn:S-Cu (1:1) Majority-Rules system at 1.0×10⁻⁶ M with 1×10⁻² M QND at RT. B: Kinetic profiles of the extraction of R-Zn from R-Zn:S-Cu:A-Cu (12.5:7.5:80) Diluted-Majority-Rules system at 1.0×10⁻⁶ M with 1×10⁻² M QND at RT.

Under the assumption that the dynamics for monomer-aggregate exchange does not strongly depend on the metal/side chain of the porphyrin, the remarkable difference in extraction kinetics between the coaggregated S-Zn:A-Cu (1:9) and the narcissistically self-sorted R-Zn:S-Cu (1:1) system can be rationalized by a shielding effect that occurs when Zn-porphyrins are coaggregated with Cu-porphyrins. This hypothesis can be explained by the exposure of porphyrin monomers when they detach from the end from the stack in order to preserve the dynamic equilibrium between monomers and aggregates. In the case of efficient coaggregation, the Zn-porphyrins are randomly distributed over the mixed stack and the monomers that keep the whole coaggregate in the equilibrated state comprise of Zn- as well as Cu-porphyrins. As a result, Zn-monomer exposure occurs to a considerably lower extent than when the Zn-porphyrins form their own homo-aggregate, in which only Zn-monomers are involved in the equilibrium. In the latter, each monomer exposure event directly leads to metal-ligand complexation and removal from the self-assembly, which causes a shift in the equilibrium, hence leading to depolymerization. In this way, Cu-porphyrins “protect” the Zn-porphyrins by consistent participation in the dynamic equilibrium. We therefore postulate that Zn-monomers are removed slower when they are coaggregated with copper-monomers.

### 7.4 Selective depolymerization in a Diluted-Majority-Rules system

As demonstrated in Section 6.4, the Diluted-Majority-Rules experiment revealed that coaggregation of enantiomers is enabled upon ‘dilution’ with Soldier co-monomers that encounter a lower structural mismatch. This behavior between Sergeant-and-Soldiers and Majority-Rules is also observed in its extraction process with QND, as we show for the R-
Zn:S-Cu:A-Cu (12.5:7.5:80; ‘ce’ = 25% at 20% Sergeant) coaggregate at 1.00×10⁻⁶ M. At a concentration of 1.25×10⁻⁷ M, the receptive R-Zn Sergeant dominates the helical sense of this coaggregate, which shows a positive CD signal at 392 nm (Figure 6.9). Upon the removal of R-Zn from this Diluted-Majority-Rules system we observe slow extraction kinetics; after ~200 min all Zn-porphyrins are converted to R-Zn:QND complexes (Figure 7.5B). The extraction kinetics is in line with the Sergeant-and-Soldiers experiment, yet in this coaggregate, S-Cu and A-Cu co-monomers are also involved in the dynamic equilibrium, thereby protecting R-Zn from axial ligation (Figure 7.6). Remarkably, when we consider the chirality of the supramolecular backbone during extraction, we observe an optical response between Sergeant-and-Soldiers and Majority-Rules. Upon R-Zn removal, a direct response in CD is observed, however, the CD response does not follow the absorbance of R-Zn:QND. When all R-Zn co-monomers are removed at ~200 min, the chirality is half-way the transition from a positive to a negative helical sense, which originates from the remaining S-Cu:A-Cu (7.5:80) coaggregate. The observed chiral memory effect disappears after one day, which is in contrast with chiral memory effect of the remaining A-Cu backbone in the S-Zn:A-Cu (1:9) coaggregate that lasts over months (vide supra).

The difference between these memory effects is obviously related to frustration caused by S-Cu, which is initially incorporated in a stack of the wrong handedness. Therefore, the initial R-Zn:S-Cu:A-Cu (12.5:7.5:80) cогregates are higher in energy than the final state where R-Zn has been removed. Consequently, a rapid, enthalpy-driven atropisomerization is observed. In contrast, the remaining A-Cu backbone in the Sergeant-and-Soldiers system lacks the preference for any helical direction. Therefore, this energy difference caused by initial structural frustration is absent and slow, entropy-driven atropisomerization is observed due to the conformational inertness of the A-Cu backbone.

**Figure 7.6** Schematic depiction of the selective removal of R-Zn from the Diluted-Majority-Rules system with a reversal of the supramolecular chirality.
7.5 Conclusion

By proper choice of center metal and side chain chirality, the selective removal of Zn-porphyrins with quinuclidine was investigated from differently mixed states that were established by chiral amplification experiments. When the Zn-porphyrins were coaggregated with Cu-porphyrins, slow depolymerization kinetics were established. In contrast, conglomerates of Zn- and Cu-porphyrins revealed instant depolymerization. The difference is related to the protection of receptive Zn-porphyrins by Cu-porphyrins from Lewis bases upon their participation in the dynamic equilibrium between monomers and aggregates. These strikingly different outcomes in kinetics support the hypothesized mechanism that matched the thermodynamic data as well. According to the mechanism, free monomers predominantly interact with Lewis bases to form complexes that cannot participate in aggregation. The aggregates are depolymerized by axial ligation of free monomers into complexes that cannot participate in self-assembly, which causes a shift of the equilibrium towards free monomers, thereby sacrificing monomers in the aggregate.

A chiral memory effect has been achieved by the sole removal of a structural directing building block. The success relied on (1) the mixing of chiral and achiral building blocks according to the Sergeant-and-Soldiers principle, (2) the molecular recognition to selectively remove the chiral building block, and (3) the high conformational stability of the remaining aggregate based on achiral building to preserve chirality. This resulted in a tunable chiral memory that was sufficiently stable under ambient conditions that could be erased and partially restored by heating and cooling. The stability of the chiral memory can be tuned by the Diluted-Majority-Rules principle, in which an opposite Cu-enantiomer remains coaggregated when the major Zn-enantiomers have been removed. The helical imprint originating from the Zn-enantiomer is frustrated by the opposite Cu-enantiomer, causing a fast, enthalpy-driven atropisomerization. In contrast, the lack of chiral building blocks in the remaining aggregate for the Sergeant-and-Soldiers system causes a slow, entropy-driven atropisomerization.

7.6 Experimental

Materials and methods
The porphyrin aggregates were by chloroform injection as described in Section 7.2. The quinuclidine for the depolymerization of the Zn-porphyrins was used as received. To 10 mL of a mixed-porphyrin solution at 1.0×10⁻⁶ M, 11.1 mg QND (1×10⁻² M) was added and rapidly dissolved using a vortex.
Instrumentation
Circular dichroism (CD), ultraviolet-visible (UV-vis) were performed in the same way as described in the experimental section of Chapter 2. Excitation spectra were recorded on a JASCO FP6500 with the solutions in a 1 × 1 cm cuvet at an emission wavelength of 612 nm.

7.7 References

8. With the molar absorptivity spectra of the S-Zn:A-Cu (1:9) coaggregate and the S-Zn:QND complex, the amount of S-Zn removed from the system is estimated. It is assumed that the molar absorptivity of the aggregate remains constant.
9. It is assumed that chiral amplification behavior remains identical in the 10% drop of the porphyrin concentration. By using the g-value relationship, the CD-intensity is corrected for the concentration drop.
12. Temperature-induced switching of the chiral memory is very sensitive for small differences in experimental conditions such as the applied heating/cooling rate. It is observed that QND affects H-type aggregation of A-Cu at higher temperatures, which precludes the full restoration of the CD effect.
Towards porphyrin-based polymeric systems

Abstract. In a statistical amidation procedure, non-symmetrical porphyrin derivatives were synthesized that were covalently attached to different polymeric backbones. Two systems were explored as a platform to investigate the stimuli-responsiveness of the porphyrins when immobilized to a polymeric backbone. Firstly, the telechelic poly(ethylene-co-butylene) polymer was end-functionalized with the porphyrin moiety as a supramolecular motif for the formation of a physically cross-linked network. Secondly, a polymethacrylate co-polymer was functionalized at the side chains with porphyrins for single-chain polymeric nanoparticles. For both systems, preliminary spectroscopic studies revealed different aggregation behavior due intramolecular interactions when immobilized to the polymeric backbone.
8.1 Introduction

The solution-based studies on the porphyrin assemblies described in this thesis revealed a variety of stimuli-responsive properties that aroused in a multi-component environment. As demonstrated by the orthogonal interaction from Lewis bases, the cooperativity by which hydrogen bonded aggregates are formed strongly enhances the responsivity. This resulted in a pronounced dilution-induced self-assembly effect (Chapter 3). Moreover, this property allowed for the rational design of a photo-responsive system, in which cooperativity of the main component amplified the cis/trans-isomerization of a second component to a macroscopic response (Chapter 4). Besides cooperativity, the porphyrin aggregates revealed a high conformational stability that, by selective removal of a structure-directing agent, resulted in a tunable and stable memory effect (Chapter 6). For the construction of stimuli-responsive materials, it is impelling to convey these remarkable properties from solution state to gel/bulk state. Obviously, this transformation has drastic consequences for the behavior of the system, for instance due to phase segregation into binding domains featuring high local concentrations. Another important aspect relates to the flexibility inside the gel/polymer matrix and the diffusion of multiple components through these media. Notably, the slow supramolecular dynamics found in solution (Chapter 3, 4, 5 and 7) are conceivably hampering the dynamic behavior at lower degrees of freedom. Nonetheless, by also considering the potential optical and catalytic applications of metallo-porphyrins, their functionalization to polymeric backbones could afford new insights and research directions for functional materials. In this outlook-chapter, a synthetic approach is developed for non-symmetrical porphyrins that can be employed as pendant supramolecular recognition units for polymeric backbones. The porphyrins are employed in the end-group functionalization of telechelic poly(ethylene-co-butylene) and the side-chain functionalization of a polymethacrylate co-polymer. Besides their synthesis, preliminary spectroscopic studies are presented that demonstrate some of the consequences of immobilization on the porphyrin self-assembly.

8.2 Synthesis of non-symmetrical porphyrins

For the covalent fixation of the porphyrins to a polymeric backbone, a reactive group should be introduced that does not interfere with the hydrogen bonding array. Furthermore, the smallest deviation from the molecular design of S-Zn is desired in order to preserve its self-assembly properties. In our group, these considerations have resulted in the successful functionalization of polymeric backbones with different supramolecular motifs such as ureidopyrimidinones (UPy’s) and benzene-1,3,5-tricarboxamides (BTA’s). Analogously with the latter, this synthetic elaboration requires the preparation of non-symmetrical porphyrin derivatives having one reactive group in the periphery.
Towards porphyrin-based polymeric systems

Since we would like to refrain from synthetic procedures on the porphyrin substrate, it is decided to perform a statistical amidation reaction of the commercially available mesotetrakis-(4-carboxyphenyl)porphyrin (TCPP) with a mixture of two different aniline derivatives. Herein, we aim at the 3:1 (or “A3B1”) functionalization by chiral trialkoxy aniline wedges (3, “A”) and p-(10-azidodecyloxy)aniline (1, “B”) (Scheme 8.1). While aniline 3 has been applied in S-Zn, aniline 1 is designed to directly couple the porphyrin moiety by “click” reactions (see experimental section). In addition, the azide moiety is non-reactive in the amidation procedure and it allows for the transformation (after amidation) to other functional groups such as amines.

Scheme 8.1. Synthetic scheme for the construction of non-symmetrical “A3B1” porphyrins 5, 6 and 7 which are prepared by amidation of TCPP (4) and a statistical mixture of chiral trialkoxy aniline wedge 3 and p-(10-azidodecyloxy)aniline 1 or t-butyl-[10-(p-aminophenoxy)decyl]carbamate 2. The tetraphenyl porphyrin and the trialkoxy wedges are schematically depicted by bold figures.

To ensure full conversion of the TCPP substrate, a small excess of amine is used (1:4.75). Considering the different reactivity for both anilines and the formation of useful by-product “A3” (or S-FB) a higher feed ratio of 3 to 1 at 0.84 (4:0.75) is applied than statistically imposed (0.75 at 3:1). After amidation and work-up, a major fraction of “A3” is separated and a mixture of “A3” and “A3B1” is freed from the “A3B1” and “A3B3” derivatives by column chromatography. A second separation by Chromatotron® allows for the purification of the desired product as confirmed by 1H-NMR and MALDI-TOF MS (Figure 8.1).
Figure 8.1. A: Second purification step of 5 by Chromatotron® and the measured m/z-values of the collected fractions designated by the rings on the spinning silica disk. B: 1H-NMR spectra of 5 and 6 after purification in CDCl3 (peak labels refer to the structure in Scheme 8.1).

After obtaining azide-functionalized porphyrin 5 in 35% yield, its single-step conversion to amine-functionalized porphyrin 7 failed. Therefore, the statistic approach is repeated using aniline 2, which results in pure 6 as evidenced by 1H-NMR and MALDI-TOF MS (Figure 8.1B). The desired amine-functionalized porphyrin 7 is obtained after deprotection of 6 using trifluoroacetic acid in 30% yield (Scheme 8.1).

8.3 Porphyrin-based telechelics

The first system of interest is the functionalization of a low molecular weight telechelic polymer. Herein it is envisioned that the cooperative self-assembly of the porphyrins into rod-like domains induces phase segregation with the soft polymer matrix.1a,b,2a,b Upon the formation of hydrogen bonds between the porphyrins, the polymer gets physically cross-linked, which gives rise to thermoplastic elastomeric properties. Poly(ethylene-co-butylene) (pEB, Mw = 3500 D) end-functionalized with two alcohol groups is selected as a soft polymer matrix featuring amorphous and apolar properties and a low glass transition temperature.

The dumbbell-type of molecules are prepared by activation of the alcohol functionality of pEB 8 to the chloroformate (9) by reaction with phosgene gas saturated in toluene. Subsequently, the telechelic is reacted with an excess of amine-functionalized porphyrin 7, in which a carbamate is formed between the two (Scheme 8.2). Since the macromolecule approximately triples its mass upon coupling with two porphyrin moieties, preparative-scale recycling gel permeation chromatography (rGPC) is performed to purify the dumbbells with relative ease. The excess of porphyrin used in the reaction is separated after the third cycle and the analytical GPC shows clear shift to higher molecular weights when the porphyrin moiety is selectively probed at 420 nm (Figure 8.2A). After purification and zinc-insertion,
Towards porphyrin-based polymeric systems

the \(^1\)H-NMR spectrum of 10-Zn is recorded in D8-THF,\(^3\) in which both \(\text{CH}_2\) groups adjacent to the carbamate appear. It remains however difficult to determine the exact ratio of single- and double substituted pEB, since two different sets of alkoxy protons of pEB (\(h\) and \(h'\), Scheme 8.2) are overlapping with the porphyrin alkoxy protons and that changes in the \(^1\)H-NMR spectrum are marginal relative to starting product 7 (Figure 8.2B).

![Scheme 8.2](image-url)

**Scheme 8.2.** Synthetic scheme for the formation of dumbbell-type of molecule 10-Zn based on amine-functionalized porphyrin 7 and poly(ethylene-co-butylene). The tetraphenyl porphyrin and the trialkoxy wedges are schematically depicted by bold figures.

Besides GPC and \(^1\)H-NMR, the successful formation of dumbbell-type of molecules is macroscopically evidenced by an increase of material properties after casting a chloroform solution of 10-Zn. While pEB 8 is a viscous oil at RT, 10-Zn appears as an elastomeric material that is highly opaque (Figure 8.2C). On the other hand, casting a chloroform solution of symmetric S-Zn yields a highly brittle film. Apparently, the material gained its properties due to the formation of hydrogen bonds between the porphyrins. The infrared spectrum reveals the same vibrations of the NH-stretch, amide I and amide II for dumbbell 10-Zn and symmetric S-Zn in the bulk state (Figure 8.2D). Considering their similarity with the spectrum for S-Zn in MCH (Figure 2.2C), it is proposed that the porphyrins are hydrogen bonded in the polymer matrix. Regarding the bulk properties, multiple measurements, such as AFM, DSC and rheological studies are suggested.
Figure 8.2. A: Recycling GPC traces for crude 10-Zn (upper panel) and normalized analytical GPC traces of the crude before/after rGPC and reference 7 (lower panel). B: 1H-NMR spectra of 7 and 10-Zn in D8-THF (peak labels refer to the structure in Scheme 8.2). C: Hydroxy telechelic pEB before (left, 8) and after (right, 10-Zn) functionalization with porphyrin 7. D: Infrared spectra of S-Zn and 10-Zn in the bulk state.

In solution, the solvent-dependency of aggregation is investigated by UV-vis and CD spectroscopy. A highly concentrated chloroform solution of 10-Zn is injected to different solvents (at 1.0 v%), thereby keeping the concentration constant at \( \sim 2 \times 10^{-6} \) M for each sample. In chloroform, 10-Zn is molecularly dissolved as evidenced by the Soret band at \( \lambda_{\text{max}} \sim 420 \) nm, while for all other solvents the Soret band is red-shifted to \( \lambda_{\text{max}} \sim 428 \) nm (Figure 8.3A, upper panel). The UV-vis spectrum recorded in MCH shows a weak absorbance at \( \lambda_{\text{max}} \sim 390 \) nm, which gives rise to a strong CD effect identical to S-Zn in the same solvent (Figure 8.3A, lower panel). Especially by considering the weak CD activity observed for the major absorbance at 428 nm, the spectra are highly similar to S-Zn in the presence of a monotopic Lewis base (Figure 3.2B/4.7B/5.6B). This comparison suggests that the porphyrin assembles into stacks and dimer complexes. Perhaps the carbamate group acts as a Lewis base that forms intramolecular metal-ligand complexes. When compared to the pyridine titration to S-Zn, it is likely that the intramolecular complexation process prevails in the competition with
Towards porphyrin-based polymeric systems

intermolecular hydrogen bonding. Obviously, after establishing the dilution-induced self-assembly process, this competition is drastically affected by the (bulk-) concentration. Interestingly, after heating and cooling of the sample in MCH at 6 °C/h, the aggregate Soret band at 390 nm has fully disappeared in favor of the formation of complexes (Figure 8.3B). Here, 10-Zn is molecularly dissolved at 90 °C (λmax ~ 420 nm), while the Soret band red-shifts to the absorbance band of the complex (λmax ~ 429 nm) upon cooling. The CD effect at 390 nm has been fully erased after heating/cooling, however, it re-appears extremely slowly in the order of weeks (data not shown). Having evidenced slow supramolecular dynamics for aggregate interconversion of S-Zn in MCH (see Section 3.6/4.6/5.4), this process is even slower probably due to immobilization of the porphyrin on the polymer backbone.

![Figure 8.3.](image)

**Figure 8.3.** A: UV-vis (upper panel) and CD (lower panel) spectra of 10-Zn in different solvents at ~2×10⁻⁶ M and RT. B: Temperature-dependent UV-vis spectra of 10-Zn in MCH.

The tentative spectroscopic analysis shows the lack of cofacial aggregation, which has to be reduced in order to introduce stimuli-responsive properties that actually arise from the underlying cooperativity by which H-type aggregates are being formed. It appears that the intramolecular metal-ligand complexation hampers the ability to form these aggregates, which should be further investigated by concentration-dependent self-assembly studies. A different molecular design could assist in preventing metal-ligand associations, for instance by reducing the spacer between the porphyrin moiety and the polymer backbone to prevent possible “back-biting”. In addition, a different functional group with lower Lewis basicity can be used for connectivity or a urea linker as an additional hydrogen bonding motif. It is expected that metal substitution towards the copper-analog of 10 enhances the formation of stacks; albeit the envisioned stimuli-responsive properties are lost (vide infra), the material properties may be enhanced.
8.4 Porphyrin-based single-chain nanoparticles

The second system of interest is based on the side-chain functionalization of polymers that are able to fold into well-defined nanometer sized architectures. By using the porphyrin moiety as a pendant group, its hydrogen bond-assisted self assembly controls the folding in a reversible fashion while the process is highly responsive to external stimuli. Since the recognition unit has excellent optical properties, the folding of porphyrin-based single-chain nanoparticles can be probed by a variety of spectroscopic techniques, thereby providing novel insights into folding processes. In this investigation, a copolymer of propargyl methacrylate and racemic isobornylmethacrylate (20:80, \( M_\ell \sim 28000 \) D) is post-functionalized by a “click” reaction with azide-functionalized porphyrin 5.

Alkyne-functionalized copolymer 11 is reacted with a sub-stoichiometric amount of azide-porphyrin 5 in a copper(I)-catalyzed Huisgen cycloaddition (Scheme 8.3). The polymer backbone is for 20% functionalized with alkyne groups and the feed ratio with 5 is adapted to only functionalize half the available alkyne groups. Successful coupling is evidenced by GPC, which shows a drastic increase of the molecular weight when the porphyrin absorbance is monitored (Figure 8.5A). Despite the sub-stoichiometric feed ratio, a considerable amount of unreacted porphyrins is observed in the chromatogram, which may indicate the coupling is sterically hindered. Compared to the dumbbell system, the removal of unreacted porphyrins is facilitated considering the increased mass difference; only one cycle is required to remove residual 5 by rGPC. The analytical GPC traces reveal that 5 has almost been fully removed from the polymer after rGPC (Figure 8.5A). According to UV-vis spectroscopy, the porphyrins are metalated with copper-ions during the “click” reaction. As a result, the induced paramagnetism precludes \(^1\)H-NMR analysis of 12.\(^5\)

![Scheme 8.3. Synthetic scheme for the formation of the side-functionalized polymer 12.](image-url)
Towards porphyrin-based polymeric systems

Despite the poor characterization of 12, preliminary spectroscopy studies are performed to investigate the effect of the side-functionalization. At an optimized solvent mixture of toluene/MCH (3/7, v/v), a maximum CD effect is observed at ~390 nm indicating that this mixture provides sufficient backbone solubility while porphyrin H-type aggregates are formed.\(^\text{26}\) The UV-vis spectrum recorded at \(1\times10^{-5}\) M reveals two Soret absorbances at 390 and 420 nm that may be assigned to the presence of aggregates and monomers, respectively at RT (Figure 8.5B). The UV-vis spectrum is similar to S-Zn at higher temperatures (Figure 2.4A), which demonstrates that the porphyrins are not fully aggregated under these conditions. This may be caused by the solvent combination or by the steric inability to form cofacial aggregates when attached to the polymer chain. Since the CD intensity only reduces by 30% when 12 is dissolved in pure toluene (Figure 8.5B), the solvent effect is less pronounced for the polymeric system; even at considerably higher concentrations, “free discotics” of S-Zn (or S-Cu) are molecularly dissolved in this solvent. On the other hand, the steric constraints are likely the cause of the lower fraction of aggregated porphyrins.

![Graphs](image.png)

**Figure 8.5.** A: Recycling GPC traces for crude 12 (*upper panel*) and normalized analytical GPC traces of reference 5 and crude 12 (*lower panel*). B: UV-vis (*upper panel*) and CD (*lower panel*) spectra of 12 in 30% toluene/MCH and pure toluene at \(1\times10^{-5}\) M and RT. C: Temperature-dependent UV-vis (*upper panel*) and CD (*lower panel*) spectra of 12 in toluene/MCH (3/7, v/v). D: Cooling curves probed by CD at 392 nm at \(1\times10^{-5}\) and \(5\times10^{-7}\) M.

153
When the solution is heated to 90 °C, the aggregate Soret band and its Cotton effect have fully disappeared concomitantly with the appearance of the absorbance at $\lambda_{\text{max}} \sim 420$ nm indicative for the molecularly dissolved state. Upon cooling the solution at 6°C/h, the aggregate re-appears without intermediate formation of complexes (Figure 8.5C), which has been observed for the Zn-porphyrin-based dumbbell system. Perhaps, the copper-ions prevent the formation of metal-ligand complexes, which favors the formation of H-type aggregates only.

Compared to “free” S-Zn (or S-Cu) porphyrins, the polymeric system seems to provide a higher stability for hydrogen bonds in more polar solvents, while only a limited number of porphyrins participates in the aggregation process. These features demonstrate the consequence of immobilization, in which intramolecular self-assembly becomes the prevailing process instead of intermolecular self-assembly. Only the former process leads to the formation of single-chain polymeric nanoparticles and in order to prove their formation, concentration-dependent cooling studies are performed. A strong concentration-dependency is found for the elongation temperature ($T_e$) at which S-Zn aggregates are being formed when the solution is cooled from the molecularly dissolved state at $T > T_e$ (Figure 2.4C). By probing the CD intensity at 392 nm, the same onset of the optical activity is found when cooling a solution of 12 at 1$x10^{-5}$ and 5$x10^{-7}$ M (Figure 8.5D). This concentration-independency on $T_e$ strongly suggests that the self-assembly is driven by the local concentration instead of the total concentration indicative for an intramolecular self-assembly process. Lastly, this may also explain the shape of the cooling curves, which reveal a less sharp transition between the molecularly dissolved and aggregated state.

8.5 Conclusion and outlook

Non-symmetrical porphyrin building blocks have been successfully prepared according to a statistical amidation procedure followed by proper purifications. The presence of a reactive group in the periphery of the porphyrin moiety allowed for its covalent fixation onto polymeric backbones. This approach is necessary for the development of polymers having stimuli-responsive material properties. Preliminary feasibility studies have been performed to investigate if porphyrin-functionalized polymers offer a suitable platform to convey self-assembly properties established in solution to the gel/bulk sate. Two different systems were developed with side-chain and end-group functionalization patterns of porphyrin moieties on polymeric backbones.

The end-group functionalization of pEB with the porphyrin moiety by carbamate linkage resulted in a significant improvement of the material properties. Tentative infrared spectroscopy revealed that the porphyrin moieties are hydrogen bonded in the polymer matrix. UV-vis spectroscopy in solution revealed that cofacial aggregation is suppressed by
Towards porphyrin-based polymeric systems

the formation of metal-ligand complexes. It was hypothesized that an intramolecular complexation process of the carbamate with the Zn-porphyrin is operative, which could be reduced by synthetic modification.

The side-chain post-functionalization of a propargyl/isobornyl methacrylate copolymer by “click” chemistry resulted in the formation of single-chain nanoparticles. Solution-based studies revealed the inability to achieve a fully aggregated state when the porphyrins were connected to the polymer chain. The formation of intramolecularly self-assembled single-chain nanoparticles was evidenced by a concentration-independency of the elongation temperature. The lack of metal-ligand complexation was attributed to the copper-ions inside the porphyrins featuring low Lewis base sensitivities.

Both polymeric systems provide new research directions in the field of stimuli-responsive systems. As evidenced by the analysis in the bulk state, the porphyrin-based dumbbells can be processed into elastic films upon the formation of hydrogen bonded networks. During processing of the film, the (magnetic induced) alignment-ability of the hydrogen bonded porphyrin domains is interesting to explore for photo-catalytic purposes. The unidirectional alignment of porphyrin stacks in the polymer matrix may direct solar excitation energy to the surface, which may be doped with catalytically-active acceptors. Another possible prospect relates to the ability to gelate solvents with low-molecular weight polymers that form physical crosslinks. If the formation of a hydrogen bonded network is sufficient to induce sol-gel transitions, its photo-responsiveness can be explored by mixing-in phenylazopyridines. As shown in Chapter 4, the photo-induced aggregation in solution proceeds relatively slow and it is expected that the supramolecular dynamics slow down even more in the gel matrix due to diffusion limitations. As a result, local irradiation leads to local sol-gel transitions for reversible, macroscopic shape control. The post-functionalization approach of the nanoparticle system allows for the introduction of different porphyrin building blocks, such as donor-acceptor moieties or porphyrins with different chirality. While the former directs to constructs for catalytically-active nanoparticles, the latter allows for the introduction of conglomerate-type of domains inside a single particle similarly as demonstrated in Chapter 6. Lastly, the optical properties of this recognition unit allows for superb probing of folding processes. The characterization of UPy-functionalized nanoparticles has been restricted to GPC and AFM, while BTA-based systems the folding has been followed by CD spectroscopy as well. Additional UV-vis analysis in the present system reveals essential information on the participation level of the building block in the assembly. Moreover, metalation induces high contrast with the polymer backbone, which allows one to obtain structural information by transmission electron microscopy.
8.6 Experimental

Materials and methods
Unless specifically mentioned, reagents and solvents were obtained from commercial suppliers and used without further purification. All solvents were of AR quality and the chloroform and DMF used for synthesis was dried over 4Å molsieves. Kraton L2203 was kindly provided by Kraton Polymers Research. Poly-propargyl/isobornyl methacrylate 11 was kindly provided by Tristan Mes. Deuterated chloroform and THF for 1H-NMR analyses was provided with TMS as a 0 ppm reference. The solvents used for spectroscopy were spectroscopic grade.

Instrumentation
The same instrumentation for syntheses (NMR, MALDI-TOF MS, Column chromatography and rGPC) were used as described in the experimental section of Chapter 2. The Chromatotron® (Harrison Research, 7924T) is a preparative, centrifugally accelerated, radial, thin-layer chromatograph. The sample to be separated is applied, as a solution, near the center of a spinning disk coated with 2 mm silica. Elution by solvent forms circular bands of the separated components, which are spun off from the edge of the rotor together with solvent and collected. GPC measurements were performed on a Resi Pore column with chloroform as the eluent (1 mL·min⁻¹) and a Shimadzu SPD-M20A PDA detector. Circular dichroism (CD) and ultraviolet-visible (UV-vis) measurements were performed in the same way as described in the experimental section of Chapter 2. Infrared spectra were recorded on a Perkin Elmer Spectrum One equipped with a universal ATR detector (Diamond Zn/Se)

Synthesis of functionalized aniline derivatives 1 and 2.
The synthesis of aniline derivatives 1 and 2 is based on p-nitrophenol (Scheme 8.4). Protective chemistry is applied for 2 in order to perform the amidation on the benzylic amine rather than the aliphatic amine.

Scheme 8.4. Synthetic scheme for the formation functionalized aniline derivatives 1 and 2 used in the statistical amidation reaction.
Towards porphyrin-based polymeric systems

• p-(10-Azidodecyleoxy)aniline 1 (Scheme 8.4)

(a) p-nitrophenol (4.0 g, 28.6 mmol), 1,10-dibromodecane (25.8 g, 86.2 mmol), K₂CO₃ (11.9 g, 86.2 mmol) and tetra-butyrammonium bromide (1.4 g, 4.3 mmol) were suspended in acetone (150 mL) and refluxed overnight. After filtration, the filtrate was evaporated and the product was partitioned between water (50 mL) and diethyl ether (75 mL) in a separating funnel. The organic layer was washed with 2 M HCl (2 × 50 mL), H₂O (2 × 100 mL) and subsequently dried with MgSO₄. After filtration and evaporation, the product was purified by column chromatography (Biotage®; 15%→50% over 8 cv’s (SNAP 100 g) DCM/Heptane). A white solid powder is obtained. Yield: 8 g (78%).

(b) 10-(p-Nitrophenoxy)decylbromide (4 g, 11.2 mmol) was dissolved in EtOAc (20 mL) and saturated with Ar by flushing for 15 min. Pd/C (10%, 50 mg) was added and the suspension was shaken in a Parr apparatus under hydrogen atmosphere at 70 psi overnight. The catalyst was removed by filtration and the solvent was evaporated in order to obtain a white powder in quantitative yield, which did not require further purification.

(c) p-(10-Bromodecyleoxy)aniline (3.5 g, 9.8 mmol) and sodium azide (1.58 g, 24.4 mmol) were dissolved in DMF (25 mL) and stirred at 50 °C overnight. The mixture was poured in 0.1 M HCl (200 mL) and extracted with diethyl ether (2 × 100 mL). The organic layer was washed with 1 M HCl (2 × 50 mL), H₂O (2 × 50 mL) and brine (100 mL) and dried with MgSO₄. After filtration, the solvent was removed and the crude product was purified by column chromatography (Biotage®; 30%→60% over 10 cv’s (SNAP 50 g) MixC/DCM; mixC = DCM with 5% methanol). Yield: 2.33 g (82 %). ¹H-NMR (400 MHz, CDCl₃): δ = 1.2-1.8 (m, 18H, CH₂), 3.25 (t, 2H, CH₂N₂), 3.87 (t, 2H, OCH₂), 6.64 (d, 2H, ArH), 7.73 (d, 2H, ArH). MALDI-TOF MS: [M⁺] calcd. for C₅₂H₄₀N₄O: 290.21; found: 290.27 D.

• t-Butyl-[10-(p-aminophenoxo)decyl]carbamate 2 (Scheme 8.4)

(d) 10-(p-Nitrophenoxy)decylbromide (2.0 g, 5.58 mmol) and potassium phthalimide (1.13 g, 6.14 mmol) were dissolved in DMF (20 mL) and stirred for 24 hours at 50 °C. After cooling to RT, the KBr salt was removed by filtration and the filtrate was partitioned between DCM (100 mL) and 1M HCl (100 mL) in a separating funnel. The organic layer was washed with 1 M HCl (2 × 50 mL) and H₂O (2 × 50 mL). The organic layer was dried with MgSO₄, filtered and the solvent was evaporated in vacuo to afford the phthalimide derivative.

(e) The phthalimide was subsequently reduced under mild conditions in order to prevent reduction of the phenyl-nitro group. In this reaction, 1 mL hydrazine monohydrate was added to the substrate (~2 g) in THF (50 mL). The mixture was stirred at 100 °C overnight. After cooling to RT, the phthalimide salt was removed by filtration and the filtrate was evaporated to dryness. The solid was triturated with diethyl ether (50 mL) and the solution was washed with 1 M NaOH (2 × 50 mL) and brine (1 × 100 mL). The organic layer was dried with magnesium sulfate and evaporated in vacuo to obtain the aliphatic amine derivative.

(f) The aliphatic amine was subsequently BOC-protected, in which the substrate (1.2 g, 4 mmol) and di-tert-butyl dicarbonate (3.55 g, 16.3 mmol) were dissolved in dry THF (30 mL) and refluxed under Ar for 12 hours. The solvent was evaporated in vacuo and the resulting product was redissolved in diethyl ether (50 mL) washed with 1 M HCl (3 × 30 mL), saturated NaHCO₃ (1 × 50 mL) and H₂O (50 mL). After drying the organic layer with MgSO₄ the crude product was purified by column
chromatography (Biotage®; 0%→15% over 8 cv’s (SNAP 25 g) EtOAc/DCM). A white solid is obtained. Yield: 1.4 g (64 %).

(g) t-Butyl-[10-(p-nitrophenoxy)decyl]carbamate (1.3 g, 3.29 mmol) was dissolved in EtOAc/ethanol (4/1, v/v) and saturated with Ar by flushing for 15 min. Pd/C (10%, 40 mg) was added and the suspension was shaken in a Parr apparatus under H2 overnight. The catalyst was removed by filtration and the solvent was evaporated in order to obtain a white powder in quantitative yield, which did not require further purification. A yellow viscous oil is obtained that slowly crystallized.

1H-NMR (400 MHz, CDCl3): δ = 1.55-1.28 (m, 16H, CH2), 1.44 (s, 9H, CH3-t-butyl), 3.09 (t, 2H, CH2N), 3.32 (s, 2H, ArNH2), 3.86 (t, 2H, OCH2), 4.67 (s, 1H, NH), 6.62 (d, J = 8.6 Hz, 2H, ArH), 6.72 (d, J = 8.6 Hz, 2H, ArH). MALDI-TOF MS: [M]+ calcd. for C32H38N4O5: 564.27; found: 564.22 D.

General procedure non-symmetrical porphyrins 5 and 6 (Scheme 8.1)
The statistical amidation is performed with wedge 3 (see Scheme 2.3), aniline derivative 1 or 2 and TCPP using benzotriazol-1-yl-oxytritylridinophosphonium hexafluorophosphate (PyBOP) as a coupling agent in DMF. 3 (853 mg, 1.52 mmol), 1 (82.6 mg, 0.28 mmol) or 2 (104 mg, 0.28 mmol), TCPP (300 mg, 0.38 mmol), N,N-Diisopropylethylamine (DIPEA, 523 μL, 3 mmol) and PyBOP (1.17 g, 2.25 mmol) were dissolved in 30 mL DMF. The mixture was stirred for 24 hours at 40 °C. The reaction mixture was poured in 1M HCl (150 mL) (product turned green) and extracted with diethyl ether (2 × 75 mL). The organic layer was washed with 1M NaOH (100 mL) (product turned red) and brine (2 × 100 mL) and dried with Na2SO4. After filtration, the solvent was removed in vacuo and purified by two silica-based chromatographic operations. First separation was used to collect pure “Aa” (Rf = 0.55 in MixA) and remove “AaBz” (Rf = 0.30 in MixA) and “AaBz” (Rf < 0.30 in MixA) from a mixture of desired “AaBz” (Rf = 0.45 in MixA) with residual amounts of “Aa”. This separation was performed with the Biotage®; 0%→100% over 12 cv’s (SNAP 100 g) MixA/MixB; MixA = 4/4/1 (Heptane/Chloroform/EtOAc) and MixB = 1/1 (Heptane/Chloroform). The second separation was performed with the Chromatotron® using a 2 mm silica plate. The plate was equilibrated with pure chloroform and the product was applied and eluted in a mixture of MixA/Chloroform 4/6. This resulted in the separation of “Aa” and “AaBz” (Figure 8.1A).

5: 1H-NMR (400 MHz, CDCl3): δ = -2.1 (s, 2H, NH), 0.8-1.8 (m, 187H, aliphaticH), 3.18 (t, 2H, CH2N), 3.96-4.06 (m, 20H, OCH2), 6.90 (d, 2H, ArH), 7.06 (s, 6H, ArH), 7.41 (d, 2H, ArH), 7.69 (s, 2H, NH), 8.06 (s, 2H, NH), 8.19 (d, 8H, ArH), 8.25 (d, 8H, ArH), 8.86 (s-overlap, 8H, β-pyrrylro protons) (Figure 8.1B). MALDI-TOF MS: [M]+ calcd. for C172H190N11O16: 2694.92; found: 2693.9.

6: 1H-NMR (400 MHz, CDCl3): δ = -2.1 (s, 2H, NH), 0.87-1.93 (m, 187H, aliphaticH), 1.46 (s, 9H, CH3-t-butyl), 3.11 (t, 2H, CH2N), 3.91-4.12 (m, 20H, OCH2), 4.52 (s, 1H, NH), 6.89 (d, 2H, ArH), 7.11 (s, 6H, ArH), 7.69 (d, 2H, ArH), 8.12 (s-overlap, 4H, NH), 8.26 (d, J = 8.5, 8H, ArH), 8.31 (d, J = 8.5, 8H, ArH), 8.81 (s-overlap, 8H, β-pyrrylro protons) (Figure 8.1B). MALDI-TOF MS: [M]+ calcd. for C172H190N11O16: 2768.99; found: 2767.9 D.

Amine-functionalized porphyrin 7 (Scheme 8.1)
Compound 6 (500 mg, mmol) was dissolved in DCM/TFA (1:1, 30 mL) and stirred for 4 hours at RT (product turned green). The solvent was removed in vacuo and redissolved DCM/TFA (1:1, 30 mL) and this process was repeated 4 times. After evaporation to dryness, the product was redissolved in DCM
Towards porphyrin-based polymeric systems

(50 mL) and the organic layer was neutralized with in 1M NaOH (2 × 50 mL, product turned red) and brine (50 mL). The solution was dried with NaSO₄, filtered and the solvent was removed in vacuo. A considerable increase in polarity is observed of the product (Rt = 0.2 in MixD), which was purified by column chromatography (Biotage®; 50%→100% over 6 cv’s (SNAP 50 g) Chloroform/MixD; MixD = chloroform with 6% methanol and 3% triethylamine). ¹H-NMR (400 MHz, D₈-THF): δ = -2.76 (s, 2H, NH), 0.72-1.87 (m, 187H, aliphaticH), 3.79-4.08 (m, 20H, OCH₂), 6.83 (d, 2H, ArH), 7.24 (s, 6H, ArH), 7.74 (d, 2H, ArH), 8.02-8.36 (m, 16H, ArH), 8.59-8.85 (s-overlap, 8H, β-pyrrolic protons), 9.56 (s-overlap, 4H, NH). N.B. CH₃NH₂ protons are not observed due to water peak at 2.55 ppm (Figure 8.1B). MALDI-TOF MS: [M]+ calcd. for C₁₇H₂₃N₅O₄: 2667.92; found: 2668.74 D.

Chloroformate-activated pEB 9 (Scheme 8.2)
Alcohol end-functionalized pEB 8 (Kraton L2203; Mₙ = 3500 D; Mₘ/Mₙ = 1.08; 2 g, 0.56 mmol) was dissolved in 10 mL toluene and a 1M phosgene solution in toluene (6 mL) was added by syringe. The reaction was stirred under Ar at RT overnight while emitted gasses were allowed to escape via a gas-trap containing NaOH. The mixture was heated to 70 °C for 1 hour to remove phosgene gas and the solvent was subsequently removed in vacuo. The product was a light-yellow oil and used without purification. ¹H-NMR (400 MHz, CDCl₃): δ = 0.70-1.81 (m, aliphaticH pEB), 4.04 (s, 2H, C-CH₂O), 4.34 (t, 2H, CH-CH₂O).

Zn-porphyrinate-functionalized pEB 10-Zn (Scheme 8.2)
Activated-pEB 9 (285 mg, 0.08 mmol) was dissolved in 5 mL dry chloroform and added dropwise to a solution of porphyrin 7 (500 mg, 0.19 mmol) and DIPEA (320 µL, 1.9 mmol) in 5 mL dry chloroform. The mixture was stirred for 2 days under Ar and after reaction evaporated to dryness. The crude was redissolved in chloroform (5 mL) and precipitated in cold methanol (10 mL). After filtration and drying, the crude was redissolved in DCM and suspended with ZnOAc. After stirring overnight, the suspension was filtered and the filtrate was evaporated to dryness. A red/purple waxy solid was dissolved in chloroform at high concentration and purified by preparative-scale rGPC. ¹H-NMR (400 MHz, D₈-THF): No inner pyrrolic NH observed at δ < 0 ppm after Zn-insertion, δ = 0.71-1.89 (m, aliphaticH pEB + porphyrin), 2.98 (m, 2H, CH₂N), 3.83-4.05 (m, 20H, OCH₂), 4.06 (br, 2H, C-CH₂O), 6.83 (d, 2H, ArH), 7.23 (s, 6H, ArH), 7.71 (d, 2H, ArH), 8.06-8.35 (m, 16H, ArH), 8.79 (br, 8H, β-pyrrolic protons), 9.43 (s-overlap, 4H, NH). N.B. Only one of the pEB CH₂ endgroups is visible (Figure 8.1B).

Post-functionalization of poly-propargyl/isobornyl methacrylate 11 with porphyrin 5 (Scheme 8.3)
Azide-functionalized porphyrin 5 (39 mg, 0.014 mmol), co-polymer 11 (28 mg, 5.6×10⁻⁴ mmol; 0.028 mmol alkyn groups), N,N′,N′′,N′-pentamethyldiethenetetramine (PMDETA, 1 drop), Sn(II)-2-ethylhexanoate (1 drop) and a copper-wire-twisted stirring bar were charged in a 10 mL dry Schlenk tube. Dry THF (5 mL) was added and the solution was 35 °C under Ar atmosphere. After stirring for 25 hours, the solvent was evaporated under a nitrogen stream and the crude was redissolved in chloroform. The organic phase was washed with a 0.065 M EDTA solution (2 × 25 mL) and 1 M HCl (25 mL). After drying with NaSO₄, the solvent was removed in vacuo. The crude polymer was dissolved in CDCl₃ and precipitated from cold methanol. The polymer was purified by rGPC (Figure 8.5A).
8.7 References


3. The deprotection of 6 is accompanied by a considerable increase in polarity. The $^1$H-NMR spectrum of 7 in CDCl$_3$ shows peak broadening, while reasonable spectra were acquired in D8-THF.

4. The bimodal distribution between H-type aggregates and dimer complexes was also observed for the zinc-analogue of 5. Concentration-dependent studies revealed an enhanced formation of complexes upon dilution, which could explain that metal-ligand association is an intramolecular process.

5. Unlike zinc-ions, copper (and manganese) ions cannot be removed from the porphyrin core. The $^1$H-NMR spectrum of 12 shows no peaks in the porphyrin region (7-9 ppm) and considerable peak broadening upfield.
Multi-Component Porphyrin Self-Assembly

The self-assembly of organic molecules offers an attractive bottom-up approach to create nano-meter sized objects. Supramolecular assemblies become highly interesting for numerous applications in the fields of sensing, catalysis and light harvesting by usage of chromophoric building blocks in a multi-component environment. Regarding the development of functional supramolecular materials and mimicking natural systems, it is highly important to understand self-assembly processes in detail as well as the ability to control them; particularly the control over the arrangement and number of molecules in an aggregate. However, due to the presence of multiple interacting components in a dynamic assembly, these systems are inherently complex, which requires in-depth analyses in multi-component self-assembly. Rather than the description of their functional properties, the focus in this thesis is on insights into multi-component self-assembly of porphyrin monomers into non-discrete helical architectures. By the employment of modeling tools, the thermodynamic aspects of different interacting moieties via orthogonal supramolecular interactions are addressed, which allows one to predict the behavior of several systems comprising of Zn-porphyrins and different axial ligands. In these analyses, the role of cooperativity is closely examined, which strongly enhances the stimuli-responsiveness of the system. The supramolecular chirality has been applied as an additional probe to study the multi-component porphyrin self-assembly. In addition, chiral amplification experiments reveal that the supramolecular chirality provides a level of control over the mixing of different porphyrin monomers in an aggregate. Lastly, besides thermodynamic assessments, the kinetic properties of multi-component porphyrin assemblies have been studied. Here, different dynamic processes such as the exchange of monomers in an aggregate, aggregate interconversions and the imprint of helical conformations have been investigated.

In Chapter 1, a literature overview is presented on the formation of porphyrin-based assemblies, in which different non-covalent interactions are used to construct well-defined architectures. The versatility of the porphyrin building block allows for a diversity of supramolecular motifs, which self-assemble by different mechanisms. Functional properties arise in multi-component mixtures, in which strategies are presented to control the mutual chromophore arrangement in discrete and non-discrete assemblies. Besides stoichiometric and positional control, a special focus is on cooperativity and the stimuli-responsiveness of porphyrin-based aggregates in multi-component systems.

A library of metallo-porphyrin derivatives is developed in Chapter 2, in which the effect of metal center, amide linker and side-chain chirality on the one-component self-assembly is investigated. A hydrogen bond-assisted and highly cooperative self-assembly process is deduced for all amide-functionalized metallo-porphyrins. Their cofacial arrangement results into extended, helical, 1-dimensional H-type aggregates, which are fully analyzed for self-assembled S-chiral zinc-porphyrin “S-Zn” in methylcyclohexane. Temperature- and
concentration-dependent UV-vis and CD measurements have been performed to obtain a thermodynamic description for the cooperative self-assembly. The resulting thermodynamic parameters for S-Zn have been deduced and applied in multiple equilibrium models. These models describe the self-assembly of S-Zn in the presence of different axial ligands in Chapter 3/4/5.

In Chapter 3, the self-assembly of S-Zn is studied in the presence of pyridine, which depolymerizes the porphyrin stacks in a bimodal fashion into hydrogen-bonded, pyridine-capped dimers. As a result of cooperativity, a monomer-driven depolymerization mechanism is validated by fitting spectroscopy data of the pyridine titration to a corresponding thermodynamic model. Simulations on this depolymerization model are used to assess the competition between hydrogen bonding and metal-ligand association in a coupled system, which reveals a dilution-induced self-assembly of the porphyrin stacks. A slow interconversion between dimers and stacks is observed upon the addition of solvent and this kinetic property is used to control the distribution between both aggregate types by diffusive mass transfer in a microfluidic H-cell.

Using the design rules for a strong pyridine-responsiveness between stacks and dimers established in Chapter 3, the photo-induced alteration of the binding constant of phenylazopyridines is explored to photo-regulate the self-assembly of S-Zn in Chapter 4. In the absence of hydrogen bonding, the thermodynamic properties of the photo-induced (de)complexation have been deduced by titration and irradiation studies, which have subsequently been introduced in a modified depolymerization model. High conversion ratios and a large difference in binding constant between both isomers induce a strong photo-switch-ability, which is predicted between 2% and 90% of stacked S-Zn monomers. Regardless the experimental deviation from the model, a reversible photo-induced (de)polymerization of the porphyrin stacks between 1% and 81% is achieved based on CD spectroscopy. Corroborating the spectroscopic measurements, the irradiation of the auxiliary causes a change in solution viscosity.

In Chapter 5, the self-assembly of S-Zn is studied in the presence of the bidentate axial ligand DABCO. In the absence of hydrogen bonding, the thermodynamic properties of the Zn-porphyrin:DABCO 2:1 sandwich complexation have been deduced by UV-vis and 1H-NMR titrations, which reveal that coordination of the second nitrogen of DABCO is less favorable than the first. This negative cooperativity has subsequently been introduced in a modified depolymerization model, which describes the DABCO-induced formation of an alternating supramolecular block copolymer comprising of DABCO units and hydrogen bonded, Zn-porphyrin dimers. Using multiple analytical techniques, DABCO titration experiments reveal the formation of chiral, elongated structures at a 2:1 stoichiometry of S-Zn and DABCO, respectively. The unexpected stability of the alternating copolymer towards excessive amounts of DABCO is analyzed by the model, which demonstrates that stability is
provided by positive cooperativity. Unlike their stability towards excessive amounts of DABCO, preliminary chain-stopping experiments indicate that the alternating copolymers readily depolymerize upon the addition of monotopic Mn(III)-porphyrins, which reveal energy transfer upon chain stopping.

In Chapter 6, the coaggregation of porphyrin monomers with different chirality is studied by chiral amplification experiments. Efficient coaggregation has been observed between achiral and chiral porphyrins, as evidenced by a strong Sergeant-and-Soldiers effect. On the other hand, no chiral amplification is observed in the Majority-Rules experiment as a consequence of narcissistic self-sorting. The distinctive behavior in chiral amplification is quantified by modeling studies that reveal a combination of high helix reversal and high mismatch penalties. The latter penalty is also operative at the end of the stack as evidenced by the induction of the supramolecular chirality upon the addition of a chiral chain stopper. For mixed-metal Sergeants-and-Soldiers and Majority-Rules studies, the same trends in chiral amplification are also observed by fluorescence quenching between Zn and Cu-porphyrins. Within the same library, the limits of coaggregation are explored by a Diluted-Majority-Rules experiment, which demonstrate that opposite enantiomers only coaggregate when achiral comonomers are added to the system.

In Chapter 7, the dynamic properties of mixed-metal porphyrin assemblies are investigated by the selective removal of Zn-porphyrin comonomers by axial ligation with quinuclidine. The extraction process proceeds at different time scales depending on the coaggregated state; slow extraction kinetics are found for the Sergeant-and-Soldiers and Diluted-Majority-Rules systems, while an instant extraction process has been deduced for the self-sorted Majority-Rules system. By simultaneously monitoring the supramolecular chirality during extraction, a chiral memory effect is observed for both systems that showed slow extraction kinetics. For the Sergeant-and-Soldiers system, the remaining supramolecular backbone comprises of achiral Cu-porphyrins only, which give rise to a long-lasting chiral memory with slow, entropy-driven atropisomerization. The stability of the chiral memory is analyzed by time- and temperature-dependent CD studies; for the latter, the memory can be erased and partially restored by respective heating and cooling of the solutions. In case of the Diluted-Majority-Rules experiment, the remaining supramolecular backbone comprises of a mixture of achiral and chiral Cu-porphyrins. Being present in an aggregate with the unpreferred helicity, the remaining chiral Cu-porphyrins induce a short chiral memory with enthalpy-driven atropisomerization.

The final chapter is an outlook towards porphyrin-based polymeric systems, in which nonsymmetrical porphyrins are covalently linked to polymeric backbones. Preliminary feasibility studies have been performed to investigate if porphyrin-functionalized polymers offer a suitable platform to convey the stimuli-responsiveness deduced in solution to the macroscopic level.
Curriculum Vitae

Floris Helmich was born on September 28th, 1981 in Eindhoven, The Netherlands. After secondary education at the Lorentz-Casimir Lyceum in Eindhoven, he started studying Chemical Engineering and Chemistry at the Eindhoven University of Technology, which he completed cum laude in 2007. In his master's program on Chemical Reactor Engineering, he performed his research project in the group of prof.dr.ir. J.C. (Jaap) Schouten on the development of ruthenium and tin promoted platinum catalysts supported on mesoporous silica films. The work on these catalytically active coatings for micro-reactors was partly conducted in the group of prof. B.F.G. (Brian) Johnson at the Department of Chemistry, University of Cambridge (UK). This graduation project was awarded with the “Unilever price 2008” and nominated for the “TU/e afstudeerprijs 2008”. After his internship at PURAC Biochem in September 2007, Floris took up a PhD position with dr. A.P.H.J. (Albert) Schenning and prof.dr. E.W. (“Bert”) Meijer in the Molecular Science and Technology (MST) group and the Institute for Complex Molecular Systems (ICMS) at the Eindhoven University of Technology. His PhD activities focused on the multi-component self-assembly of porphyrins, which encompassed stimuli-responsive behavior, thermodynamic modeling, chirality and kinetic phenomena of supramolecular porphyrin systems. The most important results of this research are presented in this thesis.
List of publications

Effect of Stereogenic Centers on the Self-Sorting, Depolymerization, and Atropisomerization Kinetics of Porphyrin-Based Aggregates (Chapter 6/7)

Chiral Memory via Chiral Amplification and Selective Depolymerization of Porphyrin Aggregates (Chapter 6/7)

Dilution-Induced Self-Assembly of Porphyrin Aggregates: A Consequence of Coupled Equilibria (Chapter 2/3)

Investigation of Lipase-Catalyzed Ring-Opening Polymerizations of Lactones with Various Ring Sizes: Kinetic Evaluation

(to be) submitted

Controlled Perturbation of the Thermodynamic Equilibrium by Microfluidic Separation of Porphyrin-Based Aggregates in a Multi-Component Self-Assembling System (Chapter 3)
Helmich, F.; Meijer, E. W., submitted to Chem. Comm..

Photo-Control of Cooperative Porphyrin Aggregation with Photoresponsive Phenylazopyridine Ligands (Chapter 4)
Hirose, T; Helmich, F.; Meijer, E. W., to be submitted.

DABCO-Induced Cooperative Self-Assembly of a Porphyrin-Based Supramolecular Copolymer (Chapter 5)
Acknowledgements

All scientific facts described in the preceding 8 chapters were gathered during the best four years of my life so far. Until this part, I could not express feelings of pleasure, happiness and gratitude that predominated during my PhD studies. Many people’s support and confidence considerably facilitated the switch from the reactor engineering group to this fantastic group.

First of all, I would like to thank my supervisor prof. Bert Meijer for giving me the opportunity to work in his research group on a project that allowed for a highly personal interpretation. Bert, I admire the way you manage your group; by setting your priority to education, you offer all possible prerequisites for success to the members of your group, not only facility-wise, but also by giving personal attention with care. With your educational and scientific scopes, you provided original suggestions and directions when necessary. I feel honored that I was given the chance to take advantage of all opportunities provided, which strongly assisted in my personal development. Without any doubt, this unique environment is highly appreciated by many colleagues and the reputation of our group in the scientific community is in keeping with this.

I want to thank my daily supervisor dr. Albert Schenning for his highly appreciated guidance and support. Albert, with your assistance I remained focused on my research and you clearly demonstrated how to (re)define research-lines and how to deal with experimental problems. Soon after our first publication, I reached a level of confidence that guaranteed a satisfactory continuation of my project; despite your departure from the group, our collaboration remained extremely pleasant and efficient. Thank you for your critical input to improve the quality of this thesis and I wish you lots of success with your new research on organic materials that are truly functional.

I want to express my gratitude to the members of my reading committee. Prof. Yashima, I would like to thank you for your warm hospitality during my visit to your research group at Nagoya University in Japan. Visiting your and prof. Aida’s group has been an amazing experience and I am looking forward to meeting you again as an honored committee member at my PhD defense. I wish you and the whole Japanese community a prosperous future. Prof. Nolte, thank you very much for all your efforts and I wish you a happy and healthy retirement. Prof. Sijbesma, dear Rint, thank you for you availability during my research and I wish you lots of success.

After working on BTA and perylene molecules in my first year, I started collaborating with dr. Cameron Lee who initiated the porphyrin project. Dear Cameron, thank you so much for your advise, guidance and ingenious ideas in this project. You definitely set the basis for our published work and I truly appreciate your continuous curiosity, even after you returned to the US. It has been a brave decision to move for a post-doc to Eindhoven with your entire family and I wish you, Megan and the kids all the best for the future.

The last period of my research I collaborated with dr. Takashi Hirose. Taka-san, one paragraph is too short to express my gratitude for everything you have done. Before our friendship, I never believed in a perfect match when it comes to collaborations, however, I soon found out differently when I realized how much we have learned from each other. It is amazing how quick, well-organized and dedicated you started on the photo-responsive systems and how you turned it into an absolute success. I feel honored to include your accomplishments in Chapter 4, which will definitely result in some beautiful publications. The pace at which you picked-up computational modeling and the English language is indescribable; in an extremely short time, you became the central figure in this group who was willing to help out anyone, anytime. I wish you all the best and lots of success in Kyoto and happiness with Yumi. Yumi-san, I am happy you were able to continue your post-doctoral activities in Eindhoven. With your synthetic skills, we have gained many insights into the porphyrin-based polymers described in Chapter 8. I sincerely thank you for your input and I wish you all the best.

I would like to thank my office mates in STO-4.47; Cameron, Michel, Yoko, Peter, Adrien, Maarten and Marko for the great atmosphere and their availability for fruitful discussions. Marko Nieuwenhuizen, thank you very much for the modeling and NMR work you performed on the porphyrin systems. With your incredible know-how on self-assembly and computational modeling, you established the “systems-approach” in this project. I learned a lot
from our daily discussions; thank you for your anytime-availability and the quality time we spent inside and outside the lab. Maarten Smulders, thank you very much for stimulating discussions on self-assembly and chirality and your highly appreciated input for Chapter 6 and 7, the best of luck in your academic career. Ronald Gosens, you performed your internship and graduation under my supervision. I want to thank you for your contributions, which resulted in Chapter 8 of this thesis. With your skills, we learned a lot on the synthesis and characterization of porphyrin-based polymers that turned out to be highly complex. We have had incredible amount of fun together and I wish you lots of success during your master’s at our university. I had the privilege to guide many other great students who supported me: Roger, Nina, Evert, Rik and Peter, thank you very much. Also, I would like to thank these other people for their collaboration, support or donations: Jeroen Gielen, Paul Schlebos, Antje Larsen, Philippe Leclère, Motonori Banno, Jolanda Spiering, Wilco Appel, Martijn Gillissen, Ilja Voets, Martin Wolffs, Martijn Veld, Thomas Hermans, Niels Brankaert, Anderson Shum and Tristan Mes.

Tristan, we now swap places in this particular three-unity, hence Pol needs to assist at another PhD ceremony; thank you both for being my “little-helpers” during my defense and I sincerely value our friendship. Tristan, we were on the same boat in our PhD career, in which we shared tons of experiences with lots of laughter; I wish you a lot of success at SupraPolix. Pol, I will never forget our interesting road-trip along the West-Coast before we actually arrived at the ACS National Meeting in Anaheim. I wish you and Melissa all the best in your academic careers and lots of happiness together.

I would like to thank the academic staff for their availability to support me when necessary: Jef Vekemans, Marcel van Genderen, René Janssen, Martijn Wienk, Stefan Meskers and Anja Palms. Dear Anja, after my activities at the ‘Spinoza Junior Research Institute’, I started in the group under your supervision that I truly enjoyed. Thank you for critically reading article manuscripts your open-door throughout the years.

Also, I would like to acknowledge the supporting staff for creating perfect conditions to do science in a pleasant way. Joost van Dongen, Xianwen Lou and Ralf Boeve, thank you for your help analyzing samples. Hans Damen, thank you for maintaining all necessary facilities on the lab. I also would like to thank Henk E., Angela, Nora, Patricia vd E., Carine and Joke for their great support. Lastly, I want to thank Henk Janssen and his people at SyMO-Chem, the people at the ICMS (Sagitta Peters, Janna Verkaik, Tom de Greef and Hans Wyss) and the ICMS Animation Studio (Koen Pieterse, Isabelle Aerts and Johan Holwerda) for creating a marvelous animation on the porphyrin-pyridine system described in Chapter 3.

I want to thank many great colleagues with whom I have spent quality time inside and outside the lab. Definitely including the people mentioned above and the ones I forgot, I want to thank Matt + Shanna, Erik + Dana G., Pablo + Roxanne, Johan F., Davide, Ewelina, Elisa, Alessio, Bart, Carel, Pim, Arjan, Edith, Subi, Amparo, Patrick, Rob, Isja, Janus, Bram, Seda, Louis, Stanislav, Paco, Daniele, Mellany, Maartje, Marcel K. + Dana U., Patricia D., Katja, Bob, Bas, Tonny and “the other people in Die Gesellschaft (Thorsten and Jean-Luc)”. I will never forget the precious moments with my dear Japanese friends; Takashi, Yumi, Nobuhiko, Yoko, Yuko (it was great meeting you again in Tokyo) and Takaya (we shared a great weekend in Kyoto, I wish you, Aya and Reiya all the best); arigatou! Lastly, I specially would like to thank my dear friends and former-colleagues Marloes Verbruggen and Lars van der Mee.

I thank all of my friends outside the university for showing interest and support. Dear Karin, thank you for your patience, warm support and your terrific cover design.

My very last words are fully dedicated to my dearest parents and sister. Who would have thought I had come this far? I simply cannot express how much I appreciate your support, patience and confidence; fortunately, we are all aware how deep these feelings are rooted. You were always there to strengthen me while I was suffering from my weaknesses; once in a while I fall back, you always pick me up and gradually I learn to deal with it myself, thanks to your love and care. Thank you very much!

Floris