Summary

Coordination–Driven Encapsulation of Transition Metal Complexes in Molecular Capsules and their Application in Hydroformylation and Proton Reduction Catalysis

Traditional homogeneous catalysis involves the use of catalysts based on organometallic complexes which are tuned by changing the metal and/or the ligands that are coordinated to it. Catalyst-substrate interactions which dictate the outcome of a reaction occur solely on the metal, i.e. the *'first coordination sphere'* (left in Figure 1). Modulation of the sterics and electronics of the ligands offers an easy platform to steer the selectivity and activity of a reaction of interest. Still today various reactions cannot be controlled to the extent that is needed. Enzymes, the molecular catalysts of nature, use a more complex chemical toolbox to steer reactions towards desired products. The active site is embedded deep in a protein matrix and thereby isolated from bulk solution. This confinement also leads to preorganization of substrates close to the active site. On size does not fit all, but a highly customized region around the active site, the '*second coordination sphere*' (right in Figure 1), is necessary to steer the activity and selectivity of a particular reaction. Inspired by nature, we seek to control homogeneous transition metal catalysts through synthetic second coordination spheres to allow for activity and selectivity control that is otherwise not possible, we refer to this approach as '*Homogeneous Catalysis 2.0*'. Our approach is the encapsulation of known catalysts in supramolecular metal-organic cages. The focus of this thesis is on studying the effect of synthetic second coordination spheres on encapsulated rhodium-based catalysts and bio-inspired hydrogenase mimics.

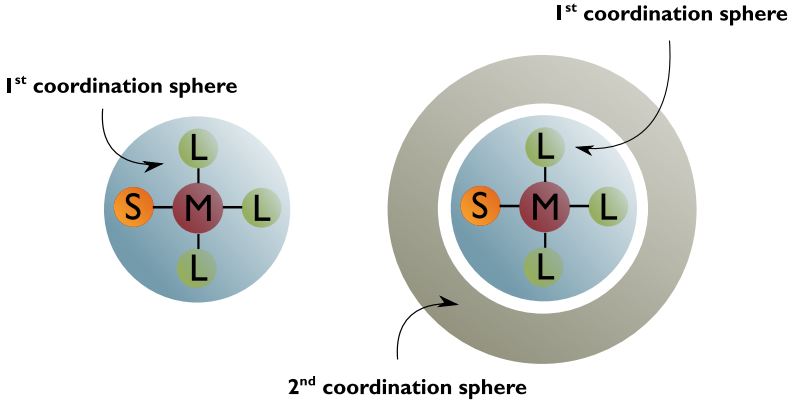

Figure 1. Catalyst encapsulation in a second coordination sphere results in interesting new properties as a result of secondary interactions between the catalyst and the surrounding cage, coined '*Homogeneous Catalysis 2.0*'.

The first part of this thesis describes the use of porphyrin-based cages for the encapsulation of rhodium hydroformylation catalysts by the ligand-template approach, in which the ligand coordinates simultaneously to the cage and the catalytically active transition metal. Modulation of the activity, substrate and product selectivity of the encapsulated rhodium catalysts by the surrounding porphyrin cage is of particular interest. Inspired by the natural [FeFe]hydrogenase enzyme that catalyzes the reduction of protons to molecular hydrogen, synthetic mimics of the active site of this enzyme are subject of intensive research. For these systems the applied porphyrin cage serves a dual role as it confines the catalyst in addition to serving as photosensitizer for photocatalytic proton reduction.

In Chapter 2 we present a rhodium complex that is encapsulated in a porpholactone-based supramolecular assembly (**C2** in Figure 2). The confinement of the complex is shown to lead to the selective formation of rhodium monophosphine complexes, which results in enhanced catalytic activity and branched product selectivity in the hydroformylation of propene. The strong binding of the applied porpholactone cage building blocks with the pyridine-functionalized phosphine ligand ensures the structural integrity of the applied capsule in polar solvents as well as at elevated temperatures. This increased stability allows for the selective hydroformylation reaction to be conducted in industrially relevant, more polar and coordinating solvents. This study represents the catalyst with the highest selectivity for the branched aldehyde in the hydroformylation of

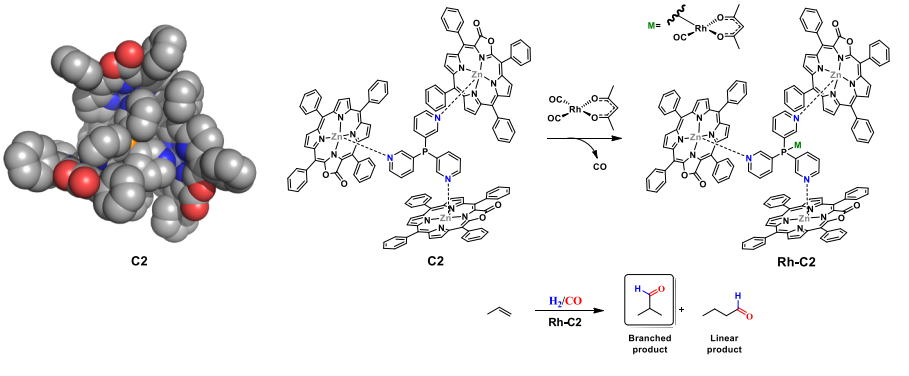

Figure 2. The self-assembled porphyrin cage **C2** used in Chapter 2 as a second coordination sphere for rhodium catalyzed branched-selective hydroformylation of propene.

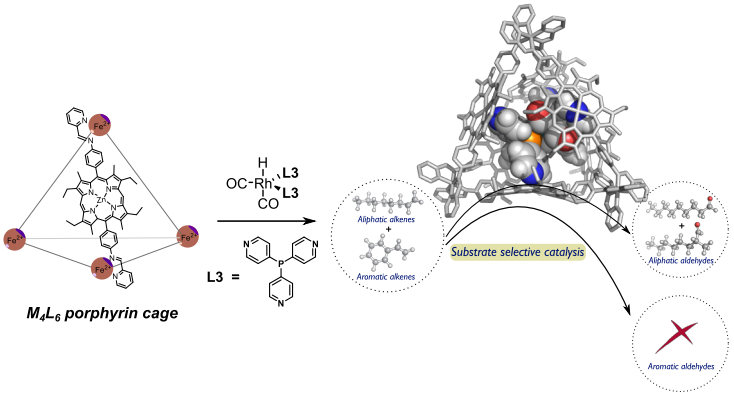

Figure 3. (left) Molecular structure of the M_4L_6 porphyrin cage applied in Chapters 3 and 4. For clarity only one of the cage ligands is shown. (right) Substrate-selective hydroformylation of terminal alkenes by a rhodium bisphosphine catalyst encapsulated in a porphyrin-based metal-organic cage.

propene reported to date.

Chapter 3 discusses the first example of substrate-selective hydroformylation of terminal alkenes by steric confinement of a rhodium bisphosphine complex in a metal-organic porphyrin cage. The porphyrin cage applied in Chapter 2 was expected to be too dynamic for substrate-selective catalysis and therefore in Chapter 3 a more stable and rigid M_4L_6 porphyrin cage is utilized (see Figure 3). Catalyst encapsulation relies again on the ligand-template approach but in this case the cage has sufficient space to accommodate two phosphine ligands in its apolar cavity, yielding a supramolecular bidentate rhodium bisphosphine complex. The relatively small window aperture size of the cage limits the diffusion of larger substrates into the cage. As a consequence, the encapsulated catalyst displays substrate selectivity where a preference for the conversion of smaller substrates is observed. A surprising odd-even effect is seen in the conversion of a series of substrates with increasing alkyl chain lengths. Based on DFT calculations this is ascribed to the favorable folding of odd-numbered alkenes in the cage which slows down their reactivity.

Chapter 4 elaborates on the use of the M_4L_6 porphyrin cage as second coordination sphere for a synthetic [FeFe]hydrogenase mimic (left in Figure 3 and see also Figure 4). Encapsulation of the complex is driven by ditopic pyridine-zinc porphyrin interactions established between the complex and the zinc porphyrins of the cage. By time-resolved infrared spectroscopy electron transfer from the

excited state of the cage porphyrins to the encapsulated catalyst after visible light excitation is confirmed. The quantum yield of the electron transfer is low (1%) as a result of non-selective electron transfer. The cage possesses redox-active corners which, in addition to the catalyst, can also be photo-reduced. Light-driven proton reduction is achieved by irradiation of an acidic solution of the catalyst-cage complex with visible light. Although the obtained turnover number is low, the system represents one of the few successful examples with zinc porphyrins as photosensitizers for photocatalytic proton reduction. This is interesting as the light-harvesting antennae of the natural photosynthetic machinery also apply porphyrins in their structure.

In Chapter 5 we report a novel porphyrin-based cage which bears structural resemblance to the cage used in Chapter 4, but with redox-innocent corners (Figure 4). An [FeFe]hydrogenase mimic with a milder reduction potential than that of the mimic applied in Chapter 4 is encapsulated in the cage in a 1:1 stoichiometry. The encapsulation is again driven by pyridine-zinc porphyrin interactions. As anticipated, the photo-induced electron transfer is selective to the catalyst (the cage corners are redox-innocent in this potential window). As a result, the quantum yield for the formation of the mono-anion has increased by nearly an order of magnitude (from 1% to 8%). Photocatalytic proton reduction is achieved, but no increase in turnover number is observed. The challenge lies in the fast electron transfer kinetics back and forth as enabled by the close proximity of the catalyst and cage. Interestingly, electrocatalytic experiments

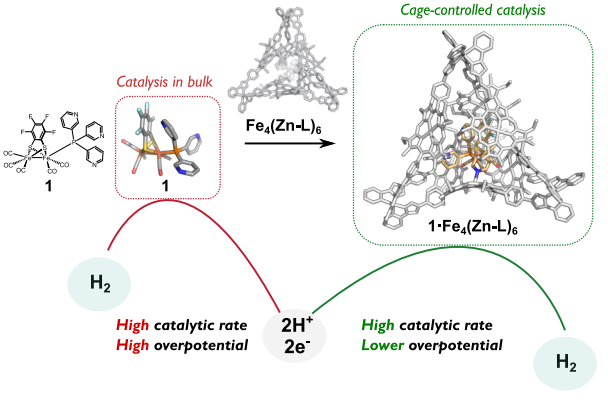

Figure 4. Control of the overpotential of a synthetic [FeFe]hydrogenase mimic by a porphyrin-based second coordination sphere.

reveal that the encapsulated catalyst reduces protons to molecular hydrogen with a 150 mV milder overpotential compared to the same catalyst in bulk solution. This large decrease is attributed to the second coordination sphere around the catalyst preventing the formation of a bridging hydride after reduction and protonation of the catalyst.

In this thesis we show how simple self-assembled synthetic metal-organic cages around transition metal catalysts can dramatically alter their catalytic and physical properties. We have demonstrated that porphyrin-based metal-organic cages are sufficiently rigid to promote enzyme-like substrate selectivity in hydroformylation catalysis. This approach is applicable for well-defined systems with a single substrate present, but for catalysis to work in complex mixtures, more sophisticated strategies are needed. Nature operates in a complex chemical mixture containing reactive molecules and still succeeds at controlling both the activity and selectivity of its catalytic transformations. The key is that reactions are switchable as a result of being stimuli-responsive and they are turned 'on' only when needed. Mechanically interlocked molecules have served as the foundation of the field of molecular machines as they can be switched in response to an external trigger. The great promise of the field became clear after the 2016 Nobel prize was awarded to three pioneers working in this field. Along these lines, in the last chapter of this thesis we aimed at combining the fields of metal-organic cages and rotaxanes to generate a cage rotaxane that is switchable in response to an external co-factor. Even though the final structure was not generated yet, the system shows great promise as a novel method to control homogeneous transition metal catalysts. We believe that the field of '*Homogeneous Catalysis 2.0*' transitions towards '*Homogeneous Catalysis 3.0*' when the current systems can be selectively switched in complex chemical mixtures.