Ligand based encapsulation strategies in homogeneous catalysis

Catalysis is essential for the production of many functional molecules used in society. The development of new catalysts is important to perform increasingly difficult reactions that are associated to, for example, the transition to a clean energy future. Development of new catalysts in the field of homogeneous catalysis has traditionally focused on tuning the activity and selectivity of transition metal complexes through modifications made to the ligands directly bound to the metal of the complexes. A relatively new strategy is to use supramolecular interactions to create a second coordination sphere around transition metal complexes to control the catalytic properties in a similar way as enzymes do. The use of supramolecular capsules as catalysts and as vessels to encapsulate homogeneous catalysts has led to new product selectivity, increased activity and improved catalyst stability as a result of the confinement effects caused by encapsulation. Encapsulation of transition metal complexes is not always straightforward, especially when the properties of the transition metal complex change during the catalytic cycle. We decided to address this problem by focusing on the encapsulation of transition metal complexes by using the ligand coordinated to the transition metal. For most catalytic cycles it is known which ligands will remain attached to the transition metal during catalysis. Using ligands that can interact with supramolecular capsules ensures encapsulation throughout the catalytic cycle. In this thesis we studied the encapsulation of transition metal complexes based on the structure of the ligands used and the application of these complexes in various catalytic reactions.

Ligands with multiple orthogonal binding sites had been studied in our group for a longer time in the context of encapsulation of transition metal complexes. In **chapter 1** we have summarized the previous effort of our group as well as relevant contributions from other groups active in the field in the ligand-template strategy for catalyst encapsulation. These efforts focused on the use of ligand templates that can be encapsulated by capsule-forming building blocks, while a central donor atom can be used to coordinate to a transition metal (figure 1). Application of the ligand-template approach in catalysis has led to several examples of product selectivities that cannot be achieved using traditional catalyst design strategies. Ligand-

template encapsulated catalysts have been applied in several different reactions, most notably rhodium-catalyzed hydroformylation and gold-catalyzed cyclization reactions.

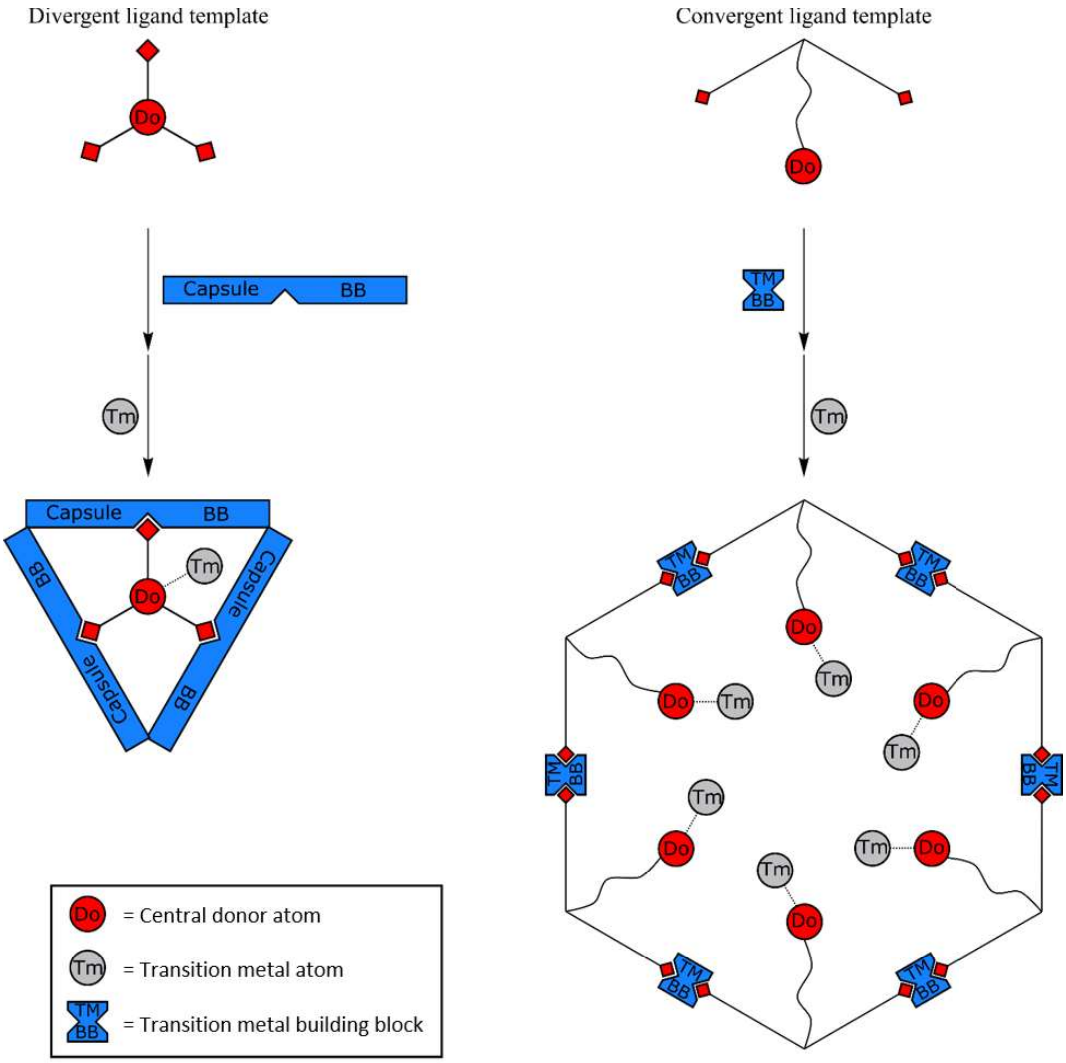

Figure 1. Schematic representation of the two distinct ligand template approaches for encapsulation of catalysts: for the mononuclear approach a divergent ligand template is encapsulated by capsule building blocks, forming a confined space around a single transition metal atom. For the multinuclear approach, multiple convergent ligand template molecules self-assemble into a nanosphere with a number of metal complexes in confined space, leading to very high local concentration of transition metal atoms

In **chapter 2** we expand on the ligand template strategy by developing a system in which encapsulation of a *tris*-3-pyridyl ligand template with zinc porphyrins can be triggered by addition of a small cofactor molecule (figure 2). The effect of encapsulation on rhodium catalyzed hydroformylation of 1-octene was studied in detail. This revealed that when the cofactor molecule is not present in solution the rhodium complex formed is a slow hydroformylation catalyst that produces the aldehyde products in a ratio characteristic for a rhodium complex containing two phosphine ligands. Addition of the cofactor produces a rhodium complex which has an eightfold higher activity in 1-octene hydroformylation and a product selectivity typical for a ligand template encapsulated catalyst. The activity and selectivity of the catalyst can thus effectively be switched by addition of the cofactor.

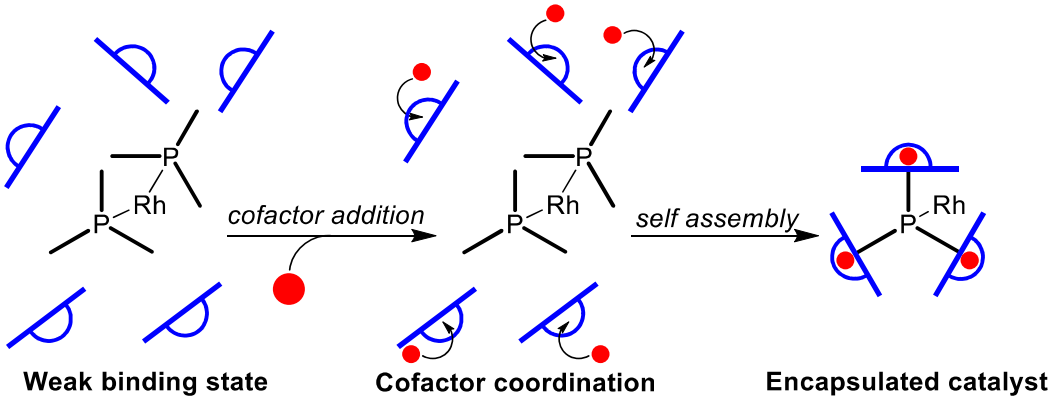

Figure 2. Schematic representation of cofactor-controlled encapsulation: the individual components present in solution form a bisphosphine rhodium complex, the introduction of the cofactor activates the porphyrin for coordination initiating capsule formation around the catalyst.

In **chapter 3** we show that an achiral tris-3-pyridyl phosphine ligand template can be encapsulated by chiral porphyrins to yield a chiral capsule (figure 3). Application of this capsule in rhodium-catalyzed hydroformylation showed that this approach can be used to produce chiral aldehydes in *enantiomeric excess*, yielding a maximum of 33% *ee*. The structure of the chiral group introduced on the porphyrin building blocks is of importance for activity and (enantio)selectivity of the catalyst formed, as no *ee* is observed when the chiral substituents are too small. In some cases, the steric and electronic properties of the chiral substituent lead to the formation of a capsule that is too rigid to facilitate effective catalysis.

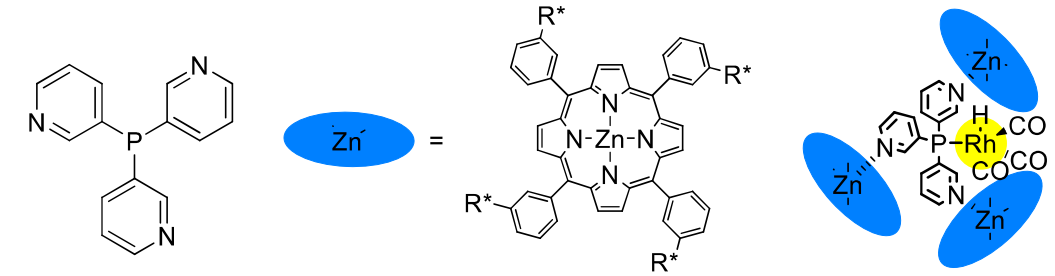

Figure 3. An achiral ligand template can be encapsulated with chiral capsule building blocks to form a chiral capsule that can be used in chiral catalysis

In **chapter 4** we explored the ligand based encapsulation strategy with the cationic PTA-Me ligand. We show that a cationic ligand can be encapsulated in two different cages known to encapsulate cationic guests (figure 4). Application of the encapsulated ligand in rhodium-catalyzed hydroformylation reactions showed that the coordination of the PTA-Me ligand to rhodium is strongly influenced by the encapsulation of the ligand. The free PTA-Me ligand coordinated to rhodium forms a rhodium bisphosphine complex that is active in catalysis or an insoluble rhodium complex, dependent on which solvent is used. Encapsulation of the PTA-Me ligand prevents the ligand from coordinating to rhodium. When the encapsulated ligand is present in solution in a rhodium-catalyzed hydroformylation reaction free rhodium catalysis is observed. The two different catalytic states produced when the PTA-Me ligand is used in rhodium catalyzed hydroformylation in presence or in absence of the capsules could be used as a basis for the development of a switchable catalytic system.

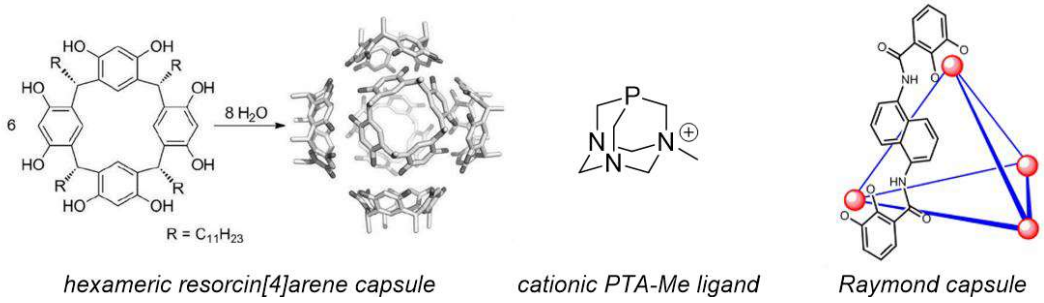

Figure 4. A cationic PTA-Me ligand (middle) can be encapsulated in the hexameric resorcin[4]arene capsule (left) and the Raymond capsule (right)

In **chapter 5** we use the ligand based encapsulation strategy for the encapsulation of ruthenium metathesis catalysts. Encapsulation of the metathesis catalysts in the resorcin[4]arene capsule is achieved by using cationic ligands that can interact with the capsule and the metathesis catalysts are still active in ring-closing metathesis reactions (figure 5). The encapsulation of the metathesis catalysts increase the catalyst stability of the ruthenium complexes, which is attributed to the encapsulation of the catalyst, which prevents bimetallic deactivation pathways.

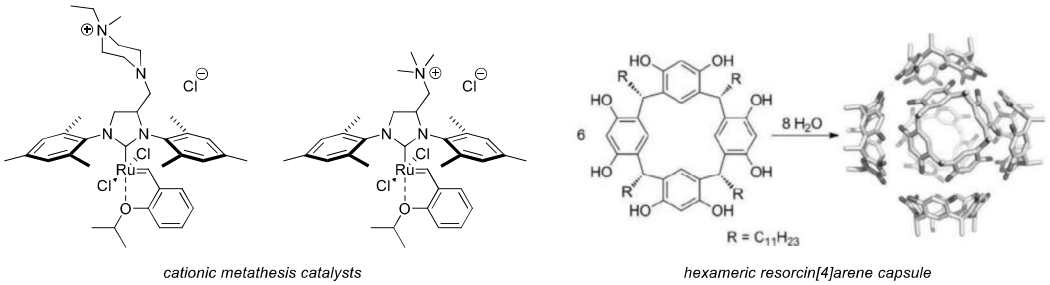

Figure 5. Two cationic metathesis catalysts that can be encapsulated in the hexameric resorcin[4]arene capsule based on the interaction of their cationic ligand structure with the capsule building blocks

In this thesis we have shown the importance of ligand structures for the encapsulation of transition metal complexes. Using the ligand as a template to generate a second coordination sphere around a transition metal complex and this can also be used as a basis for switchable catalysis. Encapsulation of an achiral ligand with chiral capsule building blocks can yield a structure suitable for asymmetric catalysis. Cationic ligand structures known in literature can be encapsulated in well-known capsule, greatly effecting the catalytic properties of the encapsulated ligands or complexes.

In chapters 2 and 4 we report systems that we envision to be used for switchable catalysis. A clear follow-up to this research would include the development of fully switchable systems based on these results. Two approaches seem most viable in that case, either to use the supramolecular approach and introduce a competing guest to obtain a switchable system, or to use electrochemistry to switch the property of the guest molecules *in situ* from binding to non-binding molecules.

In chapters 4 and 5 we report catalysis with systems in which the ligand has an interaction with a supramolecular capsule. Although in the

system reported in chapter 4 the catalyst formed was not encapsulated, several other reactions could be attempted using this ligand encapsulated in the two capsules reported. The PTA-Me ligand has been used as a ligand for numerous transition metals and this approach should be a viable method to encapsulate different transition metal complexes. The results of chapter 4 suggested that reactions in which competing ligands, such as carbon monoxide, are present may not be compatible with the encapsulated PTA-Me ligand. The cationic catalysts that were successfully encapsulated in chapter 5 form a precedent for further exploration of these cationic N-heterocyclic carbene ligands as suitable ligands that can be used to encapsulate transition metal complexes.

The encapsulation of homogeneous catalysts has led to an additional method to control the activity and selectivity of transition metal complexes. The ligand template approach and the ligand based encapsulation strategy highlighted in this thesis can potentially play an important role in finding more general methods for creating homogeneous catalysts with a second coordination sphere that influences catalysis. Many supramolecular capsules have been reported in literature, while only a handful were successfully used as vessels for the encapsulation of transition metal complexes. By carefully selecting ligands that have the right properties to be encapsulated in a specific capsule many more examples of ligand based encapsulation of homogeneous catalysts can be achieved. The development of more encapsulation strategies will contribute to the development of the increasingly complex, active and selective catalysts required for future applications.