Summary

The most powerful tool in homogeneous transition metal catalysis is ligand design and optimization. However, as the complexity of the ligands increases, synthetic routes towards these ligands are generally more difficult and time-consuming. Supramolecular chemistry provides all the tools to facilitate the synthesis of new ligands for transition metal catalyst systems. In this thesis we describe two strategies in supramolecular transition metal catalysis which result from the introduction of supramolecular chemistry in traditional transition metal catalysis. The first strategy comprises the encapsulation of a transition metal catalyst by the formation of template-assisted multi-component assemblies resulting in catalysts in specific nano-environments (Chapter 2 and 3). The second strategy comprises the formation of self-assembled chelating (hetero)bidentate ligands using supramolecular interactions (Chapters 4, 5 and 6). In Chapter 1 (The introduction) illustrative examples of the recent developments in the rapidly growing field of supramolecular ligands in transition metal catalysis are discussed.

Detailed studies on the encapsulation of (transition metal) catalysts by the formation of molecular capsules are described in Chapter 2. We have extended our previously introduced templated approach for the encapsulation of transition metal catalysts, demonstrating that the supramolecular approach provides a range of catalysts with specific properties, depending on the building blocks used. Encapsulation of a rhodium catalyst system using a tris(*meta*-pyridyl)phosphine template ligand in combination with porphyrin building blocks resulted in the formation of a rhodium complex with one phosphine coordinated. In this way a unique nano-reaction chamber was created that resulted in very selective catalysts in the rhodium-catalyzed hydroformylation of 1-octene. Based on preliminary kinetic experiments we propose that during the selectivity determining hydride migration, the alkene has to rotate which is hindered by encapsulation. The high selectivity for the branched aldehyde induced by the encapsulated rhodium complex is therefore a direct consequence of the steric restrictions imposed by the capsule. In the rhodium-catalyzed hydroformylation of internal alkenes, the catalyst showed an unprecedented high selectivity for the formation of one of the branched aldehydes. This is the first catalyst system that is able to discriminate between carbon atoms C3 and C4 in trans-3-octene, and the current findings can lead to new routes in organic synthesis.

We have also shown that the geometry of the template ligand affects the encapsulation of transition metal catalysts. The use of a tris(*para*-pyridyl)phosphine

template ligand in combination with several porphyrin and salphen building blocks provided bis-phosphine rhodium complexes, as was indicated by preliminary catalysis data. A covalent approach for the encapsulation of a rhodium complex using a bulky bowl-shaped phosphine ligand also afforded a bis-coordinated rhodium complex under reaction conditions as was evidenced by high-pressure IR and catalysis data. Certainly, a more bulky ligand needs to be synthesized to obtain selectively a mono-coordinated phosphine rhodium-complex; a goal which will be much harder to achieve in the case of covalent ligand synthesis compared to the supramolecular approach for ligand encapsulation.

In Chapter 3 we have described a combinatorial approach for the non-covalent anchoring of non-chiral transition metal catalysts to simple, chiral building blocks. For this study we used a library of 276 self-assembled chiral ligands based on 6 different non-chiral pyridyl phosphorus ligands and 46 chiral zinc(II) salen building blocks. These salen building blocks were synthesized using automated synthesis. The library of chiral palladium complexes based on these assemblies was examined in the palladium-catalyzed asymmetric allylic alkylation of 1,3-diphenylallyl acetate. Although only moderate enantioselectivities (up to 52 %) were observed so far, we demonstrated that the encapsulation effect induced by these simple chiral salphen complexes afforded the most enantioselective palladium catalysts. With the experiments described in this Chapter we have introduced a new method for the facile preparation of chiral ligands that can be used in a combinatorial fashion for various asymmetric transformations.

In the second part of this thesis (Chapters 4-6), we report the formation of self-assembled structures using a bis-zinc(II)-salphen as a template. Chapter 4 describes the use of a bis-zinc(II)-salphen template in combination with ditopic nitrogen ligands generating, depending on the distance between the two nitrogen donor atoms, organic coordination polymers or supramolecular box assemblies. Most supramolecular complexes based on the bis-zinc(II)-salphen complex crystallized readily, which facilitated structural analysis and enables the preparation of functional solid materials. Moreover, the packing of the supramolecular boxes led to porous materials in the solid state. We also prepared a chiral supramolecular box assembly, which is potentially useful in a number of applications (*e.g.* chiral separation, recognition, absorption etc.).

In Chapters 5 and 6 we discuss a template-induced formation of chelating (hetero)bidentate ligands by the selective self-assembly of two monodentate ligands on a rigid bis-zinc(II)-salphen template with two identical binding sites. For the construction of templated self-assembled homobidentate ligands we used two identical monomeric pyridyl phosphorus ligands and the assemblies were characterized by UV-vis, NMR-

spectroscopy and X-ray analysis (Chapter 5). Transition metal complexes based on these templated homobidentate ligands were explored in various catalytic transformations and they outperformed in most cases their non-templated analogues.

In Chapter 6 we show, for the first time, the formation of templated chelating heterobidentate ligands by the selective self-assembly of two *different* monodentate ligands on a rigid bis-zinc(II)-salphen template with two *identical* binding sites. Interestingly, these templated heterobidentate ligands give rise to catalysts that provide much higher enantioselectivities (up to 72 % ee) in the asymmetric rhodium-catalyzed hydroformylation of styrene than any of the corresponding homobidentate ligands or non-templated mixed ligand combinations (up to 13% ee). With the experiments described in this Chapter we have introduced a new method for the easy preparation of heterobidentate ligands that can be used for asymmetric catalysis.

The implementation of supramolecular strategies in traditional transition metal catalysis clearly results in new opportunities for catalysis. For example, supramolecular interactions can be used to mimic a cavity around the active site of an enzyme by encapsulation of a transition metal catalyst using simple building blocks. This has resulted in the formation of a high-precision catalyst, which is the first catalyst that is able to form predominantly one of the branched aldehydes in the rhodium-catalyzed hydroformylation of internal alkenes. In analogy to enzymes, the cavity around the transition metal center is of crucial importance for the formation of products in a highly selective manner. Supramolecular chemistry is also ideally suited for the development of large libraries of chiral ligands by using easy accessible building blocks that form ligands by just mixing. Because the progress in catalyst optimization by rational ligand design in asymmetric catalysis is very slow, it still depends to a great extent on trial-and-error experimentation and sophisticated guesses. Supramolecular chemistry provides all the tools to create sufficiently large ligand libraries that will be necessary to find the proper catalyst for every reaction.

Certainly, the development of supramolecular transition metal catalysis is only at its early stages, but it has already resulted in the formation of highly selective catalysts that outperformed their covalent analogues. Clearly, there is a bright future for supramolecular transition metal catalysis.