Abstract

Suitably functionalized organometallic and coordination transition metal complexes can be applied as molecular building blocks for the (supramolecular) construction of new materials which can be applicable as catalysts or sensor materials. This chapter illustrates their use in (supramolecular) catalysis, self-assembly, crystal engineering, and bio-organometallic chemistry by presenting selected examples from the respective fields.
1.1 Introduction
A rapidly evolving field in inorganic chemistry is the application of organometallic and coordination complexes as building blocks or active components in the construction of new materials exhibiting specific catalytic, redox, optical or sensor activities.\textsuperscript{1} Coordinatively unsaturated transition metal complexes can self-assemble in the presence of suitable ligands to form superstructures. The wide range of bonding geometries available in transition metal chemistry allows the targeted construction of linear, square, cubic, spherical, or other geometrical assemblies. These structures can be functional as catalysts, sensors and molecular devices, or are prepared for purely aesthetic reasons.\textsuperscript{2} Besides this, functionalization of catalytically active transition metal complexes allows regulation of their solubility behavior or immobilization on supports. This offers the opportunity to separate homogeneous catalysts from the reaction products for recycling of the expensive transition metal or ligand system, generating cleaner product streams. An exciting development in the field of ligand functionalization is the design and construction of supramolecular catalysts.\textsuperscript{3} Catalytically active transition metal building blocks can be combined with strategically placed receptor/host moieties, metal ions, functional groups or steric bulk, to mimic the substrate and product selectivities encountered in biological enzymatic systems.

The availability and synthetic accessibility of suitably functionalized organometallic building blocks forms a crucial factor in the expanding field of organometallic materials science. Since the metal-to-ligand bonds are often the most reactive part of transition metal complexes, ligands are generally metallated in the final stage of the synthesis. Coordination complexes based on ligands such as phosphanes, pyridines, and oxazolines, are prepared by facile treatment of the ligand with a suitable metal salt. In contrast, the formation of a metal-to-carbon bond often requires more stringent conditions, which should be compatible with the functional groups already present in the ligand. Consequently, the use of coordination complexes as molecular synthons is further developed compared to organometallic complexes, with heterocyclic nitrogen ligands dominating the field. This chapter highlights the use of organometallic and coordination complexes as building blocks with illustrative examples concerning (catalyst) assembly, crystal engineering, catalyst immobilization, supramolecular catalysis, and bio-organometallic chemistry. Furthermore, ligand functionalization offers the opportunity to tune the electronic properties of its metal complex. The final paragraph describes the aim and scope of this thesis.

1.2 Assembly in Solution and in the Solid State
The assembly of organic building blocks in solution or in the solid state (crystal engineering) relies on weak intermolecular interactions such as hydrogen bonding, π-π stacking, dipole-
dipole interactions, and coulombic interactions. Strong hydrogen bond donor and acceptor groups, *e.g.* COOH, OH, CONH$_2$, and CONHR groups, form essentially the same type of hydrogen bonding interactions whether part of an organic molecule or of a metal-coordinating ligand. In contrast, (transition) metal complexes offer additional bonding features, namely coordinate and covalent bonds. As a result, materials containing covalent or metal-based coordination networks are generally more robust than those relying on weak interactions between organic building blocks alone. In addition, the presence of metal atoms in the molecular building block generates new types of interactions, which are characteristic of inorganic and organometallic systems, including $M\cdots M$ interactions and $M\cdots X\cdots H$ hydrogen bonds. The ample availability of metal-binding ligands, and the varying coordination geometries and numbers of different metal ions allows the formation of any imaginable structure. The strategic use of kinetically labile or inert metal ions, and conversions between them during or after the assembly process, allows efficient scanning of the potential energy surface for the thermodynamically most stable product and subsequent kinetic immobilization of the obtained structure.

### 1.2.1 Self-Assembly in Solution

Porphyric systems, in particular zinc(II) tetraphenylporphyrin (ZnTPP), offer readily accessible building blocks for the construction of supramolecular assemblies, utilizing the complexation of nitrogen based (pyridyl) ligands to the zinc(II) ion. Additionally, numerous functionalizations on porphyric systems have made them highly versatile building blocks in supramolecular transition metal chemistry. Pyridyl functionalized Zn(II) porphyrins were found to self-assemble in solution and in the solid state. Combinations of free-base porphyrins and various degrees of pyridyl functionalisation on the porphyrins allows self-assembly in controllable supramolecular architectures (Figure 1).
The group of Hupp applied the complexing abilities of ZnTTP towards pyridyl groups for the introduction of steric bulk around a chiral manganese(III) salen based catalyst (4, Figure 2). The presence of the ZnTPP moieties in the vicinity of the catalyst improved its activity and lifetime, but hardly altered its enantioselectivity.\textsuperscript{11}

\textbf{Figure 2.} Chiral manganese(III) salen catalyst with ZnTPP.\textsuperscript{11}

A more complex system published by this group uses large supramolecular assemblies of pyridyl functionalized zinc(II) and manganese(III) porphyrins, held together by coordination to rhenium atoms (5, Figure 3). The authors state that this assembly resembles the catalytic core of cytochrome P450, both structurally and functionally. Although the catalyst is embedded in steric bulk, an apical ligand is missing on the central manganese porphyrin. This ligand is of crucial importance in the structure and catalytic activity of cytochrome P450, but not included in its mimic 5. In epoxidation experiments with several functionalized \textit{cis}-stilbenes, shape selectivity was observed. The least bulky substrates were epoxidized preferentially over the bulky substrates.\textsuperscript{12}

\textbf{Figure 3.} Self-assembled Mn(III) based epoxidation catalyst.\textsuperscript{12}
The group of van Leeuwen prepared hemispherical assemblies with the metal center completely encapsulated in steric bulk by combining pyridylphosphanes, ZnTPP and transition metal salts. Ligand 6 can complex to three porphyrin moieties forming an extremely bulky phosphane (Figure 4).\(^\text{13}\)

![Figure 4. Supramolecular assembly of encapsulated transition metal catalysts with altered activities and selectivities.\(^\text{13}\)](image)

The palladium(II) complex of ligand 6 has hardly any activity in the Heck reaction of styrene and iodobenzene, in the absence of zinc(II)porphyrins. However, the addition of ZnTPP to the complex leads to the assembly of a highly active Heck catalyst when compared to its triphenylphosphane analogue. A similar effect is observed for ligand 6 in the rhodium(I) catalysed hydroformylation of 1-octene, showing a significant drop in the linear to branched ratio and higher activities in the presence of the porphyrin. The enhanced activity and altered selectivity of the catalyst is attributed to the preferred formation of monophosphane complexes as a result of the steric bulk of the assembled ligands.

The versatility of pyridyl-type ligands in the construction of supramolecular assemblies is represented by the work of Fujita et al. The combination of designed ligands, appropriate metal salts, and templates allows the supramolecular assembly of various rings, cages, and two- or three-dimensional synthetic receptors.\(^\text{14}\) One illustrative example involves the spontaneous assembly of pyridyl-based ligands and metal salts into two interlocked coordination cages (7, Figure 5).\(^\text{15}\) This assembly uses ten components, which have to be organized in a specific way. While at first a statistically distributed mixture is formed, a gradual increase in the thermodynamic product (7) is observed after prolonged heating.
Functionalized transition metal terpyridine units have been studied in detail as building blocks for the construction of coordination dendrimers. Main emphasis in these studies has been put on the ruthenium terpyridines, since these can exhibit interesting electrochemical, photophysical and photochemical properties. An interesting assembly is prepared by the selective reaction of a polyol functionalized coordination dendrimer with [(tpy)Ru(tpyCl)]^{2+} moieties, affording a fully functionalized coordination dendrimer (8, Figure 6). Functionalisation of the polyol dendrimer is quantitative and selective, and is a rare example of ligand functionalization on metallated amine ligands.
The concept of preparing dendritic macromolecules based on metal complexation was used by the group of Reinhoudt for the construction of organometallic coordination dendrimers from cyclopalladated SCS-pincer (SCS-pincer = 2,6-bis((thiophenolato)methyl)phenyl anion) complexes. The building blocks are activated upon dehalogenation to afford Lewis acidic palladium complexes, forming coordinative bonds with cyano-ligands (Figure 7). Dendrimers of generation one (9) to five were obtained via a step-wise growth strategy.20

Figure 7. Step-wise assembly of coordination dendrimers.20

Highly elegant examples using transition metal complexes as building blocks and active units have been reported by Sauvage et al.21 Linear ‘molecular machines’ resembling shuttles and muscles, were prepared making use of the ability of copper(I) to assemble two phenanthroline ligands in a stable tetrahedral environment, combined with the affinity of copper(II) species for higher coordination numbers. A molecular rod functionalized with phenanthroline and terpyridine building blocks was combined with a phenanthroline based rotaxane copper(I) complex (10, Figure 8). In the 1+ oxidation state the copper ion is accommodated between both phenanthroline units. Oxidation of the copper ion to its 2+ oxidation state increases the affinity of the phenanthroline rotaxane copper complex towards the terpyridine unit, resulting in shuttling of the macrocycle over the molecular rod. This process is fully reversible and could also be induced photochemically by irradiating the MLCT transition of the bis-
phenanthroline copper(I) complex. These studies were extended to mimic muscle action by designing a molecular assembly in which two filaments can glide along one another.

![Diagram of copper(I) phenanthroline rotaxanes over a molecular rod.](image)

Figure 8. Shuttling of copper(I) phenanthroline rotaxanes over a molecular rod.

### 1.2.2. Crystal Engineering

The design, modeling and synthesis of ordered solids, i.e. crystal engineering, by predefined aggregation of molecules and ions is of interest for applications in fields within material science, such as (opto)electronics and the construction of nanoporous or biomimetic materials. A prerequisite for success is the understanding of the intermolecular forces involved in the assembly of the individual parts. The fast majority of molecular architectures in the field of inorganic crystal engineering are covered by coordination networks. The coordination bonding capacity of transition metals is utilized to build-up three-dimensional supramolecular arrangements with crystalline periodicity. These networks generally utilize bipyridyl-type ligands with the N-donor atoms situated in a predefined geometrical arrangement to act as a bridge or joint between (late transition) metal atoms. The suitability of the obtained materials for solid-state reactivity, catalysis, or in sensor applications appears to be dependent on the availability of large accessible spaces. It is often difficult to obtain this nanoporosity, since self-entanglement or interpenetration of the networks, can lead to densely packed structures. Crystallization in the presence of removable guest molecules has given some success in this respect, creating channels and cavities in the crystal lattice. A special
case in the adsorption and desorption of guest molecules in the crystalline state is based on the SO₂ adsorbing properties of platinum(II) NCN-pincer complexes (NCN = 2,6-bis(dimethylamino)methyl]phenyl anion).²⁴ The para-hydroxy functionalized cyclopatinated NCN-pincer complex (11) forms α-type linear hydrogen bonded networks in the crystalline state, an example of M−X⁻...H bonding. Adsorption and desorption of SO₂ on the platinum center of 11 is fully reversible in the crystalline state (Figure 9) and occurs via crystal-to-crystal transformations accompanied by a color change, and expansion and shrinkage of the crystal. Interestingly, the crystalline gas sensor material does not contain a channeled structure, indicating that large voids in the structure are no prerequisite for nanoporosity.

Apart from ligand coordination, hydrogen bonds are widely employed to obtain predefined crystalline architectures.²⁵ Hydrogen bonds are considered to be essentially electrostatic in nature, are relatively strong and possess a highly directional character. Their strength can be improved by employing ionic charges, i.e. cationic donors and anionic acceptors, combining the hydrogen bond directionality and the strength of coulombic forces. Additionally, the use of metal ions permits a larger choice of components, which may possess different topologies, as well as different bonding and electronic characteristics.² An illustrative example in this respect is the study of metallocene dicarboxylic acid structures.²⁶ The solid-state structure of various hydrogen bonded, nearly isostructural, organometallic building blocks depends on their charges. While neutral ferrocene dicarboxylic acid (12) forms dimers in the solid state, its positively charged cobalt(III) analogue (13) forms chains, as well as the anionic singly deprotonated ferrocene dicarboxylic acid (14) (Figure 10). These studies were also performed with carboxylic acid functionalized chromium bis-arene complexes, showing similar trends.²⁷
In addition to the carboxylic acid functionalized complexes, Braga et al. introduced alcohols and amines on the cyclopentadienyl ring to extend their library of ferrocene based organometallic building blocks for crystal engineering. The group of Brammer prepared hydrogen bonded zigzag ribbons based on the $\pi$-bonded Cr(CO)$_3$ benzene tricarboxylic acid building block. While two carboxylic acid moieties are involved in the formation of the ribbon, the third is hydrogen bonded to an ether molecule. No honeycomb structure, as is known for benzene tricarboxylic acid, is observed. Recently, a catalytically active indium(III) three-dimensional solid-state framework was obtained by assembly of 1,4-benzene dicarboxylic acid and an indium(III) salt in the presence of water and base. The crystals are constructed from [In$_2$(OH)$_3$]$_{3+}$ sheets which are interconnected by 1,4-benzene dicarboxylate units acting as pillars, with each carboxylate connected to two indium ions. This material is active in the reduction of nitroaromatics and the oxidation of sulfides. Kinetic data suggest that the catalyzed reactions only take place at the surface of the material, due to the small size of the pores in this structure.

Although ligand coordination and hydrogen bonding can be considered as most useful for crystal engineering purposes, other interactions also possess a sufficient degree of directionality. The $\pi-\pi$ stacking of arene ligands, especially porphyrins, forms a reoccurring motive in crystalline systems. Hosseini et al applied weak van der Waals interaction in the construction of linear one-dimensional networks based on unsymmetrical bis-calixarene molecules (coilands) and appropriate connectors. The linear rods are hold together by a lock-and-key fit of the connector in the coiland, with van der Waals interactions acting as single attractive force.
1.3 Catalyst Immobilization

Immobilization of homogeneous transition metal catalyst on (solid) supports allows facile separation of catalyst and reaction products. This makes recycling of expensive transition metals and ligand systems feasible. The efficient removal of the catalysts leads to cleaner product streams in fine-chemical synthesis. In general, the ligand is grafted on the support system prior to introduction of the transition metal. Ligands are, for this purpose, functionalized at positions distal from the metal binding site, with suitable anchoring groups. Alternatively, metallated ligands can be immobilized directly on the support in either a covalent or non-covalent fashion. While immobilization on regular polymers\textsuperscript{33} and solid supports\textsuperscript{34} has attracted considerable attention, much research has been directed to the use of dendrimers as support systems for catalyst immobilization.\textsuperscript{35} These tree-like macromolecules possess well-defined structures and can be functionalized selectively at their core, shell or periphery, depending on their composition. This makes them ideal systems to study various properties of immobilized transition metal complexes in great detail.

An illustrative example in this field was published by Togni \textit{et al.} and involves the use of dendrimers functionalized at their periphery with chiral \((R)-(S)-\text{Josiphos}\) ligands.\textsuperscript{36} The dendrimer is constructed from cores based on a cyclophosphazene core (15\textsuperscript{a})\textsuperscript{36a} or polycarboxylic acids (15\textsuperscript{b-c}),\textsuperscript{36b} functionalized with aryl based branching points, containing the phosphane ligand attached by amide linkages (Figure 11). Conversion into their corresponding rhodium(I) complexes was achieved by treatment with [Rh\((\text{cod})\)]\((\text{BF}_4)\) affording chiral catalysts for the asymmetric hydrogenation of dimethyl itaconate in methanol. High enantioselectivities (>98%), only slightly lower than those of the parent \((R)-(S)-\text{Josiphos}\) complex, were obtained with these dendritic systems.

\begin{figure}
\centering
\includegraphics[width=\textwidth]{ Figure 11. Chiral dendritic phosphane ligands for asymmetric rhodium(I) catalysis.\textsuperscript{36} }
\end{figure}

The ferrocenyl based phosphane functionalized dendritic wedge forms the essential organometallic building block in the preparation of this system, since the catalytically active rhodium(I) complex is prepared \textit{in situ} as final step of the total synthesis. This exemplifies the
stability of selected organometallic fragments such as ferrocene, which can be treated as inert functional groups in organic synthesis.

The encapsulation of a catalytically active transition metal complex within dendrimer wedges allows shielding of the catalytic system and tuning of its microenvironment. Starting from a chiral TALDOL building block, Seebach et al prepared titanium(IV) TALDOLates functionalised with Fréchet-type wedges up to the fourth generation (16, Figure 12). The chiral catalyst shows very high enantioselectivities (98:2) in the addition of diethyl zinc to benzaldehydes. Additional functionalisation of the dendritic wedges with styrene moieties allowed cross-linking of the system in a polystyrene support, making successful catalyst recycling facile.

![Figure 12. Dendrimer/polystyrene encapsulated Ti(IV) TALDOLates for the enantioselective addition of ZnEt2 to benzaldehyde.](image)

A recent alternative approach for catalyst immobilization is the non-covalent anchoring of transition metal complexes onto dendritic support systems. Loading of the dendrimer by non-covalent interactions allows separate construction of support and catalyst, followed by facile immobilization under mild conditions. Additional advantages involve refuctionalization of the support in the case of catalyst deactivation, and eventually immobilization of mixtures of catalytically active components. While the use of dendrimers for the supramolecular immobilization of organic guest molecules has been well established, there are only few examples involving the non-covalent immobilization of homogeneous catalysts. Reek and Meijer reported the non-covalent immobilization of phosphane ligands on urea adamantyl functionalized poly(propylene imine) dendrimers (16, Figure 13). Multiple hydrogen bonding interactions, in addition to a strong coulombic attraction, between the urea-functionalized phosphane ligand and the dendrimer allow selective binding of 32 ligands on
the periphery of the dendrimer. Subsequent treatment of the material with \([(\text{cod})\text{PdMeCl}]\) afforded a supramolecularly assembled system with catalytic activity in allylic amination reactions. The coordination complexes formed with a phosphane-to-palladium ratio of 2 showed high retentions in a continuous flow membrane reactor. Lower phosphane:palladium ratios led to considerable leaching of the catalyst.

![Figure 13. Immobilized phosphane ligand on the periphery of urea adamantyl functionalized poly(propylene imine) dendrimer.](image)

In our group, coulombic interactions were applied for the immobilization of organometallic NCN-pincer complexes. Polycationic dendrimers, based on a polybenzylammonium core and Fréchet-type dendritic wedges, were loaded with sulfate functionalized NCN-pincer palladium complexes using anion exchange (17, Figure 14). Activation of the complex by halide abstraction afforded an assembly with catalytic activity in Lewis-acid catalyzed aldol reactions. Alternatively, the NCN-pincer palladium complex could be activated prior to assembly onto the dendrimer. The efficiency and retention of 17 in continuous flow membrane reactors was not investigated.

Systems 16 and 17 differ with respect to the assembling method. In the preparation of the palladium complex of 16 the metal center is introduced in the final stage of the synthesis by forming coordinative bonds to already immobilized phosphane ligands. These polyphosphane ligands can be used for the complexation of various metals with different catalytic properties. However, leaching of the metal by decomplexation of the ligand can occur even when the ligand is retained in the dendrimer host. In contrast, 17 is prepared by the assembly of the organometallic building block and dendritic host in one step. The covalent M–C bond ensures that the metal is retained in the coordination sphere of the ligand, and leaching of the transition metal can only occur in case of complete removal of the complex from the dendritic host.
1.4 Supramolecular Catalysis

An exciting application of transition metal building blocks is the design, construction, and evaluation of supramolecular catalysts. A key source of inspiration in the development of supramolecular catalysts is found in enzymatic catalysis. Enzymatic catalysts have evolved over millions of years through mutation and selection, and represent the highest expression of chemical catalysis. They achieve astonishing selectivities by deploying intermolecular forces to guide the substrate precisely along a predestinated reaction pathway. Catalysis takes place within a supramolecular aggregate, resulting in high effective concentrations of substrate near the catalytic site, leading to high catalytic activities. Another feature of (enzymatic) catalysts involves selective stabilization of the highest energy transition state, thereby reducing the activation enthalpy of the reaction. Transition metal based supramolecular catalysts are generally constructed by combining known homogeneous catalysts with known host molecules, such as crown ethers, cyclodextrins, cyclophanes, and calixarenes. Modification of the ligand, allowing strategic placement of receptor sites with respect to the catalyst, forms an
essential step in the preparation of supramolecular catalysts. Examples are ordered with respect to the type of catalyzed reactions, and thus the type of catalytic building block.

1.4.1 Ester Hydrolysis

The fast majority of supramolecular catalysts is active in ester cleavage reactions, based on either fully organic groups for general acid-base catalysis, or on the use of zinc(II), cobalt(III), barium(II) or copper(II) coordination complexes. The combination of multiple metal sites on a linker is often a successful approach to obtain highly active catalysts with synergic action of the metal sites in catalysis.

The cation complexing abilities of crown ethers have been applied in the construction of a dinuclear barium(II) complex (18) for ester and amide cleavage (Figure 15). Complex 18 has two identical Ba$^{2+}$ sites, which perform different functions. One of the metal ions binds and activates the ethoxide nucleophile, while the other side anchors the amide or ester by the distal carboxylate moiety on the substrate. Hence, the amide or ester moiety is in close vicinity of the activated ethoxide, resulting in cleavage.

![Figure 15. Dinuclear barium(II) complex for supramolecular ester and amide cleavage.](image)

Extended studies were performed towards the hydrolytic activity of di- (and tri-)nuclear metal ion complexes based on calix[4]arenes and N-donor ligands as molecular scaffolds by Reinhoudt et al. The metal ions in complexes 19 and 20 are placed at the upper rim of the calix[4]arene, at diametrical positions (Figure 16). The substituents on the lower ring (ethoxyethyl) prevent inversion of the aromatic units through the cavity of the macrocycle.

![Figure 16. Calix[4]arene based dinuclear complexes as metallo-phosphodiesterase model.](image)
In the studies, various phosphate esters and RNA 3',5'-dinucleotides (NpN) were used to screen the catalysts for their phosphodiesterase activity. The activity of the dinuclear complexes 19 and 20 was increased considerably when compared to the mononuclear complex (50-fold), or the mononuclear complex lacking the calix[4]arene scaffold (300-fold). The bimetallic complexes show saturation kinetics, with binding constants with the substrate in the order of $10^4$ M$^{-1}$. Both the flexibility and the preorganizing ability of the calix[4]arene, are important factors in their efficiency. A decrease in flexibility by connecting the oxygens on the lower rim with a rigid spacer, resulted in reduced activity. The pH-rate profiles of both catalysts are bell-shaped with optimums located at pH 7.4 and 6.4 for 19 and 20, respectively. Introduction of a third metal binding site at the upper rim leads to a threefold increase in turnover rate, while the binding affinity of the substrate is reduced considerably. The application of a statistical 1:2 mixture of copper(II) and zinc(II) leads to species with higher activity than their homonuclear analogues.43

Another successful example in the supramolecular cleavage of esters is published by the group of Breslow.44 Two β-cyclodextrins are attached to a bipyridine moiety, according to a design based on computer models (21, Figure 17). Complexation of a metal(II) ion (Cu(II), Ni(II), Zn(II)) to the bipyridine fragment places the metal in an ideal place to coordinate to the carbonyl oxygen, and to deliver a hydroxide anion to the substrate. Since the sum of the binding energy of the products is less compared to the binding energy of the substrate alone, product inhibition is not observed. Rate enhancements up to 225,000 for designed substrates (22) are observed. In the absence of the copper(II) ion this rate enhancement is only 80-fold. Copper(II) is the most active metal, albeit that in the presence of a nucleophilic bound oxime ligand zinc(II) ions give rate accelerations up to 1,700,000 in the hydrolysis of 22.

Porphyrin complexes are, apart from their application as (ep)oxidation and hydroxylation catalysts, useful building blocks in the construction of host molecules. Sanders et al. synthesized a cyclic zinc(II) porphyrin trimer (23) which is capable of acyl transfer by holding the substrates in close proximity (Figure 18).45
The substrates are functionalized with pyridyl and imidazole groups which can coordinate to the zinc(II) ions, positioning the substrates in an optimal way to react. The reaction rate was enhanced 16 fold compared to a monomeric zinc(II) porphyrin. The reaction is inhibited by 1,3-bis(4-pyridyl)propane, and the average turnover number per trimer after 160 hours is around 25, without detectable decomposition or loss in activity.45

1.4.2 Oxidation Reactions

Selective (mild) oxidations, epoxidations and hydroxylations form an important class of reactions in organic synthesis. Most homogeneous catalysts in these fields are based on their biological counterparts, for their astonishing substrate and product selectivities. Metalloporphyrins constitute an important class of epoxidation and hydroxylation catalysts in attempts to mimic the behavior of the enzyme cytochrome P450, which converts alkanes into alcohols. The naked manganese porphyrins degrade fairly rapidly under catalytic reaction conditions, like the iron heme mimics. The primary mode of deactivation under these conditions is the formation of an inactive \(\mu\)-oxo bridged dimer (Mn–O–Mn).46 In analogy with the protein superstructure, with the metalloporphyrin encapsulated in a regulated nanospace formed by the folded amino acid chain, synthetic metalloporphyrins have been functionalized with bulky substituents and other functional units. The steric bulk not only prevents the primary deactivation mode, but also introduces regioselectivity in, for example, alkane hydroxylations.47

Apart from creating steric bulk around the metalloporphyrin to induce shape selectivity, iron(III) porphyrins 'capped' with chiral bridging groups have been applied in asymmetric catalysis (24 and 25, Figure 19). Iron(III) porphyrin 24 is an elegant example of asymmetric
induction in the hydroxylation of ethylbenzenes. The chiral binaphtyl cavity imposes a preferential orientation of the substrate to the catalyst, leading to a stereoselective outcome of the reaction. In the iron(III) binaphtyl 'capped' porphyrin two chiral binaphtyl groups are placed above each face of the metalloporphyrin. The ether linkages force the binaphtyl groups into close proximity to the metal center, imposing a rigid chiral environment. Asymmetric epoxidations of various aromatic alkenes with iodosylbenzene as oxygen donor gave high ee's (up to 63%) for monosubstituted alkenes. The more sterically demanding disubstituted alkenes gave only moderate ee's (20-30%).

Substrate binding in the vicinity of the metalloporphyrin was accomplished by Breslow and co-workers, giving access to the regioselective hydroxylation of steroids. A manganese(III) TPP with β-cyclodextrins connected to the phenyl rings, hydroxylated an andostanediol derivative selectively at the 6α-position (Figure 20). The substituents attached to andostanediol are chosen to optimize complexation of the substrate in two opposite cyclodextrins, placing the 6α-carbon atom on top of the oxygenated manganese atom for hydroxylation. The stability of the catalyst against oxidative degradation is increased to a great extent by fluorination of the four phenyl rings, improving the turnover number from 3-5 to 95.
A similar system was synthesized by Woggon et al. for the central (15,15') cleavage of $\beta,\beta$-carotene (Figure 21), mimicking carotene dioxygenases. Two cyclodextrin moieties are attached with their primary rim on the two opposite sites of a tetraphenylporphyrin using ether linkages instead of the thioether links used in 26. This spatial orientation makes it an ideal host to complex both distal aliphatic groups of the $\beta,\beta$-carotene in the cyclodextrin cavities with binding constants in the order of $10^6$ M$^{-1}$, enforcing the central C=C bond above the metal coordination site of the porphyrin. Its ruthenium complex is capable of central cleavage of $\beta,\beta$-carotene, however competitive cleavage of the C11'-C12' and the C9'-C10' double bonds form serious site reactions due to lateral movement of the carotene in the cyclodextrin cavities. Modification of the substrate into Phe-$\beta$-carotene, suppresses the lateral movement, giving exclusive central cleavage at C15–C15'. Exocentric cleavage at C7'–C8' is in both cases not observed.\textsuperscript{51}
Supramolecular catalysis with systems based on cyclophane hosts has been extensively studied by the group of Diederich. Cyclophanes provide excellent hosts for the encapsulation of aromatic guest molecules in aqueous and other protic solvents. A porphyrin bridge was introduced on a tetramine cyclophane and tested for its catalytic activity in the oxidation ofacenaphtylene, a substrate which binds strongly in the macrocyclic cyclophane ring (27, Figure 22). Acenaphten-1-one is the major isolable product in the oxidation with iodosylbenzene as oxygen-transfer reagent. Support for supramolecular catalysis is provided in a competition experiment with the unreactive phenanthrene, reducing the yield of naphten-1-one considerably.

1.4.3 Carbon-Carbon bond formation and activation

In contrast to supramolecular ester hydrolysis and oxidation reactions, less is known concerning supramolecular catalysis of C–C bond forming reactions. While homogeneous transition metal catalysts play a crucial role in important organic transformations involving the C–C bond, they were hardly studied in the context of supramolecular catalysis. A cyclophane-type host molecule, functionalized with a bisoxazoline ligand incorporated in the macrocyclic ring, was applied in the supramolecular Cu(I) catalysed cyclopropanation of styrene with diazoacetate (28, Figure 23). The cyclophane ligand forms a $C_2$-symmetric complex with copper(I) inducing a certain degree of helicity to the bridge. The cyclopropane ring is formed in the catalytic cycle by nucleophilic attack of the copper-bound carbene to the prochiral alkene. The helicity of the macrocyclic ring can be seen as an extension of the symmetry around the metal center, and can transfer its chiral information over to the substrate bound inside the cavity. The effectiveness of this concept is evident from the high ee’s and even more from the high diastereoselectivities observed in the test reactions, compared to those of the parent complex without macrocycle.
Diphenylglycoluryl molecular clips, intensively studied by the group of Nolte, were applied as hosts for supramolecular transition metal catalysed hydroformylation and hydrogenation reactions. Although various architectures failed to show activity or increased selectivity, a molecular clip functionalized with aza-crown ether bis-phosphite building blocks shows substrate selectivity in hydrogenation reactions of functionalized allylarenes (29, Figure 24).\(^{55}\) The exchange of the phosphite ligands for phosphane ligands (30) afforded metallohosts capable of shape selective hydroformylations.\(^{56}\)

Substrates with the ability to bind in the cleft by a combination of hydrogen bonding to the carbonyl groups and \(\pi-\pi\) stacking with the aromatic walls, such as allylresorcinol and allylcaotic, are converted preferentially over substrates incapable of hydrogen bonding interactions. Surprisingly, the metallohost hardly influences the linear to branched ratio in the hydroformylation reactions with 30.

1.5 Bio-Organometallic Chemistry

The modification of biologically active molecules, such as proteins or sugars, with transition metal complexes can give useful insights in structure and function of biomolecules and has given rise to various medicinal applications.\(^{57}\) Werner-type complexes with hard N, O, or S
donor ligands have been applied mostly in this respect. Of recent interest is the application of robust organometallic complexes in biochemistry. Characteristic chemical and spectroscopic properties of organometallic complexes can be applied for site-selective reaction with biomolecules, or as markers for the direct detection of the bio-organometallic material.

The use of transition metal carbonyl complexes is attractive, since the carbonyl stretching frequency forms a valuable probe for (drug) detection purposes. Characteristic bands are formed for adducts of the carbonyl complexes with peptides or steroid hormones, allowing a simultaneous qualitative and quantitative essay of multiple components with very small detection limits without the need for radioactive markers. Grotjahn et al applied donor substituted cyclopentadienyl ruthenium complexes (31) for selective labeling of amino acids in a peptide chain. Treatment of a model polypeptide with 31 resulted in the selective formation of $\eta^6$-bonded ruthenium complexes on the arene rings of the phenylalanine residues of the polypeptide (Figure 25). This method was effective for the selective labeling of the 27 amino acid polypeptide secretin.

![Figure 25. Labeling of polypeptides with ruthenium complexes.](image)

NCN-pincer platinum complexes are used in our group as peptide labels with potential applications as diagnostic biomarkers and biosensors. NCN-pincer platinum complexes exhibit characteristic $^{195}$Pt-NMR signals, which is a valuable tool for probing the steric and electronic environment of the metal. Additionally they form bright orange complexes in the presence of SO$_2$ making facile detection of the complex feasible. The high robustness of the NCN-pincer platinum complexes allows their application in the aqueous and aerobic conditions encountered in biological systems. As a consequence of this stability, pincer platinum species could be covalently bonded to the N-terminus of L-valine, or on the side-chain of L-lysine. Interestingly, transformations on the ligand were possible after metallation of the ligand, generating more flexibility in the synthesis of the bio-organometallic species. Indeed, NCN-pincer palladium complexes could be functionalized at the N- and C- terminus of L-valine, and on the N-terminus of the dipeptide L-Phe-L-Val-OMe (32, Figure 26).
1.6. Tuning of Transition Metal Complexes

Apart from ligand-functionalization employed for anchoring opportunities, i.e. the building block approach, it can be used to tune the metal center of the resulting complexes electronically. This methodology can be especially useful in cases where the influence of the substituent can be rationalized. The empirical Hammett equation has been used widely for treating the effect of substituents on rates and equilibria of organic reactions. Furthermore, correlation analysis is applied with success with several other properties, such as $^{13}$C- and $^{19}$F-NMR chemical shifts. The use of the Hammett correlation to quantify the influence of substituted (aromatic) ligands on transition metal complexes, and consequently on their catalytic and/or optical properties has been used with varying success. However, if successful it allows theoretical prediction of properties from the resulting complexes.

In studies directed toward the prediction of the oxidative reactivity of vanadium peroxo complexes, Di Furia et al. found Hammett-type correlations between the $^{51}$V-NMR chemical shift and the $\sigma$ values of the substituents on meta- and para-substituted pyridine and aniline ligands (33, Figure 27). Upon increasing the electron density on the vanadium nucleus by placement of electron donating substituents, the chemical shift of the complexes decreases. By calculation of the $^{51}$V gyromagnetic ratios from the chemical shift data of various N$\cap$O or O$\cap$O ligated peroxo vanadium complexes (not shown), the authors found linear correlations between the gyromagnetic ratios and $\lambda_{\text{max}}$ values of the lowest energy electronic (n$\rightarrow$d) transition. These correlations allow the prediction of reactivity for the peroxo vanadium complexes and tuning of the band gap of the frontier orbitals, based on $^{51}$V-NMR chemical shift data.
Reinhoudt et al. studied the coordination chemistry of cationic SCS-pincer palladium complexes with substituted pyridines (34, Figure 28). Linear Hammett correlations were found between σ⁺ substituent constants and the stability of the resulting pyridine-palladium complex, reflected in their association constants.

![Figure 28. SCS-pincer palladium complexes with substituted pyridines.](image)

An example from our group involves the electronic tuning of NCN-pincer nickel complexes by para-substitution (35, Figure 29). Investigation of the complexes by ¹³C-NMR and electrochemistry revealed Hammett-type correlations for ¹³C chemical shift differences (δC_{ipso}-δC_{ortho}), as well as for the oxidation potentials (E_{p,a}) of the nickel complexes with the σₚ substituent constants. Especially the quantification of the substituent effect on the Ni(II)/Ni(III) oxidation potential by correlation analysis is a powerful tool for tuning the reactivity of the catalytically active NCN-pincer nickel complexes. Their catalytic activity in the Kharasch addition of polyhalogenated alkanes to alkenes, involving one-electron transfer of the nickel(II) atom to the substrate, is directly affected by para-functionalization. Electron donating substituents decrease the oxidation potential of the Ni(II)/Ni(III) couple, resulting in more active one-electron transfer catalysts.

![Figure 29. Para-substituted NCN-pincer nickel complexes.](image)

1.7 Conclusions and Outlook
Organometallic and coordination chemistry is originally mainly focused on the metal center itself, tuning its direct coordination environment, and consequently its properties by subtle variations in the ligand system. By choosing the appropriate combination of metal and ligand systems, transition metal complexes can exhibit characteristic properties, allowing applications as catalyst or as sensor materials. A more recent challenge in inorganic chemistry forms the application of organometallic and coordination complexes as building blocks in the construction of new (transition) metal based materials, as is evident from the ample examples available in literature. The selected examples shown in this chapter illustrate the broad field of potential applications, but should not be considered as comprehensive. Key sources of
inspiration are found in biological systems, but also in organic chemistry, which is more developed with respect to supramolecular chemistry and crystal engineering.

Apart from few selected examples, ligands are functionalized or immobilized prior to the introduction of the metal, making the suitably functionalized ligand the actual building block in the syntheses. The transition metal complex is recognizable as building block in the final product, but is often not introduced as such. This is especially true for coordination complexes, which are prepared under mild conditions by treatment of the ligand with a metal salt. The formation of organometallic complexes in the final stage of the synthesis is often more problematic, as formation of M–C bonds requires more demanding reaction conditions. Metallation in earlier stages of the synthesis forms an attractive alternative, generating true organometallic building blocks. Obviously, this approach is only applicable for relatively stable organometallic complexes. The increasing availability of easily accessible transition metal building blocks, and the stability of part of them, generates a transition metal complex ‘meccano kit’ for the preparation of materials ranging from engineering solids to supramolecular catalysts and bio-organometallic materials.

Apart from the use of functionalized transition metal complexes as (supramolecular) building blocks, ligand substitution offers a powerful tool to tune the metal center of the resulting complexes electronically. In cases where correlation analysis can be applied to rationalize the influence of the substituent, theoretical prediction of their properties becomes feasible.

1.8 Aim and Scope of this Thesis

The work described in this thesis was part of the CW/STW project 'Molecular Recognition in Dendritic Catalysts'. The aim of this project was the use of supramolecular interactions for either substrate binding in catalytic dendrimers or catalyst immobilization in dendrimers. Both concepts combine the advantage found in homogeneous (supramolecular) catalysis, i.e. well-defined catalytic sites with high substrate and product selectivities, with the ease of separation and recycling found in heterogeneous catalysis. Essential for the development of these systems is the availability of suitably functionalized organometallic building blocks. The NCN-pincer ligand forms an attractive ligand to use in this respect, since it has shown its versatility in various catalytic and sensor applications. The central theme in this thesis is the preparation and application of organometallic NCN-pincer complexes as building blocks in the construction of new (macromolecular) organometallic materials. Chapter Two describes the development of synthetic routes towards new para-functionalized NCN-pincer complexes, and the influence of the substituent on the properties of the complex. Surprisingly, various substitution reactions, involving rather vigorous reaction conditions, can be performed after
metalation of the ligand, exemplifying the high stability of these complexes. The NCN-pincer palladium and platinum complexes presented in Chapter Two form the essential building blocks for the preparation of the organometallic materials described later in this thesis. One aspect of the functional groups introduced on the pincer ligand system can give rise to new interactions and assembly features, in solution as well as in the solid state. Chapter Three describes the formation of para-nitro functionalized NCN-pincer palladium dimers in the solid state by electron donor-acceptor interactions between the metal center and the nitro substituent.

The availability of an additional anchoring point on the NCN-pincer ligand in the form of a para-substituent makes the introduction of additional functional moieties feasible. The synthesis, properties and catalytic application of a tweezer shaped complex based on an NCN-pincer palladium complex and a polycyclic aromatic pyrenoxy unit is presented in Chapter Four. The flexibility of the tweezer is studied in detail using various analytical tools, among which the pyrenoxy unit is used as fluorescent probe. Chapter Five describes the synthesis of NCN-pincer palladium complexes for immobilization purposes containing an additional binding site for functional groups.

The final chapters of this thesis are directed to the use of hyperbranched polymers (polyether polyols), as alternative for dendrimers as macromolecular support systems. These polymers are randomly branched, but still possess a low polydispersity, and offer the advantage of being synthesized in a one-step polymerization step. In Chapter Six, nanocapsules based on hyperbranched polyglycerol are applied in the non-covalent encapsulation of sulfonated NCN-pincer platinum complexes. Chapter Seven describes the covalent immobilization of metalated NCN-pincer platinum complexes on hyperbranched polyglycerols. The size and shape of the resulting materials is investigated by TEM, making imaging of these relatively small-sized molecules feasible without staining procedures. The research presented in Chapter Eight makes use of chiral hyperbranched polyglycerols for immobilization of NCN-pincer platinum complexes in either a non-covalent or covalent manner, using the methodologies described in Chapter Six and Seven.
1.7 References


34. For a review see: Clark, J. H.; Macquarrie, D. J. *Chem. Commun.* **1998**, *853-860


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