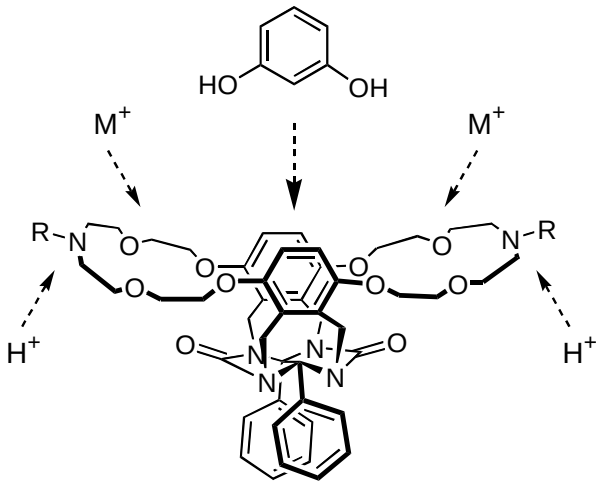
# Summary

This thesis describes the development of several new, basket-shaped host molecules. The hosts are based on the same molecular building-block of diphenylglycoluril (DPGU) and possess a cavity in which (di-)hydroxybenzenes (guests) can be bound. This association process is achieved by hydrogen bonds between the hydroxy groups of the guest and the carbonyl groups of the host, π-π stacking interactions between the aromatic ring of the guest and the aromatic side walls of the host, and finally electrostatic interactions between the two molecules.

In addition to a cavity, these hosts possess a macrocyclic crown-ether ring to which different types of guests (cations) can be bound. This association process involves mainly electrostatic interactions of the cation with the electron-rich oxygen atoms of the ethylene glycol units (cation-dipole interaction).

Finally, some of the hosts contain nitrogen atoms, which can be protonated by acids.



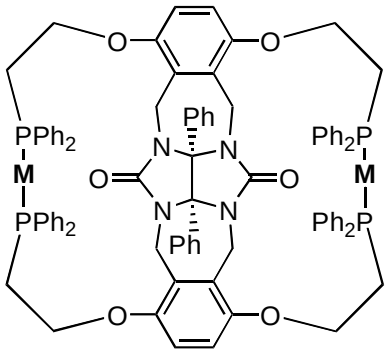

Chapter 2 describes the syntheses of various resorcinol derivatives. These molecules can be used as guests in combination with the above-mentioned hosts. A minor drawback of these guest molecules is that only few are commercially available. In order to have access to a number of guests we decided to synthesise them *via* palladium catalysed cross-coupling reactions. These reactions can often be applied under mild conditions and therefore this method was preferred to other routes. First 3,5-dimethoxyphenylboronic

acid, 1-iodo-3,5-dimethoxy benzene and 1-trimethyltin-3,5-dimethoxy benzene were prepared starting from 1-chloro-3,5-dimethoxybenzene. Subsequently, they were made to react, in the presence of small amounts of a palladium catalyst, with nucleophilic and electrophilic reagents.

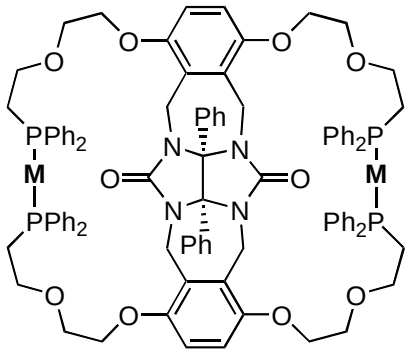
The use of this synthetic pathway afforded several 5-substituted dimethoxybenzenes, which were transformed into their respective resorcinol derivatives *via* a demethylation reaction. The syntheses described in this chapter can be readily used in the synthesis of biologically active analogues, which might open up new areas in the development of resorcinol derivatives with antileukemic properties.

In chapter 3 two novel, tetradentate phosphine ligands are presented. Both ligands are based on the DPGU building-block, but have different spacer groups separating the phosphine moieties from the binding unit. The ligands were obtained after a nucleophilic displacement of chlorine atoms by diphenylphosphine units. These ligands are capable of co-ordinating transition metals and can bind resorcinol derivatives in their cavity.

To determine binding affinities between the host and guests NMR-titrations were performed, in which the guest concentration was varied at constant host concentration. For comparison of the binding abilities of the different hosts they were measured using olivetol as guest. These measurements have shown that the length of the flexible spacer groups and the size of their end groups (chlorine or phosphine) influence the binding affinity between host and guest; large spacers and large end groups decrease the binding due to an extra loss in entropy for the larger molecules.




**1**




**2**

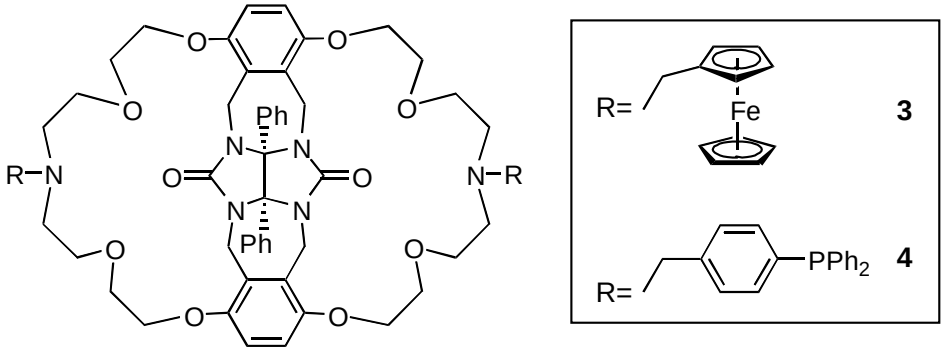
The basket-shaped metallohosts (**1** and **2**) were also used in binding studies with olivetol and again an influence of the spacer-size was found. If the spacers are too short, as in the case of type **1** complexes, guests cannot be bound in the host because the basket formed is

too small. Type **2** complexes, on the other hand, are capable of binding guests and generally gave higher association constants with olivetol than the free ligand. Since there is no interaction between the transition metal and the guest, the fixation of the flexible spacer groups seems most likely to explain this increase in binding.
The absence of an interaction between the metal centre and the guest was confirmed by the use of rhodium- and platinum-NMR. Additionally, IR measurements proved the absence of hydrogen bonds between the hydroxyl groups of the guest and ligands of the metal centre.
The free ligand with the large spacer groups was also used in a binding study using the resorcinol derivatives synthesised in chapter 2. This study has shown that substituents on resorcinol have a large effect on the magnitude of the association constant. A substituent influences the acidity of the hydroxyl groups of the guest, which determines the strength of the hydrogen bonds between host and guest. Electron-withdrawing groups show a positive effect on the association constant because they increase the acidity of the hydroxyl group (analogous to findings by Nolte and co-workers).

Chapter 4 deals with a study towards the effect of cations on the redox potential of a ferrocene-modified basket-shaped host molecule (**3**). Ferrocene is reduced or oxidised easily and it has often been used in electrochemical studies. The novelty of our receptor is its ability to bind both organic molecules and cations. Differential pulse voltammetry (DPV) measurements showed that the oxidation potential of the ferrocene units shift to more positive values in the presence of $Na^+$, $K^+$ or $NH_4^+$ ions, illustrating that this host can be used as a cation sensor. The host was not responsive to the addition of uncharged molecules like resorcinol derivatives.
NMR and IR spectroscopy were used to investigate the process of binding that occurs between host and guest in the presence of cations. The formation of a new type of supermolecule, *i.e.* one host, two $Na^+$ ions and one resorcinol derivative has been proposed. The binding is established through a bond between the oxygen atoms of the guest and two $Na^+$ ions bound in the host and not through hydrogen bonds between the hydroxyl groups of the guest and the carbonyl groups of the host. The sodium ions are bound to the crown-ether moieties *via* cation-dipole interactions. In the presence of a resorcinol derivative, each sodium ion has an additional cation-dipole interaction with an oxygen atom of the guest molecule. This novel type of binding resulted in an increased binding affinity by a factor of four compared to the sodium-free host-guest complex.

The knowledge obtained in the previous chapters was used in the development of a

supramolecular hydroformylation catalyst, as described in chapter 5. To achieve this goal, a basket-shaped host was modified with phosphine ligands (**4**) that formed a catalyst for the hydroformylation of allylbenzenes in combination with a rhodium precursor. Nine substituted allylbenzenes bearing hydroxy and/or methoxy groups were used to investigate substrate-selective properties of the catalyst.




First, these substrates were hydroformylated using the Wilkinson's hydride-catalyst ($HRh(CO)(PPh_3)_3$). The substrates reacted at comparable rate, except for the hydroxyl-substituted substrates, which were converted at lower rate. The supramolecular catalyst, on the other hand, converted substrates with hydroxyl groups at higher rates, due to binding in the receptor-part of the catalyst. Rate differences up to a factor of five were found between bound and non-bound substrates. The substrate with the highest binding affinity for the host (5-allylresorcinol) was converted at the highest initial rate. After approximately 1 hour of reaction time product inhibition occurred, resulting in an overall lower conversion of this particular substrate.

Addition of guest molecules, inactive in hydroformylation themselves, afforded different trends in the hydroformylation. Guests having a stronger binding affinity for the host than the substrate slowed down the conversion of 5-allylresorcinol dramatically. Guests with a comparable binding affinity for the host on the other hand, had a positive effect on the rate. Competition experiments in which a combination of 5-allylresorcinol and another allylbenzene derivative was hydroformylated clearly illustrated the principle of a supramolecular catalyst; the catalyst was substrate-selective and hydroformylated 5-allylresorcinol at the highest rate.