Transition metals enclosed in supramolecular capsules: assembly, characterization and application in catalysis

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Citation for published version (APA):

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Chapter 5

Bismetallo Capsules
Based on Two Ionic Diphosphines
5.1 Introduction

Supramolecular chemistry concerns the application of programmed molecules that assemble via intermolecular noncovalent bonds into larger molecular architectures, such as molecular capsules. The novel finite microenvironment within nanocapsules and their reversible encapsulation properties have stimulated their application as nanoreactors. Encapsulation of a transition metal within these nanoreactors resulted in new selectivities and activities for the transition metal catalyst. We have introduced a templated approach for metal encapsulation which involves a bifunctional diphosphine ligand containing a donor-atom site for metal complexation as well as functional groups for capsule formation. Self-assembly of a tetracationic diphosphine ligand, or the transition metal complex thereof, with a tetraanionic calix[4]arene resulted in capsule formation and metal encapsulation (Figure 1a). The transition metal complex is an integrated part of the capsule with the transition metal located inside the capsule. As it is not involved in the assembly process it is available for catalytic transformations. In this Chapter we report a new type of capsules which are composed of two oppositely charged diphosphine ligands or the transition metal complexes thereof (Figure 1b). The novel hetero bis-diphosphine capsule can simultaneously encapsulate two transition metals within its cavity to give a bismetallo-capsule.

![Figure 1](image-url)

Figure 1 Schematic picture of a metallodiphosphine and calix[4]arene based capsule (a) and a bis-metallodiphosphine capsule (b).

5.2 Synthesis of ionic building blocks

Water soluble sulfonated phosphine ligands have been applied in two-phase catalysis and in aqueous-phase catalysis, for example the rhodium-TPPTS (trisodium salt triphenylphosphine trisulfonate) catalyst for the hydroformylation of propene in water. Xantphos-type ligands with sulfonato-groups have also been reported, for example sulfoxantphos which contains two sulfonato-groups on the xanthene backbone, and the aggregating amphiphilic xantphos where the four arylphosphines are substituted with a second p-sulfonatophenyl separated by a bridge of aliphatic carbon atoms.
We have synthesized a novel tetraanionic xantphos-type ligand by direct sulfonation of the four arylphosphine rings. The precursor tetrakis(2-methoxyphenyl)-xantphos \((\text{o-OMe)}\)-xantphos is prepared by a reaction of the lithiated product of 2-bromoanisole with 4,5-bis(diethoxyphosphonito)-9,9-dimethylxanthene in 22% yield (Scheme 1a). Sulfonation of the arylphosphine rings of \((\text{o-OMe)}\)-xantphos was achieved by a reaction with concentrated sulfuric acid. Hydrolysis of the reaction mixture with water resulted in tetrakis(2-methoxy-5-sulfonicacid-phenyl)-xantphos \(a'\) (Scheme 1b). We have observed that \(a'\) (partly) precipitates from the reaction mixture as a sticky white solid at temperatures lower than \(-20\,^\circ\text{C}\) but immediately redissolves at higher temperatures. Consequently, isolation of the tetraacid by filtration was not successful. Neutralization of the reaction mixture by sodium hydroxide and product extraction with methanol afforded tetrakis(2-methoxy-5-sulfonatophenyl)-xantphos tetrasioumdsalt \(a\) in 74% yield (Scheme 1b). An attempt was made to remove the trace amounts of sodium sulfate salts from the product by reverse-phase silica chromatography (eluens: water/ethanol). The salt rests were removed but the diphosphine was oxidized during column chromatography because no air-free conditions were used (in reverse-phase silica chromatography the solvent flow is restricted and therefore a pump or pressurized gas is required to drive the solvent through the column). Consequently, the tetrasulfonato-xantphos \(a\) used in this Chapter contained trace amounts of sodium sulfate salts. All new compounds described in this Chapter have been characterized by NMR, IR and mass spectrometry techniques (see Experimental section).

Methoxy groups are ortho- and para directing groups in electrophilic aromatic substitution reactions. Indeed, sulfonation occurred exclusively on the arylphosphine rings para to the 2-methoxy substituent and meta to the phosphorus atom, as is confirmed by \(^1\text{H}\) NMR, H-H-COSY and \(^{13}\text{P}\{^1\text{H}\}\) NMR spectroscopy. No sulfonation of the xanthene backbone is observed under the conditions applied and therefore no alkyl groups at the 2 and 7 position of the xanthene backbone were necessary. The resonances in the \(^{13}\text{P}\{^1\text{H}\}\) NMR spectrum of the non-isolated tetrapsulfonicacid-xantphos \(a'\) \((-25.6\,\text{ppm})\) are downfield shifted compared to the resonance of the sodium salt \(a\) \((-34.8\,\text{ppm})\). This downfield shift indicates that the phosphorus atoms of \(a'\) are protonated, which is a result of the acidic environment or the bis-zwitterionic nature of \(a'\), as was previously reported by Mul and co-workers. During the reaction the phosphorus atoms were protected as phosphonium salt by protonation and indeed no phosphine-oxide was formed.

Reaction of rhodium(I) dimer \([\text{Rh(\(\mu\)-Cl)(CO)}_2]\)_2 with 2 equiv. of tetraanionic diphosphine \(a\) in methanol resulted in the formation of the corresponding Rh(I) carbonyl chloride complex \([\text{Rh(a)(CO)}\text{Cl]}\) \((1a)\) (Scheme 2). The bidentate ligand \(a\) of the distorted square planar Rh(I)-complex \(1a\) coordinates to the rhodium atom in a trans-fashion, as is indicated by \(^{31}\text{P}\{^1\text{H}\}\) NMR spectroscopy: \(\delta\) 22.7 ppm (d) \(J_{\text{Rh-P}} = 130.6\,\text{Hz}\). The tetracationic tetrakis(ammoniumchloride)-calix[4]arene \(z\) was synthesized by N-protonation of tetrakis(amino)-calix[4]arene by HCl in diethyl ether (Scheme 3).
5.3 Capsule self-assembly

All hetero-dimeric capsules reported in this Chapter are formed by ionic interactions and are composed of one tetraanionic building block and one complementary tetracationic building block. Self-assembly of these capsules is simply achieved by mixing methanol solutions containing these building blocks (Scheme 4). The capsules are formed instantaneously and are in equilibrium with the building blocks in monomeric form containing the original counter ions. Capsule formation is evidenced by NMR spectroscopy and mass spectrometry. A single set of proton resonances for the free and associated building blocks was observed in the $^1$H NMR
spectra for all the capsules described in this Chapter. This indicates a fast exchange process on the NMR time scale between the building blocks that are in the monomeric form (free) and those in the capsular form (bound).

![Scheme 4](image)

**Scheme 4** Self-assembly of ionic-based supramolecular capsules (schematic picture).

5.4 Metallo-capsule based on one diphosphine and one calix[4]arene

In Chapters 2 and 3 of this thesis we have reported (metallo) capsules composed of one tetracationic diphosphine, or the transition metal complex thereof, and one tetraanionic calix[4]arene. We were interested to know if a capsule composed of one tetraanionic diphosphine, or the transition metal complex thereof, and one tetracationic calix[4]arene will also be formed. In this section we report capsule \( z\cdot a \) which is composed of the tetraanionic xantphos-type diphosphine \( a \) and the tetracationic calix[4]arene \( z \), and metallo-capsule \( z\cdot 1a \) which is composed of the rhodium complex \( 1a \) containing the tetraanionic ligand and \( z \) (Figure 2). Encapsulation of a transition metal within capsule \( z\cdot a \) is achieved by using the rhodium complex \( 1a \).

**Characterization.** The \(^1\)H NMR spectra of capsules \( z\cdot a \) and \( z\cdot 1a \) in CD\(_3\)OD at 20 °C show sharp resonances, with the exception of the broad singlet resonance of the aromatic protons of the calix[4]arene \( z \) (Figure 3). Capsules \( z\cdot a \) and \( z\cdot 1a \) show significant upfield shifts for the aromatic proton of \( z \), with respect to that of the corresponding free \( z \): \( \Delta\delta_{z\cdot a} = 0.42 \) ppm and \( \Delta\delta_{z\cdot 1a} = 0.21 \) ppm. The observed upfield shifts are likely caused by interaction with the sulfonato groups of \( a \) and \( 1a \), and support capsule formation. Additional evidence for capsule formation and their stabilities in the gas-phase is obtained by electrospray ionization mass spectrometry (ESI-MS).\(^{10}\) The ESI-MS spectra of capsules \( z\cdot a \) and \( z\cdot 1a \) in CH\(_3\)OH show prominent ion peaks of the capsules at \( m/z \) 892.83 for \([z\cdot a + 2H]^2+ \) and at \( m/z \) 957.80 for \([z\cdot 1a - Cl + H]^2+ \) (Figure 4). All the capsules ion peaks correspond to 1:1 complexes and no ion peaks for higher aggregates were detected.

**Molecular modeling.** The four negative charges of tetrasulfonato-xantphos \( a \) are located at the meta position of its arylphosphine rings and the four positive charges of the calix[4]arene \( z \) are located at the para position of its aryl rings. The modeled structure (PM3 level) of capsule \( z\cdot a \)
shows that the rigid tetrasulfonato-xantphos \( a \) and the rigid concave calix[4]arene \( z \) are complementary in shape and that the 1:1 assembly has a highly symmetrical capsular structure (Figure 2a). The methoxy groups of \( a \) do not interfere with capsule formation. The four aryl groups of \( a \) are situated perpendicularly to the capsule equator with the sulfonato groups pointing down, and the charges of \( a \) and \( z \) are arranged in an array around the capsule equator. The structure of capsule \( z\cdot a \) is similar to that of a capsule composed of a xantphos-\( m \)-anilinium and a sulfonato calix[4]arene described in Chapter 3. Rhodium complex \([\text{Rh}(a)(CO)\text{Cl}] (1a)\) adopts a distorted square planar geometry with the ligand coordinating in a \textit{trans}\-fashion. The modeled structure (PM3 level) of the metallo capsule \( z\cdot 1a \) illustrates that \( 1a \) and \( z \) fit nicely and can form a capsule via interaction between the ammonium and sulfonato groups. In addition, the rhodium metal is located inside the capsule and the chloride and carbonyl groups of \( 1a \) are sticking out of the capsule (Figure 2b).

**Figure 2** Modeled and molecular structures of diphosphine capsule \( z\cdot a \) (a) and metallo-capsule \( z\cdot 1a \) (b). The NH hydrogen atoms are visible.

**Figure 3** \(^1\)H NMR spectra in CD\(_3\)OD at 20 °C. \textit{Top}: calix \( z \); \textit{Middle}: capsule \( z\cdot a \) (\( z/a = 1/2, [a] = 4 \text{ mM} \)); \textit{Bottom}: diphosphine \( a \).
5.5 Capsules based on two diphosphines

All capsules described by us so far are formed by ionic interactions and are composed of one calix[4]arene and one diphosphine. Our next challenge is to form capsules composed of two oppositely charged diphosphine ligands. In this section we report the bis-diphosphine capsules b·a, c·a and d·a which are based on the tetracationic diphosphine a and on a tetracationic tetrakis(p-diethylbenzylammoniumchloride)-diphosphine with an ethylene- b, diphenyl ether- c or xanthene- d backbone (Figure 5). The three tetracationic diphosphines b, c and d have different flexibilities and shapes but all form a hetero-dimeric capsule with a concave rigid tetrakisulfonato calix[4]arene, as is reported in Chapter 3. The xantphos-type ligand a is less rigid than calix[4]arene, and thus we were interested to know if this xantphos-type ligand will form a 1:1 capsule with a second diphosphine that is equally or less rigid.

Characterization. The $^1$H NMR spectra of capsules b·a, c·a and d·a in CD$_3$OD at 20 °C show significant upfield shifts for the diethylammoniummethyl substituents, CH$_2$NH(CH$_2$CH$_3$)$_3$, with respect to those of the corresponding free diphosphines b, c and d: $\Delta\delta$(CH$_2$CH$_3$)$_3$ = 0.21–0.23, $\Delta\delta$(CH$_2$CH$_3$)$_2$ = 0.31–0.35, $\Delta\delta$(CH$_2$N) = 0.34–0.39 ppm (Figure 6). The upfield shifts point to partial inclusion of the diethylammoniummethyl substituents inside the hydrophobic cavity of the capsules. The capsule’s proton resonances are relatively sharp. The 1D-NOESY spectrum of the hetero-dimeric capsule c·a in CD$_3$OD display negative intermolecular NOE contacts between the NH(CH$_2$CH$_3$)$_2$ protons of c, and the aromatic proton of a, i.e. H$^6$ of PAr$_2$, upon selective saturation of the methyl protons of c (Figure 7). Another NOE contact is observed between the NH(CH$_2$CH$_3$)$_2$ protons of c and the OMe group of a. This illustrates that the aryl-substituents of the two diphosphines are facing one another to form the dimeric 1:1 capsular
structure. The observed negative NOE enhancements confirm the large size of the capsules.\textsuperscript{12} For the hetero-dimeric capsule \(\text{d-a}\) similar NOE contacts are observed.

Additional evidence for capsule formation and their stabilities in the gas-phase is obtained by ESI-MS. The ESI-MS spectra of the bis-diphosphine capsules \(\text{b-a}, \text{c-a}\) and \(\text{d-a}\) in CH\(_3\)OH show prominent ion peaks of the capsules at \(m/z\) 879.80 for \([\text{b-a} + 2\text{H}]^{2+}\), at \(m/z\) 963.89 for \([\text{c-a} + 2\text{H}]^{2+}\) and at \(m/z\) 969.82 for \([\text{d-a} + 2\text{H}]^{2+}\) (Figure 8). All the capsule’s ion peaks correspond to 1:1 complexes and no ion peaks for higher aggregates were detected. The assignment of the capsule’s ion peaks is in agreement with the ESI-MS/MS collision induced dissociation, upon which the isolated capsule’s ion peak (partly) disappeared and product ion peaks appeared that correspond to the capsule building blocks (Figure 9).

![Figure 5](image.png)

**Figure 5** Modeled and molecular structures of the bis-diphosphine capsules \(\text{b-a}\) (a), \(\text{c-a}\) (b) and \(\text{d-a}\) (c).

**Molecular modeling.** Self-assembly of capsules \(\text{b-a}, \text{c-a}\) and \(\text{d-a}\) is primarily driven by the formation of multiple intermolecular ionic interactions between the oppositely charged diphosphine ligands. The tetracationic diphosphines contain the same \(p\)-diethylbenzylammonium groups but have different backbones: ethylene \(\text{b}\), diphenyl ether \(\text{c}\), and xanthene \(\text{d}\) (respectively ethane-1,2-diyl, diphenyl ether-2,2’-diyl, 9,9-dimethylxanthene-4,5-diyl). According to modeling studies (PM3 level) the molecular sizes of \(\text{b, c, d}\) are similar to \(\text{a}\) but their shapes and conformational rigidity differ. The xantphos-type ligands \(\text{a}\) and \(\text{d}\) have a rigid backbone and a concave-like structure while dppe \(\text{b}\) and DPEphos \(\text{c}\) have more flexible backbones and no
concave structures. The modeled structures of capsules b·a, c·a and d·a show that the diphosphines are facing one another and that their opposite charges are arranged in an array around the capsule equator (Figure 5). The cavities of the capsules are defined by the eight phosphorus aryl rings. The rigid and concave-like xantphos-type ligand a fixes the flexible diphosphines b and c into the proper conformation needed to form a capsule. Hence, one rigid building block is sufficient to form an ionic-based capsule. Interestingly, the free electron pairs on the phosphorus atoms of b·a are pointing away from the capsule, unlike in c·a and d·a where they are pointing to the capsule’s interior. In order to form the corresponding bismetallo capsule, capsule b·a will have to undergo a conformational change.

Figure 6 $^1$H NMR spectra in CD$_3$OD at 20 °C. Top: diphosphine b; Middle: capsule b·a (b/a = 1/2, [a] = 4 mM); Bottom: diphosphine a. Asterisks indicate solvent signals.

Figure 7 1D-NOESY spectrum of bis-diphosphine capsule c·a in CD$_3$OD (c/a = 1/2, [a] = 4 mM) (inset: 1D-NOESY spectrum enlargement).
Figure 8 ESI-MS spectrum of bis-diphosphine capsule c·a in CH$_3$OH (inset: measured isotope pattern).

Figure 9 ESI-MS spectra: isolation of bis-diphosphine capsule c·a (a) and collision induced dissociation of capsule c·a (ESI-MS/MS) (b).
5.6 Bismetallo capsules based on two diphosphines

In section 5.4 we have described the encapsulation of one transition metal within capsule \( z \cdot a \) composed of a tetraanionic diphosphine \( a \) and a tetracationic calix[4]arene \( z \) by using the corresponding rhodium complex \( 1a \). We anticipated that simultaneous encapsulation of two transition metals in the bis-diphosphine capsules reported in section 5.5, would provide a new class of easily accessible bismetallo capsules. Simultaneous encapsulation of two metals can be achieved by mixing solutions of a transition metal complex containing a tetraanionic diphosphine and a transition metal complex containing a tetracationic diphosphine. We have used the rhodium complex \( 1a \) as the tetraanionic building block, and the palladium and platinum complexes \( \text{trans-}[\text{Pd}(\text{d})(p\text{-C}_6\text{H}_4\text{CN})(\text{Br})] (2d), \text{cis-}[\text{Pt}(\text{d})\text{Cl}_2] (3d) \) and \( \text{cis-}[\text{Pd}(\text{b})\text{Cl}_2] (4b) \) as the tetracationic building block. The bismetallo capsules \( 2d \cdot 1a \) and \( 4b \cdot 1a \) encapsulate one palladium atom and one rhodium atom, and capsule \( 3d \cdot 1a \) encapsulates one platinum atom and one rhodium atom (Figure 10).

**Characterization.** The bismetallo capsules hardly dissolve in methanol but addition of 10–20% (v) of dichloromethane resulted in a better solubility of the capsules. As can be seen in Figure 11 the \(^1\)H NMR spectra of the bismetallo capsules \( 2d \cdot 1a, 3d \cdot 1a \) and \( 4b \cdot 1a \) in CD\(_3\)OD/CD\(_2\)Cl\(_2\) (80/20 v) at 20 °C show significant upfield shifts for the diethylammoniummethyl substituents, CH\(_2\)NH\(^+\)(CH\(_2\)CH\(_3\))\(_3\), with respect to those of the corresponding free metal complexes \( 2d, 3d \) and \( 4b \): \( \Delta\delta(\text{CH}_2\text{CH}_3)_2 = 0.08–0.18, \Delta\delta(\text{CH}_2\text{CH}_3)_2 = 0.21–0.30, \Delta\delta(\text{CH}_2\text{N}) = 0.29–0.33 \) ppm. These upfield shifts point to partial inclusion of the diethylammoniummethyl substituents inside the hydrophobic cavity of the capsules. Variable temperature \(^1\)H NMR spectra of the bismetallo capsules show line-broadening only for the CH\(_2\)N and N(CH\(_2\)CH\(_3\))\(_2\) protons of \( 2d, 3d \) and \( 4b \) at 20 °C and sharper resonances for these protons at higher temperatures (40 and 60 °C).

Additional evidence for capsule formation and their stabilities in the gas-phase was obtained by ESI-MS. The ESI-MS spectra of the bismetallo capsules \( 2d \cdot 1a, 3d \cdot 1a \) and \( 4b \cdot 1a \) in CH\(_3\)OH show prominent ion peaks of the capsules at \( m/z \) 759.52 for \([2d \cdot 1a – \text{Br} – \text{Cl} + \text{H}]^3+\), at \( m/z \) 754.53 for \([3d \cdot 1a – 3\text{Cl}]^3+\) and at \( m/z \) 664.52 for \([4b \cdot 1a – 3\text{Cl}]^3+\) (Figure 12). All the capsule ion peaks correspond to 1:1 complexes and no ion peaks for higher aggregates were detected.

**Molecular modeling.** According to modeling studies (PM3 level), in line with literature, the palladium complex \([\text{Pd}(\text{d})(p\text{-C}_6\text{H}_4\text{CN})(\text{Br})] (2d)\) adopts a distorted square planar geometry with the oxygen atom of the xanthene backbone in the apical position and the diphosphine ligand coordinated in a \text{trans} fashion. The palladium dichloride complex \([\text{Pd}(\text{b})\text{Cl}_2] (4b)\) adopts a square planar geometry with the diphosphine ligand coordinated in a \text{cis} fashion. The modeled structures of the bismetallo capsules \( 2d \cdot 1a \) and \( 4b \cdot 1a \) illustrate that the Pd-complexes \( 2d \) and \( 4b \) and the square planar \text{trans-Rh-complex 1a} fit nicely and are facing one another (Figure 10). In each capsule, the two transition metals are located inside the capsule. The
chloride and carbonyl groups of 1a and aryl and bromide groups of 2d are sticking out of the capsule while the two chlorides of 4b are pointing into the capsule’s interior. The modeled structures of the bismetallo capsules show that the distance between the two metals is 8.5 Å for the bisxantphos-based capsule 2d·1a and 4.9 Å for the dppe- and xantphos-based capsule 4b·1a.

**Figure 10** Modeled and molecular structures of bismetallo capsules 2d·1a (a) and 4b·1a (b).

**Discussion.** The two transition metals within the bismetallo capsule are situated close to each other. We were interested to know if this will promote a metal exchange reaction or if the two metals interact. The variable temperature 1H NMR spectra of the bismetallo capsules remain unchanged (at least for 1 h at 20, 40 and 60 °C), indicating that no metal exchange occurred under these conditions. Considering the calculated distances between the two metals of the bismetallo capsules 2d·1a and 4b·1a (8.5 and 4.9 Å, respectively), it is unlikely that the two metals will interact with each other, i.e. form a metal–metal bond. However, interaction between e.g. a cationic metal center and a cyanophenyl group (located inside the capsule) of the second metal might be possible.
Figure 11 $^1$H NMR spectra in CD$_3$OD/CD$_2$Cl$_2$ (80/20 v) at 20 °C. Top: Pd-complex 2d; Middle: capsule 2d·1a (2d/1a = 1/2, [1a] = 4 mM); Bottom: Rh-complex 1a. Asterisks indicate solvent signals.

Figure 12 ESI-MS spectrum of capsule 4b·1a in CH$_3$OH (inset: measured isotope pattern).
5.7 Monometallo capsule based on two diphosphines

In section 5.6 we have described the encapsulation of two transition metals within a bis-diphosphine capsule. Encapsulation of only one transition metal within a bis-diphosphine capsule can also be achieved e.g. by mixing solutions of a transition metal complex containing a tetracationic ligand, and a tetraanionic diphosphine. To this end the formation of the monometallo capsule $2d\cdot a$ based on trans-[Pd(d)(p-C$_6$H$_4$CN)(Br)] ($2d$) and on the tetrusulfonato-xantphos ligand $a$ was studied (Scheme 5).

$^1$H NMR study. As can be seen in Figure 13 (top), the $^1$H NMR spectrum of capsule $2d\cdot a$ (at a $2d/a$ ratio of 1/2) shows significant upfield shifts for the diethylammoniummethyl substituents, CH$_2$NH$^+$ (CH$_2$CH$_3$)$_2$, with respect to those of $2d$: $\Delta$$\delta$(CH$_2$CH$_3$)$_2$ = 0.25, $\Delta$$\delta$(CH$_2$CH$_3$)$_2$ = 0.44, $\Delta$$\delta$(CH$_3$N) = 0.47 ppm. We observed that upon leaving the NMR tube at 20 °C or heating it to 40 °C, another set of signals started to appear for the diethylammoniummethyl substituents (Figure 13). The ratio between the two signal sets did not change anymore after 3.5 h at 40 °C (‘$2d$’/$d$’ = 3/7, vide infra). The chemical shifts of the new set of signals resemble that of the bis-diphosphine capsule $d\cdot a$ (Figure 13 bottom). Metal exchange between palladium complex $2d$ and diphosphine $a$ resulted in the formation of diphosphine $d$ and Pd-complex $2a$. The simultaneous presence of the tetracationic building blocks $d$ and $2d$, and the tetraanionic building blocks $a$ and $2a$ in solution resulted in the formation of four capsules: the monometallo capsules $2d\cdot a$ and $d\cdot 2a$, the bismetallo capsule $2d\cdot 2a$, and the bis-diphosphine capsule $d\cdot a$ (Scheme 5). The remaining question is how can four different capsules that are simultaneously present in solution, give only two signal sets in the $^1$H NMR spectrum. As is reported in section 5.3 the free- and bound building blocks of all the ionic-based capsules are in a fast exchange on the NMR time scale. This results in a single set of proton resonances which represent the average of the free- and bound building blocks. The same fast exchange process also occurs between the four capsules, which results in this case in two sets of signals for the CH$_2$NH$^+$ (CH$_2$CH$_3$)$_3$ protons of $d$ and $2d$: one signal set for the protons of free $d$, capsule $d\cdot a$ and capsule $d\cdot 2a$, and another signal set for the protons of free $2d$, capsule $2d\cdot a$ and capsule $2d\cdot 2a$.

Metal exchange reaction between $2d$ and $a$, and consequently the simultaneous presence of the corresponding four building blocks $2d$, $2a$, $d$ and $a$ is confirmed by $^{31}$P{^1}H NMR: $2d$ 13.6 (br s), $2a$ 10.4 (s), $d$ −17.3 (s) and $a$ −34.2 (s) ppm. ESI-MS also support the occurrence of metal exchange between $2d$ and $a$, and consequently the formation of four capsules. The ESI-MS spectrum of capsule $2d\cdot a$ in CH$_3$OH, after being stirred overnight at room temperature, show prominent ion peaks of the four capsules at m/z 730.95 for [2(d•a) – Br + 2Na]$^{3+}$, at m/z 792.60 [2d•2a – 2Br + Na]$^{3+}$ and at m/z 969.98 [d•a + 2H]$^{2+}$. Noteworthy, the monometallo capsules $2d\cdot a$ and $d\cdot 2a$ have the same elemental composition and hence give the same m/z (these capsules are designated as $2(d\cdot a)$).
**Discussion.** The exchange rate of the building blocks between various capsules is much faster than the metal exchange rate between the ligands. We were interested to know if the capsule effects the rate and product distribution of the metal exchange reaction. Heating a solution containing two building blocks that can not form a capsule, *i.e.* a and 2d’ (d’ is the neutral tetraamine-xantphos ligand) also resulted in metal exchange to give 2d’, 2a, d’ and a, as is evidenced by an NMR study. Comparison of the metal exchange reaction between a and 2d with that between a and 2d’ suggests that the capsule does not effect the reaction rate and product distribution.

**Scheme 5** Molecular structure of monometallo capsule 2d·a, and the resulting capsules upon metal exchange.

**Figure 13** ¹H NMR spectra in CD₃OD/CD₂Cl₂ (8/2 v). *Top:* capsule 2d·a (2d/a = 1/2, [a] = 4 mM); *Middle:* stirring capsule 2d·a at 40 °C for 1–3 h; *Bottom:* capsule d·a. Asterisks indicate solvent signals.
5.8 Conclusions

In this Chapter we have demonstrated that the scope of ionic-based capsules based on functionalized diphosphine ligands, or metal complexes thereof, can easily be extended. The first type of capsules is composed of one novel tetraanionic diphosphine ligand and one complementary tetracationic calix[4]arene. Encapsulation of a transition metal is achieved by self-assembly of a transition metal complex (Rh) containing a tetracationic ligand, and a tetracationic calix[4]arene. The second type of capsules is composed of two oppositely charged diphosphine ligands. Simultaneous encapsulation of two different transition metals is achieved by self-assembly of a transition metal complex containing a tetracationic ligand (Pd, Pt) and a transition metal complex containing a tetraanionic ligand (Rh). Diphosphine ligands with different flexibilities and shapes (i.e. different backbones) assemble into (metallo) capsules with a proper capsular structure, as is indicated by $^1$H NMR, 1D-NOESY, ESI-MS and modeling studies. This approach for encapsulation of two different metals within one cavity opens up new opportunities for bimetallic catalysis to control the activity, stability and selectivity of the potential homogeneous catalysts.

5.9 Experimental section

General remarks. All reactions were carried out under a dry, inert atmosphere of purified nitrogen or argon using standard Schlenk techniques, unless stated otherwise. Solvents were dried and distilled under nitrogen prior to use. Diethyl ether and tetrahydrofuran (THF) were distilled from sodium/benzophenone. Dichloromethane and methanol were distilled from CaH₂. Deuterated solvents were distilled from the appropriate drying agents. Unless stated otherwise, all chemicals were obtained from commercial suppliers and used as received. 5,11,17,23-Tetrakis(amo)no)-25,26,27,28-tetraakis(pentoxy)calix[4]arene, 9, 4,5-bis(diehtoxyphosphonito)-9,9-dimethylxanthene, 4b,18 1,2-bis[bis(p-(diethylammoniumchloride)-methyl)phenyl]phosphino]ethane b,4b 2,2’-bis[bis(p-((diethylammoniumchloride)methyl)phenyl)-phosphino]-4,4’-dimethylidiphenylether c,4c 4,5-bis[bis(p-((diethylammoniumchloride)methyl)phenyl)-phosphino]-9,9-dimethylxanthene d,4c trans-[Pd(d-4HCl)(p-C₆H₄CN)(Br)] 2d,4b cis-[Pt(d-4HOTs)Cl₂] 3d,14 and cis-[Pd(b-4HOTs)Cl₂] 4b were synthesized according to reported procedures. NMR spectra were recorded on Varian Inova 500, Bruker Avance DRX 300 and Varian Mercury 300 NMR spectrometers. Chemical shifts are given relative to TMS ($^1$H and $^{13}$C NMR) and 85% H₃PO₄ ($^{31}$P NMR). Chemical shifts are given in ppm. 1D-NOESY measurements (1D transient NOE) were carried out with a DPFGSE excitation (double pulsed field gradient spin-echo). High-resolution fast atom bombardment mass spectrometry (HRMS FAB) measurements were carried out on a JEOL JMS SX/SX 102A at the Department of Mass Spectrometry at the University of Amsterdam. Electrospray ionization mass spectrometry (ESI-MS) measurements were carried out on a Q-TOF (Micromass, Waters, Whyttenshawe, UK) mass spectrometer equipped with a Z-spray orthogonal nanoelectrospray source, using Econo Tips (New Objective, Woburn, MA) to create an off-line nanospray, at the Department of Mass Spectrometry.
of Biomacromolecules at the University of Amsterdam. Infrared spectra were recorded on a Nicolet 510 FT-IR spectrophotometer. Molecular modeling calculations were performed using Spartan ’04 V1.0.3 software, on the semi-empirical PM3-level.

**Synthesis**

**4,5-Bis[4,5-(methoxy-phenyl)phosphino]-9,9-dimethylxanthene: \((\text{o-OMe})\)-xantphos**

\[ \text{n-Butyllithium (2.5 M in hexanes, 18.34 ml, 45.84 mmol) is added slowly to a solution of 2-bromoanisole (5.72 ml, 45.84 mmol) in 60 ml diethyl ether at} \] 0 °C. The solution was allowed to warm slowly to room temperature and was stirred overnight. Next morning, the solution of 2-lithioanisol was cooled to –45 °C and subsequently a solution of 4,5-bis(dioxyphosphonito)-9,9-dimethylxanthene (4.13 g, 9.17 mmol) in 60 ml THF was added slowly. The resulted green reaction mixture was allowed to warm to room temperature and was stirred overnight. Next morning, the clear red reaction mixture was hydrolyzed with 5 ml degassed water, and the solvents were removed in vacuo. Subsequently, the orange viscous oil was dissolved in dichloromethane and washed with degassed brine. The organic layer was separated, and the aqueous layer was extracted with dichloromethane. The combined organic layers were dried with MgSO₄, and the solvent was removed in vacuo. The crude product was purified by column chromatography (silica gel: EtOAc/PE 40-60). The product \((\text{o-OMe})\)-xantphos was obtained as a white powder (1.42 g, 2.03 mmol, 22%).

\[ \text{\textsuperscript{1}H NMR (300 MHz, CDCl} \text{3, 293 K):} \delta = 7.35 \text{ (d, } J = 7.7 \text{ Hz, 2H, PC} \text{C} \text{H}_3), 7.11 \text{ (t, } J = 7.7 \text{ Hz, 4H, PC} \text{C} \text{H}_4), 6.87 \text{ (t, } J = 7.5 \text{ Hz, 2H, PC} \text{C} \text{H}_3), 6.69 \text{ (br d, } J = 7.7 \text{ Hz, 4H, PC} \text{C} \text{H}_4), 6.61 \text{ (t, } J = 7.3 \text{ Hz, 4H, PC} \text{C} \text{H}_4), 6.51 \text{ (m, 6H, PC} \text{C} \text{H}_3 + \text{PC} \text{C} \text{H}_4), 3.61 \text{ (s, 12H, OCH}_3), 1.63 \text{ (s, 6H, C(CH}_3)_2); \text{\textsuperscript{3}P\{\textsuperscript{1}H\} NMR (121.5 MHz, CDCl}_3, 293 K):} \delta = –34.2 \text{ (s);} \text{\textsuperscript{13}C\{\textsuperscript{1}H\} NMR (75 MHz, CDCl}_3, 293 K):} \delta = 161.3 \text{ (t, } J = 8.0 \text{ Hz, Cq, C}_A), 153.3 \text{ (br s, Cq, C}_A), 133.4 \text{ (s, CH, C}_A), 132.2 \text{ (s, CH, C}_A), 129.7 \text{ (s, Cq, C}_A), 129.3 \text{ (s, CH, C}_A), 125.9 \text{ (br s, Cq, C}_A), 125.6 \text{ (s, CH, C}_A), 123.0 \text{ (s, CH, C}_A), 120.5 \text{ (s, CH, C}_A), 110.1 \text{ (s, CH, C}_A), 55.6 \text{ (s, OCH}_3), 34.5 \text{ (s, C(CH}_3)_2), 31.7 \text{ (s, C(CH}_3)_2);} \text{HRMS (FAB\+: found 699.2439, calcd. for [C}_43\text{H}_40\text{O}_5\text{P}_2 + \text{H}]\text{+ 699.2429.} \]

**4,5-Bis[4,5-(methoxy-5-sulfonatophenyl)phosphino]-9,9-dimethylxanthene tetrasodiumsalt: a**

\[ \text{A solution of (o-OMe)-xantphos (0.56 g, 0.80 mmol) in 1 ml dichloromethane was cooled to} \] –10 °C and concentrated sulfuric acid (96%, 2.05 ml, 38.4 mmol) was added dropwise. After the diphosphine was completely dissolved in the concentrated sulfuric acid, dichloromethane was removed in vacuo. The brown reaction mixture was slowly warmed to room temperature and was stirred for 6 days. A second portion of concentrated sulfuric acid (2.05 ml, 38.4 mmol) was added at –10 °C and the reaction mixture was stirred for 4 more days at room temperature. Next, the reaction mixture was hydrolyzed by slow addition of 16 ml degassed ice water at –10 °C to give the tetrasulfonic acid diphosphine \(a'\), upon which the reaction mixture decolorized. Subsequently, the reaction mixture was carefully neutralized with aqueous NaOH (27%, w/w) at 0 °C until a pH of 8-10 was reached. The solution was thoroughly evaporated to dryness at 75 °C resulting in a white powder. Methanol (100 ml) was added to the crude product and the suspension was refluxed for 2 h. After the suspension was cooled to room temperature the white salts (Na₂SO₄) were allowed to precipitate and were filtered off. After a second extraction with methanol the product \(a\) was obtained as a white powder (0.65 g, 0.59 mmol, 74
Tetrasodiumsalt a: $^1$H NMR (300 MHz, CD$_3$OD, 293 K): $\delta$ = 7.76 (dd, $J$ = 8.6 Hz, $J$ = 2.2 Hz, 4H, PC$_6$H$_3$-SO$_3$Na), 7.42 (d, $J$ = 7.7 Hz, 2H, PC$_6$H$_3$), 7.23 (s, 4H, PC$_6$H$_3$-SO$_3$Na), 6.92 (d, $J$ = 8.6 Hz, 4H, PC$_6$H$_3$-SO$_3$Na), 6.86 (t, $J$ = 7.6 Hz, 2H, PC$_6$H$_3$), 6.54 (t, $J$ = 7.4 Hz, 2H, PC$_6$H$_3$), 3.67 (s, 12H, OCH$_3$), 1.67 (s, 6H, C(CH$_3$)$_2$); 31P{1H} NMR (121.5 MHz, CD$_3$OD, 293 K): $\delta$ = –34.8 (s); 13C{1H} NMR (75 MHz, D$_2$O, 293 K): $\delta$ = 163.1 (t, $J$ = 7.7 Hz, Cq, C Ar), 152.5 (br t, Cq, C Ar), 135.3 (s, Cq, C Ar), 131.4 (s, CH, CAr), 131.0 (s, Cq, CAr), 130.4 (s, CH, CAr), 128.3 (s, CH, CAr), 127.4 (s, CH, CAr), 124.2 (s, CH, CAr), 124.1 (s, Cq, C Ar), 124.0 (s, Cq, C Ar), 110.9 (s, CH, C Ar), 56.0 (s, OCH$_3$), 34.3 (s, C(CH$_3$)$_2$), 30.2 (s, C(CH$_3$)$_2$); HRMS (FAB+): found 1107.0020, calcd. for [C$_{43}$H$_{36}$Na$_4$O$_{17}$P$_2$S$_4$ + H] $^+$ 1106.9980.

Non-isolated tetrasulfonicacid a': (4,5-bis[bis(2-methoxy-5-sulfonicacid-phenyl)phosphino]-9,9-dimethylxanthene): $^1$H NMR (300 MHz, CD$_3$OD, 293 K): $\delta$ = 8.05 (dd, $J$ = 8.7 Hz, $J$ = 2.2 Hz, 4H, PC$_6$H$_3$-SO$_3$Na), 7.84 (d, $J$ = 6.9 Hz, 2H, PC$_6$H$_3$), 7.43 (m, 4H, PC$_6$H$_3$-SO$_3$Na), 7.25 (m, 6H, PC$_6$H$_3$-SO$_3$Na + PC$_6$H$_3$), 6.88 (m, 2H, PC$_6$H$_3$), 3.77 (s, 12H, OCH$_3$), 1.77 (s, 6H, C(CH$_3$)$_2$); 31P{1H} NMR (121.5 MHz, CD$_3$OD, 293 K): $\delta$ = –25.6 (br s); ESI-MS (m/z, CH$_3$OH): [M + H]$^+$ found 1019.15, calcd. (C$_{43}$H$_{41}$O$_{17}$P$_2$S$_4$ + H) 1019.16.

trans-[Rh(a)(CO)Cl]: A solution of a (84.6 mg, 76.4 $\mu$mol) in 7 ml methanol was added to a clear yellow solution of [Rh($\mu$-Cl)(CO)$_2$]$_2$ (14.9 mg, 38.9 $\mu$mol) in 1 ml methanol. The reaction mixture was stirred for 30 min. at room temperature and subsequently was refluxed at 70 °C for 4 h. After cooling the brown reaction mixture to room temperature the solvent was evaporated in vacuo. After washing with diethyl ether and drying in vacuo the product 1a was obtained as a brown powder. $^1$H NMR (300 MHz, CD$_3$OD, 293 K): $\delta$ = 8.01 (dd, $J$ = 8.7 Hz, $J$ = 2.1 Hz, 4H, PC$_6$H$_3$-SO$_3$Na), 7.96 (m, 2H, PC$_6$H$_3$), 7.68 (dt, $J$ = 8.7 Hz, $J$ = 2.6 Hz, 4H, PC$_6$H$_3$-SO$_3$Na), 3.65 (s, 12H, OCH$_3$), 1.81 (s, 6H, C(CH$_3$)$_2$); 31P{1H} NMR (121.5 MHz, CD$_3$OD, 293 K): $\delta$ = 22.7 (d, $J$$_{Rh-P}$ = 130.6 Hz); 13C{1H} NMR (75 MHz, CD$_3$OD, 293 K): $\delta$ = 156.2 (s), 136.2 (s), 124.6 (s), 123.0 (s), 75.6 (s, C$_5$H$_{11}$), 30.2 (s, ArC$_5$H$_{11}$), 29.8 (s, C$_5$H$_{11}$) +; HRMS (FAB+): found 1236.8972, calcd. for [C$_{44}$H$_{36}$ClNa$_4$O$_{18}$P$_2$RhS$_4$ – Cl$^-$] $^+$ 1236.8906; IR (CH$_3$OH, 293 K, cm$^{-1}$): $\nu$ = 2013 (CO).

5,11,17,23-Tetrakis(ammoniumchloride)-25,26,27,28-tetrakis(pentoxy)calix[4]arene: A 2 M solution of HCl in diethyl ether (1.50 ml, 3.00 mmol) was added dropwise to a solution of 5,11,17,23-tetrakis(amino)-25,26,27,28-tetrakis(pentoxy)calix[4]arene (0.230 g, 300 $\mu$mol) in 25 ml diethyl ether, upon which a fine pink precipitation appeared. After stirring for 30 min. the volatiles were removed in vacuo and z was obtained as a red powder in quantitative yield. $^1$H NMR (300 MHz, CD$_3$OD, 293 K): $\delta$ = 6.78 (s, 8H, H$_{Ar}$), 5.50 (d, $J$ = 13.4 Hz, 4H, C$_5$H$_{11}$), 3.94 (t, $J$ = 7.3 Hz, 8H, OCH$_2$), 3.36 (d, $J$ = 14.2 Hz, 4H, CHF$^+$), 0.95 (t, $J$ = 6.6 Hz, 12H, CH$_3$); 13C{1H} NMR (75 MHz, CD$_3$OD, 293 K): $\delta$ = 156.2 (s), 136.2 (s), 124.6 (s), 123.0 (s), 75.6 (s, C$_5$H$_{11}$), 30.2 (s, ArCH$_2$Ar), 29.8 (s, C$_5$H$_{11}$), 28.2 (s, C$_5$H$_{11}$), 22.5 (s, C$_5$H$_{11}$), 13.2 (s, C$_5$H$_{11}$); HRMS (FAB+): found 765.5311, calcd. for [C$_{48}$H$_{72}$O$_{4}$N$_{4}$Cl$_{4}$ – 3H – 4Cl] $^+$ 765.5319.
General procedure for capsules self-assembly
Capsule self-assembly was done in situ. Equimolar methanol, methanol/dichloromethane (80-90% (v) methanol), dmso or water solutions of the tetracationic building block and the tetraanionic building block were mixed at room temperature and stirred for 5-20 min., resulting in the formation of the corresponding capsules.

1H NMR characterization of the capsules
Upfield shifts (\(\Delta\delta_H\)) upon capsule formation are given for the protons of the bound building blocks, with respect to those of the corresponding free building blocks (Table 1).

<table>
<thead>
<tr>
<th>Capsule</th>
<th>Solvent/temp</th>
<th>(\Delta\delta(CH_2CH_3)) (ppm)</th>
<th>(\Delta\delta(CH_2CH_3)) (ppm)</th>
<th>(\Delta\delta(CH_2N)) (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>b·a (^b)</td>
<td>CD_3OD / 20 °C</td>
<td>0.22</td>
<td>0.31</td>
<td>0.34</td>
</tr>
<tr>
<td>c·a (^b)</td>
<td>CD_3OD / 20 °C</td>
<td>0.23</td>
<td>0.35</td>
<td>0.39</td>
</tr>
<tr>
<td>d·a (^b)</td>
<td>CD_3OD / 20 °C</td>
<td>0.21</td>
<td>0.34</td>
<td>0.36</td>
</tr>
<tr>
<td>2d·1a</td>
<td>CD_3OD/CD_2Cl_2 8/2 vol% / 20 °C</td>
<td>0.18</td>
<td>0.30</td>
<td>0.32</td>
</tr>
<tr>
<td>3d·1a</td>
<td>CD_3OD/CD_2Cl_2 8/2 vol% / 20 °C</td>
<td>0.11</td>
<td>0.26</td>
<td>0.33</td>
</tr>
<tr>
<td>4b·1a</td>
<td>CD_3OD/CD_2Cl_2 8/2 vol% / 20 °C</td>
<td>0.08</td>
<td>0.21</td>
<td>0.29</td>
</tr>
<tr>
<td>2d·a</td>
<td>CD_3OD/CD_2Cl_2 8/2 vol% / 20 °C</td>
<td>0.25</td>
<td>0.44</td>
<td>0.47</td>
</tr>
</tbody>
</table>

\(^a\) [a] = 4 mM. PP/a = 1/2. PP = b, c, d, 2d, 3d and 4b. The NH\(^+\) proton resonance was not visible because of H–D exchange with CD\(_3\)OD. \(^b\) The assignment of the 1H NMR spectra of the capsules is fully supported by COSY NMR.

ESI-MS
Samples of the capsules with initial concentrations of 100-250 μM were diluted in MeOH to a final concentration of 1%. Comparison of the measured isotope patterns of the capsules with the calculated ones confirm their elemental composition and charge state. The capsules ion peaks correspond to 1:1 complexes and no ion peaks for higher aggregates were detected. From the survey MS spectra individual candidate ions were selected for collision induced dissociation (CID) MSMS with Argon as collision gas. The assignment of the capsule’s ion peaks is confirmed by CID experiments: upon collision induced dissociation of the capsule’s ion peaks, product peaks appeared that correspond to the capsule’s building blocks. The reported m/z correspond to the 100% ion peak (isotope with the highest intensity).

Self-assembly of following capsules was done in CH\(_3\)OH upon which the capsules remained soluble, hence sodium cations were present in solution: Capsule za (C91H108N4O21P2S4) ESI-MS (m/z, CH\(_3\)OH): [za + 2H + O]\(^2+\) found 900.85, calcd. 900.80; [za + 2H]\(^2+\) found 892.83, calcd. 892.80. Capsule ba (C89H108N4O17P4S4) ESI-MS (m/z, CH\(_3\)OH): [ba + 2Na]\(^2+\) found 901.83, calcd. 901.77; [ba + H + Na]\(^2+\) found 899.81, calcd. 899.78; [ba + 2H]\(^2+\) found 897.80, calcd. 897.79; [ba + 3Na]\(^3+\) found 608.89, calcd. 608.84; [ba + H + 2Na]\(^3+\) found 601.56, calcd. 601.51; [ba + 2H + Na]\(^2+\) found
5.10 Acknowledgments

Henk Dekker is gratefully acknowledged for the ESI-MS measurements. Han Peeters is gratefully acknowledged for the high resolution mass spectra measurements.
5.11 References and notes


See *Chapter 4* of this Thesis.

Complexes 2d, 3d and 4b contain tetrakis(p-diethylbenzylammoniumchloride)-xantphos, tetrakis(p-diethylbenzylammoniumtosylate)-xantphos and tetrakis(p-diethylbenzylammonium-tosylate)-dppe, respectively.

