Controlling radical-type reactivity with transition metals and supramolecular cages

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Chapter 2

Encapsulation and Reactivity of Metallo-Porphyrins in a Self-Assembled Cubic $M_8L_6$ Cage.

Abstract: The synthesis of a new, cubic $M_L_6$ cage is described. The new supramolecular assembly was characterized by NMR spectroscopy, DOSY, Cryo-UHR-ESI-ToF mass spectrometry and molecular modelling techniques. The increased cavity size of this new supramolecular assembly compared to the previously described cubic cage compound allows the selective encapsulation of tetraakis(4-pyridyl)porphyrins ([M(TPyP)], $M=H_2, Zn, Co$). The substrate accessibility of this system was demonstrated through radical-trapping experiments and its catalytic activity was studied in two different radical-type transformations. The reactivity of the encapsulated [Co$^{II}$(TPyP)] complex is significantly increased compared to free [Co$^{II}$(TPyP)] and related cobalt-porphyrin complexes. The reactions catalyzed by this system are the first examples of cobalt-porphyrin catalyzed radical-type transformations involving diazo compounds that occur inside a supramolecular cage.

2.1 Introduction

The creation of complex, well-defined three dimensional structures through self-assembly is an important and fast growing field of modern chemistry. The obtained supramolecular architectures exhibit unprecedented new functionalities (see Chapter 1).\textsuperscript{1} Elegant examples are reported in which such supramolecular assemblies act as hosts for small ions\textsuperscript{2-4} or molecules,\textsuperscript{5-7} large organic compounds\textsuperscript{8} or transition metal complexes.\textsuperscript{9} In particular, the ability to encapsulate guests in so-called ‘molecular flasks’ leading to unusual reactivities and selectivities is interesting,\textsuperscript{10-16} as it offers new opportunities to steer and control catalytic reactions. In this perspective, catalyst encapsulation is a fascinating method to achieve site-isolation in homogeneous catalysis. In addition to control over selectivity, the catalyst is also protected from the bulk, potentially suppressing (self)deactivation. For example, unwanted radical-radical coupling is an important catalyst deactivation pathway\textsuperscript{17} in metallo-radical catalysis\textsuperscript{18-22} that can possibly be prevented by encapsulation of the metallo-radical catalyst in a supramolecular cage. Such a site-isolation methodology mimics in a way the protective protein matrix surrounding the active sites of metallo-enzymes (which frequently follow related metallo-radical pathways). Self-deactivation is particularly important in metallo-porphyrin catalyzed processes, and hence the development of new hosts that are capable of encapsulating metallo-porphyrins is an important goal to advance porphyrin-based (radical-type) catalysis. Only a few examples have so far been reported that address this problem of self-deactivation in metallo-porphyrin catalyzed processes using supramolecular approaches.\textsuperscript{23-25}
Due to their symmetry and versatility, porphyrins are widely used for the design of supramolecular host-complexes. They are easily accessible and adjustable in terms of substituents and metals, and hence offer various synthetic handles to steer the electronic and structural parameters of new (supramolecular) catalysts. While the encapsulation of porphyrins in so-called metal-organic frameworks (MOFs) is well-established, fewer examples are known where they are guests in soluble, molecular hosts. Here we report the synthesis of a new, self-assembled cubic $M_8L_6$ cage compound that efficiently encapsulates tetrakis(4-pyridyl)porphyrins [M(TPyP)]. The cage is accessible for additional organic substrates and allows catalytic turnover inside the self-assembled cage.

2.2 Results and Discussion

The deactivation of catalysts via the formation of bridged dimers is an important issue in metallo-porphyrin catalyzed processes. Prominent examples are the oxo-bridged dimers in manganese-porphyrin catalyzed epoxidations of olefins, which has been addressed by Hupp and co-workers. In our previous studies we reported that dimerization can also occur in cobalt(II)-porphyrin catalyzed reactions of diazo compounds. While this reaction provided additional experimental proof for radical-type pathways in cobalt-porphyrin catalyzed carbene transfer reactions, it also reveals the problem of unwanted catalyst self-deactivation through radical-radical coupling processes. We took it as a challenge to avoid such self-deactivation processes, and hence we became interested in the use of supramolecular hosts capable of encapsulating porphyrins while leaving enough space available for organic substrates to react inside the cavity. Diamagnetic $M_8L_6$ cage 1 (Scheme 1), which has been described by Nitschke and co-workers, initially looked promising for this purpose.
Scheme 1: Synthesis of Nitschke’s cubic $M_8L_6$ cage 1,\textsuperscript{37} and attempted guests for encapsulation.

The zinc-porphyrin planes of 1 allow, in principle, directed interactions with pyridine functionalized guests such as meso-tetakis(4-pyridyl)porphyrin ([H$_2$(TPyP)], 2-H$_2$) and the metallo-porphyrin analogues ([M$^{II}$(TPyP)], 2-M)$^{40}$ to give host-guest complexes [2-H$_2$@1] or [2-M@1]. However, the cubic cage host 1 is not large enough to encapsulate pyridine-appended porphyrins such as 2-Zn or 2-Co. The Zn–Zn distance between two cube planes in 1 is about 15.0 Å, which is smaller than the N–N distance between two trans-pyridyl nitrogens in 2 (15.5 Å). Furthermore, encapsulation of meso-tetraphenylporphyrin complexes ([Co(TPP)], 3-Co) were also unsuccessful. We therefore decided to design and synthesize a new $M_8L_6$ cubic cage which is large enough to host 2. In principle, the synthesis of cubic $M_8L_6$ cages offering an increased cavity size can be accomplished by changing either one of the three building blocks (zinc tetrakis(4-aminophenyl)porphyrin (Zn-TAPP, 4), 2-pyridine-5-carbox-aldehyde (5) or iron triflate (Fe(OTf)$_2$, 6). The influence of the employed metal salts on the size and shape of related tetrahedral $M_4L_6$ cages to yield a variety of new supramolecular complexes has been described recently.$^{41}$
2.2.1 Synthesis and Characterization of the large cubic M₈L₆ cage 8

We approached the synthesis of a larger cubic cage by replacing the 2-pyridine-aldehyde (5) building block used in the synthesis of Nitschke’s cubic cage by the 2,2’-bipyridine-5-carboxaldehyde 7 (Scheme 2). Indeed, reaction of 24 equivalents of 7 with 6 equivalents of Zn-TAPP 4 in the presence of 8 equivalents of Fe(OTf)₂ results in the selective formation of the new, larger cubic cage complex 8 through self-assembly. Notably, 8 is formed in high yield (96%) and the reaction is relatively easy to scale-up, yielding 8 in 400 mg isolated yield.

![Scheme 2: Synthesis of the new and large cubic M₈L₆ cage 8.](image)

Figure 1a shows the ¹H-NMR spectrum of cage 8. Except for one signal being masked by an overlapping solvent signal, the chemical shifts, relative integrals and multiplicity of the signals observed match well with the structure of 8. Other signals stem from the solvents used (and a minor trace of 7; signal at 10.3 ppm). Solutions of 8 in DMF are remarkably stable, and remain unchanged for several days at room temperature.
To reveal any missing signal hidden under the solvent peaks we performed a DOSY experiment (Figure 2). The DOSY separated spectrum clearly revealed that all signals assigned to the cage indeed belong to only one compound (Figure 1b). Furthermore, DOSY helped to assign the missing $^1$H-NMR signal of the porphyrin building block hidden under the DMF-$d_7$ solvent peak at 8.0 ppm, which could not be identified using $^1$H, $^1$H-COSY techniques. $^{13}$C-NMR data further support the structure of 8 in solution. $^{19}$F-NMR data showed no indication for encapsulation of the triflate counterions by 8.
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Figure 2: DOSY spectrum of M₈L₆ cubic cage 8 in DMF-d₇.

The exact mass of 8 was unambiguously confirmed by cryo-spray ultra-high resolution electrospray ionization time-of-flight (Cryo-UHR-ESI-ToF) mass spectrometry (Figure 3).

Figure 3: Cryo-UHR-ESI-TOF mass spectrum of cubic cage 8 recorded using a spray temperature of -40 °C and a dry gas temperature of -35 °C. Right: Cryo-UHR ESI-TOF mass spectrum of 8¹¹⁺ {[(C₅₂₈H₃₃₆Fe₈N₉₆Zn₆)(CF₃SO₃)₅]¹¹⁺} (above) and simulated isotopic distribution (below).
We were thus far unable to grow crystals suitable for X-ray diffraction (XRD). A MM-minimized model (Spartan '08, SYBYL force field) of 8 is shown in Figure 4.

![Model (MM) of empty cage 8 (hydrogen atoms and counter ions omitted for clarity).](image)

From this model it is clear that cage 8 is larger than cage 1. The average Zn-Zn distance between two opposite planes in the empty cage 8 (19.5 Å) is ca. 4.5 Å larger than the corresponding plane distance in 1. Hence, by modifying the aldehyde building block, derivatives of 1 can be synthesized that offer significantly larger cavities, expanding the scope of host-guest chemistry applications for this new family of M₃L₆ cubic cages.

### 2.2.2 Encapsulation of metallo-porphyrins by cubic host 8

With the new large cubic cage compound 8 in hand, we evaluated its ability to encapsulate guests (Scheme 3, left). The cavity of 8 is, according to molecular modelling, sufficiently large to host tetrakis(4-pyridyl)porphyrins 2. Indeed, reaction of a 1:1 mixture of 8 and 2-Zn ([Zn(TPyP)]) gives the new diamagnetic host-guest complex [2-Zn@8] in 86% yield (Scheme 3).
Scheme 3: Left: Encapsulation of 2-M (M = Zn, Co) in 8. Right: One step synthesis of [2-Zn@8] from the building blocks.

The $^1$H-NMR spectra clearly show the appearance of two new, strongly upfield shifted signals at 6.3 and 5.7 ppm stemming from encapsulated 2-Zn (Figure 5c). For assignment see Figure 5 and Scheme 3.

Figure 5: a) $^1$H-NMR spectrum of 8; b) $^1$H-NMR spectrum of 2-Zn; c) $^1$H-NMR spectrum of [2-Zn@8]; d) $^1$H-DOSY separated NMR spectrum of [2-Zn@8]. All spectra were recorded in DMF-$d_7$. 
The observed strong upfield shifts for 2-Zn are expected due to anisotropic ring-current effects in the confined nanospace of 8, and are consistent with data reported in related host-guest assemblies.\textsuperscript{35} The signals of 2-Zn reveal C\textsubscript{4}-symmetry of this encapsulated guest, showing that 2-Zn is symmetrically bound in 8. Moreover, as a consequence of the reduced symmetry of host 8 upon binding 2-Zn (see Figure 6), the signals belonging to the cage are broadened. The DOSY separated spectrum of [2-Zn@8] (Figure 5d) was required to detect the signal at 2.7 ppm stemming from encapsulated 2-Zn, and confirms that the assembly [2-Zn@8] is present as a single species in solution. The symmetry, the upfield shifts for all pyridine moieties and the integrals of the \textsuperscript{1}H-NMR signals rule out that guest 2-Zn binds to host 8 from the outside of the cage.

Figure 6: Model (MM) of [2-Co@8] (hydrogen atoms and counter ions omitted for clarity).

The exact mass of [2-Zn@8] was unambiguously confirmed by UHR-ESI-ToF mass spectrometry, thus confirming inclusion of exactly one molecule of 2-Zn in host 8. No other assemblies with different stoichiometries (e.g. [(2-Zn)\textsubscript{2}@8] or [2-Zn@8\textsubscript{2}]) were observed. Moreover, no signals corresponding to empty cage 8 were observed, indicating that no empty host remains after reaction with one equivalent of porphyrin. The NMR spectra shown in Figure 5d and Figure 5e confirm that no empty cage is left (red lines as a guide for the eyes). In a separate experiment we demonstrated that formation of the assembly [2-Zn@8] can also be achieved in a one-pot synthetic procedure by mixing 2-Zn, 4, 7 and Fe(OTf)\textsubscript{2} in the correct stoichiometric amounts (Scheme 3, right). These results underline the highly selective assembly to [2-Zn@8] and expanded scope of M\textsubscript{8}L\textsubscript{6} cubic cages through selective cavity size variation. Similar
results were obtained when using 8 and the related tetra-pyridine-metalloporphyrin [Co(TPyP)] (2-Co), showing that the approach to encapsulate metallo-porphyrins in host 8 is general. The stoichiometry and exact mass of the paramagnetic host-guest assembly [2-Co@8] was revealed by Cryo-UHR-ESI-ToF mass spectrometry (Figure 7). Again, no signals corresponding to empty cage 8 were observed.

A MM-minimized model of [2-Co@8] is shown in Figure 6, illustrating that metallo-porphyrins of the type 2-M fit perfectly in the cavity of the cubic cage 8. EPR spectra of [2-Co@8] are clearly different from those of free 2-Co, illustrative for selective encapsulation of 2-Co in 8 (Figure 8). The EPR spectrum of 2-Co in frozen DMF reveals a broad, featureless signal. In the region between 5000-1500 gauss only a single broad line was detected (Figure 8, left). Similar signals, albeit much sharper (and therefore revealing resolved cobalt hyperfine couplings), have been reported for S= ½ (por)Co systems with axially bound pyridine or related σ-donor ligands.42-44 Strong dilution of the sample had no effect, and did not lead to sharper or different signal shapes. The spectrum indicates a mixture of self-aggregated assemblies due to intermolecular Co-pyridine interactions between different species 2-Co.

Importantly, the EPR spectrum of [2-Co@8] is markedly different (Figure 8, right). It is much sharper, shows a larger anisotropy and reveals clearly resolved cobalt hyperfine
couplings. The signal is typical for S=½ Co\(\text{II}\)(por) metallo-radicals with weakly coordinating axial ligands (likely DMF).\(^{45,46}\) Clearly, encapsulation of 2-Co by host 8 protects the system from self-aggregation, and the cubic M\(_8\)L\(_6\) host nicely keeps the paramagnetic centers [2-Co@8] separated from each other.

Additional evidence for encapsulation of 2-Co in 8 was obtained through metallo-radical trapping experiments. The paramagnetic nature of [2-Co@8] prevented us from directly detecting the characteristic NMR signals of encapsulated 2-Co, and therefore we decided to convert the metallo-radical [2-Co\(\text{II}\)@8] into a diamagnetic species ([2-Co\(\text{III}\)-R@8]) by reaction of the Co\(\text{II}\) center with ethyl diazoacetate (9) in the presence of the hydrogen-atom-transfer (HAT) agent 1,4-cyclohexadiene (10) (Scheme 4).

![Scheme 4: Radical trapping experiment to yield [Co\(\text{III}\)-CH\(_2\)CO\(_2\)Et@8].](image)

In this way, diamagnetic [2-Co\(\text{III}\)-CH\(_2\)CO\(_2\)Et@8] could be obtained. The assembly [2-Co\(\text{III}\)-CH\(_2\)CO\(_2\)Et@8] indeed revealed clear upfield-shifted tetra(4-pyridyl)porphyrin signals comparable to those observed for [2-Zn@8] (Figure 9). In addition, the signals marked with * in the separated \(^1\text{H}-\text{NMR}\) spectrum (Figure 9) indicates formation of
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Oligomers from ethyl diazoacetate (EDA) with a similar diffusion constant. Oligomers are easily formed from ethyl diazoacetate with a variety of different metal catalysts.\(^{47-49}\)

Figure 9: \(^1\text{H}-\text{NMR DOSY}\) separated spectrum of \([2-\text{Co}^{\text{III}}-\text{CH}_2\text{CO}_2\text{Et}@8]\). Signals marked with * likely correspond to oligomers formed from ethyl diazoacetate with a similar diffusion constant as \([2-\text{Co}^{\text{III}}-\text{CH}_2\text{CO}_2\text{Et}@8]\).

The exact mass of \([2-\text{Co}^{\text{III}}-\text{CH}_2\text{CO}_2\text{Et}@8]\) was unambiguously confirmed by Cryo-UHR-ESI-ToF mass spectrometry (Figure 10). This proofs not only selective encapsulation of \(2-\text{Co}\) in \(8\), but also reveals the accessibility of the catalytically active \([\text{Co}^{\text{II}}(\text{TPyP})]\) moiety within the cavity of \(8\) for substrates.

![Figure 10: Cryo-UHR-ESI-TOF mass spectrum of host-guest assembly \([2-\text{Co}^{\text{III}}-\text{CH}_2\text{CO}_2\text{Et}@8]\) with a spray temperature of -40 °C and a dry gas temperature of -35 °C. Right: Cryo-UHR ESI-TOF mass spectrum of host-guest assembly \([2-\text{Co}^{\text{III}}-\text{CH}_2\text{CO}_2\text{Et}@8]\) with a spray temperature of -40 °C and a dry gas temperature of -35 °C.](image-url)
\[
\text{CH}_2\text{CO}_2\text{Et}@8^{11+} \quad \{(\text{C}_{528}\text{H}_{336}\text{N}_{96}\text{Zn}_{6}\text{Fe}_{8})(\text{C}_{40}\text{H}_{24}\text{CoN}_{8})(\text{CF}_3\text{SO}_3)_5(\text{CH}_2\text{CO}_2\text{CH}_2\text{CH}_2)(+\text{H})\}^{11+}
\]

(above) and simulated isotopic distribution (below).

### 2.3 Metallo-radical Catalysis

To prove that \([\text{2-Co@8}]\) is a catalytically active ‘molecular flask’, and to study the effect of encapsulation on the catalytic performance of metallo-radical catalysts, we studied the activity of \([\text{2-Co@8}]\) to catalyze transformations of diazo compounds. Moreover, we compared the obtained results with several other cobalt(II)-porphyrins, namely \([\text{Co}^{II}\text{(TPyP)}\text{]}\) (\text{2-Co}), \([\text{Co}^{II}\text{(TPP)}\text{]}\) (\text{3-Co}), \([\text{Co}^{II}\text{(TPyP)*4 Zn(TPP)}\text{]}\) (\text{2-Co*4(3-Zn)}) and \text{11-Co} (Figure 11).

![Figure 11: Structure of catalyst 11-Co reported by Zhang.](image)

We started our investigations with the cobalt(II)-porphyrin catalyzed radical cyclopropanation of styrene (12) with ethyl diazoacetate (9) in DMF to give cyclopropane 13 (Table 1). In coordinating solvents such as DMF, cyclopropanation reactions are generally associated with lower rates and shorter catalyst life-times. This makes it easier to investigate the effect of catalyst encapsulation in terms of catalyst activity and stability. The encapsulated catalyst \([\text{2-Co@8}]\) is indeed active even at small catalyst loadings (0.8 mol%), leading to the formation of 13 (Entry 6, 28%, TON = 33; TON (turnover number) = Number cycles / Number sites within the indicated time). Control experiments show that \([\text{2-Co@8}]\) is substantially more active than the free tetrakis(4-pyridyl)porphyrin catalyst \text{2-Co} (Entry 3, 7%, TON = 9), which is not surprising given the self-aggregation behavior of \text{2-Co} (See Figure 8). Encapsulation of \text{2-Co} in 8 protects the cobalt-porphyrin catalyst \text{2-Co} from deactivating itself via pyridine-cobalt coordination (which blocks its active sites). More noteworthy is the fact that \([\text{2-Co@8}]\) is almost as active as free tetraphenylporphyrin catalyst \text{3-Co} (compare Entry 2 and 6). Hence, \text{2-Co} must be tightly bound in the protective cage 8 and
apparently does not easily escape from the cage (in which case a similar poor activity as observed for free \( \text{2-Co} \) would be expected; Entry 3).

Table 1: Cobalt-catalyzed cyclopropanation of styrene.

<table>
<thead>
<tr>
<th>Entry(^a)</th>
<th>Catalyst</th>
<th>Time (h)</th>
<th>Yield (%)</th>
<th>d.r.(^b) (trans:cis)</th>
<th>TON(^c)</th>
</tr>
</thead>
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<td>---</td>
<td>1</td>
<td>Trace</td>
<td>unknown</td>
<td>---</td>
</tr>
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<td>2</td>
<td>\text{3-Co}</td>
<td>1</td>
<td>34</td>
<td>78:22</td>
<td>41</td>
</tr>
<tr>
<td>3</td>
<td>\text{2-Co}</td>
<td>1</td>
<td>7</td>
<td>67:33</td>
<td>9</td>
</tr>
<tr>
<td>4</td>
<td>[\text{2-Co}(*4(3-Zn)])</td>
<td>1</td>
<td>10</td>
<td>79:21</td>
<td>13</td>
</tr>
<tr>
<td>5</td>
<td>\text{8}</td>
<td>1</td>
<td>Trace</td>
<td>unknown</td>
<td>---</td>
</tr>
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<td>6</td>
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<td>28</td>
<td>65:35</td>
<td>33</td>
</tr>
<tr>
<td>7</td>
<td>---</td>
<td>4</td>
<td>Trace</td>
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<td>---</td>
</tr>
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<td>8</td>
<td>\text{3-Co}</td>
<td>4</td>
<td>37</td>
<td>78:22</td>
<td>44</td>
</tr>
<tr>
<td>9</td>
<td>\text{2-Co}</td>
<td>4</td>
<td>15</td>
<td>75:25</td>
<td>18</td>
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<tr>
<td>10</td>
<td>[\text{2-Co}(*4(3-Zn)])</td>
<td>4</td>
<td>15</td>
<td>78:22</td>
<td>18</td>
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<tr>
<td>11</td>
<td>[\text{2-Co}@8]</td>
<td>4</td>
<td>50</td>
<td>63:37</td>
<td>60</td>
</tr>
<tr>
<td>12</td>
<td>\text{11-Co}</td>
<td>4</td>
<td>56</td>
<td>74:26</td>
<td>70</td>
</tr>
</tbody>
</table>

\(^a\) Reaction conditions: \text{12} (1.16 mmol), \text{9} (960 μmol), catalyst (8 μmol), DMF (3.2 mL), 70°C, argon atmosphere. \(^b\) diastereoselectivity. \(^c\) TON (turnover number) = Number cycles / Number sites within 1 or 4 h.\(^52\)

This protective effect of cage 8 on the activity of encapsulated \( \text{2-Co} \) is not just a simple effect of protecting the pyridine moieties of \( \text{2-Co} \) with a Lewis acid, as a mixture of \( \text{2-Co} \) with four equivalents of [Zn(TPP)] (\( \text{3-Zn} \)) (\( \text{2-Co}\(*4(3-Zn)]\)) gave very poor results in this reaction (Entry 4, 10%, TON = 13).
The improved activity and enhanced catalytic lifetime of [2-Co@8] compared to [2-Co*4(3-Zn)] can be explained by a stronger binding and better protection of 2-Co in 8. Importantly, the empty cage 8 shows no catalytic activity at all, thus ruling out that the iron cage corners are involved in the cyclopropanation reaction (Entry 5). To the best of our knowledge, these are the first examples of transition-metal catalyzed radical-type reactions of diazo compounds occurring inside the cavity of a supramolecular cage. The M₈L₆ cage 8 has two major effects on the activity of cobalt-porphyrin 2-Co in [2-Co@8]: (1) It activates the encapsulated guest as a catalytically active species, and (2) it prevents or at least delays unwanted radical-radical dimerization.

The yield and turnover number achieved with encapsulated catalyst [2-Co@8] (Entry 11, 50%, TON = 60) after a longer reaction time (4 h) is substantially higher than with the non-protected catalysts 3-Co (Entry 8, 37%, TON = 44) or 2-Co (Entry 9, 15%, TON = 18). Also [2-Co*4(3-Zn)] gave a lower yield and turnover number (Entry 10, 15%, TON = 18). Moreover, the turnover numbers of 3-Co do not differ significantly between 1 and 4 hours reaction time, indicating that 3-Co became inactive after 1 h of reaction (Entries 2 and 8), while the encapsulated catalyst [2-Co@8] remains active in this period (Entries 6 and 11) effectively leading to higher yields (50%) than obtained with 3-Co (37%) after 4 h in DMF. Out of all tested catalysts, 11-Co remains the only catalyst performing overall better than [2-Co@8] (Entry 12, 56%, TON = 70) under the applied reactions conditions. In a way, the steric bulk of this catalyst provides a similar protective ‘cage’ around the metal as it is the case for [2-Co@8], but likely the H-bonding motifs contribute additionally to the relatively high activity of 11-Co.¹⁷

To further explore the scope of [2-Co@8] towards diazo compounds capable of entering the cage and reacting with the encapsulated cobalt center, we studied the reactivity of diazo ester 14 (Scheme 5). Activation of 14 using cobalt(II)-porphyrins yields carbon-centered radical 15. In the absence of any external radical acceptor, intermediate 15 can in principle undergo two different reaction pathways. Intramolecular radical addition to the aromatic ring results in the formation of 16, similar to the approach described by Gansäuer, Flowers and co-workers.⁵³ Alternatively, a 1,2-hydrogen atom shift yields the olefins 17. While olefin formation from diazo compounds has been described for other catalysts based on rhodium or copper⁵⁴ cobalt(II)-porphyrin catalyzed olefin formation from diazo esters like 14 has not been described to date.
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Scheme 5: Intramolecular reactions of carbene radical intermediate 15.

Table 2: Cobalt-catalyzed synthesis of olefins 17.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Mol%</th>
<th>Time (h)</th>
<th>Yield 17 (%)</th>
<th>d.r. (^{b} ) (E:Z)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3-Co</td>
<td>1</td>
<td>1</td>
<td>10</td>
<td>40:60</td>
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<tr>
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<td>[2-Co@8]</td>
<td>1</td>
<td>1</td>
<td>30</td>
<td>13:87</td>
</tr>
<tr>
<td>4</td>
<td>[2-Co@8]</td>
<td>1</td>
<td>3</td>
<td>40</td>
<td>16:84</td>
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<td>5</td>
<td>11-Co</td>
<td>1</td>
<td>3</td>
<td>20</td>
<td>10:90</td>
</tr>
<tr>
<td>6</td>
<td>3-Co</td>
<td>2</td>
<td>3</td>
<td>22</td>
<td>43:57</td>
</tr>
<tr>
<td>7</td>
<td>2-Co</td>
<td>2</td>
<td>3</td>
<td>&lt;7</td>
<td>22:78</td>
</tr>
<tr>
<td>8</td>
<td>2-Co*4(3-Zn)</td>
<td>2</td>
<td>3</td>
<td>15</td>
<td>29:71</td>
</tr>
<tr>
<td>9</td>
<td>[2-Co@8]</td>
<td>2</td>
<td>3</td>
<td>72</td>
<td>16:84</td>
</tr>
</tbody>
</table>

a) Reaction conditions: 14 (0.5 mmol), DMF (2.5 mL), 70°C, argon atmosphere.
b) Diastereoselectivity was determined from the \(^{1} \text{H-NMR} \) ratio of the alkene products.
Increasing the reaction time to 3 hours further improved the yield (Entry 4, 40%, \(E:Z = 14:86\)). Remarkably, while 11-Co gave better results in the cyclopropanation of styrene than [2-Co@8], the situation is clearly reversed for the transformation of 14 to 17. Catalyst 11-Co produces olefin 17 with a significant lower yield but slightly higher diastereoselectivity (Entry 5, 20%, \(E:Z = 10:90\)) than [2-Co@8] (Entry 4, 40%, \(E:Z = 16:84\)). Increasing the loading of the employed catalyst further improved the yield. Catalyst [2-Co@8] gave, with 72% yield, the best results of all studied catalysts (Entry 9, 72%, \(E:Z = 16:84\)). The mixture of 2-Co with four equivalents of [Zn(TPP)] (3-Zn) ([2-Co*4(3-Zn)]) gave only 15% of 17 in 3 h under similar reaction conditions (Entry 8). These results undoubtedly demonstrate that the reactivity of a cobalt-porphyrin can be dramatically influenced by encapsulation in a supramolecular host.

## 2.4 Conclusion

We here presented the design, synthesis and characterization of a new ‘molecular flask’. This \(M_3L_6\) cubic cage is sufficiently large to encapsulate tetrakis(4-pyridyl)porphyrins, which represent an important class of catalysts. The synthesis of this host is based on a self-assembly process using bipyridine-functionalized porphyrin building blocks. The encapsulation of tetrakis(4-pyridyl)porphyrins provides the first examples of encapsulated transition metal complexes in such hosts. Importantly, the encapsulated cobalt porphyrin is an active catalyst and shows higher TON than the non-encapsulated analogues in radical-type transformations. The number of unwanted side reactions of reactive radical intermediates could be reduced due to the shielded environment. The systems presented in this chapter are rare examples of (molecularly) encapsulated metallo-porphyrins capable of catalytic turnover. The encapsulated cobalt tetrakis(4-pyridyl)porphyrin [Co\(^{11}\)(TPyP)] (2-Co) showed to be active in radical-type cyclopropanation of styrene with ethyl diazoacetate as well as Z-selective olefin synthesis using a disubstituted diazo compound as the substrate. Improved activities and catalyst life-times were demonstrated through a combination of control experiments. Therefore, the results show that the reactivity of a transition-metal complex can be influenced by encapsulation in a supramolecular host.
2.5 Experimental Section

2.5.1 General Information

All reactions involving air- or moisture sensitive compounds were carried out under argon or nitrogen using standard Schlenk and vacuum line techniques. Dimethylformamide (DMF) was purchased from Aldrich without purification before use. The toluene used was dried and deoxygenated over sodium according to standard procedures. All other chemicals were purchased from commercial suppliers without purification before use.

$^1$H NMR, $^{13}$C NMR and $^{19}$F NMR spectra were measured on Mercury Varian 300MHz, Bruker 400 MHz or Bruker 500 MHz spectrometer. $^1$H NMR chemical shifts are reported in ppm, and were calibrated by using the residual non-deuterated solvent as internal reference (CHCl$_3$ (7.26 ppm), DMF-d$_7$ (8.03 ppm, 2.92 ppm and 2.75 ppm)). $^{13}$C NMR chemical shifts were recorded in ppm from the solvent peak employed as internal reference (CDCl$_3$ (77.0 ppm), DMF-d$_7$ (163.2 ppm, 34.9 ppm, 29.8 ppm)). $^{19}$F NMR chemical shifts are reported with CFCl$_3$ (0.0 ppm) added as internal standard. IR spectra were measured on a Bruker Alpha-P instrument as neat film. UV-vis spectra were measured on a Hewlett Packard 8453.

MS measurements were performed on a UHR-ToF Bruker Daltonik (Bremen, Germany) maXis, which was coupled to a Bruker cryospray unit, an ESI-ToF MS capable of resolution of at least 40.000 FWHM. Detection was in positive-ion mode and the source voltage was 5 kV. The flow rates were 500 µL/hour. The drying gas (N$_2$), was held at -35 °C (-55 °C) and the spray gas was held at -40 °C (-60 °C). The machine was calibrated prior to every experiment via direct infusion of the Agilent ESI-ToF low concentration tuning mixture, which provided an m/z range of singly charged peaks up to 2700 Da in both ion modes.

2.5.2 Synthesis of described compounds

Compounds 1, 37 2-Zn, 55 2-Co, 56 4, 37 11, 57 18 58 and 19 59 were synthesized as described in the literature.

Synthesis of 2,2’-bipyridine-5-carbaldehyde (7)

To an oven dried Schlenk flask were added bis(triphenylphosphine)palladium(II) dichloride (104 mg, 0.15 mmol), triphenylphosphine (77 mg, 0.30 mmol), 2-(tributylstannyl)pyridine (18, 1.09 g, 2.95 mmol), 6-bromo-3-pyridinecarbaldehyde (19, 660 mg, 3.54 mmol) and toluene (40 mL) under argon. The resulting mixture was stirred for 72 hours under reflux. The mixture was cooled to room temperature and the solvent was removed under reduced pressure. The obtained solid was
redissolved in CH$_2$Cl$_2$ (50 ml) and washed with a saturated NH$_4$Cl-solution (30 mL). The aqueous phase was extracted with CH$_2$Cl$_2$.

The organic layers were combined, the solvent was removed under reduced pressure and the crude product was purified by column chromatography (SiO$_2$, 20% EtOAc, 20% CH$_2$Cl$_2$ and 60% cyclohexane, $R_f = 0.16$) to give 7 (200 mg, 1.09 mmol, 37%) as a colorless solid. $^1$H-NMR (300MHz, CDCl$_3$): 10.18 (s, 1H), 9.13 (d, $J = 2.1$ Hz, 1H), 8.76-8.71 (m, 1H), 8.63 (d, $J = 8.5$ Hz, 1H) 8.52 (m, 1H), 8.30 (dd, $J = 8.2$ Hz, $J = 2.1$ Hz, 1H), 7.89 (td, $J = 7.8$ Hz, $J = 1.9$ Hz, 1H), 7.40 (dd, $J = 7.5$ Hz, $J = 4.8$ Hz, $J = 1.2$ Hz, 1H); $^{13}$C-NMR (75MHz, CDCl$_3$): 190.8, 160.7, 154.8, 151.8, 149.6, 127.4, 137.1, 131.2, 125.0, 122.4, 121.5; $^1$H- and $^{13}$C-NMR data are in agreement with published data.$^{60}$

**Synthesis of supramolecular cubic M$_8$L$_6$ cage 8**

4 (48.8 mg, 66 µmol), Fe(OTf)$_2$ (30.5 mg, 88 µmol), 2,2'-bipyridine-5-carbaldehyde 7 (48.6 mg, 264 µmol) and 5 ml DMF were mixed in an oven dried Schlenk flask under an argon atmosphere. The mixture was degassed three times and stirred for 16 h at 70 °C. The mixture was cooled to room temperature and diethyl ether was added. The precipitate was collected by filtration and washed with diethyl ether. The remaining solid was collected quantitatively with DMF. The solvent was removed under reduced pressure to give 8 as a purple solid (119 mg, 10.6 µmol, 96%). $^1$H-NMR (400MHz, DMF-d$_7$): 9.33 (d, $J = 9.3$ Hz, 24H, H-5), 9.24 (d, $J = 8.4$ Hz, 24H, H-4), 9.05 (d, $J = 8.2$ Hz, 24H, H-6), 8.93 (s, 48H, H-11), 8.79 (s, 24H, H-8), 8.66 (s, 24H, H-7), 8.45 (m, 24H, H-3), 8.25 (d, $J = 8.6$ Hz, 24H, H-10), 8.10 (m, 24H, H-10'), 7.87-7.79 (m, 48H, H-1, H-2), 7.60 (d, $J = 8.4$ Hz, 24H, H-9), 7.48 (d, $J = 8.5$ Hz, 24H, H-10'); $^{13}$C-NMR (125MHz, DMF-d$_7$): 160.5, 159.6, 158.4, 156.0, 152.8, 152.3, 151.0, 150.8, 142.4, 140.5, 137.4, 137.2, 137.0, 136.7, 132.8, 132.5, 129.6, 126.7, 125.9, 124.1, 121.5, 121.4, 118.7; $^{19}$F-NMR (282 MHz, DMF-d$_7$): -77.5; IR (neat, cm$^{-1}$): 2970, 2360, 2340, 1660, 1390, 1255, 1155, 1090, 1030; UV-vis (DMF, $\lambda_{max}$, nm): 312, 359, 424, 443, 565, 607; Exact mass ESI-MS:
Reactivity of Metallo-Porphyrins in a Self-Assembled Cubic M8L6 Cage

Table 3: Exact mass ESI-MS signals of cubic cage 8.

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<th>Identified as</th>
</tr>
</thead>
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<td>654.4201</td>
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<td>873.6124</td>
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<tr>
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<td>1100.8497</td>
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<td>[M-8*(CF₃SO₃)]²₀⁺</td>
</tr>
</tbody>
</table>

Synthesis of [2-Zn@8]

Encapsulation of 2-Zn in preformed cubic cage 8:

To an oven dried Schlenk flask under an argon atmosphere were added 2-Zn (9.1 mg, 134 µmol), 8 (150 mg, 134 µmol) and DMF (20 mL). The mixture was degassed three times and heated for 16 h at 70 °C. After reaching room temperature diethyl ether was added. The mixture was filtered and the precipitate was washed with diethyl ether (100 mL). The remaining solid was collected with DMF (25 mL). The solvent was removed under reduced pressure to give [2-Zn@8] as a purple solid (137 mg, 11.4 µmol, 85 %). The analysis data was in agreement to the data found for the one step synthesis described below.

One step synthesis of [2-Zn@8] starting from 4:

To an oven dried Schlenk flask under argon atmosphere were added tetrakis(4-aminophenyl)porphyrin 4 (30 mg, 41 µmol), Fe(OTf)₂ (19 mg, 53 µmol), 7 (30 mg, 164 µmol), 2-Zn (4.2 mg, 6.8 µmol) and DMF (5.0 mL). The mixture was degassed three times and stirred for 16 h at 70 °C. The mixture was cooled to room temperature and diethyl ether (50 mL) was added to precipitate the product. The mixture was filtered and the obtained solid was washed with diethyl ether (100 mL). The remaining solid was collected with DMF (10 mL). The solvent was removed under reduced pressure to give [2-Zn@8] as a purple solid (53 mg, 4.4 µmol, 65 %).
Table 4: Exact mass ESI-MS signals of host-guest assembly [2-Zn@8]. Methanol has not been used as a solvent during the synthesis or measurement. However, there are always small amounts of methanol present in the spectrometer since it is the main rinsing solvent used to clean the instrument.

<table>
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<th>Peak m/z</th>
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<td>839.5026</td>
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<td>[M-13⁺(CF₃SO₂)⁺+(CH₃OH)⁺(CH₂O)⁺(H₂O)]¹²⁺</td>
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<td>[M-13⁺(CF₃SO₂)⁺+(CH₃OH)⁺(CH₂O)⁺(H₂O)]¹²⁺</td>
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<td>846.6626</td>
<td>846.6614</td>
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<tr>
<td>927.8111</td>
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<td>[M-12⁺(CF₃SO₂)⁺⁺(CH₂O)]¹¹⁺</td>
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<td>935.6264</td>
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<td>[M-10⁺(CF₃SO₂)⁺⁺(H₂O)]¹⁰⁺</td>
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</tbody>
</table>
Synthesis of [2-Co@8]

2-Co (7.4 mg, 11 µmol), 8 (125 mg, 11 µmol) and DMF (10 mL) were treated in the same manner as for the synthesis of [2-Zn@8] to give [2-Co@8] as a purple solid (115 mg, 9.6 µmol, 87 %). 19F-NMR (282 MHz, DMF-d7): -77.5; IR (neat): 2365, 2340, 1655, 1250, 1225, 1150, 1030, 990, 790, 635, 635, 435, 410; UV-vis (DMF): λ<sub>max</sub>, nm: 316, 357, 420, 443, 567, 610; Exact mass ESI-MS.

Table 5: Exact mass ESI-MS Signals of host-guest assembly [2-Co@8].

<table>
<thead>
<tr>
<th>Peak m/z</th>
<th>Simulated m/z</th>
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<td>702.7142</td>
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<td>[M-14*(CF3SO3)+(H2O)]&lt;sub&gt;14+&lt;/sub&gt;</td>
</tr>
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<td>705.2180</td>
<td>705.2180</td>
<td>[([C52H35N6O6Zn6Fe6)(C6H5CoN6)(CF3SO3)&lt;sub&gt;2&lt;/sub&gt;+(H2O)&lt;sub&gt;2&lt;/sub&gt;]&lt;sub&gt;14+&lt;/sub&gt;)</td>
<td>[M-14*(CF3SO3)+(H2O)&lt;sub&gt;2&lt;/sub&gt;]&lt;sub&gt;14+&lt;/sub&gt;</td>
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<td>[M-13*(CF3SO3)+(H2O)&lt;sub&gt;2&lt;/sub&gt;]&lt;sub&gt;13&lt;/sub&gt;</td>
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1045.1873 1045.1846 [(C₅₂H₃₃N₉Zn₆Fe₉)(C₆H₅CoN₉)(CF₃SO₃)₃]·(H₂O) [M-10*(CF₃SO₃)+(H₂O)]¹⁰⁺

1175.8661 1175.8663 [(C₅₂H₃₃N₉Zn₆Fe₉)(C₆H₅CoN₉)(CF₃SO₃)₃]·(H₂O)³⁺

1177.8674 1177.8674 [(C₅₂H₃₃N₉Zn₆Fe₉)(C₆H₅CoN₉)(CF₃SO₃)₃]·(H₂O)³⁺

Synthesis of [2-CoIII-CH₂CO₂Et@8]

To an oven-dried Schlenk flask were added under nitrogen [2-Co@8] (32 mg, 2.7 µmol) and DMF (0.5 mL). Ethyl diazoacetate (12, 70 mg, 620 µmol) and 1,4-cyclohexadiene (13, 9 mg, 110 µmol) were added to the stirred solution and the mixture was heated to 70 ºC. After 90 minutes drying under reduced pressure, [2-CoIII-CH₂CO₂Et@8] was obtained as a dark purple solid (17 mg). ¹H-NMR (400MHz, DMF-d₇): 9.45–8.69 (m, 155 H), 8.69–8.13 (m, 72 H), 8.13–7.89 (m, 44H), 7.89–7.07 (m, 65H), 6.50–6.31 (m, 8H), 5.84–5.68 (m, 8H), 2.96–2.82 (m, 8H). Exact mass ESI-MS:

Table 6: Exact mass ESI-MS Signals of host-guest assembly [2-CoIII-R@8].

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<td>710.2920</td>
<td>710.2920</td>
<td>[(C₅₂H₃₃N₉Zn₆Fe₉)(C₆H₅CoN₉)(CF₃SO₃)₃+(H₂O)(CH₂CO₂CH₂CH₃)]¹⁴⁺</td>
<td>[M-14*(CF₃SO₃)+(H₂O)(CH₂CO₂CH₂CH₃)]¹⁴⁺</td>
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<tr>
<td>775.0016</td>
<td>775.0023</td>
<td>[(C₅₂H₃₃N₉Zn₆Fe₉)(C₆H₅CoN₉)(CF₃SO₃)₃(CH₂CO₂CH₂CH₃)]¹³⁺</td>
<td>[M-13*(CF₃SO₃)+(CH₂CO₂CH₂CH₃)]¹³⁺</td>
</tr>
<tr>
<td>776.3868</td>
<td>776.3878</td>
<td>[(C₅₂H₃₃N₉Zn₆Fe₉)(C₆H₅CoN₉)(CF₃SO₃)₃+(H₂O)(CH₂CO₂CH₂CH₃)]¹³⁺</td>
<td>[M-13*(CF₃SO₃)+(H₂O)(CH₂CO₂CH₂CH₃)]¹³⁺</td>
</tr>
<tr>
<td>851.9985</td>
<td>851.9986</td>
<td>[(C₅₂H₃₃N₉Zn₆Fe₉)(C₆H₅CoN₉)(CF₃SO₃)₃(CH₂CO₂CH₂CH₃)]¹²⁺</td>
<td>[M-12*(CF₃SO₃)+(CH₂CO₂CH₂CH₃)]¹²⁺</td>
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<tr>
<td>853.4987</td>
<td>853.4995</td>
<td>[(C₅₂H₃₃N₉Zn₆Fe₉)(C₆H₅CoN₉)(CF₃SO₃)₃+(H₂O)(CH₂CO₂CH₂CH₃)]¹²⁺</td>
<td>[M-12*(CF₃SO₃)+(H₂O)(CH₂CO₂CH₂CH₃)]¹²⁺</td>
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<tr>
<td>942.9943</td>
<td>942.9941</td>
<td>[(C₅₂H₃₃N₉Zn₆Fe₉)(C₆H₅CoN₉)(CF₃SO₃)₃(CH₂CO₂CH₂CH₃)]¹¹⁺</td>
<td>[M-11*(CF₃SO₃)+(CH₂CO₂CH₂CH₃)]¹¹⁺</td>
</tr>
<tr>
<td>944.6307</td>
<td>944.6315</td>
<td>[(C₅₂H₃₃N₉Zn₆Fe₉)(C₆H₅CoN₉)(CF₃SO₃)₃+(H₂O)(CH₂CO₂CH₂CH₃)]¹¹⁺</td>
<td>[M-11*(CF₃SO₃)+(H₂O)(CH₂CO₂CH₂CH₃)]¹¹⁺</td>
</tr>
</tbody>
</table>
Reactivity of Metallo-Porphyrins in a Self-Assembled Cubic M8L6 Cage

| 1052.189 | 1052.188 | \[[\text{C}_{52}H_{38}N_{96}Zn_{6}Fe_{8}](\text{CH}_{2}CO_{2}CH_{2}CH_{3})\]^{10+} | \[[\text{M}-10^{+}(\text{CF}_{3}\text{SO}_{3})_{6}(\text{CH}_{2}CO_{2}CH_{2}CH_{3})]^{10+}\]  
| 1053.9897 | 1053.9899 | \[[\text{C}_{52}H_{38}N_{96}Zn_{6}Fe_{8}](\text{H}_{2}O)(\text{CH}_{2}CO_{2}CH_{2}CH_{3})\]^{10+} | \[[\text{M}-10^{+}(\text{CF}_{3}\text{SO}_{3})_{6}+(\text{H}_{2}O)(\text{CH}_{2}CO_{2}CH_{2}CH_{3})]^{10+}\]  
| 1185.6480 | 1185.6490 | \[[\text{C}_{52}H_{38}N_{96}Zn_{6}Fe_{8}](\text{CF}_{3}\text{SO}_{3})_{7}(\text{CH}_{2}CO_{2}CH_{2}CH_{3})\]^{9+} | \[[\text{M}-9^{+}(\text{CF}_{3}\text{SO}_{3})_{7}+(\text{H}_{2}O)(\text{CH}_{2}CO_{2}CH_{2}CH_{3})]^{9+}\]  
| 1187.5377 | 1187.6501 | \[[\text{C}_{52}H_{38}N_{96}Zn_{6}Fe_{8}](\text{CF}_{3}\text{SO}_{3})_{7}+(\text{H}_{2}O)(\text{CH}_{2}CO_{2}CH_{2}CH_{3})\]^{9+} | \[[\text{M}-9^{+}(\text{CF}_{3}\text{SO}_{3})_{7}+(\text{H}_{2}O)(\text{CH}_{2}CO_{2}CH_{2}CH_{3})]^{9+}\]  

**Synthesis of 2-Co* (3-Zn)**

To an oven-dried schlenk flask was added under nitrogen 2-Co (49.8 mg, 73.7 mmol), 4-Zn (200 mg, 295 mmol) and DMF (10 mL). The stirred reaction mixture was degassed three times and heated to 70 °C for 16 h. After the reaction mixture was cooled to room temperature all solvents were removed under vacuum to yield a purple powder (249 mg).

**EPR spectroscopy**

[CoII(TPyP)] (2-Co) or [2-Co@8] was dissolved in DMF in a N₂-filled glovebox, after which the solution was transferred into an EPR tube. The samples were immediately frozen in liquid N₂ before recording the X-band EPR spectra on a Bruker EMX spectrometer at 20 K. Measurements were performed with the microwave frequency at 9.374749 GHz For the measurement of 2-Co and 9.376376 GHz for [2-Co@8], microwave power at 0.2 mW and modular amplitude at 4 Gauss.

**General procedure for the catalytic cyclopropanation experiments**

\[
\text{12} \quad \text{1.2 eq.} \quad + \quad \text{11} \quad \text{1.0 eq.} \quad \xrightarrow{\text{catalyst (0.8 mol-%)}} \quad \text{DMF, 70°C} \quad \text{13} \quad \text{1.0 eq.} \quad \text{CO}_2\text{Et}
\]

To an oven dried Schlenk flask were added the cobalt-catalyst (8 μmol) and DMF (3.2 mL) under argon. 12 (120 mg, 1.16 mmol) and 9 (109 mg, 960 μmol) were added to the mixture and the reaction mixture was stirred for one or four hours at an oil bath temperature of 70 °C. The mixture was cooled to room temperature and EtOAc was added. After filtration and washing with EtOAc the solvents were removed under reduced pressure and the crude product was purified by column chromatography (SiO₂, 25 % EtOAc, 75% cyclohexane) to give 13 as a pale yellow oil. ¹H-NMR data of the obtained cyclopropane product 13 were in agreement with published data. ⁵¹
General procedure for the synthesis of 17

\[
\begin{align*}
\text{N}_2 & \quad \text{catalyst (1.0 mol-%)} \\
14 & \quad \text{DMF, 70°C} \\
& \quad 17
\end{align*}
\]

To an oven dried Schlenk flask were added the cobalt-catalyst (10 μmol) and DMF (2.5 mL) under argon. 109 mg 14 (500 μmol) was added to the mixture and the reaction mixture was stirred for the indicated time at 70 °C. The mixture was cooled to room temperature and EtOAc was added. After filtration and washing with EtOAc the solvents were removed under reduced pressure and the mixtures of product 17 and substrate 14 was obtained and weighted. \(^1\)H-NMR analysis of olefins 17-E \(^61\) and 17-Z \(^62\) are in agreement with published data. The diastereoselectivity was determined from the relative intensity of the \(^1\)H-NMR signals of the two isomers.

### 2.6 Acknowledgements

Matthias Otte is gratefully acknowledged for collaborating in this project. M. Otte performed the initial cage synthesis and encapsulation studies, P. Kuijpers performed the radical trapping experiments and characterization. Both M. Otte and P. Kuijpers participated in the catalytic studies and preparation of the manuscript. Oliver Troeppner is thanked for the ESI-MS analysis of the cages described in this chapter. Financial support from the Netherlands Organization for Scientific Research is appreciated (NWO-CW VICI project 016.122.613).
2.6 References


