Controlling radical-type reactivity with transition metals and supramolecular cages

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Publication date
2017

Document Version
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Citation for published version (APA):
Chapter 3

An Encapsulated Cobalt-Porphyrin as Catalyst for Size-Selective Radical-Type Cyclopropanation Reactions.

**Abstract:** A cobalt-porphyrin catalyst encapsulated in a cubic $M_8L_6$ cage allows cyclopropanation reactions in aqueous media. The encapsulated catalyst shows enhanced activities in acetone/water as compared to pure acetone. Interestingly, the $M_8L_6$-encapsulated catalyst reveals size-selectivity. Smaller substrates penetrate through the pores of the supramolecular cage more easily and are therefore converted faster than bigger substrates.

### 3.1 Introduction

Bio-inspired supramolecular caged catalysts, sometimes referred to as molecular flasks, attracted much attention in recent years.\(^1\)\(^-\)\(^9\) The aim of these fascinating man-made architectures is to translate some of the operational modes of enzymes to synthetic systems. One of their main characteristics is that the catalyzed transformations take place in a confined space (see also Chapter 1 of this Thesis). Unfortunately, the design of such molecular flasks is very challenging while offering mostly only a very limited scope of substrates for catalysis.\(^10\)\(^-\)\(^14\) In Chapter 2 of this Thesis, the synthesis of the Nitschke-type $M_8L_6$ cubic cage 1 via self-assembly was described (Scheme 1).\(^15\) Cage 1 is suitable to encapsulate tetrakis(4-pyridyl)porphyrins ($M$(TPyP) (2); $M = Zn, Co$) to yield the $M_8L_6P_1$ cubic cages [\(2-Zn@1\)] and [\(2-Co@1\)] ($P =$ porphyrin guest). In particular, the encapsulation of a cobalt-porphyrin is interesting as these complexes are well known for their catalytic activity in radical-type reactions.\(^16\)\(^-\)\(^25\) Indeed, we were able to show that [\(2-Co@1\)] is a catalytically active supramolecular catalyst (see Chapter 2).

However, the solvent for the reactions catalyzed by the cubic cage were so far limited to dimethylformamide (DMF). Furthermore, the substrate scope is unexplored, and it remained unclear if size-selective transformations are possible with encapsulated catalysts such as [\(2-Co@1\)], which is the topic of the investigations described in this chapter.

Shape and size selectivity plays a tremendously important role in several enzymatic processes,\(^26\)\(^,\)\(^27\) as well as a wide range of catalytic reactions with zeolites,\(^28\)\(^,\)\(^29\) zeolite-based encapsulated catalysts,\(^30\) metal-organic frameworks\(^31\) and related systems.\(^32\) In marked contrast, homogeneously catalyzed processes with soluble, encapsulated (supramolecular) catalysts showing shape or size-selectivity are rare.\(^33\)\(^-\)\(^40\) The development of such systems is of importance for, among others, the advancement of selective tandem catalytic processes and/or one-pot, multicomponent reactions with complex mixtures of catalysts and substrates. In this chapter we present, to the best of
our knowledge, the first example of an encapsulated catalyst in a supramolecular cage capable of size-selective radical-type cyclopropanation reactions. In addition, an unexpected beneficial effect of water on the rate and selectivity of cobalt-porphyrin catalyzed cyclopropanation reactions is described.

### 3.2 Results and discussion

We started our investigations by improving the solubility of cage 1, aiming for a cage that is soluble in different solvents and/or solvent mixtures. Since modification of the aldehyde or porphyrin structure might interfere with the selective cage formation, we decided to manipulate the counter-ion. As such, by replacing Fe(OTf)₂ by Fe(NTf₂)₂ as a building block in the cage synthesis protocol, we were able to synthesize cage compound 3 in 97% yield (see Scheme 1).

Scheme 1: Synthesis of cubic cages 1 and 3 with subsequent encapsulation of 2-M. [2-M@1] is shown as a model (Spartan '08, MM SYBYL FF; hydrogen atoms and counter ions omitted for clarity).
Cage compound 3 proved to be soluble in acetone, acetonitrile and DMF as well as in solvent mixtures like 1,2-dichlorobenzene/acetonitrile or water/acetone. The aromatic signals from the cage 3 shift depending on the solvent used, which could be caused by the ability of the cage to contract and expand slightly. However, the signals remained relatively sharp and well resolved in all solvents, characteristic for the symmetrical cubic shape of the cage (Figure 1).

![Figure 1: \(^1\)H-NMR spectra of cage 3 in DMF (top), acetone (middle) and acetonitrile (bottom).](image)

High resolution mass spectrometry confirmed that the stoichiometry of the assemblies does not change in the different solvents (Figure 2). In all solvents a peak pattern was observed corresponding to the supramolecular cage after loss of up to nine triflimide counter ions resulting in signals for the 15+ to 8+ charged assemblies.
An Encapsulated Catalyst for Size-Selective Cyclopropanation Reactions

Figure 2: Cryo-UHR-ESI-TOF mass spectrum of cubic cage 3 using a spray temperature of -40 °C and a dry gas temperature of -35 °C in different solvents; DMF (top); acetone (middle) and acetonitrile (bottom).

Analogous to 1, cage 3 is also able to encapsulate metallo-porphyrins 2-Zn and 2-Co to give the encapsulated complexes [2-Zn@3] and [2-Co@3] in good yields (Scheme 1). Furthermore, 3 and [2-Zn@3] were studied using $^1$H-NMR DOSY techniques revealing that both compounds behave as single, intact supramolecular entities in solution (Figure 3). The spectra show a distortion around the solvent peak (8.03 ppm) which is caused by the exchange of solvent molecules in the supramolecular cage.

Figure 3: DOSY spectra of 3 (left) and [2-Zn@3] (right) in DMF-d$_7$. 
The encapsulated catalyst [2-Co@3] was examined in the cyclopropanation of styrene (4) with ethyl diazoacetate (5) in different solvents (Table 1).

Table 1: Cobalt-catalyzed cyclopropanation of styrene.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Solvent</th>
<th>Yield (%)</th>
<th>d.r.</th>
<th>TON</th>
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</thead>
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<tr>
<td>1۵</td>
<td>[2-Co@1]</td>
<td>DMF</td>
<td>28</td>
<td>65:35</td>
<td>33</td>
</tr>
<tr>
<td>2۵</td>
<td>[2-Co@3]</td>
<td>DMF</td>
<td>25</td>
<td>65:35</td>
<td>30</td>
</tr>
<tr>
<td>3</td>
<td>[2-Co@3]</td>
<td>DMF</td>
<td>6</td>
<td>65:35</td>
<td>27</td>
</tr>
<tr>
<td>4</td>
<td>[2-Co@3]</td>
<td>Acetone</td>
<td>19</td>
<td>65:35</td>
<td>77</td>
</tr>
<tr>
<td>5</td>
<td>[2-Co@3]</td>
<td>Acetone/Water</td>
<td>46</td>
<td>66:34</td>
<td>182</td>
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<tr>
<td>6</td>
<td>3</td>
<td>Acetone/Water</td>
<td>1:5</td>
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<td>---</td>
</tr>
<tr>
<td>7</td>
<td>2-Co</td>
<td>Acetone/Water</td>
<td>1:5</td>
<td>3</td>
<td>83:17</td>
</tr>
<tr>
<td>8</td>
<td>7</td>
<td>Acetone/Water</td>
<td>1:5</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>9</td>
<td>8</td>
<td>Acetone/Water</td>
<td>1:5</td>
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<td>---</td>
</tr>
<tr>
<td>10</td>
<td>9</td>
<td>Acetone/Water</td>
<td>1:5</td>
<td>75</td>
<td>73:27</td>
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<tr>
<td>11</td>
<td>9</td>
<td>Acetone</td>
<td>63</td>
<td>78:22</td>
<td>252</td>
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<tr>
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<td>10</td>
<td>Acetone/Water</td>
<td>1:5</td>
<td>64</td>
<td>79:21</td>
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<tr>
<td>13۵</td>
<td>[2-Co@3]</td>
<td>Acetone/Water</td>
<td>1:5</td>
<td>73</td>
<td>65:35</td>
</tr>
<tr>
<td>14۵</td>
<td>[2-Co@3]</td>
<td>Acetone/Water</td>
<td>1:5</td>
<td>76</td>
<td>66:34</td>
</tr>
</tbody>
</table>

a) 0.8 mol% catalyst loading, 1.2 eq. 4. b) Reaction time 24 h. c) Acetone-d₆ has been used. d) d.r. = diastereomeric ratio.
These catalysis experiments showed that the change of the counter ion has only a minor influence on the synthesis of 6 catalyzed by the encapsulated catalysts [2-Co@1] and [2-Co@3] (Table 1, Entry 1 and 2, TON = 33 and 30 respectively, (TON = turnover number)). Reducing the catalyst loading to 0.25 mol% results in a decreased yield of only 6% after 1 h and a comparable TON of 27 (Entry 3). However, employing acetone-d₆ as the solvent increased the yield to 19% (Entry 4, TON = 77). Remarkably, the reactivity of [2-Co@3] increased further by carrying out the reaction in a 5:1 mixture of water and acetone-d₆ yielding 46% of cyclopropane 6 after 1 h (Entry 5, TON = 182). Only a few catalysts have previously been described for efficient cyclopropanation in aqueous solutions. Control experiments with empty cage 3 show no catalytic activity in the cyclopropanation reaction (Entry 6). Importantly, [2-Co@3] is substantially more productive than the free cobalt tetrakis(4-pyridyl)porphyrin catalyst ([Co(TPyP)], 2-Co, Entry 7, 3%, TON = 10). Furthermore, water soluble cobalt(II) tetrakis(4-N-methylpyridyl)porphyrin tetraiodide [Co(TMePyP)*4I], 7, Figure 4) and cobalt(II) tetrasodium tetrakis(4-sulfonatophenyl)porphyrin [Co(TPPS)*4Na], 8, Figure 4) showed no reactivity under the applied conditions (Entries 8 and 9 respectively).

Figure 4: Structures of catalysts [Co(TMePyP)*4I] (7), [Co(TPPS)*4Na] (8), [Co(TPP)] (9) and porphyrin 10.
It has to be noted that [2-Co@3] (although soluble in acetone/water mixtures) can migrate to some extent into the water insoluble substrate phase. This means that [2-Co@3] may act as a phase-transfer catalyst (with the cyclopropanation catalyst embedded). On the other hand, due to encapsulation in the hydrophobic cavity of [2-Co@3] substrates might be pulled into the aqueous phase. Inspired by these hypotheses we also studied cobalt(II) tetraphenylporphyrin ([Co(TPP)], 9, Figure 4) as a catalyst. Interestingly, with catalyst 9 in acetone/water, high yields (75%) of product 6 were obtained already after 1 hour (d.r. = 73:27, TON = 302, Table 1, Entry 10). Again, the results reveal a positive influence of water on the outcome of the reaction, as the reaction in pure acetone yields 6 only in 63% (Entry 11).

A possible explanation for these observations is stabilization of the catalytic carbene intermediate through hydrogen bonding interactions with water. Catalyst 10 (Figure 4) developed by Zhang and co-workers is known to be superior to 9 in dichloromethane.\textsuperscript{48,49} However, in acetone/water the simpler complex 9 outperforms catalyst 10 (64%, d.r. = 79:21, TON = 255, Entry 12). The reactions using the apolar catalysts 9 and 10 probably do not take place in the aqueous phase. Phase separation of the catalyst into the organic substrate layer might well play a role in the observed rate enhancements. However, reactions in strongly concentrated solutions (organic solvents) typically lead to lower yields due to enhanced carbene dimerization and faster catalyst deactivation. Hence, water does have a true beneficial effect on these reactions. With these additional results, explaining the enhanced rates and higher TONs obtained with [2-Co@3] in acetone/water mixtures compared to pure acetone is not so straightforward and the effect of water on these reactions requires more research in the future. Such a detailed study of these water effects is beyond the scope of this chapter. So far, the optimal reaction conditions of [2-Co@3] are obtained by performing the reactions in acetone/water mixtures, using catalyst loadings of 0.25 mol%. Following the reaction over time revealed that [2-Co@3] is still active after the initial 1 hour reaction time. Using [2-Co@3] as catalyst for a prolonged reaction time of 24 h resulted in a higher TON of 292 and gave 73% yield of cyclopropane 6 (Entry 13). Reducing the temperature to 50 °C gave similar results, showing that the reaction can be performed under milder conditions (Entry 14, 76%, TON = 304).

With the above reaction conditions optimized for the caged-catalyst [2-Co@3] we explored the scope of suitable alkenes as substrates (Scheme 2). We started our investigations by studying a variety of styrene derivatives. Styrenes with electron donating groups gave the corresponding cyclopropanes in high yields (11, 75%, TON =
302, d.r. = 77:23; 12, 88%, TON = 351, d.r. = 76:24). Additionally, styrenes with electron withdrawing substituents also react smoothly, giving cyclopropanes 13 and 14 in good to high yields (13, 78%, TON = 320, d.r. = 82:18; 14, 66%, TON = 265, 80:20). 2-Vinylnaphtalene is also a suitable substrate leading to 15 in 69% yield (TON = 273), while sterically demanding cyclopropane 16 is only obtained in 18% yield (TON = 73). The lower yield could be an indication that it is more challenging to assemble both the bulky styrene and diazo compound 5 in the cavity of [2-Co@3]. Another reason might be substrate or product inhibition due to π-stacking, although [2-Co@3] still reaches a TON of 73.

\[ \text{Scheme 2: Substrate scope of alkenes suitable for [2-Co@3]-catalyzed cyclopropanation with 5.} \]
Cyclopropanation of other alkenes using catalyst [2-Co@3] was less successful. Using phenyl or methyl methacrylate as substrates gave 17 and 18 in moderate yields (17, 25%, TON = 100, d.r. = 82:18; 18, 20%, TON = 82, d.r. = 53:47). Unsubstituted acrylates like n-butyl acrylate reacted via a [3+2]-cycloaddition, yielding 1H-pyrazoles instead. Simple olefins like 1-octene and 3-phenyl-1-propene gave cyclopropanation products in low yields of 5% or less (see 19 and 20).

To further study the substrate scope, we focused on the use of various diazo compounds in the cyclopropanation of styrene 4 (Scheme 3). Benzyl diazoacetate gave cyclopropane 21 in 72% yield (TON = 287). This result is similar to ethyl diazoacetate 5 which gave 6 under the same conditions in 76% yield. However, using the bulky tert-butyldiazoacetate (27, R₁=H, R₂=t-Bu) resulted in the formation of 22 in only 22% (TON = 88). This is in agreement with the results described in Scheme 2 where the bulky 4-benzhydrylstyrene gave a low yield of 16 in comparison to other styrene derived substrates. Disubstituted diazo compounds (27, R₁≠H) seem to be unreactive when using [2-Co@3] as the catalyst.

![Scheme 3: Substrate scope of diazo compounds suitable for [2-Co@3]-catalyzed cyclopropanation of 4.](image)

Formation of rather bulky products such as 22 and 16 shows that the large cavity of [2-Co@3] is accessible for rather large substrates. However, the rather low yields obtained in these reactions also suggest that the cage should show size-selectivity. We investigated this aspect through a series of competition experiments between styrenes of different sizes (Table 2). Initially, we employed a 1:1 mixture of the substrates styrene 4 and 4-benzhydrylstyrene 24 (in total 2 equivalents) and 1 equivalent of ethyl diazoacetate 5, using the optimized reaction conditions described above.
An Encapsulated Catalyst for Size-Selective Cyclopropanation Reactions

Table 2: Competition experiments.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Styrene</th>
<th>Diazo</th>
<th>Products</th>
<th>Product ratio c:d</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>[2-Co@3]</td>
<td>4</td>
<td>24</td>
<td>5</td>
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<td>9</td>
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<td>6</td>
<td>9b</td>
<td>4</td>
<td>25</td>
<td>27</td>
<td>22</td>
</tr>
</tbody>
</table>

a) 0.25 mol% catalyst loading, 1.0 eq. 4, 1.0 eq. styrene 24 or 25, 1.0 eq. diazo compound 5 or 27, reaction time 24 h, 50°C, in acetone-d6/water 1:5. b) 0.5 mol% catalyst loading.
These experiments indeed show that [2-Co@3] acts as a size-selective catalyst, which clearly favors the formation of 6 over 16 (70:30; Table 2, entry 1). The reports described in Chapter 2, using different diazo substrates, showed that substrate activation takes place inside the cavity of these types of molecular flasks, thus leading to different selectivities compared to similar but non-encapsulated catalysts. In good agreement, the results described in this chapter show that encapsulated catalyst [2-Co@3] allows size-selective substrate transformations. This is most easily explained by a slower diffusion of larger substrates through the pores of the cage as compared to smaller substrates (Figure 5).

Figure 5: Schematic representation of the proposed pore-size controlled, size-selective transformations catalyzed by encapsulated catalyst [2-Co@3].

Partial and reversible opening of the supramolecular assembly cannot be fully excluded in the process of substrate binding and product release through the pores (e.g. involving reversible imine hydrolysis and/or bipyridine dissociation from the Fe corners). This would alter the pore-sizes of [2-Co@3] during catalysis, and hence might facilitate the entrance of larger substrates into the cage (and product release from the cage) leading to a lower size-selectivity than in the absence of reversible cage opening. Nevertheless, the pores of the molecular flask surrounding the cobalt catalyst in [2-Co@3] make it possible to distinguish between substrates of similar reactivity but different size. It is important to note that Co-TPP (9) is not able to distinguish between these sets of substrates at all (Table 2, Entries 4–6).
3.3 Conclusions

To develop a size-selective radical-type cyclopropanation reaction we described in this chapter the synthesis of a new molecularly encapsulated catalyst [2-Co@3]. The new supramolecular cage is still capable of encapsulated porphyrin complexes and is soluble in different solvents and solvent mixtures, including water/acetone. Employing water/acetone mixtures as the solvent increased the catalytic performance of [2-Co@3] in styrene cyclopropanation reactions dramatically. The caged catalyst [2-Co@3] shows a preference for cyclopropanation of styrenes over other vinylic substrates. While exploring the substrate scope, it became clear that [2-Co@3] is a size-selective catalyst showing preference for cyclopropanation of smaller styrene and diazo substrates. Bulkier substrates react slower than smaller ones, thus allowing size-selective competition reactions. To the best of our knowledge, [2-Co@3] is the first well-documented homogeneous catalyst capable of size-selective radical-type cyclopropanation reactions.

3.4 Experimental Section

3.4.1 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. Acetone-d6 was purchased from Euriso-Top without purification before use. Deionized water used was used without further purification. All other chemicals were purchased from Alfa Aesar, Acros, Fluka and Aldrich without purification before use. 1H-NMR, 13C-NMR and 19F-NMR spectra were measured on Mercury Varian 300MHz, Bruker 400 MHz or Bruker 500 MHz spectrometer. 1H NMR chemical shifts are given 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), Acetone-d$_6$ (2.05 ppm) Acetonitrile-d$_3$ (1.94 ppm)). 13C-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)). 19F-NMR chemical shifts are reported with respect to internal CFCl$_3$ (0.0 ppm). 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 (N₂), 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.

3.4.2 Synthesis of described compounds

Compounds 1, 15 [2-Zn@1], 15 [2-Co@1], 15 2-Zn, 50 2-Co, 51 7, 52 8, 52 10, 53 22, 54 31, 10 32, 55 7, 52 10, 53 22, 54 31, 10 32, 55 3 and 36 were synthesized as described in the literature.

Synthesis of supramolecular cubic M₈L₆ cage 3

To an oven-dried Schlenk flask under argon atmosphere were added zinc(II) tetrakis(4-aminophenyl)porphyrin (31) (65 mg, 87 μmol), Fe(N(Tf)₂)₂ (32) (72 mg, 117 μmol), 2,2'-bipyridine-5-carbaldehyde (33) (64.5 mg, 351 μmol) and DMF (5.0 mL). The mixture was degassed three times and heated for 16 h at 70 °C. The mixture was cooled to room temperature and diethyl ether was added. The mixture was filtered and washed with diethyl ether. The remaining solid was dissolved in DMF. The solvent was removed under reduced pressure to give 3 as a purple solid (188 mg, 14 μmol, 97 %). ¹H-NMR (400MHz, DMF-d₇): 9.34 (d, J = 8.5 Hz, 24H), 9.25 (d, J = 8.3 Hz, 24H), 9.05 (d, J = 8.1 Hz, 24H), 8.93 (m, 48H, H-11), 8.78 (d, J = 4.6 Hz, 24H), 8.66 (s, 24H), 8.55-8.47 (m, 24H), 8.29 (d, J = 8.6 Hz, 24H), 8.10 (d, J = 8.4 Hz, 24H), 7.91-780 (m, 48H), 7.60 (d, J = 8.3 Hz, 24H), 7.40 (m, 24H, J = 8.1 Hz, 24H); ¹³C-NMR (125MHz, DMF-d₇): 159.4, 158.7, 157.2, 155.1, 151.8, 150.0, 141.3, 139.5, 136.4, 136.1, 135.8, 135.5, 131.8, 128.7, 125.7, 124.1, 121.5, 120.4, 120.2, 119.0, 117.9, 116.4; ¹⁹F-NMR (282 MHz, DMF-d₇): -78.6; IR (neat): 2370, 2360, 1660, 1350, 1185, 1055, 450, 410 cm⁻¹; Exact mass ESI-MS: See Table 3.
Table 3: Exact mass ESI-MS signals of cubic cage 3.

<table>
<thead>
<tr>
<th>Peak m/z</th>
<th>Simulated m/z</th>
<th>Identified as</th>
<th>Identified as</th>
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<td>609.5933</td>
<td>609.5930</td>
<td>[(C$<em>{528}$H$</em>{336}$N$<em>{96}$Zn$</em>{6}$Fe$_{8}$)(N(SO$_2$CF$_3$)$_2$)$_2$]$^{14+}$</td>
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<td>673.1295</td>
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<td>[M-$8^*$ (N(SO$_2$CF$_3$)$_2$)]$^{7+}$</td>
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</table>

Synthesis of supramolecular host-guest complex [2-Zn@3]

To an oven dried Schlenk flask under an argon atmosphere were added 2-Zn (2 mg, 3 µmol), 3 (40 mg, 3 µmol) and DMF (2 mL). The mixture was degassed three times and heated for 16 h at 70 °C. The mixture was cooled to room temperature and diethyl ether was added. The mixture was filtered and washed with diethyl ether. The remaining solid was dissolved in DMF. The solvent was removed under reduced pressure to give [2-Zn@3] as a purple solid (30.8 mg, 2.3 µmol, 70 %).

$^1$H-NMR (400MHz, DMF-d$_7$): 9.70 – 9.35 (m, 45H), 9.34 – 8.85 (m, 102 H), 8.84 – 8.64 (m, 42H) 8.63 – 8.23 (m, 42H), 8.22 – 7.98 (m, 61H), 7.97 – 7.28 (m, 44H), 6.41 (s, 8H), 5.80 (s, 8H)
2.88 (s, 8H); $^{19}$F-NMR (282 MHz, DMF-d$_7$): -78.5; IR (neat): 2360, 2325, 2105, 2000, 1345, 1185, 1055, 790, 490, 415 cm$^{-1}$; Exact mass ESI-MS: See Table S2.

Table 4: Exact mass ESI-MS signals of host-guest complex [2-Zn@3].

<table>
<thead>
<tr>
<th>Peak m/z</th>
<th>Simulated m/z</th>
<th>Identified as</th>
<th>Identified as</th>
</tr>
</thead>
<tbody>
<tr>
<td>888.8997</td>
<td>888.8991</td>
<td>$<a href="%5Ctext%7BC%7D_%7B40%7D%5Ctext%7BH%7D_%7B24%7D%5Ctext%7BZnN%7D_%7B8%7D">\text{C}<em>{88}\text{H}</em>{56}\text{N}<em>{16}\text{Zn},\text{Fe}</em>{8}</a>$(\text{CF}_3\text{SO}<em>3)</em>{12}$</td>
<td>$[\text{M}-12^{+}(\text{CF}_3\text{SO}_3)]^{12^{+}}$</td>
</tr>
<tr>
<td>995.1540</td>
<td>995.1552</td>
<td>$<a href="%5Ctext%7BC%7D_%7B40%7D%5Ctext%7BH%7D_%7B24%7D%5Ctext%7BZnN%7D_%7B8%7D">\text{C}<em>{88}\text{H}</em>{56}\text{N}<em>{16}\text{Zn},\text{Fe}</em>{8}</a>$(\text{CF}_3\text{SO}<em>3)</em>{11}$</td>
<td>$[\text{M}-11^{+}(\text{CF}_3\text{SO}_3)]^{11^{+}}$</td>
</tr>
<tr>
<td>1122.6608</td>
<td>1122.6625</td>
<td>$<a href="%5Ctext%7BC%7D_%7B40%7D%5Ctext%7BH%7D_%7B24%7D%5Ctext%7BZnN%7D_%7B8%7D">\text{C}<em>{88}\text{H}</em>{56}\text{N}<em>{16}\text{Zn},\text{Fe}</em>{8}</a>$(\text{CF}_3\text{SO}<em>3)</em>{10}$</td>
<td>$[\text{M}-10^{+}(\text{CF}_3\text{SO}_3)]^{10^{+}}$</td>
</tr>
<tr>
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<td>1278.5047</td>
<td>$<a href="%5Ctext%7BC%7D_%7B40%7D%5Ctext%7BH%7D_%7B24%7D%5Ctext%7BZnN%7D_%7B8%7D">\text{C}<em>{88}\text{H}</em>{56}\text{N}<em>{16}\text{Zn},\text{Fe}</em>{8}</a>$(\text{CF}_3\text{SO}<em>3)</em>{9}$</td>
<td>$[\text{M}-9^{+}(\text{CF}_3\text{SO}_3)]^{9^{+}}$</td>
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<tr>
<td>1473.4315</td>
<td>1473.4325</td>
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<td>$[\text{M}-8^{+}(\text{CF}_3\text{SO}_3)]^{8^{+}}$</td>
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<td>1723.9111</td>
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<td>$[\text{M}-7^{+}(\text{CF}_3\text{SO}_3)]^{7^{+}}$</td>
</tr>
</tbody>
</table>

Synthesis of supramolecular host-guest complex [2-Co@3]

To an oven dried Schlenk flask under an argon atmosphere were added 2-Co (10.7 mg, 16 µmol), 3 (214 mg, 16 µmol) and DMF (11 mL). The mixture was degassed three times and heated for 16 h at 70 °C. The mixture was cooled to room temperature and diethyl ether was added. The mixture was filtered and washed with diethyl ether. The remaining solid was dissolved in DMF. The solvent was removed under reduced pressure to give [2-Co@3] as a purple solid (184 mg, 13.8 µmol, 86 %). IR (neat): 2365, 2360, 2010, 1660, 1345, 1180, 1050, 790, 405 cm$^{-1}$; Exact mass ESI-MS: see Table 5.
Table 5: Exact mass ESI-MS signals of host-guest complex [2-Co@3].

<table>
<thead>
<tr>
<th>Peak m/z</th>
<th>Simulated m/z</th>
<th>Identified as</th>
<th>Identified as</th>
</tr>
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<td>([\text{M}-15*(\text{N(SO}<em>{2}\text{CF}</em>{3})_{2})]^{15})</td>
</tr>
<tr>
<td>721.5004</td>
<td>721.4972</td>
<td>([\text{C}<em>{528}\text{H}</em>{336}\text{N}<em>{96}\text{Zn}</em>{6}\text{Fe}<em>{8}\text{CoN}</em>{8}]) ((\text{N(SO}<em>{2}\text{CF}</em>{3})<em>{2})</em>{4}) (^{14})</td>
<td>([\text{M}-14*(\text{N(SO}<em>{2}\text{CF}</em>{3})_{2})]^{14})</td>
</tr>
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<td>798.4548</td>
<td>798.4521</td>
<td>([\text{C}<em>{528}\text{H}</em>{336}\text{N}<em>{96}\text{Zn}</em>{6}\text{Fe}<em>{8}\text{CoN}</em>{8}]) ((\text{N(SO}<em>{2}\text{CF}</em>{3})<em>{2})</em>{3}) (^{13})</td>
<td>([\text{M}-13*(\text{N(SO}<em>{2}\text{CF}</em>{3})_{2})]^{13})</td>
</tr>
<tr>
<td>888.4020</td>
<td>888.3997</td>
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<td>([\text{M}-12*(\text{N(SO}<em>{2}\text{CF}</em>{3})_{2})]^{12})</td>
</tr>
<tr>
<td>994.5210</td>
<td>994.5194</td>
<td>([\text{C}<em>{528}\text{H}</em>{336}\text{N}<em>{96}\text{Zn}</em>{6}\text{Fe}<em>{8}\text{CoN}</em>{8}]) ((\text{N(SO}<em>{2}\text{CF}</em>{3})<em>{2})</em>{1}) (^{11})</td>
<td>([\text{M}-11*(\text{N(SO}<em>{2}\text{CF}</em>{3})_{2})]^{11})</td>
</tr>
<tr>
<td>1122.0638</td>
<td>1122.0631</td>
<td>([\text{C}<em>{528}\text{H}</em>{336}\text{N}<em>{96}\text{Zn}</em>{6}\text{Fe}<em>{8}\text{CoN}</em>{8}]) ((\text{N(SO}<em>{2}\text{CF}</em>{3})<em>{2})</em>{1}) (^{10})</td>
<td>([\text{M}-10*(\text{N(SO}<em>{2}\text{CF}</em>{3})_{2})]^{10})</td>
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<tr>
<td>1277.8381</td>
<td>1277.8388</td>
<td>([\text{C}<em>{528}\text{H}</em>{336}\text{N}<em>{96}\text{Zn}</em>{6}\text{Fe}<em>{8}\text{CoN}</em>{8}]) ((\text{N(SO}<em>{2}\text{CF}</em>{3})<em>{2})</em>{1}) (^{9})</td>
<td>([\text{M}-9*(\text{N(SO}<em>{2}\text{CF}</em>{3})_{2})]^{9})</td>
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<td>1472.8096</td>
<td>1472.8080</td>
<td>([\text{C}<em>{528}\text{H}</em>{336}\text{N}<em>{96}\text{Zn}</em>{6}\text{Fe}<em>{8}\text{CoN}</em>{8}]) ((\text{N(SO}<em>{2}\text{CF}</em>{3})<em>{2})</em>{1}) (^{8})</td>
<td>([\text{M}-8*(\text{N(SO}<em>{2}\text{CF}</em>{3})_{2})]^{8})</td>
</tr>
</tbody>
</table>

General procedure for the catalytic cyclopropanation experiments

To an oven dried Schlenk flask was added [2-Co@3] (0.0025 eq.), acetone-d<sub>6</sub> (0.5 mL/mmol alkene) and water (2.5 mL/mmol alkene). Argon was bubbled 3 min through the reaction mixture. The alkene (1.0 eq.) and diazo compound (1.0 eq.) were added and the reaction mixture was stirred for 24 h at 50 °C. The mixture was cooled to room temperature and acetone was added. The solvents were removed under reduced pressure and the crude product was purified by column chromatography.
Synthesis of ethyl 2-phenylcyclopropanecarboxylate (6)

\[
\begin{align*}
\text{[2-Co@3]} & \quad (0.25 \text{ mol-%}) \\
\text{Water/acetone-}d_6 & \quad 5:1, \\
& \quad 50^\circ\text{C}, 24\text{h}
\end{align*}
\]

[2-Co@3] (35 mg, 2.5 µmol), acetone-\(d_6\) (0.5 mL), water (2.5 mL), 4 (104 mg, 1.0 mmol) and 5 (114 mg 1.0 mmol) were handled according to the general procedure for the catalytic cyclopropanation experiments to give 6 (145 mg, 760 µmol, 76%, d.r. (trans:cis) = 66:34). Data for cyclopropane 6 were in agreement with published data.\(^{57}\)

Synthesis of ethyl 2-(4-methoxyphenyl)cyclopropanecarboxylate (11)

\[
\begin{align*}
\text{MeO-} & \quad + \\
\text{[2-Co@3]} & \quad (0.25 \text{ mol-%}) \\
\text{Water/acetone-}d_6 & \quad 5:1, \\
& \quad 50^\circ\text{C}, 24\text{h}
\end{align*}
\]

[2-Co@3] (17.5 mg, 1.25 µmol), acetone-\(d_6\) (0.25 mL), water (1.25 mL), 34 (67 mg, 500 µmol) and 5 (57 mg, 500 µmol) were handled according to the general procedure for the catalytic cyclopropanation experiments to give 11 (83 mg, 377 µmol, 75%, d.r. (trans:cis) = 77:23). Data for cyclopropane 11 were in agreement with published data.\(^{58,59}\)

Synthesis of ethyl 2-(4-methylphenyl)cyclopropanecarboxylate (12)

\[
\begin{align*}
\text{[2-Co@3]} & \quad (0.25 \text{ mol-%}) \\
\text{Water/acetone-}d_6 & \quad 5:1, \\
& \quad 50^\circ\text{C}, 24\text{h}
\end{align*}
\]

[2-Co@3] (17.5 mg, 1.25 µmol), acetone-\(d_6\) (0.25 mL), water (1.25 mL), 35 (67 mg, 570 µmol) and 5 (57 mg, 500 µmol) were handled according to the general procedure for the catalytic cyclopropanation experiments to give 12 (90 mg, 440 µmol, 88%, d.r. (trans:cis) = 76:24). Data for cyclopropane 12 were in agreement with published data.\(^{60}\)
Synthesis of 4-(2-(ethoxycarbonyl)cyclopropyl)benzoic acid (13)

\[
\text{MeO}_2\text{C} - \text{C} - \text{MeO}_2\text{C} + \begin{array}{c}
\text{N}_2 \\
\text{Et}
\end{array} \xrightarrow{\text{[2-Co@3] (0.25 mol-%)}} \text{CO}_2\text{Et}
\]

[2-Co@3] (17.5 mg, 1.25 µmol), acetone-d₆ (0.25 mL), water (1.25 mL), 36 (81 mg, 500 µmol) and 5 (57 mg, 500 µmol) were handled according to the general procedure for the catalytic cyclopropanation experiments to give 13 as a white solid (97 mg, 390 µmol, 78%, d.r. (trans:cis) = 82:18). \textit{trans}-13: ¹H-NMR (300MHz, CDCl₃): 7.97-7.91 (m, 2H), 7.17-7.10 (m, 2H), 4.17 (q, \(J = 7.2\) Hz, 2H), 3.90 (s, 3H), 2.55 (ddd, \(J = 9.1\) Hz, \(J = 6.4\) Hz, \(J = 4.1\) Hz, 1H), 1.96 (ddd, \(J = 8.5\) Hz, \(J = 5.5\) Hz, \(J = 4.1\) Hz, 1H), 1.66 (ddd, \(J = 9.2\) Hz, \(J = 5.5\) Hz, \(J = 4.6\) Hz, 1H), 1.35 (ddd, \(J = 8.5\) Hz, \(J = 6.4\) Hz, \(J = 4.7\) Hz, 1H), 1.28 (q, \(J = 7.2\) Hz, 3H); ¹³C-NMR (75 MHz, CDCl₃): 173.1, 167.0, 145.8, 130.0, 128.5, 126.2, 61.0, 52.2, 26.2, 24.9, 17.7, 14.4; \(R_f = 0.50\) (CH:EE = 90:10); IR (neat): 2985, 2360, 2340, 1720, 1610, 1220, 1190, 1180, 1110, 1085, 855, 770, 430; cm⁻¹; Exact mass ESI-MS: C₁₄H₁₄O₄Na calculated: 271.0946 found: 271.0945. Data for \textit{cis}-13 were in agreement with published data.⁶¹

Synthesis of ethyl 2-(4-fluorophenyl)cyclopropanecarboxylate 14

\[
\text{F} - \text{C} - \text{F} + \begin{array}{c}
\text{N}_2 \\
\text{Et}
\end{array} \xrightarrow{\text{[2-Co@3] (0.25 mol-%)}} \text{CO}_2\text{Et}
\]

[2-Co@3] (17.5 mg, 1.25 µmol), acetone-d₆ (0.25 mL), water (1.25 mL), 37 (61 mg, 500 µmol) and 5 (57 mg, 500 µmol) were handled according to the general procedure for the catalytic cyclopropanation experiments to give 14 (69 mg, 331 µmol, 66%, d.r. (trans:cis) = 80:20). Data for cyclopropane 14 were in agreement with published data.⁶⁰
Synthesis of ethyl 2-(naphthalen-2-yl)cyclopropanecarboxylate (15)

\[ \text{[2-Co@3] (17.5 mg, 1.25 µmol), acetone-d}_6 (0.25 mL), \text{ water (1.25 mL), 38 (67 mg, 500 µmol) and 5 (57 mg, 500 µmol) were handled according to the general procedure for the catalytic cyclopropanation experiments to give 15 (82 mg, 340 µmol, 69%, d.r. (trans:cis) = 77:23). Data for cyclopropane 15 were in agreement with published data}^{59,60} \]

Synthesis of ethyl 2-(4-benzhydrylphenyl)cyclopropanecarboxylate (16)

\[ \text{[2-Co@3] (17.5 mg, 1.25 µmol), acetone-d}_6 (0.25 mL), \text{ water (1.25 mL), 24 (135 mg, 500 µmol) and 5 (57 mg, 500 µmol) were handled according to the general procedure for the catalytic cyclopropanation experiments to give 16 (33 mg, 90 µmol, 18%, d.r. (trans:cis) = 67:33). trans-16: } ^1\text{H-NMR (300MHz, CDCl}_3\text{): 7.32-6.98 (m, 14H), 5.51 (s, 1H), 4.16 (q, } J = 7.1 \text{ Hz, 2H), 2.48 (ddd, } J = 9.2 \text{ Hz, } J = 6.5 \text{ Hz, } J = 4.1 \text{ Hz, 1H), 1.87 (ddd, } J = 8.4 \text{ Hz, } J = 5.3 \text{ Hz, } J = 4.1 \text{ Hz, 1H), 1.63-1.54 \text{ (m, 1H), 1.32-1.23 (m, 1H), 1.27 (t, } J = 7.1 \text{ Hz, 3H); } ^1\text{C-NMR (75MHz, CDCl}_3\text{): 173.6, 144.0, 142.4, 138.3, 129.7, 129.5, 128.5, 126.5, 126.2, 60.8, 56.6, 26.1, 24.4, 17.2, 14.4; } R_F = 0.69 \text{ (CH:EE = 90:10); cis-16: } ^1\text{H-NMR (300MHz, CDCl}_3\text{): 7.44-6.75 (m, 14H), 5.50 (s, 1H), 3.86 (qd, } J = 7.1 \text{ Hz, } J = 2.0 \text{ Hz, 2H), 2.54 (q, } J = 8.6 \text{ Hz, 1H), 2.05 (ddd, } J = 9.4 \text{ Hz, } J = 7.7 \text{ Hz, } J = 5.6 \text{ Hz, 1H), 1.69 (dt, } J = 7.4 \text{ Hz, } J = 5.4 \text{ Hz, 1H); 13C-NMR (75MHz, CDCl}_3\text{): 171.1, 144.1, 142.4, 134.7, 129.6, 129.3, 129.1, 128.4, 126.4, 60.3, 56.7, 25.2, 22.1, 14.2, 11.2; } R_F = 0.59 \text{ (CH:EA = 90:10); IR (neat): 3085, 2925, 1720, 1175, 1015, 700, 605, 530; cm}^1; \text{ Exact mass ESI-MS: } C_{25}H_{24}O_2Na \text{ calculated: 379.1674 found: 379.1680.} \]
An Encapsulated Catalyst for Size-Selective Cyclopropanation Reactions

Synthesis of 2-ethyl 1-phenyl 1-methylcyclopropane-1,2-dicarboxylate (17)

\[
\begin{align*}
\text{PhO}_2\text{C} & \quad + \quad \begin{array}{c}
\text{O} \\
\text{Et}
\end{array} \\
\text{N}_2 & \quad \xrightarrow{[2-\text{Co@3} \text{ (0.25 mol-%)}]} \\
\text{PhO}_2\text{C} & \quad \text{CO}_2\text{Et}
\end{align*}
\]

[2-Co@3] (17.5 mg, 1.25 µmol), acetone-d₆ (0.25 mL), water (1.25 mL), 39 (81.1 mg, 500 µmol) and 5 (58.0 mg, 508 µmol) were handled according to the general procedure for the catalytic cyclopropanation experiments to give 17 (36.8 mg, 148 µmol, 29%, d.r. (trans:cis) = 82:18).

trans-17: ¹H-NMR (300MHz, CDCl₃): 7.44-7.32 (m, 2H), 7.28-7.18 (m, 1H), 7.01-7.14 (m, 1H), 4.21 (q, J = 7.2 Hz), 2.52 (dd, J = 8.8 Hz, J = 6.6 Hz, 1H), 1.76 (dd, J = 8.8 Hz, J = 4.4 Hz, 1H), 1.54 (s, 3H), 1.48 (dd, J = 6.6 Hz, J = 4.4 Hz), 1.31 (t, J = 7.1 Hz); ¹³C-NMR (75MHz, CDCl₃): 172.4, 170.3, 150.9, 129.5, 126.0, 121.5, 61.2, 28.4, 27.2, 21.5, 14.4, 13.3. Cis-17: ¹H-NMR (300MHz, CDCl₃): 7.44-7.32 (m, 2H), 7.28-7.18 (m, 1H), 7.01-7.14 (m, 2H), 4.15 (dq, J = 7.2 Hz, J = 1.3 Hz, 2H), 1.99-1.89 (m, 1H), 1.75-1.70 (m, 1H), 1.55 (s, 3H), 1.19 (dd, J = 7.1 Hz, J = 3.6 Hz). ¹³C-NMR (75MHz, CDCl₃): 170.6, 170.3, 151.0, 129.5, 125.9, 121.6, 61.2, 29.1, 21.3, 20.0, 14.3, 13.3; Rₘ = 0.58 (CH:EA = 90:10); IR (EA): 3011, 2926, 2900, 1777, 1768, 1064, 937, 926, 911, 656, 633, 513, 493 cm⁻¹. Exact mass ESI-MS: C₁₄H₁₆O₄Na calculated: 271.0946 found: 271.0966.

Synthesis of 2-ethyl 1-methyl 1-methylcyclopropane-1,2-dicarboxylate (18)

\[
\begin{align*}
\text{MeO}_2\text{C} & \quad + \quad \begin{array}{c}
\text{O} \\
\text{Et}
\end{array} \\
\text{N}_2 & \quad \xrightarrow{[2-\text{Co@3} \text{ (0.25 mol-%)}]} \\
\text{MeO}_2\text{C} & \quad \text{CO}_2\text{Et}
\end{align*}
\]

[2-Co@3] (17.5 mg, 1.25 µmol), acetone-d₆ (0.25 mL), water (1.25 mL), 40 (50.1 mg, 500 µmol) and 5 (60 mg, 526 µmol) were handled according to the general procedure for the catalytic cyclopropanation experiments to give 18 (19.0 mg, 102 µmol, 20%, d.r. (trans:cis) = 53:47). Data for cyclopropane 18 were in agreement with published data.¹⁷
Synthesis of ethyl 2-hexylcyclopropanecarboxylate (19)

\[
\text{Hex} + \text{5} \xrightarrow{[\text{2-Co@3} \ (0.25 \text{ mol-\%})]} \text{CO}_2\text{Et} \quad \text{Water/acetone-}\text{d}_6 \ 5:1, \ 50^\circ\text{C, 24h}
\]

[2-Co@3] (17.5 mg, 1.25 µmol), acetone-d_6 (0.25 mL), water (1.25 mL), 41 (56.1 mg, 500 µmol) and 5 (57.3 mg, 502 µmol) were handled according to the general procedure for the catalytic cyclopropanation experiments to give 19 (4.9 mg, 24.7 µmol, 5%, d.r. (trans:cis) = 82:18). Data for cyclopropane 19 were in agreement with published data.\(^{62}\)

Synthesis of ethyl 2-benzylcyclopropanecarboxylate (20)

\[
\text{Ph} + \text{5} \xrightarrow{[\text{2-Co@3} \ (0.25 \text{ mol-\%})]} \text{CO}_2\text{Et} \quad \text{Water/acetone-}\text{d}_6 \ 5:1, \ 50^\circ\text{C, 24h}
\]

[2-Co@3] (17.5 mg, 1.25 µmol), acetone-d_6 (0.25 mL), water (1.25 mL), 42 (59 mg, 500 µmol) and 5 (57 mg 500 µmol) were handled according to the general procedure for the catalytic cyclopropanation experiments to yield trace amounts of 20.\(^{63}\)

Synthesis of benzyl 2-phenylcyclopropanecarboxylate (21)

\[
\text{4} + \text{43} \xrightarrow{[\text{2-Co@3} \ (0.25 \text{ mol-\%})]} \text{CO}_2\text{Bn} \quad \text{Water/acetone-}\text{d}_6 \ 5:1, \ 50^\circ\text{C, 24h}
\]

[2-Co@3] (17.5 mg, 1.25 µmol), acetone-d_6 (0.25 mL), water (1.25 mL), 4 (52 mg, 500 µmol) and 43 (88 mg 500 µmol) were handled according to the general procedure for the catalytic cyclopropanation experiments to give 21 (90.3 mg, 358 µmol, 72%, d.r. (trans:cis) = 65:35). Data for cyclopropane 21 were in agreement with published data.\(^{64}\)
Synthesis of tert-butyl 2-phenylcyclopropanecarboxylate (22)

\[
\text{4} + \text{44} \xrightarrow{[2-\text{Co@3}] (0.25 \text{ mol-\%})} \text{22}
\]

[2-Co@3] (17.5 mg, 1.25 µmol), acetone-d₆ (0.25 mL), water (1.25 mL), 4 (52 mg, 500 µmol) and 44 (71 mg 500 µmol) were handled according to the general procedure for the catalytic cyclopropanation experiments to give 22 (24.2 mg, 111 µmol, 22%, d.r. (trans:cis) = 76:24). Data for cyclopropane 22 were in agreement with published data.⁵⁵

Synthesis of dimethyl 2-phenylcyclopropane-1,1-dicarboxylate (23)

\[
\text{4} + \text{45} \xrightarrow{[2-\text{Co@3}] (0.25 \text{ mol-\%})} \text{23}
\]

[2-Co@3] (17.5 mg, 1.25 µmol), acetone-d₆ (0.25 mL), water (1.25 mL), 4 (52 mg, 499 µmol) and 5 (57 mg, 500 µmol) were handled according to the general procedure for the catalytic cyclopropanation experiments. No conversion of the substrates was observed.

Competition experiment between styrene derivatives 4 and 24

To an oven dried Schlenk flask were added [2-Co@3] (17.5 mg, 1.25 µmol), acetone-d₆ (0.25 mL) and water (1.25 mL). Argon was bubbled 3 min through the reaction mixture. Styrene 4 (52 mg, 500 µmol), 4-benzhydrylstyrene 24 (135 mg, 500 µmol) and ethyldiazoacetate 5 (57 mg, 500 µmol) were added and the reaction mixture was stirred for 24 h at 50 °C. The mixture was cooled to room temperature and acetone was added. The solvents were removed under reduced pressure and the crude product was analyzed by ¹H-NMR to yield the products (6:13) in a ratio of 70:30.
Co-TPP (9, 0.5 mg, 0.74 µmol, 0.26 mol%) was added to a dried schlenk flask and dissolved in acetone-d<sub>6</sub>/water (1:5, total volume 0.9 mL). To the stirred solution was added 4-benzhydrylstyrene 24 (79 mg; 0.29 mmol), styrene 4 (30 mg, 0.29 mmol) and ethyldiazoacetate 5 (33 mg, 0.29 mmol). Nitrogen was bubbled through the solution for 3 minutes and the mixture was placed in an oil bath at 50 °C for 24 h. After cooling the mixture to room temperature the products were collected with acetone (10 mL). The solvents and volatile starting materials were removed at reduced pressure and the product mixture was analyzed by ¹H-NMR (CDCl<sub>3</sub>) to yield the products (16:6) in a ratio of 50:50.

**Competition experiment between styrene derivatives 4 and 25**

2-Co@3 (17.5 mg, 1.25 µmol, 0.25 mol%) was added to a dried schlenk flask and dissolved in acetone-d<sub>6</sub>/water (1:5, total volume 1.5 mL). To the stirred solution was added 3,5-di-tert-butylstyrene 25 (108 mg; 0.5 mmol), styrene 4 (52 mg, 0.5 mmol) and ethyldiazoacetate 5 (57 mg, 0.5 mmol). Nitrogen was bubbled through the solution for 3 minutes and the mixture was placed in an oil bath at 50 °C for 24 h. After cooling the mixture to room temperature the products were collected with acetone (10 mL). The solvents and volatile starting materials were removed at reduced pressure and the product mixture was analyzed by ¹H-NMR (CDCl<sub>3</sub>) to yield the products (26:6) in a ratio of 36:64.

Co-TPP (9, 0.8 mg, 1.25 µmol, 0.25 mol%) was added to a dried schlenk flask and dissolved in acetone-d<sub>6</sub>/water (1:5, total volume 1.5 mL). To the stirred solution was added 3,5-di-tert-butylstyrene 25 (108 mg; 0.5 mmol), styrene 4 (52 mg, 0.5 mmol) and ethyldiazoacetate 5 (57 mg, 0.5 mmol). Nitrogen was bubbled through the solution for 3 minutes and the mixture was placed in an oil bath at 50 °C for 24 h. After cooling the mixture to room temperature the products were collected with acetone (10 mL). The solvents and volatile starting materials were removed at reduced pressure and the product mixture was analyzed by ¹H-NMR (CDCl<sub>3</sub>) to yield the products (26:6) in a ratio of 51:49.
trans-26: ¹H-NMR (300MHz, CDCl₃): 7.28 (t, J = 1.8 Hz, 1H), 6.93 (d, J = 1.8 Hz, 2H), 4.18 (q, J = 7.1 Hz, 2H), 2.55-2.48 (m, 1H), 1.97-1.89 (m, 1H), 1.64-1.55 (m, 1H), 1.41-1.30 (m, 1H), 1.31 (s, 18H), 1.28 (t, J = 7.2 Hz, 3H); ¹³C-NMR (75MHz, CDCl₃): 173.7, 151.0, 139.2, 120.9, 120.3, 60.8, 35.0, 31.6, 26.9, 24.4, 17.5, 14.4; cis-26: ¹H-NMR (300MHz, CDCl₃): 7.25 (t, J = 1.7 Hz, 1H), 6.93 (d, J = 1.5 Hz, 2H), 3.83 (q, J = 7.1 Hz, 2H), 2.52-2.64 (m, 1H), 3.10-2.01 (m, 1H), 1.73-1.65 (m, 1H), 1.41-1.30 (m, 1H), 1.30 (s, 18H), 0.87 (d, J = 7.1 Hz, 3H); ¹³C-NMR (75MHz, CDCl₃): 171.3, 150.2, 136.0, 123.7, 120.6, 60.1, 34.9, 31.6, 26.1, 21.9, 14.0, 11.4; R₉ = 0.57 (CH:EA = 90:10); Exact mass ESI-MS: C₂₀H₃₀O₂H calculated: 303.2324 found: 303.2347.

2-Co@3 (35.0 mg, 2.5 µmol, 0.50 mol%) was added to a dried schlenk flask and dissolved in acetone-d₆/water (1:5, total volume 1.5 mL). To the stirred solution was added 3,5-di-tert-butylstyrene 25 (108 mg; 0.5 mmol), styrene 4 (52 mg, 0.5 mmol) and tert-butyl diazoacetate 27 (71 mg, 0.5 mmol). Nitrogen was bubbled through the solution for 3 minutes and the mixture was placed in an oil bath at 50 °C for 24 h. After cooling the mixture to room temperature the products were collected with acetone (10 mL). The solvents and volatile starting materials were removed at reduced pressure and the product mixture was analyzed by ¹H-NMR (CDCl₃) to yield the products (28:22) in a ratio of 21:79.

Co-TPP (9, 1.6 mg, 2.4 µmol, 0.54 mol%) was added to a dried schlenk flask and dissolved in acetone-d₆/water (1:5, total volume 1.5 mL). To the stirred solution was added 3,5-di-tert-butylstyrene 25 (95 mg; 0.44 mmol), styrene 4 (46 mg, 0.44 mmol) and tert-butyl diazoacetate 27 (55 mg, 0.38 mmol). Nitrogen was bubbled through the solution for 3 minutes and the mixture was placed in an oil bath at 50 °C for 24 h. After cooling the mixture to room temperature the products were collected with acetone (10 mL). The solvents and volatile starting materials were removed at reduced pressure and the product mixture was analyzed by ¹H-NMR (CDCl₃) to yield the products (28:22) in a ratio of 51:49.
trans-28: $^1$H-NMR (300MHz, CDCl$_3$): 7.22 (t, $J = 1.6$ Hz, 1H), 6.87 (d, $J = 1.6$ Hz, 2H), 2.38 (ddd, $J = 9.0$ Hz, 6.4 Hz, 4.1 Hz, 1H), 1.86-1.78 (m, 1H), 1.52-1.45 (m, 1H), 1.42 (s, 9H), 1.26 (s, 18H), 1.25-1.14 (m, 1H); $^{13}$C-NMR (75MHz, CDCl$_3$): 172.9, 151.0, 139.6, 120.7, 120.1, 80.6, 35.0, 31.6, 28.3, 26.5, 25.6, 17.6; cis-28: $^1$H-NMR (300MHz, CDCl$_3$): 7.21 (s, 1H), 7.07 (s, 2H), 2.48 (q, $J = 8.6$ Hz, 1H), 1.91 (ddd, $J = 9.4$, 7.6, 5.5 Hz, 1H), 1.60 (dt, $J = 7.3$, 5.2 Hz, 1H), 1.26 (s, 18H), 1.25-1.14 (m, 1H), 1.01 (s, 9H); $^{13}$C-NMR (75MHz, CDCl$_3$): 170.5, 150.1, 135.9, 123.7, 120.8, 79.8, 34.9, 31.6, 27.9, 25.7, 23.0, 10.7. $R_F = 0.74$ (CH:EA = 90:10). Exact mass ESI-MS: $^{22}$C$_{24}$H$_{34}$O$_2$Na calculated: 353.2456 found: 353.2441.

### 3.5 Acknowledgements

Matthias Otte is gratefully acknowledged for the collaboration on the project described in this chapter. M. Otte prepared and analyzed the new supramolecular cage 3. Both M. Otte and P. Kuijpers performed the catalyst optimisation and exploration of the substrate scope. P. Kuijpers performed the direct competition experiments. Financial support from the Netherlands Organization for Scientific Research (NWO-CW VICI project 016.122.613) is acknowledged. Oliver Troepner is thanked for the ESI-MS analysis of the cages described in this chapter. Henk Kleijn is acknowledged for technical support on the analysis of cyclopropane products.
3.6 References