Supramolecular encapsulation of a rhodium hydroformylation catalyst: a mechanistic study
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CHAPTER 5

Supramolecular Encapsulation and Selectivity in Hydroformylation of Internal Alkenes

Abstract. Herein we report mechanistic studies of a rhodium hydroformylation catalyst, encapsulated using the ligand-template strategy developed previously in our group (Angew. Chem. Int. Ed. 2001, J. Am. Chem. Soc. 2004). We address the origin of the curious selectivity in hydroformylation of linear internal alkenes, which are transformed without isomerisation into branched aldehydes. Using combined experimental (gas-uptake kinetics, catalysis using isotopically labelled gas, in situ FT-IR spectroscopy) and computational (DFT of the catalytic cycle followed by the simulation of catalysis kinetics) approach, we found that the rate-limiting processes depend greatly on the reaction conditions. The selectivity of the catalyst is determined in the hydride migration, where the transition state energies towards the minor aldehyde product are raised more than those towards the major aldehyde; this is due to the energies for the capsule reorganisation required to accommodate the corresponding transition states. Thus, the capsule rearrangement energy, which is higher for one product than for the other, is the crucial energy contribution that ultimately leads to the observed selectivity.

5.1. Introduction

Reactions occurring in confined spaces within biological systems, i.e. in binding pockets of enzymes, proceed with excellent selectivity and very high rates. Reactions of similar efficiency within synthetic confined spaces and capsules are scarce. There are, however, several examples where the application of synthetic supramolecular capsules as nano-reactors has led to high reaction rates and previously inaccessible selectivities. In 2007, Raymond and co-workers reported a supramolecular capsule whose inner space caused a $pK_a$ shift leading to easy protonation of a reaction intermediate as compared to the reaction medium, thereby enabling an acid catalysed reaction in a basic aqueous solution. Other research groups have reported acceleration of a Diels-Alder reaction within a spherical supramolecular capsule, and within an octahedral metal-ligand assembly. Besides accelerating the reaction, unusual product distributions were observed when reactions were taking place in these confined spaces.

In our group, a ligand-templated strategy for the encapsulation of transition metal catalysts was developed. Encapsulation of a rhodium hydroformylation catalyst using this approach led to a more than tenfold increase of activity and high selectivities in transformation of terminal alkenes. Also in hydroformylation of very difficult, non-functionalised linear internal alkenes (Fig. 5.1.1), high activities and selectivities were observed, with the hydroformylation of 2-alkenes resulting mainly in the C3-aldehyde. A detailed review with more examples of catalysis in confined spaces has been published recently. In some of the examples described above and in the mentioned review, the mechanism of the reaction and the role of
5. SELECTIVITY AND THE ROLE OF THE CAPSULE – MECHANISM

Figure 5.1.1. Assembly of the supramolecular capsule, and formation of the rhodium hydroformylation catalyst with unusual transformation of trans-2-octene mainly to the 3-aldehyde (P3).

the capsule in it is well understood. For instance, the steric conditions inside the octahedral (by Fujita) or spherical (by Rebek) capsules allow only one orientation of the reactants relative to one another, leading to unusual selectivities in the Diels-Alder reactions within these capsules.\(^1\)\(^2\)\(^4\)\(^5\) However, in most other examples the role of the (supramolecular) capsule is not, or only partly understood.

It is of fundamental interest, and importance to the field, to understand the mechanisms of reactions in which the difficult, non-functionalised substrate molecules are converted to the desired products with high selectivities. This might potentially lead to an economical and more efficient utilisation of feed stocks as well as to the production of high added value intermediates for the fine chemicals industry.\(^1\) Moreover, insights into general principles regarding the reactions in confined spaces may be gained, drawing parallels between synthetic and natural systems like enzymes, thus contributing to a better general understanding of these phenomena.

Herein we report the mechanistic details of the hydroformylation catalysis performed by the encapsulated rhodium hydroformylation catalyst, aiming to identify the steps which determine its (unusual) selectivity, and, in particular, to cast light on the role of the capsule in this process. Using the slightly extended hydroformylation cycle of Breslow and Heck\(^4\)\(^,\)\(^7\)\(^,\)\(^24\) as the working model, we look into the details

\(^1\) Large amounts of alkenes used in hydroformylation are produced in ethylene oligomerisation processes, which delivers mixtures of alkenes; however, only terminal alkenes can be converted to (linear) aldehydes with high selectivity. Internal alkenes, less reactive in hydroformylation, are first converted to terminal alkenes in isomerisation processes, and subsequently hydroformylated to linear aldehydes. Potentially high added-value products (highly branched aldehydes) are not accessible directly from the internal alkenes due to the lack of selective catalysts. The ZnTPP-encapsulated rhodium catalyst was the only one capable of achieving high selectivity (combined with high activity) in the hydroformylation of these linear, non-functionalised internal 2- and 3-alkenes.
5.2. RESULTS AND DISCUSSION

Using various techniques. By performing gas-uptake experiments we monitor the kinetics and look into the rate limiting processes. Additionally, we use high pressure FT-IR spectroscopy to monitor the catalyst resting states in situ to support the conclusions from the kinetics experiments. Closer insight into the cycle, obtained by combining the data from the kinetics, in situ FT-IR spectroscopy, and deuterof ormation experiments with the DFT-based simulation model of the kinetics of the catalytic cycle, conclusively identify the selectivity-determining step of the catalysis. Moreover, the molecular models and the analysis of the catalytic pathways unveil the role of the capsule in the selectivity-determining step as an effective steric block for paths to the minor product. In addition, we demonstrate that the DFT model is suitable for prediction of product distribution using two similar – and previously not studied – substrates. These substrates differ only in the position of a substituent by one carbon atom – remote from the double bond – causing them to be converted with different selectivities by the ZnTPP-encapsulated catalyst, as we also predict using the theoretical model.

5.2. Results and Discussion

Typically, the hydroformylation reaction (the cycle is depicted in Fig. 5.2.1) is discussed in terms of two kinetics types, which are conveniently called type I and type II kinetics. In type I kinetics the rate limiting step is usually

**Figure 5.2.1.** Schematic representation of the hydroformylation catalytic cycle with monophosphine rhodium catalyst and a generic trans-2-alkene as substrate. Resting states for both types of kinetics are indicated (rsI, rsII), and hydrogenolysis is assumed to consist of oxidative addition of H$_2$ and subsequent reductive elimination of the aldehyde. Formation of dormant dirhodium species, as well as β-H elimination pathways (leading to isomeric alkenes) are not shown.

early in the catalytic cycle and difficult to pinpoint exactly. Most likely it is
either CO dissociation from the rhodiumhydrido resting state (rsI, Fig. 5.2.1) and subsequent alkene coordination to the electronically unsaturated species f, leading to the rhodium alkene complexes a. Alternatively, the hydride migration from Rh (species a) to the alkene, forming the alkylrhodium species b may be rate-limiting, with a rapid pre-equilibrium from rsI. The hydride migration step is also considered to be the selectivity determining in the type I kinetics, provided it is irreversible. Characteristic of the type I kinetics is that the reaction rate order is one (1) with respect to the substrate, −1 with respect to the CO, and zero (0) with respect to the H2 concentration. Also, it is usually observed when phosphines (or other poor πaccepting ligands) are used as ligands to form the Rh catalyst.

The type II kinetics is typical for electron-poor ligands which are also moderate to good πacceptors, like phosphites. The characteristic of the type II kinetics is the often observed high isomerisation rate, the hydrogenolysis is the rate determining process, and the electronically saturated rhodium acyl species rsII is observed as the resting state. The rate order in type II kinetics is one (1) with respect to the H2, negative with respect to the CO, and zero (0) with respect to the substrate concentration.

5.2.1. Kinetics and in situ HP-FTIR. The kinetics of the trans-2-octene hydroformylation by the ZnTPP-encapsulated rhodium catalyst were studied at 40°C by measuring the gas uptake during the reaction. From these data, using the reaction progress kinetics analysis approach, we were able to determine the reaction rate orders in reactant concentrations. The raw gas uptake data were not fitted to analytical expressions describing potential rate laws. Instead, the data were numerically differentiated to obtain the reaction rate (at any moment). The rate orders in CO (m) and H2 (n) were obtained by fitting the rate vs. partial pressure data to the equations \( r = K' \cdot p^m(CO) \) (for \( p(H_2) = \text{const.} \)) and \( r = K'' \cdot p^n(H_2) \) (for \( p(CO) = \text{const.} \)), as shown in the Figure 5.2.2a. The logarithmic plot of rate vs. substrate concentration gave the rate order in substrate as the slope of the straight line (three examples shown in Fig. 5.2.2b, for CO/H2 = 1 : 2; 1 : 1; and 2 : 1). Thus we found broken orders in all three reactants: −0.9 in CO, +0.7 in H2 and +0.8 in trans-2-octene. None of the rate orders was zero, suggesting that the kinetics type under these conditions is neither type I nor type II, but intermediate. This implies that both resting states, rsI and rsII, should be present during catalysis under these conditions.

We used infrared spectroscopy to monitor the reaction in situ, under the conditions similar to those of the gas-uptake experiments, and we indeed found signals belonging to both resting states during catalysis. The Figure 5.2.3a shows the rhodiumhydrido resting state rsI at 40°C before the addition of substrate (three bands at 2089, 2042 and 2006 cm⁻¹, Fig 5.2.3a) Similar HP-IR experiments carried out at 25°C showed the appearance of the same three bands, indicative of the reaction progress kinetics analysis approach.

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This and further species denominators refer to those in Fig. 5.2.1, if not specified otherwise.

In Figure 5.2.1 shown as sequence of steps: hydrogen oxidative addition + reductive elimination of the aldehyde.

Alternatively, the orders in partial pressures of the gases were also obtained by fitting the reaction rate vs. \( (p(CO), p(H_2)) \) surface to the equation \( r = K \cdot p^m(CO) \cdot p^n(H_2) \) at different conversions, please see the Experimental Section for more details.

40°C, 20–25 bar syngas pressure, low rhodium concentration (0.50·10⁻³ mol·l⁻¹), variable temperatures and syngas composition.
5.2. RESULTS AND DISCUSSION

![Graphs and equations]

(a) Influence of H₂ and CO partial pressures on reaction rate at 20% conversion

(b) Reaction rate vs. substrate concentration

**Figure 5.2.2.** Reaction rate orders in respect to gases (left) and substrate (right). Left: order is $-0.8$ to $-0.9$ in CO, and 0.6 to 0.7 in H₂ concentration; the data were fitted to the equation of type $r = K' \cdot p^{\text{order}}(\text{gas})$; Fitting the reaction rate over the whole partial pressures surface $r = f(p(\text{CO}), p(\text{H}_2))$ to the equation $r = K' \cdot p^m(\text{CO}) \cdot p^n(\text{H}_2)$ gave $n = -0.90$ and $m = 0.73$ (in the Experimental Section). Right: the slope of the logarithmic plot of the reaction rate vs. substrate concentration is 0.8 and represents the order in trans-2-octene concentration for these reactions. The initial non-linearity is most likely caused by the incomplete catalyst incubation and/or mass transfer phenomena at the beginning of the reaction (CO/H₂ = 1:2; 1:1; and 2:1). The values of these parameters (at given reaction conditions) suggest that kinetics follows neither pure type I nor type II profile, but could rather be characterised as “mainly” type I mixed with type II.

the rsI. Upon injection of trans-2-octene at 40°C, the intensities of these three bands decrease (Fig. 5.2.3b), and new bands at 2056, 2025 and 1992 cm⁻¹ appear, as is shown in the difference spectrum in Figure 5.2.3c. The new bands indicate appearance of the acylrhodium resting state rsII, which co-exists with the rhodiumhydrido resting rsI state during catalysis, in agreement with the kinetics studies.

Interestingly, the addition of trans-2-octene to rsI at 25°C does not lead to any spectral changes (see Fig. 5.2.3d), indicating that the kinetics at this temperature is mainly of type I. This was also suggested earlier by Kuil et al., who found that the conversion was not influenced by the H₂ partial pressure at 25°C, in line with the type I kinetics.

Although the reaction rate was significantly influenced by reaction conditions (overall pressure, substrate concentration, and CO/H₂ ratio), the selectivity towards the C3-aldehyde remained essentially constant regardless of the conditions (Fig. 5.2.4). This suggests that, either the reaction rate and the selectivity are determined in separate steps of the catalytic cycle, or – more likely – that the reaction rates leading to the C2- and the C3-aldehyde are equally affected by the changes in reaction conditions, keeping the product ratio constant. Conversely, what might be expected at 40°C, the selectivity did not drop significantly compared to the reaction carried out at 25°C, but is largely retained with 62–67% C3-aldehyde as the major product.
Figure 5.2.3. In situ HP-IR showing the catalyst resting states at 40°C and 25°C (20 bar syngas, CO/H₂ = 1 : 1). Top left: the hydride resting state rsI (RhP(CO)₃H) before substrate addition at 40°C. Top right: Upon substrate addition (at 40°C) and reaction start the initial resting state bands changed; they decreased in intensity (negative in the difference spectrum, lower left), while new ones appeared (positive, arrows point upwards), indicating the formation of RhP(CO)₃(acyl) rsII resting state and the intermediate kinetics type. Lower right: resting state rsI before and during catalysis at 25°C, typical for type I mechanism. P=(meta−pyridyl)₃P·(ZnTPP)₃.

At 25°C the catalysis follows mainly the type I kinetics, as no acylrhodium resting state (rsII) was observed in HP-IR at this temperature (and CO/H₂ = 1 : 1). Under these conditions, only the RhP(CO)₃H species (rsI) is visible in the autoclave, as is evidenced by the FT-IR spectra in the Fig. 5.2.3d. Thus, the catalysis rate at 25°C is most likely determined by the CO dissociation/trans-2-octene coordination/hydride migration processes, while temperature elevation leads to intermediate kinetics, where H₂ oxidative addition is rate limiting as well.
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Figure 5.2.4. Influence of syngas pressure and composition on conversion and selectivity of hydroformylation of trans-2-octene catalysed by the ZnTPP-encapsulated rhodium catalyst at 40°C. The conversion and reaction rates decrease with increasing pressure, especially when CO is in excess. The selectivity for the C3-aldehyde is practically not influenced by CO or H\(_2\) pressures, while the yield of the C2-aldehyde grows slightly with increasing pressure at the expense of the isomerisation products (not shown).

Table 5.2.1. Deuteroformylation experiments results showing selective isomerisation of trans-2-octene to cis-2-octene with two encapsulated catalysts under encapsulation conditions, while the non-encapsulated catalysts produce statistical mixture of isomers. Conditions: [Rh] = 0.50 \cdot 10^5mol⋅l\(^{-1}\), [P]/[Rh] = 5.0, [Zn]/[P] = 3.0, p = 20 bar, CO/\(^2\)H\(_2\) = 1 : 1, [trans-2-octene]/[Rh] = 1000, 120 hours. Reaction mixture was quenched with tributylphosphite, diluted with CH\(_2\)Cl\(_2\) and analysed directly by GC and \(^2\)H NMR spectroscopy.

<table>
<thead>
<tr>
<th>Ligand</th>
<th>encapsulated by</th>
<th>non-encapsulated</th>
<th>calc.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ZnTPP</td>
<td>ZnTPP(m-OMe)</td>
<td>P(m-py)(_3)</td>
</tr>
<tr>
<td>conversion(^a)</td>
<td>14</td>
<td>12</td>
<td>4</td>
</tr>
<tr>
<td>isomers(^b)</td>
<td>5.4</td>
<td>3.5</td>
<td>9</td>
</tr>
<tr>
<td>1-octene(^c)</td>
<td>7</td>
<td>17</td>
<td>32</td>
</tr>
<tr>
<td>cis-2-octene(^c)</td>
<td>85</td>
<td>70</td>
<td>26</td>
</tr>
<tr>
<td>trans-3-octene(^c)</td>
<td>8</td>
<td>13</td>
<td>42</td>
</tr>
<tr>
<td>C1-aldehyde(^b)</td>
<td>n.d.</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>C2-aldehyde(^b)</td>
<td>8</td>
<td>10</td>
<td>56</td>
</tr>
<tr>
<td>C3-aldehyde(^b)</td>
<td>87</td>
<td>85</td>
<td>33</td>
</tr>
<tr>
<td>C4-aldehyde(^b)</td>
<td>n.d.</td>
<td>n.d.</td>
<td>n.d.</td>
</tr>
</tbody>
</table>

\(^a\) % of total converted substrate; \(^b\) % of formed products (aldehydes + isomers); \(^c\) % of total amount of isomeric octenes, excluding the substrate

5.2.2. Deuteroformylation, hydride migration, \(\beta\)-H elimination and selectivity. Deuteroformylation experiments show that, when no deuterium is incorporated into the substrate (via hydride migration/\(\beta\)-H elimination processes), the deuteride (and the hydride, by analogy) migration step is irreversible, making it therefore the selectivity determining step of the catalytic cycle.\(^{188,189,249}\) This
is valid if the isomerisation process shares the same pathway as the hydroformylation. However, in a complex system with multiple possible catalytic pathways there might be those which are reversible and possibly do not even lead to the acylrhodium species, resulting (only) in isomerised alkenes. Also, other pathways may have an irreversible hydride migration and the subsequent full cycle to the aldehyde product, determining the selectivity of the hydroformylation.

Figure 5.2.5. $^2$H NMR spectra of the trans-2-octene deuteroformylation reaction mixture, showing the signals of deuterium incorporated into aldehyde products (9.3 and 1.3 ppm) and alkenes ($C^{sp^2}-2^2$H signal at 5.4 ppm). At 25°C (top spectrum), the isomerisation with the ZnTPP-encapsulated catalyst is selective. Opposite to that, isomerisation at 80°C (middle spectrum) is not selective, leading to the statistical distribution of isomeric octenes. This result correlates with the non-selective production of aldehydes at this temperature, indicating that the loss of selectivity in these processes might have the same cause. Legend: ♠ $C^2$H(O) (aldehyde); ★ $C^{sp^2}-2^2$H (alkene); ♦ toluene; ♣ $C^{sp^3}-2^2$H (3-octene); ♦ $C^{sp^3}-2^2$H (aldehyde); ♫ $C^{sp^3}-2^2$H signals belonging to 1- and 3-octene.

Our deuteroformylation study was conducted analogously to the hydroformylation catalysis experiments using two C3-selective, Zn$^{II}$(porphyrin)-encapsulated catalysts and also two non-encapsulated rhodium catalysts modified with tris-(3-pyridyl)-phosphine and triphenylphosphine. We analysed the quenched crude reaction mixtures by gas chromatography and $^2$H NMR spectroscopy. The results are summarised in the Table 5.2.1. Isomeric octenes were found with all catalytic systems we studied. The $^2$H NMR spectra of the reaction mixtures of the ZnTPP-encapsulated catalyst (at 25 and 80°C, Fig. 5.2.5) display clearly the signal of

$^vii$with 1000 or 2000 equivalents of substrate instead of 500 used in hydroformylation
5.2. RESULTS AND DISCUSSION

Figure 5.2.6. Isomerisation to 2 octenes under hydroformylation and deuteroformylation conditions. Due to the kinetic isotope effect, cis-2-octene is formed faster than trans-2-octene under deuteroformylation conditions.

the deuterium atom at the $sp^2$ carbon atom of the isomerised substrate (peak at 5.4 ppm; the corresponding $C^{sp^2}-H$ signal is at 1.3 ppm). No signals between 2 and 3 ppm were found, indicating that there no deuterium atoms were incorporated on the carbon that bears the aldehyde group.

Interestingly, while the non-encapsulated catalysts produced a nearly statistical mixture of isomeric 1-, 2-, and 3-octene, the ZnTPP-encapsulated catalysts produced selectively one isomer in 85% at 25°C.\(^{\text{viii}}\) The other C3-selective catalyst, encapsulated by a methoxy-substituted ZnTPP-analogue, ZnTPP\((m\text{-OMe})\) (see Chapter 4), gave rise to an essentially identical isomerisation pattern as the ZnTPP-encapsulated catalyst. Importantly, with both encapsulated catalysts, the major isomeric octene was the cis-2-octene (from trans-2-octene as the starting alkene\(^{\text{ix}}\)). This isomerisation pattern differs greatly from the one observed in hydroformylation, with cis-2-octene as the selective isomerisation product and the most striking difference. In hydroformylation, any of the trans-2-octene potentially formed by $\beta_{-1}^1$H elimination would not be visible in GC. In deuteroformylation however, $\beta_{-1}^1$H elimination is faster than $\beta_{-2}^2$H elimination,\(^{249–253}\) and instead of trans-2-octene, cis-2-octene is formed, which is visible in GC, as is illustrated in Figure 5.2.6. In other words, most of the isomerisation processes in hydroformylation that lead back to the starting material (“invisible”) become largely visible in deuteroformylation, allowing for a better insight into the hydride/deuteride migration – $\beta$-H elimination isomerisation processes. That the cis-2-octene is the major isomer in deuteroformylation, but not in hydroformylation, implies that the trans-2-octene is one of the main isomers formed in the hydroformylation of trans-2-octene.

As shown in the scheme in Figure 5.2.7, the most relevant paths to cis-2-octene from C2- and C3-alkylrhodium species involve rotation of an alkyl group (n-hexyl in b1 or ethyl in b3, Fig. 5.2.7) and elimination of a $\beta_{-1}^1$H atom, which is faster than the $\beta_{-2}^2$H elimination from the same carbon atom (KIE\(^{249–253}\)). If there were no preference for deuteride migration, indicated by 50% yield probability on reaction arrows from the species a, Fig. 5.2.7, one would expect to observe 20–25% of cis-2-octene (path1 + path3, Fig. 5.2.7) in the octenes mixture. In fact, the distribution pattern of isomeric octenes as depicted in Fig. 5.2.7 is almost identical to the distribution of isomers we observed experimentally with the non-encapsulated

\(^{\text{viii}}\) At 80°C all catalysts displayed similar, statistical distribution of isomeric octenes and their follow-up aldehyde products.

\(^{\text{ix}}\) and vice versa, trans-2-octene was the major produced isomer in deuteroformylation using cis-2-octene as substrate; cis-2-octene is hydroformylated by the ZnTPP-encapsulated catalyst giving 83% C3-aldehyde, and deuteroformylated giving 85% of the same product (not shown in the table).
catalysts (at 25°C), suggesting that the deuteride migration and the subsequent β-^1^H elimination processes with the non-selective catalysts very likely proceed as in Figure 5.2.7.

With the encapsulated catalysts, however, these reactions must proceed with other probabilities, i.e., the yields of these reactions or their relative rates must differ significantly in order to result in the observed isomerisation pattern with 70-90% cis-2-octene. It is very likely that the deuteride/hydride migration step proceeds selectively, producing preferentially the C3-alkylrhodium species. The major isomeric alkene, cis-2-octene, is then produced via path 3, involving the rotation of the ethyl group within the capsule. The alternative, β-^1^H elimination in the path 4 leading to 3-octene, requires rotations of the n-pentyl group, which is very likely sterically more hindered than rotation of the ethyl group in the competing path 3. Thus, the isomerisations from either alkylrhodium species could proceed taking the pathways of lesser steric hindrance, accounting for the distribution of isomers. Also, both alkylrhodium species are free to undergo forward reactions with similar rates, producing the aldehydes in required C3/C2 ratios. This hypothesis certainly
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offers the simplest and the most attractive explanation for the observed distributions of isomers and aldehydes, and is also supported by DFT calculations as we show below.

5.2.3. DFT study, kinetic simulation of the catalytic cycle and selectivity. In order to gain qualitative insight into the catalytic cycle, especially into the crucial initial steps, a DFT study was performed, which included the full hydroformylation cycle using the non-encapsulated and the ZnTPP-encapsulated catalyst. For these calculations we used the pbe1pbe functional with the dgdzvp basis set as implemented in the Gaussian 03 program package. The optimised structures of the non-encapsulated rhodium species were used to construct the ZnTPP-encapsulated molecules, which were further optimised using the two layer ONIOM method.

We considered four possible rhodium-trans-2-octene complexes (Fig. 5.2.8a), each of which can take two hydride migration pathways (“inner” or “outer”, see Fig. 5.2.8), leading to C2- or C3- alkylrhodium species (generically shown as species b in Fig. 5.2.1). Next, CO coordination to b giving c, and alkene migration to CO lead to the electronically unsaturated acylrhodium species d. The species d can either react reversibly with CO, leading to the acylrhodium resting state rsII, or undergo oxidative addition of H2 to give the hexacoordinated species e. This species can in turn undergo reductive elimination either of H2 (and return to d), or of the aldehyde, regenerating the catalytically active species f (full details of the computed reaction pathways are provided in the Experimental Section).

In order to relate the DFT-computed pathways to the experiments more precisely, we used the DFT results to simulate and predict the kinetics. From the DFT-computed activation barriers in the catalytic cycle we calculated the rate

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x Other possibilities are less likely. For instance, in one hypothetical case the formation of the C2-alkylrhodium is not preferred over C3-alkylrhodium species, i.e. that the deuteride/hydride migration is not selective. In order to satisfy the isomer and aldehyde distribution, the forward reactions (with respect to the catalytic cycle; β-H elimination reactions in Figure 5.2.7 are backward with respect to the aldehyde production cycle) from the C3-alkylrhodium (towards the C3-aldehyde) would have to be much faster than those from the C2-alkylrhodium (these would have to be disfavoured or blocked). Also, it means that isomerisation from the C3-alkylrhodium would largely be suppressed, due to acceleration of the forward reactions. Thus, the only way to produce cis-2-octene as major isomer would be to block forward reactions from C2-alkylrhodium and selectively favour the isomerisation through the path 1 over the path 2. How this might happen is unclear, since the first path requires rotation of the n-hexyl group within the capsule and it is very likely that it would be more hindered than the path 2. The path 2, in turn, would lead to formation of large amount of 1-octene. In addition, this scenario would eventually lead either to production of near equal amounts of isomers and aldehydes, or to catalyst deactivation due to the blocked forward reactions from C2-alkylrhodium. Since neither was observed, this scenario is highly unlikely. Similarly, if one assumes that C2-alkylrhodium is preferentially formed in the deuteride/hydride migration step, the only mechanism to achieve the peculiar distribution of isomers an aldehydes would have to include the blocking of the forward reactions from the C2-alkylrhodium species, as well as acceleration of β-1H elimination through path 1 from C2-alkylrhodium.

With pbe1pbe/dgdzvp for the high level (rhodium fragment + substrate) and pbe1pbe/3-21g** for the low level (ZnTPP molecules).

The other four, on the opposite side of the Rh atom are their mirror images and therefore not considered. Isomers with the substrate in positions other than equatorial were either too high in energy to be accessible or too distorted, so we did not include them in further analysis.
Figure 5.2.8. Four rhodium-alkene isomer complexes (above) and two possible hydride migration pathways (below) shown for the encapsulated isomer a1. With four isomers, there are eight hydride migration pathways in total.

Table 5.2.2. Hydride migration activation energies for the non-encapsulated and the ZnTPP-encapsulated rhodium catalyst and trans-2-octene as substrate.

<table>
<thead>
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<th>entry</th>
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<th>ZnTPP-encapsulation</th>
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<tr>
<td></td>
<td>starting species</td>
<td>$\Delta G^#(C3)$</td>
<td>$\Delta G^#(C2)$</td>
</tr>
<tr>
<td>1</td>
<td>a1</td>
<td>9.79</td>
<td>9.13</td>
</tr>
<tr>
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</tr>
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<td>4</td>
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<td>10.67</td>
<td>11.41</td>
</tr>
<tr>
<td>5</td>
<td>major product</td>
<td>C2: 84% (79%)</td>
<td>C3: 93% (70%)</td>
</tr>
<tr>
<td>6</td>
<td>experiment</td>
<td></td>
<td>C3: 85–91%</td>
</tr>
</tbody>
</table>

* obtained from simulation of the hydride migration step; in parentheses: amount obtained from whole-cycle simulations; ** the non-encapsulated, monophosphine-rhodium catalyst is only a model, as it is not accessible experimentally other than as in mixture with bis-phosphine- and as possibly tris-phosphine-rhodium species; $\Delta(G)E^\#_A(C3)$ is the (free) activation energy of the hydride transfer to the C2 atom, forming the C3-alkylrhodium species, $\Delta(G)E^\#_A(C2)$ is the equivalent for the formation of the C2-alkylrhodium species.
5.2. RESULTS AND DISCUSSION

We used these microconstants to build a kinetic model simulating the catalytic cycle (and the kinetics). For all the steps, except for the reductive elimination of the aldehyde, the backward reactions were taken into account. The kinetic simulation of the catalysis produces the concentrations of the species involved in the cycle, of which especially interesting were the concentrations of the aldehyde products, and the catalyst resting states. The kinetic model of the non-encapsulated catalyst predicts the C2-aldehyde as the major product in 79%. The closest experimental comparison available for this model catalyst is the ZnPc-encapsulated catalyst (see Chapter 3), whose spacious capsule allows unhindered motion of the substrate within it, and leads to 60–70% C2-aldehyde from long-chained \textit{trans}-2-alkenes (2-octene to 2-decene). Importantly, for the ZnTPP-encapsulated catalyst the kinetic model correctly predicts the C3-aldehyde as the major product in up to 70% (Fig. 5.2.9a), which is in excellent agreement with the experimental results (85-91%, entries 5 and 6, Tab. 5.2.2). In further agreement with the experiments, the kinetic simulation model predicts that the resting states (rsI and rsII, Fig. 5.2.1) of the ZnTPP-encapsulated catalyst would both be present during catalysis, as is illustrated in Fig. 5.2.9b. As we have shown, both resting states can indeed be observed during catalysis.

In order to analyse the initial steps of the catalytic cycle, we also built the kinetic models (with both catalyst systems), taking into account only the hydride

\[ k = A \cdot e^{-\frac{E}{RT}}, \quad A = 10^{12}[k] \]

For both, the non-encapsulated model and the ZnTPP-encapsulated catalyst. We used the Simbiology module in MATLAB® (R2010a, The Mathworks Inc.™); for rate expressions we use the simple Mass Action Law: \( r = k \cdot c^a(a) \cdot c^m(b) \cdot \ldots \cdot c^n):\) concentration of species \( a, m, n: \) reaction rate orders with respect to the corresponding reactants; for further details please see the Experimental Section.

Isomerisation pathways to octenes other than to the starting substrate, \textit{trans}-2-octene, were not considered.
migration and the $\beta$-H elimination steps. In either catalyst case, the predicted major product corresponds to the one predicted by the whole cycle (and which is also observed experimentally), although the numbers are slightly different:

- non-encapsulated – 84% C2 (H-migration) vs. 79% C2 (full cycle)
- ZnTPP-encapsulated – 93% C3 (H-migration) vs. 70% C3 (full cycle)
- ZnTPP-encapsulated – experiment: 85-91% C3, (see Tab. 5.2.2).

The product distribution initially determined in the hydride migration step is thus largely preserved in the later stages of the catalytic cycle. The DFT computations and the simulation of the kinetics built using the DFT data clearly point out that the hydride migration determines the selectivity. Importantly, this is in line with the discussion in the deuteroformylation section, where we found that the selectivity in the hydride migration is the most likely explanation for the observed isomerisation and hydroformylation product distributions.

It might seem contradictory to simultaneously find the hydride migration to be reversible and the selectivity-determining step. However, we would like to emphasize that there are eight hydride migration pathways (which we considered in the DFT-study), and 28 possible $\beta$-H elimination pathways. Some of these elimination pathways are accessible, producing the isomers, while others are inaccessible, determining the aldehyde distribution. If we look at the energy diagrams of the hydride migration with the ZnTPP-encapsulated catalyst (shown in Fig. 5.2.10), we see that some activation barriers for $\beta$-H elimination are very similar to those of their corresponding hydride migration steps, making the backward reaction possible (according to the principle of the microscopic reversibility). At closer inspection, we see that in all alkylrhodium pairs in Fig. 5.2.10, the species lying higher in energy is always the one where the alkyl moiety coordinates to Rh cis to the P atom. The alkyl group is deep inside the capsule, as is shown in Figure 5.2.11a for the example of the alkylrhodium complex stemming from the a3 species, and it is most likely that the steric crowding within the capsule destabilises the whole complex. On the other hand, the species where the alkyl group lies trans to the P atom (Fig. 5.2.11b) is usually lower in energy (more stable), most likely because in this configuration the alkyl chain avoids steric crowding with the capsule.

Therefore, the capsule seems to be destabilising the products of the hydride migration in which the alkyl group lies cis to the P atom, creating steric crowding within the capsule; this destabilisation lowers the barrier for $\beta$-H elimination from these alkylrhodium species. At the same time, the reaction forward from this species may be associated with high energy barriers. Thus it is possible to have hydride migration as the selectivity determining step (because there are irreversible H-migration pathways), and simultaneously observe isomerisation (because some $\beta$-H elimination pathways are accessible, and do not lead to acylrhodium or aldehyde species). In the case of the ZnTPP-encapsulated catalyst, the main produced isomer

\footnote{xvi}{non-encapsulated and ZnTPP-encapsulated}
\footnote{xvii}{That it does not remain constant may be a manifestation of the imperfection of the model, or, it may suggest that it is not one single step that determines the selectivity absolutely, but that more catalytic steps influence it. In this case it seems that the selectivity determined by the hydride migration step is moderated to a certain degree by the latter catalysis steps.}
\footnote{xviii}{from each of the four C2-alkylrhodium species there are three, and from each of the four C3-alkylrhodium species there are 4 $\beta$-H elimination possibilities, making in total: 4 \cdot (3 + 4) = 28.}
\footnote{xix}{electronic effects can also contribute to its stability.
5.2. RESULTS AND DISCUSSION

Figure 5.2.10. Energy diagrams of the eight hydride migration pathways. Three out of four rhodium-alkene complexes favour the formation of the C3-alkylrhodium species. The isomer a3 has the lowest activation barrier towards the C3-alkylrhodium complex and it most probably dominates the catalysis. \( \Delta E = \Delta E_A^\# (C2) - \Delta E_A^\# (C3) \).

of a 2-alkene is also a 2-alkene, so that the effect of the isomerisation processes is very small on the final product distribution.

5.2.4. Selectivity and the role of the capsule. Having shown which step determines the selectivity, we will take a look at how the unusual selectivity is achieved and what the role of the supramolecular capsule is in the selection of hydride migration pathways.

The activation barriers for the hydride migration pathways of the encapsulated rhodium-alkene isomers show that the C3-path is preferred from the intermediate a1 (by 8.5 kcal·mol\(^{-1}\)), a2 (by 0.8 kcal·mol\(^{-1}\)), and a3 (by 2.5 kcal·mol\(^{-1}\)) isomers, while the C2-alkylrhodium is clearly the preferred product of the a4 isomer (see Tab. 5.2.2 and Fig. 5.2.10). Product distribution analysis of the individual reaction
Figure 5.2.11. The alkylrhodium species formed from the \textit{a3} rhodium alkene isomer showing the alkyl group within the capsule in the \textit{cis} position to the P atom (left), and outside of the capsule in the \textit{trans} position to the P atom (right). The \textit{cis}-alkylrhodium isomers are generally higher in energy than the \textit{trans} isomers (in this case ca. 10 kcal·mol$^{-1}$), and thus more prone to $\beta$-H elimination.

Table 5.2.3. Contributions of individual reaction pathways to the total product distribution according to the simulation of the full catalytic cycle.

<table>
<thead>
<tr>
<th>entry</th>
<th>isomer</th>
<th>contribution [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>P2</td>
<td>P3</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>a1</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>a2</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>a3</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>a4</td>
<td>25</td>
</tr>
<tr>
<td>5</td>
<td>total</td>
<td>30</td>
</tr>
</tbody>
</table>

pathways\textsuperscript{,x(1)} (starting with the species \textit{a1} to \textit{a4}) confirms the qualitative estimate based on the hydride migration. The individual contributions to the total amount of the produced aldehydes in the simulation of the full cycle are shown in Table 5.2.12. The pathways to the C2-aldehyde starting from the rhodium-alkene isomers \textit{a1} and \textit{a3} are blocked, as is the pathway to the C3-aldehyde in the case of the \textit{a4} isomer (Fig. 5.2.12). Both the C2- and the C3-aldehyde are formed only from the \textit{a2} isomer, which clearly favours the C3-aldehyde (Fig. 5.2.12b). The effect of the supramolecular capsule is most pronounced – and best to visualise – in the case of the rhodium-alkene complex (isomer) \textit{a1} (Fig. 5.2.8c). For the non-encapsulated catalyst, the activation energies for hydride migration to C3- and C2-pathways differ only by 0.7 kcal·mol$^{-1}$, whereas this difference is 8.5 kcal·mol$^{-1}$ when the catalyst is encapsulated. The main contribution to this increase of the activation barrier is the energy required for capsule rearrangement from the rhodium-alkene species (\textit{a1}) to

\textsuperscript{x(1)}according the the DFT-based kinetic simulation of the catalytic cycle
5.2. RESULTS AND DISCUSSION

Figure 5.2.12. Contribution of individual reaction pathways to the overall product distribution, showing which aldehydes are the preferred products in each of the pathways, according to the simulation including the full catalytic cycle.

the transition state geometry. Single point energies of the supramolecular capsules (the assembly (meta−pyridyl)$_3$P·(ZnTPP)$_3$) in the conformations of the hydride migration transition states towards the C2- and C3-products have been calculated by removing the Rh-fragments from the intermediates of the previously calculated pathways; the corresponding energy diagrams are shown in Fig. 5.2.13). These reorganisation energies of the capsules that accommodate the transition states for the C3-aldehyde are 6–8 kcal·mol$^{-1}$ lower in energy than those towards the C2-aldehyde, except in the example of the isomer a$_4$, where the pathway to the C2-aldehyde is favoured (Fig. 5.2.13). The rearrangement energy in the case of the isomer a$_1$ is 3.8 and 12.5 kcal·mol$^{-1}$ for the C3- and the C2-pathway respectively. This difference of 8.7 kcal·mol$^{-1}$ in capsule rearrangement energies corresponds very well to the difference in the activation energies of 8.5 kcal·mol$^{-1}$ (see Tab. 5.2.2 and Fig. 5.2.10a) demonstrating that in this pathway the capsule rearrangement energy is the main cause for the selectivity. The capsule of the other rhodium
Figure 5.2.13. Single point energies of the ZnTPP-capsule in conformations corresponding to the indicated catalyst intermediates and the hydride migration transition states with trans-2-octene as substrate. The capsule rearrangement energies are the energy differences between these conformations, and they are in three out of four pathways larger for the hydride migration towards formation of the C2-product. The overall hydride migration activation barriers for the C2-paths are thus increased and these reaction pathways clearly disfavoured.

alkene complexes display similar behaviour, and the overall trend confirms the importance of the capsule rearrangement energy in the selectivity determining step. The reason for the different capsule conformations in the hydride migration step are the steric requirements for accommodation of the substrate alkyl chain for the C2-alkyl path, as is illustrated in Fig. 5.2.14. In order to form the C2-alkylrhodium, the substrate must rotate the “outer” C (the C3, Fig. 5.2.8b) towards the hydride (which is transferred to it), and in this process the alkyl chain of the substrate collides with the capsule (ZnTPP molecules). These must rearrange in order to accommodate the substrate (Fig. 5.2.14c and 5.2.14d), what is associated with an energy penalty. In the case of the path to the C3-alkylrhodium, the “inner” C

\footnote{The isomer \textit{a4} displays the same mechanism, except that the C2-product is favoured.}

\footnote{One need also recall here the attractive interactions responsible for the cooperativity in the capsule assembly: at least one pair must be broken for the rearrangement to occur.}
Figure 5.2.14. The role of the capsule in the selectivity determining step: it hinders the hydride migration pathways for which the capsule rearrangement energy is higher, which is mainly towards C2-alkylrhodium species (and the P2-aldehyde). Here the hydride migration in the case of a1 species is shown: steric crowding of the substrate alkyl chain with the capsule raises the energy of the transition state that leads to the C2-alkylrhodium (5.2.14d) 8.5 kcal mol$^{-1}$ higher than that of the transition state leading to the C3-product (5.2.14b). Thus, the reaction pathway towards the C2-aldehyde is efficiently blocked.
(the C2) rotates towards the hydride, leading to a small steric rearrangement of the capsule (Fig. 5.2.14a and 5.2.14b) and causing the C3-alkylrhodium to be produced much faster than the C2-product.

Probably the most important aspect concerning the high catalytic activity and selectivity of enzymes is that the enzymes “bring the reacting species together in a geometry that favours” one specific reaction, often imposing this geometry by additional substrate binding sites or by the shape of their substrate binding pocket. The restrictions of the rotational freedom of the substrate (2-alkene) within our synthetic capsule and its favourable conformations in the transition states leading to formation of the C3-aldehyde represents a concept that is similar to that exercised in Nature by enzymes.

5.2.5. Predicting the outcome of hydroformylation: two new substrates.

In order to evaluate the predictive power of our method, we calculated the capsule effect of the hydride migration step in the hydroformylation of two substituted trans-2-hexenes, (5-phenyl)- and (6-phenyl)-trans-2-hexene. These alkenes differ only in the position of the phenyl substituent by one carbon atom, but we anticipated that this would largely affect the occupation of space within the capsule at the active site. To estimate this effect the encapsulated rhodium alkene complexes with these two substrates were calculated using DFT (two-layer ONIOM method as described earlier).

![Figure 5.2.15](image)

**Figure 5.2.15.** ZnTPP-encapsulated catalyst with coordinated substituted substrates. Left: (5-phenyl)-trans-2-hexene and right: (6-phenyl)-trans-2-hexene. In both structures the alkene is positioned as in a2 species (Fig. 5.2.8a)

The DFT-optimised molecular models show that the phenyl group in position five (C5) is mainly within the capsule (Fig. 5.2.15a), while that on the C6 is just outside the capsule (Fig. 5.2.15b). The 5-phenyl group might thus distort the capsule during the selectivity determining hydride transfer also in the C3-pathways, potentially leading to changes in selectivity. The 6-phenyl group, being outside of
Table 5.2.4. Activation energies for the hydride migration step with (5-phenyl)-trans-2-hexene and (6-phenyl)-trans-2-hexene as substrates for the ZnTPP-encapsulated rhodium catalyst. The calculated values show excellent correlation with the experimental results.

<table>
<thead>
<tr>
<th>entry</th>
<th>$E_i$/[kcal·mol$^{-1}$]</th>
<th>(5-phenyl)-2-hexene</th>
<th>(6-phenyl)-2-hexene</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>starting species</td>
<td>$\Delta E_A^#(C3)$</td>
<td>$\Delta E_A^#(C2)$</td>
</tr>
<tr>
<td>1</td>
<td>a1</td>
<td>16.42</td>
<td>16.12</td>
</tr>
<tr>
<td>2</td>
<td>a2</td>
<td>20.86</td>
<td>24.90</td>
</tr>
<tr>
<td>3</td>
<td>a3</td>
<td>8.40</td>
<td>7.64</td>
</tr>
<tr>
<td>4</td>
<td>a4</td>
<td>13.66</td>
<td>14.63</td>
</tr>
<tr>
<td>5</td>
<td>calculation</td>
<td>C3, 37%</td>
<td>C3, 77%</td>
</tr>
<tr>
<td>6</td>
<td>experiment</td>
<td>C3, 44%</td>
<td>C3, 86%</td>
</tr>
</tbody>
</table>

Figure 5.2.16. Predicted (DFT/kinetics simulation) aldehyde distributions of (5-phenyl)-trans-2-hexene (left) and (6-phenyl)-trans-2-hexene (right) hydroformylation. The kinetics simulation is based only on the DFT-computed hydride migration, and the results are in excellent agreement with the experiments.

Indeed, the (DFT-)calculation of the product ratio$^{xxiii}$ based on the hydride migration predicts that the major product in the (6-phenyl)-trans-2-hexene hydroformylation would be the C3-aldehyde in 77%, while only 37% C3-aldehyde would be obtained from (5-phenyl)-trans-2-hexene (Fig. 5.2.16). These results are in excellent agreement with the experiments: the major product in each of the cases is predicted correctly, with the numeric values differing only slightly from

$^{xxiii}$using the kinetic simulation model built with the DFT-computed activation barriers
the experiments: 86% C3-aldehyde (77% calc.), and 44% C3-product (37% calc.) from (6-phenyl)- and (5-phenyl)-trans-2-hexene respectively (see entries 5 and 6 in Tab. 5.2.4). Importantly, these experiments confirm our model, in which the hydride migration determines the selectivity. It gives us a solid method for qualitative (and even near-quantitative) prediction of the distribution of regioisomers in the hydroformylation of internal alkenes by the ZnTPP-encapsulated catalyst.

5.3. Summary and Conclusions

In this contribution the mechanistic aspects of the internal alkene hydroformylation catalysed by the ZnTPP-encapsulated rhodium catalyst was reported. This catalyst was studied by detailed kinetics, \textit{in situ} spectroscopy, DFT calculations, and evaluation of deuteroformylation experiments, allowing identification of the rate- and selectivity-determining processes. The role of the supramolecular capsule in determining the selectivity for the hydroformylation of \textit{trans}-2-octene as archetypal substrate has been uncovered. Using the knowledge thus acquired, we were able to predict the regioselectivity of hydroformylation of two substituted 2-alkenes, and confirm this prediction experimentally.

From kinetics studies we found that the encapsulated catalyst follows an intermediate kinetics type, showing characteristics of type I and type II at 40°C or low CO concentrations, with CO dissociation/alkene coordination and hydrogenolysis determining the rate of reaction. At a lower temperature (25°C) and higher CO concentrations, type I kinetics dominates, and the rate limiting step is early in the cycle (the CO dissociation from the rhodiumhydrido resting state \textit{rsI}, subsequent alkene coordination step, and possibly the hydride migration). Deuteroformylation studies, together with the DFT computation coupled with the kinetic model of the catalytic cycle using the DFT-calculated activation barriers, allowed identification of the hydride migration as the selectivity-determining step. Moreover, the molecular models and the analysis of the hydride migration pathways unveiled the role of the capsule in determining the selectivity. The supramolecular capsule blocks or hinders the pathways by increasing the energies of the respective hydride migration transition states, for which the required capsule rearrangement energy is too high. For \textit{trans}-2-octene as substrate, most of the blocked pathways are those towards the C2-aldehyde, leaving the C3-aldehyde as the main product. In addition, using the combined DFT/kinetic model including only the hydride migration step with two novel substrates, (5-phenyl)- and (6-phenyl)-trans-2-hexene, we were able to predict the outcome of their hydroformylation with the ZnTPP-encapsulated catalyst. Thus, the ZnTPP-encapsulated catalyst is not only substrate-specific, but its substrate specificity is also predictable.

Thus, we are now in possession of a practical tool for predicting the outcome of internal alkene hydroformylation catalysed by the ZnTPP-encapsulated catalyst. Moreover, we found a similarity between the role of our synthetic capsule and that of the enzymes in the catalysis mechanism, indicating that the reactions in confined spaces – natural or synthetic – may have some common general guiding rules.

5.4. Experimental Section

5.4.1. General. Solvents used for pyridyl-phosphine synthesis, catalysis, spectroscopic (HP-FTIR, UV-Vis) and crystallisation experiments were dried and freshly distilled prior to use: toluene and hexane over Na/benzophenone and CH\textsubscript{2}Cl\textsubscript{2} over
CaH₂. Solvents for synthesis and column chromatography of porphyrins were used as obtained from the supplier. The deuterated solvents were dried and degassed using the freeze–pump–thaw technique and kept under Ar over 4 Å molecular sieves. 1-Octene and trans-2-octene were purified by filtration over alumina plug and degassed by Ar bubbling. All handling and manipulations, except synthesis and chromatographic purification of porphyrins, were performed under oxygen- and water-free atmosphere (dinitrogen, Ar or syngas).

NMR spectra were acquired on the Varian Mercury-VX 300, Bruker DRX300 or Bruker ARX400. The resonances are referenced to solvent itself as internal standard and are reported in parts per million (ppm). IR spectra were recorded on the Nicolet Nexus 670 FT-IR spectrometer operated by Omnic 6.2 Software. Gas chromatography (GC) analysis were done on the Shimadzu GC-17A chromatograph equipped with an FID detector using a 30 mm long column with 0.32 mm diameter and dimethylsiloxane cross-linked phase of 3 µm thickness.

Catalytic experiments were performed in mini-4-autoclaves, each equipped with a magnetic stirring bar and a glass insert, connected to the same high-pressure line, allowing all four reactions to be ran under the same pressure. Before each run the autoclaves were evacuated, flushed with nitrogen, and tested for leaks at ca. 35 bar syngas.

High-pressure FTIR spectroscopy experiments were conducted in an autoclave designed for the in situ monitoring of the reaction using infrared spectroscopy. The autoclave was cleaned, dried, tested for leaks (pressurized with 40 bar hydrogen for 16 hours), and flushed (3×15 bar) with syngas prior to every use.

The geometry optimisations of were performed using Gaussian 03 Rev. C.02 on the Dutch national computing cluster Lisa, which was installed by SARA, The Dutch National High Performance Computing and e-Science Support Center.

Molecular graphics images were produced using the UCSF Chimera package from the Resource for Biocomputing, Visualization, and Informatics at the University of California, San Francisco.

5.4.2. Synthesis of ZnII(porphyrin) complexes. Synthesis of porphyrins were performed according to the published procedures, in general following the Rothemund-Adler-Longo methodology of pyrrole condensation with the corresponding aldehyde (in 1:1 ratio) in boiling propionic acid under air atmosphere (described in the Section 4.4). Free-base porphyrins were precipitated by addition of methanol and cooling at 3°C. They were collected by filtration, washed thoroughly with cold methanol and purified by column chromatography (column material: basic alumina, eluent methylene chloride with 0.1 - 1 % methanol). The (NMR) purity of of thus obtained porphyrins was >90%. Metallation of the free-base porphyrins was performed by refluxing (3–5 hours) with 2.5–3.5 equivalents of Zn(CH₃COO)₂·2H₂O in ca. 5:1 chloroform/methanol mixture. The metallated porphyrin was obtained in >95% purity (NMR) after evaporation of the reaction solvent mixture, column chromatography (column material and eluent same as above) and filtration of insoluble residue (column material dissolved during chromatography). Yields of this step were 80–90%.

The tris-(meta-pyridyl)phosphine ligand was prepared using previously published procedure.
Table 5.4.1. Amounts of chemicals used in catalysis (per experiment). Total reaction volume was 4.0 ml, rhodium concentration 0.50·10\(^{-3}\) mol\(\cdot\)l\(^{-1}\).

<table>
<thead>
<tr>
<th>Compound</th>
<th>(m/(10^{-3}g))</th>
<th>equiv.</th>
<th>Substrate</th>
<th>(V/(10^{-6}l))</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZnTPP</td>
<td>20.35</td>
<td>15</td>
<td>trans-2-octene</td>
<td>157</td>
</tr>
<tr>
<td>Rh(acac)(CO)(_2)</td>
<td>0.516</td>
<td>1.0</td>
<td>cis-2-octene</td>
<td>157</td>
</tr>
<tr>
<td>(3- pyridyl)(_3)P</td>
<td>2.652</td>
<td>5.0</td>
<td>(5-Ph)-trans-2-hexene</td>
<td>182</td>
</tr>
<tr>
<td>diisopropylethylamine</td>
<td>10</td>
<td>30</td>
<td>(6-Ph)-trans-2-hexene</td>
<td>182</td>
</tr>
</tbody>
</table>

5.4.3. Catalytic Experiments. Typical procedure involved weighing of Zn\(^{II}\)-complex directly in the glass inserts of the autoclaves, which were then closed, set under inert atmosphere and filled with stock solutions (all in toluene, dipea was added neat) of ligand ((3- pyridyl)\(_3\)P), DIPEA (diisopropylethylamine), Rh(acac)(CO)\(_2\), 500 equivalents substrate, and was topped with toluene to 4.0 ml total volume. Alternatively, stock solutions of Zn\(^{II}\) complexes were used instead of weighing them directly. After filling, the autoclaves were flushed (3×25bar) with syngas, pressurised to 20 bar (CO/H\(_2\) = 1 : 1), immersed in an oil bath tempered at required temperature and stirred. The autoclaves were opened after the pressure release and flushing with nitrogen. Few drops of n-tributylphosphite were added to each reaction mixture for quenching. The crude reaction mixture (about 50 µl) was diluted with dichloromethane and injected into GC directly without work-up or product isolation.

Figure 5.4.1. \(^2\)H NMR spectra of the trans-2-octene deuteroformylation reaction mixture at 25 and 80\(^\circ\)C. The isomerisation is random and identical for both non-encapsulated, and the encapsulated catalyst. Legend: ♣ – aldehyde; ★ – C\(^{13}\)\(^{15}\)\(^{15}\)\(^{15}\)-2H; ♠ – toluene (solvent); rest – various C\(^{13}\)\(^{15}\)\(^{15}\)-2H, with ♣ most likely 3-octene.
Table 5.4.2. Deuteroformylation experiments results showing selective isomerisation of \(\text{trans}-2\)-octene to \(\text{cis}-2\)-octene with two encapsulated catalysts under encapsulation conditions, while the non-encapsulated catalysts produce statistical mixture of isomers. Conditions: \([\text{Rh}]=0.50 \cdot 10^3 \text{mol} \cdot \text{l}^{-1}, [\text{P}]/[\text{Rh}]=5.0, [\text{Zn}]/[\text{P}]=3.0, p=20 \text{bar}, \text{CO}/\text{H}_2=1:1, [\text{trans}-2\text{-octene}]/[\text{Rh}]=1000, 120\text{h}. \) Reaction mixture was quenched with tributylphosphite, diluted with \(\text{CH}_2\text{Cl}_2\) and analysed directly by GC.

(a) Deuteroformylation at 25°C. All numbers in %.

<table>
<thead>
<tr>
<th>Ligand</th>
<th>ZnTPP</th>
<th>ZnTPP((m)-OMe)</th>
<th>(P(m-py)_3)</th>
<th>PPh(_3)</th>
<th>calc.</th>
</tr>
</thead>
<tbody>
<tr>
<td>conversion(^a)</td>
<td>14</td>
<td>12</td>
<td>4</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>isomers(^b)</td>
<td>5.4</td>
<td>3.5</td>
<td>9</td>
<td>13</td>
<td>-</td>
</tr>
<tr>
<td>1-octene(^c)</td>
<td>7</td>
<td>17</td>
<td>32</td>
<td>36</td>
<td>(\sim 37)</td>
</tr>
<tr>
<td>(\text{cis}-2)-octene(^c)</td>
<td>85</td>
<td>70</td>
<td>26</td>
<td>20</td>
<td>(\sim 24)</td>
</tr>
<tr>
<td>(\text{trans}-3)-octene(^c)</td>
<td>8</td>
<td>13</td>
<td>42</td>
<td>44</td>
<td>(\sim 33)</td>
</tr>
<tr>
<td>C1-aldehyde(^b)</td>
<td>n.d.</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>-</td>
</tr>
<tr>
<td>C2-aldehyde(^b)</td>
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<td>10</td>
<td>56</td>
<td>54</td>
<td>-</td>
</tr>
<tr>
<td>C3-aldehyde(^b)</td>
<td>87</td>
<td>85</td>
<td>33</td>
<td>29</td>
<td>-</td>
</tr>
<tr>
<td>C4-aldehyde(^b)</td>
<td>n.d.</td>
<td>n.d.</td>
<td>n.d.</td>
<td>2</td>
<td>-</td>
</tr>
</tbody>
</table>

(b) Deuteroformylation at 80°C. All numbers in %.

<table>
<thead>
<tr>
<th>Ligand</th>
<th>ZnTPP</th>
<th>(P(m-py)_3)</th>
<th>PPh(_3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>conversion(^a)</td>
<td>44</td>
<td>35</td>
<td>87</td>
</tr>
<tr>
<td>isomers(^b)</td>
<td>78</td>
<td>18</td>
<td>6</td>
</tr>
<tr>
<td>1-octene(^c)</td>
<td>4</td>
<td>6</td>
<td>n.d.</td>
</tr>
<tr>
<td>(\text{cis}-2)-octene(^c)</td>
<td>41</td>
<td>40</td>
<td>22</td>
</tr>
<tr>
<td>(\text{trans}-3)-octene(^c)</td>
<td>55</td>
<td>55</td>
<td>78</td>
</tr>
<tr>
<td>C1-aldehyde(^b)</td>
<td>9</td>
<td>36</td>
<td>6</td>
</tr>
<tr>
<td>C2-aldehyde(^b)</td>
<td>11</td>
<td>42</td>
<td>53</td>
</tr>
<tr>
<td>C3-aldehyde(^b)</td>
<td>2</td>
<td>4</td>
<td>28</td>
</tr>
<tr>
<td>C4-aldehyde(^b)</td>
<td>1</td>
<td>n.d.</td>
<td>7</td>
</tr>
</tbody>
</table>

\(^a\) percentage of total converted substrate; \(^b\) percentage of formed products (aldehydes + isomers); \(^c\) percentage of total amount of isomeric octenes, excluding the substrate.

5.4.3.1. \textit{Deuteroformylation Experiments}. These experiments were performed analogously to the standard catalysis experiments (same solvent, catalyst concentration and overall pressure). The reaction time at 25°C was significantly prolonged (from 85 to 135 hours) in order to obtain sufficient (for NMR) amount of isomeric octenes, and the starting amount of 2-octene was increased to 1000 equivalents (314\(\cdot10^{-6}\)l). The temperature was elevated (to 85°C) in some experiments in order to study the isomerisation at lower encapsulation degrees; for same purposes we performed the experiments without ZnTPP (at both temperatures). Samples for GC-analysis were prepared as described, and ca. 0.7 ml of the raw reaction solution were taken for \(^2\text{H}\) NMR in deuteroformylation experiments (no other solvents added). By correlating the peaks in the GC with those in the NMR it was possible to assign them to isomeric alkenes formed in the reaction, as well as quantify their amounts. The results are listed in the Table 5.4.2.
5.4.4. Gas-Uptake Kinetics. The kinetics study was performed by monitoring the syngas uptake rate during the reaction \((p = \text{const.})\) at various pressures and three syngas compositions using the AMTEC robot.\(^{xxv}\) The reaction temperature of 40°C was chosen in order to obtain measurable gas flow rates. The concentrations of the catalyst and substrate were identical to those described above, however, the reaction volume was 8.0 instead of 4.0 ml, so that the amounts of compounds used for a single run were double of those given in the Table 5.4.1.

Procedure. ZnTPP, \((\text{meta-pyridyl})_3\)P and diisopropylethylamine were stirred in toluene (under Ar) for 30 minutes at room temperature, before Rh(acac)(CO)\(_2\) and trans-2-octene were added. Portions of 8.0 ml of this stock solution were transferred into the stainless steel autoclaves (all under Ar), which were flushed with syngas \((3 \times 15 \text{ bar})\) and pressurised to 20 bar. Gas uptake measurement started upon finished pressurisation of all autoclaves.

\(^{xxv}\)We kindly acknowledge the help of Dr. R. Detz, Dr. A. Kluwer and R. Bellini in these experiments.
Table 5.4.3. GC-analysis results of the reactions monitored by gas-uptake in the AMTEC robot.

<table>
<thead>
<tr>
<th>p/bar</th>
<th>Conv. [%]</th>
<th>Isomers [%]</th>
<th>Aldehydes [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>total</td>
<td>1-oct.</td>
</tr>
<tr>
<td>CO/H₂ = 1 : 1, 90 hours reaction time, c₀(substrate) = 0.25 mol·l⁻¹</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>97.6</td>
<td>2.8</td>
<td>0.0</td>
</tr>
<tr>
<td>20</td>
<td>95.1</td>
<td>2.6</td>
<td>0.2</td>
</tr>
<tr>
<td>30</td>
<td>93.0</td>
<td>2.5</td>
<td>0.2</td>
</tr>
<tr>
<td>40</td>
<td>87.7</td>
<td>3.3</td>
<td>0.2</td>
</tr>
<tr>
<td>CO/H₂ = 1 : 1, 60 hours reaction time, c₀(substrate) = 0.60 mol·l⁻¹</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>86.2</td>
<td>8.3</td>
<td>0.2</td>
</tr>
<tr>
<td>20</td>
<td>83.0</td>
<td>7.0</td>
<td>0.1</td>
</tr>
<tr>
<td>30</td>
<td>86.1</td>
<td>3.8</td>
<td>0.0</td>
</tr>
<tr>
<td>40</td>
<td>81.5</td>
<td>4.6</td>
<td>0.1</td>
</tr>
<tr>
<td>CO/H₂ = 1 : 2, 50 hours reaction time, c₀(substrate) = 0.25 mol·l⁻¹</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>95.8</td>
<td>2.8</td>
<td>0.0</td>
</tr>
<tr>
<td>23</td>
<td>95.6</td>
<td>2.2</td>
<td>0.0</td>
</tr>
<tr>
<td>30</td>
<td>94.6</td>
<td>2.1</td>
<td>0.0</td>
</tr>
<tr>
<td>45</td>
<td>91.6</td>
<td>2.2</td>
<td>0.0</td>
</tr>
<tr>
<td>CO/H₂ = 2 : 1, 50 hours reaction time, c₀(substrate) = 0.25 mol·l⁻¹</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>61.3</td>
<td>13.9</td>
<td>0.0</td>
</tr>
<tr>
<td>15</td>
<td>67.1</td>
<td>7.7</td>
<td>0.0</td>
</tr>
<tr>
<td>23</td>
<td>67.1</td>
<td>5.6</td>
<td>0.0</td>
</tr>
<tr>
<td>30</td>
<td>62.3</td>
<td>4.8</td>
<td>0.0</td>
</tr>
</tbody>
</table>

*percentage consumed trans-2-octene; †percentage of consumed trans-2-octene

Since the catalysis was started without prior gas-liquid equilibration and catalyst incubation period, the initial gas uptake data is not caused solely by substrate conversion (in the first 3-5 hours). The consequences thereof can be observed to a larger (at smaller pressures/higher CO concentration) or a smaller (higher pressures/lower CO concentration) degree, depending on the reaction conditions. Typically, the rates at the beginning of the reaction deviate from the trend displayed during the most of the reaction period. Therefore, the gas uptake values in the initial period were not taken in account, when this effect was significant, although the full data are shown in the graphs throughout this and the main text.

Three syngas compositions were employed, at four different total pressures:

CO/H₂ = 1 : 1: 10, 20, 30, and 40 bar; total reaction time 90 hours;xxvi
CO/H₂ = 1 : 2: 15, 23, 30, and 45 bar; total reaction time 50 hours;
CO/H₂ = 2 : 1: 8, 15, 23, and 30 bar; total reaction time 45 hours.

In addition, a series of four experiments at CO/H₂ = 1 : 1 (at 10, 20, 30, and 40 bar) was performed with 0.60 mol·l⁻¹ substrate (in other experiments it was 0.25 mol·l⁻¹). Upon de-pressurisation, tributylphosphite was added for quenching, and the samples were analysed by GC in a usual way (reaction mixture diluted with methylene chloride without product isolation). The results are shown in the

xxviFor initial substrate concentration of 0.25·10⁻³ mol·l⁻¹. The reaction time was 60 hours when 0.60·10⁻³ mol·l⁻¹ initial substrate concentration was used.
Table 5.4.3. The raw data, in ml gas, was correlated with conversion using the final values of either, so that the data pairs (substrate) concentration vs. time could be reconstructed. These data vectors were subject to as little numeric manipulation as possible,\textsuperscript{xxvii} the data points were smoothed, in order to perform numerical differentiation and obtain the substrate consumption rates ($r = -(dc/dt)$).

Applying reaction progress kinetic analysis\textsuperscript{187} to the data, we extracted thus the reaction rates, the rate orders in CO, H$_2$, and substrate concentration. Additionally, plot of the graphical rate equation was done in order to investigate potential decomposition or deactivation phenomena during catalysis. The orders in partial pressures of the gases were obtained by fitting the reaction rate vs. ($p(\text{CO}), p(\text{H}_2)$) surface to the equation $r = K \cdot p^m(\text{CO}) \cdot p^n(\text{H}_2)$ at different conversions (Fig. 5.4.3a).

The orders in CO and H$_2$ ($m$ and $n$) were also obtained from two-dimensional projections of the curves $r = f(p(\text{CO})|p(\text{H}_2)=$ const. and $r = f(p(\text{H}_2)|p(\text{CO})=$ const. by fitting the rate to the simplified equations $r = K' \cdot p^m(\text{CO})$ and $r = K'' \cdot p^n(\text{H}_2)$, respectively.

\textsuperscript{xxvii}No equation with physical meaning could be used for fitting the kinetics data.
Figure 5.4.5. Graphical rate equation of hydroformylation of trans-2-octene at four different pressures and 1:1 syngas. The overlap of the curves at 10 and 20 bar is a clear evidence that the catalyst decomposition does not occur under these conditions. At higher pressures (30 and 40 bar) the lines are a lot noisier and do not overlap, although they do have similar slope. This could be the consequence of the lowered signal-to-noise ratio at higher pressures or formation of dormant rhodium species, which decrease the available amount of catalytically active rhodium.

5.4.5. In-Situ High-Pressure Infrared Spectroscopy. These experiments were performed under conditions identical to those under which the catalytic experiments were done, with the only exceptions being the solvent and substrate concentration: here we used methylene chloride instead of toluene and 200 equivalents substrate (trans-2-octene) instead of 500. ZnTPP (86.45 \times 10^{-3} g, 12.75 \times 10^{-5} mol) and tris-meta-pyridyl)-phosphine (11.26 \times 10^{-3} g, 4.25 \times 10^{-5} mol, were stirred with DIPEA (46 \times 10^{-6} l ) in 13 \times 10^{-3} l methylene chloride in a Schlenk flask at ambient temperature for ca. 30 minutes. The mixture was transferred into the IR-autoclave under Ar, which was then flushed with syngas (3 \times 25 bar) and pressurised to 19 bar (CO/H₂ = 1:1). This solution was used for background correction spectrum (after the equilibrium was established between the gas and the liquid). The injection chamber of the autoclave was charged with solution of
Rh(acac)(CO)$_2$ (2.193 · 10$^{-3}$ g, 0.85 · 10$^{-5}$ mol) in 1.5-10$^{-3}$ l methylene chloride and pressurised to ca. 35 bar. Opening the valve to the main autoclave chamber injected the rhodium precursor to the ligand solution.

Formation of the rhodium-carbonyl complex was followed in the region around 2000 cm$^{-1}$, and after the system stabilised (1–2 hours), three bands at 2011, 2039, and 2089 cm$^{-1}$ were observed, corresponding to RhH(CO)$_3$L complex, with L being the supramolecular ligand [(3 – pyridyl)$_3$P·(ZnTPP)$_3$] (Fig. 5.4.7a).

The geometry of this pentacoordinated rhodiumhydrido complex is most likely the trigonal bipyramid, with the P atom in the equatorial plane and the hydride in one apical position. This is supported by DFT (pbe1pbe/dgdzvp) calculations.
5.4. EXPERIMENTAL SECTION

Figure 5.4.7. HP-FTIR of RhP(CO)$_3$H species and the carbonyl vibrational modes.

on a model system (without the ZnTPP molecules) as well, as the DFT-computed spectrum displays the same number of bands in approximately similar intensity ratio.\textsuperscript{xxviii} The bands at 2039 and 2089 cm$^{-1}$ are produced by combined CO and Rh–H stretches (vibrational modes 1 and 2, Fig. 5.4.7b), while the band at 2011 cm$^{-1}$ is due to the asymmetric stretch of the CO molecules (vibrational mode 3, Fig. 5.4.7b). Therefore, if the hydrogen were replaced with deuterium, only those vibrational modes in which the Rh–H stretch participates should be affected and, due to the higher reduced mass $\mu$ of the vibrational system ($\tilde{\nu} \sim \frac{1}{\sqrt{\mu}}$), they should be shifted towards lower wavenumbers. The DFT-computed spectrum of the analogous rhodiumdeuterido species shows indeed that exactly those bands shift, which correspond to the vibrational modes 1 and 2 (Fig. 5.4.8a). Also, the calculated shift was 7-10 cm$^{-1}$ to lower energies.

Repeating this experiment but using syngas with deuterium instead of hydrogen (CO/$^2$H$_2$ = 1 : 1) confirmed the DFT-computed changes, strongly supporting the proposed geometry of the rhodiumhydrido (-deuterido) complex (Fig. 5.4.8b). The shifts of the bands are:

1: 2089 (hydride) $\rightarrow$ 2082 cm$^{-1}$ (deuteride)
2: 2039 (hydride) $\rightarrow$ 2030 cm$^{-1}$ (deuteride)
3: 2011 cm$^{-1}$ - no change.

Injection of trans-2-octene to the rhodiumhydrido (-deuterido) species into the autoclave was performed under various conditions:

- 25°C and CO/$^2$H$_2$ = 1 : 1, 20 bar; this led to no changes in the region around 2000 cm$^{-1}$
- 40°C and CO/$^2$H$_2$ = 1 : 1, bar; the three bands decreased in intensity, and three new ones appeared at 2056 (weak), 2025 and 1992 cm$^{-1}$; all bands present

\textsuperscript{xxviii}The DFT-computed IR spectrum of the rhodiumhydrido species with all three CO molecules in the equatorial plane of the complex displays two very close bands of similar intensity at around 2000 cm$^{-1}$, and one very weak band at higher frequency ($\sim$2060 cm$^{-1}$). This IR-bands pattern is clearly different from the observed and therefore the structure with all three CO molecules in the equatorial plane is considered unlikely.
Figure 5.4.8. Comparison of DFT-computed and measured IR spectra of the RhP(CO)$_3$$^1$H rhodiumhydrido (rsI, black full line) and analogous RhP(CO)$_3$$^2$H rhodiumdeuterido (dash-dotted red line) species. Only those vibrational modes shift frequencies, which include Rh–H or Rh–D stretches.

- 25°C and excess hydrogen: CO/H$_2$ = 1 : 4, 23 bar; the three bands were replaced completely by the new three at 2050 (weak), 2023, and 1994 cm$^{-1}$ (Fig. 5.4.9a);
- 25°C and CO$_2$/H$_2$ = 1 : 1, 20 bar; acylrhodium species is visible due to slower activation of $^2$H$_2$ compared to $^1$H$_2$, thus allowing the accumulation of the acylrhodium resting state rsII (bands at 2051, 2023 and 1995 cm$^{-1}$, see Fig. 5.4.9d).

Clearly, this pattern indicates trigonal-bipyramidal geometry with three CO molecules in the equatorial plane, as is also supported by DFT-calculation of the acylrhodium species rsII with all-equatorial arrangement of the CO molecules (Fig. 5.4.9b). Similar spectra have been observed and assigned to the acylrhodium resting state rsII.$^{230, 231}$ The spectrum in Fig. 5.4.9a (formed under 23 bar CO/H$_2$ = 1 : 4 syngas) changes when the syngas composition is altered and CO is introduced to it in excess (CO/H$_2$ = 4.5 : 1, 25 bar total pressure). Then three bands of the rhodiumhydrido species rsI start reappearing slowly at 2011, 2039, and 2089 cm$^{-1}$. Comparison of reaction rates in these experiments at 25°C is shown in Fig. 5.4.10. Clearly, excess hydrogen does not accelerate the reaction as much as excess CO inhibits the catalysis.

5.4.6. Computational Details. The DFT computations were performed using Gaussian 03.$^{190}$, as indicated above, using the combination of the hybrid functional of Perdew, Burke, and Ernzerhof$^{217, 218}$ (pbe1pbe) with the DGAuss double-ζ double valence polarisation$^{215, 216}$ (dgdzvp) all-electron basis set.$^{254}$

5.4.6.1. The non-encapsulated catalyst. A similar computational study was performed by using ethylene as substrate, what circumvented the calculation of multiple pathways due to different rhodium-alkene intermediates.$^{255, 256}$ Our model catalyst is the monophosphine rhodium species with tris-(meta-pyridyl)-phosphine
as ligand in the rhodium equatorial plane, as supported by the in situ infrared spectroscopy. The equilibrium geometry optimisations of the non-encapsulated structures were performed with additional frequency calculation after the optimisation was finished, in order to obtain the free energy of the system (per default it was computed at 298 K, and those values are also given in the Table 5.4.4). The transition states were found by performing the relaxed scan computation along the reaction coordinate (backwards for the hydride migration and oxidative addition of hydrogen, forwards for the alkyl (CO) migratory insertion and reductive elimination of the aldehydes) in order to locate the preliminary, near-saddle point structure. Next, the transition state search with calculation of forces at every search step led to the saddle point structure in 3-5 steps. All transition state structures displayed an imaginary frequency in their infrared spectra, describing the motion of the bond breaking and/or the bond forming event in the transition state.

Figure 5.4.9. HP- IR Spectra of the catalyst resting states under various conditions.
5. SELECTIVITY AND THE ROLE OF THE CAPSULE – MECHANISM

![Graph](image)

**Figure 5.4.10.** Reaction rate and syngas composition: excess hydrogen accelerated the reaction less than the excess CO inhibits it.

![Energy diagrams](image)

**Figure 5.4.11.** Energy diagrams of the hydroformylation catalytic cycle with the non-encapsulated model catalyst.

The four rhodium alkene isomers a1–a4 undergo separate reaction pathways for the C3- and the C2-aldehydes. However, we have found that the different C3-paths merge into one after the alkyl migration step, since they all undergo this
Table 5.4.4. Free energies of the species participating in the catalytic cycle with the non-encapsulated catalyst (in kcal·mol$^{-1}$, at 25$^\circ$C). In parentheses are the energies of the alternative pathways for reductive elimination of the aldehyde (either of the H atoms of the dihydridorhodium species $e$ can undergo this reaction).

<table>
<thead>
<tr>
<th>species</th>
<th>starting rhodium-alkene isomer</th>
<th>a1</th>
<th>a2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>C3-path</td>
<td>C2-path</td>
</tr>
<tr>
<td>rsI + CO + H$_2$ + trans-2-octene</td>
<td>-7.92</td>
<td>-7.92</td>
<td>-7.92</td>
</tr>
<tr>
<td>f + 2CO + H$_2$ + trans-2-octene</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>a + 2CO + H$_2$</td>
<td>8.02</td>
<td>8.02</td>
<td>6.64</td>
</tr>
<tr>
<td>H-migration TS + 2CO + H$_2$</td>
<td>17.15</td>
<td>17.81</td>
<td>20.13</td>
</tr>
<tr>
<td>b + 2CO + H$_2$</td>
<td>2.83</td>
<td>6.69</td>
<td>2.16</td>
</tr>
<tr>
<td>c + CO + H$_2$</td>
<td>-2.12</td>
<td>-0.55</td>
<td>-2.12</td>
</tr>
<tr>
<td>alkyl migration TS + 2CO + H$_2$</td>
<td>13.15</td>
<td>14.05</td>
<td>13.15</td>
</tr>
<tr>
<td>d + CO + H$_2$</td>
<td>-11.92</td>
<td>-11.56</td>
<td>-11.92</td>
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<tr>
<td>rsII + H$_2$</td>
<td>-16.10</td>
<td>-15.84</td>
<td>-16.10</td>
</tr>
<tr>
<td>H$_2$ oxidative addition TS + CO</td>
<td>5.04</td>
<td>6.38</td>
<td>5.04</td>
</tr>
<tr>
<td>e + CO</td>
<td>-0.29</td>
<td>0.10</td>
<td>-0.29</td>
</tr>
<tr>
<td>aldehyde red. elimin. TS + CO</td>
<td>7.22 (7.78)</td>
<td>6.45 (7.47)</td>
<td>7.22 (7.49)</td>
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<tr>
<td>rs1 + aldehyde</td>
<td>-29.29</td>
<td>-29.48</td>
<td>-29.29</td>
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</table>

<table>
<thead>
<tr>
<th>species</th>
<th>a3</th>
<th>a4</th>
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<tbody>
<tr>
<td></td>
<td>C3-path</td>
<td>C2-path</td>
</tr>
<tr>
<td>rsI + CO + H$_2$ + trans-2-octene</td>
<td>-7.92</td>
<td>-7.92</td>
</tr>
<tr>
<td>f + 2CO + H$_2$ + trans-2-octene</td>
<td>0.00</td>
<td>0.00</td>
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<tr>
<td>a + 2CO + H$_2$</td>
<td>7.28</td>
<td>7.28</td>
</tr>
<tr>
<td>H-migration TS + 2CO + H$_2$</td>
<td>17.64</td>
<td>17.57</td>
</tr>
<tr>
<td>b + 2CO + H$_2$</td>
<td>8.71</td>
<td>4.40</td>
</tr>
<tr>
<td>c + CO + H$_2$</td>
<td>3.76</td>
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<tr>
<td>alkyl migration TS + 2CO + H$_2$</td>
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<td>14.05</td>
</tr>
<tr>
<td>d + CO + H$_2$</td>
<td>-8.03</td>
<td>-13.64</td>
</tr>
<tr>
<td>rsII + H$_2$</td>
<td>-15.87</td>
<td>-18.20</td>
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<tr>
<td>H$_2$ oxidative addition TS + CO</td>
<td>9.83</td>
<td>3.90</td>
</tr>
<tr>
<td>e + CO</td>
<td>-0.29</td>
<td>0.10</td>
</tr>
<tr>
<td>aldehyde red. elimin. TS + CO</td>
<td>6.65 (8.83)</td>
<td>5.89 (6.49)</td>
</tr>
<tr>
<td>rs1 + aldehyde</td>
<td>-29.29</td>
<td>-29.48</td>
</tr>
</tbody>
</table>

reaction (migration of the alkyl group to the coordinated CO and formation of the acylrhodium species $d$) through identical transition state. Equivalent is valid also for the C2-pathways. The free energy diagrams displayed in Figure 5.4.11, and Table 5.4.4 were obtained by summation of the free energies (at 298K) of the molecules participating in one catalytic cycle: the rhodium catalyst, CO, H$_2$, substrate and/or products.

5.4.6.2. The encapsulated catalyst. The optimised non-encapsulated structures of the model catalyst were used to construct the ZnTPP-encapsulated catalyst.
Table 5.4.5. Entropy-corrected SCF-energies of the species participating in the catalytic cycle with the ZnTPP-encapsulated catalyst (in kcal·mol⁻¹, at 25°C). Only one pathway for aldehyde elimination is shown, which is energetically more favourable. Entropy correction of 10 kcal·mol⁻¹ was applied to the species participating in reactions where the number of molecules changed (formation: -10 kcal·mol⁻¹ and consumption: +10 kcal·mol⁻¹ of molecules).

<table>
<thead>
<tr>
<th>species</th>
<th>starting rhodium-alkene isomer</th>
<th>a1</th>
<th>a2</th>
<th>a3</th>
<th>a4</th>
</tr>
</thead>
<tbody>
<tr>
<td>rsI + CO + H₂ + trans-2-octene</td>
<td>C3-path</td>
<td>-22.81</td>
<td>-22.81</td>
<td>-22.81</td>
<td>-22.81</td>
</tr>
<tr>
<td>f + 2CO + H₂ + trans-2-octene</td>
<td>C3-path</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>a + 2CO + H₂</td>
<td>C3-path</td>
<td>-13.05</td>
<td>-13.05</td>
<td>-12.31</td>
<td>-12.31</td>
</tr>
<tr>
<td>H-migration TS + 2CO + H₂</td>
<td>C3-path</td>
<td>1.07</td>
<td>9.50</td>
<td>-0.36</td>
<td>0.47</td>
</tr>
<tr>
<td>b + 2CO + H₂</td>
<td>C3-path</td>
<td>-20.43</td>
<td>-17.82</td>
<td>-26.17</td>
<td>-13.99</td>
</tr>
<tr>
<td>c + CO + H₂</td>
<td>C3-path</td>
<td>-35.70</td>
<td>-29.89</td>
<td>-35.70</td>
<td>-29.89</td>
</tr>
<tr>
<td>alkyl migration TS + 2CO + H₂</td>
<td>C3-path</td>
<td>-15.47</td>
<td>-24.96</td>
<td>-15.47</td>
<td>-24.96</td>
</tr>
<tr>
<td>d + CO + H₂</td>
<td>C3-path</td>
<td>-42.78</td>
<td>-47.36</td>
<td>-42.78</td>
<td>-47.36</td>
</tr>
<tr>
<td>rsI + H₂</td>
<td>C3-path</td>
<td>-68.11</td>
<td>-69.37</td>
<td>-68.11</td>
<td>-69.37</td>
</tr>
<tr>
<td>H₂ oxidative addition TS + CO</td>
<td>C3-path</td>
<td>-12.88</td>
<td>-16.25</td>
<td>-12.88</td>
<td>-16.25</td>
</tr>
<tr>
<td>e + CO</td>
<td>C3-path</td>
<td>-19.84</td>
<td>-25-28</td>
<td>-19.84</td>
<td>-25-28</td>
</tr>
<tr>
<td>aldehyde red. elimin. TS + CO</td>
<td>C3-path</td>
<td>-11.45</td>
<td>-12.06</td>
<td>-11.45</td>
<td>-12.06</td>
</tr>
<tr>
<td>f + CO + aldehyde</td>
<td>C3-path</td>
<td>-52.89</td>
<td>-53.24</td>
<td>-52.89</td>
<td>-53.24</td>
</tr>
<tr>
<td>rs1 + aldehyde</td>
<td>C3-path</td>
<td>-75.70</td>
<td>-76.05</td>
<td>-75.70</td>
<td>-76.05</td>
</tr>
</tbody>
</table>

molecules by simply replacing the tris-(meta-pyridyl)-phosphine with the crystal structure of the supramolecular capsule. The geometry optimisation was performed using the two-layer ONIOM\textsuperscript{191,192} method, with all except the ZnTPP molecules belonged to the high layer. The high layer was calculated using pbe1pbe/dgdzvp functional and basis set, while the three ZnTPP molecules in the low level were calculated with pbe1pbe/3-21g** level of theory. The cut between the levels was
Figure 5.4.12. Energy diagrams of the hydroformylation catalysis cycle with the ZnTPP-encapsulated catalyst.

Thus between the Zn (low layer) and the N\textsuperscript{py} (high layer) atoms. No dummy atoms were used. The energies of the transition states were computed by performing a normal geometry optimisation of the structure in which the atoms participating in the transition state were kept frozen (structure from the previously calculated non-encapsulated complex). Due to the size of the catalyst system, neither a proper transition state search, nor the calculation of forces could be conducted. A numerical evaluation of forces on one example molecule was not finished even after three months of continuing computations. We assumed that the geometry of the transition states would not differ greatly (if at all) in the non-encapsulated and the ZnTPP-encapsulated molecules, and by freezing the geometry from the non-encapsulated case, we were able to look mainly at steric effects affecting the energies of the transition states in the capsule. Moreover, the trends, rather than the exact energies were our main interest, and these could be well observed in spite of these approximations.

The SCF-energies obtained in calculations were corrected for entropy contributions to energy (at 298 K) in the reaction steps consuming, or creating a molecule by +10 and −10 kcal·mol\(^{-1}\) respectively.\textsuperscript{xix} The energies obtained in this way and the corresponding diagrams are shown in Table 5.4.5 and Figure 5.4.12.

5.4.6.3. ZnTPP-Encapsulation and Phenyl-Substituted Substrates. Using the structures optimised with trans-2-octene and analogous DFT method, computation of

\textsuperscript{xix}The entropy contribution to energy in the non-encapsulated case was 9.7 and 9.8 kcal·mol\(^{-1}\) in two arbitrary reactions.
the hydride migration step was performed with the two substituted trans-2-hexenes, (5-phenyl)- and (6-phenyl)-trans-2-hexene.

5.4.6.4. Capsule rearrangement energy. These energies were computed by removing the rhodium fragments from the previously optimised encapsulated complexes with trans-2-octene as substrate, leaving only the capsules ([3−pyridyl]₃P/(ZnTPP)₃) behind, which were then subject to single point energy calculations (DFT, pbe1pbe/dgdzvp). The energies of the capsules in their various conformations through the catalytic cycle obtained in this way are shown in the Table 5.4.7 and in the Figure 5.4.14.

5.4.6.5. The kinetic model of the catalytic cycle. The data obtained from the DFT calculations contains the geometries and relative energies of the species involved in the catalytic cycle. Also the (free in the case of the non-encapsulated model) activation energies could be obtained as differences between the equilibrium geometries and the neighbouring resting states. Using the Arrhenius equation

\[ k = A \cdot e^{-\frac{E}{RT}} \]

with \( A = 1 \cdot 10^{12} \text{s}^{-1} \), and the activation energies we were able to calculate the microconstants of the reaction steps (forward and backward) in the catalytic cycle. These microconstants were subsequently entered as parameters into
5.4. EXPERIMENTAL SECTION

(a) $\Delta E_A^{#} = 16.1 \text{ kcal} \cdot \text{mol}^{-1}$, (5-phenyl)-trans-2-hexene, C2-path

(b) $\Delta E_A^{#} = 18.2 \text{ kcal} \cdot \text{mol}^{-1}$, (6-phenyl)-trans-2-hexene, C2-path

(c) $\Delta E_A^{#} = 16.4 \text{ kcal} \cdot \text{mol}^{-1}$, (5-phenyl)-trans-2-hexene, C3-path

(d) $\Delta E_A^{#} = 16.6 \text{ kcal} \cdot \text{mol}^{-1}$, (6-phenyl)-trans-2-hexene, C3-path

Figure 5.4.13. Hydride migration transition states (from the a2-analogue rhodium alkene isomer as example) towards the C2- (first row) and the C3-alkylrhodium (second row) species with (5-phenyl)- (left) and (6-phenyl)-trans-2-hexene (right) as substrate.

The simulation model of the catalytic cycle, built with the Simbiology module (provided with the MATLAB® program package). In addition, in order to obtain the product distribution after hydride migration, a kinetic model was built using only the hydride migration step, whereby forward and backward (β-H elimination) reactions were taken in account. As rate law simple mass action law ($r = k \cdot c(a) \cdot c(b)$) was used. The flow charts of the simulation model (full catalytic cycle) is shown in Figure 5.4.16 as an illustration of the simplified, but still complex reaction network in this hydroformylation reaction.

R2010a, The Mathworks Inc.™
Since the transition states for CO or \textit{trans}-2-octene dissociation/association were not calculated, we assumed that their values were low in comparison to other reaction steps; therefore we used the barrier of 2 kcal mol\(^{-1}\) for CO, and 3 kcal mol\(^{-1}\) for \textit{trans}-2-octene dissociation/association as correction to the activation energies of the steps in which these events occur. Also, a correction of the activation barrier of the \(\text{H}_2\) oxidative addition to the ZnTPP-encapsulated species was necessary, since it was clearly overestimated by the computation (\(\sim 30\) kcal mol\(^{-1}\)). Increasing the order of magnitude of the corresponding microconstants (but keeping their relative ratio unchanged) let the simulation run within reasonable time frame. Initial concentrations of the rhodium catalyst and \textit{trans}-2-octene in the simulation were set to be identical as in the experiments, \(0.50 \times 10^{-3}\) mol l\(^{-1}\) and \(0.25\) mol l\(^{-1}\), respectively. The concentrations of CO and \(\text{H}_2\) were set at a constant value of 0.10 mol l\(^{-1}\).\(^{257}\)

As simulation output the concentrations of the aldehyde products and of the catalyst resting states were obtained (see the main text). In Figure 5.4.17 are

### Table 5.4.7. Capsule energies in the conformations during the catalytic cycle.

<table>
<thead>
<tr>
<th>species</th>
<th>(\text{a1})</th>
<th>(\text{a2})</th>
<th>(\text{a3})</th>
<th>(\text{a4})</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\text{rsI})</td>
<td>0.24</td>
<td>0.24</td>
<td>0.24</td>
<td>0.24</td>
</tr>
<tr>
<td>(\text{f})</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>(\text{a})</td>
<td>(-3.77)</td>
<td>(-3.77)</td>
<td>0.50</td>
<td>0.50</td>
</tr>
<tr>
<td>H-migration TS</td>
<td>0.05</td>
<td>8.74</td>
<td>0.03</td>
<td>8.73</td>
</tr>
<tr>
<td>(\text{b})</td>
<td>(-1.05)</td>
<td>1.19</td>
<td>(-2.13)</td>
<td>(-0.58)</td>
</tr>
<tr>
<td>(\text{c})</td>
<td>2.87</td>
<td>(-0.97)</td>
<td>2.87</td>
<td>(-0.97)</td>
</tr>
<tr>
<td>alkyl migration TS</td>
<td>4.25</td>
<td>(-4.65)</td>
<td>4.25</td>
<td>(-4.65)</td>
</tr>
<tr>
<td>(\text{d})</td>
<td>5.00</td>
<td>1.95</td>
<td>5.00</td>
<td>1.95</td>
</tr>
<tr>
<td>(\text{rsII})</td>
<td>(-3.81)</td>
<td>0.41</td>
<td>(-3.81)</td>
<td>0.41</td>
</tr>
<tr>
<td>(\text{H}_2) oxidative addition TS</td>
<td>1.34</td>
<td>(-0.30)</td>
<td>1.34</td>
<td>(-0.30)</td>
</tr>
<tr>
<td>(\text{e})</td>
<td>(-2.38)</td>
<td>(-3.32)</td>
<td>(-2.38)</td>
<td>(-3.32)</td>
</tr>
<tr>
<td>aldehyde red. elim. TS</td>
<td>(-1.08)</td>
<td>(-2.34)</td>
<td>(-1.08)</td>
<td>(-2.34)</td>
</tr>
</tbody>
</table>

Starting rhodium-alkene isomer C3-path C2-path C3-path C2-path C3-path C2-path C3-path C2-path
Figure 5.4.14. Energy diagrams of the capsule conformations in the hydroformylation catalytic cycle with the ZnTPP-encapsulated catalyst.
Figure 5.4.15. Energy diagrams of the capsule conformations in the hydroformylation catalytic cycle with the ZnTPP-encapsulated catalyst (continued).
Figure 5.4.16. The flow diagram of the kinetic simulation model for the full hydroformylation cycle. The catalysis intermediates, resting states, gases, substrate, and the products are represented as squares with rounded corners. The circles represent reactions, i.e., the transition states. Black lines with arrows connect the reacting species.

(a) full cycle, no encapsulation  
(b) H-migration, no encapsulation  
(c) resting states, no encapsulation  
(d) H-migration, ZnTPP-encapsulation

Figure 5.4.17. The simulated concentrations of the aldehydes, trans-2-octene, and the resting states during catalysis by the non-encapsulated catalyst. The results of the simulated product distribution for the ZnTPP-encapsulated catalyst based on the hydride migration are also shown (right).

According to
the simulation, the C3-aldehyde will be produced in 37% (Fig. 5.4.17) by the non-encapsulated monophosphine rhodium catalyst, while the (C2-acyl)rhodium resting state $\text{rsII}$ should be the major resting state (Fig. 5.4.17c). The simulations including the full catalytic cycle (Fig. 5.4.17a), as well as only hydride migration step (Fig. 5.4.17b) predict the product distribution close to that observed in experiments with the non-selective catalysts. The main resting state, however, with monophosphine rhodium catalyst should be the acylrhodium species (Fig. 5.4.17c), what is in agreement with our observation in experiments using the ZnPc-encapsulated catalyst (that also showed preference toward production of C2-aldehydes). Importantly, the simulation with the ZnTPP-encapsulated catalyst is in agreement with the experiments, here we show the results based on the hydride migration step (Fig. 5.4.17d).

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