Transition metal catalysts for the conversion of biomass inspired substrates
Jansen, E.

Link to publication

Citation for published version (APA):
Jansen, E. (2014). Transition metal catalysts for the conversion of biomass inspired substrates

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: http://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.

UvA-DARE is a service provided by the library of the University of Amsterdam (http://dare.uva.nl)
Chapter 5

Catalytic Hydrogenation of Polar Bonds Using Ru, Rh and Ir Catalysts with Bidentate NHC-Amine Ligands

**Abstract**

The use of a series of Ru, Rh and Ir half-sandwich complexes, bearing different bidentate NHC-amine ligands, in the hydrogenation of ketones and hydrogenolysis of esters was explored. Structural variations in the chelate ring size of the bidentate NHC-amine-type ligands revealed that smaller chelate ring-sizes in combination with ring-conjugation in the ligand is beneficial for the activity of these types of catalysts. Clear mechanistic differences between (p-cym)Ru(NHC-amine) and (Cp*)M(NHC-amine) complexes (M = Rh, Ir) were observed in the catalytic H₂-hydrogenation of acetophenone. Our results are consistent with reported calculations that p-cymene containing complexes favor an inner-sphere coordination pathway, while the Cp* containing complexes favor an outer-sphere coordination pathway. Additionally, increasing the steric bulk of the alkyl substituent on the NHC aided the reaction, showing almost no induction period and formation of a more active catalyst for the n-Bu complex compared to complexes with smaller Me and Et substituents. As is common in hydrogenation reactions, the activity of the complexes decreases in the order Ru > Ir > Rh. The application of complex 1, [Ru(p-cym)(NHC-amine)]PF₆ which outperforms its reported analogues, was successfully extended to hydrogenation of more challenging biomass-inspired substrates.

**5.1 Introduction**

As was described in the general introduction, hydrogenation of polar bonds can take place via an outer-sphere or an inner-sphere mechanism. Generally, reactions proceeding through outer sphere mechanisms are much faster since the reaction can take place without coordination of the substrate to the metal center, usually assisted by a bifunctional ligand.⁶ In this chapter, we focus on the hydrogenation of polar bonds and investigate the performance of several late transition metal complexes containing the potentially bifunctional NHC-amine (C₅H₅-N=NH₂) ligand A, described in Chapter 3 (shown in Figure 1).

![Image of ligands A, B, C](image)

**Figure 1.** The types of C₅H₅-N=NH₂ ligands referred to in this chapter. Ligand A is the NHC-aniline ligand synthesized by us, as described in Chapter 3. Ligand B and C were previously reported by Morris.⁵⁵ B is not reported in this form as the free ligand but is reduced on the transmetallating agent via reduction of an isonitrile group.
Our research is supported and complemented by reports of the group of Morris,\textsuperscript{[2-6]} who showed that, based on DFT calculations, a ruthenium complex of general structure I (Figure 2) containing C\textsubscript{NHC-NH\textsubscript{2}} ligand B in the H\textsubscript{2}-hydrogenation of acetophenone favors an inner sphere bifunctional mechanism, while a ruthenium complex of general structure II, with a Cp\textsuperscript{*} substituent instead of a p-cymene, facilitates a much faster outer sphere bifunctional mechanism. Illustratively, for the Ru-complexes I-B and II-B in the hydrogenation of acetophenone with H\textsubscript{2}, TOFs of 213 and 10800 mmol\cdot mmol\textsuperscript{-1}\textsuperscript{-1} hour\textsuperscript{-1} respectively, have been reported.\textsuperscript{[7,4]}

\textbf{Figure 2.} General structures of two types of complexes containing different chelate ring size C\textsubscript{NHC-NH\textsubscript{2}} ligands. Complexes I contain the neutral p-cymene as ancillary ligand and complexes II contain the anionic Cp\textsuperscript{*}.

Building on this work, we investigate the effect of structural variations of the catalyst on catalytic activity in H\textsubscript{2}-hydrogenation of ketones in more detail. In general, the activity of a catalyst is closely related to its structure: a small structural change can bring about large differences in activity and selectivity. To this end, we studied the influence of the chelate ring size of ligand A, B and C when coordinated to a metal center, the size of the alkyl substituent on the ligand and we varied the metal, correlating the structural parameters as reported in Chapter 2 to catalyst activity.

Based on the calculations of Morris, we can anticipate that also other complexes of general structure I follow the inner sphere route, and complexes of general structure II follow an outer sphere mechanism. This means that we anticipate to observe two possible trends in the catalytic reactions for general structures I and II when changing the ligand structure:

1 – The difference in chelate ring size is not expected to significantly influence the outer sphere mechanism, since the pre-organization of the substrate takes place in the second coordination sphere. The structure of the ligand and the smaller chelate will therefore only have minor influence on the catalytic performance. This will be seen for complexes with general structure II.

2 – The difference in chelate ring size is, however, expected to influence the inner sphere
mechanism significantly since the structure of the ligand and the smaller chelate push a lot of electron density into the NHC, enlarging the electron donating effect of the carbene. The possibility that the orbital overlap between amine and metal is less optimal due to the strained chelate ring can influence the coordination / decoordination of the amine which is needed if the substrate has to bind to the metal. This influence should be most pronounced for the complexes of general structure I.

Additionally, to rule out the influence of the different alkyl substituent on the NHC which is found between our complexes (nBu) and Morris (Me) we synthesized complexes with differing alkyl substituent and evaluated their catalytic activity as well.

The benchmark reaction that was used to investigate these influences is the hydrogenation of acetophenone. To evaluate the potential of the NHC-amine motif, we investigated the performance of these types of catalysts on more challenging compounds: biomass inspired model substrates such as cinnamaldehyde, and actual platform chemicals such as levulinic acid (LA) and hydroxymethyl furfural (HMF). Additionally, esters such as methyl butyrate (MB) or dimethyl oxalate (DMO) were tested. In doing so, we initiate broadening of the substrate scope of these NHC-amine containing complexes to include these platform chemicals. These substrates are of particular interest in the fine-chemical and pharmaceutical sector since they are all key building blocks or precursors for sustainable chemicals, materials and biofuels.

5.2 Results and Discussion

The Influence of Chelate Ring Size and Ligand Structure

First, we evaluated the influence of the chelate ring size of Ru-complexes of general structure II combined with ligands A, B and C in catalysis. The complexes are depicted in Figure 3.

Figure 3. [Ru(p-cym)Cl(C\text{NHC-NH}_2)]PF_6 complexes with different C\text{NHC-NH}_2 ligands. The synthesis of 1, containing ligand A is described in Chapter 3. Complexes 2 and 3 have been reported in literature, containing ligand C and B respectively.
Chapter 5

The results we obtained by applying 1 were compared with the activity reported for 2[3] and 3[7]. In Chapter 3 we investigated the structural parameters of the catalysts shown in Figure 3. The chelate ring size of these complexes decreases in the order 3 > 2 > 1 and the NHC ligands for complexes 1 and 2 appear to be more electron rich than 3 (for further structural details see Chapter 3).

Scheme 1. Benchmark catalytic hydrogenation of acetophenone with H₂.

As a benchmark reaction, the catalytic hydrogenation of acetophenone with H₂ in the presence of KOtBu in THF to 1-phenylethanol was investigated (see Scheme 1 and Table 1). The results in Table 1 show that the TOF value increases with decreasing chelate ring size: TOF (3) = 213 h⁻¹, TOF (2) = 298 h⁻¹ and TOF (1) = 548 h⁻¹ (entry 6, 4 and 1 respectively). Additionally, increasing the substrate loading leads to a linear increase of the TOF (entry 1-3, 548 vs 1202 vs 3609 h⁻¹) within the (limited) range studied. Such a high activity is unprecedented for this type of halfsandwich NHC-amine complexes in this reaction.

Table 1. H₂-hydrogenation of acetophenone with ruthenium complexes 1-3 of various chelating ring size.

<table>
<thead>
<tr>
<th>Entry[a]</th>
<th>Complex</th>
<th>C/B/S[b]</th>
<th>Conv (%/hr)[c]</th>
<th>TOF[d]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>1/8/100</td>
<td>99/0.5</td>
<td>548</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>1/8/200</td>
<td>99/0.5</td>
<td>1202</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>1/8/600</td>
<td>99/0.5</td>
<td>3609</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>1/8/200</td>
<td>99/1</td>
<td>298</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
<td>1/8/600</td>
<td>99/2</td>
<td>595</td>
</tr>
<tr>
<td>6</td>
<td>3</td>
<td>1/8/200</td>
<td>99/2</td>
<td>213</td>
</tr>
<tr>
<td>7</td>
<td>3</td>
<td>1/8/600</td>
<td>57/2.5</td>
<td>122</td>
</tr>
</tbody>
</table>

General Conditions: [a] Reactions (Scheme 1) were carried out at 25 bar H₂ and at 50 °C, in 15 ml THF using KOtBu as base. [b] C/B/S = catalyst/base/substrate ratio. [c] Conversions were determined by GC using p-xylene as an internal standard. [d] TOF = turnover frequency in mmol·mmol⁻¹·hr⁻¹ determined in steepest part of the plot (between 40-60% conversion). Details from complex 2[3] and 3[7] were taken from literature.

A linear dependence of the TOF with respect to the substrate concentration was also observed for complex 2 (entry 4 and 5, from 298 to 595 h⁻¹). Curiously, the opposite has been reported for complex 3[7]. The reported sandwich species RuCp*Cl(η⁶-(C(NHC-NH₂)) species...
Chapter 5

(see Chapter 3) was also tested in a catalysis run. In absence of a coordinating, electron donating NHC the catalytic activity of this Ru-sandwich species is low, converting 84% of acetophenone in 17 hr at 50°C and 25 bar H₂. To further investigate the effect of the chelate ring size, we turned our attention to the iridium and rhodium complexes 4, 5 and 6 shown in Figure 4. The chelate ring size of the Ir-complexes decreases in the order 5 > 4 and also here structural parameters indicate that the NHC of 4 is more electron rich compared to 5 (see Chapter 3).

**Figure 4.** [MCp*Cl(NHC-NH₂)]PF₆ complexes (M = Ir, Rh). Complexes 4 and 6 contain ligand A and the synthesis is described in Chapter 3. Ir-complex 5, containing ligand B, was reported in literature.[5]

While the iridium systems are less active than the ruthenium catalysts, indeed a similar relation between the TOF and the chelate ring effect was observed between the IrCp* complexes 4 and 5 (Table 2, entry 8 and 9). The effect is, however, much less pronounced. For the even less active rhodium complex 6 (entry 10, 11) we lack comparison with the larger 7-membered ring-sized equivalent.

**Table 2.** H₂-hydrogenation of acetophenone with iridium and rhodium complexes 4-6 of different chelating ring size

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>4</td>
<td>1/8/200</td>
<td>95/4</td>
<td>190</td>
</tr>
<tr>
<td>9</td>
<td>5</td>
<td>1/8/200</td>
<td>98/3</td>
<td>154</td>
</tr>
<tr>
<td>10</td>
<td>6</td>
<td>1/8/200</td>
<td>0</td>
<td>nd</td>
</tr>
</tbody>
</table>

General Conditions: [a] Reactions (Scheme 1) were carried out at 25 bar H₂ and at 50°C, in 15 ml THF using KOtBu as base. [b] C/B/S = catalyst/base/substrate ratio. [c] Conversions were determined by GC using p-xylene as an internal standard. [d] TOF = turnover frequency in mmol•mmol⁻¹•hr⁻¹ determined in steepest part of the plot (between 40-60% conversion). [e] p(H₂)=50 bar. Details from complex 5 were taken from literature.[6]

Besides Cross,[13] another related rhodium example containing a secondary amino tethered NHC, [Rh(cod)(L)] (L = 1-Mes-3-(2-(Mes-NH)ethyl)imidazolium), was reported by Fryzuk. [14] This complex did not show any activity in hydrogenation of polar bonds at all and only alkene hydrogenation was reported. Complex 6 thus seems to be the first Rh-NHC-amine
complex reported to be active in the direct hydrogenation of ketones. It becomes apparent that the influence of the structural variation in the NHC-amine ligand motif is smallest for the IrCp* complexes 4 and 5, that are assumed to follow an outer-sphere coordination pathway, and are largest for the Ru(p-cym) complexes 1-3, which are assumed to follow an inner-sphere coordination pathway, as was described in the introduction. The coordination of the substrate in the outer sphere is apparently less susceptible for the structural variations, and the electron donating strength of the NHC is in that case only of minor influence. The increased TOF for the Ru(p-cym) complexes (largest for complex 1, containing our C\textsuperscript{NH2}-NH\textsubscript{2} ligand) can be explained by two contributing effects:

1 – The smaller chelating ring size can account for a less tightly bound amine, since the system is more strained. The aniline is also less basic than the benzyl amine (pK\textsubscript{a} 4.6 vs 9.3)\textsuperscript{[15]} and both factors could cause the amine to dissociate more readily (necessary when following an inner-sphere pathway) thereby promoting coordination of the substrate.

2 – Additionally, the conjugated system renders the NHC more electron rich, therefore making it a stronger donor.

Variation of the Alkyl N-Substituent

Figure 5 depicts a series of synthesized complexes of general structure 1 with varying N-alkyl substituents on the NHC. The structure of 7c is identical to 1 except for the anion: PF\textsubscript{6} is replaced by I\textsuperscript{-}, which is also the anion for structures 7a and 7b.

We evaluated the influence of the N-alkyl substituent on the ligand, by testing complexes 7a-c in the H\textsubscript{2}-hydrogenation of acetophenone (Scheme 1, Table 3). This was initially done to rule out any influence of the differently substituted NHC of 3 (Me) and 1 (nBu) but, surprisingly, a substantial increase of the TOF was observed on going from the Me/Et complexes 7a/b to the nBu complex 7c (see Table 3).

**Figure 5.** [Ru(p-cym)\textsubscript{Cl}(C\textsuperscript{NH2}-NH\textsubscript{2})]I complexes with differently N-alkyl substituted C\textsuperscript{NH2}-NH\textsubscript{2} ligands. The synthesis of 7a (R = Me), 7b (R = Et) and 7c (R = nBu) is described in Chapter 3.
Table 3. H₂-hydrogenation of acetophenone with Ru-complexes 7a-c with varying alkyl substituents.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Complex</th>
<th>C/B/S</th>
<th>Conv (%/hr)</th>
<th>TOF</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>7a (R = Me)</td>
<td>1/8/200</td>
<td>99/0.5</td>
<td>909</td>
</tr>
<tr>
<td>13</td>
<td>7b (R = Et)</td>
<td>1/8/200</td>
<td>99/0.5</td>
<td>915</td>
</tr>
<tr>
<td>14</td>
<td>7c (R = nBu)</td>
<td>1/8/200</td>
<td>99/0.5</td>
<td>1543</td>
</tr>
</tbody>
</table>

General conditions: [a] Reactions (Scheme 2) were carried out at 25 bar H₂ and at 50 °C, in 15 ml THF using KOTBu as base. [b] C/B/S = catalyst/base/substrate ratio. [c] Conversions were determined by GC using p-xylene as an internal standard. [d] TOF = turnover frequency in mmol:mmol•hr⁻¹ determined in steepest part of the plot (between 40-60% conversion) and as an average of two runs.

Probably, this effect is primarily caused by differences in catalyst activation rates. Inspection of the reaction profile indeed reveals that the induction period for all complexes is different (Figure 6).

Figure 6. Performance in time of Ru(p-cym)Cl(C₅H₄N₂H₂) complexes 7a-7c in H₂-hydrogenation of acetophenone with varying alkyl substituents on the ligand. R = Me (red triangles), Et (green circles), nBu (blue squares).

At t = 0 the reaction mixture containing deprotonated complex and substrate is pressurized with H₂ forming the active species (Scheme 2). Going from nBu to Me the induction period becomes much longer, clearly pointing to differences in the rates of formation of the active species in each case. The larger bulk of the nBu group with respect to Me and Et substituents likely influences the spatial positioning of the ligand in such a way that the amine is tilted into a position closer to the metal center, rendering the complex better suited for activation of the incoming dihydrogen reagent, thus leading to more efficient catalyst activation (Scheme 2). Alternatively, the bulk of the nBu group might help to speed up elimination of the product in order to regenerate a new active species.¹⁶
Scheme 2. Catalyst activation by amine deprotonation followed by (bifunctional) dihydrogen activation involving heterolytic splitting of $H_2$ over the M-amine bond leading to the proposed activated species.

Complex 1 was shown to be the most active complex of the ones tested in acetophenone hydrogenation. Although we did not investigate the kinetics of this reaction, the fact that the electron donating strength of $C_{\text{NHNC-NH}_2}$ ligand A has a large influence on the catalytic activity suggests that the reaction proceeds via an inner sphere coordination pathway (see Scheme 3). This points to a classical mechanism in which the substrate coordinates directly to the metal and in which a stronger ligand donor leads to an enhanced 'hydridic character' beneficial for migration to the coordinated ketone substrate, which is a key step in the inner sphere catalytic cycle.

Scheme 3. A putative reaction scheme for the hydrogenation of a polar substrate (here acetophenone) for the [Ru(p-cym)Cl($C_{\text{NHNC-NH}_2}$)]PF$_6$ complex 1. After formation of the active species decoordination of the amine is needed to facilitate binding of the substrate, which is subsequently hydrogenated.

**Conversion of Platform Chemicals and Model Compounds Thereof**

To further investigate the performance of 1, several relevant types of biomass inspired substrates have been subjected to hydrogenation. More challenging and with a higher degree
of functionalization than acetophenone, these substrates are a good measure of the capacities of this type of NHC-amine containing catalysts for application in biomass conversion. The results are summarized in Table 4. When using levulinic acid (LA) as the substrate, only minor conversion to the ring-closed product γ-valerolactone was observed (Table 4, entry 1a), probably due to incompatibility of the acid with the amine functionality of the catalyst. Upon mixing the deprotonated complex with this acid, a color change from brown to green was observed showing that the conditions become acidic enough to protonate the amino-functionality\(^{[17]}\) to form a different active species. Raising the temperature as well as the pressure does improve the conversion (entry 1b) but increasing the substrate loading (entry 1c and 1b) does not. Applying the methyl ester of LA, methyl levulinate, in hydrogenation also showed selective conversion of the ketone functionality (Table 4, entry 2).

Table 4. Biomass inspired substrates tested in H\(_2\)-hydrogenation using [Ru(p-cym)Cl(C\(^{NHC}\)-NH\(_2\))]PF\(_6\) as catalyst.

<table>
<thead>
<tr>
<th>Entry(^{[a]})</th>
<th>Substrate</th>
<th>Conditions</th>
<th>Product</th>
<th>Conversion(^{[b]}) %</th>
<th>hr</th>
</tr>
</thead>
</table>
| 1a           | \[\text{\begin{tikzpicture}[baseline=-0.5ex]
    \node[anchor=west] at (0,0) {\text{O}};
    \node[anchor=west] at (0.5,0) {\text{O}};
    \node[anchor=west] at (1,0) {\text{OH}};
\end{tikzpicture}}\] | 50 °C, 25 bar H\(_2\) | \[\text{\begin{tikzpicture}[baseline=-0.5ex]
    \node[anchor=west] at (0,0) {\text{O}};
    \node[anchor=west] at (1,0) {\text{O}};
    \node[anchor=west] at (2,0) {\text{OH}};
\end{tikzpicture}}\] | 15 | 17 |
| 1b           | \[\text{\begin{tikzpicture}[baseline=-0.5ex]
    \node[anchor=west] at (0,0) {\text{O}};
    \node[anchor=west] at (0.5,0) {\text{O}};
    \node[anchor=west] at (1,0) {\text{OH}};
\end{tikzpicture}}\] | 70 °C, 50 bar H\(_2\) | \[\text{\begin{tikzpicture}[baseline=-0.5ex]
    \node[anchor=west] at (0,0) {\text{O}};
    \node[anchor=west] at (1,0) {\text{O}};
    \node[anchor=west] at (2,0) {\text{OH}};
\end{tikzpicture}}\] | 85 | 17 |
| 1c\(^{[c]}\) | \[\text{\begin{tikzpicture}[baseline=-0.5ex]
    \node[anchor=west] at (0,0) {\text{O}};
    \node[anchor=west] at (0.5,0) {\text{O}};
    \node[anchor=west] at (1,0) {\text{OH}};
\end{tikzpicture}}\] | 70 °C, 50 bar H\(_2\) | \[\text{\begin{tikzpicture}[baseline=-0.5ex]
    \node[anchor=west] at (0,0) {\text{O}};
    \node[anchor=west] at (1,0) {\text{O}};
    \node[anchor=west] at (2,0) {\text{OH}};
\end{tikzpicture}}\] | 15 | 17 |
| 1d\(^{[d]}\) | \[\text{\begin{tikzpicture}[baseline=-0.5ex]
    \node[anchor=west] at (0,0) {\text{O}};
    \node[anchor=west] at (0.5,0) {\text{O}};
    \node[anchor=west] at (1,0) {\text{OH}};
\end{tikzpicture}}\] | 70 °C, 50 bar H\(_2\) | \[\text{\begin{tikzpicture}[baseline=-0.5ex]
    \node[anchor=west] at (0,0) {\text{O}};
    \node[anchor=west] at (1,0) {\text{O}};
    \node[anchor=west] at (2,0) {\text{OH}};
\end{tikzpicture}}\] | 35 | 17 |
| 2            | \[\text{\begin{tikzpicture}[baseline=-0.5ex]
    \node[anchor=west] at (0,0) {\text{O}};
    \node[anchor=west] at (0.5,0) {\text{O}};
    \node[anchor=west] at (1,0) {\text{OH}};
\end{tikzpicture}}\] | 70 °C, 50 bar H\(_2\) | \[\text{\begin{tikzpicture}[baseline=-0.5ex]
    \node[anchor=west] at (0,0) {\text{O}};
    \node[anchor=west] at (1,0) {\text{O}};
    \node[anchor=west] at (2,0) {\text{OH}};
\end{tikzpicture}}\] | 86 | 17 |
| 3\(^{[e]}\)  | \[\text{\begin{tikzpicture}[baseline=-0.5ex]
    \node[anchor=west] at (0,0) {\text{O}};
    \node[anchor=west] at (0.5,0) {\text{O}};
    \node[anchor=west] at (1,0) {\text{OH}};
\end{tikzpicture}}\] | 80 °C, 80 bar H\(_2\) | \[\text{\begin{tikzpicture}[baseline=-0.5ex]
    \node[anchor=west] at (0,0) {\text{O}};
    \node[anchor=west] at (1,0) {\text{O}};
    \node[anchor=west] at (2,0) {\text{OH}};
\end{tikzpicture}}\] | 0  | 17 |
| 4            | \[\text{\begin{tikzpicture}[baseline=-0.5ex]
    \node[anchor=west] at (0,0) {\text{O}};
    \node[anchor=west] at (0.5,0) {\text{O}};
    \node[anchor=west] at (1,0) {\text{OH}};
\end{tikzpicture}}\] | 80 °C, 80 bar H\(_2\) | \[\text{\begin{tikzpicture}[baseline=-0.5ex]
    \node[anchor=west] at (0,0) {\text{O}};
    \node[anchor=west] at (1,0) {\text{O}};
    \node[anchor=west] at (2,0) {\text{OH}};
\end{tikzpicture}}\] | 29 | 24 |
| 5            | \[\text{\begin{tikzpicture}[baseline=-0.5ex]
    \node[anchor=west] at (0,0) {\text{O}};
    \node[anchor=west] at (0.5,0) {\text{O}};
    \node[anchor=west] at (1,0) {\text{OH}};
\end{tikzpicture}}\] | 70 °C, 50 bar H\(_2\) | \[\text{\begin{tikzpicture}[baseline=-0.5ex]
    \node[anchor=west] at (0,0) {\text{O}};
    \node[anchor=west] at (1,0) {\text{O}};
    \node[anchor=west] at (2,0) {\text{OH}};
\end{tikzpicture}}\] | 99 | 2  |
| 6            | \[\text{\begin{tikzpicture}[baseline=-0.5ex]
    \node[anchor=west] at (0,0) {\text{O}};
    \node[anchor=west] at (0.5,0) {\text{O}};
    \node[anchor=west] at (1,0) {\text{OH}};
\end{tikzpicture}}\] | 70 °C, 50 bar H\(_2\) | \[\text{\begin{tikzpicture}[baseline=-0.5ex]
    \node[anchor=west] at (0,0) {\text{O}};
    \node[anchor=west] at (1,0) {\text{O}};
    \node[anchor=west] at (2,0) {\text{OH}};
\end{tikzpicture}}\] | 47/2/38 | 6 |

General conditions: [a] Reactions were carried out at 25 bar H\(_2\) and at 50 °C, in 15 ml THF using KOtBu as base and complex 1 as cat; C/B/S = 1/8/200. [b] Conversions were determined by GC using p-xylene as an internal standard. [c] C/B/S = 1/8/2000 in 2 ml THF. [d] C/B/S = 1/8/1000. [e] C/B/S/\text{S}/ = 1/8/600.
Again, higher temperatures and pressures than those used in the benchmark reaction with acetophenone were required, resulting in 86% conversion overnight. The lower activity might be attributed to competition between coordination of the ketone and the ester functionality.

Substrates with linear ester functionalities are an important class of esters when it comes to biomass, as they are frequently found in natural oils. There have been several reports of the conversion of natural oils using ruthenium systems but, as is clear from entry 3, linear ester functionalities such as those in methyl butyrate are not converted by 1. However, the conjugated diester dimethyl oxalate (DMO), where one ester functionality activates the other one for hydrogenation, is converted slowly (29% conversion in 24 hr) to methyl glycolate (Table 4, entry 4). This is slower than previously reported activity from our group using a ruthenium system (Ru(acac)₃/triphos, see Chapter 2), but for this NHC-amine motif it’s a promising result, partly because no additives were needed and THF instead of fluorinated alcohols was used. The highly functionalized aldehyde HMF is converted to the bishydroxy compound furan-2,5-dimethanol in 2 hr at 70 °C and 50 bar H₂ (Table 4, entry 5). Application of the α,β-unsaturated compound cinnamaldehyde is a good measure for the selectivity of the catalyst. After 6 hr at elevated temperature and pressure, a roughly 50:50 product distribution of the hydrogenated ketone and the completely hydrogenated product was detected. The latter is probably formed by hydrogenation of the hydrocinnamaldehyde intermediate, which is only present in trace amounts throughout the entire reaction (Table 4, entry 6).

5.3 Summary and Conclusions

In conclusion, we have shown that half-sandwich complexes with an amino-tethered NHC, most notably ruthenium complexes, show good activity in hydrogenation of polar functionalities. Acetophenone is hydrogenated by [Ru(p-cym)Cl(C\text{NHC-NH}_2)]A (1, 7a-c) which likely proceeds via an inner-sphere mechanism showing excellent activity with TOFs as high as 3600 hr⁻¹ for complex 1 (Table 1). We are also the first to report a Rh-NHC-amine species of this type, [RhCp*Cl(C\text{NHC-NH}_2)]PF₆, to be active in the direct hydrogenation of ketones.

From the results we can conclude that the activity of this type of catalyst is influenced by the type of chelating ligand and the \textit{N}-substituent on the NHC: a conjugating, small chelate ring is beneficial for the activity. However, the influence is significantly more pronounced for catalysts that follow inner-sphere mechanism, the Ru(p-cym) complexes 1 and 7a-c. The catalysts that follow an outer-sphere mechanism, IrCp* 4 (and RhCp* 6) only have minor benefit from the structure of our ligand. This indicates that the most significant change, in
this case, is the additional electron density that stems from the conjugated aniline and is pushed into the NHC. A larger alkyl substituent on the NHC promoted the formation of the active species and thereby greatly reduces the induction period. Also, the bulk can help in the elimination of the formed product, thereby speeding up the reaction.

The applicability of complex 1 was successfully extended to key biomass derived substrates. Functionalized aldehydes, ketones and activated diesters were (partially) converted at moderate pressures and temperatures (50-80 bar H₂, 70-80 °C).

The combined results from this chapter and Chapter 3 have provided more thorough knowledge concerning the workings of Ru-, Ir- and Rh NHC-amine complexes in direct hydrogenation of polar functionalities, which will aid the future rational design of hydrogenation catalysts for conversion of biomass into useful and/or added-value compounds.

5.4 Experimental Section

General Remarks

All experiments were carried out under an atmosphere of purified nitrogen using standard Schlenk techniques. Solvents were freshly distilled under an argon atmosphere from sodium benzophenoneketyl (Toluene, THF, pentane and diethyl ether) and from CaH₂ (CH₂Cl₂ and MeCN). MeOH and i-prop were distilled from CaH₂ under a nitrogen atmosphere and were stored over 4Å molecular sieves. Acetophenone, methyl butyrate and methyl levulinate were distilled from CaH₂ under reduced pressure and stored in a dry nitrogen atmosphere over 4Å molsieves prior to use. Dimethyl oxalate was repeatedly crystallized from EtOH, dried under high vacuum and stored under a dry nitrogen atmosphere. Levulinic acid, hydroxymethylfurfural and cinnamaldehyde were degassed and stored under a dried nitrogen atmosphere prior to use. Hydrogen gas (purity 5.0) was obtained from Hoek Loos B.V. Holland, and used without additional purification or drying. Other reagents were obtained commercially and were used as received. Deuterated solvents (CDCl₃ and CD₂Cl₂) were distilled from CaH₂ under a nitrogen atmosphere and stored over 4Å molecular sieves. Synthetic procedures for 1, 4, 5, 6 and 7a-c are described in Chapter 3. Other reagents were obtained commercially and used as received. NMR spectra were recorded on either a Bruker AMX400 MHz, Bruker DRX 300 MHz, Varian Mercury 300 MHz or Varian INOVA 500 MHz. Products were determined with gas chromatography using p-xylene as internal standard, on a Thermo Scientific Trace GC Ultra system with a Restek RTX®-200 (30 meters, 0.25 mmID) capillary column with a split injecting method.
Chapter 5

General Procedure for Hydrogenations

Catalyst (0.014 mmol) and KOtBu (0.12 mmol) were weighed in a Schlenk tube, dissolved in 15 ml THF and stirred for 30 min to ensure formation of the deprotonated complex. The appropriate amount of substrate and p-xylene (internal standard, 1.4 mmol) were then added. A homebuilt stainless steel autoclave (with a volume of 200 ml; equipped with sample port, manometer and sample inlet) was flushed three times with nitrogen and the mixture was inserted into the autoclave under an outflow of nitrogen. The autoclave was then heated till the desired temperature (50-80 °C) was reached, flushed three times with H2 and filled with hydrogen gas until the appropriate pressure was reached (25-80 bar H2). If the reaction was monitored in time, samples were taken via a sample port (1st aliquot was discarded). After the reaction the autoclave was cooled to about 20 °C with an ice bath and the autoclave was vented carefully. The products were determined with gas chromatography using p-xylene as internal standard, on a Thermo Scientific Trace GC Ultra system with a Restek RTX®-200 (30 meters, 0.25 mmID) capillary column with a split injecting method. Additional characterization of several of the known products obtained from conversion of biomass inspired substrates was performed using 1H-NMR. The spectra of γ-valerolactone[22], n-butanol[23] and furan-2,5-dimethanol[24] were used for identification.

Acknowledgements

Linda Jongbloed is kindly acknowledged for her contributions to the work described in this chapter.

5.5 References

### Chapter 5


