Chapter 6

Mechanistic study of the L₂Pd catalyzed reduction of nitrobenzene with CO in methanol; a comparative study between diphosphane and 1,10-phenanthroline ligated complexes.

Abstract: The reactivity of Pd^{II} compounds supported by 1,10-phenanthroline (‘phen’) or the bidentate diaryl phosphane ‘L₄X’ has been studied in the reaction of nitrobenzene with CO in methanol. Both are ~70% selective for the ‘NPh-containing’ coupling products azo(xy)benzene (azo(xy)), but also produce carbonylation products (methylphenyl carbamate (MPC), N,N-diphenylurea (DPU)) and hydrogenation products (aniline and DPU (derived form aniline)). Only the Pd^{II}(L₄X) system concurrently produced significant amounts of methanol oxidation products (dimethyl carbonate (DMC), dimethyl oxalate (DMO), water). These findings could be rationalized by the mechanism developed for Pd/diphosphane catalysts, that is centred around a palladium-imido complex (Pd=NPh) being the terminal product of nitrobenzene de-oxygenation, and the sole product releasing species for all ‘NPh-containing’ products.

The palladacycle C₇ (Pd(OC)(N(Ph)OC(O))) was considered as an alternative carbonylation product releasing species, but the ESI-MS spectrum of ‘phen–C₇’, a ligand exchange experiment of ‘phen–C₇’ with L₄X, and a DFT study of nitrobenzene deoxygenation to (ligand)Pd=NPh all suggest that this is not the case; the barrier for C₇ decarbonylation (~CO) is lower than decarboxylation (~CO₂). Instead, C₇ is part of several CO-equilibrated palladacycles that merely act as temporary ‘NPh-reservoir’. As suggested by the catalytic data and other literature reports however, under acidic conditions the decarboxylation barrier is lowered; for ‘phen–C₇’ to the point where CO₂ extrusion is favored relative to decarbonylation, but for ‘L₄X–C₇’ the decarbonylation barrier is still lowest due to the destabilizing effect that this bulkier ligand has on such palladacycles.

It is thus concluded that the Pd=NPh complex is the prime ‘NPh’ product releasing intermediate and only under acidic condition C₇ may –depending on the ligand– become carbonylation product releasing.
6.1. Introduction

Studies in homogeneous catalysis are often motivated by financial and/or ecological incentives. One process in which both motivators are in play is the synthesis of the aromatic isocyanates\cite{1,2} such as the polymer precursors MDI and TDI\cite{3,4} (Figure 6.1). Both molecules are produced on the megaton scale per annum, using nitrobenzene as feedstock and employing the highly toxic\cite{5,6} and corrosive\cite{2} phosgene as carbonylating reagent.

![Figure 6.1. Two industrially produced aromatic isocyanates.](image)

Phosgene can in principal be replaced by the less toxic carbon monoxide as deoxygenating and carbonylating reagent, which in known to proceed in the presence of a transition metal catalyst.\cite{7} When this reaction is conducted in a protic medium such as an alcohol or an amine, a carbamate or urea is obtained (Scheme 6.1a) which can by pyrolyzed to the isocyanate with the recovery of the alcohol/amine (Scheme 6.1b).

![Scheme 6.1. Alternative route to make aromatic isocyanates by a carbonylation (a), followed by a pyrolysis (b).](image)

It was disclosed already in the advent of the 1980s working in methanol as the solvent, that reasonably active (~500 turn over numbers) palladium–based catalysts were obtained if the Pd–centre was stabilized by bidentate N–, or P–ligands.\cite{8} The ligand 1,10–phenanthroline (phen) proved most active (in the presence of an acid co–catalyst), which resulted in the focus of the scientific community on this Pd/phen/H\textsuperscript{+}/CH\textsubscript{3}OH catalytic system.\cite{12–23} Despite the fact that a very active catalytic system has been reported (~10\textsuperscript{5} turn over numbers),\cite{9} a clear–cut mechanism for this reaction involving common intermediates has yet to emerge. In general however, most proposals start from an in situ formed zero–valent palladium species, which is oxidized by nitrobenzene and CO to a
palladacyclic compound such as the one shown in Scheme 6.2a. Methylphenylcarbamate (MPC) can then be formed by a reaction with methanol.

![Scheme 6.2](image)

Scheme 6.2. Two simplified mechanistic proposals for the reductive carbonylation of nitrobenzene, catalyzed by a L₂Pd–catalyst wherein: a) L₂ is the N₂–donor ligand 1,10–phenanthroline; b) L₂ is a P₂–donor ligand such as bidentate diarylphosphines.

Chapters 3–5 reported on mechanistic studies of this carbonylation reaction in methanol, using bidentate diarylphosphane ligands and palladium.[10, 11] During these studies, a detailed mechanistic scheme was unravelled, wherein a palladium imido complex (‘Pd=NPh’) is the central key–intermediate species, rationalizing the formation of all observed products.[10, 11] A simplified version of this mechanism to rationalize the formation of MPC is shown in Scheme 6.2b. It was found that the postulation of a palladacyclic intermediate such as the one shown in Scheme 6.2a is, as product releasing species, both unlikely and explanatorily redundant in the Pd/P₂/CH₃OH catalytic system (see Chapters 3 and 4).[11]

During the studies described in the preceding chapters, it was unexpectedly found that the product distribution of the aryl–containing nitrobenzene reduction products is very similar when employing the N–donor ligand phen Figure 6.2, left) or the P–donor ligand L4X (Figure 6.2, right). Fascinated by this finding, it was investigated in what way proposed reaction mechanism (for phosphane stabalized Pd complexes) as outlined in Chapters 3–5 might be (a)similar for phen stabalized Pd complexes.

![Figure 6.2](image)

Figure 6.2. The N–donor ligand (phen) and the P–donor ligand (L4X) used in this study.
6.2. Results

6.2.1. General considerations

In all catalytic reactions, the catalyst precursor was formed *in situ* from 0.05 mmol Pd(OAc)$_2$ and a certain amount of ligand, as testing the catalytic activity of pre–formed complex gave identical results. By thoroughly drying of the reagents (see experimental), it was ensured that the reaction conditions were strictly anhydrous (<100 ppm H$_2$O).

The products that were observed in the catalytic reactions are shown in Scheme 6.3. Full analytical details for these products are given in Table AV.1 in Appendix V for all catalytic reactions. The aryl containing reduction products of nitrobenzene can be divided in the carbonylation products (‘NCO’) methylphenylcarbamate (MPC), and N,N’-diphenylurea (DPU), the coupling products (‘N=N’) azobenzene (Azo) and azoxybenzene (Azoxy), and the hydrogenation products (‘NH’) aniline (PhNH$_2$) and also DPU (derived from aniline).\(^{[12]}\)

![Scheme 6.3.](image)

Scheme 6.3. Overview of the different products that are formed in the palladium–catalyzed reaction of nitrobenzene with CO in methanol.

Azo and azoxy are frequently reported side–products, as are aniline and DPU.\(^{[7]}\)

Azo and azoxy are derived from nitrobenzene only, but for the formation of aniline and DPU, H-atoms are required. Their formation is therefore commonly attributed to the presence of water, either in the reagents or formed *in situ*, e.g. via acid–catalyzed etherification of methanol. However, it was shown in Chapter 3 that these H-atoms can also originate from methanol oxidation, resulting in the oxidative carbonylation products dimethyl carbonate (DMC) and dimethyl oxalate (DMO), and in the oxidative dehydrogenation products methyl formate (MF) and
carbon monoxide. The H-atoms are then transferred to water, and aniline (and thus also DPU; see Chapter 3 for details).

It is noteworthy that neither dimethyl ether (DME) nor dimethoxy methane (DMM, commonly observed in palladium catalyzed carbonylation experiments under reducing or redox neutral conditions involving methanol as substrate)\cite{13} has been observed as a reaction product. This indeed excludes methanol self-etherification or etherification with any possibly formed (uncoordinated) formaldehyde under reaction conditions as a source of water and/or protons for aniline and DPU.

As it is known that at reaction temperatures (110–130 ºC) DPU reacts with methanol to MPC and aniline,\cite{10} it is best to view DPU and MPC together as carbonylation products, and aniline and DPU together as hydrogenation products. Although the coupling products Azo and Azoxy were almost always detected, Azoxy is always the major product and Azo the minor product (< 2% selectivity).

6.2.2. Catalytic experiments

6.2.2.1 Reactivity without additives or co–catalysts

Using GLC analysis of the reaction mixtures, all products could be quantified with calibration lines made from authentic samples. The accuracy of the quantitative analysis of the phenyl–containing products is excellent as confirmed by the sum of the aryl rings (column $\Sigma\phi$ in Table 6.1).

When employing Pd$^{II}$(phen), and operating at 110 ºC (entry 1), only 17% conversion was achieved, whereas operating at 130 ºC (entry 2), 56% nitrobenzene was converted. This reactivity at 130 ºC is similar as for the Pd$^{II}$(L4X) catalytic system at 110 ºC (52% conversion, entry 3).

Both catalytic systems are roughly equally selective for the reductive coupling product Azoxy (~70%); Pd$^{II}$(phen) is more selective towards carbonylation (20%) while Pd$^{II}$(L4X) is more selective towards hydrogenation (20%). Notably, using Pd$^{II}$(L4X), large quantities of oxidation products of methanol were co-produced (DMC, DMO, MF, and H$_2$O), whereas these products are hardly formed when using Pd$^{II}$(phen).
Table 6.1. Reactions of nitrobenzene with CO in methanol, using Pd\(^{II}\)(phen)(OAc)\(_2\) or Pd\(^{II}\)(L4X)(OAc)\(_2\) as catalyst precursor.\([a]\)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ligand</th>
<th>Temp. (°C)</th>
<th>Conv. (%)([b])</th>
<th>(\Sigma_{X})</th>
<th>Selectivity (%)</th>
<th>mmol</th>
<th>MF</th>
<th>H₂O</th>
<th>DMC/O</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>phen</td>
<td>110</td>
<td>17</td>
<td>24.7</td>
<td>NCO([c]) = 23</td>
<td>71</td>
<td>6</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>2</td>
<td>phen</td>
<td>130</td>
<td>56</td>
<td>24.3</td>
<td>N=N([d]) = 22</td>
<td>71</td>
<td>7</td>
<td>0.2</td>
<td>0.3</td>
</tr>
<tr>
<td>3</td>
<td>L4X</td>
<td>110</td>
<td>52</td>
<td>24.4</td>
<td>NH([e]) = 8</td>
<td>73</td>
<td>19</td>
<td>0.2</td>
<td>10.1</td>
</tr>
</tbody>
</table>

[a] Reactions were heated for four hours at the indicated temperature in 25.0 ml dry and degassed methanol under 50 bar CO. The catalyst was always generated in situ from 0.05 mmol Pd(OAc)\(_2\). Mole ratio’s are: Pd(OAc)\(_2\) : Ligand : nitrobenzene = 1 : 1.5 : 488. All reactions were performed in quadruplet and the relative standard deviation of all analytes was < 5% in all cases. [b] Conversion = (\(\Sigma_{aryl\ converted}\))/24.4 \(\times\) 100%. [c] Selectivity towards carbonylation products = (MPC + DPU) / \(\Sigma_{aryl\ converted}\) \(\times\) 100%. [d] Selectivity towards coupling products = (2 \(\times\) Azo + 2 \(\times\) Azoxy) / \(\Sigma_{aryl\ converted}\) \(\times\) 100%. [e] Selectivity towards hydrogenation products = (PhNH\(_2\) + DPU) / \(\Sigma_{aryl\ converted}\) \(\times\) 100%.

6.2.2.2 The effects of the initial nitrobenzene concentration

Intrigued by the similar selectivity for reductive coupling products (mainly Azoxy) of Pd\(^{II}\)(phen) and Pd\(^{II}\)(L4X) catalyst systems, it was investigated if the selectivity for these coupling products can also be manipulated in the same way. As it was suspected that the coupling products stem from a disproportionation or ‘metathesis’ of a palladium–imido complex (“Pd=NPh”) and nitrobenzene,\([10]\) and because it is known that the selectivity towards coupling products depends on the concentration of nitrobenzene when using Pd\(^{II}\)(L4X),\([11]\) the initial concentration of the nitrobenzene was varied in the Pd\(^{II}\)(phen) catalytic system. As is shown in Figure 6.3 (derived from data in Table S1), the relative ratio of carbonylation (NCO) and hydrogenation (NH) products over coupling (N=N) products decreases significantly with increasing nitrobenzene concentrations. This suggests that the formation of Azo(xy) coupling products from nitrobenzene involves a directly competing step with its carbonylation and hydrogenation, but with higher order kinetics in nitrobenzene.

Figure 6.3. Plot of the ratio of (carbonylation (NCO) and hydrogenation (NH) products) relative to the amount of coupling products (N=N) as a function of the initial concentration of nitrobenzene in mol.L\(^{-1}\), when using Pd\(^{II}\)(phen) as catalyst precursor. The line is added as an aid for the eye.
6.2.2.3 The effects of the added acid

The selectivity towards coupling products in the Pd\textsuperscript{II}(L4X) catalytic system is sensitive to (sub)stoichiometric amounts of acid.\textsuperscript{[10]} It is known that stoichiometric amounts of acid influence the selectivity for the Pd\textsuperscript{II}(phen) catalytic system.\textsuperscript{[14-16]} Thus, some experiments were conducted wherein sub-stoichiometric amounts (on Pd) of \textit{para}–toluenesulfonic acid (HOTs) were added, using the standard experimental conditions (i.e., 110 °C for Pd\textsuperscript{II}(L4X) and 130 °C for Pd\textsuperscript{II}(phen)).

As shown in Figure 6.4a for the Pd\textsuperscript{II}(L4X) catalytic system, the conversion increases when adding more HOTs, whereas for the Pd\textsuperscript{II}(phen) catalytic system (Figure 6.4b), the conversion remains constant. Interestingly, in both systems the coupling reaction is significantly suppressed already when adding sub-stoichiometric amounts of HOTs. The selectivity becomes however, drastically different for the two catalysts: when using Pd\textsuperscript{II}(L4X) as catalyst precursor, both the hydrogenation and carbonylation reactions become more important, whereas the carbonylation reaction becomes highly dominant when employing Pd\textsuperscript{II}(phen). This indicates that the influence of acid operates through a different reaction mechanism for both systems.

![Figure 6.4. Plot of the conversion (+) and selectivity towards coupling products (●, Azo(xy)), hydrogenation products (○, DPU+PhNH\textsubscript{2}), and carbonylation products (○, MPC+DPU) as a function of the amount of \textit{p}–toluenesulphonic acid added (relative to Pd), when using the ligands L4X @ 110 °C (a) and phen @ 130 °C (b). The lines are added as a guide for the eye.]

To investigate if this effect may be related to the anion of the acid, rather than the acidity itself, some reactions were performed, adding half an equivalent of 1,3,5–trimethylbenzoic acid (TMBA, \(pK_a = 3.43\)),\textsuperscript{[17]} HOTs (\(pK_a = -2.7\)),\textsuperscript{[17]} or the dibasic phenylphosphonic acid (PPA, \(pK_{a1} = 1.85\)).\textsuperscript{[17]} For the Pd\textsuperscript{II}(L4X) catalytic system (Figure 6.5a), the conversion increases in the order TMBA < HOTs < PPA, and the coupling is always suppressed mainly in favor of the hydrogenation.
For the Pd\textsuperscript{II}(phen) catalytic system, the conversion also increases in the order TMBA < HOTs < PPA, and the coupling reaction is also suppressed, but now very predominantly in favor of the carbonylation reaction.

That the effect with TMBA is less pronounced in the Pd\textsuperscript{II}(phen) system can be due to the relatively low acidity of this acid (compared to HOTs and PPA) or because TMBA can be partly esterificated with methanol at 130 °C, as it has been reported that adding more of this acid also results in higher selectivity towards carbonylation products when using Pd\textsuperscript{II}(phen).\cite{15}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure6.5}
\caption{The selectivity when using Pd\textsuperscript{II}(L4X) @ 110 °C (a) or Pd\textsuperscript{II}(phen) @ 130 °C (b), and adding 0.5 equivalent (on Pd) of the indicated acid. Carbonylation products = □ (MPC+DPU), coupling products = ■ (Azo+Azoxy) and hydrogenation products = ▼ (PhNH\textsubscript{2}+DPU). The conversion based on nitrobenzene (within parentheses) is also given. All experiments were performed (using the same conditions as reported in Table 6.1) in triplo and the relative standard deviation of all analytes was always < 5%.
}
\end{figure}

To further investigate if the effect of adding HOTs to the Pd\textsuperscript{II}(phen) system is really due to the proton concentration, it was attempted to buffer this strong acid by adding a weak base in the form of extra phen ligand. Shown in Figure 6.6a and b are the control experiments wherein the Pd:phen:HOTs molar ratio is 1:1.5:0 (Figure 6.6a) or 1:1.5:0.5 (Figure 6.6b), showing a ~7-fold decrease in coupling products on addition of acid. When using 5 equivalents of phen on Pd (Figure 6.6c), and adding 0.5 equivalents of HOTs (Figure 6.6d) led to ~5-fold decrease in coupling products. Adding more HOTs (Figure 6.6e), gives a gain in carbonylation selectivity to about 90 %, while a ~12 fold decrease in coupling products results compared to the experiment without adding HOTs (Figure 6.6c).
Note that in all three experiments using 5 equivalents of phen ligand (Figure 6.6c–e) the conversion increased (roughly from 50 to 90%). This can be ascribed to the stabilizing effect that extra phen ligand can have on zero valent palladium reaction intermediates.\textsuperscript{[16]}

![Figure 6.6](image)

**Figure 6.6.** The selectivity when using a Pd(OAc)\textsubscript{2}:phen:HOTs ratio of: (a) 1:1.5:0; (b) 1:1.5:0.5; (c) 1:5:0; (d) 1:5:0.5; (e) 1:5:2. Carbonylation products = (MPC+DPU), coupling products = (Azo+Azoxy) and hydrogenation products = (PhNH\textsubscript{2}+DPU). The conversion based on nitrobenzene (within parentheses) is also given. All experiments were performed (using the same conditions as reported in Table 6.1) in triplo and the relative standard deviation of all analytes was always < 5%.

It thus appears for both catalytic systems, that when working under (mildly) acidic conditions, the coupling reaction is suppressed in favour of either the carbonylation product (Pd\textsuperscript{II}(phen)) or of both carbonylation and hydrogenation products (Pd\textsuperscript{II}(L4X)). For the Pd\textsuperscript{II}(phen) system, HOTs could be buffered by adding a weak base in the form of extra phen ligand.

### 6.2.2.4 Nitrosobenzene as intermediate for Azo or Azoxy?

It has been suggested that in the Pd\textsuperscript{II}(phen) catalytic system, nitrobenzene becomes first reduced to ‘free’ nitrosobenzene and then reacts further to form mainly Azoxy (and some Azo).\textsuperscript{[18, 19]} It was investigated if elevated amounts of Azo and Azoxy could be detected when adding 2.5 mmol nitrosobenzene during a catalytic run (see experimental for details). As can be seen in Figure 6.7 however, when employing either Pd\textsuperscript{II}(L4X) or Pd\textsuperscript{II}(phen), both the conversion and selectivity are nearly identical to a ‘normal’ catalytic experiment. No significant increase in the selectivity for Azo (max. 1.5%) and Azoxy could be observed. Interestingly, no nitrosobenzene could be detected after the catalytic run, while a
significant amount of nitrobenzene was still present. This shows, that, consistent with the observation of only traces of nitrosobenzene in ordinary catalytic experiments, whereas nitrosobenzene is more prone to reductive carbonylation reactions\cite{20} than is nitrobenzene, still a very similar product composition is obtained, and that nitrosobenzene must thus not be considered as prime intermediate towards Azo or Azoxy.

![Figure 6.7](image)

**Figure 6.7.** The selectivity when using Pd\textsuperscript{II}(L4X) @ 110 °C (left) or Pd\textsuperscript{II}(phen) @ 130 °C (right), with or without adding 2.5 mmol nitrosobenzene during a catalytic run. Carbonylation products = □ (MPC+DPU), coupling products = ■ (Azo+Azoxy) and hydrogenation products = ◼ (PhNH\textsubscript{2}+DPU). The conversion based on nitrobenzene(nitrosobenzene) is given within parentheses. Conversion is based on (Σaryl converted)/(24.4+mmol PhNO added) × 100%. Reaction conditions were as reported in Table 6.1.

6.2.2.5 Azo or Azoxy as intermediate for MPC, DPU or aniline?

Azo or Azoxy, might be themselves intermediately produced and could react further to MPC, DPU and/or aniline, as is suggested when working with the Pd/phen/H\textsuperscript{+} system at 155 °C.\cite{21} As shown in Table 6.2 however, when adding 2.5 mmol Azo (entry 2) or Azoxy (entry 3) to the Pd\textsuperscript{II}(phen) catalytic system, the same amount (plus the amount formed, entry 1) could be detected after the catalytic run, even when using 1 equivalent of HOTs and 2.5 mmol Azoxy (entry 4). This means that Azo and Azoxy are stable reaction products and cannot be intermediates towards MPC, DPU or aniline employing the standard reaction conditions of 130 °C and 50 bar CO.
Table 6.2. Catalytic reaction employing Pd\textsuperscript{II}(phen)(OAc)\textsubscript{2} and using 4.9 mmol PhNO\textsubscript{2} and the indicated additives.\textsuperscript{[a]}

<table>
<thead>
<tr>
<th>Entry</th>
<th>Additive (mmol)</th>
<th>(\Sigma)</th>
<th>PhNO\textsubscript{2}</th>
<th>PhNH\textsubscript{2}</th>
<th>MPC</th>
<th>DPU\textsuperscript{[b]}</th>
<th>Azo</th>
<th>Azoxy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>–</td>
<td>4.8</td>
<td>0.1</td>
<td>0.5</td>
<td>1.6</td>
<td>–</td>
<td>0.2</td>
<td>1.1</td>
</tr>
<tr>
<td>2</td>
<td>2.5 Azo</td>
<td>10.0</td>
<td>0.8</td>
<td>0.4</td>
<td>1.5</td>
<td>–</td>
<td>2.7</td>
<td>1.0</td>
</tr>
<tr>
<td>3</td>
<td>2.5 Azoxy</td>
<td>10.1</td>
<td>1.4</td>
<td>0.3</td>
<td>0.5</td>
<td>–</td>
<td>0.3</td>
<td>3.6</td>
</tr>
<tr>
<td>4</td>
<td>2.5 Azoxy + 0.025 HOTs</td>
<td>10.1</td>
<td>0.3</td>
<td>0.4</td>
<td>1.3</td>
<td>–</td>
<td>0.5</td>
<td>3.6</td>
</tr>
</tbody>
</table>

\[a\] Reactions were heated for four hours at 130 °C in 25.0 ml dry and degassed methanol under 50 bar CO pressure. The catalyst was always generated \textit{in situ} from 0.05 mmol Pd(OAc)\textsubscript{2}. Mole ratio’s are: Pd(OAc)\textsubscript{2} : phen : nitrobenzene = 1 : 1.5 : 98. \[b\] not detected as the reaction mixture was a clear solution.

### 6.2.3. Synthesis and characterisation of possible palladium intermediates

#### 6.2.3.1 (Attempted) synthesis of a palladacyclic complex and DFT calculations

Most mechanistic proposals for the Pd/phen catalytic system are centered around palladacyclic intermediates, in particular the one shown in Scheme 6.2a.\textsuperscript{[7, 21-23]} This five-membered palladacyclic complex is thermally stable to about 170 °C,\textsuperscript{[23]} but upon addition of an acid and heating to 90 °C in ethanol this complex smoothly decomposes to yield ethylphenylcarbamate (80%).\textsuperscript{[23]} This complex was therefore also considered as a possible (MPC, DPU) product releasing intermediate for the L4X-palladium catalytic system.

The palladacycle with phen as the supporting ligand could easily be obtained (see experimental for details) according to a literature procedure.\textsuperscript{[23]} When applying the same procedure and using L4X as the ligand however, the anticipated ‘L4X-palladacycle’ could not be obtained, nor was an asymmetric complex observed in the resulting reaction mixture, such as previously detected in \((^{31}\text{P}\{^1\text{H}\}\text{NMR})\) measurements for other phosphane-palladium catalysts.\textsuperscript{[11]} One possible explanation for the apparent lack of ‘L4X-palladacycle’ formation, is that the steric constraints in the equatorial position of such five–membered ring species lead to its de-stabilisation. Especially since the steric constraints in such complexes is influenced by the ligand bite angle (\(\beta\)), which is much smaller for the ligand phen (\(~78^\circ\) ), than for bidentate diaryl phosphane ligands with a butylene backbone (96°). Indeed, when the above experiment was conducted with the sterically less demanding ‘L3X’ (i.e. 1,3–bis(diphenylphosphino)–...
2,2′-dimethylpropane), the asymmetric complex, be it initially clearly formed, is gradually disappearing over time (during the workup). DFT calculations of the palladacycle with L3X,[10] but also with L4X and L4 (a simplified version of L4X) as the supporting ligand (see section AV.1. of Appendix V for details), indeed suggest that phosphane ligands can significantly (ca. 15 kcal.mol\(^{-1}\)) destabilize the palladacycle relative to the phen-analogue.

6.2.3.2 Ligand exchange experiment of ‘phen-palladacycle’ with L4X
An alternative strategy was envisaged to obtain a ‘di-phosphane–palladacycle’ by ligand exchange reaction between ‘phen–palladacycle’ and a phosphane ligand, such as shown successful for the L3X-palladium system.[11] When this ligand exchange experiment was repeated with L4X as the ligand (see experimental for details), the anticipated asymmetric palladacyclic species could not be detected however, but the final product of the palladacycle decomposition process, namely [Pd\(^0\)(L4X)\(_2\)], as well as ‘free’ phen ligand clearly evolved (see section AV.2 of Appendix V for details). This suggests that (like with L3X) a ligand exchange indeed took place, but that the decomposition of the resulting strained 5-ring is expedited so much as to prevent significant build-up of intermediate concentrations, probably due to the even larger bite angle of L4X (96º) compared to L3X (90º).[24]

6.2.3.3 ESI-MS analysis of ‘phen-palladacycle’
The decomposition pathway of ‘L3X-palladacycle’ (and probably also of ‘L4X-palladacycle’) was shown to proceed likely first via a reversible decarboxylation (–CO), and followed by an irreversible decarboxylation (–CO\(_2\)) to give a reactive palladium-imido (‘Pd\(^{II}\)=NPh’) complex from which organic ‘PhN’ containing products ultimately evolve.[10, 11] This means that, at least under the mild ligand-exchange conditions, the barrier for decarboxylation of ‘L3X-palladacycle’ must be lower than that of the decarboxylation (in which case the palladacycle would have been an isocyanate releasing species). A prime source of evidence for this reaction sequence was the defragmentation pattern of ‘L3X–palladacycle’ as obtained from an electron spray ionization mass spectrum (ESI–MS) taken directly after the ligand exchange took place. As the ‘phen–palladacycle’ could be synthesized and isolated as a thermodynamically stable compound (see
A comparative study between the Pd/phen and Pd/L4X catalytic systems,\textsuperscript{[23]} its defragmentation with ESI–MS was studied in order to see whether the ‘phen–palladacycle’ would decompose in a similar manner as the ‘L3X–palladacycle’.

Due to the poor solubility of ‘phen–palladacycle’ in various common solvents, a saturated solution of ‘phen–palladacycle’ in nitrobenzene was introduced directly into the ESI–source (instead of using an injector with an eluent). However, when using the same ionization conditions that were successful for measuring the defragmentation of ‘L3X–palladacycle’ (i.e., 3 kV and 300 °C), no clear mass spectrum could be obtained. Only when the ionization temperature was elevated to 450 °C could a proper mass spectrum be recorded; this is in line with the DFT–calculations, which suggested that the palladacycle is more stable when the supporting ligand is phen, relative to a diphosphane ligand such as L3X\textsuperscript{[10]} or L4X (\textit{vide supra}). The mass spectrum of this experiment is shown in Figure 6.8a and a simulation of the most prominent peaks is given in Figure 6.8b.

![Mass spectrum and simulation](image)

\textit{Figure 6.8.} (a) ESI mass spectrum of a saturated solution of ‘phen–palladacycle’ (M) in nitrobenzene; (b) simulation of the most prominent MS peaks.

The highest significant mass around \(m/z = 571.8\) is consistent with a nitrobenzene solvent adduct of ‘phen–palladacycle’ (exact mass is 572.0; recall that the solid state structure of ‘phen–palladacycle’ also contains a nitrobenzene molecule in its
lattice). The mass and isotope distributions of the two features found around \( m/z = 466.7 \) and 484.9 are in perfect agreement with \([M + H_2O]^+\) and \([M + 2 \text{H}_2\text{O}]^+\) respectively, as is also explicitly shown in Figure 6.9. The H\(_2\)O in these adducts probably derives from trace amounts of water in the solvent nitrobenzene.

![Figure 6.9. Zoom-in and assignment of the ESI mass spectrum of ‘phen–palladacycle’ (‘M’, see Figure 6.8) together with a simulation of the mass and isotope distribution.](image)

Although the structure of ‘phen–palladacycle’ is well-documented\(^{[22, 23]}\) and the purity of the batch used was verified by elemental analysis, IR–, and \(^1\)H–\(^1\)H–COSY–NMR spectroscopy (see experimental and Appendix V, Figure AV.3), the \([M]^+\) peak (exact mass is 449.0) was not observed. Also, the mono–decarbonylated fragment \((M–\text{CO})^+\), exact mass of 421.0) was not observed, while the mass of the di–decarbonylated fragment \([M–2\text{CO}]^+\) (i.e. a nitrosobenzene complex) is present around \(m/z = 392.7\) (exact mass 393.0).

Surprisingly, the feature around \( m/z = 407.9 \) cannot be ascribed to the anticipated palladium bound phenylisocyanate (i.e. \([M–\text{CO}_2]^+\)), as the exact mass of this species (405.0) differs three units. Instead, it is tentatively assigned to a \([\text{phen}][\text{Pd}–\text{C}_6\text{H}_4\text{NO}_2]^+]\) complex as follows. The most abundant mass observed is that of \([\text{phen}][\text{Pd}]^+\) around \(m/z = 285.9\) (exact mass 286.0), and a phenyl–adduct of this species seems also to be present (i.e., \(m/z = 362.9; [\text{phen}][\text{Pd}–\text{Ph}]^+, \text{exact mass 363.0}\)). As the experiment was performed in a nitrobenzene solvent matrix, the mass around 407.9 can thus best be assigned to a nitrophenyl–adduct of \([\text{phen}][\text{Pd}]^+\), i.e.: \([\text{phen}][\text{Pd}–\text{C}_6\text{H}_4\text{NO}_2]^+(\text{exact mass is 408.0})\). Interestingly, the mass of the very small peak around \(m/z = 377.9\) is in agreement with a (phen)Pd\(^{i=3}\)=NPh complex (i.e., \([M−\text{CO}_2–\text{CO}]^+, \text{exact mass 378.0}\)).

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As the ESI mass spectrum is very likely to reflect the thermal decomposition of ‘phen-palladacycle’, the defragmentation pattern surprisingly suggests that ‘phen–palladacycle’ may decompose (like ‘L3X–palladacycle’) predominantly via an initial decarboxylation (–CO) instead of a direct decarboxylation (–CO₂), to palladium bound phenylisocyanate. After the first decarboxylation a second may follow, or CO₂ can be extruded to form the imido intermediate ‘(phen)Pd\textsuperscript{II}=NPh’, which may decompose further to [(phen)Pd]\textsuperscript{+} (thus giving rise to the observed adducts thereof).

6.2.3.4 In situ trapping of a Pd–imido complex in the Pd\textsuperscript{II}(phen) system

It was demonstrated elsewhere in Chapters 3 and 4\textsuperscript{[10]} that a palladium imido complex ‘Pd\textsuperscript{II}=NPh’ is by far the most likely species to be considered as prime intermediate in Pd/diphosphane catalyzed reductive carbonylation of nitrobenzene. One piece of additional evidence for the possible intermediacy of ‘Pd\textsuperscript{II}=NPh’ under reaction conditions when employing diphenyl phosphane ligands such as L4X, comes from nitrobenzene carbonylation experiments in which cyclohexene\textsuperscript{[25]} was added to trap the nitrene ligand (‘NPh’) in these species; a reaction analogous to trapping of carbenes by alkenes\textsuperscript{[26–29]} Convincing mass spectroscopic evidence was thus obtained for the formation of a three membered cyclic amine via a reaction as depicted in Scheme 6.4:

\[
\text{Scheme 6.4. Trapping reaction of an imido complex with cyclohexene.}
\]

As the above ESI–MS experiment suggests that ‘(phen)Pd\textsuperscript{II}=NPh’ may be formed from ‘phen–palladacycle’, it seems likely that such an imido complex may be an intermediate in Pd/phen catalytic system as well. The trapping experiment was therefore repeated with Pd\textsuperscript{II}(phen) as the catalyst precursor (at 130 °C, see experimental for details), indeed revealing the presence of the same trapping product (GLC–MS analysis). This thus lends credibility to the presence of a palladium–imido complex (‘Pd\textsuperscript{II}=NPh’) under actual catalytic carbonylation conditions.
6.2.4. DFT study of nitrobenzene de-oxygenation with CO

The above data suggests that the palladacyclic species shown in Scheme 6.2a may decompose to an imido intermediate when the supporting ligand is either phen or a phosphane ligand such as L3X or L4X. To relate these data to the actual catalytic process under carbonylation conditions, the possible deoxygenation pathways of nitrobenzene to the palladacyclic and/or palladium-imido complex were studied using DFT calculations. Because of computational limitations, no attempts were undertaken to estimate the reaction barrier from one complex to another. Instead, the approach here was to estimate the Gibbs free energies for the relevant complexes (see Scheme 6.5), via the methodology explained and validated in sections AV.3. and AV.4. of Appendix V. In essence, the enthalpy differences were estimated using DFT calculations and the changes in entropy were estimated at the relevant reaction temperature from literature data (standard molar entropy ($S^\circ$) in J.mol$^{-1}$.K$^{-1}$). Hence, the data shown in Scheme 6.5 are the estimated Gibbs free energies at 110 °C for complexes containing L4X, and at 130 °C for complexes containing phen as the supporting ligand.

Scheme 6.5. L$_2$Pd-catalyzed nitrobenzene de-oxygenation process with CO, as computed with DFT calculations (see sections AV.3. and AV.4. of Appendix V for details) for L$_2$ is phen (@ 130 °C) or L4X (@ 110 °C). Data is given in kcal.mol$^{-1}$ relative to complex C0.
The starting compound for the nitrobenzene reduction process is most likely the zero-valent complex \( L_2\text{Pd(CO)}_2 \) (C0), which is therefore defined as \( 0.0 \text{ kcal.mol}^{-1} \). The oxidative coupling of C0 with nitrobenzene can proceed either via C1 or C4. No preference can be given as C1 and C4 are similar in energy for both phen and L4X. Also, the irreversible CO\(_2\) extrusions C1→C2 and C4→C5 are both roughly equally highly exothermic (ca. –50 kcal.mol\(^{-1}\)), thereby completing the first deoxygenation step of nitrobenzene.

Complexes C2 and C5 differ merely ca. 8 kcal.mol\(^{-1}\); both may thus very well interconvert into each other via a reversible carboligation/decarboligation process. Likewise, the equilibrium reactions C2⇌C7, C5⇌C6, and C6⇌C7 are all likely to be reversible carboligation/decarboligation reactions, meaning that C2, C5, C6 and C7 are probably all interconvertible into one another. Note that the palladacycle C7 in the most stable complex of these (presumably) CO equilibrated species, both when phen and when L4X is the supporting ligand. Note also that the oxidative coupling of nitrosobenzene with CO (i.e. C5⇌C2 and C5⇌C6) is exothermic by ca. –8 kcal.mol\(^{-1}\) whereas the oxidative coupling of nitrobenzene with CO is endothermic (i.e., C0⇌C1 and C0⇌C4) by ca. +20 kcal.mol\(^{-1}\); this is in line with the finding (section 3.2.2.4) and literature data\(^{[20]}\) that nitrosobenzene is more easily reduced than nitrobenzene.

The second de-oxygenation of nitrobenzene can only occur by the irreversible CO\(_2\) extrusion from C2 to the imido complex C3, which is also the most thermodynamically stable complex (ca. –62 kcal.mol\(^{-1}\)). Finally, it is worth noting that all the palladacycles that are formally Pd\(^{III}\) species and sterically crowded in the equatorial positions of Pd (i.e., C1, C2, C4, and C7) are all destabilized by ca. 10 kcal.mol\(^{-1}\) by the bulkier L4X ligand relative to phen. The formally zero-valent palladium-nitrosobenzene complex C5 is more stable when L4X is the supporting ligand due to the increased acidity of palladium as induced by the increased \( \pi \)-backbonding from Pd to P.

These data thus strongly suggest that the main de-oxygenation pathway is C0⇌C1→C2→C3, and that complexes C5, C6, and C7 can be seen as carboligation/decarboligation equilibrated equivalents of C2.
6.3. Discussion

6.3.1. Overall mechanism with $P_2Pd$ catalysts: a network centered around a $P_2Pd^{II}=NPh$ complex

During the studies into the reductive carbyonlation of nitrobenzene in methanol, as described in Chapters 3–5, it was discovered that besides CO, methanol acts as the (co-)reductant for nitrobenzene to eventually give a palladium-imido complex as the central ‘PhN’ product releasing species.\cite{10,11} This deoxygenation process involves oxidation of $Pd^0$ to $Pd^{II}$, and can be described by the half–reactions given in Equations 1a–c.

$$P_2Pd^0 + PhNO_2 + 2 CO \rightarrow P_2Pd^{II}=NPh + 2 CO_2 \quad (1a)$$
$$P_2Pd^0 + PhNO_2 + 2 CO + 2 CH_3OH \rightarrow P_2Pd^{II}=NPh + H_2O + CO_2 + DMC \quad (1b)$$
$$[P_2Pd^0 + PhNO_2 + 3 CO + 2 CH_3OH \rightarrow P_2Pd^{II}=NPh + H_2O + CO_2 + DMC (1b)*]$$
$$P_2Pd^0 + PhNO_2 + CH_3OH \rightarrow P_2Pd^{II}=NPh + CO + 2 H_2O \quad (1c)$$
$$[P_2Pd^0 + PhNO_2 + 2 CH_3OH \rightarrow P_2Pd^{II}=NPh + MF + 2 H_2O \quad (1c)*]$$

The reduction of $Pd^{II}=NPh$ to $Pd^0$ and the various ‘PhN’ containing products as described by Equations 2a–c makes the process catalytic.

$$P_2Pd^{II}=NPh + CO + CH_3OH \rightarrow P_2Pd^0 + MPC \quad (2a)$$
$$[P_2Pd^{II}=NPh + CO + PhNH_2 \rightarrow P_2Pd^0 + DPU \quad (2a)*]$$
$$P_2Pd^{II}=NPh + CO + 2 CH_3OH \rightarrow P_2Pd^0 + PhNH_2 + DMC \quad (2b)$$
$$[P_2Pd^{II}=NPh + 2CO + 2 CH_3OH \rightarrow P_2Pd^0 + PhNH_2 + DMO \quad (2b)*]$$
$$P_2Pd^{II}=NPh + CO + PhNO_2 \rightarrow P_2Pd^0 + Azoxy + CO_2 \quad (2c)$$
$$[P_2Pd^{II}=NPh + 2CO + PhNO_2 \rightarrow P_2Pd^0 + Azo + 2 CO_2 \quad (2c)*]$$

A combination of the half–reactions that oxidize $Pd^0$ to $Pd^{II}$ (eq. 1) with the half–reactions that reduce $Pd^{II}$ to $Pd^0$ (eq. 2), naturally leads to the overall possible stoichiometries as described in detail in Chapter 3.\cite{10} Such a combination allows for the construction of a relatively simple and unifying catalytic scheme, rationalizing the formation of all methanol oxidation products and all nitrobenzene reduction products (Scheme 6.6).
6.3.2. Molecular mechanism of nitrobenzene deoxygenation

The current understanding of the molecular basis underlying the de-oxygenation stoichiometries given by Equations 1a-c for phosphanes as the supporting ligand (L₂) is shown in Scheme 6.7.[11]

Scheme 6.7. Working hypothesis for the formation the palladacyclic intermediate (top) and the Pd–imido intermediate (centre and bottom), in the deoxygenation of nitrobenzene.
As also supported by the DFT calculations reported in this chapter, the most likely CO-only deoxygenation route commences with an oxidative coupling of nitrobenzene and CO in L\(_2\)Pd\(^{0}\)(CO)\(_2\) (C0) to form C1, followed by a series of irreversible decarboxylation steps (i.e., C1→C2→C3, centre in Scheme 6.7). The final product C3, i.e., the Pd-imido complex, is then the sole ‘PhN’-containing product releasing species (i.e., producing MPC, DPU, PhNH\(_2\), and Axo(xy), vide infra).\(^{10, 11}\) The carbo(noylation/decarbo(nylation) equilibrated species C5, C6, and C7 (top in Scheme 6.7) all act merely as temporary reservoir of the ‘PhN’ fragment, and none are likely to be a product releasing species. Not even the palladacycle C7 should be considered as such, as it was found that the barrier for decarboxylation (CO\(_2\) loss) is higher than the barrier for decarboxylation (CO loss) of C7, at least when using bidentate diaryl phosphane ligands (see Chapter 4).\(^{11}\) The methanol de-oxygenation routes are thought to commence by oxidative addition of methanol on ‘L\(_2\)Pd\(^{0}\)’ (bottom in Scheme 6.7) to C8 and most likely proceed via (C8=C9=C10=C11) palladium hydride chemistry to eventually form the same palladium-imido intermediate C3, as is discussed in more detail elsewhere.\(^{11}\)

Clearly, the fraction of nitrobenzene that is de-oxygenated with CO-only or (also) with methanol must depend on the characteristics of the catalyst employed, as predetermined by the properties of the supporting ligand. Indeed, when employing L4X in the catalyst, the CO-only de-oxygenation route contributes merely 9%, whereas this is 72% when this ligand is functionalized with electron-donating methoxy groups.\(^{10}\) Likewise, when using the even more basic phen as the supporting ligand, the CO-only de-oxygenation pathway contributes 97%\(^{30}\), meaning that the oxidation of methanol is almost completely suppressed. This relationship between the basicity of the Pd-centre (induced by that of the ligand) and the fraction of CO-only de-oxygenation may come as no surprise: it is indeed well-known that when palladium is made more basic, it binds stronger to carbon monoxide by increased electron backdonation of the filled d\(\pi\) orbitals of Pd into the empty \(\pi^*\) orbitals of CO.\(^{31}\) Hence, the dissociation of CO from C0 to open the pathway towards C8 will be hampered, thus effectively blocking methanol oxidation while facilitating the CO-only de-oxygenation.

Based on the ESI-MS spectrum of the ‘phen-palladacycle’ (i.e. ‘phen-C7’), the trapping experiment with cyclohexene, the ligand exchange experiment, the
dependency of the Azo(xy) selectivity on the nitrobenzene concentration, and the DFT results, it is propose here that the molecular mechanism of the CO-only deoxygenation shown in Scheme 6.7 is a general one and is also valid for the Pd/phen catalytic system. That is, it is proposed that ‘phen-C7’ – commonly thought to be the product releasing species– in not a (main) product releasing species under normal (acid-free) catalytic carboxylation conditions. Instead, ‘phen-C7’ merely is part of the several CO-equilibrated species (C2, C5, and C6) that together act as temporary ‘PhN’ reservoir.

This insight, together with the DFT studies also explains why ‘phen-C7’ can be obtained under mild carboxylation conditions (60 °C, ethanol);[23] C7 is the thermodynamically most stable of the CO-equilibrated species and is therefore thought to be the resting state of the catalyst. At elevated temperatures, ‘phen-C7’ may be decarboxylated to phenylisocyanate (and thus MPC and DPU), but judging from the product distribution of the reaction under ‘normal’ conditions, this cannot be the (dominant) pathway; merely 20% MPC but 70% Azoxy are produced. This must mean that, in line with the results reported above, that the reaction barrier for ‘phen-C7’ decarboxylation (to ‘PhNCO’) is higher than that of ‘phen-C7’ decarboxylation (to C2 and/or C6). Irreversible decarboxylation of C2→C3 then removes the catalyst from the CO-equilibrated ‘PhN’ reservoir.

The different temperature required when phen (130 °C) or L4X (110 °C) is used as the supporting ligands may be ascribed to the destabilizing effect that the bulkier L4X has on palladacycles such as C7 (as indicated by DFT); both the decarboxylation barriers (of e.g. C7→C2), as well as the barrier for decarboxylation of C2→C3 will be lowered, thus allowing the ‘PhN’ fragment to escape the temporary reservoir more easily and thus also allowing the application of milder temperatures.

6.3.3. Molecular mechanism of reaction of the Pd\textsuperscript{II}=NPh intermediate

As is shown in Scheme 6.8,[10, 11] once the imido intermediate C3 has been formed, it can undergo a disproportionation reaction with nitrobenzene and CO to produce and azoxybenzene and CO\textsubscript{2} as stable end products. It has been proposed that Azoxy stems from a reaction between ‘free’ nitrosobenzene and a nitrene (‘PhN’),[15, 18] or a supposed condensation reaction of nitrobenzene with aniline.[19]
It was shown however, that adding extra nitrosobenzene during a catalytic run did not result in more Azoxy. It was also observed that nitrosobenzene is more easily reduced than nitrobenzene, which is corroborated by the DFT-studies reported in this chapter, and finds support in literature as well.\textsuperscript{[18, 32, 33]} Besides, it is known that Azoxy cannot be formed by a condensation reaction of aniline and nitrobenzene during catalysis, as a carbonylation experiment with deuterated nitrobenzene and undeuterated aniline gave only fully deuterated Azoxy when working with the Pd/phen catalytic system.\textsuperscript{[34]} As an alternative to the disproportionation, the imido intermediate $C_3$ can also be protonated by methanol to produce PhNH$_2$ (bottom right) and/or MPC (top right); all three reactions result in a zero-valent palladium species that can re-enter the catalytic cycle and thus make the overall processes catalytic (see also Scheme 6.6).

Because one N=O bond in nitrobenzene is formally fully polarized, nitrobenzene is thought to associate strongest to the (also very polarized) Pd=N bond in $C_3$ (relative to charge-neutral methanol). As a result, the disproportionation reaction dominates, resulting in the observed selectivity towards Azoxy (70\%) for both catalyst systems.

![Scheme 6.8. Working hypothesis for the molecular mechanism of $L_2Pd^{II}=NPh$ ($C_3$) reduction to $L_2Pd^{0}$ and the various aryl-containing nitrobenzene reduction products.](image_url)

The protonation of $C_3$ by methanol will give $C_{12}$ which may undergo a carbonylation to $C_{13}$ via an associative displacement of CH$_3$O$^-$ by the smaller and charge neutral CO, followed by nucleophilic attack of nearby CH$_3$O$^-$ on
coordinated CO and finally a reductive elimination to produce MPC. Such a mechanism to produce MPC is very similar to the one recently proposed by Ragaini and co-workers involving first full reduction of nitrobenzene to aniline and a phenPd(C(O)OCH$_3$)$_2$ species, which is supposed to react with aniline to give the isocyanate.$^{[19, 35]}$ Yet the mechanism proposed in this chapter differs significantly in that it is the precursor for aniline formation –i.e. the palladium imido intermediate– that is methoxycarbonylated to MPC. Any Pd-imido that escapes methoxy carbonylation may convert to azoxy (by a reaction with nitrobenzene) or aniline by protonation by methanol and subsequent DMC/O formation. Thus, as an alternative to MPC formation, C$_{12}$ may be protonated to C$_{14}$ while liberating aniline. C$_{14}$ will then be carbonylated once or twice via associative displacement/nucleophilic attack to give C$_{15}$ and C$_{16}$, from which reductive elimination will produce DMC and DMO respectively.

As it appears from the data in this chapter, the carbonylation of C$_{12}$ is favoured when phen is the supporting ligand (20% MPC), whereas the protonation of C$_{12}$ is favored in case of L$_4$X (20% PhNH$_2$). This effect can be understood by the difference in basicity of both ligands; the more basic phen will destabilize the Pd–OCH$_3$ bond in C$_{12}$ more, thus facilitating the associative displacement by CO leading to MPC ($via$ C$_{13}$).

What all the above means, is that the mechanistic understanding of nitrobenzene reductive carbonylation in a CO/CH$_3$OH environment with diphosphane stabilized palladium complexes (as developed in this thesis), translates directly to the mechanism of this reaction when phen is the supporting ligand. Here too the network of catalytic cycles centered around a palladium-imido intermediate (Scheme 6.6) can rationalize the formation of all the products observed, and – moreover– can relate the catalyst performance to its characteristics as imposed by the supporting ligand (Scheme 6.7 and Scheme 6.8), whether this is a N- or P-donor.

### 6.3.4. Effect of added acid

With the understanding of the mechanism unfolded above, it can also be easily rationalized why adding sub-stoichiometric amounts (on Pd) of acid has such a dramatically different effect on the selectivity of the Pd$^{II}$(phen) (> MPC) and the
Pd\textsuperscript{II}(L4X) (>PhNH\textsubscript{2}) catalytic systems. As explained above, under ‘normal’ conditions, the palladacycle C\textsubscript{7} (with either phen or L4X) is not a (main) product releasing species due to the too high barrier for decarboxylation relative to decarboxylation. When an acid as co-catalyst is added however, the decarboxylation barrier is dramatically lowered, presumably by protonation at N of the palladacycle; in the case of ‘phen-C\textsubscript{7}’ apparently to the point where CO\textsubscript{2} extrusion is favored relative to decarboxylation. As a result, now ‘phen-C\textsubscript{7}’ becomes the main product releasing species, selectively producing MPC. The imido-intermediate ‘phen-C\textsubscript{3}’ will then only scarcely be formed, hence explaining the strongly decreased azoxybenzene selectivity (from 71 to \textasciitilde15\%). This is in line with the findings of Osborn and co-workers, whom reported that ‘phen-C\textsubscript{7}’ is thermally very stable, but in the presence of an acid (catalyst) smoothly decomposes to ethyl phenyl carbamate when heated in ethanol at merely 90 °C.\textsuperscript{[23]}

For the Pd\textsuperscript{II}(L4X) system however, although the barrier for ‘L4X-C\textsubscript{7}’ decarboxylation is most probably also lowered when adding acid, the barrier for ‘phen-C\textsubscript{7}’ decarboxylation is still lowest. This is most likely due to the fact that, as corroborated by DFT, ‘L4X-C\textsubscript{7}’ is less stable than ‘phen-C\textsubscript{7}’ which surely must have a similar effect of the ‘L4X-C\textsubscript{7}’ decarboxylation reaction barrier. As a consequence, ‘L4X-C\textsubscript{3}’ will still be formed predominantly, and thus remains the (main) product releasing species. The suppressing effect on azoxybenzene production in favor of the carbonylation and hydrogenation (see Figure 6.4), can be rationalized by an acid-assisted protonation of C\textsubscript{3} to C\textsubscript{12}, thereby hampering the disproportionation. Note that the suppressing effect on Azoxy production is less than that observed for the Pd/phen/H\textsuperscript{+} system, because the ‘Pd=NPh’ species is hardly formed in this phen/H\textsuperscript{+}-system in the first place. That in the Pd/L4X/H\textsuperscript{+} system the hydrogenation is promoted somewhat more that the carbonylation can easily be understood; protonation of the [PhNH\textsuperscript{-}] ligand in C\textsubscript{12} to aniline will be facilitated by the acid, in expense of the associative replacement of the [CH\textsubscript{3}O\textsuperscript{-}] ligand in C\textsubscript{12} by CO. It is important to note that in line with this mechanism, when adding an acid to the Pd\textsuperscript{II}(phen) system, the amount of DMC+DMO produced declines (from 0.5 to 0.2 mmol being very small), whereas the amount of DMC+DMO is increased (from 8.2 to \textasciitilde13 mmol) when employing Pd\textsuperscript{II}(L4X) (see Table S1 for details).
6.4. Conclusions

The palladium-imido species L2Pd=NPh (C3) and the palladacycle L2PdC(O)N(Ph)OC(O) (C7) were considered as possible carbonylation product-releasing species for both phen and L4X. The results of catalytic experiments, supported by spectroscopic (ESI-MS and NMR) evidence and a DFT study suggest that the palladacyclic compound C7 is not the major product-releasing intermediate in reactions performed in the absence of acid. The unified mechanistic proposal for the carbonylation of nitrobenzene in methanol, catalyzed by the palladium-phenanthroline system is illustrated in Scheme 6.9. In the absence of acid the proposed mechanism for Pd/diphosphane catalysts (Scheme 6.6)\cite{10, 11} applies directly to the Pd/phen catalytic system: the Pd-imido complex C3 is the central ‘PhN-containing’ (Azoxy, MPC, PhNH$_2$) product releasing species, producing mainly the coupling product Azoxy. On the other hand, in the presence of acid the palladacyclic complex C7 becomes the major product-releasing species, resulting in the selective formation of the nitrobenzene carbonylation product MPC.

\[
\text{Scheme 6.9. Working hypothesis for the overall catalytic processes in the palladium catalyzed reduction reactions of nitrobenzene when 1,10-phenanthroline (N$_2$) is the supporting ligand.}
\]
6.5. Experimental section

6.5.1. General remarks

All solids were purchased from Acros organics and used as received. Methanol, nitrobenzene and aniline were all of analytical reagent purity, and were distilled under an argon atmosphere over the appropriate drying agent\(^{[36]}\). After the distillation, these liquids were saturated with argon. It was ensured that no water was present using an analytical reaction with trimethylorthoformate according to a literature procedure\(^{[37]}\). Carbon monoxide (> 99% pure)\(^{[38]}\) was purchased from Linde gas benelux B.V. and used as received.

\(^{1}\)H–, and \(^{13}\)C–NMR spectra were recorded on a Bruker DPX300 (300 MHz) or a Bruker DMX400 (400 MHz) machine. A Finnigan Aqua Mass Spectrometer (MS) with electro spray ionization (ESI) was used to record mass spectra. Samples were directly introduced into ESI–source that was heated at 450 °C. The voltage of the capillary and the voltage for the aquamax were set at 3 kV and 50 V respectively. High pressure experiments were conducted in stainless steel autoclaves (100 ml) equipped with two inlet/outlet valves, a burst disc, a pressure sensor, and a thermocouple. The autoclaves were heated by a Hell\(^{©}\) polyBLOCK electrical heating system. Temperatures and pressures where measured with probes connected to a computer interface making it possible to record these parameters throughout the course of the reaction.

6.5.2. Catalytic / high pressure reactions

In a typical catalytic experiment, 0.05 mmol Pd(OAc)\(_2\) and 0.075 mmol ligand (and if relevant another additive) were weighed and transferred into an autoclave, together with a magnetic stirring rod. The autoclave was tightly closed and subsequently filled with argon using a Schlenk–system that was connected to the one of the valves of the autoclave. Through the other valve was added 2.50 ml (24.4 mmol) dried and degassed nitrobenzene, under a continuous flow of argon. In a similar fashion, 25.0 ml dried and degassed methanol was then added. This reaction mixture was allows to stir at 500 rpm for about 15 minutes to ensure that complex formation was complete\(^{[39]}\). The autoclave was then inserted into the heating block and put under 50 bar carbon monoxide gas. The reaction mixture was heated to 110 or 130 ºC (within 30 minutes) under stirring at 500 rpm. After standing for four hours at a certain temperature, the autoclave was cooled to room temperature in about one hour. The autoclave was then slowly vented to atmospheric pressure and the reaction mixture was analyzed as described in Chapter 3\(^{[10]}\). To ensure reproducibility, some standard catalytic reactions were performed in quadruplet, and the relative standard deviation was always less than 5% for each analyte.

6.5.3. Adding a reactant during a catalytic run

In experiments wherein a compound was added during a catalytic run, the experiment was first started as a normal high pressure experiment (see above). A stainless steel hollow pipe (10 ml), sealed with two valves on each side was then put under an argon atmosphere, and nitrosobenzene (2.5 mmol in 5 ml methanol) or cyclohexene (2.5 mmol, 0.25 ml) were transferred into the hollow pipe using standard Schlenk techniques. The bottom valve of the hollow pipe was then mounted on one of the valves of the autoclave, connected to the CO supply, and pressurized to about five bar above the pressure inside the autoclave. At about one hour reaction time, nitrosobenzene or cyclohexene was added to the reaction mixture by opening the two valves in between the autoclave and the hollow pipe. The reaction was then allowed to run for the remaining reaction time, and treated as any other catalytic experiment.
6.5.4. NMR experiment
4.50 mg (10 μmol) of ‘phen–C7’ \[23\] was weighed into an NMR tube and put under argon. In another tube, 8.96 mg (18 μmol) of L4X was dissolved in 0.6 ml d5–nitrobenzene under an argon atmosphere. Of this solution, 0.5 ml (15 μmol of L4X) was added to the ‘phen–C7’ complex using a 1 ml syringe, which was dry and flushed with argon. The thus obtained mixture (30 mM L4X, 20 mM ‘phen–C7’) was thoroughly mixed using a vortex mixer and measured with 31P{1H}–NMR spectroscopy. After the first measurements, the yellow suspension was carefully heated to about 50 ºC, resulting in a clear yellow–orange solution which was again measured. While maintaining the temperature within the NMR spectrometer at 50 ± 2 ºC, \[39\] proton and phosphorus spectra were recorded with 15 minute intervals for several hours. The number of free inductive decays (FIDs) for the phosphorus and proton NMR spectra was 40 and 16 respectively.

6.5.5. DFT studies
Calculations were done with the SPARTAN ‘04 package (Wavefunction, Inc; www.wavefun.com), using density functional theory (DFT) \[40, 41\] with the Becke and Perdew (BP) functional. \[42, 43\] Geometry optimizations were carried out using Pople’s 6–31G* \((d,p)\) for H, C, O, and P atoms \[44\] and the LANL2DZ effective core potential for palladium. \[45-47\] All of the geometrical parameters were fully optimized, and all of the structures located on the PESs were characterized as minima. No constraints to bonds, angles, or dihedral angles were applied in the calculations, and all atoms were free to be optimized.

6.5.6. Synthesis of ‘phen–palladacycle’ / ‘phen-C7’
‘phen–palladacycle’ (i.e., ‘phen-C7’) was synthesized according to a literature procedure, \[23\] and the product was isolated as a bright yellow powder in 83% yield. 1H–NMR (300 MHz, d5–PhNO2): δ 10.2 (d, 4.8 Hz, 1H, o–phen1), 10.1 (d, 4.8 Hz, 1H, o–phen2), 8.7 (t, 6.9 Hz, 2H, p–phen1+2), 8.2 (m, 3H, m–phen1+o–Ph), 8.1 (s, 2H, phen), 8.0 (dd, 8.1 Hz, 1H, m–phen2), 7.6 (dd, 7.8 Hz, 2H, m–Ph), 7.3 (t, 7.2 Hz, 1H, p–Ph) ppm (see Figure AV.3 for 1H–1H–COSY spectrum); Main IR absorptions: 1691 (OC=O), 1622 (NC=O), 1587 (N–O), 1428 (OC–O), 1253 (OC–N), 1045, 950, 850, 722 \((\text{C=C and C=N})\) cm\(^{-1}\); Elemental analysis for ‘phen–palladacycle’, C\(_{20}\)H\(_{13}\)N\(_3\)O\(_3\)Pd (449.0) • 0.2 Pd: calcd. C 50.64, H 2.76, N 8.86; found C 50.47, H 2.72, N 8.97. ESI Mass Spectroscopy, \(m/z\) found (calcd): [M+H\(_2\)O\(^+\)] = 466.7 (467.0); [M+2H\(_2\)O\(^+\)] = 484.9 (485.0); see also Figure 6.8 and Figure 6.9.

References

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Note that DPU can be formed by the reaction of nitrobenzene, CO and \textit{(in situ) generated} aniline, but also by the transesterification of MPC with aniline. In both cases, aniline is formed first and DPU is thus derived from aniline.

When performing an analysis for the simulation of the products distribution as described in Chapter 3 (and in more detail in the supporting information for that chapter in Appendix II), and using the reaction stoichiometries described therein, the following results (NB: the equation numbers refer to those in Chapter 3 and Appendix II): For Pd$^{2+}$(Phen), added water is hardly (net) consumed, meaning that the contribution of eq. 10/11*, 13/14*, and 16/17* should be kept as low as possible relative to eq. 11, eq. 14, and eq. 17 (together accounting for the aniline produced). Thus, various fraction (of eq. X vs eq. X*) were considered and an excellent fit was obtained when the water ‘consuming’ reactions (eq. X*) contribute for 35.0%. The (aryl) product distribution is: MPC (34.5%); PhNH$_2$ (11.5%); Azoxy (54.0%), with PhNH$_2$/MPC = 0.33, and Azoxy/MPC = 1.57. 0.28 mmol nitrobenzene was reduced with methanol alone, so: C$_3$H$_6$OH reduction: (0.28 x 0.345 x eq. 16) + (0.28 x 0.115 x 0.65 x eq. 17) + (0.28 x 0.115 x 0.35 x eq. 16/17*) + (0.28 x 0.540 x eq. 18) = 0.10 MPC + 0.03 PhNH$_2$ + 0.15 Azoxy + 0.55 H$_2$O + 0.02 DMC. As next calibration point, we can take MPC; there is still 3.00 - 0.10 = 2.90 mmol unaccounted for. This must have been produced via CO-only reduction and/or via the co-reduction of CO and the acidic protons of CH$_3$OH molecules. Thus, there must be an optimal fraction of CO-only reduction, so that the simulation approaches perfection (and the aryl product distribution is respected). Several options were considered, and a fraction of 1.00 CO reduction was found to fit best, meaning that 2.90 mmol nitrobenzene was reduced with CO alone, and none by CO/2CH$_3$OH. Thus: CO only reduction: (2.90 x 1.00 x eq. 10) + (2.90 x 0.33 x 0.650 x eq. 11) + (2.90 x 0.33 x 0.350 x eq. 10/11*) + (2.90 x
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1.57 × eq. 12) = 2.90 MPC + 0.95 PhNH₂ + 4.55 Azoxy + 0.62 DMC + (-0.33) H₂O. Adding all three reduction pathways leads to an excellent simulation of sim. (exp.) = 3.0 (3.0) MPC; 1.0 (1.0) PhNH₂; 4.7 (4.7) Azoxy; 0.6 (0.5) DMC; 0.2 (0.3) H₂O. This means that the respective contributions of CO-only / CO+2CH₃OH / CH₃OH -only = 97% / 0% / 3%.
