The Pd-catalyzed semihydrogenation of alkynes to Z-alkenes: Catalyst systems and the type of active species

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Chapter 5

Pd-Catalyzed Z-Selective Semihydrogenation of Alkynes: Determining the Type of Active Species

Abstract

A protocol was developed to distinguish between well-defined molecular and nanoparticle-based catalysts for the Pd-catalyzed semihydrogenation reaction of alkynes to Z-alkenes. The protocol applies quantitative partial poisoning and dynamic light scattering methods, which allows the institution of additional validation experiments. For the quantitative partial poisoning method, tetramethylthiourea was developed as an alternative for the standard poison ligand CS$_2$, and was found to be superior in its applicability. The protocol and the TMTU poison ligand were validated using the well-described [Pd$^{II}$ (phenanthroline)]-catalyzed copolymerization of styrene and CO. The protocol is applied to three catalyst systems for the semihydrogenation of alkynes. The first catalyst system was proposed to be a molecular [Pd$^{0}$ (IMes)] catalyst that uses molecular hydrogen, however, nanoparticles were found to be the true catalysts. The second catalyst system was proposed to operate through an in situ generated molecular [Pd$^{0}$ (IMes)] catalyst for the transfer semihydrogenation using formic acid as the hydrogen source. The investigations show that only a small fraction of the Pd is active and that NPs are formed. We propose three types of catalyst system for this reaction. The third investigated system is also applied in the transfer semihydrogenation and is based on a [Pd$^{II}$ (IMes)(η$_3$-allyl)Cl] precatalyst with additive ligands. The combined data are multi-interpretable, but suggest that a partially deactivated molecular catalyst that dominates the catalytic reaction is active.

5.1 Introduction

Critical mechanistic studies of molecular catalysis\textsuperscript{1-11} and developments in the field of soluble nanoparticle (NP) catalysts\textsuperscript{12-22} have demonstrated that under certain circumstances molecular precatalysts may form active NPs or nanocluster catalysts, which consist of a small number of metal atoms. The opposite, in which anticipated NP or nanocluster materials can be precursors for molecular catalysts, has been demonstrated as well.\textsuperscript{11,23-26} It is important to know the type of active catalyst, especially for the development of molecular catalysts. These catalysts are developed based on mechanistic understanding by varying reaction conditions accordingly.\textsuperscript{10,27,28}

When, instead of a molecular catalyst, an \textit{in situ} generated metal particle based catalyst is active, the assumed mechanism is incorrect. In that case, altering the reaction conditions, varying the ligand design and computational studies will most likely not lead to improved catalyst systems. Studies on the nature of the active catalyst in the Heck-reaction illustrate the importance of knowing the type of a catalyst and the benefits thereof. These investigations provided a rationale for the observed reactivities, disproved wrong mechanistic assumptions, and have realized that Heck-reaction can now be performed at ultra-low metal loadings.\textsuperscript{3,4,29-32}

According to experts in the field of the determination of the type of active species, the number of catalyst systems that are erroneously assumed to be well-defined molecular catalysts is underestimated.\textsuperscript{10,11} This holds especially for Pd-catalyzed coupling and hydrogenation reactions,\textsuperscript{11,25,33} because many of those reactions can be performed by both transition metal based complexes and metal particles.\textsuperscript{4,5,10,34-48} The Pd-catalyzed semihydrogenation of alkynes toward \textit{Z}-alkenes is such a reaction. It is catalyzed by Pd transition metal complexes, as well as metal particles such as Pd on carbon and Lindlar’s catalyst.\textsuperscript{48-52} Chemoselectivity of the catalyst system is crucial in this reaction that is applied from laboratory to bulk scale.\textsuperscript{45,46,52,53} Especially for such a reaction, an understanding of the type of active species and the reaction mechanism are required to improve catalyst systems that meet the required chemoselectivities. In this chapter the type of active species is studied for three catalyst systems; one system for the Pd\textsuperscript{0}-catalyzed \textit{Z}-selective semihydrogenation of alkynes using molecular hydrogen, and two catalyst systems for the Pd\textsuperscript{0}-catalyzed \textit{Z}-selective transfer semihydrogenation of alkynes using formic acid. The mercury poisoning\textsuperscript{7,24,54-58} test and the Crabtree test,\textsuperscript{59} which are often applied methods for the determination of the type of catalyst proved not suitable for the investigated [Pd\textsuperscript{0}(NHC)] complexes. We found that mercury decomposes the precatalysts. The active catalyst could not be incubated with the dibenzo[\textit{a,e}]cyclootraene ligand. To determine the type of active species a protocol was developed that uses quantitative partial poisoning and
dynamic light scattering (DLS) methods. New protocols require careful validation, and therefore we applied the protocol to the [PdII(phenanthroline)]-catalyzed copolymerization reaction of CO and styrene. This reaction has been thoroughly studied with NMR and kinetic experiments. The true catalyst is a well-defined transition metal complex, which makes this reaction a good testbed for the validation of the protocol.

5.2 The Protocol and its Application

A variety of methods to distinguish between well-defined, molecular catalysts and less-defined systems based on (nano)particles has been developed.1,6,9,21,24,29,33,59-62 Excellent reviews by Finke et al. and Crabtree give an overview of the experiments applied and methods used for the determination of the type of catalyst.10,11 Especially the methodology by Finke et al. has provided a basis for determining the type of active catalyst.33 The key to the success of the methodology and others based thereon is that multiple determination methods are combined.3,11,13,33,63,64

Here, DLS and quantitative partial poisoning are applied to study the type of active catalyst of the semihydrogenation reactions. DLS gives information about the presence of NPs, but not on their activity. On the other hand, quantitative partial poisoning gives an estimate of the number of actively participating Pd atoms in the catalytic reaction.

The first advantage of DLS is that it is non-invasive. This means its application does not influence the reaction conditions and does not require sample treatment. DLS is able to detect particles of 1 to ca 250 nm even at very low concentrations in the nM range.10,24,65-67 Although its main task is to show the presence or absence of scattering particles, this technique also provides information about the average size of the particles, assuming single scattering conditions, which is generally the case in catalytic reactions. Another advantage of DLS is that it is a simple and fast technique: it takes about the same time to perform a DLS measurement as it takes to record a 1H NMR spectrum. The detected particles in a scattering experiment indicate the presence of transition metal based NPs, however, salts, dust and any other type of particles also cause light-scattering. Hence, to avoid misinterpretations control reactions are required. These consist of measuring the scattering of all the individual reagents and combinations thereof. Furthermore, DLS does not show whether the observed NPs are catalytically active. Therefore, we combine DLS experiments with the quantitative partial poisoning method to obtain more information about the number of active Pd atoms.
Quantitative poisoning is used to estimate the fraction of active metal atoms by applying ranges of sub-stoichiometric amounts of poison and measuring the corresponding decrease in catalytic activity. The amount of active metal atoms is indicative for the type of the catalyst. Only the atoms on the outer sphere of NPs are catalytically active, leaving many non-participating metal atoms in the interior of the NP (see Scheme 1). Rarely more than 15 percent of the metal atoms participate when NPs are the active catalysts. In case of active molecular catalysts typically most of the metal atoms can participate.

**Scheme 1.** A schematic representation of a partial poisoning experiment.

Using quantitative poisoning to determine the type of active species is appealing, because it has only a few experimental constraints, it is a simple method and it does not require additional analytical methods. The quantitative data that this method provides make it more reliable than the more often applied qualitative poisoning methods and because it uses only sub-stoichiometric amounts of poison it is also less invasive. However, there are three situations where quantitative poisoning can give misleading results: I) When the applied poison binds too weakly to the catalyst, then a partial poisoning test may erroneously indicate that a molecular catalyst is active, while the activity actually originates from (nano)particles; II) Experiments may falsely indicate particles as active catalysts when only a small fraction of the precatalyst is converted into an active molecular form; III) An incorrect estimation of the fraction of active metal atoms is obtained if the poison decomposes a molecular catalyst non-stoichiometrically (or if the catalyst decomposes the poison). To circumvent these three problems, the protocol includes validation experiments such as:

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• Testing the poison ligand with authentic NP catalysts to demonstrate sufficient deactivation of the NPs by the poison ligand.
• Demonstrating that the reactivity of an isolated poisoned analogue of the proposed molecular catalyst is minimal.
• Isolation of the proposed poisoned molecular species, which is a good indication that the poison ligand does not decompose the active species to form nanoparticles.

The combination of DLS and quantitative partial poisoning allows the institution of several additional controls, which improve the reliability of the determination of the type of active species. These additional controls are:

• Performing DLS on the reaction without poison, with poison, and with the poisoned analogue of the proposed active catalyst. This indicates if the poison ligand facilitates NP formation.
• Verifying that NPs are present if quantitative poisoning shows that only a small fraction of the metal is active.
• Verifying that the percentage of active metal atoms determined by quantitative poisoning is in agreement with the number of surface atoms that is derived from the average particle size. If the poison is appropriate, and the number of surface atoms based on DLS is significantly smaller than the estimated metal fraction, species that are not observed by scattering are most likely active.

The DLS and quantitative poisoning methods and the related validation experiments provide a significant amount of data. A guiding principle in the interpretation of the data is that the type of catalyst should be consistent with all the data. The protocol derived is shown in Scheme 2.
Scheme 2. A schematic presentation of the protocol for the determination of the type of active catalyst for soluble (pre)catalysts using DLS and quantitative poisoning and the DLS (α), poison (β) and combined (γ) validation experiments.

5.3 TMTU as a Poison Ligand

The selection of an appropriate poison is crucial. The herein investigated reactions are catalyzed by Pd, which is a soft and electron-rich metal. Sulfur-based poisons are ideal candidates for such type of metals, of which CS₂ is the most commonly used. However, CS₂ has several disadvantages, of which the high volatility, its limited use at elevated temperatures, and high toxicity are the most significant. Not surprisingly, research towards alternative poisoning ligands has been noted as one of the key issues for the further development of poisoning tests. To that end, we investigated the use of alternative poison ligands, specifically tetramethylthiourea (TMTU) (Figure 1). Its strong π-acceptor properties combined with its strong σ-donor properties originate from its resonance structures, which make it a strongly binding ligand for low-valent as well as high-valent complexes (Figure 1).

![Figure 1. The structure of tetramethylthiourea, its resonance structures and coordination modes.](image)

Thioureas have been exploited as ligand for Pd-complexes, Pd-catalyzed reactions, the removal of trace metal salts from aqueous solutions and the preparation of coordination polymers. TMTU possesses qualities that are
advantageous for poison ligands. It is a stable, inexpensive, commercially available compound, that is a solid at room temperature with a high boiling point and low vapor pressure. In comparison to CS₂ TMTU has only one defined binding mode, is less toxic and is not easily decomposed in fragments that can bind to multiple metal centers. TMTU can also easily be monitored because the thiourea and thiocarbonyl IR-vibrations have high absorption coefficients and the frequencies shift significantly upon coordination to a metal.

To validate the use of TMTU as a new poison ligand we studied the coordination behavior of TMTU by X-ray diffraction. Secondly, the performance was validated in the copolymerization of CO and styrene by a [Pd(Phenanthroline)] catalyst. Finally we compare the performance of TMTU to that of CS₂.

### 5.4 [Pd(TMTU)] complexes

We synthesized the proposed poisoned molecular catalysts. From these complexes we learn whether such compounds may exist, what the stoichiometry of the poison and the molecular catalyst is and the coordination mode of the poison ligands. In the following sections, these compounds were subsequently applied as precatalysts to test whether these compounds are catalytically active, how strongly deactivating the poison ligand is, and whether these compounds give rise to NP formation.

\[ [\text{Pd}^{II}(\text{phenanthroline})(\text{TMTU})(\text{Me})]^+\text{PF}_6^- \]

We first investigated the coordination of TMTU to the molecular [Pd\text{\textsuperscript{II}}(\text{phenanthroline})] system 1 (Scheme 3), which is a catalyst for the copolymerization of CO and styrene. Addition of TMTU to the proposed catalyst 1 in DCM afforded 2, which is the analogue of the TMTU-poisoned complex 2 (Scheme 3). We obtained an X-ray crystal structure of the compound, which confirmed the proposed TMTU-coordination mode (Figure 2).
Scheme 3. Catalyst 1 used in CO/styrene copolymerization, its resting state 3, its TMTU-poisoned analogue 2 and the TMTU resting state 4.

Figure 2. The structure of the TMTU-poisoned analogue 2 obtained by X-ray crystal structure determination. Displacement ellipsoids are drawn at 50% probability.

NMR measurements showed that when complex 2 is placed under an atmosphere of CO at room temperature cationic species 4 (Scheme 3) is formed. While for standard catalyst 1 the cationic 3 species is formed. That 3 is not formed indicates that the TMTU ligand binds strongly and that CO does not replace it. It also shows that TMTU does not lead to decomposition of the original complex (1).

[Pd\(^{\text{II}}\)(IMes)] complexes

We synthesized the CS\(_2\) (6) and TMTU (7) poisoned analogues of 5, which is the proposed (pre)catalyst for the semihydrogenation reactions (Figure 3). For all three compounds we determined their molecular structure through single crystal X-ray structure analysis (Figure 4).
Figure 3. The proposed catalyst 5 for the semihydrogenation and its CS₂ (6) and TMTU (7) poisoned analogues.

Figure 4. ORTEP representation of [Pd⁰(IMes)(MA)₃] complex 5 and its CS₂-poisoned analogue 6. The crystal structure of the TMTU-poisoned analogue 7 was refined with a disorder model. 7a shows the major disorder form (86.4% occupancy) and 7b the minor disorder form (13.6% occupancy). Displacement ellipsoids are drawn at 50% probability. Hydrogen atoms are omitted for clarity’s sake.

Through these X-ray crystal structures the coordination properties of the complexes and poison ligands could be studied in further depth. All three structures adopt a planar Y-shaped structure around the Pd⁰-atom.

We note that the maleic anhydride ligands (MA) of 5 are directed in opposite directions. This corroborates the inequivalence of the MA as was proposed by NMR-studies. The inequivalence is also displayed in the significant difference in lengths of the olefinic bond in the MA as well as in the MA-Pd distances.
The X-ray crystal structure of the putative TMTU poisoned catalyst 7 is the first example of a palladium(0) TMTU complex. The structure was disordered with two positions of the Pd atom and two orientations of the MA ligand. Two steric interactions give rise to the formation of these two conformers. In the major disorder form (7a) the anhydride carbonylic oxygen has a steric interaction with the methyl of the thiourea, and in the minor disorder form (7b) the MA ligand is rotated and its olefinic bond is directed to the methyl group of the thiourea. These steric interactions are clearly shown in the CPK model of both disorder forms. A comparison of bond geometries between compound 5 and its TMTU poisoned analogue is severely hampered by the disorder in 7. The geometrical parameters of the palladium complexes 5 and 7 are given in Table 1.

Table 1. Selected bond lengths of the X-ray crystal structures of 5 and 7. 7a and 7b are the major and minor disorder forms in the crystal structure of 7.

<table>
<thead>
<tr>
<th>Bond lengths (Å)</th>
<th>7a</th>
<th>7b</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pd–NHC</td>
<td>2.069 (5)</td>
<td>1.978 (6)</td>
<td>2.1062 (14)</td>
</tr>
<tr>
<td>Pd–MA</td>
<td>1.9486 (6)*</td>
<td>1.956 (3)*</td>
<td>2.0333 (2)*</td>
</tr>
<tr>
<td>Pd–MA[2]</td>
<td></td>
<td>2.0117 (3)*</td>
<td></td>
</tr>
<tr>
<td>MA (olefin)</td>
<td>1.437 (7)**</td>
<td>1.436 (12)**</td>
<td>1.393 (2)</td>
</tr>
<tr>
<td>MA (2) (olefin)</td>
<td></td>
<td></td>
<td>1.401 (2)</td>
</tr>
<tr>
<td>Pd–S</td>
<td>2.3592 (12)</td>
<td>2.503 (3)</td>
<td></td>
</tr>
<tr>
<td>S–C</td>
<td>1.721 (5)</td>
<td>1.721 (5)</td>
<td></td>
</tr>
</tbody>
</table>

*distance between metal and least-square plane of the ring
**restraints have been used in the refinement of the disorder model

The dinuclear compound 6 is located on an exact, crystallographic inversion center between the two metal atoms, and the IMes ligand has an approximate, non-crystallographic C2-symmetry. The general formula is [Pd0(IMes-μ(κ-S,η2)-(CS)2)]2 (Figure 3). The Pd0(IMes) moieties are bridged by two CS2 molecules. Each bridging CS2 ligand binds in a π-fashion to one of the Pd-centers and in a σ-fashion to the other. This results in a planar structure around the two Pd0-nuclei. The wing tips of the NHC are directed perpendicularly to this plane to minimize steric interactions.
Table 2. Comparison of 6 to the analogous phosphine Pd₂(P(Bu)₂Ph)₂(CS₂)₂ compound\textsuperscript{89}.

<table>
<thead>
<tr>
<th>Atom-Atom distance (Å)</th>
<th>NHC-CS₂ complex</th>
<th>P-CS₂ complex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pd–Pdi</td>
<td>4.1790 (8)</td>
<td>-</td>
</tr>
<tr>
<td>Pd–S(side)</td>
<td>2.3342 (7)</td>
<td>2.313 (1)</td>
</tr>
<tr>
<td>Pd–S(end)</td>
<td>2.3193 (7)</td>
<td>2.316 (1)</td>
</tr>
<tr>
<td>Pd–C</td>
<td>1.964 (2)</td>
<td>1.980 (5)</td>
</tr>
<tr>
<td>C–S(side)</td>
<td>1.664 (3)</td>
<td>1.643 (5)</td>
</tr>
<tr>
<td>C–S(end)</td>
<td>1.654 (2)</td>
<td>1.650 (5)</td>
</tr>
<tr>
<td>NHC–Pd</td>
<td>2.092 (2)</td>
<td></td>
</tr>
</tbody>
</table>

Symmetry code i: 2/3-x, 1/3-y, 1/3-z.

Complexes of the form of 6 are quite rare in literature: only a single X-ray crystal structure of such a binuclear binding motif with CS₂ was reported by Farrar et al.,\textsuperscript{89} with a general formula Pd₂(P(Bu)₂Ph)₂(CS₂)₂. Overall, the metrics and shapes of the bimetallic Pd-planes of both molecules are similar (Table 2). However, we observe significant differences in the bond lengths of the π-coordinated part of the CS₂ molecule to the palladium center. This is presumably caused by the stronger σ-donating properties of the NHC with respect to the phosphine. Interestingly, for both compounds there is only a minor difference between the C–S(η²) and C–S(η¹) bond lengths. An elongation of both bonds with respect to CS₂ is expected. However, a more significant difference between the lengths of the two CS bonds would be expected as π-back donation into the η²-CS-bond would affect this bond strongest. A somewhat larger difference is observed between the Pd–S(η¹) and Pd–S(η²) distance, but it is still minimal. Neither the publication by Farrar et al.,\textsuperscript{89} nor we are able to give a satisfactory explanation for this phenomenon. Comparing the obtained structure of compound 6 to that of the other two Pd⁰ compounds shows that the Pd–NHC distance is similar to that of the [Pd⁰(NHC)(TMTU)] compound \textsuperscript{7b}, and the Pd–S(η¹) distance is significantly shorter. This may mainly be caused by steric factors as there is a significant interaction between the MA and TMTU moieties in complex \textsuperscript{7a}, which is not an issue for the small CS₂ ligand.

In summary, we have studied the coordination properties of TMTU, and we were able to isolate and characterize the proposed poisoned catalyst analogues. The X-ray crystal structures of the phenanthroline (2) and NHC compounds (6 and 7) show that TMTU binds to Pd atoms via the sulfur atom in a single, defined binding mode. All these studies indicate that TMTU may be a good poison for the investigated catalyst systems. The synthesis of these compounds allows the further studies of the poisoning
capabilities of the TMTU ligand by using the poisoned catalyst analogues as precatalysts in their respective reactions.

### 5.5 Copolymerization of Styrene and CO by a [Pd\textsuperscript{II}(Phenanthroline)] Catalyst

Aromatic polyketones are interesting materials both as high-performance plastics and as precursors for polyalcohols, polyamines and polyimines.\textsuperscript{90} Bidentate nitrogen ligands, such as phenanthroline, have proven to be excellent ligands for this cationic Pd\textsuperscript{II}-catalyzed reaction (Scheme 4).\textsuperscript{91–93}

**Scheme 4.** The copolymerization of CO and styrene by [Pd\textsuperscript{II}(phenanthroline)(Me)]PF\textsubscript{6}.

The [Pd\textsuperscript{II}(phenanthroline)] (1) catalyzed copolymerization of CO and styrene was chosen as a first test-case of the poisoning method and the applicability of TMTU as a poison ligand for two reasons. First of all, the reaction has been intensively studied and all these studies indicate that the catalytic polymerization reaction involves well-defined molecular compounds. A second reason is that the proposed intermediates have been characterized by NMR-spectroscopy. This enabled the studies of the “poisoned” species, which demonstrated that TMTU is a good ligand for catalyst 1 (Section 5.4). A minor disadvantage is that not all parts of protocol can be tested for this reaction, since \textit{in situ} DLS measurements of the solution cannot be performed because insoluble polymers are formed. However, this is compensated by all the previously performed studies. Therefore, this reaction is highly suitable to validate the quantitative poisoning protocol using TMTU as a poison ligand.

**Validation**

Following the protocol (Scheme 2) poison validation was performed. The synthesis of compound 2 and NMR studies showed that the TMTU poisoned analogue can form and that TMTU binds strongly to the complex. DLS experiments showed that NPs were not
present in precatalyst 1 and that NPs were not generated when a solution was exposed to CO.

Subsequently, we tested the TMTU-poisoned analogue complex 2 as a precatalyst in the reaction. The test demonstrated that the poison ligand was highly effective because only a negligible activity was obtained, from which we conclude that the poison binds strongly and that the putative poisoned complex (2) is not catalytically active itself (Figure 5). The combined poison validation and DLS experiments indicate that TMTU does not decompose the compound and binds strongly to the precatalyst. Therefore, TMTU is an appropriate poison ligand for this reaction.

Quantitative partial poisoning

We performed a quantitative poisoning experiment by variation of the amount of TMTU between 0 and 0.5 equivalents of poisoning ligand with respect to the catalyst. An induction period of 5 minutes was instituted between the start of the reaction and the addition of the poison ligand to avoid interference of the poison ligand with the generation of the active catalyst species. We measured the total yield in polyketone after 24 hours as a function of the amount of TMTU that was added (Figure 5).

![Figure 5. Quantitative partial poisoning studies of 1 and 2 showing the relative activity as a function of the added amount of poison ligand.](image)

The fact that the TMTU-poisoned analogue of the (pre)catalyst is virtually inactive in this reaction indicates that TMTU is such a strong-binding poison. When a strong-binding poison is applied to an efficiently activated molecular catalyst, a linear negative relationship between the activity and the amount of poison is expected.\(^{68,73}\) Indeed, plotting the activity versus the poison fraction yields a straight line with a negative slope (Figure 5), indicating that the applied system behaves as is expected for
a molecular catalyst. The active metal fraction can then be derived by the determination of the slope of this line and calculating the intersection with the horizontal axis.\textsuperscript{61,94} In this case the intercept is at 0.84 equivalents of TMTU per Pd-atom, which is strongly indicative of a molecular catalyst, which is in good agreement with all previous studies.

In order to place the performance of the TMTU poisoning ligand in context, we compared the efficiency of TMTU to that of the standard poison, CS\textsubscript{2}. We applied 0.3 equivalent of CS\textsubscript{2} and compared the decrease in activity of the reaction caused by both poison ligands. TMTU reduced the catalyst activity of \textit{1} by \(~25\%\) (Figure 5). However, addition of 0.3 equivalent of CS\textsubscript{2} to \textit{1} did not influence the activity of the catalyst. We therefore conclude that CS\textsubscript{2} is a poor poison for this reaction. Probably, this is caused by a reversible binding of CS\textsubscript{2} to the catalyst, which in combination with the high volatility of CS\textsubscript{2} led to removal of the poison ligand from the reaction mixture.

From the above experiments and validations we conclude that the quantitative TMTU poisoning protocol is valid. The protocol indicates that a molecular catalyst is active, which is in line with the previous studies of this reaction. In addition the quantitative partial poisoning tests show that TMTU is a superior poison compared to CS\textsubscript{2} for this reaction.

\textbf{5.6 The Semihydrogenation of 1-phenyl-1-propyne to Z-1-phenyl-1-propene Using Molecular Hydrogen}

The semihydrogenation of alkynes that yields synthetic and pharmaceutically relevant \textit{Z}-alkenes is an important catalytic synthetic reaction. An interesting feature of this reaction is that both molecular and particle catalyst systems are active in this reaction.\textsuperscript{45,50,51,95-100} Our group has previously reported a catalytic system for this reaction that was proposed to proceed via an \textit{in situ} generated molecular [Pd\textsuperscript{2}(IMes)] species as the active catalysts (Scheme 5).\textsuperscript{46,101-103}

Sprengers et al. reported that the in situ generated catalyst is significantly more active than the isolated catalyst. One explanation for the reduced activity is that less of the MA ligands is applied. However, this observation may also be an indication that NPs may actually be participating as active species. In combination with the fact that NPs have been reported as active catalysts for this system, this merits further investigations into the nature of the true catalyst. For this reason we studied whether the isolated [Pd⁰(NHC)] complex 5 is a precatalyst for well-defined molecular species or a precursor for active (nano)particles. Using an isolated system instead of an in situ generated system is beneficial, because it circumvents issues that could arise from inefficient or incomplete formation of the active catalyst and generation of (active) NPs in that step.

Validation and synthesis of precursors devoid of NPs

We started with DLS analysis of 5 and its precursors to ensure that all tested species were NP-free. Bis(dibenzylideneacetone)palladium⁰ ([Pd⁰(DBA)₂]), is reported to contain NPs even when bought from the suppliers. Indeed, we observed the presence of NPs with DLS measurements in batches stored for a longer period, but not for samples of [Pd⁰(DBA)₂] freshly bought from the supplier. We were unable to obtain palladium⁰(1,4-di-tertbutyl-diazobutadiene)(maleic anhydride) ([Pd(ʻBuDAB)(MA)]) (8) and palladium(0)(norbornadiene)(maleic anhydride) ([Pd⁰(NBD)(MA)]) in a NP-free form when following the original synthetic procedures (Figure 6). Filtration over Celite was insufficient to remove all particle species. Complex 8 could be obtained devoid of NPs by flash column chromatography. However, we were unable to do so for 9, presumably due to the highly labile and volatile nature of the norbornadiene ligand.
With a suitable precursor in hand, the synthesis of NP-free 6 was attempted. Again, following literature procedure, NPs were observed with DLS after synthesis. It is impossible to discriminate between Pd NPs and other particles using only DLS measurements. Therefore, we performed TEM-EDX measurements, which confirmed that the particles that were observed with DLS were indeed Pd NPs. We were, however, able to obtain complex 6 devoid of NPs, based on DLS, through flash chromatography.

**Figure 6.** \([\text{Pd}^{0}(\text{tBuDAB})(\text{MA})] \) 8 and \([(\text{Pd}^{0}(\text{NBD})(\text{MA})] \) 9.

*Poison validation by applying the analogues of the poisoned catalysts in catalysis*

Complexes 6 and 7, the CS₂- and TMTU-poisoned analogues of the proposed molecular catalyst, were tested as (pre)catalysts in the semihydrogenation reaction for poison validation. Both complexes did not display any activity nor was the generation of NPs observed by DLS. Therefore, we concluded that the poisons are appropriate poisons for the molecular catalysts (or NP catalyst precursors) in this reaction.

*Poison validation with particle-based (pre)catalyst materials*

The next validation step is determining whether the poison ligands are also appropriate poisons for (preformed) NPs. Therefore, we tested the ability of the poison ligand to deactivate authentic particle-based precatalyst materials. We chose Pd on carbon to simulate poorly defined NPs and the BASF Nano-Cat on titanium sulfide as a control for well-defined small NPs. For the BASF Nano-Cat it was already proven that the active species are authentic NPs. For completeness, we first verified that Pd on carbon is also an authentic particle based catalyst instead of a precursor for atomic substrate-ligated compounds. For this purpose, we performed a (Maitlis) “hot filtration” test. When active soluble species are formed during a reaction, the filtrate should display activity. However, we did not observe any activity in the filtrate. Additionally, the amount of Pd that had leached from the support during the reaction was minimal according to inductively coupled plasma - atomic emission
spectrometry (ICP-AES) measurements. Therefore, we concluded that for both materials particles are the active catalysts.

Subsequently, we tested the ability of the poison ligand to deactivate these authentic particle-based precatalyst materials. The particle catalysts, without poison ligands, are quite active under the standard conditions (Figure 7). The Nano-Cat is faster than Pd on carbon, which is not surprising, because it has smaller particles and thus a higher degree of Pd is available for the reaction. We performed a partial poison test with TMTU and CS₂ to be able to compare the efficiency of both poisons. 0.25 equivalent of the appropriate poison with respect to the total amount of Pd was added to the reaction mixture and the reaction was followed in time. (Figure 7). We evaluated the poisons at room temperature and at 70 °C (Figure 8), since poisons are generally less effective at higher temperature. Evaluation of the poison efficiency at elevated temperatures is therefore an important aspect in the development of new poison ligands.

CS₂ (0.25 mol/mol Pd) did not deactivate the catalyst activity completely. Instead, an induction period was observed, after which catalytic activity starts. Possibly, this is the result of CS₂ escaping from the reaction mixture, since elevated temperatures shortened the induction period dramatically. The sigmoidal curve could also be caused by the “dissolution”¹⁰ of the Pd-particles by CS₂. However, ICP-AES showed that CS₂ and TMTU did not increase the Pd leaching (see Figure 9), from which we concluded that the observed induction times are not caused by disassembly of the NPs by the poison ligands. When CS₂ was applied as a poison ligand the Pd leaching even decreased compared to the standard reaction. Apparently, the CS₂ ligand possesses a stabilizing effect on the catalyst system, for which we do not know the cause.

TMTU has an advantage over CS₂ as a poison ligand (Figures 7 and 8). Initially, TMTU (0.25 mol/mol Pd) reduces the catalytic activity somewhat less effectively than CS₂, nonetheless, it still reduces the catalytic activity of the reaction by a respectable 96% or more. However, TMTU is a more reliable poison than CS₂, because it poisons the active catalyst for a much longer period. The advantages of TMTU as poison ligand are even more pronounced at 70 °C. Under these conditions the efficiency of both poisons decreases somewhat, but the induction period caused by CS₂ lasts significantly shorter. This clearly shows that TMTU is the better poison for this reaction, especially at elevated temperatures.
Figure 7. The semihydrogenation of 1-phenyl-1-propyne at 20 °C for Pd on carbon and the BASF Nano-Cat using either 0.25 equivalent of TMTU or CS₂.

Figure 8. The semihydrogenation of 1-phenyl-1-propyne at 70 °C for Pd on carbon and the BASF Nano-Cat using either 0.25 equivalent of TMTU or CS₂ as a poison.

Figure 9. Leaching of Pd from Pd on Carbon in the semihydrogenation of 1-phenyl-1-propyne and the influence of the poison ligands thereon.
Partial poisoning studies

Having demonstrated that TMTU and CS₂ are potent poisons under the applied reaction conditions, partial poisoning tests were performed with precatalyst 5 (Figure 10). We first performed a partial poisoning analysis of the precatalyst that was prepared according to the literature procedure, which thus contained NPs. In order not to hinder the generation of the active catalyst, the reaction was started by placing a solution containing the catalyst, the substrate and the internal standard in acetonitrile under an H₂ atmosphere. After 5 minutes 0.25 equivalent of the selected poison, with respect to the amount of precatalyst, was added, and the reaction was monitored in time. Both poisons decreased the activity significantly more than 25%, which is suggestive of NPs being the active species in this case.

![Graph showing partial poisoning test results](image)

**Figure 10.** The partial poisoning test at standard reaction conditions using compound 5 with and without NPs. When poison was applied, 0.25 equivalent was used.

However, since there were already NPs present in the applied precatalyst, we were unable to determine whether these particles or particles that were generated during the catalytic hydrogenation reaction were responsible for the observed activity. Therefore, we tested the (pre)catalyst 5 that was devoid of NPs and this did not display any activity. Catalytic activity is only observed when NPs are present with 5, thus the NPs that were formed during the synthesis must be the active catalysts.

We have demonstrated that TMTU and CS₂ poison particle-based catalysts, of which TMTU is a more reliable poison ligand. DLS measurements determined that in the original synthesis of precatalyst 5 NPs are formed. Subsequently, we applied partial
poisoning to determine the type of catalyst. The results from the partial poisoning experiments are sufficient to reliably determine the type of active catalyst and therefore, a full quantitative poisoning study was not performed. The developed protocol is thus capable to determine that the NPs that were formed in the synthesis of NHC complex 5 are the active species, instead of the complex itself.

5.7 Transfer Semihydrogenation of 1-phenyl-1-propyne to Z-1-phenyl-1-propene Using an In Situ Generated \([\text{Pd}^0(\text{IMes})(\text{MA})(\text{MeCN})])\) Catalyst

Other work in our group concerns a system for the transfer semihydrogenation of internal alkynes using an in situ generated catalyst 10 (Scheme 6), which applied a triethyl ammine-formic acid donor-pair as the hydrogen source. An ionic hydrogen donor-pair is applied, which circumvents the oxidative addition of hydrogen and a \([\text{Pd}^{II}(\text{NHC})])\) dihydride species. The system is reported to involve an anionic \([\text{Pd}^0(\text{NHC})(\text{H})])\) mono-hydride species 11 (See also Chapter 1, Scheme 9), thus it operates through a different mechanism from the previously discussed semihydrogenation reaction that uses molecular hydrogen. The system for the transfer semihydrogenation was intensively studied because it was the first system that did not show over-reduction and isomerization of the product Z-alkene at full conversion of the substrate.49,107

Scheme 6. The transfer semihydrogenation of 1-phenyl-1-propyne to Z-1-phenyl-1-propene and its side products by in situ generated catalyst 10 and proposed active species 11.
Several kinetic studies were performed on this catalyst system, such as the determination of the order in the substrate of both the hydrogen donors and the transition metal. Based on these studies an anionic mono-hydride [Pd\(^{0}\)(NHC)(H)] complex 11 was proposed to be the active catalyst. Two reasons were given for a molecular catalyst. The first was the observed first-order dependence of the reaction rate on the precursor concentration. However, several NP-based hydrogenation catalysts were reported to also give a first order in transition metal. A first order in transition metal does not necessarily signify a molecular active catalyst; it only demonstrates a linear relationship between the activity and the concentration of the applied precatalyst. The second reason for the catalyst being molecular was the unprecedented selectivity. It was hypothesized that NPs would not possess the required chemoselectivity to differentiate between alkenes and alkynes. Since this catalyst system is a key element in our current research, this aspect was investigated with the newly developed protocol.

Poison validation

The proposed CS\(_2\) (6) and TMTU (7) poisoned molecular catalysts were applied as (pre)catalysts in the semihydrogenation reaction. The CS\(_2\)-poisoned compound (6) showed no activity in the semihydrogenation and NPs were not observed with DLS measurements. The TMTU-poisoned compound showed some activity and NPs were not observed with DLS. The activity of the TMTU-poisoned compound was reduced by 83% with respect to the catalyst without poison ligand. The validation experiments indicate that the CS\(_2\) and TMTU are appropriate poisons for the transfer semihydrogenation reaction as well.

In order to investigate the efficiency of the poison ligands on authentic particle catalysts, we first tested whether or not particle-based catalysts are active in the transfer semihydrogenation of 1-phenyl-1-propyne (Figure 11). We found that not all types of NP (pre)catalysts are active in the semihydrogenation reaction. Most surprising was the inactivity of the BASF Nano-Cat, which is one of the most active catalysts for the hydrogenation of alkynes using molecular hydrogen. The commercially available Pd nanopowder <25 nm from Aldrich was also inactive. Lindlar's catalyst (Pd on CaCO\(_3\) poisoned with lead acetate) and Pd on carbon, on the other hand, displayed reasonable activities.
Figure 11. The transfer semihydrogenation of 1-phenyl-1-propyne using 3 mol% of several palladium NP catalysts with and without 0.25 equivalents of TMTU or CS$_2$, conversion after 24 hours.

Subsequently, we performed a Maitlis filtration test in reactions with these supported catalysts, in which cases no activity of the filtrate was observed. Additionally ICP-AES measurements showed that the leaching of Pd from the particle (pre)catalysts is minimal (Figure 12). Based on these observations it seems that for these supported particle-based catalysts the activity originates from Pd on the support.

Figure 12. Pd leaching from the catalyst materials in the transfer semihydrogenation reaction and the influence of the poison ligands thereon (ICP-AES).

We continued with the validation of the poison ligands for particle catalysts. Both CS$_2$ and TMTU efficiently reduced the activity of the catalysts (>90%). Especially CS$_2$ was highly efficient. However, when CS$_2$ was applied as a poison ligand, the Pd leaching
was increased by more than an order of magnitude. Therefore, even though CS$_2$ reduces the activity of the catalyst in an efficient manner, it also has an additional ill-defined interaction with the (pre)catalyst, possibly making it a "non-innocent" poison.

From the validation experiments we conclude that TMTU strongly reduces the activity of both molecular and particle catalysts, thus binding sufficiently strong to the catalyst. Additionally, TMTU does not seem to cause NP formation because no NPs were observed when the TMTU-poisoned analogue of the molecular catalyst was applied as a (pre)catalyst.

**DLS and quantitative partial poisoning studies on the transfer semihydrogenation reaction**

In the catalytic procedure for the transfer semihydrogenation reaction the NHC-species 5 is first generated from [Pd($\text{tBuDAB})(\text{MA})]$ (8), after which the reagents and substrate are added (Scheme 6). Therefore, DLS measurements were performed after each addition. The measurements showed that particles had formed after the generation of the catalyst. Upon addition of formic acid, a white suspension formed, which is most likely triethylammonium formate. After filtration of the suspension over a 0.4 μm filter, DLS did not show any NPs. The particles that were present up to this point, have probably been taken up in the agglomeration of the macroscopic particles. Half an hour after the start of the reaction another DLS measurement was performed, and particles of ~44 nm in size were observed. After an hour Pd black formation was observed, and no further DLS measurements were performed.

Subsequently, we performed quantitative partial poisoning studies of the transfer semihydrogenation reaction with the *in situ* generated catalyst 10 ([Pd($^\text{Imes})(\text{Ma})(\text{MeCN})]$, Scheme 6). We applied 0.25 equivalent of TMTU or of CS$_2$ respectively, as poison ligands in the reaction. According to these experiments, TMTU and CS$_2$ caused an equal decrease in turn-over frequency, which provides another indication that the poisons are not inducing catalyst decomposition or NP formation: It is highly unlikely that the two poison ligands decompose the proposed molecular catalyst at the same rate. Based on this observation and the other validation experiments we conclude that the poison ligands are behaving only as a poison and that NP formation is inherent to the applied reaction conditions.

The quantitative poisoning study shows that only a fraction of the Pd is active (Figure 13). Drawing a tangent line for the initial decrease in activity gives an estimation that ~12% of the Pd is active in the reaction. Such a value is indicative of catalytically active NPs, if all quantitative poisoning criteria are met.$^{68}$ In the quantitative
poisoning experiment the activity does not decrease to zero in a linear fashion. This behavior is typically observed when the binding of the poison to the active catalyst is not infinitely large with respect to the substrate. The substrate alkyne binds strongly to Pd. Therefore, the alkyne (which is present in excess) may well be in competition with the TMTU poison ligand. As a result of this competition the degree of binding is concentration dependent, thus yielding a non-linear inhibition-concentration relationship. This phenomenon is actually normal in literature. A competition between alkyne and poison ligand is also consistent with the data from the poison validation with particle-based precatalysts, where the poison ligand does not fully deactivate the particle-based precatalysts as well. The percentage of active Pd is likely overestimated because there are few points in the “linear” area of the partial poisoning study. Hence, the estimated amount of 12% of the Pd that is active, is most likely lower in reality.

Figure 13. The quantitative partial poisoning of the proposed in situ generated catalyst 10. The TOF was determined at 15 % conversion.

We evaluated whether the particles that were observed by DLS could correspond to the percentage of Pd that is active. Based on the DLS measurements the average particle size is in the order of 40 nm. Assuming all Pd is present as spherical particles, a density of palladium of 12.02 g/cm³ (the density of Pd) and an atomic surface that is simplified to squares with edges that are equal to the atomic diameter of Pd, we estimate that about 3% of the Pd atoms are on the outside of the particle. For NPs not all of the metal on the outside can be catalytically active, since there are also coordinating “ligands” and other stabilizing species present on the surface of the particle. Assuming 30 % of the metal on the surface of a NP to be active, this is a high amount. Using this for an estimation means that an amount of ~1 % of the Pd would be expected to be active. This value does not correspond with the
(over)estimated value of 12% of active Pd in the reaction. Hence, the observed NPs may not be the (sole) source of catalytic activity.

If the observed NPs are not the main source of catalytic activity, the active species does not make up 100% of the applied Pd either. In that case a lower percentage of active Pd is expected. We do not know the amount of applied Pd that is present in a NP form. Therefore, we also do not know the amount of active Pd that could be expected. Hence, the results obtained by DLS and quantitative poisoning are open to multiple interpretations.

As such, the results of the determination experiments could stem from four types of catalyst systems. I) The observed NPs are the active catalyst. Based on the active metal fraction and the observed first order in Pd concentration this is less likely. II) Nanoclusters, which are not detected by DLS are the active catalysts. These clusters must be highly defined to provide the observed first-order kinetic behavior in Pd III) The observed NPs are not the (main) source of catalytic activity, but are in equilibrium with a molecular species, which is responsible for the majority of the catalyst activity. Similar systems have also been reported for Heck reactions3-5 (Chapter 1, Scheme 11) and other Pd-catalyzed cross-coupling reactions.109,110 However, for such systems, the substrate-Pd ratio is, usually, at least two orders of magnitude higher than for our system. 4) Only a small fraction of the total amount of Pd is active in the form of a molecular active species. A molecular active species is supported by the activity of the TMTU-poisoned analogue of the putative molecular catalyst. This species shows a low activity, and NPs are not observed on DLS. The observed first order in Pd concentration is not definitive evidence. However, it fits well with a molecular catalyst system.

In summary, the poison validation showed that both TMTU and CS₂ are efficient poisons for this reaction. However, CS₂ was found to have an interaction with the particle-based precatalyst materials that causes an increase in the leaching of Pd. For this reason, CS₂ could be a “non-innocent” poison. As such, TMTU is preferred as a poison ligand.

The results of the protocol to determine the type of catalyst are not clear cut. We have proposed four possible catalyst systems that could give rise to the obtained results. A three-phase test may provide further information on the type of the catalyst. However, this requires that the reaction components are in three different phases. To apply this approach to this system two components must be heterogenized, which may alter the system and thus make the result of the three-phase test less reliable. The results of the protocol show that the type of active catalyst system for the transfer
semihydrogenation is not as simple, as was previously proposed. The amount of active Pd is low and NPs are generated in the reaction. Therefore, regardless of the type of catalyst, the protocol has demonstrated that significant improvements can be made on this system.

5.8 The Transfer Semihydrogenation of 1-phenyl-1-propyne to Z-1-phenyl-1-propene Using [PdII(IMes)(η^3-C_3H_5)(Cl)] with Additional PPh₃ Ligands as Catalyst System

We reported another system for the transfer semihydrogenation of alkynes in chapters 2 and 3. This system applies a precatalyst that is transformed to a [Pd⁰(IMes)] species in situ by triethylammonium formate, which is stabilized by additional selectivity-enhancing PPh₃ ligands (Scheme 7).

Scheme 7. [PdII(IMes)(allyl)(Cl)] precatalyst (12) that is converted under reaction conditions to a PPh₃-stabilized Pd⁰ catalyst system for the transfer semihydrogenation.

We performed several mechanistic studies on this system in order to determine the role of the additive and find what mechanism lies behind the high selectivities that were observed. For this system first-order reaction kinetics were observed in catalyst concentration when the precatalyst was applied without any additives. As mentioned before, such kinetic behavior does not unequivocally prove that the reaction is catalyzed by a molecular catalyst, but at the time we nevertheless interpreted the data as such. From mechanistic studies (Chapter 3) we conclude that the high selectivities that are induced by the additive are the result of the relative coordination strengths of the substrate, the phosphine and the products. The coordination of the phosphine ligand to the catalyst prevents the isomerization and over-reduction of the Z-alkene product.
In the light of the results for the other transfer semihydrogenation catalyst system, determining the type of active catalyst is also relevant for this system. Additionally, determining the type of active catalyst for the PdII-precatalyst system may show the viability of additive methodologies to prevent the formation of active NPs and to stabilize molecular catalysts.

**Quantitative partial poisoning studies and DLS measurements**

We validated the particle-based catalysts, the capabilities of the poison ligands to stop particle based-catalysts and the reduction of the catalytic activity of the analogues of the poisoned molecular catalysts in the previous section. We performed DLS measurements of the reaction using two equivalents of PPh₃ and precatalyst 12 and precatalyst with two equivalents of PPh₃ and 0.25 equivalent of TMTU or CS₂, respectively. In all three cases NPs were observed. Therefore, DLS could not be used to prove that TMTU and CS₂ do not lead to decomposition of the catalyst. We found that CS₂ and TMTU reduced the activity of the reaction equally. The equal reduction in activity indicates that the poisons are “innocent”, since it is highly unlikely that CS₂ and TMTU decompose the catalyst at the same rate. Based on all validation experiments we conclude that TMTU is an appropriate poison for the transfer semihydrogenation and has a similar efficiency as CS₂.

Subsequently, we performed a quantitative partial poisoning analysis by variation of the applied amount of TMTU, from which we estimated the percentage of the metal that is active (Figure 14). The plot of the relative activity as a function of the TMTU -Pd ratio for the transfer semihydrogenation seems to show a concentration-dependent relation just as for the system described previously (Section 5.5). The initial part of the plot shows a linear correlation between the applied poison and the activity, which is another indication of strong binding of the poison. Drawing a tangent line through these points gives an estimate that ~42% of the applied Pd atoms are active.
Figure 14. A quantitative poisoning analysis of the transfer semihydrogenation with 12 by variation of the TMTU over Pd ratio and determining the initial TOF.

The value is too high for NPs as the sole catalysts. We compared the size of the observed NPs to the percentage of Pd that is active to estimate quantitatively whether the observed NPs can be the active catalyst. DLS gives an average particle size of ca 30 nm after 40 minutes. Using the same assumptions as in the previous section, we estimate that about 4% of the Pd atoms is exposed to the substrate and available for catalysis at the particle surface. Clearly, this does not correspond to the estimated 42% of the Pd that is active according to the quantitative poisoning studies. The percentage of active Pd atoms is an order of magnitude larger than may be expected on the basis of the observed NPs. Therefore, we conclude that the observed NPs cannot be the sole active catalysts.

Further assignment of the type of active catalyst based on the quantitative partial poisoning is not straightforward. The obtained value of the percentage of Pd that is active and the observed NPs are multi-interpretable and could be obtained from four systems. I) Nanocluster active catalysts, where also less active or inactive NPs are formed. II) Dissoluted substrate-ligated species that are in equilibrium with NPs/nanoclusters. III) A well-defined, molecular species is active and at the same time less active, or inactive NPs are formed. The developed protocol does not allow a reliable and clear-cut distinction between these cases. Making such a distinction is extremely difficult and sometimes impossible. In such cases one may only indicate which case is more plausible.

The percentage of the metal that is active in nanoclusters has been scarcely studied. If ~40% of all Pd is in an active state, this is a high but not
unrealistic value for nanoclusters, more so, considering that part of the applied Pd is present in the observed NPs. Nanoclusters could also give rise to the observed kinetic first-order in Pd that was observed for this system.

A molecular active species could also be obtained if an equilibrium exists between NPs and substrate ligated species. Such an equilibrium would explain the observed NPs and could also give rise to the estimated percentage of active Pd. A similar mechanism was derived for a [Pd\textsuperscript{II}NHC] catalyst system for Suzuki–Miyaura cross-coupling reaction proposed for catalysts.\textsuperscript{110} The NHC ligand is proposed to be part of the molecular active species that is in equilibrium with the NPs in this system. However, the substrate to Pd ratios of such catalyst systems are generally orders of magnitude higher than for our system.\textsuperscript{4,109}

Efficient well-defined molecular catalyst systems are expected to give values greater than 40% of active metal. However, we proposed that the phosphine coordination to the [Pd\textsuperscript{II}(NHC)] species leads to an inactive state,\textsuperscript{111} which was also proposed for a Pd(NHC)PCy\textsubscript{3} system by Cazin et al.\textsuperscript{41,115} The presence of an inactive species could explain why a lower fraction of Pd that is active in the reaction is obtained for a molecular catalyst. The degree of Pd that is in a poison-independent inactive state depends on the binding strength of the phosphine ligand compared to that of the alkyne substrate. Unfortunately, we were unable to determine the binding constants for both species. Therefore, we cannot quantify or estimate the amount of catalyst that is in a dormant state and correlate this to the observed active metal fraction. On a qualitative basis, we can derive that the binding of the phosphine ligand is strong. By application of 1.0 equivalent of PPh\textsubscript{3} the catalytic activity is reduced by 80%. Based on the observed strong binding of PPh\textsubscript{3}, a significant fraction of the Pd may be in an inactive state. In this case, the obtained percentage of active Pd fits well with a molecular active compound. The data obtained in the previous mechanistic studies are also circumstantial evidence of a molecular catalyst. The proposed molecular catalyst would yield a kinetic first-order in catalyst concentration. The [Pd\textsuperscript{II}Mes(TMTU)(MA)] compound shows some activity, but does not form NPs. An influence of the NHC ligand is observed. Based on these observations a form of molecular species is the most likely catalyst.

By comparing both the discussed systems for the transfer semihydrogenation more insight may be gained in the role of the phosphine additive ligand and the type of active catalyst. There is a significant difference in the percentage of active Pd between both catalyst systems. About 40% is active when PPh\textsubscript{3} is applied with precatalyst \textsuperscript{12}, and only ~10% is active when the \textit{in situ} generated system is applied. Most likely the
phosphine ligand stabilizes the molecular (or nanocluster) catalyst and prevents the degradation of the catalyst into (less active) NPs. Such an effect has previously been observed for a catalyst system for Heck coupling reactions that uses Pd(OAc)$_2$ as a precatalyst. Without PPh$_3$ ligands the system was reported to form NPs. However, in the presence of 4 equivalents of PPh$_3$ no colloids were observed.$^{36,116}$ Stabilization of the active catalyst by the PPh$_3$ ligand also explains the observed reactivities in the transfer semihydrogenation reaction. As expected, the initial catalytic activity decreases at higher PPh$_3$ loadings. However, at longer reaction times the reaction becomes faster at higher PPh$_3$ loadings. Stabilization of the catalyst by the PPh$_3$ ligand causes more Pd to remain active throughout the reaction, which results in higher overall activities.

To summarize this part, the type of catalyst for transfer semihydrogenation reaction using [Pd$^{II}$Mes] precatalyst 12 and PPh$_3$ additive ligands was investigated. Their results do not definitively allow the assignment of any type of active catalyst. From the obtained data three catalyst systems have been proposed. Based on known properties of the different types of suggested catalysts and the indirect evidence provided by the mechanistic studies (Chapter 3), the data suggest a partially deactivated molecular catalyst system that dominates the catalytic reaction. Comparison of both systems for the transfer semihydrogenation reaction indicates that the phosphine additive ligand increases the percentage of active Pd by stabilization of the catalytically active species.

5.9 Conclusion

We have developed a protocol for the determination of the type of active catalyst for several Pd catalyzed semihydrogenation reactions of alkynes to Z-alkenes. In this protocol, we applied quantitative partial poisoning and DLS methods, which also incorporated various validation experiments. As a part of these validation experiments we studied the coordination of TMTU and CS$_2$ to Pd$^0$ complexes, which showed that TMTU is a good ligand for Pd. In these studies we obtained the corresponding X-ray crystal structures of 5, 6 and 7. Next to the semihydrogenation reactions, we studied the Pd-catalyzed copolymerization of CO and styrene. The copolymerization is an extensively studied, molecularly catalyzed reaction, and is therefore ideal as additional validation of the protocol. Next to the protocol, we have introduced TMTU as an alternative poison ligand to the standard sulfur-based poison CS$_2$. According to the protocol the copolymerization reaction is indeed catalyzed by a molecular species, which is in line with the extensive previous research on this reaction. Therefore, both the additional validation of the protocol and the validation of
TMTU as a poison ligand were successful. We also demonstrated that TMTU is a superior poison ligand to CS$_2$ for the copolymerization reaction.

The protocol demonstrated that the semihydrogenation with molecular hydrogen is not catalyzed by its proposed NHC-catalyst 5. Instead, it is catalyzed by NPs that were most likely generated during the synthesis of the NHC complexes.

Subsequently, the protocol was applied to two transfer semihydrogenation reactions. The first, an in situ generated [Pd(NHC)] system 10, does not operate as efficiently as it was proposed. Only about 10% of the applied palladium is active in the reaction and NPs are observed. Multiple Pd species are present in this catalyst system, which complicates the assignment of the type of active catalyst. Therefore, no clear-cut assignment of the type of catalyst for this system could be made. However, based on the results of the protocol we find that the observed NPs are most likely not the (main) source of catalytic activity. Either molecular catalysts or nanoclusters are likely responsible for the bulk of the activity.

The second catalyst system that was investigated uses precatalyst 12 and PPh$_3$ as additive. The methods for determination did not allow the definitive assignment of a type of catalyst. Based on the obtained results and in combination with the previous mechanistic studies, the active catalyst for this system may well be a molecular species. A comparison of both transfer semihydrogenation catalyst system indicates that PPh$_3$ stabilizes the type of active catalyst and results in a higher percentage of Pd that is active in the reaction compared to the in situ generated system.

For the development of TMTU as a poison ligand we also evaluated its performance relative to the standard poison ligand CS$_2$ in the investigated reactions. We found that TMTU is a superior poison ligand for the copolymerization and the semihydrogenation reaction. Additionally, we found that CS$_2$ and TMTU perform equally well for the transfer semihydrogenation reactions. The beneficial properties of TMTU make it a valuable addition to the available poison ligands and therefore, it may be well suited in poisoning studies of other late transition metals.

Overall, these studies have, once more, demonstrated the importance of determining the type of active catalyst. None of the semihydrogenation reactions appear to be as straightforward as they were originally presented. Critical evaluation of such systems, in early stages, is therefore essential. Protocols as the one presented here may facilitate such critical evaluations. The protocol is straightforward and reliable and will also be applicable to various other types of reactions, making it a valuable tool for catalyst development.
5.10 Experimental Section

Complex synthesis and catalytic experiments were performed using Schlenk techniques under dry nitrogen. Solvents were dried according to standard procedures and distilled prior to use,\(^\text{117}\) unless stated otherwise. Maleic anhydride was crystallized from hot DCM. [Pd(η\(^3\)-C\(_3\)H\(_5\))\(_2\), triethyl amine, formic acid, potassium tert-butoxide triphenylphosphine, Pd nano-powder, Pd on carbon (10 wt%), Pd on BaSO\(_4\) (10 wt%) and Lindlar’s catalyst (5 wt%) were purchased from Sigma Aldrich. The BASF NanoCat was purchased from Strem chemicals. A Pd-DVTMS (1,3-divinyl-1,1,3,3-tetramethyl-disiloxane palladium\(^{0}\)) solution was generously provided by Umicore. Compounds 5\(^\text{111}\) and 12\(^\text{118}\) were synthesized according to literature procedures. NMR spectra were recorded on Bruker AV 400 MHz, Bruker DRX 300 MHz and Varian Mercury 300 MHz spectrometers. HR mass spectrometry was performed on a Bruker MicrOTOF-Q machine using ESI. GC analysis were performed on a Thermo Scientific Trace GC Ultra equipped with a R-Rxi 5ms column (30 m, ID 0.25 mm) and quantified using the response factor corrected GC-areas in respect to the internal standard. ICP-AES analyses were performed by Mikroanalytisches Laboratorium Kolbe, Mülheim an der Ruhr, Germany. DLS data were obtained on an ALV/LSE 5003 light scattering electronics and multiple Tau digital correlator.

[Palladium(II)phenanthroline(tetramethylthiourea)(methyl)] hexafluorophosphate (2). To a solution of [Pd(phenanthroline)(Me)Cl] (0.21 mmol) in DCM (6 mL) a solution of TMTU (0.42 mmol) n DCM (1 mL) was added leading to a clear solution. To the latter a solution of AgPF\(_6\) (0.24 mmol) in DCM (1.5 mL) was added. The system was stirred at room temperature for 30 min leading to the precipitation of AgCl. The suspension was filtered over Celite, and washed with DCM. The filtrate was concentrated up to one third of volume and a yellow solid was isolated upon addition of diethyl ether. The solid was filtered and dried under vacuum. The NMR analysis indicates that the solid is a mixture of the desired product and of the unreacted starting Pd-complex. The solid was purified by completing the reaction. The solid (0.0122 mmol) was dissolved in DCM (6 mL). To this solution TMTU (0.0244 mmol) dissolved in DCM (0.5 mL) was added. To the obtained solution, a solution of AgPF\(_6\) in DCM (0.01403 in 0.5 mL) was added. The final solution was stirred for 30 min, afterwards the precipitated AgCl was filtered over Celite, washed with DCM. The filtrate was concentrated under vacuum and the product precipitated upon addition of diethyl ether. The yellow solid was filtered and dried under vacuum. Total yield: 46 %. \(^1\)H-NMR (500MHz, CD\(_2\)Cl\(_2\)) \(\delta = 9.08\) (d, 1H, Phen(H\(^9\))), 8.98 (d, 1H, Phen(H\(^2\))), 8.68 (dd, 1H, Phen(H\(^9\))), 8.64 (dd, 1H, Phen(H\(^7\))), 8.09 (s, 2H, Phen(H\(^5,6\))), 7.97 (m, 2H, Phen(H\(^3,8\))), 3.31 (12H, s, NCH\(_3\)), 0.80 (s, 3H, Pd-CH\(_3\)).
(1,4-Di tert butyl-dia z o buadiene)(maleic anhydride)palladium(0) (8). The compound was synthesized according to the procedure of Cav ell et al.\textsuperscript{105} Further purification was performed by flash column chromatography. The compound was dissolved in a minimum amount of 1:1 DCM THF and brought on the column. The compound was then eluted with pure THF. The fractions were collected and the solvent was removed giving the compound in a 90% yield. Subsequently, no particles were observed by DLS indicating that the compound is devoid of NPs.

**Bis-[palladium(0)-(1,3-dimesityl-imidazolylidene)-μ(κ-Sη²)-carbon disulfide]** (6). The corresponding imidazolium salt (0.15 g, 0.44 mmol) was stripped twice with 3 mL toluene and suspended in THF (30 mL). Potassium tert-butoxide (65 mg, 0.53 mmol) was added and a lightly discolorated solution was obtained. Subsequently, [Pd(DVTMS)] in solution (10.87 mass % Pd) (0.431 g, 0.44 mmol) was added and an orange solution was obtained. The solution was stirred for an hour and CS₂ (5M in THF, 4.4 mmol, 0.9 mL) was added. Upon addition the solution turned yellow, but in time the color changed to orange again. The solution was stirred overnight. Then 10 mL of pentane was added and the solution was filtered over Celite (in air). The solution was concentrated to ca 3 mL. The product was precipitated with pentane and washed with pentane twice, yielding a yellow powder. This was dissolved in DCM with 1% 5M CS₂ solution in THF and was flashed over a silica column (0.183 g, 83% yield). A DLS measurement was performed, which showed that the sample was devoid of particles. X-ray quality crystals were obtained by slow diffusion of pentane 2 mL to 0.5 mL THF with 15 mg compound.\textsuperscript{111} \textsuperscript{1}H-NMR (300 MHz, CD₂Cl₂) δ 7.11 (s, 2H, Im-bb), 7.01 (s, 4H, Mes), 2.37 (s, 6H, Mes(p-Me), 2.14 (s, 12H, Mes(o-Me)). \textsuperscript{13}C-NMR (75 MHz, CDCl₃) δ (CS₂ \textsuperscript{13}C not observed), 188.19 (NCN), 139.57 (p-Mes), 136.54 (i-Mes), 135.77 (o-Mes), 129.66 (m-Mes), 123.51 (Im-bb), 21.64 (Mes(p-Me)), 18.33 (Mes(o-Me)). IR: 1119 cm⁻¹ CS (s), 716 cm⁻¹ CS (s).

**Palladium(0)-(1,3-Mesityl-imidazolylidene)(maleic anhydride)(tetramethyl-thiourea)** (7). 1,3-Dimesitylimidazolium chloride (0.200 g, 0.58 mmol) was stripped with toluene three times and, subsequently, suspended in 30 mL THF. First potassium tert-butoxide (0.093 g, 0.76 mmol), second [Pd('BuDAB)(MA)] \textsuperscript{8} (0.218 g, 0.58 mmol) and third, TMTU (0.100 g, 0.76 mmol) were added. The solution was stirred for one hour, after which it was filtered over a thick layer of Celite and rinsed with an additional 10 mL of THF. The solution was concentrated to approximately 2 mL and 2 mL of Et₂O was added. While stirring 20 mL pentane was added drop-wise, upon which the compound precipitated as a light yellow powder. The precipitation step was repeated, but \textsuperscript{1}H NMR showed that an unidentified byproduct was still present. The compound was further purified by column chromatography over silica (in air) using a 5% acetone in DCM eluent and 0.19 g of a yellow powder, (0.30 mmol) was obtained, which corresponds to a yield of 51%. \textsuperscript{1}H NMR (300 MHz, CD₂Cl₂) δ 7.09 (s, 2H, Im-bb), 7.01 (s, 4H, Mes), 3.01 (d, J = 3.7 Hz, 1H, MA), 2.90 (s, 12H, NMe₃), 2.83 (d, J = 3.7 Hz, 1H, MA), 2.36 (s, 6H, Mes(p-Me)), 2.19 (s+s, 12H, Mes(o-Me)). \textsuperscript{13}C NMR 75 MHz (CDCl₃) δ: 191.14 (NCN), 190.74 (thiourea), 172.71 (C=O), 172.21 (C=O), 138.17 (p-Mes), 136.97 (i-Mes), 136.11 (o-
The copolymerization of CO and styrene. A three-necked, thermostated 75 mL glass reactor equipped with a magnetic stirrer and connected to a temperature controller was heated to 30°C. After establishment of the reaction temperature 20 mL 2,2,2-trifluoroethanol (TFE), 10 mL of styrene, 0.0127 mmol of the selected precatalyst and 0.0635 mmol of 1,4-benzochinone were added, after which the solution was bubbled through with CO for 10 minutes. Subsequently, if required, the appropriate amount of poison was added and, a previously filled, 4 L balloon was connected to the reactor. The system was stirred for 24 hours, after which the reaction mixture was poured onto methanol (100 mL) and stirred for 1.5 h at room temperature. The obtained solid was filtered, washed thoroughly with methanol and dried under vacuum until a constant weight was obtained and analysed by NMR spectroscopy.

Semihydrogenation of 1-phenyl-1-propyne with authentic particle-based precursors and molecular precursors. The appropriate catalyst precursor (0.008 mmol, 0.4 mol% based on Pd content) was added to a 2-necked Schlenk that was equipped with a hydrogen gas bag and a valve with a septum containing 10 mL of a previously prepared, degassed stock solution of MeCN with 0.83 M 1-phenyl-1-propyne and 8.3 M p-xylene. If required, 0.002 mmol of the appropriate poison was added as 0.5 mL of a stock solution of the poison. Then the mixture was placed under a hydrogen atmosphere by ten cycles of evacuation and subjecting to hydrogen atmosphere. Periodic sampling was performed by taking 0.05 mL of the mixture, filtering over a plug of silica with 1 mL of DCM which was analyzed by GC. DLS-measurements were performed by taking 1.5 mL of the solution, which was filtered over a 0.4 μm filter and transferred to a custom made cuvette that was adapted with a Schlenk connector that allowed inert handling.

A "hot" filtration test for the semihydrogenation of 1-phenyl-1-propyne with supported catalyst materials. The normal catalytic procedure was performed, only after 5 minutes a sample was taken and the reaction mixture was filtered over a column of Celite. The filtrate was transferred to another 2-necked Schlenk and exposed to hydrogen and the solution was allowed to react further and periodic samples were taken to determine the activity of the liquid phase.

Determination of the Pd leaching from the particle precatalyst materials in the semihydrogenation of 1-phenyl-1-propyne. Using ten times the standard amount of Pd on C and five times the standard volume of stock solution the reaction was run for twenty-one hours and filtered over Celite. The solution was concentrated on a rotatory evaporation device and dried under higher vacuum 3·10⁻² mbar. The obtained oil was analyzed for Pd content using ICP-AES.

Transfer semihydrogenation of 1-phenyl-1-propyne using the proposed in situ generated [Pd⁰IMes(MA)] catalyst. The procedure was performed according to the procedure as described by Hauwert et al., with a few minor adaptations in volumes and instead of Schlenks a Radleys' twelve-place reaction station with integrated heating and cooling setup was used for these experiments. In a typical experiment
mesityl imidazolium chloride (12.5 mg, 0.037 mmol) was suspended in 20 mL MeCN and stirred overnight. KOtBu (18 mg, 0.15 mmol) was added to generate the free carbene and the mixture was stirred for one hour. [Pd(BuDAB)(MA)] (8) (12.4 mg, 0.033 mmol) was added and the reaction was stirred for another hour. Subsequently, determining the exact amounts by post-weighing, 1-phenyl-1-propyne (0.38 g, 3.3 mmol), p-xylene (0.35 g, 3.3 mmol), NEt₃ (1.69 g, 16.7 mmol) and formic acid (0.77 g, 16.7 mmol) were added in that order. After addition of the formic acid the reaction was heated to 70°C. At this temperature the appropriate amount of poison was added. Samples for GC-analysis were taken at regular intervals by taking 0.05 mL of the reaction mixture, and filtering it over a plug of silica with 1 mL DCM. DLS samples were prepared by taking 1.5 mL of the reaction mixture, filtering it over a 0.4 μm filter and transferring it to a specially designed cuvette that was adapted with a Schlenk connection. The TOFs for the quantitative poisoning analysis were determined around 15% conversion.

Transfer semihydrogenation of 1-phenyl-1-propyne using preformed or Pd³⁺(IMes) precatalysts with PPh₃ additives. A stock solution was prepared, adding in their respective order: acetonitrile (320 mL, 250.3 g), 1-phenyl-1-propyne (6.4 g, 55 mmol), p-xylene (internal standard, 5.68 g, 54 mmol), triethylamine (27.00 g, 267 mmol) and formic acid (11.48 g, 267 mmol), which was saturated with nitrogen gas by gently bubbling N₂ through the solution for 20 minutes. From the stock solution 20 mL was taken, by a syringe, and added to one of the twelve reaction vessels. The exact amount of added stock solution was determined by weighing; for this reason, molar and weight percentages were applied to determine quantities and further calculations. The Radleys’ station was heated to 70 °C, after which 0.03 mmol of the appropriate catalyst, and, if required, the PPh₃ additive was added. After 10 minutes the corresponding amount of the appropriate poison was added. Samples for GC analysis were taken at regular intervals by taking 0.05 mL of the reaction mixture and filtering it over a plug of silica with 1 mL DCM. DLS samples were taken by taking 1 mL of the reaction mixture, filtering it over a 0.4 μm filter and transferring it to a specially designed cuvette that was adapted with a Schlenk connection. The TOFs for the quantitative poisoning analysis were determined around 15% conversion.

Transfer semihydrogenation of 1-phenyl-1-propyne using particle-based precatalyst materials. The experiment was performed as described for the molecular catalysts. However, for Pd on C, Pd nano-powder and Lindlar’s catalyst 3 mol% (0.09 mmol) of the precatalyst material was applied. For the poison validation 0.25 equivalent of the appropriate poison (with respect to the Pd) was applied (0.0023 mmol).

The “hot” filtration test for the semihydrogenation of 1-phenyl-1-propyne using particle-based precatalyst materials. A standard experiment, as described previously, was performed. After one hour the reaction mixture was filtered over Celite and the filtrate was allowed to react further, after which the activity was monitored by GC.

Determining the degree of leaching of Pd from the supported precatalyst material and the influence thereon for the transfer Semihydrogenation of 1-
phenyl-1-propyne. The experiment was performed as the standard experiment, but on a two and a half time larger scale. The reaction was run for an hour and the mixture was filtered over Celite. Subsequently, the volatiles were removed with a rotatory evaporation device and further drying was performed at higher vacuum ($3 \times 10^{-2}$ mbar). The Pd content was determined by ICP-AES.

**X-ray crystal structure determination of 2.** Data collections were performed at the X-ray diffraction beamline (XRDL) of the Eletra Synchrotron, Trieste (Italy), with a Pilatus 2M image plate detector. Complete datasets were collected at 100 K (nitrogen stream supplied using an Oxford Cryostream 700) with a monochromatic wavelength of 0.700 Å through the rotating crystal method. Crystals of poisoned analogue complex compound 2 were dipped in N-paratone and mounted on the goniometer head with a nylon loop. The diffraction data were indexed, integrated and scaled using XDS. Complete datasets for the triclinic crystal form found were obtained by merging three different data collections done on different crystals mounted with different orientations. The structures were solved by direct methods using SIR2011, Fourier analyzed and refined by the full-matrix least-squares based on $F^2$ implemented in SHELXL-2013. The Coot program was used for modeling. Empirical absorption correction has been applied as implemented in the XABS2 program. Anisotropic thermal motion modeling was then applied to atoms with full occupancy. Hydrogen atoms were included (except for disordered water molecules) at calculated positions with isotropic $U_{	ext{eq}} = 1.2 U_{	ext{eq}}$.

The asymmetric unit contains one complex molecule and a PF$_6^-$ ion that counterbalances its positive charge (Figure 2). The angle between the TMTU ligand and the plane defined by the inner coordination sphere of Palladium is 61.0°: this value is intermediate between angles reported in other Pd-TMTU structures published (where values are ~54° or ~80°).

**X-ray crystal structure determination of 5.** $C_{29}H_{28}N_2O_6Pd$, Fw = 606.93, colorless plate, 0.41 × 0.35 × 0.10 mm$^3$, monoclinic, $P2_1/c$ (no. 14), $a = 17.5665(6)$ Å, $b = 13.6471(3)$ Å, $c = 11.6294(3)$ Å, $\beta = 109.070(1)$°, $V = 2634.94(13)$ Å$^3$, $Z = 4$, $D_x = 1.530$ g/cm$^3$, $\mu = 0.75$ mm$^{-1}$. 47521 Reflections were measured on a Bruker Kappa Apex diffractometer with sealed tube and Triumph monochromator ($\lambda = 0.71073$ Å) at a temperature of 150(2) K up to a resolution of $(\sin \theta/\lambda)_{\text{max}} = 0.65$ Å$^{-1}$. Intensity data were integrated with the Eval15 software. Analytical absorption correction and scaling was performed with SADABS (correction range 0.82-0.94). 6040 Reflections were unique ($R_{	ext{int}} = 0.015$), of which 5765 were observed [I>2\sigma(I)]. The structure was solved with Direct Methods using the program SHELXS-97. Least-squares refinement was performed with SHELXL-2013 against $F^2$ of all reflections. Nonhydrogen atoms were refined freely with anisotropic displacement parameters. All hydrogen atoms were located in difference Fourier maps. Hydrogen atoms on the five-membered rings were refined freely with isotropic displacement parameters. All other hydrogen atoms were refined with a riding model. 373 Parameters were refined with no restraints. $R_1/\text{wr} R_2 [I > 2\sigma(I)]: 0.0176 / 0.0471$. $R_1/\text{wr} R_2 [\text{all refls}]: 0.0187 / 0.0478$. $S = 1.068$. Residual electron density between -0.32 and 0.36 e/Å$^3$. Geometry calculations and checking for higher symmetry was performed with the PLATON.
The metric of the lattice is approximately orthorhombic-C, but we see no indications for the presence of this higher symmetry.

**X-ray crystal structure determination of 6.** \( \text{C}_{44}\text{H}_{48}\text{N}_{4}\text{Pd}_{2}\text{S}_{4} \) 2\( \text{C}_{4}\text{H}_{8}\text{O} \) + disordered solvent, \( \text{Fw} = 1118.11^{[11]} \), yellow needle, \( 0.48 \times 0.19 \times 0.09 \text{ mm}^3 \), trigonal, \( R \ 3 \) (no. 148), \( a = b = 35.8920(7), c = 11.0473(5) \ \text{Å}, \alpha = \beta = 90, \gamma = 120^{\circ} \), \( V = 12324.9(9) \ \text{Å}^3, \ Z = 9, \ \text{D}_e = 1.356 \text{ g/cm}^3, \ \mu = 0.85 \text{ mm}^{-1}^{[1]} \). 52468 Reflections were measured on a Bruker Kappa Apex II diffractometer with sealed tube and Triumph monochromator (\( \lambda = 0.71073 \ \text{Å} \) at a temperature of 150(2) K up to a resolution of (\( \sin \theta / \lambda \))\text{max} = 0.65 \ \text{Å}^{-1}. Intensity data were integrated with the Eval15 software.\(^{124}\) Absorption correction and scaling was performed with SADABS\(^{125}\) based on multiple measured reflections (correction range 0.61-0.75). 6297 Reflections were unique (\( R_{int} = 0.018 \)), of which 5153 were observed \([I>2\sigma(I)]\). The structure was solved using the program SHELXT.\(^{128}\) Least-squares refinement was performed with SHELXL-2013\(^{126}\) against \( F^2 \) of all reflections. The crystal structure contains voids (809 \text{ Å}^3 / unit cell) filled with disordered solvent molecules. Their contribution to the structure factors was taken into account using the SQUEEZE routine of the PLATON software\(^{127}\) (127 electrons / unit cell). Non-hydrogen atoms were refined freely with anisotropic displacement parameters. All hydrogen atoms were introduced in calculated positions and refined with a riding model. 295 Parameters were refined with no restraints. \( R1/\text{wrR2} \ [I > 2\sigma(I)] : 0.0306 / 0.0765. \ R1/\text{wrR2} \ \text{[all refl.]} : 0.0417 / 0.0832. \ S = 1.061. \) Residual electron density between -0.51 and 0.42 \text{ e/Å}^3. Geometry calculations and checking for higher symmetry was performed with the PLATON program.\(^{127}\)\(^{[*]} \) Derived values do not contain the contribution of the disordered solvent molecules.

**X-ray crystal structure determination of 7.** \( \text{C}_{30}\text{H}_{38}\text{N}_{4}\text{O}_{3}\text{PdS}, \text{Fw} = 641.10, \text{yellow needle,} \ 0.44 \times 0.23 \times 0.10 \ \text{mm}^3, \text{monoclinic,} \ P2_1/n \ (\text{no. 14}), \ a = 13.2975(5), b = 14.2960(6), c = 15.7136(7) \ \text{Å}, \beta = 90.4304(13)^{\circ}, \ V = 2987.1(2) \ \text{Å}^3, \ Z = 4, \ \text{D}_e \ = \ 1.426 \text{ g/cm}^3, \ \mu = 0.73 \text{ mm}^{-1}^{[1]} \). 43869 Reflections were measured on a Bruker Kappa Apex II diffractometer with sealed tube and Triumph monochromator (\( \lambda = 0.71073 \ \text{Å} \) at a temperature of 150(2) K up to a resolution of (\( \sin \theta / \lambda \))\text{max} = 0.65 \ \text{Å}^{-1}. Intensity data were integrated with the Saint software.\(^{129}\) Absorption correction and scaling was performed with SADABS\(^{125}\) based on multiple measured reflections (correction range 0.65-0.75). 6878 Reflections were unique (\( R_{int} = 0.051 \)), of which 6248 were observed \([I>2\sigma(I)]\). The structure was solved with Direct Methods using the program SHELXS-97.\(^{126}\) Least-squares refinement was performed with SHELXL-2013\(^{126}\) against \( F^2 \) of all reflections. Non-hydrogen atoms were refined freely with anisotropic displacement parameters. The Palladium atom and the maleic anhydride ligand were refined with a disorder model for positional disorder (occupancy 0.863(3):0.136(3)). All hydrogen atoms were introduced in calculated positions and refined with a riding model. 400 Parameters were refined with 41 restraints (1,2 and 1,3 distances in the disordered groups, flatness of the MA ligand). \( R1/\text{wrR2} \ [I > 2\sigma(I)] : 0.0562 / 0.1326. \ R1/\text{wrR2} \ \text{[all refl.]} : 0.0619 / 0.1346. \ S = 1.253. \) Residual electron density between -0.76 and 1.15 \text{ e/Å}^3. Geometry calculations and checking for higher symmetry was performed with the PLATON program.\(^{127}\)\(^{[*]} \)
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5.12 References

125. Sheldrick, G. M. SADBS. 1999, Universität Göttingen, Germany.
128. Sheldrick, G. M. SHELXT. 2013, Universität Göttingen, Germany.