Palladium and rhodium allyl complexes in catalysis

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Ik bedank iedereen die een bijdrage heeft geleverd aan de verwezenlijking van dit proefschrift en/ of aan de goede sfeer in de groep.
Chapter 1
General introduction:
Towards green chemistry

1.1 Chemistry and the environment

Chemical products have become an integral part of our life, for instance in commodities and pharmaceutics. The advent of the chemical industry in the 19th century was triggered by the large scale synthesis of dyes and simple medical drugs. Throughout the 20th century, the discovery of synthetic polymers led to a further increase of the importance of the chemistry for the everyday-life. At present, important developments in chemical industry take place in the fields of material science, catalysis, medicin and biotechnology.

Lack of knowledge of polluting effects of chemicals has caused grave damage to the environment. Nowadays, the knowledge and awareness of environmental effects have increased, which is for instance reflected in the recently awarded Nobel-prize for Crutzen and others for their study of chemistry in the atmosphere.

The increasing knowledge and awareness of the effects of chemicals on the environment led to many improvements of existing chemical processes and the development of new, less polluting chemicals. One of the key-issues in this field is replacing existing stoichiometric routes by catalytic routes. The traditional routes often involve the production of large amounts of side products (waste), low yields and harsh reaction conditions. In many cases, an alternative catalytic pathway is possible, which often leads to a more efficient use of starting materials (higher atom economy), less reaction steps, milder conditions, less energy consumption, higher selectivities and less side products. An illustrative example is the catalyzed synthesis of Ibuprofen. The traditional route consists of seven steps, with an atom economy of only 40%. The new, catalytic route involves only four steps and the atom efficiency is nearly doubled to 77%. Thus, successful application of catalysis leads to processes with both economical and ecological gain!

1.2 Background of this research

For large scale industrial processes for base chemicals, both heterogeneous and homogeneous catalysts are often used. In addition, homogeneous catalysts are used for small scale batch reactions (pharmaceutics). Heterogeneous catalysts have the advantage of easy separation of the catalyst from the reaction mixture. The separation of homogeneous catalysts is more difficult, but these catalysts offer the advantage of fine-tuning and consequently a much higher (stereo)-selectivity. In this thesis we will focus on the use of homogeneous catalysts.
Chapter 1

The large scale use of homogeneous systems is hampered by the high development costs, the above mentioned difficult separation and the degradation of the catalyst, which prevents recycling. So far, most research has been devoted to optimizing the activity and the selectivity of catalysts. Much less studies have been devoted to the origin of catalyst degradation.\[^2\]

Recently, the combination of the advantage-of-separation of the heterogeneous and the advantage-of-activity-and-selectivity of the homogeneous systems has become a topic of intensive research. Binding the catalyst in the core or the periphery of dendrimers has proven to increase the stability of the catalyst and it is possible to recycle the catalyst several times, thereby improving the turn-over-number.\[^3\] In a similar fashion, the embedding of the catalyst in silica particles, either trapped in the pores or covalently bonded, has led to very selective and stable catalyst.\[^4\]

*Industrial and academic research*

The above examples have been developed in collaborations of industry with academia, thus combining their efforts in applied and fundamental research. This approach has proven useful in many research topics. A good example is the Carilon process for the homogeneously catalyzed synthesis of the alternating ethylene-CO copolymer.\[^4\] Many research projects in academia have been devoted to elucidate different aspects of this reaction.\[^5\]

### 1.3 Aim of this research

The project described in this thesis, has been funded by DSM Research and forms part of the EET program (ministerie van Economische Zaken) for green chemistry. We investigated some fundamental backgrounds of a large scale homogeneously catalyzed reaction involving the palladium catalyzed alkoxycarbonylation of dienes. This is a key step in the catalyzed synthesis of ε-caprolactam (figure 1), the starting material for nylon-6.\[^6\] The chemistry involved is relevant for many more potential applications.

DSM Research has developed this novel, catalytic route to caprolactam as the green alternative for the current stoichiometric route. After much fundamental work, the industrial research has reached the process-development stage. In our collaboration, the role of academia is to investigate some fundamental features of the new catalytic route, for instance:

- what factors cause the formation of side products and how can this be influenced ?
- why are certain catalysts more / less active than others ?
- can alternative catalysts be developed?
General introduction.

\[
\text{Figure 1: The palladium catalyzed alkoxy carbonylation of dienes.}
\]

It was shown that in the reaction mixture of the palladium catalyzed carbonylation, Pd(\(\eta^3\)-allyl) complexes are present. These species could be the active catalyst, but could also lead to the formation of side products via nucleophilic attack on the allyl moiety. It was found, that the performance of the catalyst mainly depends on the nature of the ligands. We decided therefore, to investigate the effect of the ligand on the structure, the properties and the reactivity of Pd(\(\eta^3\)-allyl) complexes.

As a model reaction for the nucleophilic attack we have chosen the well known allylic alkylation reaction.\(^7\) Because of the importance of the regiochemistry of the side products, we decided to focus on the regioselectivity of the reaction. Although much research had been devoted to the enantioselective allylic alkylation, the subject of regioselectivity has received considerably less attention. The results of the studies described in this thesis have lead to several new mechanistic insights in the factors governing the regioselectivity. In addition, we studied the reactivity of the Pd(\(\eta^3\)-allyl) complexes towards CO and in the catalytic carbonylation. Based on our findings, we will propose a novel mechanistic pathway for the carbonylation reaction.

The results prompted us to investigate the structure and reactivity of the analogous rhodium catalysts. Although there is only a relatively small difference between the rhodium and the palladium atom, the properties of the corresponding catalytic complexes are significantly different.

The fundamental research described in this thesis has yielded several useful leads that could be used by the industrial research to improve the current process.
1.4 Spin-offs

In addition to our core activities concerning the properties and reactivity of palladium and rhodium allyl complexes, we were especially interested in increasing the recyclability of the catalyst. To this end, we have been involved in a number of collaborations, in which we used our newly gained knowledge to immobilize the palladium catalyst.

With G. E. Oosterom (University of Amsterdam):\(^{[8]}\)
A dendrimer with a dppf-based core was used to bind the palladium-allyl catalyst. This new system was active in the palladium catalyzed allylic alkylation. Increasing the size of the dendrimer led to a decrease of the local polarity around the catalytic core and thus the regioselectivity can be influenced. More importantly, the catalyst remained relatively stable and could be recycled several times via membrane filtration.

With D. G. de Groot (University of Amsterdam):\(^{[9]}\)
By using similar system involving a dendrimer with the phosphine functionalities on the periphery, the catalyst could be recycled via membrane filtration.

With A. J. Sandee (University of Amsterdam):\(^{[10]}\)
In a slightly different approach, a palladium catalyst was coupled to a silica particle via covalent bonds. Also this catalyst system is active in the palladium catalyzed alkylation and shows the same regioselectivity as found for the analogous homogeneous catalyst.

With M. Tromp (University of Utrecht, ESRF Grenoble):\(^{[11]}\)
In view of improving the recyclability of the catalyst, it is important to understand and control the factors governing the degradation of the catalyst. The general assumption is that Pd(\(\eta^3\)-allyl) complexes are very stable, but during the course of our studies several degradation pathways have been observed.\(^{[12]}\) To gain more insight, we recently started a project with the group of Koningsberger to study the controlled degradation of the catalyst via time-resolved UV and EXAFS techniques.\(^{[11]}\)
1.5 References


Chapter 2

Palladium catalyzed allylic alkylation
(introduction to chapters 3-9)

2.1 Introduction

The allylic alkylation reaction (figure 1), first discovered by Tsuji\textsuperscript{1} and its enantioselective variant, later developed by Trost and others,\textsuperscript{2, 3} has become a powerful and versatile tool in synthetic organic chemistry. The reaction allows for a variety of allylic substrates as well as a variety of nucleophiles. An example of an application of the allylic substitution in the total synthesis of the alkaloid (+)-γ-lycorane is shown in figure 2.\textsuperscript{3c}

Although initially palladium was used for this reaction, it now appears that virtually every metal capable of binding to an allylic substrate can be used.\textsuperscript{4} This reaction has become one of the standard reactions for testing new chiral ligands. To obtain a high enantioselectivity, there seem to be no restrictions concerning either the type and number of ligand donor atoms or the type and size of substituents on the ligand. Because of the high reaction rates and high yields, palladium is still the metal of choice in most cases. The use of
other metals may be desirable for certain substrates, since it may lead to selectivities different from those found for palladium\textsuperscript{[4]}\textsuperscript{). As mentioned in chapter 1, our studies will focus on palladium.}

### 2.2 Enantioselectivity

A vast amount of studies has been published, reporting the use of many different kinds of ligands for the enantioselective alkylation of various substrates (figure 3). Most often substrates are used with large substituents, such as two phenyl rings. Because ligands having completely different electronic and steric properties show similar (high) enantioselectivities,\textsuperscript{[2, 3]} the substitution pattern on the allyl moiety seems to be the most important factor determining the enantioselectivity of the reaction. Much less studies are known, concerning the use of smaller substrates. Smaller substituents on the allyl moiety lead to less steric interaction between the ligand and the allyl group and consequently to a less efficient transfer of chiral information. For such substrates, therefore, only ligands bearing the chiral center in close proximity to the metal center have been successful\textsuperscript{[2a, 5]}.

![Figure 3: Several allylic substrates often used as models in the enantioselective allylic alkylation.](image)

**Steric models**

Several years ago, Trost has presented a model for the mechanism of the chiral induction in the allylic alkylation (figure 4).\textsuperscript{[2]} The model explains the observed enantioselectivities in terms of steric hindrance. Trost proposed that the main factor influencing the outcome of the reaction is the steric interaction between the ligand and the substituents on the allyl group. Upon nucleophilic attack, the substituents will have to bend in the direction of the Pd(ligand) fragment, giving rise to steric interactions. During the formation of the new carbon-carbon bond, the allyl moiety rotates to form the olefin product. Upon rotation, the substituents on the allyl and the (former) nucleophile interact with the Pd(ligand) fragment. The resulting selectivity depends on the relative contributions of the various steric interactions. The model has proven to be very useful in the explanation of many enantioselectivity studies.\textsuperscript{[2, 3, 5]}
2.3 Regioselectivity

Considerably less has been reported concerning the enantioselective alkylation of substrates that lead to intermediate palladium complexes bearing a non-symmetrically substituted allyl moiety.\textsuperscript{[14]} To obtain a high enantioselectivity, regioselectivity is required in addition to enantiocontrol (figure 5). Attack on the non-substituted C1 atom in figure 5b leads to the formation of the non-chiral linear product, whereas attack on the substituted C3 atom leads to the chiral branched product. For most ligands the formation of the linear product is highly favored over that of the chiral branched product.\textsuperscript{[6]} Although the use of other metals such as molybdenum\textsuperscript{[4]} or rhodium\textsuperscript{[4]} may lead to 99\% selective formation of the branched product, palladium still offers the advantage of a higher reaction rate, higher yield and a large tolerance for many functional groups.\textsuperscript{[2]}

Figure 5: Regioselectivity in the palladium catalyzed allylic alkylation: a): enantiocontrol, b): regiocontrol prior to enantiocontrol.
Several methods are known to influence the regioselectivity of the reaction. In some cases, the nucleophile can be forced to attack on the branched position by modifying the allylic substrate in such a way that attack on the branched position is favored for geometric reasons. An example is presented in figure 6, in which the nucleophilic attack occurs intramolecularly. The preference for the formation of a six-membered ring compared to an eighth-membered ring.

Another method involves the use of bidentate ligands bearing two different donor atoms. Extensive NMR studies by Pregosin have shown, that apart from steric interactions, the regioselectivity of the nucleophilic attack is for a large part determined by the different trans influences of the ligand donor atoms. Using bidentate P-N or P-S ligands, the nucleophile primarily attacks the allylic carbon atom trans to the phosphorus.

In recent years several studies have been devoted to the so-called "memory effect". In some cases, it has been found, that the nucleophile shows a preference for attack on the allylic carbon atom, to which the leaving group in the substrate was bonded prior to oxidative addition (figure 7). Thus, although both substrates lead to the formation of the same intermediate Pd(allyl) complex, the use of substrate a mainly yield product a', while use of substrate b leads to b'. Such a "memory effect" was found for monodentate
ligands, but also for some mixed bidentate ligands. Several sophisticated studies have been performed to elucidate the origins of these observations.\[^9\] A number of explanations for this observation has been presented, e.g. involving ion pairs. We, however, propose a simple alternative explanation to account for the observations.

![Diagram](image)

**Figure 8:** A possible, simple explanation for the "memory effect". L is a phosphine ligand.

For Pd(monoridentate phosphine) complexes, it is known that the oxidative addition of allylic substrates to palladium occurs in a cis fashion.\[^10\] Thus, after oxidative addition of a to Pd-P, initially the complex a-Pd is formed (figure 8), in which the substituted carbon is located cis to the phosphorus ligand. The subsequent nucleophilic attack is known to primarily take place trans to phosphorus and for steric and electronic reasons product a' will be formed as the main product.\[^8\] Using the substrate with the leaving group on the other terminal carbon atom will yield intermediate b. Nucleophilic attack trans to phosphorus yields the other regio-isomer, b'. It is known that the intermediate b-Pd, bearing the substituent on the allyl moiety trans to phosphorus, is thermodynamically more stable than intermediate a-Pd (chapter 6). The overall regioselectivity of the reaction therefore is determined by the rate of a-Pd ↔ b-Pd isomerization, the a-Pd / b-Pd equilibrium value and the rate of alkylation for the two isomers. Thus, the "memory effect" can be explained by kinetic versus thermodynamic control of the regioselectivity of the reaction (figure 8).

The a-Pd ↔ b-Pd isomerization is known to be dependent on the coordinating abilities of the counterion and consequently also on the solvent (chapter 6), which explains the observed effects of solvent and counterion on the "strength" of the "memory effect".\[^9\]
Chapter 2

2.4 Modeling studies

With the increasing availability of cheaper CPU-time and the demand for better mechanistic insights, high level modeling studies are increasingly used to help the elucidation of reaction mechanisms. In recent years, a large number of theoretical studies dealing with the nucleophilic attack on Pd(η³-allyl) complexes has appeared.\[111\]

The accuracy of these calculations, however, are hampered by the electrostatic attraction between the negatively charged nucleophile and the positively charged palladium atom. Because the interaction between charged molecules is ill described in the gas phase, the neutral ammonia nucleophile is often used as a model. Solvent models can be used to diminish the electrostatic interactions between palladium and the nucleophile, but this requires many extra calculations. To date, no fully conclusive calculations concerning the regioselectivity of the alkylation have been reported.\[110d\]

The modeling studies reported so far, have confirmed some of the features of the model presented by Trost. Upon nucleophilic attack of NH₃, the allyl moiety rotates in such a way that the newly formed C=C double bond will be in the Pd(ligand) plane. Following the reaction at low temperature by means of NMR spectroscopy, such olefin complexes have indeed been observed.\[114\] The reaction is essentially controlled by the frontier orbitals, but the overall results are the same as predicted by a purely steric model. Because the used theoretical models lack large steric groups, the full steric implications of the "Trost"-model have not been evaluated yet.

Extrapolation of details of these calculations to the alkylation reaction is questionable. Åkermark has investigated experimentally the influence of the strength of the nucleophile on the regioselectivity.\[12\] It was found that for relatively hard nucleophiles, such as malonate, electronic factors are more important for the regioselectivity than they are for less reactive, softer nucleophiles. An extrapolation of calculations for attack of ammonia will thus underestimate the contribution of electronic factors.

In conclusion, although the steric model and the theoretical studies can explain some features of the regioselectivity, the predictions are valid only for certain nucleophiles, certain allyl moieties and certain ligands. We will show that these explanations fail for some borderline cases.
2.5 Scope and content of the chapters on allylic alkylation

In the next chapters (3-9), the factors governing the regioselectivity of the palladium catalyzed allylic alkylation will be studied in more detail. First (chapter 3), the mentioned reported modeling studies are discussed in more detail and new calculations are presented that apply directly to the complexes used in the following chapters. In the experimental chapters, the regioselectivity is studied systematically using several series of ligands and a series of allylic substrates. Since preliminary studies in our laboratories had yielded promising results, we chose to focus on the influence of the bite angle of bidentate ligands. In the first experimental chapter (chapter 4), we study the relation between the influence of the bite angle on the structure of palladium complexes bearing the monosubstituted crotyl moiety (3-CH₂-C₃H₄) and the regioselectivity in the allylic alkylation. Using the findings of chapter 4, the alkylation of cis- and trans-substrates is investigated in more detail in chapter 5. The influence of two different donor atoms (P-N) on the alkylation of crotyl and cinnamyl moieties (3-Ph-C₃H₄) is studied in chapter 6. A detailed investigation of the effect of the bite angle on the bond between palladium and a disubstituted allyl moiety (3,3-(CH₂)₂-C₃H₃) is presented in chapter 7. The last experimental chapter, chapter 8, deals with the influence of different donor atoms in a series of ligands based on the xanthene backbone. Finally, in chapter 9, the results of the allylic alkylation are evaluated and a model is presented that accounts for all our observations.

2.6 References

Chapter 2


Our first step to investigate the limits of the existing late transition state models for the palladium catalyzed allylic alkylation is made in this chapter. We focus on the possible use of an early transition state model to predict the regioselectivity of the reaction.

Abstract

We studied the geometry and the electronic properties of a series of (bidentate ligand)Pd(η^3-allyl) complexes, that vary in the number and the position of substituents on the allyl moiety, in the nature of the ligand donor atoms and the bite angle of the ligand.

After a detailed discussion of reported modeling studies, we show that the presence of substituents on the allyl distorts the η^3-character of the Pd(η^3-allyl) bond. A larger bite angle of the ligand enhances this effect. The use of two different ligands, PH₃ and NH₃, also leads to a larger distortion of the Pd(η^3-allyl) bond. Based on these results we predict the regioselectivity of the allylic alkylation provided that an early transition state is involved.
3.1 Introduction

Figure 1: Late transition state model for the palladium catalyzed allylic alkylation. Left: steric interactions upon attack of the nucleophile, right: steric interactions after nucleophilic attack, during rotation of the attacked allyl moiety.[13]

At present, the late transition state model presented by Trost (chapter 2) is commonly accepted and is often used to explain the observed regio- and enantioselectivities of the palladium catalyzed allylic alkylation (figure 1).[11] The possibility of a product-like intermediate was confirmed by several theoretical studies of the reaction path of nucleophilic attack on L2Pd(η3-allyl) model complexes.[2] Several groups found further experimental indications for a late transition state mechanism.[3] Experimental mechanistic studies pointing to a late transition state, however, involve a) weak nucleophiles such as amines instead of the more reactive malonates or / and b) bulky substituents on the allyl moiety and / or the ligand. We expect that these weakened electronic and these increased steric interactions possibly favor the occurrence of the late transition state. Furthermore, in the reported theoretical studies the pathway of the reaction has been investigated using an uncharged amine instead of a charged malonate as the nucleophile.

For these reasons, we decided to explore the possibility of an early transition state mechanism, in which the regioselectivity is mainly explained by the structure of the Pd(allyl) complex.[4] To our opinion, some reported results could be explained more easily using this alternative mechanism (see section 3.2).[5] Therefore, we were interested in the limits of the late transition state mechanism and decided to study the regioselectivity of the alkylation under the following conditions:

a) use of an allyl moiety that is electronically activated for nucleophilic attack
b) use of small substituents on the allyl moiety
c) use of a charged nucleophile.

In this chapter, first a short overview is presented of studies concerning the structure of the Pd(η3-allyl) bond (section 3.2). Next, the influence of the bite angle of the ligand on the Pd(η3-allyl) bond is investigated using DFT calculations (section 3.3) and the implications for the regioselectivity are discussed (section 3.4).
3.2 Literature survey

3.2.1 Experimental studies

Åkermark has studied the influence of substituents on the allyl moiety and of ligands on the regioselectivity of the allylic alkylation.\[4c-6\] He presented a relation between the $^{13}$C-resonances of the allylic carbon atoms in $L_2$Pd-(3,3-(CH$_3$)$_2$-C$_3$H$_3$) complexes and the regioselectivity (figure 2). More recently, Moreno-Manas has found similar results for dppe (1,2-bis(diphenylphosphino)ethane) modified complexes of para-substituted cinnamyl derivatives.\[7\] Even though there is still no theoretical basis that validates a direct relation between the $^{13}$C-chemical shifts and the charge, the observed trends (see below) seem to be in line with estimated charges on the terminal allylic carbon atoms.

![Figure 2: (L)$_2$Pd-(3,3-(CH$_3$)$_2$-C$_3$H$_3$)$^+$OTf and products of allylic alkylation.](image)

Åkermark found that, in general, the signals of the substituted allylic carbon atoms C2 and C3 are shifted downfield relative to the non-substituted allyl moiety (table 1).\[6\] The effect is enhanced when π-acceptor ligands are used. The downfield shift of C2 and C3 could indicate an enhanced olefinic character of the C2-C3 bond. Several reported crystal structures of Pd(allyl) complexes indeed show a relatively short C2-C3 bond and a relatively long C1-C2 bond. In addition, a slight distortion of the bonding mode of the allyl moiety has been found. The Pd-C1 bond is shortened and the Pd-C2 and Pd-C3 bonds are elongated,

![Figure 3: Distortion of the Pd-(3,3-(CH$_3$)$_2$-C$_3$H$_3$) bond.](image)
The complexes listed in table 1 have been used by Åkerman in the stoichiometric alkylation using sodium diethyl 2-methylmalonate as the nucleophile. Nucleophilic attack can take place either at the non-substituted C1 atom (forming the linear product) or at the substituted C3 atom, forming the branched product. The results are presented in table 1 and the relation between the shifts in $^{13}$C-NMR and the regioselectivity are presented graphically in figures 4 and 5. It was found that a larger difference in chemical shift between the substituted C3 and the non-substituted C1 atom corresponds to a higher regioselectivity for attack on C3. The increase of the chemical shift of C3 relative to C1 was explained by an increased strength of the Pd-C1 bond and a decreased Pd-C3 bond strength. This distortion of the Pd($\eta^1$-allyl) bond to $\eta^1$(Pd-C1)-$\eta^1$(Pd-C2C3) results in an increase of the electrophilicity of the substituted C3 atom.

The observed relation depends mainly on the results using the ligands tmdea, pyridine and P(OPh)$_3$ (omission of these points would lead to a very poor correlation). Inspection of table 1, however, shows that for the phosphine ligands the relation is rather good. In later studies by the same authors a similar, more convincing correlation is found between the non-symmetry of the Pd($\eta^3$-allyl) bond in a non-systematic series of (N-N)Pd(allylic ligand) complexes (averaged over X-ray crystal structures in the CSD) and the regioselectivity.$^{[6]}$

The observed relation, however, is the opposite of what would be predicted using the late transition state model. The more the allyl moiety is bonded in a pre-linear product-like manner, the more branched product is found.

Table 1: Relation between $^{13}$C-chemical shifts in L-Pd-(3,3-(CH$_3$)$_2$C$_2$H$_5$)$^+$OTf complexes and the regioselectivity in the stoichiometric allylic alkylation.$^{[6]}$

<table>
<thead>
<tr>
<th>L</th>
<th>$\delta$(C3)</th>
<th>$\Delta(\delta$(C3)-$\delta$(C1))</th>
<th>% branched</th>
<th>% linear</th>
</tr>
</thead>
<tbody>
<tr>
<td>L = tmdea</td>
<td>88</td>
<td>32</td>
<td>1</td>
<td>99</td>
</tr>
<tr>
<td>2 pyridine</td>
<td>92</td>
<td>37</td>
<td>1</td>
<td>99</td>
</tr>
<tr>
<td>2 Ph$_2$PS</td>
<td>106</td>
<td>46</td>
<td>21</td>
<td>79</td>
</tr>
<tr>
<td>PhS-CH$_2$CH$_2$-SPh</td>
<td>108</td>
<td>45</td>
<td>5</td>
<td>95</td>
</tr>
<tr>
<td>dppe</td>
<td>109</td>
<td>48</td>
<td>8</td>
<td>92</td>
</tr>
<tr>
<td>2 MeCN</td>
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<td>87</td>
</tr>
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<td>2 P(OMe)$_3$</td>
<td>116</td>
<td>57</td>
<td>8</td>
<td>92</td>
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<td>2 P(OPh)$_3$</td>
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<td>43</td>
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</tr>
</tbody>
</table>
DFT study of the distortion of the $\text{Pd}(\eta^1$-allyl) bond.

Figure 4: Relation between $\delta(C3)$ and regioselectivity of the alkylation. The bigger points correspond to the results obtained for phosphorus ligands. Omission of the points with arrows would lead to a poor correlation.\(^6\)

Figure 5: Relation between $\Delta(\delta(C3)-\delta(C1))$ and regioselectivity of the alkylation. The bigger points correspond to the results obtained for phosphorus ligands. Omission of the points with arrows would lead to a poor correlation.\(^6\)
3.2.2 Modeling study of \((\text{PH}_3)_2\text{Pd(}C_3\text{H}_5)\)\(^+\)

The above presented studies of Åkerman and co-workers have mainly been concerned with the use of nitrogen ligands. Because it can be expected that the observed electronic effects on the Pd-allyl bond will be enhanced by ligands with a stronger trans influence, we were interested in the non-symmetry of the Pd-allyl bond using phosphine ligands. For these ligands, only few theoretical studies have been reported, describing the Pd(\(\eta^3\)-allyl) bond in detail.\(^8\)

In these modeling studies, the non-substituted cationic \((\text{PH}_3)_2\text{Pd(}C_3\text{H}_5)\)\(^+\) complex (1a) (figure 6) was used as a model for the much larger experimental systems. Use of such a model complex has the advantage of a small amount of atoms (and electrons). The main disadvantages, however, are the relatively poor description of the electronic properties of the phosphine ligand (using PH\(_3\) instead of PR\(_3\)) and the absence of stabilizing interactions of the cationic complex with the counterion and the solvent molecules. Several theoretical studies have been devoted to this complex; the results presented here are taken from a recent study by Szabo.\(^8\)

The structure of \((\text{PH}_3)_2\text{Pd(}C_3\text{H}_5)\)\(^+\) (1a) is presented in figure 6 and values for some parameters are given in table 2. The complex is square planar with the phosphines cis to one another and the allyl moiety is bonded in an \(\eta^1\)-fashion. The bond is formed by an allyl-to-metal interaction (the filled \(\varphi 1\) of the allyl with the empty sp, of the palladium) and a metal-to-allyl interaction (the empty \(\varphi 2\) on the allyl with the filled \(d_{xz}\) on the palladium). The general orbital diagram for the Pd-(\(\eta^3\)-allyl) bond, obtained from \textit{ab} initio calculations, is depicted in figure 7.

![Figure 6: Structure of \((\text{PH}_3)_2\text{Pd(}C_3\text{H}_5)\)\(^+\) (1a) (structure on the right is slightly turned).](image)
DFT study of the distortion of the Pd(π^3-allyl) bond.

Table 2: Values of selected parameters of (PH\textsubscript{3})\textsubscript{2}Pd(C\textsubscript{3}H\textsubscript{5})\textsuperscript{+} (1a), taken from ref [8], distances in Å, angles in °, charges in electrons.

<table>
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<th>value</th>
<th>parameter</th>
<th>value</th>
</tr>
</thead>
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<tr>
<td></td>
<td></td>
<td>q C\textsubscript{3}H\textsubscript{5}</td>
<td>+0.379</td>
</tr>
</tbody>
</table>

Figure 7: Orbital interaction diagram (taken from ref [8]).

Because the L-Pd-L angle in the optimized structure is around 90°, the overlap of the ligand lone pair orbitals with the Pd-d\textsubscript{xy} orbital is more efficient than that with the Pd-p\textsubscript{x} orbital. This results in a lower level of the empty antibonding combination a" depicted in figure 7. This leads to a lower energy level for the 2a" orbital. The π-orbital on the allyl moiety (φ1) interacts with a' and mixes slightly with the allyl π*-orbital (φ3). Analogously, the non-bonding allyl n\textsubscript{x}-orbital (φ2) interacts with the a" orbital. The anti-bonding orbitals, 2a" and 2a' respectively, are close in energy level, but differ in the LUMO coefficients on the allylic carbon atoms. The 2a' orbital, originating from φ3, has the largest coefficient on C2 (central carbon) atom, whereas the 2a" orbital has the largest coefficient on the Ct (terminal carbon, C1 or C3) atoms. The relative energy
levels of these two unoccupied molecular orbitals depend on the energy levels of and the overlap with the a' and a'' Pd-fragment orbitals.

It has been found that strong σ-donor ligands, such as NH₃, have a strong interaction with the Pd-dₓ orbitals and the energy level of the corresponding antibonding a'' orbital will be raised. The N-Pd-N angle has a value around 90° and the interaction with the Pd-pₓ orbital will be less efficient than with the Pd-dₓ orbital, which results in a lowering of the energy level of a'.

For L-Pd-L angles between 80° and 100°, the s-p-s overlap has a stronger angular dependence relative to the s-d-s overlap. A smaller bite angle will thus have a stronger influence on energy level a'' than on level a' and consequently, a decrease in the bite angle will lower the 2a' energy level relative to the 2a'' energy level.

Strong σ-donor ligands with a small bite angle will cause the 2a' orbital to be the LUMO. Nucleophilic attack will take place on C2, forming a cyclopropane product. If, on the other hand, 2a'' is the LUMO, a nucleophile will attack at C3 and an olefin will be formed.

These calculations of Szabo are in line with reported experimental results. Nucleophilic attack on the (tmeda)Pd(allyl)⁺ complexes may take place at C2[9], whereas (P-P)Pd(C₃H₅)⁺ complexes are attacked at C1[10]. The mechanism of the nucleophilic attack at C2 proceeds via the formation of a palladacyclobutane intermediate[9] and will not be discussed here.

Although complex Ia is formally treated as L₂Pd₂⁺(allyl)²⁺, the analysis of the Mulliken charges shows that the palladium fragment bears a charge of only +0.6123 whereas the allyl moiety also bears a positive charge (+0.3277). Considering the positive charge on the allyl moiety, we deduced that the non-bonding orbital ϕ₂ on the allyl will be located primarily on the palladium. The corresponding anti-bonding combination 2a'' therefore, is primarily located on the allyl moiety, thus favoring nucleophilic attack on the allyl.

Preliminary EXAFS experiments, carried out in collaboration with the University of Utrecht and the ESRF in Grenoble, show that the charge on the palladium atom in cationic Pd(P-P)(allyl)⁺ complexes is between 0 and +1, which is well below its formal charge of +2.[18]

3.2.3 Effect of substituents

During the course of our studies, a DFT study was reported (B3LYP / LANL2DZ) concerning the effect of substituents on the symmetry of the Pd-(η³-allyl) bond.[2a] It was shown that substituting the allyl with an electron donating group on one of the terminal carbon atoms, leads to a polarization of the frontier orbitals of the allyl moiety (figure 8) in the sense expected. The ϕ₁ and the ϕ₂ orbital are polarized in the direction of the non-substituted C1 atom, whereas the ϕ₃ orbital is polarized to the substituted C3 atom. Furthermore, the node on C2 in ϕ₂ has disappeared. Due to this polarization, the three allyl frontier orbitals can mix. Because of the out-of-phase mixing for the atomic orbital on C1, the contribution of this orbital to the allyl-to-metal interaction (bonding) will decrease, whereas this contribution will increase for the C3 atom. More
importantly, the mixing of the allyl orbitals will increase the coefficient on C3 in the atomic orbital $\varphi_2$, that is involved in the metal-to-allyl (backbonding) interaction.

We reasoned that the bond of the polarized allyl moiety to the Pd fragment leads to the formation of a $2a^\pi$ (LUMO) level in which the coefficient on the C3 atom is larger than that on the C1 atom. A large coefficient on C3 in the occupied orbitals of the complex will decrease the electrophilicity of C3 relative to C1, whereas a large coefficient on C3 in the LUMO of the complex will accelerate the nucleophilic attack on C3. For our studies, the overall results of these two effects are important. As discussed in the previous paragraph, the bite angle of the ligand influences the energy levels of the complex. We decided therefore, to use for our theoretical studies allyl moieties with different substitution patterns and ligands with different bite angles.

![Figure 8: Polarization of the frontier orbitals of the substituted allyl moiety, R = CH$_3$.][2a]

### 3.3 Results and discussion

In the previous sections, several parameters have been identified that may influence the regioselectivity of the allylic alkylation: the presence of substituents on the allyl moiety, the bite angle of the ligand and the trans influence of the ligand donor atoms.

In this section, the influence of these parameters on the structure of Pd(allyl) complexes is studied by DFT calculations. In the chapters 4-8, the experimental results will be presented.

We calculated the structures of model complexes, using 2 PH$_3$ groups as a model for the bidentate phosphine ligand and NH$_3$ as a model for a nitrogen ligand. All calculations were performed on the B3LYP level of theory using the LANL2DZ basis-set, which is one of the accepted methods for calculations of such complexes.[2] In general, the obtained structures are in excellent agreement with those in reported ab initio[8] and DFT studies.[2a]

First the effect of the bite angle on the bonding in the above introduced ($\eta^1$-C$_3$H$_3$)Pd(PH$_3$)$_2^+$ model complex is investigated. Next, the effect of substituents on the allyl moiety, the effect of the bite angle and the effect of different ligand donor atoms will be discussed. Both for our calculations and our experimental work, we used the mono-substituted syn and anti 3-CH$_3$-C$_3$H$_4$ (crotyl) moieties and the dimethyl substituted 3,3-(CH$_3$_)$_2$-C$_3$H$_3$ moiety (figure 9).
Figure 9: Numbering scheme of the used complexes. 2: syn crotyl (CH$_3$ syn with respect to the central H-atom on the allyl), 3: anti crotyl (CH$_3$ anti with respect to the central H-atom on the allyl), 4: dimethyl allyl, bis-PH$_3$, 5: dimethyl allyl, PH$_3$-NH$_3$. Complex 1-80° means: complex 1 with a bite angle of 80°.

3.3.1 Effect of the bite angle on the structure of complex 1

To study the effect of the bite angle on the Pd-allyl bond in complex 1, the P-Pd-P angle was constrained and changed from 80 to 120° in steps of 10°. Selected results are presented in table 3.

For all angles studied, the allyl remains bonded in a symmetric η$^1$-fashion. Increasing the bite angle from 80 to 120°, the Pd-C distances become longer and the C-C distances become shorter. The corresponding bond orders change accordingly, indicating a shift of electron density from the region between the metal and the allyl to the allyl moiety itself. The Pd-P distances decrease and the corresponding bond strengths increase. This can be explained by the effect of the bite angle on the overlap of the ligand and the palladium orbitals (see above). An increase of the bite angle results in a lowering of the a" level (the d$_{xz}$ orbital which interacts with q2 of the allyl) and an increase of the a' energy level (the sp$_z$ orbital which interacts with q1 of the allyl). This is in agreement with the calculated changes in bond strength. A decrease in the bonding and the backbonding interactions will lead to decrease of the strength of the Pd-allyl bond and an increased C-C bond strength.

The Mulliken charges on the Pd atom and the PH$_3$ groups change only little and suggest a slight shift of electron density from PH$_3$ to Pd.
DFT study of the distortion of the Pd(η'-allyl) bond.

Table 3: Values of some parameters of (PH₃)₂Pd(C₃H₅)⁺ (1) and at different values of the bite angle, (q: Mulliken charge in electrons, distances in Å).

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*: bo = Mulliken bond order

3.3.2 Frontier orbitals of the palladium(ligand) fragment

Because the charge on the Pd(PH₃)₂ fragment is closer to a value of +1 than to +2, the energy levels of the orbitals involved in the Pd-allyl bond were calculated for the Pd(PH₃)₂ fragment bearing a charge of +1 (doublet) (table 4).
A direct comparison between the orbitals of the uncharged allyl moiety and the positively charged Pd(PH₃)₂⁺⁺ fragment is not useful, since in the complex the charges on both fragments are different from respectively 0 and +1. The effect of the change in the energy levels of the Pd(PH₃)₂⁺⁺ fragment on the Pd-allyl bond depends on the energy level of φ₁ and φ₂ of the allyl moiety.

According to Szabo[81], and as can be derived from the charge distribution in the complex, the energy level of φ₁ is below that of the dₓ orbital of the Pd(PH₃)₂ fragment and the level of φ₂ is in between the levels of dₓ and the spₓ (figure 7). An increase of the bite angle then results in a decrease of the bonding interaction between φ₁ and spₓ and also in a decrease of the backbonding interaction between φ₂ and dₓ. In addition, the bonding combination between φ₂ and dₓ will be located primarily on Pd whereas the corresponding antibonding combination, the LUMO of the complex (2a⁺ in figure 7), will be lower in energy and will be located more on the allyl moiety. A larger bite angle of the ligand may therefore result in an enhanced reactivity towards nucleophilic attack.

### 3.3.3 Effect of bite angle on the geometry of substituted allyl moieties

In the introduction it was shown that one or more substituents on one of the terminal carbon atoms of the allyl distorts the symmetry of the Pd-allyl bond and a trend had been observed between this distortion and the regioselectivity in the allylic alkylation (see also chapter 7). Therefore, we calculated the geometries for different bite angle values of (PH₃)₂Pd(syn-3-CH₃-C₃H₄)⁺ (2), (PH₃)₂Pd(anti-3-CH₃-C₃H₄)⁺ (3), (PH₃)₂Pd(3,3-(CH₃)₂-C₃H₃)⁺ (4) and its P-N analogue (PH₃)(NH₃)Pd(3,3-(CH₃)₂-C₃H₃)⁺ (5) (figure 9, see above). Selected results are presented in tables 5-8 and some derived parameters are presented in figures 10-13.

### Table 5: Heats of formation (in kJ / mole) of different complexes for different values of the bite angle.

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<th>3</th>
<th>4</th>
<th>5</th>
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DFT study of the distortion of the Pd(\eta^1\text{-allyl}) bond.

Table 6: Bond distances (Å) in different complexes for different values of the bite angle.

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Table 7: Mulliken bond orders in different complexes for different values of the bite angle.

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DFT study of the distortion of the Pd(η^1-allyl) bond.

Table 8: Mulliken charges (electrons) for different complexes for different values of the bite angle.

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</table>
Chapter 3

Figure 10: Palladium - terminal-allylic-carbon distances in complexes 2-5 for various bite angles: d(PdC3) - d(PdC1).

Figure 11: Carbon-carbon distances in complexes 2-5 for various bite angles: d(C1C2) - d(C2C3).
DFT study of the distortion of the Pd(η²-allyl) bond.

Figure 12: Charges on terminal allylic carbon atoms in complexes 2-5 for various bite angles: q(C3)-q(C1).

Figure 13: Fragment charges on terminal allylic carbon atoms in complexes 2-3 for different bite angles: q(C3H2)-q(C1H2), for complexes 4-5 q(C3)-q(C1H2).

Independent of the allyl moiety (1-5), the energy minima of the complexes are found for a bite angle around 100° (table 5). The substituted allyl complexes 2-5 show a slight distortion of the Pd-allyl bond from pure η³ to η¹-η² (tables 6 and 7, figures 10 and 11). The Pd-C1 bond distance is shorter than the Pd-C3 distance (table 6, figure 10) and the C1C2 distance increases while the C2C3 distance decreases (table 7, figure 11). The trend towards η¹-η² is strong for the dimethyl substituted complex 4 and relatively weak for the anti-complex 3. The above effects increase when the bite angle is larger and when the allyl bears more substituents. For all structures, the substituted C3 atom is less negatively charged than the non-substituted C1.
atom (table 8, figures 12 and 13). The calculations, therefore, confirm the trends proposed by Åkermark (section 3.2).\cite{akermark6}

In the following sections, the effect of the bite angle on the bonding is discussed, followed by an analysis of the differences between the use of a syn- and an anti-crotyl moiety, and between the use of PH$_3$-NH$_3$ and PH$_3$-PH$_3$ complexes.

### 3.3.4 Frontier orbitals of the substituted allyl moiety

As discussed in section 3.3.2, a comparison of the energy levels of frontier orbitals of the allyl moiety with those of the cationic palladium fragment is not useful. Nevertheless, a comparison of the energy levels of the various allyl moieties may give more insight in the reactivity towards nucleophiles. Because the Mulliken charge on the allyl moiety is close to zero the energy levels of the involved frontier orbitals of the various uncharged allyl moieties (taken from the optimized structures of 1, 2, 3, 4-120) are compared (table 9).

**Table 9**: Energy levels (in Hartrees) of the frontier orbitals of different allyl moieties. The calculations were performed on allyl$^0$ fragments (doublet) taken from the optimized geometries of the corresponding complexes.

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<th>anti 3-CH$_3$-C$_3$H$_4$ (3)</th>
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</table>

The energy difference between the non-occupied $\varphi_3$ level and the single-occupied $\varphi_2$ level is about half the difference between the $\varphi_1$ and the $\varphi_2$ level. Substitution of the allyl moiety leads to an elevation of all energy levels, but mainly of the occupied $\varphi_1$ level. These results partly confirm the polarization of the frontier orbitals on the allyl moiety upon substitution mentioned in the introduction. A mixing of $\varphi_1$ and $\varphi_2$ would lead to an increase of the energy level of the lowest level, and a decrease of $\varphi_2$, which is indeed observed. The increases of the $\varphi_3$ energy level, however, cannot be explained by mixing of the allyl fragment orbitals.

Comparing these results with the orbital interaction diagram presented in figure 7, shows that a lowering of the $\varphi_1$ energy level leads to an increase of the bonding interaction between the $\varphi_1$ and Pd-sp$_z$. Analogously, the decrease of the $\varphi_2$ level leads to an increase of the interaction between $\varphi_2$ and Pd-d$_{xz}$. Furthermore, the interaction between $\varphi_3$ and Pd-sp$_z$ will decrease, leading to a lowering of the 2a' level. However, for the phosphine complexes used in the experimental chapters, only nucleophilic attack on C1 and C3 was observed, indicating that the interaction of the nucleophile with the 2a" level leads to the alkylation product.
As stated in the introduction, an increase of the bite angle leads to a decrease of the a" level and the effect on the level of the LUMO of the complex, 2a" depends on the relative changes in energy of the involved a" and φ2 orbitals. The most important feature with respect to the reactivity therefore appears to be the polarization of the φ2 orbital, that determines the orbital coefficients of C1 and C3 in the LUMO of the complex. Nevertheless, the bite angle has a clear effect on the structure and charge distribution in the complexes. This can be explained by the non-zero orbital coefficient on C2 in the φ2 orbital, causing a stabilizing interaction between the pz orbitals on C2 and C3 and consequently an enhanced double bond character between C2 and C3. Increasing the bite angle from 80° to 120°, both the bonding and the backbonding interaction decrease. Due to the larger angular dependence of the overlap of the ligand orbital with Pd-dx z compared to Pd-sp z, the effect on the backbonding is more pronounced than the effect on the bonding interaction. The decrease of the bonding interaction leads to an enhanced interaction between the pz orbitals on C1, C2 and C3. The decrease of the backbonding interaction, however, leads to an antibonding interaction between C1 and C2. These two effects lead to an enhanced double bond character between C2 and C3. The allyl will adapt its geometry, which enhances the η1-η2 bonding fashion. Thus, the overall bite angle effect is a result of both the polarization of the frontier orbitals on the allyl fragment and of the bite angle effect on the energy levels of the Pd fragment.

These considerations are confirmed by comparing the non- (1), mono- (2) and disubstituted (4) allyl moieties. The Pd-C1 distance decreases and the Pd-C3 distance increases going from 1 to 4; the C1-C2 distance increases and the C2-C3 distance decreases. Thus, going from 1 to 4, the η1-η2-character of the Pd-allyl bond increases.

### 3.3.5 Syn and anti crotyl (2 and 3)

Monosubstituted allyl moieties are useful substrates for the enantioselective alkylation, since attack on C3 results in a stereogenic carbon atom.[12] It is known that the monosubstituted (crotyl)Pd complex can exist as two isomers, syn and anti (figure 9, see above).[13] Because nucleophilic attack on the C3 atom in the syn and the anti isomer leads to the formation of the opposite enantiomers, insight in the factors governing the regioselectivity for the syn and anti isomer is of great importance.

Ab initio studies by Szabo showed a lower heat of formation for the syn complex.[8] This was explained by the trans configuration of the C2C3 bond and an additional stabilizing interaction between the σ* orbital of a C-H bond of the CH3 with the allyl frontier orbitals. The η3-bonding of the syn-crotyl to the palladium was found to be less distorted than the Pd(anti-crotyl) bond.

Our DFT calculations also show that the heat of formation of the syn isomer 2 is lower than that of the anti isomer 3. In contrast to the reported ab initio studies, we found a more distorted geometry of the Pd-crotyl bond for the syn than for the anti isomer. Moreover, we did not find an energy minimum for the syn-crotyl-geometry obtained from the ab initio calculations. The geometry we found resembles an X-ray crystal
structure we obtained for (syn-crotyl)Pd(dppf)OTf \[^{15}\] and therefore our DFT calculations seem more trustworthy than the reported ab initio calculations.

Both the syn complex 2 and the anti complex 3 show a distortion from \(\eta^1\) to \(\eta^2\). Compared to complex 3, the Pd-C1 distance is shorter and the bond is stronger in complex 2 and the Pd-C3 distance is longer and the bond is weaker in complex 2. An analogous pattern is observed in the allylic CC bonds. The C1-C2 distance is longer and the bond is weaker in 2, and the C2-C3 distance is shorter and stronger in 2. Remarkably, for the anti-isomer, the C2-C3 bond is longer than the C1-C2 bond and they are of similar strength. The low double-bond-character in the C2-C3 bond is reflected in the orientation of the CH\(_3\) group with respect to the CCC plane. Whereas the methyl group in the syn isomer 2 is almost located in the CCC plane (dihedral angle = 175.9° \(2-120^\circ\)), in the anti complex 3, the dihedral angle of the methyl with the allyl CCC plane is much smaller (145.3° in 3-\(120^\circ\)), indicating a shift of hydride character from \(\text{sp}^2\) to \(\text{sp}^3\) on the C3 atom. The polarization of the frontier orbitals of the crotyl fragment is therefore expected to be more pronounced in the syn-isomer 2 than in the anti-isomer 3. These structural features hardly change when the bite angle is varied from 80° to 120°.

The distribution of the Mulliken charge on the allyl reflects the differences in the geometries. The charge on C1 is more negative and the charge on C3 more positive in the syn complex 2. Remarkably, for both 2 and 3, the charge on C3 is significantly more positive than in the non substituted (1) and the disubstituted complexes (4 and 5).

Based on our calculations, it is expected that for both complexes, the nucleophilic attack will preferentially take place at the C3 atom and that this regioselectivity might be more pronounced for attack on the syn isomer. The enhanced \(\text{sp}^3\) character on the C3 atom, found in the modeling of the anti complex 3, may also contribute to a preference for attack on this carbon atom. In the alkylation product, the attacked carbon ends up as \(\text{sp}^3\) hybridized. Attack on C3 of the anti-crotyl in 3 will include a smaller shift of electron density and a smaller rearrangement of atoms than attack on C3 of the syn-crotyl 2. Since the ab initio studies report the contrary result (a less distorted bond for the syn-crotyl),\[^{18}\] it is hard to predict what experimentally may be found. Our experimental studies show (chapter 4-5), that the syn isomer reacts mainly via attack on C1, whereas the anti isomer reacts mainly via attack on C3.

3.3.6 Effect of two different donor atoms, PN (5) instead of PP (4)

To study the effect of the well known difference in trans-influence between a PH\(_3\) and a NH\(_3\) ligand, we replaced the PH\(_3\) trans to C1 in the dimethyl complex 4 by NH\(_3\). NMR studies showed that this trans isomer (PH\(_3\) trans to the substituted C3 atom) is favored over the corresponding cis isomer (chapter 6). The calculations show that the distortion of the Pd-allyl bond is slightly more pronounced compared to the P-P analogue 3 (tables 6-8). The Pd-C1 distance is shorter and the bond is stronger than in 4. The Pd-C3 distance, however, is also shorter and stronger than in 4. Thus, the Pd-allyl bond has slightly more \(\eta^1\)- and slightly less \(\eta^2\)-character. On the other hand, the CC distances in the allyl moiety show a slightly more pronounced non-
symmetry. The C1-C2 distance is longer and the bond is weaker than in 4 and the C2-C3 distance is shorter and the bond is stronger than in 4. The Mulliken charge distribution in the complex shows the same pattern; the charge on C1 is more negative than in 4 and the charge on C3 is slightly less negative.

To gain insight in the origin of the enhanced non-symmetry, the molecular orbitals of the Pd(PH₃)(NH₃)⁺ fragment were calculated. In contrast to the analogous Pd(PH₃)₂⁺ fragment, the occupied Pd-π (to combine with ϕ2) and unoccupied Pd-σ orbital (to combine with ϕ1) could not be assigned. The presumably involved Pd-π orbital (the HOMO) is significantly lower in energy than the corresponding orbital in the Pd(PH₃)₂⁺ fragment and the coefficients on the relevant orbitals are significantly smaller. Because of the different response of N compared to P to the 1+ charge on the Pd-fragment, a comparison of the energy levels between the different Pd-fragments is not useful. The identification of the involved Pd-σ orbital is more difficult, since the fragment has several unoccupied fragment molecular orbitals that are close in energy, most of them having significant Pd-s or Pd-p character. Several of these potential Pd-σ orbitals are well below the energy level of the Pd-σ orbital of the Pd(PH₃)₂⁺-fragment, so even a linear combination of these orbitals would lead to a relatively low lying Pd-σ orbital.

Therefore, it is difficult to estimate the overall effect on going from Pd(PH₃)₂⁺ to Pd(PH₃)(NH₃)⁺. The energy levels of the orbitals involved in both the bonding and the backbonding interactions are significantly lower in energy. Indeed, the Pd fragment in the complex bears less positive charge than the corresponding Pd(PH₃)₂⁺ fragment; a relatively large electron density is found on the NH₃ ligand. A more detailed analysis of the bonding in the Pd(PH₃)(NH₃)(allyl)⁺ complex and the effect of the bite angle thereupon is beyond the scope of this thesis.

3.4 Conclusions and aim of the chapters on allylic alkylation

The DFT calculations of (allyl)Pd(L1)(L2)⁺ complexes in this chapter were focused on the effect of substituents on the allyl, ligand donor atoms and the bite angle (L1-Pd-L2 angle). It was shown that for substituted allyl groups, the Pd-allyl bond is distorted from η¹ to η³. The distortion of the Pd-allyl bond can be described as follows:

1) a longer C1C2 distance relative to the C2C3 distance
2) a lower C1C2 bond order compared to the C2C3 bond order
3) a shorter PdC1 distance relative to the PdC2 and PdC3 distances
4) a higher PdC1 bond order compared to the PdC2 and PdC3 bond orders
5) a more positive Mulliken charge on C3 is compared to C1.

This distortion is more pronounced when:

a) the allyl is substituted with a CH₃ on one of its terminal carbon atoms
b) there are two substituents on C3 instead of one
c) the bite angle is larger

d) the PH$_3$ cis to C3 is replaced by NH$_3$.

The respective effects can be explained as follows:

ad a) the substituent(s) on the allyl group cause(s) polarization of the frontier orbitals of the allyl moiety and more specifically, an increase of the 2p$_z$-coefficient of C3 in the 2a$^\pi$ (LUMO) level of the complex.

ad b) an enhanced effect of a)

ad c) a change in the energy levels of the frontier orbitals of the palladium fragment: a bell shaped dependence is found for the Pd-π orbital and a steady increase is found for the Pd-σ orbital

ad d) a decrease in the energy difference between the involved frontier orbitals of the palladium fragment

ad e) a combination of a) - d).

3.4.1 Implications for the regioselectivity of nucleophilic attack

If the regioselectivity of the allylic alkylation is determined by an early transition state mechanism, it can be expected that alkylation of all substituted allyl moieties studied in this chapter lead to at least a significant percentage of the branched product. A relatively high selectivity is expected for the dimethyl substituted allyl, especially using P-N ligands. Based on the modeling studies, the relative regioselectivity arising from the syn and the anti crotyl group is hard to predict. If the non-symmetry of the syn isomer is less pronounced than the DFT calculations suggest, the regioselectivity of alkylation of the anti-isomer may be higher. If the partly sp$^3$ hybridization on C3 of the anti-isomer does not contribute to the regioselectivity, the regioselectivity may be higher for the syn-isomer.

3.4.2 Aim of the chapters on allylic alkylation

In the following chapters, the aforementioned predictions will be investigated experimentally. In the first part (chapters 4 and 5), the effect of one methyl substituent is studied by using crotyl (C$_4$H$_7$) complexes of a series of bidentate phosphine ligands varying in bite angle. The second part (chapter 6) deals with the allylic alkylation of a series of crotyl and cinnamyl (C$_9$H$_7$) complexes using P-N ligands. In the third part (chapter 7), the steric effect of the ligand on the solid state structure of a series of [3,3-(CH$_3$)$_2$-C$_5$H$_3$] complexes is studied in detail using X-ray crystallography. In the fourth part (chapter 8), the effect of different donor atoms is investigated using various wide-bite-angle-ligands based on the xanthene backbone. Finally, the hypothesis is evaluated in chapter 9.
DFT study of the distortion of the Pd(η^1-allyl) bond.

3.5 Experimental section

The calculations were performed using the Gaussian98 program\[^{14}\], using the hybrid B3LYP functional\[^{16}\] and the LANL2DZ basis set on all atoms. For palladium this basis set consists of the small core ECP of Hay and Wadt with a [341/321/31] contracted valence set.\[^{17}\]

The reported data for the complexes were taken from the optimized structures.

3.6 References


Chapter 4
Effect of the bite angle of bidentate phosphine ligands on the regioselectivity in allylic alkylation of crotyl complexes.

The DFT calculations in chapter 3 showed that the Pd-allyl bond is distorted, when the allyl moiety is substituted. In this chapter we study the effect on the structure and reactivity of the presence of one substituent on the allyl moiety for the case of two phosphorus donor atoms.

Abstract

The natural bite angle of bidentate phosphine ligands influences the isomer distribution (syn and anti) in (crotyl)Pd(bisphosphine) OTf complexes. It was found ($^{31}$P- and $^1$H-NMR studies) that the syn/anti ratio changes from 12 (dppp) to 1.3 (Sixantphos). Molecular orbital calculations (PM3(tm) level) indicate that for ligands inducing a large bite angle, the phenyl rings of the ligand embrace the allyl moiety, thereby influencing the syn / anti ratio. This bite angle effect on the syn / anti ratio is transferred to the regioselectivity in stoichiometric allylic alkylation. Ligands inducing large bite angles direct the regioselectivity towards the formation of the branched product 2. Catalytic alkylation of trans-2-butenyl acetate (crotyl acetate) showed that for ligands with a small bite angle the regioselectivity of the catalytic and stoichiometric alkylation are in good agreement. This correspondence is less pronounced for ligands with a larger bite angle, which is rationalised in terms of the relative rates of syn / anti isomerization and the alkylation reaction. The ligand with the largest bite angle (Sixantphos) gives the most active catalytic species.
4.1 Introduction

The palladium-catalysed allylic alkylation reaction receives much interest\textsuperscript{1-7}. Most of the research in this field focuses on asymmetric induction. Less effort is put into understanding the regioselectivity found in the alkylation of non-symmetrically substituted allyl-fragments\textsuperscript{8,13}. Åkerman\textsuperscript{8} has shown that the cone-angle of substituted phenantrolines has a large influence on both the isomer distribution of crotyl-Pd complexes and the regioselectivity of stoichiometric alkylation. The methyl substituents on the 2,9-dimethyl-1,10-phenantrolin ligand interfere with the methyl substituent on the allyl-moiety. This causes the anti-isomer of the complex to prevail over the otherwise more stable syn-isomer. It was shown that stoichiometric alkylation of the syn-complex resulted in almost exclusive formation of the linear trans-product (1). The anti-complex reacted to the branched (2) and the linear cis-product (3) in an approximately 1:1 ratio.

\[
\text{RR} = \text{H} , \quad \text{X} = \text{CMe}_2 : \text{xantphos} \\
\text{H} , \quad \text{SiMe}_2 : \text{sixantphos} \\
\text{Me} , \quad \text{S} : \text{thixantphos} \\
\text{H} , \quad \text{no atom} : \text{DPE phos}
\]

Figure 1. Generic Xantphos structure

In our group much research has been conducted concerning the effect of the natural bite angle\textsuperscript{20} (\(\beta_n\)) of bidentate phosphine ligands on transition metal catalysed reactions\textsuperscript{15}. This research led to the development of a new class of ligands that enforces (very) large bite angles up to 110° (the Xantphos type ligands; see figure 1). Significant dependencies of the catalyst performance on the natural bite angle have been observed in reactions such as the rhodium catalysed hydroformylation\textsuperscript{8} and the nickel catalysed hydrocyanation\textsuperscript{9}. Previously, we communicated on the effect found in the alkylation of trans-2-hexenyl acetate with sodium diethyl 2-methylmalonate\textsuperscript{11}. Ligands with a large natural bite angle were found to direct the regioselectivity to the linear trans-product 1 resulting in smaller amounts of the branched product (figure 2). The results were rationalized in terms of steric hindrance. In this chapter we will explore the limits of the used model by studying the influence of the bite angle on the allylic alkylation of the much smaller crotyl moiety.
4.2 Stoichiometric alkylation

4.2.1 Synthesis and characterization of the catalyst

In order to investigate the nature of this bite angle effect, we have prepared and isolated Pd(crotyl)(bisphosphine)OTf complexes of several bisphosphine ligands. NMR studies (\(^1\)H and \(^31\)P) of these compounds show that they exist as an equilibrium mixture of the syn and anti isomers. The syn / anti ratio is dependent on the bite angle of the ligand and is significantly lower in complexes of ligands inducing larger bite angles (table 1).

To understand the effect of the P-Pd-P angle\(^{19}\) (\(\beta\)) on the structure of the Pd-allyl complex, molecular orbital calculations (semi-empirical PM3(tm) level) were carried out on the cationic (crotyl)Pd(bisphosphine)\(^+\) complexes. The P-Pd-P angle (\(\beta\)), taken from the calculated structures, varies from 85° (dppe) to 110° (Sixantphos). The allyl moiety is found to be embraced by the phenyl rings of the ligand. When the bite angle is larger, the embracing becomes more pronounced. This is visualised in figure 3.
In all the complexes studied using molecular modelling, the syn-isomer has a lower energy than the anti-isomer. The energy difference between the syn- and anti-isomer, however, decreases with larger bite angle. This is in agreement with the experimental data: a lower syn / anti ratio is observed when ligands inducing larger bite angles are applied (table 1). The embracing effect in complexes of ligands inducing a small bite angle, however, is of minor influence. The relatively high syn / anti ratio of (crotyl)Pd(dppp) OTf is therefore the result of electronic rather than steric effects. Detailed DFT modeling studies are in progress to investigate the nature of this effect.

4.2.2 Stoichiometric alkylation

Table 1. Relation between the bite angle and 1) $\Delta E$ (syn-anti) calculated by molecular modelling (PM3(tm) level) and obtained from experimental data (NMR), and 2) the regioselectivity in stoichiometric alkylation of the equilibrium mixtures of (crotyl)Pd(bisphosphine)OTf complexes

<table>
<thead>
<tr>
<th>complex (ligand)</th>
<th>$\beta$</th>
<th>% syn</th>
<th>% anti</th>
<th>$\Delta E$(NMR) (kJ.mole$^{-1}$)</th>
<th>$\Delta E$ (pm3(tm)) (kJ.mole$^{-1}$)</th>
<th>% 1</th>
<th>% 3</th>
<th>% 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (dppe)</td>
<td>85</td>
<td>90</td>
<td>10</td>
<td>-5.4</td>
<td>-23.7</td>
<td>70.0</td>
<td>8.9</td>
<td>21.1</td>
</tr>
<tr>
<td>II (dppp)</td>
<td>95</td>
<td>92</td>
<td>8</td>
<td>-6.1</td>
<td>-21.9</td>
<td>79.2</td>
<td>4.6</td>
<td>16.2</td>
</tr>
<tr>
<td>III (dppb)</td>
<td>99</td>
<td>86</td>
<td>14</td>
<td>-4.5</td>
<td>-20.0</td>
<td>71.7</td>
<td>8.0</td>
<td>20.3</td>
</tr>
<tr>
<td>IV (dpff)</td>
<td>106</td>
<td>78</td>
<td>22</td>
<td>-3.1</td>
<td>-18.9</td>
<td>68.9</td>
<td>8.9</td>
<td>22.2</td>
</tr>
<tr>
<td>V DPEphos</td>
<td>108</td>
<td>72</td>
<td>28</td>
<td>-2.3</td>
<td>-15.4</td>
<td>66.4</td>
<td>9.6</td>
<td>24.0</td>
</tr>
<tr>
<td>VI Sixanphos</td>
<td>110</td>
<td>57</td>
<td>43</td>
<td>-0.7</td>
<td>-12.5</td>
<td>54.5</td>
<td>12.4</td>
<td>33.1</td>
</tr>
</tbody>
</table>

[a]: $\beta$ obtained from the calculated (crotyl)Pd(bisphosphine) complexes [b]: the relative large energy difference in the calculations is most likely the result of the absence of solvent and anion

Figure 3. The embracing effect of the phenyl rings cause the substituent on the allyl moiety to bend out of the allyl plane. Left = syn, right = anti.
The syn / anti ratio governs the regioselectivity of the stoichiometric alkylation (table 1, figure 4). In (crotyl)Pd(bisphosphine) OTf complexes of ligands inducing a small bite angle the syn isomer largely prevails and the relative amount of the linear trans product 1 is high. Going to a larger bite angle (from dppe to Sixantphos), the percentage syn isomer as well as the selectivity to 1 drops, whereas the selectivity to the branched product 2 increases. The percentage of 3 remains almost constant along the bite angle range studied.

Figure 4. Relation between isomer distribution in cationic (crotyl)Pd(bisphosphine)OTf complexes and the regioselectivity of stoichiometric alkylation

It has been suggested\textsuperscript{4} that in allylic alkylation reactions the structure of the allyl complex determines the (enantio)selectivity in an early transition state. Recent developments\textsuperscript{4, 6, 12-15}, however, indicate that in many cases a late transition state is more likely. In an early transition state, not only the electronic properties of the allyl moiety are important for the regioselectivity (chapter 3), but also the relative steric accessibility of the two carbon atoms C1 and C3. Due to steric hindrance between the substituent on the allyl moiety and the ligand, it will be bent out of the allyl plane, away from the palladium centre. Therefore the substituted allyl carbon atom C3 will be less accessible for nucleophilic attack and consequently alkylation of the unsubstituted allyl carbon atom C1 will prevail.

In a late transition state, nucleophilic attack of the malonate anion at the substituted allyl carbon atom C3 will cause a change in the hybridisation on C3 from $sp^2$ to $sp^3$. This causes the substituent to bend towards a phenyl ring of the ligand. A large bite angle results in an increase of the steric hindrance in this stage of the reaction (figure 3), which hampers the formation of 2\textsuperscript{11}.

Using a small group like a methyl substituent on the allyl moiety the steric hindrance during the nucleophilic attack is of less influence. Consequently, electronic factors may become more important. This would explain the good correlation between the syn / anti ratio and the observed regioselectivity.
Therefore it is concluded that in the alkylation of \((\text{crotyl})\text{Pd(bisphosphine)}\text{OTf}\) complexes the transition state of the reaction is not late. The relative importance of steric and electronic factors is dependent on the nature of the ligand and the (syn or anti) orientation of the substituents on the allyl moiety.

### 4.3 Catalytic alkylation

#### 4.3.1 Rate of reaction

In addition to these stoichiometric experiments we have also carried out the catalytic alkylation of crotyl acetate (table 2). The catalytic experiments have been performed using the isolated \((\text{crotyl})\text{Pd(bisphosphine)}\text{OTf}\) complexes, instead of using a precursor, such as \(\text{Pd(dba)}_2\), or \(\text{Pd(OAc)}_2\), and the ligand. This procedure excludes an incubation step which is necessary for the formation of the catalytically active species, as well as the possibility of pre-equilibria via complexation of dba to palladium\(^{17}\). The retarding effect of dba is clear, if we compare the reaction rates presented in table 2 with the reaction rates presented in a previous communication of the bite angle effect on allylic alkylation\(^{11}\). The difference in the rate of reaction is at least one order of magnitude\(^{16}\). Remarkably, the observed trend in reaction rate does not remain the same. Starting from the isolated \((\text{crotyl})\text{Pd(bisphosphine)}\text{OTf}\) complex, Sixanphos is found to yield the most active catalytic species, whereas use of \(\text{Pd(dba)}_2\) results in DPEphos or dppb to yield the most active catalyst\(^{11}\). Obviously, the catalytically active species is less easily formed from \(\text{Pd(dba)}_2\) when a rigid ligand inducing a large bite angle is used.

In contrast to most literature procedures for allylic alkylation reactions only one equivalent of ligand per palladium atom is used. When a precursor, such as \(\text{Pd(OAc)}_2\) is used, an additional equivalent of ligand might be required to reduce the \(\text{Pd}^{II}\) to the active \(\text{Pd}^0\) species\(^{16}\). The presence of an excess of ligand will also reduce the rate of the reaction, by complexation to the \(\text{Pd}^0\) species which is formed after alkylation. Before coordination of the substrate dissociation of the extra ligand is necessary. This can retard the overall reaction rate.

#### 4.3.2 Regioselectivity

The bite angle effect as observed in the stoichiometric alkylation of \((\text{crotyl})\text{Pd(bisphosphine)}\text{OTf}\) complexes is less obvious in the catalytic alkylation of crotyl acetate. The starting complex enters the catalytic cycle via alkylation of the starting \((\text{crotyl})\text{Pd(bisphosphine)}\text{OTf}\) complex. The next step involves oxidative addition of the substrate to the thus formed \(\text{Pd}^0\) species. As the substrate configuration is mainly trans (95%), initially the syn (crotyl)\text{Pd(bisphosphine)}\text{OAc} complex is formed as the main
product. This complex is cationic, so the acetate leaving group will remain as a counterion in the coordination sphere. Interaction of the counterion with the palladium centre is known to increase the rate of dynamic behaviour of the allyl moiety\[18\]. This results in an isomerization of the syn complex to the anti complex and vice versa. The resulting regioselectivity of the catalytic reaction (table 2) is dependent on the relative rates of syn-anti isomerization and alkylation.

NMR experiments with the (crotyl)Pd(bisphosphine)OTf complexes used in the alkylation reactions, indicate that the syn-anti isomerization in these complexes is slow relative to stoichiometric alkylation. The isomerization, however, may play a significant role when acetate instead of the weakly co-ordinating triflate is the counterion, as is the case in the catalytic experiments.

The correlation between the regioselectivity in stoichiometric and catalytic alkylation is good for ligands inducing a small bite angle, such as dppe and dppp, but also for dppf (table 1 and 2). Going to a larger bite angle, the selectivity follows a different trend than observed in the stoichiometric reaction. The Sixantphos ligand directs the regioselectivity towards 85% of the linear trans product. This can be rationalised in terms of a fast alkylation rate, relative to isomerization, of the complexes with ligands inducing a large bite angle.

Table 2. Catalytic alkylation of crotyl acetate using the equilibrium mixtures of (crotyl)Pd(bisphosphine)OTf complexes

<table>
<thead>
<tr>
<th>complex(ligand)</th>
<th>$\beta$[a] ($^\circ$)</th>
<th>t.o.f.[b]</th>
<th>yield[c] (%)</th>
<th>% 1</th>
<th>% 3</th>
<th>% 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (dppe)</td>
<td>85</td>
<td>2.0</td>
<td>37.3</td>
<td>68.8</td>
<td>11.1</td>
<td>20.0</td>
</tr>
<tr>
<td>II (dppp)</td>
<td>95</td>
<td>2.9</td>
<td>37.1</td>
<td>76.0</td>
<td>6.6</td>
<td>17.4</td>
</tr>
<tr>
<td>III (dppb)</td>
<td>99</td>
<td>8.9</td>
<td>90.3</td>
<td>79.0</td>
<td>3.1</td>
<td>17.9</td>
</tr>
<tr>
<td>IV (dppf)</td>
<td>106</td>
<td>8.0</td>
<td>81.5</td>
<td>74.1</td>
<td>2.5</td>
<td>23.4</td>
</tr>
<tr>
<td>V (DPEphos)</td>
<td>108</td>
<td>8.7</td>
<td>86.0</td>
<td>80.1</td>
<td>2.5</td>
<td>17.4</td>
</tr>
<tr>
<td>VI (Sixantphos)</td>
<td>110</td>
<td>9.1</td>
<td>88.3</td>
<td>85.7</td>
<td>1.4</td>
<td>12.9</td>
</tr>
</tbody>
</table>

[a]: $\beta$ obtained from the calculated (crotyl)Pd(bisphosphine) complexes
[b]: t.o.f. initial turn over frequency, determined after 10 minutes reaction time, in $10^3$ mole mole$^{-1}$ h$^{-1}$
[c]: based on the formation of 1,2 and 3, as determined after 30 minutes by GC, using the internal standard method

The catalytic reactions were performed in THF (10 mL), using 0.05 mol% of catalyst (0.00050 mmole), 1.0 mmole of substrate and 2.0 mmole of sodium diethyl 2-methylmalonate. The reaction was monitored by GC using decane as the internal standard.
4.4 Conclusion

In conclusion, we have shown that for (crotyl)Pd(bisphosphine)OTf complexes with ligands inducing a large bite angle the syn / anti ratio is much lower than in the corresponding complexes with ligands having a small bite angle. Molecular modelling studies indicate that this is caused by an increasing embrace of the allyl moiety by the phenyl rings of the ligand. This bite angle effect on the syn / anti ratio can be transferred to the regioselectivity in stoichiometric allylic alkylation. Ligands inducing large bite angles direct the regioselectivity towards the formation of 2. In the catalytic alkylation of crotyl acetate, however, the regioselectivity is also determined by the relative rates of syn-anti isomerization and alkylation. The correlation between the regioselectivity found in the stoichiometric and the catalytic alkylation is best for ligands inducing a small bite angle. The ligands with the largest bite angle (Sixantphos) is found to result in the most active catalytic species, indicating an enhanced electrophilicity of the allyl moiety (see chapter 3).
4.5 Experimental section

$^1$H NMR (300 MHz, TMS, CDCl$_3$), $^{31}$P{$^1$H} (121.5 MHz external 85% H$_3$PO$_4$, CDCl$_3$) were recorded on a Bruker AMX-300 spectrometer. Elemental analyses were performed on an Elementar Vario EL (Foss Electric).

All calculations were carried out using the commercially available SPARTAN program (version 5.0.3). The geometry optimisation was performed on the semi-empirical pm3(tm) level. The product distribution was measured on a Interscience Mega2 apparatus, equipped with a DB1 column, length 30 m, inner diameter 0.32 mm, film thickness 3.0 μm, and a F.I.D detector. All experiments were carried out using standard Schlenk techniques. All solvents were freshly distilled prior to use.

Sodium diethyl 2-methylmalonate (0.5 M in THF) was prepared from diethyl 2-methylmalonate and NaH in THF at 273 K.

The stoichiometric alkylation reactions were performed by adding an excess of sodium diethyl 2-methylmalonate (0.1 ml of a 0.5 M solution in THF) to a solution of 10 mg of the Pd-complex in 1 ml of THF. Reaction was instantaneous and after one minute, the mixture was worked up with water, filtered over silica and analysed by GC.

The catalytic reactions were performed in THF (10 mL), using 0.05 mol% of catalyst (0.00050 mmole), 1.0 mmole of substrate and 2.0 mmole of sodium diethyl 2-methylmalonate. The reaction was monitored by quenching samples from the reaction mixture with flash chromatography which were analysed by GC using decane as the internal standard.

The Pd-complexes were prepared in CH$_2$Cl$_2$ from [(crotyl)-Pd-μCl]$_2$ by adding 2 equiv. of ligand and abstracting the Cl-atom with AgOTf. The complexes were isolated in a quantitative yield (white microcrystalline powder) as their analytically pure equilibrium mixtures and were used as such in the alkylation reaction. The syntheses of DPEphos and Sixantphos have been published elsewhere$^{[6]}$. Dppe, dppp, dppb and dppf were obtained from Acros chemicals and used as received.

Analytical data of the (crotyl)-Pd-(ligand)OTf complexes are given for their equilibrium mixtures. The NMR signals of the syn and anti isomers could easily be distinguished. The syn / anti ratio was determined by comparing the intensities of the signals of the Me-substituent on the allyl moiety. NMR-data of the complexes were obtained in CDCl$_3$ (δ in ppm).
Chapter 4

Pd(dppe)(crotyl)OTf (Ia+s) was obtained in syn/anti ratio of 90/10. El.anal. (Ia+s) found: C: 52.08%, H: 4.30% (calc. C: 52.51%, H: 4.38%).

Pd(dppe)(syn-crotyl)OTf (Ia): H: 1.69 (ddd, J₁ = 6.3 Hz, J₂ = 8.4 Hz, J₃ = 8.4 Hz, 3H(Me)), 2.4-3.0 (m, 4H, 2CH₂-bridge), 3.1 (ddd, J₁=12.1 Hz, J₂= 12.1 Hz, 1H(Ha)), 4.37 (m, 1H(Hc)), 4.6 (dd, J₁=7.2 Hz, J₂= 7.2 Hz, 1H(Hb)), 5.7 (ddd, J₁= 7.4 Hz, J₂ = 13.1 Hz, J₃ = 13.1 Hz, 1H(Hd)), 7.3-7.7 (m, 20H(Ar)), ³¹P¹H: 48.5 (d, J = 33 Hz), 49.6 (d, J = 33 Hz).

Pd(dppe)(anti-crotyl)OTf (Ia): H: 0.9 (ddd, J₁= 6.9 Hz, J₂ = 7.0 Hz, J₃ = 7.0 Hz, 3H(Me)), 2.4-3.0 (m, 4H, 2CH₂-bridge), 3.5 (dd, 1H(Ha)), 4.15 (m, 1H(Hc)), 4.7 (dd, 1H(Hb)), 5.6 (m, 1H(Hd)), 7.3-7.7 (m, 20H(Ar)).

Pd(dppe)(anti-crotyl)OTf (Ia): H: 0.9 (ddd, J₁ = 6.9 Hz, J₂ = 7.0 Hz, J₃ = 7.0 Hz, 3H(Me)), 2.4-3.0 (m, 4H, 2CH₂-bridge), 3.5 (dd, 1H(Ha)), 4.15 (m, 1H(Hc)), 4.7 (dd, 1H(Hb)), 5.6 (m, 1H(Hd)), 7.3-7.7 (m, 20H(Ar)).

³¹P¹H: 49.9 (d, J = 35 Hz), 52.6 (d, J = 35 Hz).

Pd(dppe)(anti-crotyl)OTf (IIa): H: 0.88 (ddd, J₁= 6.9 Hz, J₂ = 6.9 Hz, J₃ = 6.9 Hz, 3H(Me)), 2.6-3.0 (m, 4H, 2CH₂-bridge), 3.2 (dd, J₁,J₂ >7 Hz, 1H(Ha)), 4.0 (dd, J₁,J₂ <7Hz, 1H(Hb)), 4.0 (dd, J₁= 6.9 Hz, J₂ = 6.9 Hz, 1H(Hb)), 4.7 (m, 1H(Hc)), 5.5 (m, 1H(Hd)), 7.2-7.6 (m, 20H(Ar)).

³¹P¹H: 7.1 (d), 7.9 (d)

Pd(dppe)(anti-crotyl)OTf (IIIa): H: 0.64 (ddd, J₁= 6.7 Hz, J₂ = 6.7 Hz, J₃ = 6.7 Hz, 3H(Me)), 1.7-2.0 (m, 4H, 2CH₂-bridge), 2.5-2.8 (m, 4H, 2CH₂-bridge), 2.95 (dd, J₁ = 11.3 Hz, J₂ = 11.3 Hz, 1H(Ha)), 3.7 (dd, J₁= 6.5 Hz, J₂ = 6.5 Hz, 1H(Hb)), 4.85 (m, 1H(Hc)), 5.5 (ddd, J₁= 7.4 Hz, J₂ = 13.0 Hz, J₃=13.0 Hz, 1H(Hd)), 7.4-7.7 (m, 20H(Ar)).

³¹P¹H: 20.4 (d, J= 20.8 Hz), 21.2 (d, J= 20.8 Hz).

Pd(dppe)(anti-crotyl)OTf (IIIa): H: 0.64 (ddd, J₁= 6.7 Hz, J₂ = 6.7 Hz, J₃ = 6.7 Hz, 3H(Me)), 1.7-2.0 (m, 4H, 2CH₂-bridge), 2.5-2.8 (m, 4H, 2CH₂-bridge), 3.05 (dd, 1H(Ha)), 4.85 (dd, 1H(Hb)), 5.7 (m, 1H(Hd)), 7.4-7.7 (m, 20H(Ar)).

³¹P¹H: 20.7 (d, overlap with syn-complex), 21.2 (d, overlap with syn-complex)

52
Pd(dpff)(crotyl)OTf (IV s+a) was obtained in syn/anti ratio of 78/22. El.anal. (IVa+s) found: 53.71%, H: 4.11% (calc.: C: 54.15%, H: 4.05%)

Pd(dpff)(syn-crotyl)OTf (IVs): \( ^1H \): 1.08 (ddd, \( J_1 = 6.7 \) Hz, \( J_2 = 6.7 \) Hz, \( J_3 = 10.3 \) Hz, 3H(Me)), 3.23 (dd, \( J_1 = 11.0 \) Hz, \( J_2 = 11.0 \) Hz, 1H(Ha)), 3.50 (dd, \( J_1 = 4.0 \) Hz, \( J_2 = 4.0 \) Hz, 1H(Hb)), 3.83 (s, 1H(FcH)), 3.94 (s, 1H(FcH)), 4.27 (s, 1H(FcH)), 4.32 (s, 1H(FcH)), 4.35-4.55 (m, contains FcH and Hc), 4.37 (s, 1H(FcH)), 4.46 (s, 1H(FcH)), 4.63 (s, 1H(FcH)), 4.83 (s, 1H(FcH)), 5.64 (ddd, \( J_1 = 12.9 \) Hz, \( J_2 = 12.9 \) Hz, \( J_3 = 7.4 \) Hz, 1H(Hd)), 7.3-7.8 (m, 20H, Ar, syn and anti)

\( ^{31}P{^{1H}} \): 24.9 (d, \( J = 47.5 \) Hz), 23.6 (d, \( J = 47.5 \) Hz)

Pd(dpff)(anti-crotyl)OTf (IVa): \( ^1H \): some signals appear as shoulders on IVs, some however appear as separate signals: 0.90 (ddd, \( J_1 = J_2 = J_3 = 6.8 \) Hz, 3H(Me)), 3.2 (shoulder on IVs(Ha), Ha), 3.93 (s, 1H (FcH)), 4.35-4.55 (m, contains FcH), 4.40 (s, 1H (FcH)), 4.43 (s, 1H (FcH)), 4.51 (s, 1H (FcH)), 4.65 (s, 1H (FcH)), 4.66 (s, 1H (FcH)), 4.74 (ddd, \( J_1 = J_2 = J_3 = 6.8 \) Hz, 1H, (He)), 7.3-7.8 (m, 20H, Ar, syn and anti)

\( ^{31}P{^{1H}} \): signals appear as shoulders on IVs.

Pd(DPEphos)(crotyl)OTf (V s+a) was obtained in syn/anti ratio of 72/28. El.anal. (Vla+s) found: C: 57.60%, H: 4.08% (calc. C: 57.99%, H: 4.15%)

Pd(DPEphos)(syn-crotyl)OTf (Vs): \( ^1H \): 1.1 (ddd, \( J_1 = 10.7 \) Hz, \( J_2 = 6.6 \) Hz, \( J_3 = 6.6 \) Hz, 3H(Me)), 3.4 (m, 2H(Ha and Hb)), 4.4 (m, 1H, Hc)), 5.6 (ddd, \( J_1 = 7.4 \) Hz, \( J_2 = 12.7 \) Hz, \( J_3 = 12.7 \) Hz, 1H(Hd)), 6.4-7.6 (m, Ar)

\( ^{31}P{^{1H}} \): 10.3 (d, \( J = 39.6 \) Hz), 17.1 (d, \( J = 39.6 \) Hz)

Pd(DPEphos)(anti-crotyl)OTf (Va): \( ^1H \): 0.9 (ddd, \( J_1 = 6.6 \) Hz, \( J_2 = 6.6 \) Hz, \( J_3 = 6.6 \) Hz, 3H(Me)), 3.0 (dd, \( J_1 = 9.1 \) Hz, \( J_2 = 14.1 \) Hz, 1H(Ha)), 4.2 (dd, \( J_1 = 6.4 \) Hz, \( J_2 = 6.1 \) Hz, 1H(Hb)), 4.4 (m, 1H, Hc)), 5.8 (ddd, \( J_1 = 14.0 \) Hz, \( J_2 = 7.7 \) Hz, \( J_3 = 7.7 \) Hz, 1H(Hd)), 6.4-7.6 (m, Ar)

\( ^{31}P{^{1H}} \): 10.6 (d, \( J = 40 \) Hz), 16.4 (d, \( J = 40 \) Hz)

Pd(Sixantphos)(crotyl)OTf (VI s+a) was obtained in syn/anti ratio of 57/43. El.anal. (VIa+s) found: C: 56.31%, H: 4.35% (calc. C: 55.88%, H: 4.46%)

Pd(Sixantphos)(syn-crotyl)OTf (VIs): \( ^1H \): 0.57 (s, 3H(Me-Si)), 0.61 (s, 3H(Me-Si)), 0.8 (ddd, \( J_1 = 11.3 \) Hz, \( J_2 = 6.3 \) Hz, \( J_3 = 6.3 \) Hz, 3H(Me)), 3.4 (dd, \( J_1 = 11.7 \) Hz, \( J_2 = 11.7 \) Hz, 1H(Ha)), 3.55 (dd, \( J_1 = 6.4 \) Hz, \( J_2 = 6.4 \) Hz, 1H(Hb)), 4.4 (m, 1H(Hc)), 5.4 (ddd, \( J_1 = 12.8 \) Hz, \( J_2 = 12.8 \) Hz, \( J_3 = 7.3 \) Hz, 1H(Hd)), 6.9-7.5 (m, Ar(syn and anti)), 7.7 (q, Ar(syn and anti))

\( ^{31}P{^{1H}} \): 9.8 (d, \( J = 39.3 \) Hz), 10.6 (d, \( J = 39.3 \) Hz)

Pd(Sixantphos)(anti-crotyl)OTf (Vla): \( ^1H \): 0.57 (s, 3H(Me-Si)), 0.61 (s, 3H(Me-Si)), 0.9 (ddd, \( J_1 = 6.2 \) Hz, \( J_2 = 6.2 \) Hz, \( J_3 = 6.2 \) Hz, 3H(Me)), 3.4 (dd, \( J_1 = 11.7 \) Hz, \( J_2 = 11.7 \) Hz, 1H(Ha)), 3.7 (dd, \( J_1 = 7.1 \) Hz, \( J_2 = 7.1 \) Hz,
1H(Hb)), 4.65 (m, 1H(Hc)), 5.9 (ddd, J₁=13.8 Hz, J₂=8.0 Hz, J₃=8.0 Hz, 1H(Hd)), 6.9-7.5 (m, Ar(syn and anti)), 7.7 (q, Ar(syn and anti)) ³¹P[¹H]: 5.8 (d, J=35.2 Hz), 7.0 (d, J=35.2 Hz)

4.6 References

[19] β obtained from the calculated (crotyl)Pd(bisphosphine) complexes
Chapter 5

On the influence of the bite angle on the allylic alkylation of (E) and (Z) substrates: Loss and retention of double bond stereochemistry.

The DFT calculations of chapter 3 showed that the Pd(η^3-allyl) bond is distorted, when the allyl moiety is substituted. In the previous chapter we studied the effect on the structure and reactivity of the presence of one substituent on the allyl moiety for the case of two phosphorus donor atoms. We have found that, as predicted by the modeling studies, the Pd-complexes exist as a mixture of syn and anti-isomers. In this chapter we study the influence of the bite angle on the reactivity of the syn and the anti isomer.

Abstract

To study the effect of the ligand on the regioselectivity of the allylic alkylation, (Z) and (E) pent-2-enylacetate were used as substrates. The alkylation of substrates with an (E) conformation of the double bond results in the preferential formation of the linear (E) product. A larger bite angle of the ligand results in an increase of the regioselectivity to more than 98 % linear product for the Sixantphos ligand. Analogously, the alkylation of (Z) substrates results in the formation of the linear (Z) product. Remarkably, for (Z) substrates, a larger bite angle of the ligand leads to an increased regioselectivity for the branched product, up to 47.5 % for Sixantphos. The observed regioselectivities are rationalized in terms of a) a competition between syn-anti isomerization and alkylation and b) a combination of steric and electronic effects in the transition state of the reaction. For all ligands tested, the reaction is faster for the (E) than for the (Z) substrate. However, competition experiments using the Sixantphos ligand show a relatively fast reaction rate for the (Z) substrate, which indicates that the coordination of the substrate to palladium is the discriminating, but not the rate determining step when both substrates are present.
5.1 Introduction

The transition metal catalyzed allylic alkylation is a useful tool in synthetic organic chemistry. A total control of the stereoselectivity and regioselectivity is required for most applications of this reaction. Whereas the enantioselective alkylation of symmetrically disubstituted allyl moieties (derived from e.g. cyclohexenyl acetate) has received much attention in literature, the regioselectivity of the reaction using other types of allylic substrates has been studied less extensively.

When non-symmetrically substituted allylic substrates are used, regiocontrol is required prior to enantiocontrol (figure 1). Palladium(bisphosphine) catalysts are widely studied and show for such substrates a preference for the formation of the linear product (chapter 4). Catalysts based on other metals, such as tungsten or iridium, also show a preference for the branched product, but the rate of the reaction is much lower than found for palladium.

Relatively few studies have been reported concerning the influence of the geometry of the starting allylic substrate on the regioselectivity of the palladium catalyzed reaction. Some years ago, Åkermark et al. have reported such a study in which phenantroline type ligands were used in the allylic alkylation reaction with sodium diethyl 2-methylmalonate as the nucleophile. It was found that the regioselectivity of the reaction is dependent on the geometry of the double bond (E or Z) of the substrate. The E substrate reacts with the Pd(ligand) fragment to form an allylic complex having a syn geometry, which after reaction with the nucleophile mainly yields the linear E product. Analogously, the Z substrate reacts to form a (ligand)Pd(allyl) complex with an anti geometry (see figure 1), which results in the formation of the linear Z and the branched product. They also reported that in the catalytic reactions, the regioselectivity is determined by competition between syn-anti isomerization and alkylation.
In chapter 4, it is described that a large bite angle leads to a low syn / anti ratio as a result of increased steric interactions. *Stoichiometric* alkylation of these complexes showed a correlation between the bite angle and the regioselectivity. The complexes were present as syn / anti-mixtures, which complicated interpretation of the data. Moreover, apart from the C1 to C3 selectivity, the regioselectivity of the *catalytic* reaction was also determined by the competition between syn-anti isomerization and alkylation, which obscured structure-selectivity relations.

The syn-anti isomerization of the allyl moiety involves a $\eta^1-\eta^1-\eta^3$ rearrangement during which the allyl moiety is temporarily $\sigma$-bonded to the palladium via the substituted terminal allylic carbon atom (see figure 2).[^7] Rotation about the Pd-C $\sigma$-bond and the adjacent C-C bond, followed by $\eta^1-\eta^3$ rearrangement then yields the other (syn or anti) isomer. As a result of increased steric hindrance, this process will be slower when the substituent is larger. In order to explore the influence of the size of the allyl-substituent on the regioselectivity, we have also performed the reaction with methyl-, ethyl- and propyl-substituted allylic substrates. By using $(Z)$ and $(E)$-pent-2-enyl acetate as substrates instead of $(E)$-but-2-enylacetate, we will show that a small change in steric size already results in a relatively slow syn-anti isomerization rate (see below). This way, we have been able to study the effects of the ligands on the alkylation of the transient syn and anti isomeric complexes.

[^7]: Note: The number in the superscript is the citation reference.
5.2 Results

All experiments were carried out with cationic (crotyl)Pd(ligand) complexes as catalyst precursors using four ligands, that differ significantly in the calculated bite angle (dppe, dppb, DPEphos and Sixantphos, see figure 3).

![Figure 3: The ligands (°: the bite angle has been determined by pm3(tm) geometry optimization of the cationic (crotyl)Pd(ligand) complexes that have been employed in the catalytic experiments (chapter 4)).](image)

5.2.1 (Z) and (E) allylic substrates

To study the effect of the double bond geometry of the substrate we performed the allylic alkylation of (Z) and (E) pent-2-enylacetate with sodium diethyl 2-methylmalonate as the nucleophile (table 1). Starting from the (E) substrate primarily the linear (E) product is formed. When the bite angle of the ligand is larger, the regioselectivity for the formation of this product increases. In contrast, the (Z) substrate reacts to form both the linear (Z) and the branched product. In this case, a larger bite angle of the ligand results in an increase of the regioselectivity to the branched product. Using dppe, the reaction rate is low compared to the other
ligands and remarkably, the linear \((E)\) product is formed in high regioselectivity, even starting from the \((Z)\) substrate.

The fastest reactions are observed using the relatively flexible ligands dppe and DPEphos. For all ligands, the alkylation of the \((Z)\) allylic substrate proceeds at a lower rate than that of the \((E)\) allylic substrate. Because a less-coordinating counterion may decrease the rate of syn-anti isomerization, we have also briefly studied the alkylation of the analogous trifluoro-acetate substrates. The alkylation reaction proceeded about 5 times faster, but the observed regioselectivities were similar to those using acetate as the leaving group.

Table 1: Alkylation of \((Z)\)- and \((E)\)-pent-2-enyl acetate

<table>
<thead>
<tr>
<th>substrate geometry</th>
<th>complex (ligand)</th>
<th>(\text{TOF}_{\text{mol}}^\text{a}) (mol/mol/h)</th>
<th>% branched(^b)</th>
<th>% linear (E^b)</th>
<th>% linear (Z^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(E)</td>
<td>dppe</td>
<td>2100</td>
<td>1.9</td>
<td>94.2</td>
<td>3.9</td>
</tr>
<tr>
<td>(E)</td>
<td>dppe</td>
<td>7200</td>
<td>1.4</td>
<td>96.9</td>
<td>1.7</td>
</tr>
<tr>
<td>(E)</td>
<td>DPEphos</td>
<td>16900</td>
<td>1.1</td>
<td>98.1</td>
<td>0.8</td>
</tr>
<tr>
<td>(E)</td>
<td>Sixantphos</td>
<td>5500</td>
<td>1.0</td>
<td>98.3</td>
<td>0.6</td>
</tr>
<tr>
<td>(Z)</td>
<td>dppe</td>
<td>160</td>
<td>3.1</td>
<td>86.4</td>
<td>10.5</td>
</tr>
<tr>
<td>(Z)</td>
<td>dppe</td>
<td>1400</td>
<td>15.6</td>
<td>7.3</td>
<td>77.1</td>
</tr>
<tr>
<td>(Z)</td>
<td>DPEphos</td>
<td>3200</td>
<td>26.7</td>
<td>1.1</td>
<td>72.3</td>
</tr>
<tr>
<td>(Z)</td>
<td>Sixantphos</td>
<td>950</td>
<td>47.5</td>
<td>0.8</td>
<td>51.7</td>
</tr>
</tbody>
</table>

\(a\): determined after 2 minutes reaction time  
\(b\): determined after complete conversion  

The reaction conditions are described in the experimental section.

5.2.2 Competition experiments

To gain more insight in the different courses the reaction takes for the \((E)\) and \((Z)\) pent-2-enyl acetate, competition experiments were carried out using the ligands dppe and Sixantphos (table 2). It was found, that in the separate experiments the alkylation of the \((Z)\) substrate is much slower than that of the \((E)\) substrate. Using dppe in the competition experiments, however, a much smaller difference in conversion rate is observed between the \((E)\) and \((Z)\) substrates. Furthermore, when Sixantphos is used as the ligand, the \((Z)\) substrate is consumed at a higher rate than the \((E)\) substrate. The initially predominating consumption of the \((Z)\) substrate results in the formation of primarily the linear \((Z)\) and the branched product. The regioselectivity of the reaction is dependent on the conversion and, as the reaction proceeds, the fraction of linear \((E)\) product increases.
Table 2: Competition experiment using \( E \) and \( Z \) pent-2-enyl acetate.

<table>
<thead>
<tr>
<th>complex (ligand)</th>
<th>time (minutes)</th>
<th>% ( Z ) substrate(^a)</th>
<th>% ( E ) substrate(^a)</th>
<th>% branched(^b)</th>
<th>% linear ( E )(^b)</th>
<th>% linear ( Z )(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>dppb</td>
<td>2</td>
<td>5</td>
<td>11</td>
<td>7</td>
<td>40</td>
<td>53</td>
</tr>
<tr>
<td>dppb</td>
<td>5</td>
<td>12</td>
<td>16</td>
<td>9</td>
<td>43</td>
<td>48</td>
</tr>
<tr>
<td>dppb</td>
<td>10</td>
<td>28</td>
<td>33</td>
<td>9</td>
<td>43</td>
<td>48</td>
</tr>
<tr>
<td>dppb</td>
<td>30</td>
<td>56</td>
<td>58</td>
<td>9</td>
<td>47</td>
<td>44</td>
</tr>
<tr>
<td>dppb</td>
<td>60</td>
<td>75</td>
<td>77</td>
<td>9</td>
<td>48</td>
<td>43</td>
</tr>
<tr>
<td>dppb</td>
<td>180</td>
<td>88</td>
<td>92</td>
<td>9</td>
<td>50</td>
<td>41</td>
</tr>
<tr>
<td>Sixantphos</td>
<td>2</td>
<td>12</td>
<td>8</td>
<td>36</td>
<td>23</td>
<td>41</td>
</tr>
<tr>
<td>Sixantphos</td>
<td>5</td>
<td>36</td>
<td>21</td>
<td>35</td>
<td>26</td>
<td>39</td>
</tr>
<tr>
<td>Sixantphos</td>
<td>10</td>
<td>65</td>
<td>38</td>
<td>34</td>
<td>29</td>
<td>37</td>
</tr>
<tr>
<td>Sixantphos</td>
<td>30</td>
<td>95</td>
<td>82</td>
<td>28</td>
<td>42</td>
<td>30</td>
</tr>
<tr>
<td>Sixantphos</td>
<td>60</td>
<td>100</td>
<td>98</td>
<td>25</td>
<td>48</td>
<td>27</td>
</tr>
<tr>
<td>Sixantphos</td>
<td>180</td>
<td>100</td>
<td>100</td>
<td>24</td>
<td>50</td>
<td>26</td>
</tr>
</tbody>
</table>

\( a \): percentage of substrate consumed

\( b \): regioselectivity, percentage of total yield

The reaction conditions are described in the experimental section.

5.2.3 Influence of the size of the allyl substituent

The results using \( (E) \)-pent-2-enyl acetate show a different regioselectivity than previously found for \( (E) \)-but-2-enyl acetate (chapter 4). The results of the allylic alkylation of \( (E) \) substituted allylic substrates bearing substituents of different size (methyl, ethyl, and propyl) are compared in table 3. In all cases, there is a preference for the formation of the linear \( (E) \) product. The selectivity to the formation of the \( (E) \)-product increases when ligands with a larger bite angle are used. As expected, the regioselectivity is also influenced by the size of the substituent. The selectivity increases when the substituent is larger, leading to 99.3\% linear \( (E) \) product in the alkylation of \( (E) \) hex-2-enylacetate \((R=\) propyl\) by a Sixantphos ligated palladium complex. The size of the substituent also has a pronounced effect on the rate of the reaction: the larger the substituent, the slower the reaction.
P-P ligands, E- and Z-substrates.

Table 3: Alkylation of various E substituted allylic acetates (but-2-enyl acetate, pent-2-enyl acetate, hex-2-enyl acetate)

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Complex (ligand)</th>
<th>TOF&lt;sub&gt;im&lt;/sub&gt;&lt;sup&gt;a&lt;/sup&gt; (mol/mol/h)</th>
<th>% branched&lt;sup&gt;b&lt;/sup&gt;</th>
<th>% linear E&lt;sup&gt;b&lt;/sup&gt;</th>
<th>% linear Z&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>butenyl</td>
<td>dppe</td>
<td>2000</td>
<td>20.0</td>
<td>68.8</td>
<td>11.1</td>
</tr>
<tr>
<td>butenyl</td>
<td>dppb</td>
<td>8900</td>
<td>17.9</td>
<td>79.0</td>
<td>3.1</td>
</tr>
<tr>
<td>butenyl</td>
<td>DPEphos</td>
<td>8700</td>
<td>17.4</td>
<td>80.1</td>
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</table>

a: determined after 2 minutes reaction time
b: determined after complete conversion

The reaction conditions are described in the experimental section.

5.3 Discussion

Several studies have been devoted to the origin of regioselectivity in the palladium catalyzed allylic alkylation. Two different effects have been reported. 1) It was stated, that in the case of an early transition state, the regioselectivity is determined by the relative electrophilicity of the terminal allylic carbon atoms and the steric hindrance is of minor importance. In chapter 4 we also showed the importance of steric interactions during the approach of the nucleophile. 2) In the case of a late transition state, the steric hindrance becomes important that is encountered during the nucleophilic attack and the subsequent rotation of the allyl moiety. The route to the formation of the linear product is then favored over that of the branched product.

From theoretical and experimental studies it is known that the allylic alkylation reaction proceeds via attack of the nucleophile on the cationic (η<sup>3</sup>-allyl)Pd(ligand) species (figure 4). This results in the formation of a single bond between the attacked allylic carbon atom and the nucleophile (stage a). A C=C double bond is formed between the other two allylic carbon atoms (stage b). During these processes, the allyl moiety rotates, forming a transient neutral (olefin)Pd(P-P) complex (stage b).
In a recent theoretical study, a combined explanation is presented for the apparent occurrence of either an early or a late transition state.\textsuperscript{[10c]} The nucleophilic attack at the most electrophilic terminal allylic carbon atom (early transition state) results in a lowering of the energy barrier of stage b of the reaction.

### 5.3.1 Influence of the alkene geometry

The alkylation of (E) pent-2-enylacetate does not yield more than 4% of the linear (Z) product and 2% of the branched product (table 1), thus giving almost complete retention of alkene geometry. The linear (E) product can only be formed from the syn isomer (see figure 1) indicating that for each of the tested palladium(ligand) complexes, oxidative addition of the (E) substrate yields mainly the syn isomer. Analogously, the results obtained for (Z) pent-2-enylacetate (table 1) indicate that after its oxidative addition to palladium, the anti isomer is formed, which then reacts to form the linear (Z) product. However, reaction of the (Z) substrate leads to the formation of a relatively large amount of the linear (E) product. These mixtures of products can only be formed after isomerization from anti to syn (or vice versa) has occurred. Thus, the regioselectivity is a result of (1) the syn / anti equilibrium, (2) the competition between isomerization and alkylation and (3) the C1 to C3 regioselectivity for attack on the syn and the anti isomer.\textsuperscript{[5a]}

Concerning (1) the syn / anti ratio, we have shown before that for cationic (crotyl)Pd(ligand) complexes (ligand = dppe, dpbb, DPEphos and Sixanthphos), the syn isomer is more stable than the anti isomer (chapter 4). The crotyl substrate yields an allyl group with a relatively small methyl substituent. After oxidative addition of a pentenyl substrate, an allyl moiety bearing a larger ethyl group (syn or anti) is formed which will show more steric interaction of both the syn and the anti isomer with the ligand. The data obtained from
the catalytic experiments (table 1) indicate that the relatively small difference in size between a methyl and an ethyl substituent has a large effect on the syn/anti ratio of the transient allyl complexes. Because the results indicate that the anti-to-syn isomerization prevails over the syn-to-anti isomerization (table 1), it is concluded, that for larger substituents on the allyl group, the preferred syn/anti ratio is higher than that previously observed for the methyl substituent.

The occurrence of (2) a competition between syn-anti isomerization and alkylation is supported by the concurrence of a low reaction rate and a low regioselectivity. Thus, the alkylation of the (Z) substrate occurs at a lower rate than that of the (E) substrate, allowing anti-to-syn isomerization to take place prior to nucleophilic attack, which lowers the overall regioselectivity. Especially for dppe the rate of isomerization is fast relative to the rate of alkylation; the reaction of the (Z) substrate leads almost exclusively to the formation of (E) product.

The effect of the bite angle on the C1 to C3 regioselectivity of the alkylation is different for the syn and the anti isomer (3). The selectivity of the syn isomer to the formation of the linear (E) product increases when the bite angle is larger. This can be explained in terms of steric hindrance during both stage a and b of the reaction. The linear C1 position is more accessible for the approaching nucleophile than the branched C3 position. Furthermore, during the bond formation, the substituent has to bend away from the nucleophile in the direction of the sterically crowded Pd(ligand) fragment. The nucleophilic attack on the allyl moiety results in the formation of a transient palladium-olefin complex, \([9c]\), in which the C=C double bond is located in the P-Pd-P plane and the malonate-substituted C3 atom below this plane (see figure 4). When the branched product has been formed, the substituted C3 site, bearing the ethyl group and the malonate, is rotated out of the P-Pd-P plane (stage b). In a syn substituted allyl moiety, the ethyl group points in the direction of the phenyl rings of the ligand. The steric interactions, thus encountered, are more pronounced when the bite angle of the ligand is larger. So, during both stage a and b of the reaction, steric hindrance directs the regioselectivity to the formation of the linear (E) product.

In contrast, the effect of the bite angle on the regioselectivity of the alkylation of the anti isomer shows the opposite trend. It is known, that in palladium complexes of disubstituted allylic substrates, the branched anti-position is relatively electrophilic and consequently more reactive than the branched syn-position.\([5b]\). The geometrical distortion resulting from steric interactions with the ligand, are relatively large for the anti compared to the syn isomer. An increase of the bite angle will enhance the geometrical distortion of the allyl moiety and thereby\([2c, 10c]\) enhance the relative electrophilicity of the allylic carbon atom at the branched C3 position compared to the C1 position. Thus during the approach of the nucleophile, stage a of the reaction, the electronic effects may prevail over the steric hindrance giving the branched product. During the rotation of the allyl moiety after the nucleophilic attack has taken place, stage b, the ethyl group of the anti isomer will point downward, i.e. not in the direction of the phenyl rings of the ligand and steric hindrance will be less than in the case of the syn isomer (stage b). So also for the anti isomer, in both stage a and b of the reaction, the regioselectivity is directed to the formation of the same regio-isomer, i.e. the branched product, whereas for the syn isomer in both stages the linear (E) product is favored.

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The competition experiments, carried out to gain more mechanistic insight in the reaction course of the (E) and the (Z) substrate, showed a relatively high reaction rate for the latter. Because the overall reaction rate in the separate experiments is higher for the (E) substrate than for the (Z) substrate, the discrimination in the competition experiments has to take place in an early stage of the catalytic cycle of the reaction. As a result of the better accessibility of the (Z) double bond compared to the (E) double bond, the coordination of the substrate to palladium will be faster for the (Z) than for the (E) substrate. Because in the separate experiments the (E) substrate is found to react faster, we conclude that the next steps of the reaction proceed at a higher rate for the (E) substrate than for the (Z) substrate (figure 5).

Figure 5: Schematic representation of the origin of kinetic resolution (the size of the arrows indicates the relative rate).

The change in rate difference in the competition experiments compared to the separate experiments is larger for Sixantphos, the ligand with the larger bite angle (table 2). Upon coordination of the substrate to a Pd\(^0\) (Sixantphos) complex, the steric hindrance will be larger than for the analogous complex with the dppb ligand and therefore the discrimination between the (E) and (Z) substrate will be more pronounced for Sixantphos. Possibly, for dppb the substrate discrimination does take place in this stage, but its effect may be compensated by a rate difference in the next steps of the reaction.

It can be argued, that the discriminating step, coordination of the olefin, is not the rate determining step of the reaction. If the coordination of the (E) substrate would be rate limiting and thus slower than the coordination of the (Z) substrate, the (E) substrate would not react faster in the separate experiments. Analogously, if the coordination to palladium would be the rate determining step for the (Z) substrate, it would not be found to react faster in the competition experiments.
On the other hand, if the rate determining step for the $E$ substrate is indeed the substrate coordination and for the $Z$ substrate, the subsequent oxidative addition would be rate determining and the latter being slower than the substrate coordination of the $(E)$ substrate, the above argumentations are not true. Unfortunately, the coordination of the substrate and the subsequent oxidative addition can not be distinguished in kinetic experiments.

5.3.3 Effect of the size of the substituent

The alkylation of the $(E)$ substrates with different substituents all show the same trend (table 3). Both a larger bite angle of the ligand and a larger substituent on the allyl moiety result in an increase of the regioselectivity to the formation of the linear $(E)$ product. As has been described above, the syn / anti isomer ratio will be lower for small groups, which accounts for the relatively large amount of linear $(Z)$ product formed from alkylation of $(E)$ but-2-enylacetate.

Furthermore, the relatively large size of the ethyl and propyl groups, as compared to the methyl group, hinders the attack of the nucleophile on the branched position. This explains the smaller amounts of branched product formed, when either the substituent or the bite angle of the ligand is larger.

Also the rate of the reaction is affected by the size of the substituent. The lower rate of reaction when larger substrates are used can be explained in terms of steric hindrance. During the oxidative addition and the nucleophilic attack, a larger allylic substrate will experience more steric hindrance than a small allylic substrate and the reaction may therefore proceed at a lower rate. The product dissociation will probably not be rate limiting but nevertheless, the coordination of a larger product will be more hindered than that of a small one and therefore it may dissociate faster than a small product. Which of these effects prevails, depends on the nature of the rate limiting step of the reaction, which may be determined by the size and orientation of the substituent and the bite angle of the ligand.

In the absence of significant steric interactions, a larger bite angle of the ligand results in an increase of the rate of reaction. Thus, the alkylation of $(E)$ but-2-enylacetate occurs at the highest rate when the Sixantphos ligand is used. The rate of alkylation of the larger substrates is the highest for catalysts bearing a flexible ligand favoring a relatively large bite angle, such as dpbb or DPEphos.
Chapter 5

5.4 Conclusion

We separated the effect of the bite angle on the regioselectivity resulting from on the one hand the syn and on the other hand the anti isomeric complex. The regioselectivity of the reaction of the syn isomer is determined by steric effects in both the first and the second stage of the reaction, resulting in almost exclusive formation of the linear \((E)\)-product. The geometry of the allyl moiety in the anti isomer is presumably distorted to a large extent and the electrophilicity of the branched position is enhanced compared to the linear position. The regioselectivity of its alkylation is in the first stage of the reaction mainly governed by electronic factors and in the second stage by steric effects. For syn complexes of ligands with a large bite angle, both in the first and the second stage of the reaction, the linear product is favored, whereas for the anti isomer, in both stages of the reaction, the branched product becomes the favored regio-isomer.

In competition experiments between the \((E)\) and \((Z)\) substrates, the \((Z)\) substrate is found to react at a rate that is similar or faster than that of the \((E)\) substrate, whereas in separate experiments, the reaction with the \((E)\) substrate is faster. This effect is more pronounced for Sixantphos than for dppb. The substrate-discrimination presumably takes place in the stage of coordination of the olefin to the metal center, prior to oxidative addition and prior to the rate determining step. Therefore, in a system in which both the \((E)\) and \((Z)\) substrate are present, the latter dominates the reaction rate.

5.5 Experimental section

\(^1\)H NMR (300 MHz, TMS, CDCl\(_3\)), \(^{31}\)P \(^1\)H) (121.5 MHz external 85\% H\(_3\)PO\(_4\), CDCl\(_3\)), \(^1\)C NMR (75.4 MHz, TMS, CDCl\(_3\)) were recorded on a Bruker AMX-300 spectrometer. The product distribution of the alkylation experiments was measured on a Interscience Mega2 GC apparatus, equipped with a DB1 column, length 30 m, inner diameter 0.32 mm, film thickness 3.0 \(\mu\)m, and a F.I.D. detector.

All experiments were carried out using standard Schlenk techniques. All solvents and allylic substrates were freshly distilled prior to use. Diethyl 2-methylmalonate, NaH, and E-hex-2-enyl acetate were obtained from Aldrich.

5.5.1 General synthetic procedures

**Sodium diethyl 2-methylmalonate** (0.5 M in THF) was prepared from diethyl 2-methylmalonate (20 mmol, 3.48 g) and NaH (20 mmol, 0.48 g) in THF at 273 K. The synthesis and characterisation of the complexes (chapter 4), crotyl acetate (chapter 4) and the alkylation products of the coupling of crotyl acetate and E-hex-2-enyl acetate to sodium diethyl 2-methylmalonate are described elsewhere.\(^{54b}\)
5.5.2 Alkylation reactions

The catalytic reactions were performed at 292 K in THF (5 mL), using 0.05 mol% of catalyst (0.25 μmole), 0.5 mmole of substrate (0.064 g) and 1.0 mmole of sodium diethyl 2-methylmalonate (0.20 g). All reagents were added from stock solutions. The reaction was monitored by taking samples from the reaction mixture which, after aqueous work up, were analyzed by GC using decane (0.0142 g) as the internal standard.

5.5.3 Characterization

NMR-data were obtained in CDCl₃ (δ in ppm).

Diethyl 2-methyl-[(2E)-pent-2-en-4-yl]malonate (linear E):

\[ \text{H: 0.90 (t, 3H, } ^3J = 7.3 \text{ Hz (CH}_3\text{-CH}_2\text{-CH=)}) \]; 1.22 (t, 6H, \( ^3J = 7.0 \text{ Hz (O-CH}_2\text{-CH}_3\text{)}) \); 1.32 (s, 3H (C_quaternary-CH3)); 2.00 (m, 2H (CH3-CH2-CH=)); 2.50 (d, 2H, \( ^3J = 6.9 \text{ Hz (C_quaternary-CH2-CH=)}) \); 4.12 (q, 4H, \( ^3J = 7.0 \text{ Hz (O-CH}_2\text{-CH}_3\text{)}) \); 5.25 (m, 1H, olefinic H); 5.50 (m, 1H, olefinic H)

\[ ^{13}\text{C} \left( ^1\text{H} \right): \text{14.1 (CH}_3\text{-CH}_2\text{-CH=); 14.5 (O-CH}_2\text{-CH}_3\text{); 20.1 (C_quaternary-CH}_3\text{); 26.0 (CH}_3\text{-CH}_2\text{-CH=); 39.2 (C_quaternary-CH}_2\text{-CH=); 54.3 (C_quaternary-CH}_3\text{); 61.5 (O-CH}_2\text{-CH}_3\text{); 123.1 (CH}_3\text{-CH}_2\text{-CH=); 137.4 (CH}_3\text{-CH}_2\text{-CH=)}) \]; 172.5 (C=O)

Diethyl 2-methyl-[(2Z)-pent-2-en-4-yl]malonate (linear Z):

\[ \text{H: 0.90 (t, 3H, } ^3J = 7.5 \text{ Hz (CH}_3\text{-CH}_2\text{-CH=)}) \]; 1.20 (t, 6H, \( ^3J = 7.0 \text{ Hz (O-CH}_2\text{-CH}_3\text{)}) \); 1.33 (s, 3H (C_quaternary-CH3)); 2.05 (m, 2H (CH3-CH2-CH=)); 2.56 (d, 2H, \( ^3J = 7.5 \text{ Hz (C_quaternary-CH2-CH=)}) \); 4.12 (q, 4H, \( ^3J = 7.0 \text{ Hz (O-CH}_2\text{-CH}_3\text{)}) \); 5.15 (m, 1H (CH1-CH2-CH=CH-)); 5.45 (m, 1H (CH3-CH2-CH=CH-))

\[ ^{13}\text{C} \left( ^1\text{H} \right): \text{13.9 (CH}_3\text{-CH}_2\text{-CH=); 14.4 (O-CH}_2\text{-CH}_3\text{); 17.4 (C_quaternary-CH}_3\text{); 20.0 (CH}_3\text{-CH}_2\text{-CH=); 33.4 (C_quaternary-CH}_2\text{-CH=); 51.3 (C_quaternary-CH}_3\text{); 61.6 (O-CH}_2\text{-CH}_3\text{); 122.7 (CH}_3\text{-CH}_2\text{-CH=); 135.9 (CH}_3\text{-CH}_2\text{-CH=)}) \]; 172.5 (C=O)

3-(Diethyl 2-Methyl [(1E)-pent-1-ene malonate] (branched):

\[ \text{H: 0.82 (t, 3H, } ^3J = 7.5 \text{ Hz (CH}_3\text{-CH}_2\text{-CH=)}) \]; 1.20 (t, 6H, \( ^3J = 7.0 \text{ Hz (O-CH}_2\text{-CH}_3\text{)}) \); 1.21 (m, 2H (CH3-CH2-CH3)); 1.32 (s, 3H (C_quaternary-CH3)); 3.38 (m, 1H (CH3-CH2-CH3)); 4.12 (q, 4H, \( ^3J = 7.0 \text{ Hz (O-CH}_3\text{-CH}_2\text{-CH=)}) \)); 5.01 (d, 1H, \( ^3J = 16.8 \text{ Hz (E-CH=C(H)H)}) \); 5.05 (d, 1H, \( ^3J = 10.2 \text{ Hz (Z-CH=C(H)H)}) \); 5.6 (m, 1H (-CH=C(H)H))

\[ ^{13}\text{C} \left( ^1\text{H} \right): \text{12.8 (CH}_3\text{-CH}_2\text{-CH=); 14.4 (O-CH}_2\text{-CH}_3\text{); 17.4 (C_quaternary-CH}_3\text{); 21.0 (CH}_3\text{-CH}_2\text{-CH=); 46.5 (CH}_3\text{-CH}_2\text{-CH=); 51.3 (C_quaternary-CH}_3\text{); 61.6 (O-CH}_2\text{-CH}_3\text{); 118.9 (-CH-CH=CH)=); 137.2 (-CH-CH=CH)=); 172.5 (C=O) \]
Chapter 5

5.6 References


Chapter 6

On the influence of the bite angle of bidentate P-N ligands on the regioselectivity of the allylic alkylation of monosubstituted allyl moieties.

In the previous chapters, we studied the effect of the presence of one substituent on the allyl moiety in complexes of bidentate phosphorus ligands. The DFT calculations described in chapter 3 predict, that the use of P-N instead of P-P ligands leads to an enhanced non-symmetry of the Pd(η^3-allyl) bond and consequently in a change in regioselectivity of the allylic alkylation. In this chapter, we study the effect of P-N ligands on a) the structure and reactivity of complexes of mono-substituted allyl moieties and on b) the regioselectivity of the stoichiometric and catalytic allylic alkylation.

Abstract

Two series of new bidentate P-N ligands have been synthesized. Application of these ligands in the palladium catalyzed allylic alkylation of crotyl chloride and cinnamyl chloride leads to the preferential formation of the branched product. A larger bite angle of the ligand leads to a further increase of this regioselectivity. Stoichiometric alkylation of the complex (crotyl)Pd(κ)OTf proceeds with 88% regioselectivity to the branched product.
6.1 Introduction

A tremendous research effort has been devoted to the enantioselective alkylation of symmetrically 1,3-disubstituted allylic substrates, such as 3-acetoxy-1,3-diphenyl-1-propene and cyclohex-2-enyl acetate\textsuperscript{11, 2, 3}, using malonate nucleophiles. In the case of non-symmetrically monosubstituted substrates, e.g. crotyl acetate (but-2-enyl acetate) or cinnamyl acetate (3-phenyl-prop-2-enyl acetate) regiocontrol is a prerequisite for enantiocontrol (figure 1).\textsuperscript{14} Palladium complexes have a preference for the formation of the linear, achiral product.\textsuperscript{51} Excellent regio- and enantioselectivities\textsuperscript{16} have been obtained using metals other than palladium such as iridium\textsuperscript{6a}, rhodium\textsuperscript{6b}, iron\textsuperscript{6c} and tungsten\textsuperscript{4a, ed}.

After the course of our studies, up to 96 % regioselectivity to the formation of the branched, chiral product was obtained for cinnamyl acetate, using a palladium catalyst.\textsuperscript{4b} Very high enantioselectivities have been found using phosphino-oxazoline ligands (Pfaltz\textsuperscript{4a, 4b} Williams\textsuperscript{4e, 4f} and the MAP ligand (Kocovsky\textsuperscript{4c, 4d}). These phosphino-oxazoline ligands contain a soft phosphorus donor atom and a relatively hard nitrogen donor atom. It had been established previously, that the electronic difference between phosphorus and nitrogen is important for the regioselectivity of the reaction.\textsuperscript{1, 4, 7} In the Pd(allyl) complex, the nucleophilic attack takes place at the allylic carbon atom trans to phosphorus.\textsuperscript{1, 4, 7} Although the allyl moiety remains bonded via all three carbon atoms in a covalent manner,\textsuperscript{9} the presence of a substituent on one of the terminal positions distorts its symmetry.\textsuperscript{11b} As described in chapter 3, the allylic carbon-carbon bond next to the substituent (C3-C2) will show more double bond character than the other allylic carbon-carbon bond (C1-C2). The bonding between palladium and the substituted allyl will be distorted to an $\eta^2$-(to C2-C3)-$\eta^1$-(to C1) type complex. Since phosphorus exerts a stronger trans influence than nitrogen, the Pd-allyl bond trans to phosphorus is weakened. As a result, the allylic C-C bond trans to phosphorus has more double bond character. Thus $\eta^1$-(C1-C2) will be found cis to phosphorus and $\eta^2$-(C2-C3) trans to phosphorus. The preference for nucleophilic attack on the allylic carbon atom trans to phosphorus is therefore caused both by steric and electronic effects (see figure 1).

Part of our own work in the field of allylic alkylation\textsuperscript{45} has been concerned with the effect of the bite angle of achiral, symmetric bidentate phosphine ligands on the regioselectivity (chapters 4, 5, 7, 8).\textsuperscript{45a, b} It was found that a larger bite angle of the ligand results in 100% formation of the linear, non chiral product for trans-hex-2-enylacetate. In this chapter we report the remarkable, opposite effect of the bite angle of bidentate P-N ligands on the regioselectivity of the alkylation of non symmetrically substituted allyl moieties. A series of (allyl)palladium complexes bearing new P-N ligands is synthesized and characterized. The exact orientation of the substituent on the allyl group is established by means of NMR spectroscopy. Use of the complexes in the stoichiometric and the catalytic alkylation shows a pronounced effect of the counterion of the cationic (allyl)palladium(ligand) complex.
We have prepared two series of mixed phosphorus-nitrogen ligands. One series of ligands consists of a Ph$_2$PO- unit that is connected to an ortho substituted pyridine moiety via an alkyl chain of variable length (POP$_y$-ligands (a-c); the generic structure is given in figure 2). By changing the length of the alkyl chain, the bite angle of the ligand can be tuned. Another class of ligands (d-g) is based on the same phosphorus unit, with an alkyl group of variable length linked to an imine moiety (see figure 2). At the para position of the imine moiety a substituent was introduced. By changing this substituent, the electronic properties of the ligand can be tuned.

The POP$_y$ type ligands (a-c) were conveniently prepared by coupling Ph$_2$PCl to ortho-pyridine-(CH$_2$)$_n$OH in the presence of NEt$_3$. The P-Im class of ligands (d-g) were synthesized in two steps. The imine was synthesized according to a literature procedure$^{9}$ by condensation of the para-substituted aldehyde with H$_2$N(CH$_2$)$_n$OH ($n = 3, 4$), followed by coupling to Ph$_2$PCl.
### 6.2.2 Synthesis and structures of palladium(allyl)(P-N)X complexes

We have prepared cationic crotyl (E-but-2-enyl, C₄H₇) and cinnamyl (3-phenylprop-2-E-enyl, C₉H₉) palladium complexes of these new ligands by reaction of the appropriate ligand with the [(C₄H₇ or C₉H₉)PdCl]₂ dimer, followed by chloride abstraction with silver triflate. Using these P–N ligands, four isomeric complexes can be formed: the substituent can be oriented either syn or anti with respect to Hd and cis or trans to the phosphorus atom (see figure 3). The value of the coupling constant ($^4J_{P\cdot\text{CH}_3}$) is diagnostic for the orientation of the substituent, enabling elucidation of the structure of the complexes.[⁵⁶] The value of the coupling constant of the syn oriented CH₃ groups with a trans phosphorus atom is around 10-12 Hz ($^4J_{P\cdot\text{CH}_3}$). Both a cis orientation with respect to phosphorus and an anti orientation with respect to Hd would result in a lower value of $^4J_{P\cdot\text{CH}_3}$ (around 6 Hz). When ligand a is used, all four isomers of the (crotyl)Pd(a) complex are formed. The syn-trans-P isomer predominates over the other isomers (> 90%). When the substituent is a phenyl group rather than a methyl group, the amount of syn-trans-P isomer exceeds 97%. The minor isomer (< 3%) could not be identified by NMR. Based on the results of allylic alkylation (see below) we assign the minor signal to the anti-trans-P isomer. These findings are in line with the results of the DFT calculations (chapter 3).

**Figure 2:** Generic structures of two new classes of P-N ligands

**Figure 3:** Possible isomeric structures of cationic (crotyl)Pd(P-N ligand) complexes
It was concluded from $^{31}$P and $^1$H-NMR spectroscopy, that the bite angle of the ligand has an effect on the isomer distribution. Use of the ligands b or c, having a large bite angle, results in almost exclusive formation (> 97 %) of the syn-trans-P isomer of the crotyl and cinnamyl complexes. When the ligand with the smallest bite angle is used (a), only 81 % of the syn-trans-P isomer is formed, with the anti-trans-P complex (14 %) as the other main isomer. The remaining signals (4 % and 1 %) are ascribed to the syn-trans-N and the anti-trans-N isomer.

Figure 4: Variable temperature NMR spectra of cationic (crotyl)Pd(c) a) at 223 K, b) 273 K, c) 328 K, recorded in CDCl$_3$.

In general, the signals in the $^1$H NMR spectra (at 298 K) are relatively broad, which is indicative of a dynamic exchange process. As it is crucial to determine the orientation of the substituent on the allyl moiety, we conducted variable temperature NMR experiments with the cationic (crotyl)Pd(c)-complex. The NMR spectra of the cationic (crotyl)Pd(c) complex at different temperatures are depicted in figure 4. The fast exchange limit is reached at +55°C (c) and at −55°C (a) the slow exchange limit is almost reached.$^{[11]}$ All signals in the fast exchange spectrum decoalesce into two signals when going to lower temperatures. At −55°C, the value of $^4J_{(P,CH)}$ could not be determined exactly, but was approximately the same as in the fast exchange limit.

In order to gain more insight, we have prepared the imine based ligand g, that differs from ligand e only in the nature of the nitrogen donor group. The crotyl complex of ligand g shows the same type of fluxional
behavior as the analogous complex of ligand \( \text{c} \). A low temperature (-25 °C) spectrum recorded for the complex of ligand \( \text{g} \) shows that in the slow exchange regime the methyl groups of both isomers have the same coupling constant \( ^4J_{(P-\text{CH}_3)} = 10.1 \text{ Hz} \). This indicates that both isomers have the methyl group in a \textit{syn} orientation. The spectra of all complexes ligated with the imine type ligands show the presence of two structures. All are identified as \textit{syn-trans-P} complexes.

The value for \( ^4J_{(P-\text{CH}_3)} \) in the fast exchange spectrum of the complex of ligand \( \text{c} \) is the same as in the slow exchange spectrum of the complex of ligand \( \text{g} \) (10.1 Hz). Apart from the value for \( ^4J_{(P-\text{CH}_3)} \), the chemical shift of the \( \text{CH}_3 \) group, for all complexes > 1.3 ppm, is also indicative of a \textit{trans-P} orientation. A \textit{trans-N} orientation of the methyl group would result in a signal at higher field (< 0.6 ppm).

Apart from the splitting of all signals, it can be seen that at +55°C the allylic protons \( \text{H}_a \) and \( \text{H}_b \) are in a fast exchange. At low temperature (-55°C), the one, averaged signal of these two protons is not split in only two, but in four signals, two for each proton. The signals of the \textit{ortho}-pyridine proton are separated from the rest of the signals and were used to obtain rate data by simulation of the spectra\(^{12e,f} \). The Eyring plot shows that the rate of exchange is linearly dependent of the reciprocal temperature: \(- \ln k/T = -33 + 7 \cdot 10^3 / T \). From this it follows that \( \Delta H^\ddagger = 60 \text{ kJ/mole} \) and \( \Delta S^\ddagger = 34 \text{ J/mole.K} \).

### 6.2.3 Stoichiometric alkylation

The results of the stoichiometric alkylation of these complexes with sodium diethyl 2-methylmalonate are presented in table 1 and 2 (see also figure 1). Reaction of the crotyl complex provided mainly the linear \textit{trans} and the branched product. The linear \textit{cis} product is formed in only minor amounts (up to 7 %). When the bridge length and consequently the bite angle of the ligand are larger, the regioselectivity to the branched product of the stoichiometric alkylation increases, up to 79% for ligand \( \text{c} \).

If the substituent on the allyl moiety is a bulkier phenyl rather than a methyl group, only two products are observed: the linear \textit{trans} and the branched product. Again the ligands with a larger bite angle direct the regioselectivity towards the preferential formation of the branched product up to 78% (ligand \( \text{c} \)). There is no significant change in regioselectivity when neutral instead of cationic complexes are used (entry 4).

<table>
<thead>
<tr>
<th>entry</th>
<th>ligand</th>
<th>% branched</th>
<th>% trans</th>
<th>% cis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>( \text{a} )</td>
<td>37.2</td>
<td>56.1</td>
<td>6.7</td>
</tr>
<tr>
<td>2</td>
<td>( \text{b} )</td>
<td>65.6</td>
<td>31.0</td>
<td>3.4</td>
</tr>
<tr>
<td>3</td>
<td>( \text{c} )</td>
<td>79.0</td>
<td>18.2</td>
<td>2.8</td>
</tr>
<tr>
<td>4</td>
<td>( \text{d} )</td>
<td>84.1</td>
<td>14.2</td>
<td>1.7</td>
</tr>
<tr>
<td>5</td>
<td>( \text{e} )</td>
<td>88.0</td>
<td>10.9</td>
<td>1.1</td>
</tr>
<tr>
<td>6</td>
<td>( \text{f} )</td>
<td>79.8</td>
<td>17.9</td>
<td>2.3</td>
</tr>
</tbody>
</table>

Experimental details: see experimental section.
Table 2: Stoichiometric alkylation of (cinnamyl)Pd(P-N)OTf complexes.

<table>
<thead>
<tr>
<th>entry</th>
<th>ligand</th>
<th>% branched</th>
<th>% trans</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>a</td>
<td>43.7</td>
<td>56.3</td>
</tr>
<tr>
<td>2</td>
<td>b</td>
<td>67.5</td>
<td>32.5</td>
</tr>
<tr>
<td>3</td>
<td>c</td>
<td>77.8</td>
<td>22.2</td>
</tr>
<tr>
<td>4</td>
<td>d</td>
<td>75.3</td>
<td>24.7</td>
</tr>
<tr>
<td>5</td>
<td>e</td>
<td>78.4</td>
<td>21.6</td>
</tr>
<tr>
<td>6</td>
<td>f</td>
<td>81.8</td>
<td>18.2</td>
</tr>
</tbody>
</table>

Experimental details: see experimental section.

Tables 1 (crotyl) and 2 (cinnamyl) show that the regioselectivity of stoichiometric alkylation of the complexes ligated with imine based ligands (d-f) is similar to that obtained using the pyridine based ligands (a-c). For the crotyl complexes, the highest regioselectivity is found for methoxy substituted ligand e, which gives 88% of the branched product, whereas for cinnamyl complexes, the highest regioselectivity (82%) is found using the fluoro substituted ligand f.

**6.2.4 Catalytic alkylation and kinetics**

We have studied the catalytic alkylation of crotyl chloride (trans-but-2-enyl chloride) and cinnamyl chloride (trans-3-phenyl-prop-2-enyl chloride) using the corresponding Pd(allyl) complex as the catalyst. Also in the catalytic reactions, the regioselectivity for the branched product increases when the bite angle of the pyridine based ligands is larger (entries 1-3). The branched / linear ratio obtained in the catalytic reactions, however, is lower than that found for the stoichiometric reactions.

Table 3: Catalytic alkylation of crotyl chloride. Experimental details: see experimental section.

<table>
<thead>
<tr>
<th>entry</th>
<th>complex</th>
<th>TOF&lt;sub&gt;rn&lt;/sub&gt;</th>
<th>% branched **</th>
<th>% trans **</th>
<th>% cis **</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>a</td>
<td>1000</td>
<td>33.3</td>
<td>58.6</td>
<td>8.1</td>
</tr>
<tr>
<td>2</td>
<td>b</td>
<td>200</td>
<td>41.7</td>
<td>49.6</td>
<td>8.7</td>
</tr>
<tr>
<td>3</td>
<td>c</td>
<td>1000</td>
<td>55.1</td>
<td>37.8</td>
<td>7.1</td>
</tr>
<tr>
<td>4</td>
<td>d</td>
<td>900</td>
<td>52.3</td>
<td>39.0</td>
<td>8.7</td>
</tr>
<tr>
<td>5</td>
<td>e</td>
<td>300</td>
<td>50</td>
<td>41</td>
<td>9</td>
</tr>
<tr>
<td>6</td>
<td>f</td>
<td>200</td>
<td>33</td>
<td>57</td>
<td>10</td>
</tr>
</tbody>
</table>

*: determined after 5 minutes, in mole/mole/h.

**: determined after complete conversion
Table 4: Catalytic alkylation of cinnamyl chloride. Experimental details: see experimental section.

<table>
<thead>
<tr>
<th>entry</th>
<th>complex</th>
<th>TOF\textsubscript{in} *</th>
<th>% branched **</th>
<th>% trans **</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>a</td>
<td>2700</td>
<td>29.4</td>
<td>70.6</td>
</tr>
<tr>
<td>2</td>
<td>b</td>
<td>1700</td>
<td>26.7</td>
<td>73.3</td>
</tr>
<tr>
<td>3</td>
<td>c</td>
<td>2800</td>
<td>56.9</td>
<td>43.1</td>
</tr>
<tr>
<td>4</td>
<td>d</td>
<td>7300</td>
<td>22.5</td>
<td>77.5</td>
</tr>
<tr>
<td>5</td>
<td>e</td>
<td>3000</td>
<td>31.5</td>
<td>68.5</td>
</tr>
<tr>
<td>6</td>
<td>f</td>
<td>3500</td>
<td>13</td>
<td>87</td>
</tr>
</tbody>
</table>

*: determined after 5 minutes, in mole/mole/h.

**: determined after complete conversion

The alkylation of allylic acetates compared to chlorides, resulted in a significant decrease of the regioselectivity towards the branched product: from 56.9% for crotyl chloride to 24.5% for crotyl acetate (see table 5). Addition of extra halide (LiBr) to the reaction mixture containing crotyl acetate restored the regioselectivity to a value of 50.4%.

Table 5: Regioselectivity in the catalytic alkylation of crotyl acetate\[a]\[b]

<table>
<thead>
<tr>
<th>entry</th>
<th>complex</th>
<th>% branched</th>
<th>% trans</th>
<th>% cis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>a (1)</td>
<td>29.6</td>
<td>62.3</td>
<td>8.0</td>
</tr>
<tr>
<td>2</td>
<td>a (3)</td>
<td>29.2</td>
<td>63.1</td>
<td>7.7</td>
</tr>
<tr>
<td>3</td>
<td>a (4)</td>
<td>24.5</td>
<td>68.3</td>
<td>7.2</td>
</tr>
<tr>
<td>4</td>
<td>b (1)</td>
<td>24.5</td>
<td>64.6</td>
<td>10.9</td>
</tr>
<tr>
<td>5</td>
<td>b (1)</td>
<td>50.4</td>
<td>44.0</td>
<td>5.6</td>
</tr>
<tr>
<td>6</td>
<td>b (1.5)</td>
<td>19.3</td>
<td>77.5</td>
<td>3.2</td>
</tr>
<tr>
<td>7</td>
<td>b (2)</td>
<td>13.9</td>
<td>84.1</td>
<td>2.0</td>
</tr>
<tr>
<td>8</td>
<td>c (1)</td>
<td>29.1</td>
<td>59.6</td>
<td>11.3</td>
</tr>
</tbody>
</table>

[a]: after 24 hours quantitative conversion was reached. Initial reaction rates were not determined
[b]: extra ligand was added from a stock solution to the isolated complex.
Table 6: Regioselectivity in the catalytic alkylation of cinnamyl acetate

<table>
<thead>
<tr>
<th>entry</th>
<th>complex (ligand/Pd)</th>
<th>% branched</th>
<th>% trans</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>a (1)</td>
<td>33.0</td>
<td>67.0</td>
</tr>
<tr>
<td>2</td>
<td>a (2)</td>
<td>22.4</td>
<td>77.6</td>
</tr>
<tr>
<td>3</td>
<td>a (3)</td>
<td>22.3</td>
<td>77.7</td>
</tr>
<tr>
<td>4</td>
<td>a (4)</td>
<td>5.9</td>
<td>94.1</td>
</tr>
<tr>
<td>5</td>
<td>b (1)</td>
<td>21.5</td>
<td>78.5</td>
</tr>
<tr>
<td>6</td>
<td>b (2)</td>
<td>7.7</td>
<td>92.3</td>
</tr>
<tr>
<td>7</td>
<td>b (3)</td>
<td>5.9</td>
<td>94.4</td>
</tr>
<tr>
<td>8</td>
<td>c (1)</td>
<td>39.1</td>
<td>60.9</td>
</tr>
<tr>
<td>9</td>
<td>dppe</td>
<td>4.7</td>
<td>95.3</td>
</tr>
</tbody>
</table>

[a]: after 24 hours quantitative conversion was reached. Initial reaction rates were not determined
[b]: extra ligand was added from a stock solution to the isolated complex
[c]: 1,2-bis-diphenylphosphino-ethane

When extra ligand was added to the isolated complexes, a sharp decrease in regioselectivity was observed (tables 5 and 6). The addition of two extra equivalents of ligand b resulted in the formation of only 6% of the branched product (entry 7, table 6). The effect is more pronounced for the ligand having the longer bridge length (ligand b versus a). This product distribution is similar to that obtained with the bidentate phosphine ligand dppe (entry 9, table 6).

Kinetic experiments on the catalytic alkylation of cinnamyl chloride using the ligand c were performed by variation of the concentrations of palladium, diethyl 2-methylmalonate and cinnamyl chloride. The reactions were monitored with GC. The alkylation reaction proceeds with a zero order dependency in the concentration of cinnamyl chloride, and a first order dependency in both the malonate anion and the palladium complex.

6.3 Discussion

6.3.1 Structures of the complexes

The $^1$H-NMR spectra showed that all complexes exhibit dynamic behavior at room temperature. Variable temperature NMR spectroscopy of the complex bearing ligand c showed that the observed exchange process does not involve an exchange of the syn-trans-P and one of the other isomers of the types syn-trans-N, anti-trans-P or anti-trans-N. Surprisingly, the two different isomers that were observed under the slow exchange
Chapter 6

conditions are both identified as a syn-trans-P isomer. The two isomers are proposed to be conformers differing in the orientation of the ligand backbone, which can be either up (endo) or down (exo) with respect to the orientation of the allyl moiety.

The protons Ha and Hb (see figure 1) are in fast exchange at +55°C, via the η³-η¹-η³-rearrangement\(^{[12]}\) of the allyl moiety. At +55°C, one averaged signal is observed for Ha and Hb. This one signal is split in two signals for each proton at -55°C. The fluxional behavior is thus caused by a selective η³-η¹-η³ isomerization, during which the Pd-allyl bond trans to phosphorus is broken. The syn-trans-P structure is retained during this rearrangement, but the orientation has changed from endo to exo or vice versa (see figure 5). Thus, the dynamic exchange between the endo and the exo form of the complex is a result of the η³-η¹-η³ rearrangement of the allyl moiety and not of other processes such as flopping of the backbone.

The partial decooordination of the allylic moiety during this process accounts for the observed positive \(\Delta S^+\) value. The value of the activation parameters \(\Delta H^+\) and \(\Delta S^+\) corresponds to literature values for the η³-η¹-η³ rearrangement.\(^{[12e]}\)

![Figure 5: Dynamic exchange of endo and exo isomers in cationic (crotyl)Pd(P-N) complexes via η³-η¹-η³ rearrangement](image)

6.3.2 Stoichiometric alkylation

As expected, the syn-trans-P isomeric form of the cationic (crotyl or cinnamyl)Pd(P-N ligand) complexes is the main isomer present in solution. The NMR spectra show that for a small methyl substituent, there is 3% of the anti-trans-P isomer present. The study of the dynamic behavior shows that there is no isomerization from the syn to the anti isomer on the NMR time scale. The 3% linear cis product that is found (table 1) corresponds with the 3% anti-trans-P isomer that is present. When the substituent is a larger phenyl group, only the syn-trans-P isomer is observed. This is also reflected in the absence of the linear cis product in the alkylation reactions (table 2). VT-NMR experiments show that the cationic complexes do not interconvert between the different isomers.

The regioselectivities found for the stoichiometric reactions therefore indicate that the nucleophilic attack takes place trans to the phosphorus atom, having a larger trans influence. This observation is in agreement with the early transition state model and with recent modeling studies: the regioselectivity for the branched product is higher, when the non-symmetry of the allyl moiety is enhanced.\(^{[15]}\) Substitution of the imine at the
P-N ligands, crotyl and cinnamyl substrates.

Para position with an electron donating group, such as a methoxy (e) or a dimethylamino (d) group, will increase the non-symmetry of the allyl. The results in table 1 and 2 show that this is indeed the case, both for bridge length 3 and 4. The regioselectivity towards the branched product can be increased to a value of 88% for the methoxy substituted ligand (e).

The regioselectivity for the branched product increases when going from a small bite angle (ligand a) to a larger bite angle (ligand e). This is observed both for the crotyl and the cinnamyl complexes. The regioselectivities obtained using P-N type ligands, may therefore be related to the non-symmetry of the allyl moiety. The substituted allylic carbon atom C3 is more electrophilic than C1 and becomes even more electrophilic when the bite angle is larger. This explanation is in line with the results of our DFT calculations (chapter 3).

For cinnamyl complexes, the difference between the regioselectivity obtained with the fluoro substituted ligand f and the methoxy substituted ligand e is smaller than for the corresponding crotyl complexes. The regioselectivity obtained using ligand f is slightly higher than that obtained using ligand e. Since these observations cannot be explained in terms of electronic non-symmetry of the allyl moiety only, it is concluded that in this case either steric, or other secondary interactions, such as π-π stacking, can play a role.\(^{[17]}\)

6.3.3 Catalytic alkylation, kinetics

The regioselectivity found for the catalytic reactions is lower than that found for the stoichiometric reactions. This can be explained as follows. After oxidative addition of the substrate, two types of isomeric palladium complexes can be formed: one type having the substituent oriented trans to the phosphorus atom and one type having the substituent oriented trans to the nitrogen atom. The syn-trans-P isomer is thermodynamically favored and the syn-trans-N will isomerize to the more stable syn-trans-P isomer. This isomerization is facilitated by strongly coordinating counterions, such as chloride, which is the leaving group in the catalytic reactions (tables 3 and 4).\(^{[12]}\)

If the subsequent alkylation step is slow relative to isomerization (trans-N to trans-P), the product distribution will be determined by the syn-trans-P isomer only and therefore will be equal to the regioselectivity in the stoichiometric alkylation. If the alkylation, however, occurs at a rate similar to or faster than the rate of isomerization, the observed regioselectivity is determined by the isomer ratio formed, their rate of isomerization and their respective rates of alkylation. Since nucleophilic attack will primarily take place at the carbon atom trans to phosphorus, alkylation of the syn-trans-N isomer will yield relatively large amounts of the linear trans product.

This explanation in terms of competition between isomerization and alkylation is supported by the results of the catalytic alkylation of both crotyl and cinnamyl acetate. The acetate anion coordinates not as strongly to the palladium center as the chloride anion. It was shown that a coordinating anion facilitates dynamic behavior of the allyl moiety.\(^{[12\text{d-e}]}\) It has indeed been found that the regioselectivity is lower when acetate is
the leaving group (and therefore also the counterion (table 6)). The influence of a coordinating anion is further shown by addition of LiBr to the crotyl acetate reaction mixture (Br\(^-\) replaces OAc\(^-\): entry 5, table 5). In this case the regioselectivity is similar to that obtained using crotyl chloride.

The catalytic intermediates used as precursors in the catalytic experiments contain only one ligand per palladium atom. In tables 5 and 6 it is shown that the addition of extra ligand to the isolated complex causes a significant change in regioselectivity. In experiments where extra ligand is added the regioselectivity is similar to that obtained when bidentate phosphine ligands are used (entry 9, table 6). When extra ligand is present, it is plausible that two ligands are coordinated to palladium, both via the phosphorus atom (figure 6). The resulting complex then behaves as if bearing a bidentate phosphine ligand.

![Figure 6: Proposed formation of bis-phosphine coordinated complexes by addition of extra ligand to cationic (crotyl or cinnamyl)Pd(P-N) complexes](image-url)

Extensive kinetic experiments of the alkylation of cinnamyl chloride, using (cinnamyl)Pd(c)OTf as the catalyst, show that the rate of reaction is independent of the cinnamyl chloride concentration and that it is linear dependent on the concentration of both the malonate anion and the palladium complex. This indicates that the nucleophilic attack is the rate determining step of the reaction.

Although palladium allyl complexes have been studied in great detail in literature, little is known about the influence of the properties of ion pairs, which seem to be important for this chemistry. It has been reported that solvent polarity can have an effect on the outcome of enantioselective alkylation reactions.\cite{2a} In collaboration with G. E. Oosterom, we have studied the influence of local polarity on the regioselectivity of the alkylation reaction.\cite{5a}
6.4 Conclusion

In conclusion, we have shown that mixed bidentate P-N ligands with a large bite angle direct the regioselectivity to the formation of the branched product. Since the nitrogen donor atom is incorporated in a small pyridine group, the effect is electronic in nature. This is in contrast with our previous results concerning the effect of the bite angle of bidentate phosphine ligands, which could be explained in terms of steric hindrance.\cite{5a,5b} Thus, the effect of a larger bite angle on the regioselectivity has a steric component (leading to more linear product) and an electronic component (leading to more branched product). Therefore we conclude that for a rational design of ligands that favor the formation of the branched product, the following parameters are of importance: 1) relative donor-acceptor strength of the ligand donor atoms; 2) steric hindrance in the transition state; 3) bite angle of the ligand.

6.5 Experimental section

\( ^1H\) NMR (300 MHz, TMS, CDCl\(_3\)) , \(^{31}P\) \(^1H\) (121.5 MHz external 85\% H\(_3\)PO\(_4\), CDCl\(_3\)) , \(^{13}C\) NMR (75.4 MHz, TMS, CDCl\(_3\)) were recorded on a Bruker AMX-300 spectrometer. Elemental analyses were performed on an Elementar Vario EL (Foss Electric). The product distribution of the alkylation experiments was measured on an Interscience Mega2 apparatus, equipped with a DB1 column, length 30 m, inner diameter 0.32 mm, film thickness 3.0 \(\mu\)m, and a F.I.D. detector.

All experiments were carried out using standard Schlenk techniques. All solvents were freshly distilled prior to use. Crotyl chloride, cinnamyl chloride, benzaldehyde, 4-fluorobenzaldehyde, 4-dimethylaminobenzaldehyde, 4-methoxybenzaldehyde, 3-aminopropanol, 4-aminobutanol, diethyl 2-methylmalonate, NaH, AgOTf and PdCl\(_2\) were obtained from Aldrich. Crotyl chloride and the aldehydes were distilled prior to use.

6.5.1 General synthetic procedures

Sodium diethyl 2-methylmalonate (0.5 M in THF) was prepared from diethyl 2-methylmalonate and NaH in THF at 273 K. The dimers [(crotyl)Pd(\(\mu\)-Cl)]\(_2\) and [(cinnamyl)Pd(\(\mu\)-Cl)]\(_2\) were prepared following a literature procedure\cite{10}. The synthesis and characterisation of (dppe)Pd(crotyl)OTf,\cite{5b} crotyl acetate,\cite{5b} and the alkylation products of the coupling of crotyl acetate to sodium diethyl 2-methylmalonate are described elsewhere.\cite{16}

The POP\(_y\) type ligands (a-c) were prepared via condensation of the 2-pyridinemethanol (POP\(_y\)1 (a)), ethanol (POP\(_y\)2 (b)) and \(-\)propanol (POP\(_y\)3 (c)) with Ph\(_2\)PCl in the presence of an excess NEt\(_3\). The alcohol and NEt\(_3\) were dissolved in diethyl ether and cooled to 0\(^\circ\)C, after which a solution of Ph\(_2\)PCl in diethyl ether
was added dropwise. A white precipitate was formed (NEt₃·HCl). After filtration, the reaction volume was concentrated under reduced pressure. Slow filtration (silica) of this residue yielded the ligand as a colorless oil, in a yield of around 70%, based on Ph₂PCl.

The P-Im type ligands (d-g) were synthesized using a similar procedure, but required as extra step the synthesis of the imine-alcohol.[9] In a typical procedure, the aldehyde was dissolved in toluene and the α-ω amino-alcohol was added in one portion. The equilibrium of this condensation reaction was directed towards the imine-alcohol by removing the water formed with dehydrated K₂CO₃. After stirring for 12 hours, the reaction was completed and after filtration the solvent was removed by evaporation. The alcohol was then coupled to Ph₂PCl using the same procedure as for the POPy type ligands.

As a side reaction, cyclization of the imine took place.[9] This side reaction could only be prevented by the presence of an excess of the aldehyde. It should be noted that especially aldehydes bearing electron withdrawing substituents required this excess. The aminoalcohol could be quantitatively converted to the corresponding imine. The mixture of imine and aldehyde (colorless oil) was used as such in the coupling to Ph₂PCl. The aldehyde-ligand mixture (colorless oil) was then used in the synthesis of the corresponding (allyl)palladium complexes.

The oily ligand (1.0 equivalent) was weighed in a Schlenk and dissolved in 10 mL of CH₂Cl₂. To this mixture a solution of exactly 0.5 equivalent of the [(crotyl)Pd(μ-Cl)]₂ or [(cinnamyl)Pd(μ-Cl)]₂ dimer was added (dissolved in 10 mL of CH₂Cl₂). The color of the solution changed from colorless to bright yellow instantaneously. After stirring for 15 minutes, exactly 1.0 equivalent of AgOTf was added. Immediately, a white precipitate was formed and the color of the solution changed to light yellow. After filtration over celite, the solvent was removed in vacuo. After this step, the excess aldehyde could be removed by repetitive washing with either pentane or benzene. All palladium complexes were isolated as a white microcrystalline powder in circa 90% yield based on palladium and were used in the alkylation reaction.

### 6.5.2 Alkylation reactions

The stoichiometric alkylation reactions were performed at room temperature (292 K) by adding an excess of sodium diethyl 2-methylmalonate (0.1 ml of a 0.5 M solution in THF) to a solution of 10 mg of the Pd-complex in 1 ml of THF. Reaction was instantaneous and after one minute, the mixture was worked up with water, filtered over silica and analyzed by GC.

The catalytic reactions were performed at room temperature (292 K) in THF (5 mL), using 0.05 mol% of catalyst (0.25 μmole), 0.5 mmole of substrate and 1.0 mmole of sodium diethyl 2-methylmalonate. The reaction was monitored by taking samples from the reaction mixture which, after aqueous work up, were analyzed by GC using decane as the internal standard.

The kinetic experiments were performed using stock solutions of all reaction components. The amount of each reagent was, one at the time, varied by changing the amount of stock solution added. The amount of
catalyst was varied from 0.000625 mmole to 0.0200 mmole, the amount of cinnamyl chloride from 0.125 mmole to 1.000 mmole and the amount of malonate was varied from 0.200 mmole to 2.000 mmole.

6.5.3 Characterization:

Ligands and ligand precursors:

POPyll (a): $^1$H: 5.02 (d, J = 9.1 Hz, 2H (CH$_2$)); 7.18 (t, J = 5.4 Hz, 1H (m-pyridine (N-CH=CH))); 7.38 (m, 6H (aromatic H)); 7.45 (d, J = 6 Hz, 1H); 7.56 (m, 4H (aromatic H)); 7.67 (t, J = 6 Hz, 1H (m-pyridine (N-C(CH$_2$)=CH))); 8.54 (d, J = 4 Hz, 1H (o-pyridine)); $^{31}$P($^1$H): 117.1; $^{13}$C($^1$H): (75.4 MHz): 72.0 (d, J(P-C) = 18.9 Hz, CH$_2$); 120.94 (m-pyridine, N-C=CH); 122.1 (m-pyridine, N-CH=CH); 128.2 (C meta to P in Ph); 129.3 (C para to P in Ph); 130.4 (d, J = 21.9 Hz, C ortho to P in Ph); 134.6 (m-pyridine, N-CH=CH); 141.2 (d, J(P-C) = 18.1 Hz, P-C); 148.8 (o-pyridine, N-CH); 150.0 (o-pyridine, N-C)

POPy2 (b): $^1$H: 3.19 (t, J = 6.7 Hz, 2H (P-O-CH$_2$-CH$_2$)); 4.26 (dt, J1 = J2 = 6.7 Hz, J3 = 8.3 Hz, 2H (P-O-CH$_2$-CH$_2$)); 7.1 (d, J = 7.8 Hz, 1H (m-pyridine (N-CH=CH))); 7.15 (d, J = 7.8 Hz, 1H (m-pyridine (N-C(CH$_2$)=CH))); 7.31 (m, 6H (aromatic H)); 7.41 (m, 4H (aromatic H)); 7.55 (1H (p-pyridine)); 8.54 (d, J = 4.8 Hz, 1H (o-pyridine)); $^{31}$P($^1$H): 113.3; $^{13}$C($^1$H): 40.0 (d, J(P-C) = 9.0 Hz, P-O-CH$_2$-CH$_2$); 69.1 (d, J(P-C) = 20.4 Hz, P-O-CH$_2$-CH$_2$); 121.2 (m-pyridine, N-C=CH); 123.6 (m-pyridine, N-CH=CH); 128.0 (d, J = 6.8 Hz, C meta to P in Ph); 129.0 (C para to P in Ph); 130.3 (d, J = 21.9 Hz, C ortho to P in Ph); 136.0 (m-pyridine, N-CH=CH); 141.7 (d, J = 18.1 Hz, P-C); 149.1 (o-pyridine, N-CH); 158.0 (o-pyridine, N-C)

POPy3 (c): $^1$H: 2.16 (dt, J1 = J2 = 6.4 Hz, J3 = 8.0 Hz, 2H (CH$_2$-CH$_2$-CH$_2$)); 2.91 (t, J = 7.9 Hz, 2H (O-CH$_2$-CH$_2$-CH$_2$)); 3.93 (dt, J1 = J2 = 6.4 Hz, J3 = 8.7 Hz, 2H (O-CH$_2$-CH$_2$-CH$_2$)); 7.09 (d, J = 5.8 Hz, 1H (m-pyridine (N-C(CH$_2$)=CH))); 7.09 (t, 1H (m-pyridine (N-CH=CH))); 7.35 (m, 6H (aromatic H)); 7.45-7.6 (m, 5H (aromatic H and p-pyridine)); 8.54 (d, J = 4.4 Hz, 1H (o-pyridine)); $^{31}$P($^1$H): 112.4; $^{13}$C($^1$H): 31.1 (d, J = 8.3 Hz, P-O-CH$_2$-CH$_2$-CH$_2$); 34.5 (P-O-CH$_2$-CH$_2$-CH$_2$); 69.2 (d, J = 8.3 Hz, P-O-CH$_2$-CH$_2$-CH$_2$); 120.9 (m-pyridine, N-C=CH); 122.7 (m-pyridine, N-CH=CH); 128.1 (d, J = 6.0 Hz, C meta to P in Ph); 129.0 (C para to P in Ph); 130.1 (d, J = 22 Hz, C ortho to P in Ph); 136.1 (m-pyridine, N=CH=CH); 141.9 (d, J = 17.3 Hz, P-C); 149.1 (o-pyridine, N-CH); 161.2 (o-pyridine, N-C)

4-(para-fluoro-benzimino)-butanol (not isolated: see experimental procedures): $^1$H: 1.7 (m, 4H, (N-CH$_2$-CH$_2$-CH$_2$-CH$_2$-OH)); 3.6 (m, 4H, N-CH$_2$-CH$_2$-CH$_2$-CH$_2$-OH); 4.6 (s, 1H, OH); 7.0 (m, 2H, (F-C-CH)); 7.6 (m, 2H, (F-C-CH)); 8.14 (s, N=CH)
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P-Im4F (f) (not isolated: see experimental procedures): \(^1\)H: 1.88 (m, 4H, (N-CH\(_2\)-CH\(_2\)-CH\(_2\)-CH\(_2\)-O-P)); 3.66 (m, 2H, N-CH\(_2\)-CH\(_2\)-CH\(_2\)-CH\(_2\)-O-P)); 3.98 (m, 2H, N-CH\(_2\)-CH\(_2\)-CH\(_2\)-CH\(_2\)-O-P)); 7.1 (m, 2H, (F-C-CH)); 7.4 (m, 6H (o- and p-phenyl H)); 7.6 (m, 4H (m-phenyl H)); 7.6 (m, 2H (F-C-CH-CH)); 8.22 (s, N=CH); \(^3\)P\({^1\text{H}}\) : 112.4

4-(para-methoxy-benzimino)-butanol (not isolated: see experimental procedures): \(^1\)H: 1.80 (m, 4H (N-CH\(_2\)-CH\(_2\)-CH\(_2\)-CH\(_2\)-OH)); 3.62 (t, J = , 2H (N-CH\(_2\)-CH\(_2\)-CH\(_2\)-CH\(_2\)-OH)); 3.72 (t, J = , 2H (N-CH\(_2\)-CH\(_2\)-CH\(_2\)-CH\(_2\)-OH)); 3.82 (s, 3H (OCH\(_3\))); 6.94 (d, J = 8.7 Hz, 2H (CH\(_3\)-O-C-CH)); 7.8 (d, J = 8.7 Hz, 2H (CH\(_3\)-O-C-CH-CH)); 8.18 (s, N=CH);

P-Im4OMe (e) (not isolated: see experimental procedures): \(^1\)H: 1.81 (m, 4H (N-CH\(_2\)-CH\(_2\)-CH\(_2\)-CH\(_2\)-O-P)); 3.5 (m, 2H (N-CH\(_2\)-CH\(_2\)-CH\(_2\)-CH\(_2\)-O-P)); 3.83 (s, 3H (OCH\(_3\))); 3.87 (m, 2H (N-CH\(_2\)-CH\(_2\)-CH\(_2\)-CH\(_2\)-O-P)); 6.93 (d, J = 8.7 Hz, 2H (CH\(_3\)-O-C-CH)); 7.35 (m, 6H (o- and p-phenyl H)); 7.5 (m, 4H (m-phenyl H)); 7.68 (d, J = 8.7 Hz, 2H (CH\(_3\)-O-C-CH-CH)); 8.18 (s, N=CH); \(^3\)P\({^1\text{H}}\) : 112.1

3-(para-dimethylamino-benzimino)-propanol (not isolated: see experimental procedures):
\(^1\)H: 1.99 (quintet, J = 5.7 Hz, 2H (N-CH\(_2\)-CH\(_2\)-CH\(_2\)-O)); 3.01 (s, 6H (2CH\(_3\))); 3.79 (t, J = 5.7 Hz, 2H (N-CH\(_2\)-CH\(_2\)-CH\(_2\)-O)); 3.92 (t, J = 5.7 Hz, 2H (N-CH\(_2\)-CH\(_2\)-CH\(_2\)-O)); 6.74 (d, J = 8.7 Hz, 2H (CH\(_3\)-N-C-CH)); 7.67 (d, J = 8.7 Hz, 2H ((CH\(_3\))\(_2\)N-C-CH-CH)); 8.16 (s, N=CH)

P-Im3NMe\(_2\) (d) (not isolated: see experimental procedures):
\(^1\)H: 2.09 (quintet, J = 6.5 Hz, 2H (N-CH\(_2\)-CH\(_2\)-CH\(_2\)-CH\(_2\)-O)); 3.02 (s, 6H (2CH\(_3\))); 3.67 (t, J = 6.5 Hz, 2H (N-CH\(_2\)-CH\(_2\)-CH\(_2\)-CH\(_2\)-O)); 3.96 (dt, J1 = J2 = 6.5 Hz, J3 = 9 Hz, 2H (N-CH\(_2\)-CH\(_2\)-CH\(_2\)-CH\(_2\)-O)); 6.71 (d, J = 8.9 Hz, 2H (CH\(_3\))\(_2\)N-C-CH)); 7.35 (m, 6H (o- and p-phenyl H)); 7.5 (m, 4H (m-phenyl H)); 7.55 (d, J = 8.9 Hz, 2H (CH\(_3\))\(_2\)N-C-CH-CH)); 8.10 (s, N=CH); \(^3\)P\({^1\text{H}}\) : 112.3; \(^13\)C\({^1\text{H}}\) : 33.1 (d, J(P-C) = 7.5 Hz, N-CH\(_2\)-CH\(_2\)-CH\(_2\)-O); 40.2 (CH\(_3\)); 40.4 (CH\(_3\)); 58.0 (N-CH\(_2\)-CH\(_2\)-CH\(_2\)-O); 68.2 (d, J(P-C) = 19.6 Hz, N-CH\(_2\)-CH\(_2\)-CH\(_2\)-O); 111.2 ((CH\(_3\))\(_2\)N-C-CH); 111.8 ((CH\(_3\))\(_2\)N-C-CH-CH); 124.7 (N=CH-C); 128.7 (p-phenyl); 129.4 (d, J = 7 Hz, m-phenyl); 130.5 (d, J = 21.9 Hz, o-phenyl); 142.5 (d, J = 18.1 Hz, P-C); 152.2 ((CH\(_3\))\(_2\)N-C-); 161.6 (-N=CH-)

3-benzimino-propanol (not isolated: see experimental procedures):
\(^1\)H: 1.66 (quintet, J = 5.9 Hz, 2H (N-CH\(_2\)-CH\(_2\)-CH\(_2\)-O)); 3.76 (t, J = 5.9 Hz, 2H (N-CH\(_2\)-CH\(_2\)-CH\(_2\)-O)); 3.82 (t, J = 5.9 Hz, 2H (N-CH\(_2\)-CH\(_2\)-CH\(_2\)-O)); 5.15 (s, OH); 7.4 (m, 3H (aromatic H)); 7.7 (d, J = 8.7 Hz, 2H (o-phenyl H)); 8.25 (s, N=CH)
P-N ligands, crotyl and cinnamyl substrates.

P~Im3H (not isolated: see experimental procedures):

\[ ^1H: 2.17 \text{ (quintet, } J = 6.5 \text{ Hz, } 2H \text{ (N-CH}_2\text{-CH}_2\text{-CH}_2\text{-O})}; 3.79 \text{ (t, } J = 6.5 \text{ Hz, } 2H \text{ (N-CH}_2\text{-CH}_2\text{-CH}_2\text{-O})}; 4.04 \text{ (dt, } J_1 = J_2 = 6.5 \text{ Hz, } J_3 = 9 \text{ Hz, } 2H \text{ (N-CH}_2\text{-CH}_2\text{-CH}_2\text{-O})}; 7.4 \text{ (m, } 9H \text{ (o- and p- phenyl H))}; 7.59 \text{ (dt, } J_1 = J_2 = 7.5 \text{ Hz, } J_3 = 1.9 \text{ Hz, } 4H \text{ (P-C-CH-CH-)} 7.75 \text{ (m, } -\text{N=CH-C- and aromatic H}) ; 8.27 \text{ (s, } 1H \text{ (N=CH)}) ; ^31P{^1H} : 112.3 \]

**Palladium complexes:**

Pd(POPy 1 (a))(crotyl) \[ \text{SO}_3\text{CF}_3 \]

\[ ^1H: \text{ (syn trans P isomer): 1.83 (d, } J_1 = 6.2 \text{ Hz, } J_2 = 10.6 \text{ Hz, } 3H \text{ (Me))}; 3.21 \text{ (hump, } 2H \text{ (Ha and Hb))}; 5.05 \text{ (m, } 1H \text{ (Hz)); 5.16 (d, } J = 21.9 \text{ Hz, } 2H \text{ (P-O-CH}_2\text{))}; 5.75 \text{ (dt, } J_1 = J_2 = 9.4 \text{ Hz, } J = 13.2 \text{ Hz, } 1H \text{ (Hz)); 7.5 (m, } 10H \text{ (Ar)); 7.63 (t, } J = 7.4 \text{ Hz, } 1H \text{ (m-pyridine (N-CH-CH))}; 7.65 \text{ (d, } J = 7.4 \text{ Hz, } 1H \text{ (m-pyridine (N-C-CH))}); 7.95 \text{ (t, } J = 7.4 \text{ Hz, } 1H \text{ (p-pyridine)); 8.81 (d, } J = 5.3 \text{ Hz, (o-pyridine));} \]

\[ ^13C{^1H} : 17.7, 50.6, 73.1, 103.7, 121.7, 123.3, 126.8, 127.1, 129.3, 129.5, 131.8, 132.6, 134.3, 140.7, 154.5, 155.0; ^31P{^1H} : \text{(syn trans P isomer) 128.3 (s, } 1P) \]

FAB-MS: \[ \\ m/z = 454.0550 \text{ (C}_{22}\text{H}_{23}\text{NOPPd}^+ \text{ requires 454.0552}) \]

Elem. anal.: Found: C, 45.35%; H, 3.84%. Calc. for \[ \text{C}_{22}\text{H}_{23}\text{NOPPd}^+\text{CF}_3\text{SO}_3 + 0.1 \text{ CH}_2\text{Cl}_2: C, 45.31%; H, 3.82%. \]

Pd(POPy 1 (a))(cinnamyl) \[ \text{SO}_3\text{CF}_3 \]

\[ ^1H: \text{ 3.4 (d, } J = 9.3 \text{ Hz, } 2H \text{ (Ha and Hb)); 5.18 (d, } J = 21.9 \text{ Hz, } 2H \text{ (P-O-CH}_2\text{))}; 5.98 \text{ (dd, } J_1 = 10.3 \text{ Hz, } J_2 = 13.6 \text{ Hz, } 1H \text{ (Hz)); 6.4 (dt, } J_1 = J_2 = 9.3 \text{ Hz, } J_3 = 13.6 \text{ Hz, } 1H \text{ (Hz)); 7.0 (t, } J = 6.4 \text{ Hz, } 1H \text{ (H-pyridine)); 7.3-7.6 (m, } 2H \text{ (H-Ar and H-pyridine)); 7.75 (t, } J = 7.6 \text{ Hz, } 1H \text{ (H-pyridine)); 7.81 (d, } J = 5.1 \text{ Hz, } 1H \text{ (o-pyridine));} \]

\[ ^13C{^1H} : 17.2, 39.2, 49.8, 66.7, 102.0, 120.3, 125.4, 129.1, 132.1, 132.8, 139.6, 151.2, 159.7; ^31P{^1H} : 130.3 (s, } 1P) \]

FAB-MS: \[ \\ m/z = 516.0723 \text{ (C}_{27}\text{H}_{25}\text{NOPPd}^+ \text{ requires 516.0709}) \]

Elem. anal.: Found: C, 49.80%; H, 3.65%. Calc. for \[ \text{C}_{27}\text{H}_{25}\text{NOPPd}^+\text{CF}_3\text{SO}_3 + 0.15 \text{ CH}_2\text{Cl}_2: C, 49.82%; H, 3.76%. \]

Pd(POPy 2 (b))(crotyl) \[ \text{SO}_3\text{CF}_3 \]

\[ ^1H: \text{ 1.64 (dd, } J_1 = 6.3 \text{ Hz, } J_2 = 10.7 \text{ Hz, } 3H \text{ (Me)); 2.86 (broad, } 1H \text{ (Ha)); 3.65 (broad, } 1H \text{ (Hb)); 3.75 (broad, } 2H \text{ (pyridine-CH}_2\text{)); 4.15 (broad, } 2H \text{ (P-O-CH}_2\text{)); 4.9 (m, } 1H \text{ (Hz)); 5.78 (dt, } J_1 = J_2 = 9.4 \text{ Hz, } J_3 = 13.0 \text{ Hz, } 1H \text{ (Hz)); 7.2-7.8 (broad, } 2H \text{ (aromatic H and pyridine H)); 7.89 (t, } J = 7.3 \text{ Hz, } 1H \text{ (p-pyridine)); 8.46 (d, } J = 5.3 \text{ Hz, } 1H \text{ (o-pyridine));} \]

\[ ^13C{^1H} : 17.2, 39.2, 49.8, 66.7, 102.0, 120.3, 125.4, 129.1, 132.1, 132.8, 139.6, 151.2, 159.7; ^31P{^1H} : 116.7 (s) \]

FAB-MS: \[ \\ m/z = 3059, 2973, 1604, 1437 \]

85
FAB-MS: m/z = 468.0720 (C_{22}H_{23}NOPPd\textsuperscript{+} requires 468.0709)

Elem. anal.: Found: C, 44.06%; H, 3.76%. Calc. for C_{22}H_{23}NOPPd\textsuperscript{+}CF_{3}SO_{3} + 0.30 CH_{2}Cl_{2}: C, 44.06; H, 3.90%.

Pd(POPY2 (b))(cinnamyl) SO\textsubscript{3}CF\textsubscript{3}:

\textsuperscript{1}H: 1.77 (br, 2H (H\textsubscript{a} and H\textsubscript{b})); 3.1-3.8 (br, 2H (P-O-CH\textsubscript{2}-CH\textsubscript{2})); 4.1 (br, 2H (P-O-CH\textsubscript{2}-CH\textsubscript{2})); 6.13 (dd, J\textsubscript{1} = 10.7 Hz, J\textsubscript{2} = 13.5 Hz, 1H (Hc)); 6.36 (dt, J\textsubscript{1} = J\textsubscript{2} = 9.1 Hz, J\textsubscript{3} = 13.5 Hz, 1H (Hd)); 6.89 (dd, J\textsubscript{1} = J\textsubscript{2} = 7.2 Hz, 1H (aromatic H)); 7.1-7.8 (m, 13H (aromatic H)); \textsuperscript{13}C\{\textsuperscript{1}H\}: 113.5, 129.0, 130.7, 153.0, 159.3; \textsuperscript{31}P\{\textsuperscript{1}H\}: 117.9

IR (v\textsubscript{max} / cm\textsuperscript{-1}): 3066, 2894, 1655, 1438

FAB-MS: m/z = 530.0870 (C_{28}H_{27}NOPPd\textsuperscript{+} requires 530.0873)

Elem. anal.: Found: C, 49.48%; H, 3.86%. Calc. for C_{28}H_{27}NOPPd\textsuperscript{+}CF_{3}SO_{3} + 0.40 CH_{2}Cl_{2}: C, 49.46; H, 3.92%.

Pd(POPY3 (c))(crotyl) SO\textsubscript{3}CF\textsubscript{3}:

\textsuperscript{1}H (298 K): 1.33 (dd, J\textsubscript{1} = 10.1 Hz, J\textsubscript{2} = 6.2 Hz, 3H (Me)); 2.15 (broad, 2H (P-O-CH\textsubscript{2}-CH\textsubscript{2}-CH\textsubscript{2})); 2.9 (broad, 2H (P-O-CH\textsubscript{2}-CH\textsubscript{2}-CH\textsubscript{2})); 3.4 + 3.5 (broad, 4H, (P-O-CH\textsubscript{2}-CH\textsubscript{2}-CH\textsubscript{2} and Ha + Hb)); 4.9 (broad, 1H (Hc)); 5.73 (m, broad, 1H (Hd)); 7.3-7.7 (broad, 22H (aromatic H and pyridine H)); 7.80 (t, J = 7.6 Hz, 1H (p-pyridine)); 8.88 (s (broad), 1H (o-pyridine)); \textsuperscript{31}P\{\textsuperscript{1}H\}: 127.5; \textsuperscript{13}C\{\textsuperscript{1}H\}: 16.7, 32.7, 35.9, 64.0, 102.6, 106.9, 121.1, 121.2, 124.4, 125.0, 128.9, 131.0, 131.7, 138.9, 151.9, 162.3;

IR (v\textsubscript{max} / cm\textsuperscript{-1}): 3060, 2951, 2855, 1604, 1437

FAB-MS: m/z = 482.0872 (C_{24}H_{27}NOPPd\textsuperscript{+} requires 482.0865)

Elem. anal.: Found: C, 45.52%; H, 4.34%. Calc. for C_{24}H_{27}NOPPd\textsuperscript{+}CF_{3}SO_{3} + 0.45 CH_{2}Cl_{2}: C, 45.61; H, 4.20%.

Pd(POPY3 (c))(cinnamyl) SO\textsubscript{3}CF\textsubscript{3}:

\textsuperscript{1}H (298 K): 2.06 (broad, 2H (Ha and Hb)); 3.17 (br, 2H (P-O-CH\textsubscript{2}-CH\textsubscript{2}-CH\textsubscript{2})); 3.38 (br, 2H (P-O-CH\textsubscript{2}-CH\textsubscript{2}-CH\textsubscript{2})); 3.52 (br, 2H (P-O-CH\textsubscript{2}-CH\textsubscript{2}-CH\textsubscript{2})); 5.76 (dd, J\textsubscript{1} = J\textsubscript{2} = 10.7 Hz, 1H (Hc)); 6.36 (m, 1H (Hd)); 6.97 (br, 1H (aromatic H)); 7.1 (br, 4H (aromatic H)); 7.3 (br, 3H (aromatic H)); 7.5 (br, 7H (aromatic H)); 7.6 (br, 4H (aromatic H)); 8.54 (br, 1H (o-pyridine)); \textsuperscript{31}P\{\textsuperscript{1}H\}: 128.0; \textsuperscript{13}C\{\textsuperscript{1}H\}: 31.0, 34.8, 68.7, 103.0, 112.5, 121.5, 123.2, 127.8, 132.0, 136.3, 136.7, 137.0, 149.5, 161.5

IR (v\textsubscript{max} / cm\textsuperscript{-1}): 3060, 2950, 2885

FAB-MS: m/z = 544.1026 (C_{29}H_{30}NOPPd\textsuperscript{+} requires 544.1022)

Elem. anal.: Found: C, 51.06%; H, 4.28%. Calc. for C_{29}H_{30}NOPPd\textsuperscript{+}CF_{3}SO_{3} + 0.15 CH_{2}Cl_{2}: C, 51.02; H, 4.17%.
Pd(POPPy3 (c))(cinnamyl)Cl:

^1^H (298 K): 2.15 (br, 2H (Ha and Hb)); 2.95 (br, 4H (P-O-CH2-CH2-CH2 and P-O-CH2-CH2-CH2)); 4.0 (br, 2H (P-O-CH2-CH2-CH2)); 5.4 (br, 1H (Hc)); 5.97 (br m, 1H (Hd)); 6.9-7.7 (br, 19H (aromatic H)); \(^{31}^P[^1^H ]: 121.2

Pd(P-Im3 HH (g))(crotyl)OTf: obtained as the equilibrium mixture (endo and exo) in a ratio of (determined by \(^{31}^P\): ^1^H (258 K): 0.86 (dd, J1 = 6.3 Hz, J2 = 10.1 Hz, 3H (CH3, major)); 1.28 (dd, J1 = 6.5 Hz, J2 = 9.9 Hz, 3H (CH3, minor)); 1.98 (br, 2H (CH2-CH2-N, major)); 2.3-2.5 (br m, 2H (CH2-CH2-N, minor)); 2.59 (app. t: 2d, J = 9.7 Hz, (1+1)H (Ha, major and minor)); 3.40 (d, J = 6.1 Hz, 1H (Hb, minor)); 3.51 (d, J = 4.4 Hz, 1H (Hb, major)); 3.77 (m, 1H (Hc, minor)); 4.00 (m, (2+2)H (CH2-CH2-N, major and minor)); 4.25 (m, (2+2)H (CH2-CH2-O, major and minor)); 4.65 (t, J = J2 = 9.5 Hz (backbone)); 4.79 (m, 1H (Hc, major)); 5.18 (dd, J1 = 6.5 Hz, J2 = 12.5 Hz, J3 = 12.5 Hz, 1H (Hd, major)); 5.68 (dd, J1 = 6.8 Hz, J2 = 12.4 Hz, J3 = 12.4 Hz, 1H (Hd, minor)); \(^{31}^P[^1^H ]: 129.2 (s, 1.0P, minor); 129.4 (s, 1.5P, major);

Pd(P-Im3NMe22 HH (d))(crotyl)SbF6: obtained as the equilibrium mixture (endo and exo) in a ratio of 1:1.8 (determined by \(^{31}^P\): ^1^H (298 K): most signals broad, due to significant overlap no complete interpretation could be given: 1.1 (dd, J1 = 6.6 Hz, J2 = 9 Hz, 3H (CH-CH3, minor)); 1.3 (dd, J1 = 6.6 Hz, J2 = 9.6 Hz, 3H (CH-CH3, major)); 1.91 (m, 2H (-CH2-CH2-CH2-CH2-CH2-CH2-CH2-CH2, major)); 2.3 (m, 2H (-CH2-CH2-CH2-CH2-CH2-CH2-CH2-CH2, minor)); 2.43 (d, J = 10.2 Hz, 1H (Ha, major)); 2.80 (d, J = 11.1 Hz, 1H (Ha, minor)); 3.01 (s, 2 x 6H (N-CH3, major and minor)); 3.34 (d, J = 6 Hz, 1H (Hb, minor)); 3.43 (app q, J = 7.5 Hz, 1H (bridge minor)); 3.8-4.3 (m, (-CH2-CH2-CH2-, major and minor and Hc (minor)); 4.45 (t, J = 10.5 Hz, 1H (bridge -CH2-CH2-CH2-O-P-, major)); 4.7 (m, 1H (Hc, major)); 5.4 (m, 1H (Hd, major)); 5.6 (m, 1H (Hd, minor)); 6.5 (d, J = 8.7 Hz, N-C-CH, major and minor); 7.4-7.8 (aromatic H, major and minor); 8.35 (s, N=C(H), major); 8.47 (s, N=C(H), minor); \(^{13}^C[^1^H ]: 17.9, 33.6, 40.2, 48.6, 51.7, 61.0, 66.3, 81.8, 99.3, 103.0, 111.5, 117.3, 119.9, 120.8, 129.2, 129.29, 129.34, 129.38, 129.44, 129.48, 129.59, 131.1, 131.25, 131.32, 131.5, 131.7, 132.0, 132.2, 132.5, 133.8, 134.5, 135.4, 135.6, 136.2, 153.9, 170.1; \(^{31}^P[^1^H ]: 129.9 (1.0 P, major); 129.7 (0.8 P, minor);

IR (v max / cm\(^{-1}\)): 3062, 2951, 2918, 1593, 1531, 1438, 1375
FAB-MS: m/z = 551.1461 (C\(_{28}\)H\(_{34}\)N\(_2\)OPPd\(^+\) requires 551.1443)
Elem. anal.: Found: C, 40.62%; H, 4.31%. Calc. for C\(_{28}\)H\(_{34}\)N\(_2\)OPPd\(^+\)CF\(_3\)S\(_3\) + 0.75 CH\(_2\)Cl\(_2\): C, 40.69; H, 4.21%.

Pd(P-Im40Me (e))(crotyl) SO\(_3\)CF\(_3\): obtained as the equilibrium mixture (endo and exo) in a ratio of 1:1.8 (determined by \(^{31}^P\): ^1^H (298 K): most signals broad, due to significant overlap no complete interpretation could be given: 1.27 (dd, J1 = 6.6 Hz, J2 = 9.9 Hz, 3H (CH3, major)); 1.47 (dd, J1 = 7.2 Hz, J2 = 8.7 Hz, 3H (CH3, minor)); 1.6-1.9 (m, 3-4H, -CH2- CH2- CH2- CH2-CH2-, major and minor); 2.0 (b, 1H (allylic H minor or bridge)); 2.15 (b, 1H (allylic H minor or bridge)); 2.3 (b, 1H (allylic H minor or bridge)); 2.4 (d, J = 12.0 Hz, 1H (Ha, major, or bridge H)); 2.5 (b, 1H (bridge, minor)); 2.9 (t (overlap with d), J = 12 Hz, 1H (bridge,
Chapter 6

minor); 3.0 (d, J = 11.9 Hz, 1H (Ha minor, or bridge H)); 3.08 (d, J = 6.0 Hz, 1H (Hb minor, or bridge H)); 3.55 (d, J = 6 Hz, 1H (Hb, major or bridge H)); 3.6 (m, J = 12 Hz, around 2H (bridge)); 3.83 (s, 2 x 3H, (OCH3, major and minor)); 3.94 (m, around 2H (bridge (-CH2- CH2- CH2- CH2-, major and minor or Hc (minor)))); 4.10 (m, 1H (bridge (-CH2- CH2- CH2- CH2-, minor)); 4.40 (d, J = 11.8 Hz, 2H (minor) or 1H (major) (bridge -CH2- CH2- CH2- CH2-)); 4.75 (m, 1H (Hc, major)); 5.6-5.7 (m, 2 x 1H, (Hd, major and minor)); 6.9 (d, J = 8.4 Hz, 2 x 2H, O-C-CH-, major and minor), 7.3-7.7 (m, aromatic H's, major and minor), 7.95 (d, J = 8.4 Hz, 2H, O-C-CH-CH-, major), 8.07 (d, J = 8.7 Hz, 2H, O-C-CH-CH-, minor), 8.79 (s, 1H, -N=CH-, major), 8.90 (s, 1H, -N=CH-, minor); 31P1H: 131.9 (1.59 P, major), 132.5 (1.0 P, minor); 13C1H: 26.2, 31.6, 56.9, 114.9, 115.1, 129.2, 129.6, 130.7, 131.5, 132.6

IR (vmax/cm⁻¹): 3056, 2946, 2851, 1602, 1436

FAB-MS: m/z = 552.1304 (C36H33NO3PPd⁺ requires 552.1284)

Elem. anal.: Found: C, 48.17%; H, 4.65%. Calc. for C36H33NO3PPd⁺CF3SO3 + 0.35 CH2Cl2: C, 48.17; H, 4.64%.

Pd(Im4OMe(e))(cinnamyl) SO3CF3: obtained as the equilibrium mixture (endo and exo) in a ratio of 1:1.8 (determined by 31P)

1H (298 K): most signals broad, due to significant overlap no complete interpretation could be given: 1.5 (t, J = 12.3 Hz, 2H (-CH2- CH2- CH2- CH2-, major)); 1.67 and 1.73 (b, 1H (-CH2- CH2- CH2- CH2-, minor)); 2.1 (b, 2H (Ha and Hb, major)); 2.25 (b 2H (Ha and Hb, minor)); 2.5 (broad q, 1H (-CH2- CH2- CH2- CH2-, minor)); 2.74 (d, J = 11.4 Hz, 1H (major) or 2H (minor) (-CH2- CH2- CH2- CH2-)); 3.1 (t, J = 12 Hz, 1H (major) or 2H (minor) (-CH2- CH2- CH2- CH2-)); 3.3 (d, J = 4.5 Hz, 1H (major) or 2H (minor) (-CH2- CH2- CH2- CH2-)); 3.4 (d, J = 12 Hz, 1H (major) or 2H (minor) (-CH2- CH2- CH2- CH2-)); 3.5-3.7 (broad m, 1H (-CH2- CH2- CH2- CH2-, minor)); 3.6 (d, J = 11.7 Hz, 1H (major) or 2H (minor) (-CH2- CH2- CH2- CH2-)); 3.8 (d, J = 6 Hz, 1H (-CH2- CH2- CH2- CH2-, minor)); 3.84 (s, 3H (OCH3, major)); 3.88 (s, 3H (OCH3, minor)); 3.95 (m, 1H (-CH2- CH2- CH2- CH2-, minor)); 4.44 (d, J = 12.6 Hz, 2H, P-O-CH2, minor). 5.23 (t, J1 (with Hd) = 11.4 Hz, J2 (with trans P) = 11.4 Hz, 1H (Hc, minor)), 5.68 (t, J1 (with Hd) = 12.9 Hz, J2 (with trans P) = 12.9 Hz, 1H (Hc, major)), 5.9 (b, 1H, minor), 6.4 (m, 2 x 1H, Hd, major and minor), 6.74 (d, J = 8.1 Hz, O-C-CH-, major), 6.9-7.7 (m, aromatic H, major and minor), 7.97 (s, -N=CH-, major), 8.01 (d, J = 8.1 Hz, 2 x 2H, O-C-CH-CH-, major and minor), 8.24 (s, -N=CH-, minor); 13C1H: 24.2, 30.3, 54.5, 56.1, 56.8, 65.1, 67.4, 67.6, 103.4, 115.4, 119.0, 123.2, 125.1, 127.5, 128.6-132.5, 134.1, 134.4, 134.9, 136.9, 164.0, 168.4; 31P1H: 133.6 (1.7P, major); 134.0 (1.0P, minor)

IR (vmax/cm⁻¹): 3060, 2935, 2843, 1602, 1436

FAB-MS: m/z = 614.1446 (C38H35NO3PPd⁺ requires 614.1440)

Elem. anal.: Found: C, 50.81%; H, 4.52%. Calc. for C38H35NO3PPd⁺CF3SO3 + 0.65 CH2Cl2: C, 50.80; H, 4.47%.
Pd(P~Im4FF) (f)(crotyl) SO₃CF₃: obtained as the equilibrium mixture (endo and exo) in a ratio of 1:1.8 (determined by ³¹P): 'H (298 K): most signals broad, due to significant overlap no complete interpretation could be given: 1.3 (dd, J₁ = 6.3 Hz, J₂ = 9.6 Hz, 3.8H (Me, major)); 1.5 (2H (Me, minor)); 1.7-2.0 (3H); 2.1 (1.7H); 2.3 (1.2H); 1.4 (d, J = 11.7 Hz, 1H); 2.6 (0.7H); 2.9 (t, J = 11.4 Hz, 1.7H); 3.1 (0.9H); 3.5 (1H); 3.7 (m, 1.9H); 4.0 (2.4H); 4.1 (d, J = 13.2 Hz, 1.8H (P-O-CH₂-), major); 4.3 (0.7H (Hc, minor)); 4.4 (d, J = 13.8 Hz, 1.1H (P-O-CH₂-, minor)); 4.8 (m, 1H (Hc, major)); 5.5 (m, 1.1H (Hd, major)); 5.7 (m, 0.6H (Hd, minor)); 7.0 (t, J = 8.4 Hz, 3.5H (F-CH=CH-, major)); 7.3-7.6 (18H, (aromatic H)); 8.0 (2H (aromatic H)); 8.15 (1H (aromatic H)); 9.0 (1.0H (-N=CH-, major)); 9.1 (0.55H (-N=CH-, minor)): ¹³C (¹H): 17.1, 17.7, 24.4, 24.9, 29.7, 30.3, 47.2, 53.4, 54.9, 67.6, 68.0, 102.2, 102.6, 119.7, 120.8, 128.6, 129.2, 129.3-132.6, 134.6, 167.2, 169.6; ³¹P (¹H): 131.3 (1.8P, major); 132.0 (1.0P, minor).

IR (v/cm⁻¹): 3060, 2950, 1653, 1601, 1508, 1437

FAB-MS: m/z = 540.1085 (C₂₇H₃₀FNOPPd⁺ requires 540.1084)

Elem. anal.: Found: C, 45.56%; H, 4.27%. Calc. for C₂₇H₃₀FNOPPd⁺CF₃SO₃ + 0.80 CH₂Cl₂: C, 45.64; H, 4.20%

Pd(P~Im4FF) (f)(cinnamyl) SO₃CF₃: obtained as the equilibrium mixture (endo and exo) in a ratio of 1:2.1 (determined by ³¹P)

¹H (298 K): all signals broad, due to significant overlap no complete interpretation could be given: 1.35 (1H); 1.7 (6H); 2.0-2.3 (6H); 2.5 (1H); 2.85 (2H), 3.1 (3H), 3.3 (5H), 3.5-3.8 (9H), 4.0 (2.1 x 2H (P-O-CH₂-, major)); 4.5 (2H (P-O-CH₂-, minor)); 5.2 (1H (Hc, minor)); 5.8 (2.1 x 1H (Hc, major)); 6.3 (2.1 x 1H (Hd, major)); 6.8-7.7 (aromatic H); 7.9 (2H (aromatic H)); 8.2 (2.1 x 1H (-N=CH-, major)); 8.5 (1H (-N=CH-, minor)); ¹³C (¹H): 24.3, 29.6, 30.2, 54.8, 65.1, 67.4, 67.6, 103.1, 103.4, 113.4, 113.9, 116.1, 116.4, 117.0, 117.4, 126.7, 127.5, 128.4, 128.6, 129.1-132.6, 134.2, 134.3, 134.5, 135.7, 163.7, 165.0, 168.1; ³¹P (¹H): 132.6 (0.46P, minor); 133.6 (1.0P, major)

IR (v/cm⁻¹): 3058, 2949, 1653, 1601, 1508, 1437

FAB-MS: m/z = 602.1259 (C₃₂H₃₂FNOPPd⁺ requires 602.1240)

Elem. anal.: Found: C, 52.11%; H, 4.19%. Calc. for C₃₂H₃₂FNOPPd⁺CF₃SO₃ + 0.15 CH₂Cl₂: C, 52.06; H, 4.26%

alkylation products:
Analysis and identification of diethyl 2-((trans)-but-2-en-1-yl) methylmalonate and diethyl 2-((trans)-but-2-en-2-yl) methylmalonate is described elsewhere [12e].

Diethyl 2-((trans)-1-phenyl-pent-1-en-4-yl)malonate: ¹H: 1.21 (t, J = 6.4 Hz, 6H (O-CH₂-CH₃)); 1.41 (s, 3H, (C-CH₃)); 2.73 (d, J = 7.6 Hz, 2H (CH=CH-CH₃)); 4.15 (q, J = 6.4 Hz, 4H (O-CH₂-CH₃)); 6.1 (dt, J₁ = J₂ = 7.6 Hz, J₃ = 15.6 Hz, 1H (CH=CH-CH₃)); 6.4 (d, J = 15.6 Hz, (CH=CH-CH₃)); 7.1-7.35 (m, 5H (aromatic H)); ¹³C (¹H): 14.5 (O-CH₂-CH₃); 20.4 (C-CH₃); 39.8 (C-CH₂-CH₃=); 54.7 (C-CH₃); 61.7 (O-CH₂-
CH_3); 124.7 (Ph-CH=CH-); 126.6 (aromatic C); 127.8 (aromatic C); 128.9 (aromatic C); 130.1 (aromatic C); 134.4 (Ph-CH=CH-); 172.3 (C=O)

Diethyl 2-(1-phenyl-prop-2-en-1-yl) methylnalontae: ^1^H: 1.21 (t, J = 6.4 Hz, 6H (O-CH_2-CH_3)); 1.41 (s, 3H, (C-CH_3)); 4.15 (q, J = 6.4 Hz, 4H (O-CH_2-CH_3)); 5.04 (d, J = 14.4 Hz, 1H (E-CH-CH=C(H)H)); 5.08 (d, J = 8.1 Hz, 1H ((Z-CH-CH=C(H)H)); 6.3 (m, 1H (CH-CH=CH_2)); 7.1-7.35 (m, 5H (aromatic H)); ^1^C[^1^H]: 13.9 (O-CH_2-CH_3); 18.9 (C-CH_3); 46.5 (C-CH_2-CH=); 54.3 (C-CH_3); 61.7 (O-CH_2-CH_3); 118.0 (-CH-CH=CH_2); 126.6 (aromatic C); 127.4 (aromatic C); 128.5 (aromatic C); 130.1 (aromatic C); 137.5 (-CH-CH=CH_2); 172.3 (C=O)
P-N ligands, crotyl and cinnamyl substrates.

6.6 References and notes


[11] The use of other solvents with lower boiling point did not improve the results, either because the energy barrier for the exchange process was even lower than in CDCl₃ or because of very poor solubility.


[13] The NMR data were compared to simulated spectra in 16 steps from 218K to 338K, coalescence of the ortho pyridine protons occurred at 251K, R² = 0.981. Simulation of the spectra was performed using gNMR software by Budaelaar P. H. M., gNMR version 3.5M, Ivorysoft, Amerbos 330, 1025AV, Amsterdam, Netherlands

[14] The alkylation of (cinnamyl)Pd complexes bearing other bidentate ligands resulted in similar regioselectivities.


[17] Molecular modeling (Spartan PM3(tm) method) shows that the phenyl substituent on the allyl moiety is oriented parallel to the imine functionality.
Chapter 7.

An X-ray study towards the effect of the bite angle of bidentate phosphine ligands on the geometry of palladium(allyl) complexes: implications for the regioselectivity in the allylic alkylation of a disubstituted allyl moiety.

In the previous chapters we have studied mono-substituted allyl moieties. The DFT calculations described in chapter 3 predict an enhanced non-symmetry of the $\text{Pd}(\eta^1\text{-allyl})$ bond for di-substituted allyl moieties. In this chapter we study the effect of the bite angle of bidentate phosphine ligands on the structure and reactivity of $(\text{P-P})\text{palladium}(3,3-(\text{CH}_3)_2\text{C}_3\text{H}_3)$ complexes.

Abstract

X-ray crystal structures of a series of cationic $(\text{P-P})\text{palladium}(3,3-(\text{CH}_3)_2\text{C}_3\text{H}_3)$ complexes ($\text{P-P} = \text{dppe} (1,2\text{-bis(diphenylphosphino)ethane}), \text{dpff} (1,1\text{-bis(diphenylphosphino)ferrocene}), \text{DPEphos}$) and the $(\text{Xantphos})\text{Pd}(\text{C}_3\text{H}_5)\text{BF}_4$ complex have been determined. In the solid state structure, the phenyl rings of the ligands are oriented in the direction of the non-symmetrically bound $[3,3-(\text{CH}_3)_2\text{C}_3\text{H}_3]$ moiety. An increase of the bite angle of the chelating ligand results in an increase of the cone angle. In complexes containing ligands having a large cone angle, the distances between the phenyl rings and the allyl moiety become small, resulting in a distortion of the symmetry of the palladium-allyl bond. In solution, two types of dynamic exchange have been observed, the $\eta^3-\eta^1-\eta^3$ rearrangement and the apparent rotation of the allyl moiety. At the same time, the folded structure of the ligand changes from an endo to an exo orientation or vice versa.

The regioselectivity in the palladium catalyzed allylic alkylation of 3-methyl-but-2-enylacetate is determined by the cone angle of the bidentate phosphine ligand. Nucleophilic attack by a malonate anion takes place preferentially at the allylic carbon atom having the largest distance to palladium. Ligands with a larger cone angle direct the regioselectivity to the formation of the branched product, from 8% for dppe (1) to 61% for Xantphos (6).

The influence of the cone angle on the regioselectivity has been assigned to a sterically induced electronic effect.
7.1 Introduction

In many cases, palladium is the metal of choice in the synthetically useful catalytic allylic alkylation reaction.\[1\] When substrates resulting in symmetrically substituted Pd(allyl) complexes are used, such as cyclopent-2-enyl acetate or 1,3 diphenyl-prop-2-enyl-1-acetate, high enantioselectivities can be obtained.\[2-4\] The ligands that can be employed range from monodentate phosphorus ligands\[9a\] to bidentate phosphorus\[2\], nitrogen\[3\], or mixed bidentate P-N, P-S or phosphine-phosphate ligands\[4\].

When other types of allylic substrates are used, such as crotyl acetate or cinnamyl acetate, non-symmetrically substituted Pd(allyl) complexes are formed and regiocontrol\[5\] becomes an issue prior to enantiocontrol (see scheme 1). Three products can be formed: the non-chiral \(E\) and \(Z\) linear products and the chiral branched product. Excellent regio- and enantioselectivities have been obtained using P-N ligands with palladium as the metal\[6\]. The use of other metals, such as iridium,\[7a-d\] rhodium,\[7e\] or tungsten,\[7f\] can lead to analogous results, although the reaction rates are lower than those employing palladium. At this time, palladium based systems are still the most widely studied.

![Scheme 1: Regioselectivity in the palladium catalyzed allylic alkylation.](image)

Although many papers have appeared on enantioselective allylic alkylation, the subject of regioselectivity is studied less extensively. When a bidentate P-N or P-S ligand is used, the regioselectivity is determined by the difference in trans influence of the ligand donor atoms. The nucleophilic attack consequently takes place trans to the phosphorus donor (chapter 6), which in many cases exerts the strongest trans influence.\[8\]

For complexes containing bidentate P-P or N-N ligands, it has been suggested that the regioselectivity is determined by the bonding of the allyl moiety.\[9\] When the allyl group is substituted at one of its terminal positions, the symmetry of its bond to palladium is distorted. QSAR studies by Åkermark\[9a\] and our modeling studies (chapter 3) show that the Pd-allyl bond is changed from an \(\eta^3\) to an \(\eta^1-\eta^2\) like structure (see scheme 2). The Pd-C1 bond is shorter than the Pd-C3 bond, the C1-C2 bond is elongated and the C2-C3 bond is shortened. In literature many examples are known of crystal structures of substituted allyl moieties that are not symmetrically bonded to palladium.\[10\] Based on NMR studies, it has been suggested that the electrophilicity of the substituted allylic carbon atom site is enhanced relative to the non substituted terminal site. It appears that the malonate nucleophile attacks preferentially at the allylic carbon atom with the largest Pd-C distance. This observation is supported by theoretical studies.\[8a, 9d\]
**P-P ligands, dimethyl allyl complexes.**

In chapter 4 we showed the effect of the bite angle of bidentate phosphine ligands on the structure of cationic (crotyl)Pd(ligand) complexes and their performance in the regioselective allylic alkylation. The complexes were isolated as equilibrium mixtures of two isomers, a syn and an anti isomer. Molecular modeling showed an increased embracing of the allyl moiety by the phenyl rings of the ligand when the bite angle is larger. Thus, it was predicted that an increase of the bite angle of the ligand resulted in an increase of the cone angle and consequently in a decrease of the syn / anti isomer ratio. Furthermore, the stoichiometric alkylation of these complexes with sodium diethyl 2-methylmalonate showed an increased regioselectivity for the branched product when the bite angle of the ligand is larger. To gain more insight into the factors influencing the regioselectivity, the effect of the bite angle on the symmetry of the Pd-allyl bond was studied.

To this end, cationic (3,3-(CH₃)₂-C₅H₅)Pd(ligand) complexes have been prepared, using ligands enforcing different bite angles (see scheme 3). The geometry of the complexes bearing the ligands dppe, dppf, DPEphos and Xantphos was studied in detail by X-ray crystallography. The isolated complexes have been used to determine the regioselectivity in the allylic alkylation, using sodium diethyl 2-methylmalonate as the nucleophile. In order to study the relation between the observed regioselectivity and the embracing effect of the ligand (chapter 4), we have calculated two steric ligand parameters from the crystal structures, the cone angle\(^{[11]}\) and the solid angle.\(^{[12]}\)

---

**Scheme 2:** Distorted coordination of a substituted allyl moiety to palladium.

**Scheme 3:** Structures of the complexes, numbering scheme and the ligands used.
Chapter 7

7.2 Results

A series of cationic (ligand)Pd(3,3-(CH$_3$)$_2$-C$_3$H$_3$) complexes (see scheme 3) has been prepared following a standard procedure.$^{[10]}$ The ligand was added to the [(3,3-(CH$_3$)$_2$-C$_3$H$_3$)PdCl]$_2$ dimer,$^{[13]}$ after which the chloride anion is abstracted using either AgBF$_4$ or AgOTf. The cationic (Xantphos)Pd(C$_3$H$_5$) complex (7) has been prepared in a similar way, starting from the [(C$_3$H$_5$)PdCl]$_2$ dimer.

7.2.1 Allylic alkylation

The complexes 1-6 were used in the allylic alkylation using sodium diethyl 2-methylmalonate as the nucleophile. Upon nucleophilic attack of the malonate nucleophile two regio-isomeric products can be obtained (see scheme 4). Bond formation at C1 yields the linear product, while bond formation at C3 it yields the branched product. The results of the stoichiometric reaction, presented in table 1, show that the regioselectivity towards formation of the branched product increases when the bite angle of the ligand is larger, ranging from 8% for dppe (1) to 61% for Xantphos (6). In chapter 4, a discrepancy was observed between the results of stoichiometric and catalytic alkylation due to competition between syn-anti isomerization and alkylation.$^{[8b, 10]}$ In this investigation, only one isomer is possible leading to similar regioselectivities for the stoichiometric and the catalytic reaction (table 2). The rate of the catalytic reaction is dependent on the ligand, being relatively slow for dppe (1) and relatively fast for dppf (4).

![Scheme 4: Alkylation products of complexes 1-6, X = BF$_4$, OTf, OAc (stoichiometric: BF$_4$, OTf; catalytic: OAc).](image-url)


Table 1: Product distribution in the stoichiometric alkylation of complexes 1-6 (reaction conditions are described in the experimental section). All experiments were carried out in triplo, standard deviation of the reported regioselectivities is 0.5% or less.

<table>
<thead>
<tr>
<th>Complex</th>
<th>Bite angle</th>
<th>% branched</th>
<th>% linear</th>
</tr>
</thead>
<tbody>
<tr>
<td>dppe (1)</td>
<td>85.77(6)</td>
<td>8</td>
<td>92</td>
</tr>
<tr>
<td>dppe (2)</td>
<td>95</td>
<td>5</td>
<td>95</td>
</tr>
<tr>
<td>dppe (3)</td>
<td>99</td>
<td>11</td>
<td>89</td>
</tr>
<tr>
<td>dppe (4)</td>
<td>101.2(3)</td>
<td>13</td>
<td>87</td>
</tr>
<tr>
<td>DPEphos (5)</td>
<td>103.93(6)</td>
<td>41</td>
<td>59</td>
</tr>
<tr>
<td>Xantphos (6)</td>
<td>108.11(7)</td>
<td>61</td>
<td>39</td>
</tr>
</tbody>
</table>

a: value taken from crystal structure
b: value taken from reference 10

Table 2: Results of the catalytic alkylation of 3-methyl-but-2-enyl acetate (reaction conditions are described in the experimental section). All experiments were carried out in triplo, standard deviation of the reported regioselectivities is 0.5% or less, the standard deviation of the reported rates are 5% or less.

<table>
<thead>
<tr>
<th>Complex</th>
<th>Bite angle</th>
<th>TOF (mole/mole/h)</th>
<th>% branched</th>
<th>% linear</th>
</tr>
</thead>
<tbody>
<tr>
<td>dppe (1)</td>
<td>85.77(6)</td>
<td>400</td>
<td>6</td>
<td>94</td>
</tr>
<tr>
<td>dppe (4)</td>
<td>101.2(3)</td>
<td>12000</td>
<td>13</td>
<td>87</td>
</tr>
<tr>
<td>DPEphos (5)</td>
<td>103.93(6)</td>
<td>6200</td>
<td>45</td>
<td>55</td>
</tr>
<tr>
<td>Xantphos (6)</td>
<td>108.11(7)</td>
<td>2500</td>
<td>63</td>
<td>37</td>
</tr>
</tbody>
</table>

a: initial turn over frequency, determined after 2 minutes
b: determined after complete conversion
c: value taken form crystal structure

7.2.2 NMR experiments

In the complexes, the effect of the ligand on the allyl moiety is reflected in the NMR spectra. In the $^1$H-NMR of complexes 1-6, the signals of the two methyl groups of the allyl moiety appear as separate signals. The chemical shift is dependent on the ligand and is found at higher field when the bite angle of the ligand is larger (table 3).

At room temperature, the signals of Ha and Hb are broadened in all cases, especially for complexes bearing ligands with a large bite angle. The signal of Hc appears as a triplet due to coupling with the Ha and Hb
nuclei. The phosphorus spectra show two different signals, which are broad for the Xantphos modified complex (table 3).

Table 3: Selected NMR data of the complexes 1-7, data determined at 298 K, \( \delta \) in ppm.

<table>
<thead>
<tr>
<th>Complex (ligand)</th>
<th>Bite angle(°)</th>
<th>line width ( ^{11}P ) (Hz)</th>
<th>( \delta ) Me syn</th>
<th>( \delta ) Me anti</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (dppe)</td>
<td>85.77(6)( ^{a} )</td>
<td>8</td>
<td>1.90</td>
<td>1.45</td>
</tr>
<tr>
<td>2 (dppp)</td>
<td>95( ^{b} )</td>
<td>9</td>
<td>1.28</td>
<td>1.13</td>
</tr>
<tr>
<td>3 (dppb)</td>
<td>99( ^{b} )</td>
<td>6</td>
<td>1.36</td>
<td>0.82</td>
</tr>
<tr>
<td>4 (dppf)</td>
<td>101.2(3)( ^{a} )</td>
<td>3</td>
<td>1.11</td>
<td>1.11</td>
</tr>
<tr>
<td>5 (DPEphos)</td>
<td>103.93(6)( ^{a} )</td>
<td>10</td>
<td>1.23</td>
<td>1.06</td>
</tr>
<tr>
<td>6 (Xantphos)</td>
<td>108.11(7)( ^{a} )</td>
<td>91</td>
<td>0.92</td>
<td>1.04</td>
</tr>
<tr>
<td>7 (Xantphos)</td>
<td>108.11(7)( ^{a} )</td>
<td>3</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

a: value taken from crystal structure  
b: value taken from reference 10

The broadened signals indicate the occurrence of dynamic exchange of the allyl moiety,\(^{10}\) which appears to proceed at a higher rate when the bite angle of the ligand is larger. This dynamic exchange of the allyl moiety of complex 6 has been studied in detail by means of variable temperature NMR. At -40°C the slow exchange limit is reached. Upon raising the temperature, apart from Ha and Hb, also the two methyl groups of the ligand backbone, which appear as separate signals due to its folded structure (see below), and the two phosphorus atoms exhibit exchange behavior. Rate data, obtained from simulation of the spectra show that the observed dynamic behavior is the result of two different processes. The exchange of the methyl groups of the ligand and the phosphorus atoms occur with the same rate (\( k = 450 \text{ s}^{-1} \) at 303 K, \( \Delta H^{\ddagger}_{298} = +71 \text{ kJ/mole}, \Delta S^{\ddagger}_{298} = -88 \text{ J/mole.K} \)), which is significantly higher than that of the Ha-Hb exchange (\( k = 100 \text{ s}^{-1} \) at 303 K, \( \Delta H^{\ddagger}_{298} = +56 \text{ kJ/mole}, \Delta S^{\ddagger}_{298} = -30 \text{ J/mole.K} \)).

To gain more insight in the different dynamic processes, a NOESY spectrum was recorded for complex 6 bearing the Xantphos ligand, that enforces a large bite angle. The methyl groups of the allyl appeared to have a steric interaction with the phenyl rings of the ligand. This interaction was studied in more detail by recording NOE difference spectra, in which the methyl groups were irradiated. Irradiation of the signal at 0.92 ppm, which was assigned to the syn CH\(_3\) based on the value of \( ^{3}J(P-CH_{3}) \), showed that this CH\(_3\) group has a strong interaction with He. In contrast, the irradiation of the CH\(_3\) signal at 1.04 ppm shows a much weaker interaction. These observations confirm the assignment of the signals to respectively the syn and anti CH\(_3\) groups. The two CH\(_3\) groups differ in interaction with the phenyl groups of the ligand. The interaction is stronger for the syn methyl than for the anti methyl group. This results in a shielding effect of the syn-CH\(_3\) group in complexes 6, which is reflected in its resonance at unusual high field.
7.2.3 X-ray structures

The influence of the bite angle on the steric interaction of the ligand with the allyl moiety was also studied by X-ray crystallography. After recrystallization from CH₂Cl₂ / hexane we obtained crystals suitable for X-ray structure determination of the cationic (ligand)palladium(3,3-(CH₃)₂-C₃H₅) complexes with the ligands dpppe (1), dppf (4) and DPEphos (5), whereas no suitable crystals were obtained of complexes bearing ligands with a bite angle larger than DPEphos. To study the coordination mode of the Xantphos ligand, the cationic (Xantphos)Pd(C₃H₅) complex was prepared and crystallized.

Selected structural data obtained from the X-ray structures (figures 1-4) are presented in tables 4 and 5.

Table 4: Selected bond distances obtained from the crystal structures (Å).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>1 (dppe)</th>
<th>4 (dppf)</th>
<th>5 (DPEphos)*</th>
<th>7 (Xantphos)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pd-C1</td>
<td>2.185(9)</td>
<td>2.192(15)</td>
<td>2.161(7)</td>
<td>2.17(1)</td>
</tr>
<tr>
<td>Pd-C2/C2a</td>
<td>2.174(7)</td>
<td>2.152(16)</td>
<td>2.21(1)</td>
<td>2.16(1)</td>
</tr>
<tr>
<td>Pd-C2b</td>
<td></td>
<td></td>
<td>2.21(1)</td>
<td></td>
</tr>
<tr>
<td>Pd-C3</td>
<td>2.253(7)</td>
<td>2.291(18)</td>
<td>2.37(1)</td>
<td>2.17(1)</td>
</tr>
<tr>
<td>C1-C2</td>
<td>1.42(1)</td>
<td>1.42(2)</td>
<td>1.39(1)</td>
<td>1.34(2)</td>
</tr>
<tr>
<td>C1-C2</td>
<td>1.28(1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C2/C2a-C3</td>
<td>1.41(1)</td>
<td>1.41(2)</td>
<td>1.41(2)</td>
<td>1.34(2)</td>
</tr>
<tr>
<td>C2b-C3</td>
<td></td>
<td></td>
<td>1.59(2)</td>
<td></td>
</tr>
<tr>
<td>C3-C4 (anti)</td>
<td>1.51(1)</td>
<td>1.58(2)</td>
<td>1.48(1)</td>
<td></td>
</tr>
<tr>
<td>C3-C5 (syn)</td>
<td>1.50(1)</td>
<td>1.44(2)</td>
<td>1.48(1)</td>
<td></td>
</tr>
<tr>
<td>Pd-P (cis to C1)</td>
<td>2.296(2)</td>
<td>2.313(6)</td>
<td>2.336(2)</td>
<td>2.372(2)</td>
</tr>
<tr>
<td>Pd-P (cis to C3)</td>
<td>2.293(2)</td>
<td>2.33(9)</td>
<td>2.379(2)</td>
<td>2.372(2)</td>
</tr>
</tbody>
</table>

*: C2a corresponds to C85 in figure 3 and C2b corresponds to C77 in figure 3.
Table 5: Selected geometrical data obtained from the crystal structures, distances in Å, angles in °.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>1 (dppe)</th>
<th>4 (dppf)</th>
<th>5 (DPEphos)*</th>
<th>7 (Xantphos)</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \angle (P-Pd-P) )</td>
<td>85.77(6)</td>
<td>101.2(3)</td>
<td>103.93(6)</td>
<td>108.11(7)</td>
</tr>
<tr>
<td>( \angle (C-C-C) )</td>
<td>121.2(7)</td>
<td>124(1)</td>
<td>120.2(7)(a)</td>
<td>115(1)(b)</td>
</tr>
<tr>
<td>( d(C5(syn))-closest\ Ph-plane )</td>
<td>3.44(2)</td>
<td>3.54(3)</td>
<td>3.20(1)\textsuperscript{a}</td>
<td></td>
</tr>
<tr>
<td>( d(C1)-(PPdP-plane) )</td>
<td>+0.044(10)</td>
<td>-0.17(2)</td>
<td>+0.319(8)</td>
<td>-0.35(1)</td>
</tr>
<tr>
<td>( d(C2)-(PPdP-plane) )</td>
<td>-0.440(10)</td>
<td>-0.35(3)</td>
<td>+0.91(1)\textsuperscript{c}</td>
<td>-1.01(2)</td>
</tr>
<tr>
<td>( d(C3)-(PPdP-plane) )</td>
<td>+0.329(9)</td>
<td>+0.34(3)</td>
<td>-0.13(1)</td>
<td>-0.348(3)</td>
</tr>
<tr>
<td>( \angle((CCC-plane)-(PPdP-plane)) )</td>
<td>114.4(9)</td>
<td>114(2)</td>
<td>111(1)\textsuperscript{c}</td>
<td>99(1)\textsuperscript{d}</td>
</tr>
<tr>
<td>( \angle((C4-C3-C5-plane)-closest\ Ph-plane) )</td>
<td>7.9(5)</td>
<td>5(1)</td>
<td>10.2(7)</td>
<td></td>
</tr>
</tbody>
</table>

\*a: C2a corresponds to C85 in figure 3 and C2b corresponds to C77 in figure 3.

\textsuperscript{a} C81 in figure 3

\textsuperscript{b} C65 in figure 3

\textsuperscript{c} C2 corresponds to C77 in figure 3

\textsuperscript{d} C2 corresponds to C85 in figure 3

Figure 1: Two views of the crystal structure of complex 1 (dppe).
Figure 2: Two views of the crystal structure of complex 4 (dpf).

Figure 3: Two views of the crystal structure of complex 5 (DPEphos).
Figure 4: Two views of the crystal structure of complex 7 (Xantphos).

All structures are cationic, since the counterion is located at a large, non-bonding distance from palladium. In all complexes two phenyl rings of the ligand, located in the P-Pd-P plane, point in the direction of the allyl moiety. The planes of the \(-C(CH_3)_2\) fragment and the closest phenyl ring are almost parallel (table 5). The two other phenyl ring of the ligand point in the same direction as C2.

The DPEphos ligand (β = 103.93(6))° shows an interaction between one of the aromatic rings (C--C) of the backbone and one of the phenyl rings bound to phosphorus (C--C) (figure 3). The angle between the two planes is 23.8(2)° and the minimum distance is 3.37(3) Å (d(C54-C58)). This type of orientation for DPEphos has also been observed in the two other crystal structures known of palladium complexes of this ligand, the zerovalent (tcne)Pd(DPEphos) complex\(^ {14}\) and the (DPEphos)Pd(\(para-C_6H_4-CN\))Br complex\(^ {15}\).
With respect to C2, the ferrocene unit of the dppf ligand is located under the P-Pd-P plane, and is twisted as a result of its staggered conformation (figure 2). The two Cp rings are staggered and almost parallel (angle = 3.6(5)°). Also in this complex, two phenyl rings of the ligand point in the direction of the allyl moiety.

The Xantphos complex (figure 4) has C₃ symmetry, two phenyl rings of the ligand point in the direction of the allyl moiety and two are directed upwards with respect to C₂. The latter phenyl groups are almost parallel (13.4(2)°) and the distance between the ipso carbon atoms is 3.87(2) Å.

The two aromatic rings in the backbone of the Xantphos ligand are not coplanar as a result of the sp³ carbon atom and the oxygen atom in the bridge. The value found for the angle between the planes (27.4(5)°) is similar to that found for the zerovalent (tcne)Pd(Xantphos) complex reported previously\(^{114}\). As a result of this folded structure, one of the methyl groups of the backbone is located equatorially and one axially, resulting in two different signals in the NMR spectrum (see above).

As expected, the C1-C2-C3 plane is not perpendicular to the P-Pd-P plane. The angle between these planes appears to be dependent on the ligand, as it ranges from 114.4(9)° for dppe to 100(2)° for Xantphos (table 5).

In all C₅H₉-complexes, the allyl moiety is not symmetrically bound to the palladium center. The Pd-C1 bond is shorter than the Pd-C3 bond and the C1-C2 bond is longer than the C2-C3 bond (table 4). Considering these differences between the bond lengths, the non-symmetry of the allyl moiety is more pronounced when the bite angle of the ligand is larger.

In the complex of dppe, the bond between C3 and the syn methyl substituent on the allyl moiety is slightly shorter (1.50(1) Å) than the bond from C3 to the anti substituent (1.51(1) Å). When the bite angle is larger, as in the case of dpff, the C3-C5(syn) bond becomes shorter (1.44(2) Å) and the C3-C4(anti) bond is longer (1.58(2) Å).

It has been reported, that in some cases the allyl moiety is slightly rotated around the Pd-allyl axis\(^{4c, 4d, 9}\). This rotation towards a product-like state could be important for determining the regioselectivity. In the crystal structures we present here, no significant rotated orientation of the allyl group is observed and no correlation with the bite angle of the ligand is found (table 5).

The palladium phosphorus distances are in the same range as found previously for zerovalent (P-P)Pd(tcne) complexes.\(^{114}\) In general, the bond between palladium and phosphorus cis to C1 is shorter than that to phosphorus cis to C3. This difference is more pronounced when the bite angle of the ligand is larger; it is approximately zero for the dppe ligated complex and amounts to 0.02 Å for dpff (4) and to 0.04 Å for DPEphos (5). The distance between palladium and the phosphorus atoms is also dependent on the bite angle of the ligand. A smaller bite angle results in a smaller Pd-P distance. It ranges from 2.293(2) Å for dppe to 2.372(2) Å for Xantphos.
7.2.4 Cone angle, solid angle

From the above observations it is clear, that the bite angle of the ligand influences the symmetry of the Pd-allyl bond via steric interaction. The top views of the crystal structures show that the phenyl rings are closer to the allyl moiety when the bite angle of the ligand is larger, as was already suggested by the results of the semi-empirical molecular modeling in chapter 4. The bite angle, however, is an indirect parameter for determining the amount of steric interaction a ligand induces. Therefore we decided to determine the values of two direct parameters from the X-ray structures, the cone angle \( \Theta \) \cite{111} introduced by Tolman, and the solid angle \( \Omega \) \cite{112} as introduced by Bagnall and Xing-Fu.

The results in table 6 show in general the same trend for each of these geometrical parameters. Going from dppe to Xantphos, the bite angle, the cone angle and the solid angle increase.

Table 6: Values of the bite angle, the cone angle and the solid angle, as determined from the X-ray structures.

<table>
<thead>
<tr>
<th>Complex</th>
<th>Bite angle (°)</th>
<th>Cone angle (°)</th>
<th>Solid angle (sterrad)</th>
<th>% branched product</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (dppe)</td>
<td>85.77(6)</td>
<td>224.6</td>
<td>4.47</td>
<td>8</td>
</tr>
<tr>
<td>4 (dppf)</td>
<td>101.2(3)</td>
<td>229.7</td>
<td>5.44</td>
<td>11</td>
</tr>
<tr>
<td>5 (DPEphos)</td>
<td>103.93(6)</td>
<td>240.2</td>
<td>5.00</td>
<td>41</td>
</tr>
<tr>
<td>7 (Xantphos)</td>
<td>108.11(7)</td>
<td>246.9</td>
<td>5.56</td>
<td>61</td>
</tr>
</tbody>
</table>

7.3 Discussion

7.3.1 Structure of the complexes in the solid state

From the X-ray data, it can be concluded that the presence of substituents on the allyl moiety distorts the symmetry of the bond to palladium (see scheme 5). This effect has been observed before, both in other crystal structures and in modeling studies \cite{9}. In all cases, it is observed that the bonding distance between C3 and palladium is longer than between palladium and C1. The weakened bonding between the substituted allylic site and palladium corresponds to an enhanced bond strength of the allylic C2-C3 bond. In the present case, the distortion is dependent on the ligand used and, specifically, on the bite angle of the ligand used. A larger bite angle results in an increase of the cone angle of the ligand and therefore in a more pronounced embracing of the allyl moiety by the phenyl rings of the ligand (see table 6). The increase in solid angle with larger bite angle indicates that there is less space for the allyl ligand to coordinate to palladium. In figure 5, a space-filling model of the crystal structure containing the Xantphos ligand is presented. There is enough space for the allyl moiety to coordinate but addition of two extra methyl substituents on one of its terminal positions will result in significant steric interaction (see figure 5). This leads to a lengthening of the Pd-C3
P-P ligands, dimethyl allyl complexes.

bond and changes in bond lengths as shown in scheme 5. Therefore it is argued that the steric effect of the bite angle on the dissymmetry of the Pd-allyl bond induces electronic effects on the allyl moiety.

Scheme 5: Schematic representation of the distortion of the Pd-allyl bond as observed in the X-ray structures.

Figure 5: Space filling model of the X-ray structure of complex 7, the allyl moiety at the bottom of the figure.

The distortion of an $\eta^3$ towards an $\eta^1$-$\eta^2$ bonding mode as observed in the crystal structures, will result in a lower value of the overlap integral on the $\eta^2$-site and a higher value of this integral on the $\eta^1$-site. On the $\eta^2$-site, both the donating interaction (ligand to metal) and the back-donating interaction (metal to ligand) will be decreased with respect to the symmetrically $\pi$-bonded allyl moiety$^{[8c, 9]}$. Thus, as a result of the lengthening of the Pd-C3 distance the back-donation to the LUMO of this site of the allyl moiety is lower than in a symmetrically bonded $\pi$-allyl moiety. The Pd-C1 distance is decreased and the C1-C2 distance is increased, which both indicate an increase in the L$\rightarrow$M donation as well as the M$\rightarrow$L back-donation on the $\eta^1$-site of the allyl moiety.

The difference in the two allyllic binding sites is reflected in the bond length between palladium and phosphorus. The Pd-P cis to the non-substituted C1 is shorter than the bond trans to C1. So, the two ligands that are most strongly bound to the metal center are cis to one another.

The effects of changes in donation and back-donation are also reflected in the value for the angle between the allylic CCC plane and the P-Pd-P plane. In the absence of back-donation, a value close to 90° would be expected. When the back-donation to C1 and C3 is strong, the value for this angle ($\angle((\text{CCC})-(\text{PPd}))$) will
increase. In the crystal structures presented in this chapter, the value of $\angle((CCC)-(PPdP))$ is dependent on the ligand. When the bite angle of the ligand is larger, this angle decreases. It is concluded that an increase in the bite angle results in a decrease of the back-donation. As a consequence, the allylic LUMO orbitals, which are the sites of reaction in the nucleophilic attack, remain less occupied. Therefore, a larger bite angle of the ligand results in an increase of the reactivity of the allyl moiety towards nucleophilic attack. This has indeed been observed in the catalytic alkylation of trans substrates (chapters 4 and 5). The catalytic experiments, however, show a lower reaction rate for the Xantphos ligand. This can be explained in terms of increased steric hindrance (see below).

7.3.2 Structure of the complexes in solution

The NOE experiments carried out on the cationic (3,3-(CH$_3$)$_2$-$C_6H$_3$)Pd(Xantphos)$^+$ complex (6) revealed steric interactions between the methyl groups and the phenyl rings of the ligand. The phenyl rings show a stronger interaction with the syn methyl, compared to the anti methyl group, whereas in the X-ray structure of complex 7, the anti hydrogen atom is closest to the phenyl rings. A slight rotation about the P-C bond in the X-ray structure would bring the phenyl rings at a closer distance to the syn substituent than to the anti substituent. In solution, some rotation about the P-C bond may take place and our results indicate that on average the syn substituent is at a closer distance to the phenyl rings. The crystal structures show that the steric interaction is stronger when the bite angle of the ligand is larger.

Complex 6, as well as the other complexes, can in theory be present in two pairs of enantiomeric structures (scheme 6): the methyl groups can be oriented trans to P1 or trans to P2 and the axial phenyl rings of the ligand (figure 1-4) can be oriented in the same direction as C2 (endo) or in the opposite direction (exo). In the crystal structures, only the endo isomer is found for complexes 1, 4 and 7, whereas for complex 5 both isomers are found to crystallize together. In the NMR spectra only one complex is observed, also at low temperature, which is therefore assigned to be the endo isomer. It can not be ruled out that the different complexes which are possibly present at reaction temperature show different regioselectivities in the allylic alkylation.

Scheme 6: Two pairs of enantiomers of complex 6.
Variable temperature NMR experiments carried out for complex 6, showed that several types of fluxional behavior occur simultaneously. The slower process involves the Ha/Hb exchange and the faster process involves the phosphorus atoms and the two methyl groups of the ligand, which at low temperature appear as separate signals due to the folded structure of the backbone (see above). The exchange of the methyl groups of the ligand indicates that during the faster process, the backbone of the ligand folds from one orientation to the other, thereby exchanging the methyl groups from an equatorial to an axial position and vice versa.

The relatively high negative value for the entropy of activation suggests that the faster process occurs via an associative pathway. It is known, that temporary coordination of the counterion of cationic (allyl)palladium complexes may enhance the rate of dynamic exchange of the allyl moiety.\textsuperscript{16b} In a thus formed five coordinated Pd(allyl) complex, the so-called apparent rotation of the allyl moiety can easily take place.\textsuperscript{16b} In complex 6, such a process will cause the exchange of C1 and C3 and vice versa, resulting in the equivalency of the two phosphorus atoms. Apparently, during this process, the backbone of the ligand changes its folded structure from one form to the other, thereby exchanging the two methyl groups of the ligand.

The Ha/Hb exchange, observed in the slower process, is known to be caused by a $\eta^1$-$\eta^1$-$\eta^1$ rearrangement\textsuperscript{171}. The Pd-C3 and Pd-C2 bonds are broken selectively and a Pd-C1 $\sigma$-bond is formed. Rotation about the Pd-C1 bond and the C1-C2 bond results in an exchange of the signals of Ha and Hb. As at \(-40^\circ\mathrm{C}\) only one complex is observed, it is concluded that, contrary to our previous results,\textsuperscript{8b} the $\pi$-$\sigma$ rearrangement of the allyl moiety observed for complex 6 does not lead to the exchange of the endo and exo isomeric forms of the complex.

If the $\eta^1$-$\eta^1$-$\eta^1$ rearrangement process occurs via a T-shaped palladium intermediate, in which no exchange of the coordination sites of C1 and C3 takes place, the exchange of endo to exo and vice versa will take place.\textsuperscript{8b} On the other hand, if it occurs via a C, symmetric Y-shaped intermediate, in which a C1-C3 exchange will take place, the endo-exo exchange may not occur (scheme 7). Recently, we have found evidence for coordination of the oxygen atom of the ligand backbone to palladium in cationic (Xantphos)Pd(Ph) complexes.\textsuperscript{151} This may also occur in the Y-shaped intermediate. The thus formed flat structure of the backbone can fold back to form the endo isomer of the $\eta^1$-$\eta^1$-$\eta^1$ rearranged complex. Because the $\eta^1$-$\eta^1$-$\eta^1$ rearrangement is the slower process, it can not be distinguished whether it involves a T- or a Y-shaped intermediate.
Chapter 7

7.3.3 Allylic alkylation

Several theoretical studies concerning the mechanism of the allylic alkylation reaction have been reported in literature.\textsuperscript{[9d, 17]} Recently, a theoretical rationale has been presented\textsuperscript{[9d]} for the correlation between the regioselectivity and the non-symmetry of the allyl moiety\textsuperscript{[91]}. By means of DFT calculations (ADF) it was shown, that an electronic preference for initial nucleophilic attack on the carbon atom of the allyl moiety with the largest Pd-C distance, leads to a lowering of the energy barrier encountered in a later stage of the reaction. Our results may be explained following the same rationale.

First, the malonate nucleophile selects the site of attack, based on electronic properties (charge, LUMO coefficients) and steric (accessibility) properties. Therefore, the regioselectivity for initial attack at C3 will be a trade-off between the larger steric hindrance the nucleophile encounters during attack at this position and the electronic preference.

During the process of bond formation,\textsuperscript{[17]} the allyl moiety rotates to form a transient palladium-olefin complex\textsuperscript{[18]}. When the attack takes place at C3, the branched site, a terminal C=C double bond is formed. The formation of the transient palladium-olefin complex implies that the substituted carbon atom has been rotated out of the P-Pd-P plane, thereby minimizing the steric interaction with the phenyl rings of the ligand. Alternatively, attack on C1 results in the formation of an internal C=C double bond, substituted by three groups. In the resulting palladium-olefin complex, the methyl substituents are at a closer distance to palladium than they were in the allyl complex, so the steric hindrance with the ligand is increased. In this stage of the reaction, the height of the energy barrier is also influenced by the thermodynamically favorable formation of an internal C=C double bond compared with that of a terminal alkene.

The preference for formation of the branched product when the bite angle of the ligand is larger, can therefore be explained both in steric and electronic terms. Thus, the selectivity towards the formation of the linear product for the dppe ligated complex can be explained by a less activated allyl moiety due to less steric interaction with the ligand (see above). Consequently, the steric accessibility of C3 relative to C1 is important. Also in the second stage of the reaction, when the more favored internal alkene is formed, the steric hindrance in the palladium-olefin complex will be less than that in complexes of the other ligands.

Scheme 7: Different intermediates for the $\eta^3$-\$\eta^1$-$\eta^3$ rearrangement.

\[ \text{T-shaped intermediate} \quad \leftrightarrow \quad \text{Y-shaped intermediate} \]
In contrast, the use of ligands with a larger bite angle will result in the formation of a more activated allyl moiety in the corresponding palladium complex. In the trade-off between steric access and electronic reactivity, the electronic factors may prevail. During the rotation of the allyl moiety, the steric hindrance encountered during terminal olefin formation (branched product) will be less than that for internal olefin formation (linear product). We therefore propose that the regioselectivity of the allylic alkylation is determined by a set of steric/electronic trade-off pathways (see Scheme 8).

The large difference in the amount of branched product formed from the dpff (4) and the DPEphos (5) modified complexes would not be expected based on the small difference in bite angle. In general, comparing the values found for the three different ligand parameters (bite angle, cone angle, solid angle) with the regioselectivity, reveals that the cone angle shows the best correlation.

The total effect of the ligand geometry on the rate of the catalytic reaction is dependent on several effects. The reaction consists of a number of consecutive stages: (1) substrate coordination to palladium, (2) oxidative addition, (3) nucleophilic attack and (4) product dissociation. A large cone angle will slow down stage (1), as a result of large steric hindrance. The study of the crystal structures shows that a large cone angle may enhance the reaction rate of stage (3) and (4). The oxidative addition process can be regarded as the reverse process of nucleophilic attack, so it can be expected that also stage (2) may proceed slower when the cone angle is larger. Thus, the total effect of the cone angle of the ligand on the rate is determined by a trade-off between the accelerating and the decelerating effects.

Scheme 8: Trade-off pathways that may determine the regioselectivity.
7.4 Conclusion

We have shown, that in crystal structures an increase of the bite angle of a bidentate phosphorus ligand leads to an increase in both the cone angle and solid angle of the ligand. As the effect of the ligand on the geometry and reactivity of the complexes is best described in terms of steric hindrance, the cone angle of the ligand is the parameter of choice.

The more pronounced embracing of the allyl moiety by the ligand distorts the symmetry of the Pd-(3,3-(CH$_3$)$_2$-C$_3$H$_5$) bond to an $\eta^1$-$\eta^2$ type coordination. Furthermore, the backbonding to the substituted site of the allyl moiety decreases when the cone angle is large. This sterically induced electronic effect has a pronounced influence on the reactivity of the allylic carbon atoms and the regioselectivity of stoichiometric alkylation.

A larger cone angle of the ligand enhances the electronic preference for nucleophilic attack on the branched position, but also the steric hindrance at this position is enhanced. Therefore it is concluded, that the regioselectivity of the reaction is a result of a trade-off between electronic and steric interactions.

7.5 Experimental Section

7.5.1 General procedures

$^1$H NMR (300 MHz, TMS, CDCl$_3$), $^{13}$P [$^1$H] (121.5 MHz external 85% H$_3$PO$_4$, CDCl$_3$) were recorded on a Bruker AMX-300 spectrometer.

The product distribution of allylic alkylation was measured on a Interscience Mega2 apparatus, equipped with a DB1 column, length 30 m, inner diameter 0.32 mm, film thickness 3.0 μm, and a F.I.D detector.

All experiments were carried out using standard Schlenk techniques. All solvents were freshly distilled prior to use. All reactions have been performed at room temperature (292 K).

The variable temperature NMR experiments have been carried out by measuring spectra at different temperatures, ranging from 233K (dynamic behavior frozen out) to 328 K (coalesced signals, towards fast exchange). The simulation of the spectra was carried out using gNMR software.$^{191}$

Sodium diethyl 2-methylmalonate (0.5 M in THF) was prepared from diethyl 2-methylmalonate and NaH in THF at 273 K. All alkylation experiments were carried out in triplo.

The stoichiometric alkylation reactions were performed by adding an excess of sodium diethyl 2-methylmalonate (0.1 ml of a 0.5 M solution in THF) to a solution of 10 mg of the Pd-complex in 1 ml of THF. Reaction was instantaneous and after one minute, the mixture was worked up with water, filtered over silica and analyzed by GC.

The catalytic reactions were performed in THF (10 mL), using 0.05 mol% of catalyst (0.00050 mmole), 1.0 mmole of 3-Me-but-2-enyl acetate and 2.0 mmole of sodium diethyl 2-methylmalonate. The reaction was
P-P ligands, dimethyl allyl complexes.

monitored by taking samples from the reaction mixture, which after quenching with wet ether, were analysed by GC using decane as the internal standard.

The Pd-complexes were prepared in CH$_2$Cl$_2$ from [(CsH$_5$)-Pd-μCl]$_2^{[113]}$ by adding 2 equiv. of ligand and abstracting the Cl-atom with AgOTf.$^{[10]}$ The complexes were isolated in quantitative yield (white microcrystalline powder) as their analytically pure equilibrium mixtures and were used as such in the alkylation reaction. The syntheses of DPEphos and Xantphos have been published elsewhere.$^{[28]}$ Dppe, dppp, dppb and dpff were obtained from Acros chemicals and used as received.

7.5.2 Characterization

(C$_5$H$_9$)Pd(dppe)OTf (1): $^1$H: 1.05 (t, 3H, J1 = J2 = 6.3 Hz, anti-CH$_3$); 1.90 (t, 3H, J1 = J2 = 8.4 Hz, syn-CH$_3$); 2.5-2.8 (br m, 4H, 2P-CH$_2$); 3.6-4.0 (br, 2H, allylic-CH$_2$); 5.53 (t, 1H, J1 = J2 = 11.0 Hz); 7.3-7.9 (br m, 20H, aromatic H)

$^{31}$P: 46.8 (d, 1P, J = 34 Hz); 51.1 (d, 1P, J = 34 Hz)

$^{13}$C ($^1$H): 20.2 (d, J = 5 Hz); 26.6 (d, J = 13.7 Hz); 26.8; 26.9 (d, J = 13 Hz); 28.0 (d, J = 13 Hz); 28.5 (d, J = 13 Hz); 60.6; 61.0; 103.5; 104; 107.9; 108.2; 115.0; 115.1; 115.2; 116.7; 116.8; 117.1; 117.3; 129.5 (d, J = 11 Hz); 131.8; 132.3 (d, J = 13 Hz)

HR-MS (FAB): C$_{41}$H$_{33}$P$_2$Pd$^+$ requires m/z = 573.1092, found m/z = 573.1102

(C$_5$H$_9$)Pd(dppp)OTf (2): $^1$H: 1.14 (dd, 3H, J1 = J2 = 6.3 Hz, anti-CH$_3$); 1.28 (dd, 3H, J1 = J2 = 9.6 Hz, syn-CH$_3$); 1.6 (br m, 1H, C(H)H-CH$_2$-P); 2.2 (br m, 1H, C(H)H-CH$_2$-P); 2.75 (m, 2H, -CH$_2$-P); 2.8 (dd, 1H, J1 = J2 = 13 Hz, allylic H); 2.95 (m, 2H, -CH$_2$-P); 3.65 (dd, 1H, J1 = J2 = 7.2 Hz, allylic H); 5.27 (dd, 1H, J1 = 8.1 Hz, J2 = 13.8 Hz, allylic H); 7.2-7.7 (br m, 20H, aromatic H)

$^{31}$P: 6.5 (d, J = 65.7 Hz); 9.8 (d, J = 65.3 Hz)

$^{13}$C ($^1$H): 19.0; 20.7; 25.9; 26.3; 26.6; 64.1 (d, J = 29 Hz); 110.1 (d, J = 26 Hz); 114.5; 128.4; 129.2; 129.3; 129.5; 129.6; 130.5; 131.0; 131.8; 131.9; 132.7 (d, J = 11 Hz); 133.8 (d, J = 12.4 Hz); 134.3 (d, J = 14 Hz)

HR-MS (FAB): C$_{32}$H$_{33}$P$_2$Pd$^+$ requires m/z = 587.1249, found m/z = 587.1255

(C$_5$H$_9$)Pd(dpbb)BF$_4$ (3): $^1$H: 0.82 (dd, 3H, J1 = J2 = 6.0 Hz, anti-CH$_3$); 1.36 (dd, 3H, J1 = 7.4 Hz, J2 = 10.1 Hz, syn-CH$_3$); 1.7 (br m, 4H, CH$_2$-CH$_2$-P); 2.7 (br m, 5H, CH$_2$-CH$_2$-P, allylic H); 3.7 (br, 1H, allylic H); 5.45 (t, 1H, J1 = J2 = 10.8 Hz); 7.2-7.8 (br m, 20H, aromatic H)

$^{31}$P: 21.3 (d, AB, 1P, 49 Hz); 22.2 (d, AB, 1P, 48 Hz)

$^{13}$C ($^1$H): 20.0; 22.9; 25.4; 26.3; 26.9; 63.1; 106.1; 106.9; 113.9; 116.5; 116.6; 129.2; 130.7; 131.3; 134.2; 135.0

HR-MS (FAB): C$_{33}$H$_{35}$P$_2$Pd$^+$ requires m/z = 601.1405, found m/z = 601.1400
(C₃H₅)Pd(dppf)BF₄ (4): ¹H: 1.1 (m, 6H, 2CH₃); 2.82 (t, 1H, J₁ = J₂ = 11.4 Hz, anti-allylic H); 3.68 (t, J₁ = J₂ = 7.2 Hz, syn-allylic H); 3.87 (s, 1H, FcH); 4.19 (s, 1H, FcH); 4.27 (s, 1H, FcH); 4.32 (s, 1H, FcH); 4.41 (s, 1H, FcH); 4.48 (s, 2H, FcH); 4.55 (s, 1H, FcH); 5.49 (dd, 1H, J₁ = 8.1 Hz, J₂ = 13.8 Hz, He); 7.3-7.6 (br m, 18 H, aromatic H); 7.85 (br m, 2H, aromatic H)

³¹P: 22.7 (d, 1P, J = 46 Hz); 26.9 (d, 1P, 46 Hz)

¹³C (¹H): 15.5; 21.1; 26.5; 66.1; 114.3; 116.0; 118.4; 129.2; 129.3; 129.4; 129.5; 130.3; 130.8; 131.3; 131.4; 131.5; 132.1; 132.4; 132.6; 133.1; 133.5; 134.0; 134.4; 134.9

HR-MS (FAB): C₃Η₅FeP₂Pd⁺ requires m/z = 729.0755, found m/z = 729.0748

(C₃H₅)Pd(DPPhos)BF₄ (5): ¹H: 1.06 (t, 3H, J₁ = J₂ = 5.6 Hz, anti-CH₃); 1.23 (dd, 3H, J₁ = 5 Hz, J₂ = 11 Hz, syn-CH₃); 2.84 (t, 1H, J₁ = J₂ = 12.5 Hz, anti-allylic H); 3.63 (dt, 1H, J₁ = J₂ = 7.3 Hz, J₃ = 2.0 Hz, syn-allylic H); 5.51 (dd, 1H, J₁ = 7.9 Hz, J₂ = 13.4 Hz, He); 6.6-7.6 (m, 28H, aromatic H)

³¹P: 13.8 (d, 1P, J = 41 Hz); 14.7 (d, 1P, J = 42 Hz)

¹³C (¹H): 15.1; 21.0; 26.0; 65.6; 113.1; 116.3; 116.4; 118.4; 122.2; 122.6; 122.8; 124.1 (d, J = 6.5 Hz); 125.5 (d, J = 6.5 Hz); 127.4; 128.0; 128.8; 129.0; 130.8; 131.0; 131.2; 134.3 (d, J = 13 Hz); 135.1; 157.9 (d, J = 7.9 Hz)

HR-MS (FAB): C₄H₇OP₂Pd⁺ requires m/z = 713.1354, found m/z = 713.1373

(C₃H₅)Pd(Xantphos)OTf (6): ¹H: 0.9 (t, 3H, J₁ = J₂ = 8.6 Hz, syn-CH₃); 1.04 (t, 3H, J₁ = J₂ = 5.7 Hz, anti-CH₃); 1.4-1.9 (br, 6H, ligand-CH₃'s); 2.74 (br, 1H, anti-allylic H); 3.5 (br, 1H, syn allylic H); 5.70 (t, 1H, J₁ = J₂ = 10.4 Hz); 6.67 (t, 2H, J₁ = J₂ = 7.9 Hz); 7.0-7.6 (br m, 22H, aromatic H); 7.64 (d, 2H, J = 7.6 Hz)

³¹P: 5.3 (br, 1P); 10.4 (br, 1P)

¹³C (¹H): 36.0; 116.0; 114.3; 116.4; 118.8; 123.8; 123.9; 124.6; 124.7; 127.8; 128.8; 129.0; 130.6; 131.7; 132.7; 134.0; 135.4

HR-MS (FAB): C₄H₁₀O₂Pd⁺ requires m/z = 753.1667, found m/z = 753.1685

(C₃H₅)Pd(Xantphos)BF₄ (7): ¹H: 1.54 (s, 3H, ligand-CH₃); 1.81 (s, 3H, ligand-CH₃); 3.5 (m, 2H, anti-allylic H); 3.8 (m, 2H, syn-allylic H); 6.0 (m, 1H, central allylic H); 6.6 (br t, 2H, Ar-H); 7.0-7.5 (br m, 22H, aromatic H); 7.63 (d, J = 7.8 Hz, 2H, aromatic H)

³¹P: 4.3 (s); ¹³C (¹H): 25.9; 30.1; 36.3; 118.0; 118.0; 123.1; 125.0; 128.4; 129.3; 130.9; 132.3; 132.7; 133.2; 134.4; 155.2

HR-MS (FAB): C₄H₇OP₂Pd⁺ requires m/z = 725.1354, found m/z = 725.1365
7.5.3 Calculation of cone angle and solid angle

In the crystal structures, the allyl moiety was removed and a dummy atom was placed in the center of the P-P axis at a non fixed distance to palladium. The two-dimensional cone angle in the P-Pd-P plane has been calculated viewed from the palladium atom in the direction of the dummy atom. The values thus found for the ligands are listed in table 6. In all cases, the ligand has a cone angle larger than 180°. The value found for dppe is the smallest (224.6°) and increases for ligands with a larger bite angle to 246.9° for the Xantphos ligand.

A direct comparison between the different ligands is hampered by the fact that some atoms of the phenyl rings of the ligand can be located slightly below or above the P-Pd-P plane. Since these atoms are not taken into account by the two-dimensional cone angle θ, we calculated the three-dimensional solid angle Ω of these ligands in an analogous manner (see scheme 9). The ligand is again viewed from the palladium atom in the direction of the dummy atom. The solid angle is then determined as a three-dimensional cone angle. The values listed in table 6 represent the space that the ligands occupy after projection on the central metal atom. The thus determined value for the size of the ligand appears to be dependent on the bite angle of the ligand and increases when the bite angle is larger. Again, the smallest value is found for dppe (4.47 sterrad) and the largest is found for Xantphos (5.56 sterrad). The relatively large value found for the dppf ligand is mainly due to the presence of the large ferrocene unit at a short distance to palladium.

Scheme 9: Determination of the cone angle and the solid angle, D=dummy atom (necessary for determining plane of the cone angle).


### 7.5.4 Crystal structure determination

**Table 7:** Crystallographic data for compounds 1, 4, 5 and 7.

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<thead>
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<th>Complex</th>
<th></th>
<th>4</th>
<th>5</th>
<th>7</th>
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<td><strong>Formula</strong></td>
<td>[C3H33OP2Pd]+</td>
<td>[C3H33OP2Pd]+</td>
<td>[C4H53OP2Pd]+</td>
<td>[C4H53OP2Pd]+</td>
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<td>SO3CF3</td>
<td>BF4⁻</td>
<td>BF4⁻</td>
<td>CH2Cl2</td>
<td></td>
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<tr>
<td><strong>λ, Å</strong></td>
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<td>1.5418</td>
<td>1.5418</td>
<td>1.5418</td>
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<td><strong>a, Å</strong></td>
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<td>15.827(3)</td>
<td>11.822(1)</td>
<td>9.153(2)</td>
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<tr>
<td><strong>b, Å</strong></td>
<td>16.101(2)</td>
<td>13.067(2)</td>
<td>12.519(2)</td>
<td>18.0851(9)</td>
</tr>
<tr>
<td><strong>c, Å</strong></td>
<td>18.681(1)</td>
<td>18.267(3)</td>
<td>14.435(2)</td>
<td>12.6484(8)</td>
</tr>
<tr>
<td><strong>α, °</strong></td>
<td>91.601(4)</td>
<td>108.01(1)</td>
<td>78.01(1)</td>
<td>105.409(9)</td>
</tr>
<tr>
<td><strong>β, °</strong></td>
<td>83.84(1)</td>
<td>83.31(1)</td>
<td>83.84(1)</td>
<td>83.84(1)</td>
</tr>
<tr>
<td><strong>γ, °</strong></td>
<td>67.568(8)</td>
<td>67.568(8)</td>
<td>67.568(8)</td>
<td>67.568(8)</td>
</tr>
<tr>
<td><strong>V, Å³</strong></td>
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<td>3592.7(11)</td>
<td>1930.7(5)</td>
<td>2018.5(5)</td>
</tr>
<tr>
<td><strong>Space Group</strong></td>
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<td>Cc</td>
<td>P1</td>
<td>P2₁/m</td>
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<td><strong>Z</strong></td>
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<td>2</td>
<td>2</td>
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<td><strong>Formula Weight</strong></td>
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<td>800.8</td>
<td>812.9</td>
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<td><strong>ρ(obs), g/cm³</strong></td>
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<td>1.51</td>
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<td><strong>μ, cm⁻¹</strong></td>
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<td>85.2</td>
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<td>255</td>
<td>293</td>
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<tr>
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<td>0.059</td>
<td>0.091</td>
</tr>
<tr>
<td><strong>R</strong>*</td>
<td>0.067</td>
<td>0.080</td>
<td>0.061</td>
<td>0.103</td>
</tr>
</tbody>
</table>

* R = Σ(|F_obs| - |F_calc|) / Σ(|F_obs|), ** R_w = Σ[w(|F_obs| - |F_calc|)^2] / Σ(w|F_obs|^2)

Data (table 7) were collected on an Enraf-Nonius CAD-4 diffractometer with graphite-monochromatized CuKα radiation and ω-2θ scan. Corrections for Lorentz and polarisation effects were applied.

Absorption correction was performed with the program PLATON, following the method of North et al. using Ψ-scans of five reflections for all four compounds. The structures were solved by the PATTY option of the DIRDIF96 program system. The hydrogen atoms were calculated. Full-matrix least-squares refinement was carried out on F, anisotropic for the non-hydrogen atoms and isotropic for the hydrogen atoms, restraining the latter in such a way that the distance to their carrier remained constant at approximately 1.0Å. converged Scattering factors were taken from Cromer and Mann; International Tables for X-ray
P-P ligands, dimethyl allyl complexes.

Crystallography.\textsuperscript{[24]} Anomalous scattering was taken into account.\textsuperscript{[25]} All calculations were performed with XTAL\textsuperscript{[26]} unless stated otherwise. For (4) the BF\textsubscript{4} moiety was kept fixed at ideal geometry with isotropic temperature factors U=0.15 Å\textsuperscript{2} for B and U=0.25 Å\textsuperscript{2} for F; the hydrogen atoms were kept fixed at their calculated positions with U=0.10 Å\textsuperscript{2}. (5) showed some disorder which was dealt with in the following way: C(2) was divided over two half occupied positions and all H atoms connected to atoms C(1)-C(5) were kept fixed at their calculated positions with U=0.10 Å\textsuperscript{2}; the BF\textsubscript{4} moiety also showed disorder and all F-atoms were divided over three 1/3 occupied position and were kept restrained geometrically to values from literature and were refined isotropic. After refinement some residual electron density was found in a ΔF synthesis. It was impossible to interpret this density so it was decided to correct for it by using the option SQUEEZE in the program package PLATON.\textsuperscript{[20, 21]} For compound (7) BF\textsubscript{4} was refined isotropic, the solvent molecule consists of two half occupied molecules which share their Cl-atoms through the centre of symmetry; the solvent molecule was refined isotropically and the H-atoms of the solvent were kept fixed with U=0.10 Å\textsuperscript{2} the remainder of the H-atoms were restrained with fixed temperature factors U=0.10 Å\textsuperscript{2}.

Supporting information available: X-ray crystallographic files in CIF format for the structure determinations of complexes 1, 4, 5 and 7. This material is available free of charge via the Internet at http://pubs.acs.org
7.6 References


P-P ligands, dimethyl allyl complexes.


Chapter 8.
The effect of ligand donor atoms of wide bite angle ligands on the regioselectivity in the palladium catalyzed allylic alkylation of a disubstituted allyl moiety.

In the previous chapter we showed that the non-symmetry of the Pd(\(\eta^3\)-allyl) bond is enhanced for di-, compared to mono-substituted allyl moieties. The DFT calculations in chapter 3 predict an enhanced non-symmetry when the ligand carries two different donor atoms, which is confirmed in chapter 6. In addition, the results of chapters 4-7 show that a large bite angle of the ligand generally leads to an increase of the non-symmetry and the regioselectivity for the branched product.

In this chapter, we study the combination of these parameters, using a \((3,3-(CH_3)_2-C_5H_5)\) allyl moiety, wide bite angle Xantphos based ligands, carrying different combinations of donor atoms.

Abstract

The regioselectivity of the palladium catalyzed allylic alkylation was studied systematically using bidentate ligands based on a xanthene backbone, bearing different donor atoms. The nature of the ligand donor atoms has a pronounced influence on the regioselectivity of the reaction. The results can be explained by a mechanism that distinguishes two 'stages' in the alkylation reaction. Ligands bearing strong \(\pi\)-acceptor donor atoms induce the formation of branched products (60\% for the P-P derivative), whereas the use of ligands with weak \(\pi\)-acceptor donor atoms mainly yields linear products (>99\% for the N-N derivative).

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8.1 Introduction

The palladium catalyzed allylic alkylation is a useful tool in synthetic organic chemistry\[1\]. Much research has been devoted to optimizing and understanding the enantioselectivity of the reaction, mainly using substrates such as Z-cyclohex-2-enyl acetate, E-1,3-diphenyl-prop-2-enyl-1 acetate or related compounds.\[1-4\]

In the catalytic cycle, these substrates add oxidatively to Pd(0) to form (ligand)Pd\(\eta^3\)-allylOAc complexes, bearing a symmetrically substituted allyl group. Carbon-carbon bond formation by nucleophilic attack takes place at one of the two terminal allylic carbon atoms and consequently a chiral product is formed (figure 1).

![Figure 1. Allylic alkylation of cyclohexenyl acetate.](image1)

When substrates are used that form a non-symmetric \(\eta^3\)-allyl complex, regiocontrol becomes an issue in addition to enantiocontrol (figure 2).\[5-8\] Compared to the vast amount of studies towards the enantioselective allylic alkylation, relatively few studies are concerned with the regioselectivity of this reaction.\[5-17\]

![Figure 2. Allylic alkylation of a non-symmetric \(\eta^3\)-allyl complex.](image2)

In chapter 5, we showed that for the allylic alkylation of E-hex-2-enyl acetate (R=propyl, R'=H), attack at the non substituted (R'=H), is favored for all examined ligands, leading to the non chiral linear product. The use of ligands enforcing a larger bite angle leads to an increase of the regioselectivity to the linear product up to 100%. These results were explained in terms of steric hindrance: a larger bite angle of the ligand results in a larger cone angle of the ligand.

In chapter 7, we showed the opposite trend in regioselectivity for 3-methyl-buteryl complexes. We rationalized this in terms of the symmetry of the palladium-\(\eta^3\)-allyl bond (see also references 11, 15, 17). A distortion of the symmetry of the Pd-allyl bond leads to activation for nucleophilic attack of the allylic
carbon atom having the largest Pd-C distance. For bidentate PP ligands, we showed that in the crystal
structures of a series of (P-P)Pd(3,3-(CH₃)₂-C₃H₅)OTf complexes the symmetry of the Pd-allyl bond depends
on the cone angle of the P-P ligand (figure 3). As a result of the increased steric hindrance, a large cone
angle of the ligand results in a large distortion of the Pd-η²-C₃H₅ bond. The bond is almost symmetric in the
dppe (1,2-(bisdiphenylphosphino)ethane) modified complex while in the DPEphos (bis(2-diphenylphosphino-phenyl)-ether, figure 3) modified complex the Pd-allyl bond is significantly distorted to
an η¹-η² bonding mode (figure 4). Due to this distortion, the substituted carbon atom (C3) is more
electrophilic than the non substituted allylic carbon atom (C1). A larger distortion seemed to result in a larger
difference in electrophilicity between the terminal carbon atoms. Stoichiometric reaction of these complexes
with a nucleophile (sodium diethyl 2-methyl-malonate) led to the formation of two regio-isomeric products.
Attack on the unsubstituted carbon atom (C1) yields the linear olefin B and attack on the substituted carbon
atom (C3) yields the branched olefin A. The regioselectivity of the reaction varied from 8/92 (B/A) for dppe
to 60/40 for Xantphos (chapter 7).

Figure 3. Diphosphine ligands used in chapter 7.

Figure 4. Distortion of the Pd-allyl bond in (allyl)Pd(PP) complexes and products of the allylic alkylation.
Amongst others, Vrieze and co-workers\cite{81} showed that also the nature of the donor atoms is an important factor in the allylic alkylation. To gain more insight in the factors determining the regioselectivity of the reaction, we decided to explore the electronic effect of ligands that all enforce a large bite angle, but differ in the nature of the donor atoms (figure 5).\cite{19} Using these ligands, we prepared a series of cationic (3-methyl-buteny1)Pd(ligand) complexes and used them in the stoichiometric allylic alkylation.

![Figure 5. Structure of Xanthene based ligands used in this work.](image)

8.2 Results

To study the electronic effect of the donor atom of the ligand on the allylic alkylation, the ligands a-f\cite{19} were used to synthesize the corresponding (ligand)Pd(3,3-(CH\textsubscript{3})\textsubscript{2}-C\textsubscript{3}H\textsubscript{3})OTf complexes\cite{17} la-f by coupling to [(3,3-(CH\textsubscript{3})\textsubscript{2}-C\textsubscript{3}H\textsubscript{3})PdCl\textsubscript{2}]\cite{20} followed by abstraction of the chloride atom using AgOTf.

8.2.1. Structure of the complexes (NMR, crystal structures)

As evidenced by the characteristic resonances in \textsuperscript{1}H-NMR, the allyl group is bonded in the π-fashion in all cases (see chapters 4-7). The complexes of the ligands bearing two different donor atoms (1b and 1c) were formed in two isomeric structures. In principle, the complexes 1b and 1c can exist in four different isomeric structures. The results obtained in chapter 6 indicate, that the methyl groups of the allyl can be oriented trans to P or trans to As/N and for both these structures, the allyl can be oriented up or down with respect to the Xanthene backbone. The isomeric structures can be distinguished by the chemical shift and by comparison of the values of \(J(P-H)\) in the different complexes. Unfortunately, the NMR signals of the complexes 1b and 1c are too broad to allow a definitive assignment based on \(J(P-H)\). In chapter 6 we showed, that similar complexes of PN-ligands are also formed in two isomers, identified as the 'up' and 'down' isomers of the
Wide bite angle ligands, dimethyl allyl complexes.

complex in which the substituent on the allyl was oriented trans to the phosphorus. We therefore conclude that the different isomers of the complexes 1b and 1c are also the trans-P 'up' and 'down' isomers.

![Diagram of different isomeric structures of 1b and 1c.](image)

Figure 6: Different isomeric structures of 1b and 1c.

We were able to obtain crystals of compound 1f, suitable for structure determination by X-ray crystallography (figure 7). A comparison between the crystal structure of 1f and those of the already mentioned bidentate phosphorus analogues is presented in table 1.

The distance of the triflate counterion to palladium in complex 1f is large (d(Pd-S)=7.152 Å) and the palladium complex can thus be regarded as a cationic fragment. The structure of 1f resembles the crystal structures (chapter 7) of analogous complexes bearing bidentate phosphine ligands, such as dppe, dppf, DPEphos and Xantphos (table 1, figure 3). A more detailed analysis, however, reveals some remarkable features. In the complexes of the PP ligands, the allyl moiety is not bonded symmetrically to the palladium. Compared to the C$_{6}$H$_{5}$ complex, the C1-C2 bond is elongated and the C2-C3 bond is shortened. At the same time, the Pd-C1 bond is shortened and the Pd-C2 and Pd-C3 bonds are elongated. It was found that for these ligands, two phenyl rings are located in the Pd-allyl plane. Therefore, a wide P-Pd-P bite angle results in a large cone angle and, via increased steric interaction of the ligand with the allyl moiety, induces a distorted symmetry of the Pd-allyl bond (chapter 7).
Table 1: Comparison of selected structural data of crystal structures of allyl complexes of dppe, dppf, DPEphos, Xantphos and SS-xanthene (distances in Å, angles in °).

<table>
<thead>
<tr>
<th>ligand</th>
<th>C₃H₃P₃Pd⁺ CF₅SO₃⁻</th>
<th>C₃H₃FeP₂P₂⁺ BF₄⁻</th>
<th>C₄H₅OP₂P₂⁺ BF₄⁻</th>
<th>C₂₂H₅OS₂Pd⁺ CF₅SO₃⁻</th>
</tr>
</thead>
<tbody>
<tr>
<td>dppe</td>
<td>1.42(1)</td>
<td>1.39(1)</td>
<td>1.34(2)</td>
<td>1.413(10)</td>
</tr>
<tr>
<td>dppf</td>
<td>1.41(2)</td>
<td>1.41(2)</td>
<td>1.34(2)</td>
<td>1.314(17)</td>
</tr>
<tr>
<td>DPEphos</td>
<td>1.50(1)</td>
<td>1.48(1)</td>
<td>1.482(18)</td>
<td></td>
</tr>
<tr>
<td>Xantphos</td>
<td>1.51(1)</td>
<td>1.58(2)</td>
<td>1.48(1)</td>
<td>1.628(18)</td>
</tr>
<tr>
<td>allyl</td>
<td>2.185(9)</td>
<td>2.161(7)</td>
<td>2.161(7)</td>
<td>2.144(8)</td>
</tr>
<tr>
<td>C1C2</td>
<td>2.174(7)</td>
<td>2.21(1)</td>
<td>2.16(1)</td>
<td>2.123(10)</td>
</tr>
<tr>
<td>C2C3</td>
<td>2.253(7)</td>
<td>2.291(18)</td>
<td>2.37(1)</td>
<td>2.192(10)</td>
</tr>
<tr>
<td>C3syn</td>
<td>2.296(2)</td>
<td>2.336(2)</td>
<td>2.372(2)</td>
<td>2.424(3)</td>
</tr>
<tr>
<td>C3Canti</td>
<td>2.293(2)</td>
<td>2.379(2)</td>
<td>2.372(2)</td>
<td>2.411(3)</td>
</tr>
<tr>
<td>PdC1</td>
<td>85.77(6)</td>
<td>101.1646</td>
<td>103.96(3)</td>
<td>103.35(9)</td>
</tr>
</tbody>
</table>

*obtained from chapter 7

For the disulfide ligand f, the observed bite angle of 103.35(9)° is smaller than that found for the analogous diphosphine ligand a. The Xanthene backbone is not flat, but slightly folded (figure 7). The folding of the Xanthene backbone in the disulfide ligand f is larger than that found for the diphosphine Xantphos a (35.5° versus 27.4°).

In contrast to the phenyl rings of the diphosphine ligand a, the methyl substituents on each of the sulfur atoms do not point in the direction of the allyl moiety and the steric interaction of the ligand with the allyl is minimal. The observed Pd-C₃ distances are slightly shorter than found for the diphosphine ligands. In contrast to the complexes with the bidentate phosphine ligands, however, the Pd-C1 and Pd-C3 distances, are similar. The C1-C2 distance (1.413 Å) is similar to the C1-C2 distance (1.42 Å) found for the diphosphine ligands, but the C2-C3 bond (1.314 Å) is much shorter. Furthermore, in contrast to the diphosphine-modified complexes, the allyl moiety is rotated around the Pd-allyl axis. The C2 atom is located 0.17 Å above the S-Pd-S plane and the C1 atom is 0.17 Å below the S-Pd-S plane, while C3 is located only 0.09 Å below the S-Pd-S plane. Such a rotated structure has been observed before using a 1,3-diphenyl-allyl moiety and a P-S ligand, or a P-N ligand.
Figure 7. Three views of the crystal structure of If (hydrogen atoms omitted for clarity). Top figure: showing the slight rotation of the allyl group, middle figure: showing the orientation of the Me-substituents on the sulfur atoms and bottom figure: showing folding of the Xanthene backbone.

8.2.2 Stoichiometric alkylation

To study the effect of the donor atom of the ligand on the regioselectivity of the stoichiometric allylic alkylation, the complexes 1a-f were treated with sodium diethyl 2-methylmalonate. The results presented in table 2 show that the nature of the ligand donor atoms has a pronounced effect on the regioselectivity of the reaction. The branched/linear product distribution ranges from 1/99 (A/B) for complex 1e to 60/40 (A/B) for
complex 1a. Thus, the bidentate nitrogen ligand e is much more selective in forming the linear product B than any of the bidentate phosphorus ligands used previously.

Table 2: Comparison of the regioselectivity of the stoichiometric alkylation of complexes bearing PP-ligands and of complexes 1a-f.

<table>
<thead>
<tr>
<th>ligand</th>
<th>Bite angle</th>
<th>% branched (A)</th>
<th>% linear (B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>dppe</td>
<td>85.77(6)a</td>
<td>8</td>
<td>92</td>
</tr>
<tr>
<td>dpff</td>
<td>101.2(3)a</td>
<td>13</td>
<td>87</td>
</tr>
<tr>
<td>DPEphos</td>
<td>103.96(3)a</td>
<td>41</td>
<td>59</td>
</tr>
<tr>
<td>PP-xanthene (1a)</td>
<td>108.11(7)a</td>
<td>61</td>
<td>39</td>
</tr>
<tr>
<td>P-As-xanthene (1b)</td>
<td>105.4b</td>
<td>38</td>
<td>62</td>
</tr>
<tr>
<td>P-N-xanthene (1c)</td>
<td>106.0b</td>
<td>26</td>
<td>74</td>
</tr>
<tr>
<td>As-As-xanthene (1d)</td>
<td>107.6b</td>
<td>13</td>
<td>87</td>
</tr>
<tr>
<td>N-N-xanthene (1e)</td>
<td>d</td>
<td>1</td>
<td>99</td>
</tr>
<tr>
<td>S-S-xanthene (1f)</td>
<td>103.35(9)a</td>
<td>5</td>
<td>95</td>
</tr>
</tbody>
</table>

*a bite angle determined from crystal structure.

*bite angle determined by semi-empirical PM3(tm) calculations of the corresponding complexes

c data taken from chapter 7

d no global minimum could be found using PM3(tm)

8.3 Discussion

8.3.1 Mechanism, hypothesis

Much has been reported concerning the mechanism of the palladium catalyzed allylic alkylation.¹¹⁻¹⁷ Both experimental and theoretical studies support a mechanism via a late transition state, i.e. in the transition state the allyl moiety resembles the olefin product.¹¹⁻⁴ In contrast, some results seem to support an early transition state model in which the regioselectivity is determined by electronic factors in the η³-allyl complex.¹¹⁻¹⁴,¹⁶⁻¹⁷ In summary, the relative importance of steric and electronic factors depends on the bite angle of the ligand, on the nature of the substituents (e.g. phenyl or methyl) and on the orientation of the substituents (syn or anti).¹¹⁻¹³,¹⁶⁻¹⁷ The results presented in this paper can be explained in terms of these effects. In addition to the factors mentioned above, the nature of the donor atoms (donor/acceptor properties) are important for the transition state of the reaction too.
8.3.2 Effect of the nature of the donor atoms on the structure

It has been proposed that the regioselectivity of the reaction depends on the distortion of the symmetry of the Pd-allyl bond, which in turn depends on both steric and electronic factors. In the present series of ligands, the steric bulk (cone angle) will be approximately the same for all ligands (except for the disulfide ligand). The various donor atoms used in this paper differ significantly in donor and acceptor properties. A decrease in σ-donation from the ligand to the metal will result in a decrease of electron density on the palladium and consequently will lead to an increase of the bonding interaction from the allyl to palladium. Analogously, a decrease in the π back donation from the metal to the ligand, will result in an increase of electron density in the π-system of the palladium atom and the π back donation from the palladium to the allyl moiety will be enhanced. The ligand causes a change in the donating bonding interaction of the allyl to the metal. This does not affect the allyl-LUMO, but the effect of the ligand on the π back donation of the palladium to the ligand does influence the energy level of the allyl-LUMO. A weak π acceptor ligand causes more π-back donation to the allyl which results in a higher energy level of the anti-bonding combination of the Pd-allyl bond and consequently a less electrophilic allyl moiety. Furthermore, an increase of the π-back-donation to the allyl will result in an increase of the symmetry of the Pd-allyl bond. This is reflected in the crystal structure of 1f, in which the Pd-allyl bond is shorter and much less distorted than in the corresponding diphosphine complexes.

In addition, the absence of steric interaction between the ligand and the allyl group in 1f only results in a relatively small distortion of the Pd-allyl bond. The allyl itself resembles the structure of an internal olefin. The Pd-C3 distance, however, is only slightly larger than the Pd-C1 distance, whereas in the structures of the complexes bearing bidentate phosphine ligands, the Pd-C1 distance is much shorter than the Pd-C3 distance. The C2-C3 bond in 1f is much shorter than the C1-C2 bond and is mainly olefinic in nature.

In the complexes bearing the ligands b-e with less strong π-accepting donor atoms, the allyl group will be deformed. Because the steric interaction of the allyl with the phenyl rings of these ligands will be much larger than with the methyl groups of ligand f, the π'-π type distortion of the Pd-allyl bond as found for the diphosphine ligands can be expected for steric reasons.

8.3.3 Effect of the nature of the donor atom on the regioselectivity

In the case of the diphosphine ligand a, attack on C3 is favored for electronic reasons (chapter 3). Upon nucleophilic attack, the two methyl substituents on the allyl rotate out of the P-Pd-P plane and the steric interaction with the phenyl rings of the ligand will be minimized during the rotation of the allyl group. On the other hand, allyl rotation after nucleophilic attack on C1 will leave the methyl substituents in the P-Pd-P plane, thereby maximizing the steric interactions with the phenyl rings. In the case of a late transition state,
the relative thermodynamic stability of the products may become an important factor and formation of the internal olefin B may be favored.

The selectivity for the formation of the branched product (terminal olefin A) decreases with decreasing \( \pi \)-accepting properties of the ligand donor atoms. Thus, going from P-P (a) to N-N (e), the allyl moiety compensates for the weaker \( \pi \)-accepting properties of the ligand and becomes less electrophilic. In other words, the allyl-LUMO will be higher in energy for the complex bearing the bidentate nitrogen ligand. The energy gain upon nucleophilic attack will be less than for the diphosphine modified complex and it is therefore more likely that the C-C bond formation is reversible for the diamine complex. Thus, the formation of the branched product A is favored for the diphosphine ligand as a result of the relative electrophilicity of C1 and C3, whereas product B is favored for the bidentate nitrogen ligand as a result of its relative thermodynamic stability.

For the ligands a-f, the regioselectivity of the mixed ligands is in between the results of the corresponding symmetric ligands. This statement does not apply to other mixed ligands, since many examples are known of mixed P-N ligands that favor the formation of the branched product with up to 99% regioselectivity.\(^{[5-8]}\)

In complexes 1b and 1c, C3 will be more electrophilic than C1, which is reflected in the observed regioselectivity. For the P-As complex (1b), the strong \( \pi \)-acceptor properties of the phosphorus results in an increase of the selectivity for product A relative to the As-As complex (1d). Analogously, the weaker \( \pi \)-acceptor properties of the arsine lead to a decrease of the selectivity for product A compared to the diphosphine complex (1a).

8.4 Conclusion

In the allylic alkylation catalyzed by Pd complexes with bidentate ligands based on a Xanthene backbone, the donor atoms have a pronounced influence on the regioselectivity of the reaction. The formation of the branched product A is relatively favored for the ligands bearing the stronger \( \pi \)-acceptor, whereas the ligands bearing the weaker \( \pi \)-acceptors favor the linear product B. The results are explained in terms of the relative electrophilicity of the non-substituted C1 atom (leading to B) compared to that of the substituted C3 atom (leading to A).

We propose that the overall regioselectivity of the reaction is determined by three factors:
1) the overall electrophilicity of the allyl moiety,
2) the relative electrophilicity of C1 and C3 and
3) the thermodynamic stabilities of the products.
Wide bite angle ligands, dimethyl allyl complexes.

8.5 Experimental

8.5.1 General procedures

$^1$H NMR (300 MHz, TMS, CDCl$_3$), $^{31}$P [$^1$H] (121.5 MHz external 85% H$_3$PO$_4$, CDCl$_3$) were recorded on a Bruker AMX-300 spectrometer. The product distribution of allylic alkylation was measured by GC on an Interscience Mega2 apparatus, equipped with a DB1 column, length 30 m, inner diameter 0.32 mm, film thickness 3.0 µm, and a F.I.D detector. All experiments were carried out using standard Schlenk techniques. All solvents were freshly distilled prior to use. All reactions have been performed at room temperature (292 K). Sodium diethyl 2-methylmalonate (0.5 M in THF) was prepared from diethyl 2-methylmalonate and NaH in THF at 273 K.

8.5.2 Syntheses and characterization

The syntheses of ligands a-e have been published elsewhere.$^{[19]}$

Ligand f (S-S):

1.0 gram (4.8 mmol) of xanthene was dissolved in 50 mL of diethyl ether and 2.2 mL (14.3 mmol) of TMEDA was added. After cooling to 273K, 11 mL (1.3 M in cyclo-hexane, 14.3 mmol) of sec-BuLi was slowly added to the solution. The reaction mixture was stirred for 20 hours at 293K. After cooling to 203K, 0.458 g (14.3 mmol) of S$_8$ was added and the reaction mixture was slowly warmed to 293K (6 h.). After cooling to 195K, 1.2 mL (19.0 mmol) of MeI was added and the reaction mixture was stirred overnight at room temperature. After 20 h., water was added and the mixture was extracted with CH$_2$Cl$_2$ and water. The organic fractions were dried over Na$_2$SO$_4$ and the crude product was further purified by column chromatography using 5% ethyl acetate in PE 60/80. Recrystallization from CH$_2$Cl$_2$/hexane yielded 0.42 g (29 %) as white crystals. $^1$H NMR (CDCl$_3$) 1.61 (s, 6H, CH$_3$); 2.53 (s, 6H, SCH$_3$); 7.09 (d, 4H, ArH, J = 4.7 Hz); 7.22 (t, 2H, ArH, J = 4.7 Hz).

The Pd-complexes were prepared in CH$_2$Cl$_2$ from [(C$_5$H$_5$)$_2$Pd-μCl]$_2$ $^{[20]}$ by adding 2 eq. of ligand and abstracting the chloride with AgOTf.$^{[17]}$ The complexes were isolated in quantitative yield (microcrystalline powder) and were used as such in the alkylation reaction. The synthesis and characterization of complex 1a is described elsewhere.$^{[17]}$

1b (P-As)Pd(C$_5$H$_5$)$_2$OTf$^-$:

Major isomer (70%): $^1$H-NMR: 1.10 (br b, 18H, tBu), 1.25 (br b, 6H, C(CH$_3$)$_2$), 1.41 (br b, 3H, allyl CH$_3$-anti), 1.86 (br b, 3H, allyl CH$_3$-syn), 3.06 (br d, 1H, J = 13 Hz, H-anti), 3.50 (br b, 1H, H-syn), 5.71 (br m, 1H, H-meso), 6.5-7.6 (m, 24H, H-aromatic). $^{31}$P NMR: 10.9.
Minor isomer (30%): $^1$H NMR: 1.10 (br b, 18H, tBu), 1.25 (br b, 6H, C(CH$_3$)$_2$), 1.3 (br b, 3H, allyl CH$_3$-anti), 1.75 (br b, 3H, allyl CH$_3$-syn), 3.81 (br b, 1H, H-anti), 4.2 (br m, 1H, H-syn), 5.7 (br m, 1H, H-meso), 6.5-7.6 (m, 24H, H-aromatic). $^{31}$P NMR: 7.6.

HRMS: C$_{52}$H$_{58}$AsOPPd$^+$ requires m/z=910.2476, found 909.2405 (C$_{50}$H$_{58}$AsOPPdNa$^+$)

1c (P-N)Pd(C$_4$H$_9$)′OTf$^-$:

$^1$H-NMR: 1.06 (br s, 9H, tBu), 1.23 (br s, 9H, tBu), 1.53 (br b, 6H, C(CH$_3$)$_2$), 1.85 (br b, 6H, allyl CH$_3$-syn+anti), 2.15 (br b, 2H, allyl-H-syn+anti), 4.21 (br b, 1H, H-meso), 6.3-7.6 (m, 24H, H-aromatic). $^{31}$P NMR: 22.2 (br b).

HRMS: C$_{52}$H$_{58}$NOPPd$^+$ requires m/z=849.3291, found 848.3190 (C$_{50}$H$_{58}$AsOPPdNa$^+$)

1d (As-As)Pd(C$_4$H$_9$)′OTf$^-$:

$^1$H-NMR: 1.11 (br s, 21H, tBu + allyl CH$_3$-anti), 1.33 (br s, allyl-CH$_3$-syn), 1.65 (br s, 6H, C(CH$_3$)$_2$), 3.27 (d, 1H, J = 13 Hz, H-anti), 3.81 (d, 1H, J = 6 Hz, H-syn), 5.69 (dd, 1H, J1 = 13 Hz, J2 = 6 Hz, H-meso), 6.6-7.6 (m, 24H, H-aromatic).

HRMS: C$_{52}$H$_{58}$As$_2$OPd$^+$ requires m/z=953.1876, found 953.1913

1e (N-N)Pd(C$_4$H$_9$)′OTf$^-$:

$^1$H-NMR: 1.26 (br s, 24H (t-Bu + ligand CH$_3$), 1.70 (br s, 6H, allyl-CH$_3$‘s), 2.87 (d, 1H, J = 12 Hz, H-anti), 3.85 (d, 1H, J = 7 Hz, H-syn), 5.64 (dd, 1H, J1 = 12 Hz, J2 = 7 Hz, H-meso), 6.5-7.5 (br m, 24H).

1f (S-S)Pd(C$_4$H$_9$)′OTf$^-$:

HRMS: C$_{22}$H$_{28}$OPdS$_2$ requires m/z = 478.0616, found 478.0624

8.5.3 Allylic Alkylation

The stoichiometric alkylation reactions were performed by adding an excess of sodium diethyl 2-methylmalonate (0.1 ml of a 0.5 M solution in THF) to a solution of 10 mg of the Pd-complex in 1 ml of THF. Reaction was instantaneous and after one minute, the mixture was worked up with water, filtered over silica and analysed by GC. All alkylation experiments were carried out in triplo.
8.5.4 Structure determination

A crystal with dimensions 0.20 x 0.30 x 0.40 mm approximately was used for data collection on an Enraf-Nonius CAD-4 diffractometer with graphite-monochromated CuKα radiation and ω-2θ scan. A total of 5131 unique reflections was measured within the range -9≤h≤10, 0≤k≤15, 0≤l≤31. Of these, 4225 were above the significance level of 4σ(Fobs) and were treated as observed. The range of (sin θ)/λ was 0.040-0.626Å (3.5≤θ≤74.8°). Two reference reflections ([2 2 0], [1 0 7]) were measured hourly and showed no decrease during the 84 h collecting time. Unit-cell parameters were refined by a least-squares fitting procedure using 23 reflections with 39.91≤θ≤41.70. Corrections for Lorentz and polarization effects were applied. Absorption correction was performed with the program PLATON,[21] following the method of North et al.[22] using Ψ-scans of five reflections, with coefficients in the range 0.498-0.988. The structure was solved by the PATTY option of the DIRDIF99 program system.[23] The hydrogen atoms were calculated. Full-matrix least-squares refinement on F, anisotropic for the non-hydrogen atoms and isotropic for the hydrogen atoms, restraining the latter in such a way that the distance to their carrier remained constant at approximately 1.0 Å and keeping their atomic displacement parameters fixed at U=0.10Å², converged to R=0.080, Rw=0.089, (Δσ)max=0.07, S=1.11. A weighting scheme w=[13. + 0.01*(σ(Fobs))² + 0.01/(σ(Fobs))]-¹ was used. The secondary isotropic extinction coefficient[24] refined to G=240(64). A final difference Fourier map revealed a residual electron density between −1.2 and 2.1 e Å⁻³ in the vicinity of the Pd. Scattering factors were taken from Cromer and Mann,[25] International Tables for X-ray Crystallography.[26] The anomalous scattering of Pd and S was taken into account.[27] All calculations were performed with XTAL3.7[28], unless stated otherwise.

[C₂₃H₂₇OS₃Pd]⁺ SO₃CF₃⁻, Mr=271.1, monoclinic, P2₁/n, a=8.2790(5), b=12.2683(9), c=25.136(8)Å, β=92.71(2)°, V=2550.2(8)Å³, Z=4, Dx =1.633 g cm⁻³, λ(CuKα)=1.5418Å, μ(CuKα)=86.12 cm⁻¹, F(000)=1272, room temperature, Final R=0.080 for 4225 observed reflections.
Chapter 8

8.6 References

Wide bite angle ligands, dimethyl allyl complexes.


Chapter 9
Allylic alkylation: an evaluation.

9.1 Introduction

In chapter 2 we argued that the late transition state model as described by Trost, although useful in most cases, fails to explain some of the reported regioselectivities. An early transition state mechanism may be a more useful alternative in those cases. In chapter 3, it was shown by DFT studies that both the hydrocarbyl substitution of the allyl moiety and a larger bite angle of the ligand enhance the electrophilicity of the allyl. For substituted allyl groups, the same factors cause a distortion of the Pd-(η₃-allyl) bond to η¹-η², thereby increasing the regioselectivity for attack on the substituted allylic carbon atom C3 (figure 1), leading to the branched product. In chapters 4-8 we studied the influence of several parameters on the regioselectivity in the allylic alkylation.

Figure 1: Numbering scheme.

In this chapter, an overview of the results is presented, followed by an evaluation of both the early and the late transition state mechanisms. Finally, a model is presented that accounts for our experimental results. Based on the modeling results (chapter 3) we reasoned that, if the regioselectivity is determined by an early transition state mechanism, alkylation of all substituted allyl moieties studied in chapter 3 will lead to a significant percentage of the branched product. A relatively high selectivity was expected for the dimethyl substituted allyl. Use of P-N ligands was expected to enhance the regioselectivity. Based on the calculated structures, the relative regioselectivity arising from the syn and the anti crotyl moieties was hard to predict. If the non-symmetry of the syn-isomer would be as pronounced as suggested by the DFT calculations, the regioselectivity for the branched product on alkylation of the syn-isomer could be higher. If, however, the calculated partial sp³ hybridization on C3 of the anti-isomer would be important for the regioselectivity, the regioselectivity could be higher for the anti-isomer.
9.2 Overview of alkylation results

Based on the results of the allylic alkylation experiments several parameters influencing the regioselectivity have been identified. A summary of these parameters and their effect on the regioselectivity is presented in table 1.

Table 1: Overview of the parameters influencing the regioselectivity of the palladium catalyzed allylic alkylation (chapter 4-8).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>see chapter</th>
<th>Linear product favored if (example)</th>
<th>Branched product favored if (example)</th>
<th>origin of effect</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Allyl parameters</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Size of the syn-substituent on allyl moiety</td>
<td>5</td>
<td>large (C₃H₇)</td>
<td>small (CH₃)</td>
</tr>
<tr>
<td>2</td>
<td>Number of substituents</td>
<td>7</td>
<td>1 (crotyl)</td>
<td>2 (dimethyl allyl)</td>
</tr>
<tr>
<td>3</td>
<td>Mixture of E and Z substrates</td>
<td>5</td>
<td>long reaction time</td>
<td>short reaction time</td>
</tr>
<tr>
<td>4</td>
<td>Orientation of the substituent in mono substituted allyl groups</td>
<td>4 and 5</td>
<td>syn</td>
<td>anti</td>
</tr>
<tr>
<td>5</td>
<td>Leaving group can coordinate to Pd (dissymmetric ligands)</td>
<td>6</td>
<td>no (OTFA)</td>
<td>yes (Cl)</td>
</tr>
<tr>
<td>6</td>
<td>Leaving group can coordinate to Pd (symmetric ligands)</td>
<td>4, 5, 6</td>
<td>yes (OAc)</td>
<td>no (OTf)</td>
</tr>
</tbody>
</table>
Table 1 (continued): Overview of the parameters influencing the regioselectivity of the palladium catalyzed allylic alkylation (chapter 4-8).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>see chapter</th>
<th>Linear product favored if (example)</th>
<th>Branched product favored if (example)</th>
<th>nature of effect</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ligand parameters</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7 π-acceptor capabilities of donor atoms (both are the same)</td>
<td>8</td>
<td>small (N)</td>
<td>large (P)</td>
<td>electronic</td>
</tr>
<tr>
<td>8 Symmetry of the ligand with respect to the donor atoms</td>
<td>6</td>
<td>P-P</td>
<td>P-N</td>
<td>electronic</td>
</tr>
<tr>
<td>9 Position of P in allyl complexes of P-N ligands</td>
<td>6</td>
<td>cis to C3</td>
<td>trans to C3</td>
<td>electronic</td>
</tr>
<tr>
<td>10 Bite angle</td>
<td>4-7</td>
<td>small</td>
<td>large</td>
<td>electronic</td>
</tr>
<tr>
<td>11 Cone angle, mono-substituted syn</td>
<td>4 and 5</td>
<td>large</td>
<td>small</td>
<td>steric</td>
</tr>
<tr>
<td>12 Cone angle, mono-anti and disubstituted</td>
<td>4, 5 and 7</td>
<td>small</td>
<td>large</td>
<td>electronic</td>
</tr>
<tr>
<td><strong>Other parameters</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13 Strength of nucleophile</td>
<td>ref 1</td>
<td>relatively soft</td>
<td>relatively hard</td>
<td>electronic</td>
</tr>
</tbody>
</table>

Table 2: Overview of the parameters influencing the reaction rate of the Pd catalyzed allylic alkylation.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>see chapter</th>
<th>slow if (example)</th>
<th>fast if (example)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Allyl parameters</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14 Size of the syn substituent in mono substituted allyl groups</td>
<td>5</td>
<td>large (C3H7)</td>
<td>small (CH3)</td>
</tr>
<tr>
<td>15 Orientation of the substituent in monosubstituted allyl groups</td>
<td>5</td>
<td>anti</td>
<td>syn</td>
</tr>
<tr>
<td>16 Number of substituents</td>
<td>7</td>
<td>more</td>
<td>less</td>
</tr>
<tr>
<td>17 Coordinating properties of the leaving group</td>
<td>5</td>
<td>strongly coordinating (OAc)</td>
<td>weakly coordinating (OTFA)</td>
</tr>
</tbody>
</table>
Table 2 (continued): Overview of the parameters influencing the reaction rate of the Pd catalyzed allylic alkylation.

<table>
<thead>
<tr>
<th>Ligand parameters</th>
<th>18</th>
<th>19</th>
<th>20</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \pi )-acceptor capabilities of donor atoms (both are the same)</td>
<td>8</td>
<td>weak (N)</td>
<td>strong (P)</td>
</tr>
<tr>
<td>Bite angle</td>
<td>4-7</td>
<td>small</td>
<td>large</td>
</tr>
<tr>
<td>amount of P-donor atoms per Pd</td>
<td>( \neq 2 )</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

9.3 Evaluation of the early transition state mechanism

The results show that the electronic activation of the allyl moiety is important for the regioselectivity. A clear relation was found between the regioselectivity and parameters as the number of substituents (2), the \( \pi \)-acceptor capabilities of the donor atoms (7), the symmetry of the ligand (8), the orientation of the phosphorus donor atom (9), the bite angle (10), the effect of the cone angle for the anti-crotyl and the dimethyl allyl moieties ((CH$_3$)$_2$-C$_{6}$H$_5$) (12) and the strength of the nucleophile (13).

The effect of a few parameters, however, cannot be explained by the early transition state mechanism. The modeling and X-ray studies (chapter 3, 4, 7) predicted for the syn crotyl moiety an increased distortion of the \( \eta^1 \)-bond to an \( \eta^1 \cdot \eta^3 \)-bond when the bite angle and / or cone angle is larger (11). Similarly, the non-symmetry of the Pd-allyl bond was also expected to increase with the size of the syn-substituent (1). The observed regioselectivities, however, are the opposite of the expected results. An enhanced distortion of the Pd-(syn-R)allyl bond leads to the formation of less branched product.

9.4 Evaluation of the late transition state mechanism

To predict the regioselectivity using the late transition state mechanism is less straightforward than it is for the early transition state mechanism. The model takes into account the steric interactions occurring during the whole process of bond formation. At some point, the steric interactions encountered along the reaction coordinate may conflict, favoring the other regio-isomer.

Nevertheless, some predictions can be made based purely on steric considerations. A lower selectivity for the branched product can be expected for allyl groups carrying more and / or larger substituents. Analogously, an increase of the steric hindrance (large bite and / or cone angle of the ligand) around the palladium would also lead to less branched product.
The results show that the late transition state mechanism indeed accounts for the effect of the cone angle for syn-crotyl (11) and for the effect of the size of the syn-substituent (1). For some of the results, however, it is clear that steric interactions do not play a role. The use of P-N instead of P-P ligands (8), the effect of the cis or trans orientation of the phosphorus in P-N ligands (9), the effect of the bite angle (10) and the strength of the nucleophile (13) are effects that cannot be accounted for by the late transition state mechanism.

9.5 Combination of the early and the late transition state mechanisms

The above considerations indicate that neither the early nor the late transition state mechanism satisfactorily explains all observed regioselectivities, showing the limits of these mechanistic models. In general, the former succeeds where the latter fails and vice versa. We have succeeded therefore, in exploring the limits of the early and the late transition state mechanism. A separate explanation of the effect of the different parameters in terms of early or late has a limited utilization, so we attempted to provide an explanation that accounts for all of our results.

![Figure 2: Model that accounts for our results, applied to syn and anti crotyl.](image-url)
Chapter 9

Figure 3: Model that accounts for our results, applied to the dimethyl allyl moiety.

The combined model we propose, has been introduced in the previous experimental chapters (figures 2 and 3). Going from the Pd(n³-allyl) complex to the Pd-(olefin-product) complex, the reported modeling studies show no energy minimum (relatively stable intermediate) along the reaction coordinate. Nevertheless, for the sake of argument, we treat the reaction as if it occurs in two stages. In the first stage, the nucleophile approaches the Pd(n³-allyl) complex and selects the most electrophilic carbon atom. During the first stage of bond formation, the attacked carbon gradually changes its hybridization from sp² to sp³. As a result, the substituents on the attacked carbon bend away from the nucleophile, in the direction of the Pd(ligand) fragment. At this point, steric interactions may become important.

After the initial stage, the attacked allyl moiety rotates to form the final Pd(olefin) complex. The site of the attacked carbon atom rotates out of the Pd(ligand) plane, while the site that is not attacked rotates into this plane. The formation of a more substituted double bond and its coordination to palladium are favored for electronic reasons over that of a terminal double bond, so attack on the linear position would be preferred. In contrast, for steric reasons the attack on the branched position may be favored. The rotation of the attacked branched position out of the Pd(ligand) plane decreases the steric interactions, whereas attack on the linear position would lead to a significant increase of steric interaction after rotation of the newly formed substituted double bond into the Pd(ligand) plane.

Summarizing, in the first stage of the reaction, attack on the branched position is favored for electronic reasons and in the second stage it is favored for steric reasons. The opposite applies for attack on the linear position; it is favored in the first stage for steric reasons and in the second stage for electronic reasons.

In the following this mechanism will be used to explain the influence of each parameter mentioned in table 1.
9.6 Evaluation of the combined model

1. Size of the syn-substituent on the allyl moiety (chapter 5).
A larger syn-substituent corresponds to a lower regioselectivity for the branched product. The crystal structures of dimethyl allyl-complexes (chapter 7) show, that the phenyl rings of the ligand are closer to the syn than to the anti methyl substituent. The steric hindrance in the first stage of the reaction therefore, increases with the size of the substituent and the linear product is favored. Apparently, the increase of the steric interactions in the second stage is less important than in the first stage.

2. Number of substituents (chapter 7).
The selectivity for the branched product increases with the number of substituents. Going from C3H3 via CH3-C3H4 to (CH3)2-C3H3 leads to a more pronounced distortion of the Pd-allyl bond from \( \eta^3 \) to \( \eta^1-\eta^2 \) and consequently to an increase of the relative electrophilicity of the C3 atom. The importance of the electronic factors in the first stage is thus enhanced. The increased steric bulk around C3 also leads to an increase of the importance of steric interactions in the second stage. Both effects favor the formation of the branched product.

3. Mixture of E and Z monosubstituted substrates (chapter 5).
In (1:1) mixtures, the Z substrate is alkylated (forming branched and linear product) at a faster rate than the E substrate (forming only the linear product). Therefore, after a short reaction time, the concentration of the branched product is higher than that of the linear product. The situation is reversed after a longer reaction time, i.e. when the Z substrate has been consumed completely.

4. Orientation of the substituent in mono substituted allyl groups (chapters 4 and 5).
The regioselectivity for the branched product is higher for anti complexes than for syn complexes. The modeling studies predicted a more pronounced non-symmetry for the syn substituted allyl moiety, but also a partly sp3 hybridization on C3 in the anti substituted allyl moiety. The crystal structures (chapter 7) of dimethyl allyl-complexes show, that the phenyl rings of the ligand are closer to the syn than to the anti methyl substituent. The steric interactions in the first stage therefore, are more important for the syn than for the anti substituted allyl moiety. Assuming that the steric and electronic factors in the second stage do not differ much for both isomers, the differences in the first stage determine the regioselectivity.

5. Coordinating properties of the leaving group (dissymmetric ligands) (chapter 6).
The use of chloride as the leaving group leads to a higher selectivity for the branched product when P-N ligands are used. After oxidative addition of the allylic substrate to the Pd\(^0\)(ligand) complex, the syn-cis-P allyl complex is formed. The alkylation takes place primarily on the carbon trans to the phosphorus, so the regioselectivity for attack on C1 is high. A coordinating counterion facilitates the isomerization from syn-cis
Chapter 9

- P to syn-trans-P, thereby increasing the probability for attack on C3, leading to the branched product. The steric bulk around the nitrogen functionality is small and the reaction is allowed to follow the electronically preferred pathway.

6. Coordinating properties of the leaving group (symmetric ligands) (chapter 4, 5, 6).
An other effect of the possible coordination of the counterion is its influence on the electron density on the active complex. A long distance of the negatively charged counterion (e.g. triflate) increases the cationic character of the complex and consequently its reactivity towards nucleophilic attack (the electronic factors in the first stage of the reaction). Comparison of the regioselectivity of the stoichiometric and catalytic reactions shows, that for less strongly coordinating counterions (e.g. acetate), a higher selectivity for the branched product is found.

7. The π-acceptor capabilities of donor atoms (symmetric ligands) (chapter 8).
The use of a ligand-donor atom that is a stronger π-acceptor, increases the selectivity for the branched product. The increased π-back donation of the metal to the ligand increases the orbital coefficients in the LUMO (2a") on the allyl moiety, especially on C3. Thus, the electronic factors in the first stage of the reaction are enhanced.

8. Symmetry of the ligand with respect to the donor atoms (chapters 6 and 8)
Going from P-P to P-N the selectivity for the branched product increases. The dissymmetry of the ligand increases the electrophilicity of the allyl and thereby the importance of the electronic factors in the first stage of the reaction.

9. Position of the phosphorus in complexes of P-N ligands (chapter 6)
The electrophilicity of the carbon trans to the phosphorus is larger than that of the carbon cis to phosphorus. A trans orientation of C3 therefore, increases the importance of the electronic factors in the first stage and consequently increases the regioselectivity for the branched product.

10. Bite angle of the ligand (chapters 4-7)
A larger bite angle leads to an increased distortion of the Pd(η²-allyl) bond and consequently to an enhanced electrophilicity of the allyl. Because of the polarization of the frontier orbitals of the allyl fragment, the effect is more pronounced for C3 than for C1. Thus, the electronic factors in the first stage become more important.

11. The cone angle for monosubstituted syn allyl groups (chapters 4 and 5).
Analogous to the effect of the size of the syn-substituent (parameter 1), the increase of the cone angle increases the steric interactions in the first stage of the reaction, thus decreasing the regioselectivity for the branched product.
12. The cone angle in complexes bearing monosubstituted anti allyl groups and disubstituted allyl groups (chapters 4, 5 and 7).

The increase of the cone angle leads to an increase of the regioselectivity for the branched product. Because of increased steric interactions, the symmetry of the Pd-(η^3-allyl) bond is distorted thereby leading to an enhanced electrophilicity of the allyl moiety. In addition, the steric factors in the second stage increase. Although the steric factors in the first stage increase as well, the electronic effect in the first stage and the steric effect in the second stage are more important.


Åkermark has shown that the use of weaker nucleophiles than sodium diethyl 2-methylmalonate leads to a lower selectivity for the branched product. 111 Although the electronic properties of the allyl are not influenced, they are less important in the first stage of the reaction.

14: Size of the syn substituent in mono-substituted allyl groups (chapter 5).

Larger substituents lead to a lower rate of reaction. This is in line with the above mentioned importance of steric factors in the first stage of the reaction. An increase of the steric interactions naturally decreases the rate of reaction.

15: Orientation of the substituent in monosubstituted allyl groups (chapter 5).

The reaction proceeds faster for E substrates (leading to syn complexes) than for Z substrates (leading to anti complexes), which can be explained by the aforementioned difference in steric effects in the first stage of the reaction.

16: The number of substituents (chapter 7)

Despite a larger electronic activation of the disubstituted allyl moieties compared to monosubstituted allyl moieties, the reaction proceeds at a lower rate. The allylic alkylation leads to a higher regioselectivity for the branched product than found for monosubstituted allyl moieties. Apparently, the increased steric interactions have a strong influence on both the rate and the selectivity of the reaction.

17: Coordinating properties of the leaving group (chapter 5).

A weaker coordination of the counterion to the catalytically active complex decreases the electron density on the complex and consequently on the allyl moiety. Via this way, the reactivity for nucleophilic attack increases and, assuming that the Pd(allyl) complex is not influenced, also the reaction rate will increase.
18: The π-acceptor capabilities of donor atoms (symmetric ligands) (chapter 8).

The reaction proceeds faster for bidentate phosphorus ligands than for ligands with other donor atoms. The rate decreases in the order $P > As > S > N$. As mentioned above, a stronger π-acceptor enhances the electrophilicity of the allyl and thereby also the rate of the reaction.

19: Bite angle of the ligand (chapters 4-7).

In general, the reaction proceeds faster when the bite angle of the ligand is larger. The increased electrophilicity of the allyl moiety accounts for this observation. For some substrates, however, the rate is slowed down by the increased steric interactions.

20. Number of ligand donor atoms per Pd (chapter 6 and to be published)

Because of the high trans influence and consequently the high electronic activation of the allyl moiety, the highest rates are observed for bidentate phosphine ligands. For two monodentate P-ligands, the rate is lower because of several coordination modes of the ligands (not necessarily cis) and because of the formation of multinuclear Pd-species. A higher L/Pd ratio will lead to the formation of relatively inactive (mononuclear) palladium complexes, from which the excess of ligands have to dissociate before oxidative addition can occur.

9.7 Recent developments

After completion of our studies, several modeling studies of the reaction pathway of nucleophilic attack have been reported. Some studies discuss the regioselectivity of the reaction and the results are in line with the empirical model proposed in this thesis. It is shown that the course of the reaction is controlled by frontier orbital interactions, confirming the observed relation between the distortion of the Pd-allyl and the regioselectivity. The reported studies show, that the orbital interactions and the steric interactions cooperate. Translating these results to our model, the electronic factors in the first stage and the electronic interactions in the second stage favor the same product. Our results suggest, that for some cases, this may not apply. Furthermore, the course of the reaction may be different for nucleophiles that are more reactive than the NH$_3$ group used in the modeling studies.
9.8 Conclusion

We have succeeded in exploring the limits of validity of the existing models for the allylic alkylation. In the experimental chapters 4-8 we have shown that for some cases, neither the late nor the early transition state mechanism satisfactorily explains the results. Our new model, resulting from a combination of the two existing models, covers this undefined area and provides a rationalization for all our results as well as for those of others. Recent theoretical reports support the combined mechanistic model and we are confident that it will continue to be useful in the future.

9.9 References

Chapter 10

New insights in the mechanism of the palladium catalyzed methoxycarbonylation of cinnamyl chloride.

Abstract

In this chapter, two mechanistic routes for the palladium catalyzed carbonylation of cinnamyl chloride are described, one associative and one insertion mechanism.

The associative mechanism was studied by the stepwise synthesis of potential intermediates at 1.2 bar of CO. After the formation of an intermediate \( [(\eta^3\text{-allyl})\text{Pd(L)-CO}]^{[\text{OTf}]} \) complex (L is a monodentate ligand with a group 15 donor atom), the addition of methanol to the coordinated CO leads to the formation of a transient carbomethoxy complex. Via reductive elimination of the \( \eta^3\text{-allyl} \) and the carbomethoxy group, the linear ester is formed. The catalytic carbonylation of cinnamyl chloride proceeds at room temperature and 1.2 bar of CO and requires the presence of a methoxide base. It was surprising to find an associative pathway for this reaction, since reported studies pointed to the insertion mechanism or disproved the occurrence of the associative mechanism.

When using a chloride counter ion instead of a triflate, insertion of the carbon monoxide in the Pd(\( \eta^3\text{-allyl} \)) bond occurs at elevated pressure, forming an acyl complex. The insertion proved to be completely reversible. The ester product can be formed by reaction with methanol. The catalytic reaction via the insertion mechanism requires elevated pressures (>10 bar CO) and the absence of methoxide. The insertion mechanism was also studied using the bidentate P-N ligands POPyn (see chapter 6). When the chloride counterion was used, the acyl complexes could be isolated. For the POPyn modified complex, a crystal structure could be obtained in which the acyl group is located cis to the phosphorus. Interestingly, when acetate is used as the counterion also the analogous transient trans-P complex could be observed. Kinetic studies point out that the kinetic equation depends on the nature of the solvent. In all cases the catalytic reaction proceeds with a positive order in palladium, CO and the amine base.

Remarkably, for monodentate ligands, the catalytic carbonylation can proceed via both mechanisms. Which of the two prevails (association, insertion), depends on the ligand, the CO-pressure and whether methoxide or methanol is used.
10.1 Introduction

As mentioned in chapter 1, the alkoxy carbonylation of dienes is a powerful tool in synthetic organic chemistry to form $\beta$-$\gamma$ unsaturated esters (figure 1). These products can be used as intermediates in the synthesis of nylon-6 (figure 1).

\[
\text{butadiene (A)} + \text{CO} + \text{CH}_3\text{OH} \xrightarrow{[\text{Pd}]} \text{methyl 3-pentenoate (B)}
\]

\[
\text{nylon-6 (D)} \xrightarrow{\text{Pd} (\eta^3-\text{allyl})} \text{\varepsilon-caprolactam (C)}
\]

Figure 1: Use of the alkoxy carbonylation of butadiene in the synthesis of nylon-6.

Using butadiene as the substrate, research at DSM had shown the intermediacy of Pd($\eta^3$-allyl) complexes. To obtain more insight in the carbonylation mechanism, we used the analogous allyl chlorides to obtain Pd($\eta^3$-allyl) complexes.

Carbonylation of allyl chlorides

Few studies have been reported concerning the carbonylation of allylic halides. In most cases a palladium catalyst is used for the alkoxy carbonylation of such substrates, although also rhodium or nickel based systems have been reported. Using palladium, the reaction proceeds under mild conditions and with a large tolerance for functional groups. The mechanism for the palladium system has been studied extensively by Yamamoto and Milstein. As a model for the $\eta^3$-allyl ligand the benzyl group was used, which can coordinate to palladium in an $\eta^1$- or an $\eta^3$-fashion (figure 2).

\[
\text{Pd} \quad \eta^1\text{-benzyl} \quad \eta^3\text{-benzyl}
\]

Figure 2: $\eta^1$ and $\eta^3$ coordination of the benzyl group to palladium.
The mechanisms of the palladium catalyzed carbonylation.

Initially, two mechanisms have been proposed for the carbonylation reaction, a) an insertion pathway involving an acyl species in which the product-forming step is the alcoholysis of the Pd-acyl bond[4,9] (figure 3) and b) an associative pathway involving a carbomethoxy intermediate, in which the product is formed by the reductive elimination of the π-allyl and the carbomethoxy group (figure 4).[6a]

Based on the studies using Pd-benzyl complexes as model systems, it was concluded that both the stoichiometric and the catalytic reaction proceed via an insertion pathway.[4,5,7]

Both because of the steric bulk of the phenyl group and because of the aromatic stabilization, the benzyl group will have a higher propensity to coordinate in the η¹-fashion than other allyl groups, such as cinnamyl (3-Ph-C₃H₅) or C₃H₅.[8] Furthermore, in the studies mentioned, an excess of monodentate ligand was used (P/Pd > 1) which is known to stabilize the η¹-coordination[10,11] thereby promoting the migratory insertion reaction[9] of the Pd-(aliphatic carbon) σ-bond and CO, forming the Pd-C(O)CH₂Ph acyl species.[4] The results obtained from these studies with the benzyl moiety may not be representative for an η¹-allyl group.

Thereafter we decided to perform mechanistic studies using complexes with a different allyl moiety and with only one equivalent of ligand per palladium. The use of the unsubstituted allyl ligand C₃H₅ proved not to be convenient, as (ligand)Pd(C₃H₅)X complexes were often found to be unstable.[11] The slightly larger η³-C₄H₇ (crotyl group) is known to form several isomers, such as syn and anti complexes (see chapter 4), which complicates our mechanistic study. The 3,3-(CH₃)₂-C₃H₅ group may favor the η¹-isomer (figure 5)[12] and thus is not a good model for an η³-allyl group either. We selected the η³-cinnamyl moiety for our studies, both because of the high stability of the complexes and the low tendency to form η¹-complexes.
Outline of this chapter

Using the η\(^3\)-cinnamyl group, we studied systematically the possibilities of an associative and an insertion mechanism. We will evaluate the possible mechanisms using monodentate ligands and mixed bidentate ligands, both under high and low CO pressure.

Contrary to the reported studies, we will first show, that for some palladium complexes bearing one monodentate ligand, the alkoxy-carbonylation can proceed via the associative pathway. This mechanism was studied by the stepwise synthesis of intermediates and by performing catalytic reactions under a low pressure of CO.

Secondly, it will be shown that using the same ligands, the insertion pathway can be followed at elevated pressures. The insertion reaction proceeds for monodentate and bidentate P-N ligands. Also this mechanism was studied by the stepwise synthesis of intermediates and in addition, the kinetics of the catalytic reaction were studied by the variation of the concentrations of the various reactants.

10.2 Results and discussion: Associative mechanism, monodentate ligands

10.2.1 Synthesis of Pd complexes (1a-g) bearing monodentate ligands

To study the carbonylation mechanism of η\(^3\)-cinnamyl complexes using monodentate ligands, we have prepared a series of (η\(^3\)-cinnamyl)Pd(L)Cl complexes (figure 6, table 1) (1a-g). The used ligands are based on group 15 donor atoms and differ in steric and electronic properties.

The (cinnamyl)Pd(L)Cl complexes (1a-g) were prepared via reaction of the appropriate monodentate ligand with [(cinnamyl)PdCl]\(_2\) \({}\(^{[13]}\)\). The \(^1\)H-NMR spectra showed sharp signals for all allylic protons. The coupling constant between Hc and Hd is relatively large (\(^2\)J\(_{(H_c-H_d)}\) = 13 Hz) and indicates a trans configuration around the C2-C3 bond (see chapters 4-8). For the complexes containing a phosphorus ligand, a large coupling of phosphorus to Hd was observed (\(^2\)J\(_{(P-H_d)}\) = 10 Hz), indicating that this proton is oriented trans to phosphorus. The chemical shifts of the signals of Ha-d do not differ much for the various ligands and it is concluded that
The mechanisms of the palladium catalyzed carbonylation.

for all ligands, the phenyl group of the cinnamyl moiety is oriented trans to the ligand L, in a syn fashion with respect to the central allyl hydrogen He (figure 6) (see chapters 4-8).

Figure 6: Numbering scheme of the cinnamyl moiety in the prepared complexes.

Table 1: Numbering of complexes bearing monodentate ligands.

<table>
<thead>
<tr>
<th>Complex</th>
<th>L</th>
<th>Q</th>
<th>X</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>PCy₃</td>
<td>Cl</td>
<td>---</td>
</tr>
<tr>
<td>1b</td>
<td>PPh₃</td>
<td>Cl</td>
<td>---</td>
</tr>
<tr>
<td>1c</td>
<td>AsPh₃</td>
<td>Cl</td>
<td>---</td>
</tr>
<tr>
<td>1d</td>
<td>SbPh₃</td>
<td>Cl</td>
<td>---</td>
</tr>
<tr>
<td>1e</td>
<td>P(OPh)₃</td>
<td>Cl</td>
<td>---</td>
</tr>
<tr>
<td>1f</td>
<td>phosphorus-amidite *</td>
<td>Cl</td>
<td>---</td>
</tr>
<tr>
<td>1g</td>
<td>P(o-tolyl)₃</td>
<td>Cl</td>
<td>---</td>
</tr>
<tr>
<td>2a</td>
<td>PCy₃</td>
<td>MeCN</td>
<td>OTf</td>
</tr>
<tr>
<td>2b</td>
<td>PPh₃</td>
<td>MeCN</td>
<td>OTf</td>
</tr>
<tr>
<td>2c</td>
<td>AsPh₃</td>
<td>MeCN</td>
<td>OTf</td>
</tr>
<tr>
<td>2d</td>
<td>SbPh₃</td>
<td>MeCN</td>
<td>OTf</td>
</tr>
<tr>
<td>2e</td>
<td>P(OPh)₃</td>
<td>MeCN</td>
<td>OTf</td>
</tr>
<tr>
<td>2f</td>
<td>phosphorus-amidite *</td>
<td>MeCN</td>
<td>OTf</td>
</tr>
<tr>
<td>2g</td>
<td>P(o-tolyl)₃</td>
<td>MeCN</td>
<td>OTf</td>
</tr>
<tr>
<td>3a</td>
<td>PCy₃</td>
<td>CO</td>
<td>OTf</td>
</tr>
<tr>
<td>3b</td>
<td>PPh₃</td>
<td>CO</td>
<td>OTf</td>
</tr>
<tr>
<td>3c</td>
<td>AsPh₃</td>
<td>CO</td>
<td>OTf</td>
</tr>
<tr>
<td>3d</td>
<td>SbPh₃</td>
<td>CO</td>
<td>OTf</td>
</tr>
<tr>
<td>3e</td>
<td>P(OPh)₃</td>
<td>CO</td>
<td>OTf</td>
</tr>
<tr>
<td>3f</td>
<td>phosphorus-amidite *</td>
<td>CO</td>
<td>OTf</td>
</tr>
<tr>
<td>3g</td>
<td>P(o-tolyl)₃</td>
<td>CO</td>
<td>OTf</td>
</tr>
</tbody>
</table>

*: see figure 7 for the structure of this ligand.
10.2.2 Reaction with CO

Treating 1a-g with 1.2 bar of CO resulted in a slight broadening of the $^1$H-NMR signals, but no new complexes were observed. Presumably, CO binds reversibly to complexes 1a-g, but the dynamic equilibrium strongly favors the (η$^3$-cinnamyl)Pd(L)Cl complex (1a-g). Unfortunately, this could not be observed using IR spectroscopy.

To facilitate the binding of CO to these complexes, a vacant site was created by removal of the chloride by treatment with AgOTf. To stabilize the coordinatively unsaturated palladium, CH$_3$CN was added to occupy the vacant site (2a-g) (figure 8). In the absence of acetonitrile, the complexes were found to decompose to palladium metal within minutes. Complexes 2a-g are stable for a longer time, but decompose within hours after isolation. The $^1$H-NMR spectra of these cationic complexes are similar to those of the corresponding neutral complexes, which indicates that the orientation of the cinnamyl group is the same (syn trans P).

Upon treating these cationic complexes in chloroform with 1.2 bar of CO, the loosely bonded acetonitrile was easily replaced by CO and the light yellow solution of 2a-g turned colorless. Both IR and $^{13}$C-NMR spectroscopy (using $^{13}$CO) showed the formation of the novel [(cinnamyl)Pd(L)CO][OTf] complexes 3a-g. These complexes could not be isolated, but are stable for about one hour in solution (under an atmosphere of CO), before decomposing to palladium metal. The allyl region of the $^1$H-NMR spectra of these complexes is similar to those of the neutral complexes, indicating that also in this case, the phenyl group of the cinnamyl group is oriented syn-trans L.

![Figure 7: Structure of ligand f.](image)

![Figure 8: Synthesis scheme of [(cinnamyl)Pd(L)CO][OTf] 3a-g.](image)
The formation of complexes 3a-g is faster for the more basic ligands and the decomposition to palladium metal is slower. For these ligands, the stretching vibration of the coordinated CO in 3a-g was found at lower frequency (table 2). This is indicative of a more pronounced π-back donation from the palladium to the CO ligand, which can be explained by the higher electron density on the palladium. The enhanced π-back donation indicates a stronger bond between the palladium and the CO ligand, which may cause a higher stability of the complexes. The relatively high stability of other Pd-CO complexes with basic ligands has also been reported by Yamamoto, who used PMe₃ for his mechanistic studies.[4, 5, 8]

Milstein and Yamamoto reported on the insertion mechanism, but unlike as in our studies they used at least two equivalents of ligand per palladium in their mechanistic studies.¹⁴ The [(cinnamyl)Pd(L)CO][OTf] complexes showed no sign of insertion of CO, but the addition of an extra equivalent of PCy₃-ligand to 3a, resulted in a new ¹³C resonance at 236 ppm, which was assigned to an acyl complex (see below) [¹⁴, 5, 7, 9, 26] (figure 9). The singlet resonance observed in the ³¹P-NMR spectrum suggests that both phosphorus ligands are magnetically equivalent, which can be explained by the formation of a complex bearing the two phosphines in a trans configuration.¹⁴

Apparently, the non-coordinating counterion, the strong (η³-cinnamyl)-Pd bond (compared to the (η³-benzyl)-Pd bond) and an L / Pd ratio of 1 are crucial for the formation and relative stability of the [(cinnamyl)Pd(L)CO][OTf] complexes.

![Figure 9: Effect of addition of extra ligand to [(cinnamyl)Pd(PCy₃)CO][OTf] (3a), L = PCy₃.](image)

Table 2: Selected spectral data of the [(cinnamyl)Pd(L)CO][OTf] complexes (3a-g).

<table>
<thead>
<tr>
<th>complex</th>
<th>L</th>
<th>δ(CO) NMR</th>
<th>ν (CO) IR</th>
</tr>
</thead>
<tbody>
<tr>
<td>3e</td>
<td>P(OPh)₃</td>
<td>179.5</td>
<td>2133</td>
</tr>
<tr>
<td>3f</td>
<td>phosphorus-amidite</td>
<td>179.4</td>
<td>2133</td>
</tr>
<tr>
<td>3b</td>
<td>PPh₃</td>
<td>181.4</td>
<td>2125</td>
</tr>
<tr>
<td>3g</td>
<td>P(o-tolyl)₃</td>
<td>n.d.</td>
<td>2123</td>
</tr>
<tr>
<td>3c</td>
<td>AsPh₃</td>
<td>181.1</td>
<td>2123</td>
</tr>
<tr>
<td>3a</td>
<td>PCy₃</td>
<td>181.9</td>
<td>2115</td>
</tr>
<tr>
<td>3d</td>
<td>SbPh₃</td>
<td>183.5</td>
<td>n.d.</td>
</tr>
</tbody>
</table>

n.d.: not determined

*: see figure 7 for the structure of this ligand
10.2.3 Reaction of [(cinnamyl)Pd(L)CO] complexes with nucleophiles.

To study the probability of an associative (carbomethoxy) mechanism, the most readily formed and most stable cationic CO-complex, [(cinnamyl)Pd(PCy$_3$)CO][OTf] (3a), was treated with methanol at room temperature. According to $^1$H-NMR several complexes were formed. The signals in the allyl region indicated the formation of a new ($\eta^3$-cinnamyl)Pd(L) complex, which is assigned to the novel carbomethoxy species 4a (see below). Yamamoto also studied the interaction of nucleophiles with (PMe$_3$)$_2$(benzyl-C(O))-Pd-CO. In contrast to our results it was found that alcohols only react via nucleophilic attack at the Pd-acyl group (methanolysis),$^{[4]}$ whereas primary and secondary amines attack the coordinated CO, forming a Pd(amide) complex.

Addition of ammonium hydroxide at low temperature (-78°C) in methanol to [(cinnamyl)Pd(PCy$_3$)$_{13}$CO][OTf] (3a) yielded the carbomethoxy complex (4a) nearly quantitatively (figure 10, table 3). The $^{13}$C-NMR of this compound shows a resonance at 211.1 ppm ($^{2}J_{P,C} = 23$ Hz). This chemical shift is outside the normal range of Pd-CO or Pd-acyl type complexes, but it is similar to that of ((2S, 4S)-2, 4-bis-(diphenylphosphino)-pentane)Pd(OM)(COOMe) ($\delta C = 214.4$ ppm, $^{2}J_{P,C} = 165$ Hz).$^{[14]}$ The newly formed carbomethoxy complex was stable at low temperature but upon heating to +10°C it decomposed to form the linear ester product and palladium metal.

The ($\eta^3$-cinnamyl)Pd complexes (1-3) show a difference in the resonance of Hc and Hd larger than 0.5 ppm or show both resonances above 6 ppm (table 3, see also chapter 6). Therefore, the shifts of Hc (5.70 ppm) and Hd (5.60 ppm) of the [(cinnamyl)Pd(L)(C(O)OMe)] complex (4a) are not in agreement with a syn-trans-P orientation of the Ph group of the cinnamyl moiety (see chapter 6). Therefore it is proposed that the carbomethoxy complex (4a) has the Ph group located syn-cis-P. The subsequent reductive elimination of the $\eta^3$-cinnamyl and the carbomethoxy group then yields the linear ester (E) (figure 11).

![Figure 10: Synthesis scheme of [(cinnamyl)Pd(PCy$_3$)(C(O)OMe)] (4a), L = PCy$_3$.](image-url)
The mechanisms of the palladium catalyzed carbonylation.

Table 3: Chemical shifts of Hc and Hd in complexes of PCy₃ (1-4a), δ in ppm.

<table>
<thead>
<tr>
<th>complex</th>
<th>complex</th>
<th>Hc anti</th>
<th>Hb syn</th>
<th>Hc</th>
<th>Hd</th>
<th>P</th>
<th>CO</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>X=Cl</td>
<td>2.64</td>
<td>3.28</td>
<td>5.80</td>
<td>5.20</td>
<td>45.9</td>
<td>--</td>
</tr>
<tr>
<td>2a</td>
<td>X=OTf, MeCN</td>
<td>2.90</td>
<td>3.53</td>
<td>6.06</td>
<td>5.59</td>
<td>47.0</td>
<td>--</td>
</tr>
<tr>
<td>3a</td>
<td>X=OTf, CO</td>
<td>3.56</td>
<td>4.17</td>
<td>6.56</td>
<td>6.30</td>
<td>48.5</td>
<td>181.9</td>
</tr>
<tr>
<td>4a</td>
<td>X=OMe, CO</td>
<td>4.47</td>
<td>5.00</td>
<td>5.70</td>
<td>5.60</td>
<td>45.1</td>
<td>211.1</td>
</tr>
</tbody>
</table>

![Diagram](image)

Figure 11: Reductive elimination of ester from [(cinnamyl)Pd(L)(C(0)OMe)].

The synthesis of carbomethoxy complexes (type 4) has been reported before. Milstein[7a] used Hg(C(O)OCH₃)₂ as a carbomethoxy-donor in the stoichiometric carbonylation of [(C₃H₅)PdCl]₂ and proposed a species of type 4 as an intermediate. Keim[6c] reported the preparation of (σ³-C₃H₅-C(CH₃)-CH₂)Pd(PPh₃)(C(O)OCH₃) via a one-pot procedure using [(σ³-C₃H₅-C(CH₃)-CH₂)PdCl]₂, two equivalents of PPh₃, and excesses of HC(O)OCH₃ and NaOMe. In contrast to our results, no reductive elimination to the linear ester was observed in these studies. Instead, a pathway was proposed involving an acyl group bonded to the carbomethoxy-Pd species (L₂(R-C(O)-Pd-C(O)-OR)). Although the PPh₃-analogue of 4a may show different behavior than 4a itself, it cannot be ruled out that following the one-pot procedure a mixture of compounds was obtained. In contrast, the species 4a described in this chapter, was prepared via a stepwise route and does undergo reductive elimination to the ester.
10.2.4 Catalytic carbonylation at 1.2 bar CO

The ready formation of the carbomethoxy complex (4a) and the further reaction to the ester under mild conditions suggest that the catalytic carbonylation of cinnamyl substrates at 1.2 bar of CO at room temperature in organic solution is a feasible process. Indeed, the carbonylation of allyl halides under these conditions has been reported, but a two phase system was used, with potassium hydroxide as the nucleophile.\textsuperscript{[6b, 15]}

To study the effect of the type of nucleophile on the reaction, experiments were carried out using both methoxide and hydroxide anions as the nucleophile. Sodium methoxide dissolved readily in the organic reaction medium (thf), but potassium hydroxide is much less soluble in organic solvents. Furthermore, the hydroxide anion proved to be too reactive and the direct nucleophilic attack on the allyl moiety leading to cinnamyl alcohol, prevailed over the carbonylation reaction. As a soluble alternative for KOH, we used N\textsubscript{Bu}\textsubscript{4}OH in a methanol solution.

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{figure_12.png}
\caption{Products and side products of the carbonylation of cinnamyl chloride at room temperature and 1.2 bar of CO. The analogous side product cinnamyl alcohol is not formed.}
\end{figure}

The use of cinnamyl triflate as the substrate resulted in a fast direct attack of the hydroxide or the methoxide on the cinnamyl and no carbonylation product could be observed (see chapters 4-8 for a discourse on nucleophilic attack on $\eta^3$-allyl complexes). The use of several other leaving groups instead of the triflate were examined (OAc, Br, Cl), but only cinnamyl chloride proved to be a suitable reagent for the carbonylation reaction, since the nucleophilic attack of hydroxide or methoxide is slow for this substrate.

The results of the catalytic carbonylation of cinnamyl chloride are presented in tables 4 and 5.
The mechanisms of the palladium catalyzed carboylation.

Table 4: Catalytic carboylation of cinnamyl chloride at room temperature and 1.2 bar of CO, using sodium methoxide, after 60 minutes. Substrate / Pd = 200, for further details: see experimental section.

<table>
<thead>
<tr>
<th>complex (L)</th>
<th>TOF*</th>
<th>conv. (%)</th>
<th>H (%)</th>
<th>G (%)</th>
<th>F (%)</th>
<th>E (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>la (PCy₃)</strong></td>
<td>132</td>
<td>66</td>
<td>5</td>
<td>5</td>
<td>9</td>
<td>82</td>
</tr>
<tr>
<td><strong>lb (PPh₃)</strong></td>
<td>16</td>
<td>8</td>
<td>6</td>
<td>6</td>
<td>75</td>
<td>13</td>
</tr>
<tr>
<td><strong>lc(AsPh₃)</strong></td>
<td>78</td>
<td>39</td>
<td>8</td>
<td>5</td>
<td>21</td>
<td>41</td>
</tr>
<tr>
<td><strong>ld(SbPh₃)</strong></td>
<td>80</td>
<td>40</td>
<td>8</td>
<td>5</td>
<td>18</td>
<td>70</td>
</tr>
</tbody>
</table>

*: in mole/mole/h, determined after 1 hour

Table 5: Catalytic carboylation of cinnamyl chloride at room temperature and 1.2 bar of CO, using NBu₄OH, after 60 minutes. Substrate / Pd = 200, for further details: see experimental section.

<table>
<thead>
<tr>
<th>complex (L)</th>
<th>TOF*</th>
<th>conv. (%)</th>
<th>H (%)</th>
<th>G (%)</th>
<th>F (%)</th>
<th>E (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>la (PCy₃)</strong></td>
<td>136</td>
<td>68</td>
<td>28</td>
<td>25</td>
<td>3</td>
<td>44</td>
</tr>
<tr>
<td><strong>lb (PPh₃)</strong></td>
<td>52</td>
<td>26</td>
<td>19</td>
<td>19</td>
<td>38</td>
<td>23</td>
</tr>
<tr>
<td><strong>lc(AsPh₃)</strong></td>
<td>142</td>
<td>71</td>
<td>31</td>
<td>28</td>
<td>4</td>
<td>37</td>
</tr>
<tr>
<td><strong>ld(SbPh₃)</strong></td>
<td>184</td>
<td>92</td>
<td>24</td>
<td>22</td>
<td>1</td>
<td>53</td>
</tr>
</tbody>
</table>

*: in mole/mole/h, determined after 1 hour

Both the use of methoxide (table 4) and hydroxide/methanol (table 5), yields the linear trans ester E as the only carboylation product. This indicates that in both cases, methoxide is reacting. In addition, several other, non-carboylation products are formed (F, G, H, figure 12). Remarkably, the possible side product cinnamyl alcohol (resulting from nucleophilic attack of OH) is not formed. Using NBu₄OH, both the conversion of cinnamyl chloride and the yield of the ester are higher than with NaOMe as the nucleophile, except when PCy₃ is used. On the other hand, using NBu₄OH, also the relative amount of side products (G and H) formed is higher.

The formation of cinnamyl methyl ether (F) is not surprising and arises from nucleophilic attack of methanol or a methoxide anion on the (η³-cinnamyl)Pd complex. The formation, however, of both allyl benzene (H) and β-E-methyl styrene (G) is remarkable. The ratio of allyl benzene (H) and methyl styrene (G) is approximately 1 for all ligands. The formation of these products occurs immediately after the start of the reaction and the amount does not increase in time. In the carboylation of allyl formates these products have also been observed, due to a decarboylation of the formato group, giving a hydrido intermediate.4

Obviously, this mechanism cannot be operative in the present case.

The formation of allyl benzene (H) and β-E-methyl styrene (G) can be explained by the carboxmethoxy mechanism. The hydroxide that is present in the solution, may react with [(cinnamyl)Pd(L)(CO)]⁺[Cl]⁻ (of the type 3a-d) to form [(cinnamyl)Pd(L)(C(O)OH)]. Loss of CO₂ then leads to the formation of a transient
[(cinnamyl)Pd(L)(H)] complex, which subsequently undergoes reductive elimination to form either allyl benzene \( H \) or \( \beta\-E\)-methyl styrene \( G \). An analogous mechanism has been proposed for the hydroxycarbonylation of olefins.\(^{[21]}\) The feasibility of the reductive elimination of the allyl and the hydride from such palladium complexes is supported by theoretical studies (figure 13).\(^{[22]}\)

![Figure 13: Proposed mechanism of formation of allyl benzene and \( \beta\-E\)-methyl styrene.](image)

The initial formation of the carbonylation product \( E \) is much slower than the initial formation of \( G \) and \( H \) but the absolute amount of ester \( E \) steadily increases with conversion. The carbonylation proceeds fast for SbPh\(_3\) and slow for PPh\(_3\). As discussed above, the use of chloride as the counter ion leads to an equilibrium mixture of the CO-complexes \( 3a-g \) with the starting complex \( 1a-g \). Presumably, the [(cinnamyl)Pd(L)Cl complex \( 1a-d \) is the resting state of the catalyst. The CO-coordinated [(cinnamyl)Pd(L)CO][X] complexes \( 3a-g \) are formed more readily and they are more stable for basic ligands, thereby increasing the concentration of the catalytically active species. This may be the cause of the higher overall reaction rate that is found for the basic ligands. This seems to be the major factor, although via increased \( \pi\)-back donation, the more basic ligands cause a higher electron density on the carbonyl ligand, which may decrease its reactivity towards nucleophiles.

Using the SbPh\(_3\) modified complex \( 1d \) the carbonylation was also performed at 50 bar of CO, using NBut\(_4\)OH as the nucleophile. No significant difference was observed in rate and selectivity between the experiment at 50 bar CO and 1 bar CO, indicating that when NBut\(_4\)OH is used, the occurrence of the associative mechanism does not depend on the CO-pressure.

We propose that the following catalytic cycle is operative and can account for all the results (figure 14). It is known, that the formation of the \( \eta^3\)-cinnamylPd complex \( I \) is a facile process (chapter 6, also 10.3). The next step is difficult and the dynamic equilibrium strongly favors complex \( I \). The rapid formation of \( \beta\-E\)-methyl styrene \( G \) and allyl benzene \( H \) shows that the next steps are easy for the hydroxide. The rate of reaction to form the ester \( E \), however, is much lower. The difference between the reaction rate of the
The mechanisms of the palladium catalyzed carboxylation.

hydroxide and the methoxide is either in the formation of 4 (from 3) or in the reductive elimination to form E (from 4). Our studies show that the reductive elimination proceeds rapidly at room temperature, leaving the reaction from 3 to 4 as the only candidate for the rate limiting step. More detailed kinetic studies are required to distinguish between these two steps.

![Diagram](image)

Figure 14: Proposed catalytic cycle for the methoxy-carbonylation of cinnamyl chloride at 20 bar CO.

10.3 Results and discussion: Insertion mechanism

10.3.1 High pressure NMR using monodentate ligands

For the catalytic reaction at 1.2 bar of CO, cinnamyl chloride proved to be the only useful substrate and was used instead of cinnamyl triflate (section 10.2.4). Although the stepwise synthesis using the triflate complexes lead us to the discovery of the associative mechanism, we were interested in the reactivity of the chloride complexes towards CO. For these complexes, we were unable to observe CO-frequencies using infrared spectroscopy at 1.2 bar of CO (see section 4.2). We decided therefore, to study these complexes at various pressures of CO, using NMR spectroscopy. To this end, the (cinnamyl)Pd(L)Cl complexes (1a-d) were treated with 1.2 bar of CO. As expected, the chloride analogue of 3a-g ((cinnamyl)Pd(CO)Cl) could not be observed.
Chapter 10

Raising the CO pressure to 20 bar and lowering the temperature to 233K resulted in the formation of a new complex. A characteristic pattern in the $^1$H-NMR spectrum was observed, showing $H_a$ and $H_b$ in the CH$_2$-unit around 4 ppm and the olefinic proton next to the phenyl as a doublet (figure 6). Furthermore, a resonance at 236 ppm in the $^{13}$C-spectrum indicated the formation of an acyl species (5a-b) (figure 15, table 6).\cite{4,5,7,9}

The starting $\eta^3$-cinnamyl and the acyl complex appeared to be in equilibrium. At low pressure and high temperature, the starting complex (cinnamyl)Pd(L)Cl (1a-b) was observed, whereas the acyl species was observed at low temperature and high pressure. No decomposition occurred during these NMR experiments and the formation of the acyl complex appeared to be completely reversible. After insertion of CO the formed acyl complex was found to be stable under the conditions used. Most likely, the vacant site created upon insertion will be occupied by a bridging chloride ligand, forming a dimeric complex (5a-b)\cite{18b} (figure 16). In such a complex, the ligand and the carbonyl would be located cis to one another as in (POPy1)Pd(Cl)(C(O)cinnamyl) (13a, see below).

![Figure 16: Proposed dimeric acyl species.](image)

Several authors have reported on the reductive elimination of acid chloride from L$_2$Pd(acyl)Cl complexes.\cite{18b}

For the complexes studied in this chapter, however, no reductive elimination was observed.

To study the possible formation of the carbomethoxy intermediate (4a) from the acyl complex (5a), methanol was added to the solution, but no reaction occurred.

In contrast, the acyl species was not formed when the cationic [(cinnamyl)Pd(L)(MeCN)][OTf] complexes (2a-b) were used. The [(cinnamyl)Pd(L)CO][OTf] complexes (3a-b) were readily formed, but even raising the pressure of CO to as much as 50 bar did not result in the formation of the acyl complex (5a-b) (figure 15). Apparently, either an extra equivalent of ligand (see above) or a coordinating counterion are required to obtain acyl species.
The mechanisms of the palladium catalyzed carbonylation.

![Chemical structures](image)

Figure 15: Observed species in HP-NMR using (cinnamyl)Pd(L)X complexes.

Table 6: Distribution of (cinnamyl)Pd(L)X complexes as observed using HP-NMR spectroscopy.

<table>
<thead>
<tr>
<th>L / X</th>
<th>Temperature (K)</th>
<th>p (bar)</th>
<th>% 1a/b (η3-allyl)</th>
<th>% 5a/b (acyl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCy₃</td>
<td>298</td>
<td>5</td>
<td>&gt;98</td>
<td>&lt;2</td>
</tr>
<tr>
<td>PCy₃</td>
<td>233</td>
<td>5</td>
<td>&gt;98</td>
<td>&lt;2</td>
</tr>
<tr>
<td>PCy₃</td>
<td>298</td>
<td>10</td>
<td>&gt;98</td>
<td>&lt;2</td>
</tr>
<tr>
<td>PCy₃</td>
<td>233</td>
<td>10</td>
<td>90</td>
<td>10</td>
</tr>
<tr>
<td>PCy₃</td>
<td>298</td>
<td>20</td>
<td>&gt;98</td>
<td>&lt;2</td>
</tr>
<tr>
<td>PCy₃</td>
<td>233</td>
<td>20</td>
<td>25</td>
<td>75</td>
</tr>
<tr>
<td>PCy₃ / OTf</td>
<td>298</td>
<td>50</td>
<td>&gt;98</td>
<td>&lt;2</td>
</tr>
<tr>
<td>PCy₃ / OTf</td>
<td>233</td>
<td>50</td>
<td>&gt;98</td>
<td>&lt;2</td>
</tr>
<tr>
<td>PPh₃</td>
<td>298</td>
<td>20</td>
<td>&gt;98</td>
<td>&lt;2</td>
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<td>77</td>
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<td>PPh₃</td>
<td>298</td>
<td>50</td>
<td>&gt;98</td>
<td>&lt;2</td>
</tr>
</tbody>
</table>

10.3.2 High pressure NMR using bidentate PN ligands

In the previous paragraph describing the behavior of the complexes containing monodentate ligands, it was shown that an L/Pd ratio > 1 or a coordinating chloride counterion is needed to obtain acyl complexes. We therefore considered the use of hemilabile bidentate ligands. Since it is known that the use of dissymmetric ligands facilitates the CO-insertion, we decided to use the cinnamyl complexes of the ligands...
POPyl-3 (figure 17) (chapter 6), bearing the Ph group of the cinnamyl trans to phosphorus in the syn position.\[^{[16]}\)

![Figure 17: Used PN ligands, n=1: POPyl, n=2: POPy2, n=3: POPy3.](image)

![Figure 18: Reaction of complexes of type 12, as observed by HP-NMR.](image)

Table 7: Numbering of complexes bearing POPyny ligands.

<table>
<thead>
<tr>
<th>Complex</th>
<th>Ligand</th>
<th>X</th>
<th>acyl complex?</th>
<th>remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>11a</td>
<td>POPyl</td>
<td>OTf</td>
<td>no</td>
<td></td>
</tr>
<tr>
<td>11b</td>
<td>POPy2</td>
<td>OTf</td>
<td>no</td>
<td></td>
</tr>
<tr>
<td>11c</td>
<td>POPy3</td>
<td>OTf</td>
<td>no</td>
<td></td>
</tr>
<tr>
<td>12a</td>
<td>POPyl</td>
<td>Cl</td>
<td>no</td>
<td></td>
</tr>
<tr>
<td>12b</td>
<td>POPy2</td>
<td>Cl</td>
<td>no</td>
<td></td>
</tr>
<tr>
<td>12c</td>
<td>POPy3</td>
<td>Cl</td>
<td>no</td>
<td></td>
</tr>
<tr>
<td>13a</td>
<td>POPyl</td>
<td>Cl</td>
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<td></td>
</tr>
<tr>
<td>13b</td>
<td>POPy2</td>
<td>Cl</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>13c</td>
<td>POPy3</td>
<td>Cl</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>14a</td>
<td>POPyl</td>
<td>OAc</td>
<td>no</td>
<td></td>
</tr>
<tr>
<td>14b</td>
<td>POPy2</td>
<td>OAc</td>
<td>no</td>
<td></td>
</tr>
<tr>
<td>15a1</td>
<td>POPyl</td>
<td>OAc</td>
<td>yes</td>
<td>minor</td>
</tr>
<tr>
<td>15a2</td>
<td>POPyl</td>
<td>OAc</td>
<td>yes</td>
<td>major</td>
</tr>
<tr>
<td>15b</td>
<td>POPy2</td>
<td>OAc</td>
<td>yes</td>
<td></td>
</tr>
</tbody>
</table>
The mechanisms of the palladium catalyzed carbonylation.

Contrary to what was found for the complexes bearing monodentate ligands, treating the cationic (POPy1-3)Pd(η^3-cinnamyl)OTf complexes (11a-c) with 1 bar of CO did not alter the NMR spectra. Raising the pressure to 50 bar, resulted in a slight broadening of the signals in the NMR spectra. No evidence was found, however, for coordination of CO to palladium or insertion of CO in the Pd-allyl bond. The ¹H-NMR spectrum shows that the pyridine functionality remained bonded to the palladium, thereby hampering the coordination of CO.

Since the presence of the nitrogen donor atom in the ligand did not result in the formation of the acyl complex, the corresponding chloride complexes 12a-c were prepared. The allyl signals in the ¹H-NMR spectra are broadened compared to the corresponding cationic complexes, indicating a lower barrier for the η^1-η^1 isomerization (see chapter 6). Recent EXAFS measurements show that the chloride counterion is at a large distance of the palladium, leaving the Pd-complex essentially cationic.¹¹ Again, treating these complexes with 1.2 bar of CO did not result in a reaction of the starting material.

Analogous to the complexes bearing monodentate ligands, NMR studies show that an increase of the CO pressure (> 5 bar) for the chloride containing complexes 12a-c resulted in the formation of the acyl complexes (13a-c) (figure 18, tables 7). The reaction proceeded smoothly for all three ligands, was irreversible for the POPy1 complex and was reversible for the POPy2 and the POPy3 complexes. It remains unclear, whether the different stabilities of 13a-c are only due to thermodynamic factors, or that kinetic factors may play a role as well. For instance, the low flexibility in the backbone of POPy1 may prevent rearrangements in the complex required for the reverse reaction.

The η^3-allyl complexes of POPy2 and POPy3 (12b-c) and the newly formed acyl species (13b-c) are in equilibrium. At high temperature and low pressure, the η^1-allyl complexes (12b-c) are observed, whereas at low temperature and high pressure, the acyl complexes (13b-c) are observed. As was found for the monodentate ligands, also for the bidentate PN ligands, no reductive elimination of the acyl chloride was observed under these conditions.¹⁸

10.3.3 Effect of acetate as the counterion on acyl formation

As discussed in chapter 1, the use of leaving groups other than halogen atoms, is desirable for environmental reasons. Unfortunately, the catalytic carbonylation does not proceed for cinnamyl acetate (see below). To gain more insight in the origin of this inactivity of cinnamyl acetate, we studied the reactivity of the acetate complexes 14a-b towards CO.

The (POPy)nPd(cinnamyl)OAc complexes (14a-b) were prepared by treating 12a-b with AgOAc. The acetate complexes of monodentate ligands a-g (ligand)Pd(cinnamyl)OAc decomposed rapidly after formation to cinnamyl acetate and palladium metal, but the (POPy)nPd(cinnamyl)OAc complexes (14a-b) were found to be relatively stable. NMR spectroscopy showed that these complexes are very similar to the chloride analogues 12a-b.
Chapter 10

The use of acetate instead of chloride as the counterion resulted in different behavior of the (POPy)Pd(cinnamyl)OAc complexes (14a-b) upon reaction with CO. Pressurizing to 20 bar of CO at room temperature resulted in reductive elimination of cinnamyl acetate and decomposition to palladium metal. The propensity of (allyl)PdOAc type complexes to undergo reductive elimination in the presence of carbon monoxide has been described previously.\[1b\] Below 273 K, the decomposition of 14a-b was slow and NMR-spectroscopy showed a $^{13}$C-resonance around 228 ppm, indicating the formation of the acyl species (15a-b) (table 8). In contrast to the chloride modified complexes, the (POPy2)Pd(cinnamyl)OAc (15b) complex slowly decomposed via reductive elimination to the linear anhydride (figure 19c) and palladium metal. This is in line with studies by Yamamoto, who reported on the reductive elimination of anhydrides from acyl-Pd-formato complexes.\[4\]

Apparently, the use of cinnamyl acetate in the catalytic carbonylation is hampered by fast (direct or catalyzed) nucleophilic attack on the allyl and a relatively fast decomposition of the catalyst. EXAFS studies are being performed to gain more insight in the factors governing the decomposition of Pd(allyl) complexes (chapter 1).

![Diagram](figure 19 a)

**n**

![Diagram](figure 19 b)

![Diagram](figure 19 c)

**Figure 19 a-c: Reductive elimination of acyl complexes.**

For the POPy1 modified complex (15a), NMR-spectroscopy showed the presence of two acyl species in approximately a 3 / 2 (15a1/15a2) ratio, differing slightly in the chemical shift of $^{31}$P and $^{13}$C(O). Also in this case, slow decomposition occurred to the linear anhydride. Repeating the experiment with 5 bar instead of 20 bar of $^{13}$CO, again showed the two acyl species, but in a 1 / 5 (15a1/15a2) ratio. Lowering the temperature did not alter the ratio, but complex 15a1 disappeared upon raising the temperature to above 298 K. After completion of this reaction, lowering of the temperature did not alter the NMR-spectra, indicating...
that the thermodynamically most stable isomer \((15a2)\) had been formed. The \(^{13}\text{C}-\text{NMR}\) shift is close to that of the analogous chloride complex and \(15a2\) was assigned to the cis-acyl-P isomer (figure 20).

Table 8: Selected NMR data of the acyl complexes bearing PN ligands.

<table>
<thead>
<tr>
<th>complex</th>
<th>L</th>
<th>X</th>
<th>(\delta^{(13}\text{C-O})/\text{ppm})</th>
<th>(\delta^{(31}\text{P})/\text{ppm})</th>
</tr>
</thead>
<tbody>
<tr>
<td>13a</td>
<td>POPy1</td>
<td>Cl</td>
<td>226.5</td>
<td>119.9</td>
</tr>
<tr>
<td>13b</td>
<td>POPy2</td>
<td>Cl</td>
<td>229.6</td>
<td>106.7</td>
</tr>
<tr>
<td>13c</td>
<td>POPy3</td>
<td>Cl</td>
<td>227.5</td>
<td>118.9</td>
</tr>
<tr>
<td>15a1</td>
<td>POPy1</td>
<td>OAc</td>
<td>229.8</td>
<td>119.8</td>
</tr>
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<td>15a2</td>
<td>POPy2</td>
<td>OAc</td>
<td>231.9</td>
<td>123.5</td>
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<tr>
<td>15b</td>
<td>POPy2</td>
<td>OAc</td>
<td>228.0</td>
<td>106.8</td>
</tr>
</tbody>
</table>

These observations are in agreement with the proposed mechanism of the migratory insertion reaction.\(^{[23, 24]}\) The dependence of the \(15a1/15a2\) ratio on the pressure can be explained by the relatively weak coordination of the acetate counterion. Under a high pressure of carbon monoxide, the CO may replace the acetate and retard the isomerization from \(15a1\) to \(15a2\). At a low CO pressure, the acetate is not replaced and the isomerization of \(15a1\) to \(15a2\) may be relatively fast.

Figure 20: Reaction of CO with \((\text{POPy}1)\text{Pd (cinnamyl)(OAc) 14a.}\)

10.3.4 Crystal structure of \(13a\)

For POPy1, the CO-insertion reaction is not reversible under the applied conditions and complex \(13a\) could be isolated. Recrystallization from CDCl\(_3\) / hexane yielded colorless crystals suitable for structure determination by X-ray crystallography. As shown in the molecular plot (figure 21 and 22 and table 9), the acyl group is located cis to phosphorus, which is in agreement with the small P-C coupling constant \(^{[29]}\)
10 Hz) and with previous studies on (alkyl-C(O)-)Pd(P-N) complexes that show that the acyl group is located cis to phosphorus.\[^{17}\]

The geometry around the central Pd-atom is square planar and the angles between the ligands are all close to 90°. The pyridine ring is rotated with respect to the coordination-plane and the Pd-P and Pd-N bonds are of almost equal length. The cinnamyl group is almost planar and points away from the palladium atom. The C=C double bond (C3-C4) and the phenyl rings on the phosphorus are at a distance of 4Å and are almost parallel.

![Figure 21: X-ray crystal structure of 13a.](image)

![Figure 22: Line drawing and numbering scheme of the crystal structure of 13a.](image)
The mechanisms of the palladium catalyzed carbonylation.

Table 9: Selected structural data of the crystal structure of 13a.

<table>
<thead>
<tr>
<th>Distance or angle</th>
<th>Value (distances in Å, angles in °)</th>
</tr>
</thead>
<tbody>
<tr>
<td>d(Pd-Cl)</td>
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</tr>
<tr>
<td>d(Pd-N)</td>
<td>2.210(5)</td>
</tr>
<tr>
<td>d(Pd-P)</td>
<td>2.215(2)</td>
</tr>
<tr>
<td>d(Pd-C(1))</td>
<td>1.972(6)</td>
</tr>
<tr>
<td>d(C(1)-O)</td>
<td>1.202(9)</td>
</tr>
<tr>
<td>d(C(1)-C(2))</td>
<td>1.580(13)</td>
</tr>
<tr>
<td>d(C(2)-C(3))</td>
<td>1.526(9)</td>
</tr>
<tr>
<td>d(C(3)-C(4))</td>
<td>1.305(11)</td>
</tr>
<tr>
<td>d(C(4)-C(ipso))</td>
<td>1.508(10)</td>
</tr>
<tr>
<td>θ(Cl-Pd-N)</td>
<td>92.66(16)</td>
</tr>
<tr>
<td>θ(N-Pd-P)</td>
<td>88.83(16)</td>
</tr>
<tr>
<td>θ(P-Pd-C(1))</td>
<td>89.3(2)</td>
</tr>
<tr>
<td>θ(C(1)-Pd-Cl)</td>
<td>89.4(2)</td>
</tr>
</tbody>
</table>

10.3.5 Discussion on the formation of cis-complexes

The reaction of (POPyn)Pd(Cl)(cinnamyl) complexes (12a-c) with CO resulted in the clean formation of the CO-inserted (POPyn)Pd(Cl)(C(O)cinnamyl) complexes (13a-c) with the phosphorus and the carbonyl functions cis to one another. This has been observed before for migratory insertion reactions in palladium complexes\(^{17, 23}\) (figure 23) but seems to contradict the Cossee mechanism\(^{24}\) which describes the acyl forming step as a migration reaction rather than an insertion reaction (see below).

The coalesced signals of Ha and Hb indicate that the well known \(\eta^1\)-\(\eta^1\)-\(\eta^3\) rearrangement readily occurs in the (POPyn)Pd(Cl)(cinnamyl) complexes (12a-c). In chapter 6 it was shown, that with the phenyl group of the cinnamyl trans to the phosphorus atom, the \(\eta^1\)-\(\eta^1\)-\(\eta^1\) rearrangement occurs via a selective cleavage of the Pd-allyl bond trans to the phosphorus atom, forming species 12-2 (figure 23). Consequently, the vacant site available for coordination of CO is trans to phosphorus. Migratory insertion via the Cossee mechanism, therefore, would yield the acyl group trans to phosphorus, instead of the observed cis arrangement. The trans-cis isomerization in such complexes is known to proceed easily and accounts for the observation the thermodynamic product only.\(^{23}\)

The \(\eta^1\)-\(\eta^1\)-\(\eta^1\) rearrangement, however, also takes place in the cationic complexes bearing a triflate counterion (11a-c). Even at a pressure of 50 bar, no insertion and no complexes other than (POPyn)Pd(cinnamyl)OTf (11a-c) could be observed. Apparently, the chloride counterion plays a crucial
role in the process of formation and / or stabilization of the acyl species (13). Several explanations may account for this behavior. First, the chloride may facilitate the isomerization from the trans-isomer to the cis-isomer. Thus, after formation of the kinetic trans-acyl complex, isomerization to the cis-isomer has to occur before “de-insertion” and dissociation of CO takes place. Second, the chloride counterion may be involved in a concerted mechanism, in which the CO coordinates and inserts in one step. This mechanism could proceed via either an η^1- or an η^3-complex. Attempts to study the insertion pathway in an (η^3-C_3H_5)Pd(PH_3)(NH_3)Cl complex by molecular modeling have failed as a result of the strong interaction between the chloride and the cationic palladium center.

η^1-complex

In the η^1-complex (figure 24), the coordination of both Cl and CO to the palladium may cause the η^3-cinnamyl to rearrange to the η^1-cinnamyl. As the donor ligands will be located preferentially trans to the best π-acceptor ligands, the square pyramidal five coordinated transient complex depicted in figure 24 will be formed. The phosphorus and nitrogen donor atoms are cis to one another, the CO ligand is located trans to nitrogen and the η^1-allyl trans to phosphorus. Subsequent migratory insertion will directly yield the observed (POPyl)Pd(Cl)(C(0)cinnamyl) (13a) with the phosphorus and the carbonyl functions cis to one another.

η^3-complex

In an alternative mechanism, the cinnamyl remains bonded to the palladium in an η^3-fashion (figure 25). Upon coordination of CO and a weak coordination of Cl in the second coordination sphere, a concerted insertion of CO in the η^3-cinnamyl occurs. Because the CH_2-site of the cinnamyl is cis to phosphorus, the acyl will also be cis to phosphorus.

![Figure 23 η^3-η^1 rearrangement and CO insertion, according to the Cossee mechanism, for cationic complexes.](image-url)
The mechanisms of the palladium catalyzed carbylation.

Figure 24: Proposed process for \( \eta^3-\eta^1 \)-rearrangement and CO insertion, leading directly to the formation of 13a.

Figure 25: Proposed process for CO insertion in an \( \eta^3 \)-complex.

10.3.6 Stoichiometric reactions of the acyl complex 13a

To study the reactivity of the acyl group, the isolated (POPy1)Pd(Cl)(C(O)cinnamyl) complex (13a) was subjected to stoichiometric reactions using various nucleophiles (figure 26). Reaction with methanol at room temperature resulted in slow formation of the linear ester. No evidence was found for the presence of other complexes such as a possible intermediate (POPy1)Pd(OC(OCH\(_3\)))(C(O)cinnamyl) in which the chloride would be replaced by a methoxide (figure 27). When methanol was used in the presence of the base NEt\(_3\), the methanolsysis occurred instantaneously.

Piperidine reacted slowly with the acyl species to form the corresponding linear amide (K).\(^4\) The less nucleophilic amine p-toluidine, however, did not react at all. Because for the reaction of (POPy1)Pd(Cl)(C(O)cinnamyl) (13a) with methanol or piperidine no other intermediates than the acyl complex (13a) could be observed, it is concluded that both reactions take place via nucleophilic attack on the coordinated acyl group. Yamamoto suggested that Et\(_2\)NH might react via an associative mechanism rather than nucleophilic attack on the acyl group in (benzyl-C(O)-)Pd(CO)(PMe\(_3\))\(_2\) complexes.\(^4\) For the PN ligands studied in this chapter, however, no evidence for such an amidocarboxy Pd-(C(O)-NEt\(_3\))-type intermediate was found.

Addition of a tertiary amine, NEt\(_3\), resulted in the loss of CO and the known \( \eta^3 \)-allyl complex 12a was formed quantitatively. The use of AgOTf had a similar effect; the chloride was abstracted and, as expected,
the cationic (POPyl)Pd(cinnamyl)OTf complex (11a) was formed. Apparently, the acyl decomposed via deinsertion to fill the vacant site. Thus, the more stable cationic complex (POPyl)Pd(cinnamyl)OTf complex (11a) was formed, which is known not to undergo CO-insertion (see above).

10.3.7 Catalytic carbonylation using PN ligands

The facile formation of the ester (E) from (POPyl)Pd(Cl)(C(O)cinnamyl) (13a) and methanol and NEt₃ at room temperature, prompted us to study the catalytic carbonylation of cinnamyl chloride at room temperature and elevated pressure, using various solvents and various tertiary amines (tables 10 and 11). For comparison, the reactions were also performed using complex 1a (PCy₃).
Table 10: Results of catalytic carbonylation of cinnamyl chloride at 20 bar at room temperature, yields determined after 4 hours. Experimental details: see experimental section.

<table>
<thead>
<tr>
<th>L / amine</th>
<th>solvent</th>
<th>TOF(^b)</th>
<th>conversion (4 hours)</th>
<th>% ester (E)</th>
<th>% ammonium salt (AM)(^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCy(_3) / NEt(_3)</td>
<td>thf</td>
<td>10</td>
<td>49</td>
<td>33</td>
<td>67</td>
</tr>
<tr>
<td>PCy(_3) / NEt(_3)</td>
<td>acetone</td>
<td>24</td>
<td>76</td>
<td>39</td>
<td>61</td>
</tr>
<tr>
<td>PCy(_3) / NEt(_3)</td>
<td>MeCN</td>
<td>23</td>
<td>100</td>
<td>32</td>
<td>68</td>
</tr>
<tr>
<td>POPy1 / NEt(_3)</td>
<td>MeCN</td>
<td>8</td>
<td>72</td>
<td>22</td>
<td>78</td>
</tr>
<tr>
<td>POPy2 / NEt(_3)</td>
<td>MeCN</td>
<td>22</td>
<td>36</td>
<td>8</td>
<td>92</td>
</tr>
<tr>
<td>POPy3 / NEt(_3)</td>
<td>MeCN</td>
<td>55</td>
<td>100</td>
<td>37</td>
<td>63</td>
</tr>
<tr>
<td>POPy1 / DIPEA(^b)</td>
<td>MeCN</td>
<td>3</td>
<td>8</td>
<td>88</td>
<td>13</td>
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<tr>
<td>POPy2 / DIPEA(^b)</td>
<td>MeCN</td>
<td>21</td>
<td>39</td>
<td>87</td>
<td>13</td>
</tr>
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<td>POPy3 / DIPEA(^b)</td>
<td>MeCN</td>
<td>52</td>
<td>40</td>
<td>95</td>
<td>5</td>
</tr>
</tbody>
</table>

\(^a\): initial Turn Over Frequency of substrate to ester in mole/mole/hour, determined after 60 minutes.
\(^b\): N, N-di-isopropyl ethyl amine
\(^c\): (cinnamyl)NR\(_3\)Cl

As was also found for the associative mechanism, the linear ester is the only carbonylation product. No formation of cinnamyl methyl ether (F) was observed, indicating that the carbonylation is faster than the nucleophilic attack of methanol on the Pd-allyl complex (table 10).

The only side product formed, (cinnamyl)NR\(_3\)Cl (AM), originates from nucleophilic attack of the tertiary amine on the allyl moiety. The absolute amount of ammonium salt formed depends on the ligand and increases in the following order: POPy2 < POPy1 < POPy3. This reaction is rather similar to the allylic alkylation reaction and the observed activity of the PN ligands with respect to the formation of the ammonium side product (AM) roughly corresponds to their activity in the allylic alkylation (see chapter 6).

The use of the bulkier amine DIPEA reduced the amount of ammonium salt formed and the ester was produced in nearly quantitative yield.

The catalytic carbonylation using piperidine as the nucleophile did not yield any carbonylation product; instead all cinnamyl chloride was converted to the corresponding amine (M), via the allylic amination reaction (figure 28).\(^{19}\)
Using PCy₃ as the ligand, the rate of the catalytic carbonylation at 20 bar (insertion mechanism) is much lower than for the carbonylation at 1.2 bar of CO with NBu₄OH (associative mechanism). This can be explained by a lower reactivity of methanol compared to methoxide towards the carbomethoxy species (if it would be formed at elevated pressures) and also by a low concentration of the acyl species (the equilibrium favors the η³-allyl).

Figure 28: Formation of allyl-amine using piperidine as the base.

10.3.8 Kinetics

To gain more insight in the mechanism of the carbonylation reaction and the origin of the different reaction rates found for the various ligands the kinetics of the reaction were studied. To this end, the reaction was performed with a systematic variation of the initial concentration of the reactants, using various solvents and various tertiary amines (table 11). Because of the stability of the intermediates in the catalytic reaction and their reversible formation, we were able to monitor the reaction by taking samples after releasing the pressure from the autoclave. After repressurizing, the reaction started again, without noticeable degradation of the catalyst (figure 29). At low conversion (below circa 60%) the reaction proceeded at the same rate, allowing for the reliable determination of the reaction orders for the reactants.
The mechanisms of the palladium catalyzed carbonylation.

Table 11: Kinetic data for the catalytic carbonylation of cinnamyl chloride to ester E.

\[ \text{d}[\text{P}]/\text{d}t = k_{\text{obs}} [\text{Pd}]^q [\text{cinnamyl chloride}]^p [\text{MeOH}]^r [\text{amine}]^s [\text{CO}]^t. \]

Empty fields: order not determined. Experimental details: see experimental section.

<table>
<thead>
<tr>
<th>L</th>
<th>base</th>
<th>solvent</th>
<th>( k_{\text{obs}}^{\text{**}} ) ((10^{11}))</th>
<th>p</th>
<th>q</th>
<th>r</th>
<th>s</th>
<th>t.</th>
</tr>
</thead>
<tbody>
<tr>
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<td>NEt₃</td>
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<td>0</td>
<td>1</td>
<td>0-1*</td>
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<td></td>
<td></td>
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<td>0.5</td>
</tr>
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*: not enough data points to determine the exact order.

**: in L⁴.mole⁻⁴.s⁻¹.

Figure 29: Typical example demonstrating the stability of the catalyst: each point represents a sample taken after release of the pressure. Conditions of the experiment: 0.001 mmole of catalyst 1a, 1 mmole of methanol, 1 mmole of NEt₃, 1 mmole of cinnamyl chloride, in acetonitrile at 20 bar of CO at 293K.

Under the used conditions, the reaction proceeded with a zero order dependence of both cinnamyl chloride and methanol concentration, whereas a positive order in CO concentration and a first order dependence on the palladium concentration were found. Intriguingly, the dependence of the rate of the reaction on the amine...
concentration varies strongly for the different ligands and conditions. When using PCy$_3$ in thf, a first order dependence on the amine concentration is found, but in acetone and acetonitrile the observed order is 0.5 (figure 30). For the bidentate PN ligands, in all cases a broken order in the amine concentration was found. For NEt$_3$, the observed order varies with the ligand, between 0.3 and 0.7, but for the more bulky amine DIPEA, the observed order is 0.5 for all ligands within the window of concentrations studied. This half-order dependence might point to association-dissociation behavior. It is, however, not clear what the nature of the species involved is.

![Figure 30: Typical example of the kinetic experiments. Each point represents the percentage of ester formed after 1 hour, using different concentrations of NEt$_3$. All kinetic experiments showed curves of product formation as displayed in the previous figure. The reaction conditions for the example of this graph are: 0.1-1.0 mmole of NEt$_3$, 0.005 mmole of complex 1a, 1.0 mmole of cinnamyl chloride, 1.0 mmole of MeOH, in acetone p.a. at 20 bar CO at 293K.](image_url)

10.3.9 High pressure NMR of the reaction mixture of catalytic carbonylation at 20 bar CO.

For the PCy$_3$ complex 1a, the reaction was also followed using NMR spectroscopy. To this end, excesses of cinnamyl chloride, NEt$_3$ and methanol were used. After pressurizing to 20 bar, the tube was cooled in the NMR spectrometer. Some of the substrate was already converted to the ester, but the acyl complex could still be observed. In addition, several other complexes bearing $^{13}$CO were found in the reaction mixture. Two complexes showed resonances around 180 ppm, which is indicative of a Pd-CO complex (see section 4.2) and one resonance was found at 255 ppm, which is indicative of a palladium dimer containing a bridging carbonyl ligand.\(^{[20]}\) Heating to room temperature resulted in a fast conversion of cinnamyl chloride to the ester (E). Unfortunately, as a result of broadened signals, the signal to noise ratio in the $^{31}$P and $^{13}$C-NMR
The mechanisms of the palladium catalyzed carboxylation.

spectra was too low to observe intermediate palladium complexes at room temperature. Repeating the experiment without added NEt₃ did not result in the formation of the ester. This is in agreement with the kinetic experiments, that showed a positive order in the amine concentration.

10.3.10 Discussion on the rate of the catalytic reaction

The results of the systematic variation of the initial concentrations of the substrates show that the overall kinetic equation is rather complicated. Compared to POPy₁ and POPy₂, the use of PCy₃ at 20 bar results in a similar reaction rate. The different rates for the various POPyₙ ligands are not easily explained, since several factors may influence the reaction rate.

The reaction rate increases from POPy₁ to POPy₃, resembling the bite angle trend observed for the alcoholysis of (acetyl)Pd(P-P) complexes. The kinetics, however, show a zero order dependency in methanol and a positive order in the amine. If the amine is involved in the alcoholysis, it follows the same reactivity pattern as the alcohol in the above mentioned studies. On the other hand, the amine may also be involved in stabilizing intermediate Pd clusters. For instance, Kurosawa reported cationic dimers, in which the allyl group acted as a bridge between the two palladium centers. Although we have not yet observed Pd-clusters in the reaction mixtures, their formation cannot be ruled out. The dissociation of the amine from these dimeric complexes may be rate determining, leading to the observed rate equation.

Furthermore, the interactions between the formed H⁺ and the amine may also influence the kinetics of the reaction. More studies are required to gain more insight in the catalytic cycle and in the observed differences in the rates of the catalytic reactions. Based on the results so far, we propose the following catalytic cycle for the carboxylation of cinnamyl chloride at elevated pressures of CO, using P-N ligands (figure 31).

Figure 31: Proposed catalytic cycle for the methoxy-carboxylation of cinnamyl chloride at 20 bar CO using mixed bidentate P-N ligands.
Chapter 10

A transient Pd(P-N)\(^0\) complex reacts with cinnamyl chloride to form the corresponding \((\eta^3\text{-cinnamyl})\text{Pd}(P-N)\text{Cl}\) complex. Initially, the isomer bearing the phenyl group of the cinnamyl cis to the phosphorus will be formed (see also chapter 6), which after rearrangement yields the more stable complex 12. Insertion of CO occurs and initially the isomer bearing the acyl trans to the phosphorus will be formed. After rearrangement to the more stable isomer 13, the ester E will be formed via methanolysis of complex 13. The HCl, which is formed as a side product, will react with the amine base to form the corresponding ammonium salt.

10.4 Conclusions

To study the mechanism of the palladium catalyzed alkoxy carbonylation of cinnamyl chloride we have prepared several putative intermediates of the catalytic cycle, among which a new class of \([(\eta^3\text{-cinnamyl})\text{Pd(ligand)CO}]\text{[OTf]}\) complexes (3). These palladium complexes react with a methoxide nucleophile to form \((\eta^3\text{-cinnamyl})\text{Pd(L)}\text{C(O)OMe}\) carbomethoxy complexes (type 4).

We have shown that two mechanistic pathways are possible for the palladium catalyzed methoxy carbonylation of cinnamyl chloride. Both mechanisms proceed at room temperature. The newly found carbomethoxy mechanism is favored at 1.2 bar of CO for complexes bearing a) an \(\eta^3\)-allyl moiety and b) one monodentate ligand. The acyl mechanism is favored only at higher pressures of CO and only for complexes bearing a) a coordinating counterion and b) more than one monodentate ligand or one bidentate P-N ligand.

The reagents determine the mechanism of the reaction. When monodentate ligands are used in combination with methoxide, the reaction proceeds via the carbomethoxy mechanism, both at high and low pressure. On the other hand, using methanol and amine, the reaction only proceeds via the acyl mechanism and a high CO-pressure is required.

Kinetic studies of the insertion reaction point out that the kinetic equation depends on the nature of the solvent. The catalytic reaction proceeds with a positive order in palladium, CO and the amine base.

Furthermore, we have shown for the insertion mechanism, that the catalyst remains stable after release of the CO-pressure. We expect that recycling of the catalyst is possible via anchoring the catalyst to a solid support and filtration of the reaction mixture.
10.5 Experimental section

$^1$H and $^{13}$C-NMR (300 resp. 75 MHz, TMS, CDCl$_3$), $^{31}$P ($^1$H) (121.5 MHz external 85% H$_3$PO$_4$, CDCl$_3$) were recorded on a Bruker DRX-300 spectrometer.

The product distribution of the carbonylation reaction was measured by GC on an Interscience Mega2 apparatus, equipped with a DB1 column, length 30 m, inner diameter 0.32 mm, film thickness 3.0 μm, and a F.I.D detector.

10.5.1 General procedures

All experiments were carried out using standard Schlenk techniques. All solvents were freshly distilled prior to use. All reactions have been performed at room temperature (292 K). High pressure NMR experiments were carried out using a sapphire tube.

The Pd-complexes were prepared in CH$_2$Cl$_2$ from [(C$_9$H$_9$)$_2$-Pd-μCl]$_2$ by adding 2 equiv. of ligand (i.e. one per palladium) and abstracting the chloride-atom using AgOTf (see chapter 4-8). The complexes were isolated in quantitative yield (microcrystalline powder) and were used as such in the alkylation reaction. The synthesis of the POPyn ligands has been described in chapter 6. The synthesis and characterization of 11a-c and 12c have been described in chapter 6. Ligand f was used by kind permission of Maarten Boele.[28] All other ligands and reagents have been purchased from Aldrich.

10.5.2 Synthesis of palladium complexes

Typical procedures for the synthesis of the palladium complexes (procedures are the same for all ligands):

Type 1 (table 1) and 12 (table 7):
To a yellow solution of [(C$_9$H$_9$)$_2$-Pd-μCl]$_2$ (100 mg, 193 μmole) in 20 mL of CH$_2$Cl$_2$ was added 101 mg (386 μmole) of PPh$_3$. After stirring for 30 minutes the solvent was evaporated and the complex was obtained quantitatively as a yellow microcrystalline solid.

Type 2 (table 1):
To a yellow solution (20 mL) of 1b in CH$_2$Cl$_2$ (201 mg, 386 μmole) was added 101.2 mg (39.0 μmole) of dry AgOTf. Upon addition, the color of the solution became light yellow and a fine white solid precipitates. After stirring for 3 minutes, 0.5 mL MeCN was added. The solution became even lighter yellow and the white powder changed to white flakes. After stirring for 15 minutes, active carbon was added to remove the excess of AgOTf. Filtration over cotton wool and evaporation of the solvent yielded a light yellow microcrystalline powder. The complexes should be stored at low temperature.
Chapter 10

Type 11 (table 7):
The procedure is analogous to the procedure for type 2 complexes, but no MeCN was added.

Type 3 (table 1):
CO was bubbled through a solution of 10 mg of 1b in CDCl₃. The light yellow solution turned colorless within one minute (within seconds for the more basic ligands). The product could not be isolated by either evaporation of the solvent or by precipitation using pentane or hexane.

Type 4 (table 3):
A solution of 10 mg of 3a in 0.6 mL of CDCl₃ was frozen at 195K and 0.1 ml of a 1.0 M solution of NBu₄OH in methanol was added and frozen as well. Slowly, the frozen solution was heated and upon melting, the solution was mixed thoroughly. Immediately, the tube was transferred to the precooled NMR spectrometer and complex 4a was characterized.

Type 5 (figure 15):
A solution of 20 mg of 1b in CDCl₃ was pressurized with CO to the appropriate pressure (10, 20, 50 bar).

Type 13 (table 7):
This procedure was performed similar to that of type 5, but alternatively, the pure acyl compound could also be obtained by preparation of the complex type 13(a and b) in an autoclave. Addition at high pressure of hexane (not pentane) via a pressurized addition vessel, led to the precipitation of the desired complex. The complex was isolated by removal of the solvent and slowly drying overnight (not evaporation in vacuo).

Type 14 (table 7):
Similar to type 11, but now AgOAc was used in place of AgOTf.

Type 15 (table 7):
Similar to type 13, but now complexes of type 14 were used as starting complexes.

10.5.3 Carbonylation reactions, low pressure

Standard conditions: 5 μmole of Pd complex of type 1, 1.0 mmole of cinnamyl chloride, 1.0 mmole of NaOMe or NBu₄OH, 0.2 mmole of para-methoxy-acetophenon (internal standard), total 5.0 mL of solvent (2.0 mL MeOH, 3.0 mL thf). The reactions were carried out under a CO atmosphere. Samples for GC were taken from the reaction mixture at regular time intervals. The samples were worked up by extraction (NH₄Cl in water / diethyl ether). After complete conversion, the catalyst decomposed to palladium metal.
The mechanisms of the palladium catalyzed carbonylation.

10.5.4 Carbonylation reactions, high pressure

Standard conditions: 5 μmole of Pd complex of type 1 or 12, 1.0 mmole of cinnamyl chloride, 1.0 mmole of MeOH, 1.0 mmole of amine (NEt₃ or DIPEA), 0.2 mmole of decane (internal standard), total volume of solvent. Before the reactions were carried out, the air was removed from the dried stainless steel autoclave and replaced by CO. Samples for GC were taken (after pressure release) from the reaction mixture at regular time intervals, after which the reaction was started again by repressurizing. The samples were worked up by extraction (water / diethyl ether).

For the kinetic experiments, the amount of the reactants was varied systematically. In all cases, the total volume of the reaction mixture was 5.0 mL.

10.5.5 Characterization

E (E-styrene-methyl-acetate):

\(^1\)H: 3.22 (d, 2H, J = 7 Hz, CH₂); 3.68 (s, 3H, CH₃); 6.25 (m, 1H, -CH=CH-Ph); 6.45 (d, 1H, 16 Hz, -CH=CH-Ph); 7.0-7.8 (m, 5H, aromatic)

K (amide of E-styrene-acetic acid and piperidine):

\(^1\)H: 1.6 (m, 6H, N-(CH₂CH₂)+C₂); 3.10 (d, 2H, J = 7 Hz,=CH-CH₂-C(O)-); 6.31 (m, 1H, Ph-CH=CH-CH₂-C(O)-); 6.48 (d, 1H, J = 16 Hz, Ph-CH=CH-CH₂-C(O)-); 7.2-7.9 (m, 5H, aromatic)

ammonium salt of cinnamyl and NEt₃:

\(^1\)H: 1.23 (t, 9H, J = 7 Hz, CH₃); 3.30 (q, 6H, J = 7 Hz, N-CH₂-CH₃); 4.12 (d, 2H, J = 8 Hz, -C(O)-CH₂-); 6.05 (dt, 1H, J₁ = J₂ = 8 Hz, J₃ = 16 Hz, -CH=CH-Ph); 6.85 (d, 1H, J = 16 Hz, -CH=CH-Ph); 7.15 (m, 3H, aromatic H); 7.30 (m, 2H, aromatic H)

\(^13\)C: 8.5; 53.4; 60.2; 114.3; 127.6; 129.1; 129.7; 135.0; 143.0

1a (PCy₃)Pd(n°-cinnamyl)Cl:

\(^1\)H: 1.25 (br s, 12H, Cy-ring); 1.5 (br s, 6H, Cy-ring); 1.8 (br m, 12H, Cy-ring); 2.2 (q, 2.2, J₁ = 12 Hz, J₂ = 12 Hz, H on ipso carbon of Cy-ring); 2.65 (d, 1H, J = 11 Hz, Ha); 3.28 (d, 1H, J₁ = 6 Hz, Hb); 5.20 (dd, 1H, J₁ = 10 Hz, J₂ = 13 Hz, Hd); 5.81 (ddd, 1H, J₁ = 13 Hz, J₁ = J₂ = 10 Hz, Hc); 7.2-7.3 (m, 3H, aromatic); 7.50 (d, 2H, J = 8 Hz, ortho-aromatic H)

\(^31\)P: 45.9 (s)

\(^13\)C (1H): 26.5; 26.8; 27.3 (d, J = 11 Hz); 27.9 (d, J = 11 Hz); 30.6; 35.1 (d, J = 18 Hz); 47.3; 100.8 (d, J = 26 Hz); 110.0; 128.0; 128.3; 129.0; 129.4; 137.1

HR-MS (FAB): C₂₇H₄₂PPd⁺ requires m/z = 503.2059, found 503.2029 (loss of Cl).
2a (PCy₃)Pd(η³-cinnamyl)(MeCN) OTf:

¹H: overlap of 1.25 (br s); 1.27 (br s); 1.38 (br s) together 15H, Cy-ring; 1.7-1.9 (br m, 18H, Cy-ring); 2.02 (s, 3H, CH₃-CN); 2.90 (br d, 1H, J = 11 Hz, Ha); 3.53 (br d, 1H, J = 6 Hz, Hb); 5.59 (dd, 1H, J₁ = 8 Hz, J₂ = 13 Hz, Hd); 6.07 (ddd, 1H, J₁ = 13 Hz, J₂ = J₃ = 9 Hz, Hc); 7.4 (m, 3H, aromatic); 7.6 (d, 2H, J = 8 Hz, ortho-aromatic H)

³¹P: 47.0 (s)

3a (PCy₃)Pd(η³-cinnamyl)(CO)OTf:

¹H: 1.2-1.4 (br m, 15H, Cy-ring); 1.7-2.2 (br m, 18H, Cy-ring); 3.56 (d, 1H, J = 13 Hz, Ha); 4.17 (d, 1H, J = 6 Hz, Hb); 6.3 (ddd, 1H, J₁ = 7 Hz, J₂ = J₃ = 9 Hz, Hd); 6.56 (br m, 1H, Hc); 7.4 (br m, 3H, aromatic); 7.78 (d, 2H, J = 8 Hz, ortho-aromatic H)

³¹P: 48.5 (s)

¹³C: 181.9

IR: 2115 cm⁻¹ (C=O)

4a (PCy₃)Pd(η³-cinnamyl)(C(0)OMe):

¹H: (signals of ammonium and Cy-rings omitted); 4.47 (dd, 1H, J₁ = J₂ = 12 Hz, Ha); 5.00 (dd, 1H, J₁ = J₂ = 10 Hz, Hb); 5.58 (ddd, 1H, J₁ = 8 Hz, J₂ = J₃ = 13 Hz, Hd); 5.72 (m, 1H, Hc); 7.0-7.4 (m, 5H, aromatic)

³¹P: 45.1 (d, J = 24 Hz)

¹³C: 211.0 (d, J = 23 Hz)

1b (PPh₃)Pd(η³-cinnamyl)Cl:

¹H: Ha and Hb overlap: 2.90 (d, 1H, J = 12 Hz, Ha); 2.95 (d, 1H, J = 6 Hz, Hb); 3.36 (dd, 1H, J₁ = 10 Hz, J₂ = 13 Hz, Hd); 6.01 (ddd, 1H, J₁ = 13 Hz, J₂ = J₃ = 10 Hz, Hc)

³¹P: 26.4 (s)

HR-MS (FAB): C₂₇H₂₄PPd⁺ requires m/z = 485.0650, found 485.0669 (loss of Cl⁻)

2b (PPh₃)Pd(η³-cinnamyl)(MeCN)OTf:

¹H: 1.84 (s, 3H, CH₃-CN); 3.13 (br d, 1H, J = 9 Hz, Ha); 3.47 (br b, 1H, Hb); 5.97 (dd, 1H, J₁ = 13 Hz, J₂ = 9 Hz, Hd); 6.30 (ddd, 1H, J₁ = 13 Hz, J₂ = J₃ = 9 Hz, Hc); 7.2-7.5 (m, 18H, aromatic); 7.71 (d, 2H, J = 5 Hz, ortho-aromatic H)

³¹P: 27.6 (s)
The mechanisms of the palladium catalyzed carbonylation.

3b (PPh₃)Pd(η³-cinnamyl)(CO)OTf:

1H: 3.58 (br d, 1H, J = 11 Hz, Ha); 3.86 (br b, 1H, Hb); 6.44 (ddd, 1H, J₁ = J₂ = 10 Hz, J₃ = 9 Hz, Hd); 6.59 (br t, 1H, J₁ = J₂ = 11 Hz, Hc); 7.2-7.5 (m, 18 H, aromatic); 7.80 (d, 2H, J = 5 Hz, ortho-aromatic H)

31P: 25.3 (s)

13C: 181.4 (s)

IR: 2125 cm⁻¹ (C=O)

1c (AsPh₃)Pd(η³-cinnamyl)Cl:

1H: 3.0-3.5 (br b, 2H, Ha + Hb); 5.20 (d, 1H, J = 12 Hz, Hd); 5.95 (ddd, 1H, J₁ = 12 Hz, J₂ = J₃ = 10 Hz, Hc); 7.2-7.6 (br m, 20 H, aromatic)

13C: 56.5; 96.9; 109.8; 128.4; 128.7; 129.1; 129.4; 130.4; 130.6; 131.9; 134.0; 134.8; 136.9

HR-MS (FAB): C₃₁H₂₄AsPd⁺ requires m/z = 529.0129, found 529.0127 (loss of Cl⁻).

2c (AsPh₃)Pd(η³-cinnamyl)(MeCN)OTf:

1H: 1.90 (s, 3H, CH₃-CN); 3.18 (br b, 1H, Ha); 3.74 (br b, 1H, Hb); 5.92 (br b, 1H, Hd); 6.26 (br b, 1H, Hc); 7.2-7.8 (br b, 20 H, aromatic)

13C: 181.1

IR: 2123 cm⁻¹ (C=O)

1d (SbPh₃)Pd(η³-cinnamyl)Cl:

1H: 3.00 (br b, 1H, Ha); 3.97 (br b, 1H, Hb); 5.24 (d, 1H, J = 12 Hz, Hd); 5.87 (ddd, 1H, J₁ = J₂ = 10 Hz, J₃ = 12 Hz); 7.2-7.6 (br m, 20 H, aromatic)

13C: 56.5; 108.9; 128.3; 128.7; 129.3; 129.6; 130.4; 132.0; 136.5; 137.1

HR-MS (FAB): C₂₇H₂₃PdSb⁺ requires m/z = 575.8483, found 576.9933 (loss of Cl⁻).

2d (SbPh₃)Pd(η³-cinnamyl)(MeCN)OTf:

1H: 2.01 (s, 3H, CH₃-CN); 3.20 (br b, 1H, Ha); 4.10 (br b, 1H, Hb); 4.60 (br b, 1H, Hd); 6.05 (br b, 1H, Hc); 6.8-7.8 (br m, 20 H, aromatic)

3d (SbPh₃)Pd(η³-cinnamyl)(CO)OTf:

1H: 3.67 (br b, 1H, Ha); 4.52 (br b, 1H, Hb); 6.32 (ddd, 1H, J₁ = 13 Hz, J₂ = J₃ = 8 Hz, Hc); 6.62 (br b, 1H, Hd); 7.0-7.7 (br m, 20 H, aromatic)

13C: 183.5 (s)

181
Ie (P(OPh)₃)Pd(η₃-cinnamyl)Cl:

\(^{1}H\): 2.00 (br d, 1H, J = 10 Hz, Ha); 3.18 (br b, 1H, Hb); 5.00 (dd, 1H, J₁ = 17 Hz, J₂ = 13 Hz, Hd); 5.25 (m, 1H, Hc); 7.0-7.3 (m, 20 H, aromatic) 

\(^{31}P\): 126.7 (s)

1g (P(o-tolyl)₃)Pd(η₃-cinnamyl)Cl:

\(^{1}H\): 2.23 (s, 9H, CH₃); 2.49 (br b, 1H, Ha); 2.97 (br b, 1H, Hb); 5.24 ((dd, 1H, J₁ = 11 Hz, J₂ = 13 Hz, Hd); 5.91 (dd, 1H, J₁ = J₂ = 9 Hz; J₃ = 13 Hz, Hc); 6.6-7.8 (m, 17 H, aromatic) 

\(^{31}P\): 22.6 (br s)

HR-MS (FAB): C₃₀H₃₀Pd⁺ requires m/z = 527.1120, found 527.1133 (loss of Cl)

5a (PCy₃)Pd(C(O)-cinnamyl)Cl:

\(^{1}H\): 1.0-2.0 (br m, 33 H, Cy-rings); 3.8 (br d, 2H, J = 5 Hz, CH₂); 6.3 (d, 1H, J = 18 Hz, -CH=CH-Ph); 6.50 (m, 1H, -CH=CH-Ph); 7.0-7.6 (br m, 5 H, aromatic) 

\(^{31}P\): 41.3 (s)

\(^{13}C\): 236.0 (s)

5a (PCy₃)Pd(C(O)-cinnamyl)OTf + extra PCy₃:

\(^{1}H\): 1.0-2.0 (br m, 33 H, Cy-rings); 3.8 (br d, 2H, J = 5 Hz, CH₂); 6.3 (d, 1H, J = 18 Hz, -CH=CH-Ph); 6.50 (m, 1H, -CH=CH-Ph); 7.0-7.6 (br m, 5 H, aromatic) 

\(^{31}P\): several signals among which two singlets: 31.3 and 55.1

\(^{13}C\): 236.0 (s)

5b (PPh₃)Pd(C(O)-cinnamyl)Cl:

\(^{1}H\): 3.1 (br b, 2H, CH₂); 5.63 (br b, CH=CH-Ph); 6.08 (m, 1H, -CH=CH-Ph); 7.0-7.6 (br m, 5 H, aromatic) 

\(^{31}P\): 28.6 (s)

\(^{13}C\): 229.2 (s)

12a (POPy1)Pd(η₃-cinnamyl)Cl:

\(^{1}H\): 2.77 (br b, 2H, Ha + Hb); 4.93 (d, 2H, J = 20 Hz, O-CH₂); 5.17 (d, 1H, J = 16 Hz, Hd); 6.63 (ddd, 1H, J₁ = 15 Hz, J₂ = J₃ = 9 Hz, Hc); 7.0-7.8 (m, 18H, aromatic); 9.6 (br b, 1H, ortho-pyridine) 

\(^{31}P\): 134.6

\(^{13}C\): 25.6; 71.3; 72.0; 124.5 (d, J = 149 Hz); 125.9; 126.2; 128.7; 129.1; 129.2; 132.2; 132.4; 132.9; 133.4; 133.6; 134.5; 138.9; 139.4; 154.0; 154.6

HR-MS (FAB): C₂₅H₂₅NOPPd⁺ requires 516.0709, found 516.0677 (loss of Cl)
The mechanisms of the palladium catalyzed carbonylation.

14a (POPy1)Pd(η^3-cinnamyl)OAc:

\[ \text{\( ^{1}H \)}: 2.07 \text{ (s, 3H, O}_2\text{CCH}_3\}; 2.64 \text{ (br b, 2H, Ha+Hb); 4.95 (d, 2H, } J = 20 \text{ Hz, } , \text{ O-CH}_2\}; 5.43 \text{ (d, 1H, } J = 16 \text{ Hz, Hbd); 6.41 (ddd, 1H, J1 = J2 = J3 = 7 Hz); 7.0-7.9 (m, 18H, aromatic); 9.2 (br b, 1H, ortho-pyridine) \]

\[ ^{31}\text{P}: 136.7 \]

12b (POPy2)Pd (η^3-cinnamyl)Cl:

\[ \text{\( ^{1}H \)}: 2.86 \text{ (d, 2H, } J = 9 \text{ Hz, Ha+Hb); 3.25 (t, 2H, } J = 6 \text{ Hz, -CH}_2\text{-Ar); 4.32 (app q, 2H, } J = 6 \text{ Hz, O-CH}_2\}; 5.34 \text{ (dd, 1H, J1 = 9 Hz, J2 = 14 Hz, Hbd); 6.10 (ddd, 1H, J1 = J2 = 9 Hz, J3 = 14 Hz, Hcd); 7.0-7.8 (m, 18 H, aromatic); 8.59 (d, 1H, } J = 5 \text{ Hz, ortho-pyridine) \]

\[ ^{31}\text{P}: 121.9 \]

HR-MS (FAB): C\text{\( _{28}H_{27}NO\text{Pd}^+ \) requires } m/z = 530.0865, found 530.0884 (loss of Cl).

14b (POPy2)Pd (η^3-cinnamyl)OAc:

\[ \text{\( ^{1}H \)}: 1.97 \text{ (br s, 3H, O}_2\text{CCH}_3\}; 2.80 \text{ (br b, 2H, Ha+Hb); 3.50 (br b, 2H, -CH}_2\text{-Ar); 4.42 (br b, 2H, } , \text{ O-CH}_2\}; 5.78 \text{ (br m, 1H, Hbd); 6.28 (br b, 1H, Hcc) \]

\[ ^{31}\text{P}: 117.7 \]

13a (POPy1)Pd(13C(O)cinnamyl)Cl:

\[ \text{\( ^{1}H \)}: 3.48 \text{ (d, 2H, } J = 6 \text{ Hz, -C(O)-CH}_2\}; 5.06 \text{ (d, 2H, } J = 21 \text{ Hz, O-CH}_2\}; 5.88 \text{ (d, 1H, } J = 16 \text{ Hz, -CH=CH-Ph); 6.20 (m, 1H, -CH=CH-Ph); 7.0-7.8 (br m, 18 H, aromatic); 9.38 (br b, 1 H, ortho-pyridine) \]

\[ ^{31}\text{P}: 119.9 \text{ (s) \]

\[ ^{13}\text{C}: 226.5 \text{ (d, } J = 8 \text{ Hz) \]

HR-MS (FAB): As a result of the loss of Cl, decomposition occurred in the spectrometer. M+ could not be observed, but the signal at m/z = 544.0669 corresponds to C\text{\( _{28}H_{27}NO\text{Pd}^+ \), proving the existence of a Pd complex bearing two oxygen atoms (one of the ligand and one of the carbonyl). \]

15a1 (POPy1)Pd(13C(O)cinnamyl)OAc:

\[ \text{\( ^{1}H \)}: 2.18 \text{ (s, 3H, O}_2\text{CCH}_3\}; 2.77 \text{ (br d, 2H, } J = 7 \text{ Hz, -C(O)-CH}_2\}; 5.10 \text{ (d, 2H, } J = 19 \text{ Hz, O-CH}_2\}; 5.80 \text{ (d, 1H, } J = 16 \text{ Hz, -CH=CH-Ph); 6.27 (m, 1H, -CH=CH-Ph); 7.0-7.8 (br m, 18 H, aromatic); 8.83 (br b, 1 H, ortho-pyridine) \]

\[ ^{31}\text{P}: 123.5 \]

\[ ^{13}\text{C}: 231.9 \]
15a2 (POPy1)Pd\(^{13}\)C(O)cinnamyl)OAc:

\(^1\)H: 2.24 (s, 3H, O-CCH\(_3\)); 4.69 (br d, 2H, \(J = 7\) Hz, -C(O)-CH\(_2\)-); 4.96 (d, 2H, \(J = 21\) Hz, O-CH\(_2\)); 5.65 (d, 1H, \(J = 16\) Hz, -CH=CH-Ph); 6.27 (m, 1H, -CH=CH-Ph); 7.0-7.8 (br m, 18H, aromatic); 9.30 (d, 1H, \(J = 5\) Hz, ortho-pyridine)

\(^3\)P: 121.5

\(^{13}\)C: 229.8

15b (POPy2)Pd\(^{13}\)C(O)cinnamyl)Cl:

\(^1\)H: 3.51 (d, 2H, \(J = 7\) Hz, -C(O)-CH\(_2\)-); 3.60 (br t, 2H, \(J = 5\) Hz, -CH\(_2\)-Ar); 4.11 (dt, 2H, \(J = 14\) Hz, \(J = 6\) Hz, O-CH\(_2\)); 6.05 (d, 1H, \(J = 16\) Hz, -CH=CH-Ph); 6.28 (m, 1H, -CH=CH-Ph); 7.0-7.7 (br m, 18H, aromatic); 8.97 (d, 1H, \(J = 5\) Hz, ortho-pyridine)

\(^3\)P: 107.4 (s)

\(^{13}\)C: 38.4; 56.3; 68.0; 124.2; 126.7; 127.8; 129.0; 129.5; 130.1; 131.6; 132.8; 137.2; 152.0; 158.1; 229.6 (d, \(J = 6\) Hz)

15b (POPy2)Pd(C(O)cinnamyl)OAc:

\(^1\)H: 2.22 (d, 3H, \(J = 7\) Hz, Pd-O-CCH\(_3\)); 3.50 (br t, 2H, \(J = 5\) Hz, -CH\(_2\)-Ar); 3.95 (br m, 2H, O-CH\(_2\)); 5.80 (d, 1H, \(J = 16\) Hz, -CH=CH-Ph); 6.28 (m, 1H, -CH=CH-Ph); 7.0-7.7 (br m, 18H, aromatic); 8.98 (d, 1H, \(J = 5\) Hz, ortho-pyridine)

\(^3\)P: 106.8 (s)

\(^{13}\)C: 228.0 (s)

15c (POPy3)Pd(C(O)cinnamyl)Cl:

\(^1\)H: 1.94 (br b, 2H, -CH\(_2\)-CH\(_2\)-CH\(_2\)-); 3.41 (d, 2H, \(J = 7\) Hz, -C(O)-CH\(_2\)-); 3.56 (br b, 4H, O-CH\(_2\)+-CH\(_2\)-Ar); 6.06 (d, 1H, \(J = 16\) Hz, -CH=CH-Ph); 6.29 (m, 1H, -CH=CH-Ph); 7.0-7.7 (br m, 18H, aromatic); 8.37 (d, 1H, \(J = 5\) Hz, ortho-pyridine)

\(^3\)P: 118.2 (s)

\(^{13}\)C: 227.5

10.5.6 Crystal structure determination of 13a:

C\(_{25}\)H\(_{24}\)ClNO\(_2\)PPd, M\(_w\)=580.3, triclinic, P \(\overline{1}\), \(a=9.125(1)\), \(b=11.172(2)\), \(c=13.127(4)\)\(\text{Å}\), \(\alpha=79.68(2)\), \(\beta=74.13(1)\), \(\gamma=83.96(1)\)\(^\circ\), V=1264.2(5)\(\text{Å}^3\), Z=2, \(D_x=1.52 \text{gcm}^{-3}\), \(\lambda(\text{CuK}α)=1.5418\text{Å}, \mu(\text{CuK}α)=76.94 \text{cm}^{-1}\), F(000)=588, room temperature, Final R=0.069 for 5201 reflections.

A crystal with dimensions 0.35 x 0.45 x 0.50 mm approximately was used for data collection on an Enraf-Nonius CAD-4 diffractometer with graphite-monochromated CuK\(α\) radiation and \(\omega-2\theta\) scan. A total of 5201 unique reflections was measured within the range -10\(≤\theta≤11\), -13\(≤\kappa≤13\), 0\(≤\lambda≤16\). Of these, 5040 were above

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the significance level of $4\sigma(F_{\text{obs}})$ and were treated as observed. The range of $(\sin \theta)/\lambda$ was 0.040-0.630\AA
(3.5°≤θ≤76.1°). Two reference reflections (2 2 1), (1 0 2) were measured hourly and showed 5% decrease during the 83 h collecting time, which was corrected for. Unit-cell parameters were refined by a least-squares fitting procedure using 23 reflections with 40.04°≤θ≤41.92. Corrections for Lorentz and polarization effects were applied. Absorption correction was performed with the program PLATON\cite{30}, following the method of North et al.\cite{35} using $\Psi$-scans of five reflections, with coefficients in the range 0.669-0.981. The structure was solved by the PATTY option of the DIRDIF99 program system.\cite{29}

The hydrogen atoms were calculated and a riding model was used during refinement. Full-matrix least-squares refinement on $F^2$, anisotropic for the non-hydrogen atoms and isotropic for the hydrogen atoms, converged to $R_I=0.069$, $wR_I=0.075$, $(\Delta/\sigma)_{\text{max}}=0.03$, $S=1.5$. A weighting scheme $w=[7000. + 0.01*(\sigma(F_{\text{obs}}))^2 + 0.01/(\sigma(F_{\text{obs}}))$] was used. The secondary isotropic extinction coefficient\cite{33,34} refined to $G=1181(30)$. A final difference Fourier map revealed a residual electron density between −4.56 and 2.04 e\AA$^3$ in the vicinity of the Pd. Scattering factors were taken from Cromer and Mann;\cite{30a} International Tables for X-ray Crystallography.\cite{30b} The anomalous scattering of Pd, P and Cl was taken into account.\cite{31} All calculations were performed with XTAL3.7\cite{32}, unless stated otherwise.

10.6 References


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[16] In chapter 6 we have found that on the timescale of the allylic alkylation the nitrogen functionality of the POPy ligands is not bonded to palladium in a hemilabile fashion. We were interested whether this would also apply for the conditions of the carbonylation reaction. Also in this chapter we found no evidence for a dissociation from palladium of the nitrogen functionality.


[25] A recent brief theoretical study by Yamamoto and coworkers points out that for cationic complexes an insertion mechanism involving a five-coordinated species is not feasible. Since the study is only
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concerned with cationic complexes bearing one or two phosphorus atoms, this conclusion may not apply to the neutral complexes at hand:


Chapter 11
Rhodium-allyl chemistry

Abstract

In the previous chapters we have described the use of palladium catalysts and the mechanisms of the alkylation and carbonylation reaction. In this chapter, we present an exploratory study of the use of rhodium based catalysts in the same reactions.

To this end, we have prepared several novel rhodium complexes and we have studied the structure in detail, using NMR and modeling techniques. We found that three coordination modes are possible: the known $\eta^1$ and $\eta^3$ mode and the newly found $\eta^1$-$\eta^2$ mode. A crystal structure of the $(\eta^1$-$\eta_3$-C$_3$H$_5$)Rh(Xantphos)Cl$_2$ complex shows many similarities to the crystal structure of the analogous palladium complex in chapter 7. The reactivity of these complexes was tested in the stoichiometric alkylation and in high pressure NMR experiments. We showed that these novel complexes are active in the allylic alkylation reaction. Under a pressure of CO (10-40 bar), we found that insertion of CO is a facile process and we have obtained the corresponding novel acyl complexes, which are presumably the intermediates in the catalytic carbonylation reaction.
11.1 Introduction

Previous studies in our group concerning the effect of the bite angle of bidentate phosphine ligands in the rhodium catalyzed hydroformylation of styrene, showed an interesting influence on the rate of this reaction. The reaction rate was relatively low when ligands were used that enforce a medium bite angle (95-105°). Other ligands enforcing either a smaller or a larger bite angle resulted in a more active catalyst.

For the intermediate rhodium-styrene complex, an equilibrium has been postulated between an \( \eta^1 \)-styryl (A) and an \( \eta^3 \)-styryl complex (B). Hydroformylation of A yields the non-chiral linear aldehyde, whereas after the required \( \eta^1 \)-\( \eta^3 \) rearrangement to C, the hydroformylation of C can yield the chiral branched product (figure 1). In view of our previous results with Pd(\( \eta^3 \)-allyl) complexes, it occurred to us, that a relatively stable \( \eta^3 \)-styryl complex of ligands enforcing a medium bite angle could explain the observed effect of the bite angle on the rate of the reaction.

![Figure 1: Influence of an \( \eta^3 \)-styryl complex (B) on the course of hydroformylation of \( \eta^1 \)-styryl (A and C) complexes.](image)

A reaction that involves a similar Rh-allyl intermediate is the allylic alkylation (figure 2). Although palladium is the metal of choice for many homogeneously catalyzed organic transformations, the interest for the use of catalysts based on other metals, such as rhodium and iridium, is increasing. Recently, rhodium based catalysts showed unusual regioselectivity in the allylic alkylation of monosubstituted allyl moieties. Most palladium catalysts, favor the non-chiral linear product, whereas the rhodium system shows a high preference for the formation of the chiral branched product.
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Although for the palladium catalyst the reaction is known to proceed via an η\(^3\)-allyl complex, for the rhodium system an η\(^1\)-allyl complex was postulated as the catalytically active species.\(^{[5a]}\) The alkylation on such a species would take place via an S\(_{N}2'\) attack of the nucleophile on the γ-carbon of the allyl (figure 3). Alkylation of an allyl moiety with a substituent on the γ-carbon would then yield the branched product.

![Figure 2: Regioselectivity in allylic alkylation of cinnamyl chloride.](image)

![Figure 3: The postulated S\(_{N}2'\) mechanism for the rhodium catalyzed allylic alkylation via a Rh(η\(^1\)-cinnamyl) species (left) and the alternative pathway via a Rh(η\(^3\)-cinnamyl) species (right).](image)
The rhodium catalysts in the reported alkylation studies were prepared in situ using an excess of monodentate phosphine ligands. For these systems, $\eta^1$-allyl complexes have indeed been observed, but similar complexes bearing bidentate phosphine ligands have not been studied yet. Inspired by the results of the hydroformylation, we reasoned that for bidentate ligands, the $\eta^1$-allyl coordination may not be favored over the $\eta^3$-allyl coordination. Furthermore, Cole-Hamilton has reported the rhodium catalyzed carbylination of allyl halides using PEt$_3$ as the ligand. In the late sixties (Vrieze and co-workers) and the early eighties (Fryzuk and co-workers) several studies have been reported concerning the synthesis and structure of allyl-rhodium complexes. Encouraged by these findings we decided to synthesize (diphosphine)rhodium-allyl complexes and study their structure and their reactivity in the allylic alkylation and towards CO.

11.2 Results

11.2.1 Choice of ligands and allyl moieties

To study the effect of the bite angle of the ligand on the geometry of (PP)Rh$^\text{III}$ (allyl)Cl$_2$ complex, four ligands were used (figure 4) that mainly differ in their preferred bite angle. Besides alkane bridged dppe (2), which enforces a relatively small bite angle and has a rather flexible backbone, the other three ligands are triaryl phosphines: o-dppb (1), which is a rigid ligand enforcing a small bite angle, DPEphos (3), which enforces an intermediate bite angle and has a flexible backbone and Xantphos (4), which enforces a large bite angle and has a more rigid backbone.

To study the effect of the substituent on the allyl moiety, the small unsubstituted C$_3$H$_5$ moiety (a) was used and the large phenyl substituted cinnamyl moiety (3-Ph-C$_3$H$_4$) (b). The numbering scheme of the complexes used in this study is presented in figure 4.

```
\begin{figure}
\centering
\includegraphics[width=\textwidth]{complexes.png}
\caption{Numbering scheme of the complexes used in this study.}
\end{figure}
```
11.2.2 Synthesis

Starting from a Rh\(^1\) precursor, several routes were explored to synthesize (PP)Rh\(^{111}\)(allyl)Cl\(_2\) complexes. The most convenient and versatile route proceeds via oxidative addition of the appropriate allyl chloride to (PP)Rh\(^{111}\)(COD)Cl\(^{81}\). The oxidative addition proceeded smoothly for each complex. For the DPEphos complex a small amount (<5 %) of an unidentified side product was formed that could not be removed.

11.2.3 Characterization, general remarks

In the previous chapters, the characterization of Pd(allyl) complexes has been discussed in detail. The NMR spectra of the rhodium-allyl complexes show similarities, but also differences compared to those of the palladium complexes. Some rhodium complexes clearly showed an \(\eta^3\)-coordination mode, whereas other complexes seemed to be \(\eta^1\)-complexes. To facilitate the characterization of the (PP)Rh\(^{111}\)(allyl)Cl\(_2\) complexes described in this chapter, some general remarks concerning the \(^1\)H-NMR spectra of palladium allyl complexes may prove useful for the unambiguous assignment of the observed signals. The two coordination modes of the allyl moiety (\(\eta^1\)- or \(\eta^3\)-fashion (figure 5)) can be distinguished by several differences in the \(^1\)H-NMR spectra.

![Figure 5: Bonding modes of the allyl moiety and numbering scheme of the hydrogens (left \(\eta^3\) and right \(\eta^1\)).]

11.2.4 \(\eta^3\)-allyl-palladium (see also chapter 4-8)

The results in the previous chapters and the work of others show, that the five hydrogens on the allyl moiety are inequivalent in non-symmetrical complexes, whereas in symmetrical complexes \(\{H_{\text{anti}}\text{ and } H_{\text{anti}}\}'\) and \(\{H_{\text{syn}}\text{ and } H_{\text{syn}}\}'\) are equivalent. The anti hydrogens are closer to palladium and show a signal at lower ppm-value than the syn-hydrogens. In general, the signal for \(H_{\text{anti}}\) is typically found between 2 and 3.5 ppm, whereas the signal for \(H_{\text{syn}}\) is mostly observed between 2.5 and 3.9 ppm. The signal of \(H_{\text{meso}}\) almost always appears above 5 ppm, but below 6.5 ppm. In some cases, the \(\eta^3\)-allyl moiety shows fluxional behavior and via a \(\eta^3\)-\(\eta^1\)-\(\eta^1\) rearrangement, \(H_{\text{anti}}\) and \(H_{\text{syn}}\) become equivalent, which results in only one signal for the anti- and syn-hydrogens appearing at the averaged frequency.
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The presence of a phenyl substituent at the allyl moiety (cinnamyl) disrupts the symmetry of allyl and all four protons show different signals. The phenyl can be oriented anti or syn with respect to \( H_{\text{meso}} \), but in the complexes described in this thesis, only the syn-orientation has been observed. The signals of \( H_{\text{anti}} \) and \( H_{\text{syn}} \), as compared to the \( \text{C}_2H_5 \) moiety, are in general slightly shifted to a higher ppm value. The shift of the signal of the anti hydrogen next to the phenyl is much larger, because of the partial double bond character of the \( \text{C}2-\text{C}3 \) bond (figure 4). The doublet may be observed even at higher chemical shift (between 5.9 and 6.8 ppm) than the signal of \( H_{\text{meso}} \), which is found between 5.8 and 6.6 ppm.

11.2.5 \( \eta^1\)-allyl-palladium

So far, only a few \((\eta^1\text{-C}_5H_5)\text{Pd}\) complexes have been reported. The \(^1\text{H-NMR} \) spectrum resembles that of organic allyl compounds e.g. allyl chloride.\(^9\) The aliphatic \( \text{CH}_2 \)-unit appears as one signal; the olefinic signals are magnetically inequivalent. The fine structure on and the chemical shift of the signal of \( H_{\text{meso}} \) resembles that found for \( H_{\text{meso}} \) in \( \eta^1\)-allyl complexes. The main difference, therefore, between an \( \eta^1\)- and an \( \eta^1\)-allyl will be found in the fine structure on the signal of the olefinic \( \text{CH}_2 \)-unit. The signal consists of two double doublets around 5 ppm, whereas this is not observed for the \( \eta^1\)-allyl complex.

The situation is slightly more complicated for cinnamyl complexes. In (triphos)\( \text{Pd}(\eta^1\text{-cinnamyl})\text{Cl} \),\(^{11,13}\) the cinnamyl is bonded to the metal via the \( \text{CH}_2 \)-unit, with a trans configuration of the allylic \( \text{C}={\text{C}} \) bond. The \(^1\text{H-NMR} \) spectrum of these complexes shows one signal for the \( \text{CH}_2 \)-unit, a multiplet for \( H_{\text{meso}} \) and a doublet for \( H_{\text{olefinic}} \) (\( H_{\text{olefinic}} \) is bonded to the terminal carbon atom). In other words: it yields a spectrum potentially similar to that of an \( \eta^1\)-cinnamyl group in which \( H_{\text{anti}} \) and \( H_{\text{syn}} \) are equivalent or rapidly exchanging. Contrary to the \( \eta^3\)-cinnamyl group, the \( \eta^1\)-cinnamyl moiety does not show a phosphorus coupling on the olefinic hydrogen next to the phenyl group. Another tool to distinguish between the two coordination modes is the relative chemical shift of \( H_{\text{meso}} \) and \( H_{\text{olefinic}} \). In the \( \eta^1\)-allyl complex, the chemical shift of \( H_{\text{olefinic}} \) is higher than that of \( H_{\text{meso}} \), whereas in the \( \eta^1\)-allyl complex, it is the other way round.

11.2.6 Characterization of the rhodium complexes

Using the guidelines of the previous paragraph, we have assigned the structure of the rhodium complexes (tables 1 and 2). The interpretation of the \(^1\text{H-NMR} \) spectrum of the \( \text{o-dpb} \) cinnamyl complex \( 1b \), is hampered by the overlap of \( H_{\text{olefinic}} \) and the aromatic hydrogens. Because of the similarities between the NMR spectra of \( 1b, 1a \) and \( 2b \), the signals have been assigned to an \( \eta^1\)-cinnamyl moiety. Also the Xantphos bearing complex, \( 4b \), binds the cinnamyl in an \( \eta^1 \)-fashion. Both DPEphos modified complexes, \( 3a \) and \( 3b \), have been identified as \( \eta^1\)-allylic complexes.
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Table 1: Assignment of \((\text{C}_3\text{H}_5)\text{Rh(PP)Cl}_2\) complexes (room temperature).

<table>
<thead>
<tr>
<th>number</th>
<th>PP ligand</th>
<th>hapticity</th>
<th>P's equivalent?</th>
<th>remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>o-dppb</td>
<td>(\eta^1)</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>2a</td>
<td>dppe</td>
<td>(\eta^1)</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>3a</td>
<td>DPEphos</td>
<td>(\eta^3)</td>
<td>no</td>
<td>all hydrogens inequivalent</td>
</tr>
<tr>
<td>4a</td>
<td>Xantphos</td>
<td>(\eta^3)</td>
<td>yes</td>
<td>broad (^{31}\text{P-NMR} ) signal</td>
</tr>
</tbody>
</table>

Table 2: Assignment of \((3-\text{Ph-C}_3\text{H}_4)\text{Rh(PP)Cl}_2\) complexes (room temperature).

<table>
<thead>
<tr>
<th>number</th>
<th>PP ligand</th>
<th>hapticity</th>
<th>P's equivalent?</th>
<th>remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>1b</td>
<td>o-dppb</td>
<td>probably (\eta^1)</td>
<td>yes</td>
<td>\text{Holeffect under aromatic signals}</td>
</tr>
<tr>
<td>2b</td>
<td>dppe</td>
<td>(\eta^1)</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>3b</td>
<td>DPEphos</td>
<td>(\eta^3)</td>
<td>no</td>
<td>broad signals in (^1\text{H-NMR} )</td>
</tr>
<tr>
<td>4b</td>
<td>Xantphos</td>
<td>(\eta^1)</td>
<td>yes</td>
<td></td>
</tr>
</tbody>
</table>

In most complexes the two phosphorus atoms show only one signal in the \(^{31}\text{P-NMR} \) spectra, which is indicative of a symmetric complex geometry. Rhodium(III) can adopt several geometries: octahedral, square pyramidal and trigonal bipyramidal. Although the coordination mode of the allyl is clearly identified by \(^1\text{H-NMR} \), the geometry around the rhodium is not resolved. Because the chemical shift of \(^{103}\text{Rh} \) is known to be dependent on the geometry around the metal center, attempts were made to measure the \(^{103}\text{Rh-NMR} \) signal. Due to broad signals, even at low temperature, the measurements were not conclusive.

11.2.7 Variable temperature NMR

Several complexes show broad signals in the \(^1\text{H-NMR} \), which is indicative of fluxional behavior of the allyl moiety. Because more insight in the coordination of the allyl ligand at low temperature may provide information about the geometry around rhodium, variable temperature NMR experiments were carried out using complexes 1-4a (figures 6-9, following pages).
Figure 6: VT-NMR of 1a ((o-dppb)(C₃H₅)RhCl₂), left $^1$H-NMR, right $^{31}$P-NMR.

Figure 7: VT-NMR of 2a ((dppe)(C₃H₅)RhCl₂), left $^1$H-NMR, right $^{31}$P-NMR.
Figure 8: VT-NMR of 3a ((DPEphos)(C₃H₅)RhCl₂), left ¹H-NMR, right ³¹P-NMR.
Both 1a (o-dppb) and 2a (dppe) are η¹-allyl complexes at room temperature and show similar ¹H-NMR spectra at lower temperatures. Cooling the o-dppb-complex 1a to 218 K (figure 6), the signals in the olefinic region do not shift and are slightly broadened, but the signal of the CH₂ unit is split into two separate multiplets, each representing one hydrogen. In contrast, the signals in the olefinic region of the dppe-complex 2a do shift (figure 7). At room temperature three overlapping multiplets are observed, whereas at 218 K the signals are split in one multiplet at 5.0 ppm (presumably H₃meso) and a double doublet and a triplet at 4.6 and 4.4 ppm respectively. In addition, the ³¹P-NMR spectra of 1a and 2a showed a single doublet at high temperature, but at low temperature two doublets were observed. It is clear that the species at low temperature is neither the η¹-allyl species observed at room temperature nor an η²-allyl species. We propose an η¹-η²-type coordination for the observed complex (figure 10). At low temperature, the signals of the η¹-part (2.8 ppm) are split into two signals, one for each hydrogen. Thus, if the structure would be that of an η¹-η²-allyl, the rotation about the Rh-C and the C1-C2 bond is restricted. The possible occurrence of this coordination mode is supported by the crystal structure of 4a (Xantphos, see below) and modeling studies.
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Figure 10: Proposed $\eta^1$-$\eta^2$ coordination in 1a and 2a with hindered rotation about the C1-C2 bond.

Complex 3a (DPEphos, figure 8) showed five separate signals for all hydrogens of the C$_3$H$_5$ moiety at room temperature. Lowering the temperature did not affect the $^1$H and $^3$P NMR-spectra of 3a, but the signals of the minor side product (< 5 %) sharpened and appeared to be very similar to the spectrum of 3a.

At room temperature, the $^1$H-NMR spectrum of complex 4a (figure 9) shows one coalesced signal for all hydrogens except H$_{\text{meso}}$. At low temperature, this coalesced signal splits in three broad multiplets in a 2 : 1 : 1 ratio, of which the multiplet with relative intensity 2 overlaps with one other multiplet. At low temperature, the CH$_3$ groups on the backbone of the ligand appear as two multiplet patterns, one at 1.2 ppm and one at 1.8 ppm. The inequivalence of the methyl groups of the backbone has been observed before in similar palladium complexes (chapter 7) and can be attributed to endo and an exo methyl groups of the bent xanthene moiety. The assignment of the multiplet signals to the CH$_3$ groups is discussed in section 11.2.8.

At first glance, the allyl region of the $^1$H-NMR spectrum is rather complicated. In contrast to the spectra of 1a and 2a, there are no signals in the olefinic region (except H$_{\text{meso}}$), indicating that the structure is still very similar to the $\eta^1$-allyl observed at room temperature. At room temperature, the $^1$H-NMR spectrum is similar to that of an $\eta^3$-C$_3$H$_5$ moiety with fast exchange of all 4 terminal hydrogen atoms. At low temperature, the signal at 5.5 ppm reveals two signals for H$_{\text{meso}}$, indicating the existence of two isomeric complexes. One of the isomers shows a spectrum similar to that observed at room temperature and can be assigned to a symmetrically bonded $\eta^3$-C$_3$H$_5$ moiety, in which one average signal is observed for all four terminal hydrogens due to a fast dynamic exchange. The other isomer, however, shows two different multiplet signals for the terminal hydrogen atoms. One possible explanation would be that one of the two multiplets can be assigned to the syn-protons, and the other multiplet to the anti-protons. This explanation would imply for this isomer a slow $\eta^3$-$\eta^1$-$\eta^3$ rearrangement relative to the apparent allyl rotation rearrangement, which is not observed often.
A second, more plausible explanation involves a dissymetrically $\eta^3$-bonded allyl moiety (towards $\eta^1$-$\eta^2$) as found in the crystal structure of 4a (see below). In this complex, two phenyl rings of the Xantphos ligand are stacked in a perpendicular fashion, unlike the parallel orientation which was found in the crystal structure of the analogous palladium complex (chapter 7). A non-selective $\eta^3$-$\eta^1$-$\eta^3$ rearrangement involving both C1 and C3 of the allyl moiety accounts for the two broad multiplets; one multiplet for each CH$_2$-unit. This explanation would imply a slow allyl-rotation rearrangement for this isomer, which may seem unlikely, but has been observed before in analogous palladium complexes (chapters 4-8).

In the $^{31}$P-NMR spectrum recorded at low temperature, two doublets are observed in a 1:1 ratio. Apparently, the slight distortion of the $\eta^1$-character of the Pd-allyl bond is not reflected in the $^{31}$P-NMR spectrum at the lowest temperature used (218 K).

A summary of the assignments at low temperature is presented in table 3.

![Figure 11: Selective $\eta^3$-$\eta^1$-$\eta^3$ rotation about the Rh-C$_\alpha$ bond in 4b.](image)

**Table 3**: Structural assignment of (C$_3$H$_5$)Rh(PP)Cl$_2$ complexes (low temperature).

<table>
<thead>
<tr>
<th>number</th>
<th>PP ligand</th>
<th>hapticity</th>
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<td>1a</td>
<td>o-dppb</td>
<td>$\eta^1$-$\eta^2$</td>
</tr>
<tr>
<td>2a</td>
<td>dppe</td>
<td>$\eta^1$-$\eta^2$</td>
</tr>
<tr>
<td>3a</td>
<td>DPEphos</td>
<td>$\eta^3$</td>
</tr>
<tr>
<td>4a</td>
<td>Xantphos</td>
<td>$\eta^1$-$\eta^2$ and $\eta^3$</td>
</tr>
</tbody>
</table>
11.2.8 Crystal structure of 4a

After recrystallization of (Xantphos)Rh(Cl_2)(\eta^3-C_3H_5) 4a from CH_2Cl_2 / hexane, crystals were obtained that were suitable for X-ray crystallography (figure 12). The structure of 4a is rather similar to the crystal structure of the analogous cationic (Xantphos)Pd(\eta^3-C_3H_5)OTf complex described in chapter 7 (figure 13).

Geometrical data of both complexes are presented in table 4.
Figure 13: Crystal structure of the palladium analogue of \textit{4a} (Xantphos)Pd(C\textsubscript{3}H\textsubscript{5})\textsuperscript{+} OTf\textsuperscript{−} (three points of view).

![Crystal structure diagram]

Figure 14: Numbering scheme in crystal structures, M = Rh or Pd.

![Numbering scheme diagram]
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Table 4: Selected geometrical data of the crystal structures of 4a (figure 12) and (Xantphos)Pd(C₃H₅)⁺OTf⁻ (figure 13). The numbering scheme is presented in figure 14. Distances in Å, angles in °.

<table>
<thead>
<tr>
<th></th>
<th>rhodium</th>
<th>palladium</th>
</tr>
</thead>
<tbody>
<tr>
<td>d(M-C1)</td>
<td>2.232(11)</td>
<td>2.17(1)</td>
</tr>
<tr>
<td>d(M-C2)</td>
<td>2.186(14)</td>
<td>2.16(1)</td>
</tr>
<tr>
<td>d(M-C3)</td>
<td>2.241(11)</td>
<td>2.17(1)</td>
</tr>
<tr>
<td>d(C1-C2)</td>
<td>1.414(18)</td>
<td>1.34(2)</td>
</tr>
<tr>
<td>d(C2-C3)</td>
<td>1.442(18)</td>
<td>1.34(2)</td>
</tr>
<tr>
<td>∠(C1-C2-C3)</td>
<td>124.9(14)</td>
<td>120.4(15)</td>
</tr>
<tr>
<td>d(M-P1)</td>
<td>2.394(2)</td>
<td>2.372(2)</td>
</tr>
<tr>
<td>d(M-P2)</td>
<td>2.437(2)</td>
<td>2.372(2)</td>
</tr>
<tr>
<td>d(Rh-Cl) (above in figure)</td>
<td>2.351(3)</td>
<td>2.372(2)</td>
</tr>
<tr>
<td>d(Rh-Cl) (below in figure)</td>
<td>2.363(2)</td>
<td>2.372(2)</td>
</tr>
<tr>
<td>∠(P-M-P)</td>
<td>106.89(7)</td>
<td>108.11(7)</td>
</tr>
<tr>
<td>∠(Cl-Rh-Cl)</td>
<td>177.44(10)</td>
<td></td>
</tr>
<tr>
<td>angle between xanthene planes</td>
<td>16.6571</td>
<td>27.352</td>
</tr>
<tr>
<td>d(M-O)</td>
<td>3.320(6)</td>
<td>3.445(7)</td>
</tr>
<tr>
<td>∠((P-M-P)-(C1-C2-C3))</td>
<td>58.9154</td>
<td>99.368</td>
</tr>
<tr>
<td>d(C1-(P-M-P))</td>
<td>-0.2723 (below)</td>
<td>+0.349</td>
</tr>
<tr>
<td>d(C2-(P-M-P))</td>
<td>+0.3136</td>
<td>+1.008</td>
</tr>
<tr>
<td>d(C3-(P-M-P))</td>
<td>-0.2195</td>
<td>+0.349</td>
</tr>
</tbody>
</table>

*: M=Rh for 4a and M=Pd for (Xantphos)Pd(C₃H₅)⁺OTf⁻.

The rhodium complex has a trigonal bipyramidal structure, with the two chloride ligands in the axial positions, the two phosphine atoms cis to one another and the allyl in the equatorial plane bonded in an η³-fashion. In contrast to the palladium complex, the rhodium complex has no Cs symmetry, probably because of the non-symmetric π-π interactions between the phenyl rings of the ligand. Compared to the palladium complex, the metal to allyl distance is larger and the C-C bonds in the allyl moiety are longer. Although the longer C-C bonds may suggest a less olefinic character of the allyl moiety, the C-C-C angle of the allyl is larger. In addition, the angle between the P-M-P plane and the allyl C-C-C plane is much smaller. The coordination mode of the allyl group may thus indicate a decreased bonding and an increased backbonding interaction compared to the palladium complex. The P-Rh-P bite angle is similar to the calculated natural bite angle and to the bite angle found in other rhodium complexes of Xantphos derivatives.¹¹
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The dynamic behavior observed in $^1$H-NMR can be explained in terms of $\pi-\pi$ interactions of the cinnamyl with the phenyl rings of the ligand (see above). The dissymmetric stacking observed in the crystal structure of 4a causes an $\eta^1-\eta^3$-coordination of the allyl moiety at low temperature.

The perpendicular stacking (lines represent phenyl rings) of the phenyl rings may explain the low chemical shift in the $^1$H-NMR spectrum (1.2 ppm) of one of the multiplet signals of the CH$_3$ groups of the ligand. A different orientation of the phenyl rings causes a different folding of the Xanthene backbone and also a different ring current experienced by the methyl groups. In figure 12 and 13 it is shown that because of the large folding of the Xanthene backbone in the rhodium complex 4a, the difference between the endo and exo methyl group is smaller than in the analogous palladium complex. Therefore, we assign each of the two multiplet NMR-signals of the CH$_3$ groups to an endo-exo combination of the same isomer. In the analogous palladium complex, the signals of the CH$_3$ groups was found between 1.4-1.9 ppm. Because of the different orientation of the phenyl rings and the resulting different effect of ring current, we propose that the multiplet signal of 1.2 ppm should be assigned to the $-l$ stacked isomer.

11.2.9 DFT studies

To study the effect of the bite angle on the geometry in more detail, DFT calculations on model complexes were performed on the B3LYP/LANL2DZ level of theory, which is a commonly accepted level of theory for DFT calculations of organometallic compounds.$^{[10]}$

The bonding of the allyl to the [Rh(PH$_3$)$_2$Cl$_2$] fragment was studied for both the complex bearing the non substituted [C$_3$H$_5$] 5 and the substituted [3,3-(CH$_3$)$_2$-C$_3$H$_3$] moiety 6. The latter was used as a model for the cinnamyl complexes. The influence of the bite angle of the ligand was investigated by changing the P-Rh-P angle incrementally from 90-180°.

For both allyl moieties, two minima were found in the energy curve (figure 15, table 5). The global minimum for 5 (figure 16) and a local minimum for 6 (figure 18) correspond to the $\eta^3$-complex (bite angle ~ 100°, trigonal bipyramid, figure 16). The local minimum of 5 (figure 17) and the global minimum of 6 (figure 19) correspond to an $\eta^1$-geometry (bite angle ~ 170°, square pyramidal). The relative stability of the $\eta^1$-structure for 6 compared to 5, is most likely caused by the more stable C=C double bond.

Table 5: Heat of formation (in kJ/mole) of the minimized structures of the $\eta^3$ and the $\eta^1$ isomers of 5 and 6.

<table>
<thead>
<tr>
<th>Complex (bite angle)</th>
<th>5 (C$_3$H$_5$)</th>
<th>6 (3,3-(CH$_3$)$_2$-C$_3$H$_3$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\Delta E \eta^3$ (~100°)</td>
<td>-717048</td>
<td>-923257</td>
</tr>
<tr>
<td>$\Delta E \eta^1$ (~170°)</td>
<td>-717022</td>
<td>-923258</td>
</tr>
<tr>
<td>$\Delta E (\eta^3-\eta^1)$</td>
<td>-26</td>
<td>+1</td>
</tr>
</tbody>
</table>
Rhodium-allyl chemistry.

Figure 15: Plot of the heat of formation of \((\text{C}_3\text{H}_5)\text{Rh}(\text{PH}_3)_2\text{Cl}_2\) (5) at different values of the P-Rh-P angle. For complex 6, the global minimum is found at a bite angle of \(\sim 170^\circ\).

Figure 16: The \(\eta^3\)-geometry of \((\text{C}_3\text{H}_5)\text{Rh}(\text{PH}_3)_2\text{Cl}_2\) (5) corresponding to the global minimum (two views).

Figure 17: The \(\eta^1\)-geometry of \((\text{C}_3\text{H}_5)\text{Rh}(\text{PH}_3)_2\text{Cl}_2\) (5) corresponding to the local minimum.
Figure 18: Two views of the $\eta^1$-geometry of $(C_5H_9)Rh(PH_3)_2Cl_2$ (6) corresponding to the local minimum, hydrogens omitted for clarity, phosphines axial, chlorides equatorial.

Figure 19: The $\eta^1$-geometry of $(C_5H_9)Rh(PH_3)_2Cl_2$ (6) corresponding to the global minimum.

Although complex $(C_5H_5)Rh(PH_3)_2Cl_2$ (5) has a symmetric $\eta^3$-structure in the global minimum, the symmetry is slightly distorted for larger values of the bite angle. Going from $100^\circ$ to $140^\circ$ the geometry of the complex slowly changes from trigonal bipyramidal to square pyramidal and the coordination of the allyl slowly changes from the $\eta^3$-mode to the $\eta^1$-mode. This distortion is more pronounced for the substituted [3,3-(CH$_3$)$_2$C$_3$H$_3$] moiety (figure 18) and increases further for a larger bite angle. The deviation from $\eta^3$ to $\eta^1$-$\eta^7$ of the Rh-allyl bond is stronger than found for the analogous Pd-allyl bond (chapter 7) (figure 20). For the $\eta^3$-geometry, the bond distances in the Rh-$\eta^3$-C$_3$H$_5$ bond are similar to those of the corresponding palladium complex (table 6). However, for the palladium complex, d(Pd-C1) is shorter than d(Pd-C2)
whereas for the rhodium complex, $d($Rh-C2$) < d($Rh-C1$). This indicates that for the Rh-allyl bond, the contribution of the allyl-to-rhodium electron donation is relatively more pronounced than the rhodium-to-allyl back donation.

Increasing the bite angle leads to a strong increase of the Rh-allyl distance. The C-C distances in the allyl moiety are smaller, indicating a decrease of the allyl-to-rhodium electron donation. The Mulliken charge of the allylic carbon atoms resembles that of the analogous palladium complex, although for the rhodium complex the electron density on C1 / C3 is slightly higher and that on C2 is slightly lower (table 7). An increase of the bite angle does not result in a significant change of the charge on the allylic carbon atoms.

![Figure 20: Comparison of distortion of $\eta^3$-bonding fashion in 6 (120°) viewed along the Cl-Rh-Cl axis (left) and its palladium analogue Pd(C5H5)(PH3)2 (120°) (right).](image)

Table 6: Comparison of distortion of $\eta^3$ bonding fashion between 6 and the palladium analogue (3,3-(CH3)2-C5H5)Pd(PH3)2+, bond distances in Ångström.

<table>
<thead>
<tr>
<th>bond \ bite angle</th>
<th>80°</th>
<th>100°</th>
<th>120°</th>
</tr>
</thead>
<tbody>
<tr>
<td>d(Rh-C1)</td>
<td>2,198</td>
<td>2,217</td>
<td>2,163</td>
</tr>
<tr>
<td>d(Rh-C3)</td>
<td>2,383</td>
<td>2,421</td>
<td>2,752</td>
</tr>
<tr>
<td>d(Pd-C1)</td>
<td>2,187</td>
<td>2,195</td>
<td>2,191</td>
</tr>
<tr>
<td>d(Pd-C3)</td>
<td>2,374</td>
<td>2,425</td>
<td>2,527</td>
</tr>
</tbody>
</table>
Table 7: Mulliken charge of allylic carbon atoms in \( \text{5 Rh(C}_3\text{H}_5) \), \( \text{6 Rh(3,3-(CH}_3)_2\text{-C}_3\text{H}_3) } \) and the analogous cationic palladium complexes resp. \( \text{5Pd} \) and \( \text{6Pd} \).

<table>
<thead>
<tr>
<th>atom</th>
<th>bite angle</th>
<th>5</th>
<th>6</th>
<th>5Pd</th>
<th>6Pd</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1</td>
<td>100 (( \eta^1 ))</td>
<td>-0.5027</td>
<td>-0.5286</td>
<td>-0.4915</td>
<td>-0.5252</td>
</tr>
<tr>
<td>C2</td>
<td>100 (( \eta^1 ))</td>
<td>-0.0379</td>
<td>-0.1769</td>
<td>0.0154</td>
<td>-0.1678</td>
</tr>
<tr>
<td>C3</td>
<td>100 (( \eta^1 ))</td>
<td>-0.5027</td>
<td>0.3119</td>
<td>-0.4915</td>
<td>-0.3240</td>
</tr>
<tr>
<td>C1</td>
<td>170 (( \eta^1 ))</td>
<td>-0.4361*</td>
<td>-0.4297**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C2</td>
<td>170 (( \eta^1 ))</td>
<td>-0.0179*</td>
<td>-0.2961**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C3</td>
<td>170 (( \eta^1 ))</td>
<td>-0.5606*</td>
<td>0.3842**</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*: taken from the structure at the local minimum (bite angle = 172.01°).
**: taken from the structure at the local minimum (bite angle = 171.44°).

Comparing the Mulliken charges of the allylic carbon atoms (table 7), shows that the \( \eta^1\text{-C}_3\text{H}_5 \) complex 5 resembles the palladium analogue \( \text{5Pd (C}_3\text{H}_5\text{Pd(PH}_3)_2^+ \). The charge distribution in the substituted analogue 6, however, is much more shifted to the \( \eta^1 \)-like distribution than in the palladium analogue \( \text{6Pd (3,3-(CH}_3)_2\text{-C}_3\text{H}_3\text{Pd(PH}_3)_2^+} \). As a result of the relatively large geometrical distortion, the relative electrophilicity of the substituted carbon atom C3 in 6 is larger than in \( \text{6Pd} \).

For the \( \eta^1 \)-structure of 5 the Mulliken charge of the C1 atom is more positive than for the \( \eta^3 \)-structure, whereas the charge on C3 is more negative than in the \( \eta^3 \)-structure. For the substituted complex 6, both C1 and C3 become more positively charged.

Based on the modeling studies, it is expected that alkylation of the \( \eta^3 \)-structure of a substituted allyl moiety of rhodium complexes results in a higher regioselectivity for the branched product than its palladium analogue. For the \( \eta^1\text{-C}_3\text{H}_5 \) complex 5, the distribution of the Mulliken charge is not in favor of an \( \text{S}_2\text{2'} \) attack on C3. For the substituted complex \( \eta^1\text{-6} \), however, nucleophilic attack via the \( \text{S}_2\text{2'} \) mechanism is plausible.

### 11.2.10 Reactions: Allylic alkylation

For palladium(allyl) complexes, it has been shown that nucleophilic attack takes place exclusively on an \( \eta^3 \)-coordinated allyl moiety\(^{13} \) and that for substrates such as cinnamyl, in most cases the linear product is obtained (chapters 3-9 and references therein). In contrast, studies of the allylic alkylation using rhodium phosphine complexes as the catalyst yield a very high portion (99%) of the chiral branched product.\(^{15} \) It has been suggested that the reaction does not proceed via an attack on a \( \eta^3 \)-coordinated allyl, but via an \( \text{S}_2\text{2'} \) attack on a \( \eta^1 \)-allyl (figure 2 and 3). To investigate these postulations, we used complexes 1b, 4a, 4b and the
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Palladium analogue of 4b in the stoichiometric alkylation with sodium diethyl 2-methylmalonate, which is the nucleophile we also used for the studies with palladium (table 8). Furthermore, complexes 4a and 4b were used in the catalytic alkylation of respectively allyl chloride and cinnamyl chloride (table 9). Because the rhodium catalyzed reactions proceed relatively slower, a slightly more concentrated reaction mixture was used.

Table 8: Stoichiometric alkylation of rhodium complexes using sodium diethyl 2-methylmalonate as the nucleophile (for reaction conditions: see experimental section).

<table>
<thead>
<tr>
<th>complex</th>
<th>branched (%)</th>
<th>linear (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1b (o-dppb) (cinnamyl)</td>
<td>88</td>
<td>12</td>
</tr>
<tr>
<td>4b (Xanthphos) (cinnamyl)</td>
<td>23</td>
<td>77</td>
</tr>
<tr>
<td>4a (Xanthphos) (allyl)</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Pd(Xanthphos)(cinnamyl)OTf</td>
<td>8</td>
<td>92</td>
</tr>
</tbody>
</table>

Table 9: Catalytic allylic alkylation using sodium diethyl 2-methylmalonate as the nucleophile (for reaction conditions: see experimental section).

<table>
<thead>
<tr>
<th>complex</th>
<th>TOF&lt;sub&gt;im&lt;/sub&gt;</th>
<th>% product</th>
<th>branched (%)</th>
<th>linear (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4a (allyl)</td>
<td>107</td>
<td>44</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>4b (cinnamyl)</td>
<td>15</td>
<td>13</td>
<td>21</td>
<td>79</td>
</tr>
</tbody>
</table>

*: determined after 45 minutes
**: determined after 4 hours.

The stoichiometric and the catalytic reactions show that both η³- and η¹-allyl complexes are alkylated. In the stoichiometric alkylation, the regioselectivity for the formation of the branched product is high for the o-dppb complex 1b (88 %), whereas the Xanthphos complex 4b shows the reverse regioselectivity (23%). Nevertheless, the selectivity to the branched product found using 4b is significantly higher than that found using its palladium analogue (Xanthphos)(cinnamyl)OTf (only 8% branched product). In the catalytic reaction of complex 4b, the same regioselectivity is found as in the stoichiometric reaction, suggesting that the reaction proceeds via the same intermediate. Using Xanthphos, the reaction proceeds faster for allyl chloride than for cinnamyl chloride and at a rate similar to that of the palladium complex.

11.2.11 Reaction with CO: High pressure-NMR

To study the influence of an η³- or η¹-coordination of the allyl on the interaction of the complexes with CO, the complexes 1-4a were treated with elevated pressures of $^{13}$C enriched CO.
For complexes \(1a\), \(2a\) and \(4a\), at room temperature, the NMR spectra showed the slow formation of a new complex (figures 21, 22 and 24 respectively). Upon heating to 313 K, the reaction proceeded faster and conversion was complete within 3 hours. During the reaction the \(^{31}\)P-NMR spectrum showed the formation of several transient complexes. The signals in the \(^1\)H-NMR spectrum are too broad to be conclusive; we postulate a Rh-CO complex, in which the allyl is bonded in an \(\eta^1\)-fashion. Several isomeric structures may exist for such complexes, which may account for different signals in the \(^{31}\)P-NMR spectra.

Figure 21: NMR spectra of the formation of an acyl complex of \(1a\) (o-dppb).

Figure 22: NMR spectra of the formation of an acyl complex of \(2a\) (dppe).
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Figure 23: HP-NMR spectra of the reaction of complex 3a (DPEphos) with CO.

Figure 24: NMR spectra of the formation of an acyl complex of 4a (Xantphos).
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The $^{13}$C-NMR spectra of the final product showed a doublet at 212 ppm ($^1J_{\text{Rh-C}} = 29$ Hz) (1a and 2a) or 217 ppm ($^1J_{\text{Rh-C}} = 27$ Hz, 4a). These values are similar to those of a reported acyl species (Rh(PPh$_3$)$_2$(C(O)C$_2$H$_5$)Cl)$_2$. In all cases the $^1$H-NMR showed a characteristic -CH$_2$-CH=CH$_2$ pattern, with the signals of the CH$_2$-unit at a higher ppm value than those in the starting complexes. The $^{31}$P-NMR showed that the two phosphorus atoms in the new complex are equivalent, indicating either an equatorial-equatorial coordination of the ligand in a trigonal bipyramidal or a square pyramidal structure. From this we concluded that the acyl species were formed.

After release of the CO pressure, the novel acyl complexes remained stable for a short time. The acyl product resulting from complex 4a, showed in the infrared spectrum a signal at 1676 cm$^{-1}$, which is in the range of metal-acyl complexes.

The $\eta^1$-allyl complex 3a, showed a different interaction with CO (figure 23). Several new complexes were formed, but the reaction did not proceed to form a single product.

11.3 Discussion

11.3.1 Structure

The modeling studies show that both an $\eta^3$ and an $\eta^1$ coordination of allyl to rhodium are possible and they support the feasibility of a significant distortion of the $\eta^3$ coordination to $\eta^1$-$\eta^1$. For the non substituted C$_3$H$_5$ allyl moiety, the global minimum is found for the $\eta^1$-complex, whereas the $\eta^1$-structure is more favored for the substituted allyl moiety. For both allyl groups, the $\eta^1$ structure is favored for a bite angle smaller than 130-140° and the $\eta^1$ structure for larger values.

11.3.2 dppe and o-dppb

Although the calculations predict an $\eta^1$-allyl for the used ligands, the experiments show a different result. The calculated $\eta^1$-coordination is found for DPEphos and Xanthos, but an $\eta^1$-coordinated allyl is found for dppe and o-dppb. Obviously, the Rh(PH$_3$)$_2$(C$_3$H$_5$)Cl$_2$ complex is not a good model for our system or the B3LYP/LANL2DZ level of theory is not a good method to study the geometry for small values of the bite angle ($< 100^\circ$). Although the calculations show that a trigonal bipyramidal structure is favored for small bite angles, in experimental systems, such a coordination may put too much strain on the backbone of the ligand and / or may cause too much steric hindrance for the substituents on the phosphorus atom. The geometry around the rhodium for o-dppb and dppe may therefore differ from trigonal bipyramidal and be more towards a square pyramidal geometry with the phosphorus functionalities cis to one another. The latter coordination would indeed explain the formation of $\eta^1$-complexes for these ligands.
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11.3.3 DPEphos

NMR spectroscopy shows that for DPEphos, both complex 3a and 3b are \( \eta^3 \)-structures and that a trigonal bipyramidal geometry is most likely. The NMR studies show, that in contrast to the other ligands, the two phosphorus atoms in the \( \text{C}_3\text{H}_7 \) complex 3a are not equivalent, which indicates that the Rh-allyl bond is not symmetric. This has been observed before in crystal structures of cationic (DPEphos)Pd(allyl) complexes (chapter 7). It appeared that the backbone of the DPEphos ligand is folded, such that one of the aromatic rings of the backbone has a \( \pi-\pi \) interaction with one of the phenyl rings of the phosphorus atom that is bonded to the other backbone ring.

11.3.4 Xantphos

According to NMR spectroscopy, the Xantphos complexes 4a and 4b differ in structure and presumably also in the geometry around the rhodium. The crystal structure clearly shows a trigonal bipyramidal geometry for 4a, but for the \( \eta^1 \)-complex 4b the calculations predict a square pyramidal complex. It remains unclear whether the two phosphorus atoms are cis or trans to one another. A trans coordination of Xantphos, with a coordinated oxygen, has been observed in cationic palladium complexes\(^{[12]} \), but seems less likely in a neutral rhodium complex. We therefore propose a cis coordination of the Xantphos ligand in complex 4b. The different coordination of \( \text{C}_3\text{H}_5 \) and cinnamyl to the rhodium is presumably caused by steric hindrance. In chapter 7, it was described that a large cone angle of the ligand influences the coordination of the allyl group. A strong steric interaction between Xantphos and the cinnamyl may therefore explain the difference in structure of 4a and 4b.

11.3.5 Allylic alkylation reaction

It has been suggested that, in contrast to palladium, rhodium allyl complexes react via an \( \text{S}_2\text{N}2 \)' attack on the \( \gamma \) carbon of the \( \eta^1 \)-allyl moiety. We found that both \( \eta^1 \)- and \( \eta^3 \)-complexes react with sodium diethyl 2-methylmalonate to form the corresponding alkylated products. Attack on the substituted \( \gamma \)-carbon of the \( \eta^1 \)-cinnamyl of o-dppb complex 1b results in a high regioselectivity for the branched product (88%). Remarkably, the alkylation of the analogous Xantphos \( \eta^1 \)-complex 4b results in the formation of only 23% of the branched product. This relatively low regioselectivity is more easily explained by a nucleophilic attack on an \( \eta^1 \)-allyl moiety (\( \text{S}_2\text{N}2 \)) than by the \( \text{S}_2\text{N}2 \)' mechanism. Possibly, complex 4b undergoes a rearrangement from \( \eta^1 \) to \( \eta^3 \) in the alkylation mixture. The increased polarity of the solution and an interaction between the sodium of the nucleophile and a chloride of 4b, may cause the formation of an intermediate rhodium complex with an enlarged Rh-Cl distance, which would enhance the possibility of \( \eta^3 \)-coordination of the cinnamyl. The possibility of nucleophilic attack on a rhodium allyl complex is evidenced by the successful
reaction between the η⁴-allyl complex 4a and malonate. If 4b reacts via the η¹-structure, the high selectivity for the branched product (23%) relative to the palladium analogue Pd(Xantphos)(cinnamyl)OTf (8%) can be explained by the large distortion of the Rh-cinnamyl bond (see above).

The catalytic alkylation of cinnamyl chloride using complex 4b shows the same regioselectivity as in the stoichiometric reaction, which indicates that the reactions proceed via the same intermediate. The alkylation of cinnamyl chloride using 4b proceeds relatively fast, even compared to palladium complexes (chapter 6). If complex 4b reacts via the η³-mechanism, the high reaction rate could be explained by the instability of the intermediate η³-cinnamyl complex and the large distortion of the Rh-cinnamyl bond. Furthermore, the modeling studies showed that for the η³-allyl complex, the backbonding interaction may be relatively small compared to the analogous palladium complex. In chapter 3 it was shown that a smaller backbonding interaction enhances the reactivity towards nucleophilic attack. The overall regioselectivity may therefore be a result of a competition between the SN₂' mechanism and the η³-mechanism. For η¹-complexes, a larger bite angle of the ligand will result in an increase of the reactivity and the η³-mechanism may be favored over the SN₂' mechanism.

11.3.6 Reaction with CO

Previous studies in our group to the rhodium catalyzed hydroformylation of styrene showed a remarkable dependency of the reaction rate on the bite angle of the ligand. The reaction proceeded slowly for ligands with a medium bite angle and fast for ligands with either a smaller or a larger bite angle. Our present study towards the interaction between the isolated rhodium allyl complexes and CO show the same trend. A facile insertion of CO was observed for complexes 1a and 2a, bearing ligands enforcing a small bite angle (o-dppb and dppe) and for complex 4a, bearing the large-bite-angle Xantphos ligand. The DPEphos complex 3a does show an interaction with CO, but no insertion product could be observed.

Since in complexes 1a and 2a the allyl is coordinated in an η¹-fashion, not all the coordination sites of the rhodium atom are occupied. Coordination of CO will therefore be a relatively facile process. In contrast, the allyl moiety in the Xantphos bearing complex is bonded in an η³-fashion. In studies of CO insertion (chapter 10) using analogous palladium complexes it was found that a distorted symmetry of the metal-allyl bond and a low barrier for η¹-η³ isomerization facilitate the reaction with CO. The same factors may govern the different behavior of complexes 3a and 4a. In the NMR studies, no η¹-η¹-η³ rearrangement could be observed for the DPEphos complex 3a, whereas this isomerization is an easy process for the Xantphos complex 4a. We tentatively propose an η¹-η¹ rearrangement of the allyl moiety of 4a prior to the coordination and insertion of CO (figure 25).
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Figure 25: Proposed mechanism of reaction of 4a with CO.

If our proposed mechanism for the carbonylation with Rh^{III} complexes is applicable to the Rh^{1} species in the reaction mixture of the hydroformylation of styrene and if the insertion of CO is rate determining (figure 1), we expect that for ligands enforcing an intermediate bite angle, the η^{3}-styryl species may be relatively stable. If this is the case, the catalytic reaction with ligands enforcing either a smaller or a larger bite angle will then show a different rate determining step. To date, no such kinetic studies have been reported.

11.4 Conclusion

We have synthesized and isolated a series of novel Cl_{2}Rh^{III}(diphosphine)allyl complexes. The hapticity of the rhodium-allyl bond (η^{1}, η^{3} or η^{1}-η^{2}) is highly dependent on the ligand and the substituents on the allyl moiety. The Rh(allyl) complexes react with malonate to form the alkylated product and with CO to form the CO-inserted acyl complex. The nature of the rhodium-allyl bond influences the mechanism of these reactions. In the allylic alkylation, an η^{1}-complex reacts via the S_N2' mechanism whereas an η^{3}-complex reacts via nucleophilic attack on the η^{3}-allyl moiety. DFT calculations suggest that the S_N2' mechanism may not be the favored pathway for non substituted allyl moieties.

For the reaction with CO, no insertion products could be observed for the η^{3}-allyl DPEphos complex 3a. For palladium complexes, the η^{3}-allyl square planar cationic geometry is favored whereas the crystal structure of 4a shows that neutral penta-coordinated complexes are formed for rhodium. The possibility for rhodium to adopt different geometries facilitates the formation of η^{1}-allyl complexes and causes a much stronger distortion of the η^{3}-coordination to η^{1}-η^{2} than observed for palladium. For palladium, η^{1}-allyl complexes can only be formed in using tridentate ligands and coordinating counterions, and these η^{1}-allyl species have shown to be unreactive towards nucleophiles. In contrast, η^{1}- and η^{3}-allyl rhodium complexes described in this chapter react readily to form the alkylation product with a moderately high regioselectivity for the chiral, branched product.

Thus, we have studied the structure and reactivity of a series of novel Rh(III)(allyl) complexes. Further studies are needed to reveal more details of the mechanism of the reactions and to explore the scope of the potential use as homogeneous catalysts.
11.5 Experimental Section

11.5.1 General procedure:

All reactions were performed in an atmosphere of argon unless stated otherwise. Dichloromethane was distilled under nitrogen atmosphere from P$_2$O$_5$; pentane, hexane, toluene and benzene were distilled from sodium, THF and diethyl ether from sodium/benzophenone. [RhCl$_3$3H$_2$O] was obtained from ABCR and used as obtained. [Rh(Acac)(CO)$_2$] was obtained from Merck and used as received. bis-1,2-(diphenylphosphino)-ethane and bis-1,2-(diphenylphosphino)-benzene were purchased from Aldrich and used as received. Allylchloride and cinnamylchloride were obtained from ACROS and used as received. [Rh(COD)Cl]$_2$ was synthesised according to literature procedure. $^1$H-, $^{31}$P-$^1$H- and $^{13}$C-NMR spectra were recorded at 300, 121 and 75 MHz respectively on a Varian FT NMR spectrometer. Variable temperature NMR experiments were performed on a Brucker DRX-300 FT NMR spectrometer equipped with a variable temperature unit. Cosy-spectra were recorded at 500 MHZ on a Varian Inova500 FT NMR spectrometer. Chemical shifts are reported in δ units (ppm) and referenced to the residual deuterated solvent signal for $^1$H- and $^{13}$C-NMR spectroscopy, external H$_3$PO$_4$ (δ = 0 ppm) for $^{31}$P-$^1$H-NMR spectroscopy.

11.5.2 Computational Details

The DFT/HF-hybrid calculations were performed using the Gaussian98 program. The geometries were optimised using the B3LYP / LANL2DZ level of theory. All optimisations were performed in redundant internal coordinates. No symmetry was used.

11.5.3 Synthesis and characterization

![Figure 26: Numbering scheme for $^1$H-NMR data.](image)

Rh(o-DPPB)(COD)Cl

25 mg of [Rh(COD)Cl]$_2$ (0.05 mmol) was dissolved in 5 ml of dry toluene. To this solution 47 mg of o-DPPB (0.10 mmol) in 15 ml of toluene was added. After addition the solution was stirred for 30 minutes at
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room temperature, during which an orange solid precipitated. The liquid was removed and the solid was washed twice using 25 ml of pentane. The product was dried under vacuum.

$^1$H-NMR(CDC$_3$): 8.0 - 6.2 (24H, m, aromatic protons o-DPPB), 3.9 (4H, bs, olefinic protons COD), 2.2 (4H, bs, exo - protons COD), 1.6 (4H, bd, J(H,H) = 8 Hz, endo – protons COD)

$^{31}$P$^{'1}$$H$-NMR (CDCl$_3$): 75 (d, J(Rh,P) = 198 Hz)

**Rh(DPPE)(COD)Cl**

16.1 mg of [Rh(COD)Cl]$_2$ (0.06 mmol) was dissolved in 5 ml of THF. To this solution 26.5 mg of DPPE (0.06 mmol, 97%) was added while stirring. The solution was stirred for 30 minutes. The solvent was removed in vacuo and the solid was washed twice using 10 ml of pentane.

$^1$H-NMR(CD$_2$CN): 8.0 - 7.0 (20H, m, aromatic protons DPPE), 4.1 (4H, bs, olefinic protons COD), 3.5 (2H, m, backbone protons DPPE), 2.3 (4H, bs, aliphatic protons COD), 2.1 (2H, m, backbone protons DPPE), 1.7 (4H, bs, aliphatic protons COD).

$^{31}$P$^{'1}$$H$-NMR (CD$_2$CN): 63 (d, J(Rh,P) = 133 Hz)

**Rh(Xanthphos)(COD)Cl**

25 mg of [Rh(COD)Cl]$_2$ (0.05 mmol) was suspended in 5 ml of dry Ether. To this suspension 58 mg of Xanthphos was added as a finely ground solid. After addition the solution was stirred for 30 minutes at room temperature, during which an orange solid precipitated. The orange solid was washed twice using 20 ml of Ether. The product was dried under vacuum.

$^1$H-NMR(Toluene-D$_8$): 8.0 - 7.0 (26H, m, Aromatic protons Xanthphos), 4.5 (4H, bs, olefinic protons COD), 1.9 (4H, bs, aliphatic protons COD), 1.6 (6H, bs, methyl-protons Xanthphos), 1.3 (4H, bs, aliphatic protons COD)

$^{31}$P$^{'1}$$H$-NMR (Toluene-D$_8$): 7.6 (d, 1J(Rh,P) = 91 Hz)

**Rh (C$_3$H$_5$(o-DPPB))Cl**

50 mg of [Rh(COD)Cl]$_2$ (0.10mmol) was suspended in 5 ml of toluene. To this suspension 90.1 mg of o-di(diphenylphosphino)-benzene (0.20 mmol) in 15 ml of toluene was added dropwise. After addition, the solution was stirred for 1 hour, during which the product precipitated as an orange solid. 0.05 ml of allylchloride (0.65 mmol, a large excess) was added. The mixture was stirred for another hour at room temperature, during which the colour of the suspension changed from orange to yellow. 15 ml of pentane were added to facilitate precipitation. The liquids were removed and the solid was washed twice using 20 ml of pentane. The solid was dried under vacuum.

$^1$H-NMR(CDC$_3$): 8.0 - 6.2 (24H, m, aromatic protons o-DPPB), 5.1 (1H, m, He), 5.0 (1H, dt, J(H,2H) = 4 Hz; J(H,H) = 14 Hz; Ha), 4.9 (1H, dt, J(H,2H) = 3 Hz; J(H,H) = 6Hz, Hb), 2.6 (2H, d, J(H,H) = 8 Hz, Hd and He)

$^{31}$P$^{'1}$$H$-NMR (CDCl$_3$): 62 (bd, J(Rh,P) = 124 Hz)

HR-MS (FAB): C$_{33}$H$_{29}$Cl$_2$P$_2$Rh$^+$ requires m/z = 660.0176, found: 625.0491 (loss of one Cl)
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**Rh(C₃H₅)(DPPE)Cl₂ 2a**

29 mg of Rh(DPPE)(CO)Cl (0.05 mmol) was dissolved in 5 ml of THF. To this suspension 0.05 ml of allylchloride (0.65 mmol, a large excess) was added dropwise. The mixture was stirred for 30 minutes at room temperature. The solvent was removed in vacuo and the product was washed twice using 10 ml of pentane. The yellow product was dried in vacuo.

^1^H-NMR (CDCl₃) : 8.0 - 7.0 (20H, m, aromatic protons DPPE), 5.0 (1H, m, Hc), 4.8 (2H, m, Ha and Hb), 3.1 (2H, m, Backbone protons DPPE), 2.9 (2H, bs, Hd and He), 2.5 ppm (2H, m, Backbone protons DPPE)

^3^P[^1^H]-NMR (CDCl₃) : 66 (bd, J(Rh,P) = 105 Hz)

**Rh(DPEphos)(C₃H₅)Cl₂ 3a**

25 mg of [Rh(COD)Cl]₂ (0.05 mmol) was suspended in 5 ml of dry ether. To this suspension 55 mg of DPEphos (0.10 mmol) was added as a finely ground solid. After addition the solution was stirred for 30 minutes at room temperature, during which a red solid precipitated. The solid was washed twice using 20 ml of ether. This solid was then suspended in 3 ml of THF. To this suspension 0.05 ml of allylchloride (0.65 mmol, a large excess) was added dropwise. The mixture was stirred for 2 hours during which the colour of the solution changed from red to yellow and finally a yellow solid precipitated. The liquid was removed and the solid was washed twice using 20 ml of pentane. The solid was dried under vacuum.

^1^H-NMR (CDCl₃) : 8.5 - 6.0 (aromatic protons DPEphos), 5.3 (1H, m, Hc), 4.5 (1H, dd, J(H,H) = 13 Hz, J(H,H) = 10 Hz, Hb), 4.2 (1H, dd, J(H,H) = 7 Hz, J(H,H) = 7 Hz, He), 3.1 (1H, d, J(H,H) = 7 Hz, Hd), 3.0 (1H, d, J(H,H) = 12 Hz, Ha)

^3^P[^1^H]-NMR (CDCl₃) : 30 (1P, dd, J(Rh,P) = 115 Hz, J(P,P) = 9 Hz), 12 (1P, dd, J(Rh,P) = 144 Hz, J(P,P) = 9 Hz)

HR-MS (FAB): C₃₄H₃₈Cl₂OP₂Rh⁺ requires m/z = 752.0439, found: 717.0755 (loss of one Cl)

**Rh(Xanthphos)(C₃H₅)Cl₂ 4a**

42 mg of Rh(Xanthphos)(COD)Cl (0.05 mmol) was suspended in 5 ml of toluene. To this suspension 0.1 ml of allylchloride (1.3 mmol, a large excess) was added. The reaction mixture was stirred for 2 hours at room temperature. The solvent was removed in vacuo, and the product was dried under high vacuum (5x10⁻⁵ mbar).

^1^H-NMR (CDCl₃): 8.0 - 7.0 (26H, m, aromatic H's Xanthpos), 5.5 (1H, p, J(H,4H) = 11 Hz, Hc), 3.6 (4H, bs, Ha + Hb + Hd + He), 1.5 (6H, bs, CH₃'s Xanthpos)

^3^P[^1^H]-NMR (CDCl₃) : 5 (bs)

HR-MS (FAB): C₃₉H₃₃Cl₂OP₂Rh⁺ requires m/z = 792.0752, found: 757.1068 (loss of one Cl)

**Rh (C₃H₅Ph)(o-DPPB)Cl₂ 1b**

49.2 mg of [Rh(COD)Cl]₂ (0.10 mmol) was suspended in 5 ml of toluene. To this solution 90.1 mg of o-di(diphenylphosphino)-benzene (0.20 mmol) in 15 ml of toluene was added dropwise. After addition, the
solution was stirred for 1 hour, during which the product precipitated as an orange solid. 0.10 ml of cinnamylchloride (1.3 mmol, a large excess) was added. The mixture was stirred for two hours at room temperature. 15 ml of pentane were added to facilitate precipitation. The liquids were removed and the solid was washed twice using 20 ml of pentane. The solid was dried under vacuum.

$^1$H-NMR (CDCl$_3$) : 8.0 - 7.0 (30H, m, aromatic protons o-DPPB and phenyl cinnamyl-group), 5.6 (1H, dt, J(H,H) = 8 Hz, J(H,2H) = 11 Hz, Hc), 2.3 (2H, d, J(H,H) = 11 Hz, Hd and He)

$^{31}$P$^1$H-NMR (CDCl$_3$) : 64 (d, J(Rh,P) = 164 Hz)

**Rh(DPPE)(C$_3$H$_4$Ph)Cl$_2$ 2b**

28 mg of Rh(DPPE)(CO)Cl (0.05 mmol) was dissolved in 5 ml of THF. To this solution 0.05 ml of cinnamylchloride (0.65 mmol, a large excess) was added dropwise. The mixture was stirred for 30 minutes at room temperature. The solvent was removed in vacuo and the product was washed twice using 10 ml of pentane. The yellow product was dried in vacuo.

$^1$H-NMR (CDCl$_3$) : 8.0 - 7.0 (25H, m, aromatic protons DPPE and phenyl protons cinnamyl), 6.1 (1H, d, J(H,H = 25 Hz, Ha), 5.7 (1H, dt, J(H,H) = 25 Hz, J(H,2H) = 8 Hz, Hc), 4.5 (2H, d, J(H,H) = 8 Hz, Hd and He), 3.3 (2H, m, backbone protons DPPE), 2.3 (2H, m, backbone protons DPPE)

$^{31}$P$^1$H-NMR (CDCl$_3$) : 69 (d, J(Rh,P) = 145 Hz)

**Rh(DPEphos)(C$_3$H$_4$Ph)Cl$_2$ 3b**

25 mg of [Rh(COD)Cl]$_2$ (0.05 mmol) was suspended in 5 ml of dry ether. To this suspension 55 mg of DPEphos (0.10 mmol) was added as a finely ground solid. After addition the solution was stirred for 30 minutes at room temperature, during which a red solid precipitated. The solid was washed twice using 20 ml of ether. This solid was then suspended in 3 ml of Toluene. To this suspension 0.1 ml of cinnamylchloride (0.66 mmol, a large excess) was added. The solution was stirred at room temperature for 2 hours. The product was precipitated using 20 ml of pentane. The liquids were removed, and the solid was washed twice, using 20 ml of pentane. The product was dried in vacuo.

$^1$H-NMR (CDCl$_3$): 8.0 - 7.0 (33H, m, aromatic H's Xantphos and phenyl cinnamyl-group), 6.1 (1H, bs, Hb), 5.8 (1H, m, Hc), 3.7 (1H, bs, Hd), 3.4 (1H, bs, He)

$^{31}$P$^1$H-NMR (CDCl$_3$) : 44 (1P, dd, J(Rh,P) = 180 Hz, J(P,P) = 15 Hz), 32 (1P, dd, J(Rh,P) = 134 Hz, J(P,P) = 15 Hz), 11 (0.1P, d, J(Rh,P) = 121 Hz, minor product)

**Rh(Xantphos)(C$_3$H$_4$Ph)Cl$_2$ 4b**

40 mg of Rh(Xantphos)(COD)Cl (0.05 mmol) was suspended in 5 ml of toluene. To this suspension 0.1 ml of cinnamylchloride (0.66 mmol, a large excess) was added. The reaction mixture was stirred for 2 hours at room temperature. The solvent was removed in vacuo, and the yellow solid was washed twice using 10 ml of pentane. The product was dried under high vacuum (5*10$^{-5}$ mbar).
1H-NMR (CDCl₃): 8.0 – 7.0 (31H, m, aromatic H’s Xantphos and phenyl cinnamyl-group), 6.7 (1H, d, J(H,H) = 16 Hz, Hb), 6.6 (1H, m, He), 4.4 (2H, bs, Hd and He), 1.7 (6H, s, methyl-protons Xantphos)

31P{1H}-NMR (CDCl₃): 16 (bd, J(Rh,P) = 117 Hz)

HR-MS (FAB): C₄₀H₄₁⁺Cl₂OP⁺Rh⁺ requires m/z = 868.1065, found: 833.1384 (loss of one Cl)

11.5.4 High-Pressure NMR

Rh(C₃H₃)(o-DPPB)Cl₂ 1a
34 mg of Rh(C₃H₃)(o-DPPB)Cl₂ (0.05 mmol) was dissolved in 2 ml of CDCl₃. The solution was transferred to a 10 mm sapphire high-pressure NMR-tube. The tube was pressurised using 4 bar of ¹³CO and 36 bar of ¹²CO. ¹H- and ³¹P{¹H}-spectra were taken every 15 min throughout the experiment. ¹³C-spectra were taken every hour. After 2 hours the mixture was heated to 50°C in the spectrometer. The solution was heated for 1 hour, during which time the reaction went to completion. Afterwards the solution was cooled to room temperature and ¹H- and ³¹P{¹H}-NMR spectra were obtained.

Rh(C₃H₃)(DPPE)Cl₂ 2a
32 mg of Rh(NBD)(DPPE)Cl (0.05 mmol) was dissolved in 2 ml of CD₃CN. To this solution 0.05 ml of allylchloride (1.3 mmol, a large excess) was added and the mixture was stirred thoroughly. The solution was transferred to a 10 mm sapphire high-pressure NMR-tube. The tube was pressurized using 4 bar of ¹¹CO and 36 bar of ¹²CO. ¹H- and ³¹P{¹H}-NMR spectra were obtained at room temperature before heating to 50°C. NMR-spectra were obtained after 20 min., 45 min., 1:20 h. and 1:30 h. The solution was then cooled to room temperature. ¹H- and ³¹P{¹H}-NMR spectra were taken 20 min., 40 min. and 75 min. after cooling.

Rh(C₃H₃)(DPEphos)Cl₂ 3a
37 mg of Rh(C₃H₃)(DPEphos)Cl₂ (0.05 mmol) was dissolved in 2 ml of CDCl₃. The solution was transferred to a 10 mm sapphire high-pressure NMR-tube. The tube was pressurized to 8 bar using ¹³CO. The ¹H-, ³¹P{¹H}- and ¹³C{¹H}-NMR measurements were taken at room temperature. The solution was heated to 50°C for 1 hour in the spectrometer, after which another set of measurements was taken. The NMR-tube was pressurized further using 36 bar of ¹²CO and was heated to 50°C for another hour. The mixture was analysed using ¹H-, ³¹P{¹H}- and ¹³C{¹H}-NMR.

Rh(C₃H₃)(Xantphos)Cl₂ 4a
41 mg of Rh(C₃H₃)(Xantphos)Cl₂ (0.05 mmol) was dissolved in 2 ml of CDCl₃. The solution was transferred to a 10 mm sapphire high-pressure NMR-tube. The tube was pressurized to 8 bar using ¹³CO. The ¹H- and ³¹P{¹H}-NMR spectra were taken every 15 min. for 3 hours at room temperature, ¹³C-NMR spectra were obtained every hour. Afterwards, the solution was heated to 40°C in the spectrometer for 1 hour, during
which time the reaction was completed. The solution was cooled to room temperature and $^1$H, $^{31}$P,$^1$H- and $^{13}$C-NMR spectra from the final product were obtained.

11.5.5 Crystal structure determination of 4a:

C$_{23}$H$_{37}$Cl$_2$OP$_2$Rh, $M_r$=793.5, monoclinic, P2$_1$/c, a=16.516(3), b=13.218(2), c=16.908(2)Å, $\beta$=101.15(1)$^\circ$, $V$=3621.5(10)Å$^3$, Z=4, $D_x$ =1.46 gcm$^{-3}$, $\lambda$(CuK$\alpha$)=1.5418Å, $\mu$(CuK$\alpha$)=62.56 cm$^{-1}$, $F(000)$=1624, room temperature, Final $R$=0.074 for 5558 reflections.

A crystal with dimensions 0.15 x 0.20 x 0.45 mm approximately was used for data collection on an Enraf-Nonius CAD-4 diffractometer with graphite-monochromated CuK$\alpha$ radiation and $\omega$-2$\theta$ scan. A total of 7453 unique reflections was measured within the range -20$\leq h \leq$20, 0$\leq k \leq$16, -21$\leq l \leq$0. Of these, 5558 were above the significance level of 4$\sigma$(F$_{obs}$) and were treated as observed. The range of $(\sin \theta)/\lambda$ was 0.031-0.627Å (2.7$\leq \theta \leq$75.3$^\circ$). Two reference reflections ([2 1 4],[2 1 1]) were measured hourly and showed no decrease during the 132 h collecting time. Unit-cell parameters were refined by a least-squares fitting procedure using 23 reflections with 39.91$\leq \theta \leq$41.00. Corrections for Lorentz and polarisation effects were applied. Absorption correction was performed with the program PLATON$^{[10]}$ following the method of North et al.$^{[17]}$ using $\Psi$-scans of five reflections, with coefficients in the range 0.356-0.954. The structure was solved by the PATTY option of the DIRDIF99 program system.$^{[18]}$ The hydrogen atoms were calculated. Full-matrix least-squares refinement on F, anisotropic for the non-hydrogen atoms and isotropic for the hydrogen atoms keeping the latter fixed at their calculated positions with an atomic displacement parameter of U=0.10 Å$^2$, converged to $R$=0.074, $R_w$=0.081, $(\Delta/\sigma)$max=0.18, $S$=1.07. A weighting scheme $w=[15. + 0.01*(\sigma(F_{obs}))^2 + 0.01/(\sigma(F_{obs}))]^{-1}$ was used. A final difference Fourier map revealed a residual electron density between -2.43 and 1.66 eÅ$^{-3}$ in the vicinity of the Rh. Scattering factors were taken from Cromer and Mann.$^{[19a]}$ International Tables for X-ray Crystallography.$^{[19b]}$ The anomalous scattering of Rh, P and Cl was taken into account.$^{[20]}$ All calculations were performed with XTAL3.7,$^{[21]}$ unless stated otherwise.
11.6 References and notes


[8] Many different procedures have been reported for the synthesis of such complexes and we have tried many. Our novel route was the only method that was succesful for all ligands and all allyls. For other procedures see for instance:


[13] R. J. van Haaren: characterization of (triphos)Pd(η¹-cinnamyl)Cl: ^1^H-NMR: 2.3-2.6 (2 multiplets, 4H, backbone), 2.7 (m, 2H, Pd-CH₂), 3.0-3.3 (m(ddd), 4H, backbone), 5.1 (dd, J₁ = 15.3 Hz, J₂ = 5.6 Hz, 1H, =CH-Ph), 5.8 (dt, J₁(d) = 15.0 Hz, J₂(t) = 6.3 Hz, 1H, Pd-CH₂=CH-Ph), 7.0-7.8 (m, 30 H, aromatic H); ^3¹^P-NMR: 47 (d, J = 48 Hz, 2P, -PPh₂), 99 (temperature, J = 48 Hz, 1P, PPh₂-P(Ph)-PPh₂);

This palladium complex and other Pd(η¹-cinnamyl) complexes are not reactive in the stoichiometric and the catalytic allylic alkylation.


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In the chemical industry, the use of environmentally friendly processes is of great importance. The combination of fundamental and applied research is useful for the development of these processes. The fundamental research presented in this thesis, is part of a combined industrial-academic effort for cleaning-up an existing industrial process.

Besides the general introduction (chapter 1), the thesis consist of 3 parts. Part 1 (chapters 2-9) deals with the palladium catalyzed allylic alkylation, part 2 (chapter 10) deals with the palladium catalyzed carbynlation of allylic substrates and in the third part (chapter 11) the use of rhodium instead of palladium in these reactions is explored.

The industrial process of DSM to which our research is related, the carbynlation of dienes, involves palladium-allyl intermediates. To study the formation of side products resulting from nucleophilic attack, we used the allylic alkylation as a model reaction. Because of a special interest in the origin of the formation of regio-isomers of the side products, we focused on the topic of regioselectivity. First, we studied the structure of the Pd-allyl bond in detail by DFT calculations (chapter 3) and by X-ray crystal structures (chapter 7). Via stoichiometric and catalytic alkylation reactions we found a relation between the structure of the Pd-allyl bond and the regioselectivity. We succeeded in exploring the limits of the validity of the existing mechanistic theories. To explain the results, we developed a new model for the origin of the regioselectivity (chapter 9) (figure 1). Two reaction paths may be followed, leading to the opposite regio-isomer. In the first phase of the reaction, the electronically favored path leads to the branched product, whereas in the second phase, the sterically favored path leads to the branched product. We have determined a number of parameters influencing the rate and the regioselectivity of the reaction.
Figure 1: Proposed origin of the regioselectivity in the palladium catalyzed allylic alkylation.

For the industrial process under study by DSM, the catalytic reaction of the palladium-allyl complexes with CO and alcohol to form β-γ-unsaturated esters is highly important. We investigated the mechanism of the interaction of Pd(allyl) complexes with CO and found that two pathways are possible for the formation of the ester product (chapter 10). At high pressure, the well known migratory-insertion reaction leads to the formation of an acyl complex, which reacts with an alcohol to form the corresponding ester. In addition, we found a pathway involving the direct attack of methanoate to the coordinated CO to form an intermediate carboxymethoxy species (figure 2). Reductive elimination of the carboxymethoxy group and the η³-allyl leads to the formation of the ester product. Our results show that neither the insertion reaction nor the last step of the ester formation per se are slow, the overall low rate observed is due to relatively stable η³-intermediates.
Finally, we conducted an exploratory study concerning the use of rhodium for the allylic alkylation and carbonylation reaction (chapter 11). To this end, a novel series of (diphosphine)-Rh(allyl)Cl₂ complexes has been prepared and studied in detail. It was found that depending on the ligand and the substitution pattern of the allyl, the hapticity of the Rh-allyl bond is either η¹, η¹-η³ or η³. The Rh(allyl) complexes were tested in the allylic alkylation and in the reaction with CO. Although in literature the Sₙ2' nucleophilic attack on the η¹-allyl moiety is the commonly accepted mechanism, we found that attack on complexes with other hapticities also takes place. As an additional novel mechanism for the rhodium catalyzed allylic alkylation, we proposed the direct nucleophilic attack on the η¹-η³- or η³-allyl. Concerning the reaction of Rh(allyl) complexes with CO, we showed that at elevated pressures, migratory-insertion occurs to form the corresponding acyl complexes, thus forming a possible key intermediate in the rhodium catalyzed alkoxy-carbonylation.
Hoofdstuk 13
Samenvatting

Voor de chemische industrie zijn schone processen van groot belang. Een combinatie van fundamenteel en toegepast onderzoek leidt tot synergie bij de ontwikkeling van dergelijke processen. Het fundamentele onderzoek, beschreven in dit proefschrift, maakt deel uit van een industrieel-academische samenwerking die zich richt op het opschonen van een bestaand industrieel proces.

Naast de algemene introductie (hoofdstuk 1), bestaat het proefschrift uit 3 delen. Deel 1 (hoofdstuk 2-9) behandelt de palladium gekatalyseerde allylische alkylering, deel 2 (hoofdstuk 10) behandelt de palladium gekatalyseerde carbonylering van allylische substraten en in het derde deel wordt het gebruik van rhodium als alternatief voor palladium onderzocht.

In het industriële proces van DSM waaraan dit onderzoek verwant is, de carbonylering van diënën, spelen Pd(allyl) intermediairen een rol. Om de vorming van nevenproducten als gevolg van nucleofiele aanval te bestuderen hebben we de allylische alkylering gebruikt als modelreactie. Vanwege een interesse in de vorming van regio-isomeren van een van de nevenproducten, hebben we speciale aandacht besteed aan de regioselectiviteit van de reactie.

Eerst hebben we de Pd-allyl binding in detail bestudeerd met behulp van DFT berekeningen (hoofdstuk 3) en kristalstructuren (hoofdstuk 7). Uit de resultaten van de stoichiometrische en katalytische alkylering hebben we een relatie gevonden tussen de structuur van de Pd(allyl) binding en de regioselectiviteit. Met succes hebben we de grenzen van de geldigheid van de bestaande mechanismische modellen onderzocht. Om de resultaten te verklaren, hebben we een nieuw model ontwikkeld voor de oorsprong van de regioselectiviteit van de reactie (hoofdstuk 9, figuur 1).

De reactie kan verlopen via twee paden, die leiden tot het tegenovergestelde regio-isomeer. In het eerste stadium van de reactie leidt het electronisch gunstigste pad naar het vertakte product, terwijl in het tweede stadium van de reactie het sterisch gunstigste pad naar het vertakte product leidt. We hebben een aantal factoren bepaald die van invloed zijn op de regioselectiviteit en de snelheid van de reactie.
Hoofdstuk 13

Figuur 1: Voorgestelde mechanisme van de regioselectiviteit van de allylsche alkylering.

In het door DSM bestudeerde industriële proces is de katalytische reactie belangrijk, waarin Pd(allyl) met CO en alcohol reageert om β-γ onverzadigde esters te vormen. Wij hebben het mechanisme onderzocht van de reactie van Pd(allyl) complexen met CO en hebben gevonden dat twee mechanismische routes mogelijk zijn voor de vorming van het ester product (hoofdstuk 10). Onder hoge druk verloopt de reactie via de welbekende migratie-insertie. Het als intermediair gevormde Pd-acyl complex reageert vervolgens met een alcohol tot de ester. Daarnaast hebben we een andere route gevonden, die verloopt via directe aanval van methanoaat op het gecoördineerde CO (figuur 2). Het aldus gevormde carbomethoxy complex reageert via reductieve eliminatie met de η³-allyl groep tot de ester.

Onze resultaten tonen aan dat noch de insertiestap, noch de vorming van de ester snelheidsbepalend zijn: de gevonden lage reactiesnelheid is het gevolg van de stabiliteit van de Pd(η³-allyl) intermediairen.
Samenvatting.

Figuur 2: Voorgestelde associatieve (carbomethoxy) mechanisme voor de carbonylering van Pd(η³-allyl)
complexen.

Tot slot hebben we een verkennende studie uitgevoerd naar het gebruik van rhodium in de allylische
alkylering en de carbonylering reacties (hoofdstuk 11). We hebben hiertoe een nieuwe serie (diphosphine)-
Rh(allyl)Cl₂ complexen gemaakt en in detail bestudeerd. Het blijkt, dat de hapticiteit van de Rh-allyl binding
afhankelijk is van het ligand en het substitutiepatroon op de allyl, met als mogelijke waarden η¹, η¹-η² of η³.
De Rh(allyl) complexen werden getest in de allylische alkylering en in de reactie met CO. Hoewel in de
literatuur de S₈₂' nucleofiele aanval op de η¹-allyl groep het algemeen aanvaarde mechanisme is, hebben wij
gevonden dat complexen met andere hapticiteiten ook reactief zijn voor de nucleofiele aanval. We hebben
derhalve een nieuw mechanisme voorgesteld, verlopend via directe nucleofiele aanval op de η¹-η²- of η³-
allyl. Met betrekking tot de reactie van Rh(allyl) complexen met CO hebben we aangetoond dat bij
verhoogde druk, de migratie-insertie reactie optreedt, hetgeen leidt tot de vorming van acyl complexen. Deze
complexen kunnen belangrijke intermediairen zijn in de rhodium gekatalyseerde alkoxy carbonylering.