Palladium and rhodium allyl complexes in catalysis

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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(\(\eta^1\)-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)\(\text{Pd}(\varepsilon)\text{OTf}\) 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{[4]} Palladium complexes have a preference for the formation of the linear, achiral product.\textsuperscript{[5]} Excellent regio- and enantioselectivities\textsuperscript{[6]} 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 (Pfalz\textsuperscript{[4a, 4b]}, Williams\textsuperscript{[4c, 4d]} and the MAP ligand (Kocovsky\textsuperscript{[4e, 4f]}). 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{[15b]} 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 $\eta^5$-(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 $\eta^5$-(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{[5]} 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{[5a, 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.
6.2 Results

6.2.1 Ligand synthesis

We have prepared two series of mixed phosphorus-nitrogen ligands. One series of ligands consists of a Ph₂PO- unit that is connected to an ortho substituted pyridine moiety via an alkyl chain of variable length (POPy-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 POPy type ligands (a-c) were conveniently prepared by coupling Ph₂PCl to ortho-pyridine-(CH₂)ₙOH in the presence of NEt₃. The P-Im class of ligands (d-g) were synthesized in two steps. The imine was synthesized according to a literature procedure by condensation of the para-substituted aldehyde with H₂N(CH₂)ₙOH (n = 3, 4), followed by coupling to Ph₂PCl.
Figure 2: Generic structures of two new classes of P-N ligands

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 (\(J_{PCH₃}\)) is diagnostic for the orientation of the substituent, enabling elucidation of the structure of the complexes. The value of the coupling constant of the syn oriented CH₃ groups with a trans phosphorus atom is around 10-12 Hz (\(J_{PCH₃}\)). Both a cis orientation with respect to phosphorus and an anti orientation with respect to Hd would result in a lower value of \(J_{PCH₃}\) (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 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 CDCl₃.](image)

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 c 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 c. A low temperature (-25 °C) spectrum recorded for the complex of ligand g shows that in the slow exchange regime the methyl groups of both isomers have the same coupling constant ($^4J_{(P-CH_3)} = 10.1$ Hz). This indicates that both isomers have the methyl group in a syn orientation. The spectra of all complexes ligated with the imine type ligands show the presence of two structures. All are identified as syn-trans-P complexes.

The value for $^4J_{(P-CH_3)}$ in the fast exchange spectrum of the complex of ligand c is the same as in the slow exchange spectrum of the complex of ligand g (10.1 Hz). Apart from the value for $^4J_{(P-CH_3)}$, the chemical shift of the CH$_3$ group, for all complexes > 1.3 ppm, is also indicative of a trans-P orientation. A trans-N orientation of the methyl group would result in a signal at higher field (< 0.6 ppm).[12e,f]

Apart from the splitting of all signals, it can be seen that at +55°C the allylic protons Ha and Hb 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 ortho-pyridine proton are separated from the rest of the signals and were used to obtain rate data by simulation of the spectra[13]. The Eyring plot shows that the rate of exchange is linearly dependent of the reciprocal temperature: $-\ln k/T = -33 + 7.10^3 / T$. From this it follows that $\Delta H^\ddagger = 60$ kJ/mole and $\Delta S^\ddagger = 34$ 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 trans and the branched product. The linear 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 c.

If the substituent on the allyl moiety is a bulkier phenyl rather than a methyl group, only two products are observed: the linear 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 c). There is no significant change in regioselectivity when neutral instead of cationic complexes are used (entry 4).

Table 1: Stoichiometric alkylation of (crotyl)Pd(P-N)OTf complexes.

<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>a</td>
<td>37.2</td>
<td>56.1</td>
<td>6.7</td>
</tr>
<tr>
<td>2</td>
<td>b</td>
<td>65.6</td>
<td>31.0</td>
<td>3.4</td>
</tr>
<tr>
<td>3</td>
<td>c</td>
<td>79.0</td>
<td>18.2</td>
<td>2.8</td>
</tr>
<tr>
<td>4</td>
<td>d</td>
<td>84.1</td>
<td>14.2</td>
<td>1.7</td>
</tr>
<tr>
<td>5</td>
<td>e</td>
<td>88.0</td>
<td>10.9</td>
<td>1.1</td>
</tr>
<tr>
<td>6</td>
<td>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;en&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

75
Table 4: Catalytic alkylation of cinnamyl chloride. Experimental details: see experimental section.

<table>
<thead>
<tr>
<th>entry</th>
<th>complex</th>
<th>TOF_{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]

<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[^b]</td>
<td>a (3)</td>
<td>29.2</td>
<td>63.1</td>
<td>7.7</td>
</tr>
<tr>
<td>3[^b]</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></td>
<td>20 eq LiBr/Pd</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6[^b]</td>
<td>b (1.5)</td>
<td>19.3</td>
<td>77.5</td>
<td>3.2</td>
</tr>
<tr>
<td>7[^b]</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.


P-N ligands, crotyl and cinnamyl substrates.

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). \(^{14}\)

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
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 \( \eta^3-\eta^1-\eta^3 \)-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 \( \eta^3-\eta^1-\eta^3 \) 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 \( \eta^3-\eta^1-\eta^3 \) rearrangement of the allyl moiety and not of other processes such as flopping of the backbone.

The partial decoordination of the allylic moiety during this process accounts for the observed positive \( \Delta S^\ddagger \) value. The value of the activation parameters \( \Delta H^\ddagger \) and \( \Delta S^\ddagger \) corresponds to literature values for the \( \eta^3-\eta^1-\eta^3 \) rearrangement.\(^{12} \)

![Figure 5: Dynamic exchange of endo and exo isomers in cationic (crotyl)Pd(P-N) complexes via \( \eta^3-\eta^1-\eta^3 \) 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
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 crottyl 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 crottyl 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.\textsuperscript{171}

\subsection*{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).\textsuperscript{112}

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 crottyl 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.\textsuperscript{12d-e} It has indeed been found that the regioselectivity is lower when acetate is
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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)

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.[29] In collaboration with G. E. Oosterom, we have studied the influence of local polarity on the regioselectivity of the alkylation reaction.[54]
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.\[5a, b\] 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

$^1$H NMR (300 MHz, TMS, CDCl$_3$), $^{31}$P [$^1$H] (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 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. 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(µ-Cl)]$_2$ and [(cinnamyl)Pd(µ-Cl)]$_2$ were prepared following a literature procedure\[10\]. The synthesis and characterisation of (dppe)Pd(crotyl)OTf,\[5b\] crotyl acetate\[5b\] and the alkylation products of the coupling of crotyl acetate to sodium diethyl 2-methylmalonate are described elsewhere.\[16\]

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°C, after which a solution of Ph$_2$PCl in diethyl ether
was added dropwise. A white precipitate was formed (NEt$_3$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 Ph$_2$PCl.

The P-Im type ligands (d-g) were synthesized using a similar procedure, but required an 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 K$_2$CO$_3$. After stirring for 12 hours, the reaction was completed and after filtration the solvent was removed by evaporation. The alcohol was then coupled to Ph$_2$PCl 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 Ph$_2$PCl. 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 CH$_2$Cl$_2$. 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 CH$_2$Cl$_2$). 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
P-N ligands, crotyl and cinnamyl substrates.

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:

POPy 1 (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); 136.4 (m-pyridine, N-CH=CH); 141.2 (d, J(P-C) = 18.1 Hz, P-C); 148.8 (o-pyridine, N-CH); 159.0 (o-pyridine, N-C)

POPy 2 (b): \(^1\)H: 3.19 (t, J = 6.7 Hz, 2H (P-O-CH\(_2\)-CH\(_2\))); 4.26 (dt, J\(_1\) = J\(_2\) = 6.7 Hz, J\(_3\) = 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 (o-pyridine, N-C)

POPy 3 (c): \(^1\)H: 2.16 (dt, J\(_1\) = J\(_2\) = 6.4 Hz, J\(_3\) = 8.0 Hz, 2H (CH\(_2\)-CH\(_2\)-CH\(_2\)-CH\(_2\))); 2.91 (t, J = 7.9 Hz, 2H (O-CH\(_2\)-CH\(_2\)-CH\(_2\)-CH\(_2\))); 3.93 (dt, J\(_1\) = J\(_2\) = 6.4 Hz, J\(_3\) = 8.7 Hz, 2H (O-CH\(_2\)-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\(_2\)-CH\(_2\)); 34.5 (P-O-CH\(_2\)-CH\(_2\)-CH\(_2\)-CH\(_2\)); 69.2 (d, J = 8.3 Hz, P-O-CH\(_2\)-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, 17.3 Hz, P-C); 149.1 (o-pyridine, N-CH); 161.2 (o-pyridine, N-C)

4-(para-fluoro-benzimino)-butan-1-ol (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-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); $^{31}$P {$^1$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 (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)); 3.6 (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); $^{31}$P {$^1$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$_3$)$_2$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$_2$-O)); 3.02 (s, 6H (2CH$_3$)); 3.67 (t, J = 6.5 Hz, 2H (N-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$_2$-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); $^{31}$P {$^1$H}: 112.3; $^{13}$C {$^1$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)

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P-N ligands, crotyl and cinnamyl substrates.

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

$^1$H: 2.17 (quintet, J = 6.5 Hz, 2H (N-CH$_2$-CH$_2$-CH$_2$-O)); 3.79 (t, J = 6.5 Hz, 2H (N-CH$_2$-CH$_2$-CH$_2$-O)); 4.04 (dt, J1 = J2 = 6.5 Hz, J3 = 9 Hz, 2H (N-CH$_2$-CH$_2$-CH$_2$-O)); 7.4 (m, 9H (o- and p- phenyl H)); 7.59 (dt, J1 = J2 = 7.5 Hz, J3 = 1.9 Hz, 4H (P-C-CH-CH-)); 7.75 (m, N=CH-C-CH- and aromatic H); 8.27 (s, 1H (N=CH));

$^{31}$P{$^1$H} : 112.3

Palladium complexes:

Pd(POPy (a))(crotyl) SO$_3$CF$_3$: $^1$H: (syn trans P isomer): 1.83 (d, J1 = 6.2 Hz, J2 = 10.6 Hz, 3H (Me)); 3.21 (hump, 2H (Ha and Hb)); 5.05 (m, 1H (Hc)); 5.16 (d, J = 21.9 Hz, 2H (P-O-CH$_2$)); 5.75 (dt, J1 = J2 = 9.4 Hz, J = 13.2 Hz, 1H (Hd)); 7.5 (m, 10H (Ar)); 7.63 (t, J = 7.4 Hz, 1H (m-pyridine) (N-CH-H)); 7.65 (d, J = 7.4 Hz, 1H (m-pyridine) (N-C-H)); 7.95 (t, J = 7.4 Hz, 1H (p-pyridine));

$^{13}$C{$^1$H} : 17.7, 50.6, 73.1, 103.7, 119.0, 121.7, 123.3, 126.8, 127.1, 129.3, 129.5, 131.8, 132.6, 134.3, 140.7, 154.5, 155.0; $^{31}$P{$^1$H} : (syn trans P isomer) 130.3 (s, IP), 128 (s, 0.06P); other isomers appear at 132.7 (s, 0.04P), 130.1 (s, 0.03P), 129.7 (s, 0.14P);

IR (v$_{max}$ / cm$^{-1}$): 3058, 2991, 2923, 1607, 1438

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

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

Pd(POPy (a))(cinnamyl) SO$_3$CF$_3$: $^1$H: 3.4 (d, J = 9.3 Hz, 2H (Ha and Hb)); 5.18 (d, J = 21.9 Hz, 2H (P-O-CH$_2$)); 5.98 (dd, J1 = 10.3 Hz, J2 = 13.6 Hz, 1H (Hc)); 6.4 (dt, J1 = J2 = 9.3 Hz, J3 = 13.6 Hz, 1H (Hd)); 7.0 (t, J = 6.4 Hz, 1H (H-pyridine)); 7.3-7.6 (m, 21H (H-Ar and H-pyridine)); 7.75 (t, J = 7.6 Hz, 1H (H-pyridine)); 7.81 (d, J = 5.1 Hz, 1H (o-pyridine));

$^{13}$C{$^1$H} : 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; $^{31}$P{$^1$H} : 130.3 (s, 1P), 128 (s, 0.06P)

IR (v$_{max}$ / cm$^{-1}$): 3061, 2993, 1605, 1437

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

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

Pd(POPy (b))(crotyl) SO$_3$CF$_3$: $^1$H: 1.64 (dd, J1 = 6.3 Hz, J2 = 10.7 Hz, 3H (Me)); 2.86 (broad, 1H (Ha)); 3.65 (broad, 1H (Hb)); 3.75 (broad, 2H (pyridine-CH$_2$)), 4.15 (broad, 2H (P-O-CH$_2$)); 4.9 (m, 1H (Hc)); 5.78 (dt, J1 = J2 = 9.4 Hz, J3 = 13.0 Hz, 1H (Hd)); 7.2-7.8 (broad, 22H (aromatic H and pyridine H)); 7.89 (t, J = 7.3 Hz, 1H (p-pyridine)); 8.46 (d, J = 5.3 Hz, 1H (o-pyridine));

$^{13}$C{$^1$H} : 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; $^{31}$P{$^1$H} : 116.7 (s)

IR (v$_{max}$ / cm$^{-1}$): 3059, 2973, 1604, 1437
FAB-MS: m/z = 468.0720 (C\textsubscript{22}H\textsubscript{23}NOPPd\textsuperscript{+} requires 468.0709)

Elem. anal.: Found: C, 44.06%; H, 3.76%. Calc. for C\textsubscript{22}H\textsubscript{23}NOPPd\textsuperscript{+}CF\textsubscript{3}SO\textsubscript{3} + 0.30 CH\textsubscript{2}Cl\textsubscript{2}: C, 44.06; H, 3.90%.

\textbf{Pd(POPy\textsubscript{2} (b))(cinnamyl) SO\textsubscript{3}CF\textsubscript{3}:}

\( ^1\text{H} \): 1.77 (br, 2H (Ha and Hb)); 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)); 13\text{C}[^1\text{H}]: 113.5, 129.0, 130.7, 153.0, 159.3; 31\text{P}[^1\text{H}]: 117.9

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

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

Elem. anal.: Found: C, 49.48%; H, 3.86%. Calc. for C\textsubscript{28}H\textsubscript{27}NOPPd\textsuperscript{+}CF\textsubscript{3}SO\textsubscript{3} + 0.40 CH\textsubscript{2}Cl\textsubscript{2}: C, 49.46; H, 3.92%.

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

\( ^1\text{H} \) (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)); 3\text{P}[^1\text{H}]: 127.5; 13\text{C}[^1\text{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 (\(\nu_{\text{max}}\)/cm\textsuperscript{-1}): 3060, 2951, 2855, 1604, 1437

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

Elem. anal.: Found: C, 45.52%; H, 4.34%. Calc. for C\textsubscript{24}H\textsubscript{27}NOPPd\textsuperscript{+}CF\textsubscript{3}SO\textsubscript{3} + 0.45 CH\textsubscript{2}Cl\textsubscript{2}: C, 45.61; H, 4.20%.

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

\( ^1\text{H} \) (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)); 3\text{P}[^1\text{H}]:128.0; 13\text{C}[^1\text{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 (\(\nu_{\text{max}}\)/cm\textsuperscript{-1}): 3060, 2950, 2885

FAB-MS: m/z = 544.1026 (C\textsubscript{29}H\textsubscript{29}NOPPd\textsuperscript{+} requires 544.1022)

Elem. anal.: Found: C, 51.06%; H, 4.28%. Calc. for C\textsubscript{29}H\textsubscript{29}NOPPd\textsuperscript{+}CF\textsubscript{3}SO\textsubscript{3} + 0.15 CH\textsubscript{2}Cl\textsubscript{2}: C, 51.02; H, 4.17%.
**P-N ligands, crotly and cinnamyl substrates.**

Pd(POPy3 (c))(cinnamyl)Cl:

1H (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)); \(^{31}P{^1H}\): 121.2

Pd(P-Im3 HH (g))(crotly)OTf: obtained as the equilibrium mixture (endo and exo) in a ratio of (determined by \(^{31}P\)):

1H (298 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)); \(^{31}P{^1H}\): 129.2 (s, 1.0P, minor); 129.4 (s, 1.5P, major);

Pd(P-Im3NMe22 (d))(crotly)SbF6: obtained as the equilibrium mixture (endo and exo) in a ratio of 1:1.8 (determined by \(^{31}P\)):

1H (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-., major)); 2.3 (m, 2H (-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); \(^{13}C{^1H}\): 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; \(^{31}P{^1H}\): 129.9 (1.0 P, major); 129.7 (0.8 P, minor)

IR (\(\nu_{max} / \text{cm}^{-1}\)): 3062, 2951, 2918, 1593, 1531, 1438, 1375

FAB-MS: m/z = 551.1461 (C28H34N2OPPd+ requires 551.1443)

Elem. anal.: Found: C, 40.62%; H, 4.31%. Calc. for C28H34N2OPPd+CF3SO3 + 0.75 CH2Cl2: C, 40.69; H, 4.21%.

Pd(P=Im40Me (e))(crotly) SO3CF3: obtained as the equilibrium mixture (endo and exo) in a ratio of 1:1.8 (determined by \(^{31}P\)):

1H (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-, 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,
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**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 = 11.9 Hz, 1H (Hb minor, or bridge H)); 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-CH2-, 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-); 3.84 (s, 3H, (OCH3, major)); 3.88 (s, 3H, (OCH3, 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=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); 13C{1H }: 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; 31P{1H }: 133.6 (1.7P; major); 134.0 (1.0P, minor)

IR (v max / cm⁻¹): 3060, 2935, 2843, 1602, 1512, 1436

FAB-MS: m/z = 614.1446 (C13H12NO2Pd²⁺ requires 614.1440)

Elem. anal.: Found: C, 50.81%; H, 4.52%. Calc. for C13H12NO2Pd²⁺CF3SO3 + 0.65 CH2Cl2: C, 50.80; H, 4.47%.
Pd(P~Im4FF (f))(crottyl) 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: 1.3 (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{' H }: 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, 169.5; 3P{' H }: 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 (C27H35FNOPdO requires 540.1084)

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{' H }: 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; 3P{' H }: 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 (C32H32FNOPdO requires 602.1240)

Elec. anal.: Found: C, 45.56%; H, 4.27%. Calc. for C27H35FNOPdOCF3SO3 + 0.80 CH2Cl2: C, 45.64%; H, 4.20%.

alkylation products:
Analysis and identification of diethyl 2-((trans)-but-2-en-1-yl) methylmalonate and diethyl 2-(but-3-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{' H }: 14.5 (O-CH2-CH3); 20.4 (C-CH3); 39.8 (C-CH2-CH=); 54.7 (C-CH3); 61.7 (O-CH2-
Diethyl 2-(1-phenyl-prop-2-en-1-yl) methyimalonate: $^1$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=)); 7.1-7.35 (m, 5H (aromatic H)); $^{13}$C ($^1$H): 13.9 (O-CH$_2$-CH$_3$); 18.9 (C-CH$_3$); 46.5 (C-CH$_2$-CH$_3$); 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


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[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 Budzelaar 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.