Pd-pincer complexes containing six-membered rings that are more active allylation catalysts than five-membered ring analogues

Dan E. Wise, a Natalie E. Pridmore, a Paul G. Pringle a

aSchool of Chemistry, University of Bristol, Cantock’s Close, Bristol, BS8 1TS, U.K.

Abstract
A series of symmetric and non-symmetric PCP-pincer complexes have been prepared and an evaluation of their activity in catalytic allylic alkylation carried out. The X-ray crystallography and NMR spectroscopy data suggest that metallacycles containing one (or two) 6-membered rings are inherently more rigid than initially anticipated. The observed catalyst activity is found to increase as the metallacycle size increases from 5 to 6.

Introduction

Since the pioneering work on cyclometalated phosphine pincer complexes by Shaw et al. and amine pincer complexes by van Koten et al. in the 1970s, chemists have exploited the tunability of pincer complexes to develop many thousands of variants.1,2 The rich chemistry of pincer complexes is attributed to the many points of derivatisation present, such as the donor atoms and substituents, backbone structure, metal centre, and ancillary ligands. The applications of transition metal pincer complexes in catalysis have been extensively reviewed.3–7

Most pincer complexes are derived from C2v symmetric ligands which give rise to complexes with two fused 5-membered metallacycles (i.e. 5,5-metallacycles).3 Less well studied are pincer complexes with fused 6-membered metallacycles (i.e. 6,6-metallacycles).8–10 Pincer complexes containing 6-membered metallacycles have a larger P-M-P bite angle and would be anticipated to be more conformationally flexible. In some cases, they have been shown to have superior catalytic properties compared to 5,5-metallacyclic systems.11–14 Very few pincer complexes with non-symmetric 5,6-metallacycles have been reported9,15 and the only P-containing, non-symmetric 5,6-metallacycles are bis-phosphite (A) and phosphine-phosphite Pd complexes, reported by Eberhard et al.11,16 In the 2018 review by Crabtree et al.,3 it was noted that there were very few examples of pincer ligands with non-symmetric metallacycles. The high thermal stability that pincer complexes have compared to many other organometallic complexes, is attractive for their applications in biological and catalytic contexts.17 The following examples demonstrate the enhanced reactivity that may be gained when using larger, non-symmetric pincer metallacycles.
Milstein et al. studied the difference in reactivity between a ‘normal’ 5,5-metallacyclic Pt(II) complex and the ‘long-arm’ variant (5,6-metallacyclic Pt(II) complex, B). The hemilability of the 6-membered amine metallacycle was implicated in the quantitative formation of a trinuclear Pt cluster when the PCN-Pt(II) pincer complex was reduced with H₂ at 65 °C. Under the same conditions, the ‘conventional’ 5,5-metallacycle was found to be completely inert.

Transition metal-catalysed allylic substitution reactions (Figure 1b) are useful organic transformations that have been applied in the synthesis of pharmaceuticals and natural products. van Leeuwen and Kamer reported the effect of diphosphine bite angle in Pd-catalysed allylic alkylation. As the ligand bite angle increased, a decrease in catalytic activity was observed, coupled with a stronger preference for the linear alkylation. For the largest bite angle Pd-diphosphine complex (C) employed, (Xantphos, bite angle = 110°), exclusive formation of the linear product was observed, albeit at a slow rate. The high selectivity was attributed to a steric effect of the diphosphine embracing the allyl fragment, and thereby inhibiting formation of the branched regioisomer. High linear selectivity at high catalyst activity was achieved with the moderately wide bite angle ligand DPEPhos (102.7°).

A structure-activity relationship for symmetric 5,5-metallacyclic and non-symmetric 5,6-metallacyclic Pd(II) pincer complexes was reported by Eberhard et al. These pincer complexes were applied as
catalysts for the alkylation of cinnamyl acetate with sodium dimethylmalonate and the regioselectivity was found to be sensitive to the ligand structure (Scheme 1). The 5,6-metallacycles were found to be more active catalysts than the 5,5-metallacycles while maintaining high linear to branched product ratios (up to 95% linear selectivity). It was reported that the synthesis of the analogous Pd(II) pincer complexes with two 6-membered metallacycles was not successful although it was predicted that 6,6-metallacycles may show even higher catalytic activity in allylic alkylation.

Scheme 1. Pd-pincer catalysed alkylation of cinnamyl acetate with sodium dimethylmalonate, Eberhard et al.\textsuperscript{11,16}

Herein, we report a series of symmetric and non-symmetric aminophosphine PCP-pincer complexes and an evaluation of their performance in catalytic alkylation of dimethylmalonate (Figure 1c). To investigate the effect of metallacycle ring size on the Pd coordination chemistry and catalytic activity of organometallic pincer complexes, we have studied structure-activity relationships for aminophosphine Pd-pincer complexes as catalysts for the alkylation of dimethylmalonate, and compared our novel derivatives to the current state-of-the-art catalysts.

**Results and Discussion**

**Synthesis of aminophosphine ligands**

The aminidiphosphine ligands L1-L9 were made by the routes shown in Scheme 2. They have high stability to air and moisture and were readily prepared from commercially available amine precursors. For the previously reported ligands (L1-L3), the spectroscopic data matched the literature data.\textsuperscript{29} Deprotonation of the appropriate diamine precursor using either 4-dimethylaminopyridine (DMAP) or \textsuperscript{6}BuLi, followed by reaction with the corresponding chlorophosphine gave the novel ligands L4-L9 in 75-90% yield. Full experimental and characterisation details are given in the ESI.

The two $^{31}$P NMR signals for the unsymmetrical diphos ligand L4 are singlets ($\delta_P = 81.6$ and $59.3$ ppm, $^7J_{PP}$ was not detected) with $\delta_P$ values similar to the corresponding values in the related symmetrical diphos ligands L1 ($\delta_P = 58.2$ ppm), and L7 ($\delta_P = 81.6$ ppm).

**Palladium coordination chemistry**

In view of its relevance to the catalysis (see below), a study of the Pd coordination chemistry of L1-L9 has been carried out. The symmetrical pincer L1 was reacted in a 1:1 molar ratio with [PdCl$_2$(cod)] in toluene under reflux for 18 h. Analysis of the *in situ* $^{31}$P{$_1^H$} NMR spectrum showed a singlet resonance ($\delta_P = 119.5$ ppm) assigned to the pincer complex 1a. The formation of the 5,5-metallacycle is associated with a large, positive coordination chemical shift ($\Delta\delta_P = +61.3$ ppm). As with the free ligand, the symmetry of the molecule means there are only two aryl-$C$–$H$ resonances in the $^1H$ NMR spectrum. Formation of the desired Pd–Cl complexes (1a-3a) derived from L1-L3 was confirmed by comparison with the previously reported spectroscopic data.$^{30}$
The coordination of the 5,6-\(\text{P}^\text{tBu}_2\) ligand \(\text{L4}\) to Pd(II) is surprisingly easy compared to \(\text{L1}\). Immediately upon addition of a dichloromethane solution of \(\text{L4}\) to \([\text{PdCl}_2(\text{NCPh})_2]\), the \(\text{in situ}\) \(^{31}\text{P}\{^1\text{H}\}\) NMR spectrum showed an AB pattern with a large \(^2J_{PP}\) of 406 Hz consistent with \(\text{4a}\) (Scheme 3) having a \textit{trans} geometry.\(^{11,16}\) The different chelate ring sizes influence the coordination chemical shifts which, for the 6-membered metallacycle is small (\(\Delta\delta_P = +8.2\) ppm), and for the 5-membered metallacycle is large (\(\Delta\delta_P = +63.0\) ppm); the latter \(\Delta\delta_P\) is similar to the value for the symmetrical complex \(\text{1a}\) (\(\Delta\delta_P = +61.3\) ppm).\(^{31,32}\)

![Diagram of L4 and L7 coordination to Pd(II)](image)

Scheme 3. Formation of 5,6-Pd–Cl complex \(\text{4a}\) and 6,6-Pd–Cl complex \(\text{7a}\).

Clearly, there is a difference in kinetics of the cyclopalladation of \(\text{L1}\) and \(\text{L4}\), with 5,5-metallacycle formation requiring elevated temperatures and extended reaction time while the 5,6-metallacycle formation occurred rapidly at room temperature. It was anticipated that the formation of a symmetric 6,6-metallacycle would be rapid, but this was found not to be the case. When \(\text{L7}\) and \([\text{PdCl}_2(\text{NCPh})_2]\) were mixed in \(\text{CH}_2\text{Cl}_2\) (or toluene) two broad signals (\(\delta_P = +78\) and +79 ppm) were observed in the \(\text{in situ}\) \(^{31}\text{P}\{^1\text{H}\}\) NMR spectra. The isolated product had limited solubility and was assigned to a diphos-bridged polymeric material, reminiscent of previously reported work on Pd bis(phosphite) \(\text{PCP}\)-pincer complexes.\(^{33}\) It was found that the metallacycle \(\text{7a}\) was formed when the reaction of \(\text{L7}\) and \([\text{PdCl}_2(\text{cod})]\) was carried out in toluene under reflux (Scheme 3) for 4 h. The \(^{31}\text{P}\{^1\text{H}\}\) NMR spectrum of the product formed under these more forcing conditions showed a singlet resonance at \(\delta_P = +89\) ppm and the HR-ESI-MS showed a molecular ion peak at \(m/z\) 563.1713 corresponding to \([\text{M}\text{–H}]^+\) for \(\text{7a}\) (calc. \(m/z\) 563.1713).

Difficulties were encountered when we attempted to form non-symmetric 5,6- and symmetric 6,6-Pd–Cl metallacycles using ligands with less bulky phosphorus substituents than \(\text{P}^\text{tBu}_2\) (e.g. \(\text{P}^\text{iPr}_2\) and \(\text{PPh}_2\)). In the attempted synthesis of complexes derived from \(\text{P}^\text{iPr}_2\) ligands \(\text{L5-L8}\) and \(\text{PPh}_2\) ligands \(\text{L6-L9}\), mixtures containing very insoluble precipitates were obtained (See ESI for details).\(^{34}\) The \(\text{in situ}\) \(^{31}\text{P}\{^1\text{H}\}\) NMR
spectra of the mixtures from the attempted synthesis of non-symmetric metallacycles did display the expected AB pattern along with unknown impurities (Figure S2). In these cases, the isolated material was highly insoluble coordination polymer as previously documented for related diphos ligands.\textsuperscript{35}

To investigate the coordination chemistry further, Pd(II) trifluoroacetate, [Pd(TFA)\textsubscript{2}] was used and found to be a suitable precursor to soluble, monomeric Pd–TFA pincer complexes with 5- or 6-membered metallacycles (Scheme 4). These cyclometallations occur rapidly under mild conditions (25 °C, 20 min), rather than the harsh conditions required to form some Pd–Cl complexes (110 °C, 6 h). This is a consistent with the cyclometallation being an electrophilic aromatic substitution process; the rate acceleration when using Pd(TFA)\textsubscript{2} has been previously observed in other cyclopalladations.\textsuperscript{34,36}

\[\text{Scheme 4. Formation of Pd–TFA complexes 4b-9b.}\]

The formation of soluble 6,6-metallacyclic Pd–TFA complexes was also possible using the corresponding 6,6-ligand and [Pd(TFA)\textsubscript{2}] at room temperature (Scheme 4). For the P'\text{Bu}_2 substituted ligand L7 this corresponded to a small downfield coordination chemical shift ($\Delta\delta_p = +11$ ppm), thus clarifying the previously ambiguous result in the formation of Pd–Cl complex 7a (see Scheme 3). The weakly bound nature of the trifluoroacetate ligand was evident from HR-ESI-MS experiments (see ESI).\textsuperscript{37} The mass spectrometry data support the observation that, in the gas phase, the trifluoroacetate ligand dissociates from 5,6- and 6,6-palladacycles 4b and 7b, but not from 5,5-palladacycle 1b. It is proposed that a weakly bound ligand in this position could lead to a more active catalyst, where an incoming substrate may bind to the Pd centre following ligand dissociation in this position.

**Effect of ring size on the crystal structures of the pincer complexes**

Crystals of 4a and 7a suitable for X-ray diffraction were grown by evaporation of their concentrated solutions in CH\textsubscript{2}Cl\textsubscript{2} and hexane respectively (see Figure 2 and Figure 3). The bond lengths fall within the typical range for similar complexes,\textsuperscript{38,39} for 4a, the Pd1–P2 (in the 6-membered ring) is longer than Pd1–P1 (2.3436(4) vs. 2.3096(4) Å, see Table 1), which may indicate increased strain in the larger ring. The 6-membered metallacycle is in a boat conformation and the 5-membered metallacycle in an envelope conformation. From the front-on view of 4a (Figure 3), the P'\text{Bu}_2 groups are above and below the aryl-Pd–
Cl plane. The complex adopts a square planar geometry with a tetrahedral distortion (sum of angles around the Pd1 atom, \( \Sigma(C1\text{--}Pd1\text{--}Cl1 + P1\text{--}Pd1\text{--}P2) = 334.7^\circ \), less than the ideal 360°).

Figure 2. Single crystal X-ray crystallography structures of 4a (left) and 7a (right) (side view). Hydrogen atoms have been omitted for clarity. Thermal ellipsoids at 50% probability level.

Figure 3. Single crystal X-ray crystallography structures of 4a (left) and 7a (right) (front view). Hydrogen atoms have been omitted for clarity. Thermal ellipsoids at 50% probability level.
The crystal structure of 7a (Figure 3) shows the conformations of the 6-membered chelate rings are half chairs with pseudo axial and equatorial tBu groups. Due to the two methylene groups in the ligand backbone, the P'Bu₂ substituents are held above and below the aryl-Pd–Cl plane. Complex 7a adopts a square planar geometry with a smaller tetrahedral distortion than 4a (sum of angles, Σ(C1–Pd1–Cl1 + P1–Pd1–P2) = 350.3°). Moreover, owing to the additional methylene unit in the ligand backbone, the crystallographic bite angle (P1–Pd1–P2) for 7a is 175.4° which is ~14° larger than for the non-symmetric 5,6-metallacycle 4a.

The bite angle for 7a is greater than the 5,6-PPr₂ Pd–Cl complex (A) reported by Eberhard (P–Pd–P = 168.3°, see Figure 1a), and the analogous 5,5-PPr₂ Pd–Cl complex (P–Pd–P = 160.4°). Table 1. Selected bond lengths (Å) and bond angles (°) in 5,6-metallacycle (4a) and 6,6-metallacycle (7a). For details see ESI.

<table>
<thead>
<tr>
<th>Bond</th>
<th>5,6-Pd–Cl (4a) (Å)</th>
<th>6,6-Pd–Cl (7a) (Å)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pd1–Cl1</td>
<td>2.4171(3)</td>
<td>2.3812(5)</td>
</tr>
<tr>
<td>Pd1–P1</td>
<td>2.3096(4)</td>
<td>2.3631(5)</td>
</tr>
<tr>
<td>Pd1–P2</td>
<td>2.3436(4)</td>
<td>2.3382(5)</td>
</tr>
<tr>
<td>Pd1–C1</td>
<td>2.0392(14)</td>
<td>2.0580(18)</td>
</tr>
<tr>
<td>Angle</td>
<td>5,6-Pd–Cl (4a) (°)</td>
<td>6,6-Pd–Cl (7a) (°)</td>
</tr>
<tr>
<td>P1–Pd1–Cl1</td>
<td>94.460(12)</td>
<td>89.437(17)</td>
</tr>
<tr>
<td>P2–Pd1–Cl1</td>
<td>94.674(12)</td>
<td>92.083(18)</td>
</tr>
<tr>
<td>P1–Pd1–P2</td>
<td>161.693(14)</td>
<td>175.400(18)</td>
</tr>
<tr>
<td>Cl–Pd1–Cl1</td>
<td>172.96(4)</td>
<td>174.86(5)</td>
</tr>
</tbody>
</table>

As a result of the extra methylene unit in 4a (or two units in 7a), there is a twist allowing the P'Bu₂ groups to deviate from the aryl-Pd–Cl plane. This tetrahedral distortion, that is more pronounced in 4a than 7a, results in longer Pd–P bonds compared to 5,5-palladacycles (Pd–P = 2.303 Å in [(PCP)PdCl]; PCP = 1,3-(tBu₂PCH₂)₂(C₆H₄)).

**NMR studies of the metallacycles**

The NMR inequivalence of the P'Bu₂ protons in the solution ¹H NMR spectrum of 7a (Figure S1) implies that the ring conformation is rigid on the NMR timescale. To investigate further, a crystalline sample of 7a was dissolved in 1,1,2,2-tetrachloroethane-d₂ (TCE-d₂) and its ¹H NMR spectra were recorded at intervals between 25–100 °C (Figure 4). Although significant peak broadening of the P'Bu₂ protons is observed at higher temperature, two distinct resonances persist in solution up to 100 °C. This implies that there is a high
degree of conformational rigidity, despite the complex having a potentially more flexible structure than the analogous 5,5-metallacycle 1a.

Initially it was reasoned that the 5,6- and 6,6-palladacycles would be more flexible than analogous 5,5-metallacycles due to more degrees of freedom in the ligand backbone. However, contrary to the arguments of Eberhard et al., we have found by X-ray crystallography and NMR studies, that including a 6-membered metallacycle introduces ring strain and imposes rigidity on the pincer rings. The longer Pd–P bonds and apparent rigidity of 6-membered palladacycles may be contributing factors in their enhanced catalytic activity compared with conventional 5,5-metallacycles (see below).

Figure 4. Selected region of the $^1$H VT-NMR spectra of crystals of 6,6-Pd–Cl complex 7a, dissolved in TCE-d$_2$.

For the 5,6-metallacycles, the $^{31}$P{$^1$H} NMR spectra exhibit the expected AB patterns (Figure 5) with large \(^2J_{PP}\) values typical of the trans relationship PdP$_2$ group: for 4b, 5b and 6b, \(^2J_{PP} = 367\) Hz, 388 Hz, and 447 Hz respectively (Figure 5). For Pd–TFA complex 4b, the \(^2J_{PP}\) is considerably smaller than the analogous Pd–Cl complex 4a (\(^2J_{PP} = 406\) Hz). This trend in coupling constants for 5,6-Pd–TFA complexes (\(^2J_{PP}: \text{P}^\text{iPr}_2 < \text{P}^\text{tBu}_2 < \text{P}^\text{Ph}_2\)) reflects the trans influence of the phosphine donor substituents (i.e., two good σ-donating P ligands will mutually weaken their bonds to the metal leading to a smaller \(^2J_{PP}\) coupling).
Figure 5. $^{31}$P{¹H} NMR spectra for a) 5,6-PBu₂ (L4), b) 4b, c) 5,6-PPr₂ (L5), d) 5b, e) 5,6-PPh₂ (L6), f) 6b.

A summary of the NMR spectroscopy data for L1-L9 and associated Pd complexes is given in Table S1.
**Catalytic allylation of dimethylmalonate**

**Catalysis under standard conditions**

The performance of the Pd–Cl and Pd–TFA pincer complexes of L1-L9 as catalysts for the allylation of dimethylmalonate has been investigated and the results are presented in Table 2. Two equivalents of sodium dimethylmalonate with respect to the limiting substrate cinnamyl acetate were used.

Table 2. Catalytic allylation of dimethylmalonate under standard conditions.a

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ligand</th>
<th>% Conversionb with [PdCl₂(NCPh)₂]</th>
<th>% Linear selectivity</th>
<th>% Conversionb with [Pd(TFA)₂]</th>
<th>% Linear selectivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>L1</td>
<td>11</td>
<td>88</td>
<td>16</td>
<td>95</td>
</tr>
<tr>
<td>2</td>
<td>L2</td>
<td>&gt;99</td>
<td>75</td>
<td>52</td>
<td>84</td>
</tr>
<tr>
<td>3</td>
<td>L3</td>
<td>&gt;99</td>
<td>95</td>
<td>&gt;99</td>
<td>92</td>
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<tr>
<td>4</td>
<td>L4</td>
<td>58</td>
<td>91</td>
<td>70</td>
<td>93</td>
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<tr>
<td>5</td>
<td>L5</td>
<td>&gt;99</td>
<td>71</td>
<td>93</td>
<td>82</td>
</tr>
<tr>
<td>6</td>
<td>L6</td>
<td>&gt;99</td>
<td>91</td>
<td>&gt;99</td>
<td>93</td>
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<tr>
<td>7</td>
<td>L7</td>
<td>&gt;99</td>
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<td>81</td>
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<tr>
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<td>L8</td>
<td>&gt;99</td>
<td>92</td>
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<tr>
<td>9</td>
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<td>&gt;99</td>
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<td>&gt;99</td>
<td>89</td>
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<tr>
<td>10e,f</td>
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<td>&gt;99</td>
<td>78</td>
<td>&gt;99</td>
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<td>L8</td>
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<td>87</td>
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<td>12e,f</td>
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<td>48</td>
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<tr>
<td>13c,g</td>
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<tr>
<td>14d,g</td>
<td>L8</td>
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<td>–</td>
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<td>15c,g</td>
<td>L8</td>
<td>–</td>
<td>–</td>
<td>12h</td>
<td>&gt;99</td>
</tr>
</tbody>
</table>

*aReaction conditions: 0.5 mmol of cinnamyl acetate, 1.0 mmol of sodium dimethylmalonate, 2.5 × 10⁻² mmol of [Pd], 2.5 × 10⁻² mmol of ligand, in THF, 60 °C, 6 h. Results are the average of two independent experiments. bConversion and selectivity determined by GC-MS using dodecane as internal standard. c[Pd] / L8 5 mol%. d[Pd] / L8 2.5 mol%. e[Pd] / L8 1.25 mol%. fReaction performed at 60 °C. gReaction performed at 25 °C. hReaction time 20 h.*

The progress of the reaction was monitored by GC-MS for the Pd–Cl catalysts having PPh₂ substituted ligands L1, L4 and L7 (Figure 6). From these data, the influence of metallacycle size is evident from the relative rates of reaction, with the 6,6-metallacycle reaching complete conversion in 2-3 h, the 5,5-
metallacycle had only reached ~10% conversion after 7 h, and the 5,6-metallicycle displayed intermediate behaviour (60% conversion after 7 h).

Figure 6. Conversion–time plot for the allylation of dimethylmalonate catalysed by Pd–Cl catalysts derived from L1, L4 and L7. Conversion determined by GC-MS using dodecane as internal standard.

When the catalysis was run under the same conditions but in the absence of diphos ligand, using either [Pd(TFA)2] or [PdCl2(NCPh)2], the conversions were <1%, in each case. No significant difference in catalytic activity was observed between runs using in situ or pre-formed pincer complex catalyst.

The following trends can be discerned from the data presented in Table 2. The catalysts derived from 5,5- and 5,6-PBu2 substituted aminophosphine ligands (L1 and L4 respectively) (Table 2, entries 1 and 4) showed lower activity after 6 h than the ligands with the smaller PPr2 and PPh2 substituents. Catalysts composed of 6,6-metallacycles showed superior activity to the other metallacycle sizes, with all derivatives giving >99% conversion under the standard conditions (Table 2, entries 7-9). In general, PPh2 substituents show the highest linear selectivity (88–95%), followed by PBu2 substituents (81–93%), and then PPr2 substituents (67–92%).

This high activity of catalysts derived from L8 led us to investigate it further. The catalysis with L8 and [Pd(TFA)2] or [PdCl2(NCPh)2] has been investigated as a function of the catalyst loading from 1.25–5 mol% and temperature from 25–60 °C (Table 2, entries 10-15). These results demonstrated the greater activity of the Pd–TFA catalysts than the Pd–Cl catalysts: at 60 °C, after 2 h and at 1.25 mol% catalyst loading, full conversion was observed with Pd–TFA catalysts whilst only 48% conversion was observed with the Pd–Cl catalyst (Table 2, entry 12). Excellent linear selectivity (>99%) is maintained at 25 °C for Pd–TFA catalysts,
whereas the Pd–Cl are not active at this temperature, suggesting that a more labile ligand is required for activity at low temperatures.

We performed the Hg drop test using L7-L9 with either [PdCl2(NCPh)2] or [Pd(TFA)2] to determine whether the active catalytic species was the Pd(II) pincer complexes, or if they deposited Pd(0) nanoparticles.41,42 For each of the ligands tested, the conversion and selectivity was not influenced by the addition of Hg(0) (300 eq. with respect to Pd), suggesting that the active catalyst is homogeneous Pd(II) (Table S2). It has been shown that addition of elemental Hg is highly effective at extinguishing heterogeneous Pd(0) catalysts, including those generated by PCP-pincer complexes of Pd.43 Visually, the post-catalysis mixtures containing Hg did not appear different to runs without Hg, suggesting homogeneous solutions.

To assess the scalability of the reaction, the best combination for catalyst activity and linear selectivity were selected. The catalysis was performed with cinnamyl acetate on a multi-gram scale (3.5 g, 21 mmol) with L3 and [PdCl2(NCPh)2] (both at 5 mol%) at 50 °C in THF (Scheme 5). Analysis by GC-MS indicated that, at 42× scale, the outcome of the reaction was the same (full conversion, 95% linear selectivity).

**Scheme 5.** Catalytic allylation of dimethylmalonate under optimal conditions.

It was also discovered that, at high conversion, another product was formed. The mole fraction of this unknown product varied (between 0.03–0.19) depending on the aminophosphine ligand (L1-L9) that was used. The product was isolated from the post-catalysis mixture and purified by column chromatography; it was identified as the product of di-allylation of dimethylmalonate (for full details see the ESI). It is still surprising that di-allylation occurs when the molar ratio of sodium dimethylmalonate to cinnamyl acetate is 2:1. The formation of this di-allylation product is often overlooked but was observed by Sato et al. with N-heterocyclic carbene derived Pd catalysts.37

**Mechanistic considerations**

The mechanism Pd(II)-pincer complex catalysed allylation is not yet fully understood and it remains a topic of debate whether Pd(0)/Pd(II) and Pd(II)/Pd(IV) redox cycles are involved. In the study performed by Eberhard et al. utilising bis(phosphite)-Pd(II) pincer complexes, the alkylation of deuterated allylic acetate substrate resulted in products with a 1:1 ratio of C(sp3)-deuteration and C(sp2)-deuteration (Scheme 6), implying the reaction proceeds through a symmetrical (η3-allyl)Pd intermediate.11 In their study, it was not
determined whether the X ligand (chloride, acetate, or triflate) remained bound to Pd during the catalytic cycle, and neither a Pd(0)/Pd(II) nor a Pd(II)/Pd(IV) cycle was proposed.

Scheme 6. Alkylation of deuterated allylic acetate, Eberhard *et al.*

Furthermore, Szabó and co-workers provided evidence for bis(phosphite)-Pd(II) pincer complex catalysed alkylation of aldehydes and imines via (η₁-allyl)Pd intermediates. In 2009, the Szabó group reported that Pd(II) pincer complexes could catalyse the coupling of alkenes with diaryliodonium salts via proposed aryl-Pd(IV) intermediates. In addition, they reported allylic C–H acetoxylation via proposed (η₃-allyl)Pd(IV) intermediates.

Based on our findings that 5,6- and 6,6-palladacycles are rigid scaffolds and our negative Hg drop experiments rule out decomposition to Pd(0) and instead, we propose that aminophosphine Pd(II) pincer complexes catalyse alkylation via (η₃-allyl)Pd(IV) intermediates. The properties of the PCP-pincer ligands (tridentate, rigid, monoanionic chelating ligand), would facilitate stabilisation of Pd(IV) intermediates. Therefore, the following plausible mechanism is proposed (Scheme 7): (i) oxidative addition of cinnamyl acetate to give an (η₁-allyl)Pd(IV) intermediate; (ii) η₃-allyl formation by deprotonation (loss of AcOH) to give a cationic (η₃-allyl)Pd(IV) intermediate; (iii) nucleophilic attack on the η₃-allyl predominantly at the less hindered terminus; (iv) product dissociation to complete the catalytic cycle.

Although the oxidative addition of cinnamyl acetate has not been observed with Pd(II) complexes, the formation of a Pd(IV) complex following oxidative addition with an allyl bromide was reported by Malinakova *et al.* who demonstrated that Pd(IV) oxidative addition complexes can be accessed without the use of strongly oxidising iodine(III) reagents. Through further studies, it may be possible to observe whether Pd(IV) aminophosphine pincer complexes are viable intermediates under the catalytic conditions.
Scheme 7. Plausible catalytic cycle for allylic alkylation via (η^3-allyl)Pd(IV) intermediate. R = tBu, iPr, Ph. X = Cl or CF_3CO_2.

Conclusions

We have shown that aminophosphine pincer ligands (which can be readily handled in air) are prepared in high yields and purity from commercial starting materials; the synthetic route is amenable to much variation to produce ligands that could span a wide range of steric and electronic effects.

They form palladacycles with 5,5-, 5,6-, or 6,6-membered rings, whose chemistry is sensitive to the phosphine substituents and the nature of the fourth X ligand as shown here for X = Cl or CF_3CO_2. The bulky P^tBu_2 ligands form very stable, soluble, monomeric Pd–Cl complexes in any of the three metallacycle sizes. When smaller P^iPr_2 or PPh_2 substituents are present, insoluble Pd-coordination polymers are produced. On switching the anionic ligand from Cl to CF_3CO_2, not only are the desired monomeric pincer complexes formed, but the C–H activation reaction is much more rapid and occurs under mild conditions. This provides access to highly active Pd(II) catalysts with a weakly bound TFA ligand and these have been applied in the catalytic alkylation of dimethylmalonate.

Promising preliminary results indicate that the activity of these catalysts generally increases with increasing metallacycle size: 5,5- < 5,6- < 6,6-. In addition, the linear selectivity for the alkylation product is highest for PPh_2 substituted complexes which has been shown to be scalable with no decrease in activity or
selectivity. The aminophosphine Pd-pincer complexes catalyse the allylation of dimethylmalonate with high activity and excellent linear selectivity under mild conditions.

NMR studies and the X-ray crystal structures of the pincer complexes reveal that, unexpectedly, the 6-membered metallacycles are best described as more rigid and more strained than conventional 5-membered metallacycles. The strain that is apparent in the 6-membered rings may be part of the explanation for the higher catalytic activity of the pincer complexes containing 6-membered rings. Further work is in progress to explore this concept of ‘strain-activation’ of pincer catalysts experimentally and computationally.

Conflicts of interest
There are no conflicts to declare.

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References


