

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

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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 C_{2v} 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 reported^{9,15} 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.

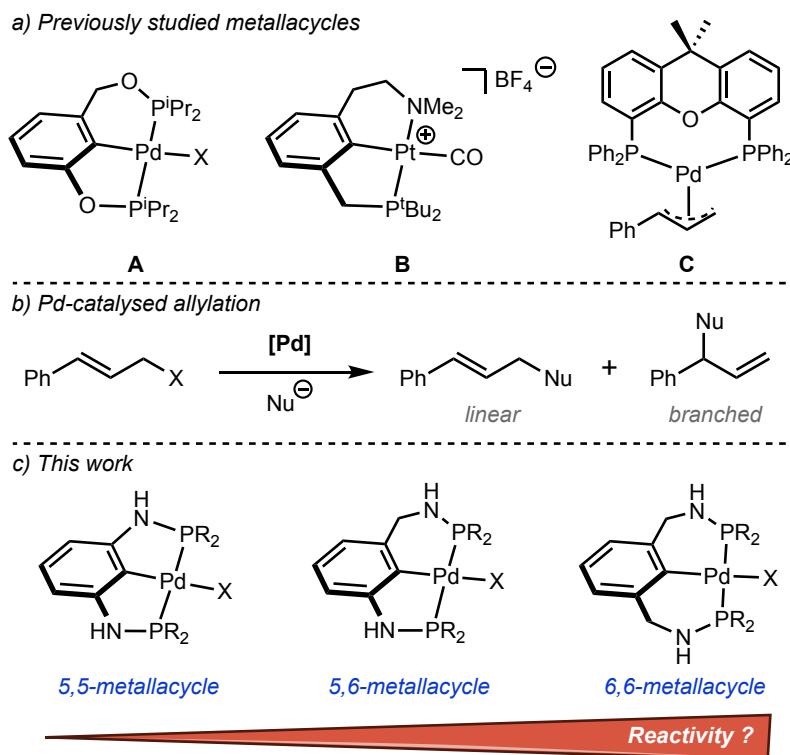


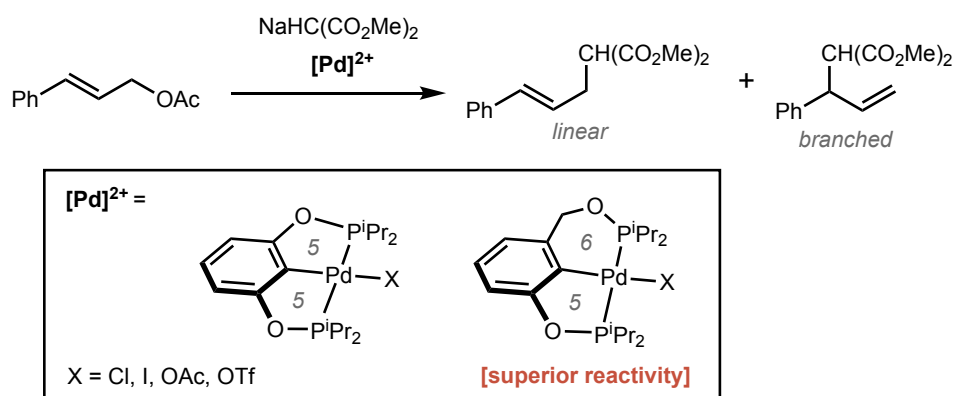
Figure 1. a) Previously reported metallacycles **A-C**.^{11,18,19} b) Pd-catalysed allylic substitution to give linear and branched products. c) Aminophosphine PCP-Pd(II) complexes studied in this work.

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**).^{18,20} 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.^{21–23} van Leeuwen and Kamer reported the effect of diphosphine bite angle in Pd-catalysed allylic alkylation.^{19,24–28} As the ligand bite angle increased, a decrease in catalytic activity was observed, coupled with a stronger preference for the linear alkylation.¹⁹ 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.*^{11,16} 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.



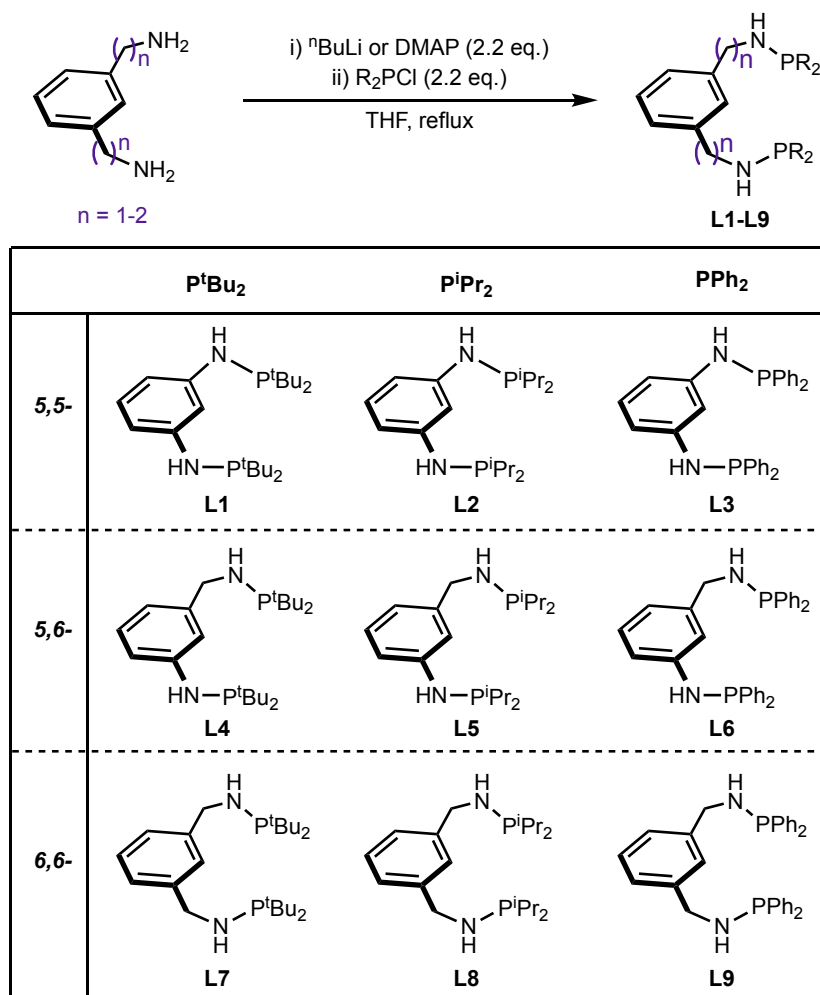
Scheme 1. Pd-pincer catalysed alkylation of cinnamyl acetate with sodium dimethylmalonate, Eberhard *et al.*^{11,16}

Herein, we report a series of symmetric and non-symmetric aminophosphine *PCP*-pincer complexes and an evaluation of their performance in catalytic allylation 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 allylation of dimethylmalonate, and compared our novel derivatives to the current state-of-the-art catalysts.

Results and Discussion

Synthesis of aminophosphine ligands

The aminodiphosphine 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.²⁹ Deprotonation of the appropriate diamine precursor using either 4-dimethylaminopyridine (DMAP) or ⁿBuLi, 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.



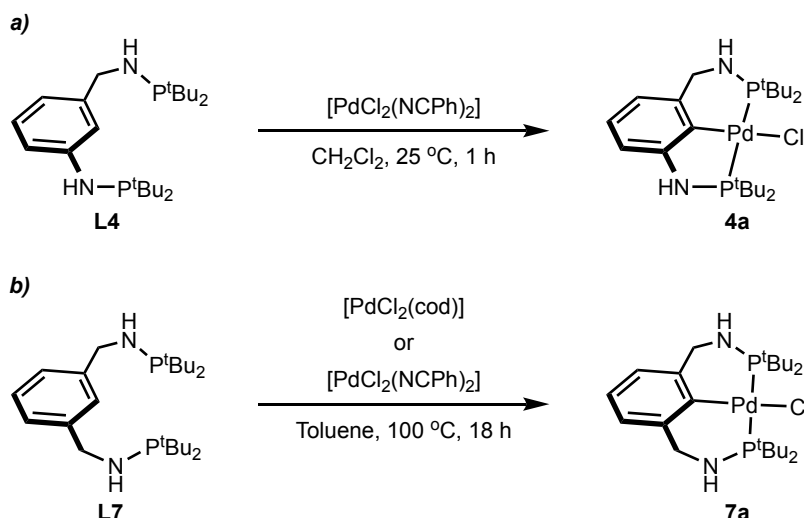
Scheme 2. Synthesis of aminophosphine ligands **L1-L9**.

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 δ_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* $^{31}P\{^1H\}$ 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- P^tBu_2 ligand **L4** to Pd(II) is surprisingly easy compared to **L1**. Immediately upon addition of a dichloromethane solution of **L4** to $[PdCl_2(NCPh)_2]$, the *in situ* $^{31}P\{^1H\}$ NMR spectrum showed an AB pattern with a large $^2J_{PP}$ of 406 Hz consistent with **4a** (Scheme 3) having a *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 **1a** ($\Delta\delta_P = +61.3$ ppm).^{31,32}



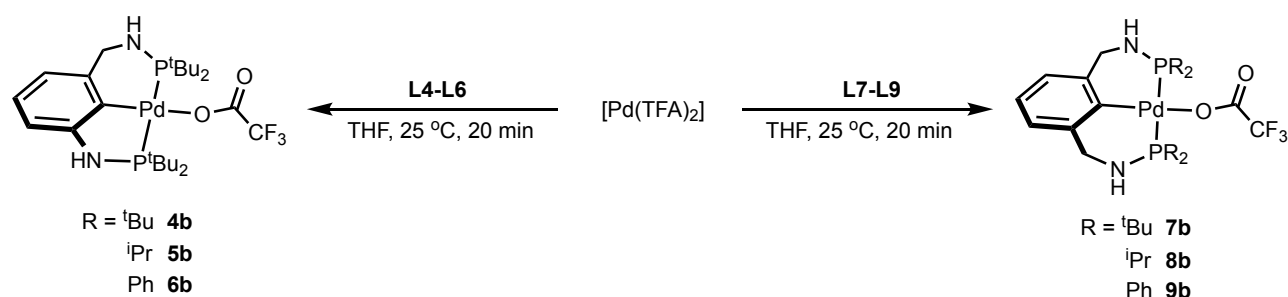
Scheme 3. Formation of 5,6-Pd-Cl complex **4a** and 6,6-Pd-Cl complex **7a**.

Clearly, there is a difference in kinetics of the cyclopalladation of **L1** and **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 **L7** and $[PdCl_2(NCPh)_2]$ were mixed in CH_2Cl_2 (or toluene) two broad signals ($\delta_P = +78$ and $+79$ ppm) were observed in the *in situ* $^{31}P\{^1H\}$ 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) *PCP*-pincer complexes.³³ It was found that the metallacycle **7a** was formed when the reaction of **L7** and $[PdCl_2(cod)]$ was carried out in toluene under reflux (Scheme 3) for 4 h. The $^{31}P\{^1H\}$ 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 $[M-H]^+$ for **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 P^tBu_2 (e.g. P^iPr_2 and PPh_2). In the attempted synthesis of complexes derived from P^iPr_2 ligands **L5-L8** and PPh_2 ligands **L6-L9**, mixtures containing very insoluble precipitates were obtained (See ESI for details).³⁴ The *in situ* $^{31}P\{^1H\}$ 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.³⁵

To investigate the coordination chemistry further, Pd(II) trifluoroacetate, [Pd(TFA)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 consistent with the cyclometallation being an electrophilic aromatic substitution process; the rate acceleration when using Pd(TFA)₂ has been previously observed in other cyclopalladations.^{34,36}



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)₂] at room temperature (Scheme 4). For the P^{*t*}Bu₂ 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).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 CH₂Cl₂ and hexane respectively (see Figure 2 and Figure 3). The bond lengths fall within the typical range for similar complexes;^{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^{*t*}Bu₂ 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, $\Sigma(\text{C1-Pd1-Cl1} + \text{P1-Pd1-P2}) = 334.7^\circ$, less than the ideal 360°).

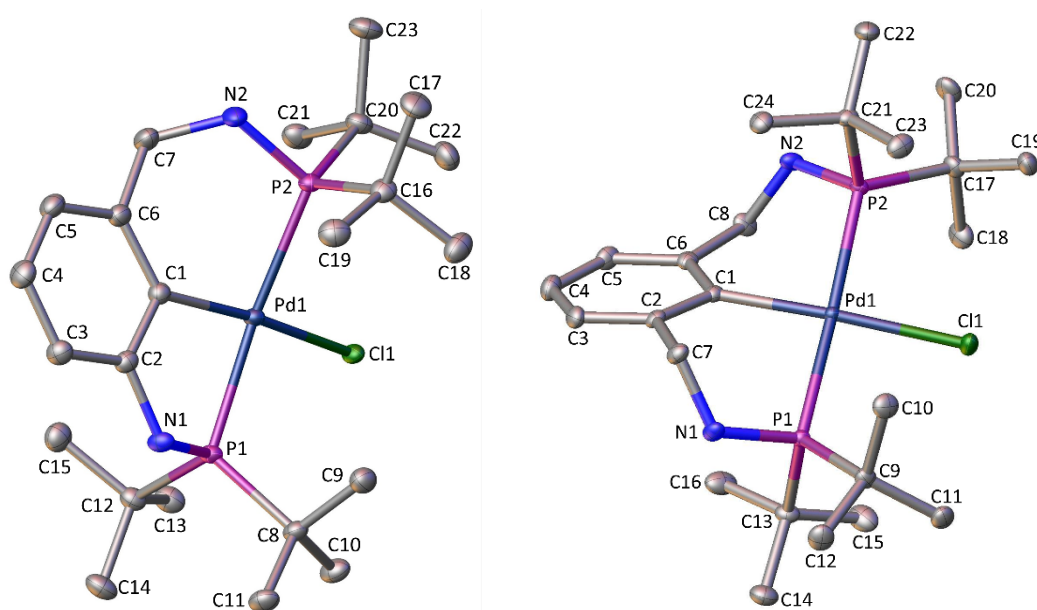


Figure 2. Single crystal X-ray crystallography structures of **4a** (left) and **7a** (right) (side view). Hydrogen atoms have been omitted for clarity. Thermal ellipsoids at 50% probability level.

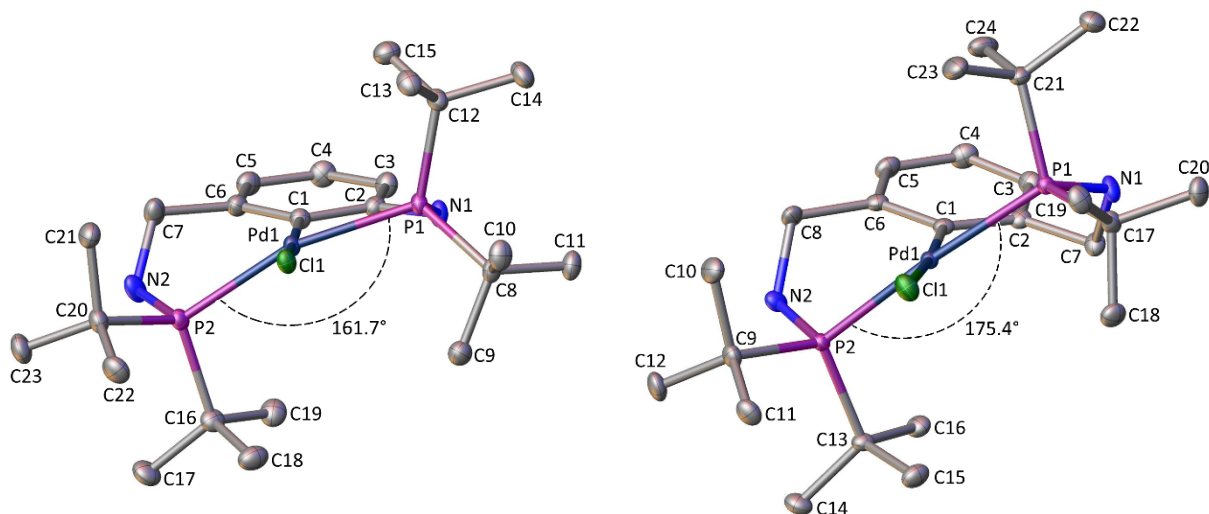


Figure 3. Single crystal X-ray crystallography structures of **4a** (left) and **7a** (right) (front view). Hydrogen atoms have been omitted for clarity. Thermal ellipsoids at 50% probability level.

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^tBu₂ 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, $\Sigma(\text{C1-Pd1-Cl1} + \text{P1-Pd1-P2}) = 350.3^\circ$). 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-PⁱPr₂ Pd-Cl complex (**A**) reported by Eberhard (P-Pd-P = 168.3°, see Figure 1a), and the analogous 5,5-PⁱPr₂ Pd-Cl complex (P-Pd-P = 160.4°).¹¹

Table 1. Selected bond lengths (Å) and bond angles (°) in 5,6-metallacycle (**4a**) and 6,6-metallacycle (**7a**). For details see ESI.

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

As a result of the extra methylene unit in **4a** (or two units in **7a**), there is a twist allowing the P^tBu₂ 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)).⁴⁰

NMR studies of the metallacycles

The NMR inequivalence of the P^tBu₂ 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-*d*₂ (TCE-*d*₂) and its ¹H NMR spectra were recorded at intervals between 25–100 °C (Figure 4). Although significant peak broadening of the P^tBu₂ 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.*,¹¹ 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).

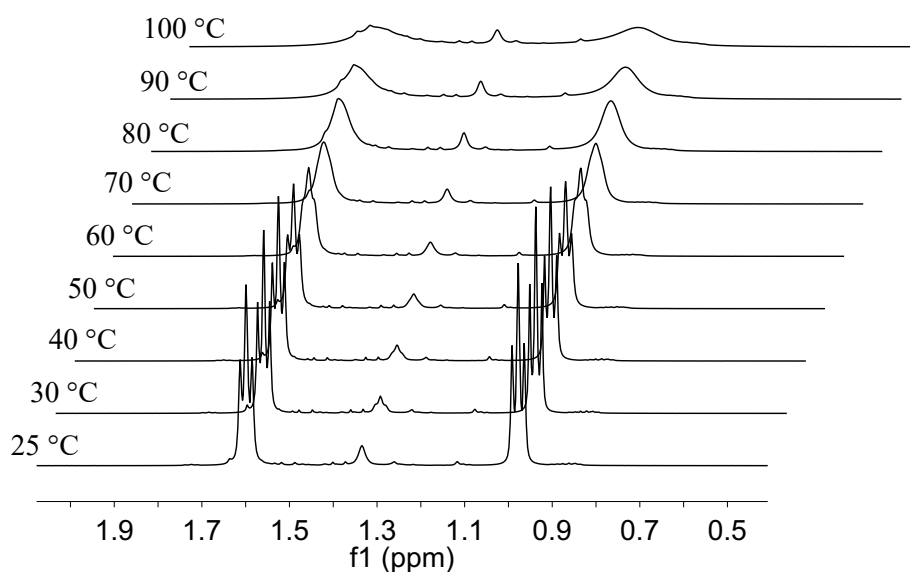


Figure 4. Selected region of the ^1H VT-NMR spectra of crystals of 6,6-Pd-Cl complex **7a**, dissolved in $\text{TCE-}d_2$.

For the 5,6-metallacycles, the $^{31}\text{P}\{^1\text{H}\}$ NMR spectra exhibit the expected AB patterns (Figure 5) with large $^2J_{\text{PP}}$ values typical of the *trans* relationship PdP_2 group: for **4b**, **5b** and **6b**, $^2J_{\text{PP}} = 367$ Hz, 388 Hz, and 447 Hz respectively (Figure 5). For Pd–TFA complex **4b**, the $^2J_{\text{PP}}$ is considerably smaller than the analogous Pd–Cl complex **4a** ($^2J_{\text{PP}} = 406$ Hz). This trend in coupling constants for 5,6-Pd–TFA complexes ($^2J_{\text{PP}}$: $\text{P}^t\text{Bu}_2 < \text{P}^i\text{Pr}_2 < \text{PPh}_2$) 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 $^2J_{\text{PP}}$ coupling).

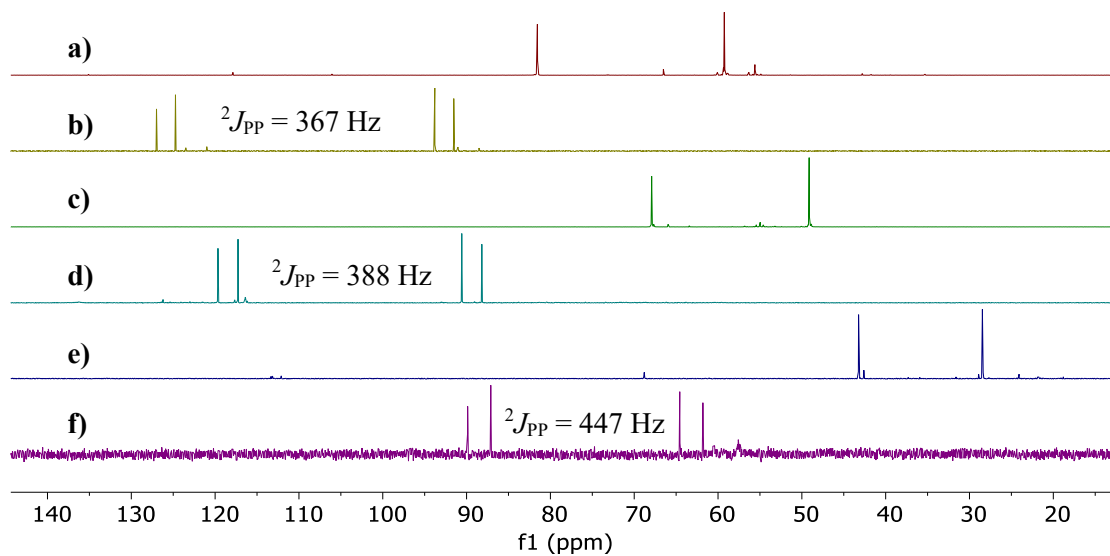


Figure 5. $^{31}\text{P}\{^1\text{H}\}$ NMR spectra for a) 5,6- P^tBu_2 (**L4**), b) **4b**, c) 5,6- P^iPr_2 (**L5**), d) **5b**, e) 5,6- PPh_2 (**L6**), f) **6b**.

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.¹¹

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

Entry	Ligand	% Conversion ^b with [PdCl ₂ (NCPH) ₂]	% Linear selectivity	% Conversion ^b with [Pd(TFA) ₂]	% Linear selectivity
1	L1	11	88	16	95
2	L2	>99	75	52	84
3	L3	>99	95	>99	92
4	L4	58	91	70	93
5	L5	>99	71	93	82
6	L6	>99	91	>99	93
7	L7	>99	82	>99	81
8	L8	>99	92	>99	67
9	L9	>99	88	>99	89
10 ^{c,f}	L8	>99	78	>99	67
11 ^{d,f}	L8	95	87	>99	63
12 ^{e,f}	L8	48	92	>99	78
13 ^{c,g}	L8	—	—	49 ^h	>99
14 ^{d,g}	L8	—	—	48 ^h	96
15 ^{e,g}	L8	—	—	12 ^h	>99

^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 P^tBu₂ 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-metallacycle displayed intermediate behaviour (60% conversion after 7 h).

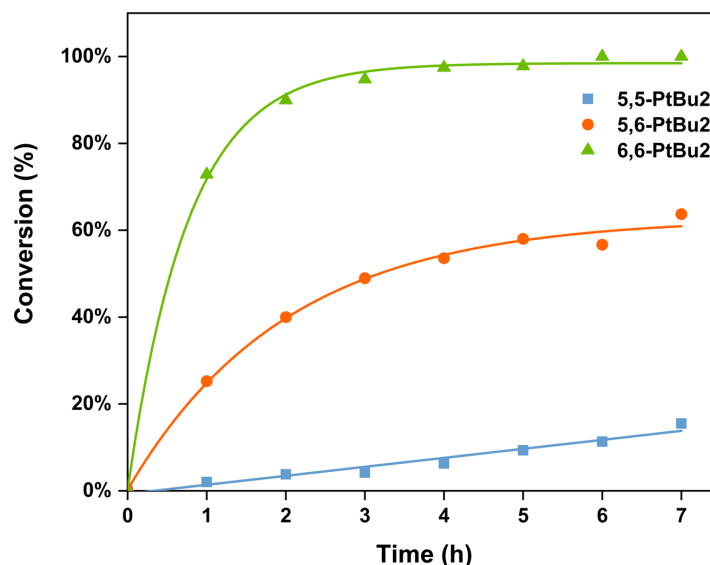


Figure 6. Conversion–time plot for the allylation of dimethylmalonate catalysed by Pd–Cl catalysts derived from **L1**, **L4** and **L7**. Conversion determined by GC–MS using dodecane as internal standard.

When the catalysis was run under the same conditions but in the absence of diphos ligand, using either $[\text{Pd}(\text{TFA})_2]$ or $[\text{PdCl}_2(\text{NCPh})_2]$, 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.

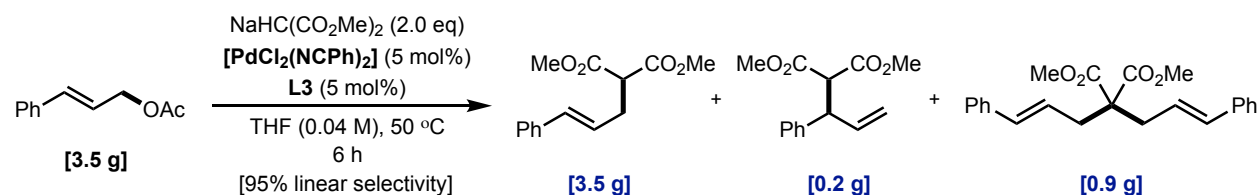
The following trends can be discerned from the data presented in Table 2. The catalysts derived from 5,5- and 5,6- P^tBu_2 substituted aminophosphine ligands (**L1** and **L4** respectively) (Table 2, entries 1 and 4) showed lower activity after 6 h than the ligands with the smaller P^iPr_2 and PPh_2 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, PPh_2 substituents show the highest linear selectivity (88–95%), followed by P^tBu_2 substituents (81–93%), and then P^iPr_2 substituents (67–92%).

This high activity of catalysts derived from **L8** led us to investigate it further. The catalysis with **L8** and $[\text{Pd}(\text{TFA})_2]$ or $[\text{PdCl}_2(\text{NCPh})_2]$ 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 $[\text{PdCl}_2(\text{NPh})_2]$ or $[\text{Pd}(\text{TFA})_2]$ 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 $[\text{PdCl}_2(\text{NPh})_2]$ (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).



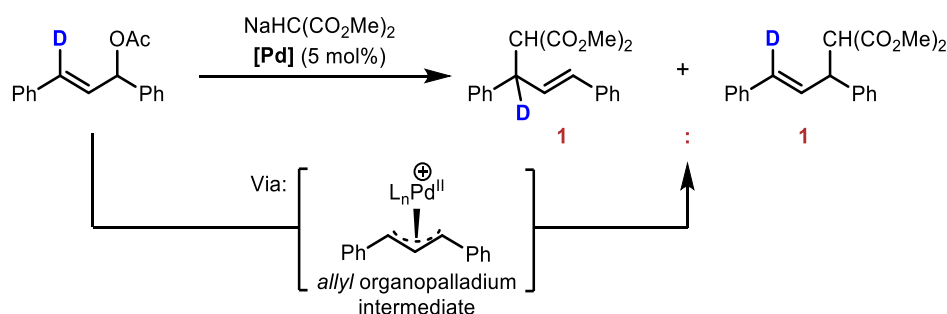
Scheme 5. Catalytic allylation of dimethylmalonate under optimal conditions.

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 (η^3 -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.

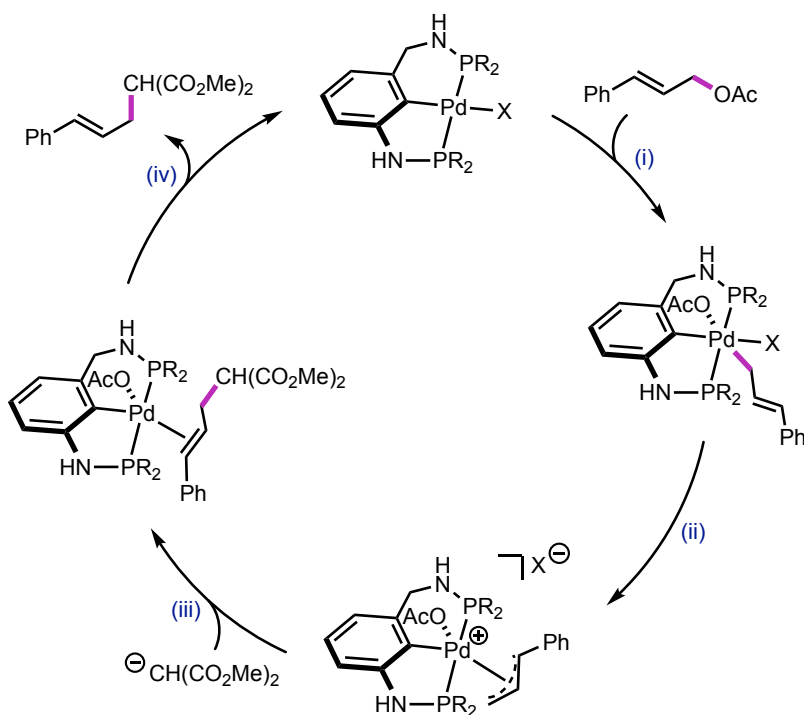


Scheme 6. Alkylation of deuterated allylic acetate, Eberhard *et al.*¹¹

Furthermore, Szabó and co-workers provided evidence for bis(phosphite)-Pd(II) pincer complex catalysed allylation of aldehydes and imines via (η^1 -allyl)Pd intermediates.⁴⁴ 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.⁴² In addition, they reported allylic C–H acetoxylation via proposed (η^3 -allyl)Pd(IV) intermediates.⁴⁵

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 allylation via (η^3 -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 (η^1 -allyl)Pd(IV) intermediate; (ii) η^3 -allyl formation by deprotonation (loss of AcOH) to give a cationic (η^3 -allyl)Pd(IV) intermediate; (iii) nucleophilic attack on the η^3 -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.*⁴⁶ 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 CF₃CO₂.

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 CF₃CO₂. The bulky P^{*t*}Bu₂ ligands form very stable, soluble, monomeric Pd–Cl complexes in any of the three metallacycle sizes. When smaller P^{*i*}Pr₂ or PPh₂ substituents are present, insoluble Pd-coordination polymers are produced. On switching the anionic ligand from Cl to CF₃CO₂, 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 allylation 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 allylation product is highest for PPh₂ 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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