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# Preformed Pd(II) Catalysts Based on Monoanionic [N,O] Ligands for Suzuki-Miyaura Cross-Coupling at Low Temperature

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**Abstract:** This paper describes the synthesis and catalytic testing of a palladium complex with a 5-membered chelating [N,O] ligand, derived from the condensation of 2,6-diisopropylphenyl aniline and maple lactone. This catalyst was active towards the Suzuki-Miyaura cross-coupling reaction, and its activity was optimised through the selection of base, solvent, catalytic loading and temperature. The optimised conditions are mild, occurring at room temperature and over a short timescale (1 h) using solvents considered to be 'green'. A substrate scope was then carried out in which the catalyst showed good activity towards aryl bromides with electron-withdrawing groups. The catalyst was active across a broad scope of electron-donating and high-withdrawing aryl bromides with the highest activity shown for weak electron-withdrawing groups. The catalyst also showed good activity across a range of boronic acids and pinacol esters with even boronic acids featuring strong electron-withdrawing groups showing some activity. The catalyst was also a capable catalyst for the cross-coupling of aryl chlorides and phenylboronic acid. This more challenging reaction requires slightly elevated temperatures over a longer timescale but is still considered mild compared to similar examples in the literature.

**Keywords:** palladium; cross-coupling; Suzuki-Miyaura; aryl Halide; sustainable



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## 1. Introduction

Suzuki-Miyaura cross-coupling is an important and popular reaction with many applications across a wide field, including the synthesis of ligands for catalysis, natural products and pharmaceuticals [1,2]. This wide applicability is due to the high tolerance of the reaction to a wide variety of functional groups and the mild reaction conditions that are required [1,3–6]. The reaction typically occurs through the reaction of an aryl boronic acid with a haloarene in the presence of a base with many different catalysts available [7]. These catalysts are typically Pd and range from heterogeneous nanoparticles to homogeneous catalysts [4–14]. Early catalysts for Suzuki-Miyaura coupling reactions were based on phosphorus ligands, of which $[Pd(PPh_3)_4]$ is a typical example, with the choice of Pd(II) pre-catalysts based on their air stability and their ready reduction to form the active Pd(0) species [1,3,14]. The choice of ligand was also observed to have a major effect. This led to much work being carried out into monoligated species through the development of bulky, electron-rich phosphines or sterically demanding N–Heterocyclic carbene (NHC) ligands [15,16]. An important advance in Suzuki-Miyaura cross-coupling reactions is the activation of aryl chlorides due to their decreased cost compared to aryl bromides, which was first achieved by Shen et al. using $Pd(OAc)_2$ with 1,3 bis(diphenylphosphino)propane (dppp) [17]. Through tuning the phosphorus ligands, it has been possible to cross-couple a wide variety of coupling partners with aryl chlorides [18]. Whilst the yields for aryl chlorides are typically poor, high reaction temperatures, such as refluxing *ortho*-xylene for 5–20 h, can be used to improve the yields [19].

Another main class of ligands in this field are NHCs, first utilised for the Suzuki–Miyaura coupling of 4–chloroacetophenone with arylboronic acid by Herrmann and co-workers [20]. Following this work, a wide range of NHCs have been utilized as ligands for catalytic cross-coupling reactions owing to the strong $\sigma$-donating properties and steric shielding [16]. A recent development in cross-coupling catalysis is the utilization of well-defined pre-catalysts that do not require the addition of ancillary ligands to metal salts. These catalysts can allow for transformations under milder conditions or at lower catalytic loadings [21]. These advantages have been demonstrated by Beller and co-workers where the use of a pre-formed catalyst improved performance over the same catalytic system generated in situ [22].

There is a large drive within the field of chemistry to work towards 'greener' reactions. These are summarized as the twelve principles of green chemistry introduced by Anastas and Warner in 1998 [23]. One of these principles is the choice of safer solvents and auxiliaries [24]. With many cross-coupling reactions requiring DMF, DMA or toluene heated under reflux, there is space here to improve these conditions and move to more sustainable alternatives since these solvents are classified by several companies as undesirable or in need of substitution where available following environmental, health and safety property analysis [25,26]. The use of better media for Suzuki-Miyaura reactions was reviewed recently across a range of solvents and catalyst types [27,28]. The switch away from solvents such as DMF is also beneficial when solvents such as methanol are used, as a simple extraction is required rather than a lengthy aqueous workup.

Schiff base-derived ligands have been shown to provide alternatives to classic phosphine-based catalysts with similar easy tuning of their steric and electronic properties [8,29–32]. One catalyst design of note was developed by Liu et al. using salicylaldimine ligands with $PdCl_2$ to form catalytic species in situ, which were capable of coupling a wide range of aryl bromides between room temperature and 60 °C under 6 h (Figure 1) [33]. The use of pre-formed neutral Pd [N,O] catalysts in green solvents has also been observed in recent work by Muthumari et al. which was capable of coupling alkyl bromides with a range of boronic acids in yields of approximately 90% after 3 h at 100 °C in water. The catalyst was also capable of coupling 4–chloroacetophenone to phenyl boronic acid, but this required 8 h at 100 °C [34].

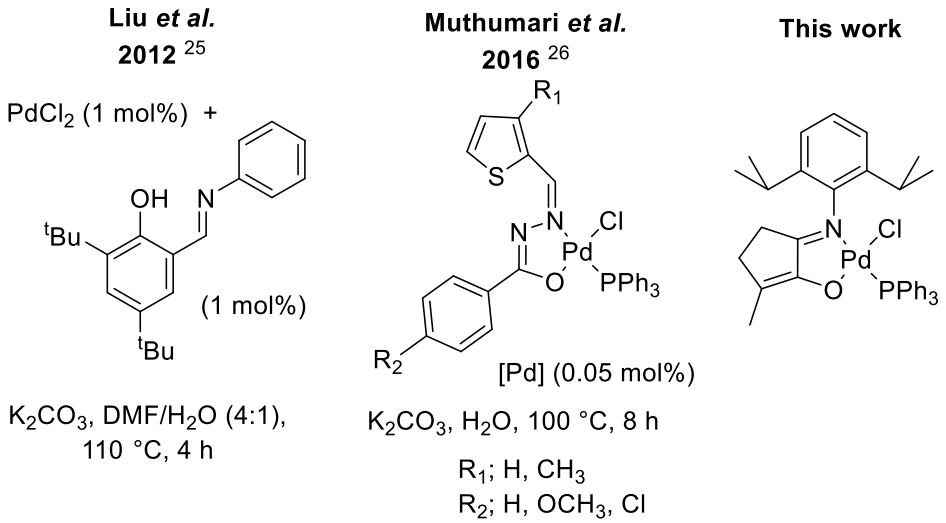



**Figure 1.** Selected [N,O] catalysts capable of Suzuki-Miyaura cross-coupling reactions [25,26].

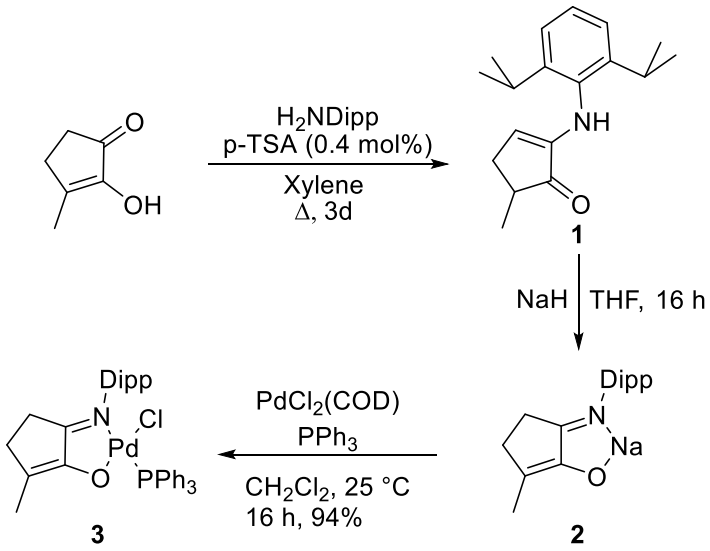
We have previously developed [N,O]-chelating ligands based on maple lactone, 2-hydroxy–3–methylcyclopent–2–enone, also called cyclotene [35,36], which when condensed with a substituted aniline, gave ligands featuring a 5-membered chelate ring and a correspondingly smaller bite-angle than salicylaldimines [37]. Complexation with [Ni(Ar)($PPh_3$)] fragments gave catalysts for ethylene polymerization generating differ-

ent polyethylene properties depending upon the initiator [38]. These ligands are based on maple lactone, a cheap, bio-sourced material that is useful in the development of catalysts with inexpensive ligand systems. With limited work into the development of [N,O]-ligated catalysts in cross-coupling, we set out to investigate the use of a Pd catalyst with a 5-membered chelating ring in Suzuki-Miyaura cross-coupling reactions using benign conditions. The work presented herein includes the synthesis, complexation and characterization of an active catalyst, optimization studies for the Suzuki–Miyaura cross-coupling reaction and a substrate scope for both cross-coupling partners.

## 2. Results and Discussion

### *2.1. Catalyst Synthesis*

Synthesis of the proligand was carried out as previously detailed through the condensation of maple lactone with 2,6–diisopropylaniline using catalytic amounts of *p*-toluenesulfonic acid (Scheme 1) with single substitution seen to occur selectively at the ketone position [38]. The reaction with NaH gave the corresponding sodium imino–enolate (**2**) that reacted smoothly with $[PdCl_2(COD)]$ and $PPh_3$ to give the desired Pd complex **3** in 94% yield.




**Scheme 1.** Synthesis of the Pd complex **3**. Dipp = 2,6–diisopropylphenyl.

**3** was characterized using multinuclear NMR spectroscopy, single-crystal X-ray diffraction (SCXRD), elemental analysis and high-resolution mass spectrometry. The NMR spectroscopic studies showed free rotation of the aniline group around the metal centre with a pair of doublets at 1.20 ppm and 1.44 ppm, each with an integration equivalent to 6H, and a septet at 3.46 ppm with an integration of 2H, indicative of two distinct environments for the Dipp protons. Alongside this, signals corresponding to the $PPh_3$ group were also seen, including a singlet at 26.6 ppm in the $^{31}P\{^1H\}$ NMR spectrum.

The molecular structure of **3** was determined using SCXRD and showed a Pd(II) complex with square planar geometry (Figure 2). The N-Pd-O bite angle was 82.74(7)° with the imine donor *trans* to $PPh_3$. This is similar to the other reported 5-membered chelating [N,O] Pd complexes displaying bite angles between 78.46(6)° and 85.27(4)°. Similar bond lengths to those in the literature were also observed with bond lengths of Pd-O; 2.018(2) Å and Pd–N; 2.099(2) Å for compound **3** [34,39,40]. The imino–enolate tautomer was identified from the short C1–C5 bond length (1.359(4) Å) and the longer C2–C3 bond length (1.497(3) Å). We note that **3** is air and moisture stable over a 3-month period, which is of significant importance for use in Suzuki-Miyaura reactions, as this allows for easier handling and the use of hydrous solvents.

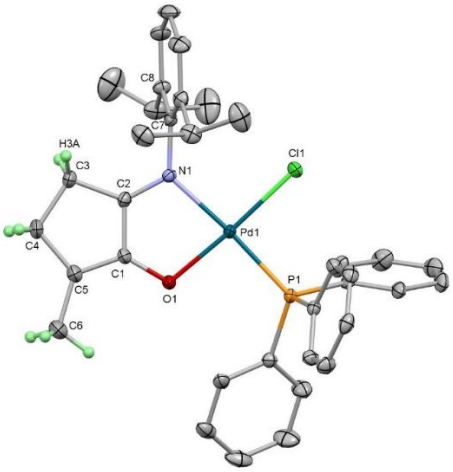
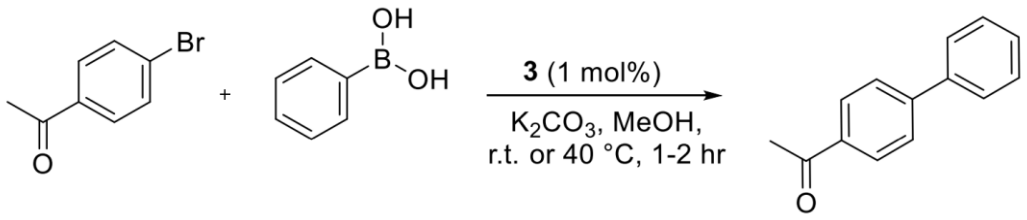



**Figure 2.** Molecular structure for compound **3** with 50% ellipsoids (all H atoms, except for selected H atoms on the imino-enolate ligand, are omitted for clarity). Selected bond lengths (Å) and bond angles (°): Pd1-Cl1 2.2905(6), Pd1-P1 2.2530(6), Pd1-O1 2.018(2), Pd1-N1 2.099(2), O1-C1 1.328(3), C1-C5 1.359(4), C1-C2 1.442(3), N1-C2 1.294(3), C2-C3 1.497(3), C3-C4 1.535(4), C4-C5 1.502(4), O1-Pd1-N1 82.74(7).

### *2.2. Cross-Coupling Reactions*

The initial reactions between 4–bromoacetophenone and phenylboronic acid were carried out using methanol as the solvent under both atmospheric conditions and in an anaerobic $N_2$ environment at either room temperature or 40 °C (Table 1). These substrates were chosen as they represent common reactions within the literature allowing for the benchmarking of results; in addition, the acetophenone group on the halogen coupling partner acts as an unambiguous $^1$H NMR spectroscopic handle for reaction monitoring through comparative integration of the respective signals in the starting material at 2.44 ppm and the product at 2.50 ppm. Assignment of these signals were confirmed through both starting material characterization and doping of additional starting material into the final reaction mixture.

**Table 1.** Initial optimization studies carried out between 4–bromoacetophenone and phenylboronic acid.




| Entry | Air/$N_2$ | Time (hr) | Temperature (°C) | NMR Conversion [a] |
|---|---|---|---|---|
| **1** | $N_2$ | 2 | r.t. | 79% |
| **2** | Air | 2 | r.t. | 90% |
| **3** | $N_2$ | 1 | r.t. | 73% |
| **4** | Air | 1 | r.t. | 85% |
| **5** | $N_2$ | 1 | 40 | 83% |
| **6** | Air | 1 | 40 | 99% |

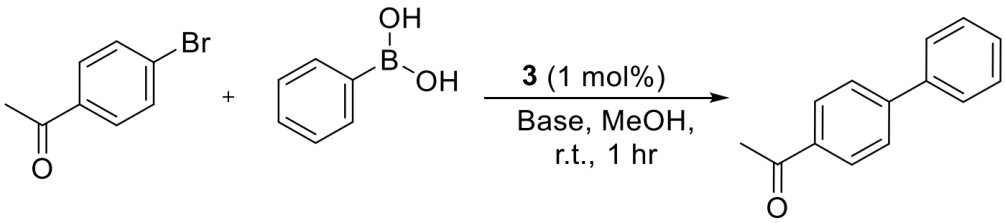
[a] Conversion was determined with $^1$H NMR spectroscopy via integration against starting material of the aryl halide and the product, as outlined above.

From these initial studies, it was determined that carrying the reaction out in air was not detrimental to the yield with a conversion of 90% (Table 1, entry 2) compared to 79%

(Table 1, entry 1) when the reaction was carried out under $N_2$ over a two-hour period at room temperature. The difference between a one-hour and two-hour reaction time was small with an 85% completion over 1 h in air (Table 1, entry 4) compared to 90% completion after 2 h in air at room temperature (Table 1, entry 2). Room temperature was selected for further reactions, incorporating 'green' chemistry principles and benign conditions, and to allow for easier observations of the different optimization studies.

Following this initial screen of reaction time and temperature, a base screen was carried out using standardised conditions of 1 h at room temperature with a 1 mol% catalytic loading in methanol. The choice of base has an important effect on the rate of the reaction with the base playing various roles within the catalytic cycle [11,41–45]. The hydroxide ion is known to promote the transmetallation and the reductive elimination steps; however, a concentration of hydroxide that is too high has a negative impact, enhancing the formation of unreactive boronates. The different bases screened can be seen in Table 2 and were chosen to give a range of anions and cations.

**Table 2.** Base optimization screen with the range of bases trialled and the NMR spectroscopic conversion obtained.




| Entry | Base | NMR Conversion |
|---|---|---|
| **7** | $Et_3N$ | No reaction observed |
| **8** | NaOH | 80% |
| **9** | $K_3PO_4$ | 65% |
| **10** | K(OAc) | 45% |
| **11** | $K_2CO_3$ | 81% |
| **12** | $Na_2CO_3$ | 82% |
| **13** | $Cs_2CO_3$ | 71% |
| **14** | No base | 2% |

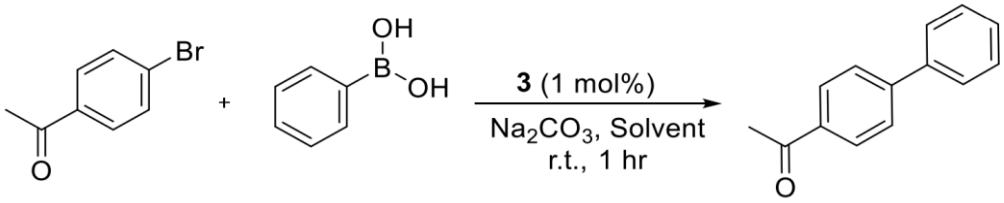
When the neutral base $Et_3N$ (Table 2, entry 7) was used, no reaction was observed. The classic ionic bases enabled the catalytic reaction to proceed; acetates and phosphates displayed moderate conversions (Table 2, entries 9, 10), whilst hydroxides and carbonates showed good conversion (Table 2, entries 8 and 11). Following these experiments, carbonate anions were chosen, and through comparison of the cations (Table 2, entries 11–13), it was seen that sodium carbonate and potassium carbonate were similar in performance; therefore, sodium carbonate was chosen for future reactions. For the control studies, the reaction was also trialled with no base added, which showed very little reaction (2% conversion, Table 2, entry 14).

A solvent screen was then carried out on this reaction at room temperature with 1 mol% catalyst and $Na_2CO_3$ as the base.

Acetone is a poor solvent for this reaction with a low conversion of 23% (Table 3, entry 15) along with dimethyl carbonate (Table 3, entry 16), trialled due to its growing relevance as a green solvent, with a poor conversion of 4%. Other typical laboratory solvents, including toluene, DCM and DMF, also showed very poor conversion of below 8% (Table 3, entries 17–20). Whilst surprising due to the common use of these solvents within the literature for Suzuki-Miyaura cross-coupling reactions [4,14,15], this could be due to

the low solubility of $Na_2CO_3$ in these solvents at room temperature with the literature examples requiring refluxing conditions. Further evidence of this low reactivity being caused by poor base solubility can be seen in entry 21 when a 50:50 DMF/$H_2O$ solvent mixture was utilised. In this entry, the NMR conversion increased from 4% to 14%, which is likely due to the increased solubility of the reagents. Following the success seen with methanol in the initial reactions, a screen of common alcohols was then carried out (Table 3, entries 22–24). This showed an increase in catalytic activity with lower molecular weight alcohols, with methanol enabling the highest catalytic activity. Methanol was then trialled with the addition of water (Table 3, entries 25–26). Entry 25 shows that the addition of water was beneficial for an improved conversion, possibly due to the increased solubility of the reagents, with the conversion increasing from 80% to 88%. There is a balance with the number of equivalents of water though, as by decreasing the proportion of water to 25% (entry 26), a further increase in conversion is seen to 97%.

**Table 3.** Solvent screen results with solvent used and NMR conversion.

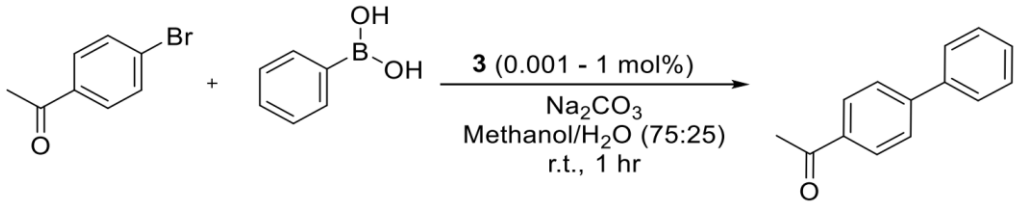



| Entry | Solvent | NMR Conversion |
|---|---|---|
| **15** | Acetone | 23% |
| **16** | Dimethylcarbonate | 4% |
| **17** | Toluene | 2% |
| **18** | THF | 7% |
| **19** | DCM | 2% |
| **20** | DMF | 4% |
| **21** | DMF/$H_2O$ (50:50) | 14% |
| **22** | IPA | 21% |
| **23** | EtOH | 52% |
| **24** | MeOH | 80% |
| **25** | MeOH/$H_2O$ (50:50) | 88% |
| **26** | MeOH/$H_2O$ (75:25) | 97% |

From the solvent scope, a mixed solvent system of MeOH/$H_2O$ (75:25) was then chosen for further reactions. This result contributes towards the initial aim of improving the reaction with the use of 'green' solvents since methanol has a low environment, health and safety (EHS) indicator of 2.67 and is, therefore, classified as a 'green' solvent alongside water [12,16].

Following these optimisations, the catalytic loading of the system was investigated to try to lower the catalytic loading from 1 mol%, using sodium carbonate as the base, with a 75:25 MeOH:$H_2O$ solvent mixture at room temperature for an hour, as outlined in Table 4.

**Table 4.** Results from the catalytic loading screen with NMR conversion and calculated TON from the conversion.




| Entry | Catalyst Loading | NMR Conversion | TON |
|---|---|---|---|
| **27** | 0.001 mol% | 0.3% | 300 |
| **28** | 0.01 mol% | 2% | 200 |
| **29** | 0.1 mol% | 43% | 430 |
| **30** | 1 mol% | 97% | 97 |

From these results, it can be seen that a very low catalyst loading of 0.001 mol% results in very little conversion (Table 4, entry 27). This also can act as a control run with very little catalyst effectively shutting off the reaction. Increasing the catalytic loading can be seen to increase the conversion. This TON is lower than other catalysts reported in the literature [8] and may be due to the mild conditions utilised in this screen. However, the TON is higher than other reported catalysts in the literature in mild conditions with the work by Wang et al. exhibiting a TON of 316. This experiment was carried out over 8 h, however, with a more comparable TON calculated after 1 h of 160 [17]. Comparisons with phosphine complexes at room temperatures are still low with a comparative TON calculated at 9900 at room temperature, but this was again calculated over 4 h [18].

The rate of conversion over time was investigated through the use of an NMR scale reaction and monitored using the addition of mesitylene to act as an internal standard with MeOD as the solvent (Figure 3). This graph shows that no induction period was observed with the fastest rate of reaction occurring at the start of the experiment (Table 4).

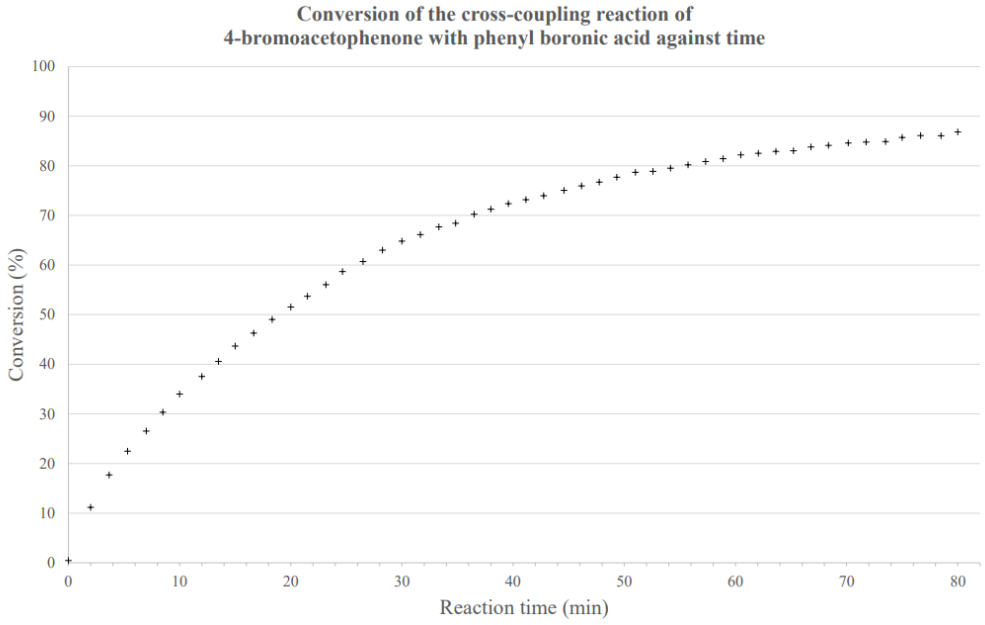
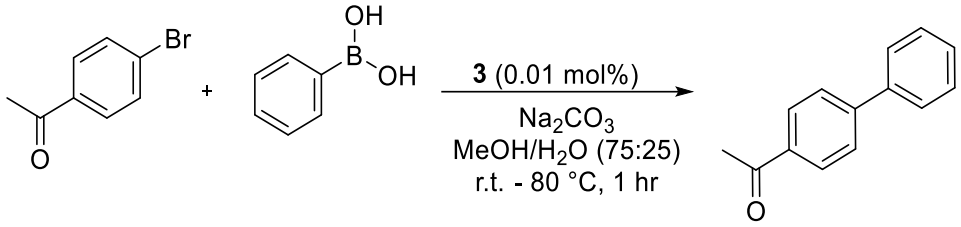



**Figure 3.** Reaction profile for the NMR conversion of the cross-coupling reaction of 4–bromoacetophenone with phenyl boronic acid against time.

The temperature of the reaction was then screened to investigate how this affected the NMR spectroscopic conversion. Due to the high conversion obtained under 1 mol% loading in mild conditions and the relative short time scale of the reaction, these experiments were carried out using 0.01 mol% of catalyst to allow for the effects to be seen (Table 5).

**Table 5.** Temperature and NMR conversion obtained from the temperature screen.




| Entry | Temperature (°C) | NMR conv. |
|---|---|---|
| **39** | 20 | 2% |
| **40** | 40 | 10% |
| **41** | 60 | 99% |
| **42** | Reflux | 99% |

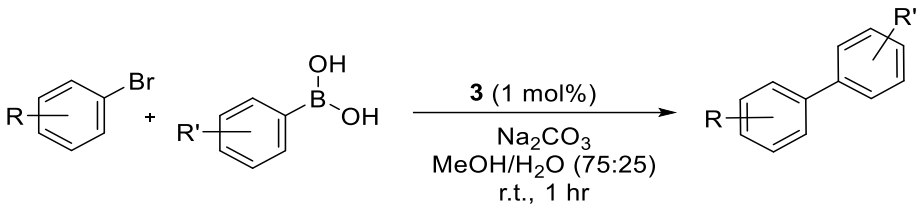
From this screen, a dramatic increase in reactivity was observed above 40 °C. This increase could be due to catalyst degradation resulting in the formation of Pd(0) nanoparticles changing, or in fact producing, the active catalytic species. In order to test for the formation of Pd(0) nanoparticles, a mercury drop test was carried out [7]. Whilst this is not a completely infallible test, we did observe a decrease in the NMR conversion from 97% to an average of 40%, leaving the role of nanoparticles as a possibility [32].

### *2.3. Substrate Scope*

With the catalytic conditions optimized, the study then progressed to establishing the substrate scope. This was first carried out across a range of aryl halides. The conditions used were a 1 mol% [Pd] loading at room temperature for an hour utilizing MeOH/$H_2O$ (75:25) as the solvent (Table 5). These conditions were chosen to maintain the 'green' chemistry of the system and limit the possible catalyst degradation through heating of the system.

An initial screen of groups with varying electron-donating/withdrawing properties showed that the cross-coupling reaction proceeded well when strong or moderate electron-withdrawing groups were used (Table 6, entries 46 and 45, respectively). When weak electron-donating groups were used at the *ortho*– and *para*– positions (Table 6, entries 47 and 48), the conversion decreased to 82% and 75%, respectively. Comparing the *ortho*– and *para*–bromotoluene to *meta*–bromotoluene (Table 6, entry 49), the conversion dropped significantly to 15%. This effect continued further when a strong electron-donating group was used in entry 50 when only trace amounts of product were obtained. Entry 45 was subjected to column chromatography to check for homo-coupling of either partner. This resulted in an isolated yield of 70% with all other components isolated relating to trace starting materials. These trends have been seen in the literature; previous salicylaldimine ligated catalysts showed decreasing activity with increasing electron-donating substituents [4]. Electron-donating groups were also seen to slow the catalysis down in the work by Ref. [23].

**Table 6.** Substrate scope investigating the effect of changing the aryl bromide coupling to phenylboronic acid.




| Entry | Aryl Bromide | NMR conv. |
|---|---|---|
| **45** | 4-bromoacetophenone | 96% |
| **46** | 4-nitrobromobenzene | 97% |
| **47** | 4-bromotoluene | 82% |
| **48** | 2-bromotoluene | 75% |
| **49** | 3-bromotoluene | 15% |
| **50** | 4-bromoaniline | Trace |
| **51** [1] | 4-bromoaniline | 29% [a] |
| **52** [2] | 4-bromoaniline | 87% [a] |

[1]: Reaction carried out at 40 °C for 24 h. [2]: Reaction carried out at 60 °C for 24 h. [a]: Isolated yield obtained.

The reaction was carried out at increased temperatures over a longer reaction time with the isolated yield recorded for added clarity because no convenient characteristic signals were observed through $^1$H NMR spectroscopy. This showed an increase in reactivity with an isolated yield of 29% obtained at 40 °C after 24 h. This was further improved with heating at 60 °C for 24 h instead, resulting in an 87% isolated yield (Table 6, entries 51 and 52).

A similar study was then carried out for the boronic acid scope with a range of electronic properties present on the aryl ring. Phenylboronic acid pinacol ester was also included in this trial for tolerance of boronic acid derivatives.

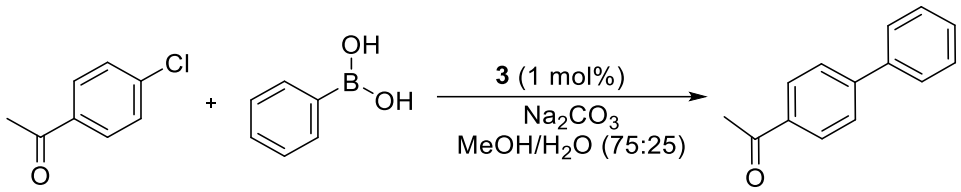
The catalyst showed a broad reaction scope tolerating many substituents except for a *para*–nitro substituent (a strong electron-withdrawing group), which displayed a low conversion of 17% (Table 7, entry 58). Phenylboronic acid pinacol ester (Table 7, entry 59) displayed quantitative conversion, indicating that the catalyst is tolerant towards pinacol esters. This trend has also been seen in the literature with electron deficient boronic acids showing reduced catalytic activity [8,23].

**Table 7.** Substrate scope investigating the effect of changing the boronic acid coupling to 4–bromoacetophenone.

| Entry | R′ | NMR Conversion |
|---|---|---|
| **53** | 4-methoxybenzene boronic acid | 99% |
| **54** | 4-tolylboronic acid | 97% |
| **55** | 2-tolylboronic acid | 94% |
| **56** | 3-tolylboronic acid | 99% |
| **57** | 4-methoxycarbonylbenzene boronic acid | Quant. |
| **58** | 4-nitrobenzene boronic acid | 17% |
| **59** | Phenylboronic acid pinacol ester | Quant. |

There is an incentive to be able to use aryl chlorides as the coupling partner in these reactions due to their decreased cost compared to aryl bromides. With that in mind, compound **3** was trialled for catalytic activity towards aryl chlorides using the conditions previously optimised (Table 8).

**Table 8.** Cross-coupling reaction between 4–chloroacetophenone and phenyl boronic acid in varying conditions.




| Entry | Temperature | Time (hr) | NMR Conversion |
|---|---|---|---|
| **60** | Room temperature | 1 hr | trace |
| **61** | 40 °C | 24 hr | 62% |
| **62** | 60 °C | 1 hr | 42% |
| **63** | 60 °C | 6 hr | 74% |
| **64** | 60 °C | 24 hr | 95% |

The initial conditions of room temperature for one hour proved insufficient for the reaction to proceed with only trace quantities of product observed. Because of this, the temperature was increased to 40 °C for 24 h (Table 8, entry 61). This increase in temperature and prolonged reaction time was sufficient for the reaction to proceed with an NMR spectroscopic conversion of 62% observed. A further increase in temperature to 60 °C allowed for a higher rate of conversion with 42% observed over 1 h, 74% over 6 h, and 95% after 24 h (Table 8, entries 62–64).

Through comparison of these results to other [N,O] catalysts in the field, compound **3** shows good catalytic activity. Work by Muthumari et al. required high temperatures of 100 °C for 8 h for the coupling of aryl chlorides when using 4-methoxychlorobenzene with phenyl boronic acid with a comparative isolated yield of 58% [8]. Cui et al. utilised an [N,O]-ligated palladium catalyst for the reaction of 4–chloroacetophenone with phenyl boronic acid, offering a more direct comparison between the catalytic systems [24]. These catalysts were capable of completing this reaction to high conversion (95%) with a lower catalytic loading of 0.5 mol% but required DMF at 110 °C for 4 h. Similar high conversions were also observed by Liu et al. with [N,O] catalysts generated in situ [4]. These reaction conditions were also forcing with a DMF:$H_2O$ (80:20) solvent heated to 110 °C for 4 h. In comparison to this, catalyst **3** was capable of cross-coupling 4–chloroacetophenone to phenyl boronic acid to moderate yields in 6 h and high yields over 24 h at 60 °C.

## 3. Experimental

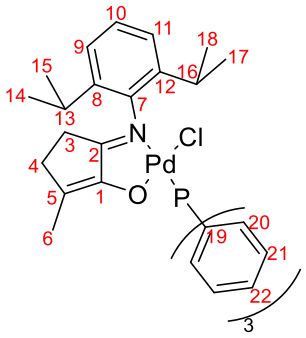
Reactions were either performed under an oxygen-free ($H_2O$, $O_2$ < 0.5 ppm) nitrogen atmosphere using standard Schlenk line techniques and an MBRAUN UNIlab Plus glovebox or in the open laboratory, as indicated. Anhydrous toluene, anhydrous DCM and anhydrous THF were obtained from an MBRAUN SPS–800,(MBRAUN, Munich, Germany) and petroleum ether 40–60 was distilled from sodium wire; benzene and benzene-$d^6$ were dried over molten potassium and distilled. All anhydrous solvents were degassed before use and stored over activated molecular sieves.

The following compounds were prepared according to the literature methods: 2–((2,6-diisopropylphenyl)amino)–5–methylcyclopent–2–en–1–one (**1**), **2**, [38] and $PdCl_2$(COD) [46]. The following were purchased from commercial suppliers and used without further purification: maple lactone, *p*–toluenesulfonic acid, sodium hydride (95%), palladium chloride, 1,5–cyclooctadiene and triphenylphosphine. 2,6–Diisopropylaniline was distilled under reduced pressure before use. Air-sensitive samples for NMR spectroscopy were prepared in NMR tubes equipped with a J. Young tap. The NMR spectra were recorded on a Bruker AV300 (Bruker, MA, USA) (300 MHz), AVI400 (400 MHz), AVIII400 (400 MHz) or AVHDIII (400 MHz) spectrometer at 25 °C unless specified. Chemical shifts $\delta$ are noted in parts per

million (ppm). $^{1}$H and $^{13}$C spectra were calibrated to the residual proton resonances of the deuterated solvent. $^{31}$P NMR spectra were referenced to external samples of 85% $H_3PO_4$ at 0 ppm. The elemental analyses were performed by Brian Hutton at Heriot-Watt University using an Exeter CE440 elemental analyser. (Exeter Analytical, Coventry, UK)The mass spectrometry analysis was performed at the UK National Mass Spectrometry Facility at Swansea University using an Atmospheric Solids Analysis Probe interfaced to a Waters Xevo G2–S instrument (Waters, MA, USA).

**[Pd(Cl)(N,O$^{Dipp}$)(PPh$_3$)] (3)**

[$PdCl_2$(cod)] (0.371 g, 1.30 mmol), **2** (0.400 g, 1.365 mmol, 1.05 eq) and $PPh_3$ (0.341 g, 1.30 mmol) were weighed into a Schlenk tube in a glovebox before $CH_2Cl_2$ (0.8 mL) was added. The solution was then stirred at room temperature overnight, and the solvent was removed via rotatory evaporation yielding a dark-brown solid. The solid was then dissolved in toluene and filtered before evaporation of the solvent under reduced pressure. Recrystallisation was then carried out using THF/petroleum ether 40–60 to yield the desired product as dark red crystals (0.826 g, 1.22 mmol, 94%).




**$^{1}$H NMR (400 Hz, 298 K, $C_6D_6$):** δ 7.73 (6H, m, $H_{20}$), 7.46 (m, 3H, $H_{22}$), 7.38 (m, 6H, $H_{21}$), 7.16 (3H, m, $H_{9\text{-}11}$), 6.24 (1H, td, J = 7.3, 1.2 Hz, $H_{Ni\text{-}o\text{-}tolyl}$), 3.46 (2H, sept, J = 7.3 Hz, $H_{13,16}$), 2.57 (bs, 2H, $H_{4/3}$), 2.02 (bs, 2H, $H_{3/4}$), 1.67 (s, 3H, $H_6$), 1.44 (6H, d, J = 6.8 Hz, $H_{iPr}$), 1.20 (6H, d, J = 6.8 Hz, $H_{iPr}$). **$^{13}$C{$^{1}$H} NMR (100.6 Hz, 298 K, $C_6D_6$):** δ 194.06 (C), 166.65 (C), 141.25 (C), 140.84 (C), 137.84 (C), 135.10 (CH), 135.00 (CH), 132.32 (CH), 130.80 (CH), 129.16 (C), 129.03 (CH), 128.62 (C), 128.21 (CH), 128.03 (CH), 127.92 (CH), 126.56 (CH), 125.29 (CH), 123.15 (CH), 34.44 ($CH_2$), 28.31 (CH), 24.82 ($CH_2$), 23.99 ($CH_3$), 23.86 ($CH_2$), 21.41 ($CH_3$), 13.15 ppm ($CH_3$). **$^{31}$P{$^{1}$H} NMR (162 Hz, 298 K, $C_6D_6$):** δ 26.6 ppm. **HRMS (ASAP):** Calculated for [M+H]: 674.1581, Found: 674.1575 m/z; calculated for [M-Cl]: 638.1818, Found: 638.1816 m/z. **Elemental analysis** calcd (%) for $C_{15}H_{19}NO$: C; 64.10, H; 5.83, N; 2.08. Found: C; 63.82, H; 5.86, N; 2.21.

### *3.1. Crystallographic Details*

The X-ray diffraction experiments were performed on single crystals of **3** with the data collected on a Bruker X8 APEX II (Bruker, MA, USA) four-circle diffractometer. The crystal was kept at 100 K during the data collection. Indexing, data collection and absorption corrections were performed, and the structures were solved using direct methods (SHELXT [47] and refined with full-matrix least-squares (SHELXL) interfaced with the programme OLEX2 [48,49].

**Crystal data** for $C_{36}H_{39}ClNOPPd$ ($M$ = 674.50 g/mol): orthorhombic, space group $P2_12_12_1$ (no. 19), $a$ = 8.9925(4) Å, $b$ = 16.4896(8) Å, $c$ = 22.0909(10) Å, $V$ = 3275.7(3) Å$^3$, $Z$ = 4, $T$ = 100.15 K, μ(synchrotron) = 0.765 mm$^{-1}$, $Dcalc$ = 1.368 g/cm$^3$, 103,238 reflections measured (4.552° ≤ 2Θ ≤ 62.764°), 9994 unique ($R_{int}$ = 0.0781, $R_{sigma}$ = 0.0398), which were used in all calculations. The final $R_1$ was 0.0298 (I > 2σ(I)), and $wR_2$ was 0.0726 (all data). CCDC deposition number: 2102831.

### *3.2. Suzuki-Miyaura Cross-Coupling Reactions*

A typical cross-coupling reaction was carried out as follows:

4–bromoacetophenone (0.100 g, 0.5 mmol, 1 eq.), phenyl boronic acid (0.092 g, 0.754 mmol, 1.5 eq.), $Na_2CO_3$ (0.1065 g, 1.005 mmol, 2 eq.) and [PdCl(N,O$^{Dipp}$)($PPh_3$)] (3.4 mg, 0.005 mmol, 1 mol%) were added to a 100 mL round-bottomed flask equipped with a stirrer bar. A solvent mixture of methanol:water 3:1 (10 mL) was added, and the mixture was stirred for 1 h at room temperature. Water (10 mL) was then added to the flask followed by diethyl ether (10 mL), and the organic phase was collected by separation. This was then dried over $MgSO_4$, filtered and the solvent removed by rotatory evaporation. $^1$H NMR spectroscopic analysis was then carried out in $CDCl_3$, and the conversion was calculated through integration of the resonances at 2.60 ppm (starting material) and 2.65 ppm (product). The product was then isolated using column chromatography (199:1 petroleum ether 40–60:ethyl acetate) as an off-white solid (0.069 g, 0.35 mmol, 70%). **$^1$H NMR (400 Hz, 298 K, $C_6D_6$):** δ 7.92 (2H, d, *J* = 8.8 Hz), 7.57 (2H, d, *J* = 8.5 Hz), 7.51 (2H, m), 7.36 (2H, m), 7.29 (1H, m), 2.52 (3H, s). The data matches the literature values [10].

### *3.3. Cross-Coupling Reaction of 4–Bromoaniline at Elevated Temperatures*

4–bromoaniline (0.0864 g, 0.5 mmol, 1 eq.), phenyl boronic acid (0.092 g, 0.754 mmol, 1.5 eq.), $Na_2CO_3$ (0.1065 g, 1.005 mmol, 2 eq.) and [PdCl(N,O$^{Dipp}$)($PPh_3$)] (3.4 mg, 0.005 mmol, 1 mol%) were added to a 100 mL round-bottomed flask equipped with a stirrer bar. A solvent mixture of methanol:water 3:1 (10 mL) was added, and the mixture was stirred at 60 °C for 24 h. The mixture was then cooled to room temperature before water (10 mL) was then added to the flask followed by diethyl ether (10 mL), and the organic phase was collected by separation. This was then dried over $MgSO_4$, filtered and the solvent removed by rotatory evaporation. The product was then isolated using column chromatography (1:1 petroleum ether 40–60:ethyl acetate) with a small amount of DCM added to improve solubility to yield a brown solid (0.0736 g, 0.43 mmol, 87%). **$^1$H NMR (400 Hz, 298 K, $C_6D_6$):** δ 7.47 (2H, d, *J* = 8.3 Hz), 7.34 (4H, m), 7.20 (1H, m), 6.69 (2H, d, *J* = 8.4 Hz), 3.66 (2H, br. s, $NH_2$). The data matches the literature values [10].

## 4. Conclusions

In conclusion, a Pd(II) complex with a 5-membered chelating [N,O] ligand derived from maple lactone was synthesized and characterized. This complex is a rare example of a pre-formed [N,O] Pd catalyst for the Suzuki-Miyaura cross-coupling reaction, and screening revealed good catalytic activity even at low temperatures. The catalytic activity was optimized through the selection of base, solvent, catalytic loading and temperature to yield conditions that involve a mild, room-temperature reaction at a short timescale (1 h) using solvents that are typically considered to be 'green'. Using these optimised conditions, a substrate scope identified that the catalyst showed good activity towards aryl bromides with electron-withdrawing groups. This activity decreased with weak electron-donating groups, and only trace quantities of products were observed with strong electron-donating groups. However, these less reactive substrates were capable of being coupled through increased temperature and timescale with an 87% isolated yield of the cross-coupled product derived from 4–bromoaniline obtained after 24 h at 60 °C. The catalyst also showed good activity across a range of boronic acids and pinacol esters with only boronic acids featuring strong electron-withdrawing groups showing limited activity. The catalyst was also a capable catalyst for the cross-coupling of aryl chlorides and phenylboronic acid. This reaction, however, required slightly elevated temperatures of 60 °C over a longer timescale but is still considered mild compared to other examples of these compounds in the literature.

**Author Contributions:** M.J.A. and S.B. synthesised and characterised the proligands and catalyst. M.J.A. carried out catalytic studies. M.J.A., S.M.M. and R.D.M. undertook the analysis of the results. M.J.A., S.M.M. and R.D.M. conceived the project and contributed to writing the paper. All authors have read and agreed to the published version of the manuscript.

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