A Thermally Stable, Alkene-Free Palladium Source for Oxidative Addition Complex Formation and High Turnover Catalysis

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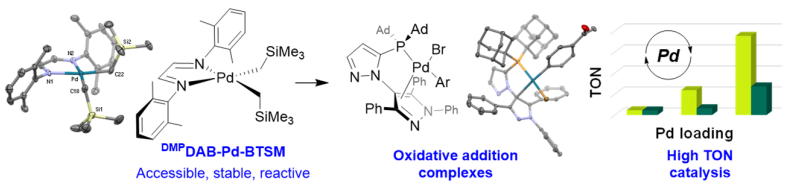
Abstract: Oxidative addition complexes play a crucial role in Pd-catalyzed transformations. They are not only key catalytic intermediates, but are also powerful and robust precatalysts, and effective reactants for late-stage functionalization of complex molecules. However, accessing a given oxidative addition complex is often challenging due to a lack of effective and stable palladium sources with the correct reactivity. Herein, we report an easily prepared and bench stable Pd(II) dialkyl complex, ^{DMP}DAB–Pd–BTSM (BTSM = bis[trimethylsilylmethyl]), that is a versatile precursor for generating Pd(II) oxidative addition complexes, and a highly active Pd source for *in situ* catalyst formation in cross-coupling reactions. A crucial aspect of this structure is the absence of alkene-based stabilizing ligands common to other Pd precursors. We demonstrate the utility of this precursor in the formation of several Pd(II) complexes, including phosphine and diimine-ligated oxidative addition complexes, and in high turnover number catalysis of C–O, Suzuki, and Heck coupling reactions.



Introduction

Palladium-catalyzed cross-coupling reactions continue to be among the most important methods for C–C and C–heteroatom bond formation.[1–3] The canonical catalytic mechanism consists of three general steps — oxidative addition, (trans)metalation, and reductive elimination — where oxidative addition is often the rate- and/or selectivity-determining step.[4–7] Palladium oxidative addition complexes (OACs), generated by R–X addition to Pd^0, play a significant role in cross-coupling catalysis (Figure 1).[6,8–11] In addition to their importance in mechanistic studies of cross-coupling reactions, these complexes are now being exploited as robust and superior (pre)catalysts in specific cases.[12–20] Notably, Buchwald and co-workers have incorporated sterically demanding biarylphosphine ligands in OACs (referred to Buchwald G6 precatalysts) and demonstrated their use for various cross-couplings (**A**).[13,15,18,21] OACs can also be used for late-stage functionalization of complex molecules, offering substantial advantages in drug discovery efforts (**B**).[18]

While using an effectively "on-cycle" species as a precatalyst seems ideal, wider use of OACs has been hampered by synthetic access. OACs are generally synthesized by combining the desired phosphine, R–X, and either Pd_2dba_3 or $(COD)Pd(CH_2SiMe_3)_2$ (**C**, COD = 1,5-cyclooctadiene)), which is a reactive but known to be thermally unstable Pd^{II} complex first reported by Young and co-workers.[22] In addition, **C** can be used to generate specific Pd^0 dimers of the form $[(\mu\text{-COD})Pd(L)]_2$ (**D**). These dimers are active precatalysts in challenging nucleophilic fluorinations as well as precursors to the aforementioned OACs;[18,23–25] However, poor solubility, solution instability, and air sensitivity limit their broader application.[23] Another OAC precursor is $(COD)Pd(CH_2CMe_2C_6H_4)$ (**E**), an air-stable palladacycle first prepared by Cámpora[26] and recently exploited for OAC formation by Buchwald and co-workers.[27] However, its lower reactivity means that pre-treatment of **E** with ligands to generate $[(\mu\text{-COD})Pd(L)]_2$ is required prior to the addition of aryl halides. Finally, a common issue with all of these precursors is that the dissociated alkene (dba or COD) can act as a competitive ligand, resulting in catalyst inhibition and/or challenging formation/ purification of the desired OAC.[28]

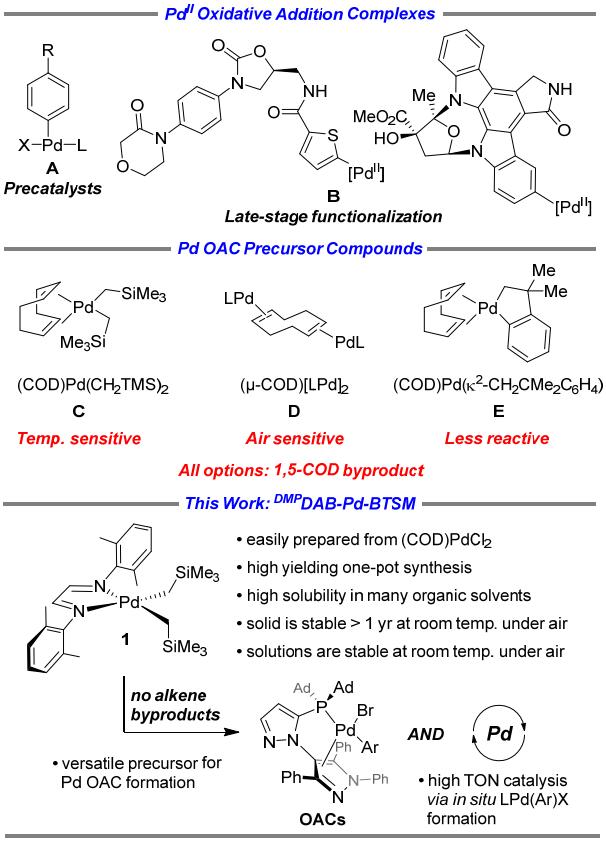


Figure 1. Importance of Pd OACs in catalysis (**A**) and late-stage functionalization (**B**), common precursors to access OACs (**C**-**E**), and new precursor ^{DMP}DAB–Pd–BTSM.

Here, we report an easily prepared, stable, and versatile Pd^{II} dialkyl compound for OAC generation and *in situ* catalyst formation: ^{DMP}DAB–Pd–BTSM (**1**, Figure 1; ^{DMP}DAB = *N*,*N*'-bis(2,6-dimethylphenyl)diazabutadiene; BTSM = bis(trimethylsilylmethyl)). This complex offers several significant advantages over existing Pd^0 and Pd^{II} sources, including high solubility in many organic solvents, thermal/air stability in both solution and the solid state, and the absence of any alkene byproducts upon activation. Complex **1** is effective for the generation of OAC complexes with several ligands, and exhibits high catalyst TONs in Suzuki and Heck couplings when used as in *in situ* catalyst precursor.

Results and Discussion

Synthesis and Characterization of Complex 1

As part of ongoing efforts in our group on precatalyst synthesis[29,30] and oxidative addition reactivity,[6] we sought a general Pd precursor to directly access OACs with no supporting alkene ligands. Inspired by extensive prior work with (α-diimine)Pd^{II} alkyl complexes in the context of alkene polymerization,[31–45] and the favorable ligand substitution chemistry observed for ^{DMP}DAB–Pd–MAH,[29,30] we targeted **1** as a candidate complex. To our surprise, there is only one prior report that discusses an attempt to access α-diimine-supported Pd^{II} complexes featuring $–CH_2SiMe_3$ ligands. Cámpora and co-workers prepared ^{DIPP}DAB–$Pd(CH_3)_2$ (^{DIPP}DAB = bis(2,6-diiso-propylphenyl)diazabutadiene) from $(py)_2Pd(CH_3)_2$ *via* ligand substitution; however, the corresponding ^{DIPP}DAB–$Pd(CH_2SiMe_3)_2$ complex could not be prepared from $(py)_2Pd(CH_2SiMe_3)_2$ due to incomplete ligand substitution and unsuccessful purification.[46] More broadly, there are only a handful of reported $LPd(CH_2SiMe_3)_2$ complexes featuring chelating N–N ligands (L = bipy, phen, TMEDA, and di(2-pyridyl)ketone),[22,47] and only one containing a more complex iminopyridine ligand (characterized only by ^{1}H NMR spectroscopy).[48,49]

Using a ligand substitution strategy, we developed two procedures to synthesize complex **1** (Figure 2A). Simple treatment of $(COD)Pd(CH_2SiMe_3)_2$ with ^{DMP}DAB in THF gives **1** in 96% isolated yield, which only requires a filtration through Celite and vacuum evaporation to remove the COD byproduct. Due to the aforementioned temperature sensitivity (and high cost) of $(COD)Pd(CH_2SiMe_3)$, we explored the potential of a telescoped, one-pot synthesis of **1** from $(COD)PdCl_2$ proceeding through $(COD)Pd(CH_2SiMe_3)_2$ as a non-isolated intermediate. Following the alkylation of $(COD)PdCl_2$ with Me_3SiCH_2MgCl, excess Grignard reagent is quenched with acetone, and the byproduct magnesium salts are complexed and precipitated with 1,4-dioxane. Simple addition of ^{DMP}DAB followed by filtration through Celite and vacuum evaporation gives **1** in 82% isolated yield. Notably, both of these procedures have been validated on 1.0 mmol scale, giving 450-500 mg **1** per batch.

We have fully characterized **1**, including by X-ray crystallography (Figure 2B). The complex exhibits the expected *pseudo* square-planar geometry, with the two aryl groups oriented to reduce steric strain between the *ortho* methyl groups and the $–SiMe_3$ groups of the alkyl ligands. Notably, the complex is darkly colored as a solid and in solution. UV/Vis absorbance spectroscopy reveals a broad, low intensity absorbance peak in the visible region (λ_{max} = 439 nm, ε = 4.69 x 10^3 M^{-1} cm^{-1}, THF), which (by analogy to related systems) may correspond to a transition from a σ(Pd–C) *HOMO* to a π*(α-diimine) *LUMO*.[43] This feature of complex **1** made us aware of potential photoinstability by Pd–C homolytic cleavage.[44,50]

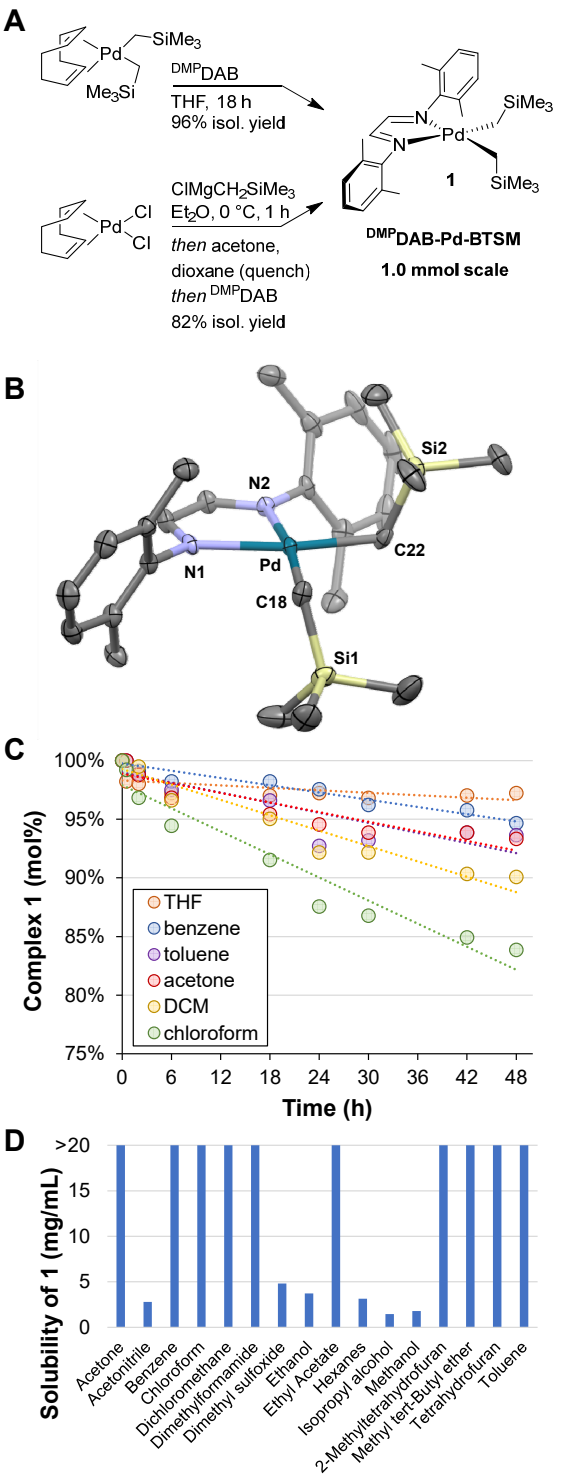


Figure 2. A) Synthesis of **1** *via* two routes, from $(COD)Pd(CH_2SiMe_3)_2$ or one-pot synthesis from $(COD)PdCl_2$ without isolation of intermediate $(COD)Pd(CH_2SiMe_3)_2$. B) Solid-state molecular structure of **1** (atom colors: C, gray; N, light blue; O, red; Si, light yellow; Pd, green/blue; ellipsoids plotted at 50% probability; hydrogen atoms removed for clarity; one of two independent molecules from asymmetric unit shown). C) Solution stability of **1** dissolved in the indicated deuterated solvent (13-14 mg/mL concentration); solutions exposed to air and held at room temperature, with mol% **1** remaining at the indicated time determined by ^{1}H NMR spectroscopy (relative integration versus 1,3,5-trimethoxybenzene as internal standard). D) Solubility of **1** (mg/mL) in various organic solvents determined using UV/Vis absorbance spectroscopy. ≥20 mg/mL indicates **1** is at least this soluble.

Given the known temperature sensitivity of (COD)Pd(CH_2SiMe_3)$_2$,[51] and the aforementioned potential for light sensitivity, we assessed the stability of **1** in both the solid state and in solution. A solid sample of **1** was unchanged after >1 year storage at room temperature under N_2 atmosphere with no precautions to limit light exposure (as judged by ^{1}H NMR spectroscopy); in addition, a solid sample stored under air at room temperature remained unchanged after >1 week. Room temperature solutions of **1** (13-14 mg/mL concentration) in six deuterated solvents (THF, benzene, toluene, acetone, DCM, and chloroform, all used-as-received) were analyzed over time (^{1}H NMR spectroscopy) after exposure to air and with no precautions to limit light exposure (Figure 2C). After 48 hours, >90% of **1** remained intact in all solvent except chloroform (~84% remaining), with the mass balance comprised of $Me_3SiCH_2CH_2SiMe_3$ (presumably generated by C–C reductive elimination).

To assess thermal stability, we heated a solution of **1** in d_6-benzene to 50 °C overnight, and observe ~80% **1** remaining. Decomposition products are free ^{DMP}DAB (~20%) and $Me_3SiCH_2CH_2SiMe_3$ (~20%), as well as Pd metal (observed). Importantly, users can be confident that stock solutions of **1** used within 6-18 hours at room temperature will have >95% of the desired complex still present (other than chloroform).

Finally, we have measured the solubility of **1** in 16 common organic solvents. Importantly for applications in microscale high-throughput experimentation (HTE), we observe >20 mg/mL solubility in all but the most polar solvents (Figure 2D). This enables solution dispensing of **1** in a wide variety of potential reaction solvents. Collectively, the features of complex **1** – ease of synthesis, long term shelf stability, and solubility/stability in key organic solvents – make it especially well-suited to further applications in synthesis and catalysis. It can also be handled without the need for an inert atmosphere glovebox, and does not need to be protected ambient heat or light.

Ligand Substitution and Oxidative Addition Reactivity

With the complex characterized, we sought to assess the potential reactivity benefits of **1** compared to those based on dba or COD supporting ligands. As an initial example, we examined the formation of (Xantphos)Pd(CH_2SiMe_3)$_2$ (**2**). Phosphine-ligated Pd dialkyl complexes are versatile intermediates and catalysts, and are often formed by ligand substitution from (COD)Pd(CH_2SiMe_3)$_2$.[22,52–59] In particular, complex **2** was reported by Ito and co-workers as an effective precatalyst for cross-coupling; however, its synthesis from (COD)Pd(CH_2SiMe_3)$_2$ must be carried out under very specific conditions.[52] Simply mixing equimolar amounts of Xantphos and (COD)Pd(CH_2SiMe_3)$_2$ in THF at room temperature results in exclusive formation of Pd^0(Xantphos)$_2$ as an insoluble product.[60] Successful synthesis of **2** requires diethyl ether solvent, 0 °C, an inert atmosphere and a 20 min reaction time to suppress this premature reduction.

The formation of Pd^0(Xantphos)$_2$ in THF is inconsistent with the observed thermal stability of isolated **2**, which was clearly established by Ito and co-workers.[52] Given these results, we hypothesized that the presence of COD must promote reductive elimination from the initially formed **2** when the reaction is carried out in THF at room temperature. Accordingly, treating **1** with Xantphos in THF at room temperature gives a yellow suspension of complex **2** (identified by ^{1}H and ^{31}P NMR spectroscopy) with no evidence of Pd^0(Xantphos)$_2$ formation. Due to difficulties removing residual THF, we carried out a preparative synthesis of **2** using diethyl ether at room temperature under air, with 68% isolated yield (eq. 1). These results clearly reveal that COD is a non-innocent byproduct of ligand substitution that can induce premature reduction to Pd^0. Use of **1** eliminates this issue, enabling straightforward access to (bisphosphine)Pd(CH_2SiMe_3)$_2$.

Encouraged by the clear benefits in ligand substitution chemistry afforded by **1** over (COD)Pd(CH_2SiMe_3)$_2$, we then assessed **1** as a precursor toward OAC formation using four monophosphine ligands important in cross-coupling reactivity: *t*BuBippyPhos (gives complex **3**), AdBippyPhos (complex **4**), XPhos (complex **5**), and PAd_3 (complex **6**). Simply mixing **1** with 1 equiv of the desired phosphine and 2-3 equivalents of 4-bromoacetophenone or 1-bromo-4-fluorobenzene (for PAd_3) in CPME (or THF for XPhos) at 50 °C under N_2 generates the OACs as determined by ^{1}H and ^{31}P NMR spectroscopy (Figure 4). Each complex was isolated, and new compounds **3**-**5** were fully characterized, including X-ray crystallography. For **3**, **4**, and **6**, the OAC product completely precipitates from CPME within 2 h; simple filtration followed by washing away the ^{DMP}DAB byproduct yields the desired complexes. Isolation of pure complex **5** required THF as the reaction solvent and longer reaction times (24 h), and repeated washing of the crude solid to remove ^{DMP}DAB.

To the best of our knowledge, **4** is the first example of an isolated and characterized OAC based on AdBippyPhos. Moreover, only two OACs based on *t*BuBippyPhos have been reported (again to the best of our knowledge): one in 39% yield from Pd_2dba_3,[61] and the other in 74% yield from (COD)Pd(CH_2SiMe_3)$_2$.[62] Importantly, our synthesis of **3** combines the advantages of the two reported synthetic pathways: high yield, short reaction time, operational convenience, and readily removable byproducts. Complex **6** was first reported by Carrow and co-workers, prepared from the Buchwald G3 mesylate dimer as a Pd source,[20] and more recently Colacot and co-workers reported its synthesis from Cámpora's palladacycle **E**.[19]

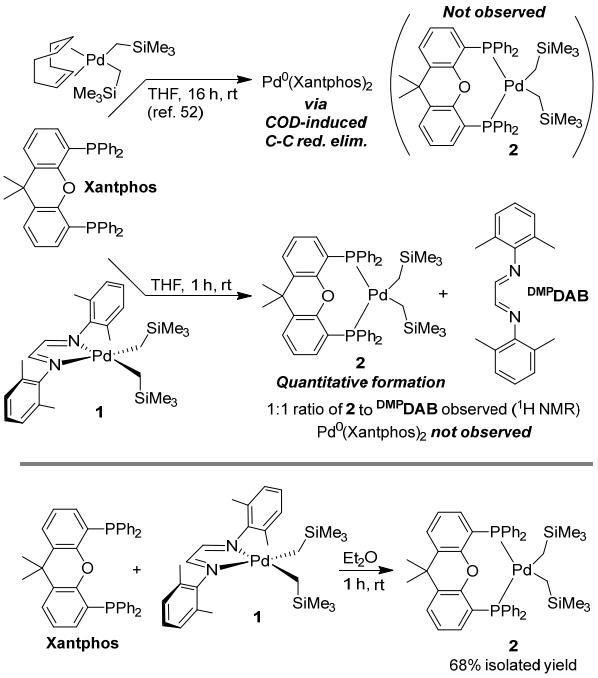


Figure 3. Comparison of (COD)Pd(CH_2SiMe_3)$_2$ and complex **1** for the formation of (Xantphos)Pd(CH_2SiMe_3)$_2$ (**2**) *via* ligand substitution. The former generates Pd^0(Xantphos)$_2$ exclusively (THF, rt),[52] whereas **1** gives the desired complex **2** with no Pd^0(Xantphos)$_2$ observed (THF, rt; 68% isolated yield using Et_2O, rt).

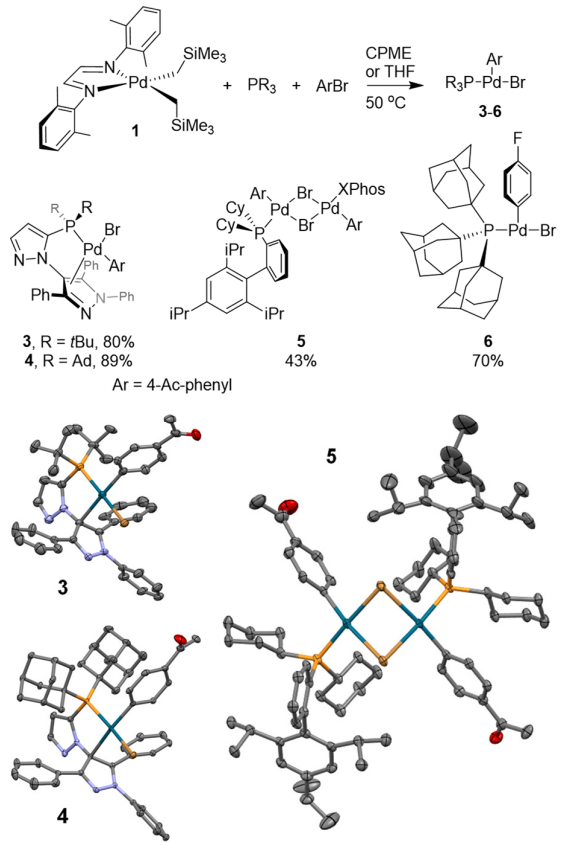


Figure 4. Synthesis and isolation of (phosphine)Pd(Ar)(Br) complexes **3**-**6** using **1** as a Pd source, and solid-state molecular structures of complexes **3**-**5** (atom colors: C, gray; N, light blue; O, red; P, bright orange; Br: dark yellow; Pd, blue; ellipsoids plotted at 50% probability; hydrogen atoms and solvent molecules removed for clarity; one orientation shown of disordered iPr group in **5**).

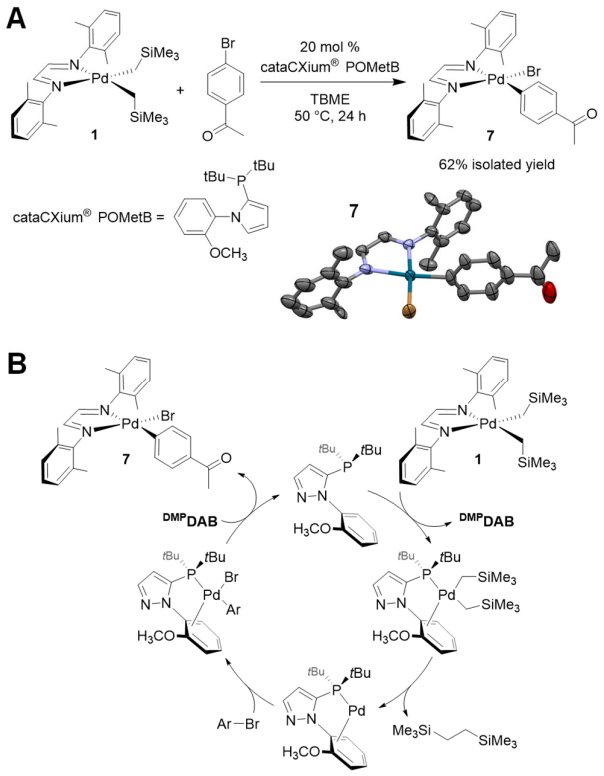


Figure 5. A) Synthesis and isolation of (^{DMP}DAB)Pd(Ar)(Br) complex **7** catalyzed by catacXCium® POMetB, and solid-state molecular structure of **7** (atom colors: C, gray; N, light blue; O, red; Br: dark yellow; Pd, blue; ellipsoids plotted at 50% probability; hydrogen atoms and solvent molecules removed for clarity; complex **7** is disordered over two positions, one of which is shown). B) Proposed mechanism of formation of **7** with catalytic cataCXium® POMetB *via* phosphine-induced reductive elimination to Pd^0, followed by oxidative addition and finally ligand substitution.

In addition to solution phase characterization, we obtained solid-state molecular structures for all three new OACs. Complexes **3** and **4** are isostructural, mononuclear *pseudo* square-planar complexes, with the fourth coordination site occupied by the second pyrazole ring through its π-system; this is analogous to one of the aforementioned *t*BuBippyPhos OACs.[62] In contrast, **5** is observed as a bromide-bridged dimer in the solid-state; we also observed the presence of dimeric molecular ions by ESI-HRMS analysis.

In an effort to explore other ligands to support OACs generated from **1**, we observed an unexpected product when using cataCXium® POMetB in combination with 4-bromoacetophenone (Figure 5). Instead of generating the anticipated (phosphine)Pd(Ar)(Br) complex, we isolated a single species lacking any phosphorus (silent in ^{31}P NMR spectroscopy). The ^{1}H NMR spectrum was instead consistent with ^{DMP}DAB–Pd(Ar)(Br) (**7**), with the α-diimine ligand retained.

Our initial hypothesis was that ligand substitution was too slow in this case, and complex **1** itself underwent C–C reductive elimination and subsequent oxidative addition to form **7**. To test this, we reacted **1** with 4-bromoacetophenone in the absence of phosphine under analogous conditions. Instead of forming **7**, no reaction was observed, with **1** remaining unchanged. We then tested the reaction of **1** and 4-bromoacetophenone with a *catalytic* amount of cataCXium® POMetB (20 mol%), which does enable the formation of **7** in 62% isolated yield (Figure 5A). Complex **7** has been fully characterized, including a disordered solid-state molecular structure that is consistent with the proposed structure. We propose that cataCXium® POMetB catalyzes the formation of **7** according to the mechanism shown in Figure 5B, where liberated ^{DMP}DAB displaces the phosphine from the initially formed (phosphine)Pd(Ar)(Br) OAC. Thus, **1** also provides a starting point for accessing α-diimine ligated OACs, and work is ongoing to identify other ligands that may exhibit similar reactivity.

High Turnover Catalysis Using Complex 1

With the feasibility of *in situ* catalyst activation established from the studies of OAC formation, we then sought to assess the catalytic activity of **1** as a precatalyst for several cross-coupling reactions. While there are a plethora of Pd precursors available to generate active complexes *in situ*, from simple $Pd(OAc)_2$[63] and Pd_2dba_3[64–67] to state-of-the-art complexes,[29,68–75] many systems undergo complex activation mechanisms that rely on the action of external reagents (e.g. reductants),[76–78] and/or generate different catalyst species/mixtures depending on the specific conditions.[79–82] Notably, (COD)Pd^{II} compounds **C** and **E** are only rarely used to generate catalysts *in situ*, despite their use to generate OACs.

To assess the suitability of **1** as a Pd source in catalysis, we investigated representative examples of three reaction classes: C–O coupling, Heck coupling, and Suzuki coupling. Alcohol O-arylation to form a C–O bond is generally challenging *via* Pd catalysis, requiring specific ligands to achieve high activity. We examined the coupling of 4-bromoacetophenone with *n*-butanol in

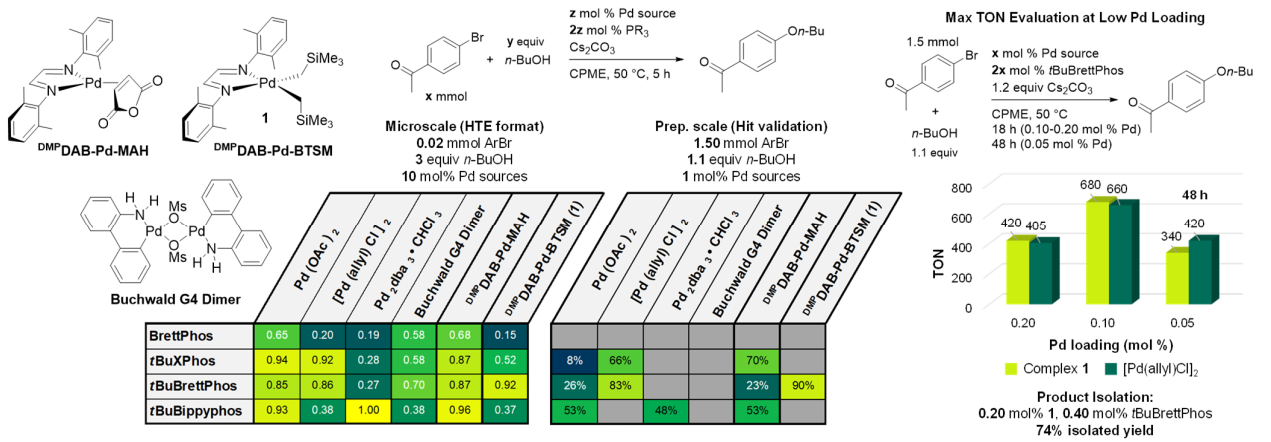


Figure 6. Comparison of complex **1** against other common Pd sources for for C–O coupling between 4-bromoacetophenone and *n*-BuOH. HTE format results are from HPLC analysis, with values representing normalized product peak area versus internal standard. Hit validation and TON evaluation results are solution yields or corresponding TON (TON = [product yield %] / [mol % Pd]) obtained by ^{1}H NMR spectroscopy by integration versus internal standard. See Supporting Information for complete comparison results table.

a 24-experiment microscale (0.020 mmol ArBr) screen under conditions often used for HTE. This enables direct comparison of **1** against our previously reported ^{DMP}DAB–Pd–MAH complex and four other Pd sources for *in situ* catalyst formation and suitability for HTE (Figure 6). Building from a prior screen on this reaction,[29] we investigated 4 ligands (BrettPhos, *t*BuXPhos, *t*BuBrettPhos, and *t*BuBippyPhos) with a 50 °C reaction temperature.

HPLC analysis of the screening experiments reveals several trends. Consistent with our prior screening results, several ligands give either active or inactive catalysts depending on the Pd source used; for example, *t*BuBippyPhos gives high product amounts when paired with $Pd(OAc)_2$, Pd_2dba_3•$CHCl_3$, or ^{DMP}DAB–Pd–MAH, but gives only modest conversion with $[Pd(allyl)Cl]_2$, the Buchwald G4 dimer, or complex **1**. The **1**/*t*BuBippyPhos experiment was repeated several times at this scale, confirming this result. In terms of hit identification, $Pd(OAc)_2$ and ^{DMP}DAB–Pd–MAH appear superior to the other sources at this high Pd loading.

The situation is different when validating the top 10 hits from the microscale screen under more synthetically-relevant conditions (Figure 6). Increasing the reaction scale 75x (1.50 mmol ArBr), and reducing the alcohol amount (1.1 equiv) and catalyst loading (1 mol %) further distinguishes these catalyst systems. Under these conditions, most catalyst systems yield poor to moderate amounts of product; however, two systems stand out with solution yields >80%: **1**/*t*BuBrettPhos (90%) and $[Pd(allyl)Cl]_2$/*t*BuBrettPhos (83%). We then conducted a more detailed comparison of these two Pd sources precursors at very low catalyst loadings to establish a maximum catalytic turnover number (TON = [product yield %] / [mol % Pd]). For both precursors, significant conversion to product is observed even at 0.05 mol %, with maximum catalyst activity achieved at 0.10 mol %. Both $[Pd(allyl)Cl]_2$ and **1** give comparable solution yields of 66% and 68% respectively, corresponding to TONs of 660 and 680. It is therefore likely that these two Pd/ligand mixtures generate the same active species in the same amount. Given the known reactivity of LPd(allyl) species toward oxygen nucleophiles, it is reasonable that the catalyst generated from $[Pd(allyl)Cl]_2$ should be highly active. Clearly, complex **1** is also capable of generating such a highly active catalyst *in situ*. Finally, we used 0.2 mol % **1** in a preparative synthesis of 4-(*n*-butoxy)acetophenone, which was isolated in 74% yield.

Another challenging reaction class for Pd-catalysis is the Heck coupling of (unactivated) aryl chlorides. Littke and Fu reported that Pd_2dba_3/P(*t*Bu)$_3$ is an effective system even for electron-rich aryl chlorides.[83] We therefore assessed the catalytic activity of **1** against both Pd_2dba_3•$CHCl_3$ and $[Pd(allyl)Cl]_2$ in the coupling of 4-chloroanisole with methyl methacrylate (MMA) under analogous conditions (Figure 7). At 2.5 mol % Pd and a 1:1 L-to-Pd ratio, the yield/TON for **1** is more than twice that for Pd_2dba_3•$CHCl_3$, and also higher than $[Pd(allyl)Cl]_2$ (82%, 38%, and 62% respectively). Further reducing the Pd loading to 1 mol % maintains the distinction, with **1** outperforming the other sources. With 1 mol% of **1**, increasing the L-to-Pd ratio to 2:1 and extending the reaction time to 48 h gives 87% yield. Under these conditions, appreciable product is observed even as low as 0.08 mol % Pd, with **1** giving double the TON (350) compared to the other sources. A preparative scale synthesis on 1.0 mmol scale yielded 66% with 1 mol % Pd, which compares favorably to the reported synthesis with 3-fold less Pd (72% yield with 3 mol % Pd).[83]

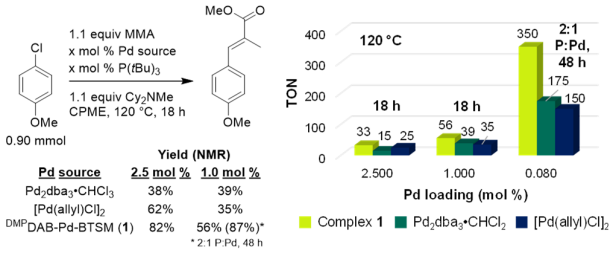


Figure 7. Comparison of complex **1** with Pd_2dba_3•$CHCl_3$ and $[Pd(allyl)Cl]_2$ for *in situ* catalyst formation with P(*t*Bu)$_3$ for Heck coupling. Yields and TON determined by ^{1}H NMR spectroscopy (integration versus internal standard). See Supporting Information for complete comparison results table.

Finally, we examined the Suzuki-Miyaura coupling of 2-chloro-5-methylpyridine with phenylboronic acid. We previously observed that ^{DMP}DAB–Pd–MAH is an inferior precursor to $Pd(OAc)_2$ for this specific reaction, giving only 46% and 86% yield respectively after 2 h at 80 °C under standard biphasic conditions.[29] Using 2 mol % **1** and 4 mol % XPhos under analogous conditions gives 83% yield, comparable to $Pd(OAc)_2$.

To further differentiate between these three precursors, we assessed the extent of reaction under milder conditions (Figure 8). Reducing the Pd loading to 0.5 mol% leads to complete conversion at 80 °C (18 h) for each Pd source; however, at lower temperature (50 °C) and shorter reaction time (1.5 h), ^{DMP}DAB–Pd–MAH fails to yield appreciable product (5% yield), whereas both $Pd(OAc)_2$ and **1** give >50% yield (TON > 100). At even lower Pd loading, complex **1** significantly outperforms $Pd(OAc)_2$: at 0.100 mol % Pd, **1**/XPhos gives 59% yield (TON = 590) after 5 h, whereas $Pd(OAc)_2$/XPhos only gives 16% yield (TON = 160). This distinction is maintained at 0.025 mol % Pd, where **1**/XPhos has a maximum TON of 1880 after 48 h (47%), while the $Pd(OAc)_2$/XPhos TON is 680 (17% yield). Finally, a preparative scale synthesis (3.00 mmol) of 2-phenyl-5-methylpyridine using **1**/XPhos (0.10 mol % Pd, 0.2 mol % XPhos) at 50 °C for 24 h gave 66% isolated yield. These results compare well with other reported low catalyst loading systems (≤ 0.1 mol %) for Suzuki-Miyaura couplings with aryl chlorides, which generally require supported Pd catalysts,[84,85] specific surfactant additives,[86,87] and/or highly activated substrates.[88]

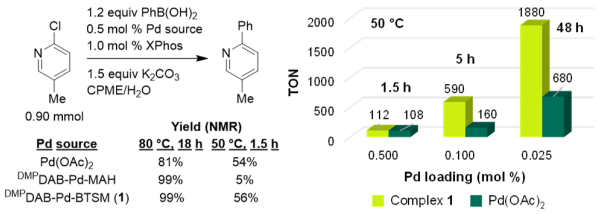


Figure 8. Comparison of complex **1** with ^{DMP}DAB–Pd–MAH and $Pd(OAc)_2$ for *in situ* catalyst formation with XPhos for Suzuki coupling. Yields and TON determined by ^{1}H NMR spectroscopy (integration versus internal standard). See Supporting Information for complete comparison results table.

Conclusion

In summary, we developed an easily prepared, bench-stable, and versatile Pd^{II} dialkyl complex (**1**) suitable for OAC generation and cross-coupling catalysis. Complex **1** is thermally stable and can be handled without the need for a glovebox. It also exhibits good solution stability in a range of solvents over two days at room temperature under air, which is more than long enough to permit solution dispensing in many applications. Successful isolation of the known complex XantPhos–Pd–$(CH_2SiMe3)_2$ as well as several OACs demonstrates that **1** is an effective, alkene-free alternative to $(COD)Pd(CH_2SiMe3)_2$. Furthermore, **1** is also an excellent precursor for *in situ* catalyst formation when combined with a phosphine ligand, as demonstrated by high TON catalysis for C–O, Heck, and Suzuki-Miyaura couplings. Complex **1** exhibits equivalent or superior catalytic activity compared to common Pd sources. Its solubility and stability make it well-suited to solution-based HTE experiments, and its high activity should enable practical synthesis with low Pd loadings.

Acknowledgements

We acknowledge and respect the Lək̓ʷəŋən (Songhees and Esquimalt) Peoples on whose territory the university stands, and the Lək̓ʷəŋən and W̱SÁNEĆ Peoples whose historical relationships with the land continue to this day. We also thank NSERC (Discovery Grant, Idea2Innovation Grant) for operating funds.

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