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Design of a Versatile and Improved Precatalyst Scaffold for Palladium-Catalyzed Cross-Coupling: (η^3-1-^{t}Bu-indenyl)$_2$(μ-Cl)$_2$Pd$_2$

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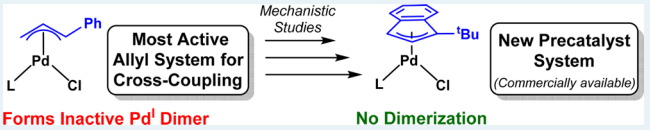
Supporting Information

ABSTRACT: We describe the development of (η^3-1-^{t}Bu-indenyl)$_2$(μ-Cl)$_2$Pd$_2$, a versatile precatalyst scaffold for Pd-catalyzed cross-coupling. Our new system is more active than commercially available (η^3-cinnamyl)$_2$(μ-Cl)$_2$Pd$_2$ and is compatible with a range of NHC and phosphine ligands. Precatalysts of the type (η^3-1-^{t}Bu-indenyl)Pd(Cl)(L) can either be isolated through the reaction of (η^3-1-^{t}Bu-indenyl)$_2$(μ-Cl)$_2$Pd$_2$ with the appropriate ligand or generated in situ, which offers advantages for ligand screening. We show that the (η^3-1-^{t}Bu-indenyl)$_2$(μ-Cl)$_2$Pd$_2$ scaffold generates highly active systems for a number of challenging cross-coupling reactions. The reason for the improved catalytic activity of systems generated from the (η^3-1-^{t}Bu-indenyl)$_2$(μ-Cl)$_2$Pd$_2$ scaffold compared to (η^3-cinnamyl)$_2$(μ-Cl)$_2$Pd$_2$ is that inactive Pd^I dimers are not formed during catalysis.



KEYWORDS: *cross-coupling, catalysis, palladium, precatalyst, Suzuki−Miyaura reaction, Buchwald−Hartwig reaction, α-arylation, DFT calculations*

INTRODUCTION

Pd-catalyzed cross-coupling has found applications in diverse areas of chemistry and is one of the most powerful and general synthetic methods.[1] A recent advance has been the development of specialized phosphine and NHC-based ligands,[2] which can promote the fundamental steps in catalysis such as oxidative addition and reductive elimination. The use of these ligands has resulted in an expanded substrate scope, milder reaction conditions, and lower catalyst loadings. However, these specialized ligands often have comparable expense with respect to the Pd precursor, which means that the traditional route for generating the active species, addition of excess ligand to a Pd^0 precursor, is not attractive. Furthermore, in many cross-coupling reactions the optimal Pd to ligand ratio is 1:1, and the active species is proposed to be monoligated Pd^0.[3] As a result, a number of well-defined Pd^{II} precatalysts with a 1:1 Pd to ligand ratio, such as Buchwald's palladacycles,[4] Organ's PEPPSI complexes[5] and Nolan's allyl-based systems[6] (Figure 1) have been developed and are now commercially available.

A major advantage of both the Buchwald and Nolan systems is the accessibility of the ligand-free precursors, (2-aminobiphenyl)$_2$(μ-OMs)$_2$Pd$_2$ or (η^3-cinnamyl)$_2$(μ-Cl)$_2$Pd$_2$, respectively, which can be converted into the ligated precatalyst in situ. This allows for a variety of different ligands to be rapidly screened, without the need for the isolation of well-defined precatalysts. At this stage, Buchwald precatalysts are more commonly utilized than Nolan-type systems, but they have not been used with NHC ligands, which generate superior catalysts for a number of cross-coupling reactions.[1h] In contrast, Nolan-type systems are compatible with both NHC and phosphine ligands, which is advantageous for ligand screening.

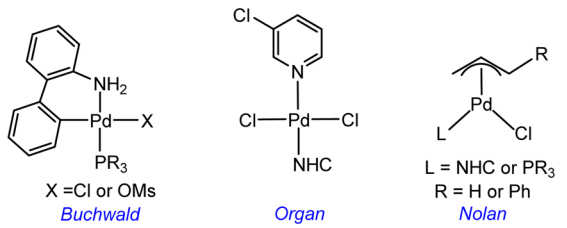


Figure 1. Three well-defined precatalyst scaffolds with a 1:1 Pd to ligand ratio that are commercially available.

Recently, we investigated the activation of Nolan-type (η^3-allyl)Pd(Cl)(L) precatalysts.[7] We established that even in the case of the highly efficient (η^3-cinnamyl)Pd(Cl)(IPr) (**Cin-IPr**; IPr = 1,3-Bis(2,6-diisopropylphenyl)-1,3-dihydro-2H-imidazol-2-ylidene) precatalyst, some of the IPr−Pd^0 active species undergoes comproportionation with unactivated Pd^{II} precatalyst to form an unreactive Pd^I dimer, (μ-cinnamyl)(μ-Cl)Pd$_2$(IPr)$_2$, instead of entering the catalytic cycle (Figure 2).[7a] This mechanistic insight prompted us to seek a related precatalyst scaffold that does not undergo unproductive Pd^I dimer formation, and here we report that our efforts have

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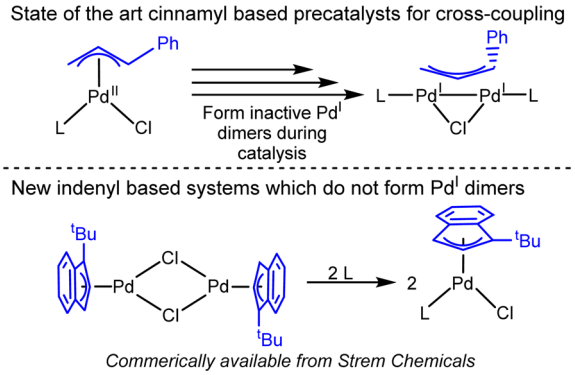


Figure 2. Comparison of state-of-the-art cinnamyl-based precatalysts with the new indenyl-based systems developed in this work.

resulted in the discovery of $(\eta^3$-1-^{t}Bu-indenyl$)_2(\mu$-Cl$)_2$Pd$_2$ (Figure 2), a highly efficient precatalyst scaffold for cross-coupling. In this work, we summarize our precatalyst development efforts, and we illustrate that our new scaffold produces highly active systems for a wide range of challenging cross-coupling reactions. Our new precatalyst scaffold is compatible with both NHC and phosphine ligands, and catalytically active systems can be generated either starting from isolated complexes of the type $(\eta^3$-1-^{t}Bu-indenyl)Pd(Cl)(L) or by generating these species in situ. The dimeric precursor $(\eta^3$-1-^{t}Bu-indenyl$)_2(\mu$-Cl$)_2$Pd$_2$ as well as complexes of the type $(\eta^3$-1-^{t}Bu-indenyl)Pd(Cl)(L) with several different ligands are now commercially available from Strem Chemicals.[8]

RESULTS AND DISCUSSION

Synthesis, Preliminary Catalytic Results, and Mechanism. Our previous work on Nolan's $(\eta^3$-allyl)Pd(IPr)(Cl) precatalysts demonstrated that the addition of steric bulk to the 1-position of the η^3-allyl ligand reduces Pd^I dimer formation, which in part explains the efficiency of the **Cin-IPr** precatalyst.[7a] We hypothesized that the use of a di- or trisubstituted allyl ligand may completely suppress dimer formation. Indenyl and 1-substituted indenyl ligands represent simple di- or trisubstituted allyl ligands,[9] which are synthetically accessible. Therefore, the monomeric indenyl series of precatalysts, $(\eta^3$-1-R-indenyl)Pd(IPr)(Cl) (R = H (**2a-IPr**), Me (**2b-IPr**), ^{i}Pr (**2c-IPr**) or ^{t}Bu (**2d-IPr**)), were synthesized using a robust and scalable sequence of reactions (Scheme 1). The dimeric precursors, $(\eta^3$-1-R-indenyl$)_2(\mu$-Cl$)_2$Pd$_2$ (R = H (**1a**), Me (**1b**), ^{i}Pr (**1c**) or ^{t}Bu (**1d**)), were formed through an allylic hydrogen abstraction[10] of the appropriate indene precursors by Pd under mildly basic conditions. Subsequently, the monomeric $(\eta^3$-1-R-indenyl)Pd(IPr)(Cl) precatalysts were generated by reacting these dimeric complexes with IPr. The new complexes **2b-IPr**, **2c-IPr** and **2d-IPr** were fully characterized, and their solid-state structures (see SI) are similar to that previously described for **2a-IPr**.[11] Our reaction sequence enabled the synthesis of the new indenyl complexes in high yield without the use of a glovebox, and the scalability of the protocol was demonstrated through the preparation of **1d** on a 20 g scale and of **2d-IPr** on a 10 g scale (see SI).

The indenyl complexes **2a-IPr**, **2b-IPr**, **2c-IPr**, and **2d-IPr** were screened as precatalysts for the Suzuki–Miyaura (SM) reaction of 4-chlorotoluene with phenylboronic acid, using both weak (K_2CO_3) and strong (KO^{t}Bu) base in a 19:1 MeOH/THF mixture (Figure 3).[12] For comparison, both Nolan's **Cin-IPr** and Organ's (3-chloropyridine)Pd(Cl)$_2$(IPr) (**PEPPSI-IPr**) precatalysts were included. The same trends in precatalyst performance were observed under both sets of reaction conditions. All of the indenyl-supported precatalysts are more active than **Cin-IPr**, and both **2c-IPr** and **2d-IPr** are also significantly more active than **PEPPSI-IPr**. Strikingly, the indenyl-supported precatalysts become more active as the size of the substituent on the indenyl ligand is increased, with **2d-IPr** being the most efficient system.

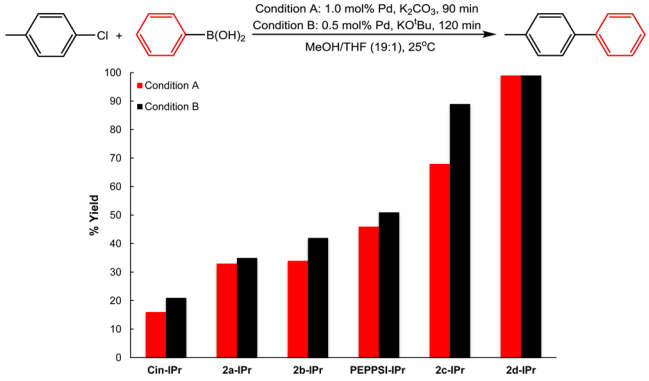
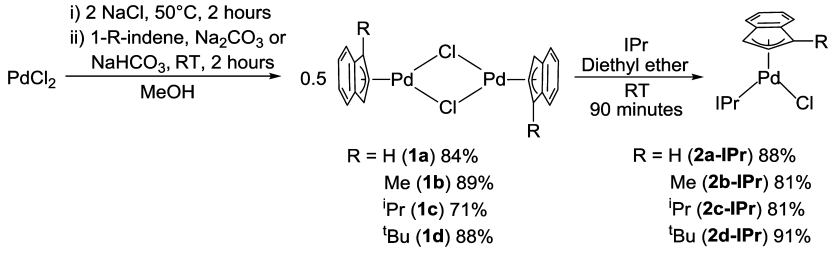


Figure 3. GC yields of product for the SM reaction catalyzed by **Cin-IPr**, **PEPPSI-IPr**, **2a-IPr**, **2b-IPr**, **2c-IPr**, and **2d-IPr**.

A possible explanation for the trend seen in Figure 3 is that the formation of unreactive Pd^I dimers is less likely to occur with more sterically demanding substituents. To probe this, the tendency of **2a-IPr** and **2d-IPr** to dimerize was examined. Treatment of **2a-IPr** with K_2CO_3 in MeOH at RT resulted in the rapid formation of the unsubstituted indenyl dimer **3** in 85% yield, indicating that dimer formation is facile (eq 1). This is the same synthetic protocol we previously used to prepare Pd^I dimers with one bridging allyl ligand and one bridging chloride ligand.[7a] Compound **3** was fully characterized, including by X-ray crystallography (see SI), and the binding of the indenyl ligand is similar to that observed in other Pd^I dimers supported by a bridging indenyl ligand.[13] In contrast to **2a-IPr**, no dimer formation was observed when **2d-IPr** was

Scheme 1. Synthesis and Yields of Indenyl Precatalyst Scaffold and IPr-Supported Precatalysts



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treated with K_2CO_3 (eq 2). Instead, only Pd^0 products, such as $Pd(IPr)_2$,[14] were observed in the reaction mixture. This observation is consistent with Pd^I dimer formation via comproportionation being more difficult for indenyl systems with greater steric bulk.

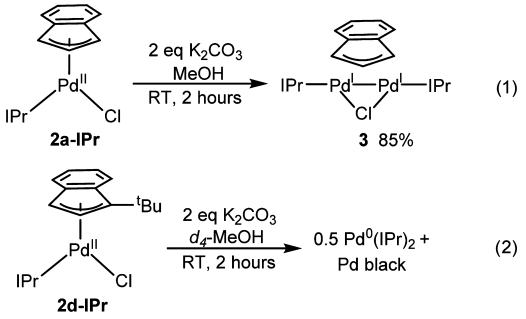
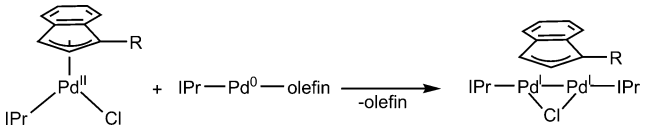


Table 1. Calculated Gibbs Energies in MeOH for Comproportionation of 2a-IPr, 2b-IPr, 2c-IPr, and 2d-IPr with the Appropriate Pd^0 Olefin Complex To Form a Pd^I Dimer and the Free Olefin[a]



Pd^{II} monomer	olefin	$\Delta G°_{MeOH}$ (kcal mol^{-1})
2a-IPr	indene	−9.4
2b-IPr	1-Me-indene	−2.0
2c-IPr	1-^{i}Pr-indene	1.8
2d-IPr	1-^{t}Bu-indene	2.6

[a]See SI for computational details.

The relevance of the Pd^I dimer **3** to catalysis was confirmed by performing a reaction under slightly modified catalytic conditions to those described in Table 1, using 4 mol % **2a** (see SI). ^{1}H NMR spectroscopy indicated that **3** was present during the catalytic reaction, and once full conversion was achieved, approximately 85% of the Pd was in the form of the Pd^I dimer. The deleterious nature of this dimerization was confirmed by testing **3** as a precatalyst for the SM coupling using the reaction conditions described in Figure 3. Complex **3** is inactive as a precatalyst under these conditions (see SI). Thus, **3** represents an off-cycle deactivation product, which reduces the amount of the active monoligated Pd^0 catalyst in solution.

Our proposed pathway for Pd^I dimer formation (see SI for full pathway) involves initial activation of the Pd^{II} precatalyst to generate a Pd^0 olefin complex. This Pd^0 complex can then comproportionate with the starting Pd^{II} species to generate a Pd^I dimer (Table 1). DFT calculations were performed to explore the thermodynamics of comproportionation of **2a-IPr**, **2b-IPr**, **2c-IPr**, and **2d-IPr** with the appropriate Pd-olefin complex to form the corresponding Pd^I dimer (Table 1). As the bulk of the 1-substituent of the indene ligand is increased, dimer formation becomes less favorable. For example, the formation of **3** from **2a-IPr** is thermodynamically favorable, consistent with **3** being isolable. However, the generation of a Pd^I dimer from **2d-IPr** and a Pd^0 complex with a 1-^{t}Bu-indene ligand is endoergic. This is due to the distortion of the metal core required to accommodate the 1-^{t}Bu substituent, which otherwise would introduce steric clashes with the ^{i}Pr substituents of the IPr ligand (for more information, see NBO and NCIPLOT calculations in the SI). These calculations are in agreement with our inability to synthetically access a Pd^I dimer with a bridging 1-^{t}Bu-indenyl ligand. We conclude from these results that one of the main features explaining the superior catalytic activity of **2d-IPr** is the absence of the deactivation pathway shown in Table 1.

Further Catalytic Reactions with NHC-Supported Complexes. A head-to-head comparison was performed between **2d-IPr** and the commercially available **Cin-IPr** for the SM reaction of a range of substrates using both weak (Figure 4) and strong base (see SI). The newly designed **2d-IPr** significantly outperforms **Cin-IPr** in all of these examples, including substrates with deactivating electron-donating groups and substituents in the *ortho* positions. The improvement from **Cin-IPr** to **2d-IPr** is most pronounced using a weak base

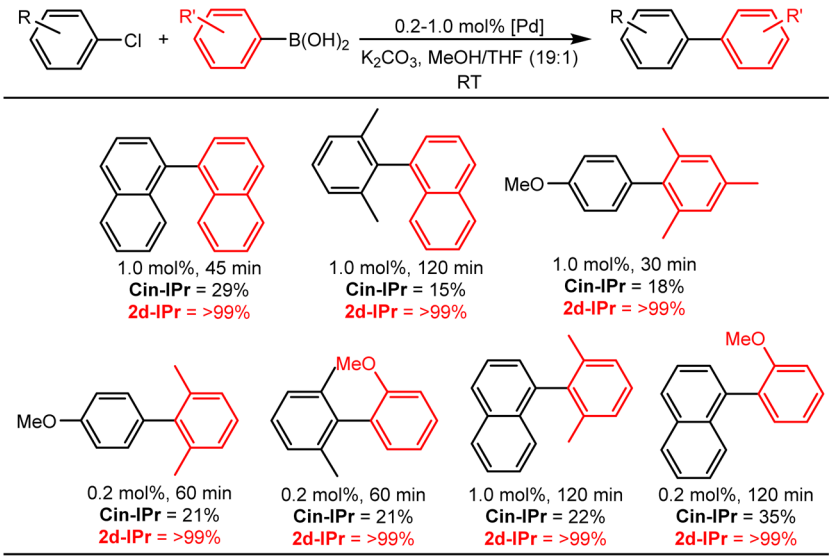


Figure 4. Yields of product for a series of SM reactions catalyzed by **Cin-IPr** and **2d-IPr**. ArCl (0.50 mmol), $ArB(OH)_2$ (0.53 mmol), K_2CO_3 (0.75 mmol), **Cin-IPr** or **2d-IPr** (0.20 or 1.0 mol %), MeOH (0.95 mL), THF (0.05 mL); GC yields average of two runs.

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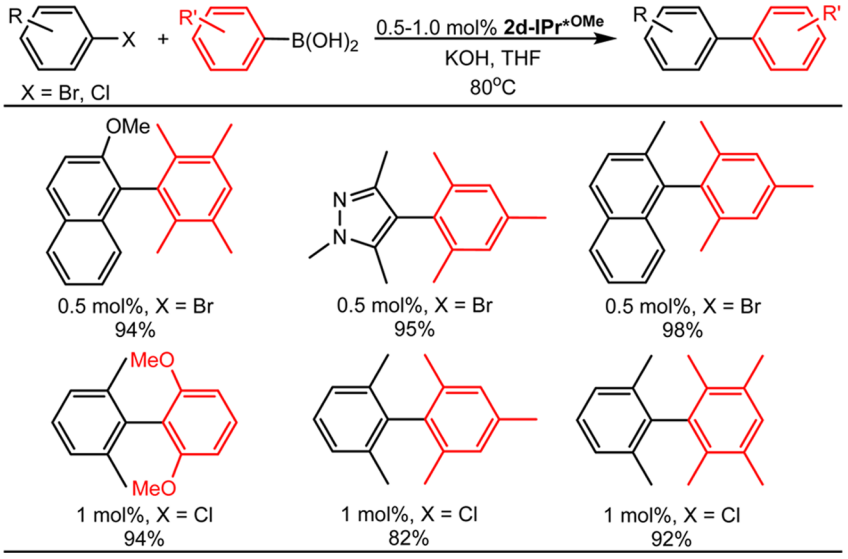

Figure 5. Yields of product for a series of SM reactions to generate tetra-*ortho*-substituted biaryl products catalyzed by **2d-IPr*^{OMe}**. ArX (0.50 mmol), $ArB(OH)_2$ (0.75 mmol), KOH (1.0 mmol), **2d-IPr*^{OMe}** (0.5 or 1.0 mol %), THF (1.0 mL); isolated yields average of two runs.

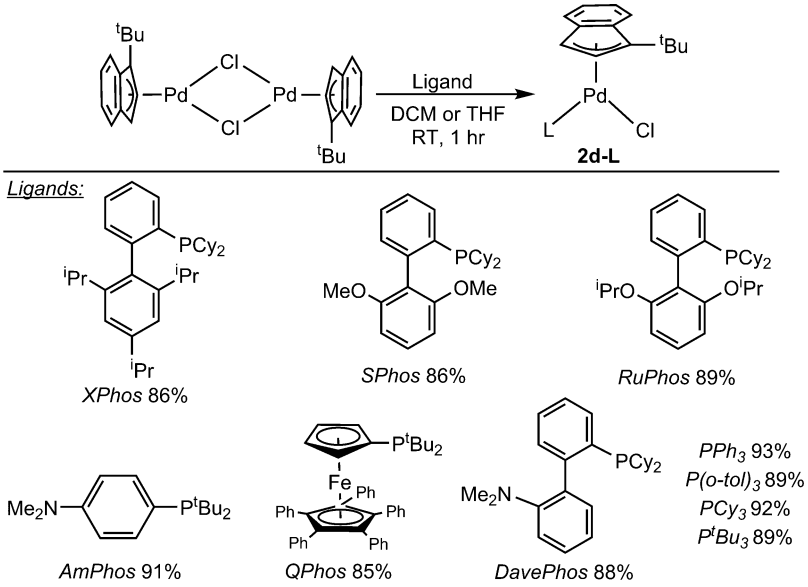

Figure 6. Preparation and yields of phosphine-supported precatalysts.

compared to a strong base. The quantitative yields obtained with **2d-IPr** using weak base are unprecedented with Nolan-type precatalysts at RT.[7a]

To show that our new precatalyst scaffold is compatible with state of the art NHC ligands, SM reactions which generate tetra-*ortho*-substituted biaryl products were performed (Figure 5). For this type of challenging reaction, it has been demonstrated that the sterically hindered ancillary ligand IPr*^{OMe} (IPr*^{OMe} = 1,3-bis(2,6-bis(diphenylmethyl)-4-methoxyphenyl)imidazol-2-ylidene) is required.[15] The complex **2d-IPr*^{OMe}** was prepared through the reaction of IPr*^{OMe} with **1d** (see SI). Using **2d-IPr*^{OMe}** as a precatalyst, a number of tetra-*ortho*-substituted products were prepared in high yield. When aryl bromides were used as substrates, reactions could be performed at lower temperature (80 °C), compared to cinnamyl systems supported by IPr*^{OMe}.[15a] Furthermore, by increasing the catalyst loading to 1.0 mol %, aryl chlorides could be used as substrates under the same reaction conditions. We believe that this method utilizes the mildest conditions reported to produce tetra-*ortho*-substituted products in high yields using aryl chlorides.

Catalytic Reactions with Phosphine-Supported Complexes. Encouraged by our results with NHC ligands, we turned our attention to expanding the ligand scope to include phosphines. Many important cross-coupling reactions are facilitated through the use of electron-rich, sterically demanding phosphines.[1e] To this end, a family of phosphine-ligated complexes with the general structure (η^3-^{t}Bu-indenyl)Pd(L)(Cl) were synthesized (Figure 6).[16] Coordination was achieved through the addition of 2 equivs of ligand to the dimeric precursor, **1d**, to afford a variety of precatalysts with excellent yields (see SI). A number of state-of-the-art ligands, including several Buchwald-type phosphines, were successfully coordinated to the dimeric scaffold.

With these complexes in hand, we screened the phosphine-supported systems for several currently challenging cross-

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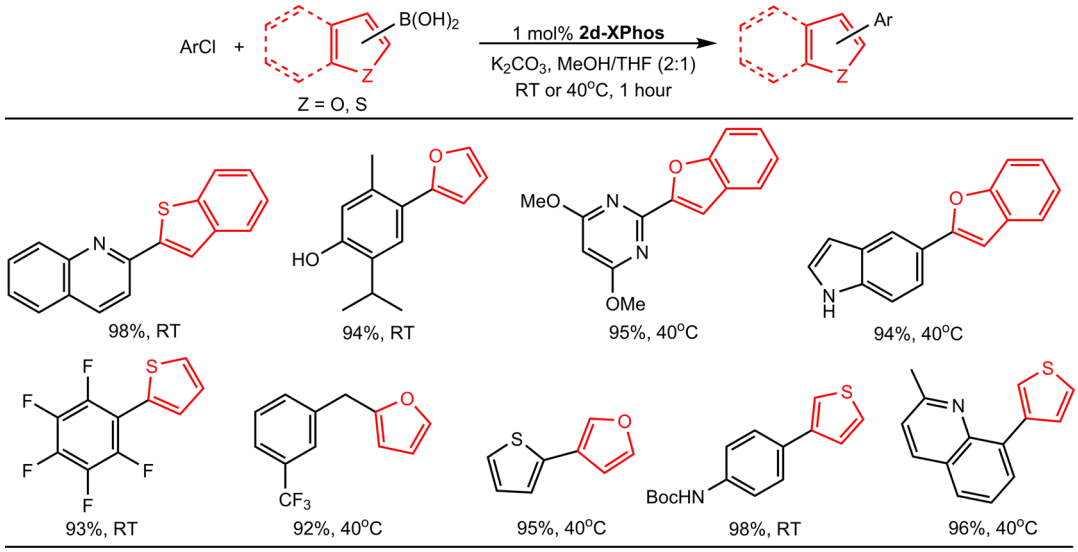

Figure 7. Yields of products for SM reactions involving 2-heterocyclic boronic acids. ArCl (1.0 mmol), $ArB(OH)_2$ (1.5 mmol), K_2CO_3 (2.0 mmol), **2d-XPhos** (1.0 mol %), MeOH (4 mL), THF (2 mL); isolated yields average of two runs.

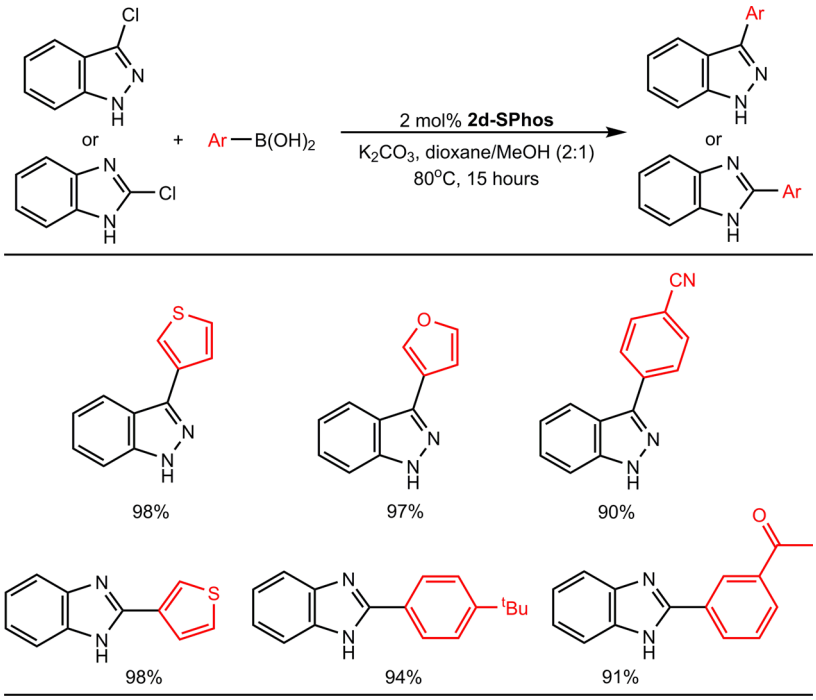

Figure 8. Yields of products for SM reactions involving unprotected indazoles or benzimidazoles. ArCl (1.0 mmol), $ArB(OH)_2$ (2.0 mmol), K_2CO_3 (2.0 mmol), **2d-SPhos** (2.0 mol %), 1,4-dioxane (4 mL), MeOH (2 mL); isolated yields average of two runs.

coupling reactions. Heterocycles are commonly found in pharmaceuticals and natural products but traditionally represent difficult substrates for cross-coupling.[1e,17] For example, SM reactions that employ boronic acids in the 2-position of 5-membered heterocycles are particularly challenging due to their tendency to undergo rapid protodeboronation.[4b] Therefore, a rapid and efficient precatalyst must be used to afford full conversion to product. Using **2d-XPhos** as the precatalyst, we were able to successfully couple a range of 2-heterocyclic boronic acids to produce biaryl products in excellent yields under mild reaction conditions (Figure 7). Our precatalyst, which gives comparable if not superior performance to the best known systems for this reaction,[4b] is also tolerant to a wide range of functional groups on the aryl chloride, including phenols, Boc-protected anilines, and free amines.

Until recently, Pd-catalyzed cross-coupling methodology was not compatible with substrates containing acidic, free N—H moieties. In 2013, the Buchwald group reported drastic improvements for the coupling of indazoles, benzimidazoles, pyrazoles, indoles, oxindoles, and azaindoles using their SPhos-supported palladacycle.[18] Employing **2d-SPhos** under similar conditions, we obtained yields of greater than 90% for reactions where the aryl chloride was either indazole or benzimidazole (Figure 8). With our catalyst system, the temperature could be lowered slightly (80 °C), with excellent yields obtained in 15 h.

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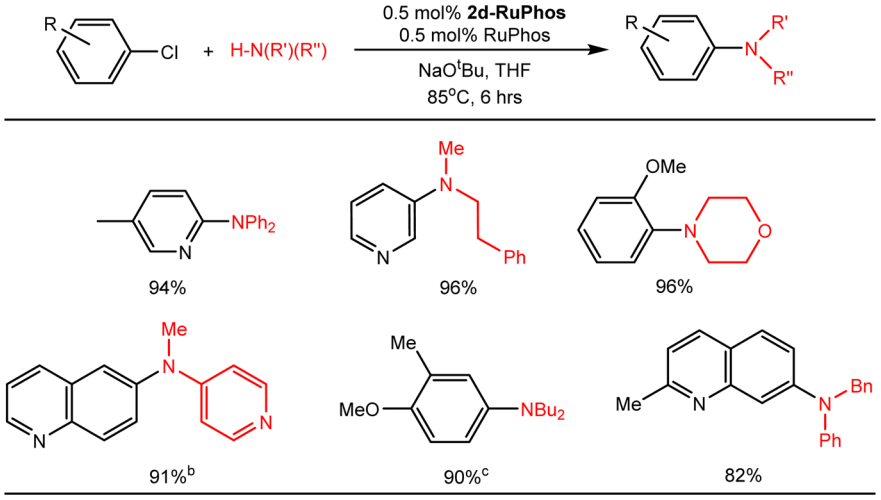

Figure 9. Yields of products for Buchwald-Hartwig reactions involving secondary amines. ArCl (1.0 mmol), amine (1.2 mmol), NaO^{t}Bu (1.2 mmol), **2d-RuPhos** (0.5 mol %), RuPhos (0.5 mol %), THF (1 mL); isolated yields average of two runs. Notes (see figure): used **2d-XPhos**[(b)]; used ArBr[(c)].

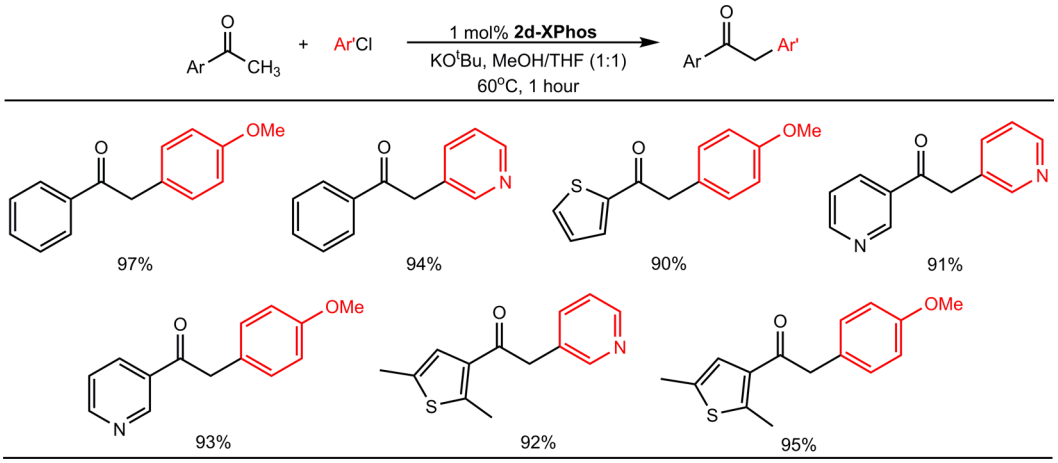

Figure 10. Yields of products from α-arylation of aryl methyl ketones. ArCl (0.53 mmol), ketone (0.5 mmol), KO^{t}Bu (1.2 mmol), **2d-XPhos** (1.0 mol %), THF (4 mL), MeOH (1 mL); isolated yields average of two runs.

As described previously, this methodology also supports the use of heteroaromatic boronic acids.

After the SM reaction, the Buchwald−Hartwig coupling is the next most commonly performed cross-coupling reaction in the synthesis of pharmaceuticals.[17] The RuPhos ligand has allowed for substantial decreases in catalyst loading for challenging secondary amine substrates.[4c] Using reaction conditions similar to those in the literature,[4c] **2d-RuPhos** is able to generate a selection of symmetrical and unsymmetrical tertiary amines in good to excellent yield (Figure 9). Various aryl chlorides containing heteroatoms and *ortho*-substituents are compatible with our system.

The monoarylation of aryl methyl ketones is important due to the prevalence of α-aryl carbonyl moieties in organic compounds with interesting pharmacological and biological properties.[19] However, this is a challenging reaction due to the possibility for diarylation of the ketone. The XPhos ligand has been shown to promote formation of the monoarylated product.[20] Using **2d-XPhos**, we observed excellent results for the monoarylation of a variety of methyl ketones under moderate conditions (Figure 10). Using a 1:1 THF/MeOH mixture and KO^{t}Bu as base, heterocyclic moieties in both the aryl chloride and aryl methyl ketone were tolerated with yields greater than 90% in each case. In fact, in two cases, the products contained heterocyclic fragments in both coupling partners.

A very recent and important advance in cross-coupling has been the utilization of unactivated alkyl coupling partners.[21] In particular, alkyl trifluoroboronates have shown promise as boronic acid mimics for the SM reaction with aryl chlorides.[22] At this stage, good yields require high catalyst loadings (5−10 mol %), high temperatures (100 °C), and long reaction times (24−48 h). By using **2d-P^{t}Bu$_3$** as the precatalyst, we were able to make sizable improvements on the existing protocol. Specifically, in some cases, catalyst loadings could be reduced to 1 mol % and shorter reaction times (8 h) utilized. Using **2d-P^{t}Bu$_3$**, both linear and cyclic alkyl trifluoroboronates salts could be coupled to a variety of aryl chlorides, including one example of a nitrogen-containing heterocycle (Figure 11). In fact, when potassium cyclopropyl trifluoroboronate was used, the temperature could be lowered to 40 °C without any loss in activity (96% yield, see SI).

Finally, to demonstrate that (η^3-1-^{t}Bu-indenyl)$_2$(μ-Cl)$_2$Pd$_2$ (**1d**) is suitable for rapid ligand screening, without the need for the isolation of well-defined precatalysts, we performed a series of catalytic reactions using an in situ-generated solution of **1d** and 2 equivs of ligand (see SI). When **1d** was mixed with the

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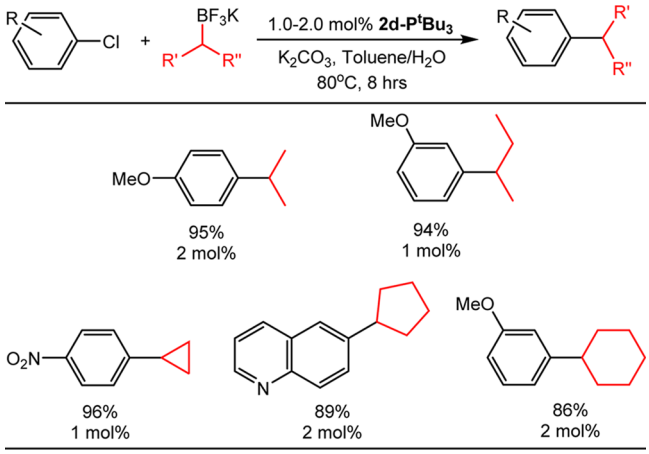


Figure 11. Yields of products for SM reactions involving alkyl trifluoroborates. ArCl (0.5 mmol), BF_3K (0.75 mmol), K_2CO_3 (1.5 mmol), **2d-P^{t}Bu$_3$** (1.0−2.0 mol %), toulene (1.0 mL), H_2O (0.5 mL); isolated yields average of two runs.

appropriate ligand for 10 min at RT, excellent activity was observed for all of the different reactions described in this work with isolated precatalysts. Comparative experiments between systems containing **1d** and IPr as well as Nolan's cinnamyl dimer and IPr showed that superior catalytic activity was observed with **1d** (see SI). Taking this one step further, a successful reaction was achieved without premixing **1d** and ligand; eq 3 shows a one-pot SM reaction where the precatalyst is generated during the reaction. Under these conditions, there is no loss in activity compared to both the in situ-generated and isolated versions of **2d-XPhos**. This methodology should allow access to a variety of general and rapid screening procedures.

CONCLUSIONS

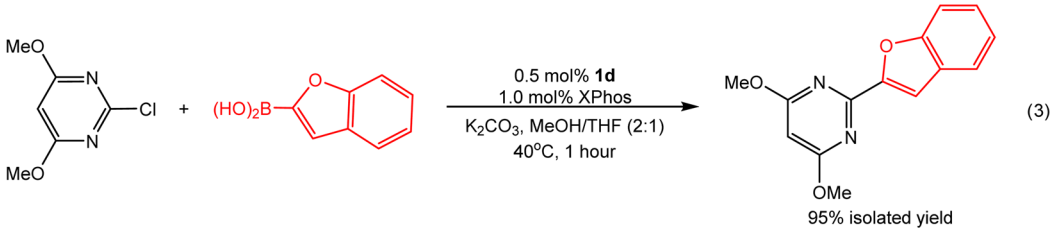
In conclusion, we have developed a highly active precatalyst scaffold for cross-coupling, which is compatible with both NHC and phosphine ligands. The inability of precatalysts formed from our $(\eta^3$-1-^{t}Bu-indenyl$)_2(\mu$-Cl$)_2$Pd$_2$ scaffold to generate unreactive Pd^I dimers significantly improves the activity of these systems compared to Nolan's commercially available cinnamyl precatalysts. Indeed, precatalysts based on our new scaffold are either the most active systems reported to date or comparable to the best systems for a number of challenging cross-coupling reactions. On the basis of the preliminary study of challenging reactions reported herein, we expect that the 1-^{t}Bu-indenyl scaffold will have wide-ranging utility for many dfferent cross-coupling and related reactions that involve monoligated Pd^0.

EXPERIMENTAL SECTION

General Methods. Experiments were performed under a dinitrogen atmosphere in an M-Braun drybox or using standard Schlenk techniques unless otherwise stated. Under standard glovebox conditions purging was not performed between uses of diethyl ether, pentane, benzene, toluene, and THF; thus, when any of these solvents were used, traces of all these solvents were in the atmosphere and could be found intermixed in the solvent bottles. Moisture- and air-sensitive liquids were transferred by stainless steel cannula on a Schlenk line or in a drybox. Pentane, THF, diethyl ether, and toluene were dried by passage through a column of activated alumina followed by storage under dinitrogen. All commercial chemicals were used as received except where noted. MeOH (J.T. Baker) and ^{i}PrOH (Macron Fine Chemicals) were not dried but were degassed by sparging with dinitrogen for 1 h and stored under dinitrogen. Ethyl acetate (Fisher Scientific) and hexanes (Macron Fine Chemicals) were used as received. Potassium *tert*-butoxide (99.99%, sublimed) was purchased from Aldrich. Potassium carbonate was purchased from Mallinckrodt and ground up with a mortar and pestle and stored in an oven at 130 °C prior to use. Flash chromatography was performed on silica gel 60 (230−400 mesh, Fisher Scientific). All liquids were degassed prior to use in a glovebox through three freeze−pump−thaw cycles. Deuterated solvents were obtained from Cambridge Isotope Laboratories. C_6D_6 was dried over sodium metal and stored under nitrogen, while $CDCl_3$, d_4-MeOH, d_8-^{i}PrOH, and d_8-THF were not dried but were degassed prior to use through three freeze−pump−thaw cycles. NMR spectra were recorded on Agilent-400, -500, and -600 spectrometers at ambient probe temperatures unless noted. For variable-temperature NMR, the sample temperature was calibrated by measuring the distance between the OH and CH_2 resonances in ethylene glycol (99%, Aldrich). Chemical shifts are reported with respect to residual internal protio solvent for ^{1}H and ^{13}C{^{1}H} NMR spectra. Robertson Microlit Laboratories, Inc. performed the elemental analyses (inert atmosphere). Gas chromatography analyses (GC) were performed on a Shimadzu GC-2010 Plus apparatus equipped with a flame ionization detector and a Shimadzu SHRXI-5MS column (30 m, 250 μm inner diameter, film: 0.25 μm). The following conditions were utilized for GC analyses: flow rate 1.23 mL/min constant flow, column temperature 50 °C (held for 5 min), 20 °C/min increase to 300 °C (held for 5 min), total time 22.5 min. High-resolution mass spectrometry was performed using an ion-cyclotron resonance (ICR) mass spectrometer equipped with a superconducting (7T) magnet. Literature procedures were used to prepare the following compounds: IPr,[23] (η^3-cinnamyl)Pd(IPr)(Cl) (**Cin-IPr**)[6d] and **PEPPSI-IPr**.[24]

COMPUTATIONAL DETAILS

All stationary points were fully optimized at the DFT level with the hybrid *meta*-GGA M06 functional[25] including dispersion, as implemented in the Gaussian09 software package (revision D.01).[26] Geometry optimizations were carried out on the full system including solvation by MeOH with the continuum SMD model.[27] Frequencies were computed with the aim of classifying all stationary points as minima and determining the thermochemistry corrections, $(G - E)$, which include the zero-point energies, thermal contributions, and entropies. Two different basis sets were used, BS1, for geometry optimizations and frequency calculations, and BS2, for single-points. BS1 includes polarization functions and small-core pseudopotentials by combining the double-ζ 6-31G** (C, N, O and H)[28] and triple-ζ LANL08* (Pd)[29] basis sets. With BS2, Pd was described at the same level, whereas C, N, O, and H were described with the triple-ζ 6-311+G** basis set,[30] including polarization and diffuse functions. The single-point calculations were performed at the DFT(M06)/SMD-



(3)

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(MeOH)/BS2 level on the DFT(M06)/SMD(MeOH)/BS1-optimized geometries with the aim of refining the potential energies (E_{sol}). The energies discussed in the text, G_{sol}, were obtained by adding the thermochemistry corrections to the refined potential energies (eq 4).

$$G_{sol} = E_{sol} + (G - E) \quad (4)$$

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acscatal.5b00878.

Characterizing data; further experimental details; X-ray information for **2b-IPr**, **2c-IPr**, **2d-IPr**, and **3**; and details of DFT calculations (PDF)

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Notes

The authors declare no competing financial interest.

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