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Preparation of a Highly Congested Carbazoyl-Derived P,N-Type Phosphine Ligand for Acetone Monoarylations

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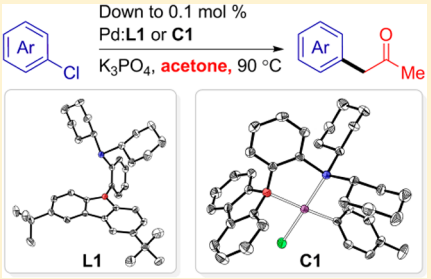
Supporting Information

ABSTRACT: We report a newly developed carbazoyl-derived P,N-type phosphine ligand (**L1**) for the monoarylation of acetone with aryl chlorides. The proposed $Pd(dba)_2$/**L1** catalyst exhibited remarkable catalytic reactivity toward highly electron rich and sterically congested aryl chlorides, with catalyst loading as low as 0.1 mol % of Pd along with excellent chemoselectivity. A reaction rate study of the system using electronically diverse aryl chlorides determined the mechanisms regarding the rate-limiting steps in this reaction. The oxidative addition adduct of Pd-PhenCar-Phos with *p*-chlorotoluene showed the participation of N−Pd coordination in the metal complex. The isolated palladium complex **C1** could be utilized as a precatalyst in the transformation and achieved performance comparable to that of the in situ generated palladium species.



INTRODUCTION

The transition-metal-catalyzed selective monoarylation of acetone[1] has emerged as a powerful synthetic tool due to its simplicity and practicality in constructing important intermediates in organic materials and pharmaceuticals.[2] Nevertheless, a challenge originated from the multiple reactive acidic protons, which render unselective multiple arylations. Since the pioneering work by Buchwald,[3] Hartwig,[4] and Miura[5] in 1997, the reaction scope of ketone arylations has been extensively expanded to allow various electrophiles, catalysts, and reaction parameters to be used.[6] Lately, development has focused on the design of ancillary ligands in the hope of pursuing enhanced reactivity and, more importantly, mono selectivity toward this arylation of methyl ketones.[1,6]

While reports on the monoarylation of ketones have been limited, the group of Stradiotto demonstrated the first monoarylation of acetone in 2011, employing a Pd catalyst with the morpholine-based P,N-type ligand Mor-DalPhos (Figure 1).[1a] Afterward, Ma and Lang independently reported Zheda-Phos and a ferrocenyl-based phosphine as effective ligands for this process (Figure 1).[1c,d] However, it was discovered that the scope might suffer from electron-deficient arenes when aryl halides or sulfonates were used.[1a,h] This is presumably due to ineffective reductive elimination (RE) or transmetalation as a result of employing highly electron-rich phosphorus donor ligands. Indeed, a decrease in electron richness on the phosphorus donor would accelerate the rate of C−C reductive elimination[1a,6p] and an increase in the steric bulkiness of the ligand (i.e., either with the bulky phosphino group or the bottom ring of the ligand in a remote fashion) can facilitate the RE process. Recently, we designed an electronically appropriate indolylphosphine ligand which can effectively promote the acetone monoarylation with electron-poor arenes,[1g] even on a scale up to 100 mmol. Nevertheless, it would be intriguing to determine whether the reductive elimination of electron-deficient substrates could be promoted when the two factors of electron-rich phosphorus donor and highly sterically encumbered bottom ring are confined in one single ligand. Whereas a few other phosphines also showed effectiveness in this reaction, they tended to employ high catalyst loadings.[1e,f] With our continuing interest in phosphine ligand design and monoarylation of methyl ketones,[1g,7] we herein disclose a newly developed P,N-type phosphine ligand for acetone monoarylation. The new P,N-Pd catalyst was found to be particularly effective against sterically hindered and electron-rich substrates, and the P,N coordination to the Pd center was also confirmed by X-ray crystallographic analysis.

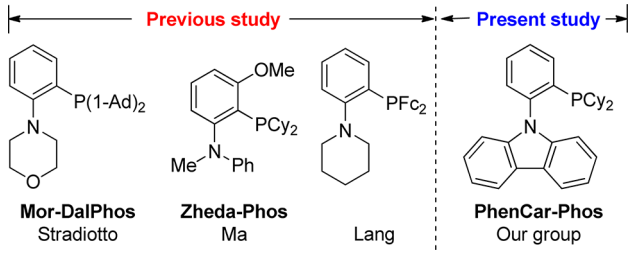


Figure 1. P,N-type phosphine ligands used in the Pd-catalyzed monoarylation of acetone and our proposed target ligand scaffold for this study.

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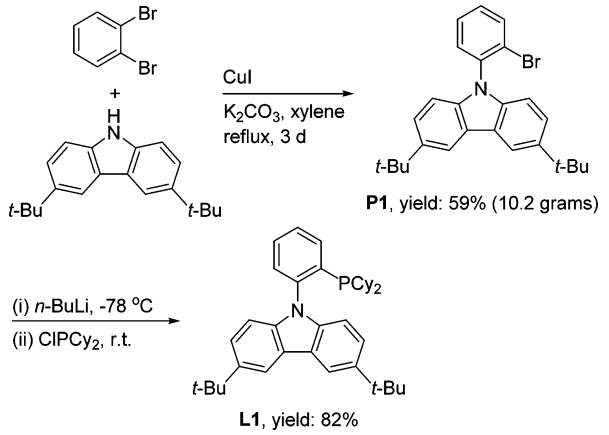
RESULTS AND DISCUSSION

Synthesis and Characterization of Carbazolyl-Based Phosphine Ligand L1. In 2011, we reported the carbazolyl-based P,N phosphine ligand PhenCar-Phos for sterically hindered biaryl syntheses (Figure 1),[7b] in which we believe the extended carbazolyl framework is the key for the difficult $C(sp^2)-C(sp^2)$ bond-forming reductive elimination. Recently, we further extended the aromatic carbazolyl framework to enable tetra-ortho-substituted biaryl syntheses.[7c] In this regard, we envisioned that the PhenCar-Phos ligand skeleton would hold great promise against the Ar–Pd–acetone enolate reductive elimination after adequate modifications. On the basis of this scaffold, we sought to incorporate steric prominence on the carbazole moiety (Scheme 1). The

Scheme 1. Preparation of Carbazolyl-Based Phosphine Ligand L1



preparation of **L1** was accomplished by a ligand-free Cu-catalyzed animation followed by nucleophilic phosphination. The basic 3,6-di-*tert*-butyl-9*H*-carbazole was prepared in good yield with a simple Friedel–Crafts reaction according to literature procedures.[8] To further realize the amenability of this procedure, the Cu-catalyzed animation was attempted on a multigram scale and 10.2 g of product was successfully obtained. A single crystal of **L1** suitable for X-ray diffraction was grown by a liquid–liquid diffusion of ethanol into a chloroform solution of **L1** at −20 °C. The X-ray analysis of **L1** confirmed an sp^2-N conformation in the carbazole structure (Figure 2).

Catalytic Studies of $Pd(dba)_2$/L1 Catalyst. With the newly developed P,N ligand in hand, we next initiated the reaction trials using electronically neutral *p*-chlorotoluene as the benchmarking substrate. In addition to **L1**, a series of other PhenCar-Phos ligands **L2**–**L6**, which are electronically and sterically diverse at the phosphorus donor, were also evaluated. At the beginning of ligand screening, we found that ligands bearing PCy_2 and P-*i*-Pr_2 groups gave superior results over the other counterparts (Table 1, entries 1–3 vs entries 4–6). Further evaluation of **L1**–**L3** with lower catalyst loadings revealed comparable performances, while **L3** provided a slightly lower product yield (Table 1, entries 7–9). **L1** was found to provide 83% product yield with lengthened reaction time, while **L2** was inferior in this respect (Table 1, entry 10 vs entry 11). Carbonated base and strongly basic hydroxide were found to be not suitable in this system (Table 1, entries 12 and 13). The use of $Pd(dba)_2$ as a metal source gave almost the same catalytic

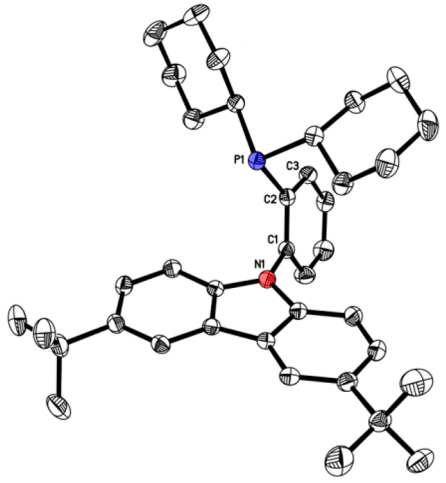
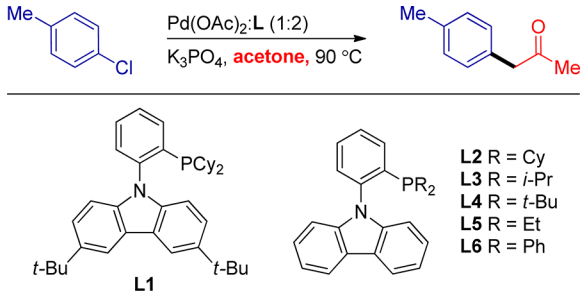


Figure 2. ORTEP diagram of **L1**. All hydrogen atoms have been omitted for clarity.

Table 1. Representative Entries for Reaction Optimization[a]



entry	amt of Pd (mol %)	L	base	time (h)	yield (%)
1	0.5	**L1**	K_3PO_4	4	99
2	0.5	**L2**	K_3PO_4	4	99
3	0.5	**L3**	K_3PO_4	4	99
4	0.5	**L4**	K_3PO_4	4	trace
5	0.5	**L5**	K_3PO_4	4	trace
6	0.5	**L6**	K_3PO_4	4	trace
7	0.1	**L1**	K_3PO_4	4	40
8	0.1	**L2**	K_3PO_4	4	39
9	0.1	**L3**	K_3PO_4	4	18
10	0.05	**L1**	K_3PO_4	18	83
11	0.05	**L2**	K_3PO_4	18	42
12	0.05	**L1**	Cs_2CO_3	18	73
13	0.05	**L1**	$CsOH·H_2O$	18	trace
14	0.05	**L1**	K_3PO_4	18	84[b]

[a]Reaction conditions unless specified otherwise: $Pd(OAc)_2$:ligand = 1:2, *p*-chlorotoluene (0.5 mmol), base (1.25 mmol), acetone (1.7 mL, 0.30 M); 90 °C for the indicated time under N_2. Calibrated GC-FID yields are reported. [b]$Pd(dba)_2$ was used as the Pd source.

performance as $Pd(OAc)_2$ (Table 1, entry 10 vs entry 14), yet it provided more reproducible results.

Having the optimal reaction conditions in hand, we sought to examine the scope of the system for the monoarylation of acetone. Generally, only 0.2 mol % of $Pd(dba)_2$/**L1** catalyst allowed good-to-excellent product yields with electron-neutral and -rich arenes (Scheme 2, compounds **1a**–**f**). It is particularly noteworthy that highly electron-rich and sterically hindered substrates, such as **1h**, were able to react and gave 99% product yield with only 0.3 mol % of Pd; the same substrate required 1.5 mol % of catalyst in our previous report. Other sterically

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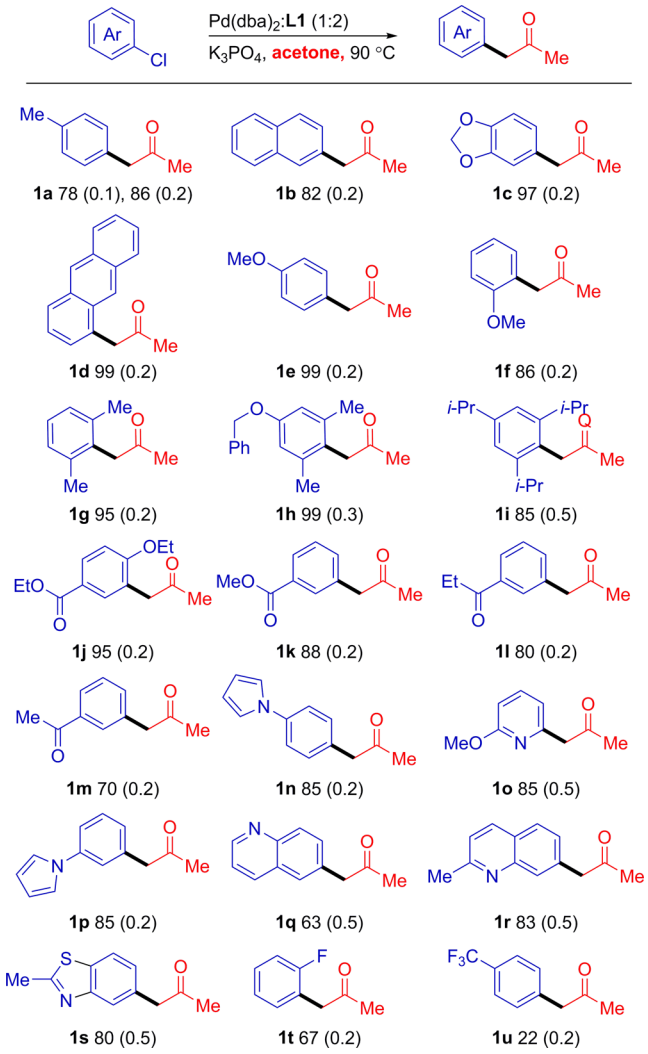
Scheme 2. Pd(dba)$_2$/L1-catalyzed Mono-α-Arylation of Acetone with Aryl and Heteroaryl Chlorides[a]

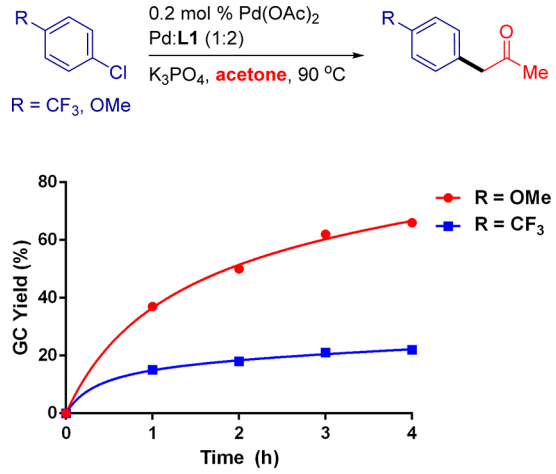


[a]Reaction conditions: Pd:**L1** = 1:2, ArCl (0.5 mmol), K_3PO_4 (1.25 mmol), acetone (1.7 mL, 0.30 M); 90 °C for 18 h under N_2. Isolated yields are reported. The catalyst loading is reported in parentheses as mol % of Pd with respect to ArCl. Reaction times were not optimized for each substrate.

hindered arenes were successfully converted to the desired products in 86−99% yield (Scheme 2, entries **1f−j**). Functionalities such as esters, enolizable ketones, and a variety of heterocycles were tolerated in our system, and up to 95% isolated yield was given (Scheme 2, compounds **1j−s**). Despite the moderate product yield afforded for compound **1t**, the reaction with the highly electron-deficient *p*-chlorobenzotrifluoride **1u** gave 22% yield. In addition to acetone, other alkyl and aryl ketones were shown to be applicable substrates in our reaction (see Scheme S1 in the Supporting Information).

Reaction Rate Study and Oxidative Addition Complex of Pd/PhenCar-Phos Catalyst. Although our system was found to be highly efficient toward electron-rich and sterically hindered substrates, para-substituted electron-deficient arenes were still problematic despite the reinforced steric hindrance provided by **L1**. To shed light on the limitations and mechanisms of the system, we studied the initial reaction rate of electronically diverse aryl chlorides (Scheme 3). Interest-

Scheme 3. Reaction Rate Study of Electronically Diverse Aryl Chlorides in Acetone Monoarylation using the Pd(dba)$_2$/L1 System



ingly, the reaction rate with electron-rich *p*-chloroanisole was found to be much higher than that with electron-poor *p*-chlorobenzotrifluoride. Notwithstanding the fact that the extended carbazole framework of **L1** was proven to greatly improve the catalytic performance of PhenCar-Phos in acetone monoarylations toward electron-rich substrates, the reaction with electron-deficient arenes was not entirely applicable. This result was consistent with a previous report regarding the use of P,N ligand[1a] but not with ours,[1g] which next drew our attention to the interaction between the PhenCar-Phos ligand and the palladium metal center.

To gain an insight into the ligand−metal interaction during the catalysis, we attempted to prepare and isolate the catalytic intermediate of the Pd/PhenCar-Phos catalyst. The oxidative addition adduct **C1** was successfully prepared by direct treatment of Pd(dba)$_2$/PhenCar-Phos with *p*-chlorotoluene in tetrahydrofuran at 90 °C, giving an isolated yield of 70% (Scheme 4). A single crystal of **C1** suitable for X-ray diffraction was obtained by vapor diffusion of diethyl ether into a dichloromethane solution containing **C1**. The crystallographic analysis of **C1** confirmed a κ^2-P,N coordination of PhenCar-Phos to the palladium while chloride bound trans to the phosphorus donor. This coordination mode is consistent with previous reports regarding the P,N-type ligand Mor-DalPhos. As suggested by the molecular structure of **C1** and reaction rate study with electron-rich aryl chlorides, we believe that the high steric hindrance of **L1** did improve the catalytic rate by facilitating the reductive elimination. However, the inferior performance with electron-poor aryl chlorides should originate from the extra electron richness or heightened basicity on the palladium center provided by the ligand through N−Pd coordination, in which it binds trans to the arene substrate. This vastly heightened basicity ultimately led to the increased reductive elimination rate with electron-rich arenes but to a significant performance drop for electron-poor substrates. We found that this phenomenon is likely in line with the results of Zheda-Phos by Ma and co-workers,[1c] where lowering the electron richness at the nitrogen atom or a secondary competitive binding atom (oxygen of methoxy group in that case) within the ligand could allow the transformation of certain electron-deficient arenes such as *p*-keto or *p*-cyano aryl chlorides.

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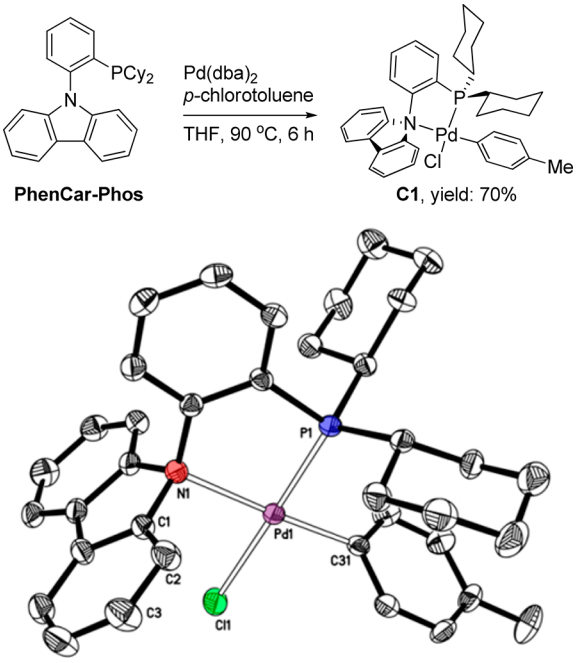
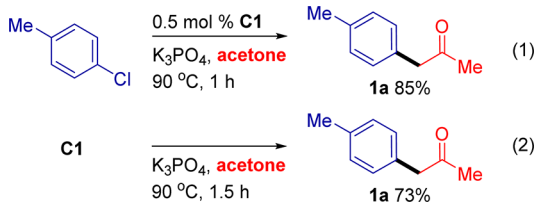
Scheme 4. Preparation of C1 and ORTEP Diagram of C1[a]



[a]All hydrogen atoms have been omitted for clarity. Reaction conditions: $Pd(dba)_2$ (1.0 mmol), PhenCar-Phos (1.2 mmol), *p*-chlorotoluene (15.0 mmol) in THF at 90 °C for 6 h under N_2. Selected distances (Å): Pd1−P1 2.216(8), Pd1−N1 2.285(2), Pd1−Cl1 2.342(8), Pd1−C31 1.990(3).

Recently, palladium precatalysts have received considerable attention due to their stability, ease of handling, and sometimes greater catalytic activity.[9] We envisioned that the isolated palladium complex **C1** could also be employed as a precatalyst for catalytic applications (Scheme 5). Without the addition of extra amounts of ligand, 0.5 mol % of **C1** catalyzed the monoarylation of acetone with *p*-chlorotoluene and afforded 85% yield in 1 h (eq 1). Direct reaction of **C1** with acetone in the presence of K_3PO_4 gave the product in 73% yield (eq 2). This air-stable precatalyst **C1** gave performance comparable to that of the in situ generated palladium species (Scheme 5, eq 1, vs Table 1, entry 2).

Scheme 5. Acetone Monoarylations using Precatalyst C1[a]



[a]Reaction conditions for eq 1: **C1** (0.5 mol %), *p*-chlorotoluene (0.5 mmol), K_3PO_4 (1.25 mmol), acetone (1.7 mL, 0.30 M); 90 °C for 1 h under N_2. The calibrated GC-FID yield is reported. Reaction conditions for eq 2: **C1** (0.05 mmol), K_3PO_4 (1.25 mmol), acetone (1.7 mL, 0.30 M); 90 °C for 1.5 h under N_2. The calibrated GC-FID yield is reported.

SUMMARY

In summary, we have developed a new catalyst ($Pd(dba)_2$/**L1**) that is specifically efficient toward electron-rich and highly congested aryl chlorides in acetone monoarylations, with catalyst loadings as low as 0.1 mol % (the lowest catalyst loading achieved so far) and exhibition of chemoselectivity. The carbazolyl-based ligand **L1** can be readily prepared by straightforward synthetic procedures with easily accessible materials and was amenable for multigram-scale synthesis. The steric prominence of the carbazolyl framework of **L1** was found to greatly enhance the catalytic performance of PhenCar-Phos in the acetone arylation process, yet the N−Pd coordination may contribute negatively to the reaction with electron-deficient arenes. We believe that these findings can offer a further understanding of the ligand−metal interaction and effect of bidentate P,N ligands and be considered as a distinctive characteristic for future phosphine ligand design. Other mechanistic and catalytic studies regarding the use of PhenCar-Phos in not only ketone arylation but also a variety of fundamentally different catalyses are now underway in our laboratory.

EXPERIMENTAL SECTION

General Considerations. Unless otherwise noted, all reagents were purchased from commercial suppliers and used without purification. All catalytic reactions were performed in resealable screw-capped Schlenk tubes (approximately 20 mL volume) in the presence of a Teflon-coated magnetic stirrer bar (4 mm × 10 mm). Acetone was dried with activated 4 Å molecular sieves under N_2 followed by vacuum distillation into a 100 mL Schlenk flask and was stored for not more than 5 days. Cs_2CO_3, $CsOH·H_2O$, and K_3PO_4 were purchased from Aldrich. $Pd(OAc)_2$ and $Pd(dba)_2$ were purchased from Strem Chemical. Ligands **L2**−**L6** were prepared according to reported literature procedures.[7b] Commercially available aryl halides were used as received. Thin-layer chromatography was performed on Merck precoated silica gel 60 F_{254} plates. Silica gel (Merck, 70−230 and 230−400 mesh) was used for column chromatography. Melting points were recorded on Büchi B-545 melting point instrument. ^1H NMR spectra were recorded on a Bruker (400 MHz) spectrometer. Spectra were referenced internally to the residual proton resonance in $CDCl_3$ (δ 7.26 ppm), or with tetramethylsilane (TMS, δ 0.00 ppm) as the internal standard. Chemical shifts (δ) are reported in parts per million (ppm) on the δ scale downfield from TMS. ^{13}C NMR spectra are referenced to $CDCl_3$ (δ 77.00 ppm, the middle peak). ^{31}P NMR spectra are referenced to external 85% H_3PO_4. Coupling constants (J) are reported in hertz (Hz). Mass spectra (EI-MS and ES-MS) were recorded on a HP 5989B mass spectrometer. High-resolution mass spectra (HRMS) were obtained on a Bruker APEX 47e FTICR mass spectrometer (ESIMS). GC-MS analysis was conducted on a HP 5973 GCD system using an HP5MS column (30 m × 0.25 mm). The GC yields described for the products were in accord with the authentic samples/dodecane calibration standard from an HP 6890 GC-FID system. All yields reported refer to isolated yields of compounds estimated to be greater than 95% purity as determined by capillary gas chromatography (GC) or ^1H NMR. Compounds described in the literature were characterized by comparison of their ^1H, and/or ^{13}C NMR spectra to the previously reported data. The procedures in this section are representative, and thus the yields may differ from those reported in the tables.

Synthesis and Characterization of Carbazolyl-Based Phosphine Ligand L1. *General Procedure for Synthesis of 9-(2-Bromophenyl)-3,6-di-tert-butyl-9H-carbazole (P1).* 3,6-Di-*tert*-butyl-9*H*-carbazole (11.1 g, 40 mmol), CuI (7.62 g, 40 mmol), K_2CO_3 (11.0 g, 80 mmol), and a Teflon-coated magnetic stir bar were placed in a two-necked round-bottom flask (250 mL) equipped with a condenser and fitted with a septum. The system was carefully evacuated and back-filled with nitrogen (three cycles). 1,2-Dibromobenzene (9.65 mL, 80 mmol) and xylene (130 mL) were added by syringe via septum. The septum was replaced with a stopper and the reaction mixture was refluxed in a preheated oil bath (185 °C) for 3 days. After completion of the reaction, the copper powder was filtered through Celite and the

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xylene was removed by distillation under high vacuum. The crude products were purified by flash column chromatography on silica gel (230−400 mesh) to afford the product as a white solid (10.2 g, 59%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.54 (s, 18H), 7.06 (d, J = 8.6 Hz, 2H), 7.39−7.43 (m, 1H), 7.47−7.54 (m, 4H), 7.90 (dd, J = 8.1, 0.9 Hz, 1H), 8.24 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 32.4, 35.0, 109.8, 116.6, 123.5, 123.9, 124.0, 129.0, 130.1, 131.3, 134.4, 137.6, 139.7, 143.1; HRMS calcd for $C_{26}H_{28}NBr$ 433.1400, found 433.1410.

*General Procedure for Synthesis of 3,6-Di-tert-butyl-9-(2-(dicyclohexylphosphanyl)phenyl)-9H-carbazole (**L1**).* The ligand precursor (**P1**) obtained from the previous step (2.17 g, 5.0 mmol) was dissolved in freshly distilled THF (25 mL) at room temperature under a nitrogen atmosphere. The solution was cooled to −78 °C in a dry ice/acetone bath. Titrated *n*-BuLi (5.5 mmol) was added dropwise with a syringe, and the reaction mixture was stirred for 30 min at −78 °C. Chlorodiphenylphosphine (1.32 mL, 6.0 mmol) was then added dropwise to the reaction mixture with a syringe. The reaction mixture was warmed to room temperature and stirred for 12 h. The solvent was then removed under reduced pressure. Methanol (10 mL) was added to the residue, and the mixture was stirred at 1250 rpm for 10 min. The white solid product was successively filtered and washed with cold methanol. The white solid was collected and dried over vacuum to afford 3,6-di-*tert*-butyl-9-(2-(dicyclohexylphosphanyl)phenyl)-9*H*-carbazole (2.26 g, 82%): ^{1}H NMR (400 MHz, C_6D_6) δ 0.98−1.17 (m, 8H), 1.41 (s, 18H), 1.51−1.72 (m, 14H), 7.10−7.12 (m, 2H), 7.18−7.20 (m, 3H), 7.51 (dd, J = 8.6, 1.6 Hz, 2H), 7.57 (d, J = 7.6 Hz, 1H), 8.38 (s, 2H); ^{13}C NMR (100 MHz, C_6D_6) δ 27.2, 28.1 (d, J = 23.4 Hz), 28.1 (d, J = 3.9 Hz), 30.6 (d, J = 11.0 Hz), 31.0 (d, J = 16.8 Hz), 32.8, 34.9 (d, J = 16.9 Hz), 35.4, 111.4 (d, J = 2.5 Hz), 117.2, 124.0, 124.6, 130.9, 134.6 (d, J = 3.4 Hz), 138.8, 139.1, 142.3, 143.0, 145.4, 145.6; ^{31}P NMR (162 MHz, C_6D_6) δ −14.54; HRMS calcd for $C_{38}H_{50}NPH^+$ 552.3759, found 552.3762.

General Procedure for Ligand and Reaction Condition Screenings. Base (1.25 mmol) was loaded into a Schlenk tube equipped with a Teflon-coated magnetic stir bar and fitted with a septum. The tube was carefully evacuated and back-filled with nitrogen for three cycles. The Pd source (0.02 mmol) and ligand (0.04 mmol) in 4.00 mL of acetone (1.00 mol % of Pd per 1.00 mL of stock solution) were then prepared under N_2 with stirring until all solids were dissolved (usually within 1 min). The corresponding volume of the stock solution was then immediately added to the Schlenk tube by syringe (in the case of 0.10 mol % of Pd, an additional 400 μL of acetone was added). The solution was stirred for 5 min at room temperature. *p*-Chlorotoluene (0.50 mmol) was added by syringe, and the solution was diluted with acetone to 1.70 mL. The septum was then replaced with a screw cap, and the solution was stirred at room temperature for 5 min. The tube was placed into a preheated oil bath (90 °C) and stirred for the desired duration. After completion of the reaction, the reaction tube was warmed to room temperature. Ethyl acetate (∼3 mL), dodecane (114 μL, internal standard), and water (∼2 mL) were added. The organic layer was subjected to GC analysis. The GC yield was previously calibrated by an authentic sample/dodecane calibration curve.

General Procedure for Mono-α-Arylation of Acetone with Aryl Chlorides. Aryl chloride (if solid, 0.50 mmol) and K_3PO_4 (1.25 mmol) were loaded into a Schlenk tube equipped with a Teflon-coated magnetic stir bar and fitted with a septum. The tube was carefully evacuated and back-filled with nitrogen for three cycles. $Pd(dba)_2$ (0.02 mmol) and **L1** (0.04 mmol) in 4.00 mL of acetone (1.00 mol % of Pd per 1.00 mL of stock solution) were then prepared under N_2 with stirring until all solids were dissolved (usually within 1 min). The corresponding volume of the stock solution was then immediately added to the Schlenk tube by syringe (in the case of 0.20 mol % of Pd, an additional 300 μL of acetone was added). The solution was stirred for 5 min at room temperature. Aryl chloride (if liquid, 0.50 mmol) was added by syringe, and the solution was diluted with acetone to 1.70 mL. The septum was then replaced with a screw cap, and the solution was stirred at room temperature for 5 min. The tube was placed into a preheated oil bath (90 °C) and stirred for 18 h. After completion of the reaction, the reaction tube was warmed to room temperature. Ethyl acetate (∼3 mL), dodecane (114 μL, internal standard), and water (∼2 mL) were added. The organic layer was separated, and the aqueous layer was washed with ethyl acetate. The filtrate was concentrated under reduced pressure. The crude products were purified by flash column chromatography on silica gel (230−400 mesh) to afford the desired product.

General Procedure for Reaction Rate Study. K_3PO_4 (1.25 mmol) was loaded into a Schlenk tube equipped with a Teflon-coated magnetic stir bar and fitted with a septum. The tube was carefully evacuated and back-filled with nitrogen for three cycles. $Pd(dba)_2$ (0.005 mmol) and **L1** (0.01 mmol) in 2.50 mL of acetone (0.2 mol % Pd per 500 μL stock solution) were then prepared under N_2 with stirring until all solids were dissolved (usually within 1 min). The stock solution (500 μL) was then immediately placed in the Schlenk tube by syringe. The solution was stirred for 5 min at room temperature. *p*-Chloroanisole (0.50 mmol) or *p*-chlorobenzotrifluororide (0.50 mmol) was added by syringe, and the solution was diluted with acetone to 1.70 mL. The tube was stirred at room temperature for another 5 min, and the septum was then replaced with a screw cap. An array of Schlenk tubes that were prepared in parallel according to the above procedure were placed in a preheated oil bath (90 °C) and stirred for the time indicated. After completion of the reaction, the reaction tube was immediately placed in an ice bath to quench the reaction. Ethyl acetate (∼3 mL), dodecane (114 μL, internal standard), and water (∼2 mL) were added. The organic layer was subjected to GC analysis. The GC yield was previously calibrated by an authentic sample/dodecane calibration curve.

Synthesis of Metal Complex C1. $Pd(dba)_2$ (1.0 mmol) and PhenCar-Phos (1.2 mmol) were loaded into a Schlenk tube (250 mL) equipped with a screw cap and Teflon-coated magnetic stir bar. The tube was carefully evacuated and back-filled with nitrogen for three cycles. *p*-Chlorotoluene (15.0 mmol) and subsequently THF (30 mL) were added by syringe. The solution was stirred at room temperature for 5 min. The tube was placed into a preheated oil bath (90 °C) and stirred for 6 h. After completion of the reaction, the reaction tube was warmed to room temperature. The unreacted palladium was filtered through Celite, and the solvent was removed; diethyl ether was then added to precipitate the product. The crude product was washed successively with diethyl ether to eliminate the unreacted materials and dibenzylideneacetone ligands. The solvent was removed under high vacuum to give the desired product as a light yellow solid (470 mg, 70%). A single crystal of **C1** suitable for X-ray diffraction was obtained by vapor diffusion of diethyl ether into a dichloromethane solution containing **C1**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85−0.95 (m, 2H), 1.20−1.53 (m, 5H), 1.74−1.89 (m, 11H), 2.11−2.19 (m, 5H), 2.32−2.37 (m, 2H), 6.31 (dd, J = 8.3, 3.1 Hz, 1H), 6.74 (d, J = 7.9 Hz, 2H), 6.99 (dd, J = 8.4, 1.8 Hz, 2H), 7.10 (d, J = 7.1 Hz, 2H), 7.30−7.41 (m, 5H), 7.46 (t, J = 7.4 Hz, 1H), 7.75 (t, J = 6.8 Hz, 1H), 8.01−8.03 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.6, 25.8, 26.9 (d, J = 11.2 Hz), 27.1 (d, J = 13.7 Hz), 28.1, 28.3 (d, J = 2.6 Hz), 33.6 (d, J = 27.4 Hz), 116.5, 120.8, 125.3, 127.3, 127.9 (d, J = 7.8 Hz), 128.3, 128.8 (d, J = 4.6 Hz), 130.9, 131.2 (d, J = 30.5 Hz), 131.5, 132.3, 133.4, 133.9 (d, J = 2.7 Hz), 136.0 (d, J = 3.7 Hz), 151.7, 154.2 (d, J = 14.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 37.12; HRMS calcd for $C_{37}H_{41}PNPd^+$ 638.2020, found 638.2023.

General Procedure for Mono-α-Arylation of Acetone using Precatalyst C1. K_3PO_4 (1.25 mmol) and **C1** (1.68 mg, 0.0025 mmol) were loaded into a Schlenk tube equipped with a Teflon-coated magnetic stir bar and fitted with a septum. The tube was carefully evacuated and back-filled with nitrogen for three cycles. *p*-Chlorotoluene (0.50 mmol) and subsequently acetone (1.70 mL) were added by syringe. The contents of the tube were stirred at room temperature for 5 min, and the septum was then replaced with a screw cap. The tube was placed into a preheated oil bath (90 °C), and the contents were stirred for 1 h. After completion of the reaction, the reaction tube was immediately placed in an ice bath to quench the reaction. Ethyl acetate (∼3 mL), dodecane (114 μL, internal standard), and water (∼2 mL) were added. The organic layer was subjected to GC analysis. The GC yield was previously calibrated by an authentic sample/dodecane calibration curve.

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General Procedure for Reaction of C1 and Acetone. K_3PO_4 (1.25 mmol) and **C1** (33.7 mg, 0.05 mmol) were loaded into a Schlenk tube equipped with a Teflon-coated magnetic stir bar and fitted with a septum. The tube was carefully evacuated and back-filled with nitrogen for three cycles. *p*-Chlorotoluene (0.50 mmol) and subsequently acetone (1.70 mL) were added by syringe. The contents of the tube were stirred at room temperature for 5 min, and the septum was then replaced with a screw cap. The tube was placed into a preheated oil bath (90 °C), and the contents were stirred for 1.5 h. After completion of the reaction, the reaction tube was immediately placed in an ice bath to quench the reaction. Ethyl acetate (~3 mL), dodecane (114 μL, internal standard), and water (~2 mL) were added. The organic layer was subjected to GC analysis. The GC yield was previously calibrated by an authentic sample/dodecane calibration curve.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.organomet.6b00154.

X-ray crystallographic data (CIF)
X-ray crystallographic data (CIF)
^{1}H, ^{13}C, and ^{31}P NMR spectra and characterization data of the compounds and crystal data and structure refinement detailss of **L1** and **C1** (PDF)
All computed molecule Cartesian coordinates (XYZ)

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Notes

The authors declare no competing financial interest.

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