Preparation of A Highly Congested Carbazoyl-Derived *P,N*-type Phosphine Ligand for Acetone Monoarylations

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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 towards highly electron-rich and sterically congested aryl chlorides, with catalyst loading as low as 0.1 mol % Pd along with excellent chemoselectivity. The reaction rate study of the system using electronically diverse aryl chlorides conferred mechanistics regarding rate-limiting steps in this reaction. The oxidative addition adduct of Pd-PhenCar-Phos with *para*-chlorotoluene showed the participation of N-Pd coordination in the metal complex. This isolated palladium complex **C1** could be utilized as a precatalyst in the transformation and achieved comparable performance as 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 to construct important intermediates in organic materials and pharmaceuticals.[2] Nevertheless, the problem originated from the multiple reactive acidic protons renders these arylations unselective. 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, the development has been focused on the design of ancillary ligands in hope to pursue enhanced reactivity and more importantly, the mono-selectivity towards this arylation of methylketones.[1,6]

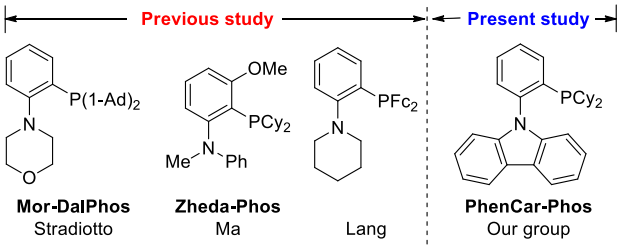


Figure 1. *P,N*-type phosphine ligands used in the Pd-catalyzed monoarylation of acetone and our proposed target ligand scaffold for this study.

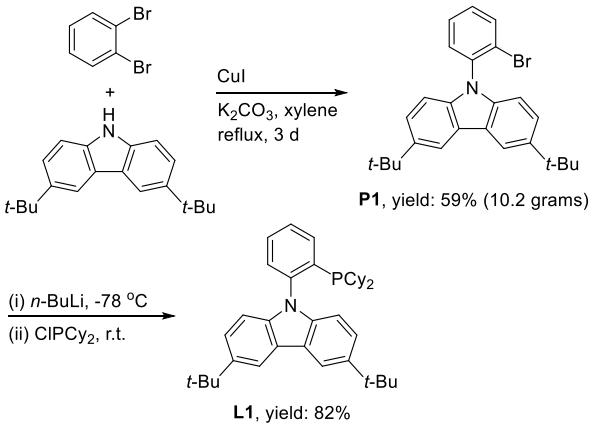
While the reports on monoarylation of ketones were limited, the group of Stradiotto demonstrated the first monoarylation of acetone in 2011, employing a Pd catalyst with morpholine-based *P,N*-type ligand Mor-DalPhos (Figure 1).[1a] Afterwards, Ma and Lang independently reported Zheda-Phos and a ferrocenyl-based phosphine as effective ligands for this process (Figure 1).[1c, 1d] However, it was discovered that the scope might suffer from electron-deficient arenes when aryl halides or sulfonates were used.[1a,1h] It is presumably due to ineffective reductive elimination or transmetalation as a result of employing highly electron-rich phosphorous donor ligands. Indeed, the decrease of electron-richness on the phosphorous donor would accelerate the rate of C-C reductive elimination,[1a,6p] and the increase of 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 is intriguing if 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,1f] With our continuing interest in phosphine ligand design and monoarylation of methylketones,[1g,7] we herein disclose a newly developed *P,N*-type phosphine ligand for acetone monoaryalation. The new *P,N*-Pd catalyst was found particularly effective against sterically hindered and electron-rich substrates, and the *P,N* coordination to Pd center was also shown by X-ray crystallographic analysis.

RESULTS AND DISCUSSION

Synthesis and characterization of carbazolyl-based phosphine ligand L1. In 2011, we reported a carbazolyl-based *P,N* phosphine ligand PhenCar-Phos for the 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 the tetra-*ortho*-substituted biaryl

syntheses.[7c] In this regard, we envisioned that the PhenCar-Phos ligand skeleton held high promise against the Ar-Pd-acetone enolate reductive elimination after adequate modifications. Based on this scaffold, we sought to incorporate steric prominence on the carbazole moiety (Scheme 1). The preparation of **L1** was accomplished by a ligand-free Cu-catalyzed animation followed by the 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 to deal with multi-gram scale and 10.2 grams of product were successfully yielded. 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 a sp^2-N conformation in the carbazole structure (Figure 2).

Scheme 1. Preparation of Carbazolyl-based Phosphine Ligand L1.



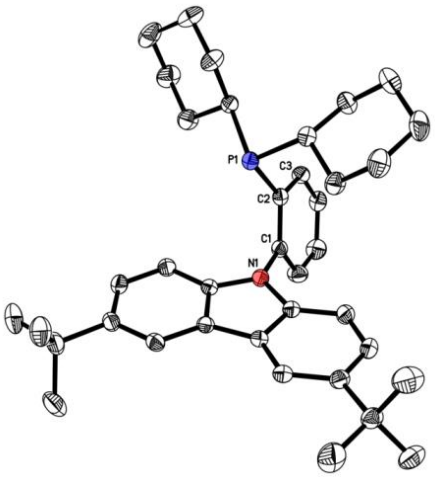
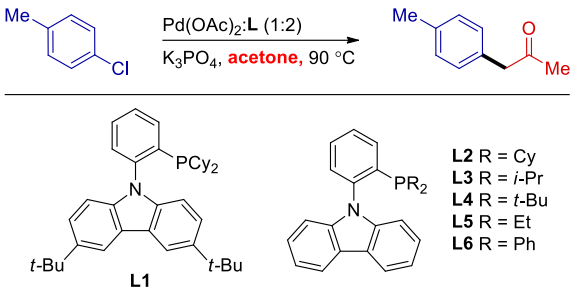


Figure 2. OPTEP diagram of **L1**. All hydrogen atoms have been omitted for clarity.

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 benching marking substrate. Apart from **L1**, a series of other PhenCar-Phos ligands **L2-L6**, which are electronically- and sterically-diverse on 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.* 4-6). Further evaluation of **L1-L3** with lower catalyst loading revealed comparable performances while **L3** provided 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 at this end (Table 1, entries 10 *vs.* 11). Carbonated base and strongly basic hydroxide were found to be not suitable in this system (Table 1, entries 12-13). The use of Pd(dba)$_2$ as metal source gave almost the same catalytic performance as Pd(OAc)$_2$ (Table 1, entries 10 *vs.* 14), yet it provided more reproducible results.

Table 1. Representative Entries for Reaction Optimization[a]



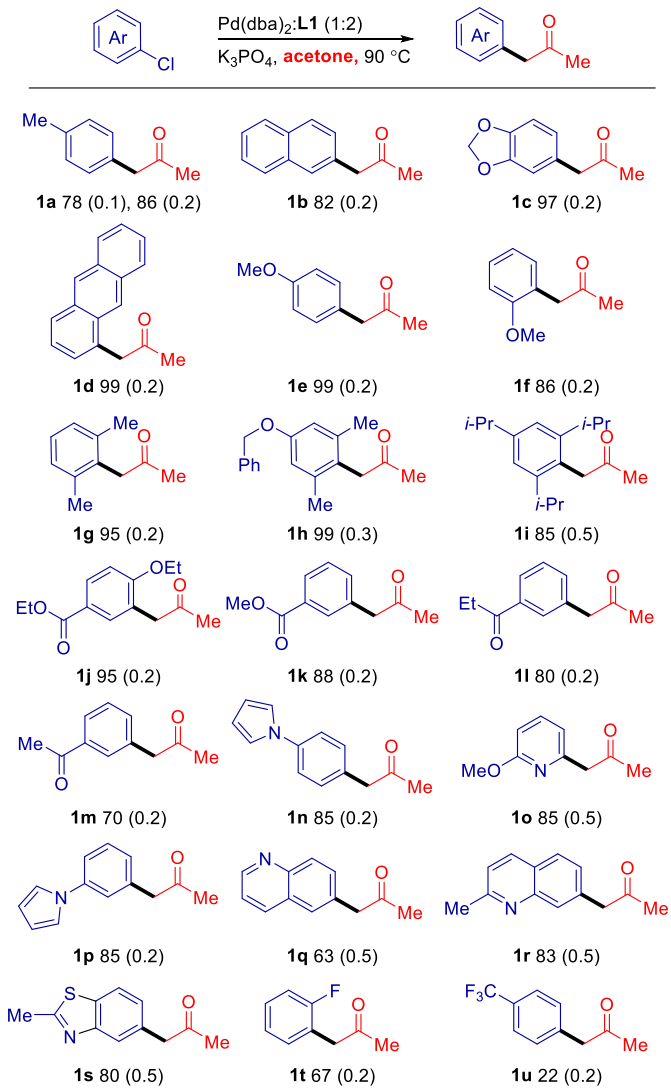
entry	Pd (mol %)	L	base	time (h)	yield (%)
1	0.5	**L1**	K_3PO_4	4	99
2	0.5	**L2**	K_3PO_4	4	99
3	0.5	**L3**	K_3PO_4	4	99
4	0.5	**L4**	K_3PO_4	4	trace
5	0.5	**L5**	K_3PO_4	4	trace
6	0.5	**L6**	K_3PO_4	4	trace
7	0.1	**L1**	K_3PO_4	4	40
8	0.1	**L2**	K_3PO_4	4	39
9	0.1	**L3**	K_3PO_4	4	18
10	0.05	**L1**	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: 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 indicated time under N_2. Calibrated GC-FID yields were reported. [b]Pd(dba)$_2$ was used as Pd source.

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 electronically–neutral and –rich arenes (Scheme 2, entries **1a-1f**). It is particularly noteworthy that highly

electron-rich and sterically hindered substrates, such as **1h** was able to react and gave 99% product yield with only 0.3 mol% of Pd, in which the same entry requires 1.5 mol% of catalyst in our previous report. Other sterically hindered arenes were successfully converted to the desired products in 86-99% yield (Scheme 2, entries **1f-1j**). Functionalities such as esters, enolizable ketones, as well as a variety of heterocycles were tolerated in our system and up to 95% isolated yield was given (Scheme 2, entries **1j-1s**). Despite the moderate product yield afforded in entry **1t**, the reaction with highly electron-deficient *p*-chlorobenzotrifluoride **1u** gave 22% yield. Apart from acetone, other alkyl and aryl ketones were shown to be applicable substrates in our reaction (See Supporting Information, Scheme S1).

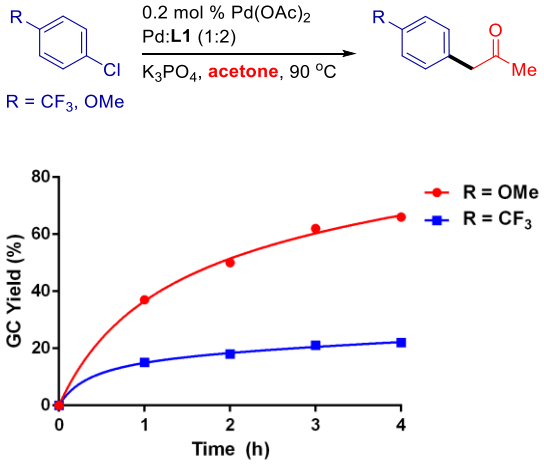
Scheme 2. Pd(dba)$_2$/L1-catalyzed Mono-α-arylation of Acetone with Aryl and Heteroaryl Chlorides[a]



[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 were reported. Catalyst loading was reported in parentheses as mol % of Pd with respect to ArCl. Reaction times were not optimized for each substrate.

Reaction rate study and oxidative addition complex of Pd/PhenCar-Phos catalyst. Although our system was found to be highly efficient towards electron-rich and sterically hindered substrates, *para*-substituted electron-deficient arenes were still problematic despite the reinforced steric hinderance provided by **L1**. To shed light on the limitation and mechanistics of the system, we studied the initial reaction rate of electronically-diverse aryl chlorides. Interestingly, the reaction rate with electron-rich *p*-chloroanisole was found to be much higher than that of electron-poor *p*-chlorobenzotrifluoride. Notwithstanding that the extended carbazole framework of **L1** was proven to greatly improve the catalytic performance of PhenCar-Phos in acetone monoarylations towards electron-rich substrates, the reaction with electron-deficient arenes was not entirely applicable. This result was consistent with the previous report regarding the use of *P,N* ligand[1a] but not ours,[1g] which next led our attention to the interaction between the PhenCar-Phos ligand and palladium metal centre.

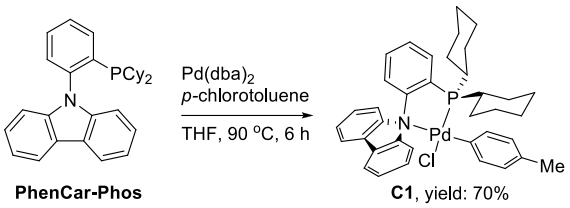
Scheme 3. Reaction Rate Study of Electronically Diverse Aryl Chlorides in Acetone Monoarylation using Pd(dba)$_2$/L1 System

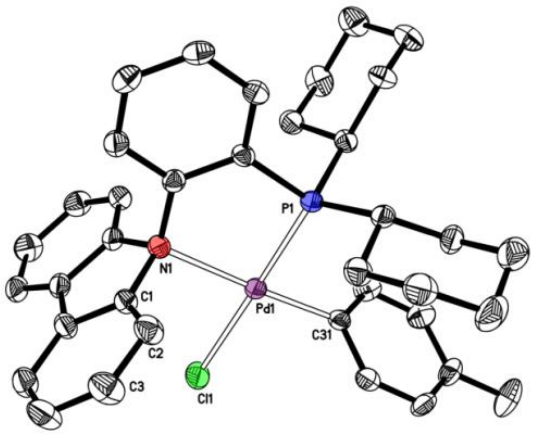


To gain an insight into the ligand-metal interaction during the catalysis, we attempted to prepare and isolate the catalytic intermediate of Pd/PhenCar-Phos catalyst. The oxidative addition adduct **C1** was successfully prepared by direct treatment of Pd(dba)$_2$/PhenCar-Phos with *p*-chlorotoluene in tetrahydrofuran at 90 °C, giving an isolated yield of 70% (Scheme 4). Single crystal of **C1** suitable for X-ray diffraction was yielded 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 binds *trans* to the phosphorus donor. This coordination mode is consistent with the 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 hinderance of **L1** did improve the catalytic rate by facilitating the reductive elimination. However, the inferior performances with electron-poor aryl chlorides shall originate from the extra electron

richness or namely heightened basicity on the palladium centre 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, yet a significant performance drop per 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 *para*-keto or *para*-cyano aryl chlorides.

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

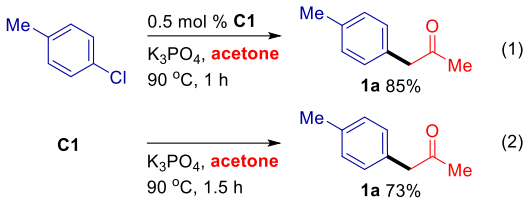




[a]All hydrogen atoms have been omitted for clarity. Reaction conditions: $Pd(dba)_2$ (1.0 mmol), **PhenCar-Phos** (1.2 mmol), *p*-chlorotoluene (15.0 mmol) in THF at 90 °C for 6 h under N_2. Selected distances (Å) and angles (deg): Pd1-P1 2.216 (8), Pd1-N1 2.285 (2), Pd1-Cl1 2.342 (8), Pd1-C31 1.990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

Recently, palladium precatalyst 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 ligand equipvalents, 0.5 mol % of **C1** catalyzed the monoarylation of acetone with *p*-chlorotoluene and afforded 85% yield in 1 hour (1). Direct reaction of **C1** with acetone in the presence of K_3PO_4 gave the product in 73% yield (2). This air-stable precatalyst **C1** gave comparable performance as the *in situ* generated palladium species (Scheme 5, 1 *vs.* Table 1, entry 2).

Scheme 5. Acetone Monoarylations using Precatalyst C1



SUMMARY

In summary, we have developed a new catalyst ($Pd(dba)_2$/**L1**) specifically efficient towards 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 multi-gram scale synthesis. The steric prominence by 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 these findings can offer 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 catalysis, 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 re-sealable screw-capped Schlenk tube (approx. 20 mL volume) in the presence of Teflon-coated magnetic stirrer bar (4 mm × 10 mm). Acetone was dried with activated 4Å molecular sieves under N_2 following by vacuum distillation to a 100 mL Schlenk flask and stored 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 and aryl boronic acids 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 Melting Point B-545 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) were reported as part per million (ppm) in δ scale downfield from TMS. ^{13}C NMR spectra were referenced to $CDCl_3$ (δ 77.00 ppm, the middle peak). ^{31}P NMR spectra were referenced to 85% H_3PO_4 externally. Coupling constants (*J*) were 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 Brüker APEX 47e FTICR mass spectrometer (ESIMS). GC-MS analysis was conducted on a HP 5973 GCD system using a HP5MS column (30 m × 0.25 mm). The products described in GC yield were accorded to the authentic samples/dodecane calibration standard from HP 6890 GC-FID system. All yields reported refer to isolated yield of compounds estimated to be greater than 95% purity as determined by capillary gas chromatography (GC) or ^{1}H NMR. Compounds described in the literature were characterized by comparison of their ^{1}H, 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 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 Teflon-coated magnetic stir bar were charged to a two-necked round bottom flask (250 mL) equipped with a condenser and fitted with a septum. The system was carefully evacuated and backfilled with nitrogen (3 cycles). 1,2-Dibromobenzene (9.65 mL, 80 mmol) and xylene (130 mL) were added by syringe via septum. The septum was switched with a stopper and the reaction mixture was allowed to reflux in a preheated oil bath (185 °C) for 3 days. After completion of reaction, the copper powder was filtered by Celite® and the 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 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 allowed to stir 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 was allowed to warm 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 filtered and washed with cold methanol successively. 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 to a Schlenk tube equipped with a Teflon-coated magnetic stir bar and fitted with septum. The tube was carefully evacuated and backfilled with nitrogen for three cycles. Pd source (0.02 mmol) and ligand (0.04 mmol) in 4.00 mL acetone (1.00 mol % Pd per 1.00 mL stock solution) was then prepared under N_2 with stirring until all solids were dissolved (usually within 1 min). The corresponding volume of stock solution was then immediately added to the Schlenk tube by syringe (In case of 0.10 mol % Pd, additional 400 μL of acetone was added). The solution was stirred for 5 minutes 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 minutes. The tube was placed into a preheated oil bath (90 °C) and stirred for desired duration. After completion of reaction, the reaction tube was allowed to reach room temperature. Ethyl acetate (~3 mL), dodecane (114 μL, internal standard), water (~2 mL) were added. The organic layer was subjected to GC analysis. The GC yield was previously calibrated by 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) was loaded to a Schlenk tube equipped with a Teflon-coated magnetic stir bar and fitted with septum. The tube was carefully evacuated and backfilled with nitrogen for three cycles. $Pd(dba)_2$ (0.02 mmol) and **L1** (0.04 mmol) in 4.00 mL acetone (1.00 mol % Pd per 1.00 mL stock solution) was then prepared under N_2 with stirring until all solids were dissolved (usually within 1 min). The corresponding volume of stock solution was then immediately added to the Schlenk tube by syringe (In case of 0.20 mol % Pd, additional 300 μL of acetone was added). The solution was stirred for 5 minutes 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 minutes. The tube was placed into a preheated oil bath (90 °C) and stirred for 18 hours. After completion of reaction, the reaction tube was allowed to reach room temperature. Ethyl acetate (~3 mL), dodecane (114 μL, internal standard), 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 to a Schlenk tube equipped with a Teflon-coated magnetic stir bar and fitted with septum. The tube was carefully evacuated and backfilled with nitrogen for three cycles. $Pd(dba)_2$ (0.005 mmol) and **L1** (0.01 mmol) in 2.50 mL acetone (0.2 mol % Pd per 500 μL stock solution)

was then prepared under N_2 with stirring until all solids were dissolved (usually within 1 min). The stock solution (500 μL) was then immediately added to the Schlenk tube by syringe. The solution was stirred for 5 minutes at room temperature. *p*-Chloroanisole (0.50 mmol) or *p*-chlorobenzotrifluroride (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 minutes and the septum was then replaced with a screw cap. An array of Schlenk tubes those were prepared in parallel according to above procedure were placed into a preheated oil bath (90 °C) and stirred for the time indicated. After completion of reaction, the reaction tube was immediately placed in an ice bath to quench the reaction. Ethyl Acetate (~3 mL), dodecane (114 μL, internal standard), water (~2 mL) were added. The organic layer was subjected to GC analysis. The GC yield was previously calibrated by authentic sample/dodecane calibration curve.

Synthesis of metal complex C1. $Pd(dba)_2$ (1.0 mmol) and PhenCar-Phos (1.2 mmol) were loaded to a Schlenk tube (250 mL) equipped with a screw cap and Teflon-coated magnetic stir bar. The tube was carefully evacuated and backfilled 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 minutes. The tube was placed into a preheated oil bath (90 °C) and stirred for 6 hours. After completion of reaction, the reaction tube was allowed to reach room temperature. The unreacted palladium was filtered by Celite® and the solvent was removed, diethyl ether was then added to precipitate the product. The crude product was washed with diethyl ether successively to eliminate the unreacted materials and dibenzylideneacetone ligands. The solvent was removed in high vacuum to give the desired product as a light yellow solid (470 mg, 70%). Single crystal of **C1** suitable for X-ray diffraction was yielded 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) was loaded to a Schlenk tube equipped with a Teflon-coated magnetic stir bar and fitted with septum. The tube was carefully evacuated and backfilled with nitrogen for three cycles. *p*-chlorotoluene (0.50 mmol) and subsequently acetone (1.70 mL) were added by syringe. The tube was stirred at room temperature for another 5 minutes and the septum was then replaced with a screw cap. The tube was placed into a preheated oil bath (90 °C) and stirred for 1 hour. After completion of reaction, the reaction tube was immediately placed in an ice bath to quench the reaction. Ethyl Acetate (~3 mL), dodecane (114 μL, internal standard), water (~2 mL) were added. The organic layer was subjected to GC analysis. The GC yield was previously calibrated by authentic sample/dodecane calibration curve.

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

ASSOCIATED CONTENT

Supporting Information. ^{1}H, ^{13}C and ^{31}P NMR spectra and characterization data of compounds. Crystal data and structure refinements of **L1** and **C1**. CIF files containing X-ray crystallographic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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