Dalton Transactions

Accepted Manuscript

ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/dalton

Design and development of POCN-pincer palladium catalysts for C−H bond arylation of azoles with aryl iodides†

Shrikant M. Khake,[a] Vineeta Soni,[a] Rajesh G. Gonnade[b] and Benudhar Punji*[a]

[a]*Organometallic Synthesis and Catalysis Group, Chemical Engineering Division, CSIR–National Chemical Laboratory (CSIR–NCL), Dr. Homi Bhabha Road, Pune – 411 008, Maharashtra, INDIA. Phone: + 91-20-2590 2733, Fax: + 91-20-2590 2621, E-mail: b.punji@ncl.res.in*

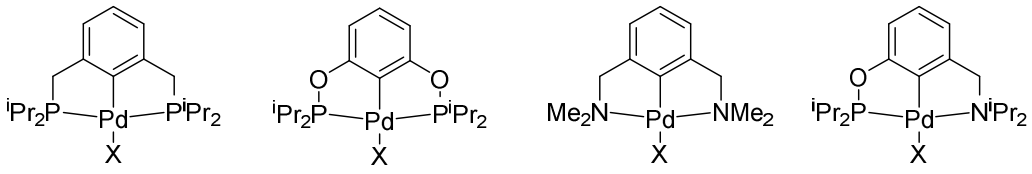
[b]*Centre for Material Characterization, CSIR–National Chemical Laboratory (CSIR–NCL), Dr. Homi Bhabha Road, Pune – 411 008, Maharashtra, INDIA*

Abstract: The well-defined and efficient POCN-ligated palladium complexes have been developed for direct C–H bond arylation of azoles with aryl iodides. The phosphinite-amine pincer ligands 1-(R_2PO)-C_6H_4-3-($CH_2N^iPr_2$), ($^{R2}POCN^{iPr2}$–H) (R = ^{i}Pr, **1a**; R = ^{t}Bu, **1b**) and corresponding palladium complexes {2-(R_2PO)-C_6H_3-6-($CH_2N^iPr_2$)}PdCl, ($^{R2}POCN^{iPr2}$)PdCl (R = ^{i}Pr, **2a**; R = ^{t}Bu, **2b**) are synthesized in good yields. Treatment of palladium complex **2a** with KI and AgOAc afforded the complexes ($^{iPr2}POCN^{iPr2}$)PdI (**3a**) and ($^{iPr2}POCN^{iPr2}$)Pd(OAc) (**4a**), respectively. Similarly, the reaction of **2a** with benzothiazolyl-lithium produces the ($^{iPr2}POCN^{iPr2}$)Pd(benzothiazolyl) (**5a**) complex in quantitative yield. The pincer palladium complex **2a** efficiently catalyzes the C–H bond arylation of benzothiazole, substituted-benzoxazoles and 5-aryl oxazoles with diverse aryl iodides in presence of CuI as co-catalyst under mild reaction conditions. This represents the first example of pincer-palladium complex being applied for direct C–H bond arylation of any heterocycles with low-catalyst loading. Preliminary mechanistic investigation reveals that palladium nanoparticles are presumably not the catalytically active form of **2a** and supports the direct involvement of catalyst **2a**, with complex **5a** being a probable key-intermediate in the catalytic reaction.

†Electronic supplementary information (ESI) available: Crystallographic information files (CIF). Detail experimental data and NMR spectra of all compounds, crystal structure data of complexes **2a** and **2b**, $^{31}P\{^1H\}$ NMR spectrum of ($^{iPr2}POCN^{iPr2}$)Pd species during arylation of azole demonstrating the catalyst resting state. CCDC-973533 (**2a**) and CCDC-973534 (**2b**).

Introduction

Direct C–H bond functionalization of heteroarenes has raised much interest as an alternative to traditional cross-coupling reactions, because such process bypasses the pre-activation steps such as halogenation or metallation of heteroarenes.[1] The transition metal-catalyzed C–H bond functionalizations like arylation, alkenylation, alkynylation and alkylation of various heteroarenes have been widely explored since last few years.[2] Most importantly, arylation of azoles has received particular attention as arylated azoles are essential building-block of diverse biological and pharmaceutical compounds.[3] The C-2 arylations of azoles to synthesize 2-arylated azoles have been realized by employment of various transition metal salts with suitable ligand sets.[4] Among them, the most convenient and inexpensive transition metal catalysts such as complexes of nickel[5] and copper[6] represents very important development for arylation of azoles in term of catalyst cost for large scale synthesis; however, in most cases the utilization of strong bases and harsh reaction conditions limits further advancement of those methodologies. The arylation of azoles has also been reported under mild conditions employing precious metal catalysts, like Ru,[2j] Rh,[7] or Pd[8]-where high loading of catalyst (> 5 mol %) is essential for the completion of reactions. Moreover, many of these catalysts were generated *in situ* (not "well-defined") with few exception;[8l] hence limits proper understanding of the catalyst reactivity and reaction system. Although, many of these *in situ* generated catalysts perform conveniently for arylation of various azoles, still there is a demand to develop well-defined catalyst which can execute the same with minimal catalyst loading. Herein, our objective is to develop well-designed, well-characterized and competent palladium catalysts for the direct C–H bond arylation of azoles, as in many cases such catalysts are more efficient than the transformations carried out by metal salts and added ligands.



"(^{iPr4}PCP)PdX" "(^{iPr4}POCOP)PdX" "(^{Me4}NCN)PdX" "(^{iPr2}POCN^{iPr2})PdX" (described in this paper)

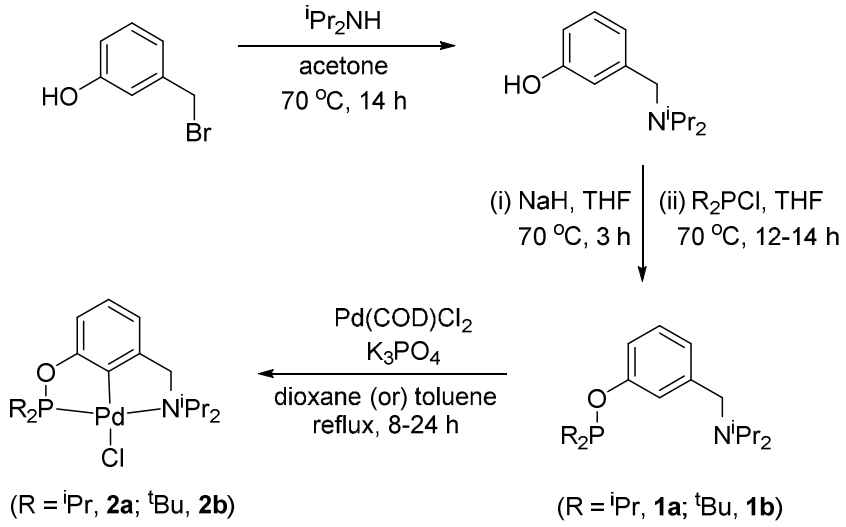
Chart 1 General representation of pincer-palladium complexes.

The pincer-ligated transition metal catalysts have shown exceptionally high thermal stability and catalytic activity for various important organic transformations than the traditional mono- or bi-dentate ligated transition metal catalysts; as the tight tridentate coordination in pincer system keeps the metal and ligand together in each catalytic step, where ligand effects are conveniently transferred to the metal center (Chart 1).[9] For example, the PCP-pincer palladium complexes, [{2,6-(^{i}Pr$_2$PCH$_2$)$_2$-C$_6$H$_3$}Pd(OCOCF$_3$)] and [{2,6-(^{i}Pr$_2$PCH$_2$)$_2$-3,5-(CH$_3$)$_2$-1-CH$_2$-C$_6$H}Pd(OCOCF$_3$)] are highly active catalysts for Heck coupling reaction with bromo- and iodo-arene electrophiles;[10] whereas, phosphinite-based POCOP-pincer palladium catalyst, [{2,6-(^{i}Pr$_2$PO)$_2$-C$_6$H$_3$}PdCl] shows efficient activity for coupling of styrene with relatively difficult aryl chloride electrophiles.[11] Similarly, aminophosphine-based pincer palladium complexes, [{2,6-(EP(piperidinyl)$_2$)$_2$-C$_6$H$_3$}PdCl] (E = NH, O) and an adamantyl core, [{2,6-(Cy$_2$PCH$_2$)$_2$-C$_{10}$H$_{13}$}PdCl] are extremely efficient catalysts for Suzuki cross-coupling reactions.[12] Driven by the high thermal stability and extraordinary catalytic efficiency of pincer palladium complexes for Suzuki and Heck coupling reactions; we became fascinated in developing novel pincer palladium catalyst for C–C bond forming reaction *via* direct C–H bond functionalization. As many of these pincer palladium catalysts are assumed to follow a Pd(II)-Pd(IV)-Pd(II) catalytic pathway during cross-coupling reaction,[12b] a pincer ligated palladium complex having strong σ-donor atom on ligand would enhance electrophilic oxidative addition at Pd(II) center and will stabilize Pd(IV) species.[13] Further, the transmetallation and electrophillic attack has opposite electron demand during such catalysis. Hence, we envisioned that an amino-phosphinite ligand,[14] where electron-rich hard donor amino-side and phosphinite segment would assist electrophilic addition and transmetallation, respectively; could be an ideal system

to stabilize the catalytically active palladium species in higher oxidation state,[15] which can lead to high conversion rate with low catalyst loading. With these entire hypotheses, here in, we have synthesized a “hybrid” pincer palladium catalyst system which efficiently catalyzes the arylation of various azoles with aryl iodides under low catalyst loading in presence of CuI as co-catalyst. The preliminary mechanistic investigation has been carried out to gain in-sight into the catalyst behaviour and reaction pathway.

Results and discussion

Synthesis of POCN–H ligands and palladium complexes. The ^{R2}POCN^{iPr2}–H {1-(R_2PO)-C_6H_4-3-($CH_2N^iPr_2$)} ligands were synthesized in two steps starting from 3-hydroxy benzyl bromide (Scheme 1). First, 3-hydroxy benzyl bromide was treated with two equivalents of diisopropyl amine in acetone to obtain colorless product of 3-((diisopropylamino)methyl)phenol in 82% isolated yield. This compound was characterized by ^{1}H and ^{13}C NMR spectroscopy as well as HRMS. The treatment of 3-((diisopropylamino)methyl)phenol with NaH, followed by reaction with dialkylchlorophosphine, R_2PCl (R = ^{i}Pr, ^{t}Bu) produces the ligands {1-(R_2PO)-C_6H_4-3-($CH_2N^iPr_2$)}, ^{R2}POCN^{iPr2}-H (R = ^{i}Pr, **1a**; R = ^{t}Bu, **1b**) as colorless viscous liquid in excellent yields. The ^{31}P{^{1}H} NMR spectrum of **1a** displayed a peak at 148.8 ppm (for O-P^{i}Pr$_2$ moiety), whereas that of **1b** displayed at 154.3 ppm (for O-P^{t}Bu$_2$ moiety). These NMR values of **1a** and **1b** are consistent with the ^{31}P NMR reported for similar compounds i.e. ^{iPr4}POCOP-H[16] (δ 149.0 ppm) and ^{tBu4}POCOP-H[17] (δ 153.1 ppm), respectively. These crude viscous liquid were used for the metallation reactions without further purification.



Scheme 1 Synthesis of (^{R2}POCN^{iPr2})-H ligands and (^{R2}POCN^{iPr2})PdCl complexes.

The metallation of ligand, ^{iPr2}POCN^{iPr2}–H with $Pd(COD)Cl_2$ in presence of K_3PO_4 in 1,4-dioxane under reflux condition gave {2-($^{i}Pr_2PO$)-C_6H_3-6-($CH_2N^{i}Pr_2$)}PdCl, (^{iPr2}POCN^{iPr2})PdCl (**2a**) as an air-stable light yellow solid. The $^{31}P\{^{1}H\}$ NMR spectrum of **2a** shows a singlet at δ 198.9 ppm (cf. (^{iPr4}POCOP)PdCl,[16] δ 187.7 ppm). The ^{1}H NMR spectrum of compound **2a** shows signals for only three protons in the aromatic region with disappearance of signal correspond to apical proton, which clearly indicates the formation of pincer-palladium complex. Similarly, the complexation of ^{tBu2}POCN^{iPr2}–H with $Pd(COD)Cl_2$ in presence of K_3PO_4 in toluene under reflux condition produced {2-($^{t}Bu_2PO$)-C_6H_3-6-($CH_2N^{i}Pr_2$)}PdCl, (^{tBu2}POCN^{iPr2})PdCl (**2b**) as yellow solid in 89% yield. The $^{31}P\{^{1}H\}$ NMR spectrum of **2b** shows a singlet at δ 204.9 ppm (cf. (^{tBu4}POCOP)PdCl,[18] δ 192.1 ppm). The complexes **2a** and **2b** were well characterized by ^{1}H and ^{13}C NMR spectroscopy as well as elemental analyses.

Compounds **2a** and **2b** were further characterized by single X-ray crystallography (Fig. 1 and Fig. 2). For both the compound, the coordination geometry around palladium is distorted square-planar. Selected bond lengths and bond angles are given in the respective figure captions. For **2a**, the Pd–C(*ipso*) bond length is 1.956(2) Å, slightly shorter than the Pd–C bond length 1.974(±1) Å of (^{iPr4}POCOP)PdCl; whereas the Pd–Cl bond length (2.3922(6) Å) is

slightly longer than the corresponding bond length (2.371(2) Å) of (^{iPr4}POCOP)PdCl.[16] This could be due to the strong σ-donor strength of (^{iPr2}POCN^{iPr2}) moiety exerted towards palladium in **2a** than the (^{iPr4}POCOP) moiety in (^{iPr4}POCOP)PdCl complex. Interestingly, the Pd–P bond length 2.1890(6) Å in **2a** is significantly shorter than the corresponding Pd–P bond lengths (2.276(±2), 2.284(±2) Å) reported for (^{iPr4}POCOP)PdCl. The Pd–N bond length 2.2204(17) Å in **2a** is slightly longer than the Pd–N bond length (2.159(±2) Å) observed for a similar palladium complex, (3-MeO-^{Ph2}POCN^{Me2})PdCl.[14h] The P–Pd–N bond angle 162.10(5)° of **2a** is slightly greater than that observed for (3-MeO-^{Ph2}POCN^{Me2})PdCl (P–Pd–N, 159.53(5)°). The C–Pd–P bond angle 80.35(7)° of **2a** is comparable with that observed for (^{iPr4}POCOP)PdCl (C–Pd–P; 80.500(±2) and 79.920(±2)°). The C–Pd–N bond angle (81.84(8)°) is slightly greater than the C–Pd–P bond angle (80.35(7)°) for **2a**. For compound **2b**, two methyl groups (C15, C16 and C20, C21) of each *tert*-butyl groups showed large anisotropic displacement parameters (ADP) due to orientational disorder. The Pd–C(*ipso*) and Pd–Cl bond lengths in **2b** are 1.958(4) and 2.3943(11) Å, respectively; which are comparable with the corresponding bond lengths in **2a**. The Pd–P bond length 2.2090(11) Å in **2b** is slightly longer than the Pd–P bond length of **2a**, whereas the Pd–N bond length 2.229(3) Å in **2b** is comparable with that observed for **2a**. The P–Pd–N (161.65(9)°), C–Pd–P (80.56(12)°) and C–Pd–N (81.35(15)°) bond angles of **2b** are comparable with the corresponding bond angles in **2a**.

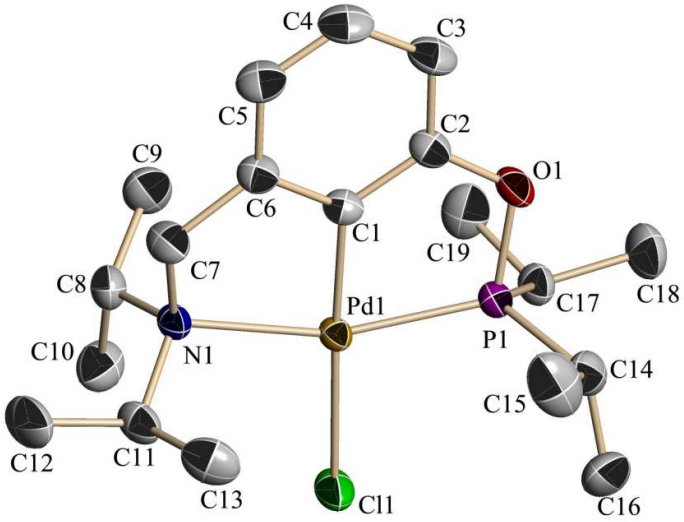


Fig. 1 Thermal ellipsoid of (^{iPr2}POCN^{iPr2})PdCl (**2a**). All the hydrogen atoms omitted for clarity. Selected bond lengths (Å): Pd(1)–C(1), 1.956(2); Pd(1)–P(1), 2.1890(6); Pd(1)–N(1), 2.2204(17); Pd(1)–Cl(1), 2.3922(6). Selected bond angles (°): C(1)–Pd(1)–P(1), 80.35(7); C(1)–Pd(1)–N(1), 81.84(8); P(1)–Pd(1)–N(1), 162.10(5); C(1)–Pd(1)–Cl(1), 177.32(7); P(1)–Pd(1)–Cl(1), 97.04(2); N(1)–Pd(1)–Cl(1), 100.79(5).

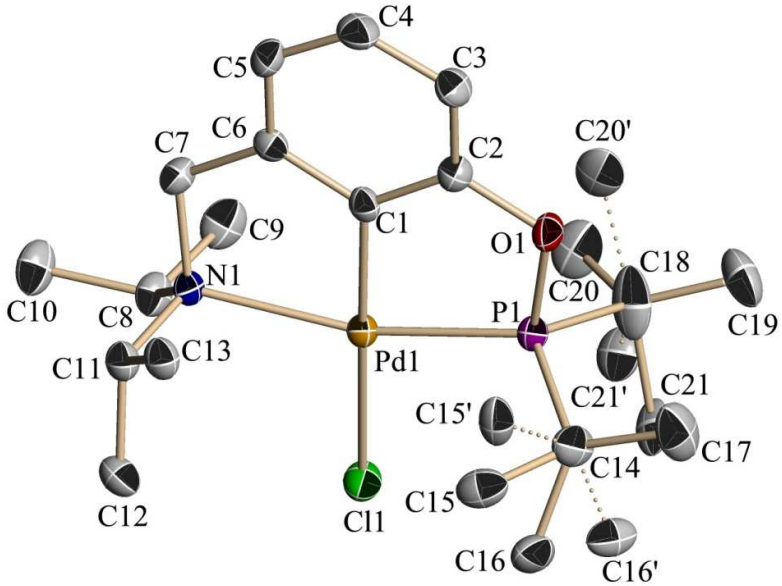
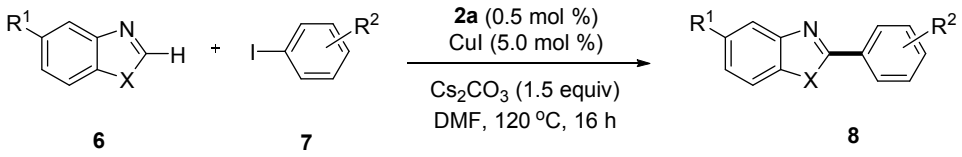


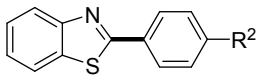
Fig. 2 Thermal ellipsoid of (^{tBu2}POCN^{iPr2})PdCl (**2b**). All the hydrogen atoms omitted for clarity. Selected bond lengths (Å): Pd(1)–C(1), 1.958(4); Pd(1)–P(1), 2.2090(11); Pd(1)–N(1), 2.229(3); Pd(1)–Cl(1), 2.3943(11). Selected bond angles (°): C(1)–Pd(1)–P(1), 80.56(12); C(1)–Pd(1)–N(1), 81.35(15); P(1)–Pd(1)–N(1), 161.65(9); C(1)–Pd(1)–Cl(1), 177.93(13); P(1)–Pd(1)–Cl(1), 99.18(4); N(1)–Pd(1)–Cl(1), 99.00(9).

Catalytic activity of (^{R2}POCN^{iPr2})PdCl complexes for C–H bond arylation of azoles. The newly developed hybrid pincer complexes, (^{iPr2}POCN^{iPr2})PdCl (**2a**) and (^{tBu2}POCN^{iPr2})PdCl (**2b**) were optimized and employed for the direct C–H bond arylation of azoles with aryl iodides. Initially, the complex **2a** was screened for C–H bond arylation of benzothiazole (**6a**, 0.50 mmol) with 4-iodotoluene (**7a**, 0.75 mmol) as electrophile, employing CuI as co-catalyst. After investigating various reaction parameters, we found that the coupled product 2-(*p*-tolyl)benzothiazole (**8aa**) could be obtained in 97% isolated yield employing 0.5 mol % of catalyst **2a** and 5.0 mol % of CuI, in presence of Cs_2CO_3 (0.75 mmol) in DMF.[19] Other carbonate bases like Na_2CO_3, K_2CO_3 as well as cesium source like CsOAc were found to be less effective (5 - 34%). The use of K_3PO_4 base also gave good yield (88%) of **8aa**. The polar aprotic solvent DMF was found to be the solvent of choice,[20] whereas solvents like dioxane, toluene led to diminished yields. The presence of CuI as co-catalyst was very much essential to obtain good conversion rate. Direct arylation proceeded even in absence of CuI co-catalyst, however with low efficacy (21% of **8aa**, TON's 42). The CuI most likely enhances the transmetallation of azoles to the palladium center.[8l] The presence of palladium catalyst **2a** under the standard condition (**6a**, 0.50 mmol; **7a**, 0.75 mmol; Cs_2CO_3, 0.75 mmol; CuI, 5 mol % in DMF at 120 ^{o}C) was necessary, in absence of which arylation product **8aa** formed in < 2% (^{1}H NMR yield), which is non-catalytic as regards to CuI. To understand the respective roles of palladium catalyst **2a** and CuI, a number of experiments were carried out by decreased **2a** loading and increased CuI loading. Hence, the catalytic reactions using 0.5% of **2a** + 5% of CuI, 0.25% of **2a** + 10% of CuI and 0.125% of **2a** + 20% of CuI under standard catalytic conditions, the yields (TON's) of **8aa** obtained were 97% (194), 76% (304) and 67% (536), respectively. Even, large amount of CuI could not replace **2a** under present catalytic conditions. For example, when the standard catalytic reaction was carried out employing 20 mol % of CuI in absence of **2a**, only 8% (^{1}H NMR yield) of coupled product was formed. This clearly indicates both the palladium catalyst **2a** and CuI are essential for the catalytic reaction to occur, and CuI act as a co-catalyst for the reaction. The catalytic reaction also proceeded with low catalyst loading (0.1 mol % of **2a** and 5 mol % of CuI) giving product **8aa** with a TON's of 650 after 48 h. The employment of bulky pincer

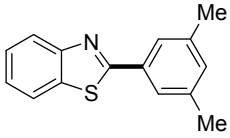
palladium catalyst, (^{tBu2}POCN^{iPr2})PdCl (**2b**) was less efficient giving the coupled product **8aa** in 47% yield; which could be due to more steric constraint.

Subsequently, the optimized reaction conditions were applied to C–H bond arylation of benzothiazole with diversely substituted aryl iodide electrophiles (Scheme 2). By employing only 0.5 mol % of catalyst **2a** and 5 mol % of CuI,[21] benzothiazole was very efficiently arylated in DMF at 120 °C. Thus, electron-rich aryl iodides were effectively employed as coupling partner including sterically demanding *ortho*-substituted partner (**7j**). The coupling of electron-deficient aryl iodides with benzothiazole were less effective, giving the products (**8af**, **8ag**) in moderate to low yields. A variety of functional groups, -OMe, -F, -Cl, -Br, -CF_3, -$COCH_3$ were tolerated on aryl iodide moiety under the catalytic conditions. The tolerability of functional groups like -Cl, -Br in the product (**8ad**, **8ai**) is significant, as they can be used for further functionalization. Heteroarene electrophiles like iodo-pyridine and iodo-pyrazine also reacted with moderate to good conversion (**8al**, **8am**). On contrary, the aryl bromide or chloride as electrophilic coupling partner did not produce arylated product satisfactorily under standard catalytic conditions. Similar to benzothiazole, substituted-benzoxazoles also reacted smoothly yielding the products **8ba**, **8ca** in good yields.

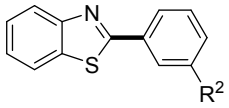




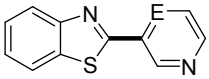
R^2 = Me (**8aa**): 97%
R^2 = H (**8ab**): 94%
R^2 = OCH_3 (**8ac**): 86%
R^2 = Cl (**8ad**): 92%
R^2 = F (**8ae**): 74%
R^2 = CF_3 (**8af**): 58%
R^2 = COMe (**8ag**): 20%



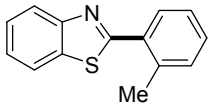
8ak: 99%



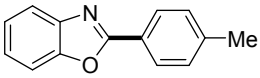
R^2 = Me (**8ah**): 94%
R^2 = Br (**8ai**): 41%



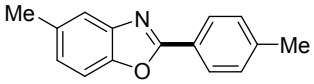
E = CH (**8al**): 70%
E = N (**8am**): 47%



8aj: 95%



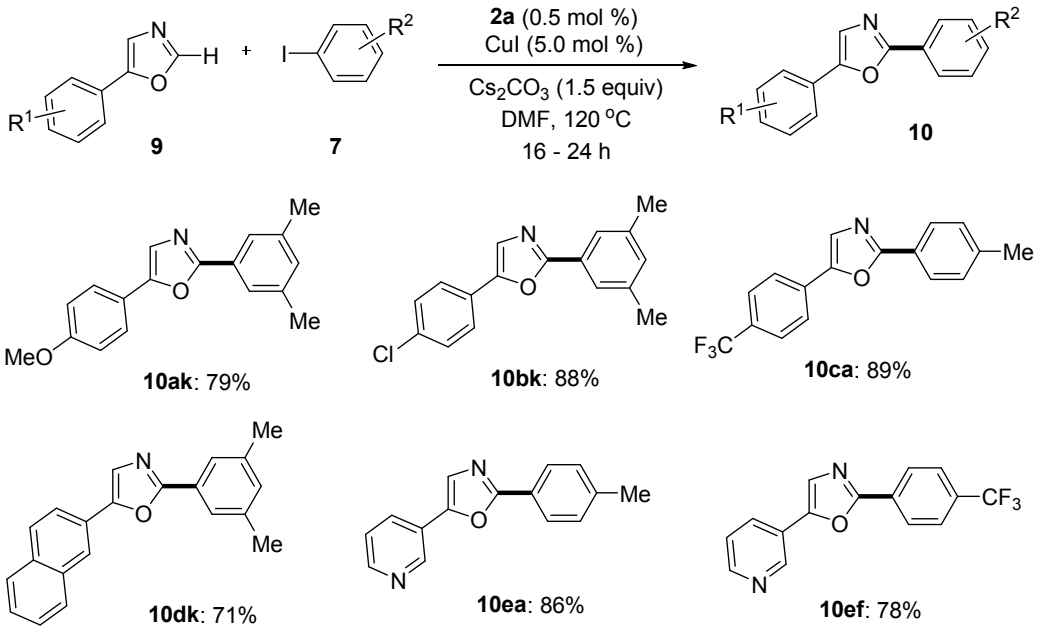
8ba: 85%



8ca: 91%

Scheme 2 Scope of the (^{iPr2}POCN^{iPr2})PdCl (**2a**) catalyzed arylations of azoles with aryl iodides. *Reagents and conditions:* Azole (0.5 mmol), aryl iodide (0.75 mmol), Cs_2CO_3 (0.75 mmol), catalyst **2a** (0.5 mol %), CuI (5.0 mol %) and DMF (1.0 mL), 120 ^oC, 16 h. Isolated yield after column chromatography on silica gel.

Further, we tested the versatility of catalyst **2a** in the arylation of various 5-substituted-oxazoles (Scheme 3). Hence, azoles containing both electron-donating as well as electron-withdrawing substituents (**9a**, **9c**) on aryl backbone reacted conveniently with aryl iodides to give the 2-arylated products in good yields. Functional groups like chloro, methoxy as well as heteroarene substituents like pyridine were well tolerated on azole substrates. Interestingly, electron-deficient aryl iodides those are moderate in coupling with benzothiazole, reacted efficiently with 5-pyridinyl azole giving the arylated product **10ef** in good yield.

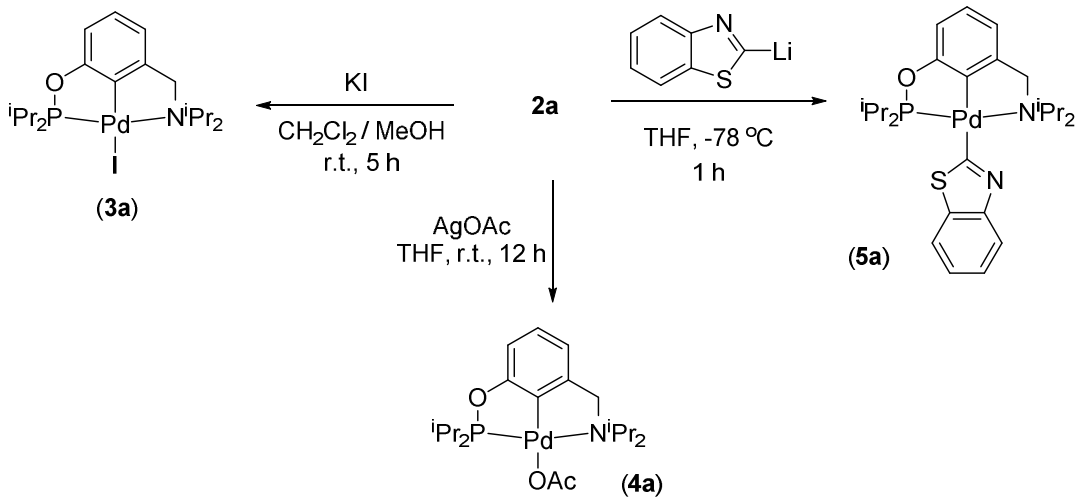


Scheme 3 Scope of the (^{iPr2}POCN^{iPr2})PdCl (**2a**) catalyzed arylations of 5-arylated azoles with aryl iodides. *Reagents and conditions:* Azole (0.5 mmol), aryl iodide (0.75 mmol), Cs_2CO_3 (0.75 mmol), catalyst **2a** (0.5 mol %), CuI (5.0 mol %) and DMF (1.0 mL), 120 °C, 16-24 h. Isolated yield after column chromatography on silica gel.

Although, the *in situ* generated palladium catalysts are known for C–H bond arylation of azoles, a minimum 5 mol % loading of precious palladium metal required in many cases.[8a,8c,8h,8k] However, the well-characterized complex **2a** catalyzes the arylation of azoles with only 0.5 mol % of catalyst loading. In addition, we were particularly fascinated by the remarkable reactivity observed by the electron-rich aryl iodides, which are generally considered as electronically deactivated coupling partner for Pd(0)/Pd(II) redox catalysis.

Synthesis of (^{iPr2}POCN^{iPr2})PdX derivatives. Assuming the possible formation of (^{iPr2}POCN^{iPr2})Pd(X) (X = I, OAc, benzothiazolyl) intermediates during the catalysis, we have independently synthesized these complexes to prove their authenticity (Scheme 4). Hence, the treatment of (^{iPr2}POCN^{iPr2})PdCl (**2a**) with KI in dichloromethane and methanol solvent mixture in a J-Young NMR tube afforded (^{iPr2}POCN^{iPr2})PdI (**3a**) at room temperature. Similarly, the reaction of (^{iPr2}POCN^{iPr2})PdCl with AgOAc in THF at room temperature gave (^{iPr2}POCN^{iPr2})Pd(OAc) (**4a**) in 73% isolated yield. The ^{31}P NMR spectrum of **3a** shows a single resonance at 203.9 ppm, whereas that of **4a** resonates at 196.7

ppm. Treatment of complex **2a** with benzothiazoly-lithium compound at -78 ^{o}C afforded the product (^{iPr2}POCN^{iPr2})Pd(benzothiazolyl) (**5a**) in quantitative conversion. The ^{31}P NMR spectrum of complex **5a** shows a singlet at 194.4 ppm. The complexes **3a**, **4a** and **5a** were further characterized by ^{1}H and ^{13}C NMR spectroscopy as well as HRMS.

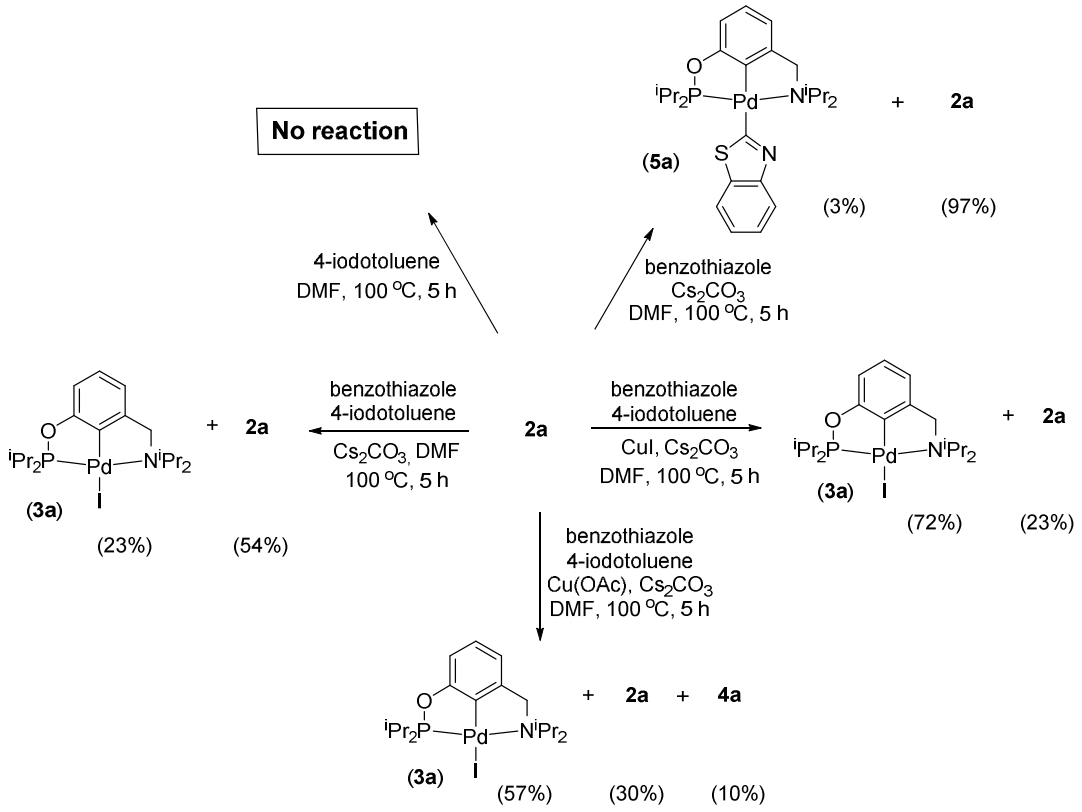


Scheme 4 Synthesis of (^{iPr2}POCN^{iPr2})Pd-derivatives.

Mechanistic aspects. Considering the excellent catalytic activity of (^{iPr2}POCN^{iPr2})PdCl (**2a**) for arylation of azoles, we became interested in looking at the working mode of catalyst. The palladium catalysts known for arylation of azoles generally undergo classical redox process, such as Pd(0)-Pd(II)-Pd(0) cycle. However, a similar catalytic cycle for complex **2a** will decompose the pincer catalyst when palladium enters to zero oxidation state; and concurrently the catalyst might transform into another active species, such as palladium(0) nanoparticle.[22] In such cases, the pincer complex do not catalyze the reaction directly, instead serves as a precatalyst and releases the active palladium(0) species. Alternatively, a hypothetical Pd(II)-Pd(IV)-Pd(II) catalytic cycle is proposed for cross-coupling reactions, where pincer complexes directly catalyzes the reaction; as palladium(IV) pincer complexes are supposed to be stable species.[12b] In order to know the precise catalytic cycle involves for **2a** during

arylation of azoles, a number of quantitative tests and NMR studies were carried out.

The addition of Bu_4NBr (10 mol %), a salt known to stabilize the palladium(0) nanoparticles,[23] to the catalytic reaction did not enhance the rate of reaction as well as yield of product. Instead, a low yield of isolated product (40% *vs* 97% in absence of Bu_4NBr) was observed in presence of Bu_4NBr salt.[24] Similarly, addition of ligands suitable for poisoning the palladium(0) nanoparticles,[25] such as PPh_3 (2.0 equiv w.r.t. **2a**) to the standard catalytic reaction has no impact on the reaction, whereas addition of molecular pyridine (150 equiv w.r.t. **2a**) to the catalytic reaction has negligible influence on overall conversion.[26] The catalytic reaction was slightly affected by incorporation of 150 equiv of basic poison poly(vinyl pyridine) (PVPy), known to quench homogeneous Pd(0) nanoparticles.[22b,22c] All these experimental finding supports the possibility of **2a** being directly involved in catalytic reaction[27] and less likely to transform into another active catalytic species (palladium nanoparticles). However, the addition of 200 equiv of mercury to the catalytic reaction reduced the reaction yield remarkably, though it could not quench the reaction completely. Generally, mercury ceases the reaction completely, if the catalyst is heterogeneous in nature by forming an amalgam with palladium nanoparticles.[28]



Scheme 5 Formation of different (^{iPr2}POCN^{iPr2})Pd-species during control experiments (% are w.r.t standard PMe_3 capillary).

Further, to gain more insight into the stature of active catalytic species, the catalytic reactions were probed by ^{31}P NMR spectroscopy (Scheme 5). The catalyst (^{iPr2}POCN^{iPr2})PdCl (**2a**) (0.012 g, 0.025 mmol) and CuI (0.005 mmol) were taken in a J-Young NMR tube along with benzothiazole (0.25 mmol), 4-iodotoluene (0.375 mmol) and Cs_2CO_3 in DMF and the reaction was monitored by ^{31}P NMR at regular interval. At room temperature, the reaction mixture exhibited two signals: a singlet at 198.8 ppm which corresponds to **2a** (89%) and another singlet at 204.5 ppm which was assigned to (^{iPr2}POCN^{iPr2})PdI (**3a**, 11%). The (^{iPr2}POCN^{iPr2})PdI being obtained from the halide exchange reaction of **2a** with CuI, which was again independently probed. Upon heating the aforementioned reaction mixture at 100 °C for 5 h, the two signals persists at 198.8 ppm (23%, **2a**) and 204.5 ppm (72%, **3a**) with the iodo-derivative **3a** being the major species.[29] An additional phosphorus signal appeared at 49.3 ppm (3%, unknown) and a slight (< 2% w.r.t. external standard PMe_3) disappearance of the

catalyst from total catalysts concentration (**2a**+**3a**) was observed; which could be due to the catalyst decomposition. In order to indentify the origin of iodide-source other than CuI and to verify the possibility of iodide from 4-iodotoluene for the formation of **3a**,[29] a reaction was carried out by replacing CuI with Cu(OAc). Hence, after heating the reaction mixture in presence of Cu(OAc) (0.016 mmol) at 100 ^{o}C for 5 h, the ^{31}P NMR spectrum exhibited four signals at 195.2 ppm (10%), 198.8 ppm (30%, **2a**), 204.5 ppm (57%, **3a**) and 49.3 ppm (2%, unknown). The signal at 195.2 ppm was assigned to (^{iPr2}POCN^{iPr2})Pd(OAc) (**4a**) complex.[30] The formation of iodo-derivative **3a** from **2a** in absence of CuI clearly demonstrates that 4-iodotoluene is the only iodide-source for the generation of **3a**. To examine the credibility of pincer complex **2a** and to rule out the possible indirect involvement of Cu(OAc)[31] in the generation of iodo-derivative **3a** during catalytic reaction, complex **2a** was treated with 4-iodotoluene and benzothiazole in absence of copper source. The ^{31}P NMR spectrum of the reaction mixture shows formation of **3a** (23%), which indicates that CuX was not necessarily required for the generation of **3a**; and (^{iPr2}POCN^{iPr2})Pd-alone can generate **3a** during catalytic reaction in presence of 4-iodotoluene and benzothiazole.

Next, the probable route for the generation of complex **3a** from the complex **2a** and 4-iodotoluene was probed. Milstein et. al. have reported that a halide exchange reaction between (pincer)Pd-Cl and Ar-I can occur *via* a redox induced binuclear Pd(0) intermediate.[32,33] However, the reactivity order of electronically different substituted aryl iodides in current system does not support oxidative addition of Ar-I to a Pd(0)-species for the formation of **3a**.[34,35] To probe further, the complex **2a** (0.025 mmol) was treated with 4-iodotoluene (0.375 mmol) in DMF at 100 ^{o}C. After heating the reaction mixture at 100 ^{o}C for 5 h, the ^{31}P NMR of reaction did not show formation of **3a**; and the complex **2a** mostly remained unreacted. This indicates 4-iodotoluene does not undergo direct halide exchange reaction with **2a**, either *via* a concerted halide exchange or *via* an oxidative pathway through Pd(IV) intermediate. Alternatively, the 4-iodotoluene can react with a (POCN)Pd(II)-intermediate species (generated from **2a**), which can lead to the formation of complex **3a**. To probe this hypothesis and to identify formation of any (POCN)Pd(II)-intermediate species, **2a** was treated with benzothiazole in absence of 4-iodotoluene and CuI. Hence, treatment of **2a** with benzothiazole in presence of Cs_2CO_3 at 100 ^{o}C for 5 h, a new peak observed at

194.4 ppm which corresponds to (POCN)Pd-benzothiazolyl (**5a**) complex. Though, the formation of complex **5a** was not competitive enough in the reaction,[36] the same has been reacted upon addition of 4-iodotoluene and a new peak correspond to **3a** appeared. Further, a stoichiometric reaction of **5a** with 4-iodotoluene in DMF at 100 ^{o}C for 5 h, exclusively produced **3a** and coupled product **8aa**; and the amount of **3a** generated was roughly same as the starting complex **5a**.[37] This indicates the complex **5a** might be a possible intermediate during the catalytic reaction. Even, a catalytic reaction employing **5a** as catalyst under standard reaction condition produces **8aa** in 95% yield, which means **5a** is as active as catalyst **2a**. This finding further supports **5a** as a feasible active intermediate during the catalytic reaction and also in the formation **3a**. Hence, the formation of **3a** in all the controlled experiments might be presumed from the concerted metathesis or oxidative addition of 4-iodotoluene to **5a**, followed by a reductive elimination of **8aa**.

With these entire results, as well as following the previously reported mechanistic observations for palladium/copper-catalyzed azole arylation[8l] and pincer-palladium-catalyzed Suzuki reaction,[12b] we have proposed a possible catalytic cycle for the arylation of azoles by complex **2a** (Fig. 3). We assume that, the catalytic cycle begins with the important base-assisted concerted metallation deprotonation of benzothiazole with CuI. The benzothiazolyl-copper species then undergo transmetallation with palladium complex **2a** to form an intermediate complex **5a**. Subsequently, oxidative addition of aryl iodide to **5a** could generate a neutral hexacoordinated pincer Pd(IV) intermediate **A**, followed by reductive elimination of the arylated azole product (Fig. 3, Path-I). Alternatively, direct formation of arylated azole product on pincer Pd(II) center of **5a** *via* a four-centered concerted transition state **B** (path-II) can be manifested. Although, the experimental evidences support a homogeneous catalysis pathway, the results of some standard test to distinguish homogeneous to heterogeneous catalysis were not conclusive. Hence, a parallel catalysis *via* trace amount of highly active palladium nanoparticle as well as by a molecular catalyst cannot be ruled out completely at this stage.

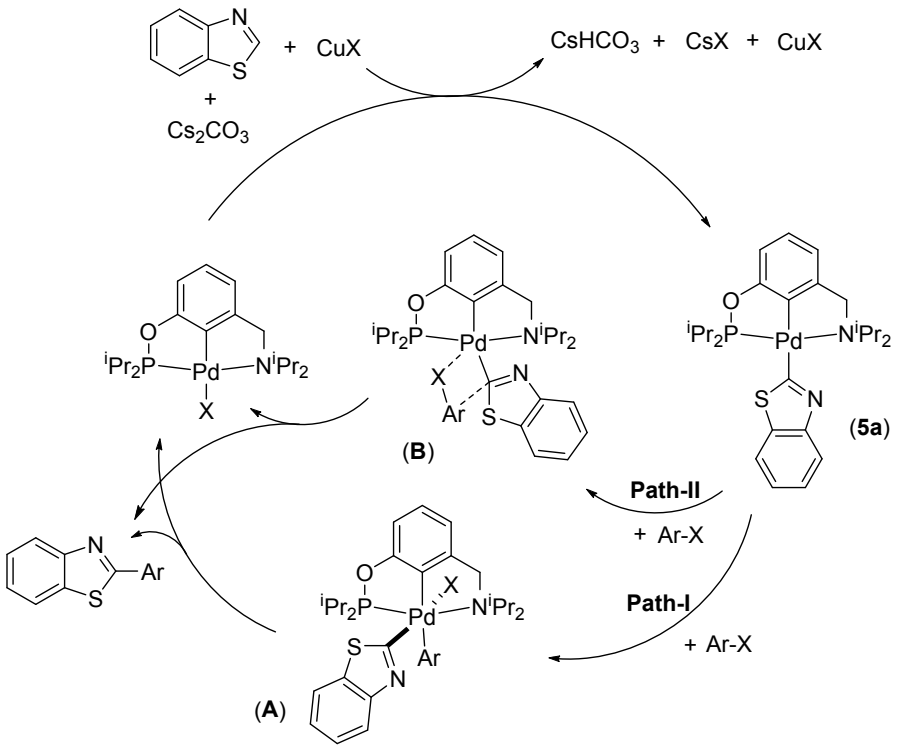


Fig. 3 Possible mechanisms for the arylation of azoles catalyzed by **2a**.

Experimental section

General information. All manipulations were conducted under an argon atmosphere either in a glove box or using standard Schlenk techniques in pre-dried glass wares. The catalytic reactions were performed in flame-dried reaction vessels with Teflon screw cap. Solvents were dried over Na/benzophenone or CaH_2 and distilled prior to use. DMF was dried over CaH_2, distilled under vacuum and stored over 4 Å molecular sieves. Liquid reagents were flushed with argon prior to use. 3-Hydroxy benzyl bromide,[38] 5-methyl benzoxazole,[39] 5-aryl azoles[40] and benzothiazolyl lithium[41] were synthesized according to previously described procedures. All other chemicals were obtained from commercial sources and were used without further purification. Yields refer to isolated compounds, estimated to be > 95% pure as determined by ^{1}H-NMR. TLC: TLC Silica gel 60 F_{254}. Detection under UV light at 254 nm. Chromatography: Separations were carried out on Spectrochem silica gel (0.120-0.250 mm, 60-120 mesh). All IR spectra were recorded on a Bruker optics alpha-E Spectrometer. High resolution mass spectroscopy (HRMS) mass spectra were recorded on a Thermo Scientific Q-Exactive, Accela 1250 pump. M. p.: Büchi 540 capillary melting point

apparatus, values are uncorrected. NMR (^{1}H and ^{13}C) spectra were recorded at 400 or 500 (^{1}H), 100 or 125 {^{13}C, DEPT (Dettached Proton Test)}, 377 (^{19}F) and 162 or 202 MHz (^{31}P{^{1}H}), respectively on Bruker AV 400 and AV 500 spectrometers in $CDCl_3$ solutions, if not otherwise specified; chemical shifts (δ) are given in ppm. The ^{1}H and ^{13}C NMR spectra are referenced to residual solvent signals ($CDCl_3$: δ H = 7.26 ppm, δ C = 77.2 ppm) and ^{31}P{^{1}H} NMR chemical shifts are referenced to an external standard, Me_3P in p-xylene-d_{10} solvent (δ –62.4 ppm), in a sealed capillary tube.

Representative procedure for the arylation of azoles: Synthesis of 2-(*p* tolyl)benzo[*d*]thiazole (8aa). To a flame-dried screw-capped Schlenk tube equipped with magnetic stir bar was introduced 4-iodotoluene **7a** (0.164 g, 0.75 mmol), Cs_2CO_3 (0.244 g, 0.75 mmol) and CuI (0.005 g, 0.025 mmol, 5.0 mol %) under argon. The screw-capped Schlenk tube with mixture was then evacuated and refilled with argon. To the above mixture was added benzothiazole **6a** (0.068 g, 0.50 mmol) and (^{iPr2}POCN^{iPr2})PdCl (0.0025 mmol, 0.5 mol %, 1.0 mL of 0.0025 M stock solution) in DMF under argon. The resultant reaction mixture was then degassed, refilled with argon and was stirred at 120 ^{o}C in a pre-heated oil bath for 16 h. At ambient temperature, H_2O (15 mL) was added and the reaction mixture was extracted with *t*-BuOMe (20 mL x 3). The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated *in vacuo*. The remaining residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc 30/1→ 20/1) to yield **8aa** (0.109 g, 97%) as an off-white solid.

General procedure for added ligand experiments. These reactions were carried out following the representative procedure for the synthesis of 2-(*p*-tolyl)benzo[*d*]thiazole (**8aa**); using **6a** (0.068 g, 0.50 mmol), **7a** (0.164 g, 0.75 mmol), Cs_2CO_3 (0.244 g, 0.75 mmol), **2a** (0.0025 mmol, 0.5 mol %), CuI (0.025 mmol, 5.0 mol %) and appropriate amount of external ligand Bu_4NBr (0.016 g, 0.05 mmol), Hg (0.1 g, 0.5 mmol), PPh_3 (0.0013 g, 0.005 mmol), Py (0.03 g, 0.375 mmol) or PVPy (0.04 g, 0.375 mmol). After stirring the reaction mixtures at 120 ^{o}C for 16 h, the products were isolated by column chromatography.

The isolated yields of **8aa** obtained in presence of Bu_4NBr, Hg, PPh_3, Py and PVPy in the reactions were 40%, 42%, 94%, 76% and 80%, respectively.

General procedure for resting state study of (^{iPr2}POCN^{iPr2})Pd during azole arylation. A mixture of (^{iPr2}POCN^{iPr2})PdCl (0.012 g, 0.025 mmol), CuX (for X = I, 0.001 g, 0.005 mmol or for X= OAc, 0.002 g, 0.016 mmol), Cs_2CO_3 (0.124 g, 0.38 mmol), benzothiazole (0.034 g, 0.25 mmol) and 4-iodotoluene (0.083 g, 0.375 mmol) was taken in J-Young NMR tube along with PMe_3 capillary (external standard), and DMF (0.5 mL) was added into it. The reaction mixtures were subsequently heated at 100 ^{o}C and progress of reaction was monitored by ^{31}P NMR. The percentage of different species formed was calculated w.r.t. standard PMe_3 capillary.

Reaction in presence of CuI. Following the general procedure and using CuI co-catalyst, when the reaction mixture was heated for 1 h, two signals appear in ^{31}P NMR spectrum at 198.8 and 204.5 ppm, which correspond to (^{iPr2}POCN^{iPr2})PdCl (68%) and (^{iPr2}POCN^{iPr2})PdI (30%), respectively. On continuation of the same reaction for 5 h, two signals persist with different intensity ratio, (^{iPr2}POCN^{iPr2})PdCl (23%) and (^{iPr2}POCN^{iPr2})PdI (72%). An additional peak appeared during the course of reaction at 49.3 ppm (3%, unknown). The total ^{31}P NMR active products concentration has became 98% {(^{iPr2}POCN^{iPr2})PdCl + (^{iPr2}POCN^{iPr2})PdI + unknown} from the actual concentration at the beginning of reaction. The remaining 2% disappearance from the actual concentration might be due to minor catalyst decomposition. Even after heating the reaction mixture at 100 ^{o}C for 16 h, the total pincer catalytic species observed were 82%. This indicates the catalyst decomposition is not significantly high.

Reaction in presence of CuOAc. Following the general procedure and using CuOAc, when the reaction mixture was heated at 100 ^{o}C for 1 h, three signals appear in ^{31}P NMR at 195.2, 198.8 and 204.5 ppm which are resembles to (^{iPr2}POCN^{iPr2})Pd(OAc) (5%), (^{iPr2}POCN^{iPr2})PdCl (87%) and (^{iPr2}POCN^{iPr2})PdI (8%), respectively. After heating for 5 h, the same three signals persist with intensity ratio, (^{iPr2}POCN^{iPr2})Pd(OAc) (10%), (^{iPr2}POCN^{iPr2})PdCl (30%) and (^{iPr2}POCN^{iPr2})PdI (57%), respectively. An additional peak appeared during the course of reaction at 49.3 ppm (2%, unknown).

Reaction in absence of CuX. Following the general procedure and without the addition of Cu-precursor, when the reaction mixture was heated at 100 ^{o}C for

5 h, two signals appear in ^{31}P NMR at 204.5 and 198.8 ppm which corresponds to (^{iPr2}POCN^{iPr2})PdI (23%) and (^{iPr2}POCN^{iPr2})PdCl (54%), respectively.

Reaction with 4-iodotoluene. Following the general procedure and without addition of CuX, benzothiazole and Cs_2CO_3; the complex **2a** (0.012 g, 0.025 mmol) was treated with 4-iodotoluene (0.083 g, 0.375 mmol) in DMF at 100 ^oC for 5 h. The ^{31}P NMR spectrum of the reaction mixture shows only the signal corresponds to **2a**. The formation of signal corresponds to **3a** was not observed.

Reaction with benzothiazole. Following the general procedure and without addition of both CuX and 4-iodotoluene, the reaction mixture was heated at 100 ^oC for 5 h. The ^{31}P NMR spectrum of the reaction mixture shows two signals at 194.4 and 198.8 ppm, which corresponds to (^{iPr2}POCN^{iPr2})Pd-benzothiazolyl (3%) and (^{iPr2}POCN^{iPr2})PdCl (97%), respectively. Upon addition of 4-iodotoluene (0.083 g, 0.375 mmol) to the resulted reaction mixture and further heating at 100 ^oC for 1 h, the peak at 194.4 ppm disappeared and peak correspond to (^{iPr2}POCN^{iPr2})PdI (**3a**) formed.

*Reaction of (^{iPr2}POCN^{iPr2})Pd-benzothiazolyl (**5a**) with 4-iodotoluene*. A mixture of (^{iPr2}POCN^{iPr2})Pd-benzothiazolyl (**5a**) (0.018 g, 0.031 mmol) and 4-iodotoluene (0.007 g, 0.031 mmol) was taken in a J-Young NMR tube and DMF (0.5 mL) was added into it. The reaction mixture was subsequently heated at 100 ^oC for 2 h. The ^{31}P NMR spectrum of the reaction mixture shows 57% conversion of **5a** to (^{iPr2}POCN^{iPr2})PdI (**3a**). Upon continuation of heating for 5 h, the complete conversion of **5a** to **3a** was observed. The formation of **3a** (92%) was roughly same as starting complex **5a** (100%).

Synthesis of 3-((diisopropylamino)methyl)phenol. To a solution of 3-hydroxy benzyl bromide (5.0 g, 26.73 mmol) in acetone (50 mL) was added diisopropylamine (7.6 mL, 53.46 mmol) at room temperature. The resultant reaction mixture was refluxed at 70 ^oC for 14 h under argon atmosphere. After cooling the reaction mixture to room temperature, the solvent was evaporated under reduced pressure and crude product obtain was treated with 10% aqueous solution of $NaHCO_3$ (70 mL). The product was extracted with Et_2O (20 mL x 3) and combined extracts were dried over $MgSO_4$. Filtration and evaporation of all the volatile gave colorless viscous product. Yield: 4.52 g (82%). ^1H-NMR (200

MHz, $CDCl_3$): δ = 7.14 (dd, *J* = 8.1, 7.8 Hz, 1H, Ar–H), 6.94-6.90 (m, 2H, Ar–H), 6.68 (dd, *J* = 8.1, 2.2 Hz, 1H, Ar–H), 3.59 (s, 2H, CH_2), 3.02 (sept, *J* = 6.7 Hz, 2H, N{CH(CH_3)$_2$}$_2$), 1.02 (d, *J* = 6.7 Hz, 12H, N{CH(CH_3)$_2$}$_2$). ^{13}C-NMR (50 MHz, $CDCl_3$): δ = 155.8 (C_q), 145.3 (C_q), 129.2 (CH), 120.4 (CH), 115.0 (CH), 113.5 (CH), 49.0 (CH_2), 48.1 (2C, N{*C*H(CH_3)$_2$}$_2$), 20.8 (4C, N{CH(*C*H_3)$_2$}$_2$). HR-MS (ESI) *m/z* calcd for $C_{13}H_{21}NO+H^+$ [M+H$^+$] 208.1701, found 208.1694.

General procedure for the synthesis of ^{R2}POCN^{iPr2}–H ligands. To the suspension of NaH (0.56 g, 23.3 mmol for **1a**; 0.42 g, 17.5 mmol for **1b**)) in THF (10 mL) was added a solution of appropriate amount of 3-((diisopropylamino)methyl)phenol (4.0 g, 19.3 mmol for **1a**; 3.0 g, 14.5 mmol for **1b**) in THF (20 mL) and the resulting mixture was refluxed at 70 ^{o}C for 3 h. After the reaction mixture was cooled to room temperature, a solution of dialkylchlorophosphine, R_2PCl (for compound **1a**, R = ^{i}Pr, 3.2 mL, 20.1 mmol; for compound **1b**, R = ^{t}Bu, 2.90 mL, 15.3 mmol) in THF (20 mL) was added and resulting reaction mixture was further refluxed at 70 ^{o}C for 12 h. The reaction mixture was cooled to ambient temperature and volatile were evaporated under reduced pressure. The compounds were extracted with *n*-hexane (60 mL x 3) and combined *n*-hexane solutions were evaporated under vacuum to obtain oily products of ^{R2}POCN^{iPr2}–H.

(^{iPr2}POCN^{iPr2})–H (1a). Yield: 5.40 g (87%). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.20-7.16 (m, 2H, Ar–H), 7.01 (d, *J* = 7.3 Hz, 1H, Ar–H), 6.94 (d, *J* = 5.8 Hz, 1H, Ar–H), 3.64 (s, 2H, CH_2), 3.04 (sept, *J* = 6.5 Hz, 2H, N{CH(CH_3)$_2$}$_2$), 1.94 (d of sept, *J* = 6.8, 2.5 Hz, 2H, P{CH(CH_3)$_2$}$_2$), 1.21 (dd, *J* = 10.5, 6.8 Hz, 6H, PCH(CH_3)$_2$), 1.14 (dd, *J* = 15.8, 7.3 Hz, 6H, PCH(CH_3)$_2$), 1.05 (d, *J* = 6.5 Hz, 12H, N{CH(CH_3)$_2$}$_2$). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 159.5 (d, J_{P-C} = 8.4 Hz, C_q), 145.2 (C_q), 128.8 (CH), 121.2 (CH), 118.2 (d, J_{P-C} = 10.3 Hz , CH), 116.6 (d, J_{P-C} = 9.9 Hz , CH), 48.9 (CH_2), 47.9 (2C, N{*C*H(CH_3)$_2$}$_2$), 28.5 (d, J_{P-C} = 17.6 Hz, 2C, P{*C*H(CH_3)$_2$}$_2$), 20.9 (4C, N{CH(*C*H_3)$_2$}$_2$), 18.0 (d, J_{P-C} = 20.5 Hz, 2C, PCH(*C*H_3)$_2$), 17.2 (d, J_{P-C} = 8.4 Hz, 2C, PCH(*C*H_3)$_2$). ^{31}P{^{1}H}-NMR (162 MHz, $CDCl_3$): δ = 148.8 (s).

(^{tBu2}POCN^{iPr2})–H (1b). Yield: 4.58 g, (90%). ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.21 (br s, 1H, Ar–H$_{ipso}$), 7.15 (t, *J* = 7.8 Hz, 1H, Ar–H), 6.98 (d, *J* = 7.8 Hz, 2H, Ar–H), 3.62 (s, 2H, CH_2), 3.02 (sept, *J* = 6.4 Hz, 2H, N{CH(CH_3)$_2$}$_2$), 1.17 (d, *J* =

11.5 Hz, 18H, P{C(CH_3)$_3$}$_2$), 1.02 (d, J = 6.4 Hz, 12H, N{CH(CH_3)$_2$}$_2$). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 160.0 (d, J_{P-C} = 8.6 Hz, C_q), 145.2 (C_q), 128.8 (CH), 120.9 (CH), 118.0 (d, J_{P-C} = 9.6 Hz, CH), 116.4 (d, J = 10.5 Hz, CH), 48.9 (CH_2), 47.9 (2C, N{*C*H(CH$_3$)$_2$}$_2$), 35.8 (d, J_{P-C} = 25.9 Hz, 2C, P{*C*(CH$_3$)$_3$}$_2$), 27.6 (d, J_{P-C} = 15.3 Hz, 6C, P{C(*C*H$_3$)$_3$}$_2$), 20.9 (4C, N{CH(*C*H$_3$)$_2$}$_2$). ^{31}P{^{1}H}-NMR (162 MHz, $CDCl_3$): δ = 154.3 (s).

General procedure for the synthesis (^{R2}POCN^{iPr2})PdCl complexes. A mixture of Pd(COD)Cl_2 (0.84 g, 2.94 mmol for compound **2a**; 0.155 g, 0.54 mmol for compound **2b**), appropriate amount of (^{R2}POCN^{iPr2})–H (1.0 g, 3.09 mmol of **1a**; 0.20 g, 0.568 mmol of **1b**) and K_3PO_4 (0.749 g, 3.53 mmol for compound **2a**; 0.137 g, 0.645 mmol for compound **2b**) were taken in a schlenk flask and 1,4-dioxane (for compound **2a**) or toluene (for compound **2b**) (30 mL) was added into it. The reaction mixture was heated at reflux (**2a**: 100 ^{o}C for 8 h or **2b**: 110 ^{o}C for 24 h) under argon atmosphere. The yellowish-black suspension formed was cooled to room temperature and the volatile were evaporated under reduced pressure. The compound was extracted with *n*-hexane (30 mL x 6; for **2a**) or THF (40 mL x 2; for **2b**) and combined organic solutions were evaporated under reduced pressure to obtain the respective complexes as light yellow crystalline solid. The compound **2a** was recrystallized from *n*-hexane solution by slow evaporation, whereas compound **2b** was recrystallized from CH_2Cl_2/*n*-hexane solvent to obtain X-ray quality single crystals.

(^{iPr2}POCN^{iPr2})PdCl (2a). Yield: 0.818 g, 60%. M.p. = 143–144 ^{o}C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 6.91 (vt, J = 7.8 Hz, 1H, Ar–H), 6.62 (d, J = 7.3 Hz, 1H, Ar–H), 6.56 (d, J = 7.8 Hz, 1H, Ar–H), 4.07 (s, 2H, CH_2), 3.55 (apparent octet,[42] J = 6.4 Hz, 2H, N{C*H*(CH$_3$)$_2$}$_2$), 2.43 (apparent octet,[42] J = 7.0 Hz, 2H, P{C*H*(CH$_3$)$_2$}$_2$), 1.65 (d, J = 6.8 Hz, 6H, NCH(CH_3)$_2$), 1.42 (dd, J = 18.8, 7.3 Hz, 6H, PCH(CH_3)$_2$), 1.30 (dd, J = 15.8, 7.1 Hz, 6H, PCH(CH_3)$_2$), 1.21 (d, J = 6.4 Hz, 6H, NCH(CH_3)$_2$). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 163.6 (d, J_{P-C} = 6.9 Hz, C_q), 153.5 (C_q), 143.2 (d, J_{P-C} = 1.5 Hz, C_q), 126.3 (CH), 114.9 (CH), 108.2 (d, J_{P-C} = 16.2 Hz, CH), 61.1 (CH_2), 57.3 (2C, N{*C*H(CH$_3$)$_2$}$_2$), 29.4 (d, J_{P-C} = 25.4 Hz, 2C, P{*C*H(CH$_3$)$_2$}$_2$), 22.5 (2C, NCH(*C*H$_3$)$_2$), 19.4 (2C, NCH(*C*H$_3$)$_2$), 17.7 (d, J = 5.4 Hz, 2C, PCH(*C*H$_3$)$_2$), 16.9 (2C, PCH(*C*H$_3$)$_2$). ^{31}P{^{1}H}-NMR (162 MHz, $CDCl_3$): δ = 198.9 (s). HR-MS (ESI) *m/z* calcd for $C_{19}H_{33}ClNOPPd–Cl^+$ $[M–Cl]^+$ 428.1335,

found 428.1331. Anal. Calcd for $C_{19}H_{33}ClNOPPd$: C, 49.15; H, 7.16; N, 3.02. Found: C, 49.07; H, 7.16; N, 2.77.

(^{tBu2}POCN^{iPr2})PdCl (2b). Yield: 0.237 g, 89%. M.p. = 167–169 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 6.91 (vt, *J* = 7.7 Hz, 1H, Ar–H), 6.59-6.57 (m, 2H, Ar–H), 4.04 (s, 2H, CH_2), 3.58 (apparent octet,[42] *J* = 6.4 Hz, 2H, N{CH(CH_3)$_2$}$_2$), 1.65 (d, *J* = 6.4 Hz, 6H, NCH(CH_3)$_2$), 1.46 (d, *J* = 15.3 Hz, 18H, P{C(CH_3)$_3$}$_2$), 1.19 (d, *J* = 6.4 Hz, 6H, NCH(CH_3)$_2$). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 164.3 (d, J_{P-C} = 5.7 Hz, C_q), 153.5 (C_q), 143.4 (C_q), 126.1 (CH), 114.7 (CH), 108.2 (d, J_{P-C} = 16.2 Hz, CH), 61.1 (*C*H_2), 57.2 (2C, N{*C*H(CH_3)$_2$}$_2$), 40.1 (d, J_{P-C} = 16.2 Hz, 2C, P{*C*(CH_3)$_3$}$_2$), 28.1 (d, J_{P-C} = 4.5 Hz, 6C, P{C(*C*H_3)$_3$)}$_2$), 22.6 (2C, NCH(*C*H_3)$_2$), 19.4 (2C, NCH(*C*H_3)$_2$). ^{31}P{^{1}H}-NMR (162 MHz, $CDCl_3$): δ = 204.9 (s). HR-MS (ESI) *m/z* calcd for $C_{21}H_{37}ClNOPPd–Cl^+$ $[M–Cl]^+$ 456.1648, found 456.1643. Anal. Calcd for $C_{21}H_{37}ClNOPPd$: C, 51.23; H, 7.57; N, 2.84. Found: C, 49.87; H, 7.26; N, 1.96.[43]

Synthesis of (^{iPr2}POCN^{iPr2})PdI (3a). To the mixture of 2,6-(^{i}Pr$_2$PO)(C_6H_3)(CH_2-N^{i}Pr$_2$)PdCl, **2a** (0.015 g, 0.032 mmol) and KI (0.008 g, 0.048 mmol) in a J-Young NMR tube was added CH_2Cl_2 (0.3 mL) and methanol (0.3 mL). Upon warming the reaction mixture at 40 °C for 14 h, the chloro-derivative **2a** is completely converted to iodo-derivative (^{iPr2}POCN^{iPr2})PdI (**3a**). At ambient temperature the volatiles were removed under vacuum to obtain light yellow compound. M.p. = 159–160 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 6.94 (vt, *J* = 7.8 Hz, 1H, Ar–H), 6.64 (d, *J* = 7.5 Hz, 1H, Ar–H), 6.61 (d, *J* = 8.0 Hz, 1H, Ar–H), 4.09 (s, 2H, CH_2), 3.61 (apparent octet,[42] *J* = 6.3 Hz, 2H, N{C*H*(CH_3)$_2$}$_2$), 2.54 (apparent octet,[42] *J* = 7.0 Hz, 2H, P{C*H*(CH_3)$_2$}$_2$), 1.66 (d, *J* = 6.3 Hz, 6H, NCH(CH_3)$_2$), 1.45 (dd, *J* = 18.8, 7.3 Hz, 6H, PCH(CH_3)$_2$), 1.28 (dd, *J* = 15.8, 7.0 Hz, 6H, PCH(CH_3)$_2$), 1.19 (d, *J* = 6.3 Hz, 6H, NCH(CH_3)$_2$). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 162.9 (d, J_{P-C} = 6.2 Hz, C_q), 153.8 (C_q), 147.1 (d, *J* = 6.9 Hz, C_q), 126.4 (CH), 115.1 (CH), 108.1 (d, J_{P-C} = 16.9 Hz, CH), 61.1 (*C*H_2), 58.2 (2C, N{*C*H(CH_3)$_2$}$_2$), 30.3 (d, J_{P-C} = 26.9 Hz, 2C, P{*C*H(CH_3)$_2$}$_2$), 23.7 (2C, NCH(*C*H_3)$_2$), 19.5 (2C, NCH(*C*H_3)$_2$), 18.8 (d, *J* = 3.9 Hz, 2C, PCH(*C*H_3)$_2$), 16.9 (s, 2C, PCH(*C*H_3)$_2$). ^{31}P{^{1}H}-NMR (162 MHz, $CDCl_3$): δ 203.9 (s). HR-MS (ESI) *m/z* calcd for $C_{19}H_{33}INOPPd–I^+$ $[M–I]^+$ 428.1335, found 428.1330.

Synthesis of (^{iPr2}POCN^{iPr2})Pd(OCOCH$_3$) (4a). The mixture of 2,6-(^{i}Pr$_2$PO)(C_6H_3)(CH_2-N^{i}Pr$_2$)PdCl (0.03 g, 0.065 mmol) and AgOAc (0.012 g, 0.072

mmol) in THF (10 mL) was stirred at room temperature for 12 h. The resultant suspension was filtered through celite and volatile were evaporated under reduced pressure to obtain light yellow compound **4a**. Yield: 0.023 g, 73%. M.p. = 134–135 ^{o}C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.89 (vt, *J* = 7.7 Hz, 1H, Ar–H), 6.56 (d, *J* = 7.5 Hz, 1H, Ar–H), 6.52 (d, *J* = 7.8 Hz, 1H, Ar–H), 4.05 (s, 2H, CH_2), 3.43 (apparent octet,[42] *J* = 6.3 Hz, 2H, N{C*H*$(CH_3)_2$}$_2$), 2.66 (apparent octet,[42] *J* = 7.0 Hz, 2H, P{C*H*$(CH_3)_2$}$_2$), 1.92 (s, 3H, COC*H*$_3$), 1.55 (d, *J* = 6.3 Hz, 6H, NCH(C*H*$_3)_2$), 1.32 (dd, *J* = 19.6, 7.3 Hz, 6H, PCH(C*H*$_3)_2$), 1.26 (dd, *J* = 14.7, 7.0 Hz, 6H, PCH(C*H*$_3)_2$), 1.23 (d, *J* = 6.3 Hz, 6H, NCH(C*H*$_3)_2$). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 176.5 (*C*OCH$_3$), 164.2 (d, J_{P-C} = 7.6 Hz, C_q), 153.4 (C_q), 140.7 (C_q), 126.0 (CH), 114.4 (CH), 107.9 (d, J_{P-C} = 15.3 Hz, CH), 60.8 (*C*H$_2$), 56.9 (2C, N{*C*H$(CH_3)_2$}$_2$), 29.9 (d, J_{P-C} = 25.8 Hz, 2C, P{*C*H$(CH_3)_2$}$_2$), 24.2 (CO*C*H$_3$), 21.9 (2C, NCH(*C*H$_3)_2$), 19.3 (2C, NCH(*C*H$_3)_2$), 18.1 (d, *J* = 6.7 Hz, 2C, PCH(*C*H$_3)_2$), 16.9 (d, J_{P-C} = 2.9 Hz, 2C, PCH(*C*H$_3)_2$). ^{31}P{^{1}H}-NMR (162 MHz, $CDCl_3$): δ = 196.7 (s). IR (neat): ν_{max}/cm^{-1} 1598 (CO). HR-MS (ESI) *m/z* calcd for $C_{21}H_{36}NO_3PPd$–$OCOCH_3^+$ [M–$OCOCH_3$]$^+$ 428.1335, found 428.1329. Anal. Calcd for $C_{21}H_{36}NO_3PPd$: C, 51.70; H, 7.44; N, 2.87. Found: C, 51.29; H, 7.46; N, 1.91.[43]

Synthesis of (^{iPr2}POCN^{iPr2})Pd-benzothiazolyl (5a). To a stirred solution of benzothiazole (0.043 g, 0.323 mmol) in THF (10 mL) was added *n*-BuLi (0.22 mL, 1.6 M in hexane) at -78 ^{o}C. After stirring the resultant light yellow lithiated benzothiazole solution at -78 ^{o}C for 20 min, a cold (-78 ^{o}C) solution of **2a** (0.03 g, 0.065 mmol) in THF (10 mL) was added via cannula. The reaction mixture was stirred at -78 ^{o}C for 1 h. The volatiles were evaporated under reduced pressure and product was extracted with *n*-hexane (20 mL). The *n*-hexane extract was evaporated to dryness to obtain crude product, which shows a mixture of **5a** (88%) and **2a** (12%) in ^{31}P NMR spectroscopy. Characterization data of (^{iPr2}POCN^{iPr2})Pd-benzothiazolyl (**5a**): ^{1}H-NMR (500 MHz, C_6D_6): δ = 8.34 (d, *J* = 7.9 Hz, 1H, Ar–H), 7.95 (d, *J* = 7.6 Hz, 1H, Ar–H), 7.24 (vt, *J* = 7.6 Hz, 1H, Ar–H), 7.08 (vt, *J* = 6.9 Hz, 1H, Ar–H), 7.00 (t, *J* = 8.2 Hz, 1H, Ar–H), 6.83 (d, *J* = 7.9 Hz, 1H, Ar–H), 6.63 (d, *J* = 7.6 Hz, 1H, Ar–H), 3.84 (s, 2H, CH_2), 3.20 (apparent octet,[42] *J* = 6.4 Hz, 2H, N{C*H*$(CH_3)_2$}$_2$), 2.26 (apparent octet,[42] *J* = 6.7 Hz, 2H, P{C*H*$(CH_3)_2$}$_2$), 1.43 (d, *J* = 6.0 Hz, 6H, NCH(C*H*$_3)_2$), 1.11 (dd, *J* = 7.0, 1.8 Hz,

6H, PCH(CH_3)$_2$), 1.07 (dd, J = 7.0, 6.7 Hz, 6H, PCH(CH_3)$_2$), 0.94 (d, J = 6.4 Hz, 6H, NCH(CH_3)$_2$). ^{13}C-NMR (100 MHz, C_6D_6): δ = 163.9 (d, J_{P-C} = 6.7 Hz, C_q), 158.4 (C_q), 154.8 (C_q), 152.6 (C_q), 139.0 (C_q), 136.4 (C_q), 127.1 (CH), 126.4 (CH), 125.2 (CH), 124.6 (CH), 122.6 (CH), 114.9 (CH), 108.1 (d, J_{P-C} = 15.3 Hz, CH), 64.7 (CH_2), 58.2 (2C, N{*C*H(CH$_3$)$_2$}$_2$), 29.2 (d, J_{P-C} = 28.6 Hz, 2C, P{*C*H(CH$_3$)$_2$}$_2$), 23.0 (2C, NCH(*C*H$_3$)$_2$), 19.4 (2C, NCH(*C*H$_3$)$_2$), 17.5 (d, J_{P-C} = 4.8 Hz, 2C, PCH(*C*H$_3$)$_2$), 16.9 (2C, PCH(*C*H$_3$)$_2$). ^{31}P{^{1}H}-NMR (202 MHz, C_6D_6): δ = 194.4 (s). HR-MS (ESI): *m/z* calcd for $C_{26}H_{37}N_2OPSPd+1^+$ $[M+1]^+$ 563.1477, found 563.1468.

Conclusion

In summary, new unsymmetrical pincer palladium complexes (^{iPr2}POCN^{iPr2})PdCl and (^{tBu2}POCN^{iPr2})PdCl have been synthesized and demonstrated for the C–H bond arylation of azoles, for the first time any pincer-ligated palladium catalyst is being employed for such reaction. Particularly, sterically less demanding catalyst (^{iPr2}POCN^{iPr2})PdCl enables the efficient coupling of a variety of activated, deactivated and functionalized azoles with diverse aryl iodides under very low-catalyst loading with TON's up to 650. Numerous functional groups such as F, Cl, Br, OMe, $COCH_3$, etc. were tolerated on the aryl backbone to give the coupled products in moderate to excellent yields. Notably, the electron-rich aryl iodide electrophiles perform better than the electron-poor counterparts, a result complimentary to the traditional Pd(0)-catalyzed reactions. Furthermore, employment of less expensive and easily available aryl chloride and bromide electrophiles for azole arylation by catalyst modification is currently under study in our group. Although, the mechanistic investigations accomplished were not conclusive, the experimental findings are indicative of homogeneous reaction mechanism with direct involvement of **2a** in catalysis; however, partial generation of another catalytic active species (palladium nanoparticles) from **2a** cannot be completely ruled out at this stage. The (^{iPr2}POCN^{iPr2})Pd-benzothiazolyl complex, **5a** assumed to be a key intermediate in the catalytic reaction. Hence, reaction mechanism is predicted *via* concerted metathesis or oxidative addition of aryl iodide to **5a**, followed by reductive elimination of coupled product.

Acknowledgements

This work was financially supported by CSIR-NCL (start-up grant, MLP025926), CSIR-New Delhi (Network project ORIGIN, CSC0108) and DST, New Delhi (SR/S1/IC-42/2012). S.M.K. and V.S. thank CSIR, New Delhi for their research fellowship. We thank a reviewer for useful suggestions during the review process.

Notes and references

1. (a) F. Diederich and P. J. Stang, *Metal-Catalyzed Cross-Coupling Reactions; Eds.; Wiley-VCH: Weinheim, Germany*, 1998; (b) L. Ackermann, *Modern Arylation Methods; Ed.; Wiley-VCH: Weinheim, Germany*, 2009.
2. For selected reviews, see: (a) T. Satoh and M. Miura, *Chem. Lett.*, 2007, **36**, 200-205; (b) D. Alberico, M. E. Scott and M. Lautens, *Chem. Rev.*, 2007, **107**, 174-238; (c) I. V. Seregin and V. Gevorgyan, *Chem. Soc. Rev.*, 2007, **36**, 1173-1193; (d) G. P. McGlacken and L. M. Bateman, *Chem. Soc. Rev.*, 2009, **38**, 2447-2464; (e) L. Ackermann, R. Vicente and A. R. Kapdi, *Angew. Chem. Int. Ed.*, 2009, **48**, 9792-9826; (f) L. Ackermann, *Chem. Commun.*, 2010, **46**, 4866-4877; (g) S. Messaoudi, J.-D. Brion and M. Alami, *Eur. J. Org. Chem.*, 2010, 6495-6516; (h) K. Hirano and M. Miura, *Synlett*, 2011, 294-307; (i) N. Kuhl, M. N. Hopkinson, J. Wencel-Delord and F. Glorius, *Angew. Chem. Int. Ed.*, 2012, **51**, 10236-10254; (j) P. B. Arockiam, C. Bruneau and P. H. Dixneuf, *Chem. Rev.*, 2012, **112**, 5879-5918; (k) S. I. Kozhushkov, H. K. Potukuchi and L. Ackermann, *Catal. Sci. Technol.*, 2013, **3**, 562-571.
3. (a) H. Razavi, S. K. Palaninathan, E. T. Powers, R. L. Wiseman, H. E. Purkey, N. N. Mohamedmohaideen, S. Deechongkit, K. P. Chiang, M. T. A. Dendle, J. C. Sacchettini and J. W. Kelly, *Angew. Chem. Int. Ed.*, 2003, **42**, 2758-2761; (b) K. Okamoto, B. T. Eger, T. Nishino, S. Kondo, E. F. Pai and T. Nishino, *J. Biol. Chem.* , 2003, **278**, 1848-1855; (c) P.-Y. Coqueron, C. Didier and M. A. Ciufolini, *Angew. Chem. Int. Ed.*, 2003, **42**, 1411-1414; (d) A. C. Giddens, H. I. M. Boshoff, S. G. Franzblau, C. E. Barry and B. R. Copp, *Tetrahedron Lett.*, 2005, **46**, 7355-7357.

4. C. Verrier, P. Lassalas, L. Théveau, G. Quéguiner, F. Trécourt, F. Marsais and C. Hoarau, *Beilstein J. Org. Chem.* , 2011, **7**, 1584-1601.

5. (a) H. Hachiya, K. Hirano, T. Satoh and M. Miura, *Org. Lett.*, 2009, **11**, 1737-1740; (b) J. Canivet, J. Yamaguchi, I. Ban and K. Itami, *Org. Lett.*, 2009, **11**, 1733-1736; (c) H. Hachiya, K. Hirano, T. Satoh and M. Miura, *Angew. Chem. Int. Ed.*, 2010, **49**, 2202-2205; (d) H. Hachiya, K. Hirano, T. Satoh and M. Miura, *ChemCatChem* 2010, **2**, 1403-1406; (e) T. Yamamoto, K. Muto, M. Komiyama, J. Canivet, J. Yamaguchi and K. Itami, *Chem. Eur. J.*, 2011, **17**, 10113-10122; (f) J. Yamaguchi, K. Muto and K. Itami, *Eur. J. Org. Chem.*, 2013, 19-30.

6. (a) H.-Q. Do and O. Daugulis, *J. Am. Chem. Soc.*, 2007, **129**, 12404-12405; (b) A. A. Kulkarni and O. Daugulis, *Synthesis*, 2009, 4087-4109; (c) Y. Han, X. Wang, X. Wang, L. Lv, G. Diao and Y. Yuan, *Synthesis*, 2012, **44**, 3027-3032.

7. (a) J. C. Lewis, S. H. Wiedemann, R. G. Bergman and J. A. Ellman, *Org. Lett.*, 2003, **6**, 35-38; (b) J. C. Lewis, R. G. Bergman and J. A. Ellman, *Acc. Chem. Res.*, 2008, **41**, 1013-1025; (c) D. A. Colby, R. G. Bergman and J. A. Ellman, *Chem. Rev.*, 2010, **110**, 624-655.

8. For selected examples, see: (a) S. Pivsa-Art, T. Satoh, Y. Kawamura, M. Miura and M. Nomura, *Bull. Chem. Soc. Jpn.*, 1998, **71**, 467-473; (b) A. Mori, A. Sekiguchi, K. Masui, T. Shimada, M. Horie, K. Osakada, M. Kawamoto and T. Ikeda, *J. Am. Chem. Soc.*, 2003, **125**, 1700-1701; (c) F. Bellina, S. Cauteruccio and R. Rossi, *Eur. J. Org. Chem.*, 2006, 1379-1382; (d) G. L. Turner, J. A. Morris and M. F. Greaney, *Angew. Chem. Int. Ed.*, 2007, **46**, 7996-8000; (e) F. Bellina, C. Calandri, S. Cauteruccio and R. Rossi, *Tetrahedron*, 2007, **63**, 1970-1980; (f) H. A. Chiong and O. Daugulis, *Org. Lett.*, 2007, **9**, 1449-1451; (g) F. Derridj, A. L. Gottumukkala, S. Djebbar and H. Doucet, *Eur. J. Inorg. Chem.*, 2008, 2550-2559; (h) L. Ackermann, A. Althammer and S. Fenner, *Angew. Chem. Int. Ed.*, 2009, **48**, 201-204; (i) L.-C. Campeau, D. R. Stuart, J.-P. Leclerc, M. Bertrand-Laperle, E. Villemure, H.-Y. Sun, S. Lasserre, N. Guimond, M. Lecavallier and K. Fagnou, *J. Am. Chem. Soc.*, 2009, **131**, 3291-3306; (j) L. Ackermann, S. Barfüsser and J. Pospech, *Org. Lett.*, 2010, **12**, 724-726; (k) F. Shibahara, E. Yamaguchi and T. Murai, *Chem.*

Commun., 2010, **46**, 2471-2473; (l) J. Huang, J. Chan, Y. Chen, C. J. Borths, K. D. Baucom, R. D. Larsen and M. M. Faul, *J. Am. Chem. Soc.*, 2010, **132**, 3674-3675; (m) G. Zhang, X. Zhao, Y. Yan and C. Ding, *Eur. J. Org. Chem.*, 2012, 669-672.

9. (a) M. E. van der Boom and D. Milstein, *Chem. Rev.*, 2003, **103**, 1759-1792; (b) N. Selander and K. Szabó, *Chem. Rev.*, 2011, **111**, 2048-2076; (c) K. J. Szabó *Top Organomet. Chem.* , 2013, **40**, 203-242.
10. M. Ohff, A. Ohff, M. E. van der Boom and D. Milstein, *J. Am. Chem. Soc.*, 1997, **119**, 11687-11688.
11. (a) D. Morales-Morales, R. Redon, C. Yung and C. M. Jensen, *Chem. Commun.*, 2000, 1619-1620; (b) A. Naghipour, S. J. Sabounchei, D. Morales-Morales, D. Canseco-González and C. M. Jensen, *Polyhedron*, 2007, **26**, 1445-1448.
12. (a) J. L. Bolliger, O. Blacque and C. M. Frech, *Angew. Chem. Int. Ed.*, 2007, **46**, 6514-6517; (b) R. Gerber, O. Blacque and C. M. Frech, *ChemCatChem*, 2009, **1**, 393-400.
13. C. Tabares-Mendoza and P. Guadarrama, *J. Organomet. Chem.*, 2006, **691**, 2978-2986.
14. For POCN-type amino-phosphinite ligand and their complexes (nickel and palladium), see: (a) G. Ebeling, M. R. Meneghetti, F. Rominger and J. Dupont, *Organometallics*, 2002, **21**, 3221-3227; (b) C. S. Consorti, G. Ebeling, F. R. Flores, F. Rominger and J. Dupont, *Adv. Synth. Catal.*, 2004, **346**, 617-624; (c) Y. Motoyama, K. Shimozono and H. Nishiyama, *Inorg. Chim. Acta*, 2006, **359**, 1725-1730; (d) J.-F. Gong, Y.-H. Zhang, M.-P. Song and C. Xu, *Organometallics*, 2007, **26**, 6487-6492; (e) D. M. Spasyuk, D. Zargarian and A. van der Est, *Organometallics*, 2009, **28**, 6531-6540; (f) D. M. Spasyuk and D. Zargarian, *Inorg. Chem.*, 2010, **49**, 6203-6213; (g) B.-S. Zhang, W. Wang, D.-D. Shao, X.-Q. Hao, J.-F. Gong and M.-P. Song, *Organometallics*, 2010, **29**, 2579-2587; (h) J. Li, M. Siegler, M. Lutz, A. L. Spek, R. J. M. Klein Gebbink and G. van Koten, *Adv. Synth. Catal.*, 2010, **352**, 2474-2488; (i) J.-L. Niu, Q.-T. Chen, X.-Q. Hao, Q.-X. Zhao, J.-F. Gong and M.-P. Song, *Organometallics*, 2010, **29**, 2148-2156; (j) D. E. Herbert and O. V. Ozerov, *Organometallics*, 2011, **30**, 6641-6654; (k) D. M. Spasyuk, S. I. Gorelsky, A. van der Est and D.

Zargarian, *Inorg. Chem.*, 2011, **50**, 2661-2674; (l) M.-J. Yang, Y.-J. Liu, J.-F. Gong and M.-P. Song, *Organometallics*, 2011, **30**, 3793-3803; (m) A.-T. Hou, Y.-J. Liu, X.-Q. Hao, J.-F. Gong and M.-P. Song, *J. Organomet. Chem.*, 2011, **696**, 2857-2862.

15. (a) J. Kjellgren, H. Sundén and K. J. Szabó, *J. Am. Chem. Soc.*, 2004, **126**, 474-475; (b) N. Selander, B. Willy and K. J. Szabó, *Angew. Chem. Int. Ed.*, 2010, **49**, 4051-4053.
16. D. Morales-Morales, C. Grause, K. Kasaoka, R. Redón, R. E. Cramer and C. M. Jensen, *Inorg. Chim. Acta*, 2000, **300-302**, 958-963.
17. I. Göttker-Schnetmann, P. White and M. Brookhart, *J. Am. Chem. Soc.*, 2004, **126**, 1804-1811.
18. A. V. Polukeev, S. A. Kuklin, P. V. Petrovskii, S. M. Peregudova, A. F. Smolyakov, F. M. Dolgushin and A. A. Koridze, *Dalton Trans.*, 2011, **40**, 7201-7209.
19. See the experimental section and supporting information (Table S1) for details.
20 The standard catalytic reaction employing crude DMF as well as DMF with added water (5 equiv w.r.t. catalyst **2a**) has been probed and both of which gave less than 2% of desired product **8aa** at 120 ^{o}C. To know the status of catalyst under such condition, the catalytic reaction was monitored by ^{31}P NMR. Hence, the treatment of catalyst **2a** (0.025 mmol) with benzothiazole (0.25 mmol) and 4-iodotoluene (0.375 mmol) under catalytic conditions in DMF in presence of H_2O (5 equiv w.r.t. **2a**) at 100 ^{o}C for 5 h, the decomposition of **2a** observed was 43% (compared to 5% under dry DMF). This decomposition could be even more at 120 ^{o}C. This indicates the Pd-system decomposes significantly in presence of moisture under catalytic conditions, which might accounts for very poor or no catalytic reaction in presence of crude DMF.
21. In many instance the reactions proceeded efficiently if 1 mol % of CuI is used (instead of 5 mol % of CuI) in addition to 0.5 mol % of **2a**.
22. (a) M. R. Eberhard, *Org. Lett.*, 2004, **6**, 2125-2128; (b) K. Yu, W. Sommer, M. Weck and C. W. Jones, *J. Catal.* , 2004, **226**, 101-110; (c) K. Yu, W. Sommer, J. M. Richardson, M. Weck and C. W. Jones, *Adv. Synth. Catal.*,

2005, **347**, 161-171; (d) D. E. Bergbreiter, P. L. Osburn and J. D. Frels, *Adv. Synth. Catal.* , 2005, **347**, 172-184.

23. (a) M. T. Reetz and E. Westermann, *Angew. Chem. Int. Ed.*, 2000, **39**, 165-168; (b) A. Zapf and M. Beller, *Chem. Eur. J.*, 2001, **7**, 2908-2915.
24. The status of catalytic species in presence of Bu_4NBr during the catalytic reaction was monitored by ^{31}P NMR spectroscopy. Hence, treatment of catalyst **2a** (0.025 mmol) with benzothiazole (0.25 mmol) and 4-iodotoluene (0.375 mmol) in presence of Bu_4NBr (0.05 mmol) under catalytic condition at 100 ^{o}C for 3 h, three major species observed in the solution are (^{iPr2}POCN^{iPr2})PdI (204.5 ppm, 43%), (^{iPr2}POCN^{iPr2})PdCl (198.8 ppm, 24%) and a peak at 201.1 ppm (29%). The peak at 201.1 ppm is most likely from the (^{iPr2}POCN^{iPr2})PdBr compound (same has been independently probed by reacting (^{iPr2}POCN^{iPr2})PdCl with Bu_4NBr (5 equiv)). The observed low yield of product in presence of Bu_4NBr may be due to impact of Bu_4NBr on CuX. The possible formation of coordinatively saturated Cu(I) or Cu(II) species in equilibrium with CuX can be envisaged; a scenario which might hinder the action of Cu(I).
25. (a) Y. Lin and R. G. Finke, *Inorg. Chem.*, 1994, **33**, 4891-4910; (b) K. S. Weddle, J. D. Aiken and R. G. Finke, *J. Am. Chem. Soc.*, 1998, **120**, 5653-5666; (c) J. A. Widegren and R. G. Finke, *J. Mol. Catal. A: Chem.*, 2003, **198**, 317-341.
26. The catalytic reactions employing CuI (5 mol %)/PPh_3 (0.007 g, 0.025 mmol, 5 mol %) or CuI (5 mol %)/Py (0.03 g, 0.375 mmol) in absence of **2a** yielded the coupled product **8aa** in < 5% and < 1% (^{1}H NMR yields), respectively. This indicates the actual catalytic reactions were not promoted by CuI/PPh_3 or CuI/Py-catalysis alone.
27. The status of catalytic species were monitored by ^{31}P NMR in presence of PPh_3, pyridine and poly(vinyl pyridine) during the catalytic reactions. The major pincer-palladium species observed in all the cases were (^{iPr2}POCN^{iPr2})PdI and (^{iPr2}POCN^{iPr2})PdCl.
28. (a) P. Foley, R. DiCosimo and G. M. Whitesides, *J. Am. Chem. Soc.*, 1980, **102**, 6713-6725; (b) D. R. Anton and R. H. Crabtree, *Organometallics*, 1983, **2**, 855-859.

29. The reaction mixture contained 20% of CuI w.r.t **2a**; however, the iodide-derivative **3a** formed was 72%. This suggest the additional 52% of iodide is coming from 4-iodotoluene.
30. The (^{iPr2}POCN^{iPr2})Pd(OAc) (**4a**) complex might have formed *via* ligand (chloride/acetate) exchange reaction of (^{iPr2}POCN^{iPr2})PdCl with CuOAc.
31. A probable ligand exchange between Cu(OAc) and 4-iodotoluene might produce CuI, which in turn can react with **2a** to generate complex **3a**.
32. C. M. Frech, L. J. W. Shimon and D. Milstein, *Angew. Chem. Int. Ed.*, 2005, **44**, 1709-1711.
33. Though, Milstein et. al. demonstrated that the halide exchange reaction (pincer-Pd-Cl/Ar-I) is possible through a redox induced Pd(0) intermediate; they have ruled out the intermediacy of the such species during cross-coupling reaction.
34. J. K. Stille and K. S. Y. Lau, *Acc. Chem. Res.*, 1977, **10**, 434-442.
35. The observed catalytic reactions were faster with aryl iodide bearing electron-donating groups (Scheme 2), which is against a conventional Pd(0)-mediated coupling reaction and is consistent with the probability of a transient Pd(IV) species.
36 The trivial formation of (POCN)Pd-benzothiazolyl (**5a**) species is most likely due to the absence of transmetallating reagent CuI in this reaction. The same reaction in presence CuI produces (POCN)PdI as the major species in addition to unreacted **2a**, and unfortunately formation of **5a** was not observed in this case. In addition, the aim of this controlled experiment was also to check the feasibility of transmetallation in absence of CuI.
37 The reaction of (POCN)Pd-benzothiazolyl (**5a**) (100%) with 4-bromotoluene and 4-chlorotoluene in DMF at 100 ^{o}C for 5 h produced (POCN)Pd-Br (75%) and (POCN)Pd-Cl (16%), respectively. This shows the reactions of 4-bromotoluene and 4-chlorotoluene with **5a** were resilient compared to that shown with 4-iodotoluene. Though, the stoichiometric reactions of 4-bromotoluene and 4-chlorotoluene with **5a** are feasible, we did not get convincing catalysis while employing Ar–Cl and Ar–Br as electrophiles, which might be due to the low catalyst concentration during catalysis (substrate/catalyst ratio is 200/1 in catalysis).
38. K. J. Przybilla and F. Vögtle, *Chem. Ber.*, 1989, **122**, 347-355.

39. K. R. Kunz, E. W. Taylor, H. M. Hutton and B. J. Blackburn, *Org. Prep. Proce. Int.*, 1990, **22**, 613-618.
40. A. M. van Leusen, B. E. Hoogenboom and H. Siderius, *Tetrahedron Lett.*, 1972, **13**, 2369-2372.
41. H. Chikashita, M. Ishibaba, K. Ori and K. Itoh, *Bull. Chem. Soc. Jpn.*, 1988, **61**, 3637-3648.
42. In principle, CH of -N{$CH(CH_3)_2$}$_2$ should show a septet (if both CH are equivalents) or two separate septet (if CH are non-equivalent); however, an apparent octet is observed most likely due to partial overlapping of two septet for each CH of -N{$CH(CH_3)_2$}$_2$.
43. A satisfactory elemental analysis is not observed for this compound.

POCN-PdCl

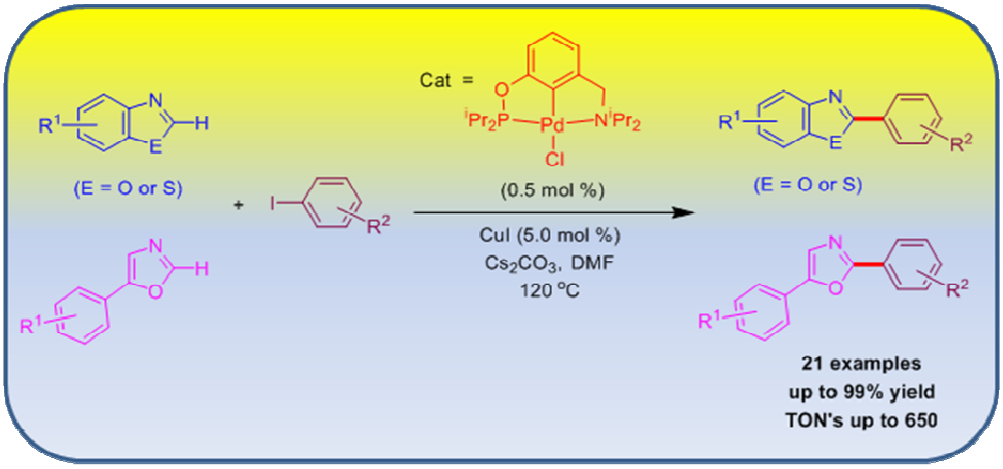
Design and development of POCN-pincer palladium catalysts for C–H bond arylation of azoles with aryl iodides

Shrikant M. Khake,[a] Vineeta Soni,[a] Rajesh G. Gonnade[b] and Benudhar Punji*[a]

[a]*Organometallic Synthesis and Catalysis Group, Chemical Engineering Division, CSIR–National Chemical Laboratory (CSIR–NCL), Dr. Homi Bhabha Road, Pune – 411 008, Maharashtra, INDIA. Phone: + 91-20-2590 2733, Fax: + 91-20-2590 2621, E-mail: b.punji@ncl.res.in*

[b]*Centre for Material Characterization, CSIR–National Chemical Laboratory (CSIR–NCL), Dr. Homi Bhabha Road, Pune – 411 008, Maharashtra, INDIA*

Table of contents entry



Well-defined highly active pincer-ligated palladium complexes are developed for the direct arylation of heteroarenes through C–H bond functionalization using aryl iodide as electrophiles with impressive reactivity.