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PAPER

Development of (quinolinyl)amido-based pincer palladium complexes: A robust and phosphine-free catalyst system for C–H arylation of benzothiazoles†

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(Quinolinyl)amido-ligated palladium(II) complexes have been synthesized and applied in the catalytic C–H bond arylation of benzothiazoles. The tridentate ligand precursors, R_2N-C(O)CH_2-(NH)-C_9H_6N [(^{R2}NNN$^{8\text{-}Q}$)–H; R_2N = morpholinyl, Me-N-piperazinyl] and the pincer palladium complexes, [κ^N,κ^N,κ^N-{R_2N-C(O)CH_2-(μ-N)-C_9H_6N}]PdX [(^{R2}NNN$^{8\text{-}Q}$)PdX {R_2N = Et_2N, morpholinyl, Me-N-piperazinyl; X = OAc or Cl}] were efficiently synthesized, and characterized by various analytical techniques. The iodo-derivative, (^{Et2}NNN$^{8\text{-}Q}$)PdI was obtained in excellent yield by the treatment of complex (^{Et2}NNN$^{8\text{-}Q}$)PdCl with KI. Molecular structures of complexes (^{Et2}NNN$^{8\text{-}Q}$)Pd(OAc) (**2a**), (^{Et2}NNN$^{8\text{-}Q}$)PdCl (**3a**) and (^{Et2}NNN$^{8\text{-}Q}$)PdI (**4a**) were elucidated by the X-ray crystallography. The complex **3a** was found to be the most efficient catalyst for direct C–H bond arylation of substituted benzothiazoles with diverse aryl iodides using a mild base, K_2CO_3. The working catalyst system **3a** is highly robust that can be recycled and reused several times for the arylation of benzothiazole without loss in the catalytic activity. Preliminary mechanistic investigations by the controlled studies and kinetic analysis have been performed, which greatly support a molecular mechanism for the arylation.

Introduction

Palladium complexes of tridentate pincer-ligands have been widely explored for diverse catalytic transformations, by virtue of their unusual thermal, moisture and air-stability.[1] Among various reactions, the pincer-palladium complexes as catalyst are commonly exploited for the traditional cross-couplings,[2] aldol and Michael reactions,[3] allylation of aldehydes and imines,[4] hydrosilylation and borylation,[5] and many other[6] reactions. Most of these reactions were reported with high turnover numbers and broad substrate scope. Additionally, the pincer-ligated palladium complexes were demonstrated for enantioselective synthesis.[3a,3d,3i,4e,7] Conversely, the application of robust pincer-ligated palladium complexesas catalysts in more promising and ubiquitous C–H bond functionalization remains scarce.[5f,8]

More specifically, the C–H bond arylation of sulphur-containing electron-rich heterocycles, such as benzothiazoles is crucial, as they constitute the building blocks of various biological and pharmaceutical compounds.[9] For example, the Thioflavin-T, which contain the C-2 arylated benzothiazole as core motif, is commonly used for histology staining and biophysical studies for protein aggregation.[9f,g] Similarly, the compound 2-(3-cyano-4-isobutoxyphenyl)-4-methyl-5-thiazolecarboxylic acid (TEI-6720) based on aryl-thiazole is an extremely potent inhibitor of xanthine oxidoreductase (XOR).[9c] Considering the significant pharmaceutical conciliation of aryl-benzothiazole motifs, it is worth exploring the design and synthesis of new and robust catalyst system for the selective C-2 arylation of benzothiazoles.

The selective C-2 arylation of substituted-benzothiazoles with aryl halides to achieve the 2-arylated benzothiazole derivatives has been established by various metal catalysts, such as Ni,[10] Cu,[11] Ru,[12] Rh[13] or Pd[14,15] with the added ligands. Though, these metal catalysts efficiently perform the arylation of benzothiazoles; very often harsh reaction conditions, strong and expensive bases, costly phosphine-based ligands are essential for the satisfactory conversion. Additionally, the catalyst stability is a major concern, which enforces the usage of high catalyst loading (more than 5 mol%) in many reactions. Recently, we have reported phosphine-amine based pincer palladium system for the arylation of azoles, which catalyzes the arylation with low catalyst loading.[16] Moreover, the described arylation by the pincer-palladium proceeded

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†Electronic Supplementary Information (ESI) available: ^{1}H and ^{13}C NMR spectra of pincer precursors and palladium complexes, CIF files for **2a** (CCDC-1487195), **3a** (CCDC-1487196) and **4a** (CCDC-1502139). See DOI: 10.1039/x0xx00000x

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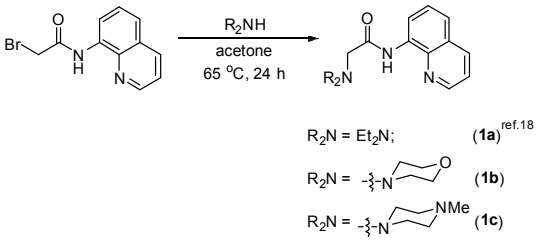
through a rare Pd^{II}-Pd^{IV}-Pd^{II} pathway, which has been validated both by the experiments and by the theoretical calculations.[16c] Motivated by these findings, we hypothesized that a pincer ligated palladium with the strong σ-donor nitrogen atoms on ligand would enhance the oxidative addition of aryl halide electrophile, and the resulting Pd(IV) intermediate would suitably be stabilized, which in turn can act as a robust catalyst system for the arylation.[17]

With the above assumption in mind, herein, we developed the phosphine-free (quinolinyl)amido-based pincer ligands and their palladium complexes, (^{R2}NNN$^{8\text{-}Q}$)PdX [$\kappa^N,\kappa^N,\kappa^N$-{$R_2$N-C(O)$CH_2$-($\mu$-N)-$C_9H_6$N}PdX], and employed them for the arylation of benzothiazoles. In fact, the synthesized palladium catalyst system catalyzes the arylation of benzothiazoles with a variety of aryl iodides employing low catalyst loading, and in the presence of a mild base, K_2CO_3. Importantly, this catalyst system demonstrated to be exceptionally robust, which was recycled and reused for several rounds without loss in the catalytic activity. Preliminary mechanistic experiments have been performed to understand the working mode of catalyst.

Results and discussion

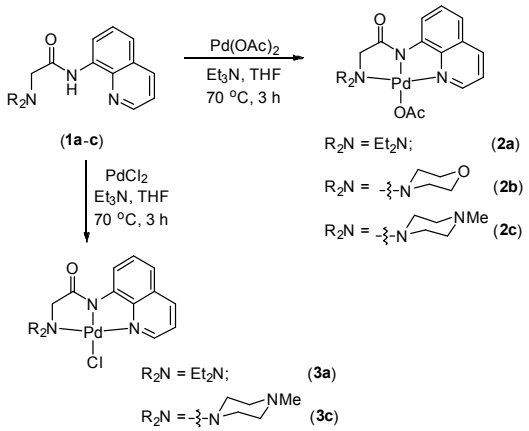
Synthesis and characterization of (^{R2}NNN$^{8\text{-}Q}$)–H ligands and palladium complexes

Recently, we have synthesized nickel complexes of Et_2N-CH_2C(O)N(H)C_9H_6N (^{Et2}NNN$^{8\text{-}Q}$–H; **1a**) ligand and demonstrated their application for the alkylation of indoles with diverse alkyl halides.[18] Similar to the synthesis of **1a**, the quinolinyl-amide ligand precursors, R_2N-CH_2C(O)N(H)C_9H_6N [^{R2}NNN$^{8\text{-}Q}$–H; R_2 = -$(CH_2)_2O(CH_2)_2$- (morpholinyl; **1b**) and -$(CH_2)_2$NMe$(CH_2)_2$- (Me-N-piperazinyl; **1c**)] were conveniently synthesized. Thus, the reaction of 2-bromo-*N*-(quinolin-8-yl)acetamide with the cyclic secondary amines, morpholine and *N*-methyl piperazine, afforded the quinolinyl-amide ligands **1b** and **1c**, respectively, in excellent yields (Scheme 1). Both the compounds **1b** and **1c** were obtained as solids in analytical pure form. These ligands were characterized by ^{1}H and ^{13}C NMR spectroscopy as well as by the HRMS analysis. Notably, the morpholinyl methylene protons in **1b** resonate as two different sets to give two multiplets (~ 3.89 and ~ 2.69 ppm), whereas those of piperazinyl (eight protons) in **1c** appeared as single multiplet (~ 2.67 ppm).



Scheme 1. Synthesis of (8-quinolinyl)amido-ligands, (^{R2}NNN$^{8\text{-}Q}$)–H.

The palladation reactions of ligand, ^{Et2}NNN$^{8\text{-}Q}$–H (**1a**) with $Pd(OAc)_2$ and $PdCl_2$ in the presence of Et_3N in THF under reflux conditions gave {Et_2N-CH_2C(O)-(μ-N)-C_9H_6N}Pd(OAc) [(^{Et2}NNN$^{8\text{-}Q}$)Pd(OAc); **2a**] and {Et_2N-CH_2C(O)-(μ-N)-C_9H_6N}PdCl [(^{Et2}NNN$^{8\text{-}Q}$)PdCl; **3a**], respectively (Scheme 2). These complexes were obtained as yellow crystalline solids in moderate to good yields. In the ^{1}H NMR spectra of compounds **2a** and **3a**, the disappearance of signal corresponds to –*N*H proton on ligand indicative of the formation amido-palladium covalent bond. Further, the methylene protons on –NEt_2 group displayed two sets of multiplets against a single set in **1a**, which suggests the coordination of –NEt_2 arm to the Pd-center. Among two multiplets for the methylene protons, one appeared in the down-field region and the other in up-field region compared to that observed in the free-ligand. The HRMS analysis of both the compounds **2a** and **3a** showed the mass ion peaks correspond to [**2a**–OAc]$^+$ (*m/z* = 362.0493) and [**3a**–Cl]$^+$ (*m/z* = 362.0474). These compounds were further characterized by ^{13}C NMR spectroscopy and elemental analysis. The molecular structures of **2a** and **3a** were determined by single crystal X-ray diffraction study (Figures 1 and 2).



Scheme 2. Synthesis of (8-quinolinyl)amido-based pincer palladium complexes.

The pincer palladium complex, (^{Morp}NNN$^{8\text{-}Q}$)Pd(OAc) (**2b**) was synthesized in good yield by the reaction of (^{Morp}NNN$^{8\text{-}Q}$)–H (**1b**) with $Pd(OAc)_2$ in the presence of Et_3N. However, the attempted synthesis of the corresponding chloro-derivative, (^{Morp}NNN$^{8\text{-}Q}$)PdCl (**3b**) was not successful. Compound **2b** was obtained as a yellow powder. The ^{1}H NMR spectrum of **2b** displayed three sets of multiplet for the methylene protons on morpholinyl moiety, in contrast to two sets in the free-ligand **1b**. This suggests the coordination of morpholinyl-arm to the Pd-center. The HRMS analysis of **2b** showed mass peak *m/z* 376.0267 for the ion [**2b**–OAc]$^+$. Pincer complexes, (^{Pip}NNN$^{8\text{-}Q}$)Pd(OAc) (**2c**) and (^{Pip}NNN$^{8\text{-}Q}$)PdCl (**3c**) were obtained by the treatment of **1c** with $Pd(OAc)_2$ and $PdCl_2$, respectively, in the

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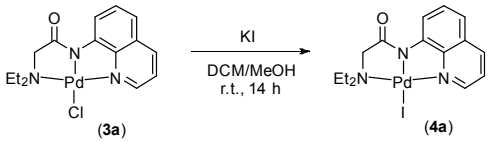
presence of Et_3N base (Scheme 2). Both the compounds **2c** and **3c** were isolated in moderate to good yields as yellow crystalline solids. Notably, the ^{1}H NMR spectra of **2c** and **3c** displayed four sets of signals each for the methylene protons on piperazinyl-moiety, which could be due to the diastereotopic nature of methylene protons, generated upon the coordination of piperazinyl arm to the palladium center. All the three complexes **2b**, **2c** and **3c** were further characterized by the ^{13}C NMR spectroscopy, HRMS and elemental analysis.

The ORTEP diagrams of the complexes **2a** and **3a** are shown in Figure 1 and Figure 2, respectively. Selected bond lengths and bond angles are given in Table 1. In both the complexes, ligand **1a** provides a tridentate coordination to the palladium through quinolinyl-*N2*, amido-*N1* and amine-*N3*, and the fourth site is occupied by anionic ligand –OAc (**2a**) or –Cl (**3a**). The coordination geometry around palladium is slightly distorted from the expected square-planar geometry in both **2a** and **3a**. The Pd–N(1) bond lengths in **2a** (1.936(5) Å) and **3a** (1.953(2) Å) are slightly longer than the Pd–N bond length (1.927(5)Å) in a similar amido-complex, {H_2N-CH(Me)C(O)-(μ-N)-C_9H_6N}PdCl;[19] whereas the Pd–N(2) {2.012(5) Å in **2a**, 2.021(1) Å in **3a**} and Pd–N(3) {2.070(5) Å in **2a**, 2.072(2) Å in **3a**} bond lengths are comparable. The Pd–Cl bond length (2.314(1) Å) in **3a** is slightly shorter than the analogous bond length (Pd–Cl = 2.322(1) Å) in the complex {H_2N-CH(Me)C(O)-(μ-N)-C_9H_6N}PdCl. This slight difference in bond length could be due to weaker σ-donor strength of amido-ligand moiety exerted towards palladium in **2a** than the {H_2N-CH(Me)C(O)NH-C_9H_6N} moiety in {H_2N-CH(Me)C(O)-(μ-N)-C_9H_6N}PdCl. The N(2)–Pd–N(3) bond angles in **2a** (166.8(2)°) and **3a** (166.99(7)°) are comparable with each other and slightly more than that reported for {H_2N-CH(Me)C(O)-(μ-N)-C_9H_6N}PdCl (N(2)-Pd-N(3) = 165.3(2)°). The N(1)–Pd–N(2) and N(1)–Pd–N(3) bond angles in **2a** and **3a** are in the range of 82.35(7)-84.67(7)°. Notably, in the complex **3a**, the N(1)–Pd–N(3) bond angle (84.67(7)°) is significantly larger than the N(1)–Pd–N(2) bond angle (82.35(7)°). The five-membered ring containing Pd, N(1), N(2) is almost planar with the quinolinyl-moiety (Pd(1)-N(2)-C(9)-C(1) = 0.2(7)°), whereas the other five-membered Pd-containing ring is slightly distorted (Pd(1)-N(1)-C(10)-C(11) torsion angle 7.2(7)°) in the complex **2a**.

The iodo-derivative, (^{Et2}NNN$^{8\text{-}Q}$)PdI (**4a**) was synthesized by the reaction of **3a** with KI in DCM/MeOH (1:1, v:v) at ambient temperature (Scheme 3). The complex **4a** was obtained as a brown solid in excellent yield. The ^{1}H NMR spectrum of **4a** has similar splitting pattern to that observed for the complex **3a**. The MALDI-TOF analysis of **4a** showed the mass ion peaks correspond to [**4a** + H]$^+$ (*m/z* = 489.8192) and [**4a** – I]$^+$ (*m/z* = 361.9155). The molecular structure of **4a** was further confirmed by single crystal X-ray diffraction analysis (Figure 3). The coordination geometry around the palladium in **4a** is slightly distorted from the expected square-planar geometry. The Pd–N(1), Pd–N(2) and Pd–N(3) bond lengths (1.967(1), 2.030(1) and 2.079(1) Å, respectively) in **4a** are slightly longer than the corresponding bond lengths (1.953(2), 2.021(1) and 2.072(2) Å) in **3a**, which is due to the larger trans effect and bigger size of iodide than that of chloride. In addition, a slight shortening of the N(1)–Pd–N(2), N(1)–Pd–N(3) and N(2)–Pd–N(3) bond angles (81.77(5), 83.88(5) and 165.64(4)°) in **4a** was observed when compared to those in complex **3a**.



Scheme 3. Synthesis of (^{R2}NNN$^{8\text{-}Q}$)PdI (**4a**) complex.

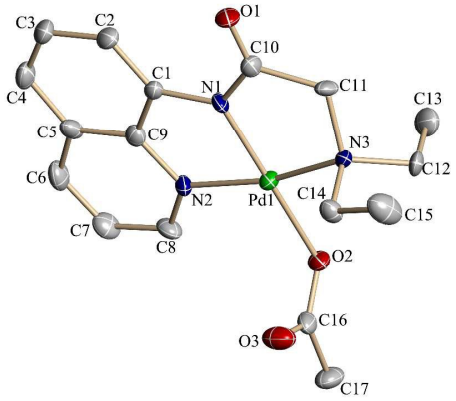


Fig. 1 Thermal ellipsoid plot of (^{Et2}NNN^{Q})Pd(OAc) (**2a**). All the hydrogen atoms are omitted for clarity.

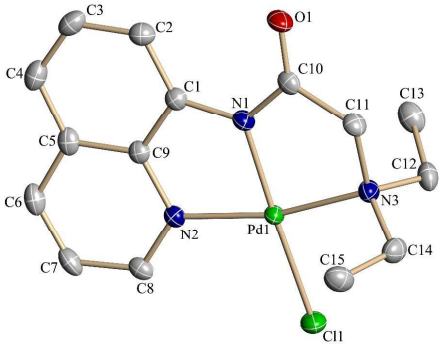


Fig. 2 Thermal ellipsoid plot of (^{Et2}NNN^{Q})PdCl (**3a**). All the hydrogen atoms are omitted for clarity.

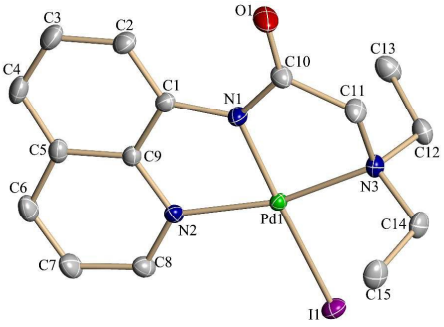


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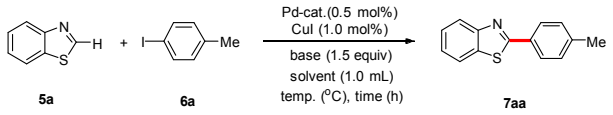
Fig. 3 Thermal ellipsoid plot of (^{Et2}NNN^{Q})PdI (**4a**). All the hydrogen atoms are omitted for clarity.

Table 1 Selected bond lengths [Å] and angles [deg] for **2a**, **3a** and **4a**

	2a	3a	4a
Pd(1)–N(1)	1.936(5)	1.953(2)	1.967(1)
Pd(1)–N(2)	2.012(5)	2.021(1)	2.030(1)
Pd(1)–N(3)	2.070(5)	2.072(2)	2.079(1)
Pd(1)–O(2)	2.055(4)	-	-
Pd(1)–Cl(1)	-	2.314(1)	-
Pd(1)–I(1)	-	-	2.624(1)
N(1)–Pd(1)–N(2)	83.1(2)	82.35(7)	81.77(5)
N(1)–Pd(1)–N(3)	83.9(2)	84.67(7)	83.88(5)
N(2)–Pd(1)–N(3)	166.8(2)	166.99(7)	165.64(4)
N(1)–Pd(1)–O(2)	176.4(2)	-	-
N(2)–Pd(1)–O(2)	94.3(2)	-	-
N(1)–Pd(1)–Cl(1)	-	175.82(5)	-
N(2)–Pd(1)–Cl(1)	-	97.61(5)	-
N(3)–Pd(1)–Cl(1)	-	95.40(5)	-
N(1)–Pd(1)–I(1)	-	-	175.08(3)
N(2)–Pd(1)–I(1)	-	-	97.71(3)
N(3)–Pd(1)–I(1)	-	-	96.55(3)

Optimization of reaction conditions for (^{R2}NNN^{8-Q})PdX catalyzed arylation of benzothiazole

Newly developed phosphine-free pincer palladium complexes were screened, optimized and employed for the direct C–H bond arylation of benzothiazoles with aryl iodides. Initially, all the pincer complexes (^{R2}NNN^{8-Q})PdX (**2a**-**3c**) were screened for the coupling of benzothiazole (**5a**; 0.30 mmol) with 4-iodotoluene (**6a**; 0.45 mmol), employing CuI (1.0 mol%) co-catalyst and K_3PO_4 base in DMF [standard conditions employed with the (^{iPr2}POCN^{iPr2})PdX catalyst][16c] (Table 2). Among all the complexes screened, **3a** performed better and afforded the coupled product **7aa** in 76% isolated yield (Table 2, entries 1-5). The arylation reaction also proceeded equally in the polar aprotic DMSO solvent using catalyst **3a** (entry 6). Interestingly, the arylation in the presence of mild base, K_2CO_3 gave 86% yield of **7aa**; albeit slight elevated temperature of 130 ^{o}C is essential (entries 7-9). Other bases like Na_2CO_3, NaOAc, KOAc were found to be less effective (entries 10-12). Similarly, the reaction was inefficient in other polar (NMP, DMA) and non-polar (toluene, 1,4-dioxane) solvents (entries 13-16). Employment of the palladium catalyst **3a** under the standard reaction conditions is essential, without which only 11% of product **7aa** was detected (entry 17). The presence of CuI as co-catalyst was very much necessary to afford good yield. Most likely, the CuI co-catalyst enhances the transmetalation of benzothiazoles to the palladium center.[16a] A catalytic reaction of the benzothiazole with iodide **6a** employing $PdCl_2$ as catalyst afforded **7aa** in 46% yield (against 99% GC yield with **3a**). This suggests that a catalyst stabilizing ligand is essential for the better conversion in arylation reaction. After investigating the various reaction parameters, we found that the coupled product 2-(*p*-tolyl)benzothiazole (**7aa**) could be obtained in 86% isolated yield, employing 0.5 mol% of catalyst **3a** and 1.0 mol% of CuI in the presence of K_2CO_3 in DMSO. Comparable yield of **7aa** has previously been reported with the catalyst $Pd(OAc)_2$, however, a strong base LiO^{t}Bu along with more loading of the catalyst and co-catalyst $Cu(TFA)_2$ were employed.[14r]



5a 6a 7aa

Table 2 Optimization of reaction conditions for arylation of benzothiazole[a]

Entry	Pd-cat.	Base	Solvent	T (^{o}C)/ time (h)	Yield (%)[b]
1	**2a**	K_3PO_4	DMF	120/16	67
2	**2b**	K_3PO_4	DMF	120/16	68
3	**2c**	K_3PO_4	DMF	120/16	49
4	**3a**	K_3PO_4	DMF	120/16	76
5	**3c**	K_3PO_4	DMF	120/16	24[c]
6	**3a**	K_3PO_4	DMSO	120/16	78
7	**3a**	K_2CO_3	DMSO	120/16	49[c]
8	**3a**	K_2CO_3	DMSO	130/16	81
9	**3a**	**K_2CO_3**	**DMSO**	**130/24**	**86** (99)[c]
10	**3a**	Na_2CO_3	DMSO	130/24	53[c]
11	**3a**	NOAc	DMSO	130/24	12[c]
12	**3a**	KOAc	DMSO	130/24	25[c]
13	**3a**	K_2CO_3	NMP	130/24	3[c]
14	**3a**	K_2CO_3	DMA	130/24	27
15	**3a**	K_2CO_3	toluene	130/24	2[c]
16	**3a**	K_2CO_3	1,4-dioxane	130/24	10[c]
17	-	K_2CO_3	DMSO	130/24	11[c]
18	**3a**	K_2CO_3	DMSO	130/24	16[d]

[a]Conditions: Benzothiazole (0.041 g, 0.30 mmol), 4-iodotoluene (0.098 g, 0.45 mmol), base (0.45 mmol), Pd-cat. (0.0015 mmol), CuI (0.0006 g, 0.003 mmol) and solvent (1.0 mL) were added inside the glove box. [b]Isolated yield. [c]G.C. yield. [d]CuI was not employed.

Complex stability and catalyst recycling studies for arylation

Since the pincer-based complexes are presumed to be the robust catalysts because of the strong and rigid pincer coordination, we examined the stability of pincer complex **3a**.

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For analysing air-stability, the complex (^{Et2}NNN$^{8\text{-}Q}$)PdCl (**3a**, in DMSO-d_6) was exposed to air for 5 days. The ^{1}H NMR was recorded at regular intervals (1 day, 2 days, 3 days and 5 days) and was analysed (using standard mesitylene in capillary), which demonstrates that the complex **3a** largely remained intact. Neither the dissociation of ligand from **3a** nor the decomposition of **3a** was occurred.

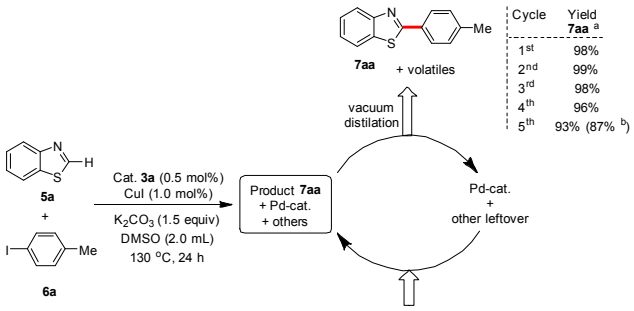

Fig. 4 Catalyst recycling experiment. [a]GC yield using *para*-xylene as internal standard. [b]Isolated yield.

Further, the catalyst performance was studied by conducting recycling experiments (Figure 4). The recycling experiment was performed by distilling out the product and other volatiles after each experiment/cycle. In a Schlenk tube, the standard catalytic experiment was performed using **5a** (0.5 mmol), **6a** (0.75 mmol), catalyst **3a** (0.0025 mmol), CuI (0.005 mmol), K_2CO_3 (0.75 mmol) and DMSO (2.0 mL). After heating the reaction mixture for 24 h (1st cycle), the internal standard *p*-xylene (0.03 mL, 0.243 mmol) was added at ambient temperature and the reaction mixture was subjected to GC analysis, wherein the yield of the coupled product **7aa** was analyzed to be 98% (GC yield w.r.t. standard *p*-xylene). Then, the product and other volatiles were distilled out under high vacuum (5 × 10^{-5} bar) at 140 ^{o}C. The reaction vessel was transferred in to the glove-box, and fresh **5a** (0.5 mmol), **6a** (0.75 mmol), K_2CO_3 (0.75 mmol) and DMSO (2.0 mL) were added. The reaction was continued for second cycle, wherein the GC yield of the product **7aa** was found to be 99%. Similarly, in the 3rd, 4th and 5th cycles, the GC yields of the product **7aa** were observed to be 98%, 96% and 93%, respectively. At the end of fifth cycle the product **7aa** was isolated and the yield was determined to be 87%. These experiments highlighted the exceptional stability and activity of the novel (quinolinyl)amido-palladium catalyst system for the arylation of benzothiazole.

Scope of the 3a-catalyzed arylation of benzothiazoles

The optimized reaction condition was applied to the arylation of benzothiazoles with diversely substituted aryl iodides. As listed in Table 3, aryl iodides with different electronic features were coupled with the benzothiazole to yield the desired arylated products in moderate to good yields. In general, with the current catalyst system, the electron-rich aryl iodides were more efficiently reacted than those with electron-deficient ones (Table 3, entries 1-9), which is contrary to the Pd(0)-catalyzed coupling reactions, and similar to our previous observations.[16] Important functional groups, such as, –OMe, –F, –Cl, –Br, –NO_2, –CF_3, –CO_2CH_3 were tolerated on the aryl iodide backbone under the current catalytic conditions, which is very crucial from the synthetic

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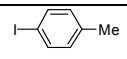
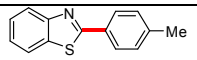
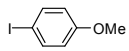
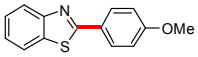
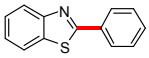
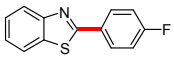
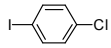
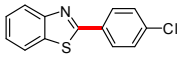
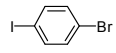
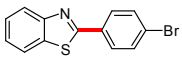
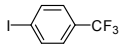
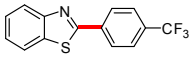
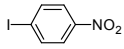
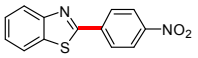
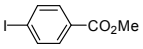
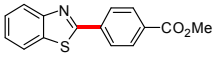
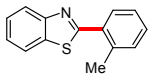
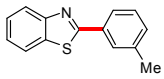
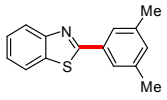
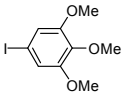
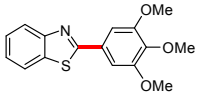
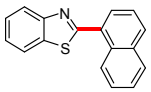
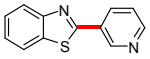
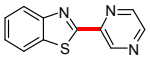
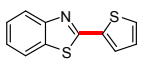
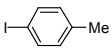
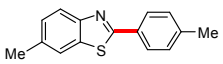
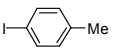
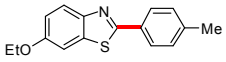
Table 3 Scope for the **3a**-catalyzed arylation of benzothiazoles with aryl halides[a]

entry	aryl halide (**6**)	product (**7**)	yield (%)[b]
1			86
2			92
3			89
4			39
5			82
6			59
7			41
8			45
9			55
10			66
11			88
12			88
13			73
14			76
15			64
16			65
17			20
18			64
19			57

[a]Conditions: Substrate **5** (0.3 mmol), iodide **6** (0.45 mmol), cat **3a** (0.0015 mmol), CuI (0.003 mmol), K_2CO_3 (0.45 mmol), DMSO (1.0 mL), 130 °C, 24 h. [b]Isolated yields.

prospective. The *para*- and *meta*-substituted aryl iodides, as well as di- and tri-substituted aryl iodides were coupled with benzothiazole to deliver the desired C-2 arylated benzothiazoles in good yields, though the coupling of sterically demanding *ortho*-substituted aryl iodide resulted in slightly lower yield (entries 10-13). Notably, the heteroaryl iodides, such as pyridinyl and pyrazinyl iodides reacted with good activity, whereas thiophenyl iodide gave poor yield of the product (entries 15-17). Synthesis of these bis-heterocycles is important, as they can be used as bidentate ligand system for transition-metal-catalyzed reactions. Methyl- and ethoxy-substituted-benzothiazoles reacted in moderate activity. Unfortunately, the less expensive aryl bromides or chlorides as electrophilic coupling partners reacted sluggishly and gave unsatisfactory yield of the product. Though, many methods are known for the arylation of azoles, the current process involves a phosphine-free catalytic system, which represents a rare example. More particularly, arylation methods of sulphur-containing azoles, such as benzothiazole, are less precedented. In addition, the contrasting reactivity of the electrophiles in the **3a**-catalyzed arylation reaction is interesting for detailed mechanistic consideration.

Mechanistic consideration

Pincer ligated palladium complexes are known for their decomposition into Pd(0) nanoparticles during the coupling reactions, and even a trace of such species can catalyze the reaction and pincer complexes merely serve as the precatalysts.[20] To investigate the probable involvement of Pd(0) nanoparticles during **3a**-catalyzed arylation, the standard catalytic reaction was performed in the presence of 300 and 1500 equiv (w.r.t catalyst **3a**) of mercury (Hg),[21] wherein the yield of coupling product **7aa** obtained was 72% and 63%, respectively. The presence of mercury slightly suppressed the arylation suggesting that minor Pd(0) particles might have formed, and are responsible for at least some of the observed reactivity. A filtration experiment was performed after the initial heating (30 min, GC yield 34%) to remove all the heterogeneous particles, and the reaction was subsequently continued upon adding fresh K_2CO_3. The arylation proceeded convincingly without much decline in the yield of **7aa** (88% yield), suggesting that the molecular palladium is responsible for major activity. Furthermore, the addition of ligands, such as PPh_3 (3.0 equiv w.r.t **3a**), poly(vinyl pyridine) (PVPy; 150 equiv w.r.t **3a**), known for poisoning the Pd(0) nanoparticles,[21,22] afforded the arylated product **7aa** in 98% and 78%, respectively. Though, the arylation reaction remains unaffected in the presence of PPh_3, the presence of PVPy slightly lowered the yield of **7aa**. The Hg and PVPy addition experiments indicate that at least some of the reactivity is promoted by Pd(0)-nanoparticles, that might generate from the partial decomposition of complex **3a**. However, as the arylation was only partially affected in the presence of Hg or PVPy, the major arylation may not have solely emerged from Pd(0) particles.[23]

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In order to identify the status of complex **3a** during the arylation, we have performed the catalytic reaction in a J-Young NMR tube using 20 mol% of (^{Et2}NNN$^{8\text{-}Q}$)PdCl (**3a**) in DMSO-d_6 and the progress of the reaction was monitored by ^{1}H-NMR spectroscopy (mesitylene was used in toluene-d_8 as an internal standard in a sealed capillary). Thus, upon heating the reaction mixture at 130 ^{o}C in a pre-heated oil bath, the major palladium species observed were (^{Et2}NNN$^{8\text{-}Q}$)PdCl (**3a**) and (^{Et2}NNN$^{8\text{-}Q}$)PdI (**4a**) in 65% and 35% (12 h), 69% and 28% (24 h), and 68% and 28% (48 h), respectively. Further, an independent catalytic reaction employing the complex **4a** afforded the coupled product **7aa** in 95% yield. These findings indicate that either **3a** or **4a** is the resting state of the catalyst during arylation reaction. The complex **4a** might have generated by the halide exchange reaction between **3a** and CuI or KI (KI will produce during the course of catalytic reaction). Further, the catalyst decomposition was negligible even after 24 h (3%) or 48 h (4%) at 130 ^{o}C. This strongly suggests that the catalyst mostly remains in molecular form and highly stable under catalytic conditions.

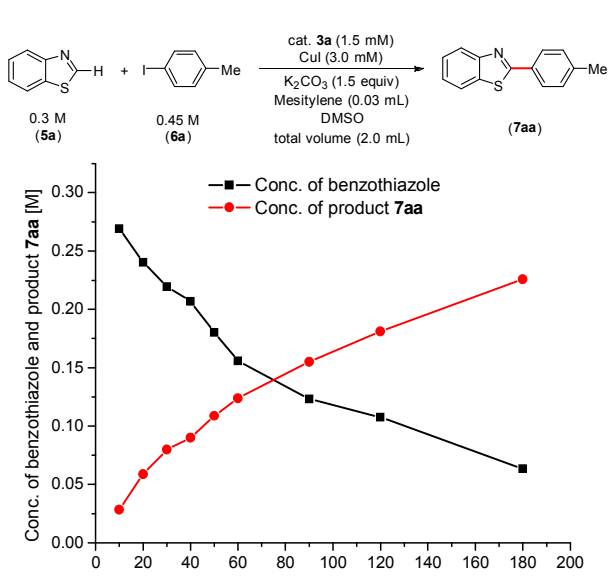

Fig. 5 Reaction profile for **3a**-catalyzed arylation of benzothiazole with 4-iodotoluene.

into a new active catalyst species is unlikely, and **3a** might directly involve in the catalytic arylation. Further, the initial rates for the arylation of benzothiazole with electronically distinct *para*-substituted aryl iodides (4-R-C_6H_4-I) were determined (Figure 6). The Hammett plot was drawn from a correlation between the initial rates and σ_p values, which resulted in linear fit with a slope of –0.853 (Figure 7). The negative slope (ρ value) indicates that a positive charge is produced in the active catalyst species and hence, the electron-donating substituents on the aryl iodide would enhance the rate of arylation.[16c,25] This strongly supports the reaction of aryl iodide to a Pd(II) species (oxidative addition or concerted path) rather to a Pd(0) center, because the electron-donating substituent is expected to stabilize the resulting palladium species in higher oxidation state, and in turn would lower the energy of the process.[16c] Additionally, the observed reactivity order of aryl iodides goes against the conventional Pd(0)-catalyzed coupling reaction,[26] which further supports the above observation.

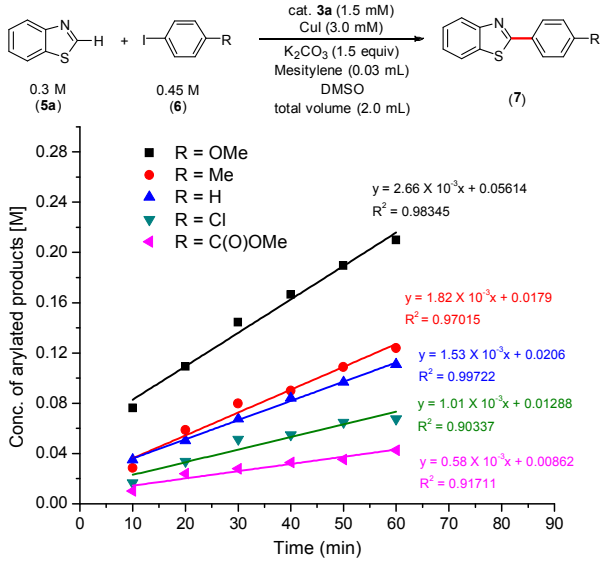

Fig. 6 Time-dependent formation of arylated products in the coupling of benzothiazole with various para-substituted aryl iodides (4-R-C_6H_4-I).

Since the Hg and PVPy addition experiments were not conclusive, we performed kinetic experiments to know the progress of the arylation as well as to understand the reactivity of electronically distinct electrophiles.[24] In a standard kinetic experiment, 1.5 mM of **3a**, 3 mM of CuI, benzothiazole (0.3 M), R-C_6H_4-I (0.45 M), K_2CO_3 (1.5 equiv) and mesitylene (0.03 mL, internal standard) were used, and DMSO was added to make total volume 2.0 mL. All the reactions were performed at 130 ^{o}C and the progress of the arylation was monitored by GC analysis. As shown in Figure 5, the formation of arylated product **7aa** followed a linear plot and induction period is absent. This suggests that decomposition of the complex **3a**

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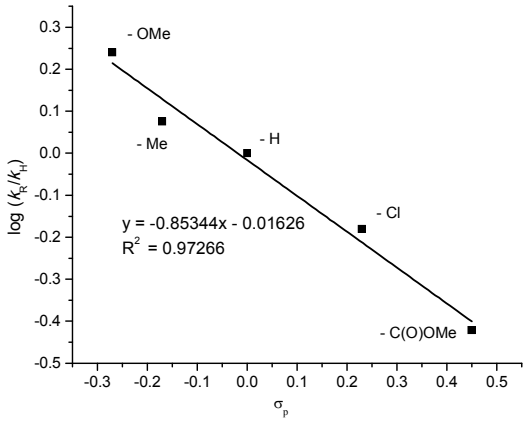

Fig. 7 Hammett correlation plot using various aryl iodides (4-R-C_6H_4-I).

Based on the mechanistic findings described above, and from the earlier observation of ours[16a,c] and others,[2o,6i] a probable catalytic cycle is shown in Figure 8. The catalytic cycle begins with the base-assisted concerted metalation deprotonation (CMD) of benzothiazole with CuI,[16c] followed by the reaction with complex **3a** to produce species **A**. Reaction of aryl iodide with **A** *via* oxidative addition would give Pd(IV) species **B** (Path I). Reductive elimination of arylated couple product from **B** will regenerate the active Pd(II) catalyst. Alternately, aryl iodide can react with **A** *via* concerted process (**C**) to deliver the product **7** and regenerate the catalyst (Path II). The MALDI-TOF-MS analysis of the reaction mixture provided evidences for the formation of the intermediates **A** and **B**. Kinetic analysis of the arylation strongly supports the reaction of aryl iodide to a Pd(II) species, hence a molecular catalytic pathway is assumed. But, the standard tests performed to distinguish between homogeneous and heterogeneous catalysis, particularly Hg test, was not conclusive; thus, a parallel catalytic reaction by the trace amount of Pd(0) nanoparticles may be operative in addition to the arylation by a molecular Pd(II) species.[27]

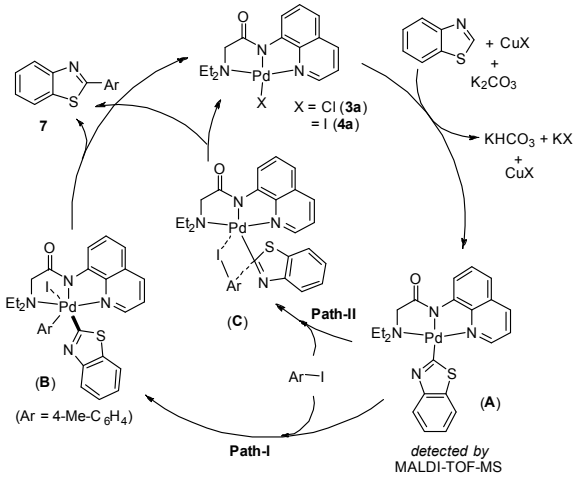

Fig. 8 Plausible mechanism for **3a**-catalyzed arylation of benzothiazole.

Conclusions

In summary, we have synthesized (quinolinyl)amido-based pincer palladium complexes and disclosed their catalytic application in the C–H bond arylation of benzothiazoles. All the pincer-palladium complexes were fully characterized by NMR spectroscopy, HRMS and elemental analysis. The molecular structures of three complexes were established by single crystal X-ray diffraction study. Complex (^{Et2}NNN$^{8\text{-}Q}$)PdCl efficiently catalyzes the arylation of benzothiazoles with substituted aryl iodides. This (quinolinyl)amido palladium catalyst system demonstrated to be highly robust, and was recycled for five rounds with consistent yield of the arylation product. Mechanistic study by the kinetic analysis strongly supports a molecular mechanism with the direct involvement of catalyst **3a**. However, a parallel reaction path by the minor formation of active palladium nanoparticles, *via* the partial decomposition of pincer-palladium complex cannot be completely ruled out.

Experimental section

General experimental

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 the flame-dried reaction vessels with Teflon screw cap. Solvents were dried over Na/benzophenone or CaH_2 and distilled prior to use. Liquid reagents were flushed with argon prior to use. The 2-bromo-*N*-(quinolin-8-yl)acetamide,[28] compound **1a**,[18] and 6-substituted benzothiazoles[29] 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, 100-200 mesh). 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 MHz (^{1}H) and 100 or 125 MHz {^{13}C, DEPT (distortionless enhancement by polarization transfer)} on Bruker AV 200, AV 400 and AV 500 spectrometers in $CDCl_3$ solutions, if not then specified; chemical shifts (δ) are given in ppm. The ^{1}H and ^{13}C NMR spectra are referenced to residual solvent signals ($CDCl_3$: δH = 7.26 ppm, δC = 77.2 ppm).

GC Method

Gas Chromatography analyses were performed using a Shimadzu GC-2010 gas chromatograph equipped with a Shimadzu AOC-20s autosampler and a Restek RTX-5 capillary column (30 m x 250 µm). The instrument was set to an injection volume of 1 µL, an inlet split ratio of 10:1, and inlet and detector temperatures of 250 and 320 °C, respectively.

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UHP-grade argon was used as carrier gas with a flow rate of 30 mL/min. The temperature program used for all the analyses is as follows: 80 °C, 1 min; 30 °C/min to 200 °C, 2 min; 30 °C/min to 260 °C, 3 min; 30 °C/min to 300 °C, 3 min.
Response factors for all the required compounds were calculated with respect to standard *para*-xylene or mesitylene from the average of three independent GC runs.

Synthesis of (^{Morp}NNN$^{8\text{-}Q}$)–H (1b). A mixture of 2-bromo-*N*-(quinolin-8-yl)acetamide (0.5 g, 1.89 mmol) and morpholine (0.49 g, 5.6 mmol) in acetone (15 mL) was refluxed for 24 h. The reaction mixture was then cooled to ambient temperature and the volatiles were evaporated under vacuum. The crude mixture was quenched with distilled H_2O (20 mL) and the aminated product was extracted with EtOAc (15 mL x 3). The combined organic extract was dried over Na_2SO_4. After filtration and evaporation of the volatiles in *vacuo* pure product of **1b** was obtained as brown solid. Yield = 0.51 g, 99%. M. p. = 122-124 °C. ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 11.46 (br s, 1H, N–H), 8.85 (dd, *J* = 4.2, 1.6 Hz, 1H, Ar–H), 8.76 (dd, *J* = 5.9, 3.1 Hz, 1H, Ar–H), 8.14 (dd, *J* = 8.3, 1.6 Hz, 1H, Ar–H), 7.55--7.49 (m, 2H, Ar–H), 7.44 (dd, *J* = 8.3, 4.3 Hz, 1H, Ar–H), 3.92-3.87 (m, 4H, CH_2), 3.28 (s, 2H, CH_2), 2.71-2.66 (m, 4H, CH_2). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 168.9 (CO), 148.7 (CH), 139.1 (C_q), 136.3 (CH), 134.4 (C_q), 128.2 (C_q), 127.4 (CH), 121.9 (CH), 121.7 (CH), 116.7 (CH), 67.4 (2C, CH_2), 62.9 (CH_2), 53.9 (2C, CH_2). HRMS (ESI): *m/z* calcd for $C_{15}H_{17}N_3O_2 + H^+$ $[M + H]^+$ 272.1394, found 272.1391.

Synthesis of (^{Pip}NNN$^{8\text{-}Q}$)–H (1c). Procedure similar to the synthesis of **1b** was followed, using 2-bromo-*N*-(quinolin-8-yl)acetamide (0.5 g, 1.89 mmol) and 1-methylpiperazine (0.56 g, 5.6 mmol). The compound **1c** was obtained as brown solid. Yield = 0.52 g, 97%. M. p. = 106-108 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 11.45 (br s, 1H, N–H), 8.85 (dd, *J* = 4.3, 1.8 Hz, 1H, Ar–H), 8.77 (dd, *J* = 6.1, 2.8 Hz, 1H, Ar–H), 8.14 (dd, *J* = 8.3, 1.8 Hz, 1H, Ar–H), 7.54-7.48 (m, 2H, Ar–H), 7.44 (dd, *J* = 8.3, 4.3 Hz, 1H, Ar–H), 3.28 (s, 2H, CH_2), 2.72-2.62 (m, 8H, CH_2), 2.37 (s, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 169.3 (CO), 148.6 (CH), 139.2 (C_q), 136.3 (CH), 134.5 (C_q), 128.2 (C_q), 127.5 (CH), 121.8 (CH), 121.7 (CH), 116.7 (CH), 62.5 (CH_2), 55.5 (2C, CH_2), 53.5 (2C, CH_2), 46.2 (CH_3). HRMS (ESI): *m/z* calcd for $C_{16}H_{20}N_4O + H^+$ $[M + H]^+$ 285.1710, found 285.1708.

Synthesis of (^{Et2}NNN$^{8\text{-}Q}$)Pd(OAc) (2a). To a Schlenk flask equipped with magnetic stir bar was introduced ligand **1a** (0.167 g, 0.649 mmol) and $Pd(OAc)_2$ (0.146 g, 0.650 mmol). To the resultant reaction mixture, freshly distilled THF (15 mL) and Et_3N (0.12 mL, 0.860 mmol) were added, and the reaction mixture was heated to reflux for 3 h. The reaction mixture was cooled to ambient temperature and the volatiles were evaporated under vacuum. The crude compound was extracted with toluene (10 mL x 2) and the solution was concentrated under vacuum. Et_2O (6.0 mL) was added to precipitate the product, which was then dried under high vacuum to obtain a yellow solid. Yield: 0.16 g, 58%. M. p. = 160 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.67 (d, *J* = 7.8 Hz, 1H, Ar–H), 8.26 (d, *J* = 8.3 Hz, 1H, Ar–H), 8.21 (d, *J* = 5.1 Hz, 1H, Ar–H), 7.49 (vt, *J* = 7.7 Hz, 1H, Ar–H), 7.39 (dd, *J* = 7.8, 4.9 Hz, 1H, Ar–H), 7.33 (d, *J* = 8.1 Hz, 1H, Ar–H), 3.69 (s, 2H, CH_2), 3.19-3.11 (m, 2H, CH_2), 2.66-2.58 (m, 2H, CH_2), 2.10 (s, 3H, CH_3), 1.80 (t, *J* = 7.3 Hz, 6H, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.2 (CO), 175.4 (CO), 149.1 (CH), 146.8 (C_q), 145.2 (C_q), 139.1 (CH), 129.9 (C_q), 129.5 (CH), 121.2 (CH), 120.8 (CH), 120.2 (CH), 65.9 (CH_2), 57.5 (2C, CH_2), 24.1 (CH_3), 12.8 (2C, CH_3). HRMS (ESI): *m/z* calcd. for $C_{17}H_{21}N_3O_3Pd - OAc^+$ $[M - OAc]^+$ 362.0479, found 362.0493. Anal. Calcd. for $C_{17}H_{21}N_3O_3Pd$: C, 48.41; H, 5.02; N, 9.96. Found: C, 47.98; H, 4.73; N, 9.71.[30]

Synthesis of (^{Morp}NNN$^{8\text{-}Q}$)Pd(OAc) (2b). To a Schlenk flask equipped with magnetic stir bar was introduced ligand **1b** (0.05 g, 0.184 mmol) and $Pd(OAc)_2$ (0.041 g, 0.183 mmol). To the resultant reaction mixture, freshly distilled THF (10 mL) and Et_3N (0.032 mL, 0.229 mmol) were added, and the reaction mixture was heated to reflux for 3 h. The reaction mixture was cooled to ambient temperature, filtered through cannula and the volatiles were evaporated under vacuum. The product was then washed with Et_2O (6.0 mL x 3) and dried under high vacuum to obtain a yellow solid compound **2b**. Yield: 0.048 g, 60%. M. p. = 230 °C (dec.). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.61 (dd, *J* = 7.6, 0.9 Hz, 1H, Ar–H), 8.27 (dd, *J* = 8.2, 1.2 Hz, 1H, Ar–H), 8.15 (dd, *J* = 5.2, 1.5 Hz, 1H, Ar–H), 7.50 (vt, *J* = 7.9 Hz, 1H, Ar–H), 7.40 (dd, *J* = 8.2, 5.2 Hz, 1H, Ar–H), 7.35 (d, *J* = 7.9 Hz, 1H, Ar–H), 4.02 (s, 2H, CH_2), 3.94-3.85 (m, 4H, CH_2), 3.83-3.79 (m, 2H, CH_2), 2.99-2.96 (m, 2H, CH_2), 2.17 (s, 3H, $COCH_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.6 (CO), 172.9 (CO), 148.7 (CH), 146.6 (C_q), 145.0 (C_q), 139.4 (CH), 129.9 (C_q), 129.6 (CH), 121.3 (CH), 121.0 (CH), 120.5 (CH), 69.4 (CH_2), 62.4 (2C, CH_2), 59.3 (2C, CH_2), 24.4 (CH_3). HRMS (ESI): *m/z* calcd. for $C_{17}H_{19}N_3O_4Pd - OAc^+$ $[M - OAc]^+$ 376.0272, found 376.0267. Anal. Calcd. for $C_{17}H_{19}N_3O_4Pd$: C, 46.86; H, 4.39; N, 9.64. Found: C, 46.93; H, 4.36; N, 9.68.

Synthesis of (^{Pip}NNN$^{8\text{-}Q}$)Pd(OAc) (2c). Procedure similar to the synthesis of **2b** was followed, using **1c** (0.05 g, 0.176 mmol), $Pd(OAc)_2$ (0.04 g, 0.178 mmol) and Et_3N (0.033 mL, 0.237 mmol). The compound **2c** was obtained as a yellow solid. Yield: 0.062 g, 78%. M. p. = 170 °C (dec.). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.62 (d, *J* = 7.6 Hz, 1H, Ar–H), 8.26 (d, *J* = 8.2 Hz, 1H, Ar–H), 8.16 (d, *J* = 4.3 Hz, 1H, Ar–H), 7.49 (vt, *J* = 7.8 Hz, 1H, Ar–H), 7.39 (dd, *J* = 7.9, 5.5 Hz, 1H, Ar–H), 7.34 (d, *J* = 7.9 Hz, 1H, Ar–H), 3.94 (s, 2H, CH_2), 3.75 (vt, *J* = 10.4 Hz, 2H, CH_2), 3.23 (br s, 2H, CH_2), 2.62 (br s, 2H, CH_2), 2.47 (br s, 2H, CH_2), 2.29 (s, 3H, CH_3), 2.16 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.5 (CO), 173.6 (CO), 148.9 (CH), 146.7 (C_q), 145.0 (C_q), 139.3 (CH), 129.9 (C_q), 129.6 (CH), 121.2 (CH), 120.9 (CH), 120.4 (CH), 58.7 (CH_2), 49.6 (4C, CH_2), 46.1 (CH_3), 24.5 (CH_3). HRMS (ESI): *m/z* calcd. for $C_{18}H_{22}N_4O_3Pd - OAc^+$ $[M - OAc]^+$ 389.0588, found 389.0576. Anal. Calcd. for $C_{18}H_{22}N_4O_3Pd$: C, 48.17; H, 4.94; N, 12.48. Found: C, 47.84; H, 4.73; N, 11.99.[30]

Synthesis of (^{Et2}NNN$^{8\text{-}Q}$)PdCl (3a). To a Schlenk flask equipped with magnetic stir bar was introduced ligand **1a** (0.30 g, 1.166 mmol) and $PdCl_2$ (0.207 g, 1.167 mmol). To the reaction

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mixture, freshly distilled THF (20 mL) and Et_3N (0.2 mL, 1.434 mmol) was added, and the reaction mixture was heated to reflux for 3 h. The reaction mixture was cooled to ambient temperature and the volatiles were evaporated under vacuum. The crude compound was extracted with toluene (10 mL x 2), concentrated under vacuum and Et_2O (6 mL) was added to obtain crystalline compound of **3a**. Yield: 0.30 g, 65%. M. p. = 165 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.93 (d, *J* = 4.3 Hz, 1H, Ar–H), 8.71 (d, *J* = 7.9 Hz, 1H, Ar–H), 8.28 (d, *J* = 8.2 Hz, 1H, Ar–H), 7.52 (vt, *J* = 7.9 Hz, 1H, Ar–H), 7.42 (dd, *J* = 8.5, 5.2 Hz, 1H, Ar–H), 7.37 (d, *J* = 8.2 Hz, 1H, Ar–H), 3.73 (s, 2H, CH_2), 3.42-3.35 (m, 2H, CH_2), 2.64-2.57 (m, 2H, CH_2), 1.82 (t, *J* = 7.0 Hz, 6H, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ 175.8 (CO), 150.4 (CH), 147.1 (C_q), 145.2 (C_q), 139.2 (CH), 130.1 (C_q), 129.6 (CH), 121.4 (CH), 120.7 (CH), 120.5 (CH), 66.4 (CH_2), 58.8 (2C, CH_2), 13.5 (CH_3). HRMS (ESI): *m/z* calcd. for $C_{15}H_{18}ClN_3OPd - Cl^+$ $[M - Cl]^+$ 362.0479, found 362.0474. Anal. Calcd for $C_{15}H_{18}ClN_3OPd$: C, 45.24; H, 4.56; N, 10.55. Found: C, 45.21; H, 4.37; N, 10.39.

Synthesis of (^{Pip}NNN$^{8\text{-}Q}$)PdCl (3c). Procedure similar to the synthesis of **3a** was followed, using **1c** (0.05 g, 0.176 mmol), $PdCl_2$ (0.032 g, 0.18 mmol), Et_3N (0.032 mL, 0.229 mmol) and THF (10 mL). The compound **3c** was obtained as a yellow crystalline solid. Yield: 0.045 g, 60%. M. p. = 210 ^{o}C (dec). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.96 (d, *J* = 4.3 Hz, 1H, Ar–H), 8.64 (d, *J* = 7.6 Hz, 1H, Ar–H), 8.23 (d, *J* = 7.9 Hz, 1H, Ar–H), 7.49 (vt, *J* = 7.9 Hz, 1H, Ar–H), 7.39 (dd, *J* = 8.2, 5.2 Hz, 1H, Ar–H), 7.34 (d, *J* = 7.9 Hz, 1H, Ar–H), 4.13 (vt, *J* = 11.6 Hz, 2H, CH_2), 4.00 (s, 2H, CH_2), 3.35 (d, *J* = 11.9 Hz, 2H, CH_2), 2.64 (br s, 2H, CH_2), 2.43 (br s, 2H, CH_2), 2.30 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.2 (CO), 150.8 (CH), 147.0 (C_q), 144.8 (C_q), 139.2 (CH), 130.0 (C_q), 129.5 (CH), 121.5 (CH), 120.7 (CH), 120.7 (CH), 59.3 (3C, CH_2), 49.4 (2C, CH_2), 46.1 (CH_3). HRMS (ESI): *m/z* calcd. for $C_{16}H_{19}ClN_4OPd - Cl^+$ $[M - Cl]^+$ 389.0588, found 389.0582. Anal. Calcd for $C_{16}H_{19}ClN_4OPd$: C, 45.19; H, 4.50; N, 13.18. Found: C, 44.87; H, 4.94; N, 12.84.[30]

Synthesis of (^{Et2}NNN$^{8\text{-}Q}$)PdI (4a). The mixture of **3a** (0.017 g, 0.043 mmol) and KI (0.011 g, 0.066 mmol) in CH_2Cl_2 (5.0 mL)/MeOH (5.0 mL) was stirred at room temperature for 14 h. Then the volatiles were evaporated under vacuum and the compound was extracted with Et_2O (5 mL x 3). Upon evaporation of the solvent, the compound **4a** was obtained as a brown solid. Yield: 0.020 g, 95%. M. p. = 176-178 ^{o}C (dec.). ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.56 (d, *J* = 4.2 Hz, 1H, Ar–H), 8.78 (d, *J* = 8.0 Hz, 1H, Ar–H), 8.25 (d, *J* = 8.0 Hz, 1H, Ar–H), 7.52 (vt, *J* = 7.8 Hz, 1H, Ar–H), 7.38 (d, *J* = 8.0 Hz, 1H, Ar–H), 7.33 (dd, *J* = 8.2, 5.2 Hz, 1H, Ar–H), 3.74 (s, 2H, CH_2), 3.64-3.57 (m, 2H, CH_2), 2.73-2.67 (m, 2H, CH_2), 1.84 (t, *J* = 7.1 Hz, 6H, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ 176.9 (CO), 156.4 (CH), 146.9 (C_q), 145.6 (C_q), 138.9 (CH), 130.4 (C_q), 129.6 (CH), 122.2 (CH), 120.8 (CH), 120.7 (CH), 67.1 (CH_2), 61.9 (2C, CH_2), 14.3 (CH_3). MALDI-TOF: *m/z* calcd for $C_{15}H_{18}IN_3OPd + H^+$ $[M + H]^+$ 489.9608, found 489.8192 and $C_{15}H_{18}IN_3OPd - I^+$ $[M - I]^+$ 362.0485, found 361.9155. Anal. Calcd for $C_{15}H_{18}IN_3OPd$: C, 36.79; H, 3.71; N, 8.58. Found: C, 37.39; H, 4.21; N, 7.73.[30]

Representative procedure for arylation of benzothiazoles

Synthesis of 2-(*p*-tolyl)benzo[*d*]thiazole (7aa). To a flame-dried Schlenk tube containing magnetic stir bar were added the catalyst **3a** (0.0015 mmol, 0.5 mol%, 240 µL of 0.0063 M stock solution in toluene) and CuI (0.003 mmol, 1.0 mol%, 60 µL of 0.0525 M stock solution in CH_3CN). The Schlenk tube with catalysts mixture was evacuated under vacuum and refilled with argon. Subsequently, 4-iodotoluene (**6a**; 0.098 g, 0.45 mmol), benzothiazole (**5a**; 0.041 g, 0.30 mmol), K_2CO_3 (0.062 g, 0.45 mmol) and DMSO (1.0 mL) were added under argon. The resultant reaction mixture was degassed, refilled with argon and was stirred at 130 ^{o}C in a pre-heated oil bath for 24 h. At ambient temperature, H_2O (10 mL) was added and the reaction mixture was extracted with EtOAc (20 mL x 3). The combined organic layers were dried over Na_2SO_4 and the volatiles were evaporated in *vacuo*. The resultant residue was purified by column chromatography on silica gel (petroleum ether/EtOAc: 50/1→30/1) to yield **7aa** (0.058 g, 86%) as an off-white solid. The ^{1}H and ^{13}C NMR data as well as HRMS of compound **7aa** and other arylated benzothiazoles were in accordance with those reported in the literature.[16]

Procedure for catalyst recycling experiment

To a flame dried Schlenk tube equipped with magnetic stir bar was introduced the catalyst **3a** (0.001 g, 0.0025 mmol), CuI (0.001g, 0.005 mmol), K_2CO_3 (0.104 g, 0.750 mmol), 4-iodotoluene (**6a**; 0.164 g, 0.750 mmol), and benzothiazole (**5a**; 0.071 g, 0.524 mmol). To this reaction mixture, DMSO (2.0 mL) was added and the reaction vessel was heated at 130 ^{o}C in a preheated oil bath for 24 h. At ambient temperature, the reaction vessel was transferred to glove box and *para*-xylene (0.030 mL, 0.243 mmol, internal standard) was added into it. The solution was shaken well and an aliquot of the sample was withdrawn and subjected to the GC analysis. The yield of the arylated product **7aa** was determined to be 98% by the GC analysis w.r.t. the internal standard *para*-xylene. The product **7aa** and other volatiles were distilled out under high vacuum (5×10^{-5} bar) at 140 ^{o}C. The GC analysis of the remaining residue confirms the absence of both the starting compounds as well as product **7aa** in the reaction vessel. The reaction vessel was further charged with fresh K_2CO_3 (0.104 g, 0.750 mmol), **6a** (0.164 g, 0.750 mmol) and **5a** (0.070 g, 0.516 mmol), and DMSO (2.0 mL) inside the glove box (cat. **3a** and CuI were not added). The resultant reaction mixture was then stirred at 130 ^{o}C in a preheated oil bath for the second cycle. Following the steps mentioned above, the yield of the arylated product **7aa** was determined to be 99% by GC analysis for the second cycle. This recycling experiment was continued for further three cycles and the yields of the product **7aa** were analyzed to be 98%, 96% and 93% for the third, fourth and fifth cycles, respectively. At the end of 5th cycle, the product was isolated by column chromatography, wherein the yield of coupled product **7aa** was 87%.

Procedure for NMR tube experiment

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A mixture of **3a** (0.015 g, 0.038 mmol), CuI (0.014 g, 0.075 mmol), K_2CO_3 (0.026 g, 0.188 mmol), benzothiazole (0.026 g, 0.192 mmol) and 4-iodotoluene (0.041 g, 0.188 mmol) was taken in a J. Young NMR tube, and DMSO-d_6 (0.5 mL) was added into it. The J. Young NMR tube with the reaction mixture was heated in a pre-heated oil-bath at 130 ^{o}C. At regular intervals, the J. Young NMR tube was taken out from the oil bath and reaction progress was monitored by ^{1}H NMR analysis. The major palladium species observed were (^{Et2}NNN$^{8\text{-}Q}$)PdCl (**3a**) and (^{Et2}NNN$^{8\text{-}Q}$)PdI (**4a**) in 65% and 35% (12 h), 69% and 28% (24 h), and 68% and 28% (48 h), respectively. The yields (%) were calculated w.r.t the external standard mesitylene (in toluene-d_8) in a sealed capillary.

Procedure for additive (Hg, PPh_3, PVPy) experiments

Additive experiments were performed following the procedure similar to the representative procedure for arylation of benzothiazoles, additionally employing Hg (0.09 g, 0.45 mmol; 0.45 g, 2.24 mmol) or PPh_3 (0.0012 g, 0.0045 mmol) or PVPy (0.024 g, 0.225 mmol). After stirring the reaction mixtures at 130 ^{o}C for 24 h, the reactions were quenched with H_2O (5.0 mL) at ambient temperature, and EtOAc (5 mL) and *para*-xylene (0.030 mL, 0.243 mmol; internal standard) were added. An aliquot of the reaction mixture was subjected to GC analysis. The GC yield of the coupled product **7aa** obtained was 72% (0.45 mmol Hg), 63% (2.24 mmol Hg), 98% (0.0045 mmol PPh_3) and 78% (0.225 mmol PVPy).

Procedure for kinetic experiment

To a flame dried Schlenk tube was introduced catalyst **3a** (0.0012 g, 0.003 mmol), CuI (0.0011 g, 0.006 mmol), K_2CO_3 (0.124 g, 0.9 mmol), benzothiazole **5a** (0.081 g, 0.6 mmol) and 4-iodootoluene (0.196 g, 0.9 mmol) or [4-iodoanisole (0.211 g, 0.9 mmol); iodobenzene (0.0184 g, 0.9 mmol); 4-chloro-iodobenzene (0.215 g, 0.9 mmol); methy-4-iodobenzoate (0.236 g, 0.9 mmol)] and required amount of DMSO to make total volume 2.0 mL. To the reaction mixture, mesitylene (0.030 mL, 0.2156 mmol) was added as an internal standard. The reaction mixture was then stirred at 130 ^{o}C in a pre-heated oil bath. At regular intervals, the reaction vessel was cooled to ambient temperature and an aliquot of sample was withdrawn under argon and subjected to GC analysis. The concentration of the product **7aa** obtained in each sample was determined with respect to the internal standard mesitylene. The data was collected till 60 min. The final data was obtained by averaging the results of two independent experiments. The initial rate for the coupling reactions are shown in Figure 6. The Hammett plot was drawn from the correlation between the initial rates and Hammett substituent constants, *i.e* log (k_R/k_H) *vs.* σ_p, and obtained a slope of -0.85344, *i.e.* Hammett reaction constant (ρ)<0 (Figure 7).

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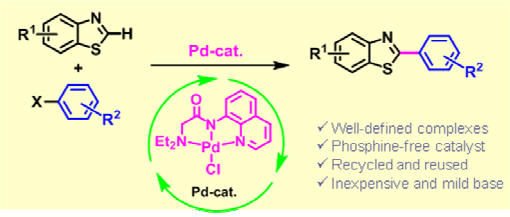

Abstract: Well-defined (quinolinyl)amido-pincer palladium complexes are developed and employed for the catalytic C–H bond arylation of benzothiazoles with aryl iodides, which can be recycled and reused for several rounds.