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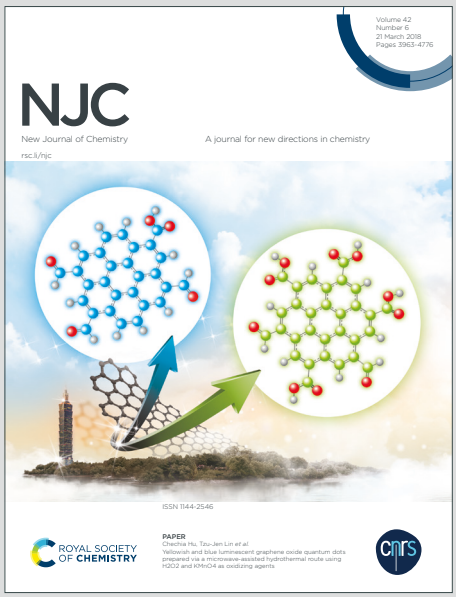

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PAPER

Sterically Enriched Bulky 1,3-Bis(*N,N'*-Aralkyl)Benzimidazolium based Pd-PEPPSI Complexes for Buchwald-Hartwig Amination Reactions

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Motakatla Venkata Krishna Reddy, Gokanapalli Anusha and Peddiahgari Vasu Govardhana Reddy*

Pd-PEPPSI (palladium-pyridine enhanced pre-catalyst preparation stabilization and initiation) complexes are now emerging as well defined catalysts for C-C and C-N bond formations. In this connection, we prepared a family of six air and moisture stable, simple to bulky benzyl substituents bearing benzimidazolium core Pd-PEPPSI complexes, **C1-C6**. Structure of **C6** is confirmed from X-ray diffraction (XRD) studies and the steric pressure of *N*-heterocyclic carbene is determined by v_{Bur} % calculation. Notably, these NHC-Pd-Py frameworks execute good **σ**-donating and π-extended electronic property of benzimidazolium NHCs which is an essential requirement for catalysis. The prepared complexes are proved to accomplish an outstanding and overwhelming reactivity than the other previously reported catalysts for the Buchwald-Hartwig cross-coupling reactions between 3-chloropyridine and various aryl/heteroaryl amines under mild reaction conditions. On the other hand, there is no need of external additives or ligands for the complete conversion of lead parent molecules to products. More remarkably, **C6** executed significant catalytic activity compared to other complexes, **C1**-**C5** for C-N bond formations. Further, the substrate scope is extended to other heteroaryl chlorides such as *N*-(5-chloro-4-methylpyridin-2-yl)acetamide, 2,4,6-trichloro-1,3,5-triazine, 3-chlorothiophene and 3-chloroquinoline.

Introduction

Transition metal mediated catalysis has emerged as widely used strategy offering a valuable tool for the synthesis of several biologically active drugs, agricultural chemicals, natural products and other building blocks.[1] This technique has been widely disseminating a variety of organic processes such as hydroamination, silylation, cyclo addition, double cyclization etc.[2] Although, different metal complexes[3-5] have been utilized to carry-out these reactions, the efficacy of palladium conjugates remained unbeaten since many years. Among various organic transformations, cross-coupling reactions like Buchwald–Hartwig and Suzuki–Miyaura couplings with palladium complexes are extensively studied by great number **of** research teams for C(sp^2)-N and C(sp^2)-C(sp^2) bond formations due to their generality and wide functional groups tolerance in organic synthesis.[6-7] In this perspective, several ligands[8] and Pd catalysts[9] were built for a range of catalysis reactions, but their usage is sometimes restricted due to the variability and less compatibility to the substrates. For instance, till today, direct amination on heteroaryl halides with conventional catalysts remains a practical challenge[10] despite of the formation of insoluble co-ordinate complexes. Moreover, the synthesis of some of the catalysts is expensive[11] and a few catalysts are known to be less tolerant to air. Hence, to protect the Pd (0) species, they should be typically run under an inert atmosphere.

Consequence to this anticipation, metal-*N*-heterocyclic carbene (NHC) complexes have come into existence. These are the gifted substitutes to phosphines, emerging as bench top class of transition-metal complexes with strong σ-donating and weak π–accepting ligands. Their electronic and steric tunability by *N,N'*-substituents adds flush catalytic activity. Ofele[12] and Wanzlick[13] identified the existence of NHCs in the year 1968. After a long period, Arduengo[14] isolated the first stable bis adamantyl NHC. Since then, many researchers across the globe have been continuously focusing on the synthesis of diverse NHCs[15] and M-NHC complexes[16] for distinct conversions. With a major effort, Nolan put forth the use of (η3-allyl)Pd(NHC)-X complexes as efficient pre-catalysts for cross-coupling reactions,[17] while extended to phosphine ligands as external additives by Colacot.[18] Although, several Pd-NHC complexes[19] were synthesized and applied to catalysis reactions, they are however set with few short comings like multi-step catalyst synthesis,[20] requirement of high catalyst load etc., Hence, Organ and team introduced a new class of air stable and environmentally benign Pd-PEPPSI pre-catalysts.[21]

Infact, a pile of reports are available on (*N,N'*-diaryl)imidazolium Pd-PEPPSI complexes,[22] but they display limited substrate scope by virtue of their stability to certain reaction conditions. Nevertheless, it is apparent that the synthesis of these complexes requires skillful workup besides low reaction yields.

Department of Chemistry, Yogi Vemana University, Kadapa-516005, Andhra Pradesh, India. Tel.: +91-8562-225410; fax: +91-8562-225419; e-mail: pvgr@yogivemanauniversity.ac.in.

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Furthermore, application of these complexes has not been firmly established.

Benzimidazole nucleus is considered to be far stable than the simple imidazole nucleus due to the extended aromaticity and hence, the current decade is witnessed with the synthesis and exploration of few massive, symmetrical and unsymmetrical benzimidazole core Pd-NHC complexes. Additionally, the steric bulk of these complexes enables the stabilization of low valent active intermediates and favors easy reductive elimination step, thereby increases the catalytic activity for several cross-coupling reactions. From the literature survey, it is identified that Baker and group introduced bulky *o*-xylyl linked alkoxybenzimidazolin-2-ylidine-Pd-NHC complexes for Mizoroki-Heck and Suzuki-Miyaura reactions.[23] Later, Akkoc and Gok reported benzimidazole based Pd-PEPPSI complexes for arylations on thiazole, furan and thiophene compounds by C-C bond formation reactions.[24] Recently, Boubakri et al. synthesized few Pd-PEPPSI complexes for Suzuki-Miyaura coupling and evaluated their biological properties.[25] Lately, benzimidazolyl Pd-NHC complexes were exercised for sustainable chemistry on aryl bromides by Zhu and his co-workers.[26]

Much before from the original discovery, many of the teams are endlessly focusing on the synthesis and applications of assorted Pd-NHC complexes precisely for C-C bond formations, while only a few are directing on C-N bond formations. For instance, Zhang[22a] reported the Buchwald-Hartwig amination reaction with imidazolyl Pd-PEPPSI-IPr$^{(NMe_2)_2}$ catalyst in 2015. Later, Lan et al. employed flexible and bulky bis(imino)acenaphthene (BIAN) Pd-PEPPSI complex for amination reaction in open air.[27] Recently, Mizusaki and group[19c] put forth the silyl supportive Pd-NHCs for these type of reactions (Scheme 1).

Most of the heteroaryl chlorides are less reactive or reluctant to cross-couplings due to their electron deficit property. Hence, several teams are continuously putting their efforts towards synthesizing abnormal metal complexes and activating them for derivatization of heterocyclic amines.

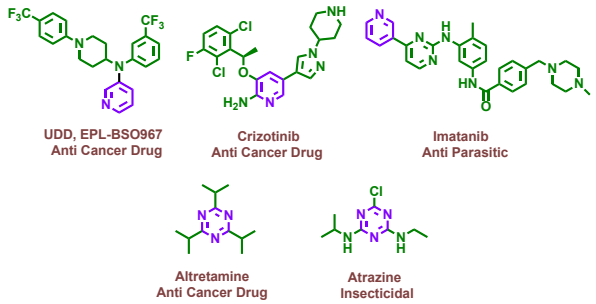
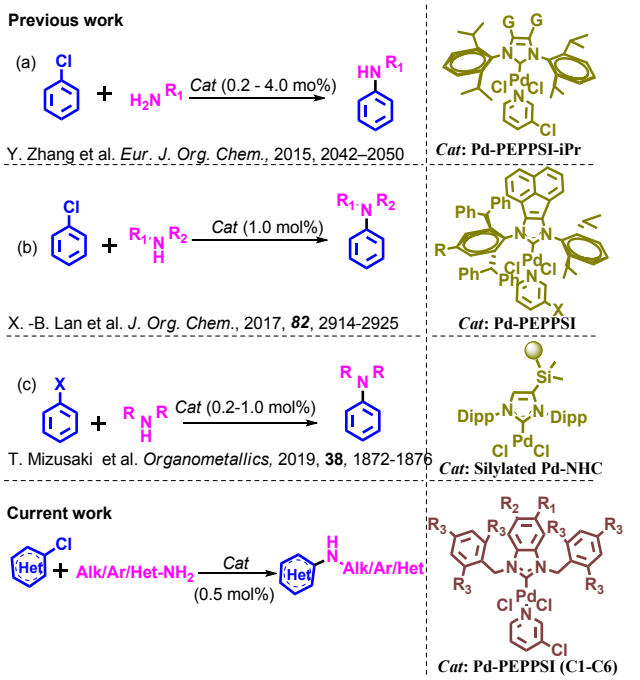


Fig. 1 Few pyridine and triazine based drugs.

Pyridine and triazine scaffolds represent important classes of heteroaromatic compounds in spite of their potential biological activities.[28,29] Some of the biologically active compounds are presented in figure 1.

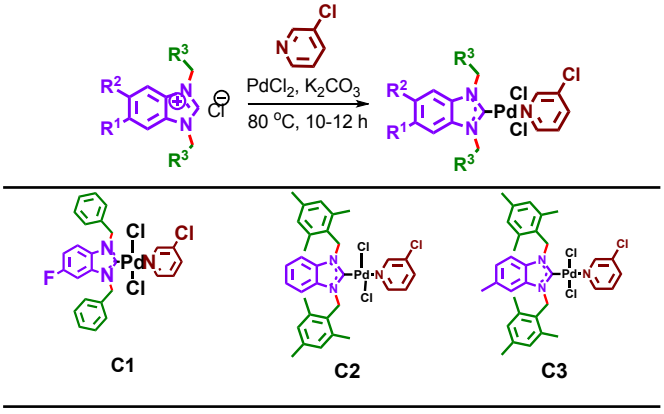
With this perception, our present study aimed at the synthesis of different series of pyridine and triazine mimics from the respective heteroaryl chlorides and aryl/heteroaryl amines in the presence of electron rich sterically encumbered benzimidazolium Pd-PEPPSI complexes (Scheme 1).



Scheme 1 Representative examples of previous and present works.

Results and discussion

Since 2016, we gained a rich experience in the development of new protocols for C-C and C-N bond formation reactions on heterocyclic compounds[30] using Pd-PEPPSI catalysts.



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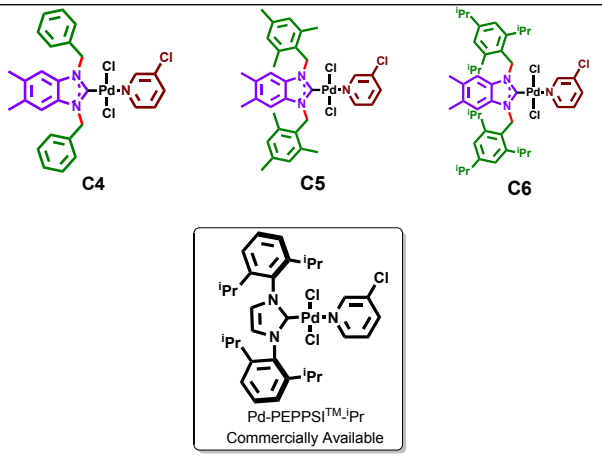

Scheme 2 Preparation of various Pd-PEPPSI complexes **C1-C6** Reagents and conditions: benzimidazolium chlorides (1.0 mmol), $PdCl_2$ (1.0 mmol), K_2CO_3 (4.0 mmol), 3-chloropyridine (4 mL), 80 °C, 10-12 h.

To further continue our efforts on NHCs, we here-in constructed an array of six different *N,N'*-symmetrically substituted benzimidazolium chloride salts from the low cost, readily available, *o*-phenylenediamines following a simple reaction pathway.[27e] These salts were then allowed to react with $PdCl_2$ and 3-chloropyridine in the presence of K_2CO_3 at 80 °C for 10-12 h to afford the highly active Pd-PEPPSI complexes **C1-C6** (Scheme 2). All the prepared candidates were well characterized by IR and NMR (^1H & ^{13}C) spectroscopies. Structure of one of the bulky and highly reactive complex, **C6** has been analyzed by single crystal X-ray diffraction spectroscopy.

X-ray crystallography study

To establish the geometry, suitable crystals of Pd-PEPPSI **C6** were grown by slow diffusion of ethanol in saturated dichloromethane solution. A good quality pale yellow colour single crystal of size 0.200 x 0.150 x 0.150 mm3 was selected for single-crystal diffraction analysis under a polarizing microscope. Data was collected on the 'Bruker axs kappa apex2 CCD diffractometer' generated from fine-focus sealed tube diffraction radiation source under graphite monochromator. Theta range employed for data collection is 2.149 to 25.000° at 296(2)K.

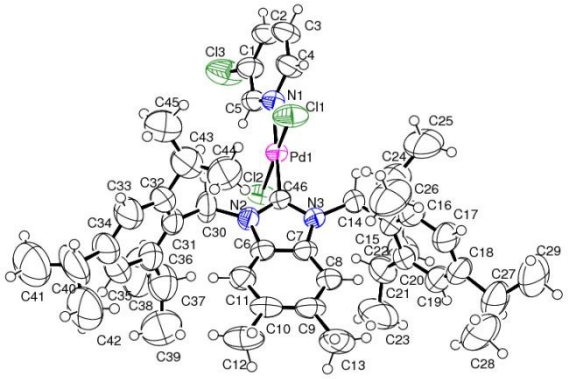

Fig. 2 ORTEP diagram drawn with 50% ellipsoid probability for non-H atoms of the crystal structure of **C6** determined at 296 K (CCDC Deposit No.: 1982273).

Crystal showed the monoclinic geometry with space group $P21_{/n}$ around the metal center. The complex has single bond character between Pd (1) and $C_{carbene}$(46) with bond length 1.939 Å while the bond distance between Pd(1) and N(1) (of pyridine) is 2.144 Å. In this complex, NHC ligand and 3-chloropyridine are oriented *trans* to each other with a bond angle of 177.45° for C(46)-Pd(1)-N(1). The 2,4,6-triisopropyl-benzyl groups on N2 and N3 are much more tilted, probably due to the skewed geometry of the NHC backbone with bond angles 118.9° and 119.4° for C(46)-N(3)-C(14) and C(46)-N(2)-C(30) respectively (Figure 2).

Besides the crystal refinement, $\%V_{Bur}$ was also calculated for **C6** complex using web application Samb*V*ca[31] by setting the bond radius scaled by 1.17, sphere radius R = 5 Å and Pd–$C_{carbene}$ distance d = 2.00 Å. The obtained percentage buried volume was 44.8% which is greater than the computed values for IPr-$PdCl_2$-3-chloropyridine and SIPr-$PdCl_2$-3-chloropyridine (34.3 and 39.3 respectively)[32] and this revealed its greater steric environment. The steric map for graphical representation of **C6** is presented in figure 3.

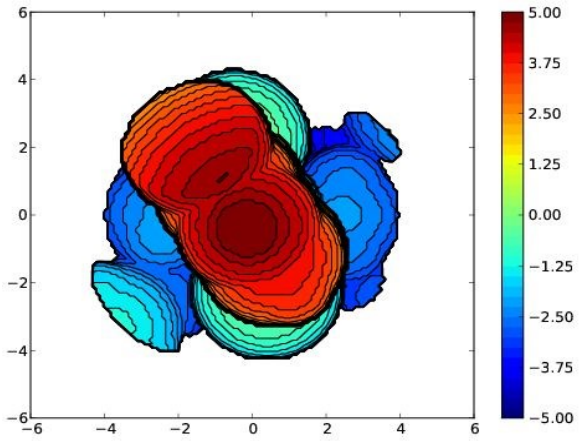

Fig. 3 Steric map of catalyst **C6**.

As an element of study, to judge the catalytic activity of various synthesized Pd-PEPPSI complexes, we have chosen Buchwald-Hartwig amination reaction. For this, we initiated C-N bond formation reaction between 3-chloropyridine and aniline in the presence of Pd-PEPPSI catalyst **C1** (0.5 mol% load), KO^{t}Bu and in toluene at room temperature for about 8 h, but obtained no desired product (Table 1, entry 1). Temperature was then raised gradually to 50 °C and 90 °C and noticed product formation with increase in the percentage yield (Table 1, entries 2 and 3). With this scope, reactivity by different complexes **C2-C6** was checked and found that bulkiness due to 2,4,6-methyl/triisopropylbenzyl groups on 1,3 positions (of NHC) and the direct methyl groups on benzimidazole core could together influence the reactivity and hence amplified result was gained with **C6** (Table 1, entries

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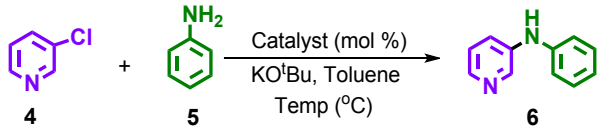
4-8). For the purpose of comparison, the catalytic activity was also monitored with Pd-PEPPSI-^{i}Pr and observed the lowering in yield (Table 1, entry 13). This states the impact of bulky yet flexible nature of 2,4,6-triisopropyl benzyl groups which is less noticed in Pd-PEPPSI-^{i}Pr.

Next, to find the exact time of conversion, the reaction was repeated with **C6** and recognized best yield formation in just 3 h (Table 1, entry 9). Finally, to reduce the effort in large scale catalyst manufacturing, effective catalyst loading was aspired. For this study, reaction was started with 0.05 mol% of **C6** and obtained 23% of yield. Later, the loading was increased to 0.1 and 0.5 mol% and received 59 and 91% yields respectively (Table 1, entries 11 and 9). An additional increase to 0.8 mol% did not offer any increase in product yield (Table 1, entry 12). Therefore, the optimum catalyst load for carrying out the reaction was set to 0.5 mol%.

Table 1. Screening of Pd-PEPPSI complexes **C1** to **C6** for the preparation of *N*-phenylpyridine-3-amine



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Entry	Catalyst (mol%)	Temp (°C)	Time (h)	Yield[a] (%)
1	**C1** (0.5)	25	8	N.P
2	**C1** (0.5)	50	8	34
3	**C1** (0.5)	90	8	58
4	**C2** (0.5)	90	8	67
5	**C3** (0.5)	90	8	76
6	**C4** (0.5)	90	8	63
7	**C5** (0.5)	90	8	85
8	**C6** (0.5)	90	8	91
9	**C6** (0.5)	90	3	91
10	**C6**(0.05)	90	3	23
11	**C6** (0.1)	90	3	59
12	**C6** (0.8)	90	3	91
13	Pd-PEPPSI™-^{i}Pr (0.5)	90	3	86

Reaction conditions: 3-chloropyridine (1.0 mmol), aniline (1.0 mmol), KO^{t}Bu (3.0 mmol), toluene (3 mL).

Subsequently, to make the condition more specific, the role of solvents was also examined. Several teams are interested in the development of green methodologies using solvents/solvent systems like dimethyl sulfoxide, water, toluene:water etc. Hence investigations were repeated with organic solvents alone/water/mixture of organic solvents and water (1:1), but unfortunately obtained ambiguous results (Table 2, entries 1-7). Hence toluene is optimized as the best solvent for this reaction (Table 1, entry 9). Apart from all the above parameters, the selection of base is also very much imortant in the area of catalysis. So, bases like K_2CO_3, Cs_2CO_3, NaO^{t}Bu, KO^{t}Bu, K_3PO_4, NEt_3 and pyridine were tested and received superior yield with KO^{t}Bu (Table 2, entries 7-13 and Table 1, entry 9).

Table 2. Effect of role of solvents and bases on C-N bond formation

Entry	Solvent (mL)	Base	Yield[a] (%)
1	Dimethylsulfoxide	KO^{t}Bu	55
2	1,4-dioxane	KO^{t}Bu	67
3	Dimethoxyethane	KO^{t}Bu	61
4	Water	KO^{t}Bu	N.P
5	Toluene:Water (1:1)	KO^{t}Bu	57
6	Dioxane:Water (1:1)	KO^{t}Bu	52
7	THF:Water (1:1)	KO^{t}Bu	49
8	Toluene	K_2CO_3	51
9	Toluene	Cs_2CO_3	73
10	Toluene	NaO^{t}Bu	69
11	Toluene	K_3PO_4	58
12	Toluene	NEt_3	38
13	Toluene	Pyridine	45

Reaction conditions: 3-chloropyridine (1.0 mmol), aniline (1.0 mmol), base (3.0 mmol), solvent (3 mL), 90 °C, 3 h.

Rate of reaction with catalysts C1-C6 towards *C-N* bond formation on 3-chloropyridine

To widen the studies, an auxiliary evaluation of rate of reaction with **C1-C6** was endeavored. With the optimum reaction condition in hand, 3-chloropyridine was coupled with aniline in the presence of series of complexes **C1-C6** (0.5 mol%) at 90 °C. In all the cases, reaction was observed to start in 30 min of time followed by a steep raise in activity between 2 to 3 h, reaches a maximium yield and therafter remained constant (Fig.4).

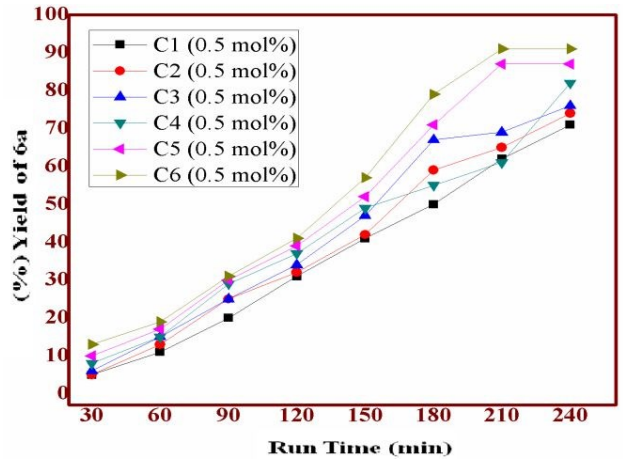

Fig. 4 Rate of Reaction.

From the above all practices, the best optimum reaction condition for the coupling of different amines with 3-chloropyridine is catalyst: **C6**, base: potassium *tert*-butoxide, solvent: toluene and temperature: 90 °C. With this tool in hand, we then explored the substrate scope and obtained good to excellent yields of products as shown in Table 3.

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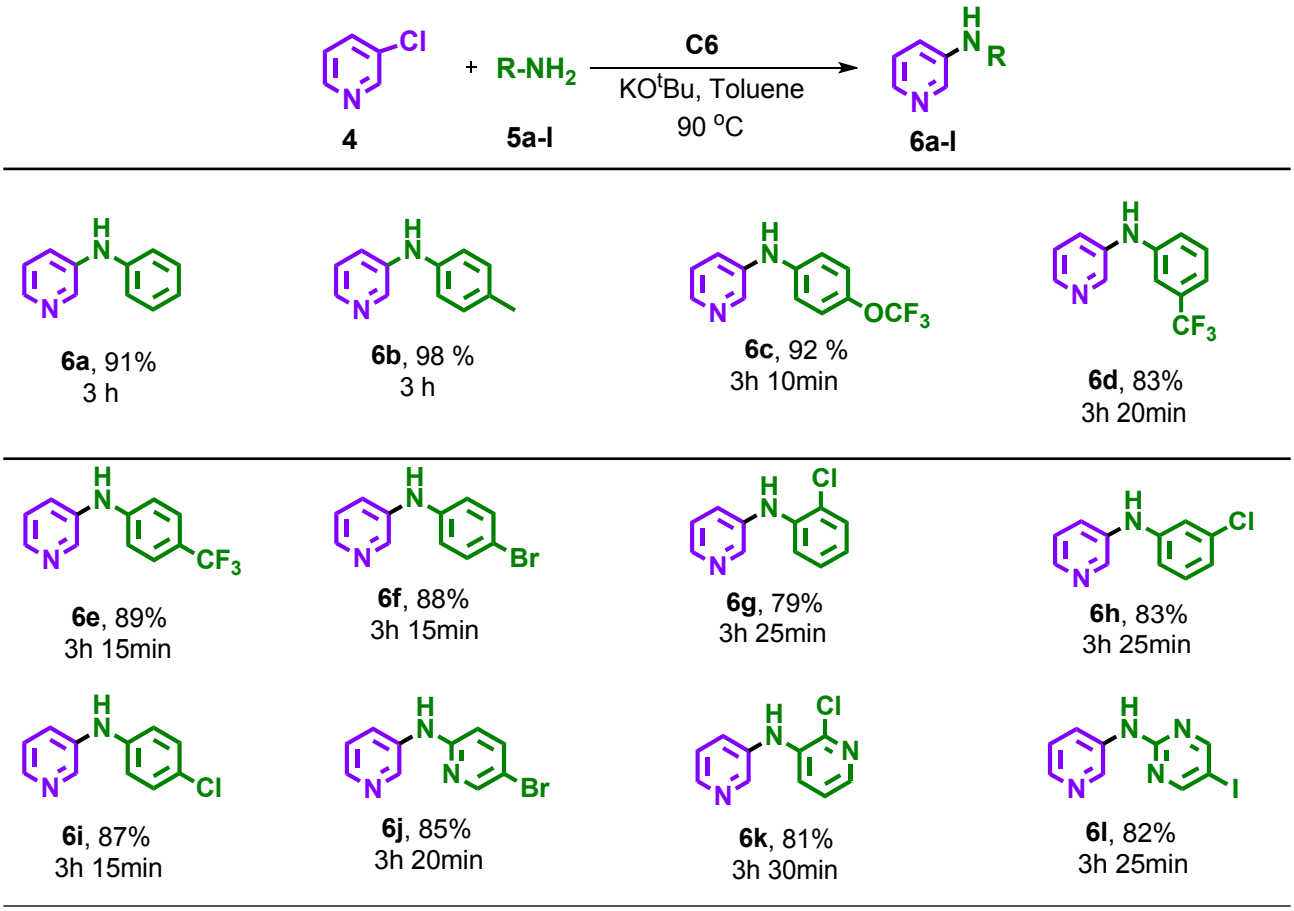
Table 3. Identification of catalyst activity for coupling of 3-chloropyridine with primary amines



Reaction conditions: 3-chloropyridine (1.0 mmol), 1° amine (1.0 mmol), **C6** (0.5 mol%), KO^{t}Bu (3.0 mmol), toluene (3 mL), 90 °C.

The study was generalized from the coupling of 3-chloropyridine with simple aniline and extended to substituted aromatic and heteroaromatic amines. Amines bearing electron donating groups like -CH_3 coupled very efficiently compared to those bearing withdrawing groups like -CF_3 (Table 3, entries **6b** and **6d, 6e**). In the other case, effect due to electron withdrawing groups at different positions was tested and observed a negligible variation in yields. In this respect, amines with -CF_3 group at *meta*-position afforded lower yield than that at *para*-position (Table 3, entries **6d** and **6e**). Similarly, when we monitored the effect of chlorines at different positions of aniline, 2-chloroaninine was observed to couple with lower yield compared to 3- and 4-chloroanilines (Table 3, entries **6g-i**).

Limited protocols are available on the coupling of aromatic halides with amines bearing bromo/iodo substituents.[33] Despite, with our objective to bring out the rationale on working of these complexes, 3-chloropyridine was allowed to react with 4-bromoaniline, 2-amino-5-bromopyridine and 5-iodopyrmidin-2-amine and gained surprising results in all these cases. Particularly 4-bromoaniline gave a little higher yield than the other two amines (Table 3, entries **6f, 6j** and **6l**). This clearly evidences the tolerability and good compatibility of the catalyst even for different halo surrogates of amines. The results also explain that the hetero aromatic amines could efficiently couple with 3-chloropyridine under satisfactory yields (Table 3, entries **6j-l**).

From the literature reports, most of the catalysts shown to execute good activity towards coupling of primary amines with aryl/heteroaryl halides than do with secondary amines. Hence, in a quest to find out the substrate scope of the catalyst, coupling of 3-chloropyridine with secondary amines was routed. For this, initially morpholine was allowed to couple with 3-chloropyridine and achieved promising yield (Table 4,

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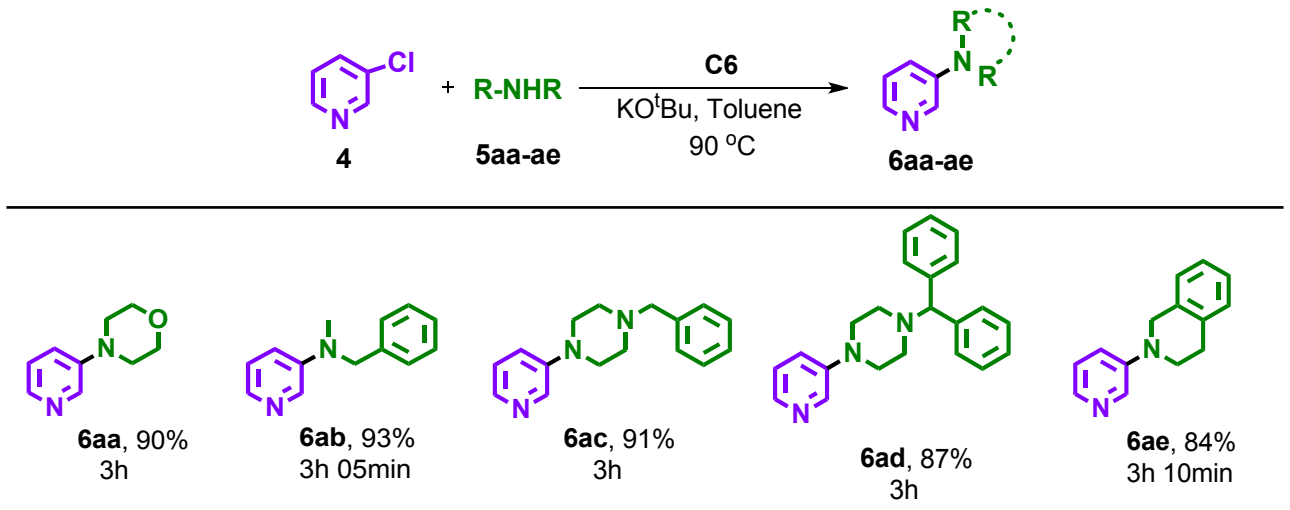
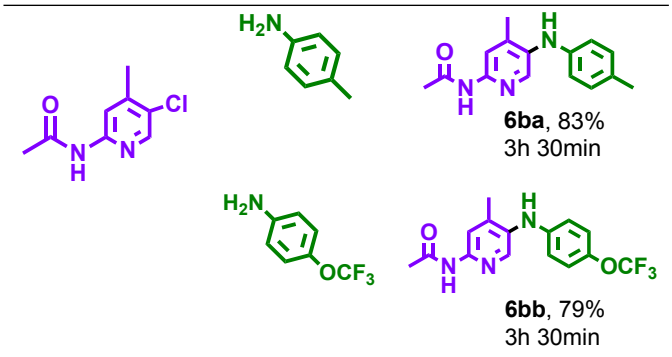
Table 4. Investigation on catalyst activity for coupling of 3-chloropyridine with secondary amines



Reaction conditions: 3-chloropyridine (1.0 mmol), 2° amine (1.0 mmol), **C6** (0.5 mol%), KO^{t}Bu (3.0 mmol), toluene (3 mL), 90 °C.

entry **6aa**). With this inception, we then proceeded to react with 1-methylbenzylamine, 1-benzylpiperazine, 1-benzhydrylpiperazine & 1,1,2,2-tetrahydroquinoline (Table 4, entries **6ab - 6ae**) and acquired un-anticipated results. The above results gives us a crystal inference of more or less same reactivity effect of **C6** for both 1° and 2° amines.

Table 5. Survey on effect of catalyst for coupling of *N*-(5-chloro-4-methylpyridin-2-yl)acetamide with 1° aromatic amines

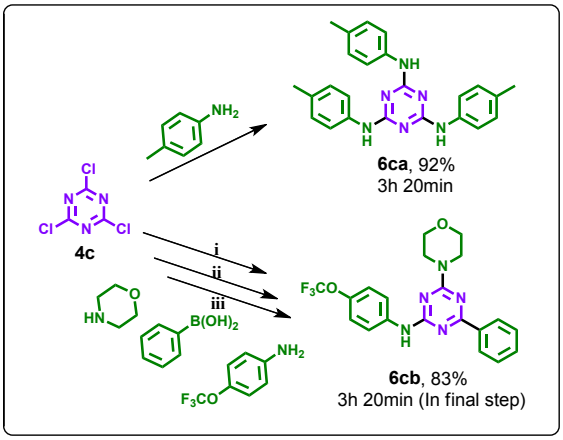


Reaction conditions: *N*-(5-chloro-4-methylpyridin-2-yl)acetamide (1.0 mmol), amine (1.0 mmol), **C6** (0.5 mol%), KO^{t}Bu (3.0 mmol), toluene (3 mL), 90 °C.

To further explore the scope of the catalyst, *N*-(5-chloro-4-methylpyridin-2-yl)acetamide was coupled with electron rich *p*-toluidine and electron deficient *p*-trifluoromethoxy aniline, and attained better result with the former than the latter owing to its electronic property (Table 5, **6ba** and **6bb**).

Next, to identify the substrate scope of the catlyst for other nitrogen heterocycles, we selected highly versatile and biologically active 2,4,6-trichlorotriazine for cross-coupling reactions.

Although, 2,4,6-trichlorotriazine can effectively couple with different nucleophilic partners under mild base conditon, they are sometimes reported with long reaction time,[34] and at high temperatures.[35,36]



Scheme 3. Rational design for the synthesis of 2,4,6-trisubstituted triazines with **C6**.

Reaction conditions: For **6ca**: 2,4,6-trichlotriazine (1.0 mmol), 4-methyl aniline (3.0 mmol), **C6** (1.0 mol%), KO^{t}Bu (5.0 mmol), toluene (3 mL), 90 °C.

For **6cb**: Step i: 2,4,6-trichlotriazine (1.0 mmol), morpholine (1.0 mmol), **C6** (0.5 mol%), K_2CO_3 (3.0 mmol), toluene (3 mL), 90 °C, 1h 20min. Yield (91%). Step ii: 4-(4,6-dichloro-1,3,5-triazin-2-yl)morpholine (1.0 mmol), phenylboronic acid (1.0 mmol), **C6** (0.5 mol%), K_2CO_3 (2.0 mmol), toluene (3 mL), 90 °C, 2h 30min. Yield (94%). Step iii: 4-(4-chloro-6-phenyl-1,3,5-triazin-2-yl)morpholine (1.0 mmol), 4-trifluoromethyl aniline (1.0 mmol), **C6** (0.5 mol%), KO^{t}Bu (3.0 mmol), toluene (3 mL), 90 °C, 3h 20min. Yield (83%).

Conversely, M. S. Muller and team displayed coupling of morpholine to 2,4,6-trichlorotriazine in the presence of

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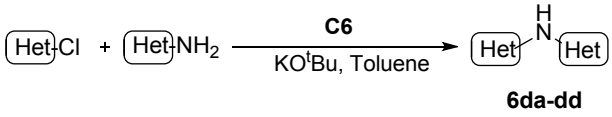
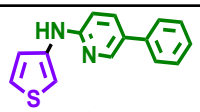
triethylamine followed by 2-substituted benzimidazole coupling in the presence of $Pd(OAc)_2$ and xantphos.[36] Similarly, palladium complexes catalyzed C-C bond formations for active 2,4,6-triazines synthesis was presented by various teams.[30e,37] Hence, to ascertain the efficiency of the synthesized Pd-PEPPSI complexes, we also conducted few more experiments. First 2,4,6-trichloro traiazine was reacted with toluidine via Buchwald coupling and obtained 92% of trisubstituted product with just 1 mol % of **C6.** With this enthusiastic report, we then proceded to examine the captivity of catalyst for Suzuki-Miyaura reaction. In this consequence, 4-(4,6-dichloro-1,3,5-triazin-2-yl)morpholine (step-i product of **6cb**) was coupled with phenylboronic acid in the presence of Pd-PEPPSI **C6** and K_2CO_3 in toluene at 90 °C and acquired 4-(4-chloro-6-phenyl-1,3,5-triazin-2-yl)morpholine in best yield. During the conversion of 2,4,6-trichlorotriazine to 4-(4-chloro-6-phenyl-1,3,5-triazin-2-yl)morpholine, sequential Buchwald-Hartwig (morpholine substitution), Suzuki-Miyaura (phenyl substitution) and Buchwald-Hartwig couplings (*p*-trifluoromethoxyphenyl substitution) were performed to achieve products in 91, 94% and 83% respectively (Scheme 3).

Table 6. Assessment of substrate scope of **C6** for different heteroaryl chlorides

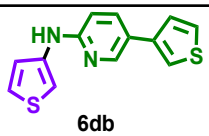


6da-dd



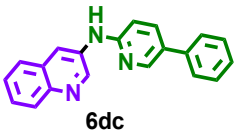
6da

Yield with Pd-PEPPSI-**C6** : [a]69%
SingaCycle™-A1: [b]48%



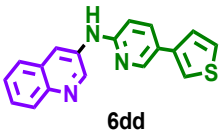
6db

Yield with Pd-PEPPSI-**C6** : [a]59%
SingaCycle™-A1: [b]43%



6dc

Yield with Pd-PEPPSI-**C6** : [a]81%
SingaCycle™-A1: [b]68%



6dd

Yield with Pd-PEPPSI-**C6** : [a]71%
SingaCycle™-A1: [b]52%

Reaction conditions: heteroarylchlorides (1.0 mmol), heteroarylamine (1.0 mmol), **C6** (0.5 mol%), KO^{t}Bu (3.0 mmol), toluene (3 mL), 90 °C, 3 h. [a]Isolated Yield. [b]Reported Yield.

The aforementioned results prompted us to further explore the synthetic utility of the complexes. Hence, we tried the application of Pd-PEPPSI **C6** for coupling of different heteroaromatic chlorides such as 3-chlorothiophene and 3-chloroquinoline which we were moderately successful with SingaCycle™-A1 in our previous report.[30c] These compounds were effectively coupled with 5-phenylpyridin-2-amine and 5-(thiophen-3-yl)pyridin-2-amine with comparatively good yields of products in the presence of Pd-PEPPSI **C6** than with SingaCycle™-A1 and all the products (**6da-dd**) were matched with the earlier literature report.[30c]

Experimental

I. General Experimental Section

o-Phenylenediamines, benzyl halides (aralkylhalide), triethylorthoformate, 3-chloropyridine, 2,4,6-trichloro-1,3,5-triazine, aromatic amines, phenylboronic acid, Pd-PEPPSI™-^{i}Pr and SingaCycle™-A1 were purchased from Sigma Aldrich and TCI companies, palladium chloride was procured from Alfa Aesar company, *N*-(5-chloro-4-methylpyridin-2-yl)acetamide was received from Avra Synthesis, solvents were acquired from Merck company and were used without any further purification. Bases were collected from Sigma Aldrich and Acros companies. Benzimidazolium salts were prepared from our recent work.[30e] All the reactions were carried out in non-inert atmosphere. Progress of the reactions was monitored from TLC analysis using Merck silica gel 60 F_{254} plates and visualized under UV lamp.

The NMR spectra were recorded on Bruker Top spin 400 MHz instrument at ambient temperature using TMS as an internal standard and $CDCl_3$ or DMSO-d6 as solvents with a decoupled nucleus. Chemical shifts (δ) are reported in ppm. Multiplicities in the ^{1}H-NMR spectra are described as: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublet, td = triplet of doublet, qd = quartet of doublet, m = multiplet; Coupling constants are reported in Hz. High Resolution Mass Spectra were recorded on microTOF-Q II-Bruker compass mass spectrometer operating at 70 eV.

Melting points of the synthesized compounds are uncorrected. Infrared spectra for all the compounds recorded on Bruker Alpha-Eco ATR-FTIR (Attenuated total reflection-Fourier transform infrared) interferometer with single reflection sampling module equipped with KBr crystal. X-ray diffraction data for single crystal of Pd-PEPPSI **C6** was obtained using the ω-2θ scan mode on a Bruker kappa apex2 CCD diffractometer with graphite monochromator under Mo Kα radiation 2.149 to 25.000° at 296(2)K. Global refinement of all positions from the reflections used for recording cell parameters. The crystal structure was solved by direct methods and refined by full-matrix least-squares on F2. Structure solution and refinement were performed by using the SHELXL-97 package. All the non-hydrogen atoms were refined anisotropically. Hydrogen atoms were introduced in calculated positions with the displacement factors of the host carbon atoms.

II. Common route for the synthesis of Benzimidazolium Pd-PEPPSI-Complexes (C1-C6)

a. Synthesis of Bis *N,N*-diaralkyl benzene-1,2-diamines

o-phenylenediamine (1.0 mmol) was taken into a clean 50 mL RBF and charged with dry acetonitrile solvent (10 mL). To that solution, triethylamine (3.0 mmol) and aralkylhalide (2.0 mmol) were added at 0 °C and allowed to stir for 30 min at 25 °C and 3 h at reflux condition. The reaction mixture was then cooled to room temperature (25 °C), monitored the progress of reaction

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by TLC, distilled off the solvent, added 5 mL of water and extracted with CH_2Cl_2 twice (2x10 mL). The combined organics was dried over anhydrous Na_2SO_4 and the CH_2Cl_2 solvent was removed under high vacuum to obtain the crude mass which was then purified through column chromatography using 100-200 silica mesh to obtain the pure colourless solids.

b. Typical method for the construction of symmetrical bis *N,N*-diaralkyl benzimidazolium chlorides

In a 25 mL round bottomed flask containing symmetrical *N,N'*-diaralkylbenzene-1,2-diamine (1.0 mmol) and triethyl orthoformate (1.0 mmol) was added conc. HCl (1.0 mmol) at 0 ^oC and the resulting mixture was refluxed for 3 h. After the completion of reaction (examined over TLC), the mixture was cooled to room temperature and evaporated the solvent under the reduced pressure to yield the crude mass. This was triturated with n-hexane/diethyl ether (2*5 mL) and dried under high vacuum to afford colourless salts.

c. Versatile procedure for the synthesis of Pd-PEPPSI complexes C1-C6

A 25mL round bottomed flask containing magnetic stir bar was charged with 3-4 mL of 3-chloropyridine, *N,N'*-symmetrically disubstituted benzimidazolium chlorides (1.0 mmol) and palladium chloride (1.0 mmol). To that, was added K_2CO_3 (3.0 mmol) and allowed to stir for 10-12 h at 80 ^oC in non-inert atmosphere during which the reaction mixture converts initially to yellow followed by deep color change to orange-red mass. After the completion of reaction, the mixture was cooled to room temperature and filtered through a pad of celite by washing with small amount of ethyl acetate (15 mL). To the filtrate was added 10 mL of water, extracted with ethyl acetate twice (2x5 mL) and the combined organics was evaporated under reduced pressure to obtain the crude mass. This was purified by gravity column using silica mesh with hexane:ethyl acetate eluent to obtain pure Pd-PEPPSI complexes **C1** to **C6** as yellow solids (Yields: 63-85%). All the complexes were characterized by ^1H and ^{13}C NMR and IR spectroscopies. Compound **C6** was also characterized by crystal XRD.

III. Typical procedure for the preparation of *N*-alkyl/aryl/heteroarylpyridine/triazine amines (6a-l, 6aa-6ae, 6ba-bb, 6ca-cb, 6da-dd)

In a dry 10 mL round bottomed flask charged with toluene (3 mL), pyridine/triazine/thiophene/quinoline chlorides (1.0 mmol), alkyl/aryl/heteroaryl 1^o or 2^o amines (1.0 mmol (3.0 mmol for **6ca**)), **C6** (0.5 mol% (1 mol% for **6ca**)) and KO^{t}Bu (3.0 mmol (5.0 mmol for **6ca**)) were added at room temperature and then stirred at 90 ^oC for 3-4 h in the absence of any inert gases. After the complete progress of reaction (monitored through TLC), the mixture was cooled to room temperature, added 3 mL of water, extracted with ethyl acetate twice (2x5 mL), dried the combined organic over anh. Na_2SO_4 and distilled-off the solvent under vacuum to get the crude material. This obtained mass was then purified through gravity column with silica gel (100-200 mesh) using hexane-ethyl acetate as eluent to obtain the pure products. **6a-l, 6aa-ae, 6ba-bb, 6ca-cb, 6da-dd** (yields: up to 98%). The identity and purity of the compounds were confirmed from NMR and HRMS spectroscopic analyses.

For **6f, 6j** and **6l**: Initially 3-chloropyridine (1.0 mmol) was added to a round bottomed flask charged with Pd-PEPPSI **C6** (0.5 mol%) in toluene (3 mL) at room temperature and stirred for 10-15 min. To that, were added corresponding aryl/heteroaryl amines (1.0 mmol) and KO^{t}Bu (3.0 mmol) and stirred at 90 ^oC for 3-4 h without inert atmosphere condition. The progress of the reaction was monitored through TLC and the reaction mixture was cooled and worked up with water and ethyl acetate. The combined organics was dried over anh. Na_2SO_4, removed the solvent under vacuum and chromatographed with 100-200 mesh silica gel using hexane-ethyl acetate as eluent and acquired pure products.

IV. Suzuki coupling for the synthesis of 4-(4-chloro-6-phenyl-1,3,5-triazin-2-yl)morpholine (Step ii for 6cb synthesis)

Int **1**, 4-(4,6-dichloro-1,3,5-triazin-2-yl)morpholine (1.0 mmol), phenylboronic acid (1.01 mmol) and K_2CO_3 (2.0 eq) were taken into a 25 mL round bottomed flask containing toluene (3 mL) and the reaction mixture was allowed to stir for 5 minutes at room temperature. Later, **C6** (0.5 mol%) was included and continued stirring for further 5 minutes at the same temperature. The reaction mixture was then transferred to a pre-heated oil bath at 90 ˚C and stirred for another 2 h. After the completion of reaction as monitored by TLC, the reaction mixture was brought to room temperature and filtered through Whatman filter paper followed by hexane washings. To the filtrate was added 5 mL of saturated sodium bicarbonate solution and extracted with ethyl acetate twice to remove the un reacted boronic acid. The combined organics was dried over anhydrous sodium sulphate and evaporated under vacuum. The obtained crude mass was purified by flash column chromatography over silica gel using hexane-ethyl acetate as the eluent to get the pure product, int **2** (yield: 94%).

Conclusions

In summary, we report a more convenient approach for the preparation of a new class of *N,N'*-symmetrical benzimidazolium clock Pd-PEPPSI complexes. From the reactivities of different catalysts **C1-C6** towards Buchwald-Hartwig cross-coupling on heterocyclic halides, it can be concluded that the bulky *N,N'*-triisopropylbenzyl substituents on benzimidazolium NHC ligands in as-synthesized Pd-PEPPSI complexes effectively influence the C-N bond formations. Moreover, all these catalysts are new and worthy to replicate the catalytic conversion in short reaction time at low loading (0.5 mol%) under non-inert atmosphere with excellent yields. Thus, the benzimidazolium Pd-PEPPSI complexes opens new route of dynamic catalytic system that could be paramount importance in constructing several new and vulnerable biologically active lagoons.

Conflicts of interest

There are no conflicts to declare.

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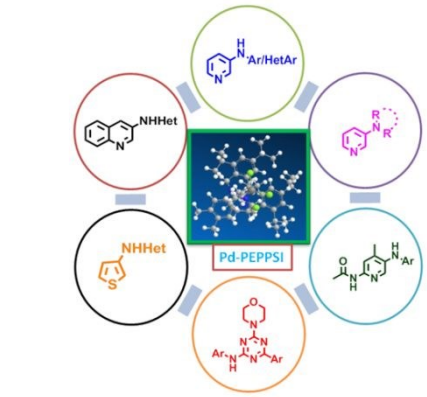
Graphical Abstract

Sterically Enriched Bulky 1,3-Bis(*N,N'*-Aralkyl)Benzimidazolium based Pd-PEPPSI Complexes for Buchwald-Hartwig Amination Reactions

Motakatla Venkata Krishna Reddy, Gokanapalli Anusha and Peddiahgari Vasu Govardhana Reddy*

A simple and efficient synthesis of a series of unexisting Pd-PEPPSI complexes is summarized. These complexes are exploited for their high catalytic activity towards Buchwald-Hartwig amination reactions without any external ligand or additive. A great influence is perhaps noticed with the increase in steric bulk of the catalysts.



✓Pd-PEPPSI Complexes C1-C6 ✓Non Inert Condition
✓Buchwald-Hartwig ✓Low Catalyst Loading