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One-pot synthesis of new N-(1-methylpyridin-4(1H)-ylidene)amine ligands for palladium-catalyzed Heck coupling reaction

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Abstract: A series of new derivatives of N-(1-methylpyridin-4(1H)-ylidene)amines, [L[1]]–[L[5]], were synthesized and characterized by FTIR, NMR, MS, and XRD analysis. These targeted compounds were synthesized by the melt reaction between N-methylated-4-chloropyridinium triflate and corresponding amines (1-naphthyl amine, o-ansidine, 2-nitroaniline, p-ansidine, and cyclohexyl amine) followed by the addition of sodium hydride in dichloromethane in the same pot. These highly electron-donating N-(1-methylpyridin-4(1H)-ylidene)amine ligands considerably improve the catalytic activity of palladium acetate towards Heck–Mizoroki carbon–carbon cross-coupling reactions.

Key words: N-(1-Methylpyridin-4(1H)-ylidene)amines, pyridinium amido, Heck–Mizoroki

1. Introduction

Phosphines and N-heterocyclic carbenes (NHCs) have gained an enormous reputation in the homogeneous catalytic world owing to their extensive utility in chemical transformations.[1] N-(1-Methylpyridin-4(1H)-ylidene) amine (PYE) as a ligand has been found to have properties comparable with these versatile ligands due to the exceptional electron donor ability towards metals in a coordination compound.[2] In addition, steric properties of PYE around metal can be altered by synthesizing various libraries of its derivatives.[3] It can resonate between zwitterion pyridinium amido and neutral N-(1-methylpyridin-4(1H)-ylidene)amine (Figure 1) similar to NHCs and thus can be categorized as a flexible electron donor and nitrogen donor ligand.[4] As it possesses an exocyclic nitrogen atom, it can provide a better environment to metal for coordination.[5]

Mizoroki–Heck cross coupling is an extremely convenient tool available to create C-C bonds in new drugs, natural products, optical devices, and industrially important starting materials, which are otherwise impossible or extremely difficult.[6–18] This technique has allowed scientists to link two organic moieties under less vigorous conditions for the creation of complex delicate molecules. The electron-rich environment around palladium via the choice of various electron donor ligands can facilitate the key oxidative addition step of alkyl or aryl halides to palladium in these types of reactions.[19–21] Palladium complexes of bidentate PYE ligands were already reported and showed strong trans influence.[3] As the electron donor properties of PYEs are similar to NHCs and phosphine donor ligands, these ligands are therefore potential candidates for palladium-catalyzed Heck coupling reactions.

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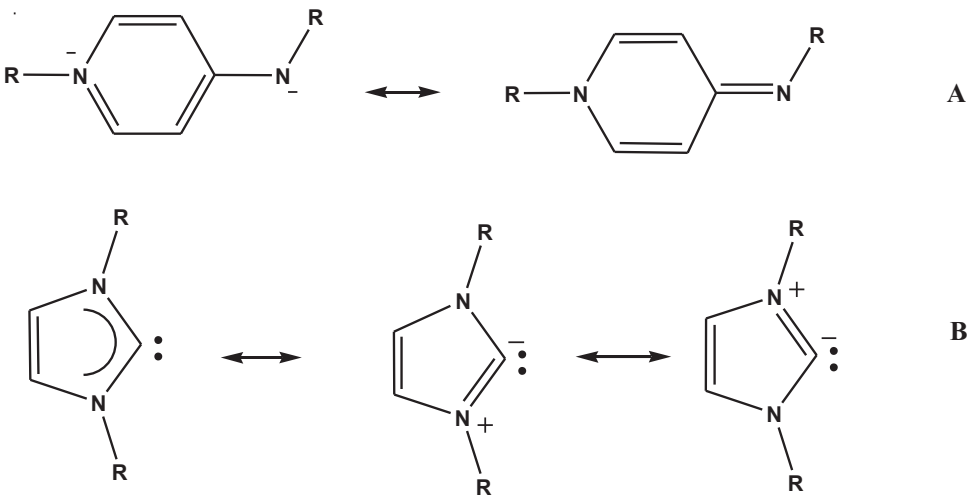


Figure 1. N-(1-Alkylpyridin-4(1H)-ylidene)amine (A) and N-heterocyclic carbene (B) ligands along with their resonance structures.

This research work presents the one-pot synthesis of five new reactive intermediates (PYEs) (Figure 2) that act as cocatalysts for palladium acetate and thus considerably enhance its catalytic activity towards the Heck–Mizoroki C-C cross-coupling reaction under various conditions. These synthesized compounds ([L^1]–[L^5]) were characterized by FTIR, ^{1}H NMR, ^{13}C NMR, mass spectrometry, and XRD analysis.

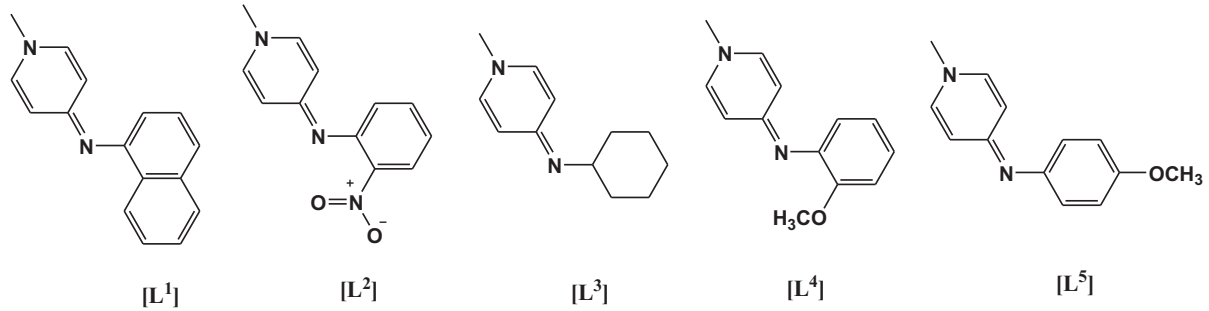


Figure 2. Structures of newly synthesized derivatives of *N*-(1-methylpyridin-4(1*H*)-ylidene)amine.

2. Results and discussion

2.1. Synthesis and characterization of compounds [L^1]–[L^5]

All five new compounds, [L^1]–[L^5], were prepared by the same method in a single pot. Initially, a melt reaction between 4-chloro-1-methylpyridin-1-ium triflate with the corresponding amine was carried out followed by deprotonation of the corresponding amine by sodium hydride (base) in dichloromethane. The sharp melting point indicates the purity of the synthesized compounds. All these compounds were characterized by FTIR, mass spectroscopy, and ^{1}H and ^{13}C NMR. Compound [L^2] was also confirmed by single-crystal analysis.

The disappearance of the NH_2 and NH peak around 5–6 and 9–11 ppm respectively in the proton NMR spectra of all five compounds clearly indicates the formation of the targeted compounds ([L^1]–[L^5]). In the aliphatic region, a singlet appears for *N*-methylated protons in the range of 3.64–3.50 ppm and *N*-methylated carbon in 42.95–39.50 ppm in all compounds along with another singlet for the methoxy group in [L^4] and

[L^5] (^{1}H NMR spectra are shown in Figure 3). The aromatic protons and carbon of all compounds appear in their normal ranges. Compound [L^3] showed cyclohexyl proton signals in the range of 3.34–1.00 ppm and 32.23–24.28 ppm in proton and carbon NMR, respectively.

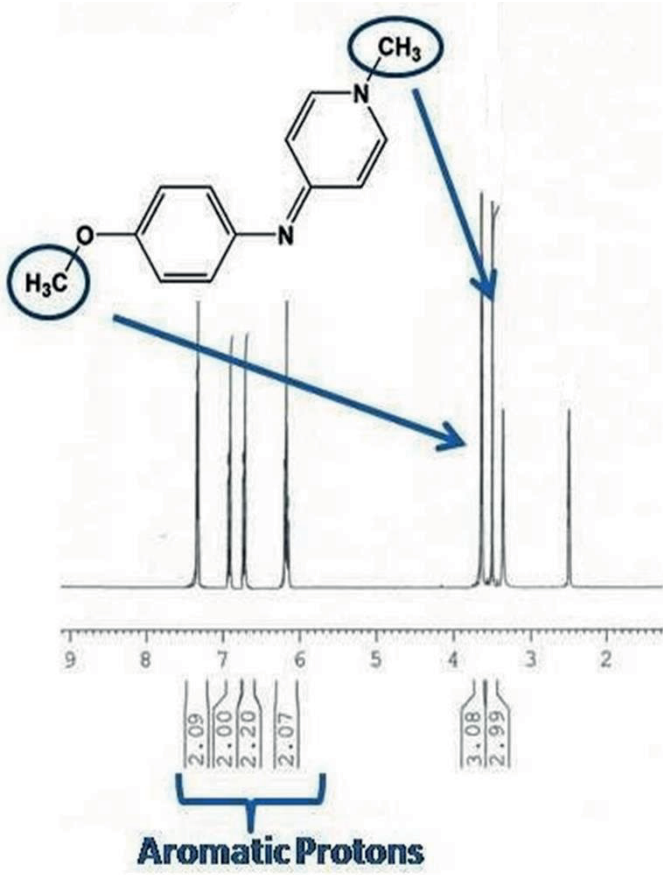


Figure 3. ^{1}H NMR spectrum of L^5.

In the IR spectra of compounds, the band between 2924 and 2829 cm^{-1} is assigned to ?(C-H). A strong band attributable to (-C= N) for all compounds is observed at 1590, 1647, 1649, 1651, and 1661 cm^{-1}, respectively. The bands in the range of 1582–1550 cm^{-1} are assigned to aromatic ?(C=C). A band due to methyl bending vibrations occurs between 1430 and 1255 cm^{-1}. In the high-resolution mass spectra of [L^1]–[L^5], the molecular ion peaks $[M+H]^+$ $[C_{16}H_{14}N_2]^+$, $[C_{12}H_{11}N_3O_2]^+$, $[C_{12}H_{19}N_2]^+$, and $[C_{13}H_{15}N_2O]^+$ were observed at m/z = 235.12283, 229.08458, 191.1543, and 215.11783, respectively (calculated 235.12297, 229.08461, 191.1546, and 215.11789).

A crystal of L^2 suitable for single-crystal X-ray diffraction studies was grown by slow evaporation of a saturated dichloromethane solution of L^2. An ORTEP depiction is given in Figure 4. Selected bond lengths and angles are presented in Tables 1 and 2, respectively. L^2 crystallizes in the space group $P2_1/c$ with four independent molecules in the asymmetric unit (Figure 5). The crystal structure showed that the C7–N2 bond length of 1.318 Å confirms that L^2 displays considerable imine character; typical bond lengths for single and double C-N bonds are 1.47 and 1.28 Å, respectively. Likewise, the C7–C11 and C7–C8 bonds of 1.424 Å and

1.430 Å are longer than a typical aromatic C-C bond. On the other hand, the C10–C11 bond and C9–C8 bond of length 1.352 Å and 1.351 Å are shorter than a typical aromatic C-C bond. The C10–N3 bond of 1.362 Å is longer than the expected 1.34 Å for pyridine N-C bonds.[3]

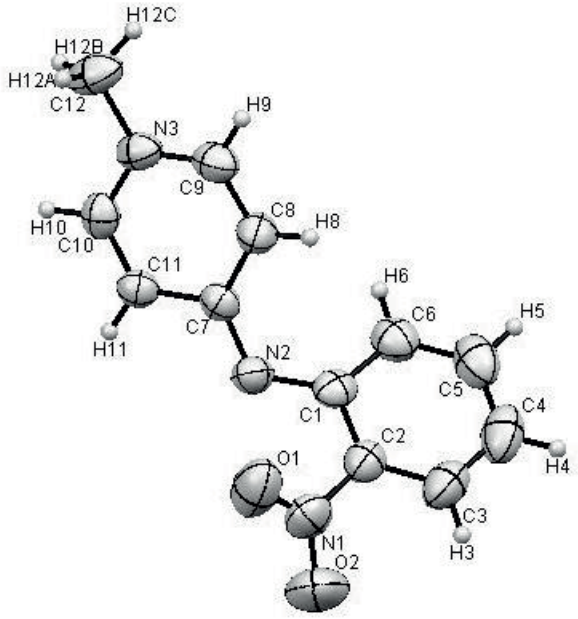


Figure 4. ORTEP diagram of L^2.

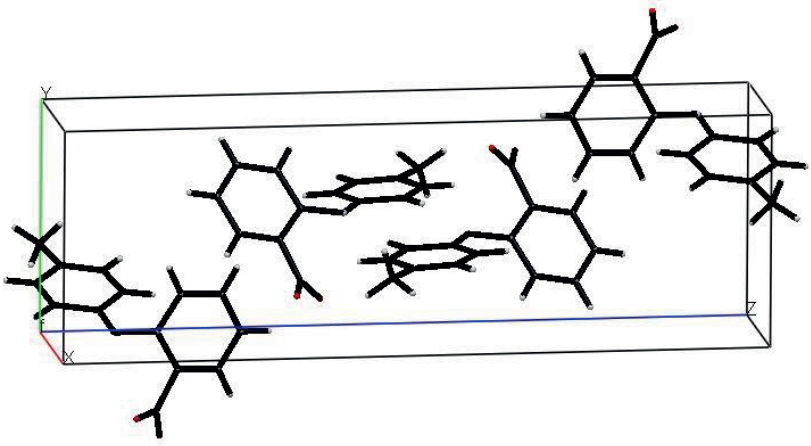


Figure 5. Packing diagram of L^2.

2.2. Catalytic Heck–Mizoroki cross-coupling reactions

To estimate the potential efficacy of PYEs (L^1–L^5) as ligands towards the Heck–Mizoroki cross-coupling reaction, each PYE (2 mol% as compared to halobenzene) was added as a cocatalyst with palladium acetate catalyst (1 mol% as compared to halobenzene) in entries 2–19 of Table 3. L^1 was used as the default ligand for the optimization of the Mizoroki–Heck reaction. First, the reaction of styrene with bromobenzene in DMA at 100 °C for 4 h in the presence of potassium carbonate, 0 mol palladium acetate, and 0.02 mol L^1 was run

Table 1. Selected bond lengths (Å) for [L^2].

Bonds	Length (Å)	Bonds	Length (Å)
O1 N1	1.208(3)	C1 C2	1.411(4)
O2 N1	1.222(4)	C2 C3	1.375(5)
N1 C2	1.457(5)	C3 C4	1.367(5)
N2 C7	1.318(3)	C4 C5	1.384(5)
N2 C1	1.373(4)	C5 C6	1.380(5)
N3 C9	1.340(5)	C7 C11	1.424(4)
N3 C10	1.362(4)	C7 C8	1.430(5)
N3 C12	1.479(3)	C8 C9	1.351(4)
C1 C6	1.401(4)	C10 C11	1.352(4)

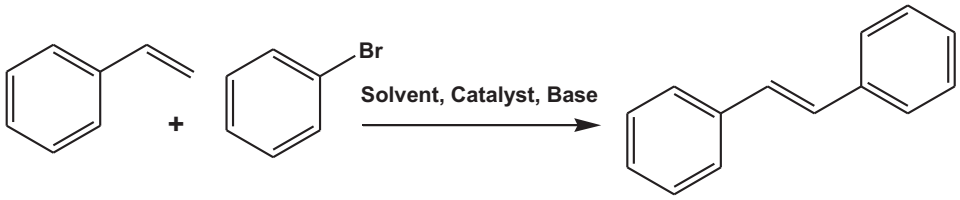
Table 2. Selected bond angles (°) for [L^2].

Bonds	Angles (°)	Bonds	Angles (°)
O1 N1 O2	122.8(3)	C1 C2 N1	119.2(3)
O1 N1 C2	119.6(3)	C4 C3 C2	120.0(4)
O2 N1 C2	117.5(3)	C3 C4 C5	118.9(4)
C7 N2 C1	121.9(3)	C6 C5 C4	120.9(4)
C9 N3 C10	118.4(3)	C5 C6 C1	122.3(3)
C9 N3 C12	121.2(3)	N2 C7 C11	118.5(3)
C10 N3 C12	120.2(3)	N2 C7 C8	127.1(3)
N2 C1 C6	123.7(3)	C11 C7 C8	114.4(3)
N2 C1 C2	121.1(3)	C9 C8 C7	120.6(4)
C6 C1 C2	114.5(3)	N3 C9 C8	123.3(4)
C3 C2 C1	123.4(4)	C11 C10 N3	121.7(3)
C3 C2 N1	117.4(3)	C10 C11 C7	121.6(3)

as a blank reaction. No product formed (Table 3, entry 1). Then a series of experiments was performed to find the optimum conditions (Table 3). Various reaction conditions including catalyst loading (Table 3, entries 1–5), solvent (Table 3, entries 5–10), base (Table 3, entries 10–15), and temperature (Table 3, entries 15–19) were examined to achieve the best condition. The $Pd(OAc)_2$:L ratio was also varied (Table 3, entries 19–23) but the initially selected 1:2 yielded maximum product (Table 3, entries 19). A control experiment in the presence of palladium acetate catalyst (1 mol% as compared to halobenzene) in the absence of the ligands indicated that the yield of the coupled product was extremely low (Table 3, entry 21). By using the optimized reaction conditions, NaOAc (1.5 mmol), DMF (2 mL), $Pd(OAc)_2$ loading (0.01 mol), ligand loading (0.02), and DMF reflux temperature (Table 3, entries 19), all the synthesized ligands, L^1–L^5, were compared as shown in Table 4. L^1 was found best among the other ligands as it yielded the maximum coupled product. The reason for this activation is the extensive resonance-based delocalization of electrons resulting in electron-rich amido nitrogen capable of activating palladium acetate more than other ligands towards coupling reactions.

Substrate scope including various olefins and aryl halides containing electron-withdrawing to electron-donating substituents for coupling reactions were also studied with the best ligand (L^1) in the presence of palladium acetate under optimized conditions. Aryl iodides coupled with olefins more efficiently and gave better yields of the desired product than aryl bromides and aryl chlorides (Table 5). Similarly, aryl halides with electron-withdrawing groups such as nitro, aldehyde, and ketone on the aryl ring showed more reactivity

Table 3. Optimizations for the Mizoroki–Heck cross-coupling reaction.[a]



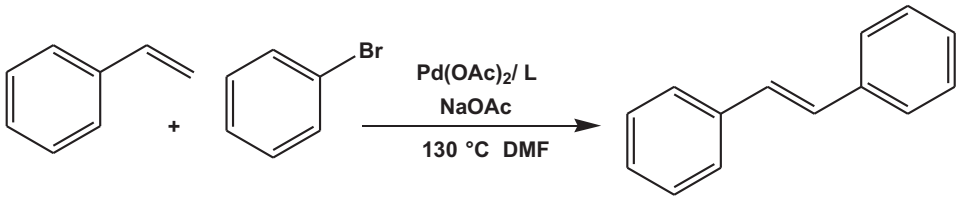
Entry	Base	$Pd(OAc)_2$ (mol)	$Pd(OAc)_2$:L	Solvent	Temperature (°C)	Yield[b]
	K_2CO_3	-	0:2	DMA	100	-
	K_2CO_3	0.1	1:2	DMA	100	81
	K_2CO_3	0.05	1:2	DMA	100	78
	K_2CO_3	0.01	1:2	DMA	100	76
	K_2CO_3	0.001	1:2	DMA	100	48
	K_2CO_3	0.01	1:2	Hexane	80	41
	K_2CO_3	0.01	1:2	Toluene	110	45
	K_2CO_3	0.01	1:2	H_2O	100	54
	K_2CO_3	0.01	1:2	Ethanol	75	66
	K_2CO_3	0.01	1:2	DMF	100	82
	Na_2CO_3	0.01	1:2	DMF	100	78
	Cs_2CO_3	0.01	1:2	DMF	100	76
	NEt_3	0.01	1:2	DMF	100	39
	Pyridine	0.01	1:2	DMF	100	44
	NaOAc	0.01	1:2	DMF	100	84
	NaOAc	0.01	1:2	DMF	25	51
	NaOAc	0.01	1:2	DMF	50	61
	NaOAc	0.01	1:2	DMF	75	70
	NaOAc	0.01	1:2	DMF	130	91
	NaOAc	0.01	1:1	DMF	130	52
	NaOAc	0.01	1:0	DMF	130	Trace
	NaOAc	0.01	1:4	DMF	130	92
	NaOAc	0.01	2:1	DMF	130	54

[a]Conditions: 4 h, styrene (1.4 equiv.) versus halobenzene.

[b]Isolated yield based on aryl halide.

than both electron-neutral group such as –H as well as electron-donating groups such as anisole and toluene as they made the aryl halides relatively inactive.[22] The challenge to activate the C-Cl bond owing to economical factors[23] prompted us to explore aryl chlorides coupling with styrene, but both electron-rich (4-chlorotoluene) and electron-neutral (chlorobenzene) groups showed low reactivity in coupling reactions (Table 5, entries 1 and 2). In spite of the fact that many reported catalysts in the literature were used in high loadings, they still showed little or no activity with aryl chloride substrates.[24] On the other hand, both electron-neutral and electron-rich aryl iodides were converted efficiently to the desired coupled products in excellent yields (Table 5, entries 3 and 4). The high reactivity of aromatic iodides is attributed to their easy oxidative addition to Pd(0) species and small C-I bond dissociation energy.[25]

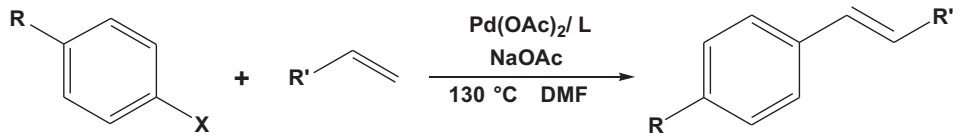
Table 4. Comparison of L^1–L^5 for the Mizoroki-Heck cross-coupling reaction.[a]



Entry	Ligands	Yield[b]
1.	L^1	91
2.	L^2	76
3.	L^3	80
4.	L^4	85
5.	L^5	87

[a] Conditions: 4 h, styrene (1.4 equiv.) versus halobenzene, NaOAc (1.5 mmol), $Pd(OAc)_2$:L ratio = 1:2, DMF (2 mL), $Pd(OAc)_2$ loading (0.01 mol), ligand loading (0.02 mol), and DMF reflux temperature. [b] Isolated yield based on aryl halide.

Table 5. Mizoroki–Heck cross-coupling reaction of aryl halides catalyzed by $Pd(OAc)_2/L^1$.[a]



Entry	Aryl halide	Olefin	Yield (%)[b]	Time (h)
	Chlorobenzene	Styrene	65	6
	4- Chlorotoluene	Styrene	63	7
	Iodobenzene	Styrene	97	4
	4-Iodotoluene	Styrene	93	5
	Bromobenzene	Styrene	91	4
	4- Bromotoluene	Styrene	87	6
	4-Bromoanisole	Styrene	85	6
	4- Bromonitrobenzene	Styrene	94	4.5
	4- Bromobenzaldehyde	Styrene	90	4
	4- Bromoacetophenone	Styrene	92	4
	1- Bromonaphthalene	Styrene	83	16
	Bromobenzene	Ethyl acrylate	94	3.5
	4- Bromotoluene	Ethyl acrylate	92	4
	4-Bromoanisole	Ethyl acrylate	91	4
	4- Bromonitrobenzene	Ethyl acrylate	97	3
	4- Bromobenzaldehyde	Ethyl acrylate	95	2
	4- Bromoacetophenone	Ethyl acrylate	96	2
	1- Bromonaphthalene	Ethyl acrylate	90	12

[a] Conditions: styrene (1.4 equiv.) versus halobenzene, NaOAc (1.5 mmol), $Pd(OAc)_2$:L ratio = 1:2, DMF (2 mL), $Pd(OAc)_2$ (0.01 mol), ligand loading 0.02, and DMF reflux temperature.
[b] Isolated yield based on aryl halide.

Different aryl bromides including electronically neutral bromobenzene; electronically activated 4-bromonitrobenzene, 4-bromobenzaldeyde, and 4-bromoacetophenone; and electronically deactivated 4-bromoanisole and 4-bromotoluene were also explored to couple with styrene and more activated olefin such as ethyl acrylate under optimized reaction conditions (Table 5, entries 5 and 18). As expected, the results obtained in Table 5 show that reaction of activated aryl bromides and activated olefin yielded maximum coupled products (Table 5, entries 15, 16, and 17). Similarly, reaction of deactivated aryl bromides and less activated olefin such as styrene yielded minimum coupled products (Table 5, entries 6, 7, and 11). To extend the scope of our work, we next investigated the coupling reaction of electronically neutral bromobenzene with both styrene and ethyl acrylate (Table 5, entries 5 and 12). Again ethyl acrylate proved to be better coupling olefin than styrene. The activated bromobenzenes gave couple products in the range of 92%–94% yield with styrene (Table 5, entries 8–10). The deactivated bromobenzenes gave coupling products in the range of 90%–92% yield with ethyl acrylate (Table 5, entries 13, 14, and 18).

In order to verify the actual identity of the true catalyst and the existence of interactions between the palladium and basic nitrogen centers of ligands, the classic mercury test was carried out with 150 to 300 equivalents of Hg(0) (relative to palladium acetate) to test reactions. However, no catalyst deactivation effect was observed in any reaction. It is already known that heterogeneous, electron-rich, unprotected zero-valent palladium particles can be poisoned and deactivated upon the addition of an excess of metallic mercury relative to the palladium catalyst and Hg(0) is not expected to have a poisoning effect on homogeneous palladium complexes, and the results of the mentioned test helped us to determine the nature of the active species.[26–28] The results of these experiments confirmed that there is no competing pathway involving the heterogeneous Pd(0) catalyst. The stable homogenous catalysts formed in situ from palladium acetate and various ligands were responsible for speedy coupling reactions.

Attempts were made to synthesize pure palladium complexes of these monodentate PYE ligands but were never fruitful as it resulted in the formation of a mixture of products owing to the strong trans effect of these ligands. Efforts were also made to separate them via various techniques but none were found fruitful. Since all the palladium catalysts were generated in situ during the Heck coupling reaction and were homogeneous in the reaction mixture, they were not recoverable.

The activity of the palladium acetate is significantly enhanced in the presence of various PYE ligands (L^1–L^5). The presented catalytic results for L^1 under optimized conditions are much higher than those reported for heterogeneous palladium acetate catalyst with no added ligands under different experimental conditions.[29] These results are also comparable to those reported with *N*-heterocyclic carbenes[30–32] and phosphines.[33]

In conclusion, each of the five new *N*-(1-methylpyridin-4(1*H*)-ylidene)amine ligands, [L^1]–[L^5], were synthesized in a single pot by a melt reaction between *N*-methylated-4-chloropyridinium triflate and the corresponding amine (1-naphthyl amine, *o*-ansidine, 2-nitroaniline, p-ansidine, or cyclohexyl amine) followed by the addition of sodium hydride and dichloromethane solvent. The synthesized compounds were characterized by FTIR, ^{1}H and ^{13}C NMR, mass spectroscopy, and XRD analysis. A novel approach was used for palladium acetate-catalyzed Heck cross-coupling reactions in the absence of NHC and phosphine ligands. The introduction of electron-donating PYE ligands, particularly L^1 with palladium acetate, was found efficient for coupling of various aryl halides with styrene and ethyl acrylate in good to excellent yields. From these initial results, an inference can be drawn that these PYEs have a strong possibility of becoming a vital class of electron-donating neutral ligands for the development of active catalysts for cross-coupling reactions and in the establishment of various other catalytic systems that require electron donor ligands.

3. Experimental

3.1. Reagents

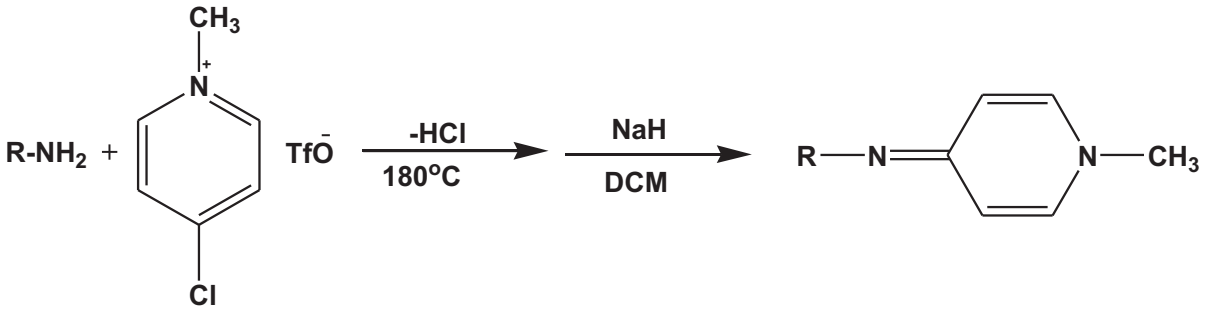
1-Naphthyl amine, 2-ansidine, 2-nitroaniline, p-ansidine, cyclohexyl amine, halobenzenes, styrene, and ethyl acrylate used were purchased from Sigma and BDH. Solvents were dried and distilled before being used. *N*-Methyl-4-chloropyridinium triflate was prepared according to the method of Schneider and Hermann.[34]

3.2. Physical measurements

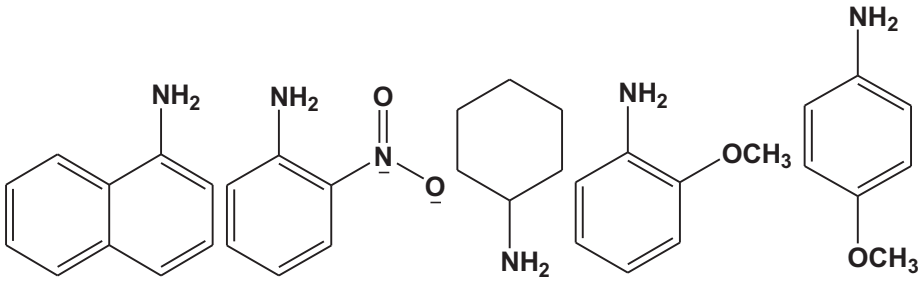
All manipulations were carried out under an oxygen-free argon atmosphere using a standard vacuum line. Melting points of the synthesized compounds were taken in capillary tubes on a Gallenkamp melting point apparatus and are uncorrected. Infrared spectra were recorded over the range 4000–400 cm^{-1} on a PerkinElmer Spectrum 400 FT-IR spectrometer. NMR spectra were obtained using a Bruker Avance spectrometer at 300 MHz (^{1}H) and 75 MHz (^{13}C) at 300 K. ^{1}H spectra were referenced to impurity of DMSO (2.50 ppm). ^{13}C NMR spectra were referenced to DMSO (39.43 ppm).

3.3. Chemistry

N-(1-Methylpyridin-4(1*H*)-ylidene)amine compounds [L^1]–[L^5] were synthesized according to the Scheme. It involved a melt reaction between *N*-methylated-4-chloropyridinium triflate and the corresponding amines (1:1 ratio) in a 25-mL two-necked round-bottomed flask for 15 min at 180 °C. After this time the melt was cooled to ambient temperature. To this flask, dichloromethane (5 mL) was added, followed by the addition of sodium hydride (1:8). The reaction mixture was stirred overnight. After that time, the solid was filtered; the solvent was removed under vacuum from filtrate to get crude products [L^1]–[L^5]. These products were recrystallized from dichloromethane and ether.



Where R-NH_2 are:



Scheme. Synthesis of derivatives of *N*-(1-methylpyridin-4(1*H*)-ylidene)amine.

3.3.1. *N*-(1-Methylpyridin-4(1*H*)-ylidene)naphthalen-1-amine [$\mathbf{L^1}$]

Light brown solid, yield 80%; m.p.: 132 °C. ^{1}H NMR δ (ppm) / DMSO-d_6 / 300 MHz: 7.86 (m, 3H, *Np-H* and *Py-H*), 7.84–7.34 (m, 6H, *Np-H*), 6.89 (d, 2H, J = 9, *Py-H*), 3.50 (s, 3H, *Me*). ^{13}C NMR δ (ppm) / DMSO-d_6 / 75 MHz: 156.1, 134.4, 127.8, 126.5, 125.7, 124.6, 123.6, 121.3, 115.8, 42.1. IR (KBr, cm^{-1}): 2943.5, 2829.7, 1590.0, 1400.0, 1114.9, 1031.6. (m/z): calcd. for $[C_{16}H_{14}N_2]^+$ $[M+H]^+$ 235.12297, found 235.12283.

3.3.2. *N*-(1-Methylpyridin-4(1*H*)-ylidene)-2-nitrobenzenamine [$\mathbf{L^2}$]

Light brown solid, yield 72%; m.p.: 147 °C. ^{1}H NMR δ (ppm) / DMSO-d_6 / 300 MHz: 7.80 (d, 1H, J = 6, *Ar-H*), 7.77 (m, 1H, *Ar-H*), 7.36 (d, 2H, J = 6, *Py-H*), 7.04–6.94 (m, 2H, *Ar-H*), 6.06 (d, 2H, J = 9, *Py-H*), 3.52 (s, 3H, *Me*). ^{13}C NMR δ (ppm) / DMSO-d_6 / 75 MHz: 156.4, 142.9, 141.6, 139.8, 133.4, 124.2, 120.7, 117.2, 110.4, 42.1. IR (KBr, cm^{-1}): 2924.2, 1647.3, 1550.0, 1400.4, 1031.9, 796.6. (m/z): calcd. for $[C_{12}H_{11}N_3O_2]^+$ $[M+H]^+$ 229.08461, found 229.08458.

3.3.3. N-Cyclohexylidene-1-methyl-1,4-dihydropyridin-4-amine [$\mathbf{L^3}$]

White solid, yield 80%; m.p.: 120 °C. ^{1}H NMR δ (ppm) / DMSO-d_6 / 300 MHz: 7.72 (apparent d, 1H, J = 7.5, *H* ***9***), 7.58 (apparent d, 1H, J = 7.2, *Ar-H*), 6.56–6.52 (m, 1H, *Ar-H*), 6.43–6.40 (m, 1H, *Ar-H*), 3.64 (s, 3H, *Me*), 3.34–3.26 (m, 1H, *Cy-H*), 1.77–1.00 (s, 10H, *Cy-H*). ^{13}C NMR δ (ppm) / DMSO-d_6 / 75 MHz: 154.8, 142.1, 139.9, 111.9, 104.7, 52.7, 42.9, 32.2, 25.2, 24.3. IR (KBr, cm^{-1}): 2929, 2861, 1649, 1581, 1549, 1452, 1372, 1255, 1146, 1028, 834, 756, 633, 571, 507. MS (m/z, ESI): calcd. for $[C_{12}H_{19}N_2]^+$ $[M+$ H$]^+$191.1546, found 191.1543.

3.3.4. 2-Methoxy-N-(1-methylpyridin-4(1H)-ylidene)benzenamine [$\mathbf{L^4}$]

Light yellow solid, yield 92%; m.p.: 129–131 °C. ^{1}H NMR δ (ppm) / DMSO-d_6 / 300 MHz: 8.30 (m, 1H, *Ar-H*), 7.57 (d, 2H, J = 6, *Py-H*), 7.25 (m, 1H, *Ar-H*), 7.08–7.01 (m, 2H, *Ar-H*), 6.91 (d, 2H, J = 6, *Py-H*), 3.74 (s, 3H, *OMe*), 3.51 (s, 3H, *Me*).^{13}C NMR δ (ppm) / DMSO-d_6 / 75 MHz: 164.6, 152.6, 143.9, 135.4, 128.3, 123.3, 122.4, 115.6, 113.7, 56.1, 39.6. IR (KBr, cm^{-1}): 2952.8, 2343.6, 1651.1, 1582.5, 1508.4, 1379.2, 1251.8, 1018.5. MS (m/z): calcd. for $[C_{13}H_{15}N_2O]^+$ $[M+$ H$]^+$ 215.11789, found 215.11783.

3.3.5. 4-Methoxy-N-(1-methylpyridin-4(1H)-ylidene)benzenamine [$\mathbf{L^5}$]

Light brown solid, yield 89%; m.p.: 120–122 °C. ^{1}H NMR δ (ppm) / DMSO-d_6 / 300 MHz: 7.33 (d, 2H, J = 6.3, *Ar-H*), 6.87 (d, 2H, J = 9, *Py-H*), 6.77 (d, 2H, J = 9, *Py-H*), 6.16 (m, 2H, *Ar-H*), 3.71 (s, 3H, *OMe*), 3.50 (s, 3H, *Me*).^{13}C NMR δ (ppm) / DMSO-d_6 / 75 MHz: 162.0, 159.2, 143.6, 141.3, 123.1, 115.2, 113.6, 55.9, 39.5. IR (KBr, cm^{-1}): 2941.5, 2829.6, 1661.1, 1558.5, 1114.3, 1031.9, 1018.1. MS (m/z): calcd. for $[C_{13}H_{15}N_2O]^+$ $[M+$ H$]^+$215.11789, found 215.11783.

3.4. Typical procedure for the Mizoroki-Heck Reactions

To a dry Schlenk tube (10 mL) equipped with a Teflon screw tap and magnetic stirrer bar, the catalyst (4 μmol, 0.01 equivalents of palladium acetate and 8 μmol, 0.02 equivalents of ligand vs. halobenzene), sodium acetate (36 mg, 440 μmol, 1.5 equivalents), halobenzene (400 μmol, 1.0 equivalent), styrene (64 μL, 560 μmol,

1.4 equivalents), and DMF (2 mL) were added under air. The was vessel immersed in an oil bath, which was maintained at 130 °C for 4 h (**caution:** a blast shield was placed in front of the reaction vessel as a precaution in the event that the increase in internal pressure on heating caused the Schlenk tube to rupture). Thin-layer chromatography was used to monitor the reactions. Upon completion of the reaction, the reaction vessel was removed from the oil bath and cooled to room temperature. At the conclusion of the reaction, the mixture was cooled, extracted with ethyl acetate/hexane (1:5), filtered through a pad of silica gel with copious washing, concentrated, and purified by recrystallization from ethanol and water or purified by silica gel column chromatography (n-hexane: EtOAc, 80:20). The purity of the compounds was checked by NMR and yields are based on halobenzene.

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