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Extending the Range of Neutral N-Donor Ligands Available for Metal Catalysts: *N*-[1-Alkylpyridin-4(1*H*)-ylidene]amides in Palladium-Catalyzed Cross-Coupling Reactions

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Supporting Information

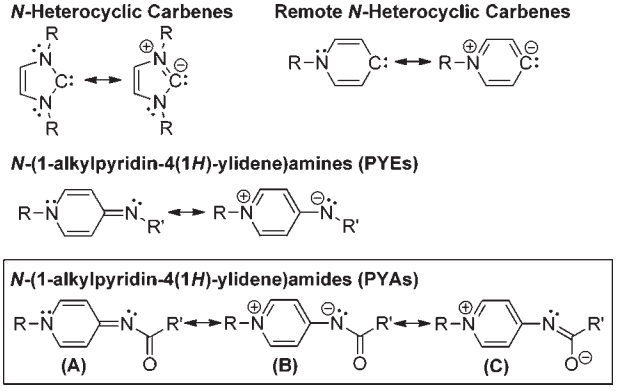
ABSTRACT: *N*-[1-Alkylpyridin-4(1*H*)-ylidene]amides (PYAs) are a new class of easily prepared, neutral N-donor ligands that share some features in common with N-heterocyclic carbenes. They are strongly electron-donating toward metal centers, and a palladium(II) complex of one of these ligands has been shown to successfully catalyze both the Heck–Mizoroki and Suzuki–Miyaura cross-coupling reactions.

The development of effective homogeneous metal catalysts has long been recognized as an important scientific endeavor.[1] A growing appreciation for the urgent need to develop sustainable chemical practices is currently providing significant impetus to studies in this area.[2,3] While the ligand compliment is a fundamental part of any homogeneous metal catalyst, it is noteworthy that relatively few classes of neutral donor ligands have been commonly utilized in successful homogeneous catalysts.[4] Among these are the phosphanes,[5] amines,[6] nitrogen-containing heterocycles such as pyridines and oxazolines,[7,8] imines,[9−11] and, more recently, N-heterocyclic carbenes (NHCs).[12−14] The discovery of new ligand classes that can be widely utilized in catalyst development is therefore an important goal.

It has recently emerged that there is a set of ligands that share the common features of neutral overall charge and one valence-bond representation in which the donor atom is negatively charged but is in π conjugation with a positively charged "iminium-like" group. Examples of classes of ligands with these features are NHCs,[12] "remote" NHCs,[14,15] and the recently reported *N*-[1-alkylpyridin-4(1*H*)-ylidene]amines (PYEs).[16−19] Valence-bond representations of each of these classes of ligands that emphasize the relationships between them are illustrated in Scheme 1. In this Communication, we now extend this set of ligands by reporting the *N*-[1-alkylpyridin-4(1*H*)-ylidene]-amides (PYAs; see Scheme 1) as a new class of neutral N-donor ligands. The valence structures **A** and **B** illustrate the relationship between PYAs and the other classes of ligands depicted in Scheme 1. The use of palladium PYA complexes to successfully catalyze cross-coupling reactions is also reported.

Amidates, which are obtained via deprotonation of the nitrogen atom of carboxamides, are well-known anionic ligands.[20] Coordination usually occurs through the nitrogen atom, and in this form, they are characteristically strong σ donors.[21,22] Deprotonation of the corresponding *N*-pyridinium-substituted carboxamides gives neutral PYAs directly. Although some compounds of this type have been reported previously,[23] to our knowledge, these have not been used directly as ligands to form coordination compounds. A small number of complexes that have PYA-like ligands and were prepared in alternative ways have been described in the literature.[24]

Scheme 1. Similarities between Valence-Bond Representations of NHCs, Remote NHCs, PYEs, and PYAs



The PYA ligands reported in this study are simple to prepare, as indicated in Scheme 2. Details of the syntheses and characterization data for all new compounds are available in the Supporting Information. The precursor pyridinium carboxamides, $[HL^{1-3}]X$, are easily deprotonated through treatment with bases such as sodium carbonate (aqueous) or sodium hydride to give L^{1-3} in excellent yield. In the IR spectrum, the bands in the amide I region of $[HL^{1-3}]X$ all decrease by ca. 40−60 cm^{-1} upon deprotonation.

Single-crystal X-ray structure determinations of $[HL^2]Cl$ and L^2 have been obtained (see the Supporting Information). The atom numbering schemes used for these compounds are identical with that used for the L^2 ligand in the structure of $[PdCl_2(L^2)]$ (**2**), depicted in Figure 2. Upon deprotonation of the pyridinium carboxamide $[HL^2]^+$ to form L^2, significant decreases are observed in the distances C6−N2 [1.382(2)−1.3562(14) Å] and N2−C7 [1.380(2)−1.3414(14) Å], while accompanying increases occur in the distances C7−C8 [1.405(2)−1.4280(15) Å] and C6−O1 [1.216(2)−1.2357(13) Å]. These data suggest that both valence-bond structures **A** and **C** in Scheme 1 should be considered in addition to **B** in a simple description of the delocalized bonding for L^2.

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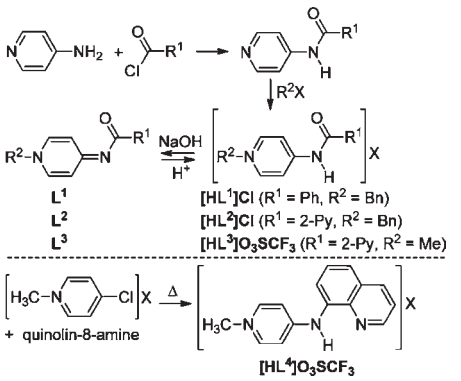
Scheme 2. Syntheses of Alkylpyridinium Carboxamides $[HL^{1-3}]X$, PYA Ligands L^{1-3}, and Methylpyridinium Amine $[HL^4]X$



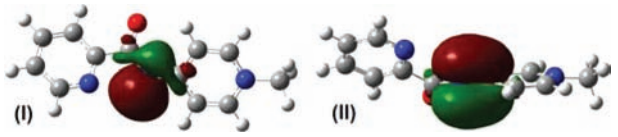


Figure 1. Frontier NBO orbitals: (I) lone pair on N2 and (II) the π bond between N2 and C7 in L^3.

Density functional theory calculations (B3LYP/def2-TZVP) carried out on L^3 and $[HL^3]^+$ support the valence-bond representation **A** in Scheme 1 as the predominant Lewis structure for L^3. A natural bond orbital (NBO) analysis of L^3 indicates the σ and π character of the double bonds represented in **A** (see the Supporting Information). The lone pair on N2 and the π bond between N2 and C7 obtained by this analysis are illustrated in Figure 1.

The ligands L^{1-3} (Scheme 2) are all air-stable crystalline solids. They remain essentially unchanged upon heating under reflux in methanol for 30 min or standing at 20 °C for 48 h in dimethyl sulfoxide containing 10% water.

Estimates of the comparative donor properties of a range of neutral ligands L (including NHCs) have been obtained previously by measuring ν_{av}(CO) for the complexes [*cis*-RhCl(CO)$_2$L].[25] The treatment of $[\{Rh(\mu\text{-Cl})(COD)\}_2]$ with L^1 gives $[Rh(Cl)(COD)L^1]$, and subsequent carbonylation produces [*cis*-RhCl(CO)$_2$L^1] (**1**). A preliminary crystal structure determination of $[Rh(Cl)(COD)L^1]$ confirms that L^1 bonds as a monodentate ligand through nitrogen in this complex, and it is reasonable to assume this is also the case in **1**. In an alternative synthesis, **1** can be obtained directly by the treatment of $[\{Rh(\mu\text{-Cl})(CO)_2\}_2]$ with L^1 (Scheme 3). The two ν(CO) bands for the *cis*-carbonyl ligands in **1** are observed in the IR spectrum at 2069 and 1987 cm^{-1} (av 2028 cm^{-1}). These values are slightly lower than those reported for [*cis*-RhCl(CO)$_2$L], where L is either a saturated NHC (2081, 1996; av 2038 cm^{-1}),[25] or a PYE ligand (2077, 1998; av 2038 cm^{-1}).[17] On the basis of these data, the donor strength of the PYA ligand L^1 in **1** is at least as great as that of typical NHC or PYE ligands, even though there are differences in the electronic structures of these three ligand classes.

The palladium complex **2** is formed in ca. 70% isolated yield through the treatment of $[PdCl_2(COD)]$ with either L^2 or, more conveniently, a mixture of $H[L^2]Cl$ and 1,8-diazabicyclo[5.4.0]-undec-7-ene (DBU; Scheme 3). The closely related complex $[PdCl_2(L^3)]$ (**3**) can be obtained through parallel reactions with L^3 or $H[L^3][O_3SCF_3]$. In both **2** and **3**, the ring protons of the alkylpyridinium groups are observed in the ^{1}H NMR spectra at positions intermediate between those found for the corresponding protonated ($H[L^{2,3}]X$) and free ligands ($[L^{2,3}]$).

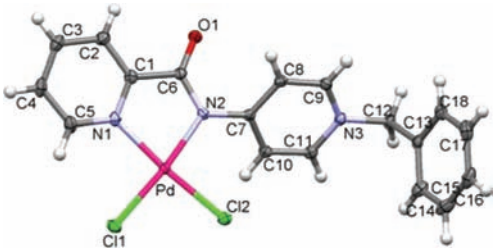
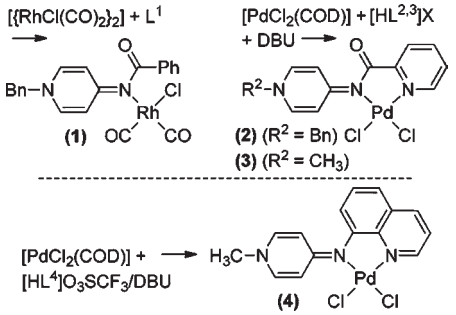


Figure 2. X-ray structure of **2**.

Scheme 3. Syntheses of Complexes 1−4



A single-crystal X-ray structure determination of **2** has been obtained (see the Supporting Information), and the molecular structure is shown in Figure 2. This confirms that coordination to palladium occurs through the two nitrogen donors of L^2. The distances C6−N2 [1.363(2) Å], N2−C7 [1.397(2) Å], C7−C8 [1.404(2) Å], and C6−O1 [1.230(2) Å] in **2** are either between the corresponding distances observed in $[HL^2]Cl$ and L^2 or close to those recorded for $[HL^2]Cl$. The Pd−Cl2 distance [2.2917(4) Å] is normal for chlorine trans to pyridine. In contrast, the Pd−Cl1 [2.3115(4) Å] distance is longer, indicating that the PYA ligand has a stronger trans influence than pyridine. The Pd−N2 distance of 2.0392(14) Å is similar to that reported for a corresponding Pd−N distance in a related PYE-containing complex.[18]

To gauge the potential utility of the PYA ligands L^2 and L^3 as supporting ligands for the important palladium-catalyzed Heck−Mizoroki and Suzuki−Miyaura cross-coupling reactions (NHCs have been extensively studied as supporting ligands for these reactions[26,27]), preliminary experiments with **2** and **3** were carried out. For comparative purposes, the PYE-containing palladium complex $[PdCl_2(L^4)]$ (**4**; see Scheme 3) was prepared from $[HL^4]O_3SCF_3$ (Scheme 2) and also studied in these reactions. The PYE ligand L^4 was designed so that it incorporates a chelating arm that is similar to the chelating pyridyl groups of $L^{2,3}$.

The results obtained for the Heck−Mizoroki reactions (not optimized) between phenyl bromide and styrene with **2**, **3**, or **4** added as precatalysts (1 mol %) are summarized in Table 1. Nearly complete conversion to stilbenes (>93% *trans*-stilbene)

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Table 1. Results for the Catalytic Experiments

Heck−Mizoroki reactions[a]			Suzuki−Miyaura reactions[c]		
catalyst no.	time (h)	product (%)[b]	catalyst no.	time (h)	product (%)[d]
4	6	49	4	4	38
2	6	61	2	4	49
2	12	75	4	6	56
2	24	93	2	6	76
3	24	93	3	6	76

[a] Conditions: DMA solvent, 140 °C, catalyst (1 mol %), sodium acetate (1.1 equiv), styrene (1.4 equiv) vs bromobenzene ($Pd(OAc)_2$ blank, 6 h, 9% conversion). [b] *trans*-1,2-Stilbene, *cis*-1,2-stilbene, and α-1,1′-stilbene. [c] Conditions: DMF solvent, 100 °C, catalyst (1 mol %), Cs_2CO_3 (2 equiv), *p*-tolylboronic acid (1.5 equiv) vs bromobenzene ($Pd(OAc)_2$ blank, 6 h, 38% conversion). [d] 4-Methylbiphenyl.

occurred after 24 h with **2** or **3**. The activities of these PYA-containing complexes are reasonable but somewhat lower than those reported for $Pd(NHC)_2$ "pincer" complexes under similar conditions.[26] The reactions to which the PYE-containing complex **4** was added formed visible amounts of palladium black after 6 h, and the unsuitability of the PYE ligands in palladium-catalyzed cross-coupling reactions has been noted previously.[19] In contrast, the reactions involving the PYA-containing **2** or **3** showed no visible signs of darkening or metal formation, even after 24 h, although this observation does not rule out the possibility that palladium nanoparticles are formed under these conditions.

Preliminary investigations into the ability of **2**−**4** to act as precatalysts for Suzuki−Miyaura cross-coupling reactions between bromobenzene and *p*-tolylboronic acid were also carried out, and the results are recorded in Table 1. No darkening or visible formation of palladium black occurred in any of the reactions, even with **4**. In all cases, catalysis was observed, but the complexes **2** and **3** (which contained the PYA ligands L^2 or L^3, respectively) again showed superior activity to that of **4** (which contained the PYE ligand L^4). Furthermore, the activities of **2** and **3** are similar to those reported for some bis(NHC) "pincer" complexes under similar conditions.[27]

The inference that can be drawn from these preliminary results is that PYAs have the potential to become an important class of neutral ligands that can be used in the development of effective, alternative catalysts for the Heck−Mizoroki and Suzuki−Miyaura cross-coupling reactions. In view of the strong σ-donor characteristics, ease of synthesis, and relative stability of these ligands, it can be anticipated that future applications might be found in numerous other catalytic systems. An additional feature of the PYA ligands that is not present in the other related ligands depicted in Scheme 1 is the possibility that the oxygen atom could serve as an alternative donor atom. This added dimension should provide PYA ligands with the flexibility to form strong interactions with a wide range of metals that include diverse oxidation states and steric demands.

■ ASSOCIATED CONTENT

Supporting Information. Experimental procedures and characterizing data, crystallographic data and material in CIF format (CCDC 825923−825925), optimized geometries, and NBO analysis. This material is available free of charge via the Internet at http://pubs.acs.org.

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