

# Synthesis and Properties of Palladium–Triazolopyridinylidene: Catalyst for Cross-Coupling Using Chloroarenes and Nitroarenes

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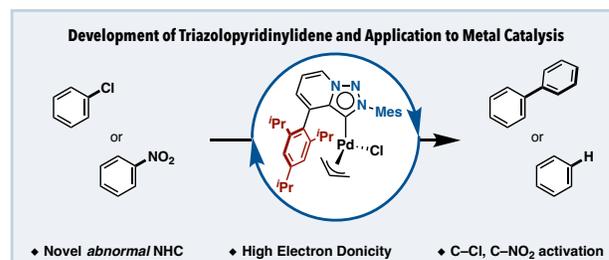
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Supporting Information Placeholder

**ABSTRACT:** The synthesis and catalytic activity of triazolopyridinylidene as a novel abnormal *N*-heterocyclic carbene (aNHC) ligand was described. The evaluation of physical properties using X-ray crystallographic analysis and infrared spectroscopy revealed that these triazolopyridinylidenes have a high electron-donating ability to the metal center. Application of triazolopyridinylidenes to palladium-catalyzed cross-coupling of chloroarenes and nitroarenes showcased its ability to activate C–Cl and C–NO<sub>2</sub> bonds.

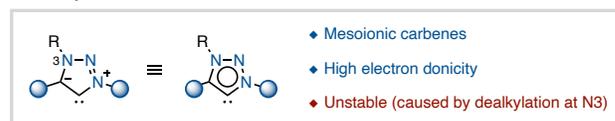
*N*-Heterocyclic carbenes (NHCs) have found wide use in organic synthesis as ligands on metal catalysts and organocatalysts.<sup>1</sup> As ligands, 1,3-imidazole- or imidazoline-based carbenes have played a pivotal role such as in Grubbs-2<sup>nd</sup> generation catalyst<sup>2</sup> and Pd-PEPPSI catalyst.<sup>3</sup> The high  $\sigma$ -donating ability as well as a robustness of these NHC ligands are the characteristic feature, often enabling bond activation that is otherwise difficult.<sup>4</sup>

Meanwhile, abnormal NHCs (aNHCs), also characterized as mesoionic carbenes, have gradually attracted attention in metal-catalyzed organic synthesis.<sup>5</sup> This class of *N*-heterocyclic carbenes lacks one nitrogen atom adjacent to the carbene, which leads to a higher electron-donating ability compared to normal NHCs. Thus, aNHCs have been expected to work as a useful ligand to achieve the oxidative addition of inert chemical bonds. Among aNHCs, 1,2,3-triazole-based carbenes, triazolylidenes, have been synthesized and evaluated for their catalytic performance (Figure 1A).<sup>6</sup> For example, it was revealed that a Pd-triazolylidene complex can efficiently activate aryl–Cl bonds in Suzuki–Miyaura coupling.<sup>7</sup> Although triazolylidene ligands were expected to be potentially useful in organic reactions involving inert bond cleavages, some drawbacks hampered further developments. Probably due to the mesoionic nature of the triazolylidenes, these ligands are known to decompose during the catalytic reaction and even during the preparation of metal carbene complexes through a dealkylation at the N3 position.<sup>6,7</sup> To circumvent this, attachment of a secondary coordinating group<sup>8</sup> and/or introduction of an aryl group on the N3 position have been evaluated (Figure 1B).<sup>9</sup> However, even when using these advanced triazolylidenes, the activation of bonds more inert than aryl–Cl bonds has remained challenging. To this end, we designed a pyridine-fused triazole core, [1,2,3]triazolo[1,5-*a*]pyridinylidenes, TriPy (Figure 1C).<sup>10</sup> On this novel core, the N8 atom, which is the same position

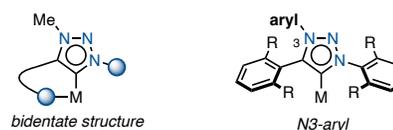


as the N3 on triazolylidenes, was “protected” by a fused pyridine ring. Therefore, TriPy is anticipated to prevent the decomposition process. Moreover, introducing an aromatic ring at the C4 position might serve as a secondary coordinating sphere to stabilize the corresponding metal–carbene complex.

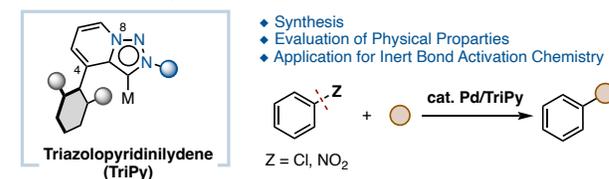
## A. Triazolylidenes



## B. Robust triazolylidene–metal complexes



## C. This Work: Triazolopyridinylidene-enabled inert bond activation



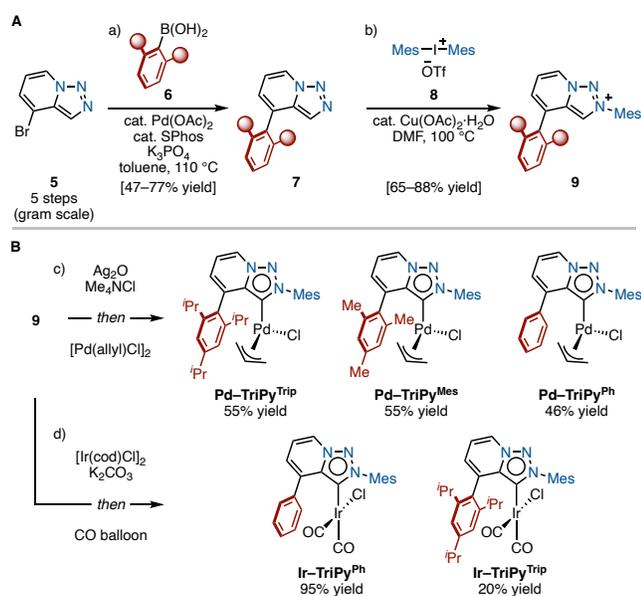
**Figure 1.** (A) General feature of triazolylidenes. (B) Attempts to increase the stability of triazolylidenes. (C) This work: triazolopyridinylidenes

A similar framework was invoked by the Nakao's group who developed imidazopyridinylidene ligands and applied them to Pd-catalyzed denitrative couplings of nitroarenes.<sup>11</sup> If such an effect could be transferred to the triazolylidene structures, this field could reach

beyond precedented bond activations. Herein, we report the synthesis of triazolopyridinylidene–metal complexes and evaluation of catalytic activity for cross-couplings involving inert bond activations.

We first embarked on the synthesis of TriPy ligand (Scheme 1). Starting from commercially available 3-bromopyridine, 4-bromo-[1,2,3]triazolo[1,5-*a*]pyridine (**5**) was synthesized in 5 steps.<sup>12</sup> The obtained **5** was coupled with various arylboronic acids **6** by Suzuki–Miyaura coupling using Pd(OAc)<sub>2</sub>/SPhos catalyst and K<sub>3</sub>PO<sub>4</sub>, furnishing aryltriazolopyridines **7** in generally good yields. This Suzuki–Miyaura coupling was able to introduce sterically congested aryl groups such as 2,4,6-trisopropylphenyl (Tri*p*) and mesityl (Mes) in moderate to good yields (47–77% yield). Next, triazolium salt formation was achieved by copper-catalyzed *N*-arylation of **7** with dimesityliodonium triflate (**8**). By using this highly convergent synthetic procedure, we rapidly constructed various carbene precursors **9** (see the Supporting Information for details). With desired triazolopyridiniums **9** in hand, we attempted the complexation of **9** with transition metal salts (Scheme 1B). A typical carbene-transfer procedure using Ag<sub>2</sub>O in the presence of Me<sub>4</sub>NCl, followed by transmetalation with [Pd(allyl)Cl]<sub>2</sub> provided a series of Pd–TriPy complexes. Moreover, we synthesized Ir(carbene)Cl(CO)<sub>2</sub> complexes through direct irradiation of **9**, followed by CO gas capturing.

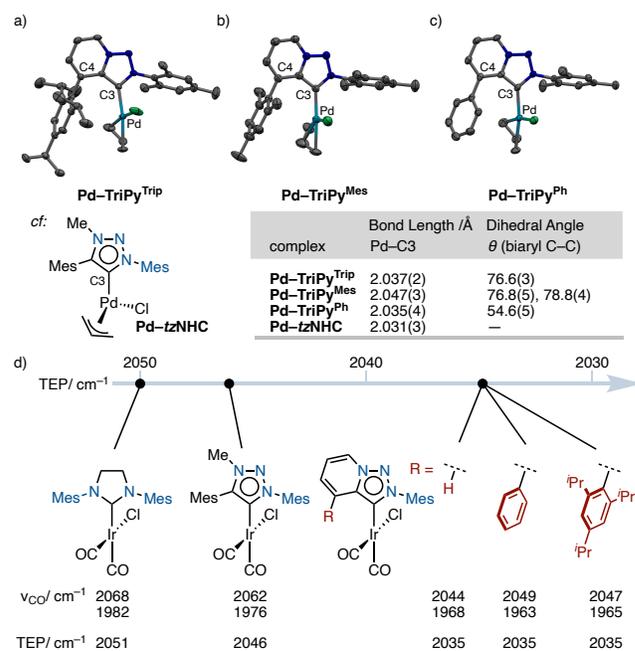
**Scheme 1.** (A) Synthesis of triazolopyridinium salts **9**. (B) Metal complexation of **9**.



Conditions: (a) **5** (1.0 equiv), **6** (1.5 equiv), Pd(OAc)<sub>2</sub> (5.0 mol %), SPhos (10 mol %), K<sub>3</sub>PO<sub>4</sub> (3.0 equiv), toluene, 110 °C, 24 h. (b) **7** (1.0 equiv), **8** (1.0 equiv), Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (5.0 mol %), DMF, 100 °C. (c) **9** (1.0 equiv), Ag<sub>2</sub>O (0.50 equiv), Me<sub>4</sub>NCl (1.0 equiv), then [Pd(allyl)Cl]<sub>2</sub> (0.50 equiv). (d) [Ir(cod)Cl]<sub>2</sub> (0.50 equiv), K<sub>2</sub>CO<sub>3</sub> (3.0 equiv), then CO balloon.

The obtained complexes were successfully analyzed by X-ray crystallographic analysis (Figure 2). Regarding the palladium complexes, the bond length of the palladium–carbene (Pd–C3) was in the range of 2.036–2.047 Å, which is almost the same value as Fukuzawa’s Pd–*tz*NHC complex.<sup>7c</sup> This bond length was not affected by an aryl group at the C4 of the pyridine core. Regarding the dihedral angle ( $\theta$ ) between the pyridine core and the pendant benzene, Pd–

TriPy<sup>Tri*p*</sup> and Pd–TriPy<sup>Mes</sup> showed a larger value than Pd–TriPy<sup>Ph</sup>. Therefore, the benzene portion of Pd–TriPy<sup>Tri*p*</sup> and Pd–TriPy<sup>Mes</sup> could be expected to function as a secondary coordinating ligand to support the corresponding Pd(0) complexes. Infrared spectroscopy was also measured to assess the CO stretching of the iridium complexes, and the TEP values of these complexes were calculated (Figure 2, bottom).<sup>13</sup> Our TriPy ligands showed a higher electron donating ability than that of Ir–SImes and triazolylidene. The benzene ring at the C4 position does not influence the electron donating ability, since almost the same TEP values were obtained.

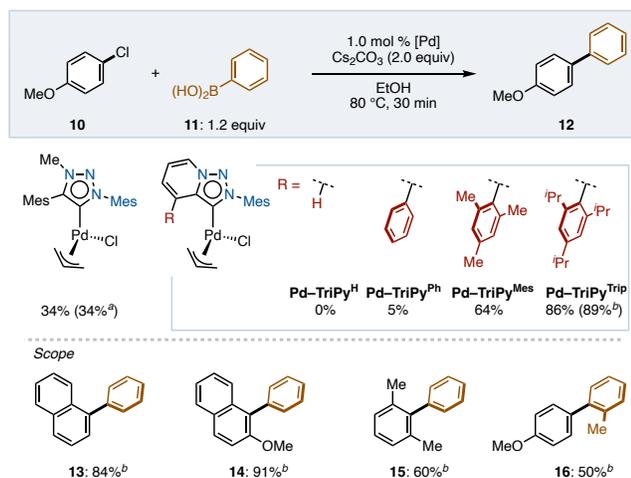


**Figure 2.** Structures of the complexes (a) Pd–TriPy<sup>Tri*p*</sup>, (b) Pd–TriPy<sup>Mes</sup>, (c) Pd–TriPy<sup>Ph</sup> as ORTEP plots with 50% thermal ellipsoid. black = C, blue = N, green = Cl, and dark cyan = Pd. Hydrogens and disordered carbon atoms were omitted for clarity. (d) TEP values of iridium–carbonyl complexes.

To prove the capability of metal–TriPy complexes as a catalyst, we applied these palladium complexes to cross-couplings (Scheme 2). As a model reaction, we selected the Suzuki–Miyaura coupling of *para*-anisyl chloride (**10**) with phenylboronic acid (**11**). As a control experiment, we used a precedented palladium–triazolylidene complex as a catalyst, resulting in the production of desired biaryl **12** in 34% yield after 30 min. Increasing the reaction time to 3 hours did not improve the yield of **12**, which suggested catalyst deactivation. Among the Pd–TriPy complexes, the ligand bearing Tri*p* at the C4 position (Pd–TriPy<sup>Tri*p*</sup>) showed the highest catalytic activity, delivering **12** in 86% yield after 30 min. Increasing the steric bulk of the pendant phenyl group led to an improvement in the yield of **12**. This result could suggest that this pendant phenyl group interacts with the palladium center (C<sub>ipso</sub>–Pd interaction), increasing the electron-donating ability of the Pd(0) active species toward the oxidative addition of the C–Cl bond. With this success, we further evaluated the complexes’ catalytic activity using Suzuki–Miyaura coupling of more challenging substrates. The coupling reaction using sterically congested aryl chlorides such as 1-chloronaphthalene and 2-methoxy-1-chloronaphthalene with **11** furnished the corresponding biaryls in high yields (**13** and **14**). 2,6-Dimethylchlorobenzene also coupled with **11** to produce **15** in 61% yield. When *ortho*-

methylphenylboronic acid was used with chloroanisole **10**, **16** was obtained in 50% yield. However, the use of even more sterically demanding arylboronic acids furnished biaryl products in low yields (see the Supporting Information for details).

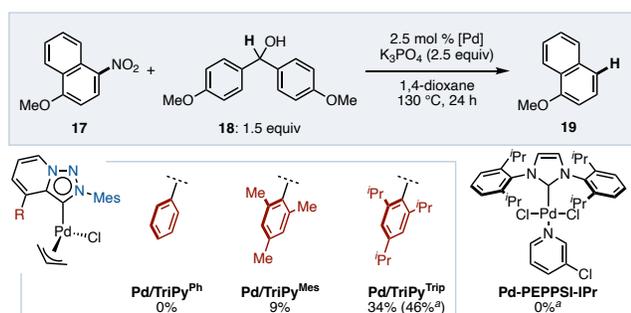
### Scheme 2. Suzuki–Miyaura Coupling



Conditions. Chloroarenes (0.20 mmol), arylboronic acids (1.2 equiv), Pd complex (1.0 mol %), Cs<sub>2</sub>CO<sub>3</sub> (2.0 equiv), EtOH (0.50 mL), 80 °C, 30 min. <sup>a</sup> 3 h. <sup>b</sup> 4 h.

Previously, Nakao reported that their Pd–imidazopyridinylidene catalyst can reduce nitroarenes through C–NO<sub>2</sub> oxidative addition.<sup>11a,14</sup> Inspired by this report, we also confirmed the catalytic performance of Pd–TriPy complexes on a denitrative hydrogenation of nitronaphthalene **17** with a secondary alcohol.<sup>15</sup> Pd–TriPy<sup>Ph</sup> was proved to be the best catalyst, as 34% yield of **19** was obtained. The yield of **19** was further improved to 46% by changing the hydride source from benzhydrol **18** to isopropyl alcohol. It is noteworthy that our ligand and Nakao's imidazopyridinylidene were the only the NHC ligands capable of achieving the denitrative reaction, as other NHCs such as IPr did not work in this reaction system.

### Scheme 3. Denitrative Hydrogenation



Conditions. Nitronaphthalene **17** (0.10 mmol), benzhydrol **18** (1.5 equiv), Pd complex (2.5 mol %), K<sub>3</sub>PO<sub>4</sub> (2.5 equiv), 1,4-dioxane (1.0 mL), 130 °C, 24 h. <sup>a</sup> Isopropyl alcohol was used instead of **18**.

In conclusion, we have synthesized triazolopyridinylidenes and evaluated their properties, revealing that triazolopyridinylidenes have higher electron-donating ability than typical triazolylidenes. When applying them to as ligands for metal-catalyzed cross-coupling, Pd/TriPy catalysts were found to be capable of activating C–Cl and C–NO<sub>2</sub> bonds. Further studies to develop alternative abnormal

NHCs and applications to bond-activation chemistry are ongoing in our laboratory.

## ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge.

Experimental procedures and spectroscopic data for compounds including <sup>1</sup>H-, <sup>13</sup>C-, and <sup>19</sup>F-NMR spectra and crystallographic data (PDF).

### Accession Codes

CCDC 2167559 (Pd–TriPy<sup>TriP</sup>), 2167560 (Pd–TriPy<sup>Mes</sup>), and 2167561 (Pd–TriPy<sup>Ph</sup>) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via [www.ccdc.cam.ac.uk/data\\_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif), or by emailing [data\\_request@ccdc.cam.ac.uk](mailto:data_request@ccdc.cam.ac.uk), or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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### Notes

The authors declare no competing financial interest.

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