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Monosubstituted, Anionic Imidazolyl Ligands from N–H NHC Precursors and Their Activity in Pd-Catalyzed Cross-Coupling Reactions

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Abstract. We report that treatment of several 2-diphenylphosphinoimidazoles with Pd(II) salts generates monosubstituted N–H NHC-Pd complexes via insertion into the C–P bond. Removal of the N–H proton in situ leads to anionic (X-type) or imidazolyl-Pd complexes that are highly stable and catalytically active, achieving up to 340,000 turnovers at 1 ppm catalyst loading in Suzuki-Miyaura reactions. DFT-calculated Tolman electronic parameters for the sterically small ligands suggest that these ligands are significantly more donating than traditional NHCs, which provides a rationale for rapid cross-coupling catalysis. Excellent reactivity is also demonstrated in Sonogashira reactions.

Keywords: carbenes; catalysis; cross-coupling; palladium; Suzuki-Miyaura.

N-Heterocyclic carbene (NHC) ligands are among the most important classes of ligands for transition metals because their strong σ-donating ability leads to highly robust and catalytically active metal complexes.[1] For imidazole-based NHC ligands, substitution at both nitrogens on the rings also enables selective tuning of the steric environment around the metal center. Monosubstituted or N–H NHCs are a unique and potentially powerful class of NHCs because of their ability to benefit from H-bonding with substrates (Figure 1a).[2] In addition, protic NHCs can be deprotonated to generate anionic (X-type) 2-imidazolyl ligands, where the Lewis basic nitrogen can then participate in substrate binding or transmetallation.[3] Recent results from the Lindsay laboratory suggest that the basic nitrogen on a benzimidazolyl ligand can coordinate a boronic ester substrate to facilitate faster transmetallation in Suzuki-Miyaura cross-coupling reactions (Figure 1a).[4] Despite these potential advantages, reports on the development and use of imidazolyl ligands in transition metal catalysis are sparse.[3]

Traditional methods for the preparation of metal-NHC complexes involve the deprotonation of the acidic imidazolium hydrogen to form the free carbene species, followed by addition of the metal salt.[1] This preparation method limits the types of carbene complexes that can be formed due to rapid dimerization of unhindered carbene intermediates. As such, methods to prepare monosubstituted imidazole-based NHC metal complexes are limited and typically require multistep synthesis,[5] proceed by oxidative addition into a halide-substituted imidazole,[6] or rely on the inherent ability of the metal to insert into the C–H bond at the 2-position of an imidazole precursor (Figure 1b).[2a,7] In addition, the majority of known monosubstituted NHC metal complexes are either multidentate (pincer type) or contain multiple NHC ligands, which is a consequence of their ease of preparation.[2a]

In this work, we demonstrate that treatment of 2-diphenylphosphinoimidazoles with Pd(II) salts leads to rapid formation of monosubstituted *N*-heterocyclic carbene palladium complexes via non-oxidative

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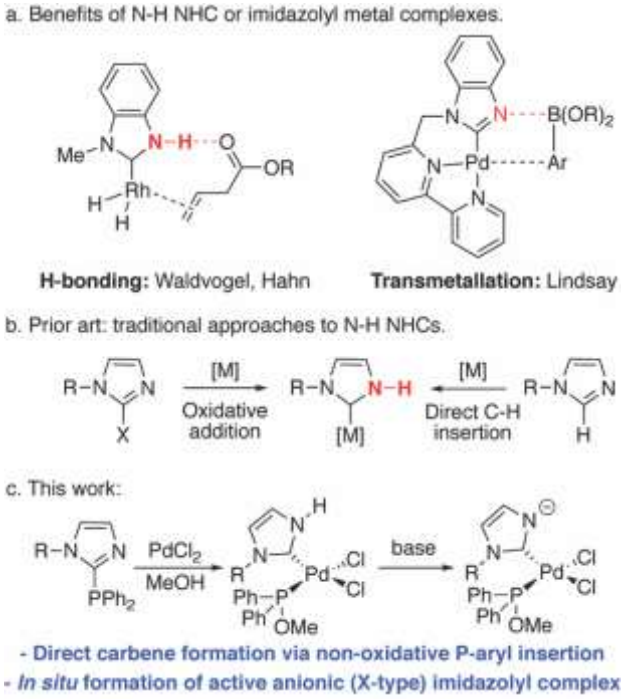

Figure 1. Benefits of and preparation methods for N–H or monosubstituted NHC metal complexes.

insertion between the C–P bond (Figure 1c).[8] While the insertion of transition metals into P-aryl bonds is known, this mechanistic pathway is typically involved in decomposition of metal phosphine catalysts.[9] Herein we demonstrate that this approach efficiently leads to a variety of monosubstituted NHC-palladium complexes and that these isolated complexes have an acidic hydrogen atom at the free nitrogen of the NHC. Our mechanistic and computational studies also show that upon removal of the N–H on the NHC ligand, an anionic (X-type) imidazolyl ligand is generated that is much more electron donating than traditional NHCs. These highly donating X-type imidazolyl ligands maintain their role as spectator ligands and do not cross couple in the reaction, suggesting that they have properties intermediate between NHC and true carbanion ligands.[4] We also demonstrate that these deprotonated Pd(II)-imidazolyl complexes are highly active precatalysts for Suzuki-Miyaura and Sonogashira cross-coupling reactions and easily achieve over 100,000 turnovers at catalyst loadings lower than 10 ppm palladium.

At the outset of our studies, we desired a general and high yielding approach to monosubstituted NHC palladium complexes that would allow us to investigate their reactivity in cross-coupling reactions. Of the reported approaches to the synthesis of N–H NHCs, we believed that insertion into a heteroatom at the 2-position of the imidazole would provide the most general approach.[8a,10] Hong and coworkers have demonstrated that palladium(II) salts can undergo non-oxidative insertion between the C–P bond in 2-imidazolylphosphine oxides. This non-oxidative reactivity derives from the fact that 2-phosphinoimidazoles can, upon protonation, be thought of as NHC-phosphenium complexes, which have been shown to serve as carbene transfer reagents (Figure 2a).[8a] Insertion of the palladium into the phosphenium intermediate, with concomitant addition of methanol to the phosphenium fragment would then provide the desired metal NHC complex. While Hong's data confirms that 2-imidazolylphosphine oxides can undergo this rearrangement, it was not known whether the reaction would proceed with 2-imidazolylphosphines as starting materials.

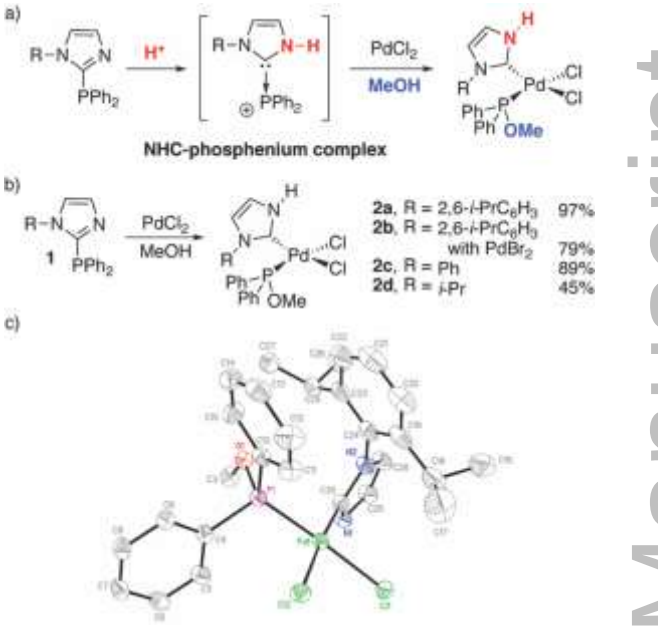

Figure 2. Synthesis and crystal structure of monosubstituted NHC-Pd(II) complexes.

Using Hong's precedent as a starting point, we were excited to find that addition of palladium(II) chloride in methanol to 2-diphosphinoimidazoles **1** led to selective formation of the NHC-Pd(II) complexes (**2**) across a range of substituted imidazole ligands (Figure 2b). Methanol as solvent was found to be necessary for efficient conversion to the NHC complex as methanol has been proposed to facilitate migration of the palladium to the carbon of the imidazole.[2a] Formation of the complex could be easily tracked by ^{31}P NMR due to appearance of a characteristic phosphorous peak near ~120 ppm that indicates formation of Pd-bound $P(OMe)Ph_2$. Using our optimized conditions, a variety of substituted NHC-Pd complexes were synthesized in good yield, including those containing *N*-aryl (**2a**–**2c**), and *N*-alkyl (**2d**) substituents. Other N-substitutions, including mesityl, benzyl, methyl, and tert-butyl efficiently formed the N–H NHC complexes with $PdCl_2$. However, purification proved challenging and these complexes could not be obtained in analytically pure form for catalytic studies. To confirm the structure of these new NHC-Pd complexes, we grew X-ray quality crystals of **2a** and obtained an X-ray crystallographic structure (Figure 2c). Unlike other N–H NHC metal complexes, palladium complexes

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formed in this fashion crystallize in monomeric and not dimeric form (Figure 2c).

One intriguing structural characteristic of these new Pd-NHC complexes is the potential to remove the N–H of the imidazole and create an anionic NHC or imidazolyl-type ligand.[3] Grotjahn and coworkers have previously demonstrated that deprotonation of the N–H on a monosubstituted Ru-NHC complex led to formation of an anionic NHC ligand with high nucleophilicity at the imidazole nitrogen.[10] We wondered whether deprotonation in this manner would lead to a more donating NHC ligand that could enhance the reactivity of the transition metal in catalysis. Indeed, anionic complexes of palladium have been implicated as highly active species in cross coupling catalysis.[11] The ^{1}H NMR spectrum of complex **2a** contains an acidic proton near 12 ppm, which exchanges for deuterium when D_2O is added to the sample in $CDCl_3$. When complex **2a** was treated with excess Et_3N or under the reaction conditions (95:5 C_6D_6:MeOH, Cs_2CO_3, rt), deprotonation of the imidazole was evident due to disappearance of the N–H peak in the ^{1}H NMR spectrum (see supporting information). We are not sure, however, whether this deprotonation leads to an anionic Pd-imidazolyl complex or a neutral complex where one of the chlorides dissociates.

To evaluate the electron donor propensity of N–H versus anionic NHC-Pd species, we performed DFT calculations in Gaussian 16[12] to estimate the Tolman electronic parameter (TEP = ν_{CO} (A_1) of $Ni(CO)_3(NHC)$). We used the mPW1PW91/6-311+G** methodology and procedure of Gusev to optimize and verify a minima for the Ni complex with carbene ligand (Figure 2d).[13] This showed that upon deprotonation of the N–H of the NHC complex **2a**, the ligand (Im*N*Dip-anion) became much more donating, greatly increasing the electron density at the metal

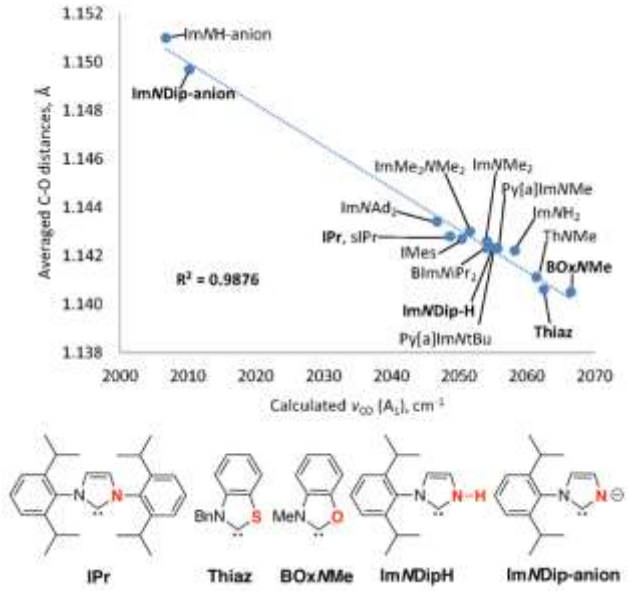
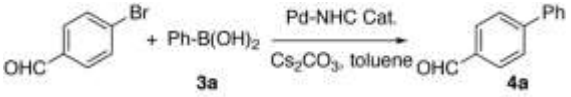


Figure 3. Electron Donor properties (TEP) of N-H and anionic NHC ligands. See supporting information for full ligand abbreviation list.

center and shifting the ν_{CO} value by >40 cm^{-1}. This increase in the donor ability of the ligand would not only make the metal more electron rich to accelerate oxidative addition type processes, it would also increase the strength of the NHC-M interaction, increasing the stability and lifetime of the catalyst.

Having developed an efficient synthesis of these new NHC-Pd complexes, we next investigated their catalytic potential in Suzuki-Miyaura reactions. As seen in Table 1, our monosubstituted Pd complexes are highly active in the Suzuki reaction when compared to other NHC-Pd complexes (entries 1–4). In particular, complexes **2a**–**2d** (entries 1, 5–7) performed as well or better than the IPr carbene (1,3-bis(2,6-diisopropylphenyl)imidazolium-2-yl, entry 2), the state-of-the-art PEPPSI catalyst (entry 3),[14] and the *N*-benzylthiazolium-2-yl carbene (entry 4).[15] Further optimization studies showed that as little as 0.001 mol% catalyst (10 ppm) was sufficient to provide high yields of the cross-coupling product (entries 8–12). When the reaction was run on just 1 ppm catalyst **2a**,

Table 1. Optimization of Suzuki-Miyaura cross-couplings.



entry[a]	catalyst	mol% Pd	time	% conv[b]
1	**2a**	1	1 h	96
2[c]	IPr-$PdCl_2$-PPh_3	1	1 h	35
3[c]	IPr-$PdCl_2$-3-Clpyr	1	1 h	>99
4[d]	Thiaz-$PdBr_2$-py	1	1 h	25
5	**2b**	1	1 h	89
6	**2c**	1	1 h	89
7	**2d**	1	1 h	89
8[e]	**2a**	1	20 min	97
9[e]	**2a**	0.1	2.5 h	95
10[e]	**2a**	0.01	2 h	>99
11[e]	**2a**	0.001	4 h	99
12[e]	**2a**	0.0001	36 h	34%
13[e]	**1a**	--	16 h	0
14[e,f]	**1a**, $PdCl_2$	0.1	30 min	>99
15[e,g]	**2a**	1	30 min	>99

[a]Reaction run on 0.5 mmol bromide, 0.75 mmol boronic acid, 1.0 mmol Cs_2CO_3, and 1 mol% catalyst in toluene (0.2M) at 100 °C for 1 h. [b]Determined by ^{1}H NMR analysis of the crude reaction mixture by comparison to an internal standard. [c]IPr = 1,3-bis(2,6-diisopropylphenyl)-imidazol-2-yl. [d]Thiaz = 3-benzylbenzo[d]thiazol-2-yl. [e]Run at 1M in 95:5 toluene:MeOH. [f]*In situ* catalyst formation with 0.1 mol% $PdCl_2$ and 0.1 mol% **2a**. [g]Reaction conducted under air.

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34% isolated yield was obtained, indicating that our catalyst is capable of up to 340,000 turnovers (entry 12). The addition of 5 vol% MeOH to the latter reactions was found to be beneficial to catalysis, presumably by helping drive the equilibrium for catalyst formation via C–P insertion (entries 10–15). Under the same conditions, and with ligand **1a** and no palladium catalyst, no product was observed (entry 13). In addition, formation of the active catalyst *in situ* via a prestir with the ligand and palladium source in methanol led to the same reactivity (entry 14), which greatly expands the opportunities for using these complexes in optimization and screening studies. Our catalyst also appears to be relatively air stable; when conducted under air, there was no apparent loss in reactivity (entry 15).

We also performed studies to test for the formation of nanoparticles, which are known to perform cross couplings at very low catalyst loadings.[16] First, we followed the reaction by ^{31}P NMR and found that a substantial amount of the active catalyst was still present in the reaction as the reaction progressed. Second, we performed the mercury drop test in an attempt to deactivate the reaction if nanoparticles were present. The addition of a drop of mercury only slightly impacted the overall rate of the reaction (87% conversion, 30 min with Hg vs 100% conversion, 20 min without Hg). Thus, we do not believe that Pd nanoparticles are participating to a great extent in this reaction, but this effect cannot be ruled out completely (see supporting information for full details).

Our optimal reaction conditions using complex **2a** were next screened against a variety of substituted bromoarene substrates (Figure 4). With as little as 0.1 mol% Pd catalyst, high yields could be consistently obtained with high functional group tolerance. In particular, aryl halides containing electron donating and electron withdrawing substituents at the ortho, meta, or para positions all reacted in high yield (**4a**–**4p**). We were especially interested in substrates that were sterically hindered, due to the unhindered nature of our palladium carbene catalyst. We found that hindered substrates, such as mesityl bromide (**4s**) and ortho-substituted aryl halides (**4b**, **4k**, **4t**) performed

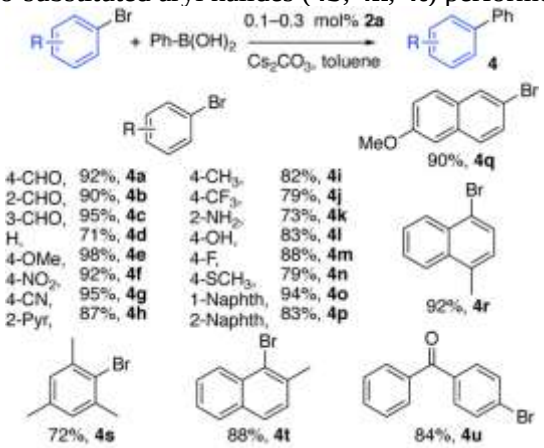

Figure 4. Substrate scope of Suzuki-Miyaura reaction. See supporting information for detailed procedures.

very well in the reaction. The reaction is also easily scalable using our standard conditions: with 0.001 mol% Pd (10 ppm) and on 11 mmol scale, 1.59 g of product **4a** (80% yield) was obtained after 14 hr. Aryl chlorides also participate in the reaction, but have much lower reactivity (4-chlorobenzaldehyde, 54% conv, 9h with 1 mol% catalyst at .75M in 95/5 toluene/MeOH).

We also investigated a variety of boronic acid substrates and found that all boronic acids tested reacted in high yield (Figure 5). Both electron-rich (**5a**–**5d**) and electron-poor (**5e**–**5g**) boronic acids reacted with good to excellent yields. Since transmetallation of the boronic acid can often be rate limiting in Suzuki cross-coupling reactions, we wanted to measure the efficiency of reactions with sterically hindered boronic acids compared when catalyst **2a** was used. As seen with products **5a**, **5j**, **5k**, and **5l**, our N–H NHC catalyst provides good to excellent yields with a variety of ortho-substituted aryl boronic acids. We believe that this effect may be due to faster transmetallation with a less hindered NHC ligand,[4] but further studies are needed to confirm this effect.

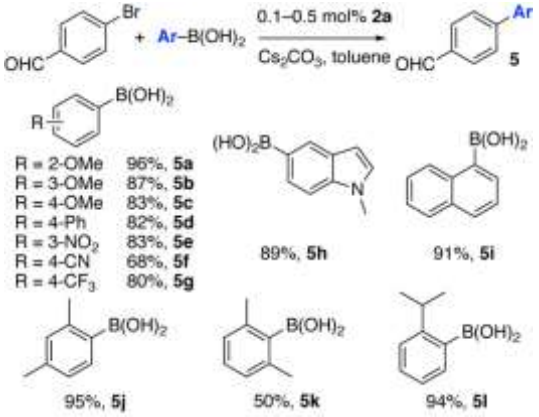

Figure 5. Boronic acid substrate scope. See supporting information for detailed procedures.

Finally, we investigated the activity of our catalyst in Sonogashira reactions under copper free conditions (Figure 6).[17] Without additional optimization, we found that our standard conditions provided the cross-coupling product in high yield for a variety of aryl iodide coupling partners (**6a**–**6e**). Aryl iodides containing a variety of electron donating and electron withdrawing substituents performed very well in the cross coupling, with electron-withdrawing substituents providing higher yields overall. These final results suggest that our monosubstituted NHC-Pd complexes can find broad application in a variety of Pd-catalyzed cross-coupling reactions.

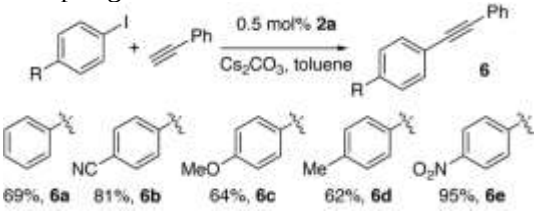

Figure 6. Substrate scope for Sonogashira reaction.

In conclusion, our results presented here provide an expeditious route to N–H NHC complexes of palladium that are highly active precatalysts for Suzuki-Miyaura and Sonogashira cross-coupling reactions. Under optimized conditions, catalyst turnover numbers over 100,000 are achieved while maintaining high yields of product. In addition, our computational studies provide insight into the donating ability of these unique carbene structures, which surpasses that of traditional NHCs. These results complement previous work with anionic imidazolyl palladium catalysts for cross-couplings[4] and provide useful insights to the potential utility of this class of ligands for transition metal catalysis. Our continuing studies on this powerful class of NHC ligands is focused on the application to other transition metals including nickel.

Experimental Section

General procedure for the synthesis of palladium catalysts. In a glove box, the phosphinoimidazole ligand (**1a-1d**, 0.100 mmol, 1 eq.) and palladium(II) chloride (17.7 mg, 0.100 mmol, 1 eq.) were dissolved in methanol (0.17 mL) and the mixture was stirred for 7-72 hours. The solvent wsa then removed under vacuum and the resulting product was dissolved in CH2Cl2 and passed through a silica gel plug. The solvent was then removed to provide the clean product.

General procedure for Suzuki-Miyaura coupling. In a N_2-filled glovebox, complex **2a** (0.67 mg, 0.0011 mmol), cesium carbonate (702 mg, 2.15 mmol), aryl halide (1.08 mmol), add boronic acid (1.62 mmol) were dissolved in toluene/methanol (95/5, 1.4 mL). The solution was then heated to 100 °C for 2-24 h until complete consumption of starting material was observed by ^{1}H NMR. The reaction was then cooled to room temperature. Water was added and the mixture was extracted 3 times with dichloromethane. The combined organic layers were dried with sodium sulfate and the solvent removed. Purification was accomplished on a silica gel column with 1:1 hexane:DCM as eluent.

General procedure for Sonogashira coupling. In a N_2-filled glovebox, complex **2a** (3.0 mg, 0.0048 mmol), cesium carbonate (628 mg, 1.93 mmol), aryl iodide (0.965 mmol), and phenylacetylene (120.7 mg, 1.16 mmol) were dissolved in toluene/methanol solution (95/5. 1.9 mL). The reaction was then stirred at 40 °C for 16-24 h until complete consumption of starting material was observed by ^{1}H NMR. The reaction was then cooled to room temperature. Water was added and the mixture was extracted 3 times with diethyl ether. The combined organic layers were dried with sodium sulfate and the solvent removed. Purification was accomplished on a silica gel column with cyclohexane as eluent.

Acknowledgements

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References

[1] (a) W. A. Herrmann, *Angew. Chem. Int Ed.* **2002**, *41*, 1290–1309. (b) R. H. Crabtree, *Oil Gas Sci. Technol.* **2007**, *62*, 739–744. (c) F. E. Hahn, M. C. Jahnke, *Angew. Chem. Int. Ed.* **2008**, *47*, 3122–3172. (d) K. Öfele, C. Taubmann, W. A. Herrmann, *Chem. Rev.* **2009**, *109*, 3408–3444. (e) S. Díez-González, N. Marion, S. P. Nolan, *Chem. Rev.* **2009**, *109*, 3612–3676. (f) E. Peris, *Chem. Rev.* **2018**, *118*, 9988–10031.

[2] (a) S. Kuwata, F. E. Hahn, *Chem. Rev.* **2018,** *118*, 9642–9677. (b) M. C. Jahnke, F. E. Hahn, *Coord. Chem. Rev.* **2015**, *293–294*, 95–115. (c) F. E. Hahn, *ChemCatChem* **2013**, *5*, 419–430. (d) S. Kuwata, T. Ikariya, *Chem Eur. J.* **2011**, *17*, 3542–3556. (e) S. Kuwata, T. Ikariya, *Chem. Commun.* **2014**, *50*, 14290–14300.

[3] M. Y. Leow, C. C. Ho, M. G. Gardiner, A. C. Bissember, *Catalysts* **2018**, *8*, 620–640.

[4] J. Zhu, V. N. G. Lindsay, *ACS Catal.* **2019**, *9*, 6993–6998.

[5] For leading references, see: (a) Y. Ito, T. Hirao, K. Tsubata, T. Saegusa, *Tetrahedron Lett.* **1978**, *19*, 1535–1538. (b) R. A. Michelin, L. Zanotto, D. Braga, P. Sabatino, R. J. Angelici, *Inorg. Chem.* **1988**, *27*, 93–99. (c) J. Ruiz, B. F. Perandones, G. García, M. E. G. Mosquera, *Organometallics* **2007**, *26*, 5687–5695.

[6] For leading references, see: (a) T. Kösterke, T. Pape, F. E. Hahn, *J. Am. Chem. Soc.* **2011**, *133*, 2112−2115. (b) R. Das, C. G. Daniliuc, F. E. Hahn, *Angew. Chem. Int. Ed.* **2014,** *53*, 1163−1166.

[7] For leading references, see: (a) K. L. Tan, R. G. Bergman, J. A. Ellman, *J. Am. Chem. Soc.* **2002**, *124*, 3202–3203. (b) K. Araki, S. Kuwata, T. Ikariya, *Organometallics* **2008**, *27*, 2176–2178. (c) V. Miranda-Soto, D. B. Grotjahn, A. G. DiPasquale, A. L. Rheingold, *J. Am. Chem. Soc.* **2008**, *130*, 13200–13201. (d) F. He, M. Wesolek, A. A. Danopoulos, P. Braunstein, *Chem.-Eur. J.* ***2016***, 22, 2658–2671. (e) D. C. Marelius, E. H. Darrow, C. E. Moore, J. A. Golen, A. L. Rheingold, D. B. Grotjahn, *Chem. - Eur. J.* **2015**, *21*, 10988−10992.

[8] (a) Y.-C. Chang, C.-H. Chang, L.-W. Wang, Y.-H. Liang, D.-F. Hu, C.-M. Weng, K.-C. Mao, F.-E. Hong, *Polyhedron* **2015**, *100*, 382–391. (b) I. Abdellah, C. Lepetit, Y. Canac, C. Duhayon, R. Chauvin, *Chem Eur. J.* **2010**, *16*, 13095–13108.

[9] P. W. N. M. Leeuwen, *Applied Catal. A: General* **2001**, *212*, 61–81.

[10] V. Miranda-Soto, D. B. Grotjahn, A. L. Cooksy, J. A. Golen, C. E. Moore, A. L. Rheingold, *Angew. Chem. Int. Ed.* **2011**, *50*, 631–635.

[11] For leading references, see: (a) C. Amatore, A. Jutand, *Acc. Chem. Res.* **2000,** *33*, 314–321. (b) F. Schroeter, J. Soellner, T. Strassner, *ACS Catal.* **2017**, *7*, 3004–3009.

[12] *Gaussian 16*, Revision B.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H.

Nakatsuji, X. Li, M. Caricato, A. V. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2016.

[13] (a) D. G. Gusev, *Organometallics* **2009**, *28*, 6458–6461. b) R. Tonner, G. Frenking, *Organometallics* **2009**, *28*, 3901–3905. (c) C. A. Tolman, *Chem. Rev.* **1977**, *77*, 313–348. (d) R. Dorta, E. D. Stevens, N. M. Scott, C. Costabile, L. Cavallo, C. D. Hoff, S. P. Nolan, *J. Am. Chem. Soc.* **2005**, *127*, 2485–2495. (e) W. A. Herrmann, L. J. Goossen, G. R. J. Artus, C. Köcher, *Organometallics*, **1997**, *16*, 2472−2477.

[14] (a) C. J. O'Brien, E. A. B. Kantchev, C. Valente, N. Hadei, G. A. Chass, A. Lough, A. C. Hopkinson, M. C. Organ, *Chem. Eur. J.* **2006**, *12*, 4743–4748. (b) O. Diebolt, V. Jurčík, R. Correa da Costa, P. Braunstein, L. Cavallo, S. P. Nolan, A. M. Z. Slawin, C. S. J. Cazin, *Organometallics* **2010**, *29*, 1443–1450.

[15] S. K. Yen, L. L. Koh, H. V. Huynh, T. S. A. Hor, *Chem. Asian J.* **2008**, *3*, 1649–1656.

[16] (a) For leading references on heterogenized Pd catalysts, see: A. Biffis, P. Centomo, A. Del Zotto, M. Zecca, *Chem. Rev*. **2018**, *118*, 2249–2295. (b) A. Molnár, *Chem. Rev.* **2011**, *111*, 2251–2320. (c) L. Yin, J. Liebscher, *Chem. Rev.* **2007**, *107*, 133–173.

[17] For leading references, see: (a) R. W. Wagner, T. E. Johnson, F. Li, J. S. Lindsey, *J. Org. Chem.* **1995**, *60*, 5266−5273. (b) T. Ljungdahl, T. Bennur, A. Dallas, H. Emtenäs, J. Mårtensson, *Organometallics* **2008**, *27*, 2490−2498. (c) M. Gazvoda, M. Virant, B. Pinter, J. Košmrlj, *Nat. Commun.* **2018**, *9*, 4814.

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