ChemComm

Cite this: *Chem. Commun.*, 2012, **48**, 555–557

www.rsc.org/chemcomm

COMMUNICATION

Abnormal N-heterocyclic carbene palladium complex: living catalyst for activation of aryl chlorides in Suzuki–Miyaura cross coupling†

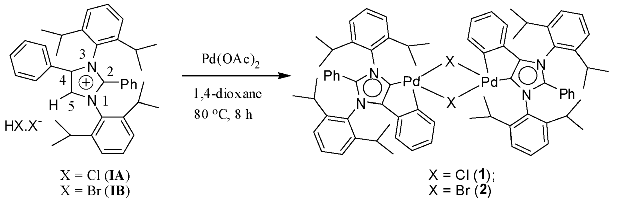
Samaresh Chandra Sau, Subhankar Santra, Tamal K. Sen, Swadhin K. Mandal* and Debasis Koley

Received 16th September 2011, Accepted 24th October 2011
DOI: 10.1039/c1cc15732a

Palladium complexes bearing abnormal N-heterocyclic carbene were used as catalysts in Suzuki–Miyaura cross coupling of aryl chlorides at 25 °C. The catalyst remained active for 10 successive catalytic runs and can activate 4-chlorotoluene at 25 °C with 0.01 mol% catalyst loading resulting in a TON of 9500 within 6 h.

The isolation of heteroatom stabilized carbenes [normal N-heterocyclic carbenes (*n*NHCs)] by Arduengo *et al.*[1] has led to numerous catalytic applications in organometallic chemistry. The N-heterocyclic carbenes also have been used as nucleophiles for organocatalytic reactions.[2] The *n*NHCs bind to a metal center through the C-2 center generating a normal mode of metal binding (refer to Scheme 1 for numbering). Crabtree, Faller and co-workers first demonstrated in 2001 that 2-pyridylmethylimidazolium salts react with $IrH_5(PPh_3)_2$ in which an abnormal mode of metal binding of the NHCs was observed through the C-4 center.[3] Later on, a few other complexes featuring the so-called abnormal mode of binding was reported.[4] The abnormal mode of bonding increases the electron density at the metal center substantially, and now a number of imidazole based carbene salts specifically designed for abnormal mode of binding have been reported.[5]

However, it took a while to isolate the abnormal N-heterocyclic carbenes (*a*NHCs).[6] Metal coordinated *a*NHCs have proven to be excellent catalysts resulting in the activation of un-reactive bonds such as C–H and H–H[7] and in some cases the *a*NHC coordinated metal complexes have outperformed the catalytic activity as compared to their normal NHC counterpart (*n*NHC). For example, in 2004, Lebel and co-workers demonstrated the catalytic activity of the *a*NHC based palladium complex towards Suzuki–Miyaura cross coupling using aryl chlorides at 80 °C whereas the corresponding *n*NHC analog remained inactive under identical conditions.[8] This report prompted us to test the catalytic activity of palladium complexes prepared from the newly reported[6] 1,3-bis(2,6-diisopropylphenyl)-2,4-diphenyl-imidazolium salts **IA** and **IB** for Suzuki–Miyaura cross coupling of aryl chlorides. It is noteworthy that the ready availability and low cost of aryl chlorides relative to aryl bromides or iodides in Suzuki–Miyaura cross coupling has been economically attractive. However, the activation of aryl chloride substrates in Suzuki–Miyaura cross coupling has been limited as compared to the activation of aryl bromide and aryl iodide substrates because of the strength of the C–Cl bond in comparison to the C–Br or C–I bond. Since the reports of activation of aryl chloride substrates during the late 1990's[9] there are now few studies available in the literature for Suzuki–Miyaura cross coupling of aryl chlorides.[10,11] However, the Suzuki–Miyaura cross coupling of aryl chlorides at room temperature has remained one of the great challenges in this area specifically at very low catalyst loading.



Scheme 1 Synthesis of compounds **1** and **2**.

Herein we report the synthesis of halobridged C–H activated palladium dimers **1** and **2** using 1,3-bis(2,6-diisopropylphenyl)-2,4-diphenyl-imidazolium salts **IA** and **IB**, respectively. Both **1** and **2** were tested for their efficacy in Suzuki–Miyaura cross coupling of aryl chlorides. The preliminary results indicate that the aryl chlorides can be activated under Suzuki–Miyaura cross coupling conditions at room temperature leading to nearly quantitative yield of the corresponding biphenyls. The catalyst remained active for 10 successive catalytic cycles without loss of any activity. The catalyst **1** successfully activated 4-chlorotoluene under a low catalyst loading of 0.01 mol% at room temperature with TON value of 9500 within 6 h.

Two imidazolium salts, **IA** and **IB** (Scheme 1), are employed for the current study as *a*NHC precursors to prepare palladium complexes. The addition of **IA** or **IB** to a dry 1,4-dioxane solution of $Pd(OAc)_2$ in 1 : 1 ratio resulted in the change of color from yellow to deep brown with the formation of a halobridged C–H activated palladium dimer **1** or **2** (Scheme 1). Previously Herrmann and co-workers have reported the synthesis of phosphorus coordinated C–H activated halobridged palladacycle dimers.[12]

Department of Chemical Sciences, Indian Institute of Science Education and Research-Kolkata, Mohanpur-741252, India. E-mail: swadhin.mandal@iiserkol.ac.in

† Electronic supplementary information (ESI) available: Experimental and theoretical details including all analytical data. CCDC 843993 (**1**) and 843992 (**2**). For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c1cc15732a

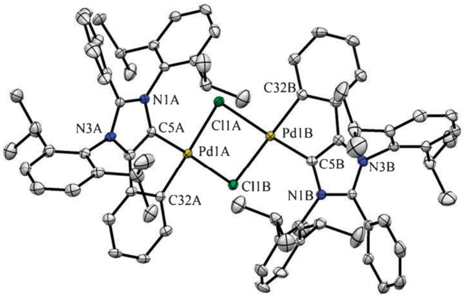
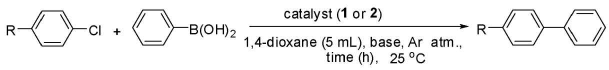
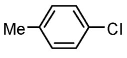
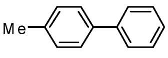
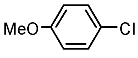
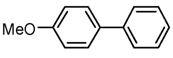
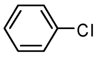
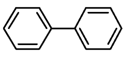
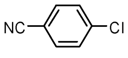
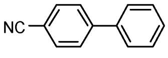
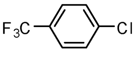
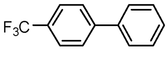


Fig. 1 Perspective ORTEP views of the molecular structure of **1**. Thermal ellipsoids are drawn with 50% probability. Hydrogen atoms and solvent molecules (diethyl ether and dichloromethane) have been omitted for the sake of clarity.

Table 1 Suzuki–Miyaura cross coupling reactions of aryl chlorides at room temperature[a]



R = H, Me, OMe, CN, CF_3

Entry	Substrate	Cat.	Time/h	Product	Yield[b] (%)
1		1	4		98
2		2	4		97
3		1	8		98
4		2	7		98
5		1	3		97
6		2	3		98
7		1	2		98
8		2	2		98
9		1	2		98
10		2	2		98

[a] Reaction conditions: 0.73 mol% catalyst (**1** or **2**), aryl chloride (1 mmol), phenylboronic acid (1.5 mmol) and base (2 mmol, NaOMe for entries 1–6 and Cs_2CO_3 for entries 7–10), 5 mL dry 1,4-dioxane. [b] Isolated yield after chromatography.

The compounds **1** and **2** were isolated by column chromatography using dichloromethane and recrystallized as yellow crystals from CH_2Cl_2/Et_2O in nearly 80% yield. The complexes were characterized by elemental analysis, NMR spectroscopy, and X-ray crystallography. The molecular structures of **1** and **2** were determined by X-ray crystallographic studies establishing the abnormal mode of binding of the carbene. The X-ray measurements (see ESI†) revealed that compounds **1** and **2** are isostructural. The solid state structures (Fig. 1 and also see ESI† for molecular structure of **2**) displayed that the *ortho* aryl C–H bond activation has taken place during the reaction. The geometry around palladium is square planar where each palladium center is bonded to the C-5 center of the carbene displaying an abnormal mode of binding, C–H activated *ortho* aryl carbon, and two chlorides. The Pd–C bond lengths revealed that Pd–C(carbene) bond distances (1.989(4) Å in **1** and 1.980(3) Å in **2**) are shorter than that observed for Pd–C (aryl) bond distances (2.017(4) Å in **1** and 2.031(1) Å in **2**). The Pd–C(carbene) bond distances are comparable to that observed in earlier studies.[8] As a part of our interest to develop an efficient palladium catalyst for the C–C coupling reaction[13] we checked the efficiency of these palladium complexes (**1** and **2**) for the Suzuki–Miyaura coupling reaction. The study begins with an optimization of the operating conditions on a model reaction involving 4-chlorotoluene and phenylboronic acid (see ESI† for details). It was observed that 1,4-dioxane/NaOMe and 1,4-dioxane/Cs_2CO_3 are the most effective combination for this particular catalytic system to carry out the Suzuki–Miyaura reaction. We tested these combinations for a number of aryl chloride substrates successfully at room temperature leading to nearly quantitative isolated yield of the biphenyl (Table 1). Chlorobenzene as well as chlorobenzene attached with electron donating groups at the *para*-position furnished the corresponding biaryl products (entries 1–6, Table 1) utilizing a strong base (NaOMe) while chlorobenzenes bearing electron withdrawing groups at the *para*-position gave the corresponding biaryls (entries 7–10, Table 1) upon applying a milder base (Cs_2CO_3). The catalytic reactions were performed with 0.73 mol% loading of the catalysts (**1** and **2**). The result revealed that activation of aryl chlorides having electron donating groups is more difficult compared to those having electron withdrawing groups at the same position. The progress of the reaction was monitored with ^1H NMR spectroscopy using 4-chlorotoluene and catalyst **1** at defined time intervals revealing that within the first 75 minutes, the reaction reaches near completion resulting in 95% conversion (see ESI†).

One of the major problems in homogeneous catalysis is catalyst's recycling inability as they are inseparable from the reaction mixture. Herein, we assessed the longevity of catalyst **1** by performing several catalytic runs into the same reaction pot to check whether the catalyst remains active for several catalytic cycles.[13a] We have carried out 10 successive catalytic runs by using 0.73 mol% of catalyst. After every 4 h interval we add a fresh batch of substrates (4-chlorotoluene and phenylboronic acid) and base without adding any additional catalyst into the reaction vessel. After each 4 h interval, we checked the substrate consumption by recording the ^1H NMR spectrum of the reaction mixture after initial workup. The ^1H NMR spectrum indicates a complete consumption of substrates within 4 h time at 25 °C for 10 successive catalytic runs (see ESI†) indicating no loss of catalytic activity. After 10 catalytic cycles the overall isolated yield of 4-methylbiphenyl is 95%. This result clearly demonstrates that the catalyst stays active for 10 consecutive catalytic runs. This result further prompted us to check the catalyst's ability to execute the Suzuki–Miyaura reaction of 4-chlorotoluene with phenylboronic acid under lower catalyst loading at room temperature. The results indicate that the catalyst **1** is almost equally active for coupling of 4-chlorotoluene with 0.01 mol% catalyst resulting in a nearly quantitative yield of the product at room temperature with a TON value of 9500 within 6 h (Table 2). Further lowering the catalyst loading to 0.005 mol% leads to 65% yield at room temperature in longer time (26 h).

We carried out DFT calculations in order to have insight into the Pd–carbene bonding. The DFT optimized (BP86/6-31G(d) level)

Table 2 Suzuki–Miyaura coupling reaction of 4-chlorotoluene at different catalyst (**1**) loading[a]

Entry	Catalyst (mol%)	Time/h	Yield[b] (%)	TON
1	0.36	4	98	272
2	0.14	4	97	692
3	0.07	5	96	1371
4	0.01	6	95	9500
5	0.005	26	65	13 000

[a] Reaction conditions: catalyst **1**, 4-chlorotoluene (1 mmol), phenylboronic acid (1.5 mmol), NaOMe (2 mmol), 5 mL dry 1,4-dioxane. [b] Isolated yield after column chromatography.

structure of **1** as well as dissociated monomer $\mathbf{1_m}$ (see ESI†) were generated. An earlier study has considered dissociation of the palladium dimer to monomers in solution.[12] To understand the nature of the Pd–C(carbene) bond and compare its strength with the Pd–C(aryl) bond we have performed Natural Bond Orbital Analysis. The Wiberg bond indices for the Pd–C(carbene) (0.5215) are relatively higher than Pd–C(aryl) (0.3891) suggesting a stronger Pd–C(carbene) bond. This fact is also manifested in the X-ray structure revealing a shorter bond length of Pd–C(carbene) in comparison with the Pd–C(aryl) bond length. The bonding analysis suggests that both the Pd–C(carbene) and Pd–C(aryl) are single bonds with occupancy of 1.289 and 1.525 *e*, respectively. The electron density contribution from the Pd itself is very less (14% in Pd–C(carbene) and 9% in Pd–C(aryl) as can be visualized from the two NBO orbitals) (Fig. 2). To further reinforce our results we have performed AIM (Atoms in Molecules) calculations for $\mathbf{1_m}$. The electron density (ρ) at the bond critical point (BCP) for the Pd–C(carbene) and Pd–C(aryl) bonds are 0.1898 and 0.1846, respectively, with a $\nabla^2\rho$ value of −0.216 and −0.218 (see Computational Details, ESI†). The values suggest that concentration of electron density along the bond path is discernable.

In summary, we prepared two halobridged palladium dimers bearing the abnormal N-heterocyclic carbene and completely characterized them. These palladium dimers are active catalysts for Suzuki–Miyaura cross coupling of a number of aryl chlorides at room temperature leading to nearly quantitative yield. The catalyst exhibits its activity at very low catalyst loading up to 0.005 mol% at room temperature. The catalyst remained active for 10 successive catalytic runs without any loss of its activity which is in line with the DFT calculation describing the Pd–carbene bond as a strong one preventing from any palladium leaching in solution.

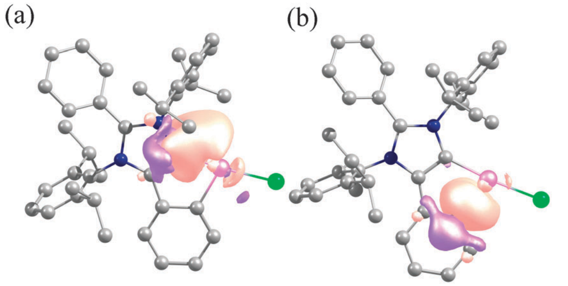


Fig. 2 Natural bond orbitals of $\mathbf{1_m}$ showing (a) Pd–C(carbene) and (b) Pd–C(aryl). Hydrogen atoms are omitted for the sake of clarity. Color code: C grey, Cl green, N blue and Pd pink.

Financial support from the Department of Science and Technology (DST), India (Grant No. SR/FT/CS-020/2008), is highly acknowledged. SCS is thankful to UGC, SS and TKS are thankful to CSIR for their research fellowships. SKM and DK thank Prof. S. Dattagupta for support and constant encouragement.

References

1 (*a*) A. J. Arduengo, R. L. Harlow and M. Kline, *J. Am. Chem. Soc.*, 1991, **113**, 361–363; (*b*) A. J. Arduengo, H. V. R. Dias, R. L. Harlow and M. Kline, *J. Am. Chem. Soc.*, 1992, **114**, 5530–5534.
2 For example see: (*a*) D. Enders, O. Niemeier and A. Henseler, *Chem. Rev.*, 2007, **107**, 5606–5655; (*b*) S. Díez-González and S. P. Nolan, *Synlett*, 2007, 2158–2167; (*c*) T. K. Sen, S. C. Sau, A. Mukherjee, A. Modak, S. K. Mandal and D. Koley, *Chem. Commun.*, 2011, **47**, 11972–11974.
3 S. Gründemann, A. Kovacevic, M. Albrecht, J. W. Faller and R. H. Crabtree, *Chem. Commun.*, 2001, 2274–2275.
4 (*a*) M. Albrecht, *Chem. Commun.*, 2008, 3601–3610; (*b*) O. Schuster, L. Yang, H. G. Raubenheimer and M. Albrecht, *Chem. Rev.*, 2009, **109**, 3445–3478.
5 (*a*) M. Heckenroth, A. Neels, M. G. Garnier, P. Aebi, A. W. Ehlers and M. Albrecht, *Chem.–Eur. J.*, 2009, **15**, 9375–9386; (*b*) G. Ung and G. Bertrand, *Chem.–Eur. J.*, 2011, **17**, 8269–8272.
6 E. Aldeco-Perez, A. J. Rosenthal, B. Donnadieu, P. Parameswaran, G. Frenking and G. Bertrand, *Science*, 2009, **326**, 556–559.
7 (*a*) M. Heckenroth, E. Kluser, A. Neels and M. Albrecht, *Angew. Chem.*, 2007, **119**, 6409–6412 (*Angew. Chem., Int. Ed.*, 2007, **46**, 6293–6296); (*b*) A. Prades, M. Viciano, M. Sanaú and E. Peris, *Organometallics*, 2008, **27**, 4254–4259.
8 H. Lebel, M. K. Janes, A. B. Charette and S. P. Nolan, *J. Am. Chem. Soc.*, 2004, **126**, 5046–5047.
9 (*a*) D. W. Old, J. P. Wolfe and S. L. Buchwald, *J. Am. Chem. Soc.*, 1998, **120**, 9722–9723; (*b*) A. F. Littke and G. C. Fu, *Angew. Chem.*, 1998, **110**, 3586–3587 (*Angew. Chem., Int. Ed.*, 1998, **37**, 3387–3388).
10 (*a*) B. Yuan, Y. Pan, Y. Li, B. Yin and H. Jiang, *Angew. Chem.*, 2010, **122**, 4148–4152 (*Angew. Chem., Int. Ed.*, 2010, **49**, 4054–4058); (*b*) N. Marion, O. Navarro, J. Mei, E. D. Stevens, N. M. Scott and S. P. Nolan, *J. Am. Chem. Soc.*, 2006, **128**, 4101–4111; (*c*) L. Wu, J. Ling and Z.-Q. Wuc, *Adv. Synth. Catal.*, 2011, **353**, 1452–1456; (*d*) R. B. Bedford, C. P. Buttsa, T. E. Hurst and P. Lidström, *Adv. Synth. Catal.*, 2004, **346**, 1627–1630; (*e*) B. Karimi and P. F. Akhavan, *Inorg. Chem.*, 2011, **50**, 6063–6072.
11 (*a*) R. B. Bedford, C. S. J. Cazin and D. Holder, *Coord. Chem. Rev.*, 2004, **248**, 2283–2321; (*b*) C. J. O'Brien, E. A. B. Kantchev, C. Valente, N. Hadei, G. A. Chass, A. Lough, A. C. Hopkinson and M. G. Organ, *Chem.–Eur. J.*, 2006, **12**, 4743–4748; (*c*) O. Navarro, N. Marion, J. Mei and S. P. Nolan, *Chem.–Eur. J.*, 2006, **12**, 5142–5148; (*d*) O. Diebolt, P. Braunstein, S. P. Nolan and C. S. J. Cazin, *Chem. Commun.*, 2008, 3190–3192.
12 W. A. Herrmann, C. Brossmer, K. Öfele, C.-P. Reisinger, T. Priermeier, M. Beller and H. Fischer, *Angew. Chem.*, 1995, **107**, 1989–1992 (*Angew. Chem., Int. Ed.*, 1995, **34**, 1844–1848).
13 (*a*) S. Santra, P. Ranjan, S. K. Mandal and P. K. Ghorai, *Inorg. Chim. Acta*, 2011, **372**, 47–52; (*b*) S. Santra, K. Dhara, P. Ranjan, J. Dash, S. K. Mandal and P. Bera, *Green Chem.*, 2011, **13**, 3238–3247.