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Synthesis of Dichlorobis(1,4-dimesityl-1*H*-1,2,3-triazol-5-ylidene)palladium [$PdCl_2(TMes)_2$] and Its Application to Suzuki–Miyaura Coupling Reaction

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The palladium complex bearing a novel NHC-ligand derived from 1,4-dimesityl-1,2,3-tirazole was prepared. The complex catalyzed the Suzuki–Miyaura coupling reaction with aryl chloride successfully to give biaryls in excellent yields, particularly very effective for the sterically hindered reaction between *o*-substituted arylchlorides and *o*-substituted phenylboronic acids.

As an extremely useful class of ligands for use in transition-metal complexes, *N*-heterocyclic carbenes (NHCs) have emerged.[1] It is well recognized that replacement of phosphines by NHCs can provide complexes with enhanced thermal stability and catalytic performance due to the higher electron-donor ability. The majority of NHC ligands used are imidazol-2-ylidenes **A** or 1,2,4-triazol-5-ylidenes **B** (Figure 1). In contrast, since Crabtree et al. first reported an NHC complex which features an imidazole ring bound at the C5 position,[2] various complexes bearing abnormal NHC ligands such as imidazol-5-ylidene **C**, pyrazolin-4-ylidenes **D**[3] and 1,2,3-triazol-5-ylidene **E**[4] have also been reported by several research groups. Although these series of abnormal NHC ligands and their complexes have been researched,[5,6] catalytic merit of abnormal NHC has yet to be developed in detail.[7] Moreover synthesis of 1,2,3-triazole NHC complexes, and application to transition metal catalytic reactions have scarcely been studied.

Since Albrecht et al. first reported novel abnormal *N*-heterocyclic carbene (abnormal NHC) ligands based on a 1,2,3-triazole framework,[4] Sankararaman and Bertrand independently disclosed two other types of abnormal NHCs and their metal complexes.[8,9] In view that 1,2,3-triazoles are readily accessible by the reaction of an organic azide and an alkyne, i.e., click chemistry, the modularity of the click chemistry would lead to diversity of 1,2,3-triazole-based abnormal NHC ligands, and to alternative NHC ligands.

Novel abnormal carbene metal complexes may be predicted to have a potential for a unique catalytic activity in organic reactions because abnormal NHC ligands are stronger donors than conventional NHC ligands.[9] Thus, Sankararaman's pyrolidinyl 1,2,3-triazol-5-ylidene palladium complex worked effectively in the Suzuki–Miyaura coupling with aryl bromide, but not with aryl chloride. We envisioned that TMes (triazole-based NHC ligand bearing mesityl groups) might be a promising and attractive ligand for coupling reactions because TMes is an analog of IMes [1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene] which is known as an effective imidazole carbene ligand due to electronically rich and steric hindered mesityl groups.

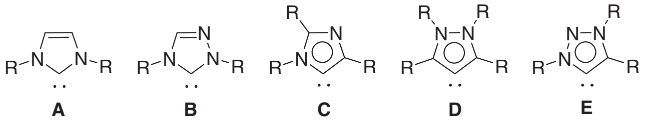
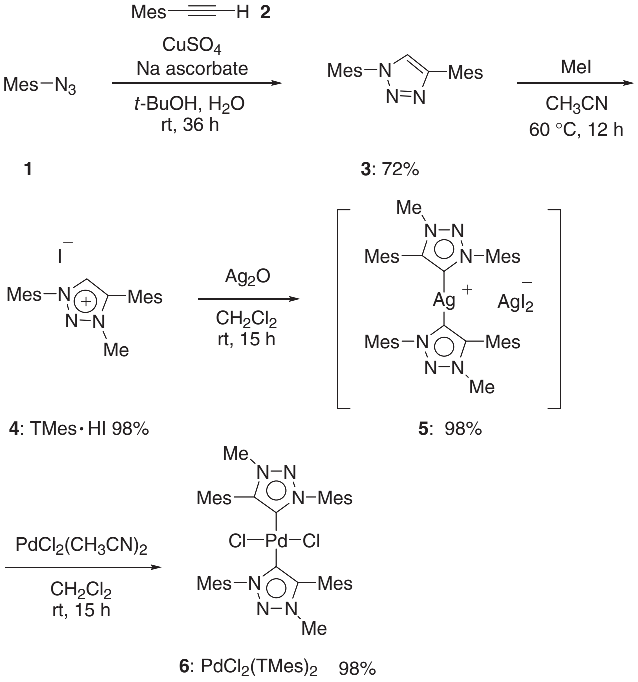


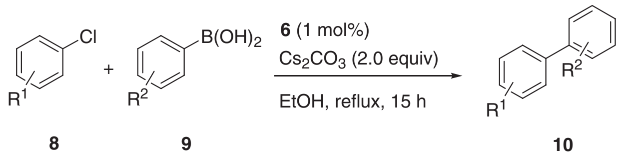
Figure 1.



Scheme 1. Synthesis of $PdCl_2(TMes)_2$ complex.

Following a general procedure reported by Sharpless et al.,[10] 1,4-dimesityl-1,2,3-triazole (**3**) was readily prepared by the reaction of mesitylazide **1** with mesitylacetylene **2** using copper(I) catalyst in the first step (Scheme 1). The triazole was converted into triazolium salt **4** quantitatively by treatment with CH_3I in excess according to Albrecht's method.[4] The reaction of the 1,2,3-triazolium salt with silver oxide successfully afforded silver 1,2,3-triazol-5-ylidene complex **5** as a stable white solid in a quantitative yield. The formation of **5** might be supported by disappearance of triazolium proton ($\delta_H = 9.38$ ppm) in ^{1}H NMR, the appearance of a metal-bond carbon signal at 155.2 ppm in ^{13}C NMR. This is consistent with the previous studies[4–6] of the synthesis of Ag–1,2,3-triazol-5-ylidene complex. The Ag complex **5** was converted successfully into the corresponding palladium carbene complex on treatment with $PdCl_2(MeCN)_2$ in CH_2Cl_2 at room temperature and dichlorobis(1,2,3-triazol-5-ylidene)palladium **6** [$PdCl_2(TMes)_2$] was obtained as an air-stable pale yellow complex. The complex was purified by column chromatography on basic alumina and characterized by

Table 1. The **6**-catalyzed Suzuki–Miyaura coupling[a]



Entry	Aryl chloride	Boronic acid	Yield/%[b]
1	**8a** ($R^1 = p$-MeO)	**9a** ($R^2 = H$)	99[c]
2[d]	**8a**	**9a**	60[c]
3	**8b** ($R^1 = m$-MeO)	**9a**	93
4	**8c** ($R^1 = o$-MeO)	**9a**	98
5	**8d** ($R^1 = p$-Me)	**9a**	98
6	**8e** ($R^1 = o$-Me)	**9a**	97
7	**8f** ($R^1 = p$-COMe)	**9a**	94
8	**8g** ($R^1 = o$-COMe)	**9a**	93
9	**8h** ($R^1 =$ 1-naphthyl)	**9a**	98
10	**8i** ($R^1 =$ 2-naphthyl)	**9a**	99
11	**8j** ($R^1 =$ 2-pyridyl)	**9a**	97
12	**8k** ($R^1 =$ 3-pyridyl)	**9a**	95
13	**8c**	**9b** ($R^2 = o$-Me)	68
14	**8e**	**9b**	99
15	**8h**	**9b**	93
16	**8j**	**9b**	98
17	**8e**	**9c** ($R^2 = o$-MeO)	64
18	**8h**	**9c**	83
19	**8j**	**9c**	83

[a] **8** (0.5 mmol), **9** (0.6 mmol), **6** (0.005 mmol), Cs_2CO_3 (1.0 mmol), EtOH (1.5 mL); reflux, 15 h. [b] Isolated yields. [c] Determined by GC. [d] **7** was used instead of **6**.

^1H and ^{13}C NMR, and combustion analysis: the metal-bond carbon was observed at 163.0 ppm in ^{13}C NMR. According to the literature,[4,8,9] carbene-carbon of Pd–1,2,3-triazol-5-ylidene complex tends to appear around 160 ppm, the signal at 163.0 ppm demonstrates the formation of the palladium carbene complex. Yet to make a single crystal for X-ray analysis failed, unsuitable crystalline solid being obtained instead.

Palladium catalysts bearing NHC ligands have been used for such cross coupling reactions as the Suzuki–Miyaura coupling. NHC ligands are a good alternative to conventional phosphine ligands in view of thermal stability.[11] Thus, we evaluated the $PdCl_2(TMes)_2$ **6** in the Suzuki–Miyaura coupling, and optimized the representative reaction between *p*-chloroanisole (**8a**: $R^1 = p$-MeO) with phenylboronic acid (**9a**: $R^2 = H$). The reactions were usually performed in the presence of **6** (1 mol %). After many optimization experiments, the optimum conditions are revealed to be refluxing in an ethanol solution for 15 h with Cs_2CO_3 as a base, affording 4-methoxybiphenyl in a quantitative yield (Table 1, Entry 1, and see Supporting Information).[12] The efficiency of bisimidazolylidene palladium dichloride **7** $[PdCl_2(IMes)_2]$[7a] (Figure 2) was tested for comparison, **7** was less effective than **6**, giving 60% yield of the coupling product (Table 1, Entry 2).

On the basis of the optimized reaction conditions, the coupling reactions between a variety of aryl chlorides and phenylboronic acid and *o*-substituted phenylboronic acid were examined to explore the general effectiveness of **6**. The results are summarized in Table 1. The coupling products with **9a** were obtained in excellent yields regardless of substituents; stereo and electronic properties of substituent of benzene hardly affected on yields. Electronically deactivated aryl chlorides and *ortho*-substituents tolerated the reaction; the corresponding biaryl-products were obtained in excellent yields (Entries 1 and 3–8). The coupling with other aromatic rings such as 1- and 2-naphthyl chlorides (Entries 9 and 10) gave the corresponding biaryls in quantitative yields as well. Such heteroaromatic chlorides as 2- and 3-pyridyl (Entries 11 and 12) coupled with **9a** to provide the corresponding products in nearly quantitative yields. Reactions using *o*-methylphenylboronic acid (**9b**: $R^2 = o$-Me, Entries 13–16) or *o*-methoxyphenylboronic acid (**9c**: $R^2 = o$-MeO, Entries 17–19) were also performed, and the yields were as good as those of phenylboronic acid **9a**. It is noteworthy that the reaction between *o*-substituted aryl chloride and *o*-substituted phenylboronic acids proceeded to give the sterically crowded biaryls in good to excellent yields. The reaction of *o*-chlorotoluene (**8e**) with *o*-methoxyphenylboronic acid (**9c**) was the exception giving the biaryl in a moderate yield (Entry 17). These results suggest that the **6**-catalyzed reaction has a broad substrate scope. The complex was also effective for the Mizoroki–Heck reaction of bromobenzene with acrylic ester (Scheme 2). Detailed study will be reported in due course.

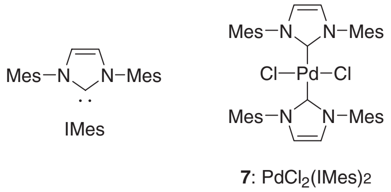
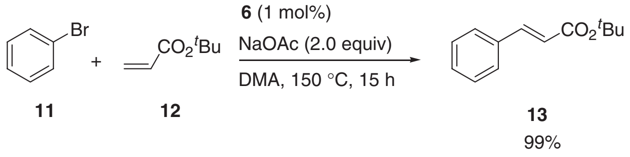


Figure 2. IMes and its Pd complex.



Scheme 2. The **6**-catalyzed Mizoroki–Heck coupling.

In conclusion, the $PdCl_2(TMes)_2$ complex **6** was an efficient catalyst for the Suzuki–Miyaura coupling reaction with aryl and heteroaryl chlorides, especially for the sterically hindered reaction between *o*-substituted arylchlorides and *o*-substituted phenylboronic acids.

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References and Notes

1 For reviews of *N*-heterocyclic carbenes, see: a) S. P. Nolan, *N-Heterocyclic Carbenes in Synthesis*, Wiley, New York, **2004**. b) W. A. Herrmann, *Angew. Chem., Int. Ed.* **2002**, *41*, 1290. c) Y. Yamaguchi, *Bull. Jpn. Soc. Coord. Chem.* **2008**, *52*, 43. d) N. Marion, S. P. Nolan, *Chem. Soc. Rev.* **2008**, *37*, 1776. e) S. Würtz, F. Glorius, *Acc. Chem. Res.* **2008**, *41*, 1523. f) K. Cavell, *Dalton Trans.* **2008**, 6676. g) O.

Schuster, L. Yang, H. G. Raubenheimer, M. Albrecht, *Chem. Rev.* **2009**, *109*, 3445.

2 S. Gründemann, A. Kovacevic, M. Albrecht, J. W. Faller, R. H. Crabtree, *Chem. Commun.* **2001**, 2274.

3 Y. Han, H. V. Huynh, *Chem. Commun.* **2007**, 1089.

4 P. Mathew, A. Neels, M. Albrecht, *J. Am. Chem. Soc.* **2008**, *130*, 13534.

5 For recent research of abnormal NHCs, see: a) L. N. Appelhans, C. D. Incarvito, R. H. Crabtree, *J. Organomet. Chem.* **2008**, *693*, 2761. b) G. Song, X. Wang, Y. Li, X. Li, *Organometallics* **2008**, *27*, 1187. c) G. Song, Y. Zhang, X. Li, *Organometallics* **2008**, *27*, 1936. d) Y. Kong, H. Ren, S. Xu, H. Song, B. Liu, B. Wang, *Organometallics* **2009**, *28*, 5934. e) E. Aldeco-Perez, A. J. Rosenthal, B. Donnadieu, P. Parameswaran, G. Frenking, G. Bertrand, *Science* **2009**, *326*, 556. f) R. Jothibasu, H. V. Huynh, *Chem. Commun.* **2010**, *46*, 2986.

6 For reviews of abnormal NHCs, see: a) P. L. Arnold, S. Pearson, *Coord. Chem. Rev.* **2007**, *251*, 596. b) M. Albrecht, *Chem. Commun.* **2008**, 3601.

7 Abnormal NHC–transition metal complex catalyzed reaction, see: a) H. Lebel, M. K. Janes, A. B. Charette, S. P. Nolan, *J. Am. Chem. Soc.* **2004**, *126*, 5046. b) V. Lavallo, Y. Canac, C. Präsang, B. Donnadieu, G. Bertrand, *Angew. Chem., Int. Ed.* **2005**, *44*, 5705. c) Y. Han, H. V. Huynh, G. K. Tan, *Organometallics* **2007**, *26*, 6581. d) L. Yang, A. Krüger, A. Neels, M. Albrecht, *Organometallics* **2008**, *27*, 3161.

8 T. Karthikeyan, S. Sankararaman, *Tetrahedron Lett.* **2009**, *50*, 5834.

9 G. Guisado-Barrios, J. Bouffard, B. Donnadieu, G. Bertrand, *Angew. Chem., Int. Ed.* **2010**, *49*, 4759.

10 H. C. Kolb, M. G. Finn, K. B. Sharpless, *Angew. Chem., Int. Ed.* **2001**, *40*, 2004.

11 For reviews of NHC–palladium catalyzed cross-coupling reactions, see: a) E. A. B. Kantchev, C. J. O'Brien, M. G. Organ, *Angew. Chem., Int. Ed.* **2007**, *46*, 2768. b) F. Glorius, *N-Heterocyclic Carbenes in Transition Metal Catalysis*, Springer-Verlag, Berlin, **2007**. c) N. Marion, S. P. Nolan, *Acc. Chem. Res.* **2008**, *41*, 1440.

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