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Palladium complexes with abnormal *N*-heterocyclic carbene ligands derived from 1,2,3-triazolium ions and their application in Suzuki coupling

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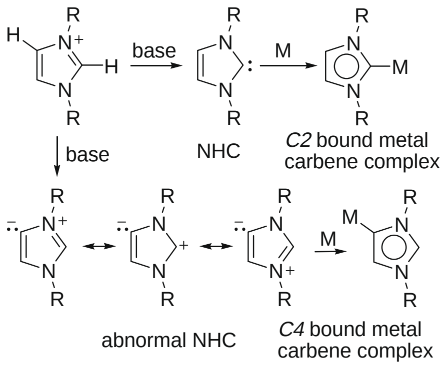
ABSTRACT

Chiral and achiral pincer type palladium complexes bearing abnormal *N*-heterocyclic carbene ligands derived from 1,2,3-triazole are reported. Both complexes are effective as catalysts for non-asymmetric Suzuki coupling reaction for the synthesis of biphenyl derivatives. However, both the complexes failed to catalyze the formation of binaphthyl derivatives, by the asymmetric Suzuki coupling in case of the chiral complex and the non-asymmetric version in case of the achiral pincer complex. Instead deboronation of arylboronic acid occurred very efficiently leaving the aryl bromide intact.

In 1968 Wanzlick and Ofele almost simultaneously and independently reported the potential of imidazolium-derived *N*-heterocyclic carbenes (NHC) as ligands for transition metals.[1] Although the ability of NHCs to act as efficient ligands by coordination through *C*2 carbon of the imidazolidene has been well established, isolation and structural characterization of free NHCs were reported only in the early 90s with the discovery of the Arduengo carbenes.[2] Recently, NHCs derived from deprotonation of imidazolium ions at the *C*4 position have been reported.[3] Unlike the Wanzlick–Ofele–Arduengo carbenes in this class of NHCs, the carbene center (*C*4) is not flanked by heteroatoms on both sides and their structures can only be represented as zwitter ions and not in the neutral canonical form (Scheme 1). Such carbenes are termed as abnormal NHCs. Metallation via *C*4-*H* activation results in the formation of *C*4-bound metal carbene complexes (Scheme 1).

A handful of abnormal NHCs from other heterocycles such as pyrazolylidene, isothiozolylidene, pyridylidene, and 1,2,3-triazolylidene have been reported.[4] Recently, we have reported pyrrolidine-1,2,3-triazole conjugates as organocatalysts for the asymmetric Michael addition reaction with excellent diastereo and enantioselectivities.[5] During our attempts to prepare the corresponding chiral quaternary ammonium hydroxide of **1**, we stumbled upon formation of the silver complex of abnormal NHC derived from **2** (Scheme 2). During the course of our investigation Albrecht[6] has reported the synthesis and structural characterization of late transition metal complexes with abnormal NHC ligands derived from 1,2,3-triazolylidenes. Herein we report the first chiral palladium complex bearing abnormal NHC ligand and the first palladium pincer complex bearing abnormal bis-NHC chelating ligand, both based on 1,2,3-triazolylidene, and their utility in Suzuki coupling reactions.

Reaction of chiral triazole derivative **1**[5] with methyl iodide yielded the corresponding quaternary ammonium iodide **2** in quantitative yield (Scheme 2). In an attempt to synthesize the corresponding chiral quaternary ammonium hydroxide (**3**), quaternary ammonium iodide **2** was treated with silver oxide. ^{1}H NMR spectrum of the crude product revealed the absence of triazole ring proton that appeared at 9.47 ppm for **2**. The crude product was identified as the silver complex (**4**) of the abnormal NHC formed from **2** (Scheme 2). This observation is consistent with the report of Albrecht.[6] The silver carbene complex (**4**) was unstable under ambient conditions and also decomposed upon exposure to light. Nevertheless it was characterized by ^{1}H NMR, ESI-MS, and HRMS. The molecular ion corresponding to the cation part of **4** showed



Scheme 1. Metal complexes derived from normal (*C*2) and abnormal (*C*4) NHCs from imidazolium ion.

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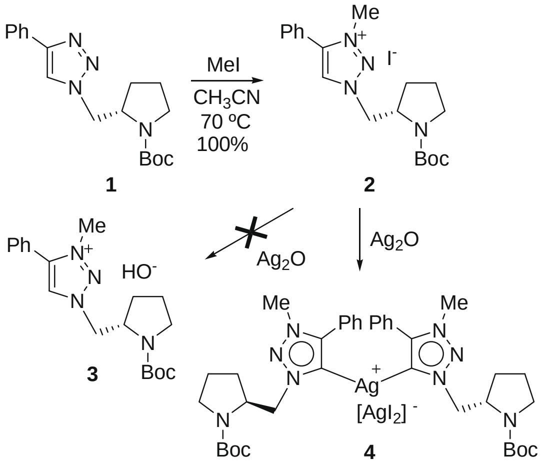
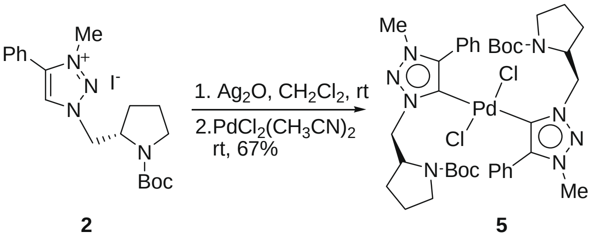


Scheme 2. Synthesis of silver complex of abnormal NHC derived from **2**.

the isotope peaks that matched with the calculated spectrum. In view of the instability of the silver complex, it was decided to prepare the palladium complex of the abnormal carbene derived from **2**. The NHC complexes of palladium have been shown to be useful in cross-coupling reactions.[7] Attempted synthesis of the corresponding palladium complex by treatment of **2** with $Pd(OAc)_2$ in DMSO, following the procedure reported by Albrecht,[6] yielded a mixture of intractable material. Therefore transmetallation of in situ-generated silver carbene complex **4** was carried out.

Treatment of **2** with silver oxide followed by $[Pd(Cl)_2(CH_3CN)_2]$ in dichloromethane afforded the corresponding palladium complex **5** (Scheme 3) in 67% yield as an air stable pale yellow solid. It was purified by chromatography over silica gel and characterized by IR, ^1H and ^{13}C NMR, ESI-MS, and HRMS data.

Attempts to grow single crystals of **5** yielded only a microcrystalline solid that was unsuitable for X-ray crystallographic analysis. Palladium catalysts bearing NHC ligands have been used for cross-coupling reactions, in particular Suzuki and Heck coupling reactions.[7] NHC ligands are good alternative to the conventional phosphine ligands, and catalysts bearing NHC ligands react with a high degree of efficiency in C–C bond forming reactions compared to ligandless catalysts. Although complex **5** is chiral it was first tested for its catalytic activity in simple non-asymmetric Suzuki reactions for the synthesis of substituted biphenyls. Various substituted aryl bromides were treated with phenylboronic acid and 4-methoxyphenylboronic acid in THF in the presence of catalytic amounts of **5**. The catalyst loading varied from 2 to 20 mol % depending upon the substrates. The coupling products were obtained in good yields and the results are summarized in Table 1. In Table 1, entries 3, 7, and 8 are noteworthy because methoxy-substituted derivatives are generally less reactive in Suzuki coupling and using the catalyst **5**, high yields of the coupling products were obtained. To rule out the possibility of the reaction being catalyzed by leached out Pd(0), the reaction of phenylboronic acid with 4-cyanobromobenzene was carried out in the presence of mercury. Though the reaction took longer time for completion (9 vs 14 h), the coupling product was obtained in 98% yield, indicating that the reaction was catalyzed by **5**. Attempted coupling of 1,4-phenylenediboronic acid with 4-methoxybromobenzene using **5** did not proceed and only starting materials were recovered under the conditions given in Table 1. The more reactive 2-bromo-5-*tert*-butylisophthalaldehyde (Table 1, entry 4, ArBr) also failed to react with 1,4-phenylenediboronic acid.

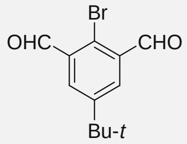
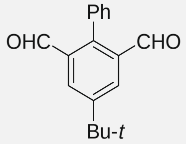


Scheme 3. Synthesis of palladium complex **5** from **2** via in situ-generated silver complex.

As stated earlier, complex **5** is chiral and it is potentially useful for the asymmetric C–C cross-coupling reactions. We focused our attention on the asymmetric Suzuki coupling for the synthesis of chiral binaphthalene derivatives. Although palladium catalysts bearing other NHC ligands have been successfully used in non-asymmetric Suzuki coupling,[8,9] to this date there has been no report on the asymmetric version of Suzuki coupling using NHC ligand based catalysts, especially of the sterically hindered substrates. Therefore, we wanted to study the utility of complex **5** for the asymmetric synthesis of chiral binaphthalene derivatives. Accordingly, 1-bromo-2-methoxynaphthalene (**6**) was treated with 2-methoxy-1-naphthylboronic acid (**7**) in the presence of K_2CO_3 and 10 mol % of **5** in THF. To our dismay only deboronation of **7** to yield 2-methoxynaphthalene (**8**) was observed and **6** remained intact. The same deboronation was observed when 2-benzyloxy-1-bromonaphthalene (**9**) was reacted with 2-benzyloxy-1-naphthylboronic acid (**10**) to yield 2-benzyloxynaphthalene (**11**) and **9** was recovered. Also reaction of 1-iodo-2-naphthol with **7** led to only deboronation, and 2-methoxynaphthalene (**8**) and 1-iodo-2-naphthol were recovered from the reaction mixture. Attempted coupling of 1-naphthylboronic acid with **6** yielded 1,1-binaphthylene as the product and **6** was recovered back from the reaction. It is well documented that sterically demanding boronic acids with two *ortho* substituents are prone to deboronation during Suzuki coupling reaction.[10] Nevertheless, some successful coupling of sterically hindered boronic acids has been reported under rigorously anhydrous conditions. Our attempts to carry out asymmetric Suzuki coupling using rigorously dried THF and DME under various conditions failed to yield the desired binaphthalene derivatives. Only deboronated products were obtained in nearly quantitative yields in all the reactions (Table 2). Deboronation in Suzuki coupling of sterically hindered substrates is explained on the basis of formation of *trans*-diarylpalladium(0) intermediate in which C–C coupling is disfavored compared to *cis*-diarylpalladium(0) intermediate. As a result of the formation of trans isomer, the catalytic cycle is stagnated and the reaction does not proceed further to the reductive elimination step to complete the catalytic cycle. Under these conditions, the boronic acid undergoes deboronation in the presence of the base and often due to the presence of adventitious water in the reaction. This problem can be addressed by using a chelating ligand for the palladium complex which prevents the conversion of the *cis*-diarylpalladium(0) intermediate to the trans isomer. Alternatively, the transmetallation of the boronic acid could be a slow step, especially in sterically demanding substrates, leading to deboronation reaction. To rule out the formation of the *trans*-diarylpalladium(0) intermediate, we proceeded to synthesize an achiral version of a pincer type palladium complex. Methylation of the bis-triazole derivative **12** (obtained by the addition of benzyl azide to 1,3-diethynylbenzene) gave the bis-quaternary ammonium iodide **13** in 95% yield. It was further treated with silver oxide followed by $PdCl_2(CH_3CN)_2$ to afford complex **15** (Scheme 4). The intermediate silver carbene complex **14** was unstable for isolation and complete characterization. Nevertheless, it was characterized by ESI-MS, and HRMS data which corresponded to $C_{26}H_{24}N_6Ag$, the cationic part of the silver carbene complex **14**. Complex **15** was characterized by IR, NMR, ESI-MS and

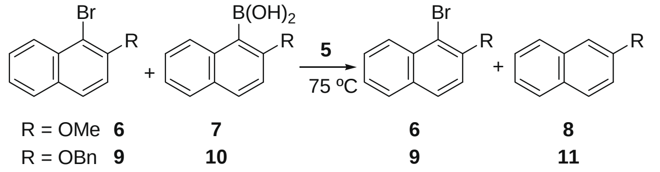
Table 1
Synthesis of biphenyls by Suzuki coupling using complex **5**[a]

$$\mathrm{ArBr} + \mathrm{Ar'B(OH)_2} \xrightarrow[\mathrm{K_2CO_3},\ 70\text{-}\ 75\ ^{\circ}\mathrm{C}]{\mathbf{5}\ (2\ \text{to}\ 20\ \text{mol\%})} \mathrm{Ar\text{-}Ar'}$$

Entry	ArBr	Ar′B(OH)$_2$	Ar–Ar′	**5** (mol %)	Time (h)	Yield (%)
1[b]	1-Bromonaphthalene	PhB(OH)$_2$	1-Phenylnaphthalene	20	16	73
2	1,2-Dibromobenzene	PhB(OH)$_2$	*o*-Terphenyl	20	18	60
3	1-Bromo-2-methoxynaphthalene	PhB(OH)$_2$	2-Methoxy-1-phenylnaphthalene	10	12	93
4		PhB(OH)$_2$		5	7	84
5	1-Bromo-4-nitrobenzene	PhB(OH)$_2$	4-Nitrobiphenyl	5	8	90
6	4-Bromobenzonitrile	PhB(OH)$_2$	4-Cyanobiphenyl	5	9	90
7[c]	1-Bromo-4-methoxybenzene	4-Methoxy-phenylboronic acid	4,4′-Dimethoxybiphenyl	2	40	79
8[c]	1-Bromo-4-methylbenzene	4-Methoxy-phenylboronic acid	4-Methoxy-4′-methylbiphenyl	2	40	96

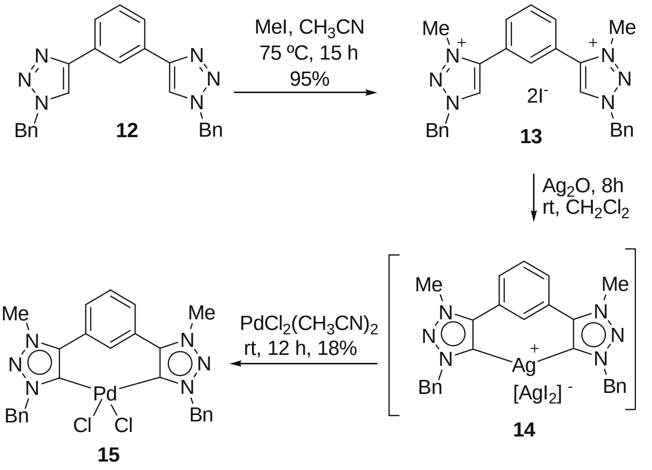
[a] Entries 1–6, 0.35 mmol scale, 1 equiv ArBr, 2 equiv PhB(OH)$_2$, 3 equiv K$_2$CO$_3$, entries 7–8, 0.88 mmol scale, 1 equiv ArBr, 1.2 equiv 4-methoxyphenylboronic acid, 3 equiv K$_2$CO$_3$.
[b] CsF as base.
[c] Yield based on 37% conversion for entry 7 and 30% conversion for entry 8.

Table 2
Attempted asymmetric Suzuki coupling for the synthesis of binaphthalene derivatives[a]



Entry	ArBr	ArB(OH)$_2$	**5** (mol %)	Base/solvent	Product
1	**6**	**7**	10	K$_2$CO$_3$/THF	**8**
2	**9**	**10**	10	K$_2$CO$_3$/THF	**11**
3	**6**	**7**	20	KOBu-*t*/DME	**8**
4	**9**	**10**	20	KOBu-*t*/DME	**11**
5	**6**	**7**	10	Cs$_2$CO$_3$/DME	**8**
6[b]	**6**	1-NpB(OH)$_2$	10	K$_2$CO$_3$/THF	Np–Np

[a] 1 equiv of ArBr, 2 equiv of ArB(OH)$_2$ and 3 equiv of base.
[b] 1-NpB(OH)$_2$ = 1-naphthylboronic acid and Np–Np = 1,1-binaphthylene.



Scheme 4. Synthesis of pincer palladium complex **15**.

HRMS. The absence of triazolium ring proton resonance at 9.47 ppm in the ^{1}H NMR spectrum indicated that both the rings had undergone deprotonation resulting in the formation of the corresponding biscarbene leading to the formation of **15** via **14**. The molecular ion peak in MS corresponded to $C_{26}H_{25}N_6Cl_2Pd$, [M+1] ion, and showed the isotope distribution pattern expected for this formula, based on the calculated spectrum. Complex **15** was tested for its catalytic activity in Suzuki coupling. Coupling of 4-bromonitrobenzene and 4-bromobenzonitrile with phenylboronic acid yielded 4-nitro- and 4-cyanobiphenyl, respectively, in >90% yields. However, attempted coupling of 1-bromo-2-methoxynaphthalene (**6**) and 2-methoxynaphthalen-1-ylboronic acid (**7**) using **15** and Cs_2CO_3 in DME resulted only in deboronation of **7** to yield 2-methoxynaphthylene (**8**) and **6** remained intact in the reaction. To our disappointment, even the use of the pincer complex **15** as catalyst in the Suzuki reaction did not result in the formation of the desired binaphthyl derivative. We speculate that the failure of the Suzuki coupling to yield binaphthyl derivatives using **5** and **15** as pre-catalysts might be due to slow transmetallation of the sterically demanding boronic acids, leading to deboronation reaction.

In conclusion, we report the first example of a chiral palladium complex (**5**) bearing an abnormal NHC ligand based on 1,2,3-triazolylidene precursor and the first example of the corresponding pincer complex (**15**) derived from bis-1,2,3-triazolylidene precursor. We have demonstrated that both the complexes are useful as catalysts for the non-asymmetric Suzuki coupling reaction for the synthesis of biphenyl derivatives. However, both the complexes failed to catalyze the formation of binaphthyl derivatives, the asymmetric version of Suzuki coupling in the case of **5** and the ordinary version in the case of **15**. Under the reaction conditions deboronation of arylboronic acid occurred very efficiently leaving the aryl bromide intact in the reaction.

Acknowledgments

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Supplementary data

Supplementary data (detailed experimental procedure, copies of ^1H NMR, ^{13}C NMR, mass spectrum of palladium complexes, characterization data for the Suzuki products are available in supplementary material) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.08.002.

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