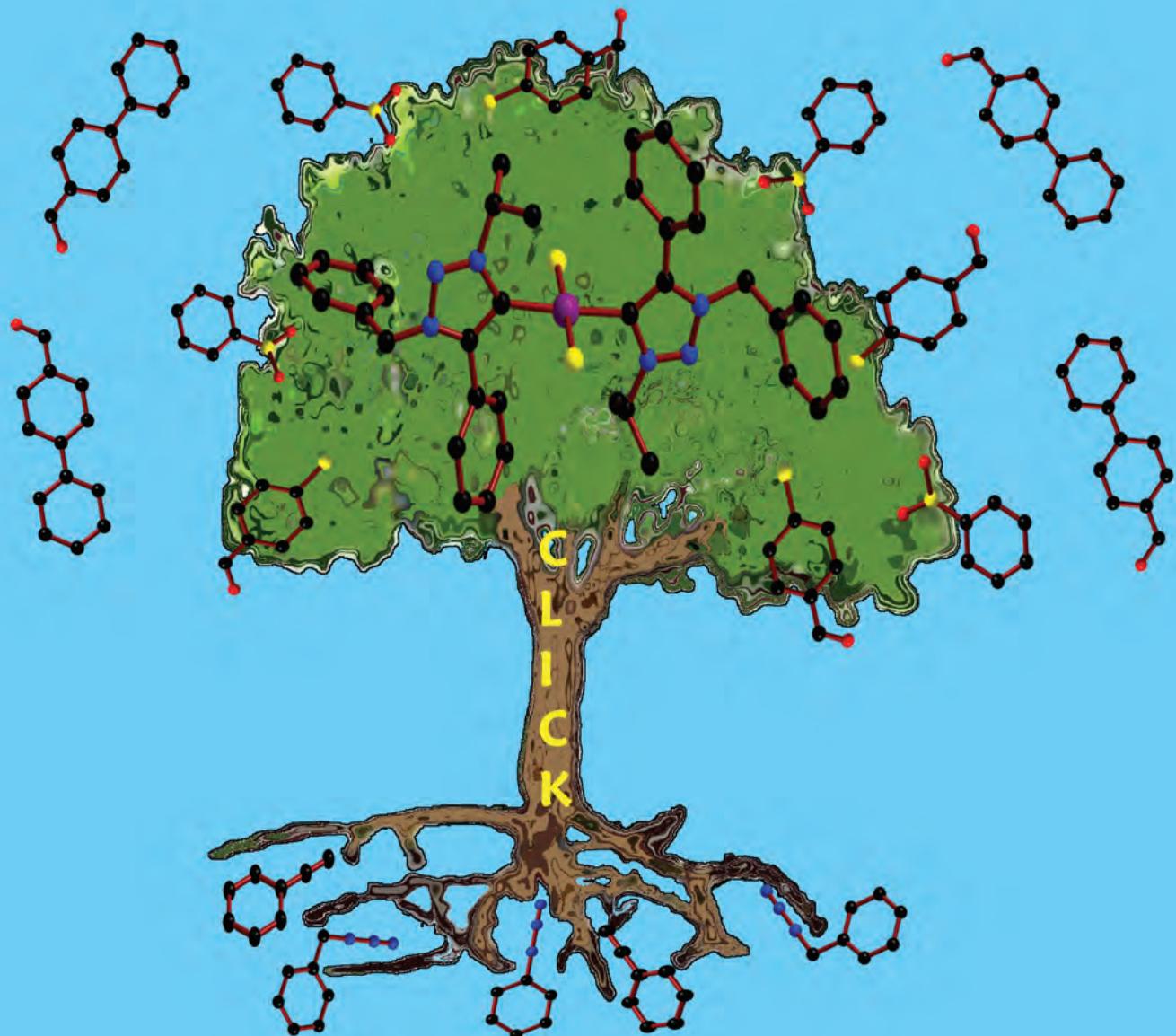


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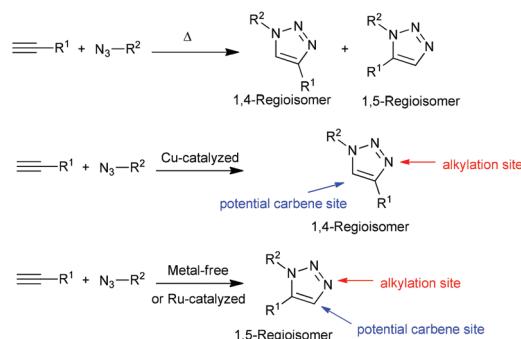
## Abnormal carbenes derived from the 1,5-cycloaddition product between azides and alkynes: structural characterization of Pd(II) complexes and their catalytic properties<sup>t</sup>

Stephan Hohloch,<sup>a</sup> Wolfgang Frey,<sup>b</sup> Cheng-Yong Su<sup>c</sup> and Biprajit Sarkar<sup>\*a</sup>

The exclusive formation of the 1,5-cycloaddition product between azides and alkynes is taken advantage of in generating the first examples of abnormal carbenes from these precursors. This new route provides unprecedented post-functionalization possibilities for such abnormal carbenes.

Since the discovery of the surprisingly robust *N*-heterocyclic carbenes (NHC) by Arduengo,<sup>1</sup> these compounds have been extensively used as ligands over the last two decades.<sup>2</sup> One reason for the huge interest in NHC chemistry is the potent nature of their metal complexes as homogeneous catalysts.<sup>2,3</sup> Redox-active properties of carbene complexes<sup>4</sup> and the discovery of abnormal carbenes (*a*NHC)<sup>5</sup> or mesoionic carbenes (MIC)<sup>5d</sup> continue to add to the richness of this field. The Huisgen cycloaddition<sup>6</sup> reaction between alkynes and azides has been popularized in recent years in its Cu(I) catalyzed form as the “Click” reaction.<sup>7</sup> One big advantage of the Cu(I) catalyzed reaction is the exclusive formation of the 1,4-cycloaddition product in a reaction where two regioisomers are, in principle, possible (Scheme 1).<sup>7</sup> The selectivity of this method and its high yields make the 1,4-isomer of this cycloaddition reaction ideal precursors for abnormal carbenes of the 1,2,3-triazol-3-ium-5-ylidene form which are excellent donors.<sup>5a</sup> Metal complexes of these abnormal carbenes have thus proven to be highly efficient catalysts for a variety of chemical transformations.<sup>8</sup>

In recent years, metal-containing as well as metal free catalysts for the generation of the 1,5-regioisomer in the azide-



Scheme 1 Thermal and catalysed version of the Huisgen cycloaddition reaction. Potential alkylation and carbene sites in the triazoles are highlighted.

alkyne cycloaddition reaction have been reported (Scheme 1).<sup>9</sup> Seeing the availability of the 1,5-regioisomer, we wanted to take advantage of this and use them as precursors for generating *a*NHCs. For the 1,4-regioisomer, the alkylating step that generates the *a*NHC occurs at a nitrogen atom that is far removed from the carbene center that eventually binds to the metal atom.<sup>8</sup> Hence the influence of the alkylating group on the properties of the carbene center is negligible and the tuning of ligand properties necessarily has to be completed at the cycloaddition stage.<sup>5a,8</sup> The 1,5-regioisomer, on the one hand, presents a unique opportunity for alkylating a nitrogen atom that is *ortho* to the potential carbene center (Scheme 1). Thus, through such alkylation reactions, the steric and electronic properties of such *a*NHC ligands (formed after deprotonation) and, in turn, their metal complexes can be influenced to a much higher degree than can be done with the 1,4-regioisomers. In the following, we present the first examples of Pd(II) complexes of *a*NHCs derived from the 1,5-regioisomers of the azide–alkyne cycloaddition reaction. The complexes have been characterized by spectroscopic methods and single crystal X-ray diffraction. We also show that the Pd(II) complexes of these *a*NHCs are potent catalysts for the Suzuki–Miyaura reaction and are also capable of activating the more robust aryl chloride bonds.

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<sup>t</sup>Electronic supplementary information (ESI) available: Synthetic and structural details and description of catalytic reactions. CCDC 846888, 929861, 846894 and 892296. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c3dt51083b

The 1,5-cycloaddition products 1,5-diphenyl-1-*H*-1,2,3-triazole (**1**) and 1-benzyl-5-phenyl-1-*H*-1,2,3-triazole (**2**) were prepared by metal free catalysis and ruthenium catalysed reactions, respectively, of the corresponding substituted azides and alkynes (see the Experimental section). These literature reported procedures<sup>9</sup> produced the 1,5-cycloaddition products exclusively in excellent yields. **1** and **2** were then alkylated to the corresponding iodide salts 3-methyl-1,5-diphenyl-1-*H*-1,2,3-triazol-3-ium iodide (**3**), 1-benzyl-3-methyl-5-phenyl-1-*H*-1,2,3-triazol-3-ium-iodide (**4**) and 1-benzyl-3-isopropyl-5-phenyl-1-*H*-1,2,3-triazol-3-ium-iodide (**5**) (see the Experimental section). Even though **3** is literature known,<sup>8b,10</sup> the known procedure requires the use of methylazide, a potentially explosive compound. The present route helps in avoiding the use of methylazide. The salts **1**, **2** and **3** are characterized in their <sup>1</sup>H-NMR spectrum by a strongly downfield shifted signal for the C-H proton of the triazolium ring.

The complexes bis-(3-methyl-1,5-diphenyl-1-*H*-1,2,3-triazol-3-ium-4-ylidene)PdCl<sub>2</sub> (**6**), bis-(1-benzyl-3-methyl-5-phenyl-1-*H*-1,2,3-triazol-3-ium-4-ylidene)PdCl<sub>2</sub> (**7**) and bis-(1-benzyl-3-isopropyl-5-phenyl-1-*H*-1,2,3-triazol-3-ium-4-ylidene)PdCl<sub>2</sub> (**8**) were synthesized using the salts **3**, **4** and **5** by taking advantage of the transmetallation method with Ag<sub>2</sub>O and Pd(MeCN)<sub>2</sub>Cl<sub>2</sub> in good yields (Scheme 2 and the Experimental section).

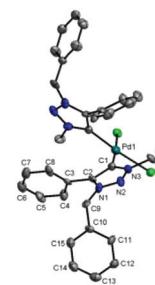
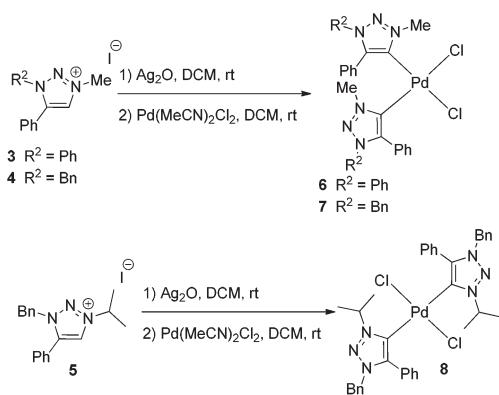
Complexes **6**, **7** and **8** were characterized by <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy, elemental analyses and mass spectrometry. The disappearance of the downfield shifted signal corresponding to the triazolium ring proton in **3**, **4** and **5** was a first indication of the formation of carbene complexes. Additionally, for **7**, signals corresponding to the carbene C atom were observed at 172.4 (*cis*) and 172.6 (*trans*) ppm respectively in their <sup>13</sup>C NMR spectrum (see the Experimental section). Unfortunately, for **6** and **8** the carbene C signal was not resolved. The metal complexes can exist either as the *cis* or *trans* isomer. In contrast to a recent report on Pd(II) complexes with 1,2,3-triazol-3-ium-5-ylidenes where a mixture of *cis* and *trans* isomers was obtained under various reaction conditions,<sup>11</sup> for **6** only the *cis*-isomer was observed after workup. Complexes **7** and **8** showed several isomers (*cis/trans-syn/anti* (depending on the relative orientation of the substituents on the triazolylidene

backbone)) in NMR at room temperature. Temperature dependent proton NMR spectroscopy in DMSO-d<sub>6</sub> showed that the benzylic signals merge into two species (*cis/trans* ratio 1 : 1) at 120 °C for complex **7**. While the *syn/anti* isomers for the *cis* form seem to converge to one species at this temperature, it seems like not all rotation barriers have been overcome at this temperature. On further heating, NMR spectra indicate that the *cis* complex becomes the more preferable isomer (*cis/trans* ratio at 150 °C 1 : 0.7) (see Fig. S1†). Heating complex **8** showed similar results.

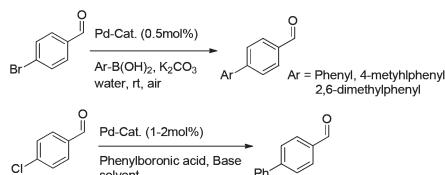
Single crystal X-ray diffraction studies were performed for **4**, **6**, **7** and **8**. The ligand **4** shows bond lengths expected for delocalized C-C and C-N bonds inside the five-membered triazolium ring (Fig. S2 and Table S2†).<sup>8a</sup> Complexes **6**, **7** and **8** are all mononuclear (Fig. 1, S3 and S4†).

The carbene ligands as well as the chlorides are *cis* to each other in **6**. For **7** we were only able to determine the structure of the *cis*-complex, whereas the *trans* isomer preferably crystallized for **8**. Increasing the steric demand using the bulky isopropyl substituents on N3 in **8** should preferably result in the *trans*-complex, because of large steric crowding in a *cis*-complex. The smaller methyl substituents on N3 in **6** and **7** seem to stabilize the complex in the *cis*-form. The structural data for **8** are unfortunately not good enough to discuss bond length and angles in detail. However, the connectivity and configuration around the metal center can be ascertained with full confidence with the data set. The Pd centers in **6**, **7** and **8** are in a distorted square planar environment as is typical of Pd(II). The Pd-C1 and Pd-Cl1 bond lengths of 1.988(2) and 2.3775(5) Å, respectively, in **6** and 1.99(1) and 2.373(3) Å, respectively, in **7** are in the typical range of such bonds in a *cis*-complex.<sup>11</sup> Even though the corresponding bond lengths in **8** cannot be discussed here with confidence they are expected to be larger than in **7** because of the operation of a larger *trans*-influence (carbene C vs. Cl<sup>-</sup>) in the *trans*-complex.<sup>11</sup> The bond lengths inside the five-membered triazolylidene ring are in the typical range of delocalized C-C and C-N bonds and are similar to those observed for the ligand **4**.<sup>8a,11</sup> The carbene ligands are largely tilted with respect to the PdCl<sub>2</sub> plane. The dihedral angle is 57.3(1)° in **6** and 54.0(5)° in **7**.

The Pd(II) complexes were tested for their efficiency in the Suzuki–Miyaura cross-coupling reaction. There have been recent reports in the literature regarding the potent nature of



**Fig. 1** ORTEP plot of **7**. Ellipsoids are drawn at 50% probability. Hydrogen atoms have been omitted for clarity.



**Scheme 3** The Suzuki–Miyaura cross-coupling reaction using the reported Pd(II) complexes as catalysts.

**Table 1** Catalysis results for aryl bromides in water at room temperature. Reaction time: 5 hours

Boronic acid	Catalyst	Conversions
Phenylboronic acid	6	93%
	7	89%
	8	93%
3,5-Dimethyl-phenylboronic acid	6	97%
	7	98%
	8	90%
4-Methyl-phenylboronic acid	6	97%
	7	95%
	8	88%

Pd(II) complexes of abnormal carbenes in catalysis of the Suzuki–Miyaura type.<sup>8b,d,g,12</sup> We were interested in investigating the corresponding complexes of substituted 1,2,3-triazol-3-ium-4-ylidene ligands. All of the complexes **6–8** show excellent activity in the cross-coupling reaction between aryl bromides and boronic acids (Scheme 3 and Table 1). Yields exceeding 90% were observed in each case with a catalyst loading of 0.5 mol%. The reactions work at room temperature, in the environmentally benign solvent water, and was complete within 5 hours. We tested three differently substituted aryl boronic acids, and the reaction worked with high yields in all cases (Table 1).

We were next interested in seeing if these complexes with new types of abnormal carbene ligands would be capable of catalysing the Suzuki–Miyaura reaction with the more challenging aryl chloride substrates. Unfortunately, no product formation was observed in water at all investigated temperatures. We then changed our focus to organic solvents, and optimised the reaction temperature by using **6** as a catalyst for a case study. Using *tert*-butanol resulted in 30% product formation at 120 °C by carrying out the reaction for 15 hours. The best conditions turned out to be dry 1,4-dioxane at 120 °C. By using 1 mol% of the catalyst in 1,4-dioxane, yields of about 50% were obtained with **6** and about 70% with **8** (Table 2). Unfortunately, the yields were poor while using **7** as a catalyst.

Summarizing, we have presented here a novel way of synthesizing metal complexes of abnormal carbene ligands by using the 1,5-cycloaddition product between azides and alkynes. The Pd(II) complexes of these carbene ligands have been shown to be potent catalysts in the Suzuki–Miyaura cross-coupling reaction, and are capable of activating the more challenging aryl chloride bonds. The synthetic route presented here offers an excellent opportunity for post-functionalization of the nitrogen

**Table 2** Catalysis results for aryl chlorides. Reaction time: 15 hours

Catalyst	Solvent	Temperature	Conversions
6	<i>tert</i> -Butanol	95 °C	17%
6	<i>tert</i> -Butanol	120 °C	30%
6	Neat	120 °C	2%
6	1,4-Dioxane	120 °C	23%
6	1,4-Dioxane dry	120 °C	48%
7	1,4-Dioxane dry	120 °C	9%
8	1,4-Dioxane dry	120 °C	68%

atom *ortho* to the carbene center in the 1,2,3-triazole ring. Such a strategy might open up new routes for introducing additional donating and hemilabile groups in such ligands, and thus create novel avenues for generating homogeneous catalysts.<sup>13</sup>

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