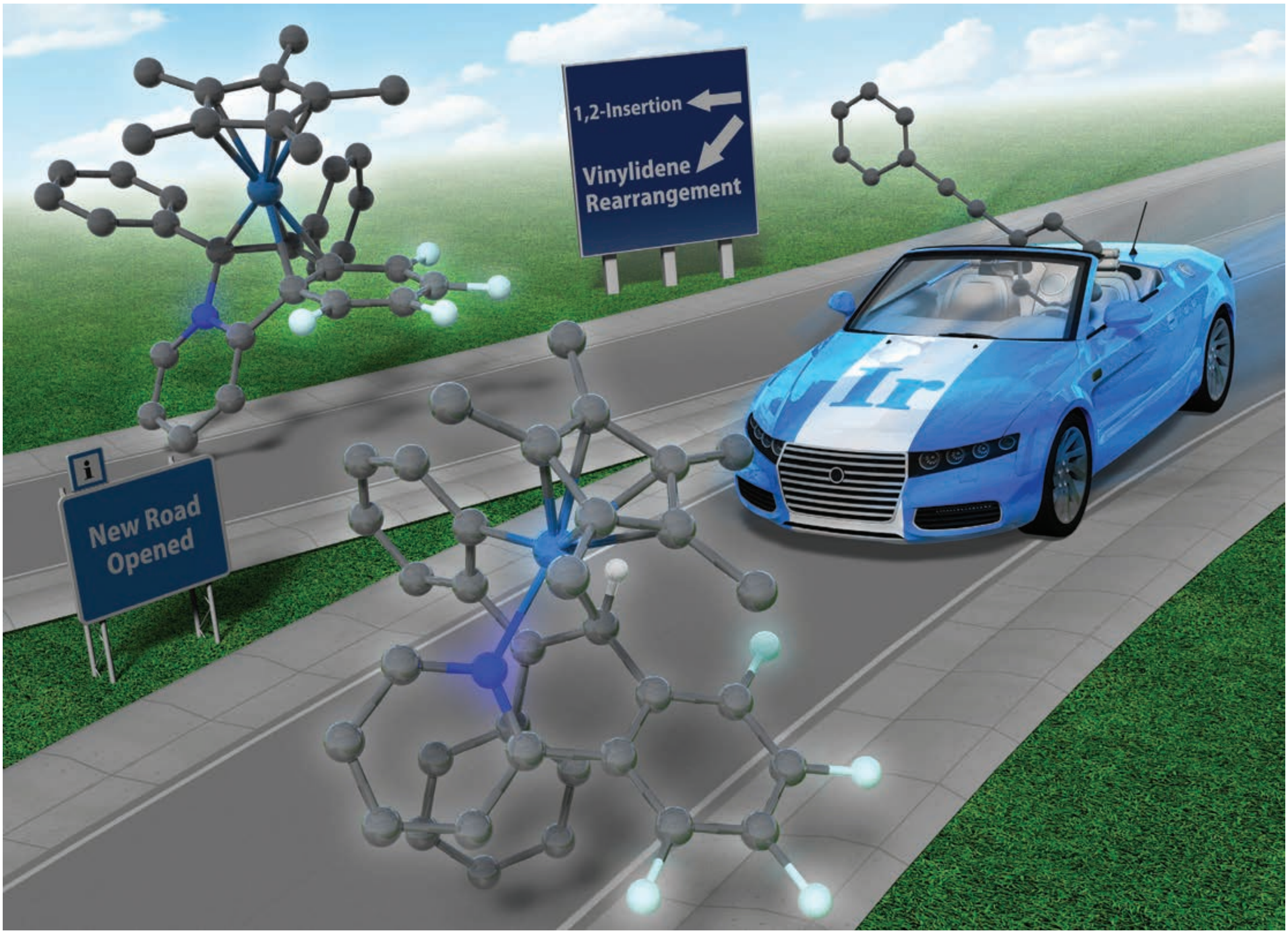

Showcasing collaborative research from the Youichi Ishii lab at Chuo University and Noriko Tsuchida lab at Saitama Medical University.

Title: Competition between vinylidene rearrangement and 1,2-insertion of carbon-disubstituted internal alkynes at a Cp*Ir(III) complex

Even carbon-disubstituted internal alkynes can select the "vinylidene rearrangement route". Vinylidene rearrangement of diarylacetylenes in an aryl-Ir(III) complex has been shown to become a kinetically (and thermodynamically) more favorable path than common 1,2-insertion.

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Competition between vinylidene rearrangement and 1,2-insertion of carbon-disubstituted internal alkynes at a Cp*Ir(III) complex†

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Competition between vinylidene rearrangement/1,1-insertion and 1,2-alkyne insertion into the Ir–Ar bond of [Cp*Ir(ppy-F_4)]$^+$ was observed on reaction with diarylacetylenes. The former process afforded the iridacycle 2 *via* the subsequent 1,4-Ir migration, whereas the latter led to the pyridoisoquinolinium complex 4. Detailed analysis revealed that 4 isomerizes to 2 by heating at 50 °C.

Vinylidene rearrangement is now recognized as one of the most valuable methods for the transformation of terminal alkynes.[1] Details of this tautomerization involving mechanistic studies[1f,2] and applications to organic synthesis[1] have been well discussed. The rich reactivities of vinylidenes as well as the accumulated mechanistic information concerning their formation brought about interest in the vinylidene rearrangement of more general alkynes.[1l] However, the tautomerization of internal alkynes is still not recognized as a common process,[1b] although a few examples of the internal alkyne-disubstituted vinylidene rearrangement have been studied by us and other groups during the last decade.[3,4] This is partly because the vinylidene rearrangement of internal alkynes is a slower process than that of terminal alkynes, hence cannot compete favorably with other metal promoted reactions. For example, internal alkynes readily insert into the metal–carbon bond of an alkyl– or aryl–metal complex in a 1,2 fashion, and therefore the vinylidene rearrangement of the alkynes does not take place. A representative reaction is found in Cp*Rh(III)-mediated annulation of 2-phenylpyridine with internal alkynes, which is first developed by Jones in 2008,[5] and the mechanism of this interesting reaction has been proposed to involve the first *ortho*-metallation of phenylpyridine to form a five-membered metallacycle [Cp*RhCl(ppy)] (ppy = 2-(2-pyridyl)phenyl) followed by the 1,2-insertion of the alkyne into the Rh–aryl bond and the reductive elimination of a C–N bond. This strategy has been applied to a variety of substrates other than 2-phenylpyridine and also expanded to catalytic versions.[6] Needless to say, vinylidene rearrangement of internal alkynes and subsequent 1,1-insertion of the disubstituted vinylidene ligand has never been observed throughout these studies.

Obviously, the general kinetic trend that the 1,2-insertion of internal alkynes is faster than their vinylidene rearrangement/1,1-insertion limits the synthetic utility of the latter process. To overcome this drawback and broaden applicability of the vinylidene rearrangement, we have explored how we can control the preference between these processes. As a model system, we have adopted [Cp*IrCl(ppy-F_4)] (**1**) (ppy-F_4 = 2,3,4,5-tetrafluoro-6-(2-pyridyl)phenyl), in which the C_6F_4 group is expected to bind to the metal more strongly than the C_6H_4 group in ppy and hence to slow down the 1,2-insertion. To our surprise, the products derived from the vinylidene rearrangement of diarylacetylenes were obtained in preference to those from the 1,2-insertion as the thermodynamic product, but not necessarily the kinetic product. This also provides the first example of vinylidene rearrangement of internal alkynes at metal complexes other than group 8 metals.

The iridium precursor **1** was readily synthesized by the reaction of $[Cp^*IrCl_2]_2$ with 2-(2,3,4,5-tetrafluorophenyl)pyridine in the presence of $NaOAc{\cdot}3H_2O$ and fully characterized by spectroscopic as well as crystallographic analysis (see ESI†). When **1** was allowed to react with diphenylacetylene and $NaBAr^F{}_4$ in $C_2H_4Cl_2$ (1,2-dichloroethane) at 50 °C for 4 h, the colour of the reaction mixture turned from yellow to dark purple (Scheme 1). Recrystallization of this mixture afforded the nine-membered iridacycle complex **2a** with an Ir–(vinyl CH) agostic interaction as dark purple crystals in 87% isolated yield, and **2a** was fully characterized by means of NMR analysis as well as a single-crystal X-ray diffraction study (Fig. 1, left). In the ^{1}H NMR spectrum, the vinyl CH signal of **2a** appears in a

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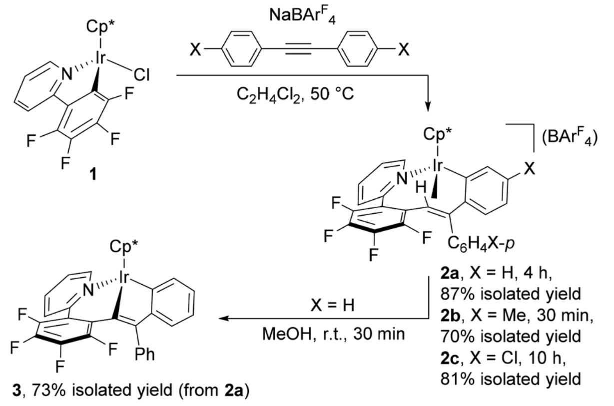
† Electronic supplementary information (ESI) available: Text, figures and CIF files giving experimental procedures and crystallographic data. CCDC 1052465–1052470. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c5dt02207j



Scheme 1 Reaction of **1** with diphenylacetylene derivatives and NaBAr$^F_4$, and deprotonation of **2a** to form **3**.

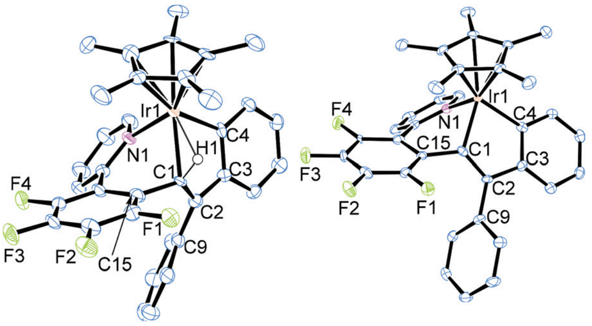
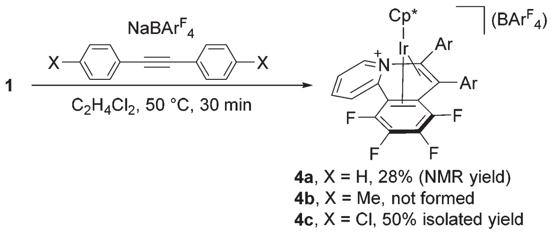


Fig. 1 ORTEP drawings of **2a** (left) and **3** (right). Anionic part and hydrogen atoms except for H1 of **2a** are omitted for clarity. Selected bond lengths (Å) and angles (°): **2a**, Ir1–N1, 2.121(5); Ir1–C1, 2.213(5); Ir1–C4, 2.026(6); Ir1–H1, 1.893; C1–C2, 1.461(9); C1–C2–C3, 114.0(5); C1–C2–C9, 123.0(6); C3–C2–C9, 122.5(6); C2–C1–C15, 119.3(5). **3**, Ir1–N1, 2.085(3); Ir1–C1, 2.033(5); Ir1–C4, 2.056(4); C1–C2, 1.346(6); Ir1–C1–C2, 120.3(3); Ir1–C1–C15, 112.8(3); C2–C1–C15, 126.0(4); C1–C2–C3, 112.5(4); C1–C2–C9, 125.4(4); C3–C2–C9, 121.7(4).

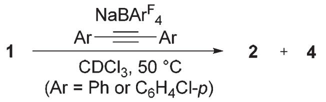
significantly low-field region (*δ* 4.16) as an agostic CH, whereas its $^{13}C\{^1H\}$ NMR signal exhibited notable high-field shift (*δ* 49.3). It is interesting to note that these spectroscopy data are in marked difference to those of the related (*o*-vinyl)aryliridium complex [Cp*Ir{*o*-$C_6H_4C(Ph){=}CHPh$}(PMe_3)][BAr$^F_4$] which showed its vinyl CH signal at *δ* −0.30 in the ^1H NMR and *δ* 86.4 in the $^{13}C\{^1H\}$ NMR spectra.[7] The molecular structure of **2a** shows that the Ir1–C1 distance at 2.214(5) Å is explicitly shorter than common agostic iridium–CH distances,[7,8] suggesting that the iridium center of **2a** interacts more strongly with the C1 atom than the common Ir–CH agostic interaction. In fact, complex **2a** easily dissociates the agostic vinyl proton by stirring in MeOH at room temperature for 30 min to form the neutral iridium(III) complex **3** in 73% isolated yield (Scheme 1). Complex **3** was fully characterized by spectroscopic as well as crystallographic analysis (Fig. 1, right). Importantly, the two Ph groups of **2a** are bound to the same carbon atom (C2), indicating that one of the Ph groups of diphenylacetylene has migrated across the C≡C bond during the reaction. In addition, one Ph group is *ortho*-metallated by the iridium center, and the H atom is transferred to the vinyl carbon (C1). These results clearly demonstrate that the formation of **2a** occurred through the initial vinylidene rearrangement to generate the diphenylvinylidene intermediate followed by the 1,1-insertion of the vinylidene ligand into the Ir–C_6F_4 bond and 1,4-Ir(III) migration[7,9] to the *ortho* position of the Ph group originated from the alkyne (*vide infra*). Similarly, *para*-substituted diphenylacetylene derivatives *p*-$XC_6H_4C{\equiv}CC_6H_4X$-*p* (X = Me, Cl) were applied to this transformation, and the corresponding cyclometallated complexes **2b** and **2c** were formed in good yield under appropriate conditions (Scheme 1). Apparently, in this system, vinylidene rearrangement of internal alkynes was more favored than 1,2-insertion into the Ir–C_{aryl} bond. It should also be mentioned that the present reaction provides the first example of the vinylidene rearrangement of carbon-disubstituted internal alkynes at an Ir complex;[10] related reactions have so far been observed only at group 8 metal complexes.[3,4]

To gain deeper insight into this reaction, we monitored the progress of the formation of **2c** at 50 °C in $CDCl_3$ by means of ^1H NMR.[11] After 30 min, **1** was consumed completely, and two Cp* signals were observed at *δ* 1.58 and 1.63 in the intensity ratio of 1 : 2.1. The former signal is assigned to **2c**, whereas the latter species was isolated in 50% yield as yellow crystals by column chromatography on silica gel and characterized unambiguously by a X-ray diffraction study (see ESI†) as the Ir(I) η^4-pyridoisoquinolinium complex **4c** (Scheme 2). A structurally related rhodium complex was already reported by Huang.[6a] Obviously complex **4c** is formed from the 1,2-insertion of the alkyne into the Ir–C_6F_4 bond to form the seven-membered metallacycle instead of the vinylidene rearrangement, and this species was further isomerized to **4c** through the reductive elimination (*vide infra*).

Surprisingly, as the reaction proceeded, isomerization of **4c** to **2c** was observed, and it was completed after 10 h (Scheme 3). Thus, complex **4c** is kinetically formed at the early stage of this reaction, and on maintaining at 50 °C, **4c** slowly isomerizes to **2c**, the thermodynamic product of this reaction. Similarly, Cp*Ir(I) complex **4a** was observed at the early stage of the reaction of **1** with PhC≡CPh as a minor species and isomerized to **2a** over 4 h (Scheme 3), although it could not be isolated in a pure form (Scheme 2).[12] On the other hand, the



Scheme 2 Formation of complexes **4**.



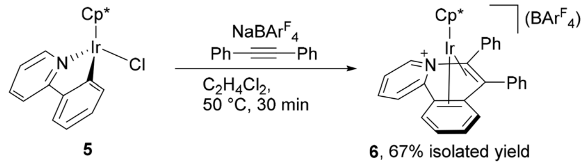
time	2a / 4a	2c / 4c
30 min	1 / 0.4	1 / 2.1
4 h	1 / 0	1 / 0.3
10 h	–	1 / 0

^{1}H NMR ratio

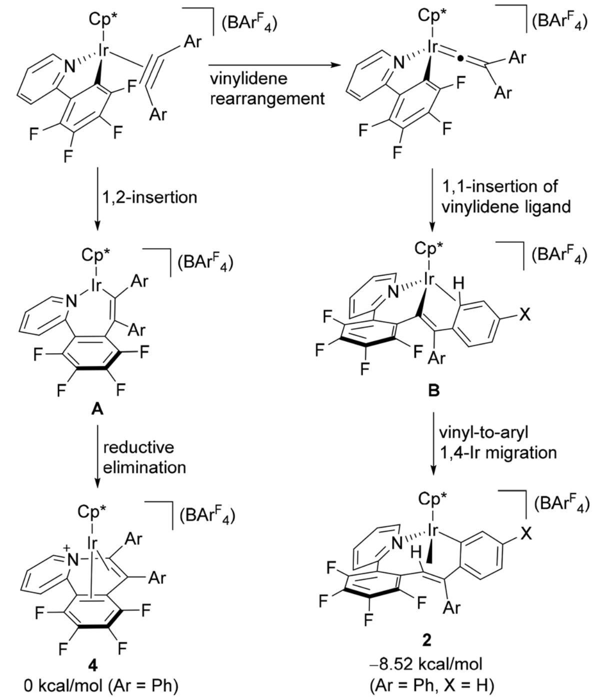
Scheme 3 Isomerization of **4** to **2** at 50 °C.

formation of **2b** was so fast that the corresponding **4b** could not be observed.

The above observation indicates that the rate of the formation of **2** is notably enhanced by introducing electron donating groups into the *para* positions of the diphenylacetylene. Recently we have shown both experimentally and theoretically that the internal alkyne-disubstituted vinylidene rearrangement at [CpRu(dppe)]$^+$ is facilitated by an electron-donating substituent,[4b,e] and this tendency is in good agreement with the present observations, suggesting that the present vinylidene rearrangement at the Ir(III) center involves nucleophilic aryl migration in the rate determining step. In addition, the ppy-F$_4$ ligand is essential for the formation of **2**; the reaction of [Cp*IrCl(ppy)] (**5**) with PhC≡CPh in the presence of NaBAr$^F_4$ at 50 °C for 30 min resulted in selective formation of **6** as the sole product in 67% yield, and the corresponding vinylaryliridium species was not formed any more (Scheme 4). For a better understanding of the above observations, preliminary density functional theory (DFT) calculations on the cationic part of **2a** and **4a** were performed with the B3PW91 functional. As expected, it was confirmed that **2a** is more stable in energy than **4a** by 8.52 kcal mol^{-1}, which gives good explanation for the selective formation of **2** as the thermodynamic product (Scheme 5). Although we must await a more detailed theoretical study, several mechanisms are considered to be plausible for the conversion of **4** to **2**. One is the C–N bond oxidative addition followed by the β-carbon elimination (back-reaction from **4**) to regenerate the η^2-alkyne complex,[13] which then undergo vinylidene rearrangement. β-Carbon elimination from a vinyl complex to form the corresponding η^2-alkyne complex is a rare process, but some examples are known in the literature.[4f,14] Alternatively, direct isomerization of the seven-membered iridacycle **A** may be operative. In this case, concerted migration of the iridium center and an aryl group (Fig. 2(a)) or an aryl group migration to eliminate C$_5$H$_4$N-C$_6$F$_4$$^-$ anion followed by its nucleophilic attack at the vinylidene α-carbon (Fig. 2(b)) is assumed to be involved.[15]



Scheme 4 Reactions of **5** with PhC≡CPh.



Scheme 5 Plausible mechanism of formation of **2** and **4**, and Gibbs energy differences between **2a** and **4a**.

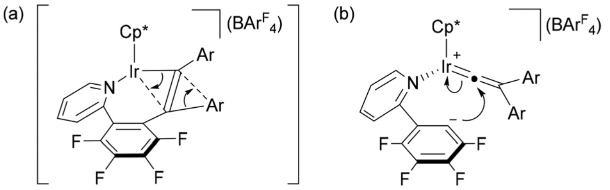
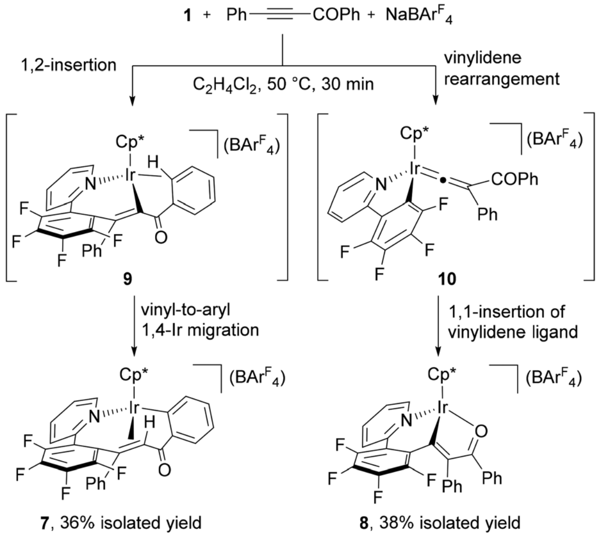


Fig. 2 Possible structures for (a) the transition state in a concerted migration of **A** into **B** (Scheme 5) and (b) the intermediate derived from aryl migration of **A** to eliminate C$_5$H$_4$N-C$_6$F$_4$$^-$ anion.

Finally, we have investigated the reactivity of **1** with acyl alkyne, which is known to be a reactive substrate towards a vinylidene rearrangement.[3,4c] When a mixture of **1** with PhC≡CCOPh and NaBAr$^F_4$ in C$_2$H$_4$Cl$_2$ was allowed to react at 50 °C for 30 min, a mixture of yellow and red crystals was obtained after recrystallization. X-ray diffraction studies disclosed that the yellow product is the ten-membered iridacycle complex **7**, while the red one is attributed to the vinyliridium complex **8** (see ESI†).[16] These complexes could be separated by column chromatography on silica gel and isolated in 36% and 38% yields, respectively.

Judging from these structures, the 1,2-insertion and vinylidene rearrangement of PhC≡CCOPh competitively occurred to generate the seven-membered vinyliridium species **9** and the iridium vinylidene species **10**. Complex **7** was formed from **9** by the 1,4-Ir migration from the vinyl to the *ortho* position of the COPh group, whereas **8** was produced by the 1,1-insertion of the vinylidene ligand in **10** into the Ir–C$_6$F$_4$ bond and the



Scheme 6 Reactions of **1** with PhC≡CCOPh and NaBAr$^F_4$.

final coordination of the oxygen atom of the carbonyl group (Scheme 6). Unlike the reaction with diarylalkynes, the ratio of **7** and **8** was not changed by further heating at 50 °C.[17]

In conclusion, we have revealed that the reaction of [Cp*Ir(ppy-F$_4$)]$^+$ with diphenylacetylene derivatives afforded the nine-membered metallacycle complex **2** by way of the sequential vinylidene rearrangement, 1,1-insertion of the vinylidene ligand, and the 1,4-Ir migration to the Ar group. Detailed analysis of this reaction disclosed that **2** and the Ir(I) pyridoisoquinolinium complex **4**, the latter of which is a normal 1,2-insertion–reductive elimination product, are competitively generated at the early stage of the reaction, but **4** is gradually isomerized to **2**, indicating that **2** is the thermodynamically favoured product. The present reaction provides not only the first example of the internal alkyne-disubstituted vinylidene rearrangement at an iridium complex but also a rare example of actual observation of the competition between vinylidene rearrangement and 1,2-insertion of internal alkynes.

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12 The structure of **4a** was determined by a preliminary single-crystal X-ray diffraction study.

13 Preliminary DFT calculation indicated that the free energy barrier of activation for the β-carbon elimination is *ca.* 19 kcal mol^{-1} (see ESI†), and therefore we consider that the formation of the η^2-alkyne complex from **A** is acceptable in the present reaction conditions, while we have not obtained satisfactory calculation results to explain the C–N bond oxidative addition yet.

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16 The ^{1}H NMR analysis of the crude reaction mixture indicated that complexes **7** and **8** were formed in the ratio of 1.4 : 1.

17 When isolated **7** and **8** are dissolved in $C_2H_4Cl_2$ and kept at 50 °C overnight, no isomerization was observed for both complexes.