DOI: 10.1002/adsc.200800544

Substituent Effect on the Formation and Reactivity of Platinum Carbenoids

Eun Jin Cho[a] and Daesung Lee[b,*]

[a] Department of Chemistry, University of Wisconsin, Madison, Wisconsin 53706, USA
[b] Department of Chemistry, University of Illinois at Chicago, 845 West Taylor Street, Chicago, Illinois 60607, USA
Fax: (+1)-312-996-0431; phone: (+1)-312-996-5189; e-mail: dsunglee@uic.edu

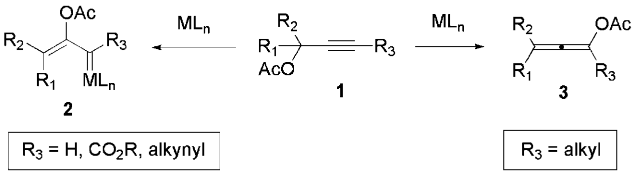
Received: September 3, 2008; Published online: November 19, 2008

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.200800544.

Abstract: A propargylic ester containing a propargylic alkoxy group has been observed to preferentially undergo [1,2]-acyl shift over [1,3]-shift. In addition, the complementary and contrasting reactivity of vinyl *vs.* alkynyl platinum carbenoids has been discovered. Vinyl platinum carbenoids are more prone to undergo [1,2]-H shift over addition to π-bonds whereas alkynyl platinum carbenoids preferentially add to π-bonds.

Keywords: alkynes; carbenoids; cyclopropanes; platinum; substituent effects

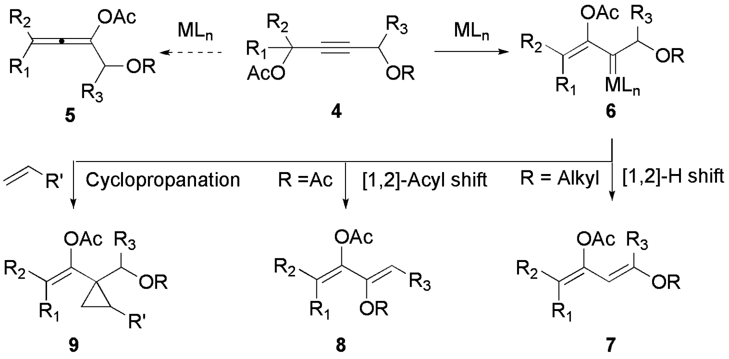
Carbenes and carbenoids are versatile intermediates in organic chemistry. Usually, diazo compounds serve as precursors to these reactive species under photolytic, thermal, or transition metal-catalyzed conditions.[1] And yet, due to the inconvenience of their preparation and their hazardous nature, an alternative source for these species is highly desirable. In this context, an alkyne such as propargylic ester **1**[2] would be an ideal precursor to generate a metal-carbenoid **2** if the alkyne can be properly activated by electrophilic transition metals[3] under appropriate conditions (Scheme 1). However, the potential of this transition metal-based alkyne activation is significantly reduced by the propensity of **1** to undergo a [1,3]-acyl shift to generate allene **3**[4] over a [1,2]-shift to form vinyl metal carbenoid **2**, if the alkyne moiety is internal. In general, only terminal alkynes ($R_3 = H$)[5] and internal alkynes with electron-withdrawing substituent ($R_3 = CO_2R$)[6] were known to provide the metal carbenoid **2**.



Scheme 1. [1,2]- *vs.* [1,3]-acyl shift.

Recently, in the study of the metallotropic [1,3]-shift[7] of electrophilic metal complexes, we have shown that a 1,3-diyne-containing system ($R_3 =$ alkynyl group) provided strong preference for [1,2]-acyl shift, thereby selectively generating vinyl carbenoid **2**.[8] Recognizing the subtlety of the electronic influence by the R_3 substituent for the [1,2]- and [1,3]-acyl shift, we envisioned that the introduction of an electron-withdrawing oxygen substituent at the propargylic carbon of **4** would provide enough driving force for the formation of carbenoid **6** over **5** *via* an [1,2]-acyl shift (Scheme 2).[9] Furthermore, the oxygen substituent would also allow an alternative trapping mechanism of metal carbenoid **6** to form 1,3-diene **7** through a [1,2]-hydride shift[5f,10] due to an electronic effect of the oxygen substituent. This would nicely complement the more prevailing trapping manifolds of reactions of **6** through [1,2]-acyl migration forming **8** or intra-/intermolecular cyclopropanation generating **9**. We report herein a prominent role of the propargylic oxygen substituent to induce [1,2]-acyl migration in the initiation step and a favorable [1,2]-hydride shift at the termination step. This ultimately allowed us to observe the conspicuous difference in trapping preference between vinyl and alkynyl carbenoids, where the former have a higher tendency to undergo [1,2]-hydride shift whereas the latter favour an addition to alkenes and alkynes.

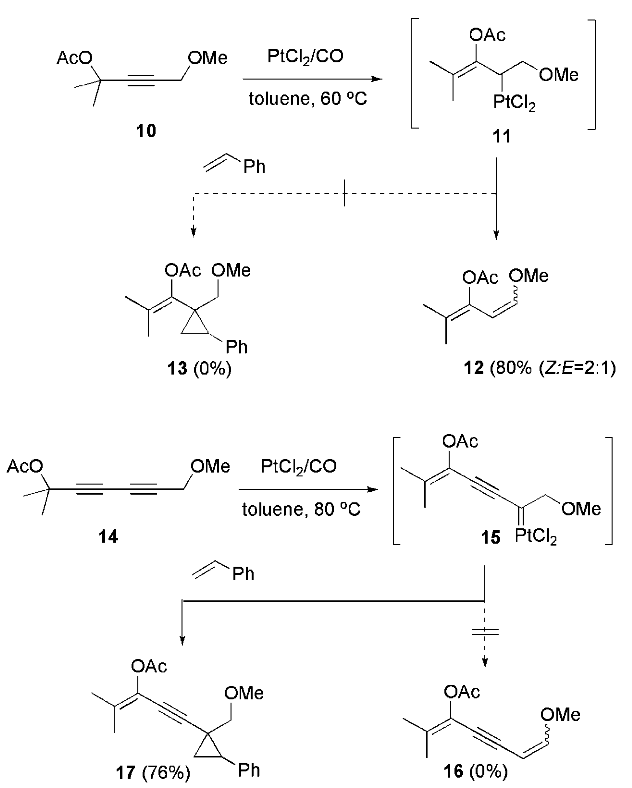
First, we examined substrate **10** containing a propargylic methoxy substituent for its [1,2]-acyl shift and the termination behaviour of the resultant carbenoid. When **10** was subjected to typical reaction conditions (5 mol% $PtCl_2$ under CO,[11] toluene, 80 °C) the ex-



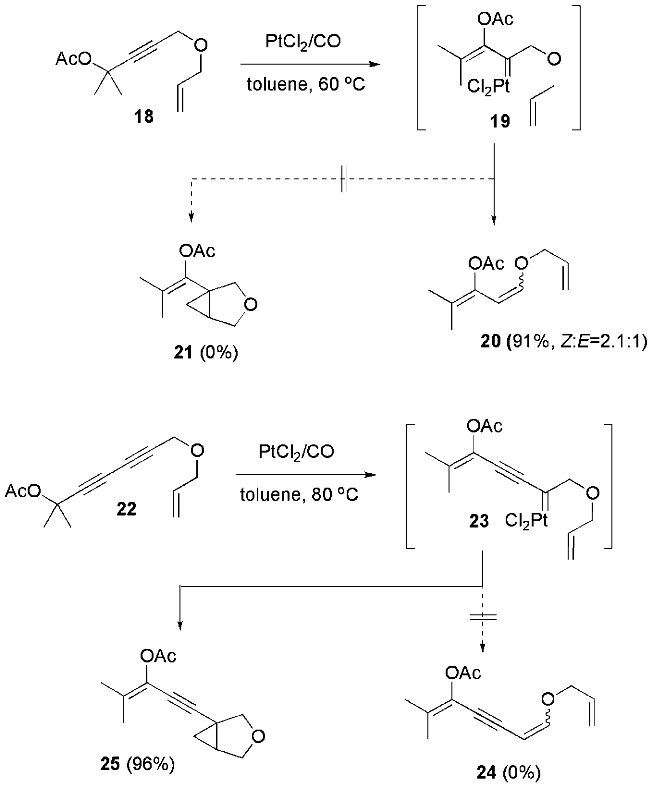
Scheme 2. Controlled [1,2]-acyl shift to form vinyl carbenoid and its trapping.

pected 1,3-diene **12** was obtained in high yield as a mixture of *Z/E* isomers (Scheme 3). Based on the known examples of intermolecular trapping of vinyl carbenoid of type **11** with styrene,[12] we expected that in the presence of an excess amount of styrene, it should deliver cyclopropanated product **13**. However, even in the presence of an excess amount of styrene the cyclopropanated product **13** was not obtained, instead still **12** was produced as the sole product. In comparison, under identical conditions, 1,3-diyne **14** did not lead to [1,2]-hydride shifted product **16** and most starting material was recovered unchanged. On the other hand, efficient intermolecular cyclopropanation occurred in the presence of styrene to yield product **17** in 76% (3.8:1). This result clearly suggests that vinyl carbenoid **11** preferentially undergoes [1,2]-hydride shift[13] whereas alkynyl carbenoid **15** prefers to react with double bond of styrene, thereby indicating significant differences in reactivity between these carbenoids.[12,14]

This reactivity difference manifested by putative vinyl carbenoid **11** and alkynyl carbenoid **15** was further examined by using substrates **18** and **22** that contain an allyl ether moiety by which the respective carbenoid intermediates would be readily trapped intramolecularly (Scheme 4). We surmised that the reac-



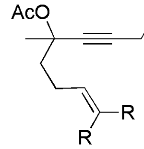
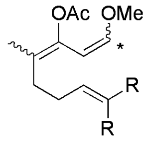
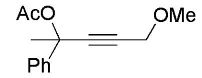
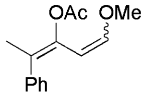
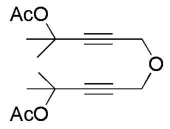
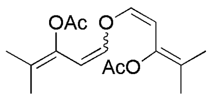
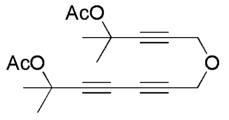
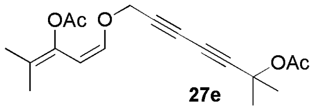
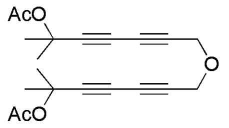
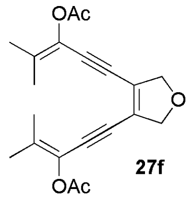
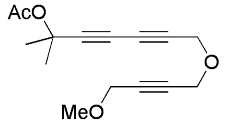
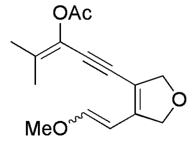
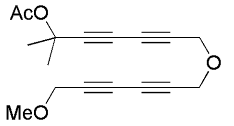
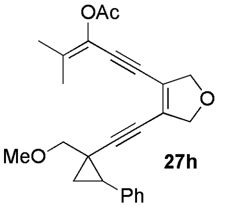
Scheme 3. The reactivity difference between vinyl and alkynyl Pt-carbenoids.



Scheme 4. The reactivity difference between vinyl and alkynyl Pt-carbenoids.

tions with these substrates would eliminate any uncertainty related to the entropy-based kinetic barrier, thereby showing the inherent reactivity difference more clearly. Under standard conditions (5 mol% $PtCl_2$ under CO, toluene, 60 °C), the reaction of substrate **18** selectively produced [1,2]-hydride shifted product **20** (91%, Z:E = 2.1:1) without any indication of formation of cyclopropanated product **21**. On the other hand, the related 1,3-diyne **22** gave only cyclopropanated product **25** in 96% yield devoid of [1,2]-hydride shifted product **24**.[15] Again, this result is believed to be caused by the reactivity difference between vinyl carbenoid **19** and alkynyl carbenoid **23**, which further corroborates the previous conclusion that vinyl Pt-carbenoids prefer [1,2]-hydride shift whereas alkynyl Pt-carbenoids favour cyclopropanation. It is worth emphasizing that propargylic acetoxyalkynes **10/18** and **14/22**, although internal alkynes

Table 1. Products from [1,2]-H shift of vinyl carbenoids and addition to alkenes and alkynes of alkynyl carbenoids.[a]

Entry		Substrate	Temp (°C)	Product		Yield (%)^b	Z/E ratio^c
1	**26a** (R = H)		60		**27a** (R = H)	70^d	1 : 2.8^e
2	**26b** (R = Me)		60		**27b** (R = Me)	92	5.1 : 1^e
3	**26c**		40		**27c**	77	2.2 : 1
4	**26d**		40		**27d**	75	1.7 : 1
5	**26e**		60		**27e**	67	1.0 : 1
6	**26f**		80		**27f**	92	—
7	**26g**		80		**27g**	47	1 : 1.2
8	**26h**		80		**27h**	26^f	—

[a] Conditions: 5 mol% $PtCl_2$, under CO, toluene.

[b] Isolated yield.

[c] Z/E ratio of crude products.

[d] Additional 20% of the corresponding hydrolyzed aldehyde was isolated.

[e] Z/E ratio of the methyl enol ether (*).

[f] Mixture of diastereomers in 2.9:1 ratio.

are known to promote allene formation, did not provide any allenes *via* [1,3]-acetoxy shift. They delivered products only derived from the putative vinyl Pt-carbenoids, which can be rationalized by the presence of electron-withdrawing methoxy and allyloxy substituents for the monoynes and the alkynyl substituent for the diynes.

Having shown the salient reactivity difference between vinyl and alkynyl Pt-carbenoids, diverse substrates were employed to confirm the observed reactivity in broader context. Especially, the trapping of initially formed alkynyl Pt-carbenoids by tethered alkynes instead of alkenes in substrates **26f** will further bolster their preferred reactivity toward π-bonds over [1,2]-hydride shift (Table 1). Substrate **26a** that contains a tethered terminal alkene provided only [1,2]-hydride shifted product **27a** in 70% yield as a mixture of *E/Z* isomers (entry 1). Similarly, a trisubstituted alkene-containing substrate **26b** also gave **27b** in 92% yield without any sign of cyclopropanated product (entry 2). An aromatic substituent[16] in **26c** did not perturb the reactivity of the corresponding vinyl Pt-carbenoid, producing 1,3-diene product **27c** in 77% yield (entry 3). The reaction of symmetrical monoyne **26d** yielded **27d** *via* a consecutive [1,2]-OAc shift followed by a [1,2]-hydride shift in 75% yield (*Z:E*=1.7:1) at 40 °C (entry 4). On the other hand, substrate **26e** (entry 5), containing mono- and diyne moieties that can potentially compete, yielded product **27e** (*Z*-isomer, 67% at 47% conversion), where only the monoyne was transformed to a 1,3-diene moiety presumably *via* a vinyl Pt-carbenoid. This result suggests that a monoyne is more reactive than the corresponding diyne. In comparison, the reaction of symmetrical diyne **26f** gave symmetrical enediyne **27f** in 92% yield, which is the result of the favourable addition over a [1,2]-H shift of the initially formed alkynyl carbenoid onto the other 1,3-diyne moiety across the tether (entry 6). The differential reactivity of vinyl and alkynyl Pt-carbenoids was further examined using a diyne initiator moiety of substrates **26g** and **26h**. The reaction of **26g** containing a monoyne terminating group gave **27g** in 47% yield (*Z:E*=1:1.2) *via* the penultimate vinyl Pt-carbenoid, which ultimately delivered the observed product *via* a [1,2]-hydride shift (entry 7). On the other hand, **26h** with diyne terminating group, which eventually generated an alkynyl carbenoid at the penultimate stage of the catalytic cycle, did not give any product in the absence of styrene but yielded cyclopropanated product **27h** in 26% yield in the presence of styrene (entry 8). Decomposition of products as well as other side reactions such as aromatization seem to account for the low yields of the last two reactions.

In conclusion, we have observed that propargylic esters containing a propargylic alkoxy group preferentially undergo [1,2]-acyl shift over [1,3]-shift with $PtCl_2$. In this study, we also have demonstrated that vinyl and alkynyl Pt-carbenenoids have significantly different reactivity: vinyl Pt-carbenoids have the propensity to undergo [1,2]-H shift whereas alkynyl Pt-carbenoids preferentially add to π-bonds in both intra- and intermolecular reactions. Further study to elucidate the origin of the difference between these carbenoids will be reported in due course.

Experimental Section

General Procedure for $PtCl_2$-Catalyzed Reactions

$PtCl_2$ (5 mol%) was added to a solution of the alkyne in toluene (0.05 M), and CO was bubbled through the solution. The mixture was warmed to the appropriate temperature (40 °C, 60 °C, or 80 °C) and stirred until the reaction was complete (30 min–2 h). The mixture was cooled to room temperature and the solvent was evaporated under vacuum. Purification by flash chromatography on silica gel (hexane/ethyl ether) afforded the product.

Acknowledgements

We thank the NIH for financial support of this work as well as the NSF and NIH for NMR and Mass Spectrometry instrumentation.

References

[1] a) G. Mass, *Top. Curr. Chem.* **1987**, *137*, 75–253; b) M. P. Doyle, M. A. McKervey, T. Ye, *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds* Wiley-Interscience, New York, **1998**; c) T. Ye, M. A. Mckervey, *Chem. Rev.* **1994**, *94*, 1091–1160; d) A. Padwa, M. D. Weinngarten, *Chem. Rev.* **1996**, *96*, 223–269.

[2] Reviews on metal-catalyzed reactions of propargylic esters: a) N. Marion, S. P. Nolan, *Angew. Chem. Int. Ed.* **2007**, *46*, 2750–2752; b) J. Marco-Contelles, E. Soriano, *Chem. Eur. J.* **2007**, *13*, 1350–1357.

[3] Recent reviews on gold and platinum-catalyzed reactions: a) A. Fürstner, P. W. Davies, *Angew. Chem. Int. Ed.* **2007**, *46*, 3410–3449; b) D. J. Gorin, F. D. Toste, *Nature* **2007**, *446*, 395–403; c) A. S. K. Hashmi, *Chem. Rev.* **2007**, *107*, 3180–3211; d) E. Jimenez-Nunez, A. M. Echavarren, *Chem. Commun.* **2007**, 333–346; e) L. Zhang, J. Sun, S. A. Kozmin, *Adv. Synth. Catal.* **2006**, *348*, 2271–2296.

[4] Examples of [1,3]-acyl shift in gold and platinum- catalyzed reactions: a) L. Zhang, *J. Am. Chem. Soc.* **2005**, *127*, 16804–16805; b) N. Marion, S. Díez-González, P. de Frémont, A. R. Noble, S. P. Nolan, *Angew. Chem. Int. Ed.* **2006**, *45*, 3647–3650; c) J. Zhao, C. O. Hughes, F. D. Toste, *J. Am. Chem. Soc.* **2006**, *128*, 7436–7437; d) C. H. Oh, A. Kim, W. Park, D. I. Park, N. Kim, *Synlett* **2006**, 2781–2784; e) L. Zhang, S. Wang, *J. Am. Chem. Soc.* **2006**, *128*, 1442–1443; f) S. Wang, L.

Zhang, *J. Am. Chem. Soc.* **2006**, *128*, 8414–8415; g) S. Wang, L. Zhang, *Org. Lett.* **2006**, *8*, 4585–4587; h) A. Buzas, F. Istrate, F. Gagosz, *Org. Lett.* **2006**, *8*, 1957–1959; i) A. Buzas, F. Gagosz, *J. Am. Chem. Soc.* **2006**, *128*, 12614–12615; j) M. Yu, G. Li, S. Wang, G. Zhang, *Adv. Synth. Catal.* **2007**, *349*, 871–875.

[5] Examples of [1,2]-acyl shift: a) V. Rautenstrauch, *J. Org. Chem.* **1984**, *49*, 950–952; b) E. Mainetti, V. Mouriès, L. Fensterbank, M. Malacria, J. Macro-Contelles, *Angew. Chem. Int. Ed.* **2002**, *41*, 2132–2135; c) K. Miki, K. Ohe, S. Uemura, *J. Org. Chem.* **2003**, *68*, 8505–8513; d) V. Mamane, T. Gress, H. Krause, A. Fürstner, *J. Am. Chem. Soc.* **2004**, *126*, 8654–8655; e) D. J. Gorin, S. T. Staben, F. D. Toste, *J. Am. Chem. Soc.* **2005**, *127*, 18002–18003; an exception to this general trend, see: f) L. Zhang, G. Li, G. Zhang, *J. Am. Chem. Soc.* **2008**, *130*, 3740–3741; application to natural products, see: g) A. Fürstner, P. Hannen, *Chem. Eur. J.* **2006**, *12*, 3006–3019; h) C. Fehr, J. Galindo, *Angew. Chem. Int. Ed.* **2006**, *45*, 2901–2904.

[6] B. A. B. Prasad, F. K. Yoshimoto, R. Sarpong, *J. Am. Chem. Soc.* **2005**, *127*, 12468–12469.

[7] A recent review on metallotropic shift of alkynyl carbenoids: D. Lee, M. Kim, *Org. Biomol. Chem.* **2007**, *5*, 3418–3427.

[8] Reactions of diynes: a) E. J. Cho, M. Kim, D. Lee, *Eur. J. Org. Chem.* **2006**, 3074–3078; b) E. J. Cho, M. Kim, D. Lee, *Org. Lett.* **2006**, *8*, 5413–5416; c) D. J. Gorin, P. Dubé, F. D. Toste, *J. Am. Chem. Soc.* **2006**, *128*, 14480–14481.

[9] It was observed that the alkyl and aryl substituents at the propargylic site (R_1 and R_2 are alkyl or aryl) increase the reactivity of the substrates significantly probably due to both the electronic and steric reasons (see ref.[8a]) but their role to affect the selectivity between [1,2]- *vs.* [1,3]-acyl shift has not been confirmed. DFT study for [1,2]- *vs.* [1,3]-acyl shift, see: A. Correa, N. Marion, L. Fensterbank, M. Malacria, S. P. Nolan, L. Cavallo, *Angew. Chem. Int. Ed.* **2008**, *47*, 718–721.

[10] Examples of [1,2]-hydride shift: a) A. Padwa, D. J. Austin, Y. Gareau, J. M. Kassir, S. L. Xu, *J. Am. Chem. Soc.* **1993**, *115*, 2637–2647; b) A. Furstner, F. Stelzer, H. Szillat, *J. Am. Chem. Soc.* **2001**, *123*, 11863–11869; c) C. A. Witham, P. Mauleon, N. D. Shapiro, B. D. Sherry, F. D. Toste, *J. Am. Chem. Soc.* **2007**, *129*, 5838–5839.

[11] Reactions with Pt-catalyst under CO atmosphere: a) J. M. Lutton, R. W. Parry, *J. Am. Chem. Soc.* **1954**, *76*, 4271–4274; b) A. Fürstner, P. W. Davies, T. Gress, *J. Am. Chem. Soc.* **2005**, *127*, 8244–8245; c) A. Fürstner, C. Aissa, *J. Am. Chem. Soc.* **2006**, *128*, 6306–6307.

[12] Examples of intermolecular cyclopropanation of vinyl Ru-carbenoid, and Au-carbenoids, see refs.[5c,e].

[13] It is interesting to note that vinyl Rh-carbenoid selectively undergo allylic C–H insertion over addition to double bonds. Considering that [1,2]-hydride shift can be viewed as a C–H insertion to a vicinal C–H bond, the preferred reactivity of vinyl Pt-carbenoid for [1,2]-hydride shift and that of Rh-carbenoid for C–H insertion seems to have close mechanistic similarity. For an excellent review on donor-acceptor substituted Rh-carbenoids, see: a) H. M. L. Davies, J, Nikolai, *Org. Biomol. Chem.* **2005**, *3*, 4176–4187. For an example of C–H insertion by Pt-carbenoid, see: b) C. H. Oh, J. H. Lee, S. J. Lee, J. I. Kim, C. S. Hong, *Angew. Chem. Int. Ed.* **2008**, *47*, 7505–7507.

[14] An example of intermolecular cyclopropanation of alkynyl Au-carbenoids, see ref.[8c].

[15] Vinyl Pt-carbenoid preferentially reacts with double bond intramolecularly over [1,2]-hydride shift at the termination step, see ref.[11b]

[16] The participation of an aryl group at the propargylic position in the reaction, see refs.[4b,6].