DOI: 10.1002/chem.201103799

Factors Controlling the Equilibrium of Pt-Catalyzed [1,2]- versus [1,3]-Acyloxy Migration

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The development of reactions involving electrophilic transition-metal-catalyzed activation of alkynes have revealed the various hidden reactivity of alkynes.[1] In platinum- and gold-catalyzed reactions, the substituent pattern and electronic variation on and near the alkyne have profound impacts on the reaction pathway of substrates. When activated by platinum or gold, the propargylic acetate **1** has a propensity to undergo [1,2]-acyloxy migration to form vinyl carbenoid **2**, or, it generates allenyl acetate **3** by [1,3]-acyloxy migration, an example of [3,3]-sigmatropic rearrangement (Figure 1).[2] It is widely accepted that terminal or internal alkynes with an electron-withdrawing R substituent preferentially undergo reactions through pathway **A**,[3,4] whereas reactions of other internal alkynes generally proceed through pathway **B**.[5]

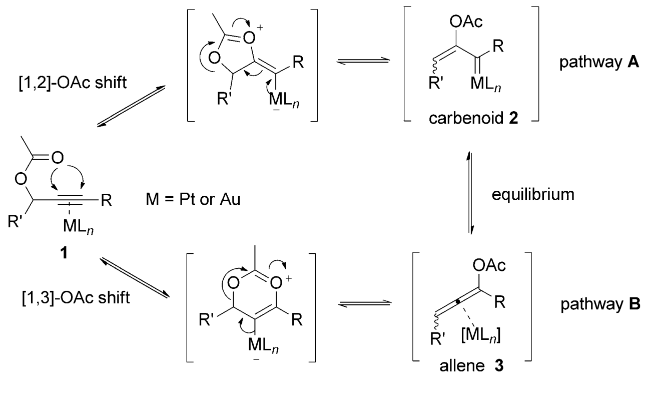


Figure 1. Pt- and Au-catalyzed reaction pathways of propargylic esters.

Although these two competing pathways are generally assumed to be reversible, this theory lacks direct experimental evidence.[6] Furthermore, controlling the [1,2]- versus [1,3]-acyloxy migration is a mechanistically controversial issue.[7] Herein, clear evidence for the reversible interconversion between carbenoid **2** and allene **3** is presented. In addition, it is shown that [1,2]- versus [1,3]-acyloxy migration can be controlled by reaction temperature, alkyne substituent pattern, and the nature of the catalyst.

First, the interconversion between the carbenoid and allene intermediates was observed from the reactions of substrates containing a propargylic alkoxy group. These reactions were found to be dependent on the reaction temperature. It was previously reported that reactions of alkoxy group-containing substrates (of type **4**) generated exclusively 1,3-dienes **6** with $PtCl_2$ under CO at 40–60 °C through [1,2]-acyloxy migration followed by a [1,2]-hydride shift (Figure 2).[8]

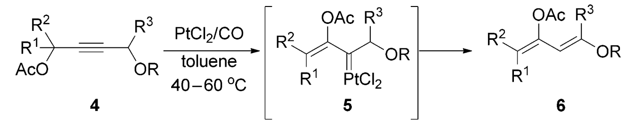
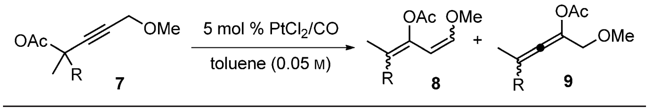
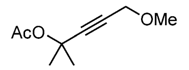
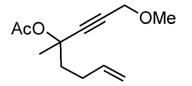


Figure 2. The formation of 1,3-diene by using propargylic esters containing an alkoxy group.

However, at a lower reaction temperatures, the same substrates could also yield allenes through a [1,3]-acyloxy migration under otherwise identical conditions (5 mol% $PtCl_2$ under CO[9] in toluene). The reaction of **7a** produced a mixture of [1,2]- and [1,3]-acyloxy-migrated products **8a** and **9a**, respectively, in a ratio of 1.5:1 at room temperature, whereas only 1,3-diene **8a** was generated at 60 °C (Table 1,

Table 1. Product distribution dependent on reaction temperature.



Entry	Reaction	T [°C]	Yield[a] [% (Z/E ratio)]	
	R = Me		R = Me	
1	 **7a**	25 60	**8a**, 48 (5.3:1) **8a**, 80 (2:1)	**9a**, 32 **9a**, 0
	$R = CH_2CH_2CH_2CH_2$		$R = CH_2CH_2CH_2CH_2$	
2	 **7b**	25 60	**8b**, 33 (2:1) **8b**, 70 (2:1)	**9b**, 57 **9b**, 0

[a] Isolated product yield.

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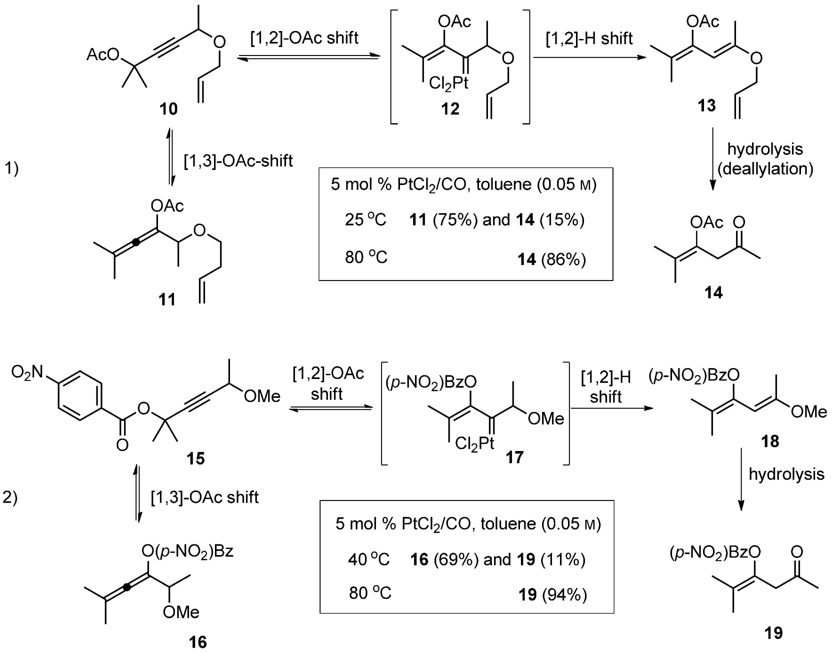
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201103799.



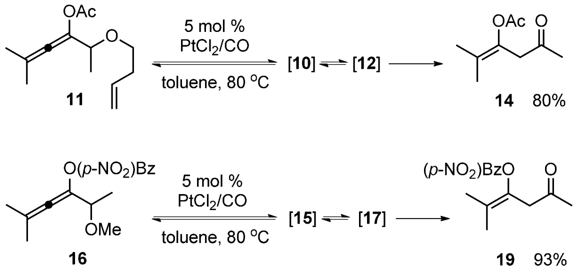
Scheme 1. Product distribution dependent on reaction temperature.

entry 1). The reaction of **7b**, which gave exclusively **8b** at 60 °C, also generated a mixture of **8b** and **9b** in a ratio of 1: 1.7 (Table 2, entry 2).[10] These results imply that, at a higher temperature, the initially formed allenes revert back to the starting materials so that the equilibrium eventually drains down to the observed 1,3-diene products.

Reactions of compounds **10** and **15** further demonstrate the temperature-dependent product distribution through the interconversion of [1,2]- and [1,3]-acyloxy-migrated intermediates (Scheme 1). The reaction of **10** gave a mixture of **11** and **14** in a ratio of 5:1 at room temperature, but it gave only **14** at 80 °C. This is likely the consequence of interconversion between **11** and **12** through propargylic acetate **10** and an irreversible [1,2]-H shift of **12** to **13** followed by hydrolysis to form **14** at higher temperatures. The reaction of **15**, which contains a propargylic methoxy group and *para*-nitrobenzoate, showed a similar behavior. A mixture of [1,3]- and [1,2]-acyloxy-shifted products **16** and **19** were isolated in a ratio of 6.3:1 at lower temperatures (at 40 °C) but only the [1,2]-acyl-shifted product **19** was obtained at 80 °C.

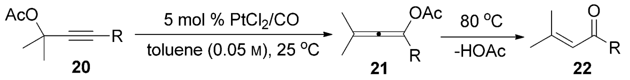
The conversion of the isolated [1,3]-shifted products to the corresponding [1,2]-shifted products further confirmed the interconversion of allenes and vinyl carbenoids. When isolated allenes **11** and **16** were subjected to the same reaction conditions again ($PtCl_2$/CO, toluene) at 80 °C, only the [1,2]-shifted products **14** and **19** were generated (Scheme 2). These results should be the consequence of the reverse [1,3]-acyloxy migration of **11** and **16** to propargylic esters **10** and **15** and subsequent [1,2]-acyloxy migration to form vinyl carbenoids followed by their [1,2]-H shift and hydrolysis.

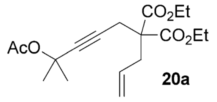
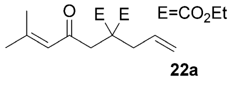
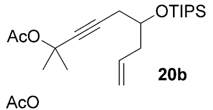
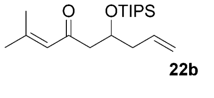
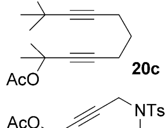
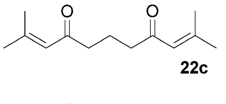
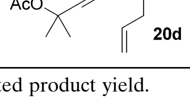
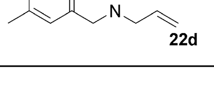
The equilibrium between [1,2]- and [1,3]-acyloxy migrations was also studied with other systems. As expected from the propensity of internal alkynes to undergo [1,3]-acyloxy migration, allene products **21** were obtained from the reactions of **20a**–**20d** under the same conditions (5 mol % $PtCl_2$ under CO, toluene, 25 °C; Table 2). Interestingly, unreacted substrates and allenyl intermediates were transformed into α,β-unsaturated ketones **22a**–**22d** at 80 °C through hydrolysis presumably by adventitious water. The lack of α-alkylidene-β-diketone formation from reactions with $PtCl_2$ implies a subtle difference in reactivity between Pt- and Au-catalysts.[11] Based on the observed product distribution, it is also concluded that the irreversible [1,2]-hydride shifts of vinyl Pt-carbenoids **12** and **17** to **13** and **18** in Scheme 1 are much



Scheme 2. Evidence for the interconversion of allenes and carbenoids through reversible acyloxy migration.

Table 2. Enone formation of internal propagylic acetates through [1,3]-acyloxy migration followed by hydrolysis.

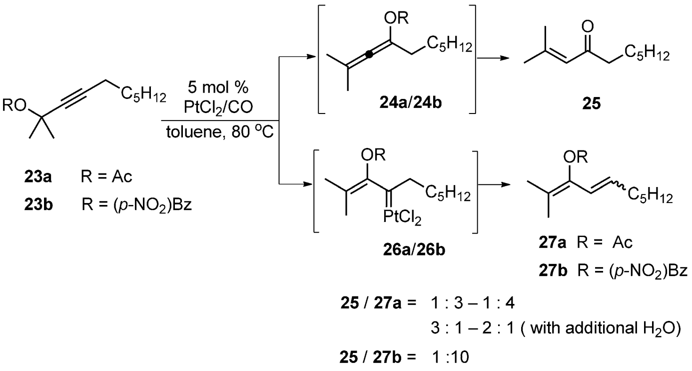


Entry	Substrates	Products	Yield[a] [%]
1	 **20a**	 **22a**	91
2	 **20b**	 **22b**	87
3	 **20c**	 **22c**	66
4	 **20d**	 **22d**	80

[a] Isolated product yield.

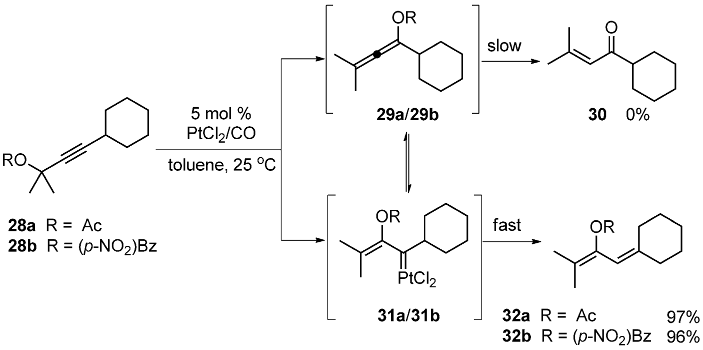
faster than the hydrolysis of allenes **11** and **16**. Otherwise, enone products would be obtained from the hydrolysis of allenes at 80 °C as shown in Table 2.

Although alkynes preferentially undergo [1,3]-acyloxy migration, trace amounts of [1,2]-OAc-shifted products were also obtained from **20c** and **20d** with major [1,3]-OAc-shifted products **22c** and **22d** in Table 2. In this context, **23a** and **23b** were next used to examine whether [1,2]- versus [1,3]-acyloxy migration could be controlled even in electronically unbiased internal alkynes (Scheme 3).[12] The reactions of **23a** and **23b** yielded a mixture of products **25** and **27a**/**27b** from [1,3]-acyloxy migration and [1,2]-acyloxy migration, respectively. Acetate **23a** gave a 1:3 to 1:4 ratio of **25** (from a [1,3]-OAc shift and hydrolysis) and **27a** (from a [1,2]-OAc shift followed by [1,2]-H shift) with the same catalyst system (5 mol% $PtCl_2$ under CO) in dry toluene at 80 °C. The addition of a small amount of water increased the yield of **25** by promoting the hydrolysis of allene **24a**. Interestingly, the use of *para*-nitrobenzoate gave **27b** as a major product via the [1,2]-shift of benzoate and a [1,2]-H shift. It is likely that the use of sterically hindered ester retards the hydrolysis of **24b**, reducing the formation of enone compound **25**, thus giving **27b** as a major product.



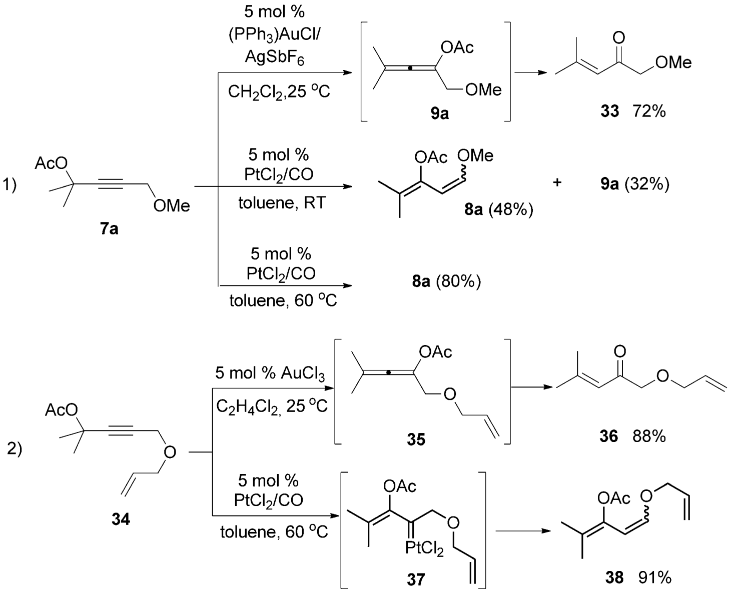
Scheme 3. Steric effect of sterically demanding propargylic ester for the selectivity of [1,2]- versus [1,3]-acyloxy migration.

The substituent pattern around the alkyne affects the reaction course as well. The reaction of **23a**/**23b** with a linear alkyl group at the propargylic position generated a mixture of [1,3]- and [1,2]-acyloxy-migrated products, as shown in Scheme 3. However, the reaction of **28a**/**28b** with a branched alkyl group at the same position gave only 1,3-diene **32a**/**32b** through [1,2]-acyloxy migration followed by [1,2]-H shift, regardless of the kind of ester (Scheme 4). This suggests that the extra alkyl group at the propargylic center of **29a**/**29b** should slow down the deacylation whereby the formation of enone **30** was prohibited. Moreover, the [1,2]-H shift of the tertiary C–H of **31a**/**31b** is faster than that of the corresponding secondary C–H, resulting in the efficient formation of trisubstituted alkene **32a**/**32b**. It was recognized that reactions of **23a**/**23b** with a secondary C–H bond required a higher reaction temperature (80 °C) in Scheme 3, whereas reactions of **28a**/**28b** with a tertiary C–H bond provided products **32a**/**32b** in excellent yield even at room temperature.



Scheme 4. Steric effect of the tertiary alkyl group at the propargylic center.

In addition to the reaction temperature and the substituent pattern around the alkyne, the nature of the catalyst also affected the reaction course. Au-catalyzed reactions provided different results from Pt-catalyzed reactions. Although **7a** yielded a mixture of [1,2]- and [1,3]-acyloxy-shifted products with $PtCl_2$ at room temperature, and only [1,2]-shifted product **8a** at 60 °C as shown in Table 1 and Scheme 5, the same substrate underwent [1,3]-acyloxy migration to give only compound **33** in 72 % yield after hydrolysis with 5 mol% $(PPh_3)AuCl/AgSbF_6$ (Scheme 5). Similarly, the reaction of **34** with 5 mol% $AuCl_3$ exclusively provided the [1,3]-OAc shift-hydolysis product **36** in 88 % yield at room temperature, whereas the reaction with $PtCl_2$ gave 1,3-diene **38** by [1,2]-acyloxy migration followed by a [1,2]-H shift.[13] These discrepancies are likely the result of faster hydrolysis of allenes **9a** and **35** to 1,3-enone **33** and **36** in Au-catalyzed reactions.



Scheme 5. Effect of the nature of catalysts for the selectivity of [1,2]- versus [1,3]-acyloxy migration.

In conclusion, clear evidence has been presented for the equilibrium between [1,2]- and [1,3]-acyloxy migration in the Pt-catalyzed reactions of propargylic esters. A temperature-dependent interconversion between vinyl carbenoids (1,2-acyloxy-migrated intermediate) and allenes (1,3-acyloxy-migrated product) has been observed in systems of propargylic esters containing propargylic alkoxy groups. In addition to reaction temperature, several factors exert significant influence in the reaction course of propargylic esters, including the substituent pattern around the alkyne and the nature of the catalysts. Gaining insight into the role of these factors in the Pt-catalyzed reactions of propargylic esters can lead to better control over [1,2]- versus [1,3]-acyloxy migration.

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 stirred at the appropriate temperature (25, 40, 60, or 80°C) until the reaction was complete (0.5–2 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

This work was supported by the National Research Foundation of Korea (NRF) under Grant NRF-2011-0013118. E.J.C. thanks Prof. Daesung Lee (University of Illinois at Chicago) for the advice and help with this work.

Keywords: acyloxy migration • platinum • propargylic acetate • reaction mechanisms • transition-metal catalysis

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[10] Transformations of **7a** and **7b** to **8a** and **8b** at 60°C were reported, see ref. [8].

[11] α-Alkylidene-β-diketones were formed by further activation of allene intermediate with a Au^{III} complex followed by acyl migration, see: S. Wang, L. Zhang, *J. Am. Chem. Soc.* **2006**, *128*, 8414–8415.

[12] Propargylic pivalates with electronically unbiased internal alkynes underwent a gold-catalyzed [1,2]-acyloxy migration, see: L. Zhang, G. Li, G. Zhang, *J. Am. Chem. Soc.* **2008**, *130*, 3740–3741.

[13] A transformation of **34** to **38** at 60°C was reported, see ref. [8].

Received: December 3, 2011