JOC*Note*

Platinum-Catalyzed Cycloisomerization Reaction of 1,6-Enyne Coupling with Rearrangement of Propargylic Esters

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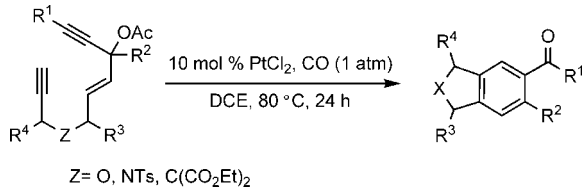
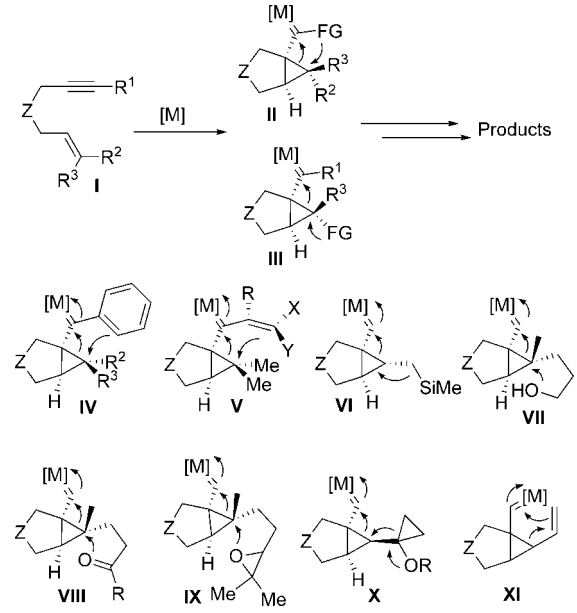


A platinum-catalyzed cycloisomerization of 1,6-enyne coupling with the rearrangement chemistry of propargylic ester has been developed. Most probably, under platinum catalysis, propargylic ester undergoes the 1,3-acyloxy migration to afford metal allene intermediate, which is followed by the Diels−Alder-type reaction. 1,3-Acyloxy migration is the key step during the transformation.

In the last decades, platinum and gold complexes have emerged as powerful carbophilic π-acids for the activation of alkynes toward a variety of nucleophiles.[1] This strategy has been well applied in the cycloisomerization reactions of 1,*n*-enynes, which are attractive processes due to the high demands for atom economy in newly developed reactions.[2–7] Particularly intriguing of this transformation is the diversity and complexity generated by both the skeleton rearrangement and the influence of functional groups. In this content, aromatic groups,[3] alkenes,[3,4] silyl ethers,[5] alcohols,[6] aldehydes,[7] epoxides,[7] and ethers[7] are excellent partners in the cycloisomerization of 1,6-enynes. However, in most cases, these functional groups follow the same path in nucleophilic attack to promote the ring-opening of the intermediate cyclopropyl metal carbenes (Scheme 1). A limited exception was reported recently by Fürstner and co-workers.[4] It was found that the 1,6-enynes bearing another alkene group in the alkene position undergo formal intramolecular Diels−Alder reactions to afford desired products.[4] The mechanism was proposed via the rearrangement of the intermediate vinylcyclopropyl metal carbenes **XI**. Consequently, further studies on the reaction diversity of enynes governed by different functional groups are still attractive.

SCHEME 1



On the other hand, platinum- and gold-catalyzed transformations of readily available propargylic esters have received much attention in recent years.[8] The metal allene complexes are considered as common intermediates, which further react with various functional groups to give astonishingly diverse products (Scheme 2). What we are interested in is the effect of this functional group when introduced into the cycloisomerization of enynes. On the basis of previous efforts in this area,[9] we envision that 1,6-enyne **A** with the propargylic

(1) For selected reviews on Au and/or Pt catalysis, see (a) Jimènez-Nùñez, E.; Echavarren, A. M. *Chem. Rev* **2008**, *108*, 3326–3350. (b) Li, Z.; Brouwer, C.; He, C. *Chem. Rev.* **2008**, *108*, 3239–3265. (c) Muzart, J. *Tetrahedron* **2008**, *64*, 5815–5849. (d) Michelet, V.; Toullec, P. Y.; Genét, J.-P. *Angew. Chem., Int. Ed.* **2008**, *47*, 4268–4315. (e) Gorin, D. J.; Toste, F. D. *Nature* **2007**, *446*, 395–403. (f) Hashmi, A. S. K. *Chem. Rev.* **2007**, *107*, 3180–3211. (g) Chianese, A. R.; Lee, S. J.; Gagné, M. R. *Angew. Chem., Int. Ed.* **2007**, *46*, 4042–4059. (h) Nieto-Oberhuber, C.; López, S.; Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Eur. J.* **2006**, *12*, 5916–5923. (i) Zhang, L.; Sun, J.; Kozmin, S. A. *Adv. Synth. Catal.* **2006**, *348*, 2271–2296.

(2) (a) For selected reviews on metal-catalyzed isomerizations of enynes, see: (a) Ref 1a,d,h,i. (b) Ma, S.; Yu, S.; Gu, Z. *Angew. Chem., Int. Ed.* **2006**, *45*, 200–203. (c) Bruneau, C. *Angew. Chem., Int. Ed.* **2005**, *44*, 2328–2334. (d) Diver, S. T.; Giessert, A. J. *Chem. Rev.* **2004**, *104*, 1317–1382. (e) Añorbe, L.; Domínguez, G.; Pérez-Castells, J. *Chem. Eur. J.* **2004**, *10*, 4938–4943. (f) Echavarren, A. M.; Nevado, C. *Chem. Soc. Rev.* **2004**, *33*, 431–436. (g) Aubert, C.; Buisine, O.; Malacria, M. *Chem. Rev.* **2002**, *102*, 813–834, For selected examples, see. (h) Toullec, P. Y.; Genin, E.; Leseurre, L.; Genet, J.-P.; Michelet, V. *Angew. Chem., Int. Ed.* **2006**, *45*, 7427–7430. (i) Cho, E. J.; Kim, M.; Lee, D. *Org. Lett.* **2006**, *8*, 5413–5416. (j) Zhang, L.; Kozmin, S. A. *J. Am. Chem. Soc.* **2004**, *126*, 11806–11807. (k) Mendez, M.; Munoz, M. P.; Nevado, C.; Cardenas, D. J.; Echavarren, A. M. *J. Am. Chem. Soc.* **2001**, *123*, 10511–10520. (l) Chatani, N.; Kataoka, K.; Murai, S. *J. Am. Chem. Soc.* **1998**, *120*, 9104–9105. (m) Chatani, N.; Furukawa, N.; Sakurai, H.; Murai, S. *Organometallics.* **1996**, *15*, 901–903. (n) Fürstner, A.; Szillat, H.; Gabor, B.; Mynott, R. *J. Am. Chem. Soc.* **1998**, *120*, 8305–8314. (o) Fürstner, A.; Stelzer, F.; Szillat, H. *J. Am. Chem. Soc.* **2001**, *123*, 11863–11869.

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(4) Fürstner, A.; Stimson, C. C. *Angew. Chem., Int. Ed.* **2007**, *46*, 8845–8849.

(5) (a) Fernández-Rivas, C.; Méndes, M.; Nieto-Oberhuber, C.; Echavarren, A. M. *J. Org. Chem.* **2002**, *67*, 5197–5201. (b) Fernández-Rivas, C.; Méndes, M.; Echavarren, A. M. *J. Am. Chem. Soc.* **2000**, *122*, 1221–1222.

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SCHEME 2

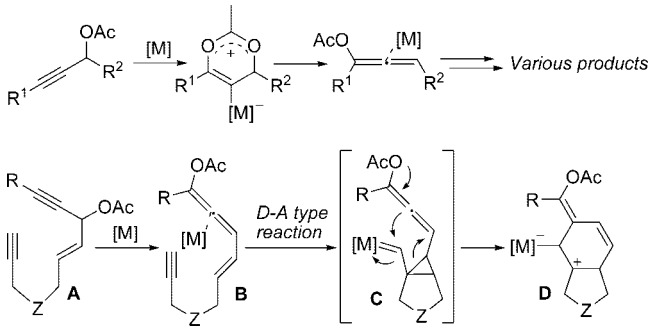
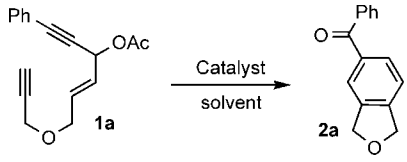


TABLE 1. Optimization of Reaction Conditions[a]



entry	catalyst (mol %)	solution	*t*, °C	time, h	yield, %
1	$PtCl_2$ (10), CO (1 atm)	toluene	80	24	65
2	$PtCl_2$ (10), CO (1 atm)	CH_3CN	80	24	NR[b]
3	$PtCl_2$ (10), CO (1 atm)	Dioxane	80	24	NR
4	$PtCl_2$ (10), CO (1 atm)	DCE	80	24	83
5	$PtCl_2$ (10), COD (40)	DCE	80	24	46
6	$PtCl_2$ (10)	DCE	80	36	41
7	$Au(PPh_3)BF_4$ (5)	DCE	rt	3	6[c]
8	$Au(PPh_3)SbF_6$ (5)	DCE	rt	3	11[c]
9	$Au(PPh_3)OTf$ (5)	DCE	rt	3	trace[c]
10	$AuCl_3$ (5)	DCE	rt	3	8[c]
11	AuCl (5)	DCE	rt	3	trace[c]

[a] Reactions were conducted with 0.4 mmol of **1a** in 3 mL of solvent. [b] No reaction. [c] Most of the material was decomposed.

ester in its alkene position might undergo Diels−Alder reaction after 1,3-migration of the acetate group, where the intermediate vinylcyclopropyl metal carbenes **C** might be involved (Scheme 2).[4] Herein, we report a platinum-catalyzed cycloisomerization of 1,6-enyne coupling with migration chemistry of propargylic esters.

Optimization studies of this transformation started with the use of enyne **1a** as the model substrate (Table 1). To our delight, the concept works nicely. Treatment of **1a** in the presence of 10 mol % of $PtCl_2$ under CO (1 atm)[10] afforded the desired aryl ketone **2a** in 65% yield after the reaction mixture was stirred in toluene (3 mL) at 80 °C for 24 h (entry 1). The nature of the solvent had a substantial effect on the efficiency of the reaction. No reaction was observed in either CH_3CN or dioxane, whereas 1,2-dichloroethane (DCE) gave the best result (entries 1−4).

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(7) Jiménez-Núñez, E.; Claverie, C. K.; Nieto-Oberhuber, C.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2006**, *45*, 5452–5455.

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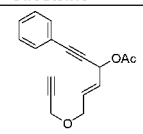
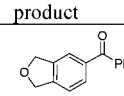
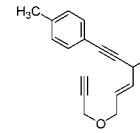
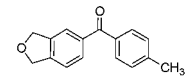
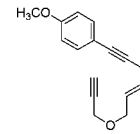
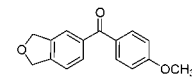
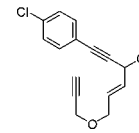
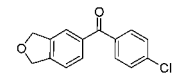
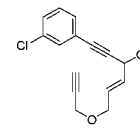
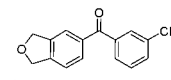
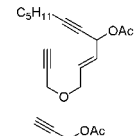
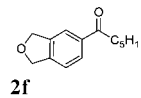
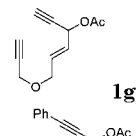
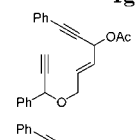
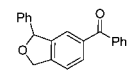
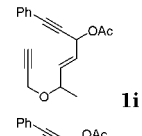
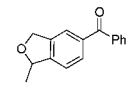
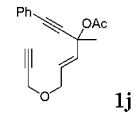
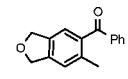
TABLE 2. Scope Study of Platinum-Catalyzed Cyclization of Enynes[a]

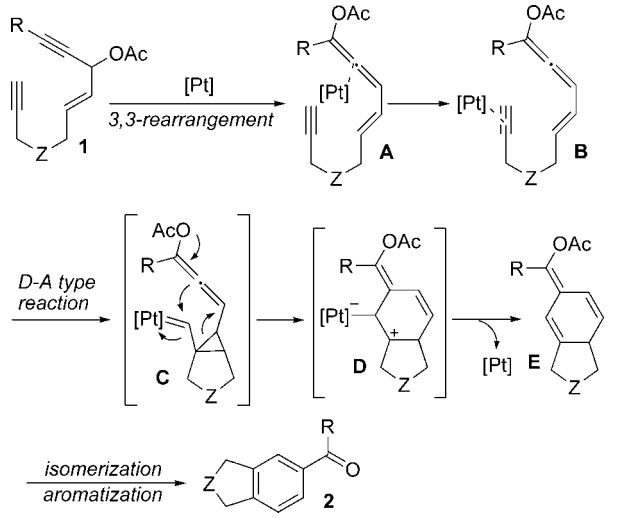
entry	substrate	product	yield
1	 **1a**	 **2a**	83%
2	 **1b**	 **2b**	78%
3	 **1c**	 **2c**	81%
4	 **1d**	 **2d**	53%
5	 **1e**	 **2e**	67%
6	 **1f**	 **2f**	78%
7	 **1g**	—	NR[b]
8	 **1h**	 **2h**	78%
9	 **1i**	 **2i**	65%
10	 **1j**	 **2j**	58%

[a] All reactions were carried out with **1** (0.4 mmol) with 10 mol % of $PtCl_2$ under CO (1 atm) in DCE (3 mL) at 80 °C for 24 h. [b] No reaction.

Other platinum catalyst systems did not lead to an increase in yield (entries 5 and 6). Gold catalysts also catalyzed this cyclization, but in poor yields (entries 7−11). Thus, the use of $PtCl_2$ (10 mol %) and CO (1 atm) in DCE (3 mL) at 80 °C was found to be the most efficient and was subsequently used as the standard condition.

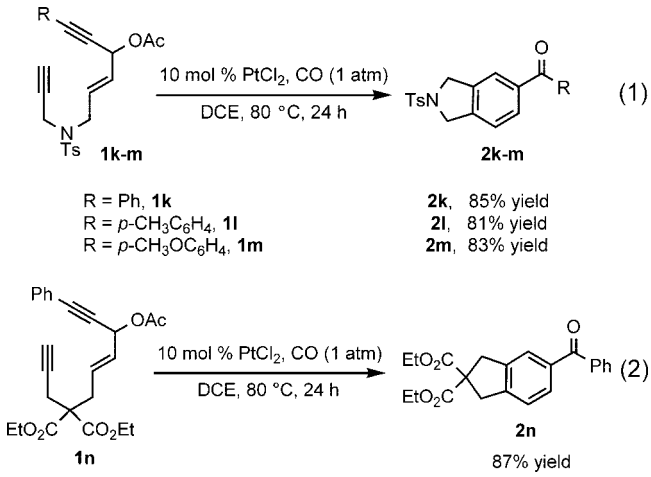
Under the optimized reaction conditions, various O-tethered enynes were investigated, as shown in Table 2. In most cases, the desired cyclized products were generated in good to high yields. The electronic properties of the substituent on the aryl group[11] attached to the alkyne affected the reaction. Electron-rich substituents gave results superior to those obtained from electron-

SCHEME 3. Proposed Mechanism



withdrawing ones (entries 2 and 3 vs 4 and 5). When an aromatic substituent was exchanged with an alkyl group, the desired aryl ketone **2f** was also obtained in high yield (entry 6). However, terminal alkyne **1g** did not afford any cyclized product, with most of the starting material recovered after 24 h. This might be due to the fact that the propargylic ester with the terminal triple bond normally undergoes 1,2-acyloxy migration without generating an allene intermediate (entry 7).[11] Substrates with a phenyl or methyl group at the position adjacent to the oxygen atom reacted smoothly[12] to afford the respective products **2h** and **2i** in good yields (entries 8 and 9). Furthermore, a substituent at the propargylic position was also tolerated (entry 10).

To further explore the scope of application of this method, the tether effect was further investigated. Various N-tethered enynes reacted efficiently to afford the corresponding products **2k**−**m** in good yields (eq 1). The results were similar to those obtained from **1a**−**c**. Moreover, this tandem transformation was not limited to the heteroatom-tethered substrates. Enyne **1n** gave a superior result, affording the carbocyclic skeleton **2n** in 87% yield (eq 2).



The proposed mechanism of this transformation was shown in Scheme 3. Platinum-promoted 1,3-acyloxy migration[8,14] of the propargylic ester led to the formation of the allene metal intermediate **A**. This coordinated metal catalyst might have efficiently participated in the activation of another triple bond to afford the complex **B**. Formal Diels−Alder-type reaction of compound **B** generated the adducts **E**, which underwent further isomerization and aromatization[14] to give the desired product **2**. The nature of the Diels−Alder-type reaction from **B** to **E** might be consistent with that reported by Fürstner and coworkers recently.[4] Electrophilic metal carbene **C**, generated from the attack of the alkene moiety to the platinum-activated triple bond, might have cyclized to the six-membered-ring cation **D**, which could have released cycloadduct **E** and regenerated the catalyst.

In conclusion, we have reported a platinum-catalyzed tandem reaction of propargylic ester isomerization and subsequent cyclizations with 1,6-enyne. The allene metal intermediate generated from 1,3-acyloxy migration of propargylic ester was proved to be an excellent candidate in the Diels−Alder-type reaction. Platinum catalyst, regenerated from the migration process, efficiently participated in the activation of another triple bond, which might have been a crucial factor for this transformation.

Experimental Section

General Procedure for the Platinum-Catalyzed Cycloisomerization of 1,6-Enynes. To a stirred solution of enyne **1** (0.4 mmol) in DCE (3.0 mL) was added 10.6 mg (10 mol %) of $PtCl_2$ under CO atmosphere (1 atm). When the mixture was stirred at 80 °C for 24 h, ethyl acetate (30 mL) was added. The mixture was evaporated under reduced pressure. The residue was purified by chromatography on silica gel to afford corresponding products **2**.

(1,3-Dihydroisobenzofuran-5-yl)(phenyl)methanone (2a). 2a was prepared according to the above method in 83% yield as a solid: mp 84−86 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80−7.69 (m, 4 H), 7.59−7.56 (m, 1 H), 7.51−7.45 (m, 2 H), 7.35−7.32 (m, 1 H), 5.16 (s, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.3, 143.7, 139.4, 137.5, 137.0, 132.4, 129.8, 129.7, 128.2, 122.6, 120.7, 73.3, 73.1; IR (KBr, cm^{-1}) 3060, 2926, 2857, 1768, 1658, 1616, 1315, 1281, 1048. Anal. Calcd for $C_{15}H_{12}O_2$: C, 80.34; H, 5.39. Found: C, 80.31; H, 5.45.

Phenyl(2-tosylisoindolin-5-yl)methanone (2k). 2k was prepared according to the above method in 85% yield as a solid: mp 138−140 °C; ^{1}H NMR(400 MHz, $CDCl_3$) δ 7.79−7.56 (m, 7 H), 7.48−7.45 (m, 2 H), 7.34−7.26 (m, 3 H), 4.68 (s, 2 H), 4.66 (s, 2 H), 2.41 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.9, 143.8, 140.7, 137.5,

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137.3, 136.6, 135.1, 133.6, 132.6, 129.9, 128.3, 127.6, 125.0, 124.2, 122.5, 53.6, 53.4, 21.5; IR (KBr, cm^{-1}) 2923, 2853, 2255, 1739, 1660, 1597, 1448, 1348, 1281, 1167, 1092, 911, 730. Anal. Calcd for $C_{22}H_{19}NO_3S$: C, 70.00; H, 5.07; N, 3.71. Found: C, 69.93; H, 4.89; N, 3.77.

Diethyl 5-Benzoyl-1*H*-2,2(3*H*)-dicarboxylate (2n). 2n was prepared according to the above method in 67% yield as an oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78−7.76 (d, J = 8.1 Hz, 2 H), 7.66−7.55 (m, 3 H), 7.49−7.44 (m, 2 H), 7.31−7.28 (d, J = 7.8 Hz, 1 H), 4.26−4.19 (q, J = 6.9 Hz, 4 H), 3.66 (s, 2 H), 3.65 (s, 2 H), 1.29−1.24 (t, J = 6.9 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.4, 171.2, 145.2, 140.4, 137.8, 136.6, 132.1, 129.8, 129.4, 128.1, 125.8, 123.9, 61.8, 60.3, 40.4, 40.1, 13.9; IR (neat, cm^{-1}) 2920, 2853, 1650, 1612, 1566, 1427, 1286, 1254, 1045, 904, 744. Anal. Calcd for $C_{22}H_{22}O_5$: C, 72.12; H, 6.05. Found: C, 72.03; H, 6.22.

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Supporting Information Available: Detailed experimental procedure and copies of ^{1}H NMR and ^{13}C NMR spectra of all compounds as well as X-ray crystallography of **2d**. This material is available free of charge via the Internet at http://pubs.acs.org.

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