Rhodium-Catalyzed Carbonylative Skeleton Rearrangement of 1,4-Enynes Tethered by a Cyclopropane Group

Gen-Qiang Chen, Xiang-Ying Tang,* Min Shi*

State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Road, Shanghai 200032, P. R. of China
Fax +86(21)64166128; E-mail: mshi@mail.sioc.ac.cn

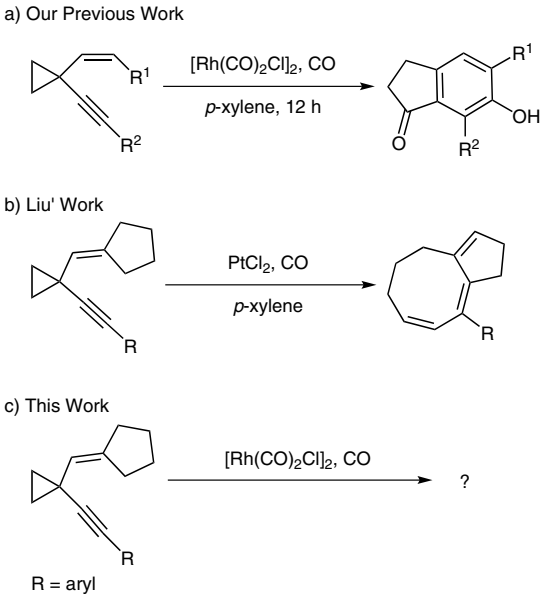
Received: 22.07.2014; Accepted after revision: 24.07.2014

Abstract: The carbonylative skeleton rearrangement of 1,4 enynes tethered by a cyclopropane group proceeded smoothly in the presence of $[Rh(CO)_2Cl]_2$ under CO atmosphere to give the corresponding 1,2,4,5,6,7-hexahydrocyclopenta[*a*]inden-3(3*bH*)-one derivatives in moderate yields.

Key words: rhodium(I), carbonylation, skeleton rearrangement, 1,4-enyne, cyclopropane

Transition-metal-catalyzed carbonylation functions as a primary and efficient route for introducing carbonyl groups into an organic molecule.[1] The versatility of carbonylation technology has been extended to the formation of a diverse array of organic carbonyl compounds via reactions of aziridines,[2] epoxides,[3] oxazolines,[4] methylenecyclopropanes,[5] vinyl cyclopropanes,[6,13] spiropentane,[7] and primary alkyl- or arylmethyl halides.[8] Some of the carbonylation reactions such as the well-known Monsanto process has been commercialized, and CO-free carbonylations have been also developed.[9] Furthermore, CO can also serve as an one carbon unit for cycloadditions, including [2+2+1],[10] [3+3+1],[11] [2+2+2+1],[12] [5+2+1],[13] etc.

Transition-metal-catalyzed enyne cycloisomerization has been studied extensively during the last few decades. However, only a few examples with regard to 1,4-enynes have been reported,[14] and the carbonylative cycloisomerization of 1,4-enyne was very rare.[15] In 2013, we reported a novel rhodium(I)-catalyzed Pauson–Khand-type reaction of cyclopropane group tethered 1,4-enynes,[16] in which the 1,4-enyne first undergoes an intramolecular Pauson–Khand reaction and then the subsequent carbonylative cleavage of the spiropentane unit to produce 6-hydroxy-2,3-dihydro-1*H*-inden-1-one derivatives in moderate yields. The ring opening of the cyclopropane group and the aromatization process comprise the two driving forces for this reaction to take place (Scheme 1, a). Liu's group also reported a novel cycloisomerization of 1,4-enynes in the presence of $PtCl_2$ under CO atmosphere. The reaction was initiated by a π-alkyne-activated sp^3-hydride shift, a 6-*endo*-*dig* cyclization and the subsequent ring expansion, giving eight-membered carbocycles in high yields (Scheme 1, b).[17] We envisaged that if the olefin unit of 1,4-enyne was a alkylidenecycloalkane, the intramolecular Pauson–Khand reaction and the subsequent aromatization would be inhibited and the reaction may take place through a new pathway. Herein, we wish to report an interesting rhodium(I)-catalyzed carbonylative rearrangement of 1,4-enynes tethered by a cyclopropane group.



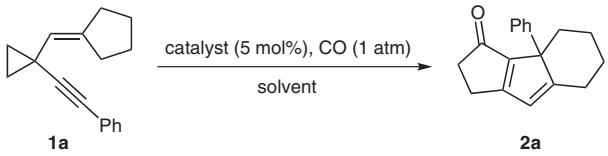
Scheme 1 Previous work and this work

We initiated our investigations by seeking the optimal conditions for the carbonylative skeleton rearrangement of 1,4-enyne **1a** in the presence of transition-metal catalyst, and the results are shown in Table 1. With $Rh(PPh_3)_3Cl$ as the catalyst, the corresponding product **2a** was afforded in 29% yield (Table 1, entry 1), and the desired product was not detected when the temperature was raised to 140 °C (Table 1, entry 2). Using $[Rh(CO)_2Cl]_2$ as the catalyst, the yield of **2a** was improved to 46% (Table 1, entry 3). Raising the temperature to 140 °C, the reaction gave no desired product again (Table 1, entry 4). Other rhodium catalysts such as $Rh(PPh_3)_2(CO)Cl$, $[Rh(cod)Cl]_2$, $Rh(CO)_2(acac)$, $Rh(dppp)_2Cl$, $[Cp^*RhCl_2]_2$, and $Rh_6(CO)_{16}$ were found to be ineffective to catalyze this transformation (Table 1, entries 7–13). Other transition-metal catalysts such as $Ni(cod)_2$ and Vaska's complex were also found to be ineffective in this reaction (Table 1, entries 14 and 15). $[Rh(CO)_2Cl]_2$ was identified

SYNLETT 2014, 25, 2311–2315
Advanced online publication: 21.08.2014
DOI: 10.1055/s-0034-1378633; Art ID: st-2014-s0618-c

to be the best catalyst. When the reactions were carried out in other solvents such as PhCl, *p*-DCB, tetrachloroethane, MeCN, and PhCN, the formation of **2a** was not observed (Table 1, entries 16–20). Addition of NMO has been found to be able to accelerate the Pauson–Khand reaction by removing a CO ligand from the metal oxidatively as carbon dioxide,[18] but it was also ineffective to our reaction. Other additives such as $AgSbF_6$ and phosphine ligands[19] $(C_6F_5)_3P$, DPEphos and dppe have no effect to improve the yield of **2a** (Table 1, entries 21–25). It should

Table 1 Optimization of the Reaction Conditions



1a **2a**

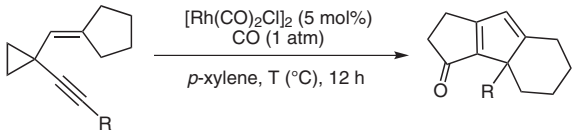
Entry[a]	Catalyst	Additive	Solvent	Temp (°C)	Yield (%)[b]
1	$Rh(PPh_3)_3Cl$	–	*p*-xylene	100	29
2	$Rh(PPh_3)_3Cl$	–	*p*-xylene	140	n.d.[d]
3	$[Rh(CO)_2Cl]_2$	–	*p*-xylene	120	46
4	$[Rh(CO)_2Cl]_2$	–	*p*-xylene	140	n.d.[d]
5	$[Rh(CO)_2Cl]_2$	–	*p*-xylene	60–130[c]	32
6	$[Rh(dppp)(CO)Cl]_2$	–	*p*-xylene	130	28
7	$[Rh(cod)Cl]_2$	–	*p*-xylene	100	n.d.[d]
8	$Rh(CO)_2(acac)$	–	*p*-xylene	100	n.d.[d]
9	$[Rh(C_2H_4)_2Cl]_2$	–	*p*-xylene	100	n.d.[d]
10	$Rh(dppp)_2Cl$	–	*p*-xylene	100	n.d.[d]
11	$Rh(CO)(PPh_3)_2Cl$	–	*p*-xylene	100	n.d.[d]
12	$Rh_6(CO)_{16}$	–	*p*-xylene	100	n.d.[d]
13	$[Cp^*RhCl_2]_2$	–	*p*-xylene	100	n.d.[d]
14	$Ir(PPh_3)_2(CO)Cl$	–	*p*-xylene	130	n.d.[d]
15	$Ni(cod)_2$	–	*p*-xylene	120	n.d.[d]
16	$[Rh(CO)_2Cl]_2$	–	PhCl	120	n.d.[d]
17	$[Rh(CO)_2Cl]_2$	–	*p*-DCB	120	n.d.[d]
18	$[Rh(CO)_2Cl]_2$	–	tetrachlorethane	120	trace[e]
19	$[Rh(CO)_2Cl]_2$	–	MeCN	80	n.d.[d]
20	$[Rh(CO)_2Cl]_2$	–	PhCN	120	n.d.[d]
21	$[Rh(CO)_2Cl]_2$	$AgBF_4$	*p*-xylene	100	n.d.[d]
22	$[Rh(CO)_2Cl]_2$	dppe	*p*-xylene	100	n.d.[d]
23	$[Rh(CO)_2Cl]_2$	NMO	*p*-xylene	100	n.d.[d]
24	$[Rh(CO)_2Cl]_2$	DPEphos	*p*-xylene	100	n.d.[d]
25	$[Rh(CO)_2Cl]_2$	$(4\text{-}F_3CC_6H_4)_3P$	*p*-xylene	120	trace[e]

[a] The reaction was performed in a 25 mL flame- and vacuum-dried Schlenk tube. Compound **1** (0.2 mmol) and the catalyst (5 mol%) were added, and the tube was evacuated and backfilled with CO. Then, the solvent was added, and the reaction mixtures were allowed to stir in an oil bath at indicated temperature for 12 h.
[b] Isolated yields.
[c] The temperature was raised from 60 °C to 130 °C gradually.
[d] Not detected.
[e] Detected by the ^1H NMR of the crude product.

be also noted that when this $[Rh(CO)_2Cl]_2$-catalyzed reaction was conducted without CO, the conversion of **1a** was very low (<5%) and only trace amount of product **2a** was afforded.

To evaluate the generality of the reaction, different substrates with varying substituents were synthesized and investigated under the standard reaction conditions. The results are shown in Table 2. All of the reactions proceeded smoothly when the substituents were introduced on the aromatic ring regardless of whether they have electron-donating or electron-withdrawing substituents (Table 2, entries 1–10). The structure of **2a** was unambiguously confirmed by the X-ray diffraction (Figure 1).[20]

Table 2 Substrate Scope of the Carbonylative Skeleton Rearrangement



1 2

Entry[a]	R	Temp (°C)	Yield (%)[b]
1	**1b** 4-MeC_6H_4	120	**2b** 34
2	**1c** 3-MeC_6H_4	100	**2c** 32
3	**1d** 3,5-$Me_2C_6H_4$	120	**2d** 34
4	**1e** 4-PhC_6H_4	120	**2e** 43
5	**1f** 4$MeOC_6H_4$	100	**2f** 39
6	**1g** 4-ClC_6H_4	100	**2g** 30
7	**1h** 4-FC_6H_4	120	**2h** 35
8	**1i** 4-AcC_6H_4	100	**2i** 31
9	**1j** 4-$MeO_2CC_6H_4$	100	**2j** 32
10	**1k** 4-$F_3CC_6H_4$	100	**2k** 28

[a] The reaction was performed on 0.2 mmol scale.
[b] Isolated yields.

The mechanism of this reaction is still unclear at this stage. A plausible reaction mechanism is shown in Scheme 2 using **1a** as a model substrate.[21] Compound **1a** first undergoes oxidative addition in the presence of rhodium(I) catalyst to give rhodacyclobutane intermediate **A**. The subsequent rearrangement of intermediate **A** produces intermediate **B**, which undergoes carbonylation to generate intermediate **C**. The reductive elimination in intermediate **C** produces compound **2a′**. Compound **2a′** is a relatively labile substance, which can easily produce **2a** via 1,2-alkyl migration.[22]

In summary, we have developed a novel carbonylative skeleton rearrangement of cyclopropane-tethered 1,4-enynes catalyzed by $[Rh(CO)_2Cl]_2$ under CO atmosphere, affording the corresponding 1,2,4,5,6,7-hexahydrocyclopenta[*a*]inden-3(3*bH*)-one derivatives in moderate yields. A plausible reaction mechanism has also been proposed.

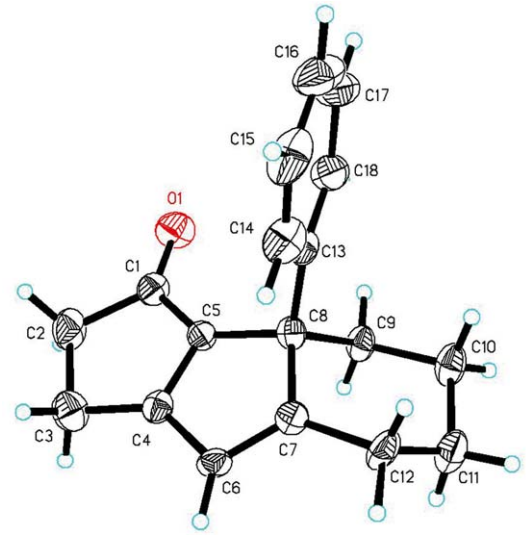
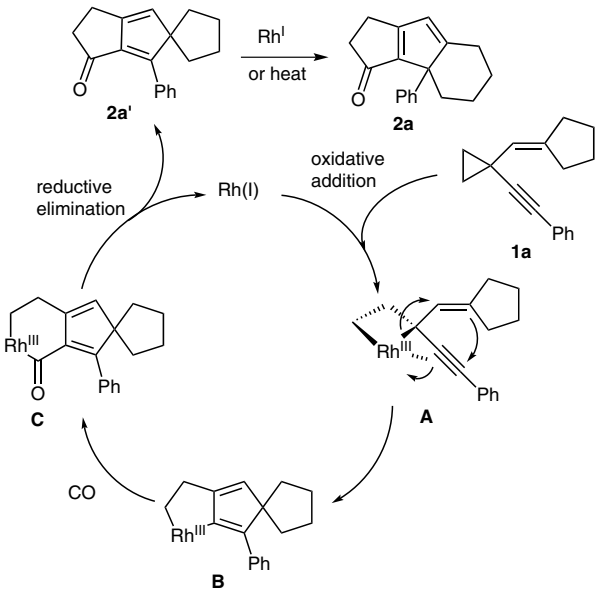


Figure 1 X-ray crystal structure of compound **2a**



Scheme 2 A plausible reaction mechanism

General Procedure for the Rhodium-Catalyzed Carbonylative Skeleton Rearrangement

To a 25 mL flame- and vacuum-dried Schlenk tube were added the substrate 1 (0.2 mmol) and $[Rh(CO)_2Cl]_2$ (0.005 mmol). The Schlenk tube was evacuated and backfilled with CO, then *p*-xylene (2 mL) was added, and the reaction mixture was allowed to stir at indicated temperature for 12 h. The product was purified by column chromatography or preparative silica gel plate using PE and EtOAc as eluent (PE–EtOAc = 8:1).

Compound 2a

A white solid; mp 104–107 °C. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 1.13–1.17 (m, 1 H, CH_2), 1.20–1.30 (m, 2 H, CH_2), 1.56–1.58

(m, 1 H, CH_2), 1.965–1.973 (m, 1 H, CH_2), 2.36–2.37 (m, 1 H, CH_2), 2.63–2.71 (m, 4 H, CH_2), 2.76–2.81 (m, 1 H, CH_2), 3.10–3.14 (m, 1 H, CH_2), 6.36 (d, J = 1.5 Hz, 1 H, Ar), 7.18–7.21 (m, 1 H, Ar), 7.26–7.28 (m, 4 H, Ar). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 21.3, 23.9, 29.0, 29.6, 36.3, 40.8, 56.9, 122.4, 126.5, 127.1, 128.6, 138.2, 155.7, 173.2, 181.6, 197.8. IR (CH_2Cl_2): ν = 2950, 1720, 1604, 1435, 1275, 1107, 858, 765, 750, 698 cm^{-1}. MS (%): *m/e* (%) = 250 (48.56) [M^+], 222 (12.62), 208 (100.00), 193 (17.25), 179 (34.08), 165 (42.13), 152 (13.64), 128 (13.34), 115 (26.15), 89 (11.25). HRMS (EI): *m/z* calcd for $C_{18}H_{18}O$: 250.1358; found: 250.1357.

Compound 2b

A white solid; mp 123–125 °C. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 1.15–1.19 (m, 1 H, CH_2), 1.26–1.34 (m, 2 H, CH_2), 1.55–1.56 (m, 1 H, CH_2), 1.69–1.75 (m, 1 H, CH_2), 1.93–1.98 (m, 1 H, CH_2), 2.29 (s, 3 H, CH_3), 2.33–2.40 (m, 1 H, CH_2), 2.59–2.75 (m, 4 H, 2 CH_2), 2.77 (d, J = 13.6 Hz, 1 H, CH_2), 3.09 (dd, J_1 = 13.6 Hz, J_2 = 2.0 Hz, 1 H, CH_2), 6.35 (d, J = 1.6 Hz, 1 H, =CH), 7.09 (d, J = 8.0 Hz, 2 H, Ar), 7.17 (d, J = 8.0 Hz, 2 H, Ar). ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 21.0, 21.3, 23.9, 28.9, 29.6, 36.2, 40.9, 56.6, 122.3, 126.9, 129.3, 135.1, 136.1, 155.9, 173.4, 181.5, 197.9. IR (CH_2Cl_2): ν = 2930, 2856, 1674, 1541, 1386, 1327, 1054, 846, 730 cm^{-1}. MS: *m/e* (%) = 264 (58.45) [M^+], 236 (17.47), 222 (100.00), 207 (33.57), 193 (21.75), 179 (33.86), 165 (21.79), 128 (11.00), 115 (20.07), 89 (18.94). HRMS (EI): *m/z* calcd for $C_{19}H_{20}O$: 264.1514; found: 264.1513.

Acknowledgment

We thank the Shanghai Municipal Committee of Science and Technology (11JC1402600), the National Basic Research Program of China (973)-2010CB833302, and the National Natural Science Foundation of China (20472096, 21372241, 21361140350, 20672127, 21102166, 21121062, 21302203 and 20732008).

Supporting Information for this article is available online at http://www.thieme-connect.com/products/ejournals/journal/10.1055/s-00000083.

References and Notes

(1) (a) Beller, M. *Catalytic Carbonylation Reactions*, In *Topics in Organometallic Chemistry*; Vol. 18; Springer: Berlin, **2006**. (b) Hegedus, L. S. *Transition Metals in the Synthesis of Complex Organic Molecules*; University Science Books: Mill Valley, **1994**. (c) Kollar, L. *Modern Carbonylation Methods*; Wiley-VCH: Weinheim, **2008**. (d) Kiss, G. *Chem. Rev.* **2001**, *101*, 3435.

(2) Mahadevan, V.; Getzler, Y. D. Y. L.; Coates, G. W. *Angew. Chem. Int. Ed.* **2001**, *41*, 2781.

(3) (a) Lee, J. T.; Thomas, P. J.; Alper, H. *J. Org. Chem.* **2001**, *66*, 5424. (b) Schmidt, J. A. R.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2005**, *127*, 11426.

(4) Jia, L.; Xu, H. *Org. Lett.* **2003**, *5*, 1575.

(5) Kurahashi, T.; de Meijere, A. *Angew. Chem. Int. Ed.* **2005**, *44*, 7881.

(6) (a) Jiang, G.-J.; Fu, X.-F.; Li, Q.; Yu, Z.-X. *Org. Lett.* **2012**, *14*, 692. (b) Yao, Z.-K.; Li, J.; Yu, Z.-X. *Org. Lett.* **2011**, *13*, 134. (c) Wender, P. A.; Gamber, G. G.; Hubbard, R. D.; Pham, S. M.; Zhang, L. *J. Am. Chem. Soc.* **2005**, *127*, 2836. (d) Wender, P. A.; Gamber, G. G.; Hubbard, R. D.; Zhang, L. *J. Am. Chem. Soc.* **2002**, *123*, 2876.

(7) Matsuda, T.; Tsuboi, T.; Murakami, M. *J. Am. Chem. Soc.* **2007**, *129*, 12596.

(8) (a) Jones, R. V. H.; Lindsell, W. E.; Palmer, D. D.; Prestonb, P. N.; Whitton, A. J. *Tetrahedron Lett.* **2005**, *46*, 8695. (b) Lindsell, W. E.; Palmer, D. D.; Preston, P. N.; Rosair, G. M. *Organometallics* **2005**, *24*, 1119.

(9) Morimoto, T.; Fujioka, M.; Fuji, K.; Tsutsumi, K.; Kakiuchi, K. *Pure Appl. Chem.* **2008**, *80*, 1079.

(10) (a) Fukuyama, T.; Nakashima, N.; Okada, T.; Ryu, I. *J. Am. Chem. Soc.* **2013**, *135*, 1006. (b) Lin, M.; Li, F.; Jiao, L.; Yu, Z.-X. *J. Am. Chem. Soc.* **2011**, *133*, 1690. (c) Kondo, T.; Nomura, M.; Ura, Y.; Wada, K.; Mitsudo, T. *J. Am. Chem. Soc.* **2006**, *128*, 14816. (d) Wender, P. A.; Croatt, M. P.; Deschamps, N. M. *J. Am. Chem. Soc.* **2004**, *126*, 5948. (e) Jiao, L.; Yuan, C.; Yu, Z.-X. *J. Am. Chem. Soc.* **2008**, *130*, 4421. (f) Wender, P. A.; Croatt, M. P.; Deschamps, N. M. *J. Am. Chem. Soc.* **2004**, *126*, 5948. (g) Khand, I. U.; Knox, G. R.; Pauson, P. L.; Watts, W. E. *J. Chem. Soc., Perkin Trans. 1* **1973**, *1*, 977.

(11) (a) Kim, S. Y.; Lee, S. I.; Choi, S. Y.; Chung, Y. K. *Angew. Chem. Int. Ed.* **2008**, *47*, 4914. (b) Kim, S. Y.; Chung, Y. K. *J. Org. Chem.* **2010**, *75*, 1281.

(12) Bennacer, B.; Fujiwara, M.; Lee, S.-Y.; Ojima, I. *J. Am. Chem. Soc.* **2005**, *127*, 17756.

(13) (a) Wender, P. A.; Gamber, G. G.; Hubbard, R. D.; Zhang, L. *J. Am. Chem. Soc.* **2002**, *124*, 2876. (b) Wang, Y.; Wang, J.; Su, J.; Huang, F.; Jiao, L.; Liang, Y.; Yang, D.; Zhang, S.; Wender, P. A.; Yu, Z.-X. *J. Am. Chem. Soc.* **2007**, *129*, 10060.

(14) For transition-metal-catalyzed cyclizations of 1,4-enynes, see: (a) Shi, X.; Gorin, D. J.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 5802. (b) Buzas, A.; Gagosz, F. *J. Am. Chem. Soc.* **2006**, *128*, 12614. (c) Marion, N.; Diez-Gonzalez, S.; De Fremont, P.; Noble, A. R.; Nolan, S. P. *Angew. Chem. Int. Ed.* **2006**, *45*, 3647. (d) Shu, X.; Schienebeck, C. M.; Song, W.; Guzei, I. A.; Tang, W. *Angew. Chem. Int. Ed.* **2013**, *52*, 13601. (e) Schienebeck, C. M.; Robichaux, P. J.; Li, X.; Chen, L.; Tang, W. *Chem. Commun.* **2013**, *49*, 2616. (f) Xu, X.; Liu, P.; Shu, X.; Tang, W.; Houk, K. N. *J. Am. Chem. Soc.* **2013**, *135*, 9271. (g) Shu, X.; Li, X.; Shu, D.; Huang, S.; Schienebeck, C. M.; Zhou, X.; Robichaux, P. J.; Tang, W. *J. Am. Chem. Soc.* **2012**, *134*, 5211. (h) Shu, X.; Huang, S.; Shu, D.; Guzei, I. A.; Tang, W. *Angew. Chem. Int. Ed.* **2011**, *50*, 8153.

(15) For carbonylative cycloisomerisation of 1,4-enynes, see: (a) Fukuyama, T.; Ohta, Y.; Brancour, C.; Miyagawa, K.; Ryu, I.; Dhimane, A.-L.; Fensterbank, L.; Malacria, M. *Chem. Eur. J.* **2012**, *18*, 7243. (b) Li, X.; Song, W.; Tang, W. *J. Am. Chem. Soc.* **2013**, *135*, 16797. (c) Li, X.; Huang, S.; Schienebeck, C. M.; Shu, D.; Tang, W. *Org. Lett.* **2012**, *14*, 1584.

(16) Chen, G.-Q.; Shi, M. *Chem. Commun.* **2013**, *49*, 698.

(17) Vasu, D.; Das, A.; Liu, R.-S. *Chem. Commun.* **2010**, *46*, 4115.

(18) (a) Shambayati, S.; Crowe, W. E.; Schreiber, S. L. *Tetrahedron Lett.* **1990**, *31*, 5289. (b) Jeong, N.; Chung, Y. K.; Lee, B. Y.; Lee, S. H.; Yoo, S.-E. *Synlett* **1991**, 204.

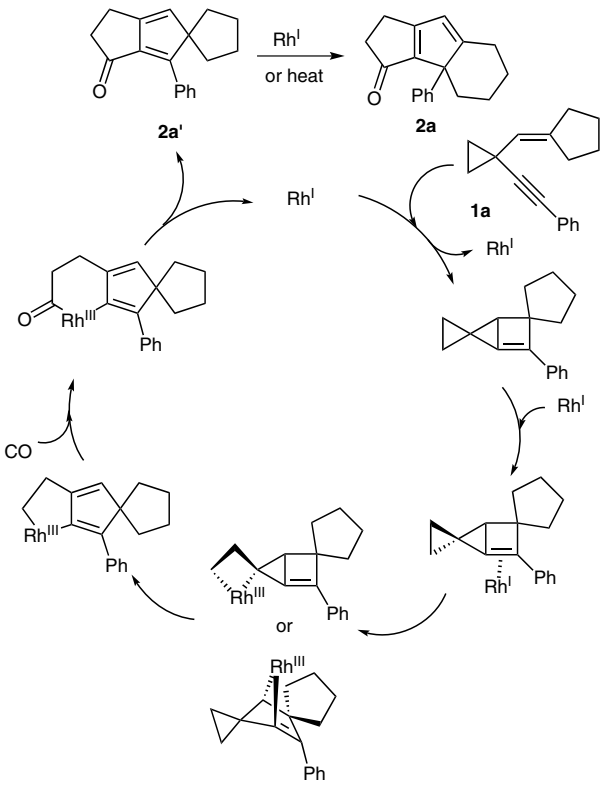
(19) It has been reported that electron-deficient CO or phosphine ligands were critical to increase the π-acidity of the rhodium center, see: (a) Huang, S.; Li, X.; Lin, C. L.; Guzeic, I. A.; Tang, W. *Chem. Commun.* **2012**, *48*, 2204. (b) Shu, X.-Z.; Shu, D.; Schienebeck, C. M.; Tang, W. *Chem. Soc. Rev.* **2012**, *41*, 7698. Phosphine ligands have great influence on

rhodium-catalyzed carbonylation and decarbonylation and a π-acidic phosphine ligand can promote decarbonylation in some cases, see: (c) Chen, P.-H.; Xu, T.; Dong, G. *Angew. Chem. Int. Ed.* **2014**, *53*, 1674. (d) Xu, T.; Savage, N. A.; Dong, G. *Angew. Chem. Int. Ed.* **2014**, *53*, 1891; however, concerning about that phosphine ligands have no effect in our current reaction, the reason is still not clear at the present stage.

(20) The crystal data of **2a** have been deposited in CCDC with number 906119.

(21) There is still another mechanism that can explain the formation of product **2a**. However, this mechanism involves the formation of a very strained intermediate, which makes this mechanism seems less possible (Scheme 3).

(22) For a similar migration at cyclopentadiene ring, see: (a) Replogle, K. S.; Carpenter, B. K. *J. Am. Chem. Soc.* **1984**, *106*, 5751. (b) Li, Z.; Vasella, A. *Helv. Chim. Acta* **1996**, *79*, 2201. (c) Ye, B.; Cramer, N. *J. Am. Chem. Soc.* **2013**, *135*, 636.



Scheme 3