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Rh(I)-Catalyzed Intramolecular Allenic Pauson−Khand Reaction: Construction of a Bicyclo[5.3.0]dec-1,7-dien-9-one Skeleton

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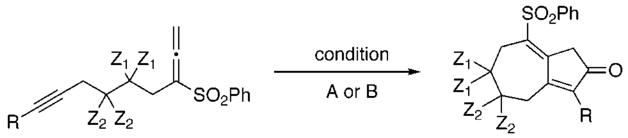
ABSTRACT



a : $Z_1 = Z_2 = H$, **b** = $Z_1 = H$, $Z_2 = CO_2Me$, **c** : $Z_1 = CO_2Me$, $Z_2 = H$

Condition A : $[RhCl(CO)_2]_2$, toluene, 1 atm CO
Condition B : $[RhCl(CO)dppp]_2$, toluene, 1 atm CO

1-Phenylsulfonylallenes possessing a hexynyl appendage in refluxing toluene in the presence of catalytic amount of rhodium(I) catalyst under a carbon monoxide atmosphere underwent regioselective formal [2 + 2 + 1]-cycloaddition to produce the corresponding bicyclo[5.3.0]dec-1,7-dien-9-one derivatives in acceptable yields.

The $Co_2(CO)_8$-mediated Pauson−Khand reaction (PKR) is a formal [2 + 2 + 1]-cyclization of an alkene, an alkyne, and carbon monoxide moieties.[1] The intramolecular version of this intriguing cyclization has been well recognized as one of the most powerful and reliable tools for constructing cyclopentenone-fused bicyclic derivatives. Thus, both bicyclo[3.3.0]octenone **1** and bicyclo[4.3.0]nonenone **2** frameworks[2] can be efficiently synthesized from the corresponding enyne derivatives. In sharp contrast, the application of this intramolecular $Co_2(CO)_8$-mediated PKR to the synthesis of bicyclo[5.3.0]decenone derivatives **3**[2e,3] has not yet been realized, except for the synthesis of azabicyclo[5.3.0]decenone derivatives[4] and medium-sized oxabicyclic compounds[5,6] from enynes with an aromatic ring as a template. On the other hand, the alkyne derivative **4** with an allenyl functionality[7−10]

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[1] For leading reviews, see: (a) Schore, N. E. *Org. React.* **1991**, *40*, 1. (b) Schore, N. E. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: Oxford, 1991; Vol. 5, p 1037. (c) Frühauf, H.-W. *Chem. Rev.* **1997**, *97*, 523. (d) Jeong, N. *Transition Met. Org. Synth.* **1998**, *1*, 560. (e) Geis, O.; Schmalz, H.-G. *Angew. Chem., Int. Ed.* **1998**, *37*, 911. (f) Brummond, K. M.; Kent, J. L. *Tetrahedron* **2000**, *56*, 3263.

[2] (a) Mukai, C.; Uchiyama, M.; Sakamoto, S.; Hanaoka, M. *Tetrahedron Lett.* **1995**, *36*, 5761. (b) Mukai, C.; Kim, J. S.; Uchiyama, M.; Sakamoto, S. Hanaoka, M. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2903. (c) Mukai, C.; Kim, J. S.; Uchiyama, M.; Hanaoka, M. *Tetrahedron Lett.* **1998**, *39*, 7909. (d) Mukai, C.; Kim, J. S.; Sonobe, H.; Hanaoka, M. *J. Org. Chem.* **1999**, *64*, 6822. (e) Mukai, C.; Sonobe, H.; Kim, J. S.; Hanaoka, M. *J. Org. Chem.* **2000**, *65*, 6654.

[3] A bicyclo[5.3.0]decenone framework with an oxygen-bridged structure was constructed in 29% yield by the zirconocene-mediated PKR. See: Wender, P. A.; McDonald, F. E. *Tetrahedron Lett.* **1990**, *31*, 3691. However, this structure can be regarded as an oxabicyclo[4.3.0]nonenone skeleton. In addition, an attempt at $Co_2(CO)_8$-mediated PKR was unsuccessful.

[4] Pérez-Serrano, L.; Casarrubios, L.; Domínguez, G.; Pérez-Castells, J. *J. Chem. Soc., Chem. Commun.* **2001**, 2602.

[5] (a) Kraft, M. E.; Fu, Z.; Boñaga, V. R. *Tetrahedron Lett.* **2001**, *42*, 1427. (b) Lovely, C. J.; Seshadri, H.; Wayland, B. R.; Cordes, A. W. *Org. Lett.* **2001**, *3*, 2607.

[6] Zr-mediated PKR for the preparation of medium-sized rings with an aromatic ring was also reported. Barluenga, J.; Sanz, R.; Fañanás, F. J. *Chem. Eur. J.* **1997**, *3*, 1324.

[7] Co-mediated PKR of alleynes: (a) Ahmar, M.; Antras, F.; Cazes, B. *Tetrahedron Lett.* **1995**, *36*, 4417. (b) Ahmar, M.; Chabanis, O.; Gauthier, J.; Cazes, B. *Tetrahedron Lett.* **1997**, *38*, 5277. (c) Ahmar, M.; Locatelli, C.; Colombier, D.; Cazes B. *Tetrahedron Lett.* **1997**, *38*, 5281. (d)

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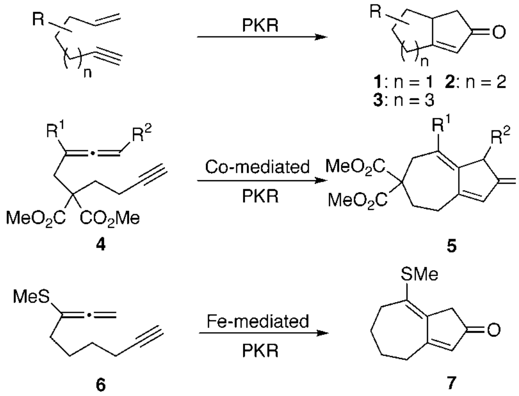
instead of an olefin group produced the bicyclo[5.3.0]dec-1,7-dien-9-one **5**[7c] under $Co_2(CO)_8$-mediated PKR conditions, although the chemical yields were rather low (10−25%). $Fe(CO)_4(NMe_3)$[9] was also found to promote the Pauson−Khand-type [2 + 2 + 1]-cyclization of an allenyne **6**, resulting in the formation of the bicyclo[5.3.0]dec-1,7-dien-9-one derivative **7** in 15% yield (Scheme 1).

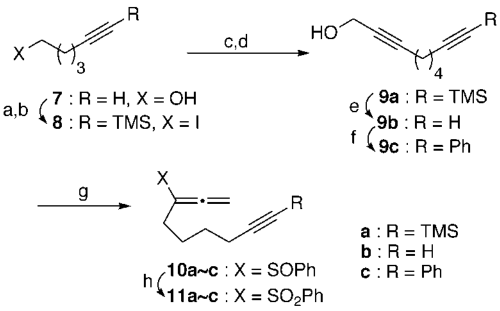
Scheme 1



Many bioactive natural products have a bicyclo[5.3.0]decane skeleton[11] as a basic carbon framework. Therefore, the straightforward and efficient preparation of a bicyclo[5.3.0]decane ring system under PKR conditions with an acceptable yield could become an alternative and useful method for the synthesis of these natural products. Recent reports from Jeong[12] and Narasaka[13] independently disclosed that rhodium(I) catalysts are effective in the PKR of enynes. To develop a reliable as well as straightforward procedure for preparing the bicyclo[5.3.0]decane framework by a Pauson−Khand-type reaction, we sought to combine these rhodium catalysts with allenyne derivatives. We paid much attention to allenynes having a sulfinyl or sulfonyl group as a starting material for this investigation, because these allenynes could be easily prepared from the corresponding propargyl alcohols and chemical transformation of these sulfur-containing groups to other functionalities was already reported. This Letter deals with our preliminary results regarding the efficient rhodium(I)-catalyzed PKR of allenynes[14] for the construction of 2-phenylsulfonylbicyclo[5.3.0]dec-1,7-dien-9-one derivatives.

The simple precursors **11** for the cyclization in this investigation were readily prepared from 5-hexyn-1-ol (**7**) (Scheme 2). Protection of the acetylenic terminus of **7** with a silyl group was followed by iodination to give **8**. The iodo compound **8** was then coupled with the acetylide, derived from the *O*-protected propargyl alcohol, to afford the diyne derivative, which was hydrolyzed under acidic conditions to give **9a** in 54% overall yield along with **9b** (16%). Desilylation of **9a** was easily performed with TBAF to give **9b** in 96% yield. Palladium-mediated Sonogashira coupling[15] of **9b** with iodobenzene proceeded under standard conditions to give **9c** in 68% yield. The three propargyl alcohols **9a**−**c** were independently exposed to benzenesulfenyl chloride[16] in the presence of Et_3N to give the corresponding sulfoxides, which were directly oxidized with *m*CPBA to furnish the allenyl sulfones **11** in yields of 69−78%.

Scheme 2[a]



[a] Reaction conditions: (a) (i) BuLi, TMSCl, THF, (ii) 10% HCl; (b) I_2, PPh_3, imid., CH_2Cl_2; (c) LiC≡CCH_2OTBS, THF−DMPU; (d) 10% HCl, MeOH, **9a** (54%), **9b** (16%); (e) TBAF, THF, (96%); (f) PhI, $PdCl_2(PPh_3)_2$, $^{i}Pr_2NH$, CuI, THF, (68%); (g) PhSCl, Et_3N, THF; (h) *m*CPBA, CH_2Cl_2, **11a** (78%), **11b** (69%), **11c** (69%).

For the initial evaluation of the rhodium-catalyzed PKR of the resulting allenynes, we first attempted the cyclization of compound **11b**.[17] A solution of **11b** in toluene was refluxed in the presence of 5 mol % of $[RhCl(CO)_2]_2$[13] under an atmosphere of carbon monoxide (condition A) for 1 h to give the bicyclo[5.3.0]dec-1,7-dien-9-one **12b** in 58% yield as a sole isolable product (Table 1, entry 3). Reducing the amount of the catalyst to 2.5 mol % in the same reaction gave a lower yield (41%). When 5 mol % of [RhCl(CO)-

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Pagenkopf, B. L.; Belanger, D. B.; O'Mahony, D. J. R.; Livinghouse, T. *Synthesis* **2000**, 1009. (e) Antras, F.; Ahmar, M.; Cazes, B. *Tetrahedron Lett.* **2001**, *42*, 8153. (f) Antras, F.; Ahmar, M.; Cazes, B. *Tetrahedron Lett.* **2001**, *42*, 8157.

(8) Mo-mediated PKR of alleynes: (a) Kent, J. L.; Wan, H.; Brummond, K. M. *Tetrahedron Lett.* **1995**, *36*, 2407. (b) Brummond, K. M.; Wan, H. *Tetrahedron Lett.* **1998**, *39*, 931. (c) Brummond, K. M.; Wan, H.; Kent, J. L. *J. Org. Chem.* **1998**, *63*, 6535. (d) Brummond, K. M.; Lu, J. *J. Am. Chem. Soc.* **1999**, *121*, 5087. (e) Brummond, K. M.; Lu, J.; Petersen, J. *J. Am. Chem. Soc.* **2000**, *122*, 4915. (f) Xiong, H.; Hsung, R. P.; Wei, L.-L.; Berry, C. R.; Mulder, J. A.; Stockwell, B. *Org. Lett.* **2000**, *2*, 2869.

(9) Fe-mediated PKR of allenynes: Shibata, T.; Koga, Y.; Narasaka, K. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 911.

(10) For Zr-mediated PKR of alleynes, see: refs 8b and 8c

(11) For example: (a) Herz, H.; Santhanam, P. S. *J. Org. Chem.* **1965**, *30*, 4340. (b) Lansburg, P. T.; Hangauer, D. G., Jr.; Vacca, J. P. *J. Am. Chem. Soc.* **1980**, *102*, 3964. (c) Heathcock, C. H.; DelMar, E. G.; Graham, S. L. *J. Am. Chem. Soc.* **1982**, *104*, 1907. (d) Grieco, P. A.; Majetich, G. F.; Ohfune, Y. *J. Am. Chem. Soc.* **1982**, *104*, 4226. (e) Heathcock, C. H.; Tice, C. M.; Germroth, T. C. *J. Am. Chem. Soc.* **1982**, *104*, 6081.

(12) (a) Jeong, N.; Lee, S.; Sung, B. K.*Organometallics* **1998**, *17*, 3642. (b) Jeong, N.; Sung, B. K.; Choi, Y. K. *J. Am. Chem. Soc.* **2000**, *122*, 6771.

(13) (a) Koga, Y.; Kobayashi, T.; Narasaka, K. *Chem. Lett.* **1998**, 249. (b) Kobayashi, T.; Koga, Y.; Narasaka, K. *J. Organomet. Chem.* **2001**, *624*, 73.

(14) During this investigation, the Rh(I)-catalyzed PKR of an allenyne leading to formation of the bicyclo[4.3.0]non-1,6-dien-8-one derivative in 61% yield was reported. See ref 13b.

(15) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467.

(16) Horner, L.; Binder, V. *Ann. Chem.* **1972**, *37*, 757.

(17) Rh(I)-catalyzed PKR of the sulfoxide derivative **10b** was examined under conditions A and B; however, no reaction took place and the starting sulfoxide was completely recovered intact.

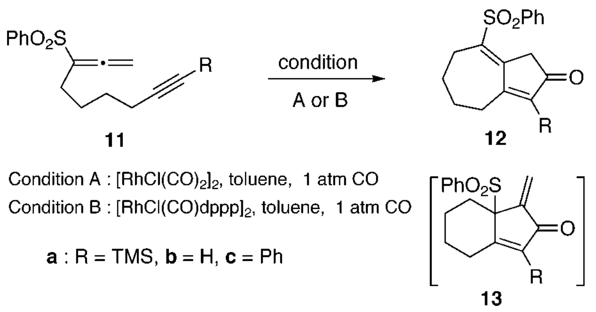


Table 1. Ring Closure of Allenes **1**

entry	allene	R	condition	mol %	product	yield (%)
1	**11a**	TMS	A	5	**12a**	45
2	**11a**	TMS	B	5	**12a**	7[a]
3	**11b**	H	A	5	**12b**	58[b]
4	**11b**	H	B	5	**12b**	75[c]
5	**11c**	Ph	A	2.5	**12c**	51
6	**11c**	Ph	B	2.5	**12c**	84

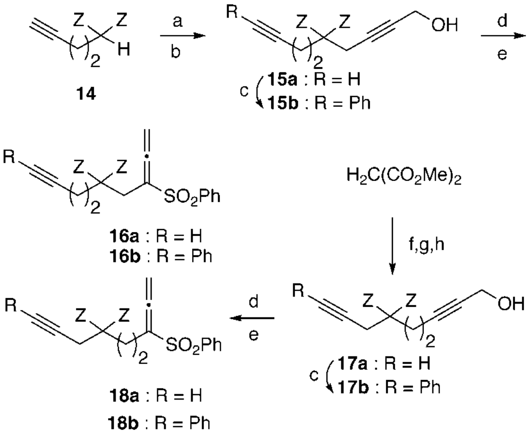
[a] The starting material **11b** was recovered in 45% yield. [b] The cyclized product **12b** was obtained in 41% yield when 2.5 mol % of $[RhCl(CO)_2]_2$ was used. [c] The cyclized product **12b** was obtained in 56% yield when 2.5 mol % of $[RhCl(CO)dppp]_2$ was used.

dppp]$_2$[12] (condition B) was used instead of $[RhCl(CO)_2]_2$, the ring-closed product **12b** was formed in a higher yield (75%, entry 4). Similar treatment of the phenyl derivative **11c** under both conditions A and B gave the corresponding bicyclo[5.3.0]dec-1,7-dien-9-one **12c** in respective yields of 51% and 84% (entries 5 and 6). Upon exposure to condition A, **11a** gave **12a** in 45% yield (entry 1). However, condition B gave **12a** in only 7% yield along with recovery of the starting material **11a** in 45% yield (entry 2). These results are summarized in Table 1. Several points deserve comment. (i) The bicyclo[5.3.0] skeleton was constructed in acceptable yields compared to those in previous works.[7c,9] (ii) Complete chemoselectivity was observed in the formal [2 + 2 + 1]-cycloaddition, leading to the exclusive construction of the bicyclo[5.3.0]dec-1,7-dien-9-one framework **12**, while the corresponding bicyclo[4.3.0]nonenone derivative **13** was not detected in the reaction mixture.

Our next step was to see whether conditions A and B could be applied to other allenynes. Therefore, we investigated the rhodium-catalyzed PKR of four additional alleynes **16a,b** and **18a,b**. The allenynes required for the cyclization were prepared as depicted in Scheme 3. Treatment of the malonate **14** with the iodobutyne derivative was followed by desilylation to give **15a** in 80% yield. According to the procedure described for the transformation of **9** into **11**, **15a** was easily converted through [2,3]-sigmatropic rearrangement[16] to the corresponding alleyne **16a** in 78% yield. The Sonogashira coupling[15] of **15a** with iodobenzene produced **15b**, which was subsequently converted to the phenyl congener **16b**. The two other starting allenynes **18a,b** could also be easily obtained from dimethyl malonate by conventional means (Scheme 3).

The rhodium-catalyzed PKR of two allenynes **16a,b** proceeded under both two conditions A and B as expected

Scheme 3[a]



[a] Reaction conditions: (a) NaH, $ICH_2C\equiv CCH_2OTBDPS$, THF; (b) TBAF, THF, (80%); (c) PhI, $PdCl_2(PPh_3)_2$, $^iPr_2NH$, CuI, THF, **15b** (82%), **17b** (95%); (d) PhSCl, Et_3N, THF; (e) *m*CPBA, CH_2Cl_2, **16a** (78%), **16b** (80%), **18a** (77%), **18b** (80%); (f) NaH, DMF, $I(CH_2)_2C\equiv CCH_2OTHP$; (g) NaH, $BrCH_2C\equiv CH$, THF; (h) *p*-TsOH, MeOH, (56%).

to produce the bicyclo[5.3.0]dec-1,7-dien-9-one derivatives **17a,b** in good yields. A similar result was observed when alleynes **18a,b** were exposed to conditions A and B, although the yields with the latter compounds seemed to be somewhat lower. The results are shown in Table 2.

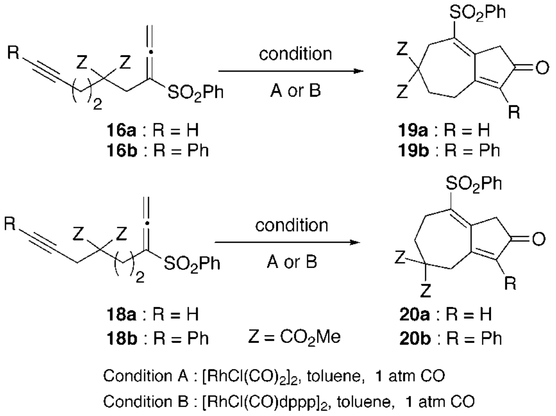
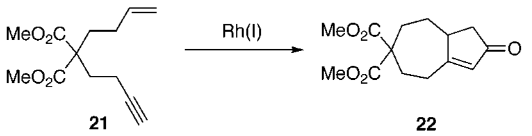


Table 2. Ring Closure of Allene **16** and **18**

entry	allene	R	condition	mol %	product	yield (%)
1	**16a**	H	A	2.5	**19a**	84
2	**16a**	H	B	2.5	**19a**	70
3	**16b**	Ph	A	2.5	**19b**	70
4	**16b**	Ph	B	2.5	**19b**	71
5	**18a**	H	A	2.5	**20a**	58
6	**18a**	H	B	2.5	**20a**	59
7	**18b**	Ph	A	2.5	**20b**	40
8	**18b**	Ph	B	2.5	**20b**	69

We next examined the PKR of the enyne derivative **21** by applying conditions A and B, which effectively catalyzed

Scheme 4



the PKR of allenynes. Thus, a solution of **21** in toluene was refluxed for a long time in the presence of catalytic amounts of rhodium catalyst under a carbon monoxide atmosphere. However, no cyclized product **22** could be detected in the reaction mixture, and the starting material **21** was completely recovered intact.

In summary, we have developed a reliable procedure for constructing a bicyclo[5.3.0]decane ring system by the rhodium-catalyzed PKR of allenynes with a sulfonyl group.[18] Acceptable yields could be achieved through the proper choice of the rhodium catalyst ([RhCl(CO)$_2$]$_2$ or [RhCl(CO)dppp]$_2$) depending on the starting allenyne. The application of this rhodium-catalyzed PKR of allenynes to the construction of other ring systems, such as the bicyclo[6.3.0]undec-1,8-dien-10-one framework, is now in progress.

Acknowledgment. We wish to thank Professor Nakcheol Jeong, Korea University, Korea, for useful discussions on the rhodium(I) catalyst.

Supporting Information Available: Experimental procedures for ring closure and preparation of compound **16a** and spectral data and ^{1}H and ^{13}C NMR spectra for **11a−c**, **12a−c**, **16a,b**, **18a,b**, **19a,b**, and **20a,b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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[18] Preliminary experiments revealed that the compound having a diethylphosphono group [PO(OEt)$_2$] at the C-1 position of an allenyl moiety instead of a sulfonyl group (e.g., **16a**), upon exposure to the Rh(I)-catalyzed cyclization conditions, produced the corresponding bicyclo[5.3.0]dec-1,7-dien-9-one skeleton. The details of these results will be reported later.