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The exclusive formation of cyclopentenones from molybdenum hexacarbonyl-catalyzed Pauson–Khand reactions of 5-allenyl-1-ynes

Arun Kumar Gupta, Dai In Park and Chang Ho Oh*

Department of Chemistry, Hanyang University, Sungdong-Gu, Seoul 133-791, North Korea

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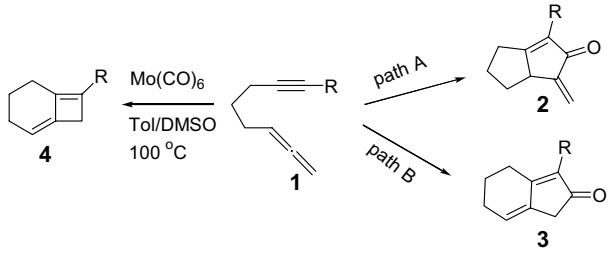
Abstract—The exclusive formation of cyclopentenones (via path B) was observed in molybdenum hexacarbonyl (10 mol %) catalyzed Pauson–Khand reactions of 1,6-allenynes under 1 atm of CO (balloon) without any substitutent effect.

Allenynes have been found to be of great importance in the field of organometallics[1] and in the construction of natural product frameworks.[2] This may be because of the unique reactivity due to the existence of the two orthogonal π-bonds. Recently, Brummond et al. have greatly enhanced the synthetic utility of allenes in the field of Pauson–Khand reactions (PKR) in place of alkenes.[3] Despite early documentation of the catalytic PKR (CPKR) by Pauson and co-workers, applications of the PKR have to date almost exclusively exploited the stoichiometric approach.[4] In the light of the developments in recent years, we are now entering the catalytic age of the PKR and the stoichiometric use of toxic metal complexes becomes increasingly difficult to justify. In the last decade, many practical alternatives to the original catalyst, $[Co_2(CO)_8]$, have been designed and investigations of other transition metal complexes based on titanium, rhodium, ruthenium, and iridium have been rewarded with an impressive catalytic activity.[5] In the case of the intramolecular coupling of allenynes, there are two possible products based on the reaction site of an allenic moiety (Scheme 1). Reaction with the internal π-bond of the allene **1** gives a bicyclic cyclopentenone possessing an alkylidene substituent **2** (path A), while reaction with the external π-bond gives a bicyclic dienone **3** (path B). As in the first report of intramolecular coupling of allenynes mediated by $Fe(CO)_4(NMe_3)$,[6] cobalt-mediated and rhodium-catalyzed reactions followed path B.[7] On the other hand, the use of a stoichiometric amount of molybdenum carbonyl complex generally gave only α-methylene-cyclopentenones **2** via path A.[8] Under the same reaction condition, however, 3,3-disubstituted allenynes gave bicyclo[4.3.0] nonane ring system via path B by utilizing the external π-bond.[9] However, there are only a few examples of this type of substrate dependence in the [2+2+1] reactions reported in the literature.[10] It is interesting to note that each pathway in cyclization gives interesting structures that are substructures in a variety of biologically important compounds such as illudins, hydroxymethylacylfulvene, crinipellin A, and the prostaglandins.[2]



Scheme 1.

Recently, Shin and Hammond[11] reported the intramolecular [2+2] cycloaddition (product **4**) from molybdenum-catalyzed reaction of 1,7-allenyne, where the

Keywords: Molybdenum hexacarbonyl; 1,6-Allenynes; Pauson–Khand reaction; Cyclopentenones.
* Corresponding author. Tel.: +82 2 2220 0932; fax: +82 2 2299 0762; e-mail: akg1966@yahoo.com

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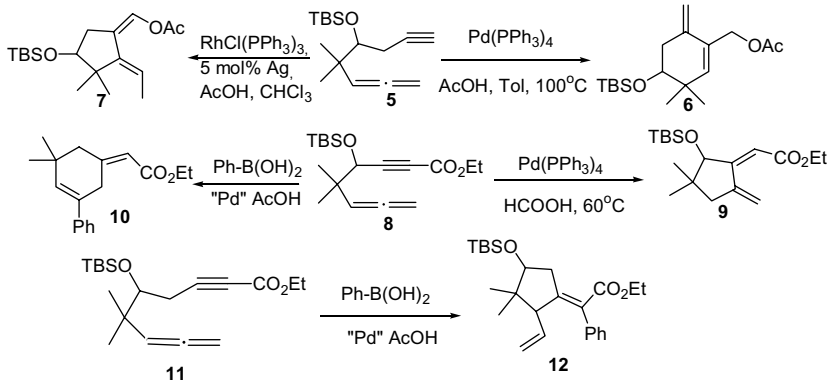
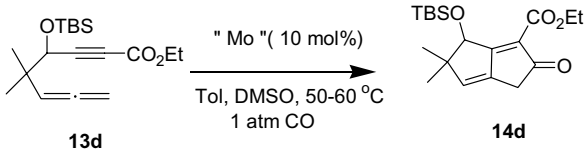


Scheme 2.

metal complex was used in a catalytic amount. The reactivity of allenyne is very much metal dependent. Allenynes, in particular, 6-allen-1-ynes **5**, give six-membered carbocycles **6** in the presence of $Pd(PPh_3)_4$ and five-membered carbocycles **7** in the presence of $RhCl(PPh_3)_3$ chemoselectively.[12] More recently, we reported Pd(0) catalyzed cycloreduction of 5-allen-1-yne **8** to **9** (Scheme 2).[13] We have also demonstrated that 1,6-allenyne **8** upon addition of organoboronic acid gave six-membered ring **10** while 1,7-alleneyne **11** gave five-membered ring **12**. Thus it suggests that, besides to the reaction conditions and metal complexes used in the reaction, lengths of the thether between allene and alkyne also influence the reaction pathway.[14]

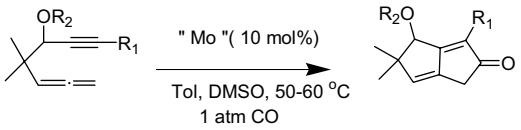
It is evident that the allenic PK cycloaddition reaction provides quick access to naturally occurring products, which otherwise would be very difficult to prepare or would need numerous steps to produce the cyclopentenones.[15] However, PKR reactions of 1,6-allenyne has not been much explored. As a part of our ongoing research project for the construction of bicyclic cyclopentenones, the characteristic behavior of allenynes inspired us to take this assignment; thus we have prepared 1,6-allenynes **13a**–**p** for our study. In order to test the feasibility of the allenic PK cycloaddition, compound **13d** was used as a representative starting material. PK cycloaddition of **13d** with dicobalt octacarbonyl was unsuccessful and with other metal complexes such as rhodium carbonyl complexes such as $[RhCl(CO)_2]_2$ and ruthenium carbonyl complexes such as $[Ru_3(CO)_{12}]$ resulted in limited success. However, treatment of **13d** with molybdenum hexacarbonyl $[Mo(CO)_6]$ in toluene containing a trace amount of DMSO at 60–80 °C under 1 atm of carbon monoxide (balloon) gave the desired product **14d**[16] in 89% yield. Although the reaction was monitored by GC–MS, the color of the reaction medium has also proven to be diagnostic of the progress of the reaction. As the reaction temperature approached to 50–60 °C, the molybdenum complex started to dissolve and the clear heterogeneous mixture turned to brightly yellow. Soon after, the solution turned to a greenish-grey and TLC monitoring showed a spot indicating product formation. Eventually, a blue precipitate was formed on the walls of the flask and the starting material was no longer consumed (Table 1).



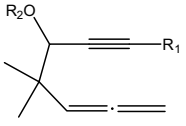
After the initial success of this allenic PK cycloaddition, we were interested in examining the effect of substituents on the alkyne as well as on the allene in order to explore the scope of the reaction. TBS protected 1,6-allenynols did not produce any significant improvement in terms of yields. We have also checked the influence of substitution on the alkyne site. We have performed reactions with free terminal alkyne (**13a**, **b**, **i**, **j**), and substitution with carbethoxy (**13c**, **d**, **k**, **l**, **n**, **p**) *n*-butyl (**13e**, **f**) and phenyl (**13g**, **h**) groups. In fact, the presence of an electron-withdrawing group such as the carbethoxy group (**13c**, **d**, **k**, **l**, **m**, **p**) enhanced the rate of reaction when compared with *n*-butyl **13e**–**f** and also phenyl ring **13g**–**h** substitution. Next, we examined substitutions on the allene moiety, since there are numerous natural products possessing cyclopentenone, and the allenic [2+2+1] cycloaddition provides a direct route to this structure. As we anticipated, compounds **13i**–**l** underwent PKR cyclizations by path B to give **14i**–**l** in 79%, 75%, 83% and 82% yields, respectively. It is noteworthy that 1,3-disubstituted allenynes **13m**–**p** did not involve any cycloisomerization during the process of the PKR reaction and gave **14m**–**p** in good yields. The nitrogen allenynes **13q** and **r** also under went PKR reaction smoothly and gave **14q** and **r**, respectively.

In summary, we have demonstrated that all 1,6-allenynes underwent the Pauson–Khand reaction in the presence of a catalytic amount of molybdenum hexacarbonyl complex under 1 atm carbon monoxide to give only cyclopentenones. We have not observed any limitation of the substituent and/or protecting group effect on the substrate. In particular, substitution on the terminal allene carbon did not give any isomerized product. All the reported reactions gave good to excellent yields at milder reaction temperature with an easy isolation procedure.

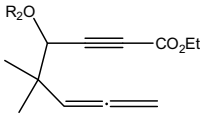
Table 1. Mo-catalyzed PKR reactions of 1,6-allenynes



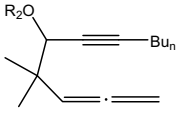
Compd	Temp (°C)/time (h)	Product	Yield (%)
13a	60, 5	**14a**	79
13b	60, 5	**14b**	83
13c	60, 4	**14c**	85
13d	**60**, **4**	**14d**	**89**
13e	60, 5	**14e**	80
13f	60, 5	**14f**	81
13g	60, 5	**14g**	87
13h	60, 5	**14h**	91
13i	60, 5	**14i**	79
13j	60, 7	**14j**	75
13k	60, 6	**14k**	83
13l	60, 6	**14l**	82
13m	60, 6	**14m**	75
13n	60, 6	**14n**	83
13o	60, 4	**14o**	85
13p	60, 4	**14p**	89
13q	60, 4	**14q**	63
13r	60, 4	**14r**	68



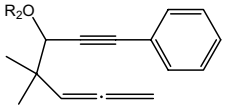
R_1=R_2=H **13a**
R_1=H, R_2=OTBS **13b**



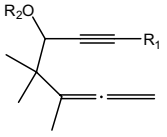
R_2 = H **13c**
R_2 = OTBS **13d**



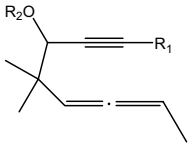
R_2 = H **13e**
R_2 = OTBS **13f**



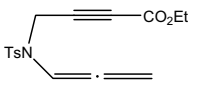
R_2 = H **13g**
R_2 = OTBS **13h**



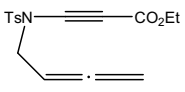
R_1= R_2 = H **13i**
R_1= H, R_2 = OTBS **13j**
R_1=CO_2Et, R_2 = H **13k**
R_1=CO_2Et, R_2 = OTBS **13l**



R_1= R_2 = H **13m**
R_1= H, R_2 = OTBS **13n**
R_1=CO_2Et, R_2 = H **13o**
R_1=CO_2Et, R_2 = OTBS **13p**



13q



13r

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16. General experimental procedure: To a solution of molybdenum hexacarbonyl (10 mol %) in degassed toluene (0.5 mL) containing 25 μL of DMSO under 1 atm of CO (balloon), allenyne **13** (0.1 mmol) in toluene (0.5 mL) was added via a cannula. After 10 min stirring at room temperature, the resulting solution was heated to 60 °C in a constant temperature bath until consumption of starting material was observed by TLC. The reaction mixture was cooled to room temperature, diluted with 5–10 mL of diethyl ether and filtered through Celite. The solvent was evaporated under vacuum to give the crude product with almost 95% HPLC purity. Finally, the crude product was passed through silica gel flash chromatography by eluting with an EA/*n*-hexane mixture to give the pure product **14**. All the products were characterized by IR, ^{1}H NMR, ^{13}C NMR, and finally with HRMS.