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Catalyst precursors for the catalytic Pauson–Khand reaction

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Abstract

Dicobalt hexacarbonyl complexes of enynes serve as $Co_2(CO)_8$ surrogates for the intramolecular Pauson–Khand cycloaddition. Enynes with polar functional groups allow for easy separation of the catalyst cyclopentenone by-product (acid or base wash, silica gel plug column) from the desired cyclopentenone. © 1999 Elsevier Science Ltd. All rights reserved.

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The Pauson–Khand [2+2+1] cycloaddition of an alkene, an alkyne and carbon monoxide to generate cyclopentenones has proven to be of significant synthetic utility.[1,2] The stoichiometric reaction proceeds thermally or via amine oxide promotion[3] at ambient temperature or below. The catalytic version of the cycloaddition has also been the subject of a number of reports.[4] Recently, Livinghouse reported two protocols[5,6] for catalytic thermal Pauson–Khand reactions under normal laboratory conditions, i.e. 1 atm of carbon monoxide pressure. In the first communication,[5] high purity $Co_2(CO)_8$ was required for efficient catalysis. An alternative procedure[6] used a pre-made and purified alkyne–$Co_2(CO)_6$ complex as a dicobalt octacarbonyl surrogate. A subsequent in situ reduction of the initial alkyne–$Co_2(CO)_6$ complex with Et_3SiH was used to generate the active catalyst. Herein we report the preparation and use of new catalyst precursors which obviate the need for the additional reduction step (Scheme 1).

Once the catalytic cycle had been demonstrated by Livinghouse as an efficient process under normal laboratory conditions, it seemed reasonable that a suitably substituted enyne complex could serve as the catalyst precursor. The Pauson–Khand reaction of a dicobalt hexacarbonyl-complexed enyne, under a carbon monoxide atmosphere, would generate the appropriate catalyst thus making the reduction step unnecessary. In designing a catalyst precursor, we envisioned several requirements that needed to be met: (1) the enyne complex must be sufficiently reactive in order to undergo cycloaddition and liberate the catalyst at a reasonable rate upon heating. Complexes of enynes bearing terminal alkynes or having Thorpe–Ingold assistance generally cyclize at a sufficient rate; (2) the product of cycloaddition from the catalyst precursor must differ in polarity from the desired product to eliminate any separation problems after reaction; and (3) the catalyst precursor must be shelf-stable, preferably crystalline, and easy to

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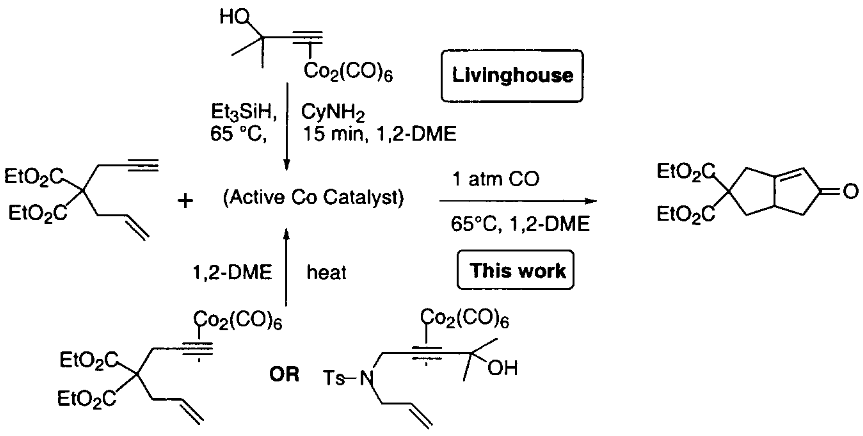
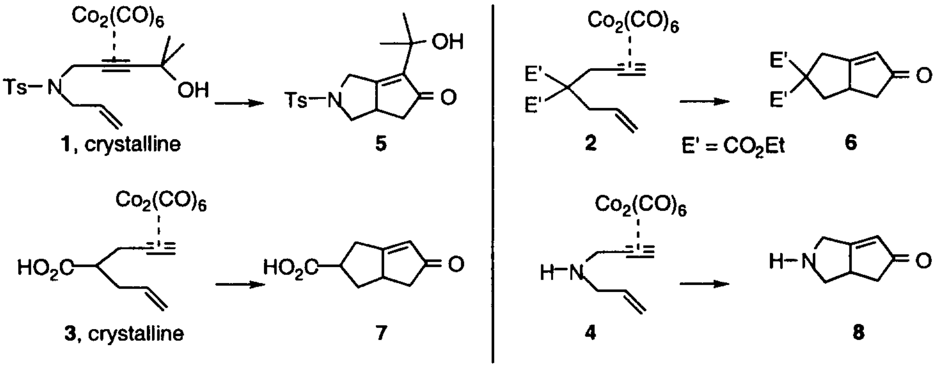


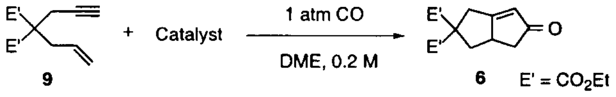
Scheme 1.

purify. Although it may not always be practical, one can easily envision using a catalytic amount of the dicobalthexacarbonyl complex of the actual substrate of interest. The dicobalt hexacarbonyl complexes **1–4** were chosen as representative catalyst precursors to demonstrate the generality of using enyne complexes to initiate the catalytic cycle (Scheme 2). Comparative Pauson–Khand reactions of enyne **9** with the dicobalt hexacarbonyl complexes **1–4** are listed in Table 1.



Scheme 2.

Table 1
Evaluation of catalyst precursors



Entry	Cat.	Cat.(%)	Temp(°C)	Time(h)	**6** Yield(%)
1	$Co_2(CO)_8$	10	65	15	80
2	**1**	10	70	2	78
3	**2**	10	70	5	79*
4	**3**	10	70	1	75
5	**4**	10	70	1	92

* Percent yield calculation based on expected product from the catalyst plus the substrate

The results in Table 1 illustrate that the catalyst precursors listed above were very effective in initiating the cycloaddition. Catalyst precursor **2** illustrates the use of the substrate as catalyst. Enone **5**, generated from reaction of enyne complex **1**, is polar enough to be readily separated from most cycloadducts. Enone **7**, generated from pre-catalyst **3**, can be washed out with base or removed by flushing the reaction mixture through a plug of silica gel which is necessary to remove cobalt residues. In the same manner, enone **8**, from precursor **4**, can be removed via an acid wash or with a silica gel plug.

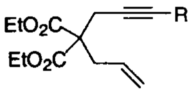
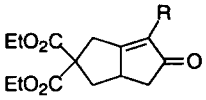
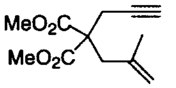
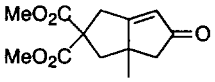
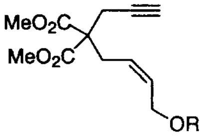
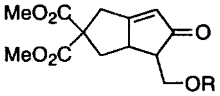
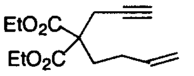
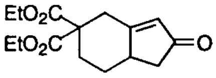
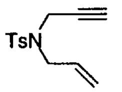
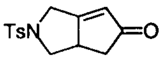
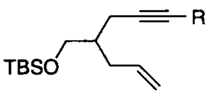
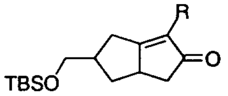
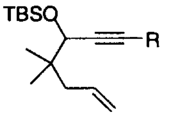
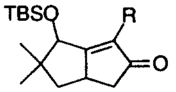
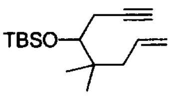
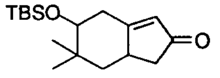
The examples in Table 2 illustrate the generality of catalyst precursor **1** in initiating the intramolecular Pauson–Khand reaction. Some of the cycloadditions proceeded in higher yield in the presence of cyclohexylamine. Sugihara[7] has shown that additives such as $CyNH_2$ promote the Pauson–Khand reaction. The reason for this enhancement in yield is not entirely clear and the outcome does not appear to be predictable with these examples. While the amine may serve in several capacities during the reaction manifold, a significant role may be as a catalyst carrier thereby increasing the longevity of the intermediate complexes. As can be seen from the results, a delicate balance of $CyNH_2$ and $Co_2(CO)_8$ is essential to the efficiency of this method.

In summary, we have shown that dicobalt hexacarbonyl complexes of enynes act as efficient catalyst precursors for the intramolecular Pauson–Khand reaction. Further work on the catalytic Pauson–Khand reaction is in progress.

Preparation of complex **1**: To a solution of *N*-tosyl-*N*-allyl-propargylamine[9] (492 mg, 1.97 mmol) in THF (20 mL) at −78°C was added 1.3 M *sec*-BuLi in cyclohexane (2.0 mL, 2.6 mmol). The reaction was then warmed to ambient temperature and acetone was added (2.0 mL). After stirring for 30 min, the resulting mixture was quenched with water and extracted with ethyl acetate. The organic layer was dried over sodium sulfate and concentrated in vacuo. Flash column chromatography (silica gel, hexane:ethyl acetate=1:1) yielded *N*-tosyl-*N*-allyl-4-hydoxy-4-methyl-2-pentynylamine (347 mg, 1.13 g) as a colorless oil in 57% yield. To a solution of *N*-tosyl-*N*-allyl-4-hydoxy-4-methyl-2-pentynylamine (159 mg, 0.488 mmol) in a 1:1 mixture of petroleum ether:dichloromethane (5 mL) was added solid dicobalt octacarbonyl[10] (220 mg, 0.643 mmol) [$Co_2(CO)_8$ was obtained from Strem Chemical Co. stabilized with 1–5% hexane] at ambient temperature. After stirring for 30 min, the reaction mixture was directly subjected to column chromatography (silica gel, petroleum ether:ether=1:1). Concentration of the eluent at room temperature in vacuo gave **1** as a red-brown solid (260 mg, 0.438 mol) in 90% yield.

Representative experimental procedure: A *carefully base-washed* 10 mL flask equipped with a three-way stopper, a condenser and a balloon of CO containing a mixture of enyne **9** (50.9 mg, 0.213 mmol) and catalyst **1** (12.1 mg, 0.0204 mmol) was pumped briefly and purged three times with CO. Freshly distilled 1,2-DME (1.0 mL) was added and the resulting solution was heated to 70°C and stirred for 2 h. Upon completion of the reaction the mixture was cooled to room temperature, quenched with water and extracted with ethyl acetate. The organic layer was dried over sodium sulfate and concentrated in vacuo. Flash column chromatography (SiO_2, hexane:ethyl acetate=2:1) yielded **6** (44.3 mg, 0.166 mmol) in 78% yield. If appropriate, cyclohexylamine was added prior to heating. Alternatively, the reaction could be worked up by dilution with 10% EtOAc in hexanes and plugged through a pad of silica gel using hexane/ethyl acetate as the eluent. It was further observed that *inadvertent introduction of air into the system from frequent checking of the reaction by TLC resulted in incomplete consumption of the starting material.*

Table 2
Pauson–Khand reactions using catalyst precursor **1**[a]

Entry	Substrate	Product[8]	% Yield (time, h)
			
1		R=H	78 (2)
2		R=nPr	67 (9)[b]
3			84 (16)
			
4		R=TBS	94 (6)[b,c]
5		R=Ac	93(16)[b,c]
6			81 (20)[b]
7			94 (8)[b]
			
8		R=H	81 (16)[b,d]
9		R=nPr	72 (16)[d,e]
			
10		R=H	83 (16)[f]
11		R=Me	61 (6)[d]
12		R=TMS	NR
13			75 (5)[g]

a. All reactions were carried out using a substrate concentration of 0.2 M in dimethoxyethane (DME) with 10 mol% of catalyst **1** under a CO atmosphere at 70 °C, unless stated otherwise. b. 20 mol% of cyclohexylamine was used. c. >20:1 ratio of diastereomers. d. 1:3 ratio of diastereomers. e. 40 mol% of cyclohexylamine was used. f. 1:1 ratio of diastereomers. g. 1:4 ratio of diastereomers.

Acknowledgements

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