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Synthesis of Cyclopentenones: The New Catalytic Cocyclization Reaction of Alkyne, Alkene, and Carbon Monoxide employing Catalytic Co(acac)$_2$ and NaBH$_4$

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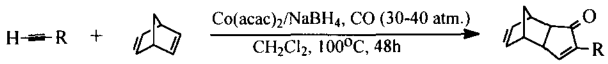
Abstract: A new catalytic cycloaddition reaction of alkyne, alkene, and carbon monoxide employing catalytic amount of Co(acac)$_2$ and NaBH$_4$ was developed for the synthesis of cyclopentenones. This catalytic system worked quite effectively for both intermolecular and intramolecular reactions.

Cyclopentenone systems are often embedded in numerous natural and unnatural organic compounds and have been the subject of intensive synthetic efforts.[1] The metal-promoted synthesis of cyclopentenones from readily available substrates has been recognized as an efficient synthetic method[2] and among them Pauson-Khand reaction (PKR)[3] represents one of the most powerful metal-promoted methods for the construction of the cyclopentenone system. However, most PKRs are stoichiometric reactions. There have been many attempts to catalyze the PKR, but the truly catalytic reactions described so far are very limited.[4] A number of alternatives to the PKR have been reported.[5] Recently we reported[6] a catalytic system (indenyl)Co(COD) to give cyclopentenones in excellent yields. Herein we report a new catalyst system that proceeds under mild reaction conditions to afford cyclopetenones in excellent yields.



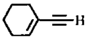
Incorporation of Co(acac)$_2$ and NaBH$_4$ as a catalyst system was a key to the development of the new process. In comparison to the (indenyl)Co(COD) system, this new system tolerates functionalities such as halide and ester and is applicable to the reaction employing acetylene.

We envisioned that a system could be catalytic if it can generate in situ low valent cobalts[7] which can complex with dienes and alkynes or can produce cobalt carbonyls under CO. In fact, we screened several cobalt salts such as Co(acac)$_n$ (n = 2, 3) with/without NaBH$_4$, CoCl(PPh$_3$)$_3$, CoCl$_2$, and CpCo(CO)$_2$ using norbornene and phenylacetylene as substrates. As we expected, most of them showed marginal catalytic activities.[8] We have found that a system of Co(acac)$_2$ with NaBH$_4$ provided the best chemical yield under the reaction conditions. The use of Co(acac)$_n$ (n = 2 or 3) as a catalyst in the cycloaddition of norbornadiene has been recently reported.[9]

A representative experimental procedure for the intermolecular cocyclization reaction of alkyne with norbornadiene is as follows. When a mixture of alkyne (5 mmol), alkene (15 mmol), Co(acac)$_2$[10] (65 mg, 5 mole %) and NaBH$_4$ (10 mg, 2 equiv. based on cobalt) in 20 mL of CH$_2$Cl$_2$ was heated under carbon monoxide

(40 atm at room temperature) at 80 - 100 °C for 2 d - 3 d, the corresponding cyclopentenone derivative was obtained in a high yield after column chromatography. Results obtained from several representative substrates under standard conditions are summarized in Table 1.

Table 1. Intermolecular Cocyclization Catalyzed by $Co(acac)_2$ and $NaBH_4$

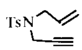
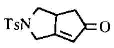
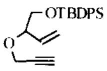
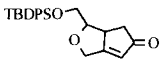
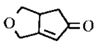
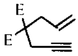
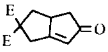
entry	alkyne	alkene	$Co(acac)_2$, mol%	$NaBH_4$, mol%[a]	yield (%)[b]
1	Ph$-\equiv-$H		0.02	0	quant.
2	Ph$-\equiv-$H		0.01	0	65
3	Ph$-\equiv-$H		0.01	0.02	quant.[c]
4	Ph$-\equiv-(CH_2)_nCH_3$ (n=3,4)		0.05	0.10	quant.
5	Ph$-\equiv-(CH_2)_n-\equiv-$H (n=4,5)		0.05	0.10	80-85
6			0.05	0.10	80
7	H$-\equiv-(CH_2)_3Cl$		0.05	0.10	83
8	H$-\equiv-CH_2OH$		0.05	0.10	69
9	H$-\equiv-CO_2Et$		0.05	0.10	33
10	H$-\equiv-$H				1225[d]

[a] Based on alkyne. [b] All given in this table are isolated yields. [c] This reaction was carried out in DME. [d] Acetylene (5 atm.) and CO (20 atm.) were used. This reaction was carried in C_6H_6 at 150 °C for 120 h. The yield was based on the $Co(acac)_2$.

Table 1 gives details on the amounts of reagents and conditions of catalytic runs for intermolecular cycloaddition reaction. For all the reactions in Table 1, only exo-products were obtained. The reaction proceeded well even without $NaBH_4$ (entry 1). However, for other reactions, the use of $NaBH_4$ was required. Phenylacetylene exhibited a higher reactivity and yield in the presence of $NaBH_4$ (entries 2 vs. 3). Acetylenes bearing n-alkyl chains (entry 4) and n-alkyl halide (entry 7), an alkyne conjugated with double bond (entry 6), and diynes (entry 5) also gave excellent yields. Propargyl alcohol (entry 8) and ethyl propiolate (entry 9) known as poor substrates for the Pauson-Khand reaction gave 69 and 33% yields, respectively. While with the new catalytic system, the yields for entries 7 and 9 were 83 and 33%, respectively, (indenyl)Co(COD) was not effective[6] for both entries. When acetylene was used as an alkyne substrate (entry 10), we obtained the expected product in 1225% yield based on $Co(acac)_2$ used. Acetylene was not a satisfactory substrate for (indenyl)Co(COD) system. Thus, this catalyst system is quite effective for intermolecular cycloaddition reaction. However, with the less reactive alkenes such as cyclopentene, indene, and cyclohexadiene, this catalytic system was not effective.

The scope of this catalytic process was examined for intramolecular cycloaddition reaction (Table 2). The intramolecular reaction was not as effective as intermolecular reaction. However, enynes were transformed into the corresponding cyclopentenones.

Table 2. Intramolecular Cocyclization Catalyzed by $Co(acac)_2$ and $NaBH_4$

substrate	$Co(acac)_2$, mol%	$NaBH_4$, mol%	product	yield (%)[a]
	0.046	0.092		85
	0.10	0.20		82 [b]
	0.10	0.20		59
	0.05	0.10		66

[a] All yields given in this table are isolated yields. [b] A diastereomeric mixture was obtained in the ratio of 3.7: 1.

The following observations might provide some mechanistic insights for the catalysis. The formation of some cobalt carbonyls was observed in every reaction. In fact, when 1-cyclohexenylethyne was used as a substrate, (1-hexyne)$Co_2(CO)_6$ was isolated When 1-hexyne and ethylene were used as substrates, a small amount of bifurandione was obtained.[11] Ethylene did not participate in the reaction because of low reactivity. Pauson *et al.* reported[12] the formation of bifurandiones from the reaction of $Co_2(CO)_8$ with acetylenes and carbon monoxide. Thus it can be inferred that in our catalytic system cobalt carbonyls, presumably $Co_2(CO)_8$, are generated in situ and participate in the reaction with alkyne and then with alkene to give the product. However, the use of $Co_2(CO)_8$ as a catalyst was not successful.[13] The main obstacle to the thermal PKR is the formation of either metal clusters or inactive cobalt carbonyl species. Thus in the thermal PKR, phosphite or phosphine ligands were added to prevent the formation of inactive cobalt species.[4] It is presumed that the role of $NaBH_4$ might be to prevent the formation of cobalt clusters or inactive cobalt species.[14] Thus, in the presence of $NaBH_4$, the catalytic cycle continues.

In conclusion, a new catalytic cocyclization of alkyne, alkene and, carbon monoxide employing readily available $Co(acac)_2$ and $NaBH_4$ provides a simple and mild way to synthesize cyclopentenone systems. This catalyst system is quite effective to both intermolecular- and intramolecular cycloaddition reactions. While work is in progress to study detailed reaction mechanism of this new catalytic ststem, the simplicity and availablity of the catalyst system should encourage the use of this catalytic system among synthetic organic chemists.

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14. According to our preliminary experiments, in the presence of NaBH$_4$ the alkyne dicobalt hexacarbonyls react catalytically with strained alkenes under CO. Now a manuscript is in preparation.

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