

## Rhodium-catalyzed CO gas-free carbonylative cyclization using aldehydes\*

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**Abstract:** A new protocol for CO gas-free carbonylation, in which aldehydes are used as a substitute for CO, is described. The protocol consists of two Rh-mediated processes; the Rh-mediated decarbonylation of aldehydes, which leads to the formation of Rh carbonyl, and subsequent Rh-catalyzed carbonylative cyclization utilizing the *in situ* formed Rh carbonyl species.

**Keywords:** homogeneous catalysis; carbonylation; transition metals; carbonyl; aldehydes.

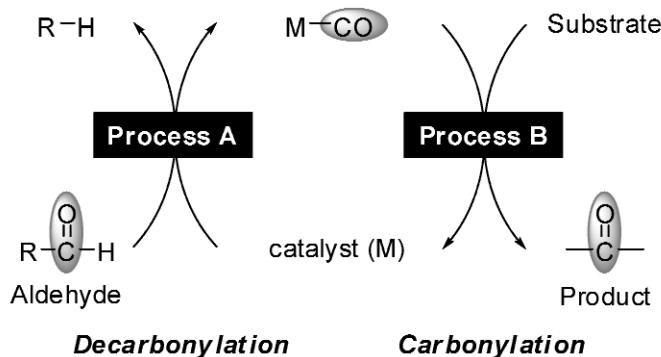
### INTRODUCTION

Transition-metal-catalyzed carbonylation is recognized as a powerful tool for the direct synthesis of a wide variety of carbonyl compounds [1]. In carbonylation chemistry, considerable attention is now being paid to developing carbonylation methods that do not use CO per se, because of experimental simplicity and ease of use. Consequently, researchers are finding that various organic and inorganic carbonyl compounds, such as formic acid, formates, formamides, chloroform, and metal carbonyls, are effective substitutes for CO in carbonylation [2]. These compounds are used because they allow *in situ* generation of CO by thermal or chemical decomposition.

An alternative approach is to generate metal carbonyl species, which are essential key intermediates in the reaction, without the use of CO. In catalytic carbonylation reactions, the coordination of CO to the metal center results in the generation of metal carbonyls. Decarbonylation of aldehydes, mediated by transition metals, is an alternative approach to the formation of metal carbonyls (Scheme 1, process A). Coupling the decarbonylation and carbonylation reactions of processes A and B would allow the transfer of the carbonyl moieties of aldehydes to the substrate via a metal carbonyl. The purpose of the present study was to verify this strategy and demonstrate its applicability to carbonylation reactions.

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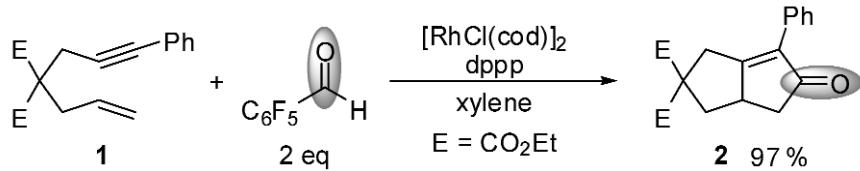
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**Scheme 1** A novel strategy for CO gas-free carbonylation.

### CO GAS-FREE CYCLOCARBONYLATION OF ENYNES USING ALDEHYDES

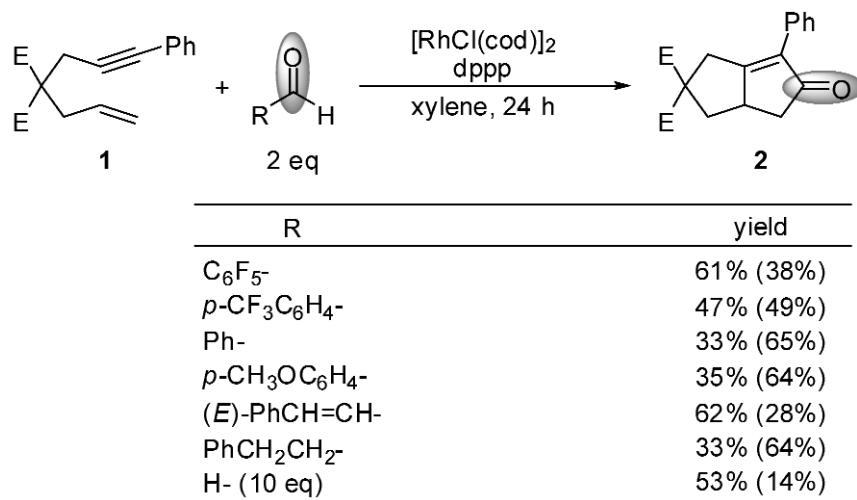
Initial studies examined the feasibility of Rh-catalyzed CO-transfer from an aldehyde to an enyne because the cyclocarbonylation of enynes is catalyzed by Rh complexes [3], which mediate decarbonylation of aldehydes [4]. The reaction of enyne **1** with pentafluorobenzaldehyde in the presence of a catalytic amount of  $[\text{RhCl}(\text{cod})]_2$  and dppp [1,3-bis(diphenylphosphino)propane] at 130 °C for 60 h gave the bicyclic cyclopentenone **2** quantitatively (Scheme 2) [5]. This result clearly shows that the aldehyde acts as a CO equivalent and that its carbonyl moiety is incorporated into the carbonylated product **2**. To our knowledge, this study was the first to report examples of a CO-transfer carbonylation [6–7].



**Scheme 2**

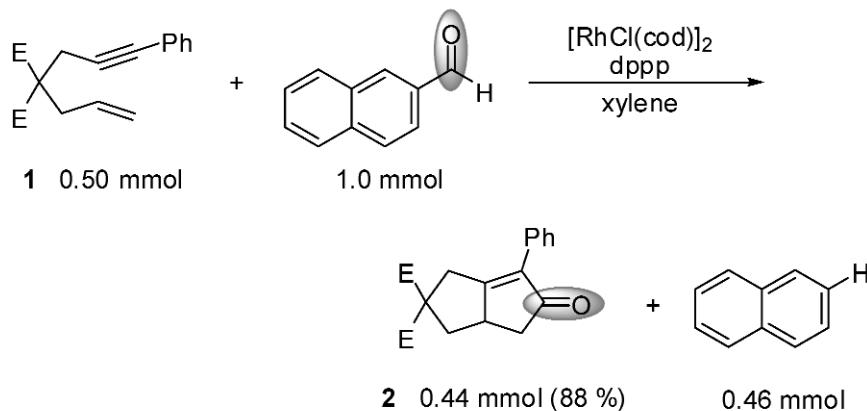
To investigate the efficiency of CO-transfer, reactions with various aldehydes as a carbonyl source were examined, and the results are shown in Table 1. All of the aldehydes examined were an effective carbonyl donor. Moreover, the efficiency of the CO-transfer catalysis depended heavily on the electrochemical nature of the aldehydes as follows: aldehydes with electron-withdrawing substituents donated a carbonyl moiety more efficiently than those with electron-releasing substituents. This observation is consistent with the general tendency of alkyl groups to migrate from acyl-metal complexes leading to the formation of metal carbonyls [8]. Thus, the smooth decarbonylation is responsible for the efficiency of the entire catalytic reaction.

**Table 1** Cyclocarbonylation of enyne **1** with various aldehydes as a CO substitute.



Values in parentheses are the yields of the recovered enyne.

The carbonyl moiety on an aldehyde was transferred efficiently to an enyne. The reaction of enyne **1** (0.50 mmol) with 2-naphthaldehyde (1.0 mmol) afforded 0.44 mmol of the carbonylated product **2**, along with 0.46 mmol of the decarbonylated counterpart, naphthalene (Scheme 3). This result demonstrates that 95 % of the carbonyl moiety abstracted from the aldehyde was utilized in carbonylation of enyne **1**. Figure 1 shows the reaction profile of Scheme 3. The abstraction and incorporation of the carbonyl moiety proceeded cooperatively with negligible loss of the carbonyl moiety.



**Scheme 3**

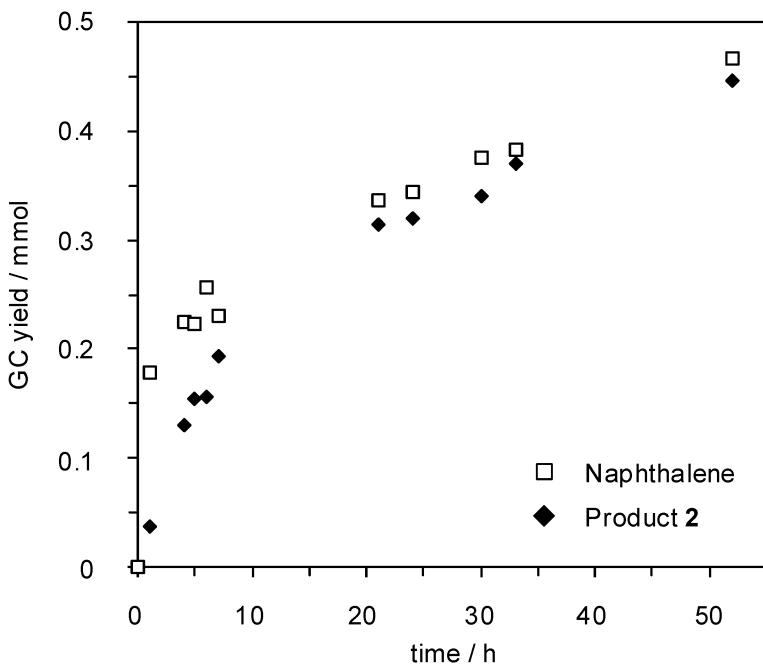
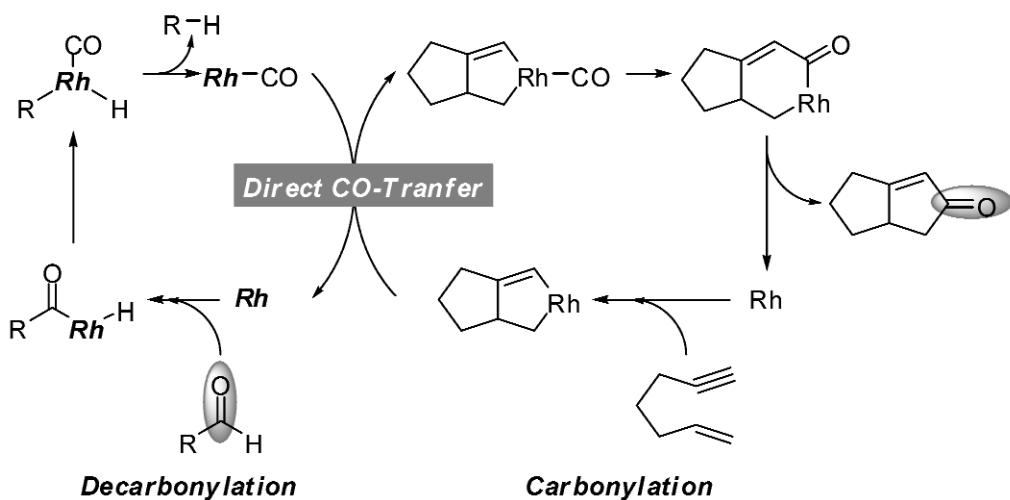


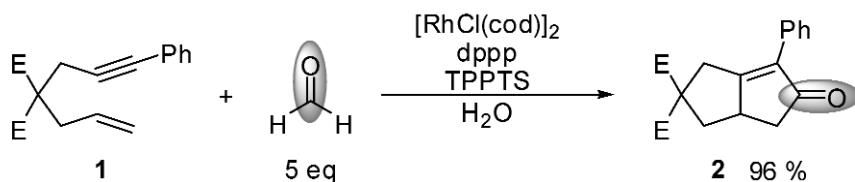
Fig. 1 The reaction profile of Scheme 3.

Based on these observations, a reaction pathway for the present CO gas-free cyclocarbonylation was proposed, consisting of two Rh-catalyzed processes, as follows: the decarbonylation of an aldehyde leading to the formation of Rh carbonyl species (the left cycle shown in Scheme 4); and, the carbonylation of an enyne utilizing the in situ formed Rh carbonyl species (the right cycle). Within this reaction scheme, there is direct transfer of the carbonyl moiety, resulting in an efficient CO gas-free cyclocarbonylation of an enyne. The high efficiency of CO-transfer arises from the general observation that decarbonylation of aldehydes by Rh complexes is not readily catalyzed by Rh, in other words, the carbonyl moiety abstracted from aldehydes is not easily released as free CO.



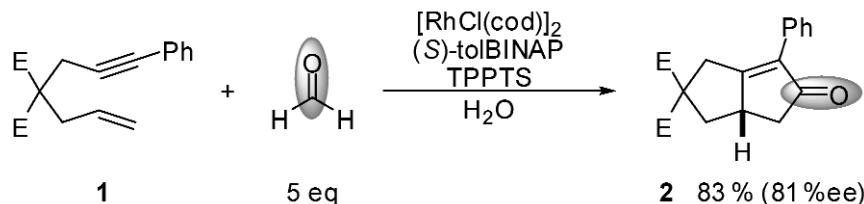
Scheme 4

Next, the utilization of formalin (an aqueous solution of formaldehyde), a low-cost C1 feedstock, was examined as a substitute for CO. The CO gas-free cyclocarbonylation reaction using formalin proceeded in aqueous media to give the carbonylated product **2** in 96 % yield (Scheme 5) [9]. In this case, the combined use of a hydrophobic phosphine, dppp, and a water-soluble phosphine, TPPTS (tri-phenylphosphine-3,3',3"-trisulfonic acid trisodium salt), led to highly efficient cyclocarbonylation, requiring a lower reaction temperature (100 °C) and a much shorter reaction time (5 h) than the reaction in organic solvent (Scheme 2).



Scheme 5

Furthermore, after changing the hydrophobic phosphine from dppp to chiral (*S*)-tolBINAP [2,2'-bis(di-*p*-tolylphosphino)-1,1'-binaphthyl], the reaction proceeded with high enantioselectivity, resulting in an aqueous, asymmetric, CO gas-free cyclocarbonylation (Scheme 6) [10].



Scheme 6

### CO GAS-FREE CARBONYLATIVE CYCLIZATION OF ARYL HALIDES WITH TETHERED NUCLEOPHILES USING ALDEHYDES

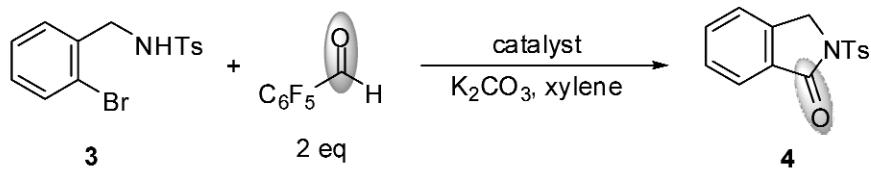
Carbonylative coupling of organic halides and pseudohalides with various nucleophiles using transition-metal complexes constitutes a large family of catalytic carbonylation reactions [11]. Intramolecular variants of this type of carbonylation, in which the substrates contain both an organic halide unit and a nucleophilic counterpart, also have been widely used for a long time [12] due to their versatility in the synthesis of cyclic carbonyl compounds [13]. More recently, the present CO gas-free carbonylation protocol was applied to carbonylation of aryl halides with tethered nucleophiles.

It is noteworthy that, in general, Pd catalysts have been used in these carbonylation reactions. Because the current strategy utilizes the decarbonylation of aldehydes by Rh complexes, a hypothetical dual catalysis system, consisting of the Rh-catalyzed decarbonylation of aldehydes and the subsequent Pd-catalyzed carbonylation of organic halides, was envisioned.

When the reaction of *N*-Ts-2-bromobenzylamine **3** with pentafluorobenzaldehyde was allowed to proceed in the presence of a catalytic amount of  $\text{Pd}(\text{PPh}_3)_4$  and  $[\text{RhCl}(\text{cod})_2]/\text{dppp}$ , the CO gas-free carbonylation system worked well, giving the desired product **4** in 48 % yield (Table 2, entry 1) [14–15]. Surprisingly, even when the reaction was run using only the Rh catalyst, the product yield was nearly same as when both catalysts were used (entry 2). Based on the similar product yields, regardless of whether the Pd catalyst was used, it was concluded that the Pd catalyst does not function as a carbonylation catalyst and that the Rh catalyst is effective in both decarbonylation and carbonylation. Under

these catalytic conditions, when the reaction time was extended to 10 h, the substrate was completely consumed, affording benzolactam **4** in excellent yield (entry 3). As demonstrated by the results described above, this carbonylation reaction also involves sequential dual-catalysis by the Rh catalyst as well as cyclocarbonylation of enyne.

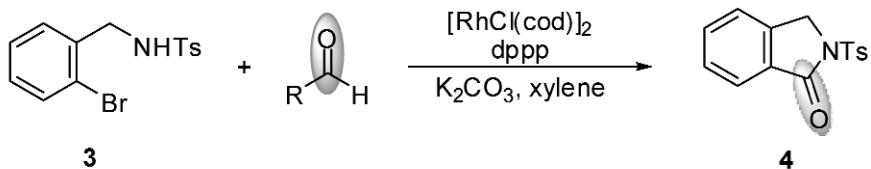
**Table 2** Rh- and/or Pd-catalyzed CO gas-free carbonylative cyclization of bromobenzene **3**.



entry	catalyst	time	yield
1	{ 2.5 mol% Pd( <i>PPh</i> <sub>3</sub> ) <sub>4</sub> 2.5 mol% [RhCl(cod)] <sub>2</sub> / 5 mol % dppp	3 h	48 %
2	2.5 mol% [RhCl(cod)] <sub>2</sub> / 5 mol % dppp	3 h	45 %
3	2.5 mol% [RhCl(cod)] <sub>2</sub> / 5 mol % dppp	10 h	92 %
4	2.5 mol% Pd( <i>PPh</i> <sub>3</sub> ) <sub>4</sub>	5 h	0 %

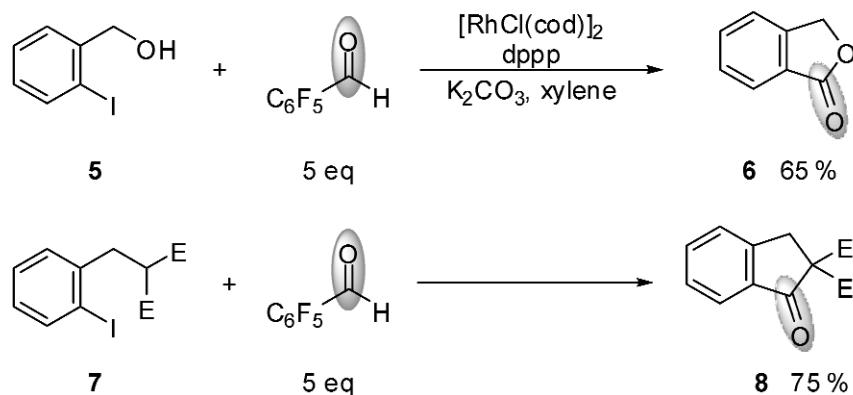
The ability of other aldehydes to donate a carbonyl was investigated (Table 3). Among them, the reaction of *trans*-cinnamaldehyde and paraformaldehyde resulted in the formation of **4** in 93 and 69 % yields, respectively (entries 1 and 2), while *p*-trifluoromethylbenzaldehyde and 2-naphthaldehyde afforded **4** in lower yields (entries 3 and 4). In the case of benzaldehyde, *p*-anisaldehyde and decanal, **4** was produced in only trace amounts. (entries 5–7).

**Table 3** Carbonylative cyclization of bromobenzene **3** with various aldehydes as a CO substitute.



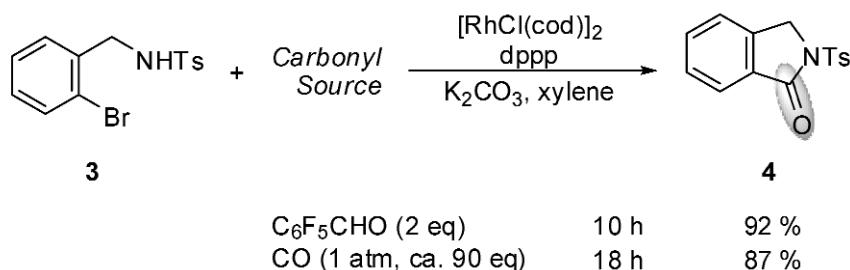
entry	R	time	yield
1	(E)-Ph-CH=CH <sub>2</sub> - (5 eq)	4 h	93 %
2	H- (10 eq)	8 h	69 %
3	p-CF <sub>3</sub> C <sub>6</sub> H <sub>4</sub> - (2 eq)	9 h	14 %
4	2-Naphthyl- (5 eq)	24 h	14 %
5	Ph- (2 eq)	17 h	trace
6	p-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> - (2 eq)	10 h	trace
7	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>8</sub> - (2 eq)	9 h	trace

Moreover, the present protocol was applicable to the carbonylative cyclization of aryl halides with tethered oxygen- and carbon-nucleophiles. The reaction of aryl iodides having other nucleophilic moieties, such as a hydroxyl group (**5**) or an active methyne group (**7**), gave the corresponding carbonylated products—the benzolactone **6** and the indane **8**, respectively—in good yields (Scheme 7) [14b].

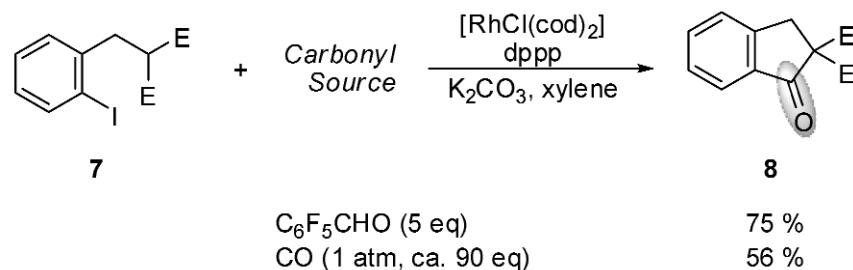


Scheme 7

Finally, the difference between the present CO gas-free protocol and the CO-based method was investigated. In the case of the reaction of benzylamine **3** using atmospheric CO under the same catalytic conditions, the carbonylated product was obtained in 87 % yield (Scheme 8). However, a longer reaction time (18 h) was required for complete consumption of the substrate. For the iodobenzene having a carbon-nucleophile (**7**), the reaction proceeded more efficiently using an aldehyde than using CO (Scheme 9). These results indicate that the presence of excess CO inhibits catalysis of carbonylation.



Scheme 8



Scheme 9

## CONCLUSION

As described above, a new CO gas-free carbonylation protocol using aldehydes as a substitute for CO was developed. The protocol consists of a sequential dual-catalysis of two Rh-catalyzed processes: Rh-catalyzed decarbonylation of aldehydes, and successive Rh-catalyzed carbonylation utilizing the in situ formed Rh carbonyl species. Additional studies of the possible applications of this new strategy to various carbonylations are in progress.

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