

## Ru<sub>3</sub>(CO)<sub>12</sub>-Catalyzed Cyclocarbonylation of Yne-Aldehydes to Bicyclic $\alpha,\beta$ -Unsaturated $\gamma$ -Butyrolactones

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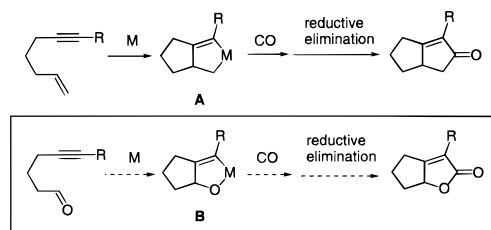
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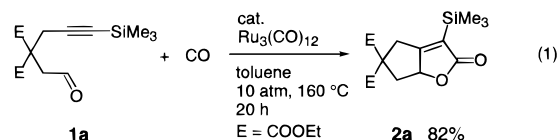
Metallacycles are involved as key species in many reactions such as olefin metathesis and a variety of cyclization reactions.<sup>1</sup> Metallacyclopentenes are usually produced via the cycloaddition of a coordinated acetylene and an olefin. It is well established that the reaction of 1,6-enynes with a transition metal gives rise to bicyclic metallacyclopentene **A** or related complexes which may then undergo insertion of CO followed by reductive elimination to give cyclopentenones, i.e., the Pauson-Khand reaction. This transformation is accomplished by the presence of a stoichiometric amount of a variety of complexes which contain metals, such as Ti,<sup>2</sup> Zr,<sup>3</sup> W,<sup>4,5</sup> Cr,<sup>5</sup> Mo,<sup>6</sup> Fe,<sup>7</sup> and Co.<sup>8</sup> The catalytic transformation of enynes to bicyclic  $\alpha,\beta$ -unsaturated ketones using Co<sub>2</sub>(CO)<sub>8</sub>,<sup>9</sup> Cp<sub>2</sub>Ti(CO)<sub>2</sub>,<sup>10</sup> Ru<sub>3</sub>(CO)<sub>12</sub>,<sup>11</sup> and [RhCl(CO)<sub>2</sub>]<sub>2</sub><sup>12</sup> as catalysts are also believed to proceed via **A** or its related complexes. Although heteroatom containing metallacyclopentenes **B**, which contain early transition metals such as Ti and Zr, are well-known,<sup>13,14</sup> there are very few examples of **B** containing a late transition metal.<sup>15</sup> If the metallacyclopentene

**B** is formed from the reaction of yne-aldehydes with a late transition metal, it would be expected that **B** could undergo insertion of CO and the resultant carbonylated metallacycle could then undergo reductive elimination to give bicyclic  $\alpha,\beta$ -unsaturated lactones. Such a catalytic transformation has not been observed. The use of a late transition metal complex could possibly make the sequence catalytic, while the strength of the early transition metal–oxygen bond renders catalysis use difficult.<sup>16</sup> We report herein the realization of the working hypothesis proposed above. To our knowledge, this represents the first example of a transition metal catalyzed hetero-Pauson-Khand reaction.

### Scheme 1



The reaction of yne-aldehyde **1a** (1 mmol) with CO (10 atm) in toluene (5 mL) in the presence of a catalytic amount of Ru<sub>3</sub>(CO)<sub>12</sub> (0.02 mmol) at 160 °C gave a bicyclic lactone **2a**<sup>17</sup> in 82% isolated yield (eq 1). When the reaction was carried out at 140 °C, no reaction was observed. The reaction also proceeded under 5 atm of CO (78% yield). A higher CO pressure (30 atm) decreased the yield to 30% yield with 38% of **1a** being recovered. Changing the solvent to dioxane (82%), CH<sub>3</sub>CN (74%), or cyclohexane (78%) had no significant effect on the product yields. No reaction was observed when other complexes, such as Ru(CO)<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub>, [RuCl<sub>2</sub>(CO)<sub>3</sub>]<sub>2</sub>, Ru(acac)<sub>3</sub>, Co<sub>2</sub>(CO)<sub>8</sub>, Rh<sub>4</sub>(CO)<sub>12</sub>, RhCl(PPh<sub>3</sub>)<sub>3</sub>, and Ir<sub>4</sub>(CO)<sub>12</sub> were used as catalysts. The standard reaction conditions established thus constitutes 2 mol % of Ru<sub>3</sub>(CO)<sub>12</sub>, 10 atm of CO, in toluene, and at 160 °C for 20 h. This reaction is the first catalytic transformation of yne-aldehydes to bicyclic  $\alpha,\beta$ -unsaturated lactones. This reaction also represents the first reported catalytic synthesis of five-membered lactones via a [2 + 2 + 1]cyclocoupling reaction, incorporating the aldehyde  $\pi$ -bond, the alkyne  $\pi$ -bond, and the carbon atom of CO into a five-membered ring.<sup>18</sup>



Selected results are shown in Table 1. The reaction of phenyl-substituted yne-aldehyde **1b** gave the corresponding lactone **2b** in 62% yield (entry 1). The alkyl substituents at the terminal acetylenic carbon had no significant effect on the reaction (entry 2). Interestingly, an olefinic and even acetylenic substituents

(16) A similar transformation mediated by Cp<sub>2</sub>Ti(PMe<sub>3</sub>)<sub>2</sub> was reported independently by Crowe and Buchwald. Crowe, W. E.; Vu, A. T. *J. Am. Chem. Soc.* **1996**, *118*, 1557. Kablaoui, N. M.; Hicks, F. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 5818. Kablaoui, N. M.; Hicks, F. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1997**, *119*, 4424.

(17) All new compounds were characterized by NMR, IR, mass spectral data, and by elemental analyses or high-resolution mass spectra. See the Supporting Information.

(18) A stoichiometric synthesis of five-membered lactones via [2 + 2 + 1]cyclocoupling reaction, incorporating the imine  $\pi$ -bond, the alkyne  $\pi$ -bond, and the carbon atom of CO was reported. Feiken, N.; Schreuder, P.; Siebenlist, R.; Frühauf, H.; Vrieze, K.; Kooijman, H.; Veldman, N.; Spek, A. L.; Fraanje, J.; Goubitz, K. *Organometallics* **1996**, *15*, 2148.

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**Table 1.** Ru<sub>3</sub>(CO)<sub>12</sub>-Catalyzed Cyclocarbonylation of Yne-Aldehydes<sup>a</sup>

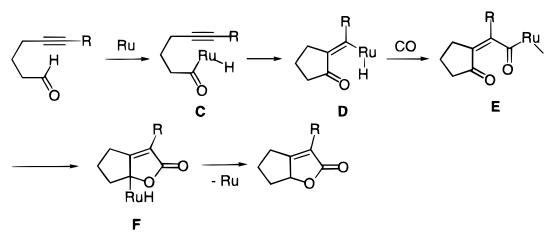
entry	yne-aldehyde	lactone <sup>b</sup>
1		
2		
3		
4		
5		
6		
7		
8		

<sup>a</sup> Reaction conditions: yne-aldehyde (1 mmol), CO (10 atm), Ru<sub>3</sub>(CO)<sub>12</sub> (0.02 mmol), toluene (5 mL) at 160 °C for 20 h. <sup>b</sup> Isolated yields. <sup>c</sup> The reaction was run at 180 °C.

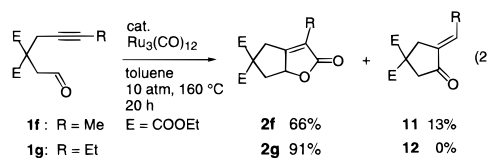
remained intact under the reaction conditions (entries 3 and 4). An yne-aldehyde having a terminal acetylenic moiety failed to give desirable results.<sup>19</sup> The result of entry 5 shows that the presence of geminal substituents in the tether is not essential for the reaction to proceed, although higher reaction temperatures are required. The present reaction is applicable to the formation of a cyclohexane-fused  $\gamma$ -butyrolactone (entry 6). Yne-aldehydes containing heteroatoms, such as oxygen and nitrogen, in the tether worked well, and heterocycle-fused  $\gamma$ -butyrolactones were obtained in high yields (entries 7 and 8). The formation of polyfunctional compounds such as **8** and **10** in a single step is also quite noteworthy, since they are amenable to further elaboration, and no simple alternative methods are available to give these multifunctionalized compounds.

Although we initiated this study guided by our working hypothesis shown in Scheme 1, we wish to point out that another very interesting mechanistic alternative is also plausible. The

(19) Many small peaks or spots were observed by GC or TLC analysis, although the starting material was completely consumed. After bulb-to-bulb distillation of the reaction mixture, more than 90% of the compounds remained in the residue.

**Scheme 2.** Alternative Mechanism

mechanism involves the oxidative addition of an aldehyde C–H bond<sup>20</sup> to ruthenium, as shown in Scheme 2.<sup>21</sup> In fact, cleavage of an aldehyde C–H bond by ruthenium was proposed by Watanabe for the case of the Ru<sub>3</sub>(CO)<sub>12</sub>-catalyzed hydroacylation of benzaldehydes with intermolecular olefins.<sup>20c</sup> The reaction of **1f** with CO gave two products, one being the expected lactone **2f** and the other the exo-methylene ketone **11** (eq 2). While intermediate **B** in Scheme 1 can account for the route to **11**, the formation of **11** can also be rationalized by assuming a reductive elimination from a vinyl complex **D**. When R is a small group, such as a methyl group, a reductive elimination from **D** takes place to some extent. The more bulky R group facilitates the insertion of CO (**D** → **E**) because of release of steric congestion around the metal in **D**. Indeed, even the ethyl isomer **1g** selectively gave only lactones. We are conducting a mechanistic study of the cyclocarbonylation of yne-aldehydes.<sup>22</sup>



In summary, we have demonstrated a new Ru-catalyzed cyclocarbonylation of yne-aldehydes. This reaction is the first example of a catalytic transformation of yne-aldehydes with CO to bicyclic  $\gamma$ -butenolides. We are continuing to investigate the scope of the cyclocarbonylation of yne-aldehydes, with special regard to the functional group and substrate skeleton compatibility of the reaction.

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**Supporting Information Available:** Lists of special data and elemental analyses for the products (18 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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(21) A similar conversion of **D** to **F** by metal migration was proposed in the related Ni complex. Carmona, E.; Gutiérrez-Puebla, E.; Monge, A.; Marín, J. M.; Paneque, M.; Poveda, M. L. *Organometallics* **1989**, 8, 967. Another possibility is direct, thermal conversion of a keto-aldehyde, derived from reductive elimination of **E**, to the lactone.

(22) In Ni-catalyzed reaction of alkynes with aldehydes leading to  $\alpha$ ,  $\beta$ -enones, both of paths, oxametallacycle and oxidative addition of a C–H bond to Ni, were proposed. Tsuda, T.; Kiyoi, T.; Saegusa, T. *J. Org. Chem.* **1990**, 55, 2554.