

# Rh(I)-catalyzed CO gas-free cyclohydrocarbonylation of alkynes with formaldehyde to $\alpha,\beta$ -butenolides†

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Received (in Cambridge, UK) 17th March 2005, Accepted 4th May 2005

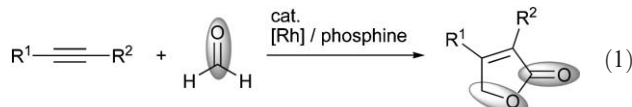
First published as an Advance Article on the web 1st June 2005

DOI: 10.1039/b503816b

The rhodium(I)-catalyzed reaction of alkynes with formaldehyde proceeds *via* the double incorporation of a carbonyl moiety from formaldehyde, resulting in a CO gas-free cyclohydrocarbonylation leading to  $\alpha,\beta$ -butenolides.

Methods for incorporating carbon monoxide into simple organic substrates for the construction of value-added chemicals can take advantage of the availability of a wide variety of transition metal catalysts.<sup>1</sup> However, the methods suffer from one major disadvantage, namely the difficulty of handling toxic, gaseous carbon monoxide. Considerable attention has been paid to developing catalytic CO gas-free carbonylation reactions, because of their experimental simplicity and ease of use. Consequently, the use of various organic and inorganic carbonyl compounds as a substitute for carbon monoxide would be highly desirable, since it would eliminate the direct use of carbon monoxide, in reactions such as the hydroesterification, hydroamidation and hydrocarboxylation of alkenes and alkynes, the hydroformylation of alkenes, the alkoxy-, amino- and hydroxycarbonylation of aromatic and alkenyl halides, and the Pauson–Khand reaction.<sup>2</sup> All of the above reactions are *mono* carbonylations, in which one organic substrate incorporates only one carbonyl moiety from the substitutes.

Our recent studies have demonstrated that a combination of aldehydes with a rhodium(I) catalyst affords an alternative protocol for CO gas-free carbonylation.<sup>3</sup> The methodology utilizes a compatible synergy of two catalytic processes, the decarbonylation of aldehydes by the transition-metal catalyst and the successive carbonylation of organic substrates by carbonyl transfer from the metal carbonyl that is formed. During the course of our studies of this methodology, we discovered a new type of catalytic CO gas-free carbonylation reaction, which proceeds *via* the *double* incorporation of a carbonyl moiety from formaldehyde. Herein we report on the rhodium(I)-catalyzed CO gas-free cyclohydrocarbonylation of alkynes with formaldehyde leading to the production of  $\alpha,\beta$ -butenolides [eqn (1)].



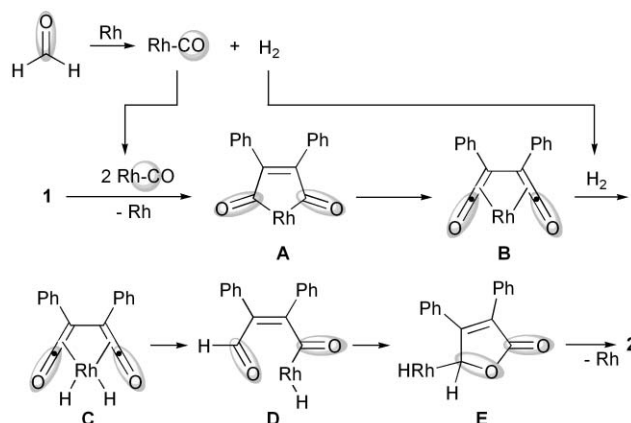
Using the same conditions as described in a previous report,<sup>3c</sup> which consist of 5 mol% of  $[\text{RhCl}(\text{cod})]_2$ , 10 mol% of dppp, and 10 mol% of TPPTS as a catalyst system, and 2 equiv. of SDS as a surfactant in water at 100 °C,<sup>4</sup> a mixture of diphenylacetylene (**1**) and formaldehyde was reacted in the presence of the rhodium

catalyst in a sealed tube, leading to the quantitative formation of  $\alpha,\beta$ -butenolide **2** (Table 1, entry 1). Apparently, two units of formaldehyde carbonyl group participate in the construction of the butenolide ring; one of which is incorporated as a carbonyl group of **2**, and the other as a  $\text{CH}_2\text{O}$  unit in the butenolide ring. Similar catalytic transformations of alkynes with highly pressurized carbon monoxide or synthesis gas ( $\text{CO—H}_2$ ) have been reported to date.<sup>5</sup> Thus, the present reaction is available as an accessible alternative to them. The use of dppp or TPPTS as a ligand resulted in a sharp decrease in the yield (42%) or no formation of **2**, respectively. A lower catalyst loading (2.5 mol% of  $[\text{RhCl}(\text{cod})]_2$ , 5 mol% of dppp,

**Table 1** Rh(I)-catalyzed cyclohydrocarbonylation of **1** using various carbonyl source

Entry	Conditions <sup>a</sup>	Carbonyl source	Yield of <b>2</b> (%) <sup>b</sup>
1	A	Formalin (3 equiv.)	98
2	A	Benzaldehyde (5 equiv.)	0 (79)
3	A	CO (1 atm)	0 (84)
4	B	$(\text{CH}_2\text{O})_n$ (5 equiv.) <sup>c</sup>	72
5	B	$\text{CO—H}_2 = 1 : 1$ (1 atm)	6 (68)

<sup>a</sup> Condition A:  $[\text{RhCl}(\text{cod})]_2$  (5 mol%), dppp (10 mol%), TPPTS (10 mol%), and SDS (2 equiv.) in  $\text{H}_2\text{O}$  at 100 °C; condition B:  $[\text{RhCl}(\text{cod})]_2$  (5 mol%) and dppp (10 mol%) in xylene at 100 °C.  
<sup>b</sup> Isolated yields. Values in parentheses are the yields of recovered **1**.  
<sup>c</sup> Paraformaldehyde was used.



**Scheme 1** Proposed pathway for Rh(I)-catalyzed cyclohydrocarbonylation of **1** using formaldehyde.

† Electronic supplementary information (ESI) available: Experimental details. See <http://www.rsc.org/suppdata/cc/b5/b503816b/>  
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and 5 mol% of TPPTS) resulted in no significant decrease in the yield of **2** (95%).

The present cyclohydrocarbonylation reaction was found to be unique to formaldehyde. Under the same conditions as entry 1, the reaction of **1** with benzaldehyde, instead of formaldehyde, afforded no trace of the butenolide **2**, and the unreacted alkyne was recovered in 79% yield (Table 1, entry 2). Moreover, under atmospheric gaseous carbon monoxide conditions, no formation of **1** was observed (entry 3). Interestingly, the use of paraformaldehyde in a *non-aqueous* system (in dry xylene as a solvent) led to the formation of **2** in 72% yield (entry 4). The results from entries 1–3 show clearly that the hydrogens on the  $\gamma$ -carbon of **2** formed in the reaction of entry 1 are derived not from H<sub>2</sub>O, but from the aldehydic hydrogen of formaldehyde.<sup>6</sup> Moreover, the reaction with 1 atm of CO–H<sub>2</sub> (1 : 1) afforded **2** although in low yield (6%) (entry 5).<sup>7</sup> This would mean that the use of (para)formaldehyde in the presence of the rhodium catalyst yields the hydroformylation conditions.<sup>8</sup>

Although details of the reaction mechanism are unclear, a probable pathway that rationalizes the results obtained in Table 1 is shown in Scheme 1. Initially, the decarbonylation of formaldehyde by the rhodium would proceed to yield Rh–CO and H<sub>2</sub>. The carbonylative cyclization of the alkyne **1** with two carbonyl moieties on the rhodium would give a maleoylrhodium **A**, analogues of which have been frequently proposed as a key intermediate in the catalytic transformation of alkynes with CO or CO–H<sub>2</sub> to butenolides.<sup>5a,d,f</sup> The subsequent isomerization of **A** affords a ( $\eta^4$ -bisetene)rhodium **C**.<sup>9</sup> The oxidative addition of H<sub>2</sub>, followed by the 1,4-addition of a Rh–H in **C**, produces the  $\beta$ -formyl-acylrhodium intermediate **D**. Finally, the addition of the Rh-acyl bond to the formyl group in **D** followed by reductive elimination gives the  $\alpha,\beta$ -butenolide **2**.<sup>10</sup>

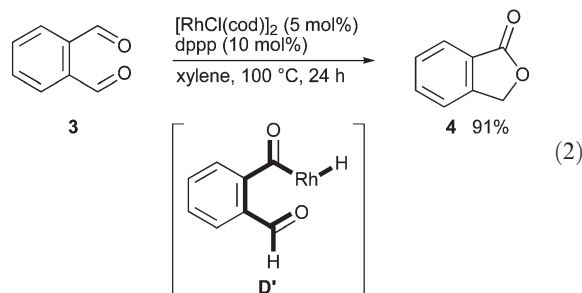
The possibility of a lactonization process *via* **D** was demonstrated by the following reaction in which the corresponding intermediate **D'** is presumed to be generated. Thus, upon the exposure of *o*-phthalaldehyde (**3**) to conditions B in Table 1, the

**Table 2** Rh(I)-catalyzed cyclohydrocarbonylation of alkynes using formaldehyde

Entry	Conditions <sup>a</sup>	Product	Yield (%) <sup>b,c</sup>	Entry	Conditions <sup>a</sup>	Product	Yield (%) <sup>b,c</sup>
1	A		93	8	A		74 (74/26)
2	A	R <sup>1</sup> = R <sup>2</sup> = C <sub>3</sub> H <sub>7</sub>	0				
3	A	R <sup>1</sup> = Ph, R <sup>2</sup> = H	0				
4	A	R <sup>1</sup> = Ph, R <sup>2</sup> = SiMe <sub>3</sub>	0	9	A		94 (81/19)
5	A	R <sup>1</sup> = Ph, R <sup>2</sup> = CH <sub>3</sub>	92 (66/34)	10	A		95 (56/44)
6	A	R <sup>1</sup> = <i>p</i> -C <sub>6</sub> H <sub>4</sub> CN, R <sup>2</sup> = Ph	76 (96/4)	11	B		71 (63/37)
		R <sup>1</sup> = Ph, R <sup>2</sup> = <i>p</i> -C <sub>6</sub> H <sub>4</sub> OCH <sub>3</sub>	76 (52/48)	12	B		69 (54/46)
7	B		91 (52/48)	13	B		65 (99/1)
				14	B		80 (57/43)

<sup>a</sup> Condition A: formalin, [RhCl(cod)]<sub>2</sub> (5 mol%), dppe (10 mol%), TPPTS (10 mol%), and SDS (2 equiv.) in H<sub>2</sub>O at 100 °C; condition B: paraformaldehyde as a precursor of formaldehyde, [RhCl(cod)]<sub>2</sub> (5 mol%) and dppe (10 mol%) in xylene at 100 °C. <sup>b</sup> Isolated yields. <sup>c</sup> Major regioisomers are depicted. Ratios are the regioselectivities with respect to substituents on the termini of alkynes. The ratios of major isomers are shown at the left of the values in parentheses.

highly efficient formation of benzolactone **4** occurred [eqn (2)], probably *via* the similar transformation from **D'** to that from **D** to butenolide **2** in Scheme 1.<sup>11</sup>



The scope of the reaction with respect to substitution of alkynes and compatibility of functional groups was investigated next (Table 2). The use of analogues of **1**, in which two propyl groups replace the two phenyl groups on the termini of **1**, also resulted in the formation of the corresponding butenolide (entry 1). Unfortunately, the reaction of phenylsilylacetylene or phenylacetylene gave none of the desired products, probably because of the polymerization of the desilylated alkyne or phenylacetylene itself, respectively (entries 2 and 3). When an unsymmetrically substituted alkyne contains phenyl and methyl groups, a moderate regioselectivity with respect to the substituents on the  $\alpha$ - and  $\beta$ -carbon was observed (entry 4). Diarylacetylene, having an electron-withdrawing group (CN) on the aromatic ring, reacted with formaldehyde to yield the corresponding butenolide with high regioselectivity, while the introduction of an electron-donating group showed almost no regioselectivity (entries 5 and 6). Although an alkyne substituted with a heteroaromatic ring, such as a furyl group, did not react under aqueous conditions (conditions A), the reaction proceeded smoothly to give the butenolide when non-aqueous conditions were used (conditions B) (entry 7). Benzyl-protected alkynols were carbonylated under aqueous conditions to yield the corresponding butenolides in high yields with moderate selectivities (entries 8–10), while, for non-protected alkynols, non-aqueous conditions were needed (entries 11 and 12). Nitrogen-functionalities, such as morpholino and phthalimide groups, were also tolerated, but only for non-aqueous reactions (entries 13 and 14).

In conclusion, we describe the Rh(I)-catalyzed cyclohydrocarbonylation reactions of alkynes with formaldehyde. The strategy has the potential for application to more *double* carbonylations as well as *mono* carbonylation.<sup>12</sup> Furthermore, the present reaction should provide a new, readily accessible tool for the synthesis of  $\alpha,\beta$ -butenolides, which have been of continuous interest due to their utility as synthetic intermediates and their biological activity.<sup>13</sup>

This work was financially supported, in part, by a Grant-in-Aid for Scientific Research (No. 15036247, “Reaction Control of Dynamic Complexes”, and No. 15750133) from MEXT, and by The Association for the Progress of New Chemistry granted to T.M. K.F. acknowledges JSPS Research Fellowship for Young Scientists. We also thank Ms Yoshiko Nishikawa for assistance in obtaining HRMS spectra.

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- Abbreviation: dppp = 1,3-bis(diphenylphosphino)propane; TPPTS = triphenylphosphine-3,3',3''-trisulfonic acid trisodium salt; SDS = sodium dodecylsulfate.
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