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Carbonylation of Terminal Alkynes Using a Multicatalytic System, Pd(II) / Chlorohydroquinone / NPMoV, under Carbon Monoxide and Dioxygen

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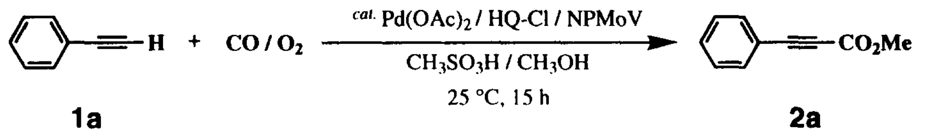
Abstract: Carbonylation of terminal alkynes was performed using a new triple catalytic system, Pd(II) / chlorohydroquinone / NPMoV, under carbon monoxide and oxygen. For instance, phenylacetylene was converted into methyl phenylpropiolate (85%) in methanol and phenylmaleic anhydride (62%) in dioxane. The reaction did not take place in the absence of oxygen.

Palladium-catalyzed carbonylation of alkynes is a useful reaction for the synthesis of alkynic carbonylates[1], carbapenem intermediates[2] as well as steroidal compounds.[3] To our knowledge, however, these reactions are carried out using $PdCl_2$ as catalyst and $CuCl_2$ as reoxidation agent under carbon monoxide. From the synthetic and industrial points of view, it is important to develop a new reoxidant system in which the redox couple CuCl / $CuCl_2$ is substituted with a halogen-free system so as to avoid the presence of the Cl ion in the solution. In recent years, Bäckvall *et al* have reported a new oxidation system, $Pd(OAc)_2$ / cobalt tetraphenylporphyrin / hydroquinone / O_2, in the oxidation of cyclohexadiene.[4]

In a previous paper, we reported that oxidative reactions like acetoxylation and acetalization of olefinic compounds are efficiently achieved by using a triple catalytic system which consists of $Pd(OAc)_2$, hydroquinone and molybdovanadophosphate (NPMoV)[5] under dioxygen atmosphere. Thus, cyclohexene and acrylonitrile are readily converted into cyclohexenyl acetate and cyanoacetaldehyde diethylacetal, respectively, in quantitative yields under mild conditions.

In order to extend our work on the triple catalytic system in synthetic reaction, we examined the carbonylation of terminal alkynes under CO and O_2 (Eq. 1).



(1)

1a **2a**

A typical reaction is carried out as follows. A solution of $Pd(OAc)_2$ (0.1 mmol), chlorohydroquinone (HQ-Cl) (0.4 mmol), NPMoV (35 mg), CH_3SO_3H (20 mg) and phenylacetylene (**1a**) (2 mmol) in methanol (10 mL) was placed in a stainless autoclave (50 mL) and then 0.5 atm of O_2 and 10 atm of CO were charged,

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and the reaction mixture was allowed to react under stirring at 25 °C for 15 h. The reaction was quenched with wet ether and the products were extracted with *n*-hexane. After removal of the solvent under reduced pressure, the products were isolated by column chromatography over silica gel by hexane/ethyl acetate (gradient up to 5:1) to give methyl phenylpropiolate (**2a**) as a yellow liquid (Eq. 1).

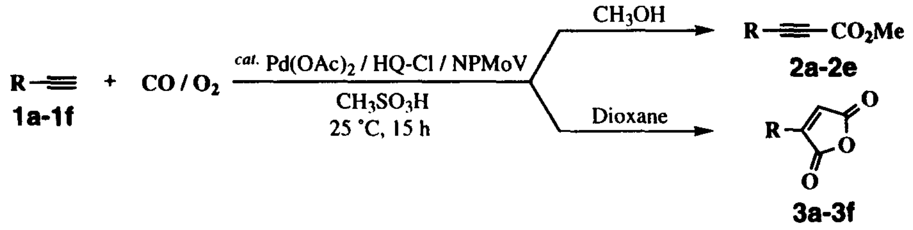
Table 1. Carbonylation of Phenylacetylene (1a) to Methyl phenylpropiolate (2a) under Various Reaction Conditions[a]

Run	CO / atm	O_2 / atm	Temp. / °C	Conv. / %	Yield / %
1	10	0.5	25	97	85
2	20	1	25	93	64
3	10	0	25	26	4
4[b]	10	0.5	25	20	2
5[c]	10	0.5	25	67	39
6	10	0.5	40	>99	60
7[d]	10	0.5	25	88	49
8[e]	10	0.5	25	94	57
9[f]	10	0.5	25	87	49
10[g]	10	0.5	25	33	13
11[h]	10	0.5	25	98	73

[a] A solution of phenylacetylene (**1a**) (2 mmol), $Pd(OAc)_2$ (0.1 mmol), HQ-Cl (0.4 mmol), NPMoV (35 mg) and CH_3SO_3H (20 mg) in methanol (10 mL) was stirred under CO / O_2 (10 / 0.5 atm) at 25 °C for 15 h.
[b] In the absence of NPMoV.
[c] In the absence of HQ-Cl.
[d] Hydroquinone was used instead of HQ-Cl.
[e] Ethanol was used instead of methanol. Ethyl phenylpropiolate was formed.
[f] *t*-Butyl alcohol was used instead of methanol. *t*-Butyl phenylpropiolate was formed.
[g] In the absence of CH_3SO_3H.
[h] *p*-Toluenesulfonic acid was used instead of CH_3SO_3H.

Table 1 shows the representative results for the carbonylation of **1a** under various reaction conditions. The reaction of **1a** with CO / O_2 (10 / 0.5 atm) gave **2a** in satisfactory yield (85 %) (Run 1). Tsuji *et al* have reported that the carbonylation of **1a** by using $PdCl_2$ and a stoichiometric amount of $CuCl_2$ under atmospheric CO in methanol forms **2a** in 74 % yield.[5] In our system, however, the resulting Pd(0) was smoothly reoxidized with molecular oxygen at room temperature by using a triple catalytic system. Thus, the palladium-catalyzed carbonylation of terminal alkynes to alkynyl carbonylates by the halogen-free reoxidation system was first achieved at room temperature. Under higher pressure of CO / O_2 (20 / 1 atm), the yield of **2a** was lowered to 64 % (Run 2). No reaction took place in the absence of dioxygen (Run 3). The carbonylation occurred with difficulty in the absence of either NPMoV or HQ-Cl of the multicatalytic system (Runs 4 and 5). The reaction of **1a** at 40 °C gave **2a** in lower yield, although the conversion was high (>99 %) (Run 6). The use of hydroquinone in place of HQ-Cl brought about **2a** in lower selectivity (Run 7). When ethanol and *t*-butyl alcohol were used instead of methanol as solvents, ethyl phenylpropiolate and *t*-butyl phenylpropiolate were obtained in 57 % and 49 % yields, respectively (Runs 8 and 9). The reaction occurred very slowly without CH_3SO_3H (Run 10). Almost the same results were obtained when *p*-toluenesulfonic acid was used in place of CH_3SO_3H (Run 11). It is believed that the reoxidation of the reduced NPMoV to the original NPMoV proceeds more smoothly by adding the acid to the reaction system. Similar results have been obtained by the oxidation of isophorone with O_2 by NPMoV.[6]

We next examined the effect of several solvents (dioxane, acetone, THF, CH_3CN and DME) on the present carbonylation under these conditions. When dioxane was employed instead of methanol, phenylmaleic anhydride (**3a**) was obtained in place of **2a** as a principal product. Among the solvents, only dioxane resulted in the formation of **3a** in a considerable yield.



(2)

Table 2. Carboxylation of Various Alkynes by Pd(II) / HQ-Cl / NPMoV under CO and O_2 [a]

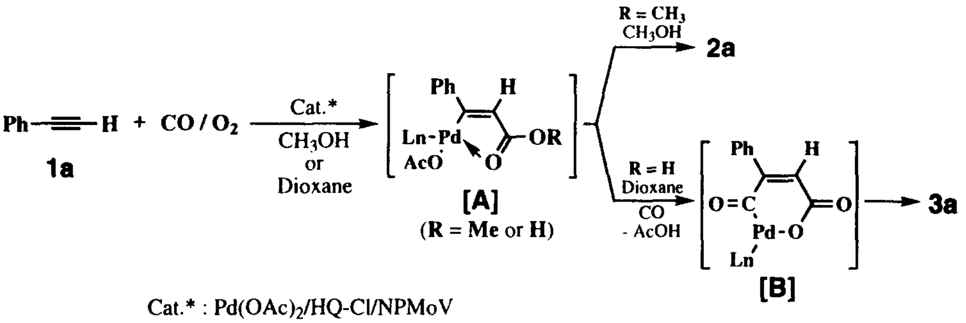
Run	Substrate R—≡—H	In methanol [b] (yield / %)	In dioxane [c] (yield / %)
1	R : C_6H_5 (**1a**)	**2a** (85)	**3a** (62)
2	R : *p*-$CH_3C_6H_5$ (**1b**)	**2b** (61)	**3b** (63)
3	R : *p*-ClC_6H_5 (**1c**)	**2c** (62)	**3c** (36)
4	R : *t*-C_4H_9 (**1d**)	**2d** (70)	**3d** (13)
5	R : *n*-C_6H_{13} (**1e**)	**2e** (63)	**3e** (18)
6	R : *n*-$C_5H_{11}CH(OH)$ (**1f**)	complex mixture	**3f** (36)

[a] Alkyne (2 mmol) was added to a solution of $Pd(OAc)_2$ (5 mol%), HQ-Cl (20 mol%), NPMoV (35 mg) and CH_3SO_3H (20 mg) in solvent (10 mL) and stirred under CO and O_2 at 25 °C for 15 h. [b] Under CO / O_2 (10 / 0.5 atm). [c] Under CO / O_2 (20 / 1 atm).

Table 2 shows the representative results for the carboxylation of several terminal alkynes by the triple catalytic system, Pd(II) / HQ-Cl / NPMoV, under the influence of CO / O_2. Both aromatic and aliphatic alkynes, 4-ethynyl toluene (**1b**), 1-chrolo-4-ethynyl benzene (**1c**), *t*-butyl acetylene (**1d**) and 1-octyne (**1e**), in methanol gave methyl *p*-tolylpropiolate (**2b**), methyl *p*-chlorophenylpropiolate (**2c**), methyl 4,4-dimethyl-2-pentynoate (**2d**) and methyl 2-nonynoate (**2e**), respectively, as major products (Runs 2-5). By the use of dioxane as the solvent, aromatic terminal alkynes, **1b** and **1c**, were converted into *p*-tolylmaleic anhydride (**3b**) and *p*-chlorophenylmaleic anhydride (**3c**) in 63 % and 36 % yields, respectively (Runs 2 and 3). For example, the reaction of **1a** under CO / O_2 (20 / 1 atm) in dioxane proceeded favorably to give **3a** in 62 %

yield. For aliphatic terminal alkynes such as **1d** and **1e** in dioxane, *t*-butylmaleic anhydride (**3d**) and *n*-hexylmaleic anhydride (**3e**) were formed in low yields (Runs 4 and 5). In the case of 1-octyn-3-ol (**1f**), the carboxylation in dioxane gave 5-pentylidene furanone (**3f**), although a complex mixture of products was formed in methanol (Run 6).

Although the detailed reaction pathway is not clear at the present time, the reaction is considered to proceed via similar mechanisms as shown by Heck[7] for carboalkoxylation and by Alper[8] for dicarbonylation of terminal alkynes.



(3)

Cat.* : Pd(OAc)$_2$/HQ-Cl/NPMoV

A vinyl carboxyl palladium complex [**A**] is thought to be a key intermediate in the present carbonylation. The β-elimination of H-Pd-OAc from the vinyl palladium complex **A** affords **2a**, Pd(0) and AcOH. In the case of the reaction in dioxane, the insertion of CO to the vinyl complex **A** (R = H) and elimination of AcOH successively take place to form a palladium complex [**B**] which subsequently undergoes reductive elimination to give the corresponding anhydride **3a**. Yamamoto *et al* have reported that the carbonylation of 3-butenoic acid with CO by a Pd- complex proceeds through a Pd-containing cyclic intermediate to give anhydride.[9]

In summary, we have found that the carbonylation of some terminal alkynes in methanol by using a triple catalyst, Pd(II) / HQ-Cl / NPMoV, under carbon monoxide and oxygen produces 2-alkynylcarbonylates in satisfactory yields. The reaction of aromatic acetylenes such as **1a**, **1b** and **1c** in dioxane under these conditions resulted in the corresponding maleic anhydrides in fair yields.

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