Catalytic Tricarbonylation of Alkynes with Palladium Catalysts

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A novel catalytic process of introducing *three* CO units into alkynes by palladium-catalyzed alkoxycarbonylation was developed. Based on the fundamental studies on the behavior of organopalladium complexes, mechanisms to account for the mono- and tricarbonylation processes are proposed.

Catalytic carbonylation of alkynes provides convenient routes to various unsaturated carboxylates that can be utilized for synthesis of a variety of important organic compounds.[1] Alkynes can be oxidatively carbonylated into alkynecarboxylates with retention of the C≡C bond or hydrocarbonylated into alkenecarboxylates having the C=C bond in the presence of palladium catalysts under carbon monoxide. However, mechanisms of these carbonylation processes have not been satisfactorily clarified and conditions to selectively produce mono- and/or di-carbonylation products have not been well established.[2] In the previous paper we have shown that a clean palladium-catalyzed monocarbonylation proceeded *under atmospheric pressure of CO and oxygen* without adding any other oxidant, such as Cu(II) compound (Chart 1).[3]

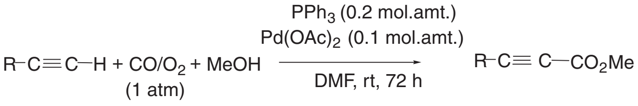


Chart 1.

A mechanism proceeding through an intermediate palladium complex having a methoxycarbonyl ligand coupled with an alkynyl ligand was proposed to account for the oxidative carbonylation of alkynes to produce alkyl alkynoates based on properties of the isolated methoxycarbonyl- and alkynylpalladium complexes.

Further examination of the reaction conditions on the oxidative carbonylation process *under the pressure of CO and oxygen* revealed that the oxidative *tricarbonylation* as well as dicarbonylation took place when the reaction was performed under certain conditions *in the presence of iodide*, such as NaI and NEt_4I (Chart 2). Table 1 shows that the catalytic carbonylation of 4-ethynyltoluene (*p*-tolylacetylene) depends strongly on the nature of the solvent employed. When 4-ethynyltoluene was treated with the mixture of methanol and THF under the pressure of 15 atm of CO and 5 atm of O_2, the monocarbonylation product **6** was obtained predominantly, whereas the use of DMF in higher proportions in combination with methanol afforded tricarbonylation products **2** and **3** (Runs 2 and 3 in Table 1) without producing the monocarbonylation product under otherwise similar conditions. However, upon reduction of the proportion of DMF relative to methanol or by carrying out the reaction in methanol, the amounts of the dicarbonylation products **4** and **5** were increased.

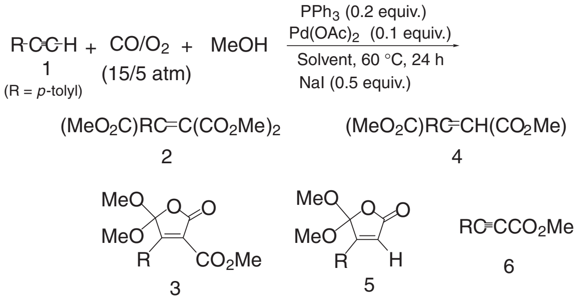


Chart 2.

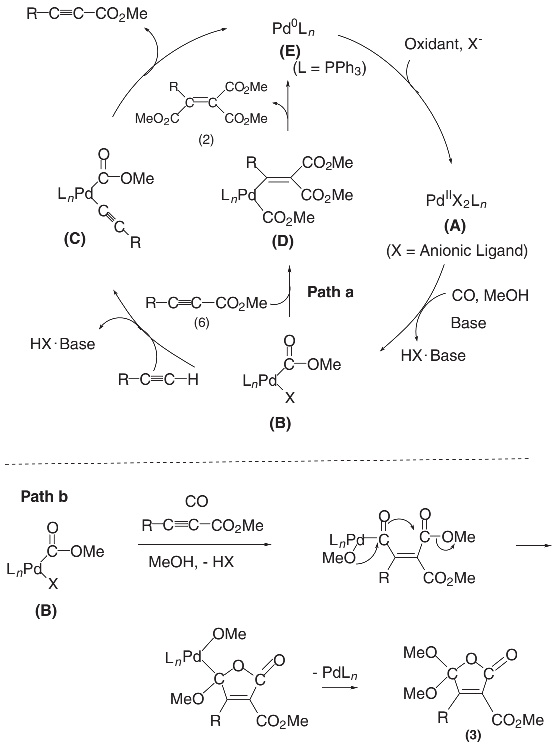
Table 1. Oxidative carbonylation of 4-ethynyltoluene in various solvents

Run	Solvent	Product Yield[a]/%				
		2	**3**	**4**	**5**	**6**
1	MeOH (2 mL)/THF (10 mL)	trace				66
2	MeOH (2 mL)/DMF (10 mL)	18[b]	9			
3	MeOH (5 mL)/DMF (5 mL)	35[b]	36			
4	MeOH (8 mL)/DMF (2 mL)	11	10	4	trace	59
5	MeOH	13	19	37	16	

[a]Determined by ^1H NMR. [b]Isolated yield.

Decrease in the CO pressure caused increase in the monocarbonylation product **6** at the cost of tricarbonylation product. The tricarbonylation did not proceed at room temperature and the starting alkyne was recovered unreacted. In the absence of the iodide salt, only monocarbonylation product **6** was produced. The use of NaBr or NaCl instead of the iodide gave no tricarbonylation product. Aliphatic alkynes such as 1-heptyne gave the tricarbonylation products as well as aromatic alkynes without giving any mono- or dicarbonylation products, when the reactions were carried out in the mixture containing methanol and DMF in a comparable ratio under the pressure of CO (15 atm) and O_2 (5 atm).

Scheme 1 shows the mechanisms proposed to account for the monocarbonylation as well as tricarbonylation proceeding through a common methoxycarbonylpalladium intermediate (**B**). Our previous work[3] established the course of oxidation of a Pd(0) complex **E** with molecular oxygen to a Pd(II) complex **A** that is subsequently converted into the methoxycarbonylpalladium species **B** upon reaction with CO and methanol with a base. We have further confirmed that an isolated methoxycarbonylpalladium complex **B** reacted with an alkyne in the presence of a base to release methyl alkynecarboxylate, probably through an intermediate **C** that produces the methyl alkynoate by reductive elimination of the methoxycarbonyl and the alkynyl ligands.



Scheme 1. Proposed mechanism for the palldium-catalyzed oxidative mono- and tricarbonylation of a terminal alkyne.

The tricarbonylation process found in the present study can be accounted for by assuming insertion of the alkynecarboxylate, the monocarbonylation product **6**, into the Pd-methoxycarbonyl bond in **B** (**Path a**) as shown in the center of Scheme 1. The insertion of **6** coupled with another methoxycarbonylation of **B** produces an intermediate **D** having the vinyl and the methoxycarbonyl ligands. The reductive elimination of the vinyl group substituted with the two methoxycarbonyl groups with another methoxycarbonyl ligand in **D** produces the olefin **2** substituted with three methoxycarbonyl groups with regeneration of the Pd(0) species **E** to carry the catalytic cycle.

Path b in Scheme 1 shows one of the possible routes for production of the lactone **3** as the tricarbonylation product. The process involves additional CO insertion into the vinyl-Pd bond followed by cyclization and the transfer of the methoxy groups. A similar palladium-catalyzed dicarbonylation of 1-alkynes to produce lactones has been observed in the catalytic dicarbonylation of alkynes under atmospheric pressure of CO.[4] Effectiveness of the iodide in the catalytic tricarbonylation process and the delicate influence of the compositions of the solvent mixtures in performing the carbonylation process may be associated with the dissociation of X from the palladium center. Further detailed examination of the effect of the solvent nature on the carbonylation process is required to maximize the yield of the tricarbonylation products.

A typical catalytic carbonylation of 4-ethynyltoluene under the pressure of CO (15 atm) and O_2 (5 atm) was performed in a 100 mL stainless autoclave containing 4-ethynyltoluene (131 μL, 1.00 mmol), $Pd(OAc)_2$ (22.5 mg, 0.100 mmol), PPh_3 (52.4 mg, 0.200 mmol), and NEt_4I (129 mg, 0.502 mmol) dissolved in DMF (5 mL) and MeOH (5 mL). The autoclave was immersed in an oil bath heated at 60 °C for 24 h. The reaction mixture was separated by passing through a celite column and the organic layer was collected after washing with water followed by drying with $MgSO_4$. The tricarbonylation products were collected by separation with column chromatography over silica gel by eluting with a hexane/ethyl acetate mixture (1:10 ratio).

Use of aliphatic alkyne also gave the tricarbonylation products **2** and **3**. Treatment of hept-1-yne under similar conditions under the pressure of CO/O_2 yielded the tricarbonylation product **2** and **3** in 32% and 15%, respectively.

The di- and tricarbonylation products were identified with spectroscopic methods (^1H, $^{13}C\{^1H\}$ NMR, IR, and GC-MS) and elemental analysis after purification by chromatography (supplementary material attached).

References

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2 For recent reports, see: B. Gabriele, L. Veltri, G. Salerno, M. Costa, and G. P. Chiusoli, *Eur. J. Org. Chem.*, **2003**, 1722, and references cited therein.

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