A novel palladium complex catalyst for carbonylation of alkynes under mild conditions

S. Jayasree, A. Seayad, S.P. Gupte and R.V. Chaudhari [*]

Homogeneous Catalysis Division, National Chemical Laboratory, Pune 411 008, India

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Carbonylation of alkynes has been carried out using a catalyst system consisting of Pd(OAc)$_2$, a monophosphine, p-toluene sulphonic acid and semilabile anionic bidentate ligands such as pyridine or piperidine carboxylic acids. Turnover frequencies (TOF) upto 3500 h^{-1} and 98% selectivity to 2-substituted 2-propenoic acid/ester have been achieved under mild CO pressures of 1–3 atm at 373 K.

Keywords: carbonylation, alkynes, phenylacetylene, 2-pyridinecarboxylic acid, palladium

1. Introduction

Carbonylation of alkynes is one of the promising synthetic routes for α,β-unsaturated carboxylic acids/esters, having wide ranging applications as monomers for polymer synthesis, fine chemicals and pharmaceutical intermediates, etc. An important example of industrial application is the single step carbonylation of methyl acetylene to methyl methacrylate (MMA) using palladium complex catalysts. Similarly, carbonylation of aryl acetylenes such as 4-isobutylphenylacetylene and 4-methoxynaphthylacetylene is viewed as a potential route for the synthesis of optically pure anti-inflammatory drugs such as S-ibuprofen and S-naproxen. In the previous work on carbonylation of alkynes, palladium complexes with different type of ligands have been reported. Catalyst systems such as Pd(PPh$_3$)$_4$, Pd(OAc)$_2$/dppf [1], Pd(OAc)$_2$/PPh$_3$/dppb [2], Pd(dba)$_2$/4PPh$_3$ [3] have been demonstrated to catalyse the carbonylation of alkynes at low CO pressures. But in all these cases, lower reaction rates and selectivities were observed. In a recent development, Pd(OAc)$_2$/2-pyridylphosphine-catalysed carbonylation has been reported to give high yields for the branched ester product in the hydroesterification of propyne at 60 atm pressure and 333 K [4]. In another case, a catalyst system consisting of Pd(OAc)$_2$ and 2-pyrimidylphosphine ligand has been reported for the hydroesterification of alkynes [5], though with a lower activity and selectivity compared to the Pd(OAc)$_2$/2-pyridylphosphine catalyst.

The aim of this work was to develop an improved catalyst system for the carbonylation of alkynes, which can give higher reaction rates and higher selectivities for the 2-substituted propenoic acid/ester (branched isomer) derivatives under low-pressure conditions. Experimental results using Pd(OAc)$_2$/monophosphine/p-toluene sulphonic acid monohydrate (p-tsa)/2-pyridine carboxylic acid (pyca) or 2-piperidine carboxylic acid (pypca) as catalyst in the carbonylation of phenylacetylene have been reported to demonstrate that turnover frequencies (TOF) in a range of 3500 h^{-1} with a branched isomer selectivity of 98% has been achieved at lower CO pressures. A synergistic effect of the monophosphine and 2-pyridine carboxylic acid ligand in improving the catalytic activity has been discussed.

2. Experimental

The carbonylation reactions were carried out in a Parr Hastelloy C autoclave (50 ml). In a typical reaction, known quantities of the catalyst, ligands and p-tsa were dissolved in a mixture of the alkyne, alcohol and the solvent and charged to the autoclave. The contents were flushed few times with nitrogen followed by carbon monoxide and heated to the desired temperature. After attaining the temperature the autoclave was pressurized with CO and the reaction was started by agitation (900 rpm). To maintain the pressure in the reactor, CO was fed through a constant-pressure regulator from a reservoir vessel. The pressure drop in the reservoir vessel was recorded by means of a pressure transducer. Intermediate liquid samples were also taken at regular intervals of time. The reaction was continued until the CO absorption was stopped. After the reaction, the autoclave was cooled to room temperature, CO depressurized, flushed with nitrogen and the reaction mixture removed. The analysis of the substrate and product in the liquid samples was carried out using a gas chromatograph (HP 5890) using a HP-FFAP capillary column. The products were further confirmed by GC-MS, NMR and IR analysis. The gas-phase analysis was carried out by using a gas chromatograph (AIMIL NUCON GC-5500) using a Porapack-Q ($10' \times 1/8''$) column.

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[*] To whom correspondence should be addressed.

Table 1
Carbonylation of phenylacetylene using various catalyst systems.[a]

No.	Catalyst system[b]	Conversion (%)	Selectivity **2a** (%)	Reaction time[c] (h)	TOF (h^{-1})
1	$Pd(OAc)_2/PPh_3$	30[d]	89	1.45	100
2	$Pd(OAc)_2/PPh_3$/pyca	75	94	0.90	400
3	$Pd(OAc)_2/P(p\text{-}FPh)_3$	66[d]	95	0.60	530
4	$Pd(OAc)_2/P(p\text{-}FPh)_3$/pyca	80	96	0.60	650
5	$Pd(OAc)_2/P(p\text{-}ClPh)_3$/pyca	90	96	0.72	600
6	$Pd(OAc)_2/PPh_3$/pypca	85	95	0.90	450
7	$Pd(OAc)_2/PPh_3$/pyca[e]	25[d]	97	0.48	250
8	$Pd(OAc)_2/PPh_3$/pyca[f]	85	97	0.16	2500
9	$Pd(OAc)_2/PPh_3$/pyca[f,g]	40[d]	96	0.35	550
10	$Pd(OAc)_2/PPh_3$/pyca[f,h]	10[d]	97	0.12	400
11	$Pd(OAc)_2/P(p\text{-}FPh)_3$/pyca[f]	95	98	0.13	3500
12	$Pd(acac)_2/PPh_3$/pyca[f]	90	96	0.18	2400
13	$PdCl_2/PPh_3$/pyca[f]	10	80	2.4	20

[a] Reaction conditions: phenylacetylene: 0.0147 mol; Pd $= 3.0625 \times 10^{-5}$ mol; Pd : phosphine : pyca : p-tsa $= 1:4:2:10$; butanol: 3.75 ml; toluene: 19 ml; total water content: 500–1500 ppm; $P_{CO} = 2$ atm; $T = 373$ K.

[b] pyca = 2-pyridine carboxylic acid, pypca = 2-piperidine carboxylic acid.

[c] Time at which the CO absorption slows down and at which the conversion and TOF are calculated.

[d] Conversions at which the reaction stopped.

[e] p-tsa : Pd = 40.

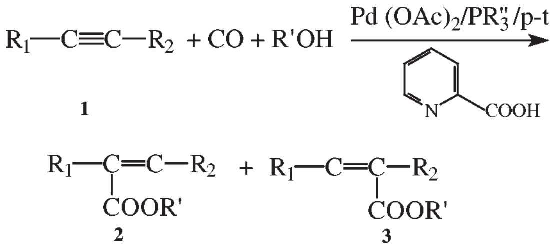
[f] Pd : phosphine : pyca : p-tsa $= 1:30:15:40$.

[g] H_2O instead of butanol.

[h] Methanol instead of butanol.

3. Results and discussion

The carbonylation of alkynes to produce esters of α,β-unsaturated carboxylic acids is described as



1a: $R_1 = C_6H_5$; $R_2 = H$
1b: $R_1 = C_6H_5\text{–}CH_3$; $R_2 = H$
1c: $R_1 = C_6H_9$; $R_2 = H$
1d: $R_1 = R_2 = C_6H_5$
1e: $R_1 = CH_3$; $R_2 = C_6H_5$
1f: $R_1 = CH_2OH$; $R_2 = H$

A preliminary examination of the carbonylation of phenylacetylene (**1a**) with the catalyst system composed of $Pd(OAc)_2/PPh_3/p$-tsa gave only very low activity and low branched isomer (**2a**) selectivity. In this case, the phenylacetylene conversion was only 30% with a selectivity of 89% for **2a**. The introduction of 2-pyridine carboxylic acid ligand in addition to $Pd(OAc)_2/PPh_3/p$-tsa resulted in improving the conversion to 80% with 95% selectivity of **2a** with an overall TOF of 400 h^{-1}. Phosphine ligands with electron withdrawing substituents at the para position such as tris(4-fluorophenyl)phosphine ($P(p\text{-}FPh)_3$) and tris(4-chlorophenyl)phosphine ($P(p\text{-}ClPh)_3$) in combination with the 2-pyridine or 2-piperidine carboxylic acid as ligands provided the best activity and selectivity, as indicated by the results in table 1.

It was also observed that the concentration of the acid promoter (p-tsa) has a strong effect on the reaction rates. The reaction rate increased steadily with the p-tsa concentration upto a p-tsa : Pd ratio of 10. At higher concentrations, i.e., at p-tsa : Pd ratio of 40, even though the initial reaction rates were high, the catalyst decomposed to Pd metal after a 25% conversion of phenylacetylene. In order to stabilize the catalyst, reactions were carried out using excess ligands (Pd : PPh_3 : pyca $= 1:30:15$) which resulted in 95% conversion of phenylacetylene with 97% selectivity to **2a** with an average TOF of 2500 h^{-1}. A typical concentration–time profile for this reaction is given in figure 1. The first-order rate constant values (k_1) for consumption of phenylacetylene were evaluated using the relationship

$$\ln\left(\frac{C}{C_0}\right) = -k_1 t,$$

where C_0 is the initial concentration and C is the concentration at time t (table 2). These values of k_1 varied within ±3–5% from the average k_1 value of 3.28×10^{-3} s^{-1}. These data indicate consistency of catalytic activity and its stability during an experiment.

The catalytic activity was found to be strongly influenced by the polarity of the medium. Less polar solvents such as toluene, xylene, benzene and chlorobenzene gave the highest catalytic activity. In the case of polar solvents such as acetonitrile, methyl ethyl ketone and N-methylpyrrolidinone, the phenylacetylene conversion was too low and the catalyst was found deactivated to Pd metal after the reaction. The enhanced catalytic activity in less polar solvents indicates a possible involvement of neutral palladium complexes as active catalytic intermediates rather than cationic complexes. When methanol was used instead of butanol, only 10% conversion of phenylacetylene was observed. With water as the nucleophile the corresponding acid was obtained but the reaction rate was comparatively lower and the reaction stopped at almost 40% conversion.

The catalyst system was applicable to the carbonylation of various terminal as well as internal alkynes (see table 3). In general, terminal alkynes showed higher reaction rates as compared to internal alkynes.

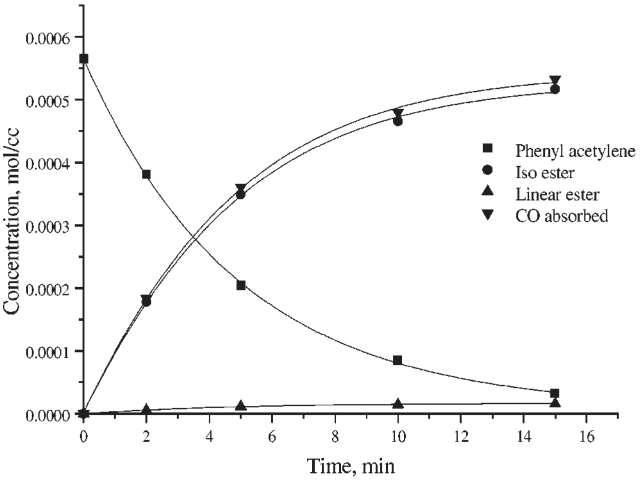


Figure 1. A typical concentration–time profile for the carbonylation of phenylacetylene. Reaction conditions: phenylacetylene: 0.0147 mol; Pd $= 3.0625 \times 10^{-5}$ mol; $\mathrm{Pd : PPh_3 : pyca} : p\text{-tsa} = 1 : 30 : 15 : 40$; butanol: 3.75 ml; total water content: 500–1500 ppm; toluene: 19 ml; $P_{\mathrm{CO}} = 2$ atm; $T = 373$ K.

Table 2
First-order rate constants determined at different time intervals.[a]

Time (s)	k_1 (s^{-1})
120	3.273×10^{-3}
300	3.388×10^{-3}
600	3.155×10^{-3}
900	3.179×10^{-3}

[a] Table 1, run 8.

An interesting observation was that neither of the catalyst systems $\mathrm{Pd(OAc)_2/PPh_3}/p$-tsa or $\mathrm{Pd(OAc)_2}$/pyca/p-tsa gave good catalytic activity. Both the phosphine and pyridine carboxylic acid ligand were needed together to achieve good catalytic activity. A similar kind of ligand synergism has been observed in a few other carbonylation reactions [3, 6,7]. When only $\mathrm{Pd(OAc)_2/PPh_3}/p$-tsa was used as the catalyst system, cationic hydride or alkoxy species such as $\mathrm{[HPd(PPh_3)_3]^+OTs^-}$ or $\mathrm{[Pd(COOR)(PPh_3)_3]^+OTs^-}$ may be formed as the active catalytic species. Under highly acidic conditions such as that of the present system it is reasonable to assume the hydride species as the major active form. Such cationic hydride species may easily get deactivated to inactive Pd(0) complexes under reducing reaction conditions [8–11], which may result in reduced catalytic activity.

In the presence of the semilabile anionic "pyca" ligand, the active catalyst species formed may be a neutral hydrido palladium(II) species of the type **B**, which can be formed through a kind of water–gas shift reaction, as given in scheme 1. The formation of complex **A** was confirmed by isolation from the stoichiometric reaction between $\mathrm{Pd(OAc)_2}$, $\mathrm{PPh_3}$, pyca and p-tsa {IR (KBr) 1668vs [ν(C=O)], 1604s [ν(C=C)], 1330s [ν(O=C–O)]; ^{31}P ($\mathrm{CDCl_3}$) δ 34.58s, δ 36.19w (cis/trans isomers); ^{1}H ($\mathrm{CDCl_3}$) δ 2.3s (3H, tolyl $\mathrm{CH_3}$), δ 7–7.9m (Ph and pyridyl)}. The complex A showed comparable catalytic activity (TOF $= 2200$ $\mathrm{h^{-1}}$) and selectivity (96%) for the carbonylation of phenylacetylene. The formation of $\mathrm{CO_2}$ is confirmed by GC analysis of the gas phase of the reaction using excess catalyst precursor. These observations strongly indicate the formation of the hydrido palladium(II) species (**B**), which may initiate the catalytic cycle.

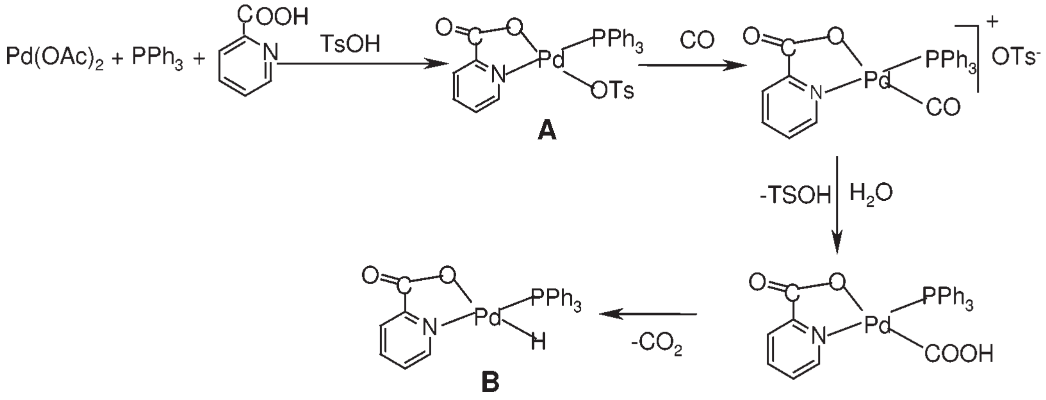
Pyridine carboxylic acid along with monophosphines is known to form neutral and stable alkyl Pd complexes, which are active for CO insertion reactions [12]. It was shown that the nature of the phosphine ligand has a significant effect on the CO insertion rates, less basic, more labile and more trans influencing ligands showing high CO insertion rates. In such circumstances the improved catalytic activity in the presence of P(p-FPh)$_3$ and P(p-ClPh)$_3$ in the carbonylation reaction is quite expected. In addition, the electron withdrawing property or lower basicity of the imino nitrogen as well as the phosphine ligand may also

Table 3
Carbonylation of various alkynes.[a]

No.	Alkyne	Conversion (%)	Selectivity (%) 2	3	Reaction time[b] (h)	TOF ($\mathrm{h^{-1}}$)
1	Phenylacetylene (**1a**)	85	97	3	0.16	2500
2	Ethynyltoluene (**1b**)	90	97	3	0.19	2300
3	1-ethynylcyclohexene (**1c**)	70	94	4	1.35	250
3	Diphenylacetylene (**1d**)	90	100	–	1.25	350
4	1-phenyl-1-propyne (**1e**)	90	47	53	1.45	300
5	Propargyl alcohol (**1f**)	50	85	10	2.40	100

[a] Reaction conditions: alkyne: 0.0147 mol; Pd $= 3.0625 \times 10^{-5}$ mol; $\mathrm{Pd : phosphine : pyca} : p\text{-tsa} = 1 : 30 : 15 : 40$; butanol: 3.75 ml; toluene: 19 ml; total water content: 500–1500 ppm; $P_{\mathrm{CO}} = 2$ atm; $T = 373$ K.

[b] Time at which the CO absorption slows down and conversion and TOF are calculated.



Scheme 1.

provide easy coordination of highly electron rich alkyne to the Pd centre. The reduced catalytic activity in the presence of methanol may be due to its ability to reduce the Pd^{2+} species easily to inactive Pd(I) or Pd(0) complexes or to Pd metal by several different pathways [9,13–15]. Another possibility for the deactivation of the catalyst under certain conditions is that the phosphine ligand may get quaternized with activated olefin product [16,17] resulting in lowering of its concentration, which ultimately may result in the decomposition of the catalyst to Pd metal. However, under the conditions of our best experiments (table 1, runs 8 and 11) with $Pd(OAc)_2$/phosphine/pyca/p-tsa $(1:30:15:40)$, the quaternization may not be significant as the catalytic activity was found to be nearly constant throughout an experiment.

Although more studies are required to further investigate the effect of the ligands and the reaction mechanism, it is noteworthy that the use of such a simple catalyst system showed remarkable favorable effects on the carbonylation of alkynes under mild conditions.

4. Conclusions

Carbonylation of alkynes has been studied using a catalyst system which contains $Pd(OAc)_2$, a monophosphine, p-toluene sulphonic acid and anionic semilabile bidentate ligands such as 2-pyridine or 2-piperidine carboxylic acid. Higher turnover frequencies (TOF) (upto 3500 h^{-1}) and selectivity (98%) have been achieved under mild CO pressures. Phosphines with electron withdrawing substituents at the para position such as $P(p\text{-}FPh)_3$ and $P(p\text{-}ClPh)_3$ showed better activity. A synergistic effect of the monophosphine and the pyridine carboxylic acid ligands has been demonstrated in improving catalytic activity. The catalyst activity was found strongly influenced by the reaction medium (solvents and the alcohol) and the concentration of acid promoter and ligands. The reaction is proposed to proceed through the formation of palladium hydride species.

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