

# One pot formation of catalyst and double carbonylation of benzyl chloride

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## Abstract

The double carbonylation of benzyl chloride to phenylpyruvic acid (PPA) catalyzed by  $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$  and potassium pyridine-2-carboxylate (KPyca) in  $\text{Ca}(\text{OH})_2/\text{dioxane}/\text{H}_2\text{O}$  system has been studied. The effects of ligands, concentration of catalysts, solvents, temperature, CO pressure and the molar ratio of  $\text{Ca}(\text{OH})_2/\text{PhCH}_2\text{Cl}$  on the conversion and selectivity have been investigated. The conversion of benzyl chloride was 71.3%, and the yield of PPA was 70.1% with selectivity 98.3% when the reaction was carried out for 10 h at 353 K and 2.8 MPa of CO in the  $\text{Ca}(\text{OH})_2/\text{dioxane}/\text{H}_2\text{O}$  system, with  $\text{CoCl}_2$  0.035 mol/l, KPyca 0.13 mol/l, and the ratio of  $\text{Ca}(\text{OH})_2/\text{PhCH}_2\text{Cl}$  2.0. The product PPA was characterized by IR,  $^1\text{H}$  NMR, MS and UV. The mechanism of this catalytic reaction has also been discussed.

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*Keywords:* Catalysis; Double carbonylation; Phenylpyruvic acid; Cobalt pyridine-2-carboxylate

## 1. Introduction

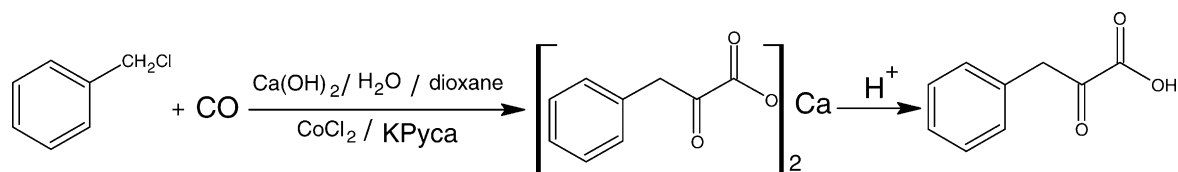
The catalytic double carbonylation of aryl halides to  $\alpha$ -keto acids has been recently investigated by several research groups, both from industry and university [1,2]. In order to find a new and useful catalyst, a number of compounds such as cobalt and palladium complexes,  $\text{Co}_2(\text{CO})_8$  and  $\text{PdCl}_2\text{Ln}$ , have been studied in the reaction [3,4]. Despite the good yield of  $\alpha$ -keto acid, these catalysts often exhibit some disadvantages such as sensitivity to  $\text{O}_2$  and  $\text{H}_2\text{O}$  in the reaction, and they are difficult to prepare because of harsh conditions.

It is reported that cobalt complexes with Schiff-base ligands show very good catalytic activity in the

oxidative carbonylation for the synthesis of dimethyl carbonate and the catalyst has also some advantages such as ease of preparation and handling [5]. It was considered interesting to test the catalytic activity of cobalt bis(2-pyridinecarboxylate)-tetrahydrate ( $\text{Co}(\text{Pyca})_2 \cdot 4\text{H}_2\text{O}$ ) in the double carbonylation of benzyl chloride to  $\alpha$ -keto acid.

Recently a novel synthesis of PPA by double carbonylation of benzyl chloride catalyzed by  $\text{Co}(\text{Pyca})_2 \cdot 4\text{H}_2\text{O}$  in mild conditions has been reported by our group [6]. On the basis of preliminary studies we explored a convenient method of putting  $\text{CoCl}_2$  and KPyca into the autoclave to carry out the preparation of catalyst and double carbonylation simultaneously, as shown in Scheme 1. This “one pot” method avoids the preparation of either  $\text{Co}_2(\text{CO})_8$  or  $\text{Co}(\text{Pyca})_2 \cdot 4\text{H}_2\text{O}$ , so it simplifies the process of synthesis. Here we report the details of our study on one pot formation of catalyst and double carbonylation of benzyl chloride.

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Scheme 1. Synthesis of PPA by double carbonylation of benzyl chloride.

## 2. Experimental

All carbonylation reactions were conducted under CO in a 250 ml autoclave. The experiments were carried out according to literature methods [6]. All reagents were used as received without further purification and CO purity is over 99.8%. IR spectra were recorded with an EQUINOX55 (BRUKER) spectrometer by using KBr pellers.

$^1\text{H}$  NMR were obtained on a Varian MERCURY-VX300 spectrometer in deuterodimethyl sulfoxide with tetramethylsilane as the internal standard. Mass spectra were recorded with a VG ZAB-3F. UV-Vis spectra were recorded on an UV-240 spectrometer. The basic data of PPA were characterized by IR, MS,  $^1\text{H}$  NMR and UV, and listed as following: Melting point: 156–157 °C. MS ( $m/e$ ): 164 ( $\text{M}^+$ ), 119, 91 (100%), 65, 45, 39.  $^1\text{H}$  NMR (300 MHz, DMSO,  $\delta$ , ppm/TMS): 4.124 (s, 1 H), 6.381 (s, 1 H), 7.184–7.748 (m, 5H), 9.268 (s, 1OH). IR ( $\text{cm}^{-1}$ ): 3473.42, 3220.50, 3112.56, 1697.25, 1624.38, 1492.06, 1456.49, 1382.32, 1294.70. UV(nm): 240, 365.

## 3. Results and discussion

### 3.1. Screening of Schiff-base ligands

N,N-donating and O,N-donating chelates are good bi-dentate ligands for metals. They have broad use in the field of wet analysis and homogeneous catalysis. Some Schiff-bases used as ligands in the catalytic system have been investigated, and shown in the Table 1. It is found that KPyca has the highest catalysis activity among these species. Nicotinic acid and *i*-nicotinic acid whose structures are similar to KPyca have been found to have no activity. It is known that Co(II) coordinated with KPyca could form the

active catalyst of five-membered ring structure (see the Scheme 2), but nicotinic acid and *i*-nicotinic acid are not beneficial to coordinate with Co(II) in that structure. 1,10-Phenanthroline and 2,2'-bipyridine are ligands of having expanded conjugated ring system. When they coordinate with Co(II), it is not advantageous to the insertion of CO molecular because of their larger steric demand compared with KPyca. This kind of structure leads to rather low yield of PPA in carbonylation. Imidazole has no catalysis function because it cannot coordinate with Co(II) to yield the active species.

### 3.2. Effects of the concentration of catalysts

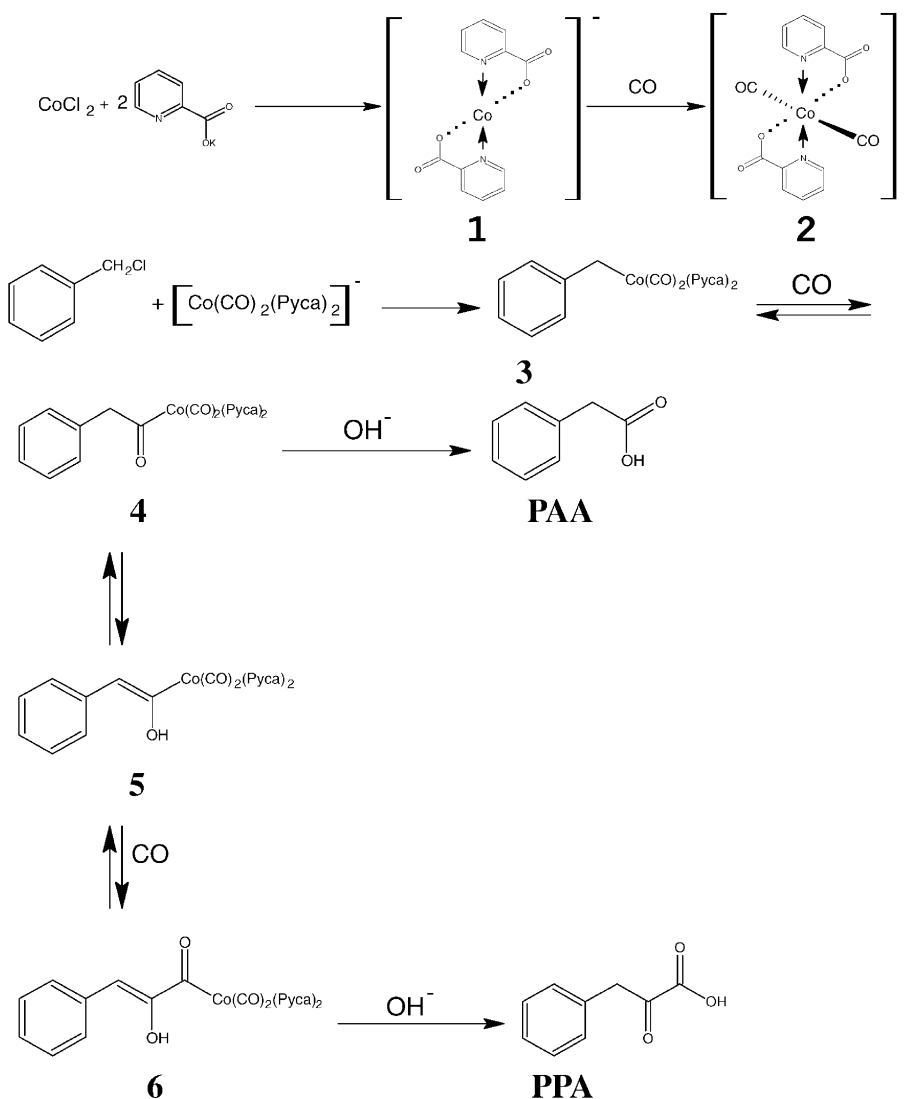
The effects of the concentration of catalysts on the yield are presented in Table 2. When the concentration of KPyca keep 0.13 mol/l, the yield of PPA increases at first and then decreases with the change of the concentration of  $\text{CoCl}_2$  from 0.07 to 0.0035 mol/l, but no significant increase in the yield of PAA is observed under the reported experimental conditions. When the

Table 1  
Effects of different Schiff-base ligands on activity

Schiff-base	Yield (%)		Conversion of PhCH <sub>2</sub> Cl (%)	Selectivity to PPA (%)
	PPA	PAA		
NO <sup>a</sup>	12.0	2.4	14.4	83.3
KPyca	70.1	1.2	71.3	98.3
1,10-Phenanthroline	58.1	0	58.1	100
2,2'-Bipyridine	28.1	0	28.1	100
Nicotinic acid	0	0	0	0
<i>i</i> -Nicotinic acid	0	0	0	0
Imidazole	0	0	0	0

PhCH<sub>2</sub>Cl: 0.06 mol, Ca(OH)<sub>2</sub>: 0.16 mol, CoCl<sub>2</sub>: 0.035 mol/l, ligand: 0.13 mol/l, T: 353 K, P: 2.8 MPa, DO: dioxane, DO(100 ml)/H<sub>2</sub>O(20 ml), 10 h, stirring speed: 2500 r/min, PAA: phenylacetic acid.

<sup>a</sup> Without ligand.

Scheme 2. Proposed mechanism for carbonylation catalyzed by  $\text{CoCl}_2/\text{KPyca}$ .

concentration of  $\text{CoCl}_2$  is too high with  $\text{KPyca}$  only 0.13 mol/l,  $\text{CoCl}_2$  cannot convert into the catalyst rapidly and completely. The excess  $\text{CoCl}_2$  tends to produce  $\text{Co(OH)}_2$  in the basic environment, which reduces the activity of catalyst. While the concentration of  $\text{CoCl}_2$  is too low, it cannot produce enough active intermediates to catalyze the double carbonylation. In the reaction process,  $\text{KPyca}$  is a Schiff-base ligand to coordinate with cobalt. When the concentration of

$\text{KPyca}$  is too high with the concentration of  $\text{CoCl}_2$  only 0.007 mol/l, the activity of catalyst in the double carbonylation will not increase very rapidly and the excess  $\text{KPyca}$  will be brought into the product, which is difficult to separate. When the concentration of  $\text{KPyca}$  is too low, it cannot produce enough intermediate. Taking into account of the yield of  $\text{PPA}$  and  $\text{TON}$ , the optimum concentration of  $\text{CoCl}_2$  is about 0.007 mol/l with  $\text{KPyca}$  0.054 mol/l.

Table 2  
Effects of the concentration of catalysts on the reaction

CoCl <sub>2</sub> (mol/l)	KPyca (mol/l)	Yield (%)		Conversion of PhCH <sub>2</sub> Cl (%)	Selectivity to PPA (%)	TON
		PPA	PAA			
0.07	0.13	45.1	4.8	49.9	90.3	3
0.035	0.13	70.1	1.2	71.3	98.3	10
0.018	0.13	55.1	2.4	57.5	95.8	16
0.007	0.13	55.1	3.6	58.7	93.8	40
0.0035	0.13	48.1	3.6	51.7	93.0	70
0.007	0.068	55.1	2.4	57.5	95.8	40
0.007	0.054	52.1	1.2	53.3	97.7	38
0.007	0.028	30.1	1.2	31.3	96.1	22

PhCH<sub>2</sub>Cl: 0.06 mol, Ca(OH)<sub>2</sub>: 0.16 mol, T: 353 K, P: 2.8 MPa, DO(100 ml)/H<sub>2</sub>O(20 ml), stirring speed: 2500 r/min.

### 3.3. Effect of solvents

Table 3 shows that the selectivity of products in reaction is critically influenced by the solvents. Miura reported that in the cobalt-catalyzed carbonylation of aryl halides using calcium hydroxide as the base in aqueous organic solvents, both the identity of the solvents and the content of water were the main factors determining the product composition [7]. In liquid reaction system, the solvent molecule tends to complex the central ion with the ligand. The stronger is the capability of donating electron pair of the solvent, the stronger is the capability of complexing the central ion from the original complex. Compared with other solvents, DO's ability to donate electron pair is lower [8], so its capability of competing for the Co is lower, which results in the better stability of cobalt complex in DO. DO is a proton inactive solvent, which is different from the proton donor solvent that can lead to the disassociation of the cobalt complex to a certain

extent because the ligand of Co can form hydrogen bond with the solvent molecule. In this way DO has the function of stabilizing and promoting for the form of intermediate in double carbonylation. On the other hand, the polar of solvent is an important factor. The lower polar solvent is favorable to the form of olefinic alcohol structure, and then is useful to the double carbonylation, which is consistent with the results of Foa and Francalanci [9].

### 3.4. Effect of ratio of Ca(OH)<sub>2</sub>/PhCH<sub>2</sub>Cl

The effect of the molar ratio of Ca(OH)<sub>2</sub>/PhCH<sub>2</sub>Cl is shown in Table 4. The highest yield of PPA is obtained when the ratio of Ca(OH)<sub>2</sub>/PhCH<sub>2</sub>Cl is about 2.0. These facts suggest that Ca(OH)<sub>2</sub> might be not strong enough to attack the carbon atom of the acyl intermediate, seeing Scheme 2, to give the product when the molar ratio of Ca(OH)<sub>2</sub>/PhCH<sub>2</sub>Cl is less than 2.0. However, when the ratio is greater than 2.0, the

Table 3  
Effect of solvents on the reaction

H <sub>2</sub> O/vol (%)	Solvent/ml	ε (°C)	Yield (%)		Conversion of PhCH <sub>2</sub> Cl (%)	Selectivity to PPA (%)
			PPA	PAA		
16.7	MeOH(100)	31.2 (20)	0	3.6	3.6	0
16.7	<i>i</i> -PrOH(100)	18.3 (25)	23.1	8.5	31.6	73.3
16.7	<i>t</i> -BuOH(100)	11.4 (19)	43.1	2.4	45.5	94.7
16.7	DO(100)	2.209 (25)	55.1	2.4	57.5	95.8
33.3	DO(100)	2.209 (25)	53.1	2.4	55.5	95.7
45.8	DO(100)	2.209 (25)	47.1	1.2	48.3	97.5

PhCH<sub>2</sub>Cl: 0.06 mol, Ca(OH)<sub>2</sub>: 0.16 mol, CoCl<sub>2</sub>: 0.007 mol/l, KPyca: 0.068 mol/l, P: 2.8 MPa, T: 353 K, 10 h, stirring speed: 2500 r/min.

Table 4  
Effect of molar ratio of Ca(OH)<sub>2</sub>/PhCH<sub>2</sub>Cl on the reaction

Ca(OH) <sub>2</sub> / PhCH <sub>2</sub> Cl	Yield (%)		Conversion of PhCH <sub>2</sub> Cl (%)	Selectivity to PPA (%)
	PPA	PAA		
4.5	45.6	4.2	49.8	91.5
3.0	47.3	2.1	49.4	95.7
2.0	63.1	2.1	65.2	96.8
1.0	50.8	10.6	61.4	82.8

PhCH<sub>2</sub>Cl: 0.04 mol, CoCl<sub>2</sub>: 0.007 mol/l, KPyca: 0.068 mol/l, P: 2.8 MPa, T: 353 K, DO (100 ml)/H<sub>2</sub>O (20 ml), 10 h.

hydroxide in the liquid solvent may react with CoCl<sub>2</sub> to produce Co(OH)<sub>2</sub> and decreases the activity of the catalyst.

### 3.5. Effect of temperature

Temperature strongly affects the yield of PPA in the reaction. The yield of PPA will increase with the elevation of temperature below 353 K and will decrease above 353 K as shown in Fig. 1. In the carbonylation of organic halides by Co<sub>2</sub>(CO)<sub>8</sub> or organic palladium catalyst system, the optimum temperature is 323 K [10], which is different from the temperature range in our reaction system. The reason is that the catalyst in our reaction system is not Co(CO)<sub>4</sub><sup>-</sup> but Co(Pyca)<sub>2</sub>. When the temperature is above 353 K, it is not favorable to the synthesis of catalyst and the form of olefinic alcohol intermediate. Moreover the carbonyl is easy to fall off from PPA when the temperature is increased.

### 3.6. Effect of CO pressure

The effect of carbon monoxide pressure on the yield of PPA and PAA is shown in Fig. 2. As expected, for the reaction of benzyl chloride, higher CO pressure enhances both the yield of PPA and PAA, but the increase of the yield of PPA is much greater than that of PAA. The increase of the yield of double carbonylation by means of increasing the CO pressure is usually common in catalytic carbonylation of organic chlorides [11]. A second insertion of carbon monoxide into intermediate is favored by increasing CO pressure.

### 3.7. Proposed catalytic mechanism

The mechanism of carbonylation of halides to α-keto acids in our new catalytic system is accounted by the pathway outlined in Scheme 2. The elementary processes inferred on the mechanism are: (a) coordination of CoCl<sub>2</sub> and KPyca to give the intermediate **1**, which is coordinated with CO rapidly to form the saturated complex **2**; (b) oxidative addition of PhCH<sub>2</sub>Cl to **2** to give acylcobalt halide **3**; (c) a molecule of carbon monoxide inserts into the Co–C bond in intermediate **3** to produce **4**; (d) nucleophilic attack of hydroxyl ion on the carbon atom of the acyl intermediate **4** to give mono-carbonylation product PAA; (e) there is a tautomeric equilibrium of ketone and olefinic alcohol structure in **4**. Some conditions such as lower polar solvent or high CO pressure can promote the equilibrium moving to the side of olefinic alcohol; (f) in the weak alkali condition such

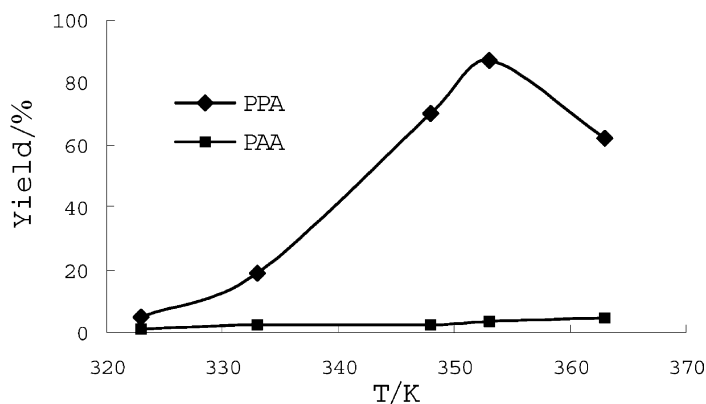


Fig. 1. Effect of temperature on the reaction, PhCH<sub>2</sub>Cl: 0.06 mol, Ca(OH)<sub>2</sub>: 0.16 mol, CoCl<sub>2</sub>: 0.035 mol/l, KPyca: 0.13 mol/l, P: 2.8 MPa, DO (100 ml)/H<sub>2</sub>O (20 ml), stirring speed: 3000 r/min.

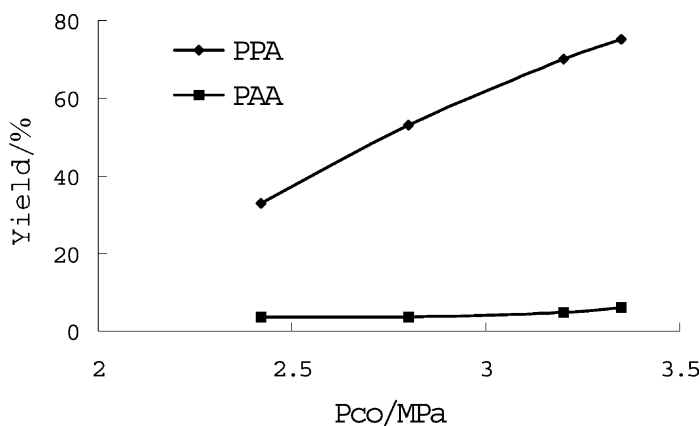


Fig. 2. Effect of CO pressure on the reaction  $\text{PhCH}_2\text{Cl}$ : 0.06 mol,  $\text{Ca}(\text{OH})_2$ : 0.16 mol,  $\text{CoCl}_2$ : 0.035 mol/l,  $\text{KPyca}$ : 0.13 mol/l,  $T$ : 353 K,  $\text{DO}$  (100 ml)/ $\text{H}_2\text{O}$  (20 ml), 10 h.

as  $\text{Ca}(\text{OH})_2$ , a second carbon monoxide is absorbed by **5** to produce **6**, perhaps because the nucleophilic ability of  $\text{Ca}(\text{OH})_2$  is so poor that intermediate **5** is less susceptible to attack by hydroxide ion; (g) the attack of hydroxyl ion on species **6** to give double carbonylation product **PPA**.

#### 4. Conclusions

The work reported here has demonstrated the possibility of  $\text{CoCl}_2$  and potassium pyridine-2-carboxylate as a novel catalyst system in double carbonylation of benzyl chloride to phenylpyruvic acid. This one pot reaction could take place under mild condition and the catalyst is very easy to prepare and handle. Under the optimized reaction conditions, the yield of PPA is reasonable high. The mechanism of mono- and double carbonylation has been proposed.

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