

# An efficient carbonylation of aryl halides catalysed by palladium complexes with phosphite ligands in supercritical carbon dioxide

Yoshihito Kayaki,<sup>a</sup> Yushi Noguchi,<sup>a</sup> Seiji Iwasa,<sup>a</sup> Takao Ikariya\*<sup>a</sup> and Ryoji Noyori<sup>b</sup>

<sup>a</sup> Department of Chemical Technology, Tokyo Institute of Technology and CREST, Japan Science and Technology Corporation, O-okayama, Meguro-ku, Tokyo 152-8552, Japan. E-mail: tikariya@o.cc.titech.ac.jp

<sup>b</sup> Department of Chemistry and Research Center for Materials Science, Nagoya University, Chikusa, Nagoya 464-8602, Japan

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The carbonylation of aryl halides catalysed by CO<sub>2</sub> soluble Pd complexes with trialkyl or triaryl phosphite ligands proceeds rapidly in scCO<sub>2</sub>, in which the rate of the reaction is higher than those attained in solution phase reactions.

Supercritical fluids (SCFs) are attractive alternatives to organic solvents as reaction media for chemical reactions for a number of reasons. These reasons include their pressure tunable physical properties and solvent powers as well as the high miscibility of the reactant gases, efficient mass transfer, local clustering, and possible weakening of the solvation of the reactants.<sup>1</sup> In particular, homogeneous transition metal-catalysed reactions involving gaseous reactants in SCFs have been intensively investigated, *e.g.* hydrogenation of olefins,<sup>1a,2</sup> hydroformylation,<sup>3</sup> hydrogenation of carbon dioxide,<sup>4</sup> and oxidation by O<sub>2</sub>.<sup>2e,5</sup> However, no discernible benefit in terms of rate was obtained by performing the reactions under supercritical conditions except for a rapid hydrogenation of supercritical carbon dioxide (scCO<sub>2</sub>) with Ru complexes<sup>4</sup> and an olefin hydroformylation catalysed by Rh complexes.<sup>3b,c</sup> This report describes the first carbonylation reactions of aryl halides catalysed by CO<sub>2</sub> soluble Pd complexes which proceed rapidly in scCO<sub>2</sub>. The rate of the reaction is higher than those attained in solution phase reactions.

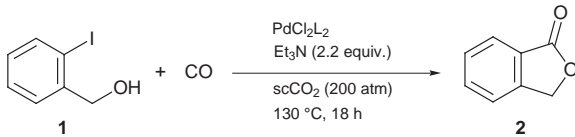
We first examined the intramolecular carbonylation of 2-iodobenzyl alcohol **1** catalysed by palladium complex [PdCl<sub>2</sub>(MeCN)<sub>2</sub>] **3a** in a supercritical mixture of CO<sub>2</sub> and CO (*P*<sub>CO<sub>2</sub></sub> = 200 atm and *P*<sub>CO</sub> = 10 atm)<sup>†</sup> at 130 °C (Table 1). The reaction proceeds smoothly in the presence of 2.2 equiv. of Et<sub>3</sub>N (1: Pd: Et<sub>3</sub>N = 5000:1:11000) to give phthalide, **2** in a moderate yield, with the TON (turnover number, mol product per mol catalyst) = 2190 after 2 h. A visual inspection of the reaction mixture in the window-equipped reactor vessel confirms that all the reactants as well as the product **2** are soluble in scCO<sub>2</sub>, although the catalyst **3a** is only partly soluble. The reaction was started by introducing CO<sub>2</sub> and then CO into the reactor containing the reactants and the catalyst at the reaction temperature (Method A). In this procedure, the reaction proceeded rapidly in the liquid phase which formed before reaching the supercritical homogeneous state. Therefore, the outcome of the reaction is at least partly due to the reaction in the liquid phase. In fact, the reaction performed in a liquid phase consisting of **1** and Et<sub>3</sub>N without CO<sub>2</sub> under otherwise identical conditions (neat condition) (substrate: catalyst = 5000:1, *P*<sub>CO</sub> = 10 atm, 130 °C, 2 h) produced **2** with a TON of 3570. Such reactions in the liquid phase can be prevented by separating the catalyst from the reactants using a small glass container (Method B, standard procedure).<sup>‡</sup> Reactions using this standard procedure gave a TON of 120 after 2 h and 1880 after 18 h as shown in Table 1, which clearly indicates that the carbonylation proceeds in the homogeneous scCO<sub>2</sub> phase.

Encouraged by the marked catalytic activity of the less soluble catalyst precursor **3a** in scCO<sub>2</sub>, we then tried to employ Pd complexes with trialkyl phosphite ligands, which are highly soluble even in nonpolar hydrocarbons.<sup>7</sup> The solubility test

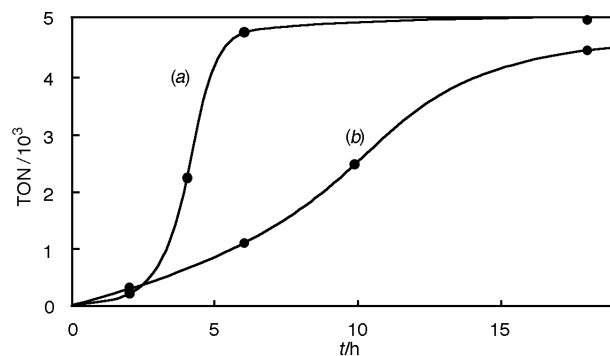
clearly demonstrated that 1 × 10<sup>-2</sup> mmol (5.1 mg) of [PdCl<sub>2</sub>{P(OEt)<sub>3</sub>}<sub>2</sub>] **3b** were dissolved in scCO<sub>2</sub> (300 atm) at 130 °C in a 50 mL reactor vessel. The success of this strategy is shown by the greater TON attained in the reaction catalysed by **3b** under the standard conditions mentioned above compared to that with **3a**. The reaction of **1** with **3b** proceeded efficiently at 130 °C in a homogeneous single phase containing all the reactants and the catalyst to provide quantitatively the product **2** (Table 1).

The phosphite compounds are the best choice of ligand for an increase in the solubility of the Pd complex. The compound's structure and electronic properties strongly affect the outcome of the reactions, as listed in Table 1. The scCO<sub>2</sub> soluble Pd complexes with trialkyl or triphenyl phosphite ligands (**3b** and **3c**) are highly efficient catalyst precursors. The complex **3g** with PMe<sub>3</sub> ligands was less reactive because the strongly coordinated ligand retards slightly the reaction in scCO<sub>2</sub> as observed in conventional liquid solvents.<sup>8</sup> Replacement of the phenyl groups in PPh<sub>3</sub> with methoxy groups (**3d** and **3e**) facilitates the carbonylation due to an increase in the solubility of the Pd catalyst precursor. On the other hand, the reaction with the CO<sub>2</sub> insoluble PPh<sub>3</sub> complex **3f** proceeded rapidly almost to completion accompanied with metal deposition. One possible explanation is that the phosphorous ligand-free, CO<sub>2</sub> soluble Pd carbonyl species<sup>9,10</sup> generated might be extracted into the

**Table 1** Pd complex catalysed carbonylation of 2-iodobenzyl alcohol **1** in scCO<sub>2</sub><sup>a</sup>

					
Run	L (Pd complex)	Medium (atm)	CO/atm	t/h	TON
1 <sup>b</sup>	MeCN <b>3a</b>	CO <sub>2</sub> (200)	10	2	2190
2 <sup>c</sup>	MeCN <b>3a</b>	—	10	2	3570
3	MeCN <b>3a</b>	CO <sub>2</sub> (200)	10	2	120
4	MeCN <b>3a</b>	CO <sub>2</sub> (200)	10	18	1880
5	P(OEt) <sub>3</sub> <b>3b</b>	CO <sub>2</sub> (200)	10	18	5000
6	P(OPh) <sub>3</sub> <b>3c</b>	CO <sub>2</sub> (200)	10	18	4510
7	PPh(OMe) <sub>2</sub> <b>3d</b>	CO <sub>2</sub> (200)	10	18	4470
8	PPh <sub>2</sub> (OMe) <b>3e</b>	CO <sub>2</sub> (200)	10	18	3880
9	PPh <sub>3</sub> <b>3f</b>	CO <sub>2</sub> (200)	10	18	4800
10	PMe <sub>3</sub> <b>3g</b>	CO <sub>2</sub> (200)	10	18	3180
11	P(OEt) <sub>3</sub> <b>3b</b>	CO <sub>2</sub> (200)	1	18	4650
12	P(OEt) <sub>3</sub> <b>3b</b>	CO <sub>2</sub> (200)	5	18	5000
13	P(OEt) <sub>3</sub> <b>3b</b>	toluene <sup>d</sup>	1	18	3100
14	P(OEt) <sub>3</sub> <b>3b</b>	toluene <sup>d</sup>	5	18	3800

<sup>a</sup> Reaction was conducted at 130 °C in a 50 mL reaction vessel containing 0.1 μmol of Pd catalyst (10 μL DMF solution), substrate and Et<sub>3</sub>N (Method B). Substrate: Pd catalyst: Et<sub>3</sub>N = 5000:1:11000. TON = product mol/catalyst mol. <sup>b</sup> The catalyst was not separated from the substrate (Method A). <sup>c</sup> Neat. <sup>d</sup> 50 mL.



**Fig. 1** Time vs. TON plots for the carbonylation of **1** catalysed by  $[\text{PdCl}_2\{\text{P}(\text{OEt})_3\}_2]$  **3b**, in (a)  $\text{scCO}_2$  (standard procedure) or (b) toluene (substrate:catalyst = 5000:1, catalyst = 0.1  $\mu\text{mol}$ ).

$\text{scCO}_2$  phase, where the carbonyl complex effects the reaction highly efficiently and is deactivated during the later stages of the reaction because of the lack of a stabilizing ligand in the  $\text{scCO}_2$  phase. In order to increase the solubility of the transition metal complexes in  $\text{scCO}_2$ , ligand modifications such as replacement of ligands containing aryl substituents to ligands bearing alkyl or perfluoroalkyl groups or introduction of  $\text{CO}_2$ -philic ponytails as substituents on the aryl groups have been developed previously.<sup>4b,c,11</sup> The use of phosphonate ligands has proved to be a practical alternative ligand modification for increasing the solubility of transition metal complexes in supercritical fluids.

The advantage of performing the carbonylation in supercritical fluids is that there is no marked effect of the CO pressure on the TON values obtained in  $\text{scCO}_2$ . Because of the higher diffusivity of  $\text{scCO}_2$  compared to organic solvents as well as the high solubility of CO in this medium, the carbonylation even at 1 atm of CO pressure (CO:substrate = ca. 1.5:1) proceeded to near completion (TON = 4650). The yield of the product **2** (TON ~ 5000) is independent of the CO pressure over a range of 1–5 atm in  $\text{scCO}_2$  (200 atm), whereas the reaction in toluene under otherwise identical conditions provided lower TON values (3100–3800) over a range of 1–5 atm of CO. The time conversion curve obtained by batch-wise experiments, illustrated in Fig. 1, as well as direct monitoring of the reaction by on-line FTIR revealed that the reaction proceeds rapidly to completion within 3–4 h after a ca. 2 h induction period.

The phosphonate–Pd catalyst can be applied to the intermolecular carbonylation of iodobenzene **4** and methanol (substrate:catalyst = 500:1) under the standard conditions in  $\text{scCO}_2$  to yield methyl benzoate (TON = 260). Further optimization of the reaction is now in progress.

In conclusion, the carbonylation of aryl halides catalysed by Pd complexes with phosphonate ligands proceeds rapidly in  $\text{scCO}_2$ . The rate of the reaction is higher than that in the liquid phase.

## Notes and references

† **SAFETY WARNING:** Operators of high-pressure equipment should take proper precautions to minimize the risk of personal injury [ref. 4(b)].

‡ **Standard procedure** for the carbonylation: The reactor equipped with a small vial was charged with argon gas in a desiccator. Then, a DMF (10 ml) solution of Pd catalyst (0.1 mmol) was charged in this vial, and the reactor was placed in an oven. After reaching the desired temperature of 130 °C (for ca. 1.5 h), a mixture of the substrate (0.5 mmol) and  $\text{Et}_3\text{N}$  (1.1 mmol) was added into the reactor (outside the vial) with a syringe through an opening against a flow of  $\text{CO}_2$ . Subsequently, CO (1–10 atm) was introduced, and then  $\text{CO}_2$  (200 atm) was added with an HPLC pump. After stirring for 18 h, the reactor was cooled in a bath of MeOH and dry ice. The mixture of CO and  $\text{CO}_2$  was vented, and the reactor was slowly warmed to room temperature. The yield of **2** was determined by  $^1\text{H}$  NMR and GC analyses of  $\text{CDCl}_3$  solutions of the products. On-line analysis was conducted by using a reactor vessel connected to the FT-IR equipment (JASCO FT/IR-610). The reaction was monitored by collecting spectra at intervals over the period of the reaction.

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