

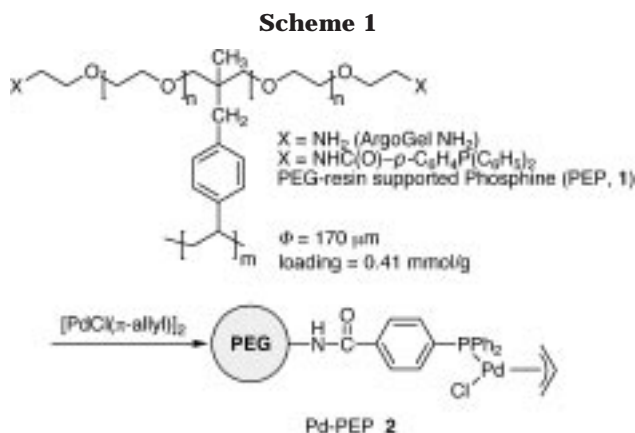
# Green Catalysis: Hydroxycarbonylation of Aryl Halides in Water Catalyzed by an Amphiphilic Resin-Supported Phosphine–Palladium Complex

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Received April 14, 1999

The development of environmentally friendly catalysts for organic transformation is becoming an area of growing importance.<sup>1</sup> Our research interests, recently, lie in the development of solid-supported transition metal complexes<sup>2,3</sup> realizing high catalytic activity in aqueous media<sup>4,5</sup> which would provide a safe, resource-saving, and environmentally benign process. Solid-phase catalytic reactions are also useful means of high-throughput organic syntheses as well as industrial production of fine chemicals.<sup>6</sup> We have previously reported the design and preparation of amphiphilic palladium–phosphine complexes bound to PEG–PS resin which exhibit high catalytic activity in the Tsuji–Trost reaction and Suzuki–Miyaura cross-coupling.<sup>2,7,8</sup> Here we report a four-phase protocol of the palladium-catalyzed hydroxycarbonylation<sup>9,10</sup> of aryl or alkenyl halides which was



performed in water in the presence of an amphiphilic solid-supported phosphine–palladium complex under an atmospheric pressure of carbon monoxide to give the corresponding carboxylic acids in high yields under mild reaction conditions.

The amphiphilic resin-supported palladium catalyst was prepared according to the procedures previously reported.<sup>2c</sup> Thus, the palladium–triarylphosphine complex, Pd–PEP (2),<sup>11</sup> bound to amphiphilic solid supports was prepared on poly(ethylene glycol)–polystyrene graft copolymer (PEG–PS) resin, ArgoGel NH<sub>2</sub>, which has been well-documented to exhibit good swelling properties in water (Scheme 1).<sup>12</sup> The Pd–PEP complex 2 catalyzed the hydroxycarbonylation of aryl iodides 3 in water under very mild reaction conditions to give benzoic acids 4 (Scheme 2). A mixture of iodobenzene (0.4 mmol) and potassium carbonate (3.6 mmol) in 2 mL of water was agitated vigorously with shaking on a wrist-action shaker under an atmospheric pressure of carbon monoxide in the presence of 3 mol % palladium of the Pd–PEP at 25 °C for 20 h. A small amount of metal leaching was observed during the reaction. The reaction mixture was filtered, and the resin was rinsed twice with a small amount of aqueous sodium bicarbonate. The combined filtrate was acidified (pH ≈ 1) with concentrated hydrochloric acid to make a precipitate of benzoic acid and extracted with ether. Concentration of the extract gave 97% yield of benzoic acid (4a), and the purity of 4a was assessed by

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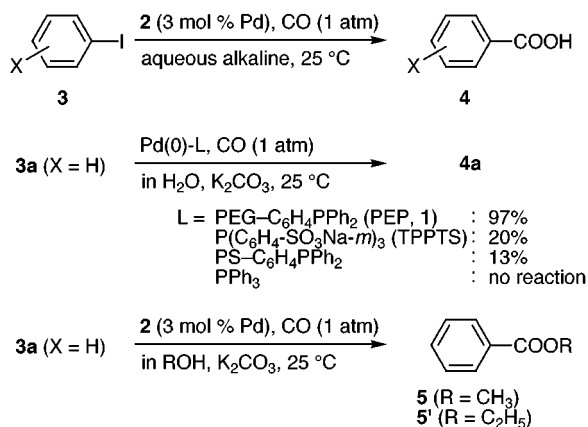
(11) Gel-phase <sup>13</sup>C and <sup>31</sup>P NMR studies on Pd–PEP (2) have been reported<sup>2c</sup> in which an η<sup>3</sup>-C<sub>3</sub>H<sub>5</sub> group and a phosphorus atom coordinated to palladium were observed, respectively. In addition, elemental analysis and ICP–atomic emission spectroscopy of 2 showed the ratio of palladium, phosphorus, and chlorine to be 1.1/1.0/1.0 (Pd/P/Cl). These results demonstrate that the structure of the palladium complex moiety at the terminus of PEG chain is PdCl(η<sup>3</sup>-C<sub>3</sub>H<sub>5</sub>)(Ph<sub>2</sub>PC<sub>6</sub>H<sub>4</sub>-resin).

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**Table 1. Hydroxycarbonylation of Aryl Halides in Water Catalyzed by Pd-PEP (2)<sup>a</sup>**

entry	aryl halide	base	product	yield (%) <sup>b</sup>	entry	aryl halide	base	product	yield (%) <sup>b</sup>
1	<b>3a</b> (X = H)	K <sub>2</sub> CO <sub>3</sub>	<b>4a</b>	97	10 <sup>c</sup>	<b>3g</b> (X = 4-Br)	K <sub>2</sub> CO <sub>3</sub>	<b>4g</b>	100
2	<b>3b</b> (X = 2-CH <sub>3</sub> )	K <sub>2</sub> CO <sub>3</sub>	<b>4b</b>	55	11 <sup>c</sup>	<b>3h</b> (X = 4-NO <sub>2</sub> )	K <sub>2</sub> CO <sub>3</sub>	<b>4h</b>	100
3	<b>3b</b> (X = 2-CH <sub>3</sub> )	KOH	<b>4b</b>	96	12	<b>3i</b> (X = 4-CF <sub>3</sub> )	K <sub>2</sub> CO <sub>3</sub>	<b>4i</b>	96
4	<b>3c</b> (X = 3-CH <sub>3</sub> )	K <sub>2</sub> CO <sub>3</sub>	<b>4c</b>	99	13	<b>3j</b> (X = 3-COOEt)	K <sub>2</sub> CO <sub>3</sub>	<b>4j</b>	93
5 <sup>c</sup>	<b>3d</b> (X = 4-CH <sub>3</sub> )	K <sub>2</sub> CO <sub>3</sub>	<b>4d</b>	55	14 <sup>c</sup>	<b>3k</b> (X = 3-I)	KOH	<b>6</b>	92 <sup>e</sup>
6 <sup>c</sup>	<b>3d</b> (X = 4-CH <sub>3</sub> )	KOH	<b>4d</b>	100	15 <sup>c</sup>	<b>3l</b> (X = 4-I)	KOH	<b>7</b>	93
7 <sup>c</sup>	<b>3e</b> (X = 4-OCH <sub>3</sub> )	K <sub>2</sub> CO <sub>3</sub>	<b>4e</b>	53	16	<b>8</b>	K <sub>2</sub> CO <sub>3</sub>	<b>9</b>	78
8 <sup>c</sup>	<b>3e</b> (X = 4-OCH <sub>3</sub> )	KOH	<b>4e</b>	96	17 <sup>f</sup>	bromobenzene	KOH	<b>4a</b>	45
9 <sup>c,d</sup>	<b>3f</b> (X = 4-Cl)	K <sub>2</sub> CO <sub>3</sub>	<b>4f</b>	99					

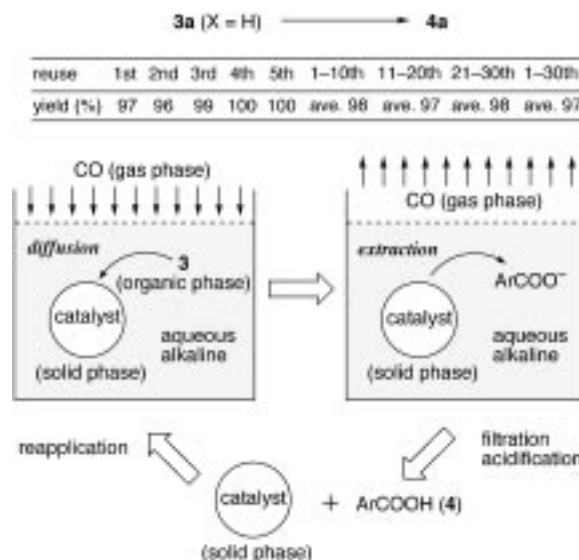
<sup>a</sup> All reactions were carried out with shaking in water under carbon monoxide (1 atm) at 25 °C for 12–20 h, unless otherwise noted: aryl halide (0.4 mmol), H<sub>2</sub>O (2.0 mL), K<sub>2</sub>CO<sub>3</sub> (3.6 mmol), **2** (3 mol % Pd). <sup>b</sup> Isolated yield. Purities of all products were assessed by <sup>1</sup>H NMR study (400 MHz) to be >98%. <sup>c</sup> 200 μL of benzene was used as a cosolvent. <sup>d</sup> Reaction for 40 h. <sup>e</sup> A mixture with a small amount of 3-iodobenzoic acid. <sup>f</sup> 10 mol % palladium of PEP-Pd catalyst was used.

**Scheme 2**

<sup>1</sup>H NMR study (400 MHz) to be >98%. The carbonylation using water-soluble phosphine ligand TPPTS<sup>13</sup> and polystyrene-supported triphenylphosphine showed much lower catalytic activity under the reaction conditions giving 20% and 13% yield of **4a**, respectively. A number of commercially available phosphine ligands (e.g., triphenylphosphine) are unsuitable for use in water owing to their insolubility. The resin-supported complex **2** also catalyzed the carbonylation of iodobenzene in methanol or ethanol under the same conditions to give an 81% yield of methyl or ethyl benzoate (**5** or **5'**).

The hydroxycarbonylation is comprised of four phases, gas, solid, organic, and aqueous phases. By using this four-phase protocol, carbon monoxide (gas phase) and the starting halide (organic phase) should diffuse into the catalyst resin (solid phase) during the reaction, and the resulting carboxylic acid is immediately extracted with alkaline solution (aqueous phase). They are readily separated each other, and subsequent reapplication of the catalyst is made facile (Scheme 3). Thus, after the workup, the recovered catalyst resin was subjected to a second series of the reaction to give 96% yield of **4a** under otherwise the same reaction conditions. The chemical yield observed in the 30 continuous runs ranged between 94 and 100%, the average being 97% yield (Scheme 3).

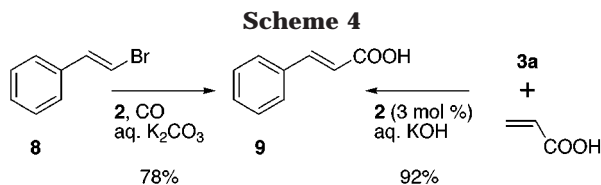
Table 1 summarizes the representative results of the hydroxycarbonylation. The hydroxycarbonylation of *m*-tolyl iodide (**3c**), 4-chlorophenyl iodide (**3f**), 4-bromophenyl iodide (**3g**), 4-nitrophenyl iodide (**3h**), 4-(trifluoromethyl)phenyl iodide (**3i**), and *m*-ethyl iodobenzoate (**3j**) gave **4c,f–j** in 96–100% yield, respectively (entries

**Scheme 3**

4, 9–13). *o*-Tolyl iodide (**3b**), *p*-tolyl iodide (**3d**), and *p*-anisyl iodide (**3e**) showed a little lower reactivity under the reaction conditions, presumably because of steric bulkiness and/or electron-donating character of the substituents. A significant improvement of the catalytic activity of Pd-PEP was observed in the carbonylation of **3b,d,e** when potassium hydroxide was used as a base (entries 2, 3, 5–8). Thus, for example, the hydroxycarbonylation of **3e** in aqueous potassium hydroxide gave **4e** in 96% under otherwise the same reaction conditions, while that in aqueous potassium carbonate gave only 53% yield of the desired acid. The hydroxycarbonylation took place successively on the two iodides of 1,3- and 1,4-diodobenzenes (**3k,l**), which gave quantitative yields of isophthalic acid **6** and terephthalic acid **7**, respectively (entries 14 and 15). All these products were obtained without chromatographical purification, the workup consisting of only filtration and extraction.

This simple protocol for the preparation of carboxylic acids was also successfully applied to alkenyl and aryl bromides under the same reaction conditions. Bromostyrene **8** underwent hydroxycarbonylation to give a 78% yield of cinnamic acid (**9**) (Scheme 4) (Table 1, entry 16). It is noteworthy that bromobenzene undergoes palladium-catalyzed hydroxycarbonylation at 25 °C in water (entry 17), though the oxidative addition of aryl bromides to palladium(0) species requires 80 °C or higher reaction temperature in general.<sup>14</sup> A mixture of bromobenzene and 10 mol % palladium of resin-supported complex **2** in 2.0

(13) TPPTS = triphenylphosphinetrisulfonate sodium salt. (a) Kuntz, E. G. German Patent No. 2627354, 1976. (b) Sinou, D. *Bull. Soc. Chim. Fr.* **1987**, 3, 480. See also refs 7a–g.



mL of 1.8 M solution of potassium hydroxide was agitated under an atmospheric pressure of carbon monoxide to give 45% yield of benzoic acid.

Pd-PEP was an effective catalyst for the Heck reaction. Thus, the preparation of cinnamic acid **9** was examined by the Heck reaction of iodobenzene with acrylic acid (5.0 equiv) in aqueous potassium carbonate in the presence of 3 mol % palladium of Pd-PEP **2** to give 92% yield of **9** (Scheme 4).

### Experimental Section

**General Methods.** The amphiphilic resin-supported palladium-triarylphosphine **2** was prepared on commercially available poly(ethylene glycol)-polystyrene graft copolymer beads, ArgoGel NH<sub>2</sub> (Argonaut Technologies, CA), according to the reported procedure. All starting substrates **3a**-**1**, **8**, and bromobenzene are commercially available. TPPTS and polystyrene-supported triphenylphosphine were purchased from Aldrich Chemical Inc. Water was deionized and distilled prior to each catalytic reaction. The agitation of the reaction mixture was

(14) For a recent review, see: J. Tsuji, *Palladium Reagents and Catalysts*, John Wiley and Sons: Chichester, U.K., 1995.

performed on a wrist-action shaker (Burrel Scientific, Inc.). All products shown in Table 1 are known compounds.

**General Procedure for Hydroxycarbonylation of Aryl Iodide Catalyzed by Pd-PEP.** A Merrifield vessel was charged with aryl iodide (**3**) (0.4 mmol), potassium carbonate (498 mg, 3.6 mmol), Pd-PEP (**2**) (29 mg, 12 μmol of Pd), and 2.0 mL of water. The reaction mixture was shaken on a wrist-action shaker under an atmospheric pressure of carbon monoxide at 25 °C for 12 h. The reaction mixture was filtered, and the resin was rinsed with saturated NaHCO<sub>3</sub> (3 × 1.5 mL). The combined filtrate was acidified (pH ≈ 1) with concentrated hydrochloric acid and extracted with ether. The extract was dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure to give benzoic acid (**4**).

**Heck Reaction of Iodobenzene (2a) with Acrylic Acid.** A Merrifield vessel was charged with **3a** (41 mg, 0.2 mmol), acrylic acid (144 mg, 2.0 mmol), potassium carbonate (124 mg, 0.9 mmol), **2** (29 mg, 12 μmol of Pd), and 500 μL of water. The reaction mixture was shaken on a wrist-action shaker at 25 °C for 20 h. The reaction mixture was filtered, and the resin was rinsed with saturated NaHCO<sub>3</sub> (3 × 1.5 mL). The combined filtrate was washed with chloroform, acidified (pH ≈ 1) with concentrated hydrochloric acid, and extracted with ether. The extract was dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure to give 55 mg of cinnamic acid (**7**) (92%).

**Acknowledgment.** The authors are grateful to Dr. John A. Porco, Jr., at Argonaut Technologies for provision of the PEG-PS resin. This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education of Japan. Y.U. thanks the Shorai Foundation for Science and Technology and the ASPRONC Foundation for partial financial support of this work.

JO990631F