

# A Solid-Phase Self-Organized Catalyst of Nanopalladium with Main-Chain Viologen Polymers: $\alpha$ -Alkylation of Ketones with Primary Alcohols

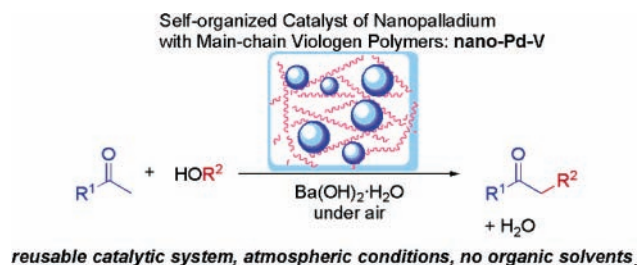
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## ABSTRACT



A novel solid-phase self-organized catalyst of palladium nanoparticles was prepared from PdCl<sub>2</sub> with main-chain viologen polymers via complexation and reduction. This insoluble nanocatalyst nano-Pd-V efficiently promoted  $\alpha$ -alkylation of ketones with primary alcohols in the presence of Ba(OH)<sub>2</sub>·H<sub>2</sub>O under atmospheric conditions without organic solvents. The nano-Pd-V catalyst was reused without loss of catalytic activity.

The development of solid-phase metal–nanoparticle catalysts is an important topic for organic synthesis and for chemical and pharmaceutical processes.<sup>1</sup> Because they can be recovered easily by simple operations thereby preventing contamination of products by toxic metals, nanoparticle catalysts are considered promising candidates for useful, safe, and reusable catalysts. Although immobilized nanoparticle catalysts have been reported, they are generally deactivated during their reuse owing to leaching of the metal species from their supports and/or aggregation of the metal–nanoparticles. Recently, we<sup>2</sup> and others<sup>3</sup> have been involved in developing improved nanoparticle catalysts to overcome these problems.

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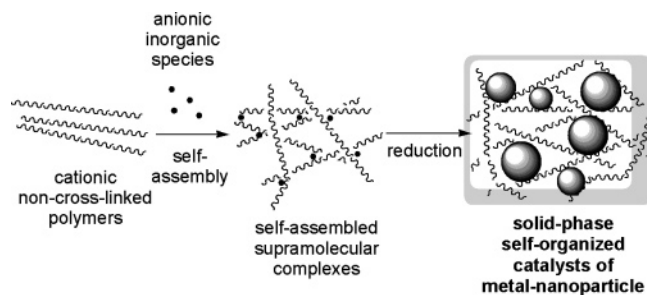
We have developed a new strategy for the preparation of highly active and reusable solid-phase metal catalysts via self-assembly of inorganic materials with non-cross-linked polymeric ligands.<sup>4</sup> Thus, complexation of inorganic materials and non-cross-linked polymeric ligands gives networked, supramolecular and insoluble complexes in which the polymeric ligands are cross-linked by the inorganic species.

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Using this methodology, we prepared insoluble catalysts and applied them to heterogeneous organic synthetic reactions. These catalysts showed outstanding stability and reusability in reaction media such as water and aqueous or anhydrous organic solvents.

We planned to expand this methodology to the preparation of solid-phase metal–nanoparticles via self-organization of inorganic materials and non-cross-linked polymers. Anionic inorganic materials self-assembled with non-cross-linked cationic polymers to give insoluble supramolecular complexes, which were converted by reduction into insoluble self-organized metal–nanoparticles having the polymers as matrixes (Scheme 1). These metal–nanoparticles should be

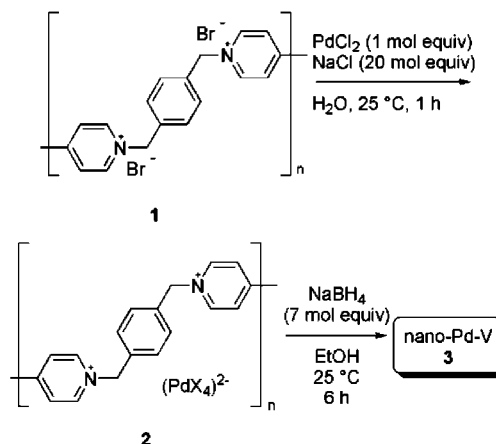
**Scheme 1.** Working Hypothesis for the Preparation of Solid-Phase Metal–Nanoparticles via Self-Organization of Inorganic Materials and Non-cross-linked Polymers



stabilized by matrix polymers to prevent leaching, aggregation, and deactivation, so that they can become active and recyclable solid-phase catalysts. In this Letter, we would like to report the development of an environmentally benign solid-phase polymeric catalyst of nanopalladium particles (nano-Pd–V) and its application to the  $\alpha$ -alkylation of ketones with primary alcohols. It should be emphasized that this novel catalyst was reused in the absence of organic solvents under atmospheric conditions without any loss of catalytic activity.

The novel nanopalladium catalyst nano-Pd–V **3** was prepared as shown in Scheme 2. When PdCl<sub>2</sub> and 20 mol equiv of NaCl in water was added to an aqueous solution of the main-chain viologen polymer **1**<sup>5</sup> at 25 °C, the components self-assembled to give the insoluble palladium complex **2** as an orange powder. Compound **2** was reduced by NaBH<sub>4</sub>

**Scheme 2.** Preparation of Solid-Phase Metal–Nanoparticles Nano-Pd–V **3** via Self-Organization of PdCl<sub>2</sub> and Non-cross-linked Polymer **1**



at 25 °C in EtOH to afford the black polymeric palladium nanoparticles nano-Pd–V **3**, which were insoluble in water, ethanol, ethyl acetate, dichloromethane, toluene, and hexane.

To elucidate the structure of **3**, several spectroscopic measurements were carried out. The morphology of **3** was evaluated by scanning electron microscopic (SEM) observation, which confirmed **3** to be a macroporous material (Figure 1, top and Figure S-1, Supporting Information). The images revealed a spongelike structure with a disordered arrangement of interconnected pores in the size range of approximately 1  $\mu$ m. An energy dispersive spectrum (EDS) collected in the SEM showed the presence of palladium and bromide with a trace amount of chloride in **3**. Transmission electron microscopy (TEM) and scanning transmission electron microscopy-energy dispersive spectroscopy (STEM/EDS) analysis proved the existence of palladium nanoparticles in **3** (Figure S-2, Supporting Information). TEM analysis showed that the palladium particles have a mean diameter of 2 nm with a narrow size distribution (Figure 1, bottom, and Figure S-2, Supporting Information).

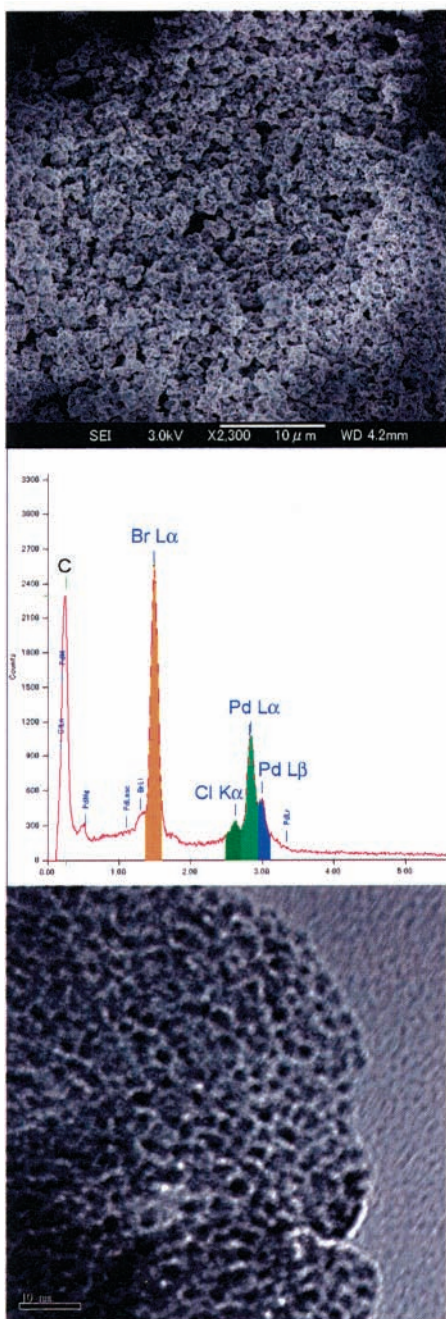
To demonstrate the potency of nano-Pd–V **3** as a reusable heterogeneous catalyst for organic synthesis,  $\alpha$ -alkylation of ketones with primary alcohols was selected because this reaction system is environmentally benign: it does not use harmful alkyl halides as electrophiles, and the resulting products are only the desired  $\alpha$ -alkylated ketones and water.<sup>6,7</sup> In 2004, Kaneda et al. reported the first heterogeneous  $\alpha$ -alkylation of ketones with alcohols at 180 °C in toluene catalyzed by Ru-hydroxalcite.<sup>7a</sup> Recently, Cho re-

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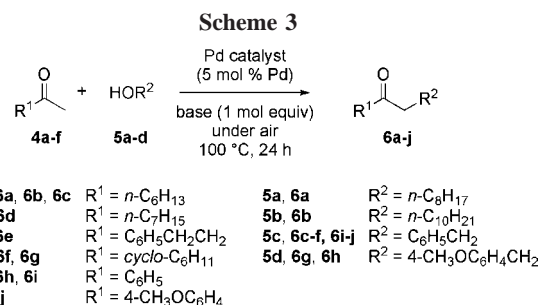
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**Figure 1.** SEM (top), TEM (bottom) images, and EDS analysis (center) of nano-Pd-V **3** (bar length: SEM 10  $\mu\text{m}$ ; TEM 10 nm).

ported Pd/C-catalyzed  $\alpha$ -alkylation of ketones with alcohols at 100  $^{\circ}\text{C}$  in dioxane in the presence of 1-decene as an additive.<sup>7b</sup> Park et al. reported the first reusable catalytic system of  $\alpha$ -alkylation of ketones with alcohols catalyzed by Pd/AIO(OH) catalyzed at 80 or 110  $^{\circ}\text{C}$  in toluene.<sup>7c</sup> We decided to use this nanoparticle catalyst under atmospheric conditions without organic solvents to comply with the goals of green chemistry. As shown in Scheme 3 and Table 1, reaction of 2-octanone (**4a**) with 2 mol equiv of 1-octanol (**5a**) was performed in the presence of 5 mol % palladium of a catalyst and 1 mol equiv of barium hydroxide octahy-



**Table 1.**  $\alpha$ -Alkylation of **4a** with **5a** in the Presence of Catalyst and Barium Hydroxide<sup>a</sup>

entry	catalyst/base	additive	<b>6a</b> : yield (%) <sup>b</sup>
1	<b>3</b> /Ba(OH) <sub>2</sub> ·8H <sub>2</sub> O		59
2	<b>1</b> /Ba(OH) <sub>2</sub> ·8H <sub>2</sub> O		no reaction
3	Pd-C/Ba(OH) <sub>2</sub> ·8H <sub>2</sub> O		4
4	ARP-Pd/Ba(OH) <sub>2</sub> ·8H <sub>2</sub> O		14
5	PdAS/Ba(OH) <sub>2</sub> ·8H <sub>2</sub> O		24
6	<b>3</b> /Ba(OH) <sub>2</sub> ·H <sub>2</sub> O	H <sub>2</sub> O (7 mol equiv)	83
7	<b>2</b> /Ba(OH) <sub>2</sub> ·H <sub>2</sub> O	H <sub>2</sub> O (7 mol equiv)	12

<sup>a</sup> All the reactions were carried out in the presence of 5 mol % palladium of the catalyst and a base (1 mol equiv) at 100  $^{\circ}\text{C}$  for 24 h under atmospheric conditions. <sup>b</sup> GC yield.

drate at 100  $^{\circ}\text{C}$  for 24 h. The dehydrative  $\alpha$ -alkylation was found to proceed with nano-Pd-V **3** to provide 59% yield of the desired product 7-hexadecanone (**6a**) (entry 1). In a control experiment, it was confirmed that the viologen polymer **1** used as a redox material<sup>5b</sup> had no catalytic activity (entry 2), and that the heterogeneous catalysts Pd/C, ARP-Pd,<sup>2</sup> and PdAS<sup>4d,g</sup> promoted the reaction sluggishly (entries 3–5). It was gratifying to see that, after thorough optimization, the combination of nano-Pd-V **3**, Ba(OH)<sub>2</sub>·H<sub>2</sub>O, and 7 mol equiv of water is essential to construct an efficient catalyst system with much higher activity. Thus, when a mixture of **4a**, **5a**, Ba(OH)<sub>2</sub>·H<sub>2</sub>O, and 7 mol equiv of H<sub>2</sub>O was stirred at 100  $^{\circ}\text{C}$  for 24 h in the presence of 5 mol % palladium of nano-Pd-V catalyst **3**, the  $\alpha$ -alkylation took place under atmospheric conditions to give 83% yield of **6a** (entry 6). The precursor **2** had low catalytic activity to give **6a** in 12% yield (entry 7).<sup>8</sup>

By using the catalyst system identified above, the reaction of a variety of ketones with primary alcohols was investigated as shown in Table 2. The following reactions were performed under the same conditions as that for entry 6, Table 1, and the  $\alpha$ -alkylated products **6b–j** were isolated via purification by column chromatography. The  $\alpha$ -alkylation of 2-octanone (**4a**) with 1-octanol (**5a**) and 1-decanol (**5b**) proceeded regioselectively to afford 7-hexadecanone (**6a**) and 7-octa-

(8) The working hypothesis of our catalytic reaction is unclear although the  $\alpha$ -alkylation with alcohols should consist of the hydrogen transfer process catalyzed by metal species and the aldol condensation promoted by a base (see refs 6 and 7). A reviewer pointed out that the metal hydride intermediates are prone to react with molecular oxygen. However, our catalytic system worked under the aerobic conditions, so that other mechanisms might participate in this reaction. We are thankful to the reviewer for the kind and proper suggestion.



**Table 2.**  $\alpha$ -Alkylation of Ketones **4** with Primary Alcohols **5** Promoted by Nano-Pd–V **3** and Ba(OH)<sub>2</sub>·H<sub>2</sub>O<sup>a</sup>

entry	ketones <b>4</b> (R <sup>1</sup> )	primary alcohols <b>5</b> (R <sup>2</sup> )	<b>6</b> : yield (%) <sup>b</sup>
1	<b>4a</b> (R <sup>1</sup> = <i>n</i> -C <sub>6</sub> H <sub>13</sub> )	<b>5a</b> (R <sup>2</sup> = <i>n</i> -C <sub>8</sub> H <sub>17</sub> )	<b>6a</b> : 83 <sup>f</sup>
2 <sup>c</sup>	<b>4a</b>	<b>5a</b>	<b>6a</b> : 90 <sup>f</sup>
3 <sup>d</sup>	<b>4a</b>	<b>5a</b>	<b>6a</b> : 91 <sup>f</sup>
4	<b>4a</b>	<b>5b</b> (R <sup>2</sup> = <i>n</i> -C <sub>10</sub> H <sub>21</sub> )	<b>6b</b> : 84
5	<b>4a</b>	<b>5c</b> (R <sup>2</sup> = C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> )	<b>6c</b> : 91
6	<b>4b</b> (R <sup>1</sup> = <i>n</i> -C <sub>7</sub> H <sub>15</sub> )	<b>5c</b>	<b>6d</b> : 84
7	<b>4c</b> (R <sup>1</sup> = C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> CH <sub>2</sub> )	<b>5c</b>	<b>6e</b> : 93
8	<b>4d</b> (R <sup>1</sup> = <i>c</i> -C <sub>6</sub> H <sub>11</sub> )	<b>5c</b>	<b>6f</b> : 81
9	<b>4d</b>	<b>5d</b> (R <sup>2</sup> = 4-CH <sub>3</sub> O-C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> )	<b>6g</b> : 83
10	<b>4e</b> (R <sup>1</sup> = C <sub>6</sub> H <sub>5</sub> )	<b>5d</b>	<b>6h</b> : 90
11 <sup>e</sup>	<b>4e</b>	<b>5c</b>	<b>6i</b> : 82
12	<b>4f</b> (R <sup>1</sup> = 4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> )	<b>5c</b>	<b>6j</b> : 95

<sup>a</sup> All the reactions were carried out in the presence of 5 mol % palladium of nano-Pd–V catalyst and 1 mol equiv of Ba(OH)<sub>2</sub>·H<sub>2</sub>O at 100 °C for 24 h under atmospheric conditions. **4/5** = 1.0/2.0. H<sub>2</sub>O (7 mol equiv) was added except for entries 2 and 3. <sup>b</sup> Isolated yields unless otherwise noted. <sup>c</sup> Second use of **3**. <sup>d</sup> Third use of **3**. <sup>e</sup> The reaction was performed at 80 °C for 12 h. <sup>f</sup> GC yield.

decanone (**6b**) in 83% and 84% yields, respectively (entries 1 and 4). The reaction of the aliphatic ketones **4a–d** with benzyl alcohol (**5c**) gave the corresponding  $\alpha$ -alkylated ketones **6c–f** in 81–93% yields (entries 5–8). When **4d** and 4-methoxybenzyl alcohol (**5d**) were used, 1-cyclohexyl-3-(4-methoxyphenyl)-1-propanone (**6g**) was obtained in 83% yield (entry 9). The catalytic system was applied to the coupling of aromatic ketones with benzylic alcohols (entries 10–12). Thus, the alkylation of acetophenone (**4e**) with **5d** proceeded smoothly to give 3-(4-methoxyphenyl)-1-phenyl-1-propanone (**6h**) in 90% yield. The ketone **4e** and the solid ketone 4-methoxyacetophenone (**4f**) were alkylated with **5c** to afford 1,3-diphenyl-1-propanone (**6i**) and 1-(4-methoxyphenyl)-3-phenyl-1-propanone (**6j**) in yields of 82% (at 80 °C for 12 h) and 95%, respectively. Although  $\alpha$ -alkylation of ketones generally suffers from poor regioselectivity, it was

found that the reactions in Table 2 gave no regioisomers. Recyclability of the nano-Pd–V catalyst **3** was examined for the subsequent reaction of **4a** and **5a**. Thus, after the first reaction, which gave 83% yield of **6a** (Table 2, entry 1), the catalyst polymer was recovered by centrifugation and successively subjected to a second and third series of reactions under the same conditions to afford 90% and 91% yields of **6a** (Table 2, entries 2 and 3).

In conclusion, we have developed a novel polymeric catalyst nano-Pd–V **3** of palladium nanoparticles with viologen polymers via the self-organization process. The  $\alpha$ -alkylation of a variety of ketones with primary alcohols using the catalyst **3** afforded the desired products in high yields. This catalyst was applied to reactions under atmospheric conditions without organic solvents. The catalyst **3** could be reused while still retaining its activity. Since the reaction system itself exhibited great potential and was promoted efficiently, applications to other reactions catalyzed by the nano-Pd–V system are currently under study in our labs.

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**Supporting Information Available:** Experimental details plus SEM and TEM and STEM/EDS of **3**, CP-MAS <sup>13</sup>C NMR spectra of **2** and nano-Pd–V **3**, and <sup>1</sup>H NMR and <sup>13</sup>C NMR of **6g**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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