

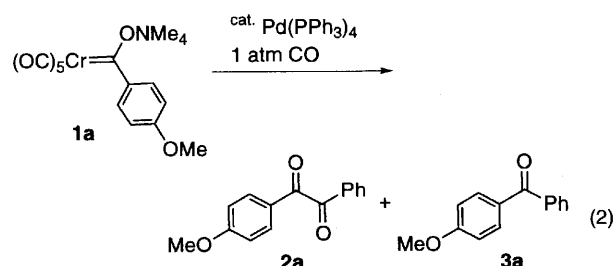
## Palladium-Catalyzed Synthesis of $\alpha$ -Diketones from Acylchromates, Iodoarenes, and Carbon Monoxide

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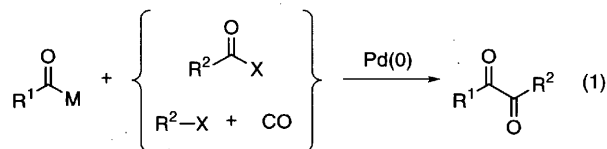
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(Received October 26, 1999, CL-990914)

A three-component coupling of tetramethylammonium pentacarbonyl(acyl)chromates, aryl iodides, and CO takes place under CO atmosphere in the presence of a catalytic amount of Pd(PPh<sub>3</sub>)<sub>4</sub> to afford the corresponding unsymmetrical  $\alpha$ -diketones in good yield. By performing the reaction under argon atmosphere, unsymmetrical ketones are prepared instead of  $\alpha$ -diketones.



Palladium-catalyzed ketone synthesis has attracted much attention, and a variety of ketones have been synthesized starting from organometallic compounds and acyl halides or alkyl halides with CO under mild reaction conditions.<sup>1</sup> In contrast to the synthesis of ketones,  $\alpha$ -diketones are hard to be prepared by the palladium-catalyzed process because good acyl donors, usually acylmetals, are necessary instead of alkylmetals in order to avoid difficult double insertion of CO (Eq 1).<sup>2</sup>



Although acyltins are one of the representative acylmetal compounds, they are unstable and give  $\alpha$ -diketones in low yield in the Pd-catalyzed coupling with acyl halides.<sup>3</sup>  $\alpha$ -Alkoxyvinyltins are used as acylmetal equivalents and react with alkenyl halides under the atmospheric CO. This process is suitable for the preparation of methyl  $\alpha$ -diketones (MeCOCOR) but cannot be applied to the synthesis of aromatic  $\alpha$ -diketones.<sup>4</sup> Recently the reaction of acylzirconium and acyl halides has been reported, though giving  $\alpha$ -diketones in unsatisfactory yield.<sup>5</sup>

In the previous paper, we demonstrated that acylchromates **1** can be employed as good acyl donors for the Pd-catalyzed acylation of allylic halides.<sup>6</sup> Based on this finding, the preparation of unsymmetrical  $\alpha$ -diketones from iodoarenes and carbon monoxide was examined by using the acylchromates **1**.

Tetramethylammonium pentacarbonyl(4-methoxybenzoyl)chromate **1a** and iodobenzene were treated with a catalytic amount of Pd(PPh<sub>3</sub>)<sub>4</sub> under 1 atm CO (Eq. 2, Table 1). When CH<sub>2</sub>Cl<sub>2</sub> or THF was used as a solvent, monoketone **3a** was obtained along with the desired  $\alpha$ -diketone **2a** (entries 3 and 4). The formation of the monoketone **3a** was suppressed in toluene and the  $\alpha$ -diketone **2a** was obtained as a sole product (entry 5). Excess amounts of PhI were needed in order to obtain the  $\alpha$ -diketone **2a** in good yield at room temperature (entries 6-8), whereas **2a** can be synthesized in 74% yield (1 mol% Pd) or 84% yield (2 mol% Pd) by employing only 1.5 molar amounts of PhI when the reaction was performed at 50 °C (entries 9 and 10).

Table 1. Reaction conditions for **2a** preparation

Entry	Solvent	PhI / equiv.	Pd / mol%	Temp. / °C	Time / h	Yield / %	
						<b>2a</b>	<b>3a</b>
1	DMF	1.5	2	rt	19	4	4
2	CH <sub>3</sub> CN	1.5	2	rt	19	6	5
3	CH <sub>2</sub> Cl <sub>2</sub>	1.5	2	rt	19	28	47
4	THF	1.5	2	rt	19	40	46
5	Toluene	1.3	1	rt	21	16	0
6	Toluene	5.0	1	rt	19	54	0
7	Toluene	5.0	1	rt	62	67	0
8	Toluene	10	1	rt	19	82	0
9	Toluene	1.5	1	50	10	74	0
10	Toluene	1.5	2	50	10	84	0

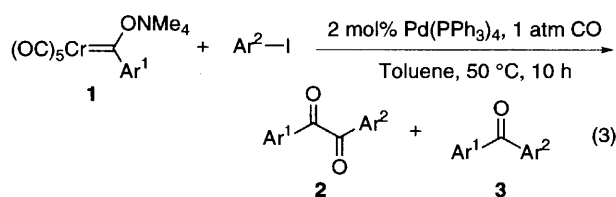
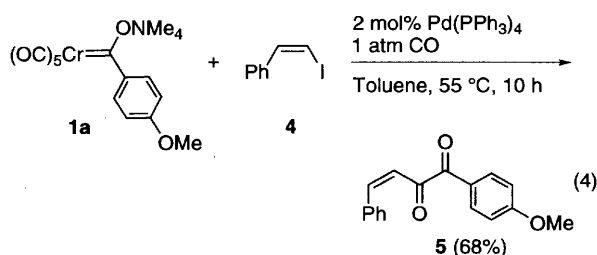


Table 2. Preparation of unsymmetrical  $\alpha$ -diketones

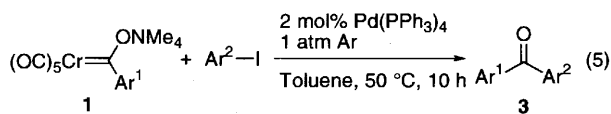
Entry	Ar <sup>1</sup>	Ar <sup>2</sup>	Yield / %	
			<b>2</b>	<b>3</b>
1	4-MeOC <sub>6</sub> H <sub>4</sub>	C <sub>6</sub> H <sub>5</sub>	84	0
2	4-MeC <sub>6</sub> H <sub>4</sub>	C <sub>6</sub> H <sub>5</sub>	69	0
3	4-CF <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	C <sub>6</sub> H <sub>5</sub>	59	31
4	4-MeOC <sub>6</sub> H <sub>4</sub>	4-MeOC <sub>6</sub> H <sub>4</sub>	83	0
5	4-MeOC <sub>6</sub> H <sub>4</sub>	4-HOC <sub>6</sub> H <sub>4</sub>	70	0
6	4-MeOC <sub>6</sub> H <sub>4</sub>	4-H <sub>2</sub> NC <sub>6</sub> H <sub>4</sub>	71	0
7	4-MeOC <sub>6</sub> H <sub>4</sub>	4-MeCOC <sub>6</sub> H <sub>4</sub>	67	21

The reactions of various acylchromates **1** and iodoarenes were carried out under the conditions listed in entry 10 of Table 1, and the results are shown in Table 2. When an electron donating substituent was introduced on aryl group of the chromates ( $\text{Ar}^1$ ), the corresponding  $\alpha$ -diketone **2** was produced in good yield, while introduction of electron withdrawing group such as  $\text{CF}_3$  diminished the yield of **2** and the mono-ketone **3** was also obtained (entries 1-3). Substituent effect on the iodoarene ( $\text{Ar}^2$ ) showed a similar inclination (entries 4-7). That is, the  $\alpha$ -diketones **2** were generally obtained selectively, whereas the reaction with 4-iodoacetophenone gave both of **2** and **3**.

Iodoalkenes are also available for this reaction as well as iodoarenes. For example, *Z*-isomer (*Z* : *E* = >98 : <2) of 1-iodo-2-phenylethene<sup>8</sup> and the chromate **1a** reacted under the above conditions to give *Z*-diketone **5** (*Z* : *E* = >98 : <2) stereospecifically in 68% yield (Eq. 4).



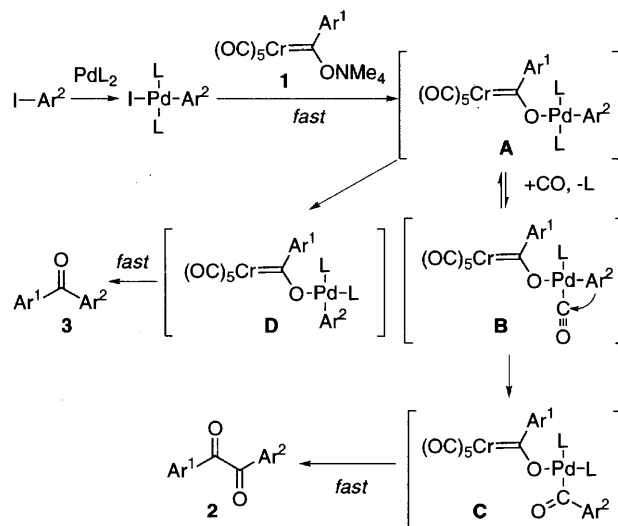
When the reaction of the chromates **1** and iodoarenes was conducted under argon atmosphere in place of CO, the unsymmetrical ketones **3** were obtained without forming the  $\alpha$ -diketone **2** (Table 3).<sup>9</sup>



**Table 3.** Preparation of unsymmetrical ketones

$\text{Ar}^1$	$\text{Ar}^2$	Yield / %
4-MeOC <sub>6</sub> H <sub>4</sub>	C <sub>6</sub> H <sub>5</sub>	79
4-MeOC <sub>6</sub> H <sub>4</sub>	4-MeCOC <sub>6</sub> H <sub>4</sub>	82
4-CF <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	4-MeCOC <sub>6</sub> H <sub>4</sub>	78

A possible mechanism is shown in Scheme 1. The reaction of acylchromate with arylpalladium iodide seems to be very facile to form *trans*-bimetallic complex **A**. If aryl ( $\text{Ar}^2$ ) migration to CO proceeds fast from the complex **B**, which is generated by the ligand exchange from phosphine to CO, *cis*-diacyl-like complex **C** might be generated. From the complex **C**, reductive elimination proceeds smoothly to give the  $\alpha$ -diketone **2**.<sup>10</sup> Both substituent on the aryl groups of acylchromate ( $\text{Ar}^1$ ) and iodoarene ( $\text{Ar}^2$ ) might influence the migration step. The substituent effects on  $\text{Ar}^2$  can be explained by decreasing the rate of  $\text{Ar}^2$  group migration to CO, when electron withdrawing group is introduced.<sup>12</sup> Although substituent effects on  $\text{Ar}^1$  are still speculative, migration might be accelerated by the *trans*  $\sigma$ -donor ligand by some kind of *trans* effect.<sup>13</sup> Acylchromate unit plays a role as a  $\sigma$ -donor ligand and the introduction of electron withdrawing group such as  $\text{CF}_3$  diminishes the  $\sigma$ -donor character.



**Scheme 1.** A possible mechanism.

This work was partially supported by a Grant-in-Aid for Scientific Research on Priority Area No.11119211 from the Ministry of Education, Science, Sports and Culture of Japanese Government.

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- General procedure. A mixture of the chromium complex **1** (0.67 mmol), iodoarene (1 mmol), and  $\text{Pd}(\text{PPh}_3)_4$  (0.013 mmol) in toluene (15 mL) are stirred at 50 °C for 10 h under CO atmosphere. After the reaction mixture is diluted with  $\text{Et}_2\text{O}$ , the solution is passed through Celite pad and the solvent is evaporated. The products **2** and **3** are separated by silica gel chromatography.
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