

# Palladium-catalyzed coupling reaction of acylzirconocene chlorides with hypervalent iodonium salts: synthesis of aryl-substituted ketones

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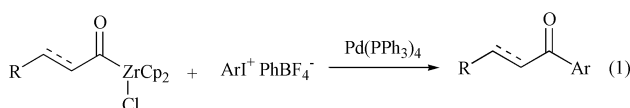
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**The palladium-catalyzed acylation reaction of alkenoyl- and alkanoylzirconocene chlorides with hypervalent iodonium salts afforded the acylated aromatic compounds under mild conditions.**

Alkenyl- and alkyl substituted acylzirconocene dichlorides, which are stable and readily available complexes through hydrozirconation of alkynes and alkenes with zirconocene hydrochloride ( $\text{Cp}_2\text{ZrHCl}$ , Schwartz reagent),<sup>1</sup> with subsequent insertion of carbon monoxide<sup>2</sup> are versatile intermediates as “unmasked” acyl anions for the preparation of aldehydes, carboxylic acids, ketols, and alkylketones as developed by Hanzawa and Taguchi and their co-workers.<sup>3</sup> Alkyl-substituted acylzirconium chloride as an “unmasked” acyl anion was coupled with iodobenzene and utilizing the palladium-catalyst under harsh conditions at 100 °C for 20 h gave alkyl phenyl ketone in a low (32%) yield. It is necessary to conduct this coupling under milder conditions and to obtain a better yield. In connection with our program to utilize hypervalent iodonium salts in cross-coupling reactions,<sup>4</sup> we have found that hypervalent iodonium salts are excellent electrophiles in the palladium-catalyzed coupling reaction of alkenyl- and alkyl-substituted acylzirconocene chlorides, to form aryl-substituted alkyl and vinyl ketones under mild conditions (Scheme 1).



Scheme 1

The results of palladium-catalyzed cross-coupling of the acylzirconocene chlorides with hypervalent iodonium salts are summarized in Table 1.

(*E*)- $\beta$ -Styrylacylzirconocene chloride prepared *in situ* from phenylacetylene **1a**,  $\text{Cp}_2\text{Zr}(\text{H})\text{Cl}$ , and carbon monoxide was reacted in the presence of  $\text{Pd}(\text{PPh}_3)_4$  (5 mol%) at room temperature for 2 h to afford the  $\alpha,\beta$ -unsaturated aromatic ketone **3a**<sup>5</sup> in 75% yield (entry 1 in Table 1). Under the same conditions with (*p*-methoxyphenyl)(phenyl)iodonium tetrafluoroborate (**2b**) as an electrophile, the *p*-methoxyphenyl substituted  $\alpha,\beta$ -unsaturated ketone **3b**<sup>6</sup> was afforded as the sole product in 73% yield (entry 2). This method was applied to the alkenyl-substituted iodonium salt **2c**.  $\beta$ -Styrylacylzirconocene chloride generated *in situ* was treated with alkenyl-substituted iodonium salt **2c** to provide dibenzylideneacetone **3c**<sup>7</sup> in 83% yield (entry 3). Alkyl-substituted acetylene **1b** was utilized in the hydrozirconation and carbon monoxide insertion followed by the palladium-catalyzed coupling with **2a**, **2b**, and **2c** to give the coupled products **3d**,<sup>8</sup> **3e**,<sup>9</sup> and **3f**<sup>10</sup> in 94, 70, and 75% yields, respectively (entries 4–6). Propargyl alcohol methyl ether (1-methoxyprop-2-yne) **1c** was converted to the corresponding acylzirconocene chloride and then coupled in the presence of palladium catalyst with **2a**, **2b**, and **2c** to furnish **3g**,<sup>11</sup> **3h**,<sup>11</sup> and

**3i**<sup>12</sup> in 77, 78, and 84% yields, respectively (entries 7–9). This coupling method was extended to the substituted alkenes. The hydrozirconation followed by carbonylation of styrene **1d** gave the alkyl-substituted zirconocene chloride, which readily coupled with **2a** to afford ketone **3j**<sup>13</sup> in 70% yield (entry 10). Under the same conditions with **2b** and **2c**, **3k**<sup>13</sup> and **3l**<sup>14</sup> were afforded (entries 11 and 12). Finally, it is notable that the alkyl-substituted zirconocene from oct-1-ene **1e**,  $\text{Cp}_2\text{Zr}(\text{H})\text{Cl}$  and CO coupled with **2a**, **2b**, and **2c** to give **3m**,<sup>15</sup> **3n**,<sup>16</sup> and **3o**<sup>17</sup> in moderate yield (entries 13–15).

In summary, the palladium-catalyzed acylation of alkenoyl- and alkanoylzirconocene and carbonylation was accomplished with hypervalent iodonium salts to afford acylated aromatic compounds under mild conditions.

## Experimental

### Typical procedure for the synthesis of 1,3-diphenylprop-2-enone **3a**

To a stirred solution of  $\text{Cp}_2\text{Zr}(\text{H})\text{Cl}$  (469 mg, 1.82 mmol) in dry THF (10 mL) at room temperature under a nitrogen balloon was added phenylacetylene **1a** (93 mg, 0.91 mmol) and the reaction mixture was stirred for 30 min. After the nitrogen balloon was changed to a CO balloon, the mixture was stirred for 2 h at room temperature. To this solution was added diphenyliodonium tetrafluoroborate **2a** (335 mg, 0.91 mmol) and  $\text{Pd}(\text{PPh}_3)_4$  (53.2 mg, 0.045 mmol) and the reaction mixture was stirred for 2 h. The reaction mixture was extracted with diethyl ether (20 mL  $\times$  3) and the organic layer was dried over  $\text{MgSO}_4$ , and evaporated *in vacuo*. The crude product was separated by  $\text{SiO}_2$  column chromatography (hexanes–EtOAc = 10 : 1,  $R_f$  = 0.35) to give 1,3-diphenylprop-2-enone **3a** (142 mg, 75%).


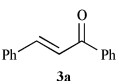
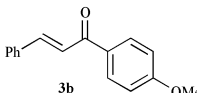
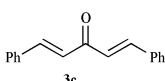

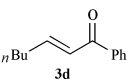
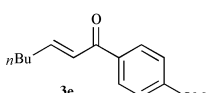
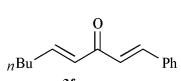

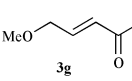
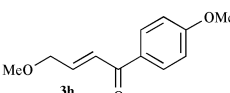
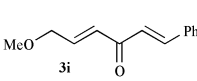

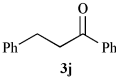
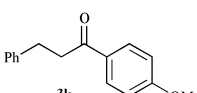
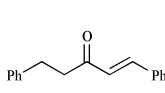

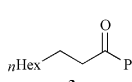
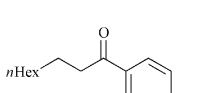
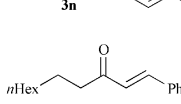
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**Table 1** The palladium-catalyzed coupling of acylzirconocene chlorides with hypervalent iodonium salts

Entry	Substrate	Iodonium salts	Products	Isolated yield (%)
1	 <b>1a</b>	$\text{Ph}_2\text{I}^+\text{BF}_4^-$ <b>2a</b>	 <b>3a</b>	75
2	<b>1a</b>	$(p\text{-MeO-C}_6\text{H}_4)\text{I}^+\text{PhBF}_4^-$ <b>2b</b>	 <b>3b</b>	73
3	<b>1a</b>	$\text{Ph-CH=CH-I}^+\text{PhBF}_4^-$ <b>2c</b>	 <b>3c</b>	83
4	 <b>1b</b>	<b>2a</b>	 <b>3d</b>	94
5	<b>1b</b>	<b>2b</b>	 <b>3e</b>	70
6	<b>1b</b>	<b>2c</b>	 <b>3f</b>	75
7	 <b>1c</b>	<b>2a</b>	 <b>3g</b>	77
8	<b>1c</b>	<b>2b</b>	 <b>3h</b>	78
9	<b>1c</b>	<b>2c</b>	 <b>3i</b>	84
10	 <b>1d</b>	<b>2a</b>	 <b>3j</b>	70
11	<b>1d</b>	<b>2b</b>	 <b>3k</b>	69
12	<b>1d</b>	<b>2c</b>	 <b>3l</b>	72
13	 <b>1e</b>	<b>2a</b>	 <b>3m</b>	68
14	<b>1e</b>	<b>2b</b>	 <b>3n</b>	69
15	<b>1e</b>	<b>2c</b>	 <b>3o</b>	69

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