

## Palladium-Catalyzed Aldol-Type Condensation by Enol Esters with SnCl<sub>2</sub>

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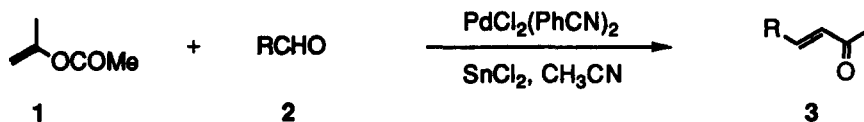
**Key Words:** Aldol-type condensation; enol ester; palladium; tin(II) chloride.

**Abstract:** Using PdCl<sub>2</sub>(PhCN)<sub>2</sub>-SnCl<sub>2</sub>, enol esters caused aldol-type condensation with aldehydes at 50°C in acetonitrile to produce (*E*)- $\alpha$ ,  $\beta$ -unsaturated carbonyl compounds. Cyclic enol ester such as  $\alpha$ -angelicalactone also reacted with aldehydes under the same conditions to afford  $\gamma$ -substituted  $\beta$ -acetyl- $\gamma$ -butyrolactones and/or 5-substituted 4-acetyl-2(5*H*)-furanones.

Enol esters, which are easily prepared and are tractable as nucleophiles, can be applied to C-C bond formation under acidic conditions<sup>1</sup> or neutral conditions.<sup>2</sup> However, the aldol-type condensation of simple enol esters such as available isopropenyl acetate (**1**) with aldehydes except for benzaldehyde has not yet been developed. Here we report that PdCl<sub>2</sub>(PhCN)<sub>2</sub>-SnCl<sub>2</sub> reagent can be utilized in the aldol-type condensation of **1** with aldehydes.

The addition reaction of **1** to 4-methoxycarbonylbenzaldehyde (**2**, R=4-MeOCC<sub>6</sub>H<sub>4</sub>) with SnCl<sub>2</sub> was investigated under various reaction conditions, as summarized in Table 1. The addition reaction occurred at 50 °C in acetonitrile without PdCl<sub>2</sub>(PhCN)<sub>2</sub> to give 4-(4-methoxycarbonylphenyl)-3-buten-2-one (**3**, R=4-MeOCC<sub>6</sub>H<sub>4</sub>) (entry 1). Then, the addition of a catalytic amount of PdCl<sub>2</sub>(PhCN)<sub>2</sub> accelerated the reaction (entry 3). In the absence of SnCl<sub>2</sub>, PdCl<sub>2</sub>(PhCN)<sub>2</sub> exhibited no catalytic activity. In the presence of PdCl<sub>2</sub>(PhCN)<sub>2</sub>, use of a catalytic amount (4 mol%) of SnCl<sub>2</sub> did not cause the reaction and use of an amount of SnCl<sub>2</sub> equimolar to that of benzaldehyde lowered the yield of **3** (R=4-MeOCC<sub>6</sub>H<sub>4</sub>, 50 °C, 48 h, 33%). The addition of phosphine or phosphite ligands inhibited the catalytic activity of palladium complex (entries 5-7). Solvents such as DMF, DMI, and THF were not effective for the reaction under the same conditions as those in DMSO shown in entry 8. A major product in 1,2-dichloroethane was 4-acetoxy-4-(4-methoxycarbonylphenyl)-butan-2-one (49%), and a mixture of **3** (R=4-MeOCC<sub>6</sub>H<sub>4</sub>, 15%) and 4-chloro-4-(4-methoxycarbonylphenyl)-butan-2-one (31%) was obtained in dichloromethane. The addition reaction in refluxing dichloromethane did not proceed in the absence of either PdCl<sub>2</sub>(PhCN)<sub>2</sub> or SnCl<sub>2</sub>. The addition reaction did not occur at 30 °C (entry 2), and many undetermined by-products were produced at 80 °C (entry 4). This reaction might be promoted either by the coordination of carbonyl oxygen of **2** (R=4-MeOCC<sub>6</sub>H<sub>4</sub>) to Pd(SnCl<sub>3</sub>)<sub>2</sub>(PhCN)<sub>2</sub> derived from PdCl<sub>2</sub>(PhCN)<sub>2</sub>-SnCl<sub>2</sub><sup>3</sup> or by the oxidative addition to palladium complex (or SnCl<sub>2</sub>), accompanied by the cleavage of an acyl-oxygen bond of **1**,<sup>4</sup> followed by the transmetalation of palladium enolate into tin enolate.<sup>5,6</sup>

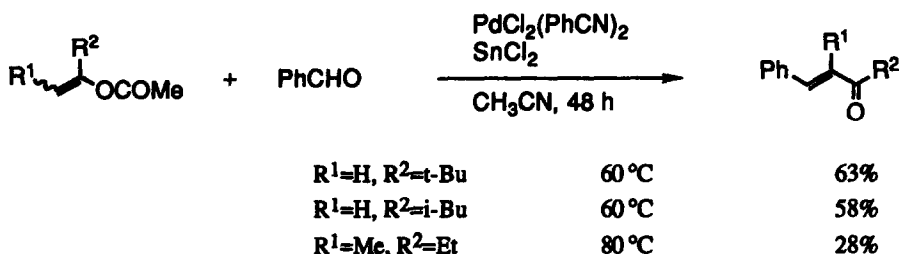
Palladium-catalyzed nucleophilic addition of **1** to several carbonyl compounds with SnCl<sub>2</sub> proceeded in acetonitrile to produce (*E*)-3-buten-2-one derivatives **3** selectively, in contrast with the reaction of **1** and benzaldehyde with Lewis acids.<sup>1a,7</sup> The results are summarized in Table 1. Arenecarbaldehydes were converted to 4-aryl-3-buten-2-ones in good yields (entry 3 and 9-18). However, alkanecarbaldehydes such as heptanal and cyclohexanecarbaldehyde do not contribute so much to the addition reaction. Alkanecarbaldehydes bearing functional groups such as C-C double bond and aryl can be employed (entries 20 and 21).

Table 1. Palladium-Catalyzed Aldol-Type Condensation of 1 and 2 with SnCl<sub>2</sub><sup>a</sup>

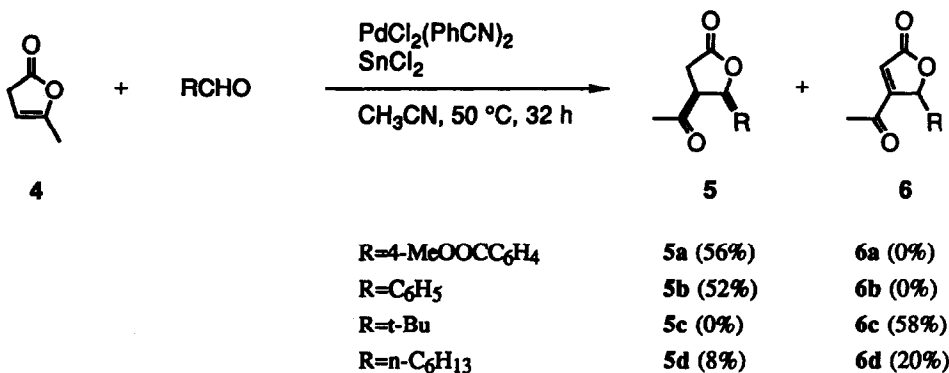
entry	R	ligand <sup>b</sup>	temp (°C)	time (h)	3, yield (%) <sup>c</sup>
1	4-MeOCC <sub>6</sub> H <sub>4</sub>	---	50	72	45 <sup>d</sup>
2	4-MeOCC <sub>6</sub> H <sub>4</sub>	---	30	48	trace
3	4-MeOCC <sub>6</sub> H <sub>4</sub>	---	50	33	88
4	4-MeOCC <sub>6</sub> H <sub>4</sub>	---	80	48	56
5	4-MeOCC <sub>6</sub> H <sub>4</sub>	PBu <sub>3</sub>	50	72	48
6	4-MeOCC <sub>6</sub> H <sub>4</sub>	PPh <sub>3</sub>	50	72	28
7	4-MeOCC <sub>6</sub> H <sub>4</sub>	P(OMe) <sub>3</sub>	50	72	35
8	4-MeOCC <sub>6</sub> H <sub>4</sub>	---	50	48	28 <sup>e</sup>
9	C <sub>6</sub> H <sub>5</sub>	---	50	48	58
10	3,4-(CH <sub>2</sub> O <sub>2</sub> )C <sub>6</sub> H <sub>3</sub>	---	50	40	78
11	2-MeOC <sub>6</sub> H <sub>4</sub>	---	50	30	79
12	3-MeOC <sub>6</sub> H <sub>4</sub>	---	50	48	63
13	4-MeOC <sub>6</sub> H <sub>4</sub>	---	50	33	68
14	2-O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub>	---	50	42	61
15	4-O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub>	---	50	40	82
16	4-NCC <sub>6</sub> H <sub>4</sub>	---	50	35	92
17	4-ClC <sub>6</sub> H <sub>4</sub>	---	50	33	83
18	3-OHCC <sub>6</sub> H <sub>4</sub>	---	50	40	53 <sup>f</sup>
19	PhCH=CH	---	50	35	28
20	PhCH <sub>2</sub> CH <sub>2</sub>	---	50	32	18
21	CH <sub>2</sub> =CH(CH <sub>2</sub> ) <sub>8</sub>	---	50	30	32

(a) The addition reaction of 1 (3 mmol) to 2 (1 mmol) with PdCl<sub>2</sub>(PhCN)<sub>2</sub> (0.02 mmol) and SnCl<sub>2</sub> (3 mmol) was carried out in solvent (5 ml) under a nitrogen atmosphere. (b) Ligand (0.04 mmol) was used. (c) Isolated yields based on 2. (d) No Pd cat. was added. (e) DMSO as a solvent was used. (f) 1,3-Bis(3-oxo-1-butenyl)benzene was obtained.

## Scheme 1



## Scheme 2



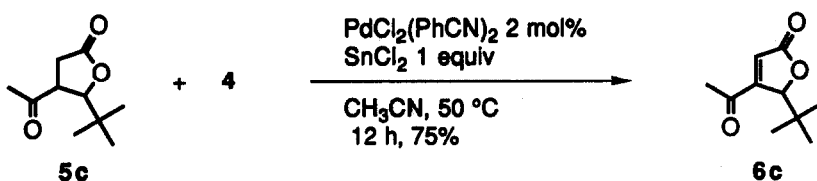
As shown in Scheme 1, some enol esters also reacted with benzaldehyde under the similar conditions to produce the corresponding (*E*)- $\alpha$ ,  $\beta$ -unsaturated ketones. The reactivity of an internally olefinic ester such as 1-ethyl-1-propenyl acetate is lower than that of terminally olefinic esters.

A cyclic enol ester,  $\alpha$ -angelicalactone **4**, which had been applied to the condensation with aldehydes in the presence of Lewis acids,<sup>1b</sup> reacted with aldehydes under the same conditions as those of the reaction of **1** to afford *syn*  $\gamma$ -substituted  $\beta$ -acetyl- $\gamma$ -butyrolactones **5**<sup>8</sup> and/or 5-substituted 4-acetyl-2(*5H*)-furanones **6**<sup>9</sup> (Scheme 2).  $\gamma$ -Butyrolactones **5a** and **5b** were only obtained in cases of arenecarbaldehydes, and furanones **6c** and **6d** were produced in cases of alkanecarbaldehydes. Furanone **6** should be produced via the formation of **5** (aldol-type reaction), followed by its dehydrogenation in the presence of  $\text{PdCl}_2(\text{PhCN})_2\text{-SnCl}_2$  and **4**.<sup>10</sup>

## REFERENCES AND NOTES

- For aldol-type reaction with Lewis acid, see: (a) Mukaiyama, T.; Izawa, T.; Saigo, K. *Chem. Lett.* **1974**, 323-326. (b) Mukaiyama, T.; Hanna, J.; Inoue, T.; Sato, T. *Chem. Lett.* **1974**, 381-382. (c) Izawa, T.; Mukaiyama, T. *Chem. Lett.* **1975**, 161-164.
- For palladium-catalyzed arylation, vinylation, and allylation of ketone with  $\text{Bu}_3\text{SnOMe}$ , see: (a) Kosugi, M.; Hagiwara, I.; Sumiya, T.; Migita, T. *J. Chem. Soc., Chem. Commun.* **1983**, 344-345. (b) Kosugi,

- M.; Hagiwara, I.; Migita, T. *Chem. Lett.* **1983**, 839~840. (c) Tsuji, J.; Minami, I.; Shimizu, I. *Tetrahedron Lett.* **1983**, 24, 4713~4714.
- Murray, T. F.; Norton, J. R. *J. Am. Chem. Soc.* **1979**, 101, 4107~4119.
  - For oxidative addition of acyl-oxygen bond to metal complex, see: Yamamoto, T.; Ishizu, J.; Kohara, T.; Komiya, S.; Yamamoto, A. *J. Am. Chem. Soc.* **1980**, 102, 3758~3764.
  - The oxidative addition of **1** to palladium seems to have higher possibility than the coordination of **2** to  $\text{Pd}(\text{SnCl}_3)_2(\text{PhCN})_2$ , since dimethyl acetals of **2** do not react with **1** under the same conditions as those shown in Table 1, entry 3. The reaction of **1** with acetals is promoted by Lewis acids. Benzaldehyde dimethyl acetal is more active than benzaldehyde. See ref. 1a.
  - For the preparation of tin enolates, see: (a) Mukaiyama, T. *Pure Appl. Chem.* **1986**, 58, 505~512. (b) Mukaiyama, T.; Iwasawa, N. *Nippon Kagaku Kaishi* **1987**, 1099~1107. (c) Pereyre, M.; Quintard, J.-P.; Rahm, A. *Tin in Organic Synthesis*; Butterworths: London, 1987; pp. 286~296.
  - 4-Acetoxybutan-2-one, 4-chlorobutan-2-one, and 4-hydroxybutan-2-one derivatives, which had been prepared by the reaction of **1** and benzaldehyde with Lewis acids,<sup>1a</sup> were not detected in the reaction with  $\text{PdCl}_2(\text{PhCN})_2\text{-SnCl}_2$  in acetonitrile.
  - The structure of *syn*-lactones **5a** and **5b** was confirmed by the coupling constant ( $J=7.6$  and  $8.7$  Hz, respectively) between  $\beta$ - and  $\gamma$ -proton on  $^1\text{H}$  NMR observation; see: Okuda, Y.; Nakatsukasa, S.; Oshima, K.; Nozaki, H. *Chem. Lett.* **1985**, 481~484. **5b**: IR (KBr) 3066, 3035, 3006, 2929, 1773, 1717, 1497, 1458, 1419, 1363, 1300, 1270, 1174, 1016, 956, 765, 701;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  2.16 (s, 3H), 2.86 (dd,  $J=19.7$ , 10.4 Hz, 1H), 2.96 (dd,  $J=19.7$ , 10.4 Hz, 1H), 3.51 (dt,  $J=10.4$ , 8.7 Hz, 1H), 5.57 (d,  $J=8.7$  Hz, 1H), 7.30~7.43 (m, 5H); MS (relative intensity)  $m/z$  204 ( $M^+$ , 50), 176 (22), 162 (92), 161 (100), 147 (66), 133 (26), 115 (21), 105 (59), 98 (43), 77 (28), 71 (26), 70 (20), 57 (36), 55 (47); HRMS calcd for  $\text{C}_{12}\text{H}_{12}\text{O}_3$ : 204.0786, found: 204.0787.
  - 6c**: IR (neat) 2964, 2872, 1785, 1766, 1644, 1478, 1465, 1442, 1383, 1366, 1284, 1233, 1170, 1153, 1050, 1026, 928, 745  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  1.20 (s, 9H), 2.11 (s, 3H), 5.98 (s, 1H), 6.57 (s, 1H); MS (relative intensity)  $m/z$  182 ( $M^+$ , 16), 181 (15), 142 (38), 139 (32), 126 (45), 125 (33), 124 (92), 98 (35), 97 (20), 57 (100); HRMS calcd for  $\text{C}_{10}\text{H}_{14}\text{O}_3$ : 182.0942, found: 182.0930.
  - 5c**, derived from **4** and pivalaldehyde with Lewis acid,<sup>1b</sup> was transformed into **6c** at  $50^\circ\text{C}$  in acetonitrile in the presence of  $\text{PdCl}_2(\text{PhCN})_2\text{-SnCl}_2$  and **4**. Dehydrogenation of **5b** did not proceed under the same conditions as those of **5c** but at  $80^\circ\text{C}$  for 8 h (82%). For palladium-catalyzed dehydrogenation of 1,4-diketone, see: (a) Theissen, R. J. *J. Org. Chem.* **1971**, 36, 752~757. (b) Kirschke, K.; Muller, H.; Timm, D. *J. Prakt. Chem.* **1975**, 317, 807.



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