## PALLADIUM-CATALYZED CARBONYL ALLYLATION BY 2-(HYDROXYMETHYL)ACRYLATE DERIVATIVES: SYNTHESIS OF $\alpha$ -METHYLENE- $\gamma$ -BUTYROLACTONES

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Abstract. Ethyl 2-(hydroxymethyl)acrylate derivatives serve as reagents for 2ethoxycarbonylallylation of carbonyl compounds using PdCl<sub>2</sub>(PhCN)<sub>2</sub>-SnCl<sub>2</sub> system to produce  $\alpha$ methylene- $\gamma$ -butyrolactones diastereoselectively.

Metal-mediated 2-alkoxycarbonylallylation of aldehydes by 2-(bromomethyl)acrylates is one of the most attractive methods for preparation of  $\alpha$ -methylene- $\gamma$ -butyrolactones.<sup>1</sup> However, 2-(bromomethyl)acrylates cannot be easily prepared and are not so stable. Thus, the development of 2-alkoxycarbonylallylating reagents, which are available and stable, is required.<sup>2</sup> Here, we employ available and stable 2-(hydroxymethyl)acrylates,<sup>3</sup> which are applied to palladium-catalyzed carbonyl allylation with SnCl<sub>2</sub> to accomplish the preparation of  $\alpha$ -methylene- $\gamma$ -butyrolactones.<sup>4</sup>

$$\begin{array}{c} \text{COOEt} \\ \text{X} \\ \text{X} \\ \text{Y} \\ \text{RCHO} \\ 1; X:OH \\ 2; X:OCOOMe \end{array} \xrightarrow{\text{PdCl}_2(\text{PhCN})_2} \\ \begin{array}{c} \text{O} \\ \text{PdCl}_2(\text{PhCN})_2 \\ \hline \\ \text{SnCl}_2 \\ \text{DMI-H}_2O \\ \end{array} \xrightarrow{\text{O}} \\ \begin{array}{c} \text{O} \\ \text{O$$

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Palladium-catalyzed allylation of carbonyl compounds by ethyl 2-(hydroxymethyl)acrylate (1)<sup>3a</sup> with SnCl<sub>2</sub> proceeded at 80°C in 1,3-dimethylimidazolidinone (DMI)-H<sub>2</sub>O to give the corresponding  $\alpha$ -methylene- $\gamma$ -butyrolactones **3** after purification by column chromatography on silica gel (Scheme 1). Some representative results are summarized in Table 1. Aromatic, aliphatic, and  $\alpha$ , $\beta$ -unsaturated aldehydes can be used in this palladium-catalyzed allylation (entries 1~5). A ketone such as cyclohexanone also reacted under the same conditions to give spiro[cyclohexane-1,4'-(2'-methylene)butyrolactone] in 23% yield (entry 6). This reaction did not occur at less than 50°C. The use of ethyl 2-(methoxycarbonyloxymethyl)acrylate (**2**) instead of **1** made it possible to lower the reaction temperature (50°C),<sup>5</sup> and allowed the yields of **3** to enhance (entries 7~12). The polymerization of **2** at 50°C might be depressed, compared with that of **1** at 80°C. However, taking into account the troublesomeness of the preparation of allylic carbonate **2** from allylic alcohol **1**, the reaction of **1** might be superior to that of **2**.

entry	acrylate	carbonyl compound	temp.(°C)	time(h)	3, yield(%) <sup>b</sup>
1	1	benzaldehyde	80	47	33
2	1	piperonal	80	25	47
3	1	octanal	80	70	36
4	1	cyclohexanecarboxaldehyde	80	90	30
5	1	cinnamaldehyde	80	120	44
6	1	cyclohexanone	80	110	23
7	2	benzaldehyde	50	52	36
8	2	piperonal	50	25	52
9	2	octanal	50	60	51
10	2	cyclohexanecarboxaldehyde	50	48	61
11	2	cinnamaldehyde	50	80	47
12	2	cyclohexanone	80	90	36

 Table 1. Palladium-Catalyzed Carbonyl Allylation by Ethyl 2-(Hydroxymethyl)acrylate (1) and Ethyl 2-(Methoxycarbonyloxymethyl)acrylate (2)<sup>a</sup>

a)The allylation of carbonyl compounds (1.2 mmol) by ethyl 2-(hydroxymethyl)acrylate or ethyl 2-(methoxycarbonyloxymethyl)acrylate (2.0 mmol) with  $PdCl_2(PhCN)_2$  (0.02 mmol) and  $SnCl_2$  (4.0 mmol) was carried out in DMI (3 ml) and  $H_2O$  (0.5 ml). b)Isolated yield based on the carbonyl compound.

Diastereoselection was investigated in the allylation of aldehydes with 2-(hydroxymethyl)acrylates 4, 5, and  $6^{3b}$  bearing a substituent (R<sup>1</sup>) at an allylic position at 80°C in DMI-H<sub>2</sub>O (Scheme 2). An addition reaction of 4 to aldehydes, such as 4-methoxycarbonylbenzaldehyde, cyclohexanecarboxaldehyde, and pentanal, led to syn selection (>95%) to afford cis-lactones 7, 8, and 9, without the influence of bulkiness of R<sup>2,6</sup> The reaction of 5 or 6, bearing a more bulky substituent (R<sup>1</sup>=Bu or Ph) than that (R<sup>1</sup>=Me) in 4, with 4-methoxycarbonylbenzaldehyde exhibited complete syn selectivity. This syn addition probably proceeds via an acyclic antiperiplanar transition state 15,<sup>1f</sup> which suggests the existence of chelation of oxygen of ester group to Sn(IV) in allylic tin intermediate 14 to disturb the formation of a six-membered cyclic transition state (Scheme 3).<sup>4d</sup> The palladium-catalyzed carbonyl allylation by 1-substituted allylic alcohol 12 proves itself a powerful diastereoselective allylation method, since 12 is prepared more easily than 3-substituted allylic alcohol and is regioselectively converted into 3-substituted allylic tin intermediates 14 via the formation of  $\pi$ -allylpalladium complexes 13.<sup>4</sup>

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Scheme 3
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- (5) Y. Masuyama, J. P. Takahara, and Y. Kurusu, unpublished results: High chemoselectivity toward methoxycarbonyloxy group was observed in the reaction of 4-methoxycarbonyloxy-2-butenol with benzaldehyde, as shown below. Thus, methoxycarbonyloxy group is superior to hydroxy group as a leaving group in the formation of  $\pi$ -allylpalladium complex.



(6) The diastereomer ratio was determined by 270 MHz <sup>1</sup>H NMR (Jeolco GX-270) and GC (capillary column: PEG 20M, 0.25 mm x 30 m). The structure of cis-lactones was confirmed by the coupling constant (J=7.0~8.3 Hz) between  $\beta$ - and  $\gamma$ -proton on <sup>1</sup>H NMR observation.<sup>1</sup>f 7a:<sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  0.78 (d, J=7.2 Hz, 3H), 3.49 (dtq, J=8.0, 7.2, 2.6 Hz, 1H), 3.92 (s, 3H), 5.61 (d, J=2.6 Hz, 1H), 5.66 (d, J=8.0 Hz, 1H), 6.35 (d, J=2.6 Hz, 1H), 7.27 (d, J=8.7 Hz, 2H), 8.05 (d, J=8.7 Hz, 2H). 8a:<sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  0.95~1.40 (m, 6H), 1.17 (d, J=7.2 Hz, 3H), 1.55~1.93 (m, 5H), 3.13 (m, 1H), 4.13 (t, J=7.0 Hz, 1H), 5.53 (d, J=1.9 Hz, 1H), 6.13 (d, J=2.3 Hz, 1H). 9a:<sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  0.92 (t, J=7.2 Hz, 3H), 1.16 (d, J=7.2 Hz, 3H), 1.20~1.60 (m, 6H), 3.17 (dtq, J=7.4, 7.2, 2.6 Hz, 1H), 4.53 (m, 1H), 5.54 (d, J=2.6 Hz, 1H), 6.19 (d,J=2.3 Hz, 1H). 10a:<sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  0.75 (t, J=6.8 Hz, 3H), 1.05~1.33 (m, 6H), 3.21~3.32 (m, 1H), 3.93 (s, 3H), 5.64 (d, J=2.3 Hz, 1H), 5.65 (d, J=7.19 Hz, 1H), 6.34 (d, J=2.3 Hz, 1H), 7.33 (d, J=8.3 Hz, 2H), 8.06 (d, J=8.3 Hz, 2H). 11a:<sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  3.86 (s, 3H), 4.72 (dt, J=8.3, 2.6 Hz, 1H), 5.62 (d, J=2.6 Hz, 1H), 5.87 (d, J=8.3 Hz, 1H), 6.54 (d, J=2.6 Hz, 1H), 6.54 (d, J=2.6 Hz, 1H), 6.72~6.77 (m, 2H), 6.94 (d, J=8.0 Hz, 2H), 7.02~7.12 (m, 3H), 7.78 (d, J=8.0 Hz, 2H).

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