

**THE PALLADIUM-CATALYZED MICHAEL ADDITION REACTION OF THE KETONE ENOLATES GENERATED BY THE DECARBOXYLATION OF ALLYL  $\beta$ -KETO CARBOXYLATES UNDER NEUTRAL CONDITIONS**

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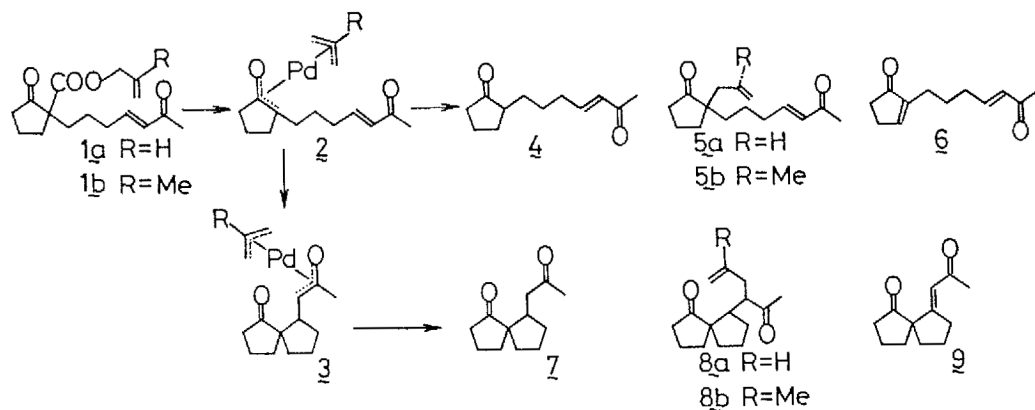
**Summary:** The palladium-catalyzed intramolecular Michael addition reaction of allyl  $\beta$ -keto carboxylates with enones under neutral conditions gave the cyclic Michael adducts **7** via ( $\pi$ -allyl)palladium enolates **2** and **3**. Also the Michael-allylation and Michael-dehydrogenation took place to give **8** and **9**.

In the course of our continuing studies on the palladium-catalyzed reaction of allyl  $\beta$ -keto carboxylates, and particularly the new chemistry of palladium enolate, we have recently reported the palladium-catalyzed aldol reaction of ketone enolates generated regioselectively by the decarboxylation of allyl  $\beta$ -keto carboxylates with aldehydes under neutral conditions as the first example of the typical enolate reaction of palladium.<sup>1</sup> Considering that aldol condensation and Michael addition are two representative reactions of various metal enolates, we have successfully attempted the intramolecular palladium-catalyzed Michael addition reaction of allyl  $\beta$ -keto carboxylates to enones via decarboxylation, and the results of our preliminary studies are presented in this paper.<sup>2</sup>

2-Allyloxycarbonylcyclopentanone **1a**, which has the enone moiety in the same molecule was prepared, and subjected to the reactions with palladium phosphine catalysts ( $\text{Pd}(\text{OAc})_2$ - $\text{PPh}_3$  or  $\text{dppe}$  and  $\text{Pd}(\text{PPh}_3)_4$ ) under various reaction conditions. The reaction proceeded smoothly in THF or MeCN, and a mixture of the products **4-9** was obtained. The ratios of these products changed depending on the reaction conditions. The results obtained under various conditions are shown in Table 1.

The formation of these products can be explained by Scheme 1. The minor products **4-6** were formed by the known palladium-catalyzed reactions of allyl  $\beta$ -keto carboxylates<sup>3</sup> without undergoing the Michael addition. Namely, the product **4** was formed by the protonation, **5** by the allylation,<sup>4</sup> and **6** by the dehydrogenation<sup>5</sup> of the ( $\pi$ -allyl)palladium enolate **2** formed by the decarboxylation of **1**.

The main reaction path is the formation of the second ( $\pi$ -allyl)palladium enolates **3** via an intramolecular 1,4-addition of the palladium enolate **2** to the enone moiety, followed by further transformations. The major product was the Michael adduct **7**, which was formed by the protonation of **3**. But the source of the proton is unknown and there remains ambiguity particularly about how the catalytic species of Pd is regenerated from **3** after giving the Michael adduct **7**. In addition to the Michael adduct **7**, two other products **8** and **9** were

Table 1 Palladium-catalyzed Reaction of Allyl  $\beta$ -Keto Carboxylate 1

Pd (mol%)	phosphine <sup>a</sup> (mol%)	solvent	temp. °C	time h	4	5	6	7	8	9
Pd(OAc) <sub>2</sub> (5)	PPh <sub>3</sub> (10)	MeCN	40	10	3.4		3.4	69.1		
Pd(OAc) <sub>2</sub> (5)	DPPE (10)	MeCN	40	15				80.6		
Pd(OAc) <sub>2</sub> (5)	DPPE (10)	MeCN	80	0.5	5.4			77.0	5.9	
Pd(OAc) <sub>2</sub> (5)	DPPE (5)	MeCN	80	1	7.2		39.8	18.2		18.1
Pd(PPh <sub>3</sub> ) <sub>4</sub> (7)		MeCN	r.t.	1				84.2		
Pd(OAc) <sub>2</sub> (5)	PPh <sub>3</sub> (10)	THF	40	4	7.2		3.6	64.5	4.5	
Pd(OAc) <sub>2</sub> (5)	PPh <sub>3</sub> (10)	THF	80	0.5	5.4	11.8		16.1	46.0	
Pd(PPh <sub>3</sub> ) <sub>4</sub> (7)		THF	r.t.	1		30.9		16.1	31.2	
Pd(PPh <sub>3</sub> ) <sub>4</sub> (2)		THF	80	0.2		22.1		17.9	47.5	
Pd(PPh <sub>3</sub> ) <sub>4</sub> (7)		THF	80	0.2		5.8 <sup>c,d</sup>		13.2 <sup>c</sup>	64.7 <sup>c,e</sup>	

a. DPPE:1,2-bis(diphenylphosphino)ethane. b. Produced from **1a** unless otherwise noted, and isolated by column chromatography on silica gel. c. Produced from **1b**. d. **5b**. e. **8b**.

obtained. The product **9** was formed by the elimination of  $\beta$ -hydrogen from the palladium enolate **3**, which seems to be the reasonable path and **9** was expected to be the main product. But it was obtained as a minor product by the reaction in boiling MeCN using Pd(OAc)<sub>2</sub> and dppe in a ratio of 1:1. This is the same condition employed before for the selective dehydrogenation of the palladium enolate.<sup>4</sup> The formation of this product is competitive with another dehydrogenation product **6**. The product **8** was formed by the tandem allylation of the intermediate **3**. This the most interesting one, which was obtained as a major product in 46% yield in boiling THF. Although the yield was not very high, this tandem Michael addition-allylation reaction seems to have potentially useful synthetic application and we are trying to improve selectivity of this reaction.

Also the palladium-catalyzed reactions of some other allyl  $\beta$ -keto carboxylates **10** and **13** which have enone moieties were carried out in order to increase the selectivities for the tandem allylation and dehydrogenation, and results are shown in Table 2. The Michael-allylation products **12a** and **12b** were obtained as the major products from **10a** and **10b** in boiling THF. Also the Michael-dehydrogenation product **15** was obtained in MeCN as the main product from **13** by decreasing a relative amount of PPh<sub>3</sub>.

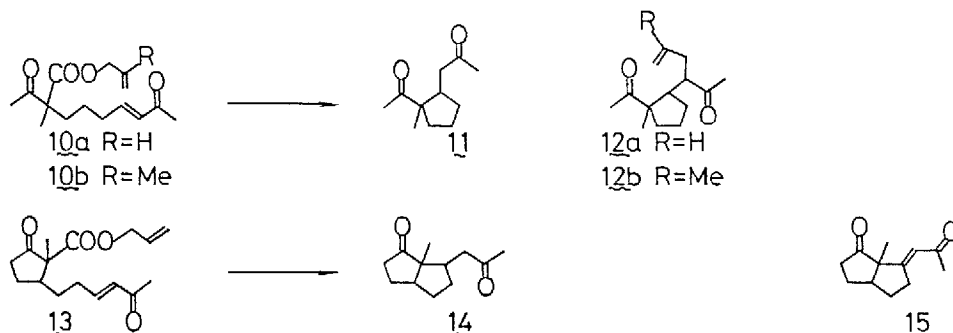


Table 2 Palladium-catalyzed Michael Reaction of Allyl(-ic)  $\beta$ -Keto Carboxylates (**10a,b**, **13**)

allyl ester	reaction condition <sup>a</sup> (mmol)	reaction time (h)	product yield(%)
<b>10a</b>	B(5), PPh <sub>3</sub> (10), THF, reflux	0.5	<b>11</b> 25.1 <b>12a</b> 42.8
<b>10a</b>	A(7), THF, reflux	0.2	<b>11</b> 23.0 <b>12a</b> 47.9
<b>10b</b>	A(7), THF, reflux	0.2	<b>11</b> 17.3 <b>12b</b> 51.9
<b>13</b>	B(5), PPh <sub>3</sub> (1), MeCN, 40 °C	7	<b>14</b> 20.5 <b>15</b> 41.4

a. A: Pd(PPh<sub>3</sub>)<sub>4</sub>, B: Pd(OAc)<sub>2</sub>

In summary, we found that the palladium-catalyzed regioselective intramolecular Michael addition reaction of ketone enolates, formed from allyl  $\beta$ -keto carboxylates, can be carried out under neutral conditions. This is the second example of the typical reactions of palladium enolates, which suggests further interesting application.

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