

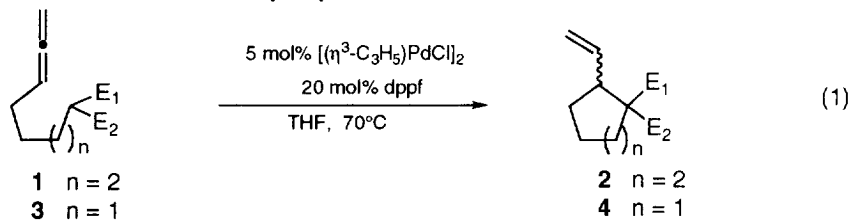
## Palladium Catalyzed Intramolecular Hydrocarbonation of Allenes Leading to Carbocycles

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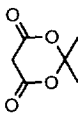


**Abstract:** The intramolecular hydrocarbonation of certain allenes (**1** and **3**), bearing active methyne groups at the terminus of the carbon chain, proceeded smoothly in the presence of catalytic amounts of palladium complex ( $[(\eta^3\text{-C}_3\text{H}_5)\text{PdCl}]_2\text{-dppf}$ ) to give the corresponding carbocycles (**2** and **4**, respectively) in good to high yields.  
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The addition reaction of a carbon nucleophile to an olefinic double bond has been regarded as one of the most important method for C-C bond formation in organic synthesis. The reaction of anionic organometallics with activated olefins (Michael acceptors)<sup>1</sup> and the carbometallation<sup>2</sup> of certain activated organometallics with unactivated olefins have been used frequently for this purpose. More recently, it has been found that certain activated methylenes and methynes (pronucleophiles) undergo the addition reaction to unactivated C-C multiple bonds<sup>3</sup> in the presence of transition metal catalysts; this is a direct addition of H-C bond to a double bond and the so-called "hydrocarbonation".<sup>4, 5</sup> We previously reported that the addition of pronucleophiles to allenes proceeds very smoothly in the presence of  $\text{Pd}_2(\text{dba})_3\cdot\text{CHCl}_3$  catalyst (neutral condition).<sup>4a</sup> Later, Trost and Gerusz reported similar addition reaction using  $\pi$ -allylpalladium chloride dimer-dppf-*t*-BuOK catalyst (basic condition);<sup>3b</sup> they reported not only intermolecular addition but also intramolecular C-H addition. Now, we report that the intramolecular addition of pronucleophiles to allenes **1** and **3** proceeds very well in the presence of a neutral palladium catalyst system to give the corresponding carbocycles **2** and **4**, respectively, in good to high yields (eq 1); the use of the neutral catalyst system gives better result than that of the basic catalyst system.



Initially, the cyclization of the allene **1a** having malononitrile group at the terminus of the carbon chain was investigated (Table 1). The cyclization in the presence of Trost catalyst ( $[(\eta^3\text{-C}_3\text{H}_5)\text{PdCl}]_2\text{-dppf-}t\text{-BuOK}$ ) gave the six-membered carbocycle **2a** in only 10% yield (entry 1), but the use of  $[(\eta^3\text{-C}_3\text{H}_5)\text{PdCl}]_2\text{-dppf}$  afforded **2a** in 62% yield (entry 2). The former reaction proceeded under basic conditions (condition A) while the latter under neutral conditions (condition B). The use of other catalysts lead to unsatisfactory result.<sup>6</sup> The cyclization of **1b** having

Table 1. Pd Catalyzed Intramolecular Hydrocarbonation of Allenes.

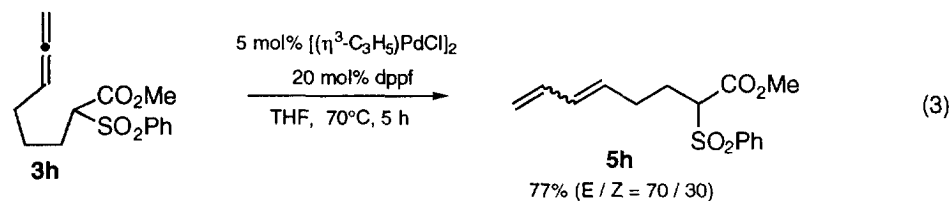
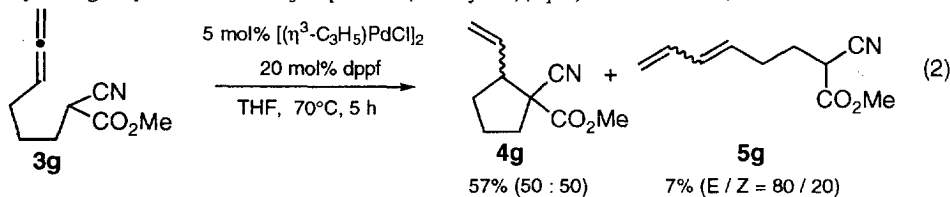
Entry	n	Allene E <sub>1</sub>	E <sub>2</sub>		Condition <sup>a</sup>	Reaction time, h	Product	Yield, <sup>b</sup> %
1	2	CN	CN	<b>1a</b>	A	5	<b>2a</b>	10
2	2	CN	CN	<b>1a</b>	B	5	<b>2a</b>	62
3	2	CO <sub>2</sub> Me	CO <sub>2</sub> Me	<b>1b</b>	B	24	<b>2b</b>	~0 <sup>c</sup>
4	1	CN	CN	<b>3a</b>	A	3	<b>4a</b>	28
5	1	CN	CN	<b>3a</b>	B	1.5	<b>4a</b>	88
6	1	CO <sub>2</sub> Me	CO <sub>2</sub> Me	<b>3b</b>	B	24	<b>4b</b>	~0 <sup>c</sup>
7	1			<b>3c</b>	A	1	<b>4c</b>	70
8	1			<b>3c</b>	B	1	<b>4c</b>	77
9	1	CN	SO <sub>2</sub> Ph	<b>3d</b>	B	5	<b>4d</b>	82 (70 : 30) <sup>d</sup>
10	1	SO <sub>2</sub> Ph	SO <sub>2</sub> Ph	<b>3e</b>	A	6	<b>4e</b>	65
11	1	SO <sub>2</sub> Ph	SO <sub>2</sub> Ph	<b>3e</b>	B	6	<b>4e</b>	74
12	1			<b>3f</b>	B	24	<b>4f</b>	~0 <sup>c</sup>

<sup>a</sup> Condition A : 5 mol% [(η<sup>3</sup>-C<sub>3</sub>H<sub>3</sub>)PdCl<sub>2</sub>] / 20 mol% dpfp / 10 mol% *t*-BuOK. The reaction was carried out in dilute solutions (0.025 M of the allenenes). Condition B : 5 mol% [(η<sup>3</sup>-C<sub>3</sub>H<sub>3</sub>)PdCl<sub>2</sub>] / 20 mol% dpfp. The reaction was carried out in dilute solutions (0.025 M of the allenenes). <sup>b</sup> Isolated yield. <sup>c</sup> Significant amounts of the starting material were recovered. <sup>d</sup> The stereoisomer ratio was determined by <sup>1</sup>H-NMR.

dimethyl malonate group at the terminus of the carbon chain did not proceed at all even under the condition B (entry 3). Compared to six-membered ring formation, the cyclization of **3** proceeded smoothly in the "5-exo-trig<sup>7</sup>" manner, giving the corresponding five-membered vinyl cyclopentanes **4** in good to high yields (entries 4-11). It should be noted that only exo cyclized products were obtained in the cyclization of **3** and no endo-cyclization was observed. The malononitrile derivative **3a** was converted to **4a** in 88 % yield under the condition B, while it gave **4a** in only 28% yield under the condition A (entry 5 vs. 4). Here again, the cyclization of the dimethyl malonate derivative **3b** did not proceed at all (entry 6). The cyclization of the Meldrum's acid derivative **3c** proceeded smoothly under the condition A and B to give **4c** in good yields (entries 7 and 8). The allenenes **3d** and **3e** bearing phenylsulfonyl group gave the corresponding five-membered carbocycles **4d** and **4e**, respectively, in good to high yields (entries

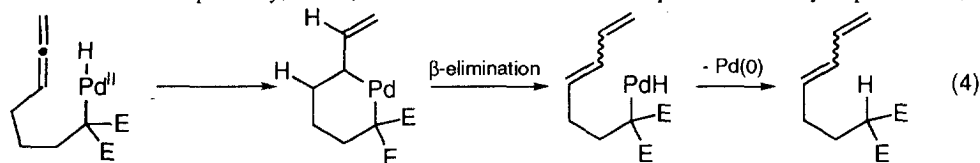
9-11). However, the allene **3f** having 1,3-benzodithiole tetraoxide<sup>8</sup> did not undergo cyclization even under the condition B (entry 12).

Very interestingly, the cyclization of the cyanoacetate derivative **3g** under the condition B gave the 1,3-diene derivative **5g** (E/Z = 80/20) in 7% yield along with the five-membered carbocycle **4g** expected as a major product (57% yield)(eq 2). Furthermore, the reaction of the



(phenylsulfonyl)acetate derivative **3h** afforded the 1,3-diene derivative **5h** in 77% yield as a sole product (eq 3). 1,3-Diene products were not obtained in the reactions of **3a** - **3f**. Although it is not clear why only **3h** and **3g** gave the corresponding 1,3-diene derivatives, the formation of such products suggests intervention of a hydridopalladium intermediate as mentioned below.

The following mechanistic rationale may account for the present Pd-catalyzed cyclization although it is speculative. Initially, Pd(0) catalyst would add oxidatively to the C-H bond of the pronucleophiles<sup>9</sup> to give a hydridopalladium(II) intermediate. Either "hydropalladation" or "carbopalladation" of the intermediate would give the cyclized products.<sup>4a</sup> However, the formation of the 1,3-diene derivatives **5g** and **5h** strongly supports the hydropalladation mechanism. Most probably, the 1,3-diene derivatives would be produced via hydropalladation,



$\beta$ -hydride elimination, and reductive elimination of Pd(0) catalyst (eq 4). The carbopalladation mechanism can not explain the formation of such products. Although further investigation is needed to settle the precise mechanism, the present cyclization reaction provides a new procedure for constructing carbocycles under essentially neutral conditions.

The intramolecular hydrocarbonylation of the Meldrum's acid derivative **3c** is representative. To a solution of  $[(\eta^3\text{-C}_3\text{H}_5)\text{PdCl}_2]$  (14.6 mg, 0.040 mmol) and dpf (88.7 mg, 0.16 mmol) in THF (12.0 ml) was added a THF (20.0 ml) solution of **3c** (179.4 mg, 0.80 mmol) under Ar atmosphere. The reaction mixture was stirred at 70°C and the reaction progress was monitored

by TLC. After consumption of the starting material, the solvent was evaporated and the residue was filtered through a silica gel short column using ethyl acetate as an eluent. The solvent was evaporated and the product was purified by silica gel column chromatography using *n*-hexane-ethyl acetate (15 : 1) as an eluent. 8,8-Dimethyl-7,9-dioxo-1-vinylspiro[4.5]decan-6,10-dione **4c** was obtained in 77% yield (138.1 mg).

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