

# A palladium catalyzed efficient synthesis of $\gamma$ -methylene- $\alpha,\beta$ -unsaturated $\gamma$ -lactones via cyclization of 3,4-alkadienoic acids

Shengming Ma\* and Fei Yu

State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences,  
354 Fenglin Lu, Shanghai 200032, People's Republic of China

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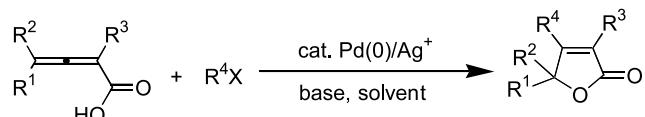
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**Abstract**—An efficient method was developed for the synthesis of  $\gamma$ -methylene- $\alpha,\beta$ -unsaturated  $\gamma$ -lactones from the Pd-catalyzed cyclization of 3,4-alkadienoic acids. Control experiment shows that the reaction should be carried out under a  $N_2$  atmosphere to ensure the high purity of the products.

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## 1. Introduction

Recently, the chemistry of Allenes has been attracting the attention of more and more chemists.<sup>1,2</sup> During the course of our studies on the chemistry of Allenes,<sup>3,4</sup> we have developed some new methodologies for the synthesis of butenolides from  $\alpha$ -allenic acids (**Scheme 1**).<sup>5</sup>

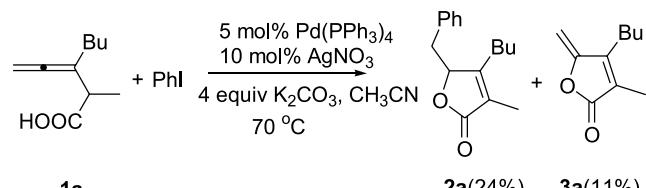


**Scheme 1.**

## 2. Results and discussion

When we turned our attention from the  $\alpha$ -allenic acids to the  $\beta$ -allenic acids **1a**, we found that under the catalysis of  $Pd(0)/Ag^+$  the reaction of 2-methyl-3-(n-butyl)-3,4-pentadienoic acid with iodobenzene in MeCN afforded not only the coupling-cyclization product **2a** but also 5-methylene-2(5H)-furanone **3a** (**Scheme 2**). Recently, the  $\gamma$ -alkylidene- $\alpha,\beta$ -unsaturated  $\gamma$ -lactones<sup>6</sup> has also attracted the attention of many organic chemists because of their biological activities<sup>7,8</sup> and versatile use in organic synthesis.<sup>9</sup> When we found product **3a** was obtained in 29% yield in DMF under the catalysis of  $Pd(PPh_3)_4$  (entry 1, **Table 1**), we went on to search a set of reaction conditions for the sole formation of **3a**. When 4 equiv  $CuCl_2$  were used instead of

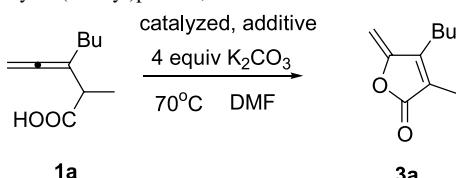
$PhI$ , 5-methylene-2(5H)-furanone **3a** was afforded under the catalysis of  $PdCl_2(PPh_3)_2$  (entry 2, **Table 1**). However, the product was contaminated by other inseparable by-products. Furthermore, it is lucky for us to observe that when the reaction was conducted under a  $N_2$  atmosphere, **3a** was isolated as the single product in 88% yield with a very high purity (entry 3, **Table 1**). When  $CuBr_2$  was used instead of  $CuCl_2$ , the reaction was complicated (entry 4, **Table 1**). In the presence of  $H_2O$  or  $O_2$ , the purity of the product was also not high (entries 2, 5, and 6, **Table 1**). When a less amount of  $CuCl_2$  was applied, the yield of **3a** was obviously lower (entries 7 and 8, **Table 1**). Thus, after screening several commonly used catalyst,  $PdCl_2(PPh_3)_2$  appeared to be the best (compare entries 9–11 with entry 3, **Table 1**). The reaction could proceed in the absence of  $PdCl_2(PPh_3)_2$  albeit in much lower yield (entry 12, **Table 1**). Obviously this cyclization reaction can also be mediated by  $CuCl_2$  (entry 13, **Table 1**). In the absence of the base the yield was also low (entry 14, **Table 1**). When only 3 equiv of  $K_2CO_3$  were added, the product isolated was not pure (entry 15, **Table 1**). When 5 equiv of  $CuCl_2$  were applied, no obvious improvement was observed (entry 16, **Table 1**). From these results we concluded the best reaction conditions:



**Scheme 2.**

**Keywords:** 3,4-Alkadienoic acids; Palladium;  $CuCl_2$ ; Cyclization.

\* Corresponding author. Tel.: +86 21 6416 3300; fax: +86 21 6416 7510;  
e-mail: masm@mail.sioc.ac.cn

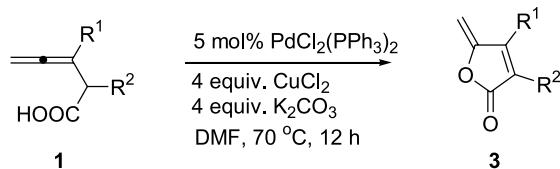
**Table 1.** Pd-catalyzed cyclization reaction of 2-methyl-3-(*n*-butyl)penta-3,4-dienoic acid **1a**

Entry	Catalyst (5 mol%)	Additive (equiv)	Time (h)	Yield of <b>3a</b> (%)
1	Pd(PPh <sub>3</sub> ) <sub>4</sub>	PhI (1.5)	24	29
2 <sup>a</sup>	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	CuCl <sub>2</sub> (4)	12	<87 <sup>b</sup>
3	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	CuCl <sub>2</sub> (4)	12	88
4	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	CuBr <sub>2</sub> (5)	24	complicated
5 <sup>c</sup>	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	CuCl <sub>2</sub> (4)	12	<50 <sup>b</sup>
6 <sup>d</sup>	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	CuCl <sub>2</sub> (4)	12	<70 <sup>b</sup>
7	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	CuCl <sub>2</sub> (2.5)	24	75
8	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	CuCl <sub>2</sub> (0.8)	24	22
9	PdCl <sub>2</sub>	CuCl <sub>2</sub> (4)	24	54
10	Pd(OAc) <sub>2</sub>	CuCl <sub>2</sub> (4)	24	40
11	PdCl <sub>2</sub> (CH <sub>3</sub> CN) <sub>2</sub>	CuCl <sub>2</sub> (4)	24	34
12	—	CuCl <sub>2</sub> (4)	24	60
13	—	CuCl <sub>2</sub> (1)	12	18
14 <sup>e</sup>	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	CuCl <sub>2</sub> (4)	12	70
15 <sup>f</sup>	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	CuCl <sub>2</sub> (4)	12	<87 <sup>b</sup>
16 <sup>g</sup>	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	CuCl <sub>2</sub> (4)	12	89

<sup>a</sup> The reaction was exposed to air.<sup>b</sup> The product is not pure.<sup>c</sup> The reaction was conducted under 1 atm of pure O<sub>2</sub>.<sup>d</sup> Four equivalents H<sub>2</sub>O was added.<sup>e</sup> No K<sub>2</sub>CO<sub>3</sub> was used.<sup>f</sup> Three equivalents K<sub>2</sub>CO<sub>3</sub> were used.<sup>g</sup> Five equivalents K<sub>2</sub>CO<sub>3</sub> were used.

5 mol% PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub>, 4 equiv of CuCl<sub>2</sub>, 4 equiv of K<sub>2</sub>CO<sub>3</sub> in DMF at 70 °C for 12 h under N<sub>2</sub>.

β-Alenoic acids can be conveniently prepared from the hydrolysis of the corresponding β-alenoic acid esters.<sup>10</sup> Subsequently, we studied the scope of this cyclization reaction of β-alenoic acids (Table 2). From the data listed in Table 2, it is obvious that the scope of the reactant is broad: R<sup>1</sup> can be H, alkyl, allyl, Bn or *t*-Bu and R<sup>2</sup> can be H or alkyl. With simple unsubstituted pentadienoic acid, the

**Table 2.** PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub>-catalyzed cyclization reaction of β-alenoic acids **1**

Entry	R <sup>1</sup>	R <sup>2</sup>	Yield of <b>3</b> (%)
1	<i>n</i> -Bu	Me	(1a) 88 (3a)
2	<i>n</i> -Bu	H	(1b) 78 (3b)
3	<i>n</i> -Bu	Et	(1c) 81 (3c)
4	<i>n</i> -Bu	<i>n</i> -Pr	(1d) 84 (3d)
5	Me	Me	(1e) 64 (3e)
6	<i>n</i> -C <sub>7</sub> H <sub>15</sub>	Me	(1f) 84 (3f)
7	<i>t</i> -Bu	Me	(1g) 71 (3g)
8	Allyl	Me	(1h) 66 (3h)
9	Bn	Me	(1i) 89 (3i)
10	H	<i>n</i> -Pr	(1j) 51 (3j)
11	H	H	(1k) 31 <sup>a</sup> (3k)

<sup>a</sup> The yield was determined by NMR using *p*-methoxyiodobenzene as the internal standard.

yield of **3k** (protoanemonin)<sup>7</sup> is 31% by NMR (entry 11, Table 2).

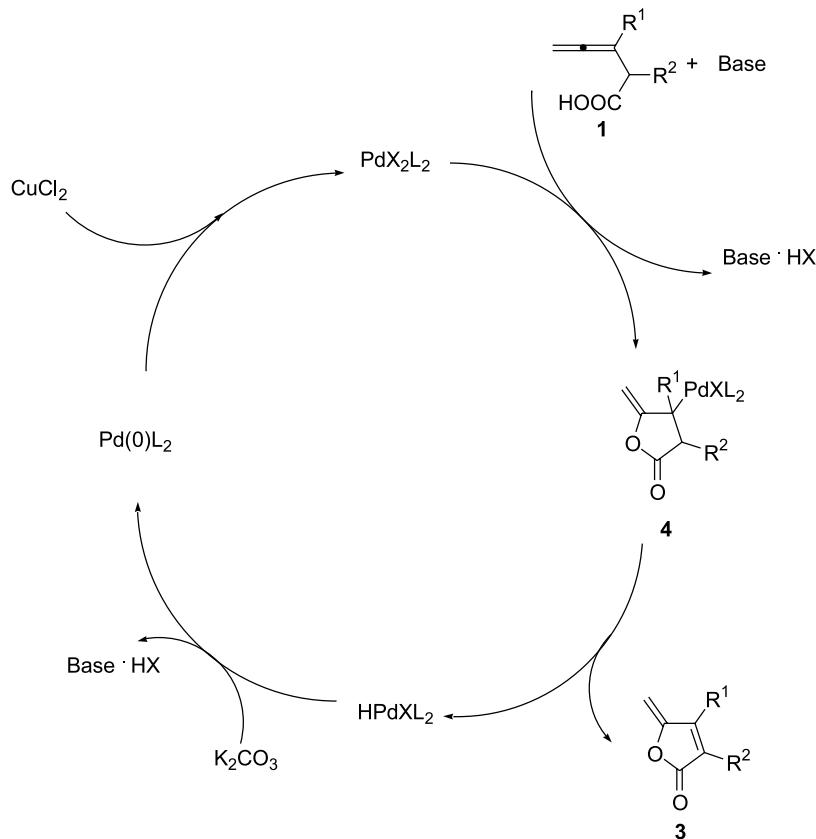
A palladium catalyzed mechanism was proposed for this reaction: *endo*-mode cyclic anti-oxypalladation of the non-terminal carbon–carbon double bonds in the 3,4-alenoic acids would form **4**, which would afford the products **3** via *syn*-β-H elimination, which may be facilitated by the presence of the base and the electron-withdrawing carbonyl group in **4**. The in situ generated palladium hydride species would form Pd(0) species upon its action with K<sub>2</sub>CO<sub>3</sub>. The catalytically active Pd(II) species would be regenerated via the oxidation with CuCl<sub>2</sub> (Scheme 3).

In conclusion, we have described a convenient method for the preparation of the valuable γ-methylene-2(5*H*)-furanes from 3,4-alenoic acids in high yield. The reaction demonstrated high efficiency and regioselectivity. Further studies in this area are being conducted in our laboratory.

### 3. Experimental

#### 3.1. General procedure for the synthesis of β-alenoic acids **1**

**Conditions A.** A solution of the corresponding β-alenoic acid ethyl ester<sup>10</sup> (6 mmol), and LiOH (288 mg, 12 mmol) was stirred in the mixed solvent of 12 mL of H<sub>2</sub>O and 24 mL of MeOH at 30 °C for 3 days. After acidification with 1 N HCl, extraction with ether, drying over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and evaporation, the mixture was submitted to flash

**Scheme 3.**

chromatography on silica gel ( $\text{CH}_2\text{Cl}_2/\text{MeOH} = 10/1$ ) to produce compound **1**.

*Conditions B.* A solution of the corresponding  $\beta$ -allenic acid ethyl ester<sup>10</sup> (6.6 mmol) was stirred in the mixed solvent of 27 mL of 20% hydrochloric acid, 20 mL of 1,4-dioxane, and 7 mL of THF at 30 °C for 3 days. After extraction with ether, drying over anhydrous  $\text{Na}_2\text{SO}_4$ , and evaporation, the mixture was submitted to flash chromatography on silica gel ( $\text{CH}_2\text{Cl}_2/\text{MeOH} = 10/1$ ) to produce compound **1**.

**3.1.1. 2-Methyl-3-(n-butyl)penta-3,4-dienoic acid (1a).** The reaction of the corresponding allenic acid ester (1044 mg, 5.3 mmol) with LiOH (250 mg, 10.4 mmol) afforded 817 mg (91%) of **1a** under conditions A: liquid;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  11.64 (br s, 1H), 4.85–4.81 (m, 2H), 3.05–2.95 (m, 1H), 2.08–1.93 (m, 2H), 1.47–1.30 (m, 4H), 1.27 (d,  $J = 7.2$  Hz, 3H), 0.89 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (75.4 MHz,  $\text{CDCl}_3$ )  $\delta$  205.9, 181.3, 103.3, 78.3, 42.1, 30.2, 29.6, 22.3, 15.8, 13.9; IR (neat) 1958, 1711, 1459, 1222  $\text{cm}^{-1}$ ; MS ( $m/z$ ) 168 ( $M^+$ , 4.83), 111 (100); HRMS calcd for  $\text{C}_{10}\text{H}_{16}\text{O}_2(\text{M}^+)$  168.11503; Found 168.11785.

**3.1.2. 3-(n-Butyl)penta-3,4-dienoic acid (1b).** The reaction of the corresponding allenic acid ester (1.132 g, 6.2 mmol) with LiOH (314 mg, 13 mmol) afforded 275 mg (29%) of **1b** under conditions A: liquid;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  10.83 (br s, 1H), 4.78–4.70 (m, 2H), 3.03 (t,  $J = 2.4$  Hz, 2H), 2.08–1.99 (m, 2H), 1.48–1.25 (m, 4H), 0.89 (t,  $J =$

7.2 Hz, 3H);  $^{13}\text{C}$  NMR (75.4 MHz,  $\text{CDCl}_3$ )  $\delta$  207.1, 178.0, 96.7, 76.1, 38.5, 31.2, 29.4, 22.2, 13.8; IR (neat) 1961, 1740  $\text{cm}^{-1}$ ; MS ( $m/z$ ) 154 ( $M^+$ , 11.97), 41 (100); HRMS calcd for  $\text{C}_9\text{H}_{14}\text{O}_2(\text{M}^+)$  154.09938; Found 154.10058.

**3.1.3. 2-Ethyl-3-(n-butyl)penta-3,4-dienoic acid (1c).** The reaction of the corresponding allenic acid ester (3654 mg, 17.4 mmol) with LiOH (945 mg, 39.4 mmol) afforded 3060 mg (97%) of **1c** under conditions A: liquid;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  11.52 (br s, 1H), 4.84–4.79 (m, 2H), 2.77 (t,  $J = 7.5$  Hz, 1H), 2.08–1.92 (m, 2H), 1.85–1.71 (m, 1H), 1.69–1.56 (m, 1H), 1.48–1.25 (m, 4H), 0.94 (t,  $J = 7.5$  Hz, 3H), 0.89 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (75.4 MHz,  $\text{CDCl}_3$ )  $\delta$  206.2, 180.7, 101.8, 77.8, 49.9, 30.3, 29.5, 23.5, 22.3, 13.9, 12.0; IR (neat) 1957, 1707, 1460, 1219  $\text{cm}^{-1}$ ; MS ( $m/z$ ) 182 ( $M^+$ , 1.59), 153 (100); HRMS calcd for  $\text{C}_{11}\text{H}_{18}\text{O}_2\text{Na}(\text{MNa}^+)$  205.1223; Found 205.1219.

**3.1.4. 2-n-(Propyl)-3-n-(butyl)penta-3,4-dienoic acid (1d).** The reaction of the corresponding allenic acid ester (4613 mg, 20.6 mmol) with LiOH (1198 mg, 50 mmol) afforded 3300 mg (82%) of **1d** under conditions A: liquid;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  11.50 (br s, 1H), 4.84–4.76 (m, 2H), 2.87 (t,  $J = 7.5$  Hz, 1H), 2.06–1.92 (m, 2H), 1.63–1.52 (m, 1H), 1.45–1.25 (m, 4H), 1.49–1.25 (m, 6H), 0.91 (t,  $J = 6.9$  Hz, 3H), 0.89 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (75.4 MHz,  $\text{CDCl}_3$ )  $\delta$  206.2, 180.9, 102.0, 77.8, 48.0, 32.4, 30.2, 29.5, 22.3, 20.6, 13.9, 13.8; IR (neat) 1957, 1708, 1466, 1210  $\text{cm}^{-1}$ ; MS ( $m/z$ ) 196 ( $M^+$ , 1.19), 153 (100); HRMS calcd for  $\text{C}_{12}\text{H}_{20}\text{O}_2\text{Na}(\text{MNa}^+)$  219.1355; Found 219.1377.

**3.1.5. 2,3-Dimethylpenta-3,4-dienoic acid (1e).** The reaction of the corresponding allenoic acid ester (1.541 g, 10 mmol) with LiOH (480 mg, 20 mmol) afforded 639 mg (51%) of **1e** under conditions A: liquid;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  11.77 (br s, 1H), 4.79–4.72 (m, 2H), 3.08–2.96 (m, 1H), 1.76 (t,  $J=3.3$  Hz, 3H), 1.28 (d,  $J=6.9$  Hz, 3H);  $^{13}\text{C}$  NMR (75.4 MHz,  $\text{CDCl}_3$ )  $\delta$  206.5, 181.1, 98.0, 76.3, 42.9, 17.1, 15.5; IR (neat) 1962, 1712, 1456, 1223  $\text{cm}^{-1}$ ; MS ( $m/z$ ) 126 ( $\text{M}^+$ , 7.53), 111 (100); HRMS calcd for  $\text{C}_7\text{H}_{10}\text{O}_2(\text{M}^+)$  126.06635; Found 126.06681.

**3.1.6. 2-Methyl-3-(*n*-heptyl)penta-3,4-dienoic acid (1f).** The reaction of the corresponding allenoic acid ester (1.357 g, 5.7 mmol) with LiOH (297 mg, 12.4 mmol) afforded 639 mg (53%) of **1f** under conditions A: liquid;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  11.43 (br s, 1H), 4.86–4.81 (m, 2H), 3.08–2.95 (m, 1H), 2.14–1.92 (m, 2H), 1.48–1.26 (m, 13H), 0.88 (d,  $J=7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (75.4 MHz,  $\text{CDCl}_3$ )  $\delta$  205.9, 181.3, 103.4, 78.2, 42.1, 31.8, 30.5, 29.2, 29.1, 27.4, 22.6, 15.8, 14.1; IR (neat) 1958, 1709, 1459, 1221  $\text{cm}^{-1}$ ; MS ( $m/z$ ) 210 ( $\text{M}^+$ , 3.75), 111 (100); HRMS calcd for  $\text{C}_{13}\text{H}_{22}\text{O}_2(\text{M}^+)$  210.16198; Found 210.16407.

**3.1.7. 2-Methyl-3-(*tert*-butyl)penta-3,4-dienoic acid (1g).** The reaction of the corresponding allenoic acid ester (538 mg, 2.7 mmol) with LiOH (145 mg, 5.5 mmol) afforded 143 mg (31%) of **1g** under conditions A: solid; mp 44 °C (ether);  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  4.86 (s, 2H), 3.06 (q,  $J=6.9$  Hz, 1H), 1.29 (d,  $J=7.2$  Hz, 3H), 1.08 (s, 9H);  $^{13}\text{C}$  NMR (75.4 MHz,  $\text{CDCl}_3$ )  $\delta$  205.3, 181.6, 112.8, 79.1, 37.6, 33.6, 29.0, 18.4; IR (neat) 1950, 1707, 1233  $\text{cm}^{-1}$ ; MS ( $m/z$ ) 169 ( $\text{M}^++1$ , 93.02), 168 ( $\text{M}^+$ , 20.46), 153 (100). Anal. Calcd for  $\text{C}_{10}\text{H}_{16}\text{O}_2$ : C, 71.39; H, 9.59. Found C, 71.46; H, 9.31.

**3.1.8. 2-Methyl-3-allylpenta-3,4-dienoic acid (1h).** The reaction of the corresponding allenoic acid ester (2745 mg, 15.2 mmol) with LiOH (719 mg, 30 mmol) afforded 553 mg (24%) of **1h** under conditions A: liquid;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  10.57 (br s, 1H), 5.88–5.71 (m, 1H), 5.12–5.02 (m, 2H), 4.88–4.83 (m, 2H), 3.09–2.98 (m, 1H), 2.90–2.73 (m, 2H), 1.28 (d,  $J=6.6$  Hz, 3H);  $^{13}\text{C}$  NMR (75.4 MHz,  $\text{CDCl}_3$ )  $\delta$  206.3, 180.9, 135.1, 116.5, 101.6, 78.3, 41.2, 35.7, 15.7; IR (neat) 1958, 1712, 1641  $\text{cm}^{-1}$ ; MS ( $m/z$ ) 153 ( $\text{M}^++1$ , 38.90), 152 ( $\text{M}^+$ , 14.13), 107 (100); HRMS calcd for  $\text{C}_9\text{H}_{12}\text{O}_2(\text{M}^+)$  152.08373; Found 152.08326.

**3.1.9. 2-Methyl-3-benzylpenta-3,4-dienoic acid (1i).** The reaction of the corresponding allenoic acid ester (1.798 g, 7.8 mmol) with LiOH (402 mg, 16.8 mmol) afforded 1.179 g (75%) of **1i** under conditions A: liquid;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  11.78 (br s, 1H), 7.38–7.15 (m, 5H), 4.87 (br s, 2H), 3.52 (d,  $J=15.0$  Hz, 1H), 3.41 (d,  $J=15.0$  Hz, 1H), 3.03–2.92 (m, 1H), 1.28 (d,  $J=7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (75.4 MHz,  $\text{CDCl}_3$ )  $\delta$  206.9, 181.1, 138.7, 129.1, 128.2, 126.4, 102.9, 78.1, 40.6, 38.2, 15.9; IR (neat) 1958, 1705, 1455, 1226  $\text{cm}^{-1}$ ; MS ( $m/z$ ) 202 ( $\text{M}^+$ , 2.59), 129 (100); HRMS calcd for  $\text{C}_{13}\text{H}_{14}\text{O}_2(\text{M}^+)$  202.09938; Found 202.09801.

**3.1.10. 2-(*n*-Propyl)penta-3,4-dienoic acid (1j).** The reaction of the corresponding allenoic acid ester

(1693 mg, 10 mmol) afforded 453 mg (33%) of **1j** under conditions B: liquid;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  11.60 (br s, 1H), 5.20 (q,  $J=3.6$  Hz, 1H), 4.80 (d,  $J=6.9$  Hz, 2H), 3.03 (q,  $J=8.1$  Hz, 1H), 1.83–1.72 (m, 1H), 1.64–1.55 (m, 1H), 1.43–1.34 (m, 2H), 0.92 (t,  $J=7.5$  Hz, 3H);  $^{13}\text{C}$  NMR (75.4 MHz,  $\text{CDCl}_3$ )  $\delta$  208.5, 180.8, 88.7, 76.5, 44.9, 33.9, 20.2, 13.7; IR (neat) 1958, 1709, 1415, 1286, 1208  $\text{cm}^{-1}$ ; MS ( $m/z$ ) 141 ( $\text{M}^++1$ , 4.15), 97 (100); HRMS calcd for  $\text{C}_8\text{H}_{11}\text{O}(\text{M}^+-\text{OH})$  123.08099; Found 123.08177.

**3.1.11. Penta-3,4-dienoic acid (1k).**<sup>11</sup> The reaction of the corresponding allenoic acid ester (2038 mg, 16.2 mmol) afforded 1360 mg (86%) of **1k** under conditions B: liquid;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  11.91 (br s, 1H), 5.23 (pentet,  $J=6.9$  Hz, 1H), 4.79–4.71 (m, 2H), 3.12–3.04 (m, 2H);  $^{13}\text{C}$  NMR (75.4 MHz,  $\text{CDCl}_3$ )  $\delta$  209.3, 178.1, 82.7, 75.9, 33.9; IR (neat) 1960, 1713, 1440  $\text{cm}^{-1}$ ; MS ( $m/z$ ) 98 ( $\text{M}^+$ , 15.03), 97 ( $\text{M}^+-1$ , 40.04), 70 (100).

The reaction of **1a** (86 mg, 5.0 mmol), PhI (85  $\mu\text{l}$ , 7.5 mmol),  $\text{K}_2\text{CO}_3$  (273 mg, 2.0 mmol),  $\text{AgNO}_3$  (8 mg, 0.05 mmol), and  $\text{Pd}(\text{PPh}_3)_4$  (30 mg, 0.025 mmol) in 3 mL of  $\text{CH}_3\text{CN}$  at 70 °C for 33 h produced 30 mg (24%) of **2a** and 9 mg (11%) of **3a** via separation with chromatography on silica gel (petroleum ether/ether = 5/1).

**3.1.12. 3-Methyl-4-(*n*-butyl)-5-benzyl-2(5*H*)-furanone (2a).** Liquid;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.32–7.17 (m, 5H), 5.09–4.97 (m, 1H), 3.15 (dd,  $J=3.6$ , 14.1 Hz, 1H), 2.75 (dd,  $J=7.5$ , 14.1 Hz, 1H), 2.53–2.40 (m, 1H), 2.30–2.22 (m, 1H), 1.74 (s, 3H), 1.52–1.22 (m, 4H), 0.92 (t,  $J=7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (75.4 MHz,  $\text{CDCl}_3$ )  $\delta$  174.3, 162.5, 135.6, 129.2, 128.3, 126.8, 123.9, 82.1, 38.6, 29.7, 26.4, 22.5, 13.6, 8.5; IR (neat) 1754, 1675, 1455  $\text{cm}^{-1}$ ; MS ( $m/z$ ) 244 ( $\text{M}^+$ , 0.62), 84 (100); HRMS calcd for  $\text{C}_{16}\text{H}_{20}\text{O}_2(\text{M}^+)$  244.14633; Found 244.14523.

### 3.2. General procedure for $\text{PdCl}_2(\text{PPh}_3)_2$ -catalyzed cyclization reaction of $\beta$ -alleneoic acids 1

Under  $\text{N}_2$  atmosphere a solution of **1** (0.5 mmol),  $\text{PdCl}_2(\text{PPh}_3)_2$  (18 mg, 5 mol%), anhydrous  $\text{CuCl}_2$  (270 mg, 2 mmol), and  $\text{K}_2\text{CO}_3$  (276 mg, 2 mmol) was stirred in 3 mL of anhydrous DMF at 70 °C for 12 h. The reaction mixture was diluted with ether (50 mL), washed with brine, and dried over anhydrous  $\text{Na}_2\text{SO}_4$ . After evaporation, the residue was submitted to column chromatography on silica gel (petroleum ether/ether = 10/1) to produce **3**.

**3.2.1. 3-Methyl-4-(*n*-butyl)-5-methylene-2(5*H*)-furanone (3a).** The reaction of **1a** (84 mg, 0.5 mmol),  $\text{CuCl}_2$  (266 mg, 2.0 mmol),  $\text{K}_2\text{CO}_3$  (277 mg, 2.0 mmol), and  $\text{Pd}(\text{PPh}_3)_4$  (5 mol%) in 3 mL of DMF at 70 °C for 12 h produced 73 mg (88%) of **3a**: liquid;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  5.06 (d,  $J=2.7$  Hz, 1H), 4.81 (d,  $J=2.7$  Hz, 1H), 2.44 (t,  $J=7.5$  Hz, 2H), 1.91 (s, 3H), 1.56–1.46 (m, 2H), 1.41–1.30 (m, 2H), 0.93 (t,  $J=7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (75.4 MHz,  $\text{CDCl}_3$ )  $\delta$  170.7, 155.2, 150.9, 126.0, 92.5, 31.1, 24.5, 22.6, 13.8, 8.8; IR (neat) 1773, 1648, 1459, 1287  $\text{cm}^{-1}$ ; MS ( $m/z$ ) 167 ( $\text{M}^++1$ , 10.40), 166 ( $\text{M}^+$ , 10.40), 124 (100); HRMS calcd for  $\text{C}_9\text{H}_{11}\text{O}_2(\text{M}^+-\text{CH}_3)$  151.0759; Found 151.0785.

**3.2.2. 5-Methylene-4-(*n*-butyl)-2(5*H*)-furanone (3b).** The reaction of **1b** (74 mg, 0.5 mmol), CuCl<sub>2</sub> (267 mg, 2.0 mmol), K<sub>2</sub>CO<sub>3</sub> (276 mg, 2.0 mmol), and Pd(PPh<sub>3</sub>)<sub>4</sub> (5 mol%) in 3 mL of DMF at 70 °C for 12 h produced 57 mg (78%) of **3b**: liquid; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 5.95–5.92 (m, 1H), 5.13–5.10 (m, 1H), 4.91–4.89 (m, 1H), 2.45 (dt, *J*=1.2, 7.5 Hz, 2H), 1.66–1.52 (m, 2H), 1.46–1.31 (m, 2H), 0.92 (t, *J*=7.5 Hz, 3H); <sup>13</sup>C NMR (75.4 MHz, CDCl<sub>3</sub>) δ 169.2, 159.3, 155.9, 116.6, 94.1, 29.9, 25.7, 22.2, 13.6; IR (neat) 1763, 1651, 1467, 1261 cm<sup>-1</sup>; MS (*m/z*) 153 (M<sup>+</sup>+1, 21.12), 152 (M<sup>+</sup>, 12.22), 110 (100); HRMS calcd for C<sub>9</sub>H<sub>12</sub>O<sub>2</sub>(M<sup>+</sup>) 152.08373; Found 152.08498.

**3.2.3. 3-Ethyl-4-(*n*-butyl)-5-methylene-2(5*H*)-furanone (3c).** The reaction of **1c** (92 mg, 0.5 mmol), CuCl<sub>2</sub> (282 mg, 2.0 mmol), K<sub>2</sub>CO<sub>3</sub> (286 mg, 2.0 mmol), and Pd(PPh<sub>3</sub>)<sub>4</sub> (5 mol%) in 3 mL of DMF at 70 °C for 12 h produced 74 mg (81%) of **3c**: liquid; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 5.04 (d, *J*=2.7 Hz, 1H), 4.79 (d, *J*=2.4 Hz, 1H), 2.42 (t, *J*=7.5 Hz, 2H), 2.32 (q, *J*=7.5 Hz, 2H), 1.57–1.46 (m, 2H), 1.44–1.30 (m, 2H), 1.10 (t, *J*=7.5 Hz, 3H), 0.91 (t, *J*=6.9 Hz, 3H); <sup>13</sup>C NMR (75.4 MHz, CDCl<sub>3</sub>) δ 170.1, 155.1, 150.4, 131.3, 92.5, 31.7, 24.3, 22.6, 17.2, 13.7, 12.7; IR (neat) 1772, 1648, 1463, 1296, 1256 cm<sup>-1</sup>; MS (*m/z*) 181 (M<sup>+</sup>+1, 100); HRMS calcd for C<sub>11</sub>H<sub>16</sub>O<sub>2</sub>Na(MNa)<sup>+</sup> 203.1042; Found 203.1041.

**3.2.4. 3-(*n*-Propyl)-4-(*n*-butyl)-5-methylene-2(5*H*)-furanone (3d).** The reaction of **1d** (98 mg, 0.5 mmol), CuCl<sub>2</sub> (272 mg, 2.0 mmol), K<sub>2</sub>CO<sub>3</sub> (278 mg, 2.0 mmol), and Pd(PPh<sub>3</sub>)<sub>4</sub> (5 mol%) in 3 mL of DMF at 70 °C for 12 h produced 81 mg (84%) of **3d**: liquid; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 5.03 (d, *J*=2.4 Hz, 1H), 4.79 (d, *J*=2.7 Hz, 1H), 2.41 (t, *J*=7.5 Hz, 2H), 2.26 (t, *J*=7.5 Hz, 2H), 1.58–1.46 (m, 4H), 1.40–1.30 (m, 2H), 0.91 (t, *J*=7.5 Hz, 6H); <sup>13</sup>C NMR (75.4 MHz, CDCl<sub>3</sub>) δ 170.2, 155.0, 150.9, 129.9, 92.5, 31.6, 25.7, 24.4, 22.7, 21.4, 13.9, 13.7; IR (neat) 1718, 1648, 1465, 1284 cm<sup>-1</sup>; MS (*m/z*) 195 (M<sup>+</sup>+1, 32.35), 194 (M<sup>+</sup>, 15.12), 123 (100); HRMS calcd for C<sub>12</sub>H<sub>18</sub>O<sub>2</sub>(M<sup>+</sup>) 194.13068; Found 194.13200.

**3.2.5. 3,4-Dimethyl-5-methylene-2(5*H*)-furanone (3e).** The reaction of **1e** (63 mg, 0.5 mmol), CuCl<sub>2</sub> (270 mg, 2.0 mmol), K<sub>2</sub>CO<sub>3</sub> (281 mg, 2.0 mmol), and Pd(PPh<sub>3</sub>)<sub>4</sub> (5 mol%) in 3 mL of DMF at 70 °C for 12 h produced 40 mg (64%) of **3e**: solid; mp 80–81 °C (ether); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 5.03 (d, *J*=2.7 Hz, 1H), 4.79 (d, *J*=2.7 Hz, 1H), 2.04 (s, 3H), 1.89 (s, 3H); <sup>13</sup>C NMR (75.4 MHz, CDCl<sub>3</sub>) δ 170.6, 155.8, 146.6, 126.2, 92.2, 9.9, 8.7; IR (neat) 1763, 1651, 1439, 1285, 1260 cm<sup>-1</sup>; MS (*m/z*) 124 (M<sup>+</sup>, 100); HRMS calcd for C<sub>7</sub>H<sub>8</sub>O<sub>2</sub>(M<sup>+</sup>) 124.05243; Found 124.05262.

**3.2.6. 3-Methyl-4-(*n*-heptyl)-5-methylene-2(5*H*)-furanone (3f).** The reaction of **1f** (105 mg, 0.5 mmol), CuCl<sub>2</sub> (277 mg, 2.0 mmol), K<sub>2</sub>CO<sub>3</sub> (282 mg, 2.0 mmol), and Pd(PPh<sub>3</sub>)<sub>4</sub> (5 mol%) in 3 mL of DMF at 70 °C for 12 h produced 90 mg (84%) of **3f**: liquid; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 5.03 (d, *J*=2.1 Hz, 1H), 4.78 (d, *J*=2.7 Hz, 1H), 2.40 (t, *J*=7.5 Hz, 2H), 1.88 (s, 3H), 1.53–1.46 (m, 2H), 1.30–1.21 (m, 8H), 0.84 (t, *J*=6.9 Hz, 3H); <sup>13</sup>C NMR (75.4 MHz, CDCl<sub>3</sub>) δ 170.7, 155.2, 151.0, 126.0, 92.5, 31.6, 29.4, 29.0, 28.9, 24.8, 22.5, 14.0, 8.8; IR (neat) 1774, 1648,

1466, 1287 cm<sup>-1</sup>; MS (*m/z*) 208 (M<sup>+</sup>, 6.83), 124 (100); HRMS calcd for C<sub>13</sub>H<sub>20</sub>O<sub>2</sub>(M<sup>+</sup>) 208.14633; Found 208.14484.

**3.2.7. 3-Methyl-4-(*tert*-butyl)-5-methylene-2(5*H*)-furanone (3g).** The reaction of **1g** (77 mg, 0.46 mmol), CuCl<sub>2</sub> (250 mg, 1.85 mmol), K<sub>2</sub>CO<sub>3</sub> (262 mg, 1.90 mmol), and Pd(PPh<sub>3</sub>)<sub>4</sub> (5 mol%) in 3 mL of DMF at 70 °C for 12 h produced 53 mg (71%) of **3g**: liquid; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 5.21 (d, *J*=2.1 Hz, 1H), 5.09 (d, *J*=2.1 Hz, 1H), 2.08 (s, 3H), 1.39 (s, 9H); <sup>13</sup>C NMR (75.4 MHz, CDCl<sub>3</sub>) δ 170.9, 155.5, 154.0, 125.4, 97.0, 34.7, 30.9, 11.3; IR (neat) 1770, 1639, 1464, 1274 cm<sup>-1</sup>; MS (*m/z*) 166 (M<sup>+</sup>, 59.06), 123 (100); HRMS calcd for C<sub>10</sub>H<sub>14</sub>O<sub>2</sub>Na(MNa)<sup>+</sup> 189.0886; Found 189.0894.

**3.2.8. 3-Methyl-4-allyl-5-methylene-2(5*H*)-furanone (3h).** The reaction of **1h** (77 mg, 0.5 mmol), CuCl<sub>2</sub> (269 mg, 2.0 mmol), K<sub>2</sub>CO<sub>3</sub> (280 mg, 2.0 mmol), and Pd(PPh<sub>3</sub>)<sub>4</sub> (5 mol%) in 3 mL of DMF at 70 °C for 12 h produced 50 mg (66%) of **3h**: liquid; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 5.86–5.72 (m, 1H), 5.15–5.08 (m, 3H), 4.84 (d, *J*=3.0 Hz, 1H), 3.21 (d, *J*=6.0 Hz, 2H), 1.92 (s, 3H); <sup>13</sup>C NMR (75.4 MHz, CDCl<sub>3</sub>) δ 170.4, 154.8, 147.7, 132.4, 127.1, 117.5, 93.1, 28.9, 8.8; IR (neat) 1782, 1650, 1441, 1287 cm<sup>-1</sup>; MS (*m/z*) 150 (M<sup>+</sup>, 36.37), 79 (100); HRMS calcd for C<sub>9</sub>H<sub>10</sub>O<sub>2</sub>Na(MNa)<sup>+</sup> 173.0573; Found 173.0580.

**3.2.9. 3-Methyl-4-benzyl-5-methylene-2(5*H*)-furanone (3i).** The reaction of **1i** (101 mg, 0.5 mmol), CuCl<sub>2</sub> (264 mg, 2.0 mmol), K<sub>2</sub>CO<sub>3</sub> (282 mg, 2.0 mmol), and Pd(PPh<sub>3</sub>)<sub>4</sub> (5 mol%) in 3 mL of DMF at 70 °C for 12 h produced 90 mg (89%) of **3i**: liquid; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.32–7.13 (m, 5H), 5.08 (d, *J*=2.7 Hz, 1H), 4.81 (d, *J*=2.7 Hz, 1H), 3.82 (s, 2H), 1.94 (s, 3H); <sup>13</sup>C NMR (75.4 MHz, CDCl<sub>3</sub>) δ 170.3, 154.9, 148.4, 136.5, 128.8, 128.1, 127.4, 126.9, 93.7, 30.6, 9.0; IR (neat) 1770, 1648, 1496, 1454, 1287 cm<sup>-1</sup>; MS (*m/z*) 200 (M<sup>+</sup>, 41.10), 84 (100); HRMS calcd for C<sub>13</sub>H<sub>12</sub>O<sub>2</sub>Na(MNa)<sup>+</sup> 223.0729; Found 223.0737.

**3.2.10. 3-(*n*-Propyl)-5-methylene-2(5*H*)-furanone (3j).** The reaction of **1j** (70 mg, 0.5 mmol), CuCl<sub>2</sub> (270 mg, 2.0 mmol), K<sub>2</sub>CO<sub>3</sub> (286 mg, 2.0 mmol), and Pd(PPh<sub>3</sub>)<sub>4</sub> (5 mol%) in 3 mL of DMF at 70 °C for 12 h produced 36 mg (51%) of **3j**: liquid; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.02 (s, 1H), 5.08 (dd, *J*=1.2, 2.4 Hz, 1H), 4.76 (d, *J*=2.4 Hz, 1H), 2.38–2.28 (m, 2H), 1.66–1.54 (m, 2H), 0.95 (t, *J*=6.9 Hz, 3H); <sup>13</sup>C NMR (75.4 MHz, CDCl<sub>3</sub>) δ 170.5, 153.9, 136.4, 128.5, 96.5, 27.1, 20.7, 13.6; IR (neat) 1767, 1465 cm<sup>-1</sup>; MS (*m/z*) 138 (M<sup>+</sup>, 24.48), 84 (100); HRMS calcd for C<sub>8</sub>H<sub>10</sub>O<sub>2</sub>Na(MNa)<sup>+</sup> 161.0573; Found 161.0581.

**3.2.11. 5-Methylene-2(5*H*)-furanone (3k).<sup>12</sup>** The reaction of **1k** (98 mg, 1.0 mmol), CuCl<sub>2</sub> (545 mg, 4.0 mmol), K<sub>2</sub>CO<sub>3</sub> (550 mg, 4.0 mmol), and Pd(PPh<sub>3</sub>)<sub>4</sub> (5 mol%) in 3 mL of DMF at 70 °C for 12 h produced **3k** (31%) (determined by NMR using *p*-methoxyiodobenzene as the internal standard).

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