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A novel, convenient synthetic method of 5-aryl-2,2-dimethyl-3(2H)-furanones (aryl = C<sub>6</sub>H<sub>5</sub>, 2-CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>, 3-CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>, 4-CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>, 2-ClC<sub>6</sub>H<sub>4</sub>, 4-ClC<sub>6</sub>H<sub>4</sub>, 2,4-Cl<sub>2</sub>C<sub>6</sub>H<sub>3</sub>) is described. It involves the Claisen-Schmidt condensation (potassium hydroxide/ethanol) of aromatic aldehydes with 3-hydroxy-3-methyl-2-butanone to give enones, whose bromination followed by alkaline hydrolysis (sodium hydroxide/ethanol) affords 3(2H)-furanone derivatives in 54-64% overall yields. The procedure is also applicable to nicotinaldehyde and furfural, although the yields are not satisfactory.

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Skeletons with a 3(2H)-furanone ring are frequently found in nature as a structural unit of essential oils and biologically active principles such as bullatenone [1] and geiparvarin [2]. Although a number of synthetic methods for 3(2H)-furanones have been reported [3], they can be classified basically to several methodological types: a) acylation of  $\alpha$ -hydroxy ketones [4], b) hydrolysis of 2-butynyl-1,4-diols [3], c) oxidation (selenium dioxide [5] or DDQ [6]) of tetrahydro-3-furanones, and so on [7]. These methods

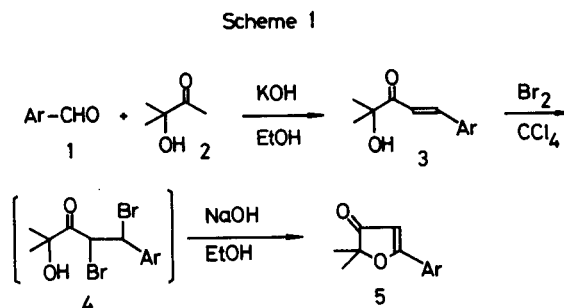


Table 1

Yields and Physical Properties of 1-Aryl-4-hydroxy-4-methyl-1-penten-3-ones **3a-i**

Compound	Aryl	Yield	Bp °C (mm Hg) and/or [Mp °C]	IR cm <sup>-1</sup>	<sup>1</sup> H NMR (carbon tetrachloride) $\delta$
<b>3a</b> [a]	C <sub>6</sub> H <sub>5</sub> -	71	160-170 (0.15)	[a]	[a]
<b>3b</b> [b]	2-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> -	78	170-180 (0.15)	3450 1679 1596	1.38 (s, 6 H), 2.44 (s, 3 H), 3.66 (br s, 1 H), 6.87 (d, 1 H, J = 16 Hz), 7.0-7.3 (m, 4 H), 8.00 (d, 1 H, J = 16 Hz)
<b>3c</b> [c]	3-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> -	75	175-180 (0.15)	3460 1682 1538	1.38 (s, 6 H), 2.35 (s, 3 H), 3.71 (br s, 1 H), 6.91 (d, 1 H, J = 16 Hz), 7.1-7.3 (m, 4 H), 7.64 (d, 1 H, J = 16 Hz)
<b>3d</b> [d]	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> -	77	194-196 (0.2) [64-65 (carbon tetrachloride)]	3460 1570 1680 1605	1.47 (s, 6 H), 2.38 (s, 3 H), 3.70 (br s, 1 H), 7.01 (d, 1 H, J = 15 Hz), 7.2-7.7 (m, 4 H), 7.87 (d, 1 H, J = 15 Hz)
<b>3e</b> [d]	2-ClC <sub>6</sub> H <sub>4</sub> -	83	200-210 (0.2) [59-61 (carbon tetrachloride)]	3440 1560 1675 1600	1.49 (s, 6 H), 3.50 (br s, 1 H), 7.03 (d, 1 H, J = 15 Hz), 7.2-7.8 (m, 4 H), 8.21 (d, 1 H, J = 15 Hz)
<b>3f</b> [d]	4-ClC <sub>6</sub> H <sub>4</sub> -	76	210-215 (0.2) [57-59 (carbon tetrachloride)]	3440 1560 1675 1600	1.37 (s, 6 H), 3.90 (br s, 1 H), 6.69 (d, 1 H, J = 16 Hz), 7.1-7.7 (m, 4 H), 7.65 (d, 1 H, J = 16 Hz)
<b>3g</b> [d]	2,4-Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub> -	72	[115-116 (carbon tetrachloride)]	3460 1583 1675 1603	1.47 (s, 6 H), 3.80 (br s, 1 H), 7.08 (d, 1 H, J = 15 Hz), 7.1-7.8 (m, 3 H), 8.10 (d, 1 H, J = 15 Hz)
<b>3h</b> [e]	3-pyridyl-	79	[f]	3460 1580 1675 1603	1.37 (s, 6 H), 4.50 (br s, 1 H), 7.22 (d, 1 H, J = 17 Hz), 7.62 (d, 1 H, J = 17 Hz), 7.2-8.8 (m, 4 H)
<b>3i</b> [d]	2-furyl-	66	140-145 (2.0)	3475 1550 1675 1603	1.42 (s, 6 H), 4.0 (br s, 1 H), 6.92 (d, 1 H, J = 15 Hz), 7.51 (d, 1 H, J = 15 Hz), 6.4-7.6 (m, 3 H)

[a] See reference [8b]. [b] *Anal.* Calcd. for C<sub>13</sub>H<sub>16</sub>O<sub>2</sub>: C, 76.44; H, 7.90. Found: C, 76.31; H, 8.07. [c] *Anal.* Calcd. for C<sub>13</sub>H<sub>16</sub>O<sub>2</sub>: C, 76.44; H, 7.90. Found: C, 76.27; H, 7.96. [d] See reference [8a]. Details of ir and <sup>1</sup>H nmr spectral data are not reported. [e] *Anal.* Calcd. for C<sub>11</sub>H<sub>13</sub>O<sub>2</sub>N: C, 69.09; H, 6.85. Found: C, 68.81; H, 6.89. [f] Purification by tlc (hexane-acetone 2:1 R<sub>f</sub> 0.25-0.35).

often necessitate the use of strongly basic condition and/or starting materials which are not easily accessible. We describe here a novel and convenient synthetic method to construct 5-aryl-2,2-dimethyl-3(2*H*)-furanone and its application to the synthesis of bullatenone [1,3,7]. It involves three simple reactions sequential as shown in Scheme 1: a) Claisen-Schmidt condensation (potassium hydroxide/ethanol) [8] of aromatic aldehydes with 3-hydroxy-3-methyl-2-butanone (**2**), b) addition of bromine (bromine-carbon tetrachloride) to the resulting enone **3**, and alkaline hydrolysis (sodium hydroxide/ethanol) of the bromine adduct. As the present method utilizes inexpensive, readily available starting materials under experimentally feasible conditions, it can be effectively employed for practical purposes. The yields and physical properties of the compounds **3a-i** as well as **5a-i** are summarized in Table 1 and **2**, respectively.

The operational simplicity of the transformation can be exemplified by the following procedure to prepare bullatenone (**5a**). Condensation of benzaldehyde (**1a**) with  $\alpha$ -hydroxy ketone **2** was carried out in ethanolic potassium hydroxide (two equivalents) by modification of the procedure

reported by King [8a] and Baldwin [8b], which gave 4-hydroxy-4-methyl-1-phenyl-1-penten-3-one (**3a**) in a 71% yield. Treatment of **3a** with one equivalent of bromine in carbon tetrachloride at room temperature gave the bromide **4a** in almost quantitative yield. Compound **4a** was subsequently hydrolyzed in ethanolic sodium hydroxide (two equivalent) at room temperature to afford bullatenone **5a** in a 90% yield (from **3a**). So far as we know, this is the most excellent synthetic method of **5a**. The present method is shown very effective as well for the preparation of other aromatic 3(2*H*)-furanones **5b-i** [9] excepting two examples of homologs carrying heterocycles, *i.e.* **5h** (R = 3-pyridyl) and **5i** (R = 2-furyl).

## EXPERIMENTAL

Melting points were determined on a Yamato Model MP-21 apparatus and uncorrected. Distillation was done by use of a Büchi Kügelrohröfen. Infrared spectra were taken on a JASCO Model A-102 spectrometer. The <sup>1</sup>H nmr spectra (60 MHz) were measured with a JEOL Model JNM PMX60-SI spectrometer. Elemental analyses were carried out by Eiichiro Amano of our laboratory. Preparative tlc was accomplished on silica gel (Kieselgel 60 PF<sub>254</sub>, Merck A. G. Darmstadt).

Experimental details for compounds **3a**, **4a**, and **5a** are described

Table 2

Yields and Physical Properties of 5-Aryl-2,2-dimethyl-3(2*H*)-furanones **5a-i**

Compound	Aryl	Yield % [a]	Bp °C (mm Hg) and/or [Mp °C]	IR cm <sup>-1</sup>	<sup>1</sup> H NMR (carbon tetrachloride) $\delta$	Molecular Formula	Analysis	
							(Calcd/Found) C	H
<b>5a</b> [b]	C <sub>6</sub> H <sub>5</sub> -	90	132-134 (0.3)	[b]	[b]			
<b>5b</b>	2-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> -	74	115-120 (0.24)	1690 1603 1580	1.41 (s, 6 H), 2.48 (s, 3 H), 5.64 (s, 1 H), 7.0-7.7 (m, 4 H)	C <sub>13</sub> H <sub>14</sub> O <sub>2</sub>	77.20 77.35	6.98 6.82
<b>5c</b>	3-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> -	73	108-113 (0.2) [81.5-82.5 (hexane- ether 3:2)]	1679 1611 1567	1.42 (s, 6 H), 2.41 (s, 3 H), 5.78 (s, 1 H), 7.2-7.7 (m, 4 H)	C <sub>13</sub> H <sub>14</sub> O <sub>2</sub>	77.20 77.28	6.98 6.83
<b>5d</b>	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> -	78	108-113 (0.2) [66.5-68.0 (hexane)]	1690 1612 1590	1.42 (s, 6 H), 2.41 (s, 3 H), 5.79 (s, 1 H), 7.12-7.77 (m, 4 H)	C <sub>13</sub> H <sub>14</sub> O <sub>2</sub>	77.20 77.13	6.98 6.82
<b>5e</b>	2-ClC <sub>6</sub> H <sub>4</sub> -	73	[c]	1701 1600 1580 1562	[d] 1.50 (s, 6 H), 6.28 (s, 1 H), 7.2-7.8 (m, 4 H)	C <sub>12</sub> H <sub>11</sub> ClO <sub>2</sub>	64.73 64.58	4.98 4.76
<b>5f</b>	4-ClC <sub>6</sub> H <sub>4</sub> -	88	[132-133 (carbon tetrachloride)]	1685 1605 1590 1560	1.50 (s, 6 H), 5.97 (s, 1 H), 7.3-7.9 (m, 3 H)	C <sub>12</sub> H <sub>11</sub> ClO <sub>2</sub>	64.73 64.75	4.98 5.14
<b>5g</b>	2,4-Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub> -	86	[134-135 (acetone)]	1685 1590	[d] 1.48 (s, 6 H), 6.24 (s, 1 H), 7.1-7.9 (m, 3 H)	C <sub>12</sub> H <sub>10</sub> Cl <sub>2</sub> O <sub>2</sub>	56.06 56.01	3.92 3.98
<b>5h</b>	3-pyridyl-	26	[117-119 (carbon tetrachloride)]	1680 1600 1580	1.50 (s, 6 H), 6.02 (s, 1 H), 7.3-9.1 (m, 4 H)	C <sub>11</sub> H <sub>11</sub> O <sub>2</sub> N	69.83 69.65	5.86 5.72
<b>5i</b>	2-furyl-	14	[e]	1701 1630	[d] 1.48 (s, 6 H), 5.80 (s, 1H), 6.56 (dd, 1 H, J = 2 Hz and 4 Hz), 7.05 (d, 1 H, J = 4 Hz), 7.61 (d, 1 H, J = 2 Hz)	C <sub>10</sub> H <sub>10</sub> O <sub>3</sub>		[f]

[a] Isolated yield from enone **3**. [b] See reference [7a]. [c] Purification by tlc (hexane-acetone 3:1, R<sub>f</sub> 0.33-0.44). [d] Recorded in deuteriochloroform. [e] Purification by tlc (hexane-acetone 3:1, R<sub>f</sub> 0.46-0.58). [f] The compound got darkened on standing for a few days and satisfactory data for elemental analysis could not be obtained.

below as typical procedures. Synthesis of compounds **3b-i**, **4b-i** [9], and **5b-i** were carried out in the similar way.

#### 4-Hydroxy-4-methyl-1-phenyl-1-penten-3-one (**3a**).

To a solution of 3-hydroxy-3-methyl-2-butanone (**2**) (1.43 g, 14 mmoles) and benzaldehyde (**1a**) (1.50 g, 14 mmoles) in ethanol (10 ml), was added a solution of potassium hydroxide (1.57 g, 28 mmoles) in ethanol (10 ml) dropwise over a period of 20 minutes. The solution was stirred for 3 hours at room temperature and then acidified with 10% hydrochloric acid. After removal of ethanol under reduced pressure, the organic layer was extracted with ether, washed with water, dried over magnesium sulfate and then concentrated under vacuum. The crude product was subjected to vacuum distillation to give **3a** [8] (1.89 g, 71%).

#### 4,5-Dibromo-2-hydroxy-2-methyl-5-phenyl-3-pentenone (**4a**).

To a solution of enone **3a** (456 mg, 2.4 mmoles) in carbon tetrachloride (10 ml), was added bromine (384 mg, 2.4 mmoles) at room temperature over a period of 5 minutes. After being stirred for 1 hour, the solvent was removed under reduced pressure to give spectroscopically pure **4a** (684 mg) in almost quantitative yield. Recrystallization from hexane gave analytical sample of **4a**, mp 135-136°; ir (potassium bromide): 3940, 1725  $\text{cm}^{-1}$ ;  $^1\text{H}$  nmr (carbon tetrachloride):  $\delta$  1.45 (s, 3 H), 1.54 (s, 3 H), 2.61 (s, 1 H), 5.25 (d, 1 H,  $J = 11$  Hz), 5.61 (d, 1 H,  $J = 11$  Hz), 7.30 (br s, 5 H). *Anal.* Calcd. for  $\text{C}_{12}\text{H}_{14}\text{Br}_2\text{O}_2$ : C, 44.94; H, 3.77. Found: 45.01; H, 3.84.

#### 2,2-Dimethyl-5-phenyl-3(2H)-furanone (Bullatenone) (**5a**).

To a solution of **4a** (697 mg, 1.99 mmoles) in ethanol (5 ml) was added a solution of sodium hydroxide (159 mg, 3.98 mmoles) in ethanol (5 ml) at room temperature. After being stirred for 30 minutes, the solvent was removed under reduced pressure. The residue was acidified with 10% hydrochloric acid and the organic layer was extracted with ether, washed with water, dried over magnesium sulfate and then concentrated under reduced pressure. The residual oil was subjected to vacuum distillation [bp 132-134° 0.3 mm Hg] to give **5a** (289 mg, 90%), whose spectral data were identical with those reported previously [7a].

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