

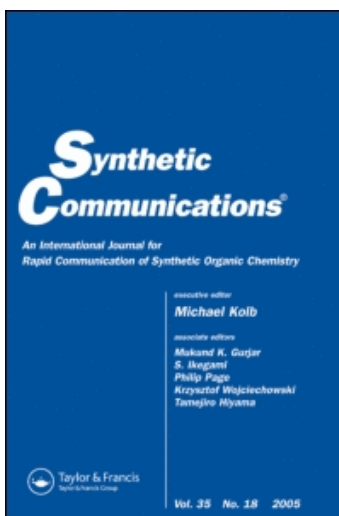
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Deevi Basavaiah<sup>a</sup>; Kannan Muthukumar<sup>a</sup>

<sup>a</sup> School of Chemistry, University of Hyderabad, Hyderabad, India

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## **RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub> CATALYZED ISOMERIZATION OF THE BAYLIS-HILLMAN ADDUCTS**

Deevi Basavaiah\* and Kannan Muthukumar

School of Chemistry, University of Hyderabad, Hyderabad-500 046, India

**Abstract** : RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub> catalyzed isomerization of the Baylis-Hillman adducts *i.e.* methyl 3-aryl-3-hydroxy-2-methylenepropanoates to methyl 3-aryl-2-methyl-3-oxopropanoates has been described.

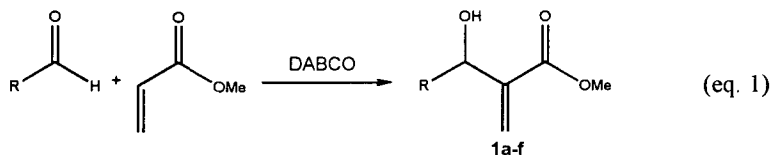
The transition metal catalyzed isomerization of allyl alcohols to saturated carbonyl molecules is an important and useful operation in synthetic organic chemistry and is of current interest.<sup>1-9</sup> In continuation of our interest in the Baylis-Hillman reaction,<sup>10-13</sup> we herein report the ruthenium catalyzed isomerization of the Baylis-Hillman adducts *i.e.* methyl 3-aryl-3-hydroxy-2-methylenepropanoates leading to the formation of methyl 3-aryl-2-methyl-3-oxopropanoates, thus describing a new aspect of Baylis-Hillman chemistry.

The Baylis-Hillman reaction provides functionalized allyl alcohols (eq. 1) which have been successfully employed in various useful organic transformations.<sup>10-19</sup> However, these allyl alcohols have not been employed as substrates for transition metal catalyzed isomerization to obtain the corresponding saturated carbonyl

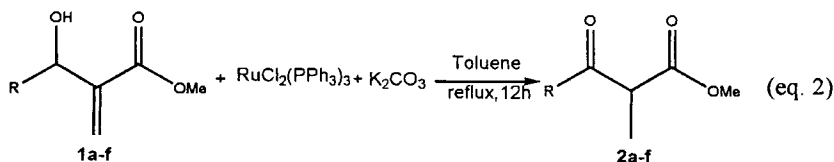
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\* To whom correspondence should be addressed

molecules. We have therefore examined the possible isomerization of these allyl alcohols *i.e.* methyl 3-hydroxy-2-methylenealkanoates (**1**) derived from methyl acrylate under the catalytic influence of  $\text{RuCl}_2(\text{PPh}_3)_3$  with a view to expand the scope of the application of the Baylis-Hillman adducts in organic synthesis. We have first selected methyl 3-hydroxy-2-methylene-3-phenylpropanoate (**1a**) as a substrate for the isomerization reaction. The best result was obtained when this molecule *i.e.* methyl 3-hydroxy-2-methylene-3-phenylpropanoate (**1a**) (1 mM) was treated with a catalytic amount of  $\text{RuCl}_2(\text{PPh}_3)_3$  (4 mol%, 0.04 mM) and  $\text{K}_2\text{CO}_3$  (1 mM) in toluene (2 mL) at reflux temperature for 12 hours to provide the desired methyl 2-methyl-3-oxo-3-phenylpropanoate (**2a**) in 53% yield.



Encouraged by this result, we have subjected a representative class of Baylis-Hillman adducts (**1a-f**) to  $\text{RuCl}_2(\text{PPh}_3)_3$  catalyzed isomerization (eq. 2) (Table) which provided the desired methyl 3-aryl-2-methyl-3-oxopropanoates (**2a-f**) in 42-61% yields.<sup>20</sup>



**Table : Isomerization of the Baylis-Hillman Adducts<sup>a, b</sup>**

Substrate	R	Product	Yield <sup>c</sup>
<b>1a</b>	C <sub>6</sub> H <sub>5</sub>	<b>2a</b>	53
<b>1b</b>	4-MeC <sub>6</sub> H <sub>4</sub>	<b>2b</b>	51
<b>1c</b>	4-EtC <sub>6</sub> H <sub>4</sub>	<b>2c</b>	42
<b>1d</b>	4-i-PrC <sub>6</sub> H <sub>4</sub>	<b>2d</b>	57
<b>1e</b>	4-MeOC <sub>6</sub> H <sub>4</sub>	<b>2e</b>	61
<b>1f</b>	2-MeOC <sub>6</sub> H <sub>4</sub>	<b>2f</b>	50

a) All reactions were carried out in 1 mM scale in toluene at reflux temperature for 12 hours.

b) All products were obtained as colorless liquids and gave satisfactory IR, <sup>1</sup>H NMR, <sup>13</sup>C NMR, mass spectral and elemental analyses.

c) Yields of the products after column chromatography (silica gel, 5% EtOAc in hexane).

In conclusion, we have successfully carried out the RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub> catalyzed isomerization of methyl 3-aryl-3-hydroxy-2-methylenepropanoates to methyl 3-aryl-2-methyl-3-oxopropanoates. Though these kind of β-keto esters can be obtained in better yields using other conventional methods, the present methodology represents a new direction for Baylis-Hillman chemistry.

## EXPERIMENTAL

IR spectra were recorded on Jasco-FT-IR model 5300 spectrometer using samples as neat liquids. <sup>1</sup>H NMR (200 MHz) and <sup>13</sup>C NMR (50 MHz) spectra were recorded on Bruker-AC-200 spectrometer using CDCl<sub>3</sub> as solvent and

tetramethylsilane (TMS,  $\delta = 0$  ppm) as internal standard. Elemental analyses were performed on Perkin-Elmer 240C-CHN analyser. Mass spectra were recorded on Hewlett Packard (model HP 5989A) or Finnigon MAT (1020C ) mass spectrometer.

**General procedure for the isomerization of methyl 3-aryl-3-hydroxy-2-methylenepropanoates:**

To a solution of the allyl alcohol (1) (1 mM) in toluene (2 mL), was added  $\text{RuCl}_2(\text{PPh}_3)_3$  (4 mol%, 0.04 mM, 38 mg) followed by  $\text{K}_2\text{CO}_3$  (1 mM, 138 mg) at room temperature and this suspension was refluxed for 12 hours. Solvent was evaporated under vacuum. The residue obtained was purified by column chromatography (silica gel, 5% EtOAc in hexane) under  $\text{N}_2$  pressure to obtain the pure  $\beta$ -keto ester (2).

**Methyl 2-methyl-3-oxo-3-phenylpropanoate (2a):**

Yield: 53%; IR (neat)/ $\text{cm}^{-1}$  : 1687, 1743;  $^1\text{H}$  NMR :  $\delta$  1.50 (d, 3H,  $J = 6.8$  Hz), 3.68 (s, 3H), 4.40 (q, 1H,  $J = 6.8$  Hz), 7.40-7.67 (m, 3H), 7.98 (d, 2H,  $J = 7.2$  Hz);  $^{13}\text{C}$  NMR :  $\delta$  13.81, 48.09, 52.38, 128.59, 128.76, 133.47, 135.88, 171.26, 195.79; MS ( $m/z$ ) : 192 ( $\text{M}^+$ ); Analysis calculated for  $\text{C}_{11}\text{H}_{12}\text{O}_3$ : C, 68.73; H, 6.29; found: C, 68.80; H, 6.32.

**Methyl 2-methyl-3-(4-methylphenyl)-3-oxopropanoate (2b):**

Yield: 51%; IR (neat)/ $\text{cm}^{-1}$  : 1682, 1743;  $^1\text{H}$  NMR :  $\delta$  1.49 (d, 3H,  $J = 7.0$  Hz), 2.42 (s, 3H), 3.68 (s, 3H), 4.38 (q, 1H,  $J = 7.0$  Hz), 7.27 (d, 2H,  $J = 8.2$  Hz), 7.88 (d, 2H,  $J = 8.2$  Hz);  $^{13}\text{C}$  NMR :  $\delta$  13.69, 21.38, 47.76, 52.11, 128.58, 129.30,

133.25, 144.23, 171.19, 195.23; MS (m/z): 206 (M<sup>+</sup>); Analysis calculated for C<sub>12</sub>H<sub>14</sub>O<sub>3</sub>: C, 69.88; H, 6.84; found: C, 70.11; H, 6.83.

**Methyl 3-(4-ethylphenyl)-2-methyl-3-oxopropanoate (2c):**

Yield: 42%; IR (neat)/cm<sup>-1</sup>: 1684, 1745; <sup>1</sup>H NMR : δ 1.26 (t, 3H, J= 7.6 Hz), 1.48 (d, 3H, J= 6.8 Hz), 2.72 (q, 2H, J= 7.6 Hz), 3.68 (s, 3H), 4.39 (q, 1H, J= 6.8 Hz), 7.30 (d, 2H, J= 8.4 Hz), 7.90 (d, 2H, J= 8.4 Hz); <sup>13</sup>C NMR : δ 13.86, 15.00, 28.91, 47.97, 52.33, 128.25, 128.84, 133.56, 150.53, 171.38, 195.38; MS (m/z): 220 (M<sup>+</sup>); Analysis calculated for C<sub>13</sub>H<sub>16</sub>O<sub>3</sub>: C, 70.88; H, 7.32; found: C, 70.57; H, 7.35.

**Methyl 3-(4-isopropylphenyl)-2-methyl-3-oxopropanoate (2d):**

Yield: 57%; IR (neat)/cm<sup>-1</sup>: 1684, 1743; <sup>1</sup>H NMR : δ 1.27 (d, 6H, J= 7.2 Hz), 1.48 (d, 3H, J=7.0 Hz), 2.95 (q, 1H, J= 7.2 Hz), 3.69 (s, 3H), 4.39 (q, 1H, J= 7.0 Hz), 7.32 (d, 2H, J= 8.0 Hz), 7.93 (d, 2H, J= 8.0 Hz); <sup>13</sup>C NMR : δ 13.80, 23.49, 34.16, 47.84, 52.23, 126.78, 128.83, 133.60, 155.00, 171.30, 195.30; MS (m/z): 234 (M<sup>+</sup>); Analysis calculated for C<sub>14</sub>H<sub>18</sub>O<sub>3</sub>: C, 71.77; H, 7.74; found: C, 71.80; H, 7.76.

**Methyl 3-(4-methoxyphenyl)-2-methyl-3-oxopropanoate (2e):**

Yield: 61%; IR (neat)/cm<sup>-1</sup>: 1678, 1743; <sup>1</sup>H NMR : δ 1.48 (d, 3H, J=7.0 Hz), 3.68 (s, 3H), 3.87 (s, 3H), 4.35 (q, 1H, J= 7.0 Hz), 6.95 (d, 2H, J= 8.8 Hz), 7.96 (d, 2H, J= 8.8 Hz); <sup>13</sup>C NMR : δ 13.78, 47.59, 52.16, 55.35, 113.86, 128.66, 130.83, 163.79, 171.33, 194.16; MS (m/z): 222 (M<sup>+</sup>); Analysis calculated for C<sub>12</sub>H<sub>14</sub>O<sub>4</sub>: C, 64.85; H, 6.34; found: C, 64.62; H, 6.32.

**Methyl 3-(2-methoxyphenyl)-2-methyl-3-oxopropanoate (2f):**

Yield: 50%; IR (neat)/cm<sup>-1</sup>: 1678, 1741; <sup>1</sup>H NMR : δ 1.43 (d, 3H, J=6.8 Hz), 3.66 (s, 3H), 3.87 (s, 3H), 4.33 (q, 1H, J= 6.8 Hz), 7.00 (m, 2H), 7.48 (m, 1H), 7.79 (d,

$^1\text{H}$ ,  $J = 7.8$  Hz);  $^{13}\text{C}$  NMR :  $\delta$  13.41, 51.94, 52.54, 55.26, 111.54, 120.88, 126.69, 131.07, 134.10, 158.47, 171.97, 197.08; MS ( $m/z$ ): 222 ( $M^+$ ); Analysis calculated for  $\text{C}_{12}\text{H}_{14}\text{O}_4$ : C, 64.85; H, 6.34; found: C, 65.00; H, 6.31.

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