

## Notes

Eschenmoser-Claisen Rearrangement of Baylis-Hillman Adducts<sup>†</sup>

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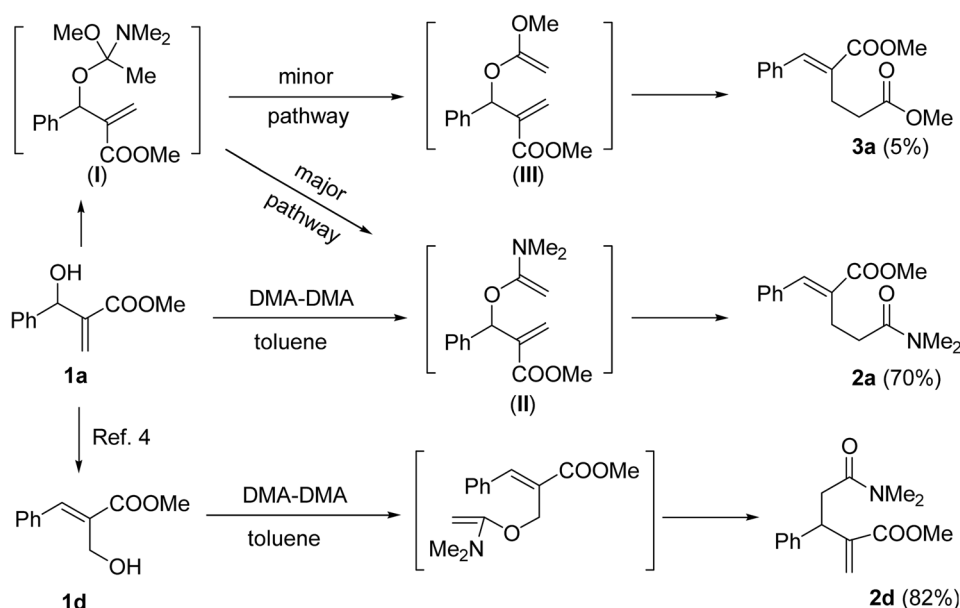
**Key Words :** Eschenmoser-Claisen rearrangement, Baylis-Hillman adducts, DMA-DMA

Johnson-Claisen rearrangement of the Baylis-Hillman adducts has been reported by Basavaiah and co-workers to produce alkyl alk-4-enoate derivatives stereoselectively.<sup>1a</sup> Das and co-workers examined the Johnson-Claisen rearrangement of Baylis-Hillman adducts with triethyl orthoacetate and reported the applicability of I<sub>2</sub>/SiO<sub>2</sub> or NaHSO<sub>4</sub>/SiO<sub>2</sub> systems.<sup>1b,c</sup> We also examined the reaction of *aza*-Baylis-Hillman adducts<sup>2a</sup> and Baylis-Hillman adducts<sup>2b</sup> with *N,N*-dimethylformamide dimethylacetal (DMF-DMA), and we obtained cinnamyl amine derivatives in both cases.<sup>2</sup>

However, literature survey revealed that Eschenmoser-Claisen rearrangement<sup>3</sup> of Baylis-Hillman adducts has not been reported.<sup>2b</sup> Thus, we decided to examine the Eschenmoser-Claisen rearrangement of Baylis-Hillman adducts (**1a-c**, **1g**, and **1h**) and cinnamyl alcohol derivatives (**1d-f**) with *N,N*-dimethylacetamide dimethylacetal (DMA-DMA) and report herein the results (Scheme 1 shows the synthesis of **2a** and **2d** as representative examples)

Required starting materials **1a-h** were synthesized accord-

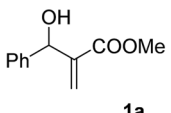
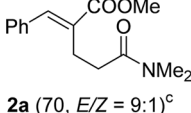
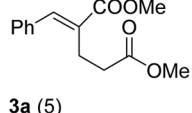
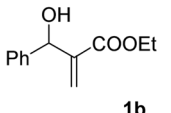
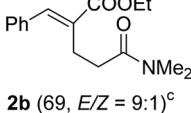
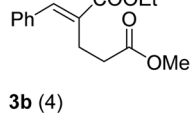
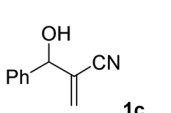
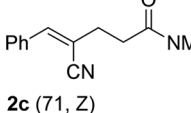
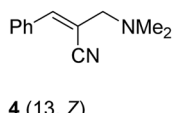
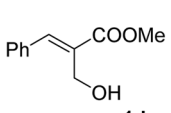
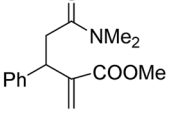
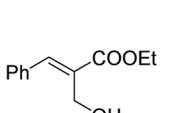
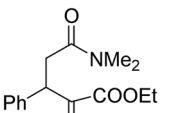
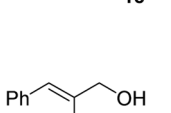
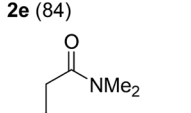
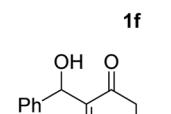
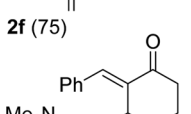
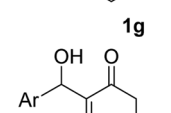
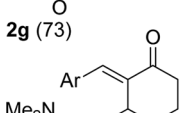
ing to the reported methods.<sup>1,2,4</sup> The reaction conditions including the amounts of DMA-DMA, solvent, and temperature were examined and we found that optimum yields were obtained with 2.0 equiv of DMA-DMA in toluene at around 80-90 °C. The results are summarized in Table 1 and the reaction mechanism is depicted in Scheme 1. For the secondary alcohol derivatives **1a-c**, some ester compounds (**3a**: 5% in entry 1 and **3b**: 4% in entry 2) were formed together (due to the competitive formation of intermediate **III**) and the yields of desired products **2a-c** were moderate (69-71%). The products **2a** and **2b** were isolated as *E/Z* mixtures (*ca.* 9:1) as in the Johnson-Claisen rearrangement of the Baylis-Hillman adducts.<sup>1</sup> The product **2c** was obtained as a pure *Z* isomer, however, 2-dimethylaminomethyl-3-phenylacrylonitrile (**4**, *Z*-form)<sup>2b</sup> was isolated together (13%). The primary alcohol derivatives **1d-f** were cleanly converted into **2d-f** in moderate to good yields (75-84%) and we could not find the corresponding ester derivatives in these cases. The Baylis-Hillman adducts of 2-cyclohexen-1-



Scheme 1

<sup>†</sup>This paper is dedicated to Professor Sang Chul Shim on the occasion of his honorable retirement.

**Table 1.** Eschenmoser-Claisen rearrangement of Baylis-Hillman adducts

Entry	B-H adduct	Product (%) <sup>a,b</sup>	
1	 <b>1a</b>	 <b>2a</b> (70, <i>E/Z</i> = 9:1) <sup>c</sup>	 <b>3a</b> (5)
2	 <b>1b</b>	 <b>2b</b> (69, <i>E/Z</i> = 9:1) <sup>c</sup>	 <b>3b</b> (4)
3	 <b>1c</b>	 <b>2c</b> (71, <i>Z</i> )	 <b>4</b> (13, <i>Z</i> )
4	 <b>1d</b>	 <b>2d</b> (82)	
5	 <b>1e</b>	 <b>2e</b> (84)	
6	 <b>1f</b>	 <b>2f</b> (75)	
7	 <b>1g</b>	 <b>2g</b> (73)	
8 <sup>d</sup>	 <b>1h</b>	 <b>2h</b> (43)	

<sup>a</sup>Isolated yields. <sup>b</sup>The reaction was carried out in toluene with DMA-DMA (2.0 equiv) at 80-90 °C for 2 h. <sup>c</sup>The ratio of *E/Z* was determined based on <sup>1</sup>H NMR. <sup>d</sup>Ar is 4-nitrophenyl.

one, **1g** and **1h**, were also converted into **2g** and **2h**, respectively, in moderate yields.

In summary, we disclosed the Eschenmoser-Claisen rearrangement of Baylis-Hillman adducts<sup>5</sup> and cinnamyl alcohol derivatives with *N,N*-dimethylacetamide-dimethylacetal (DMA-DMA) in toluene to produce 2-benzylidene 1,5-dicarbonyl compounds and 2-methylene 1,5-dicarbonyl derivatives in moderate yields.

### Experimental Section

#### Typical procedure for the synthesis of **2a** and the

**spectroscopic data of 2a-h,3a,3b, and 4 are as follows.** A mixture of **1a** (192 mg, 1.0 mmol) and DMA-DMA (266 mg, 2.0 mmol) in toluene (3 mL) was stirred at 80-90 °C for 2 h. After removal of solvent desired product was separated by column chromatographic purification process (hexanes/EtOAc, 3:5) as pale yellow oil, 183 mg (70%).

Compound **2a**: 70% (*E/Z* = 9:1); pale yellow oil; IR (film) 2950, 1708, 1654, 1648, 1250 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ 2.53-2.58 (m, 2H), 2.86-2.90 (m, 2H), 2.94 (s, 3H), 3.00 (s, 3H), 3.83 (s, 3H), 7.25-7.40 (m, 5H), 7.73 (s, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) δ 23.52, 32.77, 35.34, 37.16, 52.05, 128.65, 128.66, 129.29, 131.61, 135.20, 140.24, 168.62, 171.97.

Compound **2b**:<sup>2b</sup> 69% (*E/Z* = 9:1); pale yellow oil; IR (film) 2935, 1704, 1650 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ 1.35 (t, *J* = 7.2 Hz, 3H), 2.53-2.60 (m, 2H), 2.73-2.76 (m, 2H), 2.94 (s, 3H), 3.00 (s, 3H), 4.28 (q, *J* = 7.2 Hz, 2H), 7.30-7.42 (m, 5H), 7.73 (s, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) δ 14.29, 23.51, 32.78, 35.29, 37.14, 60.84, 128.55, 128.61, 129.25, 130.87, 135.25, 139.92, 168.09, 172.00.

Compound **2c**: 71% (*Z*); yellow solid, mp 47-49 °C; IR (film) 2919, 2203, 1650, 1644 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ 2.66 (t, *J* = 6.9 Hz, 2H), 2.78 (t, *J* = 6.9 Hz, 2H), 2.96 (s, 3H), 3.04 (s, 3H), 7.08 (s, 1H), 7.35-7.44 (m, 3H), 7.70-7.74 (m, 2H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) δ 31.45, 31.64, 35.49, 37.11, 109.82, 118.64, 128.61, 128.76, 130.03, 133.59, 144.71, 170.63.

Compound **2d**: 82%; white solid, mp 73-74 °C; IR (film) 2945, 1720, 1654, 1648, 1642 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ 2.77-2.96 (m, 2H), 2.88 (s, 3H), 2.90 (s, 3H), 3.66 (s, 3H), 4.53 (t, *J* = 7.5 Hz, 1H), 5.63 (s, 1H), 6.32 (s, 1H), 7.16-7.30 (m, 5H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) δ 35.46, 37.15, 38.06, 43.06, 51.83, 124.33, 126.63, 127.81, 128.41, 142.03, 142.89, 166.98, 170.67.

Compound **2e**: 84%; white solid, mp 63-64 °C; IR (film) 2976, 2925, 1716, 1651, 1649 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ 1.18 (t, *J* = 7.2 Hz, 3H), 2.77-2.95 (m, 2H), 2.88 (s, 3H), 2.89 (s, 3H), 4.04-4.15 (m, 2H), 4.52 (t, *J* = 7.5 Hz, 1H), 5.61 (s, 1H), 6.32 (s, 1H), 7.16-7.30 (m, 5H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) δ 14.00, 35.47, 37.17, 38.04, 43.14, 60.69, 123.97, 126.60, 127.86, 128.36, 142.16, 143.17, 166.53, 170.74.

Compound **2f**: 75%; pale yellow solid, mp 71-72 °C; IR (film) 2924, 2211, 1647 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ 2.77-3.08 (m, 2H), 2.93 (s, 3H), 3.02 (s, 3H), 4.24-4.29 (m, 1H), 5.60 (s, 1H), 5.93 (s, 1H), 7.25-7.38 (m, 5H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) δ 35.59, 36.80, 37.20, 46.05, 117.92, 126.10, 127.43, 127.60, 128.97, 131.29, 140.16, 169.54.

Compound **2g**: 73%; pale yellow oil; IR (film) 2936, 1681, 1643 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ 1.83-2.04 (m, 4H), 2.25-2.50 (m, 2H), 2.58-2.66 (m, 2H), 2.88 (s, 3H), 2.92 (s, 3H), 4.01-4.08 (m, 1H), 7.27-7.48 (m, 6H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) δ 19.21, 27.49, 33.34, 35.38, 35.95, 37.11, 40.51, 128.63, 128.78, 129.84, 134.94, 135.02, 141.34, 170.54, 202.97.

Compound **2h**: 43%; pale yellow oil; IR (film) 2930, 1689, 1644 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ 1.88-2.04

(m, 4H), 2.23-2.30 (m, 1H), 2.41-2.50 (m, 1H), 2.60-2.72 (m, 2H), 2.93 (s, 6H), 4.00-4.04 (m, 1H), 7.24 (s, 1H), 7.60 (d,  $J = 8.4$  Hz, 2H), 8.25 (d,  $J = 8.4$  Hz, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  19.39, 27.76, 33.76, 35.58, 35.74, 37.26, 40.79, 123.88, 130.43, 131.75, 141.59, 144.94, 147.29, 170.06, 202.78.

Compound **3a**: 5%; colorless oil;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  2.54-2.60 (m, 2H), 2.85-2.91 (m, 2H), 3.65 (s, 3H), 3.83 (s, 3H), 7.28-7.43 (m, 5H), 7.74 (s, 1H).

Compound **3b**: 4%; colorless oil;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  1.35 (t,  $J = 7.2$  Hz, 3H), 2.54-2.60 (m, 2H), 2.85-2.90 (m, 2H), 3.65 (s, 3H), 4.28 (q,  $J = 7.2$  Hz, 2H), 7.31-7.43 (m, 5H), 7.73 (s, 1H).

Compound **4**:<sup>2b</sup> 13%; colorless oil;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  2.34 (s, 6H), 3.22 (s, 2H), 7.10 (s, 1H), 7.27-7.45 (m, 3H), 7.77-7.81 (m, 2H).

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#### References and Notes

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