

Note

# Tandem Reaction of Deprotonation-Oxidation-Wittig Reaction: Stereoselective Synthesis of (*E*)- $\alpha$ , $\beta$ -Unsaturated Enoates<sup>†</sup>

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Phosphonium or arsonium salt with primary alcohol can undergo the tandem reaction of deprotonation-oxidation-Wittig reaction in the presence of sodium hydroxide and manganese dioxide, providing a general and efficient method for the stereoselective synthesis of (*E*)- $\alpha$ ,  $\beta$ -unsaturated enoates.

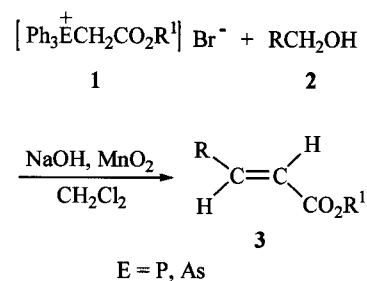
**Keywords** phosphonium or arsonium salt, alcohol, ylide,  $\alpha$ ,  $\beta$ -unsaturated enoate, synthesis, deprotonation, oxidation, Wittig reaction, tandem reaction

Since its discovery, Wittig reaction has become one of primary methods for the formation of carbon-carbon double bonds and been widely used in the synthesis of natural products.<sup>1,2</sup> Recently, it was found that primary alcohols can undergo the tandem reaction of oxidation-Wittig reaction with phosphonium ylides to give corresponding olefination products, which shows great utilities in organic synthesis.<sup>3,4</sup> In order to simplify and improve the reaction, we considered to combine the deprotonation of phosphonium salt, oxidation of alcohol and Wittig reaction into one tandem reaction. To expand this type of tandem reaction further, we extended our study on arsonium ylide.

At the beginning of the study, potassium carbonate was used as a weak base to deprotonate the phosphonium salt **1**, but the tandem reaction of deprotonation-oxidation-Wittig reaction can not take place. It may be due to the fact that the concentration of the *in-situ* formed phosphonium ylide is too low to react with aldehyde. Then we used a stronger base, *i. e.*, sodium hydroxide and found that in the presence of active manganese dioxide, phos-

phonium or arsonium salt **1** and primary alcohols **2** underwent the tandem reaction of deprotonation-oxidation-Wittig reaction smoothly to form the desired products **3** (Scheme 1) with moderate to excellent yields (Table 1). The configurations of the products **3** are *E*-form since the coupling constants of vinyl protons range from 15 to 18 Hz (See Experimental). The protocol has very high stereoselectivity and in most cases, only *E*-isomer was formed. The primary alcohols can be aromatic, allylic, propargylic and unactive aliphatic.

## Scheme 1



In conclusion, the previous reported tandem reaction of oxidation-Wittig reaction is simplified or improved further by the present tandem deprotonation-oxidation-Wittig reaction. For arsonium ylides the present tandem reaction appears more important because most of them are unstable. This tandem protocol also has the advantages of mild reaction conditions, good yields and high stereoselectivities and can be used as a general method for the stereoselective synthesis of (*E*)- $\alpha$ ,  $\beta$ -unsaturated enoates.

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**Table 1** Tandem deprotonation-oxidation-Wittig reaction of phosphonium or arsonium salt **1** with alcohol **2**

Entry	E	R	R <sup>1</sup>	Temp. (°C)	Reaction time (h)	Isolated yields (%) <sup>a</sup>	E/Z <sup>b</sup>
1	P	C <sub>6</sub> H <sub>5</sub>	Et	r. t.	1	95 <sup>5</sup> ( <b>3a</b> )	100/0
2	P	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	Et	r. t.	3	73 <sup>6</sup> ( <b>3b</b> )	99/1
3	P	C <sub>6</sub> H <sub>5</sub> CH=CH	Et	r. t.	2	80 <sup>7</sup> ( <b>3c</b> )	100/0
4	P	CH <sub>2</sub> =CH	Et	Reflux	18	58 <sup>8</sup> ( <b>3d</b> )	98/2
5	P	CH≡C	Et	Reflux	37	61 <sup>9</sup> ( <b>3e</b> )	100/0
6	P	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>14</sub>	Et	Reflux	48	52 <sup>10</sup> ( <b>3f</b> )	100/0
7	P	C <sub>6</sub> H <sub>5</sub>	Me	r. t.	1	81 <sup>5</sup> ( <b>3g</b> )	99/1
8	P	C <sub>6</sub> H <sub>5</sub> CH=CH	Me	r. t.	3	72 <sup>8</sup> ( <b>3h</b> )	100/0
9	As	C <sub>6</sub> H <sub>5</sub>	Et	Reflux	2	85 <sup>5</sup> ( <b>3a</b> )	99/1
10	As	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	Et	Reflux	4	68 <sup>6</sup> ( <b>3b</b> )	98/2
11	As	C <sub>6</sub> H <sub>5</sub> CH=CH	Et	Reflux	3	73 <sup>7</sup> ( <b>3c</b> )	100/0

<sup>a</sup>All products are confirmed by <sup>1</sup>H NMR, IR and MS spectra. <sup>b</sup>The ratio of *Z*-isomer to *E*-isomer is determined by <sup>1</sup>H NMR spectra or GC analysis.

## Experimental

All reactions were carried out in a Schlenk apparatus under nitrogen atmosphere. <sup>1</sup>H NMR spectra were determined in CDCl<sub>3</sub> on a Bruker Advance 400 (400 MHz) spectrometer with TMS as the internal standard. Mass spectra (EI) were obtained on an HP5989B mass spectrometer. IR spectra were taken with a Bruker Vector 22 spectrometer.

### General procedure for the stereoselective synthesis of (*E*)- $\alpha$ , $\beta$ -unsaturated enoates **3a**–**3h**

A mixture of phosphonium or arsonium salt **1** (1.4 mmol), alcohol (1.2 mmol), sodium hydroxide (0.080 g, 2.0 mmol) and manganese dioxide (0.87g, 10 mmol) in dry dichloromethane was stirred at r. t. or under reflux (Table 1). After the reaction was completed (monitored by TLC), the mixture was filtered. The filtrate was concentrated and the crude product was subjected to preparative TLC (hexane-ethyl acetate as eluant) to give **3a**–**3h**.

**3a** Oil (lit.<sup>5</sup>). <sup>1</sup>H NMR  $\delta$ : 7.69 (d, *J* = 16.0 Hz, 1H, =CH), 7.54–7.26 (m, 5H, ArH), 6.44 (d, *J* = 16.0 Hz, 1H, =CH), 4.27 (q, *J* = 7.1 Hz, 2H, OCH<sub>2</sub>), 1.34 (t, *J* = 7.1 Hz, 3H, CH<sub>3</sub>); IR  $\nu$ : 3100, 2981, 1713, 1638, 1495, 768, 712 cm<sup>-1</sup>; MS *m/z* (%): 176 (M<sup>+</sup>, 39), 131 (100).

**3b** Oil (lit.<sup>6</sup>). <sup>1</sup>H NMR  $\delta$ : 7.64 (d, *J* = 16.0 Hz, 1H, =CH), 7.47 (d, *J* = 8.4 Hz, 2H, ArH), 6.90 (d, *J* = 8.6 Hz, 2H, ArH), 6.31 (d, *J* = 15.9 Hz, 1H, =CH), 4.26 (q, *J* = 7.1 Hz, 2H,

OCH<sub>2</sub>), 3.83 (s, 3H, OCH<sub>3</sub>), 1.33 (t, *J* = 7.1 Hz, 3H, CH<sub>3</sub>); IR  $\nu$ : 3050, 2980, 1709, 1605, 1513, 829 cm<sup>-1</sup>; MS *m/z* (%): 206 (M<sup>+</sup>, 100), 162 (97).

**3c** Oil (lit.<sup>7</sup>). <sup>1</sup>H NMR  $\delta$ : 7.50–7.41 (m, 3H, ArH), 7.35–7.22 (m, 3H, ArH + =CH), 6.90–6.85 (m, 2H, =CH), 5.99 (d, *J* = 15.3 Hz, 1H, =CH), 4.23 (q, *J* = 7.1 Hz, 2H, OCH<sub>2</sub>), 1.31 (t, *J* = 7.1 Hz, 3H, CH<sub>3</sub>); IR  $\nu$ : 3100, 2982, 1707, 1626, 1448, 733, 689 cm<sup>-1</sup>; MS *m/z* (%): 202 (M<sup>+</sup>, 22), 129 (100).

**3d** Oil (lit.<sup>8</sup>). <sup>1</sup>H NMR  $\delta$ : 7.27 (dd, *J* = 14.1, 11.0 Hz, 1H, =CH), 6.52–6.40 (m, 1H, =CH), 5.91 (d, *J* = 15.6 Hz, 1H, =CH), 5.61 (dd, *J* = 17.6, 0.7 Hz, 1H, =CH), 5.49 (dd, *J* = 9.6, 0.7 Hz, 1H, =CH), 4.22 (q, *J* = 7.1 Hz, 2H, OCH<sub>2</sub>), 1.32 (t, *J* = 7.1 Hz, 3H, CH<sub>3</sub>); IR  $\nu$ : 3000, 2924, 1722, 1616, 1239, 1155 cm<sup>-1</sup>; MS *m/z* (%): 126 (M<sup>+</sup>, 32), 81 (100).

**3e** Oil (lit.<sup>9</sup>). <sup>1</sup>H NMR  $\delta$ : 6.73 (dd, *J* = 16.0, 2.3 Hz, 1H, =CH), 6.32 (d, *J* = 16.0 Hz, 1H, =CH), 4.22 (q, *J* = 7.1 Hz, 2H, OCH<sub>2</sub>), 3.35 (d, *J* = 2.3 Hz, 1H, =CH), 1.30 (t, *J* = 7.1 Hz, 3H, CH<sub>3</sub>); IR  $\nu$ : 3385, 2925, 1724, 1465, 1377, 1071 cm<sup>-1</sup>; MS *m/z* (%): 125 (M<sup>+</sup> + 1, 51), 79 (100).

**3f** Oil (lit.<sup>10</sup>). <sup>1</sup>H NMR  $\delta$ : 7.02–6.90 (m, 1H, =CH), 5.81 (d, *J* = 15.6 Hz, 1H, =CH), 4.18 (q, *J* = 7.1 Hz, 2H, OCH<sub>2</sub>), 2.30–2.10 (m, 2H, CH<sub>2</sub>), 1.48–1.40 (m, 2H, CH<sub>2</sub>), 1.32–1.24 (m, 27H, 12 × CH<sub>2</sub> + CH<sub>3</sub>), 0.88 (t, *J* = 6.0 Hz,

3H, CH<sub>3</sub>); IR  $\nu$ : 2925, 1725, 1655, 1467, 980 cm<sup>-1</sup>; MS  $m/z$  (%): 311 (M<sup>+</sup> - 1, 4), 43 (100).

**3g** Oil (lit.<sup>5</sup>). <sup>1</sup>H NMR  $\delta$ : 7.70 (d,  $J$  = 16.0 Hz, 1H, = CH), 7.55—7.50 (m, 2H, ArH), 7.40—7.35 (m, 3H, ArH), 6.45 (d,  $J$  = 16.0 Hz, 1H, = CH), 3.81 (s, 3H, OCH<sub>3</sub>); IR  $\nu$ : 3062, 2950, 1698, 1634, 1496, 769, 713 cm<sup>-1</sup>; MS  $m/z$  (%): 162 (M<sup>+</sup>, 64), 131 (100).

**3h** Oil (lit.<sup>8</sup>). <sup>1</sup>H NMR  $\delta$ : 7.50—7.43 (m, 3H, ArH), 7.40—7.28 (m, 3H, ArH + = CH), 6.95—6.80 (m, 2H, 2 × = CH), 6.00 (d,  $J$  = 15.3 Hz, 1H, = CH), 3.78 (s, 3H, OCH<sub>3</sub>); IR  $\nu$ : 3058, 2945, 1716, 1627, 1451, 760, 715 cm<sup>-1</sup>; MS  $m/z$  (%): 188 (M<sup>+</sup>, 34), 129 (100).

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