



# High yield preparation of $\alpha$ -ketophosphonates by oxidation of $\alpha$ -hydroxyphosphonates with zinc dichromate trihydrate ( $ZnCr_2O_7 \cdot 3H_2O$ ) under solvent-free conditions

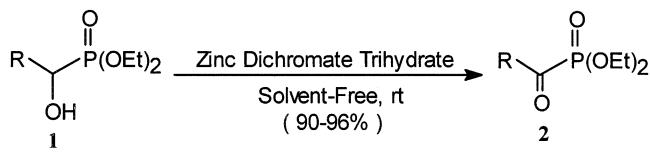
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**Abstract**—Various types of  $\alpha$ -hydroxyphosphonates were converted to  $\alpha$ -ketophosphonates by zinc dichromate trihydrate in high yields and rates under solvent-free conditions. © 2001 Elsevier Science Ltd. All rights reserved.

$\alpha$ -Ketophosphonates are fascinating and versatile compounds in organic synthesis.<sup>1</sup> The chemical properties of  $\alpha$ -ketophosphonates are mainly determined by the phosphorus substituents, but in general are a hybrid between ketones and secondary amides.<sup>2</sup> For instance, it is possible to derive hydrazones,<sup>3</sup> imines,<sup>4</sup> and oximes<sup>5</sup> from the carbonyl function; to reduce  $\alpha$ -ketophosphonates to the corresponding  $\alpha$ -hydroxyphosphonates<sup>6</sup> or use them in Wittig reactions.<sup>7</sup> The C(O)-P bonds in these compounds are known to be sensitive towards hydrolysis.<sup>8</sup> Therefore, handling  $\alpha$ -ketophosphonates is not so easy and requires special precautions.<sup>8</sup> The Michael-Arbuzov reaction is a general method for the preparation of  $\alpha$ -ketophosphonates from acyl chlorides and trialkylphosphites.<sup>9</sup> Oxidation of  $\alpha$ -hydroxyphosphonates<sup>10</sup> is another reaction for the preparation of  $\alpha$ -ketophosphonates. However, a survey of the literature indicates that reports of the oxidation of  $\alpha$ -hydroxyphosphonates are rare. Oxidation by known reagents requires long reaction times, high molar ratios of the oxidant/substrate or special treatment for the activation of the reagent.<sup>11</sup>



**Scheme 1.**

On the other hand, in view of economical and environmental demands, simplicity in processes and low costs, solvent-free reactions in organic synthesis have recently been receiving interest.<sup>12</sup> Along this line, we have reported new methods for functional group transformations.<sup>13</sup>

**Table 1.** Oxidation of  $\alpha$ -hydroxyphosphonates to  $\alpha$ -ketophosphonates by zinc dichromate trihydrate at room temperature under solvent-free conditions; comparison with  $\text{CrO}_3/\text{Al}_2\text{O}_3$ <sup>11b</sup>

Product	R-	$\text{ZnCr}_2\text{O}_7 \cdot 3\text{H}_2\text{O}$	$\text{CrO}_3/\text{Al}_2\text{O}_3$ <sup>11b</sup>		
			Yield <sup>a</sup> (%)	Time <sup>b</sup> (h)	Yield <sup>b</sup> (%)
<b>a</b>	$C_6H_5^-$	95	4	89	
<b>b</b>	$4-\text{CH}_3\text{C}_6\text{H}_4^-$	95	6	85	
<b>c</b>	$4-\text{CH}_3\text{OC}_6\text{H}_4^-$	90	8	78	
<b>d</b>	$2,4,6-(\text{CH}_3)_3\text{C}_6\text{H}_2^-$	90	—	—	
<b>e</b>	$2-\text{ClC}_6\text{H}_4^-$	96	6	75	
<b>f</b>	$3-\text{ClC}_6\text{H}_4^-$	95	—	—	
<b>g</b>	$4-\text{ClC}_6\text{H}_4^-$	94	4	90	
<b>h</b>	$2,6-\text{Cl}_2\text{C}_6\text{H}_3^-$	95	—	—	
<b>i</b>	$2-\text{O}_2\text{NC}_6\text{H}_4^-$	95	4	70	
<b>j</b>	$3-\text{O}_2\text{NC}_6\text{H}_4^-$	90	3	85	
<b>k</b>	$4-\text{O}_2\text{NC}_6\text{H}_4^-$	90	2.5	85	
<b>l</b>	2-naphthyl	91	4	85	
<b>m</b>	$i-\text{C}_3\text{H}_7^-$	92	—	—	

<sup>a</sup> Isolated yields, oxidant/substrate = 1:1, immediate reaction occurred.

<sup>b</sup> Oxidant/substrate = 3:1.

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Herein we report that zinc dichromate trihydrate<sup>14</sup> is an efficient reagent for the preparation of  $\alpha$ -ketophosphonates by oxidation of  $\alpha$ -hydroxyphosphonates at room temperature under solvent-free conditions (Scheme 1). We have compared our results with those reported for CrO<sub>3</sub>/Al<sub>2</sub>O<sub>3</sub> (Table 1).<sup>11b</sup>

As shown in Table 1, in the presence of zinc dichromate trihydrate, various ( $\alpha$ -hydroxyphenylmethyl) phosphonates (**1a–k**) were cleanly converted into the corresponding  $\alpha$ -ketophosphonates (**2a–k**) in excellent yields (90–96%).  $\alpha$ -Hydroxy-2-naphthyl and alkyl phosphonates (**1l,m**) were also oxidized efficiently giving the corresponding  $\alpha$ -ketophosphonates (**2l,m**) in 91–92% yields.

Comparison of the results in the presence of zinc dichromate trihydrate with those reported by CrO<sub>3</sub>/Al<sub>2</sub>O<sub>3</sub> indicated that: (1) the yields are higher; (2) the reaction occurs immediately; (3) the support for the oxidation was not required,<sup>15</sup> and (4) the ratio of the oxidant used was less.<sup>16,17</sup>

In conclusion, mild reaction conditions, high reaction rates, high yields, solventless conditions deserve to be mentioned for the present procedure and make it a useful method for the preparation of various  $\alpha$ -ketophosphonates without requiring a large amount of the oxidant.

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- In our laboratory, we tried similar oxidations with unsupported CrO<sub>3</sub>. The results showed that this reagent was sluggish for this aim and a messy reaction mixture was obtained.
- Typical procedure for the preparation of  $\alpha$ -ketophosphonates from 1-hydroxyphosphonates:* A mixture of the  $\alpha$ -hydroxyphosphonate **1** (5 mmol) and zinc dichromate trihydrate<sup>14</sup> (5 mmol) was ground together in a mortar with a pestle. The reaction occurred immediately and the mixture was washed with carbon tetrachloride (4× 15 ml) and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. The solvent was evaporated to give the desired crude product. The pure product(s) were obtained by vacuum distillation in 90–96% yields (Table 1).
- Spectral data of some  $\alpha$ -ketophosphonates: **2a** [<sup>1</sup>H NMR (CDCl<sub>3</sub>, TMS):  $\delta$  1.37–1.68 (t, 6H,  $J_{HH}$ =7 Hz, 2-OCH<sub>2</sub>CH<sub>3</sub>), 4.08–4.28 (dq, 4H,  $J_{POCH}$ =7.1 Hz,  $J_{HH}$ =7 Hz, 2-OCH<sub>2</sub>CH<sub>3</sub>), 7.28–7.6 (m, 3H), 8.03–8.25 (m, 2H) ppm; IR (neat):  $\nu$  1660 (C=O), 1250 (P=O) cm<sup>-1</sup>; MS: M<sup>+</sup> (242)]. **2b** [<sup>1</sup>H NMR (CDCl<sub>3</sub>, TMS):  $\delta$  1.29–1.42 (t, 6H,  $J_{HH}$ =7 Hz, 2-OCH<sub>2</sub>CH<sub>3</sub>), 2.35 (s, 3H, -CH<sub>3</sub>), 4.11–4.16 (dq, 4H,  $J_{POCH}$ =7.1 Hz,  $J_{HH}$ =7 Hz, 2-OCH<sub>2</sub>CH<sub>3</sub>), 7.12–7.21 (m, 2H), 8.04–8.07 (m, 2H) ppm; IR (neat):  $\nu$  1650 (C=O), 1260 (P=O) cm<sup>-1</sup>; MS: M<sup>+</sup> (256)]. **2c** [<sup>1</sup>H NMR (CDCl<sub>3</sub>, TMS):  $\delta$  1.11–1.29 (t, 6H,  $J_{HH}$ =7 Hz, 2-OCH<sub>2</sub>CH<sub>3</sub>), 3.80 (s, 3H, -CH<sub>3</sub>), 3.90–4.10 (dq, 4H,  $J_{POCH}$ =7.1 Hz,  $J_{HH}$ =7 Hz, 2-OCH<sub>2</sub>CH<sub>3</sub>), 6.84–6.90 (m, 2H), 7.42–7.50 (m, 2H) ppm; IR (neat):  $\nu$  1650 (C=O), 1265 (P=O) cm<sup>-1</sup>; MS: M<sup>+</sup> (272)]. **2d** [<sup>1</sup>H NMR (CDCl<sub>3</sub>, TMS):  $\delta$  1.25–1.32 (t, 6H,  $J_{HH}$ =7 Hz, 2-OCH<sub>2</sub>CH<sub>3</sub>), 2.23 (s, 6H, 2-CH<sub>3</sub>, 6-CH<sub>3</sub>), 2.27 (s, 3H, 4-Me), 4.06–4.17 (dq, 4H,  $J_{POCH}$ =7.1 Hz,  $J_{HH}$ =7 Hz, 2-OCH<sub>2</sub>CH<sub>3</sub>), 6.83 (s, 2H) ppm; IR (neat):  $\nu$  1660 (C=O), 1250 (P=O) cm<sup>-1</sup>; MS: M<sup>+</sup> (284)]. **2g** [<sup>1</sup>H NMR (CDCl<sub>3</sub>, TMS):  $\delta$  1.13–1.42 (t, 6H,  $J_{HH}$ =7 Hz, 2-OCH<sub>2</sub>CH<sub>3</sub>), 4.15–4.33 (dq, 4H,  $J_{POCH}$ =7.1 Hz,  $J_{HH}$ =7 Hz, 2-OCH<sub>2</sub>CH<sub>3</sub>), 7.47–7.50 (m, 2H), 8.21–8.24 (m, 2H) ppm; IR (neat):  $\nu$  1660 (C=O), 1260 (P=O) cm<sup>-1</sup>;

MS: M<sup>+</sup> (277), M<sup>+</sup>+2 (279). **2h** [<sup>1</sup>H NMR (CDCl<sub>3</sub>, TMS): δ 1.04–1.24 (t, 6H, J<sub>HH</sub>=7 Hz, 2-OCH<sub>2</sub>CH<sub>3</sub>), 3.95–4.23 (dq, 4H, J<sub>PoCH</sub>=7.1 Hz, J<sub>HH</sub>=7 Hz, 2-OCH<sub>2</sub>CH<sub>3</sub>), 6.90–7.09 (m, 3H) ppm; IR (neat): ν 1690 (C=O), 1260 (P=O) cm<sup>-1</sup>]. **2i** [<sup>1</sup>H NMR (CDCl<sub>3</sub>, TMS): δ

1.19–1.27 (t, 6H, J<sub>HH</sub>=7 Hz, 2-OCH<sub>2</sub>CH<sub>3</sub>), 4.08–4.18 (dq, 4H, J<sub>PoCH</sub>=7.1 Hz, J<sub>HH</sub>=7 Hz, 2-OCH<sub>2</sub>CH<sub>3</sub>), 7.42–7.47 (m, 1H), 7.64–7.70 (m, 1H), 7.94–8.01 (m, 2H) ppm; IR (neat): ν 1650 (C=O), 1250 (P=O) cm<sup>-1</sup>; MS: M<sup>+</sup> (287)].