## One-pot Synthesis of $\alpha,\beta$ -Butenolides from Methyl (Z)-3-Chloroacrylate

## José Barluenga,\* José R. Fernández, and Miguel Yus

Departamento de Química Orgánica, Facultad de Química, Universidad de Oviedo, Oviedo, Spain

A one-pot synthesis of 4,4-disubstituted  $\alpha$ , $\beta$ -butenolides from methyl (*Z*)-3-chloroacrylate by successive addition of a Grignard reagent, lithiation, and carbonation is described.

The  $\alpha,\beta$ -butenolide ring is present in a large number of biologically important natural products.<sup>1</sup> Recently, we reported the preparation of different dianionic synthons such as (1),<sup>2</sup> (2),<sup>2b</sup> (3),<sup>2c</sup> and (4)<sup>2d</sup> by metallation of the corresponding chlorinated precursors and studied their reactivity toward electrophilic reagents. We report here the preparation of a new type of dianion (5) and its application to the synthesis of  $\alpha,\beta$ -butenolides.

$-0-(c)_{n}-c^{-1}$	-o-c-c=c-	-o-c-c=c-
(1) n = 1	(4)	(5)
(2) n = 2		
(3) n = 3		

 $\alpha,\beta$ -Butenolides (7) were obtained from (6) [in turn obtained from propargyl alcohol by i, oxidation with chromium trioxide;<sup>3</sup> ii, reaction with copper(1) chloride in hydrochloric acid;<sup>4</sup> and iii, methylation with diazomethane in the following way. In a typical procedure a solution of (Z)-3chloroacrylate (6) (15 mmol) in tetrahydrofuran (20 ml) was added to a diethyl ether solution of a Grignard reagent [30 mmol or 15 mmol in the case of (7e)] at -20 °C under argon and the mixture was stirred for 2 h allowing the temperature to rise to 20 °C. Then lithium powder (45 mmol) was added to the resulting suspension at 0 °C and it was stirred overnight. Carbon dioxide was bubbled through the resulting suspension for 3 h at 0 °C and then it was carefully hydrolysed with water, extracted with diethyl ether, and the ethereal layer was washed with water and dried (Na<sub>2</sub>SO<sub>4</sub>). The solvents were distilled or evaporated (15 mmHg) and the residue condensed or distilled at reduced pressure (0.1 mm Hg) to give (7).

Table 1.  $\alpha$ ,  $\beta$ -Butenolides (7) and deuterioalcohols (9).

Entry	Compound	% Yield <sup>a</sup>	B.p. °C/mmHg <sup>b</sup>	<sup>13</sup> C N.m.r. δ <sub>C=O</sub>	Selected data <sup>c</sup> δ <sub>C=C</sub> (ring)
1 2	(7a) (7a)	$\left. \begin{array}{c} 62^{d} \\ 51^{f} \end{array} \right\}$	37—39/0.1e	172.4	162.4, 118.6
3 4	(7b) (7b)	75 <sup>a</sup> 56 <sup>f</sup>	59—61/0.1g	171.6	158.65, 121.3
5	(7c)	51d	62-65/0.1h	171.75	159.7, 120.8
6	(7d)	61 <sup>d</sup>	63-66/0.1	171.7	159.1, 121.55
7	(7e)	58ª	54-57/0.1 <sup>i</sup>	171.9	159.8, 119.6
8	(9b)	80	ii	<u> </u>	142.6, 111.2 <sup>k</sup>
9	(9d)	74	i		142.1, 112.7 <sup>1</sup>

<sup>a</sup> Isolated yield based on the starting material (6). <sup>b</sup> Distillation interval. <sup>c</sup> Neat (Me<sub>4</sub>Si + D<sub>2</sub>O capillary); recorded on a Varian FT-80 spectrometer. <sup>d</sup> Corresponding to the reaction with carbon dioxide. <sup>e</sup> Lit.<sup>5</sup> b.p. 85—88 °C/10 mmHg. <sup>f</sup> Corresponding to the reaction with ethyl chloroformate. <sup>g</sup> Lit.<sup>5</sup> b.p. 122—124 °C/19 mmHg. <sup>h</sup> Lit.<sup>6</sup> b.p. 128 °C/7 mmHg. <sup>i</sup> Lit.<sup>7</sup> b.p. 112—113 °C/1 mmHg. <sup>j</sup> This compound was condensed at room temperature under reduced pressure (0.1 mmHg). <sup>k</sup>  $\delta_{C=CD}$ ,  $J_{CD}$  23.8 Hz. <sup>1</sup>  $\delta_{C=CD}$ ,  $J_{CD}$  23.9 Hz.

Scheme 1. Reagents: i, 2 RMgBr; ii, Li; iii, CO<sub>2</sub> or ClCO<sub>2</sub>Et; iv, H<sub>2</sub>O-HCl.



The use of ethyl chloroformate instead of carbon dioxide afforded the same reaction products (Table 1, entries 2 and 4). After lithiation the intermediates (8)/(8') were formed. Thus, when the reaction was quenched with deuterium oxide, after metallation the corresponding (Z)-3-deuterioallylic alcohols (9) were isolated (Table 1, entries 8 and 9). When ethyl

chloroformate or deuterium oxide were used, the suspension resulting from metallation was filtered off and the corresponding electrophilic agent (15 mmol or 1 ml, respectively) was added to the solution, which was stirred for 3 h and then hydrolysed and worked up as above.

Received, 25th October 1985; Com. 1515

## References

- For general information see: Y. S. Rao, *Chem. Rev.*, 1976, **76**, 625;
  A. A. Avetisyan and M. T. Dangyan, *Russ. Chem. Rev.*, 1977, **46**, 643;
  R. C. Larock, B. Riefling, and C. A. Fellows, *J. Org. Chem.*, 1978, **43**, 131;
  D. Caine and A. S. Frobese, *Tetrahedron Lett.*, 1978, 5167.
- (a) J. Barluenga, J. Flórez, and M. Yus, J. Chem. Soc., Chem. Commun., 1982, 1153; C. Nájera, M. Yus, and D. Seebach, Helv. Chim. Acta, 1984, 67, 289; (b) J. Barluenga, J. Flórez, and M. Yus, Synthesis, 1983, 378; (c) J. Barluenga, J. R. Fernández, J. Flórez, and M. Yus, Synthesis, 1983, 736; (d) J. Barluenga, J. R. Fernández, and M. Yus, J. Chem. Soc., Perkin Trans. 1, 1985, 447.
   W. Viktor, Chem. Ber., 1953, 86, 735.
- 4 A. N. Kurtz, W. E. Billups, R. B. Greenlee, H. F. Hamil, and W. T. Pace, J. Org. Chem., 1965, 30, 3141.
- 5 A. Nobuhara, Agr. Biol. Chem., 1970, 34, 1745.
- 6 P. Canonne, M. Akssira, and G. Lemay, *Tetrahedron Lett.*, 1981, 2611.
- 7 S. Torii, T. Okamoto, and H. Tanaka, J. Org. Chem., 1974, 39, 2486.