

## A Novel Regioselective Ring-opening Oxidation of Cyclobutenones with VO(OEt)Cl<sub>2</sub>

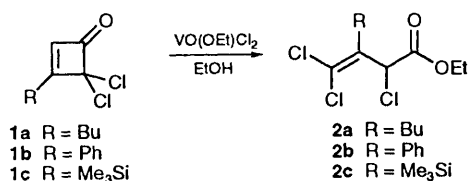
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2,2-Dichlorocyclobut-3-enones undergo VO(OEt)Cl<sub>2</sub>-induced ring-opening oxidation in ethanol to give ethyl 2,4,4-trichlorobut-3-enoates regioselectively.

Ring-opening transformations of small ring compounds have synthetic potential in regioselective construction of carbon skeletons. Such a transformation induced by one-electron oxidation should provide a useful route to radical intermediates. In previous papers, the ring cleavage of cyclobutanones<sup>1</sup> and diketene<sup>2</sup> has been achieved by one-electron oxidation of the alkoxide intermediates with oxovanadium(v). Application to small ring carbonyl compounds, readily derived by cyclizations would make the oxidative ring-opening transformation more versatile. 2,2-Dichlorocyclobut-3-enones **1**, bearing three sp<sup>2</sup> carbons, are obtained by the addition of dichloroketene to acetylenes and have been reported to be versatile synthetic intermediates.<sup>3</sup> The oxidation mode of the strained cyclobutenone **1** is of interest from a structural viewpoint because five- and six-membered cyclic  $\alpha,\beta$ -unsaturated ketones undergo allylic oxidation<sup>4</sup> or dehydrogenative aromatization,<sup>5</sup> respectively. We herein report a novel ring-opening esterification of the cyclobutenone **1** induced by VO(OEt)Cl<sub>2</sub>.

Oxidation of **1** with VO(OEt)Cl<sub>2</sub> in refluxing ethanol led to regioselective ring fission between the carbonyl and dichloro-substituted carbons giving the deconjugate ester **2**, ethyl 2,4,4-trichlorobut-3-enoates, with regioselective introduction of a chloro group at the 2-position (Scheme 1). The  $\gamma,\gamma,\gamma$ -trichloro



Scheme 1

and  $\alpha,\gamma,\gamma$ -trichloro  $\alpha,\beta$ -unsaturated esters were not detected by GLC and <sup>1</sup>H NMR spectroscopy of the crude reaction mixture. The results are listed in Table 1. The addition of lithium chloride or copper(II) chloride increased the yield of **2a**. In contrast, iron(III) chloride interfered with the VO(OEt)Cl<sub>2</sub>-induced ring-opening oxidation. Although VO(OEt)Cl<sub>2</sub> is capable of oxidative cleavage of the carbon-silicon bond of allylic and benzylic silanes,<sup>6</sup> the 3-trimethylsilyl group of **1c** was left intact under the conditions employed here.

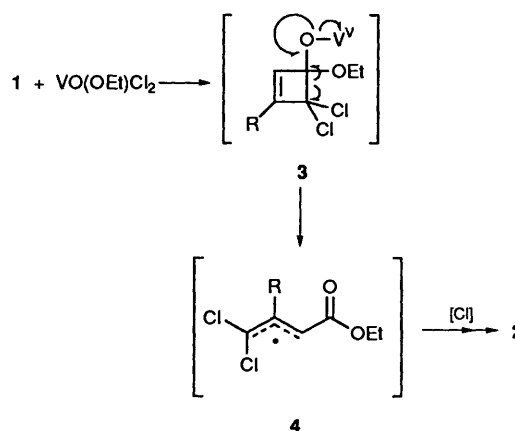
A plausible reaction path is illustrated in Scheme 2. The alkoxide **3** is formed by the addition of VO(OEt)Cl<sub>2</sub> to **1** as an initial step. One-electron oxidation induces the regioselective bond fission between carbonyl and dichloro-substituted carbons to give the more stable allylic radical **4** than the vinylic radical. Regioselective chlorination at the 2-position leads to the  $\beta,\gamma$ -unsaturated ester **2**.

The total transformation from acetylenes is illustrated in Scheme 3. Ethoxycarbonyl and dichloromethylene moieties are regioselectively introduced at the vicinal positions of the

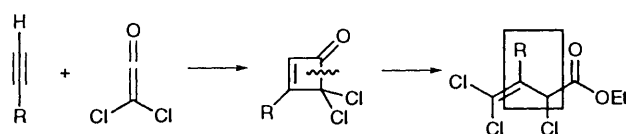
Table 1 VO(OEt)Cl<sub>2</sub>-induced ring-opening oxidation of **1**<sup>a</sup>

Substrate	Additive (mol. equiv.)	t/h	Product	Yield (%)
<b>1a</b>	—	10	<b>2a</b>	15
<b>1a</b>	LiCl (3)	2	<b>2a</b>	25
<b>1a</b>	CuCl <sub>2</sub> (1)	2	<b>2a</b>	33
<b>1a</b>	FeCl <sub>3</sub> (2)	5	<b>2a</b>	trace
<b>1b</b>	—	10	<b>2b</b>	50
<b>1c</b>	—	3	<b>2c</b>	65

<sup>a</sup> VO(OEt)Cl<sub>2</sub> (3 mol. equiv.), EtOH, reflux.



Scheme 2



Scheme 3

acetylenes. The  $\beta,\gamma$ -unsaturated esters obtained should be useful for further synthetic transformations based on, *e.g.*, the allylic chloride or  $\alpha$ -chloro ester function.

VO(OEt)Cl<sub>2</sub> can be considered to be a Lewis acid with one-electron oxidation capability and it is these properties which enable its use in versatile oxidative transformations of small ring carbonyl compounds.

### Experimental

Satisfactory elemental analyses of compounds **2** were obtained. *J* Values are given in Hz.

*General Procedure for the VO(OEt)Cl<sub>2</sub>-induced Oxidation of the Cyclobutenone 1.*—To a solution of the cyclobutenone **1** (1.0 mmol) in ethanol (2 cm<sup>3</sup>) was added VO(OEt)Cl<sub>2</sub> (0.549 g, 3.0

mmol). The mixture was refluxed for the time listed in Table 1 during which time the colour changed to green or blue. Diethyl ether (10 cm<sup>3</sup>) and conc. HCl (0.5 cm<sup>3</sup>) were added to the resultant mixture. The aqueous solution was separated and then extracted with diethyl ether (5 × 10 cm<sup>3</sup>). The combined ethereal solutions were washed with saturated aqueous NH<sub>4</sub>Cl and brine, dried (MgSO<sub>4</sub>) and then concentrated. Preparative TLC of the residue eluting with hexane–ethyl acetate (10–5: 1 v/v) gave the β,γ-unsaturated ester **2** as shown in Table 1.

*Ethyl 3-butyl-2,4,4-trichlorobut-3-enoate 2a.*  $\nu_{\max}(\text{neat})/\text{cm}^{-1}$  1764, 1740 and 1606;  $\delta_{\text{H}}(\text{CDCl}_3; 270 \text{ MHz})$  0.91 (t, 3 H, *J* 7.2), 1.2–1.7 (m, 4 H), 1.31 (t, 3 H, *J* 7.1), 2.25 (ddd, 1 H, *J* 13.5, 10.6, 5.4), 2.42 (ddd, 1 H, *J* 13.5, 11.0, 5.1), 4.26 (q, 2 H, *J* 7.1) and 5.52 (s, 1 H);  $\delta_{\text{C}}(\text{CDCl}_3)$  166.6, 134.2, 123.3, 62.8, 57.8, 30.8, 29.7, 22.8, 14.0 and 13.6; *m/z* (CI) 273 ( $M^+ + 1$ ), 275 ( $M^+ + 3$ ), 277 ( $M^+ + 5$ ) and 279 ( $M^+ + 7$ ).

*Ethyl 2,4,4-trichloro-3-phenylbut-3-enoate 2b.*  $\nu_{\max}(\text{neat})/\text{cm}^{-1}$  1768, 1736 and 1602;  $\delta_{\text{H}}(\text{CDCl}_3; 90 \text{ MHz})$  1.08 (t, 3 H, *J* 7.0), 4.02 (q, 2 H, *J* 7.0), 5.78 (s, 1 H) and 7.1–7.5 (m, 5 H); *m/z* (EI) 292 ( $M^+$ ), 294 ( $M^+ + 2$ ) and 296 ( $M^+ + 4$ ).

*Ethyl 2,4,4-trichloro-3-trimethylsilylbut-3-enoate 2c.*  $\nu_{\max}(\text{neat})/\text{cm}^{-1}$  1764, 1738 and 1550;  $\delta_{\text{H}}(\text{CDCl}_3; 90 \text{ MHz})$  0.32 (s, 9 H), 1.32 (t, 3 H, *J* 6.6), 4.24 (q, 2 H, *J* 6.6) and 5.52 (s, 1 H); *m/z*

(CI) 289 ( $M^+ + 1$ ), 291 ( $M^+ + 3$ ), 293 ( $M^+ + 5$ ) and 295 ( $M^+ + 7$ ).

#### Acknowledgements

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