



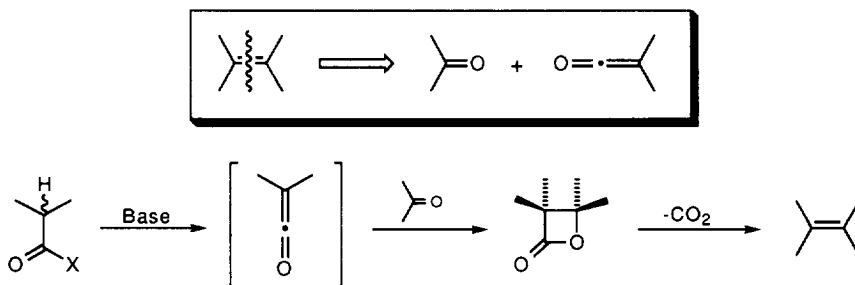
## Tandem [2+2] Cycloaddition-Cycloreversion Reactions in Highly Polar Media: A Convergent One-Pot Entry to Substituted Alkenes and Dienes

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**Abstract.** Reaction at room temperature between acyl chlorides and aromatic or  $\alpha,\beta$ -unsaturated aldehydes in the presence of a tertiary base and in 5M lithium perchlorate-diethyl ether (5M LPDE) as solvent yields substituted alkenes in satisfactory yields. The reaction is formally conceived as a [2+2] cycloaddition between the aldehyde and the *in situ* formed ketene, followed by thermal decarboxylation of the intermediate 2-oxetanone. Ketene itself yields  $\alpha,\beta$ -unsaturated acids under these reaction conditions. Copyright © 1996 Published by Elsevier Science Ltd

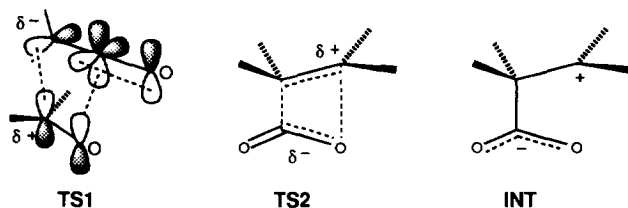
The Wittig<sup>1</sup> and Peterson<sup>2</sup> reactions are among the most useful methods for the convergent synthesis of alkenes. A possible alternative to these reactions consists in a [2+2] cycloaddition between a ketene and a carbonyl compound to form the corresponding 2-oxetanone, whose thermal decarboxylation yields an alkene, usually with total retention of configuration<sup>3</sup> (Scheme 1). These [2+2] cycloaddition-cycloreversion processes have been described separately with highly reactive ketenes such as halo-<sup>4</sup> or cyano ketenes<sup>5</sup> and are usually conducted at relatively high temperatures (80-160°C).



The possible substituents at the different positions are not specified.

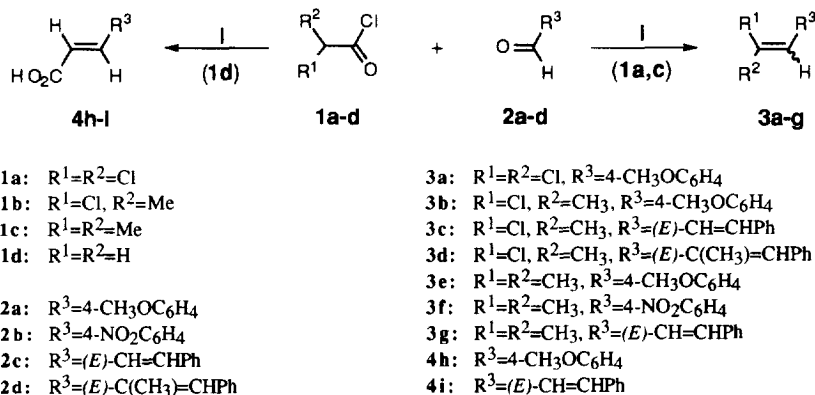
### Scheme 1

Recently, we have studied the mechanism of the former reaction and have found that zwitterionic transition structures such as **TS1** (Scheme 2) are involved,<sup>6</sup> *via* a concerted [ $\pi^2s + (\pi^2s + \pi^2s)$ ] mechanism. Although the mechanism of the second transformation, namely the [2+2] thermal decarboxylation of 2-oxetanones is still controversial,<sup>3b</sup> both transition structures<sup>7</sup> such as **TS2** (Scheme 2) or zwitterionic intermediates<sup>8</sup> such as **INT** are also presumed to be highly polar in nature. Therefore, a polar solvent and/or Lewis catalyst should accelerate *both* processes, thus providing an one-pot entry to the convergent synthesis of alkenes from ketenes and carbonyl compounds.



Scheme 2

With these considerations in mind, we reasoned that, since polar protic media are not compatible with the ketene functionality, a suitable candidate could be the highly polar aprotic solvent 5M lithium perchlorate in diethyl ether discovered by Grieco<sup>9</sup> and successfully applied to several cycloadditions.<sup>10</sup> Therefore, we decided to explore the reaction between aldehydes and ketenes, the latter generated *in situ* from the corresponding acyl chloride in the presence of a tertiary base such as triethylamine and 5M LPDE (Scheme 3). The results obtained are shown in Table 1. A representative experimental procedure is as follows: Triethylamine (4.4 mmol) was added at 0°C under inert atmosphere over a stirred solution of the acyl chloride **1** (4 mmol) and the carbonyl compound **2** (1 mmol) in 2 mL of 5M LPDE.<sup>11</sup> After stirring at room temperature for a certain time (see Table 1), the reaction mixture was diluted with dichloromethane (15 mL) and the resulting solution was washed with water, 1N HCl and saturated solution of sodium bicarbonate. The organic layer was dried, the solvent was evaporated *in vacuo* and the resulting oily residue was purified by bulb-to-bulb distillation or by flash chromatography.



Scheme 3

Reagents and conditions: i: 5M LPDE, NEt<sub>3</sub>, r.t., see Table 1 for reaction times.

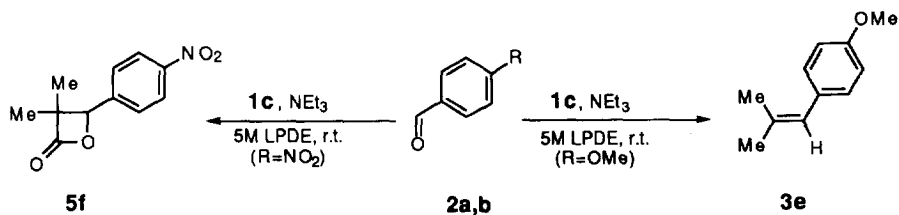
As it can be seen from the data collected in Table 1, the tandem reaction works well with aromatic and  $\alpha,\beta$ -unsaturated aldehydes. Quite surprisingly, dichloroketene was found to be reluctant to react with *p*-anisaldehyde (see Table 1, entry 1). However, when the same reaction was repeated in the absence of lithium perchlorate the conversion was even lower (*ca.* 12% after 6h of reaction time). It is interesting to note that

**Table 1.** Reaction Between Acyl Chlorides **1a-d** and Aldehydes **2a-d**.

Entry	Reactants	Product(s)	Time(h)	E/Z <sup>b</sup>	Yield, % <sup>c</sup>	b.p., °C <sup>d</sup> (P, mmHg)
1	<b>1a</b> + <b>2a</b>	<b>3a</b>	6 <sup>e</sup>		40 (85)	110 (0.4) <sup>i</sup>
2	<b>1b</b> + <b>2a</b>	<b>3b</b>	6	25:75	77	140 (0.5)
3	<b>1b</b> + <b>2c</b>	<b>3c</b>	6	40:60	71	110 (0.25)
4	<b>1b</b> + <b>2d</b>	<b>3d</b>	6 <sup>f</sup>	44:66	67 (75)	130 (0.2)
5	<b>1c</b> + <b>2a</b>	<b>3e</b>	6		81	118 (0.2)
6	<b>1c</b> + <b>2b</b>	<b>5f</b>	6		90	---- <sup>h</sup>
7	<b>1c</b> + <b>2c</b>	<b>3g</b>	6		95	110 (0.15) <sup>j</sup>
8	<b>1d</b> + <b>2a</b>	<b>4h</b>	72		65	m.p.= 170-171 <sup>ok</sup>
9	<b>1d</b> + <b>2c</b>	<b>4i</b>	6 <sup>g</sup>		26 (41)	m.p.= 159-162 <sup>ol</sup>

<sup>a</sup>All the reported products exhibited satisfactory <sup>1</sup>H-NMR, <sup>13</sup>C-NMR, IR and EI-MS analysis. <sup>b</sup>Determined by <sup>1</sup>H-NMR on the crude reaction mixture. The structures were assigned by means of n.O.e experiments. <sup>c</sup>Yield of isolated pure product. Numbers in parentheses are the yields with respect to the recovered aldehyde. <sup>d</sup>Oven temperature in a Kugelrohr apparatus. <sup>e</sup>Conversion of **3a**: 47%. <sup>f</sup>Conversion of **3d**: 89%. <sup>g</sup>Conversion of **4i**: 61%. <sup>h</sup>The title 2-oxetanone decarboxylates under distillation. <sup>i</sup>lit. val.: 120 (1) (see ref. 14). <sup>j</sup>This compound is described in the literature, although its b.p. was not reported (see ref. 15). <sup>k</sup>lit. val.: 172-5° (see ref. 16). <sup>l</sup>lit. val.: 164-165° (see ref. 17).

non-activated ketenes such as dimethylketene (generated *in situ* from **1c**) react at room temperature under the reported reaction conditions. In this case, the reaction virtually does not take place in the absence of lithium perchlorate. 4-Nitrobenzaldehyde forms the intermediate 2-oxetanone **5f** instead of the alkene **3f** (Scheme 4). This result can be explained by the destabilizing effect of the nitro group on the electron deficient center present in the corresponding TS2 or INT species (Scheme 2).  $\alpha,\beta$ -Unsaturated aldehydes **2c,d** also yield the corresponding dienes **3c,d,g** in high yields<sup>12</sup> (entries 3,4,7). In the case of the unsymmetrically substituted chloromethylketene the dienes are obtained as (E)/(Z) mixtures with low stereocontrol. The E/Z ratio remains almost unchanged when (E)- $\alpha$ -methylcynamaldehyde **2d** is used. Unfortunately, acetophenone was unreactive toward **1a** or **1c** in the presence of triethylamine and 5M LPDE.

**Scheme 4**

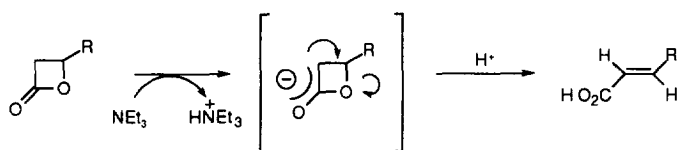
Ketene itself reacts under these conditions. However, it yields (E)- $\alpha,\beta$ -unsaturated acids **4** instead of the corresponding alkenes **3** (see Scheme 3 and Table 1, entries 8 and 9). This result can be interpreted assuming a E1 process from the intermediate INT (Scheme 2) or *via* deprotonation of the corresponding 3-unsubstituted 2-oxetanone.<sup>13</sup>

In summary, we have found that 5M-LPDE promotes the direct conversion of ketenes and aldehydes into alkenes. This transformation is achieved at room temperature and the method works even when unactivated ketenes are used. Further work on this one-pot convergent entry to alkenes is under study in our laboratory and the results will be published in due course.

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11. Lithium perchlorate (A.C.S. reagent, purchased from Aldrich) was heated at 160°C and 0.05 mm Hg in the presence of silica gel or P<sub>2</sub>O<sub>5</sub> for 4 h prior to use. We have found that this treatment is essential for a successful experiment.
12. However, Brady *et al.* have reported that dichloroketene reacts with β-alkoxy-α,β-unsaturated ketones (C<sub>6</sub>H<sub>6</sub>, reflux) to yield [4+2] cycloadducts. See Brady, W. T.; Agno, M. O. *J. Org. Chem.* . **1983**, *48*, 5337.
13. This process has been postulated by Mulzer and can be schematized as follows:



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