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# Simple Access to $\alpha$ , $\beta$ Unsaturated Ketones by Acid-Catalyzed Solvent-Free Reactions

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### SIMPLE ACCESS TO $\alpha$ , $\beta$ UNSATURATED KETONES BY ACID-CATALYZED SOLVENT-FREE REACTIONS

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Abstract : Various chalcones and dibenzylidene cycloalkanones were readily prepared in a few minutes with good yields by simply mixing aromatic aldehydes with substituted acetophenones or benzaldehyde with cycloalkanones in the presence of catalytic amounts of p-toluene sulfonic acid under focused microwave irradiation.

Substituted or unsubstituted chalcones, and their derivatives and more generally  $\alpha,\beta$  unsaturated ketones are important intermediates in organic synthesis which can be engaged in Michael additions<sup>1</sup>, oximation<sup>2</sup> and epoxydation<sup>3</sup>. They also exhibit important pharmacological and biological activities<sup>4</sup>, and are used as U.V. filters in solar creams<sup>5</sup>. Furthermore, symetrical or unsymetrical chalcones are useful intermediates in the synthesis of mesomorphic heteroaromatic salts as dithiolium<sup>6,7</sup> and pyrilium salts<sup>8</sup>. Heterocyclisation of chalcones with P<sub>4</sub>S<sub>10</sub> leads to salts which could exhibit liquid cristal properties.

Usually, the preparation of enones or dienones is achieved with NaOH, KOH or  $Ba(OH)_2$  in hydroalcoholic medium from benzaldehyde and ketones<sup>9-12</sup>. The yields are generally excellent but in the case of cycloalkanones, they are very poor. Alumina and more recently bis(p-ethoxyphenyl) telluroxide have also been used<sup>13</sup>.

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The literature shows that their preparation could be realized in AcOH/H<sub>2</sub>SO<sub>4</sub> mixtures<sup>14</sup>.

We report here our results related to the preparation of  $\alpha$ ,  $\beta$ -unsaturated ketones, without solvent, catalyzed by solid acids under focused microwave irradiation<sup>15</sup>, which to our knowledge, was not attempted up to now. We first studied the reaction of benzaldehyde with acetophénone, without solvent, under microwave irradiation in the presence of a solid acid. The mixture was irradiated during 7 minutes at 30 watts in a single mode microwave oven (Synthewave 402®). The results are reported in Table I.

Table I: Reaction of benzaldehyde with acetophenone leading to chalcone 3a



Entry <sup>a</sup>	Support	Weight	Yield <sup>b</sup>	
	or catalyst	(g)	(%)	
1	K10 (clay)	3	39	
2	K10 (clay)	5	56	
3	K10 (clay)	б	51	
4	KSF (clay)	3	59	
5	KSF (clay)	5	44	
6	PTSA <sup>c</sup>	0.10	65	
7	PTSA	0.20	85	
8	PTSA	0.25	88	

a- All reactions were run with 10 mmoles of benzaldehyde and acetophenone (Final temperature : 105°C).

b- Isolated yield.

c- p-toluene-sulfonic acid.

In order to compare with conventional heating the reaction was monitored at 105°C during 3 minutes in the microwave oven to give 61% yield. In an oil bath previously heated in order to get 105°C in the flask, the yield is 50% after 3 minutes which is comparable.

If montmorillonite K10 or KSF are able to catalyze the formation of chalcone, p-toluene sulfonic acid (PTSA) in catalytic amount (13% mol.) prove to be the more

efficient (entry 8). In all cases, there is an optimal amount of solid acid and for instance a stoichiometric amount of PTSA leads to the formation of tars.

The work-up is particularly easy : addition of ethanol removes PTSA and allows the crystallization of chalcone. A power higher than 30 watts leads to the degradation of the chalcone in some cases. The mechanism of the chalcone formation is outlined on the following scheme : the enolic acetophenone reacts with the protonated carbonyl of benzaldehyde and leads to the hydroxylated compound (which with this method is not isolated) followed by proton loss and dehydration to generate the chalcone 3a.

#### Scheme



The reaction was extended to various aromatic aldehydes and substituted acetophenones (Table II).

On the other hand, we were interested by the reaction of various cycloalkanones with benzaldehyde. The product of the reaction depends on the size of the ring. Dicondensation occurs with n = 4, 5, 6 monocondensation when n = 7. The results are reported in Table III.

In summary, we have realized a very simple, fast and environmentally benign preparation of various chalcones and  $\alpha$ ,  $\beta$ -unsaturated cyclic ketones by simple mixing of the reactants without solvent and irradiation under focused microwaves.

#### Experimental

Reactions under microwave irradiation were performed into a Prolabo Synthewave 402<sup>16</sup> apparatus (2.45 GHz) with a focused system.





<b>3</b> a	Rl	R <sup>2</sup>	Reaction	Yield <sup>b</sup>	mp(°C)	mp(°C)
			time (min)	(%)	EtOH	lit
a	Н	Н	7	88	54	5517
b	Cl	Н	7	80	114	11218
с	$NO_2$	Н	7	84	162	165 <sup>19</sup>
d	MeO	Н	7	73	74	7620
e	Me	Н	8	79	94	9621
f	Н	MeO	7	77	108	10621
g	Н	Me	8	84	78	7721

a- All reactions were run with 30 mmoles of 1 and 2 in presence of PTSA (9%; 0.50g) except for chalcone 3a (40 mmoles; PTSA (13%); 1g).

b- Isolated pure product.

#### General procedure

The inorganic solid (clay) dried in a domestic microwave oven (PHILIPS M 026) during 5 minutes at 400 watts or the acid catalyst (PTSA) were mixed without solvent with the aromatic aldehydes and substituted acetophenones for the preparation of **3a-g**, or with benzaldehyde and cycloketones for **5**, **6**, **7**, **8** then placed in a quartz or pyrex tube and introduced into Synthewave 402 Prolabo microwave reactor, fitted with a stirring device, adjustable power within the range 30-300W and a wave guide (monomode  $T_{01}$ ) for the appropriate time and power (see tables II, III). After cooling and treatment with CH<sub>2</sub>Cl<sub>2</sub>, filtration and concentration in the case of clays, addition of EtOH 95° and cooling at -18° afforded pure crystals of **3a-g**.



Table III : Reaction of benzaldehyde with cyclic ketones 4



a- 30 mmoles of cyclic ketones and 30 or 60 mmoles of benzaldehyde were used.

b- The amount of PTSA and the irradiation power must be adjusted for each particular case.

c- Isolated pure product.

**5** - **8** were crystallized in the appropriate solvent (see table III). All compounds exhibit data in agreement with literature.

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