

## KF-Al<sub>2</sub>O<sub>3</sub> catalysed synthesis of 3-phenyl-2-propenoic acids in dry media under microwave irradiation.

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Malonic acid was condensed with several aryl-substituted aldehydes to the corresponding 3-phenyl-2-propenoic acids under microwave irradiation in solvent-free conditions on potassium fluoride impregnated alumina. Yields were dramatically improved in comparison with classical heating under the same conditions.

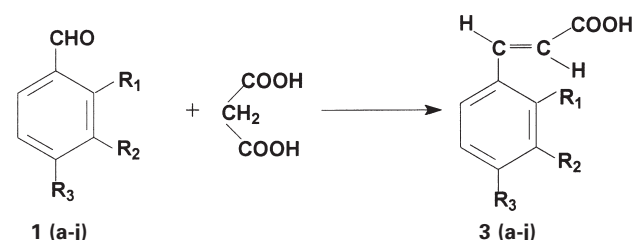
**Key words:** dry media, KF-alumina, 3-phenyl-2-propenoic acid

The aryl-substituted derivatives of 3-phenyl-2-propenoic acids are of practical interest in the preparation of bioactive compounds.<sup>1-4</sup>

Classical methods to obtain these compounds show several difficulties involving undesirable effects of the solvents. These reactions are also classically carried out under refluxing conditions for long durations, frequently with some decomposition of the reagents or products.

Recently, "non-classical" methods have been developed in organic synthesis in order to improve both yields, selectivity and experimental conditions.<sup>5</sup> In particular the use of microwave technology in conjugation with the use of solvent-free conditions allows efficient procedures in organic synthesis.<sup>6-9</sup> The salient features of these high yield protocols lie in enhanced reaction rates, higher purity of products, and very simplified ease of manipulation and work-up. They clearly constitute an eco-friendly approach.<sup>10</sup>

In the present work, we report the convenient and efficient synthesis of 3-phenyl-2-propenoic acids (**3**) under microwave irradiation in dry media using several inorganic solid supports.



(a) R<sub>1</sub>=R<sub>2</sub>=R<sub>3</sub>=H (d) R<sub>1</sub>=R<sub>3</sub>=H, R<sub>2</sub>=NO<sub>2</sub> (g) R<sub>1</sub>=R<sub>2</sub>=H, R<sub>3</sub>=OCH<sub>3</sub>  
 (b) R<sub>1</sub>=Cl, R<sub>2</sub>=R<sub>3</sub>=H (e) R<sub>1</sub>=R<sub>2</sub>=H, R<sub>3</sub>=NO<sub>2</sub> (h) R<sub>1</sub>=H, R<sub>2</sub>=R<sub>3</sub>=OCH<sub>3</sub>  
 (c) R<sub>1</sub>=R<sub>2</sub>=H, R<sub>3</sub>=Cl (f) R<sub>1</sub>=R<sub>2</sub>=H, R<sub>3</sub>=CH<sub>3</sub> (i) R<sub>1</sub>=H, R<sub>2</sub>=OCH<sub>3</sub>, R<sub>3</sub>=OH

**Scheme 1**

Microwave experiments were carried out testing several inorganic supports in order to achieve the best yields whilst avoiding decomposition of both reagents and products. The support/substrate relative amounts were previously optimised. Experiments were replicated in order to ensure reproducibility.

Final temperatures were measured immediately after the reaction using a glass thermometer. In order to check the possible intervention of specific (non-purely thermal) microwave effects, the reactions were also carried out using a thermostatic oil bath 90–100°C with the same reaction medium and conditions as for microwave experiments.

**Table 1** Synthesis of **3a** under microwave (power 800 watts) using several inorganic supports

Support <sup>a</sup>	Reaction time <sup>c</sup> /min	Temperature/°C	Yield/%
No support <sup>d</sup>	5	60	< 10
Al <sub>2</sub> O <sub>3</sub> -KF	2	100	90
Neutral Al <sub>2</sub> O <sub>3</sub>	3	93	59
Basic Al <sub>2</sub> O <sub>3</sub>	4	95	80
Acidic Al <sub>2</sub> O <sub>3</sub> <sup>b</sup>	4	98	46
K10	4	90	30
KSF	5	97	41

<sup>a</sup> 1g by reacting equivalent amounts of malonic acid and benzaldehyde (2 mmol)

<sup>b</sup> Previously calcinated at 500°C.

<sup>c</sup> Time at which maximum yield was obtained

Table 1 shows the most significant results obtained in the synthesis of **3a** (R<sub>1</sub>=R<sub>2</sub>=R<sub>3</sub>=H) under microwave irradiation in dry media. The best yield (90% in isolated product) was reached using potassium fluoride impregnated in dry media. Experiments performed at higher output power and for longer exposure times were unsuccessful (no higher yields were observed and more decomposition products were detected by TLC analysis from the reaction mixture). Yields were determined from isolated products.

Experiments performed in a thermostated oil bath lead to low yields as shown in Table 2, with the starting materials and decomposition products as the complements.

The results in Table 2 allow us to propose the microwave-dry media coupled method with potassium fluoride impregnated alumina as an efficient and selective technique to prepare the 3-phenyl-2-propenoic acids (**3 a-I**). In each case the time specified is that at which maximum yield was obtained. A strong specific non-thermal microwave effect was evidenced, as yields were incremented from 4–25% to 88–96%.

We could suggest two explanations for the improvement achieved with this method both on products yields and reaction selectivity.

- (i) The more polar charged intermediates could have a strong microwave absorption with a consequent rise of temperature, which accelerates the formation of very polar and volatile water and also avoids the reversibility of the process.
- (ii) The second effect could be the strong basicity of KF-alumina: It is believed that KF-Al<sub>2</sub>O<sub>3</sub> owes its efficient and versatile reactivity as a heterogeneous base for organic synthesis to at least three possible mechanisms: dispersion and increased surface area of KF giving coordinately unsaturated F<sup>-</sup>; liberation of strong base during preparation, and the co-operative action of F<sup>-</sup> and the hydrated alumina surface.

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**Table 2** Comparison between microwave and oil bath (90 – 100°C) for synthesis of **3 (a-i)**

Entry	Microwave		Oil bath/%		Melting point/°C Found/Reported	H <sup>1</sup> NMR (CDCl <sub>3</sub> );(MS, M <sup>+</sup> )
	Time/min	Yield/%	60 min	300 min		
<b>3a</b>	2	90	15	25	132–134/131–132 <sup>11</sup>	6.36(d,1H, = CH); 7.4–7.52 (m,5H,ArH); 7.72 (d,1H, =CH); 12.0 (OH); (148).
<b>3b</b>	2	88	9	13	208–210/211–212 <sup>14</sup>	6.54 (d,1H, = CH), 6.95–7.22 (m,3H ,ArH), 7.52(dd,1H, ArH) 7.67((d,1H, =CH); 12.5 (OH); (182).
<b>3c</b>	3	89	10	15	243–245/245 <sup>14</sup>	6.42 (d,1H, = CH), 7.33–7.36 (m,2H ,ArH), 7.70((d,1H, = CH), 7.76–7.79 (m,2H ,ArH); 12.3 (OH); (182).
<b>3d</b>	3	90	9	12	196–198/196–197 <sup>12</sup>	6.41 (d,1H, = CH), 7.47 (t, 1H, ArH), 7.87((d,1H, = CH), 7.91–8.05 (m,2H ,ArH), 8.58(d,1H, ArH), 12.7 (OH); (193).
<b>3e</b>	2	90	Traces	8	283–285/284–285 <sup>12</sup>	6.62 (d,1H, = CH), 7.63(d,1H, = CH), 7.85–7.88 (m,2H,ArH), 7.90–7.93(m,2H, ArH), 12.6 (OH); (193).
<b>3f</b>	3	96	Traces	4	196–198/197–198 <sup>13</sup>	2.10 (s, 3H, CH <sub>3</sub> ), 6.62(d,1H, = CH),7.32–7.34 (m,2H ,ArH), 7.56–7.60(m,2H, ArH), 7.9((d,1H, = CH), 12.3 (OH); (162).
<b>3g</b>	3	89	Traces	6	169–171/170–171 <sup>13</sup>	3.83 (s, 3H, OCH <sub>3</sub> ), 6.31(d,1H, = CH), 6.90–6.93 (m,2H,ArH), 7.50–7.53 (m,2H, ArH), 7.71((d,1H, = CH), 12.2 (OH); (178).
<b>3h</b>	4	90	Traces	6	181–183/180 <sup>15</sup>	3.87 (s, 3H, OCH <sub>3</sub> ), 3.87(s, 3H, OCH <sub>3</sub> ), 6.35 (d,1H, = CH), 6.87–6.89 (t,1H,ArH), 7.08 (m,1H,ArH), 7.13–7.15 (dd,1H,ArH), 7.73 (d,1H, = CH), 12.0 (OH); (208).
<b>3i</b>	4	92	9	10	172–174/172–174 <sup>15</sup>	3.88 (s,3H,OCH <sub>3</sub> ), 6.40(d,1H, = CH), 6.86–6.8 (qq,1H,ArH), 7.13–7.15(dd,1H,ArH), 7.32 (m,1H,ArH), 7.62(d,1H, = CH), 12.5 (OH); (196).

## Experimental

**General:** Microwave irradiation were carried out using a commercial oven (Panasonic NN-S539WF) operating at a frequency 2450 MHz. Melting points (uncorrected) were recorded on a Gallenkamp apparatus. IR spectra were recorded as KBr disks on a Phillips analytical PU 9600 FTIR spectrometer. <sup>1</sup>H NMR data were determined on a Bruker 250FAC spectrometer with CDCl<sub>3</sub> as solvent and TMS as internal reference. Mass spectra were recorded on quadrupolar TRIO 1000 instrument. Malonic acid and aromatic aldehydes used were commercial samples.

**Typical procedure:** malonic acid **1** (2 mmol) was dissolved in acetone. An equimolar quantity of indicated aldehydes were then added and the mixture then smoothly mixed with 1g of KF – alumina. The solvent was removed under reduced pressure. The resulting mixture was placed into a Pyrex-glass open vassel and irradiated in a microwave domestic oven at 800 watts for the times and final temperatures as indicated in Tables 1 and 2. The products were extracted from the support with acetone (3 × 10 ml) and precipitated with ice water.

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