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**APPLICATION OF MICROWAVE IRRADIATION TECHNIQUES FOR  
THE SYNTHESSES OF CINNAMIC ACIDS BY DOEBNER  
CONDENSATION**

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**Abstract :** The reaction rate of Doebner condensation to achieve cinnamic acids can be dramatically enhanced by irradiating the reaction mixture containing an aromatic aldehyde, malonic acid, pyridine and a trace of piperidine with a commercial microwave oven. Ten cinnamic acids were synthesized within 2-5 min in excellent yields.

In the recent years the use of microwave irradiation in organic reactions is rapidly increasing, because of the short reaction time and the operational simplicity. It has been commonly employed as thermal energy source in various organic reactions<sup>1</sup>. The use of domestic microwave oven in this regard is now a well established procedure in MORE<sup>2</sup> (microwave-induced organic reaction enhancement) chemistry. It has been reported that a variety of reactions such as Diels-Alder<sup>3</sup>, ene<sup>4</sup>, Claisen reactions<sup>5</sup>, Knoevenagel condensation<sup>6</sup>, Fischer cyclization<sup>7</sup>, Hantzsch synthesis<sup>8</sup>, Michael addition<sup>9</sup>, Heck reaction<sup>10</sup>, oxidation<sup>11</sup>,

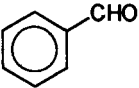
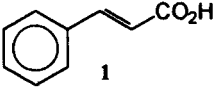
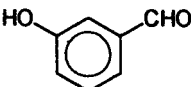
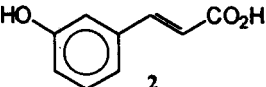
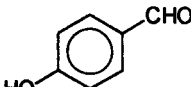
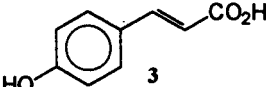
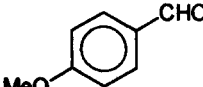
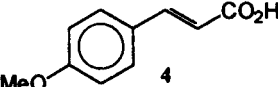
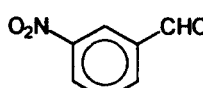
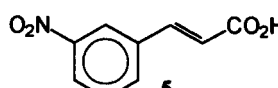
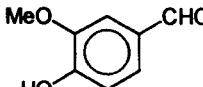
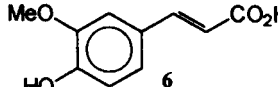
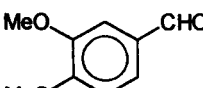
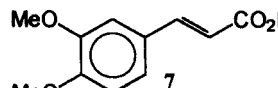
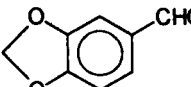
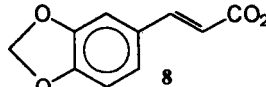
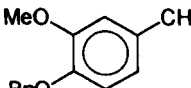
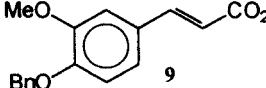
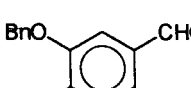
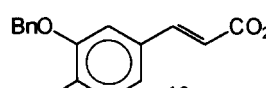
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reduction<sup>12</sup>, hydrolysis of ester<sup>13</sup>, diacetylation<sup>14</sup>, deacetylation<sup>15</sup>, synthesis of oxazolines<sup>16</sup>, nitriles<sup>17</sup>, coumarins<sup>18</sup> could be facilitated by microwave irradiation.

In continuation of our work<sup>19</sup> in lignan synthesis we needed to prepare a variety of cinnamic acids. Condensation of malonic acid with various aromatic aldehydes in the presence of pyridine and a trace of piperidine by Doebner reaction<sup>20</sup> condition have previously been effected to produce cinnamic acids by using conventional heating<sup>21</sup> for 2-4.5 hr. Herein we wish to report the rapid syntheses of a number of cinnamic acids (1-10) in very high yield by Doebner condensation between malonic acid and various aromatic aldehydes containing electron donating groups such as hydroxy, methoxy and electron withdrawing group like nitro under microwave irradiation in domestic microwave oven. Some of these cinnamic acids are naturally occurring compounds *viz.* p-coumaric acid<sup>22,23</sup> (3), coumaric acid methyl ether<sup>22</sup> (4), ferulic acid<sup>22</sup> (6), 3,4-dimethoxycinnamic acid<sup>22</sup> (7) etc. They have been successfully exploited as synthetic intermediates in the synthesis of several lignans<sup>24</sup> and cyclobutane derivatives<sup>25</sup>. To carry out this condensation an Erlenmeyer flask with a funnel as a loose top and over the funnel a round bottomed flask containing some amount of ice acting as a condenser, was used as the reaction vessel. The reactions were usually completed within 2-5 min at power level 5 and gave improved yields over conventional heating method. The results from microwave method of the syntheses of cinnamic acids (1-10) by Doebner condensation of malonic acid with various aromatic aldehydes are summerized in Table 1. Spectacular results have been obtained giving clear indications on the potentialities and advantages of this new technique when

Table 1

Entry	Substrate	Product	Time (min)	Yield (%)	mp (°C)	Lit.mp (°C)
1		 1	2	97	133	133 <sup>26</sup>
2		 2	3	95	198	—
3		 3	3	96	208	206 <sup>26</sup>
4		 4	5	97	171	172 <sup>26</sup>
5		 5	2	97	197	197 <sup>27</sup>
6		 6	5	94	166	168 <sup>22</sup>
7		 7	5	96	178	180 <sup>22</sup>
8		 8	5	96	237	238 <sup>27</sup>
9		 9	5	96	190-191	—
10		 10	5	96	206-208	—

compared to conventional methods. Performing the reaction in such conditions result in faster and cleaner reactions due to less thermal decomposition of products and minimization of secondary processes. All the products were characterized by IR and  $^1\text{H}$  NMR spectral data. The well corroborated melting points of the known compounds (reported<sup>22,26,27</sup> as *trans*) and the coupling constants ( $J \simeq 16$  Hz) of 2-H and 3-H of the products indicate that the  $\alpha,\beta$ -unsaturated acids are in *trans* form.

In summary, we have demonstrated a practical application of the microwave enhanced syntheses of cinnamic acids by Doebner condensation, in which even deactivated aldehydes with electron donating substituents can undergo the desired condensation with nearly quantitative yield in a few minutes.

## Experimental

Melting points were taken in open capillary on an electrically heated metal block and are uncorrected. The IR spectra were run on Perkin-Elmer 782 spectrophotometer.  $^1\text{H}$  NMR spectra were determined in *d*-chloroform solution except **3** which was run in  $\text{d}_6$ -DMSO on a FT NMR Bruker AM 300L operating at 300 MHz and reported in  $\delta$  ppm using tetramethylsilane as the internal standard. The reactions were carried out in a domestic microwave oven (BPL, BMO-700T, 1200W).

## General Procedure

A mixture of aromatic aldehyde (3.0 mmol), malonic acid (6.0 mmol), pyridine (1.0 mL) and piperidine (0.01 mL) was irradiated for 2-5 min in a

microwave oven at power level 5. The mixture was cooled. The excess pyridine was neutralized by the addition of cold 1:1 hydrochloric acid. The precipitated acid was filtered and washed with cold water and recrystallized from ethanol.

$^1\text{H}$  NMR spectral data of the substituted cinnamic acids (**2-10**) are given below.

**2** :  $\delta_{\text{H}}$  7.57 (1H, d,  $J = 15.9$  Hz, 3-H), 7.14-6.70 (4H, m, Ar-H), 6.33 (1H, d,  $J = 15.9$  Hz, 2-H), 5.81 (1H, br.s, OH).

**3** :  $\delta_{\text{H}}$  7.44 (1H, d,  $J = 16$  Hz, 3-H), 7.43 (2H, d,  $J = 8.3$  Hz, Ar-H), 6.74 (2H, d,  $J = 8.4$  Hz, Ar-H), 6.23 (1H, d,  $J = 16$  Hz, 2-H), 3.56 (1H, br.s, OH).

**4** :  $\delta_{\text{H}}$  7.67 (1H, d,  $J = 15.9$  Hz, 3-H), 7.44 (2H, d,  $J = 8.6$  Hz, Ar-H), 6.85 (2H, d,  $J = 8.6$  Hz, Ar-H), 6.25 (1H, d,  $J = 15.9$  Hz, 2-H), 3.78 (3H, s,  $\text{OCH}_3$ ).

**5** :  $\delta_{\text{H}}$  8.35 (1H, s, Ar-H), 8.20-7.80 (2H, m, Ar-H), 7.75 (1H, d,  $J = 16$  Hz, 3-H), 7.55 (1H, m, Ar-H), 6.53 (1H, d,  $J = 16$  Hz, 2-H).

**6** :  $\delta_{\text{H}}$  7.64 (1H, d,  $J = 15.9$  Hz, 3-H), 7.36-6.85 (3H, m, Ar-H), 6.23 (1H, d,  $J = 15.9$  Hz, 2-H), 4.72 (1H, br.s, OH), 3.86 (3H, s,  $\text{OCH}_3$ ).

**7** :  $\delta_{\text{H}}$  7.74 (1H, d,  $J = 15.9$  Hz, 3-H), 7.15-6.88 (3H, m, Ar-H), 6.32 (1H, d,  $J = 15.9$  Hz, 2-H), 3.91 (6H, s,  $2 \times \text{OCH}_3$ ).

**8** :  $\delta_{\text{H}}$  7.60 (1H, d,  $J = 15.9$  Hz, 3-H), 6.97-6.76 (3H, m, Ar-H), 6.20 (1H, d,  $J = 15.9$  Hz, 2-H), 5.95 (2H, s,  $\text{OCH}_2\text{O}$ ).

**9** :  $\delta_{\text{H}}$  : 7.70 (1H, d,  $J = 15.9$  Hz, 3-H), 7.74-6.86 (8H, m, Ar-H), 6.30 (1H, d,  $J = 15.8$  Hz, 2-H), 5.20 (2H, s,  $\text{OCH}_2$ ), 3.92 (3H, s,  $\text{OCH}_3$ ).

**10** :  $\delta_{\text{H}}$  7.60 (1H, d,  $J = 15.9$  Hz, 3-H), 7.39-6.81 (8H, m, Ar-H), 6.16 (1H, d,  $J = 15.9$  Hz, 2-H), 5.12 (2H, s,  $\text{OCH}_2$ ), 3.86 (3H, s,  $\text{OCH}_3$ ).

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