

# An Efficient Synthesis of Novel *N,N'*-Dibenzoyl-pyrimidin-2(1*H*)-Ones Using Microwave Irradiation via Three-Component Biginelli Reaction

V. DEEPTHI, S.TRILOKNADH, B.NAGARAJU and C. VENKATA RAO\*

Department of Chemistry, Sri Venkateswara University, Tirupati-517502, India  
cvrsvu@gmail.com

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**Abstract:** Environmentally benign microwave induced method of organic synthesis has been taken up to carry out three component Biginelli reaction for the synthesis of *N,N'*-dibenzoyl pyrimidin-2-one derivatives. The advantages of this protocol include enhanced yield, reduced reaction time, operational simplicity, avoidance of organic solvents and eco-friendly preparation that directs towards new trends in green synthesis.

**Keywords:** Microwave induced organic synthesis, Biginelli reaction, *N,N'*-dibenzoyl pyrimidin-2-one derivatives, green synthesis

## Introduction

Nature is diversified with enormous variety of natural products having number of scaffolds, unique structures and specific activity, more precisely, heterocyclic moiety containing Nitrogen constitute a privileged substructure with remarkable pharmacological efficacy and promising bioactivity. Owing to their wide spread of biological significance<sup>1</sup>, 3,4-dihydro pyrimidine-2-ones (DHPMs) have received considerable attention in the current years. These compounds can readily be assembled by one-pot three component cyclocondensation of  $\beta$ -dicarbonyl compounds with aldehydes (aromatic and aliphatic aldehydes) and urea under strong acidic conditions, reported by Pietro Biginelli<sup>2</sup> in 1983. Since then, a number of improved variants employing new reagents<sup>3-6</sup>, catalysts<sup>7-10</sup>, methodologies<sup>11-13</sup> and techniques were developed.

In spite of the potential utility, many of the existing methods involve expensive reagents, stoichiometric amount of catalyst, strong acidic conditions, longer reaction times, lower yields (20-50%) and incompatibility with other functional groups, cumbersome product isolation and environmental pollution. The development of versatile, simple and eco-friendly processes for the synthesis of DHPMs extended the scope of Biginelli reaction. The literature survey reveals that, the application of microwave irradiation as a thermal source to

accelerate organic reactions has gained popularity after Gedye's<sup>13</sup> pioneering report on the use of microwaves in organic synthesis. This technique is advantageous over conventional methods due to shorter reaction times, dry media, cleaner reactions, easy work up and minimization of thermal decomposition products.

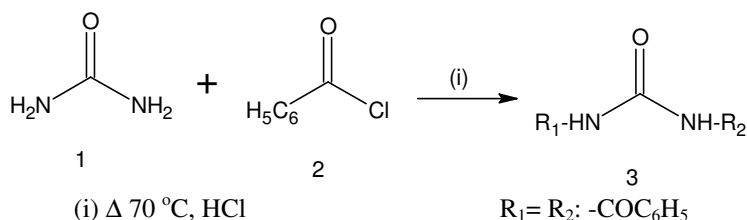
In the present study, an environmentally benign protocol has been adopted for the synthesis of different *N,N'*-dibenzoyl pyrimidin-2-ones by microwave irradiation under solvent free conditions. The synthetic potential of this new heterocyclic ring formation increased the scope of the original cyclocondensation reaction and was extended by variation to all three building blocks, allowing access to a large number of multifunctional pyrimidinone derivatives.

## Experimental

Chemicals and reagents are of analytical grade and used as obtained from Sigma-Aldrich, SDFCL and Himedia. Melting points were determined in open capillary tubes and are uncorrected. The progress of reaction was monitored at various stages by silica gel-G coated TLC plates. IR spectra were obtained by Fourier transform-infrared spectroscopy system (FT-IR, Bruker Victor 22) using KBr pellets. NMR spectra were measured on Bruker avance at 400 MHz and 75MHz respectively using CDCl<sub>3</sub> and chemical shift values are recorded in  $\delta$  ppm relative to tetramethylsilane as an internal standard. Mass spectra were recorded on Shimadzu 2010 at 70 eV. Microwave irradiation was carried out on convection (unmodified) domestic LG microwave oven with 800 watts output.

### General procedure for synthesis of *N,N'*-dibenzoylurea (3)

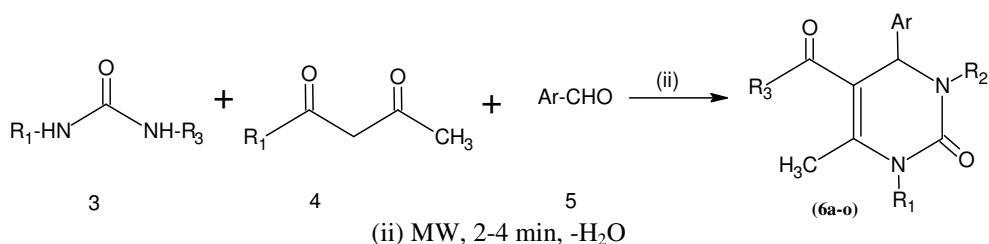
A mixture of benzoyl chloride **1** (2 mmol) and urea **2** (1 mmol) was taken into a 50 mL beaker, stirred gently and heated over water bath at 70 °C for 15 min. After the completion of the reaction (as indicated by TLC), 25 mL of ice cold water was added to the reaction mixture and the solid obtained was filtered under vacuum. The crude compound was recrystallized from aqueous ethanol to get essentially pure product **3** (Scheme 1).



**Scheme 1**

### General procedure for synthesis of *N,N'*-Dibenzoyl pyrimidine-2-one derivatives (6a-o)

An equimolar mixture (2mmol each) of *N,N'*-dibenzoyl urea (**3**),  $\beta$ -diketone (**4**), aromatic aldehyde (**5**) was subjected to microwave irradiation for appropriate time (Table 1) at 40% power level in 800 watts microwave oven at 100 °C with successive intervals of 30 s. The reaction progress was monitored by TLC till the completion of the reaction and the product was cooled to room temperature, washed with ice cold water, filtered and dried under suction. The compounds obtained were recrystallized from ethanol to afford *N,N'*-Dibenzoyl pyrimidine-2-one derivatives (**6a-o**) in excellent yields (Scheme 2).



Scheme 2

**Spectral data of the compounds****(5-Acetyl-4-(4-methoxyphenyl)-6-methyl-2-oxopyrimidine-1,3(2H,4H)-diyl)bis(phenylmethanone) (6a)**

Mol.formula: C<sub>28</sub>H<sub>24</sub>N<sub>2</sub>O<sub>5</sub>; MW: 468; IR (KBr,  $\nu$  (cm<sup>-1</sup>): 1148 (C-O), 1278 (C-N), 1513 (C=C), 1672 (C=O), 2842 (C-H, Alip), 3080 (C-H, Ar); <sup>1</sup>H NMR  $\delta$  ppm: 2.13 (s, 3H, CH<sub>3</sub>), 2.32 (s, 3H, CH<sub>3</sub>), 3.82 (s, 3H, OCH<sub>3</sub>), 6.16 (s, 1H, CH), 6.91-7.16 (m, 4H, Ar-H), 7.52-7.63 (m, 5H, Ar-H), 7.91-8.03 (m, 5H, Ar-H); ESI-MS: 468 (M<sup>+</sup>).

**Ethyl-1,3-dibenzoyl-4-(4-methoxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydro pyrimidine-5-carboxylate (6b)**

Mol.formula: C<sub>29</sub>H<sub>26</sub>N<sub>2</sub>O<sub>6</sub>; MW: 498; IR (KBr,  $\nu$  (cm<sup>-1</sup>): 1183 (C-O), 1230 (C-N), 1501 (C=C), 1684 (C=O), 2839 (C-H, Alip), 3063 (C-H, Ar); <sup>1</sup>H NMR  $\delta$  ppm: 1.22 (t, 3H, CH<sub>3</sub>), 2.25 (s, 3H, CH<sub>3</sub>), 3.80 (s, 3H, OCH<sub>3</sub>), 4.11 (q, 2H, CH<sub>2</sub>), 6.09 (s, 1H, CH), 6.71-6.82 (m, 4H, Ar-H), 7.11-7.20 (m, 6H, Ar-H), 7.57-7.65 (m, 4H, Ar-H); ESI-MS: 498 (M<sup>+</sup>).

**Allyl-1,3-dibenzoyl-4-(4-methoxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydro pyrimidine-5-carboxylate (6c)**

Mol.formula: C<sub>30</sub>H<sub>26</sub>N<sub>2</sub>O<sub>6</sub>; MW: 510; IR (KBr,  $\nu$  (cm<sup>-1</sup>): 1186 (C-O), 1275 (C-N), 1498 (C=C), 1662 (C=O), 2837 (C-H, Alip), 3045 (C-H, Ar); <sup>1</sup>H NMR  $\delta$  ppm: 2.26 (s, 3H, CH<sub>3</sub>), 3.87 (s, 3H, OCH<sub>3</sub>), 4.76 (d, 2H, CH<sub>2</sub>), 5.32 (m, 2H, =CH<sub>2</sub>), 6.04 (m, 1H, =CH), 6.17 (s, 1H, CH), 6.70-6.76 (m, 4H, Ar-H), 7.56-7.62 (m, 6H, Ar-H), 7.95 (m, 4H, Ar-H); ESI-MS: 510 (M<sup>+</sup>).

**(5-acetyl-4-(4-bromophenyl)-6-methyl-2-oxopyrimidine-1,3(2H,4H)-diyl)bis(phenylmethanone) (6d)**

Mol.formula: C<sub>27</sub>H<sub>21</sub>BrN<sub>2</sub>O<sub>4</sub>; MW: 516; IR (KBr,  $\nu$  (cm<sup>-1</sup>): 1122 (C-O), 1226 (C-N), 1502 (C=C), 1667 (C=O), 2845 (C-H, Alip), 3047 (C-H, Ar); <sup>1</sup>H NMR  $\delta$  ppm: 2.13 (s, 3H, CH<sub>3</sub>), 2.24 (s, 3H, CH<sub>3</sub>), 6.14 (s, 1H, CH), 7.17 (m, 2H, Ar-H), 7.4-7.62 (m, 6H, Ar-H), 7.88 (m, 2H, Ar-H), 7.89 (m, 4H, Ar-H); ESI-MS: 516 (M<sup>+</sup>).

**Ethyl-1,3-dibenzoyl-4-(4-bromophenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydro pyrimidine-5-carboxylate (6e)**

Mol.formula: C<sub>28</sub>H<sub>23</sub>BrN<sub>2</sub>O<sub>5</sub>; MW: 546; IR (KBr,  $\nu$  (cm<sup>-1</sup>): 1173 (C-O), 1258 (C-N), 1491 (C=C), 1661 (C=O), 2853 (C-H, Alip), 3022 (C-H, Ar); <sup>1</sup>H NMR  $\delta$  ppm: 1.18 (t, 3H, CH<sub>3</sub>), 2.21 (s, 3H, CH<sub>3</sub>), 4.12 (q, 2H, CH<sub>2</sub>), 6.08 (s, 1H, CH), 7.20 (m, 2H, Ar-H), 7.58-7.66 (m, 6H, Ar-H), 7.78 (m, 2H, Ar-H), 7.82-7.91 (m, 4H, Ar-H); ESI-MS: 546 (M<sup>+</sup>).

*Allyl-1,3-dibenzoyl-4-(4-bromophenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (6f)*

Mol.formula: C<sub>29</sub>H<sub>23</sub>BrN<sub>2</sub>O<sub>5</sub>; MW: 558; IR (KBr,  $\nu$  (cm<sup>-1</sup>): 1164 (C-O), 1249 (C-N), 1503 (C=C), 1663 (C=O), 2831 (C-H, Alip), 3029 (C-H, Ar); <sup>1</sup>H NMR  $\delta$  ppm: 2.26 (s, 3H, CH<sub>3</sub>), 4.62 (d, 2H, CH<sub>2</sub>), 5.21 (m, 2H, =CH<sub>2</sub>) 6.02 (m, 1H, =CH), 6.15 (s, 1H, Ar-H), 7.27 (m, 2H, Ar-H), 7.54-7.62 (m, 6H, Ar-H), 7.75-7.85 (m, 6H, Ar-H); ESI-MS: 558 (M<sup>+</sup>).

*(5-acetyl-4-(4-benzylphenyl)-6-methyl-2-oxopyrimidine-1,3(2H,4H)-diyl)bis(phenylmethanone) (6g)*

Mol.formula: C<sub>34</sub>H<sub>28</sub>N<sub>2</sub>O<sub>4</sub>; MW: 528; IR (KBr,  $\nu$  (cm<sup>-1</sup>): 1157 (C-O), 1261 (C-N), 1508 (C=C), 1664 (C=O), 2829 (C-H, Alip), 3021 (C-H, Ar); <sup>1</sup>H NMR  $\delta$  ppm: 2.12 (s, 3H, CH<sub>3</sub>), 2.28 (s, 3H, CH<sub>3</sub>), 4.10 (s, 2H, CH<sub>2</sub>), 6.19 (s, 1H, CH), 7.21-7.29 (m, 9H, Ar-H), 7.54-7.62 (m, 6H, Ar-H), 7.97 (m, 4H, Ar-H); ESI-MS: 528 (M<sup>+</sup>).

*Ethyl-1,3-dibenzoyl-4-(4-benzylphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (6h)*

Mol.formula: C<sub>35</sub>H<sub>30</sub>N<sub>2</sub>O<sub>5</sub>; MW: 558; IR (KBr,  $\nu$  (cm<sup>-1</sup>): 1192 (C-O), 1256 (C-N), 1502 (C=C), 1683 (C=O), 2842 (C-H, Alip), 3038 (C-H, Ar); <sup>1</sup>H NMR  $\delta$  ppm: 1.16 (t, 3H, CH<sub>3</sub>), 2.19 (s, 3H, CH<sub>3</sub>), 4.11 (q, 2H, CH<sub>2</sub>), 4.17 (s, 2H, CH<sub>2</sub>), 6.29 (s, 1H, CH), 7.15-7.25 (m, 9H, Ar-H), 7.59-7.68 (m, 6H, Ar-H), 7.95 (m, 4H, Ar-H); ESI-MS: 558 (M<sup>+</sup>).

*Allyl-1,3-dibenzoyl-4-(4-benzylphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (6i)*

Mol.formula: C<sub>36</sub>H<sub>30</sub>N<sub>2</sub>O<sub>5</sub>; MW: 570; IR (KBr,  $\nu$  (cm<sup>-1</sup>): 1149 (C-O), 1270 (C-N), 1517 (C=C), 1675 (C=O), 2813 (C-H, Alip), 3045 (C-H, Ar); <sup>1</sup>H NMR  $\delta$  ppm: 2.16 (s, 3H, CH<sub>3</sub>), 4.10 (s, 2H, CH<sub>2</sub>), 4.68 (d, 2H, CH<sub>2</sub>), 5.24-5.32 (m, 2H, =CH<sub>2</sub>), 6.05 (m, 1H, =CH), 6.18 (s, 1H, CH), 7.20-7.28 (m, 9H, Ar-H), 7.56-7.64 (m, 6H, Ar-H), 7.95 (m, 4H, Ar-H); ESI-MS: 570 (M<sup>+</sup>).

*(5-Acetyl-4-(4-hydroxy-3-methoxyphenyl)-6-methyl-2-oxopyrimidine-1,3(2H,4H)-diyl)bis(phenylmethanone) (6j)*

Mol.formula: C<sub>28</sub>H<sub>24</sub>N<sub>2</sub>O<sub>6</sub>, MW: 484; IR (KBr,  $\nu$  (cm<sup>-1</sup>): 1158 (C-O), 1238 (C-N), 1498 (C=C), 1674 (C=O), 2827 (C-H, Alip), 3027 (C-H, Ar); <sup>1</sup>H NMR  $\delta$  ppm: 2.13 (s, 3H, CH<sub>3</sub>), 2.26 (s, 3H, CH<sub>3</sub>), 3.37 (s, 3H, OCH<sub>3</sub>), 6.17 (s, 1H, CH), 6.56-6.78 (m, 3H, Ar-H), 7.54-7.62 (m, 6H, Ar-H), 7.86 (m, 4H, Ar-H), 9.56 (s, broad, 1H, -OH); ESI-MS: 484 (M<sup>+</sup>).

*Ethyl-1,3-dibenzoyl-4-(4-hydroxy-3-methoxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (6k)*

Mol.formula: C<sub>29</sub>H<sub>26</sub>N<sub>2</sub>O<sub>7</sub>; MW: 514; IR (KBr,  $\nu$  (cm<sup>-1</sup>): 1127 (C-O), 1281 (C-N), 1512 (C=C), 1687 (C=O), 2829 (C-H, Alip), 3019 (C-H, Ar); <sup>1</sup>H NMR  $\delta$  ppm: 1.15 (t, 3H, CH<sub>3</sub>), 2.13 (s, 3H, CH<sub>3</sub>), 3.84 (s, 3H, OCH<sub>3</sub>), 4.02 (q, 2H, CH<sub>2</sub>), 6.38 (s, 1H, CH), 6.72-6.96 (m, 3H, Ar-H), 7.51-7.59 (m, 6H, Ar-H), 7.72 (m, 4H, Ar-H), 9.77 (s, broad, 1H, -OH); ESI-MS: 514 (M<sup>+</sup>).

*Allyl-1,3-dibenzoyl-4-(4-hydroxy-3-methoxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (6l)*

Mol.formula: C<sub>30</sub>H<sub>26</sub>N<sub>2</sub>O<sub>7</sub>; MW: 526; IR (KBr,  $\nu$  (cm<sup>-1</sup>): 1133 (C-O), 1282 (C-N), 1507 (C=C), 1678 (C=O), 2822 (C-H, Alip), 3057 (C-H, Ar); <sup>1</sup>H NMR  $\delta$  ppm: 2.19 (s, 3H, CH<sub>3</sub>), 3.84 (s, 3H, OCH<sub>3</sub>), 4.72 (d, 2H, CH<sub>2</sub>), 5.26-5.32 (m, 2H, =CH<sub>2</sub>), 6.05 (m, 1H, =CH), 6.23 (s, 1H, CH), 6.76-6.89 (m, 3H, Ar-H), 7.54-7.62 (m, 6H, Ar-H), 7.98 (m, 4H, Ar-H), 9.62 (s, 1H, OH); ESI-MS: 526 (M<sup>+</sup>).

*(5-Acetyl-4-(4-hydroxyphenyl)-6-methyl-2-oxopyrimidine-1,3(2H,4H)-diyl) bis(phenylmethanone) (6m)*

Mol.formula: C<sub>27</sub>H<sub>22</sub>N<sub>2</sub>O<sub>5</sub>; MW: 454; IR (KBr,  $\nu$  (cm<sup>-1</sup>): 1125 (C-O), 1258 (C-N), 1501 (C=C), 1669 (C=O), 2832 (C-H, Alip), 3023 (C-H, Ar); <sup>1</sup>H NMR  $\delta$  ppm: 2.12 (s, 3H, CH<sub>3</sub>), 2.18(s, 3H, CH<sub>3</sub>), 6.19 (s, 1H, CH), 6.83-6.92 (m, 4H, Ar-H), 7.55 (m, 6H, Ar-H), 7.70 (m, 4H, Ar-H), 9.06 (s, 1H, OH); ESI-MS: 454 (M<sup>+</sup>).

*Ethyl-1,3-dibenzoyl-4-(4-hydroxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydro pyrimidine-5-carboxylate (6n)*

Mol.formula: C<sub>28</sub>H<sub>24</sub>N<sub>2</sub>O<sub>6</sub>; MW: 484; IR (KBr,  $\nu$  (cm<sup>-1</sup>): 1139 (C-O), 1276 (C-N), 1505 (C=C), 1673 (C=O), 2842 (C-H, Alip), 3029 (C-H, Ar); <sup>1</sup>H NMR  $\delta$  ppm: 1.16 (t, 3H, CH<sub>3</sub>), 2.25 (s, 3H, CH<sub>3</sub>), 4.02 (q, 2H, CH<sub>2</sub>), 6.16 (s, 1H, CH), 6.79-6.87 (m, 4H, Ar-H), 7.51-7.59 (m, 6H, Ar-H), 7.71 (m, 4H, Ar-H), 9.06 (s, 1H, OH); ESI-MS: 484 (M<sup>+</sup>).

*Allyl-1,3-dibenzoyl-4-(4-hydroxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydro pyrimidine-5-carboxylate (6o)*

Mol.formula: C<sub>29</sub>H<sub>24</sub>N<sub>2</sub>O<sub>6</sub>; MW: 496; IR (KBr,  $\nu$  (cm<sup>-1</sup>): 1154 (C-O), 1282 (C-N), 1508 (C=C), 1688 (C=O), 2851 (C-H, Alip), 3031 (C-H, Ar); <sup>1</sup>H NMR  $\delta$  ppm: 2.21 (s, 3H, CH<sub>3</sub>), 4.63 (d, 2H, CH<sub>2</sub>), 5.22 (m, 2H, =CH<sub>2</sub>), 6.05 (m, 1H, =CH), 6.24 (s, 1H, CH), 6.71-6.99 (m, 4H, Ar-H), 7.55 (m, 6H, Ar-H), 7.69 (m, 4H, Ar-H), 9.16 (s, 1H, OH); ESI-MS: 496 (M<sup>+</sup>).

## Results and Discussion

In view of the limitations mentioned in the reported methods of Biginelli reaction, efforts were made to investigate an efficient and environmentally benign method for the synthesis of DHPMs. Thus a facile, rapid and expeditious solvent-less method was developed in agreement with the green principles. A series of *N,N'*-Dibenzoyl pyrimidine-2-ones were synthesized by coupling of a wide range of structurally varied araldehydes,  $\beta$ -diketones and *N,N'*-dibenzoyl urea. All the reactions were carried out under mild conditions promoted by microwave irradiation to produce corresponding title compounds (**6a-x**) in excellent yields.

**Table 1.** Microwave assisted synthesis of *N,N'*-Dibenzoyl pyrimidine-2-ones using various aldehydes with  $\beta$ -diketones

Entry	R <sub>3</sub>	Ar	Time, min	MP °C	Yield%
<b>6a</b>	-CH <sub>3</sub>	-C <sub>6</sub> H <sub>4</sub> (4-OCH <sub>3</sub> )	2.5	219	92
<b>6b</b>	-OC <sub>2</sub> H <sub>5</sub>	-C <sub>6</sub> H <sub>4</sub> (4-OCH <sub>3</sub> )	3.0	243	94
<b>6c</b>	-OCH <sub>2</sub> CH=CH <sub>2</sub>	-C <sub>6</sub> H <sub>4</sub> (4-OCH <sub>3</sub> )	4.0	228	93
<b>6d</b>	-CH <sub>3</sub>	-C <sub>6</sub> H <sub>4</sub> (4-Br)	3.5	217	89
<b>6e</b>	-OC <sub>2</sub> H <sub>5</sub>	-C <sub>6</sub> H <sub>4</sub> (4-Br)	4.0	236	92
<b>6f</b>	-OCH <sub>2</sub> CH=CH <sub>2</sub>	-C <sub>6</sub> H <sub>4</sub> (4-Br)	4.0	230	90
<b>6g</b>	-CH <sub>3</sub>	-C <sub>6</sub> H <sub>4</sub> (4-CH <sub>2</sub> C <sub>6</sub> H <sub>5</sub> )	3.5	192	87
<b>6h</b>	-OC <sub>2</sub> H <sub>5</sub>	-C <sub>6</sub> H <sub>4</sub> (4-CH <sub>2</sub> C <sub>6</sub> H <sub>5</sub> )	4.0	197	91
<b>6i</b>	-OCH <sub>2</sub> CH=CH <sub>2</sub>	-C <sub>6</sub> H <sub>4</sub> (4-CH <sub>2</sub> C <sub>6</sub> H <sub>5</sub> )	4.0	202	90
<b>6j</b>	-CH <sub>3</sub>	-C <sub>6</sub> H <sub>3</sub> (3-OCH <sub>3</sub> ,4-OH)	4.0	201	91
<b>6k</b>	-OC <sub>2</sub> H <sub>5</sub>	-C <sub>6</sub> H <sub>3</sub> (3-OCH <sub>3</sub> ,4-OH)	3.5	231	94
<b>6l</b>	-OCH <sub>2</sub> CH=CH <sub>2</sub>	-C <sub>6</sub> H <sub>3</sub> (3-OCH <sub>3</sub> ,4-OH)	4.0	183	92
<b>6m</b>	-CH <sub>3</sub>	-C <sub>6</sub> H <sub>4</sub> (4-OH)	2.8	202	85
<b>6n</b>	-OC <sub>2</sub> H <sub>5</sub>	-C <sub>6</sub> H <sub>4</sub> (4-OH)	3.4	231	87
<b>6o</b>	-OCH <sub>2</sub> CH=CH <sub>2</sub>	-C <sub>6</sub> H <sub>4</sub> (4-OH)	3.5	185	84

After establishing the optimal conditions, we herein report the results and generality of microwave assisted Biginelli reaction (Table 1). As per the obtained results, by the increasing of power from 300 watts to 600 watts there was a noticeable increment in yields and reduction in reaction times were observed. Beyond output power of 600 watts there was no significant change in reaction time and yield.

## Conclusion

An efficient synthesis of a series of novel *N,N'*-Dibenzoyl pyrimidine-2-one derivatives promoted by microwave irradiation under solvent-free conditions was established. The reaction is multicomponent reaction with characteristic of shorter reaction times, simple and easy work-up. This protocol developed a facile and green methodology thereby extended the utility of substituted urea in the venerable Biginelli reaction. However, there are many heterocyclic reactions with great potential for automated medicinal and combinatorial chemistry which traditionally have been performed with long reaction times that might be dramatically accelerated by microwave irradiation.

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