Effective microwave synthesis of some ring fused quinolines

V. Nadaraj¹, J. Umamaheswari¹ and S. Thamarai Selvi²
¹Department of Chemistry, Tamilnadu College of Engineering, Karumathampatti, Coimbatore-641659.
²Department of Chemistry, L.R.G. Govt. Arts College for Women, Tirupur, India.

ABSTRACT
Pyrano[2,3-b]quinolin-2-ones was synthesized by cyclic condensation of 2-chloro-3-formylquinolines with sodium acetate and acetic acid in microwave reactor. Microwave reactions are very inexpensive, operational simplicity, eco-friendly method and good yield in a very short reaction time. Unexpectedly, 3-formylquinolin-2(1H)-ones were exclusively formed in very high yield by changing the molar ratio of acetic acid and sodium acetate in just 1.5 to 2.5 min. The synthesized compounds were characterised by IR, NMR, and Mass Spectra.

Introduction
MICROWAVE irradiation using commercial domestic oven has been recently used to accelerate organic reactions, the high heating efficiency giving remarkable rate enhancement and dramatic reduction in reaction time.¹² As a part of a research project to develop environmentally benign organic reactions, we have recently reported the synthesis of simple quinolines, pyrimido- and pyrazoloquinolines under microwaves.¹⁰⁻¹¹ Hence, our new approach reported herein involves the use of microwave irradiation in the synthesis of pyrano[2,3-b]quinolin-2ones under mild conditions and unexpected formation of 3-formylquinolin-2(1H)-ones as intermediates.

The preparation of pyranoquinolines has received significant attention¹⁰⁻¹¹ in previous years because of the broad spectrum of their biological properties such as psychotropic, antiallergic, anti-inflammatory and estrogenic activities.¹⁰ In addition, pyranoquinoline derivatives are found to possess a wide range of pharmacological activity.¹ⁱ Further, several bioactive alkaloids which are widely distributed in nature contain a pyranoquinoline moiety.¹² Among the pyranoquinolines, pyrano[2,3-b]quinolin-2-one systems are of interest because they are linear benzaza analogues of coumarins and they constitute the parent ring structures of pyranoquinoline alkaloids such as kaphlofoline, which occurs in the rutaceae plant family.¹²

So far, only a few methods have been reported¹³⁻¹⁵ for the construction of pyrano[2,3-b]quinolin-2-ones, which generally involve 2-chloro-3-formylquinolines (I) as starting materials. However, these methods have some disadvantages, which include multiple steps, longer reaction time, and use of toxic organic solvents, harsh reaction conditions and requirement of excess of reagents such as HCl, acetic anhydride and PPA.

Result and discussion
To identify an efficient reagent for the synthesis of pyrano[2,3-b]quinolin-2-one derivatives, from 2-chloro-3-formylquinolines. We initially examined the reaction of 2-chloro-3-formylquinoline (1) with acetic acid under microwave irradiation for 10 min. But unfortunately we got mixture of product, such as target compound pyrano[2,3-b]quinoline (2a, 30%) and unknown compound 3a in 58% (Scheme 1). IR spectrum of 3a showed absorption at 1680 cm⁻¹ corresponding to free aldehyde group. The spectral [(¹H-NMR & Mass) and analytical data attested the compound 3a to be 3-formylquinolin-2(1H)-one, which is also a good intermediate in the synthesis of other quinoline heterocycles.²⁰⁻²¹

Scheme1. (i) Method 3 and (ii) Method 4

Table 1
Microwave irradiation of 2-chloro-3-formylquinoline (1a) with acetic acid and sodium acetate under different conditions

<table>
<thead>
<tr>
<th>Methods</th>
<th>Reagent / Catalyst</th>
<th>Molar ratio (mmol)</th>
<th>Irradiation Power (W)</th>
<th>Time (min)</th>
<th>Product formed</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Acetic acid</td>
<td>175</td>
<td>480</td>
<td>10</td>
<td>2a &amp; 3a</td>
<td>30 &amp; 58</td>
</tr>
<tr>
<td>2</td>
<td>Acetic acid and sodium acetate</td>
<td>87.5 and 25</td>
<td>320</td>
<td>10.00</td>
<td>2a &amp; 3a</td>
<td>45 &amp; 45</td>
</tr>
<tr>
<td>3</td>
<td>Acetic acid and sodium acetate</td>
<td>123 and 50</td>
<td>320</td>
<td>5.00</td>
<td>2a</td>
<td>92</td>
</tr>
<tr>
<td>4</td>
<td>Sodium acetate</td>
<td>50</td>
<td>480</td>
<td>2.20</td>
<td>3a</td>
<td>98</td>
</tr>
</tbody>
</table>

a - Microwave irradiations were carried out using Kenstar, OM-20ESP, 2450 MHz, domestic microwave oven with adjustable irradiation power.
Next we improve the yield of target product using sodium acetate in the reaction sequence. When we irradiated of 2-chloro-3-formyquinoline (1a) with acetic acid/ sodium acetate using various parameters such as different molar ratio of acetic acid/ sodium acetate, irradiation power and time were studied and optimized (Table 1, Methods 1–4).

From the results obtained by using different parameters, it is obvious that method 3 is the most suitable for the synthesis of pyrano[2,3-b]quinolin-2-one 2a, as it reduces the reaction time to minimum and increases the yield of the product to maximum (Table 1). The solid-state condition was also checked for the reaction, unexpectedly, 3-formylquinolin-2(1H)-ones were exclusively formed in very high yields by changing the molar ratio of acetic acid and sodium acetate in just 1.5 to 2.5 min (Method 4, Table I).

To establish the generality and applicability of these methods, various substituted 2-chloro-3-formyquinolines (1b-g) were subjected to the same reaction conditions (Method 3) to furnish the corresponding quinolines 2b-g and in good yields (Table II).

### Table II. Microwave Synthesis of 2-oxo-2H-pyrano[2,3-b]quinolines (2a-g)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Product R¹</th>
<th>R²</th>
<th>R³</th>
<th>Time (min)</th>
<th>Yield (%)</th>
<th>mp (Lit. mp)°C</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2a</td>
<td>H</td>
<td>H</td>
<td>5.00</td>
<td>92</td>
<td>243-244        (243)</td>
</tr>
<tr>
<td>2</td>
<td>2b</td>
<td>CH₃</td>
<td>H</td>
<td>6.20</td>
<td>95</td>
<td>245-247        (240)</td>
</tr>
<tr>
<td>3</td>
<td>2c</td>
<td>H</td>
<td>CH₃</td>
<td>6.40</td>
<td>86</td>
<td>231-232        (230)</td>
</tr>
<tr>
<td>4</td>
<td>2d</td>
<td>OCH₃</td>
<td>H</td>
<td>5.00</td>
<td>78</td>
<td>224-225</td>
</tr>
<tr>
<td>5</td>
<td>2e</td>
<td>H</td>
<td>OCH₃</td>
<td>6.00</td>
<td>89</td>
<td>260-262</td>
</tr>
<tr>
<td>6</td>
<td>2f</td>
<td>Br</td>
<td>H</td>
<td>9.00</td>
<td>70</td>
<td>262-264</td>
</tr>
<tr>
<td>7</td>
<td>2g</td>
<td>Cl</td>
<td>H</td>
<td>8.20</td>
<td>75</td>
<td>210-212 (215)</td>
</tr>
</tbody>
</table>

All the yields were calculated from crystallized products and the products were identified by comparison of analytical data (mp, mmp, IR, NMR, and Mass) with those reported or with authentic samples prepared by the conventional methods. Some new derivatives were also prepared and reported.

### Conclusion

The procedures described above provide a useful, clean, fast and efficient alternative for the preparation of both pyrano[2,3-b]quinolin-2(1H)-ones and 3-formylquinolin-2(1H)-ones. Prominent among the advantages of these new methods are operational simplicity, good yield in a very short reaction time, solvent-free conditions, very inexpensive, easily available reagent and catalyst and easy workup procedure employed.

### Acknowledgment

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### Reference


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[19]. Spectral data of 3-formyquinolin-2(1H)-one (3a): IR (KBr): ν=1550 cm⁻¹, 1680 cm⁻¹ (C=O), 3200 cm⁻¹; H NMR (DMSO-d$_6$): δ=7.25 (t, 1H; C$_6$-H), 7.35 (d, 1H; C$_7$-H), 7.66 (t, 1H; C$_8$-H), 7.92 (d, 1H; C$_9$-H), 8.52 (s, 1H; C$_{10}$-H), 10.24 (s, 1H; CHO), 12.25 (s, 1H; NH); $^{13}$C NMR (DMSO-d$_6$): δ=118.2, 120.1, 126.3, 132.5, 134.3, 138.2, 142.8, 144.3, 164.3, 191.2; MS m/z: 173 [M$^+$]; elemental analysis calcd (%) for C$_{9}$H$_7$NO$_2$: C 69.36, H 4.07, N 13.09; found: C 69.33, H 4.05, N 13.06.


[22]. Spectral data of pyra[2,3-b]quinolin-2-one (2a): IR (KBr): ν=1621 cm⁻¹, 1740 cm⁻¹ (C=O); $^1$H NMR (DMSO-d$_6$): δ=6.56 (d, $^3$J (H,H) = 9 Hz, 1H; C$_5$-H), 7.50-7.85 (m, 3H; C$_7$-H, C$_9$-H & C$_{10}$-H), 7.95 (d, $^3$J (H,H)= 8.3 Hz, 1H; C$_{11}$-H), 8.10 (d, $^3$J (H,H) = 9 Hz, 1H; C$_{12}$-H), 8.41 (s, 1H; C$_{13}$-H); $^{13}$C NMR (DMSO-d$_6$): δ=117.5, 122.5, 126.5, 132.3, 134.2, 136.8, 137.9, 140.5, 143.2, 146.2, 156.3, 162.3; MS m/z: 197 [M$^+$]; elemental analysis calcd (%) for C$_{10}$H$_7$NO$_2$: C 73.09, H 3.58, N 7.10; found: C 73.07, H 3.58, N 7.06.

Dr. V. Nadaraj received M. Sc. and Ph.D. from Bharathiar University, Coimbatore, Tamilnadu, India in 2002 and 2008, respectively. He is an Asst. Professor in the Department of Chemistry, Tamilnadu College of Engineering, India. He has published more than 20 research papers in national and international journal. His current research interests are mainly focused on the synthesis of nitrogen heterocyclic compounds. His research interests include isolation of natural products and antimicrobial studies of heterocyclic compounds.

Dr. S. Thamarai Selvi is an Assistant Professor in the Department of Chemistry, L.R.G. Govt. Arts College for Women’s, Tiruput, Tamilnadu, India. She has more than 10 years of experience in teaching and research. Her current area of research includes Synthetic Organic chemistry, Photochemistry, Natural Products. She has published more than thirty papers in referred international journals. She has also presented more than fifteen articles in national and international conferences.

J. Umamaheswari received M. Sc. and M.Phil. from Bharathiar University, Coimbatore, Tamilnadu, India in 2008 and 2009, respectively. She is a lecturer in the Department of Chemistry, Coimbatore College of Engineering, India. She has published 4 research papers in international journal. Her current research interests are mainly focused on the synthesis of nitrogen heterocyclic compounds.