

## Research Article

# An Efficient One-Pot Multicomponent Synthesis of 4-Aza-Podophyllotoxin Derivatives in Ionic Liquid

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A simple, green, and efficient procedure for the synthesis of 4-aza-podophyllotoxin derivatives by using a one-pot three-component reaction of benzaldehydes, 1,3-cyclohexanediones, and anilinolactones in the presence of catalytic amount of alum in 1-butyl-3-methylimidazolium triflate as green media is described. This reaction proceeded under mild conditions with the use of an inexpensive and readily available catalyst, high to excellent yields, and simple workup procedure.

## 1. Introduction

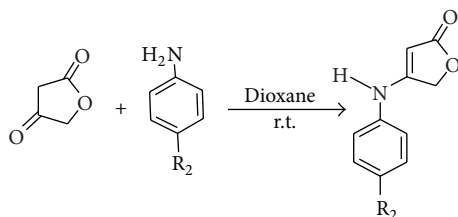
Multicomponent reactions (MCRs) are one-pot processes in which three or more reactants come together in a single reaction vessel to give a final product containing substantial elements of all the reactants [1–4], and in recent year much attention has been directed toward the one-pot multicomponent reactions, because of their wide range of applications in pharmaceutical chemistry for the production of structural scaffolds and combinatorial libraries for drug discovery [5–8]. The strategies of MCRs offer significant advantages over conventional linear-type syntheses because of high degree of atom economy, high selectivity, and procedural simplicity due to formation of carbon-carbon and carbon-heteroatom bonds in one-pot procedure [9–11]. MCRs, particularly those performed in green and eco-friendly media, have become increasingly useful tools for the synthesis of chemically and biologically important compounds because of their environmentally friendly atom economy and green characteristics, and the “greening” of global chemical processes has become a major issue in the chemical industry [12, 13].

Organic reactions in ionic liquid (IL) media have received the considerable attention of synthetic organic chemists in recent years; IL is an environmentally friendly solvent with unique properties such as high ionic conductivity, nonvolatility, high thermal stability, nonflammability, and

miscibility with organic compounds, especially with the heterocyclic compounds [14–17]. Because of these useful properties numerous works have been published in the last decades reporting the possibility to perform several organic reactions and catalyzed processes in these green media [18–20].

1,4-Dihydropyridine compounds are molecules based upon pyridine and this nucleus is one of the significant core structures among the most extensively natural and unnatural heterocyclic compounds, have been recognized as vital drugs for the treatment of cardiovascular diseases, and are well known as calcium channel modulators [21, 22]. 1,4-Dihydropyridine derivatives exhibit a variety of biological properties such as antihypertensive, antianginal [23–25], antitumor [26], anti-inflammatory [27, 28], antitubercular [29], analgesic [30], and antithrombotic [31, 32].

The biological activity of 1,4-dihydropyridine derivatives has led to extensive structural modifications resulting in several clinically useful compounds as a source of valuable drug candidates. Extensive structural modifications have been performed to obtain more potent and less toxic anticancer agents [33–35]. Among these compounds, furo[3,4-b]quinoline-1,8(3H,4H)-dione (podophyllotoxin) derivatives, which were reported as powerful DNA topoisomerase inhibitors and inhibit microtubule assembly as an antitumor ligand [36–38], have attracted attention in the recent decade [39–42].



SCHEME 1: Synthesis of anilinolactones.

With the aim to develop efficient synthetic processes using green and eco-friendly methods and to reduce laborious multistep techniques and minimize by-products, we report herein a novel and clean synthesis of some 4-azapodophyllotoxin derivatives in ionic liquid through a three-component condensation reaction of benzaldehydes **1**, 1,3-cyclohexanediones **2**, and anilinolactones **3** in the presence of catalytic amount of alum as catalyst.

## 2. Results and Discussion

In this study, firstly, the anilinolactones were prepared from the condensation reaction of tetronic acid with various anilines. As shown in Scheme 1, when tetronic acid reacted with an equimolar amount of various anilines in dioxane solution at room temperature, the corresponding products were obtained in excellent yields, appropriate reaction times, and high purity [43].

In continuation of this research, investigation on the preparation of 4-aza-podophyllotoxin derivatives **4** by using a one-pot three-component condensation reaction of benzaldehydes **1**, 1,3-cyclohexanediones **2**, and anilinolactones **3** was surveyed (Scheme 2).

To achieve suitable conditions for the synthesis of tetrahydrofuro[3,4-b]quinoline-1,8(3*H*,4*H*)-dione derivatives, the reaction of 4-bromobenzaldehyde **1d**, dimedone **2b**, and 4-(4-methylphenylamino)furan-2(3*H*)-one **3d** was chosen as a model reaction (Scheme 3). This reaction was first performed in various solvents in the presence of a catalytic amount of *p*-toluene sulfonic acid (*p*-TSA) as an inexpensive and readily available catalyst at 90°C. The results are summarized in Table 1.

It was observed that, among all solvents and media, the best result was obtained when 1-butyl-3-methylimidazolium triflate was chosen in the presence of catalytic amount of *p*-TSA at 90°C. The desired product was obtained in excellent yield and high purity.

The catalyst plays a crucial role in the success of the reaction in terms of rate of the reaction and yield. After determining the optimized conditions, we investigated the scope of the catalyst. To find the best catalyst, we screened the model reaction in the presence of different catalysts. The obtained results are outlined in Table 2.

These results indicate that, among all the catalyst systems tested, alum proved to be the most efficient since the reaction could be carried out and the desired product was obtained in excellent yield and high purity. In the absence of the catalyst, the model reaction could be carried out but the product was

TABLE 1: Different polar and nonpolar used solvents, for the synthesis of **4i**<sup>a</sup> under reflux conditions.

Entry	Solvent	Time (min)	Yield (%) <sup>b</sup>
1	MeOH	120	72
2	EtOH	120	75
3	1,4-Dioxane	120	60
4	DMF	120	70
5	Toluene	120	65
6	[bmim][triflate]	30	90
7	[bmim]OH	30	75
8	[bmim]PF <sub>6</sub>	30	88
9	[bmim]BF <sub>4</sub>	30	83
10	[bmim]Br	30	80

<sup>a</sup>Reaction conditions: 4-bromobenzaldehyde **1d** (1 mmol), dimedone **2b** (1 mmol), and 4-(4-methylphenylamino)furan-2(3*H*)-one **3d** (1 mmol), *p*-TSA (20 mol%).

<sup>b</sup>Isolated yields.

TABLE 2: Diverse used catalyst in a model reaction for the synthesis of **4i**<sup>a</sup> in [bmim][triflate].

Entry	Catalyst (20 mol%)	Yield (%) <sup>b</sup>
1	Alum	94
2	<i>p</i> -TSA	90
3	K-10	85
4	S.S.A	80
5	AlCl <sub>3</sub>	55
6	Et <sub>3</sub> N	63

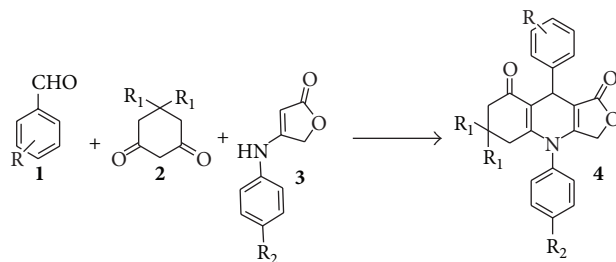
<sup>a</sup>Reaction conditions: 4-bromobenzaldehyde **1d** (1 mmol), dimedone **2b** (1 mmol), and 4-(4-methylphenylamino)furan-2(3*H*)-one **3d** (1 mmol), IL (0.2 mL).

<sup>b</sup>Isolated yields.

obtained in very low yield during 48 h and gives by TLC analysis only traces of the product.

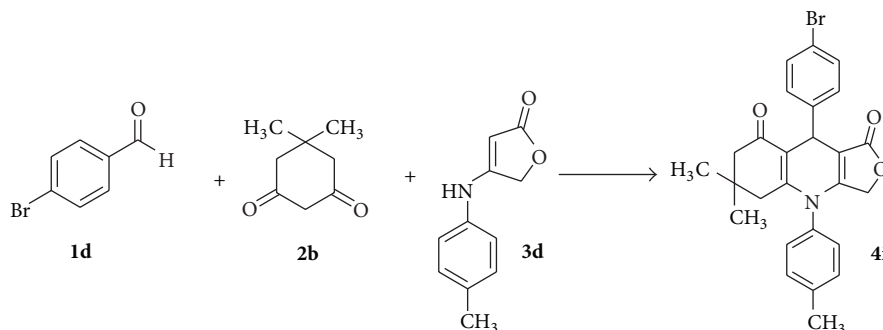
In order to optimize the more suitable reaction conditions for the preparation of 4-aza-podophyllotoxin derivatives via this novel green chemical approach, quantity of the catalyst required was determined. It was found that, when the reaction was carried out in the presence of 5 mol% of catalyst, 51% of yield was obtained. As we increase the percentage of the catalyst to 5 mol%, 10 mol%, and 15 mol%, the yields were also found to be increased up to 65%, 81%, and 95%, respectively, but beyond 20 mol% there is no significant improvement of the rate as well as yield of the reaction, and further increase in the quantity of catalyst did not show appreciable improvement in the yield of product. Thus, 20 mol% of catalyst was chosen as maximum quantity of the catalyst for the reaction (Table 3).

To optimize the reaction temperature, the reaction of dimedone **1**, bromobenzaldehyde **2**, and 4-(4-methylphenylamino)furan-2(3*H*)-one **3**, as model substrates, was studied in the ionic liquid 1-butyl-3-methylimidazolium triflate in the presence of 20 mol% alum, at different temperatures such as room temperature, 70°C, 90°C, and 110°C, respectively. The results are summarized in Table 4.



**1a** = 4-Cl, **1b** = H, **1c** = 4-CH<sub>3</sub>O, **1d** = 4-Br, **1e** = 4-F, **1f** = 3-NO<sub>2</sub>, **1g** = 4-CH<sub>3</sub>  
**2a** = H, **2b** = CH<sub>3</sub>  
**3a** = H, **3b** = F, **3c** = Cl, **3d** = CH<sub>3</sub>

SCHEME 2: Synthesis of 4-aza-podophyllotoxin.



SCHEME 3: Model reaction.

TABLE 3: Different amounts of the alum as catalyst for the synthesis of **4i**<sup>a</sup>.

Entry	Alum (mol%)	Yield (%) <sup>b</sup>
1	5	51
2	10	65
3	15	81
4	20	94
5	30	96

<sup>a</sup>Reaction conditions: 4-bromobenzaldehyde **1d** (1 mmol), dimedone **2b** (1 mmol), and 4-(4-methylphenylamino)furan-2(3H)-one **3d** (1 mmol), IL (0.2 mL).

<sup>b</sup>Isolated yields.

TABLE 4: Different reaction temperatures in model reaction for the synthesis of **4i**<sup>a</sup>.

Entry	Reaction temperature (°C)	Reaction time (min)	Yield (%) <sup>b</sup>
1	r.t.	120	Trace
2	70	60	87
3	90	30	94
4	110	30	95

<sup>a</sup>Reaction conditions: 4-bromobenzaldehyde **1d** (1 mmol), dimedone **2b** (1 mmol), and 4-(4-methylphenylamino)furan-2(3H)-one **3d** (1 mmol), IL (0.2 mL), alum (20 mol%).

<sup>b</sup>Isolated yields.

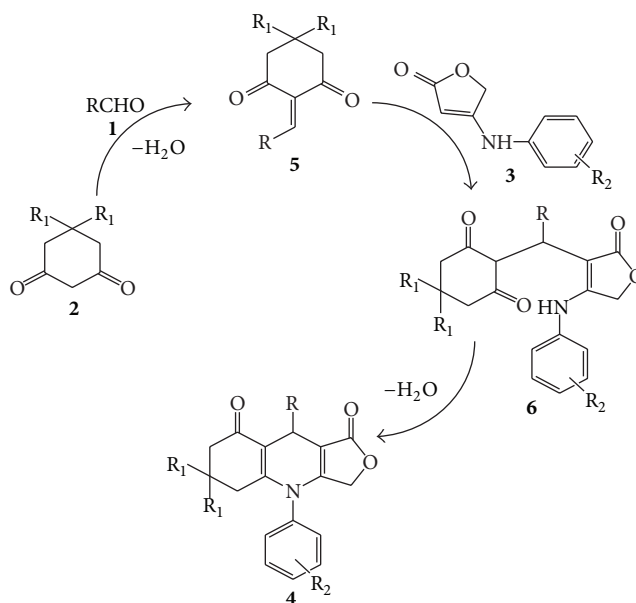
As shown in Table 4, the reaction at 90°C proceeded in the highest yield and shortest reaction time among four reaction temperatures tested. No significant increase in the yield of product was observed as the reaction temperature was raised from 70°C to 110°C. Therefore, 90°C was chosen for this reaction.

Although the detailed mechanism of the reaction remains to be unclear, a reasonable suggestion is offered in Scheme 4. Firstly, intermediate **5** was formed via the Knoevenagel condensation reaction between aldehyde **1** and cyclohexanediones **2** followed by Michael addition reaction between **5** and **3** furnished **6**, which upon intermolecular cyclization and dehydration gave rise to **4**.

With the optimized conditions, a variety of benzaldehydes possessing either electron-donating or -withdrawing

substituents, 1,3-cyclohexanediones, and substituted anilino-lactones were next explored to investigate the generality of this methodology; when this reaction was carried out with an aliphatic aldehyde such as propionaldehyde or butanaldehyde in the same conditions ([bmim][triflate]/alum), the TLC and <sup>1</sup>H NMR spectra of the crude reaction mixture showed the presence of a combination of starting materials and numerous by-products that can be synthesized via some reactions such as autocondensation reactions, with the yield of the expected product being very poor. The detailed results were presented in Table 5.

In conclusion, we have developed an extremely efficient and green procedure for the synthesis of biologically active natural product 4-aza-podophyllotoxin derivatives. These products were synthesized previously by the condensation of



SCHEME 4: Proposed mechanism.

benzaldehydes, enaminones, and tetronic acid [44, 45]. This is the first report of the synthesis of these compounds via a multicomponent condensation of various benzaldehydes, 1,3-cyclohexanediones, and anilinolactones in the presence of Alum as an inexpensive and available catalyst. The advantages of this new method are operational simplicity, high to excellent yields of products in short reaction times, and easy workup procedures.

### 2.1. Experimental Part

**General.** The chemicals used in this work were obtained from Fluka and Merck and were used without purification. Melting points were measured on an Electrothermal 9200 apparatus.  $^1\text{H}$  NMR spectra were recorded in DMSO- $d_6$  solvents on a Bruker DRX-400 spectrometer with tetramethylsilane as internal reference. The elemental analyses (C.H.N) were obtained from a Carlo ERBA Model EA 1108 analyzer. The purity determination of the substrates and reaction monitoring were accomplished by TLC on silica-gel polygram SILG/UV 254 plates (from Merck company).

All the products **4(a-r)** are known compounds and were characterized by comparison of their  $^1\text{H}$  NMR spectrum, physical properties, and elemental analyses data with previous synthetic products [44, 45].

**Typical Procedure for the Preparation of 4-Aza-Podophyllotoxin Derivatives.** To a mixture of benzaldehyde (1 mmol), dimedone (1 mmol), anilinolactone (1 mmol), and alum (20 mol%), [bmim][triflate] (0.2 mL) was added. The resulting mixture was stirred at  $90^\circ\text{C}$  for an appropriate time. After completion of the reaction as indicated by TLC, water (5 mL) was added and the product was extracted. The reaction mixture was filtered and the precipitate washed with water

and recrystallized by EtOH to afford the pure product and was identified by physical and spectroscopic data.

**9-(4-Methoxyphenyl)-4-p-tolyl-5,6,7,9-tetrahydrofuro[3,4-b]quinoline-1,8(3H,4H)-dione (4c).** Yield 93%; mp:  $255\text{--}257^\circ\text{C}$ ;  $^1\text{H}$  NMR (DMSO- $d_6$ ):  $\delta$  1.67–1.95 (2H, m,  $\text{CH}_2$ ), 2.12–2.20 (2H, m,  $\text{CH}_2$ ), 2.21–2.30 (2H, m,  $\text{CH}_2$ ), 2.38 (3H, s,  $\text{CH}_3$ ), 3.75 (3H, s,  $\text{CH}_3$ ), 4.39–4.55 (2H, m,  $\text{CH}_2$ ), 4.79 (1H, s, CH), 6.80–7.47 (8H, m, ArH). Anal. Calcd for  $\text{C}_{25}\text{H}_{23}\text{NO}_4$ : C, 74.79; H, 5.77; N, 3.49. Found C, 74.72; H, 5.71; N, 3.55.

**9-(4-Methoxyphenyl)-6,6-dimethyl-4-p-tolyl-5,6,7,9-tetrahydrofuro[3,4-b]quinoline-1,8(3H,4H)-dione (4h).** Yield 95%; mp:  $257\text{--}258^\circ\text{C}$ ;  $^1\text{H}$  NMR (DMSO- $d_6$ ):  $\delta$  0.85 (3H, s,  $\text{CH}_3$ ), 0.95 (3H, s,  $\text{CH}_3$ ), 1.95–2.10 (2H, m,  $\text{CH}_2$ ), 2.20–2.28 (2H, m,  $\text{CH}_2$ ), 2.44 (3H, s,  $\text{CH}_3$ ), 3.75 (3H, s,  $\text{OCH}_3$ ), 4.51–4.58 (2H, m,  $\text{CH}_2$ ), 4.73 (1H, s, CH), 6.81–7.45 (8H, m, ArH). Anal. Calcd for  $\text{C}_{27}\text{H}_{27}\text{NO}_4$ : C, 75.50; H, 6.34; N, 3.26. Found C, 75.45; H, 6.41; N, 3.20.

**9-(4-Bromophenyl)-6,6-dimethyl-4-p-tolyl-5,6,7,9-tetrahydrofuro[3,4-b]quinoline-1,8(3H,4H)-dione (4i).** Yield 94%; mp:  $271\text{--}273^\circ\text{C}$ ;  $^1\text{H}$  NMR (DMSO- $d_6$ ):  $\delta$  0.87 (3H, s,  $\text{CH}_3$ ), 0.95 (3H, s,  $\text{CH}_3$ ), 2.04–2.11 (2H, m,  $\text{CH}_2$ ), 2.18–2.23 (2H, m,  $\text{CH}_2$ ), 2.42 (3H, s,  $\text{CH}_3$ ), 4.50–4.54 (2H, m,  $\text{CH}_2$ ), 4.71 (1H, s, CH), 7.27–7.50 (8H, m, ArH). Anal. Calcd for  $\text{C}_{26}\text{H}_{24}\text{BrNO}_3$ : C, 65.28; H, 5.06; N, 2.93. Found C, 65.30; H, 5.04; N, 2.88.

**9-(4-Methoxyphenyl)-6,6-dimethyl-4-phenyl-5,6,7,9-tetrahydrofuro[3,4-b]quinoline-1,8(3H,4H)-dione (4l).** Yield 92%; mp:  $260\text{--}262^\circ\text{C}$ ;  $^1\text{H}$  NMR (DMSO- $d_6$ ):  $\delta$  0.84 (3H, s,  $\text{CH}_3$ ), 0.95 (3H, s,  $\text{CH}_3$ ), 2.02–2.11 (2H, m,  $\text{CH}_2$ ), 2.18–2.25 (2H, m,  $\text{CH}_2$ ), 3.74 (3H, s,  $\text{CH}_3$ ), 4.45–4.61 (2H, m,  $\text{CH}_2$ ), 4.75 (1H, s, CH), 6.83–7.58 (9H, m, ArH). Anal. Calcd for  $\text{C}_{26}\text{H}_{25}\text{NO}_4$ : C, 75.16; H, 6.06; N, 3.37. Found C, 75.11; H, 6.10; N, 3.43.

**4,9-Bis(4-chlorophenyl)-6,6-dimethyl-5,6,7,9-tetrahydrofuro[3,4-b]quinoline-1,8(3H,4H)-dione (4n).** Yield 93%; mp:

TABLE 5: Synthesis of 4-aza-podophyllotoxin derivatives (**4a-r**)<sup>a</sup>.

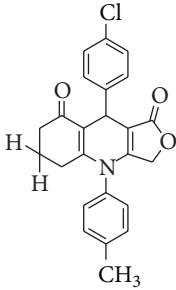
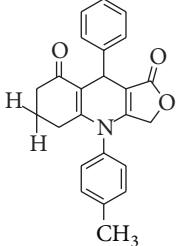
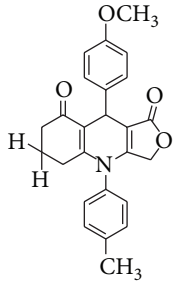
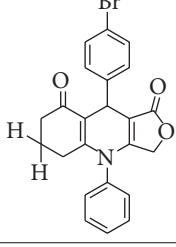
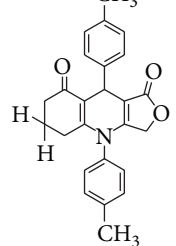
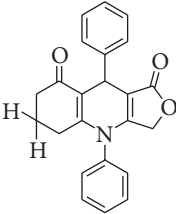
Entry	R	R <sub>1</sub>	R <sub>2</sub>	Product	Yield (%) <sup>b</sup>	Lit. Mp (°C)	Found Mp (°C)
<b>4a</b>	4-Cl	H	<i>p</i> -CH <sub>3</sub>		92	274-275	275-276
<b>4b</b>	H	H	<i>p</i> -CH <sub>3</sub>		91	280-281	281-282
<b>4c</b>	4-CH <sub>3</sub> O	H	<i>p</i> -CH <sub>3</sub>		93	254-255	255-257
<b>4d</b>	4-Br	H	H		89	280-281	281-282
<b>4e</b>	4-CH <sub>3</sub>	H	<i>p</i> -CH <sub>3</sub>		93	263-264	264-266
<b>4f</b>	H	H	H		90	275-276	276-277

TABLE 5: Continued.

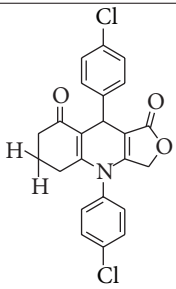
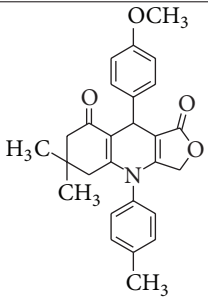
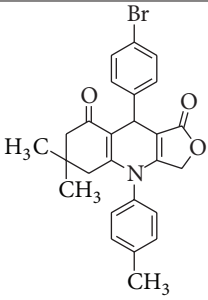
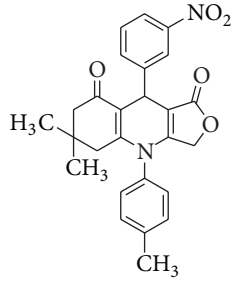
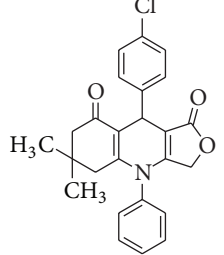
Entry	R	R <sub>1</sub>	R <sub>2</sub>	Product	Yield (%) <sup>b</sup>	Lit. Mp (°C)	Found Mp (°C)
4g	4-Cl	H	<i>p</i> -Cl		92	227-228	228-230
4h	4-CH <sub>3</sub> O	CH <sub>3</sub>	<i>p</i> -CH <sub>3</sub>		95	256-257	257-258
4i	4-Br	CH <sub>3</sub>	<i>p</i> -CH <sub>3</sub>		94	269-270	271-273
4j	3-NO <sub>2</sub>	CH <sub>3</sub>	<i>p</i> -CH <sub>3</sub>		92	232-233	232-233
4k	4-Cl	CH <sub>3</sub>	H		94	260-261	262-263

TABLE 5: Continued.

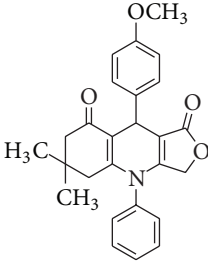
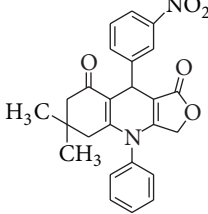
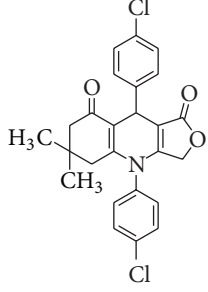
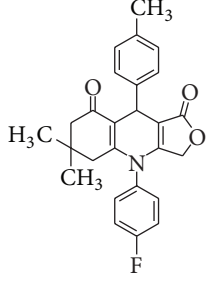
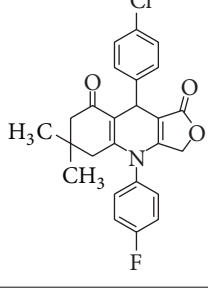
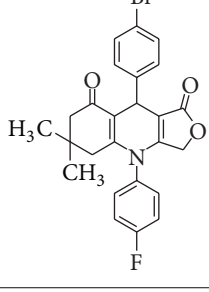
Entry	R	R <sub>1</sub>	R <sub>2</sub>	Product	Yield (%) <sup>b</sup>	Lit. Mp (°C)	Found Mp (°C)
4l	4-CH <sub>3</sub> O	CH <sub>3</sub>	H		92	258-259	260-262
4m	3-NO <sub>2</sub>	CH <sub>3</sub>	H		89	293-294	294-295
4n	4-Cl	CH <sub>3</sub>	<i>p</i> -Cl		93	>300	>300
4o	4-CH <sub>3</sub>	CH <sub>3</sub>	<i>p</i> -F		93	281-283	283-285
4p	4-Cl	CH <sub>3</sub>	<i>p</i> -F		92	297-299	299-300
4q	4-Br	CH <sub>3</sub>	<i>p</i> -F		88	283-285	285-287

TABLE 5: Continued.

Entry	R	R <sub>1</sub>	R <sub>2</sub>	Product	Yield (%) <sup>b</sup>	Lit. Mp (°C)	Found Mp (°C)
4r	4-OCH <sub>3</sub>	CH <sub>3</sub>	<i>p</i> -F		92	266–268	268–270

<sup>a</sup>Reaction conditions: benzaldehydes **1** (1 mmol), cyclohexanediones **2** (1 mmol), and anilinolactones **3** (1 mmol), IL (0.2 mL), alum (20 mol%), at 90 °C.

<sup>b</sup>Isolated yields.

>300 °C; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): δ 0.83 (3H, s, CH<sub>3</sub>), 0.96 (3H, s, CH<sub>3</sub>), 2.02–2.11 (2H, m, CH<sub>2</sub>), 2.18–2.27 (2H, m, CH<sub>2</sub>), 4.50–4.63 (2H, m, CH<sub>2</sub>), 4.74 (1H, s, CH), 7.35–7.62 (8H, m, ArH). Anal. Calcd for C<sub>25</sub>H<sub>21</sub>Cl<sub>2</sub>NO<sub>3</sub>: C, 66.09; H, 4.66; N, 3.08. Found C, 66.14; H, 4.71; N, 3.05.

4-(4-Fluorophenyl)-6,6-dimethyl-9-*p*-tolyl-5,6,7,9-tetrahydrofuro[3,4-*b*]quinoline-1,8(3H,4H)-dione (**4o**). Yield 93%; mp: 283–285 °C; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): δ 0.84 (3H, s, CH<sub>3</sub>), 0.91 (3H, s, CH<sub>3</sub>), 1.97–2.10 (2H, m, CH<sub>2</sub>), 2.15–2.24 (2H, m, CH<sub>2</sub>), 2.26 (3H, s, CH<sub>3</sub>), 4.53–4.60 (2H, m, CH<sub>2</sub>), 4.75 (1H, s, CH), 7.06–7.66 (8H, m, ArH). Anal. Calcd for C<sub>26</sub>H<sub>24</sub>FNO<sub>3</sub>: C, 74.80; H, 5.79; F, 4.55; N, 3.36. Found C, 74.85; H, 5.75; N, 3.40.

9-(4-Chlorophenyl)-4-(4-fluorophenyl)-6,6-dimethyl-5,6,7,9-tetrahydrofuro[3,4-*b*]quinoline-1,8(3H,4H)-dione (**4p**). Yield 92%; mp: 299–300 °C; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): δ 0.84 (3H, s, CH<sub>3</sub>), 0.96 (3H, s, CH<sub>3</sub>), 2.01–2.11 (2H, m, CH<sub>2</sub>), 2.16–2.22 (2H, m, CH<sub>2</sub>), 4.50–4.62 (2H, m, CH<sub>2</sub>), 4.76 (1H, s, CH), 7.32–7.62 (8H, m, ArH). Anal. Calcd for C<sub>25</sub>H<sub>21</sub>ClFNO<sub>3</sub>: C, 68.57; H, 4.83; N, 3.20. Found C, 68.63; H, 4.78; N, 3.22.

9-(4-Bromophenyl)-4-(4-fluorophenyl)-6,6-dimethyl-5,6,7,9-tetrahydrofuro[3,4-*b*]quinoline-1,8(3H,4H)-dione (**4q**). Yield 88%; mp: 285–287 °C; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): δ 0.85 (3H, s, CH<sub>3</sub>), 0.97 (3H, s, CH<sub>3</sub>), 2.00–2.11 (2H, m, CH<sub>2</sub>), 2.15–2.20 (2H, m, CH<sub>2</sub>), 4.49–4.58 (2H, m, CH<sub>2</sub>), 4.74 (1H, s, CH), 7.28–7.61 (8H, m, ArH). Anal. Calcd for C<sub>25</sub>H<sub>21</sub>BrFNO<sub>3</sub>: C, 62.25; H, 4.39; N, 2.90. Found C, 62.19; H, 4.44; N, 2.88.

4-(4-Fluorophenyl)-9-(4-methoxyphenyl)-6,6-dimethyl-5,6,7,9-tetrahydrofuro[3,4-*b*]quinoline-1,8(3H,4H)-dione (**4r**). Yield 92%; mp: 268–270 °C; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): δ 0.88 (3H, s, CH<sub>3</sub>), 0.94 (3H, s, CH<sub>3</sub>), 1.98–2.04 (2H, m, CH<sub>2</sub>), 2.15–2.22 (2H, m, CH<sub>2</sub>), 3.74 (3H, s, OCH<sub>3</sub>), 4.48–4.60 (2H, m, CH<sub>2</sub>), 4.75 (1H, s, CH), 6.88–7.60 (8H, m, ArH). Anal. Calcd for C<sub>26</sub>H<sub>24</sub>FNO<sub>4</sub>: C, 72.04; H, 5.58; N, 3.23. Found C, 72.10; H, 5.52; N, 3.25.

## Acknowledgments


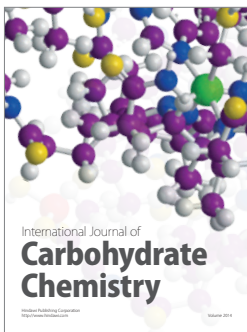
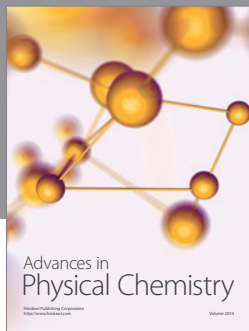
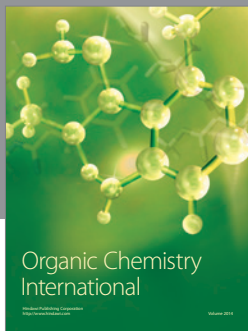
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