# An Efficient Synthesis of Pyrimido[4,5-*b*]quinoline and Indeno[2',1':5,6]pyrido[2,3-*d*]pyrimidine Derivatives via Multicomponent Reactions in Ionic Liquid

Da-Qing Shi<sup>\*</sup>, Sai-Nan Ni,<sup>b</sup> Fang Yang,<sup>b</sup> Jing-Wen Shi,<sup>b</sup> Guo-Lan Dou,<sup>b</sup> Xiao-Yue Li,<sup>b</sup> Xiang-Shan Wang,<sup>b,c</sup> Shun-Jun Ji<sup>a</sup>

<sup>a</sup> College of Chemistry and Chemical Engineering, Key Laboratory of Organic Synthesis of Jiangsu Province, Suzhou University, Suzhou 215123, P. R. China

<sup>b</sup> Department of Chemistry, Xuzhou Normal University, Xuzhou 221116, P. R. China

<sup>c</sup> Key Laboratory of Biotechnology on Medical Plants of Jiangsu Province, Xuzhou 221116, P. R. China

E-mail: dqshi@263.net

Received April 3, 2007



A series of pyrimido[4,5-*b*]quinoline and indeno[2',1':5,6]pyrido[2,3-*d*]pyrimidine derivatives were synthesized *via* the three-component reaction of an aldehyde, 6-aminopyrimidine-2,4-dione and 5,5-dimethyl-1,3-cyclohexanedione or 1,3-indanedione in ionic liquid 1-*n*-butyl-3-methylimidazolium bromide ([bmim]Br). This protocol has the advantages of easier work-up, milder reaction conditions, high yields and an environmentally benign procedure compared with other methods.

J. Heterocyclic Chem., 45, 963 (2008).

## **INTRODUCTION**

The importance of uracil and its annelated derivatives is well recognized by synthetic [1] as well as biological [2] chemists. With the development of clinically useful anticancer and antiviral drugs [3], there has recently been remarkable interest in the synthetic manipulations of uracils [4]. Pyrido[2,3-d]pyrimidines represent a heterocyclic ring system of considerable interest because of several biological activities associated with this scaffold. Some analogues have been found to act as anticancer agents inhibiting dihydrofolate reductases or tyrosine kinases [5], while others are known antiviral agents [6]. Therefore, for the preparation of these complex molecules large efforts have been directed towards the synthetic manipulation of uracils. As a result, a number of reports have appeared in the literature that usually describe forcing conditions, long reaction times using organic solvent and complex synthetic pathways [7]. Thus new routes for the synthesis of these molecules have attracted considerable attention in search for a rapid entry to these heterocycles.

Multi-component reactions (MCRs) are economically and environmentally very advantageous because multi-step syntheses produce considerable amounts of waste mainly due to complex isolation procedures often involving expensive, toxic and hazardous solvents after each step. MCRs are perfectly suited for combinatorial library synthesis, and thus are finding increasing use in the discovery process for new drugs and agrochemicals [8].

The ionic liquids have been the subject of considerable current interest as environmentally benign reaction media in organic synthesis because of their unique properties of nonvolatility, nonflammability, and recyclability, among others [9]. There has been growing recognition that ionic liquids are an attractive medium for many organic reactions and many MCRs in ionic liquids have been reported [10]. As part of our current studies on the development of new routes to heterocyclic systems [11], we now report an efficient and clean synthetic route to indeno[2',1':5,6]pyrido[2,3-d]pyrimidine derivatives and pyrimido[4,5-b]quinoline derivatives in ionic liquid without any catalyst.

# **RESULTS AND DISCUSSION**

When the three-components of aromatic aldehyde 1, 6aminopyrimidine-2,4-dione 2 and 5,5-dimethyl-1,3-cyclohexanedione or 1,3-cyclohexanedione 3 were treated in 1*n*-butyl-3-methylimidazolium bromide ([bmim]Br) at 95 °C for a few hours (Scheme 1), the desired 5-aryl-7,8,9,10-tetrahydropyrimido[4,5-*b*]quinoline-2,4,6-trione 4 were obtained in high yields (Table 1).

Entry	Ar	$\mathbb{R}^1$	$\mathbb{R}^2$	Time (h)	Yield (%)
4a	$4-CH_3OC_6H_4$	CH <sub>3</sub>	CH <sub>3</sub>	3	95
4b	$4-CH_3C_6H_4$	CH <sub>3</sub>	$CH_3$	3	93
4c	$4-BrC_6H_4$	$CH_3$	$CH_3$	4	89
4d	$4-ClC_6H_4$	$CH_3$	$CH_3$	3.5	90
<b>4e</b>	$2-CH_3OC_6H_4$	$CH_3$	$CH_3$	5	78
<b>4f</b>	$3,4-Cl_2C_6H_3$	$CH_3$	$CH_3$	4	97
4g	$2,4-Cl_2C_6H_3$	$CH_3$	$CH_3$	4	98
4h	$3,4-(CH_3)_2C_6H_3$	$CH_3$	$CH_3$	3.5	90
4i	$2-ClC_6H_4$	$CH_3$	$CH_3$	4.5	85
4j	Thiophen-2-yl	$CH_3$	$CH_3$	3	78
4k	$4-CH_3OC_6H_4$	Н	$CH_3$	4	85
41	$4-CH_3C_6H_4$	Н	$CH_3$	4	81
4m	$4-BrC_6H_4$	Н	$CH_3$	5	82
4n	$4-ClC_6H_4$	Н	$CH_3$	4	80
40	$2,4-Cl_2C_6H_3$	Н	$CH_3$	3	99
4p	$4-FC_6H_4$	Н	$CH_3$	3	92
4q	$2-CH_3OC_6H_4$	Н	$CH_3$	3.5	93
4r	$3,4-OCH_2OC_6H_3$	Н	$CH_3$	4	89
<b>4</b> s	$2-ClC_6H_4$	Н	$CH_3$	4	97
4t	Thiophen-2-yl	Н	$CH_3$	5	85
4u	$4-CH_3C_6H_4$	$CH_3$	Н	3	87
4v	$4-FC_6H_4$	$CH_3$	Н	2	91
4w	$4-ClC_6H_4$	$CH_3$	Н	2	86
4x	Thiophen-2-yl	$CH_3$	Н	3.5	80
4y	$4-CH_3OC_6H_4$	Н	Н	2	91
4z	$3,4-(CH_3)_2C_6H_3$	Н	Н	2.5	93

 Table 1

 Synthesis of 4 in ionic liquid [bmim]Br.



Scheme 1

As shown in Table 1, this protocol could be applied not only to the aromatic aldehydes with either electronwithdrawing groups (such as halide groups) or electrondonating groups (such as alkyl, hydroxy groups), but also to heterocyclic aldehydes. Therefore, we concluded that the electronic nature of the substituents of aldehydes has no significant effect on this reaction.

However, when an alphatic aldehyde was treated with 2 and 3 in [bmim]Br, the desired product 4 was not obtained, but the uncyclized product 5 was obtained (Scheme 2 and Table 2).



It is interesting, when phenylacetaldehyde was treated with 6-amino-1,3-dimethylpyrimidine-2,4-dione and 5,5dimethyl-1,3-cyclohexanedione, only 1,3,8,8-tetramethyl-

6,7,8,9-tetrahydropyrimido[4,5-b]quinoline-2,4,6-trione **6** was obtained in 67 % yield (Scheme 3). In this reaction the phenylacetaldehyde serves as a one carbon source in the forming the central ring of the product by losing the toluene or its equivalent under mild conditions. This method has not been reported in the literature.

#### Scheme 3



As expected, when the aromatic aldehydes 1 was replaced by dicarboxaldehydes 7, another series of bis(pyrimido[4,5-*b*]quinolin-2,4,6-trione) **8** were obtained under the same reaction conditions (Scheme 4). The results are summarized in Table 2.

#### Scheme 4



Entry R  $\mathbb{R}^1$  $\mathbb{R}^2$ Time (h) Yield (%) 72 5a iso-propyl CH<sub>3</sub> CH<sub>3</sub> 4 5b 4 64 CH<sub>3</sub> iso-propyl Н 8a 1,4-C<sub>6</sub>H<sub>4</sub>  $CH_3$  $CH_3$ 4 71 8b 82 1,3-C<sub>6</sub>H<sub>4</sub> Н  $CH_3$ 4 8c 1,4-C<sub>6</sub>H<sub>4</sub> CH 3.5 70 Η

Table 2

Synthesis of 5 and 8 in ionic liquid [bmim]Br.

In order to expand the scope of the present method, the replacement of 1,3-cyclohexanedione **3** with 1,3-indanedione **9** was examined. This is particularly attractive because compounds with indenopyridine motif show a wide range of biological activities such as calcium antagonistic [12], antioxidant [13], antihistamine and antidepressant [14] activities, and also act as phosphodiesterase (PDE) inhibitors [15], NK-1 and dopamine receptor ligands [16]. To our delight, under the above optimized conditions, the reactions proceeded smoothly. A series of indeno[2',1':5,6]-pyrido[2,3-d]py-rimidines **10** were obtained (Scheme 5) in excellent yields. The results are summarized in Table 3.

### Scheme 5



 Table 3

 Synthesis of 10 in ionic liquid [bmim]Br.

Entry	Ar	R	Time (h)	Yield (%)
10a	$4-CH_3C_6H_4$	CH <sub>3</sub>	4	86
10b	$4-FC_6H_4$	$CH_3$	3	90
10c	4-ClC <sub>6</sub> H <sub>4</sub>	$CH_3$	3	92
10d	$4-BrC_6H_4$	$CH_3$	3	92
10e	$4-NO_2C_6H_4$	$CH_3$	3.5	91
10f	3-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	$CH_3$	4	90
10g	2-NO <sub>2</sub> -5-ClC <sub>6</sub> H <sub>3</sub>	CH <sub>3</sub>	3.5	90
10h	3,4-Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	$CH_3$	3.5	93
10i	3-ClC <sub>6</sub> H <sub>4</sub>	$CH_3$	3	90
10j	$2,4-Cl_2C_6H_3$	$CH_3$	3	92
10k	3,4-OCH <sub>2</sub> OC <sub>6</sub> H <sub>3</sub>	$CH_3$	3	90
<b>101</b>	Thiophen-2-yl	$CH_3$	4.5	75
10m	Pyridin-4-yl	$CH_3$	5	77
10n	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	Н	2	91
<b>10</b> 0	4-ClC <sub>6</sub> H <sub>4</sub>	Н	2	93
10p	$4-BrC_6H_4$	Н	2.5	91
10q	$4-NO_2C_6H_4$	Н	2	89

Although the detailed mechanism of the above reaction remains to be fully clarified, the formation of indeno-[2',1':5,6]pyrido[2,3-*d*]pyrimidine derivatives **10** could be explained by a reaction sequence presented in Scheme 6. We proposed that the reaction proceeded *via* a reaction sequence of condensation, addition, cyclization, dehydration and aromatization. First, the condensation of aldehyde **1** and 1,3indanedione 9 gave the intermediate product 11. The addition of 11 to 6-aminopyrimidine-2,4-dione 2 then furnished the intermediate product 13, which upon intramolecular cyclization, dehydration and aromatization gave rise to 10.





Evidence supporting this proposed mechanism came from the observation that when **11a** and **2** were reacted under same conditions, the expected product **10a** was obtained in a yield similar to that obtained in the one-pot reaction (Scheme 7).

Scheme 7





Figure 1. X-ray structure of 4a

All the products 4, 5, 6, 8 and 10 were characterized by IR, <sup>1</sup>H NMR and elemental analysis. The structures of 4a, 5a and 10b were further confirmed by single crystal X-ray diffraction analysis. Figure 1, Figure 2 and Figure 3 show the molecular structures of 4a, 5a and 10b, respectively. The crystallographic data of these compounds are summarized in Table 4

![](_page_3_Figure_2.jpeg)

Figure 2. X-ray structure of 5a

![](_page_3_Figure_4.jpeg)

Figure 3. X-ray structure of 10b

In conclusion, a series of 5-aryl-5,6,7,8,9,10-hexhydropyrimido[4,5-*b*]quinoline-2,4,6-triones and 5-arylindeno-[2',1':5,6]pyrido[2,3-*d*]pyrimidine-2,4,6-triones were synthesized *via* three-component reaction of aldehyde, 6aminopyrimidine-2,4-dione and 5,5-dimethyl-1,3-cyclohexanedione or 1,3-cyclohexanedione or 1,3-indanedione in ionic liquid [bmim]Br. The advantages of this method are easier work-up, milder reaction conditions, high yields and environmentally benign procedure.

 Table 4

 Crystallographic data for 4a, 5a and 10b.

	4a	5a	10b
Empirical formula	C22H25N3O4	$C_{16}H_{23}N_{3}O_{4}$	C22H14FN3O3
Formula weight	395.45	321.37	387.36
Temperature (K)	298(2)	298(2)	298(2)
Wavelength (Å)	0.71073	0.71073	0.71073
Crystal system	monoclinic	monoclinic	monoclinic
Space group	$P2_1/n$	$P2_1/n$	$P2_1/c$
a (Å)	10.827(13)	9.119(2)	11.765(2)
b (Å)	16.65(2)	19.354(5)	15.455(3)
c (Å)	11.160(3)	9.200(2)	10.041(2)
(°)	90	90	90
$(\circ)$	100.022(17)	96.867(4)	103.423(2)
(°)	90	90	90
$V(Å^3)$	1981(4)	1611.9(7)	1775.9(6)
Z	4	4	4
$D_{calc}$ (Mg/m <sup>3</sup> )	1.326	1.324	1.449
Absorption coefficient (mm <sup>-1</sup> )	0.092	0.096	0.106
F (000)	840	688	800
Crystal size (mm)	$0.48 \times 0.39 \times 0.32$	$0.42 \times 0.23 \times 0.19$	$0.62 \times 0.50 \times 0.43$
Range (°)	2.22 to 25.01	2.10 to 25.01	1.78 to 25.01
Limiting indices	$-10 \le h \le 12$	$-10 \le h \le 10$	-13 ≤h ≤13
-	-19 ≤k ≤14	$-22 \leq k \leq 23$	$-12 \leq k \leq 18$
	-12 ≤1 ≤13	-8 ≤1 ≤10	-11 ≤1 ≤10
Reflections collected	9910	8368	9003
Independent reflections	3489	2838	3124
Data/restraints/parameters	3489/0/262	2838/0/208	3124/0/262
Goodness-of-fit on F <sup>2</sup>	1.019	1.032	1.046
Final R indices $[I > 2 (I)]$	0.0477	0.0531	0.0450
R indices (all data)	0.1118	0.1333	0.1085
Largest diff. Peak and hole (e·Å <sup>-3</sup> )	0.220 and -0.181	0.352 and -0.174	0.197 and -0.189

### EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on a Tensor 27 spectrometer. <sup>1</sup>H NMR spectra were measured on a Bruker DPX-400 M Hz spectrometer using TMS as internal standard, DMSO- $d_6$  as solvent. Microanalyses were carried out on Perkin-Elmer 2400 II instruments. X-ray diffraction was recorded on a Siemens Smart-1000 CCD diffractometer.

General Procedure for the Synthesis of 4, 5 and 6. A dry 50 mL flask was charged with aldehydes 1 (1 mmol), 6aminopyrimidine-2,4-dione (1 mmol), 5,5-dimethyl-1,3cyclohexanedione or 1,3-cyclohexanedione (1 mmol) and ionic liquid [bmim]Br (2 mL). The mixture was stirred at 95 °C for 2-5 h to complete the reaction (monitored by TLC), then 5 mL H<sub>2</sub>O was added. The yellow solid was filtered off and washed with water. The filtrate was the recovered for reuse by drying at 80 °C several hours in a vacuum. The crude product was purified by recrystallization from DMF and H<sub>2</sub>O to give 4 or 5 or 6.

**5-(4-Methoxyphenyl)-1,3,8,8-tetramethyl-7,8,9,10-tetrahydropyrimido**[**4,5-***b*]**quinoline-2,4,6(1***H***,3***H***,5***H***)-trione (<b>4a**). This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3283, 3095, 2953, 2884, 1705, 1636, 1489, 1426, 1379, 1338, 1291, 1243, 1207, 1147, 1080, 1036, 962, 884, 847, 787, 757, 728 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>):  $\delta$  0.89 (s, 3H, CH<sub>3</sub>), 1.04 (s, 3H, CH<sub>3</sub>), 2.04 (d, *J* = 16.4 Hz, 1H, CH), 2.21 (d, *J* = 16.4 Hz, 1H, CH), 2.53 (d, *J* = 17.2 Hz, 1H, CH), 2.60 (d, *J* = 17.2 Hz, 1H, CH), 3.09 (s, 3H, CH<sub>3</sub>N), 3.45 (s, 3H, CH<sub>3</sub>N), 3.67 (s, 3H, CH<sub>3</sub>O), 4.82 (s, 1H, CH), 6.74 (d, *J* = 8.4 Hz, 2H, ArH), 7.12 (d, *J* = 8.4 Hz, 2H, ArH), 8.98 (br., s, 1H, NH). *Anal.* Calcd. for C<sub>22</sub>H<sub>25</sub>N<sub>3</sub>O<sub>4</sub>: C, 66.82; H, 6.37; N, 10.63. Found: C, 66.95; H, 6.31; N, 10.72.

**1,3,8,8-Tetramethyl-5**-*p*-tolyl-7,8,9,10-tetrahydropyrimido-[**4,5**-*b*]quinoline-2,4,6(1*H*,3*H*,5*H*)-trione (**4b**). This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3221, 3091, 2959, 1702, 1661, 1642, 1595, 1493, 1379, 1338, 1289, 1244, 1208, 1149, 1124, 1080, 1042, 961, 845, 825, 786, 756 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>):  $\delta$  0.89 (s, 3H, CH<sub>3</sub>), 1.04 (s, 3H, CH<sub>3</sub>), 2.03 (d, *J* = 16.0 Hz, 1H, CH), 2.19 (s, 3H, CH<sub>3</sub>), 2.21 (d, *J* = 16.0 Hz, 1H, CH), 2.53 (d, *J* = 16.8 Hz, 1H, CH), 2.60 (d, *J* = 16.8 Hz, 1H, CH), 3.08 (s, 3H, CH<sub>3</sub>N), 3.45 (s, 3H, CH<sub>3</sub>N), 4.83 (s, 1H, CH), 6.97 (d, *J* = 8.0 Hz, 2H, ArH), 7.10 (d, *J* = 8.0 Hz, 2H, ArH), 8.98 (br., s, 1H, NH).*Anal*. Calcd. for C<sub>22</sub>H<sub>25</sub>N<sub>3</sub>O<sub>3</sub>: C, 69.64; H, 6.64; N, 11.07. Found: C, 69.70; H, 6.58; N, 11.15.

**5-(4-Bromophenyl)-1,3,8,8-tetramethyl-7,8,9,10-tetrahydropyrimido[4,5-***b***]quinoline-2,4,6(1***H***,3***H***,5***H***)-trione (4c). This compound was obtained as solid with mp 281-283 °C; ir (potassium bromide): 3381, 3063, 2963, 1696, 1654, 1637, 1503, 1377, 1360, 1289, 1244, 1210, 1150, 1076, 1012, 959, 848, 826, 751, 723, 690 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-***d***<sub>6</sub>): \delta 0.88 (s, 3H, CH<sub>3</sub>), 1.04 (s, 3H, CH<sub>3</sub>), 2.04 (d,** *J* **= 16.0 Hz, 1H, CH), 2.22 (d,** *J* **= 16.0 Hz, 1H, CH), 2.53 (d,** *J* **= 16.4 Hz, 1H, CH), 2.60 (d,** *J* **= 16.4 Hz, 1H, CH), 3.09 (s, 3H, CH<sub>3</sub>N), 3.45 (s, 3H, CH<sub>3</sub>N), 4.84 (s, 1H, CH), 7.18 (d,** *J* **= 8.4 Hz, 2H, ArH), 7.38 (d,** *J* **= 8.4 Hz, 2H, ArH), 9.05 (br., s, 1H, NH).** *Anal.* **Calcd. for C<sub>21</sub>H<sub>22</sub>BrN<sub>3</sub>O<sub>3</sub>: C, 56.77; H, 4.99; N, 9.46. Found: C, 56.84; H, 4.94; N, 9.37.** 

5-(4-Chlorophenyl)-1,3,8,8-tetramethyl-7,8,9,10-tetrahydropyrimido[4,5-b]quinoline-2,4,6(1H,3H,5H)-trione (4d). This compound was obtained as solid with mp 292-294 °C; ir (potassium bromide): 3387, 3048, 2964, 1691, 1654, 1627, 1505, 1377, 1326, 1288, 1243, 1209, 1149, 1092, 1049, 1016, 958, 848, 825, 776, 749, 691 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO- $d_6$ ):  $\delta$  0.88 (s, 3H, CH<sub>3</sub>), 1.04 (s, 3H, CH<sub>3</sub>), 2.04 (d, *J* = 16.4 Hz, 1H, CH), 2.22 (d, *J* = 16.4 Hz, 1H, CH), 2.53 (d, *J* = 17.6 Hz, 1H, CH), 2.61 (d, *J* = 17.6 Hz, 1H, CH), 3.09 (s, 3H, CH<sub>3</sub>N), 3.45 (s, 3H, CH<sub>3</sub>N), 4.86 (s, 1H, CH), 7.24 (s, 4H, ArH), 9.05 (br., s, 1H, NH). *Anal.* Calcd. for C<sub>21</sub>H<sub>22</sub>ClN<sub>3</sub>O<sub>3</sub>: C, 63.08; H, 5.55; N, 10.51. Found: C, 63.27; H, 5.59; N, 10.43.

**5-(2-Methoxyphenyl)-1,3,8,8-tetramethyl-7,8,9,10-tetrahydropyrimido**[4,5-*b*]quinoline-2,4,6(1*H*,3*H*,5*H*)-trione (4e). This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3209, 3071, 2943, 2835, 1704, 1647, 1602, 1514, 1382, 1353, 1289, 1243, 1176, 1147, 1110, 1082, 1050, 1026, 961, 860, 784, 767, 748 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>):  $\delta$  0.83 (s, 3H, CH<sub>3</sub>), 1.03 (s, 3H, CH<sub>3</sub>), 1.93 (d, *J* = 16.0 Hz, 1H, CH), 2.17 (d, *J* = 16.0 Hz, 1H, CH), 2.48 (d, *J* = 16.4 Hz, 1H, CH), 2.54 (d, *J* = 16.4 Hz, 1H, CH), 3.04 (s, 3H, CH<sub>3</sub>N), 3.67 (s, 3H, CH<sub>3</sub>O), 4.94 (s, 1H, CH), 6.74-6.78 (m, 1H, ArH), 7.23 (d, *J* = 7.6 Hz, 1H, ArH), 8.96 (br., s, 1H, NH). Anal. Calcd. for C<sub>22</sub>H<sub>25</sub>N<sub>3</sub>O<sub>4</sub>: C, 66.82; H, 6.37; N, 10.63. Found: C, 66.94; H, 6.31; N, 10.73.

**5-(3,4-Dichlorophenyl)-1,3,8,8-tetramethyl-7,8,9,10-tetrahydropyrimido**[**4,5-***b*]**quinoline-2,4,6(1***H***,3***H***,5***H***)-trione (<b>4f**). This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3212, 3092, 2954, 2891, 1699, 1661, 1635, 1595, 1490, 1376, 1345, 1288, 1245, 1198, 1153, 1127, 1081, 1052, 1028, 960, 833, 783, 750 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>):  $\delta$  0.89 (s, 3H, CH<sub>3</sub>), 1.04 (s, 3H, CH<sub>3</sub>), 2.06 (d, *J* = 16.0 Hz, 1H, CH), 2.22 (d, *J* = 16.0 Hz, 1H, CH), 2.54 (d, *J* = 17.2 Hz, 1H, CH), 2.63 (d, *J* = 17.2 Hz, 1H, CH), 3.09 (s, 3H, CH<sub>3</sub>N), 3.45 (s, 3H, CH<sub>3</sub>N), 4.84 (s, 1H, CH), 7.21 (dd, *J*<sub>1</sub> = 2.0 Hz, *J*<sub>2</sub> = 8.0 Hz, 1H, ArH), 7.40 (d, *J* = 2.0 Hz, 1H, ArH), 7.45 (d, *J* = 8.0 Hz, 1H, ArH), 9.09 (br., s, 1H, NH). *Anal.* Calcd. for C<sub>21</sub>H<sub>21</sub> Cl<sub>2</sub>N<sub>3</sub>O<sub>3</sub>: C, 58.07; H, 4.87; N, 9.68. Found: C, 58.21; H, 4.83; N, 9.59.

**5-(2,4-Dichlorophenyl)-1,3,8,8-tetramethyl-7,8,9,10-tetrahydropyrimido**[**4,5-***b***]quinoline-2,4,6(1***H***,3***H***,5***H***)-trione (<b>4g**). This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3219, 3092, 2953, 2871, 1704, 1654, 1644, 1602, 1495, 1459, 1379, 1358, 1288, 1243, 1211, 1149, 1125, 1099, 1082, 1045, 962, 863, 841, 754 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>):  $\delta$  0.89 (s, 3H, CH<sub>3</sub>), 1.03 (s, 3H, CH<sub>3</sub>), 1.98 (d, *J* = 16.0 Hz, 1H, CH), 2.20 (d, *J* = 16.0 Hz, 1H, CH), 2.53 (d, *J* = 17.2 Hz, 2H, CH<sub>2</sub>), 3.05 (s, 3H, CH<sub>3</sub>N), 3.45 (s, 3H, CH<sub>3</sub>N), 5.13 (s, 1H, CH), 7.25 (dd, *J*<sub>1</sub> = 2.0 Hz, *J*<sub>2</sub> = 8.4 Hz, 1H, ArH), 7.33 (d, *J* = 8.4 Hz, 1H, ArH), 7.35 (d, *J* = 2.0 Hz, 1H, ArH), 9.04 (br., s, 1H, NH). *Anal.* Calcd. for C<sub>21</sub>H<sub>21</sub>Cl<sub>2</sub>N<sub>3</sub>O<sub>3</sub>: C, 58.07; H, 4.87; N, 9.68. Found: C, 58.24; H, 4.92; N, 9.57.

**5-(3,4-Dimethylphenyl)-1,3,8,8-tetramethyl-7,8,910-tetrahydropyrimido**[**4,5-***b***]quinoline-2,4,6(1***H***,3***H***,5***H***)-trione (<b>4h**). This compound was obtained as solid with mp 294-296 °C; ir (potassium bromide): 3204, 3089, 2963, 1699, 1661, 1632, 1595, 1492, 1371, 1287, 1245, 1209, 1148, 1129, 1082, 1052, 960, 883, 838, 797, 758, 685 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>):  $\delta$  0.90 (s, 3H, CH<sub>3</sub>), 1.04 (s, 3H, CH<sub>3</sub>), 2.03 (d, *J* = 16.4 Hz, 1H, CH), 2.10 (s, 3H, CH<sub>3</sub>), 2.12 (s, 3H, CH<sub>3</sub>), 2.21 (d, *J* = 16.4 Hz, 1H, CH), 2.53 (d, *J* = 17.2 Hz, 1H, CH), 2.60 (d, *J* = 17.2 Hz, 1H, CH), 3.08 (s, 3H, CH<sub>3</sub>N), 3.44 (s, 3H, CH<sub>3</sub>N), 4.78 (s, 1H, CH), 6.89-6.93 (m, 2H, ArH), 6.98 (s, 1H, ArH), 8.98 (br., s, 1H, NH). *Anal.* Calcd. for C<sub>23</sub>H<sub>27</sub>N<sub>3</sub>O<sub>3</sub>: C, 70.21; H, 6.92; N, 10.68. Found: C, 70.35; H, 6.99; N, 10.62.

**5-(2-Chlorophenyl)-1,3,8,8-tetramethyl-7,8,9,10-tetrahydropyrimido[4,5-***b***]quinoline-2,4,6(1***H***,3***H***,5***H***)-trione (4i). This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3222, 3093, 2959, 1702, 1661, 1632, 1606, 1493, 1438, 1379, 1359, 1288, 1244, 1210, 1150, 1128, 1080, 1050, 962, 836, 769, 752 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-***d***<sub>6</sub>): \delta 0.88 (s, 3H, CH<sub>3</sub>), 1.03 (s, 3H, CH<sub>3</sub>), 1.97 (d,** *J* **= 16.0 Hz, 1H, CH), 2.19 (d,** *J* **= 16.0 Hz, 1H, CH), 2.58 (d,** *J* **= 17.2 Hz, 2H, CH<sub>2</sub>), 3.04 (s, 3H, CH<sub>3</sub>N), 3.45 (s, 3H, CH<sub>3</sub>N), 5.16 (s, 1H, CH), 7.05-7.10 (m, 1H, ArH), 7.14-7.22 (m, 2H, ArH), 7.33 (d,** *J* **= 7.6 Hz, 1H, ArH), 9.02 (br., s, 1H, NH).** *Anal***. Calcd. for C<sub>21</sub> H<sub>21</sub>ClN<sub>3</sub>O<sub>3</sub>: C, 63.08; H, 5.55; N, 10.51. Found: C, 63.17; H, 5.42; N, 10.64.** 

**1,3,8,8-Tetramethyl-5-(thiophen-2-yl)-7,8,9,10-tetrahydropyrimido**[**4,5-***b*]**quinoline-2,4,6(1***H*,3*H*,5*H*)-**trione (4j).** This compound was obtained as solid with mp 295-296 °C; ir (potassium bromide): 3299, 3239, 2961, 2944, 2869, 1702, 1661, 1640, 1614, 1494, 1437, 1380, 1359, 1342, 1280, 1247, 1210, 1202, 1148, 1071, 1051, 1035, 959, 873, 841, 811, 784, 753, 715 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>):  $\delta$  0.97 (s, 3H, CH<sub>3</sub>), 1.06 (s, 3H, CH<sub>3</sub>), 2.14 (d, *J* = 16.4 Hz, 1H, CH), 2.27 (d, *J* = 16.4 Hz, 1H, CH), 2.57 (d, *J* = 16.4 Hz, 1H, CH), 2.61 (d, *J* = 16.4 Hz, 1H, CH), 3.15 (s, 3H, CH<sub>3</sub>N), 3.41 (s, 3H, CH<sub>3</sub>N), 5.20 (s, 1H, CH), 6.75-6.83 (m, 2H, ArH), 7.17-7.21 (m, 1H, ArH), 9.19 (br., s, 1H, NH). *Anal.* Calcd. for C<sub>19</sub>H<sub>21</sub>N<sub>3</sub>O<sub>3</sub>S: C, 61.44; H, 5.70; N, 11.31. Found: C, 61.63; H, 5.60; N, 11.47.

**5-(4-Methoxyphenyl)-1,8,8-trimethyl-7,8,9,10-tetrahydropyrimido**[**4,5-***b*]**quinoline-2,4,6**(1*H,3H,5H*)-**trione** (**4k**). This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3278, 3218, 3092, 2968, 2832, 1721, 1654, 1644, 1492, 1420, 1383, 1356, 1284, 1237, 1213, 1171, 1154, 1104, 1039, 879, 838, 747 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-d<sub>6</sub>):  $\delta$  0.89 (s, 3H, CH<sub>3</sub>), 1.04 (s, 3H, CH<sub>3</sub>), 2.04 (d, *J* = 16.0 Hz, 1H, CH), 2.52 (d, *J* = 17.2 Hz, 1H, CH), 2.59 (d, *J* = 17.2 Hz, 1H, CH), 3.36 (s, 3H, CH<sub>3</sub>N), 3.67 (s, 3H, CH<sub>3</sub>O), 4.77 (s, 1H, CH), 6.74 (d, *J* = 8.4 Hz, 2H, ArH), 7.11 (d, *J* = 8.4 Hz, 2H, ArH), 8.92 (br., s, 1H, NH), 10.98 (br., s, 1H, NH). *Anal.* Calcd. for C<sub>21</sub>H<sub>23</sub>N<sub>3</sub>O<sub>4</sub>: C, 66.13; H, 6.08; N, 11.02. Found: C, 66.27; H, 6.02; N, 11.19.

**1,8,8-Trimethyl-5**-*p*-tolyl-7,8,9,10-tetrahydropyrimido[4,5*b*]quinoline-2,4,6(1*H*,3*H*,5*H*)-trione (41). This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3276, 3218, 3092, 2970, 2888, 1724, 1663, 1647, 1620, 1491, 1383, 1345, 1281, 1237, 1211, 1169, 1154, 1105, 1064, 880, 848, 830 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>):  $\delta$  0.88 (s, 3H, CH<sub>3</sub>), 1.04 (s, 3H, CH<sub>3</sub>), 2.03 (d, *J* = 16.0 Hz, 1H, CH), 2.19 (s, 3H, CH<sub>3</sub>), 2.21 (d, *J* = 16.0 Hz, 1H, CH), 2.52 (d, *J* = 17.6 Hz, 1H, CH), 2.59 (d, *J* = 17.6 Hz, 1H, CH), 3.37 (s, 3H, CH<sub>3</sub>N), 4.79 (s, 1H, CH), 6.98 (d, *J* = 8.0 Hz, 2H, ArH), 7.08 (d, *J* = 8.0 Hz, 2H, ArH), 8.93 (br., s, 1H, NH). 10.98 (br., s, 1H, NH). Anal. Calcd. for C<sub>21</sub>H<sub>23</sub>N<sub>3</sub>O<sub>3</sub>: C, 69.02; H, 6.34; N, 11.50. Found: C, 69.18; H, 6.29; N, 11.63.

**5-(4-Bromophenyl)-1,8,8-trimethyl-7,8,9,10-tetrahydropyrimido[4,5-***b***]<b>quinoline-2,4,6(1***H***,3***H***,5***H***)-<b>trione** (4m). This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3279, 3220, 3092, 2966, 2889, 1724, 1661, 1645, 1614, 1490, 1382, 1355, 1277, 1238, 1212, 1169, 1153, 1067, 1008, 879, 849, 833, 750 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>):  $\delta 0.87$  (s, 3H, CH<sub>3</sub>), 1.04 (s, 3H, CH<sub>3</sub>), 2.04 (d, *J* = 16.0 Hz, 1H, CH), 2.22 (d, *J* = 16.0 Hz, 1H, CH), 2.52 (d, *J* = 17.2 Hz, 1H, CH), 2.60 (d, *J* = 17.2 Hz, 1H, CH), 3.37 (s, 3H, CH<sub>3</sub>N), 4.80 (s, 1H, CH), 7.17 (d, *J* = 8.4 Hz, 2H, ArH), 7.38 (d, *J* = 8.4 Hz, 2H, ArH), 8.98 (br., s, 1H, NH), 11.03 (br., s, 1H, NH). *Anal.* Calcd. for C<sub>20</sub>H<sub>20</sub>BrN<sub>3</sub>O<sub>3</sub>: C, 55.83; H, 4.68; N, 9.77. Found: C, 55.95; H, 4.64; N, 9.82.

**5-(4-Chlorophenyl)-1,8,8-trimethyl-7,8,9,10-tetrahydropyrimido[4,5-b]quinoline-2,4,6(1***H***,3***H***,5***H***)-trione (4n). This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3276, 3219, 3092, 2968, 2890, 1742, 1663, 1639, 1617, 1490, 1383, 1355, 1278, 1237, 1213, 1169, 1153, 1086, 1012, 879, 850, 834, 751 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-***d***<sub>6</sub>): \delta 0.87 (s, 3H, CH<sub>3</sub>), 1.04 (s, 3H, CH<sub>3</sub>), 2.04 (d,** *J* **= 16.0 Hz, 1H, CH), 2.22 (d,** *J* **= 16.0 Hz, 1H, CH), 2.53 (d,** *J* **= 17.6 Hz, 1H, CH), 2.60 (d,** *J* **= 17.6 Hz, 1H, CH), 3.38 (s, 3H, CH<sub>3</sub>N), 4.82 (s, 1H, CH), 7.22 (d,** *J* **= 8.8 Hz, 2H, ArH), 7.25 (d,** *J* **= 8.8 Hz, 2H, ArH), 8.99 (br., s, 1H, NH), 11.03 (br., s, 1H, NH). Anal. Calcd. for C<sub>20</sub>H<sub>20</sub>ClN<sub>3</sub>O<sub>3</sub>: C, 62.26; H, 5.22; N, 10.89. Found: C, 62.27; H, 5.16; N, 10.94.** 

**5-(2,4-Dichlorophenyl)-1,8,8-trimethyl-7,8,9,10-tetrahydropyrimido[4,5-***b***]quinoline-2,4,6(1***H***,3***H***,5***H***)-trione (40). This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3279, 3201, 3087, 2960, 1718, 1676, 1649, 1632, 1585, 1496, 1381, 1357, 1281, 1236, 1214, 1151, 1103, 1064, 1046, 846, 757 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-***d***<sub>6</sub>): \delta 0.89 (s, 3H, CH<sub>3</sub>), 1.03 (s, 3H, CH<sub>3</sub>), 1.98 (d,** *J* **= 16.0 Hz, 1H, CH), 2.20 (d,** *J* **= 16.0 Hz, 1H, CH), 2.53 (d,** *J* **= 17.6 Hz, 2H, CH<sub>2</sub>), 3.38 (s, 3H, CH<sub>3</sub>N), 5.09 (s, 1H, CH), 7.26 (dd,** *J***<sub>1</sub> = 2.0 Hz,** *J***<sub>2</sub> = 8.4 Hz, 1H, ArH), 7.33 (d,** *J* **= 8.4 Hz, 1H, ArH), 7.35 (d,** *J* **= 2.0 Hz, 1H, ArH), 8.98 (br., s, 1H, NH), 10.96 (br., s, 1H, NH).** *Anal.* **Calcd. for C<sub>20</sub>H<sub>19</sub>Cl<sub>2</sub>N<sub>3</sub>O<sub>3</sub>: C, 57.15; H, 4.56; N, 10.00. Found: C, 57.32; H, 4.51; N, 10.12.** 

**5-(4-Fluorophenyl)-1,8,8-trimethyl-7,8,9,10-tetrahydropyrimido[4,5-***b***]quinoline-2,4,6(1***H***,3***H***,5***H***)-trione (4p). This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3282, 3224, 3095, 3017, 2962, 2889, 1724, 1661, 1646, 1617, 1491, 1420, 1384, 1344, 1282, 1218, 1154, 1112, 1066, 846, 753, 713 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-***d***<sub>6</sub>): \delta 0.87 (s, 3H, CH<sub>3</sub>), 1.04 (s, 3H, CH<sub>3</sub>), 2.05 (d,** *J* **= 16.0 Hz, 1H, CH), 2.22 (d,** *J* **= 16.0 Hz, 1H, CH), 2.53 (d,** *J* **= 17.2 Hz, 1H, CH), 2.60 (d,** *J* **= 17.2 Hz, 1H, CH), 3.38 (s, 3H, CH<sub>3</sub>N), 4.83 (s, 1H, CH), 6.98-7.03 (m, 2H, ArH), 7.21-7.24 (m, 2H, ArH), 8.98 (br., s, 1H, NH), 11.02 (br., s, 1H, NH).** *Anal.* **Calcd. for C<sub>20</sub>H<sub>20</sub>FN<sub>3</sub> O<sub>3</sub>: C, 65.03; H, 5.46; N, 11.38. Found: C, 65.16; H, 5.51; N, 11.32.** 

**5-(2-Methoxyphenyl)-1,8,8-trimethyl-7,8,9,10-tetrahydropyrimido[4,5-***b***]quinoline-2,4,6(1***H***,3***H***,5***H***)-trione (4q). This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3238, 3209, 3088, 2952, 2834, 1714, 1648, 1617, 1499, 1383, 1358, 1286, 1250, 1235, 1198, 1158, 1119, 1029, 856, 789, 757 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-***d***<sub>6</sub>): \delta 0.83 (s, 3H, CH<sub>3</sub>), 1.03 (s, 3H, CH<sub>3</sub>), 1.93 (d,** *J* **= 16.4 Hz, 1H, CH), 2.17 (d,** *J* **= 16.4 Hz, 1H, CH), 2.48 (d,** *J* **= 17.2 Hz, 1H, CH), 2.53 (d,** *J* **= 17.2 Hz, 1H, CH), 6.75-6.78 (m, 1H, ArH), 6.84 (d,** *J* **= 8.0 Hz, 1H, ArH), 7.04-7.08 (m, 1H, ArH), 7.20 (dd,** *J***<sub>1</sub> = 1.6 Hz,** *J***<sub>2</sub> = 7.2 Hz, 1H, ArH), 8.89 (br., s, 1H, NH), 10.84 (br., s, 1H, NH).** *Anal.* **Calcd. for C<sub>21</sub>H<sub>23</sub>N<sub>3</sub>O<sub>4</sub>: C, 66.13; H, 6.08; N, 11.02. Found: C, 66.25; H, 6.21; N, 11.09.** 

**5-(3,4-Methylidenedioxyphenyl)-1,8,8-trimethyl-7,8,9,10tetrahydropyrimido[4,5-***b***]quinoline-2,4,6(1***H***,3***H***, 5***H***)-trione (<b>4r**). This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3296, 3164, 3058, 2953, 2804, 1720, 1691, 1671, 1641, 1625, 1495, 1439, 1415, 1367, 1357, 1246, 1212, 1169, 1151, 1104, 1036, 927, 857, 794, 778, 759 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>):  $\delta$  0.90 (s, 3H, CH<sub>3</sub>), 1.04 (s, 3H, CH<sub>3</sub>), 2.06 (d, *J* = 16.0 Hz, 1H, CH), 2.21 (d, *J* = 16.0 Hz, 1H, CH), 2.52 (d, *J*  = 17.6 Hz, 1H, CH), 2.60 (d, J = 17.6 Hz, 1H, CH), 3.37 (s, 3H, CH<sub>3</sub>N), 4.76 (s, 1H, CH), 5.91 (s, 2H, OCH<sub>2</sub>O), 6.51-6.67 (m, 1H, ArH), 6.71-6.73 (m, 2H, ArH), 8.94 (br., s, 1H, NH), 11.00 (br., s, 1H, NH). *Anal.* Calcd. for C<sub>21</sub>H<sub>21</sub>N<sub>3</sub>O<sub>5</sub>: C, 63.79; H, 5.35; N, 10.63. Found: C, 63.71; H, 5.42; N, 10.74.

**5-(2-Chlorophenyl)-1,8,8-trimethyl-7,8,9,10-tetrahydropyrimido**[**4,5-***b*]**quinoline-2,4,6(1***H,3H,5H*)-**trione (4s).** This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3282, 3223, 3087, 2954, 2869, 1684, 1625, 1609, 1497, 1438, 1378, 1356, 1342, 1283, 1239, 1214, 1169, 1148, 1100, 1037, 790, 755 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>):  $\delta$ 0.88 (s, 3H, CH<sub>3</sub>), 1.03 (s, 3H, CH<sub>3</sub>), 1.97 (d, *J* = 16.0 Hz, 1H, CH), 2.19 (d, *J* = 16.0 Hz, 1H, CH), 2.53 (d, *J* = 17.2 Hz, 2H, CH<sub>2</sub>), 3.38 (s, 3H, CH<sub>3</sub>N), 5.12 (s, 1H, CH), 7.06-7.11 (m, 1H, ArH), 7.15-7.23 (m, 2H, ArH), 7.32-7.35 (m, 1H, ArH), 8.96 (br., s, 1H, NH), 10.93 (br., s, 1H, NH). *Anal.* Calcd. for C<sub>20</sub>H<sub>20</sub>ClN<sub>3</sub>O<sub>3</sub>: C, 62.26; H, 5.22; N, 10.89. Found: C, 62.39; H, 5.14; N, 10.94.

**5-(Thiophen-2-yl)-1,8,8-trimethyl-7,8,9,10-tetrahydropyrimido[4,5-***b***]<b>quinoline-2,4,6(1***H***,3***H***,5***H***)-<b>trione (4t).** This compound was obtained as solid with mp 294-296 °C; ir (potassium bromide): 3332, 3187, 3064, 2959, 1706, 1664, 1625, 1498, 1384, 1352, 1278, 1256, 1214, 1148, 1090, 1061, 1035, 887, 834, 786, 764, 696 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>):  $\delta$  0.97 (s, 3H, CH<sub>3</sub>), 1.06 (s, 3H, CH<sub>3</sub>), 2.14 (d, *J* = 16.0 Hz, 1H, CH), 2.57 (d, *J* = 16.0 Hz, 1H, CH), 2.53 (d, *J* = 17.6 Hz, 1H, CH), 2.60 (d, *J* = 17.6 Hz, 1H, CH), 3.36 (s, 3H, CH<sub>3</sub>N), 5.15 (s, 1H, CH), 6.74 (d, *J* = 3.2 Hz, 1H, ArH), 6.82 (dd, *J*<sub>1</sub> = 3.2 Hz, *J*<sub>2</sub> = 4.8 Hz, 1H, ArH), 7.19 (dd, *J*<sub>1</sub> = 1.2 Hz, *J*<sub>2</sub> = 5.2 Hz, 1H, ArH), 9.12 (br., s, 1H, NH), 11.11 (br., s, 1H, NH). *Anal.* Calcd. for C<sub>18</sub>H<sub>19</sub>N<sub>3</sub>O<sub>3</sub>S: C, 60.49; H, 5.36; N, 11.76. Found: C, 60.33; H, 5.29; N, 11.91.

**1,3-Dimethyl-5**-*p*-tolyl-7,8,9,10-tetrahydropyrimido[4,5-*b*]quinoline-2,4,6(1*H*,3*H*,5*H*)-trione (4u). This compound was obtained as solid with mp 284-285 °C; ir (potassium bromide): 3285, 3096, 2937, 1702, 1687, 1661, 1637, 1605, 1506, 1396, 1380, 1354, 1288, 1245, 1201, 1171, 1150, 1124, 1082, 1043, 949, 758 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>):  $\delta$  1.75-1.83 (m, 1H, CH), 1.91-1.96 (m, 1H, CH), 2.19 (s, 3H, CH<sub>3</sub>), 2.21-2.27 (m, 2H, CH<sub>2</sub>), 2.55-2.61 (m, 1H, CH), 2.74-2.79 (m, 1H, CH), 3.09 (s, 3H, CH<sub>3</sub>N), 3.45 (s, 3H, CH<sub>3</sub>N), 4.87 (s, 1H, CH), 6.97 (d, *J* = 8.0 Hz, 2H, ArH), 7.10 (d, *J* = 8.0 Hz, 2H, ArH), 9.07 (br., s, 1H, NH). Anal. Calcd. for C<sub>20</sub>H<sub>21</sub>N<sub>3</sub>O<sub>3</sub>: C, 68.36; H, 6.02; N, 11.96. Found: C, 68.43; H, 5.94; N, 12.06.

**1,3-Dimethyl-5-(4-fluorophenyl)-7,8,9,10-tetrahydropyr-imido[4,5-b]quinoline-2,4,6(1***H***,3***H***,5***H***)-trione (4v). This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3302, 2947, 1700, 1653, 1610, 1503, 1443, 1379, 1355, 1289, 1254, 1238, 1214, 1198, 1170, 1153, 1142, 1094, 1048, 950, 834, 764, 753 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-***d***<sub>6</sub>): \delta 1.77-1.84 (m, 1H, CH), 1.92-1.98 (m, 1H, CH), 2.23-2.27 (m, 2H, CH<sub>2</sub>), 2.54-2.62 (m, 1H, CH), 2.74-2.81 (m, 1H, CH), 3.09 (s, 3H, CH<sub>3</sub>N), 3.45 (s, 3H, CH<sub>3</sub>N), 4.91 (s, 1H, CH), 6.97-7.01 (m, 2H, ArH), 7.22-7.26 (m, 2H, ArH), 9.11 (br., s, 1H, NH).** *Anal.* **Calcd. for C<sub>19</sub>H<sub>18</sub>FN<sub>3</sub>O<sub>3</sub>: C, 64.22; H, 5.11; N, 11.82. Found: C, 64.37; H, 5.04; N, 11.93.** 

**5-(4-Chlorophenyl)-1,3-dimethyl-7,8,9,10-tetrahydropyrimido[4,5-***b***]<b>quinoline-2,4,6(1***H***,3***H***,5***H***)-<b>trione** (4w). This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3298, 3234, 3094, 2957, 2890, 1700, 1639, 1612, 1499, 1443, 1378, 1355, 1289, 1256, 1238, 1198, 1170, 1142, 1047, 1012, 949, 840, 752 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO- **5-(Thiophen-2-yl)-1,3-dimethyl-7,8,9,10-tetrahydropyrimido**[**4,5-***b***]<b>quinoline-2,4,6(1***H***,3***H***,5***H***)-<b>trione** (**4x**). This compound was obtained as solid with mp 288-290 °C; ir (potassium bromide): 3271, 3228, 3086, 3069, 2952, 2883, 1699, 1650, 1604, 1503, 1378, 1348, 1335, 1294, 1236, 1201, 1168, 1141, 1083, 1040, 949, 911, 882, 856, 787, 754, 712 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>):  $\delta$  1.78-2.05 (m, 2H, CH<sub>2</sub>), 2.28-2.34 (m, 2H, CH<sub>2</sub>), 2.53-2.63 (m, 1H, CH), 2.72-2.83 (m, 1H, CH), 3.16 (s, 3H, CH<sub>3</sub>N), 3.44 (s, 3H, CH<sub>3</sub>N), 5.22 (s, 1H, CH), 6.74 (d, *J* = 3.2 Hz, 1H, ArH), 6.81 (dd, *J*<sub>1</sub> = 3.6 Hz, *J*<sub>2</sub> = 4.8 Hz, 1H, ArH), 7.18 (d, *J* = 4.8 Hz, 1H, ArH), 9.24 (br., s, 1H, NH). *Anal.* Calcd. for C<sub>17</sub>H<sub>17</sub>N<sub>3</sub>O<sub>3</sub>S: C, 59.46; H, 4.99; N, 12.24. Found: C, 59.62; H, 4.86; N, 12.35.

**5-(4-Methoxyphenyl)-1-methyl-7,8,9,10-tetrahydropyrimido**[**4,5-***b***]quinoline-2,4,6(1***H***,3***H***,5***H***)-trione (<b>4y**). This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3184, 3058, 2941, 2809, 1727, 1654, 1602, 1506, 1426, 1379, 1330, 1238, 1205, 1195, 1161, 1127, 1106, 1052, 1036, 908, 892, 842, 761, 714 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>):  $\delta$  1.75-1.85 (m, 1H, CH), 1.90-1.98 (m, 1H, CH), 2.21-2.26 (m, 2H, CH<sub>2</sub>), 2.55-2.60 (m, 1H, CH), 2.75-2.80 (m, 1H, CH), 3.38 (s, 3H, CH<sub>3</sub>N), 3.67 (s, 3H, CH<sub>3</sub>O), 4.82 (s, 1H, CH), 6.74 (d, *J* = 8.4 Hz, 2H, ArH), 7.11 (d, *J* = 8.4 Hz, 2H, ArH), 9.00 (br., s, 1H, NH), 10.98 (br., s, 1H, NH). Anal. Calcd. for C<sub>19</sub>H<sub>19</sub>N<sub>3</sub>O<sub>4</sub>: C, 64.58; H, 5.42; N, 11.89. Found: C, 64.72; H, 5.38; N, 11.97.

**5-(3,4-Dimethylphenyl)-1-methyl-7,8,9,10-tetrahydropyrimido[4,5-***b***]<b>quinoline-2,4,6(1***H***,3***H***,5***H***)-<b>trione (4z).** This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3209, 3090, 3033, 2961, 1711, 1644, 1507, 1413, 1382, 1355, 1341, 1269, 1216, 1186, 1146, 1134, 1104, 896, 831, 799, 761, 712 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>):  $\delta$  1.73-1.80 (m, 1H, CH), 1.81-1.97 (m, 1H, CH), 2.10 (s, 3H, CH<sub>3</sub>), 2.13 (s, 3H, CH<sub>3</sub>), 2.22-2.27 (m, 2H, CH<sub>2</sub>), 2.53-2.60 (m, 1H, CH), 2.74-2.78 (m, 1H, CH), 3.38 (s, 3H, CH<sub>3</sub>N), 4.81 (s, 1H, CH), 6.88-6.96 (m, 3H, ArH), 9.00 (br., s, 1H, NH), 10.97 (br., s, 1H, NH). *Anal.* Calcd. for C<sub>20</sub>H<sub>21</sub>N<sub>3</sub>O<sub>3</sub>: C, 68.36; H, 6.02; N, 11.96. Found: C, 68.42; H, 5.94; N, 12.07.

**6-Amino-5-(1-(2-hydroxy-4,4-dimethyl-6-oxocyclohex-1enyl)-2-methylpropyl)-1,3-dimethylpyrimidine-2,4(1***H***,3***H***)-<b>dione (5a).** This compound was obtained as solid with mp 230-231 °C; ir (potassium bromide): 3383, 3208, 2954, 2867, 1691, 1656, 1611, 1589, 1506, 1472, 1453, 1382, 1353, 1322, 1305, 1249, 1214, 1151, 1128, 1108, 1050, 968, 942, 927, 895, 795, 761, 674 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>):  $\delta$  0.74 (d, *J* = 6.4 Hz, 3H, CH<sub>3</sub>), 0.79 (d, *J* = 6.4 Hz, 3H, CH<sub>3</sub>), 0.99 (s, 6H, 2 × CH<sub>3</sub>), 2.13 (d, *J* = 17.6 Hz, 1H, CH), 2.22 (d, *J* = 16.4 Hz, 2H, CH<sub>2</sub>), 2.35 (d, *J* = 17.6 Hz, 1H, CH), 2.85-2.97 (m, 1H, CH), 3.17 (s, 3H, CH<sub>3</sub>), 3.30 (s, 3H, CH<sub>3</sub>), 3.46 (d, *J* = 11.2 Hz, 1H, CH), 7.20 (s, 2H, NH<sub>2</sub>), 13.18 (s, 1H, OH). *Anal.* Calcd. for C<sub>18</sub>H<sub>27</sub>N<sub>3</sub>O<sub>4</sub>: C, 61.87; H, 7.79; N, 12.03. Found: C, 62.04; H, 7.58; N, 12.28.

**6-Amino-5-(1-(2-hydroxy-6-oxocyclohex-1-enyl)-2-methylpropyl)-1,3-dimethylpyrimidine-2,4(1***H***,3***H***)-dione (5b). This compound was obtained as solid with mp 234-235 °C; ir (potassium bromide): 3357, 3177, 2948, 2873, 1698, 1654, 1614, 1583, 1501, 1452, 1370, 1352, 1269, 1195, 1148, 1111,**  1046, 980, 963, 935, 784, 753, 704, 678 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSOd<sub>6</sub>):  $\delta$  0.73 (d, J = 6.4 Hz, 3H, CH<sub>3</sub>), 0.77 (d, J = 6.4 Hz, 3H, CH<sub>3</sub>), 1.75-1.86 (m, 2H, CH<sub>2</sub>), 2.18-2.40 (m, 4H, 2 × CH<sub>2</sub>), 2.82-2.90 (m, 1H, CH), 3.17 (s, 3H, CH<sub>3</sub>), 3.31 (s, 3H, CH<sub>3</sub>), 3.45 (d, J = 10.8 Hz, 1H, CH), 7.29 (s, 2H, NH<sub>2</sub>), 13.24 (s, 1H, OH). *Anal.* Calcd. for C<sub>16</sub>H<sub>23</sub>N<sub>3</sub>O<sub>4</sub>: C, 59.80; H, 7.21; N, 13.08. Found: C, 60.13; H, 7.06; N, 12.87.

**1,3,8,8-Tetramethyl-8,9-dihydropyrimido**[**4,5-***b*]quinoline-**2,4,6**(**1***H*,**3***H*,**7***H*)-trione (6). This compound was obtained as solid with mp 193-195 °C; ir (potassium bromide): 2959, 2873, 1717, 1691, 1664, 1597, 1498, 1476, 1414, 1370, 1357, 1326, 1303, 1271, 1224, 1140, 1115, 1067, 1039, 985, 965, 822, 793, 753, 696 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>):  $\delta$  1.06 (s, 6H, 2 × CH<sub>3</sub>), 2.54 (s, 2H, CH<sub>2</sub>), 3.07 (s, 2H, CH<sub>2</sub>), 3.31 (s, 3H, CH<sub>3</sub>), 3.60 (s, 3H, CH<sub>3</sub>), 8.62 (s, 1H, CH). HRMS [Found: m/z, 287.1267 (M<sup>+</sup>); Calcd. for C<sub>15</sub>H<sub>17</sub>N<sub>3</sub>O<sub>3</sub>: M, 287.1270].

**1,3,8,8-Tetramethyl-5-(4-(1,3,8,8-tetramethyl-2,4,6-tri-oxo-1,2,3,4,5,5a,6,7,8,9,9a,10-dodecahydropyrimido[4,5-***b***]quinoline-<b>5-yl)phenyl)-7,8,9,10-tetrahydropyrimido[4,5-***b***]quinoline-<b>2,4,6(1***H*,3*H*,5*H*)-trione (8a). This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3280, 3229, 3092, 2956, 2868, 1698, 1654, 1636, 1508, 1375, 1286, 1241, 1208, 1149, 1125, 1098, 1049, 978, 960, 891, 858, 811, 762, 752, 685 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>):  $\delta$  0.91 (s, 6H, 2 × CH<sub>3</sub>), 1.02 (s, 6H, 2 × CH<sub>3</sub>), 2.08 (d, *J* = 16.4 Hz, 2H, 2 × CH), 2.17 (d, *J* = 16.4 Hz, 2H, 2 × CH), 2.50 (d, *J* = 16.4 Hz, 2H, 2 × CH), 2.63 (d, *J* = 16.4 Hz, 2H, 2 × CH), 3.08 (s, 6H, 2 × CH<sub>3</sub>), 3.42 (s, 6H, 2 × CH<sub>3</sub>), 4.82 (s, 2H, 2 × CH), 7.02 (s, 4H, ArH), 9.00 (s, 2H, 2 × NH). *Anal.* Calcd. for C<sub>36</sub>H<sub>40</sub>N<sub>6</sub>O<sub>6</sub>: C, 66.24; H, 6.18; N, 12.88. Found: C, 66.49; H, 6.05; N, 13.06.

**1,8,8-Trimethyl-5-(3-(1,8,8-trimethyl-2,4,6-trioxo-1,2,3,4,5, 5a,6,7,8,9,9a,10-dodecahydropyrimido**[**4,5-b**]quinolin-5-yl)**phenyl)-7,8,9,10-tetrahydropyrimido**[**4,5-b**]quinoline-2,4,6 (**1H,3H,5H)-trione (8b).** This compound was obtained as solid with mp 298-299 °C; ir (potassium bromide): 3527, 3177, 3024, 2958, 2808, 1717, 1655, 1503, 1437, 1415, 1372, 1357, 1282, 1257, 1233, 1205, 1170, 1151, 1101, 1062, 885, 861, 819, 774, 753, 704, 662 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO- $d_6$ ):  $\delta$  0.70 (s, 6H, 2 × CH<sub>3</sub>), 1.02 (s, 6H, 2 × CH<sub>3</sub>), 1.95 (d, *J* = 16.4 Hz, 2H, 2 × CH), 2.19 (d, *J* = 16.4 Hz, 2H, 2 × CH), 2.44-2.56 (m, 4H, 4 × CH), 3.39 (s, 6H, 2 × CH<sub>3</sub>), 4.70 (s, 2H, 2 × CH), 6.94-6.98 (m, 4H, ArH), 8.83 (s, 2H, 2 × NH), 10.95 (s, 2H, 2 × NH). *Anal.* Calcd. for C<sub>34</sub>H<sub>36</sub>N<sub>6</sub>O<sub>6</sub>; C, 65.37; H, 5.81; N, 13.45. Found: C, 65.56; H, 5.53; N, 13.28.

**5**-(4-(1,3-Dimethyl-2,4,6-trioxo-1,2,3,4,5,5a,6,7,8,9,9a,10dodecahydropyrimido[4,5-*b*]quinoline-5-yl)phenyl)-1,3-dimethyl-7,8,9,10-tetrahydropyrimido[4,5-*b*]quinoline-2,4, **6**(1*H*,3*H*,5*H*)-trione (8c). This compound was obtained as solid with mp 288-290 °C; ir (potassium bromide): 3411, 3308, 3213, 3086, 2952, 1697, 1660, 1631, 1500, 1380, 1359, 1290, 1260, 1238, 1201, 1170, 1141, 1045, 948, 815, 748 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>): δ 1.77-2.00 (m, 4H, 2 × CH<sub>2</sub>), 2.18-2.31 (m, 4H, 2 × CH<sub>2</sub>), 2.54-2.63 (m, 2H, CH<sub>2</sub>), 2.75-2.83 (m, 2H, CH<sub>2</sub>), 3.08 (s, 6H, 2 × CH<sub>3</sub>), 3.43 (s, 6H, 2 × CH<sub>3</sub>), 4.85 (s, 2H, 2 × CH), 7.03 (s, 4H, ArH), 9.08 (s, 2H, 2 × NH). *Anal.* Calcd. for C<sub>32</sub>H<sub>32</sub>N<sub>6</sub>O<sub>6</sub>: C, 64.42; H, 5.41; N, 14.09. Found: C, 64.67; H, 5.26; N, 14.31.

**1,3-Dimethyl-5**-*p*-tolylindeno[2',1':5,6]pyrido[2,3-*d*]pyrimidine-2,4,6(1*H*,3*H*)-trione (10a). This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3034, 2949, 2843, 1715, 1681, 1669, 1609, 1596, 1558, 1513, 1469, 1445, 1433, 1381, 1357, 1317, 1286, 1270, 1249, 1176, 1156, 1079, 1022, 887, 834, 796, 735, 678 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>):  $\delta$  2.41 (s, 3H, CH<sub>3</sub>), 3.14 (s, 3H, CH<sub>3</sub>), 3.74 (s, 3H, CH<sub>3</sub>), 7.12 (d, J = 7.6 Hz, 2H, ArH), 7.20 (d, J = 7.6 Hz, 2H, ArH), 7.59 (d, J = 7.2 Hz, 1H, ArH), 7.63 (t, J = 7.2 Hz, 1H, ArH), 7.77 (t, J = 7.2 Hz, 1H, ArH), 7.97 (d, J = 7.6 Hz, 1H, ArH). *Anal.* Calcd. for C<sub>23</sub>H<sub>17</sub>N<sub>3</sub>O<sub>3</sub>: C, 72.05; H, 4.47; N, 10.96. Found: C, 72.24; H, 4.38; N, 11.04.

**1,3-Dimethyl-5-(4-fluorophenyl)indeno[2',1':5,6]pyrido-[2,3-***d***]pyrimidine-2,4,6(1***H***,3***H***)-trione (10b). This compound was obtained as solid with mp 294-297 °C; ir (potassium bromide): 3074, 2955, 1714, 1678, 1604, 1563, 1498, 1409, 1383, 1360, 1318, 1289, 1214, 1178, 1160, 1138, 1094, 1081, 1032, 1010, 981, 938, 890, 838, 798, 776, 747, 702, 677 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-d\_6): \delta 3.16 (s, 3H, CH<sub>3</sub>), 3.77 (s, 3H, CH<sub>3</sub>), 7.20-7.31 (m, 4H, ArH), 7.62-7.68 (m, 2H, ArH), 7.77-7.82 (m, 1H, ArH), 8.01 (d,** *J* **= 8.0 Hz, 1H, ArH).** *Anal.* **Calcd. for C<sub>22</sub>H<sub>14</sub>FN<sub>3</sub>O<sub>3</sub>: C, 68.21; H, 3.64; N, 10.85. Found: C, 68.43; H, 3.78; N, 10.62.** 

**5-(4-Chlorophenyl)-1,3-dimethyl-indeno[2',1':5,6]pyrido-**[**2,3-***d*]**pyrimidine-2,4,6(1***H***,3***H***)-<b>trione (10c).** This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3054, 2955, 1714, 1661, 1598, 1563, 1494, 1469, 1408, 1380, 1361, 1315, 1287, 1224, 1172, 1156, 1140, 1084, 1033, 1014, 981, 940, 887, 824, 796, 779, 750, 701 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>):  $\delta$  3.15 (s, 3H, CH<sub>3</sub>), 3.76 (s, 3H, CH<sub>3</sub>), 7.27 (d, *J* = 8.0 Hz, 2H, ArH), 7.47 (d, *J* = 8.0 Hz, 2H, ArH), 7.61-7.67 (m, 2H, ArH), 7.79 (t, *J* = 7.2 Hz, 1H, ArH), 8.00 (d, *J* = 7.2 Hz, 1H, ArH). *Anal.* Calcd. for C<sub>22</sub>H<sub>14</sub>ClN<sub>3</sub>O<sub>3</sub>: C, 65.43; H, 3.49; N, 10.41. Found: C, 65.18; H, 3.63; N, 10.61.

**5-(4-Bromophenyl)-1,3-dimethyl-indeno[2',1':5,6]pyrido-**[**2,3-***d*]**pyrimidine-2,4,6(1***H***,3***H***)-<b>trione (10d).** This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3042, 2958, 1720, 1669, 1592, 1571, 1503, 1491, 1466, 1449, 1414, 1381, 1361, 1319, 1289, 1223, 1172, 1140, 1094, 1082, 1068, 982, 941, 824, 796, 778, 701, 672 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>):  $\delta$  3.15 (s, 3H, CH<sub>3</sub>), 3.75 (s, 3H, CH<sub>3</sub>), 7.21 (d, *J* = 8.0 Hz, 2H, ArH), 7.59-7.67 (m, 4H, ArH), 7.79 (t, *J* = 7.2 Hz, 1H, ArH), 8.00 (d, *J* = 7.2 Hz, 1H, ArH). *Anal.* Calcd. for C<sub>22</sub>H<sub>14</sub>BrN<sub>3</sub>O<sub>3</sub>: C, 58.95; H, 3.15; N, 9.37. Found: C, 59.23; H, 3.02; N, 9.65.

**1,3-Dimethyl-5-(4-nitrophenyl)indeno[2',1':5,6]pyrido[2,3***d***]pyrimidine-2,4,6(1***H***,3***H***)-trione (10e). This compound was obtained as solid with mp 254-256 °C; ir (potassium bromide): 3078, 2942, 1717, 1670, 1601, 1568, 1517, 1505, 1464, 1411, 1381, 1344, 1316, 1291, 1222, 1196, 1173, 1140, 1093, 1081, 1031, 1007, 889, 855, 820, 797, 779, 750, 727, 703 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-***d***<sub>6</sub>): \delta 3.14 (s, 3H, CH<sub>3</sub>), 3.76 (s, 3H, CH<sub>3</sub>), 7.56 (d,** *J* **= 8.4 Hz, 2H, ArH), 7.60-7.67 (m, 2H, ArH), 7.80 (t,** *J* **= 7.2 Hz, 1H, ArH), 8.02 (d,** *J* **= 7.2 Hz, 1H, ArH), 8.30 (d,** *J* **= 8.4 Hz, 2H, ArH).** *C***alcd. for C<sub>22</sub>H<sub>14</sub>N<sub>4</sub>O<sub>5</sub>: C, 63.77; H, 3.41; N, 13.52. Found: C, 63.89; H, 3.24; N, 13.73.** 

**1,3-Dimethyl-5-(3-nitrophenyl)indeno[2',1':5,6]pyrido[2,3***d*]**pyrimidine-2,4,6(1***H***,3***H***)-<b>trione (10f).** This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3080, 2952, 1716, 1669, 1607, 1567, 1527, 1501, 1463, 1409, 1380, 1344, 1318, 1289, 1221, 1171, 1143, 1106, 1081, 1036, 983, 943, 879, 796, 777, 748, 728, 718, 702, 692 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>):  $\delta$  3.16 (s, 3H, CH<sub>3</sub>), 3.79 (s, 3H, CH<sub>3</sub>), 7.62-7.68 (m, 2H, ArH), 7.73-7.76 (m, 2H, ArH), 7.81 (d, *J* = 7.2 Hz, 1H, ArH), 8.03 (d, *J* = 7.6 Hz, 1H, ArH), 8.20 (s, 1H, ArH), 8.32 (d, *J* = 7.2 Hz, 1H, ArH). *Anal.* Calcd. for C<sub>22</sub>H<sub>14</sub>N<sub>4</sub>O<sub>5</sub>: C, 63.77; H, 3.41; N, 13.52. Found: C, 64.01; H, 3.54; N, 13.26.

1,3-Dimethyl-5-(2-nitrophenyl)indeno[2',1':5,6]pyrido[2,3*d*]pyrimidine-2,4,6(1*H*,3*H*)-trione (10g). This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3060, 2955, 2858, 1716, 1667, 1603, 1567, 1525, 1504, 1462, 1415, 1384, 1344, 1319, 1287, 1268, 1222, 1193, 1174, 1144, 1103, 1035, 942, 895, 876, 843, 796, 778, 749, 702, 690 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO- $d_6$ ):  $\delta$  3.17 (s, 3H, CH<sub>3</sub>), 3.79 (s, 3H, CH<sub>3</sub>), 7.58 (s, 1H, ArH), 7.65-7.70 (m, 2H, ArH), 7.81-7.85 (m, 2H, ArH), 8.04 (d, *J* = 7.6 Hz, 1H, ArH), 8.38 (d, *J* = 8.8 Hz, 1H, ArH). *Anal.* Calcd. for C<sub>22</sub>H<sub>13</sub>ClN<sub>4</sub>O<sub>5</sub>: C, 58.87; H, 2.92; N, 12.48. Found: C, 59.13; H, 3.08; N, 12.25.

**5-(3,4-Dichlorophenyl)-1,3-dimethylindeno[2',1':5,6]pyrido[2,3-***d***]<b>pyrimidine-2,4,6(1***H***,3***H***)-<b>trione** (10**h**). This compound was obtained as solid with mp 253-256 °C; ir (potassium bromide): 3094, 3072, 2957, 1712, 1667, 1609, 1570, 1548, 1497, 1451, 1412, 1386, 1357, 1317, 1285, 1211, 1203, 1170, 1159, 1135, 1094, 1077, 1029, 1006, 861, 823, 797, 778, 751, 700 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>):  $\delta$  3.17 (s, 3H, CH<sub>3</sub>), 3.77 (s, 3H, CH<sub>3</sub>), 7.26 (d, *J* = 8.4 Hz, 1H, ArH), 7.57 (s, 1H, ArH), 7.65-7.70 (m, 3H, ArH), 7.81 (t, *J* = 7.2 Hz, 1H, ArH), 8.01 (d, *J* = 7.2 Hz, 1H, ArH). *Anal*. Calcd. for C<sub>22</sub>H<sub>13</sub>Cl<sub>2</sub>N<sub>3</sub>O<sub>3</sub>: C, 60.29; H, 2.99; N, 9.59. Found: C, 60.04; H, 3.09; N, 9.36.

**5-(3-Chlorophenyl)-1,3-dimethyl-indeno[2',1':5,6]pyrido-**[**2,3-***d*]**pyrimidine-2,4,6(1***H***,3***H***)-<b>trione** (**10i**). This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3072, 2953, 1716, 1669, 1603, 1565, 1520, 1461, 1411, 1380, 1359, 1318, 1288, 1224, 1203, 1192, 1174, 1141, 1103, 1081, 1035, 1007, 983, 941, 891, 858, 795, 776, 749, 728, 698 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>):  $\delta$  3.16 (s, 3H, CH<sub>3</sub>), 3.76 (s, 3H, CH<sub>3</sub>), 7.20 (d, *J* = 7.6 Hz, 1H, ArH), 7.33 (s, 1H, ArH), 7.42-7.50 (m, 2H, ArH), 7.61-7.67 (m, 2H, ArH), 7.79 (t, *J* = 7.2 Hz, 1H, ArH), 8.00 (d, *J* = 7.6 Hz, 1H, ArH). *Anal.* Calcd. for C<sub>22</sub>H<sub>14</sub>ClN<sub>3</sub>O<sub>3</sub>: C, 65.43; H, 3.49; N, 10.41. Found: C, 65.62; H, 3.27; N, 10.55.

**5-(2,4-Dichlorophenyl)-1,3-dimethyl-indeno[2',1':5,6]pyr-ido[2,3-***d***]pyrimidine-2,4,6(1***H*,3*H***)-trione (10j).** This compound was obtained as solid with mp 297-298 °C; ir (potassium bromide): 3062, 2956, 1718, 1676, 1593, 1571, 1505, 1482, 1413, 1382, 1360, 1317, 1288, 1251, 1221, 1171, 1157, 1145, 1100, 1083, 1057, 1027, 982, 888, 844, 820, 795, 778, 766, 747, 700 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>):  $\delta$  3.18 (s, 3H, CH<sub>3</sub>), 3.77 (s, 3H, CH<sub>3</sub>), 7.28 (d, *J* = 8.4 Hz, 1H, ArH), 7.65-7.70 (m, 2H, ArH), 7.72 (s, 1H, ArH), 7.82 (t, *J* = 7.2 Hz, 1H, ArH), 8.03 (d, *J* = 7.2 Hz, 1H, ArH). *Anal.* Calcd. for C<sub>22</sub>H<sub>13</sub>Cl<sub>2</sub>N<sub>3</sub>O<sub>3</sub>: C, 60.29; H, 2.99; N, 9.59. Found: C, 60.52; H, 3.07; N, 9.42.

**1,3-Dimethyl-5-(3,4-methylenedioxylphenyl)indeno-[2',1': 5,6]pyrido[2,3-***d*]**pyrimidine-2,4,6(1***H***,3***H***)-<b>trione (10k).** This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3071, 2958, 2915, 1717, 1673, 1605, 1566, 1493, 1438, 1411, 1381, 1361, 1337, 1291, 1238, 1174, 1153, 1125, 1104, 1081, 1031, 1007, 982, 926, 911, 883, 812, 796, 778, 749, 702 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>):  $\delta$  3.17 (s, 3H, CH<sub>3</sub>), 3.75 (s, 3H, CH<sub>3</sub>), 6.10 (s, 2H, OCH<sub>2</sub>O), 6.71 (d, *J* = 8.0 Hz, 1H, ArH), 6.83 (s, 1H, ArH), 6.94 (d, *J* = 8.0 Hz, 1H, ArH), 7.77-7.80 (m, 1H, ArH), 7.99 (d, *J* = 7.6 Hz, 1H, ArH). *Anal.* Calcd. for C<sub>23</sub>H<sub>15</sub>N<sub>3</sub>O<sub>5</sub>: C, 66.83; H, 3.66; N, 10.16. Found: C, 66.54; H, 3.77; N, 10.34.

**1,3-Dimethyl-5-(thiophen-2-yl)indeno[2',1':5,6]pyrido[2,3***d*]**pyrimidine-2,4,6(1***H***,3***H***)-<b>trione (101).** This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3099, 1714, 1666, 1568, 1533, 1499, 1408, 1382, 1362, 1343, 1286, 1231, 1204, 1172, 1133, 1080, 1044, 1020, 978, 884, 857, 797, 780, 748, 702 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>):  $\delta$  3.19 (s, 3H, CH<sub>3</sub>), 3.75 (s, 3H, CH<sub>3</sub>), 7.00-7.03 (m, 1H, ArH), 7.12-7.14 (m, 1H, ArH), 7.64-7.68 (m, 2H, ArH), 7.72 (d, J = 5.2 Hz, 1H, ArH), 7.78-7.82 (m, 1H, ArH), 8.01 (d, J = 7.6 Hz, 1H, ArH).Anal. Calcd. for C<sub>20</sub>H<sub>13</sub>N<sub>3</sub>O<sub>3</sub>S: C, 63.99; H, 3.49; N, 11.19. Found: C, 64.23; H, 3.32; N, 11.38.

**1,3-Dimethyl-5-(pyridine-4-yl)indeno[2',1':5,6]pyrido[2,3***d*]**pyrimidine-2,4,6(1***H***,3***H***)-<b>trione (10m).** This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3068, 1715, 1667, 1601, 1569, 1548, 1498, 1464, 1410, 1378, 1360, 1319, 1305, 1291, 1222, 1171, 1140, 1093, 1084, 1034, 991, 889, 824, 797, 778, 749, 702 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>):  $\delta$  3.17 (s, 3H, CH<sub>3</sub>), 3.78 (s, 3H, CH<sub>3</sub>), 7.28 (d, *J* = 5.2 Hz, 2H, ArH), 7.63-7.68 (m, 2H, ArH), 7.81 (t, *J* = 6.8 Hz, 1H, ArH), 8.03 (d, *J* = 7.2 Hz, 1H, ArH), 8.62 (d, *J* = 5.2 Hz, 2H, ArH). *Anal.* Calcd. for C<sub>21</sub>H<sub>14</sub>N<sub>4</sub>O<sub>3</sub>: C, 68.10; H, 3.81; N, 15.13. Found: C, 68.35; H, 3.67; N, 15.32.

**1,3-Dimethyl-5-(4-methoxyphenyl)indeno[2',1':5,6]pyrido-[2,3-***d***]pyrimidine-2,4,6(1***H***,3***H***)-trione (10n). This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3169, 3118, 3034, 2963, 2852, 1721, 1694, 1609, 1561, 1491, 1414, 1362, 1317, 1288, 1251, 1174, 1155, 1129, 1110, 1025, 990, 879, 836, 826, 797, 777, 751, 743 cm<sup>-1</sup>; <sup>1</sup>H nmr (DMSO-***d***<sub>6</sub>): \delta 3.68 (s, 3H, CH<sub>3</sub>), 3.84 (s, 3H, CH<sub>3</sub>O), 6.94 (d,** *J* **= 8.4 Hz, 2H, ArH), 7.21 (d,** *J* **= 8.8 Hz, 2H, ArH), 7.63-7.66 (m, 2H, ArH), 7.77-7.80 (m, 1H, ArH), 7.98 (d,** *J* **= 6.8 Hz, 1H, ArH), 11.57 (s, 1H, NH).** *Anal.* **Calcd. for C<sub>22</sub>H<sub>15</sub>N<sub>3</sub>O<sub>4</sub>: C, 68.57; H, 3.92; N, 10.90. Found: C, 68.72; H, 3.75; N, 11.07.** 

**5-(4-Chlorophenyl)-1,3-dimethyl-indeno[2',1':5,6]pyrido-**[**2,3-***d*]**pyrimidine-2,4,6(1***H***,3***H***)-<b>trione** (**10o**). This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3171, 3125, 3045, 2844, 1720, 1689, 1597, 1562, 1490, 1449, 1396, 1361, 1316, 1301, 1287, 1227, 1189, 1174, 1156, 1131, 1090, 1070, 1016, 992, 879, 838, 828, 796, 777, 752, 744, 720, 696 cm<sup>-1</sup>, <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>):  $\delta$  3.68 (s, 3H, CH<sub>3</sub>), 7.29 (d, *J* = 8.4 Hz, 2H, ArH), 7.45 (d, *J* = 8.4 Hz, 2H, ArH), 7.63-7.66 (m, 2H, ArH), 7.78-7.81 (m, 1H, ArH), 8.00 (d, *J* = 7.6 Hz, 1H, ArH), 11.65 (s, 1H, NH). Anal. Calcd. for C<sub>21</sub>H<sub>12</sub>Cl N<sub>3</sub>O<sub>3</sub>: C, 64.71; H, 3.10; N, 10.78. Found: C, 64.93; H, 2.91; N, 10.89.

**5-(4-Bromophenyl)-1-methyl-indeno[2',1':5,6]pyrido[2,3-d]pyrimidine-2,4,6(1***H***,3***H***)-trione (10p). This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3168, 3050, 2845, 1719, 1647, 1607, 1594, 1565, 1490, 1447, 1380, 1359, 1317, 1287, 1229, 1173, 1156, 1131, 1101, 1077, 1012, 992, 879, 834, 797, 778, 745, 713 cm<sup>-1</sup>, <sup>1</sup>H nmr (DMSO***d***<sub>6</sub>): \delta 3.68 (s, 3H, CH<sub>3</sub>), 7.23 (d,** *J* **= 8.0 Hz, 2H, ArH), 7.59 (d,** *J* **= 8.4 Hz, 2H, ArH), 7.63-7.66 (m, 2H, ArH), 7.80 (t,** *J* **= 7.6 Hz, 1H, ArH), 8.00 (d,** *J* **= 7.6 Hz, 1H, ArH), 11.66 (s, 1H, NH).** *Anal.* **Calcd. for C<sub>21</sub>H<sub>12</sub>BrN<sub>3</sub>O<sub>3</sub>: C, 58.08; H, 2.79; N, 9.68. Found: C, 58.32; H, 2.55; N, 9.84.** 

**5-(4-Hydroxyphenyl)-1-methyl-indeno[2',1':5,6]pyrido-**[**2,3-***d*]**pyrimidine-2,4,6(1***H***,3***H***)-<b>trione (10q).** This compound was obtained as solid with mp > 300 °C; ir (potassium bromide): 3228, 3098, 2924, 1715, 1649, 1607, 1588, 1516, 1489, 1418, 1389, 1371, 1350, 1280, 1258, 1223, 1170, 1109, 1067, 1016, 989, 879, 852, 827, 797, 782, 768, 751, 739 cm<sup>-1</sup>, <sup>1</sup>H nmr (DMSO-*d*<sub>6</sub>):  $\delta$  3.67 (s, 3H, CH<sub>3</sub>), 6.75 (d, *J* = 8.4 Hz, 2H, ArH), 7.09 (d, *J* = 8.4 Hz, 2H, ArH), 7.61-7.65 (m, 2H, ArH), 7.78 (t, *J* = 7.6 Hz, 1H, ArH), 7.96 (d, *J* = 7.2 Hz, 1H, ArH), 9.58 (s, 1H, OH), 11.54 (s, 1H, NH). *Anal.* Calcd. for C<sub>21</sub>H<sub>13</sub>N<sub>3</sub>O<sub>4</sub>: C, 67.92; H, 3.53; N, 11.32. Found: C, 68.11; H, 3.70; N, 11.14. Acknowledgement. We are grateful to the National Nature Science Foundation of China (20472062 and 20672079), the Natural Science Foundation of Jiangsu Province (BK2006048) and the Natural Science Foundation of Jiangsu Education Department (06KJA15007) for financial support.

#### REFERENCES AND NOTES

[1a] Bradshaw, T. K.; Hutchison, D. W. Chem. Soc. Rev. 1977, 6,
43; [b] Sasaki, T.; Minamoto, K.; Suzuki, T.; Yamashita, S. Tetrahedron
1980, 36, 865; [c] Prajapati, D.; Bhuyan, P. J.; Sandhu, J. S. J. Chem.
Soc., Perkin Trans. 1 1988, 607; [d] Bhuyan, P. J.; Borah, H. N.;
Sandhu, J. S. J. Chem. Soc., Perkin Trans. 1 1999, 3083.

[2a] Marumoto, R.; Furukawa, Y. Chem. Pharm. Bull. 1997, 25, 2974; [b] Griengl, R.; Wack, E.; Schwarz, W.; Streicher, W.; Rosenwirth, B.; Clercq, E. D. J. Med. Chem. 1987, 1199; [c] Clercq, E. D.; Bernaerts, R. J. Biol. Chem. 1987, 262, 14905; [d] Jones, A. S.; Sayers, J. R.; Walker, R. T.; Clercq, E. D. J. Med. Chem. 1988, 31, 268; [e] Mitsuya, H.; Yarchoan, R.; Broder, S. Science 1990, 249, 1533; [f] Pontikis, R.; Monneret, C. Tetrahedron Lett. 1994, 35, 4351.

[3a] Heidelberger, C.; Arafield, F. J. Cancer Res. 1963, 23, 1226;
[b] Baba, M.; Pauwels, R.; Herdwig, P.; Clercq, E. D.; Desmyster, J.; Vandepulfe, M. Biochem. Biophys. Res. Commun. 1987, 142, 128; [c] Clercq, E. D. J. Med. Chem. 1986, 29, 1561; [d] Clercq, E. D. Anticancer Res. 1986, 6, 549; [e] Jones, A. S.; Verhalst, G.; Walker, R. T. Tetrahedron Lett. 1974, 15, 4415.

[4a] Hirota, K.; Kitade, Y.; Senda, S.; Halat, M. J.; Watanabe, K. A.; Fox, J. J. *J. Org. Chem.* **1981**, *46*, 846; [b] Su, T. L.; Huang, J. T.; Burchanal, J. H.; Watanabe, K. A.; Fox, J. J. *J. Med. Chem.* **1986**, *29*, 709; [c] Prajapati, D.; Sandhu, J. S. *Synthesis* **1988**, 342.

[5a] Gangjee, A.; Adair, O.; Queener, S. F. J. Med. Chem. 1999,
42, 2447; [b] Gangjee, A.; Vasudevan, A.; Queener, S. F. J. Med. Chem.
1996, 39, 1438; [c] Hamby, J. M.; Connolly, J. C.; Schroeder, M. C.;
Winters, R. T.; Showalter, H. D. H.; Panek, R. L.; Major, T. C.;
Olsewski, B.; Ryan, M. J.; Dahring, T.; Lu, G. H.; Keiser, J. A.; Aneesa,
S. C.; Kraker, A. J.; Slintak, V.; Nelson, J. M.; Fry, D. W.; Bradford, L.;

Hallak. H.; Doherty, A. M. J. Med. Chem. 1997, 40, 2296.

[6] Nasr, M. N.; Gineinah, M. M. Arch. Pharm. 2002, 335, 289.
[7a] Broom, A. D.; Shim, J. L.; Anderson, G. L. J. Org. Chem.

**1976**, *41*, 1095; [b] Shim, J. L.; Niess, R.; Broom, A. D. J. Org. Chem. **1972**, *37*, 578; [c] Bhuyan, P.; Boruah, R. C.; Sandhu, J. S. J. Org. Chem. **1990**, *55*, 568; [d] Devi, I.; Kumar, B. S. D.; Bhuyan, P. J. Tetrahedron Lett. **2003**, *44*, 8307.

[8a] Domling, A.; Ugi, I. Angew. *Chem. Int. Ed.* 2000, *39*, 3168;
[b] Ugi, I.; Domling, A. *Endeavour* 1994, *18*, 115; [c] Heck, S.; Domling, A. *Synlett* 2000, 424.

[9a] Welton, T. Chem. Rev. 1999, 99, 2071; [b] Wasserscheid, P.;
Keim, W. Angew. Chem. Int. Ed. 2000, 39, 3773; [c] Sheldon, R. Chem.
Commun. 2001, 2399; [d] Wilkes, J. S. Green Chem. 2002, 4, 73; [e]
Yao, Q. Org. Lett. 2002, 4, 2197; [f] Zerth, H. M.; Leonard, N. M.;
Mohan, R. S. Org. Lett. 2003, 5, 55; [g] Su, C.; Chen, Z. C.; Zheng, Q.
G. Synthesis 2003, 555; [h] Rajagopal, R.; Jarikote, D. V.; Lahoti, R. J.;
Daniel, T.; Srinivasan, K. V. Tetrahedron Lett. 2003, 44, 1815; [i]
Kumar, A.; Pawar, S. S. J. Org. Chem. 2004, 69, 1419.

[10a] Li, D.; Shi, F.; Peng, J.; Guo, S.; Deng, Y. J. Org. Chem.
 2004, 69, 3582; [b] Ranu, B. C.; Banerjee, S. J. Org. Chem. 2005, 70, 4517.

[11] Shi, D. Q.; Ni, S. N.; Yang, F.; Wang, X. S.; Ji, S. J. J. Heterocyclic Chem. Submitted.

[12] Safak, C.; Simsek, R.; Altas, Y.; Boydag, S.; Erol, K. Boll. Chim. Farm. 1997, 136, 665.

[13] Bisenieks, E.; Uldrikis, J.; Kirule, I.; Tirzite, G.; Dubur, G. *Khim. Geterotsikl. Soedin* **1982**, 1528.

[14a] Augstein, J.; Ham, A. L.; Leeming, P. R. J. Med. Chem.
1972, 15, 466; [b] Kunstmann, R.; Fischer, G. J. Med. Chem. 1984, 27, 1312; [c] Kunstmann, R.; Lerch, U.; Gerhards, H.; Leven, M.; Schacht, U. J. Med. Chem. 1984, 27, 432.

[15] Rentzea, C.; Meyer, N.; Kast, J.; Plath, P.; Koenig, H.; Harreus, A.; Kardorff, U.; Gerber, M.; Walter, H. Ger. Offen. DE 4301426 A121, **1994**; Chem. Abstr. **1994**, 121, 133986.

[16a] Van Emelen, K.; De Wit, T.; Hoornaert, G. J.; Compernolle,
F. *Tetrahedron* 2002, 58, 4225; [b] De Wit, T.; Van Emelen, K.;
Maertens, F.; Hoornaert, G. J.; Compernolle, F. *Tetrahedron Lett.* 2001, 42, 4919.