

A Convenient Synthesis of Novel 1,3,4-Triaryl-3,4-dihydropyrimidin-2(1H)-ones by Cyclization of Aromatic Isocyanates with β -Arylamino-1-phenylpropan-1-ones

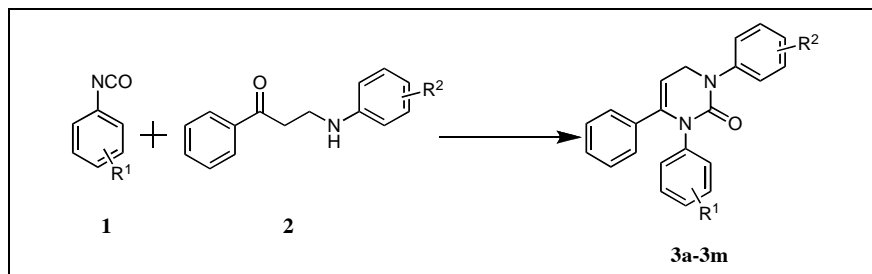
Na Xue,^{1,2} Xiuyang Lu² and Yongzhou Hu^{*1}

¹ZJU-ENS joint laboratory of medicinal chemistry, College of Pharmaceutical Sciences, Zhejiang University, Hangzhou, 310058, Zhejiang, P. R. China.

²Department of Chemical and Biochemical Engineering, College of Material Sciences and Chemical Engineering, Zhejiang University

huyz@zjuem.zju.edu.cn

Received August 30, 2007



A simple one-step method for preparation of novel 1,3,4-triaryl-3,4-dihydropyrimidin-2(1H)-ones has been developed by reaction of aromatic isocyanates with β -arylamino-1-phenylpropan-1-ones in refluxing toluene in the presence of KHSO₄ and HCl.

J. Heterocyclic Chem., **45**, 1095 (2008).

INTRODUCTION

Dihydropyrimidin-2(1H)-ones (DHPMs) and their derivatives represent heterocyclic system that have drawn significant attention due to their diverse therapeutic and pharmacological properties [1]. They are medicinally important as antiviral agents, antitumor agents, antibacterial agents and anti-inflammatory agents [1a,2]. In the last two decades, appropriately functionalized DHPM analogues have emerged as orally active antihypertensive agents [3] and α -1a adrenoceptor-selective antagonists [4]. In addition, several marine alkaloids containing the dihydropyrimidinone-5-carboxylate motifs also show interesting biological activities [5]. A conventional synthesis of DHPMs first performed by P. Biginelli in 1893 involves a three-component condensation of 1,3-dicarbonyl compounds, aldehydes and urea under strongly acidic conditions with relatively low yields [6]. In order to improve the efficiency of the Biginelli reaction, more efficient conditions have been found using Lewis acids as catalysts [7]. Additionally, the use of ionic liquids [8], microwave irradiation [9] and ultrasonic [10] mediated methods have also been developed for synthesis of 3,4-dihydropyrimidin-2(1H)-one derivatives. Besides, Mamaev *et al.* reported a two-steps synthesis method to prepare 3,4-dihydropyrimidin-2(1H)-one derivatives using 3-phenylamino-1-propanones and substituted isocyanates and giving the intermediates β -(*N*-phenylureido)ketones, but the total yields were very poor [11]. In addition, to our knowledge, the synthesis of the 3,4-dihydropyrimidin-2(1H)-ones with triaryl group

simultaneously occupying 1,3,4-position of the pyrimidin-2-one nucleus has seldom been reported. Thus, it is significant to develop a method to obtain novel triaryl-3,4-dihydropyrimidin-2(1H)-one derivatives due to the potential biological profile of such compounds. In continuation of Mamaev's work, we developed a simple and one-step method to prepare a series of new triaryl-3,4-dihydropyrimidin-2(1H)-one derivatives using easily available aromatic isocyanates and β -arylamino-1-phenylpropan-1-ones.

RESULTS AND DISCUSSION

The starting materials, substituted phenyl isocyanates **1**, are commercially available and substituted β -phenylamino-1-phenylpropan-1-ones **2** were easily prepared according to the reported procedure [12,13]. A mixture of 1.1 equimolar 4-chlorophenyl isocyanate **1a** and β -4-chlorophenylamino-1-phenylpropan-1-one **2a** was refluxed in toluene in the presence of KHSO₄ and HCl for 3 h. To our delight, the reaction proceeded smoothly and afforded the target compound 1,3-bis(4-chlorophenyl)-4-phenyl-3,4-dihydropyrimidin-2(1H)-one **3a** in 54% yield (Scheme 1) (Table 1, entry 1).

With the reaction condition described above, various hitherto unknown triaryl-3,4-dihydropyrimidin-2(1H)-ones were obtained in moderate yields, as shown in Table 1 (entries 1-13). Aromatic isocyanate with both electron-withdrawing and electron-releasing substituents readily provided triaryl-3,4-dihydropyrimidin-2(1H)-ones. The assigned molecular structures of new compounds **3a-m**

Scheme 1

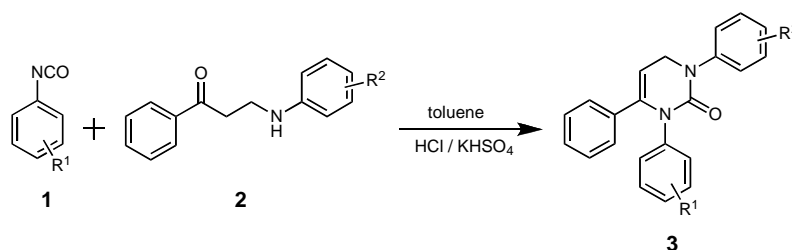


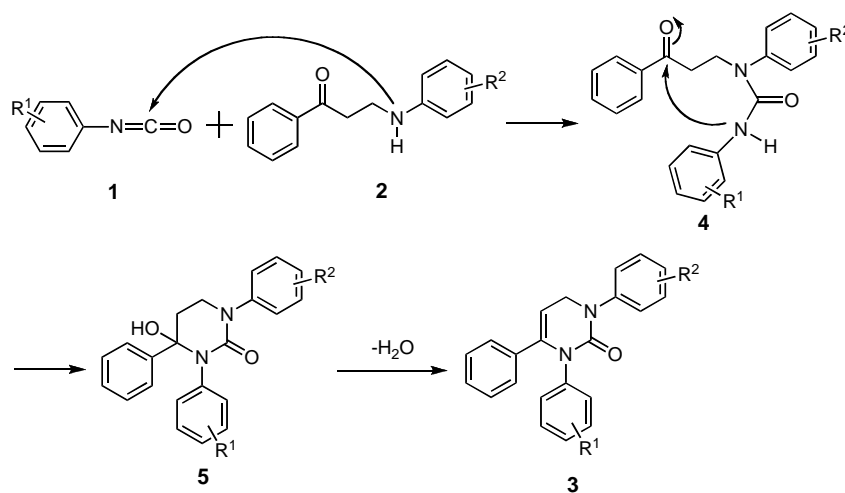
Table 1.

Synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones **3** by cyclization reaction of aromatic isocyanates **1** with β -arylamino-1-phenylpropan-1-ones **2**

Entry	Product	R ¹	R ²	Yield (%) [a]
1	3a	4-Cl	4-Cl	54
2	3b	4-CH ₃	4-Cl	48
3	3c	4-OCH ₃	4-Cl	35
4	3d	3,4,5-(OCH ₃) ₃	4-Cl	32
5	3e	4-Cl	H	43
6	3f	3,4,5-(OCH ₃) ₃	H	30
7	3g	H	H	45
8	3h	H	4-OCH ₃	37
9	3i	4-OCH ₃	4-CH ₃	39
10	3j	4-Cl	3-Cl	46
11	3k	H	3-Cl	40
12	3l	H	3-Br	34
13	3m	H	3-CH ₃	38

[a] Isolated yields of purified products.

Scheme 2



are based on rigorous spectroscopic analysis including ¹H NMR, MS and elemental analysis.

Furthermore, the most plausible mechanism for the formation of 3,4-dihydropyrimidin-2(1*H*)-ones is presented in Scheme 2. First, nucleophilic addition reaction of β -arylamino-1-phenylpropan-1-one **2** to aromatic isocyanate **1** generate the intermediate **4**, which is rapidly cyclized by intramolecular nucleophilic addition to give tetrahydro-

pyrimidin-2(1*H*)-one **5**. Then, dehydration of **5** under acidic conditions gives the target compound **3**.

In summary, a simple and one-step method for preparation novel 1,3,4-triaryl-3,4-dihydropyrimidin-2(1*H*)-ones had been developed by reaction of aromatic isocyanates with β -arylamino-1-phenylpropan-1-ones in the presence of KHSO₄ and HCl in refluxing toluene. The starting materials were easily obtained and the operation

was convenient. Further work is in progress to screen the biological activities of the series of 1,3,4-triaryl-3,4-dihydropyrimidin-2(1H)-one derivatives.

EXPERIMENTAL

Melting points were measured on a B-540 Büchi melting point apparatus and are uncorrected. ¹H NMR spectra were recorded on a Bruker Advance DMX 400-MHz spectrometer with TMS as the internal standard. Chemical shifts are expressed in parts per million (ppm). Mass Spectra (MS) analyses, ESI (positive) were performed with an Esquire-LC-00075 spectrometer. Elemental analysis was carried out on an ERBA-1110 analyzer.

General Procedure for the Synthesis of β-Arylamino-1-phenylpropan-1-ones 2. **Procedure (i):** A suspension of acetophenone (0.1 mol), dimethyl amine hydrochloride (0.13 mol) and paraformaldehyde (0.13 mol) in a mixture of 18 mL of ethanol and 0.3 mL of conc. HCl was refluxed for 2 hrs. After cooling, 100 mL of acetone was added. The white crystals formed were collected, washed with acetone and dried *in vacuo* to yield 16.9 g (79%) of β-dimethylaminopropiophenone hydrochloride, mp 152-154 °C (lit. [12], mp 153 °C).

Procedure (ii): Equimolar quantities of β-dimethylaminopropiophenone hydrochloride and arylamines (aniline; *p*-anisidine; *m,p*-toluidine; *m,p*-chloroaniline; and *m*-bromoaniline) were refluxed for 2 hrs on a boiling water-bath using 50% ethyl alcohol as solvent. The solid which separated out on cooling was filtered and thoroughly washed with water and cold ethyl alcohol. The resulting β-arylamino-1-phenylpropan-1-ones 2 were crystallised from EtOH.

3-[(4-Chlorophenyl)amino]-1-phenyl-1-propanone (2a). 92% Yield, mp 134-135 °C (lit. [14], mp 133-134.5 °C); ¹H NMR (400 MHz, CDCl₃) δ: 3.25-3.28 (t, 2H, *J* = 6.4 Hz, CH₂), 3.56-3.60 (t, 2H, *J* = 6.4 Hz, CH₂), 4.16 (br, 1H, NH), 6.55-6.57 (d, 2H, *J* = 8.8 Hz, Ar-H), 7.11-7.13 (d, 2H, *J* = 8.8 Hz, Ar-H), 7.45-7.49 (t, 2H, *J* = 7.6 Hz, Ar-H), 7.56-7.60 (t, 1H, *J* = 7.6 Hz, Ar-H), 7.94-7.96 (d, 2H, *J* = 7.6 Hz, Ar-H).

3-(Phenylamino)-1-phenyl-1-propanone (2b). 71% Yield, mp 109-111 °C (lit. [14], mp 109-111 °C); ¹H NMR (400 MHz, CDCl₃) δ: 3.28-3.31 (t, 2H, *J* = 6.4 Hz, CH₂), 3.61-3.64 (t, 2H, *J* = 6.4 Hz, CH₂), 4.12 (br, 1H, NH), 6.64-6.66 (d, 2H, *J* = 8.0 Hz, Ar-H), 6.69-6.73 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.16-7.20 (t, 2H, *J* = 8.0 Hz, Ar-H), 7.45-7.48 (t, 2H, *J* = 8.0 Hz, Ar-H), 7.56-7.59 (t, 1H, *J* = 8.0 Hz, Ar-H), 7.94-7.96 (d, 2H, *J* = 8.0 Hz, Ar-H).

3-[(4-Methoxyphenyl)amino]-1-phenyl-1-propanone (2c). 67% Yield, mp 110-111 °C (lit. [14], mp 111 °C); ¹H NMR (400 MHz, CDCl₃) δ: 3.25-3.28 (t, 2H, *J* = 6.4 Hz, CH₂), 3.55-3.58 (t, 2H, *J* = 6.4 Hz, CH₂), 3.75 (s, 3H, OCH₃), 6.62-6.64 (d, 2H, *J* = 8.0 Hz, Ar-H), 6.78-6.80 (d, 2H, *J* = 8.0 Hz, Ar-H), 7.44-7.48 (t, 2H, *J* = 8.0 Hz, Ar-H), 7.55-7.59 (t, 1H, *J* = 8.0 Hz, Ar-H), 7.94-7.96 (d, 2H, *J* = 8.0 Hz, Ar-H).

3-[(4-Methylphenyl)amino]-1-phenyl-1-propanone (2d). 78% Yield, mp 109-111 °C (lit. [14], mp 109-111 °C); ¹H NMR (400 MHz, CDCl₃) δ: 2.24 (s, 3H, CH₃), 3.26-3.29 (t, 2H, *J* = 6.4 Hz, CH₂), 3.58-3.62 (t, 2H, *J* = 6.4 Hz, CH₂), 4.12 (br, 1H, NH), 6.58-6.60 (d, 2H, *J* = 8.0 Hz, Ar-H), 6.99-7.01 (d, 2H, *J* = 8.0 Hz, Ar-H), 7.44-7.48 (t, 2H, *J* = 7.6 Hz, Ar-H), 7.55-7.59 (t, 1H, *J* = 7.6 Hz, Ar-H), 7.94-7.96 (d, 2H, *J* = 7.6 Hz, Ar-H).

3-[(3-Chlorophenyl)amino]-1-phenyl-1-propanone (2e). 55% Yield, mp 111-113 °C; ¹H NMR (400 MHz, CDCl₃) δ:

3.26-3.29 (t, 2H, *J* = 6.4 Hz, CH₂), 3.58-3.61 (t, 2H, *J* = 6.4 Hz, CH₂), 4.30 (br, 1H, NH), 6.49-6.51 (d, 1H, *J* = 8.0 Hz, Ar-H), 6.62 (s, 1H, Ar-H), 6.65-6.67 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.05-7.08 (t, 1H, *J* = 8.0 Hz, Ar-H), 7.45-7.49 (t, 2H, *J* = 8.0 Hz, Ar-H), 7.56-7.60 (t, 1H, *J* = 8.0 Hz, Ar-H), 7.94-7.96 (d, 2H, *J* = 8.0 Hz, Ar-H).

3-[(3-Bromophenyl)amino]-1-phenyl-1-propanone (2f). 57% Yield, mp 116-118 °C; ¹H NMR (400 MHz, CDCl₃) δ: 3.26-3.28 (t, 2H, *J* = 6.4 Hz, CH₂), 3.57-3.60 (t, 2H, *J* = 6.4 Hz, CH₂), 4.25 (br, 1H, NH), 6.53-6.55 (d, 1H, *J* = 8.0 Hz, Ar-H), 6.77 (s, 1H, Ar-H), 6.80-6.82 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.00-7.03 (t, 1H, *J* = 8.0 Hz, Ar-H), 7.45-7.49 (t, 2H, *J* = 8.0 Hz, Ar-H), 7.56-7.60 (t, 1H, *J* = 8.0 Hz, Ar-H), 7.94-7.96 (d, 2H, *J* = 8.0 Hz, Ar-H).

3-[(3-Methylphenyl)amino]-1-phenyl-1-propanone (2g). 51% Yield, mp 88-90 °C; ¹H NMR (400 MHz, CDCl₃) δ: 2.29 (s, 3H, CH₃), 3.27-3.30 (t, 2H, *J* = 6.4 Hz, CH₂), 3.61-3.64 (t, 2H, *J* = 6.4 Hz, CH₂), 4.07 (br, 1H, NH), 6.47-6.49 (m, 2H, Ar-H), 6.54-6.56 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.06-7.11 (t, 1H, *J* = 8.0 Hz, Ar-H), 7.45-7.49 (t, 2H, *J* = 8.0 Hz, Ar-H), 7.56-7.58 (t, 1H, *J* = 8.0 Hz, Ar-H), 7.95-7.97 (d, 2H, *J* = 8.0 Hz, Ar-H).

General Procedure for the Synthesis of 1,3,4-Triaryl-3,4-dihydropyrimidin-2(1H)-ones (compound 3a as example). To a solution of 4-chlorophenyl isocyanate **1a** (1.1 mmol) and β-4-chlorophenylamino-1-phenylpropan-1-one **2a** (1 mmol) in 5 mL toluene, added KHSO₄ (0.01 mmol) and HCl saturated toluene (0.2 mL). The reaction mixture was stirred and refluxed for 3 hrs. After cooling to room temperature, the reaction mixture was quenched with H₂O (10 mL), and extracted with ethyl acetate (3×20 mL). The organic layer was dried over anhydrous Na₂SO₄. After evaporation of the solvent, the crude product was purified by chromatography on silica gel using petroleum ether-ethyl acetate (4:1) as eluent, to offer pure product **3a**.

1,3-Bis(4-chlorophenyl)-6-phenyl-3,4-dihydropyrimidin-2(1H)-one (3a). Mp 112-114 °C; ¹H NMR (400 MHz, CDCl₃) δ: 4.43-4.44 (d, 2H, *J* = 4.4 Hz, CH₂), 5.38-5.40 (t, 1H, *J* = 4.4 Hz, =CH-), 7.10-7.13 (m, 2H, Ar-H), 7.34-7.35 (m, 4H, Ar-H), 7.16-7.18 (m, 7H, Ar-H). ESIMS *m/z* = 395 (MH⁺); *Anal.* Calcd. for C₂₂H₁₆Cl₂N₂O: C, 66.85; H, 4.08; N, 7.09. Found: C, 66.89; H, 4.13; N, 7.05.

1-(4-Methylphenyl)-3-(4-chlorophenyl)-6-phenyl-3,4-dihydropyrimidin-2(1H)-one (3b). Mp 135-137 °C; ¹H NMR (400 MHz, CDCl₃) δ: 1.67 (s, 3H, CH₃), 4.42-4.44 (d, 2H, *J* = 4.4 Hz, CH₂), 5.32-5.34 (t, 1H, *J* = 4.4 Hz, =CH-), 6.93-6.95 (d, 2H, *J* = 8.0 Hz, Ar-H), 7.08-7.10 (d, 2H, *J* = 8.0 Hz, Ar-H), 7.14-7.18 (m, 5H, Ar-H), 7.33-7.35 (m, 4H, Ar-H). ESIMS *m/z* = 375 (MH⁺); *Anal.* Calcd. for C₂₃H₁₉ClN₂O: C, 73.69; H, 5.11; N, 7.47. Found: C, 73.63; H, 5.16; N, 7.42.

1-(4-Methoxyphenyl)-3-(4-chlorophenyl)-6-phenyl-3,4-dihydropyrimidin-2(1H)-one (3c). Oil; ¹H NMR (400 MHz, CDCl₃) δ: 3.68 (s, 3H, OCH₃), 4.43-4.44 (d, 2H, *J* = 4.4 Hz, CH₂), 5.29-5.31 (t, 1H, *J* = 4.4 Hz, =CH-), 6.66-6.68 (d, 2H, *J* = 8.4 Hz, Ar-H), 7.11-7.18 (m, 7H, Ar-H), 7.34-7.38 (m, 4H, Ar-H). ESIMS *m/z* = 391 (MH⁺); *Anal.* Calcd. for C₂₃H₁₉ClN₂O₂: C, 70.68; H, 4.90; N, 7.17. Found: C, 70.63; H, 4.95; N, 7.12.

1-(3,4,5-Trimethoxyphenyl)-3-(4-chlorophenyl)-6-phenyl-3,4-dihydropyrimidin-2(1H)-one (3d). Oil; ¹H NMR (400 MHz, CDCl₃) δ: 3.68 (s, 6H, OCH₃×2), 3.72 (s, 3H, OCH₃), 4.43-4.45 (d, 2H, *J* = 4.4 Hz, CH₂), 5.35-5.37 (t, 1H, *J* = 4.4 Hz, =CH-), 6.47 (s, 2H, Ar-H), 7.16-7.19 (m, 5H, Ar-H), 7.35-7.38 (m, 4H, Ar-H). ESIMS *m/z* = 451 (MH⁺); *Anal.* Calcd. for C₂₅H₂₃ClN₂O₄: C, 66.59; H, 5.14; N, 6.21. Found: C, 66.63; H, 5.10; N, 6.18.

1-(4-Chlorophenyl)-3-phenyl-6-phenyl-3,4-dihydropyrimidin-2(1H)-one (3e). Mp 107-109 °C; ¹H NMR (400 MHz, CDCl₃) δ: 4.48-4.49 (d, 2H, *J* = 4.4 Hz, CH₂), 5.41-5.43 (t, 1H, *J* = 4.4 Hz, =CH-), 7.11-7.15 (m, 2H, Ar-H), 7.20-7.23 (m, 7H, Ar-H), 7.25-7.28 (m, 1H, Ar-H), 7.41-7.42 (m, 4H, Ar-H). ESIMS *m/z* = 361 (MH⁺); *Anal.* Calcd. for C₂₂H₁₇ClN₂O: C, 72.23; H, 4.75; N, 7.76. Found: C, 72.26; H, 4.79; N, 7.73.

1-(3,4,5-Trimethoxyphenyl)-3-phenyl-6-phenyl-3,4-dihydropyrimidin-2(1H)-one (3f). Mp 119-121 °C; ¹H NMR (400 MHz, CDCl₃) δ: 3.69 (s, 6H, OCH₃×2), 3.73 (s, 3H, OCH₃), 4.48-4.49 (d, 2H, *J* = 4.4 Hz, CH₂), 5.38-5.40 (t, 1H, *J* = 4.4 Hz, =CH-), 6.52 (s, 2H, Ar-H), 7.15-7.23 (m, 6H, Ar-H), 7.42-7.43 (m, 4H, Ar-H). ESIMS *m/z* = 417 (MH⁺); *Anal.* Calcd. for C₂₅H₂₄N₂O₄: C, 72.10; H, 5.81; N, 6.73. Found: C, 72.07; H, 5.86; N, 6.69.

1,3,6-Triphenyl-3,4-dihydropyrimidin-2(1H)-one (3g). Oil; ¹H NMR (400 MHz, CDCl₃) δ: 4.46-4.47 (d, 2H, *J* = 4.4 Hz, CH₂), 5.35-5.37 (t, 1H, *J* = 4.4 Hz, =CH-), 6.69-6.74 (m, 2H, Ar-H), 6.91-6.95 (m, 2H, Ar-H), 7.01-7.05 (m, 1H, Ar-H), 7.21-7.24 (m, 2H, Ar-H), 7.26-7.29 (m, 4H, Ar-H), 7.43-7.45 (m, 4H, Ar-H). ESIMS *m/z* = 327 (MH⁺); *Anal.* Calcd. for C₂₂H₁₈N₂O: C, 80.96; H, 5.56; N, 8.58. Found: C, 80.94; H, 5.57; N, 8.59.

1-Phenyl-3-(4-methoxyphenyl)-6-phenyl-3,4-dihydropyrimidin-2(1H)-one (3h). Mp 132-134 °C; ¹H NMR (400 MHz, CDCl₃) δ: 3.40 (s, 3H, OCH₃), 4.12-4.14 (d, 2H, *J* = 4.4 Hz, CH₂), 5.29-5.30 (t, 1H, *J* = 4.4 Hz, =CH-), 6.94-6.96 (d, 2H, *J* = 8.8 Hz, Ar-H), 7.22-7.24 (m, 1H, Ar-H), 7.29-7.33 (m, 5H, Ar-H), 7.38-7.40 (m, 4H, Ar-H), 7.66-7.69 (m, 2H, Ar-H). ESIMS *m/z* = 357 (MH⁺); *Anal.* Calcd. for C₂₃H₂₀N₂O₂: C, 77.51; H, 5.66; N, 7.86. Found: C, 77.55; H, 5.70; N, 7.89.

1-(4-Methoxyphenyl)-3-(4-methylphenyl)-6-phenyl-3,4-dihydropyrimidin-2(1H)-one (3i). Oil; ¹H NMR (400 MHz, CDCl₃) δ: 2.35 (s, 3H, CH₃), 3.68 (s, 3H, OCH₃), 4.44-4.45 (d, 2H, *J* = 4.4 Hz, CH₂), 5.29-5.31 (t, 1H, *J* = 4.4 Hz, =CH-), 6.65-6.67 (d, 2H, *J* = 8.4 Hz, Ar-H), 7.13-7.20 (m, 9H, Ar-H), 7.26-7.30 (d, 2H, *J* = 8.4 Hz, Ar-H). ESIMS *m/z* = 371 (MH⁺); *Anal.* Calcd. for C₂₄H₂₂N₂O₂: C, 77.81; H, 5.99; N, 7.56. Found: C, 77.85; H, 6.01; N, 7.53.

1-(4-Chlorophenyl)-3-(3-chlorophenyl)-6-phenyl-3,4-dihydropyrimidin-2(1H)-one (3j). Oil; ¹H NMR (400 MHz, CDCl₃) δ: 4.47-4.48 (d, 2H, *J* = 4.4 Hz, CH₂), 5.42-5.44 (t, 1H, *J* = 4.4 Hz, =CH-), 7.14-7.16 (m, 2H, Ar-H), 7.20-7.24 (m, 6H, Ar-H), 7.29-7.33 (m, 2H, Ar-H), 7.35-7.38 (m, 2H, Ar-H), 7.45 (s, 1H, Ar-H). ESIMS *m/z* = 395 (MH⁺); *Anal.* Calcd. for C₂₂H₁₆Cl₂N₂O: C, 66.85; H, 4.08; N, 7.09. Found: C, 66.81; H, 4.12; N, 7.11.

1-Phenyl-3-(3-chlorophenyl)-6-phenyl-3,4-dihydropyrimidin-2(1H)-one (3k). Mp 135-137 °C; ¹H NMR (400 MHz, CDCl₃) δ: 4.37-4.38 (d, 2H, *J* = 4.4 Hz, CH₂), 5.42-5.44 (t, 1H, *J* = 4.4 Hz, =CH-), 7.14-7.16 (m, 2H, Ar-H), 7.20-7.21 (m, 7H, Ar-H), 7.29-7.33 (m, 2H, Ar-H), 7.35-7.38 (m, 2H, Ar-H), 7.45 (s, 1H, Ar-H). ESIMS *m/z* = 361 (MH⁺); *Anal.* Calcd. for C₂₂H₁₇ClN₂O: C, 73.23; H, 4.75; N, 7.76. Found: C, 73.19; H, 4.77; N, 7.72.

1-Phenyl-3-(3-bromophenyl)-6-phenyl-3,4-dihydropyrimidin-2(1H)-one (3l). Mp 132-134 °C; ¹H NMR (400 MHz, CDCl₃) δ: 4.39-4.40 (d, 2H, *J* = 4.4 Hz, CH₂), 5.42-5.43 (t, 1H, *J* = 4.4 Hz, =CH-), 7.29-7.33 (m, 3H, Ar-H), 7.37-7.46 (m, 7H, Ar-H), 7.58-7.59 (m, 2H, Ar-H), 7.67-7.69 (m, 2H, Ar-H). ESIMS *m/z* = 405 (MH⁺); *Anal.* Calcd. for C₂₂H₁₇BrN₂O: C, 65.20; H, 4.23; N, 6.91. Found: C, 65.16; H, 4.25; N, 6.88.

1-Phenyl-3-(3-methylphenyl)-6-phenyl-3,4-dihydropyrimidin-2(1H)-one (3m). Mp 110-112 °C; ¹H NMR (400 MHz, CDCl₃) δ: 2.39 (s, 3H, CH₃), 4.38-4.39 (d, 2H, *J* = 4.4 Hz, CH₂), 5.40-5.42 (t, 1H, *J* = 4.4 Hz, =CH-), 7.09-7.15 (m, 2H, Ar-H), 7.19-7.23 (m, 3H, Ar-H), 7.31-7.35 (m, 3H, Ar-H), 7.39-7.41 (m, 4H, Ar-H), 7.67-7.70 (m, 2H, Ar-H). ESIMS *m/z* = 341 (MH⁺); *Anal.* Calcd. for C₂₃H₂₀N₂O: C, 81.15; H, 5.92; N, 8.23. Found: C, 81.10; H, 5.86; N, 8.33.

REFERENCES AND NOTES

- [1a] Kappe, C. O. *Tetrahedron* **1993**, *49*, 6937. (b) Kappe, C. O. *Acc. Chem. Res.* **2000**, *33*, 6937. (c) Kappe, C. O. *Eur. J. Med. Chem.* **2000**, *35*, 1043.
- [2] Russowsky, D.; Canto, R. F. S.; Sanches, S. A. A.; D'Oca, M. G. M.; Fatima, A. D.; Carvalho, J. E. D. *Bioorg. Chem.* **2006**, *34*, 173.
- [3a] Rovnyak, G. C.; Atwal, K. S.; Hedberg, A.; Kimball, S. D.; Moreland, S.; Gougoutas, J. Z.; O'Reilly, B. C.; Schewartz, J.; Mallay, M. F. *J. Med. Chem.* **1992**, *35*, 3254. (b) Grover, G. J.; Dzwonczyk, S.; McMullen, D. M.; Normandin, D. E.; Pharham, C. S.; Slep, P. G.; Moreland, S. *J. Cardiovasc. Pharmacol.* **1995**, *26*, 289.
- [4a] Nagarathnam, D.; Miao, S. W.; Lagu, B.; Harrell, M. C.; Vyas, K. P.; Gluchowski, C. *J. Med. Chem.* **1999**, *42*, 4764. (b) Barrow, J. C.; Nantermet, P. G.; Nagarathnam, D.; Forray, C. *J. Med. Chem.* **2000**, *43*, 2703.
- [5a] Overman, L. E.; Rabinowitz, M. H.; Renhowe, P. A. *J. Am. Chem. Soc.* **1995**, *117*, 2657. (b) Mayer, T. U.; Kapoer, T. M.; Haggarty, S. J.; King, R. W.; Schreiber, S. L. *Science* **1998**, *286*, 971. (c) Gartner, M.; Sunder-Plassmann, N.; Seiler, J.; Utz, M.; Vernos, I.; Surrey, T.; Giannis, A. *Chem. Bio. Chem.* **2005**, *6*, 1173.
- [6a] Biginelli, P. *Gazz. Chim. Ital.* **1893**, *23*, 360. (b) Folkers, K.; Johnson, T. B. *J. Am. Chem. Soc.* **1933**, *55*, 3781.
- [7a] Kappe, C. O.; Falsone, S. F. *Synlett* **1998**, 718. (b) Hu, E. H.; Sidler, D. R.; Dolling, U. H. *J. Org. Chem.* **1998**, *63*, 3454. (c) Lu, J.; Ma, H. *Synlett* **2000**, 63. (d) Ma, Y.; Qian, C.; Wang, L.; Yang, M. *J. Org. Chem.* **2000**, *65*, 3864. (e) Ranu, B. C.; Hayra, A.; Jana, U. *J. Org. Chem.* **2000**, *65*, 6270.
- [8] Peng, J.; Deng, Y. *Tetrahedron Lett.* **2001**, *42*, 5917.
- [9] Kappe, C. O.; Kumar, D.; Varma, R. S. *Synthesis* **1999**, 1799.
- [10] Zhang, X.; Li, Y.; Liu, C.; Wang, J. *J. Mol. Catal. A: Chem.* **2006**, *253*, 207.
- [11] Mamaev, V. P.; Nilko'skaya, G. S.; Lyubimova, E. N. *Izv. Sibir. Otd. Akad. Nauk SSSR, Ser. Khim. Nauk* (Russian) **1971**, *2*, 86; *Chem. Abstr.* **1972**, *76*, 14479g.
- [12] Abid, M.; Azam, A. *Eur. J. Med. Chem.* **2005**, *9*, 935.
- [13] Modak, A. S.; Gogte, V. N.; Tilak, B. D. *Indian J. Chem. Sect. B* **1984**, *10*, 907.
- [14] Xu, X. J.; Chen, G. X. *Acta. Chemica. Sinica*. (Chinese) **1982**, *4*, 362; *Chem. Abstr.* **1982**, *96*, 162498g.