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# Preparation of Some Fused Pyridopyrimidine and Pyridothienotriazine Derivatives for Biological Evaluation

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Compounds 2 and 9 were formed using 3-(4-chloro-phenyl)-1-pyridin-2-yl propenone (1) and malononitrile or ethyl cyanoacetate, respectively. The pyridine derivative 2 was in turn used as a precursor for the preparation of some pyridopyrimidine and fused pyridopyrimidine derivatives 3-8. On the other hand, the pyridine derivative 9 was used for the preparation of thienopyridine derivatives 11 and 12. Nitrozation of compound 12 afforded pyridothienotriazine derivative 13. Some of the prepared products showed potent antimicrobial activity.

**Keywords** Fused pyridopyrimidine; pyridopyrimidine; pyridothienotriazine; thienopyridine

# INTRODUCTION

Pyridines, pyridopyrimidines, and their fused heterocyclic ring systems are of current interest<sup>1-4</sup> by virtue of their exceptional and versatile biological activities as calcium antagonists,<sup>4</sup> arteriolar vasodilators,<sup>5</sup> antitumor agents,<sup>6</sup> herbicide antidotes,<sup>7</sup> antibacterial agents,<sup>8-10</sup> diuretics,<sup>11,12</sup> analgesics,<sup>13</sup> CNS depressing agents,<sup>14</sup> and hypotensive agents.<sup>15,16</sup> Similarly, pyridopyrimidine moiety was considered as the best-known tyrosin kinase inhibitor for the treatment of chronic myelogenous leukemia and drug resistance emerges by amplification of the

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development of a mutation.<sup>17</sup> Also, pyridopyrimidines have antimicrobial activity against a number of bacteria and fungi.<sup>18,19</sup> On the other hand, certain pyridothienotriazines, inhibit the immunologicallyinduced release of histamine.<sup>20</sup> So, it is used clinically for the oral treatment of asthma.<sup>21</sup> These findings encouraged us to undertake the synthesis of some newly pyridopyrimidine and pyridothienotriazine ring systems in hoping that they could have some chemical and biological interest.

### DISCUSSION

Compounds **2** and **9** were used as starting materials for this study and for further syntheses of other fused heterocyclic compounds. Thus, on refluxing a mixture of 3-(4-chloro-phenyl)-1-pyridin-2-yl propenone  $1^{22,24}$  with malononitrile or ethyl cyanoacetate in the presence of anhydrous ammonium acetate, gave compound **2** or **9**, respectively (Scheme 1). The structure of compounds **2** and **9** were confirmed with spectral data. The IR spectra showed bands at ( $\nu$ , cm<sup>-1</sup>): 3410, 3360 (NH<sub>2</sub>), and 2210 (CN) for compound **2** and 3250 (NH), 2210 (CN), and 1695 (CO) for compound **9**. The <sup>1</sup>H NMR spectra showed signals at ( $\delta$ , ppm): 6.80 (brs, 2H, NH<sub>2</sub>, exchangeable with D<sub>2</sub>O) for compound **2** and 10.20 (s, 1H, NH, exchangeable with D<sub>2</sub>O) for compound **9**. The MS gave the molecular ion peaks at m/z = 306 and 307 for compounds **2** and **9**, respectively.

On heating compound 2 with formic acid, it afforded pyrido[2,3d]pyrimidin-4-one derivative **3** (Scheme 1). Its IR spectrum showed the absence of a cyano group and showed bands at  $(v, \text{ cm}^{-1})$ : 3150 (NH) and 1700 (CO). Its <sup>1</sup>H NMR spectrum gave signals at  $(\delta,$ ppm): 7.20-8.80 (m, 10H, Ar-H), and 11.20 (s, 1H, NH exchangeable with  $D_2O$ ). The reaction of compound 2 with carbon disulphide in the presence of aqueous potassium hydroxide<sup>24</sup> gave pyrido[2,3d]pyrimidine-2,4-dithione 4 (Scheme 1). The spectral data of compound 4 assigned its structure (cf. Experimental section). The latter compound reacted with  $\beta$ -bromopropionic acid or chloroacetic acid to afford pyrido[2',3':4,5]pyrimido[2,1-b][1,3]thiazine **5** or pyrido[2',3':4,5] pyrimido[2,1-b][1,3]thiazole 6, respectively (Scheme 1). The IR spectra showed bands at  $(\nu, \text{cm}^{-1})$ : 1700 and 1705 (CO) for compounds 5 and 6, respectively. The <sup>1</sup>H NMR spectra showed signals at ( $\delta$ , ppm): 2.60 (t, 2H,  $CH_2$ ) and 3.00 (t, 2H,  $CH_2$ ) for compound 5 and 3.80 (s, 2H,  $CH_2$ ) for compound **6**. The MS spectra gave the molecular ion peaks at m/z =436 and 422 for compounds 5 and 6, respectively. When compounds **5** or **6** were condensed with p-chlorobenzaldehyde, they afforded compounds 7 or 8, respectively (Scheme 1). The latter compounds could be prepared directly *via* a one-pot reaction by treating compound **4** with  $\beta$ -bromopropionic acid or chloroacetic acid and p-chlorobenzaldehyde. The spectral data of compounds **7** and **8** assigned their structures (cf. Experimental section) (Scheme 1).



SCHEME 1

Thionation of compound **9** with phosphorus pentasulfide in dry pyridine afforded the corresponding pyridinethione derivative **10** (Scheme 1); its MS spectra gave the molecular ion peak at m/z = 323.

Condensation of compound **10** with ethyl chloroacetate in the presence of sodium methoxide<sup>25</sup> afforded 3-amino-thieno[2,3-*b*]pyridine-2-carboxylic acid ethyl ester **11** (Scheme 1). The structure of compound **11** was confirmed with spectral data because the IR spectrum showed bands at ( $\nu$ , cm<sup>-1</sup>): 3400, 3350 (NH<sub>2</sub>), and 1725 (CO). The <sup>1</sup>H NMR spectra showed signals at ( $\delta$ , ppm): 1.30 (t, 3H, CH<sub>3</sub>), 4.40 (q, 2H, CH<sub>2</sub>), and 5.10 (brs, 2H, NH<sub>2</sub> exchangeable with D<sub>2</sub>O); its MS spectra gave the molecular ion peak at m/z = 409. The latter compound was ammoniated to give its corresponding aminoamide derivative **12**, which annulated with nitrous acid to give 9-(4-chloro-phenyl)-7-pyridin-2-yl-3*H*-pyrido[3',2':4,5] thieno[3,2-*d*][1,2,3] triazin-4-one (**13**) (Scheme 1). The IR spectrum showed bands at ( $\nu$ , cm<sup>-1</sup>): 3200 (NH) and 1675 (CO); <sup>1</sup>H NMR spectrum showed signals at ( $\delta$ , ppm): 10.40 (s, 1H, and NH exchangeable with D<sub>2</sub>O).

# **BIOLOGICAL EVALUATION**

The antimicrobial activity of some newly synthesized compounds 4, 7, 11, 12, and 13 were tested at concentration of 0.1 g/mL using dimethyl-formamide as a solvent.

# **Microorganisms' Species**

Bacteria \*Gram-negative bacteria, Escherichia coli \*Gram-positive bacteria, Bacillus subtilis Yeast: Candida albicans Fungi: Aspergillus niger

# Medium

The cap-assay method containing (g/L) peptone 6.0, yeast extract 3.0, meat extract 1.5, glucose 1.0 and agar 20.0 were used. The medium was sterilized and divided while hot  $(50-60^{\circ}C)$  in 15 mL portions among sterile petri-dishes of 9 cm diameter and one mL of the spore suspension of each microorganism was spread over the surface of the cold solid medium placed in the petri-dish.

# Method<sup>26</sup>

 $0.5~{\rm g}$  of each the tested compounds was dissolved in  $5~{\rm mL}$  of dimethyl-formamide. An amount of  $0.1~{\rm mL}$  of test solution was placed on watman

	Inhibition Zone (mm) Microorganism			
Tested compounds and standers	Bacteria			
	Gram-negative Escherichia coli.	Gram-positive Bacillus subtilis	Fungi Aspergillus niger	Yeast Candida albicans
Streptomycin	+ + +	+ + +	+	+ + +
Erythromycin	_	+ + +	_	_
Ampicillin	++	_	_	_
Amoxicillin	++	_	_	_
Fusidic Acid	_	_	+ + +	+ + +
4	++	++	++	+ + +
7	+	_	_	+
11	_	_	-	-
12	_	_	_	_
13	_	_	_	_

TABLE I Antimicrobial Activity of Some Newly SynthesizedCompounds

+++, Highly sensitive (inhibition zone = 21–25 mm). ++, Fairly sensitive (inhibition zone = 16–20 mm). + Slightly sensitive (inhibition zone = 10–15 mm). -, Not sensitive.

paper disc of 9 mm in diameter and the solvent was left to evaporate. These saturated discs were placed carefully on the surface of the inoculated solid medium; each petri-dish contains at least 3 discs. The petri-dishes were incubated at  $5^{\circ}$ C for 1 h to permit good diffusion and then were transferred to an incubator of  $85^{\circ}$ C overnight, and then examined. The results were then recorded by measuring the inhibition zone diameters (Table I).

# Result

Among the tested compounds, it was noticed that compound **4** showed more significant antibacterial and antifungal activity more than some known drugs (standers) (Table I). Compound **7** demonstrated inhibitory activity against Gram negative and yeast. On the other hand, compounds **11**, **12**, and **13** showed no inhibitory effect on bacteria and fungi.

# Experimental

All melting points are uncorrected and were measured using an Electrothermal IA 9100 apparatus. Analytical data were performed by Vario El Mentar apparatus, organic microanalysis section at the National Research Centre. Their results were found to be in agreement with the calculated values (±0.3). The IR spectra (KBr) were recorded on a Perkin-Elmer 1650 spectrophotometer. <sup>1</sup>H NMR spectra were determined on a Jeol 300 MHz in DMSO-d<sub>6</sub> or CDCl<sub>3</sub> and the chemical shifts were expressed in ppm relative to TMS as internal reference. Mass spectra were run at 70 eV on EI + Q1 MSLMR UPLR.

# 6-Amino-4-(4-chloro-phenyl)-2-pyridin-2-yl-pyridine-5carbonitrile (2)

A mixture of 3-(4-chloro-phenyl)-1-pyridin-2-yl propenone 1 (2.43 gm, 0.01 mole) and malononitrile (0.66 gm, 0.01 mole) in 30 mL glacial acetic acid containing anhydrous ammonium acetate (1.53 g, 0.02 mole) was refluxed for 6 h. The reaction mixture was cooled and poured into water. The formed solid was filtered off, dried, and recrystallized from ethanol to give **2** in an 85% yield; m.p. 194–195°C. IR spectrum (KBr,  $\nu$ , cm<sup>-1</sup>): 3410, 3360 (NH<sub>2</sub>) and 2210 (CN); <sup>1</sup>H NMR spectrum (CDCl<sub>3</sub>,  $\delta$  ppm): 7.12–8.60 (m, 9H, Ar-H), 6.80 (s, 2H, NH<sub>2</sub> exchangeable with D<sub>2</sub>O); MS, m/z (%): 306 (M<sup>+</sup>, 100). Analysis for C<sub>17</sub>H<sub>11</sub>ClN<sub>4</sub> (306.75): required C, 66.56; H, 3.61; Cl, 11.56; N, 18.26; found C, 66.33; H, 3.50; Cl, 11.55; N, 18.00.

# 5-(4-Chloro-phenyl)-7-pyridin-2-yl-3*H*-pyrido[2,3-*d*]pyrimidin-4-one (3)

Compound **2** (1.12 gm, 4 mmol) was heated under reflux temperature in formic acid (20 mL, 85%) for 12 h. The reaction mixture was cooled and poured into water. The formed solid was filtered off, dried, and recrystallized from dioxane to give **3** in a 50% yield; m.p. 258–260°C. IR spectrum (KBr,  $\nu$ , cm<sup>-1</sup>): 3150 (NH), and 1700 (CO); <sup>1</sup>H NMR spectrum (DMSO-d<sub>6</sub>,  $\delta$  ppm): 7.20–8.80 (m, 10H, Ar-H), 11.2 (s, 1H, NH exchangeable with D<sub>2</sub>O). MS, m/z (%): 334 (M<sup>+</sup>, 15.20). Analysis for C<sub>18</sub>H<sub>11</sub>ClN<sub>4</sub>O (334.76): required C, 64.58; H, 3.31; Cl, 10.59; N, 16.74; found C, 64.35; H, 3.30; Cl, 10.61; N, 16.60.

# 5-(4-Chloro-phenyl)-7-pyridin-2-yl-1*H*-pyrido[2,3-*d*]pyrimidine-2,4-dithione (4)

To a solution of 2 (1.12 gm, 4 mmol) in a 5% alcoholic potassium hydroxide (20 mL), carbon disulfide (10 mL) was added. The reaction mixture was stirred for 1 h, followed by refluxing for 2 h. The reaction mixture was cooled, poured into water, and neutralized with hydrochloric acid (5 mL, 34%). The formed solid was filtered off, dried, and recrystallized from dioxane to give 4 in a 60% yield; m.p. 234–235°C. IR spectrum (KBr,  $\nu$ , cm<sup>-1</sup>): 3300 (NH), 3250 (NH), 1200 (CS), 1220 (CS); <sup>1</sup>H NMR spectrum (DMSO-d<sub>6</sub>,  $\delta$  ppm): 7.20–8.70 (9H, m, Ar-H), 9.80 (s, 1H, NH exchangeable with D<sub>2</sub>O), 11.00 (s, 1H, NH exchangeable with D<sub>2</sub>O). MS, m/z (%): 382 (M<sup>+</sup>, 14.68). Analysis for C<sub>18</sub>H<sub>11</sub>ClN<sub>4</sub>S<sub>2</sub> (382.89): required C, 56.46; H, 2.90; Cl, 9.26; N, 14.63; S, 16.75; found C, 56.53; H, 2.93; Cl, 9.22; N, 14.48; S, 16.83.

#### 4-(4-Chloro-phenyl)-2-pyridin-2-yl-5-thioxo-7,8-dihydropyrido[2',3':4,5] pyrimido[2,1-*b*][1,3]thiazin-9-one (5)

A mixture of 4 (1.53 gm, 4 mmol) and  $\beta$ -bromopropionic acid (0.61 gm, 4 mmol) was refluxed in a mixture of glacial acetic acid/acetic anhydride (3:1) containing anhydrous sodium acetate (0.35 gm, 4 mmol) for 3 h. The reaction mixture was cooled and poured into water. The formed solid was filtered off, dried and recrystallized from methanol to give **5** in a 55% yield; m.p. 204–205°C. IR spectrum (KBr,  $\nu$ , cm<sup>-1</sup>): 1700 (CO), 1180 (CS); <sup>1</sup>H NMR spectrum (CDCL<sub>3</sub>,  $\delta$  ppm): 2.60 (t, 2H, CH<sub>2</sub>), 3.00 (t, 2H, CH<sub>2</sub>), 7.00–8.80 (m, 9H, Ar-H). MS, m/z (%): 436 (M<sup>+</sup>, 8.23). Analysis for C<sub>21</sub>H<sub>13</sub>ClN<sub>4</sub>OS<sub>2</sub> (436.94): required C, 57.73; H, 3.0; Cl, 8.11; N, 12.82; S, 14.68; found C, 57.53; H, 2.98; Cl, 8.26; N, 12.84; S, 17.73.

# 4-(4-Chloro-phenyl)-2-pyridin-2-yl-5-thioxo-pyrido[2',3': 4,5]pyrimido[2,1-*b*] [1,3]thiazol-8-one (6)

A mixture of 4 (1.53 gm, 4 mmol) and chloroacetic acid (0.56 gm, 4 mmol) was refluxed in a mixture of glacial acetic acid/acetic anhydride (3:1) containing anhydrous sodium acetate (0.35 gm, 4 mmol) for 3 h. The reaction mixture was cooled and poured into water. The formed solid was filtered off, dried, and recrystallized from methanol to give **6** in a 60% yield; m.p. 178–180°C. IR spectrum (KBr,  $\nu$ , cm<sup>-1</sup>): 1705 (CO), 1185 (CS); <sup>1</sup>H NMR spectrum (CDCL<sub>3</sub>,  $\delta$  ppm): 3.80 (s, 2H, CH<sub>2</sub>), 7.20–9.00 (m, 9H, Ar-H). MS, *m*/*z* (%): 422 (M<sup>+</sup>, 11.90). Analysis for C<sub>20</sub>H<sub>11</sub>ClN<sub>4</sub>OS<sub>2</sub> (422.92): required C, 56.80; H, 2.62; Cl, 8.38; N, 13.25; S, 15.16; found C, 56.73; H, 2.71; Cl, 8.22; N, 13.28; S, 14.93.

#### Preparation of Compounds 7 and 8

#### Method A

8-(4-Chloro-benzylidene)-4-(4-chloro-phenyl)-2-pyridin-2-yl-5thioxo-7,8-dihydro-pyrido[2,3:4,5]pyrimido[2,1-b][1,3]thiazin-9-one (7). A mixture of **5** (1.3 gm, 3 mmol) and *p*-chlorobenzaldhyde (0.42 gm, 3 mmol) was refluxed in glacial acetic acid containing anhydrous sodium acetate (0.35 gm, 4 mmol). The reaction mixture was cooled and poured into water. The formed solid was filtered off, dried, and recrystallized from acetic acid to give **7** in a 65% yield; m.p. 256–257°C. IR spectrum (KBr,  $\nu$ , cm<sup>-1</sup>): 1715 (CO), 1180 (CS); <sup>1</sup>H NMR spectrum (DMSO-d<sub>6</sub>,  $\delta$  ppm): 3.40 (s, 2H, CH<sub>2</sub>), 7.20–9.20 (m, 13H, Ar-H and 1H arylmethylene). MS, m/z (%): 559 (M<sup>+</sup>, 10.55). Analysis for C<sub>28</sub>H<sub>16</sub>Cl<sub>2</sub>N<sub>4</sub>OS<sub>2</sub> (559.49): required C, 60.11; H, 2.88; Cl, 12.67; N, 10.01; S, 11.46; found C, 60.00; H, 2.93; Cl, 12.60; N, 10.20; S, 11.35.

7-(4-Chloro-benzylidene)-4-(4-chloro-phenyl)-2-pyridin-2-yl-5thioxo-pyrido[2',3':4,5]pyrimido[2,1-b][1,3]thiazol-8-one (8). A mixture of **6** (1.26 gm, 3 mmol) and *p*-chlorobenzaldhyde (0.42 gm, 3 mmol) was refluxed in glacial acetic acid containing anhydrous sodium acetate (0.35 gm, 4 mmol). The reaction mixture was cooled and poured into water. The formed solid was filtered off, dried, and recrystallized from acetic acid to give **8** in a 70% yield; m.p. 248–250°C. IR spectrum (KBr,  $\nu$ , cm<sup>-1</sup>): 1710 (CO), 1188 (CS); <sup>1</sup>H NMR spectrum (DMSO-d<sub>6</sub>,  $\delta$  ppm): 7.10–9.00 (m, 13H, Ar-H and 1H arylmethylene). MS, m/z (%): 545 (M<sup>+</sup>, 17.22). Analysis for C<sub>27</sub>H<sub>14</sub>Cl<sub>2</sub>N<sub>4</sub>OS<sub>2</sub> (545.46): required C, 59.45; H, 2.59; Cl, 13.00; N, 10.27; S, 11.76; found C, 59.90; H, 2.52; Cl, 12.90; N, 10.16; S, 11.50.

#### Method B

General procedure. Compound **7** or **8** was prepared directly by refluxing compound **4** (4 mmol) and  $\beta$ -bromopropionic acid or chloroacetic acid (4 mmol) and *p*-chlorobenzaldhyde (4 mmol) in a mixture of glacial acetic acid/acetic anhydride (3:1) containing anhydrous sodium acetate (1.2 gm, 8 mmol) for 3 h. Then the reaction mixture was cooled, poured into water, and the precipitates that formed were filtered off, dried, and recrystallized from an appropriate solvent to give **7** (72%) or **8** (84%), respectively. The obtained products were identified by m.p. and TLC in comparison with authentic samples from Method A.

### 4-(4-Chloro-phenyl)-6-oxo-2-pyridin-2-yl-1,6-dihydro-pyridine-5-carbonitrile (9)

A mixture of compound 1 (1.2 gm, 5 mmol) and ethyl cyanoacetate (0.33 gm, 5 mmol) was refluxed in glacial acetic acid containing anhydrous ammonium acetate (0.80 gm, 10 mmol) for 6 h. The reaction mixture was cooled and poured into water. The formed solid was filtered off, dried, and recrystallized from dioxane to give **9** in a 80% yield; m.p. 209–211°C. IR spectrum (KBr,  $\nu$ , cm<sup>-1</sup>): 3250 (NH), 2210 (CN), 1695 (CO); <sup>1</sup>H NMR spectrum (DMSO-d<sub>6</sub>,  $\delta$  ppm): 6.7 (s, 1H, pyridine), 7.30–8.60

(m, 8H, Ar-H), 10.2 (s, 1H, NH exchangeable with  $D_2O$ ); MS, m/z (%): 307 (M<sup>+</sup>, 100). Analysis for  $C_{17}H_{10}ClN_3O$  (307.74): required C, 66.35; H, 3.28; Cl, 11.52; N, 13.65; found C, 66.42; H, 3.30; Cl, 11.48; N, 13.56.

4-(4-Chloro-phenyl)-6-thioxo-2-pyridin-2-yl-1,6-dihydro-pyridine-5carbonitrile (10). A mixture of compound **9** (3.07 gm, 10 mmol) and  $P_2S_5$  (6.44 gm, 20 mmol) was refluxed in 50 mL of dry pyridine for 6 h. The reaction mixture cooled and poured into ice water. The solid formed filtered off, dried, and recrystallized from dioxane to give **10** in a 55% yield; m.p. 243–245°C. IR spectrum (KBr,  $\nu$ , cm<sup>-1</sup>): 3300 (NH), 2215 (CN), 1200 (CS); <sup>1</sup>H NMR spectrum (DMSO-d<sub>6</sub>,  $\delta$  ppm): 7.20–8.50 (m, 9H,Ar-H), 10.6 (s, 1H, NH exchangeable with D<sub>2</sub>O); MS, *m/z* (%): 323 (M<sup>+</sup>, 27.39). Analysis for C<sub>17</sub>H<sub>10</sub>ClN<sub>3</sub>S (323.80): required C, 63.06; H, 3.11; Cl, 10.95; N, 12.98; S, 9.90; found C, 62.88; H, 3.20; Cl, 10.99; N, 12.77; S, 9.63.

#### 3-Amino-4-(4-chloro-phenyl)-6-pyridin-2-yl-thieno[2,3b]pyridine-2-carboxylic acid ethyl ester (11)

A mixture of **10** (3.23 gm, 10 mmol) and ethyl chloroacetate (2.50 mL, 20 mmol) was stirred in 50 mL of anhydrous ethanol containing sodium ethoxide (2%) for 2 h, and then was refluxed with stirring for 4 h. The reaction mixture was cooled and poured into ice water. The solid formed was filtered off, dried, and recrystallized from methanol to give **11** in a 56% yield; m.p. 197–198°C. IR spectrum (KBr,  $\nu$ , cm<sup>-1</sup>): 3400–3350 (NH<sub>2</sub>), 1725 (CO); <sup>1</sup>H NMR spectrum (CDCl<sub>3</sub>,  $\delta$  ppm): 1.30 (t, 3H, CH<sub>3</sub>), 4.40 (q, 2H, CH<sub>2</sub>), 5.10 (brs, 2H, NH<sub>2</sub> exchangeable with D<sub>2</sub>O), 7.10–8.80 (m, 9H, Ar); MS, *m/z* (%): 409 (M<sup>+</sup>, 31.10). Analysis for C<sub>21</sub>H<sub>16</sub>ClN<sub>3</sub>O<sub>2</sub>S (409.90): required C, 61.54; H, 3.93; Cl, 8.65; N, 10.25; S, 7.82; found C, 61.44; H, 3.86; Cl, 8.76; N, 10.32; S, 7.80.

### 3-Amino-4-(4-chloro-phenyl)-6-pyridin-2-yl-thieno[2,3*b*]pyridine-2-carboxylic acid amide (12)

Compound **11** (2.05 mL, 5 mmol) was dissolved in 50 mL of ethanol, and then a current of NH<sub>3</sub>was passed at 0°C tell saturation. The reaction mixture was left in a refrigerator at  $-4^{\circ}$ C over night; the solid substance was filtered off, washed with water, and recrystallized from dioxane to give **12** in a 66% yield; m.p. 228–230°C. IR spectrum (KBr,  $\nu$ , cm<sup>-1</sup>): 3410–3360 (NH<sub>2</sub>), 1680 (CO); <sup>1</sup>H NMR spectrum (DMSO-d<sub>6</sub>,  $\delta$  ppm): 4.80 (brs, 2H, NH<sub>2</sub> exchangeable with D<sub>2</sub>O), 7.30–8.90 (m, 9H, Ar-H), 9.30 (brs, 2H, NH<sub>2</sub> exchangeable with D<sub>2</sub>O); MS, *m/z* (%): 380 (M<sup>+</sup>, 7.20). Analysis for C<sub>19</sub>H<sub>13</sub>ClN<sub>4</sub>OS (380.86): required C, 59.92; H, 3.44; Cl, 9.31; N, 14.71; S, 8.42; found C, 60.10; H, 3.38; Cl, 9.26; N, 14.74; S, 8.39.

#### 9-(4-Chloro-phenyl)-7-pyridin-2-yl-3*H*pyrido[3',2':4,5]thieno[3,2-*d*] [1,2,3]triazin-4-one (13)

To a suspended solution of compound **12** (0.38 gm, 1 mmol) in a mixture of concentrated sulfuric acid (5 mL, 95%) and glacial acetic acid (10 mL) at 0–5°C, a solution of sodium nitrite (3.00 g) in water (5 mL) was added dropwise with continuous stirring over 20 min. After 2 h of stirring at room temperature the foamy mixture was diluted with water, filtered off, and recrystallized from (DMF/EtOH) to give **13** in a 50% yield; m.p. 266–268°C. IR spectrum (KBr,  $\nu$ , cm<sup>-1</sup>): 3200 (NH), 1675 (CO); <sup>1</sup>H NMR spectrum (DMSO-d<sub>6</sub>,  $\delta$  ppm): 7.10– 8.70 (m, 9H, Ar-H), 10.40 (s, 1H, NH exchangeable with D<sub>2</sub>O); MS, *m*/*z* (%): 391 (M<sup>+</sup>, 13.40). Analysis for C<sub>19</sub>H<sub>10</sub>ClN<sub>5</sub>OS (391.83): required C, 58.24; H, 2.57; Cl, 9.05; N, 17.87; S, 8.18; found C, 58.00; H, 2.55; Cl, 9.15; N, 17.59; S, 8.00.

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