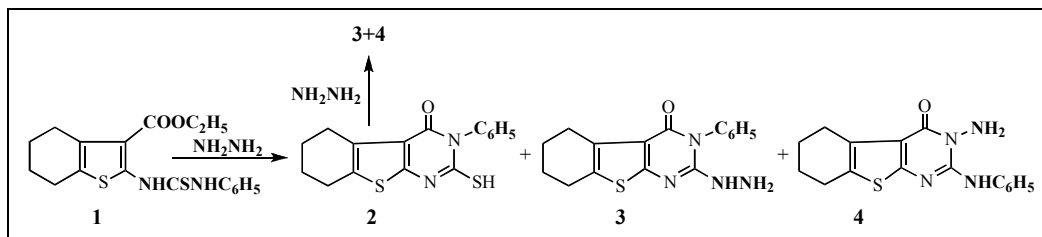


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The reaction of *N*-(3-carbethoxy-4,5,6,7-tetrahydrobenzo[*b*]thien-2-yl)-*N'*-phenylthiourea (**1**) with hydrazine hydrate in 1-butanol afforded a mixture of compounds **2**, **3** and **4**. Treatment of **3** and **4** with nitrous acid gave **6** and **8** respectively, while reactions of **3** with acetylacetone gave **7**. Synthesis of tetracyclic compounds **9a-f** and **11** from the reactions of **3** with ethyl orthoformate or appropriate acids, acid chloride, carbon disulphide and/or ethyl chloroformate. Also its reaction with isothiocyanate derivatives gave the corresponding thiosemicarbazides **12a,b** which on, refluxing in alcoholic KOH gave the unexpected tetracyclic products **14a,b**. Similarly the tetracyclic compounds **16a-e** and **19** were obtained by cyclization of **4** and **18** respectively.

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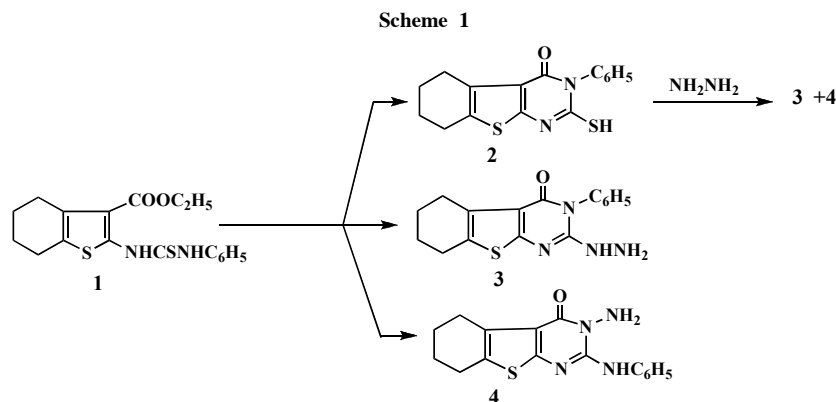
## INTRODUCTION

Thienopyrimidines, have been evaluated pharmacologically as anti-malarial [1] antibacterial [1,6], analgesic and anti-inflammatory [7,11], diuretic activity in rats [12], antiviral [13], antifungal effect [14], herbicidal activity and antimycotoxigenic activity [15]. Besides the synthetic methods of 3-amino-3,4-dihydro-2-arylamino-thieno[2,3-*d*]pyrimidin-4(3*H*)-ones, a new route has appeared in the literature by refluxing of *N*-(3-carbethoxythien-2-yl)-*N'*-arylthiourea **1** with neat hydrazine hydrate [16-18], or in ethanol. Investigation of the reported results show different melting points for the same compound besides the low yield of reaction products aroused our interest in reinvestigation of these reactions and their cyclization reactions.

## RESULTS AND DISCUSSION

The starting compound **1** was prepared by treatment of 2-amino-3-carbethoxy-4,5,6,7-tetrahydrobenzo[*b*]thiophene with phenylisothiocyanate in boiling ethanol. Refluxing of **1** with hydrazine hydrate in ethanol for 12 hours gave a solid crystalline product with mp. 205-207 °C in 50% yield as previously reported [16]. A tlc of the reaction products showed the presence of two compounds which could be separated by recrystallization and identified as the two isomeric products 2-hydrazino-3-phenyl-5,6,7,8-tetrahydrobenzo[*b*]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (**3**) and 3-amino-2-phenylamino-5,6,7,8-tetrahydrobenzo[*b*]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (**4**).

Further, the product obtained by dilution and neutralization of the basic filtrate was characterized as 2-

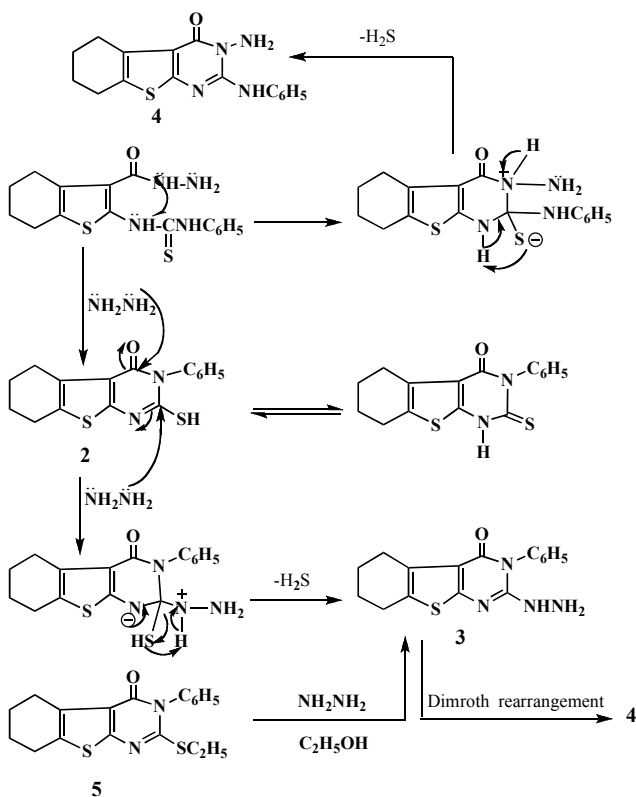


mercapto-3-phenyl-5,6,7,8-tetrahydrobenzo[*b*]thieno[2,3-*d*]pyrimidin-4(3*H*)-one **2** in 42% yield (Scheme 1). However the yield, of the latter compound was decreased either by using 1-butanol instead of ethanol as a solvent, or by increasing the reaction time.

This behaviour may be due to the conversion of **2** to **3** and **4**, which was formed at first then reacted with hydrazine (Scheme 1).

The conversion of **2** to **3** and **4** may be explained by nucleophilic attacking of hydrazine on the electrophilic centers C<sub>2</sub> and C<sub>4</sub> respectively (Scheme 2).

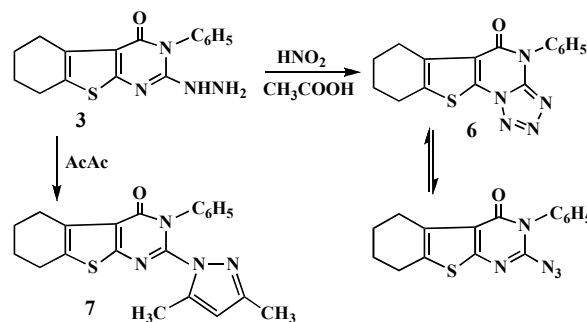
Scheme 2



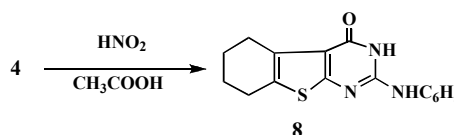
On the other hand, it may be assumed that **3** was formed at the beginning of the reaction as a kinetic product then transformed to **4** as a thermodynamic product through the Dimroth [19] rearrangement. This assumption was clarified as the 2-hydrazino derivative **3** was obtained in 90% yield when **5** was reacted with hydrazine hydrate (Scheme 2). Further, the conversion of **3** to the tetrazolo derivative **6** via its reaction with HNO<sub>2</sub>, and the formation of 2-[3,5-dimethylpyrazol-1-yl]-3-phenyl-5,6,7,8-tetrahydrobenzo[*b*]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (**7**) via its condensation with acetylacetone, are considered as additional evidence of its structure as 2-hydrazino derivative **3** (Scheme 3).

Also, the structure of **4** was chemically confirmed via its reactions with HNO<sub>2</sub>, which yielded 2-phenylamino-

Scheme 3



5,6,7,8-tetrahydrobenzo[*b*]thieno[2,3-*d*]pyrimidin-4(3*H*)-one **8**, as previously reported with similar compounds [20].



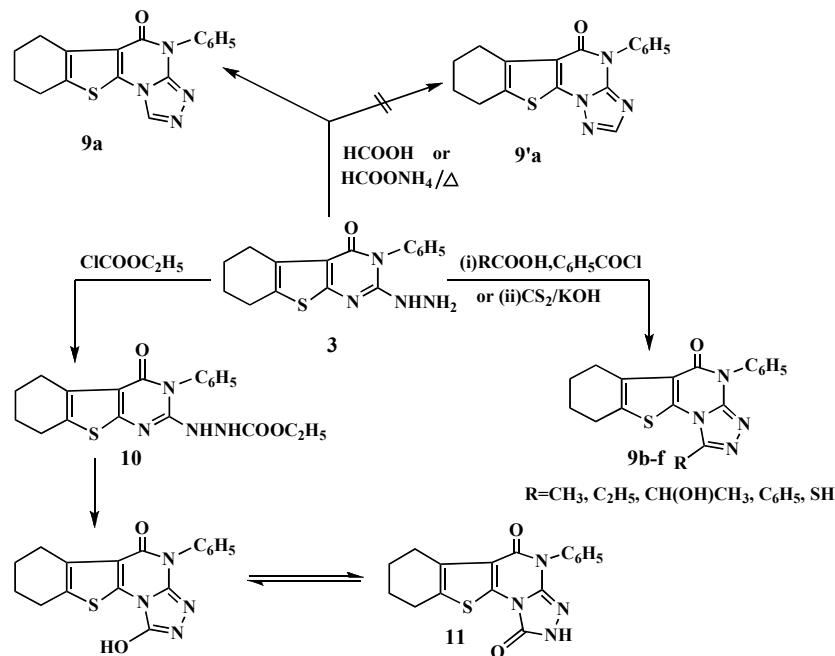
In continuation of our earlier work [21-24] on the cyclization reactions of heterocyclic hydrazines with different carbonyl compounds, it was of interest to investigate the susceptibility of 2-hydrazino-3-phenylthienopyrimidine **3** towards ring closure reactions with different reagents. Refluxing of **3** with triethyl orthoformate or with either formic acid or formamide afforded the same product 4-phenyl-6,7,8,9-tetrahydrobenzo[*b*]thieno[3,2-*e*]-1,2,4-triazolo[4,3-*a*]pyrimidin-5-one **9a**. It appears that when boiling formic acid or formamide is used for the cyclization of compound **3**, the [4,3-*a*]triazolo derivative **9a** does not undergo rearrangement to its [2,3-*a*] isomer **9a'** as previously reported [25,26]. Similarly the 2-hydrazino compound **3** was reacted with acetic acid or acetic anhydride, propionic acid, and lactic acid to give the corresponding 1-substituted triazolo[4,3-*a*]thienopyrimidine derivatives **9b-d**. While refluxing with benzoyl chloride afforded 1,4-diphenyl triazolo[4,3-*a*]thienopyrimidine **9e**. Further, the reaction with carbon disulfide in boiling alcoholic KOH gave 1-mercapto-4-phenyltriazolo [4,3-*a*]thienopyrimidine **9f**. The hydrazino compound **3** was also reacted with ethyl chloroformate to give 2-ethoxycarbonylhydrazino-4-phenylthienopyrimidine derivative **10**, which was cyclized to 4-phenyltriazolo-[4,3-*a*]thienopyrimidin-1,5-dione **11** on heating over its melting temperature (Scheme 4).

Treatment of the hydrazino derivative **3** with ethylisothiocyanate in boiling 1-butanol afforded the thiosemicarbazide derivative **12a**. Refluxing of **12a** in alcoholic KOH to prepare 1-ethylamino-1,2,4-triazolo[4,3-*a*]thienopyrimidine **13** as previously reported with similar systems [27], afforded an unexpected product in which aromatic

proton resonances were not observed in its NMR spectrum. On the basis of elemental analysis, IR, <sup>1</sup>H NMR

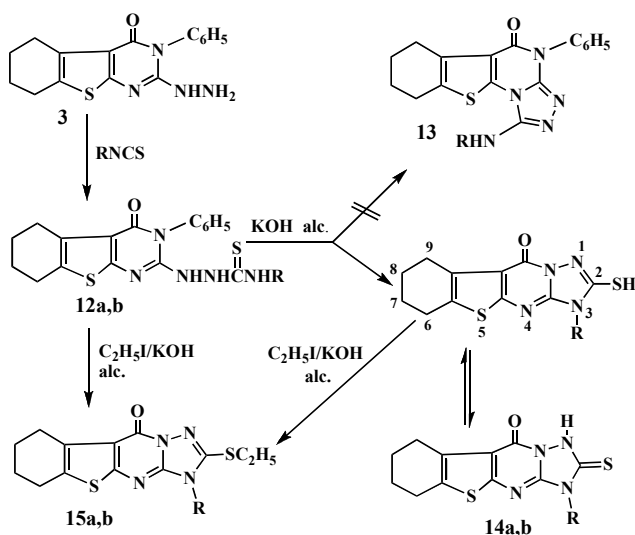
The formation of **14a,b** could be explained as shown in (Scheme 6).

Scheme 4



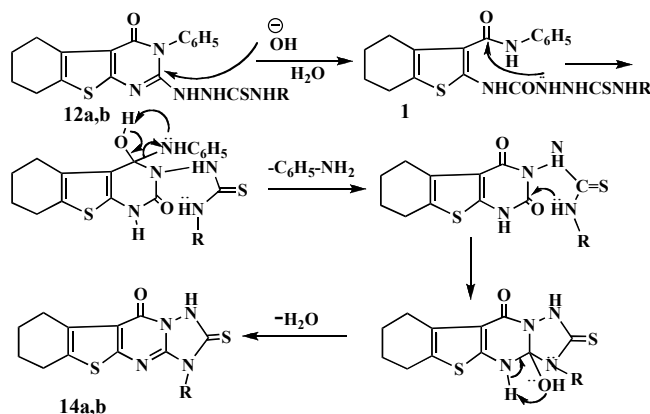
and mass spectra data, the reaction product was characterized as 3-ethyl-2-mercapto-1,2,4-triazolo-[1,5-*a*]-6,7,8,9-tetrahydrobenzo[*b*]thieno[2,3-*d*]pyrimidin-10-one (**14a**), similarly, treatment of **3** with phenylisothiocyanate afforded the corresponding thiosemicarbazide derivative **12b**, which on refluxing with alcoholic KOH afforded 2-mercapto-3-phenyl-1,2,4-triazolo[1,5-*a*]-6,7,8,9-tetrahydro[*b*]thieno[2,3-*d*]pyrimidin-10-one (**14b**) (Scheme 5).

Scheme 5



12,13,14,15,a;R=C<sub>2</sub>H<sub>5</sub>;b;R=C<sub>6</sub>H<sub>5</sub>

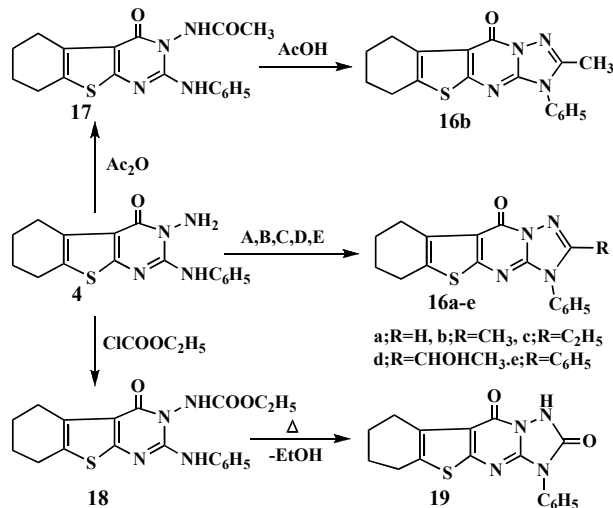
Scheme 6



On the other hand, refluxing of 3-amino-2-phenylamino-5,6,7,8-tetrahydrobenzo[*b*]thieno[2,3-*d*]pyrimidin-4-one (**4**) with triethyl orthoformate gave 3-phenyltriazolo[1,5-*a*]-6,7,8,9-tetrahydrobenzo[*b*]thieno[2,3-*d*]pyrimidin-10-one (**16a**). The same product was obtained on refluxing of **4** with formic acid or formamide. Further, refluxing of **4** with acetic acid and acetic anhydride afforded **16b** and **17** respectively. Refluxing of **17** in AcOH gave **16b** in good yield. Similarly, refluxing of **4** with propionic acid, lactic acid, benzoyl chloride gave the tetracyclic products **16c-e** respectively. While with ethyl chloroformate gave 3-ethoxycarbonylamino-2-phenylamino-5,6,7,8-

tetrahydro-benzo[*b*]thieno-[2,3-*d*]pyrimidin-4-one (**18**), which was cyclized to 3-phenyl-triazolo[1,5-*a*]-6,7,8,9-tetrahydrobenzo[*b*]thieno[2,3-*d*]pyrimidin-2,10-dione **19** on heating over its melting (Scheme 7).

Scheme 7



A;HC(OC<sub>2</sub>H<sub>5</sub>)<sub>3</sub>, HCOOH,HCONH<sub>2</sub>. B;CH<sub>3</sub>COOH, C,C<sub>2</sub>H<sub>5</sub>COOH.  
d;CH<sub>3</sub>CH(OH)COOH .E ;C<sub>6</sub>H<sub>5</sub>COCl.

## EXPERIMENTAL

**General.** Melting points were measured on a Gallen-Kamp melting point apparatus and are uncorrected. The ultraviolet spectra were recorded using UV-2011 PC, UV-Vis scanning spectrophotometer-shimadzu. The infrared spectra were recorded on IR-470, IR spectrophotometer-shimadzu-using KBr and CCl<sub>4</sub>. The <sup>1</sup>H-NMR spectra were recorded by either varian EM-390 (90 MHz) or by <sup>1</sup>H NMR LA 400 MHz (Jeol) Assiut University. Elemental analysis was carried out by Elemental analyzer system CmbH vario El at Assiut University. Ethyl acetate (EA), Benzene (B) mixture was used as an eleuent in tl chromatography.

**N-(3-Carboethoxy-4,5,6,7-tetrahydrobenzo[*b*]thien-2-yl-N'-phenylthiourea (1).** A mixture of 2-amino-3-carboethoxy-4,5,6,7-tetrahydrobenzo[*b*]thiophene (11.25 g 0.05 mol) and phenyl isothiocyanate (7 g, 0.052 mol) was refluxed 5 hours in ethanol (25 ml). A crude solid product formed while hot and was collected by filtration and recrystallized from ethanol. Yield 95%; mp 192°C (ethanol) (reported) 184-187°C [28].

**2,3-Disubstituted-5,6,7,8-tetrahydrobenzo[*b*]thieno[2,3-*d*]pyrimidin-4(3*H*)-ones (2-4).** A mixture of thiourea derivative **1** (10.8 g, 0.03 mmol) and excess of hydrazine hydrate in ethanol or 1-butanol was refluxed for about 10-50 hours. Separated solid product was collected by filtration, washed several times with KOH solution (2.5%), then with water and dried. The crude product was recrystallized from DMF several times to isolate **3** and **4** in pure state.

**2-Mercapto-3-phenyl-5,6,7,8-tetrahydrobenzo[*b*]thieno-[2,3-*d*]pyrimidin-4(3*H*)-one (2).** Was obtained by neutralization of the reaction filtrate with dilute iced HCl then collection by filtration and recrystallized from ethanol. Mp. 330°C (reported)

315°C [29]; R<sub>f</sub> 0.83 (EA/B 3:7).

**2-Hydrazino-3-phenyl-5,6,7,8-tetrahydrobenzo[*b*]thieno-[2,3-*d*]pyrimidin-4(3*H*)-one (3).** Mp. 250°C (DMF), (reported) 250°C [30] (benzene). R<sub>f</sub> 0.37 (EA/B 3:7). IR (KBr) ν 3200 (NH<sub>2</sub>, NH), 2920-2810 (C-H aliphatic), 1660 (C=O), 1535 (C = N) cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 1.85 (m, 4H, H<sub>6</sub>, H<sub>7</sub>), 2.85 (m, 4H, H<sub>5</sub>, H<sub>8</sub>), 3.85 (s, 2H, NH<sub>2</sub>), 5.55 (s, 1H, NH exchangeable by deuteration), 7.40 (m, 5H, C<sub>6</sub>H<sub>5</sub>) ppm. MS m/z (%) [M<sup>+</sup>, 312 (100)], 296 (0.7), 281 (33.1). Elemental analysis for C<sub>16</sub>H<sub>16</sub>N<sub>4</sub>OS (312), calcd: C; 61.52, H; 5.16, N; 17.93, S; 10.26. Found: C; 61.42, H; 5.38, N; 17.74, S; 10.12.

**3-Amino-2-phenylamino-5,6,7,8-tetrahydrobenzo[*b*]thieno-[2,3-*d*]pyrimidin-4(3*H*)-one (4).** Mp 197°C (ethanol) (reported) 205-208 °C [16] ,230-32 °C [17] , 227-29 °C [31] . R<sub>f</sub> 0.57 (EA/B 3:7). IR (KBr)/ν 3300-3200 (NH), 2920-2840 (C-H aliphatic), 1650 (C=O) cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.77 (m, 4H, H<sub>6</sub>, H<sub>7</sub>), 2.48 (m, 2H, H<sub>5</sub>), 2.74 (m, 2H, H<sub>8</sub>), 4.52 (s, 2H, NH<sub>2</sub> exchangeable by deuteration), 7.25 (m, 5H, C<sub>6</sub>H<sub>5</sub>), 8.43 (s, 1H, NH exchangeable by deuteration) ppm. Ms m/z (%) [M<sup>+</sup>, 312 (100%)]. Elemental analysis for C<sub>16</sub>H<sub>16</sub>N<sub>4</sub>OS (312), Calcd: C; 61.52, H; 5.16, N; 17.93, S; 10.26%. Found: C; 62.04, H; 4.59, N; 18.06, S; 10.28%.

**2-Ethylthio-3-phenyl-5,6,7,8-tetrahydrobenzo[*b*]thieno-[2,3-*d*]pyrimidin-4(3*H*)-one (5).** Compound **5** was obtained by refluxing **2** (0.3 g 0.001 mol) with ethyl iodide (excess) in 20 ml alcoholic KOH (3%) for 4 hours. The separated product was crystallized from ethanol. Yellowish crystals, mp 186°C (reported) 194°C [32]. <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 1.28 (t, 3H, CH<sub>3</sub>), 1.82 (m, 4H, H<sub>7</sub>, H<sub>8</sub>), 2.71 (m, 4H, H<sub>6</sub>, H<sub>9</sub>), 3.22 (q, 2H, -SCH<sub>2</sub>-), 7.23 (m, 5H, C<sub>6</sub>H<sub>5</sub>) ppm. R<sub>f</sub> 0.83 (EA/B 1:1). Elemental analysis for C<sub>18</sub>H<sub>18</sub>N<sub>4</sub>OS<sub>2</sub> (338): S; 18.75. Found S; 18.70).

**4-Phenyl-1,2,3,4-tetrazolo[1,5-*a*]-6,7,8,9-tetrahydrobenzo[*b*]thieno-[3,2-*e*]pyrimidin-5-one (6).** Stirring of **3** (1 g, 0.003 mol) with 50 ml acetic acid at 0°C, 3 ml saturated solution of NaNO<sub>2</sub> was added dropwise at 15 min. to the reaction mixture. Stirring was continued for about 3 hours, then the product was extracted using benzene which was evaporated under reduced pressure and crystallized from petroleum ether, mp 205°C; R<sub>f</sub> 0.72 (EA/B 1:1). The IR (KBr) spectra lacked the NHH<sub>2</sub> absorption at 3300-3100 cm<sup>-1</sup> and the azide absorption in the region 2200-2100 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.80 (m, 4H, H<sub>7</sub>, H<sub>8</sub>), 2.70 (s, 2H, H<sub>6</sub>), 2.85 (s, 2H, H<sub>9</sub>), 7.20 (m, 5H, aromatic protons) ppm. MS m/z (%) [M<sup>+</sup>, 323 (52)], 295 (76), 267 (100). Elemental analysis for C<sub>16</sub>H<sub>13</sub>N<sub>5</sub>OS (323), Calcd: C, 59.43 H; 4.05, N; 21.66, S; 9.92%. Found: C; 59.79, H; 4.51, N; 20.90, S; 9.67%.

**2-[3,5-Dimethylpyrazol-1-yl]-3-phenyl-5,6,7,8-tetrahydrobenzo[*b*]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (7).** 2-Hydrazino derivative **3** (1 g 0.003 mol) was refluxed in 10 ml acetylacetone for 7 hours. The excess acetylacetone was evaporated on a water bath. The separated product was crystallized from benzene-petroleum ether mixture, mp 156 °C. R<sub>f</sub> 0.76 (EA/B 3:7). UV: λ<sub>max</sub> 325.5, (1.254), 243.5 (1.246). <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 1.85 (m, 4H, H<sub>6</sub>, H<sub>7</sub>), two singlets at 2.00, 2.20 (6H, two CH<sub>3</sub> groups), 2.80 (s, 2H, H<sub>5</sub>), 3.00 (s, 2H, H<sub>8</sub>), 5.60, (s, 1H, CH), 7.25 (m, 5H, C<sub>6</sub>H<sub>5</sub>) ppm. MS m/z (%) [M<sup>+</sup>, 376 (85.3)]. Elemental analysis for C<sub>21</sub>H<sub>20</sub>N<sub>4</sub>OS (376), Calcd: C; 67.00, H; 5.35, N; 14.88, S; 8.52%. Found: C; 66.84, H; 5.60, N; 14.54, S; 8.24%.

**2-Phenylamino-5,6,7,8-tetrahydrobenzo[*b*]thieno[2,3-*d*]pyrimidin-4(3*H*)-one (8).** Using the same method as for the synthesis of compound **6**; mp 286°C from cyclohexane (reported) 284-286 °C [33]. R<sub>f</sub> 0.54 (EA/B 1:1). IR (KBr) ν

3350 (NH)  $\text{cm}^{-1}$ . MS  $m/z$  (%) [ $M^+$ , 297 (100)]. Elemental analysis for  $\text{C}_{16}\text{H}_{15}\text{N}_3\text{OS}$  (297), Calcd: C; 64.62, H; 5.08, N; 14.13, S; 10.78. Found: C; 64.40, H; 4.55, N; 14.01, S; 9.72%.

**1,4-Disubstituted-6,7,8,9-tetrahydrobenzo[b]thieno[3,2-*e*]-[1,2,4]triazolo[4,3-*a*]pyrimidin-5-ones (9a-d).** **General.** A mixture of **3** (1 g, 0.003 mol) with the appropriate acid, ethyl orthoformate, acetic anhydride, was refluxed for about 6-8 hours. A white ppt formed and was washed with iced ammonia. The crude product was crystallized from an ethanol-benzene mixture in 90-96% yield.

**9a.** Yield (90%); mp. 302 °C (reported) 298-300 °C [30]  $R_f$  0.83 (EA/B 6:4). IR (KBr)  $\nu$  1680 (C=O), 3030 (C-H aromatic), 2960-2940 (C-H aliphatic)  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  8.44 (s, 1H, triazole-H), 7.49 (m, 5H, aromatic-H), 2.90 (m, 4H,  $\text{H}_6$ ,  $\text{H}_9$ ), 1.88 (d, 4H,  $\text{H}_7$ ,  $\text{H}_8$ ). Elemental analysis for  $\text{C}_{17}\text{H}_{14}\text{N}_4\text{OS}$  (302), Calcd: C; 63.33, H; 4.38, N; 17.38, S; 9.95. Found: C; 63.60, H; 5.00, N; 17.55, S; 10.31.

**9b.** Yield (91%), mp 290 °C (reported) 290-92°C [30] .  $R_f$  0.53 (EA/B 6:4). IR (KBr)  $\nu$  1670 (C=O), 3030 (C-H aromatic), 2960-2940 (C-H aliphatic)  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  1.85 (m, 2H,  $\text{H}_7$ ), 1.91 (m, 2H,  $\text{H}_8$ ), 2.80 (m, 5H,  $\text{CH}_3$  and  $\text{H}_6$ ,  $\text{H}_9$ ), 3.00 (m, 2H,  $\text{H}_9$ ), 7.50 (m, 5H,  $\text{C}_6\text{H}_5$ ) ppm. Elemental analysis for  $\text{C}_{18}\text{H}_{16}\text{N}_4\text{OS}$  (336), Calcd: C; 64.26, H; 4.79, N; 16.65, S; 9.53%. Found: C; 64.07, H; 5.12, N; 16.76, S; 9.25%.

**9c.** Yield (92%) mp 275 °C (reported) 270-72°C [30],  $R_f$  0.51 (EA/B 6:4), IR (KBr)  $\nu$  1680 (C=O), 3030 (C-H aromatic), 2960-2940 (C-H aliphatic)  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR, ( $\text{CDCl}_3$ )  $\delta$  1.6 (t, 3H,  $\text{CH}_3$ ), 3.1 (q, 2H,  $\text{CH}_2$ ), 1.77 (m, 4H,  $\text{H}_7$ ,  $\text{H}_8$ ), 2.78 (m, 2H,  $\text{H}_6$ ), 2.85 (m, 2H,  $\text{H}_9$ ), 7.50 ppm (m, 5H,  $\text{C}_6\text{H}_5$ ); MS  $m/z$  (%) [ $M^+$ , 350 (65.7)]. Elemental analysis for  $\text{C}_{19}\text{H}_{18}\text{N}_4\text{OS}$  (350), Calcd: C; 65.12, H; 5.18, N; 15.99, S; 9.15%. Found: C; 65.04, H; 5.16, N; 15.82; H; 8.36%.

**9d.** Yield (96%), mp. 319°C,  $R_f$  0.43 (EA/B 6:4); IR (KBr)  $\nu$  1680 (C=O), 3300 (OH), 3030 (C-H aromatic), 2960-2940 (C-H aliphatic)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CHCl}_3$ )  $\delta$  1.6 (d, 3H,  $\text{CH}_3$ ), 5.1 (m, 1H, CH), 4.6 (br, 1H, OH), 1.77 (m, 4H  $\text{H}_7$ ,  $\text{H}_8$ ), 2.78 (m, 2H,  $\text{H}_6$ ), 2.85 (m, 2H,  $\text{H}_9$ ), 7.50 ppm (m, 5H,  $\text{C}_6\text{H}_5$ ) ; MS:  $m/z$  (%) [ $M^+$ , 366 (100)]. Elemental analysis for  $\text{C}_{19}\text{H}_{18}\text{N}_4\text{O}_2\text{S}$  (366), Calcd: C; 62.30, H; 4.96, N; 15.30, S; 8.74. Found: C; 61.94, H; 5.16, N; 14.96, S; 8.98.

**1,4-Diphenyl-1,2,4-triazolo[4,3-*a*]-6,7,8,9-tetrahydrobenzo[b]thieno[3,2-*e*]pyrimidin-5-one (9e).** A mixture of **3** (1 g, 0.003 mol) and benzoyl chloride (10 ml) was refluxed for 8 hours, filtered, cooled and poured into ammonia solution. The white precipitate thus formed was collected by filtration, washed with water, dried and recrystallized from benzene to give **9e** in 81% yield. Mp 338°C (reported) 242-44°C [30],  $R_f$  0.25 (EA/B 1:1)  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  1.85 (m, 2H,  $\text{H}_7$ ), 1.91 (m, 2H,  $\text{H}_8$ ), 2.80 (m, 2H,  $\text{CH}_2$ ,  $\text{H}_6$ ), 3.00 (m, 2H,  $\text{H}_9$ ), 7.30 (m, 10H, 2  $\text{C}_6\text{H}_5$ ) ppm. MS  $m/z$  (%) [ $M^+$ , 398 (12)]. Elemental analysis for  $\text{C}_{23}\text{H}_{18}\text{N}_4\text{OS}$  (398), Calcd: C; 69.32, H; 4.55, N; 14.06, S; 8.05%. Found: C; 68.82, H; 5.03, N; 14.05, S, 8.18%.

**1-Mercapto-4-phenyl-1,2,4-triazolo[4,3-*a*]-6,7,8,9-tetrahydrobenzo[b]thieno[3,2-*e*]pyrimidin-5-one (9f).** To a solution of **3** (1 g, 0.003 mmol) in 10 ml (3%) alcoholic KOH,  $\text{CS}_2$  (1.5 ml) was added. The mixture was refluxed for 16 hours. The precipitate formed on acidification with dilute HCl was collected and crystallized from ethanol in 68% yield. mp. 360°C (reported) 342-44 °C [30],  $R_f$  0.83 (EA/B 1:1). IR (KBr)  $\nu$  3300 (NH), 3090 (C-H aromatic), 2920-2850 (C-H aliphatic), 1680 (C=O)  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{DMSO}-d_6$ )  $\delta$  1.77 (m, 4H,  $\text{H}_7$ ,  $\text{H}_8$ ), 2.78 (m, 2H,  $\text{H}_6$ ), 2.85 (m, 2H,  $\text{H}_9$ ), 7.50 (m, 5H,  $\text{C}_6\text{H}_5$ ), 3.97 (s, 1H,

NH) ppm. MS  $m/z$  [ $M^+$ , 354 (100)], 326 (31.9), 321 (14.8), 296 (57.8). Elemental analysis for  $\text{C}_{17}\text{H}_{14}\text{N}_4\text{OS}_2$  (354), calcd: C; 57.61, H; 3.98, N; 15.81, S; 18.09. Found: C; 57.56, H; 4.40, N; 15.90, S; 18.33.

**2-Ethoxycarbonylhydrazino-4-phenyl-5,6,7,8-tetrahydrobenzo[b]thieno[2,3-*d*]pyrimidin-4(3H)-one (10) and 4-phenyl-6,7,8,9-tetrahydrobenzo[b]thieno[3,2-*e*]-1,2,4-triazolo[4,3-*a*]pyrimidin-1,5-dione (11).** A mixture of **3** (1 g, 0.003 mol) with ethyl chloroformate (10 mol) was refluxed for 12 hours and/or in the presence of anhydrous  $\text{K}_2\text{CO}_3$ . The excess of ester removed by evaporation on water bath, after cooling the solid crude product obtained washed with ammonia solution, then with water and crystallized from ethanol to give the uncyclized product **10**. The cyclized product **11** was obtained by heating **10** over its melting point for 5 min and crystallized from ethanol.

**10.** Yield 84%, mp 190°C (ethanol),  $R_f$  0.52 (EA/B 4:6). IR (KBr) $\nu$ , 3300 (NH), 3090 (C-H aromatic), 2910, 2820(C-H aliphatic), 1725 (C=O of ester), 1680 (C=O)  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  1.18 (t, 3H,  $\text{CH}_3$ ), 1.64 (m, 4H,  $\text{H}_6$ ,  $\text{H}_7$ ), 2.60 (m, 4H,  $\text{H}_5$ ,  $\text{H}_8$ ), 4.2 (q, 2H,  $\text{CH}_2$ ), 7.20 (m, 5H,  $\text{C}_6\text{H}_5$ ), 7.8, 9.1 (d, 2H, NH) ppm. MS  $m/z$  (%) [ $M^+$ , 384 (23.6)], 383 (100), 356 (6.0), 338 (35.1). Elemental analysis for  $\text{C}_{19}\text{H}_{20}\text{N}_4\text{O}_3\text{S}$  (384), Calcd: C; 59.36, H; 5.24, N; 14.57, S; 8.34(%). Found: C; 60.01, H; 5.17, N; 14.82, S; 7.91(%).

**11.** Yield 76%, mp 360°C (ethanol) (reported) 282-84°C [30],  $R_f$  0.76 (EA/B 4:6). IR (KBr)  $\nu$  lacked the C=O at 1725  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{DMSO}-d_6$ )  $\delta$  1.70 (m, 4H,  $\text{H}_6$ ,  $\text{H}_7$ ), 2.68 (s, 2H,  $\text{H}_5$ ), 2.78 (s, 2H,  $\text{H}_8$ ), 7.50 (m, 5H,  $\text{C}_6\text{H}_5$ ), 12.1 (s, 1H, NH) ppm. MS  $m/z$  (%) [ $M^+$ , 338 (100)].

**3-Alkyl-2-mercapto/ethylthio-1,2,4-triazolo[1,5-*a*]-6,7,8,9-tetrahydrobenzo[b]thieno[2,3-*d*]pyrimidin-10-one (14a,b, 15a,b).** **General.** Refluxing of the thiourea derivatives **12a,b** (0.01 mol) in (50 ml) alcoholic KOH (3%) for 7 hours followed by acidification by HCl afforded the corresponding **14a,b**. Refluxing of **12a,b** with alcoholic KOH in the presence of ethyl iodide for about 7-9 hours gave **15a,b**. Treatment of **14a,b** with ethyl iodide in alcoholic KOH afforded **15a,b**.

**14a.** Yield 81%, mp 336°C. IR (KBr)  $\nu$  3300 (NH)  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  1.18 (t, 3H,  $\text{CH}_3$ ), 1.64 (m, 4H,  $\text{H}_6$ ,  $\text{H}_7$ ), 2.60 (m, 4H,  $\text{H}_5$ ,  $\text{H}_8$ ), 4.2 (q, 2H,  $\text{CH}_2$ ), 12.1(s, 1H, NH) ppm, MS  $m/z$  (%) [ $M^+$ , 306 (60.4)], 290 (100), 262 (56.5). Elemental analysis for  $\text{C}_{13}\text{H}_{14}\text{N}_4\text{OS}_2$  (306), Calcd: C; 50.96, H; 4.61, N; 18.29, S; 20.93(%). Found: C; 51.56, H; 5.21, N; 18.20, S; 20.70(%).

**14b.** Yield 77%, mp 354°C (reported) 294-96°C [31]. IR (KBr)  $\nu$  3370 (NH), 3100 (C-H aromatic), 2950, 2870 (C-H aliphatic), 1690 (C=O)  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  1.80 (m, 4H,  $\text{H}_7$ ,  $\text{H}_8$ ), 2.70 (m, 2H,  $\text{H}_6$ ), 2.85 (m, 2H,  $\text{H}_9$ ), 7.20 (m, 5H,  $\text{C}_6\text{H}_5$ ), 12.2 (s, 1H, NH) ppm. MS  $m/z$  (%) [ $M^+$ , 354 (100)], 325 (35.50), 296 (65). Elemental analysis for  $\text{C}_{17}\text{H}_{14}\text{N}_4\text{OS}_2$  (354), Calcd: C; 57.61, H; 3.98, N; 15.81, S; 18.09%. Found: C; 57.53, H; 4.58, N; 15.92, S; 17.50%.

**15a.** Yield 72% mp 208°C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  1.24 (t, 3H,  $\text{CH}_3$ ), 1.31 (t, 3H,  $\text{CH}_3$ ), 1.77 (m, 4H,  $\text{H}_7$ ,  $\text{H}_8$ ), 2.76 (m, 4H,  $\text{H}_6$ ,  $\text{H}_9$ ), 3.73 (q, 2H,  $\text{CH}_2\text{S}$ ), 4.14 (q, 2H,  $\text{CH}_2\text{N}$ ) ppm. MS  $m/z$  (%) [ $M^+$ , 334 (100%)], 306 (64). Elemental analysis for  $\text{C}_{15}\text{H}_{18}\text{N}_4\text{OS}_2$  (334), Calcd: C; 53.87, H; 5.42, N; 16.75, S; 19.17%; Found: C; 54.34, H; 4.88, N; 15.54, S; 18.45%.

**15b.** Yield 76% mp 202°C, IR (KBr)  $\nu$  3370 (NH), 3050 (C-H aromatic) 2920, 2820 (C-H aliphatic), 1670 (C=O)  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR  $\delta$  1.28 (t, 3H,  $\text{CH}_3$ ), 1.8 (m, 4H,  $\text{H}_7$ ,  $\text{H}_8$ ), 2.7 (m, 4H,  $\text{H}_6$ ,  $\text{H}_9$ ), 3.0 (q, 2H,  $-\text{CH}_2\text{S}-$ ), 7.5 (m, 5H,  $\text{C}_6\text{H}_5$ ). MS  $m/z$  (%) [ $M^+$ , 382 (100)]. Elemental analysis for  $\text{C}_{19}\text{H}_{18}\text{N}_4\text{OS}_2$  (382), Calcd: C;

59.66, H; 4.74, N; 14.65, S; 16.77%. Found: C; 59.52, H; 5.30, N; 13.97, S; 16.59%.

**3-Phenyl-2-substituted-1,2,4-triazolo[1,5-a]-6,7,8,9-tetrahydrobenzo[b]thieno[2,3-d]pyrimidin-10-ones (16a-e).** A mixture of **4** (1 g, 0.003 mol) and triethyl orthoformate, appropriate aliphatic acid, benzoyl chloride and/or ethyl chloroformate (15 ml) was refluxed for 8 hours. The product thus formed by cooling was collected by filtration, washed with ammonia, then with water several times and recrystallized from ethanol-benzene mixture to give the compounds **16a-e** in variant yields.

**16a.** Yield 97%, mp 241°C (reported) 242-44 °C [16], 254-56°C [17]. IR (KBr)  $\nu$  3050 (C-H aromatic), 2920-2820 (C-H aliphatic), 1680 (C=O), 1570 (C=N), lacked the NH<sub>2</sub> bands at 3400-3100 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  1.74 (m, 4H, H<sub>7</sub>, H<sub>8</sub>), 2.58 (s, 2H, H<sub>9</sub>), 2.80 (s, 2H, H<sub>6</sub>), 7.24 (m, 5H, C<sub>6</sub>H<sub>5</sub>), 9.05 (s, 1H, CH: triazole ring) ppm; MS m/z (%) [M<sup>+</sup>, 322 (100)]. Elemental analysis for C<sub>17</sub>H<sub>14</sub>N<sub>4</sub>O (322), Calcd: C; 63.33, H; 4.38, N; 17.38, S; 9.95%. Found: C; 63.60, H; 4.07, N; 17.50, S; 9.31%.

**16b.** Yield 88%, mp 230°C (reported) 279-80°C [17,31]. IR (KBr)  $\nu$  lacked any bands at 3400-3100 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  1.85 (m, 4H, H<sub>7</sub>, H<sub>8</sub>), 2.42 (s, 3H, CH<sub>3</sub>), 2.67 (m, 2H, H<sub>6</sub>), 3.00 (m, 2H, H<sub>9</sub>), 7.53 (m, 5H, C<sub>6</sub>H<sub>5</sub>) ppm. MS m/z (%) [M<sup>+</sup>, 336 (63)]. Elemental analysis for C<sub>18</sub>H<sub>16</sub>N<sub>4</sub>O (336), Calcd: C; 64.26, H; 4.79, N; 16.65, S; 9.53%. Found: C; 64.88, H; 4.31, N; 16.79, S; 9.32%.

**16c.** Yield 91%, mp 242°C; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  1.6 (t, 3H, CH<sub>3</sub>), 3.1 (q, 2H, CH<sub>2</sub>) 1.77 (m, 4H, H<sub>7</sub>, H<sub>8</sub>), 2.78 (m, 2H, H<sub>6</sub>), 2.85 (m, 2H, H<sub>9</sub>), 7.50 ppm (m, 5H, C<sub>6</sub>H<sub>5</sub>); MS m/z (%) [M<sup>+</sup>, 350 (100)]. Elemental analysis for C<sub>19</sub>H<sub>18</sub>N<sub>4</sub>O (350), Calcd: C; 65.12, H; 5.18, N; 15.99, S; 9.15%. Found: C; 64.95, H; 5.90, N; 16.04, S; 9.00%.

**16d.** Yield 92%, mp 262°C; <sup>1</sup>H NMR (CHCl<sub>3</sub>)  $\delta$  1.6 (d, 3H, CH<sub>3</sub>), 1.77 (m, 4H, H<sub>7</sub>, H<sub>8</sub>), 2.78 (m, 2H, H<sub>6</sub>), 2.85 (m, 2H, H<sub>9</sub>), 5.1 (m, 1H, CH), 4.6 (br, 1H, OH), 7.50 ppm (m, 5H, C<sub>6</sub>H<sub>5</sub>); MS m/z (%) [M<sup>+</sup>, 66 (100)]. Elemental analysis for C<sub>19</sub>H<sub>18</sub>N<sub>4</sub>O<sub>2</sub>S (366), calcd: C; 62.28, H; 4.95, N; 15.29, S; 8.75%. Found: C; 61.88, H; 5.36, N; 15.07, S; 8.72%.

**16e.** Yield 87%, mp 342°C (reported) >300 °C [31]. <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  1.85 (m, 2H, H<sub>7</sub>), 1.91 (m, 2H, H<sub>8</sub>), 2.80 (m, 2H, H<sub>6</sub>), 3.00 (m, 2H, H<sub>9</sub>), 7.50 (m, 10H, 2C<sub>6</sub>H<sub>5</sub>) pp. MS m/z (%) [M<sup>+</sup>, 98 (100)]. Elemental analysis for C<sub>23</sub>H<sub>18</sub>N<sub>4</sub>O (398), Calcd: C; 69.32, H; 4.55, N; 14.06, S; 8.05%. Found: C; 68.82, H; 5.03, N; 14.06, S; 8.18%.

**3-Acetylamino-2-phenylamino-5,6,7,8-tetrahydrobenzo[b]thieno[2,3-d]pyrimidin-4(3H)-one(17).** 3-Amino derivative **4** (1 g 0.003 mol) was refluxed in acetic anhydride (10 ml) for 8 hours, cooled, the ppt formed poured into iced ammonia solution, filtered and crystallized from ethanol/benzene to give **17** in 97% yield, mp 252°C. IR (KBr)  $\nu$  3300 (NH), 2900, 2850 (C-H aliphatic) 1685 (C=O), 1665 (CONH) cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  1.73 (m, 4H, H<sub>7</sub>, H<sub>8</sub>), 2.14 (s, 3H, CH<sub>3</sub>), 2.59 (m, 2H, H<sub>9</sub>), 2.77 (m, 2H, H<sub>6</sub>), 7.27 (m, 5H, C<sub>6</sub>H<sub>5</sub>), 8.74, 10.35 (s, 2NH) ppm. Elemental analysis for C<sub>18</sub>H<sub>18</sub>N<sub>4</sub>O<sub>2</sub>S (354), Calcd: C; 61.02, H; 5.08, N; 15.82, S; 9.04%. Found: C; 60.90, H; 5.26, N; 15.53, S; 8.86%.

**3-Ethoxycarbonylamino-2-phenylamino-5,6,7,8-tetrahydrobenzo[b]thieno[2,3-d]pyrimidin-4(3H)-4-one (18) and 3-phenyltriazolo[1,5-a]-6,7,8,9-tetrahydrobenzo[b]thieno[2,3-d]pyrimidin-2,10-dione (19).**

**Method A.** **4** (1 g, 0.003 mol) was allowed to reflux in ethyl chloroformate (15 ml) for 2 hours, cooled, the solid collected by

filtration, washed with ethanol and recrystallized from ethanol as a colorless crystals of **18** in 93.2% yield.

**Method B.** A mixture of **4** (1 g 0.003 mole) and ethyl chloroformate (5 ml) in dry acetone (20 ml) in the presence of anhydrous K<sub>2</sub>CO<sub>3</sub> was refluxed for 3 hours on water bath, filtered, the solvent evaporated on water bath, compound **18** filtered and crystallized from ethanol in 87% yield. Heating of **18** over its mp for 5 minutes gave **19** in high yield.

**18.** mp 222°C (ethanol), IR (KBr)  $\nu$  3310 (NH), 1725, 1660 (2 C=O). <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  1.20 (t, 3H, CH<sub>3</sub>), 1.74 (m, 4H, H<sub>6</sub>, H<sub>7</sub>), 2.59 (m, 2H, H<sub>5</sub>), 2.80 (m, 2H, H<sub>8</sub>), 4.19 (q, 2H, CH<sub>2</sub>), 7.35 (m, 5H, C<sub>6</sub>H<sub>5</sub>), 8.10 (s, 1H, NH), 9.420 (s, 1H, NH) ppm. MS m/z (%) [M<sup>+</sup>, 384 (100)]. Elemental analysis of C<sub>19</sub>H<sub>20</sub>N<sub>4</sub>O<sub>3</sub>S (384), Calcd: C; 59.36, H; 5.24, N; 14.57, S; 8.34%. Found: C; 59.98, H; 4.81, N; 15.06, S; 8.59%.

**19.** mp over 360°C. IR (KBr)  $\nu$  3300 (NH), 1750 (C=O) of triazole ring, 1670 (C=O) cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  1.74 (m, 4H, H<sub>6</sub>, H<sub>7</sub>), 2.59 (m, 2H, H<sub>5</sub>), 2.80 (m, 2H, H<sub>8</sub>), 7.35 (m, 5H, C<sub>6</sub>H<sub>5</sub>), 8.22 (s, 1H, NH) ppm MS m/z (%) [M<sup>+</sup>, 338 (100)]. Elemental analysis for C<sub>17</sub>H<sub>14</sub> N<sub>4</sub>O<sub>2</sub>S (338), Calcd: C; 60.34, H; 4.17, N; 16.56, S; 9.48. Found: C; 60.79, H; 4.23, N; 17.19, S; 9.86.

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