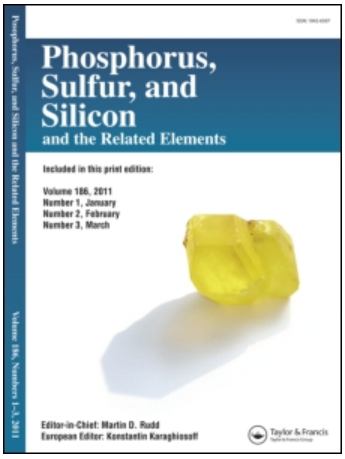

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SYNTHESIS OF SOME NEW PYRAZOLOPYRIDINES, PYRAZOLOTHIENOPYRIDINES, PYRAZOLOPYRIDOTHIENOPYRIMIDINES AND PYRAZOLOPYRIDOTHIENOTRIAZINES

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Pyrazolo[3,4-b]pyridine derivative ***3a*** *was prepared and reacted with methyl iodide to give* ***4*** *or* ***5*** *depending on reaction conditions. Oxidation of* ***3a*** *with iodine produced the corresponding disulphide derivative* ***6****, whereas oxidation with* $KMnO_4$ *gave the corresponding oxo derivative* ***7****. Oxidation of* ***4*** *afforded the corresponding sulphone derivative* ***8****, which on boiling in NaOH solution gave* ***7****. The reaction of compound* ***3a*** *with chloroacetonitrile, ethyl chloroacetate, phenacyl bromide, and chloroacetanilide afforded* ***9a,b****,* ***11****, and* ***12*** *respectively. Cyclication of the products* ***9a,b****,* ***11****, and* ***12*** *yielded* ***10a,b****,* ***13****, and* ***14*** *respectively. The reaction of compound* ***14*** *with ethyl orthoformate, nitrous acid, acetic anhydride, benzaldehyde, urea,* CS_2*, and phenyl isothiocyanate afforded compounds* ***15–21*** *respectively.*

Keywords: Pyrazolopyridines; pyrazolopyridothienopyrimidines; pyrazolopyridothienotriazines; pyrazolothienopyridines

It has been reported that thieno[2,3-b]pyridine[1–3] derivatives possess good antibacterial,[4–6] antihypertensive,[7] and gonadotropin-releasing hormone antagonizing activity.[8,9] Pyridothienopyrimidine derivatives have been used as analgesics,[10] antipyritics,[11] and antiinflammatories.[12] Also, some pyridothienotriazines exhibit antianaphylactic[13] and antiallergic[14] activity. This prompted us to synthesize the title compounds searching for better pharmacological and biological properties.

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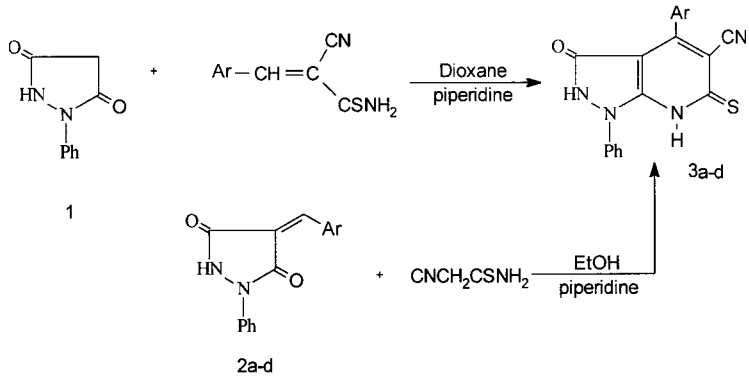
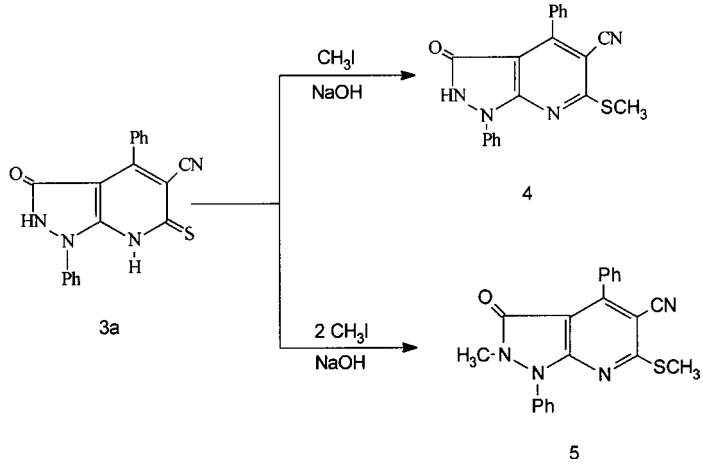
RESULTS AND DISCUSSION

4-Aryl-5-cyano-6-mercapto-3-oxo-1-phenyl-1,2,3-trihydropyrazolo[3,4-b]-pyridines **3a–d** were synthesized from the reaction of compound **1**[15] with arylidenecyanothioacetamide or by the reaction of 4-arylidene-1-phenyl-3,5-pyrazolidinediones **2a–d**[16] with cyanothioacetamide.



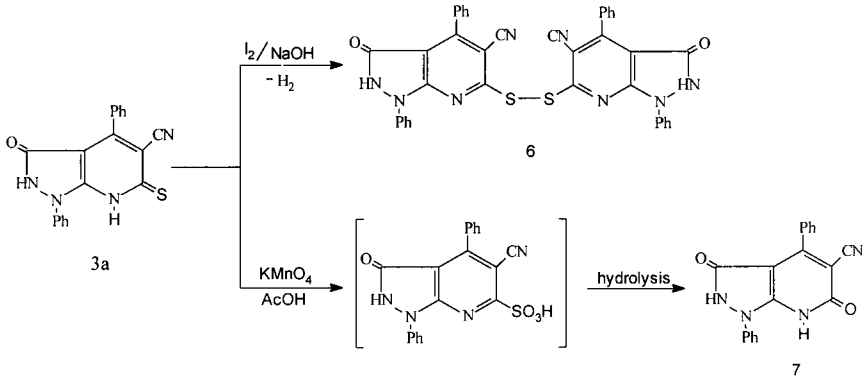
SCHEME 1 Ar; a, Ph; b, *p* chlorophenyl; c, *p* flourophenyl; d, Thienyl.

Methylation of compound **3a** with methyl iodide (1:1 molar ratio) in an alkaline medium afforded 5-cyano-1,4-diphenyl-6-methylthio-3-oxo-1,2,3-trihydropyrazolo[3,4-b]pyridine (**4**), but when the reaction is carried out using 2 mmol of methyl iodide (1:2 molar ratio), the product is identified as 5-cyano-1,4-diphenyl-2-methyl-6-methylthio-3-oxo-1,2,3-trihydropyrazolo[3,4-b]pyridine (**5**).



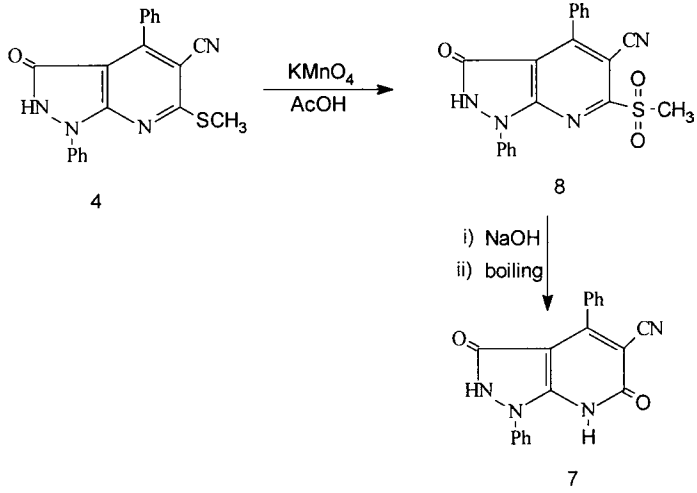
SCHEME 2

Oxidation of compound **3a** with iodine in an alkaline medium gave the corresponding disulphide derivative **6**, whereas oxidation with potassium permanganate in an acidic medium afforded 5-cyano-1,4-diphenyl-3,6-dioxo-1,2,3-trihydropyrazolo[3,4-b]pyridine (**7**).



SCHEME 3

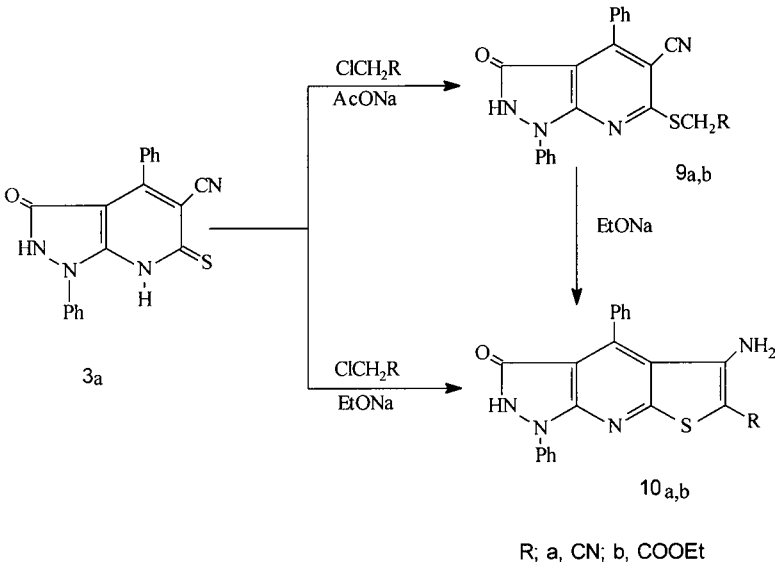
Oxidation of compound **4** with potassium permanganate in an acidic medium afforded the corresponding sulphone derivative **8**, which on hydrolysis with 10% sodium hydroxide solution afforded a compound identical in all respects with compound **7**.



SCHEME 4

Compound **3a** was used as starting material for the synthesis of thienopyridines. Thus, the reaction of compound **3a** with

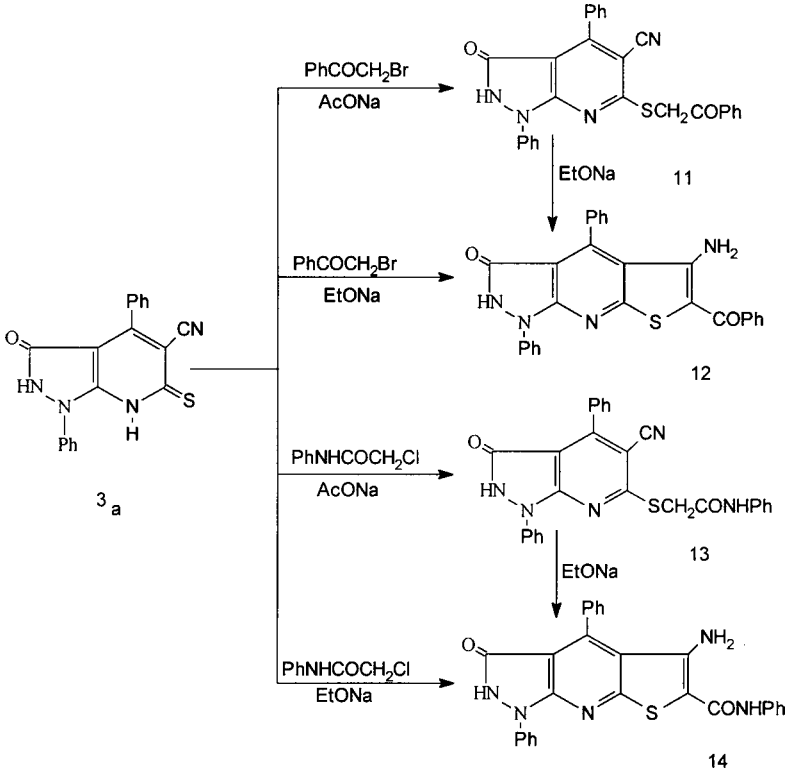
chloroacetonitrile or ethyl chloroacetate in ethanol containing sodium acetate, gave the corresponding 2-(5-cyano-3-oxo-1,4-diphenyl-1,2,3-trihydropyrazolo[3,4-b]pyridin-6-ylthio)acetonitrile (**9a**) and ethyl[5-cyano-3-oxo-1,4-diphenyl-1,2,3-trihydropyrazolo[3,4-b]pyridin-6-ylthio]acetate (**10a**). On refluxing of these compounds in ethanol in the presence of catalytic amount of sodium ethoxide, they underwent intramolecular Thorpe-Ziegler cyclization to furnish the corresponding 5-amino-6-cyano-3-oxo-1,4-diphenyl-1,2,3-trihydropyrazolo[3,4-b]thieno[3,2-e]pyridine (**9b**) and 5-amino-6-carbethoxy-1,4-diphenyl-3-oxo-1,2,3-trihydropyrazolo[3,4-b]thieno[3,2-e]pyridine (**10b**). The latter compounds also were synthesized via direct interaction of compound **3a** with the appropriate chloro compound in the presence of sodium ethoxide.



SCHEME 5

Similarly, the pyrazolopyridine derivative **3a** reacted with phenacyl bromide or N-chloroacetanilide in presence of sodium acetate to give 5-cyano-1,4-diphenyl-3-oxo-6-phenacylthio)-1,2,3-trihydropyrazolo[3,4-b]pyridine (**11**) and 5-cyano-1,4-diphenyl-3-oxo-6-acetanilidethio-1,2,3-trihydropyrazolo[3,4-b]pyridine (**13**) respectively. When the above reaction was carried out using sodium ethoxide, 5-amino-1,4-diphenyl-3-oxo-6-benzoyl-1,2,3-trihydropyrazolo[3,4-b]thieno[3,2-e]-pyridine (**12**), and 5-amino-1,4-diphenyl-3-oxo-6-phenylcarbamoyl-1,2,3-trihydro-pyrazolo[3,4-b]-thieno[3,2-e]pyridine (**14**) were

produced respectively. The latter compounds were obtained also upon refluxing of compounds **11** and **13** with sodium ethoxide in ethanol.

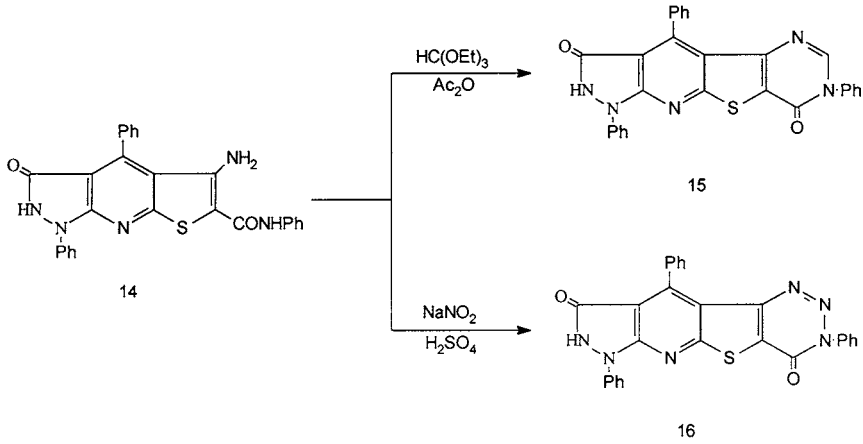


SCHEME 6

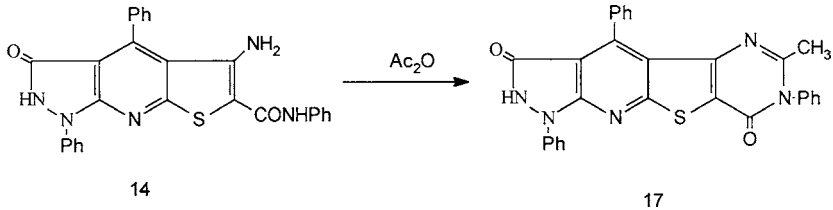
The cyclocondensation of compound **14** with ethyl orthoformate by refluxing in acetic anhydride led to 1,4,7-triphenyl-2,3,7,8-tetrahydro-1H-pyrazolo-[4″,3″:-5′,6′]pyrido[3′,2′:4,5]thieno[3,2-d]pyrimidine-3,8-dione **15**. 3,7,10-Triphenyl-4,7,8,9-tetrahydro-3H-pyrazolo-[4″,3″:5′,6′]pyrido[3′,2′:4,5]thieno[3,2-d] [1,2,3]triazine 4,9-dione **16** was obtained upon treatment of compound **14** with nitrous acid.

When compond **14** was refluxed in acetic anhydride, 6-methyl-1,4,7-triphenyl-2,3,7,8-tetrahydro-1H-pyrazolo[4″,3″:5′,6′]pyrido[3′,2′:4,5]thieno[3,2-d]pyrimidine 3,8-dione (**17**) was obtained.

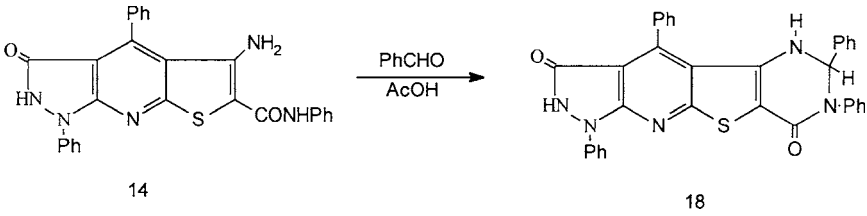
Treatment of compound **14** with benzaldehyde in boiling acetic acid afforded 1,4,6,7-tetraphenyl-2,3,5,6,7,8-hexahydro-1H-pyrazolo[4″,3″:5′,6′]pyrido[3′,2′:4,5] thieno[3,2-d]pyrimidine-3,8-dione (**18**).



SCHEME 7

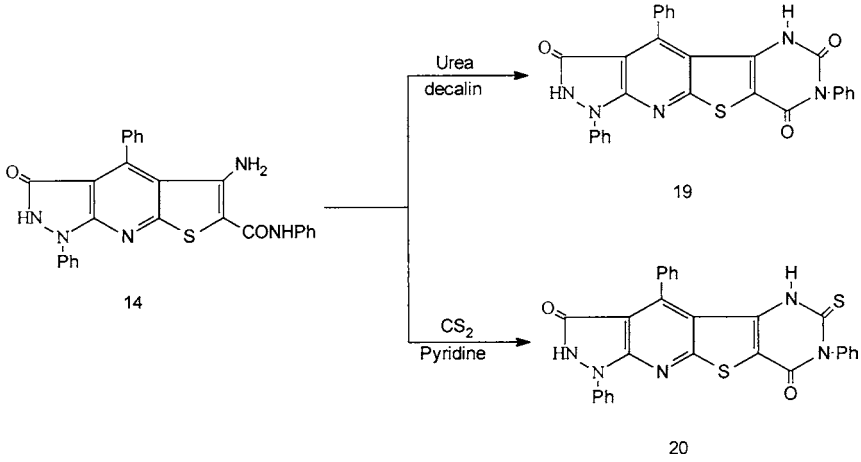


SCHEME 8



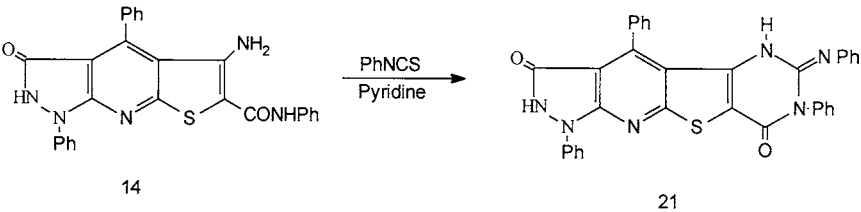
SCHEME 9

The reaction of compound **14** with urea in boiling decalin led to the formation of 1,4,7-triphenyl-2,3,5,6,7,8-hexahydro-1H-pyrazolo[4″,3″:5′,6′]pyrido[3′,2′:4,5]thieno[3,2-d]pyrimidine-3,6,8-trione (**19**). The thiono analogue 1,4,7-triphenyl-6-thioxo-2,3,5,6,7,8-hexahydro-1H-pyrazolo[4″,3″:5′,6′]pyrido[3′,2′:4,5]thieno-[3,2-d]pyrimidine-3,8-dione (**20**) was obtained by refluxing compound **14** with carbon disulfide in pyridine.



SCHEME 10

1,4,7-Triphenyl-6-aminophenyl-2,3,5,6,7,8-hexahydro-1H-pyrazolo-[4″,3″:5′,6′]pyrido[3′,2′:4,5]thieno[3,2-d]pyrimidine-3,8-dione (**21**) was obtained via the reaction of compound **14** with phenyl isothiocyanate in pyridine.



SCHEME 11

EXPERIMENTAL

All melting points were determined on a Koffler melting points apparatus and are uncorrected. IR spectra were obtained on a Nicolet 710 FT-IR spectrometer. H-NMR spectra were recorded on a Varian EM 360 at 60 MHz using TMS as an internal reference. Elemental analyses were carried out with an elemental analyzer model 240 C. Satisfactory microanalysis (C $\pm$ 0.4, H $\pm$ 0.4, N $\pm$ 0.3%) were obtained for all newly prepared compounds.

Synthesis of Compounds 3a–d

*Method A: From 1-phenyl-3,5-pyrazolidinedione (**1**):* A mixture of 1-phenyl-3,5-pyrazolidinedione **1** (0.01 mmol, 1.76 g), the appropriate arylidenecyanothioacetamide (0.01 mmol), and catalytic amount of piperidine was refluxed in dioxane (20 mL) for 2 h, the formed precipitate was recrystallized from appropriate solvent to give compounds **3a–d** (cf. Table I).

*Method B: From 4-arylidene-1-phenyl-3,5-pyrazolidinediones (**2a–d**):* A mixture of the appropriate arylidene derivative **2a–d** (0.01 mmol), cyanothioacetamide (0.01 mmol), and catalytic amount of piperidine was refluxed in ethanol (30 mL) for 2 h, the solid that formed was collected and recrystallized from appropriate solvent to give compounds **3a–d** (cf. Table I).

*Synthesis of 5-cyano-1,4-diphenyl-6-methylthio-3-oxo-1,2,3-trihydropyrazolo[3,4-b]pyridine (**4**):* A mixture of compound **3a** (0.005 mmol, 1.72 g) in ethanol (20 mL), methyl iodide (0.005 mmol, 0.15 mL), and sodium hydroxide solution (0.005 mmol, 0.2 g in 5 mL water) were added. The reaction mixture was stirred at room temperature for 2 h, the precipitate was collected, washed with water, and recrystallized from ethanol to give compound **4** (cf. Table I).

*Synthesis of 5-cyano-1,4-diphenyl-2-methyl-6-methylthio-3-oxo-1,2,3-trihydropyrazolo[3,4-b]pyridine (**5**):* A mixture of compound **3a** (0.005 mmol, 1.72 g) in ethanol (20 mL), methyl iodide (0.01 mmol, 0.3 mL), and sodium hydroxide solution (0.01 mmol, 0.4 g in 5 mL water) were added. The reaction mixture was stirred at room temperature for 2 h, the precipitate was collected, washed with water, and recrystallized from ethanol to give compound **5** (cf. Table I).

*Synthesis of (5-cyano-3-oxo-1,4-diphenyl-2,3-dihydro-1H-pyrazolo[3,4-b]-pyridin-6-ylthio)-3-oxo-1,4-diphenyl-2,3-dihydro-1H-pyrazolo[3,4-b]pyridine (**6**):* A solution of iodine (0.005 mmol, 0.32 g) in potassium iodide solution (0.005 mmol, 0.5 g in 2 mL water) was added to compound **3a** (0.005 mmol, 1.72 g) in 10% sodium hydroxide solution (20 mL) with stirring at room temperature for 2 h, the precipitate was collected and recrystallized from methanol to give compound **6** (cf. Table I).

*Synthesis of compounds 5-cyano-1,4-diphenyl-3,6-dioxo-1,2,3-trihydropyrazolo[3,4-b]pyridine (**7**) and 5-cyano-1,4-diphenyl-2,3-dihydro-6-methylsulfonyl-3-oxo-1H-pyrazolo[3,4-b]pyridine (**8**):* Potassium permanganate solution (0.008 mmol in 1.26 g, 2 mL water) was added dropwise to compound **3a** (0.005 mmol, 1.72 g) or **4** (0.005 mmol, 1.79 g) in acetic acid (20 mL) with stirring at room temperature for 2 h, the precipitate was collected and recrystallized from the appropriate solvent to give the products **7** and **8** respectively (cf. Table I).

TABLE I Charactarization Data of the Prepared Compounds

Comp No.	m.p. (°C) Crys. Solvent	Yield (%)	Mol. Form. (mol. wt.)	Analytical Data Cal./Found C	H	N	S	Spectral Data IR/^{1}H-NMR
3a	140 (Benzene + Ethanol)	84	$C_{19}H_{12}N_4OS$ (344.39)	66.26 66.49	3.51 3.34	16.27 16.19	9.31 9.55	IR: 3200 (NH), 2214 (CN), 1666 $(CO)_{amidic.}$ ^{1}H NMR 7.8–6.8 (m, 11H, 9H arom. + 2NH). MS: 343 ($M^+ - 1$, 0.8%); 265 (0.8%); 237 (0.8%); 196 (21%); 176 (1.5%); 77 (28.8%); 32 (100%); 28 (100%)
3b	160 Benzene	90	$C_{19}H_{11}ClN_4OS$ (378.83)	60.24 60.54	2.93 2.73	14.79 14.59	8.46 8.56	IR: 3220 (NH), 2220 (CN), 1676 $(CO)_{amidic}$. MS: 378.8 (M^+, 3.6%); 375.1 ($M^+ - 3$, 10.7%); 357 (20%); 328 (37%); 319 (52%); 257 (50%); 241 (71%); 215 (100%)
3c	195 Benzene	85	$C_{19}H_{11}FN_4OS$ (362.38)	62.98 62.88	3.06 3.26	15.46 15.62	8.58 8.48	IR: 3200 (NH), 2195 (CN), 1688 $(CO)_{amidic}$. MS: 360 ($M^+ - 2$, 5.7%); 341 (31%); 340 (100%); 322 (23%); 274 (17%); 257 (63%)
3d	130 Benzene	92	$C_{17}H_{10}N_4OS$ (350.41)	58.27 58.57	2.88 2.68	15.99 15.79	8.85 8.98	IR: 3180 (NH), 2224 (CN), 1659 $(CO)_{amidic}$. 350.4 (M^+, 3.6%); 328 (14%); 319 (39%); 302 (50%); 274 (80%); 265 (36%); 257 (100%); 241 (25%); 215 (38%)
4	120 Ethanol	86	$C_{20}H_{14}N_4OS$ (358.42)	67.02 67.32	3.94 3.78	15.63 15.83	8.94 8.74	IR: 3217 (NH), 3064 $(CH)_{arom.}$; 2920 $(CH)_{aliph.}$; 2216 (CN); 1687 $(CO)_{amidic}$
5	150 Methanol	78	$C_{21}H_{16}N_4OS$ (372.44)	67.72 67.90	4.33 4.53	15.04 15.26	8.61 8.41	IR: 3049 $(CH)_{arom.}$; 2930 $(CH)_{aliph.}$; 2212 (CN)
6	160 Benzene	94	$C_{38}H_{22}N_8O_2S_2$ (686.71)	66.46 66.26	3.23 3.55	16.32 16.12	9.34 9.59	IR: 3200 (NH); 3060 $(CH)_{arom.}$; 2224 (CN); 1686 $(CO)_{amidic}$
7	240 Methanol	95	$C_{19}H_{12}N_4O_2$ (328.33)	69.51 69.84	3.68 3.46	17.06 17.18	9.75 9.58	IR: 3432 (OH); 2218 (CN); 1679 $(CO)_{amidic}$
8	190 Ethanol	90	$C_{20}H_{14}N_4O_3S$ (390.41)	61.53 61.68	3.61 3.80	14.35 14.22	8.21 8.35	IR: 3220 (NH); 2218 (CN); 1687 $(CO)_{amidic.}$; 1315, 1160 (SO_2)

(Continued on next page)

TABLE I Charactarization Data of the Prepared Compounds *(Continued)*

Comp No.	m.p. (°C) Crys. Solvent	Yield (%)	Mol. Form. (mol. wt.)	Analytical Data Cal./Found C	H	N	S	Spectral Data IR/^{1}H-NMR
9a	120 Methanol	76	$C_{21}H_{13}N_5OS$ (383.43)	65.78 65.98	3.42 3.22	18.27 18.45	8.36 8.59	IR: 3217 (NH); 2191 (CN), 1411 (S-R). ^{1}H NMR 7.9–7.1 (m, 11H, arom + NH); 2.3 (s, 2H, CH_2)
9b	110 Ethanol	79	$C_{23}H_{18}N_4O_3S$ (430.48)	64.17 64.33	4.21 4.40	13.01 13.23	7.45 7.30	IR: 3330 (NH); 2213 (CN);1720 (CO)ester. ^{1}H NMR 7.9 (s, 1H, NH); 7.1–6.1 (m, 10H, arom.); 3.8–3.4 (m, 4H, $2CH_2$); 1.3–1.0 (t, 3H, CH_3)
10a	165 Pet. ether	80	$C_{21}H_{13}N_5OS$ (383.43)	65.78 65.93	3.42 3.22	18.27 18.40	8.36 8.56	IR: 3340–3220 (NH_2, NH); 2208 (CN), 1400 (S-R). ^{1}H NMR 7.2–6.4 (m, 11H, arom., + NH); 4.5–4.2 (br., 2H, NH_2)
10b	163 Benzene	84	$C_{23}H_{18}N_4O_3S$ (430.48)	64.17 64.40	4.21 4.00	13.01 13.23	7.45 7.30	IR: 3320–3430 IR: (NH_2); 1720 (CO)ester. ^{1}H NMR 7.8 (s, 1H, NH); 7.8–6.6 (m, 10 H, arom.); 6–5.8 (br., 2H, NH_2); 4.1–3.8 (q, 2H, CH_2); 1.2–0.9 (t, 3H, CH_3)
11	130 Ethanol	89	$C_{27}H_{18}N_4O_2S$ (462.52)	70.11 70.44	3.92 3.79	12.11 12.33	6.93 6.73	IR: 3235 (NH); 2218 (CN); 1690 $(CO)_{benzoyl}$. ^{1}H NMR 8.4–6.8 (m, 16H, arom. + NH); 3.2 (s, 2H, CH_2)
12	170 Pet. ether	90	$C_{27}H_{18}N_4O_2S$ (462.52)	70.11 70.37	3.92 3.80	12.11 12.37	6.93 6.77	IR: 3320–3180 (NH, NH_2); 1695 $(CO)_{benzoyl}$. ^{1}H NMR 7.6–6.4 (m, 16H, arom. + NH); 4.1–3.7 (br., 2H, NH_2)

13	110	77	$C_{27}H_{19}N_5O_2S$	67.91	4.01	14.67	6.71	IR: 3225 (NH); 3209 (NH); 2211 (CN); 1660
	Ethanol		(477.57)	67.76	3.87	14.89	6.92	$(CO)_{amidic}$. ^1H NMR 7.8–6.3 (m, 17H, arom. +2NH); 2.8 (s, 2H, CH_2)
14	180	92	$C_{27}H_{19}N_5O_2S$	67.91	4.01	14.67	6.71	IR: 3337–3180 (NH_2, NH); 1665 $(CO)_{amidic}$.
	Benzene		(477.57)	67.69	4.25	14.50	6.94	^1H NMR 8.2–7.6 (m, 17H, arom. + 2NH); 4.8–4.2 (br., 2H, NH_2)
15	122	89	$C_{28}H_{17}N_5O_2S$	68.98	3.51	14.36	6.58	IR: 3230 (NH); 3050 $(CH)_{arom.}$; 1676
	Methanol		(487.53)	68.78	3.61	14.24	6.50	$(CO)_{amidic}$
16	130	88	$C_{27}H_{16}N_6O_2S$	66.38	3.30	17.20	6.56	IR: 3150 (NH); 3045 $(CH)_{arom.}$; 1688 (CO);
	Ethanol		(488.52)	66.58	3.15	17.28	6.76	1667 $(CO)_{amidic}$
17	120	80	$C_{29}H_{19}N_5O_2S$	69.45	3.82	13.96	6.39	IR: 3230 (NH), 2933 $(CH)_{aliph.}$, 1712
	Ethanol		(501.56)	69.60	3.72	13.84	6.52	$(CO)_{diacetyl}$
18	285	92	$C_{34}H_{23}N_5O_2S$	72.20	4.10	12.38	5.67	IR: 3178 (NH), 3059 $(CH)_{arom.}$, 2867
	Dioxane		(565.65)	72.30	4.28	12.58	5.54	$(CH)_{aliph.}$, 1668 $(CO)_{amidic}$
19	270	85	$C_{28}H_{17}N_5O_3S$	66.79	3.40	13.90	6.37	IR: 3210 (NH), 1680 $(CO)_{amidic}$
	Dioxane		(503.53)	66.59	3.22	13.72	6.42	
20	140	87	$C_{28}H_{17}N_5O_2S$	64.73	3.30	13.48	6.17	IR: 3150 (NH); 3045 $(CH)_{arom.}$; 1688 (CO);
	Ethanol		(519.59)	64.95	3.38	13.66	6.37	1667 $(CO)_{amidic}$; 1150 (CS)
21	130	94	$C_{34}H_{22}N_6O_2S$	70.57	3.83	14.52	5.54	IR: 3338 (NH), 3200 (NH), 1681 $(CO)_{amidic}$.
	Ethanol		(578.65)	70.87	3.63	14.44	5.34	MS: 576.23($M^+ - 2$, 0.3 %); 487 (1.4 %); 432 (3.1%); 395 (10.3%); 344.6 (12.4%); 264 (31.7%); 176 (26.6%); 76.6 (100%); 28 (28.8%)

*Synthesis of compounds **9a**, **10a**, **11**, and **13** (General procedure):* A mixture of compound **3a** (0.005 mmol, 1.72 g), (0.005 mmol) from the appropriate chloro compound [chloroacetonitrile (0.31 mL), ethyl chloroacetate (0.54 mL), phenacyl bromide (0.93 g), or N-chloroacetanilide (0.85 g)] and sodium acetate (0.05 mmol, 0.41 g) in ethanol (20 mL) was refluxed for 2 h, the precipitate was collected, washed with water, and recrystallized from the appropriate solvent to give the compounds **9a**, **10a**, **11**, and **13** respectively (cf. Table I).

*Synthesis of compounds **9b**, **10b**, **12**, and **14** (General procedure—Method A):* Compound **9a**, **10a**, **11**, or **13** was suspended in sodium ethoxide solution (0.35 g Na. in 30 mL absolute ethanol) and refluxed for 3 h, the solid that formed after cooling was collected, washed with water, and recrystallized from the appropriate solvent to give the compounds **9b**, **10b**, **12**, and **14** respectively (cf. Table I).

*Synthesis of compounds **9b**, **10b**, **12**, and **14** (General procedure—Method B):* To a suspension of compound **3a** (0.005 mmol, 1.72 g) in sodium ethoxide solution (0.15 g Na. in 30 mL absolute ethanol), the appropriate chloro compound (0.01 mmol) was added. The reaction mixture was refluxed for 2 h, and was allowed to cool. The precipitate was collected, washed with water, dried, and recrystallized from the appropriate solvent to give the compounds **9b**, **10b**, **12**, and **14** respectively (cf. Table I).

*Synthesis of 1,4,7-triphenyl-2,3,7,8-tetrahydro-1H-pyrazolo[4″,3″:5′,6′]pyrido[3′,2′:4,5]thieno[3,2-d]pyrimidine-3,8-dione (**15**):* A mixture of compond **14** (0.003 mmol, 1.43 g) and ethyl orthoformate (0.003 mmol, 0.5 mL) in acetic anhydride (20 mL) was refluxed for 3 h, The solid that formed was recrystallized from methanol to give compound **15** (cf. Table I).

*Synthesis of 3,7,10-triphenyl-4,7,8,9-tetrahydro-3H-pyrazolo[4″,3″:5′,6′]pyrido[3′,2′:4,5]thieno[3,2-d][1,2,3]triazine-4,9-dione (**16**):* Sodium nitrite solution (0.005 mmol, 0.35 g in 5 mL water) was added dropwise to compound **14** (0.003 mmol, 1.43 g) in conc. H_2SO_4 (5 mL) and glacial acetic acid (5 mL) at 0–5°C with stirring. The solid that formed, washed with water, dried, and crystallized from ethanol to give compound **16** (cf. Table I).

*Synthesis of 6-methyl-1,4,7-triphenyl-2,3,7,8-tetrahydro-1H-pyrazolo[4″,3″:5′,6′]pyrido[3′,2′:4,5]thieno[3,2-d]pyrimidine-3,8-dione (**17**):* Compound **14** (0.003 mmol, 1.43 g) in redistilled acetic anhydride (20 mL) was refluxed for 8 h. The solid that precipitated after cooling was filtered off, washed with water, dried, and recrystallized from ethanol to give compound **17** (cf. Table I).

*Synthesis of 1,4,6,7-tetraphenyl-2,3,5,6,7,8-hexahydro-1H-pyrazolo-[4″,3″:5′,6′]pyrido[3′,2′:4,5]thieno[3,2-d]pyrimidine-3,8-dione (**18**):* A

mixture of compound **14** (0.003 mmol, 1.43 g) and benzaldehyde (0.003 mmol, 0.32 mL) in glacial acetic acid (15 mL) was refluxed for 3 h, the product was collected and recrystallized from dioxane to give compound **18** (cf. Table I).

*Synthesis of 1,4,7-triphenyl-2,3,5,6,7,8-hexahydro-1H-pyrazolo-[4″,3″:5′,6′]pyrido[3′,2′:4,5]thieno[3,2-d]pyrimidine-3,6,8-trione (**19**):* A mixture of compound **14** (0.003 mmol, 1.43 g) and urea (0.003 mmol, 0.18 g) in decalin (30 mL) was refluxed for 4 h, the product was collected and crystallized from dioxane to give compound **19** (cf. Table I).

*Synthesis of 1,4,7-Triphenyl-6-thioxo-2,3,5,6,7,8-hexahydro-1H-pyrazolo[4″,3″:5′,6′]pyrido[3′,2′:4,5]thieno[3,2-d]pyrimidine-3,8-dione (**20**):* A mixture of compound **14** (0.003 mmol, 1.43 g) and CS_2 (0.003 mmol, 0.23 mL) in dry pyridine (30 mL), was refluxed for 20 h, the solvent was removed by evaporation under reduced pressure and the residue was crystallized from ethanol to give compound **20** (cf. Table I).

*Synthesis of 1,4,7-triphenyl-6-phenylamino-2,3,5,6,7,8-hexahydro-1H-pyrazolo[4″,3″:5′,6′]pyrido[3′,2′:4,5]thieno[3,2-d]pyrimidine-3,8-dione (**21**):* A mixture of **14** (0.003 mmol, 1.43 g) and phenyl isothiocyanate (0.003 mmol, 0.4 mL) in dry pyridine (30 mL), was refluxed for 20 h, the solvent was evaporated and the residue was crystallized from ethanol to give compound **21** (cf. Table I).

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