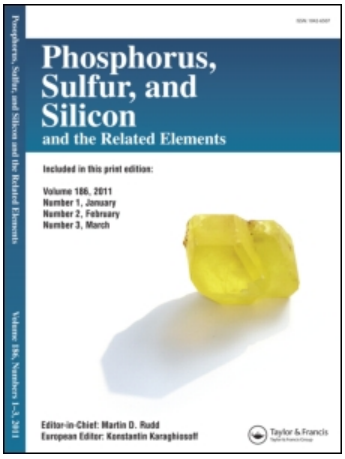

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Studies on the Synthesis of Some New Cyanopyridine-Thione and Thieno[2,3-*b*]pyridine Derivatives

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Studies on the Synthesis of Some New Cyanopyridine-Thione and Thieno[2,3-*b*]pyridine Derivatives

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*The work included in this article involves the synthesis of new cyanopyridinethiones as good synthons for new thieno[2,3-b]pyridines with anticipated biological activities. Thus, the reaction of β–aryl-α-thiocarbamoylacrylonitrile (**1a–c**) with (2-thenoyl)-ω,ω,ω-trifluoroacetone led to an unexpected formation of 4-aryl-3-cyano-6-(2-thienyl)pyridine-2(1H)-thiones (**4a–c**). In contrast, the reaction of **1a,b** with ethyl acetoacetate produced 4-aryl-3-cyano-5-ethoxycarbonyl-6-methylpyridine-2(1H)-thiones (**12a,b**). The reaction of compound **4a** with methyl iodide gave 2-methylthio derivative **6**, which upon treatment with hydrazine hydrate furnished pyrazolopyridine **7**. Treatment of **4a–c** with chloroacetaimde, in the presence of sodium ethoxide, led to the formation of 3-amino-4-aryl-6-(2-thienyl)thieno[2,3-b]pyridine-2-carboxamides (**8a–c**). The reactions of **8a** with some aromatic aldehydes and/or cycloalkanones were carried out and their products were identified. Compounds **12a,b** were reacted with chloro-N-arylacetamides to give ethyl 4-aryl-2-(N-aryl)carbamoylmethylthio-3-cyano-6-methylpyridine-5-carboxylates (**13a–j**). Upon treatment of compounds **13a–j** with sodium alkoxide in alcohol, they underwent an intramolecular Thorpe-Ziegler cyclization to furnish ethyl 3-amino-4-aryl-2-(N-aryl)carbamoyl-6-methylthieno[2,3-b]pyridine-5-carboxylates (**14a–j**). Compounds **14a–j**, in turn, were reacted with triethyl orthoformate and/or carbon disulfide to give corresponding pyridothienopyrimidinone derivatives **15a–j** and **18**. Pyridothienotriazinone analogs **17a–j** were synthesized via diazotisation of compounds **14a–j**.*

Keywords Cyanopyridinethiones; pyridothienopyrimidines; pyridothienotriazines; thienopyridines

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INTRODUCTION

The biological activities of condensed pyrimidines as sedatives, antibacterials, and antimalarials are well documented.[1,2] Numerous thieno[2,3-b]pyridines have been investigated in relation with their biological and pharmacological activities. Some of them proved to possess antibacterial,[3,4] antiviral,[5] antihypertensive,[6] and immunostimulating[7] activities. Others are useful as gonadtropin-releasing hormone antagonists[8–13] and as lipoxygenases inhibitors.[14] Recently, certain thieno[2,3-b] pyridine derivatives were prepared as antinflammatory agents, particularly for treating arthritis and bone–resorption inhibiting agents.[15] Pyridothienopyrimidine derivatives have found applications as analgesics,[16] antipyretics,[17] and anti-inflammatories.[18] In view of all these facts and as a continuation of work on the synthesis of new condensed thieno[2,3-b]pyridines,[19–22] we undertook the synthesis and reactions of the title compounds, which might have shown good biological and medicinal applications.

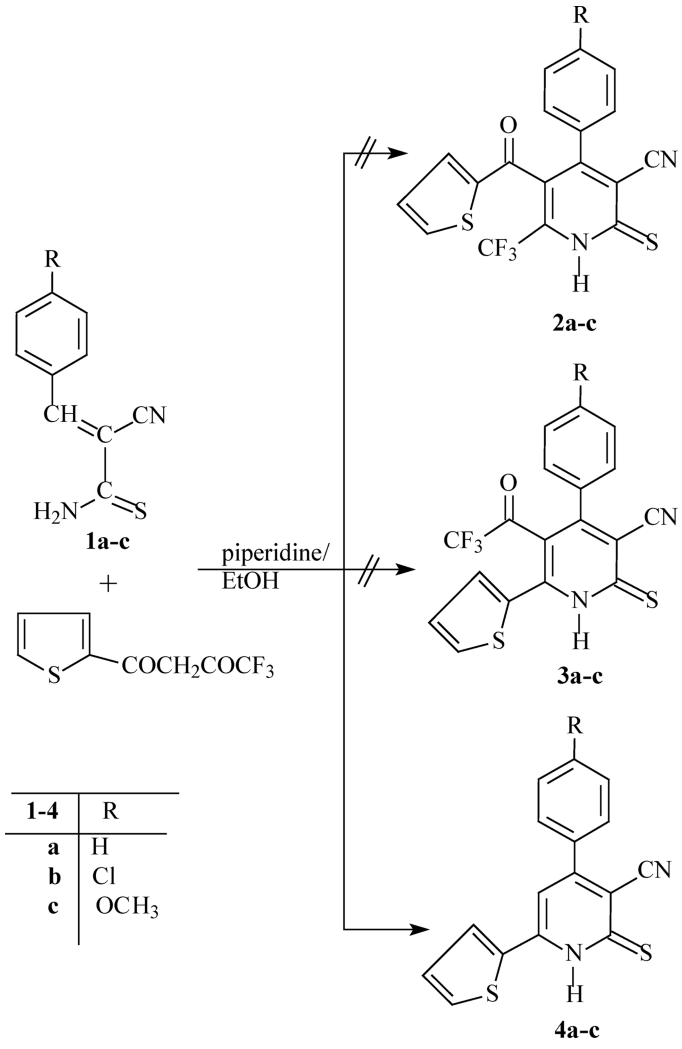
RESULTS AND DISCUSSION

Our approach to the synthesis of the target compounds started from the reaction of β–aryl-α-thiocarbamoylacrylonitriles (**1a–c**) with (2-thenoyl)-ω,ω,ω-trifluoro-acetone in boiling ethanol containing a catalytic amount of piperidine, which gave orange crystalline products. The structure of them was assigned as 4-aryl-3-cyano-6-(2-thienyl)pyridine-2(1*H*)-thiones (**4a–c**) rather than the others, **2a–c** and **3a–c**. The latter assignment was based on elemental and spectral analyses (Scheme 1).

The pathway of the latter reaction may have involved a Michael addition of cyanothioacetamide on the activated double bond of **1a–c** to give intermediate **A**, which, in turn, underwent enolization, deacylation, cyclodehydration, and spontaneous dehydrogenation to afford target compounds **4a–c** [23,24] (Scheme 2).

The structural formulas of compounds **4a–c** were confirmed by comparison with authentic samples prepared according to our reported method[22] by reaction of chalcones **5a–c** with cyanothioacetamide (Scheme 2).

The reaction of 3-cyano-4-phenyl-6-(2-thienyl)pyridine-2(1*H*)-thione (**4a**) with methyl iodide, in the presence of sodium acetate, gave the corresponding 2-methylthio derivative **6**. Heating compound **6** with hydrazine hydrate under a neat condition furnished pyrazolopyridine **7** (Scheme 3).



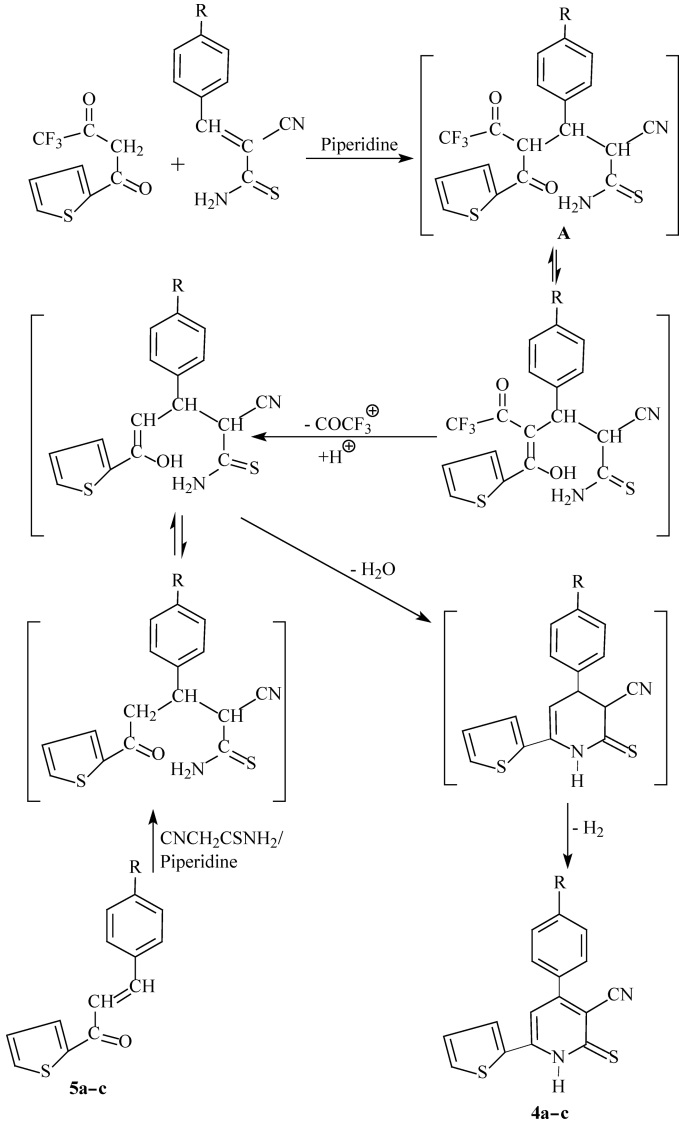
1-4	R
a	H
b	Cl
c	OCH_3

SCHEME 1

The reactivity of compounds **4a–c** as bifunctions was test through a reaction with chloroacetamide in the presence of sodium ethoxide wherein 3-aminothieno[2,3-b]pyridines **8a–c** were obtained (Scheme 3).

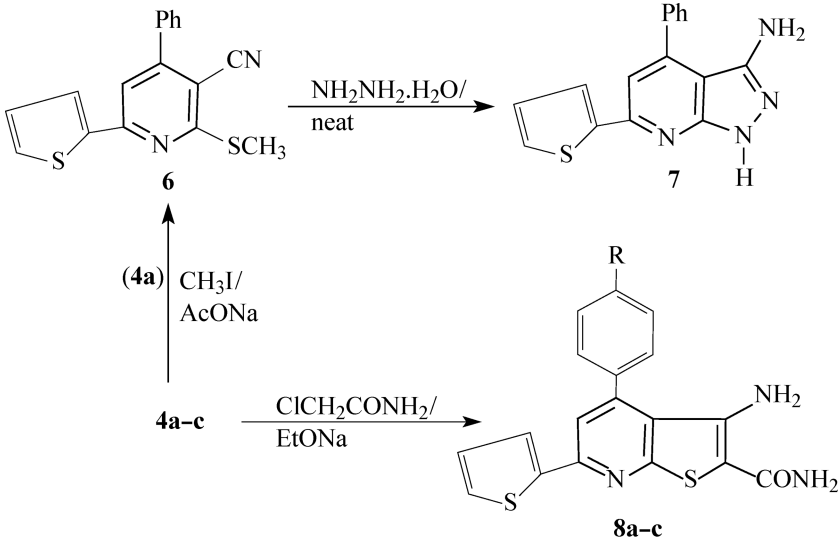
The characterization data of compounds **8a–c** were in agreement with those reported before by us.[21]

Heating *o*-aminoamide **8a** with some aromatic aldehydes in ethanol containing a few drops of acetic acid afforded the corresponding



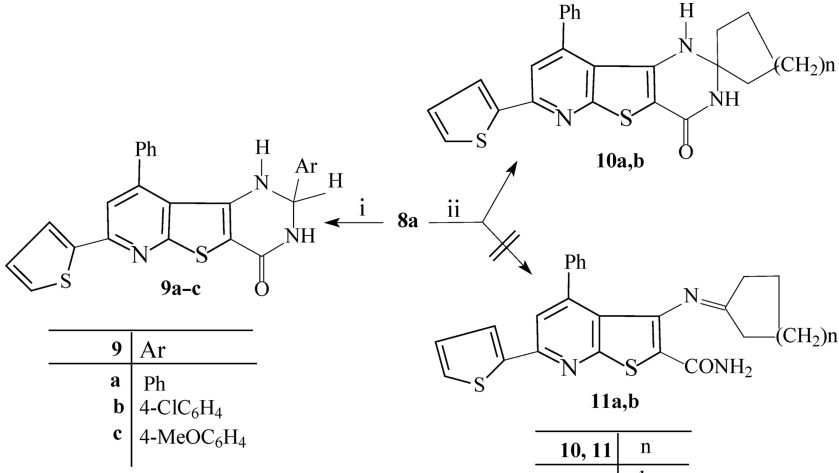
SCHEME 2

tetrahdyropyridothienopyrimidinones **9a–c**. Upon treatment of **8a** with cyclopentanone or cyclohexanone under the same conditions, the products were identified as spiro compounds **10a,b** rather than Schiff's bases **11a,b**[25](Scheme 4).



8	R
a	H
b	Cl
c	OCH_3

SCHEME 3



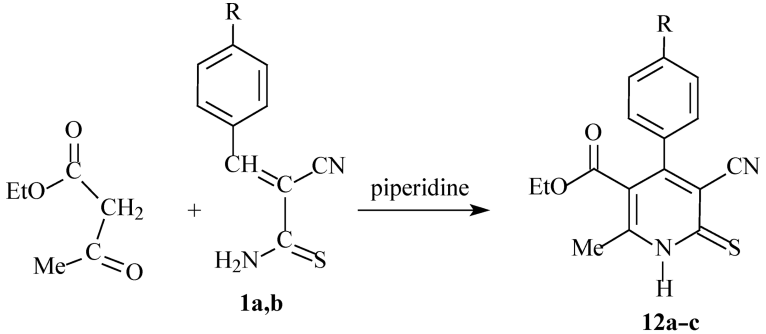
9	Ar
a	Ph
b	4-ClC_6H_4
c	4-$MeOC_6H_4$

10, 11	n
a	1
b	2

i: ArCHO/EtOH-AcOH
ii: Cyclopentanone or cyclohexanone/EtOH-AcOH

SCHEME 4

In contrast, the reaction of β–aryl-α-thiocarbamoylacrylonitriles (**1a,b**) with ethyl acetoacetate, by refluxing in ethanol containing a catalytic amount of piperidine, gave a good yield of 4-aryl-3-cyano-5-ethoxycarbonyl-6-methylpyridine-2(1*H*)-thiones (**12a,b**)[25] (Scheme 5).



1a,b

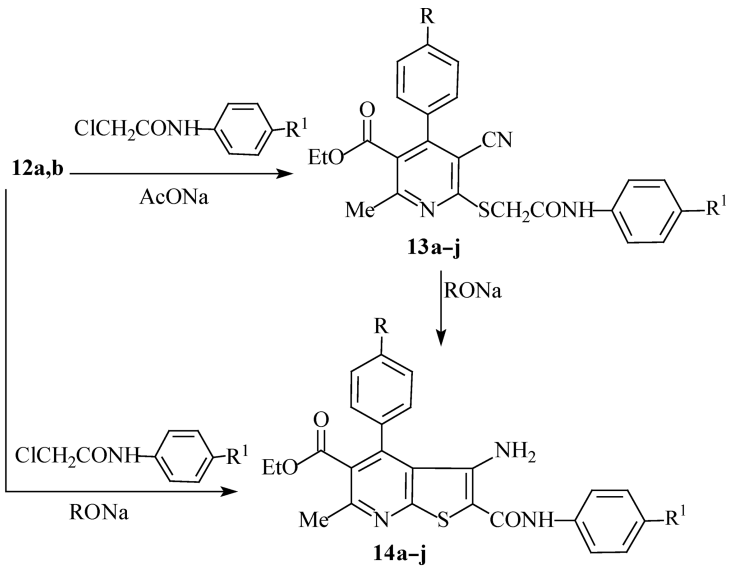
12a–c

12	R
a	Cl
b	OCH_3

SCHEME 5

The reaction of **12a,b** with chloro-*N*-arylacetamides in ethanol, in the presence of sodium acetate, as a basic catalyst, gave ethyl 4-aryl-2-(*N*-aryl)carbamoylmethylthio-3-cyano-6-methyl-pyridine-5-carboxylates (**13a–j**). Upon treatment of products **13a–i** with sodium ethoxide in ethanol, they underwent intramolecular Thorpe-Ziegler cyclization to furnish ethyl 3-amino-4-aryl-2-(*N*-aryl)carbamoyl-6-methylthieno[2,3-b]pyridine-5-carboxylates (**14a–j**). Similarly, cyclization of compound **13j** to the corresponding thienopyridine **14j** was achieved by using sodium methoxide in boiling methanol. The latter thienopyridines **14a–j** were also prepared via direct reaction of **12a,b** with the respective chloroacetamide derivative in the presence of the appropriate sodium alkoxide as a basic catalyst (Scheme 6).

Compounds **14a–j** seem to be good synthons for other new condensed thienopyridines. Thus, the cyclocondensation of **14a–j** with triethyl orthoformate in the presence of acetic anhydride afforded pyrido[3′,2′:4,5]thieno[3,2-d]pyrimidine-4(3*H*)-ones (**15a–j**). The reactivity of the acetyl group of compound **15g** was tested via its condensation with phenylhydrazine or thiosemicarbazide where the corresponding condensation products **16a,b** were obtained in a nearly quantitative yield. Triazinone derivatives **17a–j** were prepared by diazotisation of **14a–j** using sodium nitrite and an acetic acid–sulfuric acid mixture at a low temperature. The interaction of **14a** with carbon



13,14	R	R^1	13,14	R	R^1
a	Cl	H	f	OMe	OMe
b	Cl	OMe	g	OMe	COMe
c	Cl	COMe	h	OMe	Cl
d	OMe	H	i	OMe	CO_2Et
e	OMe	Me	j	OMe	CO_2Me

SCHEME 6

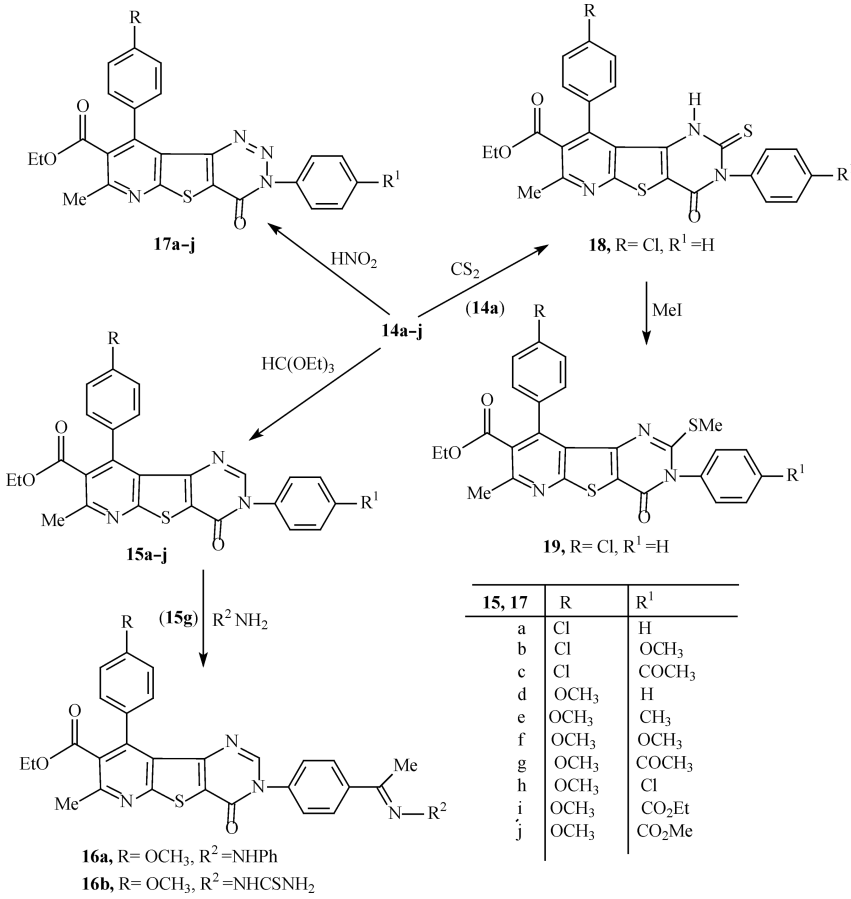
disulfide in hot pyridine resulted in the formation of thioxopyrimidinone derivative **18**. Methylthiopyrimidine derivative **19** was synthesized through the reaction of **18** with methyl iodide in the presence of sodium hydroxide (Scheme 7).

In conclusion, 3-cyanopyridine-2(1*H*)-thiones **4a–c** and **12a–c** that were investigated are good starting materials to synthesize 1,3-diamino compounds **8a–c** and 3-aminoimine derivatives **14a–j**. Compounds **8a** and **14a–j**, in turn, were used as precursors to construct pyridothienopyrimidine and pyridothienotriazine systems.

The structures of all newly synthesized compounds were confirmed by elemental analyses, IR, ^{1}H NMR, and mass spectral data.

EXPERIMENTAL

All melting points are uncorrected and were measured on a Gallan-Kamp apparatus. IR spectra: Shmiadzu 470 IR-spectrophotometer



15, 17	R	R^1
a	Cl	H
b	Cl	OCH_3
c	Cl	$COCH_3$
d	OCH_3	H
e	OCH_3	CH_3
f	OCH_3	OCH_3
g	OCH_3	$COCH_3$
h	OCH_3	Cl
i	OCH_3	CO_2Et
j	OCH_3	CO_2Me

SCHEME 7

(KBr; υ_{max} in cm^{-1}). ^1H NMR spectra: Varian EM-390, 90 MHz ^1H NMR spectrometer using TMS as an internal standard (δ in ppm); MS: Jeol JMS-600; elemental analyses: Elementar Analysensystem GmbH VARIOEL V2.3 July 1998 CHNS Mode; their results were in good agreement with the calculated values.

Reaction of β-aryl-α-thiocarbamoylacrylonitrile (1a–c) with (2-thenoyl)-ω,ω,ω-trifluoroacetone; General procedure

To a mixture of β–aryl-α-thiocarbamoylacrylonitrile (**1a–c**) (10 mmol) and (2-thenoyl)-ω,ω,ω-trifluoroacetone (2.22 g, 10 mmol) in ethanol (20 mL), a few drops of piperidine were added. The reaction mixture

was refluxed for 3 h and then left to cool. The solid that formed was collected and recrystallized from acetic acid to give orange crystalline compounds. The structure of them was assigned as 4-aryl-3-cyano-6-(2-thienyl)pyridine-2(1*H*)-thiones (**4a–c**).

3-Cyano-4-phenyl-6-(2-thienyl)pyridine-2(1*H*)-thione (4a)

Prepared from **1a**. Yield: 63%; m.p. 246°C, (Lit. m.p. 245°C). Anal. calcd. for $C_{16}H_{10}N_2S_2$(294.4): C, 65.28; H, 3.42; N, 9.52; S, 21.78%. Found: C, 65.45; H, 3.19; N, 9.30; S, 21.54%.

4-(4-Chlorophenyl)-3-cyano-6-(2-thienyl)pyridine-2(1*H*)-thione (4b)

Prepared from **1b**. Yield: 72%; m.p. 242°C, (Lit. m.p. 242°C). Anal. calcd. for $C_{16}H_9ClN_2S_2$(329.9): C, 58.44; H, 2.76; N, 8.52; S, 19.50; Cl, 10.78%. Found: C, 58.58; H, 3.01; N, 8.26; S, 19.78; Cl, 10.64%.

3-Cyano-4-(4-methoxyphenyl)-6-(2-thienyl)pyridine-2(1*H*)-thione (4c)

Prepared from **1c**. Yield: 75%; m.p. 253°C, (Lit. m.p. 250°C). Anal. calcd. for $C_{17}H_{12}N_2OS_2$(324.4): C, 62.94; H, 3.73; N, 8.63; S, 19.77%. Found: C, 63.13; H, 3.81; N, 8.26; S, 19.55%.

Synthesis of 4-aryl-3-cyano-6-(2-thienyl)pyridine-2(1*H*)-thione (4a–c)

To a solution of chalcone **5a–c** (10 mmol) and cyanothioacetamide (1.0 g, 10 mmol) in ethanol (30 mL), a few drops of piperidine were added. The reaction mixture was refluxed for 4 h. The solid that formed while hot was collected and recrystallized from acetic acid as orange needles of **4a–c** (yield: 43–62%). These products were identical in all aspects to those previously described.

Synthesis of 3-cyano-2-methylthio-4-phenyl-6-(2-thienyl)pyridine (6)

A mixture of **4a** (2.94 g, 10 mmol), methyl iodide (10 mmol), and sodium acetate trihydrate (1.4 g, 10 mmol) in ethanol (20 mL) was heated under reflux for 1 h. The precipitate that formed on cooling was collected and recrystallized from ethanol as pale yellow needles of **6**, yield: 2.5 g (81%);

m.p. 140–141°C. Anal. calcd. for $C_{17}H_{12}N_2S_2$ (308.4): C, 66.20; H, 3.92; N, 9.08; S, 20.79%. Found: C, 66.38; H, 3.87; N, 9.03; S, 20.91%.

Synthesis of 3-amino-4-phenyl-6-(2-thienyl)-1*H*-pyrazolo[3,4-b]pyridine (7)

Compound **6** (1.54 g, 5 mmol), in an excess amount of hydrazine hydrate (5 mL, 100 mmol), was heated under reflux for 4 h. The reaction mixture was triturated with ethanol (10 mL) and left to cool. The precipitated solid was collected and recrystallized from ethanol to give yellow fine needles of **7**, yield: 1.1 g (75%); m. p: 243–244°C. Anal. calcd. for $C_{16}H_{12}N_4S$ (292.3): C, 65.73; H, 4.14; N, 19.16; S, 10.97%. Found: C, 65.50; H, 4.11; N, 19.32; S, 11.20%.

Synthesis of 3-amino-4-aryl-6-(2-thienyl)thieno[2,3-b]pyridine-2-carboxamides (8a–c): General Procedure

To a solution of compound **4a–c** (10 mmol) in sodium ethoxide solution (0.35 g sodium in 40 mL abs. ethanol), chloroacetamide (0.94 g, 10 mmol) was added. The reaction mixture was refluxed for 20 min and then left to cool. The precipitated product was collected and recrystallized from an ethanol-chloroform mixture to give compounds **8a–c**.

3-Amino-4-phenyl-6-(2-thienyl)thieno[2,3-b]pyridine-2-carboxamide (8a)

Prepared from **4a**. Yield: 78%; m.p. 235–238°C. Anal. calcd. for $C_{18}H_{13}N_3OS_2$(351.4): C, 61.51; H, 3.73; N, 11.96; S, 18.25%. Found: C, 61.68; H, 3.91; N, 11.66; S, 17.98%.

3-Amino-4-(4-chlorophenyl)-6-(2-thienyl)thieno[2,3-b]pyridine-2-carboxamide (8b)

Prepared from **4b**. Yield: 76%; m.p. 240–243°C. Anal. calcd. for $C_{18}H_{12}ClN_3OS_2$(385.9): C, 56.10, H, 3.11; N, 10.90; S, 16.62; Cl, 9.09%. Found: C, 55.71; H, 3.26; N, 11.15; S, 16.82; Cl, 9.25%.

3-Amino-4-(4-methoxyphenyl)-6-(2-thienyl)thieno[2,3-b]-pyridine-2-carboxamide (8c)

Prepared from **4c**. Yield: 83%; m.p. 231°C. Anal. calcd. for $C_{19}H_{15}N_3O_2S_2$(381.4): C, 59.82; H, 3.96; N, 11.02; S, 16.81%. Found: C, 59.74; H, 4.11; N, 11.12; S, 16.79%.

Synthesis of 2-Aryl-9-phenyl-7-(2-thienyl)-4-oxo-1,2,3,4-tetrahydropyrido[3′,2′: 4,5]thieno[3,2-d]pyrimidines (9a-c). General Procedure

To a mixture of **8a** (0.7 g, 2 mmol) and the respective aldehyde (0.002 mol) in ethanol (20 mL), a few drops of glacial acetic acid was added. The reaction mixture was heated under reflux for 3 h. The product that formed was collected and recrystallized from chloroform to give yellow crystals of **9a–c**.

2,9-Diphenyl-7-(2-thienyl)-4-oxo-1,2,3,4-tetrahydropyrido-[3′,2′:4,5]thieno[3,2-d] pyrimidines (9a)

This compound was prepared by using benzaldehyde, yield 80%; m.p. 292–293°C. Anal. calcd. for $C_{25}H_{17}N_3OS_2$(439.55): C, 68.31; H, 3.90; N, 9.56; S, 14.59%. Found: C, 68.12; H, 3.77; N, 9.53; S, 14.70%.

2-(4-Chlorophenyl)-9-phenyl-7-(2-thienyl)-4-oxo-1,2,3,4-tetrahydropyrido[3′,2′: 4,5]thieno[3,2-d]pyrimidines (9b)

This compound was prepared by using 4-chlorobenzaldehyde, yield: 90%; m.p. 295–296°C. Anal. calcd. for $C_{25}H_{16}ClN_3OS_2$(473.99): C, 63.53; H, 3.40; N, 8.68; S, 13.53%. Found: C, 63.35; H, 3.36; N, 8.42; S, 13.78%.

2-(4-Methoxyphenyl)-9-phenyl-7-(2-thienyl)-4-oxo-1,2,3,4-tetrahydropyrido [3′,2′: 4,5]thieno[3,2-d]pyrimidines (9c)

This compound was prepared by using 4-methoxybenzaldehyde, yield 88%; m.p. 287–288°C. Anal. calcd. for $C_{26}H_{19}N_3O_2S_2$(469.58): C, 66.50; H, 4.08; N, 8.95; S, 13.66%. Found: C, 66.38; H, 4.18; N, 9.18; S, 13.37%.

Reaction of 8a with Cyclopentanone or Cyclohexanone, the Formation of Spiro Compounds 10a,b: General Procedure

A mixture of **8a** (0.7 g, 2 mmol) and cyclopentanone or cyclohexanone (0.002 mol) in ethanol (20 mL) containing a few drops of glacial acetic acid was heated under reflux for 3 h. The product that formed was collected and recrystallized from ethanol to give yellow needles of **10a,b**.

9-Phenyl-7-(2-thienyl)-4-oxo-1,2,3,4-tetrahydro-2,2-tetramethylene-pyrido[3′,2′: 4,5]thieno[3,2-d]pyrimidine (10a)

This compound was prepared using cyclopentanone, yield: 83%; m.p. 261–262°C. Anal. calcd. for $C_{23}H_{19}N_3OS_2$ (417.55): C, 66.16; H, 4.59; N, 10.06; S, 15.36%. Found: C, 66.00; H, 4.69; N, 10.23; S, 15.11%.

9-Phenyl-7-(2-thienyl)-4-oxo-2,2-pentamethylene-1,2,3,4-tetrahydropyrido[3′,2′: 4,5]thieno[3,2-d]pyrimidine (10b)

This compound was prepared using cyclohexanone, yield: 80%; m.p. 287–288°C. Anal. calcd. for $C_{24}H_{21}N_3OS_2$(431.57): C, 66.79; H, 4.90; N, 9.74; S, 14.86%. Found: C, 66.54; H, 4.97; N, 9.55; S, 14.67%.

4-Aryl-3-cyano-5-ethoxycarbonyl-6-methylpyridine-2(1 *H*)-thiones (12a,b)

These compounds were prepared according to the reported method.[25]

Synthesis of ethyl 4-aryl-2-(*N*-aryl)carbamoylmethylthio-3-cyano-6-methyl-pyridine-5-carboxylates (13a–j)

To a suspension of compound **12b** (5 mmol) and sodium acetate trihydrate (3.0 g, 22 mmol) in ethanol (50 mL), the respective chloro-*N*-arylacetamide (20 mmol) was added. The resulting mixture was heated under reflux for 2 h. The precipitate that formed on cooling was collected and recrystallized from ethanol as white needles of **13a–j**. Melting points, yields, and analytical data of these compounds are given in Table I.

Synthesis of Ethyl 3-amino-4-aryl-2-(*N*-aryl)carbamoyl–6-methylthieno[2,3-b] pyridine-5-carboxylates (14a–i)

Method A

Compounds **13a–i** (10 mmol) were suspended in sodium ethoxide solution (0.12 g sodium in 30 mL abs. ethanol) and heated under reflux for 5 mins. The solid that formed after cooling was collected and recrystallized from ethanol as canary yellow crystals of **14a–i**. Melting points, yields, and analytical data of these compounds are given in Table I.

Method B

To a suspension of compound **12a,b** (10 mmol) in sodium ethoxide solution (0.35 g sodium in 40 mL abs. ethanol), the respective

TABLE I Melting Points, Yields, and Analytical Data of Compounds 13a–j, 14a–j, 15a–j, 16a,b, 17a–j, 18, and 19

Compound	M.P., °C, Yield, %	Formula (M.W.)	Calculated/Found (%) C	H	N	S	Cl
13a	139–140	$C_{24}H_{20}ClN_3O_3S$	61.87	4.33	9.02	6.88	7.61
	88	(465.96)	61.93	4.15	9.34	6.58	7.70
13b	157–158	$C_{25}H_{22}ClN_3O_4S$	60.54	4.47	8.47	6.46	7.15
	85	(495.98)	60.24	4.45	8.52	6.39	6.80
13c	171–172	$C_{26}H_{22}ClN_3O_4S$	61.47	4.36	8.27	6.31	6.98
	90	(507.99)	61.32	4.24	8.19	6.48	6.77
13d	125–126	$C_{25}H_{23}N_3O_4S$	65.06	5.02	9.10	6.95	
	86	(461.54)	65.19	4.91	9.00	6.88	
+							
13e	150–151	$C_{26}H_{25}N_3O_4S$	65.67	5.30	8.84	6.74	
	91	(475.56)	65.77	5.14	8.52	6.59	
13f	155–156	$C_{26}H_{25}N_3O_5S$	63.53	5.13	8.55	6.52	
	87	(491.56)	63.56	5.34	8.71	6.35	
13g	168–169	$C_{27}H_{25}N_3O_5S$	64.40	5.00	8.34	6.37	
	90	(503.57)	64.14	5.19	8.22	6.36	
13h	125–126	$C_{25}H_{22}ClN_3O_4S$	60.54	4.47	8.47	7.15	
	92	(495.98)	60.29	4.30	8.41	7.33	
13i	148–149	$C_{28}H_{27}N_3O_6S$	63.03	5.10	7.87	6.01	
	85	(533.60)	62.78	5.15	8.11	6.90	
13j	153–154	$C_{27}H_{25}N_3O_6S$	62.42	4.85	8.09	6.17	
	85	(519.57)	62.31	4.96	8.22	6.19	
14a	175–176.	$C_{24}H_{20}ClN_3O_3S$	61.87	4.33	9.02	6.88	7.61
	94	(465.96)	62.13	4.35	8.91	6.97	7.92
14b	184–185	$C_{25}H_{22}ClN_3O_4S$	60.54	4.47	8.47	6.46	7.15
	95	(495.98)	60.45	4.37	8.28	6.31	7.22
14c	239–240	$C_{26}H_{22}ClN_3O_4S$	61.47	4.36	8.27	6.31	6.98
	90	(507.99)	61.55	4.34	8.44	6.19	7.12
14d	158–159	$C_{25}H_{23}N_3O_4S$	65.06	5.02	9.10	6.95	
	92	(461.54)	65.08	5.21	8.93	7.06	
14e	175–176	$C_{26}H_{25}N_3O_4S$	65.67	5.30	8.84	6.74	
	94	(475.56)	65.40	5.18	9.02	6.89	
14f	172–173	$C_{26}H_{25}N_3O_5S$	63.53	5.13	8.55	6.52	
	95	(491.56)	63.70	5.33	8.34	6.71	
14g	204–204	$C_{27}H_{25}N_3O_5S$	64.40	5.00	8.34	6.37	
	93	(503.57)	64.37	5.23	8.60	6.57	
14h	194–195	$C_{25}H_{22}ClN_3O_4S$	60.54	4.47	8.47	7.15	
	96	(495.98)	60.29	4.58	8.60	7.12	
14i	189–190	$C_{28}H_{27}N_3O_6S$	63.03	5.10	7.87	6.01	
	95	(533.60)	62.78	5.15	8.11	6.90	
14j	210–211	$C_{27}H_{25}N_3O_6S$	62.42	4.85	8.09	6.17	
	90	(519.57)	62.40	506	8.01	6.00	
15a	215–216	$C_{25}H_{18}ClN_3O_3S$	63.09	3.81	8.83	6.74	7.54
	87	(475.95)	63.16	3.94	8.75	6.78	7.20

(Continued on next page)

TABLE I Melting Points, Yields and Analytical Data of Compounds 13a–j, 14a–j, 15a–j, 16a,b, 17a–j, 18, and 19 *(Continued)*

Compound	M.P., °C, Yield, %	Formula (M.W.)	Calculated/Found (%) C	H	N	S	Cl
15b	231–232	$C_{26}H_{20}ClN_3O_4S$	61.72	3.98	8.30	6.34	7.01
	84	(505.98)	61.75	4.11	8.16	6.70	7.13
15c	208–209	$C_{27}H_{20}ClN_3O_4S$	62.61	3.89	8.11	6.19	6.84
	84	(517.99)	62.35	3.80	8.16	6.09	6.95
15d	230–232	$C_{26}H_{21}N_3O_4S$	66.23	4.49	8.91	6.80	
	85	(471.53)	66.00	4.51	8.53	6.92	
15e	242–243	$C_{27}H_{23}N_3O_4S$	66.79	4.77	8.65	6.60	
	86	(485.56)	66.89	4.34	8.90	6.79	
15f	236–237	$C_{27}H_{23}N_3O_5S$	64.66	4.62	8.38	6.39	
	85	(501.56)	64.42	4.91	8.49	6.22	
15g	185–186	$C_{28}H_{23}N_3O_5S$	65.48	4.51	8.18	6.24	
	80	(513.57)	65.63	4.24	8.50	6.40	
15h	186–187	$C_{26}H_{20}ClN_3O_4S$	61.72	3.98	8.30	6.34	7.01
	84	(505.98)	61.66	4.91	8.12	6.63	6.82
15i	195–196	$C_{29}H_{25}N_3O_6S$	64.08	4.64	7.73	5.90	
	89	(543.59)	64.32	4.30	7.59	5.78	
15j	180–181	$C_{28}H_{23}N_3O_6S$	63.51	4.38	7.93	6.05	
	86	(529.57)	63.66	4.40	7.81	5.82	
16a	265–266	$C_{34}H_{29}N_5O_4S$	67.66	4.81	11.61	5.31	
	80	(603.00)	67.51	4.85	11.78	5.00	
16b	281–282	$C_{29}H_{26}N_6O_4S_2$	59.38	4.44	14.33	10.92	
	84	(586.00)	59.13	4.36	14.24	10.71	
17a	180–181	$C_{24}H_{17}ClN_4O_3S$	60.44	3.59	11.75	6.72	7.43
	81	(476.94)	60.19	3.50	11.84	6.56	7.34
17b	188-189	$C_{25}H_{19}ClN_4O_4S$	59.23	3.78	11.05	6.32	6.99
	83	(506.96)	59.01	3.73	10.79	6.25	6.80
17c	197–198	$C_{26}H_{19}ClN_4O_4S$	60.17	3.69	10.80	6.18	6.83
	80	(518.98)	60.36	3.71	10.58	6.00	6.55
17d	228–229	$C_{25}H_{20}N_4O_4S$	63.55	4.27	11.86	6.79	
	82	(472.52)	63.20	4.21	11.97	6.56	
17e	197–198	$C_{26}H_{22}N_4O_4S$	64.18	4.56	11.52	6.59	
	80	(486.55)	64.09	4.59	11.61	6.44	
17f	198–199	$C_{26}H_{22}N_4O_5S$	62.14	4.41	11.15	6.38	
	86	(502.54)	62.41	4.55	11.30	6.30	
17g	164–165	$C_{27}H_{22}N_4O_5S$	63.02	4.31	10.89	6.23	
	82	(514.56)	62.74	4.38	10.78	6.00	
17h	174–175	$C_{25}H_{19}ClN_4O_4S$	59.23	3.78	11.05	6.32	6.99
	80	(506.96)	59.27	3.52	11.00	6.49	6.92
17i	170–171	$C_{28}H_{24}N_4O_6S$	61.76	4.44	10.29	5.89	
	85	(544.58)	61.46	4.67	11.00	5.70	
17j	173–174	$C_{27}H_{22}N_4O_6S$	61.12	4.18	10.56	6.04	
	86	(530.56)	61.33	4.02	10.41	5.80	
18	267–268	$C_{22}H_{18}ClN_3O_3S_2$	59.17	3.55	8.28	12.62	6.90
	78	(507.00)	59.08	3.68	8.00	12.73	6.79
19	204–205	$C_{23}H_{20}ClN_3O_3S_2$	59.88	3.84	8.06	12.28	6.72
	85	(521.00)	59.60	3.91	8.11	12.19	6.78

TABLE II IR, ^{1}H NMR, and MS Spectral Data of All Newly Synthesized Compounds

Compound	Spectral Data
4a	IR: ν = 3190 (NH), 2210 (C≡N) cm^{-1}. ^{1}H NMR (DMSO-d$_6$): δ = 8.3 (d, 1H, CH thienyl), 7.6–8.2 (m, 6H: 5ArH's and CH pyridine), 7.3 (d, 1H, CH thienyl) and 7.1 (t, 1H, CH thienyl) ppm. MS: 294 (M^+, 100%).
4b	IR: ν = 3190 (NH), 2210 (C≡N) cm^{-1}. ^{1}H NMR (DMSO-d$_6$): δ = 8.2 (d, 1H, CH thienyl), 7.5–7.8 (m, 6H: 4ArH's, CH thienyl and CH pyridine) and 7.2 (t, 1H, CH thienyl) ppm.
4c	IR: ν = 3190 (NH), 2210 (C≡N) cm^{-1}. ^{1}H NMR (TFA): δ = 7.8–8.2 (m, 5H: 2ArH's, 2CH thienyl and CH pyridine), 7.2–7.5 (m, 3H: 2ArH's and CH thienyl) and 4.0 (s, 3H, OCH_3) ppm.
6	IR: ν = 2200 (C≡N) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 8.1 (d, 1H, CH thienyl), 7.5–8.0 (m, 6H: 5ArH's and CH pyridine), 7.3 (d, 1H, CH thienyl), 7.1 (t, 1H, CH thienyl) and 2.7 (s, 3H, SCH_3) ppm.
7	IR: ν = 3480, 3320, 3200 (NH_2, NH) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 12.5 (1H, NH), 8.1 (d, 1H, CH thienyl), 7.4–7.9 (m, 6H: 5ArH's and CH pyridine), 7.2 (d, 1H, CH thienyl), 6.9 (t, 1H, CH thienyl) and 4.5 (s, 2H, NH_2) ppm.
8a	IR: ν = 3480, 3300, 3150 (2NH_2), 1640 (C═O) cm.$^{-1}$ ^{1}H NMR (DMSO-d$_6$): δ = 8.3 (d, 1H, CH thienyl), 7.6–8.2 (m, 6H: 5ArH's and CH pyridine), 7.3 (d, 1H, CH thienyl), 7.1 (m, 3H:CH thienyl and $CONH_2$) and 6.0 (s, 2H, NH_2) ppm.
8b	IR: ν = 3480, 3300, 3150 (2NH_2), 1640 (C═O) cm.$^{-1}$ ^{1}H NMR (DMSO-d$_6$): δ = 8.0 (d, 1H, CH thienyl), 7.5–7.8 (m, 6H: 4ArH's, CH thienyl and CH pyridine), 7.3 (m, 3H:CH thienyl and $CONH_2$) and 5.9 (s, 2H, NH_2) ppm ms.
8c	IR: ν = 3480, 3300, 3150 (2NH_2), 1640 (C═O) cm.$^{-1}$ ^{1}H NMR (DMSO-d$_6$): δ = 7.1–8.1 (m, 10H: 4ArH's, 3CH thienyl, CH pyridine and $CONH_2$), 5.9 (s, 2H, NH_2) and 3.5 (s, 3H, OCH_3) ppm.
9a	IR: ν = 3400, 3200 (2NH), 1650 (C═O) cm^{-1}. ^{1}H NMR (TFA): δ = 8.3 (d, 1H, CH thienyl), 7.4–8.2 (m, 11H: 10ArH's and CH pyridine), 7.3 (d, 1H, CH thienyl) and 7.1 (t, 1H, CH thienyl) and 6.0 (s, 1H, CH at C-2) ppm.
9b	IR: ν = 3400, 3200 (2NH), 1650 (C═O) cm^{-1}. ^{1}H NMR (TFA): δ = 8.4 (d, 1H, CH thienyl), 7.5–8.2 (m, 10H: 9ArH's and CH pyridine), 7.3 (d, 1H, CH thienyl) and 7.0 (t, 1H, CH thienyl) and 6.0 (s, 1H, CH at C-2) ppm.
9c	IR: ν = 3400, 3200 (2NH), 1650 (C═O) cm^{-1}. ^{1}H NMR (TFA): δ = 8.2 (d, 1H, CH thienyl), 7.2–8.2 (m, 10H: 9ArH's and CH pyridine), 7.2 (d, 1H, CH thienyl) and 6.9 (t, 1H, CH thienyl), 6.0 (s, 1H, CH at C-2) and 3.9 (s, 3H, OCH_3) ppm.
10a	IR: ν = 3400, 3200 (2NH), 1650 (C═O) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 8.1 (d, 1H, CH thienyl), 7.3–7.8 (m, 6H: 5ArH's and CH pyridine), 7.1 (d, 1H, CH thienyl), 6.9 (t, 1H, CH thienyl), 6.6 (s, 1H, CONH), 3.7 (s, 1H, NH), 1.7–2.0 (br s, 6H, $(CH_2)_3$ of cyclopentane ring) and 1.2–1.5 (br s, 2H, CH_2 of cyclopentane ring) ppm.
10b	IR: ν = 3400, 3200 (2NH), 1650 (C═O) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 8.2 (d, 1H, CH thienyl), 7.4–7.9 (m, 6H: 5ArH's and CH pyridine), 7.2 (d, 1H, CH thienyl), 7.0 (t, 1H, CH thienyl), 6.8 (s, 1H, CONH), 3.6 (s, 1H, NH), 1.9–2.2 (m, 4H, $(CH_2)_2$ of cyclohexane ring) and 1.3–1.6 (m, 4H, $(CH_2)_2$ of cyclohexane ring), 0.6–0.9 (m, 2H, CH_2 of cyclohexane ring) ppm.

(Continued on next page)

TABLE II IR, ^{1}H NMR, and MS Spectral Data of All Newly Synthesized Compounds *(Continued)*

Compound	Spectral Data
13a	IR: ν = 3200 (NH), 2200 (C ≡N), 1720 (C═O, ester), 1670 (C═O, amide), cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 8.6 (s, 1H, NH), 7.0–7.5 (m, 9H, ArH's), 3.9–4.2 (m, 4H: SCH_2 and OCH_2), 2.7 (s, 3H, CH_3 at C-6), 0.9–1.2 (t, 3H, CH_3 of ester) ppm. MS: 466 (M^+, 79%).
13b	IR: ν = 3200 (NH), 2200 (C ≡N), 1720 (C═O, ester), 1670 (C═O, amide) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 8.8 (s, 1H, NH), 7.3–7.7 (m, 6H, ArH's), 6.8–7.0 (d, 2H, ArH's), 4.0–4.3 (m, 4H: $SCH_2$and OCH_2), 3.8 (s, 3H, OCH_3), 2.7 (s, 3H, CH_3 at C-6), 0.9–1.2 (t, 3H, CH_3 of ester) ppm. MS: 496 (M^+, 100%). .
13c	IR: ν = 3200 (NH), 2200(C ≡N), 1720 (C═O, ester), 1680 (2C═O, amide and acety) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 8.7 (s, 1H, NH), 7.3–7.8 (m, 6H, ArH's), 6.8–7.0 (d, 2H, ArH's), 4.0–4.3 (m, 4H: $SCH_2$and OCH_2), 2.7 (s, 3H, CH_3 at C-6), 2.6 (s, 3H, $COCH_3$), 1.0–1.3 (t, 3H, CH_3 of ester) ppm.
13d	IR: ν = 3200 (NH), 2200 (C ≡N), 1720 (C═O, ester), 1670 (C═O, amide) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 8.9 (s, 1H, NH), 6.9–7.5 (m, 9H, ArH's), 3.9–4.3 (m, 4H: $SCH_2$and OCH_2), 3.8 (s, 3H, OCH_3), 2.7 (s, 3H, CH_3 at C-6), 0.9–1.2 (t, 3H, CH_3 of ester) ppm.
13e	IR: ν = 3200 (NH), 2200 (C ≡N), 1720 (C═O, ester), 1670 (C═O, amide) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 8.9 (s, 1H, NH), 7.0–7.5 (m, 8H, ArH's), 3.9–4.3 (m, 4H: $SCH_2$and OCH_2), 3.8 (s, 3H, OCH_3), 2.7 (s, 3H, CH_3 at C-6), 2.4 (s, 3H, CH_3), 0.9–1.2 (t, 3H, CH_3 of ester) ppm.
13f	IR: ν = 3200 (NH), 2200 (C ≡N), 1720 (C═O, ester), 1670 (C═O, amide) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 8.8 (s, 1H, NH), 7.0–7.7 (m, 8H, ArH's), 4.0–4.4 (m, 4H: $SCH_2$and OCH_2), 3.9 (s, 3H, OCH_3), 3.8 (s, 3H, OCH_3), 2.7 (s, 3H, CH_3 at C-6), 0.9–1.2 (t, 3H, CH_3 of ester) ppm.
13g	IR: ν = 3200 (NH), 2200 (C ≡N), 1720 (C═O, ester), 1670 (2 C═O, amide and acetyl) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 9.3 (s, 1H, NH), 7.5–8.0 (dd, 4H, ArH's), 6.9–7.4 (dd, 4H, ArH's), 3.9–4.3 (m, 4H: $SCH_2$and OCH_2), 3.8 (s, 3H, OCH_3), 2.6 (s, 3H, $COCH_3$), 2.5 (s, 3H, CH_3 at C-6), 0.8–1.1 (t, 3H, CH_3 of ester) ppm.
13h	IR: ν = 3200 (NH), 2200 (C ≡N), 1720 (C═O, ester), 1670 (C═O, amide) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 9.0 (s, 1H, NH), 6.8–7.6 (m, 8H, ArH's), 4.0–4.3 (m, 4H: $SCH_2$and OCH_2), 3.8 (s, 3H, OCH_3), 2.7 (s, 3H, CH_3 at C-6), 0.9–1.2 (t, 3H, CH_3 of ester) ppm.
13i	IR: ν = 3200 (NH), 2200 (C ≡N), 1720 (C═O, ester), 1700 (C═O, ester), 1680 (C═O, amide) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 9.3 (s, 1H, NH), 7.5–8.1 (dd, 4H, ArH's), 6.9–7.5 (dd, 4H, ArH's), 4.0–4.3 (m, 6H: $SCH_2$and $2OCH_2$), 3.8 (s, 3H, OCH_3), 2.7 (s, 3H, CH_3 at C-6), 1.2–1.5 (t, 3H, CH_3 of ester), 0.8–1.1 (t, 3H, CH_3 of ester) ppm.
13j	IR: ν = 3200 (NH), 2200 (C≡N), 1720 (C═O, ester), 1700 (C═O, ester), 1680 (C═O, amide) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 9.3 (s, 1H, NH), 7.5–8.1 (dd, 4H, ArH's), 6.9–7.5 (dd, 4H, ArH's), 4.0–4.3 (m, 4H: $SCH_2$and OCH_2), 3.9 (s, 3H, CO_2CH_3), 3.8 (s, 3H, OCH_3), 2.7 (s, 3H, CH_3 at C-6), 0.9–1.2 (t, 3H, CH_3 of ester) ppm.
14a	IR: ν = 3500, 3300 (NH_2), 3200 (NH), 1720 (C═O, ester), 1660 (C═O, amide) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 8.7 (s, 1H, NH), 7.0–7.7 (m, 9H, ArH's), 5.7 (s, 2H, NH_2), 3.8–4.2 (q, 2H, OCH_2), 2.6 (s, 3H, CH_3 at C-6), 0.7–1.0 (t, 3H, CH_3 of ester) ppm.

TABLE II IR, ^{1}H NMR, and MS Spectral Data of All Newly Synthesized Compounds *(Continued)*

Compound	Spectral Data
14b	IR: ν = 3500, 3300 (NH_2), 3200 (NH), 1720 (C═O, ester), 1660 (C═O, amide) cm.$^{-1}$ ^{1}H NMR ($CDCl_3$): δ = 8.8 (s, 1H, NH), 7.0–7.8 (m, 8H, ArH's), 5.7(s, 2H, NH_2), 3.8–4.1 (q, 2H, OCH_2), 3.8 (s, 3H, OCH_3), 2.7 (s, 3H, CH_3 at C-6), 0.9–1.2 (t, 3H, CH_3 of ester) ppm.
14c	IR: ν = 3500, 3300 (NH_2), 3200 (NH), 1720 (C═O, ester), 1680 (C═O, acetyl), 1660 (C═O, amide) cm.$^{-1}$ ^{1}H NMR (DMSO-d_6): δ = 8.9 (s, 1H, NH), 7.3–8.0 (m, 8H, ArH's), 5.6 (s, 2H, NH_2), 3.9–4.2 (q, 2H, OCH_2), 2.7 (s, 3H, $COCH_3$), 2.6 (s, 3H, CH_3 at C-6), 0.8–1.1 (t, 3H, CH_3 of ester) ppm. MS: 508 (M^+, 100%).
14d	IR: ν = 3500, 3300 (NH_2), 3200 (NH), 1720 (C═O, ester), 1660 (C═O, amide) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 8.7 (s, 1H, NH), 6.9–7.7 (m, 9H, ArH's), 5.8 (s, 2H, NH_2), 3.9–4.2(q, 2H, OCH_2), 3.8 (s, 3H, OCH_3), 2.6 (s, 3H, CH_3 at C-6), 0.8–1.1 (t, 3H, CH_3 of ester) ppm.
14e	IR: ν = 3500, 3300 (NH_2), 3200 (NH), 1720 (C═O, ester), 1660 (C═O, amide) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 8.7 (s, 1H, NH), 6.8–7.7 (m, 8H, ArH's), 5.8 (s, 2H, NH_2), 4.0–4.3 (q, 2H, OCH_2), 3.8 (s, 3H, OCH_3), 2.6 (s, 3H, CH_3 at C-6), 2.4 (s, 3H, CH_3), 0.9–1.1 (t, 3H, CH_3 of ester) ppm.
14f	IR: ν = 3500, 3300 (NH_2), 3200 (NH), 1720 (C═O, ester), 1660 (C═O, amide) cm^{-1}. ^{1}H NMR ((DMSO-d_6): δ = 8.7 (s, 1H, NH), 6.8–7.7 (m, 8H, ArH's), 5.8 (s, 2H, NH_2), 4.0–4.3 (q, 2H, OCH_2), 3.9 (s, 3H, OCH_3), 3.8 (s, 3H, OCH_3), 2.6 (s, 3H, CH_3 at C-6), 0.9–1.1 (t, 3H, CH_3 of ester) ppm.
14g	IR: ν = 3500, 3300 (NH_2), 3200 (NH), 1720 (C═O, ester), 1680 (C═O, acetyl), 1660 (C═O, amide) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 9.0 (s, 1H, NH), 7.7–8.2 (dd, 4H, ArH's), 7.1–7.6 (dd, 4H, ArH's), 6.0 (s, 2H, NH_2), 4.1–4.4 (q, 2H, OCH_2), 4.0 (s, 3H, OCH_3), 2.8 (s, 3H, $COCH_3$), 2.6 (s, 3H, CH_3 at C-6), 1.0–1.3 (t, 3H, CH_3 of ester) ppm.
14h	IR: ν = 3500, 3300 (NH_2), 3200 (NH), 1720 (C═O, ester), 1660 (C═O, amide) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 9.1 (s, 1H, NH), 6.9–7.6 (m, 8H, ArH's), 5.8 (s, 2H, NH_2), 3.9–4.2 (q, 2H, OCH_2), 3.8 (s, 3H, OCH_3), 2.6 (s, 3H, CH_3 at C-6), 0.8–1.1 (t, 3H, CH_3 of ester) ppm.
14i	IR: ν = 3500, 3300 (NH_2), 3200 (NH), 1720 (C═O, ester), 1700 (C═O, ester), 1660 (C═O, amide) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 9.1 (s, 1H, NH), 7.5–8.1 (dd, 4H, ArH's), 6.9–7.4 (dd, 4H, ArH's), 5.9 (s, 2H, NH_2), 4.3–4.6 (q, 2H, OCH_2), 3.9–4.2 (q, 2H, OCH_2), 3.8 (s, 3H, OCH_3), 2.7 (s, 3H, CH_3 at C-6), 1.3–1.6 (t, 3H, CH_3 of ester), 0.9–1.2 (t, 3H, CH_3 of ester) ppm.
14j	IR: ν = 3500, 3300(NH_2), 3200 (NH), 1720 (C═O, ester), 1700 (C═O, ester), 1660 (C═O, amide) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 9.2 (s, 1H, NH), 7.5–8.1 (dd, 4H, ArH's), 6.9–7.5 (dd, 4H, ArH's), 5.9 (s, 2H, NH_2), 4.3–4.6 (q, 2H, OCH_2), 3.9 (s, 6H: OCH_3 and CO_2CH_3), 2.6 (s, 3H, CH_3 at C-6), 0.9–1.2 (t, 3H, CH_3 of ester) ppm.
15a	IR: ν = 1720 (C═O, ester), 1660 (C═O, pyrimidinone) cm^{-1}. ^{1}NMR ($CDCl_3$): δ = 8.0 (s, 1H, CH pyrimidinone), 7.2–7.6 (m, 9H, ArH's), 4.0–4.3(q, 2H, OCH_2), 2.8 (s, 3H, CH_3 at C-7), 1.0–1.3 (t, 3H, CH_3 of ester)
15b	IR: ν = 1720 (C═O, ester), 1660 (C═O, pyrimidinone) cm^{-1}. ^{1}NMR ($CDCl_3$): δ = 8.0 (s, 1H, CH pyrimidinone), 7.0–7.5 (m, 8H, ArH's), 4.0–4.3 (q, 2H, OCH_2), 3.8 (s, 3H, OCH_3), 2.8 (s, 3H, CH_3 at C-7), 1.0–1.3 (t, 3H, CH_3 of ester) ppm.

(Continued on next page)

TABLE II IR, ^{1}H NMR, and MS Spectral Data of All Newly Synthesized Compounds *(Continued)*

Compound	Spectral Data
15c	IR: ν = 1720 (C═O, ester), 1680 (C═O, acetyl), 1660 (C═O, pyrimidinone) cm^{-1}. ^{1}NMR ($CDCl_3$): δ = 8.2 (d, 2H, ArH's), 8.0 (s, 1H, CH pyrimidinone), 7.2–7.6 (m, 6H, ArH's), 4.0–4.3 (q, 2H, OCH_2), 2.8 (s, 3H, $COCH_3$), 2.6 (s, 3H, CH_3 at C-7), 1.0–1.3 (t, 3H, CH_3 of ester) ppm.
15d	IR: ν = 1720 (C═O, ester), 1660 (C═O, pyrimidinone) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 7.9 (s, 1H, CH pyrimidinone), 6.8–7.6 (m, 9H, ArH's), 4.0–4.3 (q, 2H, OCH_2), 3.8 (s, 3H, OCH_3), 2.8(s, 3H, CH_3 at C-7), 0.9–1.2 (t, 3H, CH_3 of ester) ppm.
15e	IR: ν = 1720 (C═O, ester), 1660 (C═O, pyrimidinone) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 8.0 (s, 1H, CH pyrimidinone), 6.8–7.4 (m, 8H, ArH's), 4.0–4.3 (q, 2H, OCH_2), 3.9 (s, 3H, OCH_3), 2.8 (s, 3H, CH_3 at C-7), 2.4 (s, 3H, CH_3), 0.9–1.2 (t, 3H, CH_3 of ester) ppm.
15f	IR: ν = 1720 (C═O, ester), 1660 (C═O, pyrimidinone) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 8.0 (s, 1H, CH pyrimidinone), 6.9–7.4 (m, 8H, ArH's), 4.0–4.3 (q, 2H, OCH_2), 3.8 (s, 6H, two OCH_3), 2.8 (s, 3H, CH_3 at C-7), 0.9–1.2 (t, 3H, CH_3 of ester) ppm. MS: 501 (M^+, 56%).
15g	IR: ν = 1720 (C═O, ester), 1680 (C═O, acetyl), 1660 (C═O, pyrimidinone) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 8.2 (s, 1H, CH pyrimidinone), 7.5–8.0 (dd, 4H, ArH's), 6.9–7.4 (dd, 4H, ArH's),), 4.0–4.3 (q, 2H, OCH_2), 3.8 (s, 3H, OCH_3), 2.8 (s, 3H, $COCH_3$), 2.7 (s, 3H, CH_3 at C-7), 0.9–1.2 (t, 3H, CH_3 of ester) ppm.
15h	IR: ν = 1720 (C═O, ester), 1660 (C═O, pyrimidinone) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 8.1 (s, 1H, CH pyrimidinone), 6.9–7.5 (m, 8H, ArH's), 4.0-4.3 (q, 2H, OCH_2), 3.8 (s, 3H, OCH_3), 2.7 (s, 3H, CH_3 at C-7), 0.9–1.2 (t, 3H, CH_3 of ester) ppm.
15i	IR: ν = 1720 (C═O, ester), 1700 (C═O, esterl), 1660 (C═O, pyrimidinone) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 6.9–8.3 (m, 9H: 8ArH's and CH pyrimidinone), 4.3–4.6 (q, 2H, OCH_2), 3.9–4.2 (q, 2H, OCH_2), 3.8 (s, 3H, OCH_3), 2.8 (s, 3H, CH_3 at C-7), 1.3–1.6 (t, 3H, CH_3 of ester), 0.9–1.2 (t, 3H, CH_3 of ester) ppm.
15j	IR: ν = 1720 (C═O, ester), 1700 (C═O, ester), 1660 (C═O, pyrimidinone) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 8.2 (s, 1H, CH pyrimidinone), 7.4–8.0 (dd, 4H, ArH's), 6.9–7.5 (dd, 4H, ArH's), 4.3–4.6 (q, 2H, OCH_2), 3.9 (s, 6H: OCH_3 and CO_2CH_3), 2.7 (s, 3H, CH_3 at C-7), 0.9–1.2 (t, 3H, CH_3 of ester)
16a	IR: ν = 3400 (NH), 1720 (C═O, ester), 1660 (C═O, pyrimidinone), 1600 (C=N) cm^{-1}. ^{1}NMR (TFA): δ = 8.2 (s, 1H, CH pyrimidinone), 6.8–8.0 (m, 15H, ArH's), 4.0–4.3 (q, 2H, OCH_2), 3.8 (s, 3H, OCH_3), 2.8 (s, 3H, CH_3 at C-7), 2.4 (s, 3H, CH_3C=N), 1.0–1.3 (t, 3H, CH_3 of ester) ppm.
16b	IR: ν = 3500–3400 (NH_2, NH), 1720 (C═O, ester), 1660 (C═O, pyrimidinone), 1600 (C=N) cm^{-1}. ^{1}H NMR (DMSO-d_6):: δ = 8.2 (s, 1H, CH pyrimidinone), 6.8–8.0 (m, 8H, ArH's), 5.5 (s, 2H, NH_2), 4.0–4.3 (q, 2H, OCH_2), 3.9 (s, 3H, OCH_3), 2.7(s, 3H, CH_3C=N), 2.5 (s, 3H, CH_3 at C-6), 1.0–1.3 (t, 3H, CH_3 of ester) ppm.
17a	IR: ν = 1720 (C═O, ester), 1660 (C═O, triazinone) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 7.1–7.6 (m, 9H, ArH's), 3.9–4.2 (q, 2H, OCH_2), 2.8 (s, 3H, CH_3 at C-7), 1.0–1.3 (t, 3H, CH_3 of ester) ppm.

TABLE II IR, ^{1}H NMR, and MS Spectral Data of All Newly Synthesized Compounds *(Continued)*

Compound	Spectral Data
17b	IR: ν = 1720 (C═O, ester), 1660 (C═O, triazinone) cm^{-1}. ^{1}NMR ($CDCl_3$): δ = 7.0–7.6 (m, 8H, ArH's), 4.0–4.3 (q, 2H, OCH_2), 3.8 (s, 3H, OCH_3), 2.7 (s, 3H, CH_3 at C-7), 1.0–1.3 (t, 3H, CH_3 of ester) ppm.
17c	IR: ν = 1720 (C═O, ester), 1680 (C═O, acetyl), 1660 (C═O, triazinone) cm^{-1}. ^{1}NMR ($CDCl_3$): δ = 8.1 (d, 2H, ArH's), 7.2–7.5 (m, 6H, ArH's), 4.0–4.3 (q, 2H, OCH_2), 2.8 (s, 3H, $COCH_3$), 2.6 (s, 3H, CH_3 at C-7), 0.9–1.2 (t, 3H, CH_3 of ester) ppm.
17d	IR: ν = 1720 (C═O, ester), 1660 (C═O, triazinone) cm^{-1}. ^{1}NMR ($CDCl_3$): δ = 6.9–7.7 (m, 9H, ArH's), 4.1–4.4 (q, 2H, OCH_2), 3.9 (s, 3H, OCH_3), 2.8 (s, 3H, CH_3 at C-6), 0.9–1.2 (t, 3H, CH_3 of ester) ppm. MS: 472 (M^+, 100%).
17e	IR: ν = 1720 (C═O, ester), 1660 (C═O, triazinone) cm^{-1}. ^{1}NMR ($CDCl_3$): δ = 6.8–7.5 (m, 8H, ArH's), 4.0–4.3 (q, 2H, OCH_2), 3.8 (s, 3H, OCH_3), 2.7 (s, 3H, CH_3 at C-7), 2.4 (s, 3H, CH_3), 0.9–1.2 (t, 3H, CH_3 of ester) ppm.
17f	IR: ν = 1720 (C═O, ester), 1660 (C═O, triazinone) cm^{-1}. ^{1}NMR ($CDCl_3$): δ = 6.9–7.6 (m, 8H, ArH's), 4.0–4.3 (q, 2H, OCH_2), 3.8 (s, 6H, two OCH_3), 2.8 (s, 3H, CH_3 at C-7), 0.9–1.2 (t, 3H, CH_3 of ester) ppm. .
17g	IR: ν = 1720 (C═O, ester), 1680 (C═O, acetyl),1660 (C═O, triazinone) cm^{-1}. ^{1}NMR ($CDCl_3$): δ = 7.7–8.2 (dd, 4H, ArH's), 6.9–7.4 (dd, 4H, ArH's),), 4.0–4.3 (q, 2H, OCH_2), 3.8 (s, 3H, OCH_3), 2.8 (s, 3H, $COCH_3$), 2.7 (s, 3H, CH_3 at C-7), 0.9–1.2 (t, 3H, CH_3 of ester) ppm.
17h	IR: ν = 1720 (C═O, ester), 1660 (C═O, triazinone) cm^{-1}. ^{1}NMR ($CDCl_3$): δ = 7.1–7.6 (m, 8H, ArH's), 4.0–4.3 (q, 2H, OCH_2), 3.9 (s, 3H, OCH_3), 2.8 (s, 3H, CH_3 at C-7), 1.0–1.3 (t, 3H, CH_3 of ester) ppm.
17i	IR: ν = 1720 (C═O, ester), 1700 (C═O, ester),1660 (C═O, triazinone) cm.$^{-1}$. ^{1}H NMR ($CDCl_3$): δ = 7.0–8.4 (m, 8H, ArH's), 4.3–4.6 (q, 2H, OCH_2), 3.9–4.2 (q, 2H, OCH_2), 3.8 (s, 3H, OCH_3), 2.7 (s, 3H, CH_3 at C-7), 1.3–1.6 (t, 3H, CH_3 of ester), 0.9–1.2 (t, 3H, CH_3 of ester) ppm.
17j	IR: ν = 1720 (C═O, ester), 1700 (C═O, ester), 1660 (C═O, triazinone) cm.$^{-1}$. ^{1}H NMR ($CDCl_3$): δ = 7.4–8.0 (dd, 4H, ArH's), 6.9–7.5 (dd, 4H, ArH's), 4.3–4.6 (q, 2H, OCH_2), 3.9 (s, 6H: OCH_3 and CO_2CH_3), 2.8 (s, 3H, CH_3 at C-7), 1.0–1.3 (t, 3H, CH_3 of ester) ppm.
18	IR: ν = 3300 (NH), 1720 (C═O, ester), 1660 (C═O, triazinone) cm^{-1}. ^{1}NMR (TFA): δ = 7.2–7.7 (m, 9H, ArH's), 3.9–4.2 (q, 2H, OCH_2), 2.8 (s, 3H, CH_3 at C-7), 0.9–1.2 (t, 3H, CH_3 of ester) ppm.
19	IR: ν = 1720 (C═O, ester), 1660 (C═O, triazinone) cm^{-1}. ^{1}NMR (TFA): δ = 7.2–7.7 (m, 9H, ArH's), 3.9–4.2 (q, 2H, OCH_2), 2.9 (s, 3H, CH_3 at C-7), 1.8 (s, 3H, SCH_3), 1.0–1.3 (t, 3H, CH_3 of ester) ppm.

chloro-*N*-arylacetamide (10 mmol) was added. The resulting mixture was refluxed for 20 min. The yellow precipitate that formed on cooling was collected and recrystallized from ethanol to give compounds **14a–i**. These products were identical in all aspects to those described in Method A.

Synthesis of Ethyl 3-amino-4-aryl-2-[*N*-(4-methoxycarbonylphenyl)]carbamoyl–6-methylthieno[2,3-b]pyridine-5-carboxylate (14j)

Method A

Compound **13j** (2.6 g, 5 mmol) was suspended in sodium methoxide solution (0.11 g sodium in 30 mL abs. methanol) and heated under reflux for 5 min. The solid that formed on cooling was collected and recrystallized from ethanol to give canary yellow crystals of **14j** (Table I).

Method B

To a suspension of compound **12a,b** (5 mmol) in sodium methoxide solution (0.23 g sodium in 30 mL abs. methanol), the respective chloro-*N*-(4-methoxycarbonylpheny) acetamide (10 mmol) was added. The resulting mixture was refluxed for 20 min. The yellow precipitate that formed on cooling was collected and recrystallized from ethanol to give compound **14j** (yield: 76%). This product was identical in all aspects to that described in Method A

Synthesis of 3,9-diaryl-8-ethoxycarbonyl-7-methylpyrido [3′,2′:4,5]thieno[3,2-d]pyrimidine-4(3*H*)-ones (15a–j)

A mixture of **14a–j** (2 mmol) and triethyl orthoformate (1 mL) in acetic anhydride (5 mL) was refluxed for 4 h. The solid that formed while hot was collected and recrystallized from an ethanol-chloroform mixture to give white needles of **15a–j**. Melting points, yields, and analytical data of these compounds are given in Table I.

Condensation of Compound 15g with Aniline or Thiosemicarbazide; General Procedure

To a mixture of **15 g** (1.03 g, 2 mmol) and aniline or thiosemicarbazide (2 mmol) in ethanol (20 mL), a few drops of acetic acid were added. The reaction mixture was refluxed for 2 h. and then left to cool. The precipitated solid was collected and recrystalized from an ethanol-chloroform mixture to give white crystals of **16a** or **16b**, respectively. Melting points, yields, and analytical data of these compounds are given in Table I.

Synthesis of 3,9-Diaryl-8-ethoxycarbonyl-7-methylpyrido [3′,2′:4,5]thieno[3,2-d][1,2,3] triazine-4(3*H*)-ones (17a–j)

Sodium nitrite solution 10% (4 mL) was added to a solution of compound **14a–j** (2 mmol) in concentrated sulphuric acid (4 mL) and glacial acetic acid (4 mL) at 0°C during 5 min. with stirring. The mixture was allowed

to stand at r.t. for 30 min. The solid that precipitated on dilution with water was collected and recrystallized from ethanol as white needles of **17a–j**. Melting points, yields, and analytical data of these compounds are given in Table I.

Synthesis of 9-(4-Chlorophenyl)-8-ethoxycarbonyl-7-methyl-4-oxo-3-phenyl-1,2,3,4-tetrahydro-2-thioxopyrido [3′,2′:4,5]thieno[3,2-d]pyrimidine (18)

A mixture of **14a** (1.4 g, 3 mmol) and carbon disulphide (3 mL) in dry pyridine (20 mL) was refluxed on a water bath for 48 h. During the reaction time, hydrogen sulphide evolved. The solvent was removed by distillation under reduced pressure and the residue was crystallized from acetic acid to give pale yellow crystals of **18** (Table I).

Synthesis of 9-(4-Chlorophenyl)-5-ethoxycarbonyl-2-methylthio-7-methyl-3-phenylpyrido [3′,2′:4,5]thieno[3,2-d]pyrimidine-4(3*H*)-one (19)

Compound **18** (0.5 g, 2 mmol) was dissolved in 4% (5 mL, 5 mmol) ethanolic sodium hydroxide solution. To this solution methyl iodide (0.2 mL, 3 mmol) was added. The reaction mixture was refluxed for 2 h. The precipitate on cooling was filtered off and recrsytallized from ethanol as white needles of **19** (Table I).

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