Synthesis and Reactions of Some New Heterocyclic Compounds Containing Cycloalka[e]thieno[2,3-b]pyridine Moiety

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Hydrolysis of ethyl 3-amino-4-aryl-cycloalka[e]thieno[2,3-b]pyridine-2-carboxylates (**3a-d)** gave the corresponding *o*-aminocarboxylic acids **4a-d**. Heating the latter compounds (**4a-d)** with acetic anhydride furnished the oxazinone derivatives **5a-d** which, in turn, underwent recyclization reaction to give the corresponding pyrimidinones **6a-d** upon treatment with ammonium acetate in acetic acid. Reaction of 3-amino-4-aryl-cycloalka[e]thieno[2,3-b]pyridine-2-carboxamides (**3f,h**) with triethyl orthoformate gave pyrimidinone derivatives **7a,b**. Reaction of 3-amino-4-phenyl-cycloalka[e]thieno[2,3-b]pyridine-2-carboxamides **3e,h** with aromatic aldehydes furnished tetrahydropyridothienopyrimidinones **8a-d**. Chlorination of **7a,b** and **6a-d** by using phosphorous oxychloride produced 4-chlorocycloalka[5′,6′]pyrido[3′,2′:4,5]thieno[3,2-d]pyrimidine derivatives **9a-f** which were used as key intermediates in the synthesis of several new cycloalkapyridothienopyrimidines **10a-f**~**14a-f**. Moreover, some cycloalkapyridothienotriazinones **15a,b-17a,b** were synthesized.

Keywords: Cycloalkathienopyridines; Cycloalkapyridothienooxazinones; Cycloalkapyridothienopyrimidines; Cycloalkapyridothienotriazinones.

INTRODUCTION

Numerous thieno[2,3-b]pyridines have been investigated in relation with their biological and pharmacological activities. Some of them have proved to possess antibaterial,[1,2] antiviral,[3] antihypertensive,[4] and immunostimulating[5] activities. Others are useful as gonadtropin-releasing hormone antagonists[6-11] and as lipoxygenases inhibitors.[12] Recently, certain thieno[2,3-b]pyridine derivatives were prepared as antinflammatory agents, particularly for treating arthritis and bone resorption inhibiting agents.[13] In view of all these benefits and as a continuation of our interest in the field of heterocyclic compounds particularly condensed pyrimidines,[14-17,19,20] we undertook the synthesis of new condensed thieno[2,3-b]pyridine derivatives with anticipated biological and medicinal properties.

RESULTS AND DISCUSSION

Our approach to the synthesis of the target compounds started from 3-cyano-4-aryl-cycloalka[b]pyridine-2(1*H*)-thiones (**1a-f**) which were reacted with ethyl chloroacetate, chloroacetamide or Chloro-*N*-arylacetamides, in the presence of sodium acetate as a basic catalyst, to give *S*-substituted thiopyridines **2a-j**. The latter compounds underwent intramolecular *Thorpe-Ziegler* cyclization to give the corresponding 2-functionalized 3-amino-4-aryl-cycloalka[e]thieno[2,3-b]pyridines (**3a-j**) upon boiling with ethanol containing a catalytic amount of sodium ethoxide. The compounds **3a-j** were also syntheisized *via* direct reaction of **1a-f** with the respective halo compounds in the presence of a slightly excess amount of sodium ethoxide as a basic catalyst (Scheme I).

Saponification of the *o*-aminoester **3a-d** with an ethanolic sodium hydroxide solution followed by acidification with acetic acid gave the corresponding carboxylic acids **4a-d**. These compounds underwent ring closure reaction upon treatment with acetic anhydride to afford the oxazinone derivatives **5a-d**. Recyclization of the latter compounds into the corresponding pyrimidinone derivatives **6a-d** were achieved upon heating with ammonium acetate in glacial acetic acid (Scheme II).

Reaction of *o*-aminoamide derivatives **3f,h** with triethyl orthoformate in the presence of acetic anhydride furnished 9-aryl-cycloalka[5′,6′]pyrido[3′,2′:4,5]thieno[3,2-d]pyrimi-

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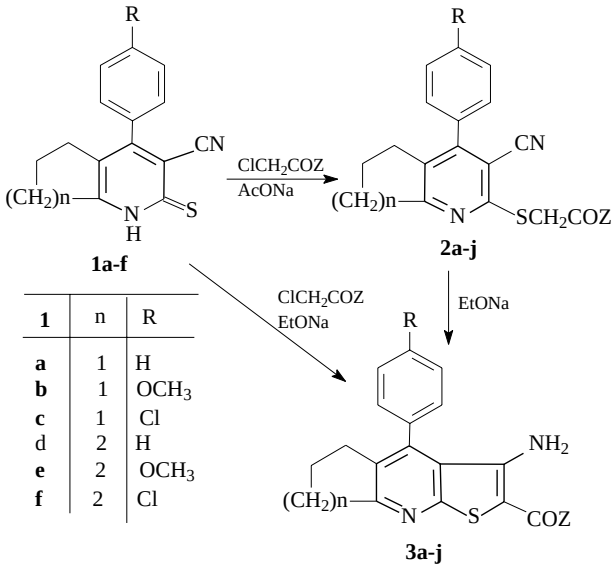
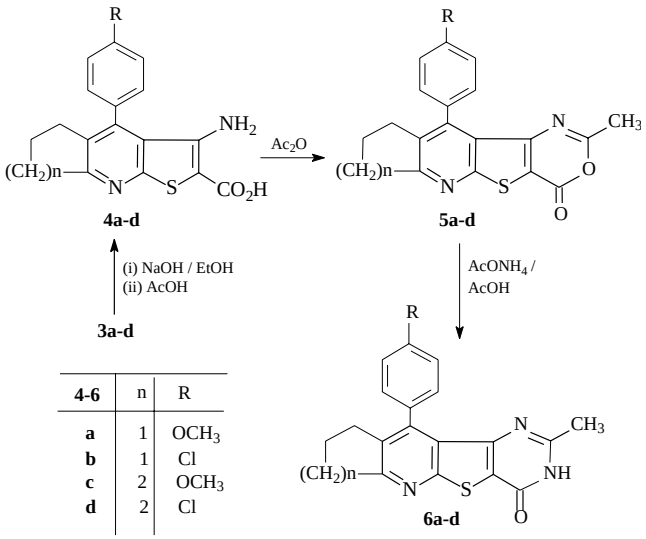
Scheme I



1	n	R
a	1	H
b	1	OCH_3
c	1	Cl
d	2	H
e	2	OCH_3
f	2	Cl

2, 3	n	R	Z
a	1	OCH_3	OEt
b	1	Cl	OEt
c	2	OCH_3	OEt
d	2	Cl	OEt
e	1	H	NH_2
f	1	Cl	NH_2
g	2	H	NH_2
h	2	OCH_3	NH_2
i	2	OCH_3	NHPh
j	2	OCH_3	$NHC_6H_4OCH_3(p)$

Scheme II



4-6	n	R
a	1	OCH_3
b	1	Cl
c	2	OCH_3
d	2	Cl

dine-4(3*H*)-ones (**7a,b**). Reaction of *o*-aminoamide derivatives **3e,g** with aromatic aldehydes in the presence of a catalytic amount of HCl furnished 1,2,3,4-tetrahydro-cycloalka-[5′,6′]pyrido[3′,2′:4,5]thieno[3,2-d]pyrimidine-4(3*H*)-ones **8a-d** in excellent yield (Scheme III).

Chlorination of pyrimidinones **7a,b** and **6a-d** to produce the corresponding 4-chloropyrimidine derivatives **9a,b** and **9c-f** was achieved upon boiling with an excess amount of phosphorus oxychloride. The reaction of **9a-f** with thiourea, followed by treatment of the resulting adduct with sodium hydroxide solution and then acidification with acetic acid gave cycloalka[5′,6′]pyrido[3′,2′:4,5]thieno[3,2-d]pyrimidine-4(3*H*)-thione derivatives **10a-f**. When **10a-f** was allowed to react with methyl iodide or ethyl chloroacetate in the presence of sodium acetate, the corresponding 4-substituted thiopyrimidines **11a-g** were obtained (Scheme IV).

The chloropyrimidine derivatives **9a-f** underwent another nucleophilic displacement upon treatment with hydrazine hydrate to afford the corresponding 4-hydrazinopyridothienopyrimidines **12a-f**. On treatment of **12a-f** with benzaldehyde in refluxing ethanol, the corresponding 4-benzylidenehydrazinopyridothienopyrimidines **13a-f** were obtained. The cyclocondensation of **9a-f** with acetylacetone under neat conditions furnished the dimethylpyrazolyl derivatives **14a-f** (Scheme V).

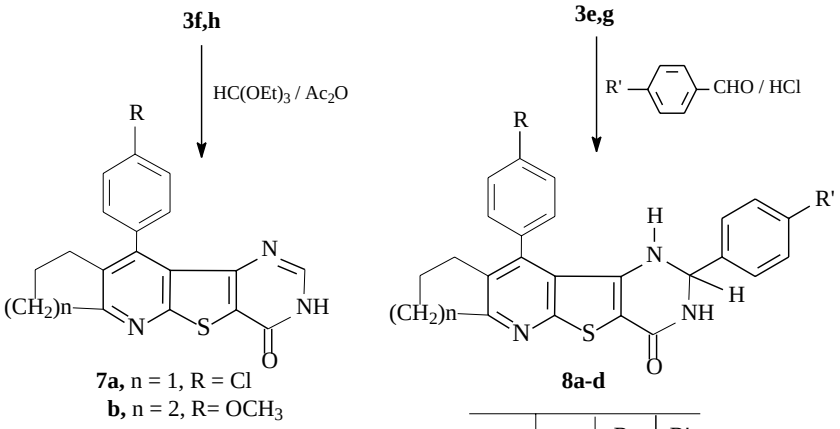
Diazotization of compounds **3f,h** and/or **3i,j** in AcOH-H_2SO_4 mixture by using sodium nitrite solution at low temperature resulted in the formation of 1,2,3-triazinone derivatives **15a,b** and **16a,b**, respectively. The reaction of compound **15a** with ethyl chloroacetate or chloroacetamide in DMF containing anhydrous K_2CO_3 led to the formation of the *N*-alkylated triazinone derivatives **17a,b** in high yield (Scheme VI).

The structures of all newly synthesized compounds were elucidated and confirmed by elemental analyses, IR, ^{1}H NMR and mass spectral data (*cf.* Tables 1, 2).

EXPERIMENTAL

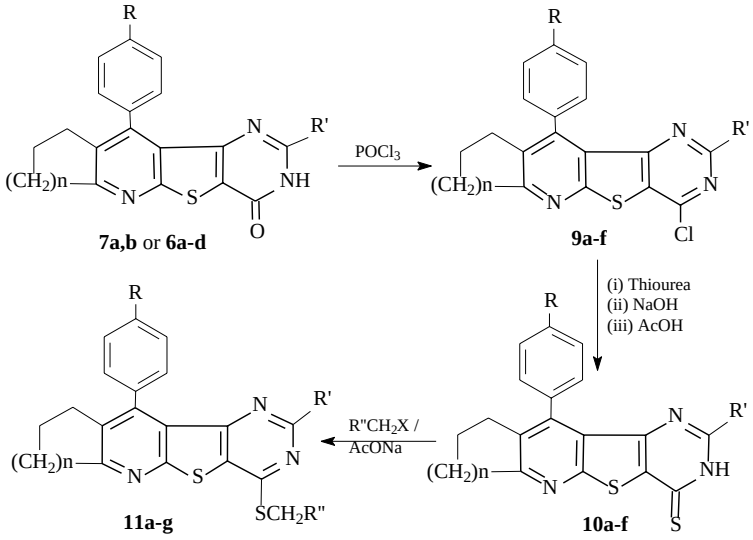
All melting points are uncorrected and measured on a Gallen-Kamp apparatus. IR spectra were recorded on a Shimadzu 470 IR-spectrophotometer using KBr pellets (ν_{max} in cm^{-1}). ^{1}H NMR spectra were obtained on a Varian EM-390, 90 MHz spectrometer using TMS as internal reference (chemical shifts in δ; ppm) and MS on a Jeol JMS-600 mass spectrometer. Elemental analyses (C, H, N, S) were carried

Scheme III



8	n	R	R'
a	1	H	H
b	1	H	OCH_3
c	2	H	H
d	2	H	OCH_3

Scheme IV

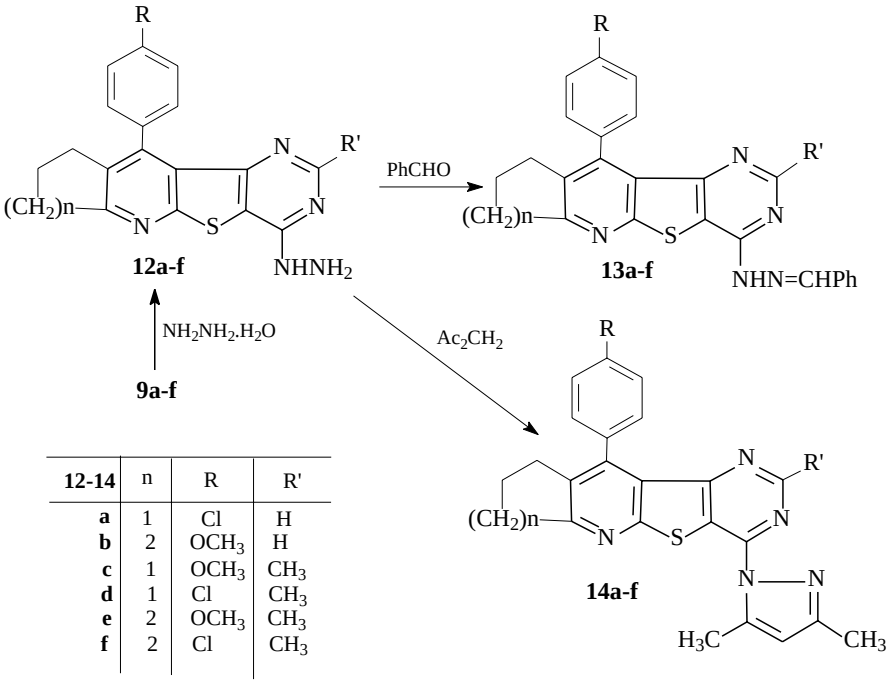


11	n	R	R'	R"
a	1	Cl	H	H
b	2	OCH_3	H	H
c	2	OCH_3	H	CO_2Et
d	1	OCH_3	CH_3	H
e	1	OCH_3	CH_3	CO_2Et
f	2	OCH_3	CH_3	H
g	2	OCH_3	CH_3	CO_2Et

9, 10	n	R	R'
a	1	Cl	H
b	2	OCH_3	H
c	1	OCH_3	CH_3
d	1	Cl	CH_3
e	2	OCH_3	CH_3
f	2	Cl	CH_3

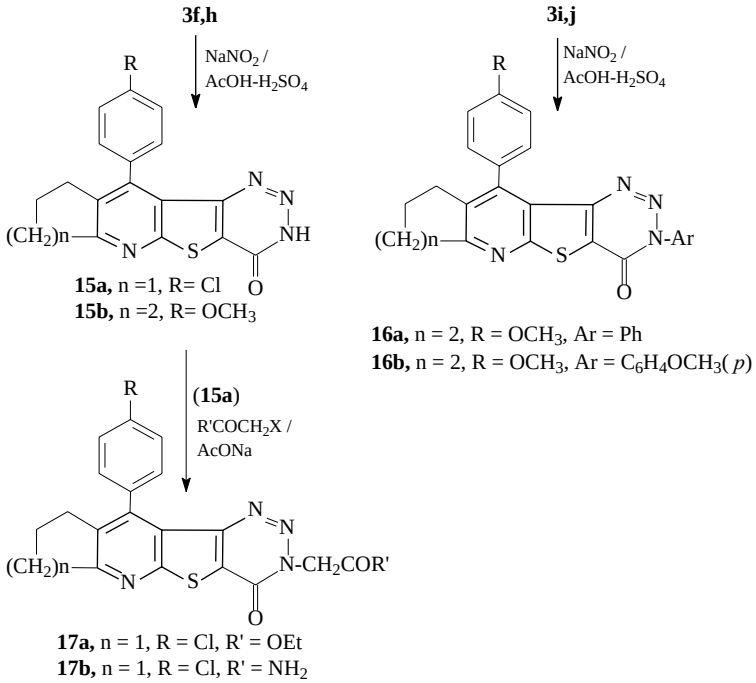
out on an Elemental Analyses System GmbH VARIOEL V2.3 July 1998 CHNS Mode. Chlorine analyses were determined using oxygen flask method by the Microanalytical Unit at Assiut University. The purity of all synthesized compounds was checked by TLC. The compounds **1a-c**,[14,15] **1d-f**,[18] **2a,e**,[14] **2c,h**,[19] **2d,g**,[18] **3a,e**,[14] **3c,h**,[19] **3d,g**,[18] **4a**,[14] **4c**,[19] **4d**,[20] **5a**[14] and **5d**,[20] **6a**[14]and **6d**[20] were prepared according to the reported methods.

Scheme V



12-14	n	R	R'
a	1	Cl	H
b	2	OCH_3	H
c	1	OCH_3	CH_3
d	1	Cl	CH_3
e	2	OCH_3	CH_3
f	2	Cl	CH_3

Scheme VI



Reaction of compounds 1c,e with ethyl chloroacetate, chloroacetamide or chloro-*N*-arylacetamides: Formation of *S*-substituted thiopyridines 2b,f,i,j

To a suspension of compound **1c,e** (0.02 mol) and sodium acetate trihydrate (3.0 g, 0.022 mol) in ethanol (50 mL), the respective halo compound (ethyl chloroacetate, chloroacetamide or chloro-*N*-arylacetamide) (0.02 mol) was added. The resulting mixture was heated under reflux for 2 h. The

Table 1. Melting points, yields, and analytical data of all new compounds

Compd. No.	Mp (°C)/ Yield (%)	Formula (M. Wt.)	Analysis (calculated/found %)				
			C	H	N	S	Cl
2b	126-127	$C_{19}H_{17}ClN_2O_2S$	61.20	4.60	7.51	8.60	9.51
	88	(372.87)	61.12	4.63	7.46	8.92	9.20
2f	189-190	$C_{17}H_{14}ClN_3OS$	59.39	4.10	12.22	9.32	10.31
	87	(343.83)	59.18	3.92	12.51	9.00	10.00
2i	186-187	$C_{25}H_{23}N_3O_2S$	69.91	5.40	9.78	7.46	-
	84	(429.54)	70.19	5.44	9.76	7.71	-
2j	183-184	$C_{26}H_{25}N_3O_3S$	67.95	5.48	9.14	6.98	-
	83	(459.55)	68.15	5.31	9.37	7.10	-
3b	198-199	$C_{19}H_{17}ClN_2O_2S$	61.20	4.60	7.51	8.60	9.51
	90	(372.87)	61.43	4.48	7.66	8.30	9.45
3f	219-220	$C_{17}H_{14}ClN_3OS$	59.39	4.10	12.22	9.32	10.31
	91	(343.83)	59.18	4.02	12.45	9.47	10.00
3i	251-252	$C_{25}H_{23}N_3O_2S$	69.91	5.40	9.78	7.46	-
	93	(429.54)	70.09	5.78	9.64	7.71	-
3j	285-286	$C_{26}H_{25}N_3O_3S$	67.95	5.48	9.14	6.98	-
	90	(459.55)	67.67	5.50	8.91	7.20	-
4b	192-193	$C_{17}H_{13}ClN_2O_2S$	59.22	3.80	8.12	9.30	10.28
	82	(344.82)	59.11	3.76	8.29	9.42	10.00
5b	206-207	$C_{19}H_{13}ClN_2O_2S$	61.87	3.55	7.60	8.69	9.61
	90	(368.84)	62.02	3.49	7.33	9.00	9.48
5c	198-199	$C_{21}H_{18}N_2O_3S$	66.65	4.79	7.40	8.47	-
	87	(378.45)	66.74	4.82	7.11	8.29	-
6b	351-352	$C_{19}H_{14}ClN_3OS$	62.04	3.84	11.42	8.72	9.64
	79	(367.85)	62.17	3.87	11.56	8.53	9.40
6c	346-347	$C_{21}H_{19}N_3O_2S$	66.82	5.07	11.13	8.49	-
	84	(377.46)	62.69	5.11	11.51	8.20	-
7a	357-358	$C_{18}H_{12}ClN_3OS$	61.10	3.42	11.88	9.06	10.02
	80	(353.83)	61.00	3.26	12.25	9.27	9.80
7b	340-341	$C_{20}H_{17}N_3O_2S$	66.10	4.71	11.56	8.82	-
	92	(363.43)	65.93	4.76	11.74	9.02	-
8a	320-321	$C_{24}H_{19}N_3OS$	72.52	4.82	10.57	8.07	-
	78	(397.49)	72.55	4.88	10.63	8.04	-
8b	289-290	$C_{25}H_{21}N_3O_2S$	70.24	4.96	9.83	7.50	-
	77	(427.52)	70.31	5.07	9.60	7.29	-
8c	316-317	$C_{25}H_{21}N_3OS$	72.97	5.14	10.21	7.79	-
	80	(411.52)	72.86	5.05	10.30	7.92	-
8d	288-289	$C_{26}H_{23}N_3O_2S$	70.72	5.25	9.52	7.26	-
	79	(441.55)	70.89	5.31	9.54	7.34	-
9a	213-214	$C_{18}H_{11}Cl_2N_3S$	45.78	2.35	8.90	6.79	15.01
	80	(472.27)	45.60	2.32	8.78	6.87	15.40
9b	191-192	$C_{20}H_{16}ClN_3OS$	62.90	4.22	11.00	8.40	9.28
	83	(381.88)	63.16	4.07	11.15	8.58	9.00
9c	185-186	$C_{20}H_{16}ClN_3OS$	62.90	4.22	11.00	8.40	9.28
	81	(381.88)	62.71	4.10	11.11	8.69	9.50
9d	200-201	$C_{19}H_{13}Cl_2N_3S$	59.08	3.39	10.88	8.30	18.36
	82	(386.30)	59.37	3.62	11.02	8.61	18.10
9e	180-181	$C_{21}H_{18}ClN_3OS$	63.71	4.58	10.61	8.10	8.95
	79	(395.91)	63.89	4.68	10.54	8.34	9.10
9f	197-198	$C_{20}H_{15}Cl_2N_3S$	60.01	3.78	10.50	8.01	17.71
	80	(400.33)	60.34	3.89	10.41	8.20	17.50
10a	308-309	$C_{18}H_{12}ClN_3S_2$	58.45	3.27	11.36	17.33	9.58
	73	(369.89)	58.71	3.01	11.48	17.56	9.35
10b	291-292	$C_{20}H_{17}N_3OS_2$	63.30	4.52	11.07	16.90	-
	77	(379.49)	63.07	4.66	10.93	16.97	-
10c	308-309	$C_{20}H_{17}N_3OS_2$	63.30	4.52	11.07	16.90	-
	75	(379.49)	63.22	4.40	10.96	16.67	-
10d	315-316	$C_{19}H_{14}ClN_3S_2$	59.44	3.68	10.95	16.70	9.23
	74	(383.91)	59.54	3.63	11.22	16.55	9.15
10e	312-313	$C_{21}H_{19}N_3OS_2$	64.10	4.87	10.68	16.29	-
	76	(393.52)	64.14	4.87	10.71	16.42	-

10f	318-319	$C_{20}H_{16}ClN_3S_2$	60.37	4.05	10.56	16.11	8.91
	77	(397.94)	60.13	3.89	10.68	16.16	9.10
11a	234-235	$C_{19}H_{14}ClN_3S_2$	59.44	3.68	10.95	16.70	9.23
	82	(383.91)	59.35	3.64	11.25	16.59	9.00
11b	192-193	$C_{21}H_{19}N_3OS_2$	64.10	4.87	10.68	16.29	-
	84	(393.52)	63.89	4.85	10.82	16.13	-
11c	140-141	$C_{24}H_{23}N_3O_3S_2$	61.92	4.98	9.03	13.77	-
	80	(465.58)	61.84	4.89	9.33	13.61	-
11d	218-219	$C_{21}H_{19}N_3OS_2$	64.10	4.87	10.68	16.29	-
	81	(393.52)	63.86	4.64	10.92	16.19	-
11e	172-173	$C_{24}H_{23}N_3O_3S_2$	61.92	4.98	9.03	13.77	-
	78	(465.58)	61.96	4.73	9.11	13.82	-
11f	184-185	$C_{22}H_{21}N_3OS_2$	64.84	5.19	10.31	15.73	-
	75	(407.55)	65.02	5.18	10.17	15.77	-
11g	171-172	$C_{25}H_{25}N_3O_3S_2$	62.61	5.25	8.76	13.37	-
	78	(479.61)	62.79	5.53	8.50	13.51	-
12a	290-291	$C_{18}H_{14}ClN_5S$	58.77	3.84	19.04	8.72	9.64
	86	(367.86)	58.64	3.75	19.21	8.48	9.50
12b	297-298	$C_{20}H_{19}N_5OS$	63.64	5.07	18.55	8.49	-
	88	(377.46)	63.35	5.08	18.39	8.43	-
12c	288-289	$C_{20}H_{19}N_5OS$	63.64	5.07	18.55	8.49	-
	83	(377.46)	63.61	5.00	18.44	8.56	-
12d	305-306	$C_{19}H_{16}ClN_5S$	59.76	4.22	18.34	8.40	9.28
	88	(381.88)	59.72	4.17	18.52	8.34	9.15
12e	297-298	$C_{21}H_{21}N_5OS$	64.43	5.41	17.89	8.19	-
	85	(391.48)	64.34	5.36	17.74	7.90	-
12f	284-285	$C_{20}H_{18}ClN_5S$	60.68	4.58	17.69	8.10	8.95
	85	(395.91)	60.99	4.56	17.87	7.77	9.10
13a	318-319	$C_{25}H_{18}ClN_5S$	65.86	3.98	15.36	7.03	7.78
	86	(455.96)	66.02	3.72	15.49	7.26	8.00
13b	332-333	$C_{27}H_{23}N_5OS$	69.66	4.98	15.04	6.89	-
	81	(465.57)	69.73	4.79	15.25	6.82	-
13c	319-320	$C_{27}H_{23}N_5OS$	69.66	4.98	15.04	6.89	-
	80	(465.57)	69.56	4.90	15.18	7.11	-
13d	331-332	$C_{26}H_{20}ClN_5S$	66.45	4.29	14.90	6.82	7.54
	86	(469.99)	66.52	4.24	15.17	6.71	7.50
13e	342-343	$C_{28}H_{25}N_5OS$	70.12	5.25	14.60	6.68	-
	84	(479.60)	70.14	7.36	14.82	6.50	-
13f	317-318	$C_{27}H_{22}ClN_5S$	67.00	4.58	14.47	6.62	7.32
	82	(484.02)	67.11	4.56	14.82	6.57	7.30
14a	238-239	$C_{23}H_{18}ClN_5S$	63.96	4.20	16.21	7.42	8.21
	87	(431.94)	63.77	4.21	16.12	7.33	8.00
14b	260-261	$C_{25}H_{23}N_5OS$	68.00	5.25	15.86	7.26	-
	86	(441.55)	68.13	5.16	15.49	7.19	-
14c	268-269	$C_{25}H_{23}N_5OS$	68.00	5.25	15.86	7.26	-
	90	(441.55)	67.88	5.29	16.03	7.39	-
14d	235-236	$C_{24}H_{20}ClN_5S$	64.64	4.52	15.70	7.19	7.95
	88	(445.97)	64.67	4.45	15.92	7.42	7.80
14e	218-219	$C_{26}H_{25}N_5OS$	68.55	5.53	15.37	7.04	-
	80	(455.57)	68.34	5.48	15.41	7.17	-
14f	236-237	$C_{25}H_{22}ClN_5S$	65.28	4.82	15.22	6.97	7.71
	82	(460.00)	65.45	4.92	15.16	7.10	7.90
15a	360-361	$C_{17}H_{11}ClN_4OS$	57.55	3.12	15.79	9.04	9.99
	80	(354.81)	57.67	3.11	15.64	8.97	9.85
15b	310-311	$C_{19}H_{16}N_4O_2S$	62.62	4.43	15.37	8.80	-
	87	(364.42)	62.39	4.56	15.62	8.73	-
16a	253-254	$C_{25}H_{20}N_4O_2S$	68.16	4.58	12.72	7.28	-
	92	(440.52)	68.04	4.72	12.95	7.18	-
16b	255-256	$C_{26}H_{22}N_4O_3S$	66.37	4.71	11.91	6.81	-
	91	(470.55)	66.12	4.73	11.96	6.94	-
17a	194-195	$C_{21}H_{17}ClN_4O_3S$	57.21	3.89	12.71	7.27	8.04
	73	(440.90)	57.00	3.87	12.90	7.42	8.30
17b	310-311	$C_{19}H_{14}ClN_5O_2S$	55.41	3.43	17.00	7.78	8.61
	73	(411.87)	55.78	3.46	16.83	7.49	8.35

Table 2. Spectral data of all new compounds

Compd. No.	Spectral Data
2b	IR: 2200 (C≡N), 1730 (C=O). ^{1}H NMR ($CDCl_3$): 7.0-7.4 (dd, 4H, ArH's), 4.2 (q, 2H, OCH_2), 3.9 (s, 2H, SCH_2), 3.0 (t, 2H, CH_2 at C-7), 2.6 (t, 2H, CH_2 at C-5), 2.1 (p, 2H, CH_2 at C-6), 1.3 (t, 3H, CH_3 of ester group).
2f	IR: 3420-3150 (NH_2), 2200 (C≡N), 1660 (C=O). ^{1}H NMR ($CDCl_3$): 7.0-7.4 (dd, 4H, ArH's), 6.8 (s, 2H, NH_2), 3.8 (s, 2H, SCH_2), 3.0 (t, 2H, CH_2 at C-7), 2.6 (t, 2H, CH_2 at C-5), 2.1 (p, 2H, CH_2 at C-6).
2i	IR: 3200 (NH), 2200 (C≡N), 1660 (C=O). ^{1}H NMR ($CDCl_3$): 9.0 (s, 1H, NH), 6.9-7.5 (m, 9H, ArH's), 4.0 (s, 3H, OCH_3), 3.8 (s, 2H, SCH_2), 3.0 (t, 2H, CH_2 at C-8), 2.6 (t, 2H, CH_2 at C-5), 1.6-2.1 (m, 4H, $2CH_2$ at C-6,7). MS; *m/z* = 429 (M^+, 100%).
2j	IR: 3200 (NH), 2200 (C≡N), 1660 (C=O). ^{1}H NMR ($CDCl_3$): 8.9 (s, 1H, NH), 6.9-7.5 (m, 8H, ArH's), 4.0 (s, 6H, $2OCH_3$), 3.8 (s, 2H, SCH_2), 3.0 (t, 2H, CH_2 at C-8), 2.6 (t, 2H, CH_2 at C-5), 1.6-2.1 (m, 4H, $2CH_2$ at C-6,7).
3b	IR: 3500, 3340 (NH_2), 1660 (C=O). ^{1}H NMR ($CDCl_3$): 7.0-7.4 (dd, 4H, ArH's), 5.6 (s, 2H, NH_2), 4.2 (q, 2H, OCH_2), 3.0 (t, 2H, CH_2 at C-7), 2.6 (t, 2H, CH_2 at C-5), 2.1 (p, 2H, CH_2 at C-6), 1.3 (t, 3H, CH_3 of ester group).
3f	IR: 3450, 3330, 3150 ($2NH_2$), 1650 (C=O). ^{1}H NMR ($CDCl_3$): 7.0-7.6 (m, 6H, ArH's and $CONH_2$), 5.8 (s, 2H, NH_2), 3.0 (t, 2H, CH_2 at C-7), 2.6 (t, 2H, CH_2 at C-5), 2.1 (p, 2H, CH_2 at C-6).
3i	IR: 3500, 3300, 3200 (NH_2, NH), 1650 (C=O). ^{1}H NMR ($CDCl_3$): 9.2 (s, 1H, NH), 7.0-7.6 (m, 9H, ArH's), 5.5 (s, 2H, NH_2), 4.0 (s, 3H, OCH_3), 3.0 (t, 2H, CH_2 at C-8), 2.6 (t, 2H, CH_2 at C-5), 1.6-2.1 (m, 4H, $2CH_2$ at C-6,7).
3j	IR: 3500, 3300, 3200 (NH_2, NH), 1650 (C=O). ^{1}H NMR ($CDCl_3$): 9.0 (s, 1H, NH), 7.0-7.6 (m, 9H, ArH's), 5.5 (s, 2H, NH_2), 4.0 (s, 6H, $2OCH_3$), 3.0 (t, 2H, CH_2 at C-8), 2.6 (t, 2H, CH_2 at C-5), 1.6-2.1 (m, 4H, $2CH_2$ at C-6,7). MS; *m/z* = 459 (M^+, 90%).
4b	IR: 3480, 3320 (NH_2), 1640 (C=O). ^{1}H NMR ($CDCl_3$): 10.1 (s, 1H, CO_2H), 7.1-7.5 (dd, 4H, ArH's), 6.0 (s, 2H, NH_2), 3.1 (t, 2H, CH_2 at C-7), 2.7 (t, 2H, CH_2 at C-5), 2.1 (p, 2H, CH_2 at C-6).
5b	IR: 1740 (C=O). ^{1}H NMR ($CDCl_3$): 7.0-7.4 (dd, 4H, ArH's), 3.1 (t, 2H, CH_2 at C-7), 2.8 (t, 2H, CH_2 at C-9), 1.9-2.4 (m, 5H, CH_3 at C-2 and CH_2 at C-8).
5c	IR: 1750 (C=O). ^{1}H NMR ($CDCl_3$): 7.0-7.4 (dd, 4H, ArH's), 3.9 (s, 3H, OCH_3), 3.0 (t, 2H, CH_2 at C-7), 2.5 (t, 2H, CH_2 at C-10), 2.2 (s, 3H, CH_3), 1.5-1.9 (m, 4H, $2CH_2$ at C-8,9).
6b	IR: 3200-3400 (NH), 1650 (C=O). ^{1}H NMR (TFA): 6.9-7.4 (dd, 4H, ArH's), 3.1 (t, 2H, CH_2 at C-7), 2.8 (t, 2H, CH_2 at C-9), 2.0-2.5 (m, 5H, CH_3 at C-2 and CH_2 at C-8).
6c	IR: 3200-3400 (NH), 1660 (C=O). ^{1}H NMR (TFA): 7.1-7.5 (dd, 4H, ArH's), 4.1 (s, 3H, OCH_3), 3.2 (t, 2H, CH_2 at C-7), 2.7 (t, 2H, CH_2 at C-10), 2.4 (s, 3H, CH_3 at C-2), 1.7-2.1 (m, 4H, $2CH_2$ at C-8,9).
7a	IR: 3200-3400 (NH), 1660 (C=O). ^{1}H NMR (TFA): 8.5 (s, 1H, CH pyrimidine), 7.0-7.4 (dd, 4H, ArH's), 3.1 (t, 2H, CH_2 at C-7), 2.8 (t, 2H, CH_2 at C-9), 2.2 (p, 2H, CH_2 at C-8).
7b	IR: 3200-3400 (NH), 1650 (C=O). ^{1}H NMR (TFA): 8.6 (s, 1H, CH pyrimidine), 7.1-7.5 (dd, 4H, ArH's), 4.0 (s, 3H, OCH_3), 3.2 (t, 2H, CH_2 at C-7), 2.6 (t, 2H, CH_2 at C-10), 1.7-2.1 (m, 4H, $2CH_2$ at C-8,9). MS; *m/z* = 363 (M^+, 100%).
8a	IR: 3400, 3200 (2NH), 1640 (C=O). ^{1}H NMR (DMSO-d_6): 8.5 (d, 1H, CONH), 7.0-7.5 (m, 10H, ArH's), 5.8 (t, 1H, CH), 5.4 (d, 1H, NH), 3.1 (t, 2H, CH_2 at C-7), 2.7 (t, 2H, CH_2 at C-9), 2.1 (p, 2H, CH_2 at C-8).
8b	IR: 3400, 3200 (2NH), 1640 (C=O). ^{1}H NMR (DMSO-d_6): 8.4 (d, 1H, CONH), 7.1-7.6 (m, 9H, ArH's), 5.9 (t, 1H, CH), 5.4 (d, 1H, NH), 3.9 (s, 3H, OCH_3), 3.1 (t, 2H, CH_2 at C-7), 2.6 (t, 2H, CH_2 at C-9), 2.1 (p, 2H, CH_2 at C-8).
8c	IR: 3400, 3200 (2NH), 1640 (C=O). ^{1}H NMR (DMSO-d_6): 8.4 (d, 1H, CONH), 7.0-7.6 (m, 10H, ArH's), 5.8 (t, 1H, CH), 5.3 (d, 1H, NH), 3.1 (t, 2H, CH_2 at C-7), 2.6 (t, 2H, CH_2 at C-10), 1.5-2.0 (m, 4H, $2CH_2$ at C-8,9).
8d	IR: 3400, 3200 (2NH), 1640 (C=O). ^{1}H NMR (DMSO-d_6): 8.5 (d, 1H, CONH), 7.1-7.6 (m, 9H, ArH's), 6.0 (t, 1H, CH), 5.4 (d, 1H, NH), 3.9 (s, 3H, OCH_3), 3.2 (t, 2H, CH_2 at C-7), 2.6 (t, 2H, CH_2 at C-10), 1.5-2.0 (m, 4H, $2CH_2$ at C-8,9).
9a	IR: 1600 (C=N). ^{1}H NMR ($CDCl_3$): 8.5 (s, 1H, CH pyrimidine), 7.0-7.4 (dd, 4H, ArH's), 3.1 (t, 2H, CH_2 at C-7), 2.7 (t, 2H, CH_2 at C-9), 2.1 (p, 2H, CH_2 at C-8).
9b	IR: 1600 (C=N). ^{1}H NMR ($CDCl_3$): 8.6 (s, 1H, CH pyrimidine), 7.1-7.5 (dd, 4H, ArH's), 4.0 (s, 3H, OCH_3), 3.0 (t, 2H, CH_2 at C-7), 2.6 (t, 2H, CH_2 at C-10), 1.6-2.1 (m, 4H, $2CH_2$ at C-8,9).
9c	IR: 1600 (C=N). ^{1}H NMR ($CDCl_3$): 6.9-7.3 (dd, 4H, ArH's), 3.9 (s, 3H, OCH_3), 3.0 (t, 2H, CH_2 at C-7), 2.6 (t, 2H, CH_2 at C-9), 2.3 (s, 3H, CH_3 at C-2), 1.9-2.1 (p, 2H, CH_2 at C-8).

9d IR: 1600 (C=N). ^{1}H NMR ($CDCl_3$): 7.0-7.4 (dd, 4H, ArH's), 3.1 (t, 2H, CH_2 at C-7), 2.6 (t, 2H, CH_2 at C-9), 2.3 (s, 3H, CH_3 at C-2), 1.9-2.1 (p, 2H, CH_2 at C-8). MS; *m/z* = 386 (M^+, 100%).

9e IR: 1600 (C=N). ^{1}H NMR ($CDCl_3$): 7.0-7.4 (dd, 4H, ArH's), 3.9 (s, 3H, OCH_3), 3.1 (t, 2H, CH_2 at C-7), 2.7 (t, 2H, CH_2 at C-10), 2.2 (s, 3H, CH_3 at C-2), 1.5-2.0 (m, 4H, $2CH_2$ at C-8,9).

9f IR: 1600 (C=N). ^{1}H NMR ($CDCl_3$): 7.0-7.4 (dd, 4H, ArH's), 3.0 (t, 2H, CH_2 at C-7), 2.6 (t, 2H, CH_2 at C-10), 2.2 (s, 3H, CH_3 at C-2), 1.5-2.0 (m, 4H, $2CH_2$ at C-8,9).

10a IR: 3200 (NH). ^{1}H NMR (TFA): 8.6 (s, 1H, CH pyrimidine), 7.0-7.4 (dd, 4H, ArH's), 3.1 (t, 2H, CH_2 at C-7), 2.7 (t, 2H, CH_2 at C-9), 2.2 (p, 2H, CH_2 at C-8).

10b IR: 3200 (NH). ^{1}H NMR (TFA): 8.6 (s, 1H, CH pyrimidine), 7.0-7.4 (dd, 4H, ArH's), 4.0 (s, 3H, OCH_3), 3.0 (t, 2H, CH_2 at C-7), 2.6 (t, 2H, CH_2 at C-10), 1.6-2.1 (m, 4H, $2CH_2$ at C-8,9).

10c IR: 3200 (NH). ^{1}H NMR (TFA): 7.1-7.5 (dd, 4H, ArH's), 4.0 (s, 3H, OCH_3), 3.1 (t, 2H, CH_2 at C-7), 2.7 (t, 2H, CH_2 at C-9), 2.4 (s, 3H, CH_3 at C-2), 2.2 (p, 2H, CH_2 at C-8).

10d IR: 3200 (NH). ^{1}H NMR (TFA): 7.0-7.4 (dd, 4H, ArH's), 3.0 (t, 2H, CH_2 at C-7), 2.6 (t, 2H, CH_2 at C-9), 2.3 (3H, CH_3 at C-2), 2.1 (p, 2H, CH_2 at C-8). MS; *m/z* = 384 (M^+, 67%).

10e IR: 3200 (NH). ^{1}H NMR (TFA): 7.0-7.4 (dd, 4H, ArH's), 3.9 (s, 3H, OCH_3), 3.1 (t, 2H, CH_2 at C-7), 2.7 (t, 2H, CH_2 at C-10), 2.2 (s, 3H, CH_3 at C-2), 1.5-2.0 (m, 4H, $2CH_2$ at C-8,9).

10f IR: 3200 (NH). ^{1}H NMR (TFA): 7.0-7.4 (dd, 4H, ArH's), 3.1 (t, 2H, CH_2 at C-7), 2.6 (t, 2H, CH_2 at C-10), 2.2 (s, 3H, CH_3 at C-2), 1.5-2.0 (m, 4H, $2CH_2$ at C-8,9).

11a IR: 1600 (C=N). ^{1}H NMR ($CDCl_3$): 8.5 (s, 1H, CH pyrimidine), 7.0-7.4 (dd, 4H, ArH's), 3.1 (t, 2H, CH_2 at C-7), 2.8 (s, 3H, SCH_3), 2.6 (t, 2H, CH_2 at C-9), 2.2 (p, 2H, CH_2 at C-8).

11b IR: 1600 (C=N). ^{1}H NMR ($CDCl_3$): 8.6 (s, 1H, CH pyrimidine), 7.0-7.4 (dd, 4H, ArH's), 4.0 (s, 3H, OCH_3), 3.0 (t, 2H, CH_2 at C-7), 2.8 (s, 3H, SCH_3), 2.6 (t, 2H, CH_2 at C-10), 1.6-2.1 (m, 4H, $2CH_2$ at C-8,9). MS; *m/z* = 393 (M^+, 100%).

11c IR: 1730 (C=O). ^{1}H NMR ($CDCl_3$): 8.6 (s, 1H, CH pyrimidine), 7.0-7.4 (dd, 4H, ArH's), 4.2 (q, 2H, OCH_2), 3.9 (s, 2H, SCH_2), 3.7 (s, 3H, OCH_3), 3.0 (t, 2H, CH_2 at C-7), 2.6 (t, 2H, CH_2 at C-10), 1.5-2.0 (m, 4H, $2CH_2$ at C-8,9), 1.2 (t, 3H, CH_3 of ester).

11d IR: 1600 (C=N). ^{1}H NMR ($CDCl_3$): 7.0-7.4 (dd, 4H, ArH's), 4.0 (s, 3H, OCH_3), 3.0 (t, 2H, CH_2 at C-7), 2.8 (s, 3H, SCH_3), 2.6 (t, 2H, CH_2 at C-9), 2.2 (s, 3H, CH_3 at C-2), 2.1 (p, 2H, CH_2 at C-8).

11e IR: 1730 (C=O). ^{1}H NMR ($CDCl_3$): 7.0-7.4 (dd, 4H, ArH's), 4.2 (q, 2H, OCH_2), 3.9 (s, 2H, SCH_2), 3.7 (s, 3H, OCH_3), 3.0 (t, 2H, CH_2 at C-7), 2.6 (t, 2H, CH_2 at C-9), 2.3 (3H, CH_3 at C-2), 2.1 (p, 2H, CH_2 at C-8), 1.2 (t, 3H, CH_3 of ester).

11f IR: 1600 (C=N). ^{1}H NMR ($CDCl_3$): 7.0-7.4 (dd, 4H, ArH's), 3.9 (s, 3H, OCH_3), 3.1 (t, 2H, CH_2 at C-7), 2.9 (s, 3H, SCH_3), 2.6 (t, 2H, CH_2 at C-10), 2.2 (s, 3H, CH_3 at C-2), 1.5-2.0 (m, 4H, $2CH_2$ at C-8,9).

11g IR: 1730 (C=O). ^{1}H NMR ($CDCl_3$): 7.0-7.4 (dd, 4H, ArH's), 4.2 (q, 2H, OCH_2), 3.9 (s, 2H, SCH_2), 3.7 (s, 3H, OCH_3), 3.0 (t, 2H, CH_2 at C-7), 2.6 (t, 2H, CH_2 at C-10), 2.3 (3H, CH_3 at C-2), 2.1-1.5 (m, 4H, $2CH_2$ at C-8,9), 1.2 (t, 3H, CH_3 of ester).

12a IR: 3460, 3320, 3180 ($NHNH_2$), 1640 (C=N). ^{1}H NMR (DMSO-d_6): 8.5 (s, 1H, CH pyrimidine), 8.1 (br, 1H, NH), 7.0-7.4 (dd, 4H, ArH's), 4.2 (br, 2H, NH_2), 3.1 (t, 2H, CH_2 at C-7), 2.7 (t, 2H, CH_2 at C-9), 2.1 (p, 2H, CH_2 at C-8).

12b IR: 3460, 3320, 3180 ($NHNH_2$), 1640 (C=N). ^{1}H NMR (DMSO-d_6): 8.6 (s, 1H, CH pyrimidine), 8.0 (br, 1H, NH), 7.1-7.5 (dd, 4H, ArH's), 4.3 (br, 2H, NH_2), 4.0 (s, 3H, OCH_3), 3.0 (t, 2H, CH_2 at C-7), 2.6 (t, 2H, CH_2 at C-10), 1.6-2.1 (m, 4H, $2CH_2$ at C-8,9).

12c IR: 3460, 3320, 3180 ($NHNH_2$), 1640 (C=N). ^{1}H NMR (DMSO-d_6): 8.0 (br, 1H, NH), 6.9-7.3 (dd, 4H, ArH's), 4.3 (br, 2H, NH_2), 3.9 (s, 3H, OCH_3), 3.0 (t, 2H, CH_2 at C-7), 2.6 (t, 2H, CH_2 at C-9), 2.3 (s, 3H, CH_3 at C-2), 1.9-2.1 (p, 2H, CH_2 at C-8).

12d IR: 3460, 3320, 3180 ($NHNH_2$), 1640 (C=N). ^{1}H NMR (DMSO-d_6): 8.1 (br, 1H, NH), 7.0-7.4 (dd, 4H, ArH's), 4.3 (br, 2H, NH_2), 3.1 (t, 2H, CH_2 at C-7), 2.6 (t, 2H, CH_2 at C-9), 2.3 (s, 3H, CH_3 at C-2), 1.9-2.1 (p, 2H, CH_2 at C-8).

12e IR: 3460, 3320, 3180 ($NHNH_2$), 1640 (C=N). ^{1}H NMR (DMSO-d_6): 8.0 (br, 1H, NH), 7.0-7.4 (dd, 4H, ArH's), 4.3 (br, 2H, NH_2), 3.9 (s, 3H, OCH_3), 3.1 (t, 2H, CH_2 at C-7), 2.7 (t, 2H, CH_2 at C-10), 2.2 (s, 3H, CH_3 at C-2), 1.5-2.0 (m, 4H, $2CH_2$ at C-8,9).

12f IR: 3460, 3320, 3180 ($NHNH_2$), 1640 (C=N). ^{1}H NMR (DMSO-d_6): 8.0 (br, 1H, NH), 7.0-7.4 (dd, 4H, ArH's), 4.2 (br, 2H, NH_2), 3.0 (t, 2H, CH_2 at C-7), 2.6 (t, 2H, CH_2 at C-10), 2.2 (s, 3H, CH_3 at C-2), 1.5-2.0 (m, 4H, $2CH_2$ at C-8,9).

13a IR: 3200 (NH). ^{1}H NMR (TFA): 8.5 (s, 1H, CH pyrimidine), 7.0-7.4 (m, 10H, ArH's and N=CH), 3.1 (t, 2H, CH_2 at C-7), 2.6 (t, 2H, CH_2 at C-9), 2.1 (p, 2H, CH_2 at C-8).

13b	IR: 3200 (NH). ^{1}H NMR (TFA): 8.6 (s, 1H, CH pyrimidine), 7.1-7.5 (m, 10H, ArH's and N=CH), 4.0 (s, 3H, OCH_3), 3.0 (t, 2H, CH_2 at C-7), 2.6 (t, 2H, CH_2 at C-10), 1.6-2.1 (m, 4H, $2CH_2$ at C-8,9).
13c	IR: 3200 (NH). ^{1}H NMR (TFA): 6.9-7.3 (m, 10H, ArH's and N=CH), 3.9 (s, 3H, OCH_3), 3.0 (t, 2H, CH_2 at C-7), 2.6 (t, 2H, CH_2 at C-9), 2.3 (s, 3H, CH_3 at C-2), 1.9-2.1 (p, 2H, CH_2 at C-8).
13d	IR: 3200 (NH). ^{1}H NMR (TFA): 7.0-7.4 (m, 10H, ArH's and N=CH), 3.1 (t, 2H, CH_2 at C-7), 2.6 (t, 2H, CH_2 at C-9), 2.3 (s, 3H, CH_3 at C-2), 1.9-2.1 (p, 2H, CH_2 at C-8).
13e	IR: 3200 (NH). ^{1}H NMR (TFA): 7.0-7.4 (m, 10H, ArH's and N=CH), 3.9 (s, 3H, OCH_3), 3.1 (t, 2H, CH_2 at C-7), 2.6 (t, 2H, CH_2 at C-10), 2.2 (s, 3H, CH_3 at C-2), 1.5-2.0 (m, 4H, $2CH_2$ at C-8,9).
13f	IR: 3200 (NH). ^{1}H NMR (TFA): 7.0-7.4 (m, 10H, ArH's and N=CH), 3.0 (t, 2H, CH_2 at C-7), 2.6 (t, 2H, CH_2 at C-10), 2.2 (s, 3H, CH_3 at C-2), 1.5-2.0 (m, 4H, $2CH_2$ at C-8,9).
14a	IR: 1600 (C=N). ^{1}H NMR (DMSO-d_6): 8.5 (s, 1H, CH pyrimid-ine), 7.0-7.4 (dd, 4H, ArH's), 6.0 (s, 1H, CH pyrazole), 3.1 (t, 2H, CH_2 at C-7), 2.8 (s, 3H, CH_3 attached to pyrazole ring), 2.6 (t, 2H, CH_2 at C-9), 2.3 (s, 3H, CH_3 attached to pyrazole ring), 2.1 (p, 2H, CH_2 at C-8).
14b	IR: 1600 (C=N). ^{1}H NMR (DMSO-d_6): 8.6 (s, 1H, CH pyrimid-ine), 7.1-7.5 (dd, 4H, ArH's), 6.1 (s, 1H, CH pyrazole), 4.0 (s, 3H, OCH_3), 3.0 (t, 2H, CH_2 at C-7), 2.8 (s, 3H, CH_3 attached to pyrazole ring), 2.6 (t, 2H, CH_2 at C-10), 2.4 (s, 3H, CH_3 attached to pyrazole ring), 1.6-2.1 (m, 4H, $2CH_2$ at C-8,9).
14c	IR: 1600 (C=N). ^{1}H NMR (DMSO-d_6): 6.9-7.3 (dd, 4H, ArH's), 5.9 (s, 1H, CH pyrazole), 3.9 (s, 3H, OCH_3), 3.0 (t, 2H, CH_2 at C-7), 2.8 (s, 3H, CH_3 attached to pyrazole ring), 2.6 (t, 2H, CH_2 at C-9), 2.4 (s, 3H, CH_3 attached to pyrazole ring), 2.2 (s, 3H, CH_3 at C-2), 1.9-2.1 (p, 2H, CH_2 at C-8).
14d	IR: 1600 (C=N). ^{1}H NMR (DMSO-d_6): 7.0-7.4 (dd, 4H, ArH's), 6.0 (s, 1H, CH pyrazole), 3.1 (t, 2H, CH_2 at C-7), 2.8 (s, 3H, CH_3 attached to pyrazole ring), 2.6 (t, 2H, CH_2 at C-9), 2.4 (s, 3H, CH_3 attached to pyrazole ring), 2.2 (s, 3H, CH_3 at C-2), 1.9-2.1 (p, 2H, CH_2 at C-8).
14e	IR: 1600 (C=N). ^{1}H NMR (DMSO-d_6): 7.0-7.4 (dd, 4H, ArH's), 6.1 (s, 1H, CH pyrazole), 3.9 (s, 3H, OCH_3), 3.1 (t, 2H, CH_2 at C-7), 2.8 (s, 3H, CH_3), 2.6 (t, 2H, CH_2 at C-10), 2.4 (s, 3H, CH_3), 2.2 (s, 3H, CH_3), 1.5-2.0 (m, 4H, $2CH_2$ at C-8,9).
14f	IR: 1600 (C=N). ^{1}H NMR (DMSO-d_6): 7.0-7.4 (dd, 4H, ArH's), 6.0 (s, 1H, CH pyrazole), 3.0 (t, 2H, CH_2 at C-7), 2.8 (s, 3H, CH_3 attached to pyrazole ring), 2.6 (t, 2H, CH_2 at C-10), 2.4 (s, 3H, CH_3 attached to pyrazole ring), 2.2 (s, 3H, CH_3 at C-2), 1.5-2.0 (m, 4H, $2CH_2$ at C-8,9).
15a	IR: 3200-3400 (NH), 1660 (C=O). ^{1}H NMR (TFA): 7.0-7.4 (dd, 4H, ArH's), 3.1 (t, 2H, CH_2 at C-7), 2.8 (t, 2H, CH_2 at C-9), 2.2 (p, 2H, CH_2 at C-8).
15b	IR: 3200-3400 (NH), 1650 (C=O). ^{1}H NMR (TFA): 7.1-7.5 (dd, 4H, ArH's), 4.0 (s, 3H, OCH_3), 3.2 (t, 2H, CH_2 at C-7), 2.6 (t, 2H, CH_2 at C-10), 1.7-2.1 (m, 4H, $2CH_2$ at C-8,9).
16a	IR: 1670 (C=O). ^{1}H NMR ($CDCl_3$): 7.0-7.6 (m, 9H, ArH's), 4.0 (s, 3H, OCH_3), 3.2 (t, 2H, CH_2 at C-7), 2.6 (t, 2H, CH_2 at C-10), 1.7-2.1 (m, 4H, $2CH_2$ at C-8,9).
16b	IR: 1670 (C=O). ^{1}H NMR ($CDCl_3$): 7.0-7.6 (m, 8H, ArH's), 4.0 (s, 6H, $2OCH_3$), 3.2 (t, 2H, CH_2 at C-7), 2.6 (t, 2H, CH_2 at C-10), 1.7-2.1 (m, 4H, $2CH_2$ at C-8,9).
17a	IR: 1740 (C=O, ester), 1680 (C=O, triazinone). ^{1}H NMR ($CDCl_3$): 7.1-7.5 (dd, 4H, ArH's), 5.2 (s, 2H, NCH_2), 4.2 (q, 2H, OCH_2), 3.1 (t, 2H, CH_2 at C-7), 2.8 (t, 2H, CH_2 at C-9), 2.2 (p, 2H, CH_2 at C-8), 1.2 (t, 3H,CH_3 of ester).
17b	IR: 3350, 3150 (NH_2), 1680 (2C=O). ^{1}H NMR ($CDCl_3$): 7.1-7.5 (dd, 4H, ArH's), 6.8 (s, 2H, $CONH_2$), 5.2 (s, 2H, NCH_2), 3.1 (t, 2H, CH_2 at C-7), 2.8 (t, 2H, CH_2 at C-9), 2.2 (p, 2H, CH_2 at C-8).

precipitate that formed on cooling was collected by filtration and recrystallized from ethanol as white needles of **2b,f,i,j**.

2-Functionalized 3-amino-4-aryl-cycloalka[e]thieno[2,3-b]pyridines (3b,f,i,j)

Method A

Compounds **2b,f,i,j** (0.01 mol) were suspended in sodium ethoxide solution (0.12 g sodium in 30 mL abs. ethanol) and heated under reflux for 5 min. The solid that formed while hot was collected and recrystallized from ethanol-chloroform to give canary yellow crystals of **3b,f,i,j**.

Method B

To a suspension of compound **1c,e** (0.01 mol) in sodium ethoxide solution (0.35 g sodium in 40 mL abs. ethanol), ethyl chloroacetate, chloroacetamide or chloro-*N*-arylacetamides (0.01 mol) was added. The resulting mixture was refluxed for 20 min. and then left to cool. The formed yellow precipitate was collected and recrystallized from ethanol-chloroform to give compounds **3b,f,i,j** (yield; 76-83%). These products were identical in all aspects to those de-

scribed in method A.

3-Amino-4-(4-chlorophenyl)-cyclopenta[e]thieno[2,3-b]-pyridine-2-carboxylic acid (4b)

A suspension of **3b** (0.03 mol) in an ethanolic sodium hydroxide solution 7% (70 mL) was heated under reflux for 4 h and then allowed to cool. The reaction mixture was diluted with 50 mL water, filtered and then the clear filtrate was acidified with dilute acetic acid. The precipitate was collected and crystallized from ethanol to give yellow crystals of **4b**.

2-Methyl-cycloalka[5′,6′]pyrido[3′,2′:4,5]thieno[3,2-d]-oxazine-4-ones 5b,c

Compound **4b,c** (0.01 mol) in redistilled acetic anhydride (40 mL) was heated under reflux for 4 h. The reaction mixture was then concentrated by normal distillation and allowed to cool. The solid that separated was collected by filtration and dried in air to give yellowish white needles of **5b,c**.

2-Methyl-cycloalka[5′,6′]pyrido[3′,2′:4,5]thieno[3,2-d]pyrimidine-4(3*H*)-ones 6b,c

A mixture of **5b,c** (0.001 mol) and ammonium acetate (0.3 g, 0.004 mol) in glacial acetic acid (25 mL) was refluxed for 3 h and then left to cool. The product was collected by filtration and recrystallized from ethanol to give white needles of **6b,c**.

Cycloalka[5′,6′]pyrido[3′,2′:4,5]thieno[3,2-d]pyrimidine-4(3*H*)-ones 7a,b

A mixture of compound **3f,h** (0.005 mol) and triethyl orthoformate (5 mL) in acetic anhydride (20 mL) was refluxed for 4 h. The solid that formed on cooling was collected and recrystallized from an ethanol-chloroform mixture to give white crystals of **7a,b**.

4-Oxo-1,2,3,4-tetrahydro-cycloalka[5′,6′]pyrido[3′,2′:4,5]-thieno[3,2-d]pyrimidines 8a-d

A mixture of compound **3e,g** (0.002 mol) and the respective aldehyde (0.002 mol) in ethanol (20 mL) containing a few drops of HCl was heated under reflux for 3 h. The product that formed while hot was collected and recrystallized from acetic acid to give **8a-d** in the form of yellow needles.

4-Chloro-cyloalka[5′,6′]pyrido[3′,2′:4,5]thieno[3,2-d]pyrimidine 9a-f

Compound **7a,b** or **6a-d** (0.01 mol) in an excess amount of phosphorus oxychloride (25 mL) was gently refluxed for 4 h. The cooled reaction mixture was poured with vigorous stirring into ice-water (100 mL). The separated solid was collected and crystallized from ethanol as white needles of **9a-f**.

Cycloalka[5′,6′]pyrido[3′,2′:4,5]thieno[3,2-d]pyrimidine-4(3*H*)-thiones 10a-f

A mixture of chloro compound **9a-f** (0.005 mol) and thiourea (0.76 g, 0.01 mol) in DMF (20 mL) was gently refluxed for 3 h. The precipitate that formed on cooling was collected, dissolved in warm 10% sodium hydroxide solution and then filtered off. The clear filtrate was acidified with dilute aceitc acid whereby a yellow precipitate separated. It was collected and crystallized from an ethanol-chloroform mixture as yellow needles of **10a-f**.

4-(*S*-Substituted)methylthio-cycloalka[5′,6′]pyrido-[3′,2′:4,5]thieno[3,2-d]pyrimidines 11a-g

To a mixture of **10a-c** or **10e** (0.004 mol) and sodium acetate trihydrate (1.36 g, 0.01 mol) in ethanol (30 mL), methyl iodide or ethyl chloroacetate (0.005 mol) was added. The reaction mixture was refluxed for 2 h. The precipitate that formed on cooling was collected and recrystallized from ethanol as white crystals of **11a-g**.

4-Hydrazino-cycloalka[5′,6′]pyrido[3′,2′:4,5]thieno[3,2-d]-pyrimidines 12a-f

A mixture of **9a-f** (0.005 mol) and hydrazine hydrate 99% (1.0 mL, 0.02 mol) in ethanol (20 mL) was refluxed for 2 h. The product that formed was collected and recrystallized from dioxane to give pale yellow needles of **12a-f**.

4-Benzylidenehydrazino-cycloaka[5′,6′]pyrido[3′,2′:4,5]-thieno[3,2-d]pyrimidines 13a-f

A mixture of **12a-f** (0.004 mol) and benzaldehyde (0.005 mol) in ethanol (30 mL) was refluxed for 3 h. The product that precipitated on cooling was collected and recrystallized from dioxane as white needles of **13a-f**.

4-(3,5-Dimethylpyrazol-1-yl)-cycloaka[5′,6′]pyrido-[3′,2′:4,5]thieno[3,2-d]pyrimidines 14a-f

A mixture of **12a-f** (0.004 mol) and acetylacetone (10 mL) was gently refluxed for 4 h. The reaction mixture was then triturated with ethanol (15 mL) and left to cool. The precipitated product was collected and recrystallized from ethanol to give white needles of **14a-f**.

Cycloalka[5′,6′]pyrido[3′,2′:4,5]thieno[3,2-d][1,2,3]triazines 15a,b and 16a,b

Sodium nitrate solution 10% (12 mL, 0.015 mol) was

added to a solution of **3f,h** and/or **3i,j** (0.01 mol) in conc. sulfuric acid (5 mL) and glacial acetic acid (5 mL) at 0 °C during 5 min. with stirring. The solid that precipitated on dilution with cold water was collected and crystallized from ethanol as white crystals of **15a,b** and **16a,b**, respectively.

3-Substituted 10-(4-chlorophenyl)cyclopenta[5′,6′]pyrido-[3′,2′:4,5]thieno[3,2-d][1,2,3]triazines 17a,b

A solution of triazinone **15a** (0.002 mol) in DMF (15 mL) was stirred for a while with anhydrous potassium carbonate (0.8 g), and then the respective halo compound (ethyl chloroacetate or chloroacetamide) (0.002 mol) was added. The mixture was stirred at 80 °C for 2 h. and then diluted with water (25 mL). The precipitated solid was collected and crystallized from ethanol to give white needles of **17a,b**.

Received November 9, 2004.

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