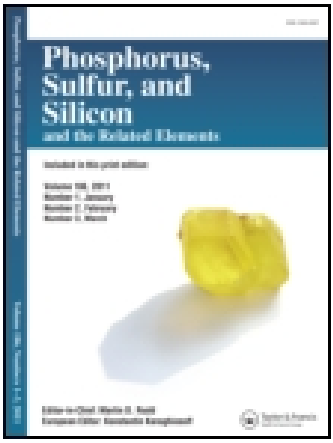

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Synthesis and Reactions of Some New Heterocyclic Compounds Related to Pyrrolylthieno[2,3-d]Pyrimidines and Thieno[2,3-d][4,5-d] Dipyrimidines

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Synthesis and Reactions of Some New Heterocyclic Compounds Related to Pyrrolylthieno[2,3-d]Pyrimidines and Thieno[2,3-d][4,5-d] Dipyrimidines

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*Condensation of ethyl-5-amino-2,4-diphenylthieno[2,3-d]pyrimidine-6-carboxylate (**3a**) with 2,5-dimethoxy tetrahydrofurane in acetic acid gives the corresponding 5-pyrrolyl derivative **4**, which in turn could be easily reacted with hydrazine hydrate in ethanol yielding the carbohydrazide derivative **5**. Reaction of **5** with aromatic aldehydes, acetylacetone, carbon disulfide or phenylisothiocyanate gave pyrrolyl derivatives **6–9** respectively. On the other hand, condensation of 5-(1-pyrrolyl)-6-acetyl-2,4-diphenylthieno[2,3-d]pyrimidine **11** with benzaldehyde afforded the corresponding chalcone **12**, which on treatment with hydrazine hydrate, phenyl hydrazine, or thiourea gave the pyrazolinyl derivatives **13**, **14** and pyrimidinyl derivative **15**, respectively. Furthermore, some new pyrimidothienopyrimidne **16**, **17a–d**, **19**, **20$_{a-c}$** were obtained using 5-amino-carboxamide **3c** as starting material.*

Keywords Thienopyrimidine–pyrrolylthienopyrimidine–pyrimidothienopyrimidine

INTRODUCTION

The structural diversity and biological significance of fused pyrimidines have aroused much attention in the past few years owing to their wide range of biological activity.[1] Many potential drugs have been modeled on them, particularly in cancer and virus research.[2,3] Also, thienodipyrimidines show anaphylactic activity,[4] while thieno[2,3-d]pyrimidine prove to exhibit antituberculouses[5] and herpes virus inhibitory,[6] and can be used in fertility regulation therapies.[7] On the other hand many pyrroles have been investigated in relation to their pharmacological activities, and they prove to exhibit anti-inflammatory activities,[8] antitumer[9] and antibiotic activities against various microorganisms.[10] Within this context and also as a part of our research program

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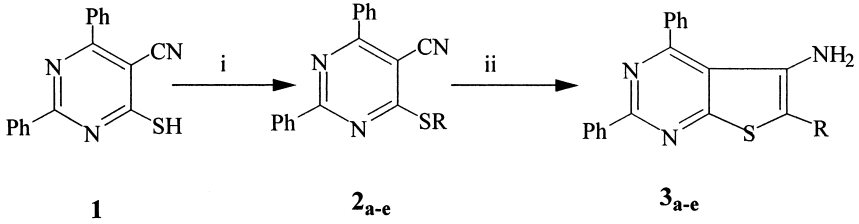
dealing with the syntheses of several thieno[2,3-d]pyrimidines.[11,12] We planned to investigate a new route for the synthesis of novel thieno[2,3-d]pyrimidines, pyrrolylthieno[2,3-d]pyrimidines, and thieno[2,3-d][4,5-d]dipyrimidines with potential biological activities.

DISCUSSION

The starting 5-Cyano-2,6-diphenylpyrimidine-4(3H)thione (**1**) was readily obtained by a previously described procedure.[13] Compound **1** was reacted with different α-halocompounds, ethyl chloroacetate, chloroacetone, chloroacetamide, phenacyl bromide, and chloroacetanilide in refluxing ethanol containing sodium acetate, to give the expected 5-alkyl derivatives **2a–e** in excellent yield. The latter compounds **2a–e** were cyclized to the required compounds **3a–e** by heating in ethanol containing sodium ethoxide.

Compound $\mathbf{3_a}$ was condensed with 2,5-dimethoxytetrahydorofurane in acetic acid to give the corresponding 5-pyrrolyl derivative **4**,[14] which could easily be reacted with hydrazine hydrate in ethanol affording the carbohydrazide derivative **5**. Condensation of **5** with aromatic aldehydes in refluxing ethanol afforded the hydrazone derivatives **6a–d**. Similarly, reaction of **5** with acetylacetone furnished the dimethylpyrazolyl derivative **7**.



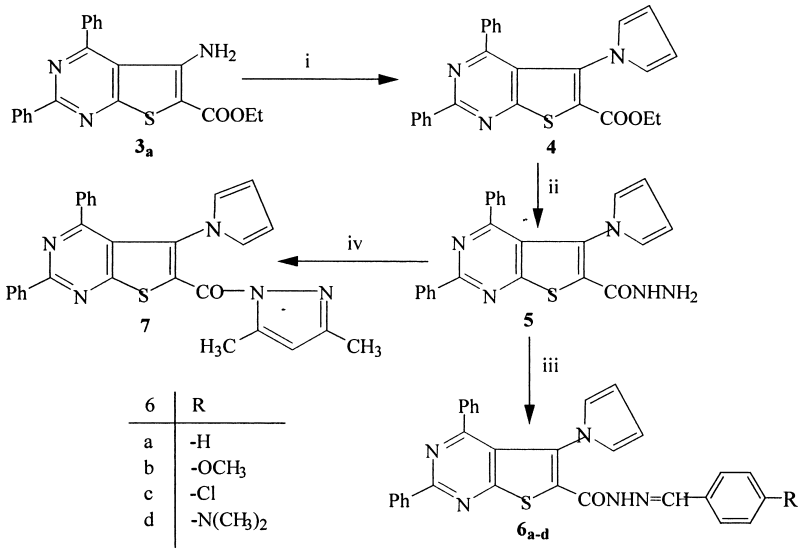
1 **2_{a-e}** **3_{a-e}**

2	R
a	$-CH_2COOEt$
b	$-CH_2COCH_3$
c	$-CH_2CONH_2$
d	$-CH_2COPh$
e	$-CH_2CONHPh$

3	R
a	$-COOEt$
b	$-COCH_3$
c	$-CONH_2$
d	$-COPh$
e	$-CONHPh$

Reagents: i , R X/AcONa; ii, EtOH/EtONa

SCHEME 1



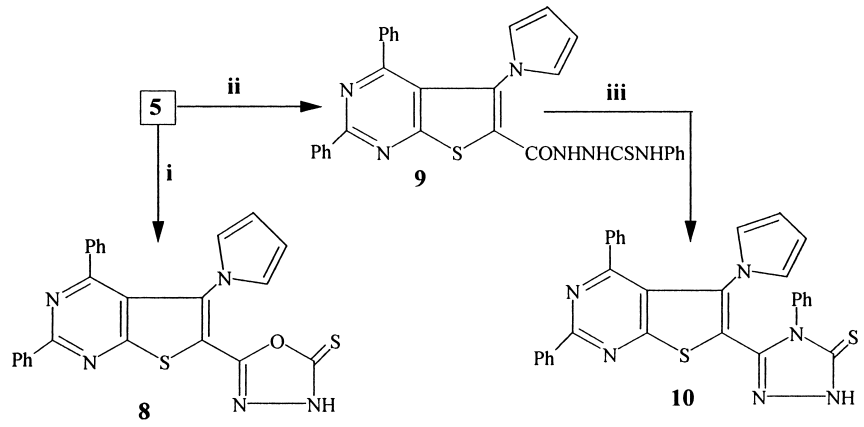
Reagents : i, DMTHF/AcOH; ii, $NH_2NH_2.H_2O$/EtOH; iii ArCHO/EtOH; iv, $ClCH_2$/EtOH

SCHEME 2

Carbohydrazide **5** reacted with carbon disulfide in pyridine afforded oxadiazolyl thione **8**. Furthermore, when **5** was allowed to react with phenylisothiocyanate in absolute ethanol, the product was identified as N′-5-(1-pyrrolyl)-N_4-phenyl-2,4-diphenylthieno[2,3-d]pyrimidin-6-yl)carbonylthio-semicarbazide (**9**). Cyclization of thiosemicarbazide **9** into triazolyl derivative 10 was achieved in alcoholic sodium hydroxide solution (Scheme 3).

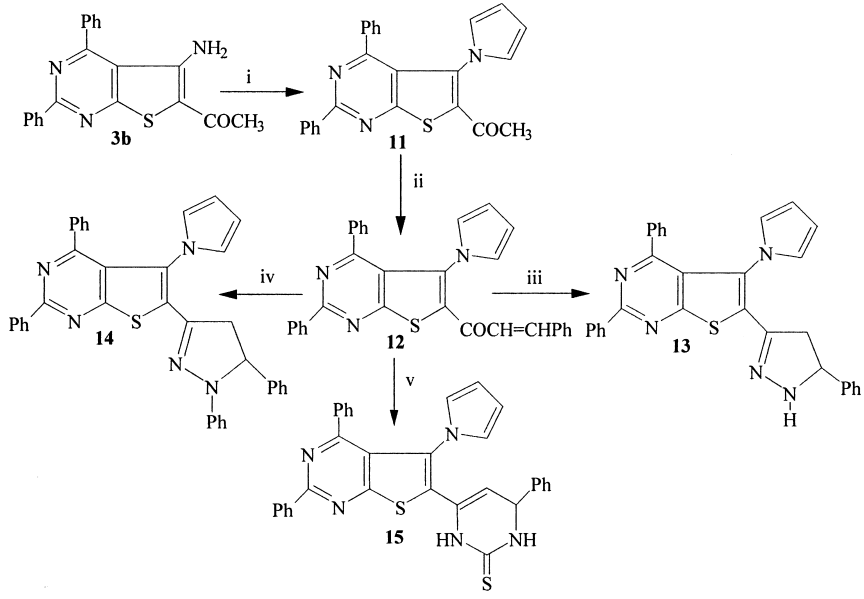
Other new pyrrolylthieno[2,3-d]pyrimidines were obtained using 5-amino-6-acetyl-2,4-diphemyl thieno[2,3-d]pyrimidine (**3b**) as starting material. Thus, **3b** was condensed with DMTHF in acetic acid to give the corresponding pyrrolyl derivative **11** which was allowed to undergo base-catalyzed Claisen–Schmidt reaction with benzaldehyde to give the chalcone derivative **12**, which was produced in good yield. The reactivity of **12** as cholcone was tested via their cydocondensation reactions with hydrazines and thiourea, affording pyrazolyl **13**, **14** and pyrimidinyl **15** derivatives, respectively.

5-Amino-2,4-diphenylthieno[2,3-d]pyrimidine-6-carboxamide (**3c**) also proved to be a versatile synthon for some newly fused thienopyrimidine moieties. Thus the reaction of **3c** with carbon disulfide in hot pyridine led to the formation of oxopyrimidothienopyrimidine **16**, which was easily S-alkylated with different halo compounds in ethanol



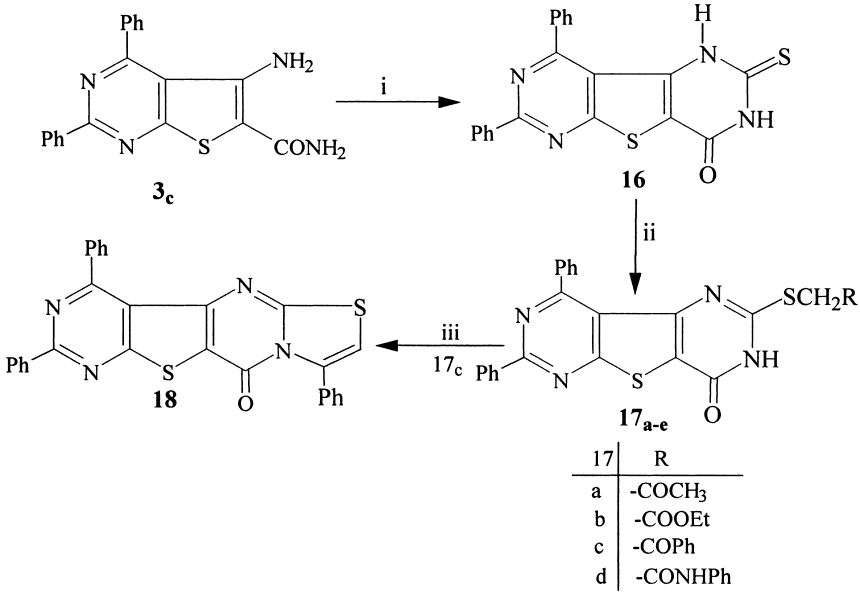
Reagents: i, CS_2 /pyridine; ii, PhNCS/EtOH; iii, NaOH/EtOH

SCHEME 3



Reagents: i, DMTHF/AcOH; ii, ArCHO/EtOH; iii, $N_2H_2.H_2O$/EtOH
iv, $PhNHNH_2$/EtOH; v, NH_2CSNH_2/EtOH/piperidine

SCHEME 4



17	R
a	-COCH$_3$
b	-COOEt
c	-COPh
d	-CONHPh

Reagents : i, CS_2 / Pyridine; ii, X-CH_2-R/EtOH/AcONa; iii, H_2SO_4/AcOH

SCHEME 5

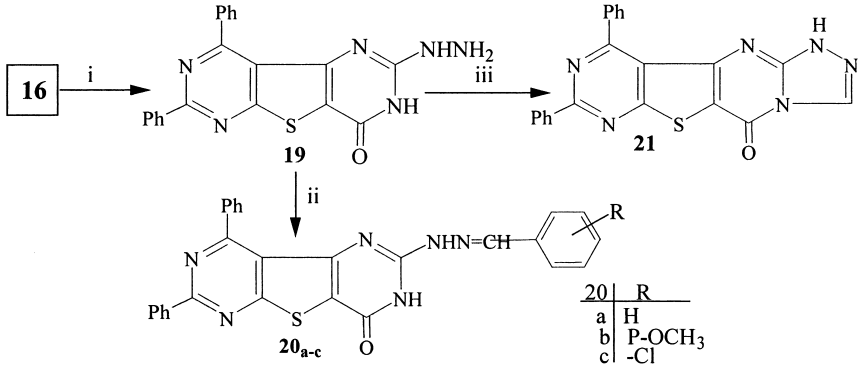
containing a catalytic amount of sodium acetate to give the expected S-alkylated products **17a–d** in good yields. Compound **17c** underwent smooth cyclodehydration in concentrated sulfuric acid[15] to furnish thiazolopyrimido-thienopyrimidine **18** in moderate yield (Scheme 5).

Treatment of **16** with hydrazine hydrate in pyridine led to the formation of 2,4-diphenyl-6-hydrazinothieno[2,3-d][4,5-d]dipyrimidin-8(7H)-one (**19**), which reacts easily with aromatic aldehydes in ethanol to give the corresponding hydrazones **20a–c**. Condensation of **19** with triethylorthoformate in ethanol in presence of a few drops of acetic acid afforded the triazolo derivative **21**[16] (Scheme 6).

The structural formulae of all newly synthesized compounds were elucidated and confirmed by elemental and spectroscopic analyses (cf. Tables I, II).

EXPERIMENTAL

All melting points are uncorrected and measured on a Fisher–Johns apparatus. IR spectra: Shimadzu IR-Spectrophotometer (KBr; ν_{max} in Cm^{-1}); ^{1}H-NMR spectra: Varian EM-390, 90 MHz spectrometer, TMS as internal standard; MS: Jeol JMS-600; elemental analyses (C, H, N):



Reagents: i, $NH_2NH_2.H_2O$/Pyridine; ii, ArCHO/EtOH;
iii, $CH(OEt)_3$/EtOH/AcOH

SCHEME 6

Perkin. Elmer 240c elemental analyzer: sulpher and chlorine analysis: oxygen flask method by the Micro Analytical Unite at Assiut University.

Reaction of 1 with Ethyl Chloroacetate, Chloroacetone, Chloroacetamide, Phenacyl Bromide or Chloroacetanilide

Formation of Compounds 2a–e, General Procedure

A mixture of compound **1** (0.02 mol), sodium acetate (4.68 g, 0.03 mol) and the respective halo-compound (0.02 mol) in ethanol (100 ml) was heated under reflux for 2 h. The precipitate that formed on cooling was collected and recrystallized from ethanol to give **2a–e**.

Cyclization of Compounds 2a–e; Formation of 3a–e; General Procedure

Compounds **2a–e** (0.01 mol) in sodium ethoxide solution (50 mg Na in 25 ml absolute ethanol) was heated under reflux for 15 min. The solid that formed while hot was collected and recrystallized from ethanol to give yellow crystals **3a–e**.

Ethyl 2,4-Diphenyl-5-(1-pyrrolyl)thieno[2,3-d]pyrimidine-6-carboxylate (4)

A mixture of **3a** (3.75 g; 0.01 mol) and 2, 5-dimethoxytetrahydrofurane (0.01 mol) was refluxed in acetic acid (20 ml) for 3 h and then allowed to cool. The solvent was removed under reduced pressure and the residue was triturated several times with ethanol. The solid product was filtered off and recrystallized from acetic acid as pale yellow crystals of **4**.

TABLE I Melting Points, Yield and Analytical Data (Cale/Found) of the Prepared Compounds

Comp.	M.P. [°C]	Yield [%]	Mol. formula (mol. wt)	C	H	N	S
2a	155–157	89	$C_{21}H_{17}N_3O_2S$	67.18	4.48	11.19	8.54
			(375.43)	67.35	4.41	11.27	8.73
2b	160–161	91	$C_{20}H_{15}N_3OS$	69.56	4.34	12.17	9.27
			((345.41)	69.71	4.11	12.52	9.36
2c	173–175	88	$C_{19}H_{14}N_4OS$	65.90	4.07	16.18	9.24
			(346.29)	65.77	4.31	16.35	9.09
2d	178–180	85	$C_{25}H_{17}N_3OS$	73.71	4.17	10.31	7.86
			(407.48)	73.56	4.03	10.55	7.34
2e	244–245	87	$C_{25}H_{18}N_4OS$	71.09	4.26	13.27	7.58
			(422.35)	71.17	4.32	13.52	7.74
3a	184–185	85	$C_{21}H_{17}N_3O_2S$	67.18	4.48	11.19	8.54
			(375.43)	67.33	4.06	11.52	8.72
3b	229–230	81	$C_{20}H_{15}N_3OS$	69.56	4.34	12.17	9.27
			(345.41)	69.17	4.03	12.52	8.87
3c	259–260	83	$C_{19}H_{14}N_4OS$	65.90	4.07	16.18	9.24
			(346.29)	66.04	4.51	16.39	9.58
3d	209–210	85	$C_{25}H_{17}N_3OS$	73.71	4.17	10.31	7.86
			(407.48)	73.54	4.22	10.82	7.71
3e	194–195	85	$C_{25}H_{18}N_4OS$	71.09	4.26	13.27	7.58
			(422.35)	71.26	4.41	13.18	7.98
4	178–180	79	$C_{25}H_{19}N_3O_2S$	70.59	4.47	9.87	7.52
			(425.34)	70.32	4.77	9.90	7.83
5	229–230	76	$C_{23}H_{17}N_5OS$	67.15	4.13	17.02	7.78
			(411.34)	67.54	4.47	16.94	7.57
6a	288–290	71	$C_{30}H_{21}N_5OS$	72.13	4.23	14.02	6.41
			(499.51)	72.48	4.42	13.90	6.12
6b	298–300	73	$C_{31}H_{23}N_5O_2S$	70.30	4.37	13.22	6.05
			(529.60)	70.09	4.50	13.49	6.21
6c	278–280	71	$C_{30}H_{20}N_5OSCl$	67.48	3.77	13.11	6.00
			(533.96)	67.94	3.31	13.05	5.82
6d	308–310	75	$C_{32}H_{26}N_6OS$	70.84	4.83	15.49	5.91
			(542.51)	70.33	4.50	15.39	6.07
7	145–147	73	$C_{28}H_{21}N_5OS$	70.71	4.42	14.73	6.73
			(475.56)	70.32	4.47	14.06	6.61
8	188–200	72	$C_{24}H_{15}N_5OS_2$	63.57	3.31	15.44	14.12
			(453.41)	63.09	3.11	15.15	13.97
9	248–250	77	$C_{30}H_{22}N_6OS_2$	65.90	4.05	15.37	11.72
			(546.73)	65.64	4.30	15.05	11.44
10	259–260	65	$C_{30}H_{20}N_6S_2$	68.17	3.81	15.90	12.13
			(528.50)	68.43	3.25	16.07	12.32
11	173–175	79	$C_{24}H_{17}N_3OS$	72.89	4.32	10.62	8.10
			(395.47)	72.62	4.08	10.34	8.37
12	164–165	87	$C_{31}H_{21}N_3OS$	76.99	4.37	8.68	6.63
			(483.58)	77.21	4.29	8.26	6.94

(Continued on next page)

TABLE I Melting Points, Yield and Analytical Data (Cale/Found) of the Prepared Compounds *(Continued)*

Comp.	M.P. [°C]	Yield [%]	Mol. formula (mol. wt)	C	H	N	S
13	193–195	71	$C_{31}H_{23}N_5S$	74.82	4.65	14.07	6.44
			(497.61)	74.57	4.81	14.33	6.09
14	223–225	73	$C_{37}H_{27}N_5S$	77.46	4.70	12.20	5.58
			(573.71)	77.62	4.21	12.65	5.37
15	183–185	75	$C_{32}H_{23}N_5S_2$	70.97	4.27	12.93	11.84
			(541.51)	70.49	4.62	12.50	11.60
16	308–310	84	$C_{20}H_{12}N_4OS_2$	61.85	3.08	14.42	16.51
			(388.36)	61.64	3.46	14.61	16.45
17a	258–260	87	$C_{23}H_{16}N_4O_2S_2$	62.16	3.65	12.60	13.99
			(444.40)	62.46	3.13	12.06	14.43
17b	280–282	85	$C_{24}H_{18}N_4O_3S_2$	60.74	3.82	11.80	13.51
			(474.52)	61.27	3.96	11.07	13.30
17c	263–265	87	$C_{28}H_{18}N_4O_2S_2$	66.38	3.58	11.05	12.65
			(506.58)	65.62	3.85	11.07	13.13
17d	>300	81	$C_{28}H_{19}N_5O_2S_2$	64.47	3.67	13.42	12.29
			(521.59)	64.37	3.41	13.37	12.06
18	298–300	63	$C_{28}H_{20}N_4OS_2$	68.29	4.06	11.37	13.02
			(492.45)	68.14	4.21	11.62	12.97
19	283–285	79	$C_{20}H_{14}N_6OS$	62.18	3.62	21.75	8.30
			(386.31)	61.94	3.31	21.52	8.11
20a	>360	73	$C_{27}H_{18}N_6OS$	68.36	3.79	17.71	6.75
			(474.39)	68.09	3.46	17.63	6.46
20b	>360	73	$C_{28}H_{20}N_6O_2S$	66.67	3.96	16.66	6.35
			(504.39)	66.70	3.34	16.17	6.09
20c	>300	71	$C_{27}H_{17}N_6OSCl$	63.71	3.34	16.51	6.29
			(508.5)	63.88	3.13	16.94	6.18
21	>300	69	$C_{21}H_{12}N_6OS$	63.65	3.02	21.20	8.07
			(396.26)	63.41	3.52	20.93	7.89

2,4-Diphenyl-5-(1-pyrrolyl)thieno[2,3-d]pyrimidine-6-carbohydrazide (5)

A mixture of **4** (4.25 g; 0.01 mol) and hydrazine hydrate (3 ml) in ethanol (20 ml) was refluxed for 3 h. The sold product which formed in hot mixture was filtered off and crystallized from dioxane as orange crystals from **5**.

Arylidine 2,4-Diphenyl-5-(1-pyrrolyl)thieno[2,3-d]pyrimidine-6-carbohydrazone (6a–d)

A mixture of carbohydrazide **5** (4.11 g; 0.01 mol) and appropriate aromatic aldehyde (0.01 mol) in ethanol (30 ml) was refluxed for 4 h, then allowed to cool. The solid product was collected and crystallized from ethanol into yellow–orange crystals from **6a–d**.

TABLE II TR, ^{1}HNMR and Mass Spectral Data

Compound no.	IR [Cm^{-1}]	^{1}HNMR [ppm]
2a	2900 (—CH aliphatic); 2200 (C≡N); 1710 (C═O)	(DMSO-d_6): 7.3–8.2 (m, 10H, Ar-H); 4.5 (s, 2H, SCH_2); 3.7–3.9 (q, J = 7.0, 2H, CH_2 ester); 1.2–1.3 (t, J = 7.0, 3H, CH_3 ester)
2b	2200 (C≡N); 1690 (C═O)	(DMSO-d_6): 7.2–8.2 (m, 10H, Ar-H); 3.9 (s, 2H, SCH_2); 2.4 (s, 3H, CH_3)
2c	3400–3300 (NH_2); 2200 (C≡N); 1670 (C═O)	(DMSO-d_6): 7.5–8.5 (m, 10H, Ar-H); 4.2 (s, 2H, SCH_2); 5.6 (s, 2H, NH_2)
2d	2200 (C≡N); 1670 (C═O)	(DMSO-d_6): 7.2–8.5 (m, 15H, Ar-H); 5.1 (s, 2H, SCH_2)
2e	3200 (NH); 2200 (C≡N); 1670 (C═O).	(DMSO-d_6): 11.0 (s, 1H, NH); 7.5–8.7 (m, 15H, Ar-H); 4.3 (s, 2H, SCH_2)
3a	3400, 3310 (NH_2); 2900 (—CH aliphatic); 1710 (C═O)	(DMSo-d_6): 7.3–8.1 (m, 10H, Ar-H); 5.5 (s, 2H, NH_2); 3.3–3.5 (q, J = 7.0, 2H, CH_2 ester); 1.3–1.5 (t, J = 7.0, 3H, CH_3 ester)
3b	3480–3300 (NH_2); 1690 (C═O)	(DMSo-d_6): 7.5–8.8 (m, 10H, Ar-H) 5.9 (s, 2H, NH_2); 2.5 (s, 3H, CH_3)
3c	3400–3300 (NH_2); 1670 (C═O)	—
3d	3450–3300 (NH_2); 1690 (C═O)	(DMSo-d_6): 7.3–8.5 (m, 15H, Ar-H); 5.5 (s, 2H, NH_2)
3e	3100, 3450, 3300 (NH, NH_2) 1670(C═O)	(DMSo-d_6): 10.7 (s, 1H, NH); 7.5–8.9 (m, 15H, Ar-H); 5.8 (s, 2H, NH_2)
4	2950 (—CH aliphatic); 1715 (C═O)	($CDCl_3$): 7.5–8.6 (m, 10H, Ar-H) 6.3–6.5 (m, 2H, 2CH pyrryl); 5.7–5.9 (m, 2H, 2CH pyrryl); 4.2 (q, J = 7.0, 2H, CH_2 ester); 1.3–1.5 (t, J = 7.0, 3H, CH_3 ester)
5	3310, 3300, 3230 (—$NHNH_2$) 1650 (C═O)	(DMSO-d_6): 9.5 (s, 1H, NH); 7.5–8.6 (m, 10H, Ar-H); 6.1–6.3 (m, 2H, 2CH pyrryl); 5.6–5.8 (m, 2H, 2CH pyrryl); 5.5(s, 2H (NH_2)
6a	3180 (NH); 1650 (C═O)	(DMSO-d_6): 9.3 (s, 1H, NH); 7.3–8.9 (m, 16H, Ar-H + N═CH); 5.7–5.9 (m, 2H, 2CH pyrryl); 6.2–6.5 (m, 2H, 2CH pyrryl)
6b	3170 (NH); 1645 (C═O)	(DMSO-d_6): 9.5 (s, 1H, NH); 7.5–8.8 (m, 16H, Ar-H + —N═CH); 5.8–6 (m, 2H, 2CH pyrryl); 6.2–6.3 (m, 2H, 2CH pyrryl); 3.5 (s, 3H, OCH_3)
6c	3170 (NH); 1650 (C═O)	—
6d	3170 (NH); 1650 (C═O)	—
7	1650 (C═O); 1590 (C═N)	(DMSO-d_6): 7.2–8.3 (m, 10H, Ar-H); 6.2–6.4 (m, 2H, 2 CH pyrryl); 6.1 (s, $1H_1$—CH pyrazole); 5.9–6.0 (m, 2H, 2-CH pyrryl); 2.4, 2.2 (2s, 6H, $2CH_3$)

(Continued on next page)

TABLE II TR, ^{1}HNMR and Mass Spectral Data *(Continued)*

Compound no.	IR [Cm^{-1}]	^{1}HNMR [ppm]
8	3210 (NH); 1610 (C═N)	(DMSO-d_6): 10.1 (s, 1H, NH); 7.7–8.5 (m, 10H, Ar-H); 5.9–6.1 (m, 2H, 2CH pyrryl); 6.2–6.5 (m, 2H, 2CH pyrryl)
9	3310, 3200, 3150 (3NH) 1640 (C═O); 1590 (C═N)	(DMSO-d_6): 9.5(s, 2H, 2NH); 10.3 (s, 1H, NH); 7.3–8.6 (m, 15H, Ar-H); 5.9–6.1 (m, 2H, 2CH pyrryl); 6.2–6.4 (m, 2H, 2CH pyrryl)
10*	3210 (NH); 1600 (C═N)	(DMSO-d_6): 9.5 (s, 1H, NH); 7.8–8.9 (m, 15H, Ar-H); 6.2–6.4 (m, 2H, 2CH pyrryl); 5.6–5.8 (m, 2H, 2CH pyrryl).
11	1660 (C═O)	(DMSO-d_6): 7.7–8.9 (m, 10H, Ar-H); 6.1–6.3 (m, $2H_1$ 2CH pyrryl); 5.8–5.6 (m, 2H, 2CH pyrryl); 2.7 (s, 3H, $COCH_3$)
12*	1660 (C═O) and 1590 (C═N)	(DMSO-d_6): 7.9–8.2 (m, 17H, Ar-H and -─CH═CH-); 6.2–6.1 (m, 2H, 2CH pyrryl); 6.5–6.3 (m, 2H, 2CH pyrryl)
13	3200 (NH) and 1590 (C═N)	(DMSO-d_6): 12.1 (s, 1H, NH); 7.7–8.6 (m, 15H, Ar-H); 5.9–6.1 (m, 2H, 2CH pyrryl); 6.4–6.2 (m, 2H, 2CH pyrryl); 4.6–4.8 (t, 1H, ─CH pyrazoline); 3.3–3.5 (m, $2H_1$─CH_2 pyrazoline)
14*	1600(C═N)	—
15**	3320, 3100 (2NH); 1590 (C═N) and 1230 (C═S)	(DMSO-d_6): 9.7, 10.5 (2s, 2H, 2NH); 7.5–8.8 (m, 17H, 15Ar-H and 2CH pyrimidine); 6.1–6.3 (m, 2H, 2CH pyrryl); 6.5–6.6 (m, 2H, 2CH pyrryl)
16	3400, 3100 (2NH) and 1660 (C═O)	(T.FA): 7.5-8.7 (m, 10H, Ar-H)
17a	3200 (NH); 1680, 1640 (2C═O) and 1610 (C═N)	(DMSO-d_6): 10.3 (s, 1H, NH); 7.3–8.6 (m, 10H, Ar-H); 4.5 (s, 2H, SCH_2); 2.9 (s, 3H, CH_3)
17b	3290 (NH); 2900 (─CH aliphatic); 1710, 1660 (2C═O) and 1600 (C═N)	(DMSO-d_6): 10.1 (s, 1H, NH); 7.2–8.5 (m, 10H, Ar-H); 4.5 (s, 2H, SCH_2); 3.9 (q, 2H, CH_2 ester); 1.5 (t, 3H, CH_3 ester)
17c	3200 (NH); 1680 (C═O) and 1600 (C═N)	—
17d	3220, 3100 (2NH); 1670 (C═O) and 1590 (C═N)	(DMSO-d_6): 9.5, 10.3 (2s, 2H, 2NH); 7.3–8.6 (m, 15H, Ar-H); 4.6 (s, 2H, SCH_2)
18**	1690 (C═O) and 1600 (C═N)	(TFA): 8.2 (s, 1H, thiazole-CH); 7.1–8 (m, 10H, Ar-H)
19	3380, 3280, 3200 ($NHNH_2$, NH); 1670 (C═O) and 1600 (C═N)	(DMSO-d_6): 9.5, 10.3 (2s, 2H, 2NH); 7.6–8.7 (m, 10H, Ar-H); 4.7 (br, 2H, NH_2)

(Continued on next page)

TABLE II TR, ^{1}HNMR and Mass Spectral Data *(Continued)*

Compound no.	IR [Cm^{-1}]	^{1}HNMR [ppm]
20a	3310, 3200 (2NH); 1670 (C═O) and 1610 (C═N)	(DMSO-d_6): 9.3, 10.1 (2s, 2H, 2NH); 7.2–8.6 (m, 16H, Ar-H and N═CH)
20b	3320, 3200 (2NH); 1675 (C═O) and 1600 (C═N)	(DMSO-d_6): 9.5, 10.1 (2s, 2H, 2NH) 7.5–8.7 (m, 15H, Ar-H and ─N═CH-); 2.7 CS, 3H, OCH_3)
20c	3310, 3200 (2NH) 1670 (C═O) and 1590 (C═N)	—
21[*]	3400 (NH); 1670 (C═O) and 1590 (C═N).	(DMSO-d_6): 10.5 (s, 1H, NH); 8.6 (s, 1H, triazol ─CH); 7.2–8.5 (m, 10H, Ar-H)

[a]MS of 10: m/z (fragment, %): 529 (M^+, 80); 463 (M^+-C_4H_4N, 90).
[b]MS of 12: m/z (fragment, %): 484 (M^+, 56); 407 (M^+-C_6H_5, 100).
[c]MS of 14: m/z (fragment, %): 574 (M^+, 60); 497 (M^+-C_6H_5, 90).
[d]MS of 15: m/z (fragment, %): 542 (M^+, 45); 476 (M^+-C_4H_4N, 85).
[e]MS of 21: m/z (fragment, %): 396 (M^+, 25); 395 (M^+-1, 70); 394 (M^+-2, 73).
[f]C^{13}-NMR spectra of compounds 15, 18 were recorded on a Jeol LA 400 MH_zFT-NMR.
[g]C^{13}-NMR of 15: 164, 166, 128, 130 (pyrimidine); 127, 137 (thiophene); 118, 110 (pyrryl); 103, 59, 149, 179 (thioxopyrimidine); 126–142 (Aromatic).
[h]C^{13}-NMR of 18: 163, 165, 127, 136 (pyrimidine); 144, 136 (thiophene) 163, 165 (pyimidinone); 86, 145 (thiazole); 127–136 (aromatic).

6-[3′,5′-Dimethyl-pyrazoleylcarbonyl]- 2,4-Diphenyl-5-(1-pyrrolyl)thieno[2,3-d]pyrimidine (7)

A mixture of **5** (4.11 g; 0.01 mol) and acetylacetone (1 g; 0.01 mol) in ethanol in the presence of a few drops from AcOH was refluxed for 6 h. The solid product which separated was collected by filtration and recrystallized from acetic acid to give yellow crystals of **7**.

2,4-Diphenyl-5-(1-pyrrolyl)-6-(5′-thioxo-1,3,4-oxadiazol-2-yl)-thieno[2,3-d]pyrimidine 8

A mixture of compound **5** (4.11 g; 0.01 mol) and carbon disulfide (5 ml) in pyridine (20 ml) was heated on a water bath for 12 h. The solid product which separated from the hot mixture was collected by filtration and recrystallized from dioxane as orange crystals from **8**.

2,4-Diphenyl-6-(oxophenylthiosemicarbazide)-5-(1-pyrrolyl)-thieno[2,3-d]pyrimidine (9)

A mixture of **5** (4.11 g; 0.01 mol) and phenylisothiocyanate (1.35 g; 0.01 mol) in ethanol was refluxed for 4 h. Pale yellow crystalline product

obtained on heating was collected by filtration and recrystallized from dioxane.

2,4-Diphenyl-6-(1,5-dihydro-4-phenyl-5-thioxo-s-triazol-3-yl)-5-(1-pyrrolyl)thieno [2,3-d]pyrimidine (10)

Thiosemicarbazide **9** (5.46 g; 0.01 mol) was dissolved in 2N alcoholic sodium hydroxide (20 ml) and heated for 3 h. the solution was cooled and acidified with dilute. HCl, the separated product, was collected by filtration and crystallized from dioxane as yellow crystals from **10**.

2,4-Diphenyl-6-methylcarbonyl-5-(1-Pyrrolyl)thieno[2,3-d]-pyrimidine (11)

This compound was synthesized following an analogous procedure that for compound **4**. Compound 11 was separated from dioxane as deep yellow crystals.

1 (2,4-Diphenyl-5-(1-pyrrolyl)thieno[2,3-d]pyrimidine-6-yl)-3-phenyl-2-propen-1-one (12)

To a solution of **11** (3.95 g; 0.0l mol) in hot ethanol (100 ml) containing sodium hydroxide (2 g, 0.05 mol), the benzaldehyde (1.06 g; 0.01 mol) was added. The resulting mixture was stirred at 50–55 for 4 h and then left to cool. The separated solid was collected and recrystallized from dioxane to give orange crystals of **12**.

2,4-Diphenyl-6-(5-phenyl-Δ^2-pyrazolin-3-yl)-5-(1-pyrrolyl)-thieno[2,3-d]pyrimidine (13)

A mixture of **12** (0.96 g; 0.002 mol) and hydrazine hydrate (3 ml) in ethanol (30 ml) was heated under reflux for 4 h. The separated solid product was collected and recrystallized from ethanol-$CHCl_3$ mixture to give yellow crystals of **13**.

2,4-Diphenyl-6-(1,5-diphenylpyrazolin-3-yl)-5-(1-pyrrolyl)-thieno[2,3-d]pyrimidine (14)

A mixture of **12** (4.83 g; 0.01 mol) and phenyl hydrazine (1.08 g; 0.01 mol) in ethanol (30 ml) was heated under reflux. The solid product which separated during heating was collected and recrystallized from ethanol-$CHCl_3$ mixture as orange crystals from **14**.

2,4-Diphenyl-6-(2,3-dihydro-2-thioxo-1,3-pyrimidin-6-yl)-5-(1-pyrrolyl)thieno[2,3-d]pyramidine (15)

A mixture of **12** (4.83 g; 0.01 mol) and thiourea (0.76 g; 0.01 mol) in ethanol (30 ml) and a few drops of piperidine were added. The reaction mixture was heated under reflux for 4 h. The precipitate that formed

while hot was collected by filtration and recrystallized from dioxane as deep yellow crystals of **15**.

2,4-Diphenyl-5,6-dihydro-6-thioxothieno[2,3-d][4,5-d]-dipyrimidin-8(7H)one (16)

A mixture of compound **3C** (3.46 g; 0.01 mol) and carbon disulfide (5 ml) in pyridine (20 ml) was heated on a water bath for 12 h. The solid product which separated from hot mixture was collected by filtration and crystallized from dioxane as orange needles from **16**.

Reactions of 16 with Chloroacetone, Ethyl Chloroactate, Phenacylbromide, and Chloroacetanilide

Formation of Compounds 17_{a-d}; General Procedure

A mixture of compound **16** (3.88 g; 0.01 mol), sodium acetate (1.46 g; 0.02 mol), and respective halo compounds (0.01 mol) was heated under reflux for 1–2 h. The precipitate that formed on cooling was collected by filtration, washed with water, and crystallized from ethanol-$CHCl_3$ mixture as pale yellow crystals of **17a–d**.

2,4,8-Triphenylthiazole[3″,2″:1′,2′]pyrimido[4′,5′:4,5]thieno-[2,3-d]pyrimidin-9-one (18)

To a solution of **17c** (1.0 g; 0.002 mol) in glacial acetic acid (15 ml), concentrated H_2SO_4 (10 ml) was added and the mixture was gently heated for 8 h. After cooling reaction mixture was poured into ice water and neutralized with 5% aqueous sodium bicarbonate. The precipitated was filtered off, washed well with water, and crystallized from dioxane as yellow crystals of **18**.

2,4-Diphenyl-6-hydrazinothieno[2,3-d][4,5-d]dipyrimidin-8(7H) one (19)

A mixture of compound **16** (0.77 g; 0.002 mol) and 99% hydrazine hydrate (2 ml) in pyridine (10 ml) was heated under reflux for 10 h until H_2S gas ceased, then allowed to cool. The solid product was collected, washed well with ethanol, and recrystallized from pyridine as orange crystals of **19**.

6-Arylidenehydrazion-2,4-diphenyl-5,6-dihydrothieno[2,3-d]-[4,5-d]dipyrimi-din-8 (7H) one (20a–c)

A mixture of 19 (3.86 g; 0.01 mol) and the respective aldehyde (0.01 mol) in ethanol (25 ml) was refluxed for 3 h. The solid product that precipitated by cooling was collected and recrystallized from dioxane as orange crystals of **20a–c**.

2,4-Diphenyl-6(H)-s-triazolo[3″,4″:1′,2′]pyrimido[4′,5′:4,5]-thieno[2,3-d]pyrimidine (21)

A mixture of hydrazion derivative **19** (3.86 g; 0.01 mol) and triethylorthoformate (0.12 mol) in ethanol in presence of few drops of acetic acid, was refluxed for 3 h. The solid product which separated from the hot mixture was filtered off and recrystallized from acetic acid as yellow crystals of **21**.

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