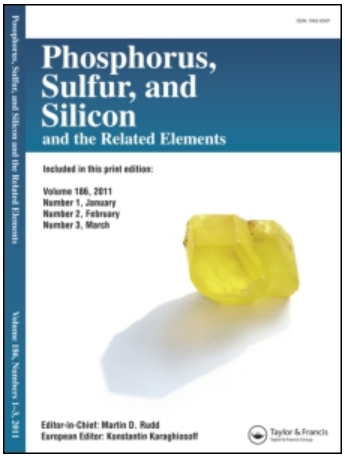


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

The Synthesis of Some Pyrazolyl- and Thiazolylthienopyridines

A. M. Kamal El-Dean[a]; A. A. Geies[a]; Y. A. El-Ossaily[a]
[a] Chemistry Department, Assiut University, Assiut, Egypt

To cite this Article El-Dean, A. M. Kamal , Geies, A. A. and El-Ossaily, Y. A.(2006) 'The Synthesis of Some Pyrazolyl- and Thiazolylthienopyridines', Phosphorus, Sulfur, and Silicon and the Related Elements, 181: 9, 2013 — 2022
To link to this Article: DOI: 10.1080/10426500600605665
URL: http://dx.doi.org/10.1080/10426500600605665

Phosphorus, Sulfur, and Silicon, 181:2013–2022, 2006

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426500600605665

Taylor & Francis
Taylor & Francis Group

The Synthesis of Some Pyrazolyl- and Thiazolylthienopyridines

A. M. Kamal El-Dean
A. A. Geies
Y. A. El-Ossaily
Chemistry Department, Assiut University, Assiut, Egypt

*2-acetyl-3-amino-4,6-dimethylthieno[2,3-b]pyridine **1** reacted with dimethoxytetrahydrofuran in acetic acid and ethyl cyanoacetate in the presence of ammonium acetate or with $NaNO_2$ in the presence of an AcOH/HCl mixture to produce **2–4**. Compound **2** reacted with aromatic aldehydes, semicarbazide hydrochloride, thiosemicarbazide, and phenyl hydrazine or with hydrazine hydrate to give compounds **5a–c** and **11a–d**, respectively.*

*Chalcone **5** reacted with hydrazines, hydroxylamine hydrochloride, or thiourea to produce compounds **6–9**. Thiosemicarbazone **11b** reacted with α-haloester to produce the corresponding thiazolidinone derivatives **12a,b**; also it reacted with ω-bromoacetophenone to give thiazoline derivatives **13a,b**.*

Keywords Pyrrolylthiazolylthienopyridines; pyrrolylthienopyridines; thienopyridines

INTRODUCTION

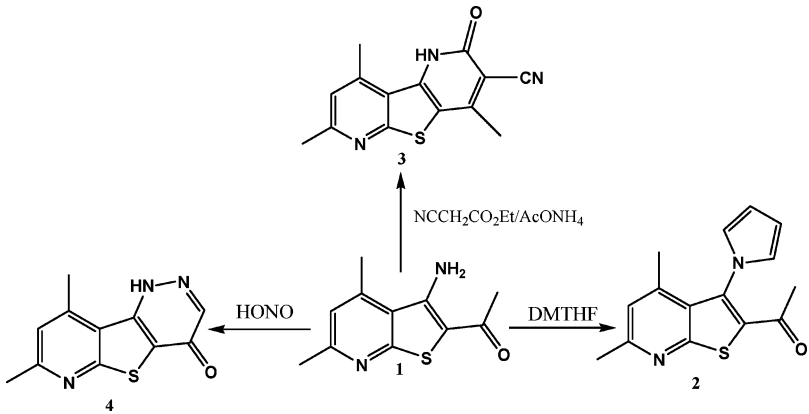
Thieno[2,3-b]pyridines are useful for multiple pharmacological applications. Thus, dihydrothieno[2,3-b]pyridine shows remarkable effects as a calcium antagonist[1] and has been also used in the treatment of epilepsy, Alzheimer's disease, and Huntington's corea.[2] Some thieno[2,3-b] pyridines have shown interesting as an antiatherosclerotic,[3] and other thienopyridines show antimicrobial effects.[4]

In view of the previously discussed benefits and in continuation of our work with thienopyridines,[3–5] herein in this article we report the synthesis of some new thienopyridines.

Received October 1, 2005; accepted November 25, 2005.
Address correspondence to A. M. Kamal El-Dean, Assiut University, Chemistry Department, Faculty of Science, Assiut 71516, Egypt. E-mail: a.eldean@acc.aun.edu.eg

RESULTS AND DISCUSSION

2-acetyl-3-amino-4,6-dimethylthieno[2,3-b]pyridine[6] **1** reacted with dimethoxy-tetrahydrofuran in acetic acid, ethyl cyanoacetate in ammonium acetate, and sod. Nitrite in acetic acid/HCl mixture to produce 2-acetyl-3(1-pyrrolyl)-4,6-dimethylthieno[2,3-b]pyridine **2**, pyridothienopyridine **3**, and pyridothienopyridazine **4**, respectively.



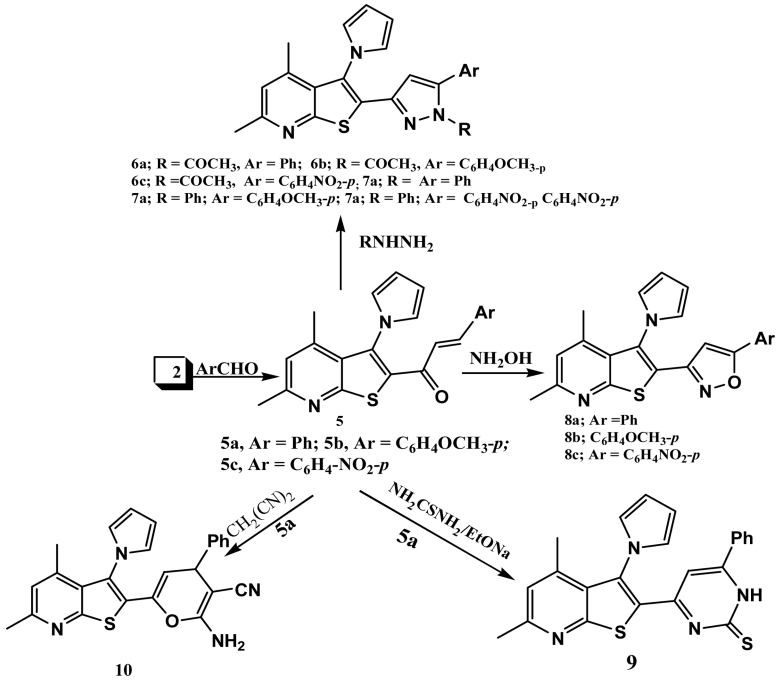
SCHEME 1

Compound **2** reacted with aromatic aldehydes in alcoholic NaOH (10%) to produce the corresponding substituted benzalacetyl derivative **5**. The produced chalcone reacted with hydrazine hydrate in acetic acid to give a pyrazolinyl derivative, which spontaneously oxidized under the reaction condition and lost 2H, followed by acylation to give **6a**,**b**. Another pyrazolyl derivatives **7a**,**b** was produced by the same manner by refluxing compound **5** with phenyl hydrazine in ethanol.

Also, when compounds **5a–c** were allowed to react with hydroxylamine hydrochloride in ethanol in the presence of sodium acetate, isoxazolyl derivatives **8a–c** were obtained.

The pyrimidine derivative **9** was synthesized by the reaction of chalcone **5a** with thiourea in ethanol in the presence of sodium ethoxide, while the dihydropyrimidine derivative was produced, followed by dehydrogenation under the reaction condition. When chalcone compound **5** was allowed to react with malononitrile in ethanol in the presence of catalytic amount of piperidine, pyrano derivative **10** was obtained.

Compound **2** was condensed with amino compounds, namely semicarbazide hydrochloride in ethanol in the presence of sodium acetate, thiosemicarbazide in acetic acid, phenyl hydrazine in ethanol, or with hydrazine hydrat in ethanol, to give compounds **11a–d**.



SCHEME 2

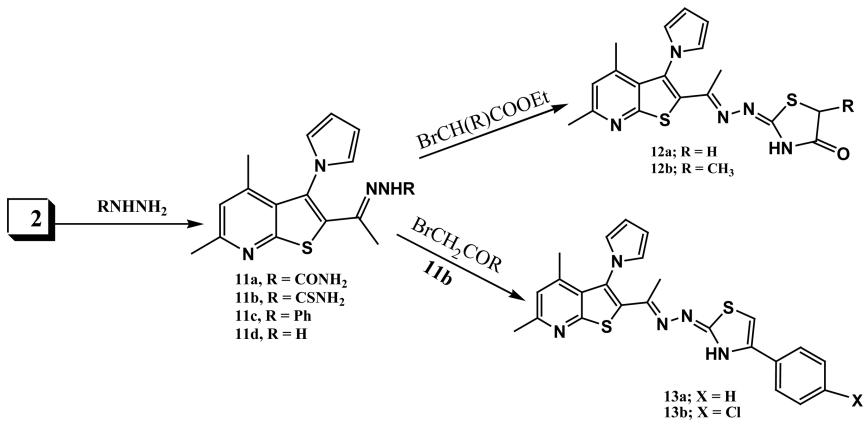
Thiosemicarbazone **11b** reacted with α-halocompounds, such as α-haloester (2-ethyl chloroacetate, α-bromomethylpropionate), to give thiazolidinone derivatives **12a**,**b**. Also, when compound **11b** was allowed to react with ω-bromoacetophenones to give thiazoline derivatives **13a**,**b**.

EXPERIMENTAL

Melting points were determined on a Kofler melting point apparatus and are uncorrected. IR spectra were recorded on potassium bromide disks on a Pye Unicam spectrophotometer using the KBr Wafer technique. ^{1}H NMR spectra were obtained on Varian 390 90-MHz spectrometer in a suitable deuterated solvent. Chemical shifts were determined on the δ scale by using tetramethylsilan as the internal standard. Elemental analyses were obtained on Perkin Elmer 240 C microanalyzer.

2-Acetyl-3-amino-4,6-dimethylthieno[2,3-b]pyridine (1)

Prepared according to the literature method; m.p. 207°C; Lit.[9] m.p. 206–207°C.



SCHEME 3

2-Acetyl-3(1-pyrrolyl)-4,6-dimethylthieno[2,3-b]pyridine (2)

A mixture of compound **1** (2.23 g, 0.01 mol) and dimethoxytetrahydrofuran (0.01 mol) in acetic acid (20 mL) was heated under reflux for one h, allowed to cool, and poured into cold water. The solid product was collected and washed with Na_2CO_3 (10% solution) several times and recrystallized from ethanol as white crystals, 2.00 gm, 74% yield, m.p. 207°C.

Anal. calcd. for $C_{15}H_{14}N_2OS$(270.36): C, 66.64; H, 5.22; N, 10.36; S, 11.86%. Found: C, 66.46; H, 5.55; N, 10.14; S, 11.88%. IR: $\nu = 1700\ cm^{-1}$ (C═O) and showed the disappearance of band characteristic of NH_2 group in the starting material. ^{1}HNMR($CDCl_3$): $\delta = 1.85$, 2.2, 2.7 (3s, 9H, CH_3), 6.2–6.4, 6.55–6.75 (2m, 4H, 4CH-pyrrolyl ring), 6.9 (s, 1H, CH-pyridine).

3-Cyano-4,7,9-trimethylpyrido[3′.2′:2,3]thieno[5,4-b]pyridin-1(2H)-one (3)

A mixture of compound **1** (2.23 gm, 0.01 mol), ethyl cyanoacetate, and ammonium acetate (10 g) was heated under reflux for 2 h; then ethanol (30 mL) was added and refluxed for an additional 2 h. The solid product was filtered off in hot, washed well with ethanol, and recrystallized from dioxan as yellow crystals, 1.7 gm, 62% yield, m.p. > 300°C.

Anal. calcd. for $C_{14}H_{11}N_3OS$(269.33): C, 62.44; H, 4.12; N, 15.60; S, 11.91% Found: C, 62.18; H, 3.88; N, 15.44; S, 12.13%. IR: $\nu = 3250\ cm^{-1}$ (NH), 1675 cm^{-1} (C═O). ^{1}HNMR(CF_3CO_2D): $\delta = 2.1$, 2.5, 2.9 (3s, 9H, $3CH_3$), 6.9 (s, 1H, CH-pyridine).

1,4-Dihydro-8,9-dimethylpyrido[2,3:5′,4′]thieno[2,3-c]pyridazin-4-one (4)

To a stirred ice cooled solution of compound **1** (1.1 gm, 0.005 mol) in a mixture of HCl (2 mL, 11 N), and acetic acid (5 mL), sodium nitrite solution (0.01 mol in 3 mL of H_2O) was added dropwise for 10 min. The stirring was continued for 30 min and then allowed to stand for 2 h. The solid product was collected and recrystallized from ethanol as yellow crystals, 0.77 gm, 67% yield, m.p. 289°C.

Anal. calcd. for $C_{11}H_9N_3OS$(231.28): C, 57.13; H, 3.92; N, 18.17; S, 13.86%. Found: C, 56.88; H, 4. 21; N, 18.00; S, 14.07%. IR: $\nu = 3340\ cm^{-1}$ (NH) and 1670 cm^{-1} (CO). ^{1}HNMR (DMSO-d_6): $\delta = 2.4$, 2.8 (2s, 6H, $2CH_3$), 6.95 (s, 1H, CH-pyridine), 7.6 (s, 1H, CH-pyridazine), and 9.9 (s, 1H, NH).

2-Arylideneacetyl-3(pyrrol-1yl)-4,6-dimethylthieno[2,3-b]pyridine (5a–c)

A mixture of compound **2** (2.7 gm, 0.01 mol) and aromatic aldehyde (0.01 mol) in alcholic NaOH solution (10%, 30 mL) was stirried for 5 h.The solid product was collected and washed well with water and recrystallized from acetic acid. Physical constants and spectral data of compounds **5a–c** are listed in Tables I and II.

4,6-Dimethyl-3(pyrrol-1-yl)-2(2-acetyl-3-diaryl-pyrazolin-5yl)thieno[2,3-b]pyridine (6)

A mixture of chalcone compounds **5a–c** (0.01 mol) and hydrazine hydrate (0.01 mol) in acetic acid (20 mL) was heated under reflux for 4 h, allowed to cool, and then poured into cold water (100 mL). The solid product was collected and recrystallized from ethanol. Physical constants and spectral data of compounds **4a**,**b** are listed in Tables I and II.

4,6-Dimethyl-3(pyrrol-1-yl)-2(2,3-diaryl-pyrazolin-5-yl)thieno[2,3-b]pyridine (7)

A mixture of chalcone compound **5** (0.01 mol) and phenyl hydrazine (0.01 mol) in ethanol (25 mL) was heated under reflux for 5 h and then allowed to cool. The solid product was collected and recrystallized from ethanol. Physical constants and spectral data of compounds **7a–c** are listed in Tables I and II.

TABLE I Physical Constants and Analytical Data of compounds 5a–c

No.	M.P. °C	Yield %	Molecular formula	Analytical data (calcd./found) C	H	N	S
5a	252	75	$C_{22}H_{18}N_2OS$	73.72	5.06	7.81	8.94
			(358.46)	73.95	4.86	8.03	9.18
5b	220	72	$C_{23}H_{20}N_2O_2S$	71.11	5.19	7.21	8.25
			(388.48)	70.87	4.99	7.47	8.03
5c	285–287	68	$C_{22}H_{17}N_3O_3S$	65.49	4.25	10.42	7.95
			(403.46)	65.63	4.03	10.13	8.15
6a	212	60	$C_{24}H_{20}N_4OS$	69.88	4.89	13.58	7.77
			(412.52)	69.66	5.12	13.36	7.91
6b	232	64	$C_{25}H_{22}N_4O_2S$	67.85	5.01	12.66	7.23
			(442.54)	67.94	4.78	12.45	7.15
6c	289	71	$C_{24}H_{19}N_5O_3S$	63.01	4.19	15.31	7.01
			(457.51)	63.01	4.19	15.31	7.01
7a	254	67	$C_{28}H_{22}N_4S$	75.31	4.97	12.55	7.18
			(446.58)	75.20	5.19	12.49	6.92
7b	235	74	$C_{29}H_{24}N_4OS$	73.08	5.08	11.76	6.73
			(476.60)	72.88	5.32	11.54	6.50
7c	310	77	$C_{28}H_{21}N_5O_2S$	68.42	4.31	14.25	6.52
			(491.58)	68.19	4.53	14.08	6.32
8a	210	63	$C_{22}H_{17}N_3OS$	71.14	4.61	11.31	8.63
			(371.46)	70.93	4.89	11.21	8.59
8b	225	67	$C_{23}H_{19}N_3O_2S$	68.81	4.77	10.47	7.99
			(401.49)	68.67	5.0	10.33	8.18
8c	241	71	$C_{22}H_{16}N_4O_3S$	63.45	3.87	13.45	7.70
			(416.46)	63.24	4.04	13.52	7.66
12a	237	65	$C_{18}H_{17}N_5OS_2$	56.38	4.474	18.261	16.72
			(383.50)	55.16	.21	8.19	16.57
12b	233	69	$C_{19}H_{19}N_5OS_2$	57.41	4.82	17.62	16.13
			(397.52)	57.57	4.72	17.82	16.37
13a	289	72	$C_{24}H_{21}N_5S_2$	64.98	4.77	15.79	14.46
			(443.60)	64.65	4.70	15.98	14.44
13b*	299	75	$C_{24}H_{20}ClN_5S_2$	60.30	4.22	14.65	13.41
			(478.04)	60.70	4.12	14.85	13.58

*Calcd, Cl = 7.42; Found = 7.65.

4,6-Dimethyl-3(pyrrol-1-yl)-2(5-aryl-[1,2]oxzazolin-3-yl)thieno[2,3-b]pyridine (8)

A mixture of chalcone compound **5** (0.01 mol), sod. acetate (0.015 mol), and hydroxylamine hydrochloride (0.01 mol) in ethanol (25 mL) was heated under reflux for 5 h, allowed to cool, and then poured into cold water. The solid product was collected and recrystallized from ethanol. Physical constants and spectral data of compounds **8a–c** are listed in Tables I and II.

TABLE II Spectral Data of Compounds 5a–c

No.	IR	^{1}HNMR
5a	1705 cm^{-1} (C═O), 1600 cm^{-1} (C═C)	($CDCl_3$): 1.9, 2.5 (2s, 6H, $2CH_3$), 6.2–6.4, 6.55–6.75 (2m, 4H, 4CH-pyrrolyl ring), 6.85 (s, 1H, CH-pyridine) and 7.0–7.8 (m, 7H, CH═CH—, Ar-H)
5b	1705 cm^{-1} (C═O), 1600 cm^{-1} (C═C)	($CDCl_3$): 1.9, 2.5, 3.8 (3s, 9H, $3CH_3$), 6.2–6.4, 6.55–6.75(2m, 4H, 4CH-pyrrolyl ring), 6.9 (s, 1H, CH-pyridine) and 7.0–7.8 (m, 6H, CH═CH—, Ar-H)
5c	1710 cm^{-1} (C═O), 1600 cm^{-1} (C═C)	($CDCl_3$): 1.9, 2.5, 3.2 (3s, 9H, $3CH_3$), 6.2–6.4, 6.55–6.75 (2m, 4H, 4CH-pyrrolyl ring), 6.9 (s, 1H, CH-pyridine) and 7.0–7.8 (m, 6H, CH═CH—, Ar-H)
6a	1690 cm^{-1} (C═O), 1610 cm^{-1} (C═N)	2.2, 2.4, 2.8 (3s, 9H, $3CH_3$), 6.4 (s, 1H, CH pyrazole), 6.1–6.4, 6.55–6.75 (2m, 4H, 4CH-pyrrolyl ring), 7.05 (s, 1H, CH-pyridine) and 7.3–7.7 (m, 5H, Ar-H)
6b	1690 cm^{-1} (C═O), 1600 cm^{-1} (C═N)	2.2, 2.4, 2.8, 3.9 (4s, 12H, $4CH_3$), 6.4 (s, 1H, CH pyrazole), 6.2–6.4, 6.55–6.75 (2m, 4H, 4CH-pyrrolyl ring), 7.1 (s, 1H, CH-pyridine) and 7.2, 7.6 (2d, 4H, Ar-H)
6c	1690 cm^{-1} (C═O), 1610 cm^{-1} (C═N)	2.2, 2.4, 2.9 (3s, 9H, $3CH_3$), 6.5 (s, 1H, CH pyrazole), 6.2–6.4, 6.55–6.75 (2m, 4H, 4CH-pyrrolyl ring), 7.1 (s, 1H, CH-pyridine) and 7.6, 8.2 (2d, 4H, Ar-H)
7a	3050 cm^{-1} (CH-aromatic), 1620 cm^{-1} (C═N)	1.9, 2.5 (2s, 6H, $2CH_3$), 6.5 (s, 1H, CH pyrazole), 6.2–6.4, 6.55–6.75 (2m, 4H, 4CH-pyrrolyl ring), 6.9 (s, 1H, CH-pyridine) and 7.0–7.8 (m, 10H, Ar-H)
7b	3050 cm^{-1} (CH-aromatic), 1620 cm^{-1} (C═N)	1.9, 2.5, 3.9 (3s, 9H, $3CH_3$), 6.5 (s, 1H, CH pyrazole), 6.2–6.4, 6.55–6.75 (2m, 4H, 4CH-pyrrolyl ring), 6.9 (s, 1H, CH-pyridine) and 7.0–7.8 (m, 9H, Ar-H)
7c	3050 cm^{-1} (CH-aromatic), 1630 cm^{-1} (C═N)	2.3, 2.6(2s, 6H, $2CH_3$), 6.5 (s, 1H, CH pyrazole), 6.2–6.4, 6.55–6.75 (2m, 4H, 4CH-pyrrolyl ring), 6.9 (s, 1H, CH-pyridine) and 7.0–7.8 (m, 9H, Ar-H)
8a	3050 cm^{-1} (CH-aromatic), 1630 cm^{-1} (C═N)	DMSO-d_6: 2.35, 2.7(2s, 6H, $2CH_3$), 6.1 (s, 1H, CH oxazole); 6.2–6.4, 6.55–6.75 (2m, 4H, 4CH-pyrrolyl ring), 6.9 (s, 1H, CH-pyridine) and 7.0–7.8 (m, 5H, Ar-H)
8b	3050 cm^{-1} (CH-aromatic), 1630 cm^{-1} (C═N)	DMSO-d_6: 2.3, 2.7(2s, 6H, $2CH_3$), 3.7 (s, 3H, CH_3), 6.1 (s, 1H, CH oxazole); 6.2–6.4, 6.55–6.75 (2m, 4H, 4CH-pyrrolyl ring), 7.0 (s, 1H, CH-pyridine) and 7.1–7.3 (2d, 4H, Ar-H)
8c	3050 cm^{-1} (CH-aromatic), 1630 cm^{-1} (C═N)	DMSO-d_6: 2.4, 2.75(2s, 6H, $2CH_3$), 6.1 (s, 1H, CH oxazole); 6.3–6.4, 6.6–6.8 (2m, 4H, 4CH-pyrrolyl ring), 7.05 (s, 1H, CH-pyridine) and 7.2, 7.8 (2d, 4H, Ar-H)

(Continued on next page)

TABLE II Spectral Data of Compounds 5a–c *(Continued)*

No.	IR	^{1}HNMR
12a	3350 cm^{-1}(NH), 3050 cm^{-1} (CH-aromatic), 1720 cm^{-1} (CO), 1630 cm^{-1} (C═N)	DMSO-d_6: 1.9, 2.5, 3.3 (3s, 9H, 3CH_3), 4.2 (s, 2H, CH_2), 6.2–6.4, 6.55–6.75 (2m, 4H, 4CH-pyrrolyl ring), 6.9 (s, 1H, CH-pyridine) and 10.2 (s, 1H, NH)
12b	3320 cm^{-1}(NH), 1720 cm^{-1} (CO), 1630 cm^{-1} (C═N)	DMSO-d_6: 1.9, 2.5, 3.3 (3s, 9H, 3CH_3), 2.8 (d, 3H, CH_3), 4.2 (q, 1H, CH), 6.2–6.4, 6.55–6.75 (2m, 4H, 4CH-pyrrolyl ring), 6.9 (s, 1H, CH-pyridine) and 10.2 (s, 1H, NH)
13a	3360 cm^{-1}(NH), 1610 cm^{-1} (C═N)	DMSO-d_6: 1.9, 2.5, 3.3 (3s, 9H, 3CH_3), 6.2–6.4, 6.55–6.75 (2m, 4H, 4CH-pyrrolyl ring), 6.9 (s, 1H, CH-pyridine) and 7.0-7.8 (m, 6H, Ar-H, CH thiazol)
13b	3340 cm^{-1}(NH), 1620 cm^{-1} (C=N)	DMSO-d_6: 1.9, 2.5, 3.3 (3s, 9H, 3CH_3), 6.2–6.4, 6.55–6.75 (2m, 4H, 4CH-pyrrolyl ring), 6.9 (s, 1H, CH-pyridine) and 7.2, 7.8 (2d, 4H Ar-H), 7.0 (s, 1H, CH thiazol)

6-Aryl-4-[4,6-Dimethyl-3(pyrrol-1-yl)thieno[2,3-b]pyridine-2-yl]pyrimidin-2(1H)-thione (9)

A mixture of chalcone compound **5a** (3.58 gm, 0.01 mol) and thiourea (0.01 mol) in absolute ethanol (25 mL) containing sod. ethoxide (0.01 mol) was heated under reflux for 6 h, allowed to cool, and poured into cold water. The produced solution was acidified with HCl (0.1 N) to just pH 7. The solid product was collected and recrystallized from dioxane as yellow crystals, 2.6 gm, 63% yield, m.p. > 300°C.

Anal. calcd. for $C_{23}H_{18}N_4S_2$(414.55): C, 66.64; H, 4.38; N; 13.51, S, 15.47%. Found: C, 66.83; H, 4.54; N; 13.32, S, 15.63%. IR: $\nu = 3340$ cm^{-1} (NH) and 1620 cm^{-1} (C═N—). ^{1}HNMR(DMSO-d_6): $\delta = 2.4$, 2.7 (2s, 6H, 2CH_3), 6.2, 6.8(2d, 4H, CH-pyrryl), 7.05 (s, 1H, CH-pyridine), 7.3–7.8 (m, 5H, CH-aromatic), 8.1 (s, 1H, CH-pyrimidine) and 11.9 (s, 1H, NH).

4,6-Dimethyl-2-[2-amino-3-cyano-4(H)-4phenylpyran-6-yl]-3-(pyrrol-1yl)thieno[2,3-b]pyridine (10)

To a mixture of chalcone compound **5a** (3.58 gm, 0.01 mol) and malononitrile (0.01 mol) in absolute ethanol (25 mL), a few drops of piperidine were added. The mixture was heated under reflux for 5 h, allowed to cool, and poured into cold water. The solid product was collected and recrystallized from dioxane as yellowish white crystals, 2.8 gm, 66% yield, m.p. > 300°C.

Anal. calcd. for $C_{25}H_{20}N_4OS$(424.53): C, 70.73; H, 4.75; N, 13.20; S, 7.55%. Found: C, 70.91; H, 4.88; N, 12.98; S, 7.72%. IR: $\nu = 3440$, 3340 cm^{-1} (NH_2) and 1220 cm^{-1} (CN). ^{1}HNMR(DMSO-d_6): $\delta = 2.35$, 2.7 (2s, 6H, $2CH_3$), 4.05 (s, 1H, CH-pyran), 6.6 (s, 2H, NH_2), 6.2, 6.9 (2d, 4H, CH-pyrryl), 7.05 (s, 1H, CH-pyridine), 7.2–7.7 (m, 5H, CH-aromatic).

4,6-Dimethyl-3(pyrrol-1yl)thieno[2,3-b]pyridin-2-acetylsemicarbazone (11a)

A mixture of compound **2** (2.73 gm, 0.01 mol), semicarbazidehydrochloride (1.11 gm, 0.01 mol), and sodium acetate (1.23 gm, 0.015 mol) in ethanol (20 mL) was heated under reflux for 5 h, allowed to cool, and poured into cold water. The solid product was collected and recrystallized from ethanol as yellow crystals, 2.23 gm, 68% yield, m.p. 298°C.

Anal. calcd. for $C_{16}H_{17}N_5OS$(327.40): C, 58.70; H, 5.23; N, 21.39; S, 9.79%. Found: C, 58.85; H, 5.05; N, 21.17; S, 10.00%. IR: $\nu = 3370, 3270$, 3120 cm^{-1} (NH, NH_2), 1675 cm^{-1} (C=O). ^{1}HNMR(DMSO-d_6): $\delta = 2.1$, 2.5, 2.9 (3s, 9H, $3CH_3$) , 6.2–6.4, 6.55–6.75 (2m, 4H, 4CH-pyrrolyl ring), 6.9 (s, 1H, CH-pyridine), 5.5 (s, 2H, NH_2) and 9.8 (s, 1H, NH).

4,6-Dimethyl-3(pyrrol-1yl)thieno[2,3-b]pyridin-2-acetylthiosemicarbazone (11b)

A mixture of compound **2** (2.73 gm, 0.01 mol) and thiosemicarbazide (0.91 gm, 0.01 mol) in acetic acid (20 mL) was heated under reflux for 2 h and then allowed to cool. The solid product was collected and recrystallized from acetic acid as yellow crystals, 2.47 gm, 72% yield, m.p. 270°C.

Anal. calcd. for $C_{16}H_{17}N_5S_2$(343.46): C, 55.95; H, 4.99; N, 20.39; S, 18.67%. Found: C, 56.15; H, 5.21; N, 20.12; S, 18.86%. IR: $\nu = 3370$, 3270, 3120 cm^{-1} (NH, NH_2). ^{1}HNMR (DMSO-d_6): $\delta = 2.1$, 2.5, 2.9 (3s, 9H, $3CH_3$) , 6.2–6.4, 6.55–6.75 (2m, 4H, 4CH-pyrrolyl ring), 6.9 (s, 1H, CH-pyridine), 5.5 (s, 2H, NH_2) and 9.8 (s, 1H, NH).

4,6-Dimethyl-3(pyrrol-1yl)thieno[2,3-b]pyridin-2-acetylphenylhydrazone (11c)

A mixture of compound **2** (2.73 gm, 0.01 mol) and phenyl hydrazine (1.1 gm, 0.01 mol) in ethanol (20 mL) was heated under reflux for 5 h, allowed to cool, and poured into cold water. The solid product was collected and recrystallized from ethanol as yellow crystals in 74% yield, m.p. 235°C. Anal. calcd. for $C_{21}H_{20}N_4S$(360.48): C, 69.97; H, 5.59; N, 15.54; S, 8.89%. Found: C, 70.07; H, 5.40; N, 15.51; S, 9.08%. IR: $\nu = 3410$ cm^{-1} (NH). ^{1}HNMR(DMSO-d_6): $\delta = 2.1$, 2.5, 2.9 (3s, 9H, $3CH_3$) , 6.2–6.4, 6.55–6.75

(2m, 4H, 4CH-pyrrolyl ring), 6.9 (s, 1H, CH-pyridine), and 10.8 (s, 1H, NH).

4,6-Dimethyl-3(pyrrol-1yl)thieno[2,3-b]pyridin-2-acetyhydrazone (11d)

A mixture of compound **2** (2.73 gm, 0.01 mol) and hydrazine hydrate (0.5 gm, 99%, 0.01 mol) in ethanol (20 mL) was heated under reflux for 5 h, allowed to cool, and poured into cold water. The solid product was collected and recrystallized from ethanol as yellow crystals, 2.1 gm, 74% yield, m.p. 208°C.

Anal. calcd. for $C_{15}H_{16}N_4S$(284.38): C, 63.35; H, 5.67; N, 19.70; S, 11.27%. Found: C, 63.52; H, 5.80; N, 19.52; S, 11.05%. IR: $\nu = 3370$, 3270, 3120 cm^{-1} (NH, NH_2). ^{1}HNMR (DMSO-d_6): $\delta = 2.1$, 2.5, 2.9 (3s, 9H, $3CH_3$), 6.2–6.4, 6.55–6.75 (2m, 4H, 4CH-pyrrolyl ring), 6.9 (s, 1H, CH-pyridine), 4.6 (s, 2H NH_2).

The Cyclization of Thiosemicarbazone 11b with α-Halocompounds

General Procedure

A mixture of compound **11b** (3.4 gm, 0.01 mol), α-halocompound (0.01 mol), and sod. acetate (0.012 mol) in ethanol (30 mL) was refluxed for 5 h and allowed to cool. The solid product was collected, washed well with water, and recrystallized from dioxan. Physical constants and spectral data of compounds **12a**,**b** and **13a**,**b** are listed in Tables I and II.

REFERENCES

[1] I. Adachi, T. Yamamori, Y. Hiramatsu, K. Sakai, S. Mihara, M. Kawakami, M. Masui, O. Uno, and M. Ueda, *Chem. Pharm. Bull.*, **36,** 4389 (1988).
[2] M. Ueda, T. Gemba, M. Eigyo, and Y. Adachi, European Patent Appl; EP: 519,602 (1992); *C.A.*, **118,** 94335t (1993).
[3] Y. Saito, M. Yasushi, M. Sakashita, K. Toyoda, and T. Shibazalti, European Patent Appl; EP 535,548 (1993); *C.A.*, **119,** 117112e (1993).
[4] M. Z. A. Badr, S. A. Mahgoub, F. F. Abdel-Latif, and A. A. Abd El-Hafez, *Phosphorus, Sulfur, and Silicon*, **55,** 175 (1991).
[5] H. S. El-Kashef, A. A. Geies, A. M. Kamal El-Dean, and A. A. Abdel-Hafez, *J. Chem. Tech., Biotechnol.*, **57,** 15 (1993).
[6] E. A. Bakhite, A. A. Geies, A. M. Kamal El-Dean, and H. S. El-Kashef, *Phosphorus, Sulfur, and Silicon*, **104,** 143 (1995).
[7] H. S. El-Kashef, A. M. Kamal El-Dean, A. A. Geies, J. C. Lancelot, P. Dallemagne, and S. Rault, *J. Heterocyclic Chem.*, **37,** 1521 (2000).
[8] Kh. M. Hassan, A. M. Kamal El-Dean, M. S. K. Youssef, F. M. Atta, and M. S. Abbady, *Phosphorus, Sulfur, and Silicon*, **47,** 181 (1990).
[9] Y. W. Ho and I. J. Wang, *J. Heterocycl. Chem.*, **32,** 819 (1995).