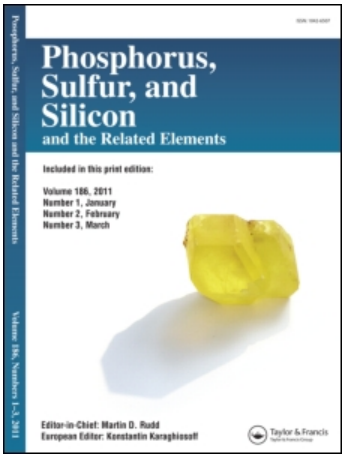

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Thieno[2,3-b]pyridine-2-carbohydrazide in Polyheterocyclic Synthesis: The Synthesis of Pyrido[3',2':4,5]thieno[3,2-d]pyrimidine, Pyrido[3',2':4,5]thieno[3,2-d][1,2,3]triazine, and Pyrazolyl, Oxadiazolylthieno[2,3-b]pyridine Derivatives

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Thieno[2,3-*b*]pyridine-2-carbohydrazide in Polyheterocyclic Synthesis: The Synthesis of Pyrido[3′,2′:4,5]thieno[3,2-*d*]pyrimidine, Pyrido[3′,2′:4,5]thieno[3,2-*d*][1,2,3]triazine, and Pyrazolyl, Oxadiazolylthieno[2,3-*b*]pyridine Derivatives

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*Pyrdine-2(1*H*)-thione **1** reacted with ethyl chloroacetate **2** to give 2-*S*-ethoxycarbonylmethylpyridine derivative **3**, which could be cyclized into thieno[2,3-*b*]pyridine-2-carbohydrazide derivative **5** by boiling with hydrazine hydrate. The latter compound reacted with cinnamonitrile derivatives **6a**,**b**, triethylorthoformate, formic acid, dimethylformamide-dimethylacetal, and diethyl carbonate to give the corresponding shiff base **7a**, **b** and pyrido[3′,2′;4,5]thieno[3,2-d]pyrimidine derivatives **10–13** in respective manner. On the other hand, compound **5** also reacted with carbondisulphide and phenyl isothiocyanate to afford the corresponding 2-(1,3,4-oxadiazolo-2-yl)thieno[2,3-b]pyridine derivatives **18** and **22**. Finally, compound **5** reacted with some β-dicarbonyl compounds, such as ethyl acetoacetate, acetylacetone and ethyl β-arylazoacetoacetate, to yield the corresponding 2-(pyrazol-1-ylcarbonyl)thieno[2,3-b]pyridine derivatives **24**, **25**, and **27** respectively.*

Keywords 2-(1,3,4-Oxadiazolo-2-yl)thieno[2,3-*b*]pyridine; 2-(pyrazol-1-ylcarbonyl)-thieno[2,3-*b*]pyridine; pyridine-2(1*H*)-thiones; thieno[2,3-*b*]pyridine-2-carbohydrazide, thieno[2,3-*b*]pyridines; pyrido[3′,2′:4,5]thieno[3,2-*d*]pyrimidines

INTRODUCTION

Thieno[2,3-*b*]pyridines are of special importance due to the reported biological activities, such as antimicrobial,[1–5] anti-inflammatory,[6] and

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ganadotropin-releasing hormone antagonizing activities,[7] they also have neurotropic activity.[8] Furthermore, pyridothienopyrimidines were reported to have antiallergic,[9] antiparasitic,[10] antianaphylactic,[11,12] and anti-microbial[1,2] activities. In addition, pyridothienotriazines were reported to have antiparasitic activity.[10] The interesting biological activities reported for these classes of compounds, and in continuation of our efforts on the synthesis of expected biologically active heterocyclic compounds utilizing thieno[2,3-*b*]-pyridine,[4,13–20] have stimulated us to investigate the reaction of thieno[2,3-*b*]pyridine **4**[13] with different reagents for the synthesis of some novel of heterocyclic moieties.

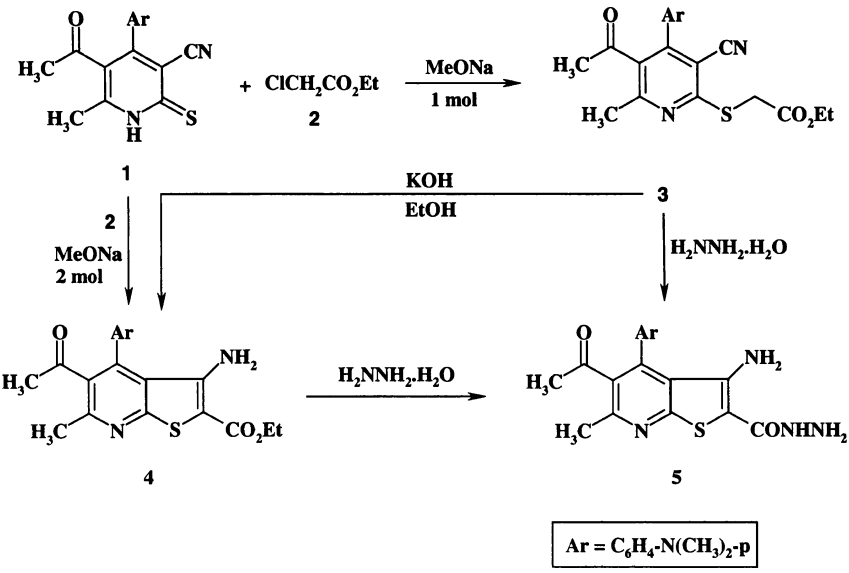
RESULTS AND DISCUSSION

It has been found that pyridine-2(1*H*)-thione **1** reacted with ethyl chloroacetate **2** in sodium methoxide solution (prepared from 1 mole of sodium and 30 mL of methanol) to give the corresponding 2-ethoxycarbonylmethylthiopyridine derivative **3**, which could be, in turn, cyclized to the 2-hyrazinocrbonylthieno[2,3-*b*]pyridine derivative **5** via its reaction with hydrazine hydrate. The IR spectrum of compound **5** showed the absorption bands (3472, 3338, and 3199) corresponded to NH_2 and $NHNH_2$; two carbonyl groups (1696.2 and 1659) corresponded to acetyl carbonyl and hydrazidic carbonyl and did not show any absorption band attributed to the nitrile function, which could be consumed in the reaction via the addition of the methylene group of **3** to the cyano group. ^{1}H-NMR of **5** revealed the signals of NH and NH_2 and did not reveal any signals attributed to the ethyl function. Moreover, the mass spectrum of **5** gave the molecular ion peak M^+ at m/z = 383 (38.9%) and the base peak at m/z = 309 (100%) corresponding to M^+ (383) − [HN-NH_2 (31) + $CONH_2$(44)] + H (1).

The structure of compound **5** was confirmed via its synthesis by the reaction of **4** (prepared from the reaction of **1** with **2** in the presence of two moles of sodium methoxide in boiling methanol or by heating **3** in ethanolic potassium hydroxide solution)[13] with hydrazine hydrate (c.f. Scheme 1, Figure 1, and Experimental section).

Compound **5** could be used as starting material to synthesize new heterocyclic moieties, such as pyrido[3′,2′:4,5]thieno[3,2-*d*][1,2,3]-triazin-4-one **9a,b**, pyrido[3′,2′:4,5]thieno[3,2-*d*]pyrimidine **10–13**, imidazo[4′,5′:4,5]thieno[2,3-*d*]pyridine **16**, and pyrazolo[3′,4′:4,5]thieno-[2,3-*b*]pyridine **17** derivatives.

It has been found that compound **5** reacted with cinnamonitrile derivative **6a** to afford the corresponding 3-amino-N′-{[4-(dimethylamino)phenyl]methylene}thieno[2,3-*b*]pyridine-2-carbohydrazide



SCHEME 1

derivative **7a**. The IR spectrum of **7a** showed absorption bands of NH and NH_2 (3457.7, 3315.1, and 3260.1), acetyl carbonyl (1697.2), and hydrazidic carbonyl (1632). Its ^{1}H-NMR revealed a new signal at $\delta = 7.69$, which corresponded to the imino-CH proton. The reaction between **5** and **6a** proceeded via a ylidene exchange with the elimination of one molecule of malononitrile. Compound **7a** could be prepared via another route by the reaction of **5** with 4-(*N,N*-dimethylamino)benzaldehyde **8a**, compound **7a** synthesized via this route and was found to be identical in all aspects (spectral data, m.p., and mixed m.p.) with **7a** previously prepared.

A third elucidation of the structure of compound **7a** came from its cyclization by the reaction with sodium nitrite in the presence of concentrated hydrochloric acid[21] to give the corresponding pyrido-[3′,2′:4,5]thieno[3,2-*d*][1,2,3]triazinone derivative **9a**. The IR spectrum of compound **9a** did not show any absorption bands that corresponded to the NH or NH_2, indicating that they were consumed in the reaction to form the salt of diazonium chloride, which underwent self coupling with the loss of one molecule of hydrogen chloride under experimental reaction conditions. Moreover, its ^{1}H-NMR spectrum didn't reveal any signals that corresponded to NH or NH_2. Based on the previously discussed data compound **9a** could be formulated as 3-({[4-(dimethylamino)phenyl]methylene}amino)pyrido-[3′,2′:4,5]

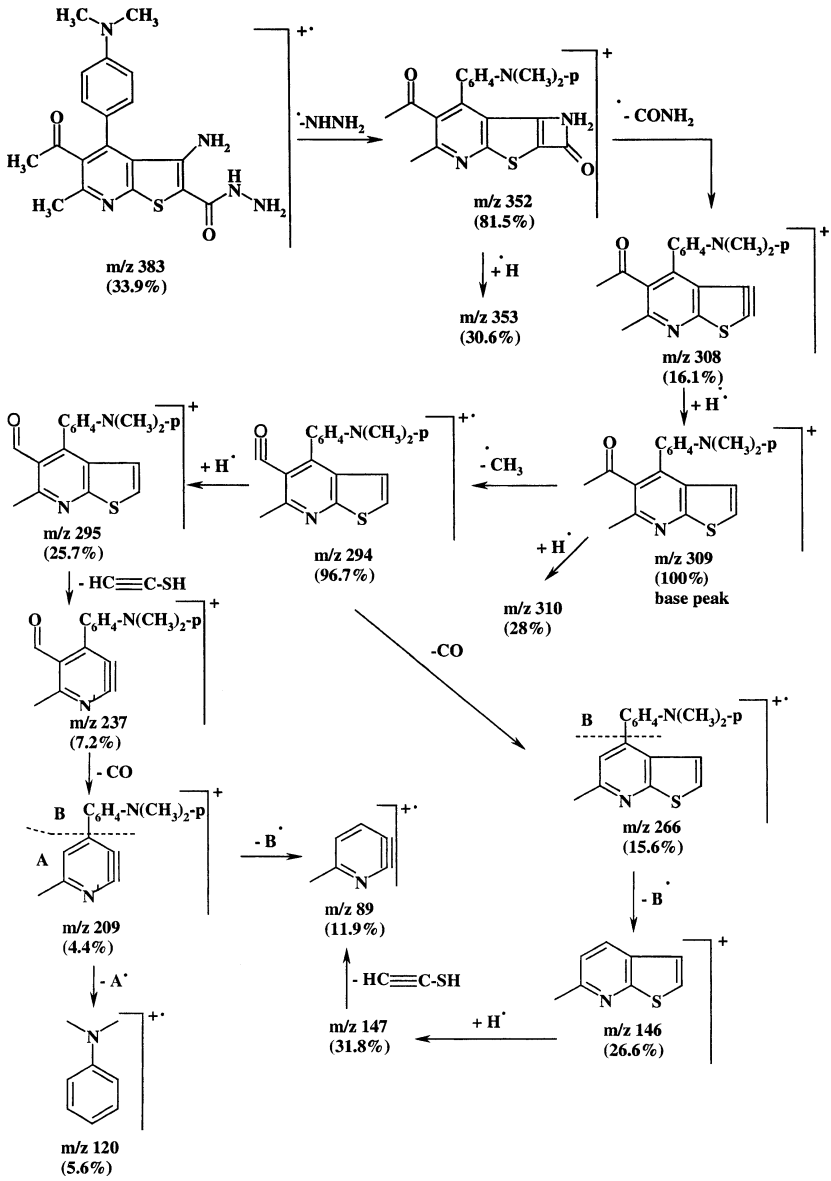
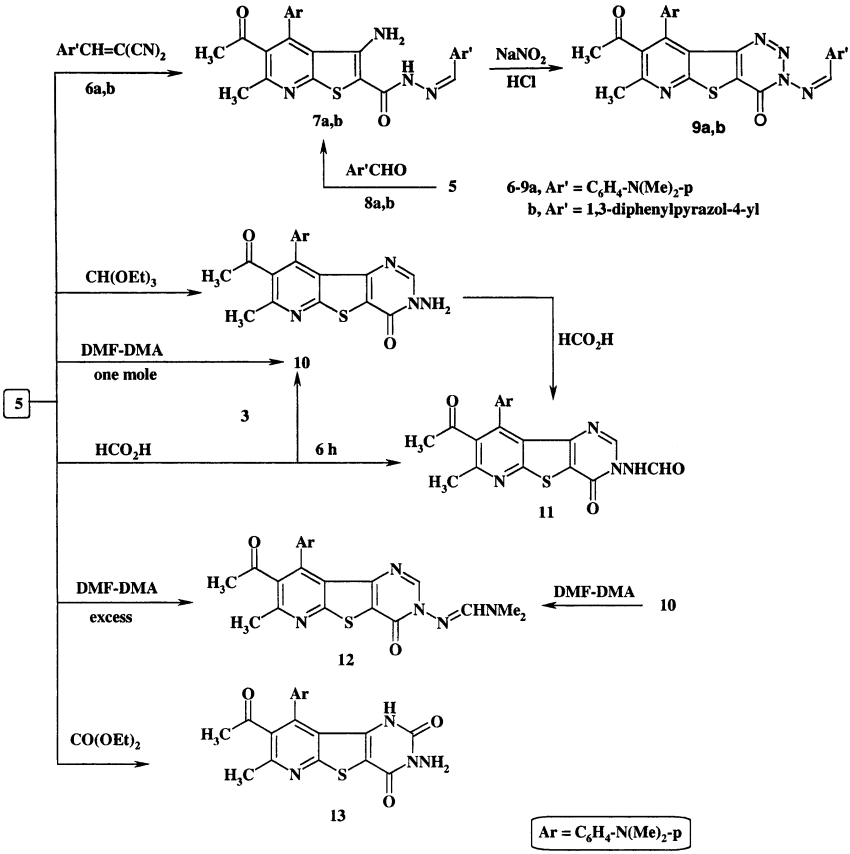


FIGURE 1 Fragmentation pattern of compound **5**.

thieno[3,2-*d*][1,2,3]triazin-4(3*H*)-one derivative. In the same manner, compounds **5** reacted with cinnamonitrile derivative **6b** to afford the corresponding 3-amino-N′-[(1,3-diphenyl-1*H*-pyrzol-4-yl)-methylene]thieno[2,3-*b*]pyridine-2-carbohydrazide derivative **7b**. The

structure of compound **7b** was confirmed via its synthesis by the reaction of **5** with aromatic aldehyde **8b** to give **7b**. Compound **7b** reacted with sodium nitrite in the presence of concentrated hydrochloric acid to afford the corresponding 3-{[(1,3-diphenyl-1*H*-pyrzol-4-yl)-methylene]amino}pyrido[3′,2′:4,5]thieno[3,2-*d*][1,2,3]triazin-4(3*H*)-one derivative **9b** (c.f. Scheme 2 and Experimental section).



SCHEME 2

Work was also extended to shed more light on the synthetic potential of compound **5** to synthesize a new moiety of pyrido[3′,2′:4,5]thieno-[3,2-*d*]pyrimidinone derivatives **10–13** by using available reagents, such as triethylorthoformate, formic acid, dimethylformamide-dimthylacetal (DMF-DMA), and diethyl carbonate. Thus, it has been found that compound **5** reacted with triethylorthoformate to give the corresponding 3-aminopyrido[3′,2′:4,5]thieno[3,2-*d*]pyrimidine

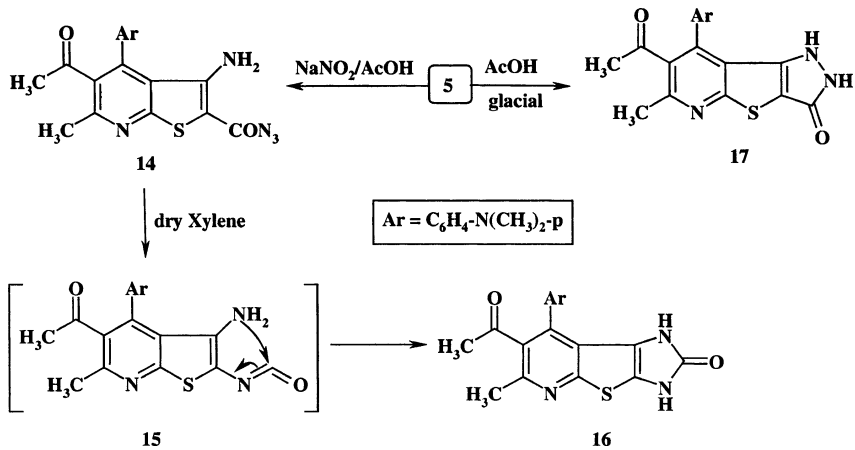
derivative **10**. The IR of **10** showed absorption bands of amino (3310.6, 3200.4), acetyl-CO (1699.8), and pyrimidine-CO (1645.5) groups. The ^{1}H-NMR of **10** revealed a singlet signal at $\delta = 5.99$ that corresponded to NH_2 and a singlet signal at $\delta = 8.28$, which corresponded to pyrimidine-2H (c.f. Scheme 2 and Experimental section).[22] Compound **10** could be prepared via another route by the condensation of **5** with formic acid or one mole of DMF-DMA under reflux for 3 h. Compound **10** that formed via this route was found to be identical in all aspects as **10** was previously prepared (spectral data, m.p., and mixed m.p.). Further elucidation for the structure of **10** came from its reaction with formic acid again to yield 3-fomylaminopyrido[3′,2′:4,5]thieno[3,2-*d*]pyrimidin-4-one derivative **11**. The IR spectrum of **11** showed absorption bands corresponded to NH (3310.9) and CO of the formyl group (1721.3). Moreover, its ^{1}H-NMR spectrum revealed a singlet signal at $\delta = 8.47$, which corresponded to the aldehydic proton, and a singlet signal at $\delta = 11.54$, which corresponded to the NH. Compound **11** could be prepared via another route by heating **5** with formic acid[23] for 6 h (c.f. Scheme 2 and Experimental section).

The condensation of compound **5** with excess DMF-DMA in dry xylene to give the corresponding 3-{(dimethylaminomethylene)amino}-pyrido[3′,2′:4,5]thieno[3,2-*d*]pyrimidinone derivative **12**. The IR spectrum of **12** showed absorption bands corresponded to acetyl-CO and pyrimidine-CO groups and didn't show any absorption band that corresponded to the amino group, which was consumed in the reaction. Moreover, its ^{1}H-NMR spectrum revealed two new singlets at $\delta = 8.09$ and $\delta = 8.16$, which corresponded to the pyrimidine-2H and methyne-protons and didn't reveal any signal that corresponded to the NH_2 group. The structure of compound **12** could be confirmed via its synthesis from the reaction of **10** and DMF-DMA in boiling dry xylene (c.f. Scheme 2 and Experimental section).

Finally, due to broad biological activities of the pyrido-[3′,2′:4,5]thieno[3,2-*d*]pyrimidinone moiety, compound **5** reacted with diethyl carbonate to afford the corresponding 3-aminopyrido[3′,2′:4,5]-thieno[3,2-*d*]pyrimidin-2,4-dione derivative **13**. The structure of **13** was confirmed based on the elemental analysis and spectral data (c.f. Scheme 2 and Experimental section).

The work was extended to synthesize novel heterocyclic derivatives containing a five membered-ring with two nitrogen atoms. Thus, it has been found that compound **5** reacted with a cold solution of sodium nitrite in the presence of acetic acid to give the corresponding 3-aminothieno[2,3-*b*]pyridine-2-carbonylazide derivative **14**. The IR spectrum of **14** showed the new absorption band at 2137.6, which was attributed to the azide[22,23] function and NH_2 (3473.7 and 3321.2). Its

^{1}H-NMR revealed a singlet signal at $\delta = 10$ ppm, which corresponded to NH_2 and did not reveal any signals that may be attributed to the $NHNH_2$ protons, which were consumed in the formation of the azide function.[22,23] Further confirmation of structure **14** came from its cyclization in dry xylene into the corresponding imidazo[4′, 5′ : 4, 5]thieno-[2,3-*b*]pyridine derivative **16**. Compound **16** was formed via a Curtius rearrangement[22,23] of compound **14** into isocyanate **15** followed by a nucleophilic addition of the NH_2 function of **15** to the N=C=O to yield the novel condensed imidazole **16**. The IR spectrum of **16** showed new absorption bands of two NH and CO groups of a new imidazole moiety and absence of any absorption band due to the azide function. The ^{1}H-NMR spectrum of the latter compound revealed new signals at $\delta = 9.38$, and $\delta = 11.08$, which corresponded to the two NH protons (c.f. Scheme 3 and Experimental section).

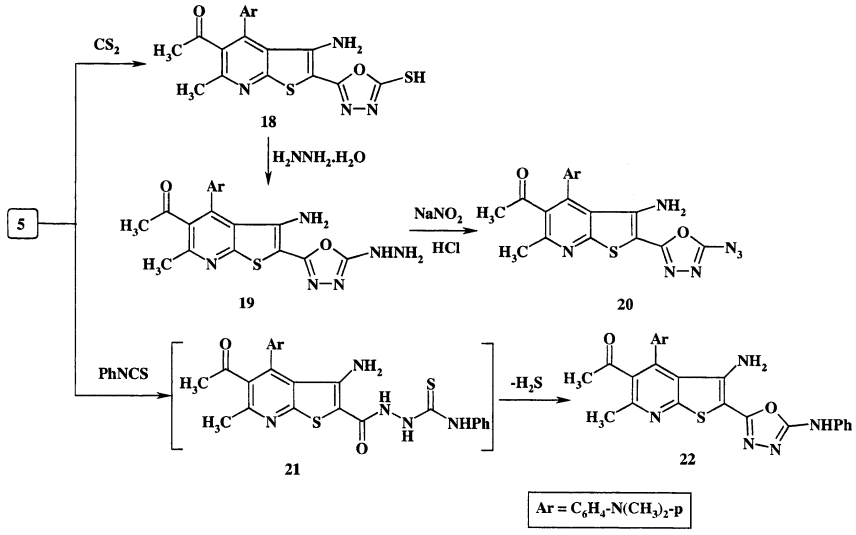


SCHEME 3

A new pyrazolo[3′,4′:4,5]thieno[2,3-*b*]pyridine derivative **17** was formed via the treatment of **5** with glacial acetic acid under reflux for 4 h, the structure of the latter compound was elucidated based on the elemental analysis and spectral data (c.f. Scheme 3 and Experimental section).

In continuation of the present work, compound **5** reacted with sulfur-containing compounds, such as carbon disulphide and phenylisothiocynate, to synthesize new heterocyclic rings such as 2-(1,3,4-oxadiazolo-2-yl)thieno[2,3-*b*]pyridine derivatives **18–20**, **22** respectively. Thus, it has been found that compound **5** reacted with carbon disulphide in pyridine to give the corresponding 3-amino-2-(5-mercapto-1,3,4-oxadiazol-2-yl)thieno[2,3-*b*]pyridine derivative **18**. The structure of **18**

was inferred by elemental analysis and chemical transformation. The ^{1}H-NMR spectrum of compound **18** revealed a new signal at $\delta = 7.35$, which corresponded to the -SH proton. The reaction of **18** with hydrazine hydrate afforded the corresponding 3-amino-2-(5-hydrazino-1,3,4-oxadiazol-2-yl)thieno[2,3-*b*]pyridine derivative **19** via the loss of one molecule of hydrogen sulfide. The latter compound was further confirmed via its reaction with sodium nitrite in the presence of concentrated hydrochloric acid to give the corresponding 3-amino-2-(5-azido-1,3,4-oxadiazol-2-yl)thieno[2,3-*b*]pyridine derivative **20**. The structure of compounds **18–20** was confirmed based on the elemental analysis and spectral data. (c.f. Scheme 4 and Experimental section).

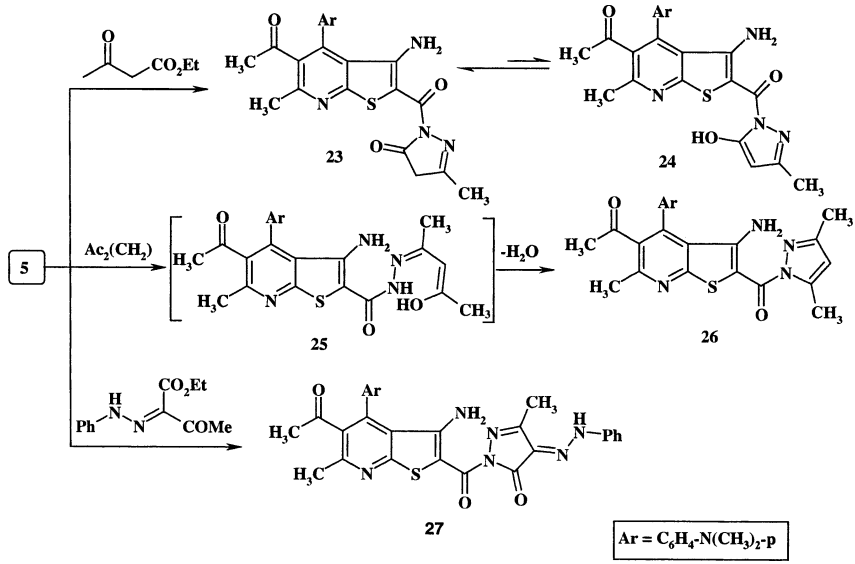


SCHEME 4

On the other hand, compound **5** reacted with phenylisothiocyanate to give the corresponding 3-amino-2-(5-phenylamino-1,3,4-oxadiazol-2-yl)thieno[2,3-*b*]pyridine derivative **22** via the loss of one molecule of hydrogen sulfide through the formation of the intermediate **21**. (c.f. Scheme 4 and Experimental section).

Finally, compound **5** reacted with different β-dicarbonyl compounds to form 2-(pyrazol-2-yl)thieno[2,3-*b*]pyridine derivative **23**, **26**, and **27**. Thus, it has been found that compound **5** reacted with ethyl acetoacetate in boiling glacial acetic acid and gave the corresponding 2-(pyrazol-1-yl)thieno[2,3-*b*]pyridine derivative **23** or **24**. The IR spectrum of the reaction product showed absorption bands corresponded to amino and carbonyl groups and didn't show any absorption band attributed to

the hydroxyl group. Moreover, its ^{1}H-NMR revealed a singlet signal at $\delta = 2.29$ that corresponded to the pyrazolyl-CH_2 and absence of any signals that corresponded to the OH or CH of the pyrazole moietyl. Based on the previously discussed data the reaction product was formulated as 5-acetyl-3-amino-4-(4-dimethylaminophenyl)-2-[carbonyl(3-methyl-4,5-dihydro-5*H*-pyrazol-5- on-1-yl)]-6-methylthieno[2,3-*b*]pyridine **23** and not the enol form **24** (c.f. Scheme 5 and Experimental section).



SCHEME 5

In the same manner, compound **5** reacted with acetylacetone and ethyl 2-arylazoacetoacetate to give the corresponding 2-(pyrazol-1-yl)-thieno[2,3-*b*]pyridine derivative **26** and the hydrazo form 2-(4-phenylhydrazonopyrazol-1-yl)thieno[2,3-*b*]pyridine derivative **27** based on the elemental analyses and spectral data (c.f. Scheme 5 and Experimental section).

EXPERIMENTAL

All melting points were measured on a Gallenkamp electrothermal melting point apparatus and are uncorrected. The infrared spectra were recorded in potassium bromide on Pye Unicam SP 3-300 infrared and FT-IR 8101PC Schimadzu spectrophotometer. The ^{1}H-NMR spectra were recorded in deutrated chloroform or dimethyl sulphoxide on a

Varian Gemini 200 NMR and varian Mercury 300 MHz spectrometer using tetramethylsilane (TMS) as an internal reference; mass spectra were recorded on GCMS-QP 1000 EX Shimatzu mass spectrometer at 70 eV. Elemental analyses were carried out at the Microanalytical Center of Cairo University, Giza, Egypt.

Compound **1** and **4** were prepared according to the literature procedure.[13]

The Synthesis of 3

A solution of each of **1** (0.01 mol) and ethyl chloroacetate **2** (0.01 mol) in sodium methoxide (prepared from 0.01 g of sodium and 30 mL of methanol) was heated under reflux for 4 h, cooled, poured onto ice cold water, and neutralized (pH = 7) with concentrated hydrochloric acid, the solid was collected by filtration, dried, and crystallized from dioxane to give **3** (c.f. Tables I and II).

The Synthesis of 5 and 19

A solution of each of **3** or **4** and **18** (0.01 mol) in hydrazine hydrate (15 mL) and ethanol (20 mL) was heated under reflux for 6 h; the excess solvents were evaporated in vacuo (to 1/3 of the solution) and cooled. The solid was collected by filtration, dried, and crystallized from the proper solvent to give **5** and **19**, respectively (c.f. Tables I and II).

The Synthesis of 7a,b

Method A

A solution of each of **5** (0.01 mol) and cinnamonitrile derivatives **6a**, **b** (0.01 mol) in pyridine (15 mL) and ethanol (20 mL) was heated under reflux for 2 h, the excess solvents were evaporated in vacuo (to 1/3 of the solution) and cooled, the solid was collected by filtration, dried, and crystallized from the acetic acid to give **7a**, **b** respectively (c.f. Tables I and II).

Method B

A solution of each of **5** (0.01 mol) and aromatic aldehydes **8a**, **b** (0.01 mol) in pyridine (15 mL) and ethanol (20 mL) was heated under reflux for 2 h. Excess solvents were evaporated in vacuo (to 1/3 of the solution) and cooled, the solid was collected by filtration, dried, and crystallized from the acetic acid to give **7a**, **b** respectively (c.f. Tables I and II).

TABLE I Elemental Analyses of the Newly Synthesized Compounds

Compound no.	Mol. formula/ mol. wt.	Solvent of cry. yield %	Colour/ m.p.°C	Analyses calc./found			
				C	H	N	S
3	$C_{21}H_{23}N_3O_3S$	Dioxane	Yellow	63.46	5.83	10.57	8.07
	397.50	70	167–169	63.20	6.10	10.90	7.9
5	$C_{19}H_{21}N_5O_2S$	Ethanol	Yellow	59.51	5.52	18.26	8.36
	383.48	75	236–238	59.80	5.80	18.50	8.1
7a	$C_{28}H_{30}N_6O_2S$	Acetic acid	Yellow	65.35	5.88	16.33	6.23
	514.65	69	296–298	65.00	5.50	16.50	6.60
7b	$C_{35}H_{31}N_7O_2S$	Acetic acid	Yellow	68.50	5.09	15.98	5.22
	613.75	78	288–290	68.20	4.90	15.70	5.00
9a	$C_{28}H_{27}N_7O_2S$	Dioxane	Yellow	63.98	5.18	18.65	6.10
	525.64	85	230–232	63.80	5.10	18.30	5.90
9b	$C_{35}H_{28}N_8O_2S$	Dioxane	Yellow	67.29	4.52	17.94	5.13
	624.73	75	222–224	67.50	4.40	17.90	5.00
10	$C_{20}H_{19}N_5O_2S$	Ethanol	Yellow	61.05	4.87	17.80	8.15
	393.47	73	266–268	61.00	4.70	17.70	8.10
11	$C_{21}H_{19}N_5O_3S$	Acetic acid	Yellow	59.84	4.54	16.62	7.61
	421.48	71	180–182	59.60	4.40	16.40	7.40
12	$C_{23}H_{24}N_6O_2S$	Dioxane	Yellow	61.59	5.39	18.74	7.15
	448.55	68	279–281	61.40	5.50	18.70	7.30
13	$C_{20}H_{19}N_5O_3S$	Ethanol	Yellow	58.67	4.68	17.10	7.83
	409.47	67	318–320	58.30	4.30	17.00	7.60
14	$C_{19}H_{18}N_6O_2S$	Ethanol	Brown	57.85	4.60	21.31	8.13
	394.46	79	180–182	57.70	4.30	21.20	8.20
16	$C_{17}H_{12}N_4O_2S$	DMF/H_2O	Brown	60.70	3.60	16.66	9.53
	336.37	76	>300	60.50	3.40	16.50	9.40
17	$C_{19}H_{18}N_4O_2S$	Acetic acid	Yellow	62.28	4.95	15.29	8.75
	366.44	74	290–292	61.90	5.00	15.10	8.60
18	$C_{20}H_{19}N_5O_2S_2$	Ethanol	Pale/Brown	56.45	4.50	16.46	15.07
	425.53	75	284–286	56.10	4.30	16.40	15.10
19	$C_{20}H_{21}N_7O_2S$	Dioxane	Yellow	56.72	5.00	23.15	7.57
	423.50	76	236–238	56.50	4.90	23.00	7.30
20	$C_{20}H_{18}N_8O_2S$	Dioxane	Yellow	55.29	4.18	25.79	7.38
	434.476	75	>330	55.60	4.50	25.70	7.50
22	$C_{26}H_{24}N_6O_2S$	Ethanol	Brown	64.44	4.99	17.34	6.62
	484.58	81	168–170	64.20	4.80	17.10	6.50
23	$C_{23}H_{23}N_5O_3S$	Acetic acid	Yellow	61.45	5.16	15.58	7.13
	449.54	73	>320	61.20	5.30	15.60	7.40
26	$C_{24}H_{25}N_5O_2S$	Acetic acid	Yellow	64.41	5.63	15.65	7.16
	447.56	79	250–252	64.30	5.60	16.50	6.90
27	$C_{29}H_{27}N_7O_3S$	Acetic acid	Brown	62.91	4.92	17.71	5.79
	553.65	70	276–178	62.70	5.22	17.50	5.60

The Synthesis of 9a,b, 14, and 20

A stirred solution (0–5°C) of the appropriate of thieno[2,3-*b*]pyridine derivatives **7a**, **b**, **5**, and **19** (0.01 mol) in acetic acid (20 mL) and

TABLE II IR (cm^{-1}) and ^{1}H-NMR Spectra of Newly Synthesized Compounds

Compound no.	IR (cm^{-1})	^{1}H-NMR δ (ppm)
3	2218.7 (CN) and 17461, 1694.4 (two C=O)	$CDCl_3$, 1.19 (t, 3H, $CH_2\underline{CH_3}$), 1.80 (s, 3H, CH_3), 2.34 (s, 3H, $COCH_3$), 2.97 (s, 6H, $N(CH_3)_2$), 3.71 (s, 2H, -SCH_2), 3.91 (q, 2H, $\underline{CH_2}CH_3$), 6.73 (d, J = 8.8 Hz, 2H, Ar-H) and 7.15 (d, J = 8.8 Hz, 2H, Ar-H)
5	3472.1, 3338.4, 3199.5 (NH & NH_2) and 1696.2, 1659 (two C=O)	$CDCl_3$, 1.88 (s, 3H, CH_3), 2.48 (s, 3H, $COCH_3$), 2.97 (s, 6H, $N(CH_3)_2$), 3.64–4.09 (br. 3H, $NHNH_2$), 5.78 (br. 2H, NH_2), 6.68 (d, J = 8.4 Hz, 2H, Ar-H) and 7.08 (d, J = 8.4 Hz, 2H, Ar-H)
7a	3475.7, 3315.1, 3260.1 (NH_2 & NH) and 1697.2, 1632 (two C=O)	$CDCl_3$, 1.9 (s, 3H, CH_3), 2.57 (s, 3H, $COCH_3$), 2.99 (s, 12H, two $N(CH_3)_2$), 6.72 (d, J = 8.7 Hz, 2H, Ar-H), 6.90 (2H, s, NH_2), 7.13 (d, J = 8.7 Hz, 2H, Ar-H), 7.69 (s, 1H, CH) and 7.72 (NH)
7b	3475.7, 3315.1, 3260.1 (NH_2 & $NHNH_2$) and 1697.2, 1632 (two C=O)	DMSO-d_6, 1.89 (s, 3H, CH_3), 2.55 (s, 3H, $COCH_3$), 2.80 (s, 6H, $N(CH_3)_2$), 6.81 (2H, s, NH_2), 7.16-7.61 (m, 14H, Ar-H), 8.0 (s, 1H, CH), 8.21 (s, 1H, CH) and 8.90 (s, 1H, NH)
9a	1696.5, 1661.9 (two C=O)	DMSO-d_6, 2.13 (s, 3H, CH_3), 2.56 (s, 3H, $COCH_3$), 2.93 (s, 12H, two $N(CH_3)_2$), 7.26 (d, J = 8.3 Hz, 2H, Ar-H), 7.50 (d, J = 8.3 Hz, 2H, Ar-H) and 7.84 (s, 1H, CH)
9b	1696.5, 1661.9 (two C=O)	$CDCl_3$, 2.02 (s, 3H, CH_3), 2.62 (s, 3H, $COCH_3$), 3.04 (s, 6H, $N(CH_3)_2$), 7.18–7.76 (m, 14H, Ar-H), 8.47 (s, 1H, CH) and 8.78 (s, 1H, CH)
10	3310.6, 3200.4 (NH_2) and 1699.8, 1645.5 (two C=O)	DMSO-d6, 1.89 (3H, s, CH_3); 2.54 (3H, s, $COCH_3$); 2.99 (6H, s, $N(CH_3)_2$); 5.99 (2H, s, NH_2); 6.75 (d, J = 8.1 Hz, 2H, Ar-H), 7.14 (d, J = 8.1 Hz, 2H, Ar-H) and 8.28 (1H, s, CH- at pyrimidine)
11	3214.4 (NH) and 1721.3, 1678.2, 1610.9 (three C=O)	DMSO-d_6, 1.9 (s, 3H, CH_3), 2.50 (s, 3H, $COCH_3$), 2.99 (s, 6H, $N(CH_3)_2$), 6.75 (d, J = 8.2 Hz, 2H, Ar-H), 7.14 (d, J = 8.2 Hz, 2H, Ar-H), 8.28 (s, 1H, CH- at pyrimidine), 8.47 (s,1H, CHO) and 11.54 (s,1H, NH)
12	1695.9, 1669.4 (two C=O)	DMSO-d_6, 1.89 (3H, s, CH_3); 2.54 (3H, s, $COCH_3$); 2.99 (12H, s, -$N(CH_3)_2$); 6.74 (d, J = 8.7 Hz, 2H, Ar-H), 7.14 (d, J = 8.7 Hz, 2H, Ar-H), 8.09 (1H, s, -N=CH-) and 8.16 (1H, s, CH- at pyrimidine)
13	3459.9, 3301.33193 (NH_2 & NH) and 1687.8, 1650 (C=O)	DMSO-d_6, 1.89 (s, 3H, CH_3), 2.43 (s, 3H, $COCH_3$), 2.98 (s, 6H, $N(CH_3)_2$), 4.41 (2H, s, NH_2), 6.84 (d, J = 8.5 Hz, 2H, Ar-H) and 7.16 (d, J = 8.5 Hz, 2H, Ar-H) and 12.15 (s, 1H, NH)

TABLE II IR (cm^{-1}) and ^{1}H-NMR Spectra of Newly Synthesized Compounds *(Continued)*

Compound no.	IR (cm^{-1})	^{1}H-NMR δ (ppm)
14	3473.7, 3321.2 (NH_2); 2137.6 (azide N_3) and 1688, 1642 (two C=O)	DMSO-d_6, 1.9 (s, 3H, CH_3), 2.51 (s, 3H, $COCH_3$), 3.0 (s, 6H, $N(CH_3)_2$), 7.67 (d, J = 7.8 Hz, 2H, Ar-H), 7.67 (d, J = 7.8 Hz, 2H, Ar-H) and 10.0 (2H, s, NH_2)
16	3397.6 (two NH) and 1695.4, 1662.5 (two C=O)	DMSO-d_6, 1.90 (s, 3H, CH_3), 2.50 (s, 3H, $COCH_3$), 3.01 (s, 6H, $N(CH_3)_2$), 6.86 (d, J = 8.4 Hz, 2H, Ar-H), 7.11 (d, J = 8.4 Hz, 2H, Ar-H), 9.38 (s, 1H, NH) and 11.08 (s, 1H, NH).
17	3221.4 (two NH) and 1724.3, 1681.9 (two C=O)	$CDCl_3$, 1.88 (s, 3H, CH_3), 2.4 (s, 3H, $COCH_3$), 2.98 (s, 6H, $N(CH_3)_2$), 4.85 (s, 1H, NH), 6.73 (d, J = 8.4 Hz, 2H, Ar-H), 7.17 (d, J = 8.4 Hz, 2H, Ar-H), and 8.86 (s, 1H, NH).
18	3407, 3259.3 (NH_2) and 16997, 1664.9 (two C=O).	DMSO-d_6, 1.84 (s, 3H, CH_3), 2.55 (s, 3H, $COCH_3$), 2.58 (s, 2H, NH_2), 2.99 (s, 6H, $N(CH_3)_2$), 6.63 (d, J = 8.7 Hz, 2H, Ar-H), 7.11 (d, J = 8.7 Hz, 2H, Ar-H) and 7.35 (s, 1H, -SH)
19	3303.1, 3183.4 (NH & NH_2) and 1695.4, 1667.2 (C=O)	DMSO-d_6, 1.86 (s, 3H, CH_3), 2.50 (s, 3H, $COCH_3$), 2.91 (s, 6H, $N(CH_3)_2$), 4.08-4.56 (br, 4H, two NH_2) and 6.63-7.5 (m, 5H, Ar-H & NH)
20	3474, 3350 (NH_2), 2147.4 (azide N_3) and 1697.8 (C=O)	DMSO-d_6, 1.90 (s, 3H, CH_3), 2.60 (s, 3H, $COCH_3$), 2.98 (s, 6H, $N(CH_3)_2$), 3.40 (s, 2H, NH_2), 6.78 (d, J = 8.6 Hz, 2H, Ar-H) and 7.32 (d, J = 8.6 Hz, 2H, Ar-H)
22	3350.2 (NH) and 1695.9 (C=O)	$CDCl_3$, 1.93 (s, 3H, CH_3), 2.58 (s, 3H, $COCH_3$), 2.96 (s, 6H, $N(CH_3)_2$), 3.09 (s, 2H, NH_2), 6.77-7.42 (m, 11H, Ar-H & NH_2) and 9.89 (s, 1H, NH)
23	3377.4 (OH) and 1692.7 (C=O)	$CDCl_3$, 2.0 (s, 6H, two CH_3), 2.29 (s, 2H, CH_2), 2.57 (s, 3H, $COCH_3$), 3.03 (s, 6H, $N(CH_3)_2$), 5.58 (s, 2H, NH_2), 6.84 (d, J = 8.4 Hz, 2H, Ar-H) and 7.19 (d, J = 8.4 Hz, 2H, Ar-H)
26	3425.9, 3265 (NH_2) and 1698.8, 1659 (two C=O)	DMSO-d_6, 1.34 (s, 3H, CH_3), 1.88 (s, 3H, CH_3), 1.91 (s, 3H, CH_3), 2.43 (s, 3H, $COCH_3$), 2.95 (s, 6H, $N(CH_3)_2$), 3.53 (s, 2H, NH_2), 6.72 (d, J = 8.8 Hz, 2H, Ar-H), 6.97 (d, J = 8.8 Hz, 2H, Ar-H) and 9.12 (s, 1H, 4H-pyrazole)
27	3473.9, 3319.9 (NH_2) and 1696.2, 1638.1 and 1608.3 (three C=O)	$CDCl_3$, 1.91 (s, 3H, CH_3), 2.51 (s, 3H, CH_3), 2.57 (s, 3H, $COCH_3$), 2.91 (s, 2H, NH_2), 3.01 (s, 6H, $N(CH_3)_2$), 6.78 (d, 2H, Ar-H), 7.15 (s, 1H, NH) and 7.51-7.65 (m, 9H, Ar-H)

concentrated hydrochloric acid (3 mL) was treated with a cold solution of sodium nitrite (0.23 g in 5 mL of water) over 5 min. Stirring was continued for 1 h at 0–5°C; the solid was collected by filtration, dried, and crystallized from the proper solvent to give **9a**, **b**, **14**, and **20**, respectively (c.f. Tables I and II).

The Synthesis of 10

Method A

A solution of each of **5** (0.01 mol) and triethylorthoformate (10 mL) was heated under reflux for 4 h; the excess solvent was evaporated in vacuo (to 1/3 of the solution) and cooled. The solid was collected by filtration dried, and crystallized from ethanol to give **10** (c.f. Tables I and II).

Method B

A solution of each of **5** (0.01 mol) and formic acid (20 mL) or DMF-DMA (0.01 mol) was heated under reflux for 3 h. The excess solvent was evaporated in vacuo (to 1/3 of the solution) and cooled; the solid was collected by filtration, dried, and crystallized from ethanol to give **10** (c.f. Tables I and II).

The Synthesis of 11

A solution of each of **5** or **10** (0.01 mol) and formic acid (30 ml) was heated under reflux for 6 h. The excess solvent was evaporated in vacuo (to 1/3 of the solution) and cooled; the solid was collected by filtration, dried, and crystallized from the proper acetic acid to give **11** (c.f. Tables I and II).

The Synthesis of 12

A solution of each of **5** or **10** (0.01 mol) and dimethylformamaide-dimethylacetal (0.025 mol) in dry dioxane (30 mL) was heated under reflux for 6 h. The excess solvent was evaporated in vacuo (to 1/3 of the solution) and cooled; the solid was triturated with petroleum ether and collected by filtration, dried, and crystallized from dioxane to give **12** (c.f. Tables I and II).

The Synthesis of 13

A solution of each of **5** and diethyl carbonate (30 mL) was heated under reflux for 5 h. The excess solvent was evaporated in vacuo(to 1/3 of the

solution) and cooled; the solid was collected by filtration, dried, and crystallized from ethanol to give **13** (c.f. Tables I and II).

The Synthesis of 16

A solution of **14** in dry xylene (30 mL) was heated under reflux for 5 h. The excess solvent was evaporated in vacuo (to 1/3 of the solution) and cooled. The solid was triturated with petroleum ether and collected by filtration, dried, and crystallized from DMF/H_2O (2:1) to give **16** (c.f. Tables I and II).

The Synthesis of 17

A solution of **5** in acetic acid (30 mL) was heated under reflux for 5 h. The excess solvent was evaporated in vacuo (to 1/3 of the solution) and cooled. The solid was collected by filtration, dried, and crystallized from acetic acid to give **17** (c.f. Tables I and II).

The Synthesis of 18 and 22

A solution of **5** (0.01 mol) and either carbon disulphide (5 mL) or phenylisothiocyanate (0.01 mol) in pyridine (30 mL) was heated under reflux for 5 h, cooled, poured onto ice-cold water, and neutralized (pH = 7) with hydrochloric acid; the solid was collected by filtration, dried, and crystallized from the ethanol to give **18** or **22** (c.f. Tables I and II).

The Synthesis of 23, 26, and 27

A solution of **5** and either ethyl acetoacetate, acetylacetone, or 2-phenylazoethylacetoacetate (0.01 mol) in acetic acid (30 mL) was heated under reflux for 5 h. The excess solvent was evaporated in vacuo (to 1/3 of the solution) and cooled; the solid was collected by filtration, dried and crystallized from the acetic acid to give **23**, **26** or **27** (c.f. Tables I and II).

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