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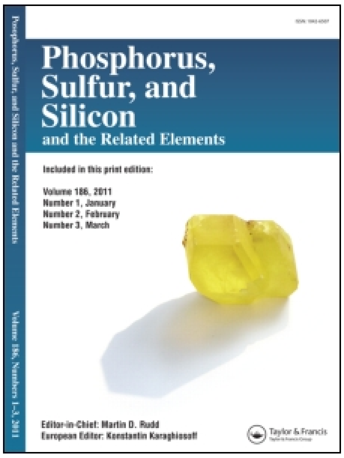

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SYNTHESIS AND REACTIONS OF SOME NEW THIENO[2,3-b]QUINOXALINES AND THEIR RELATED COMPOUNDS

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SYNTHESIS AND REACTIONS OF SOME NEW THIENO[2,3-b]QUINOXALINES AND THEIR RELATED COMPOUNDS

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Key words: Thieno[2,3-b]quinoxalines; synthesis and reactions.

Reaction of 2-chloroquinoxaline-3-carbonitril (I) with different types of nucleophiles such as thiourea, sodium methoxide, aniline, α-mercaptoacetic acid, ethyl-α-mercaptoacetate and anthranilic acid have been studied. Hydrolysis of 3-carbonitril-2(1H)-quinoxalinthione (II) with HCl gave 2(1H)-quinoxalinone-3-carboxamide (VIII). Compound II was reacted with bromoacetone, phenacylbromide and chloroacetonitrile in sodium ethoxide solution to yield thieno[2,3-b]quinoxaline derivatives IX, X, XII respectively. Compound X was reacted with ethylacetoacetate to give pyrido[5′,4′:4,5]thieno[2,3-b]quinoxaline-2-one (XI). Compound XII was reacted with ethylcyanoacetate to give 4-amino-3-cyano pyrido[4′,4′:4,5] thieno[2,3-b]quinoxaline-2-one (XVIII). Acylation of XII with Ac$_2$O and benzoylchloride gave the monoacyl derivatives XIII and XIV respectively. Hydrolysis of XII gave the corresponding carboxamide XIX. A number of pyrimido[5′,4′: 4,5]thieno[2,3-b]quinoxalines have been prepared by three other independent routes. Method 1 involves the cyclization of 3-amino-2-carbonitril thieno[2,3-b]quinoxaline (XII) with reagents such as formamide, formic acid and urea to give XV, XVI, XVII. Method 2 involves the cyclization of 3-aminothieno[2,3-b]quinoxaline-3-carboxamide (XIX) with formamide and phenyl-isocyanate to give XVI, XXI respectively. Method 3 involves the cyclization of ethyl-3-aminothieno[2,3-b]quinoxaline-3-carboxylate V with formamide to give XVI.

Quinoxalines and several compounds containing the thieno, thieno[2,3-b]pyrimidine and thieno[2,3-b]pyridine moiety show biological activity.[1-5] In continuation of our interest in the synthesis of different heterocycles[6] of expected biological potential, the aim of this study was to synthesize new quinoxalines, their pyridino thieno and pyrimido thieno derivatives.

As a part of our study on the reactivity of the chloro compound[7] (I) towards different nucleophilic reagents I was submitted to reaction with thiourea in boiling ethanol to give 3-carbonitrile-2(1H)quinoxalinthione (II) which exists as thiol-thione tautomers II$_a$, II$_b$. (II) was used as starting material for preparing the thieno[2,3-b]quinoxaline derivatives. The structure of II was confirmed by elemental analysis and IR spectrum (c.f. Scheme I, Table I), II was hydrolyzed by hydrochloric acid to give 3-carbamoyl-1,2-dihydroquinoxaline-2-one VIII, whose structure was confirmed by elemental analysis and spectral means and by comparison with a reference sample.[8] The reaction of compound I with sodium methoxide in methanol gave

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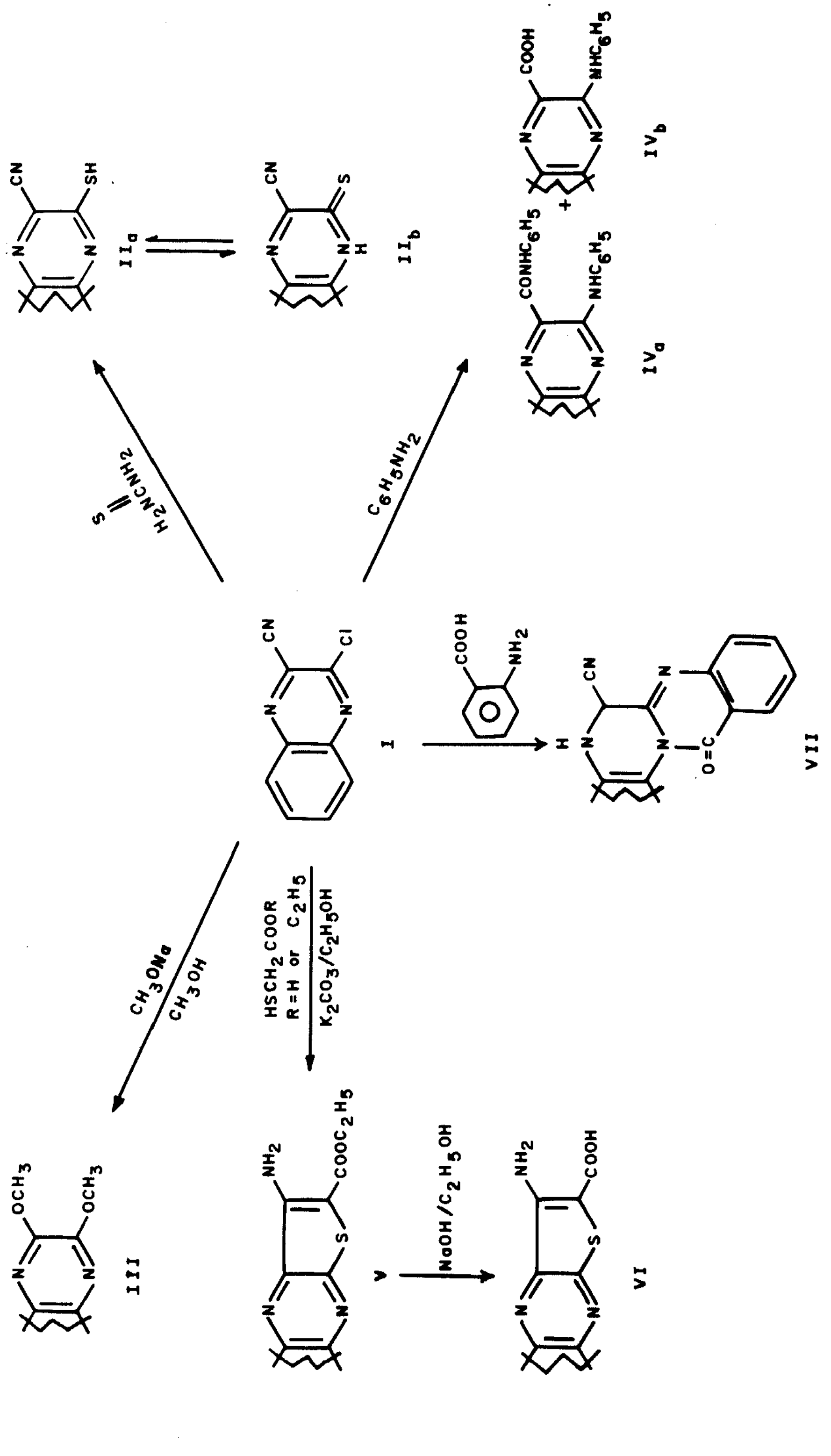

Scheme I

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TABLE I

Physical and analytical data of compounds **II–VII**

Compound	M.P. °C (Solvent)	Yield % Colour	Molecular formula	Elemental analysis Calculated/Found C	H	N	S	IR (KBr) cm^{-1}	^{1}H-NMR (CDCl$_3$) δppm
II	260	85	$C_9H_5N_3S$	57.75	2.67	22.45	17.11	2260(CN).	
	Ethanol	Orang		57.68	2.94	22.29	17.60		
III	93	95	$C_{10}H_{10}N_2O_2$	63.20	5.30	14.70	-		4.1[s,6H,2(OCH$_3$)], 7.3-7.8 (m,4H,Ar.).
	Methanol	Colourless		62.96	5.31	14.53	-		
IV$_a$	200	75	$C_{21}H_{16}N_4O$	74.10	4.74	16.46	-	3290(NH), 1665(C=O), 1620(C=N) of ring.	2.1(s,1H,CONH), 6.2-8(m,14H, Ar.), 13.05(s,1H,NH).
	Aq.acetic Acid	Greenish		74.70	5.33	17.05			
IV$_b$	172	33	$C_{15}H_{11}N_3O_2$	67.91	4.18	15.84	-	3300(NH,1670(C=O), 1590(C=N), of ring.	7.0(m,9H,Ar.), 10.15(s,1H, OH), 11.2(s,1H,NH).
	Acetic acid	Brown		68.05	4.24	16.21	-		
V	145	75	$C_{13}H_{11}N_3O_2S$	57.14	4.06	15.38	11.71	3460,3330(NH$_2$), 1680(C=O).	1.34-1.5(t,3H,CH$_3$), 4.25-4.5 (q,2H,CH$_2$), 6.3(s,2H,NH$_2$), 7.55-8.15(m,4H,Ar.).
	Aq. ethanol	Red		57.16	4.07	15.42	11.73		
VI	265	65	$C_{11}H_7N_3SO_2$	53.88	2.88	17.14	13.05		
	Ethanol	Reddish		53.87	2.86	17.05	12.89		
VII	260	95	$C_{16}H_8N_4O$	67.73	3.25	22.57	-	2240(C≡N), 1690(C=O).	
	Aq. butanol	Yellow		67.80	3.26	22.49	-		

the corresponding 2,3-dimethoxy derivative (**III**) via an ipso substitution[9] as established by analysis (c.f. Scheme I, Table I) and by comparison with a reference sample.[10] Fusion of compound **I** with aniline resulted in the formation of 2-anilino quinoxaline-2-phenylcarboxamide (**IV$_a$**) and 2-anilinoquinoxaline-3-carboxylic acid (**IV$_b$**) (c.f. Scheme I, Table I). The IR spectrum of (**IV$_b$**) showed low acid caronyl stretching frequency at 1670 cm^{-1} as a result of intramolecular hydrogen bonding with the ortho substituted amino group.[11] The most direct and versatile route into the thieno ring system which would also provide the necessary functionality for fusion of the desired pyrimidine ring, was found to be via ethyl-3-aminothieno[2,3-b]quinoxaline-2-carboxylate (**V**). Compound **V** was prepared by utilizing the K_2CO_3 mediated reaction of α-mercaptoacetic acid and/or ethyl-α-mercaptoacetate instead of the sodium carbonate method[12] with 2-chloroquinoxaline-3-carbonitrile (**I**) in absolute ethanol as shown in Scheme I. It has been observed in the present study that ethyl esterification occurs when compound **I** reacts with α-mercaptoacetic acid to give the same ethylthieno ester compound (**V**), whose ^{1}H NMR spectrum determined in $CDCl_3$ showed a triplet at δ1.34–1.5 (3H, CH_3), a quartet at δ4.25–4.5 (2H, CH_2), a singlet at δ6.3 (2H, NH_2), (which disappear upon adding D_2O) and a multiplet at δ7.55–8.15 (4H, Ar) and the structure of **V** was also supported by its mass spectrum at m/e 273 (c.f. Scheme I; Table I). Attempts to prepare **V** by reaction of α-mercaptoacetic acid with 2-chloroquinoxaline-3-carbonitrile **I** in absolute ethanol in the absence of anhydrous K_2CO_3 were unsuccessful. When ethyl-3-aminothieno[2,3-b] quinoxaline-2-carboxylate (**V**) was hydrolyzed by ethanolic KOH the corresponding acid (**VI**) was produced (c.f. Scheme I, Table I).

The 2-chloroquinoxaline (**I**) proved to be a useful precursor for the synthesis of fused nitrogen bridged benzopyrimidinoquinoxaline (**VII**) in good yield (c.f. Scheme I, Table I). Compound **II** reacted with bromoacetone, phenacylbromide and chloroacetonitrile in ethanol containing anhydrous sodium acetate or in ethanolic sodium ethoxide solution leading to the formation of quinoxaline derivatives (**IX**, **X$_{(a-c)}$**, **XII**) without the isolation of the intermediate S-substituted methyl derivatives. An examination of IR spectra of these thieno compounds showed the absence of a band in the C≡N stretching region. Also ^{1}H NMR spectra of these compounds showed absence of signal for S—CH_2-group (c.f. Scheme II, Table II). Compound **X** was reacted with ethylacetoacetate to give 3-acetoacetamidio-2-substituted benzoylthieno[2,3-b]-quinoxaline which under intramolecular cyclocondensation gave the corresponding 3-aceto-4-arylpyrido[5′,4′:4,5]thieno[2,3-b]quinoxalin-2-one (**XI$_{a,b}$**). The heterocyclization was supported by the elemental analysis, ^{1}H NMR (absence of ethyl group) and IR spectral data (c.f. Scheme II, Table II). Another derivative of pyridothieno-quinoxalinone (**XVIII**) was also formed when compound **XII** was allowed to react with ethylcyanoacetate (c.f. Scheme II). Compound **XII** was easily acylated using acetic anhydride or benzoyl chloride to give N-acyl derivatives **XIII** and **XIV**, respectively. When benzoyl chloride was used as the acylating agent hydrolysis of the C≡N group also occurred. Compound **XII** was hydrolyzed with alkali to give the corresponding 3-amino-2-carboxamide (**XIX**) its IR spectrum lacked ν(C≡N), but exhibited ν(C=O) at 1660 cm^{-1} and multiple bands at 3490–3170 cm^{-1} (NH_2). Three new independent synthetic routes which allow the preparation of many pyrimidine derivatives have been developed. Route 1 involves the cyclization of 3-amino-2-cyanothieno[2,3-b]quinoxaline (**XII**) with

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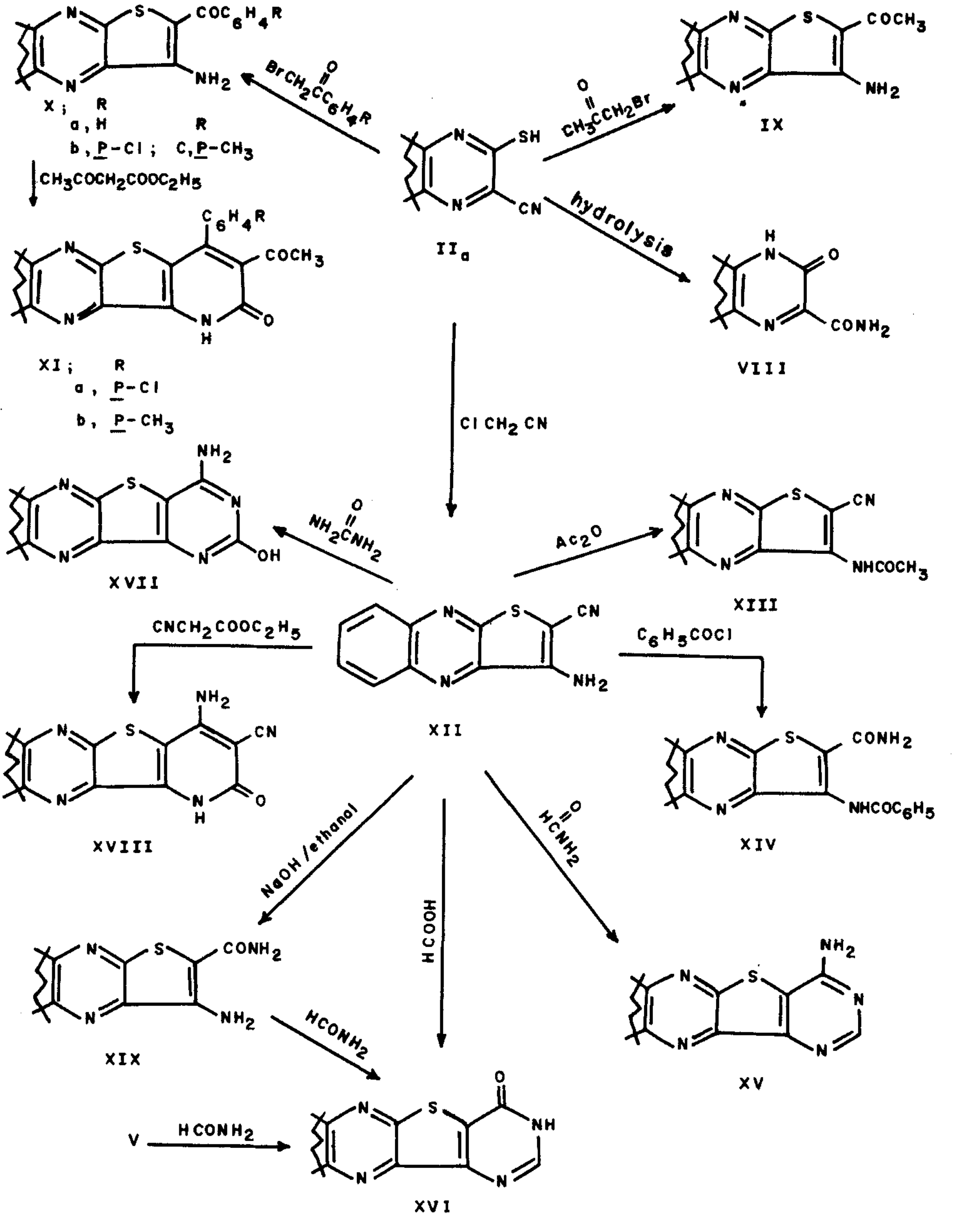

Scheme II

reagents such as formamide, formic acid and urea to give a variety of pyrimido-[5′,4′:4,5]thieno[2,3-b]quinoxaline **XV, XVI, XVII** respectively. Route 2 involves cyclization with 2-aminothieno[2,3-b]quinoxaline-3-carboxamide (**XIX**). The cyclization of an o-aminoamide with suitable one-carbon intermediates has been widely used for the preparation of numerous heterocyclic systems containing a fused py-

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TABLE II

Physical and analytical data of compounds IX–XXI

Compound	M.P. °C (Solvent)	Yield % Colour	Molecular formula	Elemental analysis calculated/found				I.R.(KBr) cm^{-1}	^1H-NMR $(CDCl_3)^*$ δppm
				C	H	N	S		
IX	210	85	$C_{12}H_9N_3OS$	59.26	3.73	17.28	13.15	3360,3480(NH_2),	
	Ethanol	Brownish		59.31	3.74	17.19	13.23	1660(C=O).	
X_a	175	90	$C_{17}H_{11}N_3OS$	66.88	3.63	13.77	10.48	3210,3310(NH_2),	1.6(s,2H,NH_2), 7.25-8.2
	Ethanol	Brown		66.86	3.63	13.83	10.46	1670(C=O).	(m,9H,Ar.).
X_b	300	75	$C_{17}H_{10}N_3OSCl$	60.09	2.97	12.36	9.44		
	Ethanol	Red		60.12	2.95	12.35	9.39		
X_c	220	93	$C_{18}H_{13}N_3OS$	67.70	4.11	13.16	10.02		
	Ethanol	Brown		67.65	4.12	13.19	10.07		
XI_a	310	65	$C_{21}H_{12}N_3O_2SCl$	62.14	2.98	10.35	7.89		2.4(s,3H,CH_3), 7.35-8.5(m,9H,
	Acetic acid	Yellow		62.15	2.98	10.40	7.97		NH,Ar.).
XI_b	330	95	$C_{22}H_{15}N_3O_2S$	68.56	3.92	10.91	8.30	1710(C=O), 1685	2.35(s,3H,$COCH_3$); 2.42(s,3H,
	Ethanol	Yellow		68.49	3.93	10.85	8.33	(C=O).	CH_3), 7.3-8.2(m,9H,NH,Ar.).
XII	280	84	$C_{11}H_6N_4S$	58.41	2.67	24.77	14.14	3380-3160(NH_2),	
	Ethanol	Brown		58.39	2.69	24.85	14.06	2210(C≡N).	
XIII	265	70	$C_{13}H_8N_4OS$	58.21	3.01	20.89	11.93	3240(NH), 2220	2.3(s,3H,CH_3), 7.89-8.34
	Acetic acid	Greenish		58.21	3.01	20.91	11.85	(C≡N),1680(C=O).	(m,4H,Ar.).
XIV	>350	95	$C_{18}H_{12}N_4O_2S$	62.07	3.47	16.09	9.19	3310-3200(NH_2),	
		Lemon		61.99	3.49	16.14	9.22	3180(NH), 1710	
								(C=O),1690(C=O).	

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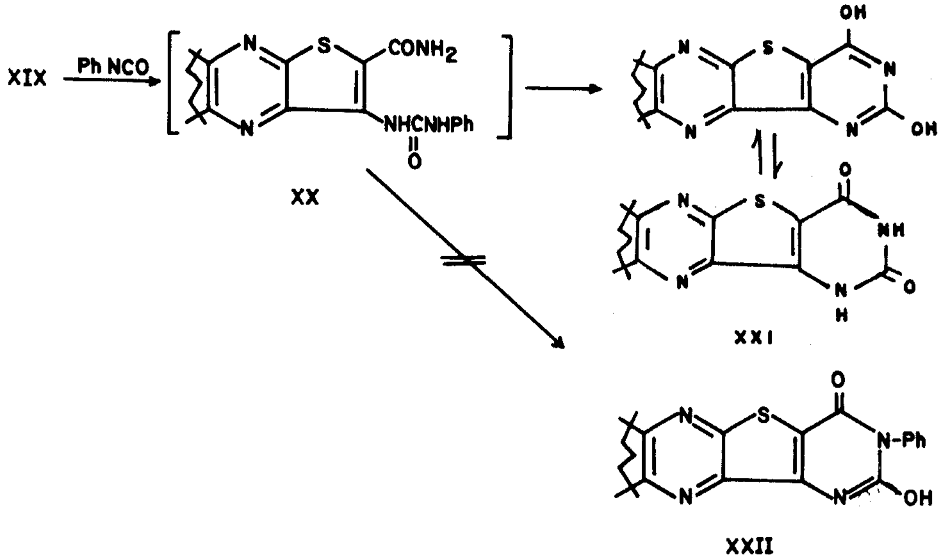
XV	350 Ethanol	65 Brown	$C_{12}H_7N_5S$	56.91 56.87	2.79 2.79	27.66 27.74	12.63 12.60	3260,3140(NH_2)	
XVI	>360 Ethanol	60 Yellow	$C_{12}H_6N_4OS$	56.70 56.69	2.38 2.38	22.04 22.01	12.58 12.62	3180(NH), 1690 (C=0).	
XVII	>320 Ethanol	35 Brown	$C_{12}H_7N_5OS$	53.53 53.60	2.62 2.62	26.02 26.00	11.89 11.88	3310(OH), 3280, 3180(NH_2).	
XVIII	310 Acetic acid	78 Orang	$C_{13}H_7N_5OS$	55.52 55.50	2.51 2.51	24.90 24.87	11.39 11.35	333o-3130(NH,NH_2) 2210(C≡N), 1670 (C=0).	7.43(s,2H,NH_2), 7.8-8.23 (m,5H,NH,Ar.).
XIX	304 Acetic acid	95 Brown	$C_{11}H_8N_4OS$	54.10 54.06	3.30 3.31	22.94 22.88	13.10 13.05	3480-3160(2NH_2), 1665(C=0),	7.0(s,2H,$CONH_2$), 7.40 (s,2H,NH_2), 7.8-8.25 (m,4H,Ar.).
XXI	330°C Acetic acid	75 Yellow	$C_{12}H_6N_4O_2S$	53.34 53.34	2.24 2.24	20.74 20.56	11.84 11.69	3570(OH),3500(OH), 3160(NH),3080(NH), 1725(C=0), 1680 (C=0).	6.40-7.2(m,4H,Ar.), 7.50-7.72[s,2H,(2OH)].

*XIII DMSO ; XVIII DMSO ; XIX DMSO ; DMSO ; XXI Acetone.

rimidine ring.[13] Thus reaction of **XIX** with phenylisocyanate in pyridine solution did not give 3-phenylpyrimido[5′,4′:4,5]thieno[2,3-b]quinoxaline-2,4(1H, 3H)-dione (**XXII**) as expected but rather 2,4-dihydroxypyrimido[5′,4′:4,5]thieno[2,3-b]quinoxaline (**XXI**) (c.f. Table II). Evidently 3-(3-phenylureido)thieno-[2,3-b]quinoxaline-2-carboxamide (**XX**) which was formed initially underwent subsequent ring closure with loss of aniline rather than ammonia. This mode of cyclization was unexpected, since it has been shown that 2-amino-5,6-diphenylpyrazine-3-carboxamide yields 3,6,7-triphenylpteridine-2,4-(1H, 3H)-dione upon treatment with phenylisocyanate and pyridine under similar conditions.[14]



Treatment of **V** with formamide yielded the pyrimidione **XVI** (Route 3).

EXPERIMENTAL

Melting points are uncorrected IR (KBr) spectra were recorded on Cye-Unicam infrared spectrophotometer and ^{1}H NMR spectra in DMSO-d_6 or $CDCl_3$ on a varian EM-390 spectrometer using TMS as internal standard, and chemical shifts are given as δ values. The mass spectrum was recorded by kratos MS-80 R.F.A. spectrometer at an ionizing potential 70 ev, at Calgary University, Canada. Analytical data were obtained from the microanalytical data of Assiut University.

2-Chloroquinoxaline-3-carbonitrile (**I**). Was prepared and isolated as reported earlier.[8]

3-Carbonitrile-2(1H)-quinoxalinthione (**II**). A mixture of 2-chloroquinoxaline-3-carbonitrile (**I**) (18.9 g, 0.1 mol) and thiourea 7.6 g, 0.1 mol) in ethanol (200 ml) was heated under reflux for two hours. The product obtained after concentration and cooling was treated with (200 ml 20%) sodium hydroxide and then acidified with dilute HCl. The solid that separated was collected by filtration and recrystallized (Table 1).

2,3-Dimethoxy quinoxaline (**III**). A solution of (**I**) (0.01 mol) in dry CH_3OH and CH_3ONa (0.01 mol) was refluxed for three hours, poured into water (100 ml) and the solid obtained recrystallized (Table I).

2-Anilinoquinoxaline-3-phenylcarboxamide (**IV**) *and 2-anilinoquinoxaline-3-carboxylic acid* (**V**). A mixture of 2-chloroquinoxaline-3-carbonitrile (**I**) (3.8 g, 0.02 mol) and aniline (9.3 g, 0.1 mol) was kept at 160° in an oil bath for five hours. The mixture was poured into water and the product was collected by

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filtration and recrystallized from acetic acid. A brown solid precipitated and after three years the solution was filtered. Yielding 40% $\mathbf{IV_b}$ and the compound $\mathbf{IV_a}$ was isolated by concentration of the filtrate in 50% yield.

Ethyl-3-aminothieno[2,3-b]quinoxaline-2-carboxylate (**V**). To (1.9 g, 0.01 mol) of 2-chloroquinoxaline-3-carbonitrile (**I**) in 20 ml absolute ethanol was added (0.01 mol) of α-mercapto acetic acid or/and ethyl-α-mercapto acetic acid and (0.01 mol) of anhydrous potassium carbonate and the mixture was refluxed for five hours. The residue was stirred with 50 ml of water, filtered and the insoluble material recrystallized (Table I).

3-Aminothieno[2,3-b]quinoxaline-2-carboxylic acid (**VI**). A mixture of **V** (1.35 g, 0.005 mol) and (2.5 g) of KOH in 50 ml absolute ethanol was refluxed for one hour. After cooling the precipitate was filtered, dissolved in water then acidified by acetic acid. The solid obtained was recrystallized (Table I).

2-Cyano-8H-quinozolo[4,3-a]quinoxaline-8-one (**VII**). Anthranilic acid (1.3 g, 0.01 mol) was refluxed for five hours with 2-chloroquinoxaline-3-carbonitrile (**I**) (1.9 g, 0.01 mol) in butanol (50 ml). After evaporation, the residue was treated with hot water to remove unreacted substances. The residue was separated and crystallized (Table I).

2-(1H)-Quinoxalinone-3-carboxamide (**VIII**). 3-carbonitrile-2-(1H)-quinoxalin thione (**II**) (1 g) was heated under reflux for five hours with 15 ml of hydrochloric acid. The product obtained after cooling was collected and washed with water, m.p. 308° (Lit[9] m.p. 308).

2-Acetyl-3-amino thieno[2,3-b]quinoxaline (**IX**). 3-amino-2-substituted benzoyl thieno[2,3-b]quinoxaline (**X**) and 3-amino-2-cyano thieno[2,3-b]quinoxaline (**XII**). General procedure: To a solution of (**II**) (3.64 g, 0.02 mol) and sodium ethoxide (from 0.70 g of sodium in ethanol (30 ml) or 3 g fused sodium acetate in 30 ml ethanol, freshly prepared bromo acetone (0.02 mol) or phenacyl bromide (0.02 mol) or chloroacetonitril (0.02 mol) was added. The reaction mixture was refluxed for one hour. A crystalline matter was separated, washed with water and recrystallized (Table II).

3-Aceto-4-aryl-pyrido[5',4':4,5]thieno[2,3-b]quinoxalin-2-one ($\mathbf{XI_{a,b}}$). General procedure: A mixture of $\mathbf{X_{a,b}}$ (0.01 mol) and ethyl aceto acetate (0.01 mol) was refluxed for three hours. On cooling, the crystals of ($\mathbf{XI_{a,b}}$) were filtered off and then recrystallized (Table II).

N-Acyl derivatives **XIII, XIV** *respectively*. General procedure: A mixture of **XII** (2.26 g, 0.01 mol) and acetic anhydride benzoyl chloride (20 ml) was refluxed for three hours. The product obtained after cooling was collected and recrystallized (Table II).

4-Aminopyrimido[5',4';4,5]thieno[2,3-b]quinoxaline (**XV**). A mixture of 0.5 g of 3-amino-2-cyano-thieno[2,3-b]quinoxaline (**XII**) and 2 ml of formamide was heated under reflux for 30 minutes, cooled, diluted with 40 ml of water and filtered. The solid which separated was collected by filtration, washed well with water and crystallized (Table II).

Pyrimido[5',4':4,5]thieno[2,3-b]quinoxaline-4(3H)-one (**XVI**). (a) A mixture of **XII** (1.13 g, 0.005 mol) and 10 ml formic acid was heated under reflux for three hours. After cooling the solid which separated was collected by filtration and crystallized (Table II).

(b) A mixture of 1.0 g of 2-aminothieno[2,3-b]quinoxaline-3-carboxamide (**XIX**) and 15 ml of formamide was heated for two hours in an oil-bath maintained at 160–170°. Cooling caused the separation of solid material which was crystallized (Table II).

(c) A mixture of ethyl 3-aminothieno[2,3-b]quinoxaline-2-carboxylate (**V**) (2.7 g, 0.01 mol) in (30 ml) of formamide was refluxed 3 hours. Cooling caused the separation of solid material which was crystallized (Table II).

4-Amino-2-hydroxypyrimido[5',4':4,5]thieno[2,3-b]quinoxaline (**XVII**). An intimat mixture of 1 g of **XII** and 2.5 g of urea was heated in an oil-bath at 300° for 30 minutes. The material first liquified and then quickly set to a hard, reddish solid. After cooling, the solid was powdered, extracted with cold water followed by boiling ethanol and the solid residue recrystallized (Table II).

4-Amino-3-cyanopyrido[5',5':4,5]thieno[2,3-b]quinoxaline-2-one (**XVIII**). A solution of **XII** (1 g) in ethylcyanoacetate (10 ml) was heated under reflux for four hours, the solvent was then concentrated to half its original volume and left to cool, the solid product that separated on standing was collected by filtration and washed with ethanol and recrystallized (Table II).

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2-Aminothieno[2,3-b]quinoxaline-3-carboxamide **XIX**. 3-Amino-2-cyanothieno[2,3-b]quinoxaline (**XII**) (3 g), was heated under reflux for two hours with 3 g NaOH in 30 ml ethanol. The separated crystalline product was filtered and recrystallized (Table II).

3-Phenyl pyrimido[5′,4′:4,5]thieno[2,3-b]quinoxaline-2(1H), 4(3H)-dione (**XX**). A mixture of 1.00 g of 2-aminothieno [2,3-b]quinoxaline-3-carboxamide (**XIX**), 1.0 ml of phenylisocyanate and 20 ml of dry pyridine was heated under reflux for one hour. During the reaction a precipitate formed. Cooling and filtering was followed by recrystallization to give the product (Table II).

3-Phenyl pyrimido[5′,4′:4,5]thieno[2,3-b]quinoxaline-2(1H)thione-4(3H)-one (**XXI**). A mixture of 1.00 g of **XIX**, 1.0 ml of phenylisothiocyanate and 30 ml of dry pyridine was heated under reflux for three hours and then poured into an excess of ethyl alcohol. A solid was collected and recrystallized (Table II).

REFERENCES

1. (a) C. W. Hofmann, J. J. Krajeurski, Ph. J. Kotz, J. T. Traxler and S. S. Ristich, *J. Agr. Food Chem.*, **1**, 298 (1971). (b) D. Bucchini, M. Fiszman, and M. Girard, *Intervirology*, **3**, 281 (1974).
2. Gozyo. Sakata; Kenzi. Makino and Yoshihisa, *Heterocycles Review*, **27**, 2481–2515 (1988).
3. K. Eichenberger, E. Schweizer and P. Schmidt, U.S. Patent, 2,627,766 December 14, 1971, *Chem. Abstr.*, **74**, 88638w (1971).
4. "Medicinal Chemistry," 3*rd* Ed., A. Burger, Ed., Wiley. Intersciences, New York, N.Y., 1970, pp. 72, 544 and 719.
5. J. M. Briker, *Adv. Heterocycl. Chem.*, **21**, 65 (1977).
6. (a) S. A. Mahgoub, A. M. Fahmy, M. M. Aly and M. Z. A. Badr, *Acta Chim. Hung.*, **116**, 267 (1984). (b) M. Z. A. Badr, G. M. El-Naggar, H. A. Al-Sherif and S. A. Mahgoub, *Bull. Chem. Soc. Japan*, **57**, 1653 (1984). (c) M. Z. A. Badr, H. A. El-Sherief, G. M. El-Naggar and S. A. Mahgoub, *J. Heterocycl. Chem.*, **21**, 471 (1984). (d) M. Z. A. Badr and S. A. Mahgoub, *Indian J. Chem.*, **28B**, 829 (1989). (e) M. Z. A. Badr, S. A. Mahgoub, F. F. Abdel-Latif, A. M. Fahmy and O. S. Moustafa, *J. Indian Chem. Soc.*, **67**, 216 (1990). (f) M. Z. A. Badr, S. A. Mahgoub, F. F. Abdek-Latif and A. A. A. Abdel-Hafez, *Phosphorus, Sulfur, and Silicon* 1990 in print.
7. K. Yoshida and H. Otomasu, *Chem. Pharm. Bull.*, **32**(9), 3361 (1984).
8. F. E. King and J. W. Clark-Lewis, *J. Chem. Soc.*, 172 (1953).
9. Marcello Tiecco, *Acc. Chem. Res.*, **13**, 51–57 (1980).
10. P. Stevens and Wolf, *J. Am. Chem. Soc.*, **68**, 1038 (1946).
11. F. J. Guadrado, M. A. Perez and J. L. Sato, *J. Chem. Soc., Perkin Trans.*, **1**, 2447 (1984).
12. A. A. Santilli, D. H. Kim and S. V. Wanser, *J. Heterocyclic Chem.*, **8**, 445 (1971).
13. E. C. Taylar, Jr. and N. W. Kalenda, *J. Am. Chem. Soc.*, **78**, 5108 (1956).
14. E. C. Taylar, Jr., R. B. Garland and C. F. Howell, *J. Am. Chem. Soc.*, **78**, 211 (1956).

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