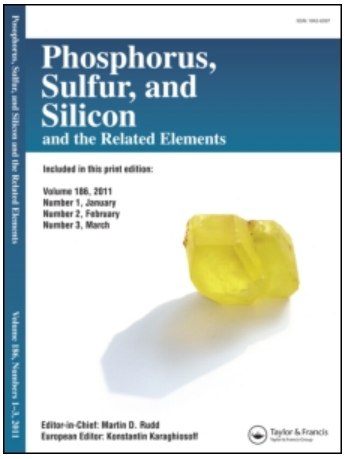

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CHEMISTRY AND CYCLIZATION REACTIONS OF THIENOQUINOXALINE DERIVATIVES: PART I†

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Reaction of 2(1H)quinoxalinethione-3-carbonitrile **1** with alkyl or aralkyl halides, chloroacetic acid, ethyl chloroacetate, or N-phenylchloroacetamide in ethanolic sodium acetate solution gives the corresponding 3-thioethers of **1**. Treatment of **3** with acetic anhydride gives the dimesoionic thiazolo[3',4'-c]-2-cyanoquinoxaline, **4**. Treatment of **6** or **10** with ethanolic sodium ethoxide solution gives the cyclization products, ethyl-3-aminothieno[2,3-b]quinoxaline-2-carboxylate **7** or 3-phenylcarboxamide **11** substituents respectively. Treatment of **11** with carbon disulfide/ethanolic potassium hydroxide soution gives 3-phenylpyromido[4',5':4,5]thieno[2,3-b]quinoxaline-4-one-2-thione **12** which is also produced by treatment of **7** with phenyl isothiocyanate in dry pyridine. Compound **11** cyclizes on treatment with benzoyl chloride, acetic anhydride, phenyl isothiocyanate, ethyl chloroformate and/or nitrous acid, to produce the corresponding pyrimidothienoquinoxalines **14–17** and [1,2,3] triazinothienoquinoxaline **18** derivatives respectively. Compound **7** cyclizes with ethanolic potassium hydroxide solution followed by acetic anhydride to give the oxazino compound **19** which gives (with different amino reagents) the corresponding 3-substituted pyrimidothienoquinoxaline-4-ones **20–25**.

Key words: Thienoquinoxaline; pyrimidothienoquinoxaline; synthesis and reactions; antimicrobial activities.

Quinoxaline derivatives have long been known as a class of biologically active compounds.[1–4] As a continuation of our earlier work[5,6] on quinoxaline derivatives, the present investigation deals with the synthesis and chemistry of a series of new thienoquinoxaline derivatives and the investigation of their expected biological potential.

Treatment of 2(1H)quinoxalinethione-3-carbonitrile **1** with alkyl or aralkyl halides and anhydrous sodium acetate in refluxing absolute ethanol gives the corresponding 3-alkyl (or aralkyl) thio products **2a–d**. However their formation does not exclude existence of **1** in solution as a mixture of 3-mercapto together with the cyclic thioamide tautomer[5] confirmed by the large red shift in electronic absorption at λ_{max} 460 nm due to the (C=S) thioamide $n - \pi$ transition (Table I) compared with the electronic absorptions at λ_{max} 390 nm observed for the separated alkylthio products **2**. It is to be noted that the absorption spectra of compound I are recorded in acid and alkaline media as well as in absolute ethanol. The recorded λ_{max} in acid medium was found to be the same as in absolute ethanol (460 nm) whereas in alkaline medium λ_{max} was 446 nm. This clearly indicates the compound exists mainly in the thioamide form where it is known that the thio tautomer predominates in acid media and the ArS^- is expected to be found in alkaline solutions. The ^{1}H-NMR spectrum of **1** and **2a** ($CDCl_3$) showed signals in agreement with the suggested structure in Table II.

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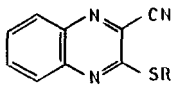
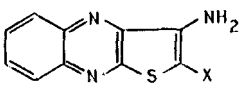
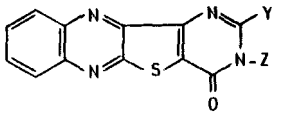
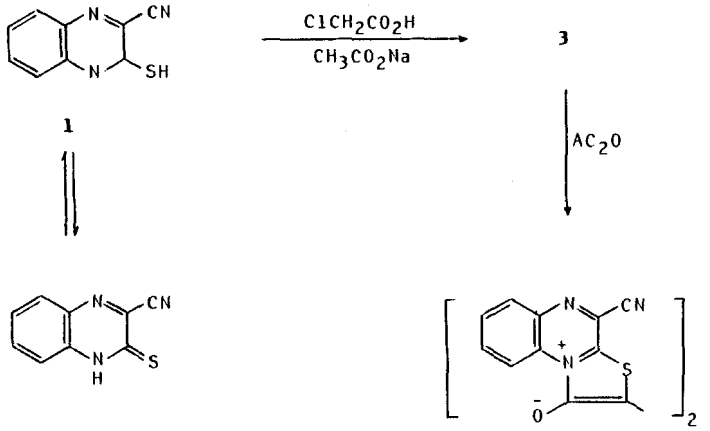




1 ; R= H
2a; R= CH_3
3 ; R= CH_2CO_2H
6 ; R= CH_2CO_2Et
10 ; R= $SCH_2CONHPh$

7; X= CO_2Et
8; X= CO_2H
11; X= CONHPh

13; Y= SCH_3 Z= Ph
14; Y= Ph Z= Ph
15; Y= CH_3 Z= Ph
16; Y= NHPh Z= Ph

20; Y= CH_3 Z= CH_3
21; Y= CH_3 Z= NH_2
22; Y= CH_3 Z= $C_6H_4COCH_3$
23; Y= CH_3 Z= CH_2Ph
24; Y= CH_3 Z= NHPh
25; Y= CH_3 Z= $CH_2CO_2CH_3$



SCHEME I

TABLE I

UV[a] spectral measurements for the compounds **1, 2a–d**

Comp.	Band 1		Band 2		Band 3	
No.	λmax_{nm}	εmax	λmax_{nm}	εmax	λmax_{nm}	εmax
1	460	$0.42x10^6$	345	$0.16x10^6$	305	$1.7x10^6$
2a	390	$0.36x10^6$	318	$0.28x10^6$	278	$1.2x10^6$
2b	390	$0.32x10^6$	318	$0.30x10^6$	278	$1.2x10^6$
2c	400	$0.58x10^6$	320	$0.48x10^6$	275	$2.2x10^6$
2d	390	$0.44x10^6$	318	$0.36x10^6$	275	$1.88x10^6$

a) In absolute ethanol solvent.

TABLE II

Characterization data of the compounds **1, 2a–d**

Comp. No.	-R	m.p. °C(c)	Yield %(d) Colour	Mol. formula	Analysis % C	H	Calcd./Found N	S	IR (KBr) cm^{-1}
(a)1	H	255	85	$C_9H_5N_3S$	57.75	2.67	22.45	17.11	(NH) br. 3400-3600 (CN) 2260
			Red		57.68	2.51	22.29	16.95	(C=N) 1610, (C=S) 1220, 1550
2a	$-CH_3$	144-45	85	$C_{10}H_7N_3S$	59.70	3.48	20.89	15.92	(CN) 2230
			Yellow		59.60	3.30	20.61	15.73	(C=N) 1590
2b	$-C_2H_5$	104-05	80	$C_{11}H_9N_3S$	61.39	4.18	19.53	14.88	(CN) 2215
			Buff		61.18	4.00	19.28	14.75	(C=N) 1580
2c	$-CH_2Ph$	179-80	78	$C_{16}H_{11}N_3S$	69.31	3.97	15.16	11.55	(CN) 2210
			Buff		69.43	4.00	15.31	11.57	(C=N) 1590
(b)2d	$-(CH_2)_3CH_3$	190-91	75	$C_{13}H_{13}N_3S$	64.19	5.34	17.28	13.16	(CN) 2220
			Pale Yellow		63.85	5.21	17.08	12.89	(C=N) 1600

(a) ^{1}H-NMR ($CDCl_3$), δ/ppm, 7.1 (s, 1H, NH) and 7.25-8.0 (m, 4H, ArH).

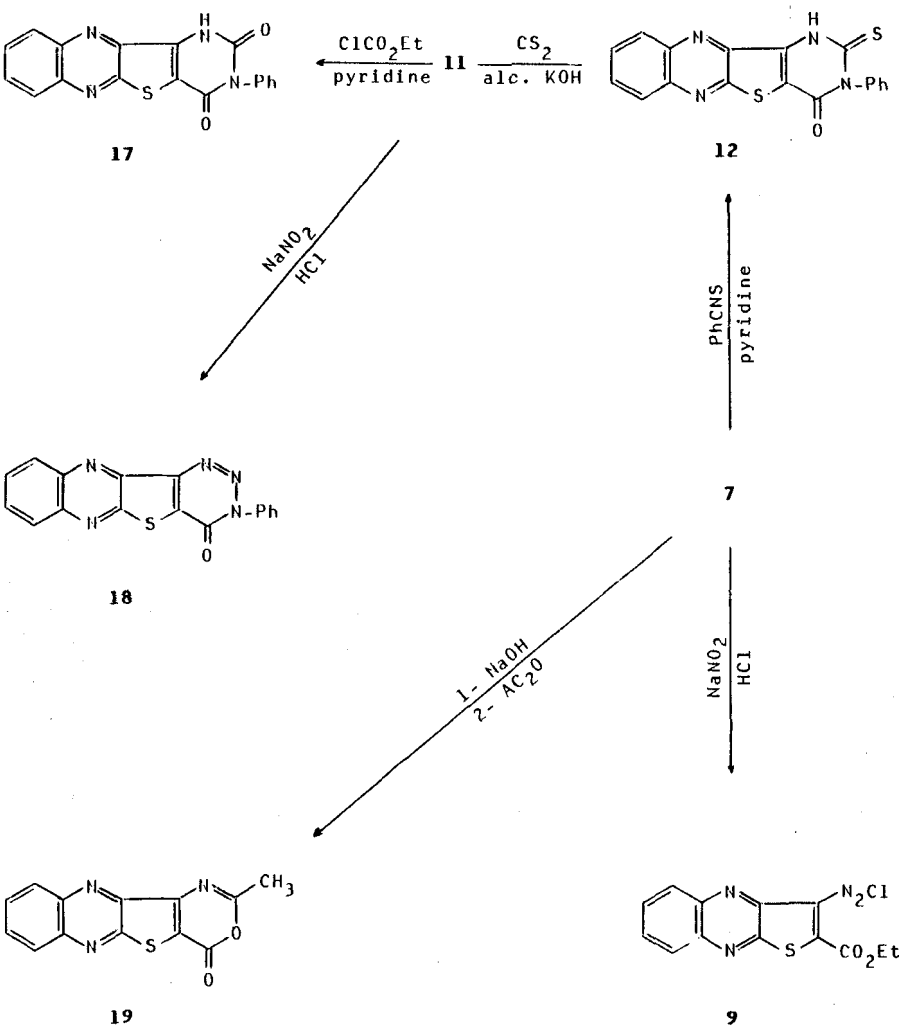
(b) ^{1}H-NMR ($CDCl_3$), δ/ppm, 0.8-1.1 (t, 3H, CH_3); 1.4-1.7 (m, 4H, $(CH_2)_2$); 3.2-3.5(t, 2H, SCH_2); 7.6-8.1 (m, 4H, ArH).

(c) Ethanol (95%) was crystallization solvent.

(d) After recrystallization.

Refluxing **1** with chloroacetic acid and sodium acetate in ethanol (30 ml) gives the corresponding 2-cyano-3-carboxylmethyl-thioquinoxaline (**3**). Its IR spectrum shows the (C=O) band at 1680 cm^{-1}. Its ^{1}H-NMR spectrum ($CDCl_3$) shows signals at δ4.1 (s, 2H, CH_2), δ6.5 (1H, OH), and δ7.6–8.1 (m, 4H, ArH). When compound **3** is refluxed with acetic anhydride it gives (through spontaneous air oxidation of the primarily formed mono) the separated dimesionic product, thiazolo[3′,4′-c]-2-cyanoquinoxaline (**4**). Its IR spectrum shows absence of the carboxyl (C=O) band at 1680 cm^{-1}. The mass spectrum shows molecular ion peak at m/e 452 which is in agreement with its molecular formula ($C_{22}H_8N_6O_2S_2$), while half mol ion peak (of the mesoionic) appears at m/e 226.

Refluxing **1** with ethyl chloroacetate and anhydrous sodium acetate in absolute ethanol gives 2-cyano-3-carboethoxymethyl-thioquinoxaline (**6**) which is further cyclized by refluxing with sodium ethoxide solution or with ethanolic anhydrous sodium acetate solution to produce ethyl 3-aminothieno[2,3-b]quinoxaline-2-carboxylate (**7**). The IR spectrum of **6** shows absorption bands, (C=O) at 1740 cm^{-1} and (—CN) at 2220 cm^{-1}. The ^{1}H-NMR spectrum ($CDCl_3$) of **6** shows signals at δ1.2–1.45 (t, 3H, CH_3), at δ4.1–4.33 (q, 2H, OCH_2), at δ4.15 (s, 2H, SCH_2) and at δ7.6–8.1 (m, 4H, ArH). The IR spectrum of **7** shows absorption bands, (NH_2) at 3460–3300 cm^{-1} and (C=O) at 1680 cm^{-1}, with disappearance of the (CN) band. The ^{1}H-NMR spectrum ($CDCl_3$) of **7** shows signals at δ1.3–1.5 (t, 3H, CH_3), δ4.2–4.5 (s, 2H, CH_2), δ6.2 (s, 2H, NH_2) which disappears on adding D_2O, and δ7.6–8.1 (m, 4H, ArH). Mass spectrum shows a molecular ion peak at m/e 273 which agree with the molecular formula ($C_{13}H_{11}N_3O_2S$). Compound **7** is also produced by the procedure of refluxing **1** with bromodiethylmalonate in ethanolic sodium ethoxide solution. Alkaline hydrolysis of **7** followed by acidification gives the corresponding product, 3-aminothienoquinoxaline-2-caboxylic acid (**8**). The IR



SCHEME II

spectrum shows absorption bands for (NH_2) at 3380–3500 cm^{-1} (C=O) 1670 cm^{-1} and (—C=N—) at 1610 cm^{-1} and which is coincident with the authentic sample.[7] Diazotization of **7** with sodium nitrite in concentrated hydrochloric acid gives the corresponding thienoquinoxaline-2-diazonium chloride (**9**). The IR spectrum shows absorption bands, (C=O) at 1740 cm^{-1} and (—N=N—) at 1680 cm^{-1}. Compound **9** was coupled with phenol or β-naphthol in sodium hydroxide solution to give the corresponding azo dye.

Compound **1** was alkylated by refluxing with N-phenylchloroacetamide and anhydrous sodium acetate in absolute ethanol solution to give 2-cyano-3-thiomethylcarboxanilide quinoxaline (**10**), which undergoes ring closure on refluxing with ethanolic sodium ethoxide solution to produce 3-aminothieno[2,3-b]quinoxaline-2-carboxanilide (**11**). IR spectrum of **10** shows absorption bands, (NH) at 3240 cm^{-1}, (CN) at 2220 cm^{-1} and (C=O) at 1645 cm^{-1}. The IR spectrum of **11** shows absorption bands, (NH_2, NH) at 3440–3340 cm^{-1}, (C=O) at 1640 cm^{-1} with

disappearance of the (CN) band. The structure of **10** and **11** is further confirmed through ^{1}H-NMR (Table III). On refluxing compound **11** with carbon disulfide in ethanolic potassium hydroxide solution undergoes a cyclization reacton to produce 3-phenylpyrimido[4',5':4,5]thieno [2,3-b]quinoxaline-4-one-2-thione (**12**), this is in agreement with an authentic sample separated from refluxing **7** with phenylisothiocyanate in dry pyridine. Its IR spectrum shows absorption bands, (NH) at 3100 cm^{-1}, (C=O) at 1690 cm^{-1}, (C=S) at 1210 cm^{-1} and (—C=N—) at 1590 cm^{-1}. Compound **12** is alkylated with methyl iodide and anhydrous sodium acetate in absolute ethanol solution to give the corresponding 2-methylthio substitution product (**13**), where the ^{1}H-NMR ($CDCl_3$) shows signals, at δ2.7 (s, 3H, CH_3) and δ7.8–8.5 (m, 9H, ArH). Compound **11** undergoes a ring closure reaction on refluxing with several reagents (benzoyl chloride, acetic anhydride, phenylisothiocyanate in dry pyridine, ethyl chloroformate in dry pyridine and/or nitrous acid) to produce the corresponding products; 2,3-diphenylpyrimido-[4',5':4,5]thieno[2,3-b]quinoxaline-4-one (**14**); its 2-methyl-3-phenyl substitutent isomer (**15**); its 2-N-phenylamino-3-phenyl substituent isomer (**16**); 3-phenyl (1H) pyrimido[4',5':4,5]-thieno[2,3-b]quinoxaline-2,4-dione (**17**) and 3-phenyl[1,2,3]triazino[4',5':4,5]thieno[2,3-b]quinaxaline-4-one (**18**). The IR spectra shows bands of pyrimido and triazino (C=O) groups at 1670–1750 cm^{-1} and with bands of other groups (Table

TABLE III

Spectral and characterization data for the compounds **3–18**

Compd.[a]	m.p.°C	Yield %[b] Colour	Mol. fomula	Analysis% Cacld./Found C	H	N	S	IR (KBr) cm^{-1}
3	192	70 Yellow	$C_{11}H_7N_3O_2S$	53.87 53.62	2.85 2.78	17.14 16.95	13.06 12.90	(CN) 2230, (CO) 1680, (-C=N-) 1650
4	>360	60 Black	$C_{22}H_8N_6O_2S_2$	58.40 58.25	1.76 1.70	18.58 18.43	14.15 14.12	(CN) 2200, (-C=N-) 1600
6	100	75 Yellow	$C_{13}H_{11}N_3O_2S$	57.14 57.13	4.02 4.01	15.38 15.36	11.72 11.73	(CN) 2220 (CO) 1740, (C=N-) 1610
7	145	85 Red	$C_{13}H_{11}N_3O_2S$	57.14 57.12	4.02 4.03	15.38 15.18	11.72 11.68	(NH_2) 3450-3300,(CO) 1680 (-C≡N) 1610
8	245	65 Red	$C_{11}H_7N_3O_2S$	53.87 53.62	2.85 2.78	17.14 16.95	13.06 12.90	(CO) 1670, (NH_2) 3470, (C=N-) 1610
(c)9	258	50 Yellow	$C_{13}H_9N_4O_2SCl$	48.67 48.49	2.80 2.85	17.47 17.36	9.98 9.80	(C=N) 1610 (CO) 1740, (N=N) 1680
10	219-20	65 White	$C_{17}H_{12}N_4OS$	63.75 63.65	3.75 3.65	17.50 17.46	10.00 9.92	(NH) 3240, (CN) 2220, (CO) 1650
11	239	70 Violet	$C_{17}H_{12}N_4OS$	63.75 63.62	3.75 3.65	17.50 17.38	10.00 9.88	(NH_2NH) 3310-3410, (CO) 1640
12	330	55 yellow	$C_{18}H_{10}N_4OS_2$	59.66 59.43	2.76 2.80	15.46 15.60	17.67 17.58	(NH), br. 3100, (CO) 1690, (C=S) 1210, (C=N-) 1590
13	269-70	75 Yellow	$C_{19}H_{12}N_4OS$	60.63 60.52	3.19 3.02	14.89 14.72	17.02 17.00	(CO) 1740, (C=N-) 1640
14	245	75 Yellow	$C_{24}H_{14}N_3OS$	70.93 70.86	3.44 3.34	13.79 13.65	7.88 7.65	(CO) 1740 (-C=N) 1670
15	341	70 Yellow	$C_{19}H_{12}N_4OS$	66.27 66.34	3.48 3.62	16.27 16.38	9.30 9.12	(CO) 1760, (C=N-) 1680
16	168	65 Yellow	$C_{24}H_{15}N_5OS$	68.40 68.30	3.56 3.45	16.62 16.51	7.60 7.50	(NH) 3220, (CO) 1750 (C=N-) 1610
17	327-28	80 Yellow	$C_{18}H_{10}N_4O_2S$	62.42 62.28	2.89 2.75	16.18 16.00	9.24 9.37	(NH) 3200, two (CO) 1740-1670
18	265	50 Green-Yellow	$C_{17}H_9N_5OS$	61.63 61.42	2.71 2.75	21.14 21.00	9.66 9.37	(CO) 1680, (N=N-) 1670, (-C=N-) 1650

(a) All compounds were crystallized from ethanol (95%) except, 4 and 18 were crystallized from acetic acid; ^{1}H NMR analysis; for (10) in ($CDCl_3$) showed signals, at δ4.1 (s, 2H, CH_2), δ7 (s, 1H, NH), δ7.2-8.2 (m, 9H, ArH); for (11) in DMSO-d_6, δ2 (s, 2H, NH_2), δ7 (s, 1H, NH), δ7.1-8.2 (m, 9H, ArH).

(b) After recrystallization.

(c) Chlorine analysis; Found, 11.07, Calcd., 11.00%.

TABLE IV

Characterization data of the compounds **19–25**

Comp. No.	-R	m.p. °C[a]	Yield %[b] Colour	Mol. formula	Analysis % Calcd./Found C	H	N	S	^{1}H-NMR ($CDCl_3$) δppm
19		278-79	80 Yellow	$C_{13}H_7N_3O_2S$	57.99 57.73	2.60 2.50	15.61 15.49	11.90 11.82	2.6(s,3H,CH_3) 7.8-8.4(m,4H,ArH)
20	$-CH_3$	330-31	90 Yellow	$C_{14}H_{10}N_4OS$	59.57 59.42	3.54 3.33	19.85 19.62	11.34 11.20	2.8(s,3H,CH_3 of pyrimidone 3.7(s,3H,N-CH_3) 7.7-8.4(m,4H,ArH)
21	$-NH_2$	299-300	80 Red	$C_{13}H_9N_5OS$	54.12 54.89	3.18 3.00	24.73 24.52	11.30 11.10	
22	$-C_6H_4COCH_3$	305-06	60 Yellow	$C_{21}H_{14}N_4O_2S$	65.28 65.36	3.62 3.70	14.50 14.47	8.29 8.10	2.7(s,3H,CH_3)of pyrimidone 2.4(s,3H,$COCH_3$) 7.4-8.5(m,8H,ArH)
23	$-CH_2Ph$	252	85 Yellow	$C_{20}H_{14}N_4OS$	67.03 66.82	3.91 3.81	15.64 15.50	8.93 8.79	2.7(s,3H,CH_3) 5.5(s,2H,CH_2) 7.3-8.5(m,9H,ArH)
24	-NHPh	309-10	70 Red	$C_{19}H_{13}N_5OS$	63.50 63.32	3.62 3.65	19.49 19.38	8.91 8.72	
25	$-CH_2COOCH_3$	141	75 Yellow	$C_{16}H_{12}N_4O_3S$	56.47 56.39	3.52 3.40	16.47 16.32	9.41 9.30	

(a) All products were crystallized from ethanol (95%).
(b) After recrystallization.

III). The ^{1}H-NMR spectrum ($CDCl_3$) of **15** showed signals, at δ2.7 (s, 3H, CH_3) and at δ7.3–8.5 (m, 9H, ArH). Compound **7** undergoes further cyclization reaction when saponified with ethanolic potassium hydroxide solution, this is followed by ring closure when refluxed with acetic anhydride to produce, 2-methyl[1,3]oxazino[4′,5′:4,5]thieno[2,3-b]quinoxaline-4-one **19**. The IR spectrum shows absorption bands (C=O) at 1740 cm^{-1} and (—C=N—) at 1620 cm^{-1}. The ^{1}H-NMR spectrum ($CDCl_3$) shows signals, at δ2.6 (s, 3H, CH_3) and at δ7.8–8.4 (m, 4H, ArH). The mass spectrum shows a molecular ion peak; at m/e = 269 in agreement with the molecular formula ($C_{13}H_7N_3O_2S$).

The oxazinone compound **19** is refluxed with an ethanolic solution of several amine reagents (methylamine, hydrazine hydrate, p-aminoacetophenone, benzylamine, phenylhydrazine, and/or methyl glycinate to produce the corresponding 3-substituted-2-methylpyrimido[4′,5′:4,5]thieno[2,3-b]quinoxaline-4-ones **20–25**. The IR spectra shows absorption bands (C=O, pyrimidone) at 1650–1720 cm^{-1} and (—C=N—) at 1600–1620 cm^{-1}, while bands for (NH_2) of **21** at 3440–3300 cm^{-1}, for (NH) of **24** at 3050–3200 cm^{-1} and for (C=O, ester) of **25** at 1740 cm^{-1}. The ^{1}H-NMR spectra showed characteristic signals as shown in Table IV.

EXPERIMENTAL

Melting points reported are uncorrected. IR spectra (Tables II and III) are recorded for potassium bromide wafers on a Pye Unicam SP3100 spectrophotometer; UV spectra (Table I) in ethanol on a Shimadzu 2005 spectrophotometer, and ^{1}H-NMR (Tables II and III) in ($CDCl_3$) or (DMSO-d_6) solvents on a Varian 90 and EM-390 spectrometers using TMS as the internal standard. The mass spectra of the solid samples are analysed by JeolD300, KRATOS MS80RFA and MAT311, mass spectrometers.

TABLE V

Bacterial and fungicidal activities of selected synthesized compounds

Compd.	Zone of inhibition* (mm)							
	B.c.	S.a.	E.c.	K.sp.	P.n.	A.fl.	A.fu.	F.s.
1	7	-	-	-	-	-	-	-
2b	9	7	6	-	-	-	10	5
2c	6	-	-	-	-	-	5	-
6	-	-	7	-	-	-	6	-
7	-	-	7	-	-	-	-	-
11	-	-	7	8	-	-	-	-
12	-	-	7	-	-	-	-	-
13	8	-	-	9	7	8	8	-
14	6	-	-	10	-	-	-	-
16	-	-	7	-	-	-	-	-
19	6	-	7	8	-	-	-	-
20	6	-	9	-	-	-	-	-
21	-	-	7	6	-	-	-	-
22	6	10	8	-	-	-	-	7
25	-	-	7	8	-	-	-	-

* B.c. = Bacillus cereus; S.a. = Staphylococus aureus; E.c. = Esherichia coil; K.sp. = Klebsiella sp.; P.n. = Penicillium nigricans; A.fl. = Aspergillus flavas; A.fu. = Aspergillus fumigatus; F.s. = Fusarium solani; Most compounds showed remarkable bacterial activity with considerable antifungal activity for some of them, as resulted of agar diffusion test.

2(1H) quinoxalinethione-3-carbonitrile (**1**) is prepared by refluxing 3-chloroquinoxaline-2-carbonitrile (18.9 g, 0.1 mol) and thiourea (7.6 g, 0.1 mol) in ethanol (200 ml) for 4 hr. Evaporation of solvent, extraction of the residue with 10% aq. sodium hydroxide then neutralization of the extract with dilute hydrochloric acid gives a red solid, which recrystallized and identified (Table II).

2-Cyano-3-alkylthioquinoxaline (**2a–d**). A mixture of an alkyl halide (methyl iodide, ethyl iodide, n-butyl bromide or benzyl bromide (0.012 mol) and **1** (1.87 g, 0.01 mol) in absolute ethanol (30 ml) in presence of anhydrous sodium acetate is refluxed for 1 hr and cooled. The solid which precipitated is recrystallized from ethanol to give the corresponding products (**2a–d**), (Table I).

2-Cyano-3-carboxylmethylthioquinoxaline (**3**). A mixture of chloroacetic acid (0.94 g, 0.01 mol) and **1** (1.87 g, 0.01 mol) and anhydrous sodium acetate in an ethanol solution (30 ml) is refluxed for 2 hr. The solid separated is filtered, recrystallized, and identified (Table III).

Dimesoionic thiazolo[3',4'-c]-2-cyanoquinoxaline (**4**). On refluxing **3** (2.45 g, 0.01 mol) in acetic anhydride (20 ml) for 2 hr a black solid is obtained, washed several times and recrystallized from acetic acid (Table III).

2-Cyano-3-carboethoxymethylthioquinoxaline (**6**). A mixture of **1** (5.61 g, 0.03 mol), ethyl chloroacetate (3.66 g, 0.03 mol) and anhydrous sodium acetate (5 gm) in ethanol (100 ml) is refluxed for 2 hr. The separated solid was recrystallized and identified (Table III).

Ethyl 3-aminothieno[2,3-b]quinoxaline-2-carboxylate (**7**) is prepared by refluxing **6** (2.7 g, 0.01 mol) in absolute ethanol (20 ml) while adding and stirring with sodium ethoxide solution (0.46 gm, sodium in (50 ml) absolute ethanol). The separated solid is recrystallized and identified. Its mixed m.p and spectrum is coincident with an authentic sample prepared by refluxing **1** (1.87 g, 0.01 mol), bromodiethylmalonate (0.01 mol) and sodium ethoxide in absolute ethanol.

3-Aminothieno[2,3-b]quinoxaline-2-carboxylic acid (**8**). Alkaline hydrolysis of **7** (2.7 g, 0.01 mol) with potassium hydroxide (5 gm) in absolute ethanol (50 ml) while refluxing for 1 hr. The separated solid is filtered, dissolved in water and acidified with acetic acid. The precipitated carboxylic acid **8** is recrystallized and identified (Table III). Its m.p and IR spectrum is coincident with an authentic sample produced by another procedure.[6]

Thieno[2,3-b]quinoxaline-2-carboethoxy-3-diazonium chloride (**9**) is prepared by diazotization of **7** (1.35 g, 0.5 mol) in concentrated hydrochloric acid (15 ml) with sodium nitrite solution while cooling at 5°C. The separated solid is filtered, recrystallized and identified (Table III).

2-Carboethoxythieno[2,3-b]quinoxaline-3-yl-azo-p-hydroxybenzene is prepared by reaction of **9** (1.35 g, 0.001 mol), with phenol (0.001 mol) in sodium hydroxide solution (5 ml). The separated solid is recrystallized from ethanol as brown crystals, m.p. 230°C, yield (63%); Found: C, 60.16; H, 3.31; N, 14.63; S, 8.31%; Calcd. for $C_{19}H_{14}N_4O_3S$; C, 60.32; H, 3.70; N, 14.82; S, 8.47%. IR spectrum shows (OH) broad band at 3470 cm^{-1}, (C=O) at 1740 cm^{-1} and (—N=N—) at 1680 cm^{-1}.

2-Carboethoxythieno[2,3-b]quinoxaline-3-yl-azo-1-yl-2-naphthol is prepared by the reaction of **9** (0.285 g, 0.001 mol), with β-naphthol (0.001 mol) in sodium hydroxide solution (5 ml). The separated solid is recrystallized from ethanol as brown crystals, m.p 245°C, yield (72%); Found: C, 63.19; H, 3.2; N, 14.36; S, 7.19%; Calcd. for $C_{23}H_{16}N_4O_3S$; C, 63.30; H, 3.66; N, 14.67; S, 7.33%. IR spectrum shows bands, broad (OH) at 3480 cm^{-1}; (C=O) at 1740 cm^{-1} and (—N=N—) at 1670 cm^{-1}.

2-Cyano-3-thiomethylcarboxanilide quinoxaline (**10**). A mixture of **1** (3.64 g, 0.02 mol), chloroacetanilide (3.4 g, 0.02 mol) and anhydrous sodium acetate (3 gm) in ethanol (30 ml) is refluxed for 1 hr. The separated solid on addition of water (50 ml) was recrystallized and identified (Table III).

3-Aminothieno[2,3-b]quinoxaline-2-carboxanilide (**11**) is prepared by cyclization of **10** (3.2 g, 0.001 mol) by refluxing in absolute ethanolic sodium ethoxide solution from sodium metal (0.5 gm) in absolute ethanol (20 ml) for 1 hr. The separated solid is recrystallized and identified (Table III).

3-Phenylpyrimido[4',5':4,5]thieno[2,3-b]quinoxaline-4-one-2-thione (**12**). A mixture of **11** (0.005 mol) and carbon disulfide (10 ml) in dry pyridine (20 ml) is refluxed for 3 hr. The separated solid is recrystallized and identified as in Table III. It is coincident with an authentic sample prepared by refluxing **7** (2.73 g, 0.01 ml) with phenyl isothiocyanate (0.01 mol) in dry pyridine (20 ml) for 5 hr., and is separated and identified as before.

2-Methylthio-3-phenylpyrimido[4',5':4,5]thieno[2,3-b]quinoxaline-4-one (**13**) is prepared by alkylation of **12** (1.75 g, 0.005 mol) in ethanol (20 ml) containing anhydrous sodium acetate (1.5 gm) with methyl iodide (10 ml) while stirring and warming for 1 hr. The solid separated on addition of water (20 ml) is filtered, recrystallized and identified (Table III).

2,3-Diphenylpyrimido[4',5':4,5]thieno[2,3-b]quinoxaline-4-one (**14**). A mixture of **11** (1.6 g, 0.005 mol) and benzoyl chloride (10 ml) is refluxed for 3 hr. The separated solid is filtered, recrystallized and identified (Table III).

2-Methyl-3-phenylpyrimido[4',5':4,5]thieno[2,3-b]quinoxaline-4-one (**15**). A mixture of **11** (3.2 g, 0.01 mol) and acetic anhydride (30 ml) is refluxed for 2 hr. The separated solid is filtered, recrystallized and identified as in Table III.

3-Phenyl-2-N-phenylamino-pyrimido[4',5':4,5]thieno[2,3-b]quinoxaline-4-one (**16**). A mixture of **11** (1.6 g, 0.005 mol) in dry pyridine (20 ml) and phenyl isothiocyanate (0.005 mol) is refluxed for 5 hr. The separated solid on water addition (10 ml) is filtered, recrystallized and identified (Table III).

3-Phenylpyrimido[4',5':4,5]thieno[2,3-b]quinoxaline-2,4(1H)dione (**17**). A mixture of **11** (1.6 g, 0.005 mol) and ethyl chloroformate (5 ml) in dry pyridine (15 ml) is refluxed for 6 hr. The separated solid on water addition (20 ml) is filtered, recrystallized and identified (Table III).

3-Phenyl[1,2,3]triazino[4',5':4,5]thieno[2,3-b]quinoxaline-4-one (**18**) is prepared by reaction of **11** (3.2 g, 0.01 mol) in concentrated hydrochloric acid (10 ml) with addition of sodium nitrite solution (14 ml. 10%, 0.01 mol) while cooling at 0°C and stirring for 20 minutes. The separated solid is recrystallized and identified (Table III).

2-Methyl[1,3]oxazino[4',5':4,5]thieno[2,3-b]quinoxaline-4-one (**19**) is prepared by saponification of **7** (2.5 g, 0.01 mol) in ethanolic sodium hydroxide solution (20 ml. 10%) by boiling for 30 min. and the

separated sodium salt was boiled with acetic anhydride (20 ml) for 1 hr. The separated solid is filtered, recrystallized and identified (Table IV).

2-Methyl-3-substituted pyrimido[4',5':4,5]thieno[2,3-b]quinoxaline-4-one (**20–25**). General procedure: Each compound is prepared by refluxing **19** (2.7 g, 0.01 mol) in absolute ethanol (30 ml) for 3 hr with the corresponding amino compound. The separated product is recrystallized and identified (Table IV).

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