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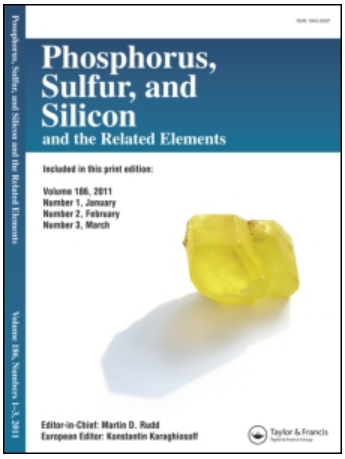

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SYNTHESIS OF NEW PYRIDYL QUINOXALINEMETHYL SULFIDES

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SYNTHESIS OF NEW PYRIDYL QUINOXALINEMETHYL SULFIDES

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3-Bromomethyl quinoxalin-2(1H) one (**1**) reacts easily with 2-mercapto-4,6-dimethyl pyridine-3-carbonitrile to give pyridiyl quinoxalinemethyl sulfide (**3**). Compound **3** was boiled with $POCl_3$ yielding pyridothieno pyrroloquinoxaline (**5**). Compound **5** was obtained also by boiling compound 6 with $POCl_3$ or Ac_2O. The mercapto compound **3** was produced by two routes: reacting compound **4** with thiourea, followed by treatment with HCl and NaOH, or by boiling compound **3** with P_2S_5 in pyridine.

Key words: Synthesis, reactions, pyridyl quinoxalino methylsulfide, pyridothienopyrroloquinoxaline, thieno pyridyl quinoxaline.

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INTRODUCTION

The insecticidal and acricidal properties of many phosphoric, phosphonic, thionophosphoric, and thionophosphamic esters of 6-hydroxy quinoxaline have been patented.[1] Many substituted quinoxalines such as chloroquinoxaline, methoxy quinoxalines derivatives, and metal salts of 2 mercaptoquinoxaline-1-oxide, have been tested and showed fungicidal, bactericidal, and insecticidal activity.[2–4]

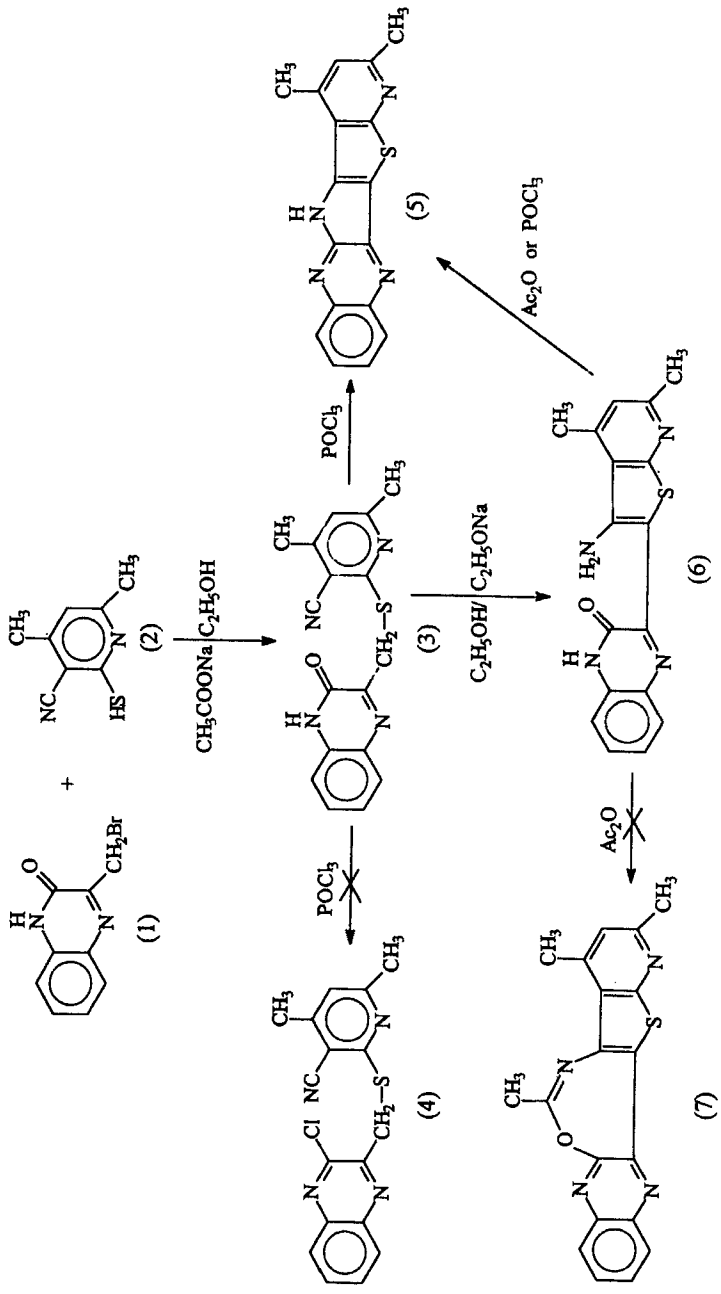
The literature reports the synthesis and activity of substituted diaryl sulfides as antileprotic, nematoidal, bactericidal,[5,6] and insecticidal activities.[7]

RESULTS AND DISCUSSION

In continuation of our work in synthesis of heterocyclic compounds containing the pyridine moiety,[8–14] we synthesized some heterocyclic compounds containing pyridine of quinoxaline moieties and with a sulfide linkage in one system.

3-Bromomethylquinoxalin-2(1H)-one [15] (**1**) reacted easily with 2-mercapto-4,6-dimethylpyridine-3-carbonitrile (**2**) in boiling ethanol and in the presence of sodium acetate to give pyridylquinoxalinomethyl sulfide (**3**).

In an attempt to convert compound **3** into 2-chloro-3-methyl-mercapto(2,4-dimethyl-5-cyanopyridin-6-yl)quinoxaline (**4**) by boiling compound **3** with $POCl_3$, a deep red compound, m.p. >300°C, was obtained. This gave a mass spectrum with $[M]^+$ 304, elemental analysis, corresponded to the molecular formula $C_{17}H_{12}N_4S$. This compound may have structure **5**. This was confirmed by another method of preparation of compound **5**. From the cyclization of compound **3** in boiling ethanol in the presence of sodium ethoxide, compound **6** was produced which was converted to compound (**5**) by the abstraction of water by boiling it in acetic anhydride or



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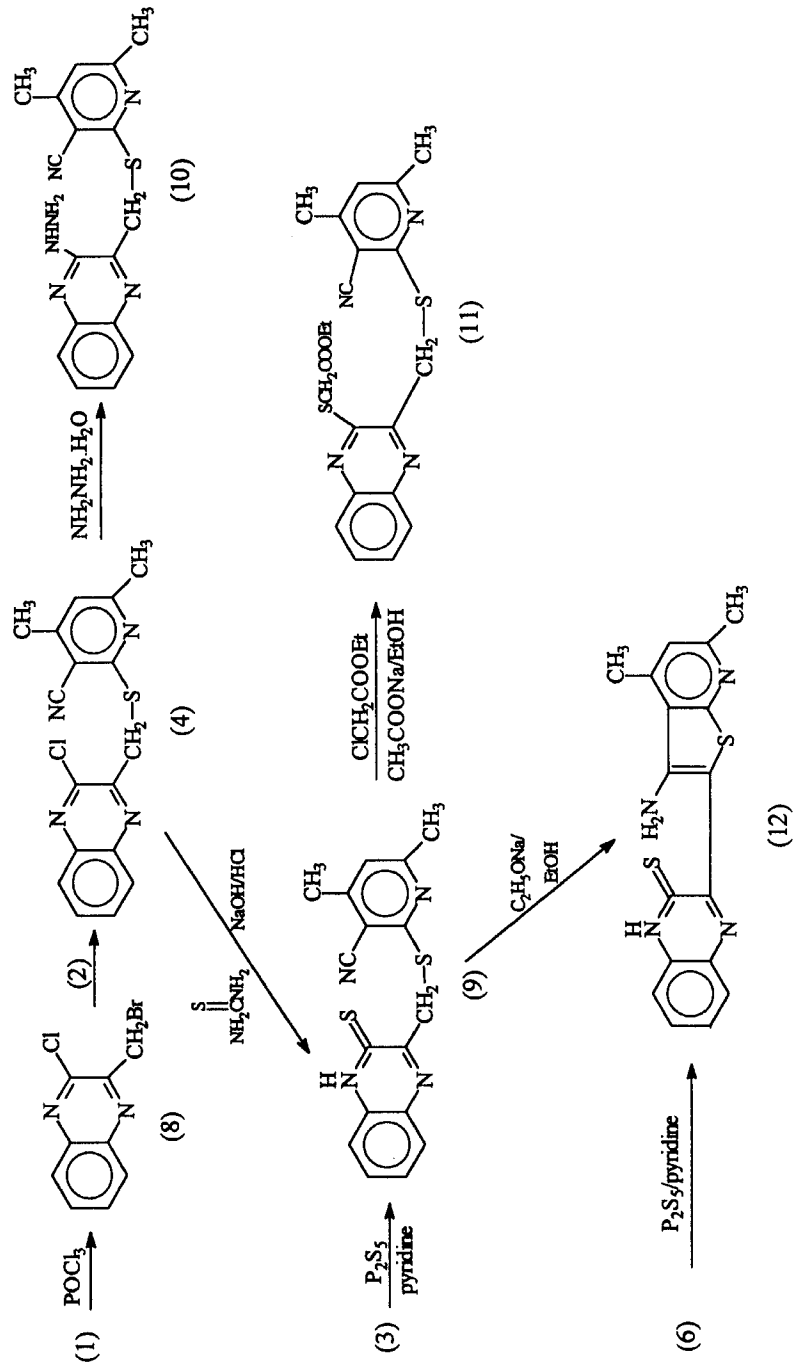

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$POCl_3$. The compound produced was identical in all physical constants with those produced from the refluxing of compound (**3**) or (**6**) with $POCl_3$.

The chloro compound (**4**) was obtained by another route, when compound (**1**) allowed to reflux with $POCl_3$, the 2 bromomethyl-3-chloroquinoxaline (**8**) was obtained. Compound (**8**) was produced when allowed to reflux with compound (**2**) in ethanol in the presence of sodium acetate, compound (**4**) was obtained.

2-Methylmercapto(2,4-dimethyl-5-cyanopyridin-6-yl]quinoxaline-3(4H) thione (**9**) was obtained by two routes, either by conversion of chloro compound (**4**) into mercapto compound **9** by refluxing it with thiourea followed by treating with NaOH and HCl or by thionation of compound (**3**) by refluxing it with P_2S_5 in pyridine.

Compound **4** reacts with hydrazine hydrate in refluxed ethanol to produce 3-hydrazino-2-methylmercapto(2,4-dimethyl-5-cyanopyridin-6-yl)quinoxaline (**10**). When compound (**9**) allowed to react with ethyl chloroacetate in refluxing ethanol and in the presence of sodium acetate, the mercapto ethyl acetate derivative (**11**) was produced, but when compound (**9**) refluxed in ethanol and in the presence of sodium ethoxide, the 2[5-amino-2,4-dimethylthieno[2,3-b]pyridine-6-yl]quinoxaline-3[4H]thione (**12**) was obtained, which also was obtained by refluxing compound (**6**) with P_2S_5 in pyridine.

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EXPERIMENTAL

Melting points are uncorrected and determined on Fisher-Johns melting point apparatus. IR spectra were recorded on a Pye-Unicam spectrophotometer using KBr-Wafer technique ^{1}H-NMR spectra were recorded by 90 MHz Varian NMR spectrometer using tetramethyl silane as internal standard. Mass spectra were determined on Dupont 21-492 B mass spectrometer at an ionizing potential 75 e.v, ionizing current 300 A, and source temperature 200°C. Elemental analysis was performed on Perkin-Elmer 240 C Microanalyzer.

2-Methylmercapto(2,4-dimethyl-5-cyanopyridin-6-yl)-quinoxalin-3(4H)-one (**3**): A mixture of compound (**1**) (2.39 g, 0.01 mol), compound (**2**) (1.64 g, 0.01 mol) and sod. acetate (0.984 g, 0.012 mol.) in ethanol of 30 ml was boiled for two hours, and then allowed to cool. The solid product was collected, washed with water and recrystallized from ethanol as yellowish white crystals, in 90% yield, mp 225°C.

Anal. Calcd. for: $C_{17}H_{14}N_4OS$: C, 63.35; H, 4.34; N, 17.39; S, 9.38%
Found: C, 63.50; H, 4.16; N, 17.18; S, 10.16%
IR: ν3400 cm^{-1} (NH), ν2220 cm^{-1} (C≡N), and ν1660 cm^{-1} (C=O); ^{1}H-NMR in DMSO-d_6: δ2.1, 2.35 (2s, 6H, $2CH_3$), 4,2(s, 2H, CH_2), 7.05 (s, 1H, CH pyridine, 7.2–7.8 (m, 4H, Ar-H) and 8.4 (s, 1H, NH).

2,4-Dimethylpyrido[2",3":2',3']thieno[2',3':2,3]pyrrolo-[4,5-b]quinoxaline (**5**): *Method (a)*: A sample of compound (**3**) (1 gm) in $POCl_3$ (10 ml) was boiled for 2 hrs, then allowed to cool and poured into ice/water mixture with stirring. The solid product was filtered off and recrystallized from dioxane as deep red crystals in 80% yield, m.p. >300.

Method (b): A sample of compound (**6**) (1 g) in acetic anhydride (10 ml) was refluxed for 10 hrs, then allowed to cool and poured into cold water. The solid product was collected and recrystallized from dioxane as red crystals in 70% yield, m.p. >300°C.

Anal. Calcd. for: $C_{17}H_{12}N_4S$: C, 67.10; H, 3.95; N, 18.42; S, 10.52%
Found: C, 66.90; H, 4.15; N, 18.20; S, 10.74%
IR: ν3400 cm^{-1} (NH) and showed the disappearance of bands characteristic for (C=O) and (C≡N) groups. ^{1}H-NMR in DMSO-d_6: 2.1, 2.4 (2s, 6H, $2CH_3$), 7.00 (s, 1H, CH pyridine), 7.3–7.7 (m, 4H, Ar-H), and 8.3 (s, 1H, NH), MS (m/e = 304).

2-(5-Amino-2,4-dimethylthieno[2,3-b]pyridin-6-yl)quinoxaline 3(4H) one (**6**): To a sample of compound (**3**) (1 gm) in ethanol absolute (20 ml) drops of sodium ethoxide solution in ethanol was added, the mixture was heated for 10 minutes, then allowed to cool, acidified with acetic acid. The solid product was filtered off and recrystallized from dimethyl formamide/water as red crystals in 85% yield, m.p. >300°C.

Anal. Calcd. for: $C_{17}H_{14}N_4OS$: C, 63.35; H, 4.34; N, 17.39; S, 9.94%
Found: C, 63.12; H, 4.56; N, 17.14; S, 10.12%
IR: ν3400–3100 cm^{-1} (NH_2) and (NH) and at ν1660 cm^{-1} (C=O) and showed the disappearance of band characteristic for (C≡N). ^{1}H-NMR in DMSO-d_6: 2.1, 2,5(2s, 6H, $2CH_3$), 4.6 (s, 2H, NH_2), 7.0 (s, 1H, CH pyridine), 7.2–7.7 (m, 4H, ArH), and 8.4 (s, 1H, NH) MS: m/e = 322.

2-Bromomethyl-3-chloroquinoxaline (**8**): A sample of compound (**1**) (2 gm) in $POCl_3$ (10 ml) was boiled for 2 hours, then allowed to cool and poured into ice/water mixture. The solid product was collected, and recrystallized from ethanol as yellowish green crystals in 65% yield, m.p. 120–22°C.

Anal. Calcd. for: $C_9H_6BrClN_2$: C, 41.94; H, 2.33; Br, 31.06; Cl, 13.78; N, 10.87%
Found: C, 42.12; H, 2.50; Br, 30.86; Cl, 13.52; N, 11.00%
IR: showed the disappearance of bands characteristic for (NH) and (C=O) in compound (**1**). ^{1}H-NMR in $CDCl_3$: 4,3(s, 2H, CH_2) and 7.2–7.8 (m, 4H, Ar-H).

2-Methylmercapto(2,4-dimethyl-5-cyanopyridin-6-yl)-4-chloro-quinoxaline (**4**): A mixture of compound (**8**) (2.575 g, 0.01 mol), compound (**2**) (1.64 g, 0.01 mol) and sod. acetate (0.984 g, 0.012 mol) in ethanol (30 ml) was refluxed for one hour, then allowed to cool. The solid product was collected and recrystallized from ethanol as yellowish white crystals, in 68% yield, m.p. 143–5°C.

Anal. Calcd. for: $C_{17}H_{13}ClN_4S$: C, 59.91; H, 3.81; Cl, 10.42; N, 16.44; S, 9.39%
Found: C, 60.10; H, 4.18; Cl, 10.22; N, 16.30; S, 9.40%
IR: Showed the disappearance of bands characteristic for (NH) and (C=O) groups. ^{1}H-NMR in DMSO-d_6: 2.1, 2,5(2s, 6H, $2CH_3$), 4.5 (s, 2H, CH_2), 7.00 (s, 1H, CH pyridine) and 7.2–7.8 (m, 4Hm Ar-H).

2-Methylmercapto[2,4-Dimethyl-5-cyanopyridin-6-yl]quinoxalin 3(4H) thione (**9**): *Method (a)*: A mixture of compound (**4**) (1.7 g, 0.005 mol) and thiourea (0.76 g, 0.01 mol) in ethanol (30 ml) was refluxed for 2 hrs, allowed to cool, then the solid product was collected and dissolved in sodium hydroxide (10 ml, 10%) followed by acidification with HCl till acidic, the solid product was collected and recrystallized from ethanol as red crystals in 70% yield, m.p. 237°C.
Method (b): A mixture of compound (**3**) (3.22 g, 0.01 mol) and phosphorous pentasulphide (2.22 g, 0.01 mol) in dry pyridine (30 ml) was refluxed for 5 hrs, then allowed to cool and poured into cold water (200 ml). The solid product was collected and recrystallized from ethanol as red crystals in 65% yield, m.p. 235–7°C.

Anal. Calcd. for: $C_{17}H_{14}N_4S_2$: C, 60.35; H, 4.14; N, 16.56; S, 18.93%
Found: C, 60.50; H, 4.95; N, 16.34; S, 19.12%.
IR: ν3400 cm^{-1} (NH), 2220 cm^{-1} (C≡N) and showed the disappearance of band characteristic for (C=O). ^{1}H-NMR in DMSO-d_6: 2,1,2,5(2s, 6H, $2CH_3$), 4,6(s, 2H, CH_2); 7.00 (s, 1H, CH pyridine), 7.2–7.7 (m, 4H, Ar-H), and 8.6 (s, 1H, NH).

3-Hydrazino-2-methylmercapto[2,4-dimethyl-5-cyano-pyridin-6-yl]-quinoxaline (**10**): A mixture of compound (**4**) (3.4 g, 0.01 mol), and hydrazin hydrate (0.5 g, 0.01 mol) in ethanol (20 ml) was refluxed for ½ hr, then allowed to cool. The solid product was collected and recrystallized from ethanol as brown crystals in 67% yield, m.p. 195°C.

Anal. Calcd. for: $C_{17}H_{16}N_6S$: C, 60.71; H, 4.76; N, 25.00; S, 9.52%
Found: C, 61.00; H, 4.88; N, 24.84; S, 9.76%
IR: ν3450–3250 cm^{-1} (NH_2, NH), ν2220 cm^{-1} (C≡N).

3-[Thoxycarbonylmethylmercapto]-2-methylmercapto[2,3-dimethyl-5-cyano-pyridin-6-yl]quinoxaline (**11**): A mixture of compound (**10**) (1.2 g, 0.005 mole), ethyl chloroacetate (0.61 g, 0.005 mol), and sod. acetate (0.49 g, 0.006 mol) in ethanol (20 ml) was refluxed for 5 hrs, then allowed to cool. The solid product was collected, washed by water, and recrystallized from ethanol as white crystals in 78% yield, m.p. 80°C.

Anal. Calcd. for: $C_{21}H_{20}N_4O_2S_2$: C, 59.43; H, 4.71; N, 13.20; S, 15.09%
Found: C, 59.60; H, 4.90; N, 13.42; S, 14.90%.
IR: ν2220 cm^{-1} (C≡N), and ν1720 cm^{-1} (C=O). ^{1}H-NMR: in $CDCl_3$: 1.3 (t, 3H, CH_3 ester), 2.1, 2.5 (2s, 6H, $2CH_3$), 4.1 (q, 2H, CH_2 ester), 4.5, 4.7 (2s, 4H, $2CH_2S$), 7.0 (s, 1H, CH pyridin), 7.2–9.8 (m, 4H, Ar-H).

2-[5-Amino-2,4-dimethyl thieno[2,3-b]pyridin-6-yl]quinoxaline-3(4H)thione (**12**): A sample of compound (**9**) (1.2 g, 0.005 mol) in ethanolic solution of sodium ethoxide (0.115 g, 0.005 mol) was refluxed for ½ hr, then allowed to cool and acidified with acetic acid. The solid product was collected and recrystallized from dioxane as red crystals in 75% yield, m.p. >300°C.

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Anal. Calcd. for: $C_{17}H_{14}N_4S_2$: C, 60.35; H, 4.14; N, 16.56; S, 18.93%
Found: C, 60.18; H, 3.95; N, 16.72; S, 19.12%.
IR: ν3450–3300 cm^{-1} (NH_2, NH) groups and showed the disappearance of band characteristic for (C≡N). ^{1}H-NMR in DMSO-d_6: 2.1, 2,5(2s, 6H, $2CH_3$), 4,7(s, 2H, NH_2), 7.1 (s, 1H, CH, pyridine), 7.2–7.9 (m, 4H, Ar-H), 8.7 (s, 1H, NH).

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