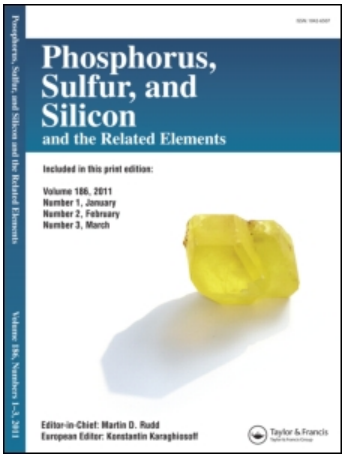

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

PYRIDAZINE DERIVATIVES: SOME REACTIONS OF 5-AMINOTHIENO[2,3-c]PYRIDAZINE-6-CARBONITRILES, SYNTHESIS OF NEW CONDENSED PYRIMIDO AND TRIAZINOTHIENOPYRIDAZINES

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To cite this Article Radwan, Sh. M.(1999) 'PYRIDAZINE DERIVATIVES: SOME REACTIONS OF 5-AMINOTHIENO[2,3-c]PYRIDAZINE-6-CARBONITRILES, SYNTHESIS OF NEW CONDENSED PYRIMIDO AND TRIAZINOTHIENOPYRIDAZINES', Phosphorus, Sulfur, and Silicon and the Related Elements, 155: 1, 175 — 188
To link to this Article: DOI: 10.1080/10426509908044981
URL: http://dx.doi.org/10.1080/10426509908044981

Phosphorus, Sulfur, and Silicon, 1999, Vol. 155, pp. 175-188
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PYRIDAZINE DERIVATIVES: SOME REACTIONS OF 5-AMINOTHIENO[2,3-c]PYRIDAZINE-6-CARBONITRILES, SYNTHESIS OF NEW CONDENSED PYRIMIDO AND TRIAZINOTHIENOPYRIDAZINES

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(Received February 23, 1999; In final form April 27, 1999)

3,4-Difuryl or 3,4-diphenyl-5-aminothieno[2,3-c]pyridazine-6-carbonitriles **2a,b** were prepared and subjected to some sequence reactions to afford new condensed polycyclic compounds containing thieno[2,3-c]-pyridazines with anticipated biological activity.

Keywords: Thienopyridazine; tetrazolopyrimidothienopyridazine; pyridazinothienopyrimidotriazepeine; imidazopyrimidothienopyridazine

Pyridazine and condensed pyridazine derivatives are reported to have good biological activities, and consequently substituted 4,5-diarylpyridazinones are used as analgesic, antiinflammatory and antipyretic agents.[1] Some tetrahydropyridazine carboxamides are also useful as pesticides.[2] Condensed pyridazines such as some 6-alkylthio imidazo[1,2-b]pyridazine derivatives are associated with CNS nervous system activity[3] and some thieno-pyridazine derivatives are reported to posses considerable antiasthmatic properties[4]. In view of the forementioned facts and as a continuation on our previous work on the chemistry of pyridazine compounds[5,6], we report the synthesis of different heterocyclic systems condensed with pyridazine ring with potential biological activity. The starting compounds, 5-amino-3,4-difuryl or 3,4-diphenylthieno[2,3-c]pyridazine-6-carbonitriles **2a, b** were obtained by the reaction of pyridazine thione derivatives

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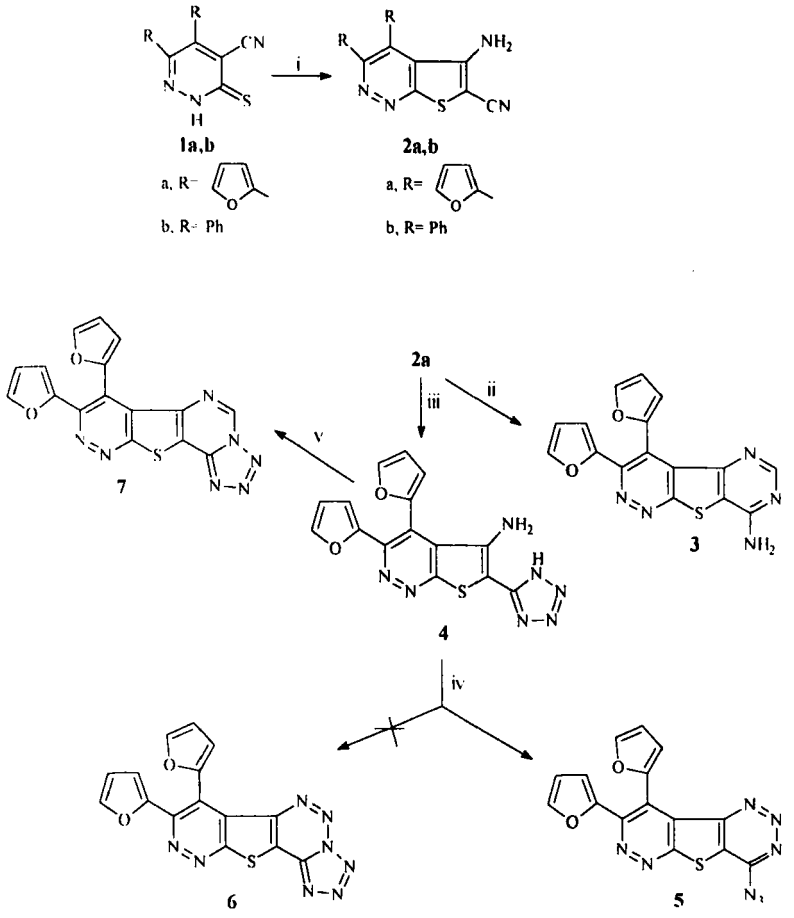
1a, b with chloroacetonitrile in refluxing ethanol in the presence of anhydrous sodium carbonate (Scheme 1).



Reagents: i $ClCH_2CN/Na_2CO_3$, ii $HCONH_2$, iii NaN_3/DMF, iv $NaNO_2/AcOH$, HCl, v $CH(OEt)_3$

SCHEME 1

Thieno[2,3-c]pyridazine derivatives **2a, b** were used as verastile compounds for building of fused heterocyclic systems. Thus, the reaction of **2a**, with formamide gaves the expected substituted pyrim-

ido[4′,5′:4,5]-thieno[2,3-c]pyridazine **3**. On the other hand reaction with sodium azide[7] in dimethyl formamide and in the presence of ammonium chloride afforded the tetrazoyl derivative **4**.

When a solution of **4** in a mixture of acetic acid and hydrochloric acid was treated with sodium nitrite solution, the product was identified as the azido compound **5**. The identification of this compound was based on the elemental analyses and IR sepctrum data which showed strong band at 2120 cm^{-1} (N_3) favoring the azido structure **5** and eliminating the expected tetrazolo [1,2-f]pyridazino[3′,4′:5,4]thieno[2,3-d] 1,2,3-triazine (**6**).

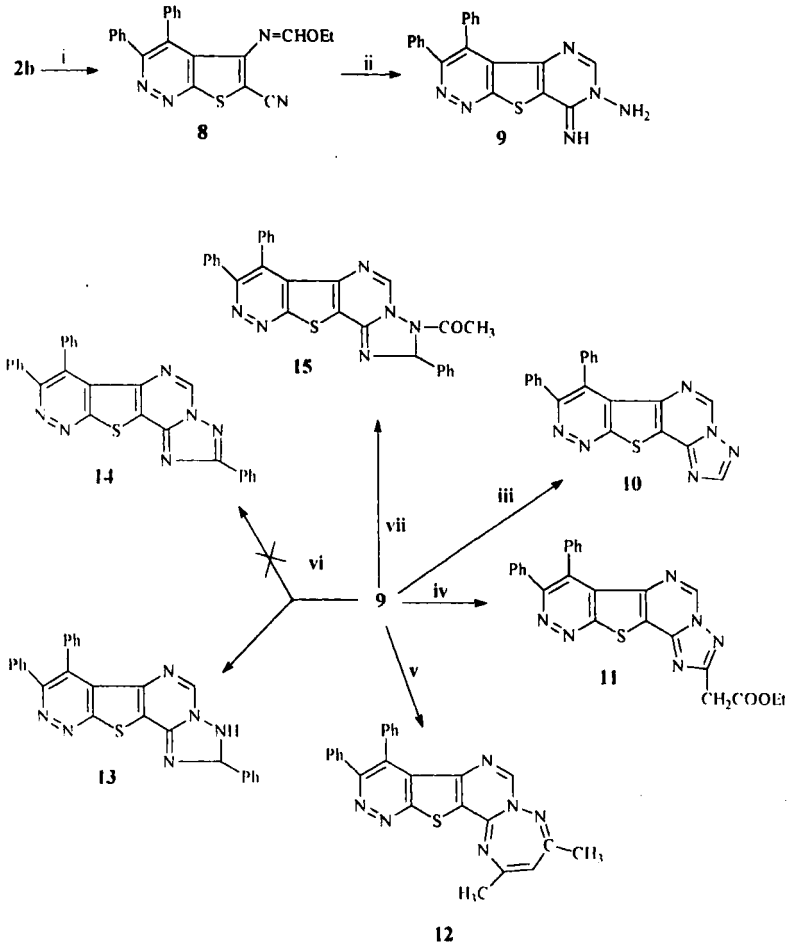
Moreover refluxing **4** with triethyl orthoformate furnished substituted tetrazolo[1",5":1′,6′]pyrimido[4′,5′:4,5]thieno[2,3-c]pyridazine **7** (Scheme 1).

Heating of compound **2b** with an equimolar amount of triethyl orthoformate in acetic anydride gave the methanimidate derivative **8**. Stirring the latter compound with an equivalent of hydrazine hydrate[8] in ethanol at room temperature produced substituted pyrimido[4′,5′:4,5]thieno [2,3-c]pyridazine **9**.

Boiling of compound **9** with riethyl orthformate, diethyl malonate, and/or acetyl acetone afforded 3,4-diphenyl-1,2,4-triazolo[1",5"1′,6′] pyrimido[4′,5′:4,5]thieno[2,3-c]pyridazine (**10**), 3,4-diphenyl-9-ethoxycarbonylmethyl-1,2,4-triazolo[1",5":1′,6′]pyrimido[4′,5′:4,5]thien[2,3-c] pyridazine (**11**) and 3,4-diphenyl-9,11-dimethyl pyridazino [3",4":5′,4′]-thieno[2′,3′:5,4]pyrimido[1.6-b]-1,2,4-triazepine (**12**) respectively.

Reaction of compound **9** with benzaldehyde in ethanol in the presence of piperidine gives the triazolo[1",2":1′,6′]pyrimido[4′,5′:4,5]-thieno[2,3-c] pyridazine (**13**) instead of the oxidized form **14**. Meanwhile on reaction of **9** with benzaldehyde in refluxing acetic acid, the product was identified as acetyl triazolo[1",2":1′,6′]pyrimido[4′,5′:4,5]thieno [2,3-c] pyridazine (**15**). This proves that the reaction proceeds via a condensation followed by the addition of the mino group to azomethine function to give the triazoline ring which under the reaction condition acetylated to give **15** (Scheme 2).

Incorporating the imidazole ring with the thieno[2,3-c]pyridazine system was achieved by the reaction of compound **2a, b** with ethylene diamine in the presence of carbon disulfide to give the imidazoyl derivative **16a, b**. Compound **16b**, when allowed to react with triethyl orthoformate, carbon disulfide, and/or nitrous acid, yielded 3,4-diphenyl-8,9-dihydroimi-

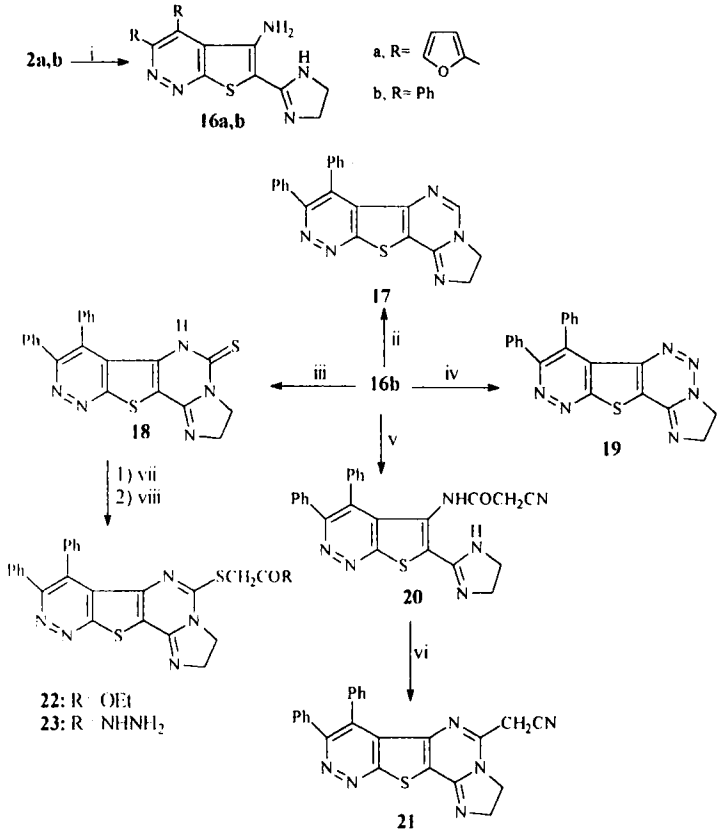


Reagents i $CH(OEt)_3/Ac_2O$, ii $NH_2NH_2/EtOH$, iii $CH(OEt)_3$, iv $CH_2(CO_2Et)_2$/reflux, v Ac_2CH_2/reflux, vi PhCHO/EtOH, vii PhCHO/AcOH

SCHEME 2

dazo[1",2":1′,6′]pyrimido[1′,5′:4,5]thieno[2,3-c]pyridazine (**17**), 3,4-diphenyl-8,9-dihydroimidazo[1′,2":1′,6′]pyrimido[4′,5′:4,5]thieno [2,3-c]pyridazine-6-thione (**18**) and 3,4-diphenyl-8,9-dihydroimidazo [1,2--f] pyridazine[3′,4′:5,4]thieno[2,3-d]-1,2,4-triazine (**19**) respectively.

Compound **21** was prepared by refluxing **16b** with ethyl cyanoacetate followed by heating of the resulting intermediate **20** with acetic anhydride. However, S-alkation of compound **18** with ethyl chloroacetate in ethanol in the presence of fused sodium acetate furnished the S-alkylated product **22**. The latter compound upon reaction with hydrazine hydrate in refluxing ethanol gives the carbohydrazide **23** (Scheme 3).



Reagents: i $NH_2(CH_2)_2NH_2/CS_2$, ii $CH(OEt)_3$, iii CS_2/Pyridine, iv $NaNO_2$/HCl, v $CNCH_2CO_2Et$, vi Ac_2O, vii $ClCH_2CO_2Et$/Fused AcONa, viii NH_2NH_2/EtOH

SCHEME 3

The structure of all the synthesized compounds was confirmed by elemental analysis, IR, ^{1}H NMR, and MS spectroscopy.

EXPERIMENTAL

All melting points are uncorrected and measured on a Fisher-John apparatus. Elemental analyses were performed on a Perkin-Elmer 240C elemental analyser. IR spectra were recorded on a Pye Unicam SP-100 spectrophtometer using KBr wafer technique. ^{1}HNMR spectra were recorded on a Varian EM-390 90 MHz. NMR spectrometer in suitable deuterated solvent using TMS as internal standard. MS spectra were recorded on Jeol-JMS-600 apparatus.

5,6-Difuryl or 5,6-diphenyl 4- cyanopyridazine-3(2H)thione 1a, b)

These compounds were prepared according to the reported methods. [9, 10]

Synthesis of 5-amino-3,4 difuryl or 3,4- diphenylthieno[2,3-c] pyridazine 6-carbonitrile (2a, b)

General procedure

A mixture of **1a, b** (0.01 mol), chloroacetonitrile 0.73 g, 0.01 mol), and anhydrous sodium carbonate (2 g) in absolute ehtanol (30 ml) was gently refluxed for 2 hours. Upon cooling, the solid product obtained was filtered off, washed with water, and recrystallized from ethanol to give **2a, b** respectively.

2a: Yellow greenish crystals, yield (88%), m.p. 237–239 °C. IR: 3340, 3300 cm^{-1} (NH_2) and 2200 cm^{-1} (CN). ^{1}HNMR DMSO-d_6): δ 5.9 (s, 2H, NH_2), 6.3–6.9 (m, 4H, 2×H-3, 2×H-4 furyl ring), 7.7, 8.1 (2s, 2H, 2×H-5 furyl ring).

Anal. Calcd. for $C_{15}H_8N_4O_2S$:	C: 58.43, H: 2.61, N: 18.77, S: 9.61.
Found:	C: 58.11, H: 2.53, N: 18.42, S: 9.63.

2b: Yellow crystals, yield (89%), m.p. 207–9 °C. Lit.[11] 208–210 °C.

Anal. Calcd for $C_{19}H_{12}N_4S$: C: 69.49, H: 3.68, N: 17.06, S: 9.76.

Found: C: 69.13, H: 3.54, N: 16.98, S: 9.66.

8-Amino-3,4 difuryl pyrimido[4′,5′:4,5]thieno[2,3-c]pyridazine (3)

Compound **2a** (0.5 g) and formamide (5 ml) were gently refluxed for 2 hours, and upon cooling, a precipitated formed was filtered off and recrystallized (acetic acid) to afford **3**, (73%), m.p. >300 °C. IR: 3400, 3200 cm^{-1} (NH_2) and 1640 cm^{-1} (C=NH). ^{1}HNMR (CF_3CO_2D): δ 6.4–7.1 (m, 4H, 2×H-3, 2×H-4 furyl ring), 7.8–8.1 (2s, 2×H-5 furyl ring) and 8.6 (s, 1H, CH pyrimidine ring).

Anal. Calcd. for $C_{16}H_9N_5O_2S$: C: 57.30, H: 2.70, N: 20.88, S: 9.56

Found: C: 57.08, H: 2.63, N: 20.68, S: 9.66

5-Amino-6-(tetrazol-2′-yl)-3,4-difuryl thieno[2,3-c]pyridazine (4)

A mixture of **2a** (3 g, 0.01 mol), sodium azide (1.5 g), and ammonium chloride (1.5 g) in dimethyl formamide (30 ml) was heated with stirring at 120 °C for 4 hours. Upon cooling the mixture was treated with 10% hydrochloric acid solution (15 ml). The product formed was filtered off and recrystallized from dimethylformamide-ethanol to give **4**, (74%), m.p. 273–275 °C (dec.). IR: 3450, 3350, 3150 cm^{-1} (NH) and 1600 cm^{-1} (C=N). ^{1}HNMR (DMSO-d_6): δ 5.7 (s, 2H, NH_2), 5.9 (s, 1H, NH), 6.3–7.0 (m, 4H, 2×H-3, 2×H-4) and 7.7–8.0 (2s, 2×H5 furyl ring).

Anal. Calcd. for $C_{15}H_9N_7O_2S$: C: 51.27, H: 2.58, N: 27.30, S: 9.12.

Found: C: 50.97, H: 2.43, N: 27.01, S: 8.97.

9-Azido-3,4-difurylpyridaizino[4′,3′:4,5]thieno[3,2-d]-1,2,4 triazine (5)

Compound **4** (0.7 g, 0.002 mol) in a mixture of acetic acid (10 ml) and hydrochloric acid (2 ml) in an ice bath was added with stirring a solution of sodium nitrate (0.15 g in 5 ml H_2O). After addition, the ice bath was removed and stirring was continued for 2 hours. The product formed was

filtered off, washed with water, and recrystallized from benzene to give **5**, (65%), m.p. 190°C (dec.). IR: 2120 cm^{-1} (N_3) and 1600 cm^{-1} (C=N).

Anal. Calcd. for $C_{15}H_6N_8O_2S$:	C: 49.72, H: 1.66, N: 30.92, S: 8.84.
Found:	C: 49.16, H: 1.55, N: 30.73, S: 8.73.

3,4-Difuryl tetrazolo[1'',5'':1',6']pyrimido[4',5':4,5]thieno [2,3-c]-pyridazine (7)

Compound **4** (0.7 g, 0.002 mol) and triethyl orthoformate (10 ml) were heated under reflux for 3 hours. After cooling, the solid product obtained was filtered off and recrystallized (acetic acid) to afford **7**, (81%), m.p. 233–235 °C. IR: 1630 cm^{-1} (C=N). Compound **7** was nsoluble in most organic solvent. MS: m/z fragment, %) 361 (M^+, 21), 360 (M^+-H, 100), 334 (M^+-HCN, 18), 333 (M^+-CO, 7).

Anal. Calcd. for $C_{16}H_7N_7O_2S$:	C: 53.18, H: 1.95, N: 27.13, S: 8.87.
Found:	C: 52.97, H: 1.93, N: 27.06, S: 8.73.

Ethyl N-(6-cyano-3,4-diphenylthieno[2,3-c]pyridazin-5-yl) methane-imidate (8)

A mixture of **2b** (3.9 g, 0.01 mol), triethyl orthoformate (1.5 g, 0.01 mol), and acetic anhydride (20 ml) was heated under reflux fur 2 hours. On cooling, the precipitated formed was filtered off, washed with petrolum ether and recrystallized (ethanol) to give **8**, (87%), m.p. 165–167 °C. IR: 2200 cm^{-1} (CN) and 1620 cm^{-1} (C=N). ^{1}HNMR ($CDCl_3$): δ 1.2–1.5 (t, 3H, CH_3), 4.1–4.4 (q, 2H, OCH_2) and 7.1–7.4 (m, 11H, 10H ArH and 1H, N=CH).

Anal. Calcd. for $C_{22}H_{16}N_4OS$:	C: 68.73, H: 4.19, N: 14.57, S: 8.33.
Found:	C: 68.56, H: 4.03, N: 14.23, S: 8.11.

7-Amino-8-imino-3,4-diphenyl pyrimido[4',5':4,5]thieno[2,3-c]-pyridazine (9)

A mixture of **8** (3.8 g, 0.01 mol) and hydrazine hydrate (0.5 ml, 0.01 mol) in ethanol (30 ml) was stirred at room temperature for 5 hours. The prod-

uct obtained was filtered off and recrystallized (dioxane) to afford **9**, (83%), m.p. 273–275 °C. IR: 3450, 3300, 3200 cm^{-1} (NH) and 1600 cm^{-1} C=N). ^{1}HNMR (DMSO-d_6): δ 5.5 (s, 2H, NH_2), 7.1–7.5 (m, 10H, ArH), 7.7 (s, 1H, NH) and 8.1 (s, H, CH pyrimidine).

Anal. Calcd. for $C_{20}H_{14}N_6S$:	C: 64.84, H: 3.80, N: 22.68, S: 8.60.
Found:	C: 64.73, H: 3.73, N: 22.33, S: 8.31.

3,4-Diphenyl-1 2,4-triazolo[1′,5'':1′,6′]pyrimido[4′,5′:4,5]thieno [2,3-c]-pyridazine (10)

Compound **9** (0.72 g, 0.002 mol) and triethyl orthoformate (5 ml) were heated under reflux for 3 hours. The solid product obtained after cooling was filtered off and recrystallized (ethanol) to give **10**, (80%), m.p. 274–276 °C. IR: 1615 cm^{-1} (C=N). ^{1}HNMR (DMSO-d_6): δ 7.2–7.6 (m, 10H, ArH), 8.4 (s, 1H, CH pyrimidine) and 9.6 (s, 1H, triazole).

Anal. Calcd. for $C_{21}H_{12}N_6S$:	C: 66.30, H: 3.17, N: 22.09, S: 8.42.
Found:	C: 65.99, H: 3.05, N: 21.88, S: 8.13.

3,4-Diphenyl-9-ethoxycarbonylmethyl-1,2,4-triazolo[1'',5′:4′,5′] pyrimido[4′,5′:4,5]thieno[2,3-c]pyridazine (11)

Compound **9** (0.72 g, 0.002 mol) and diethylmalonate (5 ml) were heated under reflux for 5 hours. The precipitate formed after cooling was filtered off, washed with petrolum ether and recrystallized (ethanol) to afford **11**, (67%), m.p. 218–220 °C. IR: 1720 cm^{-1} (C=O) and 1630 cm^{-1} (C=N). ^{1}HNMR ($CDCl_3$): δ 1.1–1.3 (t, 3H, CH_3), 3.3 (s, 2H, CH_2), 4.1–4.3 (q, 2H, OCH_2), 7.2–7.6 (m, 10H, ArH) and 9.6 (s, 1H, CH pyrimidine).

Anal. Calcd. for $C_{25}H_{18}N_6O_2S$:	C: 64.36, H: 3.88, N: 18.01, S: 6.87.
Found:	C: 64.67, H: 3.77, N: 17.83, S: 6.74.

3,4-Diphenyl-9,11-dimethyl pyridazino[3'',4'':5′,4′]thieno[2′,3′:5,4]-pyrimido[1,6-b]1,2,4-triazepine (12)

A mixture of **9** (1.1 g, 0.003 mol) and acetyl acetone (6 ml) was gently refluxed for 3 hours. After cooling the solid product obtained was filtered

off and recrystallized (ethanol) to give **12**, (72%), m.p. 253–255 °C. IR: 1610 cm^{-1} (C=N). ^{1}HNMR (CF_3CO_2D): δ 2.8 (2s, 6H, $2CH_3$), 7.2–7.6 (m, 11H, 10 ArH and 1H triazepine) and 9.7 (s, 1H, CH pyrimidine). MS: m/z (Fragment, %): 434 (M, 30), 433 (M-H, 51), 432 (M-2H, 42), 393 (M-CH_3-C≡N, 68), 392 (M-H-CH_3-C≡N, 100%), 77 (Ph^+, 19).

Anal. Calcd. for $C_{25}H_{18}N_6S$:	C: 69.10, H: 4.17, N: 19.34, S: 7.37.
Found:	C: 68.88, H: 4.02, N: 19.12, S: 7.14.

3,4,9-Triphenyl-8,9-dihydro-1,2,4-triazolo[1'',2'':1,6']pyrimido-4',5': 4,5]thieno[2,3-c]pyridazine(13)

Compound **9** (0.072 g, 0.002 mol), excess benzaldehyde (4 ml) and piperidine (0.3 ml) were mixed for 10 minutes, and absolute ethanol (20 ml) was added. Then the mixture was refluxed for 2 hours. The precipitated formed while hot was cooled, collected and recrystallized (dioxane) to afford **13**, (68%), m.p. >300 °C. IR: 3200 cm^{-1} (NH) and 1590 cm^{-1} (C=N). ^{1}HNMR (CF_3CO_2D): δ 7.2–7.8 (m, 15H, 15 ArH), 8.5 (s, 1H, CH triazoline) and 8.6 (s, 1H, CH pyrimidine).

Anal. Calcd. for $C_{27}H_{18}N_6S$:	C : 70.72, H: 3.95, N: 18.90, S: 6.93
Found:	C: 70.63, H: 3.88, N: 18.63, S: 6.88

7-Acetyl-3,4–9-triphenyl-7H-1,2,4-triazolo[1'',2'':1',6'] pyrimido-4',5':4,5]thieno[2,3-c]pyridine (15)

A mixture of **9** (0.72 g, 0.002 mol) and benzaldehyde (0.32 g, 0.003 mol) in glacial acetic acid (20 ml) was refluxed for 2 hours. The solid product obtained while hot after cooling was filtered off and recrystallized from dioxane o give **5**, yield (71%), m.p. >300°C. IR: 1690 cm^{-1} (C=O) and 590 cm^{-1} (C=N). ^{1}HNMR (CF_3CO_2D): δ 3.2 (s, 3H, CH_3), 7.2–7.5 (m, 15H, ArH), 8.6 (s, 1H, CH triazoline) and 8.7 (s, 1H, CH pyrimidine).

Anal. Calcd. for $C_{29}H_{20}N_6OS$:	C: 69.58, H: 4.07, N: 16.78, S: 6.40
Found:	C: 69.32, H: 3.88, N: 16.63, S: 6.29

5-Amino-3,4-difuryl or diphenyl-6-(4,5-dihydro-1H-imidaz-1H-yl) thieno[2,3-c]pyridazine (16a, b)

General procedure

A mixture of **2a, b** (0.01 mol), ethylene diamine (5 ml) and carbon disulfide (2 ml) was heated on water bath for one hour. After cooling, the mixture was treated with ethanol and the product obtained was filtered off and recrystallized from ethanol to afford **16a, b**.

16a: Yield (83%), m.p. >300°C. IR: 3450, 3300 cm^{-1}(NH) and 1590 cm-^{1} (C=N). ^{1}HNMR ($CDCl_3$): δ 3.4–3.6 (m, 4H, midazole ring), 5.7 (s, 2H, NH_2), 5.9 (s, 1H, NH), 6.3–6.7 (m, 4H, 2×H-3, 2×H-4 furyl ring) and 7.8, 8.0 (2s, 2H, 2×H-5 furyl ring).

Anal. Calcd. for $C_{17}H_{13}N_5O_2S$:	C: 58.11, H: 3.72, N: 19.90, S: 9.12
Found:	C: 57.93, H: 3.68, N: 19.72, S: 8.80

16b: Yield (84%), m.p. 263–265 °C. IR: 3400, 3300 cm^{-1} (NH) and 1600 cm^{-1} (C=N). ^{1}HNMR ($CDCl_3$): δ 3.3–3.6 (m, 4H, midazole ring), 5.6 (s, 2H, NH_2), 5.8 (s, 1H, NH) and 7.3–7.6 (m, 10H, ArH).

Anal. Calcd. for $C_{21}H_{17}N_5S$:	C: 67.90, H: 4.61, N: 18.85, S: 8.89.
Found:	C: 67.63, H: 4.56, N: 18.62, S: 8.62.

3,4-Diphenyl-8,9-dihydro imidazo[1'',2'':1',6']pyrimido [4',5' 4,5]-thieno[2,3-c]pyridazine (17)

Compound **16b** (0.37 g, 0.001 mol) and triethyl orthoformate (6 ml) were refluxed for 3 hours. The solid product obtained after cooling was collected and recrystallized (ethanol) to give **17**, (79%), m.p. >300 °C. IR 1630 cm^{-1} (C=N). ^{1}HNMR (DMSO-d_6): δ 3.4–3.7 (m, 4H, midazole ring), 7.3–7.6 (m, 10H, ArH) and 8.4 (s, 1H, CH pyrimidine).

Anal. Calcd. for $C_{22}H_{15}N_5S$:	C: 69.27, H: 3.96, N: 18.35, S: 8.40.
Found:	C: 69.11, H: 3.87, N: 18.15, S: 8.17.

3,4-Diphenyl-5,6,8,9-tetrahydro imidazo[1",2":1′,6′]pyrimido-4′,5′: 4,5]thieno[2,3-c] pyridazine 6-thione (18)

Compound **16b** (1 g) and carbon disulfide (5 ml) in pyridine (10 ml) were heated on a water bath for 20 hours. The product obtained after cooling was filtered off and recrystallized (acetic acid) to afford **18** (76%), m.p. >300 °C. IR 3450 cm^{-1}(NH) and 1610 cm^{-1} (C=N).

Anal. Calcd. for $C_{22}H_{15}N_5S_2$:	C: 67.90, H: 3.65, N: 16.93, S: 15.50
Found:	C: 67.78, H: 3.73, N: 16.67, S: 15.11

3,4-Diphenyl-8,9-dihydro midazo[1,2-F]pyridazino[3′,4′:5,4] thieno[2,3-d]-1,2,3-triazine (19)

To compound **16b** (0.002 mol) in a mixture of acetic acid (10 ml) and hydrochloric acid (2 ml) in an ice bath was added with stirring a solution of sodium nitrite (0.15 g in 5 ml H_2O). After addition, the ice bath was removed, and stirring was continued for 5 hours. The mixture was diluted with water and the solid product obtained was collected and recrystallized (ethanol) to give **19**, (32%), m.p. 221–223 °C. IR: 1630 cm^{-1} (C=N). ^{1}HNMR ($CDCl_3$): δ 3.1–3.3 (m, 4H, midazole ring) and 7.2–7.5 (m, 10H, ArH).

Anal. Calcd. for $C_{21}H_{14}N_6S$:	C: 65.95, H: 3.68, N: 21.97, S: 8.38.
Found:	C: 65.73, H: 3.53, N: 21.63, S: 8.6.

5-Cyanoacetylamino-3,4-diphenyl-6-(4,5-dihydro-1H-imidazo-1H-yl)-thieno[2,3-c]pyridazine (20)

A mixture of **16b** (1 g) and ethyl cyanoacetate (4 ml) was heated under reflux for one hour. Upon cooling, the product obtained was collected and recrystallized (acetic acid) to give **20**, (76%), m.p. >300 °C. IR: 3450, 3300 cm^{-1} (NH), 2200 cm^{-1} (CN) and 1660 cm^{-1} (CC=0).

Anal. Calcd. for $C_{24}H_{18}N_6OS$:	C: 65.73, H: 4.13, N: 19.16, S: 7.31.
Found:	C: 65.48, H: 4.08, N: 18.98, S: 7.46.

3,4-Diphenyl-6-cyanomethyl-8,9-dihydro[1",2":1′,6′] pyrimido-[4′,5′:4,5][thieno[2,3-c]pyridazine (21)

Compound **20** (0.5 g) and acetic anhydride (10 ml) was heated under reflux for 4 hours. The solid product obtained after cooling was filtered off and recrystallized (acetic acid) to afford **21**, (63%), m.p. >300 °C. IR: 2200 cm^{-1} (CN) and 1620 cm^{-1} (C=N). ^{1}HNMR (DMSO-d_6): δ 3.2–3.5 (m, 6H, 4H imidazole ring and 2H-CH_2CN) and 7.2–7.6 (m, 10 H, ArH).

Anal. Calcd. for $C_{24}H_{16}N_6S$:	C: 68.00, H: 3.83, N: 19.98, S: 7.62.
Found:	C: 67.78, H: 3.76, N: 19.73, S: 7.41.

3,4-Diphenyl-6-ethoxycarbonyl methylthio-8,9-dihydroimidazo-[1",2":1′,6′]pyrimido[4′,5′:4,5]thieno[2,3-c]pyridazine (22)

A mixture of **18** (2.06 g, 0.005 mol), ethyl chloroacetate (0.62 g, 0.005 mol), and anhydrous sodium acetate (1 g) in ethanol (20 ml) was refluxed for 5 hours. The product obtained after cooling was filtered off, washed with water and recrystallized (ethanol) to give **22**, (68%), m.p. 231–233°C. IR: 1720 cm^{-1} (C=O) and 1630 cm^{-1}(C=N). ^{1}HNMR ($CDCl_3$): δ 1.3–1.4 (t, 3H, CH_3), 3.3–3.6 (m, 6H, 4H imidazole ring and 2H-S-CH_2), 3.9–4.2 (q, 2H, OCH_2) and 7.1–7.5 (m, 10H, ArH).

Anal. Calcd. for $C_{26}H_{21}N_5O_2S_2$:	C: 62.25, H: 4. 23, N: 14.17, S: 12.83.
Found:	C: 62.43, H: 4.11, N: 14.08, S: 12.63.

Reaction of 22 with hydrazine hydrate, formation of the carbohydrazide derivative (23)

Compound **22** (0.4 g, 0.001 nol) and hydrazine hydrate (0.1 ml) in ethanol (10 ml) were refluxed for 4 hours. Upon cooling, the product obtained was filtered off and recrystallized (acetic acid) to afford **23**, yield 77%), m.p. 283–285°C. IR: 3300, 3100 cm^{-1} (NH) and 1640 cm^{-1} (C=O). ^{1}HNMR (CF_3CO_2D): δ 3.3–3.6 (m, 6H, midazole ring and SCH_2) and 7.2–7.5 (m, 10H, ArH).

Anal. Calcd. for $C_{24}H_{19}N_7OS_2$:	C: 59.37, H: 3.94, N: 20.19, S: 13.20.
Found:	C: 59.14, H: 3.78, N: 20.38, S: 12.96.

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