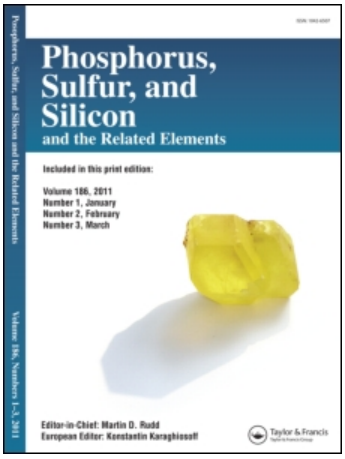

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Pyridazine Derivatives and Related Compounds Part 19:[1] The Synthesis of Different Heterocycles from Ethyl 5-Amino-3,4-diphenylthieno[2, 3-*c*]pyridazine-6-carboxylate

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Pyridazine Derivatives and Related Compounds Part 19:[1] The Synthesis of Different Heterocycles from Ethyl 5-Amino-3,4-diphenylthieno[2,3-*c*]pyridazine-6-carboxylate

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*7-substituted pyrido[2′,3′:4,5]thieno[2,3-c]pyridazines and 6-substituted pyrimido-[4′,5′:4,5]thieno[2,3-c]pyridazines were synthesized starting from ethyl 5-aminothieno[2,3-c]pyridazino-6-carboxylate **1**. The reaction of amino ester **1** with benzoyl isothiocyanate affords thiourea derivative **8**, which undergoes further transformation to the related fused heterocyclic systems.*

Keywords Pyridazinotienothiazine; pyrimdothenopyridazine; substituted pyridothienopyridazine

As a part of our research program[2] aimed at the preparation of novel thiophene-fused heterocycles of therapeutical significance, we report on the synthesis of two heteropolycyclic compounds, namely pyrido[2′,3′:4,5]thieno[2,3-*c*]pyridazine and pyrimido[4′,5′:4,5]thieno-[2,3-*c*]pyridazine.

Thiophene derivatives, which are both commercially available drugs and agents under clinical investigation, were the subject of a comprehensive review.[3] Many compounds containing the pyridothieno and pyridazinothieno ring systems are known to have interesting pharma-cological properties.[4,5] All these properties aroused our interest in synthesing new heterocyclic compounds including the thieno[2,3-*c*]pyridazine moiety.

The readily prepared ethyl 5-amino-3,4-diphenylthieno[2,3-*c*]pyridazine-6-carboxylate **1**[6] was used as the starting material because it has suitable substituents for building on a third heterocyclic ring.

The base-catalyzed cyclization of amides derived from anthranilic esters and β-keto esters or diethyl malonate is an established route

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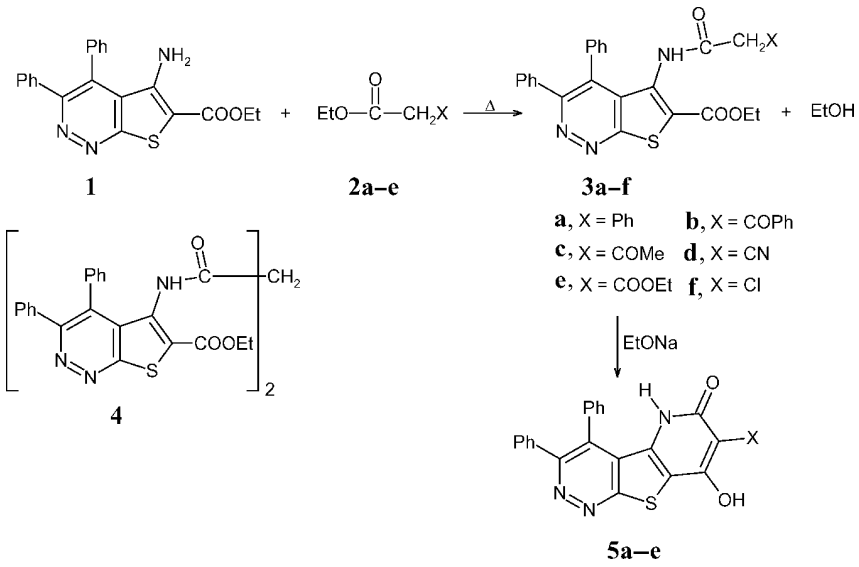
to substituted 4-hydroxy-2-quinolones.[7,8] We now wish to report the application of this approach to the synthesis of 7-substituted-8-hydroxy-pyrido[2′,3′:4,5]-thieno[2,3-*c*]pyridazines **5a–e**. The intermediate amides **3a–e** were obtained by boiling together under reflux ethyl 5-amino-3,4-diphenylthieno[2,3-*c*]pyridazine-6-carboxylate **1** and the appropriate substituted acetic ester **2a–e** (Scheme 1). In all cases, the condensation took the indicated course, and there was no evidence for the formation of the enamine rather than the amide in the reaction giving **3b** and **3c**. In one reaction (that lead to **3e**), a byproduct was isolated and was identified as the bis-amide **4**.



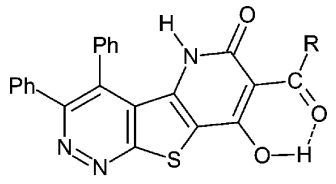
SCHEME 1

The chloroacetylation of the amino-ester **1** with chloroacetylchloride in dioxane afforded **3f**. The assignment of structure of **3a–f** was based on analytical and spectral data. The feasibility of chlorine atom in 5-chloroacetylamino derivative **3f** to undergo nucleophilic displacement was proved by the reaction with potassium cyanide, which gave 5-cyanoacetylamino derivative **3d**. The structure was assigned by comparison with an authentic sample prepared from the reaction of compound **1** and ethyl cyanoacetate.

The cyclization of the amide **3a–e** to the pyrido[2′,3′:4,5]thieno[2,3-*c*]pyridazines **5a–e** was affected by treatment with sodium ethoxide in ethanol (Scheme 1).

A point of considerable interest in the study of quinolines bearing oxygenated substituents in the pyridine ring concerns keto-enol

tautomerism. Of the various possibilities available in 2,4-dioxygenated quinoxalines, the 4-hydroxy-2-quinolone from is preferred in the solid state, with strong OH···O=C intermolecular hydrogen bonding.[9] The same is apparently true of the various 6,8-dioxygenerated pyrido-[2′,3′:4,5]thieno[2,3-*c*]pyridazines prepared in the present work. The infrared spectra of compounds **5b–e** showed strong rather broad bands in the region 1650–1660 cm^{-1}, which is typical of the 2- rather than the 4-quinolone type. Further, in several of these structures, there is the strong possibility that intramolecular hydrogen bonding would occur, reinforcing the normal preference for the 2-quinolone form.



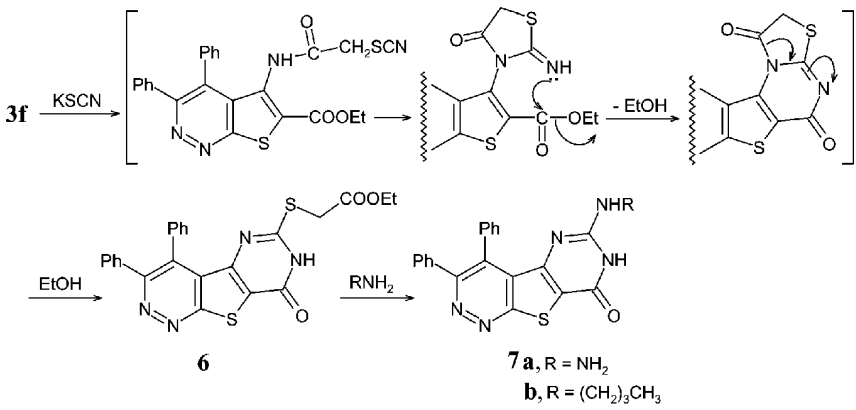
5c

SCHEME 2

In all the 6,8-dioxypyrido[2′,3′:4,5]thieno[2,3-*c*]pyridazines **5a–e**, there is a very broad band in the region 3200–3000 cm^{-1} and a comparatively weak absorption in the region 3290–3230 cm^{-1}, which we ascribe to H-bonded OH stretching (inter- or intramolecular, as appropriate) and to N-H stretching, respectively. The structures of these compounds were assigned by elemental analyses as well as IR, mass, and NMR spectral data.

Ethyl 5-chloroacetylamino-3,4-diphenylthieno[2,3-*c*]pyridazine-6-carbox-ylate **3f** also proved to be a versatile synthon for the preparation of other new thienopyridazines. Thus, on heating a suspension of **3f** and potassium thiocyanate in ethanol furnished compound **6** (Scheme 3). The indicated intermediates cannot be isolated but can be rationalized as follows: the 5-thiocyanoacetylamino is directly converted to the 5-(imino-4-oxothiazol-3-yl), which underwent smooth cyclization to the corresponding fused thiazolone and finally to (8-oxo-3,4-diphenyl-7,8-dihydropyrimido[4′,5′:4,5]thieno[2,3-*c*]pyridazin-6-ylsulfanyl)acetic acid ethyl ester **6** (Scheme 3).

The structural elucidation of compound **6** was accomplished from their analytical and spectral data. The mass spectra showed the expected molecular ion peak, and the IR spectra exhibited a strong absorption band at 3448 (NH), 1731 (C=O ester), and 1670 cm^{-1} (C=O amide), while the ^{1}H-NMR showed signals at 9.85 due to NH,



SCHEME 3

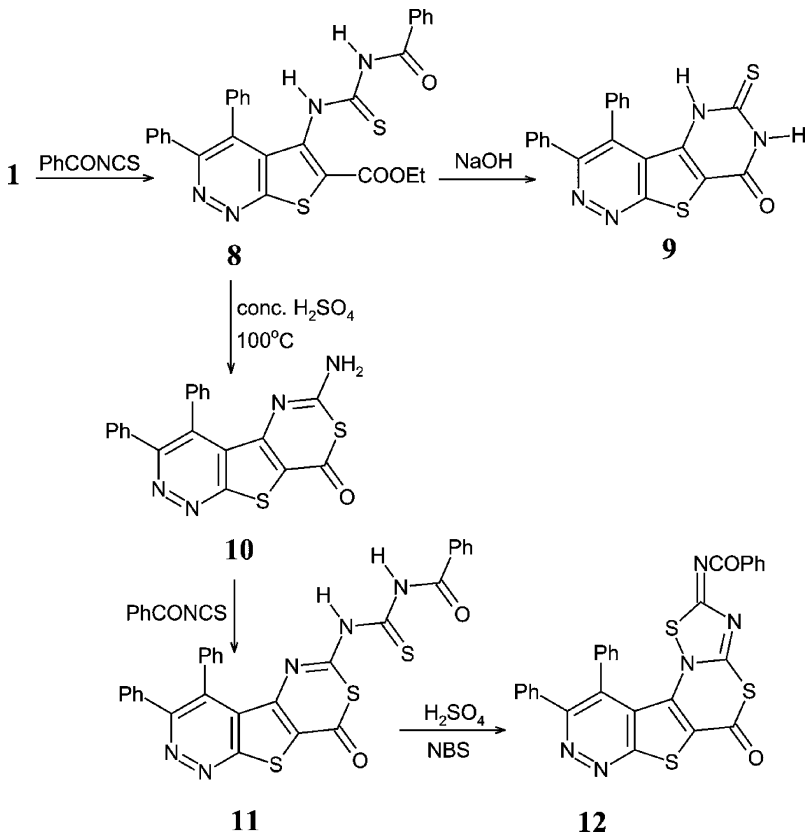
7.31–6.90 due to 2Ph, 4.64 due to SCH_2, 4.25 due to OCH_2, and 1.31 due to CH_3.

The aminolysis of compound **6** with hydrazine and with n-butylamine gave the corresponding 6-substituted derivatives **7a,b** under the elimination of the thioacetic acid moiety (Scheme 3). The data used to characterize all the compounds prepared are given in the Experimental section.

On the other hand, the reaction of benzoyl isothiocyanate with the amino-ester **1** in boiling acetone led to the formation of the benzoyl thiourea derivative **8** in a 70% yield. In an alkaline medium, compound **8** underwent a ring closure followed by debenzoylation to form 1,2-dihydro-8,9-diphenyl-2-thioxopyrimido[4′,5′:4,5]thieno[2,3-*c*]pyridazin-4(3H)-one **9**. The structure was established by microanalyses and spectral data.

The cyclic amide structure of compound **9** furthermore was defined using as a comparison its cyclic thioester isomer **10** obtained by ring closure in 98% sulfuric acid at 100°C. The two isomeric derivatives **9** and **10** are well differentiated according to the alkaline solubility and their infrared spectra. Compound **10** was proven to be 2-amino-8,9-diphenylpyridazino[4′,3′:5,4]thieno[3,2-*d*]-1,3-thiazin-4-one from its microanalyses and spectroscopic data. It should be noted that no sulfonated byproducts were observed even when benzoylthiourea derivative **8** was heated in sulfuric acid to prepare **10**.

The 2-amino derivative **10** could be converted with benzoylisothiocyanate to afford the corresponding heterocyclic substituted benzoylisothiocyanate **11**.



SCHEME 4

On treatment of **11** with concentrated sulfuric acid at r.t., compound **12** was obtained and established to be a derivative of the new hetero system 1,2,4-thiadiazole condensed system **12** (Scheme 4). The structural elucidation of compounds **11** and **12** were accomplished on the basis of microanalyses and spectral data. From the structural assignment of the product, it became clear that sulfuric acid has acted as an oxidizing agent. The yield of **12** could be improved by adding an equimolar amount of N-bromosuccinimide[10] to the reaction mixture. The oxidative cyclization to afford fused 1,2,4-thiadiazoles from substituted thioureas (e.g. from pyridyl- or pyrimidylthioureas with bromine or sulfuryl chloride)[11] is well known.

EXPERIMENTAL

Melting points were determined on a Büchi 510 apparatus and are reported uncorrected. IR spectra were recorded as potassium bromide

disks on a Perkin-Elmer 383 spectrophotometer. ^{1}H-NMR spectra were observed on a Perkin-Elmer R12 B-200 MHz, and chemical shifts (δ) are in ppm relative to internal TMS. Mass spectra were obtained at 70 eV by using a AE MS 30 mass spectrometer. All reactions were monitored by thin layer chromatography and carried out on 0.2 mm silica gel 60 F-254 (Merck) plates using U.V. light (254 and 366 nm).

Ethyl 5-Phenylacetylamino-3,4-diphenylthieno[2,3-*c*]-pyridazine-6-carboxylate 3a

A mixture of compound **1** (0.5 g, 1.33 mmol) and ethyl phenylacetate (5 mL) was boiled under an air condenser for 3 h; after cooling, the precipitate was collected by filtration, washed with ether, dried, and recrystallized from n-butanol, (0.43 g, 65.7%), m.p. 187–188°C; IR: 3313 (NH), 1732 (C=O ester), and 1669 (C=O amide) cm^{-1}. ^{1}H-NMR (DMSO-d_6): 8.10 (s, 1H, NH), 7.40–7.20 (m, 15H, 3Ph), 4.20 (q, 2H, $J = 7.0$ Hz, CH_2), 2.60 (s, 2H, CH_2) and 1.20 (t, 3H, $J = 7.0$ Hz CH_3). Anal. calcd. for $C_{29}H_{23}N_3O_3S$: C, 70.56; H, 4.69; N, 8.51. Found: C, 70.40; H, 4.50; N, 8.40.

Ethyl 5-Benzoylacetylamino-3,4-diphenylthieno[2,3-*c*]-pyridazine-6-carboxylate 3b

To a solution of compound **1** (0.5 g, 1.33 mmol) in 1,2-dichlorobenzene (10 ml), ethyl benzoyl acetate (0.25 g, 1.33 mmol) was added. The reaction mixture was refluxed for 6 h; the cooled reaction mixture was poured into pet. ether 40/60°C (50 mL). The precipitate was filtered off, dried, and recrystallized from ethanol, (0.49 g, 71.9%), m.p. 132–133°C. IR: 3329 (NH), 1722 (C=O, ketone), 1700 (C=O, ester), 1680 (C=O amide) cm^{-1}. ^{1}H-NMR (DMSO-d_6): 10.20 (s, 1H, NH), 7.40–7.00 (m, 15H, 3Ph), 4.30 (q, 2H, $J = 7.2$ Hz, CH_2), 2.20 (s, 2H, CH_2) and 1.20 (t, 3H, $J = 7.2$ Hz, CH_3). Anal. calcd. for $C_{30}H_{23}N_3O_3S$: C, 69.08; H, 4.44; N, 8.05. Found: C, 68.90; H, 4.30, N, 7.80.

Ethyl 5-Acetoacetylamino-3,4-diphenylthieno[2,3-*c*]-pyridazine-6-carboxylate 3c

A mixture of compound **1** (0.5 g, 1.33 mmol) and ethyl acetoacetate (10 mL) was boiled under an air condenser for 2 h. After cooling, the precipitate was collected by filtration, washed with ether, and recrystallized from ethanol, (0.42 g, 69.4%), m.p. 185–186°C. IR : 3260 (NH), 1750 (C=O, ketone), 1710 (C=O, ester), 1680 (C=O, amide) cm^{-1}. Anal.

calcd. for $C_{25}H_{21}N_3O_4S$: C, 65.34; H, 4.60; N, 9.14. Found: C, 65.10; H, 4.50; N, 9.00.

Ethyl 5-Cyanoacetylamino-3,4-diphenylthieno[2,3-*c*]-pyridazine-6-carboxylate 3d

To a solution of compound **1** (0.5 g, 1.33 mmol) in 1,2-dichlorobenzene (10 mL), ethyl cyanoacetate (0.1 g, 1.33 mmol) was added. The reaction mixture was refluxed for 4 h; the cooled reaction mixture was poured into pet. ether 40/60°C (50 mL). The precipitate was filleted off, dried, and recrystallized from ethanol, (0.4 g, 67.8%), m.p. 100–101°C. IR: 3448 (NH), 2100 (CN), 1731 (C=O, ester), 1670 (C=O, amide) cm^{-1}. Anal. Calcd. for $C_{24}H_{18}N_4O_3S$: C, 65.14; H, 4.10; N, 12.66. Found: C, 65.00; H, 3.90; N, 12.50.

Reaction of Ethyl 5-Amino-3,4-diphenylthieno[2,3-*c*]-pyridazine-6-carboxylate 1 With Diethyl Malonate

A mixture of compound **1** (1.0 g, 2.66 mmol) and diethyl malonate (10 mL) was boiled together under an air condenser for 2 h. The excess of the malonic ester was removed under reduced pressure to give material (0.8 g) that was shown by thin layer chromatography to consist of two components. The mixture was applied to a column of silica gel (40 g), and the column was eluted with 4:1 petroleum ether/ether. The first fraction eluted was ethyl 5-ethoxycarbonylacetylamino-3,4-diphenylthieno[2,3-*c*]pyridazine-6-carboxylate **3e** (0.5 g, 38%), m.p. 184–185°C. IR: 3450 (NH), 1732 (C=O, ester), 1669 (C=O, amide), 1595 (C=C) cm^{-1}. Anal. calcd. for $C_{26}H_{23}N_3O_5S$: C, 63.78; H, 4.73; N, 8.58. Found: C, 63.60; H, 4.60; N, 8.30.

The second fraction to be eluted from the column was N,N′-bis-(6-ethoxycarbonyl-3,4-diphenylthieno[2,3-*c*]pyridazine-5-yl)propan-1,3-diamide **4** (0.3 g, 13.8%), m.p. 109–111°C (from light petroleum, b.p. 100–120°C), IR: 3370 (NH), 1710 (C=O, ester), 1670 (C=O, amide), 1570 (C=C) cm^{-1}. Anal. calcd. for $C_{45}H_{34}N_6O_6S_2$: C, 65.99; H, 4.18; N, 10.26. Found: C, 65.80; H, 4.00; N, 10.00.

Ethyl 5-Chloroacetylamino-3,4-diphenylthieno[2,3-*c*]-pyridazine-6-carboxylate 3f

To s solution of compound **1** (0.5 g, 1.33 mmol) in dioxane (5 mL) chloroacetylchloride (0.17 g, 1.59 mmol) was added; the reaction mixture was refluxed for 8 h. The cooled reaction mixture was poured into ice water (100 mL), and the precipitate was filtered off, dried, and recrystallized from ethanol (0.42 g, 70.1%) of **3f**, m.p. 130–131°C. IR:

3380 (NH), 1733 (C=O ester), 1655 (C=O amide), 1618 (C=C) cm^{-1}; ^{1}H-NMR ($CDCl_3$): 7.60–7.20 (m, 10H, 2Ph), 6.10 (s, 1H, NH), 4.30 (q, 2H, $J = 7.0$ Hz, CH_2), 2.10 (s, 2H, CH_2), 1.20 (t, 3H, $J = 7.0$ Hz, CH_3). Anal. calcd. for $C_{23}H_{18}ClN_3O_3S$: C, 61.12; H, 4.01; N, 9.29. Found: C, 60.90; H, 3.90; N, 9.00.

The Reaction of 3f With Potassium Cyanide

To a solution of compound **3f** (0.5 g, 1.1 mmol) in ethanol (10 mL) potassium cyanide (0.07 g, 1.1 mmol) was added; the reaction mixture was refluxed for 2 h, the solvent was then evaporated under reduced pressure, and the residue was treated with water. The precipitate was filtered off, dried, and recrystallized from ethanol (0.3 g, 62.5%), m.p. 100–101°C; it was identical with compound **3d**.

7-Substituted 8-hydroxy-3,4-diphenyl[2′,3′:4,5]thieno[2,3-*c*]-pyridazin-6(5H)-one 5a–e: General Procedure

Amides **3a–e** (1.0 mmol) were boiled under reflux for 1–10 h (until all starting material had disappeared as checked by tlc) with a solution of sodium ethoxide (from 0.1 g sodium) in ethanol (10 mL). The mixture was evaporated to dryness under reduced pressure; water (30 mL) was added to the residue, and the solution was washed with dichloromethane (washings discarded) and then partially saturated with salt. The solution was cooled in ice and acidified with concentrated hydrochloric acid (2 N). The solid formed was filtered off and recystallized from ethanol. The following derivatives (**5a–e**) were obtained.

8-Hydroxy-3,4,7-triphenylpyrido[2′,3′:4,5]thieno[2,3-*c*]-pyridazin-6(5H)-one 5a

Yield : (45.7%); m.p. 230–231°C. IR: 3260 (NH), 3200–3100 (H-bonded OH), 1660 (C=O), 1590 (C=C) cm^{-1}; ^{1}H-NMR (DMSO-d_6): 10.20 (s, 1H, NH), 7.40–7.00 (m, 15H, 3Ph), 2.20 (s, 1H, OH). Anal. calcd. for $C_{27}H_{17}N_3O_2S$: C, 72.46; H, 3.82; N, 9.39. Found: C, 72.30; H, 3.70; N, 9.20.

7-Benzoyl-8-hydroxy-3,4-diphenylpyrido[2′,3′:4,5]thieno[2,3-*c*]-pyridazin-6(5H)-one 5b

Yield: (69.9%); m.p. 185–186°C. IR: 3260 (NH), 3210–3000 (H-bonded OH), 1720 (C=O ketone), 1658 (C=O amide) cm^{-1}. Anal. calcd. for $C_{28}H_{17}N_3O_3S$: C, 70.72; H, 3.60; N, 8.83. Found: C, 70.60; H, 3.40; N, 8.60.

7-Acetyl-8-hydroxy-3,4-diphenylpyrido[2′,3′:4,5]thieno[2,3-*c*]-pyridazin-6(5H)-one 5c

Yield: (54%); m.p. 198–199°C. IR: 3260 (NH), 3200–3100 (H-bonded OH), 1726 (C=O ketone), 1640 (C=O amide) cm^{-1}; MS: *m/z* (%): 414 (M^+ +1, 8.8), 385 (M^+ −CO, 1.8, ion A), 301 (ion A−OH, C=C-COMe, 2.5). Anal. calcd. for $C_{23}H_{15}N_3O_3S$: C, 66.81; H, 3.65; N, 10.16. Found: C, 66.70; H, 3.40; N, 9.90.

7-Cyano-8-hydroxy-3,4-diphenylpyrido[2′,3′:4,5]thieno[2,3-*c*]-pyriazin-6(5H)-one 5d

Yield: (66.9%), m.p. 199–200°C. IR: 3260 (NH), 3200–3100 (H-bonded OH), 2360 (CN), 1660 (C=O) cm^{-1}; MS: *m/z* (%): 396 (M^+, 4.2), 369 (M^+−CO, 9.6, ion A), 301 (ion A−NC-C=C−OH, 71.5). Anal. calcd. for $C_{22}H_{12}N_4O_2S$: C, 66.65; H, 3.05; N, 14.13. Found: C, 66.30; H, 2.90; N, 14.00.

7-Ethoxycarbonyl-8-hydroxy-3,4-diphenylpyrido[2′,3′:4,5]-thieno[2,3-*c*]pyridazin-6(5H)-one 5e

Yield: (88.3%), m.p. 148–149°C. IR: 3260 (NH), 3200–3100 (H-bonded OH), 1734 (C=O ester), 1660 (broad C=O amide) cm^{-1}; MS: *m/z* (%): 443 (M^+, 54), 301 (M^+−NHCOC(COOEt)=C−OH, 100). Anal. calcd. for $C_{24}H_{17}N_3O_4S$: C, 64.99; H, 3.86; N, 9.47. Found: C, 64.70; H, 3.70; N, 9.30.

6-Carbethoxymethylmercapto-3,4-diphenylpyrimido[4′,5′:4,5]-thieno[2,3-*c*]pyridazin-8(7H)-one 6

A suspension of **3f** (0.5 g, 1.1 mmol) and potassium thiocyanate (0.32 g, 3.3 mmol) in abs. ethanol (20 mL) was heated to reflux for 6 h. The reaction mixture was concentrated to its half volume; after cooling, the precipitate was separated and washed with water several times, dried, and recrystallized from abs. ethanol to give **6** (0.41 g, 78.4%), m.p. 160–161°C. IR: 3248 (NH), 1731 (C=O ester) 1660 (C=O amide), 1630 (C=N), 1610 (C=C) cm^{-1}; ^{1}H-NMR (DMSO-d_6): 9.85 (s, 1H, NH), 7.31–6.91 (m, 10H, 2Ph), 4.64 (s, 2H, SCH_2), 4.25 (q, 2H, $J = 7.1$ Hz, OCH_2), 1.31 (t, 3H, $J = 7.1$ Hz, CH_3). Anal. calcd. for $C_{24}H_{18}N_4O_3S_2$: C, 60.74; H, 3.82; N, 11.80. Found: C, 60.60; H; 3.60; N, 11.60.

6-Hydrazino-3,4-diphenylpyrimido[4′,5′:4,5]thieno[2,3-*c*]-pyridazin-8(7H)-one 7a

To a solution of compound **6** (0.5 g, 1.05 mmol) in ethanol (10 mL), hydrazine hydrate 85% (0.1 g, 1.99 mmol) was added; the reaction

mixture was refluxed for 4 h, the solvent was evaporated under reduced pressure, and the residue was treated with water. The precipitate was filtered off, dried, and recrystallized from ethanol to give **7a** (0.3 g, 63.8%), m.p. 110–111°C. IR: 3409, 3220 (NH, NH_2), 1625 (C=O), 1610 (C=N), 1596 (C=C) cm^{-1}. MS: *m/z* (%): 386 (M^+, 2.37). Anal. calcd. for $C_{20}H_{14}N_6OS$: C, 62.16; H, 3.65; N, 21.74. Found: C, 62.00; H, 3.50; N, 21.50.

6-Butylamino-3,4-diphenylpyrimido[4′,5′:4,5]thieno[2,3-*c*]-pyridazin-8(7H)-one 7b

To a solution of compound **6** (0.5 g, 1.05 mmol) in ethanol (10 mL), n-butylamine (0.1 g, 1.38 mmol) was added; the reaction mixture was refluxed for 6 h, the solvent was evaporated under reduced pressure, and the residue was treated with water. The precipitate was filtered off, dried, and recrystallized from ethanol to give **7b** (0.19 g, 44.4%), m.p. 180–181°C. IR: 3312 (NH), 1639 (C=O), 1620 (C=N), 1600 (C=C) cm^{-1}. Anal. calcd. for $C_{24}H_{21}N_5OS$: C, 67.42; H, 4.95; N, 16.38. Found: C, 67.20; H, 4.80; N, 16.10.

N-(6-Ethoxycarbonyl-3,4-diphenylthieno[2,3-*c*]pyridazin-5-Yl)-N′-benzoylthiourea 8

To a stirred solution of in situ prepared benzoyl isothiocyanate (0.2 g, 1.28 mmol) in dry acetone (10 mL), a solution of compound **1** (0.5 g, 1.33 mmol) in dry acetone (10 mL) was slowly added dropwise, and the mixture was gently refluxed for 30 min. The mixture was cooled, and the solid was collected, dried, and recrystallized from benzene to give **8** (0.4 g, 69.7%), m.p. 120–121°C. IR: 3449, 3310 (NH), 1731 (C=O ester), 1661 (C=O amide), 1162 (C=S) cm^{-1}; ^{1}H-NMR (DMSO-d_6): 8.10 (s, 1H, NH), 7.90 (s, 1H, NH), 7.40–7.10 (m, 15H, 3Ph), 4.20 (q, 2H, $J = 7.3$ Hz, CH_2, 1.20 (t, 3H, $J = 7.3$ Hz, CH_3). Anal. calcd. for $C_{29}H_{22}N_4O_3S_2$: C, 64.66; H, 4.11; N, 10.40. Found: C, 64.40; H, 4.00; N, 10.20.

1,2-Dihydro-8,9-diphenyl-2-thioxopyrimido[4′,5′:4,5]thieno-[2,3-*c*]pyridazin-4(3H)-one 9

A solution of compound **8** (0.5 g, 0.92 mmol) in 2 N methanolic sodium hydroxide (10 mL) was refluxed for 8 h and then filtered. The clear solution acidified (pH = 5–6) with 10% hydrochloric acid gave the compound **9**, recrystallized from ethanol (0.17 g, 58%), m.p. 165–166°C. IR: 3176 (NH), 1676 (C=O), 1194 (C=S) cm^{-1}; ^{1}H-NMR (DMSO-d_6): 10.24 (s, 1H, NH), 7.40–7.20 (m, 10H, 2Ph), 6.98 (s, 1H, NH). Anal. calcd. for

$C_{20}H_{12}N_4OS_2$: C, 61.83; H, 3.11; N, 14.42. Found: C, 61.70; H, 3.00; N, 14.20.

2-Amino-8,9-diphenylpyridazino[4′,3′:5,4]thieno[3,2-*d*]-1,3-thiazin-4-one 10

A suspension of compound **8** (0.5 g, 0.92 mmol) in 98% sulphuric acid (5 mL) and 3 drops of water was heated at 100°C for 6 h; the resultant clear solution was slowly added to ice water (30 mL), and the solid product was collected, washed with sodium bicarbonate solution (5%) and cold water, dried, and recrystallized from ethanol to give **10** (0.2 g, 67%), m.p. 160–161°C. IR: 3346, 3162 (NH_2), 1672 (C=O), 1612 (C=N) cm^{-1}; ^{1}H-NMR (DMSO-d_6): 7.80–7.10 (m, 10H, 2Ph), 8.06 (s, 2H, NH_2). Anal. calcd. for $C_{20}H_{12}N_4OS_2$: C, 61.83; H, 3.11; N, 14.42. Found: C, 61.60; H, 2.90; N, 14.10.

2-(3-Benzoylthioureido)-8,9-diphenylpyridazino[4′,3′:5,4]-thieno[3,2-*d*]-1,3-thiazin-4-one 11

Compound **10** (0.5 g, 1.28 mmol) was dissolved in dry acetone (10 mL). A solution of benzoyl isothiocyanate in acetone (1.3 mmol in 20 mL) was added. The mixture was refluxed for 3 h and kept at r.t. over night. The precipitate was collected by filtration, washed with n-hexane, dried and recrystallized from ethanol (0.4 g, 57.1%) of **11**, m.p. 264–165°C. IR: 3344, 3162 (NH), 1735 (C=O, cyclic), 1666 (C=O amide), 1154 (C=S) cm^{-1}; ^{1}H-NMR (DMSO-d_6): 8.05 (s, 1H, NH), 7.80 (s, 1H, NH), 7.40–7.20 (m, 15H, 3Ph). Anal. calcd. for $C_{28}H_{17}N_5O_2S_3$: C, 90.95; H, 3.10; N, 12.69. Found: C, 90.70; H, 2.90; N, 12.50.

2-Benzoylimino-9,10-diphenyl-2H,5H-pyridazino [4″,3″: 4′,5′] thieno[2′,3′:5,4]-1,2,4-thiadiazolo[3,2-*b*]-1,3-thiazin-5-one 12

A mixture of compound **11** (0.5 g, 0.9 mmol), N-bromosuccinimide (0.13 g, 0.9 mmol), and concentrated sulfuric acid (5 mL) was kept at r.t. for 7 days. The mixture was poured into ice water (50 mL). The precipitate was collected by filtration, washed with a solution of sodium bicarbonate (5%), and dried; the crude product was recrystallized from ethanol to give **12** (0.24 g, 50%), m.p. 220–221°C. IR: 1722 (C=O cyclic), 1673 (C=O amide), 1631 (C=N), 1610 (C=C) cm^{-1}; ^{1}H-NMR (DMSO-d_6): 8.07–7.10 (m, 15H, 3Ph). Anal. calcd. for $C_{28}H_{15}N_5O_2S_3$: C, 61.18; H, 2.75; N, 12.74. Found: C, 61.00; H, 2.50; N, 12.60.

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