

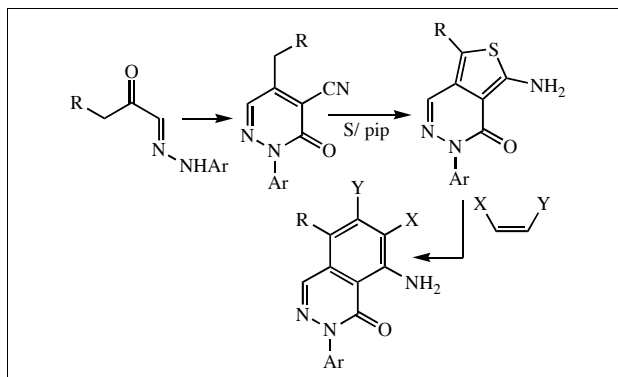
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The phenylhydrazones **1a-d** condensed with ethyl cyanoacetate to yield pyridazinones **2a-d** that reacted with sulphur in presence of piperidine to yield the aminothienopyridazineones **3a,b** that reacted with electron poor olefins and acetylenes to yield phthalazines **10-12**. The condensed aminothiophenes **3a,b** reacted with dimethylformamide dimethylacetal to yield amidines **13a,b**. Compounds **2a,b** condensed with dimethylformamide dimethylacetal to yield the *trans* enamines **16a,b** that cyclized readily into the pyridopyridazinones **17a,b** on treatment with ammonium acetate in presence of acetic acid. Compounds **2a-d** reacted also with benzylidenemalononitrile to yield the phthalazinones **21a-d**. The reactions were conducted both by microwave heating and conventional heating. Better yields in much shorter reaction times were achieved by microwave heating.

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In conjunction to previous recent interest in adopting microwaves as energy source for synthesis of polyfunctional heteroaromatics [1-5], we report here efficient synthesis of title compounds utilizing **1a-d** as starting materials and microwaves as energy source. The title compounds are biologically interesting molecules and their chemistry and pharmacology is receiving considerable recent interest [6-8]. Moreover utilizing microwaves as environmentally eco-friendly energy sources is being also now explored [9-12].

The starting **1a-d** condensed with ethyl cyanoacetate on heating in focused microwave at 170 °C for 4 minutes in presence of ammonium acetate to yield pyridazinones **2a-d** in 52 to 62% yields. The same compounds could also be obtained on heating **1a-d** with ethyl cyanoacetate in acetic acid and in presence of ammonium acetate for ten hours, in 50 to 55% yields.

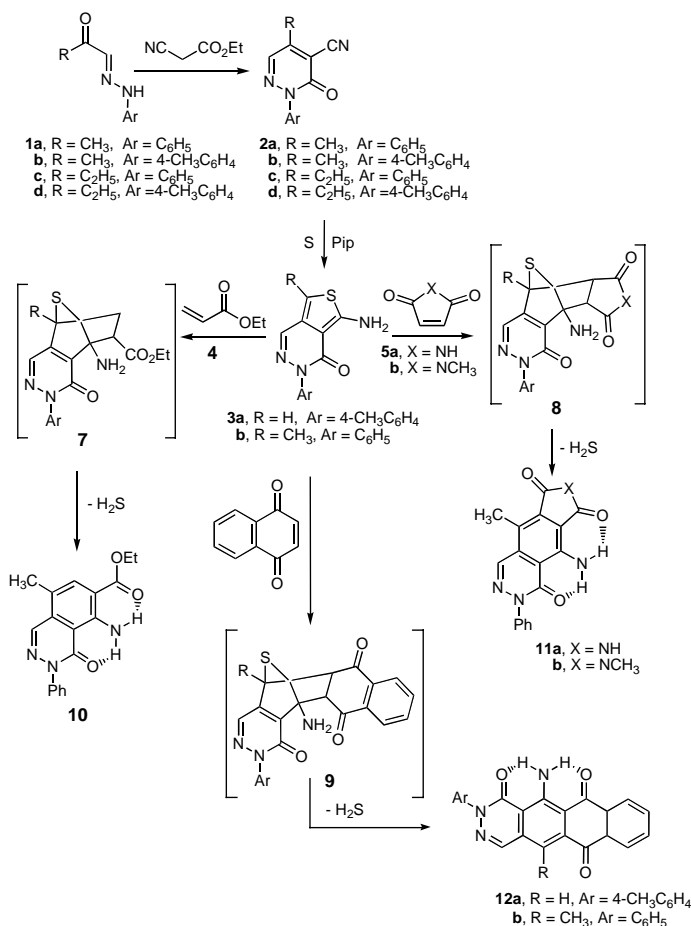
The pyridazinones **2a-d** readily reacted with sulphur in presence of piperidine on heating in a focused microwave oven for 5 minutes in dioxane as reaction medium to yield aminothienopyridazines **3a,b** in 74 and 76% yields. Again thienopyridazines **3a,b** were obtained in 69 and 72%

yields on refluxing **3a,b** with sulphur in DMF solution in presence of piperidine for 4 hours. The synthesis of **2** and **3** is an extension to our previously well-established synthesis 3-carboxylic ester derivatives of **2** and **3** [13-15].

Compound **3b** reacted readily with ethyl acrylate **4**, maleimide **5a** and *N*-methylmaleimide **5b** in a mixture of acetic acid and dioxane in focused microwave at 210 °C for 15 minutes and compounds **3a,b** reacted with naphthoquinone **6** in ethanol at 100 °C for 15 minutes in focused microwave to yield products of addition and hydrogen sulphide elimination. These products were also obtained on refluxing **3a,b** with **4-6** in the same solvents for 8 hours.

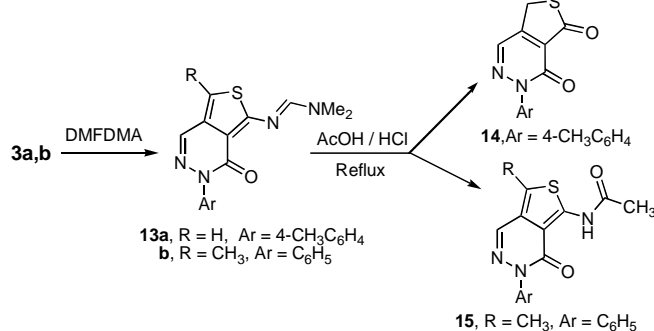
The condensation products of **3** with **4-6** were assumed to be formed *via* intermediary of 4+2 cycloadducts **7-9** which readily loses hydrogen sulphide to yield products **10-12** respectively. In no case C-1 alkylation products of thiepinines similar to those claimed earlier to be formed on reacting thienocoumarin with dimethyl acetylenedicarboxylate and ethyl propiolate were formed [16-20] (Scheme 1).

Scheme 1



Reaction of compounds **3a,b** with dimethylformamide dimethylacetal (DMFDMA) in focused microwave at 200 °C for 15 minutes in the presence of a few drops of dimethylformamide afforded condensation products **13a,b**; no trace of C-1 alkylation products were observed. Compounds **3a** upon reflux in AcOH/c.HCl mixture (3:1 by volume), afforded derivative **14** whose structure based on the ¹H NMR and ¹³C NMR spectra, that reveal the presence of methylene proton at $\delta_{\text{H}} = ca$ 4.41 and $\delta_{\text{C}} = ca$ 32.7 ppm respectively, while compound **3b** when treated

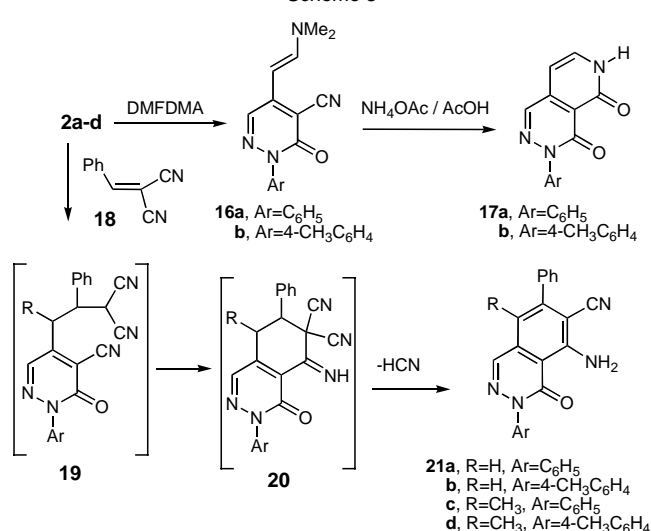
Scheme 2



with the same reagent and under the same reaction condition, formed compound **15** (Scheme 2).

Compounds **2a,b** reacted with dimethylformamide dimethylacetal on heating in focused microwave oven at 180 °C for 5 minutes or on reflux in DMF for 6 hours. The condensation products were assigned the *trans* structure **16a,b** based on the ¹H NMR which showed olefinic doublets at $\sim \delta_{\text{H}}$ 5.1 and 8.3 ($J = 12.8$ Hz). Cis-olefinic protons should show lower J values (8-10 Hz). Compounds **16a,b** were readily converted into the pyrido[3,4-*d*]pyridazine-4,5-diones **17a,b** on treatment with ammonium acetate and acetic acid in focused microwave oven at 150 °C for 5 minutes or on reflux in the same mixture for 3 hours. Compounds **2a-d** reacted with benzylidenemalononitrile **18** in pyridine in focused microwave oven at 175 °C for 5 minutes to yield **21a-d** or on reflux in pyridine for 5 hours. This is a further extension to our established phthalazine synthesis [21,22], which is believed to proceed *via* intermediary of **19** and **20** (Scheme 3).

Scheme 3



In conclusion microwaves heating is an efficient method for obtaining polyfunctionally substituted title compounds in equal or much higher yields than those obtained by conventional heating in much shorter time.

EXPERIMENTAL

All melting points are uncorrected. IR spectra were recorded in KBr disks using a Perkin-Elmer System 2000 FT-IR spectrophotometer. ¹H and ¹³C-NMR spectra were recorded on a Bruker DPX 400, 400MHz super-conducting NMR spectrometer in deuteriochloroform or dimethylsulfoxide-*d*₆ as solvent and TMS as internal standard; chemical shifts are reported in δ units (ppm). Mass spectra were measured on a VG Autospec-Q (high resolution, high performance, tri-sector GC/MS/MS).

Microanalyses were performed on a LECO CHNS-932 Elemental Analyzer. Focused microwave experiments were conducted in a CEM Explorer microwave. Compounds **1a** was prepared following published procedure [23].

General Procedure for the Preparation of Compounds **1a-d**.

The mixture of (3.5 g) of potassium hydroxide in (100 ml) of water, (6.5 g) of ethyl acetoacetate was allowed to stir at room temperature for 24 hours. The solution of potassium acetate was cooled to 0 °C and (4.5 ml) of concentrated hydrochloric acid in (15 ml) of ice-water was added slowly with stirring, then gradually treated under stirring with a solution of aryldiazonium chloride (prepared from the corresponding aromatic amine (0.01 mol) and the appropriate quantities of both hydrochloric acid and sodium nitrite. The mixture is made basic by addition of (8.2 g) of sodium acetate dissolved in (30 ml) of water. The solid product, so formed, was collected by filtration and crystallized from toluene.

1-(Phenyl-hydrazone)-propan-2-one (**1a**).

Compound **1a** was obtained as yellowish green crystals (1.44 g, 89%), mp. 152 °C (Lit., 150 °C), ir (KBr) ν_{\max} = 3249 (NH), 1649 (CO) cm^{-1} ; ms: m/z = 162 (M^+); ^1H nmr (dimethylsulfoxide- d_6): δ = 2.31 (s, 3H, CH_3), 6.93 (t, 1H, J = 7.4 Hz, phenyl-H), 7.17 (t, 2H, J = 7.7 Hz, phenyl-H), 7.24 (s, 1H, imine-H), 7.29 (d, 2H, J = 8 Hz, phenyl-H), 11.33 (s, 1H, NH, D_2O exchangeable).

Anal. Calcd. For $\text{C}_9\text{H}_{10}\text{N}_2\text{O}$ (162.19): C, 66.65; H, 6.21; N, 17.27. Found C, 66.63; H, 6.07; N, 17.27.

1-(*p*-Tolyl-hydrazone)-propan-2-one (**1b**).

Compound **1b** was obtained as light green crystals (1.06 g, 60%), mp. 128-130 °C, ir (KBr) ν_{\max} = 3246 (NH), 1652 (CO) cm^{-1} ; ms: m/z = 176 (M^+); ^1H nmr (dimethylsulfoxide- d_6): δ = 2.24 (s, 3H, CH_3), 2.30 (s, 3H, CH_3), 7.07 (d, 2H, J = 8.6 Hz, *p*-tolyl-H), 7.11 (d, 2H, J = 8.6 Hz, *p*-tolyl-H), 7.21 (s, 1H, imine-H), 11.25 (s, 1H, NH, D_2O exchangeable), ^{13}C nmr (dimethylsulfoxide- d_6): δ = 197.0 (CO), 141.9, 135.0, 131.5, 130.8, 114.4, 25.1 (CH_3), 21.3 (CH_3).

Anal. Calcd. For $\text{C}_{10}\text{H}_{12}\text{N}_2\text{O}$ (176.22): C, 68.16; H, 6.86; N, 15.90. Found C, 68.26; H, 6.81; N, 15.91.

1-(Phenyl-hydrazone)-butan-2-one (**1c**).

Compound **1c** was obtained as red crystals (1.08 g, 61%), mp. 150-152 °C, ir (KBr) ν_{\max} = 3251 (NH), 1656 (CO) cm^{-1} ; ms: m/z = 176 (M^+); ^1H nmr (dimethylsulfoxide- d_6): δ = 1.01 (s, 3H, J = 7.6 Hz, CH_3), 2.77 (q, 2H, J = 7.2 Hz, CH_2), 6.92 (t, 1H, J = 7.4 Hz, phenyl-H), 7.17 (t, 2H, J = 7.7 Hz, phenyl-H), 7.24 (s, 1H, imine-H), 7.29 (d, 2H, J = 8 Hz, phenyl-H), 11.27 (s, 1H, NH, D_2O exchangeable), ^{13}C nmr (dimethylsulfoxide- d_6): δ = 200.2 (CO), 144.3, 134.9, 130.4, 122.5, 114.4, 30.1 (CH_2), 9.5 (CH_3).

Anal. Calcd. For $\text{C}_{10}\text{H}_{12}\text{N}_2\text{O}$ (176.22): C, 68.16; H, 6.86; N, 15.90. Found C, 68.50; H, 6.89; N, 15.92.

1-(*p*-Tolyl-hydrazone)-butan-2-one (**1d**).

Compound **1d** was obtained as wine red crystals (1.26 g, 66%), mp. 134-136 °C, ir (KBr) ν_{\max} = 3236 (NH), 1651 (CO) cm^{-1} ; ms: m/z = 190 (M^+); ^1H nmr (dimethylsulfoxide- d_6): δ = 1.01 (t, 3H, J = 7.4 Hz, CH_3), 2.24 (s, 3H, CH_3), 2.75 (q, 2H, J = 7.4 Hz, CH_2), 7.05 (d, 2H, J = 8.4 Hz, *p*-tolyl-H), 7.10 (d, 2H, J = 8.4 Hz, *p*-tolyl-H), 7.21 (s, 1H, imine-H), 11.21 (s, 1H, NH,

D_2O exchangeable), ^{13}C nmr (dimethylsulfoxide- d_6): δ = 200.0 (CO), 142.0, 134.3, 131.4, 130.4, 114.4, 30.0 (CH_2), 21.3 (CH_3), 9.5 (CH_3).

Anal. Calcd. For $\text{C}_{11}\text{H}_{14}\text{N}_2\text{O}$ (190.24): C, 69.45; H, 7.42; N, 14.73. Found C, 69.56; H, 7.34; N, 14.73.

General Procedure for the Preparation of Compounds **2a-d**.

A mixture of **1a-d** (0.01 mol), ethyl cyanoacetate (1.13 g, 0.01 mol), ammonium acetate (2 g) and acetic acid (0.6 mol) was irradiated in focused microwave at 150 Watt, 170 °C for 4 minutes, then left to cool and triturated with ethanol. The solid product, so formed, was collected by filtration and crystallized from toluene.

5-Methyl-3-oxo-2-phenyl-2,3-dihydropyridazine-4-carbonitrile (**2a**).

Compound **2a** was obtained as gray crystals (1.21 g, 57%), mp. 158.160 °C, ir (KBr) ν_{\max} = 2233 (CN), 1659 (CO) cm^{-1} ; ms: m/z = 211 (M^+); ^1H nmr (dimethylsulfoxide- d_6): δ = 2.60 (s, 3H, CH_3), 7.53-7.55 (m, 5H, phenyl-H), 8.24 (s, 1H, pyridazine-H), ^{13}C nmr (dimethylsulfoxide- d_6): δ = 157.0 (CO), 152.6, 141.5, 139.9, 129.8, 129.7, 126.8, 114.4, 114.0, 19.1 (CH_3).

Anal. Calcd. For $\text{C}_{12}\text{H}_9\text{N}_3\text{O}$ (211.22): C, 68.24; H, 4.29; N, 19.89. Found C, 68.37; H, 4.38; N, 19.42.

5-Methyl-3-oxo-2-*p*-tolyl-2,3-dihydropyridazine-4-carbonitrile (**2b**).

Compound **2b** was obtained as gray crystals (1.18 g, 52%), mp. 209 °C, ir (KBr) ν_{\max} = 2229 (CN), 1658 (CO) cm^{-1} ; ms: m/z = 225 (M^+); ^1H nmr (dimethylsulfoxide- d_6): δ = 2.37 (s, 3H, CH_3), 2.50 (s, 3H, CH_3), 7.31 (d, 2H, J = 8.3 Hz, *p*-tolyl-H), 7.41 (d, 2H, J = 8.3 Hz, *p*-tolyl-H), 8.22 (s, 1H, pyridazine-H), ^{13}C nmr (dimethylsulfoxide- d_6): δ = 157.0 (CO), 152.4, 139.7, 139.3, 139.1, 130.2, 126.3, 114.5, 113.9, 21.7 (CH_3), 19.0 (CH_3).

Anal. Calcd. For $\text{C}_{13}\text{H}_{11}\text{N}_3\text{O}$ (225.25): C, 69.32; H, 4.92; N, 18.66. Found C, 69.18; H, 4.90; N, 18.34.

5-Ethyl-3-oxo-2-phenyl-2,3-dihydropyridazine-4-carbonitrile (**2c**).

Compound **2c** was obtained as light green crystals (1.26 g, 56%), mp. 100 °C, ir (KBr) ν_{\max} = 2234 (CN), 1657 (CO) cm^{-1} ; ms: m/z = 225 (M^+); ^1H nmr (dimethylsulfoxide- d_6): δ = 1.26 (t, 3H, J = 7.6 Hz, CH_3), 2.74 (q, 2H, J = 7.6 Hz, CH_2), 7.47-7.57 (m, 5H, phenyl-H), 8.32 (s, 1H, pyridazine-H), ^{13}C nmr (dimethylsulfoxide- d_6): δ = 157.2 (CO), 157.0, 141.6, 138.9, 129.8, 129.7, 126.6, 114.2, 113.2, 26.4 (CH_2), 13.8 (CH_3).

Anal. Calcd. For $\text{C}_{13}\text{H}_{11}\text{N}_3\text{O}$ (225.25): C, 69.32; H, 4.92; N, 18.66. Found C, 69.56; H, 5.05; N, 18.77.

5-Ethyl-3-oxo-2-*p*-tolyl-2,3-dihydropyridazine-4-carbonitrile (**2d**).

Compound **2d** was obtained as light green crystals (1.49 g, 62%), mp. 91 °C, ir (KBr) ν_{\max} = 2231 (CN), 1659 (CO) cm^{-1} ; ms: m/z = 239 (M^+); ^1H nmr (dimethylsulfoxide- d_6): δ = 1.26 (t, 3H, J = 7.6 Hz, CH_3), 2.37 (s, 3H, CH_3), 2.73 (q, 2H, J = 7.6 Hz, CH_2), 7.31 (d, 2H, J = 8.2 Hz, *p*-tolyl-H), 7.42 (d, 2H, J = 8.2 Hz, *p*-tolyl-H), 8.30 (s, 1H, pyridazine-H), ^{13}C nmr (dimethylsulfoxide- d_6): δ = 157.2 (CO), 156.8, 139.3, 139.2, 138.8, 130.2, 126.3, 114.2, 113.1, 26.3 (CH_2), 21.7 (CH_3), 13.7 (CH_3).

Anal. Calcd. For $\text{C}_{14}\text{H}_{13}\text{N}_3\text{O}$ (239.27): C, 70.28; H, 5.48; N, 17.56. Found C, 70.21; H, 5.52; N, 17.51.

General Procedure for the Preparation of Compounds **3a,b**.

To a suspension of compounds **2a** or **2c** (0.01 mol) in dioxane (2 ml), elemental sulphur (0.32 g, 0.01 mol) and few

drops of piperidine were added. The reaction mixture was irradiated in focused microwave at 150 Watt, 200 °C for 5 minutes and then poured onto water. The solid product, so formed, was collected by filtration and crystallized from ethanol.

7-Amino-2-*p*-tolyl-2*H*-thieno[3,4-*d*]pyridazin-1-one (3a).

Compound **3a** was obtained as green crystals (1.91 g, 74%), mp. 135 °C, ir (KBr) ν_{\max} = 3410 and 3299 (NH₂), 1648 (CO) cm⁻¹; ms: m/z = 257 (M⁺); ¹H nmr (dimethylsulfoxide-*d*₆): δ = 2.33 (s, 3H, CH₃), 6.76 (s, 1H, H-5), 7.21 (d, 2H, *J* = 7.7 Hz, *p*-tolyl-H), 7.36 (d, 2H, *J* = 8.0 Hz, *p*-tolyl-H), 7.48 (s, 2H, NH₂, D₂O exchangeable), 7.93 (s, 1H, pyridazine-H), ¹³C nmr (deuteriochloroform): δ = 168.1 (CO), 164.2, 144.5, 141.7, 135.5, 134.9, 134.4, 131.0, 109.8, 107.8, 26.4 (CH₃).

Anal. Calcd. For C₁₃H₁₁N₃OS (257.31): C, 60.68; H, 4.31; N, 16.33; S, 12.46. Found C, 60.79; H, 4.30; N, 16.30; S, 11.87.

7-Amino-5-methyl-2-phenyl-2*H*-thieno[3,4-*d*]pyridazin-1-one (3b).

Compound **3b** was obtained as brown crystals (1.96 g, 76%), mp. 209 °C, ir (KBr) ν_{\max} = 3422 and 3285 (NH₂), 1627 (CO) cm⁻¹; ms: m/z = 257 (M⁺); ¹H nmr (dimethylsulfoxide-*d*₆): δ = 2.44 (s, 3H, CH₃), 7.27 (t, 1H, *J* = 7.6 Hz, phenyl-H), 7.33 (s, 2H, NH₂, D₂O exchangeable), 7.40 (t, 2H, *J* = 8.3 Hz, phenyl-H), 7.48 (d, 2H, *J* = 8.6 Hz, phenyl-H), 8.01 (s, 1H, pyridazine-H), ¹³C nmr (dimethylsulfoxide-*d*₆): δ = 160.8 (CO), 159.4, 142.3, 135.4, 129.8, 128.9, 127.3, 126.6, 116.7, 104.2, 12.4 (CH₃).

Anal. Calcd. For C₁₃H₁₁N₃OS (257.31): C, 60.68; H, 4.31; N, 16.33; S, 12.46. Found C, 60.73; H, 4.34; N, 16.33; S, 12.57.

General Procedure for the Preparation of Compounds **10** and **11a,b**.

A mixture each of maleimide, *N*-methylmaleimide and ethyl acrylate (0.01 mol) and **3b** (2.57 g, 0.01 mol) in a mixture of acetic acid (2 ml) and dioxane (2 ml) was irradiated in focused microwave at 250 Watt, 210 °C for 15 minutes. The reaction mixture was evaporated then washed with ethanol. The solid products, so formed, were collected by filtration and crystallized from dioxane.

Ethyl 5-Amino-8-methyl-4-oxo-3-phenyl-3,4-dihydrophthalazine-6-carboxylate (10).

Compound **10** was obtained as wine red crystals (2.23 g, 69%), mp. 185 °C, ir (KBr) ν_{\max} = 3419 and 3288 (NH₂), 1687, 1638 (CO) cm⁻¹; ms: m/z = 323 (M⁺); ¹H nmr (dimethylsulfoxide-*d*₆): δ = 1.32 (t, 3H, *J* = 7.0 Hz, CH₃), 2.57 (s, 3H, CH₃), 4.27 (q, 2H, *J* = 7.0 Hz, CH₂), 7.41-7.57 (m, 5H, phenyl-H), 8.01 (s, 1H, H-7), 8.14 (br s, 1H, NH, D₂O exchangeable), 8.46 (s, 1H, pyridazine-H), 9.17 (br s, 1H, NH, D₂O exchangeable). ¹³C nmr (dimethylsulfoxide-*d*₆): δ = 167.5, 161.7 (CO), 152.1, 142.5, 138.4, 137.3, 133.7, 129.8, 128.8, 127.3, 119.1, 113.0, 110.3, 67.3 (CH₂), 18.0 (CH₃), 15.1 (CH₃).

Anal. Calcd. For C₁₈H₁₇N₃O₃ (323.35): C, 66.86; H, 5.30; N, 13.00. Found C, 66.48; H, 5.29; N, 13.01.

9-Amino-5-methyl-2-phenyl-2*H*-pyrrolo[3,4-*g*]phthalazine-1,6,8-trione (11a).

Compound **11a** was obtained as yellow crystals (2.02 g, 63%), mp. > 300 °C, ir (KBr) ν_{\max} = 3426 and 3289 (NH₂), 3180 (NH), 1751, 1708, 1651 (CO) cm⁻¹; ms: m/z = 320 (M⁺); ¹H nmr (dimethylsulfoxide-*d*₆): δ = 2.72 (s, 3H, CH₃), 7.11 (br s, 1H,

NH, D₂O exchangeable), 7.43 (t, 1H, *J* = 7.0 Hz, phenyl-H), 7.51 (t, 2H, *J* = 7.4 Hz, phenyl-H), 7.58 (d, 2H, *J* = 7.8 Hz, phenyl-H), 8.56 (br s, 1H, NH, D₂O exchangeable), 8.67 (s, 1H, pyridazine-H), 11.38 (br s, 1H, NH, D₂O exchangeable). ¹³C nmr (dimethylsulfoxide-*d*₆): δ = 170.8, 170.0, 161.3 (CO), 146.6, 142.1, 137.3, 136.3, 134.6, 129.7, 129.1, 127.1, 120.6, 117.1, 111.3, 12.1 (CH₃).

Anal. Calcd. For C₁₇H₁₂N₄O₃ (320.30): C, 63.75; H, 3.78; N, 17.49. Found C, 63.77; H, 3.92; N, 17.69.

9-Amino-5,7-dimethyl-2-phenyl-2*H*-pyrrolo[3,4-*g*]phthalazine-1,6,8-trione (11b).

Compound **11b** was obtained as yellow crystals (1.98 g, 59%), mp. 273 °C, ir (KBr) ν_{\max} = 3444 and 3307 (NH₂), 1747, 1696, 1650 (CO) cm⁻¹; ms: m/z = 334 (M⁺); ¹H nmr (deuteriochloroform): δ = 2.82 (s, 3H, CH₃), 3.14 (s, 3H, CH₃), 6.99 (br s, 1H, NH, D₂O exchangeable), 7.44 (t, 1H, *J* = 7.0 Hz, phenyl-H), 7.52 (t, 2H, *J* = 7.4 Hz, phenyl-H), 7.61 (d, 2H, *J* = 8.0 Hz, phenyl-H), 8.48 (s, 1H, pyridazine-H), 8.77 (br s, 1H, NH, D₂O exchangeable). ¹³C nmr (deuteriochloroform): δ = 169.6, 169.0, 161.5 (CO), 146.9, 141.5, 136.3, 136.1, 133.7, 129.5, 129.0, 126.3, 120.8, 117.6, 110.5, 24.3 (CH₃), 12.2 (CH₃).

Anal. Calcd. For C₁₈H₁₄N₄O₃ (334.33): C, 64.66; H, 4.22; N, 16.76. Found C, 64.23; H, 4.33; N, 16.77.

Reaction of Compounds **3a,b** with 1,4-Naphthoquinone.

A mixture of each of **3a,b** (10 mmol) with 1,4-naphthoquinone (1.58 g, 0.01 mol) in ethanol (4 ml) was irradiated in focused microwave at 125 Watt, 100 °C for 15 minutes. The solvent was removed and the residue cooled to deposit a solid, which was crystallized from dimethylformamide.

12-Amino-2-*p*-tolyl-2*H*-2,3-diazanaphthacene-1,6,11-trione (12a).

Compound **12a** was obtained as red crystals (2.13 g, 82%), mp. 264 °C, ir (KBr) ν_{\max} = 3349 and 3235 (NH₂), 1658 (br) (CO), 1573 (CO) cm⁻¹; ms: m/z = 381 (M⁺); ¹H nmr (deuteriochloroform): δ = 2.45 (s, 3H, CH₃), 7.34 (d, 2H, *J* = 8.0 Hz, *p*-tolyl-H), 7.49 (d, 2H, *J* = 8.2 Hz, *p*-tolyl-H), 7.73-7.81 (m, 2H, arom-H), 7.84 (t, 1H, *J* = 7.4 Hz, arom-H), 8.28 (s, 1H, pyridazine-H), 8.30 (d, 1H, *J* = 7.6 Hz, arom-H), 8.38 (d, 1H, *J* = 7.6 Hz, arom-H), 9.98 (br s, 1H, NH, D₂O exchangeable), 10.21 (br s, 1H, NH, D₂O exchangeable). ¹³C nmr (dimethylsulfoxide-*d*₆): δ = 184.6, 183.3, 161.5 (CO), 154.9, 139.4, 139.1, 139.0, 138.8, 137.0, 135.8, 135.4, 135.2, 134.0, 133.1, 130.1, 127.7, 127.6, 126.1, 116.6, 111.5, 21.8 (CH₃).

Anal. Calcd. For C₂₃H₁₅N₃O₃ (381.38): C, 72.43; H, 3.96; N, 11.02. Found C, 71.97; H, 4.07; N, 11.27.

12-Amino-5-methyl-2-phenyl-2*H*-2,3-diazanaphthacene-1,6,11-trione (12b).

Compound **12b** was obtained as wine red crystals (3.24 g, 85%), mp. > 300 °C, ir (KBr) ν_{\max} = 3351 and 3240 (NH₂), 1650 (br) (CO), 1593 (CO) cm⁻¹; ms: m/z = 381 (M⁺); ¹H nmr (deuteriochloroform): δ = 2.66 (s, 3H, CH₃), 7.45 (t, 1H, *J* = 7.2 Hz, arom-H), 7.54 (t, 2H, *J* = 7.6 Hz, arom-H), 7.63 (d, 2H, *J* = 7.9 Hz, arom-H), 7.74-7.82 (m, 2H, arom-H), 8.17 (d, 1H, *J* = 7.4 Hz, arom-H), 8.27 (d, 1H, *J* = 7.4 Hz, arom-H), 8.64 (s, 1H, pyridazine-H), 10.10 (s, 1H, NH, D₂O exchangeable), 10.42 (s, 1H, NH, D₂O exchangeable).

Anal. Calcd. For C₂₃H₁₅N₃O₃ (381.38): C, 72.43; H, 3.96; N, 11.02. Found C, 72.15; H, 4.08; N, 11.31

General Procedure for the Preparation of Compounds **13a,b**.

A solution of each of **3a,b** (10 mmol) and DMFDMA (1.19 g, 10 mmol) in the presence of a few drops of dimethylformamide was irradiated in focused microwave at 250 Watt, 200 °C for 15 minutes. The solid products obtained were crystallized from ethanol.

N,N-Dimethyl-*N'*-(4-oxo-3-*p*-tolyl-3,4-dihydrothieno[3,4-*d*]pyridazin-5-yl) formamidine (**13a**).

Compound **13a** was obtained as brown crystals (2.00 g, 64%), mp. 198-200 °C, ir (KBr) ν_{\max} = 1648 (CO) cm⁻¹; ms: *m/z* = 312 (M⁺); ¹H nmr (dimethylsulfoxide-*d*₆): δ = 2.30 (s, 3H, CH₃), 2.98 (s, 3H, N-CH₃), 3.06 (s, 3H, N-CH₃), 7.12 (s, 1H, thiophene-H), 7.22 (d, 2H, *J* = 8.2 Hz, *p*-tolyl-H), 7.32(d, 2H, *J* = 8.2 Hz, *p*-tolyl-H), 7.39 (s, 1H, amidine-H), 8.06 (s, 1H, pyridazine-H), ¹³C nmr (dimethylsulfoxide-*d*₆): δ = 167.4 (CO), 158.4, 157.6, 140.5, 136.9, 136.2, 132.6, 130.3, 127.2, 126.5, 112.1, 35.1 (N-CH₃), 21.6 (CH₃).

Anal. Calcd. For C₁₆H₁₆N₄OS (312.39): C, 61.52; H, 5.16; N, 17.93; S, 10.26. Found C, 61.47; H, 5.16; N, 17.69; S, 10.01.

N,N-Dimethyl-*N'*-(7-methyl-4-oxo-3-phenyl-3,4-dihydrothieno[3,4-*d*]pyridazin-5-yl) formamidine (**13b**).

Compound **13b** was obtained as light green crystals (2.23 g, 71%), mp. 165 °C, ir (KBr) ν_{\max} = 1655 (CO) cm⁻¹; ms: *m/z* = 312 (M⁺); ¹H nmr (dimethylsulfoxide-*d*₆): δ = 2.57 (s, 3H, CH₃), 2.96 (s, 3H, N-CH₃), 3.04 (s, 3H, N-CH₃), 7.29-7.47 (m, 5H, phenyl-H), 7.99 (s, 1H, amidine-H), 8.15 (s, 1H, pyridazine-H), ¹³C nmr (dimethylsulfoxide-*d*₆): δ = 164.0 (CO), 158.1, 157.6, 143.0, 134.9, 129.7, 128.9, 127.5, 127.0, 125.6, 112.4, 35.1 (N-CH₃), 13.0 (CH₃).

Anal. Calcd. For C₁₆H₁₆N₄OS (312.39): C, 61.52; H, 5.16; N, 17.93; S, 10.26. Found C, 61.51; H, 5.25; N, 17.82; S, 10.08.

General Procedure for the Preparation of Compounds **14** and **15**.

A solution of each of **13a,b** (0.01 mol) in acetic acid / hydrochloric acid (4 ml, 3:1 by volume) was refluxed for 3 hrs, and then allowed to cool to room temperature. The solid product so formed was collected by filtration and crystallized from ethanol.

2-*p*-Tolyl-2*H*,5*H*-thieno[3,4-*d*]pyridazine-1,7-dione (**14**).

Compound **13a** was obtained as green crystals (1.60 g, 62%), mp. 196 °C, ir (KBr) ν_{\max} = 1794 and 1692 (CO) cm⁻¹; ms: *m/z* = 258 (M⁺); ¹H nmr (deuteriochloroform): δ = 2.32 (s, 3H, CH₃), 4.41 (s, 2H, CH₂), 7.28 (d, 2H, *J* = 7.6 Hz, *p*-tolyl-H), 7.47 (d, 2H, *J* = 7.6 Hz, *p*-tolyl-H), 8.15 (s, 1H, pyridazine-H), ¹³C nmr (deuteriochloroform): δ = 192.2, 155.7 (CO), 139.5, 138.6, 134.6, 131.5, 130.0, 126.1, 125.6, 32.7 (CH₂), 21.8 (CH₃).

Anal. Calcd. For C₁₃H₁₀N₂O₂S (258.30): C, 60.45; H, 3.90; N, 10.85; S, 12.41. Found C, 60.37; H, 4.08; N, 11.52; S, 12.38.

N-(7-Methyl-4-oxo-3-phenyl-3,4-dihydrothieno[3,4-*d*]pyridazin-5-yl)acetamide (**15**).

Compound **13b** was obtained as light green crystals (2.10 g, 70%), mp. 235 °C, ir (KBr) ν_{\max} = 3306 (NH), 1684 and 1637 (CO) cm⁻¹; ms: *m/z* = 299 (M⁺); ¹H nmr (deuteriochloroform): δ

= 2.29 (s, 3H, CH₃), 2.69 (s, 3H, CH₃), 7.28-7.59 (m, 5H, phenyl-H), 8.07 (s, 1H, pyridazine-H), 10.97 (s, 1H, NH, D₂O exchangeable). ¹³C nmr (deuteriochloroform): δ = 167.6, 159.7 (CO), 142.9, 141.2, 134.7, 129.4, 128.2, 127.8, 126.4, 124.9, 112.1, 23.7 (CH₃), 12.4 (CH₃)

Anal. Calcd. For C₁₅H₁₃N₃O₂S (299.35): C, 60.18; H, 4.38; N, 14.04; S, 10.71. Found C, 60.19; H, 4.44; N, 14.18; S, 10.77.

General Procedure for the Preparation of Compounds **16a,b**.

A solution of each of **2a,b** (10 mmol) and DMFDMA (1.19 g, 10 mmol) was irradiated in a focused microwave at 150 Watt, 180 °C for 5 minutes. The solid product obtained was crystallized from dioxane.

5-(2-Dimethylamino-vinyl)-3-oxo-2-phenyl-2,3-dihydropyridazine-4-carbonitrile (**16a**).

Compound **16a** was obtained as yellowish green crystals (1.92 g, 72%), mp. 225 °C, ir (KBr) ν_{\max} = 2203 (CN), 1616 (CO) cm⁻¹; ms: *m/z* = 266 (M⁺); ¹H nmr (dimethylsulfoxide-*d*₆): δ = 2.99 (s, 3H, N-CH₃), 3.24 (s, 3H, N-CH₃), 5.17 (d, 1H, *J* = 12.8 Hz, vinylic-H), 7.36-7.52 (m, 5H, phenyl-H), 8.32 (d, 1H, *J* = 12.8 Hz, vinylic-H), 8.43 (s, 1H, pyridazine-H), ¹³C nmr (dimethylsulfoxide-*d*₆): δ = 158.4 (CO), 154.1, 148.8, 142.0, 134.4, 129.5, 128.5, 126.5, 117.2, 92.0, 90.3, 46.1 (N-CH₃), 37.8 (N-CH₃).

Anal. Calcd. For C₁₅H₁₄N₄O (266.30): C, 67.69; H, 5.30; N, 21.04. Found C, 67.58; H, 5.41; N, 20.96.

5-(2-Dimethylamino-vinyl)-3-oxo-2-*p*-tolyl-2,3-dihydropyridazine-4-carbonitrile (**16b**).

Compound **16b** was obtained as green crystals (2.10 g, 75%), mp. 210 °C, ir (KBr) ν_{\max} = 2209 (CN), 1630 (CO) cm⁻¹; ms: *m/z* = 280 (M⁺); ¹H nmr (dimethylsulfoxide-*d*₆): δ = 2.34 (s, 3H, CH₃), 2.97 (s, 3H, N-CH₃), 3.22 (s, 3H, N-CH₃), 5.15 (d, 1H, *J* = 12.8 Hz, vinylic-H), 7.24 (d, 2H, *J* = 8.2 Hz, *p*-tolyl-H), 7.37 (d, 2H, *J* = 8.2 Hz, *p*-tolyl-H), 8.18 (d, 1H, *J* = 12.8 Hz, vinylic-H), 8.39 (s, 1H, pyridazine-H), ¹³C nmr (dimethylsulfoxide-*d*₆): δ = 158.4 (CO), 154.0, 148.7, 139.6, 137.9, 134.2, 129.9, 126.1, 117.2, 92.1, 90.2, 46.1 (N-CH₃), 37.9 (N-CH₃), 21.6 (CH₃).

Anal. Calcd. For C₁₆H₁₆N₄O (280.32): C, 68.55; H, 5.75; N, 19.99. Found C, 68.52; H, 5.87; N, 19.96.

General Procedure for the Preparation of Compounds **17a,b**.

A solution of each of **16a,b** (0.01 mol), acetic acid (2 ml) and ammonium acetate (1 g) was irradiated in focused microwave at 150 Watt, 150 °C for 5 minutes, then allowed to cool to room temperature. The solid product so formed was collected by filtration and crystallized from acetic acid.

3-Phenyl-3*H*,6*H*-pyrido[3,4-*d*]pyridazine-4,5-dione (**17a**).

Compound **17a** was obtained as light green crystals (1.87 g, 89%), mp. 298 °C, ir (KBr) ν_{\max} = 3300 (NH), 1691 (CO) cm⁻¹; ms: *m/z* = 239 (M⁺); ¹H nmr (dimethylsulfoxide-*d*₆): δ = 6.49 (d, 1H, *J* = 6.4 Hz H-8), 7.39-7.52 (m, 5H, phenyl-H), 7.80 (d, 1H, *J* = 6.4 Hz H-7), 8.28 (s, 1H, pyridazine-H), 12.10 (s, 1H, NH, D₂O exchangeable). ¹³C nmr (dimethylsulfoxide-*d*₆): δ = 159.7, 157.2 (CO), 154.7, 142.8, 142.3, 139.0, 137.1, 129.6, 127.2, 107.7, 101.7.

Anal. Calcd. For C₁₃H₉N₃O₂ (239.23): C, 65.27; H, 3.79; N, 17.56. Found C, 65.09; H, 3.98; N, 17.64.

3-*p*-Tolyl-3*H*,6*H*-pyrido[3,4-*d*]pyridazine-4,5-dione (**17b**).

Compound **17b** was obtained as light green crystals (1.62 g, 64%), mp. 295 °C, ir (KBr) ν_{\max} = 3290 (NH), 1689 (CO) cm^{-1} ; ms: m/z = 253 (M^+); ^1H nmr (dimethylsulfoxide- d_6): δ = 2.36 (s, 3H, CH_3), 6.48 (d, 1H, J = 6.4 Hz H-8), 7.27 (d, 2H, J = 8.0 Hz, *p*-tolyl-H), 7.29 (d, 2H, J = 8.0 Hz, *p*-tolyl-H), 7.79 (d, 1H, J = 6.4 Hz H-7), 8.25 (s, 1H, pyridazine-H), 12.00 (s, 1H, NH, D_2O exchangeable). ^{13}C nmr (dimethylsulfoxide- d_6): δ = 159.7, 157.2 (CO), 154.8, 142.7, 140.0, 138.2, 136.9, 130.0, 126.8, 107.7, 101.7, 21.7 (CH_3).

Anal. Calcd. For $\text{C}_{14}\text{H}_{11}\text{N}_3\text{O}_2$ (253.26): C, 66.40; H, 4.38; N, 16.59. Found C, 66.30; H, 4.45; N, 16.60.

General Procedure for the Preparation of Compounds **21a-d**.

A solution of each of **2a-d** (10 mmol) in pyridine (3 ml) was treated with benzylidenemalononitrile (1.54 g, 0.01 mol). The reaction mixture was irradiated in a focused microwave at 150 Watt, 175 °C for 5 minutes, then poured onto water and acidified with dilute hydrochloric acid. The solid product obtained was crystallized from dioxane

5-Amino-4-oxo-3,7-diphenyl-3,4-dihydrophthalazine-6-carbonitrile (**21a**).

Compound **21a** was obtained as gray crystals (2.21 g, 65%), mp. 259-261 °C, ir (KBr) ν_{\max} = 3455 and 3301 (NH_2), 2208 (CN), 1658 (CO) cm^{-1} ; ms: m/z = 338 (M^+); ^1H nmr (deuteriochloroform): δ = 6.92 (s, 1H, H-8), 7.28 (br s, 2H, NH_2 , D_2O exchangeable), 7.43-7.47 (m, 1H, arom-H), 7.53-7.57 (m, 5H, arom-H), 7.61-7.64 (m, 4H, arom-H), 8.17 (s, 1H, pyridazine-H), ^{13}C nmr (deuteriochloroform): δ = 161.0 (CO), 154.2, 151.5, 141.6, 139.2, 138.1, 134.2, 130.2, 129.6, 129.3, 129.0, 128.9, 126.4, 117.0, 113.8, 110.8, 96.4.

Anal. Calcd. For $\text{C}_{21}\text{H}_{14}\text{N}_4\text{O}$ (338.36): C, 74.54; H, 4.17; N, 16.56. Found C, 74.66; H, 4.17; N, 16.59.

5-Amino-4-oxo-7-phenyl-3-*p*-tolyl-3,4-dihydrophthalazine-6-carbonitrile (**21b**).

Compound **21b** was obtained as light green crystals (2.36 g, 67%), mp. 283 °C, ir (KBr) ν_{\max} = 3454 and 3302 (NH_2), 2207 (CN), 1656 (CO) cm^{-1} ; ms: m/z = 352 (M^+); ^1H nmr (dimethylsulfoxide- d_6): δ = 2.38 (s, 3H, CH_3), 7.11 (s, 1H, H-8), 7.31 (d, 2H, J = 8.0 Hz, *p*-tolyl-H), 7.44 (d, 2H, J = 8.0 Hz, *p*-tolyl-H), 7.56-7.64 (m, 7H, arom-H and NH_2), 8.43 (s, 1H, pyridazine-H), ^{13}C nmr (dimethylsulfoxide- d_6): δ = 161.0 (CO), 154.6, 151.2, 139.8, 138.6, 138.4, 134.8, 130.4, 130.2, 130.1, 129.8, 129.5, 127.0, 126.3, 117.5, 114.2, 110.7, 21.7 (CH_3).

Anal. Calcd. For $\text{C}_{22}\text{H}_{16}\text{N}_4\text{O}$ (352.39): C, 74.98; H, 4.58; N, 15.90. Found C, 74.54; H, 4.72; N, 16.22.

5-Amino-8-methyl-4-oxo-3,7-diphenyl-3,4-dihydrophthalazine-6-carbonitrile (**21c**).

Compound **21c** was obtained as brown crystals (2.15 g, 61%), mp. 260 °C, ir (KBr) ν_{\max} = 3464 and 3322 (NH_2), 2208 (CN), 1647 (CO) cm^{-1} ; ms: m/z = 352 (M^+); ^1H nmr (deuteriochloroform): δ = 2.26 (s, 3H, CH_3), 7.28 (br s, 2H, NH_2 , D_2O exchangeable), 7.30-7.33 (m, 2H, arom-H), 7.45-7.64 (m, 8H, arom-H), 8.43 (s, 1H, pyridazine-H), ^{13}C nmr (deuteriochloroform): δ = 161.1 (CO), 151.6, 151.0, 141.7, 138.1, 136.8, 132.9, 130.7, 129.9, 129.7, 129.2, 128.9, 126.0, 119.4, 118.8, 112.0, 98.8, 15.4 (CH_3).

Anal. Calcd. For $\text{C}_{22}\text{H}_{16}\text{N}_4\text{O}$ (352.39): C, 74.98; H, 4.58; N, 15.90. Found C, 75.36; H, 4.62; N, 15.92.

5-Amino-8-methyl-4-oxo-7-phenyl-3-*p*-tolyl-3,4-dihydrophthalazine-6-carbonitrile (**21d**).

Compound **21d** was obtained as yellowish green crystals (2.50 g, 68%), mp. 238 °C, ir (KBr) ν_{\max} = 3454 and 3310 (NH_2), 2207 (CN), 1651 (CO) cm^{-1} ; ms: m/z = 366 (M^+); ^1H nmr (dimethylsulfoxide- d_6): δ = 2.15 (s, 3H, CH_3), 2.39 (s, 3H, CH_3), 7.28 (br s, 2H, NH_2 , D_2O exchangeable), 7.32-7.35 (m, 4H, arom-H), 7.42-7.47 (m, 2H, arom-H), 7.50-7.58 (m, 3H, arom-H), 8.59 (s, 1H, pyridazine-H), ^{13}C nmr (dimethylsulfoxide- d_6): δ = 161.0 (CO), 152.1, 151.0, 139.8, 138.8, 138.4, 137.5, 133.2, 130.2, 130.1, 129.6, 126.9, 126.3, 119.3, 117.2, 111.8, 97.8, 21.7 (CH_3), 15.6 (CH_3).

Anal. Calcd. For $\text{C}_{23}\text{H}_{18}\text{N}_4\text{O}$ (366.42): C, 75.39; H, 4.95; N, 15.29. Found C, 74.88; H, 5.09; N, 15.40.

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