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Pyridazine Derivatives and Related Compounds, Part 8: Synthesis of Different Heterocycles from 3-Hydrazinopyridazine

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ABSTRACT: *The reaction of 3-hydrazino-4,5,6-triphenylpyridazine* **1** *with phenylisothiocyanate in ethanol gave thiocarbamoylhydrazine* **2** *while in butanol gave triazolo[4,3-b]pyridazinethione* **3**. *Reaction of* **1** *with ethyl chloroformate gave ethoxycarbamoylhydrazinopyridazine* **5** *which upon heating it furnished triazolopyridazine* **6**. *Also, the reaction of* **1** *with chloroacetylchloride gave triazolopyridazine* **7**. *Reaction of* **1** *with a number of aromatic aldehydes,* D-*glucose, and pyruvic acid gave the corresponding hydrazones* **9,11**. *Oxidative cyclization of* **9a,b** *gave triazolo[4,3-b]pyridazine* **10a,b**. *On the other hand, reactions of* **1** *with diethyl oxalate, ethyl acetoacetate, acetylacetone, ethyl cyanoacetate, diacetyl, and with phthalic anhydride are also reported.* © 2005 Wiley Periodicals, Inc. Heteroatom Chem 16:278–284, 2005; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20110

INTRODUCTION

Pyridazine and related compounds find wide application in different biological and medicinal fields [1]. Also a good deal of importance is being given to pyrazole, triazole, and their derivatives due to their wide use in medicinal chemistry [2]. Hence, it was thought that incorporation of the latter heterocyclic moieties into pyridazines moiety might modify their biological activity. The present investigation, which is a continuation of our previous work [3] on pyridazine, deals with the synthesis of different 3-substituted heterocycles pyridazines.

For this purpose, 3-hydrazino-4,5,6-triphenylpyridazine **1** was prepared by the reaction of 3-chloro-4,5,6-triphenylpyridazine with hydrazine hydrate in *n*-butanol [4]. The reaction of the hydrazine **1** with phenyl isothiocyanate in boiling ethanol afforded thiocarbamoylhydrazine **2**, while in boiling butanol afforded, unexpectedly, a single product. The isolated product was proven to be identical with 6,7,8-triphenyl-2,3-dihydro-[1,2,4]triazolo[4,3-*b*]pyridazine-3-thione **3**. The latter compound was unequivocally prepared following the reported procedure [2], by refluxing **1** with carbon disulfide. Mechanistically, the formation of the bicyclic compound **3** from **1** involves the initial formation of **2** which undergoes immediate intramolecular nucleophilic attack of ring-2 nitrogen on the thione group with elimination of the phenylamino group. This mechanism was proved by converting **2** to **3** when boiled with butanol. Reaction of compound **3** with methyliodide under basic condition afforded 3-methylthio derivative **4** (Scheme 1).

Compound **1** reacted with ethyl chloroformate at room temperature; it produced 3-(2-ethoxycarbonylhydrazino)-4,5,6-triphenylpyridazine **5**. Heating of compound **5** up to its melting point gave compound **6** in 81% yield. Compound **6** could also be prepared by refluxing ethyl hydrazinoformate and 3-chloro-4,5,6-triphenylpyridazine as described earlier [2]. Reaction of **1** with chloroacetyl chloride

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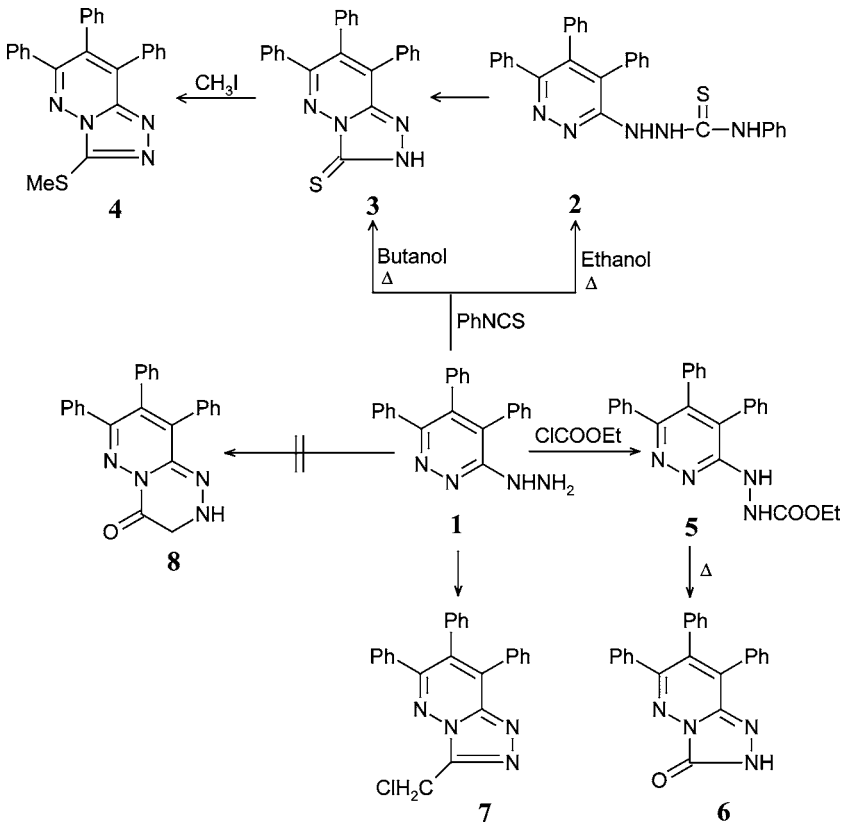


SCHEME 1

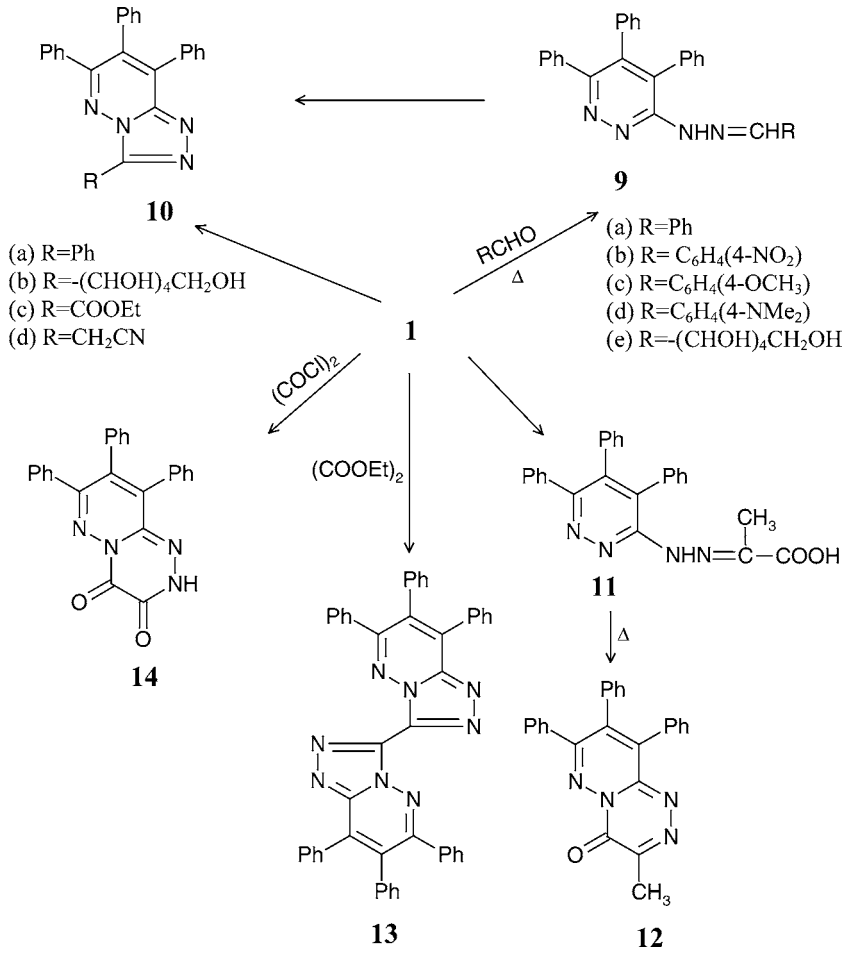
gave 3-chloromethyl-6,7,8-triphenyl-1,2,4-triazolo-[4,3-*b*]pyridazine **7** instead of the anticipated product **8**. The feasibility of chlorine atom in **7** to undergo nucleophilic displacement was proved by reaction with potassium cyanide giving 3-cyano-methyl-6,7,8-triphenyl-1,2,4-triazolo[4,3-*b*]pyrida-zine **10d** in good yield. The infrared analysis revealed the presence of cyano group at 2100 cm^{-1}.

Reaction of hydrazine **1** with aromatic aldehy-des yielded the corresponding hydrazones, also the condensation with D-glucose gave the corresponding hydrazone. The hydrazones **9a,e** subsequently un-derwent oxidative cyclization to give the correspond-ing 1,2,4-triazolo[4,3-*b*]pyridazine derivatives **10a,b**. (Scheme 2).

The reaction of hydrazine **1** with pyruvic acid yielded the hydrazone **11** which when heated to its melting point or upon refluxing with acetic acid it undergoes cyclodehydration to give 3-methyl-7,8,9-triphenylpyridazino[3,2-*c*]-as-triazin-4-one **12**. From the reaction of the hydrazine **1** with di-ethyloxalate, the product isolated (90% yield) was not the expected ethyl *s*-triazolo[4,3-*c*]pyridazine-3-carboxylate **10c**, but instead 3,3′-bis(triazolo[4,3-*c*]-pyridazine) derivative **13**, as evidenced from its ana-lytical and spectral data. However, when compound **1** was treated with oxalyl chloride afforded a prod-uct, which during purification by recrystallization from ethanol, we noticed the formation of another component as pointed out by TLC and change in the color of the alcohol solution. IR spectral analysis of the latter displayed no NH groups and showed an absorption band at 1720 cm^{-1} (C=O). The ^1H NMR spectrum showed signals at $\delta = 7.2–6.9$ (m, 15H, 3Ph), 4.8–4.4 (q, 2H, CH_2), and 1.2 (t, 3H, CH_3) ppm, so that the isolated material was iden-tified as ethyl triazolopyridazinecarboxylate **10c**. On the other hand, when the reaction was car-ried out in pyridine, the isolated product was iden-tified as 2,3,4-trihydro-7,8,9-triphenylpyridazino-[3,2-*c*]-1,2,4-triazine-3,4-dione **14**.

On heating equimolar amounts of **1** and diacetyl, it gave only the corresponding monohydrazone **15**. However, in the presence of 2 moles of **1** the corre-sponding dihydrazone **16** was produced. The same result was also obtained when the monohydrazone **15** was heated with the hydrazine **1** (Scheme 3).

Reaction of hydrazine **1** with phthalic acid an-hydride in ethanol afforded isoindole derivative **17**, while in acetic acid afforded *N*-phthalazine deriva-tive **18**. The hydrazone **19** was obtained by reaction of compound **1** with ethyl acetoacetate in ethanol,



SCHEME 2

while on fusion afforded pyrazolinylpyridazine **20a**, as confirmed by IR, ^{1}H NMR, and elemental analysis. In the same manner, on refluxing **1** with acetylacetone afforded **20b**. Reaction of hydrazine **1** with ethyl cyanoacetate in acetic acid afforded triazolo[4,3-*b*]pyridazine derivative **10d**, rather than pyrazolinylpyridazine **20c**. The structure of compound **10d** was ascertained by its spectral data and elemental analysis.

All the compounds synthesized were evaluated for insecticidal, fungicidal, bactericidal, and virucidal activities, but none of the test chemicals exhibited significant activity.

EXPERIMENTAL

All the melting points are uncorrected. The IR spectra of the compounds were recorded on a Perkin Elmer spectrophotometer model 1310, ^{1}H NMR spectra on a Perkin Elmer R12B spectrometer, and chemical shifts (δ) are in ppm relative to internal tetramethylsilane.

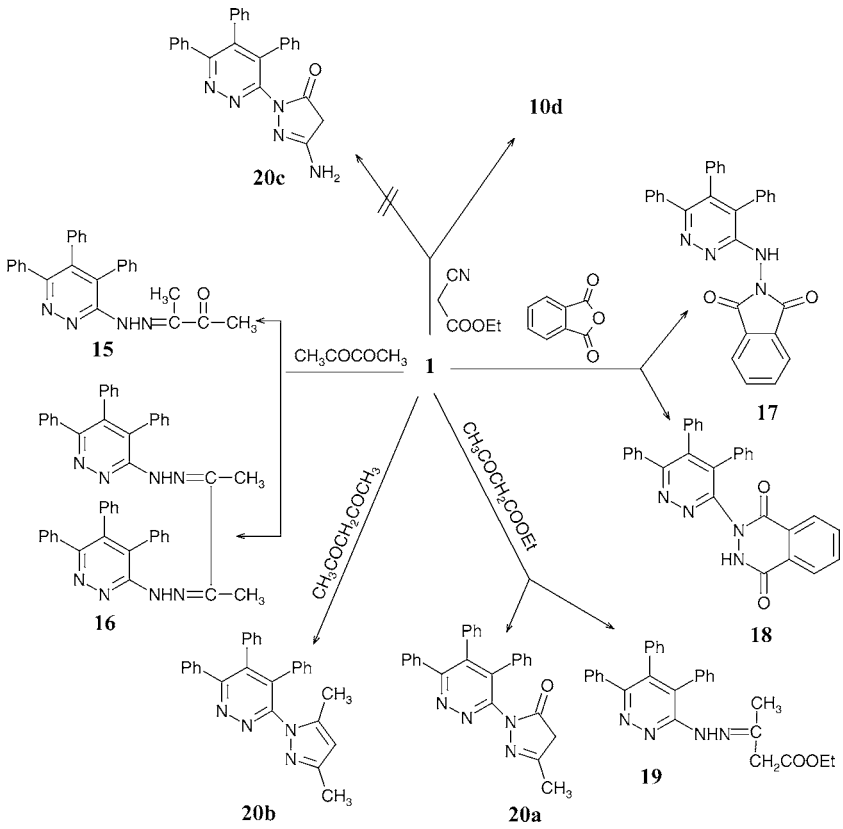
1-(4,5,6-Triphenylpyridazin-3-yl)-4-phenylthiosemicarbazide **2**

To a solution of compound **1** (1.69 g, 5 mmol) in ethanol (40 mL) phenylisothiocyanate (0.68 g, 5 mmol) was added; the mixture was refluxed for 6 h. After cooling the solid **2** was collected by filtration, 2.32 g (98%); mp 274–276° (1-butanol); IR (potassium bromide) ν 3290, 3100 (NH), 1635, 1575, 1555, 1520 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 9.6–9.5 (s, 3H, 3NH), 7.9–6.9 (m, 20H, Ar-H) ppm.

Anal. Calcd for $C_{29}H_{23}N_5S$: C, 73.55; H, 4.90; N, 14.79. Found: C, 73.40; H, 4.90; N, 14.70.

6,7,8-Triphenyl-2,3-dihydro-[1,2,4]triazolo-[4,3-b]pyridazine-3-thione **3**

Method A. To a solution of compound **1** (0.68 g, 2 mmol) in 1-butanol (20 mL), phenyl isothiocyanate (0.27 g, 2 mmol) was added. The mixture was refluxed for 4 h. Upon cooling the precipitated product was filtered to give 0.54 g (70%) of **3**, mp 262–264°



SCHEME 3

(methanol) (Lit. [4] 260–261°); IR: 3150 (NH), 1650 (C=N), 1515 (C=C), and 480 cm^{-1} (C=S).

Anal. Calcd for $C_{23}H_{16}N_4S$: C, 72.61; H, 4.24; N, 14.73. Found: C, 72.50; H, 4.10; N, 14.60.

Method B. A solution of compound **2** (1.00 g 2.11 mmol) in 1-butanol (20 mL) was refluxed for 4 h. Upon cooling the precipitated product was filtered to give 0.6 g, (75%) of **3**. It was identical with that prepared by method A.

3-Methylthio-6,7,8-triphenyl-1,2,4-triazolo-[4,3-b]pyridazine **4**

To a solution of compound **3** (1.9 g, 5 mmol) in ethanol (30 mL), a solution of potassium hydroxide (0.28 g in 2 mL of H_2O) and methyliodide (0.7 g, 5 mmol) was added. The mixture was stirred at r.t. overnight. The light yellow deposit was filtered to give 1.15 g (58%) of compound **4**; mp 204–205° (ethanol); IR: 3060 (ArH), 2930 (C–H), 1610 (C=N), and 1520 cm^{-1}; ^1H NMR (DMSO-d_6)δ (ppm): 7.8–7.6 (m, 15H, 3Ph) and 2.88 (s, 3H, CH_3).

Anal. Calcd for $C_{24}H_{18}N_4S$: C, 73.07; H, 4.60; N, 14.20. Found: C, 72.90; H, 4.50; N, 14.10.

3-(2-Ethoxycarbonylhydrazino)-4,5,6-triphenylpyridazine **5**

A mixture of compound **1** (1.69 g, 5 mmol) and ethyl chloroformate (10 mL) was stirred at r.t. for 3 h, the precipitate formed was filtered and dried to give 1.93 g (94%) of compound **5**; mp 147–148° (toluene); IR : 3210 (NH), 3110 (C–H), 1650 (C=O), and 1615 cm^{-1} (C=N).

Anal. Calcd for $C_{25}H_{22}N_4O_2$: C, 73.15; H, 5.40; N, 13.65. Found: C, 73.00; H, 5.30; N, 13.50.

6,7,8-Triphenyl-2H-[1,2,4]triazolo-[4,3-b]pyridazin-3-one **6**

Compound **5** (1.6 g, 4 mmol) was heated at 150° for 30 min. The residue was triturated with ethanol and the solid product was filtered, 1.1 g (75%) of compound **6**; mp 279–280° (ethanol) (Lit. [4] 280–281°).

3-Chloromethyl-6,7,8-triphenyl-1,2,4-triazolo[4,3-b]pyridazine **7**

To a solution of compound **1** (1.69 g, 5 mmol) in dimethylformamide (15 mL), chloroacetyl chloride

(0.57 g, 5 mmol) was added. The mixture was heated at 100° for 3 h. The cooled mixture was poured into water (100 mL). The solid product was collected by filtration, 1.69 g (85%) of **7**; mp 106–107° (ethanol), IR : 1630 (C=N) and 1550 cm^{-1} (C=C); ^1H NMR ($CDCl_3$): δ (ppm) : 7.5–6.8 (m, 15H, 3Ph) and 5.2 (s, 2H, CH_2).

Anal. Calcd for $C_{24}H_{17}ClN_4$: C, 72.63; H, 4.32; N, 14.12. Found: C, 72.50; H, 4.30; N, 14.10.

3-Cyanomethyl-6,7,8-triphenyl-1,2,4-triazolo[4,3-b]pyridazine **10d**

Method A. To a solution of compound **7** (2.0 g, 5 mmol) in ethanol (70 mL), potassium cyanide (0.33 g, 5 mmol) was added. The mixture was refluxed for 4 h and filtered. The solvent was evaporated, and the residue was crystallized from ethanol to give 1.7 g (87%) of **10d**; mp 152–153°; IR : 2100 (CN), 1628 (C=N), and 1523 cm^{-1} (C=C); ^1H NMR (DMSO-d_6): δ (ppm): 7.4–6.8 (m, 15H, 3Ph) and 2.8 (s, 2H, CH_2).

Anal. Calcd for $C_{25}H_{17}N_5$: C, 77.50; H, 4.42; N, 18.08. Found: C, 77.40; H, 4.30; N, 17.90.

Method B. A mixture of **1** (1.69 g, 5 mmol) and ethyl cyanoacetate (0.56 g, 5 mmol) in glacial acetic acid (20 mL) was refluxed for 3 h. The cooled reaction mixture was poured onto water (100 mL) followed by adding ammonium hydroxide until pH 7–8. The solid product was filtered, 1.78 g (92%) of **10d**. It was identical in every respect with that prepared by method A.

N-Arylidine-N′-(4,5,6-triphenylpyridazin-3-yl)hydrazine **9a-d**

General procedure: A mixture of **1** (1.69 g, 5 mmol) and the appropriate aldehyde (5 mmol) in ethanol (40 mL) was refluxed for 1 h. After cooling the precipitate was filtered and recrystallized from proper solvent.

N-Benzylidene-N′-(4,5,6-triphenylpyridazin-3-yl)-hydrazine **9a**. 67% yield; mp 232–234° (ethanol); IR: 3200 (NH), 1610 (C=N), and 1530 cm^{-1} (C=C).

Anal. Calcd for $C_{29}H_{22}N_4$: C, 81.66; H, 5.20; N, 13.14. Found: C, 81.60; H, 5.00; N, 13.00.

N-(4-Nitrobenzylidene)-N′-(4,5,6-triphenylpyridazin-3-yl)hydrazine **9b**. 70% yield; mp 266–267° (*n*-BuOH); IR : 3220 (NH), 1615 (C=N), 1560 and 1310 cm^{-1} (NO_2).

Anal. Calcd for $C_{29}H_{21}N_5O_2$: C, 73.87; H, 4.49; N, 14.85. Found: C, 73.80; H, 4.40; N, 14.70.

N-(4-Methoxybenzylidene)-N′-4,5,6-triphenylpyridazin-3-yl)hydrazine **9c**. 74% yield; mp 252–253° (*n*-BuOH); IR : 3200 (NH), 1610 (C=N) and 1525 cm^{-1} (C=C); ^1H NMR (DMSO-d_6): δ (ppm): 7.5–6.8 (m, 20H, 3Ph, 4H aromatic, NH), 6.3 (s, 1H, CH), and 3.8 (s, 3H, OCH_3).

Anal. Calcd for $C_{30}H_{24}N_4O$: C, 78.92; H, 5.30; N, 12.27. Found: C, 78.80; H, 5.10; N, 12.10.

N-(4-Dimethylaminobenzylidene)-N′-(4,5,6-triphenylpyridazin-3-yl)hydrazine **9d**. 90% yield; mp 238–239° (ethanol); IR : 3210 (NH), 1600 (C=N), 1515 and (C=C); ^1H NMR (DMSO-d_6): δ (ppm): 8.0–7.6 (m, 20H, 3Ph, 4H aromatic, NH), 6.5 (s, 1H, CH), and 2.8 (s, 6H, $2CH_3$).

Anal. Calcd for $C_{31}H_{27}N_5$: C, 79.29; H, 5.80; N, 14.91. Found: C, 79.20; H, 5.60; N, 14.80.

D-*Glucose, (4,5,6-triphenyl-3-pyridazinyl)-hydrazone* **9e**

To a solution of **1** (1.69 g, 5 mmol) in ethanol (50 mL), D-glucose (0.9 g, 5 mmol) and few drops of acetic acid were added. The mixture was refluxed for 1.5 h. The solid product, which separated out on cooling was filtered to give 1.9 g (76%); mp 187–188° (ethanol); IR : 3347 (OH), 3240 (NH), 1600 cm^{-1} (C=N); ^1H NMR : (DMSO-d_6) : δ (ppm): 7.4–6.8 (m, 16H, 3Ph, NH); 6.7 (s, 1H, NH=CH–), 5.0–3.35 (m, 11H, sugar-H).

Anal. Calcd for $C_{28}H_{28}N_4O_5$: C, 67.19; H, 5.64; N, 11.19. Found: C, 67.00; H, 5.40; N, 11.00.

3,6,7,8-Tetraphenyl-1,2,4-triazolo[4,3-b]-pyridazine **10a**

A solution of **9a** (2.1 g, 5 mmol) in glacial acetic acid (5 mL) was treated with bromine (0.8 g, 5 mmol) in acetic acid and stirred at r.t. for 30 min. The reaction mixture was diluted with water and filtered to obtain 1.88 g (90%) of **10a**; mp 202–203° (ethanol); IR: 1620 (C=N), 1520 cm^{-1} (C=C); ^1H NMR (DMSO-d_6): δ (ppm): 7.6–6.9 (m, 20H, 4Ph).

Anal. Calcd for $C_{29}H_{20}N_4$: C, 82.05; H, 4.75; N, 13.20. Found: C, 81.90; H, 4.70; N, 13.10.

3-Pentahydroxypentyl-6,7,8-triphenyl-1,2,4-triazolo[4,3-b]pyridazine **10b**

A 2 M solution of iron III chloride in ethanol (1 mL) was added dropwise to a boiling solution of **9e** (1.0 g, 2 mmol) in ethanol (100 mL). Heating was continued for 10 min. The mixture was then kept overnight at r.t. The pale yellow precipitate was filtered, washed with water, 0.8 g (80%) of **10b**; mp

168–169° (ethanol); IR: 3390–3260 (OH), 1611 (C=N) and 1520 cm^{-1} (C=C); ^1H NMR (DMSO-d_6): δ (ppm): 7.4–6.9 (m, 15H, 3Ph) and 5.63–3.10 (m, 11H, sugar-H).

Anal. Calcd for $C_{28}H_{26}N_4O_5$: C, 67.46; H, 5.26; N, 11.24. Found: C, 67.30; H, 5.10; N, 11.10.

2-(4,5,6-Triphenylpyridazin-3-yl)hydrazonopropionic Acid **11**

A stirred solution of **1** (1.0 g, 3 mmol) in acetic acid (10 mL) was treated with pyruvic acid (0.26 g, 3 mmol). The white precipitate that separated out immediately was filtered off and washed with water, affording 0.89 g (73%) of **11**; mp 162–163° (ethanol); IR : 3350 (OH), 1720 (C=O), 1600 (C=N), and 1525 cm^{-1} (C=C); ^1H NMR (DMSO-d_6): δ (ppm): 7.5–6.8 (m, 15H, 3Ph) and 1.8 (s, 3H, CH_3).

Anal. Calcd for $C_{25}H_{20}N_4O_2$: C, 73.51; H, 4.94; N, 13.72. Found: C, 73.40; H, 4.80; N, 13.60.

3-Methyl-7,8,9-triphenylpyridazino[3,2-c]-1,2,4-triazin-4-one **12**

Compound **11** (1.0 g, 2.4 mmol) was heated in oil bath at 150° for 10 min upon cooling to r.t. followed by trituration with ethanol. The solid product was filtered, 0.67 g (70%) of **12**; mp 288–289° (ethanol); IR: 1700 (C=O), 1620 (C=N), and 1515 cm^{-1} (C=C); ^1H NMR (DMSO-d_6): δ (ppm) : 7.6–6.9 (m, 15H, 3Ph) and 2.0 (s, 3H, CH_3).

Anal. Calcd for $C_{25}H_{18}N_4O$: C, 76.91; H, 4.65; N, 14.35. Found: C, 76.80; H, 4.60; N, 14.20.

3,3′-Bis(6,7,8-triphenyl-1,2,4-triazolo[4,3-b]-pyridazine) **13**

To a solution of **1** (2.0 g, 5.9 mmol) in acetic acid (30 mL), diethyl oxalate (15.0 g, 0.1 mol) was added. The mixture was refluxed for 1 h. The solid product, which separated out on cooling was filtered, 1.84 g (90%) of **13**; mp > 300° (DMF); IR : 1610 (C=N) and 1520 cm^{-1} (C=C); ^1H NMR (DMSO-d_6): δ (ppm): 7.6–7.0 (m, 30H, 6Ph).

Anal. Calcd for $C_{46}H_{30}N_8$: C, 79.52; H, 4.35; N, 16.13. Found: C, 79.40; H, 4.30; N, 16.00.

Ethyl 6,7,8-triphenyl-1,2,4-triazolo[4,3-b]-pyridazine-3-carboxylate **10c**

A mixture of **1** (2.0 g, 5.9 mmol) and oxalylchloride (15 mL) was stirred at r.t. for 30 min. The separated solid product was collected, then refluxed in ethanol (30 mL) for 5 min. The solid product, which separated out on cooling was filtered, 2.0 g (80%) of **10c**; mp 200–201° (ethanol); IR : 1720 (C=O), 1625 (C=N), and 1510 cm^{-1} (C=C); ^1H NMR (DMSO-d_6): δ (ppm): 7.2–6.9 (m, 15H, 3Ph), 4.8–4.4 (q, 2H, CH_2), and 1.2 (t, 3H, CH_3).

Anal. Calcd for $C_{26}H_{20}N_4O_2$: C, 74.27; H, 4.79; N, 13.33. Found: C, 74.10; H, 4.70; N, 13.20.

2,3,4-Trihydro-7,8,9-triphenylpyridazino[3,2-c]-1,2,4-triazine-3,4-dione **14**

To a solution of **1** (1.0 g, 3 mmol) in pyridine (15 mL), oxalyl chloride (0.4 g, 3 mmol) was added. The mixture was stirred at r.t. for 30 min. The reaction mixture was then poured onto water (100 mL). The separated solid product was filtered, 0.8 g (69%) of **14**; mp > 300° (ethanol); IR : 1720–1680 (2C=O), 1610 (C=N), and 1525 cm^{-1} (C=C); ^1H NMR ($CDCl_3$): δ (ppm): 7.8–6.3 (m, 15H, 3Ph).

Anal. Calcd for $C_{24}H_{16}N_4O_2$: C, 73.46; H, 4.11; N, 14.28. Found: C, 73.40; H, 4.00; N, 14.10.

3-[(4,5,6-Triphenylpyridazin-3-yl)-hydrazono]-butan-2-one **15**

A mixture of **1** (1.0 g, 3 mmol) and diacetyl (0.26 g, 3 mmol) in absolute ethanol (30 mL) was refluxed for 3 h. Upon cooling the solid product was filtered, 0.48 g (40%) of **15**; mp 257–258° (ethanol); IR: 3400–3250 (NH), 2980–2840 (CH), 1670 (C=O), 1620 (C=N), and 1490 cm^{-1} (C=C).

Anal. Calcd for $C_{26}H_{22}N_4O$: C, 76.83; H, 5.46; N, 13.78. Found: C, 76.70; H, 5.40; N, 13.60.

2,3-Butanedione-2,3-bis(4,5,6-triphenylpyridazin-3-ylhydrazone) **16**

Method A. By refluxing of compound **1** (6.77 g, 20 mmol) and diacetyl (0.86 g, 10 mmol) in glacial acetic acid (30 mL) for 3 h, upon cooling the solid product was filtered, 5.8 g (80%) of **16**; mp 172–173° (DMF); IR: 3410–3320 (NH), 2980–2930 (CH), 1620 (C=N), and 1510 cm^{-1} (C=C).

Anal. Calcd for $C_{48}H_{38}N_8$: C, 79.31; H, 5.27; N, 15.42. Found: C, 79.20; H, 5.00; N, 15.30.

Method B. By refluxing of compound **15** (0.8 g, 2 mmol) and **1** (1.0 g, 3 mmol) in glacial acetic acid (30 mL) for 3 h, upon cooling the solid product was filtered and crystallized from DMF to give 1.4 g (96%) of **16**. It was identical in every respect with that prepared by method A.

3-[N-(1,3-Dihydro-1,3-dioxo-2H-isoindol-2-yl)]amino-4,5,6-triphenylpyridazine **17**

A mixture of **1** (1.69 g, 5 mmol) and phthalic acid anhydride (0.74 g, 5 mmol) in absolute ethanol (50 mL)

was refluxed for 2 h. Upon cooling the solid product was filtered, to give 2.2 g (94%) of **17**; mp 257–258° (ethanol); IR: 3380 (NH), 1730 (C=O), 1630 (C=N), and 1550 cm^{-1} (C=C). ^1H NMR (DMSO-d_6): δ (ppm): 8.0 (s, 4H, aromatic protons) and 7.4–6.8 (m, 15H, 3Ph).

Anal. Calcd for $C_{30}H_{20}N_4O_2$: C, 76.91; H, 4.30; N, 11.96. Found: C, 76.90; H, 4.20; N, 11.80.

2-(4,5,6-Triphenylpyridazin-3-yl)phthalazine-1,4-dione **18**

A mixture of **1** (1.69 g, 5 mmol) and phthalic acid anhydride (0.74 g, 5 mmol) in glacial acetic acid (30 mL) was refluxed for 2 h. The cooled reaction mixture was diluted with water and filtered, 2.1 g (89%) of **18**; mp 262–263° (methanol); IR: 3180 (NH), 1720, 1660 (C=O groups), 1620 (C=N), and 1570 cm^{-1} (C=C); ^1H NMR (DMSO-d_6): δ (ppm): 9.5 (br, s, 1H, NH), 8.2–7.8 (m, 4H, aromatic protons), and 7.5–6.9 (m, 15H, 3Ph).

Anal. Calcd for $C_{30}H_{20}N_4O_2$: C, 76.91; H, 4.30; N, 11.96. Found: C, 76.80; H, 4.20; N, 11.90.

Ethyl 3-butanoate-(4,5,6-triphenylpyridazin-3-yl)hydrazone **19**

A mixture of compound **1** (1.0 g, 3 mmol) and ethyl acetoacetate (0.39 g, 3 mmol) was refluxed in absolute ethanol (30 mL) for 2 h. The solvent was then evaporated in vacuo, and the residue was triturated with diethylether. The solid product was filtered, 1.0 g (75%) of **19**; mp 175–176° (ethanol); IR: 3355 (NH), 1730 (C=O), 1627 (C=N), and 1550 cm^{-1} (C=C); ^1H NMR (DMSO-d_6): δ (ppm): 7.4–6.8 (m, 15H, 3Ph), 4.2–3.8 (q, 2H, $\underline{CH_2}CH_3$), 3.25 (s, 2H, $\underline{CH_2}COOC_2H_5$), 1.6 (s, 3H, CH_3), and 1.2 (t, 3H, $CH_2\underline{CH_3}$).

Anal. Calcd for $C_{28}H_{26}N_4O_2$: C, 74.65; H, 5.82; N, 12.44. Found: C, 74.60; H, 5.70; N, 12.30.

3-(3-Methyl-5-oxo-2-pyrazolin-1-yl)-4,5,6-triphenylpyridazine **20a**

A mixture of compound **1** (1.0 g, 3 mmol) and ethyl acetoacetate (0.5 g, 3.84 mmol) was heated at 150° for 10 min. The solid product separated on cooling was filtered, 1.0 g (84%) of **20a**; mp 152–153° (methanol); IR: 1645 (C=O amide), 1620 (C=N), and 1510 cm^{-1} (C=C); ^1H NMR (DMSO-d_6): δ (ppm): 7.4–6.8 (m, 16H, aromatic protons), 3.3 (br, s, 1H, OH), and 1.8 (s, 2H, CH_3).

Anal. Calcd for $C_{26}H_{20}N_4O$: C, 77.21; H, 4.98; N, 13.85. Found: C, 77.10; H, 4.90; N, 13.70.

3-(3,5-Dimethylpyrazol-1-yl)-4,5,6-triphenylpyridazine **20b**

A mixture of compound **1** (1.69 g, 5 mmol) and 2,4-pentanedione (0.5 g, 5 mmol) in absolute ethanol (50 mL) was refluxed for 5 h. The solid product separated on cooling was filtered, 1.39 g (69%) of **20b**; mp 172–173° (methanol); IR: 1625 (C=N) and 1560 cm^{-1} (C=C); ^1H NMR (DMSO-d_6): δ (ppm): 7.5–6.7 (m, 16H, aromatic protons) and 2.2 (s, 6H, $2CH_3$.

Anal. Calcd for $C_{27}H_{22}N_4$: C, 80.57; H, 5.51; N, 13.92. Found: C, 80.40; H, 5.40; N, 13.80.

Chemotherapeutic Activities

All the compounds synthesized were screened for antibacterial, antifungal, antiviral, and insecticidal activities, but none of the tested chemicals showed any significant activities in a primary screening.

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For part 7, see [5].

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