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# SYNTHESIS OF SOME NEW HETARYL-PYRANOPYRIDAZINES, CINNOLINES, AND HETARYLPYRIDAZINE DERIVATIVES

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*4-Acetyl-5,6-diphenylpyridazin-3(2H)-one was condensed with 6-chloro-3-formylchromone under different reaction conditions to yield the enone or pyranopyridazine. Both compounds were used in the synthesis of some new hetarylpyranopyridazines. Pyranodipyridazine was obtained via a sequence of reactions of 4-acetyl-5,6-diphenylpyridazin-3(2H)-one with diethyl carbonate, acetic anhydride, and 4-bromobenzenediazonium chloride. The reactions of pyridazinylbutane-1,3-dione with conc. $H_2SO_4$, $POCl_3$, hydrazines, hydroxylamine hydrochloride, cyanoacetamide, thiourea, and thiosemicarbazone were also studied.*

**Keywords:** cinnolines, pyranopyridazines, ring–chain tautomerism.

N-Containing heterocycles are of biological importance. The design of newer strategies for their synthesis is an important area of research in organic chemistry [1]. Pyridazines are an important class of nitrogen heterocycles, which are known for a wide range of biological activities [2]. It has been reported that pyridazinones displayed antinociceptive activity such as reduction of blood pressure [3], anti-inflammatory activity [4], inhibition of platelet aggregation [5], and positive inotropic effects [6].

Motivated by these facts and as a part of our program directed to the synthesis of some new pyridazine derivatives [7, 8] the present investigation deals with the combination of pyridazine with γ-pyrone in a molecular frame-work *via* different methods starting from 4-acetyl-5,6-diphenylpyridazin-3(2H)-one (**1**) [9].

Condensation of 4-acetyl-5,6-diphenylpyridazin-3(2H)-one (**1**) with 6-chloro- 3-formylchromone [10] (**2**) in sodium ethoxide solution afforded 4-[3-(6-chlorochromen-3-yl)prop-2-enoyl]-5,6-diphenylpyridazin-3(2H)-one (**3**) in good yield. Heating of compound **3** in boiling ethanol containing a catalytic amount of piperidine and intramolecular Michael addition of the lactam OH group to the olefinic CH=CH bond [11] yielded the ring–chain tautomer of compound **3** 7-(6-chloro-4-oxochromen-3-yl)-3,4-diphenyl-6,7-dihydropyrano[2,3-*c*]-pyridazin-5-one (**4**)**.** Compound **4** was also obtained directly on heating compound **1** with compound **2** in ethanol-containing piperidine as a catalyst (Scheme 1).

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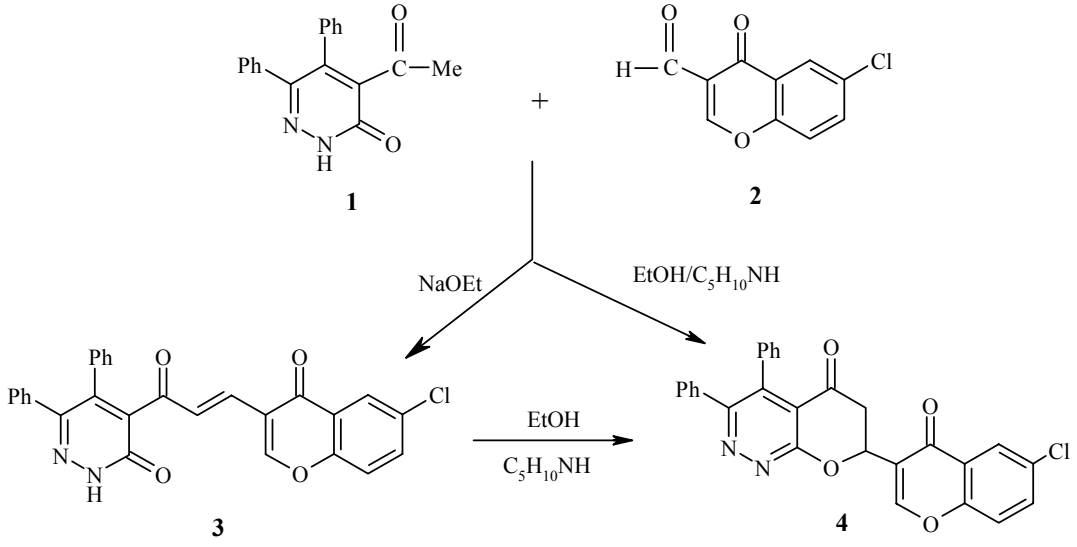
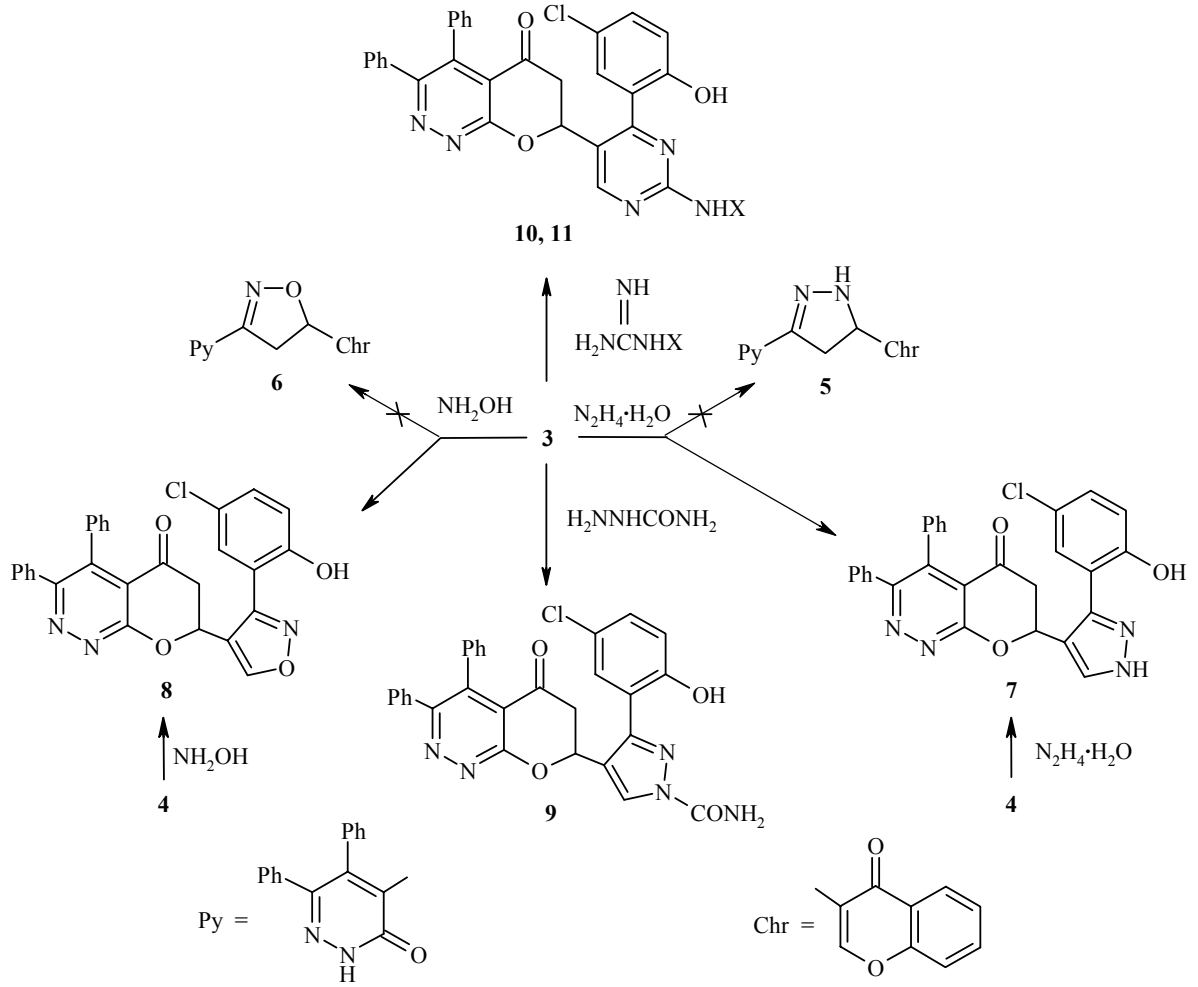
Scheme 1



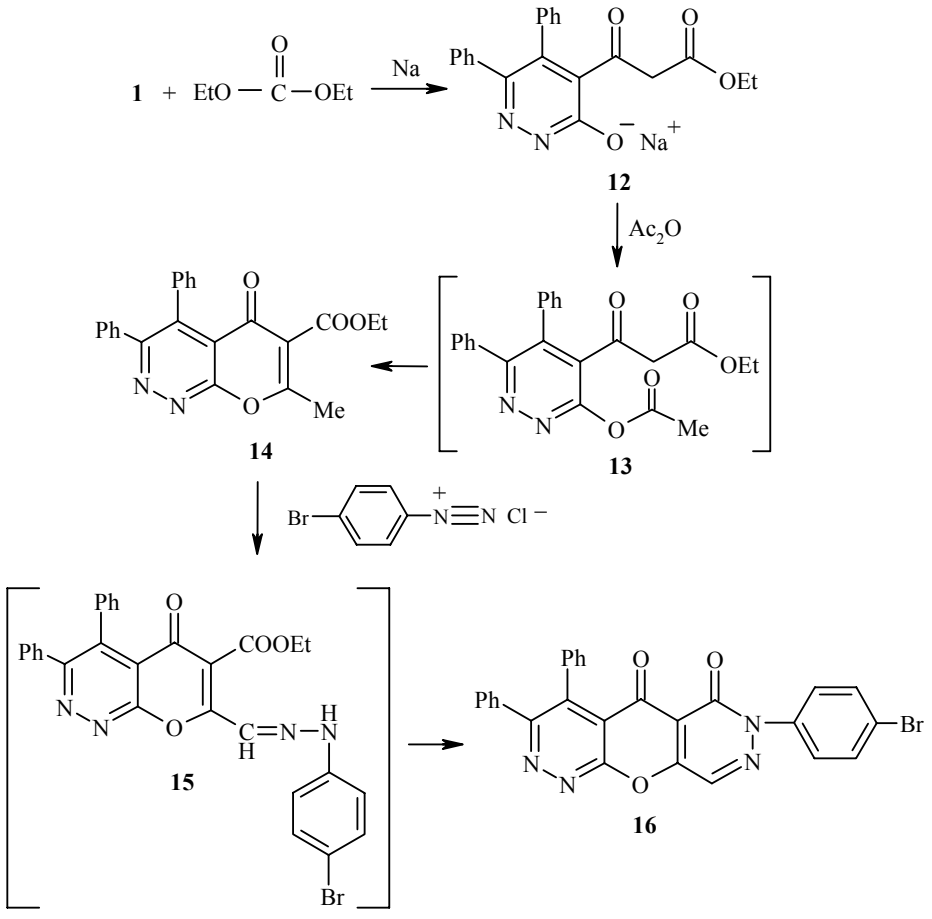

Scheme 2




**10** X = H, **11** X = CN

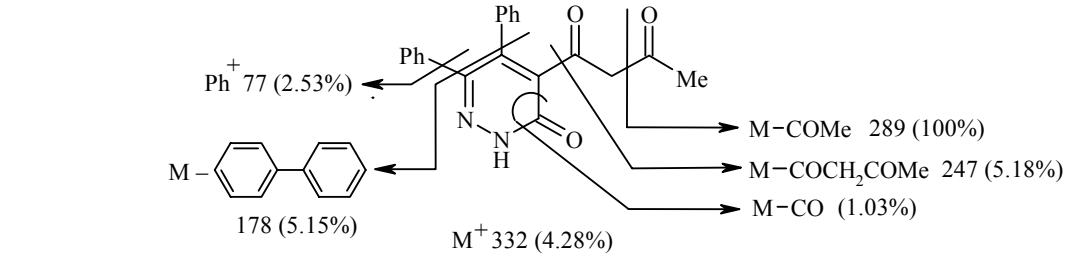
The structure of compound **4** was deduced from its $^1$H NMR spectrum (DMSO-$d_6$), which revealed the presence of a triplet at δ 4.81-5.10 and a doublet at 3.15-3.40 ppm, which indicated the presence of $CHCH_2$ moiety formed as a result of addition of lactam OH to the β-position of the CH=CH bond. In continuation of our work on biheterocyclic enones [12, 13], azoles [14], and pyrimidines [15, 16], we observed that the pyridazinyl-chromenylenone **3** exhibited an interesting reaction with nitrogen bifunctional reagents different from the normal characteristic reactions of α,β-unsaturated ketonic moiety. Thus, when compound **3** was subjected to react with hydrazine hydrate and hydroxylamine in boiling ethanol containing triethylamine, the expected pyrazoline **5** or isoxazoline **6** were not formed but instead of them pyrazolylpyranopyridazine **7** and isoxazolpyranopyridazine **8** derivatives were produced. Formation of compounds **7** and **8** involves nucleophilic attack by the amino group to position 2 of the chromone ring to form the pyrazole and isoxazole ring and addition of the lactam OH to the β-position of the CH=CH bond to form the pyranopyridazine moiety under the same reaction conditions. The structure of compounds **7** and **8** was confirmed by their identity with an authentic sample prepared by the reaction of compound **4** with hydrazine hydrate or hydroxylamine, respectively. Similarly, the pyrazolylpyranopyridazine derivative **9** was obtained on treatment of either compound **3** or compound **4** with semicarbazide hydrochloride in boiling ethanol. Moreover, interaction of compound **3** or compound **4** with guanidine hydrochloride and/or cyanoguanidine afforded the respective pyrimidinylpyranopyridazines **10** and **11**. The IR spectrum of compound **11** showed a band at 2218 $cm^{-1}$ attributed to the CN function in addition to those reported for the pyranopyridazines. All of the compounds **7**-**11** gave a violet coloration with neutral $FeCl_3$ solution, which proved the presence of the phenolic OH group arising from the broken γ-pyrone ring in chromone (Scheme 2).

Scheme 3

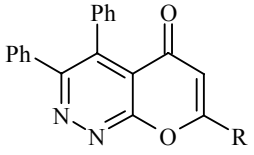


In searching for another route for the synthesis of the target compounds, it has been found that the acetylpyridazine **1** reacted with diethyl carbonate in the presence of finely divided sodium to yield ethyl 3-oxo-3-(3-hydroxy-5,6-diphenyl-2H-pyridazin-4-yl)propanoate (**12**) in the form of the sodium salt. Its mass spectrum showed the highest *m*/*z* value at 384 attributed to $M^+ + 23$. Acetylation of compound **12** with acetic anhydride–sodium acetate mixture afforded the intermediate **13**, which underwent a ring closure to give 6-ethoxycarbonyl-7-methyl-5-oxo-3,4-diphenylpyrano[2,3-*c*]pyridazine (**14**)**.** Also, the reaction of compound **14** with *p*-bromobenzenediazonium chloride gave the hydrazone intermediate **15**, which on cyclocondensation yielded the pyranodipyridazine derivative **16** (Scheme 3).

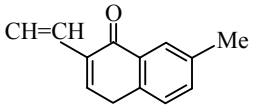
Moreover, 1-(3-oxo-5,6-diphenyl-2H-pyridazin-4-yl)butane-1,3-dione (**17**), which was obtained from the reaction of 4-acetyl-5,6-diphenylpyridazin-3(2H)-one (**1**) with ethyl acetate under Claisen condensation, was used to synthesize some new pyranopyridazines and cinnolines. The structure of compound **17** was established on the basis of its correct elemental analysis and spectroscopic data. Its $^1$H NMR spectrum (DMSO-$d_6$) displayed signals at δ 3.36 and 1.92 ppm attributed to $CH_2$ and $CH_3$, respectively. The mass spectrum of compound **17** showed a molecular ion peak at *m/z* 332 and base peak at 289 (100%), which was formed as a result of loss of the acetyl radical ($CH_3CO^{\bullet}$) from the molecular ion (*cf.* fragmentation pattern). When compound **17** was treated with concentrated sulfuric acid, ring closure of the pyrano[2,3-*c*]pyridazine-5-one derivative **18** took place. The mass spectrum of compound **18** exhibited a peak at *m/z* 314 (100%) corresponding to both molecular ion and base peak, which showed the higher stability of the mentioned compound. The presence of a methyl group at position **7** was deduced from its ability to condense with both benzaldehyde and 3-formyl-6-methylchromone [10] to afford 7-styrylpyrano[2,3-*c*]pyridazin-5-one **19** and 1-(chromon-3-yl)-2-(pyranopyridazin-7-yl)ethene **20** derivatives, respectively.




**17**

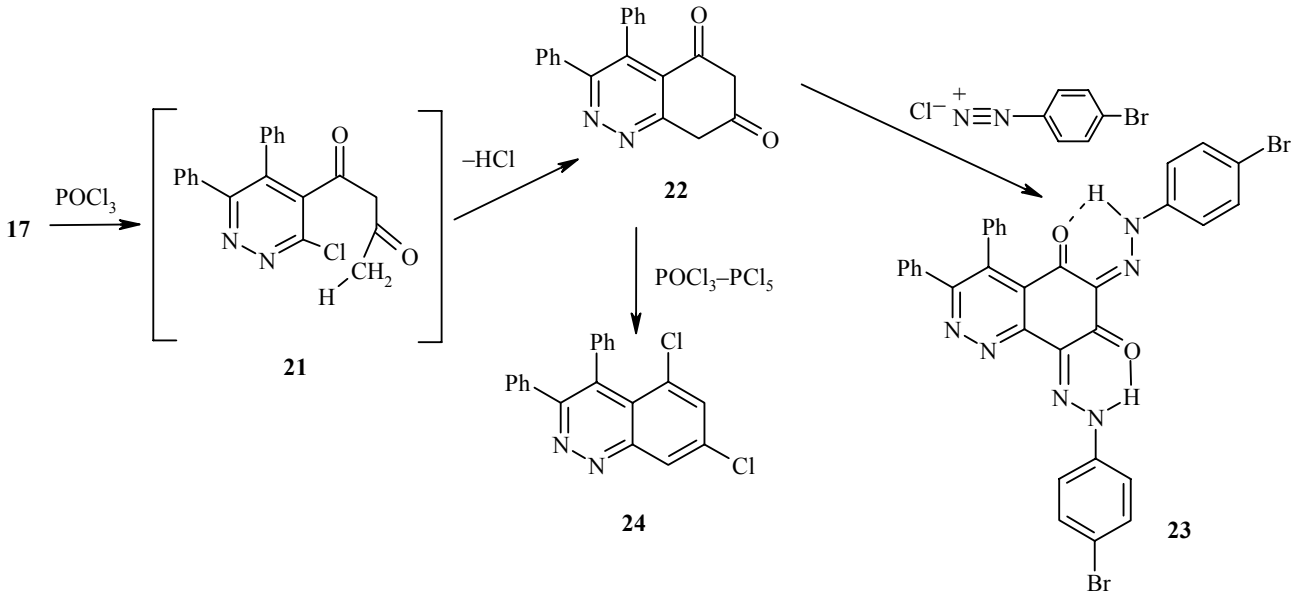



**18 – 20**

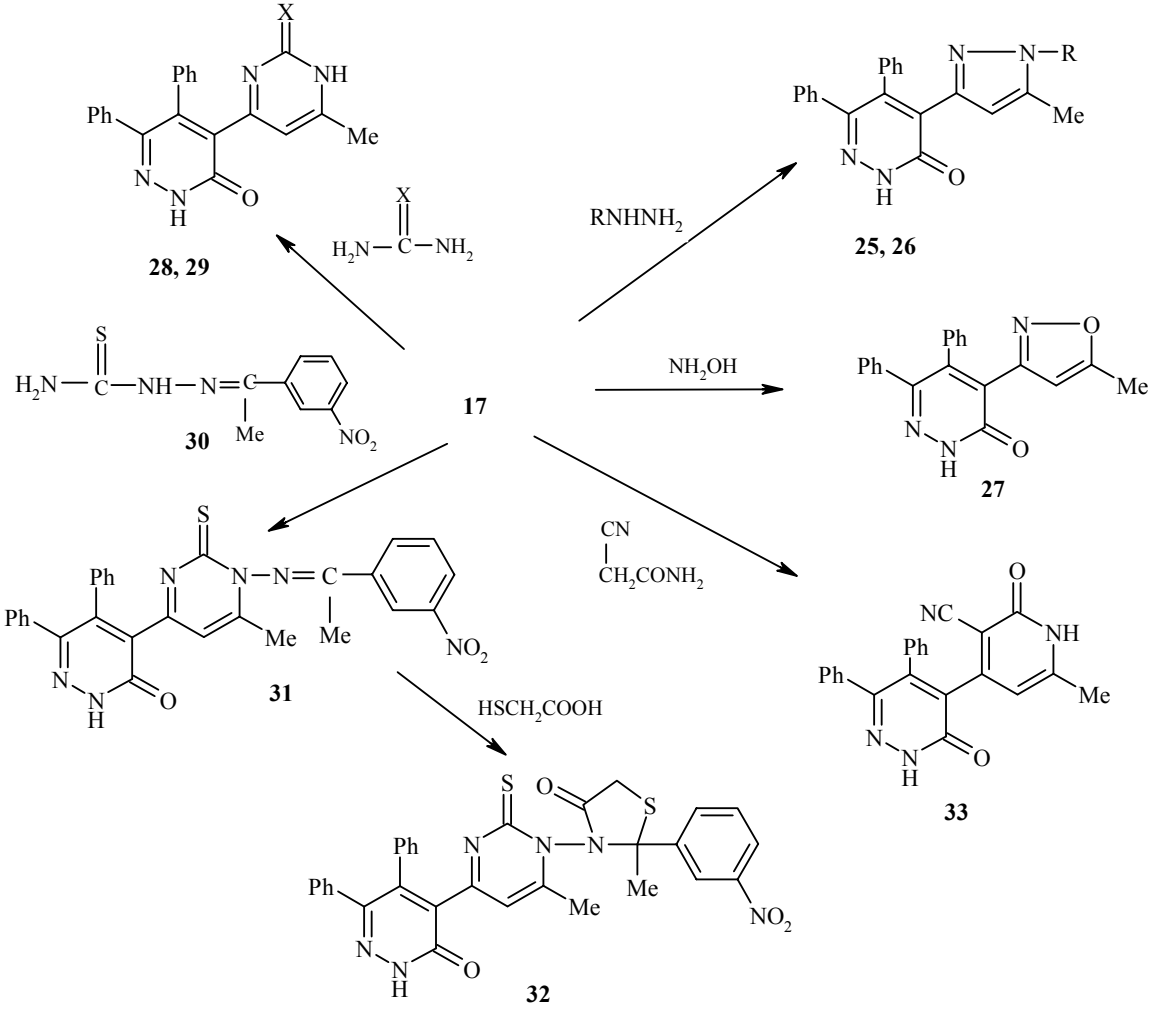
**18** R = Me, **19** R = CH=CH–Ph, **20** R = 


Treatment of compound **17** with phosphorous oxychloride in a water bath furnished a compound showing a peak at *m/z* 314 (100%) in its mass spectrum corresponding to both molecular ion and base peak, indicating its higher stability under electron impact spectroscopy and represented by the structure of compound **22**. The formation of compound **22** was explained *via* the formation of 3-chloropyridazine derivative **21** as an intermediate, which underwent cyclocondensation with the removal of hydrogen chloride molecule to yield the tetrahydrocinnolinedione derivative **22**. The presence of two active methylene groups in compound **22** was proved by its $^1$H NMR spectrum, which exhibited a broad singlet at 5.02–5.43 ppm attributed to four protons. Compound **22** was coupled with 4-bromobenzenediazonium chloride to afford 6,8-bis[(4-bromophenyl)-hydrazono]-3,4-diphenylcinnoline-5,7-dione **23**, which showed a higher stability due to the intramolecular hydrogen bonding. 5,7-Dichloro-3,4-diphenylcinnoline **24** was obtained on treatment of compound **22** with a $POCl_3$–$PCl_5$ mixture (Scheme 4).

Scheme 4



Scheme 5



**25** R = H, **26** R = Ph; **28** X = S, **29** X = NH

In view of the wide biological activities of pyrazoles and pyrimidines, it was of interest to combine pyrazole and pyrimidine moieties with pyridazine in a molecular frame which this may enhance their biological applications. Therefore, when compound **17** was subjected to reaction with hydrazine hydrate and phenylhydrazine, pyrazolylpyridazinones **25** and **26** were obtained, respectively, while interaction of compound **17** with hydroxylamine hydrochloride gave isoxazolylpyridazinone **27.**

On the other hand, treatment of compound **17** with thiourea and guanidine hydrochloride in boiling ethanol containing catalytic amount of triethylamine afforded the pyrimidinylpyridazinones **28** and **29**, respectively.

Moreover, when compound **17** was allowed to react with N-1-(3-nitrophenyl)ethylidenethiosemi-carbazone **30**, the thioxopyrimidinylpyridazinone derivative **31** was obtained. When it reacted with thioglycolic acid in dry benzene, cyclocondensation took place to yield oxothiazolidinyl pyrimidinylpyridazinone derivative **32**.

Furthermore, 4-[3-cyano-6-methyl-2-oxo-1H-pyridin-4-yl]-5,6-diphenyl-2H-pyridazinone **33** was synthesized by the reaction of compound **17** with cyanoacetamide in boiling ethanol containing a catalytic amount of triethylamine (Scheme 5). The IR spectrum of compound **33** showed absorption bands at 2220 $cm^{-1}$ corresponding to the C≡N group.

## EXPERIMENTAL

Melting points were determined on a Stuart SMP10 apparatus. The IR spectra were recorded on FTIR Brücher Vector 22 spectrophotometer using the KBr wafer technique. $^1$H NMR spectra were measured on a Varian Gemini spectrophotometer (200 MHz) in DMSO-$d_6$ using TMS as internal standard. Mass spectra were obtained using a gas chromatography/mass spectrometry GCMS Hewlett Packard 5988 Shimadzu instrument at 70 eV. Elemental analyses were done at the Microanalytical Center, Cairo University.

**4-Acetyl-5,6-diphenylpyridazin-3(2H)-one (1)** was prepared according to the reported method [9].

**6-Chloro-3-formylchromone (2)** was prepared according to the reported method [10].

**4-[3-(6-Chloro-4-oxochromen-3-yl)prop-2-enoyl]-5,6-diphenylpyridazin-3(2H)-one (3).** To a solution of sodium ethoxide prepared from sodium (0.23 g, 10 mmol) in absolute ethanol (20 ml), equimolar amounts of compounds **1** and **2** (2.9 and 2.08 g, 10 mmol) were added. The reaction mixture was refluxed for 6 h, then cooled and neutralized with dil. HCl. The solid obtained was filtered off and dried to give compound **3** (4.2 g, 87%) as yellow crystals; mp 97°C (ethanol). IR spectrum, ν, $cm^{-1}$: 3186 (NH); 3056 (CH olefinic), 1713, 1640 (2C=O), 1604 (C=N). $^1$H NMR spectrum, δ, ppm: 7.11–7.88 (13H, m, H Ar); 8.02 (1H, s, H-2 pyrone); 8.26, 8.69 (2H, 2s, CH=CH); 13.60 (1H, s, enolic OH pyridazine). Mass spectrum, *m/z* (*I*, %): 480.5 [$M^+$] (0.91), 290 (100), 391 (4.08), 383 (3.42), 191(60.80), 105 (16.69), 77 (33.50). Found, %: C 70.05; H 3.66; Cl 7.39; N 5.88. $C_{28}H_{17}ClN_2O_4$. Calculated, %: C 69.93; H 3.54; Cl 7.39; N 5.83.

**7-(6-Chloro-4-oxochromen-3-yl)-3,4-diphenyl-6,7-dihydropyrano[2,3-*c*]pyridazin-5-one (4).** Method A. A mixture of compound **1** (2.9 g, 10 mmol) and compound **2** (2.08 g, 10 mmol) in ethanol (20 ml) and a few drops of piperidine were refluxed for 8 h. The reaction mixture was cooled and then poured into crushed ice, and the solid obtained was filtered off to give compound **4** (2.64 g, 55%) as yellow crystals; mp 226°C (ethanol–water). IR spectrum, ν, $cm^{-1}$: 3470 (OH), 3031 (CH olefinic), 1703, 1688 (2C=O), 1616 (C=N). $^1$H NMR spectrum, δ, ppm (*J*, Hz): 3.15-3.40 (2H, d, *J* = 6, H-6); 4.81–5.10 (1H, t, *J* = 6, H-7); 7.01–7.71 (13H, m, H Ar); 8.02 (1H, s, H-2 chromone). Mass spectrum, *m/z* (*I*, %): 480.5 [$M^+$] (6.00), 289 (100), 385 (42.09), 317 (17.5), 282 (50.19), 182 (54.26), 77 (59.9). Found, %: C 70.15; H 3.65; Cl 7.59; N 5.88. $C_{28}H_{17}ClN_2O_4$. Calculated, %: C 69.93; H 3.54; Cl 7.39; N 5.83.

Method B. Compound **3** (2.4 g, 10 mmol) in absolute ethanol (20 ml) containing a few drops of piperidine was heated under reflux for 3 h. The solid obtained was collected and crystallized from ethanol–water to give compound **4**; mp 266-267°C and mixed mp 265°C.

**7-[3-(5-Chloro-2-hydroxyphenyl)pyrazol-4-yl]-3,4-diphenyl-6,7-dihydropyrano-[2,3-*c*]pyridazin-5-one (7).** Method A. A mixture of compound **3** (4.8 g, 10 mmol) and hydrazine hydrate (0.5 g, 10 mmol) in absolute ethanol (20 ml) was refluxed for 6 h. The solid obtained was filtered to give compound **7** (4.1 g, 83%) as yellowish-white crystals; mp 295–296°C (ethanol). IR spectrum, ν, $cm^{-1}$: 3652 (OH, phenolic), 3190 (NH), 1703 (C=O pyrone), 1614 (C=N). $^1$H NMR, δ, ppm (*J*, Hz): 3.13–3.38 (2H, d, *J* = 6, H-6); 4.79–5.07 (1H, t, *J* = 6, H-7); 7.00–7.53 (14H, m, H Ar and H-3 pyrazole); 9.68 (1H, s, OH); 9.91 (1H, s, NH). Mass spectrum, *m/z* (*I*, %): 494.5 [$M^+$] (2.09), 288 (100), 396 (6.00), 317 (17.5), 382 (1.71), 245 (4.10), 77 (6.74). Found, %: C 68.10; H 4.35; Cl 7.35; N 11.45. $C_{28}H_{19}ClN_4O_3$. Calculated, %: C 67.95; H 3.84; Cl 7.18; N 11.32.

Method B. A mixture of compound **4** (4.8 g, 10 mmol) and hydrazine hydrate (0.5 g, 10 mmol) in absolute ethanol (20 ml) was refluxed for 6 h. The solid obtained was filtered off and recrystallized from ethanol to give compound **7** (4.1 g, 83%) as yellowish-white crystals; mp 295°C and mixed mp 295°C.

**7-[3-(5-Chloro-2-hydroxyphenyl)isoxazol-4-yl]-3,4-diphenyl-6,7-dihydropyrano[2,3-*c*]pyridazin-5-one (8).** Method A. A mixture of compound **3** (4.8 g, 10 mmol) and hydroxylamine hydrochloride (0.7 g, 10 mmol) in ethanol (20 ml) containing a few drops of DMF was heated under reflux for 5 h. The solid obtained was filtered off to give compound **8** (4.2 g, 84%) as pale yellow crystals; mp above 300°C (ethanol). IR spectrum, ν, $cm^{-1}$: 3447 (OH), 3002 (CH olefinic), 1656 (C=O), 1626 (C=N). $^1$H NMR spectrum, δ, ppm (*J*, Hz): 3.13-3.35 (2H, d, *J* = 6, H-6); 4.80–5.15 (1H, t, *J* = 6, H-7); 7.38–7.95 (13H, m, H Ar); 8.34 (1H, s, H-5 isoxazole); 10.95 (1H, s, OH). Mass spectrum, *m/z* (*I*, %): 495.5 [$M^+$] (1.7), 55 (100), 391 (1.62), 333 (12.26), 288 (13.36), 264 (9.19), 77 (17.90). Found, %: C 67.55; H 3.65; Cl 7.46; N 8.55. $C_{28}H_{18}ClN_3O_4$. Calculated, %: C 67.81; H 3.636; Cl 7.16; N 8.47.

Method B. A mixture of compound **4** (4.8 g, 10 mmol) and hydroxylamine hydrochloride (0.7 g, 10 mmol) in ethanol (20 ml) containing a few drops of DMF was heated under reflux for 5 h. The solid obtained was filtered off and recrystallized from ethanol to give compound **8** (84%) as pale-yellow crystals; mp and mixed mp above 300°C.

**7-[1-Carboxamido-3-(5-chloro-2-hydroxyphenyl)pyrazol-4-yl]-3,4-diphenyl-6,7-dihydropyrano-[2,3-*c*]pyridazin-5-one (9).** A mixture of compound **3** (4.8 g, 10 mmol) and semicarbazide hydrochloride (1.11 g, 10 mmol) in ethanol (20 ml) containing a few drops of triethylamine was heated under reflux for 4 h. The solid obtained was filtered off to give compound **9** (3.6 g, 67%) as yellow crystals; mp 211°C (ethanol–water). IR spectrum, ν, $cm^{-1}$: 3408 (OH), 3295–3207 ($NH_2$), 1702, 1659 (2C=O), 1624 (C=N). Mass spectrum, *m/z* (*I*, %): 537.5 [$M^+$] (6.39), 289 (100), 523 (6.60), 477 (7.42), 368 (34.14), 188 (53.25), 77 (33.20). Found, %: C 64.62; H 3.35; Cl 6.50; N 13.25. $C_{29}H_{20}ClN_5O_4$. Calculated, %: C 64.74; H 3.72; Cl 6.60; N 13.02.

**7-[2-Amino-4-(5-chloro-2-hydroxyphenyl)pyrimidin-5-yl]-3,4-diphenyl-6,7-dihydropyrano-[2,3-*c*]pyridazin-5-one (10).** A mixture of compound **3** (4.8 g, 10 mmol), guanidine hydrochloride (1.0 g, 10 mmol), and a few drops of piperidine in DMF (30 ml) was heated under reflux for 3 h. The mixture was left to cool at room temperature, and the solid product so formed was collected to give compound **10** (2.7 g, 51%) as pale-brown crystals; mp 209°C (ethanol–water). IR spectrum, ν, $cm^{-1}$: 3484 ($OH_,$), 3281–3186 ($NH_2$), 1713 (C=O), 1614 (C=N). Mass spectrum, *m/z* (*I*, %): 521.5 [$M^+$] (2.39), 288 (100), 477 (29.88), 465 (7.71), 391(57.54), 286 (32.89), 133 (13.48), 97 (26.51). Found, %: C 67.05; H 3.35; Cl 6.80; N 13.88. $C_{29}H_{20}ClN_5O_3$. Calculated, %: C 66.73; H 3.83; Cl 6.81; N 13.42.

**7-[4-(5-Chloro-2-hydroxyphenyl)-2-cyanoaminopyrimidin-5-yl]-3,4-diphenyl-6,7-dihydropyrano-[2,3-*c*]pyridazin-5-one (11).** A mixture of compound **3** (4.8 g, 10 mmol) and cyanoguanidine (0.84 g, 10 mmol) in absolute ethanol (20 ml) containing a few drops of piperidine was heated under reflux for 4 h. The solid obtained was filtered off to give compound **11** (3.9 g, 71%) as brown crystals; mp 227°C (ethanol). IR spectrum, ν, $cm^{-1}$: 3486 (OH), 3231 (NH), 2204 (CN), 1713 (C=O). Mass spectrum, *m/z* (*I*, %): 546.5 [$M^+$] (13.48), 479 (16), 384 (31.56), 300 (18.85), 288 (57.54), 134 (44.87), 58 (48.19). Found, %: C 65.98; H 3.35; Cl 6.60; N 15.55. $C_{30}H_{19}ClN_6O_3$. Calculated, %: C 65.87; H 3.48; Cl 6.50; N 15.37.

**Sodium salt of ethyl 3-(3-hydroxy-5,6-diphenyl-2H-pyridazin-4-yl)-3-oxo-propanoate (12).** A mixture of compound **1** (2.9 g, 10 mmol), finely divided sodium (0.46 g, 20 mmol), and diethyl carbonate (20 ml) was refluxed for 4 h. The reaction mixture on neutralization with diluted AcOH was filtered off to give compound **12** (2.2 g, 56%) as pale yellow crystals; mp > 300°C (water). IR spectrum, ν, $cm^{-1}$: 3470 (OH, H–bonded), 2931 (CH aliphatic), 1703 (C=O ester), 1614 (C=N). $^1$H NMR spectrum, δ, ppm (*J*, Hz): 1.05 (3H, t, *J* = 7.5, $CH_3$); 1.71 (2H, s, $COCH_2CO$); 3.41–3.61 (2H, q, *J* = 7.5, $OCH_2$); 7.01-7.71 (10H, m, H Ar). Mass spectrum, *m/z* (*I*, %): 384 [$M^+$] (56.00), 385 [M+1] (16.58), 177 (100), 383 (92.09), 317 (17.5), 282 (52.79), 152 (24.26), 77 (39.91). Found, %: C 65.98; H 4.35; N 7.38. $C_{21}H_{17}N_2O_4Na$. Calculated, %: C 65.63; H 4.43; N 7.29.

**6-Ethoxycarbonyl-7-methyl-5-oxo-3,4-diphenylpyrano[2,3-*c*]pyridazine (14).** A mixture of compound **12** (3.84 g, 10 mmol), acetic anhydride (10 ml), and sodium acetate (0.82 g, 10 mmol) was refluxed for 6 h. The reaction mixture was poured gradually into crushed ice. The solid obtained was filtered off to give compound **14** (3.1 g, 81%) as yellow crystals; mp 81–82°C (ethanol). IR spectrum, ν, $cm^{-1}$: 3085 (CH aromatic), 2980 (CH aliphatic), 1705 (C=O ester), 1643 (C=O pyrone), 1411 (C–O–C). Mass spectrum, *m/z* (*I*, %): 386 [$M^+$] (2.47), 57 (100), 368 (1.92), 279 (2.90), 149 (37.78), 97 (51.45), 77 (2.30). Found, %: C 71.68; H 4.55; N 7.58. $C_{23}H_{18}N_2O_4$. Calculated, %: C 71.50; H 4.66; N 7.25.

**1-(4-Bromophenyl)-7,8-diphenylpyridazino[4,5-*b*]pyrano[2,3-*c*]pyridazine-9,10-dione (16) .** An ice cold solution of 4-bromobenzenediazonium chloride (3.3 g, 15 mmol) (prepared from the reaction of sodium nitrite, hydrochloric acid, and *p*-bromoaniline) was added dropwise to an ice cold solution of compound **14** (3.86 g, 10 mmol) in ethanol (20 ml) containing sodium acetate (0.82 g, 10 mmol). The solid obtained was filtered off to give compound **16** (2.9 g, 55%) as dark brown crystals; mp 255-256°C (ethanol). IR spectrum, ν, $cm^{-1}$: 3088 (CH, aromatic), 1652 (C=O pyridazinone), 1400 (C–O–C). Mass spectrum, *m/z* (*I*, %): 523 [$M^+$] (3.90), 55 (100), 417 (19.86), 388 (13.92), 289 (14.43), 149 (84.00), 77 (56.20). Found, %: C 61.55; H 3.01; Br 15.50; N 10.44. $C_{27}H_{15}BrN_4O_3$. Calculated, %: C 61.95; H 2.87; Br 15.30; N 10.71.

**1-(3-Oxo-5,6-diphenyl-2H-pyridazin-4-yl)butane-1,3-dione (17).** A mixture of compound **1** (2.9 g, 10 mmol), finely divided sodium metal (0.28 g, 12 mmol), and dry sodium acetate (1.64 g, 20 mmol) was refluxed for 6 h. The reaction mixture was kept at room temperature overnight then poured into dilute acetic acid. The solid obtained was washed with water and dried to give compound **17** (2.8 g, 83%) as pale yellow crystals; mp 281=282°C (ethanol). IR spectrum, ν, $cm^{-1}$: 3191 (NH), 2994 (CH aliphatic), 1646 (C=O), 1580 (C=N). $^1$H NMR spectrum, δ, ppm (*J*, Hz): 1.92 (3H, s, $CH_3$); 3.36 (2H, s, $CH_2$); 7.1–7.5 (10H, m, H Ar); 13.01 (1H, s, enolic OH, pyridazine). Mass spectrum, *m/z* (*I*, %): 332 [$M^+$] (4.28), 289 (100), 304 (1.03), 247 (5.18), 196 (1.82), 189 (6.68), 129 (2.77), 89 (2.15), 77 (2.53). Found, %: C 72.55; H 4.89; N 8.66. $C_{20}H_{16}N_2O_3$. Calculated, %: C 72.29; H 4.82; N 8.43.

**7-Methyl-3,4-diphenylpyrano[2,3-*c*]pyridazin-5-one (18).** A mixture of compound **17** (3.32 g, 10 mmol) and concentrated sulfuric acid (10 ml) was stirred for 5 min at room temperature. The reaction mixture was poured into crushed ice. The solid obtained was filtered off to give compound **18** (2.8 g, 89%) as dark-brown crystals; mp 190-192°C (ethanol–water). IR spectrum, ν, $cm^{-1}$: 2996 (CH aliphatic), 1648 (C=O), 1580 (C=N) 1294 (C–O pyran). Mass spectrum, *m/z* (*I*, %): 314 [$M^+$] (100), 285 (8.78), 229 (8.20), 189 (34.66), 97 (12.287), 77 (12.24), 57 (21.6). Found, %: C 76.65; H 4.89; N 8.66. $C_{20}H_{14}N_2O_2$. Calculated, %: C 76.43; H 4.46; N 8.92.

**3,4-Diphenyl-7-styrylpyrano[2,3-*c*]pyridazin-5-one (19).** A mixture of compound **18** (3.14 g, 10 mmol) and benzaldehyde (1.6 g, 12 mmol) in ethanol (20 ml) containing a few drops of concentrated hydrochloric acid was heated under reflux for 6 h. The solid obtained upon cooling was collected to give compound **19** (2.3 g, 57%) as brown crystals; mp 116-118°C (ethanol). IR spectrum, ν, $cm^{-1}$: 3059 (CH olefinic), 1699 (C=O), 1648, 1580 (C=N and C=C), 1277 (C–O pyran). Mass spectrum, *m/z* (*I*, %): 402 [$M^+$] (4.30), 377 (100), 256 (12.24), 188 (32.19), 157 (14.04), 129 (38.30), 77 (19.38). Found, %: C 80.99; H 4.56; N 6.66. $C_{27}H_{18}N_2O_2$. Calculated, %: C 80.60; H 4.48; N 6.97.

**1-(6-Methyl-4-oxo-chromen-3-yl)-2-(4-oxo-3,4-diphenylpyrano[2,3-*c*]pyridazin-7-yl)ethene (20).** The titled compound was obtained by the same method applied for compound **19** using 6-chloro-3-formylchromone instead of benzaldehyde. Compound **20** (4.2 g, 86%) was recrystallized from ethanol as brown crystals; mp 105–106°C. IR spectrum, ν, $cm^{-1}$: 3059 (CH olefinic), 2927 (CH aliphatic), 1697, 1654 (2C=O), 1610 (C=N), 1281 (C–O pyran). Mass spectrum, *m/z* (*I*, %): 484 [$M^+$] (1.34 %), 185 (100), 460 (3.13), 431 (2.3), 330 (8.15), 314 (22.07) 227 (13.30), 160 (29.26), 77 (22.87). Found, %: C 76.67; H 4.25; N 5.82. $C_{31}H_{20}N_2O_4$. Calculated, %: C 76.86; H 4.13; N 5.79.

**3,4-Diphenyl-6,8-dihydrocinnoline-5,7-dione (22).** A mixture of compound **17** (3.32 g, 10 mmol) and phosphorus oxychloride (5 ml) was refluxed in a water bath for 2 h. The reaction mixture was cooled and poured gradually onto crushed ice. The solid obtained was filtered off and dried to give compound **22** (2.85 g, 91%) as dark-brown crystals; mp 242°C (DMF–water). IR spectrum, ν, $cm^{-1}$: 3424 (OH enolic), 3057 (CH olefinic), 1700-1648 (C=O), 1585 (C=N). $^1$H NMR spectrum, δ, ppm: 5.02–5.43 (4H, br. s, H-6, H-8); 7.28 (10H, m, H Ar). Mass spectrum, *m/z* (*I*, %): 314 [$M^+$] (100), 287 (54.41), 265 (15.25), 227 (11.93), 129 (32.62), 77 (18.37). Found, %: C 76.98; H 4.35; N 8.88. $C_{20}H_{14}N_2O_2$. Calculated, %: C 76.43; H 4.46; N 8.92.

**6,8-Bis[(4-bromophenyl)hydrazono]-3,4-diphenylcinnoline-5,7-dione (23).** 4-Bromobenzenediazonium chloride (5.25 g, 25 mmol) (prepared from the reaction of hydrochloric acid, sodium nitrite, and 4-bromoaniline) was added to an ice cold solution of compound **22** (3.14 g, 10 mmol) in ethanol (20 ml) containing sodium chloride (1.16 g, 20 mmol). The solid obtained was filtered off to give compound **23** (4.3 g, 63%) as brown crystals; mp > 300°C (DMF). IR spectrum, ν, $cm^{-1}$: 3650-3150 (NH, OH hydrogen bonded), 3058 (CH aromatic), 1652 (C=O). Mass spectrum, *m/z* (*I*, %): 680 [$M^+$] (1.20), 313 (13.10), 577 (36.65), 551 (30.61), 466 (10.58), 499 (11.00). Found, %: C 56.55; H 3.01; Br 23.24; N 12.44. $C_{32}H_{20}Br_2N_6O_2$. Calculated, %: C 56.47; H 2.94; Br 23.53; N 12.35.

**5,7-Dichloro-3,4-diphenylcinnoline (24).** A mixture of compound **22** (3.14 g, 10 mmol), phosphorous oxychloride (10 ml), and phosphorus pentachloride (2 g) was refluxed in water bath for 6 h. The reaction mixture was cooled and poured gradually onto crushed ice. The solid obtained was filtered off to give compound **24** (2.35 g, 67%) as yellow crystals; mp 288-289°C (1-propanol). IR spectrum, ν, $cm^{-1}$: 3055 (CH aromatic), 1617 (C=N). Mass spectrum, *m/z* (*I*, %): 351 [$M^+$] (12.60), 313 (100), 262 (17.25), 236 (27.14), 211 (10.65), 129 (42.12), 77 (16.55). Found, %: C 58.55; H 4.31; Cl 20.19; N 7.44. $C_{20}H_{12}Cl_2N_2$. Calculated, %: C 68.38; H 3.42; Cl 20.23; N 7.98.

**4-(5-Methyl-1H-pyrazol-3-yl)-5,6-diphenylpyridazin-3(2H)-one (25).** A mixture of compound **17** (3.32 g, 10 mmol) and hydrazine hydrate (0.6 g, 12 mmol) in absolute ethanol (20 ml) was refluxed for 4 h. The reaction mixture was cooled and poured gradually onto crushed ice. The solid obtained after cooling was filtered off to give compound **25** (2.9 g, 88%) as colorless crystals; mp 250-252°C (ethanol). IR spectrum, ν, $cm^{-1}$: 3279, 3159 (NH), 2926 (CH aliphatic), 1641 (C=O), 1587 (C=N). $^1$H NMR spectrum, δ, ppm: 2.03 (3H, s, $CH_3$); 6.09 (1H, s, H-4 pyrazole); 7.13-7.20 (10H, m, H Ar); 12.94 (1H, s, NH pyrazole); 13.58 (1H, s, enolic OH pyridazine). Mass spectrum, *m/z* (*I*, %): 328 [$M^+$] (100), 286 (8.34), 266 (5.29), 202 (7.59), 77 (12.17) 57 (5.92). Found, %: C 73.31; H 4.86; N 16.88. $C_{20}H_{16}N_4O$. Calculated, %: C 73.17; H 4.88; N 17.07.

**4-(5-Methyl-1-phenylpyrazol-3-yl)-5,6-diphenylpyridazin-3(2H)-one (26).** This compound was prepared by the same manner used for compound **25** using phenylhydrazine instead of hydrazine hydrate. Compound **26** (2.8 g, 72%) was recrystallized from ethanol; mp above 300°C. IR spectrum, ν, $cm^{-1}$: 3291 (NH), 2911 (CH aliphatic), 1647 (C=O), 1597 (C=N). $^1$H NMR spectrum, δ, ppm: 2.22 (3H, s, $CH_3$); 6.15 (1H, s, H-4 pyrazole); 6.96-7.40 (15H, m, H Ar); 13.54 (1H, s, enolic OH pyridazine). Mass spectrum, *m/z* (*I*, %): 404 [$M^+$] (100), 327 (29.37), 300 (41.63) 258 (13.70), 169 (24.78), 77 (45.8). Found, %: C 77.27; H 4.73; N 13.66. $C_{26}H_{20}N_4O$. Calculated, %: C 77.23; H 4.95; N 13.86.

**4-(5-Methylisoxazol-3-yl)-5,6-diphenylpyridazin-3(2H)-one (27).** A mixture of compound **17** (3.32 g, 10 mmol) and hydroxylamine hydrochloride (0.7 g, 10 mmol) in ethanol (20 ml) containing a few drops of triethylamine was refluxed for 5 h. The solid obtained upon cooling was filtered off and dried to give compound

**27** (2.85 g, 87%) as colorless crystals; mp 255-256°C (ethanol). IR spectrum, ν, $cm^{-1}$: 3292 (NH), 3003 (CH aromatic), 2924 (CH aliphatic), 1646 (C=O pyridazinone). Mass spectrum, *m/z* (*I*, %): 329 [$M^+$] (14.44), 330 [M+1] (3.44), 287 (100), 227 (11.93), 289 (10.96), 176 (20.75) 149 (19.64), 77 (0.36). Found, %: C 72.98; H 4.35; N 12.85. $C_{20}H_{15}N_3O_2$. Calculated, %: C 72.95; H 4.56; N 12.77.

**4-(6-Methyl-1H-2-thioxopyrimidin-4-yl)-5,6-diphenylpyridazin-3(2H)-one (28).** This compound was prepared by the same method used in preparing compound **25** using thiourea instead of hydrazine hydrate. It was crystallized from absolute ethanol (2.57 g, 69%) as yellowish crystals; mp 203-205°C. IR spectrum, ν, $cm^{-1}$: 3191 (NH), 2994 (CH aliphatic), 1646 (C=O), 1580 (C=N), 1193 (C=S). $^1$H NMR spectrum, δ, ppm (*J*, Hz): 1.97 (3H, s, $CH_3$); 5.66 (1H, s, H-5 pyrimidine); 7.12-7.30 (10H, m, H Ar); 13.64, 13.77 (2H, 2s, 2NH). Mass spectrum, *m/z* (*I*, %): 372 [$M^+$] (0.23), 369 [M–3] (1.82), 289 (100), 77 (7.92), 57 (15.29). Found, %: C 67.56; H 4.45; N 15.22; S 8.55. $C_{21}H_{16}N_4OS$. Calculated, %: C 67.74; H 4.30; N 15.05; S 8.60.

**4-(2-Imino-6-methyl-1H-pyrimidin-4-yl)-5,6-diphenylpyridazin-3(2H)-one (29).** This compound was prepared by the same method used for compound **25** using guanidine hydrochloride instead of hydrazine hydrate. Compound **29** (2.4 g, 67%) was recrystallized from ethanol as brownish-red crystals; mp 215–216°C. IR spectrum, ν, $cm^{-1}$: 3422, 3298 and 3190 (NH and $NH_2$), 2993 (CH aliphatic), 1647 (C=O), 1580 (C=N). $^1$H NMR spectrum, δ, ppm: 1.97 (3H, s, $CH_3$); 5.67 (1H, s, H-5 pyrimidine); 7.12–7.23 (10H, m, H Ar); 13.60, 13.77 (2H, s, 2NH pyrimidine); 13.78 (1H, s, enolic OH pyridazine). Mass spectrum, *m/z* (*I*, %): 355 [M+] (8.45), 289 (100), 129 (13.15), 89 (22.07), 77 (24.41). Found, %: C 70.70; H 4.69; N 19.66. $C_{21}H_{17}N_5O$. Calculated, %: C 70.99; H 4.79; N 19.72.

**4-[*α*-(3-Nitrophenylethylideneamino)-6-methyl-2-thioxopyrimidin-4-yl]-5,6-diphenylpyridazin-3(2H)-one (31).** This compound was prepared by the same method applied for compound **25** using N-1-(*m*-nitrophenylethylidene)thiosemicarbazide **30** (obtained from condensation of acetophenone with thiosemicarbazide). Compound **31** (3.3 g, 62%) was crystallized from ethanol as colorless crystals; mp 212-213°C. IR spectrum, ν, $cm^{-1}$: 3370, 3219 (NH), 2996 (CH aliphatic), 1646 (C=O), 1603 (C=N), 1180 (C=S). $^1$H NMR spectrum, δ, ppm: 1.97 (3H, s, 6-$CH_3$ pyrimidine); 2.39 (s, 3H, $CH_3$); 5.65 (s, 1H, H-5 pyrimidine); 7.11-7.61 (14H, m, H Ar); 10.41 (1H, s, NH). Mass spectrum, *m/z* (*I*, %): 534 [$M^+$] (30), 310 (100), 521 (17.86), 500 (33.33), 295 (55.95), 334 (52.76), 56 (19.05). Found, %: C 65.37; H 4.32; N 15.80; S 6.00. $C_{29}H_{22}N_6O_3S$. Calculated, %: C 65.17; H 4.12; N 15.73; S 5.99.

**4-{6-Methyl-1-[(2-methyl-2-(3-nitrophenyl)-4-oxothiazolidin-3-yl]-2-thioxo-1,2-dihydropyrimidin-4-yl}-5,6-diphenylpyridazin-3(2H)-one (32).** A mixture of compound **31** (5.35 g, 10 mmol) and thioglycolic acid (1.1 g, 12 mmol) in dry benzene was refluxed in water bath for 4 h. The solid obtained was collected to give compound **32** (3.84 g, 63%) as colorless crystals; mp 218-220°C (ethanol). IR spectrum, ν, $cm^{-1}$: 3369 (OH enolic thiazolidinone), 3214 (NH), 2975 (CH aliphatic), 1637 (C=O), 1602 (C=N). $^1$H NMR spectrum, δ, ppm: 2.02 (3H, s, 6-$CH_3$ pyrimidine); 2.38 (3H, s, 2-$CH_3$, thiazolidinone); 7.06–8.62 (15H, m, H Ar and H-5 pyrimidine); 10.42 (1H, s, enolic OH thiazolidinone); 13.58 (1H, s, enolic OH pyridazine). Mass spectrum, *m/z* (*I*, %): 608 [$M^+$] (22.3), 388 (20.27), 333 (14.70), 238 (22.05). Found, %: C 60.90; H 4.01; N 13.67; S 10.36. $C_{31}H_{24}N_6O_4S_2$. Calculated, %: C 61.18; H 3.95; N 13.82; S 10.53.

**4-(3-Cyano-6-methyl-2-oxo-1,2-dihydropyridin-4-yl)-5,6-diphenylpyridazin-3(2H)-one (33).** A mixture of compound **17** (3.32 g, 10 mmol) and cyanoacetamide (1 g, 12 mmol) in absolute ethanol (20 ml) containing a catalytic amount of triethylamine was heated under reflux for 4 h. The solid obtained upon cooling was collected to give compound **33** (3.26 g, 83%) as yellow crystals; mp 201–203°C (ethanol). IR spectrum, ν, $cm^{-1}$: 3407 (OH enolic pyridine), 3192 (NH), 2967 (CH aliphatic), 2270 (C≡N), 1646 (C=O), 1580 (C=N) $cm^{-1}$. $^1$H NMR spectrum, δ, ppm: 2.05 (3H, s, $CH_3$); 5.64 (1H, s, H-3 pyridine); 7.11–7.26 (10H, m, H Ar); 7.66 (1H, s, NH pyridine); 13.63 (1H, s, enolic OH pyridazine). Mass spectrum, *m/z* (*I*, %): 380 [$M^+$] (0.22), 289 (100), 332 (8.08), 304 (8.51), 290 (24.71), 77 (20.01). Found, %: C 72.50; H 4.15; N 14.55. $C_{23}H_{16}N_4O_2$. Calculated, %: C 72.63; H 4.21; N 14.74.

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