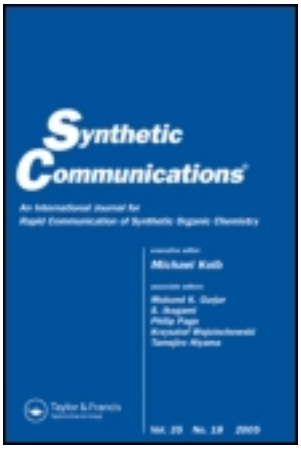

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Facile Route for the Synthesis of Pyridazine Derivatives: Unexpected Pathway to Benzothiazole, Benzimidazole, and Triazole Derivatives

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Facile Route for the Synthesis of Pyridazine Derivatives: Unexpected Pathway to Benzothiazole, Benzimidazole, and Triazole Derivatives

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Abstract: 4-Amino-5-arylmethylidene-3-phenyl-pyridazin-6-ones **7** have been synthesized and reacted with selected nucleophile reagents such as phenyl hydrazine, semicarbazide, semithiocarbazide, cyanoacetohydrazide, 2-aminothiophenol, and 2-phenylenediamine in ethanol triethyl-amine solution. An unexpected 1-phenyl-3-arylaziridene **10**, 3-aryl-5-oxo(thio)-1,2,4-triazole **21**, 4-amino-3-aryl-6-hydroxy-pridazine **27**, 2-arylbenzothiazole **30a–c**, and 2-arylbenzimidazole **30d–f** have been obtained, respectively. Also, 2-aminothiophenol and 2-phenylenediamine were reacted with *N*-phenylmethylidene-2-cyanoacetohydrazide **2**, affording the new 1,4-benzodiazepine derivatives **35.**

Keywords: 4-Aminopyridazine, 2-aminothiophenol, phenylaziridine, *N*-phenylmethylidene-2-cyanoacetohydrazide, 1,2,4-triazole

N-arylmethylidene-2-cyanoacetohydrazides are versatile intermediates for the synthesis of a variety of heterocyclic systems.[1,2] In continuation of our interest in the synthesis of polyfunctionally substituted heterocyclic compounds,[3–8] we report herein a facile and new one-pot synthesis of the title compounds.

The reaction of known *N*-phenylmethylidene-2-cyanoacetohydrazide[1] **2** with aromatic aldehydes in ethanolic piperidine solution at reflux temperature afforded a product identified as **7**, as is shown in Scheme 1. The desired target

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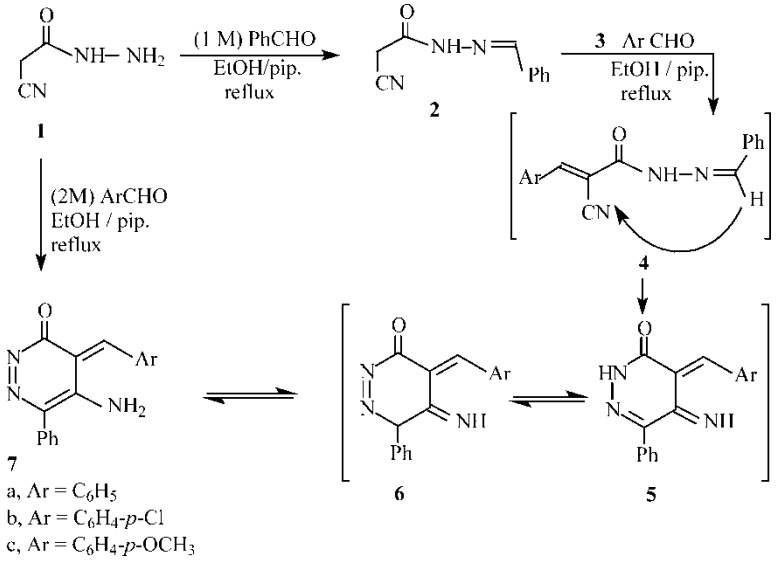
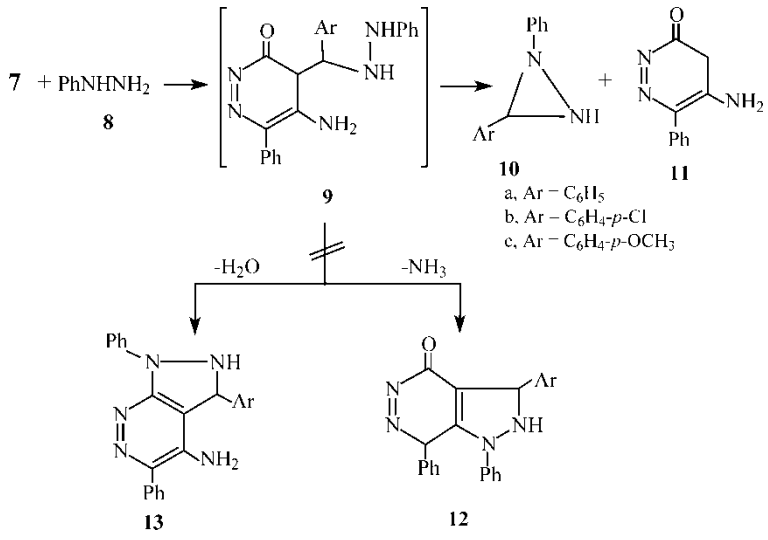


Scheme 1.

was compound **4** because it contains an α,β-unsaturated ketone with cyano function at the α-position and also contains Schiff's moiety. The nonisolable intermediate **4** readily cyclized via intramolecular cycloaddition of benzylic hydrogen into cyano function to afford the pyridazine **7** via its isomers **5**, **6**. Pyridazine **7** was obtained directly via reaction of **1** with two moles of aromatics aldehydes under the same reaction pathway. The structures of **7a–c** were based on analytical and spectroscopic data. The IR spectra of **7a–c** revealed absorption bands at 3390–3380 and 1684–1690 cm^{-1}, assigned for amino and carbonyl groups, respectively. The MS of **7a** showed m/z at 275 (M^+, 25), 247 ($M-N_2$, 5), 171 (35), 156 (25), 130 (35). The ^1H NMR of **7a** showed signals at 7.1–7.9 ppm for aromatic protons and at 9.3 ppm assigned for NH_2 protons. However, it thought that the new pyridazine **7** represents a cyclic α,β-unsaturated ketone system and would undergo the classical and known reactions of this system. So, reaction with phenyl hydrazine **8**, semicarbazide **17a**, semithiocarbazide **17b**, cyanoacetohydrazide **22**, 2-aminothiophenol **28a**, and 2-phenylendiamine **28b** have been carried out.

Reaction of **7** with phenyl hydrazine **8** afforded two different products separated by fractional crystallization from methanol. The insoluble product showed m/z at 196 as molecular ion, whereas it revealed an absorption band at ν 3311 cm^{-1} assigned to NH group. However, the soluble product revealed m/z at 187 (M^+, 80), and two intense absorption bands were recorded at ν 3356 and 1689 cm^{-1} due to NH_2 and C=O groups, respectively (Scheme 2). It is plausible that the mechanistic pathway that accounted for the formation of **10** and **11** is shown in Chart 1. It is seemed that the intermediate **9**



Scheme 2.

formed via Michael addition on the activated double bond is highly unstable and may split into two fragments, **14** and **16**. A nucleophilic attack of hydrazine nitrogen on the benzyl carbon leads to the azirdinium cation **15**, which releases a hydrogen ion to the pyridazine anion **16** to finally yield both **10** and **11**. The fragmentation patteren of the MS of both **10a** and **11** may support the proposed structures. Thus, the MS of **10a** showed m/z at 196 (M^+, 100), 119 (M-Ph, 20), and 103 (M–$PhNH_2$, 7), whereas the MS

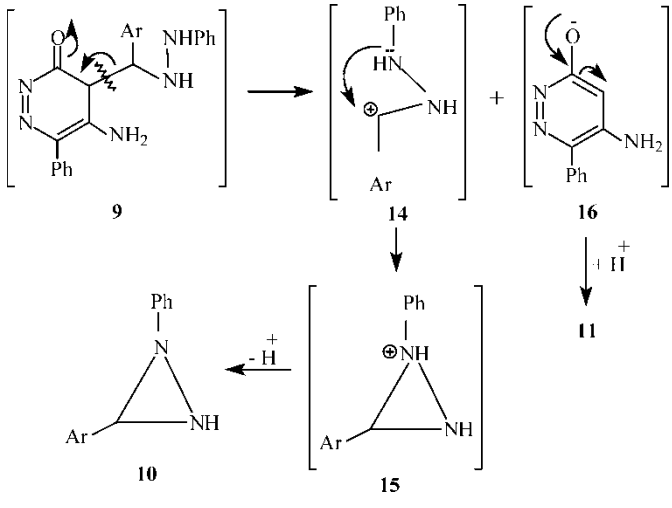


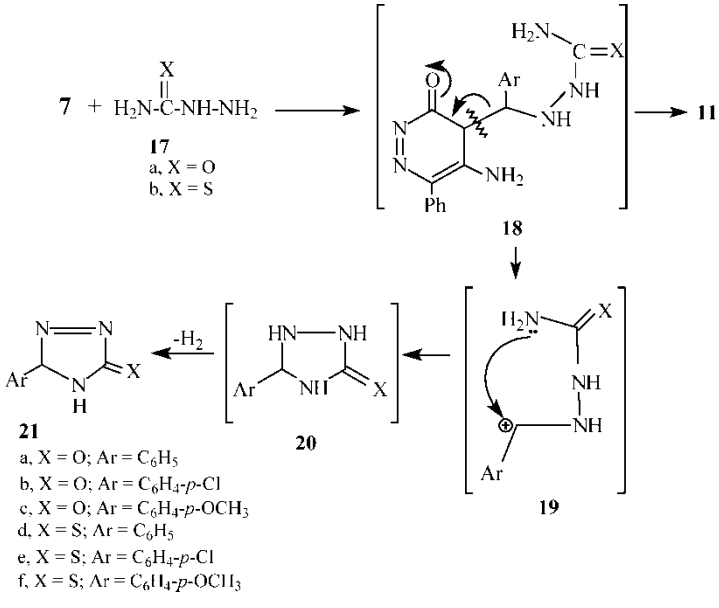
Chart 1.

of **11** revealed m/z at 187 (M^+, 80), 171 (M–NH_2, 25), and 110 (M-Ph, 30). However, the expected products (**12** or **13**) have been not found.

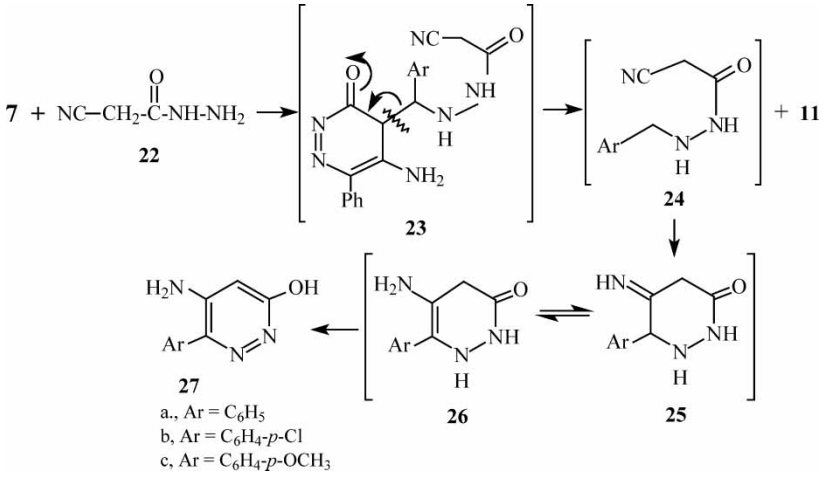
However, semicarbazide **17a** and semithiocarbazide **17b** were reacted with **7** under the same reaction conditions to yield a colorless product during reflux. The MS showed m/z at 163 (M^{+2}, 50). The IR spectrum revealed absorption bands at ν 3194 and 1688 cm^{-1} due to NH and CO groups, respectively. It is seemed that the intermediate **18** underwent breaking to yield pyridazine compound **11** under the same previous mechanism, and the formed semicarbazide cation readily undergoes intramolecular cycoladdition to the 1,2,4-triazole compound **21** as shown in Scheme 3. The ^1H NMR of **21a** showed signals at 6.5 and 10.3 ppm due to H-3 and NH and multiplets at 7.1–7.9 ppm for aryl protons, respectively. The mass fragmentation pattern supports the proposed structure as revealed M^{+2} at 163 (50), 117 (M-$CONH_2$, 100), 101 (M–H_2NCONH_2, 65), 93 (50), and 77 (60).

Reaction of **7** with cyanoacetohydrazide **22** is shown in Scheme 4. Michael addition of amine function on the activated double bond yielded the intermediate **23**, which underwent splitting into the pyridazine **11** and the nonisolable fragment **24**. An intramolecular cycloaddition led to the 4-aminopyridazine derivatives **27a–c** via their isomers **25**, **26**. The MS of **27a** showed m/z at 187 (100). The IR spectrum revealed broad bands at 3350, 3335, and 3310 cm^{-1} assigned for OH and NH_2 groups, respectively.

However, the reaction of **7** with 2-aminothiophenol **28a** and 2-phenyldiamine **28b** afforded 2-phenylbenzothiazoles **30a–c** and



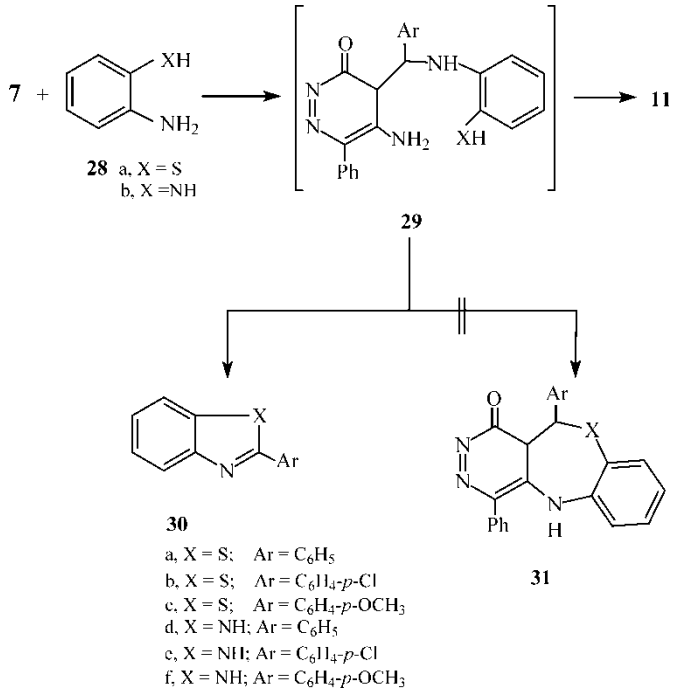
Scheme 3.



Scheme 4.

2-phenylbenzimidazoles **30d–f**, respectively, which have been previously reported,[9] and the pyridazine compound **11** (Scheme 5). Formation of 2-arylbenzothiazole **30a–c** and 2-arylbenzimidazole **30d–f** seems to proceed from the intermediate **29** as suggested in Chart 2. The intermediate **29** loses pyridazine moiety **11** to yield the intermediate cation **32**. An intramolecular nucleophilic attack by the lone pair of electrons of sulfur or nitrogen atoms on the electrophilic carbon leads to the intermediate **33**, which is readily oxidized under an aerobic conditions to give **30**. The MS of **30a** showed m/z at 211 (M^+, 89) and 134 (M-Ph, 92). The expected 1,5-benzodi(thi)azepine derivatives were not isolated.

The reactivity of **2** toward 2-substituted aniline **28a, b** was further investigated to prepare new seven-membered ring systems, which represent a part of our interest.[10,11] Reaction of **2** with 2-aminothiophenol **28a** in refluxing ethanolic piperidine solution afforded 1,5-benzodiazepine derivatives **35** during reflux via intermediate **34a**, which formed through addition of amine function of **28** to the cyano function of **2**. The intermediate **34** releases hydrogen sulfide and/or ammonia under the reaction conditions to yield finally the new 1,5-benzodiazepine derivatives **35**. The MS of **35** showed m/z at 278 (60). The IR spectrum of **35** revealed absorption bands at 3335 and 1680 cm^{-1} assigned for NH_2 and C═O. The ^1H NMR of **35** showed signals at 2.5, 7.1–7.8, 8.3, and 9.5 ppm because of CH_2, aryl-H, Ph-CH═N–, and NH_2 protons, respectively. However, reaction of **2** with 2-phenylenediamine **28b** under the same reaction conditions afforded the isolated product **34b** (X═NH). The MS of **34b** showed MS at m/z at (295). The IR spectrum revealed bands at ν 3340, 3220, and 1680 cm^{-1} because of NH_2, NH, and C═O groups, respectively. Repeating the reaction in pyridine at reflux temperature afforded the same 1,5-benzodiazipine **35**. Meanwhile, boiling **34b** in pyridine yielded the same 1,5-benzodiazipine **35**,



Scheme 5.

which showed the same spectroscopic and elemental analysis data (Scheme 6). Thus, the intermediate **34a** may release a hydrogen ion from the NH group neighbor to the carbonyl into the thiol function to give the intermediates **40**, **41**, which lose a hydrogen sulfide from the transient intermediate **41**,

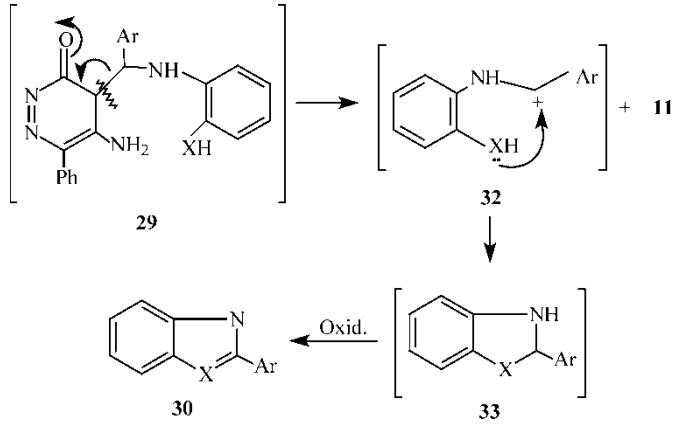
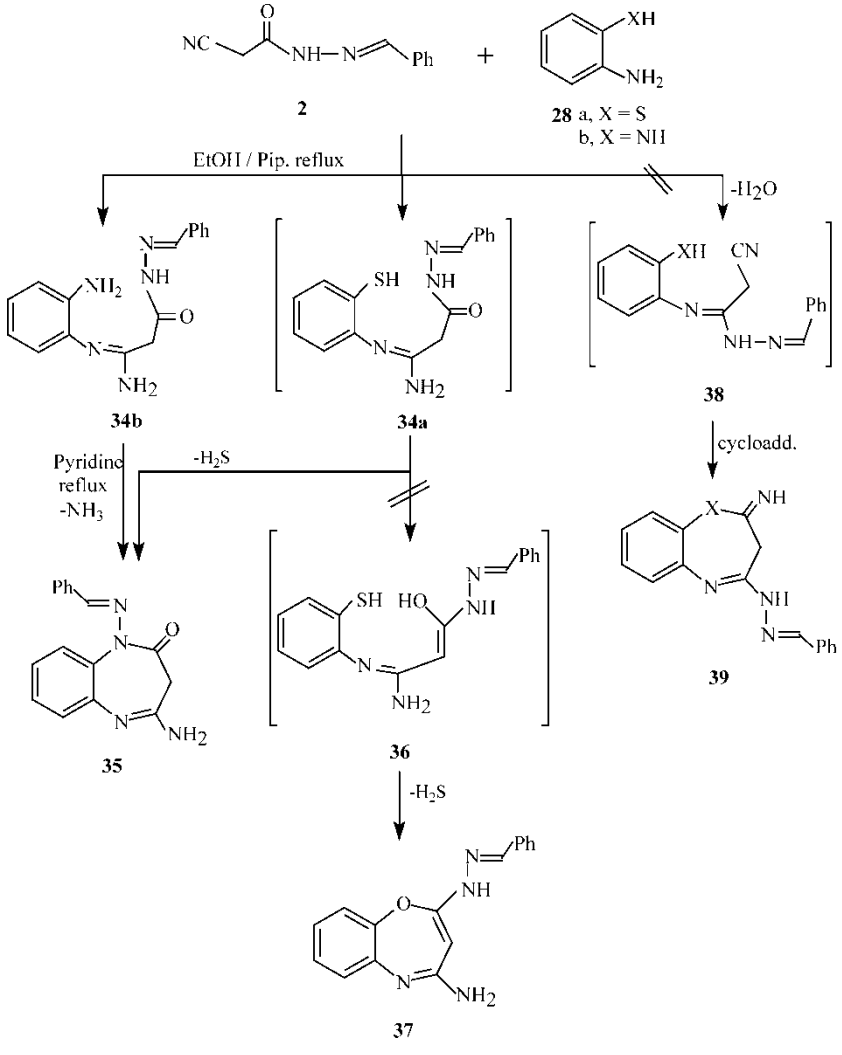


Chart 2.

leading finally to **35** (Chart 3). However, elimination of hydrogen sulfide from intermediate **36** probably formed from **34a** to give the oxazepine **37** is ruled out, since the IR spectrum showed an intense absorption band at ν 1680 cm^{-1} because of the presence of a carbonyl group.

EXPERIMENTAL

Melting points are uncorrected. The IR spectra (potassium bromide, ν in cm^{-1}) were recorded on a Pye-Unicam SP-1100 spectrophotometer.



Scheme 6.

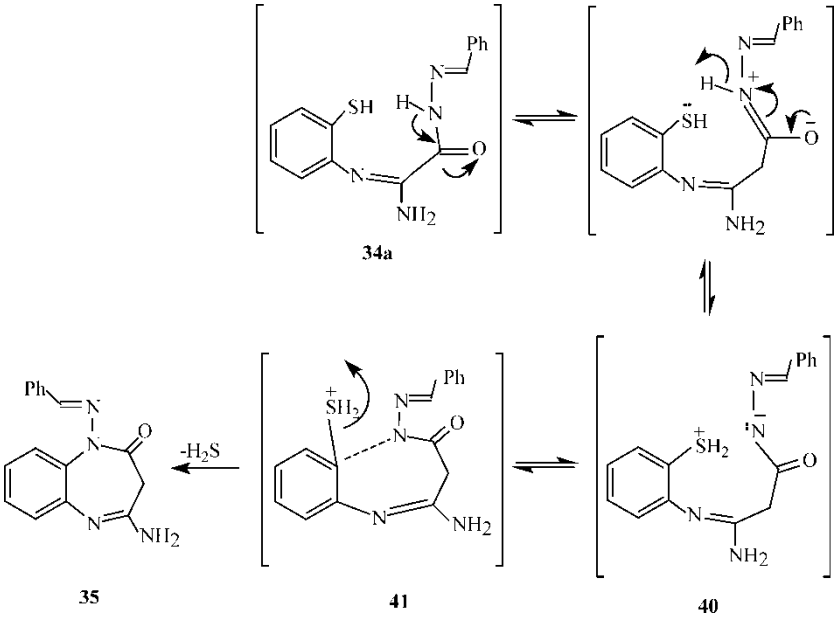


Chart 3.

^{1}H NMR spectra (deuterodimethyl-sulfoxide, δ in ppm) were run on a Varian EM-390 spectrometer using tetramethylsilane as internal standard. Mass spectra were recorded on a Varian MAT 311 A spectrometer, and the elemental analyses were determined at the Micro-analytical Center, Cairo University, Egypt.

Preparation of Compounds 7a–c

A solution of **2** (0.38 g, 1 mmol), benzaldehyde **3a** (0.2 g, 1 mmol), and 0.5 mL of piperidine in 30 mL of dry ethanol was warmed to reflux for 5 h and concentrated under vacuum. The solid formed after addition of cold diluted HCl (1 mL, 20 ml H_2O) was collected by filtration, washed well with 100 mL of cold water, and crystallized from ethanol to give **7a** as yellow compound. Analogously, **2** (0.38 g, 1 mmol) was reacted with **3b** to give **7b**, and **3c** to afford **7c**, respectively.

4-Amino-5-phenylmethylidene-3-phenyl-pyridazin-6-one **7a:** Yield: 85%. Mp: 205°C, IR: ν 3390 (NH_2), 1684 (CO) cm^{-1}; ^{1}H NMR: δ 7.1–7.9 (*m*, 11H, Ar-*H*), 9.3 (*s*, 2H, NH_2); MS (70 eV) m/z (%): 275 (M^+, 25). Anal. calcd. for $C_{17}H_{13}N_3O$ (275.31): C, 74.17; H, 4.76; N, 15.26. Found: C, 74.47; H, 4.96; N, 15.46.

4-Amino-5-(4-chlorophenylmethylidene)-3-phenyl-pyridazin-6-one **7b:** Yield: 80%. Mp: 220°C, IR: ν 3380 (NH_2), 1688 (CO) cm^{-1}; ^{1}H NMR: δ

7.1–7.8 (*m*, 10H, Ar-*H*), 9.9 (*s*, 2H, NH_2); MS (70 eV) m/z (%): 309 (M^+, 15). Anal. calcd. for $C_{17}H_{12}ClN_3O$ (309.76): C, 65.92; H, 3.90; N, 13.57. Found: C, 65.61; H, 4.12; N, 13.27.

4-Amino-5-(4-methoxyphenylmethylidene)-3-phenyl-pyridazin-6-one **7c:** Yield: 78%. Mp: 200°C, IR: ν 3385 (NH_2), 1690 (CO) cm^{-1}; ^1H NMR: δ 2.1 (*s*, 3H, CH_3), 7.1–8.0 (*m*, 10H, Ar-*H*), 8.9 (*s*, 2H, NH_2); MS (70 eV) m/z (%): 305 (M^+, 24). Anal. calcd. for $C_{18}H_{15}N_3O_2$ (305.34): C, 70.81; H, 4.95; N, 13.76. Found: C, 70.50; H, 4.65; N, 13.47.

Preparation of Aziridine 10a–c and Pyridazine 11

A solution of **7** (0.38 g 1 mmol), phenylhydrazine **8** (1 mmol), and 0.2 mL of triethylamine in 30 mL of dry ethanol was warmed to reflux for 7 h and concentrated under vacuum. The solid compound that formed was collected by filtration, washed well with 5 mL of methanol, and crystallized from ethanol to give **10a**. The residue solution was poured into water and acidified with diluted hydrochloric acid. The resulting product was filtered, washed with 50 mL of cooled water, dried, and crystallized from a mixture of methanol and water (3 : 1) to give pyridazine **11**.

1,3-Diphenylaziridene **10a:** Yield: 55%. MP: 155°C, IR: ν 3311 (NH) cm^{-1}; ^1H NMR: δ 6.2 (*d*, 1H, NCH), 7.1–7.9 (*m*, 10H, Ar-*H*), 10.3 (*d*, 1H, NH); MS (70 eV) m/z (%): 196 (M^+, 100). Anal. calcd. for $C_{13}H_{12}N_2$ (196.25): C, 79.56; H, 6.16; N, 14.27. Found: C, 79.37; H, 5.86; N, 14.46.

1-Phenyl-3-(4-chlorophenyl)-aziridene **10b:** Yield: 52%. Mp: 105°C, IR: ν 3319 (NH) cm^{-1}; ^1H NMR: δ 5.7 (*d*, 1H, NCH), 7.1–7.8 (*m*, 9H, Ar-*H*), 10.2 (*d*, 1H, NH); MS (70 eV) m/z (%): 230 (M^+, 45). Anal. calcd. for $C_{13}H_{11}ClN_2$ (230.70): C, 67.68; H, 4.81; N, 12.14. Found: C, 67.41; H, 4.99; N, 12.32.

1-Phenyl-3-(4-methoxyphenyl)-aziridene **10c:** Yield: 58%. Mp: 192°C, IR: ν 3316 (NH) cm^{-1}; ^1H NMR: δ 2.1 (*s*, 3H, CH_3), 5.9 (d, 1H, NCH), 7.1–8.0 (*m*, 9H, Ar-*H*), 10.1 (*d*, 1H, NH); MS (70 eV) m/z (%): 226 (M^+, 24). Anal. calcd. for $C_{14}H_{14}N_2O$ (226.28): C, 74.31; H, 6.24; N, 12.38. Found: C, 74.55; H, 6.47; N, 12.62.

4-Amino-3-phenyl-pyridazine-6-one **11:** Yield: 22%. Mp: 200°C, IR: ν 3356, 3340 (NH_2), 1689 (CO) cm^{-1}; ^1H NMR: δ 3.3 (*s*, 2H, CH_2), 7.1–7.9 (*m*, 5H, Ar-*H*), 8.9 (*s*, 2H, NH_2); MS (70 eV) m/z (%): 187 (M^+, 80). Anal. calcd. for $C_{10}H_9N_3O$ (187.20): C, 64.16; H, 4.85; N, 22.45. Found: C, 64.37; H, 4.99; N, 22.66.

Preparation of Compounds 21a–f

A solution of **7a** (0.38 g, 1 mmol), semicarbazide **17a** (0.15 g, 1 mmol), and 0.5 mL of triethylamine in 30 mL of dry ethanol was warmed to reflux for 8 h. The solid formed during reflux was collected by filtration, washed well

with 5 mL of methanol, and crystallized from a mixture of ethanol/DMF (3 : 1) to give **21a** as yellow compound. The residue solution poured into water acidified with diluted hydrochloric acid, the resulting product was filtered and washed with cooled water, dried and crystallized from mixture of methanol and water (3 : 1) to give **11**. Analogously, **7b,c** (1 mmol) was reacted with **17a** to give **21b**, **c**, and **7a–c** reacted with semithiocarbazide **17b** to give **21d–f**.

***3-Phenyl-1,2,4-triazol-5-one* 21a:** Yield: 65%. Mp: 215°C, IR: ν 3194 (NH), 1688 (CO) cm^{-1}; ^1H NMR: δ 6.5 (*d*, 1H, triazole-H-3), 7.1–7.9 (*m*, 5H, Ar-*H*), 10.3 (br. *d*, 1H, NH); MS (70 eV) *m/z* (%): 163 (M + 2, 50). Anal. calcd. for $C_8H_7N_3O$ (161.16): C, 59.62; H, 4.38; N, 26.07. Found: C, 59.85; H, 4.49; N, 26.25.

***3-(4-Chlorophenyl)-1,2,4-triazol-5-one* 21b:** Yield: 60%. Mp: 218°C, IR: ν 3189 (NH), 1689 (CO) cm^{-1}; ^1H NMR: δ 6.6 (*d*, 1H, triazole-H-3), 7.2–7.9 (*m*, 4H, Ar-*H*), 10.3 (br. *d*, 1H, NH); MS (70 eV) *m/z* (%): 195 (M^+, 35). Anal. calcd. for $C_8H_6ClN_3O$ (195.61): C, 49.12; H, 3.09; N, 21.48. Found: C, 49.33; H, 3.41; N, 21.67.

***3-(4-Methoxyphenyl)-1,2,4-triazol-5-one* 21c:** Yield: 68%. Mp: > 300°C, IR: ν 3189 (NH), 1686 (CO) cm^{-1}; ^1H NMR: δ 2.3 (s, 3H, CH_3), 6.2 (*d*, 1H, triazole-H-3), 7.1–7.8 (*m*, 4H, Ar-*H*), 10.5 (br. *d*, 1H, NH); MS (70 eV) *m/z* (%): 191 (M^+, 24). Anal. calcd. for $C_9H_9N_3O_2$ (191.19): C, 56.54; H, 4.75; N, 21.98. Found: C, 56.70; H, 4.99; N, 22.02.

***3-Phenyl-1,2,4-triazol-5-thione* 21d:** Yield: 55%. Mp: 150°C, IR: ν 3186 (NH) cm^{-1}; ^1H NMR: δ 6.4 (*d*, 1H, triazole-H-3), 7.1–7.9 (*m*, 5H, Ar-*H*), 10.3 (br. *d*, 1H, NH); MS (70 eV) *m/z* (%): 179 (M + 2, 59). Anal. calcd. for $C_8H_7N_3S$ (177.23): C, 54.22; H, 3.98; N, 23.71. Found: C, 54.37; H, 4.02; N, 23.99.

***3-(4-Chlorophenyl)-1,2,4-triazol-5-thione* 21e:** Yield: 60%. Mp: 180°C, IR: ν 3180 (NH) cm^{-1}; ^1H NMR: δ 6.3 (*d*, 1H, triazole-H-3), 7.1–7.9 (*m*, 4H, Ar-*H*), 10.6 (br. *d*, 1H, NH); MS (70 eV) *m/z* (%): 213 (M + 2, 38). Anal. calcd. for $C_8H_6ClN_3S$ (211.67): C, 45.40; H, 2.86; N, 19.85. Found: C, 45.57; H, 2.99; N, 19.99.

***3-(4-Methoxyphenyl)-1,2,4-triazol-5-thione* 21f:** Yield: 64%. Mp: 190°C, IR: ν 3180 (NH) cm^{-1}; ^1H NMR: δ 2.3 (s, 3H, CH_3), 6.5 (*d*, 1H, triazole-H-3), 7.3–7.9 (*m*, 4H, Ar-*H*), 10.3 (br. *d*, 1H, NH); MS (70 eV) *m/z* (%): 209 (M + 2, 24). Anal. calcd. for $C_9H_9N_3OS$ (207.25): C, 52.16; H, 4.38; N, 20.28. Found: C, 52.31; H, 4.69; N, 20.39.

Preparation of Compounds 27a–c

A solution of **7a** (0.38 g, 1 mmol), cyanoacetohydrazide **22** (0.14 g, 1 mmol), and 0.5 mL of triethylamine in 30 mL of dry ethanol was warmed to reflux for 10 h. The solid formed during reflux was collected by filtration, washed well with 5 mL of methanol, and crystallized from DMF to give **27a** as brown

compound. The filtrate was poured into water acidified with dilute hydrochloric acid, the resulting solid product which formed was collected by filtration and washed well with 50 ml of cooled water, dried and crystallized from mixture of methanol and water (3 : 1) to give **11**. Analogously, **7b,c** (1 mmol) was reacted with **22** to give **27b,c**.

***4-Amino-6-hydroxy-3-phenyl-pyridazine* 27a:** Yield: 65%. Mp: 250°C, IR: ν 3350, 3335, 3310 (OH, NH_2) cm^{-1}; ^1H NMR: δ 7.0 (*s*, 1H, pyridazine-H-5), 7.1–7.9 (*m*, 6H, Ar-*H* + *OH*), 8.9 (*s*, 2H, NH_2); MS (70 eV) *m*/*z* (%): 187 (M^+, 100). Anal. calcd. for $C_{10}H_9N_3O$ (187.20): C, 64.16; H, 4.85; N, 22.45. Found: C, 64.41; H, 4.56; N, 22.16.

***4-Amino-6-hydroxy-3-(4-chlorophenyl)pyridazine* 27b:** Yield: 60%. Mp: 205°C, IR: ν 3330, 3318 (OH, NH_2) cm^{-1}; ^1H NMR: δ 6.9 (*s*, 1H, pyridazine-H-5), 7.1–7.8 (*m*, 5H, Ar-*H* + *OH*), 8.7 (*s*, 2H, NH_2); MS (70 eV) *m*/*z* (%): 221 (M^+, 35). Anal. calcd. for $C_{10}H_8ClN_3O$ (221.65): C, 54.19; H, 3.64; N, 18.96. Found:C, 54.32; H, 3.40; N, 18.67.

***4-Amino-6-hydroxy-3-(4-methoxyphenyl)pyridazine* 27c:** Yield: 60%. Mp: 265°C, IR: ν 3330, 3318 (OH, NH_2) cm^{-1}; ^1H NMR: δ 2.1 (*s*, 3H, CH_3), 6.9 (*s*, 1H, pyridazine-H-5), 7.1–8.0 (*m*, 5H, Ar-*H* + *OH*), 8.5 (*s*, 2H, NH_2); MS (70 eV) *m*/*z* (%): 217 (M^+, 34). Anal. calcd. for $C_{11}H_{11}N_3O_2$ (217.23): C, 60.82; H, 5.10; N, 19.34. Found: C, 60.65; H, 5.37; N, 19.63.

Preparation of 2-Arylbenzothiazole Derivatives 30a–c and 2-Arylbenzimdazole Derivatives 30d–f

A solution of **7** (1 mmol), 2-aminothiophenole **28a** (1 mmol), and 0.1 mL of piperidine in 30 mL of dry ethanol was warmed to reflux for 5 h. The colorless product that formed after cooling was collected by filtration and washed well with methanol to give **30a.** The residue solution was poured into 10 mL of cold water and 0.5 mL of diluted HCl; the resulting solid product was collected by filtration and washed well with 20 mL of cooled water and crystallized from methanol to give **11.** Analogously, **7b, c** (1 mmol) was reacted with **28a** to give **30b, c**, and **7a–c** reacted with **28b** to give **30d–f**.

***2-Phenylbenzothiazole* 30a:** Yield: 45%. Mp: 240°C, ^1H NMR: δ 7.1–7.9 (*m*, 9H, Ar-*H*); MS (70 eV) *m*/*z* (%): 211 (M^+, 89). Anal. calcd. for $C_{13}H_9NS$ (211.28): C, 73.90; H, 4.29; N, 6.63; S, 15.17. Found: C, 73.72; H, 4.38; N, 6.53; S, 15.35.

***2-(4-Chlorophenyl)-benzothiazole* 30b:** Yield: 38%. Mp: 220°C, ^1H NMR: δ 7.1–7.9 (*m*, 8H, Ar-*H*); MS (70 eV) *m*/*z* (%): 245 (M^+, 89). Anal. calcd. for $C_{13}H_8ClNS$ (245.73): C, 63.54; H, 3.28; N, 5.70; S, 13.05. Found: C, 63.73; H, 3.60; N, 5.93; S, 13.20.

***2-(4-Methoxyphenyl)-benzothiazole* 30c:** Yield: 40%. Mp: 102°C, ^1H NMR: δ 2.1 (*s*, 3H, CH_3), 7.1–7.9 (*m*, 8H, Ar-*H*); MS (70 eV) *m*/*z* (%): 242 (M + 1, 80). Anal. calcd. for $C_{14}H_{11}NSO$ (241.31): C, 69.68; H, 4.59; N, 5.80; S, 13.28. Found: C, 69.99; H, 4.67; N, 5.99; S, 13.58.

2-Phenylbenzimidazole **30d:** Yield: 38%. Mp: 294°C, IR: ν 3168 (NH) cm^{-1}; ^1H NMR: δ 7.1–7.9 (*m*, 10H, Ar-*H* + *NH*); MS (70 eV) *m*/*z* (%): 195 (M + 1, 89). Anal. calcd. for $C_{13}H_{10}N_2$ (194.24): C, 80.39; H, 5.19; N, 14.42. Found: C, 80.62; H, 5.48; N, 14.82.

2-(4-Chlorophenyl)-benzimidazole **30e:** Yield: 31%. Mp: 190°C, IR: ν 3180 (NH) cm^{-1}; ^1H NMR: δ 7.0–7.8 (*m*, 9H, Ar-*H* + *NH*); MS (70 eV) *m*/*z* (%): 229 (M + 1, 89). Anal. calcd. for $C_{13}H_9ClN_2$ (228.68): C, 68.28; H, 3.97; N, 12.25. Found: C, 68.72; H, 4.68; N, 12.60.

2-(4-Methoxyphenyl)-benzimidazole **30f:** Yield: 29%. Mp: 160°C, IR: ν 3189 (NH) cm^{-1}; ^1H NMR: δ 1.9 (*s*, 3H, CH_3), 7.1–7.9 (*m*, 9H, Ar-*H* + *NH*); MS (70 eV) *m*/*z* (%): 225 (M + 1, 89). Anal. calcd. for $C_{14}H_{12}N_2O$ (224.26): C, 74.98; H, 5.39; N, 12.49. Found: C, 74.62; H, 5.62; N, 12.63.

Preparation of Compound 34b

A solution of **2** (1 mmol), 2-phenylenediamine **28b** (1 mmol), and 0.1 mL of piperidine in 30 mL of dry ethanol was warmed to reflux for 5 h. The colorless product that formed after triturating with 5 mL of methanol was collected by filtration and washed well with methanol to give **34b**.

Yield: 28%. Mp: 195°C, IR: ν 3340 (NH_2), 3220 (NH), 1680 (CO) cm^{-1}; ^1H NMR: δ 3.9 (*s*, 2H, CH_2), 7.1–7.9 (*m*, 11H, Ar-*H* + *NH*), 9.1 (*s*, 2H, NH_2), 10.3 (*s*, 2H, NH_2); MS (70 eV) *m*/*z* (%): 295 (M^+, 29). Anal. calcd. for $C_{16}H_{17}N_5O$ (295.35): C, 65.07; H, 5.80; N, 23.71. Found: C, 65.36; H, 5.99; N, 23.99.

Preparation of 1,5-Benzodiazepine 35

A solution of **2** (1 mmol), 2-aminothiophenole **28a** (1 mmol), and 0.1 mL of piperidine in 30 mL of dry ethanol was warmed to reflux for 4 h. The colorless product that formed during reflux was collected by filtration and washed well with methanol to give **35**. Analogously, **2** (1 mmol) was reacted with **28b** in pyridine for 7 h to give **35**.

Yield: 55 %. Mp: 240°C, IR: ν 3335 (NH_2), 1680 (CO) cm^{-1}; ^1H NMR: δ 2.5 (*s*, 2H, CH_2), 7.1–7.9 (*m*, 9H, Ar-*H*), 8.3 (*s*, 1H, CH), 9.5 (*s*, 2H, NH_2); MS (70 eV) *m*/*z* (%): 278 (M^+, 60). Anal. calcd. for $C_{16}H_{14}N_4O$ (278.32): C, 69.05; H, 5.07; N, 20.13. Found: C, 69.35; H, 5.12; N, 20.50.

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