An Efficient Synthesis of Some New Isolated and Fused Triazole Derivatives

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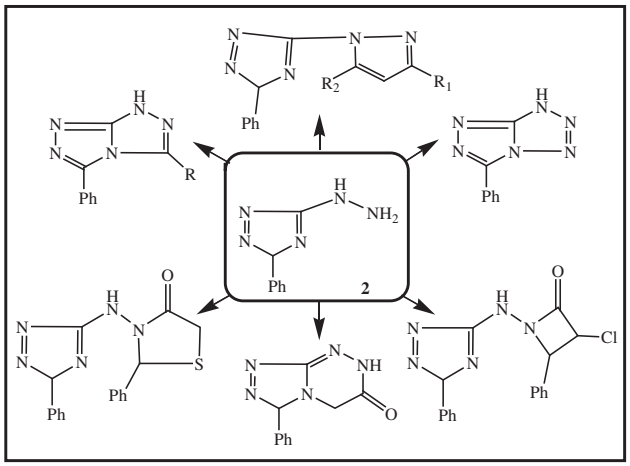
Received August 2, 2011
DOI 10.1002/jhet.1110
Published online 2 April 2013 in Wiley Online Library (wileyonlinelibrary.com).



A facile and efficient route to 5-hydrazinyl-3-phenyl-3*H*-[1,2,4]triazole **2** from the reaction of triazol-3-one **1** and hydrazine hydrate is described. In addition, the formation of isolated and fused triazole derivatives was prepared via reaction of **2** with some selected electrophilic reagents in basic medium.

J. Heterocyclic Chem., **50**, E228 (2013).

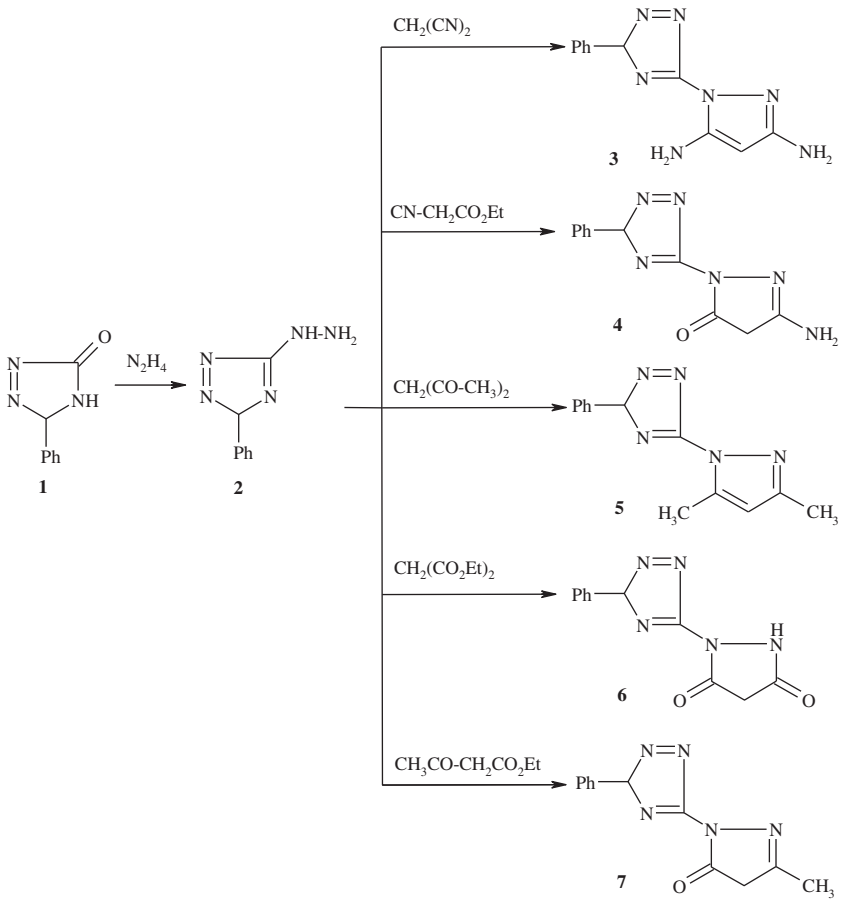
INTRODUCTION

1,2,4-Triazoles are an important class of heterocyclic compounds; they are well-known for their biological properties [1], such as antifungal [2–4], antimicrobial [5–9], antitumor, antiviral [10–13], anti-asthmatic [14], hypotonic [15], anticonvulsant [16,17], and anti-arthritic activities [18]. Also, 1,2,4-triazole derivatives were found as potential antitubercular agents [19,20], anticancer [21], as receptor antagonists [22–24], and exhibits efficacy against a broad range of viruses *in vitro* [25,26]. On the other hand, cytotoxicity and effects of some 1,2,4-triazoles on immunocompetent cells were investigated. Since, triazoles were ascertained to exhibit high cytotoxicity in test *in vitro* against thymocytes and lymphocytes [27,28]. In view of the aforementioned versatile benefits of 1,2,4-triazoles and as a continuation of our efforts to the synthesis of isolated and fused heterocyclic compounds [29–35], we report herein a facile and convenient route to 5-hydrazinyl-3-phenyl-3*H*-[1,2,4]triazole **2**, which is considered as a key intermediate for the synthesis of new triazolylpyrazole, triazolo[3,4-*c*][1,2,4]triazole, triazolo[4,3-*d*]tetrazole, triazolo[3,4-*c*][1,2,4]triazine, triazolyl-thiazolidinone, and triazolyl-azetidinone.

RESULTS AND DISCUSSION

The 5-hydrazinyl-3-phenyl-3*H*-[1,2,4]triazole **2** was synthesized by the reaction of triazol-3-one **1** [35] with hydrazine hydrate in pyridine at refluxing temperature. The formation of compound **2** may proceed via an elimination of water (Scheme 1). The structure of compound **2** was established on the basis of analytical and spectral analyses. The IR spectrum of compound **2** confirmed the presence of intense absorption bands at ν 3450, 3455, and 3120 cm^{-1} due to amino and imino groups, respectively. The ^1H NMR spectrum of compound **2** showed one singlet signal at δ 2.56 ppm due to amino, in addition to multiplets at δ 7.40–7.84 ppm attributed to aromatic protons, H-3 triazole, and imino group, respectively. The MS of compound **2** showed *m/z* at 175 (M^+, 70%). Compound **2** considered a good and available starting material for the synthesis of new functionalized heterocyclic compounds, since; it contains a nucleophillic hydrazinyl group. Thus, triazolylpyrazole **3–7** have been synthesized by the reaction of 5-hydrazinyl triazole **2** with active methylene reagents and/or 1,3 diketones in the presence of catalytic amount of piperidine in ethanol at reflux temperature (Scheme 1). The progress of the reaction has been monitored using TLC, and the final yields for these

Scheme 1. Synthesis of 1,2,4-triazolyl pyrazoles (**3–7**).

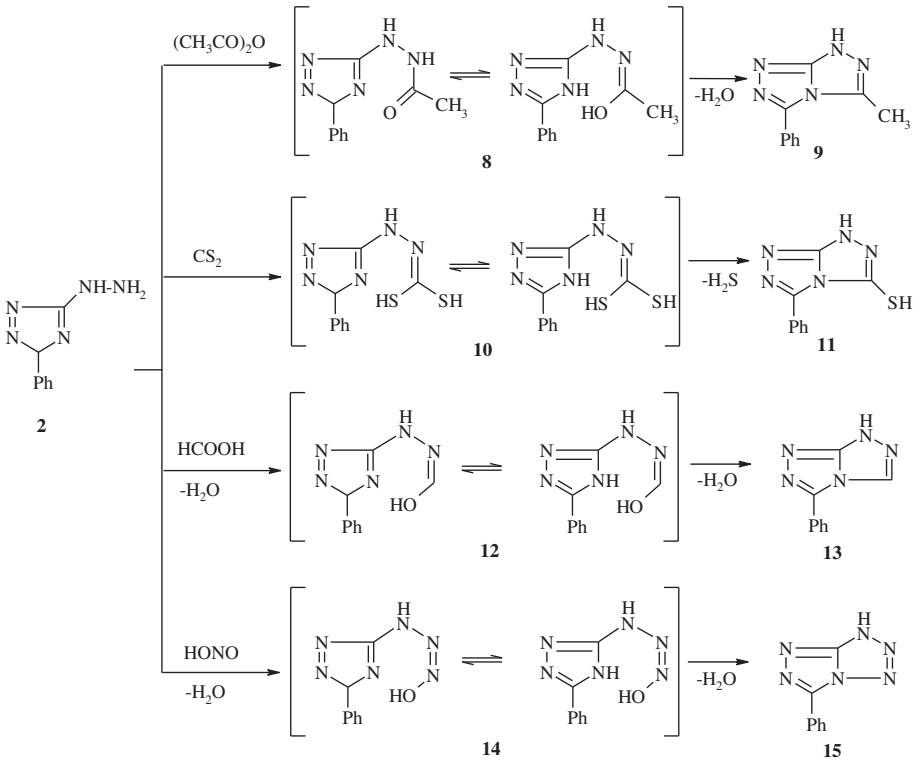


reactions ranges from 40 to 60%. IR spectroscopy data of compounds **3–7** have variable intensity, sometimes broad absorption bands as well as stretching vibrations typical for the functional groups in their structure. Compound **3** has strong absorption bands at ν 3450 and 3500 cm^{-1} for the two amino groups, and compound **4** has medium absorption bands at ν 3400 and 1690 cm^{-1} for one amino group and one carbonyl group, respectively. Also, compound **6** gave strong absorption bands at ν 1700 and 1710 cm^{-1} for two carbonyl groups. However, in their ^1H NMR spectra, the multiplet signals appears between δ 7.23–7.77 ppm due to aromatic and H-3 triazole protons. The single proton of the pyrazole ring **(3** and **5)** has a signal in the area of 7.12–722 ppm, and the two protons of the pyrazole ring **(4**, **6**, and **7)** have a signal in the area of 5.22–5.75 ppm. The two amino groups of the pyrazole ring in compound **3** have two singlet signals at 3.21 and 3.32 ppm, whereas a singlet signal is recorded at δ 2.51 ppm due to the amino protons of compound **4**. The two methyl groups of the pyrazole ring in compound **5** have two singlet signals at 2.89 and 2.98 ppm, and the methyl group of compound **7** appears as one singlet signal at δ 1.33 ppm. The mass spectroscopic molecular ion observed in the spectra of all compounds confirms their structures.

Also, the 5-hydrazinyl-3-phenyl-3*H*-[1,2,4]triazole **2** underwent other several cyclization reactions (Scheme 2). Thus, treatment of compound **2** with acetic anhydride in pyridine solution gave the corresponding 3-methyl-5-phenyl-1*H*-[1,2,4]triazolo[3,4-*c*][1,2,4]triazole **9**. The IR spectrum of compound **9** showed the lack of absorption band due to amino function and exhibited characteristic absorption band at ν 3140 cm^{-1} due to imino group. The ^1H NMR spectrum of compound **9** displayed one singlet signal at δ 1.32 ppm due to methyl, in addition to multiplet at δ 7.22–7.94 ppm for aromatic and NH-triazole protons. The MS of compound **9** showed an intense ion peak at *m/z* at 199 (M^+, 60%).

The reactivity of the hydrazinyl group in compound **2** is also explored through its reaction with carbon disulfide. Thus, refluxing of compound **2** with carbon disulfide in pyridine at refluxing temperature gave 5-phenyl-1*H*-[1,2,4]triazolo [3,4-*c*][1,2,4]triazole-3-thiol **11**. The IR spectrum of compound **11** showed the absence of absorption band assignable to amino group and displayed absorption band at ν 3170 cm^{-1} due to imino group. The formation of **11** may proceed through the addition of the amino protons to CS_2 via the formation of intermediate **10**, which is followed by cyclization through elimination of hydrogen sulfide (Scheme 2).

Scheme 2. Synthesis of [1,2,4]triazolo[3,4-*c*][1,2,4]triazoles and [1,2,4]triazolo[4,3-*d*]tetrazole.



Similarly, 5-phenyl-1*H*-[1,2,4]triazolo[3,4-*c*][1,2,4]triazole **13** was obtained via treatment of compound **2** with formic acid. The IR spectrum revealed the absence of absorption band attributed to amino group. The MS of compound **13** showed *m*/*z* at 185 (M^+, 55%).

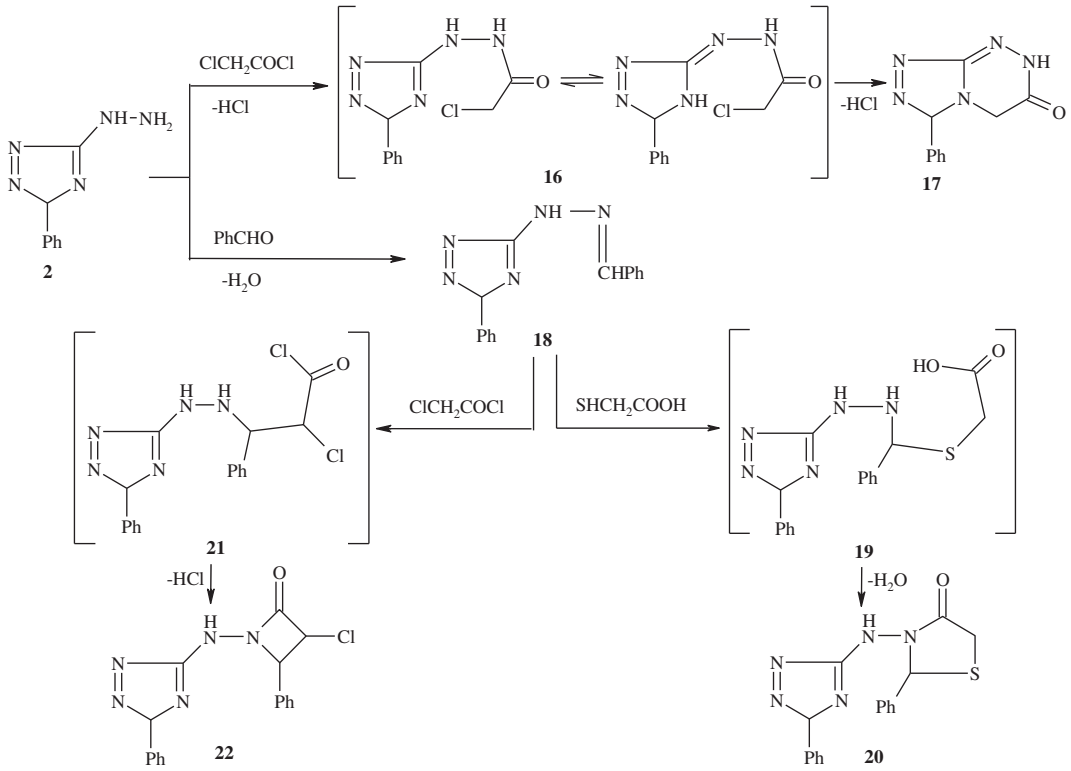
On the other hand, compound **2** reacted with nitrous acid to afford 6-phenyl-3*H*-[1,2,4] triazolo [4,3-*d*] tetrazole **15**, which may be formed via elimination of water through intermediate **14**. The IR spectrum of compound **15** revealed the absence of absorption band attributed to amino group and showed absorption band at ν 3135 cm^{-1} due to imino function. The MS of compound **15** showed an intense ion peak at 186 (M^+, 56%) (Scheme 2).

3-Phenyl-3,7-dihydro[1,2,4]triazolo[3,4-*c*][1,2,4]triazin-6 (5*H*)-one **17** could be obtained through the reaction of compound **2** with chloroacetyl chloride in ethanolic piperidine solution at refluxing temperature. The formation of compound **17** may proceed via an elimination of hydrogen chloride through intermediate **16**, then cyclized via an elimination of other molecule of hydrogen chloride. The IR spectrum of compound **17** revealed the absence of absorption band attributed to amino group and appearance of absorption bands at ν 3150 and 1690 cm^{-1} due to NH and CO groups. The ^{1}H NMR spectrum of compound **17** showed singlet signal at δ 3.44 ppm for triazine-CH_2 protons and multiplet between δ 7.23 and 7.88 ppm for H-3 triazole, imino, and aromatic protons. The MS of compound **17** showed an intense ion peak at 215 (M^+, 45%) (Scheme 3).

Also, compound **2** is condensed with benzaldehyde in ethanolic piperidine solution at refluxing temperature affording the corresponding Schiff base **18**. The IR spectrum of compound **18** showed the absence of the absorption band of the amino group and exhibited the presence of absorption bands at ν 3134 cm^{-1} due to NH function. The ^{1}H NMR spectrum of compound **18** showed singlet signal at δ 6.12 ppm for N=CH group. The MS of compound **18** showed an intense ion peak at *m*/*z* at 263 (M^+, 50%). The reactivity of Schiff base **18** could be shown by the reaction of thioglycolic acid; the isolated thiazolidinone **20** may be formed by a nucleophilic addition of thiol function to the imino carbon of compound **18** through intermediate **19** that underwent a cyclization to **20** via loss of water. The MS of compound **20** showed a peak at *m*/*z* 337 (M^+, 50%) (Scheme 3).

However, the addition of chloroacetyl chloride to Schiff base **18** gave intermediate **21**, which in turn undergoes cyclization via elimination of hydrogen chloride to afford the new β-lactam compound **22**. The IR spectrum of compound **22** showed the presence of absorption bands at ν 3132 and 1697 cm^{-1} due to (NH) and (CO) functions, respectively. The ^{1}H NMR spectrum of compound **22** showed two doublet signals at δ 5.12 and 5.29 ppm for the protons at C3 and C4 of the azetidinone. The MS of

Scheme 3. Synthesis of [1,2,4]triazolo[3,4-*c*]triazine, [1,2,4]triazolyl thiazolidine, and [1,2,4]triazolyl azetidine.



compound **22** displayed an intense ion peak at *m/z* 339 (M^+, 52%) (Scheme 3).

CONCLUSION

Despite the several existing methods for the synthesis of triazole derivatives, there still is demand for general strategies, which can efficiently provide variously substituted triazole systems. Thus, this work opened a simple avenue for the synthesis of a variety of isolated and fused triazole derivatives with the use of 5-hydrazinyl-3-phenyl-3*H*-[1,2,4] triazole.

EXPERIMENTAL

Melting points were determined on a Gallenkamp electrothermal melting point apparatus and are uncorrected. IR spectra were recorded as potassium bromide pellets with the use of an FTIR unit Bruker-vector 22 spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were obtained in DMSO-d_6 as solvent at 300 and 75 MHz, respectively on a Varian Gemini NMR spectrometer using TMS as internal standard. Chemical shifts are reported in δ units (ppm). Mass spectra were recorded on a Hewlett Packard MS-5988 spectrometer at 70 eV. Elemental analysis was carried out at the Micro analytical Center of Cairo University, Egypt.

Synthesis of 5-hydrazinyl-3-phenyl-3*H*-[1,2,4]triazole (2). A solution of 5-phenyl-4,5-dihydro-3*H*-1,2,4-triazol-3-one **1** (10 mmol) and hydrazine hydrate (10 mmol) in 20 mL of pyridine was refluxed for 4 h, then allowed to cool, and poured into acidified cold water. The solid product formed was filtered off, washed with cold water, dried, and recrystallized with ethanol to give **2** as buff powder. Yield 73%, 0.13 g, mp 180–182°C; IR (ν_{max}, cm^{-1}): 3450 and 3455 (NH_2), 3120 (NH). ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 2.56 (s, 2H, NH_2), 7.40–7.84 (m, 7H, Ar-H + H-3 triazole + NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 73.55, 125.82, 128.77, 129.55, 137.23, 163.55. MS, *m/z* (%) = 175 ($[M]^+$, 70), 144 ($[M]^+$–$NHNH_2$, 60), 98 ($[M]^+$–Ph, 40). *Anal.* Calcd for $C_8H_9N_5$ (175.19): C, 54.85; H, 5.18; N, 39.98%. Found: C, 54.91; H, 5.27; N, 39.99%.

1-(3-Phenyl-3*H*-1,2,4-triazol-5-yl)-1*H*-pyrazole-3,5-diamine (3). A mixture of **2** (1.75 g, 10 mmol) and malononitrile (0.6 g, 10 mmol) in 30 mL of ethanol containing 0.2 mL of piperidine was refluxed for 5 h. The solvent was evaporated under vacuum, and the residue was triturated with methanol. The solid product was filtered and recrystallized from methanol as colorless crystals. Yield 40%, 0.11 g, mp 225–227°C; IR (ν_{max}, cm^{-1}): 3450 and 3500 (NH_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 3.21 (s, 2H, NH_2), 3.32 (s, 2H, NH_2), 7.22 (s, 1H, H-pyrazole), 7.28–7.67 (m, 6H, Ar-H + H-3 triazole). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 71.85, 78.77, 125.83, 128.75, 129.54, 137.23, 148.12, 149.88, 163.55. MS, *m/z* (%) = 241 ($[M]^+$, 50), 225 ($[M]^+$–NH_2, 60), 209 ($[M]^+$–$2NH_2$, 20), 132 ($C_{11}H_5$–Ph, 54). *Anal.* Calcd for $C_{11}H_{11}N_7$ (241.25): C, 54.76; H, 4.60; N, 40.64%. Found: C, 54.81; H, 4.76; N, 40.74%.

3-Amino-1-(3-phenyl-3*H*-1,2,4-triazol-5-yl)-1*H*-pyrazole-5(4*H*)-one (4). A mixture of **2** (1.75 g, 10 mmol) and ethylcyanoacetate (1.13 g, 10 mmol) in 30 mL of ethanol containing 0.2 mL of piperidine was refluxed for 5 h. The solvent was evaporated under vacuum, and the residue was triturated with methanol.

The solid product was filtered and recrystallized from methanol as white crystals. Yield 50%, 0.12 g, mp 230–232°C; IR (ν_{max}, cm^{-1}): 3400 (NH_2), 1690 (CO). ^1H NMR (300 MHz, $CDCl_3$): δ ppm 2.51 (s, 2H, NH_2), 5.75 (s, 2H, CH_2-pyrazole), 7.25–7.69 (m, 6H, Ar-H + H-3 triazole). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 70.85, 72.76, 125.82, 128.75, 129.53, 137.23, 159.88, 163.55, 164.78. MS, *m/z* (%) = 242 ($[M]^+$, 55), 216 ($[M]^+$–NH_2, 20), 165 ($[M]^+$–Ph, 30). *Anal*. Calcd for $C_{11}H_{10}N_6O$ (242.24): C, 54.54; H, 4.16; N, 34.69%. Found: C, 54.63; H, 4.23; N, 34.74%.

3,5-Dimethyl-1-(3-phenyl-3*H*-1,2,4-triazol-5-yl)pyrazole (5). A mixture of **2** (1.75 g, 10 mmol) and acetylacetone (1.3 g, 10 mmol) in 30 mL of ethanol containing 0.2 mL of piperidine was refluxed for 5 h. The solvent was evaporated under vacuum, and the residue was triturated with methanol. The solid product was filtered and recrystallized from methanol as colorless crystals. Yield 60%, 0.14 g, mp 235–237°C; ^1H NMR (300 MHz, $CDCl_3$): δ ppm 2.89 (s, 3H, CH_3), 2.98 (s, 3H, CH_3), 7.12 (s, 1H, H-pyrazole), 7.23–7.70 (m, 6H, Ar-H + H-3 triazole). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 11.47, 17.88, 71.76, 105.76, 125.82, 128.77, 129.59, 137.34, 143.89, 149.88, 163.55. MS, *m/z* (%) = 239 ($[M]^+$, 65), 209 ($[M]^+$–$2CH_3$, 43), 132 ($[M]^+$–Ph, –$2CH_3$, 32). *Anal*. Calcd for $C_{13}H_{13}N_5$ (239.28): C, 65.25; H, 5.48; N, 29.27%. Found: C, 65.36; H, 5.58; N, 29.39%.

1-(3-Phenyl-3*H*-1,2,4-triazol-5-yl)-pyrazolidine-3,5-dione (6). A mixture of **2** (1.75 g, 10 mmol) and diethymalonate (1.3 g, 10 mmol) in 30 mL of ethanol containing 0.2 mL of piperidine was refluxed for 5 h. The solvent was evaporated under vacuum, and the residue was triturated with methanol. The solid product was filtered and recrystallized from methanol as colorless crystals. Yield 60%, 0.15 g, mp 227–229°C; IR (ν_{max}, cm^{-1}): 3140 (NH), 1700 and 1710 (CO). ^1H NMR (300 MHz, $CDCl_3$): δ ppm 5.22 (s, 2H, CH_2-pyrazolidine), 7.28–7.77 (m, 7H, Ar-H + H-3 triazole + NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 47.89, 70.95, 125.82, 128.75, 129.53, 137.21, 163.85, 170.78, 170.99. MS, *m/z* (%) = 243 ($[M]^+$, 63), 225 ($[M]^+ - 18$, 20), 166 ($[M]^+$-Ph, 35). *Anal*. Calcd for $C_{11}H_9N_5O_2$ (243.22): C, 54.32; H, 3.73; N, 28.79%. Found: C, 54.41; H, 3.82; N, 28.88%.

3-Methyl-1-(3-phenyl-3*H*-1,2,4-triazol-5-yl)-1*H*-pyrazol-5(4*H*)-one (7). A mixture of **2** (1.75 g, 10 mmol) and ethylacetoacetate (1.1 g, 10 mmol) in 30 mL of ethanol containing 0.2 mL of piperidine was refluxed for 5 h. The solvent was evaporated under vacuum, and the residue was triturated with methanol. The solid product was filtered and recrystallized from methanol as colorless crystals. Yield 59%, 0.14 g, mp 237–239°C; IR (ν_{max}, cm^{-1}): 1705 (CO). ^1H NMR (300 MHz, $CDCl_3$): δ ppm 1.33 (s, 3H, CH_3), 5.35 (s, 2H, CH_2-pyrazole), 7.25–7.72 (m, 6H, Ar-H + H-3 triazole). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 22.90, 33.89, 40.89, 70.80, 125.82, 128.75, 129.53, 137.24, 159.23, 163.55, 172.78. MS, *m/z* (%) = 241 ($[M]^+$, 60), 223 ($[M]^+$–H_2O, 30), 226 ($[M]^+$–CH_3, 20), 131 ($C_{11}H_4N_5$–Ph, 33). *Anal*. Calcd for $C_{12}H_{11}N_5O$ (241.25): C, 59.74; H, 4.60; N, 29.03%. Found: C, 59.82; H, 4.66; N, 29.12%.

3-Methyl-5-phenyl-1*H*-[1,2,4]triazolo[3,4-*c*][1,2,4]triazole (9). A mixture of **2** (1.75 g, 10 mmol) and acetic anhydride (15 mL) was heated at reflux for 4 h and then allowed to cool. The solid product was collected by filtration and recrystallized from methanol. Yield 60%, 0.12 g, mp 130–132°C; IR (ν_{max}, cm^{-1}): 3140 (NH). ^1H NMR (300 MHz, $CDCl_3$): δ ppm 1.32 (s, 3H, CH_3), 7.22–7.94 (m, 6H, Ar-H + NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 15.88, 126.84, 128.75, 129.59, 130.21, 148.96, 149.56, 152.87. MS, *m/z* (%) = 199 (M^+, 60). *Anal*. Calcd for $C_{10}H_9N_5$ (199.21): C, 60.29; H, 4.55; N, 35.16%. Found: C, 60.37; H, 4.64; N, 35.24%.

5-Phenyl-1*H*-[1,2,4]triazolo[3,4-*c*][1,2,4]triazole-3-thiol (11). A mixture of **2** (1.75 g, 10 mmol) and carbon disulfide (10 mmol) was heated at reflux for 4 h and then allowed to cool. The solid product was collected by filtration and recrystallized from methanol. Yield 50%, 0.11 g, mp 200–202°C; IR (ν_{max}, cm^{-1}): 3170 (NH); ^1H NMR (300 MHz, $CDCl_3$): δ ppm 7.23–7.90 (m, 6H, Ar-H + NH), 10.55 (s, 1H, SH). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 126.82, 128.77, 129.53, 130.45, 148.88, 152.55, 168.76. MS, *m/z* (%) = 217 ($[M]^+$, 60), 219 (M + 2, 4%). *Anal*. Calcd for $C_9H_7N_5S$ (217.25): C, 49.76; H, 3.25; N, 32.24%. Found: C, 49.85; H, 3.32; N, 32.35%.

5-Phenyl-1*H*-[1,2,4]triazolo[3,4-*c*][1,2,4]triazole (13). A mixture of **2** (1.75 g, 10 mmol) and formic acid (15 mL) was heated under reflux for 4 h and then allowed to cool. The solid product was collected by filtration and recrystallized from methanol. Yield 60%, 0.11 g, mp 233–235°C; IR (ν_{max}, cm^{-1}): 3190 (NH); ^1H NMR (300 MHz, $CDCl_3$): δ ppm 7.23–7.97 (m, 7H, Ar-H + CH-triazole + NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 126.82, 128.75, 129.53, 130.43, 139.99, 148.44, 152.54. MS, *m/z* (%) = 185 ($[M]^+$, 55). *Anal*. Calcd for $C_9H_7N_5$ (185.19): C, 58.37; H, 3.81; N, 37.82%. Found: C, 58.45; H, 3.92; N, 37.90%.

6-Phenyl-3*H*-[1,2,4]triazolo[4,3-*d*]tetrazole (15). To an ice-cooled solution of **2** (1.75 g, 10 mmol) in hydrochloric acid/acetic acid (20:10 v/v), a solution of sodium nitrite (10 mmol) in water (10 mL) was added dropwise. The solution was stirred at room temperature for an additional 2 h; the crude product obtained was filtered off and recrystallized from ethanol as buff powder. Yield 60%, 0.11 g, mp 190–192°C; IR (υ cm^{-1}): 3160 (NH). ^1H NMR (300 MHz, $CDCl_3$): δ ppm 7.22–7.94 (m, 6H, Ar-H + NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 126.82, 128.77, 129.58, 130.47, 148.15, 148.99. MS, *m/z* (%) = 186 ($[M]^+$, 56). *Anal*. Calcd for $C_8H_6N_6$ (186.17): C, 51.61; H, 3.25; N, 45.14%. Found: C, 51.72; H, 3.36; N, 45.26%.

3-Phenyl-3,7-dihydro[1,2,4]triazolo[3,4-*c*][1,2,4]triazin-6(5*H*)-one (17). An equimolar mixture of **2** (1.75 g, 10 mmol) and chloroacetylchloride (1.0 g, 10 mmol) in 30 mL of ethanol containing 0.2 mL of piperidine was refluxed for 6 h. The reaction mixture was concentrated and poured into acidified cold water. The solid product formed was filtered off, washed with cold water, dried, and recrystallized with ethanol/H_2O (3:1) to yield brown powder. Yield 45%, 0.11 g, mp 222–224°C; IR (ν_{max}, cm^{-1}): 3150 (NH), 1690 (CO). ^1H NMR (300 MHz, $CDCl_3$): δ ppm 3.44 (s, 2H, CH_2-triazine), 7.23–7.88 (m, 7H, Ar-H + H-3 triazole + NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 40.87, 76.87, 125.81, 128.79, 129.53, 140.23, 159.37, 160.81. MS, *m/z* (%) = 215 ($[M]^+$, 50), 187 (M–CO, 45), 138 ($[M]^+$–Ph, 30). *Anal*. Calcd for $C_{10}H_9N_5O$ (215.21): C, 55.81; H, 4.22; N, 32.54%. Found: C, 55.92; H, 4.34; N, 32.66%.

2-Benzylidene-1-(5-phenyl-5*H*-1,2,4-triazol-3-yl)hydrazine (18). An equimolar mixture of **2** (1.75 g, 10 mmol) and benzaldehyde (1.06 g, 10 mmol) in ethanol (30 mL) in the presence of piperidine (0.3 mL) was refluxed for 6 h. The reaction mixture was concentrated and poured into acidified cold water. The solid product formed was filtered off, washed with cold water, dried, and recrystallized with ethanol/H_2O (3:1) to yield brown powder. Yield 45%, 0.12 g, mp 230–232°C; IR (ν_{max}, cm^{-1}): 3134 (NH). ^1H NMR (300 MHz, $CDCl_3$): δ ppm 6.12 (s, 1H, –N=CH), 7.23–7.88 (m, 12 H, Ar-H + NH + H-3 triazole). MS, *m/z* (%) = 263 ($[M]^+$, 50). 159 ($[M]^+$–PhCHN,

20). *Anal*. Calcd for $C_{15}H_{13}N_5$ (263.30): C, 68.42; H, 4.98; N, 26.60%. Found: C, 68.55; H, 5.06; N, 26.77%.

2-Phenyl-3-[(3-phenyl-3*H*-1,2,4-triazol-5-yl) amino]-1,3-thiazolidin-4-one (20). An equimolar mixture of **18** (0.32 g, 2 mmol) and thioglycolic acid (0.28 mL, 2 mmol) in dry benzene (20 mL) was refluxed for 10 h. The reaction mixture was evaporated to dryness under reduced pressure. The thiazolidinone was separated off, washed with ether, and recrystallized from ethanol as brown powder. Yield 45%, 0.15 g, mp 224–226°C; IR (ν_{max}, cm^{-1}): 3130 (NH), 1695 (CO). ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 3.39 (s, 2H, CH_2 thiazole), 5.96 (s, 1H, CH thiazole), 7.23–7.88 (m, 12 H, Ar-H + NH + H-3 triazole). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 36.73, 57.45, 76.62, 125.82, 127.54, 128.75, 128.99, 129.53, 129. 89, 133.78, 139.43, 163.89, 168.67. MS, *m/z* (%) = 337 ($[M]^+$, 50), 309 ($[M]^+$–CO, 30), 305 ($[M]^+$–S, 20), 260 ($[M]^+$–Ph, 25). *Anal*. Calcd for $C_{17}H_{15}N_5OS$ (337.40): C, 60.52; H, 4.48; N, 20.76%. Found: C, 60.63; H, 4.59; N, 20.79%.

3-Chloro-4-phenyl-1-[(3-phenyl-3*H*-1,2,4-triazol-5-yl)amino] azetidin-2-one (22). To a well-stirred solution of **18** (0.32 g, 2 mmol) and triethylamine (0.1 mL) in dry dioxane (20 mL), chloroacetyl chloride (0.22 mL, 2 mmol) was added dropwise at room temperature, then the reaction mixture was refluxed for 8 h. The precipitate of triethylamine hydrochloride was filtered and washed thoroughly with dioxane. The filtrate was evaporated to one third of its original volume, cooled and poured into acidified ice/water, and the precipitate formed washed with water thoroughly, dried, and recrystallized from methanol as brown powder. Yield 47%, 0.16 g, mp 228–230°C; IR (ν_{max}, cm^{-1}): 3132 (NH), 1697 (CO). ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 5.12 (d, 1 H, H-4 azetidine), 5.29 (d, 1H, H-3 azetidine), 7.23–7.88 (m, 12 H, Ar-H + H-3 triazole + NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 62.47, 63.63, 76.68, 125.82, 127.87, 128.79, 128.99, 129.44, 129.89, 133.78, 144.43, 163.67, 164.34. MS, *m/z* (%) = 339 ($[M]^+$, 52), 303 ($[M]^+$–Cl, 30), 311 ($[M]^+$–CO, 20), 185 ($[M]^+$–2Ph, 15). *Anal.* Calcd for $C_{17}H_{14}ClN_5O$ (339.78): C, 60.09; H, 4.15; N, 20.61%. Found: C, 60.15; H, 4.25; N, 20.74%.

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