Synthesis of Some New 1,3,4-Thiadiazole, Thiazole and Pyridine Derivatives Containing 1,2,3-Triazole Moiety

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Abstract: In this study, 1-(5-Methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)ethan-1-one, was reacted with Thiosemicarbazide, alkyl carbodithioate and benzaldehyde to give thiosemicarbazone, alkylidenehydrazinecarbodithioate and 3-phenylprop-2-en-1-one-1,2,3-triazole derivatives. The 1,3,4-thiadiazole derivatives containing the 1,2,3-triazole moiety were obtained via reaction of alkylidenecarbodithioate with hydrazonoyl halides. Also, hydrazonoyl halides were reacted with thiosemicarbazone and pyrazolylthioamide to give 1,3-thiazoles derivatives. Subsequently, 3-phenyl-2-en-1-one was used to synthesize substituted pyridines and substituted nicotinic acid ester. The latter was converted to its azide compound which was reacted with aromatic amines and phenol to give substituted urea and phenyl carbamate containing 1,2,3-triazole moiety. The newly synthesized compounds were established by elemental analysis, spectral data and alternative synthesis whenever possible.

Keywords: 1,3,4-thiadiazoles; 1,2,3-triazoles; hydrazonoyl halides; pyridines; nicotinic ester

1. Introduction

In synthesis, 1,2,3-triazoles are useful building blocks and are additionally important due to their broad range of biological activities [1,2]—they are stable to moisture, oxygen, light and metabolic process. A series of novel 1,2,3-triazoles were synthesized [3] and found to have cytotoxic activity against human cancer cell lines such as U937, THP-1, HL60 and B16-F10. The 1,3,4-thiadiazole ring is one of the most important and well-known heterocyclic nuclei, as a common and integral feature of a variety of natural products and medicinal agents. As a core structural component, 1,2,4-thiadiazole is present in an array of drug categories such as antimicrobial, anti-inflammatory, analgesic, antiepileptic, antiviral, antineoplastic, antitubercular and antinociceptive agents [4,5]. Thiazoles display a broad range of biological activities and are found in many potent biologically active molecules such as antimicrobial, antifungal and antineoplastic drugs [6]. However, they are mostly known for their anticancer [7] and antimicrobial [8] activities. Also, pyridine derivatives, including those bearing various heterocyclic nuclei, have shown potent pharmacological properties, including antifungal [9,10], antitubercular [11], antimalarial [12], antibacterial [13], antimicrobial [14], or insecticide [15]. We report here the synthesis of new 1,3,4-thiadiazoles, 5-arylothiazoles, and pyridines containing 1,2,3-triazole moiety.

2. Results

Treatment of 1-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)ethan-1-one (1) [16] with methyl or benzyl carbodithioate [16,17] in 2-propanol gave the corresponding methyls 2-(1-(5-methyl-1-(p-tolyl)-1H-
1,2,3-triazol-4-yl)ethylidene)hydrazinecarbodithioate (2a) [17] and benzyl 2-(1-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)ethylidene)hydrazinecarbodithioate (2b) [18], respectively (Scheme 1). Structures 2a and 2b were elucidated by elemental analyses, spectral data and chemical transformation. Thus, treatment of 2a or 2b with ethyl 2-chloro-2-(2-phenylhydrazono)acetate (3a) in ethanolic triethylamine at room temperature gave one isolated product formulated as ethyl 5-((1-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)ethylidene)hydrazono)-4-phenyl-4,5-dihydro-1,3,4-thiadiazole-2-carboxylate (7a) (Scheme 1). The latter was confirmed by elemental analysis, spectral data, and an alternative synthesis route. Thus, ethyl 5-hydrazono-4-phenyl-4,5-dihydro-1,3,4-thiadiazole-2-carboxylate (8) [19] was reacted with compound 1, in 2-propanol to give a product identical in all aspects (m.p., mixed m.p., and spectra) with 7a.

![Scheme 1. Synthesis of 1,3,4-thiadiazoles 7a,b.](image)

In light of these results, the mechanism outlined in Scheme 1 seems to be the most plausible pathway for the formation of 7a from the reaction of the 2a (or 2b) with 3a. The reaction involves initial formation of thiohydrazonate 5, which undergoes intermolecular cyclization as soon as it is formed to yield the intermediate 6 or via 1,3-dipolar cycloaddition of nitrilimine 4a (generated in situ from 3a with triethylamine) to the C=S double bond of 2. The formations of 5 and 6 are similar to the reactions of hydrazonoyl halides with 1-phenyl-1,4-dihydrotetrazole-5-thione [20] and 5-phenyl-1,3,4-thiadiazole-2(3H)-thione [21]. Intermediate 6 was converted to 7 by elimination of methanethiol (or benzylthiol). Analogously, treatment of the appropriate 2a (or 2b) with 3b gave 2,3-dihydro-1,3,4-thiadiazoles 7b, in good yield (Scheme 1).

After 2-(1-(5-Methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)ethylidene)hydrazinecarbothioamide (9) [21] was reacted with hydrazonoyl chloride 3c in ethanolic triethylamine under reflux to give the
corresponding (2-(2-(1-(5-methyl-1-\((\text{p-tolyl})\)-1H-1,2,3-triazol-4-yl)ethylidene)-hydrazinyl)-4-phenyl-5-(phenyldiazenyl)thiazole (11b) in quantitative yield (Scheme 2), structure 11b was confirmed by elemental analysis, spectral data and alternative synthesis. Thus, 2-(2-(1-(5-methyl-1-\((\text{p-tolyl})\)-1H-1,2,3-triazol-4-yl)ethylidene)-hydrazinyl)-4-phenylthiazole (12) [22], prepared from reaction of 1 with 2-hydrazinyl-4-phenylthiazole (13) [23], or reaction of 9 with α-bromoacetophenone [21], was coupled with benzenediazonium chloride in ethanolic sodium acetate at 0–5 °C to furnish a product identical in all aspects (m.p., mixed m.p., and spectra) to 11b. Analogously, treatment of 9 with the appropriate 3b,d,e gave thiazole derivatives 11a,c,d respectively, in good yields (Scheme 2).

A similar treatment of 9 with ethyl 2-chloro-2-(2-phenylhydrazono)acetate (3a) in ethanolic triethylamine gave 2-(2-(1-(5-methyl-1-\((\text{p-tolyl})\)-1H-1,2,3-triazol-4-yl)ethylidene)-hydrazinyl)-5-(2-phenylhydrazono)thiazol-4(5H)-one (14a) (Scheme 3). Structure 14a was elucidated by elemental analysis, spectral data and an alternative synthetic route. Thus, treatment of benzenediazonium chloride with 2-(2-(1-(5-methyl-1-\((\text{p-tolyl})\)-1H-1,2,3-triazol-4-yl)ethylidene)-hydrazinyl)thiazol-4(5H)-one (15), prepared via reaction of 9 with ethyl chloroacetate in boiling ethanol, in a cold ethanolic sodium acetate solution, afforded a product identical in all aspects (m.p., mixed m.p., and spectra) with 14a. Analogously, the appropriate arenediazonium chloride was coupled with 15 in ethanolic sodium acetate afforded 2-(2-(1-(5-methyl-1-\((\text{p-tolyl})\)-1H-1,2,3-triazol-4-yl)ethylidene)-hydrazinyl)-5-(2-aryldiazenyl)thiazol-4(5H)-one 14b and 14c; respectively (Scheme 3). Also, compound 15 was reacted with benzaldehyde in ethanol in the presence of a catalytic amount of piperidine, giving 5-(benzylidene)-2-(2-(1-(5-methyl-1-\((\text{p-tolyl})\)-1H-1,2,3-triazol-4-yl)ethylidene)-hydrazinyl)thiazol-4(5H)-one (16).

Treatment of 3-(5-methyl-1-\((\text{p-tolyl})\)-1H-1,2,3-triazol-4-yl)-5-phenyl-4,5-dihydro-1H-pyrazole-1-carbothioamide (17) [24,25] with the appropriate α-keto-hydrazonoyl halides 3a,c,e,f in ethanolic triethylamine afforded 5-(aryl diazenyl)-4-substituted-2-(3-(5-methyl-1-\((\text{p-tolyl})\)-1H-1,2,3-triazol-4-yl)-5-phenyl-4,5-dihydro-1H-pyrazol-1-yl)-5-(aryl diazenyl)-4-substituted thiazole 20a-d, respectively (Scheme 4). Structures 20a–d were elucidated via elemental analyses, spectral data and alternative synthetic routes. Thus, 2-(3-(5-methyl-1-\((\text{p-tolyl})\)-1H-1,2,3-triazol-4-yl)-5-phenyl-4,5-dihydro-1H-pyrazol-1-yl)-4-phenylthiazole (21) was coupled with benzenediazonium chloride in ethanolic sodium acetate solution at 0–5 °C, affording a product identical in all aspects (m.p., mixed m.p., and spectra) with 20b.
Scheme 3. Synthesis of thiazolone 14a–d.

Scheme 4. The 2-(3-(5-Methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-5-phenyl-4,5-dihydro-1H-pyrazol-1-yl)-5-(aryldiazenyl)-4-substituted thiazole 20a–d.
In the light of these results, the mechanism outlined in Scheme 4 seems to be the most plausible pathway for the formation of 20 from the reaction of 17 with 3. The reaction involves initial formation of thiohydrazonate 18, which undergoes cyclization as soon as it is formed to yield the intermediate 19. The latter suffers dehydration to the final product 20.

Treatment of 17 with 3b in ethanolic triethylamine gave 2-(3-(5-methyl-1-((p-tolyl)-1H-1,2,3-triazol-4-yl)-5-phenyl-4,5-dihydro-1H-pyrazol-1-yl)-5-(2-phenylhydrazono)thiazol-4(5H)-one (22) in a good yield. Structure 22 was confirmed by elemental analysis and spectral data.

Next, treatment of compound 23 with each of ethyl acetoacetate, acetylacetone, malononitrile, ethyl cyanoacacetate, cyanothioacetamide and benzoylacetonitrile in acetic acid containing ammonium acetate afforded pyridine derivatives 24–29, respectively (Scheme 5). Structures 24–29 were elucidated on the basis of elemental analysis, spectral data and chemical transformation (cf. Experimental and Scheme 5). $^1$H-NMR spectrum of 24 showed signals at $\delta = 1.34$ (t, 3H, CH$_3$CH$_2$O), 2.4 (s, 3H, 4-CH$_3$C$_6$H$_4$), 2.60 (s, 3H, CH$_3$, pyridine H-2), 2.69 (s, 3H, CH$_3$, triazole H-5), 4.2 (q, 2H, CH$_3$O), 7.27–7.73 (m, 9H, ArH’s), 7.90 (s, 1H, pyridine H-5).

Thus, treatment of 24 with hydrazine hydrate in boiling ethanol gave 2-methyl-6-(5-methyl-1-((p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenylnicotinohydrazide (31) in a good yield. Structure 31 was elucidated via elemental analyses, spectral data and chemical transformation. Compound 31 was reacted with each of acetylacetone, ethyl acetoacetate, or with sodium nitrite in the presence of acetic acid to give 32, 33 and azido 34, respectively (Scheme 6).

Meanwhile, each of the compounds 32 and 33 were reacted with benzenediazonium chloride in ethanolic sodium acetate solution, giving (3,5-dimethyl-4-(phenyl diazenyl)-1H-pyrazol-1-yl)-(2-methyl-6-(5-methyl-1-((p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenylpyridin-3-yl)methane (35a) and
5-methyl-2-[2-methyl-6-(5-methyl-1-(p-tolyl)-1H-[1,2,3]triazol-4-yl)-4-phenylpyridine-3-carbonyl]-4-(phenyl-hydrazono)-2,4-dihydro-pyrazol-3-one (36a) (Scheme 6). The structure of compounds 35a and 36a were confirmed by alternative synthesis, by treatment of the hydrazide 31 with each of 3-(2-phenylhydrazono)pentane-2,4-dione (37a) [26] and ethyl 3-oxo-2-(phenylhydrazono)butanoate (37b) [27] in boiling acetic acid for products identical in all aspects (m.p., mixed m.p., and spectra) with 35a and 36a, respectively.

Analogously, p-tolyl diazonium chloride was reacted with each 32 and 33, giving (3,5-dimethyl-4-(p-tolyl diazenyl)-1H-pyrazol-1-yl)(2-methyl-6-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenylpyridin-3-yl)methanone (35b) and 5-methyl-2-(2-methyl-6-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenylnicotinoyl)-4-(2-(p-tolyl)-hydrazono)-2,4-dihydro-3H-pyrazol-3-one (36b), respectively (Scheme 6).

Azido(2-methyl-6-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenylpyridin-3-yl)methanone (34) can be converted into urea derivatives, 38a,b and 3-(2-methyl-6-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenylpyridin-3-yl)quinazoline-2,4(1H,3H)-dione (39) by being boiled with the appropriate aromatic amines, or anthranilic acid in dry dioxane, respectively. Also, phenyl 2-methyl-6-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenylpyridin-3-yl carbamate (40) can be obtained by boiling the azido 34 with phenol in dry benzene (Scheme 6).

Scheme 6. Synthesis of pyrazoles, urea, quinazoline and carbamate.
3. Materials and Methods

All meeting points were determined on an electro thermal Gallen Kamp melting point apparatus (Laim George, Calgary, AB, Canada) and are uncorrected. IR (cm⁻¹) spectra were recorded on KBr disk on a FTIR-8201 spectrophotometer (Shimadzu, Tokyo, Japan). ¹H-NMR and ¹³C-NMR spectra were measured in deuterated dimethyl sulfoxide (DMSO-d₆) using a Varian Gemini 300 NMR spectrometer (Varian, Inc., Karlsruhe, Germany). Mass spectra were recorded on a Shimadzu GCMS-QP1000 EX mass spectrometer (Tokyo, Japan) at 70 eV. Measurements of the elemental analysis were carried out at the Microanalytical Centre of Cairo University, Giza, Egypt. All reactions were followed by TLC (Silica gel, Merck, Kenilworth, NJ, USA). Hydrazonoyl halides were prepared as previously reported [28–31]

### 3.1. Alkyl 2-(1-(5-Methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-ethylidene)hydrazine-1-carboxdiethioate 2a and 2b

A mixture of 1-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)ethanone (1) [16] (1 g, 5 mmol) and alkyl carbodithioate (5 mmol) in 2-propanol (20 mL) was refluxed for 30 min. The reaction mixture was cooled and the resulting solid was collected and crystallized from the proper solvent to give 2a,b.

**Methyl 2-(1-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-ethylidene)hydrazine-1-carboxdiethioate (2a).** Buff crystals from ethanol: yield: 75%, m.p.: 186 °C, FT-IR (KBr, cm⁻¹): 3330, 3280 (NH), 1696 (CO), 1603 (C=N), 1561 (C=C); δ = 2.36 (s, 3H, CH₃), 2.45 (s, 3H, CH₃), 2.50 (s, 3H, CH₃), 3.20 (s, 3H, CH₃), 7.38–7.51 (m, 4H, ArH’s) and 12.4 (s, br, 1H, NH). Anal. Calcld. For C₁₄H₁₇N₃S₂ (319.46) C, 52.64; H, 5.35; N, 17.71; S, 16.21 Found C, 52.70; H, 5.40; N, 17.68; S, 16.30.

**Benzyl 2-(1-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-ethylidene)hydrazine-1-carboxdiethioate (2b).** Buff crystals from DMF: yield 75%, m.p.: 324 °C, FT-IR (KBr, cm⁻¹): 3421 (NH), 3052 (CH), 1611 (C≡N), 1553 (C=C); ¹H-NMR (300 MHz, DMSO-d₆): δ = 2.41 (s, 3H, CH₃), 2.50 (s, 3H, CH₃), 2.73 (s, 3H, CH₃), 3.28 (s, 2H, CH₂), 7.39–7.47 (m, 9H, ArH’s) and 12.35 (s, br, 1H, NH). Anal. Calcld. For C₂₀H₂₁N₃S₂ (395.54) C, 60.73; H, 5.35; N, 17.71; S, 16.21 Found C, 60.69; H, 5.32; N, 17.68; S, 16.30.

3.2. 5-[(1-(5-Methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)ethylidene-4-phenyl-4,5-dihydro-1,3,4-thiadiazole-derivatives 7a,b

**Method A:** Triethyl amine (0.75 mL, 0.5 g, 5 mmol) was added dropwise with stirring to a mixture of the appropriate alkyl carbodithioate 2a or 2b (5 mmol) and the appropriate hydrazonoyl halides 3a,b (5 mmol) in ethanol (20 mL). The resulting solid which formed after 30 min was collected and crystallized from the proper solution to give the corresponding thiaidazole derivatives 7a,b.

**Ethyl 5-[(1-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)ethylidene)hydrazono]-4-phenyl-4,5-dihydro-1,3,4-thiadiazole-2-carboxylate (7a).** Yellow crystals from acetic acid Yield: 70%, m.p.: 205–207 °C; FT-IR (KBr, cm⁻¹): 3047 (CH), 1708 (CO), 1616 (C≡N), 1573 (C=C); ¹H-NMR (300 MHz, CDCl₃): δ = 1.59 (t, 3H, CH₂-CH₃), 2.48 (s, 3H, CH₃), 2.64 (s, 3H, CH₃), 2.71 (s, 3H, CH₃), 4.50 (q, 2H, CH₂-CH₃), and 7.26–8.14 (m, 9H, ArH’s); MS (EI, m/z (%)): 461 (M⁺, 100), 433 (20), 400 (80), 289 (20), 243 (20), 184 (30), 91 (30), 80 (100), 64 (40); Anal. Calcld. For C₂₃H₂₃N₇SO₂ (461.55) C, 59.85; H, 5.02; N, 24.10; S, 19.00 Found C, 59.90; H, 5.12; N, 21.34; S, 6.99

11(5-[(1-(5-Methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)ethylidene)hydrazono]-4-phenyl-4,5-dihydro-1,3,4-thiadiazol-2-yl)ethan-1-one (7b). Yellow crystals from ethanol. Yield: 80%, m.p.: 270–271 °C; FT-IR (KBr, cm⁻¹): 2924 (CH), 1678 (CO), 1616 (C≡N), 1573 (C=C); ¹H-NMR (300 MHz, CDCl₃): δ = 2.48 (s, 3H, CH₃), 2.63 (s, 3H, CH₃), 2.65 (s, 3H, CH₃), 2.71 (s, 3H, CH₃), and 7.26–8.14 (m, 9H, ArH’s); ¹³C-NMR in CHCl₃ δ = 9.4 (5-CH₃ triazole), 13.9 (=CH₃), 19.9 (4-CH₃C₆H₄), 24.7 (CH₃CO), 123.3, 125.4, 127.2, 127.8, 129.3, 130.2, 132.4, 139.7, 140.7, 142.33, 147.8, 152.7, 163.8, 189.1 (CO), MS (EI, m/z (%)): 431 (M⁺, 100), 403 (5), 370 (10), 360 (30), 301 (10), 259 (15), 194 (55), 184 (3), 172 (40), 91 (50), 80 (100), 64 (50); Anal. Calcld. For C₂₂H₂₁N₇O₂S (431.52) C, 61.23; H, 4.91; N, 22.72; S, 7.43 Found C, 61.40; H, 4.89; N, 22.80; S, 7.80
Alternative synthesis of Ethyl 5-(1-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)ethylidene-4-phenyl-4,5-dihydro-1,3,4-thiadiazole-2-carboxylate (7a).

**Method B:** A mixture of ethyl 5-hydrazono-4-phenyl-4,5-dihydro-1,3,4-thiadiazole-2-carboxylate (8) [18] (1.3 g, 5 mmol) and 1-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)ethanone (1) (1 g, 5 mmol) in 2-propanol were heated for 30 min. The crude solid that was collected and crystallized from ethanol gave a product identical in all aspects (m.p., mixed m.p. and spectra) with 7a.

### 3.3. 2-(2-(5-Methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)ethylidene-4-phenylthiazole derivatives

**Method A:** A mixture of 9 (1.4 g, 5 mmol), the appropriate hydrazonoyl halides 3b–e (5 mmol) and triethylamine (0.5 g, 0.7 mL, 5 mmol) in ethanol was heated under reflux for 3 h. The resulting solid that was collected and recrystallized gave thiazole derivatives 11a–d.

### 4-Methyl-2-(2-(5-Methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)ethylidenehydrazinyl)-5-((E)-phenylidiazinyl) thiazole (11a). Orange crystals from acetic acid; Yield: 70%, m.p.: 245 °C; FT-IR (KBr, cm\(^{-1}\)): 3417 (NH), 1578 (C=C); \(^{1}\)H-NMR (300 MHz, CDCl\(_3\)): \(\delta = 2.45\) (s, 3H, CH\(_3\)), 2.50 (s, 3H, CH\(_3\)) 2.54 (s, 3H, CH\(_3\)), 2.62 (s, 3H, CH\(_3\)), 6.96–7.55 (m, 9H, ArH's) and 9.18 (s, br, 1H, NH). \(^{13}\)C-NMR (DMSO-\(d_6\)) \(\delta = 8.1, 12.9, 13.7, 20.8, 114.4, 121.6, 123.8, 129.0, 129.6, 129.9, 130.4, 139.1, 139.6, 146.2, 154.6, 160.1, 164.9. Anal. Calcd. For C\(_{22}\)H\(_{22}\)N\(_8\)S: C, 65.83; H, 4.55; N, 24.10, S, 6.51. Found C, 65.79, N, 22.78, S, 6.561.

### 2-(2-(5-Methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)ethylidenehydrazinyl)-4-phenyl-5-((E)-phenylidiazinyl) thiazole (11b). Orange crystals from ethanol, Yield: 70%, m.p.: 240 °C; FT-IR (KBr, cm\(^{-1}\)): 3421 (NH), 1593 (C=C); \(^{1}\)H-NMR (300 MHz, CDCl\(_3\)): \(\delta = 2.45\) (s, 3H, CH\(_3\)), 2.50 (s, 3H, CH\(_3\)) 2.54 (s, 3H, CH\(_3\)), 2.62 (s, 3H, CH\(_3\)), 6.95–7.55 (m, 9H, ArH's) and 9.18 (s, br, 1H, NH). Anal. Calcd. For C\(_{22}\)H\(_{22}\)N\(_8\)S: C, 65.83; H, 4.55; N, 24.10, S, 6.51. Found C, 65.79, N, 22.78, S, 6.561.

### 4-Methyl-2-(2-(5-Methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)ethylidenehydrazinyl)-5-((Z)-phenylidiazinyl) thiazole (11c). Gray crystals from acetic acid, Yield: 70%, m.p.: 240 °C; FT-IR (KBr, cm\(^{-1}\)): 3417 (NH), 1578 (C=C); \(^{1}\)H-NMR (300 MHz, DMSO-\(d_6\)): \(\delta = 2.29\) (s, 3H, CH\(_3\)), 2.45 (s, 3H, CH\(_3\)), 2.54 (s, 3H, CH\(_3\)) 2.62 (s, 3H, CH\(_3\)), 6.95–7.55 (m, 9H, ArH's) and 9.18 (s, br, 1H, NH). \(^{13}\)C-NMR (DMSO-\(d_6\)) \(\delta = 8.1, 12.9, 13.7, 20.8, 114.2, 121.6, 123.8, 129.0, 129.6, 129.9, 130.4, 139.1, 139.6, 146.2, 154.6, 160.1, 164.7. Anal. Calcd. For C\(_{27}\)H\(_{24}\)N\(_8\)S: C, 65.63; H, 4.91; N, 22.75; S, 6.51. Found C, 65.79, N, 22.78, S, 6.561.

### 5-((Z)-(4-Chlorophenylidiazinyl)-4-methyl-2-(2-(5-Methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)ethylidene) hydrazinyl)thiazole (11d). Red crystals from ethanol, Yield: 70%, m.p.: 240 °C; FT-IR (KBr, cm\(^{-1}\)): 3387 (NH), 3089, 3028 (CH), 1585 (C=C); \(^{1}\)H-NMR (300 MHz, DMSO-\(d_6\)): \(\delta = 2.49\) (s, 3H, CH\(_3\)), 2.58 (s, 3H, CH\(_3\)), 2.65 (s, 3H, CH\(_3\)), 3.30 (s, 3H, CH\(_3\)), 7.34–7.54 (m, 8H, ArH's), and 10.65 (s, br, 1H, NH). Anal. Calcd. For C\(_{27}\)H\(_{24}\)N\(_8\)S: C, 56.83; H, 5.83; N, 26.13; S, 7.50. Found C, 56.89; H, 5.80; N, 26.13; S, 7.50.

### Method B: Benzenediazonium chloride (5 mmol), prepared in the usual way from aniline (0.46 g, 5 mmol), hydrochloric acid (1.5 mL, 6 M) and sodium nitrite (0.35 g, 5 mmol), was added dropwise with stirring to a cold solution of 2-(2-(1-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)ethylidene)hydrazinyl)-4-phenylthiazole (12) (1.9 g, 5 mmol) and sodium acetate (1.3 g, 10 mmol) in ethanol (30 mL) at 0–5 °C. The reaction mixture was stirred for 3 h in an ice bath and was left in refrigerator overnight. The solid was collected and crystallized from ethanol, giving a product identical (m.p., mixed mp and spectra) with 11b.

### 3.4. 2-(2-(5-Methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)ethylidene)hydrazinyl)-4-phenylthiazole (13)

**Method A:** A mixture of 9 (1.4 g, 5 mmol) and \(\omega\)-bromoaacetophenone (1 g, 5 mmol) in ethanol was refluxed for 4 h. The resulting solid that was collected and crystallized from ethanol gave a white crystal of 13, Yield: 75%, m.p. 290 °C (Lit. m.p. 273 °C [22]).
Method B: A mixture of 2-hydrazinyl-4-phenylthiazole (12) (1.76 g, 10 mmol), I (2.1 g, 5 mmol) in ethanol (20 mL) and conc. hydrochloric acid (2 drops) was heated under reflux for 15 min. The solid was collected and crystallized from ethanol giving a product identical in all aspects (m.p., mixed m.p., and spectra) with the above sample obtained by Method A.

3.5. (E)-5-(2-(4-Chlorophenyl)hydrazono)-2-((Z)-2-(1-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)ethylidene)-hydrazinyl)thiazol-4(5H)-one 14a–c

Method A: A mixture of 9 (1.4 g, 5 mmol), hydrazonoyl halide 3a (5 mmol) and triethylamine (0.5 g, 0.7 ml, 5 mmol) in ethanol was boiled under reflux for 3 h. The resulting solid was collected and recrystallized from acetic acid afforded by 14a.

Method B: Dropwise addition of arenediazonium chlorides (5 mmol), which was prepared via reaction of the appropriate aniline, p-toluidine, p-chloroaniline (5 mmol), hydrochloric acid (1.5 ml, 6 M), sodium nitrite (0.37 g, 5 mmol) at 0–5 °C, to a mixture of 15 (1.64 g, 5 mmol) and sodium acetate (0.66 g, 5 mmol) in ethanol at 0–5 °C, while stirring. The reaction mixture was stirred for 3 h. The resulting solid was collected, washed with water and crystallized, giving 14a–c.

(E)-2-((Z)-2-((1-(5-Methyl-1-((p-tolyl)-1H-1,2,3-triazol-4-yl)ethylidene)hydrazinyl)-5-(2-p-tolyl)hydrazono)thiazol-4(5H)-one (14a). Yellow crystals from acetic acid, Yield 75%, m.p. >300 °C; FT-IR (KBr, cm⁻¹): 3431, 3211 (NH), 1581 (C=C), 1659 (CO), 1604 (C=N); 1H-NMR (300 MHz, DMSO-d₆): δ = 2.44 (s, 3H, CH₃), 2.49 (s, 3H, CH₃), 3.22 (s, 3H, CH₃), 7.41–7.50 (m, 8H, ArH's), 7.42–8.32 (m, 4H, ArH's), 8.12 (br, 1H, NH) and 10.9 (s, br, 1H, NH). 13C-NMR (DMSO-d₆) δ = 8.1, 19.2, 21.0, 115.4, 123.8, 127.7, 129.8, 130.1, 139.2, 139.8, 145.7, 146.3, 147.2, 159.4, 167.9, 176.1. Anal. Calcd. For C₂₁H₂₀N₆OS (432.51), C, 58.32; H, 4.66; N, 25.91; S, 4.70; Found C, 58.30; H, 4.69; N, 25.80; S, 7.50.

(E)-2-((Z)-2-((1-(5-Methyl-1-((p-tolyl)-1H-1,2,3-triazol-4-yl)ethylidene)hydrazinyl)-5-(2-p-tolyl)hydrazono)thiazol-4(5H)-one (14b). Brown crystals from ethanol, Yield: 80%, m.p. >300 °C; FT-IR (KBr, cm⁻¹): 3431, 3267 (NH), 1581 (C=C), 1659 (CO), 1604 (C=N); 1H-NMR (300 MHz, DMSO-d₆): δ = 2.26 (s, 3H, CH₃), 2.47 (s, 3H, CH₃), 2.49 (s, 3H, CH₃), 2.53 (s, 3H, CH₃), 7.41–7.50 (m, 8H, ArH's), 8.11 (s, br, 1H, NH) and 10.9 (s, br, 1H, NH). 13C-NMR (DMSO-d₆) δ = 8.1, 19.2, 20.6, 21.0, 117.4, 123.9, 128.6, 129.9, 130.2, 136.8, 139.2, 139.8, 145.2, 145.8, 146.3, 159.6, 167.9, 176.0. Anal. Calcd. For C₂₂H₂₅N₆OS (446.54), C, 59.18; H, 4.97; N, 25.09; S, 7.18 Found C, 59.28; H, 4.89; N, 25.11; S, 7.28.

(E)-5-(2-(4-Chlorophenyl)hydrazono)-2-((Z)-2-((1-(5-methyl-1-((p-tolyl)-1H-1,2,3-triazol-4-yl)ethylidene)hydrazinyl)-5-(2-p-tolyl)hydrazono)thiazol-4(5H)-one (14c). Pale brown crystals from ethanol, Yield: 70%, m.p.: 263–265 °C; FT-IR (KBr, cm⁻¹): 3431,3108 (NH), 2972 (CH), 1664 (CO), 1634 (C=N); 1H-NMR (300 MHz, DMSO-d₆): δ = 2.42 (s, 3H, CH₃), 2.53 (s, 3H, CH₃), 3.30 (s, 3H, CH₃), 7.42–7.51 (m, 8H, ArH's), 8.32 (s, br, 1H, NH) and 11.99 (s, br, 1H, NH). Anal. Calcd. For C₂₁H₁₉N₆OCl (466.96), C, 54.02; H, 4.41; N, 24.00; S, 6.87; Cl, 7.59 Found: C, 54.12; H, 4.20; N, 24.05; S, 6.90.

3.6. (E)-2-((1-(5-Methyl-1-((p-tolyl)-1H-1,2,3-triazol-4-yl)ethylidene)hydrazinyl)thiazol-4(5H)-one (15)

A mixture of 9 (1.4 g, 5 mmol) and ethyl chloroacetate (0.61 g, 5 mmol) in ethanol was refluxed for 4 h. The resulting solid was collected and recrystallized from ethanol that gave white crystals of 15, Yield: 75%, m.p. 255 °C. FT-IR (KBr, cm⁻¹): 3116 (NH), 2951 (CH), 1735 (CO), 1624 (C=N); 1H-NMR (300 MHz, DMSO-d₆): δ = 2.46 (s, 3H, CH₃), 2.54 (s, 3H, CH₃), 3.30 (s, 3H, CH₃), 3.87 (s, 2H, OCH₂), 7.42–8.32 (m, 4H, ArH's) and 11.97 (s, br, 1H, NH). 13C-NMR (DMSO-d₆) δ = 8.1, 19.1, 20.8, 37.1, 123.9, 129.7, 129.9, 139.2, 139.7, 146.0, 159.7, 168.0, 183.5. Anal. Calcd. For C₁₅H₁₆N₆O₄S (328.40), C, 54.86; H, 4.91; N, 25.59; S, 9.76 Found: C, 54.90; H, 4.95; N, 25.34; S, 9.70.
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3.7. (E)-5-Benzylidene-2-((E)-2-(1-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)ethyldiene)-hydrazinyl)thiazol-4(5H)-one (16)

A mixture of 15 (1.6 g, 5 mmol) and benzaldehyde (0.53 g, 5 mmol) in ethanol and catalytic amount of piperidine (5 drops) was refluxed for 3 h. The resulting solid was collected and recrystallized from acetic acid affording white crystals of 16. Yield: 80%, m.p.: 283 °C. FT-IR (KBr, cm⁻¹): 3124 (NH), 2974 (CH), 1705 (CO), 1624 (C=N). ¹H-NMR (300 MHz, DMSO-d₆): δ = 2.49 (s, 3H, CH₃), 2.54 (s, 3H, CH₃), 3.30 (s, 3H, CH₃), 7.42–7.51 (m, 10H, ArH’s and =CH) and 11.91 (s, br, 1H, NH). ¹³C-NMR (DMSO-d₆) δ = 8.1, 19.1, 20.8, 123.9, 129.2, 129.7, 129.9, 130.7, 132.5, 138.2, 139.3, 139.6, 146.2, 159.8, 167.8, 174.1. Anal. Calcd. For C₉₂H₂₀N₈SO (416.51), C, 63.44; H, 4.84; N, 20.18; S, 7.70. Found: C, 63.50; H, 4.90; N, 20.20; S, 7.75.

3.8. 5-(Aryldiazenyl)-4-substituted-2-(3-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-5-phenyl-4,5-dihydro-1H-pyrazole-1-yl)thiazole 20a–d, 21

Method A: A mixture of 17 (1.9 g, 5 mmol), the appropriate hydrazonoyl halides 3a,c,e,f or 3b (5 mmol) and triethyl amine (0.5 mg, 0.75 mL, 5 mmol) in ethanol (20 mL) was heated under reflux for 4 h. The resulting solid was collected and recrystallized, giving thiazole derivatives 20a–d and 21.

Method B: Benzenediazonium chloride (5 mmol) which was prepared via reaction of aniline (0.55 g, 5mmol), hydrochloric acid (3 mL, 6 M), and sodium nitrite (0.35 g, 5 mmol) was added dropwise, with stirring, to a cold solution of 21. The reaction mixture was stirred for 3 h. The resulting solid was collected, washed with water and crystallized from ethanol, giving 20b.

(E)-4-Methyl-2-(3-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-5-phenyl-4,5-dihydro-1H-pyrazol-1-yl)-5-(phenylidazinyl)thiazole (20a). Orange crystals from acetic acid, Yield: 75%, m.p.: 235 °C; FT-IR (KBr, cm⁻¹): 3045, 2926, 2860 (CH), 1653 (C=N), 1587 (C=C); ¹H-NMR (300 MHz, DMSO-d₆): δ = 2.49 (s, 3H, CH₃), 2.56 (s, 3H, CH₃), 2.70 (s, 3H, CH₃), 3.72–3.74 (dd, 1H, Hₓ), 3.78 (dd, 1H, Hₓ), 5.78 (dd, 1H, Hₓ) and 7.26–7.76 (m, 14H, ArH’s). ¹³C-NMR (DMSO-d₆) δ = 8.1, 12.82, 21.0, 33.2, 63.6, 114.8, 121.7, 123.8, 127.5, 129.1, 129.8, 130.1, 130.7, 130.9, 139.2, 139.7, 144.8, 149.6, 154.1, 161.1. MS (El, m/z (%)): 518 (M⁺, 100), 489 (5), 413 (2), 273 (15), 184 (20), 170 (15), 144 (25), 91 (35%), 77 (70), 65 (17). Anal. Calcd. For C₉₂H₂₅N₈O (518.65), C, 67.16; H, 5.05; N, 21.61; S, 6.18. Found C, 67.26; H, 5.10; N, 21.69; S, 6.28.

(E)-2-(3-(5-Methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-5-phenyl-4,5-dihydro-1H-pyrazol-1-yl)-4-phenyl-5-(phenylidazinyl)thiazole (20b). Red crystals from acetic acid, Yield: 70%, m.p.: 275 °C; FT-IR (KBr, cm⁻¹): 3043, 2924 (CH), 1666 (C=N); ¹H-NMR (300 MHz, CDCl₃): δ = 2.49 (s, 3H, CH₃), 2.71 (s, 3H, CH₃), 3.73–3.78 (dd, 1H, Hₓ), 4.18 (dd, 1H, Hₓ), 5.82 (dd, 1H, Hₓ) and 7.33–8.18 (m, 19H, ArH’s). ¹³C-NMR (DMSO-d₆) δ = 8.1, 12.82, 21.0, 33.2, 63.6, 108.7, 121.7, 123.8, 126.7, 127.4, 128.2, 128.7, 128.2, 129.8, 129.9, 130.1, 130.4, 130.9, 133.1, 136.2, 139.1, 139.7, 144.7, 154.7, 168.0 MS (El, m/z (%)): 580 (M⁺, 85), 551 (30), 447 (10), 367 (30), 133 (40), 91 (50), 77 (100), 65 (20). Anal. Calcd. For C₉₂H₂₅N₈S (580.72), C, 70.32; H, 4.86; N, 19.30; S, 5.52. Found C, 70.22; H, 4.75; N, 19.20; S, 5.56.

(E)-4-Methyl-2-(3-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-5-phenyl-4,5-dihydro-1H-pyrazol-1-yl)-5-(phenylidazinyl)thiazole (20c). Red crystals from acetic acid, Yield: 70%, m.p.: 240 °C; FT-IR (KBr, cm⁻¹): 3039, 2926 (CH), 1658 (C=N); ¹H-NMR (300 MHz, CDCl₃): δ = 2.40 (s, 3H, CH₃), 2.46 (s, 3H, CH₃), 2.60 (s, 3H, CH₃), 2.72 (s, 3H, CH₃), 3.5–3.6 (dd, 1H, Hₓ), 4.1–4.2 (dd, 1H, Hₓ), 5.61–5.64 (dd, 1H, Hₓ) and 6.81–8.17 (m, 13H, ArH’s). Anal. Calcd. For C₉₀H₂₅N₈S (532.68), C, 67.65; H, 5.30; N, 2.04; S, 6.02. Found C, 67.72; H, 5.34; N, 2.14; S, 6.12.

(E)-5-((4-Chlorophenylidazinyl)-4-methyl-2-(3-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-5-phenyl-4,5-dihydro-1H-pyrazol-1-yl)thiazole (20d). Red crystals from ethanol, Yield:65%, m.p.: 220 °C; FT-IR (KBr, cm⁻¹): 3037, 2926 (CH), 1670 (C=N); ¹H-NMR (300 MHz, CDCl₃): δ = 2.48 (s, 3H, CH₃), 2.56 (s, 3H, CH₃), 2.69 (s, 3H,CH₃), 3.63–3.72 (dd, 1H, Hₓ), 4.11–4.21 (dd, 1H, Hₓ), 5.64–5.70 (dd, 1H, Hₓ) and
6.81–7.71 (m, 13H, ArH’s). Anal. Calcd. For C_{29}H_{25}N_{8}SCl (553.09), C, 62.98; H, 4.56; N, 20.26; S, 5.80; Cl, 6.41 Found C, 62.85; H, 4.55; N, 20.30; S, 5.89.

3.9. 2-(3-(5-Methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-5-phenyl-4,5-dihydro-1H-pyrazol-1-yl)-4-phenylthiazole (21)

A mixture of 17 (1.85 g, 5 mmol) and ω-bromoacephenone (1 g, 5 mmol) in ethanol was refluxed for 4 h. The resulting solid was collected and crystallized from ethanol giving white crystals of 21. Yield: 75%, m.p. 220 °C (Lit. m.p. 193 °C [25]).

3.10. 2-(3-(5-Methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-5-phenyl-4,5-dihydro-1H-pyrazol-1-yl)-5-(2-phenyl-hydrazono)thiazol-4(5H)-one (22)

A mixture of 4,5-dihydro-3-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-5-phenyl-pyrazol-1-carbothioamide (17) (1.9 g, 5 mmol) and ethyl 2-chloro-2-(2-phenylhydrazono)acetate (3b) (1.1 g, 5 mmol) in ethanol (20 mL) was heated under reflux for 3 h. The resulting solid was collected and recrystallized from acetic acid, giving 22 as pale orange crystals. Yield 75%, m.p. 294–296 °C, FT-IR (KBr, cm⁻¹): 3437 (NH), 3049, 2929 (CH), 1695 (CO), 1658 (C=Н). 1H-NMR (300 MHz, CDCl₃): δ = 2.48 (s, 3H, CH₃), 2.65 (s, 3H, CH₃), 3.73–3.85 (dd, 1H, CH), 4.09–4.19 (dd, 1H, H₆), 5.77–5.81 (dd, 1H, H₅), 7.26–7.38 (m, 15H, ArH’s and NH). 13C-NMR (DMSO-d₆) δ = 8.1, 12.82, 21.0, 33.2, 67.2, 115.3, 122.3, 123.9, 127.0, 127.8, 128.7, 129.8, 129.9, 130.7, 139.1, 139.7, 144.0, 144.6, 146.7, 149.5, 156.6, 175.1. Anal. Calcd. For C_{28}H_{24}N_{8}OS (520.62): C, 64.60; H, 4.65; N, 21.52; S, 6.16. Found, C, 64.67; H, 4.70; N, 21.60; S, 6.19.

3.11. 6-(5-Methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenylpyridine derivatives (24)–(29)

General procedure: A mixture of 23 (1.5 g, 5 mmol), the appropriate acetylacetone, ethyl acetoacetate, ethyl cyanoacetate, cyanothioacetamide, malononitrile, benzoylacetonitrile and ammonium acetate (0.38 g, 5 mmol) in acetic acid (10 mL) was heated under reflux for 4 h. The resulting solid was filtered, washed with water and crystallized from the proper solvent, giving pyridine derivatives 24–29.

Ethyl 2-methyl-6-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenylnicotinate (24). Yellow crystals from ethanol, yield 85% m.p.: 195 °C, FT-IR (KBr, cm⁻¹): 3035, 2953 (CH); 1660 (CO), 1629 (C=Н); 1579 (C=C); 1H-NMR (300 MHz, CDCl₃): δ = 1.34 (t, 3H, CH₂CH₃), 2.42 (s, 3H, CH₃), 2.60 (s, 3H, CH₃), 2.69 (s, 3H, CH₃), 4.20 (q, 2H, CH₂CH₃), 7.27–7.73 (m, 10H, ArH’s and pyridine H-5). 13C-NMR (DMSO-d₆) δ = 11.5, 13.82, 20.9, 23.5, 41.7, 63.6, 93.3, 118.6, 123.0, 125.3, 125.8, 129.4, 132.3, 133.6, 134.52, 142.4, 146.0, 154.3, 167.9, 175. MS (El, m/z (%): 412 (M⁺, 15), 395 (10), 384 (50), 325 (30), 342 (10), 247 (70), 132 (100), 103 (80), 91 (90), 77 (40), 65 (55)). Anal. Calcd. for C_{25}H_{24}O_{2}N_{4} (412.49), C, 72.80; H, 5.86; N, 13.60. Found: C, 72.86; H, 5.90; N, 13.65.

1-(2-Methyl-6-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenylpyridin-3-yl)ethan-1-one (25). Orange crystals from acetic acid, yield 70% m.p.: 190 °C, FT-IR (KBr, cm⁻¹): 3002, 2949 (CH); 1737 (CO), 1614 (C=Н); 1579 (C=C). 1H-NMR (300 MHz, CDCl₃): δ = 2.09 (s, 3H, CH₃), 2.43 (s, 3H, CH₃), 2.46 (s, 3H, CH₃), 2.66 (s, 3H, CH₃) and 7.26–8.14 (m, 10H, ArH’s and pyridine H-5). MS (El, m/z (%): 384 (M⁺², 20), 369 (10), 354 (60), 341 (70), 247 (40), 194 (35), 144 (15), 132 (95), 91 (99), 77 (40), 65 (60)). Anal. Calcd. For C_{24}H_{22}O_{2}N₄ (382.47): C, 75.37; H, 5.80; N, 14.65. Found C, 75.47; H, 5.95; N, 14.75.

2-Amino-6-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenylpyridin-3-carbonitrile (26). Yellow crystals from acetic acid, Yield 75%, m.p.: 197 °C, FT-IR (KBr, cm⁻¹): 3427, 3224 ν(NH₂), 3002, 2954 ν(CH); 2276 ν(CN); 1635 ν(C=Н); 1581 ν(C=C). 1H-NMR (300 MHz, CDCl₃): δ = 2.46 (s, 3H, CH₃), 2.65 (s, 3H, CH₃), 6.95 (s, br, 2H, NH₂), 7.26–8.14 (m, 10H, ArH’s and pyridineH-5). 13C-NMR (DMSO-d₆) δ = 11.5, 20.9, 63.6, 91.7, 97.8, 118.4, 118.8, 121.3, 127.5, 128.8, 129.7, 133.52, 133.7, 140.3, 142.5, 150.6, 160.7, 166. MS (El, m/z (%)): 366 (M⁺, 60), 351 (30), 338 (40), 247 (50), 194 (0), 144 (30), 132 (70), 103 (50),
91 (70), 80 (100), 64 (50). Anal. Calcd. for C_{22}H_{18}N_{6}O (366.43), C, 72.11; H, 4.95; N, 22.94 Found: C, 72.15; H, 4.85; N, 22.88.

6-(5-Methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-2-oxo-4-phenyl-pyridine-3-carbonitrile (27). Yellow crystals from acetic acid. Yield 75%, m.p. 193 °C, FT-IR (KBr, cm^{-1}): 3433 (NH), 3043, 2929 (CH); 1668 (CO), 1643 (C=C), 1581 (C=C). ^{1}H-NMR (300 MHz, CDCl$_3$): $\delta$ = 2.47 (s, 3H, CH$_3$), 2.65 (s, 3H, CH$_3$), 7.26–8.14 (m, 10H, ArH's and pyridine H-5), 11.65 (s, br, 1H, NH), MS (EI, m/z (%)): 368 (M$^+$, 40), 304 (10), 247 (65), 194 (55), 132 (100), 115 (30), 103 (70), 91 (85), 77 (40), 65 (50). Anal. Calcd. For C$_{22}$H$_{17}$N$_{5}$O (367.41), C, 71.92; H, 4.66; N, 19.06. Found: C, 71.89; H, 4.65; N, 19.16.

6-(5-Methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenyl-2-thioxo-pyridine-3-carbonitrile (28). Orange crystals from acetic acid. Yield 70%, m.p. 278 °C, FT-IR (KBr, cm^{-1}): 3437 (NH); 3037, 2920 (CH); 2211 (CN), 1584 (C=C), 1615 (C=N), ^{13}C-NMR (DMSO-d$_6$): $\delta$ = 8.5, 20.9, 108.4, 112.2, 118.3, 123.2, 128.8, 129.7, 129.9, 130.4, 135.4, 135.8, 139.4, 139.8, 150.3, 150.7, 177.8. MS (EI, m/z (%)): 383 (M$^+$, 40), 303 (5), 247 (50), 194 (50), 132 (100), 103 (60), 90 (100), 77 (50), 68 (60). Anal. Calcd. For C$_{22}$H$_{17}$N$_{5}$S (383.48), C, 68.91; H, 4.47; N, 18.26; S, 8.36. Found C, 68.89; H, 4.37; N, 19.03; S, 8.46.

(2-Amino-6-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenylpyridin-3-yl)methanone (29). Pale yellow crystals from ethanol, Yield 70%, m.p.: 183 °C, FT-IR (KBr, cm^{-1}): 3431, 3330 (NH$_2$), 2972, 2925 (CH), 1659 (C=C), 1596 (C=C). ^{1}H-NMR (300 MHz, CDCl$_3$): $\delta$ = 2.49 (s, 3H, CH$_3$), 2.56 (s, 3H, CH$_3$), 6.93 (s, br, 2H, NH$_2$), 7.26–8.12 (m, 15H, ArH's and pyridine H-5). Anal. Calcd. For C$_{28}$H$_{23}$N$_{6}$O (445.53), C, 75.49; H, 5.20; N, 15.72 Found C, 75.39; H, 5.43; N, 15.65.

3.12. 2-Methyl-6-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenylnicotinohydrazide (31)

Equimolar amounts of ethyl 6-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenylpyridine-3-carboxylate (24) (2.2 g, 5 mmol) and hydrazine hydrate (1 mL, 10 mmol) in ethanol (10 mL) were refluxed for 5 h. The resulting solid was collected and recrystallized, giving 31 as white crystals from ethanol, Yield 89%, m.p.: 145 °C, FT-IR (KBr, cm^{-1}): 3431, 3335 (NH$_2$), 2960, 2923 (CH); 1662 (CO); 1572 (C=C). ^{1}H-NMR (300 MHz, CDCl$_3$): $\delta$ = 2.49 (s, 3H, CH$_3$), 2.56 (s, 3H, CH$_3$), 7.21–7.57 (m, 11H, ArH's, pyridine H-5). Anal. Calcd. For C$_{23}$H$_{22}$O$_2$N$_{6}$ (398.42), C, 69.33; H, 5.57; N, 21.09 Found C, 69.35; H, 5.60; N, 21.19.

3.13. (3,5-Dimethyl-1H-pyrazol-1-yl)(2-methyl-6-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenylpyridin-3-yl)methanone (32) and 5-Methyl-2-(2-methyl-6-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenylpyridine-3-carbonyl)-2,4-dihydropyrazol-3-one (33)

Equimolar amounts of 31 and the appropriate acetylene or ethyl acetoacetate (4 mmol for each) in ethanol (10 mL), with two drops of acetic acid, were refluxed for 4 h. The resulting solid was collected and recrystallized from ethanol, giving the corresponding products 32 and 33, respectively.

(3,5-Dimethyl-1H-pyrazol-1-yl)(2-methyl-6-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenylpyridin-3-yl) methanone (32). White crystals from ethanol, Yield 80%, m.p. 207 °C, FT-IR (KBr, cm^{-1}): 3032, 2961, 2941, 2839 (CH), 1641 (CO); 1589 (C=C). ^{1}H-NMR (300 MHz, DMSO-d$_6$): $\delta$ = 2.41 (s, 3H, CH$_3$), 2.48 (s, 3H, CH$_3$), 2.49 (s, 3H, CH$_3$), 2.57 (s, 3H, CH$_3$), 7.21–7.57 (m, 11H, ArH's, pyridine H-5 and pyrazole H-4). Anal. Calcd. For C$_{28}$H$_{26}$N$_{6}$O (462.56), C, 72.71; H, 5.67; N, 18.17 Found C, 72.80; H, 5.81; N, 18.27.

5-Methyl-2-(2-methyl-6-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenylpyridine-3-carbonyl)-2,4-dihydropyrazol-3-one (33). White crystals from ethanol, Yield 80%, m.p. 217 °C, FT-IR (KBr, cm^{-1}): 3434 (OH), 2976, 2925 v(CH); 1682 (CO); 1609 (C=N); 1575 (C=C). ^{1}H-NMR (300 MHz, DMSO-d$_6$): $\delta$ = 2.21 (s, 3H, CH$_3$), 2.48 (s, 3H, CH$_3$), 2.57 (s, 3H, CH$_3$), 2.62 (s, 3H, CH$_3$), 4.67 (s, 2H, pyrazoline H-4),
7.19–7.52 (m, 10H, ArH’s, pyridine H-5). Anal. Calcd. For C_{27}H_{24}N_{6}O_{2} (464.53): C, 69.81; H, 5.21; N, 18.09 Found C, 69.91; H, 5.33; N, 18.19

3.14. Azido (2-Methyl-6-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenyl-pyridin-3-yl)-methanone (34)

To a stirred solution of 31 (5 mmol) in acetic acid (15 mL) at 0–5 °C, sodium nitrite was added portion-wise until effervescence ended. The reaction mixture was stirred for 1 h. The resulting solid was collected, filtered, washed with water and recrystallized, giving the azido derivative 34. Buff crystals from acetic acid, yield (86%) m.p. 160 °C, FT-IR (KBr, cm⁻¹): 3064, 2924 (CH); 1641 (CO), 1609 (C=C). \(^1\)H-NMR (300 MHz, DMSO-d₆): \(\delta = 2.44\) (s, 3H, CH₃), 2.50 (s, 3H, CH₃), 2.69 (s, 3H, CH₃), 7.17–7.57 (m, 10H, ArH’s and pyridine H-5). Anal. Calcd. For C_{23}H_{19}N_{7}O (409.49): C, 67.47; H, 4.68; N, 23.95 Found C, 67.50; H, 4.70; N, 23.99.

3.15. 4-(Aryldiazenyl-3,5-dimethylpyrazol-1-yl)(2-methyl-6-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenyl-pyridin-3-yl)methanone (35a, 35b) and 4-(Aryldiazenyl)-5-methyl-2(2-methyl-6-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenyl-pyridin-3-carbonyl)-2,4-dihydropyrazol-3-one (36a, 36b)

Dropwise addition of the appropriate arenediazonium chloride (5 mmol), which was prepared via reaction of appropriate aniline or p-toluidine (5 mmol), hydrochloric acid (1.5 mL, 6M) and sodium nitrite (0.37 g, 5 mmol) at 0–5 °C, to a mixture of the appropriate 32 or 33 (5 mmol) and sodium acetate (1.3 g, 5 mmol) in ethanol (30 mL) at 0–5 °C while stirring the reaction mixture was stirred for 3 h. The resulting solid was collected, washed with water and recrystallized from acetic acid, giving 35a, 35b, 36a and 36b, respectively.

(E)-(3,5-Dimethyl-4-(phenyldiazenyl)-1H-pyrazol-1-yl)(2-methyl-6-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenyl-pyridin-3-yl)methanone (35a). Orange crystals from acetic acid, Yield 70%, m.p. 170 °C, FT-IR (KBr, cm⁻¹): 2925 (CH); 1722 (CO); 1608 (C=N), 1656 (C=C). \(^1\)H-NMR (300 MHz, DMSO-d₆): \(\delta = 2.28\) (s, 3H, CH₃), 2.44 (s, 3H, CH₃), 2.50 (s, 3H, CH₃), 2.69 (s, 3H, CH₃) and 7.17–7.97 (m, 15H, ArH’s, pyridine H-5). Anal. Calcd. For C_{34}H_{30}N_{6}O (566.67): C, 72.07; H, 5.34; N, 19.77 Found C, 72.16; H, 5.29; N, 19.88.

(E)-(3,5-Dimethyl-4-(p-tolyl diazenyl)-1H-pyrazol-1-yl)(2-methyl-6-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenyl-pyridin-3-yl)methanone (35b). Orange crystals from acetic acid, Yield 70%, m.p. 175 °C, FT-IR (KBr, cm⁻¹): 2966, 2924 (CH); 1722 (CO); 1647 (C=N); 1605 (C=C). \(^1\)H-NMR (300 MHz, DMSO-d₆): \(\delta = 2.25\) (s, 3H, CH₃), 2.44 (s, 3H, CH₃), 2.49 (s, 3H, CH₃), 2.50 (s, 3H, CH₃), 2.69 (s, 3H, CH₃) and 7.17–7.98 (m, 14H, ArH’s, pyridine H-5). Anal. Calcd. For C_{35}H_{32}N_{6}O (580.70): C, 72.39; H, 5.55; N, 19.30 Found C, 72.49; H, 5.66; N, 19.40.

(E)-5-Methyl-2-(2-methyl-6-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenylnicotinoyl)-4-(phenyldiazenyl)-2,4-dihydro-3H-pyrazol-3-one (36a). Orange crystals from acetic acid, Yield 70%, m.p. 165 °C, FT-IR (KBr, cm⁻¹): 3432 (OH); 2975, 2921 (CH); 1721 (CO); 1679 (C=N); 1584 (C=C). \(^1\)H-NMR (300 MHz, DMSO-d₆): \(\delta = 2.31\) (s, 3H, CH₃), 2.43 (s, 3H, CH₃), 2.58 (s, 3H, CH₃), 2.69 (s, 3H, CH₃) and 4.35 (s, br, 1H, pyrazoline), 7.09–7.58 (m, 15H, ArH’s and pyridine H-5). \(^{13}\)C-NMR (DMSO-d₆) \(\delta = 9.6, 11.8, 20.8, 24.4, 115.3, 123.4, 125.7, 126.8, 128.4, 129.7, 130.4, 132.4, 133.3, 138.8, 139.5, 139.8, 140.8, 169.0, 171.2, 172.5, 170.0. Anal. Calcd. For C_{33}H_{28}N_{6}O_{2} (568.64): C, 69.70; H, 4.96; N, 19.71 Found C, 69.65; H, 4.85; N, 19.72.

(E)-5-Methyl-2-(2-methyl-6-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenylnicotinoyl)-4-(p-tolyl diazenyl)-2,4-dihydro-3H-pyrazol-3-one (36b). Orange crystals from acetic acid, Yield 70%, m.p. 170 °C, FT-IR (KBr, cm⁻¹): 3064, 2922 (CH); 1721 (C=O); 1649 (C=N); 1608 (C=C). \(^1\)H-NMR (300 MHz, DMSO-d₆): \(\delta = 2.42\) (s, 3H, CH₃), 4.50 (s, 1H, pyrazoline), 2.49 (s, 3H, CH₃), 2.57 (s, 3H, CH₃), 2.69 (s, 3H, CH₃) and 7.14–7.57 (m, 14H, ArH’s and pyridine H-5). Anal. Calcd. For C_{34}H_{30}N_{6}O_{2} (582.67): C, 70.09; H, 5.19; N, 19.23 Found C, 70.19; H, 5.20; N, 19.10.
3.16. 1-(2-Methyl-6-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenyl-pyridin-3-yl)-3-substituted urea (38a, 38b) and 3-(2-Methyl-6-(1-p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenyl-pyridin-3-yl)quinazoline-2,4-(1H,3H)dione (39)

A mixture of 34 (2 g, 5 mmol) and appropriate aniline, p-toluidine, anthranilic acid (or methyl anthranilate) (5 mmol) in dry dioxane (20 mL) was refluxed for 4 h. The resulting solid that was collected and recrystallized from the proper solvent gave 38a, 38b and 39, respectively.

1-(2-Methyl-6-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenylpyridin-3-yl)-3-phenylurea (38a). White crystals from acetic acid yield 70%, m.p. 180 °C. FT-IR (KBr, cm⁻¹): 3426 (NH); 2983, 2926 (CH); 1722 (CO); 1647 (C=N), 1594 (C=C).

1H-NMR (300 MHz, DMSO-d₆): δ = 2.43 (s, 3H, CH₃), 2.59 (s, 3H, CH₃), 2.71 (s, 3H, CH₃), 7.44–7.97 (m, 15H, ArH's and pyridine H-5), 8.88 (s, br, 2H, 2NH).

Anal. Calcd. For C₂₉H₂₆N₆O (474.57): C, 73.40; H, 5.52; N, 17.71 Found C, 73.37; H, 5.63; N, 17.69.

1-(2-Methyl-6-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenylpyridin-3-yl)-3-p-tolylurea (38b). White crystals from acetic acid yield 72%, m.p. 170–172 °C. FT-IR (KBr, cm⁻¹): 3423 (NH); 2984, 2962, 2952 (CH); 1722 (CO); 1592 (C=C), 1H-NMR (300 MHz, DMSO-d₆): δ = 2.44 (s, 3H, CH₃), 2.49 (s, 3H, CH₃), 2.60 (s, 3H, CH₃), 2.71 (s, 3H, CH₃), 7.27–7.98 (m, 14H, ArH's and pyridine H-5), 8.90 (s, br, 2H, 2NH).

Anal. Calcd. For C₃₀H₂₈N₆O (488.60): C, 73.75; H, 5.17; N, 17.20 Found C, 73.80; H, 5.20; N, 17.30.

3-(2-Methyl-6-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenyl-pyridin-3-yl)-quinazoline-2,4-(1H,3H)dione (39). White crystals from acetic acid, yield 72%, m.p. 170–172 °C. FT-IR (KBr, cm⁻¹): 3424 (NH); 2984, 2962, 2952 (CH); 1722 (CO); 1592 (C=C), 1H-NMR (300 MHz, DMSO-d₆): δ = 2.43 (s, 3H, CH₃), 2.50 (s, 3H, CH₃), 2.59 (s, 3H, CH₃), 7.44–7.97 (m, 14H, ArH's and pyridine H-5), 10.54 (s, br, 1H, NH), 13C-NMR (DMSO-d₆) δ = 8.8, 20.5, 21.1, 114.2, 115.6, 117.2, 121.9, 123.7, 123.8, 128.5, 129.8, 132.7, 134.2, 134.6, 135.2, 137.8, 138.4, 138.7, 139.5, 140.2, 141.3, 144.2, 153.1, 158.6, 161.7, 164.6. Anal. Calcd. For C₃₀H₂₄N₆O₂ (500.56): C, 71.99; H, 4.83; N, 16.79 Found C, 71.89; H, 4.79; N, 16.85.

3.17. Phenyl 2-Methyl-6-(5-methyl-1-(p-tolyl)-1H-1,2,3-triazol-4-yl)-4-phenylpyridin-3-yl)-carbamate (40)

A mixture of 34 (2 g, 5 mmol) and phenol (0.47 g, 5 mmol) in dry benzene (20 mL) was refluxed for 4 h. The resulting solid was collected and crystallized from ethanol, affording the corresponding 40, as buff crystals, yield 70%, m.p. 140–142 °C. FT-IR (KBr, cm⁻¹): 3425 (NH); 2983, 2926, 2875 (CH); 1722 (CO); 1594 (C=C), 1H-NMR (300 MHz, DMSO-d₆): δ = 2.43 (s, 3H, CH₃), 2.50 (s, 3H, CH₃), 2.59 (s, 3H, CH₃), 7.33–7.97 (m, 15H, ArH's and pyridine H-5), 11.65 (s, br, 1H, NH), 13C-NMR (DMSO-d₆) δ = 8.8, 20.5, 21.1, 114.2, 115.6, 117.2, 121.9, 123.7, 123.8, 128.5, 129.8, 132.7, 134.2, 134.6, 135.2, 137.8, 138.4, 138.7, 139.5, 140.2, 141.3, 144.2, 153.1, 158.6, 161.7, 164.6. Anal. Calcd. For C₃₀H₂₄N₅O₂ (500.56): C, 71.99; H, 4.83; N, 16.79 Found C, 71.89; H, 4.79; N, 16.85.

4. Conclusions

Compound 1 proved to be useful for synthesis of a new series of novel functionalized 1,3,4-thiadiazoles, 1,3-thiazoles and pyridines containing 1,2,3-triazole moiety using hydrazonoyl halides as precursors. Also, compound 31 proved to be a useful precursor in the synthesis of various pyrazoles, urea and carbamate derivatives. The biological activities of the synthesized products will be reported in extended work.

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**Sample Availability:** Samples of the synthesized compounds are available from the authors.

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