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RESEARCH ARTICLE

Synthesis and Antimicrobial Activity of 5-Arylazothiazoles, 2,3-Dihydro-1,3,4-thiadiazoles and triazolo[4,3-*a*]pyrimidine Derivatives

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Abstract

2,3-Dihydro-1,3,4-thiadiazoles, and triazolino[4,3-*a*]pyrimidines, were synthesized from the reactions of methyl (or benzyl) carbodithioate and pyrimidine-2-thione derivatives with *C*-benzofuran-2-oyl-*N*-phenylhydrazonoyl bromide. The structures of all the newly synthesized compounds were confirmed by elemental analyses, spectral data, and alternative routes synthesis whenever possible. Also, the newly synthesized compounds were tested towards different types of bacteria

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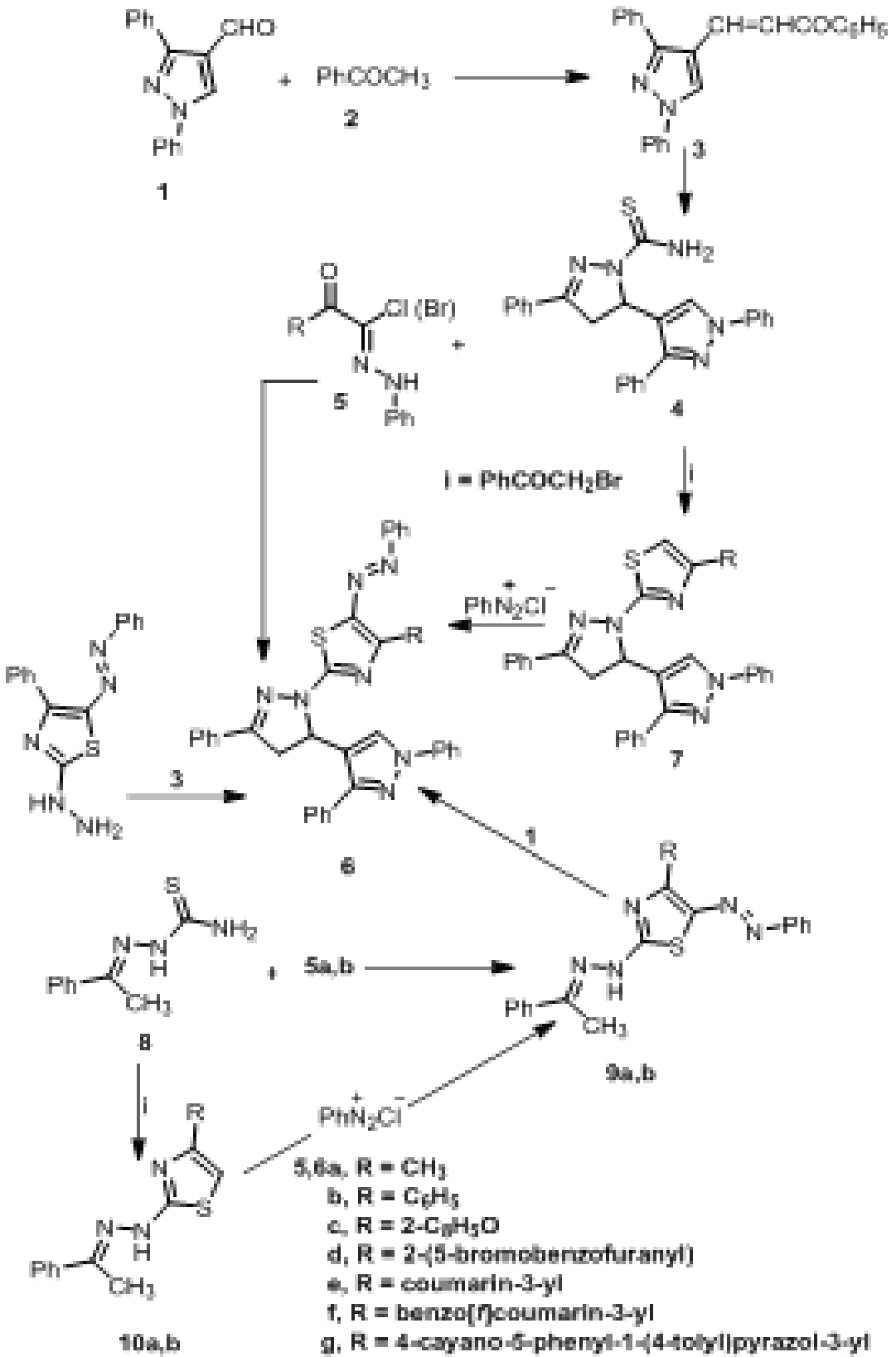
1. Introduction

Due to the interesting activity of variously substituted pyrazolines as biological agents considerable attention has been focused on this class. Various biological activities possessed by pyrazolines includes antibacterial [1], antifungal [2], antiviral [3], antiparasitic [4], antitubercular [5], insecticidal agents [6], antipyretic [7], diuretic [8], antidiabetic [9], tranquillizing [10], muscle relaxant [11], psychoanaleptic [12], anticonvulsant [13], antihypertensive [14] and antidepressant [15]. Also, certain thiadiazoles and thiosemicarbazones have been reported to exhibit antivirial and antibactrial properties and were evaluated for biological activity against various microorganism [16]. As an extension of our study [17-25] and as a part of our program aiming at the synthesis of different heterocyclic derivatives, we report here the convenient synthesis of 5-arylazothiazoles, 2,3-dihydro-1,3,4-thiadiazoles, and triazolino[4,3-*a*]pyrimidines.

2. Results and Discussion

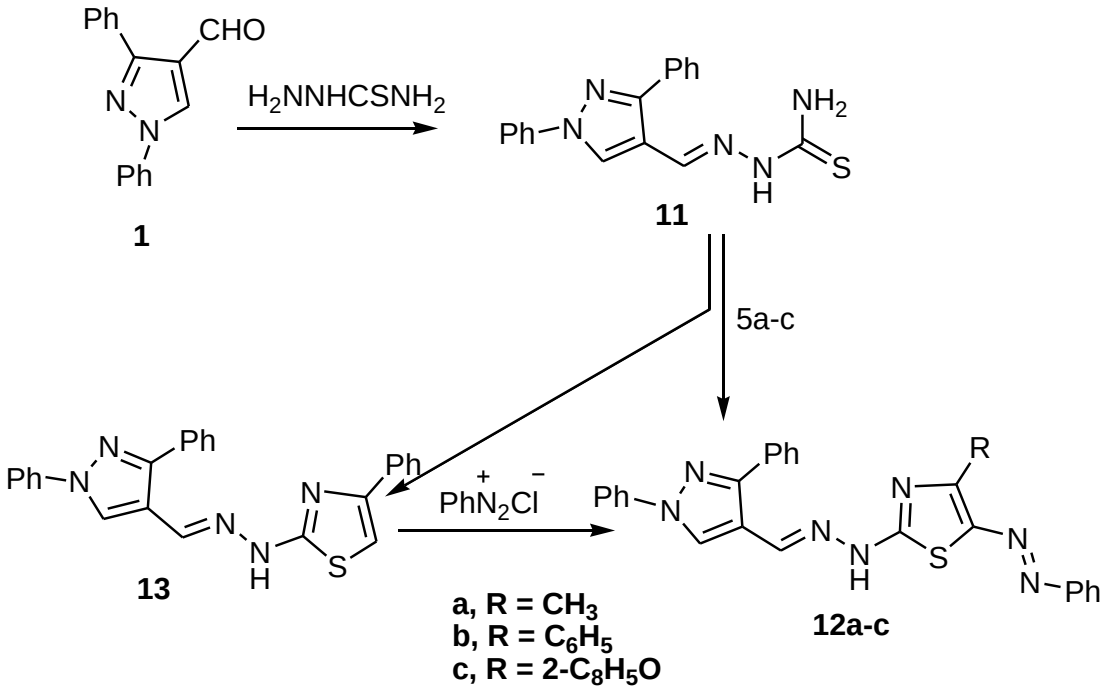
2.1. Chemistry

1-Phenyl-3-(1,3-diphenyl-1*H*-pyrazol-4-yl)prop-2-en-1-one (**3**) with thiosemicarbazide in boiling acetic acid to give 4,5-dihydro-3-phenyl-5-(1,3-diphenyl-1*H*-pyrazol-4-yl)pyrazole-1-carbothioamide (**4**). Compound **4** reacted with the appropriate hydrazonoyl halides **5a-g** in boiling chloroform containing triethylamine to give 1-(2-(4,5-dihydro-3-phenyl-5-(1,3-diphenyl-1*H*-pyrazol-4-yl)pyrazol-1-yl)-4-substituted thiazol-5-yl)-2-phenyldiazene **6a-g**, respectively (Scheme 1). Structures **6** were confirmed by elemental analyses, spectral data, and alternative synthetic routes. Thus, benzenediazonium chloride reacted with 4-(4,5-dihydro-3-phenyl-1-(4-phenylthiazol-2-yl)-1*H*-pyrazol-5-yl)-1,3-diphenyl-1*H*-pyrazole (**7b**), which prepared via reaction of **4** with ω-bromoacetophenone, in pyridine to give a product identical in all aspects (m.p., mixed m.p., and spectra) with **6b** (Scheme 1). On other hand, reaction of 1-(1-phenylethylidene)-2-(4-phenylthiazol-2-yl)hydrazine (**10b**), which synthesized by treatment of 1-(1-phenylethylidene)thiosemicarbazide (**8**) [26] with ω-bromoacetophenone, with benzenediazonium chloride to give *N*-[1-(1,3-diphenyl-1*H*-pyrazol-4-yl)-ethylidene]-*N'*-(4-phenyl-5-phenylazo-thiazol-2-yl)-hydrazine (**9b**). The later reacted with 1,3-diphenylpyrazole-4-carboxaldehyde (**1**) in ethanolic sodium hydroxide afforded product identical in all aspects (mp., mixed mp. and spectra) with **6b** (Scheme 1).


1
2
3
4
5
6
7
8
9a,b
10a,b
i = PhCOCH2Br
5,6a, R = CH3
b, R = C6H5
c, R = 2-C8H5O
d, R = 2-(5-bromobenzofuranyl)
e, R = coumarin-3-yl
f, R = benzo[f]coumarin-3-yl
g, R = 4-cayano-5-phenyl-1-(4-tolyl)pyrazol-3-yl

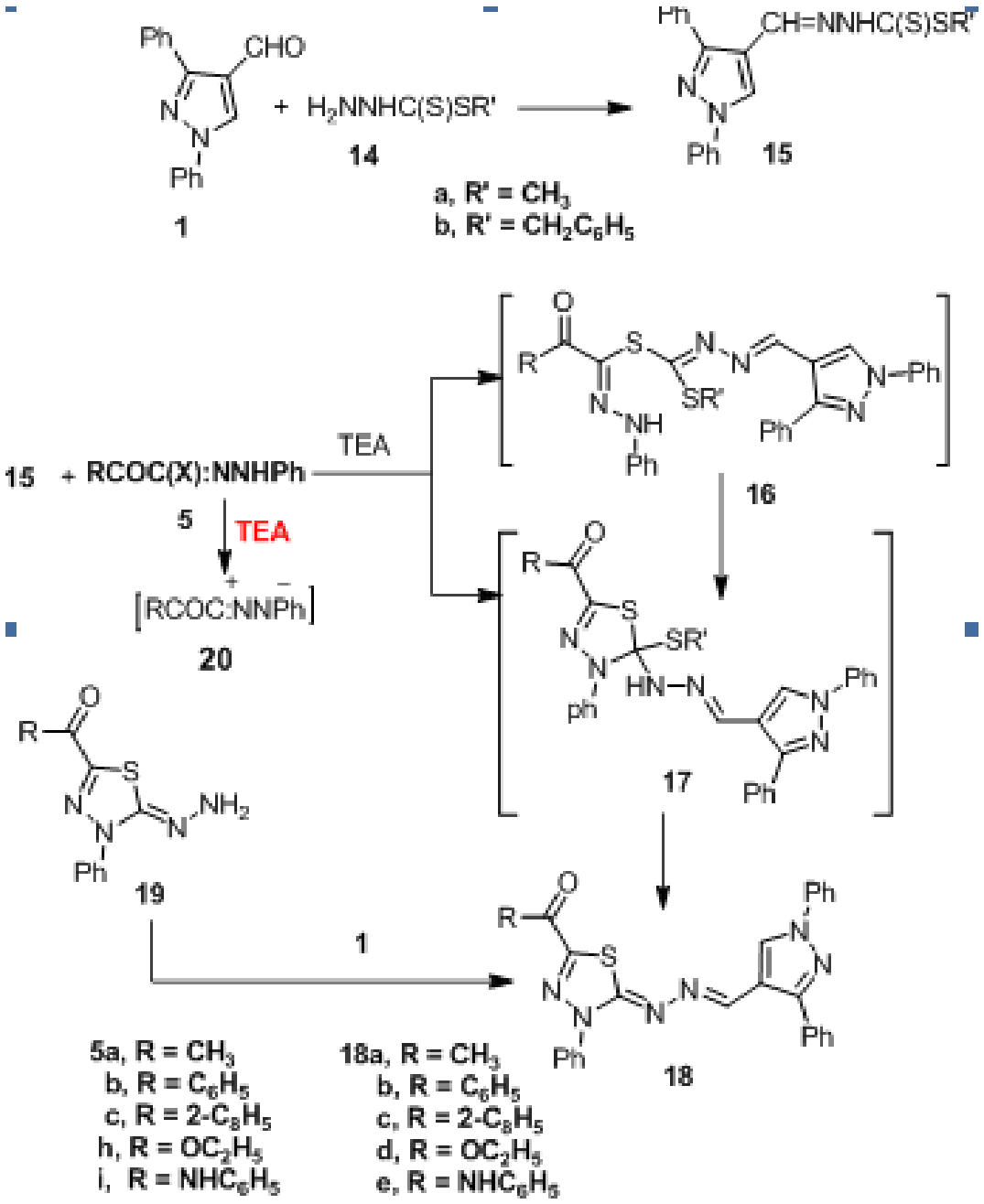
Scheme 1

Treatment of 1,3-diphenyl-1*H*-pyrazole-4-carbaldehyde (**1**) with thiosemicarbazide afforded 2-((1,3-diphenyl-1*H*-pyrazol-4-yl)methylene)hydrazine-1-carbothioamide (**11**). Compound **11** reacted with the appropriate hydrazonoyl halides **5a-c** gave *N*-(1,3-diphenyl-1*H*-pyrazol-4-ylmethylene)-N'-(4-Substiyuted 5-phenylazo-thiazol-2-yl)hydrazine **12a-c** (Scheme 2). Structures **12** were elucidated by elemental analysis, spectra and alternative synthetic routes. Thus, reaction of ω-bromoacetophenone with **11** gave 1-((1,3-diphenyl-1*H*-pyrazol-4-yl)methylene)-2-(4-phenylthiazol-2-yl)hydrazine (**13**). Latter compound reacted with benzenediazonium chloride afforded product identical in all aspects mp., mixed mp. and spectra with **12b.**



Scheme 2

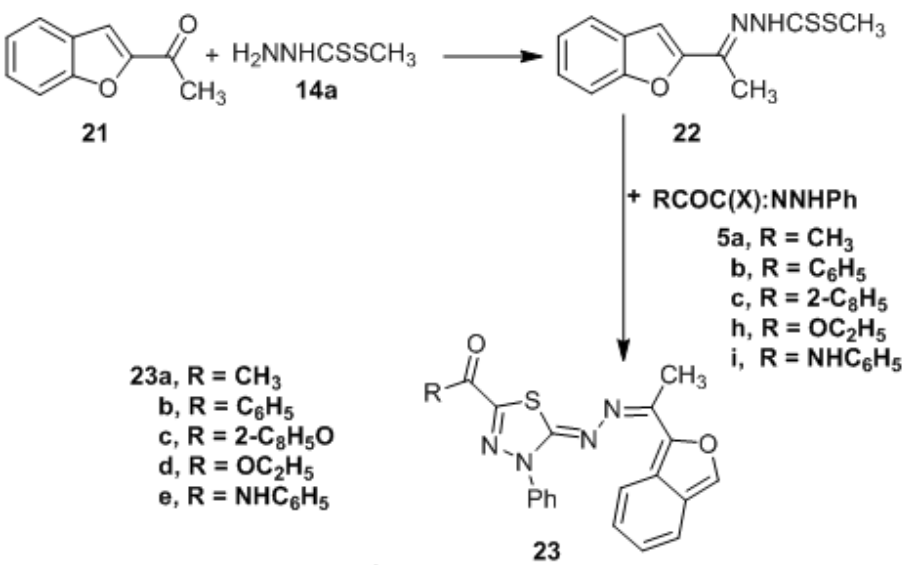
Treatment of 1,3-diphenyl-1*H*-pyrazole-4-carbaldehyde (**1**), with the appropriate alkyl hydrazinecarbodithioate **14a** and **14b** in 2-propanol gave alkyl *N'*-(1,3-diphenyl-1*H*-pyrazol-4-ylmethylene)-hydrazinecarbodithioate **15a** and **15b**, respectively (Scheme 3). Structures **15** were confirmed by elemental analyses, spectral data and chemical transformations. Thus, *C*-ethoxycarbonyl-*N*-phenylhydrazonoyl chloride (**5h**) reacted with methyl carbodithioate **15a** in ethanol containing triethylamine to afford ethyl 2-[1,2-diaza-3-(6-hydroxy-4-methoxybenzo[*b*]furan-5-yl)but-2-enylidene]-3-phenyl-1,3,4-thiadiazoline-5-carboxylate (**18d**). Structure **18** was established by elemental analyses, spectral data, and alternative syntheses. Thus, ethyl 2-hydrazono-3-phenyl-1,3,4-thidiazoline-5-carboxylate [27] (**19**) reacted with **1** in ethanol to give a product identical in all aspects (m.p., mixed m.p. and spectra) with **18d**. In addition, benzyl carbodithioate **15b** reacted with **5h** in ethanolic triethylamine to give **18d**. In the light of the foregoing results, the mechanism outlined in Scheme 3 seems to be the most plausible pathway for the formation of **18** from the reaction of the **5** with **15a** or **15b**. The reaction involves initial formation of thiohydrazonate **16**, which undergoes intermolecular cyclization as soon as it is formed to yield the intermediate **17** or via 1,3-dipolar cycloaddition of nitrilimine **20** (prepared in situ from **5** with triethylamine) to the C=S double bond of **15**.



Scheme 3

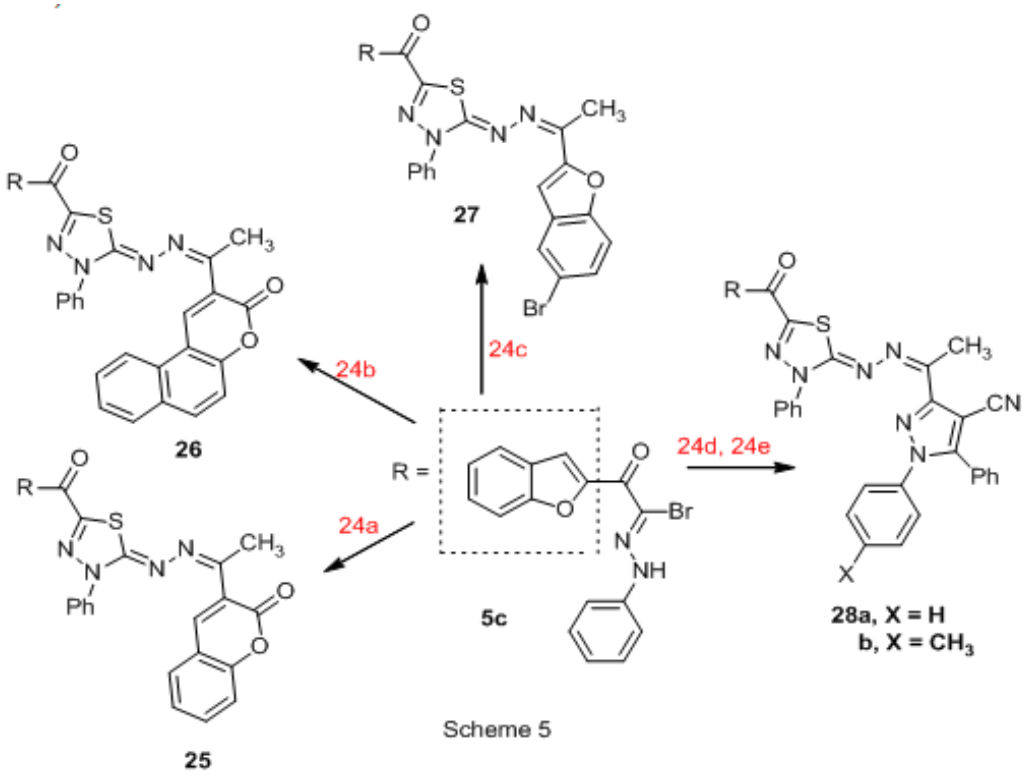
The formations of **16** and **17** are similar to the reaction of hydrazonoyl chloride with 1-phenyl-1,4-dihydrotetrazole-5-thione [28] and 5-phenyl-1,3,4-thiadiazole-2(3*H*)-thione [29]. Compound **17** was converted to **18** by elimination of alkyl mercaptan. Similarly, the appropriate **5a-c** and **5i** reacted with the appropriate **15a** or **15b** in ethanolic triethyamine to afford 2,3-dihydro-1,3,4-thiadiazoles **18a–c and 18e**, respectively.

Analogously, treatment of methyl *N'*-(1-benzofuran-2-yl-ethylidene)hydrazine-carbodithioate (**22**), which prepared via reaction of 2-acetylbenzofuran with methyl hydrazinecarbodithioate in 2-propanol, with the appropriate hydrazonoyl halides **5a-c, 5h, 5i** in ethanolic triethylamine gave 2-(1-(benzofuran-2-yl)ethylidene)-1-(5-substituted 3-phenyl-1,3,4-thiadiazol-2(3*H*)-ylidene)hydrazine **23a-c, 23h, 23i**, respectively (Scheme 4).



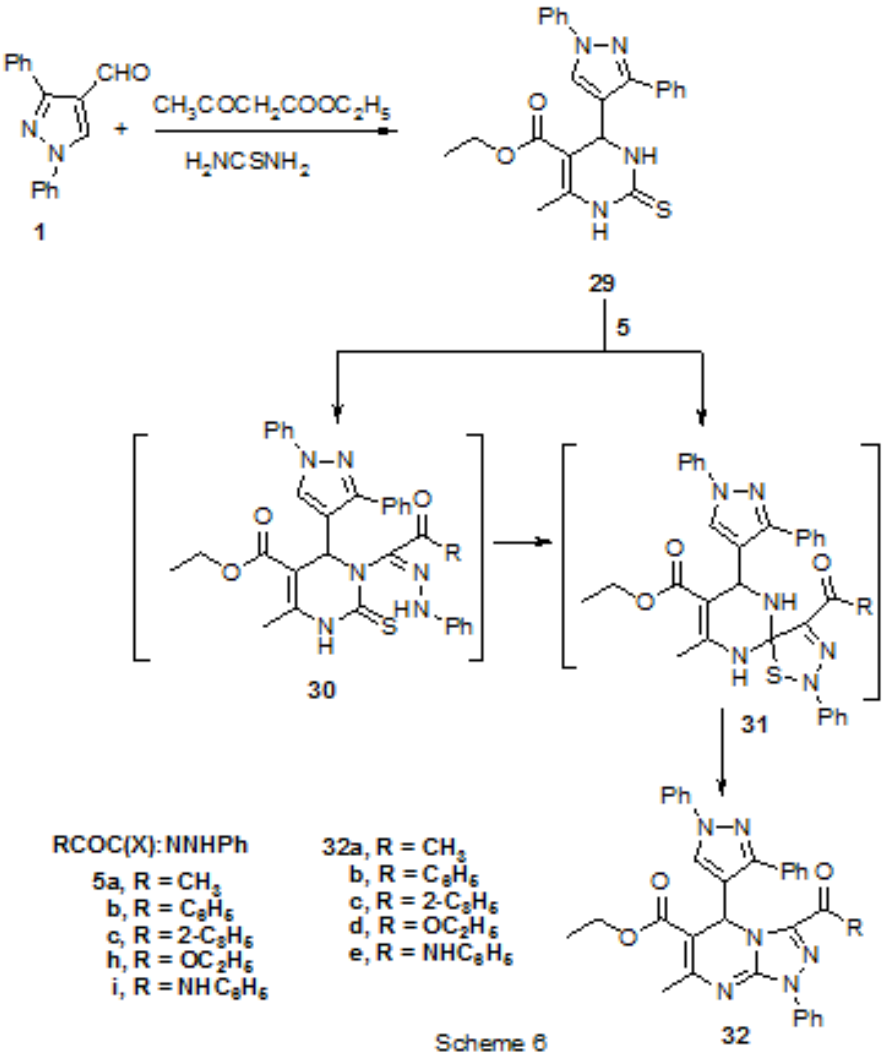
Scheme 4

Also, treatment of *C*-2-benzofuranoyl-*N*-phenylhydrazonoyl bromide **5c** with the appropriate methyl carbodithioates **24a-e** in ethanolic triethlamine gave unsymmeterical azines **25**-**28a** and **28b**, respectively in a good yield (Scheme 5).



Scheme 5

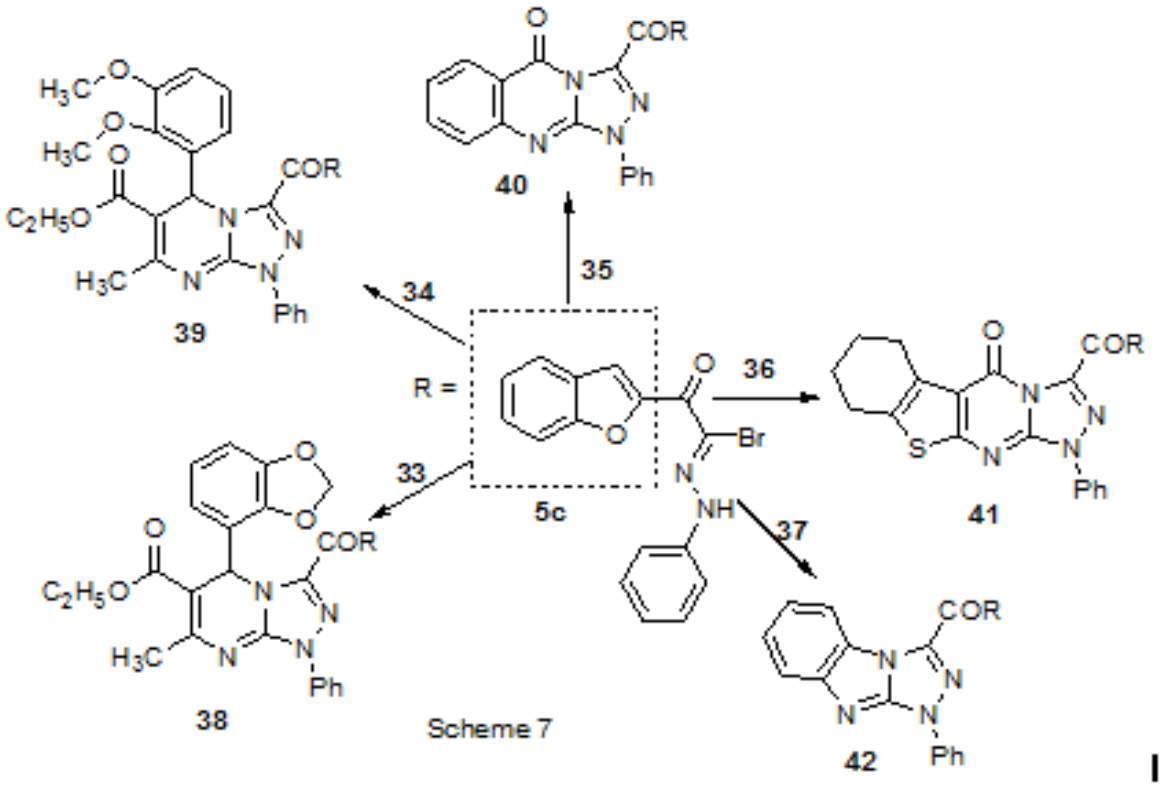
Next, compound **1** reacted with ethyl acetoacetate and thiourea in ethanol gave ethyl 1,2,3,4-tetrahydro-6-methyl-4-(1,3-diphenyl-1*H*-pyrazol-4-yl)-2-thioxo-pyrimidine-5-carboxylate (**29**) Scheme 6.



Scheme 6

Structure **29** was elucidated by elemental analysis, spectral data and chemical transformation. Thus, treatment of **5h** with the pyrimidine-2-thione **29** in boiling chloroform gave triazolino[4,3-*a*]pyrimidines **32d** in a good yields (Scheme 6). Structure of **32d** was elucidated by elemental analysis and spectral data. Thus, ^{1}H NMR spectrum of **32d** showed signals at δ = 1.29 (t, 3H, *J* = 7.5 Hz, CH_2CH_3), 1.31 (t, 3H, *J* = 7.5 Hz, CH_2CH_3), 2.27 (s, 3H, CH_3), 4.01 (q, 2H, *J* = 7.5 Hz, CH_2CH_3), 4.22 (q, 2H, *J* = 7.5 Hz, CH_2CH_3), 5.66 (s, 1H, pyrimidine H-4), 7.42-7.79 (m, 19H, ArH's). Its IR spectrum revealed bands at 1728 (CO) and 1624 (C=N). The mechanism outlined in Scheme 6 seems to be the most plausible pathway for the formation of **29** from the reaction of **5** with **29** 1)- 1,3-addition of the thiol tautomer **29** to the nitrilium imide **20** to give the thiohydrazonate ester **30** which undergoes nucleophilic cyclization to yield spiro compounds **31**. The latter ring open and cyclized to yield **32** by loss hydrogen sulfide; and 2)-1,3-cycloaddition of nitrilium imide **20** to C=S double bond of **29** to give directly **32** (Scheme 6). Attempts to isolate the thiohydrazonate ester **30** or intermidate **31** did not succeed even under mild conditions as they readily undergo *in situ* cyclization followed by elimination of hydrogen sulfide to give the final product **32** In Scheme 6.

Analogously, reactions of ethyl 4-(benzo[*d*][1,3]dioxol-7-yl)-1,2,3,4-tetrahydro-6-methyl-2-thioxopyrimidine-5-carboxylate (**33**), ethyl 1,2,3,4-tetrahydro-4-(2,3-dimethoxyphenyl)-6-methyl-2-thioxopyrimidine-5-carboxylate (**34**), 2-thioxo-2,3-dihydro-1*H*-quinazolin-4-one (**35**), 2-thioxo-2,3,5,6,7,8-hexahydro-1*H*-benzo[4,5]thieno[2,3-*d*]pyrimidin-4-one (**36**), 2-mercaptobenzimidazole (**37**) with hydrazonoyl bromide **5c** were carried out in refluxing chloroform in presence of TEA gave **38-42**, respectively (Scheme 7).



3. Experimental

Instrumentation

All melting points were determined on an electrothermal apparatus and are uncorrected. IR spectra were recorded (KBr discs) on a Shimadzu FT-IR 8201 PC spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ and $(CD_3)_2SO$ solutions on a Varian Gemini 300 MHz and 400 MHz spectrometer and chemical shifts are expressed in δ ppm units using TMS as an internal reference. Mass spectra were recorded on a GC-MS QP1000 EX Shimadzu. Elemental analyses were carried out at the Microanalytical Center of Cairo University. Hydrazonoyl halides **5a-g, 15, 16-18** [30-35] and alkyl carbodithioates **14** [36, 37] were prepared as previously reported.

3.1 4,5-Dihydro-3-phenyl-5-(1,3-diphenyl-1H-pyrazol-4-yl)pyrazole-1-carbo-thioamide (4).

A mixture of 1-phenyl-3-(1,3-diphenyl-1H-pyrazol-4-yl)prop-2-en-1-one (**3)** (1.75 g, 5 mmol) and thiosemicarbazide (0.46 g, 5 mmol) in ethanol (20 mL) was heated under refluxed for 3 h. The resulting solid was collected and recrystallized from acetic acid to give **4**

White crystals from AcOH, Yield: 94%, mp.: 134-36°C. **FT-IR (KBr, cm^{-1}):** 3259, 3139 ν (NH, NH_2), 3059 ν (CH), 1659 ν (CO), 1593 ν (C=C). **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 3.66 (dd, 1H, J = 18.1, 5.8Hz, CH_2(pyraz)), 4.01 (dd, 1H, J = 18.1, 12Hz, CH_2(pyraz)), 5.33 (dd, J = 12.2 5.8 Hz , CH(pyraz)), 5.99 (s, 1H, pyrazole H-5), 7.00–7.82 (m, 14H, ArH's), 9.34 (s, br., 2H, NH_2); **^{13}C NMR (300 MHz, DMSO-d_6):** δ = 40.52, 60.12, 117.35, 121.22, 123.41, 124.10, 125.31, 125.67, 127.47, 128.36, 129.45, 129.67, 134.44, 138.47, 141.12, 142.37, 152.24, 187.24; **MS (EI, m/z (%)):** 423 (M^+, 0.02%), 245 (40.60%), 115 (14.65%), 105 (38.55%), 77 (100%); Calcd. for $C_{25}H_{21}N_5S$ (423.53) C, 70.90; H, 5.00; N, 16.54; S, 7.57 Found: C, 71.10; H, 4.88; N, 16.56; S, 7.78 %.

3.2. 1-(2-(4,5-dihydro-3-phenyl-5-(1,3-diphenyl-1H-pyrazol-5-yl)pyrazol-1-yl)-4-substituted thiazol-5-yl)-2-phenyldiazene (6a-g).

4,5-dihydro-3-phenyl-5-(1,3-diphenyl-1*H*-pyrazol-5-yl)pyrazole-1-carbothioamide (**4**) (2.12 g, 5 mmol), the appropriate hydrazonoyl halides **5a-g** (5 mmol) and triethylamone (0.75 mL, 5 mmol) in ethanol (20 mL) were boiled under reflux for 3 hr. The resulting solid was collected and recrystallized from acetic acid to give **6a–g**, respectively.

Synthesis of 6a: Alternative Methods

Method (A): A mixture of (4-methyl-5-phenylazothiazol-2-yl)hydrazine (39) (1.47, 5 mmol) and 1-phenyl-3-(1,3-diphenyl-1*H*-pyrazol-4-yl)prop-2-en-1-one (**3)** (1.75 g, 5 mmol) in ethanol (20 mL) containing catalytically amount of piperdine (2 drops) was boiled under reflux for 2 hr to give **6a**.

Method (B):Benzenediazonium chloride (5 mmol), which prepared from aniline (0.45 mL, 5 mmol), hydrochloric acid (6 N, 6 mL), and sodium nitrite (0.35g, 5 mmol), was added dropwise with stirring to a cold solution of a mixture of 5-(4,5-dihydro-3-phenyl-1-(4-phenylthiazol-2-yl)-1*H*-pyrazol-5-yl)-1,3-diphenyl-1*H*-pyrazole (**7a**) (1.81 g, 5 mmol) and sodium acetate trihydrate (1.3 g, 10 mmol) in ethanol (50 ml). The resulting solid was collected and recrystallized to give product identical with **6a**.

3.2.1. 1-(2-(4,5-dihydro-3-phenyl-5-(1,3-diphenyl-1H-pyrazol-4-yl)pyrazol-1-yl)-4-methylthiazol-5-yl)-2-phenyldiazene (6a).

Dark brown crystals from AcOH, Yield: 91%, mp.: 129-31°C. **FT-IR (KBr, cm^{-1}):** 3052 ν (CH), 1589 ν (C=C). **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 2.49 (s, 3H, CH_3), 3.44 (dd, 1H, J = 18.0, 5.8 Hz, CH_2(pyraz)), 3.95 (dd, 1H, J = 18.8, 12Hz, CH_2(pyraz)), 4.88 (dd, 1H, J = 12.2, 5.8 Hz , CH(pyraz)), 7.20–8.08 (m, 21H, ArH's and pyrazole H-5); **^{13}C NMR (300 MHz, DMSO-d_6):**13.12 (CH_3), 36.15 (CH_2), 36.12 (CH), 59.45, 116.23, 117.58, 119.08, 121.7, 123.45, 124.21, 125.20, 125.78, 127.24, 128.56, 128.74, 129.42, 129.78, 130.12, 133.48, 138.24, 141.29, 152.45, 1252.83, 154.73, 161.22; **MS (EI, m/z (%)):** 567 (M^+, 0.38%), 242 (5.62%), 192 (4.11%), 135 (6.10%), 129 (7.03%), 128 (23.16%), 105 (60.62%), 96 (18.44%), 91 (18.85%), 76 (100%), 63 (93.33%), 60 (40.83%); Calcd. for $C_{34}H_{27}N_7S$ (565.69) C, 72.19; H, 4.81; N, 17.33; S, 5.67 Found: C, 72.21; H, 4.95; N, 17.28; S, 5.79 %.

3.2.2. 1-(2-(4,5-dihydro-3-phenyl-5-(1,3-diphenyl-1H-pyrazol-4-yl)pyrazol-1-yl)-4-phenylthiazol-5-yl)-2-phenyldiazene (6b).

Dark red crystals from AcOH, Yield: 86%, mp.: 199-201°C. **FT-IR (KBr, cm^{-1}):** 3052 ν (CH), 1595 ν (C=C). **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 3.47 (dd, 1H, J = 18, 6 Hz, CH_2(pyraz)), 3.93 (dd, 1H, J = 18, 12 Hz, CH_2(pyraz)), 4.85 (dd, 1H, J = 12, 6 Hz , CH(pyraz)), 7.18–7.88 (m, 26H, ArH's, pyrazole H-5); **MS (EI, m/z (%)):** 627 (M^+, 0.12%), 140 (5.34%), 106 (4.15%), 105 (100%), 77 (73.55%), 64 (4.10%), 51 (18.89%); Calcd. for $C_{39}H_{29}N_7S$ (627.76) C C, 74.62; H, 4.66; N, 15.62; S, 5.11 Found: C, 74.84; H, 4.75; N, 15.75; S, 5.32 %.

3.2.3. 1-(4-(Benzofuran-2-yl)-2-(4,5-dihydro-3-phenyl-5-(1,3-diphenyl-1H-pyrazol-4-yl)pyrazol-1-yl)thiazol-5-yl)-2-phenyldiazene (6c)

Brown crystals from AcOH, Yield: 86%, mp.: 198-200°C. **FT-IR (KBr, cm^{-1}):** 3057 ν (CH), 1601 ν (C=C). **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 3.46 (dd, 1H, J = 18, 5.8Hz, CH_2(pyraz)), 4.01 (dd, 1H, J = 18, 12Hz, CH_2(pyraz)), 4.86 (dd, 1H, J = 12, 5.8 Hz , CH(pyraz)), 7.18–7.95 (m, 26H, ArH's and pyrazole H-5); **MS (EI, m/z (%)):** 668 (M^+, 0.63%), 567 (6.79), 362 (75.22%), 246 (119.65%), 231 (11.83%), 219 (9.30%), 201 (6.17%), 151 (6.32%), 145 (29.29%), 127 (14.27%), 114 (10.53%), 103 (37.72%), 88 (23.20%), 77 (100%), 64 (6.87%), 63 (13.31%); Calcd. for $C_{41}H_{29}N_7OS$ (667.78) C, 73.74; H, 4.38; N, 14.68; S, 4.80 Found: C, 73.84; H, 4.28; N, 14.85; S, 4.61 %.

3.2.4. 1-(4-(5-Bromobenzofuran-2-yl)-2-(4,5-dihydro-3-phenyl-5-(1,3-diphenyl-1H-pyrazol-4-yl)pyrazol-1-yl)thiazol-5-yl)-2-phenyldiazene (6d)

Dark brown crystals from AcOH, Yield: 88%, mp.: 178-80°C. **FT-IR (KBr, cm^{-1}):** 3058 ν (CH), 1593 ν (C=C). ^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.46 (dd, 1H, J = 18, 5.9 Hz, CH_2(pyraz)), 4.01 (dd, 1H, *J* = 18, 12 Hz, CH_2(pyraz)), 4.86 (dd, 1H, *J* = 12, 6 Hz , CH(pyraz)), 7.18–7.95 (m, 25H, ArH's); **MS (EI, m/z (%)):**746 (M^+, 3.65%), 615 (4.17%), 613 (3.83), 585 (11.0%), 584 (11.48%), 363 (23.50%), 3618.18, 287 (8.29%), 231 (11.83%), 219 (9.30%), 201 (6.17%), 151 (6.32%), 145 (29.29%), 127 (14.27%), 286 (9.22%), 285 (8.18%), 156 (7.79%), 155 (10.16%), 154 (9.69%), 141 (18.24%), 139 (15.19%), 138 (4.95%), 129 (14.09%), 128 (23.77%), 127 (9.78%), 17 (10.73%), 105 (32.62%), 103 (18.66%), 91 (52.69%), 77 (100%), 69 (40.54%); Calcd. for $C_{41}H_{28}BrN_7OS$ (746.68) C, 72.50; H, 4.20; N, 14.09; S, 4.61 Found: C, 72.65; H, 4.08; N, 14.18; S, 4.87 %.

3.2.5. 3-[5-Phenylazo-2-(5,1',3'-triphenyl-3,4-dihydro-1'H-[3,4']bipyrazolyl-2-yl)-thiazol-4-yl]-chromen-2-one (6e)

Dark brown crystals from AcOH, Yield: 87%, mp.: 149-51°C. **FT-IR (KBr, cm^{-1}):** 3059 ν (CH), 1720 ν (CO), 1595 ν (C=C). **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 3.26 (dd, 1H, *J* = 18, 6 Hz, CH_2(pyraz)), 3.85 (dd, 1H, *J* = 18, 12 Hz, CH_2(pyraz)), 5.29 (dd, 1H, *J* = 12, 6 Hz , CH(pyraz)), 7.18–7.65 (m, 22H, ArH's, pyrazole H-5), 7.80-7.82 (m, 1H, ArH), 7.92 (d, 2H, *J* = 8Hz, ArH), 8.75 (s, 1H, ArH) ; **MS (EI, m/z (%)):** 697 (M+1, 0.02%), 245 (35.57%), 216 (15.64%), 105 (45.80%), 77 (100%), 64 (13.77%); Calcd. for $C_{42}H_{29}N_7O_2S$ (695.79) C, 72.50; H, 4.20; N, 14.09; S, 4.61 Found: C, 72.67; H, 4.31; N, 14.00; S, 4.45 %.

3.2.6. 2-[5-Phenylazo-2-(5,1',3'-triphenyl-3,4-dihydro-1'H-[3,4']bipyrazolyl-2-yl)-thiazol-4-yl]-benzo[f]chromen-3-one (6f)

Dark brown crystals from AcOH, Yield: 88%, mp.: 200-202°C. **FT-IR (KBr, cm^{-1}):** 3058 ν (CH), 1724 ν (CO), 1597 ν (C=C). **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 3.26 (dd, 1H, *J* = 18, 6 Hz, CH_2(pyraz)), 3.85 (dd, 1H, *J* = 18, 12 Hz, CH_2(pyraz)), 5.29 (dd, 1H, *J* = 12, 6 Hz , CH(pyraz)), 7.18–8.19 (m, 28H, ArH's, pyrazole H-5); Calcd. for $C_{46}H_{31}N_7O_2S$ (745.85) C, 74.08; H, 4.19; N, 13.15; S, 4.30 Found: C, 73.87; H, 4.00; N, 13.27; S, 4.42 %.

3.2.7. 5-Phenyl-3-[5-phenylazo-2-(5,1',3'-triphenyl-3,4-dihydro-1'H-[3,4']bipyraz-olyl-2-yl)-thiazol-4-yl]-1-p-tolyl-1H-pyrazole-4-carbonitrile (6g)

Dark brown crystals from AcOH, Yield: 89%, mp.: 145-47°C. **FT-IR (KBr, cm^{-1}):** 3055 ν (CH), 2229 ν (CN), 1658 ν (C=N), 1593 ν (C=C). **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 2.26 (s, 3H, CH_3), 3.26 (dd, 1H, *J* = 18, 6 Hz, CH_2(pyraz)), 3.85 (dd, 1H, *J* = 18 12 Hz, CH_2(pyraz)), 5.29 (dd, 1H, *J* = 12, 6 Hz, CH(pyraz)), 7.18–8.22 (m, 30H, ArH's, pyrazole H-5); **MS (EI, m/z (%)):** 809 (M^+, 0.02%), 362 (12.47%), 322 (7.07%), 286 (16.18%), 245 (50.89%), 141 (10.26%), 114 (12.18%), 104 (41.03%), 90 (33.16%), 77 (100%), 64 (26.89%), 50 (51.24%); Calcd. for $C_{50}H_{36}N_{10}S$ (808.95) C, 74.24; H, 4.49; N, 17.31; S, 3.96 Found: C, 74.12; H, 4.53; N, 17.48; S, 4.10 %.

3.3. 4-(4,5-Dihydro-1-(4-phenylthiazol-2-yl)-3-phenyl-1H-pyrazol-5-yl)-1,3-diphenyl-1H-pyrazole (7).

A mixture of 4,5-dihydro-3-phenyl-5-(1,3-diphenyl-1*H*-pyrazol-4-yl)pyrazole-1-carbothioamide (**4**) and the appropriate 2-bromo-1-phenylethanone, (1 g, 5 mmol) in ethanol (20 mL) and triethylamine (2 drops) were boiled under reflux for 2 hr. The resulting solid, which formed after cooling, was collected and crystallized from ethanol to give 4-(4,5-dihydro-1-(4-phenylthiazol-2-yl)-3-phenyl-1H-pyrazol-5-yl)-1,3-diphenyl-1H-pyrazole (**7**) as Brown crystals from AcOH, Yield: 89%, mp.: 128-30°C. **FT-IR (KBr, cm^{-1}):** 3058 ν (CH), 1628 ν (C=N), 1593 ν (C=C). **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 3.26 (dd, 1H, *J* = 18, 6 Hz, CH_2(pyraz)), 3.85 (dd, 1H, *J* = 18, 12 Hz, CH_2(pyraz)), 5.29 (dd, 1H, *J* = 12, 6 Hz, CH(pyraz)), 7.00 (s, 1H, thiazole H-5), 7.18–8.22 (m, 21H, ArH's, pyrazole H-5); Calcd. for $C_{33}H_{25}N_5S$ (523.65) C, 75.69; H, 4.81; N, 13.37; S, 6.12 Found: C, 75.54; H, 4.82; N, 13.51; S, 6.16 %.

3.4. Synthesis of N-(4-methyl-5-phenylazo-thiazol-2-yl)-N'-(1-phenyl-ethylidene)-hydrazine (9a) and N-(1-phenylethylidene)-N'-(4-phenyl-5-phenylazo-thiazol-2-yl)-hydrazine (9b)

Method A: A mixture of *C*-acetyl (or benzoyl)-*N*-phenylhdrazonoyl chloride **5a** (**5b**) (5 mmol), acetophenonethisemicarbazone (0.5 g, 5 mmol), and triethylamine (0.75 mL, 5 mmol) in ethanol (20 mL) was boiled under reflux for 2 h. The resulting solid was collected and recrystallized from ethanol to give **9a** and **9b**, respectively.

Method B: Benzenediazonium chloride (10 mmole) were added to a cold solution of each 2-(4-methylthiazol-2-yl)-1-(1-phenylethylidene)hydrazine (**10a**) or 2-(4-phenylthiazol-2-yl)-1-(1-phenylethylidene)hydrazine (**10b**) (10 mmole) and sodium acetate (1.3 g, 10 mmole) in ethanol (30 mL) while stirring at 0–5◦C. The reaction mixture was left in an ice-chest for 6 hr. The resulting solid was collected, washed with water, and recrystallized from ethanol to give **9a** and **9b,** respectively.

3.4.1. N-(4-Methyl-5-phenylazo-thiazol-2-yl)-N'-(1-phenyl-ethylidene)-hydrazine (9a) Lit m.p. 159-161^{o}C [34].

3.4.2. N-(1-Phenyl-ethylidene)-N'-(4-phenyl-5-phenylazo-thiazol-2-yl)-hydrazine (9b). Brown crystals from AcOH, Yield: 80%, mp.: 184-86°C. **FT-IR (KBr, cm^{-1}):** 3193 ν(NH) 3055 ν (CH), 1563 ν (C=C). **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 2.25 (s, 3H, CH_3), 7.25–7.89 (m, 15H, ArH's), 9.34 (s, br., 1H, NH); **MS (EI, m/z (%)):** 399 (M+2, 2.26%), 397 (M^+, 15.66%), 146 (5.32%), 133 (15.44%), 118 (18.73%), 104 (11.19%), 103 (38.89%), 92

(27.64%), 89 (7.74%), 77.90 (13.14%), 77 (100%), 64 (25.28%); Calcd. for $C_{23}H_{19}N_5S$ (397.5) C, 69.50; H, 4.82; N, 17.62; S, 8.07 Found: C, 69.65; H, 4.94; N, 17.52; S, 7.83 %.

3.5. Synthesis of 2-(4-Methylthiazol-2-yl)-1-(1-phenylethylidene)hydrazine (10a) and 2-(4-Phenylthiazol-2-yl)-1-(1-phenylethylidene)hydrazine (10b).

A mixture of the appropriate chloroacetone or ω-bromoacetophenone (5 mmol), acetophenonethisemicarbazone (0.5 g, 5 mmol), and triethylamine (0.75 mL, 5 mmol) in ethanol (20 mL) was boiled under reflux for 2 h. The resulting solid was collected and recrystallized from ethanol to give **10a** and **10b**, respectively.

3.5.1. 2-(4-Methylthiazol-2-yl)-1-(1-phenylethylidene)hydrazine (10a).

Deep brown crystals from EtOH, Yield: 84%, mp.: 167-69°C. **FT-IR (KBr, cm^{-1}):** 3421 ν (NH) 3047 ν (CH), 1616 ν (C=N) 1563 ν (C=C). **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 2.18 (s, 3H, CH_3), 2.24 (s, 3H, CH_3), 6.45 (s, 1H, thiazole H-5), 7.25–7.68 (m, 6H, ArH's), 8.42 (s, br., 1H, NH); Calcd. for $C_{12}H_{13}N_3S$ (231.32) C, 62.31; H, 5.66; N, 18.17; S, 13.86 Found: C, 62.20; H, 5.74; N, 18.29; S, 13.77 %.

3.5.2. 2-(4-Phenylthiazol-2-yl)-1-(1-phenylethylidene)hydrazine (10b).

Buff crystals from DMF, Yield: 74%, mp.: 258-60°C. **FT-IR (KBr, cm^{-1}):** 3193 ν (NH) 3055 ν (CH), 1563 ν (C=C). **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 2.31 (s, 3H, CH_3), 7.27–7.94 (m, 12H, ArH's), 9.34 (s, br., 1H, NH); Calcd. for $C_{19}H_{16}N_4O$ (316.13) C, 72.13; H, 5.10; N, 17.71 FoundC, 72.30; H, 5.22; N, 17.95

3.6. 1-((1,3-diphenyl-1H-pyrazol-4-yl)methylene)thiosemicarbazide (11).

A mixture of 1,3-diphenyl-1*H*-pyrazole-4-carbaldehyde (**1**) (1.2 g, 5 mmol) and thiosemicarbazide (0.46 g, 5 mmol) in ethanol (20 mL) was heated under refluxed for 3 hr. The resulting solid was collected and recrystallized from Acetic to give **11** as a white crystals, Yield: 94%, mp.: 208-10°C. **FT-IR (KBr, cm^{-1}):** 3352, 3259, 3139 ν (NH, NH_2), 1620 ν (C=N), 1596 ν (C=C). **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 7.27 (s, 1H, CH=), 7.28–7.78 (m, 10H, ArH's), 7.99 (s, 1H, pyrazole H-5), 8.95 (s, br., 3H, NH, NH_2); **MS (EI, m/z (%)):** 323 (M+2, 0.08%), 322 (M+1, 0.37%), 321 (M^+, 1.85%), 217 (7.96%), 141 (12.96%), 128 (9.78%), 114 (29.85%), 103 (26.94%), 88 (14.79%), 76 (100%), 62 (19.43%), 59 (43.41%); Calcd. for $C_{17}H_{15}N_5S$ (321.4) C, 63.53; H, 4.70; N, 21.79; S, 9.98 Found: C, 63.37; H, 4.82; N, 21.65; S, 10.11 %.

3.7. N-(1,3-Diphenyl-1H-pyrazol-4-ylmethylene)-N'-(4-substituted 5-phenylazothi-azol-2-yl)-hydrazine 12a-c and 1-((1,3-diphenyl-1H-pyrazol-4-yl)methylene)-2-(4-phenylthiazol-2-yl)hydrazine (13).

A mixture of the appropriate hydrazonoyl halides **5a-c** or ω-bromoacetophenone (5 mmol), **11** (1.61 g, 5 mmol), and triethylamine (0.75 mL, 5 mmol) in ethanol (20 mL) was boiled under reflux for 2 hr The resulting solid was collected and recrystallized from acetic acidl to give **12a-c** and **13**, respectively.

3.7.1. N-(1,3-Diphenyl-1H-pyrazol-4-ylmethylene)-N'-(4-methyl- 5-phenylazothi-azol-2-yl)-hydrazine (12a).

Dark red crystals, Yield: 89%, mp.: 138-140°C. **FT-IR (KBr, cm^{-1}):** 3280 ν (NH), 3055 ν (CH), 1625 ν (C=N), 1600 ν (C=C). **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 2.48 (s, 3H, CH_3), 7.29-7.98 (m, 17H, ArH's), 11.08 (s, br., 1H, NH); **^{13}C NMR (300 MHz, DMSO-d_6):** δ = 13.25 (CH_3), 113.12, 119.85, 121.45, 124.76, 128.22, 128.78, 129.13, 129.68, 129.87, 130.24, 138.21, 140.40, 154.47, 145.76, 164.23; **MS (EI, m/z (%)):** 463 (M^+, 1.01%), 114 (6.66%), 113 (5.60%), 104 (11.83%), 77 (80.64%), 65 (9.42%), 63 (10.56%); Calcd. for $C_{26}H_{21}N_7S$ (463.56) C, 67.37; H, 4.57; N, 21.15; S, 6.92 Found: C, 67.45; H, 4.38; N, 21.32; S, 7.10 %.

3.7.2. N-(1,3-Diphenyl-1H-pyrazol-4-ylmethylene)-N'-(4-phenyl- 5-phenylazothi-azol-2-yl)-hydrazine (12b).

Red crystals, Yield: 84%, mp.: 162-64°C. **FT-IR (KBr, cm^{-1}):** 3370 ν (NH), 3059 ν (CH), 1620 ν (C=N), 1593 ν (C=C). **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 7.27-8.10 (m, 22H, ArH's), 11.24 (s, br., 1H, NH); **MS (EI, m/z (%)):** 526 (M+1, 0.05%), 245 (24.36%), 217 (10.01%), 176 (39.35%), 134 (39.48%), 115 (25.92%), 103 (44.22%), 88 (21.97%), 76 (100%), 63 (15.89%); Calcd. for $C_{31}H_{23}N_7S$ (525.63) C, 70.84; H, 4.41; N, 18.65; S, 6.10 Found: C, 71.00; H, 4.52; N, 18.59; S, 6.23 %.

3.7.3. N-(4-Benzofuran-2-yl-5-phenylazo-thiazol-2-yl)-N'-(1,3-diphenyl-1H-pyrazol-4-ylmethylene)-hydrazine (12c).

Red crystals, Yield: 85%, mp.: 190-92°C. **FT-IR (KBr, cm^{-1}):** 3370 ν (NH), 3059 ν (CH), 1620 ν (C=N), 1593 ν (C=C). **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 7.10-8.17 (m, 22H, ArH's), 11.24 (s, br., 1H, NH); **MS (EI, m/z (%)):** 566 (M+1, 0.21%), 331 (11.96%), 245 (10.71%), 216 (5.22%), 212 (11.97%), 164 (8.08%), 145 (72.91%), 117 (11.95%), 103 (17.87%), 89 (100%), 77 (48.71%), 63 (14.07%); Calcd. for $C_{33}H_{23}N_7OS$ (565.65) C, 70.07; H, 4.10; N, 17.33; S, 5.67 Found: C, 69.88; H, 4.21; N, 17.45; S, 5.77 %.

3.7.4. 1-((1,3-diphenyl-1H-pyrazol-4-yl)methylene)-2-(4-phenylthiazol-2-yl)hydrazine (13).
Orange crystals, Yield: 89%, mp.: 140-42°C. **FT-IR (KBr, cm^{-1}):** 3356 ν (NH), 3055 ν (CH), 1615 ν (C=N), 1593 ν (C=C). **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 6.77 (s, 1H, thiazole H-5), 7.32-8.10 (m, 17H, ArH's), 11.10 (s, br., 1H, NH); Calcd. for $C_{25}H_{19}N_5S$ (421.52) C, 71.23; H, 4.54; N, 16.61; S, 7.61 Found: C, 71.11; H, 4.42; N, 16.78; S, 7.56 %.

3.8. Alkyl N'-(1,3-diphenyl-1H-pyrazol-4-ylmethylene)-hydrazinecarbodithioate 15a and 15b.
A mixture of the appropriate methyl (or benzyl) carbodithioate **14a** or **14b** (5 mmol), 1,3-diphenyl-1*H*-pyrazole-4-carbaldehyde (**1**)(1.2 g, 5 mmole), and triethylamine (0.75 mL, 5 mmol) in 2-propanol (20 mL) was heated under reflux for 2 hr at room temperature. The resulting solid was collected and recrystallized from acetic acid to give alkyl carbodithioates **15a** and **15b**, respectively.

3.8.1. Methyl N'-(1,3-diphenyl-1H-pyrazol-4-ylmethylene)-hydrazinecarbodithioate 15a
Beige crystals, Yield: 85%, mp.: 280-82°C. **FT-IR (KBr, cm^{-1}):** 3575 ν (NH), 3062 ν (CH), 1627 ν (C=N), 1593 ν (C=C). **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 2.45 (s, 3H, CH_3), 6.77 (s, 1H, CH=N), 7.10-8.17 (m, 11H, ArH's), 13.14 (s, br., 1H, NH); Calcd. for $C_{18}H_{16}N_4S_2$ (352.48) C, 61.34; H, 4.58; N, 15.90; S, 18.19 Found: C, 61.34; H, 4.42; N, 15.77; S, 18.23 %.

3.8.2. Benzyl N'-(1,3-diphenyl-1H-pyrazol-4-ylmethylene)-hydrazinecarbodithioate 15b.
Pale yellow crystals, Yield: 85%, mp.: 262-64°C. **FT-IR (KBr, cm^{-1}):** 3575 ν (NH), 3062 ν (CH), 1627 ν (C=N), 1593 ν (C=C). **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 4.42 (s, 2H, CH_2), 6.61 (s, 1H, CH=N), 7.10-8.17 (m, 16H, ArH's), 13.18 (s, br., 1H, NH); Calcd. for $C_{24}H_{20}N_4S_2$ (428.57) C, 67.26; H, 4.70; N, 13.07; S, 14.96 Found: C, 67.10; H, 4.82; N, 13.15; S, 15.08 %.

3.9. Synthesis of 2-(5-substituted 3-phenyl-1,3,4-thiadiazol-2(3H)-ylidene)-1-((1,3-diphenyl-1H-pyrazol-4-yl)methylene)hydrazine 18a-e
A mixture of the appropriate methyl (or benzyl) carbodithioate **15a** or **15ba** (5 mmol), appropriate hydrazonoyl halides **5a-c,5h, 5i** (5 mmoles), and triethylamine (0.75 mL, 5 mmol) in ethanol (20 mL) was stirred for 2 hrs at room temperature. The resulting solid was collected and recrystallized to give 2,3-dihydro-1,3,4-thiadiazoles **18a-e.**

3.9.1. 1-{5-[(1,3-Diphenyl-1H-pyrazol-4-ylmethylene)-hydrazono]-4-phenyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl}-ethanone (18a): Pale orange crystals from AcOH, Yield: 74%, mp.: 178-80°C. **FT-IR (KBr, cm^{-1}):** 3053 ν(CH), 1712 ν(CO), 1598 ν(C=C); **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 2.21 (s, 3H, CH_3), 7.35-8.03 (m, 15H, ArH's and CH=N), 8.86 (s, 1H, ArH), 9.12 (s, 1H, pyrazole H-5); **^{13}C NMR (300 MHz, DMSO-d_6):** δ = 23.87 (CH_3), 117.21, 119.54, 125.11, 126.57, 127.14, 128.34, 128.58, 128.88, 129.35, 129.79, 130.33, 130.96, 140.10, 141.75, 147.52, 149.52, 151.55, 159.47, 188.37 (CO); **MS (EI, m/z (%)):** 466 (M+1, 7.70%), 465 (38.28%), 245 (27.87%), 232 (78.34%), 135 (34.43%), 130 (10.15%), 128 (43.67%), 102 (34.41%), 90 (22.89%), 76 (100%); Calcd. for $C_{25}H_{20}N_6OS$ (464.54) C, 67.22; H, 4.34; N, 18.09; S, 6.90 Found: C, 67.35; H, 4.47; N, 18.13; S, 7.10 %.

3.9.2. {5-[(1,3-Diphenyl-1H-pyrazol-4-ylmethylene)-hydrazono]-4-phenyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl}-phenyl-methanone (18b): Orange crystals from AcOH, Yield: 74%, mp.: 186-88°C. **FT-IR (KBr, cm^{-1}):** 3055 ν(CH), 1711 ν(CO), 1599 ν(C=C); **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 7.52-9.14 (m, ArH's and pyrazole H-5); **MS (EI, m/z (%)):** 527 (M+1, 2.36%), 493 (11.58%), 246 (35.45%), 231 (13.28%), 217 (6.32%), 145 (24.08%), 128 (8.20%), 105 (70.42%), 88.80 (24.38%), 77 (100%); Calcd. for $C_{31}H_{22}N_6OS$ (526.61) C, 70.70; H, 4.21; N, 15.96; S, 6.09 Found: C, 70.89; H, 4.10; N, 16.20; S, 6.00 %.

3.9.3. Benzofuran-2-yl-{5-[(1,3-diphenyl-1H-pyrazol-4-ylmethylene)-hydrazono]-4-phenyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl}-methanone (18c): Orange crystals from dioxane, Yield: 73%, mp.: 249-51°C. **FT-IR (KBr,**

cm^{-1}): 3060 ν(CH), 1660 ν(CO), 1605 ν(C=N), 1620 ν(C=C); **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 7.44-8.97 (m, ArH's and pyrazole H-5); **MS (EI, m/z (%)):** 567 (M^+, 1.28%), 245 (10.19 %), 145 (21.16%), 105 (70.91%), 89 (17.41%), 77 (100%); Calcd. for $C_{33}H_{22}N_6O_2S$ (566.63) C, 69.95; H, 3.91; N, 14.83; S, 5.66 Found: C, 70.14; H, 4.11; N, 14.75; S, 5.68 %.

3.9.4. Ethyl 5-[(1,3-diphenyl-1H-pyrazol-4-ylmethylene)-hydrazono]-4-phenyl-4,5-dihydro-[1,3,4]thiadiazole-2-carboxylate (18d): Yellow crystals from AcOH, Yield: 74%, mp.: 162-64°C. **FT-IR (KBr, cm^{-1}):** 3056 ν(CH), 1720 ν(CO), 1599 ν(C=C); **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 1.32 (t, 3H, J = 7.5 Hz, $CH_2\underline{CH_3}$), 4.34 (q, 2H, J = 7.5 Hz, $CH_3\underline{CH_2}$), 7.47-9.11 (m, 17H, ArH's and pyrazole H-5); **^{13}C NMR (300 MHz, DMSO-d_6):** δ = 13.57 (CH_3), 63.48 (CH_2), 116.85, 119.45, 124.68, 126.84, 128.12, 128.46, 128.79, 129.33, 129.45, 129.85, 131.14, 140.13, 140.47, 144.52, 149.67, 151.47, 161.58; **MS (EI, m/z (%)):** 567 (M^+, 1.35%), 493 (14.32%), 245 88.36%), 232 (100%), 219 (11.64%), 204 (18.44%), 169 (34.45%), 155 (20.34%), 139 (10.34%), 130 (22.08%), 128 (34.91%), 125 (24.67%), 113 (11.10%), 111 (24.14%), 102 (26.01%), 89 (18.84%), 76 (74.44%); Calcd. for $C_{27}H_{22}N_6O_2S$ (494.57) C, 65.57; H, 4.48; N, 16.99; S, 6.48 Found: C, 65.72; H, 4.57; N, 17.11; S, 6.59 %.

3.9.5. 5-[(1,3-Diphenyl-1H-pyrazol-4-ylmethylene)-hydrazono]--2-phenyl-carbamoyl-4-phenyl-4,5-dihydro-[1,3,4]thiadiazole (18e):): Yellow crystals from AcOH, Yield: 77%, mp.: 240-42°C. **FT-IR (KBr, cm^{-1}):** 3388 ν(NH), 3056 ν(CH), 1685 ν(CO), 1600 ν(C=C); **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 7.16-9.14 (m, 22H, ArH's and pyrazole H-5), 10.72 (s, 1H, NH); **MS (EI, m/z (%)):** 542 (M+1, 1.77%), 245 (49.46%), 217 (10.43%), 128 (8.77%), 119 (8.46%), 105 (6.38%), 169 (34.45%), 155 (20.34%), 139 (10.34%), 130 (22.08%), 128 (34.91%), 125 (24.67%), 103 (26.19%), 91.30 (27.26%), 77 (100%), 64 (7.76%); Calcd. for $C_{31}H_{23}N_7OS$ (541.17) C, 68.74; H, 4.28; N, 18.10; S, 5.92 Found: C, 68.85; H, 4.41; N, 18.24; S, 6.11 %.

3.10. Methyl N'-(1-Benzofuran-2-yl-ethylidene)-hydrazinecarbodithiate (22)

A mixture of methyl carbodithioate **14a**, 1-(benzofuran-2-yl)ethanone (**1**) (1.2 g, 5 mmole), and triethylamine (0.75 mL, 5 mmol) in 2-propanol (20 mL) was heated under reflux for 2 hr at room temperature. The resulting solid was collected and recrystallized from acetic acid to give methyl carbodithioates **22**: Yellow crystals from AcOH, Yield: 77%, mp.: 230-32°C. **FT-IR (KBr, cm^{-1}):** 3259 ν(NH), 3056 ν(CH), 1635 ν(C=N), 1600 ν(C=C); **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 2.22 (s, 3H, CH_3), 2.46 (s, 3H, CH_3), 7.16-8.05 (m, 5H, ArH's), 13.72 (s, 1H, NH); Calcd. for $C_{12}H_{12}N_2OS_2$ (264.37) C, 54.52; H, 4.58; N, 10.60; S, 24.26 Found: C, 54.65; H, 4.66; N, 10.78; S, 24.37 %.

3.11. 1-{5-[(1-Benzofuran-2-yl-ethylidene)-hydrazono]-4-phenyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl}-ethanone (23a):

A mixture of methyl carbodithioate **22** (5 mmol), appropriate hydrazonoyl halides **5a-c, 5h, 5i** (5 mmoles), and triethylamine (0.75 mL, 5 mmol) in ethanol (20 mL) was stirred for 2 hrs at room temperature. The resulting solid was collected and recrystallized to give 2,3-dihydro-1,3,4-thiadiazoles **23a-e.**

3.11.1. 1-{5-[(1-Benzofuran-2-yl-ethylidene)-hydrazono]-4-phenyl-4,5-dihydro-[1,3,4]-thiadiazol-2-yl}-ethanone (23a)

Dark brown crystals from AcOH, Yield: 81%, mp.: 188-90°C. **FT-IR (KBr, cm^{-1}):** 3058 ν(CH), 1668 ν(CO), 1596 ν(C=C); **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 2.31 (s, 3H, CH_3), 2.47 (s, 3H, CH_3), 7.16-8.14 (m, 10H, ArH's); **^{13}C NMR (300 MHz, DMSO-d_6):** δ = 15.23 (CH_3), 24.66 (CH_3), 120.45, 123.73, 126.42, 127.21, 128.76, 130.21, 132.11, 132.42, 135.42, 136.75, 137.40, 142.54, 147.28, 151.55, 154.87, 190.21; **MS (EI, m/z (%)):** 376 (M^+, 0.79%), 144 (35.69%), 135 (15.50%), 115 (43.14%), 91 (17.06%), 89 (22.14%), 77 (51.50%), 65 (15.84%), 63 (44.89%); Calcd. for $C_{20}H_{16}N_4O_2S$ (376.43) C, 63.81; H, 4.28; N, 14.88; S, 8.52 Found: C, 63.95; H, 4.32; N, 15.11; S, 8.74 %.

3.11.2. {5-[(1-Benzofuran-2-yl-ethylidene)-hydrazono]-4-phenyl-4,5-dihydro-[1,3,4]-thiadiazol-2-yl}-phenyl-methanone (23b)

Red crystals from AcOH, Yield: 77%, mp.: 114-16°C. **FT-IR (KBr, cm^{-1}):** 3031 ν(CH), 1705 ν(CO), 1597 ν(C=C); **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 2.33 (s, 3H, CH_3), 7.34-8.14 (m, 15H, ArH's); **^{13}C NMR (300 MHz, DMSO-d_6):** δ = 14.81 (CH_3), 120.11, 123.35, 125.12, 127.45, 127.88, 128.49, 130.45, 131.74, 132.25, 135.7, 136.45, 137.84, 141.25, 147.58, 151.67, 154.78, 168.56; **MS (EI, m/z (%)):** 439 (M+1, 20.88%), 159 (6.98%), 144 (68.82%), 115 (48.03%), 105 (95.22%), 77 (100%), 62 (16.28%), 59 (14.97%); Calcd. for $C_{25}H_{18}N_4O_2S$ (438.5) C, 68.48; H, 4.14; N, 12.78; S, 7.31 Found: C, 68.57; H, 4.33; N, 12.89; S, 7.27 %.

3.11.3. Benzofuran-2-yl-{5-[(1-benzofuran-2-yl-ethylidene)-hydrazono]-4-phenyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl}-methanone (23c)

Brown crystals from AcOH, Yield: 74%, mp.: 124-26°C. **FT-IR (KBr, cm^{-1}):** 3031 ν(CH), 1682 ν(CO), 1597 ν(C=C); **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 2.32 (s, 3H, CH_3), 7.34-8.14 (m, 15H, ArH's); Calcd. for $C_{27}H_{18}N_4O_3S$ (478.52) C, 67.77; H, 3.79; N, 11.71; S, 6.70 Found: C, 67.68; H, 3.84; N, 11.71; S, 6.87 %.

3.11.4. Benzofuran-2-yl-{5-[(1-benzofuran-2-yl-ethylidene)-hydrazono]-4-phenyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl}-methanone (23h):

Yellowish green crystals from AcOH, Yield: 82%, mp.: 254-52°C. **FT-IR (KBr, cm^{-1}):** 3031 ν(CH), 1697 ν(CO), 1597 ν(C=C); **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 1.33 (t, 3H, J = 7.5 Hz, $CH_2\underline{CH_3}$), 2.34 (s, 3H, CH_3), 4.41 (q, 2H, J = 7.5 Hz, $\underline{CH_2}CH_3$), 7.34-8.14 (m, 10H, ArH's); **^{13}C NMR (300 MHz, DMSO-d_6):** δ = 14.22 (CH_3), 15.49 (CH_3), 120.23, 123.47, 126.34, 127.58, 128.58, 129.35, 132.11, 132.58, 135.47, 136.42, 137.81, 142.12, 144.45, 153.12, 153.78, 162.22; **MS (EI, m/z (%)):** 406 (M^+, 1.01%), 393 (15.5%), 378 (9.7%), 285 (15.7%), 244 (11.1%), 216 (21.0%), 200 (9.7%), 160 (27.0%), 158 (100%), 157 (63.9%), 144 (63.1%), 118 (27.7%), 117 (12.6%), 105 (13.7%), 93 (27.4%), 91 (46.5%), 87 (8.0%), 77 (64.2%), 65 (60.2%); Calcd. for $C_{21}H_{18}N_4O3S$ (406.46) C, 62.05; H, 4.46; N, 13.78; S, 7.89 Found: C, 62.17; H, 4.64; N, 13.89; S, 8.10%.

3.11.5. 5-[(1-Benzofuran-2-yl-ethylidene)-hydrazono]-4-phenyl-4,5-dihydro-[1,3,4]-thiadiazole-2-carboxylic acid phenylamide (23i)

Yellowish green crystals from AcOH, Yield: 84%, mp.: 210-12°C. **FT-IR (KBr, cm^{-1}):** 3382 ν(NH), 3020 ν(CH), 1647 ν(CO), 1600 ν(C=C); **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 2.35 (s, 3H, CH_3, 7.34-8.14 (m, 15H, ArH's), 9.92 (s, br., 1H, NH); **MS (EI, m/z (%)):** 452 (M-1, 4.18%), 219 (4.44%), 120 (6.11%), 119 (11.17%), 104 (11.1%), 216 (21.0%), 200 (9.7%), 160 (27.0%), 158 (100%), 157 (63.9%), 144 (12.09%), 93 (10.01%), 92 (34.92%), 90.50 (14.07%), 79 (5.24%), 77 (100%), 65 (35.70%), 62 (16.90%); Calcd. for $C_{25}H_{19}N_5O_2S$ (453.52) C, 66.21; H, 4.22; N, 15.44; S, 7.07 Found: C, 66.35; H, 4.10; N, 15.62; S, 7.24 %.

3.12. Synthesis of 1,2,4-thiadiazoles 25-28b

A mixture of *2-(2-phenylhydrazono)-1-(benzofuran-2-yl)-2-bromoethanone* (**5c**) (1.7 g, 5 mmol), the appropriate of methyl *N'*-[1-(2-oxo-2H-chromen-3-yl)-ethylidene]-hydrazinecarbodithioate (**24a**), methyl N'-[1-(3-oxo-3H-benzo[f]chromen-2-yl)-ethylidene]-hydrazinecarbodithioate (24b), methyl *N'*-[1-(5-Bromo-benzofuran-2-yl)-ethylidene]-hydrazinecarbodithioate (**24c)**, methyl *N'*-[1-(4-cyano-1,5-diphenyl-1*H*-pyrazol-3-yl)-ethylidene]-hydrazinecarbodithioate (**24d**) or methyl *N'*-[1-(4-cyano-5-phenyl-1-*p*-tolyl-1*H*-pyrazol-3-yl)-ethylidene]-hydrazinecarbodithioate (**24e)** (5 mmol) and triethylamine (0.5 g, 0.75 ml, 5 mmol) in ethanol (20 ml) was stirred at room teperature for 2 hr. The resulting solid was collected and recrystallized fromthe proper solvent to give correspondind thiadiazoles **25-28b**, respectively.

3.12.1. 3-(1-{[5-(Benzofuran-2-carbonyl)-3-phenyl-3H-[1,3,4]thiadiazol-2-ylidene]-hydrazono}-ethyl)-chromen-2-one (25)

Red crystals from DMF, Yield: 79%, mp.: 222-24°C. **FT-IR (KBr, cm^{-1}):** 3020 ν(CH), 1728 ν(CO), 1604 ν(C=C); **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 2.30 (s, 3H, CH_3, 7.14-8.14 (m, 15H, ArH's); **MS (EI, m/z (%)):** 506 (M^+, 5.9%), 441 (11.8%), 440 (34.5%), 439 (40.2%), 307 (42.6%), 306 (40.7%), 171 (5.3%), 145 (100%), 144 (100%), 157 (63.9%), 144 (12.09%), 93 (10.01%), 92 (34.92%), 90.50 (14.07%), 79 (90.5%), 106 (36.9%), 105 (27.7%), 89 (58.2%), 78 (54.3%), 77 (49.0%), 63 (17.6%); Calcd. for $C_{28}H_{18}N_4O_4S$ (506.53) C, 66.39; H, 3.58; N, 11.06; S, 6.33 Found: C, 66.45; H, 3.68; N, 11.24; S, 6.18 %.

3.12.2. 2-(1-{[5-(Benzofuran-2-carbonyl)-3-phenyl-3H-[1,3,4]thiadiazol-2-ylidene]-hydrazono}-ethyl)-benzo[f]chromen-3-one (26)

Red crystals from AcOH, Yield: 73%, mp.: 110-12°C. **FT-IR (KBr, cm^{-1}):** 3020 ν(CH), 1728 ν(CO), 1604 ν(C=C); **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 2.44 (s, 3H, CH_3, 7.26-8.36 (m, 17H, ArH's); **MS (EI, m/z (%)):** 556 (M^+, 0.18%), 170 (17.70%), 145 (100%), 128 (71.54%), 115 (51.49%), 89 (63.40%), 77 (37.89%), 62 (20.86%); Calcd. for $C_{32}H_{20}N_4O_4S$ (556.59) C, 69.05; H, 3.62; N, 10.07; S, 5.76 Found: C, 69.17; H, 3.84; N, 10.22; S, 5.60 %.

3.12.3. Benzofuran-2-yl-(5-{[1-(5-bromo-benzofuran-2-yl)-ethylidene]-hydrazono}-4-phenyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-methanone (27)

Dark red crystals from DMF, Yield: 83%, mp.: 222-24°C. **FT-IR (KBr, cm^{-1}):** 3020 ν(CH), 1666 ν(CO), 1600 ν(C=C); **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 2.33 (s, 3H, CH_3, 7.42-7.96 (m, 14H, ArH's); **MS (EI, m/z (%)):** 558 (M^+, 0.18%), 315 (12.76%), 300 (12.23%), 298 (10.07%), 279 (10.72%), 221 (15.40%), 171 (12.58%), 145 (100%), 118 (26.09%), 114 (28.68%), 102 (15.79%)91 (32.16%), 88 (90.92%), 76 (86.25%), 62 (68.37%); Calcd. for $C_{27}H_{17}BrN_4O_3S$ (557.42) C, 58.18; H, 3.07; N, 10.05; S, 5.75 Found: C, 58.25; H, 3.22; N, 10.18; S, 5.92 %.

3.12.4 3-(1-{[5-(Benzofuran-2-carbonyl)-3-phenyl-3H-[1,3,4]thiadiazol-2-ylidene]-hydrazono}-ethyl)-1,5-diphenyl-1H-pyrazole-4-carbonitrile (28a)

Brown crystals from DMF, Yield: 75%, mp.: 138-40°C. **FT-IR (KBr, cm^{-1}):** 3058 ν(CH), 2227 ν(CN), 1665 ν(CO), 1604 ν(C=C); **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 2.33 (s, 3H, CH_3), 6.90-8.11 (m, 20H, ArH's); **MS (EI, m/z (%)):** 606 (M^+, 1.41%), 145 (24.80%), 143 (9.53%), 105 (42.74%), 89 (29.04%), 77 (100%), 63 (8.05%); Calcd. for $C_{35}H_{23}N_7O_2S$ (605.67) C, 69.41; H, 3.83; N, 16.19 S, 5.29 Found: C, 69.52; H, 4.00; N, 16.32; S, 5.41 %.

3.12.5. 3-(1-{[5-(Benzofuran-2-carbonyl)-3-phenyl-3H-[1,3,4]thiadiazol-2-ylidene]-hydrazono}-ethyl)-5-phenyl-1-p-tolyl-1H-pyrazole-4-carbonitrile (28b)

Dark red crystals from DMF, Yield: 74%, mp.: 308-10°C. **FT-IR (KBr, cm^{-1}):** 3020 ν(CH), 1660 ν(CO), 1617 ν(C=C); **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 2.34 (s, 3H, CH_3), 2.57(s, 3H, CH_3), 7.42-7.79 (m, 19H, ArH's); **MS (EI, m/z (%)):** 620 (M^+, 0.77%), 619 (M-1, 1.19%)), 560 (13.72%), 584 (43.07%), 269 (34.42%), 258 (14.08%), 255 (6.55%), 245 (7.78%), 243 (10.39%), 231 (16.21%), 195 (11.31%), 145 (30.28%), 139 (9.48%), 128 (17.35%), 105 (65.17%), 91 (65.54%), 77 (100%), 65 (23.19%); Calcd. for $C_{36}H_{25}N_7O_2S$ (619.69) C, 69.77; H, 4.07; N, 15.82; S, 5.17 Found: C, 69.84; H, 4.15 N, 15.96; S, 5.24 %.

3.13. Synthesis of ethyl 1,2,3,4-tetrahydro-6-methyl-4-(1,3-diphenyl-1H-pyrazol-4-yl)-2-thioxopyrimidine-5-carboxylate (29)

A mixture of ethyl acetoacetate (6.5 g, 5 mmole), thiourea (3.8 g, 5 mmol), 1,3-diphenyl-1*H*-pyrazole-4-carbaldehyde (12.4 g, 5 mmol), hydrochloric acid (1ml, 36%)) in ethanol (40 ml) was heated under reflux for 6 hr. The resulting solid was collected and recrystallized from ethanol gave **29**: Peige crystals, Yiled: 92%, m.p., 190-92°C. **FT-IR (KBr, cm^{-1}):** 3350 ν (NH), 3020 ν(CH), 1720 ν(CO), 1607 ν(C=C); **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 1.13 (t, 3H, J = 7.5 Hz, $CH_2\underline{CH_3}$), 2.34 (s, 3H, CH_3) 4.11 (q, 2H, J = 7.5 Hz, $\underline{CH_2}CH_3$), 5.12(s, 1H, pyrimidine H-4), 7.21-7.70 (m, 11H, ArH's), 9.12 (s, br., 2H, 2NH); **MS (EI, m/z (%)):** 420 (14.67%), 419 (100%), 390 (34.15%), 346 (62.85%), 345 (19.05%), 330 (16.87%), 312 (16.18%), 286 (16.58%), 269 (12.91%), 245 (11.09%), 221 (38.69%), 216 (20.14%), 180 (10.62%), 166 (16.37%), 152 (11.16%), 140 (16.84%), 126 (11.05%), 114 (33.52%), 103 (25.14%), 77 (68.65%), 66 (15.73%); Calcd. For $C_{23}H_{22}N_4O_2S$ (418.51) C, 66.01; H, 5.30; N, 13.39; S, 7.66 Found C, 66.11; H, 5.41; N, 13.51; S, 7.82

3.14. Synthesis of (1,3-diphenyl-1H-pyrazol-4-yl)-[1,2,4]triazolo[4,3-a]pyrimidines 32a-e.

A mixture of ethyl 1,2,3,4-tetrahydro-6-methyl-4-(1,3-diphenyl-1*H*-pyrazol-4-yl)-2-thioxopyrimidine-5-carboxylate (**29**) (2.09 g, 5 mmol), appropriate hydrazonoyl halides **5a-c, h, i** (5 mmoles), and triethylamine (0.75 mL, 5 mmol) in chloroform (20 mL) was boiled under reflux for 20 hrs. The resulting solid was collected, after evaporated and triturated with pet-ether 40-60°C, and recrystallized to give [1,2,4]triazolo[4,3-*a*]pyrimidines **32a-e**.

3.14.1. Ethyl 3-acetyl-1,7-dihydro-7-methyl-1-phenyl-5-(1,3-diphenyl-1H-pyrazol-4-yl)-[1,2,4]triazolo[4,3-a]pyrimidine-6-carboxylate (32a)

Yellow crystals from EtOH, Yield: 92%, mp.: 242-44°C. **FT-IR (KBr, cm^{-1}):** 3020, 2974 ν(CH), 1674 ν(CO), 1608 ν(C=C); **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 1.31 (t, 3H, J = 7.5 Hz, CH_2CH_3), 2.34 (s, 3H, CH_3), 2.57(s, 3H, CH_3), 4.22 (q, 2H, J = 7.5 Hz, CH_2CH_3), 5.66 (s, 1H, pyrimidine H-4), 7.42-7.79 (m, 16H, ArH's); **MS (EI, m/z (%)):** 545 (M^+, 0.75%), 472 (3.24%)), 118 (18.43%), 104 (19.67%), 91 (25.56%), 77 (100%), 139 (9.48%), 128 (17.35%), 105 (65.17%), 91 (65.54%), 77 (100%), 65 (23.19%); Calcd. for $C_{32}H_{28}N_6O_3$ (544.6) C, 70.57; H, 5.18; N, 15.43 Found: C, , 70.72; H, 5.00; N, 15.37

3.14.2. Ethyl 1,7-dihydro-7-methyl-1,-diphenyl-5-(1,3-diphenyl-1H-pyrazol-4-yl)-[1,2,4]triazolo[4,3-a]pyrimidine-6-carboxylate (32b)

Red crystals from benzene, Yield: 84%, mp.: 238-40°C. **FT-IR (KBr, cm^{-1}):** 3020, 2974 ν(CH), 1674 ν(CO), 1608 ν(C=C); **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 1.31 (t, 3H, J = 7.5 Hz, $CH_2\underline{CH_3}$), 2.34 (s, 3H, CH_3), 2.57(s, 3H, CH_3), 4.22 (q, 2H, J = 7.5 Hz, $\underline{CH_2}CH_3$), 7.42-8.43 (m, 22H, ArH's); **MS (EI, m/z (%)):** 607 (M+1, 42.9%), 422

(99.9%)), 394 (11.9%), 366 (9.0%), 338 (6.0%), 310 (5.0%), 292 (6.0%), 237 (5.0%), 186 (11.9%), 121 (6.0%), 97 (16.9%), 65 (13.9%); Calcd. for $C_{37}H_{30}N_6O_3$ (606.67) C, 73.25; H, 4.98; N, 13.85 Found: C, 73.42; H, 5.12; N, 14.00

3.14.3. Ethyl 3-(benzofuran-2-carbonyl)-5-(1,3-diphenyl-1H-pyrazol-4-yl)-7-methyl-1-phenyl-1,7-dihydro-[1,2,4]triazolo[4,3-a]pyrimidine-6-carboxylate (32c)

Dark brown crystals from EtOH, Yield: 85%, mp.: 201-203°C. **FT-IR (KBr, cm^{-1}):** 3020, 2974 ν(CH), 1674 ν(CO), 1608 ν(C=C); **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 1.31 (t, 3H, J = 7.5 Hz, $CH_2\underline{CH_3}$), 2.34 (s, 3H, CH_3), 2.57(s, 3H, CH_3), 4.22 (q, 2H, J = 7.5 Hz, $\underline{CH_2}CH_3$), 7.42-8.43 (m, 22H, ArH's); **MS (EI, m/z (%)):** 646 (M^+, 56.8%), 645 (50%)), 619 (21.6%), 573 (83.3%), 427 (13.5%), 378 (16.2%), 320 (25.7%), 229 (23%), 193 (36.5%), 145 (100%), 91 (40.5%), 77 (41.9%), 65 (64.9%); Calcd. for $C_{39}H_{30}N_6O4$ (646.69) C, 72.43; H, 4.68; N, 13.00 Found: C, 72.54; H, 4.84; N, 13.15

3.14.4. Diethyl 1,7-dihydro-7-methyl-1-phenyl-5-(1,3-diphenyl-1H-pyrazol-4-yl)-[1,2,4]triazolo[4,3-a]pyrimidine-3,6-dicarboxylate (32d)

Yellow crystals from AcOH, Yield: 89%, mp.: 142-44°C. **FT-IR (KBr, cm^{-1}):** 3055, 2974 ν(CH), 1728 ν(CO), 1624 ν(C=N), 1600 ν(C=C); **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 1.29 (t, 3H, J = 7.5 Hz, $\underline{CH_2}CH_3$), 1.31 (t, 3H, J = 7.5 Hz, $\underline{CH_2}CH_3$), 2.34 (s, 3H, CH_3), 4.01 (q, 2H, J = 7.5 Hz, $\underline{CH_2}CH_3$), 4.22 (q, 2H, J = 7.5 Hz, $\underline{CH_2}CH_3$), 5.66 (s, 1H, pyrimidine H-4), 7.42-7.79 (m, 16H, ArH's); Calcd. for $C_{33}H_{30}N_6O_4$ (574.63) C, 68.98; H, 5.26; N, 14.63 Found: C, 69.10; H, 5.37; N, 14.52

3.14.5. Ethyl 5-(1,3-diphenyl-1H-pyrazol-4-yl)-7-methyl-1-phenyl-3-phenylcarbamoyl-1,7-dihydro-[1,2,4]triazolo[4,3-a]pyrimidine-6-carboxylate (32e)

Yellowish green crystals from AcOH, Yield: 82%, mp.: 214-16°C. **FT-IR (KBr, cm^{-1}):** 3350 ν(NH), 3055, 2974 ν(CH), 1680 ν(CO), 1625 ν(C=N), 1602 ν(C=C); **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 1.31 (t, 3H, J = 7.5 Hz, $1\underline{CH_2}CH_3$), 2.34 (s, 3H, CH_3), 4.22 (q, 2H, J = 7.5 Hz, $\underline{CH_2}CH_3$), 5.66 (s, 1H, pyrimidine H-4), 7.42-7.79 (m, 21H, ArH's), 9.22 (s, br., 1H, NH); **MS (EI, m/z (%)):** 621 (M^+, 48.45%), 91 (25.0%)), 77 (100%); Calcd. for $C_{37}H_{31}N_7O_3$ (621.69) CC, 71.48; H, 5.03; N, 15.77 Found: C, 71.59; H, 5.14; N, 15.89

3.15. Synthesis of 38-42

A mixture of appropriate **33-37** (5 mmol), hydrazonoyl bromide **5c** (1.7 g, 5 mmoles), and triethylamine (0.75 mL, 5 mmol) in chloroform (20 mL) was boiled under reflux for 20 hrs. The resulting solid was collected, after evaporated and triturated with pet-ether 40-60^{o}C, and recrystallized to give [1,2,4]triazolo[4,3-*a*]pyrimidines **38-42**.

3.15.1. Ethyl 5-benzo[1,3]dioxol-4-yl-3-(benzofuran-2-carbonyl)-7-methyl-1-phenyl-1,7-dihydro-[1,2,4]triazolo[4,3-a]pyrimidine-6-carboxylate (38)

Orange crystals from dioxane Yield: 81%, mp.: 208-210°C. **FT-IR (KBr, cm^{-1}):** 3068, 2920 ν(CH), 1654 ν(CO), 1612 ν(C=C); **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 1.31 (t, 3H, J = 7.5 Hz, $CH_2\underline{CH_3}$), 2.42 (s, 3H, CH_3), 4.03 (q, 2H, J = 7.5 Hz, $\underline{CH_2}CH_3$), 5.92 (s, 2H, $O\underline{CH_2}O$), 6.80-8.42 (m, 14H, ArH's); **MS (EI, m/z (%)):** 548 (M^+, 13.1%), 547 (11.1%)), 475 (44.4%), 474 (20.2%), 464 (9.1%), 427 (24.2%), 171 (25.3%), 145 (90.9%), 115 (14.1%), 89 (100%), 77 (36.4%), 65 (34.3%); Calcd. for $C_{31}H_{24}N_4O_6$ (548.55) C, 67.88; H, 4.41; N, 10.21 Found: C, 68.00; H, 4.52; N, 10.35

3.15.2. Ethyl 3-(Benzofuran-2-carbonyl)-5-(2,3-dimethoxy-phenyl)-7-methyl-1-phenyl-1,5-dihydro-[1,2,4]triazolo[4,3-a]pyrimidine-6-carboxylate (39)

Pale red crystals from dioxane Yield: 83%, mp.: 172-74°C. **FT-IR (KBr, cm^{-1}):** 3067, 2926 ν(CH), 1685 ν(CO), 1647 ν(C=N), 1615 ν(C=C); **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 1.17 (t, 3H, J = 7.5 Hz, $CH_2\underline{CH_3}$), 2.39 (s, 3H, CH_3), 3.58 (s, 3H, OCH_3), 3.66 (s, 3H, OCH_3), 4.02 (q, 2H, J = 7.5 Hz, $\underline{CH_2}CH_3$), 6.80-8.13 (m, 14H, ArH's); **MS (EI, m/z (%)):** 566 (5.7%), 564 (M^+, 18.5%), 533 (34.7%)), 491 (28.0%), 427 (54.4%), 419 (16.6%), 399 (17.2%), 211 (10.2%), 171 (14.6%), 145 (100%), 116 (14.0%), 89 (69.1%), 77 (42.0%), 65 (29.0%); Calcd. for $C_{32}H_{28}N_4O_6$ (564.59) C, 68.07; H, 5.00; N, 9.92 Found: C, 68.15; H, 5.11; N, 10.14

3.15.3. 3-(Benzofuran-2-carbonyl)-1-phenyl-1H-[1,2,4]triazolo[3,4-b]quinazolin-5-one (40)

Brown crystals from AcOH Yield: 80%, mp.: 202-204°C. **FT-IR (KBr, cm^{-1}):** 3066, 2920 ν(CH), 1665 ν(CO), 1635 ν(C=N), 1615 ν(C=C); **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 7.17 (t, 1H, J = 8Hz, ArH), 7.36 (s, 1H, furan H-

3), 6.87-7.66 (m, 6H, ArH's), 7.92 (d, 2H, J = 8Hz, ArH), 8.11 (d, 1H, J = 8Hz, ArH), 8.22 (d, 2H, J = 8Hz, ArH), 8.41 (d, 1H, J = 8Hz); **MS (EI, m/z (%)):** 406 (M^+, 1.02%), 380 (5.36%), 145 (98.02%), 117 (13.01%), 102 (13.27%), 89 (100%), 76 (44.21%), 64 (20.57%), 62 (38.21%); Calcd. for $C_{24}H_{14}N4O_3$ (406.11) C, 70.93; H, 3.47; N, 13.79 Found: C, 71.14; H, 3.62; N, 13.94

3.15.4. 3-(Benzofuran-2-carbonyl)-1-phenyl-5,6,7,8-tetrahydro-1H-9-thia-1,2,3a,10-tetra-aza-cyclopenta[b]-fluoren-4-one (41)

Brown crystals from AcOH Yield: 83%, mp.: 126-28°C. **FT-IR (KBr, cm^{-1}):** 3066, 2920 ν(CH), 1701 ν(CO), 1662 ν(CO), 1612 ν(C=N), 1577 ν(C=C); **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 1.61-1.76 (m, 4H, $2CH_2$), 2.85-2.95 (m, 4H, $2CH_2$), 7.71-8.22 (m, 10H, ArH's); **MS (EI, m/z (%)):** 467 (M^+, 38.68%), 211.35 (5.36%), 145 (100%), 118 (9.83%), 91 (20.61%), 89 (92.37%), 77 (43.30%), 64 (12.45%), 62 (24.97%); Calcd. for $C_{26}H_{18}N_4O_3S$ (466.51) C, 66.94; H, 3.89; N, 12.01; S, 6.87 Found: C, 67.15; H, 4.00; N, 12.18; S, 6.05

3.15.5. Benzofuran-2-yl-(1-phenyl-1H-benzo[4,5]imidazo[2,1-c][1,2,4]triazol-3-yl)-methanone (42)

Brown crystals from AcOH Yield: 76%, mp.: 132-34°C. **FT-IR (KBr, cm^{-1}):** 3062, 2920 ν(CH), 1682 ν(CO), 1612 ν(C=N), 1556 ν(C=C); **^{1}H NMR (300 MHz, DMSO-d_6):** δ = 7.32-7.75 (m, 10H, ArH's), 8.12-8.15 (d, 2H, J 9Hz, ArH's), 8.32-8.35 (d, 2H, J 9Hz, ArH's); **MS (EI, m/z (%)):** 378 (M^+, 6.24%), 248 (5. 06%), 229 (5.5$), 194 (7.94%), 145 (100%), 176 (8.12%), 149 (26.02%), 145 (56.84%), 134 (12.25%), 122 (11.47%), 109 (13.72%), 103 (10.71%), 89 (84.52%), 77 (100%), 69 (42.69%), 64 (38.27%); Calcd. for $C_{23}H_{14}N_4O_2$ (378.38) C, 73.01; H, 3.73; N, 14.81 Found: C, 73.20; H, 3.85; N, 15.00

4. Biological evaluation

The tested organisms were gram +ve bacteria [*Staphylococcusaureus* (RCMB 000106), Bacillis subtilis (RCMB 000108)] and gram -ve bacteria [Pseudomonas aeruginosa (RCMB 000102), Escherichia coli (RCMB 000103)]. The study followed a modification of the filter-paper-disc (3 discs / compound) method used in determining the reaction of antibiotics against various bacteria. Centrifuged pellets of bacteria from a 24 h old culture containing approximately 104-106 CFU (colony forming unit) per ml were spread on the surface of Nutrient, agar (typetone 1%, yeast extract 0.5%, NaCl 0.5%, agar 1%, 1000 ml of distilled water, PH 7.0) which was autoclaved under 121°C for at least 20 min. Wells were created in medium with the help of a sterile metallic bores and then cooled down to 45°C. The activity was determined by measuring the diameter of the inhibition zone (in mm). 100µ.1 of the tested samples. The plates were kept for incubation at 37°C for 24 h am} then the plates were examined for the formation of zone of inhibition. Each inhibition zone was measured three times by caliper to get an average value. The test was performed three times for each bacterium culture: PENICILLIN G and STREPTOMYCIN were used as antibacterial standard drugs [38].

Table 1: Response of various microorganisms to some synthesized compounds in vitro (culture)

Sample No.	*Staphylococcus aureus* (RCMB 000106)	*Bacillis subtilis* (RCMB 000108)	*Pseudomonas aeruginosa* (RCMB 000102)	*Escherichia coli* (RCMB 000103)
6a	8.4±0.2	9.1±0.2	7.8±0.2	7.4±0.2
5b	9.8±0.1	8.7±0.2	8.9±0.2	8.2±0.3
6c	10.9±0.2	9.4±0.2	9.2±0.2	7.8±0.2
12a	8.4±0.2	9.2±0.3	NA	7.9±0.2
12b	9.3±0.2	9.1±0.3	7.9±0.2	8.2±0.2
12c	11.3±0.2	10.5±0.2	10.4±0.3	9.1±0.2
18a	10.4±0.3	9.1±0.2	7.8±0.2	8.4±0.3
18b	9.6±0.3	8.8±0.1	7.8±0.2	7.4±0.2
18c	9.1±0.2	9.8±0.1	NA	7.6±0.2
18d	9.2±0.2	9.6±0.3	8.9±0.2	8.00±0.2
18c	8.9±0.2	10.1±0.3	7.4±0.2	7.1±0.2
23a	9.2±0.1	8.5±0.3	NA	8.4±0.1
23b	8.8±0.2	11.1±0.2	7.0±0.1	9.3±0.2
23c	8.2±0.1	7.8±0.2	8.9±0.1	8.1±0.2
23d	8.4±0.08	7.1±0.1	NA	8.2±0.07
23c	10.9±0.1	7.8±0.3	7.2±0.2	8.6±0.2

25	11.1±0.3	10.3±0.2	NA	7.4±0.1
26	9.2±0.1	8.1±0.3	7.9±0.2	7.4±0.2
27	8.2±0.2	NA	NA	7.1±0.1
28a	8.7±0.2	9.3±0.3	11.1±0.2	7.2±0.1
28b	8.5±0.2	NA	8.5±0.2	8.0±0.1
32a	7.8±0.2	7.9±0.3	NA	NA
32b	8.2±0.3	9.1±0.3	7.9±0.2	8.2±0.3
32c	8.9±0.3	9.3±0.2	10.1±0.2	8.8±0.3
32d	9.0±0.1	9.3±0.1	9.2±0.2	7.6±0.1
32e	9.7±0.2	8.9±0.1	8.4±0.2	7.9±0.3
38	9.7±0.3	10.4±0.1	8.3±0.2	7.3±0.3
39	9.1±0.2	9.2±0.1	8.6±0.2	7.2±0.1
40	8.2±0.1	NA	NA	7.1±0.8
41	8.8±0.2	8.0±0.1	7.9±0.2	7.2±0.1
42	8.2±0.2	7.9±0.1	7.4±0.2	NA

Table 2: ST (25µg/ mL)

Gram Positive Bacteria:	**MYCOSTATINE**	**CLOTRIMAZOLE**
***Staphylococcus aureus* (RCMB 000106)**	27.4 ± 0.2	25.1 ± 0.3
***Bacillis subtilis* (RCMB 000108)**	29.4 ± 0.3	30.1 ± 0.2
Gram negative Bacteria:	**AMPICILLIN**	**STREPTOMYCIN**
***Pseudomonas aeruginosa* (RCMB 000102)**	26.3 ± 0.3	24.3 ± 0.2
***Escherichia coli* (RCMB 000103)**	28.5 ± 0.4	25.6 ± 0.2

As shown in Table 1 and comparison with Table 2, the tested compounds showed different antibacterial activity against both Gram positive and Gram negative bacteria. Most of compounds exchibit about 30-40 % antibacterial. Compounds **27** and **40** no effect against *Bacillis subtilis*. Compounds **12a**, **18c**, **23a**, **23d**, **25**, **27**, **32a**, and **40** no effect against *Pseudomonas aeruginosa***.** Compounds **32a** and **42** are no effect against *Escherichia coli*

5. Conclusion

In summary, we have developed a simple, efficient procedure for the synthesis of **5-**arylazothiazoles, 2,3-dihydro-1,3,4-thiadiazoles and triazolo[4,3-*a*]pyrimidine derivatives, which proved to be potent wide spectrum antibacterial agents, via hydrazonoyl halides.

6. References

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