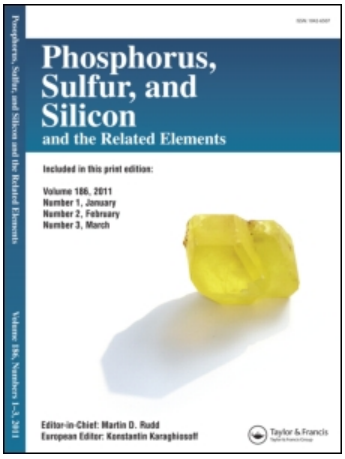

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Synthesis and Antimicrobial Activities of Some Heterocyclic Systems from 2-Furoyl Isothiocyanate

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SYNTHESIS AND ANTIMICROBIAL ACTIVITIES OF SOME HETEROCYCLIC SYSTEMS FROM 2-FUROYL ISOTHIOCYANATE

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2-Furoyl isothiocyanate (1) is used as a building block in synthesizing different heterocyclic systems of anticipated biological activities. Thus, isothiocyanate 1 was reacted with different nucleophilic reagents to produce five- and six-membered heterocyclic systems such as 1,2,4-triazoline, thiadiazolidine, quinazoline, benzothiazole, benzoxazole, benzimidazole, thiazolidine, and imidazolidine. The structures of all the synthesized compounds were confirmed by microanalytical and spectral data. The antimicrobial activity of some of the synthesized compounds was tested.

Supplemental materials are available for this article. Go to the publisher's online edition of* Phosphorus, Sulfur, and Silicon and the Related Elements *to view the free supplemental file.

Keywords Benzothiazole; 2-furoyl isothiocyanate; quinazoline; thiadiazolidine; thiourea derivatives; 1,2,4-triazoline

INTRODUCTION

1,2,4-Triazoles are known to exhibit anti-inflammatory,[1] antiviral,[2] analgesic,[3] antimicrobial,[4] anticonvulsant,[5] and antidepressant activity.[6] A series of 1,2,4-triazoles[7] has been patented and extensively employed in agriculture. In addition, it was reported that 1,3,4-thiadiazoles exhibit various biological activities due to the presence of the $=N-C-S$ moiety.[8] Quinazolines exhibit a wide variety of pharmacological activities.[9,10] The literature also states that the antiviral[11] and antibacterial[12] activities of thiourea derivatives are due to the presence of the $-NH-C(S)-NH-$ function in the molecule, and the changes in this activity depend on the nature of its substituents. In the present investigation, 2-furoyl isothiocyanate is used as a building block to synthesize some new derivatives of 1,2,4-triazole, thiadiazole, quinazoline, benzothiazole, benzoxazole, benzimidazole, thiazolidine, imidazole, and thiourea, and to investigate their antibacterial and antifungal activities.

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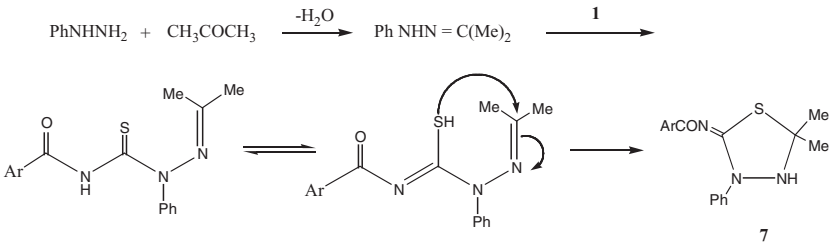
RESULTS AND DISCUSSION

The reaction of 2-furoyl isothiocyanate (**1**) with benzoyl hydrazine (**2a**) in acetonitrile produced the corresponding thiosemicarbazide derivative **3**.[13,14] Compound **3** so formed could be readily converted into 1,2,4-triazoline-5-thione derivative **4** upon treatment with polyphosphoric acid. The formation of **4** can be visualized on the basis of the removal of a molecule of water. The structures of compounds **3** and **4** were elucidated from their microanalytical and spectral data. Their IR spectra showed absorption bands corresponding to NH in the region 3102–3300 cm^{-1}, C=O in the region 1640–1674 cm^{-1}, and C=S in the region 1162–1173 cm^{-1}. The ^1H NMR spectra displayed signals due to aromatic protons at 6.61–8.02 ppm integrating eight protons, and signals of NH protons in the downfield region at 10.65–12.17 ppm. Their MS revealed molecular ion peaks at m/z 289 and m/z 271, respectively. Moreover, the appearance of 2-furoyl fragment at m/z 95 of compound **4** supported the proposed mechanism of its formation.

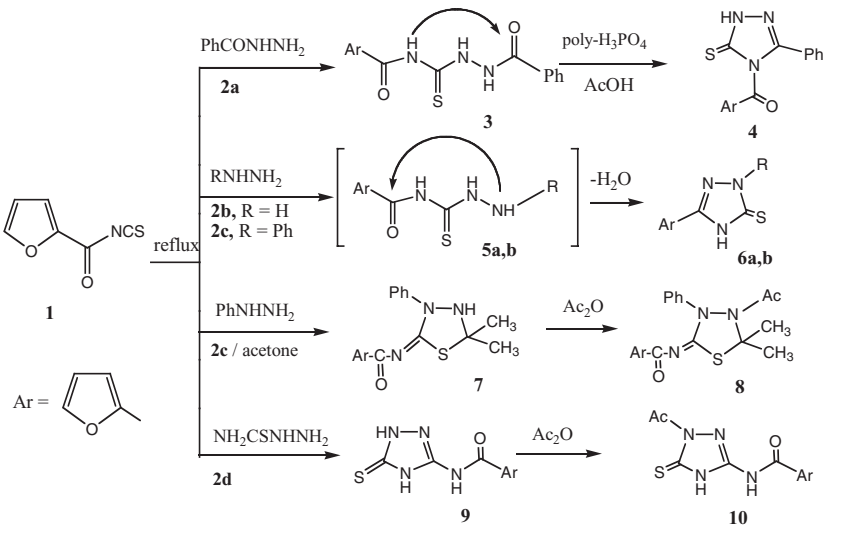
The reaction of hydrazine hydrate (**2b**) or phenyl hydrazine (**2c**) with isothiocyanate **1** in acetonitrile afforded 1,2,4-tiazoline derivatives **6a**,**b** in a one-pot reaction. However, Uher et al.[15] have reported that the formation of **6** proceeded via isolation of thiourea derivatives **5a**,**b** that underwent cyclization in an acid medium. On the other hand, when the reaction of **1** with phenyl hydrazine (**2c**) was conducted in a dry acetone, thiadiazolidine derivative **7** was obtained; these results were consistent with our previous results[14] and others.[16] The formation of compound **7** can be visualized on the basis of nucleophilic attack of isopropylidene phenylhydrazone (obtained as a side product of the reaction of phenylhydrazine with acetone) on the carbon atom of isothiocyanate group followed by cyclization (Scheme 1).



Scheme 1 Mechanism of formation of thiadiazoline derivative **7**.

The IR spectra of triazolines **6a**,**b** showed absorption bands correlated with NH and C=S groups. The IR spectrum of **7** showed absorption bands for NH and C=O groups. The ^1H NMR spectrum of **6a** displayed signals in the range 6.77–8.10 ppm corresponding to the three furan protons and signals at δ 11.99 and 14.00 ppm for two NH protons. The ^1H NMR of **7** exhibited signals due to CH_3 protons at δ 1.95 ppm, and those for aromatic protons in the range 6.49–7.84 ppm and NH proton at 4.3 ppm. Heating of compound **7** with acetic anhydride afforded its acetyl derivative **8** (Scheme 2).

Isothiocyanate **1** underwent reaction with thiosemicarbazide (**2d**) in boiling acetonitrile to yield 1,2,4-triazoline derivative **9**.[14,17] The mass spectrum of **9** showed its molecular ion peak as well as a fragment corresponding to a furoyl cation at m/z 95 as a base peak. Absorption bands correlated with NH, C=O, and C=S groups were recorded in its IR spectrum. Further proof for the assigned structure of **9** was gained from microanalytical and spectral studies of its mono acetyl derivative **10** (see the Experimental section).



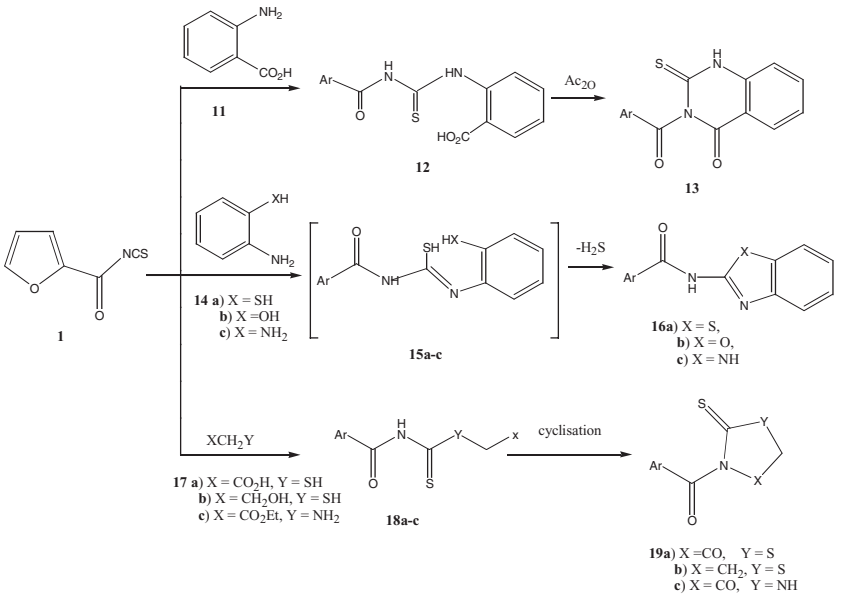
Scheme 2

The reaction of isothiocyanate **1** with anthranilic acid (**11**) yielded thiourea derivative **12**, which cyclized upon heating with acetic anhydride to produce quinazoline derivative **13**.[14] The IR spectrum of compounds **12** and **13** showed absorption bands correlated with ν NH, ν C=O, and ν C=S. The ^{1}H NMR spectrum of **13** displayed signals due to aromatic protons as well as a downfield signal due to the NH proton. Further support for the assigned structures of **12** and **13** was gained from their MS data that showed their molecular ion peaks (see the Experimental section).

A solution of isothiocyanate **1** in acetonitrile was refluxed with *o*-aminothiophenol (**14a**), *o*-aminophenol (**14b**), or *o*-phenylenediamine (**14c**), which led to products formulated as benzothiazole derivative **16a**, benzoxazole derivative **16b**, or benzimidazole derivative **16c**, respectively.[14] The compounds **16a–c** presumably formed via elimination of H_2S molecule from the non isolable thiourea derivatives **15a–c** (Scheme 3). The IR spectra of **16a–c** showed absorption bands correlated with ν NH, ν C=O. Their ^{1}H NMR spectra displayed signals in the region 6.61–8.05 ppm due to aromatic protons as well as downfield signals for the NH protons. Further highlights for the proposed structures were gained from their MS data that showed the molecular ion peaks (see the Experimental section).

Refluxing of isothiocyanate **1** with thioglycolic acid (**17a**), 2-mercaptoethanol (**17b**), or ethylglycinate (**17c**) in acetonitrile furnished adducts **18a–18c**, respectively. Compounds **18a–18c** could be readily converted into thiazolidine derivatives **19a**,**b** or imidazolidine derivative **19c** upon heating with acetic anhydride and a catalytic amount of ammonium acetate (Scheme 3). The structures of compounds **18a–c** and **19a–c** were elucidated from their microanalytical and spectral data. The ^{1}H NMR spectra of **18a–c** displayed signals of methylene protons and aromatic protons, as well as the signals of OH and NH protons in the downfield region. ^{1}H NMR spectra of **19a–c** showed methylene proton signals as well as the aromatic proton signals. The MS spectra of **18b**,**c** and **19a–c** revealed the corresponding molecular ion peaks, which were in accord with their expected molecular formulas.

The antimicrobial screening of some of the synthesized compounds was done using the agar plate diffusion method[18] (see the Supplemental Materials available online).



Scheme 3

EXPERIMENTAL

Melting points were determined in open capillary tubes on a Gallenkamp melting point apparatus and were uncorrected. The elemental analyses were done on a Perkin–Elemer 2400 CHN elemental analyzer. The infrared spectra were recorded on FTIR Maltson (infinity series) spectrometers as KBr discs. The ^{1}H NMR spectra were measured on Varian Gemini 200 MHz instrument with chemical shift (δ) expressed in ppm downfield from TMS as internal standard, in DMSO-d_6 or $CDCl_3$. Mass spectra were recorded on a Shimadzu GC-MSQP 1000 EX instrument operating at 70 eV. TLC carried out the monitoring of the progress of all reactions and homogeneity of the synthesized compounds. TLC was run using TLC aluminum sheets silica gel F_{254} (Merck). The antimicrobial activity was determined according to the method of Kavanagh.[18] 2-Furoylchloride was obtained from Merck-Schuchardt, (d 20°/4°) 1.323–1.325.

Synthesis of 2-Furoyl Isothiocyanate (1)

The solution of 2-furoyl chloride (3 mmol) in dry acetonitrile or dry acetone (30 mL) and solid ammonium thiocyanate (4 mmol) was stirred for 30 min at room temperature.[19] The precipitated ammonium chloride was filtered off to give a clear solution of 2-furoyl isothiocyanate (**1**) with 87% yield.

Reaction of 2-Furoyl Isothiocyanate (1) with 2a–d, 11, 14a–c, 17a–c

A solution of isothiocyanate **1** (3 mmol) in dry acetonitrile (30 mL) or dry acetone (30 mL) was refluxed for 2–3 h (TLC) with an equimolar amount of benzoyl hydrazine (**2a**), hydrazine hydrate **(2b)**, phenyl hydrazine (**2c**), thiosemicarbazide (**2d**), anthranilic

acid (**11**), *o*-aminothiophenol (**14a**), *o*-aminophenol (**14b**), *o*-phenylenediamine (**14c**), thioglycolic acid (**17a**), 2-mercaptothanol (**17b**), or ethylglycinate (**17c**). The precipitated solid was filtered off and recrystallized from the suitable solvent.

1-Benzoyl-4-(2-furoyl)-thiosemicarbazide (3). 86% yield; colorless crystals; mp 140–142°C (ethanol); IR (KBr) ν: 3300, 3206, and 3120, 1668, 1640, 1162 cm^{-1}; ^1H NMR (DMSO-d_6) δ: 6.76 (d, $J = 3.4$ Hz, 1H), 7.54–7.63 (m, 3H), 7.87 (d, $J = 3.6$ Hz, 1H), 7.79 (d, $J = 6.6$ Hz, 2H), 8.02 (s, 1H), 11.10 (br.s, 1H), 11.54 (br.s, 1H), 12.17 (br.s, 1H); MS (70 eV) *m/z* (%): 289 ($M^{+\cdot}$, 30), 290 ($M^{+\cdot}+1$, 13), 291 ($M^{+\cdot}+2$, 4), 272 (22), 256 (26), 105 (100), 95 (70), 77 (29); Anal. Calcd. for $C_{13}H_{11}N_3O_3S$ (289.31); C, 53.97; H, 3.83; N, 14.52. Found: C, 53.88; H, 3.76; N, 14.43%.

3-(2-Furoyl)-1,2,4-triazoline-5-thione (6a). 84% yield; colorless crystals; mp >300°C (acetic acid); IR (KBr) ν: 3283, 3118, 1670, 1170 cm^{-1}; ^1H NMR (DMSO-d_6) δ 6.77 (d, $J = 1.8$ Hz, 1H), 7.90 (d, $J = 3.6$ Hz, 1H), 8.10 (s, 1H), 11.99 (br.s, 1H), 14.00 (br.s, 1H); Anal. Calcd for $C_6H_5N_3OS$ (167.19); C, 43.10; H, 3.01; N, 25.13. Found; C, 42.93; H, 2.86; N, 24.79%.

2-Phenyl-3-(2-furayl)-1,2,4-triazoline-5-thione (6b). 84% yield; colorless crystals; mp 232–233°C (toluene); IR (KBr) ν: 3106, 1635, 1171 cm^{-1}; ^1H NMR (DMSO-d_6) δ: 6.65 (d, $J = 1.8$ Hz, 1H), 7.54 (d, $J = 2.6$ Hz, 3H,), 7.82 (d, $J = 3.6$ Hz, 1H), 7.91 (dd, $J = 2.0$, $J = 3.3$ Hz, 2H), 8.04 (s, 1H), 9.87 (br.s, 1H); MS m/z (%) 243 ($M^{+\cdot}$, 55), 245 ($M^{+\cdot}+2$, 4), 244 ($M^{+\cdot}+1$, 11), 242 (100), 91 (72), 90 (77). Anal. Calcd for $C_{12}H_9N_3OS$ (243.28); C, 59.24; H, 3.73; N, 17.27. Found; C, 59.19; H, 3.64; N, 17.19%.

2-(2-Furoylimino)-3-phenyl-5,5-dimethyl-1,3,4-thiadiazolidine (7). 78% yield; mp 176–177°C ethyl alcohol; IR (KBr) ν: 3186, 2974, 1614, 1560 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.95 (s, 6H), 4.3 (br.s, 1H), 6.49 (dd, $J = 1.8$, 2.7 Hz, 1H), 7.20 (d, $J = 3.6$ Hz, 1H), 7.24–7.32 (m, 1H), 7.47 (t, $J = 7.4$, 8.3, Hz, 2H), 7.59 (s, 1H), 7.84 (d, $J = 7.8$ 2H); Anal. Calcd for $C_{15}H_{15}N_3O_2S$ (301.36) C, 59.78; H, 5.02; N, 13.94. Found: C, 59.31; H, 4.83; N, 13.44; S, 10.32%.

3-(2-Furoylamido)-3*H*-4*H*-1,2,4-triazolin-5-thione (9). 89% yield; colorless crystals; mp 298–300°C (acetic acid); IR (KBr) ν: 3392, 3270, 3130 (NH), 1695, 1613, 1282 cm^{-1}; ^1H NMR (DMSO-d_6) δ 2.9 (br. s, 1H), 6.45–6.85 (m, 1H), 7.77–7.83 (m, 1H), 8.10 (s, 1H), 9.7 (br.s, 1H); 12.7, (br.s, 1H); MS (70 eV) *m/z* (%): 210 ($M^{+\cdot}$, 5), 182 (11), 116 (8), 95 (100); Anal. Calcd for $C_7H_6N_4O_2S$ (210.21); C, 40.00; H, 2.88; N, 26.65. Found: C, 39.83; H, 2.75; N, 26.59%.

2-(3-Furan-2-carbonylthioureido)benzoic acid (12). 82% yield; colorless crystals; mp 173°C with decomposition, (ethanol); IR (KBr) ν: 3290, br.3170–2400, 1690, 1650, 1150 cm^{-1}; ^1H NMR (DMSO-d_6) δ 6.73 (s, 1H), 7.55–7.84 (m, 4H), 7.92 (d, $J = 3.6$ Hz, 1H), 8.09 (s, 1H), 11.99 (br.s, 1H), 12.79 (br.s, 1H), 13.52 (br.s, 1H); MS (70 eV) *m/z* (%): 290 ($M^{+\cdot}$, 10), 291 (, $M^{+\cdot}+1$, 2), 262 (4), 245 (6), 95 (100); Anal. Calcd for $C_{13}H_{10}N_2O_4S$ (290.29); C, 53.79; H, 3.47; N, 9.65. Found: C, 53.47; H, 3.25; N, 9.51%.

***N*-(Benzo[d]thiazol-2-yl)furan-2-carboxamide (16a).** 65% yield; colorless crystals, mp 188–190°C (petroleum ether bp 60–80°C); IR (KBr) ν: 3314, 1656, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 6.63 (s, 1H), 7.37–7.56 (m, 4H), 7.68 (d, $J = 8.1$ Hz, 1H), 7.87 (d, $J = 7.8$ Hz, 1H), 11.77 (br.s, 1H); MS (70 eV) *m/z* (%): 244 ($M^{+\cdot}$, 23), 245 ($M^{+\cdot}+1$, 6), 246 ($M^{+\cdot}+2$, 2), 216 (47), 95 (100); Anal. Calcd for $C_{12}H_8N_2O_2S$ (244.27); C, 59.00; H, 3.30; N, 11.47. Found: C, 58.96; H, 3.15; N, 11.39%.

***N*-(Benzo[d]oxazol-2-yl)furan-2-carboxamide (16b).** 62% yield; colorless crystals, mp 135–137°C (petroleum ether b.p 60–80°C); IR (KBr) ν: 3350, 1677, 1620

cm^{-1}; ^1H NMR (DMSO-d_6) δ 6.61 (s, 2H), 7.11 (d, $J = 3.2$ Hz, 2H), 7.37 (br.s, 1H), 7.77–7.81 (m, 3H); MS (70 eV) *m/z* (%): 228 ($M^{+\cdot}$, 61), 229 ($M^{+\cdot}$+1, 10), 227 ($M^{+\cdot}$-1, 4), 118 (7), 110 (9), 109 (15), 95 (100); Anal. Calcd. $C_{12}H_8N_2O_3$ (228.20) C, 63.16; H, 3.53; N, 12.28. Found: C, 62.68; H, 3.22; N, 11.95%.

***N*-(1H-Benzo[d]imidazol-2-yl)furan-2-carboxamide (16c).** 68% yield; colorless crystals, mp 144–146°C (ethanol); IR (KBr) ν: 3300, 3195, 1671, 1622 cm^{-1}; ^1H NMR (DMSO-d_6) δ: 6.61 (d, $J = 6.4$ Hz, 1H), 6.71–6.79 (m, 2H), 6.97–7.05 (m, 1H), 7.28 (d, $J = 6.8$ Hz, 1H), 7.83 (d, $J = 3.0$ Hz, 1H), 8.05 (d, $J = 1.0$ Hz, 1H), 11.14 (br.s, 1H), 11.70, (br.s, 1H); MS (70 eV) *m/z* (%): 227 ($M^{+\cdot}$, 51), 228 ($M^{+\cdot}$+1, 8), 117 (11), 95 (100); Anal. Calcd for $C_{12}H_9N_3O_2$ (227.22); C, 63.43; H, 3.99; N, 18.49. Found: C, 63.18; H, 3.78; N, 18.33%.

Carboxymethyl N-(2-Furoyl)dithiocarbamate (18a). 79% yield; yellow crystals, mp 171°C with decomposition, (ethanol); IR (KBr) ν: 3350, (br.) 3200–2400, 1710, 1670, 1090 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 4.10 (s, 2H), 5.28 (br.s 1H), 6.75–6.77 (m, 1H), 7.84 (d, $J = 3.6$ Hz, 1H), 8.01 (s, 1H), 12.68 (br.s 1H); Anal. Calcd for $C_8H_7NO_4S_2$ (245.28); C, 39.17; H, 2.88; N, 5.71. Found: C, 38.89; H, 2.71; N, 5.55%.

2-Hydroxyethyl N-(2-Furoyl)dithiocarbamate (18b). 77% yield; yellow crystals; mp 130–132°C (petroleum ether bp 60–80°C); IR (KBr) ν: 3492, 3134, 1673, 1205 cm^{-1}; ^1H NMR (DMSO-d_6) δ: 3.34–3.39 (m, 2H), 3.69–3.74 (m, 2H), 5.04 (br. s, 1H), 6.75 (s, 1H), 7.81 (s, 1H), 8.07 (s, 1H), 12.45 (br.s, 1H); MS (70 eV) *m/z* (%): 231 ($M^{+\cdot}$, 1), 214 (5), 213 (17) 187 (8), 154 (100), 95 (14); Anal. Calcd for $C_8H_9NO_3S_2$ (231.29); C, 41.54; H, 3.92; N, 6.05. Found: C, 41.36; H, 3.78; N, 5.87%.

Ethyl-2-(3-furan-2-carbonylthioureido)acetate (18c). 91% yield; colorless crystals, mp 100–102 (ethanol); IR (KBr) ν: 3292, 3206, 1750, 1676, 1286 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 1.34 (t, $J = 7.1$ Hz, 3H), 4.30 (q, $J = 7.2$ Hz, 2H), 4.7 (d, $J = 4.8$ Hz, 2H), 6.62–6.65 (m, 1H), 7.38 (d, $J = 3.6$ Hz, 1H,), 7.61 (s, 1H), 9.24 (br.s, 1H), 11.43 (br.s, 1H); MS (70 eV) *m/z* (%): 256 ($M^{+\cdot}$, 17), 257 (M^{+}.+1, 4), 228 (15), 227 (2), 210 (5), 95 (100); Anal. Calcd for $C_{10}H_{12}N_2O_4S$ (256.28); C, 46.87; H, 4.72; N, 10.93. Found: C, 46.75; H, 4.68; N, 10.70%.

Formation of Compounds 8, 10, 13, 19a,b

The solution of corresponding compounds **7**, **9**, **12**, and **18a**,**b** (0.01 mol) in acetic anhydride was refluxed for 1–2 h (TLC) on a water bath, then left to cool at room temperature. The precipitated solid obtained after addition of ice cold water was filtered off and recrystallized from a suitable solvent.

2-(2-Furoylimino)-3-phenyl-4-acetyl-5,5-dimethyl-1,3,4-thiadiazolidine (8). 79% yield; mp 122–123°C (ethyl alcohol); IR (KBr) ν: 1694, 1666, 1630, cm^{-1}; ^1H NMR ($CDCl_3$) δ: 1.89 (s, 3H) 1.96 (s, 6H), 6.56 (dd, $J = 1.8$, 1.9 Hz, 1 H), 7.23 (d, $J =$ 3.7 Hz, 1H,), 7.28–7.35 (m, 1H), 7.51 (t, $J = 7.7$ Hz, 2H), 7.61 (s, 1H), 7.91 (d, $J = 7.3$ Hz, 2H,); Anal. Calcd for $C_{17}H_{17}N_3O_3S$ (343.30) C, 59.46; H, 4.99; N, 12.24. Found: C, 59.39; H, 4.95; N, 12.18%.

1-Acetyl-3-(2-fourylamido)-3*H*-4*H*-1,2,4-triazolin-5-thione (10). 89% yield; colorless crystals; mp 347–350°C (DMF); IR (KBr) ν: 3225, 3132, 1709, 1690, 1650, 1582 cm^{-1}; ^1H NMR (DMSO-d_6) δ 2.2 (s, 3H), 6.71–6.75 (m, 1H), 7.61–7.67 (m, 1H), 8.01 (s, 1H), 12.2 (br.s, 1H), 12.7, (br.s, 1H); MS (70 eV) *m/z* (%): 252 ($M^{+\cdot}$, 11),

210 (28), 224 (25), 158 (4), 95 (100); Anal. Calcd for $C_9H_8N_4O_3S$ (252.25*);* C, 42.85; H, 3.20; N, 22.21. Found: C, 42.77; H, 3.16; N, 22.19%.

3-(Furan-2-carbonyl)-2-thioxo-2,3-dihydroquinazolin-4(1H)-one (13). 77% yield; colorless crystals, mp 189–190°C (ethanol); IR (KBr) ν: 3220, 1690, 1635, 1190 cm^{-1}; ^1H NMR (DMSO-d_6) δ 6.75–6.79 (m, 1H), 7.54 (t, $J = 7.0$ Hz, 1H), 7.69–7.77 (m, 2H), 7.90 (t, $J = 6.8$ Hz, 1H), 8.04 (d, $J = 5.0$ Hz, 1H), 8.10 (d, $J = 5.4$ Hz, 1H), 12.34 (br.s, 1H); MS (70 eV) *m/z* (%): 272 ($M^{+\cdot}$, 24), 274 ($M^{+\cdot}+2$, 3), 273 ($M^{+\cdot}+1$, 10), 244 (100), 162 (18), 95 (80); Anal. Calcd for $C_{13}H_8N_2O_3S$ (272.28) C, 57.35; H, 2.96; N, 10.29. Found: C, 57.10; H, 2.78; N, 10.05%.

3-(Furan-2-carbonyl)-2-thioxo thiazolidin-4-one (19a). 60% yield; yellow crystals; mp 115–117°C (petroleum ether bp 60–80°C); IR (KBr) ν: 1780, 1720, 1205 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 4.22 (s, 2H), 6.65 (s, 1H), 7.82–7.84 (m, 1H), 8.08 (s, 1H); MS (70 eV) *m/z* (%): 227 ($M^{+\cdot}$, 14), 228 ($M^{+\cdot}+1$, 2), 199 (40), 95 (100); Anal. Calcd for $C_8H_5NO_3S_2$ (227.26) C, 42.28; H, 2.22; N, 6.16. Found: C, 41.95; H, 2.05; N, 5.93%.

3-(Furan-2-carbonyl)-2-thioxo thiazolidine (19b). 50% yield; yellow crystals; mp 76–78°C (petroleum ether bp 60–80°C); IR (KBr) ν: 2928, 1638, 1286 cm^{-1}; ^1H NMR (DMSO-d_6) δ: 3.78–4.39 (m, 4H), 6.73 (s, 1H), 7.83 (s, 1H), 8.05 (s, 1H); MS (70 eV) *m/z* (%):213($M^{+\cdot}$, 39), 215 ($M^{+\cdot}+2$, 4), 214 ($M^{+\cdot}+1$, 9), 185 (5), 95 (100); Anal. Calcd for $C_8H_7NO_2S_2$ (213.28) C, 45.05; H, 3.31; N, 6.57. Found: C, 44.83; H, 3.19; N, 6.44%.

3-Phenyl-4-(2-furoyl)-1*H*-1,2,4-triazoline-5-thione (4)

A solution of compound **3** (0.01 mol) in glacial acetic acid (30 mL) was added to polyphosphoric acid (20 mL). The reaction mixture was heated at 150–180°C for 1 h, then left to cool at room temperature. The precipitated solid obtained after addition of ice cold water was filtered off and recrystallized from acetic acid; 75% yield; colorless crystals; mp 261–263°C; IR (KBr) ν: 3134, 3102, 1674, 1537, 1173 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 6.61 (d, $J = 1.8$ Hz, 1H,), 7.51 (d, $J = 2.4$ Hz, 3H,), 7.62 (d, $J = 3.6$ Hz, 1H), 7.69 (s, 1H), 7.96 (dd, $J = 2.1$, $J = 3.3$ Hz, 2H), 10.65 (br.s, 1H); MS (70 eV) *m/z* (%): 271 ($M^{+\cdot}$, 7), 272 ($M^{+\cdot}+1$, 1), 242 (26),175 (3), 95 (89), 94 (100), 77 (15); Anal. Calcd. for $C_{13}H_9N_3O_2S$ (271.29) C, 57.55; H, 3.34; N, 15.49. Found: C, 57.48; H, 3.26; N, 15.44%.

3-(Furan-2-carbonyl)-2-thioxoimidazolidin-4-one (19c)

A solution of **18c** (0.01 mol) in glacial acetic acid (30 mL) and ammonium acetate (0.5 g) was refluxed for 2h, then left to cool at room temperature. The precipitated solid obtained after addition of ice cold water was filtered off and recrystallized from petroleum ether, bp 60–80°C; 76% yield; colorless crystals, mp 82–84°C IR (KBr) ν: 3182, 1666, 1272 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 4.3 (s, 2H), 6.63 (s, 1H), 7.32 (d, $J = 3.4$ Hz, 1H,), 8.01 (s, 1H), 10.43 (br.s, 1H); MS (70 eV) *m/z* (%): 210 ($M^{+\cdot}$, 11), 211($M^{+\cdot}+1$, 2), 182 (15), 95 (100); Anal. Calcd for $C_8H_6N_2O_3S$ (210.01) C, 45.71; H, 2.88; N, 13.33. Found: C, 45.35; H, 2.64; N, 13.09%.

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