Synthesis and Biological Activity of 3-(2-Furanyl)-6-Aryl-1,2,4-Triazolo[3,4-b]-1,3,4-Thiadiazoles

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Abstract: 3-(2-Furanyl)-4-amino-5-mercapto-1,2,4-triazole (1) was prepared from 2-furoic acid through a multi-step reaction sequence. Compound 1 reacted with aromatic acids in the presence of phosphorus oxychloride to give 3-(2-furanyl)-6-aryl-1,2,4-triazolo[3,4-b]-1,3,4-thiadiazoles (2). The structures of all the newly synthesized compounds have been confirmed by elemental analysis, IR, 1H-NMR, 13C-NMR and mass spectra. The bioassay indicated most of the title compounds possess significant growth promoting effects on mung bean radicles.

Keywords: Furan ring; triazolothiadiazoles; synthesis; spectral characterization; biological activity

Introduction

Various substituted 1,2,4-triazolo[3,4-b]-1,3,4–thiadiazoles are associated with diverse pharmacological activities, such as antimicrobial, bactericidal, antiinflammatory, antiviral, antihypertensive, anthelmintic and analgesic effects [1-3]. Prompted by these observations and as a continuation of our work on the synthesis of biologically active nitrogen and sulfur containing heterocycles, we report herein the reaction of aromatic acids with 3-furoyl-4-amino-5-mercapto-1,2,4-triazole in the presence of phosphoryl chloride to give 3-(2-furanyl)-6-aryl-
1,2,4-triazolo-[3,4-b]-1,3,4-thiadiazoles. The structures of all the synthesized compounds were confirmed by elemental analysis, IR, $^1$H-NMR, $^{13}$C-NMR, and mass spectral data. The bioassay indicated most of the title compounds possess significant growth promoting effects on mung bean ($Vigna radiata$) radicles, giving up to 40% increases in growth in the case of some compounds.

Results And Discussion

Synthetic route and improvement of synthetic methods

The synthetic route used is shown in Scheme 1. 2-Furoic hydrazide is a needle-like crystalline compound, but often exists in form liquid when prepared according to literature methods. Sometimes the crystals only appear after standing for up to three months. The liquid form of 2-furoic hydrazide was reacted with carbon disulphide and potassium hydroxide in ethanol, successfully giving potassium furoic hydrazide dithioformate.

Scheme 1. The synthetic route to the title compounds

After the ring-closure of compound 1 with aromatic acids in the presence of phosphorus oxychloride, the literature procedure calls for the removal of excess phosphorus oxychloride under reduced pressure, but this can result in damage to the rotatory evaporator and vacuum pump due to the strong acidity and high boiling point of phosphorus oxychloride. An improvement was made in our
experiments, in that the reaction mixture was gradually poured onto crushed ice with stirring, some solid potassium carbonate and then the appropriate amount of solid potassium hydroxide was added till the pH value was 8. The separated solid after standing overnight was filtered and thoroughly washed with cold water. Little product is lost because of its insolubility in water. This is a simple and convenient method of removing excess phosphorus oxychloride.

IR spectra of the title compounds

In the IR spectrum of compound 1 there are absorption bands at 3335, 3269 cm\(^{-1}\) due to the N-H stretching vibration, 1634, 1523, 1494, 1467, 1420 cm\(^{-1}\) due to furan and triazole ring skeleton vibrations, and 1109 cm\(^{-1}\) due to the C-O-C stretching vibration of the furan ring. Of course, the bands at 3335, 3269 cm\(^{-1}\) had disappeared in the IR spectra of compounds 2a-r. Furthermore, the strongest band in the IR of compound 1 is at 1457 cm\(^{-1}\), while in the IR of compounds 2a-r it appears at around 1470 cm\(^{-1}\). The peaks at 1634 and 1109 cm\(^{-1}\) are also shifted to 1620 and 1125 cm\(^{-1}\), respectively. The C-S-C bending vibration bands of compounds 2a-r are observed around 700 cm\(^{-1}\).

\(^1\)H-NMR spectra of the title compounds

The signals of the three furan ring hydrogens of 1 appear at \(\delta\) 7.91, 6.70 and 7.36 ppm, attributed to H-5, H-4 and H-3, respectively. In the \(^1\)H-NMR spectra of the title compounds, the \(\delta\) values of the 5-position hydrogens are noted to have shifted to 7.98-8.19, decreasing in the order of Ar = 2-HOC\(_6\)H\(_4\) > 2-ClC\(_6\)H\(_4\) > 1-naphthylmethyl > 3-ClC\(_6\)H\(_4\) > 2-furanyl > 2-NO\(_2\)C\(_6\)H\(_4\)CH\(_2\) > C\(_6\)H\(_5\) > 3,5-(NO\(_2\))\(_2\)C\(_6\)H\(_3\) > 4-NO\(_2\)C\(_6\)H\(_4\) > 3-pyridinyl > 2-CH\(_3\)OC\(_6\)H\(_4\) > 2,4-Cl\(_2\)C\(_6\)H\(_3\)OCH\(_2\) > 4-NH\(_2\)C\(_6\)H\(_4\) > C\(_6\)H\(_5\)CH\(_2\) > C\(_6\)H\(_5\)OCH\(_2\) > 2-NH\(_2\)C\(_6\)H\(_4\) > 4-CH\(_3\)OC\(_6\)H\(_4\) and 2-quinolyl (where Ar is the substituent group at the 6 position of the triazolothiadiazoles). Moreover, the \(\delta\) values of the 4-position hydrogens have increased to 6.71-6.85. Only the \(\delta\) values of the 3-position hydrogens do not show a similar trend, as they go both up and down, varying between 7.21-7.58. When an active methylene group is attached to the 6 position of the triazolothiadiazoles, the \(\delta\) values of the benzyl, o-nitrobenzyl and 1-naphthylmethyl methylene hydrogen is 4.50, 4.82 and 4.98 respectively, while the corresponding \(\delta\) values of the phenoxymethyl and 2,4-dichlorophenoxyethyl methylene hydrogen are 5.59 and 5.71, respectively.

\(^13\)C-NMR spectra of the title compounds

The \(\delta\) values of the C-2 and C-3 carbons of the furan are 142.6 and 109.6, respectively. In the \(^13\)C-NMR spectrum of the intermediate compound 1, there are peaks at 142.84, 139.91, 113.99 and 111.89 ppm, which can be attributed to 2, 5, 4 and 3 position carbons of the furan ring, respectively; the two triazole carbons have \(\delta\) values of 166.56 and 145.22. In the \(^13\)C-NMR spectra of the title compounds, the C-4 and C-3 carbons still have \(\delta\) values at 111 and 112 or so, while the chemical shifts of the C-2 and C-5 carbons vary between 135 and 145. When an active methylene group is attached to 6 position of the triazolothiadiazoles, the \(\delta\) values of benzyl and 1-naphthylmethyl methylene carbons are 37.30 and 34.95 respectively, which is different from the quantitative order seen in the \(^1\)H-NMR.
Mass spectra

All the title compounds display molecular ion peaks. In the mass spectrum of a representative compound such as 2r the molecular ion peak is also the base peak. This is probably because both substituted benzene and furan ring form a well conjugated system with the triazolothiadiazole, which makes the molecular ion especially stable. The peak at m/z 151, i.e. 3-(2-furyl)-4-amino-1,2,4-triazole, is very strong, its intensity being second only to the base peak.

Biological Activity

The effect of the title compounds on sprouting of mung bean seeds has been investigated. After treating with culture solution of 10.0µgL⁻³ of the title compounds for 48 hours, the lengths of mung bean radicles with reference of distilled water, the growth promoting percentage has been calculated. The data of biological activity test are presented in Table 1. From the data it can be seen that 2h, 2l, 2o increase mung bean sprout growth by 40% at 10⁻³ g L⁻³. Even those compounds which inhibit mung bean sprout growth at 10⁻³ g L⁻³ can show promoting effect at lower concentrations.

Table 1. Effect of the title compounds on mung bean radicle growth

| Compd. | Length of mung bean radicles (cm) | Growth promotion (%) |
|--------|-----------------------------------|----------------------|
| 2a     | 2.45                              | 1.87                 |
| 2b     | 3.34                              | 38.88                |
| 2c     | 1.26                              | -49.27               |
| 2d     | 2.485                             | 3.33                 |
| 2e     | 2.35                              | -2.29                |
| 2f     | 3.08                              | 28.07                |
| 2g     | 2.52                              | 4.78                 |
| 2h     | 3.41                              | 41.79                |
| 2i     | 2.64                              | 9.77                 |
| 2j     | 3.005                             | 24.95                |
| 2k     | 0.73                              | 30.35                |
| 2l     | 3.40                              | 41.37                |
| 2m     | 2.38                              | -6.17                |
| 2n     | 2.445                             | 1.66                 |
| 2o     | 3.40                              | 41.37                |
| 2p     | 2.79                              | 16.01                |
| 2q     | 2.01                              | -16.42               |
| 2r     | 2.26                              | -6.3                 |
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Experimental

General

All melting points were determined on an XT-4A apparatus and are uncorrected. The IR spectra (KBr disks) were taken on a Bruker Quinox 55 spectrophotometer. The $^1$H-NMR and $^{13}$C-NMR spectra were measured on a Bruker Advance 300 spectrometer for DMSO-d$_6$ solutions using TMS as internal reference. The mass spectra were recorded on an HP 5988 spectrometer. Elemental analyses were carried out with a CE 1112 elemental analyzer. All the reagents used were AR grade.

Preparation of 3-(2-furyl)-4-amino-5-mercapto-1,2,4-triazole (1).

Ethyl 2-furoate [4], was treated with 85% NH$_2$NH$_2$·H$_2$O. Reaction with CS$_2$ and KOH in ethanol gave potassium 2-furoic hydrazide dithioformate [5]. The salt underwent ring-closure in 85% hydrazine monohydrate, giving 3-(2-furyl)-4-amino-5-mercapto-1,2,4-triazole (1), which was recrystallized from absolute ethanol: $^1$H-NMR $\delta$: 13.89 (s, 1H, SH), 7.91 (d, 1H), 7.36 (d, 1H), 6.70 (q, 1H), 5.80 (s, 2H, NH$_2$); $^{13}$C-NMR $\delta$: 166.56, 145.22, 142.84, 139.91, 113.99, 111.89.

General method for the preparation of 3-(2-furanyl)-6-aryl-1,2,4-triazolo[3,4-b]-1,3,4-thiadiazoles (2a–r).

A mixture of 1 (5.0mmol) and an aromatic acid (5.5mmol) in POCl$_3$ (20mL) was refluxed for 7hr. The reaction mixture was gradually poured onto crushed ice with stirring. Some solid K$_2$CO$_3$ was added to the mixture with stirring, then an appropriate amount of solid KOH was added till the pH value was 8. The solid which separated after standing overnight was filtered, washed with cold water, dried, and recrystallized from absolute alcohol to afford the title compounds 2a–r. The physical and spectral data of the title compounds are as follows:

3-(2-furanyl)-6-(4-aminophenyl)-1,2,4-triazolo[3,4-b]-1,3,4-thiadiazole (2a): Yield 48 %; M.p. 229-231°C; IR v/cm$^{-1}$: 3422, 3220 (N-H), 1603 (C=N), 1518, 1496, 1470 (aromatic skeleton), 1226 (N-N=C), 988, 952, 903, 841,739 (Ar-H bending vibration), 699 (C-S-C); $^1$H-NMR $\delta$: 8.00, 6.78, 7.34 (3H, furan H), 6.69, 7.68 (4H,dd, J=8.7Hz, Ar-H); $^{13}$C-NMR $\delta$: 167.80, 153.72, 145.25, 140.39, 139.10, 129.04, 128.04, 115.12, 113.72, 112.18, 111.56; MS (m/z, %): 283 (M$^+$, 72.23), 136 (100), 118 (54.09), 109 (37.86), 93 (31.77), 91 (22.78), 83 (15.41), 79 (11.59), 77 (6.80), 51 (19.23), 39 (22.78). Calcd. for C$_{13}$H$_9$N$_5$OS (%): C 55.11, H 3.20, N 24.73; Found (%): C 54.87, H 3.22 , N 24.51.
3-(2-furanyl)-6-(3-pyridyl)-1,2,4-triazolo[3,4-b]-1,3,4-thiadiazole (2b): Yield 57 %; Mp. 189-191°C; IR (KBr) ν/cm⁻¹: 3128, 3063 (Ar-H), 1588, 1574, 1517, 1473, 1459 (aromatic skeleton) 1249 (N-N=C), 1224 (furan C-O-C), 989, 960, 904, 885, 809, 739 (Ar-H bending vibration), 700 (C-S-C); ¹H-NMR δ: 8.02, 6.80, 7.44 (3H, furan H), 9.23, 8.83, 8.43, 7.68 (4H, pyridine H), ¹³C-NMR δ: 164.99, 153.62, 153.43, 147.88, 145.57, 140.00, 139.45, 135.17, 125.54, 124.59, 112.31, 112.13; MS (m/z, %): 269 (M⁺, 100), 137 (11.09), 122 (66.52), 109 (70.65), 93 (52.69), 78 (12.90), 77 (17.61), 65 (20.96), 51 (35.28), 39 (18.84). Calcd. for C₁₂H₇N₅OS (%): C 53.52, H 2.62, N 26.01; Found (%): C 53.33, H 2.59, N 26.24.

3-(2-furanyl)-6-(1-naphthylmethyl)-1,2,4-triazolo[3,4-b]-1,3,4-thiadiazole (2c): Yield 64 %; Mp. 146-148°C; IR (KBr) ν/cm⁻¹: 3128, 3063 (Ar-H), 1626 (C=N), 1598, 1517, 1473, 1427 (aromatic skeleton), 1262 (N-N=C), 1226 (furan C-O-C), 989, 960, 904, 885, 799, 756, 737 (Ar-H bending vibration), 700 (C-S-C); ¹H-NMR δ: 8.13, 6.77, 7.54 (3H, furan H), 7.18-8.00 (7H, m, naphthalene H), 4.98 (2H, s, CH₂); ¹³C-NMR δ: 171.50, 153.96, 145.43, 140.21, 138.95, 133.69, 131.41, 128.89, 126.96, 126.33, 125.87, 125.63, 123.76, 112.21, 111.51, 34.95; MS (m/z, %): 332 (M⁺, 98.94), 185 (3.65), 167 (40.18), 166 (53.24), 152 (30.31), 141 (78.44), 137 (20.09), 115 (32.29), 109 (100), 93 (46.53), 83 (13.49), 65 (14.72), 63 (24.02), 51 (18.48), 39 (15.87). Calcd. for C₁₈H₁₂N₄OS (%): C 65.04, H 3.64, N 16.86; Found (%): C 64.81, H 3.60, N 16.99.

3-(2-furanyl)-6-(3,5-dinitrophenyl)-1,2,4-triazolo[3,4-b]-1,3,4-thiadiazole (2d): Yield 55 %; Mp. 290-292°C; IR (KBr) ν/cm⁻¹: 3136, 3059 (Ar-H), 1628 (C=N), 1595, 1551, 1519, 1477, 1456, 1425 (aromatic skeleton), 1252 (N-N=C), 1224 (furan C-O-C), 981, 916, 903, 886, 799, 756, 737 (Ar-H bending vibration), 696 (C-S-C); ¹H-NMR δ: 8.06, 6.83, 7.47 (3H, furan H), 9.06 (2H, s, Ar-H), 9.02 (1H, s, Ar-H); ¹³C-NMR δ: 163.86, 154.00, 148.87, 145.76, 139.86, 139.62, 131.73, 127.57, 121.84, 112.41, 112.39; MS (m/z, %): 358 (M⁺, 64.41), 266 (11.32), 211 (13.03), 165 (16.64), 137 (17.82), 119 (23.84), 111 (15.60), 109 (100), 93 (21.46), 75 (24.95), 57 (50.33), 43 (38.35). Calcd. for C₁₃H₆N₆O₅S (%): C 43.58, H 1.69, N 23.46; Found (%): C 43.23, H 1.60, N 23.66.

3-(2-furanyl)-6-benzyl-1,2,4-triazolo[3,4-b]-1,3,4-thiadiazole (2e): Yield 62 %; Mp. 111-113°C; IR (KBr) ν/cm⁻¹: 3133, 3061, 3029 (Ar-H), 1625 (C=N), 1536, 1518, 1495, 1456, 1425 (aromatic skeleton), 1265 (N-N=C), 1224 (furan C-O-C), 705 (C-S-C); ¹H-NMR δ: 8.00, 6.76, 7.21 (3H, furan H), 7.31-7.44 (5H, m, Ar-H), 4.50 (2H, s, CH₂); ¹³C-NMR δ: 171.16, 154.00, 148.87, 145.76, 139.86, 139.62, 131.73, 127.57, 121.84, 112.41, 112.39; MS (m/z, %): 282 (M⁺, 55.07), 137 (23.84), 119 (23.84), 111 (15.60), 109 (100), 93 (21.46), 75 (24.95), 57 (50.33), 43 (38.35). Calcd. for C₁₄H₁₀N₄OS (%): C 59.56, H 3.57, N 19.85; Found (%): C 59.28, H 3.65, N 20.07.

3-(2-furanyl)-6-(3-chlorophenyl)-1,2,4-triazolo[3,4-b]-1,3,4-thiadiazole (2f): Yield 66 %; M.p. 207-209°C; IR (KBr) ν/cm⁻¹: 3108, 3066 (Ar-H), 1626 (C=N), 1573, 1518, 1478, 1474, 1459, 1423 (aromatic skeleton), 1266 (N-N=C), 1226 (furan C-O-C), 694 (C-S-C); ¹H-NMR δ: 8.13, 6.80, 7.45 (3H, furan H), 7.65-8.03 (4H, m, Ar-H); ¹³C-NMR δ: 165.89, 153.56, 145.56, 140.01, 139.48, 134.52, 132.84, 131.69, 130.95, 126.75, 126.34, 112.31, 112.17; MS (m/z, %): 304 (M⁺+2, 24.00), 303
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(M⁺+1, 10.76), 302 (M⁺, 65.31), 160 (1.43), 158 (3.76), 157 (22.49), 155 (63.07), 139 (11.46), 137 (32.33), 109 (100), 93 (66.16), 75 (29.66), 65 (27.80), 51 (39.10), 39 (29.85); Calcd. for C₁₃H₇ClN₄OS (%): C 51.57, H 2.33, N 18.51; Found (%): C 51.84, H 2.40, N 18.27.

3-(2-furanyl)-6-(2-nitrophenylmethyl)-1,2,4-triazolo[3,4-b]-1,3,4-thiadiazole (2g): Yield 59 %; M.p.187-189°C; IR (KBr) ν/cm⁻¹: 3128 (Ar-H), 1620 (C=N), 1578, 1524, 1461, 1428 (aromatic skeleton), 1262 (N=N=C), 1225 (furan C-O-C), 695 (C-S-C); ¹H-NMR δ: 8.09, 6.74, 7.34 (3H, furan H), 6.84-8.15 (4H, m, Ar-H), 4.82 (2H, s, CH₂); MS (m/z, %): 327 (M⁺, 34.73), 282 (41.91), 137 (21.79), 135 (33.08), 119 (10.19), 109 (100), 77 (25.59), 64 (84.11), 51 (44.52), 39 (49.63); Calcd. for C₁₄H₉N₅O₃S (%): C 51.37, H 2.77, N 21.40; Found (%): C 51.66, H 2.74, N 21.16.

3-2-furanyl-6-(2-chlorophenyl)-1,2,4-triazolo[3,4-b]-1,3,4-thiadiazole (2h): Yield 54 %; M.p.169-171°C; IR (KBr) ν/cm⁻¹: 3130, 3073, 3013 (Ar-H), 1628 (C=N), 1592, 1517, 1454, 1427 (aromatic skeleton), 1277 (N=N=C), 1227 (furan C-O-C), 695 (C-S-C); ¹H-NMR δ: 8.14, 6.79, 7.34 (3H, furan H), 7.71-8.02 (4H, m, Ar-H); MS (m/z, %): 304 (M⁺+2, 23.52), 303 (M⁺+1, 10.71), 302 (M⁺, 60.98), 160 (1.17), 158 (3.13), 157 (18.19), 155 (49.15), 137 (27.81), 109 (100), 93 (59.72), 75 (22.51), 64 (41.34), 51 (30.21), 39 (20.59); Calcd. for C₁₃H₇ClN₄OS (%): C 51.57, H 2.33, N 18.51; Found (%): C 51.33, H 2.40, N 18.23.

3-(2-furanyl)-6-(2-hydroxyphenyl)-1,2,4-triazolo[3,4-b]-1,3,4-thiadiazole (2i): Yield 49 %; M.p.273-275°C; IR (KBr) ν/cm⁻¹: 3423 (O-H), 3126, 3070 (Ar-H), 1602 (C=N), 1519, 1477, 1460, 1425 (aromatic skeleton), 1254 (N=N=C), 1224 (furan C-O-C), 699 (C-S-C); ¹H-NMR δ: 11.70 (1H, s, OH), 8.19, 6.79, 7.39 (3H, furan H), 7.01-8.00 (4H, m, Ar-H); ¹³C-NMR δ: 163.44, 156.50, 155.16, 145.23, 140.49, 138.72, 127.69, 120.43, 117.03, 115.55, 112.23, 112.07, 111.53; MS (m/z, %): 284 (M⁺, 93.85), 137 (100), 119 (15.97), 109 (94.61), 93 (61.71), 77 (14.55), 64 (89.09), 51 (34.40), 39 (44.46); Calcd. for C₁₃H₈N₄O₂S (%): C 54.92, H 2.84, N 19.71; Found (%): C 54.68, H 2.91, N 19.98.

3,6-di(2-furanyl)-1,2,4-triazolo[3,4-b]-1,3,4-thiadiazole (2j): Yield 55 %; M.p. 204-206°C; IR (KBr) ν/cm⁻¹: 3120, 3092 (Ar-H), 1623 (C=N), 1593, 1520, 1508, 1481, 1445, 1429 (aromatic skeleton), 1254 (N=N=C), 1224 (furan C-O-C), 990, 960, 904, 886, 818, 754 (Ar-H bending vibration), 699 (C-S-C); ¹H-NMR δ: 8.12, 8.01, 7.58, 7.28, 6.85, 6.79 (6H, m, furan H); ¹³C-NMR δ: 157.05, 153.03, 147.94, 145.50, 143.07, 140.12, 139.45, 115.38, 113.54, 112.24, 111.78; Calcd. for C₁₁H₆N₄O₂S (%): C 51.15, H 2.34, N 21.70; Found (%): C 51.26, H 2.44, N 21.51.

3-(2-furanyl)-6-phenyloxymethyl-1,2,4-triazolo[3,4-b]-1,3,4-thiadiazole (2k): Yield 62 %; M.p.115-117°C; IR (KBr) ν/cm⁻¹: 3115, 3070 (Ar-H), 1624 (C=N), 1589, 1519, 1496, 1475, 1452, 1427 (aromatic skeleton), 1243 (N=N=C), 692 (C-S-C); ¹H-NMR δ: 8.00, 6.77, 7.37 (3H, furan H), 7.00-7.34 (5H, m, Ar-H), 5.59 (2H, s, OCH₂); MS (m/z, %): 298 (M⁺, 46.92), 205 (30.84), 109 (24.13), 84 (100), 77 (27.61), 65 (66.98), 57 (72.70), 51 (25.10), 39 (51.15); Calcd. for C₁₄H₁₀N₄O₂S (%): C 56.36, H 3.38, N 18.79; Found (%): C 56.09, H 3.36, N 19.04.
3-(2-furanyl)-6-(2-methoxyphenyl)-1,2,4-triazolo[3,4-b]-1,3,4-thiadiazole \((2l)\): Yield 58 \%; M.p. 162-164\(^\circ\)C; IR (KBr) v/cm\(^{-1}\): 3111, 3012 (Ar-H), 1622 (C=N), 1584, 1506, 1462, 1435, 1422 (aromatic skeleton), 1255 (N-N=C), 1223 (furan C-O-C), 699 (C-S-C); \(^1\)H-NMR \(\delta\): 8.01, 6.80, 7.40 (3H, furan H), 7.21-8.33 (4H, m, Ar-H), 4.04 (3H, s, OCH\(_3\)); MS (m/z, \%): 298 (M\(^+\), 100), 149 (33.42), 109 (84.92), 93 (59.71), 77 (23.86), 64 (68.84), 51 (35.38), 39 (48.20); Calcd. for \(\text{C}_{14}\text{H}_{10}\text{N}_4\text{O}_2\text{S}\) (%): C 56.36, H 3.38, N 18.79; Found (%): C 56.10, H 3.41, N 18.51.

3-(2-furanyl)-6-phenyl-1,2,4-triazolo[3,4-b]-1,3,4-thiadiazole \((2m)\): Yield 53 \%; M.p. 203-205\(^\circ\)C; IR (KBr) v/cm\(^{-1}\): 3131, 3078, 3024 (Ar-H), 1624 (C=N), 1518, 1469, 1444, 1426 (aromatic skeleton), 1240 (N-N=C), 1224 (furan C-O-C), 691 (C-S-C); \(^1\)H-NMR \(\delta\): 8.07, 6.78, 7.40 (3H, furan H), 7.65-8.04 (5H, m, Ar-H); MS (m/z, \%): 268 (M\(^+\), 100), 137 (15.84), 121 (88.23), 109 (77.76), 93 (52.23), 51 (41.26), 39 (26.39); Calcd. for \(\text{C}_{13}\text{H}_8\text{N}_4\text{OS}\) (%): C 58.19, H 3.00, N 20.89; Found (%): C 58.44, H 2.98, N 20.67.

3-(2-furanyl)-6-(2,4-dichlorophenoxy)methyl -1,2,4-triazolo[3,4-b]-1,3,4-thiadiazole \((2n)\): Yield 51 \%; M.p.193-195\(^\circ\)C; IR (KBr) v/cm\(^{-1}\): 3096, 3030 (Ar-H), 1625 (C=N), 1586, 1520, 1481, 1428 (aromatic skeleton), 1249 (N-N=C), 1224 (furan C-O-C), 687 (C-S-C); \(^1\)H-NMR \(\delta\): 8.01, 6.78, 7.46 (3H, furan H), 7.20-7.66 (3H, m, Ar-H), 5.71 (2H, s, OCH\(_2\)); MS (m/z, \%): 370 (M\(^+\)+4, 1.82), 368 (M\(^+\)+2, 8.86), 366 (M\(^+\), 12.83), 205 (58.79), 133 (12.64), 109 (22.09), 94 (45.70), 84 (100), 75 (6.40), 64 (19.66), 39 (9.28); Calcd. for \(\text{C}_{14}\text{H}_8\text{Cl}_2\text{N}_4\text{O}_2\text{S}\) (%): C 45.79, H 2.19, N 15.26; Found (%): C 45.83, H 2.17, N 15.50.

3-(2-furanyl)-6-(2-quinolyl ) -1,2,4-triazolo[3,4-b]-1,3,4-thiadiazole \((2o)\): Yield 48 \%; M.p. 267-269\(^\circ\)C; IR (KBr) v/cm\(^{-1}\): 3128, 3069 (Ar-H), 1622 (C-N), 1585, 1561, 1474, 1445, 1427 (aromatic skeleton), 1288 (N-N=C), 1225 (furan C-O-C), 695 (C-S-C); \(^1\)H-NMR \(\delta\): 7.98, 6.71, 7.54 (3H, furan H), 6.22-9.05 (6H, m, quinoline H); Calcd. for \(\text{C}_{16}\text{H}_9\text{N}_5\text{OS}\) (%): C 60.17, H 2.84, N 21.94; Found (%): C 60.43, H 2.88, N 21.81.

3-(2-furanyl)-6-(4-nitrophenyl)-1,2,4-triazolo[3,4-b]-1,3,4-thiadiazole \((2p)\): Yield 59 \%; M.p. 304-306\(^\circ\)C; IR (KBr) v/cm\(^{-1}\): 3099, 3061 (Ar-H), 1622 (C=N), 1527, 1486, 1469, 1428 (aromatic skeleton), 1283 (N-N=C), 1228 (furan C-O-C), 688 (C-S-C); \(^1\)H-NMR \(\delta\): 8.05, 6.83, 7.39 (3H, furan H), 8.34-8.43 (4H, dd, \(\text{J}=9.0\text{Hz}, \text{Ar-H}\)); MS (m/z, \%): 313 (M\(^+\), 78.32), 166 (29.75), 137 (19.97), 120 (34.58), 109 (100), 93 (71.97), 76 (22.26), 67 (14.30), 64 (72.07), 57 (39.21); Calcd. for \(\text{C}_{13}\text{H}_7\text{N}_5\text{O}_3\text{S}\) (%): C 49.83, H 2.25, N 22.36; Found(%): C 50.10, H 2.27, N 22.12.

3-(2-furanyl)-6-(2-aminophenyl)-1,2,4-triazolo[3,4-b]-1,3,4-thiadiazole \((2q)\): Yield 46 \%; M.p. 144-146\(^\circ\)C; R (KBr) v/cm\(^{-1}\): 3448, 3346 (N-H), 3123, 3030 (Ar-H), 1621 (C=N), 1563, 1510, 1475, 1440, 1424 (aromatic skeleton), 1273 (N-N=C), 1232 (furan C-O-C), 697 (C-S-C); \(^1\)H-NMR \(\delta\): 8.01, 6.79, 7.50 (3H, furan H), 6.81-7.27 (4H, m, Ar-H), 6.70 (2H, s, NH\(_2\) ); \(^1\)C-NMR \(\delta\): 168.01, 152.43, 147.50, 145.45, 140.34, 139.49, 133.41, 129.53, 127.08, 116.52, 112.29, 111.53, 109.95; MS (m/z, \%): 283(M\(^+\), 100), 136 (91.75), 118 (64.48), 109 (50.94), 93 (43.32), 91 (37.30), 77 (16.05), 64 (71.60), 51
(31.91), 39 (34.01); Calcd. for C_{13}H_{9}N_{5}OS (%): C 55.11, H 3.20, N 24.73; Found (%): C 54.85, H 3.22, N 24.96.

3-(2-furanyl)-6-(4-methoxyphenyl)-1,2,4-triazolo[3,4-b]-1,3,4-thiadiazole (2r): Yield 61 %; M.p. 177-179°C; IR (KBr) \( \nu / \text{cm}^{-1} \): 3102, 3003 (Ar-H), 1607 (C=N), 1576, 1518, 1496, 1473, 1420 (aromatic skeleton), 1264 (N-N=C), 1225 (furan C-O-C), 702 (C-S-C); \( ^{1}\text{H-NMR} \) \( \delta \): 8.01, 6.79, 7.38 (3H, furan H), 7.15-8.00 (4H, dd, \( J = 9.0 \text{Hz} \), Ar-H), 3.86 (3H, s, OCH\(_3\)); \( ^{13}\text{C-NMR} \) \( \delta \): 167.05, 163.07, 153.40, 145.44, 140.22, 139.34, 129.27, 121.31, 115.21, 112.28, 111.86, 55.85; MS (m/z, %): 298 (M\(^{+}\),100), 177 (8.45), 151 (98.97), 137 (28.18), 133 (21.33), 93 (35.40); Calcd. for C\(_{14}\)H\(_{10}\)N\(_4\)O\(_2\)S (%): C 56.36, H 3.38, N 18.79; Found (%): C 56.64, H 3.48, N 18.57.

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Sample Availability: Not available.

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