Synthesis of 6-Aryl-4*H*-imidazo[1,2-*b*][1,2,4]triazoles and 6-Aryl-thiazolo [3,2-*b*][1,2,4]triazoles

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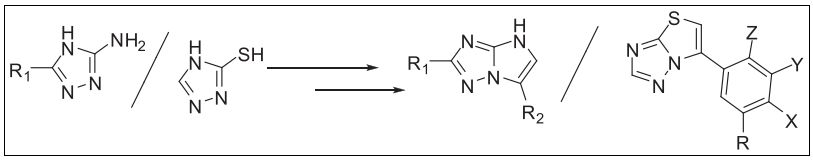

The cyclization of the derivatives of 3-aminotriazole, 2-(5-substituted 4*H*-1,2,4-triazol-3-ylamino)-1-arylethanones and 2-(4*H*-1,2,4-triazol-3-ylthio)-1-arylethanones to yield 6-aryl-4*H*-imidazo[1,2-*b*][1,2,4]triazoles and 6-aryl-thiazolo[3,2-*b*][1,2,4]triazoles has been described.

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INTRODUCTION

The synthesis of heterocyclic compounds with more nitrogen atoms in the ring has been attracting increasing interest over the past decade because of their utility in various applications, such as propellants, explosives, pyrotechnics, and especially in chemotherapy. In recent years, the chemistry of triazoles and their fused heterocyclic derivatives has received considerable attention owing to their synthetic and effective biological importance. The 1,2,4-triazole nucleus has been incorporated in a wide variety of therapeutically important agents displaying antimicrobial activities [1]. Thiazolotriazoles, which contain two rings – thiazole and triazole – fused together, can exist in both the isomeric forms, thiazolo[3,2-*b*][1,2,4]triazole and thiazolo [2,3-*c*][1,2,4]triazole. Thiazolo[3,2-*b*][1,2,4]triazoles possess a broad spectrum of biological activities – antimicrobial [2], analgesic, anti-inflammatory [3], antipyretic [4], and anticancer properties [5]. Barbuceanu et al. have synthesized a set of thiazolo[3,2-*b*][1,2,4]triazoles and evaluated their antibacterial activity [6]. A series of fluoro group containing thiazolotriazoles have been synthesized and tested for their anti-inflammatory, analgesic, and antimicrobial activities [7]. Bakali et al. have synthesized large aromatic building block-bearing cationic side chains of thiazolotriazoles and investigated them as telomeric G-quadruplex stabilizers [8]. Roy et al. have reported a series of 5,6-diarylthiazolo[3,2-*b*][1,2,4]triazoles and evaluated their potency and selectivity against human COX-1 and COX-2 enzymes [9].

RESULTS AND DISCUSSION

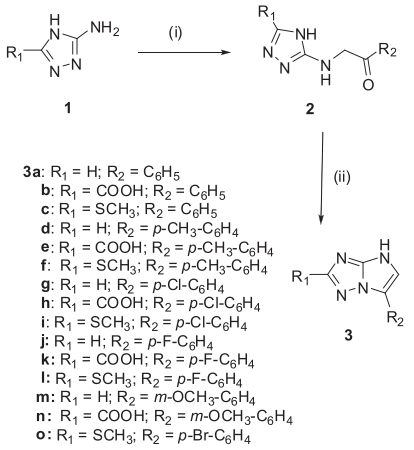
In continuation of our search of possible fused heterocycles from 3-aminotriazole [10], simple *N*-acyl derivatives of 3-amino-1,2,4-triazole and 3-mercapto-1,2,4-triazole have been subjected to intramolecular dehydration, and this has led to triazole ring fused with imidazole/thiazole ring, the common nitrogen occupying the bridge head. A set of 15 imidazo[1,2-*b*][1,2,4]triazoles **3** has been synthesized (Scheme 1). The ester (**1**, R_1 = COOEt) has been hydrolyzed during the reaction, and thus in the case of **3b**, **3e**, **3h**, **3k**, and **3n**, the corresponding carboxylic acids were obtained.

It should be mentioned that the reaction can take place through either of the tautomeric forms **2A** or **2B** or both. Thus **3A** and/or **3B** can be expected by ring tautomerized form of the initial keto compound involving in the ring closure (Scheme 2). The reaction has shown to give only one product exclusively. Unfortunately, the one dimensional NMR data are not useful enough to assign the correct structure between **3A** and **3B**. However, in **3m** (Fig. 1), the signal at 7.89 ppm gives only one HMBC contour with the carbon at 150.8 ppm. Had it been **A**, it is expected to give two HMBC contours with carbons at 150.8 and 131.3 ppm, as both can have three bond connectivity. Hence, structure **B** is the correct one, and for all compounds, it is assigned that way. In related systems also, such a cyclization has been noticed (*vide infra*).

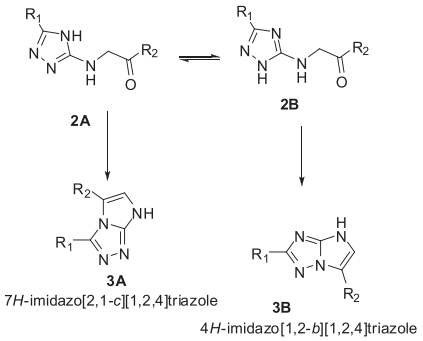
Other isomeric structures such as **C** and **D** (Fig. 2) can be ruled out for this type of compounds. This is because structures **A** and **B** of **3f** alone can account for the two dimensional NMR data, while structures **C** and **D** cannot. NH of **3f** gives HMBC contours with three carbons. This can be the case only when **A/B** is the correct structure, not with **C/D**.

In an attempt to prepare the sulfur analog of the imidazo [1,2-*b*][1,2,4]triazoles **3**, the same strategy of derivatizing the third position by an acyl group followed by dehydration was effected, now on 3-mercapto-1,2,4-triazole. There are already some reports regarding the self cyclization of the ketone **4** by different dehydrating agents [4,11,12]. In this work, we have employed sulfuric acid, and some

Scheme 1. Reagents and conditions: (i) R_2COCH_2Br, EtOH, K_2CO_3, RT, stirring, 6 h, and (ii) aqueous ethanolic KOH, 95°C, 12 h.



Scheme 2



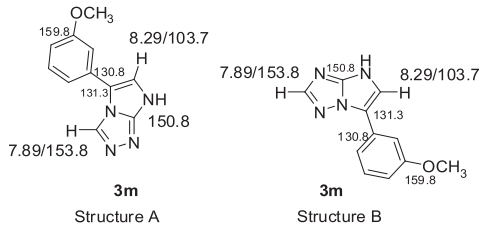


Figure 1. NMR data for **3m**.

new compounds have been targeted at. The results are interesting and presented in the succeeding texts.

Thirteen differently substituted thiazolo[3,2-*b*][1,2,4] triazoles **5** have been synthesized by this protocol (Scheme 3). In some cases, cyclization is followed by sulfonation. Thus, **4a** and **4g** undergoes sulfonation at the *para* position after cyclization. In **4i**, the position *ortho* to the methyl has been sulfonated after cyclization; while in **4m**, the position *para* to methoxy has been sulfonated. **4f** does not undergo the cyclization at all. When nitro or halogen or CF_3 group is present, the sulfonation is not taking place. When the ring does not have any substituent or if methyl or methoxy group is in the ring, the sulfonation takes place at the appropriate place. In the case of **4h**, the cyanide gets hydrolyzed to give amide after cyclization.

As in the case of imidazoltriazole **3**, in the case of thiazolotriazole **5** also, there can be two possible structures: **A** and **B**. The signal at 8.44 ppm gives only one HMBC contour in **5c** (Fig. 3), with 156.8 ppm, while the structure **A** is expected to give two contours, not only with 156.8 ppm but also with 127.3 ppm. Hence, the correct structure must be **B** and not **A**.

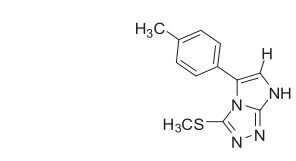
It has been shown that the cylcization of **4** by polyphosphoric acid leads to thiazolotriazole **B** and not **A** [11]. This is confirmed by X-ray studies also. However, compounds of type **4** have shown to undergo cyclization to structure **A** in anhydrous $POCl_3$. But under acidic conditions, **4** cyclizes to structure **B** [4]. This type of thiazolotriazoles has been constructed by a different route also. The triazole can be built over the thiazole ring as reported [12].

Triazoloimidazoles **3h** and **3i** have been tested for their antibacterial activities. The microdilution method for estimation of minimum inhibitory concentration (MIC) values was applied to evaluate the antimicrobial activity using agar diffusion method. They exhibited good activity against both the gram negative bacteria, *Escherichia coli* (MIC being 0.5 and 1.0 mg, respectively) and *Paratyphi A* (MIC being 0.5 and 1.0 mg, respectively), but their activities against the gram positive bacteria, *Staphylococcus aureus* and *Paratyphi A*, are not encouraging. Triazolothiazoles **5c** and **5k** are found to be active towards *E. coli* (MIC being 1.0 and 2.0 mg, respectively), *Paratyphi A* (MIC being 1.0 and 2.0 mg, respectively), *S. aureus* (MIC being 2.0 and 2.0 mg, respectively), and *Paratyphi A* (MIC being 2.0 and 2.0 mg, respectively).

EXPERIMENTAL

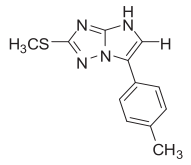
All chemicals used in this investigation were of reagent grade quality and used without further purification. All melting points were recorded in open capillaries and are uncorrected. The ^1H and ^{13}C NMR spectra were recorded on a Bruker 400 MHz spectrometer at 400 MHz and 100 MHz, respectively, in CDCl3/DMSO-d6 using TMS as internal standard. The chemical shifts are presented in δ-scale. Microanalyses were carried out on a PerkinElmer instrument (Lv Venlo, The Netherlands). All chromatographic separations were performed on 60–120 mesh silica gel using petroleum ether–ethyl acetate as eluent, unless mentioned otherwise.

For antibacterial activity experiments, the compounds were dissolved in DMSO to prepare chemical stock solution of 20 mg/mL. Gentamycin was used as the standard drug. Initially, the stock cultures of bacteria were revived by inoculating in broth media and grown at 37°C for 18 h. The agar plates of the



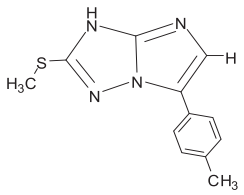
3-(methylthio)-5-(*p*-tolyl)-7*H*-imidazo[2,1-*c*][1,2,4]triazole

Structure A



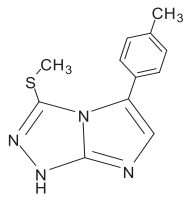
Structure B

2-(methylthio)-6-(*p*-tolyl)-4*H*-imidazo[1,2-*b*][1,2,4]triazole



Structure C

2-(methylthio)-6-(*p*-tolyl)-3*H*-imidazo[1,2-*b*][1,2,4]triazole

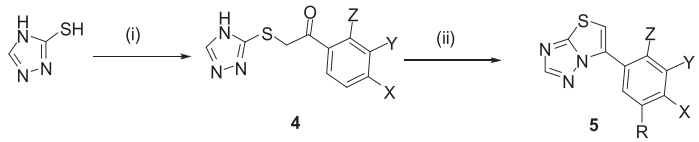


Structure D

3-(methylthio)-5-(*p*-tolyl)-1*H*-imidazo[2,1-*c*][1,2,4]triazole

Figure 2. Possible structures of **3f**.

Scheme 3. Reagents and conditions: (i) R_2COCH_2Br, EtOH, K_2CO_3, RT, stirring, 6 h, and (ii) concentrated H_2SO_4, 40°C, 5 h.

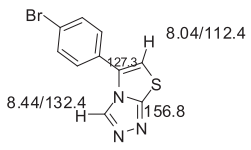


4

4a: X = Y = Z = H
b: X = Cl; Y = Z = H
c: X = Br; Y = Z = H
d: X = F; Y = Z = H
e: X = CF_3; Y = Z = H
f: X = $N(C_2H_5)_2$; Y = Z = H
g: X = C_6H_5; Y = Z = H
h: X = CN; Y = Z = H
i: X = CH_3; Y = Z = H
j: X = Z = H; Y = Cl
k: X = Z = H; Y = NO_2
l : X = Y = H; Z = Cl
m: X = Y = H; Z = OCH_3

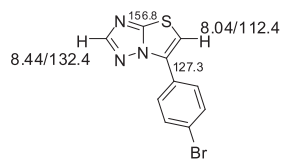
5

5a: X = SO_3H; Y = Z = H; R = H
b: X = Cl; Y = Z = H; R = H
c: X = Br; Y = Z = H; R = H
d: X = F; Y = Z = H; R = H
e: X = CF_3; Y = Z = H; R = H
g: X = *p*-SO_3H-C_6H_4; Y = Z = H; R = H
h: X = $CONH_2$; Y = Z = H; R = H
i: X = CH_3; Y = SO_3H; Z = H; R = H
j: X = Z = H; Y = Cl; R = H
k: X = Z = H; Y = NO_2 ; R = H
l : X = Y = H; Z = Cl; R = H
m: X = Y = H; Z = OCH_3; R = SO_3H



5-(4-bromophenyl)thiazolo[2,3-*c*][1,2,4]triazole

5c, Structure A



6-(4-bromophenyl)thiazolo[3,2-*b*][1,2,4]triazole

5c, Structure B

Figure 3. NMR data for **5c**.

aforementioned media were prepared, and wells were made in the plate. Each plate was inoculated with 18-h-old cultures (100 μL, 10^{-4} cfu) and spread evenly on the plate. After 20 min, the wells were filled with compound at different concentrations. The control wells with gentamycin were also prepared. All the plates were incubated at 37°C for 24 h, and the diameter of inhibition zone were noted. The derivatives of **2** and **4** were prepared by known procedures, and the analytical data for unreported **2** and **4** are alone provided here.

Ethyl 5-((2-oxo-2-phenylethyl)amino)-4*H*-1,2,4-triazole-3-carboxylate (2, R_1 = COOEt, R_2 = Ph). This compound was obtained as white solid; yield 88%; mp 195–196°C; IR (KBr) 3401, 3129, 1723, 1636 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.25 (t, J = 7.2 Hz, 3H), 4.22 (q, J = 7.2 Hz, 2H), 5.69 (s, 2H), 6.53 (bs, 2H), 7.59 (t, J = 7.4 Hz, 2H), 7.71 (t, J = 7.4 Hz, 1H), 8.02 (d, J = 7.4 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 14.1, 53.5, 60.4, 128.1, 128.9, 134.0, 134.4, 150.7, 157.4,

160.0, 192.1; ESI mass (*m/z*) Calcd $[C_{13}H_{14}N_4O_3+H]^+$274.11, found 275.2.

2-((5-(Methylthio)-4*H*-1,2,4-triazol-3-yl)amino)-1-phenylethanone (2, R_1 = SMe, R_2 = Ph). This compound was obtained as white solid; yield 92%; mp 194–195°C; IR (KBr) 3193, 2927, 1685, 1564 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 2.40 (s, 3H), 5.52 (s, 2H), 6.33 (bs, 2H), 7.59 (t, J = 7.4 Hz, 2H), 7.69 (t, J = 7.4 Hz, 1H), 8.02 (d, J = 7.4 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 13.4, 52.9, 128.0, 128.9, 133.9, 134.5, 156.3, 157.3, 192.6; ESI mass (*m/z*) Calcd $[C_{11}H_{12}N_4OS+H]^+$248.07, found 249.2.

Ethyl 5-((2-oxo-2-(*p*-tolyl)ethyl)amino)-4*H*-1,2,4-triazole-3-carboxylate (2, R_1 = COOEt, R_2 = *p*-tolyl). This compound was obtained as white solid; yield 86%; mp 210–211°C; IR (KBr) 3411, 3128, 1728, 1637 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.25 (t, J = 7.2 Hz, 3H), 2.40 (s, 3H), 4.21 (q, J = 7.2 Hz, 2H), 5.66 (s, 2H), 6.52 (bs, 2H), 7.39 (d, J = 7.9 Hz, 2H), 7.93 (d, J = 7.9 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 14.5, 21.7, 53.8, 60.8, 128.6, 129.8, 132.3, 144.9, 151.1, 157.8, 160.4, 192.0; ESI mass (*m/z*) Calcd $[C_{14}H_{16}N_4O_3]^+$288.12, found 288.9.

2-((5-(Methylthio)-4*H*-1,2,4-triazol-3-yl)amino)-1-(*p*-tolyl) ethanone (2, R_1 = SMe, R_2 = *p*-tolyl). This compound was obtained as white solid; yield 88%; mp 170–171°C; IR (KBr) 3382, 2925, 1679, 1562 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 2.39 (s, 3H), 2.40 (s, 3H), 5.47 (s, 2H), 6.31 (bs, 2H), 7.39 (d, J = 8.0 Hz, 2H), 7.91 (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 13.4, 21.3, 52.8, 128.2, 129.4, 132.1, 144.4, 156.2, 157.3, 192.1; ESI mass (*m/z*) Calcd $[C_{12}H_{14}N_4OS+H]^+$262.09, found 263.2.

Ethyl 5-((2-(4-chlorophenyl)-2-oxoethyl)amino)-4*H*-1,2,4-triazole-3-carboxylate (2, R_1 = COOEt, R_2 = 4-ClPh). This compound was obtained as white solid; yield 86%; mp 252–253° C; IR (KBr) 3405, 3121, 1723, 1640 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.25 (t, J = 7.2 Hz, 3H), 4.21 (q, J = 7.2 Hz, 2H), 5.68 (s, 2H), 6.53 (bs, 2H), 7.67 (d, J = 8.5 Hz, 2H), 8.05 (d, J = 8.5 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 14.1, 53.6, 60.4, 129.0, 130.0, 132.8, 138.9, 150.8, 157.3, 160.0, 191.5; ESI mass (*m/z*) Calcd $[C_{13}H_{13}ClN_4O_3]^+$308.07, found 308.8.

1-(4-Chlorophenyl)-2-((5-(methylthio)-4*H*-1,2,4-triazol-3-yl)amino)ethanone (2, R_1 = SMe, R_2 = 4-ClPh). This compound was obtained as white solid; yield 84%; mp 179–180° C; IR (KBr) 3383, 2914, 1683, 1589 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 2.38 (s, 3H), 5.50 (s, 2H), 6.31 (bs, 2H), 7.65 (d, J = 8.4 Hz, 2H), 8.01 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 13.3, 52.9, 128.9, 129.9, 133.2, 138.7, 156.3, 157.2, 191.7; ESI mass (*m/z*) Calcd $[C_{11}H_{11}ClN_4OS+H]^+$282.03, found 283.2.

Ethyl 5-((2-(4-fluorophenyl)-2-oxoethyl)amino)-4*H*-1,2,4-triazole-3-carboxylate (2, R_1 = COOEt, R_2 = 4-FPh). This compound was obtained as white solid; yield 88%; mp 230–231° C; IR (KBr) 3388, 3138, 1725, 1643 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.25 (t, J = 7.2 Hz, 3H), 4.21 (q, J = 7.2 Hz, 2H), 5.68 (s, 2H), 6.53 (bs, 2H), 7.43 (t, J = 8.8 Hz, 2H), 8.08–8.12 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 14.1, 53.2, 60.4, 116.0, 131.1, 131.2, 150.7, 157.4, 160.0, 165.2, 190.8; ESI mass (*m/z*) Calcd $[C_{13}H_{13}FN_4O_3\text{-}H]^+$292.10, found 290.8.

1-(4-Fluorophenyl)-2-((5-(methylthio)-4*H*-1,2,4-triazol-3-yl)amino)ethanone (2, R_1 = SMe, R_2 = 4-FPh). This compound was obtained as white solid; yield 86%; mp 166–167° C; IR (KBr) 3390, 3130, 1684, 1572 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 2.38 (s, 3H), 5.50 (s, 2H), 6.32 (bs, 2H), 7.41 (t, J = 8.2 Hz, 2H), 8.09 (d, J = 8.2 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 13.4, 52.9, 115.9, 131.0, 131.1, 156.3, 157.2, 165.1, 191.3; ESI mass (*m/z*) Calcd $[C_{11}H_{11}FN_4OS+H]^+$266.06, found 267.1.

2-((4H-1,2,4-Triazol-3-yl)amino)-1-(3-methoxyphenyl)ethanone (2, R_1 = H, R_2 = 3-MeOPh). This compound was obtained as viscous liquid; yield 85%; ^1H NMR (400 MHz, DMSO-d_6) δ 3.83 (s, 3H), 5.53 (s, 2H), 6.19 (bs, 2H), 7.27 (d, J = 8.2 Hz, 1H), 7.32–7.33 (m, 1H), 7.35 (s, 1H), 7.49 (t, J = 7.9 Hz, 1H), 7.61 (d, J = 7.9 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 53.4, 55.8, 113.0, 120.2, 120.9, 130.5, 136.3, 149.0, 156.7, 159.9, 162.9; ESI mass (*m/z*) Calcd $[C_{11}H_{12}N_4O_2]^+$232.10, found 232.8.

Ethyl 5-((2-(3-methoxyphenyl)-2-oxoethyl)amino)-4*H*-1,2,4-triazole-3-carboxylate (2, R_1 = COOEt, R_2 = 3-MeOPh). This compound was obtained as white solid; yield 87%; mp 197–198°C; IR (KBr) 3389, 3133, 1726, 1640 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.25 (t, J = 7.2 Hz, 3H), 3.83 (s, 3H), 4.20 (q, J = 7.2 Hz, 2H), 5.67 (s, 2H), 6.52 (bs, 2H), 7.29 (d, J = 8.1 Hz, 1H), 7.50–7.53 (m, 2H), 7.61 (d, J = 7.7 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 14.5, 54.1, 55.9, 60.9, 113.1, 120.3, 120.9, 130.5, 136.1, 151.1, 157.8, 159.9, 160.4, 192.4; ESI mass (*m/z*) Calcd $[C_{14}H_{16}N_4O_4]^+$304.12, found 304.8.

1-(4-Bromophenyl)-2-((5-(methylthio)-4*H*-1,2,4-triazol-3-yl) amino)ethanone (2, R_1 = SMe, R_2 = 4-BrPh). This compound was obtained as white solid; yield 82%; mp 175–176°C; IR (KBr) 3382, 2916, 1684, 1584 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 2.38 (s, 3H), 5.50 (s, 2H), 6.32 (bs, 2H), 7.79 (d, J = 8.4 Hz, 2H), 7.93 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 13.4, 53.0, 128.0, 130.1, 132.0, 133.6, 156.4, 157.3, 192.4; ESI mass (*m/z*) Calcd $[C_{11}H_{11}BrN_4OS+H]^+$325.98, found 327.4.

General procedure for the synthesis of 6-aryl-4*H*-imidazo[1,2-*b*][1,2,4]triazole (3). Compound **2** was treated with aqueous ethanolic potassium hydroxide, and the reaction mixture was heated at 95°C for 12 h. The resultant mass was acidified with concentrated hydrochloric acid to give **3**, which was purified by crystallization in ethanol.

6-Phenyl-4H-imidazo[1,2-b][1,2,4]triazole (3a). This compound was obtained as white solid; yield 86%; mp 251–252° C; IR (KBr) 1615, 1494, 1183 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.33 (t, J = 7.4 Hz, 1H), 7.45 (t, J = 7.4 Hz, 2H), 7.74 (d, J = 7.4 Hz, 2H), 7.89 (s, 1H), 8.22 (s, 1H), 12.48 (bs, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 103.9, 124.8, 128.5, 129.4, 129.9, 131.8, 151.3, 154.2; *Anal.* Calcd for $C_{10}H_8N_4$: C, 65.21; H, 4.38; N, 30.42%. Found: C, 65.38; H, 4.26; N, 30.40%; ESI mass (*m/z*) Calcd $[C_{10}H_8N_4+H]^+$184.07, found 185.2.

6-Phenyl-4H-imidazo[1,2-b][1,2,4]triazole-2-carboxylic acid (3b). This compound was obtained as white solid; yield 90%; mp 222–223°C; IR (KBr) 3358, 2940, 1630, 1355 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.38 (t, J = 7.3 Hz, 1H), 7.48 (t, J = 7.6 Hz, 2H), 7.79 (d, J = 7.6 Hz, 2H), 8.32 (s, 1H), 12.86 (bs, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 103.5, 124.8, 128.6, 129.0, 129.1, 133.4, 150.7, 156.1, 161.6; *Anal.* Calcd for $C_{11}H_8N_4O_2$: C, 57.89; H, 3.53; N, 24.55%. Found: C, 57.63; H, 3.50; N, 24.68%; ESI mass (*m/z*) Calcd $[C_{11}H_8N_4O_2]^+$228.06, found 228.8.

2-Methylthio-6-phenyl-4H-imidazo[1,2-b][1,2,4]triazole (3c). This compound was obtained as white solid; yield 86%; mp 290–291°C; IR (KBr) 3104, 2922, 1601, 1278 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 2.54 (s, 3H), 7.32 (t, J = 7.5 Hz, 1H), 7.44 (t, J = 7.5 Hz, 2H), 7.71 (d, J = 7.5 Hz, 2H), 8.17 (s, 1H), NH not seen; ^{13}C NMR (100 MHz, DMSO-d_6) δ 13.9, 103.8, 124.3, 128.0, 129.0, 129.4, 129.9, 151.3, 162.8; *Anal.* Calcd for $C_{11}H_{10}N_4S$: C, 57.37; H, 4.38; N, 24.33%. Found: C, 57.19; H,

4.43; N, 24.42%; ESI mass (*m/z*) Calcd $[C_{11}H_{10}N_4S + H]^+$230.06, found 231.1.

6-(p-Tolyl)-4H-imidazo[1,2-b][1,2,4]triazole (3d). This compound was obtained as white solid; yield 83%; mp 270–271°C; IR (KBr) 3125, 2909, 1608, 1474 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 2.33 (s, 3H), 7.28 (d, J = 8.0 Hz, 2H), 7.64 (d, J = 8.0 Hz, 2H), 7.88 (s, 1H), 8.16 (s, 1H), 12.41 (bs, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 20.8, 102.9, 124.3, 126.7, 129.5, 131.5, 137.5, 150.7, 153.6; *Anal*. Calcd for $C_{11}H_{10}N_4$: C, 66.65; H, 5.08; N, 28.26%. Found: C, 66.72; H, 5.36; N, 28.51%; ESI mass (*m/z*) Calcd $[C_{11}H_{10}N_4 + H]^+$198.09, found 199.2.

6-(p-Tolyl)-4H-imidazo[1,2-b][1,2,4]triazole-2-carboxylic acid (3e). This compound was obtained as white solid; yield 88%; mp 253–254°C; IR (KBr) 3130, 1699, 1604 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 2.34 (s, 3H), 7.29 (d, J = 7.5 Hz, 2H), 7.69 (d, J = 7.5 Hz, 2H), 8.24 (s, 1H), 12.90 (bs, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 21.2, 103.3, 125.1, 125.3, 126.8, 128.6, 129.6, 138.5, 150.8, 162.0; *Anal*. Calcd for $C_{12}H_{10}N_4O_2$: C, 59.50; H, 4.16; N, 23.13%. Found: C, 60.01; H, 4.08; N, 23.26%; ESI mass (*m/z*) Calcd $[C_{12}H_{10}N_4O_2]^+$242.08, found 242.8.

2-(Methylthio)-6-(p-tolyl)-4H-imidazo[1,2-b][1,2,4]triazole (3f). This compound was obtained as white solid; yield 82%; mp 289–290°C; IR (KBr) 3052, 1606, 1470, 1247 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 2.32 (s, 3H), 2.55 (s, 3H), 7.26 (d, J = 8.0 Hz, 2H), 7.61 (d, J = 8.0 Hz, 2H), 8.10 (s, 1H), 12.40 (bs, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 14.3, 21.2, 103.6, 124.7, 127.0, 130.0, 130.4, 137.9, 151.6, 162.9; *Anal*. Calcd for $C_{12}H_{12}N_4S$: C, 58.99; H, 4.95; N, 22.93%. Found: C, 59.12; H, 4.78; N, 22.83%; ESI mass (*m/z*) Calcd $[C_{12}H_{12}N_4S + H]^+$244.08, found 245.2.

6-(4-Chlorophenyl)-4H-imidazo[1,2-b][1,2,4]triazole (3g). This compound was obtained as white solid; yield 90%; mp 317–318°C; IR (KBr) 3115, 2853, 1617, 1490 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.53 (d, J = 8.5 Hz, 2H), 7.76 (d, J = 8.5 Hz, 2H), 7.90 (s, 1H), 8.26 (s, 1H), 12.54 (bs, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 103.9, 126.0, 128.6, 129.0, 130.6, 132.4, 151.0, 153.8; Anal. Calcd For $C_{10}H_7ClN_4$: C, 54.93; H, 3.23; N, 25.62. Found: C, 54.46; H, 3.22; N, 25.39%; ESI mass (*m/z*) Calcd $[C_{10}H_7ClN_4]^+$218.04, found 218.8.

6-(4-Chlorophenyl)-4H-imidazo[1,2-b][1,2,4]triazole-2-carboxylic acid (3h). This compound was obtained as white solid; yield 94%; mp 300–301°C; IR (KBr) 3150, 1685, 1609 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.58 (d, J = 8.4 Hz, 2H), 7.83 (d, J = 8.4 Hz, 2H), 8.38 (s, 1H), 12.93 (bs, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 104.0, 126.4, 129.1, 132.9, 150.6, 161.5, Not all carbons picked up; *Anal*. Calcd for $C_{11}H_7ClN_4O_2$: C, 50.30; H, 2.69; N, 21.33%. Found: C, 50.46; H, 2.78; N, 21.19%; ESI mass (*m/z*) Calcd $[C_{11}H_7ClN_4O_2]^+$262.03, found 262.8.

6-(4-Chlorophenyl)-2-(methylthio)-4H-imidazo[1,2-b][1,2,4]triazole (3i). This compound was obtained as white solid; yield 78%; mp 304–305°C; IR (KBr) 3048, 1610, 1488, 1248 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 2.54 (s, 3H), 7.52 (d, J = 8.5 Hz, 2H), 7.73 (d, J = 8.5 Hz, 2H), 8.21 (s, 1H), 12.50 (bs, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 13.8, 104.3, 125.9, 128.4, 128.8, 129.1. 132.3, 151.4, 163.0; *Anal*. Calcd for $C_{11}H_9ClN_4S$: C, 49.91; H, 3.43; N, 21.16%. Found: C, 50.23; H, 3.61; N, 21.07%; ESI mass (*m/z*) Calcd $[C_{11}H_9ClN_4S + H]^+$264.02, found 265.3.

6-(4-Fluorophenyl)-4H-imidazo[1,2-b][1,2,4]triazole (3j). This compound was obtained as white solid; yield 92%; mp 302–303°C; IR (KBr) 3121, 2858, 1619, 1508 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.34 (t, J = 8.8 Hz, 2H), 7.77–7.81 (m, 2H), 7.90 (s, 1H), 8.21 (s, 1H), 12.49 (bs, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 103.4, 116.0, 126.5, 126.6, 130.6, 150.8, 153.6, 161.5; *Anal*. Calcd for $C_{10}H_7FN_4$: C, 59.40; H, 3.49; N, 27.71%. Found: C, 59.37; H, 3.61; N, 27.70%; ESI mass (*m/z*) Calcd $[C_{10}H_7FN_4]^+$202.07, found 202.7.

6-(4-Fluorophenyl)-4H-imidazo[1,2-b][1,2,4]triazole-2-carboxylic acid (3k). This compound was obtained as white solid; yield 96%; mp 256°C; IR (KBr) 3163, 1684, 1616 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.37 (t, J = 8.8 Hz, 2H), 7.83–7.86 (m, 2H), 8.31 (s, 1H), 12.77 (bs, 1H), 13.09 (bs, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 103.4, 116.0, 116.2, 125.6, 127.0, 127.1, 132.5, 150.6, 161.0; *Anal*. Calcd for $C_{11}H_7FN_4O_2$: C, 53.66; H, 2.87; N, 22.76%. Found: C, 53.83; H, 2.94; N, 22.48%; ESI mass (*m/z*) Calcd $[C_{11}H_7FN_4O_2]^+$246.06, found 246.8.

6-(4-Fluorophenyl)-2-(methylthio)-4H-imidazo[1,2-b][1,2,4]triazole (3l). This compound was obtained as white solid; yield 87%; mp 301–302°C; IR (KBr) 2920, 1614, 1504 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 2.48 (s, 3H), 7.30 (t, J = 8.8 Hz, 2H), 7.72–7.75 (m, 2H), 8.13 (s, 1H), 12.46 (bs, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 13.9, 103.7, 116.1, 126.0, 126.3, 129.0, 151.2, 161.5, 162.8; *Anal*. Calcd for $C_{11}H_9FN_4S$: C, 53.21; H, 3.65; N, 22.57%. Found: C, 53.47; H, 3.24; N, 22.38%; ESI mass (*m/z*) Calcd $[C_{11}H_9FN_4S + H]^+$248.05, found 249.1.

6-(3-Methoxyphenyl)-4H-imidazo[1,2-b][1,2,4]triazole (3m). This compound was obtained as white solid; yield 92%; mp 305°C; IR (KBr) 3137, 1617, 1487 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 3.81 (s, 3H), 6.91 (d, J = 7.2 Hz, 1H), 7.31–7.38 (m, 3H), 7.89 (s, 1H), 8.29 (s, 1H), 12.46 (bs, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 55.3, 103.7, 109.9, 113.6, 116.7, 130.1, 130.8, 131.3, 150.8, 153.8, 159.8; *Anal*. Calcd for $C_{11}H_{10}N_4O$: C, 61.67; H, 4.71; N, 26.15%. Found: C, 61.48; H, 4.82; N, 26.10%; ESI mass (*m/z*) Calcd $[C_{11}H_{10}N_4O]^+$214.09, found 214.7.

6-(3-Methoxyphenyl)-4H-imidazo[1,2-b][1,2,4]triazole-2-carboxylic acid (3n). This compound was obtained as white solid; yield 96%; mp 205°C; IR (KBr) 3575, 1714, 1602 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 3.81 (s, 3H), 6.94–6.96 (m, 1H), 7.31–7.38 (m, 3H), 8.35 (s, 1H), 12.74 (bs, 1H), 13.09 (bs, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 55.3, 103.8, 110.2, 114.3, 117.0, 130.2,*133.3, 150.6, 156.1, 159.8, 161.6; *Anal*. Calcd for $C_{12}H_{10}N_4O_3$: C, 55.81; H, 3.90; N, 21.70%. Found: C, 55.63; H, 4.21; N, 27.65%; ESI mass (*m/z*) Calcd $[C_{12}H_{10}N_4O_3\text{-}H]^+$258.08, found 256.8.*Two carbon signals merged here.

6-(4-Bromophenyl)-2-(methylthio)-4H-imidazo[1,2-b][1,2,4]triazole (3o). This compound was obtained as white solid; yield 90%; mp 299–300°C; IR (KBr) 1609,1484, 1393 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 2.54 (s, 3H), 7.71 (s, 4H), 8.23 (s, 1H) NH not seen; ^{13}C NMR (100 MHz, DMSO-d_6) δ 14.3, 104.7, 121.2, 126.6, 129.3, 131.7, 132.3, 151.8, 163.4; *Anal*. Calcd for $C_{11}H_9BrN_4S$: C, 42.73; H, 2.93; N, 18.12%. Found: C, 42.56; H, 3.14; N, 18.25%; ESI mass (*m/z*) Calcd $[C_{11}H_9BrN_4S + H]^+$307.97, found 309.6.

2-((4H-1,2,4-Triazol-3-yl)thio)-1-(4-chlorophenyl)ethanone (4b). This compound was obtained as white solid; yield 86%; mp 118–119°C; IR (KBr) 3079, 2853, 1692, 1583 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 4.79 (s, 2H), 7.63 (d, J = 8.5 Hz, 2H), 8.03 (d, J = 8.5 Hz, 2H), 8.40 (s, 1H), 14.02 (bs, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 40.1, 128.9, 130.3, 134.3, 138.5, 146.2, 192.9. Not all carbons picked up; ESI mass (*m/z*) Calcd $[C_{10}H_8ClN_3OS\text{-}H]^+$253.01, found 252.2.

2-((4H-1,2,4-Triazol-3-yl)thio)-1-(4-(trifluoromethyl)phenyl)ethanone (4e). This compound was obtained as white solid; yield 72%; mp 103–104°C; IR (KBr) 3116, 2860, 1676, 1321 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 4.85 (s, 2H),

7.93 (d, $J = 8.2$ Hz, 2H), 8.21 (d, $J = 8.2$ Hz, 2H), 8.48 (s, 1H), 14.04 (bs, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 40.6, 124.8, 128.2,*129.6, 133.0, 133.3, 139.3, 193.8; ESI mass (*m/z*) Calcd $[C_{11}H_8F_3N_3OS + H]^+$287.03, found 288.2.*Two carbon signals merged here.

2-((4H-1,2,4-Triazol-3-yl)thio)-1-(4-(diethylamino)phenyl) ethanone (4f). This compound was obtained as viscous liquid; yield 71%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.22 (t, $J = 7.2$ Hz, 6H), 3.44 (q, $J = 7.2$ Hz, 4H), 4.40 (s, 2H), 6.67 (d, $J = 8.6$ Hz, 2H), 7.89 (d, $J = 8.6$ Hz, 2H), 8.03 (s, 1H) NH not seen; ^{13}C NMR (100 MHz, DMSO-d_6) δ 12.4, 38.0, 44.6, 110.3, 121.7, 130.2, 131.5, 148.9, 152.0, 192.1. Not all the carbons picked up; ESI mass (*m/z*) Calcd $[C_{14}H_{18}N_4OS + H]^+$290.12, found 291.3.

2-((4H-1,2,4-Triazol-3-yl)thio)-1-([1,1′-biphenyl]-4-yl)ethanone (4g). This compound was obtained as white solid; yield 86%; mp 148–149°C; IR (KBr) 3235, 1671, 1602, 1299 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.84 (s, 2H), 7.45 (t, $J = 7.2$ Hz, 1H), 7.52 (t, $J = 7.2$ Hz, 2H), 7.78 (d, $J = 8.5$ Hz, 2H), 7.85 (d, $J = 8.4$ Hz, 2H), 8.10 (d, $J = 8.4$ Hz, 2H), 8.39 (s, 1H), 14.02 (bs, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 40.6, 127.4, 127.5, 128.9, 129.5, 134.8, 139.3, 145.3, 146.7, 156.8, 193.7. Not all the carbons picked up; ESI mass (*m/z*) Calcd $[C_{16}H_{13}N_3OS-H]^+$295.08, found 294.2.

4-(2-((4H-1,2,4-Triazol-3-yl)thio)acetyl)benzonitrile (4h). This compound was obtained as white solid; yield 78%; mp 143–144° C; IR (KBr) 3089, 2234, 1705, 1405 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.82 (s, 2H), 8.03 (d, $J = 8.4$ Hz, 2H), 8.15 (d, $J = 8.4$ Hz, 2H), 8.39 (s, 1H) NH not seen; ^{13}C NMR (100 MHz, DMSO-d_6) δ 40.2, 115.8, 118.5, 129.4, 133.2, 139.3, 146.6, 156.7, 193.8; ESI mass (*m/z*) Calcd $[C_{11}H_8N_4OS-H]^+$244.04, found 243.1.

2-((4H-1,2,4-Triazol-3-yl)thio)-1-(p-tolyl)ethanone (4i). This compound was obtained as white solid; yield 84%; high melting; ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.37 (s, 3H), 4.76 (s, 2H), 7.33 (d, $J = 8.0$ Hz, 2H), 7.89 (d, $J = 8.0$ Hz, 2H), 8.37 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 21.6, 128.9, 129.7, 133.5, 144.4, 145.0. Not all carbons are picked up; ESI mass (*m/z*) Calcd $[C_{11}H_{11}N_3OS-H]^+$233.06, found 232.6.

2-((4H-1,2,4-Triazol-3-yl)thio)-1-(3-chlorophenyl)ethanone (4j). This compound was obtained as white solid; yield 72%; mp 133–134°C; IR (KBr) 2915, 1677, 1569 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.80 (s, 2H), 7.59 (t, $J = 7.8$ Hz, 1H), 7.73–7.76 (m, 1H), 7.96–8.02 (m, 1H), 8.03 (s, 1H), 8.41 (s, 1H), 14.03 (bs, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 40.6, 127.4, 128.4, 131.2, 133.6, 134.1, 137.9, 193.3. Not all the carbons picked up; ESI mass (*m/z*) Calcd $[C_{10}H_8ClN_3OS + H]^+$253.01, found 254.3.

2-((4H-1,2,4-Triazol-3-yl)thio)-1-(3-nitrophenyl)ethanone (4k). This compound was obtained as yellow solid; yield 76%; mp 162–163°C; IR (KBr) 2916, 1696, 1522 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.85 (s, 2H), 7.86 (t, $J = 7.9$ Hz, 1H), 8.44–8.53 (m, 3H), 8.70 (s, 1H), 14.05 (bs, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 40.6, 123.1, 128.1, 131.0, 135.0, 137.3, 145.2, 148.4, 193.2. Not all carbons picked up; ESI mass (*m/z*) Calcd $[C_{10}H_8N_4O_3S + H]^+$264.03, found 265.3.

2-((4H-1,2,4-Triazol-3-yl)thio)-1-(2-chlorophenyl)ethanone (4l). This compound was obtained as viscous liquid; yield 70%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.56 (s, 2H), 7.32–7.35 (m, 1H), 7.43–7.45 (m, 2H), 7.58 (d, $J = 7.6$ Hz, 1H), 8.13 (s, 1H) NH not seen; ^{13}C NMR (100 MHz, DMSO-d_6) δ 41.8, 126.6, 129.7, 130.1, 130.8, 132.1, 136.8, 196.9. Not all carbons picked up; ESI mass (*m/z*) Calcd $[C_{10}H_8ClN_3OS-H]^+$253.01, found 252.5.

2-((4H-1,2,4-Triazol-3-yl)thio)-1-(2-methoxyphenyl)ethanone (4m). This compound was obtained as white solid; yield 74%; mp 102–103°C; IR (KBr) 2833, 1681, 1594 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.90 (s, 3H), 4.59 (s, 2H), 7.03 (t, $J = 7.7$ Hz, 1H), 7.19 (d, $J = 7.7$ Hz, 1H), 7.55–7.61 (m, 2H), 8.33 (s, 1H) NH not seen; ^{13}C NMR (100 MHz, DMSO-d_6) δ 43.8, 56.4, 112.9, 121.0, 126.4, 130.5, 134.8, 146.8, 156.8, 159.0, 195.3; ESI mass (*m/z*) Calcd $[C_{11}H_{11}N_3O_2S + H]^+$249.06, found 250.2.

General procedure for the synthesis of substituted thiazolo [3,2-*b*][1,2,4]triazole (5). Compound **4** was treated with concentrated sulfuric acid, and the reaction mixture was heated at 40°C for 5 h. The resultant mass was basified with aqueous ammonia to give **5**, which was purified by crystallization. Compounds **5a–m** were prepared by this method (**5a**, **5g**, **5i**, and **5m** were not basified with aqueous ammonia but were added to water and filtered to give the sulfonated products).

4-(Thiazolo[3,2-b][1,2,4]triazol-6-yl)benzenesulfonic acid (5a). This compound was obtained as white solid; yield 78%; high melting: IR (KBr) 1413, 1172 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.73 (s, 1H), 7.76 (d, $J = 8.2$ Hz, 2H), 7.99 (s, 1H), 8.19 (d, $J = 8.2$ Hz, 2H), 8.44 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 112.0, 126.2, 126.5, 128.1, 131.5, 149.4, 156.6, 157.2; *Anal.* Calcd for $C_{10}H_7N_3O_3S_2$: C, 42.70; H, 2.51; N, 14.94%. Found: C, 42.58; H, 2.62; N, 15.07%; ESI mass (*m/z*) Calcd $[C_{10}H_7N_3O_3S_2]^+$280.99, found 280.2.

6-(4-Chlorophenyl)thiazolo[3,2-b][1,2,4]triazole (5b). This compound was obtained as viscous liquid; yield 76%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.64 (d, $J = 8.4$ Hz, 2H), 8.04 (s, 1H), 8.26 (d, $J = 8.4$ Hz, 2H), 8.44 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 111.9, 126.5, 127.9, 129.0, 130.3, 134.2, 156.2, 156.7; *Anal.* Calcd for $C_{10}H_6ClN_3S$: C, 50.96; H, 2.57; N, 17.83%. Found: C, 51.08; H, 2.34; N, 17.73%; ESI mass (*m/z*) Calcd $[C_{10}H_6ClN_3S + H]^+$235.00, found 236.2.

6-(4-Bromophenyl)thiazolo[3,2-b][1,2,4]triazole (5c). This compound was obtained as white solid; yield 76%; mp 180–181°C; IR (KBr) 3063, 1491,1175 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.79 (d, $J = 8.5$ Hz, 2H), 8.04 (s, 1H), 8.20 (d, $J = 8.6$ Hz, 2H), 8.44 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 112.4, 123.3, 127.3, 128.5, 130.8, 132.4, 156.6, 156.8; *Anal.* Calcd for $C_{10}H_6BrN_3S$: C, 42.87; H, 2.16; N, 15.00%. Found: C, 42.78; H, 2.32; N, 15.38%; ESI mass (*m/z*) Calcd $[C_{10}H_6BrN_3S + H]^+$278.95, found 280.3.

6-(4-Fluorophenyl)thiazolo[3,2-b][1,2,4]triazole (5d). This compound was obtained as viscous liquid; yield 70%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.43 (t, $J = 8.6$ Hz, 2H), 7.97 (s, 1H), 8.29 (d, $J = 8.6$ Hz, 2H), 8.45 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 111.4, 116.4, 124.8, 129.2, 131.0, 156.6, 157.2, 161.8; *Anal.* Calcd for $C_{10}H_6FN_3S$: C, 54.78; H, 2.76; N, 19.17%. Found: C, 54.66; H, 2.82; N, 19.18%; ESI mass (*m/z*) Calcd $[C_{10}H_6FN_3S + H]^+$219.03, found 220.2.

6-((4-Trifluoromethyl)phenyl)thiazolo[3,2-b][1,2,4]triazole (5e). This compound was obtained as viscous liquid; yield 70%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.96 (d, $J = 8.2$ Hz, 2H), 8.22 (s, 1H), 8.48 (d, $J = 8.2$ Hz, 3H), 8.49 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 113.8, 125.3, 125.8, 126.8, 129.5, 130.0, 131.3, 156.2, 156.8; *Anal.* Calcd for $C_{11}H_6F_3N_3S$: C, 49.07; H, 2.25; N, 15.61%. Found: C, 49.32; H, 2.18; N, 15.56%; ESI mass (*m/z*) Calcd $[C_{11}H_6F_3N_3S + H]^+$269.02, found 270.2.

4′-(Thiazolo[3,2-b][1,2,4]triazol-6-yl)-[1,1′-biphenyl]-4-sulfonic acid (5g). This compound was obtained as white solid; yield 82%; high melting; IR (KBr) 3183, 1428, 1180 cm^{-1}; ^{1}H NMR

(400 MHz, DMSO-d_6) δ 7.71–7.75 (m, 4H), 7.90 (d, J = 8.3 Hz, 2H), 8.06 (s, 1H), 8.34 (d, J = 8.3 Hz, 2H), 8.47 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 111.2, 126.1, 126.2, 126.7, 126.8, 127.1, 131.1, 139.1, 140.5, 147.6, 156.2. Not all carbons picked up; *Anal*. Calcd for $C_{16}H_{11}N_3O_3S_2$: C, 53.77; H, 3.10; N, 11.76%. Found: C, 53.52; H, 3.38; N, 11.52%; ESI mass (*m*/*z*) Calcd $[C_{16}H_{11}N_3O_3S_2 + H]^+$357.02, found 358.2.

4-(Thiazolo[3,2-b][1,2,4]triazol-6-yl)benzamide (5h). This compound was obtained as white solid; yield 81%; mp 227–228°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.51 (s, 2H), 8.04 (d, J = 7.9 Hz, 2H), 8.11 (s, 1H), 8.31 (d, J = 7.9 Hz, 2H), 8.46 (s,1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 113.0, 126.3, 128.5, 130.4, 131.2, 135.3, 156.6, 157.3, 167.6; *Anal*. Calcd for $C_{11}H_8N_4OS$: C, 54.09; H, 3.30; N, 22.94%. Found: C, 54.28; H, 3.29; N, 22.84%; ESI mass (*m*/*z*) Calcd $[C_{11}H_8N_4OS + H]^+$244.04, found 245.2.

2-Methyl-5-(Thiazolo[3,2-b][1,2,4]triazol-6-yl)benzenesulfonic acid (5i). This compound was obtained as white solid; yield 74%; high melting; IR (KBr) 3335, 2900, 1026 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.60 (s, 3H), 7.34–7.86 (m, 2H), 7.87 (s, 1H), 8.06 (d, J = 7.8 Hz, 1H), 8.44 (s, 1H), 8.52 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 20.1, 110.5, 124.4, 126.4, 131.4, 131.5, 137.5, 146.8, 156.0, 156.6. Not all carbon seen; *Anal*. Calcd for $C_{11}H_9N_3O_3S_2$: C, 44.73; H, 3.07; N, 14.23%. Found: C, 44.56; H, 3.12; N, 14.38%; ESI mass (*m*/*z*) Calcd $[C_{11}H_9N_3O_3S_2 + H]^+$295.01, found 296.2.

6-(3-Chlorophenyl)thiazolo[3,2-b][1,2,4]triazole (5j). This compound was obtained as white solid; yield 71%; mp 163–164° C; IR (KBr) 3064, 1468,1170 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.58–7.64 (m, 2H), 8.15 (s, 1H), 8.21 (d, J = 6.6 Hz, 1H), 8.37 (s, 1H), 8.47 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 112.8, 124.8, 125.7, 129.4, 129.5, 129.9, 130.9, 133.7, 156.2, 156.8; *Anal*. Calcd for $C_{10}H_6ClN_3S$: C, 50.96; H, 2.57; N, 17.83. Found: C, 51.03; H, 2.64; N, 17.58%; ESI mass (*m*/*z*) Calcd $[C_{10}H_6ClN_3S + H]^+$235.00, found 236.3.

6-(3-Nitrophenyl)thiazolo[3,2-b][1,2,4]triazole (5k). This compound was obtained as yellow solid; yield 73%; mp 231–232°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.88–8.37 (m, 3H), 8.52 (s, 1H), 8.64 (d, J = 7.8 Hz, 1H), 9.22 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 114.5, 121.0, 124.5, 129.5, 129.7, 131.0, 132.8, 148.6, 156.8. Not all carbon seen; *Anal*. Calcd for $C_{10}H_6N_4O_2S$: C, 48.78; H, 2.46; N, 22.75%. Found: C, 48.59; H, 2.63; N, 22.81%; ESI mass (*m*/*z*) Calcd $[C_{10}H_6N_4O_2S + H]^+$246.02, found 247.1.

6-(2-Chlorophenyl)thiazolo[3,2-b][1,2,4]triazole (5l). This compound was obtained as white solid; yield 70%; mp 139–140° C; IR (KBr) 3061, 1463,1175 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.53–7.62 (m, 2H), 7.70–7.80 (m, 3H), 8.34 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 115.0, 126.8, 127.5, 128.9, 130.1, 131.8, 132.1, 132.8, 156.1. Not all carbon seen; *Anal*. Calcd for $C_{10}H_6ClN_3S$: C, 50.96; H, 2.57; N, 17.83%. Found: C, 51.06; H, 2.63; N, 17.71%; ESI mass (*m*/*z*) Calcd $[C_{10}H_6ClN_3S + H]^+$235.00, found 236.3.

4-Methoxy-3-(thiazolo[3,2-b][1,2,4]triazol-6-yl)benzenesulfonic acid (5m). This compound was obtained as white solid; yield 72%; high melting; ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.88 (s, 3H), 7.18 (d, J = 8.6 Hz, 1H), 7.71 (d, J = 8.6 Hz, 1H), 7.84 (s, 1H), 8.37 (s, 1H), 8.45 (s, 1H), the acidic hydrogen is not seen; ^{13}C NMR (100 MHz, DMSO-d_6) δ 56.5, 111.5, 114.6, 115.8, 127.2, 128.5, 128.8, 141.1, 156.0, 157.4. Not all carbons seen; *Anal*. Calcd for $C_{11}H_9N_3O_4S_2$: C, 42.44; H, 2.91; N, 13.50%. Found: C, 42.29; H, 3.12; N, 13.49%; ESI mass (*m*/*z*) Calcd $[C_{11}H_9N_3O_4S_2 + H]^+$311.00, found 312.1.

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