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Synthesis of Some Substituted Imidazo Triazolyl-Thiazolidinones

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In this paper, a series of novel clubbed imidazo triazolyl-thiazolidinones compounds were designed which may emerge as potential antimycobacterial agents. The synthesized compounds were characterized by IR, NMR and elemental analysis.

Key Words: Synthesis, Substituted Imidazo-Triazolyl-Thiazolidinones.

INTRODUCTION

Tuberculosis is a contagious disease with comparatively high mortality worldwide. The statistics shows that around three million people throughout the world die annually from tuberculosis[1,2] and there are around eight million new cases each year, out of which developing countries shows major share[3]. In addition, about a third of the world's population harbours a dormant *Mycobacterium tuberculosis* infection, representing a significant reservoir of disease for the future.

The azole antitubercular may be regarded as a new class providing truly effective drugs, which are reported to inhibit bacteria by blocking the biosynthesis of certain bacterial lipids and/or by additional mechanisms[4,5]. Triazole and thiazole derivatives[6-10] represent a novel emerging major chemical group as antimicrobial agent. Triazoles, in particular, substituted-1,2,4-triazoles and the open-chain thiosemicarbazide counterparts of 1,2,4-triazole, are among the various heterocycles that have received the most attention during the last two decades as potential antimicrobial agents[11,12]. Substitutions including thio[13], alkylthio and alkenylthio[14] derivatives have been carried out primarily at the 3-position of the 1,2,4-triazole ring, as potential antimicrobial and antimycobacterial agents will overcome the above-mentioned resistance problems. Thiazole moiety has already been reported for its antimicrobial activity[15,16].

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In recent years, environmentally benign synthetic methods have received considerable attention and solvent-free protocols are reported[17]. A fast, highly efficient and eco-friendly solvent-free chemical transformation, for the synthesis of title compounds, under microwave irradiation, using acidic alumina is designed. Thus in continuation to establish probable pharmacological activities of triazole[17-21] herein, syntheses of new 1,2,4-triazole derivatives clubbed with thiazole moiety were reported. The synthesized compounds were also tested for their antimicrobial activity. The main advantages of the synthetic approach presented here are considerable rate enhancement in comparison with a thermal reaction, improved isolated yields of products and cleaner and environmentally safer reactions.

EXPERIMENTAL

The melting points were recorded on electrothermal apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Bruker Avance 300 MHz instrument using $CDCl_3$ as solvent using TMS as internal standard; the chemical shifts (δ) are reported in ppm and coupling constants (*J*) are given in Hz. Microwave irradiation was carried out in Raga Scientific Microwave Systems, Model RG31L at 2450 MHz. Elemental analyses were performed on a Heracus CHN-Rapid Analyzer. The purity of the compounds was checked on Merck precoated silica gel 60 F-254.

Preparation of [6-(aryl)imidazo[2,1-b]thiazol-3-yl]acetic acid hydrazide (4a-d): Compounds **4a-d** were prepared as per the reported method.

General preparation of 4-amino-6-(aryl)-imidazo[2,1-b]thiazol-3-ylmethyl]-4*H*-[1,2,4]triazole-3-thiol (5a-d): [6-(Aryl)-imidazo[2,1-b]-thiazol-3-yl]acetic acid hydrazide (**4**) (0.1 mol) and KOH (0.15 mol) were of taken in 100 mL of absolute ethanol and kept for stirring at room temperature. Later, CS_2 (0.2 mol) was added to the contents with constant stirring. It results in the formation of yellowish white thick precipitate. Then 150 mL of ethanol was added to the thick slurry and stirred for 14 h in closed condition. After ensuring the absence of **4** on TLC, dry ether was added to this mixture, to precipitate out the salt and filtered. The filtrate is taken with hydrazine hydrate (0.15 mol) and refluxed for 1-3 h and then it was cooled and poured into ice-cold water. The pH was then adjusted to 4-5 by addition of 1:1 HCl. Precipitate formed was filtered and recrystallized in ethanol to get pure **(5a-d)**.

4-Amino-5[6-phenyl-imidazo[2,1-b]thiazol-2-ylmethyl]-4*H*-[1,2,4]triazole-3-thiol (5a): Yield 66 %; m.p. 229-231 ºC; ^{1}H NMR (300 MHz DMSO), δ (ppm): 9.78 (s, 1H, SH), 8.2 (s, 1H, thiazole), 7.03-8.0 (m, 10H, Ar-H, Ar'-H and 1H imidazole), 5.65 (bs, 2H, NH_2), 4.36 (s, 2H, -CH_2-). Anal. cald. (%) for $C_{14}H_{12}N_6S_2$: C, 51.20; H, 3.68; N, 25.59. Found (%): C, 51.45; H, 3.45; N,25.75.

4-Amino-5-[6-*p*-tolyl-imidazo[2,1-b]thiazol-2-ylmethyl]-4*H*-[1,2,4]triazole-3-thiol (5b): Yield 72 %; m.p. 210-212 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.78 (s, 1H, SH), 8.2 (s, 1H, thiazole), 7.03-8.0 (m, 10H, Ar-H, Ar'-H and 1H imidazole), 5.68 (bs, 2H, NH_2), 4.32 (s, 2H, -CH_2-), 2.56 (s, 3H, CH_3) Anal. Calcd. (%) for $C_{15}H_{14}N_6S_2$: C, 52.61; H, 4.12; N, 24.54. Found (%): C, 52.82; H, 4.36; N, 24.68.

4-Amino-5-[6-(4-methoxyphenyl)-imidazo[2,1-b]thiazol-2-ylmethyl]-4*H*-[1,2,4]triazole-3-thiol (5c): Yield 69 %; m.p. 236-238 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.78 (s, 1H, SH), 8.2 (s, 1H, thiazole), 7.03-8.0 (m, 9H, Ar-H, Ar'-H and 1H imidazole), 5.71 (bs, 2H, NH_2), 4.28 (s, 2H, -CH_2-), 3.68 (s, 3H, OCH_3) Anal. calcd. (%) for $C_{15}H_{14}N_6S_2$: C, 52.61; H, 4.12; N, 24.54. Found (%): C, 52.82; H, 4.36; N, 24.68.

4-Amino-5-[6-(4-nitrophenyl)imidazo[2,1-b]thiazol-2-ylmethyl]-4*H*-[1,2,4]triazole-3-thiol (5d): Yield 75 %; m.p. 246-248 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.78 (s, 1H, SH), 7.03-8.4 (m, 10H, Ar-H, Ar'-H, 1H imidazole and 1H, thiazole), 5.74 (bs, 2H, NH_2), 4.32 (s, 2H, -CH_2-), Anal. calcd. (%) for $C_{14}H_{11}N_7O_2S_2$: C, 45.03; H, 2.97; N, 26.26. Found (%): C, 45.27; H, 2.81; N,26.42.

General procedure of 4-(benzylidene-amino)-6-(phenyl-imidazo-[2,1-b]thiazol-3-ylmethyl)-4*H*-[1,2,4]triazole-3-thiol (6a-l): 4-Amino-5-(6-aryl-imidazo[2,1-b]thiazol-3-ylmethyl)-4*H*-[1,2,4]triazole-3-thiol (**5**) (1 mmol) was dissolved in 30 mL of ethanol. A catalytic amount of *p*-toluene sulphonic acid was added. The freshly distilled aromatic aldehyde (1 mmol) was added and refluxed for 1.5 h after ensuring the absence of **5** on TLC. The reaction mixture was cooled and then poured on to crushed ice. The solid obtained was filtered, washed with water and recrystallized in ethanol to afford (**6a-l**).

5-[6-(Phenyl-imidazo[2,1-b]thiazol-2-ylmethyl)-4-{1-phenyl meth-(Z)-ylidene]amino}-4*H*-[1,2,4]triazole-3-thiol (6a): Yield 78 %; m.p. 229-231 ºC; ^{1}H NMR (300 MHZ, DMSO), δ (ppm): 9.78 (s, 1H, SH), 8.2 (s, 1H, thiazole), 7.03-8.10 (m, 12H, Ar-H, Ar'-H, 1H imidazole and 1H, Ar, CH=N), 4.87 (s, 2H, -CH_2-). Anal. calcd. (%) for $C_{14}H_{12}N_6S_2$: C, 51.20; H, 3.68; N, 25.59. Found (%): C, 51.45; H, 3.45; N,25.75.

4-{1-Phenyl meth-(Z)-ylidene]amino}-5-[6-(*p*-tolyl-imidazo[2,1-b]thiazol-2-ylmethyl)-4*H*-[1,2,4]triazole-3-thiol (6b): Yield 80 %; m.p. 229-231 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.71 (s, 1H, SH), 8.31 (s, 1H, thiazole), 6.98-8.12 (m, 10H, Ar-H, Ar'-H, 1H imidazole and 1H, Ar, CH=N), 4.81 (s, 2H, -CH_2-). 2.52 (s, 3H, CH_3) Anal. calcd. (%) for $C_{22}H_{18}N_6S_2$: C, 61.37; H, 4.21; N, 19.52. Found (%): C, 61.23; H, 4.18; N, 19.41.

5-[6-(4-Methoxyphenyl)imidazo[2,1-b]thiazol-2-ylmethyl)-4-{1-phenylmethyl-(Z)-ylidene]amino}-4*H*-[1,2,4]triazole-3-thiol (6c): Yield

81 %; m.p. 229-231 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.81 (s, 1H, SH), 8.31 (s, 1H, thiazole), 6.90-8.17 (m, 11H, Ar-H, Ar'-H, 1H imidazole and 1H, Ar, CH=N), 4.83 (s, 2H, -CH_2-). 3.67 (s, 3H, OCH_3) Anal. calcd. (%) for $C_{22}H_{18}N_6OS_2$: C, 59.16; H, 4.06; N, 18.82. Found (%): C, 59.27; H, 4.16; N, 18.91.

5-[6-(4-Nitrophenyl)imidazo[2,1-b]thiazol-2-ylmethyl)-4-{1-phenyl meth-(Z)-ylidene]amino}-4*H*-[1,2,4]triazole-3-thiol (6d): Yield 64 %; m.p. 229-231 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.85 (s, 1H, SH), 8.31 (s, 1H, thiazole), 7.00 -8.15 (m, 11H, Ar-H, Ar'-H, 1H imidazole and 1H, Ar, CH=N), 4.85 (s, 2H, -CH_2-). Anal. calcd. (%) for $C_{21}H_{15}N_7O_2S_2$: C, 54.65; H, 3.28; N, 21.24. Found (%): C, 54.71; H, 3.22; N, 21.33.

2-{[(Z)-3-Mercapto-5-[6-phenyl-imidazo[2,1-b]thiazol-2-ylmethyl)-4*H*-[1,2,4]triazole-4-ylimino]methyl}phenol (6e): Yield 78 %; m.p. 229-231 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.74 (s, 1H, SH), 8.31 (s, 1H, thiazole), 7.05-8.10 (m, 11H, Ar-H, Ar'-H, 1H imidazole and 1H, Ar, CH=N), 4.89 (s, 2H, -CH_2-) Anal. calcd. (%) for $C_{21}H_{16}N_6OS_2$: C, 58.31; H, 3.73; N, 19.43. Found (%): C, 58.46; H, 3.64; N, 19.56.

2-{[(Z)-3-Mercapto-5-[6-(*p*-tolyl-imidazo[2,1-b]thiazol-2-ylmethyl)-4*H*-[1,2,4]triazole-4-ylimino]methyl}phenol (6f): Yield 81 %; m.p. 229-231 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.78 (s, 1H, SH), 8.31 (s, 1H, thiazole), 6.95-8.15 (m, 10H, Ar-H, Ar'-H, 1H imidazole and 1H, Ar, CH=N), 4.86 (s, 2H, -CH_2-), 2.43 (s, 3H, CH_3). Anal. calcd. (%) for $C_{22}H_{18}N_6OS_2$: C, 59.17; H, 4.06; N, 18.82. Found (%): C, 59.29; H, 3.98; N,18.71

2-{[(Z)-3-Mercapto-5-[6-(4-methoxyphenyl)imidazo[2,1-b]thiazol-2-ylmethyl)-4*H*-[1,2,4]triazole-4-ylimino]methyl}phenol (6g): Yield 74 %; m.p. 229-231 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.80 (s, 1H, SH), 8.27 (s, 1H, thiazole), 7.05-8.00 (m, 10H, Ar-H, Ar'-H, 1H imidazole and 1H, Ar, CH=N), 4.73 (s, 2H, -CH_2-), 3.87 (s, 3H, OCH_3). Anal. calcd. (%) for $C_{22}H_{18}N_6O_2S_2$: C, 57.13; H, 3.92; N, 18.17. Found (%): C, 57.31; H, 3.88; N, 18.30

2-{[(Z)-3-Mercapto-5-6-(4-nitrophenyl)imidazo[2,1-b]thiazol-2-ylmethyl)-4*H*-[1,2,4]triazole-4-ylimino]methyl}phenol (6h): Yield 69 %; m.p. 229-231 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.70 (s, 1H, SH), 8.34 (s, 1H, thiazole), 7.15-8.21 (m, 10H, Ar-H, Ar'-H, 1H imidazole and 1H, Ar, CH=N), 4.71 (s, 2H, -CH_2-). Anal. calcd. (%) for $C_{21}H_{15}N_7O_{32}S_2$: C, 52.82; H, 3.17; N, 20.53. Found (%): C, 52.68; H, 3.07; N, 20.41.

4-{[1-(4-Fluoro phenyl meth-(Z)-ylidene]amino}-5-[6-phenyl imidazo-[2,1-b]thiazol-2-ylmethyl)-4H-[1,2,4]triazole-3-thiol (6i): Yield 77 %; m.p. 229-231 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.80 (s, 1H, SH), 8.23 (s, 1H, thiazole), 7.00-8.10 (m, 11H, Ar-H, Ar'-H, 1H imidazole and 1H, Ar, CH=N), 4.78 (s, 2H, -CH_2-). Anal. calcd. (%) for $C_{21}H_{15}N_6S_2F$: C, 58.05; H, 3.48; N, 19.34. Found (%): C, 58.23; H, 3.57; N,19.19.

4-{[1-(4-Fluoro phenyl meth-(Z)-ylidene]-amino}-5-[6-*p*-tolyl imidazo[2,1-b]thiazol-2-ylmethyl)-4*H*-[1,2,4]triazole-3-thiol (6j): Yield 72 %; m.p. 229-231 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.92 (s, 1H, SH), 8.38 (s, 1H, thiazole), 6.98-8.15 (m, 10H, Ar-H, Ar'-H, 1H imidazole and 1H, Ar, CH=N), 4.82 (s, 2H, -CH_2-). Anal. calcd. (%) for $C_{22}H_{17}N_6S_2F$: C, 58.91; H, 3.82; N, 18.74. Found (%): C, 58.79; H, 3.78; N,18.89.

4-{[1-(4-Fluoro phenyl meth-(Z)-ylidene]amino}-5-[6-(4-methoxy-phenyl)imidazo[2,1-b]thiazol-2-ylmethyl)-4*H*-[1,2,4]triazole-3-thiol (6k): Yield 86 %; m.p. 229-231 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.80 (s, 1H, SH), 8.43 (s, 1H, thiazole), 6.95-8.10 (m, 10H, Ar-H, Ar'-H, 1H imidazole and 1H, Ar, CH=N), 4.74 (s, 2H, -CH_2-), 3.73 (s, 3H, OCH_3) Anal. calcd. (%) for $C_{22}H_{17}N_6OS_2F$: C, 56.88; H, 3.69; N, 18.09. Found (%): C, 56.70; H, 3.78; N,18.23.

4-{[1-(4-Fluoro phenyl meth-(Z)-ylidene]-amino}-5-[6-(4-nitro-phenyl)imidazo[2,1-b]thiazol-2-ylmethyl)-4*H*-[1,2,4]triazole-3-thiol (6l): Yield 88 %; m.p. 229-231 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.75 (s, 1H, SH), 8.50 (s, 1H, thiazole), 6.95-8.25 (m, 10H, Ar-H, Ar'-H, 1H imidazole and 1H, Ar, CH=N), 4.79 (s, 2H, -CH_2-), Anal. calcd. (%) for $C_{21}H_{14}N_7O_2S_2F$: C, 52.60; H, 2.94; N, 20.45. Found (%): C, 52.75; H, 3.03; N,20.56.

General procedure 3-chloro-1-{3-mercapto-5-[6-aryl imidazo[2,1-b]-thiazol-3-ylmethyl]-[1,2,4]triazol-4-yl}-4-aryl-azetidin-2-one (7a-l): 4-(Benzylidene amino)-5-(6-phenyl-imidazo[2,1-b]thiazol-3-ylmethyl)-4*H*-[1,2,4]triazole-3-thiol (**6**) (1 mmol) and triethylamine (2 mmol) were taken in N,N-dimethyl formamide (40 mL). Chloroacetyl chloride (2 mmol) was added drop wise over a period of 0.5 h to the contents and refluxed for 5 h. After ensuring the absence of starting material on TLC the reaction mixture is cooled and salt formed was filtered. The filtrate was concentrated to half of its initial volume and then poured onto crushed ice. The solid product formed was filtered, washed with water and crystallized to furnish pure **(7a-l)**.

3-Chloro-1-{3-mercapto-5-[6-phenyl-imidazo[2,1-b]thiazol-2-ylmethyl]-[1,2,4]triazole-4-yl}-4-phenyl-azetidin-2-one (7a): Yield 68 %; m.p. 453-455 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.78 (s, 1H, SH), 8.2 (s, 1H, thiazole), 7.03-7.65 (m, 10H, Ar-H, Ar'-H and s, 1H imidazole), 4.87 (s, 2H, -CH_2-), 5.50 (d, 1H, azetidinone), 3.55 (d, 1H, azetidinone). Anal. calcd. (%) for $C_{23}H_{17}N_6OS_2Cl$: C, 56.03; H, 3.48; N, 17.05. Found (%): C, 56.21; H, 3.33; N,17.17.

3-Chloro-1-{3-mercapto-5-[6-(*p*-tolyl)-imidazo[2,1-b]thiazol-2-ylmethyl]-[1,2,4]triazole-4-yl}-4-phenyl-azetidin-2-one (7b): Yield 52 %; m.p. 460-462 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.72 (s, 1H, SH), 7.9 (s, 1H, thiazole), 6.92-7.45 (m, 10H, Ar-H, Ar'-H and 1H-imida-

zole), 4.81 (s, 2H, -CH_2-), 4.25 (d, 1H, azetidinone), 3.61 (d, 1H, azetidinone), 2.35 (s, 3H, -CH_3). Anal. calcd. (%) for $C_{24}H_{19}N_6OS_2Cl$: C, 56.85; H, 3.78; N, 16.57. Found (%): C, 56.71; H, 3.86; N,16.71.

3-Chloro-1-{3-mercapto-5-[6-(4-methoxyphenyl)-imidazo[2,1-b]-thiazol-2-yl methyl]-[1,2,4]triazole-4-yl}-4-phenyl-azetidin-2-one (7c): Yield 59 %; mp 233-235 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.74 (s, 1H, SH), 8.00 (s, 1H, thiazole), 7.13-7.55 (m, 10H, Ar-H, Ar'-H and 1H-imidazole), 4.83 (s, 2H, -CH_2-), 5.12 (d, 1H, azetidinone), 3.75 (s, 3H, -OCH_2), 3.59 (d, 1H, azetidinone). Anal. calcd. (%) for $C_{24}H_{19}N_6O_2S_2Cl$: C, 55.11; H, 3.66; N, 16.07. Found (%): C, 55.26; H, 3.74; N,16.21.

3-Chloro-1-{3-mercapto-5-[6-(4-nitrophenyl)-imidazo[2,1-b]thiazol-3-yl methyl]-[1,2,4]triazole-4-yl}-4-phenyl-azetidin-2-one (7d): Yield 69 %; m.p. 217-219 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.74 (s, 1H, SH), 7.05-8.30 (m, 11H, Ar-H, Ar'-H, 1H-imidazole 1H and thiazole), 4.85 (s, 2H, -CH_2-), 5.12 (d, 1H, azetidinone), 3.59 (d, 1H, azetidinone). Anal. calcd. (%) for $C_{23}H_{16}N_7O_3S_2Cl$: C, 51.35; H, 3.00; N, 18.22. Found (%): C, 51.48; H, 3.09; N, 18.34.

3-Chloro-4-(2-hydroxyphenyl)-1-[3-mercapto-5-(6-phenyl-imidazo-[2,1-b]thiazol-2-ylmethyl]-[1,2,4]triazole-4-yl]--azetidin-2-one (7e): Yield 77 %; m.p. 247-249 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.75 (s, 1H, SH) 7.89 (s, 1H, thiazole), 7.15-7.49 (m, 10H, Ar-H, Ar'-H and 1H- imidazole), 5.86 (d, 1H, azetidinone), 4.89 (s, 2H, -CH_2-), 5.10 (bs, 1H, OH), 3.48 (d, 1H, azetidinone). Anal. calcd. (%) for $C_{23}H_{17}N_6O_2S_2Cl$: C, 54.27; H, 3.37; N, 16.51. Found (%): C, 54.39; H, 3.57; N,16.39.

3-Chloro-4-(2-hydroxyphenyl)-1-[3-mercapto-5-(6-*p*-tolyl-imidazo-[2,1-b]thiazol-2-ylmethyl]-[1,2,4]triazole-4-yl]azetidin-2-one (7f): Yield 64 %; m.p. 245-247 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.70 (s, 1H, SH), 8.00 (s, 1H, thiazole), 7.13-7.58 (m, 9H, Ar-H, Ar'-H & 1H-imidazole), 4.86 (s, 2H, -CH_2-), 5.40 (d, 1H, azetidinone), 3.59 (d, 1H, azetidinone), 2.19 (s, 3H, CH_3). Anal. calcd. (%) for $C_{24}H_{19}N_6O_2S_2Cl$: C, 55.11; H, 3.66; N, 16.07. Found (%): C, 55.27; H, 3.55; N,16.19.

3-Chloro-4-(2-hydroxyphenyl)-1-[3-mercapto-5-(6-(4-methoxyphenyl)-imidazo[2,1-b]thiazol-2-ylmethyl]-[1,2,4]triazole-4-yl]azetidin-2-one (7g): Yield 51 %; m.p. 225-227 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.62 (s, 1H, SH), 7.10-8.25 (m, 9H, Ar-H, Ar'-H, 1H-imidazole and 1H, thiazole), 5.75 (d, 1H, azetidinone), 4.73 (s, 2H, -CH_2-), 3.56 (d, 1H, azetidinone). Anal. calcd. for $C_{24}H_{19}N_6O_3S_2Cl$: C, 53.48; H, 3.55; N, 15.59. Found (%): C, 53.32; H, 3.67; N,15.41.

3-Chloro-4-(2-hydroxyphenyl)-1-[3-mercapto-5-(6-(4-nitrophenyl)-imidazo[2,1-b]thiazol-2-ylmethyl]-[1,2,4]triazole-4-yl]azetidin-2-one (7h): Yield 48 %; m.p. 238-240 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.60 (s, 1H, SH), 3.26 (s, 3H, CH_3O), 7.11-7.47 (m, 9H, Ar-H, Ar'-H and

1H-imidazole), 6.42 (s, 1H, thiazole), 5.73 (d, 1H, azetidinone), 5.21 (bs, 1H, OH), 4.71 (s, 2H, -CH_2-), 3.53 (d, 1H, azetidinone). Anal. calcd. (%) for $C_{23}H_{16}N_7O_4S_2Cl$: C, 49.86; H, 2.91; N, 17.70. Found (%): C, 49.97; H, 2.81; N,17.82.

3-Chloro-4-(4-fluorophenyl)-1-[3-mercapto-5-[6-phenyl-imidazo-[2,1-b]thiazol-2-ylmethyl]-[1,2,4]triazole-4-yl]azetidin-2-one (7i): Yield 76 %; m.p. 240-242 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.75 (s, 1H, SH), 7.98 (s, 1H, thiazole), 7.11-7.88 (m, 10H, Ar-H, Ar'-H and 1H-imidazole), 5.69 (d, 1H, azetidinone), 4.78 (s, 2H, -CH_2-), 3.58 (d, 1H, azetidinone). Anal. calcd. (%) for $C_{23}H_{16}N_6OS_2ClF$: C, 54.06; H, 3.16; N, 16.45. Found (%): C, 54.19; H, 3.24; N,16.57.

3-Chloro-4-(4-fluorophenyl)-1-[3-mercapto-5-[6-*p*-tolyl-imidazo-[2,1-b]thiazol-2-ylmethyl]-[1,2,4]triazole-4-yl]azetidin-2-one (7j): Yield 73 %; m.p. 273-275 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.67 (s, 1H, SH), 7.77 (s, 1H, thiazole), 7.00-7.50 (m, 9H, Ar-H, Ar'-H & 1H- imidazole), 5.79 (d, 1H, azetidinone), 4.82 (s, 2H, -CH_2-), 3.48 (d, 1H, azetidinone), 2.43 (s, 1H, CH_3). Anal. calcd. (%) for $C_{24}H_{18}N_6OS_2ClF$: C, 54.90; H, 3.46; N, 16.01. Found (%): C, 54.78; H, 3.37; N, 16.16.

3-Chloro-4-(4-fluorophenyl)-1-[3-mercapto-5-[6-(4-methoxyphenyl-imidazo[2,1-b]thiazol-2-ylmethyl]-[1,2,4]triazole-4-yl]azetidin-2-one (7k): Yield 79 %; m.p. 213-215 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.73 (s, 1H, SH), 7.85 (s, 1H, thiazole), 7.17-7.64 (m, 9H, ArH and 1H imidazole), 4.74 (s, 2H, -CH_2-), 5.76 (d, 1H, azetidinone), 5.27 (bs, 1H, OH),), 3.75 (S, 3H, -OCH_3), 3.59 (d, 1H, azetidinone), Anal. calcd. (%) for $C_{24}H_{18}N_6O_2S_2ClF$: C, 53.28; H, 3.35; N, 15.53. Found (%): C, 53.40; H, 3.28; N, 15.42.

3-Chloro-4-(4-fluorophenyl)-1-[3-mercapto-5-[6-(4-nitrophenyl)-imidazo[2,1-b]thiazol-2-ylmethyl]-[1,2,4]triazole-4-yl]azetidin-2-one (7l): Yield 63 %; m.p. 208-210 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 3.60 (d, 1H, azetidinone), 9.74 (s, 1H, SH), 7.19-8.20 (m, 10H, ArH, 1H imidazole and 1H, thiazole), 4.79 (s, 2H, -CH_2-), 5.44 (d, 1H, azetidinone). Anal. calcd. (%) for $C_{23}H_{15}N_7O_3S_2ClF$: C, 49.69; H, 2.72; N, 17.63. Found (%): C, 49.81; H, 2.80; N, 17.75.

General preparation of 3-[3-mercapto-5-(6-aryl-imidazo[2,1-b]-thiazol-3-ylmethyl) -[1,2,4]triazol-4-yl]-2-aryl-thiazolidin-4-one (8a-l): 4-(Benzylidene-amino)-5-(6-phenyl-imidazo[2,1-b]thiazol-3-ylmethyl)-4*H*-[1,2,4]triazole-3-thiol (1 mmol) was refluxed with mercaptoacetic acid (2 mmol) in the presence of anhyd. aluminium chloride (0.05 g) at 120 ºC for 10-12 h. The reaction mixture was then cooled and triturated with an excess of 10 % sodium bicarbonate solution. The product obtained was filtered, washed several times with water and crystallized.

3-[3-Mercapto-5-(6-phenyl-imidazo[2,1-b]thiazol-2-ylmethyl)-[1,2,4]triazol-4-yl]-2-phenyl-thiazolidin-4-one (8a): Yield 45 %; m.p. 178-180 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.89 (s, 1H, SH), 6.92-7.95 (m, 12H, Ar-H, Ar'-H, 1H-thiazole and 1H-imidazole), 6.65 (s, 1H, thiazolidinone), 4.81 (s, 2H, -CH_2-), 4.22 (s, 2H, thiazolidinone). Anal. calcd. (%) for $C_{23}H_{18}N_6OS_3$: C, 56.31; H, 3.70; N, 17.13. Found (%): C, 56.46; H, 3.61; N, 17.26.

3-[3-Mercapto-5-(6-(*p*-tolyl)-imidazo[2,1-b]thiazol-2-ylmethyl)-[1,2,4] triazol-4-yl]-2-phenyl-thiazolidin-4-one (8b): Yield 51 %; m.p. 203-205 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.83 (s, 1H, SH), 7.80-6.97 (m, 11H, Ar-H, Ar'-H and 1H imidazole, 1H-thiazole), 6.62 (s, 1H, thiazolidinone), 4.85 (s, 2H, -CH_2-), 3.97 (s, 2H, thiazolidinone), 2.35 (s, 3H, CH_3). Anal. cacld. for $C_{24}H_{20}N_6OS_3$: C, 57.12; H, 3.99; N, 16.65. Found (%): C, 57.25; H, 3.87; N, 16.79.

3-[3-Mercapto-5-(6-(4-methoxyphenyl)-imidazo[2,1-b]thiazol-2-ylmethyl)-[1,2,4] triazol-4-yl]-2-phenyl-thiazolidin-4-one (8c): Yield 48 %; m.p. 188-190 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.75 (s, 1H, SH), 7.75-6.90 (m, 11H, Ar-H, Ar'-H and 1H imidazole, 1H-thiazole), 6.56 (s, 1H, thiazolidinone), 4.83 (s, 2H, -CH_2-), 4.10 (s, 2H, thiazolidinone), 3.74 (s, 3H, OCH_3). Anal. calcd. (%) for $C_{24}H_{20}N_5O_2S_3$: C, 55.36; H, 3.87; N, 16.14. Found (%): C, 55.23; H, 3.78; N, 16.27.

3-[3-Mercapto-5-(6-(4-nitrophenyl)-imidazo[2,1-b]thiazol-2-ylmethyl)-[1,2,4]triazol-4-yl]-2-phenyl-thiazolidin-4-one (8d): Yield 54 %; m.p. 230-232 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.8 (s, 1H, SH). 7.00-8.30 (m, 10H, Ar-H, Ar'-H, 1H imidazole and 1H, thiazole), 6.56 (s, 1H, thiazolidinone), 4.88 (s, 2H, -CH_2-), 4.3 (s, 2H, thiazolidinone), 2.56 (s, 3H, CH_3). Anal. calcd. (%) for $C_{23}H_{17}N_7O_3S_3$: C, 51.57; H, 3.20; N, 18.31. Found (%): C, 51.69; H, 3.12; N, 18.19.

2-(2-Hydroxyphenyl)3-[3-mercapto-5-(6-phenyl-imidazo[2,1-b]-thiazol-2-ylmethyl)-[1,2,4]triazol-4-yl]thiazolidin-4-one (8e): Yield 57 %; m.p. 240-242 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.79 (s, 1H, SH). 6.95-7.84 (m, 10H, ArH, Ar'-H, 1H imidazole and 1H, thiazole), 6.72 (s, 1H, thiazolidinone), 5.46 (bs, 1H, OH), 4.82 (s, 2H, -CH_2-), 4.27 (s, 2H, thiazolidinone). Anal. calcd. (%) for $C_{23}H_{18}N_6O_2S_3$: C, 54.53; H, 3.58; N, 16.59. Found: C, 54.67; H, 5.69; N, 16.46.

2-(2-Hydroxyphenyl)3-[3-mercapto-5-(6-*p*-tolyl-imidazo[2,1-b]-thiazol-2-ylmethyl)-[1,2,4]triazol-4-yl]thiazolidin-4-one (8f): Yield 44 %; m.p. 185-187 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.68 (s, 1H, SH), 7.06-7.77 (m, 9H, Ar-H, Ar'-H, 1H-imidazole and 1H-thiazole), 6.73 (s, 1H, thiazolidinone), 4.94 (s, 2H, -CH_2-), 3.94 (s, 2H, thiazolidinone), 2.24 (s, 3H, CH_3). Anal. calcd. (%) for $C_{24}H_{20}N_6O_2S_3$: C, 55.36; H, 3.87; N, 16.14. Found (%): C, 55.49; H, 3.79; N, 16.02.

2-(2-Hydroxyphenyl)3-[3-mercapto-5-(6-(4-methoxyphenyl)-imidazo[2,1-b]thiazol-2-ylmethyl)-[1,2,4]triazol-4-yl]thiazolidin-4-one (8g): Yield 61 %; m.p. 173-175 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.84 (s, 1H, SH), 6.99-7.85 (m, 10H, Ar-H, Ar'-H, 1H-imidazole and 1H-thiazole), 6.64 (s, 1H, thiazolidinone), 4.91 (s, 2H, -CH_2-), 4.40 (s, 2H, thiazolidinone), 3.70 (s, 3H, OCH_3). Anal. calcd. for $C_{24}H_{20}N_6O_3S_3$: C, 53.71; H, 3.76; N, 15.66. Found: C, 53.55; H, 3.68; N, 15.78.

2-(2-Hydroxyphenyl)3-[3-mercapto-5-(6-(4-nitrophenyl)-imidazo-[2,1-b]thiazol-2-ylmethyl)-[1,2,4]triazol-4-yl]thiazolidin-4-one (8h): Yield 58 %; m.p. 235-237 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.88 (s, 1H, SH), 7.05-8.20 (m, 10H, Ar-H, Ar'-H, 1H-imidazole and 1H-thiazole), 6.65 (s, 1H, thiazolidinone), 5.48 (bs, 1H, OH), 4.93 (s, 2H, -CH_2-), 4.29 (s, 2H, thiazolidinone). Anal. calcd. for $C_{23}H_{17}N_7O_4S_3$: C, 50.08; H, 3.11; N, 17.77. Found (%): C, 50.19; H, 3.23; N, 17.68.

2-(4-Fluorophenyl)-3-[3-mercapto-5-(6-phenyl-imidazo[2,1-b]-thiazol-2-ylmethyl)-[1,2,4]triazol-4-yl]thiazolidin-4-one (8i): Yield 73 %; m.p. 213-215 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.81 (s, 1H, SH), 6.95-7.80 (m, 11H, Ar-H, Ar'-H 1H-imidazole and 1H-thiazole), 6.81 (s, 1H, thiazolidinone), 4.76 (s, 2H, -CH_2-), 4.76 (s, 2H, thiazolidinone). Anal. calcd. (%) for $C_{23}H_{17}N_6OS_3F$: C, 54.31; H, 3.37; N, 16.52. Found (%): C, 54.49; H, 3.28; N, 16.41.

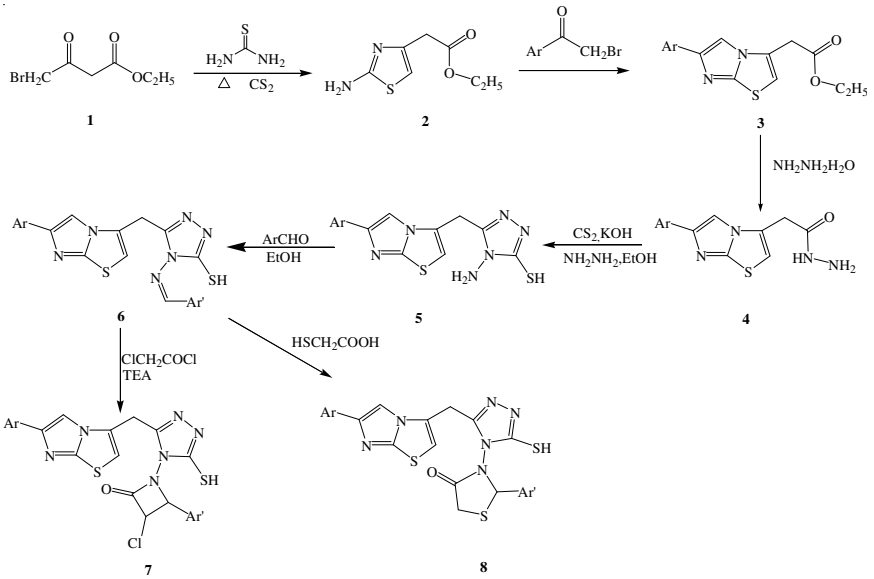
2-(4-Fluorophenyl)-3-[3-mercapto-5-(6-*p*-tolyl-imidazo[2,1-b]-thiazol-2-ylmethyl)-[1,2,4]triazol-4-yl]thiazolidin-4-one (8j): Yield 68 %; m.p. 206-208 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.79 (s, 1H, SH), 7.00-7.88 (m, 10H, Ar-H imidazole and 1H-thiazole), 6.60 (s, 1H, thiazolidinone) 4.74 (s, 2H, -CH_2-), 3.99 (s, 2H, thiazolidinone). 2.35 (s, 3H, CH_3). Anal. calcd. (%) for $C_{24}H_{19}N_6OS_3F$: C, 55.15; H, 3.66; N, 16.08. Found (%): C, 55.29; H, 3.51; N, 16.21.

2-(4-Fluorophenyl)-3-[3-mercapto-5-(6-(4-methoxyphenyl)imidazo-[2,1-b]thiazol-2-ylmethyl)-[1,2,4]triazol-4-yl]thiazolidin-4-one (8k): Yield 58 %; m.p. 195-197 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.82 (s, 1H, SH), 7.80 (s, 1H, thiazole), 6.91-7.52 (m, 9H, ArH and imidazole), 6.58 (s, 1H, thiazolidinone), 4.86 (s, 2H, -CH_2-), 5.53 (bs, 1H, OH), 4.40 (s, 2H, thiazolidinone), 3.70 (s, 3H, OCH_3). Anal. calcd. (%) for $C_{24}H_{19}N_6O_2S_3F$: C, 53.52; H, 3.56; N, 15.60. Found (%): C, 53.68; H, 3.48; N, 15.72.

2-(4-Fluorophenyl)-3-[3-mercapto-5-(6-(4-nitrophenyl)-imidazo-[2,1-b]thiazol-2-ylmethyl)-[1,2,4]triazol-4-yl]thiazolidin-4-one (8l): Yield 52 %; m.p. 182-184 ºC; ^{1}H NMR (300 MHz, DMSO), δ (ppm): 9.86 (s, 1H, SH), 7.92 (s, 1H, thiazole), 7.11-7.77 (m, 9H, Ar-H, Ar'-H and 1H-imidazole), 6.61 (s, 1H, thiazolidinone), 4.88 (s, 2H, -CH_2-), 4.41 (s, 2H, thiazolidinone). Anal. calcd. (%) for $C_{23}H_{16}N_7O_3S_3F$: C, 49.90; H, 2.91; N, 17.71. Found (%): C, 49.77; H, 2.82; N, 17.84.

RESULTS AND DISCUSSION

[6-Aryl imidazo[2,1-b]thiazol-3-yl]acetic acid hydrazides (**4a-d**) were prepared by hydrazinolysization of ethyl 6-(aryl)imidazo[2,1-b]thiazole-3-acetate (**3a-d**), which is obtained by reaction of 2-amino-4-thiazolylacetate (**1**) with bromoacetophenones (**2a-d**) and hydrazine hydrate as per the literature. ^{1}H NMR of compound **4** showed the peaks at 9.4-9.6, 8.19-8.16 and 3.6 ppm for thiazolyl ring proton, NH and NH_2, respectively which can be further confirmed by the disappearance of the peaks at 9.4 and 3.6 ppm on deuteration. The thiocarbazate salts of compound **4** obtained by the treatment with carbon disulphide and potassium hydroxide, was cyclized to traizole derivative **5** by reacting with hydrazine hydrate. The IR spectra of compound **5** showed two characteristic absorption bands, one of which appearing at 2585 cm^{-1} was attributed to SH and at 3200-3300 cm^{-1} was assigned to NH_2. Similarly, ^{1}H NMR spectra synthesized triazole derivatives showed two characteristic broad signals at 5.5-5.7 ppm and the other at 13.8-13.95 ppm for NH_2 and SH proton, these peaks disappeared on deuteration. The reactivity of **5** towards aromatic aldehyde was investigated. Thus the reaction of **5** with araldehyde in refluxing acetic acid afforded 60-70 % yield of the corresponding bezylideneamino derivatives **6**. In ^{1}H NMR a



Ar	Ar′	Ar	Ar′
a) C_6H_5	C_6H_5	g) 4-$OCH_3C_6H_4$	2-OHC_6H_4
b) 4-$CH_3C_6H_4$	C_6H_5	h) 4$NO_2C_6H_4$	2-OHC_6H_4
c) 4-$OCH_3C_6H_4$	C_6H_5	i) C_6H_5	4-FC_6H_4
d) 4-$NO_2C_6H_4$	C_6H_5	j) 4-$CH_3C_6H_4$	4-FC_6H_4
e) C_6H_5	2-OHC_6H_5	k) 4-$OCH_3C_6H_4$	4-FC_6H_4
f) 4-$CH_3C_6H_6$	2-OHC_6H_5	l) 4-$NO_2C_6H_4$	4-FC_6H_4

Scheme-I

singlet around 8.5 ppm for imine proton confirmed the formation of **6**. The Schiff's base **6** on treatment with chloroacetyl chloride in the presence of triethylamiine afforded 2-azetidinones (**7**). Similarly cyclization of **6** with thioglycolic acid afforded corresponding thiazolidinones **8**. Presence of peaks at 4.5-4.7 and 6.7-6.9 ppm for azitidinone ring and 6.5-6.8 and 4.2-4.4 ppm for of thiazolidinone ring in ^{1}H NMR spectra confirmed the formation of compounds **7** and **8** from the Schiff base **6** (**Scheme-I**).

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