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ORIGINAL ARTICLE

# Synthesis, characterization and antimicrobial activity evaluation of new 2,4-Thiazolidinediones bearing imidazo[2,1-*b*][1,3,4]thiadiazole moiety

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**Abstract** The synthesis and antimicrobial activity of 2,4-thiazolidinedione derivatives **5a–g** and **6a–g** are described. The structures of the newly synthesized compounds were confirmed by IR, NMR, mass and elemental analyses. All compounds were evaluated for their preliminary in vitro antibacterial and antifungal activity. The results revealed that most of the compounds showed high or moderate biological activity against tested microorganisms.



## 1. Introduction

The treatment of infectious diseases still remains an important and challenging problem because of a combination factors including emerging infectious diseases and increasing number of multi-drug resistant microbial pathogens with particular relevance for Gram-positive bacteria Tenover and McDonald, 2005; Pfeltz and Wilkinson, 2004; Roberts, 2004; Dessen et al., 2001; Muroi et al., 2004). In spite of the large number of antibiotics and chemotherapeutics available for medical use, the emergence of old and new antibiotic resistant bacterial strains in the last decades constitutes a substantial need for the new class of antibacterial agents (Chopra et al., 2008).

The varied biological activities of rhodanines (2-thioxo-thiazolidin-4-one) and their analogues have been known from the beginning of the 20th century. Rhodanines and 2,4-thiazolidinedione have become a pharmacologically important class of heterocyclic compounds since the introduction of various glitazones and epalrestat in to clinical use for the treatment of type II diabetes and diabetic complications, respectively (Terashima et al., 1984; Yoshioka et al., 1998). Chemical modification of these heterocycles has constantly resulted in compounds with broad spectrum of pharmacological activities. 2,4-Thiazolidinedione derivatives constitute an important class of heterocyclic compounds for which diverse biological properties such as antibacterial and antifungal (Ayhan-Kilcigil and Altanlar, 2000; Heerding et al., 2003; Tuncbilek and Altanlar, 2006; Bozdag-Dundar et al., 2007), antidiabetic (Cantello et al., 1994), cardiotonic (Andreani et al., 1993),

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anti-oedematus and analgesic (De-Lima et al., 1994), cyclooxygenase and lipoxygenase inhibitory (Boschelli et al., 1992) activities have been documented along past decades. On other hand a large number of imidazo[2,1-*b*][1,3,4]-thiadiazoles have been reported to possess various pharmacological properties such as anticancer (Terzioglu and Gursoy, 2003), antitubercular (Kolavi et al., 2006), antibacterial (Gadad et al., 2000), antifungal (Andotra et al., 1997), anticonvulsant, analgesic (Khazi et al., 1996) and antisecretory (Andreani et al., 2000).

In view of the facts mentioned above and as part of our initial efforts to discover potentially active new agents, we report herein the synthesis of 5-substituted-2,4-Thiazolidinedione derivatives and evaluation of their antibacterial and antifungal activities.

## 2. Materials and methods

### 2.1. Materials and reagents

Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. Melting point was determined by electro thermal melting point apparatus and is uncorrected. All reactions were monitored by thin-layer chromatography (TLC) on 0.25 mm silica gel (60GF-254) plates and visualized with UV light. Column chromatography was performed on silica gel (200–300 mesh). Infra red (IR) spectra were recorded on using KBr disk on a Nicolet MX-1 FTIR spectrophotometer, $^1$H NMR spectra were recorded AMX-400 and Bruker-400 liquid-state NMR spectrometer using tetramethylsilane (TMS) as internal standard (chemical shift in δ ppm). Mass spectra were recorded on a JEOL MS-DX-303 spectrometer. Elemental analysis was carried out using a Perkin Elmer 2400-CHN Analyzer. Spectra facilities and elemental analysis were carried out by Sophisticated Analytical Instruments Facility (SAIF) division of Indian Institute of Science, Bangalore, India.

### 2.2. Synthesis

#### 2.2.1. Synthesis of 2,4-thiazolidinedione (*1*)

Thiourea (0.48 mol) was added to a stirred solution of chloroacetic acid (0.5 mol) in concentrated hydrochloric acid (80 ml) and the reaction mixture was heated under reflux for 15 h. On cooling the product was precipitated, filtered, dried and recrystallized from water. Yield 78%; m.p; 123–124 °C.

$^1$H NMR (DMSO-$d_6$) δ in ppm: 12.00 (s, 1H, NH), 4.14 (s, 2H); $^1$H NMR (DMSO-$d_6$) $D_2O$ Exchange experiment δ in ppm: 4.16 (s, 2H); MS: *m/z 116.4* [M].

#### 2.2.2. Synthesis of 2-amino-5-(3,4,5-trimethoxyphenyl)-1,3,4-thiadiazole (*2*)

A mixture of equimolar quantities of 3,4,5-trimethoxy benzoic acid (0.1 mol), thiosemicarbazide (0.1 mol) and phosphorus oxychloride (30 ml) was refluxed gently for half an hour. After cooling, water was added (90 ml) and the mixture was refluxed for 4 h and filtered. The solution was neutralized by saturated solution of potassium hydroxide. The precipitate was filtered and recrystallized from ethanol. Yield 80%; m.p; 205–208 °C.

IR (KBr) cm$^{-1}$; 3590.6 ($NH_2$), 3117 (Ar—CH), 1620 (C═N). $^1$H NMR (DMSO-$d_6$) δ in ppm: 8.85 (s, 2H, —$NH_2$), 6.95 (d, 2H, C2, C6), 3.80 (s, 6H, C3—$OCH_3$, C5—$OCH_3$), 3.83 (s, 3H, C4—$OCH_3$).

#### 2.2.3. General procedure: synthesis of 2-(3,4,5-trimethoxyphenyl) 6-(4'substituted aryl)imidazo[2,1-b]-[1,3,4]-thiadiazoles ***3a–g***

A mixture of equimolar quantities of 2-amino-5-(3,4,5-trimethoxyphenyl)-1,3,4-thiadiazole (0.01 mol) and an appropriate α-bromoketones (0.01 mol) was refluxed in dry ethanol (300 ml) for 10 h. Excess of solvent was removed under reduced pressure the solid hydrobromide salts suspended in water, and neutralized by aqueous sodium carbonate solution to get free base. It was filtered, washed with water, dried and recrystallized from suitable solvent.

*2.2.3.1. 2-(3,4,5-trimethoxyphenyl)-6-phenylimidazo[2,1-b][1,3,4]-thiadiazole (**3a**).* Yield 70%; m.p; 205–208 °C; IR (KBr) cm$^{-1}$; 3095, 3033, 2943, 1576, 1490, 1339, 1130, 843; $^1$H NMR (DMSO-$d_6$) δ in ppm: 8.75 (s, 1H, H-5 imidazole), 7.40 (m, 5H, Ar—H), 7.41 (d, 2H, Ar—H), 3.89 (s, 6H, 2$OCH_3$), 3.70 (s, 3H, $OCH_3$).

*2.2.3.2. 2-(3,4,5-trimethoxyphenyl)-6-(4-methylphenyl)-imidazo[2,1-b][1,3,4]thiadiazole (**3b**).* Yield 71 %; m.p; 136–137 °C; IR (KBr) cm$^{-1}$; 3090, 3025, 2947, 1586, 1489, 1329, 1130, 839; $^1$H NMR (DMSO-$d_6$) δ in ppm: 8.64 (s, 1H, H-5 imidazole), 7.77 (d, 2H, Ar—H), 7.22 (d, 2H, Ar—H), 7.14 (d, 2H, Ar—H), 3.89 (s, 6H, 2$OCH_3$), 3.87 (s, 3H, $OCH_3$), 3.29 (s, 3H, $CH_3$).

*2.2.3.3. 2-(3,4,5-trimethoxyphenyl)-6-(4-methoxyphenyl)-imidazo[2,1-b][1,3,4]thiadiazole (**3c**).* Yield 70%; m.p; 205–208 °C; IR (KBr) cm$^{-1}$; 3085, 3043, 2973, 1596, 1481, 1343, 1150, 843; $^1$H NMR (DMSO-$d_6$) δ in ppm: 8.46 (s, 1H, H-5 imidazole), 7.62 (d, 2H, Ar—H), 7.42 (d, 2H, Ar—H), 7.14 (d, 2H, Ar—H), 3.89 (s, 6H, 2$OCH_3$), 3.87 (s, 3H, $OCH_3$), 3.85 (s, 3H, $OCH_3$).

*2.2.3.4. 2-(3,4,5-trimethoxyphenyl)-6-(4-nitrophenyl)-imidazo-[2,1-b][1,3,4]thiadiazole (**3d**).* Yield 70%; m.p; 205–208 °C; IR (KBr) cm$^{-1}$; 3060, 3021, 2959, 1587, 1494, 1346, 1128, 853; $^1$H NMR (DMSO-$d_6$) in ppm: 8.85 (s, 1H, H-5 imidazole), 8.40 (d, 2H, Ar—H), 8.16 (d, 2H, Ar—H), 8.04 (d, 2H, Ar—H), 3.89 (s, 6H, 2$OCH_3$), 3.70 (s, 3H, $OCH_3$).

*2.2.3.5. 2-(3,4,5-trimethoxyphenyl)-6-(4-bromophenyl)-imidazo-[2,1-b][1,3,4]thiadiazole (**3e**).* Yield 70%; m.p; 188–190 °C; IR (KBr) cm$^{-1}$; 3095, 3043, 2944, 1586, 1490, 1329, 1130, 833; $^1$H NMR (DMSO-$d_6$) δ in ppm: 8.74 (s, 1H, H-5 imidazole), 8.30 (d, 2H, Ar—H), 8.15 (d, 2H, Ar—H), 8.07 (d, 2H, Ar—H), 3.90 (s, 6H, 2$OCH_3$), 3.75 (s, 3H, $OCH_3$).

*2.2.3.6. 2-(3,4,5-trimethoxyphenyl)-6-(4-chlorophenyl)-imidazo-[2,1-b][1,3,4]thiadiazole (**3f**).* Yield 70%; m.p; 205–208 °C; IR (KBr) cm$^{-1}$; 3075, 3053, 2933, 1566, 1490, 1359, 1128, 833; $^1$H NMR (DMSO-$d_6$) δ in ppm: 8.76 (s, 1H, H-5 imidazole), 7.89 (d, 2H, Ar—H), 7.49 (d, 2H, Ar—H), 7.41 (d, 2H, Ar—H), 3.90 (s, 6H, 2$OCH_3$), 3.75 (s, 3H, $OCH_3$).

*2.2.3.7. 2-(3,4,5-trimethoxyphenyl)-6-(6-(2,5-methoxyphenyl)-imidazo[2,1-b][1,3,4]thiadiazole (**3g**).* Yield 70%; m.p; 205–208 °C; IR (KBr) cm$^{-1}$; 3095, 3055, 2983, 1576, 1480, 1339, 1130, 843; $^1$H NMR (DMSO-$d_6$) δ in ppm: 8.56 (s, 1H, H-5 imidazole), 7.65 (m, 3H, Ar—H), 7.24 (d, 2H, Ar—H), 3.89

(s, 6H, 2$OCH_3$), 3.87 (s, 3H, $OCH_3$), 3.85 (s, 3H, $OCH_3$), 3.8 (s, 3H, $OCH_3$).

*2.2.4. General procedure for the synthesis of 6-Aryl-2-(3,4,5-trimethoxyphenyl)imidazo[2,1-b][1,3,4]thiadiazole-5-carbaldehyde* ***4a–g***

Vilsmeier–Haak reagent was prepared by adding phosphoryl chloride (3 ml), in dimethylformamide (20 ml), at 0 °C with stirring. Then appropriately substituted 2-alkyl/aryl-6-arylimidazo[2,1-*b*][1,3,4]thiadiazole (**3a–g** 0.01 mol), was added to the reagent and stirred at 0 °C for 30 min. The mixture was further stirred for 2 h at room temperature and at 60 °C for additional 2 h. The reaction mixture was then poured in sodium carbonate solution and stirred at 90 °C for 2 h. After cooling, the mixture was diluted with water, extracted with chloroform, and collective extract was washed with water and dried over anhydrous sodium sulphate. The residue obtained after the removal of chloroform was recrystallized from suitable solvent to get the crystalline solid.

*2.2.4.1. 6-phenyl-2-(3,4,5-trimethoxyphenyl)imidazo[2,1-b][1,3,4]thiadiazole-5-carbaldehyde (**4a**).* Yield 70%; Dark brown crystals m.p; 180–182 °C; IR (KBr) $cm^{-1}$; 3016, 2840, 2737, 1674, 1130, 732. $^1$H NMR (DMSO-$d_6$) δ in ppm: 10.09 (s, 1H, CHO), 7.60 (m, 5H, Ar—H), 23 (d, 2H, Ar—H), 3.91 (s, 6H, $OCH_3$), 3.89 (s, 3H, $OCH_3$)

*2.2.4.2. 6-(4-methylphenyl)-2-(3,4,5-trimethoxyphenyl)imidazo[2,1-b][1,3,4]thiadiazole-5-carbaldehyde (**4b**).* Yield 70%; colourless crystals m.p; 145–148 °C; IR (KBr) $cm^{-1}$; 3089, 2892, 2765, 1677, 1130, 798. $^1$H NMR (DMSO-$d_6$) δ in ppm: 10.05 (s, 1H, CHO), 7.88 (d, 2H, Ar—H), 8.33 (d, 2H, Ar—H), 7.22 (d, 2H, Ar—H), 3.89 (s, 6H, $OCH_3$), 3.76 (s, 3H, $OCH_3$), 3.29 (s, 3H, $CH_3$)

*2.2.4.3. 6-(4-methoxyphenyl)-2-(3,4,5-trimethoxyphenyl)imidazo[2,1-b][1,3,4]thiadiazole-5-carbaldehyde (**4c**).* Yield 70%; brownish product m.p; 155–157 °C; IR (KBr) $cm^{-1}$; 3087, 2940, 2860, 2798, 1680, 1201, 1167, 823. $^1$H NMR (DMSO-$d_6$) δ in ppm: 10.08 (s, 1H, CHO), 7.67 (d, 2H, Ar—H), 8.43 (d, 2H, Ar—H), 7.24 (d, 2H, Ar—H), 3.90 (s, 6H, $OCH_3$), 3.74 (s, 3H, $OCH_3$), 3.70 (s, 3H, $OCH_3$)

*2.2.4.4. 6-(4-nitrophenyl)-2-(3,4,5-trimethoxyphenyl)imidazo[2,1-b][1,3,4]thiadiazole-5-carbaldehyde (**4d**).* Yield 70%; brownish-yellow crystals m.p; 175–176 °C; IR (KBr) $cm^{-1}$; 3056, 2976, 2835, 2787, 1674, 1204, 1354, 798. $^1$H NMR (DMSO-$d_6$) δ in ppm: 9.55 (s, 1H, CHO), 7.86 (d, 2H, Ar—H), 8.43 (d, 2H, Ar—H), 7.21 (d, 2H, Ar—H), 3.88 (s, 6H, $OCH_3$), 3.87 (s, 3H, $OCH_3$)

*2.2.4.5. 6-(4-bromophenyl)-2-(3,4,5-trimethoxyphenyl)imidazo[2,1-b][1,3,4]thiadiazole-5-carbaldehyde (**4e**).* Yield 70%; light brown crystals m.p; 195–196 °C; IR (KBr) $cm^{-1}$; 3050, 2945, 2854, 2789, 1680, 1167, 843, 788. $^1$H NMR (DMSO-$d_6$) δ in ppm: 9.43 (s, 1H, CHO), 8.29 (d, 2H, Ar—H), 8.15 (d, 2H, Ar—H), 7.20 (d, 2H, Ar—H), 3.87 (s, 6H, $OCH_3$), 3.75 (s, 3H, $OCH_3$)

*2.2.4.6. 6-(4-chlorophenyl)-2-(3,4,5-trimethoxyphenyl)imidazo[2,1-b][1,3,4]thiadiazole-5-carbaldehyde (**4f**).* Yield 70%; dark brown crystals m.p; 176–178 °C; IR (KBr) $cm^{-1}$; 3056, 2894, 2793, 1673, 1203, 1156, 785. $^1$H NMR (DMSO-$d_6$) δ in ppm: 10.09 (s, 1H, CHO), 8.06 (d, 2H, Ar—H), 7.60 (d, 2H, Ar—H), 7.24 (d, 2H, Ar—H), 3.91 (s, 6H, $OCH_3$), 3.89 (s, 3H, $OCH_3$)

*2.2.4.7. 6-(2,5-dimethoxyphenyl)-2-(3,4,5-trimethoxyphenyl)-imidazo[2,1-b][1,3,4]thiadiazole-5-carbaldehyde (**4g**).* Yield 70%; brownish product m.p; 177–178 °C; IR (KBr) $cm^{-1}$; 3076, 2914, 2773, 1669, 1234, 1136, 775.$^1$H NMR (DMSO-$d_6$) δ in ppm: 10.06 (s, 1H, CHO), 7.57 (m, 3H, Ar—H), 7.24 (d, 2H, Ar—H), 3.90 (s, 6H, $OCH_3$), 3.74 (s, 3H, $OCH_3$), 3.50 (s, 3H, $OCH_3$), 3.47 (s, 3H, $OCH_3$)

*2.2.5. General procedure for the synthesis of 5-[(2-(3,4,5-trimethoxyphenyl)-6-arylimidazo[2,1-b][1,3,4]thiadiazol-5-yl)methylidene]-1,3-thiazolidine-2,4-dione* ***5a–g***

A mixture of the 6-Aryl-2-(3,4,5-trimethoxyphenyl) imidazo[2,1-*b*][1,3,4]thiadiazole-5-carbaldehyde **4a–g** (0.001 mol), 2,4-thiazolidinedione (0.001 mol), piperidine (0.001 mol) and acetic acid (0.001 mol) in toluene (50 ml) was heated under reflux with azeotropic removal of water for 16 h. The mixture was cooled to 5 °C; filtration gave crude 5-[(2-(3,4,5-trimethoxyphenyl)-6-arylimidazo[2,1-*b*][1,3,4]thiadiazol-5-yl)methylidene]-1,3-thiazolidine-2,4-dione. The crude product was recrystallized from appropriate solvents.

*2.2.5.1. 5-[(2-(3,4,5-trimethoxyphenyl)-6-phenylimidazo[2,1-b][1,3,4]thiadiazol-5-yl)methylidene]-1,3-thiazolidine-2,4-dione (**5a**).* Yield 77%; light yellow crystals; m.p; 198–200 °C; IR (KBr) $cm^{-1}$; 3395, 3077, 2976, 1730, 1700, 1610, 1330, 1176. $^1$H NMR (DMSO-$d_6$) δ in ppm: 12.50 (s, 1H, NH), 8.10 (d, 2H, Ar—H), 7.77 (s, 1H, R—CH═C, TZD), 7.60 (m, 5H, Ar—H), 3.91 (s, 6H, $OCH_3$), 3.89 (s, 3H, $OCH_3$). Anal. Calcd for ($C_{23}H_{18}N_4O_5S_2$) (%): C, 50.56; H, 3.67; N, 13.33. Found; C, 50.76; H, 3.87; N, 11.37.

*2.2.5.2. 5-{[2-(3,4,5-trimethoxyphenyl)-6-(4-methylphenyl)-imidazo[2,1-b][1,3,4]thiadiazol-5-yl]methylidene}-1,3-thiazolidine-2,4-dione (**5b**).* Yield 75%; light yellow crystals; m.p; 189–191 °C; IR (KBr) $cm^{-1}$; 3380, 3060, 2965, 1725, 1696, 1615, 1330, 1166. $^1$H NMR (DMSO-$d_6$) δ in ppm: 12.40 (s, 1H, NH), 8.12 (d, 2H, Ar—H), 7.74 (s, 1H, R—CH═C,TZD), 7.50 (m, 4H, Ar—H), 3.91 (s, 6H, $OCH_3$), 3.89 (s, 3H, $OCH_3$), 3.49 (s, 3H, $CH_3$). Anal. Calcd for ($C_{24}H_{20}N_4O_5S_2$) (%): C, 56.68; H, 3.96; N, 11.02. Found; C, 50.70; H, 3.99; N, 11.35.

*2.2.5.3. 5-{[2-(3,4,5-trimethoxyphenyl)-6-(4-methoxylphenyl)-imidazo[2,1-b][1,3,4]thiadiazol-5-yl]methylidene}-1,3-thiazolidine-2,4-dione (**5c**).* Yield 70%; yellow crystals; m.p; 205–206 °C; IR (KBr) $cm^{-1}$; 3340, 3080, 2956, 1735, 1698, 1620, 1320, 1156. $^1$H NMR (DMSO-$d_6$) δ in ppm: 12.35 (s, 1H, NH), 8.14 (d, 2H, Ar—H), 7.74 (s, 1H, R—CH═C,TZD), 7.60 (d, 2H, Ar—H), 7.41 (d, 2H, Ar—H), 3.90 (s, 6H, $OCH_3$), 3.89 (s, 3H, $OCH_3$), 3.79 (s, 3H, $OCH_3$). Anal. Calcd for ($C_{24}H_{20}N_4O_6S_2$) (%): C, 54.95; H, 3.84; N, 10.68. Found; C, 54.99; H, 3.88; N, 10.86.

*2.2.5.4. 5-{[2-(3,4,5-trimethoxyphenyl)-6-(4-nitrolphenyl)imidazo[2,1-b][1,3,4]thiadiazol-5-yl]methylidene}-1,3-thiazolidine-2,4-dione (**5d**).* Yield 69%; yellow powder; m.p; 194–195 °C; IR (KBr) $cm^{-1}$; 3360, 3089, 2876, 1730, 1695, 1625, 1323, 1150. $^1$H NMR (DMSO-$d_6$) δ in ppm: 12.25 (s, 1H,

NH), 8.17 (d, 2H, Ar—H), 7.77 (s, 1H, R—CH═C, TZD), 7.59 (d, 2H, Ar—H), 7.49 (d, 2H, Ar—H), 3.91 (s, 6H, $OCH_3$), 3.89 (s, 3H, $OCH_3$), Anal. Calcd for ($C_{23}H_{17}N_5O_7S_2$) (%): C, 51.20; H, 3.18; N, 12.98. Found; C, 51.29; H, 3.19; N, 12.99.

*2.2.5.5. 5-{[2-(3,4,5-trimethoxyphenyl)-6-(4-bromophenyl)imidazo[2,1-b][1,3,4]thiadiazol-5-yl]methylidene}-1,3-thiazolidine-2,4-dione (**5e**)*. Yield 78%; yellowish orange powder; m.p; 210–211 °C; IR (KBr) $cm^{-1}$; 3370, 3069, 2897, 1720, 1695, 1620, 1325, 1155. $^1H$ NMR (DMSO-$d_6$) δ in ppm: 12.20 (s, 1H, NH), 8.27 (d, 2H, Ar—H), 8.12 (d, 2H, Ar—H), 7.67 (s, 1H, R—CH═C, TZD), 7.40 (d, 2H, Ar—H), 3.99 (s, 6H, $OCH_3$), 3.87 (s, 3H, $OCH_3$), Anal. Calcd for ($C_{23}H_{18}BrN_4O_5S_2$) (%): C, 48.17; H, 2.99; N, 9.77. Found; C, 48.29; H, 3.03; N, 8.03.

*2.2.5.6. 5-{[2-(3,4,5-trimethoxyphenyl)-6-(4-chlorophenyl)imidazo[2,1-b][1,3,4]thiadiazol-5-yl]methylidene}-1,3-thiazolidine-2,4-dione (**5f**)*. Yield 78%; light orange solid; m.p; 215–216 °C; IR (KBr) $cm^{-1}$; 3382, 3063, 2957, 1729, 1698, 1627, 1329, 1145. $^1H$ NMR (DMSO-$d_6$) δ in ppm: 12.40 (s, 1H, NH), 8.26 (d, 2H, Ar—H), 8.15 (d, 2H, Ar—H), 7.77 (s, 1H, R—CH═C, TZD), 7.45 (d, 2H, Ar—H), 3.97 (s, 6H, $OCH_3$), 3.89 (s, 3H, $OCH_3$), Anal. Calcd for ($C_{23}H_{18}ClN_4O_5S_2$) (%): C, 52.22; H, 3.24; N, 10.59. Found; C, 52.24; H, 3.26; N, 11.03.

*2.2.5.7. 5-{[2-(3,4,5-trimethoxyphenyl)-6-(2,5-dimethoxylphenyl)imidazo[2,1-b][1,3,4]thiadiazol-5-yl]methylidene}-1,3-thiazolidine-2,4-dione (**5g**)*. Yield 69%; light yellow solid; m.p; 213–215 °C; IR (KBr) $cm^{-1}$; 3362, 3054, 2966, 1733, 1698, 1637, 1339, 1148. $^1H$ NMR (DMSO-$d_6$) δ in ppm: 12.38 (s, 1H, NH), 8.26 (d, 2H, Ar—H), 7.77 (s, 1H, R—CH═C,TZD), 7.45 (m, 3H, Ar—H), 3.92 (s, 6H, $OCH_3$), 3.81 (s, 3H, $OCH_3$), 3.75 (s, 3H, $OCH_3$), 3.73 (s, 3H, $OCH_3$). Anal. Calcd for ($C_{25}H_{22}N_4O_7S_2$) (%): C, 54.14; H, 4.00; N, 10.10. Found; C, 54.16; H, 4.06; N, 10.13.

*2.2.6. General procedure for the synthesis of N-[(dimethylamino)methylidene]-5-[(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-6-arylimidazo[2,1-b][1,3,4]thiadiazole-2-sulfonamide 6a–g*

A mixture of the *N*-(dimethylaminomethylidene)-5-formyl-6-arylimidazo[2,1-b][1,3,4]thiadiazole-2-sulfonamide (0.001 mol), 2,4-thiazolidinedione (0.001 mol), piperidine (0.001 mol) and acetic acid (0.001 mol) in toluene (50 ml) was heated under reflux with azeotropic removal of water for 16 h. The mixture was cooled to 5 °C; filtration gave crude *N*-[-(dimethylamino)methylidene]-5-[-(2,4-dioxo-1,3-thiazolidin-5-ylidene)-methyl]-6-arylimidazo[2,1-b][1,3,4]thiadiazole-2-sulfonamide. The crude product was recrystallized from appropriate solvents.

*2.2.6.1. Synthesis of N-[-(dimethylamino)methylidene]-5-[-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-6-phenylimidazo[2,1-b][1,3,4]thiadiazole-2-sulfonamide (**6a**)*. Condensation of 5-formyl-6-phenylimidazo[2,1-*b*][1,3,4]thiadiazole-2-sulfonamide and 2,4-thiazolidinedione furnished bright yellow crystals of *N*-[-(dimethylamino)methylidene]-5-[-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-6-phenylimidazo[2,1-*b*][1,3,4]-thiadiazole-2-sulfonamide.

Yield 79%; light yellow solid; m.p; 236–238 °C; IR (KBr) $cm^{-1}$; 3407, 3090, 1735, 1699, 1610. $^1H$ NMR (DMSO-$d_6$) δ in ppm: 12.56 (s, 1H, NH), 8.40 (s, 1H, —N═CH—), 7.77 (s, 1H, R—CH═C, TZD), 7.63–7.51 (m, 5H, Ar—H), 3.24 (s, 3H of —$N(CH_3)_2$), 3.07 (s, 3H of —$N(CH_3)_2$). MS: *m/z* 463.53 [M + H]. Anal. Calcd for ($C_{17}H_{14}N_6O_4S_3$) (%): C, 44.15; H, 3.06; N, 18.17. Found; C, 44.00; H, 3.00; N, 18.37.

*2.2.6.2. Synthesis of N-[-(dimethylamino)methylidene]-5-[-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-6-(4-methylphenyl)imidazo[2,1-b][1,3,4]thiadiazole-2-sulfonamide(**6b**)*. Condensation of 5-formyl-6-(4-methylphenyl)imidazo[2,1-*b*][1,3,4]thiadiazole-2-sulfonamide and 2,4-thiazolidinedione furnished yellow crystals of *N*-[(dimethylamino)methylidene]-5-[-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-6-(4-methylphenyl)imidazo[2,1-*b*][1,3,4]thiadiazole-2-sulfonamide.

Yield 80%; light yellow solid; m.p; 260–261 °C; IR (KBr) $cm^{-1}$; 3433, 3080, 1730, 1707, 1612. $^1H$ NMR (DMSO-$d_6$) δ in ppm: 12.56 (s, 1H, NH), 8.38 (s, 1H, —N═CH—), 8.25–8.00 (m, 4H, Ar—H), 7.77 (s, 1H, R—CH═C,TZD), 3.28 (s, 3H, $CH_3$), 3.24 (s, 3H of —$N(CH_3)_2$), 3.03 (s, 3H of —$N(CH_3)_2$), 2.30(s, 3H, Ar—$CH_3$). MS: *m/z* 477.36 [M + H]. Anal. Calcd for ($C_{18}H_{16}N_6O_4S_3$) (%): C, 45.37; H, 3.88; N, 17.63. Found; C, 45.30; H, 3.44; N, 18.66.

*2.2.6.3. Synthesis of N-[-(dimethylamino)methylidene]-5-[-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-6-(4-methoxyphenyl)imidazo[2,1-b][1,3,4]thiadiazole-2-sulfonamide (**6c**)*. Condensation of 5-formyl-6-(4-methoxyphenyl)imidazo[2,1-*b*][1,3,4]thiadiazole-2-sulfonamide and 2,4-thiazolidinedione yielded yellow solid *N*-[-(dimethylamino)methylidene]-5-[-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-6-(4-methoxyphenyl)imidazo[2,1-*b*][1,3,4]thiadiazole-2-sulfonamide.

Yield 81%; light yellow solid; m.p; 262–264 °C; IR (KBr) $cm^{-1}$; 3427, 3085, 2960, 1730, 1707, 1610. $^1H$ NMR (DMSO-$d_6$) δ in ppm: 12.56 (s, 1H, NH), 8.40 (s, 1H, —N═CH—), 7.77 (s, 1H, R—CH═C,TZD), 7.63 (d, 2H, C3, C5, Ar—H), 7.54 (d, 2H, C2, C6, Ar—H), 3.32 (s, 3H, $OCH_3$), 3.24 (s, 3H of —$N(CH_3)_2$), 3.07 (s, 3H of —$N(CH_3)_2$). MS: *m/z* 493.36 [M + H]. Anal. Calcd for ($C_{18}H_{16}N_6O_5S_3$) (%): C, 43.89; H, 3.27; N, 17.06. Found; C, 43.85; H, 3.25; N, 17.14.

*2.2.6.4. Synthesis of N-[-(dimethylamino)methylidene]-5-[-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-6-(4-nitrophenyl)imidazo[2,1-b][1,3,4]thiadiazole-2-sulfonamide (**6d**)*. Condensation of 5-formyl-6-(4-nitroyphenyl)imidazo[2,1-*b*][1,3,4]thiadiazole-2-sulfonamide and 2,4-thiazolidinedione yielded light yellow solid of *N*-[-(dimethylamino)methylidene]-5-[-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-6-(4-nitrophenyl)imidazo[2,1-*b*][1,3,4]thiadiazole-2-sulfonamide.

Yield 83%; light yellow solid; m.p; 258–260 °C; IR (KBr) $cm^{-1}$; 3443, 3080, 1730, 1699, 1615. $^1H$ NMR (DMSO-$d_6$) δ in ppm: 12.56 (s, 1H, NH), 8.40 (s, 1H, —N═CH—), 8.29 (d, 2H, C2, C6–H phenyl), 8.14 (d, 2H, C3, C5 Ar—H), 7.77 (s, 1H, R—CH═C, TZD), 3.28 (s, 3H, $OH_3$), 3.32 (s, 3H of —N ($CH_3$)$_2$), 3.02 (s, 3H of —$N(CH_3)_2$). MS: *m/z 509* [M]. Anal. Calcd for ($C_{17}H_{15}N_7O_6S_3$) (%): C, 40.07; H, 2.97; N, 19.24. Found; C, 44.10; H, 2.97; N, 19.28.

*2.2.6.5. Synthesis of N-[-(dimethylamino)methylidene]-5-[-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-6-(4-bromophenyl)-imidazo[2,1-b][1,3,4]thiadiazole-2-sulfonamide (**6e**)*. Condensation of 6-(4-bromophenyl)-5-formylimidazo[2,1-*b*][1,3,4]thiadiazole-2-sulfonamide and 2,4-thiazolidinedione furnished

light yellow solid of 6-(4-bromophenyl)-*N*-[-(dimethylamino)-methylidene]-5-[-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-imidazo[2,1-*b*][1,3,4]thiadiazole-2-sulfonamide.

Yield 82%; light yellow solid; m.p; 264–266 °C; IR (KBr) $cm^{-1}$; 3426, 3085, 1733, 1710, 1610. $^1H$ NMR (DMSO-$d_6$) δ in ppm: 12.59 (s, 1H, NH), 8.40 (s, 1H, —N═CH—), 7.76 (s, 1H, R—CH═C,TZD), 7.75 (d, 2H, C2, C6, Ar—H), 7.60 (d, 2H, C3, C5–H, Phenyl), 3.28 (s, 3H of $—N(CH_3)_2$), 3.06 (s, 3H of $—N(CH_3)_2$). MS: *m/z* 542.8 [M + H]. Anal. Calcd for ($C_{17}H_{13}BrN_6O_4S_3$) (%): C, 37.71; H, 2.42; N, 15.52. Found; C, 37.69; H, 2.40; N, 15.50.

*2.2.6.6. Synthesis of N-[-(dimethylamino)methylidene]-5-[-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-6-(4-chlorophenyl)imidazo[2,1-b][1,3,4]thiadiazole-2-sulfonamide (**6f**).* Condensation of 6-(4-chlorophenyl)-5-formylimidazo[2,1-*b*][1,3,4]thiadiazole-2-sulfonamide and 2,4-thiazolidinedione furnished yellow crystals of 6-(4-chlorophenyl)-*N*-[-(dimethylamino)methylidene]-5-[-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]imidazo[2,1-*b*][1,3,4]thiadiazole-2-sulfonamide.

Yield 80%; light yellow solid; m.p; 272–274 °C; IR (KBr) $cm^{-1}$; 3434, 3085, 1730, 1698, 1610. $^1H$ NMR (DMSO-$d_6$) δ in ppm: 12.60 (s, 1H, NH), 8.46 (s, 1H, —N═CH—), 7.75 (s, 1H, R—CH═C,TZD), 7.68 (d, 2H, C2, C, Ar—H), 7.66 (d, 2H, C3, C5, Ar—H), 3.28 (s, 3H of $—N(CH_3)_2$), 3.06 (s, 3H of $—N(CH_3)_2$). MS: *m/z* 496.9 [M + H]. Anal. Calcd for ($C_{17}H_{13}ClN_6O_4S_3$) (%): C, 41.09; H, 2.64; N, 16.91. Found; C, 41.00; H, 2.60; N, 16.94.

*2.2.6.7. Synthesis of N-[-(dimethylamino)methylidene]-5-[-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-6-(2,5-methoxyphenyl)imidazo[2,1-b][1,3,4]thiadiazole-2-sulfonamide (**6g**).* Condensation of 5-formyl-6-(2,5-dimethoxyphenyl)imidazo[2,1-*b*][1,3,4]thiadiazole-2-sulfonamide and 2,4-thiazolidinedione yielded light yellow solid *N*-[-(dimethylamino)-methylidene]-5-[-(2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-6-(4-methoxyphenyl)imidazo[2,1-*b*][1,3,4]thiadiazole-2-sulfonamide.

Yield 78%; light yellow solid; m.p; 261–262 °C; IR (KBr) $cm^{-1}$; 3430, 3080, 2955, 1725, 1706, 1610. $^1H$ NMR (DMSO-$d_6$) δ in ppm: 12.60 (s, 1H, NH), 8.64 (s, 1H, —N═CH—), 7.67 (s, 1H, R—CH═C, TZD), 7.50 (m, 3H, Ar—H), 3.38 (s, 3H, $OCH_3$), 3.32 (s, 3H, $OCH_3$), 3.24 (s, 3H of $—N(CH_3)_2$), 3.07 (s, 3H of $—N(CH_3)_2$). MS: *m/z 553.46* [M + H]. Anal. Calcd for ($C_{19}H_{18}N_6O_6S_3$) (%): C, 43.67; H, 3.47; N, 16.08. Found; C, 43.85; H, 3.48; N, 16.01.

## 3. Antimicrobial activity

### 3.1. Microbiology

For the antibacterial and antifungal activity, the compounds were dissolved in dimethylsulfoxide (DMSO). Further dilutions of the compounds and standard drugs in the test medium were prepared at the required quantities of 256, 128, 64, 32, 16, 8, 4, 2, 1 μg/ml concentrations with Mueller–Hinton broth and Sabouraud dextrose broth. The minimum inhibitory concentrations (MIC) were determined using the twofold serial dilution technique (National Committee for Clinical Laboratory Standards, 2000). A control test was also performed containing inoculated broth supplemented with only DMSO at the same dilutions used in our experiments and found inactive in the culture medium. All the compounds were tested for their in vitro growth inhibitory activity against different bacteria and fungi.

### 3.2. Antibacterial and antifungal activity

The cultures were obtained from Mueller–Hinton broth for all the bacterial strains after 24 h of incubation at 37 ± 1 °C. Fungi were maintained in Sabouraud dextrose broth after incubation for 24 h at 25 ± 1 °C. Testing was carried out in Mueller–Hinton broth and Sabouraud dextrose broth at pH 7.4 and the twofold serial dilution technique was applied. The final inoculum size was $10^5$ CFU/ml for the antibacterial assay and $10^4$ CFU/ml for the antifungal assay. A set of tubes containing only inoculated broth was used as controls. For the antibacterial assay after incubation for 24 h at 37 ± 1 °C and after incubation for 48 h at 25 ± 1 °C for antifungal assay, the tube with no growth of microorganism was recorded to represent the MIC expressed in μg/ml. Every experiment in the antibacterial and antifungal assay was replicated twice.

## 4. Results and discussion

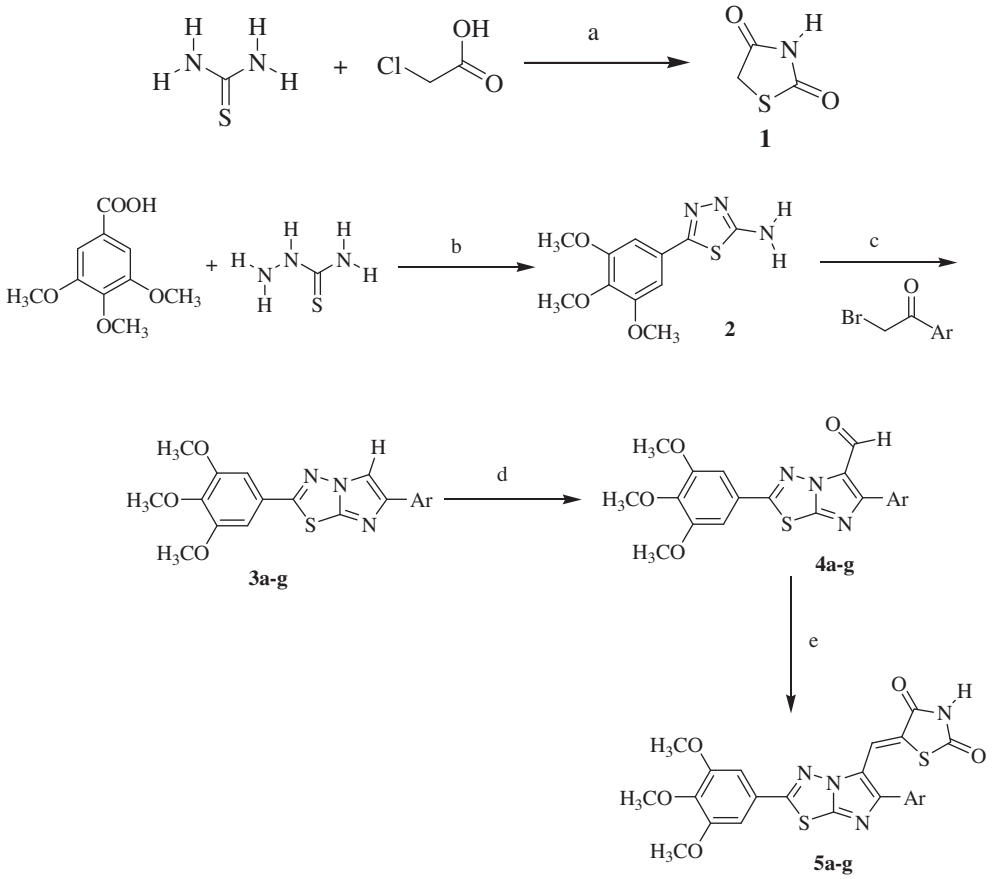
### 4.1. Chemistry

The synthetic route of the compounds (**5a–g** and **6a–g**) is outlined in Schemes 1 and 2, respectively. The 2,4-thiazolidinedione **1** was prepared by cyclisation of equimolar quantities of chloroacetic acid and thiourea by published procedures (Andreani et al., 1993). 2-Amino-5-(3,4,5-trimethoxyphenyl)-1,3,4-thiadiazole **2** was obtained by direct cyclisation of a 3,4,5-trimethoxy benzoic acid and thiosemicarbazide in the presence of phosphorus oxychloride, the latter refluxed with substituted α-haloaryl ketones in dry ethanol yielded the imidazothiadiazoles (**3a–g**) in good yield. It is well established that this reaction proceeds via the intermediate iminothiadiazole antibacterial (Gadad et al., 2000), which undergoes dehydrocyclisation to form the desired fused heterocycle under reflux temperature spontaneously. The electronic and steric factors at 5th position of 2-Amino-5-substituted-1,3,4-thiadiazole are crucial in determining the course of its reaction with substituted α-haloaryl ketones. The strongly electronegative groups impart less nucleophilic character to the nitrogen at 4th position of the 1,3,4-thiadiazole. Various α-haloaryl ketones were prepared by the bromination of the corresponding ketones.

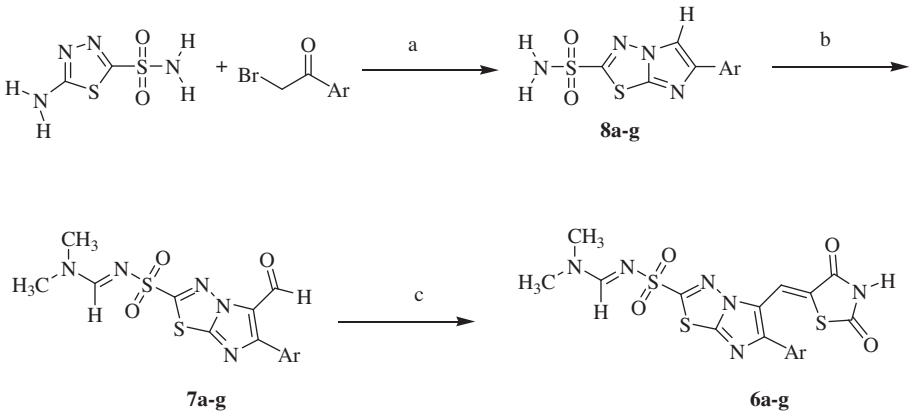
Vilsmeier–Haack reaction of imidazothiadiazoles (**3a–g**) in dimethylformamide and phosphorus oxychloride provided 6-Aryl-2-(3,4,5-trimethoxyphenyl) imidazo[2,1-*b*][1,3,4]thiadiazole–5-carbaldehyde derivatives (**4a–g**). The compounds (**7a–g**) were prepared by the multi-step reaction protocol as previously reported antibacterial (Gadad et al., 2000),

Thus, obtained imidazo[2,1-*b*][1,3,4]thiadiazoles-5-carbaldehydes (**4a–g**) and (**7a–g**) were subjected to Knoevenagel condensation with 2,4-thiazolidinedione in the presence of catalytic amount of piperidine and acetic acid to afford 5-substituted-2,4-Thiazolidinediones (**5a–g**) and (**6a–g**), respectively.

The formation of 2-Aminothiadiazole (**2**) by the reaction between 3,4,5-trimethoxy benzoic acid and thiosemicarbazide was confirmed by IR spectra, which showed the presence of



**Scheme 1** Reagents: (a) HCl (b) phosphorus oxychloride, 5 h, 80%; (c) dry ethanol, 10 h, 80–85%; (d) Vilsmeiere–Haack reagent, 8 h, 78–86%; (e) **1**, piperidine, acetic acid, toluene, 10 h, 85–90%.



**Scheme 2** Reagents: (a) dry ethanol, 10 h, 80–85%; (b) Vilsmeiere–Haack reagent, 8 h, 78–86%; (c) **1**, piperidine, acetic acid, toluene, 10 h, 85–92%.

amine (—$NH_2$) band and the absence of carbonyl stretching of carboxylic acid. Structures of imidazothiadiazole derivatives ( **3a–g**) were established by the absence of amine (—$NH_2$) band in IR spectra and appearance of imidazole proton (H-5) around δ 8.6 in the $^1$H NMR spectra. IR spectra of aldehydes (**4a–g**) displayed a sharp band for carbonyl stretching frequency ($\nu_{c=o}$) around 1675 $cm^{-1}$ and the signal for imidazole proton (H-5) in $^1$H NMR spectrum was absent. A new signal for aldehydic proton was observed around δ 10.00 in the $^1$H NMR spectra, thus substantiating the formation of imidazo[2,1-b][1,3,4]thiadiazole-5-carbaldehydes. The absence of aldehydic protons and presence of the methylidene proton around δ 7.7 in $^1$H NMR spectra of the product supported the formation of the title compounds (**5a–g**) and (**6a–g**). The

**Table 1** Physical Constants of the compounds **5a–g** and **6a–g**.

| Compounds | Ar | Yield (%) | m.p. (°C) | Molecular Formula |
|---|---|---|---|---|
| **5a** | $C_6H_5$ | 77 | 198–200 | $C_{23}H_{18}N_4O_5S_2$ |
| **5b** | 4-$CH_3$·$C_6H_4$ | 75 | 189–191 | $C_{24}H_{20}N_4O_5S_2$ |
| **5c** | 4-$OCH_3$·$C_6H_4$ | 70 | 205–206 | $C_{24}H_{20}N_4O_6S_2$ |
| **5d** | 4-$NO_2$·$C_6H_4$ | 69 | 194–195 | $C_{23}H_{17}N_5O_7S_2$ |
| **5e** | 4-Br·$C_6H_4$ | 78 | 210–211 | $C_{23}H_{18}$ $BrN_4O_5S_2$ |
| **5f** | 4-Cl·$C_6H_4$ | 78 | 215–216 | $C_{23}H_{18}$ $ClN_4O_5S_2$ |
| **5g** | 2,5-$(OCH_3)C_6H_3$ | 69 | 213–215 | $C_{25}H_{22}N_4O_7S_2$ |
| **6a** | $C_6H_5$ | 79 | 236–238 | $C_{17}H_{14}N_6O_4S_3$ |
| **6b** | 4-$CH_3$·$C_6H_4$ | 80 | 260–261 | $C_{18}H_{16}N_6O_4S_3$ |
| **6c** | 4-$OCH_3$·$C_6H_4$ | 81 | 262–264 | $C_{18}H_{16}N_6O_5S_3$ |
| **6d** | 4-$NO_2$·$C_6H_4$ | 83 | 258–260 | $C_{17}H_{15}N_7O_6S_3$ |
| **6e** | 4-Br·$C_6H_4$ | 82 | 264–266 | $C_{17}H_{13}BrN_6O_4S_3$ |
| **6f** | 4-Cl·$C_6H_4$ | 80 | 272–274 | $C_{17}H_{13}ClN_6O_4S_3$ |
| **6g** | 2,5-$(OCH_3)C_6H_3$ | 78 | 261–262 | $C_{19}H_{18}N_6O_6S_3$ |

**Table 2** Inhibitory activity of compounds **5a–g** and **6a–g** expressed as minimum inhibitory concentration (MIC) in μg/mL.

| Compounds | Ar | E.c | P.a | S.a | E.f | C.a | C.n | A.f | A.n |
|---|---|---|---|---|---|---|---|---|---|
| **5a** | $C_6H_5$ | 128 | 64 | 64 | 64 | 64 | 32 | 32 | 64 |
| **5b** | 4-$CH_3$·$C_6H_4$ | 256 | 256 | 64 | 64 | 64 | 32 | 32 | 64 |
| **5c** | 4-$OCH_3$·$C_6H_4$ | 256 | 256 | 64 | 64 | 64 | 64 | 64 | 32 |
| **5d** | 4-$NO_2$·$C_6H_4$ | 256 | 256 | 64 | 64 | 16 | 64 | 08 | 64 |
| **5e** | 4-Br·$C_6H_4$ | 256 | 256 | 32 | 32 | 4 | 8 | 4 | 4 |
| **5f** | 4-Cl·$C_6H_4$ | 128 | 64 | 32 | 32 | 4 | 8 | 32 | 32 |
| **5g** | 2,5-$(OCH_3)C_6H_3$ | 128 | 128 | 64 | 128 | 32 | 64 | 64 | 64 |
| **6a** | $C_6H_5$ | 128 | 32 | 8 | 4 | 1 | 2 | 4 | 4 |
| **6b** | 4-$CH_3$·$C_6H_4$ | 64 | 64 | 32 | 32 | 64 | 64 | 32 | 64 |
| **6c** | 4-$OCH_3$·$C_6H_4$ | 64 | 64 | 32 | 32 | 64 | 32 | 64 | 32 |
| **6d** | 4-$NO_2$·$C_6H_4$ | 64 | 64 | 32 | 64 | 32 | 64 | 64 | 32 |
| **6e** | 4-Br·$C_6H_4$ | 64 | 64 | 8 | 8 | 4 | 8 | 4 | 4 |
| **6f** | 4-Cl·$C_6H_4$ | 64 | 64 | 8 | 4 | 32 | 64 | 32 | 4 |
| **6g** | 2,5-$(OCH_3)C_6H_3$ | 128 | 128 | 64 | 64 | 32 | 8 | 32 | 64 |
| Ampicillin | | 2 | 2 | 1 | 2 | NT | NT | NT | NT |
| Ketoconazole | | NT | NT | NT | NT | 2 | 1 | 2 | 1 |

NT, not tested; E.c, *Escherichia coli*; P.a, *Pseudomonas aeruginosa*; S.a, *Staphylococcus aureus*; E.f, *Enterococcus faecalis*; C.a, *Candida albicans*; C.n, *Cryptococcus neoformans*; A.f, *Aspergillus flavus*; A.n, *Aspergillus niger*.

mass spectra and elemental analysis of these compounds further confirmed the assigned structures. The physical data and the yield of the synthesized compounds are given in Table 1.

### *4.2. Antimicrobial activity*

The synthesized compounds were tested for their in vitro antibacterial activity against the Gram-positive *Staphylococcus aureus* (ATCC25923), *Enterococcus faecalis* (ATCC35550), Gram-negative *Escherichia coli* (ATCC35218), *Pseudomonas aeruginosa* (ATCC25619) bacteria and *Candida albicans* (ATCC2091), *Aspergillus flavus* (NCIM No. 524), *Aspergillus niger* (ATCC6275), and *Cryptococcus neoformans* (Clinical isolate) fungi. The MIC values were determined by using the two-fold serial dilution technique (National Committee for Clinical Laboratory Standards, 2000) in Mueller–Hinton broth and Sabouraud dextrose agar for the antibacterial and antifungal assays, respectively. Ampicillin was used as the reference antibacterial agents; ketoconazole was used as the reference antifungal agents. All the biological results of the tested compounds are given in Table 2. The combined data were reported that the synthesized compounds **5a–g** and **6a–g** showing MIC values between 4–256 μg/ml and 4–64 μg/ml, respectively.

The investigation of antimicrobial screening revealed that some of the tested compounds showed moderate to good bacterial and fungal inhibition. Particularly compounds **5e**, **5f**, **6a**, **6b**, **6c**, **6e** and **6f** have shown good activity against *S. aureus* and *E. faecalis* with MIC values between 4 and 32 μg/ml. All compounds were active against tested fungal strains at 1–64 μg/ml concentration. Some of the compounds **5e**, **5f**, **6a** and **6e** showed good antifungal activity against *C. albicans* at 1–4 μg/ml and **5e**, **6a** and **6e** against *C. neoformans*. *A. flavus*. *A. niger* at 2–8 μg/ml concentration. Compound **5f** is active against *C. neoformans* at 8 μg/ml and **6f** against *A. niger* at 4 μg/ml concentration. From the results, it is evident that the presence of 6-p-chlorophenyl and 6-p-bromophenyl derivatives showed increased activity in series of 5-[(2-(3,4,5-trimethoxyphenyl)-6-arylimidazo[2,1-*b*][1,3,4]thiadiazol-5-yl)methylidene]-1,3-thiazolidine-2, 4-dione **5a–g** in case *N*-[(dimethylamino)methylidene]-5-[(2,4-dioxo-1,3-thiazolidin-5-ylidene)-methyl]-6-arylimidazo[2,1-b][1,3,4]thiadiazole-2-sulfonamide **6a–g** series 6-phenyl, 6-p-chlorophenyl and 6-p-bromophenyl derivatives showed very good biological activity.

## 5. Conclusion

We have synthesized series of novel 5-substituted-2,4-Thiazolidinedione derivatives. The results of antimicrobial screening revealed the discovery of new compounds series of antibacterial and antifungal agents. The mode of action of these compounds was unknown. This observation may promote a further development of this group of 2,4-Thiazolidinediones may lead to compounds with better pharmacological profile than standard antibacterial and antifungal drugs.

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