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MEDICINAL CHEMISTRY RESEARCH

ORIGINAL RESEARCH

4-Thiazolidinone and 1-thia-3,4,9-triaza fluorene conjugates: synthesis, characterization and antimicrobial screening

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Abstract Some novel 4-thiazolidinone derivatives have been synthesized by the condensation of isatin/5-chloroisatin with thiosemicarbazide to yield thiosemicarbazones, which were then cyclized to form corresponding thia-3,4,9-triaza-fluoren-2-ylamines. These were reacted with substituted aldehydes to give corresponding Schiff bases, which were cyclized using thioglycolic acid in the presence of zinc chloride to obtain the 4-thiazolidinone derivatives. All the synthesized compounds were characterized by spectral (IR, MS and NMR) and elemental analysis. The compounds were screened for their antibacterial activity against Gram-positive bacteria (*B. subtilis*, *S. aureus*, *B. pumilus* and *M. luteus*), Gram-negative bacteria (*P. aeruginosa*, *E. coli* and *P. fluorescens*) and for antifungal activity against *A. niger* and *P. chrysogenum* by agar-diffusion method. The minimum inhibitory concentrations of these compounds were also determined by tube dilution method. The antimicrobial effectiveness of all the compounds was found to be concentration dependent. Two compounds—2-methyl-3-(1-thia-3, 4, 9-triaza-fluoren-2-yl)-thiazolidin-4-one (**7aI**) and 2-naphthalen-1-yl-3-(1-thia-3, 4, 9-tri aza-fluoren-2-yl)-thiazolidin-4-one (**7aII**)—exhibited good antibacterial activity. The antibacterial activity of all the compounds was found to be better than the antifungal activity.

Keywords Antimicrobial agents · Isatin · 4-Thiazolidinone · Thiosemicarbazone · Fluorene

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Introduction

The 4-thiazolidinones are the derivatives of thiazolidine with the carbonyl group at the 4-position, belonging to an important group of heterocyclic compounds containing sulphur and nitrogen in a five membered ring. 4-Thiazolidinone template is one of the privileged structure fragments in modern medicinal chemistry considering its broad pharmacological activity (Verma and Saraf, 2008) and affinity for various biotargets as antimicrobial (Vicini *et al.,* 2006; Bondock *et al.,* 2007; Pooja *et al*., 2011a, b), anti-inflammatory (Ottana *et al.,* 2005), anti-HIV (Rawal *et al.,* 2005, 2007a, b, 2008a, b; Rao *et al.*, 2003, 2004), anti-tuberculosis (Babaoglu *et al.,* 2003), anti-convulsant (Capan *et al.,* 1996; Gursoy *et al.,* 2005; Ergenc *et al.,* 1999), etc. Isatin is an endogenous compound, i.e. derivative of indigo dye isolated in 1988 (Sridhar *et al.,* 2001). The chemistry of isatin and its derivatives is particularly interesting because of their potential application in medicinal chemistry. 2-Amino-11-hydronaphtho[2,1:5,6]pyrano[4,3-*d*]thiazole on treatment with isatin, chloroacetyl chloride and mercaptoacetic acid affords corresponding *N*[naphtha [1,2b] pyrano3,4d]thiazol-8-yl]spiro-[3*H*-indole-(1H,2H)3,4-(2H)-3chloroazetidine-2, 2-diones and *N*[naphtha [1, 2b]pyrano[3,4-d]thiazol-8-yl] spirol-[3*H*-indole-(1H, 2H)-3,2-(4H)-thiazolidine]-2,4-dione with good antimicrobial activity (Pai *et al.*, 2006). Jarrahpour *et al.* (2007) synthesized bis-Schiff bases of isatin by condensation of isatin, benzylisatin and 5-fluoroisatin with primary aromatic amines which possess significant antiviral, antibacterial and antifungal activity. Bhambi *et al.* (2009) synthesized 3′{4(1acetyl-5(4-flurophenyl)-2pyrazoline-3yl) phenyl}1-*N*-ethoxyphthalimido-4′-spiro[indole-3,2′-[1,3] thiazolidene]-2,4′-1*H*-dione, which was formed by reacting 3{4-(1-acetyl-5-(4-chlorophenyl)-2pyrazoline-3-yl)phenyl}-4′*H*-spiro[indole-3,2′-[1,3]thiazolidene]-2,4′-1*H*-dione, in DMF

and sodium hydride, which showed good antibacterial activity. Bis-Schiff bases, *N*-Mannich bases, phthalimidoxy substituted and spiro-thiazolidinone derivatives of isatin possess antimicrobial activity against a variety of Gram-positive bacteria, Gram-negative bacteria and some fungi (Pal *et al*., 2011). Bhati *et al.* (2008) synthesized various derivatives of 4-thiazolidinones with Schiff and Mannich bases of isatin and screened them for their anti-inflammatory, ulcerogenic and analgesic activities. In the present study, the compounds are conjugates of two heterocyclic moieties, i.e. isatin and thiazolidinone (Scheme 1), and are being investigated for their antimicrobial activity.

Materials and methods

Chemistry

All the chemicals and solvents used in the study were procured as LR grade from S. D. Fine Chem. Ltd., Mumbai and Sigma-Aldrich Chemie, Germany. Thin layer chromatography (TLC) was used for monitoring the progress of the reactions and product formation. The TLC of the synthesized compounds was carried out on 0.25 mm precoated plates of silica gel $60F_{254}$, E. Merck, Darmstadt, Germany with different solvent systems. Spots were detected under UV lamp (short and long wavelengths) and in an iodine chamber. The melting points were determined by open capillary method and are uncorrected. Infrared spectra (ν_{max} in cm^{-1}) of the synthesized compounds were recorded on Shimadzu FTIR-8400S and Perkin Elmer 881in the range of 400–4000 cm^{-1} in potassium bromide. Mass spectra were recorded on a JEOL SX 102/DA-600 instrument using direct analysis in real time (DART) method and fast atomic bombardment (FAB) method. ^{1}HNMR spectra (ppm, δ) were recorded on a Brucker ADVANCE DRX 300 MHz/200 MHz spectrometer, with TMS as the internal standard. Microanalyses for C, H, and N were performed on an Elementar Vario EL III at SAIF, Central Drugs Research Institute, Lucknow, India. Turbidity measurements were made on a Shimadzu 1700 UV-Visible spectrophotometer.

*General procedure for the synthesis of thiosemicarbazone derivatives (**3a–b**)*

Equimolar quantities (0.004 mol) of isatin/5-substituted isatin (**1a–b**) and thiosemicarbazide (**2**) were dissolved in 90 % ethanol and refluxed for 1 h in the presence of a few drops of glacial acetic acid. The completion of the reaction was checked by TLC using solvent system chloroform: methanol (95:5). Excess ethanol was distilled off and the residue was poured into ice water. The solid product was filtered, washed with water, dried and recrystallized using ethanol.

*3-Thiosemicarbazido indole-2-one (**3a**)* Yield 80.10 %, melting range 180–183 °C; IR (KBr) 1132, 1593 & 1466, 1674, 1593, and 3172 cm^{-1}; ms: *m/z* 221 [M + 1]. *Anal.* Calcd. for $C_9H_8N_4OS$: C, 49.08; H, 3.66; N, 25.44; O, 7.26; S, 14.56.

*5-Chloro-3-thiosemicarbazido-indole-2,3,-dione (**3b**)* Yield 68.35 %, melting range 155–160 °C; IR (KBr) 1049, 1134, 1612 & 1470, 1687, 1470, 3163 and 3478 cm^{-1}; ms: *m/z* 255 [M + 1]. *Anal.* Calcd. for $C_9H_7ClN_4OS$: C, 42.44; H, 2.77; Cl, 13.92; N, 22.00; O, 6.28; S, 12.59.

*General procedure for the synthesis of thia-3,4, 9-triaza-fluoren-2-ylamine derivatives (**4a–b**)*

Equimolar quantities of **3a–b** and 4–5 drops of cold conc. H_2SO_4 were dissolved in ethanol and refluxed for about 8 h. The completion of the reaction was checked by TLC using chloroform:methanol (98:2) as the solvent system. The reaction mixture was cooled and neutralized with liquor ammonia. The neutralized mixture was then poured into ice water, filtered, dried and recrystallized using rectified spirit.

*1-Thia-3,4,9-triaza-fluoren-2-ylamine (**4a**)* Yield 45.40 %, melting range 230–235 °C; IR (KBr) 3421, 3336, 1623, 1701, 3176 and 3421 cm^{-1}; ms: *m/z* 255 [M + 2]. *Anal.* Calcd. for $C_9H_6N_4S$: C, 53.45; H, 2.99; N, 27.70; S, 15.86.

*6-Chloro-1-thia-3,4,9-triaza-fluoren-2-ylamine (**4b**)* Yield 59.35 %, melting range 170–175 °C; IR (KBr) 3421, 3342, 1611, 1689, 3414 and 3161 cm^{-1}; ms: *m/z* 237 [M+2]. *Anal.* Calcd. for $C_9H_5ClN_4S$: C, 45.67; H, 2.13; Cl, 14.98; N, 23.67; S, 13.55.

*General procedure for the synthesis of Schiff base derivatives (**6aI–6aIII** and **6bI–6bIII**)*

Equimolar quantities of **4a–b** and appropriate aldehydes were dissolved in 20 mL of absolute ethanol, in the presence of 5–6 drops of glacial acetic acid, and the reaction mixture was refluxed till the completion of the reaction. The completion of the reaction (8–9 h) was checked by TLC using chloroform: methanol (95:5) as the solvent system. The hot mixture was then poured onto crushed ice. The crude product so obtained was purified by recrystallization from ethanol.

Ethylidene-(1-thia-3,4,9-triaza-fluoren-2-yl)-amine ***(6aI)*** Yield 77.45 %, melting range 260–265 °C; IR (KBr) 1595, 1689 and 3247 cm^{-1}; ms: *m/z* 229 [M+1]. *Anal.* Calcd. for $C_{11}H_8N_4S$: C, 57.88; H, 3.53; N, 24.54; S, 14.05.

Naphthalen-1-ylmethylene-(1-thia-3,4,9-triaza-fluoren-2-yl)-amine ***(6aII)*** Yield 61.23 %, melting range 190–195 °C; IR (KBr) 1595, 1689 and 3247 cm^{-1}; ms: *m/z* 341 [M+1]. *Anal.* Calcd. for $C_{20}H_{12}N_4S$: C, 70.57; H, 3.55; N, 16.46; S, 9.42.

Pyridin-2-ylmethylene-(1-thia-3,4,9-triaza-fluoren-2-yl)-amine ***(6aIII)*** Yield 55.65 %, melting range 176–180 °C; IR (KBr) 1620, 1720, 3174 and 3421 cm^{-1}; ms: *m/z* 292 [M+1]. *Anal.* Calcd. for $C_{15}H_9N_5S$: C, 61.84; H, 3.11; N, 24.04; S, 11.01.

6-Chloro-1-thia-3,4,9-triaza-fluoren-2-yl-ethylidene-amine ***(6bI)*** Yield 77.85 %, melting range 210–215 °C; IR (KBr) 1624, 1701, 3173 and 3422 cm^{-1}; ms: *m/z* 263 [M+1]. *Anal.* Calcd. for $C_{11}H_7ClN_4S$: C, 50.29; H, 2.69; Cl, 13.49; N, 21.33; S, 12.21.

6-Chloro-1-thia-3,4,9-triaza-fluoren-2-yl-naphthalen-1-ylmethylene-amine ***(6bII)*** Yield 88.35 %, melting range 225–230 °C; IR (KBr) 1632, 1710, 3175 and 3428 cm^{-1}; ms: *m/z* 375 [M+1]. *Anal.* Calcd. for $C_{20}H_{11}ClN_4S$: C, 64.08; H, 2.96; Cl, 9.46; N, 14.95; S, 8.55.

6-Chloro-1-thia-3,4,9-triaza-fluoren-2-yl-pyridin-2-ylmethylene-amine ***(6bIII)*** Yield 69.33 %, melting range 200–205 °C; IR (KBr) 1636, 1723, 3110 and 3437 cm^{-1}; ms: *m/z* 326 [M+1]. *Anal.* Calcd. for $C_{15}H_8ClN_5S$: C, 55.30; H, 2.48; Cl, 10.88; N, 21.50; S, 9.84.

*General procedure for the synthesis of thiazolidin-4-one derivatives (**7aI–7aIII** and **7bI–7bIII**)*

Equimolar quantities of **6aI–6aIII** and **6bI–6bIII** were dissolved in 50 mL of methanol. An equimolar quantity of thioglycolic acid was also added dropwise, in the presence of anhydrous zinc chloride and the mixture was refluxed till the completion of the reaction. The completion of the reaction was checked by TLC using different solvent systems. Excess of ethanol was distilled off and the residue was poured into ice water. The solid product was filtered, washed with water, dried and recrystallized using ethanol.

2-Methyl-3-(1-thia-3,4,9-triaza-fluoren-2-yl)-thiazolidin-4-one ***(7aI)*** Crystalline solid, yield 40.12 %, melting range 230–232 °C; IR (KBr) 1485, 1620, 1672 and 3193 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ, ppm): 1.25 (s, 3H), 2.96–2.97 (s, 2H), 3.61–3.75 (s, 1H), 6.0–7.787 (m, 4H); ms: *m/z* 301 *Anal.* Calcd. for $C_{13}H_{10}N_4OS_2$: C, 51.64; H, 3.33; N, 18.53. Found: C, 51.88; H, 3.97; N,18.86.

2-Naphthalen-1-yl-3-(1-thia-3,4,9-tri aza-fluoren-2-yl)-thiazolidin-4-one ***(7aII)*** Amorphous powder, yield 45.27 %, melting range 250–255 °C; IR (KBr) 1483, 1618, 1678 and 3193 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ, ppm): 3.23 (s, 2H), 5.76 (s, 1H), 7.10–7.77 (m, 11H); ms: *m/z* 413 *Anal.* Calcd. for $C_{22}H_{14}N_4OS_2$: C, 63.75; H, 3.40; N, 13.52. Found: C, 62.93; H, 3.23; N, 13.12.

2-Pyridin-2-yl-3-(1-thia-3,4,9-triaza-fluoren-2-yl)-thiazolidin-4-one ***(7aIII)*** Crystalline solid, yield 36.87 %, melting range 210–211 °C; IR (KBr) 1453, 1593, 1620 and 1693 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ, ppm): 3.29–3.48 (s, 2H), 5.70–5.88 (s, 1H), 7.01–7.87(m, 8H); ms: *m/z* 365 *Anal.* Calcd. for $C_{17}H_{11}N_5OS_2$. C, 55.87; H, 3.03; N, 19.16. Found: C, 55.15; H, 3.94; N, 19.78.

3-(6-Chloro-1-thia-3,4,9-triaza-fluoren-2-yl)-2-methyl-thiazolidin-4-one ***(7bI)*** Crystalline solid, yield 56.55 %, melting range 295–297 °C; IR (KBr): 767, 1378, 1443, 1474, 1611 and 1688 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ, ppm): 1.25 (s, 3H); 3.58 (s, 1H); 5.92 (s, 1H); 7.26–7.68 (m, 4H); ms: *m/z* 335. *Anal.* Calcd. for $C_{13}H_9ClN_4OS_2$. C, 46.36; H, 2.69; N, 16.63. Found: C, 46.23; H, 2.25; N, 16.38.

3-(6-Chloro-1-thia-3,4,9-triaza-fluoren-2-yl)-2-naphthalen-1-yl-thiazolidin-4-one ***(7bII)*** Crystalline solid, yield 50.23 %, melting range 265–268 °C; IR (KBr) 767, 1365, 1440, 1473, 1611 and 1688 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ, ppm): 3.83 (s, 1H); 5.58 (s, 1H); 7.26–7.89 (m, 11H); ms: *m/z* 447. *Anal.* Calcd. for $C_{22}H_{13}ClN_4OS_2$. C, 58.86; H, 2.92; N, 12.48. Found: C, 58.21; H, 2.79; N, 12.98.

3-(6-Chloro-1-thia-3, 4, 9-triaza-fluoren-2-yl)-2-pyridin-2-yl-thiazolidin-4-one ***(7bIII)*** Crystalline solid, yield 30.23 %, melting range 280–284 °C; IR (KBr) 761, 1465 and 1634 cm^{-1}. ^{1}H-NMR ($CDCl_3$, δ, ppm): 3.19 (s, 1H); 5.57 (s, 1H); 6.89–7.68 (m, 8H); ms: *m/z* 401. *Anal.* Calcd. for $C_{17}H_{10}ClN_5OS_2$. C, 51.06; H, 2.52; N, 17.51. Found: C, 51.69; H, 2.34; N, 17.98.

Microbiological activities

Test microorganisms

The standard strains were procured from the microbial type culture collection (MTCC), Institute of Microbial Technology, Chandigarh, India. The antibacterial activities of the synthesized compounds were screened against the

bacterial strains: *Bacillus pumilus* (MTCC 1456), *Pseudomonas fluorescens* (MTCC 2421), *Micrococcus luteus* (MTCC 1538), *Pseudomonas aeruginosa* (MTCC 424), *Escherichia coli* (MTCC 1573), *Bacillus subtilis* (MTCC 441) and *Staphylococcus aureus* (MTCC 1430). For antifungal screening *Penicillium chrysogenum* (MTCC 161), *Aspergillus niger* (MTCC 2546) were selected.

Antimicrobial screening

Compounds **7aI–7aIII** and **7bI–7bIII** were dissolved in 10 % DMSO at the concentrations of 100, 250, 500, 750, 1,000, 1,250 μg/mL. Norfloxacin and fluconazole were used as the standard drugs for antibacterial and antifungal studies, respectively. Nutrient broth suspension of test microorganism (10 mL) was added to 100 mL of sterile molten nutrient agar growth media (cooled to 45 °C), mixed well and poured into sterile petri plates. The agar was allowed to solidify and was then punched to make six wells/cups using a 6 mm sterile cork borer (separate borer for each organism) to ensure proper distribution of wells in periphery and one in centre. Agar plugs were removed and 50 μl solutions of test samples (each compound in six concentrations) was poured into the corresponding marked well by micropipettes. Triplicate plates of each organism were prepared. The plates were left at room temperature for 2 h to allow diffusion of samples and then incubated face upward, at corresponding temperature of each organism for 48 h (Gautam *et al.*, 2010). The diameters of zone of inhibition were measured to the nearest millimeters (the cup size also included) and are presented in Table 1.

Minimum inhibitory concentration (MIC)

A series of glass tubes containing different concentrations of the synthesized compounds (in dimethyl sulphoxide) with Mueller–Hinton broth was inoculated with the required quantity of the inoculum to obtain a suspension of microorganism which contains 10^5 colony forming units per millilitre. One growth control tube was prepared with the addition of the compound and one blank tube was prepared without the addition of the microorganism. The tubes were incubated at 37 °C for 24 h. The turbidity produced in each tube was recorded by using a UV-visible spectrometer (Agrawal *et al.,* 2011; Pandey *et al.,* 2011). The observed MICs (μg/mL) are presented in Table 2.

Results and discussion

Six novel 4-thiazolidinones of isatin were synthesized by the fusion of two heterocyclic moieties. These compounds were characterized using IR, ^{1}H-NMR, mass-spectroscopy and elemental analysis. The IR spectrum of the synthesized compounds revealed the presence of C–S–C functional group at 761–856, C–N at 1,440–1,485, C=C at 1,611–1,634, C=O at 1,672–1,694 and C–H at 3,060–3,247 cm^{-1}. In ^{1}H-NMR spectra, δ values of the synthesized compounds were found in the range of 1.25–3.83 for alkyl protons and 6.89–7.89 for aromatic protons. M^+ and M+1 peak were observed in mass spectra of the synthesized compounds. Percentage of the carbon, hydrogen, and nitrogen in all the compounds was determined by microanalysis. The compounds were screened for antimicrobial activity against four Gram-positive bacteria, three Gram-negative bacteria and two fungal strains. The MICs of all the active compounds were also determined by tube dilution method. All the compounds (**7aI–7aIII** and **7bI–7bIII**) were found more effective against Gram-negative strains than Gram-positive strains. The cell wall of Gram-negative bacteria is high in lipid content and low in peptidoglycan. On the other hand, the cell wall of the Gram-positive bacteria is low in lipid content and high in peptidoglycan. Compounds which were more lipophilic may have more penetration into the Gram-negative bacteria than the Gram-positive bacteria. Therefore, the compounds show better activity against Gram-negative strains than Gram-positive strains. Compound **7aI** exhibited good antibacterial activity, having MIC 30 μg/mL, against *Bacillus subtilis, Pseudomonas aeruginosa, Pseudomonas fluorescens* and *Bacillus pumilus*. Compound **7aII** was found to be the most effective against *B. pumilus* having lowest MIC (20 μg/mL) and good activity against *Bacillus subtilis, Pseudomonas aeruginosa, Pseudomonas fluorescens* and *Escherichia coli* having MIC 40–50 μg/mL. Two bacterial strains (*B. pumilus* and *Pseudomonas aeruginosa*) were found to be most sensitive against all the compounds at 20–50 μg/mL. *Staphylococcus aureus* was found to be the least sensitive strain against all the synthesized compounds. The antibacterial activity of all the compounds was found to be better than antifungal activity. The antibacterial activity of the compounds was in the order of **7aI > 7aII > 7bII > 7aIII > 7bI > 7bIII**. The antifungal activity was in the order of **7aIII = 7bII > 7bIII > 7aII > 7aI = 7bI**.

Conclusion

The present research encompasses the syntheses of some thiazolidinone analogs of 1-thia-3,4,9-triaza fluorene of thiazolidinones and their antimicrobial potential. The compounds were screened for antimicrobial activity by cup-plate and tube dilution methods. All the compounds

Table 1 Mean diameter of zone of inhibition (mm) of synthesized compounds (**7aI–7aIII** and **7bI–7bIII**), standard and control against various microorganisms

S. no.	Compounds (mol. wt.)	Conc. (μg/mL)	Gram +ve strains				Gram –ve strains			Fungal strains	
			BS	SA	BP	ML	PA	EC	PF	AN	PC
1.	**7aI** (302.37)	100	10	–	7	8	8	7	8	–	–
		250	13	–	9	10	11	10	10	–	–
		500	15	8	12	12	12	13	13	8	10
		750	18	11	18	14	15	15	17	11	12
		1,000	20	15	22	17	20	18	21	14	15
		1,250	22	17	25	19	24	20	24	17	17
2.	**7aII** (414.50)	100	8	–	6	–	7	8	7	–	–
		250	10	8	8	–	10	10	10	–	8
		500	13	10	11	8	13	12	14	8	9
		750	15	12	15	11	15	13	16	10	10
		1,000	17	14	20	14	17	15	19	15	12
		1,250	20	18	26	16	20	18	22	19	15
3.	**7aIII** (365.43)	100	8	–	8	–	7	7	7	–	–
		250	10	8	10	8	9	9	10	8	9
		500	12	9	15	11	13	13	13	11	12
		750	13	10	17	14	15	15	15	14	13
		1,000	15	12	19	15	18	18	18	15	15
		1,250	18	15	21	17	22	22	20	17	17
4.	**7bI** (336.82)	100	8	–	8	–	7	9	–	–	–
		250	10	8	10	–	9	11	7	–	–
		500	15	10	12	10	14	14	8	10	12
		750	17	13	13	14	17	17	12	13	14
		1,000	19	15	15	17	18	19	15	15	18
		1,250	21	19	18	19	20	21	19	17	20
5.	**7bII** (448.95)	100	–	–	8	–	8	7	8	–	–
		250	7	–	10	–	10	10	11	8	8
		500	11	6	13	8	12	13	12	11	11
		750	15	8	15	12	13	15	15	13	15
		1,000	18	10	17	15	15	17	20	15	15
		1,250	20	15	20	20	18	20	24	18	18
6.	**7bIII** (399.88)	100	–	–	10	–	7	–	7	–	–
		250	7	7	13	7	10	11	8	9	9
		500	9	9	15	8	13	12	11	12	12
		750	14	11	18	12	15	15	15	15	15
		1,000	19	13	20	15	18	20	17	18	18
		1,250	22	17	23	19	20	23	21	20	20
7.	Norfloxacin (319.34)	10	25	22	30	24	26	25	27	–	–
8.	Fluconazole (306.27)	10	–	–	–	–	–	–	–	22	23
9.	Control	–	–	–	–	–	–	–	–	–	–

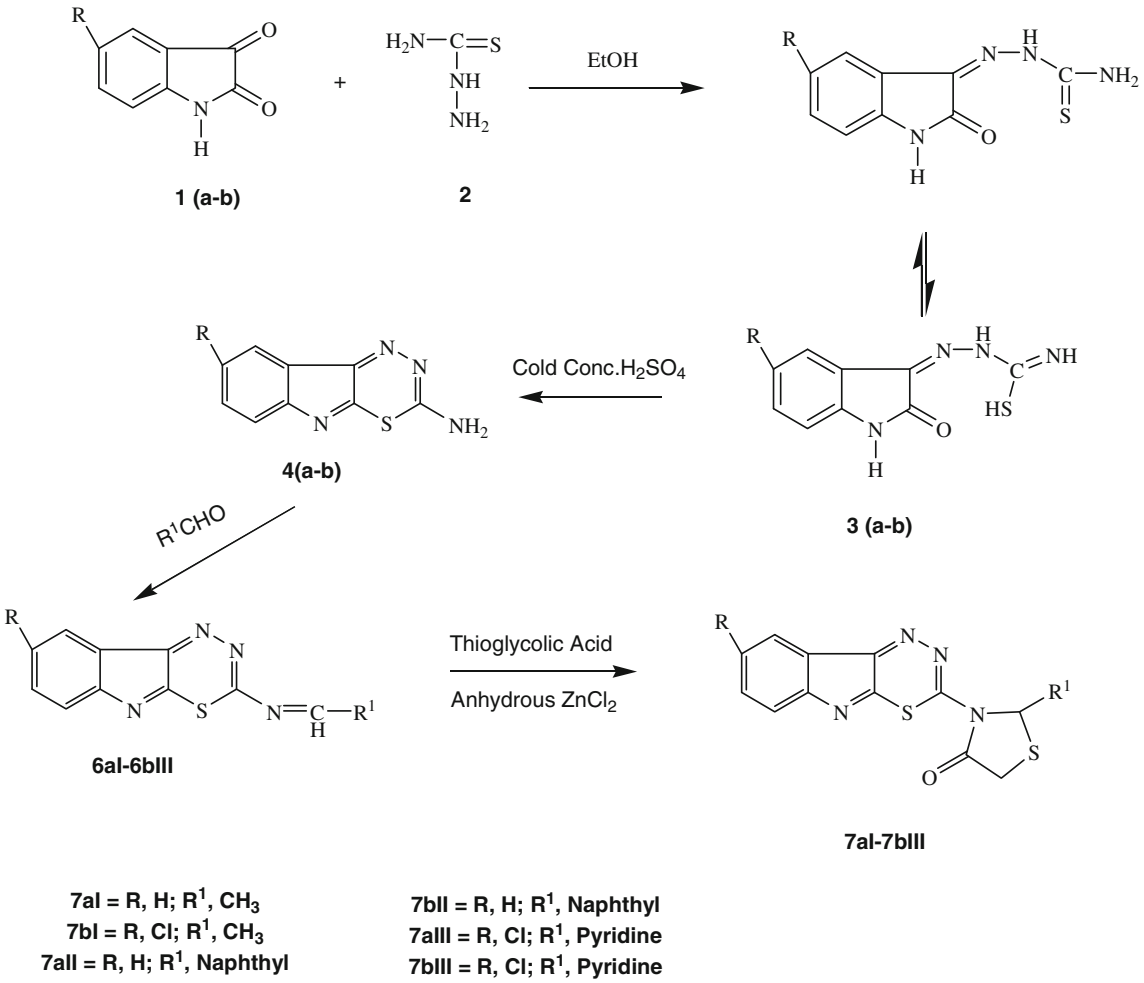
BS B. subtilis, SA S. aureus, BP B. pumilus, ML M. luteus, PA P. aeruginosa, EC E. coli , PF P. fluorescens, AN A. niger, PC P. chrysogenum
Control = 10 % v/v DMSO, (–) = no activity

exhibited more pronounced antibacterial activity than antifungal activity. The methyl and naphthyl substitutions at position-2 of the thiazolidinone ring resulted in better activity. Also, substitution with chlorine on position-6 of the 1-thia-3,4,9-triaza fluorene ring resulted in lowering of the activity. These findings lead to the conclusion that the

Table 2 Values of the minimum inhibitory concentration of the synthesized compounds and reference standards

S. no.	Strain	MIC of compounds (μg/mL)							
		7aI	7aII	7aIII	7bI	7bII	7bIII	N	F
1	*Bacillus subtilis*	30	40	40	50	150	150	2.5	–
2	*Staphylococcus aureus*	250	200	200	150	150	250	5	–
3	*Bacillus pumilus*	30	20	50	40	40	50	1.25	–
4	*Escherichia coli*	40	50	40	30	30	150	–	–
5	*Pseudomonas fluorescens*	30	40	50	150	40	50	2.5	–
6	*Micrococcus luteus*	40	250	250	150	150	250	2.5	–
7	*Pseudomonas aeruginosa*	30	40	30	50	40	30	2.5	–
8	*Aspergillus niger*	250	250	150	250	150	200	–	2.5
9	*Penicillium chrysogenum*	250	200	150	250	150	200	–	1.25

N Norfloxacin, *F* Fluconazole



Scheme 1 Synthesis of N-substituted thiazolidinones

more active analogs were the more lipophilic ones, thereby suggesting that better permeation through the microbial cell-wall could be the reason for this. Thus, lipophilic conjugates of thiazolidinone and 1-thia-3,4,9-triaza fluorene could be the potential antimicrobial agents of the future.

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