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Synthesis and antibacterial activities of *N*-chloro aryl acetamide substituted thaizole and 2,4-thazolidinedione derivatives

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ABSTRACT

A new series of 2-(2,4-dioxo-5-[4-(4-phenyl-thiazol-2-ylsulfamoyl)-benzylidene]-thiazolidin-3-yl)-n-phenyl-acetamide have been synthesized by the condensation of 2-amino-4-aryl thiazole and 4'-chlorosulphonyl benzylidine-2,4-thiazolidinedione. The novel compounds structure has been established on the basis of their substituted N-chloro aryl acetamide derivatives. All the compounds were characterized by elemental analysis, FT-IR, and ^{1}H-NMR spectroscopy. These new compounds were evaluated for their in vitro antibacterial activity against Staphylococcus Aureus, Bacillus Subtilis, Escherichia Coli, and Pseudomonas Aeruginosa.

Keywords: Thiazole, 2,4-thiazolidinedione, synthesis, antibacterial.

INTRODUCTION

The synthesis of thiazole and their derivatives have got significant awareness because of a large number of natural products and drugs comprises of this heterocyclic moviety [1,2]. The 4-thiazolidinone derivatives are known to possess antimycobacterial [3-4], anti-fungal [5], anti-tuberculosis [6-7], anti-convulsant [8], anti-inflammatory [9-11] and anti-HIV [12-14] activities. Thiazolidinediones and thiazolidones were the first parent compounds in which thiazole ring was recognized [15]. Brown reported in 1961 brief view on the close structural relationship among the various 2,4-Thiazolidinediones [16]. In the present work, we have synthesized 4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-*N*-(4-phenyl-thiazol-2-yl)-benzenesulfonamide and its *N*-chloro aryl acetamide derivatives. The synthesized compounds were examined for their antimicrobial activity against several bacteria (*Staphyloccoccus aureus* MTCC 96, *Bacillus subtilis* MTCC

619, *Escherichia coli* MTCC 739 and *Pseudomonas aeruginosa* MTCC 741 using the Kirby Bauer disk diffusion method. A general structure of synthesized compound is given in figure 1.

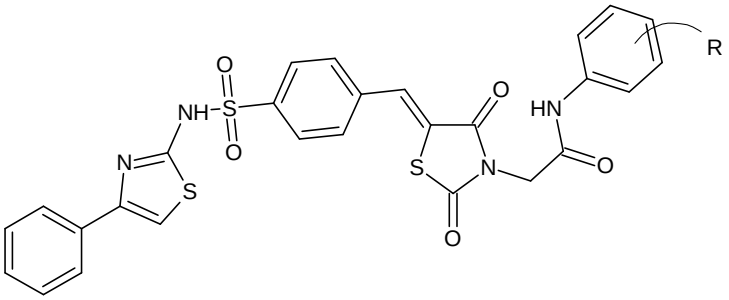
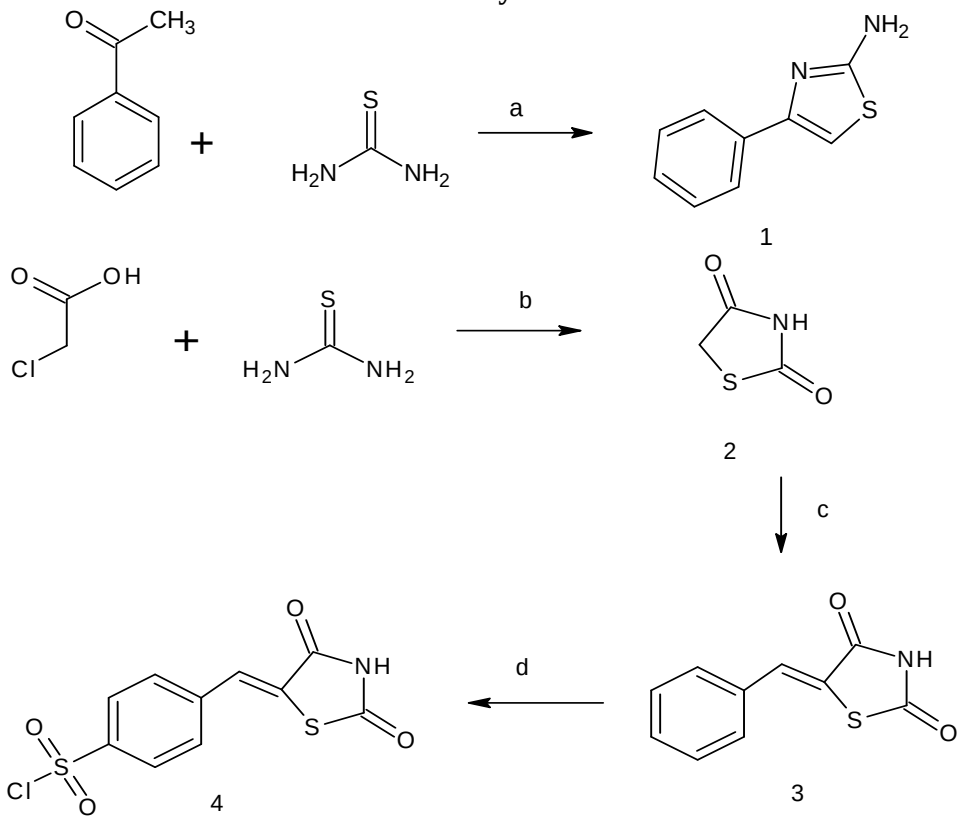


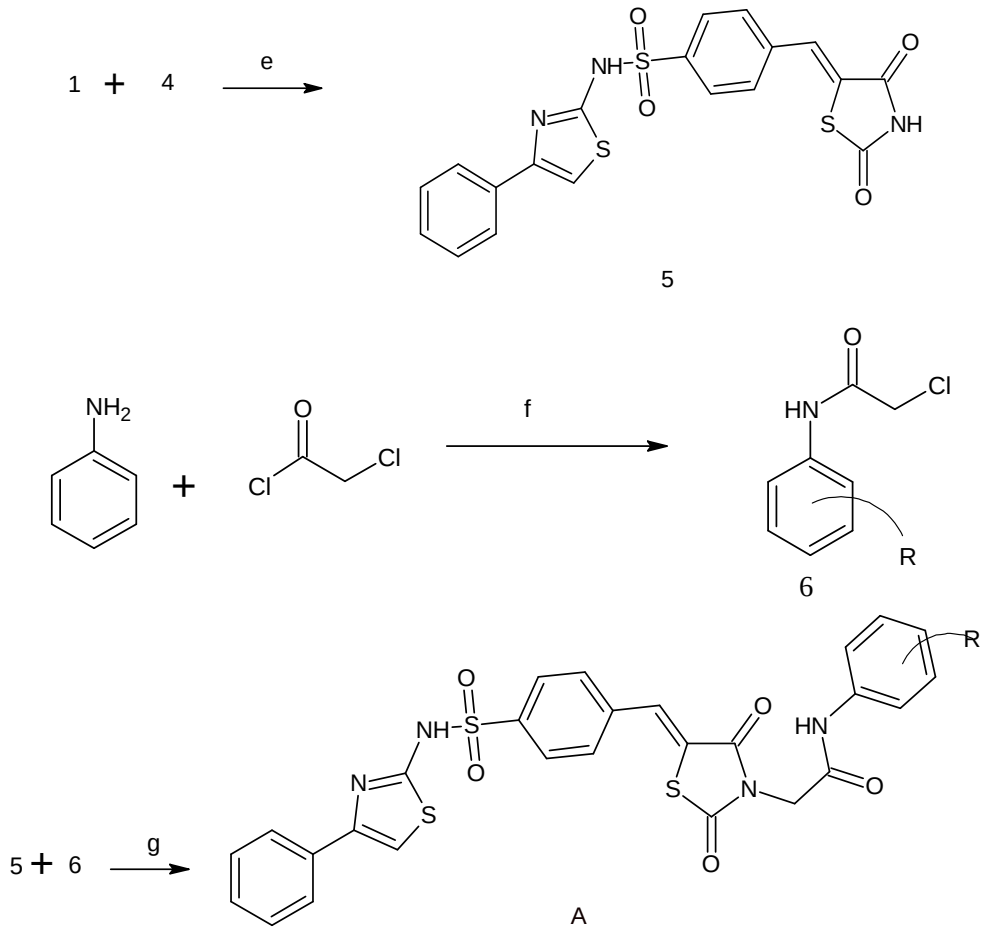
Figure 1 General structure of synthesized compounds

MATERIALS AND METHODS

All chemicals were of analytical grade and used directly. All melting points were determined in PMP-DM scientific melting point apparatus and are uncorrected. The purity of all dyes was determined by thin-layer chromatography (TLC) using silica gel-G coated Al-plates (0.5 mm thickness, Merck). Infrared spectra were recorded on a Shimadzu FT-IR 8400S model using KBr pellets. ^{1}H NMR spectra were acquired on a Varian 400 MHz model spectrophotometer using DMSO as a solvent and TMS as internal reference (chemical shifts in δ, ppm). Elemental analysis carried on Carlo Erba 1108 instrument.

Route of synthesis





R= various coupling components

Scheme 1. Reagents: *a) I_2,NH_3.H_2O, reflux 4 h, 80-90°C. b) H_2O, Conc. HCl, reflux 8-10 h, 100-110°C. c) Benzaldehyde, Piperidine, Toluene, reflux 1 h, 110°C. d) Chlorosulphonicacid, reflux 1h, 90-95°C. e) Dry Pyridine, Acetic Anhydride, reflux 2 h. f) Benzene, Tri ethyl amine, reflux 2h, 80-90°C. g) DMF, reflux 4 h.*

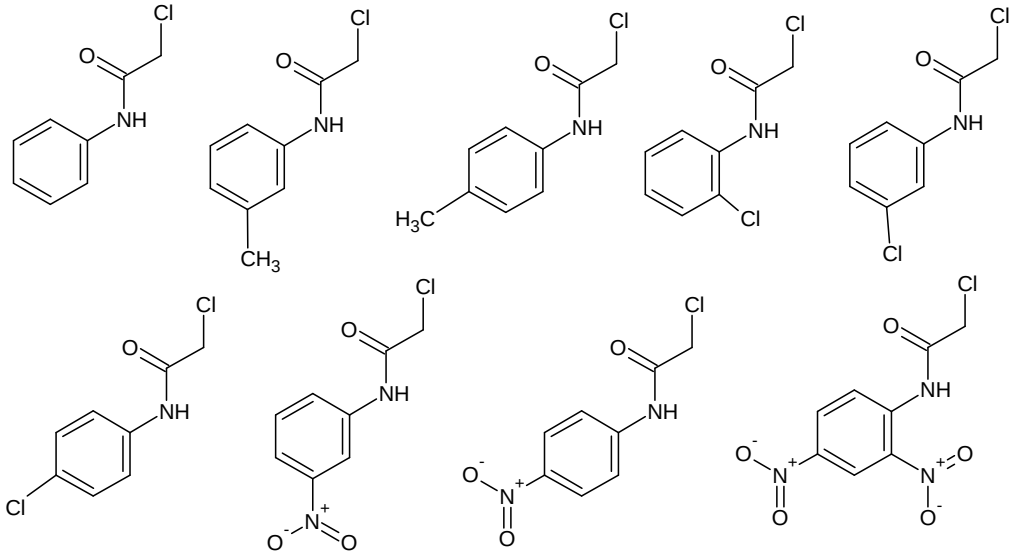


Chart 1 Various coupling components (R)

Synthesis of 2-Amino 4-Aryl Thiazole [1]
A mixture of acetophenone (0.1 mol), thiourea (0.2 mol) and Iodine (0.1 mol) was heated on a steam bath for 4 hrs. The hydroiodide, thus separated, was filtered, washed with ether and dried. It was dissolved in hot water, filtered while hot and the clear solution neutralized with a strong solution of ammonia. The solid separated was filtered, washed with water and recrystallized from Benzene. Yield: 96%, m.p. 145-150ºC.

Synthesis of 2,4-Thiazolidinedione [2]
In a 250 ml three necked round-bottomed flask was place, solution containing (0.6 mol) of chloro acetic acid in 60 ml of water and (0.6 mol) of Thiourea dissolved in 60 ml of water. The mixture was stirred for 15 min to form a white precipitate, accompanied by considerable cooling. To the contents of the flask was then added slowly 60 ml of concentrated hydrochloric acid from a dropping funnel, the flask was then connected with a reflux condenser and gentle heat applied to effect complete solution, after which the reaction mixture was stirred and refluxed for 8-10 hrs at 100-110 ºC. On cooling the contents of the flask solidified to a cluster of white needles. The product was filtered and washed with water to remove traces of hydrochloric acid and dried. It was purified by recrystallization from ethyl alcohol. Yield: 85%, m.p. 122- 127ºC.

Synthesis of 5-benzylidine 2,4- thiazolidinedione [3]
In a 250 ml three necked round-bottomed flask provided with a dean-stark apparatus, benzaldehyde (0.188 mol) and 2,4-thiazolidinedione (0.188 mol) were together suspended in ethanol. To this a catalytic amount of piperidine (1 ml) was added. The mixture was stirred and refluxed. After the complete removal of water and when the temperature reached above 110ºC the reaction mixture was stirred for a further 1 hrs. On cooling the product precipitated out from ethanol. The compound was filtered and washed with cold toluene and dry ethanol. Yield: 93%, m.p. 238-243ºC.

Synthesis of 4'-chlorosulphonyl-5-benzylidine 2,4- thiazolidinedione [4]
5-benzylidine 2,4-thiazolidinedione (0.0388 mol) was placed in a 100 ml round-bottomed flask equipped with a condenser and a dropping funnel. Chlorosulphonic acid (0.155 mol) was added at room temperature using the dropping funnel. The reaction was found to be exothermic. After addition of chlorosulphonic acid was over the reaction mass was refluxed for 1 hrs on a water bath. The reaction was cooled and poured in a thin stream with stirring into crushed ice contained in a one liter beaker. The product was filtered and dried. The product was purified by recrystallization from ethanol. Yield: 68%, m.p. 177-182ºC.

Synthesis of 4-[(z)-2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-*N*-(4-phenyl-1,3-thiazol-2-yl)benzene sulphonamide [5]
2-Amino 4-aryl thiazole [1] (0.1 mol) and 4'-chlorosulphonyl-5-benzylidine 2,4-thiazolidinedione [4] (0.1 mol) were added to a mixture of 4 ml of dry- pyridine and 20 ml acetic anhydride. The mixture was refluxed for 2 hrs, reaction mixture was poured into 20 ml of ice-water and the solid was filtered and purified by recrystallization from ethanol to give product as a white crystalline solid. Yield: 74%, m.p. 187-192ºC.

Synthesis of *N*-chloro aryl acetamide [6]
In benzene, chloro acetyl chloride (0.03 mol) and 2-3 drops of TEA were added and the mixture was stirred in water bath for 10 minute. The solution of aryl amine (0.02 mol) in benzene was added drop wise and refluxed for 2 hrs. Then cool the reaction mixture. The resulting white precipitates were filtered and washed with benzene, purified by recrystallization from ethanol.

Synthesis of 2(2,4-dioxo-5-[4-(4-phenyl-thiazol-2-ylsulfamoyl)-benzylidene]-zolidin-3-yl)-*N*-phenyl-acetamide [A]
A mixture of 4-[(z)-2,4-dioxo-1,3-thiazolidin-5-ylidene)methyl]-*N*-(4-ohenyl-1,3-thiazol-2-yl)benzene sulphonamide [5] (0.01 mol) and *N*-chloro aryl acetamide [6] (0.01 mol) in DMF were refluxed for 4 hrs. Progress of reaction was monitored by TLC using ethanol: toluene (1:4) as eluent. After the completion of reaction, the content was added to cold water. The solid product [A] was obtained and filtered, dried and purified by crystallization from Ethanol. Yield: 71%, m.p. 220ºC.

Similarly other compounds A_1-A_9 were prepared by above method from intermediate [5] and various *N*-chloro aryl acetamides [6] and purified by crystallization from ethanol.

Compound (A_1): Yield: 71%; m.p. 220^{0}C (dec.); IR (KBr,cm^{-1}) : 1328 (C-N), 1548 (C=N), 1120 & 1310 (SO_2 sym & asym), 1685 (C=O), 600-800 (C-S), 3198 cm^{-1} (-NH-), 3032-3059 cm^{-1} (-C-H) stretching of aromatic rings, ^{1}H NMR (400 MHz, DMSO- d_6) δ 4.02 (s, 1H, NH), 4.42 (s, 2H, CH_2), 6.64-7.80 (m, 16H, Ar-H), 8.10 (s, 1H, -NH); Anal. Calcd. for $C_{27}H_{20}O_5N_4S_3$: C, 56.24%; H, 3.50%; N, 9.72%; found: C, 56.48%; H,3.68%; N,10.05%.

Compound (A_2): Yield: 76%; m.p. 228^{0}C (dec.); IR (KBr,cm^{-1}) : 1330 (C-N), 1558 (C=N), 1124 & 1314 (SO_2 sym & asym), 1678 (C=O), 600-800 (C-S), 3200 cm^{-1} (-NH-), 3035-3060 cm^{-1} (-C-H) stretching of aromatic rings, ^{1}H NMR (400 MHz, DMSO- d_6) δ 2.35 (s, 3H, CH_3), 4.12 (s, 1H, NH), 4.40 (s, 2H, CH_2), 6.70-7.80 (m, 15H, Ar-H), 8.10 (s, 1H, -NH); Anal. Calcd. for $C_{28}H_{22}O_5N_4S_3$: C, 56.93%; H, 3.75%; N, 9.48%. found: C, 56.88%; H,3.84%; N,9.55%.

Compound (A_3): Yield: 78%; m.p. 235^{0}C (dec.); IR (KBr,cm^{-1}) : 1340 (C-N), 1568 (C=N), 1144 & 1334 (SO_2 sym & asym), 1668 (C=O), 600-800 (C-S), 3210 cm^{-1} (-NH-), 3035-3060 cm^{-1} (-C-H) stretching of aromatic rings, ^{1}H NMR (400 MHz, DMSO- d_6) δ 2.38 (s, 3H, CH_3), 4.18 (s, 1H, NH), 4.47 (s, 2H, CH_2), 6.70-7.80 (m, 15H, Ar-H), 8.10 (s, 1H, -NH); Anal. Calcd. for $C_{28}H_{22}O_5N_4S_3$: C, 56.93; H, 3.75; N, 9.48; found: C, 56.80%; H,3.79%; N,9.52%.

Compound (A_4): Yield: 73%; m.p. 285^{0}C (dec.); IR (KBr,cm^{-1}) : 1340 (C-N), 1568 (C=N), 1144 & 1334 (SO_2 sym & asym), 1668 (C=O), 600-800 (C-S), 3210 cm^{-1} (-NH-), 3035-3060 cm^{-1} (-C-H) stretching of aromatic rings,, 752 cm^{-1} (Cl), ^{1}H NMR (400 MHz, DMSO- d_6) δ 4.08 (s, 1H, NH), 4.45 (s, 2H, CH_2), 6.77-7.88 (m, 15H, Ar-H), 8.12 (s, 1H, -NH); Anal. Calcd. for $C_{27}H_{19}O_5N_4S_3Cl$: C, 53.07; H, 3.13; N, 9.17; found: C, 53.14%; H,3.19%; N,9.09%.

Compound (A_5): Yield: 69%; m.p. 276^{0}C (dec.); IR (KBr,cm^{-1}) : 1328 (C-N), 1578 (C=N), 1140 & 1304 (SO_2 sym & asym), 1668 (C=O), 600-800 (C-S), 3200 cm^{-1} (-NH-), 3035-3060 cm^{-1} (-C-H) stretching of aromatic rings,, 752 cm^{-1} (Cl), ^{1}H NMR (400 MHz, DMSO- d_6) δ 4.14 (s, 1H, NH), 4.45 (s, 2H, CH_2), 6.70-7.88 (m, 15H, Ar-H), 8.10 (s, 1H, -NH); Anal. Calcd. for $C_{27}H_{19}O_5N_4S_3Cl$: C, 53.07; H, 3.13; N, 9.17; found: C, 53.17%; H,3.09%; N,9.29%.

Compound (A_6): Yield: 67%; m.p. 268^{0}C (dec.); IR (KBr,cm^{-1}) : 1326 (C-N), 1588 (C=N), 1140 & 1304 (SO_2 sym & asym), 1670 (C=O), 600-800 (C-S), 3212 cm^{-1} (-NH-), 3035-3060 cm^{-1} (-C-H) stretching of aromatic rings,, 752 cm^{-1} (Cl), ^{1}H NMR (400 MHz, DMSO- d_6) δ 4.14 (s, 1H, NH), 4.45 (s, 2H, CH_2), 6.70-7.88 (m, 15H, Ar-H), 8.10 (s, 1H, -NH); Anal. Calcd. for $C_{27}H_{19}O_5N_4S_3Cl$: C, 53.07; H, 3.13; N, 9.17; found: C, 53.12%; H,3.11%; N,9.24%.

Compound (A_7): Yield: 70%; m.p. 255^{0}C (dec.); IR (KBr,cm^{-1}) : 1326 (C-N), 1588 (C=N), 1140 & 1304 (SO_2 sym & asym), 1670 (C=O), 600-800 (C-S), 3212 cm^{-1} (-NH-), 3035-3060 cm^{-1} (-C-H) stretching of aromatic rings,, 1036 & 1322 cm^{-1} (NO_2), ^{1}H NMR (400 MHz, DMSO- d_6) δ 4.44 (s, 1H, NH), 4.40 (s, 2H, CH_2), 6.77-7.80 (m, 15H, Ar-H), 8.10 (s, 1H, -NH); Anal. Calcd. for $C_{27}H_{19}O_7N_5S_3$: C, 52.16; H, 3.08; N, 11.27; found: C, 52.12%; H,3.14%; N,11.24%.

Compound (A_8): Yield: 79%; m.p. 264^{0}C (dec.); IR (KBr,cm^{-1}) : 1326 (C-N), 1588 (C=N), 1140 & 1304 (SO_2 sym & asym), 1670 (C=O), 600-800 (C-S), 3212 cm^{-1} (-NH-), 3035-3060 cm^{-1} (-C-H) stretching of aromatic rings,, 1036 & 1322 cm^{-1} (NO_2), ^{1}H NMR (400 MHz, DMSO- d_6) δ 4.44 (s, 1H, NH), 4.40 (s, 2H, CH_2), 6.77-7.80 (m, 15H, Ar-H), 8.10 (s, 1H, -NH); Anal. Calcd. for $C_{27}H_{19}O_7N_5S_3$: C, 52.16; H, 3.08; N, 11.27; found: C, 52.22%; H,3.27%; N,11.14%.

Compound (A_9): Yield: 68%; m.p. 270^{0}C (dec.); IR (KBr,cm^{-1}) : 1326 (C-N), 1588 (C=N), 1140 & 1304 (SO_2 sym & asym), 1670 (C=O), 600-800 (C-S), 3212 cm^{-1} (-NH-), 3035-3060 cm^{-1} (-C-H) stretching of aromatic rings,, 1036 & 1322 cm^{-1} (NO_2), ^{1}H NMR (400 MHz, DMSO- d_6) δ 4.44 (s, 1H, NH), 4.40 (s, 2H, CH_2), 6.77-7.80 (m, 14H, Ar-H), 8.10 (s, 1H, -NH);Anal. Calcd. for $C_{27}H_{18}O_9N_6S_3$: C, 48.64; H, 2.72; N, 12.61; found: C, 48.58; H, 2.75; N, 12.59.

Table 1 Physical data of synthesized compounds

Sr. No.	R	Molecular Formula	M.P. ºC	% Yield
A_1	H	$C_{27}H_{20}O_5N_4S_3$	220	71
A_2	3-CH_3	$C_{28}H_{22}O_5N_4S_3$	228	76
A_3	4-CH_3	$C_{28}H_{22}O_5N_4S_3$	235	78
A_4	2-Cl	$C_{27}H_{19}O_5N_4S_3Cl$	285	73
A_5	3-Cl	$C_{27}H_{19}O_5N_4S_3Cl$	276	69
A_6	4-Cl	$C_{27}H_{19}O_5N_4S_3Cl$	268	67
A_7	3-NO_2	$C_{27}H_{19}O_7N_5S_3$	255	70
A_8	4-NO_2	$C_{27}H_{19}O_7N_5S_3$	264	79
A_9	2,4-NO_2	$C_{27}H_{18}O_9N_6S_3$	270	68

RESULTS AND DISCUSSION

All the reaction was carried out under conventional methods. 4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-*N*-(4-phenyl-thiazol-2-yl)-benzenesulfonamide (5) was key intermediate that required to synthesized target product. Compound 1 was synthesized by the reaction between acetophenone and thiourea on refluxed. Compound 4 was synthesized in three steps. In first step chloro acetic acid and thiourea on reflux gave compound 2 with the removal of one mole of – H_2O. In second step above prepared compound 2 condensed with benzaldehyde in presence of toluene and catalytically amount of piperidine gave compound 3. In last step compound 3 on chlorosulphonation gave compound 4. Compound 5 was synthesized by the condensation reaction between compound 1 and compound 4 in presence of pyridine and acetic anhydride. Compound 6 was synthesized by the reaction between various aniline and chloro acetyl chloride in the presence of benzene. Finally compound 5 and compound 6 on condensation gave target compound.

All the synthesized compounds were characterized by IR and ^{1}H NMR spectra. The synthesized compounds in general showed 1340, 1568 cm^{-1} for (C-N) and (C=N) stretching respectively. SO_2 sym & asym showed band in the region of 1144 & 1334 cm^{-1} while (C=O) showed characteristic band at 1668 cm^{-1}, The (C-S) linkage showed banding vibration in the region of 600-800 cm^{-1}. The (-NH-) linkage showed stretching band at 3210 cm^{-1}, 752 cm^{-1} indicates the presence of (Cl) group. The ^{1}H-NMR spectra of all the synthesized compounds shows important signals at their respective positions, confirming the structures.

Antibacterial Activity

The antimicrobial bioassay results presented in Table 2 revealed that, all the tested compounds tended to be more active against gram-positive bacteria, than against gram-negative bacteria. Final *N*-chloro aryl acetamide derivative **A_2** showed excellent activity (MIC, 20 µg/mL, 22 mm of zone of inhibition) against gram–positive strain *S. aureus*. Compounds **A_3, A_4** and **A_1** were found half fold active (MIC, 50 µg/mL) against *S. aureus* as compared to most active analogues **A_2** tested against the same strain. Final *N*-chloro aryl acetamide derivatives **A_2** and **A_5** displayed strong inhibitory action at 20 µg/mL, 24 mm of zone of inhibition against gram–positive *B. subtilis*. Compound **A_5** exhibited similar inhibitory concentration of 20 µg/mL against *S. aureus* with 4 mm of lesser zone of inhibition (20 mm) than **A_2** and **A_3**. Compound **A_4** was found half fold active (MIC, 50 µg/mL) against *B. subtilis* as compared to most active analogues **A_2, A_5** tested against the same strain. Compound **A_5** was found to contribute promising activity (MIC, 50 µg/mL, 20 mm of zone of inhibition) towards gram–negative strain *E. coli*. Compound **A_2** exhibited similar inhibitory concentration of 50 µg/mL against *E. coli* with 1 mm of lesser zone of inhibition (19 mm) than **A_5**. Compound **A_8** was found half fold active (MIC, 100 µg/mL) against *E. coli* as compared to most active analogues **A_5** tested against the same strain. Compound **A_5** appeared with remarkable activity against gram–negative *P. aeruginosa* at 50 µg/mL of MIC, where the half fold activity was observed (MIC, 100 µg/mL) for compounds **A_8** and **A_9** against the same bacteria. All the remaining final *N*-chloro aryl acetamide derivatives exerted good to moderate activity profile at MIC level ranging from 20 to 100 µg/mL, whereas, some derivatives were found to display weak at a higher concentration of 200-500 µg/mL.

Moreover, the result showed that the compounds **A_2, A_5** were the best compounds of the series, exhibiting good antibacterial activity against both Gram-positive and Gram-negative bacteria.

Table 2 Antibacterial activity of *N*-chloro aryl acetamide derivatives

Comp. no.	R	Gram negative		Gram positive	
		E. coli	*P. aeruginosa*	*S. aureus*	*B. subtilis*
A_1	H	12 (100)	14 (100)	14 (50)	16 (50)
A_2	3-CH_3	19(50)	18 (50)	22 (20)	24 (20)
A_3	4-CH_3	16 (50)	16(50)	16(50)	16(50)
A_4	2-Cl	17(50)	15(50)	16(50)	18(50)
A_5	3-Cl	20(50)	21(50)	20(20)	24(20)
A_6	4-Cl	12 (100)	11(100)	12(100)	11(100)
A_7	3-NO_2	<10(100)	<10 (100)	14(100)	12(100)
A_8	4-NO_2	16(100)	15(100)	18(50)	20(50)
A_9	2,4-NO_2	18(100)	14(100)	18(50)	14(50)
Ciprofloxacin (100 µg/disc)		30 (≤1)	31 (≤1)	32 (≤1)	33 (≤1)

CONCLUSION

The results of study of microbial analysis revealed that the synthesized compounds are promisingly significant and possesses good antibacterial activity. We have synthesized some *N*-chloro aryl acetamide analogues combining with different substituted thaizole and thiazolidinedione derivative ring system with a view to get a good antibacterial agent with less toxic effects. We have developed an efficient and potent *N*-chloro aryl acetamide based compounds which are one of the active constituents present in many standard drugs and are well-known for its use to increase pharmacological activity of the molecules. The -NH linkage in the compounds increases the activity of compounds. Screening results clearly indicates the compounds of the scheme exhibit good antibacterial and are equipotent with the standard drugs. This is because of the presence of *N*-chloro aryl acetamide derivatives having electron donating and electron withdrawing groups and heterocyclic system attached to thiazole and thiazolidinedione nucleus. Moreover, *N*-chloro aryl acetamide as coupling component in all compounds increases activity. Hence, there is enough scope for further study in developing such compounds as a good lead activity. Most of the compounds have shown moderate to promising activity as compared to standard drug against all representative panel of bacterial strains. The compounds having *N*-chloro aryl acetamide as coupling components could be useful for derivatization to develop more effective antibacterial agents.

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REFERENCES

[1] BCC Cantello; MA Cawthorne, GP Cottam; PT Duff.; D Haigh; RM Hindley; CA Lister; SA Smith; PL Thurlby, *J. Med. Chem*. **1994**, 37, 3977-3985.
[2] G Kucukguzel; A Kocatepe; E De Clercq; F Sahin; M Gulluce, *Eur. J. Med. Chem*. **2006,** 41, 353-359.
[3] M Naeem; MN Chaudhary; FH Baloch; R Amjad, *J.chem.soc.pak*, **2009**, 31, 4, 633-637.
[4] MC Sharma; NK Shahu; DV Kohli; SC Chaturvedi; S Sharma, *Digest journal of Nanomaterials and Bio structures*, **2009**, 4, 1, 223-232.
[5] RB Patel; PS Desai; KR Desai; KH Chikhalia, *Indian journal of chemistry*, **2006**, 45B, 773.
[6] Z Turgut; C Yolacan; F Aydogan; E Bagdatli; N Ocal, *Molecules*, **2007**, 12, 2151-2159.
[7] S Bouzroura; Y Bentarzi; R Kaoua; BN Kolli; SP Martini; E Dunach, *Org. Commun*, **2010**, 3, 1, 8-14.
[8] KM Mistry; KR Desai, *E-journal of chemistry*, **2004**, 1, 4, 189-193.
[9] N Shah; PC Pant; PC Joshi, *Asian J. chem.*, **1993**, 95, 83.
[10] N Ramalakshmi; L Aruloly; S Arunkumar; K Ilango; A Puratchikody, *Malaysian journal of science*, **2009**, 28, 2, 197-203.
[11] NB Patel; VN Patel, *Iranian journal of pharmaceutical research*, **2007**, 6, 4, 251-258.
[12] MG Vigorita; R Ottana; F Monforte; R Maccari; Trovato; MT Monforte, MF Taviang, *Biorg. Med.Chem.Lett*, **2001**, 11, 2791-2794.
[13] V Murugesan; YS Prabhakar; SB Katti, *J. Mol. Graph. Model.* **2009,** 27, 735-743.
[14] J Balzarini; B Orzeszko-Krzesinska; JK Maurin; A Orzesko, *Eur. J. Med. Chem.* **2009**, 44, 303-311.
[15] SR Pattan; P Kekare; NS Dighe; SB Bhawar; MB Hole; A Nikalje; A Pati, *Asian J. Research Chem*. **2009**; 2(2): 123-126.
[16] SR Pattan; C Suresh; VD Pujar; VVK Reddy; VP Rasal; BC Koti, *Indian J. Chem*., **2005**, 44B: 2404-2408.