Journal of Applied Pharmaceutical Science Vol. 3 (11), pp. 122-127, November, 2013
Available online at http://www.japsonline.com
DOI: 10.7324/JAPS.2013.31122
ISSN 2231-3354

Synthesis and antimicrobial evaluation of novel 3-(4,6- diphenyl-6H-1,3-thiazin-2-yl)-2-(4-methoxyphenyl) thiazolidin-4-one derivatives

Sayaji S. Didwagh, Pravina B. Piste* , Aravind S. Burungale, Avinash M. Nalawade.
[1]Departmentof Chemistry,Yashavantrao Chavan Institute of Science,Satara.(Maharastra)India.
[2]Department of Chemistry, Padmabhushan Dr.Vasantraodada Patil Mahavidyalaya, Tasgaon, Sangli (Maharastra) India

ARTICLE INFO

Article history:
Received on: 02/08/2013
Revised on: 17/09/2013
Accepted on: 05/11/2013
Available online: 29/11/2013

Key words:
Synthesis, chalcone, thiazine, thiazolidin-4-one, antimicrobial activity.

ABSTRACT

A novel series of potentially biologically active 3-(4,6-diphenyl-6H-1,3-thiazin-2-yl)-2-(4-methoxyphenyl) thiazolidin-4-one derivatives **(5a-5k)** have been synthesized by the condensation-cyclization reaction of 4,6-diphenyl-6H-1,3-thiazin-2-amine, aromatic aldehyde and thioglycolic acid in polypropylene glycol at 110^0C temperature. The structure of the newly synthesized compounds has been established on the basis of their spectral data and elemental analysis. The antimicrobial activity of the synthesized compounds were tested in *vitro* against the sensitive organisms *Staphylococcus aureus, Bacillus subtilis* as a Gram positive bacteria and *Escherichia coli, Pseudomonas aeruginosa* as a Gram negative bacteria and two pathogenic fungal strains *Candida albicans, Aspergillus niger* by using the disc diffusion method. The detailed synthesis, spectroscopic data, and antimicrobial screening of synthesized compounds were reported.

INTRODUCTION

Nitrogen-containing heterocycles are undoubtedly one of the most important targets in organic chemistry. They are widely distributed in natural products and in pharmaceutical agents, and numerous studies for their chemistry and synthesis have been reported (Attanasi *et al.,* 2008) and Sulfur-containing heterocyclic ring systems, such as thiazine derivatives have shown a great potential in pharmaceutical research (Snick *et al.,* 2013). Thiazine derivatives, a versatile pharmocophore, has been the subject of great interest due to its wide range of biological activities such as antimicrobial and anti-diabetic (Faidallah *et al.,* 2011; Adly *et al.,* 2012) , anti-histaminic (Arya *et al.,* 2012), antibacterial and antifungal (Tandon *et al.,* 2006; Zia-ur Rehman *et al.,* 2009; Ganorka *et al.,* 2013), phagocytic activity of human neutrophils (Barros-Garcia *et al.,* 2011), antagonistic (Galanski *et al.,* 2006), potassium channel-opening agents (Erker *et al.,* 2000), antioxidant (Smith *et al.,* 1951) analgesic and anti-inflammatory, (Chia *et al.,* 2008; Tozkoparan *et al.,* 2002) anti-tuberculosis (Koketsua *et al.,* 2002), antitumor (Wei *et al.,* 2012), antihelminthic and insecticidal (Smith *et al.,* 1942), nitric oxide synthase inhibitor (Tung-Mei *et al.,* 2005), Smooth Muscle Relaxants (Schreder *et al.,* 2000), antimycobacterial (Indumathi *et al.,* 2009), urokinase inhibitors (Tanaka *et al.,* 1998). The derivatives of thiazine act as myocardial calcium channel modulators (Budriesi *et al.,* 2002).

Among pharmacologically important heterocyclic compounds, thiazolidinone derivatives have been known to possess a wide range of biological activities such as antimicrobial (Bhaskar *et al.,* 2008; Sah *et al.,* 2012; Ramachandran *et al.,* 2011; Bhatt *et al.,* 2012) anti-HIV(Rawal *et al.,* 2007), antifungal, antibacterial (Nagaraj *et al.,* 2012; Patel *et al.,* 2011;Omar *et al.,* 2010;Vicini *et al.,* 2006), antihyperglycemic (Datar *et al.,* 2012),anti–inflammatory (Rekha *et al.,* 2011) and antitubercular (Samadhiya *et al.,* 2013). Owing to the biological significance of these two classes of compounds and in continuation of our ongoing study on antimicrobial agents (Prasad *et al.,* 2011). Hence, considerable efforts have been carried out for the synthesis of a combined molecular framework that involves these two different chromophores.

* *Corresponding Author*
Email:sdidwagh53@gmail.com.
Phone no. (02162) 234392; Fax no. 02162234392.

Thus a novel series of potentially biologically active 3-(4,6-diphenyl-6H-1,3-thiazin-2-yl)-2- (4-methoxyphenyl) thiazolidin-4-one derivatives has been synthesized by the condensation and cyclization reaction of 4,6-diphenyl-6H-1,3-thiazin-2-amine, aromatic aldehyde and thioglycolic acid in polypropylene glycol and evaluated their antimicrobial activity.

EXPERMENTAL SECTION

The melting points were recorded on electrothermal apparatus and are uncorrected. The purity of the compounds was checked by TLC on pre-coated SiO_2 gel (HF254, 200 mesh) aluminium plates (E Merk) using hexane and ethyl acatate visualized in iodine chamber. IR spectra were recorded in KBr on a perkin-Elmer model-983. 1HNMR spectrum recorded on Varian Mercury 300MHz instrument using $CDCl_3$, DMSO-d_6 as solvent (chemical shift in δ ppm),using TMS as internal standard. Elemental analysis was performed on a Heracus CHN analyzer and was within the ±0.5% of the theoretical values.

Preparation of (2*E*)-1,3-diphenylprop-2-en-1-one derivatives (3a-3b)

Equimolar quantities of benzaldehyde / anisaldehyde (0.01mol) and acetophenone (0.01 mol) were dissolved in minimum amount of ethanol. Sodium hydroxide solution (0.02 mol) was added and the mixture stirred for 2hr until the entire mixture becomes very cloud. Then the reaction mixture was poured slowly into ice water with constant stirring and kept in refrigerator for 24 hours. The precipitates obtained was filtered ,washed with cold water and recrystallized from ethanol to give compounds **3a-3b**. The completation of the reaction was monitored by TLC.

Preparation of 4,6-diphenyl-6H-1,3-thiazin-2-amine derivatives (4a-4b)

A mixture of chalcone **(3a -3b)** (0.02mol), thiourea (0.02mol) were dissolved in ethanolic NaOH (25ml) was stirred about 2-3 hours with a magnetic stirrer. This was then poured into 400ml of cold water with continuous stirring for an hour & then kept in refrigerator for 24 hours. The separated solid was filtered,washed and recrystallized from ethanol. The completion of the reaction was monitored by TLC

Preparation of 3-(4,6-diphenyl-6H-1,3-thiazin-2-yl)-2-(4-methoxyphenyl) thiazolidin-4-one (5a-5k)

A mixture of 4,6-diphenyl-6H-1,3-thiazin-2-amine (0.01 mol), aldehyde (0.02 mol), and thioglycolic acid (0.03mol) in PPG ~ 2000 (2 ml) was heated at 110^0C for 4-11 h. After completation of the reaction as indicated by TLC, the reaction mixture was diluted with hexane , and the precipitated product was filtered. In the case of oily products, the hexane layer was decanted, and sticky material was dissolved in ethyl acetate (20 ml). The solution was washed well with saturated $NaHCO_3$ solution (15 ml) 3 times followed by water (15 ml) 3 times. The organic layer was dried over anhydrous sodium sulfate and evaporatrd under reduced pressure to afford the crude compound. The product was purified by column chromatography on silica gel using 2-4 % MeOH in benzene as eluent. In addition , the hexane layer was evaporated under reduced pressure to recover PPG which can be recycled.

Spectral characterization and elemental analysis of synthesized compounds (5a-5k)

3- (4,6- diphenyl-6H-1,3-thiazin-2-yl) -2- (4methoxyphenyl) thiazolidin-4-one (5a)

IR.(KBr,cm^{-1}): 3070(Ar-H), 1695 (>C=O), 1621, 1475 (>C=C<), 1250 (C-N), 1210 (C-O); 1HNMR (300 MHz, $CDCl_3$, DMSO-d_6,ppm): 5.41(d,1H,CH),6.37(d,1H,CH), 6.62(d,1H,Ar-H), 7.64(d,1H,Ar-H), 8.04 (d,1H,Ar-H) 7.33-7.55 (m,3H,Ar-H),5.83(s,1H,CH), 3.85 (s,2H,CH_2), 3.81 (s,3H,OCH_3); Anal. $C_{26}H_{22}N_2O_2S_2$; Calculated: C,68.09; H,4.84; N,6.11; O,6.98; S,13.98.Found: C,67.88; H,4.63; N,5.91; O,6.79; S,13.68.

2- (4- chlorophenyl) -3- (4,6- diphenyl- 6H-1,3 - thiazin-2-yl) thiazolidin-4-one (5b)

IR.(KBr,cm^{-1}):3072(Ar-H), 1695(>C=O), 1623, 1475(>C=C<), 1250(C-N), 765(C-Cl) ; 1HNMR(300 MHz,$CDCl_3$, DMSO-d_6,ppm): 5.40(d,1H,CH), 6.39(d,1H,CH), 7.23(d,1H,Ar-H),6.95 (d,1H,Ar-H), 8.04(d,1H,Ar-H) 7.33-7.55 (m,3H,Ar-H), 5.81(s,1H,CH), 3.85(s,2H,CH_2); Anal. $C_{25}H_{19}ClN_2OS_2$; Calculated: C,64.85;H,4.14; Cl,7.66; N,6.05; O,3.46; S,13.85. Found: C,64.63;H,3.97; Cl,7.43; N,5.91; O,3.26; S,13.61.

2-(2-chlorophenyl)-3-(4,6-diphenyl-6H-1,3-thiazin-2-yl)-1,3-thiazolidin-4-one(5c)

IR.(KBr,cm^{-1}):3072(Ar-H), 1698(>C=O), 1627, 1476 (>C=C<), 1250(C-N), 773(C-Cl); 1HNMR (300 MHz,$CDCl_3$, DMSO-d_6,ppm): 5.39 (d,1H,CH),6.36(d,1H,CH), 7.39(d,1H,Ar-H),6.91 (m,3H,Ar-H), 8.04(d,1H,Ar-H)7.33-7.55(m,3H,Ar-H), 5.83(s,1H,CH),3.85(s,2H,CH_2);Anal.$C_{25}H_{19}ClN_2OS_2$; Calculated: C,64.85;H,4.14; Cl,7.66; N,6.05; O,3.46; S,13.85. Found: C,64.61;H,3.92; Cl,7.46; N,5.91; O,3.26; S,13.59.

3-(4,6-diphenyl-6H-1,3-thiazin-2-yl)-2-(4-hydroxyphenyl) thiazolidin-4-one (5d)

IR.(KBr,cm^{-1}):3071(Ar-H), 1696(>C=O), 1623, 1475 (>C=C<), 1250 (C-N),1225(C-O); 1HNMR(300 MHz, $CDCl_3$, DMSO-d_6,ppm): 5.40(d,1H,CH), 6.39(d,1H,CH), 6.55(d,1H,Ar-H), 7.47(d,1H,Ar-H), 8.04(d,1H,Ar-H)7.33-7.55(m,3H,Ar-H), 5.81(s,1H,CH), 3.83(s,2H,CH_2); Anal. $C_{25}H_{20}N_2O_2S_2$; Cal culated: C,67.54; H,4.53; N,6.30; O,7.20; S,14.43. Found: C,67.24; H,4.21; N,6.15;O,7.05; S,14.23.

3-(4,6-diphenyl-6H-1,3-thiazin-2-yl)-2-phenylthiazolidin-4-one (5e)

IR.(KBr,cm^{-1}):3067(Ar-H), 1685 (>C=O), 1615,1475 (>C=C<), 1249(C-N); 1HNMR(300MHz,$CDCl_3$,DMSO-d_6,ppm): 5.40(d,1H,CH), 6.39(d,1H,CH),7.33-7.49(m,10H,Ar-H), 8.04 (d,1H,Ar-H) 7.33-7.55(m,3H,Ar-H), 5.83(s,1H,CH), 3.85

(s,2H,CH_2); Anal.$C_{25}H_{20}N_2OS_2$;Calculated:C,70.06;H, 4.70; N,6.54; O,3.73; S,14.96. Found: C,69.90; H,4.47; N,6.23; O,3.37; S,14.57.

3-(4,6-diphenyl-6H-1,3-thiazin-2-yl)-2-(2-nitrophenyl) thiazolidin-4-one(5f)

IR.(KBr,cm^{-1}):3071(ArC-H), 1694(>C=O), 1623,1475 (>C=C<), 1250(C-N),1547,1353(N=O);1HNM R(300MHz,$CDCl_3$, DMSO-d_6,ppm): 5.41(d,1H,CH), 6.38(d,1H,CH), 7.65(d,1H,Ar-H), 7.37(m,3H ,Ar-H), 8.04(d,1H,Ar-H)7.33.7.55(m,3H,Ar-H), 5.84(s,1H,CH),3.87(s,2H,CH_2);Anal.$C_{25}H_{19}N_3O_3S_2$; Calculated: C,63.41; H,4.04; N,8.87; O,10.14; S,13.54. Found: C,63.19; H,3.87; N,8.57; O,9.96; S,13.34.

3- (6- (4-methoxyphenyl) -4- phenyl-6H-1,3 - thiazin-2-yl)-2-phenylthiazolidin-4-one(5g)

IR.(KBr,cm-1):3071(Ar-H), 1691(>C=O), 1622, 1475(>C=C<), 1250(C-N), 1215(C-O); 1HNMR(300 MHz, $CDCl_3$, DMSO-d_6,ppm): 5.41(d,1H,CH), 6.37(d,1H,CH), 7.33-7.49 (m,5H,Ar-H), 8.04(d,1H ,Ar-H)6.39(d,1H,Ar-H),6.97(d,1H,Ar-H),7.33-7.55 (m,3H,Ar-H), 5.82(s,1H,CH),3.85(s,2H,CH_2) ,3.81 (s,3H,OCH_3); Anal. $C_{26}H_{22}N_2O_2S_2$; Calculated: C,68.09; H,4.84; N,6.11; O,6.98 S,13.98. Found: C,67.89; H,4.53; N,5.90; O,6.55 S,13.59.

2- (4-methoxyphenyl)-3-(6- (4-methoxyphenyl)-4-phenyl-6H-1,3-thiazin-2-yl)thiazolidin-4-one(5h)

IR.(KBr,cm^{-1}): 3075(Ar-H), 1696(>C=O), 1631, 1476 (>C=C<), 1250(C-N), 1219,1210(C-O); 1HNMR (300MHz, $CDCl_3$, DMSO-d_6,ppm): 5.41(d,1H,CH), 6.39(d,1H,CH), 7.43(d,1H,Ar-H), 8.04(d,1H, Ar-H) 6.39(d,1H,Ar-H), 6.97(d,1H,Ar-H), 7.33-7.55 (m,3H,Ar-H), 5.82(s,1H,CH), 3.85(s,2H,CH_2), 3.81 (s,3H,OCH_3); Anal. $C_{27}H_{24}N_2O_3S_2$; Calculated: C,66.37; H,4.95; N,5.73;O,9.82.S,13.12. Found: C,66.14; H,4.62; N,5.47;O,9.61.S,12.91.

2- (4-chlorophenyl)-3-(6- (4-methoxyphenyl)- 4-phenyl-6H-1,3-thiazin-2-yl)thiazolidin-4-one(5i)

IR.(KBr,cm^{-1}):3081(Ar-H), 1698 (>C=O), 1635, 1476 (>C=C<), 1250(C-N),1217(C-O),775(C-Cl);1 HNMR (300MHz, $CDCl_3$, DMSO-d_6,ppm): 5.41(d,1H,CH), 6.37(d,1H,CH), 7.25(d,1H,Ar-H),6.94 (d, 1H,Ar-H), 8.04(d,1H,Ar-H) 6.38 (d,1H,Ar-H), 6.95(d,1H,Ar-H), 7.33-7.55(m,3H,Ar-H), 5.82 (s,1H,CH),3.85(s,2H,CH_2),3.81(s,3H,OCH_3);Anal.$C_{26}H_{21}ClN_2O_2S_2$;Calculated:C,63.34;H,4.29;Cl,7.19;N,5.68;O,6.49;S,13.01.Found: C,63.11;H,4.05;Cl,7.00;N,5.37;O,6.29;S,12.90.

2-(4-hydroxyphenyl)-3- (6-(4-methoxyphenyl) -4-phenyl-6H-1,3-thiazin-2-yl)thiazolidin-4-one(5j)

IR.(KBr,cm^{-1}):3365 (O-H), 3076(Ar-H), 1693(>C=O), 1633, 1476 (>C=C<), 1250(C-N), 1211(C-O) ;1HNMR (300MHz, $CDCl_3$, DMSO-d_6,ppm): 5.41(d,1H,CH), 6.37(d,1H,CH), 6.55(d,1H,Ar-H),7.47 (d,1H,Ar-H),8.04(d,1H,Ar-H)6.38(d,1H,Ar-H), 6.95(d,1H,Ar-H),7.33-7.55(m,3H,Ar-H),5.82 (s,1H, CH), 3.85(s,2H,CH_2), 3.81(s,3H,OCH_3); Anal. $C_{26}H_{22}N_2O_3S_2$; Calculated: C;80;H,4.67; N,5.90; O,10.11; S,13.51. Found: C; 79.39;H,4.43; N,5.59; O,9.83; S,13.27.

***3- (6- (4-methoxyphenyl) -4-phenyl-6H-1,3-thiazin-2-yl) -2-(2-nitrophenyl)thiazolidin-4-one* (5k)**

IR.(KBr,cm^{-1}):3073(Ar-H), 1693(>C=O), 1627, 1476 (>C=C<),1547, 1353(N=O), 1250(C-N), 1213(C-O): 1HNMR (300MHz, $CDCl_3$,DMSO-d_6,ppm): 5.41(d,1H,CH), 6.37 (d,1H,CH), 7.65(d,1H,Ar-H), 7.37(m,3H,Ar-H), 8.04(d,1H,Ar-H), 6.38(d,1H,Ar-H),6.95(d,1H,Ar-H), 7.33-7.55(m,3H,Ar-H), 5.63 (s,1H, CH),3.75(s,2H,CH_2),3.81(s,3H,OCH_3); Anal. $C_{26}H_{21}N_3O_4S_2$; Calculated: C,62.01; H,4.20; N,8.34;O,12.71;S,12.73. Found: C,61.87; H,3.97; N,8.07;O,12.49;S,12.27.

Antimicrobial activity

The synthesised compounds (5a-5k) were screened for their in *vitro* antimicrobial activity by using disc diffusion method (Osman *et al.*, 2012). Antibacterial activity was screened against two gram positive bacteria *Staphylococcus aureus* (ATCC 9144), *Bacillus subtilis* (ATCC 6399) and two gram negative bacteria *Escherichia coli* (ATCC 25922), *Pseudomonas aeruginosa* (ATCC 17933) by measuring the zone of inhibition on agar plates at concentrations 100 µg/mL. Antifungal activity was screened against *Candida albicans* (ATCC 10231), *Aspergillus niger* (ATCC 6275) by measuring the zone of inhibition on agar plates at concentrations 100 µg/Ml. and reported in Table-2.

Disc diffusion method

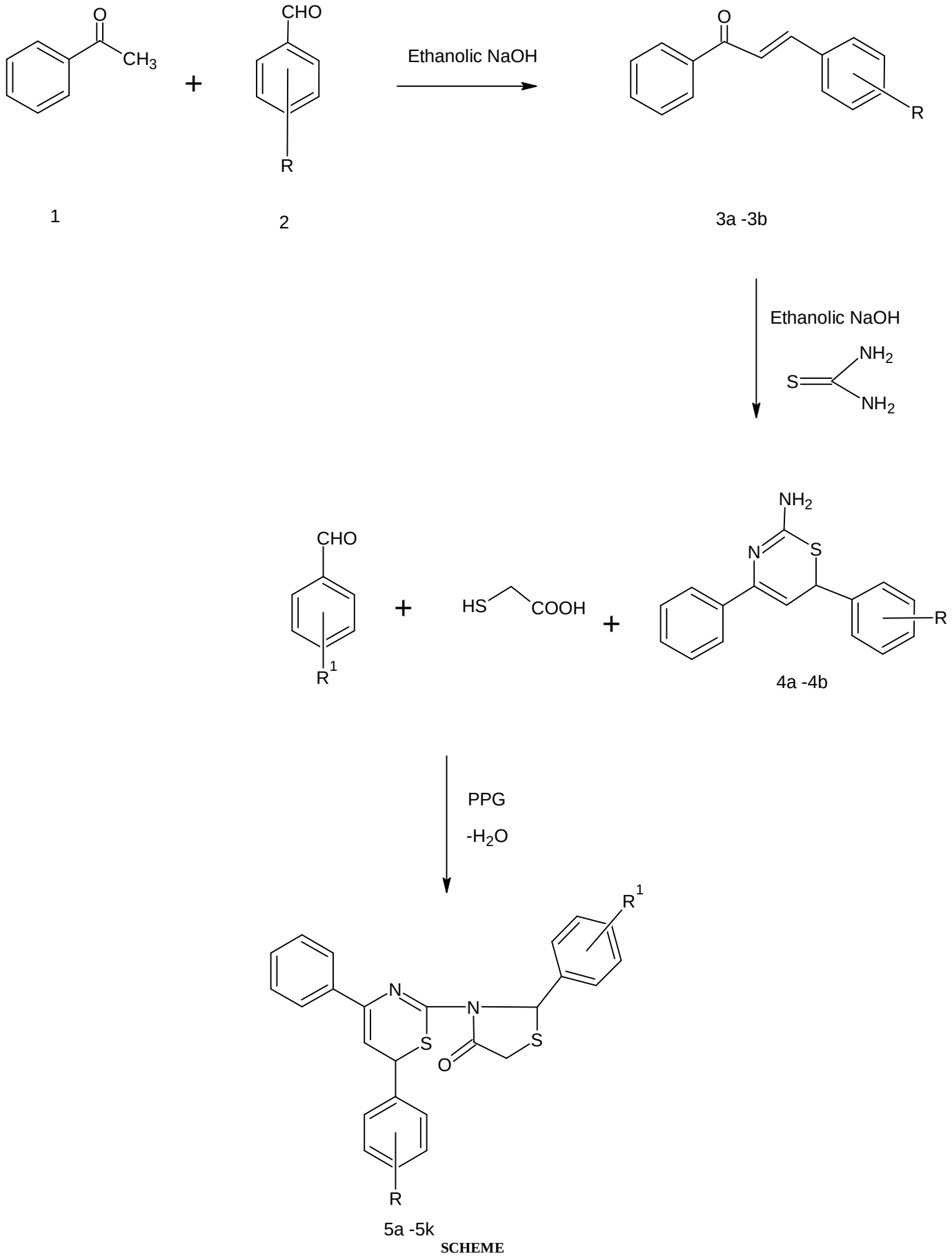
Nutrient agar and Potato Dextrose Agar plates was employed as culture medium and dimethylformamide was used as solvent control for antimicrobial activity. Ciprofloxacin and Flucanazole were used as standard for antibacterial and antifungal activities respectively.

Preparation of microbial suspension

The bacterial and fungal strains were subculture at 37℃ for six hrs in the corresponding medium of three successive days. These suspensions were used to insulate the antibiograms.

Preparation of the biograms

The agar disc diffusion method was performed on each of the tested substance solution in dimethylformamide. Filter paper discs were impregnated with 1 ml of the solution and placed on the inoculated plates. These plates after standing at 4℃ for 2 hours were incubated at 37℃ for 24 hours. Ciprofloxacin and Flucanazole were used as standard drugs for antibacterial and antifungal activities respectively. The diameters of the inhibition zones were measured in millimeters and were reported in table no. 2.


O
CH3
CHO
R
Ethanolic NaOH
O
R
1
2
3a -3b
Ethanolic NaOH
NH2
S
NH2
CHO
R1
HS
COOH
NH2
N
S
R
4a -4b
PPG
-H2O
R1
N
N
S
S
O
R
5a -5k

SCHEME

RESULTS AND DISCUSSION

Compounds **(5a-5k)** are readily obtained in 70–86% yields by the condensation and cyclization reaction of 4,6-diphenyl-6H-1,3-thiazin-2-amine, aromatic aldehyde (Prasad *et al.*, 2011) and thioglycolic acid in polypropylene glycol at 110^0C temperature. Initially , we attempted the synthesis of 3-(4,6- diphenyl - 6H - 1,3 – thiazin – 2 – yl)-2-(4-methoxyphenyl) thiazolidin-4-one derivatives by the reaction of 4,6-diphenyl-6H-1,3-thiazin-2-amine, aromatic aldehyde and thioglycolic acid at 110^0C in polyethylene glycol (PEG), as many organic transformations and multi-component reaction are reported in polyethylene glycol, but surprisingly, no product formation was observed even after 24 h of the reaction. However, the reaction proceeds well in PPG is possibly due to its immiscibility with water, which helps in the removal of a water molecule from the reaction mixture during the formation of thiazolidin-4-one ring .In addition , PPG is an eco-friendly solvent and associated with many advantages, such as low cost, less toxicity, efficient recyclability, easy work-up, and miscibility with a wide range of organic solvents. IR spectra of all the compounds (5a–5k) showed an absorption band at 1685–1698 cm $^{-}$1 due to carbon – oxygen double bond, typical of the stretching vibrations of the carbon–nitrogen single bond. No peaks were found due to starting material amino or aldehydic functionalities. ^{1}H NMR spectra of all the compounds showed the broad singlets due CH-N protons and a singlets due to CH_2–S protons. Our further object, pharmacological point of view we plan to synthesize combined molecular framework that involves these two different chromophores. All the synthesized compounds were tested for their antimicrobial activity using Ciprofloxacin and Flucanazole as standard drugs. The antibacterial activity are shown in Table 2. The Compounds 5b,5c,5d,5i,5j exhibited good activity against gram-positive bacteria *S. aureus, B. subtilis* and gram-negative bacteria *E. coli*, *P. aeruginosa*. While other compounds 5a,5e,5f,5g,5h,5k exhibited moderate to poor activity against the tested microorganisms, compared to standard drug. The antifungal activity are shown in Table 2. The Compounds 5a,5b,5c,5g,5h,5i, showed good activity against *C. albican , A. niger*. while The remaining compounds 5d,5e,5f,5j,5k, exhibited moderate to poor activity as compared to standard drugs Ciprofloxacin and Flucanazole.

Table. 1: Physical data of compounds (5a-5k).

Co Mp.	R	R1	M.P ^{0}C	M..W.	Yield
5a	C_6H_5	4-$OCH_3C_6H_4$	85	458	76
5b	C_6H_5	4- Cl C_6H_4	77	463	70
5c	C_6H_5	2-Cl C_6H_4	101	463	80
5d	C_6H_5	4- OH C_6H_4	104	444	81
5e	C_6H_5	C_6H_5	107	428	77
5f	C_6H_5	2- NO_2 C_6H_4	87	473	80
5g	4-$OCH_3C_6H_4$	C_6H_5	63	458	86
5h	4-$OCH_3C_6H_4$	4-$OCH_3C_6H_4$	71	488	83
5i	4-$OCH_3C_6H_4$	4- Cl C_6H_4	75	493	81
5j	4-$OCH_3C_6H_4$	4- OH C_6H_4	92	474	82
5k	4-$OCH_3C_6H_4$	2- NO_2 C_6H_4	79	503	78

Table. 2 : Antimicrobial activity of Synthesized Compounds.

Comp. (100µg /ml)	Antibacterial Activity				Antifungal Activity	
	S. Aureus	*B. Subtilis*	*E. Coli*	*P. aeruginosa*	C. albicans	A. niger
5a	19	15	13	09	19	20
5b	22	20	19	23	20	21
5c	19	21	23	19	18	19
5d	18	23	19	22	10	11
5e	15	14	12	19	11	13
5f	13	07	11	08	13	10
5g	13	11	15	17	20	18
5h	10	09	13	11	21	20
5i	22	19	23	20	22	19
5j	22	17	20	23	13	10
5k	14	09	17	15	10	09
Ciprofloxacin	24	26	28	25	-	-
Flucanazole	-	-	-	-	26	25

CONCLUSION

In conclusion, we have demonstrated the synthesis of novel series of potentially biologically active 3-(4,6-diphenyl-6H-1,3-thiazin-2-yl)-2-(4-methoxyphenyl)thiazolidin-4-onederivatives by the reaction of 4,6-diphenyl-6H-1,3-thiazin-2-amine, aromatic aldehyde and thioglycolic acid in polypropylene glycol at 110^0C temperature then characterization and *in-vitro* antimicrobial evaluations. The results reveal that some of the compounds of the series exhibited promising antibacterial and antifungal activity compared to standard drugs.

ACKNOWLEDGMENT

We are very thankful to the Head Department of Chemistry, Principal Y.C.I.S. Satara for providing laboratory Facilities and Shivaji University Kolhapur,National Chemical Laboratory Pune, for providing necessary instrumental facilities.

REFERENCE

Adly Omima MI. Characterization, molecular modeling and antimicrobial activity of metal

complexes of tridentate schiff base derived from 5-acetyl-4-hydroxy-2H-1,3-thiazine-2,6(3H)-dione and 2-aminophenol. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, 2012 ; 95 : 483–490.

Arya Kapil , Rawat DS, Dandia A, Sasai H . Bronsted acidic ionic liquids: Green, efficient and reusable catalyst for synthesis of fluorinated spiro [indole-thiazinones/thiazolidinones] as antihistamic agents. Journal of Fluorine Chemistry, 2012; 137 : 117–122.

Attanasi OA, Filippone P, Lillini S , Mantellini F, Nicolini S, Jesus M , Santos DL, Ignacio R, Aparicio D, Palacios F. Reactions of 1,2-diaza-1,3-dienes with thiol derivatives: a versatile construction of nitrogen/sulfur containing heterocycles. Tetrahedron, 2008; 64 : 9264–9274.

Bhaskar VH, Kumar M and Sangameswaran B. Antimicrobial screening of [(2-substituted phenyl)-4-oxo-1,3-thiazolidine-3-yl]isonicotiniamides. Rasayan J. Chem, 2008;1(2):207-211.

Bhatt HB., Sharma S. Synthesis and antimicrobial evaluation of some novel 2-(4 chlorophenyl imino) thiazolidin-4-one derivatives. Journal of the Korean Chemical Society.2012;56(6);341-347.

Budriesi R, Cosimelli B, Ioan, P, Lanza CZ, Spinelli D, Chiarini A. Cardiovascular characterization of [1,4]thiazino[3,4-*c*][1,2,4]oxadiazol-1-one derivatives: selective myocardial calcium channel modulators. J Med. Chem, 2002 ; 45: 3475 -3481.

Chia EW, Pearce AN , Berridge MV, Larsen Lesley, Perry NB , Sansom CE, Godfrey CA, L Hanton LR, Leon Lu , Walton Michaela, Denny WA, Webb VL, Copp BR, Harper JL. Synthesis and anti-inflammatory structure–activity relationships of thiazine–quinoline–quinones: Inhibitors of the neutrophil respiratory burst in a model of acute gouty arthritis. Bioorg. Med. Chem, 2008;16: 9432–9442.

Datar PA, Aher SB. 2DQSAR of novel thiazolidine-2,4-diones as antihyperglycemic agents. Journal of Current Pharmaceutical Research. 2012; 10 (1): 07-14.

Erker T, Schreder ME, Studenik C. Studies on the chemistry of thienoannelated O,N- and S,N containing heterocycles. Part 19: thieno[2,3-*b*][1,4]thiazines with calcium antagonistic and potassium opening activities. Arch. Pharm, 2000; 333: 58- 62.

Faidallah HM, Khan KA, Asiri AM. Synthesis and biological evaluation of new 3 trifluoromethylpyrazolesulfonyl-urea and thiourea derivatives as antidiabetic and antimicrobial agents. Journal of Fluorine Chemistry, 2011; 132 : 131–137.

Galanski ME, Erker T, Handler N, Lemmens-Gruber R, Kamyarb M and . Studenik CR . Studies on the chemistry of thienoanellated O,N and S,N-containing heterocycles. Part 30: Synthesis and pharmacological properties of thieno[2,3-b][1,4]thiazines with potential vasopressin receptor antagonistic activity. Bioorg. Med. Chem, 2006; 14: 826–836.

Ganorka RS, Ganorkar RP, Parhate VV .Synthesis, characterization and antibacterial activities of some new bromo/nitro 1,3 thiazines .Rasayan. J. Chem, 2013; 6 (1):65-67.

Indumathi S, Perumal S, Banerjee D, Yogeeswari P, Sriram D. L-Proline-catalysed facile green protocol for the synthesis and antimycobacterial evaluation of [1,4]-thiazines. Eur J. Med Chem,2009;44 :4978–4984.

Koketsua M, Tanakaa K, Takenakaa Y, Kwongb CD, Ishiharaa H. Synthesis of 1,3-thiazine derivatives and their evaluation as potential antimycobacterial agents. Eur. J. Pharma. Sci.2002 ; 15: 307–310.

Nagaraj A, Ravi G, Naseem, Sharath Kumar S, Nageswara RG. Synthesis of new biologically active compounds containing linked thiazolyl-thiazolidinone heterocycles. Org. Commun, 2012; 5(4): 160-170.

Omar K, Geronikaki A, Zoumpoulakis P, Camoutsis C, Sokovic M, Ciric A, Glamoclija J. Novel 4-thiazolidinone derivatives as potential antifungal and antibacterial drugs**.** Bioorg Med Chem, 2010;18:426-432.

Osman M, Hussein M, Evelin BM, Ahmed El-Mekabaty. Synthetic approaches and biological evaluation of some new sulfonate ester-containing imidazolone derivatives. American J. Org Chem, 2012; 2(4): 79-86.

Patel N, Bux FB, Parmar V, Singh A. synthesis and biological studies of novel thiazolidinones. Rasayan. J. Chem, 2011;4(4):790-794.

Prasad D, Kumar A, Shukla PK, Nath M. Design, synthesis and antimicrobial evaluation of novel 2- aryl-thiazolidino -4-one derivatives. Org Med Chem Letters, 2011;1:4.

Ramachandran S, Shanmugapandiyan P, Nalini CN. Synthasis and antimicrobial evalualution of of N-(2-(4- substituted phenyl)-4-oxothiazojidin-3-yl) isonicotinamide derivatives. Inter J Phar Sci Res, 2011; 2(6): 1564-1568.

Rawal RK, Tripathi R, Katti SB, Pannecouque C, Clercq ED. Synthesis and evaluation of 2-(2,6-dihalophenyl)-3-pyrimidinyl-1,3-thiazolidin-4-one analogues as anti-HIV-1 agents. Bioorg Med Chem, 2007;15: 3134-3142.

Rekha S, Shantharam U, Vineet Chandy.Synthesis and evaluation of novel thiazolidinediones. Inter Res J Parm. 2011;2(9):81-84.

Sah P, Gharu CH. Synthesis, characterization and antimicrobial evaluation of schiff bases of 4-thiazolidinone bearing thiadiazole moiety. Journal of Current Pharmaceutical Research, 2012;9 (1): 44-48.

Samadhiya P, Sharma R , Srivastava S K. Synthesis and antitubercular activity of 4-oxo-thiazolidine derivatives of 2-amino-5-nitrothiazole . Bull. Chem. Soc. Ethiop, 2013 ;27(2): 249-263.

Schreder ME, Erker T. Studies on the chemistry of thienoannelated O,N- and S,N-containing heterocycles. 17 Preparation of 1H-Thieno[2,3-*b*][1,4]thiazine-1-carboxamides as smooth muscle relaxants. J. Heterocycl. Chem, 2000;37: 349-354.

Smith ML. Formation and oxidation of some phenothiazine derivatives . J. Org.Chem,1951;16: 415 - 418.

Smith LE. Synthetic organic compound as potential insecticides. Ind.Engg.Chem,1942;34:499-501.

Snick WV, Aibuldinov YK, Dehaen Wim. An efficient synthetic route towards novel thienobenzothiazoles, thieno-benzothiazepines, and thienobenzothiazines. Tetrahedron, 2013; 69: 4176-4184.

Tanaka A, Mizuno H,Sakurai M. Preparation of novel benzothiophene derivatives and their use as urokinase inhibitors. PCT. Int. Appl, 1998; 9811089.

Tandon VK, Maurya HK, Yadav DB, Tripathi A, Kumar M, Shukla PK. Naphtho[2,3-b][1,4]-thiazine-5,10-diones and 3-substituted-1,4- dioxo-1,4-dihydronaphthalen-2-yl-thioalkanoate derivatives: Synthesis and biological evaluation as potential antibacterial and antifungal agents. Bioorg. Med. Chem. Lett. 2006;16:5883–5887.

Torres-Garcia P, Vinuelas-Zahinos E, Luna-Giles F, Espino J, Barros-Garcia FJ. Zinc(II) complexes with novel 1,3-thiazine/pyrazole derivative ligands: Synthesis, structural characterization and effect of coordination on the phagocytic activity of human neutrophils. Polyhedron,2011; 30: 2627–2636.

Tozkoparan B, Aktay G, Erdem Y. Synthesis of Some 1,2,4-Triazolo[3,2-*B*]-1,3-Thiazine-7-ones with potential analgesic and antiinflammatory activities. II Farmaco, 2002; 57: 145–152.

Tung-Mei T, Wen-Chuan H, Condensed naphtho [1,8- De][1,3] thiazines 2. an orientating structure modification of naphtho [1,8-De][1,2,4]- triazolo [3,4- B][1,3] thiazine ring system. Chin. Pharma, J. 2005; 57: 43-48.

Vicini P, Geronikaki A, Anastasia K, Incerti M ,Zani F. synthesis and antimicrobial activity of novel 2-thiazolylimino-5-arylidene-4-thiazolidinones. Bioorg Med Chem, 2006;14:3859-3864.

Wei W, Bing Z, Chao X, Wenpeng W. synthesis and antitumor activity of the thiazine multithioether. Int J.Org.Chem, 2012; 2; 117-120.

Zia-ur-Rehman Muhammad, Choudary JA, Elsegood MRJ, Siddiqui HL, Khan KM. A facile synthesis of novel biologically active 4-hydroxy-N0-(benzylidene)-2H-benzo[e][1,2]thiazine-3-carbohydrazide,1-dioxides. Eur. J. Med. Chem. 2009;44: 1311–1316.

How to cite this article:

Sayaji S. Didwagh, Pravina B. Piste, Aravind S. Burungale, Avinash M. Nalawade. Synthesis and antimicrobial evaluation of novel 3-(4,6- diphenyl-6H-1,3- thiazin -2-yl)-2- (4-methoxyphenyl) thiazolidin-4-one derivatives. J App Pharm Sci, 2013; 3 (11): 122-127.