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Synthesis of 4,4'-bis-(Benzylideneamino)Bibenzyls and 4,4'- bis (2"Aryl-5"-methyl-4"-oxo-thiazolidin-3"-yl)Bibenzyls from 1,2-dianilino-ethane,their characterization and study of their micro biological activities.

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ABSTRACT

4,4'-diamino-bibenzyl on refluxing with various aromatic and heteroaromatic aldehydes in alcohol in presence of catalytic amount of glacial acetic acid formed Schiff bases(I).These Schiff bases on refluxing with thioglycollic acid and thiolactic acid in alcoholic medium uing catalytic amount of fused $ZnCl_2$ on a steam bath using a Dean Stark water separator furnished the bis thiazolidinones and methyl thiazolidinones respectively in quantitative yields.The newly synthesized compounds were characterized by IR,^{1}H NMR,spectra,elemental analysis and evaluated for their in vitro antimicrobial activities against S.aureus and E.coli .

KEYWORDS:Bibenzyl,1,2-dianilinoethane,Schiff bases,bis thiazolidinones, anti microbial.

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INTRODUCTION

Heterocycles constitute one of the biggest classical divisions of organic chemicals and are of immense importance biologically to the pharmaceutical and agronomic based industries and indeed to the development of human beings.

Heterocycles bearing N and S constitute the core structure of a number of biologically interesting compounds Heterocycles constitute one of the biggest classical divisions of organic chemicals and are of immense importance biologically[1] to the pharmaceutical and agronomic based industries and indeed to the development of human beings.

Heterocycles bearing N and S constitute the core structure of a number of biologically interesting compounds.Thiazolidinones are well known for their hypnotic [2] and anti convulsant[3-5]properties.The presence of the N-C-S linkage in heterocycles is a biologically active scaffold and has been reported to have anti-tubercular[6],anthelm- intics[7],antifungal[8,9]and analgesic and anti inflammatory activity[10-12].4-thiazolidinones have also been shown to have anti HIV[13,14] activity. Diverse biological activities such as insecticidal[15,16], hypoglycemics and hypolipedemics[17,18].Thiazolidin-4-ones are extensively used anti cancer agents[18,19],as antiproliferative and metastasis agent[20,21] against cancer cell lines.Thiazolidinone derivatives have been prepared and used as parts of polymeric materials for NLO's[22] molecular and liquid crystals.

It has been found that both natural and synthetic bibenzyls show marked antifungal activity against wide range of fungi.This array of biological response profile has attracted our attention to further investigate the potential of this organic motif. Bibenzyl and thiazolidinone together as one organic motif, with the hope to achieve enhanced biological activity of the product.

The above facts and our desire to develop noveaux antimicrobials prompted us to synthesize hitherto unknown title compounds,which are derivatives of 4-thiazolidinones incorporating bibenzyl moiety4,4'-bis–(2"-aryl-5"methyl/unsubstit- uted-4"-oxo-thiazolidin-3"-yl)bibenzyl.

MATERIALS AND METHODS

All the chemicals used were of high purity grade; solvents were dried and distilled before use. Reactions were monitored by TLC using precoated 0.2mm plates of silica gel G60 F254 (Merck Germany) as the adsorbent .Visualization of the spots was done using iodine vapours or UV light.Melting points were determined by electro-thermal apparatus using open capillary tubes expressed in ^{o}C and are uncorrected. Analysis and Physical measurements: The IR spectra was recorded on a Jasco-FTIR-4100 spectrophotometer with KBr optics.NMR spectra was recorded on Bruker 400 MHz instrument using d6 -DMSO as solvent.The newly synthesized compounds were evaluated for their in vitro antimicrobial activities against S.aureus and E.coli using Ampicillin and Streptomycin as references.

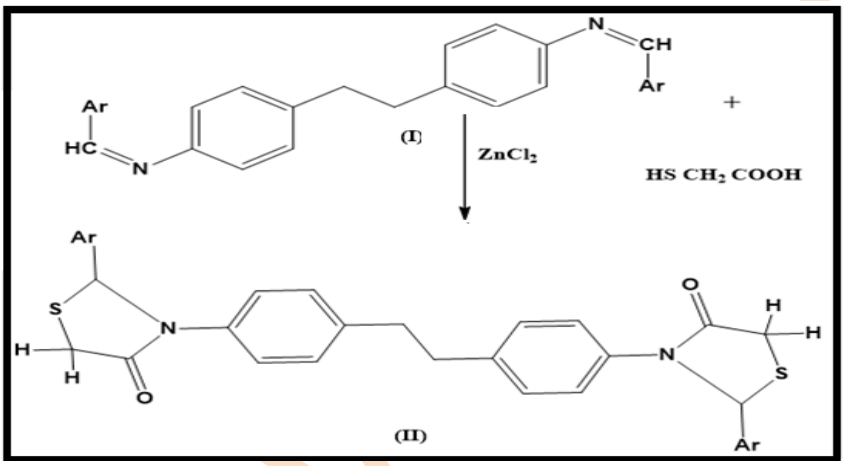
EXPERIMENTAL SECTION

General procedure for synthesis of 4,4' –bis-(Benzylideneamino) Bibenzyl (I):[23]

To a mixture of 4,4'-dianilino ethane(0.01 mole,2.12 gms) and aromatic/hetero aldehydes(0.02 mole) in 25 cm^3 of ethanol and a few drops of glacial acetic acid were added and refluxed for a period of 1-2 hours on a steam bath and cooled.The solid that separated out was filtered,washed with $NaHSO_3$, to triturate the surplus aldehyde followed by washing with water.The solids having varying shades of yellow were

purified from ethanol.

2)*General procedure for synthesis of 4,4'-bis(2Ӈryl-4ӈoxo-thiazolidin - 3ӈyl) Bi benzyls(IIa-m)*



Scheme 1 : Synthesis of 4,4'-bis(2"Aryl-4"-oxo-thiazolidin-3"-yl)Bibenzyls (II a-m)

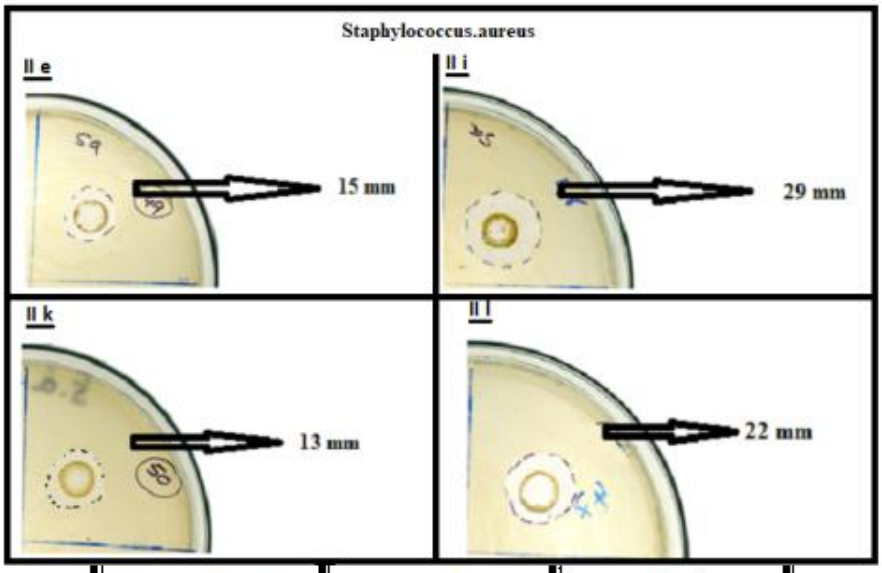
A mixture of Schiff's Base(0.01 mole) and mercapto acetic acid (0.02 mole,1.4cm^3) was taken in freshly distilled benzene(30 cm^3) and a pinch of freshly fused $ZnCl_2$. The reaction mixture was refluxed on a steam bath for a period of 6-8 hours using a Dean Stark water separator.The excess of benzene and thioglycollic acid was remov -ed from the reaction mixture by distillation under reduced pressure and cooled to room temperature.The residue obtained after removal of benzene was cooled poured onto crushed ice and filtered ,then washed successively with ice cold saturated solu - tion of $NaHCO_3$ to remove the traces of unreacted thioglycollic acid,followed by washings with copious amounts of water.The compounds were purified with aqueous ethanol to give buff coloured crystals(Scheme1).The data of these compounds is presented in the three tables given below.

Table 1 : Physico-Chemical characteristics of 4,4'-bis(2"Aryl-4"-oxo-thiazolidin-3"-yl)Bibenzyls

	R of Schiff base	Molecular Formula	Mol Wt	%yield	M.P. (°C)
a)	4 hydroxy benzaldehyde	$C_{32}H_{28}N_2O_4S_2$	568.71	67	204
b)	2 thenaldehyde	$C_{28}H_{24}N_2O_2S_4$	548.76	58	179
c)	2,3,4-trimethoxy benzaldehyde	$C_{38}H_{40}N_2O_8S_2$	716.86	67.1	156
d)	3 nitro benzaldehyde	$C_{32}H_{26}N_4O_6S_2$	626.70	64.4	190
e)	2,4-dichloro benzaldehyde	$C_{32}H_{24}Cl_4N_2O_2S_2$	674.49	59.0	193 D
f)	4,4-dimethylamino benzaldehyde	$C_{36}H_{38}N_4O_2S_2$	622.84	65	144
g)	3,4,5-trimethoxy benzaldehyde	$C_{38}H_{40}N_2O_8S_2$	716.86	62	138
h)	4 amino benzaldehyde	$C_{32}H_{30}N_4O_2S_2$	566.74	66	177
i)	Furfural	$C_{28}H_{24}N_2O_4S_2$	516.63	62	192
j)	2 nitro benzaldehyde	$C_{32}H_{26}N_4O_6S_2$	626.70	68.2	143
k)	4 nitro benzaldehyde	$C_{32}H_{26}N_4O_6S_2$	626.70	69	199
l)	4 fluoro benzaldehyde	$C_{32}H_{28}F_4N_2O_2S_2$	572.69	64.7	198
m)	2,4 -dichloro benzaldehyde	$C_{32}H_{24}Cl_4N_2O_2S_2$	674.49	57	163

Table 2 : Elemental Analysis of 4,4'-bis(2"Aryl-4"-oxo-thiazolidin-3"-yl)Bibenzyls

No	Observed Values %					Calculated Values %				
Ele	C	H	N	O	S	C	H	N	O	S
a	67.58	4.96	4.93	11.25	11.2	67.2	4.75	4.73	10.8	10.9
b	61.28	4.41	5.10	5.83	23.4	61.0	4.1	4.8	5.53	22.9
c	63.67	5.62	3.91	17.85	8.95	63.4	5.2	3.6	17.2	8.4
d	62.58	4.95	6.26	16.67	9.55	62.2	4.6	6.2	16.1	9.3
e	60.43	4.64	4.03	11.50	9.22	60.4	4.64	4.03	11.5	9.22
f	66.34	5.87	6.27	11.94	9.57	66.14	5.5	6.0	11.4	9.1
g	63.67	5.62	3.91	17.85	8.95	63.22	5.2	3.5	17.5	8.4
h	65.50	5.50	6.55	12.46	9.99	65.0	5.1	6.2	12.2	9.3
i	65.09	4.68	5.42	12.39	12.4	64.8	4.48	5.2	12.1	12.0
j	62.58	4.95	6.26	16.67	9.55	62.2	4.6	6.2	16.1	9.3
k	62.58	4.95	6.26	16.67	9.55	62.2	4.6	6.2	16.1	9.3
l	67.11	4.58	4.89	5.59	11.2	66.9	4.3	4.2	5.2	11.0
m	60.43	4.64	4.03	11.50	9.22	60.4	4.64	4.03	11.5	9.22



Streptomycin	18	20
Ampicillin	27	18

Figure 1:Pictures of petridishes showing zone of inhibition of sample and References of 4,4'-bis(2"Aryl-4"-oxo-thiazolidin - 3"-yl)Bibenzyls

Spectral Analysis of Thiazolidinones(II)

^{1}H NMR ($CDCl_3$) spectral analysis of (II l)in δ ppm

2.79(s,4H,acyclicCH_2CH_2),3.96(q,4H,cyclic,CO-CH_2-S),6.16(s,2H,cyclicS-CH-N)6.42-8.16 (m,16 H,ArH) .

I.R.Spectral analysis of (II l)(cm^{-1})

746(C–Sstr in thiazole),792,1331(C-F),829(1,4-disubstituted benzene rings),1015(CO S),1225(N-C-S),1378 (N-CH_2),693,1509,1605,1685,2341,2361(C=N & C=C Ar ring str),1894 (C=O), 2825,2921(CH_2-S),3361(Ar str &bend).

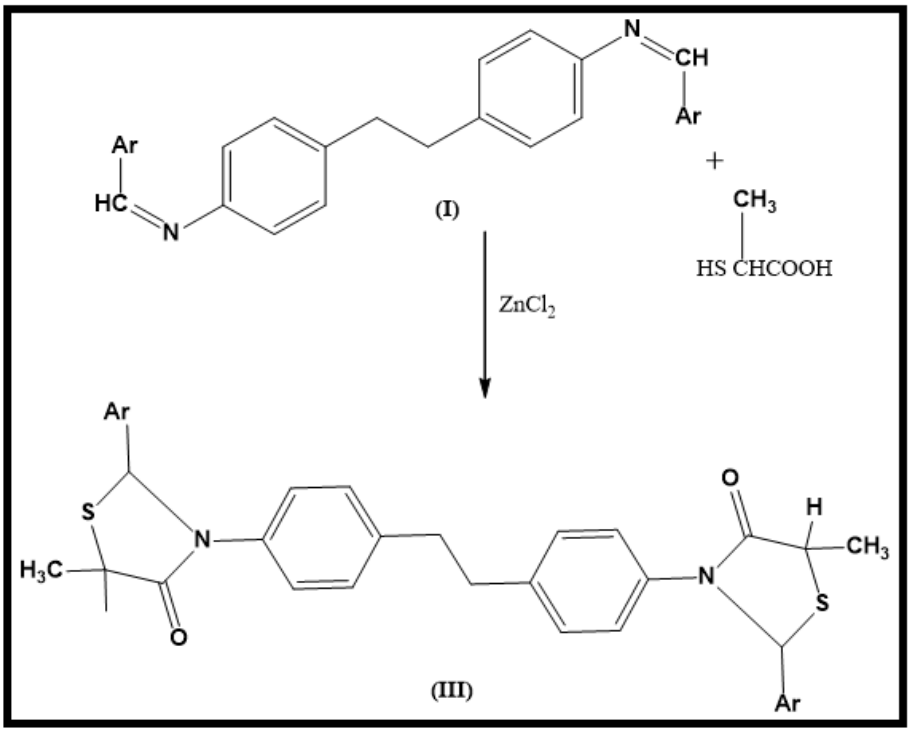
^{1}H NMR ($CDCl_3$) spectral analysis of (II k)in δ ppm

2.86(s,4H,acyclicCH_2CH_2),4.30(q,4H,cyclic,CO-CH_2-S),5.95(s,2H,cyclicS-CH-N) 7.24 -7.95(m,16 H,ArH).

I.R.Spectral analysis of (II k)(cm^{-1})

685,750,(C–Sstr in thiazole)790(1,4-disubstituted benzene rings)700,710,735,900, 940(Arstr&bend),1025,1030(CO-S),1230,1250(N-C-S),1075(CO-S),1300,1370,14 50,1550(N-O stretching for Aromatic Nitro group),1540,1550,1630(O=C-N),1720, 1750(C-N),2850,2950,2960(CH_2),3050,3350(Ar str &bend).

3)General procedure for synthesis of 4,4'-bis(2Ⱥryl-5ⱠⱠmethyl-4ⱠⱠoxo- thiazolidin -3ⱠⱠ yl)Bibenzyls (III a-m)



Scheme 2:Synthesis of 4,4'-bis (2"Aryl-5"-methyl-4"-oxo- thiazolidin -3"-yl) Bibenzyls (III a-m)

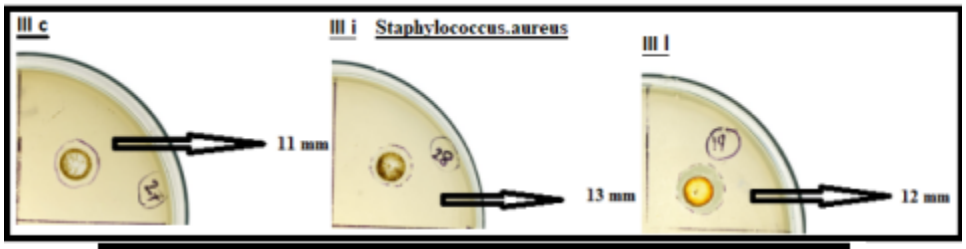
A mixture of Schiff's Base (0.01 mole) and thiolactic acid/2-mercapto propionic acid (0.02 mole,1.8cm^3)was taken in freshly distilled benzene(30 cm^3)and a pinch of freshly fused $ZnCl_2$ .The reaction mixture was refluxed on a steam bath for a period of 6-8 hours using a Dean Stark water separator.The excess of benzene and thiolactic acid was removed from the reaction mixture by distillation under reduced pressure and cooled to room temperature.The residue obtained after removal of benzene was cooled poured onto crushed ice and filtered,then washed successively with ice cold saturated solution of $NaHCO_3$ to remove the traces of unreacted thiolactic acid/ 2- mercapto propionic acid,followed by washings with copious amounts of water.The compounds were purified with aqueous ethanol to give buff coloured crystals(Scheme 2).The data of these compounds is presented in the tables given below.

Table 3 : Physico-Chemical characteristics of 4,4'-bis (2"Aryl-5"-methyl- 4"-oxo- thiazolidin-3"-yl) Bibenzyls (IIIa-m)

R of Schiff base		Molecular Formula Thiazolidinones	Mol Wt	% yield	M.P. (°C)
a)	4 hydroxy benzaldehyde	$C_{34}H_{32}N_2O_4S_2$	596.76	60	>250
b)	2 thenaldehyde	$C_{30}H_{28}N_2O_2S_4$	576.82	64	>250
c)	2,3,4-trimethoxy benzaldehyde	$C_{40}H_{44}N_2O_8S_2$	744.92	69	226
d)	3 nitro benzaldehyde	$C_{34}H_{30}N_4O_6S_2$	654.76	61.0	>250
e)	2,4-dichloro benzaldehyde	$C_{34}H_{28}Cl_4N_2O_2S_2$	702.54	67	>250
f)	4,4-dimethylamino benzaldehyde	$C_{38}H_{42}N_4O_2S_2$	650.90	58	>250
g)	3,4,5-trimethoxy benzaldehyde	$C_{40}H_{44}N_2O_8S_2$	744.92	71	>250
h)	4 amino benzaldehyde	$C_{34}H_{34}N_4O_2S_2$	594.79	54	>250
i)	Furfural	$C_{30}H_{28}N_2O_4S_2$	544.68	59	>250
j)	2 nitro benzaldehyde	$C_{34}H_{30}N_4O_6S_2$	654.76	62	249
k)	4 nitro benzaldehyde	$C_{34}H_{30}N_4O_6S_2$	654.76	73.0	>250
l)	4 fluoro benzaldehyde	$C_{34}H_{30}F_2N_2O_2S_2$	600.74	75.0	>250
m)	2,4 -dichloro benzaldehyde	$C_{34}H_{28}Cl_4N_2O_2S_2$	702.54	67	>250

Table 4 : Elemental Analysis of 4,4'-bis (2"Aryl-5"-methyl- 4"-oxo- thiazolidin-3"yl) Bibenzyls (IIIa-m)

No	Observed Values %					Calculated Values %				
Ele	C	H	N	O	S	C	H	N	O	S
a	68.43	5.40	4.69	10.7	10.7	68.2	5.0	4.2	10.3	10.4
b	65.5	5.15	4.77	8.18	16.4	65.2	4.8	4.3	7.8	16.1
c	64.49	5.95	3.76	17.2	8.61	64.2	5.5	3.6	17.0	8.1
d	63.5	5.33	6.00	16.0	9.2	63.0	5.1	5.8	15.7	9.0
e	61.4	5.01	3.87	11.05	8.86	61.1	4.6	3.2	10.7	8.4
f	70.12	6.50	8.61	4.92	9.85	70.0	6.20	8.1	4.2	9.5
g	64.49	5.95	3.76	17.2	8.61	64.2	5.5	3.6	17.0	8.1
h	66.34	5.87	6.27	11.94	9.57	66.0	5.1	6.0	11.4	9.3
i	66.15	5.18	5.14	11.75	11.8	64.8	4.9	4.7	11.5	11.6
j	63.5	5.33	6.00	16.0	9.2	63.0	5.1	5.8	15.7	9.0
k	63.5	5.33	6.00	16.0	9.2	63.0	5.1	5.8	15.7	9.0
l	67.98	5.03	4.66	5.33	10.7	67.6	4.7	4.2	5.0	10.1
m	61.4	5.01	3.87	11.05	8.86	61.1	4.6	3.2	10.7	8.4



Streptomycin	18	20
Ampicillin	27	18

Figure 2:Pictures of petridishes showing zone of inhibition of sample and References of 4,4'-bis (2"Aryl-5"-methyl-4"-oxo- thiazolidin -3"-yl) Bibenzyls

Spectral Analysis of 5-Methyl Thiazolidinones(II)

^{1}H NMR ($CDCl_3$) spectral analysis of (III i)in δ ppm

1.75(d,6H,J=8),2.74(s,4H,),4.02(s,2H,J=8) ,6.18 (s.2H),6.93-7.41(m,14 H).

I.R.Spectral analysis of (III i)(cm^{-1})

757(C-S-C cyclic);844(para- disubstituted benzene);1458(C–S–CH_2 str.),2106 (strong and broad for N-C-S);2533 for (C=O);3388 (Ar str &bend).

^{1}H NMR ($CDCl_3$) spectral analysis of (III g)in δ ppm

1.51(s,6H,J=8 ,CH_3),2.77 (s,4H, acyclic CH_2CH_2) ,3.95(q ,2H , J=8 ,cyclic,COCH S), 4.72(s,18H,OCH_3),6.49 (s ,2H, CH-N-C=O) 7.21-8.0 (m ,12 H, ArH).

I.R.Spectral analysis of (III g)(cm^{-1})

749(C-S-Ccyclic),790,1500(Ar-C-H),1020,1075,1200,1275(=C-O-C-),1750 (-C=C-O-CO-R),2250 for (C=O),3358(Ar str &bend).

RESULTS and DISCUSSION

On the basis of the above synthesis,it is noteworthy that all the the newly synthesized bibenzyl based thiazolidinones were obtained in quantitative yields.The 4,4'- di amino -bibenzyl on condensation with various hetero and aromatic aldehydic compounds gave 4,4'-bis(benzylidene amino)bibenzyls,which on cyclo condensation with mer capto acetic acid and mercapto propionic acid afforded the corresponding-4,4'-bis (2"-aryl-5"-unsubstituted/methyl-4"-oxo-thiazolidin-3'-yl)-bibenzyls.

The use of a water separator was found to be advantageous and the course of the reaction was followed by the volume of water collected and TLC.The reaction probably took place by the intermediate formation of the aldimine and ketimine formed by the addition of the thiol on the > C=N- followed by the capture of a proton by the N atom and subsequent cyclization.The effect of

electron withdrawing or releasing substituents on the positive character of the Carbon atom and the negative character of the Nitrogen of the azo methine linkage and therefore on the suscept -ibility of carbon to the nucleophilic attack by the anion of mercapto acetic acid are evident from the yields of thiazolidin-4-ones.

Nucleophilic addition of the the carbonyl carbon atom on the diamine,followed by dehydration produced the Schiff base in situ,which on nucleophilic addition on the carbon of –C=N bond with –SH group of 2-mercapto acetic acid /2 mercapto propi - onic acid followed by intramolecular nucleophilic substitution on the carboxylic group of the thio acid and cyclo dehydration gave the desired oxo-thiazolidinones. During this addition the configuration of the mercapto acids remains conserved. Although the resulting products would have been formed as diastereoisomeric pairs, but the products could not be separated into two diastereoisomers.It seems that the cis isomer probably has isomerized into the more stable trans product.The configuration was assigned on the basis of ^{1}HNMR.

The structural assignments of the synthesized products were based on the ^{1}H NMR and IR spectral studies and elemental analysis.In elemental analysis results are in good agreement with the calculated values.

The microbiological assay is based upon a comparison of inhibition of growth of micro-organisms by measured concentrations of test compounds with that produced by known concentration of a standard antibiotic Here, the presence or absence of growth is investigated.The cup plate method depends upon diffusion of antibiotic from a well through a solidified agar layer in a Petridish or plate to an extent such that growth of added micro organisms is prevented entirely in a zone around the well containing solution of the antibiotics.The cup-plate method is simple and measurement of inhibition of microorganisms is also easy. Here, we have use this method for antibacterial screening of the test compounds.The compound which having the antibacterial effect show the zone of inhibition around the well.The zone of inhibition is measured in mm.If the zone diameter is high it indicates more anti bacterial affect against respective organism.The compounds displayed excellent to good in vitro antimicrobial activity comparable to that of two antibiotics Ampicillin and Streptomycin,which have **18 mm** and **27 mm** zones of Inhibition respectively .

Of the bis thiazolidinones Compounds **(II i)** and **(II l)** showed excellent antibacterial activity with a zone of inhibition of **29** mm and **22** mm;whereas Compounds **(II e)** and **(II k)** showed good antibacterial activity with zones of inhibition of **15** mm and **13** mm with *S.aureus* respectively,indicating that bis thiazolidinones hold promising antibacterial potential as compared to Streptomycin and Ampicillin which have **18 mm** and **27 mm** zones of Inhibition respectively .

However in the case of bis-5-methyl substituted thiazolidinones Compounds **(III c), (III i)** and **(III l)**

showed moderate antibacterial activity with zones of inhibition of **11**mm,**13** mm and **12** mm with *S.aureus* respectively as compared to Streptomycin and Ampicillin which have **18 mm** and **27 mm** zones of Inhibition respectively.

These compounds and other newly synthesized thiazolidinones showed negligible or no antibacterial activity against *E.coli.*

CONCLUSIONS

The present study indicates that the 4,4' bis (oxo-thiazolidinone)bibenzyl framework reported herein might be useful for the developing of efficacious bactericides by suit able structural variations in the bibenzyl nucleus and the thiazolidinone nucleus.

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REFERENCES

1. Verma A,Saraf SK,4-Thiazolidinone-A biologically active scaffold.Eur. J. Med. Chem.,2008;43(5):897-905.
2. Ergenç N,Çapan G,Günay NS,Özkirimli S,Güngör M,Özbey S,Kendi E,Synthesis and Hypnotic Activity of New 4□Thiazolidinone and 2□Thioxo□4,5□imidazolid- inedione Derivatives, Arch.Pharm.,1999;332(10):343-347.
3. Gürsoy A,Terzioğlu N,Synthesis and isolation of new regioisomeric 4-thiazol- idinones and their anticonvulsant activity,Turk J Chem.,2005;29(3):247-254.
4. Shanmuga PS, Aanandhi V, Synthesis and Anticonvulsant activity of Thiazol-idinonederivatives,Synthesis.,2012;4(1):01-04.
5. Agarwal A,Lata S,Saxena KK,Srivastava VK,Kumar A,Synthesis and anti convul -sant activity of some potential thiazolidinonyl 2-oxo/thiobarbituric acids,Eur.J. Med.Chem.,2006;41(10):1223-1229.
6. Pathak RB,Chovatia PT,Parekh HH, Synthesis,antitubercular and antimicro bial evaluation of 3-(4-chlorophenyl)-4-substituted pyrazole derivatives,Bioorg. Med.Chem.Lett.,2012;22(15):5129-5133.
7. Sarkar S,Dwivedi J,Chauhan R,Synthesis of 1-[2 (substituted phenyl)- 4-oxo thiazolidin-3-yl]-3-(6-fluro-7-chloro-1,3-benzothiazol-2-yl)-ureas as anthelmintic agent,J Pharm Res.,2013; 7(5):439-442.
8. Omar K,Geronikaki A,Zoumpoulakis P,Camoutsis C,Soković M,Ćirić A ,Glamo člija J,Novel

4-thiazolidinone derivatives as potential antifungal and anti bacterial drugs,Bioorg.Med.Chem.,2010;18(1):426-432.

9. Patel KH,Mehta AG,Synthesis and Antifungal Activity of Azetidinone and Thiaz olidinones Derivatives of 2-Amino-6-(2-naphthalenyl)thiazolo[3,2-d] thiadiazole, J.Chem.,2006;3(4):267-273.
10. Taranalli AD,Bhat AR,Srinivas S,Saravanan E,Antiinflammatory,analgesic and antipyretic activity of certain thiazolidinones,Indian.J.Pharm.Sci.,2008;70(2):159 -164.
11. Deep A,Jain S,Sharma PC,Phogat P,Malhotra M,Synthesis of 2-(aryl)-5-(arylid- ene)-4-thiazolidinone derivatives with potential analgesic and anti- inflammatory activity,Med.Chem.Res.,2012;21(8):1652-1659.
12. Sharma A,Kumar V, JainS SharmaPC,Thiazolidin-4-one and hydrazone derivativ- es of capric acid as possible anti-inflammatory,analgesic and hydrogen peroxide-scavenging agents,J.Enzyme.Inhib.Med.Chem.,2011;26(4):546-552.
13. Rawal RK,Tripathi R,Katti SB,Pannecouque C,DeClercq E,Design and synthesis of 2-(2,6-dibromophenyl)-3-heteroaryl-1,3-thiazolidin-4-ones as anti-HIV agents, Eur.J.Med.Chem.,2008;43(12):2800-2806.
14. Ravichandran V,Kumar BP,Sankar S,Agrawal RK,Predicting anti-HIV activity of 1,3,4-thiazolidinone derivatives:3D-QSAR approach,Eur.J.Med.Chem.,2009;44 (3):1180-1187.
15. Zhong-Zhen Z,Qiong C,Guang-Fu Y,Synthesis and insecticidal activities of N-carbonylamido-2-(4-oxo-4H-1-benzopyran-3-yl)-4-thiazolidinones derivatives by microwave-assisted parallel syntheses,Chin.J.Org.Chem.,2008;28(8):1385-1392.
16. Singh T,Srivastava V K,Saxena KK,Goel SL,Kumar A,Synthesis of new thiazolyl thiazolidinylbenzothiazoles and thiazolylazetidinylbenzothiazoles as potential insecticidal,antifungal,and antibacterial agents,Arch.Pharm.,2006;339(8):466-472.
17. Choudhari P,Kumbhar S,Phalle S,Choudhari S, Desai S,Khare S,Jadhav S,Appli -cation of group-based QSAR on 2-thioxo-4-thiazolidinone for development of potent anti-diabetic compounds,J.Mol.Struct.,2017;1128:355-360.
18. Sohda T,Mizuno K,Momose Y,Ikeda H,Fujita T,Meguro K,Studies on antidiab- etic agents.11.Novel thiazolidinedione derivatives as potent hypoglycemic and hypolipidemic agents,J. Med.Chem.,1992;35(14):2617-2626.
19. Havrylyuk D,Mosula L,Zimenkovsky B, Vasylenko O,Gzella A, Lesyk R,Synth- esis and anticancer activity evaluation of 4-thiazolidinones containing benzo thiazole moiety,Eur.J.Med.Chem.,2010;45(11):5012-5021.
20. Havrylyuk D,Zimenkovsky B,Vasylenko O,Gzella A,Lesyk R,Synthesis of new 4-

thiazolidinone-,pyrazoline-,and isatin-based conjugates with promising anti tumor activity,J. Med. Chem.,2012;55(20):8630-8641.

21. Wang S,Zhao Y,Zhang G,Lv Y,Zhang N,Gong P,Design, synthesis and biological evaluation of novel 4-thiazolidinones containing indolin-2-one moiety as potential antitumor agent,Eur.J.Med.Chem.,2011;46(8):3509-3518.
22. Smokal V,Kolendo A,Krupka O,Derkowska B,Czaplicki R,Sahraoui B,New Met- hacrylic Oxazolone and Thiazolidinone Containing Polymers for Non linear Optical Applications,Mol.Cryst.Liq.Cryst.,2008;485(1):1011-1018.
23. Ramsinghani RG,Filmwala ZA, A comparative study of the synthesis of bis azo methines of 4,4-diamino-bibenzyl by conventional method and micro waves, their chacterization and study of their microbiological activities,WJPPS.,2016; 6 (2):1255-1263.