Available online at www.derpharmachemica.com

ISSN 0975-413X
CODEN (USA): PCHHAX

Der Pharma Chemica, 2017, 9(13):65-67
(http://www.derpharmachemica.com/archive.html)

Synthesis and Biological Evaluation of 4-thiazolidinone Derivatives

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ABSTRACT

A mixture of substituted quinoline-3yl-azomethines in dry dioxane containing pinch of anhydrous $ZnCl_2$ and mercaptoacetic acid was refluxed for 8 h. The reaction mixture was cooled and poured into ice cold water. The solid was separated and filtered, dried and crystallized from ethanol solvent to get novel 4-thiazolidinone Derivatives. The synthesized compounds were characterized on the basis of satisfactory elemental analytical and spectral (IR, ^{1}HNMR) data. Most of the compounds show excellent results when screened for their antimicrobial activity.

Keywords: Synthesis, Characterization, 4-thiazolidinone derivative, Antimicrobial study

INTRODUCTION

In present era heterocyclic compounds are associated with wide range of biological and pharmacological activities [1-4]. Thiazolidinones are considered as a biologically important active scaffold that possesses almost all types of biological activities. Thiazolidinone, a saturated form of thiazole with carbonyl group on fourth carbon, has been considered as magic moieties (wonder nucleus) which possess almost all types of biological activities. This diversity in the biological response profile has attracted the attention of many researchers to explore this skeleton to its multiple potential against several activities. Its derivatives belong to the most frequently studied moieties and its presence in penicillin was the first recognition of its occurrence in nature [5,6], several substituted thiazolidinone have been found to be possessed a number of biological activities like antibacterial [7-11], anticancer [12,13], antitubercular [14-17], antifungal [18,19], anti-inflammatory [20], antiviral [21,22], and analgesic [23,24]. Due to this vital role it was thought to synthesize 4-thiazolidinone derivatives and study for their biological activities.

EXPERIMENTAL

All solvents and chemicals used were of commercial or LR grade, and were used without further purification. The melting points (ºC) were recorded by open capillary method and are uncorrected. IR spectra's were recorded on Shimadzu FTIR using KBr discs. ^{1}H NMR spectra were recorded on Bruker Advance II 400 spectrometer in $CDCl_3$ using TMS as an internal standard reference.

Synthesis of substituted quinoline-3yl-azomethines (3 a-d)

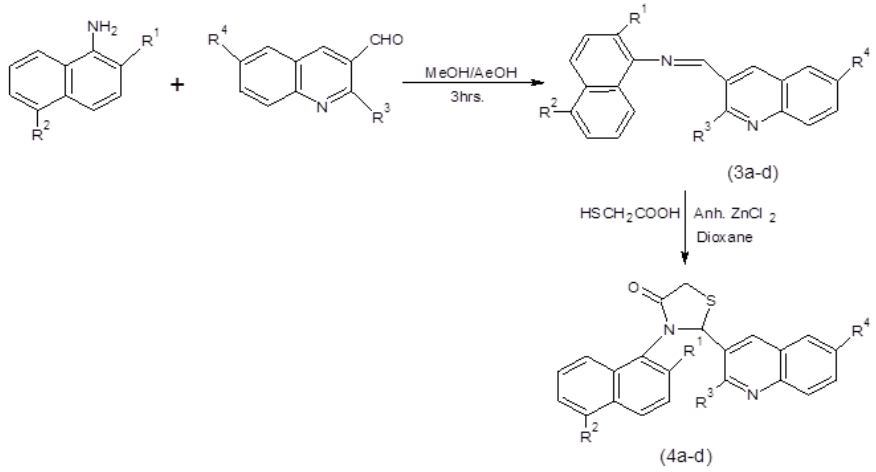
An equimolar mixture of 2,5-substituted naphthalene-1-amine (1) (0.01 M) and 2,6-substituted quinoline-3-carbaldehyde (2) (0.01 M) in methanol containing 5-6 drops of acetic acid was refluxed for 3 h. Cool and reaction mixture was poured in cold water. The solid thus separated was filtered, dried and crystallized from ethanol to gives substituted quinoline-3yl-azomethines (3a-d) (Scheme 1).

Synthesis of 4-thiazolidinone derivatives (4 a-d)

A mixture of substituted quinoline-3yl-azomethines (3a-d) (0.01 M) in dry dioxane (30 ml) containing pinch of anhydrous $ZnCl_2$ and mercaptoacetic acid (0.01 M) was refluxed for 8 h. The reaction mixture was cooled and poured into ice cold water. The solid was separated and filtered, dried and crystallized from ethanol solvent to get 4-thiazolidinone derivatives (4 a-d).

Spectral analysis (Compound No. 4d)

IR analysis (wave number in cm^{-1}): 3058 cm^{-1} (Ar-H stret.), 2951 (C-H stret.), 1682 (C=O stret.), 1248 (C-N-C stret).
NMR analysis (δ ppm): 2.41 (s, 3H, CH_3), 3.39 (s, 2H, CH_2), 5.95 (s, 1H, CH), 7.10- 8.65 (m, 11Ar-H).



Scheme 1: Synthesis of 4-thiazolidinone derivatives

The antimicrobial activity of all newly synthesized compounds was evaluated against gram-negative *Escherichia coli, Pseudomonas aeruginosa,* and gram-positive bacteria *Staphylococcus aureus, Bacillus subtilis* Table 1. The culture of each microbe's species was incubated at 37^{o}C and the zone of inhibition on agar plates (diffusion method) was measured after 24 h. Most of these compounds were found active.

Table 1: Physical property of compounds

Compounds	R1	R2	R3	R4	Molecular Formula	MP◦C	% Yield	R.F. Value	% Nitrogen	
									Found	Calculated
3a	H	SO_3H	Cl	CH_3	$C_{21}H_{15}ClN_2O_3S$	201	59	0.64	6.79	6.82
3b	CH_3	H	Cl	CH_3	$C_{22}H_{17}ClN_2$	175	60	0.57	8.10	8.13
3c	H	NO_2	Cl	CH_3	$C_{21}H_{14}ClN_3O_2$	182	61	0.70	11.15	11.19
3d	H	H	Cl	CH_3	$C_{21}H_{15}ClN_2$	199	66	0.51	8.43	8.47
4a	H	SO_3H	Cl	CH_3	$C_{23}H_{17}ClN_2O_4S_2$	192	57	0.65	5.75	5.78
4b	CH_3	H	Cl	CH_3	$C_{24}H_{19}ClN_2OS$	190	55	0.56	6.67	6.69
4c	H	NO_2	Cl	CH_3	$C_{23}H_{16}ClN_3O_3S$	187	58	0.71	9.33	9.34
4d	H	H	Cl	CH_3	$C_{23}H_{17}ClN_2OS$	193	51	0.52	6.91	6.92

Antimicrobial activity

The antimicrobial screening (Table 2) of above synthesized 4-thiazolidinone derivatives shows good activity against all microbes species. On the basis of screening data it was observed that these heterocyclic compounds can be easily used against treatment of disease caused by test microbes.

Table 2: Antimicrobial activity

S. No.	Compounds	*Escherichia coli*	*Pseudomonas aeruginosa*	*Staphylococcus Aureus*	*Bacillus subtilis*
1	3a	16	18	17	18
2	3b	14	17	15	12
3	3c	12	10	14	8
4	3d	16	15	8	15
5	4a	17	16	17	13
6	4b	7	14	10	17
7	4c	16	16	16	12
8	4d	15	15	13	18

ACKNOWLEDGEMENT

The authors are thankful to Dr.V.M. Raut, HOD, Department of Chemistry, Govt. V.I.S.H., Amravati and Director of CIL, SAIF, Panjab University, Chandigarh for providing IR, NMR data.

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