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ORIGINAL ARTICLE

Synthesis, characterization and antimicrobial evaluation of 2,5-disubstituted-4-thiazolidinone derivatives

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Abstract In the present study novel derivatives of 4-thiazolidinone were prepared from biphenyl-4-carboxylic acid and evaluated for their *in vitro* antimicrobial activity against two Gram negative strains (*Escherichia coli* and *Pseudomonas aeruginosa*) and two Gram positive strains (*Bacillus subtilis* and *Staphylococcus aureus*) and fungal strain *Candida albicans* and *Aspergillus niger*. The newly synthesized compounds were characterized by IR, ^{1}H NMR and C, H, N analyses. The results revealed that all synthesized compounds have a significant biological activity against the tested microorganisms. Among the synthesized derivatives **4g** (biphenyl-4-carboxylic acid [2-(3-bromophenyl)-5-(3-nitrobenzylidene)-4-oxo-thiazolidin-3-yl]-amide) and **4i** (biphenyl-4-carboxylic acid [5-(3-bromobenzylidene)-2-(3-bromophenyl)-4-oxo-thiazolidin-3-yl]-amide) were found to be most effective antimicrobial compounds.

1. Introduction

Microbial resistance to antimicrobial agents is of grave concern in the medical community. Hence, the development of novel, potent, and unique antimicrobial agents are the pre-eminent way to overcome microbial resistance and develop effective therapies. 4-Thiazolidinone and its derivatives have attracted considerable attention for the past few decades due to their chemotherapeutical values (Verma and Saraf, 2008).

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Table 1 Physical data of 2,5-disubstituted-4-thiazolidinones.

Compound	Ar	Ar′	Molecular formula	Molecular weight	Melting point (°C)	Yield (%)	R_f value
4a	C_6H_5–	C_6H_5–	$C_{29}H_{22}N_2O_2S$	462.56	214–216	71.32	0.63
4b	C_6H_5–	3-$NO_2C_6H_4$	$C_{29}H_{21}N_3O_4S$	507.56	217–219	78.14	0.71
4c	C_6H_5–	4-ClC_6H_4	$C_{29}H_{21}ClN_2O_2S$	497.01	223–224	82.26	0.59
4d	C_6H_5–	3-BrC_6H_4	$C_{29}H_{21}BrN_2O_2S$	541.46	216–217	79.40	0.62
4e	C_6H_5–	4-$OCH_3C_6H_4$	$C_{30}H_{24}N_2O_3S$	492.59	210–212	81.60	0.68
4f	3-BrC_6H_4	C_6H_5–	$C_{29}H_{21}BrN_2O_2S$	541.46	228–230	78.46	0.92
4g	3-BrC_6H_4	3-$NO_2C_6H_4$	$C_{29}H_{20}BrN_3O_4S$	586.46	238–239	78.40	0.88
4h	3-BrC_6H_4	4-ClC_6H_4	$C_{29}H_{20}BrClN_2O_2S$	575.90	225–227	81.20	0.79
4i	3-BrC_6H_4	3-BrC_6H_4	$C_{29}H_{20}Br_2N_2O_2S$	620.35	245–248	78.62	0.82
4j	3-BrC_6H_4	4-$OCH_3C_6H_4$	$C_{30}H_{23}BrN_2O_3S$	571.48	234–235	81.80	0.73
4k	4-FC_6H_4	C_6H_5–	$C_{29}H_{21}FN_2O_2S$	480.55	242–243	79.34	0.78
4l	4-FC_6H_4	3-$NO_2C_6H_4$	$C_{29}H_{20}FN_3O_4S$	525.55	235–237	78.86	0.84

For mobile phase: chloroform:benzene:glacial acetic acid (3:1:1, v/v/v).

These derivatives are known to possess several promising pharmacological actions such as antimicrobial (Bondock et al., 2007; Shah and Desai, 2007; Samir et al., 2007; Vicini et al., 2006; Sharma et al., 2006; Handan et al., 2005), analgesic (Knutsen et al., 2007), anti-inflammatory (Ottana et al., 2005; Goel et al., 1999), anti-HIV (Balzarini et al., 2007), cytotoxic (Mujeebur et al., 2005), and anticonvulsant (Gursoy and Terzioglu, 2005) activities. Also, 4-thiazolidinones have been found as novel inhibitors of bacterial enzyme MurB, a key enzyme responsible for the synthesis of peptidoglycon (Andres et al., 2000).

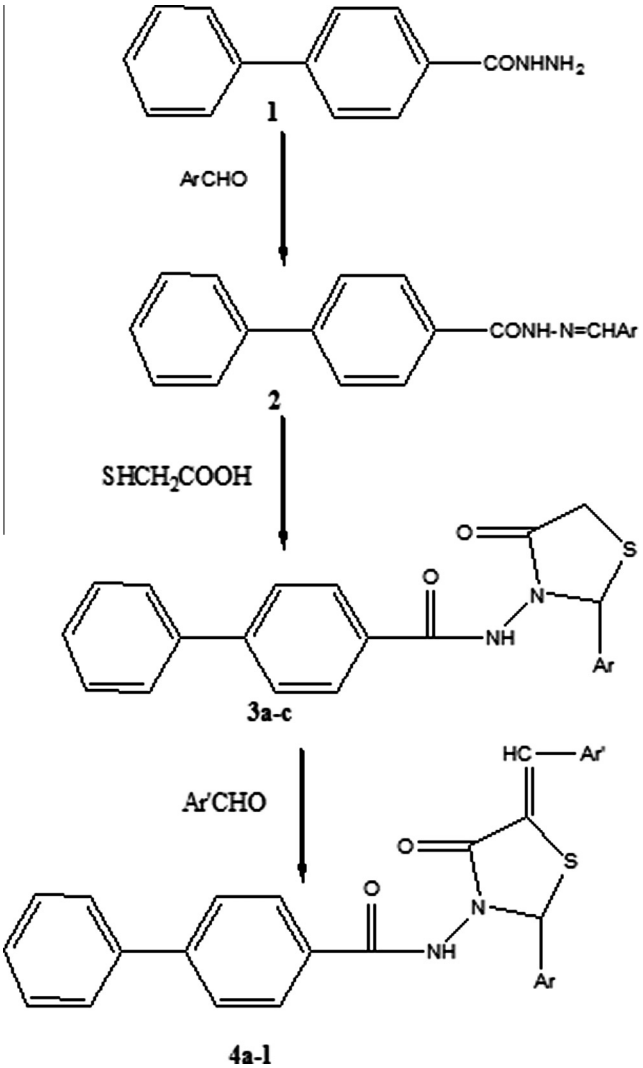
Inspired by the above facts and in continuation of our ongoing research program in the field of synthesis and antimicrobial activity of medicinally important compounds (Deep et al., 2010b; Madhukar et al., 2009; Kumar et al., 2010), we hereby report the synthesis and antimicrobial activity of 4-thiazolidinone derivatives. All these compounds have been reported with their anti-inflammatory activity elsewhere (Deep et al., 2010a). The structures of all compounds have been confirmed by elemental and spectral analysis (IR and ^{1}H NMR).

2. Experimental

The purity of the synthesized compounds were ascertained by thin layer chromatography on silica gel G in various solvent systems using iodine vapours as detecting agent. Melting points were determined by the melting point determination apparatus (TEMPO) in open capillary tubes and are uncorrected. Elemental analyses were done using Carlo Erba 1106 CHN Analyzer. Infra-red spectra were recorded on Perkin Elmer Spectrum RXI FTIR spectrophotomer in KBr phase. Proton NMR spectra were recorded on Bruker Avance II 400 NMR Ultra Shield Spectrometer using DMSO-d_6 as a solvent and tetramethyl silane as internal standard. Chemical shift value is expressed in delta parts per million (δ ppm). All the compounds have been screened *in vivo* for their anti-inflammatory activity.

2.1. Chemistry

A series of biphenyl-4-carboxylic acid-5-(arylidene)-2-(aryl)-4-oxothiazolidin-3-yl-amides has been synthesized. Reaction of acid hydrazide (**1**) with aromatic aldehydes yielded the corresponding hydrazones (**2a**–**c**) which on further reaction with thioglycolic acid in methanol afforded the corresponding 2-substituted-4-thiazolidinones (**3a**–**c**). The compounds (**3a**–**c**) were further reacted with aromatic aldehydes in presence of



Scheme 1 Preparation of biphenyl-4-carboxylic acid-5-(arylidene)-2-(aryl)-4-oxo-thiazolidin-3-yl-amides (**4a**–**l**).