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ORIGINAL ARTICLE

Synthesis and biological evaluation of 4-thiazolidinone derivatives as antitubercular and antimicrobial agents

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Abstract New series of *N*-[2-{2-(substitutedphenyl)-4-oxo-5-(substitutedbenzylidene)-1,3-thiazolidine}-iminoethyl]-2-amino-5-nitrothiazole, **5(a–m)** have been synthesized from 2-amino-5-nitrothiazole as a starting material by conventional as well as microwave methods. All the synthesized compounds **4(a–m)** were screened for their antibacterial and antifungal activities against some selected bacteria and fungi and antitubercular activity screened against *Mycobacterium tuberculosis*. The structure of all the synthesized compounds were confirmed by chemical and spectral analyses such as IR, ^{1}H NMR, ^{13}C NMR and FAB-Mass.

1. Introduction

4-Thiazolidine derivatives are an important class of heterocyclic compounds known for their potential pharmaceutical applications. Recently, this framework containing compounds were effective against antimicrobial (Young et al., 2004), antischistosomal activity (Taha and Soliman, 2007), antifungal (Asati et al., 2005), antiinflammatory (Jain et al., 2006), antimalarial (Kristina et al., 2009), herbicidal (Sanemitsu et al., 2006), antiviral (Eiichi et al., 2007), antidiabetic (Murugan et al., 2009), and antioxidant (Shih and Ke, 2004) activities. Thiazole derivatives are heterocyclic compounds containing nitrogen and sulfur atoms in their structure and are proved to be clinically useful agents against different kinds of disease. Thiazole derivatives have been employed in the preparation of different important drugs required for treatment of antimicrobial (Gouda et al., 2010), antibacterial (Bharti et al., 2010; Khalil et al., 2009), antifungal (Bharti et al., 2010; Joshi and Srivastava, 2001), antiinflammatory (Giri et al., 2009), and antitubercular (Shiradkar et al., 2007), some of the thiazole derivatives are used as antiprotozoal (Ricardo et al., 2003) drugs. All above biological activities of thiazole and thiazolidine derivatives aroused our attention and promoted to synthesis a new series of *N*-[2-{2-(substitutedphenyl)-4-oxo-5-(substitutedbenzylidene)-1,3-thiazolidine}-iminoethyl]-2-amino-

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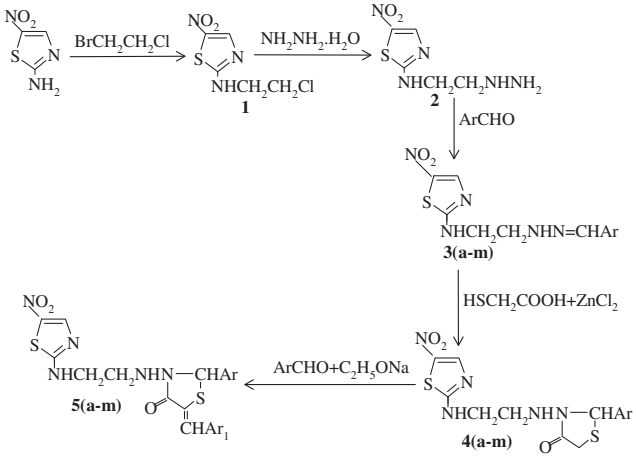

Ar = Ar_1 = substituted phenyl ring

Comp.	Ar = Ar_1	Comp.	Ar = Ar_1	Comp.	Ar = Ar_1
3a, 4a, 5a	C_6H_5	3f, 4f, 5f	3-BrC_6H_4	3k, 4k, 5k	4-$CH_3OC_6H_4$
3b, 4b, 5b	4-ClC_6H_4	3g, 4g, 5g	2-BrC_6H_4	3l, 4l, 5l	4-$CH_3C_6H_4$
3c, 4c, 5c	3-ClC_6H_4	3h, 4h, 5h	4-$NO_2C_6H_4$	3m, 4m, 5m	4-HOC_6H_4
3d, 4d, 5d	2-ClC_6H_4	3i, 4i, 5i	3-$NO_2C_6H_4$	-	-
3e, 4e, 5e	4-BrC_6H_4	3j, 4j, 5j	2-$NO_2C_6H_4$	-	-

Scheme 1

5-nitrothiazole, **5(a–m)** by conventional and microwave methods. The structure of compounds **1**, **2**, **3(a–m)**, **4(a–m)** and **5(a–m)** were confirmed by IR, ^{1}H NMR, ^{13}C NMR, FAB-Mass and chemical analysis. All the final synthesized compounds **5(a–m)** were screened for their antimicrobial activity against some selected bacteria, fungi and antituberculosis study against *M. tuberculosis*. (Scheme 1)

2. Materials and methods

2.1. Experimental

Melting points were taken in open glass capillaries and are uncorrected. Progress of the reaction was monitored by silica gel-G coated TLC plates in MeOH:$CHCl_3$ system (1:9). The spot was visualized by exposing dry plate in iodine vapours. IR spectra were recorded in KBr disc on a Schimadzu 8201 PC, FTIR spectrophotometer (ν_{max} in cm^{-1}) and ^{1}H and ^{13}C NMR spectra were measured on a Brucker DRX-300 spectrometer in $CDCl_3$ at 300 and 75 MHz respectively using TMS as an internal standard. All chemical shifts were reported on δ scales. The FAB-Mass spectra were recorded on a Jeol SX-102 mass spectrometer. Elemental analyses were performed on a Carlo Erba-1108 analyzer. Microwave irradiation was carried out in an open glass vessel. Modified microwave oven (800 W) was used for the synthesis of compounds. A thermocouple was used to monitor the temperature inside the vessel of the microwave. The analytical data of all the compounds were highly satisfactory. For column chromatographic purification of the products, Merck silica Gel 60 (230–400 Mesh) was used. The reagent grade chemicals were purchased from the commercial sources and further purified before use.

*2.2. General microwave method for synthesis of compound **1**, **2**, **3(a–m)**, **4(a–m)** and **5(a–m)***

A solid supported mixture of compounds (1:1 mol) was mixed thoroughly in open glass vessel and subjected to the microwave

Table 1 Data of yield and reaction time of all synthesized compounds.

Yield%			Reaction time			Yield%			Reaction time		
Comp.	Conv.	MW	Conv. (h)		MW (min)	Comp.	Conv.	MW	Conv. (h)		MW (min)
			1st stirr.	2nd reflux					1st stirr.	2nd reflux	
1	62	76	6.30	–	4.00	**4g**	66	80	2.35	3.25	3.30
2	70	85	5.00	–	3.10	**4h**	64	76	2.45	3.15	3.35
3a	60	78	3.00	2.15	3.35	**4i**	63	80	2.15	3.30	3.15
3b	64	86	3.15	2.00	3.45	**4j**	61	84	2.30	3.30	3.05
3c	67	83	3.10	2.00	3.35	**4k**	64	83	2.15	3.35	3.20
3d	65	85	3.15	1.45	4.10	**4l**	63	77	2.15	3.30	3.20
3e	67	84	2.30	2.15	3.15	**4m**	63	80	2.10	3.45	3.20
3f	65	81	3.30	2.30	3.05	**5a**	66	79	2.30	3.15	3.40
3g	63	80	3.35	2.00	2.40	**5b**	64	76	2.00	3.05	3.20
3h	64	77	3.30	2.30	3.15	**5c**	62	82	2.05	2.45	3.20
3i	62	78	3.30	1.40	3.30	**5d**	64	84	2.15	2.45	3.25
3j	61	82	3.25	2.30	2.55	**5e**	62	83	2.10	3.10	3.30
3k	62	81	3.30	2.30	3.45	**5f**	65	82	2.15	3.00	3.15
3l	61	79	3.30	2.20	4.15	**5g**	64	78	2.30	3.15	3.45
3m	62	81	3.30	2.00	3.25	**5h**	62	79	2.00	3.30	3.30
4a	65	75	2.45	3.05	3.35	**5i**	64	81	2.10	3.25	3.15
4b	65	79	2.30	3.15	3.35	**5j**	60	80	2.15	3.15	3.15
4c	67	84	2.45	2.30	3.15	**5k**	66	82	2.00	3.30	3.20
4d	66	82	2.30	2.30	3.10	**5l**	61	75	2.20	3.25	3.45
4e	60	80	2.30	3.00	3.30	**5m**	62	76	2.30	3.45	3.20
4f	63	83	2.15	3.15	3.05	–	–	–	–	–	–