

IN VITRO ANTIMICROBIAL ACTIVITY OF NOVEL FUNCTIONALIZED CHALCONES

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Abstract: Two series of novel chalcones (4a-4g, 5a-5g) have been synthesized by solution phase Claisen-Schmidt condensation. All the new final products have been purified by silica gel column chromatography and characterized on the basis of their infrared (IR) and proton nuclear magnetic resonance (¹H NMR) spectroscopic data, and elemental analysis. All the final compounds (4-5) were exploited for their antimicrobial activity by the cup-plate method. From the antibacterial screening it was observed that the compounds, 4 (a, d, f and g), 5 (b, c, d, e and f), shows good antibacterial activity against *Staphylococcus aureus* (zone of inhibition, 10-16 mm) as compared to standard streptomycin (zone of inhibition, 18 mm) whereas compounds 4 (a and b), 5 (b, c and d), showed good antibacterial activity against *Escherichia coli* (zone of inhibition, 10-18 mm) as compared to streptomycin (zone of inhibition, 22 mm). Fungicidal screening data also revealed that compounds 4 (b and d), 5 (a and e), imparted maximum activity against *Aspergillus niger* (zone of inhibition, 10-15 mm) as compared to standard griesofulvin (zone of inhibition, 17 mm), whereas compounds 4 (b, c, f and g), 5b, showed good activity against *Candida albicans* (zone of inhibition, 10-16 mm) as compared to griesofulvin (zone of inhibition, 20 mm).

Keywords: Chalcones, Condensation, Antimicrobial activity

INTRODUCTION

Chalcones, 1,3-diarylprop-1-enones, are a class of compounds consisting of two aryl rings linked by an α,β -unsaturated ketone moiety. Chalcones moieties are common substructures in numerous natural products belonging to the flavonoid family. The compounds with the backbone of chalcone have been reported to exhibit a wide variety of pharmacological effects including, antimalarial, antiviral, antibacterial, antituberculosis, antifungal, anticancer, antileishmanial, antiinflammatory, antipyretic, analgesic, antiulcerative, antihyperglycemic, antioxidant, antiinvasive, antiplatelet and insect antifeedent. A number of chalcone derivatives have also been found to inhibit several important enzymes in cellular systems, including xanthine oxidase, aldose reductase, epoxide hydrolase, protein tyrosine kinase and quinone reductase. Interest in chalcones as antimalarials was initiated by the discovery of antiplasmodial activity of Licochalcone A, an oxygenated chalcone isolated from the roots of the Chinese licorice during routine screening. Computational structural analysis also identified chalcones as potential plasmodial cysteine protease inhibitors consistent with the experimental data. Herein, we designed and synthesized new chalcone derivatives and evaluated their antimicrobial activity.

MATERIAL AND METHOD

All the reagents used were of analytical grade and purchased from Sigma-Aldrich, Merck, CDH, SRL

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and Spectrochem. Solvents were used after their purification by suitable methods and distillation.

Test of homogeneity/purity

Homogeneity / purity of all products were tested by conducting their thin-layer chromatography with silica gel "G" adsorbant. Sample solutions of last step products in MeOH were loaded on silica gel layers and plates were developed in petroleum ether-Ethyl acetate (8:2, v/v) solvent. Chromatograms with multispots visualized in Iodine fumes, indicate impurity of samples. Impure samples were then purified by crystallization in ethanol to obtain pure products.

Analyses and physical measurements

Melting points determined in the open capillaries were uncorrected. IR spectra and microanalyses for carbon, hydrogen and nitrogen contents of samples were obtained from I.I.T., Delhi. ¹H NMR spectra were recorded in DMSO-d₆ medium on Bruker-400 MHz spectrometer at Jamia Hamdard University, Delhi.

Antimicrobial activity, Syntheses

Twenty eight compounds have been synthesized in solution phase according to, Antimicrobial activity, following scheme.

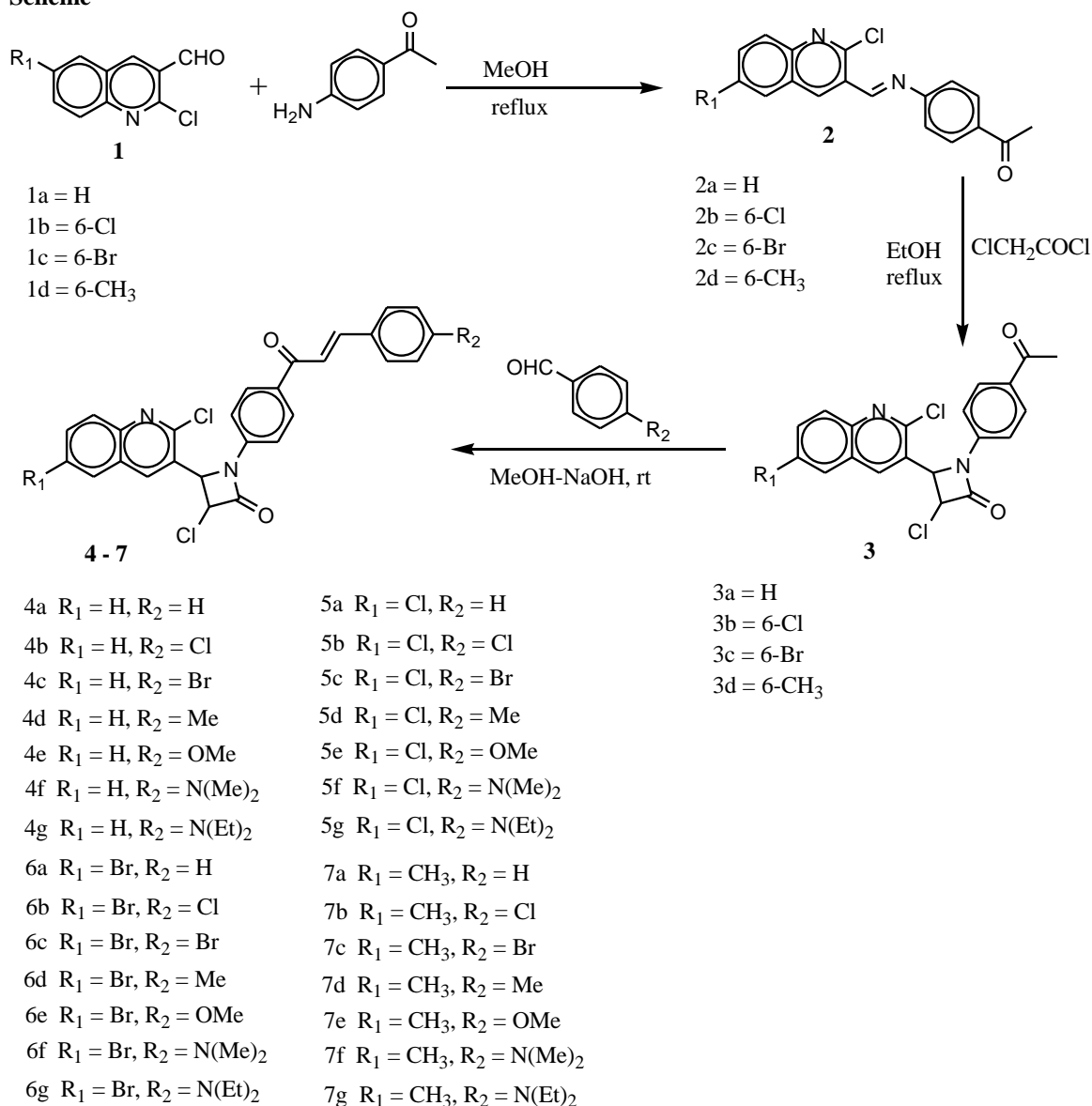
In vitro antimicrobial screening

The synthesised compounds (4-5) were screened for their *in vitro* antimicrobial activity against *Staphylococcus aureus*, *Escherichia coli* and antifungal activity against *Aspergillus niger*, *Candida albicans* by measuring the zone of

inhibition in mm. The antimicrobial activity was performed by cup plate method at concentration 500 $\mu\text{g/mL}$ and reported in Table 1. Nutrient agar was employed as culture medium and DMSO was used as

solvent control for antimicrobial activity. Streptomycin and griseofulvin were used as standard for antibacterial and antifungal activities respectively.

Scheme



Scheme General route for the synthesis of new chalcones.

Table 1. Antimicrobial activity of chalcones (4-7)

S. No	Compounds	Antibacterial ^a		Antifungal ^a	
		<i>S. aureus</i>	<i>E. coli</i>	<i>A. niger</i>	<i>C. albicans</i>
1	4a	13	14	06	09
2	4b	06	13	14	12
3	4c	08	05	07	10
4	4d	15	07	15	05
5	4e	09	06	09	07
6	4f	12	08	08	15
7	4g	10	07	10	13
8	5a	07	05	12	09
9	5b	13	15	06	14
10	5c	15	10	07	05

11	5d	12	11	09	03
12	5e	16	09	10	07
13	5f	15	05	05	04
14	5g	09	07	04	06
15	Streptomycin	18	22	--	--
16	Griesofulvin	--	--	17	20

^azone of inhibition was measured in mm. *Staphylococcus aureus* (*S. aureus*), *Escherichia coli* (*E. coli*), *Aspergillus niger* (*A. niger*) and *Candida albicans* (*C. albicans*).

RESULTS AND DISCUSSION

The antimicrobial activity of synthesized chalcones (4-5) were performed against two bacteria, *Staphylococcus aureus* (*S. aureus*) and *Escherichia coli* (*E. coli*) and two fungi, *Aspergillus niger* (*A. niger*) and *Candida albicans* (*C. albicans*) by cup plate method. Streptomycin and Griesofulvin were used as antibacterial and antifungal drug control. The activity was measured as zone of inhibition in mm and the values are depicted in table 1. From the antimicrobial screening it was observed that all the compounds exhibited activity against all the organisms employed. The compounds, 4 (a, b, d, f and g), 5 (b, c, d, e, f), shows good antibacterial activity where as other compounds showed moderate to good activity. Fungicidal screening data also revealed that compounds, 4 (b, c, d, f and g), 5 (a, b and e), imparted maximum activity against *Aspergillus niger*, where as other compounds showed moderate activity. Perusal of all results obtained from antibacterial and antifungal tests together it is concluded that entire compounds tested are active towards bacteria and fungi.

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