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Green synthesis and antimicrobial activity of some new phenothiazine chalcones

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Abstract: A new series of Phenothiazine Chalcones (3a-f) were synthesized under microwave irradiation in alcoholic KOH. The structures of these compounds were confirmed by IR, ^{1}H NMR, Mass and elemental analysis. The newly synthesized compounds were evaluated for antimicrobial activity.
Key word : Phenothiazine, Chalcones, Microwave synthesis, Biological activity.

Introduction:

Phenothiazine and related compounds have shown diverse biological activities including as tranquilizers[1] , anti-inflammatory [2], antimalarial [3], antipsychotropic [4], antimicrobial [5,6], antitubercular [7,8], antitumor [9-11] , antihistamine [12] and analgesic [13] properties.

In a recent time, there has been much interest for the use of microwave irradiation in synthesis due to substantial reduction in time as well as eco-friendly. Apart from being environmentally friendly technique, microwave irradiation has carved its importance in the field of pharmaceutical chemistry for the synthesis of new potent drugs.

In view of these above, attempts has been undertaken for the synthesis of the some novel phenothiazine chalconesunder microwave irradiation and evaluate theirantimicrobial activities.

Materials and Methods:

All chemicals were purchased from s.d fine chemicals, Mumbai (India), and were used without further purification. Melting points were determined in open capillaries using aToshniwal melting point apparatus and are uncorrected. Formation of compounds was routinely checked by TLC using Silica G, and spots were exposed to iodine vapor for visualization.

The IR spectra in KBr were recorded on a Perkin - Elmer FT-IR spectrometer (umax incm-1); and 1H NMR spectra were obtained in CDCl3 on a Brucker 300 MHz instrument usingTMS as internal standard (chemical shifts in d, ppm), Mass spectra on LCQ advantage ThermaFiniger spectrometer. Elemental analysis was performed on Carlo Erba 1108 analyzer.

General Procedure for 3a-f:

(2E)-1-(8-chloro-10,10a-dihydro-4aH-phenothiazin-2-yl)-3-phenylprop-2-en-1-one (3a):

To the solution of 8-Chloro 2-acetyl Phenothiazine 1 (10 mmol) in absolute methanol (20ml), benzaldehyde 2a (10 mmol) was added in presence of 40% methanolic KOH 5ml and the reaction was carried out under microwave irradiation (700W) for 2-5minutes.The reaction mixture was acidified with dilHCl. The solid obtained was washed with cold water finallyrecrystallised from methanol to give 3a.

IR (KBr) cm^{-1}:3352 (NH), 3056 (Ar-H), 1653 (C=O), 1606 (C=C); ^{1}H NMR ($CDCl_3$):δ 8.11 (s, 1H, NH), 7.88 (d, 1H, =CH-Ar), 7.56(d, 1H, -COCH=), 7.38 – 6.69 (m, 12H, Ar-H); Mass(m/z) :363.Anal.cald.for $C_{21}H_{14}NOSCl$: C, 69.42; H, 3.85; N, 3.85. Found: C, 69.49; H, 3.88; N, 3.73%.

Similarly, chalcones 3b-f were synthesized by condensing various 2-acetyl Phenothiazine with various aldehydes 2b-d.

Table 1. Physical data of compounds 3a-f

Comp. no	R	R1	M.F.	% Yield	M.P
3a	H	Cl	$C_{21}H_{14}NOSCl$	91	223-225
3b	OCH_3	Cl	$C_{22}H_{16}NO_2SCl$	90	281-284
3c	Cl	Cl	$C_{21}H_{13}NOSCl_2$	92	244-247
3d	H	CF_3	$C_{22}H_{14}NOSF_3$	92	208-211
3e	OCH_3	CF_3	$C_{23}H_{16}NOSF_3$	93	238-241
3f	Cl	CF_3	$C_{22}H_{13}NOSF_3Cl$	91	265-267

Antimicrobial activity

The newly synthesized compounds were screened for their antibacterial activity against *Escherichia coli*, *Bacillus subtillis* and antifungal activity against *Aspergillus niger*(recultered) , *Candida albicans* by using DMSO as solvent as 100 µg concentration by cup plate method. After 24 hrs of incubation at 37^0C the zone of inhibition were measured in mm. The activity was compared with the known antibiotics such as Ampicillin, and Fluconazole. The results of antimicrobial studies are given in Table 2.

Table2. Antbacterial and antifungal activity of the compounds 3a-f

Comp. no	Bacillus subtillis	Escherichia coli	Candida albicans	Aspergillus niger
3a	13	17	11	12
3b	16	19	13	15
3c	19	22	24	21
3d	17	17	13	12
3e	19	15	16	14
3f	24	23	22	22
Ampicillin	34	36	-	-
Fluconazole	-	-	32	30

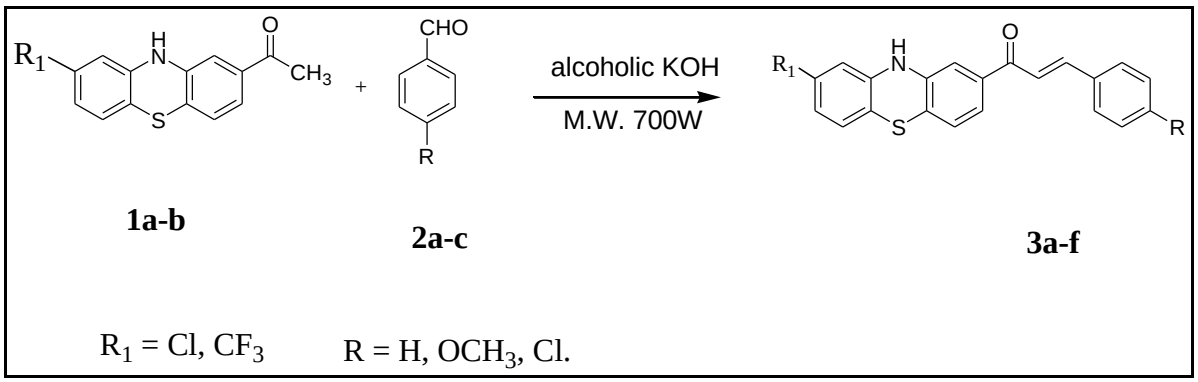
(Growth inhibition zone size, mm)

Results and Discussion:

Chalcones 3a–f were obtained by under microwave irradiation at 700 w in alcoholic KOH by treating various 2-acetylphenothiazine with various aldehydes and gave above 90% yield. The reaction sequences are outlined in Scheme 1.Formation of chalcones were confirmed on the basis of elemental analysis, IR, 1H NMR, and mass.Compounds3a showed IR absorption bands in the regions 3352 cm−1 (NH Streching), 1653cm−1 (C=O streching), and 1606 cm−1 (C==C streching).The 1H NMR spectrum of compound 3ashowedsinglet at

8.11 due phenothiazine NH proton, two doublets at 7.88 and 7.56 for olefiniv protons. It showed multiplets at 7.38–6.69 due to aromatic protons. The physical data of compounds 3a–farerecorded in Table 1.

All the newly synthesized chalcones were evaluated for antimicrobial activity and compound 3c and 3f showed good activity.



Scheme 1

Conclusions:

A mild, efficient, andconvenient method is developed for the synthesis new series of chalcones. All compounds of the seriesshowed moderate to good biological activity. Hence, it isconcluded that there is ample scope for further developingthis field.

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