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Solvent Free Microwave Assisted Synthesis of Chalcones and Their Antifungal Activities

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The microwave assisted synthesis of six chalcones was carried out by condensing the piperanal and the acetophenone (unsubstituted, 4-methyl, 4-methoxy, 4-bromo, 4-nitro, 3-chloro) in presence of zinc chloride. Minor quantities of Ketol and Michael addition product were easily removed by recrystallization. The results indicated were correlated with solvent-free synthesis. The compounds have also been screened for their antifungal activities.

Key Words: Microwave irradiation, Solvent free synthesis, Chalcone, Antifungal activities.

INTRODUCTION

Chalcones derivatives constitute an important class of compounds possessing diverse type of biological properties including antibacterial[1], antitumour[2,3], antiplasmodial[4], antiinflammatory[5], trypanocidal and leishmanicidal properties[6], antiviral activites[7]. Extensive work on synthesis of chalcones has been done by various routes. Condensation of the appropriate acetophenone and piperanal in the presence of anhydrous $ZnCl_2$ *via* microwave assisted path[8] yielded the corresponding 1,3-diarylchalcones.

The chalcones possess an α,β-unsaturated grouping in the molecules. The structural assignment of these chalcones was based on elemental analysis, IR and NMR spectral data. The antifungal activity of these chalcones has been studied by cup-plate method[9-11].

EXPERIMENTAL

Melting points were taken in open capillaries and are uncorrected. The IR spectra were recorded in KBr disc on a Nicolet Megna-FT-IR 550 spectrometer, ^{1}H NMR were recorded on model DRX 300 at 300.13 in $CDCl_3$/DMSO-d_6 using TMS as internal standard. The purity of the newly synthesized compounds were checked by TLC.

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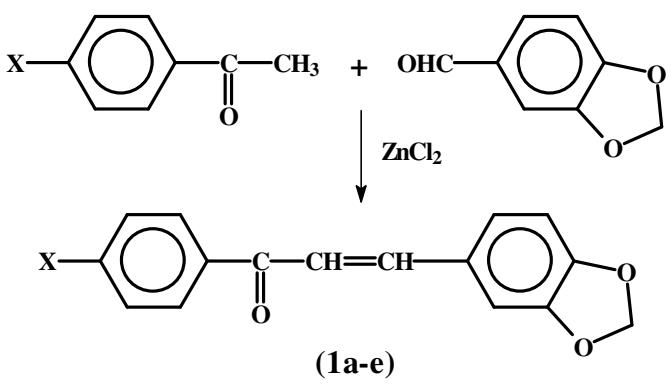
RESULTS AND DISCUSSION

Synthesis of chalcones

Solvent free synthesis of chalcone: The solvent free synthesis of chalcones was carried out by grinding the piperanol (0.05 mol) and acetophenone derivative (0.05 mol) in presence of solid sodium hydroxide (0.05 mol):petroleum ether (1:1) yielded the crystalline product. Purity of the compounds was checked by TLC using $CHCl_3$ as mobile phase.

Microwave conditions: A mixture of piperanol (0.01 mol), acetophenone derivative (0.01 mol) and $ZnCl_2$ (0.001 mol) was taken in ACE tube, flushed with argon and tightly capped. The mixture is subjected to microwave heating for 3-5 min in a domestic oven and then it is allowed to reach to room temperature. The reaction mixture was treated with aq. ethanol (20 mL) and the separated solid was filtered, washed with *n*-hexane and dried. The solid was recrystallized by benzene-hexane (**Scheme-I**).



(1a-e)

X = H, CH_3, OCH_3, Br, NO_2 Cl

Scheme-I

Spectral studies:

The IR spectra showed a characteristic bands at 1640-1632 ν(C=O), 1582-1576 cm^{-1} ν(C=C), asymmetrical C-O-C stretching band around 1265-1210 cm^{-1} and symmetrical stretching at 1070-1024 cm^{-1}. In ^1H NMR, a singlet was observed at δ 5.98-6.02 due to dioxymethylene group. Doublet at 7.82 for α-proton and 8.02 for β-proton in chalcones. A complicated pattern in the aromatic region at δ 6.9-8.0 showed the presence of seven aromatic protons. Elemental analysis and ^1H NMR data of the title compounds are given in Tables 1 and 2.

TABLE-1
SYNTHESIS OF CHALCONES UNDER MICROWAVE CONDITIONS

Compd.	Reaction time (min)	R	Yields (%)	Lit.[9] m.p. (ºC)	This work m.p. (ºC)
1a	4	H	83	109	106
1b	5	CH_3	78	33	32
1c	5	OCH_3	86	127	126
1d	3	Br	85	135	135
1e	4	NO_2	80	207	206
1f	3	Cl	74	28	27

TABLE-2
^{1}H NMR DATA OF TITLE COMPOUNDS (δ ppm)

Compd.	Ar-X	-CO<u>CH</u>=CH-	-COCH=<u>CH</u>-	OCH_2O 2H (s)
1a	6.92-8.10, complex	7.82	8.02	6.00
1b	6.72-7.89, complex	7.81	8.04	5.98
1c	6.91-8.22, complex	7.77	8.03	6.00
1d	6.77-8.23, complex	7.84	8.01	6.00
1e	6.34-7.90, complex	7.83	8.02	6.01
1f	6.88-6.99, complex	7.82	8.03	6.00

Antifungal activity: Antifungal activities of chalcones have been assessed at concentation of 300 µg/disc, against four plant pathogenic and mould fungi were studied, *viz.*, *Colletotrichum gloeosporioides* Penz. (plant pathogen), *Aspergillus niger* (mould), *Aspergillus flavus* (mould) and *Penicillium* sp. (blue mould). The inhibitory effects of compounds against these organisms are given in Table-3. Antifungal activity was assessed by the poisoned food technique, in a modified condition. Fluconazole (200 µg/disc) was used as standard fungicide. Potato dextrose agar was used as basal medium for test fungi.

TABLE-3
ZONE OF INHIBITION OF COMPOUNDS **1a-f**

Compd.	*Penicillium sp.*	*A. niger*	*A. flavus*	*C. gloeosporioides*
1a	+	–	–	–
1b	–	–	–	–
1c	++	–	–	+
1d	–	–	–	–
1e	++	–	+	–
1f	++	–	–	–
Fluconazole	–	–	+++	–

+++ = 8-10 mm, ++ = 5-7 mm, + = 2-4 mm

The screening results indicate that compounds do not show any antifungal activities against *A. niger*, *A. flavus* and *C. gloeosporioides* while they show good antifungal activities at high concentration against only *Penicillium* sp. in comparison with standard fungicides, fluconazole.

Conclusion

Microwave assisted synthesis of chalcones was a ecofriendely method for synthesis of chalcones. The chalcones were obtained in high yield and high purity. The chalcones **1a-f** were tested for their antifungal activity. The result shows that chalcones possessed weak to moderate activity against various fungus.

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