Available online at www.scholarsresearchlibrary.com

Scholars Research Library

Der Pharmacia Lettre, 2012, 4 (2):554-557
(http://scholarsresearchlibrary.com/archive.html)

Scholars Research Library
ISSN 0975-5071
USA CODEN: DPLEB4

Synthesis and evaluation of chalcone derivatives of 2-acetyl naphthalene for antifungal and antibacterial activity

Varun Arora[1*], Pragi Arora[1] and H. S. Lamba[2]

[1]R. K. S. D. College of Pharmacy, Kaithal, Haryana (India)
[2]H. R. Institute of Pharmacy, Gaziabad, U.P (India)

ABSTRACT

A series of chalcones of 2-acetyl naphthalene and substituted aryl aldehydes were synthesized and evaluated for antimicrobial activity. The structures of synthesized compounds were confirmed by IR and 1H NMR spectroscopy. The antimicrobial activity was evaluated against S. aureus, B. subtilis, E. coli and P. putida strains.

Keywords: Chalcone, 2-Acetyl naphthalene, Antimicrobial activity, Antifungal activity.

INTRODUCTION

Chalcones are the aromatic ketones belonging to 1,3-diaryl-2-propen-1-ones. Chalcones belong to flavinoids.Chemically, they consist of open chain flavinoids in which two aromatic rings are joined by a three carbon unsaturated carbonyl system[1]. Synthesis of chalcones and their derivatives has significant biological activity[2]. Among these wide variety of heterocyclic that have been explored for developing pharmaceutical important molecules pyrrole, pyrimidine[3], pyridine[4], indole[5], flavones[6] and pyrimidinethiones[7] have important role in medicinal chemistry. The presence of reactive unsaturated ketone in chalcone is responsible for antibacterial[8-10] and antifungal activities. In present study, seven chalcone derivatives were synthesized and evaluated for antimicrobial and antifungal properties.

MATERIALS AND METHODS

Chemistry

Melting points were determined by open capillary method and are uncorrected. The purity of compounds was confirmed by thin layer chromatography using Silica gel G as stationary phase and Petroleum ether: Ethyl acetate (9:1) as the mobile phase. The spots were visualized with iodine vapors. 1H NMR spectra were recorded in CDCl3 on Brucker 300 MHz instrument. Chemical shift values are expressed in parts per million (ppm, δ). IR spectra were recorded in KBr disc on Shimadzu FTIR 8400 spectrophotometer.

Synthetic procedures for chalcones (Compound1a to 1g)

Title compounds were synthesized according to *Scheme 1*. Potassium Hydroxide (0.1 mol) was dissolved in 20 ml of methanol and stirred in ice cold conditions. 2-acetyl naphthalene (0.1 mol) was dissolved in 20 ml of 95% v/v methanol and the solution was added drop wise with constant stirring under ice cold conditions. Pure benzaldehyde

or substituted benzaldehyde (0.1 mol) was dissolved in 20 ml of 95% v/v methanol and added drop wise to the previous solution with constant stirring under ice cold conditions.

The stirring was continued till the TLC had shown the disappearance of aldehyde spot (stirring time specified in Table 1). pH of the reaction mixture was made neutral by addition of dil. HCl. The product was filtered under vacuum, washed with excess distilled water and recrystallized from organic solvent absolute alcohol.

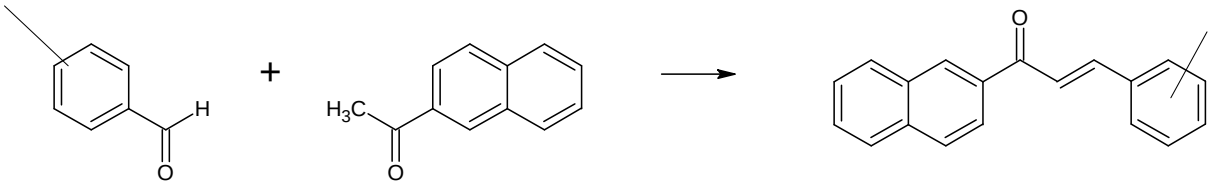

Table 1: Molecular formulae, molecular weights, reaction time, percentage yield, melting points and Rf values of compounds(1a-1g)

Compound No.	*R^1*	*Mol. Formulae*	*Mol. Weight*	*Reaction Time(hrs)*	*Percentage yield (%)*	*m.pt. (^OC)*	*Rf value*	*Analytical Calculation(%)*
1a	H	$C_{19}H_{16}O$	260	24	95	135-137	0.30	C,87.69; H,6.15; found C,87.60,H,6.10
1b	4-Cl	$C_{19}H_{15}ClO$	294.5	30	96	180-182	0.43	C,77.28; H,5.08; found C,77.60,H,5.10
1c	4-Br	$C_{19}H_{15}BrO$	339	36	85	115-117	0.57	C,67.25; H,4.42; found C,67.60,H,4.10
1d	4-F	$C_{19}H_{15}FO$	277	27	91	140-142	0.27	C,82.31; H,5.4; found C,82.20,H,5.42
1e	4-CH_3	$C_{20}H_{18}O$	274	24	98	143-145	0.35	C,87.59; H,6.5; found C,87.60,H,6.1
1f	4-OCH_3	$C_{20}H_{18}O_2$	290	24	92	145-147	0.45	C,87.75; H,6.2; found C,87.60,H,6.15
1g	4-NO_2	$C_{19}H_{15}NO_3$	309	27	91	125-127	0.54	C,73.78; H,5.8; found C,72.90,H,5.70

Table 2: Spectral data of compounds (1a-1g)

Compound No.	I.R. data(cm^{-1})	1H NMR data(ppm)
1a	1650(C=O) ,1620(CH=CH)	8.0-7.3 (m,11H,Ar-H) 7.2-7.0 (dd,1H,C=CH) 6.90-6.85 (dd,1H,CH=C)
1b	1665(C=O) , 1620(CH=CH) ,840(C-Cl)	7.8-7.3 (m,10H,Ar-H) 7.0-6.8 (dd,1H,C=CH) 6.80-6.75 (dd,1H,CH=C)
1c	1660(C=O) ,1635(CH=CH),586(C-Br)	7.9-7.3 (m,10H,Ar-H) 7.0-6.85 (dd,1H,C=CH) 6.75-6.65 (dd,1H,CH=C)
1d	1652(C=O) ,1630(CH=CH),1236(C-F)	7.8-7.3 (m,10H,Ar-H) 6.9-6.8 (dd,1H,C=CH) 6.95-6.85 (dd,1H,CH=C)
1e	1665(C=O) ,1635(CH=CH),1160(C-C)	8.0-7.2 (m,11H,Ar-H) 7.2-6.95 (dd,1H,C=CH) 6.75-6.65 (dd,1H,CH=C) 3.85 (s,3H,CH3)
1f	1670(C=O) ,1640(CH=CH),1170(C-C)	8.0-7.3 (m,11H,Ar-H) 7.2-7.0 (dd,1H,C=CH) 6.90-6.85 (dd,1H,CH=C) 3.90 (s,3H,CH3)
1g	1660(C=O) ,1635(CH=CH),1165(C-C) 870(C-N), 610(C-N-O)	7.8-7.3 (m,11H,Ar-H) 7.1-6.8 (dd,1H,C=CH) 6.80-6.70 (dd,1H,CH=C) 3.80 (s,3H,CH_3)

Biological Evaluation
All synthesized compounds were evaluated for antimicrobial activity.

Antibacterial activity
The newly synthesized compounds were screened for theirantibacterial activity against *Escherichia coli*, *Staphylococcus aureus*,*Pseudomonas aeuroginosa* and *Streptococcus pyogenes* (recultured) bacterial strains by disc diffusion method17, 18. Discs measuring 6.25 mm in diameter were punched from Whatman no. 1 filter paper. The test compounds were prepared with different concentrations using dimethylformamide. One milliliter containing 100 times the amount of chemical in each disc was added to each bottle, which contains 100 discs. The discs of each concentration were placed in triplicate in nutrient agar medium seeded with fresh bacteria separately. The incubation was carried out at 37o C for 24 h.ciprofloxacin was used as a standard drug. Solvent and growth controls were prepared and kept. Zones of inhibition and minimum inhibition concentrations (MICs) were noted. The results of antibacterial studies are given in **Table 3**

Table 3: Antibacterial activities of chalcones (1a-1g)

Compound No.	*Escherichia Coli*	*Staphylococcus aureus*	*Pseudomonas Aeruginosa*	*Streptococcus pyogenes*
1a	10	12	08	09
1b	12	13	13	12
1c	11	13	13	15
1d	14	12	14	16
1e	11	14	11	10
1f	09	11	11	07
1g	13	10	10	09
Standard	20	19	25	20

Antifungal studies
Newly prepared compounds were screened for their antifungal activity against *Aspergillus flavus*, *Aspergillus fumigatus*, *Candida albicans* and *Penicillium marneffei* (recultured) in DMSO by serial plate dilution method19, 20. Sabourands agar media were prepared by dissolving peptone (1 g), D-glucose (4 g) and agar (2 g) in distilled water (100 mL) and adjusting pH to 5.7.
Normal saline was used to make a suspension of spore of fungal strain for lowning. A loopful of particular fungal strain was transferred to 3 mL saline to get a suspension of corresponding species. Agar media (20 mL) were poured into each petri dish.Excess of suspensions was decanted and the plates were dried by placing in an incubator at 37o C for 1 h using an agar punch, wells were made and each well were labeled. A control was also prepared in triplicate and maintained at 37^{o} C for 3-4 days. Zone of inhibition and minimum inhibitory concentration (MIC) were noted. The activity of each compound was compared with flucanazole as the standard drug. The results of antifungal studies are given in **Table 4.**

Table 4: Antifungal activities of chalcones (1a-1g)

Compound No.	*Aspergillus Fumigates*	*Aspergillus flavus*	*Penicillium Marneffei*	*Candida albicans*
1a	11	08	10	09
1b	08	13	07	10
1c	10	09	13	08
1d	13	12	11	09
1e	11	13	12	12
1f	12	11	11	11
1g	07	09	10	10
Standard	20	19	18	20

RESULTS AND DISCUSSION

The results of antimicrobial studies have shown that four compounds out of seven were found to possess antimicrobial activity against all tested micro-organisms. Results have shown that all the chalcones possess mild antifungal activity against all four tested strains. The structures of the synthesized compounds (**1a-1g**) were confirmed on the basis of spectral and elemental analysis. The formulas, melting point, yield of the compounds are

listed in Table 1. Compounds with electron releasing groups such as methoxy and compounds having pharmacophores such as chloro, fluoro, bromo groups and both these groups are present in one moiety exhibited mild to moderate antimicrobial activity. Hence, it is concluded that there is ample scope for further study in developing these as good lead compounds.

Acknowledgement
The author is thankful to the Principal Dr. S.C.Arora, R.K.S.D College Of Pharmacy, Kaithal for providing laboratory facilities. Authors are also thankful to Dr. S.A.Khan ,Jamia Hamdard, New Delhi for spectral analysis of the compounds.

REFERENCES

[1] D.N. Dhar: In chemistry of chalcones and related compounds,1st ed., John Wiley, New York, **1981**, pp. 56
[2] Z. Nowakowska; *Eur J Med Chem*, **2007**, 42, 125-137
[3] C.J. Shishoo, U.S. Pathak,K.S. Jain; *Ind J Chem*; **1999**, 33B, 684-689
[4] P. Venturalla, A. Bellino, I. Piozzi; *Farmco Ed Sci*, **1971**, 591-596
[5] J.A. Mickey, H.H. Saraf; *Ind J Chem*; **1998**, 37B, 68-72
[6] S. Alam; *J App Sci*, **2005**, 5(2), 327-333
[7] D.N. Dhar: In chemistry of chalcones and related compounds,1st ed., John Wiley, New York, **1981**, pp.1-15
[8] S.S. Tiwari, A. Singh, *J.Ind Chem Soc*, **1961**, 38, 931-932
[9] A.O. Fatima; *J Heterocycl Chem*, **2004**, 41, 327-333
[10] M.S.Y. Khan; *Ind J Chem*; **2003**, 42B, 1970-1975