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Journal of Advanced Scientific Research

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ISSN
0976-9595
Research Article

SYNTHESIS AND PHRAMACOLOGICAL EVALUATION OF 3-(1-NAPHTHYL)-1-SUBSTITUTED PHENYL CHALCONES AS POTENT ANTIMICROBIAL AGENTS

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ABSTRACT

About ten numbers of (*E*)-3-(1-naphthyl)-1-substituted phenyl chalcones have been synthesized using microwave assisted Crossed-Aldol condensation of various acetophenones and 1-naphthaldehyde in the presence of Fly-ash:H_3PO_4 nano catalyst under solvent-free conditions. This methodology produced more than 90% yields. These ketones were characterized by their physico chemical quantities, micro analysis and spectroscopic data. The antimicrobial activities of these compounds have been assessed by Bauer-Kriby disc diffusion technique. From the measurement of the zone of the inhibitions against the microbes, the antibacterial and antifungal activities of these ketones were discussed.

Keywords: Crossed-Aldol condensation, Fly-ash:H_3PO_4 nano catalyst, 1-naphthyl chalcones, Solvent-free synthesis, Antimicrobial activities, Bauer-Kirby disc diffusion method

1. INTRODUCTION

Aryl enones or unsaturated ketones were derived mainly by Cross-Aldol condensation of different aldehydes and ketones in presence of alkali or acidic catalyst [1]. Numerous catalysts and synthetic techniques including microwave irradiation and ultrasonication were reported in the past years [2, 3]. The moiety of –CO–C=C– and substituents in the enones are origin for their biological effects such as antimicrobial [4], antioxidant [5], anti-HIV [6], antiplasmodial [7], anticancer [8], antiviral [9] and antimalarials[10]. These enones are key intermediates and useful for carbon block buildings in organic synthesis such as pyrazoline [11], pyrimidine [12], oxazine [13], Diels-Alder adducts [14] and so on. Their *E* or *Z* configurational geometry and *s-cis* or *s-trans* conformers of enones were determined by NMR and IR spectroscopic data [15]. Tratrat et al., have investigated the antimicrobial and molecular docking studies of thiazole based chalcones by *in-vivo* evaluation method [16]. The broad spectrum of antibacterial activity of some cationic chalcone derivative was examined by Chu et al., [17]. The Mueller Hilton well agar diffusion method was adopted for evaluating the antibacterial activity of some chalcone and dihydrochalcone isolated from *Uvariachamae* roots was reported by Koudokpon et al., [18].

A serial tube dilution method was employed for the evaluation of antimicrobial activities of some novel isobutyl chalcones against Gram-positive *Bacillus subtilis* (NCIM-2079, *Bs*), *Staphylococcus aureus* (NCIM-2063, *Sa*), Gram-negative *Escherichia coli* (NCIM-2068, *Ec*), and *Proteus vulgaris* (NCIM-2027, *Pv*) and the fungal strains *Aspergillus niger* (ATCC-6275, *An*) and *Candida tropicalis* (ATCC-1369, *Ca*.) pathogens [19]. The *in-vitro* antimicrobial activity of some aryl chalcones was assessed by Hasan et al., [20]. Cup plate method was utilized for measurement of antimicrobial activities of some poly substituted phenyl styryl ketones. Recently, Ranganathan et al., have studied the antibacterial and antifungal activities of some piperdinophenyl chalcones by Bauer-Kirby disc diffusion method [21, 22]. Within this view, there is no report available in the literature for the synthesis and evaluation of antimicrobial activities of the titled chalcones in the present and past. Hence the authors have taken effort to synthesis the titled compounds for measuring their antibacterial and antifungal activities by Bauer-Kirby [22] disc-diffusion method.

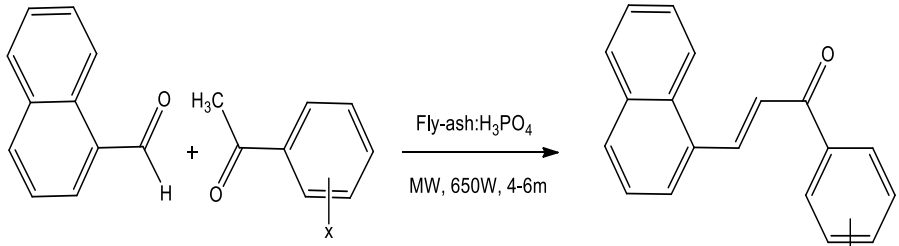
2. MATERIAL AND METHODS

2.1. General

In this experimental study, all the chemicals and solvents were procured from Sigma-Aldrich, Merck and Hi-media chemical companies. Guna make electrical meting point apparatus was employed for finding the melting points of all compounds and are uncorrected. Avatar 300 type infrared spectrophotometer and Bruker 400 MHz NMR spectrometer were employed for recording IR(ν, 400-4000cm^{-1}, KBr disc) and NMR (δ, ppm, $CDCl_3$-d_6, TMS) spectra. Mass fragments (m/z) of all ketones were recorded in Shimadzu mass spectrometer.

2.2. Synthesis procedure of (*E*)-3-(1-naphthyl)-1-substituted phenyl chalcones

This series of chalcones were prepared by Fly-ash:H_3PO_4 nano catalyst catalyzed solvent-free Aldol condensation method. An appropriate equimolar quantity of 1-naphthaldehyde (0.46 g, 2 mmol), acetophenones (0.240 g, 2 mmol) and Fly-ash:H_3PO_4 nano catalyst [23] (0.2 g) were taken in a 50 mL corning glass tube and tightly capped. The reaction mixture was subjected to microwave irradiation for 4-6 minutes in a microwave oven at 650W (Samsung, Grill Microwave Oven, 100-950W, 230v, A/c, 50Hz) and then cooled to room temperature (Scheme-1).



X= H, 4-Br, 3-Cl, 4-Cl, 2-OH, 3-OH, 4-OH, 4-CH_3, 3-NO_2, 4-NO_2

Scheme 1: Synthesis of (*E*)-3-(1-naphthyl)-1-substituted phenyl chalcones

Added 10 ml of dichloromethane, the organic layer had been separated which on evaporation yielded the solid product. The solid was recrystallized using ethanol to obtain pale yellow glittering solids. The physico-chemical constants, analytical and Mass spectral fragments of the compounds were presented in Table 1. IR and NMR spectroscopic data of ketones were presented in Table 2.

Table 1: Physico-chemical constants, analytical and Mass spectral fragments of E-3-(1-naphthyl)-1-(substituted phenyl)-2-propen-1-ones

Entry	X	MF	MW	m.p. (°C)	Mass(m/z)
1	H	$C_{19}H_{14}O$	258	96-97(95-97) [24]	258[M^+].
2	4-Br	$C_{19}H_{13}BrO$	337	118-119(117-118°C) [25]	337[M^+], 339[M^{2+}]
3	3-Cl	$C_{19}H_{13}ClO$	219	104-105	219[M^+], 221[M^{2+}]
4	4-Cl	$C_{19}H_{13}ClO$	219	112-113(110-113°C) [25]	219[M^+], 221[M^{2+}]
5	2-OH	$C_{19}H_{14}O_2$	274	97-98	274[M^+]
6	3-OH	$C_{19}H_{14}O_2$	274	118-119	274[M^+]
7	4-OH	$C_{19}H_{14}O_2$	274	125-126	274[M^+]
8	4-CH_3	$C_{20}H_{16}O$	256	132-133(132-134) [25]	256[M^+]
9	3-NO_2	$C_{19}H_{13}NO_3$	303	121-122	303[M^+]
10	4-NO_2	$C_{19}H_{13}NO_3$	303	113-114	303[M^+]

2.3. Antimicrobial activity

The compounds potato dextrose agar, Mueller Hinton agar, nutrient broth, Tween-80 solution and other materials were from Himedia, Mumbai

2.3.1. Measurement

The bacterial and antifungal activities of these ketones were measured using Bauer-Kirby disc diffusion technique according to the procedure reported in literature. Based on the procedure we prepared nutrient bath antibacterial innoculum, antifungal innoculum, agar

Table 2: Infrared stretching frequencies (ν, cm^{-1}) and NMR chemical shifts (δ, ppm) of (*E*)-3-(1-naphthyl)-1-(substituted phenyl) ketones

IR(ν, cm^{-1})							
Entry	**X**	**CO** $_{s\text{-}cis}$	**CO** $_{s\text{-}trans}$	**CH**$_{ip}$	**CH**$_{op}$	**CH=CH**$_{op}$	**C=C**$_{op}$
1	H	1661.55	1602.11	1207.88	781.53	1081.27	693.75
2	4-Br	1659.30	1600.00	1157.94	787.55	1091.55	696.56
3	3-Cl	1649.19	1608.25	1116.25	802.00	1019.95	630.21
4	4-Cl	1632.00	1600.95	1161.32	728.72	959.13	641.33
5	2-OH	1658.76	1599.28	1175.72	787.55	1004.44	670.34
6	3-OH	1669.41	1649.37	1172.48	798.85	1026.27	683.24
7	4-OH	1658.40	1606.23	1180.68	791.32	971.45	667.74
8	4-CH_3	1688.28	1643.74	1217.26	772.11	1055.94	657.31
9	3-NO_2	1688.68	1648.73	1169.82	772.24	1055.52	647.41
10	4-NO_2	1686.35	1665.76	1217.04	773.03	1082.72	691.45
NMR (δ, ppm)							
Entry	**X**	**H**$_{\alpha}$	**H**$_{\beta}$	**CO**	**C**$_{\alpha}$	**C**$_{\beta}$	
1	H	7.241	8.383	192.35	125.52	143.19	
2	4-Br	7.508	8.681	189.18	124.03	142.34	
3	3-Cl	7.598	8.689	189.01	124.09	142.31	
4	4-Cl	7.487	8.210	189.91	124.11	140.76	
5	2-OH	7.501	8.361	189.36	125.23	141.36	
6	3-OH	7.528	8.656	188.10	123.59	141.27	
7	4-OH	7.626	8.643	189.08	123.16	138.14	
8	4-CH_3	7.680	8.662	189.87	123.60	141.38	
9	3-NO_2	7.749	8.788	193.63	124.92	143.67	
10	4-NO_2	7.624	8.738	193.63	123.80	144.75	

slants, Muller-Hilton agar plates, potato dextrose agar medium and test samples. In this investigation, microbial strains such as *Bacillus subtilis, Escherichia coli, Klebsila pneumonia, Micrococcus luteus, Pseudomonas aeruginosa, Staphylococcus aureus, Aspergillus niger, Mucor species* and *Trichoderma viride* were obtained from the Department of Microbiology, Sengunthar Arts and Science College, Thiruchengode, Namakkal District, Tamilnadu. The stock cultures were kept in the refrigerator for further investigations.

2.3.2. Antibacterial sensitivity assay

Antibacterial sensitivity assay was performed using Kirby-Bauer [22] disc diffusion technique. In each Petri plate about 0.5 ml of the test bacterial sample was spread uniformly over the solidified Mueller Hinton agar using sterile glass spreader. Then the discs with 5mm diameter made up of Whatman No.1 filter paper, impregnated with the solution of the compound were placed on the medium using sterile forceps. The plates were incubated for 24 hours at 37°C by keeping the plates upside down to prevent the collection of water droplets over the medium. After 24 h, the plates were visually examined and the diameter values of the zone of inhibition were measured. Triplicate results were recorded by repeating the same procedure.

2.3.3. Antifungal sensitivity assay

Antifungal sensitivity assay was performed using Kirby-Bauer [22] disc diffusion technique. PDA medium was prepared and sterilized as above. It was poured (ear bearing heating condition) in the Petri-plate which was already filled with 1 mL of the fungal species. The plate was rotated clockwise and counter clock-wise for uniform spreading of the species. The discs were impregnated with the test solution. The test solution was prepared by dissolving 15 mg of the chalcone in 1mL of DMSO solvent. The medium could solidify and kept for 24 h. Then the plates were visually examined and the diameter values of zone of inhibition were measured.

Triplicate results were recorded by repeating the same procedure.

3. RESULTS AND DISCUSSION

3.1. Antibacterial Activity

The antibacterial effect of 3-(1-naphthyl)-1-substituted phenyl chalcones is shown in Fig. 1. for plates (1-12) and the zone of inhibition values are given in Table 3.

Table 3 inferred that the chalcones except **2, 5, 7** and **10** are possess good activity against B. *subtilis* bacterial strain. Chalcone **4** has excellent antibacterial activity against *M. luteus* strain and the compounds **2** and **3** are inactive. The chalcones **3** and **4** shows good antibacterial activity against *S. aureus* and the compounds **6, 8** and **10** were inactive. The chalcone **3** shows excellent antibacterial activity against *E. coli, and the* chalcone 6 was inactive. The chalcones **4** and **6** shows good antibacterial activities against *P. aeruginosa* and the compound **9** shows excellent activity against *K. pneumoniae*.

Table 3: Antibacterial activities of 3-(1-naphthyl)-1-substituted phenyl chalcones

Entry	X	Zone of Inhibition (mm)					
		Gram positive Bacteria			Gram negative Bacteria		
		B.subtilis	*M.luteus*	*S.aureus*	*E.coli*	*P.aeruginosa*	*k.pneumoniae*
1	H	6	6	7	7	6	6
2	4-Br	---	---	6	6	6	7
3	3-Cl	6	---	8	8	---	6
4	4-Cl	7	8	8	7	7	7
5	2-OH	---	7	6	7	---	6
6	3-OH	7	7	---	---	7	7
7	4-OH	---	6	6	6	6	6
8	4-CH_3	6	7	---	6	---	---
9	3-NO_2	7	8	7	6	6	8
10	4-NO_2	---	6	---	6	6	7
Standard (Ampicillin)		8	8	9	8	8	8
Control DMSO		---	---	---	---	---	---

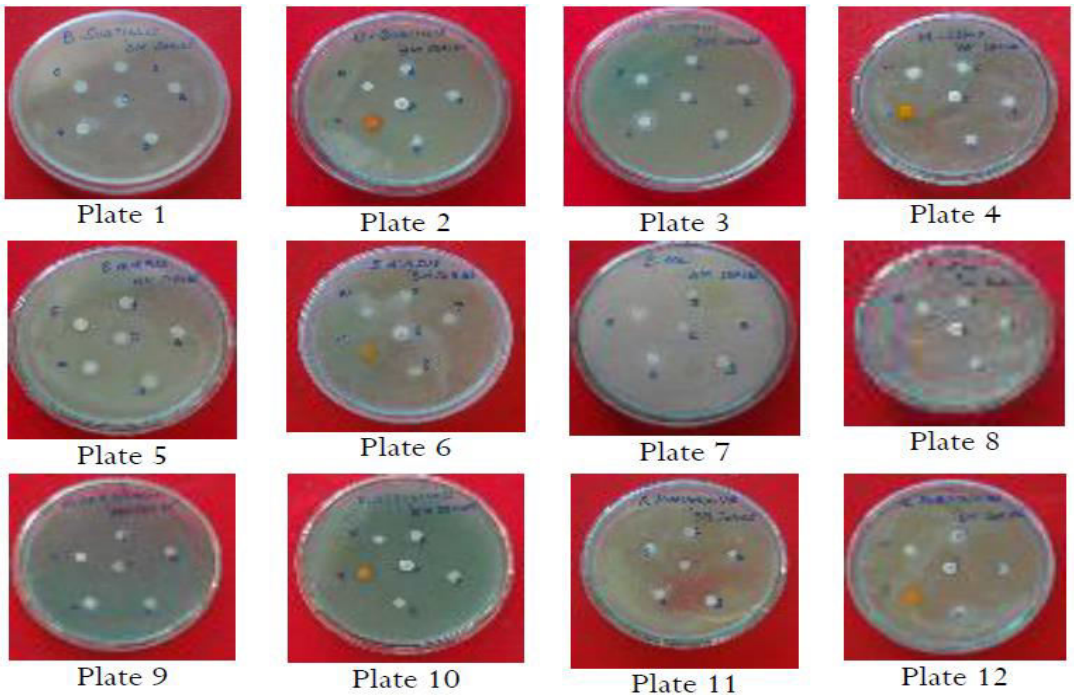


Fig. 1: Antibacterial activities of 3-(1-naphthyl)-1-substituted phenyl chalcones: Petri-dishes

3.2. Antifungal activities of 3-(1-naphthyl)-1-substituted phenyl chalcones

The antifungal effect of 3-(1-naphthyl)-1-substituted phenyl chalcones is shown in Fig. 2 for plates (1-6) and the values are given in Table 4. From the plates and table, it is indicated that all chalcones have good activity on all the three fungal species. The chalcone **10** shows very good antifungal activity against *A. niger* and the compounds **2, 3** and **7-9** were inactive. The compounds **6** and **9** show good antifungal activities against *M. species* and the compounds **2, 4** and **5** were inactive. The chalcones **1** and **8** were shows good antifungal activity against *T. viride* species.

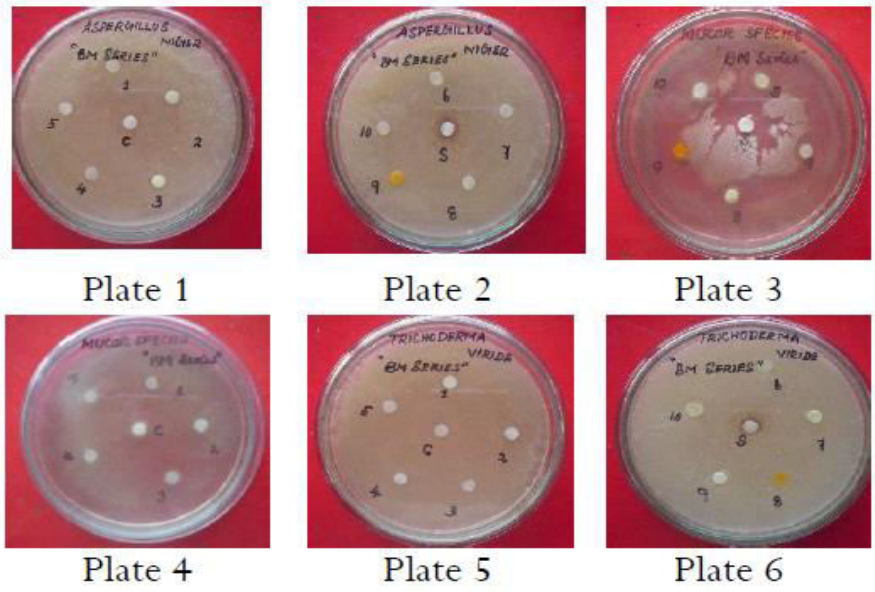


Fig. 4: Antifungal activities of 3-(1-naphthyl)-1-substituted phenyl chalcones: Perti dishes.

Table 4: Antifungal activities of 3-(1-naphthyl)-1-substituted phenyl chalcones

Entry	X	Zone of inhibition (mm)		
		A. niger	*M. species*	*T. viride*
1	H	6	6	6
2	4-Br	---	---	---
3	3-Cl	---	6	---
4	4-Cl		6	---
5	2-OH	6	7	---
6	3-OH	6		
7	4-OH	---	---	---
8	4-CH_3	---	---	6
9	3-NO_2	---	---	---
10	4-NO_2	7	7	
Standard	Miconazole	8	12	7
Control	DMSO	---	---	---

4. CONCLUSIONS

Authors prepared about ten numbers of (*E*) 3-(1-naphthyl)-1-substituted phenyl chalcones by greener synthetic methodology. All prepared ketones were characterized by their analytical and spectroscopic data. The antimicrobial activities of all ketones were measured by Bauer-Kirby disc diffusion method. The chalcones except **2, 5, 7** and **10** possess good activity against B. *subtilis* bacterial strain. Chalcone **4** has excellent antibacterial activity against *M. luteus* strain and the compounds **2** and **3** are inactive. The chalcones **3** and **4** shows good antibacterial activity against *S. aureus* and the

compounds **6, 8** and **10** were inactive. The chalcone **3** shows excellent antibacterial activity against *E.coli, and the* chalcone 6 was inactive. The chalcones **4** and **6** shows good antibacterial activities against *P. aeruginosa* and the compound **9** shows excellent activity against *K. pneumoniae*. The chalcone **10** shows very good antifungal activity against *A. niger* and the compounds **2, 3** and **7-9** were inactive. The compounds **6** and **9** show good antifungal activities against *M. species* and the compounds **2, 4** and **5** were inactive. The chalcones **1** and **8** shows good antifungal activity against on *T. viride* species.

5. ACKNOWLEDGEMENT

Authors thank DST-NMR facility, Department of Chemistry, Annamalai University, Annamalainagar for recording NMR spectra of all ketones.

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