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ULTRASOUND ASSISTED SYNTHESIS OF CHLORO-SUBSTITUTED CHALCONES FOR THEIR ANTIFUNGAL ACTIVITY

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ABSTRACT

Abstract: *Claisen- Schmidt condensation of chloro-substituted 2-acetyl-1-naphthol with aromatic aldehydes catalyzed by alkali results chalcones in 80-85% yield in alcoholic solvent under ultrasonic condition. The synthesized compounds are evaluated for their antifungal activity, the result showed all the compounds (**3a-3f**) showed good to moderate antifungal activity.*

KEY WORDS

Chloro-substituted chalcones, sonication, Antifungal activity.

INTRODUCTION:

Chalcones constitute an important group of natural products and some of them possess wide range of biological activities such as antibacterial [1, 2], anticancer [3, 4], antitubercular[5], antiviral [6, 7], antiinflammatory[8]. The presence of reactive α-β unsaturated keto function in chalcones is responsible for biological activities, which may be changed by changing the position of substituents on aromatic rings. Synthesis of chalcones via claisen-schmidt condensation of aromatic aldehydes with acetophenones has been reported in literature. Some alkalis such as NaOH[9], KOH[10] have been used to catalyze the reaction. However, there were always some problems due to long reaction time or difficult work up.

A survey of literature show that many organic reactions have been accelerated by ultrasonic irradiation[11,12]. The ultrasonic waves accelerate the reaction million-fold and many synthetically useful reactions are successfully accomplished[13,14] as compared to conventional method. In present communication the reaction of chloro-substituted 2-acetyl-1-naphthol with aromatic aldehydes to forms chloro-substituted chalcones(**3a-3f**) is reported. The structure of compounds were assigned on the basis of elemental and spectral analysis. These compounds were also screened for their antifungal activity.

MATERIAL AND METHOD:

Melting points were determined in an open capillary tube and are uncorrected. IR spectra were recorded in KBr on a Perkin-Elmer spectrometer. ^{1}H NMR spectra were recorded on a Gemini 300-MHz instrument in DMSO as solvent and TMS as an internal standard. The mass spectra were recorded on EISHIMADZU-GC-MS spectrometer. Elemental analysis was carried out on a Carlo Erba 1108 analyzer. Sonication was performed in a Toshnival model SW-4 ultrasonic bath with frequency of 37 KHz and nominal power of 500 W. The purity of products was checked by Thin Layer Chromatography (TLC) on silica gel. All solvents and chemicals were purchased from Alfa chemicals and used without further purification.

General procedure for the preparation of chalcones by ultrasound irradiation method:

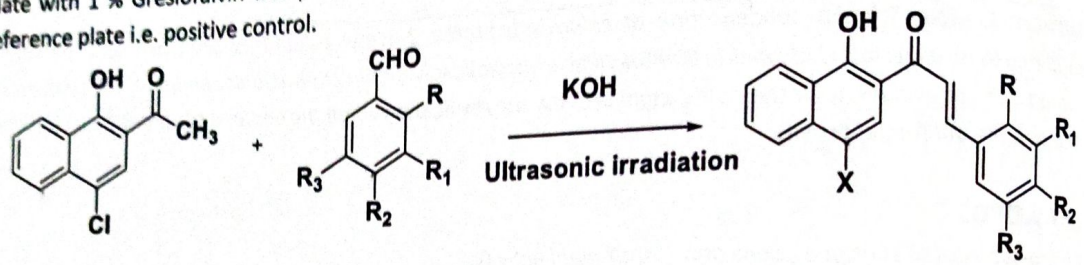
Chloro-substituted 2-acetyl-1-naphthol (1mmol), aromatic aldehydes (1mmol), 95% Ethanol (15ml) and 2*N* KOH (3ml) were taken into 100ml conical flask. The reaction mixture was sonicated by ultrasound irradiation in water bath at 30-35^{0}C for 10-11 min. The

solid obtained was diluted with cold water and neutralized with di. HCl. Then it filtered, washed and recrystalized from ehanol to afford shiny crystal (**3a-3f**), their physical characteristics and analytical data are given in **Table. 1**.

Antifungal activity:

Antifungal activity was performed by poison plate method[15]. The medium used was potato dextrose agar (Himedia). The medium was prepare and sterilized at 10psi in autoclave for 15 minutes. The compounds to be tested is added to the sterile medium in aseptic condition so as to get final concentration as 1%. A plate with DMSO was prepared as negative control similarly a plate with 1 % Gresiofulvin was prepared as standard reference plate i.e. positive control.

Aspergilus niger, Penicillium chrysogenum, Fusarium monoliforme and aspergilus flavus were selected as test fungal cultures. They were allowed to grow on slant for 48 hours so as to get profuse sporulation. 5 ml of 1:100 aqueous solution of Tween 80 was added to get the slant and spores were scraped with the help of nicrome wire loop to form suspension. The fungal suspension was spot inoculated on the plates prepared using compound with the help of nicrome wire loop. The plates were incubated at room temperature for 48 hours, after incubation plates were observed for the growth of inoculated fungi. Results were recorded as growth of fungi in percentage of zone of inhibition in **Table 2.**



3a. R= H, R_1= OCH_2CH_3 R_2= OH, R_3=H
3b. R= H, R_1=OCH_2CH_3, R_2= OH, R_3=Br
3c. R= $O\text{-}CH_3$, R_1=H, R_2= H, R_3=Cl
3d. R= OH, R_1=H, R_3= Cl, R_2=H
3e. R= OH, R_1= R_3= Br, R_2=H
3f. R= OH, R_1= R_3= I, R_2=H

Spectral and analytical data of chloro-substituted chalcone derivatives:

***2(E)-1-(4-Chloro-1-hydroxynaphthlen-2-yl)-3-(3-ethoxy-4-hydroxyphenyl)-prop-2-en-1-one* (3a)**

Brown powder, IR (KBr): ν_{max}(Cm^{-1}) 3360, 3070, 1650, 1580, 1540, ^{1}HNMR(DMSO-d_6): 2.60(t, 3H), 4.0(q, 2H), 7.80(d, 1H, J=15.6Hz,), 7.90(d, 1H, J=16.2Hz,), 6.90-7.70(m, 8H), 14.0(s, 2H). MS.m/z 368(M^+). Anal. Calcd. for Formula:$C_{21}H_{17}O_4Cl$: C, 68.47; H, 4.61; Cl, 9.78. Found: C, 68.45; H, 4.59; Cl, 9.76.

***2(E)-3-(3-bromo-5-ethoxy-4-hydroxyphenyl)-1-(4-chloro-1-hydroxynaphthalen-2-yl) prop-2-en-1-one* (3b)**

Faint brown powder, IR (KBr): ν_{max}(Cm^{-1}) 3293, 2983,1678, 1593, 1550, ^{1}HNMR(DMSO-d_6): 2.60(t, 3H), 3.90(q, 2H), 7.70(d, 1H, J=15.6Hz), 7.80(d, 1H, J=16.2Hz), 7.10-7.30(m, 7H), 13.70(s, 2H). MS.m/z 447(M^+). Anal. Calcd. for Formula:$C_{21}H_{16}O_4ClBr$: C, 56.37; H, 3.57; Cl, 8.05; Br, 17.67 Found: C, 56.35; H, 3.55; Cl,8.03; Br, 17.65.

***2(E)-1-(4-Chloro-1-hydroxynaphthlen-2-yl)-3-(5-chloro-2-methoxyphenyl)-prop-2-en-1-one* (3c)**

Brown powder, IR (KBr): ν_{max}(Cm^{-1}) 3260, 3050, 1650, 1560, 1508, ^{1}HNMR(DMSO-d_6): 2.90(s, 3H), 8.20(d, 1H, J=15.6Hz), 8.50(d, 1H, J=16.2Hz), 7.60-7.80(m, 8H), 13.95(s, 1H). MS.m/z 372(M^+). Anal. Calcd. for Formula:$C_{20}H_{14}O_3Cl_2$: C, 64.51; H, 3.76; Cl, 19.08. Found: C, 72.77; H, 4.68; Cl, 8.05.

***2(E)-3-(5-Chloro-2-hydroxyphenyl)-1-(1-Chloro-4-hydroxynaphthalen-3-yl) prop-2-en-1one* (3d)**

Redish powder, IR (KBr): ν_{max}(Cm^{-1}) 3280, 2980, 1650, 1560, 1508, ^{1}HNMR(DMSO-d_6): 8.20(d, 1H, J=15.6Hz), 8.40(d, 1H, J=16.2Hz), 7.65-7.80(m, 7H), 14.0(s, 2H). MS.m/z 357(M^+). Anal. Calcd. for Formula:$C_{19}H_{11}O_3Cl_2$: C, 63.86; H, 3.08; Cl, 19.60. Found: C, 63.84; H, 3.06; Cl, 19.58.

***2(E)-1-(4-Chloro-1-hydroxynaphthlen-2-yl)-3-(3,5-dibromo-2-hydroxyphenyl)-prop-2-en-1-one* (3e)**

Redish powder, IR (KBr): ν_{max}(Cm^{-1}) 3350, 1650, 1560, 1508, ^{1}HNMR(DMSO-d_6): 8.21(d, 1H, J=15.6Hz), 8.50(d, 1H, J=16.2Hz), 7.60-7.90(m, 7H), 14.0(s, 2H). MS.m/z 482(M^+). Anal. Calcd. for Formula: $C_{19}H_{11}O_3ClBr_2$: C, 47.30; H, 2.28; Cl, 7.26; Br, 32.19. Found: C, 47.28; H, 2.26; Cl, 7.24; Br, 32.17.

***2(E)-1-(4-Chloro-1-hydroxynaphthlen-2-yl)-3-(2-hydroxy-3,5-diiodo-phenyl)-prop-2-en-1-one* (3f)**

Redish powder, IR (KBr): ν_{max}(Cm^{-1}) 3320, 2910, 1650, 1550, 1510, ^{1}HNMR(DMSO-d_6): 8.20(d, 1H, J=15.6Hz), 8.35(d, 1H, J=16.2Hz), 7.35-7.95(m, 7H), 13.80(s, 2H). MS.m/z 576(M^+). Anal. Calcd. for Formula:$C_{19}H_{11}O_3CII_2$: C, 39.58; H, 1.90; Cl, 6.25; I, 44.09. Found: C, 39.56; H, 1.88; Cl, 6.23; I, 44.05.

RESULT AND DISCUSSION:

Synthesis of chalcones (3a-3f) was carried out in good yield by the reaction of chloro-substituted 2-acetyl-1-naphthol with aldehydes in the presence of aq. KOH, under ultrasound irradiation technique. It has been observed that the reaction proceed rapidly within 10-11 min. and yield was significantly improved as compared to conventional method.

All the synthesized compounds (3a-3f) were screened for their antifungal activity against *S.aureus, P.aeruginasa, K.pneumoniae* and *E.coli.* and it is observed that all the compounds showed good to moderate antifungal activity against fungal strain tested. A comparative study also reveals that the compounds that contain more than one chlorine atoms (3b & 3d) are more potent antifungal agent than others.

Table No. 1: Synthesis of chloro-substituted chalcones (3a-3f) by ultrasound irradiation method.

compounds	Time (min.)	Yield (%)	M.P. ^{0}C
3a	10	85	161
3b	11	82	155
3c	09	81	163
3d	10	80	167
3e	10	84	170
3f	11	85	185

Table 2. Antifungal activity of compounds (3a-3f) by poison plate method.

Compounds	Percentage zone of inhibition (%)			
	P.chrysogenum	*F.moniliforme*	*A. flavus*	*A. niger*
3a	90	70	60	59
3b	95	94	80	92
3c	50	55	54	30
3d	96	94	85	95
3e	80	60	12	10
3f	80	20	15	50
DMSO	-	-	-	-
Standard	99	99	100	99

Positive control (standard) – Griseofulvin and Negetive control (DMSO)

CONCLUSION:

In conclusion we have found an efficient and convenient procedure for the synthesis of chloro-substituted chalcones under ultrasonic condition. The main advantages of this method is milder reaction condition, higher yields and short reaction time. In case of antifungal activity, the compounds that contain electron donating group along with bromine atom showed more potent activity than others.

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REFERENCES:

1) Asiri, A.M., Khan, S.A., synthesis and antibacterial activity of a bis-chalcones derived from Thiophene and its Bis-cyclized products. Molecules.16:523-531, (2011).
2) Prasad, Y.R., Kumar, P.R., Smile, D.J., Babu, P.A., QSAR studies on chalcone derivatives as antibacterial agents against Bacillus Pumilis. Eur. J. Med. Chem. 43: 2220-2228, (2008).
3) Anto,R.J., Sukumaran, K., Kuttan, G., Rao, M.N.A., Subbaraju, V., Kuttan, R., Anticancer and antioxidant

activity of synthetic chalcones and related compounds. Cancer Lett. 97:33-37, (1995).

4) Achanta, G., Modzelewska, A., Feng, L., Khan, S.R. Hung, P., A boronic- chalcone derivative exhibits potent anticancer activity through inhibition of the proteasome. Mol. Pharmacol.70:426-433, (2006).

5) Hans *et al*. Synthesis, antimalarial and antitubercular activity of acetylenic chalcones. Biorg. Med. Chem. Lett. 20:942-944, (2010).

6) Mallikarjun, K.G., Antiviral Activity of Substituted Chalcones and their Respective Cu(ii), Ni(ii) and Zn(ii) Complexes. E. J. Chem. 2:58-61, (2005)

7) Gan, X., Wang, Y., Hu, D., Song, B., Design, Synthesis, and Antiviral Activity of Novel Chalcone Derivatives Containing a Purine Moiety. Chin. J. Chem. 20:1—8, (2007).

8) Chen *et al*. Evaluation of the Anti-Inflammatory Effect of Chalcone and Chalcone Analogues in a Zebrafish Model. Molecules,18:2052-2060, (2013).

9) Palleros, D.R., Solvent-Free Synthesis of Chalcones. J. Chem. Edu. 81:1545-1547, (2013).

10) Mandge, S., Singh, H.P., Gupta, S.D., Hari Narayan Moorty, N.S., Trends in Applied Sciences Res. 2:52-56, (2007).

11) Gupta, R., Gupta, N., Jain, A., Improved synthesis of chalcones and pyrazolines under ultrasonic irradiation. Ind. J. Chem. 49B:351-355, (2010).

12) Li *et al*. Improved synthesis of chalcones under ultrasonic irradiation. Ultrason. Sonochem. 9:237-239, (2002).

13) Kaur, Navjeet., Synthesis of six- and seven-membered heterocycles under ultrasound irradiation. Synthetic Communication. 48:135-1258, (2018).

14) Mekky, A.E.M., Abdullah, S., Al-Bogami, Ultrasound Assisted Synthesis of Some Novel Bis-Pyridazine Derivatives. J. Heterocyclic Chem. 53:595-602, (2016).

15) R. Cruickshank, J. P. Duguid, B. P. Marmion, R. R. Swain, Medicinal microbiology, Churchill livingstone, London, 1, (1998).

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