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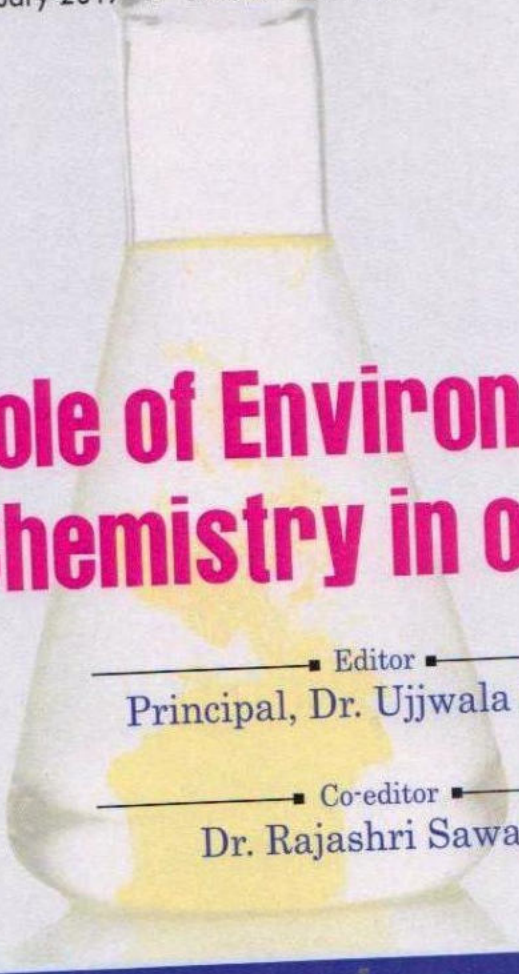

Role of Environmental Chemistry in our Life

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Improved synthesis of 2-bromothiophene incorporated chalcone under ultrasonic irradiation

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Abstract: -

Chalcones are 1, 3-diphenyl-2-propene-1-one, in which two aromatic rings are linked by a three carbon α, β-unsaturated carbonyl system. These are abundant in edible plants and are considered to be precursors of flavonoids and isoflavonoids. Chalcones were synthesized by a base catalyzed Claisen-Schmidt condensation reaction under sonochemical irradiation. The synthesized compounds were evaluated for their antimicrobial and antifungal activity against Gram +ve and Gram-ve microorganisms. Some of compounds show moderate activity against standard drugs.

Key Words: Chalcones, 2-bromothiophene, sonochemical irradiation, antimicrobial agents.

Introduction: -

Chalcones are 1, 3-diphenyl-2-propene-1-one, in which two aromatic rings are linked by a three carbon α, β-unsaturated carbonyl system. These are abundant in edible plants and are considered to be precursors of flavonoids and isoflavonoids. Chalcones are prepared by condensing 2-hydroxy acetophenones with substituted pyrazole carbaldehyde in presence of suitable condensing agents. They undergo a variety of chemical reactions and are found useful in synthesis of variety of heterocyclic compounds. Chalcones have been used as intermediate for the preparations of compounds having therapeutic value. Literature review reveals that chalcone derivatives exhibit diverse pharmacological activities[1-6] such as potential cytotoxic agents, antimicrobial agents, antiviral, anti-inflammatory, anesthetics, mydriatics etc. Based on the above observation it is worthwhile to prepare newer compounds for their antimicrobial and anti-inflammatory activities. In the view of the varied biological and pharmacological application, we synthesized some new heterocyclic derivatives of chalcones. Chalcones have been synthesized under sonochemical irradiation by Claisen–Schmidt condensation. Heterocycles bearing nitrogen, sulphur and thiazole moieties constitute the core structure of a number of biologically interesting compounds.

Antimicrobial activity:-

Compounds **3** were screened for their in vitro antimicrobial activity against *Escherichia coli*, *Pseudomonas aeruginosa, Staphylococcus albus, Staphylococcus aureus, Klebsiella pnuemoniae*

*Pseudomonas sp.*using Ciprofloxacin as a reference standard drug by paper disc diffusion method and agar well method. Antifungal activity was evaluated against *Candida sp.* using Fluconazole as standard drug. All the tests were evaluated at 100 µg/ml concentration. The culture media was Muller hinton agar. The zone of inhibition was measured in mm after 24 hr. of incubation at 37°C. 3e shows moderate antifungal activity. All the compounds show good to moderate antibacterial activity against above mentioned bacterial species.DMSO is used as control.

Experimental

Melting points were recorded in open capillaries in liquid paraffin bath and are uncorrected. The completion of reaction was monitored by TLC. IR spectra were recorded in KBr disc on Schimadzu-FT-IR Spectrophotometer. ^{1}H NMR spectra were recorded on Varian 400 MHz instrument in DMSO-d_6, $CDCl_3$ and TMS as an internal standard. Peak values are shown in δ (ppm). Mass spectra were recorded on micromass Q-Tof Micro mass spectrophotometer. Bandelin Sonorex (with a frequency of 35 KHz and a nominal power of 200W) ultrasonic bath was used for ultrasonic irradiation. The reaction vessel placed inside the ultrasonic bath containing water.

Conventional Method:

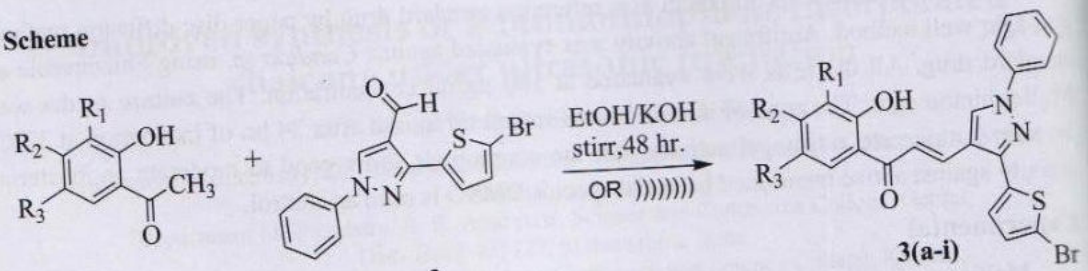
General procedure for the synthesis of (*E*)-3-(3-(5-bromothiophen-2-yl)-1-phenyl-1*H*-pyrazol-4-yl)-1-(5-chloro-2-hydroxyphenyl) prop-2-en-1-one (3c): A mixture of **1** (0.01 mol) and **2** (0.01 mol) was dissolved in 40 ml ethanol and contents were cooled to 0°C in ice bath. To this reaction mixture, 2g KOH pellets were added maintaining temperature below 5°C. The reaction mixture was stirred at room temperature for 48hr. Then reaction mixture was poured over crushed ice and contents were acidified with 2M HCl. Resulting product was separated by filtration and washed with cold water. Product was crystallized from ethanol. This typical experimental procedure was followed to prepare other analogs of this series. Their physical data are given in **Table 1**

Nonconventional Method:

A mixture of **1** (0.01 mol) and **2** (0.01 mol) was dissolved in 40 ml ethanol in 100ml round bottom flask. To this reaction mixture, 2g KOH pellets were added. The mixture was irradiated by ultrasonic generator in a water bath maintaining temperature 30-80°C for 4hr. The reaction mixture containing solid product was poured over crushed ice and contents were acidified with 2M HCl. Resulting product was separated by filtration and washed with cold water. Product was crystallized from ethanol. This typical experimental procedure was followed to prepare other analogs of this series. Their physical data are given in **Table 1**and Antimicrobial data given in **Table 2 & 3.**

3c: m.p 173°C; IR (cm^{-1}): 1018 (C-Cl), 1060 (C- Br), 1178 (C-O), 1531 (C=C), 1577, 1471 (Ar C=C), 1645 (C=O), 3410 (-OH).; ^{1}H NMR: 6.98-7.01(d, 1H, Ar-H, *J*=8.8Hz), 7.13-7.14(d, 1H, Ar-H, *J*=3.2Hz), 7.19-7.20 (d, 1H, Ar-H, *J*=3.6Hz), 7.37-7.54 (m, 5H, Ar-H), 7.79-7.81(m, 3H, Ar-H), 8.07-8.11(1H, d, CH=C, *J*=15.2 Hz), 8.42 (s, 1H, pyrazole =CH), 12.75 (s, 1H, -OH). Mass : m/z 483(M-1),485(M+2),487(M+4)

Scheme



1(a-i) **2** **3(a-i)**

Table 1: Physical data of compounds 3(a-i)

Compd.	R_1	R_2	R_3	M.P. (°C)	Conventional Method		Nonconventional Method	
					Time (hr)	Yield (%)	Time (min)	Yield (%)
3a	H	H	H	178	48	74	240	80
3b	H	H	CH_3	173	48	75	240	78
3c	H	H	Cl	173	48	62	240	69
3d	Cl	H	Cl	212	48	89	240	92
3e	H	H	OCH_3	135	48	87	240	90
3f	H	H	F	206	48	64	240	68
3g	H	CH_3	Cl	145	48	66	240	72
3h	H	H	Br	236	48	80	240	86
3i	CH_3	H	CH_3	218	48	74	240	79

Table 2: Antimicrobial data of compounds 3(a-i)

Disc Diffusion Method

Sample	Inhibition Zone Diameter (mm)					
	Candida sp.	*Staphylococcus aureus*	*Staphylococcus albus*	*Klebsiella pnuemoniae*	*Escherichia coli*	*Pseudo monas sp.*
3a	8	No zone	7	1	13	12
3b	No zone	No zone	11	9	11	12
3c	No zone	No zone	15	9	11	No zone
3d	No zone	No zone	10	7	No zone	No zone
3e	10	No zone	9	8	7	No zone
3f	8	No zone	9	8	9	No zone
3g	No zone	No zone	No zone	8	9	No zone
3h	No zone	No zone	11	No zone	7	No zone
Control (DMSO)	8	3	3	4	6	10
Ciprofloxacin	---	20	22	22	21	23
Fluconazole	23	---	---	---	---	---

Table 3: Antimicrobial data of compounds 3(a-i)

Agar Well Method

Sample	Inhibition Zone Diameter (mm)					
	Candida sp.	*Staphylococcus aureus*	*Staphylococcus albus*	*Klebsiella pnuemoniae*	*Escherichia coli*	*Pseudo monas sp.*
3a	No zone	7	5	-	3	2
3b	No zone	10	10	3	5	4
3c	No zone	5	3	5	4	10
3d	No zone	6	12	7	5	No zone
3e	No zone	8	5	7	No zone	No zone
3f	9	12	No zone	5	8	10
3g	10	6	No zone	10	8	No zone
3h	7	8	13	12	10	No zone
Control	8	3	3	4	6	10
Ciprofloxacin	---	20	22	22	21	23
Fluconazole	23	---	---	---	---	---

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