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Microwave Studies on Synthesis of Some New Heterocyclic Chalcone and Pyrimidine-2-thione Derivatives and Their Antibacterial Activity

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Chalcone derivatives [**1(a–j)**] were prepared by condensing acetophenone with various substituted aldehydes. These chalcones react with hydrazine hydrate and glacial acetic acid to give 1-acetyl pyrazolines and in turn 1-acetyl pyrazolines react with various substituted aldehydes to give various chalcone derivatives. Pyrimidine-2-thione derivatives [**2(a–j)**] were prepared by condensing substituted chalcones with thiourea in presence of dil. HCl by using ethanol as a solvent. All these reactions are carried out in borosil beaker under microwave irradiation in microwave oven. These products have been characterised by means of elemental analysis and IR spectral studies and tested for antibacterial activities against *S. aureus* and *E. coli.*

Key Words: Heterocyclic chalcone, Pyrimidine-2-thione, Antibacterial activity.

INTRODUCTION

The chemistry of chalcones has generated intensive scientific interest due to their biological and industrial applications. Chalcones and their derivatives possess some interesting biological properties such as antibacterial[1], antifungal[2], insecticidal[3], anaesthetic[4], antiinflammatory, analgesic, ulcerogenic[5] etc.

Pyrimidines and their derivatives are considered to be important for drugs and agricultural chemicals. Some substituted pyrimidines and their derivatives have been reported to possess several interesting biological activities such as hypnotic properties[6], antimicrobial, antitumour[7] and antifungal activities[8]. Many pyrimidine derivatives are used for thyroid drugs[9] and leukaemia. It has incidental antiviral activity against herpes and vaccinia infections[10].

EXPERIMENTAL

Preparation of *p*-methoxy chalcone

To a solution of *p*-methoxy acetophenone (0.01 mol) and 2,4-dichlorobenzaldehyde (0.01 mol) in dry ethanol (10 mL) taken in a borosil beaker (100 mL), a catalytic quantity of sodium hydroxide (1–2 pellets) was added and

the reaction mixture was put outside at room temperature to evaporate ethanol and the remaining mixture was placed inside a microwave oven for 50 seconds and then cooled in an ice bath and the product formed was filtered, washed with ethanol (5 mL) followed by distilled water till the washings were neutral, dried and crystallised from ethanol.

Preparation of 1-acetyl-3-(*p*-methoxyphenyl)-5-(2′,4′-dichlorophenyl)-2-pyrazoline

To a mixture of *p*-methoxy chalcone (0.01 mol) and 99 per cent hydrazine hydrate (0.015 mol) taken in a borosil beaker (100 mL), a glacial acetic acid (10 mL) was added and the reaction mixture was placed inside a microwave oven for 160 seconds. The mixture was then concentrated and cooled. The resulting solid was filtered, washed with distilled water, dried and crystallized from ethanol.

Preparation of 1-(substituted chalcone)-3-(*p*-methoxyphenyl)-5-(2′,4′-dichlorophenyl)-2-pyrazoline [1(a–j)]

To a solution of 1-acetyl-3-(*p*-methoxy phenyl)-5-(2′,4′-dichlorophenyl)-2-pyrazoline (0.01 mol) and substituted aldehyde (0.01 mol) in dry ethanol (10 mL) taken in a borosil beaker (100 mL), a catalytic quantity of sodium hydroxide (1–2 pellets) was added and the reaction mixture was put outside at room temperature to evaporate ethanol and the remaining mixture was placed inside a microwave oven for 45–50 seconds and then cooled in an ice bath and the product formed was filtered, washed with ethanol (5 mL) followed by distilled water till the washings were neutral, dried and crystallized from ethanol.

IR (cm^{-1}) (KBr): 3100–3000 ν(C—H); 2835–2815 ν(O—CH_3); 1705–1680 ν(C=O); 1680–1615 ν(C=C); 1620–1590 ν(C=N); 750–700 ν(C—Cl).

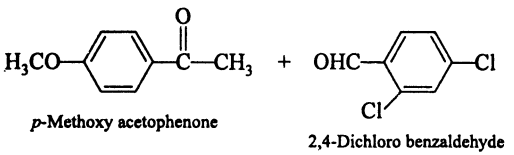
Preparation of 1-[1′-H-6′-aryl-pyrimidine-2′-thione]-3 [*p*-methoxy phenyl]-5-[2″,4″-dichloro phenyl]-2-pyrazoline [2(a–j)]

A mixture of 1-substituted chalcone-3-(*p*-methoxy phenyl)-5-(2′,4′-dichloro phenyl)-2-pyrazoline (0.001 mol), thiourea (0.001 mol) and dil. HCl (20 mL) in ethanol (10 mL) was put outside at room temperature to evaporate ethanol and the remaining mixture was placed inside a microwave oven for 55–60 seconds. The reaction was carried out in borosil beaker under microwave irradiation in microwave oven. The reaction mixture was then filtered while hot, allowed to cool and neutralized with NaOH. The resulting solid was washed several times with distilled water, dried and crystallized from ethanol.

IR (cm^{-1}) (KBr): 3350–3310 ν(N—H); 2835–2815 ν(O—CH_3); 1620–1590 ν(C=N); 1200–1050 ν(C=S); 750–700 ν(C—Cl)

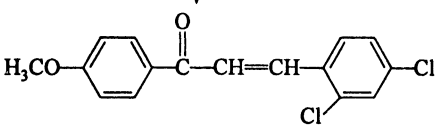
All melting points were taken in open capillary tubes and are uncorrected. IR spectra were recorded on a Perkin-Elmer spectrophotometer. All the compounds gave satisfactory elemental analysis.

Physical and Analytical data of compounds **1[a–j]** and **2[a–j]** are presented in Table-1.



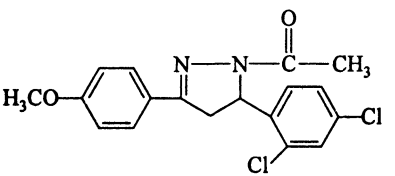
p-Methoxy acetophenone + 2,4-Dichloro benzaldehyde

Microwave irradiation
Ethanol
NaOH [1-2 pellets]



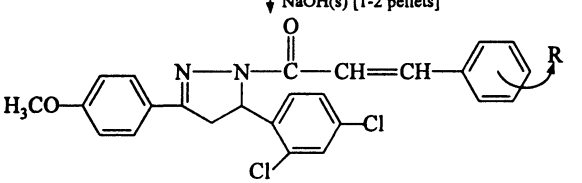
p-Methoxy chalcone

Microwave irradiation
$NH_2 \cdot NH_2 \cdot H_2O$
Glacial CH_3COOH



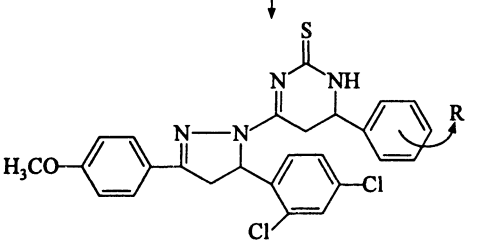
1-acetyl-3-[*p*-methoxyphenyl]-5-[2′,4′-dichlorophenyl]-2-pyrazoline

Microwave irradiation
OHC–R
Ethanol
NaOH(s) [1-2 pellets]



1-(substituted chalcone)-3-[*p*-methoxyphenyl]-5-[2′,4′-dichlorophenyl]-2-pyrazoline[1(a-j)]

Microwave irradiation
Ethanol
Thiourea
dil. HCl



1-[1′-H-6′-aryl-pyrimidine-2′-thione]-3-[*p*-methoxyphenyl]-5-[2″,4″-dichlorphenyl]-2-pyrazoline. [2(a-j)]

R = (a) phenyl (b) 2-nitrophenyl (c) 3-nitrophenyl (d) 4-bromophenyl (e) 2-chlorophenyl (f) 2,4-dichlorophenyl (g) 4-N,N′-dimethylaminophenyl (h) 3-hydroxy-4-methoxyphenyl (i) 4-methoxyphenyl (j) 3,4,5-trimethoxyphenyl

TABLE-1
PHYSICAL AND ANALYTICAL DATA OF COMPOUNDS **1[a–j]** and **2[a–j]**

Compd. No.	R	m.f.	m.w. (g/m)	m.p. (°C)	Yield (%)	C %		H %		N %	
						Found	Req.	Found	Req.	Found	Req.
1 a	phenyl	$C_{25}H_{19}N_2O_2Cl_2$	450	140	70	66.64	66.67	4.19	4.22	6.19	6.22
b	2-nitrophenyl	$C_{25}H_{18}N_3O_4Cl_2$	495	145	65	60.58	60.60	3.61	3.64	8.46	8.48
c	3-nitrophenyl	$C_{25}H_{18}N_3O_4Cl_2$	495	147	70	60.57	60.60	3.61	3.64	8.45	8.48
d	4-bromophenyl	$C_{25}H_{18}N_2O_2Cl_2Br$	529	155	68	56.69	56.71	3.37	3.40	5.26	5.29
e	2-chlorophenyl	$C_{25}H_{18}N_2O_2Cl_3$	484.5	160	65	61.89	61.92	3.69	3.72	5.76	5.78
f	2,4-dichlorophenyl	$C_{25}H_{17}N_2O_2Cl_4$	519	143	65	57.77	57.80	3.25	3.28	5.36	5.39
g	4-N,N-dimethylaminophenyl	$C_{27}H_{24}N_2O_2Cl_2$	493	130	70	65.59	65.72	4.84	4.87	8.49	8.52
h	3-hydroxy-4-methoxyphenyl	$C_{26}H_{21}N_2O_4Cl_2$	496	138	75	62.88	62.90	4.21	4.23	5.62	5.65
i	4-methoxyphenyl	$C_{26}H_{21}N_2O_3Cl_2$	480	152	63	64.97	65.00	4.36	4.38	5.80	5.83
j	3,4,5-trimethoxyphenyl	$C_{28}H_{25}N_2O_5Cl_2$	540	157	65	62.19	62.22	4.61	4.63	5.16	5.19
2 a	phenyl	$C_{26}H_{20}N_4OSCl_2$	507	125	68	61.51	61.54	3.92	3.94	11.02	11.05
b	2-nitrophenyl	$C_{26}H_{19}N_5O_3SCl_2$	552	155	65	56.49	56.52	3.42	3.44	12.65	12.68
c	3-nitrophenyl	$C_{26}H_{19}N_5O_3SCl_2$	552	157	70	56.49	56.52	3.41	3.44	12.66	12.68
d	4-bromophenyl	$C_{26}H_{19}N_4OSCl_2Br$	586	140	60	53.21	53.24	3.22	3.24	9.53	9.56
e	2-chlorophenyl	$C_{26}H_{19}N_4OSCl_3$	541.5	144	63	57.59	57.62	3.49	3.51	10.32	10.34
f	2,4-dichlorophenyl	$C_{26}H_{18}N_4OSCl_4$	576	152	60	54.14	54.17	3.11	3.13	12.12	12.15
g	4-N,N-dimethylaminophenyl	$C_{28}H_{25}N_5OSCl_2$	550	148	75	61.06	61.09	4.52	4.55	12.71	12.73
h	3-hydroxy-4-methoxyphenyl	$C_{27}H_{22}N_4O_3SCl_2$	553	145	65	58.55	58.59	3.95	3.98	10.10	10.13
i	4-methoxyphenyl	$C_{27}H_{22}N_4O_2SCl_2$	537	150	58	60.31	60.34	4.08	4.10	10.40	10.43
j	3,4,5-trimethoxy phenyl	$C_{29}H_{26}N_4O_4SCl_2$	597	143	65	58.27	58.29	4.33	4.36	9.36	9.38

Antibacterial Activity

Antibacterial screening of synthesized compounds was carried out by cup-plate method[11] using a species of gram positive bacteria *S. aureus* and gram negative bacteria *E coli.* The testing was carried out using 50 μg of sample in DMF. Antibacterial data of compounds **1[a–j]** and **2[a–j]** are presented in Table-2.

RESULTS AND DISCUSSION

From Table-2, it is clear that in case of *Staphylococcus aureus*, the maximum activities were found in compounds **1 (d), 1 (j), 2 (a), 2 (h)** (Zone of inhibition 10.0 mm) and **2 (d), 2 (i)** (zone of inhibition 13.0 mm) and minimum activities were found in compounds **1 (b), 1 (d), 1 (f), 2 (b)** (zone of inhibition 6.0 mm).

In case of *Escherichia coli*, the maximum activities were found in compounds **1 (c), 2 (f), 2 (j)** (zone of inhibition –10.0 mm) and **2 (d), 2 (i)** (zone of inhibition –13.0 mm) and minimum activities were found in compounds **1 (b), 1 (d), 1 (f), 2 (b)** (zone of inhibition –6.0 mm).

The antibacterial activities of synthesized compounds were compared with known antibiotics like ampicillin, penicillin and tetracycline. All the compounds show moderate to good activity.

TABLE-2
ANTIBACTERIAL DATA OF COMPOUNDS **1[a–j]** and **2[a–j]**

Compd. no.	R	Zone of inhibition (mm)	
		Staphylococcus aureus	*Escherichia coli*
1a	phenyl	6.0	8.0
b	2-nitrophenyl	8.0	6.0
c	3-nitrophenyl	6.0	10.0
d	4-bromophenyl	9.0	6.0
e	2-chlorophenyl	8.0	8.0
f	2,4-dichlorophenyl	7.0	6.0
g	4-N,N′-dimethylaminophenyl	8.0	7.0
h	3-hydroxy-4-methoxyphenyl	7.0	7.0
i	4-methoxyphenyl	7.0	8.0
j	3,4,5-trimethoxyphenyl	9.0	7.0
2a	phenyl	9.0	8.0
b	2-nitrophenyl	8.0	6.0
c	3-nitrophenyl	6.0	9.0
d	4-bromophenyl	8.0	13.0
e	2-chlorophenyl	6.0	7.0
f	2,4-dichlorophenyl	7.0	10.0
g	4-N,N′-dimethylaminophenyl	6.0	9.0
h	3-hydroxy-4-methoxyphenyl	9.0	8.0
i	4-methoxyphenyl	8.0	13.0
j	3,4,5-trimethoxyphenyl	8.0	10.0

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