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Synthesis and Antibacterial Activity of Some Novel Chalcones and Pyrimidine-2-one Derivatives

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Some novel chalcone derivatives have been prepared by condensation of aryl aldehyde and 2-hydroxy 3-chloro 5-ethyl acetophenone in alkaline ethanol while pyrimidine-2-one derivatives have been prepared by the condensation of chalcone and urea. Characterization and structural elucidation have been done on the basis of chemical, analytical and spectral analysis. The antibacterial activity of compounds has also been screened.

Key Words: Synthesis, Antibacterial activity, Chalcone and pyrimidine-2-one derivatives.

INTRODUCTION

Due to their wide spectrum biological properties[1], in the present age of pharmacogenetics, chalcones have been given considerable interest owing to their antifungal/antihistaminic[3], antimalarial[4] and anticancer[5] properties. Extensive work on synthesis of chalcones has been done by various routes. Pyrimidines and their derivatives are considered to be important for drugs and agricultural chemicals. Pyrimidine derivatives possess several interesting biological activities such as antimicrobial[7], antitumour[8] and antifungal activities[9]. The present investigation describes the synthesis of some novel chalcones derived from 2-hydroxy 3-chloro 5-ethyl acetophenone[6] and pyrimidine-2-one derivatives.

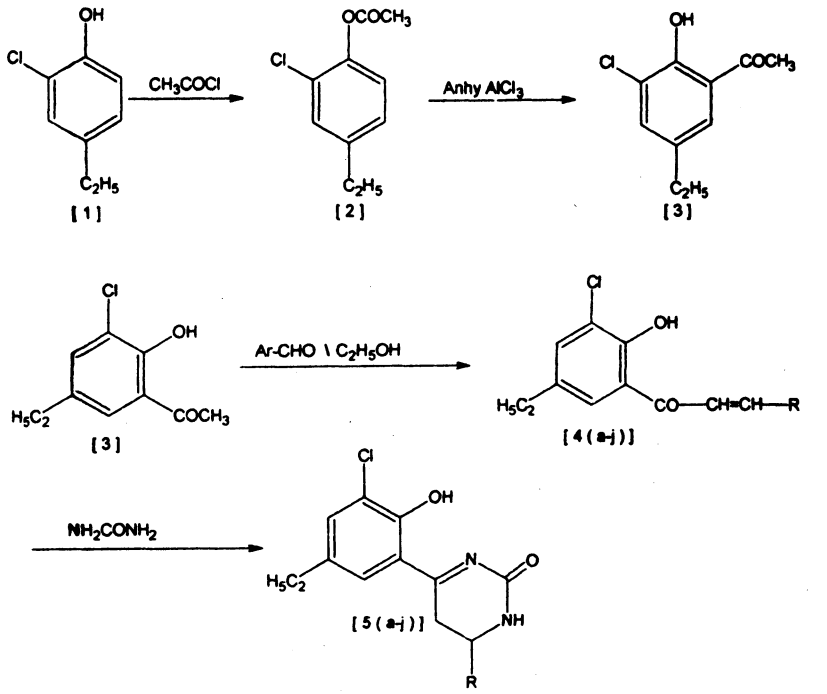
EXPERIMENTAL

All the melting points were determined on a PMP-DM Scientific melting point apparatus and are uncorrected. The purity of compounds was checked by TLC on silica gel-G coated glass plates. IR spectra were recorded with KBr on Perkin-Elmer-377 spectrophotometer, ^{1}H NMR spectra on a Brucker DRX-300 in $CDCl_3$ at 200 MHz using TMS as an internal standard.

Preparation of 2-hydroxy 3-chloro 5-ethyl acetophenone

2-Chloro 4-ethyl phenol (1) and acetyl chloride are refluxed in a water bath in presence of pyridine for 4 h, yielding 2-chloro 4-ethyl phenyl acetate (2). This

on fumigation with anhydrous $AlCl_3$ in an oil bath for 4 h with air condenser gives 2-hydroxy 3-chloro 5-ethyl acetophenone (3). Then the reaction mixture is decomposed over crushed ice and concentrated HCl. The solid separated is collected and crystallized from ethanol to yield dark brown coloured needles.



Scheme-1

m.f. $C_{10}H_{11}ClO_2$; % composition: required (found): C, 60.46 (60.42); H, 5.58 (5.52); Cl, 17.85 (17.82); O, 16.11 (16.08); yield 70%; m.p. 42°C.

^1H NMR: 9.2 (1H, s, —OH), 4.02 (3H, s, —$COCH_3$), 4.60 (2H, s, —CH_2), 1.96 (3H, s, —CH_3), 7.12–7.28 (2H, m, Ar—H).

The oxime of 2-hydroxy 3-chloro 5-ethyl acetophenone (3) is prepared by sodium acetate method. The m.p. of oxime is 111°C.

Preparation of 2-hydroxy 3-chloro 5-ethyl chalcone [4(a–h)]

A mixture of 2-hydroxy 3-chloro 5-ethyl acetophenone (1) (0.01 mol) and aryl aldehyde (0.01 mol) is stirred in ethanol (30 mL) and then an aqueous solution of KOH (40%, 15 mL) added to it. The mixture is kept overnight at room temperature. The colour of the mixture changes from yellow to orange. The content is then poured into crushed ice and acidified with HCl. The solid separated is filtered and crystallized from ethanol.

Following the same procedure, all the compounds of this series were prepared. Their characterization data are recorded in Table-1.

TABLE-1
CHARACTERIZATION DATA OF COMPOUNDS [4 (a–j)]

Compd.	R	m.p. (°C)	Yield (%)	m.f. (m.w.)	Found (Calcd.) (%)		
					C	H	N
4a	phenyl	110	75	$C_{17}H_{15}O_2Cl$ (286.75)	71.20 (71.26)	5.27 (5.22)	11.16 (11.19)
4b	4-chloro phenyl	138	70	$C_{17}H_{14}O_2Cl_2$ (321.19)	63.57 (63.53)	4.39 (4.34)	9.96 (9.94)
4c	2,4-dichloro phenyl	158	72	$C_{17}H_{13}O_2Cl_3$ (355.64)	57.41 (57.45)	3.68 (3.66)	9.00 (9.05)
4d	2-hydroxy phenyl	123	75	$C_{17}H_{15}O_3Cl$ (302.75)	67.44 (67.41)	4.99 (4.96)	15.85 (15.89)
4e	4-hydroxy phenyl	125	78	$C_{17}H_{15}O_3C$ (302.75)	67.44 (67.46)	4.99 (4.97)	15.85 (15.82)
4f	4-methyl phenyl	118	65	$C_{18}H_{17}O_2Cl$ (300.77)	71.88 (71.86)	5.70 (5.73)	10 64 (10.66)
4g	3-nitro phenyl	165	68	$C_{17}H_{14}NO_4Cl$ (331.75)	61.55 (61.58)	4.25 (4.22)	19.29 (19.27)
4h	2-methoxy phenyl	142	71	$C_{18}H_{17}O_3Cl$ (316.77)	68.25 (68.21)	5.41 (5.43)	15.15 (15.11)
4i	4-methoxy phenyl	154	75	$C_{18}H_{17}O_3Cl$ (316.77)	68.25 (68.29)	5.41 (5.46)	15.15 (15.17)
4j	4-N,N-dimethyl amino phenyl	170	70	$C_{19}H_{20}NO_2Cl$ (329.82)	69.19 (69.17)	6.11 (6.16)	9.70 (9.72)

Preparation of 1,2,5,6-tetrahydro-4-(2′-hyproxy-3′-chloro-5′-ethyl phen-1′-yl]-6-substituted phenyl-2-pyrimidinones [5(a–i)]

A mixture of 2-hydroxy 3-chloro 5-ethyl chalcone (4) (0.01 mol) in methanol was taken, urea (0.01 mol) and concentrated HCl as catalyst were added. The reaction mixture was refluxed for about 6 h and then poured into ice-cold water. The solid product formed was filtered and dried, and then recrystallised from ethanol.

Following the same procedure, all the compounds of this series are prepared. Their characterization data are recorded in Table-2.

TABLE-2
CHARACTERIZATION DATA OF COMPOUNDS [5(a–j)]

Compd.	R	m.p. (°C)	Yield (%)	m.f. (m.w.)	Found (Calcd.) (%)		
					C	H	N
4a	phenyl	155	68	$C_{18}H_{17}N_2O_2Cl$ (328.79)	65.75 (65.79)	5.21 (5.23)	8.52 (8.56)
4b	4-chloro phenyl	185	60	$C_{18}H_{16}N_2O_2Cl_2$ (363.23)	59.52 (59.55)	4.44 (4.46)	7.71 (7.76)
4c	2,4-dichloro phenyl	169	65	$C_{18}H_{15}N_2O_2Cl_3$ (397.68)	54.36 (5431)	3.80 (3.84)	7.04 (7.06)
4d	2-hydroxy phenyl	162	65	$C_{18}H_{17}N_2O_3Cl$ (344.79)	62.70 (62.75)	4.97 (4.99)	8.12 (816)
4e	4-hydroxy phenyl	161	60	$C_{18}H_{17}N_2O_3Cl$ (344.79)	62.70 (62.72)	4.97 (4.94)	8.12 (8.15)
4f	4-methyl phenyl	178	62	$C_{19}H_{19}N_2O_2Cl$ (342.81)	66.57 (66.59)	5.59 (5.53)	8.17 (8.19)
4g	3-nitro phenyl	212	70	$C_{18}H_{16}N_3O_4Cl$ (373.79)	57.84 (57.86)	4.31 (4.33)	11.24 (11.27)
4h	2-methoxy phenyl	173	58	$C_{19}H_{19}N_2O_3Cl$ (358.81)	63.60 (63.56)	5.34 (5.31)	7.81 (7.85)
4i	4-methoxy phenyl	177	60	$C_{19}H_{19}N_2O_3Cl$ (358.81)	63.60 (63.64)	5.34 (5.36)	7.81 (7.83)
4j	4-N,N-dimethyl amino phenyl	198	65	$C_{20}H_{22}N_3O_2Cl$ (371.86)	64.60 (64.63)	5.96 (5.98)	11.30 (11.34)

TABLE-3
IR, ^{1}H NMR SPECTRAL DATA OF COMPOUNDS 4 AND 5

Compd.	IR (cm^{-1}) (KBr)	^{1}H NMR ($CDCl_3$) (δ ppm)
4c	850 (—C—Cl), 3046 (—OH), 1716 (—C=O), 1637(—CH=CH)	9.1 (1H, s, —OH), 4.66 (2H, s, —CH_2), 1.95 (3H, s, —CH_3), 5.98 (1H, d, —COCH), 8.40 (IH, d, =CH—Ar), 7.00–7.23 (6H, m, Ar—H)
4e	842 (—C—Cl), 3041 (—OH), 1618 (—C=O), 1635 (—CH=CH)	9.5 (2H, s, —OH), 4.68 (2H, s, —CH_2), 1.91 (3H, s, —CH_3), 5.92 (IH, d, —COCH), 8.38 (1H, d, =CH—Ar), 7.18–7.41 (6H, m, Ar—H)
5f	835 (—C—Cl), 3053 (—OH), 1718(—C=O), 1652 (C=N), 3367 (—NH), 1312 (—CH_3)	9.8 (1H, s, —OH), 4.62 (4H, s, —CH_2), 5.46 (1H, s, —NH), 1.98 (6H, s, —CH_3, 7.11–7.39 (6H, m, Ar—H)
5j	853 (—C—Cl), 3050 (—OH), 1715 (—C=O), 1655 (C=N), 3361 (—NH),1315(—$N(CH_3)_2$)	9.3 (1H, s, —OH), 4.68 (4H, s, —CH_2), 5.41 (1H, s, —NH), 1.95 (3H, s, —CH_3), 7.18–7.46 (6H, m, Ar—H), 1.47(6H, s, —$N(CH_3)_2$)

Antibacterial activity

The synthesized compounds were tested for their antibacterial activity by measuring the zone of inhibition on agar plates (cup-plate method) with *Staphylococcus aureus* and *Escherichia coli* as test organisms.

TABLE-4
ZONE OF INHIBITION OF COMPOUNDS 4 AND 5 (mm)

No.	*S. aureus*	*E. coli*	No.	*S. aureus*	*E. coli*
4a	+++	++++	5a	+++	+++
4b	+++	++++	5b	+++	+++
4c	+++	++	5c	++++	+++
4d	++	+++	5d	+++	++
4e	+++	+++	5e	++++	+++
4f	++++	+++	5f	+++	+++
4g	+++	++	5g	+++	+++
4h	+++	+++	5h	++	+++
4i	++++	++	5i	+++	++
4j	++++	++	5j	+++	+++
Zone of inhibition of standard drugs (mm)					
	Tetracycline			+++++	-
	Gentamycine			-	+++++

++ = 5 to 7 mm, +++ = 8 to 10 mm, ++++ = 11 to 13 m, +++++ = 18 to 21 mm.

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REFERENCES

1. V.R. Naik and H.B. Naik, *Asian J. Chem.*, 12, 305 (1999).
2. Z.H. Khalil, A.S. Yanni, A.A. Abdel-Hafeez and A.A. Khalaf, *J. Indian Chem Soc.*, 67, 821 (1990).
3. H.L. Friedman and A.V. Tolstouhov, U.S. Patent 2,425,865 (1949).
4. G.B. Barlin, B. Kotecha and K.H. Reichman, *Aust. J. Chem.*, 49, 647 (1996).
5. K. Wakabayashi, M. Kochi and M. Fuji, *Chem. Abstr.*, 123, 217821m (1993).
6. P.B. Heda and B.J. Ghiya, *Asian J. Chem.*, 11, 591 (1999).
7. B.K. Karale and C.H. Gill, *Indian J. Chem.*, 41B, 1957 (2002).
8. V.M. Reddy and Rama G.V.S. Sarma, *Indian J. Heterocycl. Chem.*, 3, 111 (1993).
9. M.S. Shingare, B.K. Karale, C.H. Gil, K.N. Gange and M.T. Bachute, *Indian J. Heterocycl. Chem.*, 9, 153 (1999).

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