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Synthesis of Acetophenone Chalcone Derivatives And their Antibacterial Activity

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ABSTRACT

Chalcones[1] are the important constituent of many natural sources and have variety of biological activities. The compounds are synthesized by Claisen- Schmidt base catalyzed condensation of acetophenone with aldehyde. The structures of the synthesized compounds were confirmed by IR, 1H NMR spectroscopic data. The antimicrobial activities of these compounds were evaluated by filter paper disc diffusion method.

Keywords: Chalcones, Thiazines, Oxazines, Acetophenone, Aldehyde.

INTRODUCTION

1,3-Diphenyl-2-propene-1-one is commonly called as Chalcone. Chalcones belongs to the flavonoid family[2]. These are bi-chromophoric molecules, separated by a keto-vinyl chain. Chalcone (and related compounds "chalconoids") is an aromatic *α,β*-unsaturated ketone that forms the central core for variety of biological compounds[3]. Due to the presence of reactive α, β-unsaturated ketone, it shows various pharmacological activities.

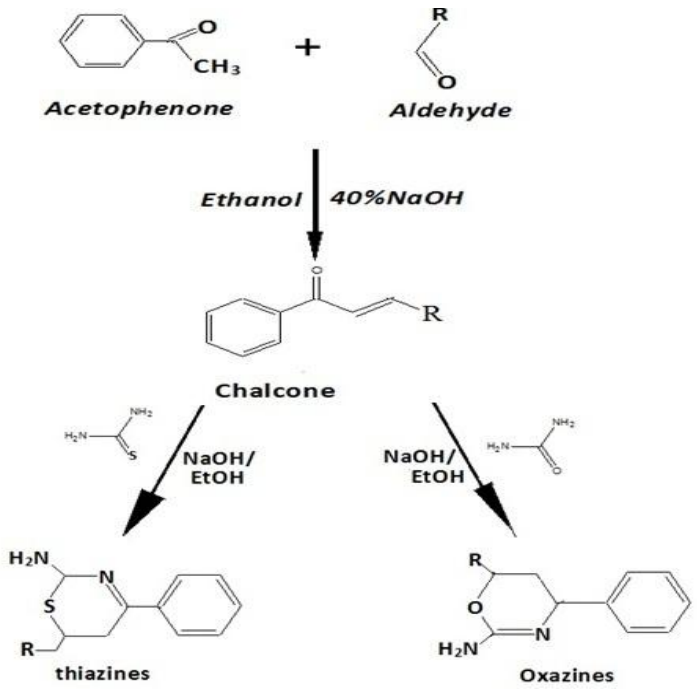
Chalcones are one of the major class of natural products with wide spread distribution in species, tea, beer, fruits, vegetables and various plant products. These are the precursor compounds in flavonoid biosynthesis in plants. In recent times, these compounds are of great interest for their pharmacological activities such as antihepatotoxic activity, antitumour activity, antitubercular activity[4], antidiabetic activity, antimalarial activity[5], antiinflammatory activity[6], antibacterial activity[7], antifungal activity[8] and antioxidative activity[9].

MATERIALS AND METHODS

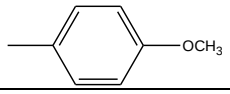
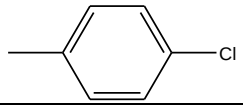
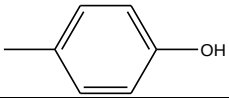
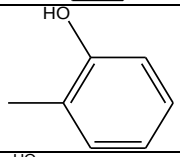
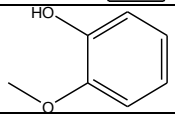
All the products were synthesized and characterized by their spectral analysis. Melting points were determined in an open capillary tube and or uncorrected. IR spectra were recorded in KBr on a JASCO FT/IR-5300. ^{1}H NMR spectra were recorded on Brucker spectrometer at 300MHz in $CdCl_3$(900W). Chalcones were synthesized by aldol condensation using NaOH/ EtOH. The chemicals and solvents used were of laboratory grade and were purified. The completion of the reactions were monitored by thin layer

chromatography of silica gel-G (Merck, Germany) using iodine vapor chamber for detection. The synthetic pathway is presented in scheme and physicochemical data and spectroscopic data for the synthesized compounds are given in tables.

Experimental:



Scheme For Synthesis

COMPOUNDS	R
Ai, Bi, Ci	
Aii, Bii, Cii	
Aiii, Biii, Ciii	
Aiv, Biv, Civ	
Av, Bv, Cv	

CHALCONES → **Ai, Aii, Aiii, Aiv, Av**
Bi, Bii, Biii, Biv, Bv → **THIAZINE DERIVATIVES**
Ci, Cii, Ciii, Civ, Cv → **OXAZINE DERIVATIVES**

Synthesis of Chalcone : Equimolar concentration of acetophenone (0.01mol) and substituted benzaldehydes (0.01mol) were dissolved in 20 ml of methanol. To it, a little amount of freshly prepared 40% sodium hydroxide solution was added (which acts as catalyst). The reaction mixture was kept undisturbed for 24 h. The mixture was then acidified with 1:1 hydrochloric acid and water. Then it was filtered through vacuum, washed with water, dried and recrystallized using methanol.

Synthesis of Thiazine / Oxazine Derivatives: A mixture of chalcone (0.02mol), thiourea/urea (0.02 mol) were dissolved in ethanolic sodium hydroxide (10ml), stirred about 2-3 h with a magnetic stirrer. This was then poured into 400 ml of cold water with continuous stirring for an hour and then kept in refrigerator for 24 h. The precipitate obtained was filtered, washed, dried and recrystallized. The completion of the reaction was monitored by TLC.

Table 1 . Characterization Data of Synthesized Compounds

S. No	SUBSTITUENT	M.P. (°C)	YIELD (%)	R_f	Molecular Formula	Nature
Ai	-C_6H_7O	129	85	0.95	$C_{16}H_{14}O_2$	Yellowish green colour
Bi	-C_6H_7O	127	50	0.83	$C_{18}H_{16}N_2OS^+$	Pale yellow colour powder
Ci	-C_6H_7O	135	60	0.85	$C_{18}H_{16}N_2O_2$	Yellow colour powder
Aii	-C_6H4Cl	125	92	0.95	$C_{15}H_{11}OCl$	Yellowish green colour powder
Bii	-C_6H4Cl	129	65	0.88	$C_{17}H_{13}N_2ClS^+$	Cream colour powder
Cii	-C_6H4Cl	130	71	0.87	$C_{17}H_{13}N_2OCl$	Pale biscuit colour powder
Aiii	-C_6H5O	195	75	0.85	$C_{15}H_{12}0_2$	Dark Brown colour powder
Biii	-C_6H5O	190	45	0.91	$C_{17}H_{14}N_2OS^+$	Cream colour Powder
Ciii	-C_6H5O	195	44	0.81	$C_{17}H_{14}N_2O_2$	Brown colour powder
Aiv	-C_6H5O	194	85	0.92	$C_{15}H_{12}O_2$	Orange red colour powder
Biv	-C_6H5O	194	72	0.89	$C_{17}H_{14}N_2OS^+$	Dark orange colour powder
Civ	-C_6H5O	187	56	0.89	$C_{17}H_{14}N_2O_2$	Pale orange colour powder

Av	$-C_5H_4O_2$	240	90	0.92	$C_{16}H_{14}O_3$	Dark violet colour powder
Bv	$-C_5H_4O_2$	250	59	0.90	$C_{18}H_{16}N_2O_2S^+$	Orange red colour powder
Cv	$-C_5H_4O_2$	270	40	0.84	$C_{18}H_{16}N_2O_3$	Red colour powder

Table 2. Spectral Data of the Synthesized Compounds

S. No.	Compound	I R (cm^{-1}, KBr)	^1H NMR (δ, ppm)	M^+ Ion (m/z)
1	**Bi**	3417 N-H (Stretching) 1219 C-N (Stretching) 1255 C-O (Stretching) 1663 C=C (Stretching) 1091 C-C (Stretching)	3.648 (1H, S, CH-NH_2) 6.78 – 6.82 (1H,d, Ar-OCH_3) 7.26 – 7.27 (5H,m,2',3',4',5',6',Ar-H)	----
2	**Bii**	3312 N-H (Stretching) 1239 C-N (Stretching) 1673 C=C (Stretching) 1096 C-C (Stretching)	7.26 – 7.27 (4H,m,2',3',5',6',Ar-H) 7.48 – 7.52 (5H,m,2',3',4',5',6',Ar-H)	317.1
3	**Cii**	3380 N-H (Stretching) 1236 C-N (Stretching) 1672 C=C (Stretching) 1090 C-C (Stretching) 1236 C-O (Stretching)	3.314 (1H, S, CH-NH_2) 7.15 – 7.19 (4H,m,2',3',5',6',Ar-H) 7.41 – 7.43 (5H,m,2',3',4',5',6',Ar-H)	----

RESULTS AND DISCUSSION

The yield of the compounds $\mathbf{A_i}$, $\mathbf{A_{ii}}$, $\mathbf{A_{iv}}$, $\mathbf{A_v}$ is high. The yield of the compounds $\mathbf{B_i}$, $\mathbf{B_{iii}}$, $\mathbf{C_{iii}}$, $\mathbf{C_{iv}}$, $\mathbf{C_v}$ is low. All the chalcones and their thiazine derivatives were easily recrystallized than oxazine derivatives of chalcones.

On the basis of the results obtained from the antibacterial activity, the following generalization could be made. The compounds $\mathbf{C_i}$, $\mathbf{B_{ii}}$, $\mathbf{C_{ii}}$, $\mathbf{B_v}$ showed weak antibacterial activity at a concentration of 10 µg/ml. The other compounds did not show the activity against *P. aeruginosa*.

APPLICATIONS

Anti Bacterial Activity: All the synthesized thiazine and oxazines derivatives of chalcones were screened for their invitro antibacterial activity at concentration of 10 µg/ml in chloroform against gram negative *Pseudomonas aeruginosa*[10,11] bacteria by the paper disc diffusion method. The zone of inhibition was measured in milli meters after 24 h of incubation at 37ºC. Ampicillin was used as standard drug and the chloroform was used as the solvent.

Table 3. Antibacterial Activity

Compounds	Zone of inhibition in mm for 10µg/ml concentration
	Pseudomonas aeruginosa
Ai	2.6mm
Bi	2.3 mm
Ci	4.3 mm

Aii	2.3 mm
Bii	5.0 mm
Cii	4.0 mm
Aiii	2.0 mm
Biii	2.1 mm
Ciii	2.4 mm
Aiv	2.8 mm
Biv	2.0 mm
Civ	2.3 mm
Av	2.9 mm
Bv	5.0 mm
Cv	2.4 mm

Compounds	**Zone of inhibition in mm for 10 µg ml^{-1} concentration**
	Pseudomonas aeruginosa
Standard (Ampicillin)	12.0 mm
Control (Chloroform)	2.0 mm

CONCLUSIONS

Some of the compounds, which were synthesised, showed weak antibacterial activity at 10 µg ml^{-1} concentration. These compounds may show more antibacterial activity at high concentrations. Substituting para and ortho positions of benzene ring with electronegative groups in acetophenone, chalcones and their derivatives may give better antibacterial activity.

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