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SYNTHESIS AND ANTIBACTERIAL ACTIVITY OF SOME NEW QUINOXALINYL CHALCONE DERIVATIVES

Dr. Sunil M. Naik
Department of Chemistry, Naran Lala College of Professional & Applied Sciences, Navsari
Email: sunilnaik669@gmail.com

ABSTRACT

Chalcones represent an essential group of natural as well as synthetic products and some of them have wide range of pharmacological activity such as anti-inflammatory, anti-fungal, antibacterial and anti-oxidnt agents. Some new 1,4-quinoxaline derivatives were synthesized from chalcones derivatives by condensation of various chalcones with benzene-1,2-diamine in methanol. All these derivatives have been screened for antibacterial activity and characterized by spectral studies.

Keywords: 4-Fluoroacetophenone, Substituted aldehyde, Chalcones, benzene-1,2-diamine, Antibacterial activity, IR/NMR Spectroscopy.

INTRODUCTION

Various chalcones derivatives can be obtained by the condensation of aryl ketone with the various substituted aldehyde in the presence of aqueous alcoholic alkali[1,2,3]. Chalcone and its related hetero cyclic derivatives such as oxazine, pyrazole, isoxazole, thiazine, pyrimidine, benzthiazepine, quinoxaline etc., shows antibacterial activity against various gram positive and gram negative bacteria[4-11]. We report the reaction of 4-Fluoroacetophenone with various substituted aromatic aldehydes to produced corresponding 4'-Fluoro chalcones [A-J], which on treatment with benzene-1,2-diamine in methanol give the corresponding derivatives of 1,4-quinoxaline derivatives[A" – J"]. The constitutions of all the synthesized compounds were characterized by elemental analysis, IR and H1 NMR spectral study. Compounds were also evaluated for antibacterial activity.

MATERIAL AND METHODS

All melting points were taken in open capillary tubes and are uncorrected. IR spectra in KBr were recorded on perkin-Elmer-377 spectrophotometer and H^1 NMR spectra were recorded on Varian NMR spectrophotometer. All compounds gave satisfactory elemental analysis.

General method for the synthesis of 4'-Flouro chalcones[A-J]

A mixture of 4-Fluoroacetophenone (0.01 mole) and aryl aldehyde (0.01 mole) in ethanol (30 ml) was stirred and to it excess of 40% potassium hydroxide (25 ml) solution was added. The mixture was kept overnight at room temperature. The colour of the reaction mixture was change from yellow to orange. The content was then poured over crushed ice and acidified with hydrochloric acid (1:1). The solid separated was filtered, washed with distilled water, dried and crystallized from ethanol, yield 60-70%.

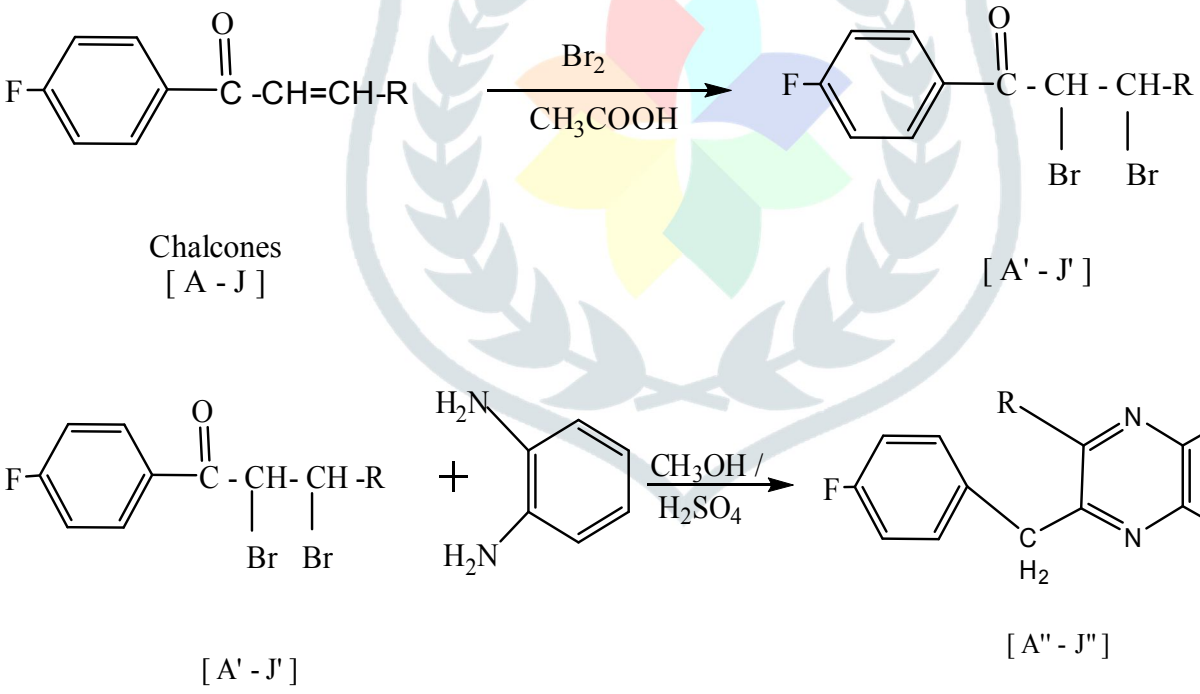
General method for the synthesis of 4'-Fluoro-α,β-dibromo chalcones[A'-J']

4'-Fluoro chalcone[A-J] (0.01 mol) was dissolved in acetic acid (30 ml) and bromine in acetic acid (2 ml, 10%), was slowly added to it. The reaction mixture is kept for 4 hours in water bath at room temperature. Then it was treated with ice-water. The solid separated was filtered, washed with sodium thiosulphate solution and then with water, dried and crystallized from absolute alcohol, yield 50-60%

General methods for the synthesis of 2-(4'-Fluoro)-benzyl-3-(substitutedphenyl)-1,4-quinoxaline[A"-J"]

A mixture of 4'-Fluoro-α,β-dibromo chalcones[A'-J'] (0.01 mol) and benzene-1,2-diamine (0.01 mol), was taken in methanol (25 ml). A few drops of conc. Sulphuric acid was added and the reaction mixture was heted on water-bath at 60-70°C for 30 minutes. It was then diluted with water and was extracted with solvent ether to remove insoluble benzene-1,2-diamine. Ether was then evaporated and solid residue was crystallized from ethanol, yield 50-60%.

REACTION SCHEME



Where R = 4-chlorophenyl, 4-hydroxyphenyl, Phenyl, 2,4-dichlorophenyl, 3-phenoxyphenyl, 2,6-dichlorophenyl, 3-nitrophenyl, 3,4,5-trimethoxyphenyl, 4-methoxyphenyl, 4-N,N-dimethylaminophenyl.

SCHEME

TABLE- 1

Characterization Table of 2-(4'-Fluoro)-benzyl-3-(substitutedphenyl)-1,4-quinoxaline[A"-J"]

Compd. No.	R	Molecular formula	(M. wt.)	Yield (%)	M.P. 0C.
A"	4-chlorophenyl	$C_{21}H_{14}N_2FCl$	348.81	58	145
B"	4-hydroxyphenyl	$C_{21}H_{16}ON_2F$	331.37	64	134
C"	Phenyl	$C_{21}H_{14}N_2F$	313.36	59	140
D"	2,4-dichlorophenyl	$C_{21}H_{14}N_2FCl_2$	384.26	55	122
E"	3-phenoxyphenyl	$C_{27}H_{20}ON_2F$	407.47	54	169
F"	2,6-dichlorophenyl	$C_{21}H_{13}N_2FCl_2$	383.25	57	155
G"	3-nitrophenyl	$C_{21}H_{14}ON_3Br_2$	484.17	49	128
H"	3,4,5-trimethoxyphenyl	$C_{24}H_{21}O_3N_2F$	404.44	51	173
I"	4-methoxyphenyl	$C_{22}H_{17}ON_2F$	344.39	65	139
J"	4-N,N-dimethylaminophenyl	$C_{23}H_{20}N_3F$	357.43	59	117

^{1}H NMR Spectroscopy

Nuclear magnetic resonance (NMR) spectroscopy is one of the latest physical methods which is use for the structure determination of organic compounds. PMR spectra of quinoxaline derivatives were recorded on varian spectrophotometer. Spectra were examined in $CDCl_3$ at room temperature using TMS as internal standard.

TABLE-2

^{1}H NMR spectral data table of 2-(4'-Fluoro)-benzyl-3-(4-methoxyphenyl)-1,4-quinoxaline. (Compound no. I")

Chemical shift	Relative Number of Protones	Assignment
3.86	2	$-CH_2-$
3.82	3	$-OCH_3$
6.72-8.15	12	Ar-H

Infrared spectra

Infrared absorption spectra were recorded using potassium bromide pallets method. The spectra were recorded using "Perkin-Elmer" spectrophotometer. The results are described in table no. 3.

TABLE-3

IR spectra of 2-(4'-Fluoro)-benzyl-3-(4-methoxyphenyl)-1,4-quinoxaline. (Compound no. I")

Position of absorption band (cm^{-1})	Intensity	Band and its mode of vibration	Functional group
1265	S	C-F stretching	Fluoro compound
1030,1250	S	C-O-C stretching	Aromatic ether compound
1295	M	C-N stretching	Compound containing C-N group
1390	Sh	O-H bending	Ar-OH intramolecular
1460	M	C-H bending	-
1595	S	C=N bending	Compound containing C=N group
2980	M	C-H stretching	-
3400	Sh	O-H stretching	Ar-OH group

S=strong, m=medium, b=broad, w=weak, sh=sharp, v=variable

Antibacterial activity:

All the synthesized compounds were tested for their antimicrobial activity against Gram negative bacteria (*Escherichia Coli*) and Gram positive bacteria (*Staphylococcus aureus*) using the agar diffusion method [11]. Each compound was dissolved in DMSO to give concentration 1ppm. The plates were then incubated at 37 0C and examined after 24 hrs. The zones of inhibition formed were measured in millimetre. All the compounds show mild activity against both bacteria in comparison with ampicillin and gentamycin. The results are described in table no. 4.

Table-4

Compound No.	**Zone of inhibition (mm)**	
	***S. aureus* (+ve)**	***E. coli* (-ve)**
A"	**10**	**12**
B"	**11**	**10**
C"	**12**	**09**
D"	**14**	**12**
E"	**10**	**10**
F"	**14**	**16**
G"	**06**	**00**
H"	**09**	**11**
I"	**13**	**14**
J"	**12**	**14**
Standard Drugs: Ampicilin Gentamycin	**18 -**	**21**

RESULTS AND DISCUSSION

From the table no. 4 quinoxaline derivatives have shown poor activity against both organisms as compared to the available routine antimicrobial compounds like Ampicilline and Gentamycin, among the tested compounds no. **F", I"** and **J"** have shown the maximum activity against all the compounds towards gram +ve bacteria and gram negative bacteria i.e. S. aureus and E.coli. Compound no. **C"** and **D"** have shown good activity against E.coli bacteria while the compound no. **G"** is found poor active

against S.aureus and inactive against E.coli bacteria. Rest of the compounds are found poor active against both bacteria S.aureus and E.coli.

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