SYNTHESIS AND ANTIBACTERIAL ACTIVITY OF SOME 1,4-QUINOXALINE DERIVATIVES OF CHALCONES

Dr.S.M. Naik
Department of Chemistry,
NaranLala College of Professional and Applied Sciences, Navsari
Gujarat.

ABSTRACT

Some new 1,4-quinoxaline derivatives were synthesized from chalcones derivatives by condensation of various chalcones with benzene-1,2-diamine in methanol. These all derivatives have been screened for antibacterial activity and characterized by spectral studies.

Keywords:1,4-Quinoxaline,Chlcones,benzene-1,2-diamine, Antibacterial activity, IR/NMR Spectroscopy.

INTRODUCTION

Quinoxalines have been extensively synthesized for their ability to antibiotic, antiviral, anti-carcinogenic and antibacterial and the like medicinal properties. Various chalcones derivatives can be obtained by the condensation of aryl ketone with the various substituted aldehyde in the presence of aqueous alcoholic alkli[1,-3]. Chalcone and its related hetero cyclic derivatives such as oxazine, pyrazole, isoxazole, thiazine, pyrimidine, benzthiazepine, quinoxalineetc shows antibacterial activity against various gram positive and gram negative bacteria[4-8].We report the reaction of 2-hydroxy-5-methyl-4,6-dibromoacetophenone with various substituted aromatic aldehydes to produced corresponding 2'-hydroxy-5'-methyl-4',6'-dibromochalcones[A-J]. Which on treatment withbenzene-1,2-diamine in methanol give the corresponding derivatives of 1,4-quinoxaline derivatives[A"-J"].The constitution of all compounds synthesized was characterized by elemental analysis, IR and H^1 NMR spectral study.Compounds were also evaluated for antibacterial activity.\

Experimental

The identification and characterization of synthesized compounds were carried out by the following procedure to determine that all the prepared compounds were of different chemical nature than the respective parent compounds. 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.

(A) Synthesisof2'-hydroxy-5'-methyl-4',6'-dibromo chalcones[A-J]

A mixture of 2-hydroxy-5-methyl-4,6-dibromoacetophenone (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%.

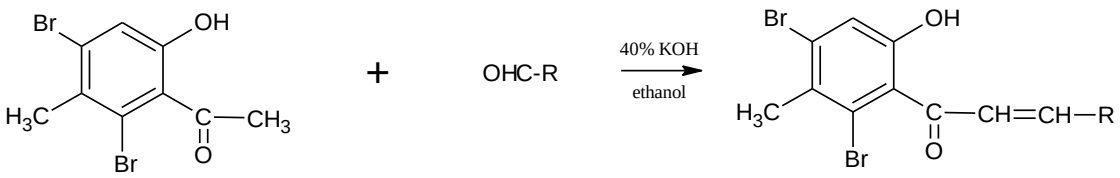
(B) Synthesis of 2'-hydroxy-5'-methyl-4',6'-α,β-tetrabromochalcones[A'-J']

2'-hydroxy-5'-methyl-4',6'-dibromo 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%

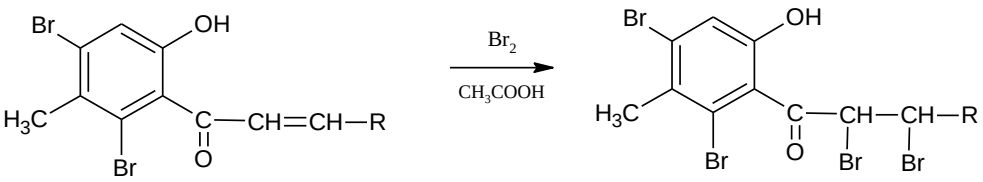
(C) Ssynthesis of 2-(2'-hydroxy-5'-methyl-4',6'-dibromo)-benzyl-3-(substitutedphenyl)-1,4-quinoxaline[A"-J"]

A mixture of 2'-hydroxy-5'-methyl-4',6'-α,β-tetrabromochalcones[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



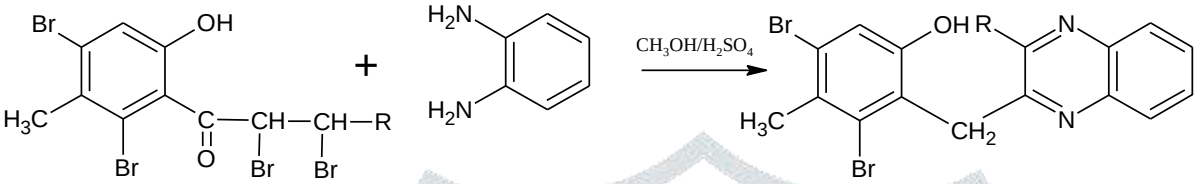
2-hydroxy-methyl-4,6-dibromoacetophenone Substituted aldehydes Chalcones [A - J]



Chalcones

[A - J]

[A' - J ']



[A' - J ']

[A" - J"]

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 Tableof 2-(2'-hydroxy-5'-methyl-4',6'-dibromo)-benzyl-3-(substitutedphenyl)-1,4-quinoxaline[A"-J"]

Compd. No.	R	Molecular formula	(Mol. wt.)	Yield (%)	M.P. 0C.	Elemental Analysis Found (Required)	
						% of N	% of X
A"	4-chlorophenyl	$C_{22}H_{15}ON_2Br_2Cl$	518.62	56	142	5.21 (5.40)	37.52 (37.65)
B"	4-hydroxyphenyl	$C_{22}H_{16}O_2N_2Br_2$	500.18	57	138	5.48 (5.60)	31.76 (31.95)
C"	Phenyl	$C_{22}H_{16}ON_2Br_2$	484.18	59	144	5.63 (5.79)	33.32 (33.01)
D"	2,4-dichlorophenyl	$C_{22}H_{14}ON_2Br_2Cl_2$	553.07	59	128	5.28 (5.07)	41.57 (41.72)
E"	3-phenoxyphenyl	$C_{28}H_{20}O_2N2Br_2$	576.27	52	164	4.67 (4.86)	27.57 (27.73)

F"	2,6-dichlorophenyl	$C_{22}H_{14}ON_2Br_2Cl_2$	553.07	51	152	5.24 (5.07)	41.56 (41.72)
G"	3-nitrophenyl	$C_{22}H_{15}O_3N_3Br_2$	529.18	47	127	7.72 (7.94)	30.06 (30.20)
H"	3,4,5-trimethoxyphenyl	$C_{25}H_{22}O_4N_2Br_2$	574.26	50	171	4.62 (4.88)	27.69 (27.83)
I"	4-methoxyphenyl	$C_{23}H_{18}O_2N_2Br_2$	514.20	49	138	5.21 (5.45)	31.27 (31.08)
J"	4-N,N-dimethylaminophenyl	$C_{24}H_{21}ON_3Br_2$	527.25	57	119	7.73 (7.97)	30.09 (30.31)

^{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-(2'-hydroxy-5'-methyl-4',6'-dibromo)-benzyl-3-(4"-methoxyphenyl)-1,4-quinoxaline (Compound no. I")

Chemical shift	Relative Number of Protones	Assignment
2.30	3	$-CH_3$
5.30	1	-OH
3.90	2	$-CH_2-$
3.82	3	$-OCH_3$
6.72-8.05	9	Ar-H

Infrared spectra

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

TABLE-3

IR spectra of 2-(2'-hydroxy-5'-methyl-4',6'-dibromo)-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
610	s	C-Br stretching	Bromo 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

The synthesized compounds were screened for their antibacterial activity using *S.aureus, E. coli*by cup plate method using DMF as solvent. All the compounds shows mild activity against both bacteria in comparison with ampicilin and gentamycin. The results are describe in table no. 4.

Table-4

Compound No.	Zone of inhabitation in mm Antibacterial (24 hrs.)	
	S.aureus (+ve)	E.coli (-ve)
A"	9	9
B"	10	9
C"	11	11
D"	11	10
E"	11	8
F"	13	15

G"	N.A.	N.A.
H"	10	10
I"	12	14
J"	13	12
Standard Drugs: Ampicilin Gentamycin	 18 -	 - 21

N.A.= Not Active

RESULTS AND DISCUSSION

The 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"**haveshownthe maximum activity against all the compounds towards gram +ve bacteria and gram negative bacteria i.e. S. aureus and E.coli. The compounds no. **C"** and **D"** have shown good activity against E.coli bacteria while the compound no. **G"** is found inactive against both bacteria. Rest of the compounds are found poor active against both bacteria S.aureus and E.coli.

ACKNOWLEDGEMENT

The authors are thankful to Department of Chemistry, South Gujarat University, Surat for providing laboratory facilities.

REFERENCES

1. Vyas G.N.; Shah N. M., Indian J. Chem. Soc., **1951**, *28*, 75.
2. Naik S. M.; Naik H. B., Orient. J. Chem., **1998**, *14(1)* 167-168.
3. Mehta P. A, Naik H. B.,Orient J Chem**1998**,*14(2)*
4. BasawarajR., Sangapure S. S., Int. J. Chem. Sci., **2008**, *6(1)*, 351-357.
5. Vekariya N. A., Khunt M. D.,Parikh A. R., Indian J. Chem.,**2003**,*42B*, 421-424.
6. Desai M. D, Desai K. K., Asian J. Chem.,**2002,** *14(2)* 947-978.
7. KaithwalM.,Gaeg P., Ahmad S., Orient. J. Chem.,**2009**, *25(4)*, 935-943.
8. KalirajanR., Sivakumar S. U., Jubie S., Gowramma B., Suresh B., Int. J. Chem. Tech. Res.,**2009,** *1(1)*,27-34.