HL **ISSN: 2231 – 3087(print) / 2230 – 9632 (Online)**
http://heteroletters.org **Vol. 3: (3), 2013, 341-347**

SYNTHESIS OF 2-METHYL-5-NITRO-N-(4-(3-((3-PHENYLQUINOXALIN-2-YL) METHYL) PHENOXY) PHENYL) BENZENESULFONAMIDE AND THEIR ANTIMICROBIAL ACTIVITY

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Abstract: Chalcones, precursors of open chain flavonoids and isoflavonoids present in edible plants, and their derivatives have attracted increasing attention due to numerous potential pharmacological applications. They have displayed a broad spectrum of pharmacological activities. Changes in their structure have offered a high degree of diversity that has proven useful for the development of new medicinal agents having improved potency and lesser toxicity. The present review highlights the recently synthesized chalcones and their derivatives possessing important pharmacological activities.

Keywords: Synthesis, heterocyclic substituted chalcone derivatives,
Sulphonamide derivatives, pyrimidin derivatives, antimicrobial activity.

INTRODUCTION

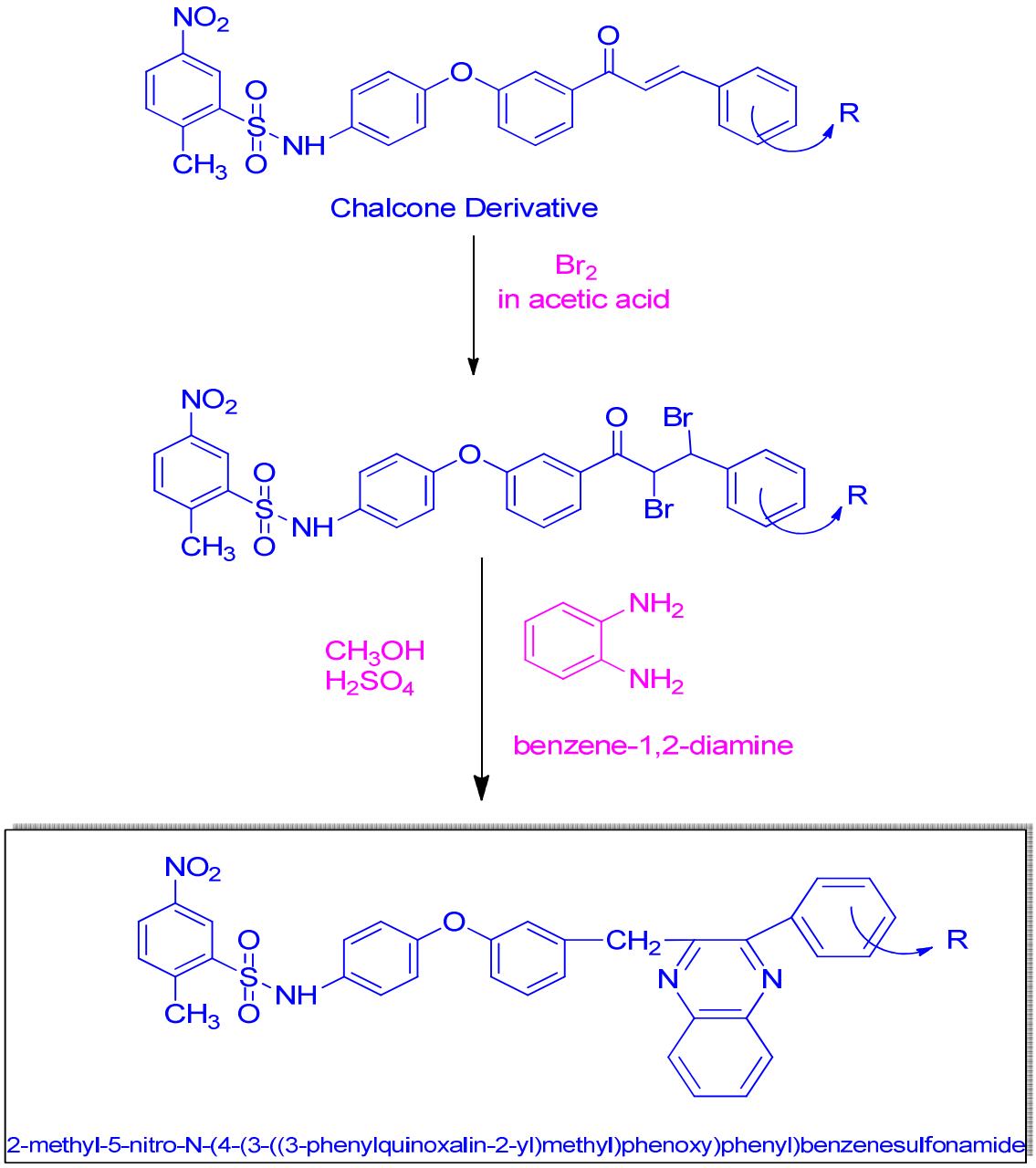
Quinoxalines as a class of heterocyclic compounds has been studied extensively for the past several years for their various pharmacological and agricultural activities.

Quinoxaline is also called as benzopyrazine. It is heterocyclic compound containing benzene ring and pyrazine ring. Pyrazine are stable, colorless compound which are soluble in water. Unlike pyridine, they are expensive, not readily available and so are seldom used as starting material for synthesis of their derivative. Diazines are fused to benzene ring to form quinoxaline.

Quinoxaline and its derivatives are important nitrogen containing heterocyclic compounds of various biologically interesting properties with several pharmaceutical applications. Substituted quinoxalines are an important class of benzoheterocycles, which constitute the building blocks of wide range of pharmacologically active compounds having antibacterial (1-2) antifungal (2), anticancer (2-3), antitubercular (2-3), antileishmania (2-3), antimalarial (2-3) and antidepressant activities (4). Some quinoxalin have been reported to show antimicrobial (3-4), novel, potent antithrombotic (4), anti-pain and anti-inflammatory (4-6) activities.

The quinoxaline is described as a bioisoster of quinoline, naphthalene, benzothiophene and other aromatic rings such as pyridine and pyrazine. Because of the similarity between some antitubercular drugs and quinoxaline, as well as the presence of the quinoxaline moiety in some broad spectrum of antibiotics, it was hoped that quinoxaline analogs would exhibit antitubercular activity (8-9). Some of quinoxaline analogues complexed with transition metals are efficient to binding with DNA(9-10).

REACTION SCHEME



(N-2)

Where R = (a) Benzaldehyde (b) 4-anisaldehyde (c) 2-anisaldehyde (d) Salicyaldehyde (e) 2-chlorobenzaldehyde (f) 4-chlorobenzaldehyde (g) 2-nitrobenzaldehyde (h) 3-bromobenzaldehyde (i) 3,4-dimethoxybenzaldehyde (j) 3,4,5- trimethoxybenzaldehyde

MATERIALS AND METHODS

PREPARATION OF N-(4-(3-(2, 3-DIBROMO-3-PHENYL PROPANOYL) PHENOXY)PHENYL)-2-METHYL-5-NITROBENZENESULFONAMIDE

The (E)-N-(4-(3-cinnamoylphenoxy)aryl)-2-methyl-5-nitrobenzenesulfonamide (3.01g, 0.01 mol) was dissolved in acetic acid (30 ml) and bromine in acetic acid (1 ml, 10%) was slowly added to it. The reaction mixture was stirred for an hour. Then it was poured over crushed ice. The white solid separated was collected, washed with distilled water, dried and crystallized from Chloroform: Methanol (1: 1) mixture

a) PREPARATION OF 2-METHYL-5-NITRO-N-(4-(3-((3-PHENYLQUINOXALIN -2-YL)METHYL)PHENOXY)PHENYL)BENZENE-SULFONAMIDE

A mixture of N-(4-(3-(2,3-dibromo-3-phenylpropanoyl)phenoxy)phenyl)-2-methyl-5-nitrobenzenesulfonamide (4.2 g, 0.01 mol) and benzene-1,2-diamine (1.08g,0.01 mol) were dissolved in methanol (25ml) . A few drops of concentrated Sulphuric acid were added and the reaction mixture was heated at 60-70 oC on water-bath for 30 minutes. It was then diluted with water and crude mass was extracted with ether to remove insoluble benzene-1,2-diamine. Ether was then removed and solid product was crystallized from ethanol (95 %).

RESULTS AND DISCUSSION

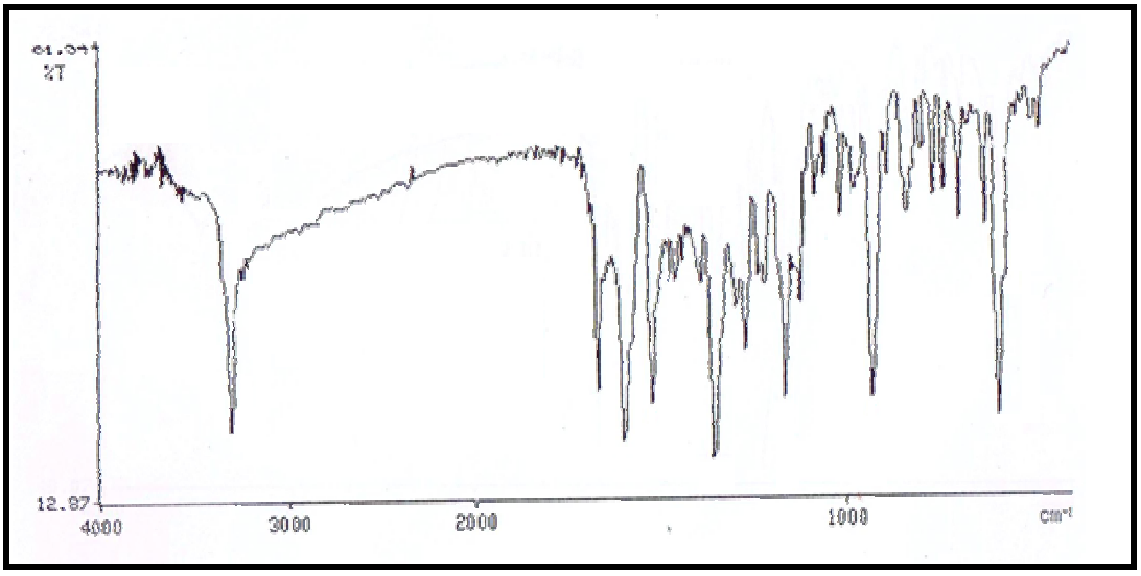
Table 1: **Physical and analytical data of compounds**

No.	Code No.	R	Molecular Formula	Molecular Weight (g/m)	Yield (%)	M.P. ^{o}C	C %	H %	N %
							Found		
1	a	H	$C_{34}H_{26}N_4O_5S$	602	84	220	67.73	4.35	9.30
2	b	4-OCH_3	$C_{35}H_{28}N_4O_6S$	603	88	213	67.05	4.30	9.17
3	c	2-OCH_3	$C_{35}H_{28}N_4O_6S$	603	86	211	67.02	4.43	9.16
4	d	2-OH	$C_{34}H_{26}N_4O_6S$	619	73	218	67.23	4.13	9.35
5	e	2-Cl	$C_{34}H_{25}ClN_4O_5S$	636	85	201	67.74	4.70	9.20
6	f	4-Cl	$C_{34}H_{25}ClN_4O_5S$	636	82	196	67.76	4.72	9.20
7	g	2-NO_2	$C_{34}H_{25}N_5O_7S$	648	77	208	67.40	4.64	9.94
8	h	3-Br	$C_{34}H_{25}BrN_4O_5S$	680	89	223	67.62	4.34	9.58
9	i	3,4-$(OCH_3)_2$	$C_{36}H_{30}N_4O_7S$	663	71	206	67.50	4.50	9.70
10	j	3,4,5-$(OCH_3)_2$	$C_{37}H_{32}N_4O_8S$	693	70	203	67.49	4.72	9.42

IR Spectral Studies

No.	Code	R	Ar-NO_2	Ar-O-Ar	C=N	-NH-	-C-R
1	a	H	1351	1264	1624	3209	-
2	b	4-OCH_3	1357	1269	1642	3205	2834
3	c	2-OCH_3	1359	1263	1626	3202	2838
4	d	2-OH	1353	1267	1619	3217	3443
5	e	2-Cl	1356	1222	1630	3192	678
6	f	4-Cl	1349	1267	1632	3218	674
7	g	2-NO_2	1361	1263	1618	3218	1321
8	h	3-Br	1355	1251	1612	3225	615
9	i	3,4-$(OCH_3)_2$	1343	1263	1621	3212	2821
10	j	3,4,5-$(OCH_3)_2$	1366	1250	1628	3203	2839

IR Spectra of sample code (a)

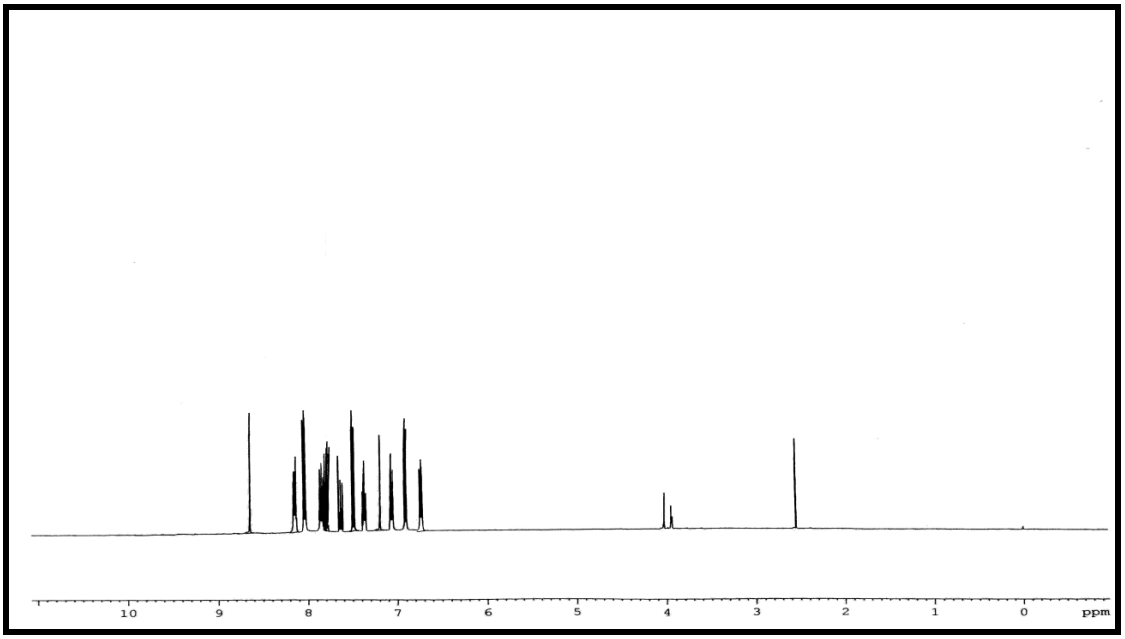


1H N.M.R. Spectral Studies:

No.	Code	R	Chemical Shift (δ ppm)			
			Ar-R	**N-H**	**-CH_3**	CH(Quinoxaline)
1	b	4-OCH_3	3.85	4.05	2.59	7.74
2	c	2-OCH_3	3.89	3.89	2.57	7.71
3	d	2-OH	5.30	4.01	2.55	7.76
4	f	4-Cl		4.02	2.60	7.77
5	g	2-NO_2	-	4.0	2.61	7.74
6	h	3-Br	-	3.87	2.59	7.78
7	i	3,4-$(OCH_3)_2$	3.80	4.07	2.62	7.70
8	j	3,4,5-$OCH_3)_2$	3.81	3.93	2.67	7.68

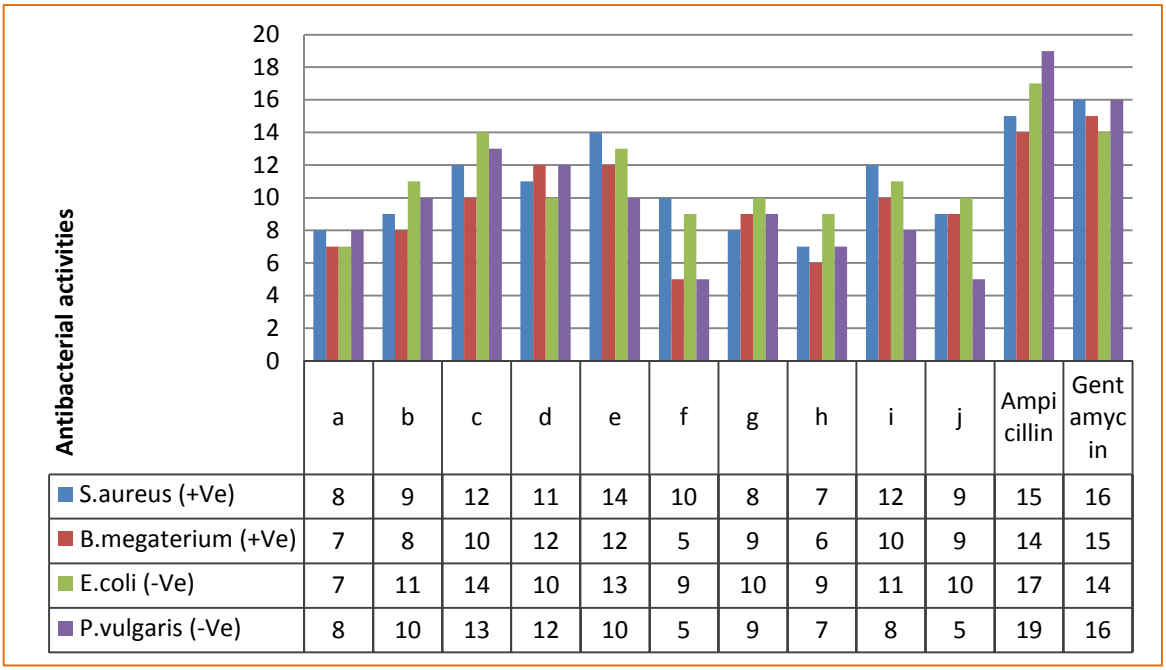
Detail data of Compound Code: (a)			
Chemical Shift (δ ppm)	**Relative number of protons**	**Peaks**	**Assignment**
4.06	1	s	C-NH
2.63	3	s	-CH_3(Aromatic)
2.83	2	s	-CH_2(Methylene)
7.82	4	q	CH(Quinoxaline)

NMR Spectra of sample code (a)



ANTIMICROBIAL ACTIVITY

The antibacterial activity of the compounds was screened by disc plate method. The test discs were containing 50 microgram per disc of the test compound. The activity was shown against gram positive bacteria are Staphylococcus aureus [MTCC(96)], Bacillus megaterium [MTCC (121)] and gram negative bacteria Escherichia coli [MTCC(443)], Proteus vulgaris [MTCC(1771)] .



	a	b	c	d	e	f	g	h	i	j	Ampicillin	Gentamycin
S.aureus (+Ve)	8	9	12	11	14	10	8	7	12	9	15	16
B.megaterium (+Ve)	7	8	10	12	12	5	9	6	10	9	14	15
E.coli (-Ve)	7	11	14	10	13	9	10	9	11	10	17	14
P.vulgaris (-Ve)	8	10	13	12	10	5	9	7	8	5	19	16

The antimicrobial activities of newly synthesised compounds were compared with known antibiotics like Ampicillin and Gentamycin; all the compounds show moderate to good activity. Structure elucidation of synthesised compounds has been made on the basis of elemental analysis, IR spectral studies and ^{1}H NMR spectral studies and all the compounds gave satisfactory results.

Conclusion:

The screening results revealed that the Compound e & c shows significant results against gram positive and gram negative bacteria respect to standard drug Ampicillin and Gentamycin.

Acknowledgements:

The authors are thankful to Shri P.M.Patel Institute of P.G Studies & Research in Science (APMS) for providing research facilities. They are also grateful to and the Department of Biosciences, Sardar Patel University, Vallabh Vidyanagar, for screening the newly synthesised compounds for their antimicrobial activities; Suleshvari Pharma ltd, for scanning the IR spectra and ^{1}H NMR spectra of newly synthesised compounds.We heartly thanks to Shri Bipinchandra sir and Parth Sir for kind support and coordination.

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Received on March 28, 2013.