AN EFFICIENT AND ECOFRIENDLY SYNTHESIS OF SOME NEW BIOACTIVE BIS BROMO α, β-UNSATURATED KETIMINES IN AQUEOUS MEDIUM UNDER MICROWAVE IRRADIATION

Nana V. Shitole, Suraj B. Ade, Pradip V. Chendkale *and* ***Subhash M. Lonkar*** [*]
[*] *P.G.Research Center, Department of Chemistry, Shri Shivaji College, Parbhani. M.S. (India)*

Abstract: A rapid, efficient and eco-friendly method for the synthesis of new biological screening effect of bis bromo α, β-unsaturated ketimines by the reactions of different substituted aromatic amines with bis bromo chalcone under microwave irradiation in water have been reported for their antimicrobial activities. A series of nine products **(3a-3i)** have been isolated, purified and characterized by IR, ^{1}HNMR, and Mass spectral analysis. Microwave irradiation technique have been found superior than conventional method and as an alternative source of energy has been proved to be one of the stepping stone towards the green synthesis, have higher yield, save energy, shorter time and mild reaction conditions.

Keywords: MWI, Bis bromo α, β--Unsaturated Ketimines, Water, Antimicrobial.

I. INTRODUCTION

Chalcones were medicinally important class of compounds. Chalcones are commonly synthesized via Claisen-Schmidt condensation reaction between acetophenone and benzaldehyde. They are products of condensation of simple or substituted aromatic benzaldehyde with simple or substituted acetophenones in presence of alkali. Chalcones are well known intermediates for synthesizing various heterocyclic compounds. The compounds with the backbone of Chalcones have been reported to possess various biological activities such as antimicrobial [1-3] anti-inflammatory [4], anti- malarial [5, 6] antileishmanial [7] antioxidant [8], anti tubercular [9, 10].

Chalconeimines have been reported to exhibit antimicrobial properties [11]. Chalconeimines are the phenolic Schiff bases which are formed when chalcones condensed with substituted aniline. Anticancer Schiff bases have been synthesised by condensation of aniline with substituted benzaldehyde. Schiff bases like chalconeimines have been reported to exhibit antimicrobial properties [12]. Chalcones (1, 3-diaryl-2-propen-1-one) and Schiff bases (substituted benzylidene aniline) belongs to a widely used groups of organic intermediates, possess broad spectrums of biological activity such as antioxidants [13, 14], antileshmanial [15, 16], antifungal [17, 18], and antimicrobial [19, 20]. Both chalcones and Schiff bases are important for synthesis of different active organic compounds such as flavones [21-22], pyrazoline [23, 24], β-lactam [25] and metal complexes [26-28]. There was some variation known, such as chalcones and Schiff bases preparation in a water suspension medium [29-30], ultrasonic [31- 33] and microwave irradiation techniques [34-35], or using different new catalysts [36- 38].

Due to wide range of pharmaceutical applications it was thought to be worthwhile synthesized some new bis bromo α, β-unsaturated ketimines under microwave irradiation in aqueous medium and tested for biological activities.

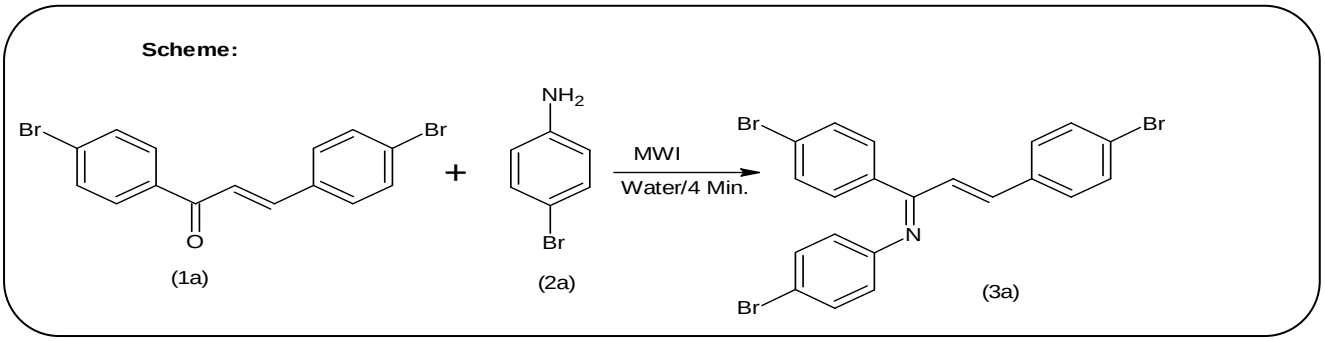
II. MATERIALS AND METHODS

All melting points were determined in an open capillary tube and are uncorrected. IR spectra were recorded in KBr on a Perkin-Elmer spectrometer ^{1}H NMR Spectra were recorded on a Gemini 300-MHz instrument in $CDCL_3$ as solvent and TMS as an internal standard. The mass spectra were recorded on GC-MS spectrometer. The purity of products was checked by thin –layer chromatography (TLC) on silica –gel. Microwave irradiation was carried out in a microwave oven (LG Smart Chef MS-255R Operating at 2450 MHz with power output of 900w)

III. EXPERIMENTAL PROCEDURE

The equimolar quantities of substituted chalcone **1a**: [*1, 3*-bis (4-bromophenyl) prop-2-en-1-one] 0.365mg (0.01M) and **2a**: (p- bromo aniline) 0.171 mg (0.01M) was taken in 100ml conical flask. Added 15 ml distilled water in it and shake well above mixture for 5 min; solution was covered with watch glass. Kept the conical flask under microwave irradiation at 180w for 4-5min, then mixture was taken out from microwave & cooled at room temperature. The reaction mixture was poured into crushed ice and stirred for 5 minutes. The solid product was filtered through suction pump, dried, recrystllized from ethanol, purity checked by TLC & subjected for antimicrobial activity.

All the chalconeimines (3b – 3i) were synthesized by same method.

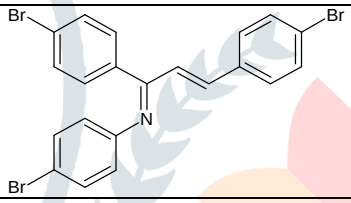
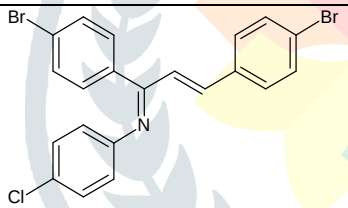
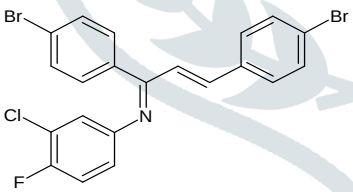
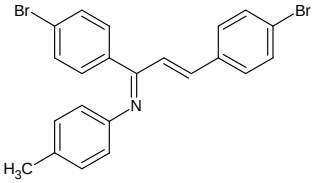
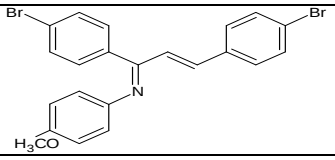
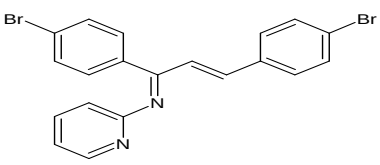


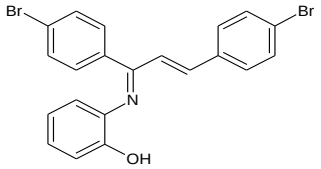
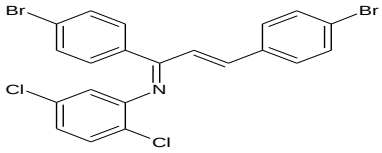
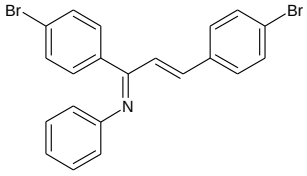
IV. RESULTS AND DISCUSSION

A series of bis bromo α, β-unsaturated ketimines (3a –3i) were synthesized from (1a) -1, 3-bis (4-bromophenyl) prop-2-en-1-one with corresponding substituted aromatic amines under MWI in water as a solvent. They were fully characterized & evaluated for their antibacterial & antifungal activity, (3a & 3f) shows antibacterial activity against *E.coli* & (3a & 3h) shows antifungal activity against *Aspergillus Niger*. Therefore, it can be concluded that this chalconeimines containing pyridine ring shows highest antibacterial activity against *E.coli*. Most of these ketimines are readily use for preparation different types of heterocyclic compounds like azitidinones, trizones, flavones, dibromochalconeimines. In continuation, earlier research work devoted towards development of green chemistry and new synthetic methodology [39-41]. MWI method is very simple, short time required, higher yields, and non hazardous due to water as a solvent and save energy.

Physical and analytical data of bis bromo α, β-unsaturated ketimines

TABLE 1

Compounds	Structures	Time in min.	M.P.in (^{0}c)	Yield in (%)
3a		5.00	148	94.32
3b		4.00	198	75.61
3c		4.20	217	85.97
3d		4.50	211	93.52
3e		4.30	180	69.73
3f		5.00	210	87.25

3g		4.00	172	79.85
3h		5.00	214	68.75
3i		4.45	210	87.25

ANTIMICROBIAL ACTIVITY

Escherichia coli and fungal strains *Aspergillus Niger* were chosen based on their clinical and pharmacological importance. The bacterial strains obtained from Shri Shivaji College, Department of microbiology, Parbhani were used for evaluating antimicrobial activity. The bacterial and fungal stock cultures were incubated for 24 hours at 37°C on nutrient agar (NA) and potato dextrose agar (PDA) medium respectively, following refrigeration storage at 4°C. The bacterial strains were grown in Mueller-Hinton agar (MHA) plates at 37°C (the bacteria were grown in the nutrient broth at 37°C and maintained on NA slants at 4°C) at 28°C. The stock cultures were maintained at 4°C.

DETERMINATION OF ZONE OF INHIBITION METHOD

In vitro antibacterial and antifungal activities were examined for chalconeimines. Antibacterial and antifungal activities chalconeimines for pathogenic bacteria and fungus was investigated by the agar disk diffusion method. Antimicrobial activity testing was carried out by using agar cup method [43, 44]. Chalconeimines dissolved in sterile distilled water, and stored at 4°C. For the determination of zone of inhibition, pure bacterial and fungal strain was taken as a standard antibiotic for comparison of the results. Chalconeimines was screened for its antibacterial and antifungal activity against the *Escherichia coli*, and the fungi, *Aspergillus Niger*. The sets of five dilutions (20, and 30 mg/ml) of chalconeimines and standard drugs were prepared in double-distilled water using nutrient agar tubes. Nutrient agar sterile plates were seeded with indicator bacterial strains (10^8 cfu) and allowed to stay at 37°C for 3 hours. Control experiments were carried out under similar condition by used tetracycline for antibacterial activity and griseofulvin for antifungal activity as standard drugs. The zones of growth inhibition around the disks/well were measured after 18 to 24 hours of in incubation at 37°C for bacteria and 48 to 96 hours for fungi at 28°C. The sensitivities of the microorganism species to chalconeimines was determined by measuring the sizes of inhibitory zones (including the diameter of disk/ well) on the agar surface around the disks were labeled and recorded in the table no. 2 values <8 mm were considered as not active against microorganisms.

ZONE OF INHIBITION IN (mm) OF CHALCONEIMINES
TABLE: 2

Compounds	Antibacterial *Escherichia Coli*	Antifungal *Aspergillus Niger*
3a	15	11
3b	08	05
3c	10	07
3d	-	05
3e	13	-
3f	15	09
3g	-	04
3h	18	12
3i	13	08
Control	00	00
Tetracycline	20	-
Griseofulvin	-	20

V. SPECTRAL ANALYSIS

3a : 1,3-bis(4-bromophenyl)prop-2-en-1-ylidene]-4-bromoaniline
IR: (C=N) - 1638 cm^{-1}, (C=C) – 1604cm^{-1}. ^{1}HNMR: 7.14 (d, 1H, -CH_β), 6.75 (d, 1H, -CH_α), 7.75- 7.21 (m, 4H, Ar-H), 7.45-7.10 (m, 4H, Ar-H), 7.32 (d,2H, Ar-H),7.21 (d, 2H, Ar-H), M/z=520.
3d : 1,3-bis(4-bromophenyl)prop-2-en-1-ylidene]-4-methylaniline
IR : (C=N) – 1632cm^{-1}, (C=C) – 1665cm^{-1}.^{1}HNMR : 7.19 (d, 2H, Ar-H), 7.32 (d, 2H, Ar-H), 2.1 (s, 1H, CH_3), 7.21 (d, 2H, Ar-H) 7.29 (d, 2H, Ar-H), 7.20 (d, 1H, CH_β), 6.84 (d, 1H, CH_α), 7.40 - 7.04 (5H, m), M/z=455.

3e : 1,3-bis(4-bromophenyl)prop-2-en-1-ylidene]-4-methoxyaniline
IR :(C=N) – 1642cm^{-1}, (C=C) – 1615cm^{-1}.^{1}HNMR: 3.82 (s, 3H, -OCH$_3$), 7.34 (d, 2H, Ar-H), 7.21 (d, 2H, Ar-H), 7.19 (d, 2H, Ar-H), 7.38 (d, 2H, Ar-H),7.24 (d, 1H, -CH$_\beta$), 6.78(d, 1H, -CHα), 7.32 (d, 2H, Ar-H),7.22 (d, 2H, Ar-H), M/z=471.
3g : 1,3-bis(4-bromophenyl)prop-2-en-1-ylidene]amino}phenol IR :(C=N) – 1648cm^{-1}, (C=C –1610cm^{-1}.^{1}HNMR: 11.62 (s, -OH), 7.30 – 7.19 (m, 4H), 7.32 (d, 2H, Ar-H),7.18 (d, 2H, Ar-H), 7.29 (d, 2H, Ar-H), 7.10(d,2H,Ar-H), M/z=557.

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