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Innovative Green synthesis of Schiff bases and their Antimicrobial Activity

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ABSTRACT

Objective: To optimize microwave assisted solvent free synthesis of Schiff bases of substituted benzaldehydes and aromatic amines (3-amino-6-bromo/Iodo-2-phenylquinazoline-4(3H) one) by using wetting reagent 000-ethoxyethanol. The goal of this study was to investigate the % yields and time required for the completion of reaction for Schiff bases by microwave and conventional conditions. **Methods:** Schiff bases have been synthesized by condensation of substituted various aromatic substituted benzaldehydes (0.001mol) with 3-amino-6-bromo/ Iodo-2-phenylquinazoline-4(3H) one (0.001mol) by two different methods as by conventional method (Heating) & Microwave accelerated synthesis by using wetting reagent 000-ethoxyethanol. The reaction time for conventional method and microwave method is in the range of 4-7 hr. and 3-5 min. respectively. The % yield for conventional method and microwave method is in the range of 56-77%. and 77-90% respectively. All synthesized compounds were characterized by elemental analyses, IR spectroscopy, mass spectroscopy, ^{1}H NMR and ^{13}C NMR spectroscopy. **Results:** The simple microwave assisted solvent-free method for the synthesis of Schiff bases using a wetting reagent (-ethoxyethanol) led to improvement in the yield of all the target compounds with reduction in their reaction byproducts & substantially reduced the overall process time as expected as compare to traditional method. Excellent isolated yields (up to 90%) were attained within short reaction times (typically, 3 min.) when the reaction was performed under microwaves irradiation. **Conclusion:** Compared with traditional methods, these methods are more convenient and reaction can be carried out in higher yield, short reactions time and milder conditions, without generation of pollution, elimination of side products and safer to analyst. From these features present methods can be correlated for safer and efficient synthesis of other products.

KEYWORDS: Schiff bases, β-ethoxyethanol, Solvent-Free, Microwave Heating, Environmentally Friendly

1.INTRODUCTION

The microwave induced enhancement of organic reactions is currently a focus of attention for chemists due to the decreased reaction time, improved yields and easier work up as compared to conventional methods[1-2]. In microwave synthesis, to avoid accidents low boiling, toxic and poisonous solvents are often avoided. The use of microwave for the synthesis of organic compounds has proved to be efficient, safe and environmentally benign techniques with shorter reaction time [3].

Compounds containing the –C=N–(azomethine group) structure are known as Schiff bases, usually synthesized from the condensation of primary amines and active carbonyl groups [4]. The reaction is acid-catalyzed and is generally carried out by refluxing the carbonyl compound and amine, with an azeotroping agent if necessary, and separating the water as formed [5]. Schiff bases are well known for their biological applications as antibacterial, antifungal, anticancer, and antiviral agents; furthermore, they have been used as intermediates inmedical substrates and as ligands in complex formation with some metal ions [6].The synthesis of imine was firstly reported by Hugo Schiff in 1864 and they have been known since then [7]. The imine compounds have been prepared using molecular sieves [8, 9], infrared irradiation [10], $Mg(ClO_4)_2$ [11], P_2O_5/SiO_2 [12], $ZnCl_2$ [13], CaO under microwave power [14], ethyl lactate as a tunable solvent [15], K10 clay [16], $TiCl_4$ [17], alumina [18], $CeCl_3.7H_2O$ [19], ultrasound irradiation [20], polymer-supported [21], nanotube TiO_2 (in sunlight) [22], and $Ti(OEt)_4$ [23]. In the recent years, microwave assisted organic reactions have emerged

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as a new tool in organic synthesis. Important advantages of this technique include highly accelerated rate of the reaction, reduction in reaction time with an improvement in the yield and quality of the product. Moreover the technique is considered as an important approach towards "Green Chemistry" because of its eco-friendly nature. Conventional methods of organic synthesis usually need longer heating time, elaborate and tedious apparatus set up, which result in higher cost of process and the excessive use of solvent/reagents leads to environmental pollution. [24] Microwave assisted reactions in solvent or solvent free conditions have gained popularity because of rapid reaction rate, cleaner reactions and ease of manipulation. [25]

Drug companies are exploiting microwaves in the area of organic/ pharmaceutical synthesis for drug screening and discovery. [26-28] Scientists have demonstrated the potential of microwave-assisted organic synthesis using ionic liquids as solvent, co solvent, additives and/or catalyst. [29-30] Among the wide variety of drug molecules that have been explored for developing microwave assisted synthetic process include pharmaceutical drugs in various biological activities like analgesic, antihypertensive, central nervous system depressant, antiviral, bactericidal and fungicidal activities. [31-33]

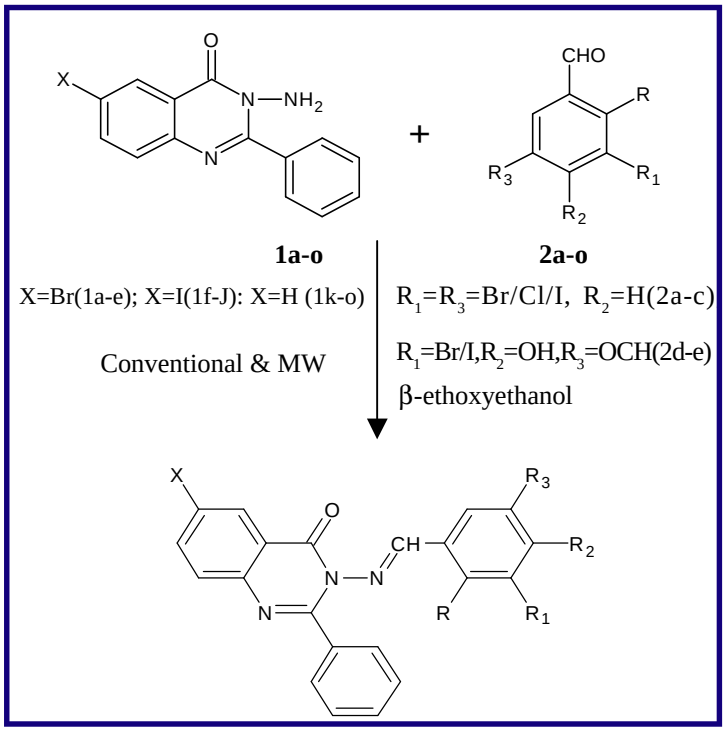
2-Ethoxyethanol is a solvent used widely in commercial and industrial applications. It is a clear, colorless, nearly odorless liquid that is miscible with water, ethanol, diethyl ether, acetone, and ethyl acetate. A polar solvent that is capable of acting as a hydron(proton) donor having property of being able to dissolve chemically diverse compounds. [34-35]

In the present paper, we have successfully to explore the possibility of a greater route with the help of microwave assisted technique and conventional method for the synthesis of Schiff bases as possible antimicrobial agents. The present work reveals the comparative aspects of condensation of some aromatic amines with aldehyde derivatives using microwave and conventional methods. The amine and aldehyde compounds as starting materials,000-ethoxyethanol as a wetting reagent and microwave power as an effective source of heating are used. The corresponding imine compounds were prepared in high yields and short reaction times using this effective and environment friendly method. The new microwave procedures were developed by considering two important parameters: minimum reaction time and minimum by-product formation leading to maximum yield of the pure product with desired quality.

2. MATERIALS AND METHODS

2.1: Instrumentation

Melting points were determined in an open capillary tube and are uncorrected. All the chemicals used were obtained from S. D. Fine Chem. Ltd. and E Merck Ltd., Mumbai while the reagents and solvents were of analytical grade & few were prepared according to standard methods. Melting points were determined with an Electrothermal 9100 apparatus. The IR spectra were recorded on Perkin-Elmer FT-IR model R XI spectrometer and absorption was expressed in cm^{-1}. The ^1H NMR spectra were recorded on a Gemini 300- MHz instrument in $CDCl_3$ and DMSO as solvent and TMS as an internal standard. The following abbreviations were used. The FAB mass spectra were recorded on a Jeol SX 102/Da-600 mass spectrometer/ data system using Argon/Xenone(6kv,10mA) as the FAB gas. Elemental analyses were carried out on a Carlo Erba 1108 analyzer. All chemicals/reagents were purchased from Aldrich and used without further purification.



Scheme 1. Synthetic pathway for preparation of Schiff bases **3a-o [** X=Br(3a-e); X=I(1f-J): X=H (1k-o); R_1=R_3=Br/Cl/I, R_2=H(2a-c); R_1=Br/I,R_2=OH, R_3=OCH(2d-e)]

Table

Compd. No	X	R	R_1	R_2	R_3
3a	Br	OH	Br	H	Br
3b	Br	OH	Cl	H	Cl
3c	Br	OH	I	H	I
3d	Br	H	Br	OH	OCH_3
3e	Br	H	I	OH	OCH_3
3f	I	OH	Br	H	Br
3g	I	OH	Cl	H	Cl
3h	I	OH	I	H	I
3i	I	H	Br	OH	OCH_3
3j	I	H	I	OH	OCH_3
3k	H	OH	Br	H	Br
3l	H	OH	Cl	H	Cl
3m	H	OH	I	H	I
3n	H	H	Br	OH	OCH_3
3o	H	H	I	OH	OCH_3

2.2. *Synthesis*

Preparation of 6-bromo-3-[(3,5-dichloro–2–hydroxyl-benzylidene) amino]-2-phenylquinazolin-4(3*H*)-one

Keeping in view the importance of quinazolin-4 (3*H*)-ones Schiff bases, a series of simple and substituted 3-amino-2-phenyl-4(3*H*)-quinazoline based Schiff bases **3a-o** were synthesized by two different method.

a) By conventional method (Heating).
b) Microwave accelerated synthesis.

Method I: Conventional method for synthesis of Schiff bases Compound

Aromatic substituted benzaldehyde i.e. 3,5-dichlrobenzaldehyde (0.175 g, 0.001 mol.) and 3-amino-6-bromo-2-phenylquinazoline-4(3*H*) one (0.316 g, 0.001 mol) dissolved in DMF (20 ml). To this solution mixture two drops of ß-ethoxyethanol as awetting reagent were mixed. This reaction mixture was refluxed 4-12 hr and the course of the reaction was monitored by TLC to completion. After that reaction mixture was cooled and the product was filtered off. The solid was dried and recrystalized obtained from appropriate solvent. By following the same procedure, all other compounds were prepared within 4-12hr.(240-720min.). All the reaction has optimized by changing reaction time and reflux time period between 240-720 min. and here impact on % yield presented for the single compound 1a in Table 2. The structure of Schiff bases were assigned on the basis of element analysis and spectral data. The physico-chemical data for synthesized Schiff base are given in Table 3.

Method II: Microwave-accelerated synthesis of Schiff bases

In microwave assisted synthesis, 3,5-dichlrobenzaldehyde (0.175 g, 0.001mol), 3-amino-6-bromo-2-phenylquinazoline-4(3*H*) one (0.316 g, 0.001 mol) and two drops of ß-ethoxyethanol as awetting reagent were mixed in a beaker. The reaction mixture was irradiated inside an MC767W (Electrolux) modified system (200 W) for about 3 minute by giving short interval of cooling. Reaction was monitored on TLC. After completion of reaction i.e. after 3 minute, the flask was cooled in ice water. It was then diluted with ice-cold water. The Schiff bases formed was filtered, dried and recrystallized from ethyl acetate. By following the same procedure, all other compounds were prepared within 3-5min.(180-300sec.). All the reaction has optimized by changing reaction time and microwave power of 180W-600W and here result presented for the single compound 1a in Table 1. The characterization data and the impact of microwave irradiation and conventional heating for the synthesis of Schiff bases compounds have been compared. Moreover, the % yield and time on the reaction were also studied and the results summarized in Tables 3.

The spectra data of the some compounds such as 3b, 3i, 3o are as follows.

3b:6-bromo-3-[(3,5-dichloro-2-hydroxybenzylidene)amino]-2-phenylquinazolin-4(3*H*)-one

IR (KBr) cm^{-1}: 3261 (Ar-OH), 1780 (C=O), 1664 (-N=CH), 1599, 1491, 1425 (Ar C=C stretch), 1294, 1242, 813 (Ar-Cl); **^{1}H NMR** ($CDCl_3$ δ ppm): 10.10 (s, 1H, Ar-OH), 8.96 (s, 1H, -N=CH), 6.83, 8.38 (m, 10H, quinazoline-H and Ar-H); **MS** (m/z): 490 (M^{+1}), 381, 353, 335, 302, 272, 256, 248, 221, 297, 190, 176, 153, 137, 116, 104, 88, 77, 61, 51.

3i: 3-[(3-bromo-4-hydroxy-5-methoxybenzylidene)amino]-6-iodo-2-phenylquinazolin-4(3*H*)-one

^{1}H NMR ($CDCl_3$ δ ppm): 10.57 (s, 1H, Ar-OH), 9.36 (s, 1H, -N=CH), 6.38-8.39 (m, 10H, quinazoline-H and Ar-H), 3.83 (s, 3H, OCH_3); **IR** (KBr) cm^{-1}: 3261 (Ar-OH), 1780 (C=O), 1664 (-N=CH), 1599, 1491, 1425 (Ar C=C stretch), 1294, 1242, 813 (Ar-Cl).

3o: 3-[(4-hydroxy-3-iodo-5-methoxybenzylidene)amino]-2-phenylquinazolin-4(3*H*)-one

^{1}H NMR ($CDCl_3$ δ ppm): 10.19 (s, 1H, OH), 8.94 (s, 1H, -N=CH), 6.522, 8.37 (m, 11H, quinazoline-H and Ar-H), 3.82 (s, 3H, OCH_3); **IR** (KBr) cm^{-1}: 3261 (Ar-OH), 1780 (C=O), 1664 (-N=CH), 1599, 1491, 1425 (Ar C=C stretch), 1294, 1242, 813 (Ar-Cl).

3.2.2 Spectral Discussion

IR Spectra

IR spectra of some representative members of the series of Schiff bases compounds showed characteristic band at near 1780-1785cm^{-1} due to C=O stretching of quinazoline ring. A band in the region 1647-1664 cm^{-1} due to C=N stretching vibration and band around 1599, 1491, 1425 cm^{-1} due to aromatic stretching.

NMR Spectra

^{1}H NMR spectra of compounds were studied in $CDCl_3$ showed characteristics signals in the region d 10.10-10.57 singlet due to Ar-OH. Azomethin proton gives singlet in the region d 8.30-8.76. All aromatic protons showed multiplet in the region δ 6.38-8.39.

MASS Spectra

The mass spectra of some representative members of the series were good agreement with their suggested structures.

2.3 *In-vitro* Antibacterial activity by cup plate method

The compounds synthesized during the present investigation were screened for their antibacterial activity. The antibacterial tests were

conducted on four common microorganisms such as *Escherichia coli ATCC 25922, Pseudomonas aureginosa ATCC 2853 and Staphylococcus aureus ATCC 25923, Bacillus substilis ATCC 29212* which are the representative types of gram positive and gram negative organisms respectively. The antibacterial activity of the compounds was assessed by cup-plate method of concentration of the test compound is 50 µg/ml & 100 µg/ ml.

2.3.1 Materials used:

Sterilized Petri dishes,Sterilized 6 mm cork borer,Sterilized inoculation loop, Sterilized test tubes, graduated pipettes and watch glasses,18-27 hours old grown culture in nutrient broth,Sterile tubercular syringes, Sterilized fine pointed forceps.

2.3.2 Preparation of Nutrient broth:

Composition:

Peptone (Bacteriological) : 20 g,Beef extract (Bacteriological) : 5 g. Sodium Chloride: 5 g,Distilled water up to: 1000 ml.

Nutrient broth is prepared by dissolving all these and steam for about 2 hour adjust the reaction mixture pH to about 7.2 and autoclave at 15 lbs pressure for 20 minutes. One day prior to the testing, the organisms obtained from the laboratory stock were subcultured into sterile nutrient broth and incubated at 37 ^{0} C for 18-24 hours. The culture growth thus obtained was used as inoculums for the antibacterial testing.

2.3.3 Preparation of nutrient agar media:

The nutrient agar media was prepared by using the following ingredients.

Peptone (Bacteriological): 20 g, Beef extract (Bacteriological): 5 g, Sodium chloride (Bacteriological): 5 g, Agar (Bacteriological): 20 g, Distilled water up to: 1000 ml.

Weighed quantities of peptone, beef extract were dissolved in distilled water by gentle warming, and then the specified amount of agar was dissolved by heating on boiling water bath. Then the pH of the above solution is adjusted by adding sodium chloride and the volume of final solution is made up to 1000 ml with distilled water. Then the above prepared nutrient agar media is sterilized by autoclave at 121^{0}C for 20 minutes at 15 lbs/in^2 pressure.

2.3.4 Preparation of test solution:

5 mg and 10 mg of the test compound were dissolved separately in 100 ml of DMF. From each of this 10 ml of solution was taken and diluted to 100 ml with DMF. Now the concentration of the test compound is 50 µg/ml & 100 µg/ ml. These sample solution were made in suitably labelled sterilized test tubes.

2.3.5 Preparation of standard solution:

The standard drug used in this testing is Ampicillin. It is water soluble; the concentration of this drug is adjusted so as to contain 25-50 µg/ml.

2.3.6 Method of testing:

The above prepared nutrient agar media is cooled to 45^0 C with gentle shaking to bring about uniform cooling. To this 0.5-0.6 ml of 18-24 hours old culture was injected aseptically and mixed well by gentle shaking. This was poured onto the Petri dishes and was allowed to set for 1 hour. Thereafter the cups were made by punching into the set agar with a sterile cork borer and scooping out the punched part of the agar. The diameter of each cup was 6 mm. To these cups 50 µl of the test compound was put, which was prepared in DMF. After adding the drug solution, it was allowed to diffuse for about 45 minutes, at room temperature. Then the plates were incubated at 37^0 C for 24 hours in an incubator. The extent of diameter of inhibition after 24 hours was measured as the zone of inhibition in millimetres.

3. RESULTS AND DISCUSSION

In this present work, we synthesized quickly and efficiently a series of imine derivatives (3a–o) (Scheme-I) by condensation of aromatic amines i.e. 3-amino-6-bromo-2-phenylquinazoline-4(3*H*) one(1a-e), 3-amino-6-iodo-2-phenylquinazoline-4(3*H*)one(1f-j) & 3-amino-2-phenylquinazoline-4(3*H*)one(1k-o) and aldehyde derivatives such as 3,5-dibromosalicylaldehyde (2a), 5-chlorosalicylaldehyde(2b), 3,5-diiodosalicylaldehyde(2c),3-bromo-4-hydroxy-5-methoxy benzaldehyde (2d), 3-iodo-4-hydroxy-5-methoxybenzaldehyde(2e) under microwave-assisted solvent free conditions and conventional method using ß-ethoxyethanol as wetting reagent. ß-ethoxyethanol that is a polar molecule quickly absorbs microwaves and therefore heats up and heats around effectively. As a result, ß-ethoxyethanol, which increases the polarity of the reaction medium, has an active role in the heating of the reaction medium by microwaves.

The general reaction was summarized in Scheme 1. In addition, we tested the effect of different microwave power such as 180, 200, 360, 600, 900W and detected the microwave power of 180W and 360W are more appropriate choices for the reaction. Hence, the optimum microwave reaction conditions were determined using 180 and 360W microwave power and neat and wetting with ß--EE for the all compound. The highest reaction yield by conventional method and microwave method was 77% & 90% respectively and reaction time by conventional method and microwave method was 12hr & 5min respectively. Yunus Bekdemir et al [36] developed a simple microwave assisted solvent-free method for the synthesis of imines using a wetting reagent (ß-ethoxyethanol). In addition, they tested the effect of different microwave power such as 180, 360, 600, 900W and detected the micro-

Table 1: The optimization of microwave conditions for compound 1a

Sr. No.	Watt	Microwave Time (s)	Method Reaction Conditions a/b	Yields %	Sr. No.	Watt	Microwave Time (s)	Method Reaction Conditions a/b	Yields %
1	180	150	a				180	a	78
2	180	180	a	80	17	360	210	a	78
3	180	210	a	80	18	360	240	a	78
4	180	240	a	80	19	360	270	a	79
5	180	270	a	82	20	360	300	a	80
6	180	300	a	82	21	360	330	a	80
7	180	330	a	82	22	180	180	b	77
8	200	150	a	82	23	200	180	b	76
9	200	180	a	85	24	360	180	b	74
10	200	210	a	84	25	180	210	b	75
11	200	240	a	84	26	200	210	b	76
12	200	270	a	82	27	360	210	b	75
13	200	300	a	79	28	180	240	b	72
14	200	330	a	80	29	200	240	b	72
15	360	150	a	79	30	360	240	b	74

[a]With wetting agent ß-ethoxyethanol, [b]Without wetting agent ß-ethoxyethanol

Table 2: The optimization of classical conditions for compound 1a

Sr. No.	Time(Min)	Reaction conditions	Yields %
1	240	Reflux	00
2	300	Reflux	00
3	360	Reflux	00
4	420	Reflux	00
5	480	Reflux	60
6	540	Reflux	62
7	600	Reflux	62
8	660	Reflux	56
9	720	Reflux	56

Table 3.Characterization data of Schiff bases compound (3a-o).

Compd. No.	M.P. (°C)	Mol. Wt.	Molecular formula	Elemental Analysis (%) Calculated (Found) N	Cl/Br/I	R_f Value
3a	176-178	578	$C_{21}H_{12}Br_3N_3O_2$	7.27 (7.35)	41.47 (41.28)	0.77
3b	196-197	489	$C_{21}H_{12}BrCl_2N_3O_2$	8.59 (8.70)	30.84 (30.82)	0.75
3c	179-181	672	$C_{21}H_{12}BrI_2N_3O_2$	6.25 (6.43)	49.66 (49.76)	0.79
3d	222-223	529	$C_{22}H_{15}Br_2N_3O_3$	7.94 (7.85)	30.20 (30.45)	0.60
3e	256-258	576	$C_{22}H_{15}BrIN_3O_3$	7.29 (7.49)	35.92 (35.81)	0.63
3f	178-180	625	$C_{21}H_{12}Br_2IN_3O_2$	6.72 (6.96)	45.91 (46.10)	0.73
3g	162-163	536	$C_{21}H_{12}Cl_2IN_3O_2$	7.84 (7.76)	36.74 (36.96)	0.72
3h	155-157	719	$C_{21}H_{12}I_3N_3O_2$	5.84 (5.97)	52.98 (52.85)	0.71
3i	216-218	576	$C_{22}H_{15}BrIN_3O_3$	7.29 (7.44)	35.90 (36.05)	0.58
3j	240-141	623	$C_{22}H_{15}I_2N_3O_3$	6.74 (6.99)	40.73 (40.93)	0.57
3k	154-156	499	$C_{21}H_{13}Br_2N_3O_2$	8.42 (8.58)	32.05 (32.25)	0.80
3l	120-122	410	$C_{21}H_{13}Cl_2N_3O_2$	10.24 (10.44)	17.06 (17.19)	0.79
3m	158-159	593	$C_{21}H_{13}I_2N_3O_2$	7.0 8(7.29)	42.82 (42.99)	0.73
3n	180-181	450	$C_{22}H_{16}BrN_3O_3$	9.3 3(9.54)	17.75 (17.98)	0.53
3o	184-185	497	$C_{22}H_{16}IN_3O_3$	8.45 (8.59)	25.52 (25.73)	0.54

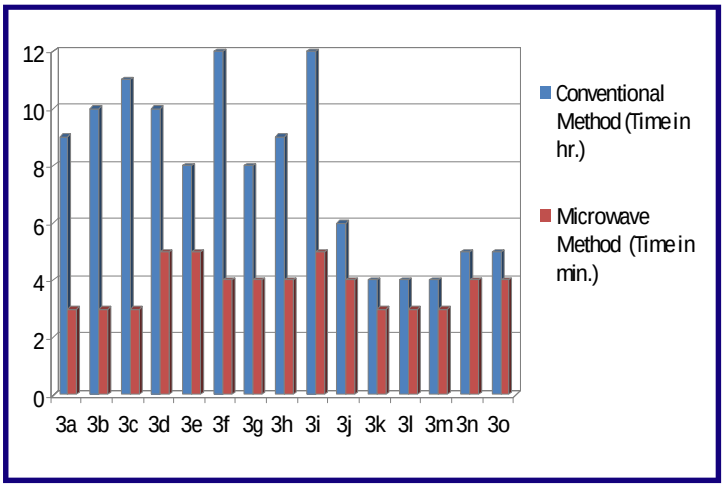


Figure 1: Comparison of time required to complete reaction under the microwave and conventional.

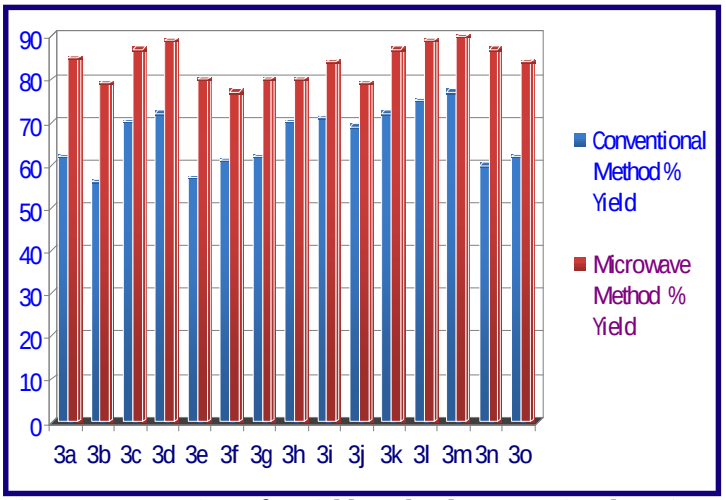


Figure 2: Comparison of % yields under the conventional & microwave Method

wave power of 180W and 360W are more appropriate choices for the reaction. Hence, the optimum microwave reaction conditions were determined using 180 and 360W microwave power and neat and wetting with (ß-ethoxyethanol. In the absence of wetting reagent, the reaction yields less amount of final compound. It is understood that the reaction yield was increased by wetting reagent (increases the

polarity of the reaction medium). The method works well for the reaction type amines & aldehydes and imine compounds were prepared in high yields and short reaction times so this method found more effective and environment friendly.

This research work reveals that, the optimum microwave reaction conditions for synthesis of novel Schiff bases by using a wetting reagent (ß-ethoxyethanol) were in between 180 and 360W microwave power. Our findings are also parallel to previous work down by Yunus Bekdemir et al & Bhusnur Omprakash et al on synthesis of imines using a wetting reagent (ß-ethoxyethanol). The method works well for the reaction type amines & aldehydes and Schiff bases compounds were prepared in high yields and short reaction times so this method is more easy, effective, economical, fast and environment friendly.

All the results such as reactions time, yields, Rf factor, elemental analysis and melting points of the compounds were presented in Table 3 & Table 4. In addition, the comparison of % yields and time required for the completion of reaction for imines by microwave and conventional conditions were expressed graphically in Fig. 1 & Fig. 2.

Table 4. Comparison of % yield and reaction time required to complete the reaction by conventional and microwave methods for synthesis of Schiff bases compound (3a-o).

Compound No.	Reaction time required		% Yield	
	Conventional Method (hrs.)	Microwave Method (min.)	Conventional Method (%)	Microwave Method (%)
3a	09	03	62	85
3b	10	03	56	79
3c	11	03	70	87
3d	10	05	72	89
3e	08	05	57	80
3f	12	04	61	77
3g	08	04	62	80
3h	09	04	70	80
3i	12	05	71	84
3j	06	04	69	79
3k	04	03	72	87
3l	04	03	75	89
3m	04	03	77	90
3n	05	04	60	87
3o	05	04	62	84

3. *In-vitro* antibacterial activity by cup plate method

The *In-vitro* antibacterial activity results presented in Table 5 conclude that the majority of the compounds tested showed good antibacterial activity against both Gram positive and Gram negative bacteria by zone of inhibition at concentration 50 µg/ml and 100 µg/ml respectively. Among the entire compound tested, 3e was equipotent against E.coli; 3h was equipotent against *P. Aeruginosa;* and *S. Aureus;* 3b showed equipotent activity against *B. Subtilies* at varied concentration of 50-100 µg/ml.

Table 5. Showing *In-vitro* Antibacterial activity by cup plate method

Compd No.	Zone of inhibition in mm							
	Gram negative bacteria				Gram positive bacteria			
	E. coli		*P.aeruginosa*		*S. aureus*		*B. subtilis*	
	50µg	100 µg	50 µg	100 µg	50µg	100 µg	50µg	100 µg
3a	08	16	12	21	07	16	08	15
3b	07	17	13	19	06	15	16	25
3c	06	12	14	22	14	26	12	20
3d	14	25	14	23	15	23	14	23
3e	15	26	13	20	15	21	11	19
3f	11	20	14	22	16	21	09	18
3g	11	19	13	24	14	21	10	20
3h	08	18	13	25	13	25	12	21
3i	14	24	11	22	10	19	14	23
3j	13	23	12	24	12	23	12	21
3k	NT	NT	NT	NT	NT	NT	NT	NT
3l	12	18	06	12	13	24	09	18
3m	09	20	07	16	18	14	09	19
3n	11	21	09	19	12	21	14	23
3o	10	20	10	18	11	19	12	20
Ampicilline	16	26	17	25	15	25	16	26
DMF (Control)	-	-	-	-	-	-	-	-

(-ve) indicate no zone of inhibition.

CONCLUSION

Our present work brings forth a novel method for the synthesis of fifteen Schiff bases 3a–o using microwave irradiation and conventional method and comparison offers significant improvements in % yield and reaction time interval. This simple microwave technique affords various Schiff base with short reaction times, excellent yields and without formation of undesirable side products. From data of antimicrobial activity, it could be observed that compounds 3e,3h and 3b showed good equipotent activity against *P. Aeruginosa, S. Aureus and B. Subtilies* at varied concentration of 50-100 µg/ml. Microwave assisted synthesis could be used as an important tool for the synthesis of various medicinally important agents.

The developed simple microwave assisted solvent-free method for the synthesis of Schiff bases using a wetting reagent (ß-ethoxyethanol) were found more efficient on overall performance compare to conventional method as desired. The microwave irradiation technique led to improvement in the yield of all the target compounds with reduction in their reaction byproducts. The microwave process also substantially reduced the overall process time as expected, by reduction in reaction time against the described conventional method.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests regarding the publication of this paper.

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ABBREVIATIONS

%: Percentage ,**Mol:** Mole,**min:** Minute,**s:** Second,**IR:** Infrared, **NMR:** Nuclear Magnetic Resonance, **cm^{-1}:** Per Centimeter,**KBr:** Potassium bromide , **^{1}HNMR:** Proton Nuclear Magnetic Resonance, **$CDCl_3$-d1:** Chloroform-δ1,**DMSO-d6**:Dimethylsulfoxide-δ6,**TMS:** Tetramethyl silane , **g:** Gram , **TLC:** Thin Layer Chromatography, **^oC:** Degree Celsius, **DMF:** Dimethylformamide, **W:** Watt, **ß-EE:** ß -ethoxyethanol, **s:** Singlet, **m:** Multiple Peak , **q:** Quadrate Peak , **t:** Triplet Peak, **MS:** Mass Spectroscopy, **M^+:** Molecular Ion Peak,**m/z:** Mass to Charge ratio, **R_f:** Retention Factor, **$CDCl_3$:** Chloroform, **ppm:** Part Per Million , **hr:** Hour, **Fig.:** Figure, **MORE:** Microwave assisted organic reaction enhancement.

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