Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2015, 7(12):720-726

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Microwave-assisted organic synthesis of some novel fluorophenyl morpholine benzene sulfonamide schiff bases and their biological studies

Loganathan Velupillai and Dhananjay V. Mane*

Department of Chemistry, Dr. Babasaheb Ambedkar Marathwada University, Aurangabad, Maharashtra, India

---

ABSTRACT

A revolution method of microwave assisted organic synthesis is one of the major roles for synthesis of new drug molecules. Considering the benefits of microwave organic synthesis we have synthesized 12 novel Schiff base compounds (10 E-10 P) of 2-amino-N-[3-fluoro-4-(morpholin-4-yl) phenyl] benzene-1-sulfonamide derivatives from commercially available 3,4-Difluoronitrobenzene. The existing conventional heating method consumes 16-24 hours, but utilizing microwave irradiation method the reaction occurs faster and the time reduced to 4–6 minutes. The structure confirmation of all the synthesized molecules was confirmed by means of ^{1}HNMR and MS study. The synthesized NCE's were further tested for their antibacterial and antifungal studies. Some of the molecules were showed better antibacterial and antifungal activity.

Keywords: Benzene-1-sulfonamide, Schiff base, Microwave, Antibacterial, Antifungal Activity.

INTRODUCTION

Microwave[1-6] oven is a better instrument for synthetic organic chemistry for fast growing drug discovery research area. Since the first study of microwave assisted organic synthesis in 1986. As a result, modern scientific microwave apparatus is the ability to control reaction conditions very specifically, monitoring temperature, pressure and reaction times. Several methods have been developed for performing reactions using microwaves including solvent free conditions. In case the reaction conducted in a solvent, the media should have high dielectric constant which to take advantage effect on micro wave heating reaction. To this conclusion, solvents like ethanol (ϵ=24.3) were employed as better solvent for conducting the reaction. Microwave irradiation has been used extensively and successfully with homogeneous solution-phase reactions include standard organic reactions in which all reagents are dissolved in the solvent[7].

The advantage of microwave irradiation for the synthesis of organic molecules showed to be a simple, safe, low pollution, eco-friendly technique, simple work-up, efficient, shorter reaction time and high yields. Additionally, Microwave synthesis gives organic chemists more time to expand their scientific creativity in medicinal chemistry. Instead of spending hours or even days synthesizing a single compound, chemists can now perform that same reaction in minutes.

The sulfonamide compounds contain sulfur in a (-SO_2NH-) moiety directly attached to a benzene ring. The sulfonamide drugs were developed in 1930 for effective medicines against the bacterial disease. It seems as miracle drug at a time of large number of people dead because of common[8] bacterial disease like pneumonia and blood poisoning. The sulfonamide derivatives widely used in variety of biological actions[9], including for antibacterial,

antitumour, diuretic and antithyroid activities. The Schiff base[10] is the compound which containing an imine group (-CH=N-) in their structure, these are usually prepared by reacting of primary amine with active carbonyl compound [11]. The presence of Schiff bases in drug moiety are produces better biological activity. From these ideas we have introduced the imine and sulfonamide functional group into our organic molecule to produce better biological activity.

The different literature survey shows that the organic molecule containing the morpholine[12-16] and fused ring morphline[17-24] produce better biological profile in verity of therapeutic field like antiviral, antimicrobial, antimalarial, antibacterial[25], anticancer, antifungal[26], anti-Inflammatory, antidiabetic etc. So the morpholine derivatives are extensively very essential in the medicinal chemistry[27] part, which induce research activity in the field of the broad range of biological activity [28] study. It is well known that the introduction of fluorine[29-32] atom into organic molecule causes dramatic changes in its biological profile, mainly due to high electro negativity of fluorine causes increase lipid solubility. Hence, in the present study, some new derivatives have been synthesized considering the importance of the functional group and fluorine element.

The present paper, reports the remarkable fast synthesis of Schiff base were carried out by the simple mixing of equimolar amounts of 2-amino-*N*-[3-fluoro-4-(morpholin-4-yl) phenyl] benzene-1-sulfonamide and corresponding aldehyde in minimum quantity of ethanol (2 volume), were irradiated in a microwave oven at 320W for 4–6 min at 65°C. The results were summarized in Table-1. Their characterization was done by spectroscopic methods like ^{1}HNMR and mass spectral data. Further, antibacterial and antifungal activities of these derivatives have been studied and the results were summarized in Table-2.

EXPERIMENTAL SECTION

All the reagents and the solvents were used as obtained from the supplier or recrystallized/redistilled as necessary. The moiety 3,4-Difluoronitrobenzene[33-38] is commercially available and is also in Sigma Aldrich. This can be also synthesized as per reported literature. Melting points were recorded on open capillary melting point apparatus and are uncorrected. Mass spectra were recorded on 'LCMS-QP2010s' instrument by direct injection method. Nuclear Magnetic Resonance spectra (^{1}HNMR) Were recorded in DMSO-d_6 & $CDCl_3$ on Bruker advance spectrometer at 400MHz using Tetramethylsilane (TMS) as internal standard and the chemical shift (δ) are reported in parts per million. The purity of the synthesized compounds was checked by Thin Layer Chromatography, Merck pre-coated plates (silica gel 60 F254) were visualized with UV light. Fungus Culture: Candida sp. Gram-positive microorganisms: Staphylococcus aureus, Staphylococcus albus, Streptococcus faecalis, Bacillus sp and Gram-negative microorganisms: Klebsiella pnuemoniae, Escherichia coli, Pseudomonas sp, Proteus sp were used for biological activity.

Antimicrobial Activity: The antimicrobial activity of all synthesized compounds (10 E- 10 P) was examined by standard literature procedure using agar diffusion method by finding the zone of inhibition of the drug sample against the standard drugs. Compounds were taken as test samples along with a standard drug Ciprofloxacin sample. 10 mg of each test compound was dissolved in 1 ml of Dimethylsulphoxide for preparing stock solution of standard drugs. The organisms employed in the in vitro testing of the compounds were gram-positive and gram-negative. Procedure for the preparation of inoculum for all the organisms was same. The inoculum was prepared from a 24-hours old growth of organism on Nutrient agar slant. With the help of sterile nichrome wire loop, the growth of the organism on slant was aseptically transferred to a tube containing sterile distilled water. The contents of the tube were then shaken properly so as to get uniform cell suspension of the organism. Optical density the innoculum was adjusted to 0.6 on the photoelectric colorimeter by using sterile distilled water, before using it as an inoculum.

The medium, 1.5 g of Nutrient agar (Microbiology grade, Hi Media) was dissolved in 100 ml of sterile distilled water. 3 g of Poloxomer 182 was added as a surfactant to the media to prevent the drug precipitation. 20 ml of this stock solution was transferred to each Petri plate. On to each Petri plate containing 20 ml of sterile Nutrient agar 0.1 ml of an authentic culture (corresponding to 5 X 10 ^{15} CFU/ml.) of test organisms was spread. Four bore wells were bored on each Petri plate and 5-20 µl of the stock solution was added to it. This corresponds to concentration range of 30 µg/ml of the test compound. The tests were carried out in duplicate. Apart from putting the controls of standard drug (Ciprofloxacin), controls with dimethylsulphoxide (positive control) and without dimethylsulphoxide (negative control) were also included in the test. The Petri plates were put in the dark conditions at 37^{0}C for 24 hours. At the end of incubation period, the results were interpreted by finding the zone of inhibition.

Antifungal Activity: The antifungal activity of all synthesized compounds (10 E- 9 P) screened against Candida sp in dimethylsulfoxide. Fluconazole was employed as standard drug during the test procedures as references. 10 mg of each test compound was dissolved in 1 ml of Dimethylsulphoxide. 3 gm of Saboraud`s dextrose agar (microbiology grade, Hi Media LABORATORY) was dissolved in 100 ml of sterile distilled water. 3 g of Poloxomer 182 was added as a surfactant to the media to prevent the drug precipitation.

On to each Petri plate containing 20 ml of sterile Saboraud`s dextrose agar (microbiology grade, Hi Media LABORATORY) 0.1 ml of an authentic culture (corresponding to 5 X 10^{15} CFU/ml.) of test organisms was spread. Four bore wells were bored on each Petri plate and 5-20 µl of the stock solution was added to it. This corresponds to concentration range of 30 µg/ml of the test compound. The tests were carried out in duplicate. Apart from putting the controls of standard drug (Fuconazole), controls with dimethyl sulphoxide (positive control) and without dimethyl sulphoxide (negative control) were also included in the test. The test tubes were put in the dark conditions at room temperature for 48 hours. At the end of incubation period, the results were interpreted by finding the zone of inhibition.

EXPERIMENTAL

Preparation of 4-(2-fluoro-4-nitrophenyl)morpholine (A): The 3,4-Difluoronitrobenzene (15g, 94mmole) was added to the solution of Morpholine (9.85g, 113mmole), N-Methyl Morpholine (14.28g, 141mmole) in Chloroform (150ml) and the mixture was stirred for 16 hr at reflux. After completion of reaction, the solution was evaporated in vacuum and the residue was suspended in water (1500ml). Stirred for 3hr at room temperature. Filtered and washed with water (30ml), after drying yielded the titled product (A) as yellow color solid.

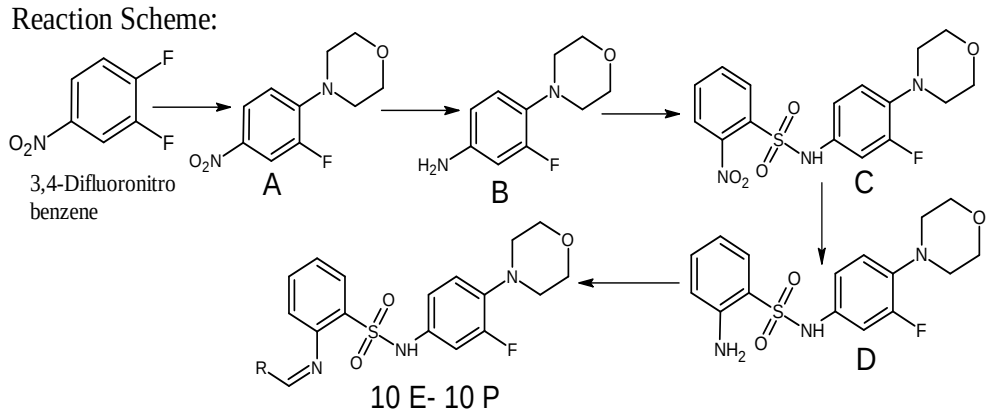


Figure 1: Synthesis of 2-amino-*N*-[3-fluoro-4-(morpholin-4-yl)phenyl]benzene-1-sulfonamide and their derivatives

Preparation of 3-fluoro-4-(morpholin-4-yl)aniline (B): The methanol (150ml), compound (A) (15g, 66mmole) and 10% palladium on carbon catalyst (1.5g) was charged into the hydrogenation parr shaker reactor, 30 PSI hydrogen gas pressure applied and the mixture was stirred for 4 hr at room temperature. After completion of reaction, the reaction mass filtered through hyflo bed washed with methanol (20ml). The filtrate was evaporated under vacuum. Yielded the titled product (B) as brown solid.

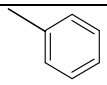
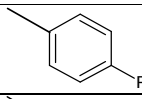
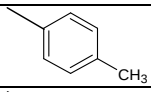
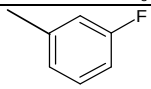
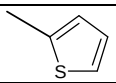
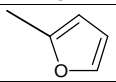
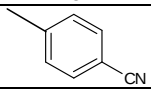
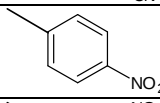
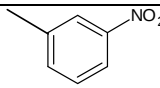
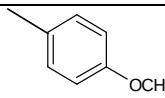
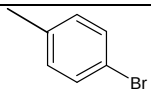
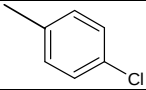
Preparation of *N*-[3-fluoro-4-(morpholin-4-yl)phenyl]-2-nitrobenzene-1-sulfonamide (C): The 2-Nitrobenzenesulfonyl Chloride (11.85g, 53mmole) in Dichloromethane (50ml) was added to the solution of compound (B) (10g, 50mmole), Triethylamine (7.72g, 76mmole) in Dichloromehane (50ml) at 0°C and the mixture was stirred for 1hr at 0°C. After completion of reaction, the solution was evaporated in vacuum and the residue was suspended in water (100ml). Stirred for 2hr at room temperature. Filtered and washed with water (20ml), after drying yielded the titled product (C) as white color solid.

Preparation of 2-amino-*N*-[3-fluoro-4-(morpholin-4-yl)phenyl]benzene-1-sulfonamide (D): The N,N-Dimethylformamide (60ml), Dichloromethane (60ml), compound (C) (15g, 39mmole) and 10% palladium on carbon catalyst (3g) was charged into the hydrogenation parr shaker reactor, 30 PSI hydrogen gas pressure applied and the mixture was stirred for 8 hr at room temperature. After completion of reaction, the reaction mass filtered through

hyflo bed washed with Dichloromethane (30ml). The filtrate was evaporated under vacuum and the residue was suspended in Diethylether (150ml). Stirred for 2hr at room temperature. Filtered and washed with diethylether (30ml), after drying yielded the titled product (D) as white color solid.

General method for the synthesis of compounds (10 E – 10 P): The equimolar amounts of compound (D) (1mol.Eq) and corresponding aldehyde (1mol.Eq) in minimum quantity of ethanol (2volume) were taken in small single neck round bottom flask. The reaction mixture was irradiated at 320W for 4–6 min in microwave at 65°C. The progress of reaction was monitored on TLC. After completion of reaction, allowed to cool RT, the crude solid product was collected through filtration and washed with ethanol. The crude product was recrystallized by 10 volume of ethanol and after drying yielded the titled product (10 E – 10 P) as white color solid.

Table1: Physical data of synthesized compounds (10 E – 10 P)

S.No	Code	-R	Molecular Formula	M.wt	M.P (°C)	% Yield
1	10 E		$C_{23}H_{22}FN_3O_3S$	439.50	176-179	86
2	10 F		$C_{23}H_{21}F_2N_3O_3S$	457.49	184-187	89
3	10 G		$C_{24}H_{24}FN_3O_3S$	453.52	186-189	92
4	10 H		$C_{23}H_{21}F_2N_3O_3S$	457.49	191-194	82
5	10 I		$C_{21}H_{20}FN_3O_3S_2$	445.53	195-198	94
6	10 J		$C_{21}H_{20}FN_3O_4S$	429.46	182-185	92
7	10 K		$C_{24}H_{21}FN_4O_3S$	464.51	189-192	88
8	10 L		$C_{23}H_{21}FN_4O_5S$	484.50	209-212	96
9	10 M		$C_{23}H_{21}FN_4O_5S$	484.50	216-219	93
10	10 N		$C_{24}H_{24}FN_3O_4S$	469.52	171-174	83
11	10 O		$C_{23}H_{21}BrFN_3O_3S$	518.39	188-191	85
12	10 P		$C_{23}H_{21}ClFN_3O_3S$	473.94	177-180	81

RESULTS AND DISCUSSION

The results are obtained from various spectral data are results discussed below.

4-(2-fluoro-4-nitrophenyl)morpholine (A):
Yellow color solid; Yield 86%; M.W: 226.2; Mol. For: $C_{10}H_{11}FN_2O_3$; LC-MS (m/z): 227.2 (M+1); ^{1}HNMR (400MHz, DMSO-d_3): δ 8.05-8.01 (1H, m), 7.18 (2H, t, J=8.8 Hz), 3.75 (4H, t, J=5.2 Hz), 3.27 (4H, t, J=4.8 Hz).

3-fluoro-4-(morpholin-4-yl) aniline (B):
Brown solid; Yield 97%; M.W: 196.2; Mol. For: $C_{10}H_{13}FN_2O$; LC-MS (m/z): 197.2 (M+1); ^{1}HNMR (400MHz, DMSO-d_3): δ 6.76 (1H, t, J= 9.6 Hz), 6.36-6.29 (2H, m), 5.01 (2H, s), 3.68 (4H, t, J=4.4 Hz), 2.80 (4H, t, J=3.6 Hz).

***N*-[3-fluoro-4-(morpholin-4-yl)phenyl]-2-nitrobenzene-1-sulfonamide (C):**
white color solid; Yield 76%; M.W: 381.3; Mol. For: $C_{16}H_{16}FN_3O_5S$; LC-MS (m/z): 382.2 (M+1); ^{1}HNMR (400MHz, DMSO-d_3): δ 10.21 (1H, s), 7.80-7.89 (3H, m), 6.96 (2H, d, J=8.8 Hz), 6.82 (2H, d, J=9.1 Hz), 3.67 (4H, t, J=5.2 Hz), 3.02 (4H, t, J=4.4 Hz).

2-amino-*N*-[3-fluoro-4-(morpholin-4-yl)phenyl]benzene-1-sulfonamide (D):
white color solid; Yield 91%; M.W: 351.39; Mol. For: $C_{16}H_{18}FN_3O_3S$; LC-MS (m/z): 352.1 (M+1); ^{1}HNMR (400MHz, DMSO-d_3): δ 9.72 (1H, s), 7.35-7.26 (3H, m), 6.71-6.79 (4H, m), 5.92 (2H, s), 3.66 (4H, t, J=4.4 Hz), 2.96 (4H, t, J=4.4 Hz).

***N*-(4-morpholino-3-fluorophenyl)-2-[benzylideneamino]benzene-1-sulfonamide (10 E):**
white color solid; Yield 86%; M.W: 421.51; Mol. For: $C_{23}H_{23}N_3O_3S$; LC-MS (m/z): 322.3 (M+1); ^{1}HNMR (400MHz, DMSO-d_3): δ 7.81 (1H, s), 7.30-7.54 (6H, m), 7.12-7.15 (1H, m), 6.69-6.89 (4H, m), 6.56 (1H, m), 3.65 (4H, t, J=4.8 Hz), 3.00 (4H, t, J=4.4 Hz).

***N*-(4-morpholino-3-fluorophenyl)-2-[(4-fluorophenyl)methylidene]amino}benzene-1-sulfonamide (10 F):**
white color solid; Yield 89%; M.W: 457.49; Mol. For: $C_{23}H_{21}F_2N_3O_3S$; LC-MS (m/z): 458.2 (M+1); ^{1}HNMR (400MHz, DMSO-d_3): δ 8.08 (1H, s), 7.03-7.78 (6H, m), 6.50-6.87 (5H, m), 3.65 (4H, s), 3.01 (4H, s).

***N*-(4-morpholino-3-fluorophenyl)-2-[(4-methylphenyl)methylidene]amino}benzene-1-sulfonamide (10 G):**
white color solid; Yield 92%; M.W: 453.52; Mol. For: $C_{24}H_{24}FN_3O_3S$; LC-MS (m/z): 454.3 (M+1); ^{1}HNMR (400MHz, DMSO-d_3): δ 8.92 (1H, s), 7.01-7.69 (7H, m), 6.45-6.78 (5H, m), 3.64 (4H, s), 3.00 (4H, s), 2.21 (3H, s).

***N*-(4-morpholino-3-fluorophenyl)-2-[(3-fluorophenyl)methylidene]amino}benzene-1-sulfonamide (10 H):**
white color solid; Yield 82%; M.W: 457.49; Mol. For: $C_{23}H_{21}F_2N_3O_3S$; LC-MS (m/z): 458.1 (M+1); ^{1}HNMR (400MHz, DMSO-d_3): δ 8.93 (1H, s), 7.03-7.49 (6H, m), 6.43-6.58 (6H, m), 3.64 (4H, t, J=4.8 Hz), 3.01 (4H, t, J=4.8 Hz).

***N*-(4-morpholino-3-fluorophenyl)-2-[(thiophen-2-yl)methylidene]amino}benzene-1-sulfonamide (10 I):**
white color solid; Yield 94%; M.W: 445.53; Mol. For: $C_{21}H_{20}FN_3O_3S_2$; LC-MS (m/z): 446.2 (M+1); ^{1}HNMR (400MHz, DMSO-d_3): δ 8.89 (1H, s), 6.71-7.89 (11H, m), 3.61 (4H, s), 2.91-3.01 (4H, m).

***N*-(4-morpholino-3-fluorophenyl)-2-[(furan-2-yl)methylidene]amino}benzene-1-sulfonamide (10 J):**
white color solid; Yield 92%; M.W: 429.46; Mol. For: $C_{21}H_{20}FN_3O_4S$; LC-MS (m/z): 430.3 (M+1); ^{1}HNMR (400MHz, DMSO-d_3): δ 8.89 (1H, s), 8.39 (1H, s), 6.31-7.78 (10H, m), 3.65 (4H, t, J=4.8 Hz), 2.95-3.03 (4H, m).

***N*-(4-Morpholino-3-fluorophenyl)-2-[(4-cyanophenyl)methylidene]amino}benzene-1-sulfonamide(10 K):**
white color solid; Yield 88%; M.W: 464.51; Mol. For: $C_{24}H_{21}FN_4O_3S$; LC-MS (m/z): 465.2 (M+1); ^{1}HNMR (400MHz, DMSO-d_3): δ 10.10 (1H, s), 9.08 (2H, s), 7.91 (1H, s), 7.84 (2H, d, J=8 Hz), 7.44-7.54 (3H, m), 7.13 (1H, d, J=8.4 Hz), 6.64-6.89 (3H, m), 3.65 (4H, t, J=4.4 Hz), 3.00 (4H, t, J=4.4 Hz).

***N*-(4-morpholino-3-fluorophenyl)-2-[(4-nitrophenyl)methylidene]amino}benzene-1-sulfonamide (10 L):**
white color solid; Yield 96%; M.W: 484.50; Mol. For: $C_{23}H_{21}FN_4O_5S$; LC-MS (m/z): 485.2 (M+1); ^{1}HNMR (400MHz, DMSO-d_3): δ 8.16 (2H, d, J=9.8 Hz), 7.92 (1H, s), 7.46-7.64 (4H, m), 7.15 (2H, d, J=8 Hz), 6.72-6.92 (4H, m), 3.66 (4H, t, J=4.4 Hz), 3.01 (4H, t, J=4.4 Hz).

***N*-(4-morpholino-3-fluorophenyl)-2-[(3-nitrophenyl)methylidene]amino}benzene-1-sulfonamide (10 M):**
white color solid; Yield 93%; M.W: 484.50; Mol. For: $C_{23}H_{21}FN_4O_5S$; LC-MS (m/z): 485.1 (M+1); ^{1}HNMR (400MHz, DMSO-d_3): δ 8.16 (2H, d, J=8.8 Hz), 8.10 (1H, s), 7.47-7.66 (3H, m), 7.17 (2H, d, J=8.4 Hz), 6.74-6.96 (4H, m), 3.66 (4H, t, J=4.4 Hz), 2.99 (4H, t, J=4.4 Hz).

***N*-(4-morpholino-3-fluorophenyl)-2-[(4-methoxyphenyl)methylidene]amino}benzene-1-sulfonamide (10 N):**
white color solid; Yield 83%; M.W: 469.52; Mol. For: $C_{24}H_{24}FN_3O_4S$; LC-MS (m/z): 470.2 (M+1); ^{1}HNMR (400MHz, DMSO-d_3): δ 8.91 (1H, s), 7.03-7.72 (7H, m), 6.43-6.76 (5H, m), 3.66 (4H, s), 3.91 (3H, s), 3.01 (4H, s).

***N*-(4-morpholino-3-fluorophenyl)-2-[(4-Bromophenyl)methylidene]amino}benzene-1-sulfonamide(10 O):**
white color solid; Yield 85%; M.W: 518.39; Mol. For: $C_{23}H_{21}BrFN_3O_3S$; LC-MS (m/z): 519.1 (M+1); ^{1}HNMR (400MHz, DMSO-d_3): δ 8.06 (1H, s), 7.05-7.81 (6H, m), 6.53-6.90 (5H, m), 3.66 (4H, s), 2.99 (4H, s).

***N*-(4-morpholino-3-fluorophenyl)-2-[(4-Chlorophenyl)methylidene]amino}benzene-1-sulfonamide(10 P):**
white color solid; Yield 81%; M.W: 473.94; Mol. For: $C_{23}H_{21}ClFN_3O_3S$; LC-MS (m/z): 474.3 (M+1); ^{1}HNMR (400MHz, DMSO-d_3): δ 8.02 (1H, s), 7.12-7.76 (6H, m), 6.50-6.67 (5H, m), 3.66 (4H, s), 3.01 (4H, s).

BIOLOGICAL EVALUATION

After the compounds synthesized the structure of the compounds are confirmed by MS and ^{1}NMR spectroscopy. Further the synthesized compounds are taken for their antibacterial and antifungal study as per standard literature procedure. After the biological study some of the synthesized compounds showed good antimicrobial activity inhibition. Antimicrobial screening results of the tested compounds are shown in Table 2. All the synthesized compounds showed moderate inhibitory activity and some compound showed superior antifungal activity inhibition. Antifungal screening results of the tested compounds are shown in Table 2.

Table 2: Antibacterial and Antifungal activity data of compounds (10 E – 10 P)

Compound No.	Inhibition Zone Diameter (mm)								
	I	**II**	**III**	**IV**	**V**	**VI**	**VII**	**VIII**	**IX**
10 E	17	25	26	24	23	26	22	27	29
10 F	15	26	22	18	19	18	21	26	31
10 G	15	22	24	16	23	17	21	24	28
10 H	16	21	24	14	22	26	24	26	29
10 I	13	24	26	25	23	24	26	29	28
10 J	15	26	20	21	24	19	28	25	26
10 K	16	27	21	19	18	18	27	22	26
10 L	11	24	24	23	26	23	21	17	24
10 M	17	25	23	22	23	22	26	22	30
10 N	13	26	19	19	19	19	22	22	28
10 O	15	25	19	22	22	24	28	26	26
10 P	12	19	22	23	24	25	25	19	30
Control (Solvent)	13	11	15	11	12	14	13	10	13
Ciprofloxacin	---	21	22	15	14	16	17	22	23
Fluconazole	15	---	---	---	---	---	---	---	---

Microbial Cultures Used to test antimicrobial Activity, Fungus Culture: I-Candida sp. Gram Positive Bacteria: II-Staphylococcus aureus, III-Staphylococcus albus, VIII-Streptococcus faecalis, IX- Bacillus sp. Gram Negative Bacteria : IV-Klebsiella pnuemoniae, V-Escherichia coli, VI- Pseudomonas sp, VII- Proteus s.

CONCLUSION

The synthesis of derivatives of 2-amino-*N*-[3-fluoro-4-(morpholin-4-yl) phenyl] benzene-1-sulfonamide Schiff bases (10 E – 10 P) was performed and their structures were confirmed by ^{1}HNMR, MS spectroscopy techniques. In addition, the newly synthesized compounds were screened for their antibacterial and antifungal activities. Here we observed that the introduction of Fluorine element in the organic molecule were increased the biological activity because of the fluorine atom has high electro negativity. We came to the conclusion after the synthesis, Characterization and their Biological activity. Some of them were found to possess good antifungal and antibacterial activity.

Also here, the main thing that we have used Microwave irradiation apparatus for the synthesis of desired organic compounds. Were we really surprised and very happy that the reaction is quickly (4–6 min at 65°C) completed because of the microwave apparatus instead using normal heating conventional methods. Also we have tried the same reaction by normal oil-bath heating method it was consumed around 16-24 hours. Also in the normal heating method we have observed that the formation of impurities more at 65°C and compound are getting colored. But in the microwave reaction method we got white compounds with good quality and quantity.

Acknowledgments
The authors are thankful to Head of the Department of Chemistry, Dr. Babasaheb Ambedkar Marathwada University, Aurangabad, Maharashtra, India for providing research facilities. The authors are also thankful to Head, Dept. Microbiology, Sub campus, Dr. Babasaheb Ambedkar Marathwada University, Aurangabad, Maharashtra for antimicrobial activity study.

REFERENCES

[1] A dela Hoz; A Loupy. Microwaves in organic synthesis, 2nd edition volume 2, bublished by Wiley-VCH, Weinheim-Germany, **2012**.
[2] S Ravichandran; E Karthikeyan. *International J. Chem Tech Research*., **2011**, 3(1), 466-470.
[3] R Gedye; F Smith; K Westaway et al . *Tetrahedron Letters.*, **1986**, 27(3), 279-282.
[4] http://en.wikipedia.org/wiki/Microwave_chemistry [Accessed twenty of October, **2015**].
[5] A de la Hoz; A Diaz-Ortiz; A Moreno. *Chemical Society Reviews*., **2005**, 34, 164-178.
[6] L Velupillai; PP Dixit; MS Shingare; BR Choudhari; DV Mane. *Int J Pharm Bio Chem*., **2015**, 4(3), 648-655.
[7] NE Leadbeater; HM Torenius. *J. Org Chem*., **2002,** 67(9), 3145-3148.
[8] http://www.encyclopedia.com/topic/sulfa_drug.aspx.
[9] M Alhassan; Z Chohan; A Scozzafava; C Supuran. *J Eur Inhib Med Chem*., **2004**, 19(3), 263-267.
[10] http://en.wikipedia.org/wiki/Hugo_Schiff [Accessed second of November, **2015**].
[11] G Kumari; D Kumari; C Singh; VB Regag. *J. Serb Chem Soc*., **2010**, 75(5), 629–637.
[12] Merck Index. Review of morpholine and its derivatives, 12th ed, Published by Merck & co, Whitehouse Station, NJ, **1996,** 1074-1075.
[13] L Velupillai; PP Dixit; MS Shingare; DV Mane. *Indo Ameri J pharm sci.*, **2015**, 2(3), 722-730.
[14] L Velupillai; PP Dixit; MS Shingare; DV Mane. *E* J Pharm Med Res., **2015**, 2(3), 269-282.
[15] L Velupillai; PP Dixit; MS Shingare; RB Choudhari; DV Mane. *E J Pharm Med Res*., **2015**, 2(4), 1099-1109.
[16] L Velupillai; MS Shingare; DV Mane. *Int J Pharm Bio Sci*., **2015**, 6(4), 340-348.
[17] P Mizar; B Myrboth. *Tetrahedron Letters*., **2006**, 47(44), 7823-26.
[18] S Sakami; K Kawai; M Maeda; T Aoki et al. *Bioorg Med Chem*., **2008**, 16(17), 7956-67.
[19] G Zhou; N Zorn; P Ting; R Aslanian et al. *Med Chem Lett*., **2014**, 5(5), 544-49.
[20] X Huang; D Pissarnitski; T Asberom et al. *Tetrahedron Letters*., **2012**, 53(47), 6451-55.
[21] L Velupillai; PP Dixit; MS Shingare; BR Choudhari; DV Mane. *World J pharm pharma sci*., **2015**, 4(8), 1413-1423.
[22] L Velupillai; PP Dixit; MS Shingare; RB houdhari; DV Mane. *Indo Ameri J pharm sci*., **2015**, 2(7), 1096-1102.
[23] L Velupillai; MS Shingare; DV Mane. *World J pharm pharma sci*., **2015**, 4 (2), 685-693.
[24] L Velupillai; PP Dixit; MS Shingare; DV Mane. *Amer J PharmTech Res*., **2015**; 5(1), 444-453.
[25] V Duhalde; B Lahillie; F camou et al. *Pathologie biologie.*, **2007,** 55(10), 478-81.
[26] C Marireau; M Guilloton; F Kartst. *Antimicrobial agents and chemo*., **1990**, 34(6), 989-93.
[27] M Chopra; VK Ahluwalia. Text Book of Medicinal Chemistry, 1st edition, Published by Ane's Books Pvt Ltd, New Delhi, **2008**.
[28] B Achari; BM Sukhendu; P Dutta et al. *Synlett*., **2004**, 14, 2449-67.
[29] D Gimemez; C Andreu; M Olmo et al. *Bioor Med Chem*., **2006**, 14(20), 6971-78.
[30] HJ Bohm; D Banner; S Bendels et al. *Chem biochem*., **2004**, 5(5), 637-43.
[31] JW Clader. *J. Med Chem*., **2004**, 47, 1-9.
[32] MA Massa; DP Spangler; RC Durley et al. *Bioor Med Chem Lett*., **2001**, 11, 1625-1628.
[33] S Keith; M Adam; GA Deboos. *J Org Chem*., **1998**, 63(23), 8448-8454.
[34] OA George; QI Wang; L Xing-Ya; B Imre. *Synthesis*., **1992**, 11, 1085-6.
[35] RD Chambers; J Hutchinson; ME Sparrowhawk et al. *J. Fluorine Chemistry*., **2000**, 102(1-2), 169-173.
[36] E Franz; S Willi. *Chemische Berichte*., **1991**, 124(1), 157-62.
[37] LM Agnes; Z Maria; D Carine; MJ Pierre; T Marc. *Advn Synt & Cat*., **2008**; 350(17), 2677-2682.
[38] Z Yun; JF Timothy; P Sejal; M Nello. *Organic Letters*., **2011**, 13(2), 280-283.