# Synthesis and biological evaluation of some Azetidinone derivatives

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**ABSTRACT:***An expeditious method for preparation of 2-Azetidinones under microwave irradiation is leveloped. This method has been assessed as greener methodology and found superior to conventional method with igher environmental factor. A series of five novel azetidinones were synthesized by cyclocondensation of various chiff bases of furfuryl amine with chloroacetylchloride in the presence of triethylamine. The newly synthesized ompounds are characterized by IR, 1H-NMR spectra. The synthesized compounds are evaluated for antibacterial nd antifungal activities .All the compounds showed good anti-bacterial activity against.Staphylococcus aureus nd E.coli.*

***Keywords:*** *Azetidinones, furfuryl amine, Schiff's base,anti-bacterial, anti-fungal*.

## I. INTRODUCTION

2-Azetidinones, commonly known as β-lactams, are well-known heterocyclic compounds among the organic and medicinal chemists. The activity of the known antibiotics such as penicillins, cephalosporins and carbapenems are attributed to the presence of 2-azetidinone ring in them. The broad and potent activity of 2-azetidinones has established them as one of the biologically important scaffold .Recently; other biological activities besides the antibacterial activity have been reported in compounds containing the 2-azetidinone ring [1]. The recent discoveries of some 1, 3, 4-trisubstituted-β-lactams as new potent cholesterol absorption inhibitors, human cytomegalovirus protease inhibitors and thrombin inhibitors justified a renewed interest in these compounds. Furthermore, interest in chemistry, synthesis and biology of 2-azetidinone pharmacophore continues to be researched due to their wide range of biological properties, such as antibacterial, ant hyperglycemic, antihyperlipidemic, CNS activity [1-5], tryptase inhibitory.

The utility of azetidinones as synthons for various biologically active compounds, as well as their recognition as antibacterial[6], anticonvulsant[7],antimicrobial[8], antitubercular[9], anti-inflammatory[10], anathematic[11] , anesthetic[12], antioxidant[13]. They also function as enzyme inhibitors [14] and are effective on the central nervous system [15]. The Staudinger's ketene-imine cycloaddition reaction [2+2] is the most common method for the synthesis of azetidinones and has been reviewed till date by several researchers. The reactions are carried out thermally or photo chemically using acid chlorides in the presence of triethylamine or α-diazoketones as ketene precursors. However the conventional methods reported for the synthesis of 2-azetidinones require longer reaction times (12–16 h reflux) at very low temperature (−70 to −90 °C) with low yields (less than 70%). The reactions also involve the use of a Dean-stark water separator for the removal of water from the reaction. The previous decade has also seen the use of microwave radiation in the synthesis of azetidinones. On the basis of the above findings and considering the need for the development of potent biologically active agents, we were stimulated to explore new simplified 2-azetidinone analogues. Here, in this paper, we are reporting the synthesis novel azetidinone analogues by a greener method

## II .MATERIALS & METHODS

All the chemicals and solvents were obtained from E-Merck, India (AR grade) and were used without further purification.

### METHODOLOGY

Due to environmental concerns, there has currently been an increasing demand for efficient synthetic processes and solvent –free reactions. Some old and new methodologies are being used to diminish and prevent pollution caused by chemical activities. Microwave-induced organic reaction enhancement (MORE) has gained popularity as

a non-conventional technique for rapid organic synthesis in the last few years and many researchers have described accelerated reaction rates, with a large number of papers that have appeared proving the synthetic utility of MORE chemistry in day to day organic synthesis. It can be termed as 'e-chemistry' because it is easy,effective, economical, and eco-friendly, and is believed to be a step toward achieving green chemistry objectives.Within the framework of 'Green Chemistry' we have now developed an environmentally benign and novel approach for the synthesis of azetidine-2-ones. The yields of synthesized compounds were found to be in the range of 60-80%

## SYNTHESIS OF SCHIFF BASE

Furfuryl amine (0.01mol) is treated with substituted aromatic aldehydes (0.01mol) in DMSO in microwave oven for 2-3 min and then mixture is cooled and poured in ice cold water to obtain Schiff bases (scheme-1).

## SYNTHESIS OF 2-AZETIDINONE DERIVATIVES

Schiff bases obtained in step 1 (0.01mol) in DMF on further treatment with base triethyl amine (0.01mol) and {acylated} with monochloroacetyl chloride (0.01 mol) as cyclising agent in microwave oven for 3 – 4mins to form 2-azetidinone (scheme-2).

## III.RESULTS AND DISCUSSION

A new method for the synthesis of various above azetidin-2-one derivatives using microwave irradiation offers significant improvements over existing procedures and thus helps facile entry into a synthesis of variety of azetidin-2-one derivatives. Also, this simple and reproducible techniques affords various azetidin-2-one derivatives with short reaction times, excellent yields, and without formation of undesirable side products. Thus

a series of five novel azetidinones are synthesized by cyclocondensation of various Schiff bases of furfuryl amine with chloroacetylchloride in the presence of triethylamine. Schiff's bases are prepared by the condensation of furfuryl amine with different aromatic aldehydes under microwave irradiation in DMSO solvent (scheme-1) and cyclocondensation of Schiff's bases with chloracetyl chloride in the presence of triethylamine and DMF under microwave irradiation resulted in the formation of corresponding azetidinone derivatives. (Scheme-2). The newly synthesized compounds are characterized by IR and 1H nmr spectra

Characteristic IR bands show several functional vibrational modes which confirm the completion of reaction.2-Azetidinone compound shows IR absorption bands at 3130-3010 cm-1 (Ar-H ), 1720-1700 cm-1 (C=O stretching) and 1360-1310 cm-1 (C-N stretching), .

.. In the 1H NMR spectra of compounds [5-10]Aromatic protons (Ar – H ) appeared as a cluster at δ 7.1 – 8.4 The doublet appearing in the region 4.1-4.4 ppm is due to CH – Cl proton The doublet in the region 3.6 3.9ppm is due the benzylic proton. Methylene protons appear as singlet at δ 2.88ppm.

**Scheme-1**

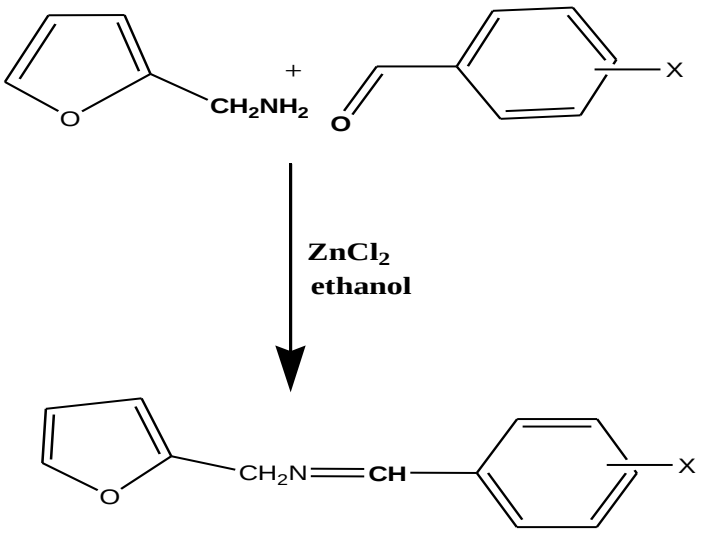


FIG.1.SCHIFF BASE

**Scheme-2**

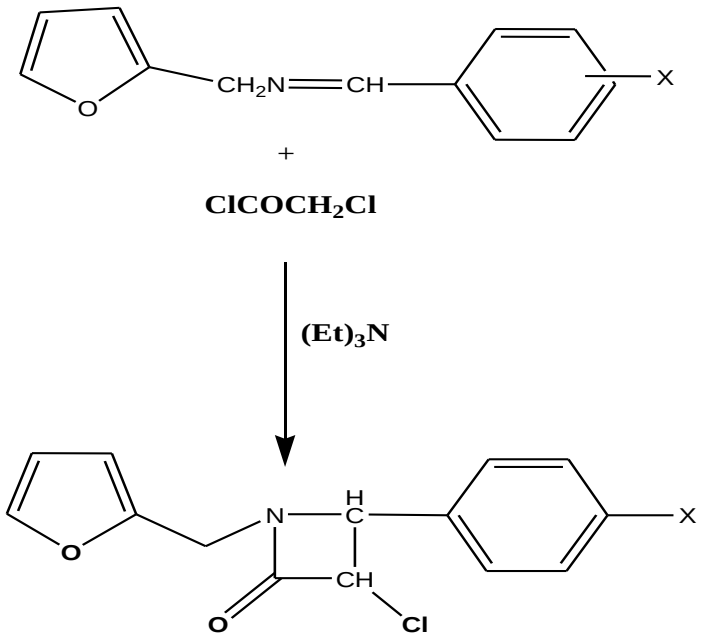


FIG.2. AZETIDINONE

Where
X = N, N-dimethyl, -CH3,-OCH3,-Cl and NO2.

**ANTIMICROBIAL ACTIVITY**

All the prepared compounds are screened for antimicrobial activity. From the microbial study it can be concluded that compounds bearing chloro, methoxy groups[cpd6&7] are more potent than remaining substituted compounds against staphylococcus auras[Table-1]. All the synthesized compounds exhibits very good activity against all the tested fungal strains.[Table-1]

**Table.1-Anti bacterial activity of azetidinone derivatives**

| Micro organism | Zone of Inhibition | | | | | |
|---|---|---|---|---|---|---|
| | 6 | 7 | 8 | 9 | 10 | Amikacin (std) |
| Salmonella typhi | 0.8 | 0.9 | 1.3 | 0.8 | 1.4 | 0.8 |
| Staphylococcus aureus | 1.4 | 1.2 | 1.0 | 0.9 | 0.8 | 1.0 |
| E.coli | 1.8 | 1.4 | 0.8 | 0.9 | 0.8 | 2.0 |
| Pseudomonas | 1.4 | 1.1 | 0.8 | 0.8 | 1.0 | 2.6 |

## CONCLUSION

An efficient and quick workup for preparation of 2-Azetidinones under microwave irradiation is developed.All the newly synthesized azetidinone derivatives were screened for antibacterial and anti fungal activities and are proved to be potent biologically active compounds.

## REFERENCE

[1]. Singh et al.,,,Arkivoc**(2007**)p.80-9
[2]. Chavan and Pai, Molecules **(2007)** p.2467.
[3]. Davis etal., Chem. Abstr**(2003)**p.375
[4]. Desai and Desai, Bioorg. Med. Chem**., (2006) p.8271**.
[5]. **Goel et al., J. Pharm. Pharm. Sci.,(2005)p.182.**
[6] A.Kaura, L.Sharama, V.J.Dhar, *Int. J. Chem. Sci.,* **2011,** 9,4, 2009.
[7] A.Rajasekharan, M.Periasamy, S.Venkatesan, *J. Dev. Biol. Tissue Eng.,* **2010**, 2,1, 5.
[8] .M. D.Basavaraj, S. M.Hipparagi, Munishamagowda. *IJPT*. **2011**, 3, 4, 3792.
[9] I.K.Bhat, S.K.Chaitanya, P.D.Satyanarayan, B. J.Kalluraya, *Serb. Chem. Soc.,* **2007,** 72, 5, 437.
[10] A.A.Chavan, N. R.Pai, *Molecules.* **2007,** 12, 2467.
[11] B.Mathew, G.E.Mathew, M.Vijayabaskaran, N.Mathew, *Der Pharma Chemica.,* **2010**, 2,6, 238.
[12]N.Ramalakshmi, R.Vijayakumar, K.Ilango, S.Arunkumar, A.Puratchikody, *Int.J.Chem.Sci*., **2008**, 6,3, 1213.
[13] P.Samadhiya, R.Sharma, S.Srivastava, S.K.Srivastava, *J. Sci. I. R. Iran.,* **2012**, 23, 2, 146.
[14] R. R.Kamble, T.Taj, T.Gireesh, B.V.Badami, *J.Chem.Sci.,* **2011**, 123,5, 657.
[15] Y.Vibhute, S.Chavan, S.Zangade, A.Vibhute, *European Journal of Chemistry*. **2013,** 4, 2, 98.