*Available online at* www.pelagiaresearchlibrary.com

Pelagia Research Library

Der Chemica Sinica, 2011, 2 (3):47-50

Pelagia Research Library
ISSN: 0976-8505
CODEN (USA) CSHIA5

# Microwave induced synthesis of some biologically active azetidinones

**Gunwanti Malhotra, Priya Gothwal and Y.K. Srivastava***

*P.G. Department of Chemistry, M.P. Govt. P.G. College, Chittorgarh, Rajasthan(India)*

---

## ABSTRACT

*Cyclcondensation of 3, 5-diaryl-2-pyrazoline-1- carbaldehyde hydrazones (2a-f)with chloroacetyl chloride yields 1-amino-4-(3,5-diaryl-2 pyrazoline -2-yl-)- azetidine -2-one using MAOS protocol. The Structure of these compounds were established on the basis of their elemental analysis, spectral data, m.m.p. and Co-TLC. The Newly synthesized compounds were evaluated for their antibacterial and antifungal activities.*

**Key Words:-** Schiff 's base , azetidinone MAOS Protocol, Cyclocondensation.

---

## INTRODUCTION

2-Azetidinone or β-lactums are well known class of heterocyclic compounds among organic and medicinal chemistry[1]. They are most prescribed antibiotic in medicine. Besides their antibiotic activity azetidinones are also known to exhibit some other types of biological activities[9], such as antibacterial[2,3] ,antimicrobial[4], antitubercular[5], local anesthetic[6], anti-inflammatory[7], anthelmintic[8], anticonvulsant[9], hypoglycemic agent[10]. They also function as enzyme inhibitors and are effective on central nervous system[11]. β-Lactum also serve as synthon for various biologically important classes of organic compounds[12].

The use of non conventional energy source for accomplishing the organic reaction is being continuously explored now a day. The usage of microwave irradiation for organic synthesis is of increasing interest, as it offers a number of advantages over conventional heating methods[13]. Microwave Assisted Organic Synthesis (MAOS) can be achieved conveniently and rapidly under solventless conditions and holds a strategic position as the common solvents are generally hazarduous, toxic, expensive and problematic to use. The reactions under microwave assisted solventless condition are ecofriendly and are a part of green chemical procedure[14-18].

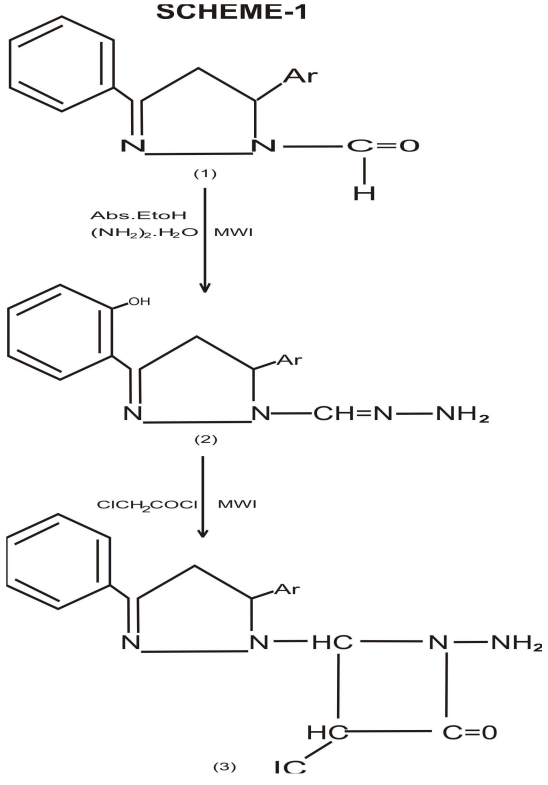
Keeping in view the advantages of MAOS protocol and pharmacological importance of azetidinone system, in the present investigation we report here in the synthesis and antimicrobial screening of some new azetidinone derivatives.

## MATERIALS AND METHODS

### General

All the melting points reported are uncorrected and were taken in open capillaries. The IR spectra (KBR, $cm^{-1}$) were recorded on shimudzu –spectrometer, PMR spectra ($CDCl_3$, δppm) were taken on Brucker DRX-600 spectrometer using TMS as internal standard and mass spectra (FAB) were recorded on Jeol SX-DA 600 mass spectrometer using m-nitro benzyl alcohol as matrix. The matrix peaks were observed at m/z 136, 137, 154, 289 and 301. The purity of compounds and progress of reaction was checked by TLC using silica Gel-G as adsorbent and benzene-ethyl acetate (9:1) as eluent. All the transformations were carried out in domestic micro wave oven (2450 MHz output, 800 watt power).

SCHEME-1




### General Procedure for Synthesis of l-amino-4-[3, 5-diaryl-2-prazoline-2-yl-]-azetidine-2-one. (3a-f).

3, 5-diaryl-2-pyrazoline-1-carbaldehyde hydrazone (2a-f) (0. 0l mol) and freshly prepared chloroacetyl chloride (0.015 mol) were mixed thoroughly to form a homogeneous paste. It was subjected to microwave irradiation at 800 watt for 2-3 minutes. After completion of reaction it

was cooled to room temperature. The reaction mixture was poured in ice cold water and left overnight in refrigerator. The separated solid was filtered off, washed with ice cold water and crystallized from ethanol to get crystals of (3a-f).

**Table – 1 Physical data of compound 2 and 3**

| Compd. | Ar | Molecular Formula (M.W.) | M.P. $^{o}$C | % Yield | Rxn Time (Min.) | %N | |
|---|---|---|---|---|---|---|---|
| | | | | | | Cal. | Found |
| 2a | Phenyl | $C_{16}H_{16}N_4O_2$ (280) | 164 | 80 | 7.0 | 20.00 | 19.80 |
| 2b | 4-OMephenyl | $C_{17}H_{18}N_4O_2$ (310) | 167 | 80 | 6.0 | 18.06 | 17.67 |
| 2c | 3, 4-DiOMephenyl | $C_{18}H_{20}N_4O_3$ (340) | 136 | 85 | 7.0 | 16.47 | 16.05 |
| 2d | 3, 4, 5-TriOMephenyl | $C_{19}H_{22}N_4O_4$ (370) | 120 | 70 | 7.0 | 15.13 | 14.88 |
| 2e | 4-ClPhenyl | $C_{16}H_{15}N_4OCl$ (314.5) | 185 | 75 | 8.0 | 17.80 | 17.08 |
| 2f | 4-$NMe_2$ Phenyl | $C_{18}H_{21}N_5O$ (323) | 148 | 70 | 8.0 | 21.67 | 21.11 |
| 3a | Phenyl | $C_{18}H_{17}N_4O_2Cl$ (356.5) | 130 | 75 | 2.0 | 15.70 | 15.11 |
| 3b | 4-OMephenyl | $C_{19}H_{19}N_4O_3Cl$ (396.5) | 135 | 80 | 2.0 | 14.12 | 13.78 |
| 3c | 3, 4-DiOMephenyl | $C_{20}H_{21}N_4O_4Cl$ (416.5) | 140 | 85 | 3.0 | 13.44 | 13.01 |
| 3d | 3, 4, 5-TriOMephenyl | $C_{21}H_{23}N_4O_5Cl$ (446.5) | 190 | 65 | 3.0 | 12.54 | 11.98 |
| 3e | 4-ClPhenyl | $C_{18}H_{16}N_4O_2Cl_2$ (390.0) | 160 | 75 | 2.0 | 14.35 | 14.01 |
| 3f | 4-$NMe_2$ Phenyl | $C_{20}H_{22}N_4O_4Cl$ (385.5) | 130 | 70 | 2.0 | 14.52 | 14.12 |

**Table – 2 Antibacterial screening of azetidinone (3a-f)**
( Zone of inhibition mm. )

| Compd. | Ar | Antibacterial activity. [Zone of inhibition (mm.)] | | | |
|---|---|---|---|---|---|
| | | E. Coli | P. Vulgaris | K. Pneumoneae | S. Aureus |
| | | | | | |
| 3a | Phenyl | + | ++ | + | + |
| 3b | 4-OMephenyl | ++ | ++ | + | + |
| 3c | 3, 4-DiOMephenyl | ++ | + | +++ | ++ |
| 3d | 3, 4,5-TriOMephenyl | ++ | ++ | + | + |
| 3e | 4-ClPhenyl | ++ | +++ | ++ | + |
| 3f | 4-$NMe_2$ Phenyl | + | ++ | ++ | ++ |
| | Ciprofloxacin(Std. Drug.) | ++++ | ++++ | ++++ | ++++ |

\+ = *<10mm*
++++ = *18-24mm*
++ = *10-14mm*
+++ = *14-18mm*

## RESULTS AND DISCUSSION

The identity of the products (3a – f ) obtained by Microwave irradiation procedure was confirmed on the basis of their elemental analysis and spectral data .

The IR spectra of these compounds gave prominent absorption bands at 3440 – 3400 $cm^{-1}$ ( -OH Stretching ), 1440, 1340 $cm^{-1}$ (N-N and C=N combined vibrations ),1680 ,1672 , $cm^{-1}$ ( >C = O stretching ) , 823 $cm^{-1}$ ( CH – Cl bending ) , The PMR spectra of the compound 3b gave signals as double doublets at δ3.01 – 3.015 ($C_4 – H_A$ ), δ3.60-3.90 ($C_4$-$H_B$) and δ4.20 – 4.50 ( $C_5 – H_X$ ) Confirming the presence of ABX pattern of pyrazoline ring . A singlet at δ8.10 for –

OH proton and a singlet at δ10.0 For – $NH_2$ protons was also observed. A doublet at δ5.5 for CH-Cl proton was observed

The mass spectra ( FAB ) of these compounds gave the molecular ion peak corresponding to their molecular masses .

The physical data of these compounds are tabulated in table -1.

**Antimicrobial Screening :-**
All the synthesized compounds were subjected to antibacterial activity against E. coli , P vulgaris . K. pneumoneae and S. aureus. Some of the compounds have shown prominent activity . ( Table -2 )

**Acknowledgment**
Authors are grateful to Dr. B.L. Verma Retd. Professor, MLSU, Udaipur for encouragement guidance and useful discussion.

## REFERENCES

[1] G.S. Singh, *Tetrahedron.* **2003**, 59, 7631.
[2] G.S. Singh, Rev. Mini. *Med. Chem.* **2004**, 4, 69.
[3] G.S. Singh, Rev.Mini. *Med. Chem*. **2004**, 4, 93.
[4] A.K.Khallafallah, M.A.Selim, R.M.A El – Hamd., M.A.Maghraby-El, H. A.Soleimon, M. A.Raslan, *Indian J. Chem.* **1995**, 34B, 1066.
[5] K.A.Parikh, P.S.Oza, and A.R. Parikh, *Indian J.Chem.* **2000**, 39B, 716.
[6] E.Costakes, G.Tastase, *Chem. Abst*.**1979**, 90, 203935q.
[7] D.Sreenivasa Rao, E.Jayachandran, G.M. Sreenivasa, B.Shivakumar, *Orient. J.Chem*. **2005**, 21(1), 113.
[8] G.M.Sreenivasa, B.Shivakumar, E.Jayachandran, *Indian Drugs.* **2006**, 43, 4.
[9] A.E.H.Abdel Ghany, H.A.W.Mohammad, *Acta Pharm.* **2003**, 53, 127.
[10] V.P.Chernykh, O.F.Sidorenko,*Chem. Abstr*. **1983**, 98, 89233.
[11] B.S.Vashi, D.S.Mehta, V.H Shah, *Indin J. Chem.* **1995**, 34B, 802.
[12] L.J.Conte, *Fluorine, Chem.* **1995**, 70, 175.
[13] S.Caddick, *Tetrahedron.* **1995**,51, 10403.
[14] R.S.Varma, *Green Chemistry.* **1999**, 1, 43.
[15] S.A.Gelena, *Chem. Soc. Rev.* **1997**,20,233.
[16] F.Langa, P.D.De Lacruz, and A.De CaHoz, *Contemp. Org. Synth.* **1997**, 373.
[17] A.K.Bose, M.S.Manhas, M.Ghosh and M.Shah, *J.Org. Chem.* **1991**, 56, (25), 6968.
[18] A.K.Bose, B.K.Banik, N.Lavlinskatia, M.Jayaraman and M.S.Manhas, *Chentech.* **1997**, 27, 18.