RJC
http://www.rasayanjournal.com

RASĀYAN *J. Chem.*
Vol.2, No.3 (2009), 641-644
ISSN: 0974-1496
CODEN: RJCABP

# ECO FRIENDLY MICROWAVE ASSISTED SYNTHESIS OF SOME 3-BENZIMIDAZOLYL -5- ARYL-2-PYRAZOLIN -1-CARBOXALDEHYDE HYDRAZONES AS POTENT ANTIMICROBIAL AGENTS

**Jayanti Rajora and Y.K. Srivastava ***
Department of Chemistry, M.P. Govt. P.G. College, Chittorgarh, 312001 (Raj) India
Email: jaya.rajora@gmail.com

**ABSTRACT**

The reaction of benzimidazolyl chalcons ( 1) with hydrazine hydrate in presence of formic acid afforded corresponding 3- benzimidazolyl -5 aryl -2-pyrazolin-1-carboxaldehyde (2) Which on treatment with hydrazine hydrate afforded the title compounds (3) in 80-89% yield under MWI condition. The newly synthesized compounds have been characterized on the basis of their elemental analysis and spectral data. Compounds (3) were screened for their antifungal and antibacterial activity in vitro. Results showed that all the compounds gave promising activity.
**Key words:** Benzimidazole, Pyrazoline, Carboxaldehyde; antifungal; antibacterial.

## INTRODUCTION

In recent years the chemical research has been focused on the eco friendly, environmentally, benign process to reduce the impact of environmental pollution. Green Chemistry [1-4] is placed in the frontier areas in this regard which involves the design, development and implementation of the performance criterion. Microwave Irradiation (MWI) [5-6] technique has gained popularity in past decade as a powerful tool for rapid, economic and efficient synthesis of variety of compounds because of selective absorption of Microwave energy by polar molecules[7]. The Application of MWI protocol to provide enhanced reaction rates, improved yields and cleaner products has been extended to modern drug discovery in complex multistep synthesis and is proving quite successful in the formation of variety of carbon hetero atom bonds. The solvent free solid phase synthesis Involving MWI exposure of neat reactants is applicable to rapid one pot assembly of heterocyclic compounds from insitu generated intermediate [8-10]. Literative survey reveals that benzimidazole derivatives play a vital role in biological field such as antidiabetic [11], antimicrobial [12], antiviral [13], antispasmodic [1]and anti cancer [15] activities. Keeping in view these facts some hydrazones containing benzimidazole moiety have been prepared under solvent less Microwave irradiation condition.

Benzimidazolyl chalcones (1) were treated with hydrazine hydrate in presence of the formic acid to get Intermediate 3- benzimidazolyl -5 aryl -2-Pyrazolin-1-Corboxaldehyde (2) . Compounds (2) were further reacted with hydrazine hydrate to afford 3-Benzimidazolyl -5- aryl-2-Pyrazolin -1-Corboxaldehyde Hydrazones in 80-89% yield. All the transformations were performed under solvent less MWI condition. The synthesized compounds have been characterized on the basis of their elemental analysis and spectral data.

## EXPERIMENTAL

All the melting points reported are uncorrected and were taken in open capillaries. IR Spectra (KBr, ν $cm^{-1}$) were recorded on Perkin Elmer spectrometer. PMR SPECTRA ($CDCl_3$ or $d_6$-DMSO δ ppm) were taken on Brucker – DRX-600 spectrometer using TMS as internal standard. Mass spectra (FAB) were recorded on Jeol-SX-DX-600 mass spectrometer using m-tetrobenzyl alcohol as matrix.

The Matrix peaks were observed at m/z 136,137,154.209 and 307. All the transformation were carried out in domestic Microwave oven (Samsung 1630 N, 600 Watt, 2450 MHz).

**Synthesis of 3- benzimidazolyl -5 aryl -2-Pyrazolin-1-carboxaldehyde (2 a-f):**
BenzImidazolyl chalcone ( 0.01 Mole), hydrazine hydrate ( 0.012 Mole) and formic acid ( 15ml), was mixed thoroughly to form a homogenous paste . It was subjected to MWI at 240 Watts for 4-6 Min. After completion of reaction the residue was washed thoroughly with water, dried and crystallized from benzene to get compounds (2a-f).
**Synthesis of 3-Benzimidazolyl -5- aryl-2-Pyrazolin -1-Corboxaldehyde Hydrazones (3 a-f):** Compounds ( 2 a-f) (0.01 Mole) and hydrazine hydrate ( 0.015 Mole) were mixed thoroughly and subjected to MWI for 3-6 Min. After complete reaction the residue was cooled to room temperature and poured on crushed ice. Separated solid was filtered, washed with water and crystallize from Benzene – alcohol as colorless crystals.

## RESULTS AND DISCUSSION

The IR Spectra of compounds (2 a-f) gave absorption bands at 3061-2960 $cm^{-1}$(C-H stret.), 1596-1495 $cm^{-1}$ (C=N and N-N combined vibration) and 1710 -1690 $cm^{-1}$ (-CHO) . The IR Spectra of compounds (3 a-f) showed absorption bands at 3040-2850$cm^{-1}$ (-CH stret.), 1470-1440 $cm^{-1}$ ( C=N and N-N Combined vibration ). The PMR Spectra of compounds (2a-f) gave prominent signals at δ3.29-3.36 (dd, C4-$H_a$), 3.83 -3.93 (dd, $C_4$-$H_b$), 5.46 -5.57 ( dd, $C_5$-$H_X$) confirming presence of ABX pattern of pyrazolin ring along with a singlet at 8.90 for aldehydic proton . The PMR Spectra of compounds ( 3a-f) gave signals at δ 3.23 -3.26 , 3.93-4.01 and 5.52-5.57 as double Doublet for $C_4$Ha, $C_4H_b$ and $C_5H_X$ protons of ABX system of pyrazoline ring the amino proton of hydrazone Amino Group were observed as singlet at δ 8.93. The Mass spectra of compounds (2a-f) and (3a -f) gave molecular ion peaks corresponding to their molecular masses.
**Antimicrobial activity:** Synthesized compounds (2a-f) and (3a-f) were screen for their anti fungal and antibacterial activity invitro at a concentration of 250 mg/ml. The Standard drugs used were Ciproflaxange and Fluncazole for antibacterial and antifungal activity respectively .The Screening results have shown that all the compounds possess good anti bacterial and anti fungal activity.

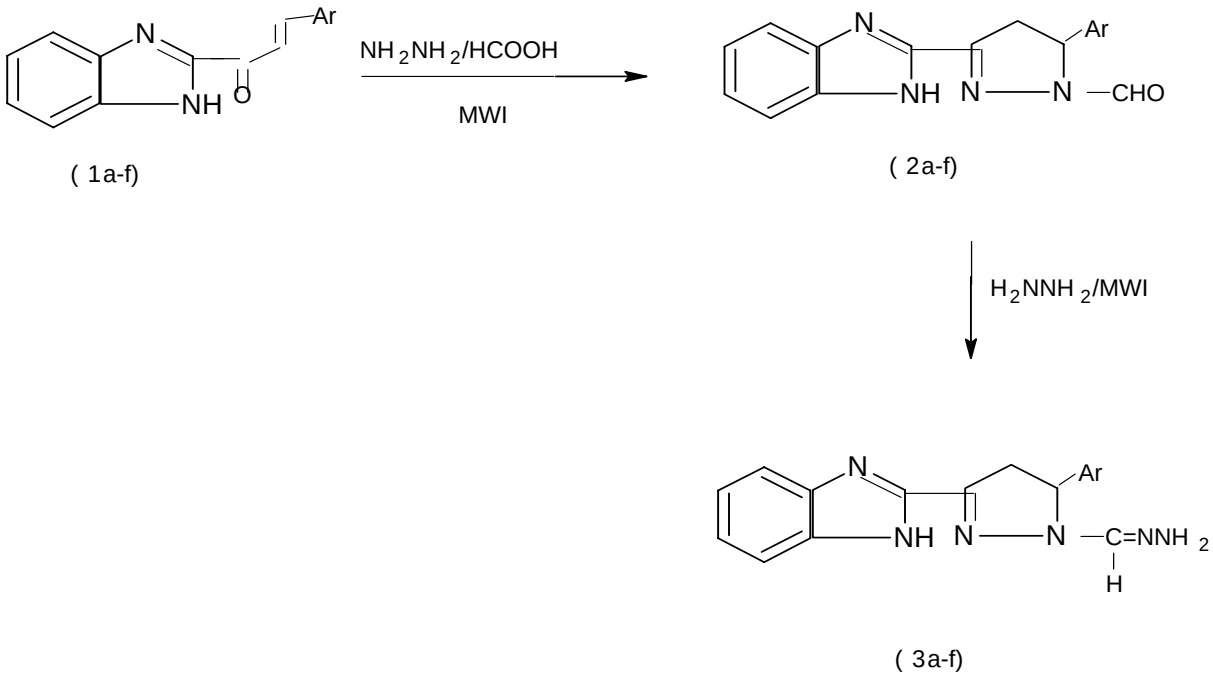
## ACKNOWLEDGEMENT

Authors are grateful to Dr. B.L. Verma (Retd. Prof., M.L.S University, Udaipur) for guidance, Valuable discussion and encouragement. Thanks are due to Head SAIF, CDRI Lucknow for Spectral analysis and Dr. Kanika Sharma, Deptt. of Microbiology M.L.S University Udaipur for antimicrobial screening.

## REFERENCES

1. P.T. Anastas , and J.C.Warner , Green Chemistry ; Theory and Practice , Oxford University Press , New York ,(1998)
2. R.S. Varma, ACS Symposium " Green Chemical synthesis and Processes , Chap 23, Pg 292-313, American Chemical Society , Washington D.C.( 2000).
3. R.S. Verma " Green Chemistry , Challenging Perspective" Oxford University Press , Oxford , Pg 221 ,( 2000)
4. R.S.Varma " Microwaves in Organic Synthesis , Chap. 6 , Wiley –VCH , Weinheim , PP 181 (2002)
5. R.S.Varma , Microwaves : Theory and application in material processing IV, American chemical society , Westerville , Ohio, PP 357 (1997)
6. S.K.Dewan, *Indian J. Chem.* , **45B**, , 2337 ,( 2006)
7. C.O.Kappe, *Aiyerv. Chem. Int. Ed.*,**43** ,6256(2004)

8. R.S.Varma ," Microwave Technology – Chemical applications ,Kirk- othmer Encyclopedia of Chemical Technology, 5th Edition (2004)
9. R.S.Varma "Advances in Green Chemistry , Chemical synthesis using Microwave irradiation , Astra -Zeneca Research Foundation , Bangalore India ( 2002)
10. C.O.Kappe , D.Kumar and R.S.Varma, *Synthesis* , 1795 ,( 1999)
11. B.B.Subudhi , P.K.Panda, T.Kundu , S.Saboo and D.Pradhan , *J.Pharm Res.*, **6** , 114(2007)
12. H.H.Fanny and S.H.abdelwad , *Molecule*, **8**, 1429,( 2000)
13. M.J.Tebbe and W.A.Spiyaer ,*J Med. Chem.*, **40** ,3937 ,(1997)
14. S.Aydin , K.Beis and D.D.Can, *Pharmazie* , **58,** 405,( 2003)
15. A.K.Bhat , H.Karadiya & M.R.Parmar ,*Indian J. Heterocyclic Chem.,* **13**,187,( 2003)




( 1a-f)

( 2a-f)

( 3a-f)

Scheme-1

Table-1 Physical Data of Compounds (2) and (3)

| Compd. | Ar | Molecular Formula | m.p. | % Yield | Reaction Time(min) | % N | |
|---|---|---|---|---|---|---|---|
| | | Mol. Weight | °C | | | Calculated | Found |
| 2a | Phenyl | $C_{17}H_{14}N4O$( 290) | 230 | 85 | 4.00 | 19.31 | 19.22 |
| 2b | 4-OMe Phenyl | $C_{18}H_{16}N_4O2$( 320) | 210 | 82 | 3.50 | 17.50 | 17.31 |
| 2c | 3-4di OMe Phenyl | $C_{19}H_{18}N_4O_3$(350) | 245 | 80 | 3.00 | 16.00 | 15.48 |
| 2d | 3-4-5 tri OMe Phenyl | $C_{20}H_{20}N_4O_4$(380) | 255 | 84 | 4.00 | 14.73 | 14.5 |
| 2e | 4-Cl-Phenyl | $C_{17}H_{13}N_4ClO$( 324.5) | 204 | 83 | 3.00 | 17.25 | 17.09 |
| 2f | 4-NMe2 Phenyl | $C_{19}H_{19}N_5O$( 333) | 190 | 83 | 3.00 | 21.02 | 20.87 |
| 3a | Phenyl | $C_{17}H_{16}N_6$( 304) | 160 | 85 | 4.00 | 27.63 | 27.08 |
| 3b | 4-OMe Phenyl | $C_{18}H_{18}N_6O$(334) | 198 | 85 | 3.00 | 25.14 | 24.98 |
| 3c | 3-4di OMe Phenyl | $C_{19}H_{20}N_6O_2$( 364) | 164 | 88 | 3.50 | 23.07 | 22.79 |
| 3d | 3-4-5 tri OMe Phenyl | $C_{20}H_{22}N_6O_3$( 394) | 105 | 89 | 4.00 | 21.31 | 21.05 |
| 3e | 4-Cl-Phenyl | $C_{17}H_{15}N_6Cl$(338.5) | 185 | 84 | 4.50 | 24.18 | 23.88 |
| 3f | 4-NMe2 Phenyl | $C_{19}H_{21}N_7$ (347) | 174 | 87 | 4.50 | 28.24 | 28.01 |

Table 2 Biological Screening Results of Compounds (2) & (3)

| | Zone Of Inhibition (mm) | | | | | |
|---|---|---|---|---|---|---|
| | Antibacterial | | | | Anti Fungal | |
| Compd. | E. Coli | P. Aeruginusa | B.Subtilis | K.Pneumoniae | Candida albicans | Aspergillus fumigatus |
| 2a | 15 | 18 | 8 | 7 | 17 | 14 |
| 2b | 16 | 19 | 4 | 7 | 18 | 5 |
| 2c | 15 | 15 | 5 | 7 | 15 | 14 |
| 2d | 13 | 12 | 5 | 9 | 16 | 18 |
| 2e | 15 | 17 | 9 | 10 | Nil | 9 |
| 2f | 10 | 11 | 4 | 7 | Nil | 13 |
| 3a | 17 | 15 | 16 | 9 | 19 | 15 |
| 3b | 11 | 10 | 9 | 5 | 19 | 10 |
| 3c | 13 | 12 | 16 | 10 | 18 | 13 |
| 3d | 15 | 12 | 12 | 2 | 18 | 11 |
| 3e | 15 | 15 | 17 | 10 | 17 | 12 |
| 3f | 13 | 17 | 16 | 8 | 16 | 10 |
| Std. Ciproflaxange | 20 | 23 | 21 | 24 | - | - |
| Std. Flucanzole | - | - | - | - | 18 | 16 |

(Received: 13 June 2009 Accepted: 25 July 2009 RJC-399)