Microwave Induced Synthesis and Antimicrobial Activities of Some Derivatives of 3, 5-Diaryl-2-pyrazoline-1-carbaldehyde

RAVINDRA KUMAR and Y. K. SRIVASTAVA *

Synthetic Organic Chemistry Laboratory, Department of Chemistry,
M. P. Govt (PG) College, Chittorgarh, Rajasthan-312001, India.

ys_cor121@yahoo.com

Received 19 January 2009; Accepted 10 March 2009

Abstract: 3, 5-Diaryl-2-pyrazoline-1-carbaldehyde (**1**) was condensed with hydrazine hydrate and *o*-phenylene diamine to afford corresponding hydrazones (**2**) and 3-benzimidazolyl-3, 5-diaryl-2-pyrazoline respectively under MWI condition. The newly synthesized compounds have been screened for their antibacterial activity *in vitro*.

Keywords: Microwave, Benzimidazolyl, Pyrazoline, Hydrazone, Carbaldehyde.

Introduction

Microwave assisted organic reaction enhancement (MORE) is now a well established technique for synthesis of various carbon-heteroatom bonds. Almost all thermally driven reactions can be accelerated by microwaves. Several advantage¹⁻⁴ such as shorter reaction time, cleaner products, easy work up, selectivity of products and synthesis under solvent free solid phase condition makes this procedure environmentally benign and hence it become a part of green chemistry.

Among nitrogen containing heterocycle, the benzimidazole constitute an important class of compounds, possessing a wide variety of pharmacological activities⁵⁻¹² such as antifungal, antihypertemina, antioxidant, cardiovascular, anticonvulsant, antiviral and HIV IPR inhibitory activity. Pyrazoline derivatives¹³⁻¹⁹ is most extensively explored class of five member heterocycles due to their versatile biological activities, diverse chemical reactivity, easy accessibility and industrial application.

Led by above fact and our continuous interest in synthesis of new pyrazoline derivatives herein, we report synthesis of some pyrazoline derivatives using 3, 5-diaryl-2-pyrazoline-1-carbaldehyde as synthon. 2-Hydroxy chalcones on treatment with hydrazine hydrate in

presence of formic acid under MWI affords²⁰ 3, 5-diaryl-2-pyrazoline-1-carbaldehyde (**1**). These carbaldehyde (**1**) were condensed with hydrazine hydrate under solvent less MWI condition to get corresponding hydrazone (**2**) in 82-90% yield. In another experiment the carbaldehyde (**1**) were condensed with *o*-phenylenediamine. The product obtained identified as 1-benzimidazolyl-3, 5-diaryl-2-pyrazoline (**5**) in 85-88% yield. (Scheme 1)

Scheme 1.

The characterization of product **2** and **3** was based on their analytical and spectral data. The IR spectra of compounds **2** exhibits absorption band at $3340\text{--}3200\text{ cm}^{-1}$ (Broad combined band for-OH and -NH stretch) and $1410\text{--}1320\text{ cm}^{-1}$ (broad, combined vibration of C=C and C=N grouping). The IR spectra of compound **3** gave a sharp band at $3440\text{--}3300\text{ cm}^{-1}$ (-OH stretch), $3260\text{--}3200\text{ cm}^{-1}$ (-NH of benzimidazolyl ring) and $1440\text{--}1320\text{ cm}^{-1}$ (combined vibration of C=N and C=C grouping).

^1H NMR spectra of compounds (**2**) gave signal at δ 2.98-3.02 (dd, 1H, $\text{C}_4\text{-H}_\text{A}$), 3.10-3.15 (dd, 1H, $\text{C}_4\text{-H}_\text{B}$) and δ 5.23-5.28 (dd, 1H, $\text{C}_5\text{-H}_\text{X}$) indicating the presence of typical ABX pattern of pyrazoline ring. Hydroxyl proton gave a singlet at δ 9.10 where as the proton attached to hydrazone nitrogen were obtained as singlet at δ 7.82. Aromatic proton of both rings gave a multiplet in the region δ 6.77-8.01. ^1H NMR spectra of compounds (**3**) gave signals at δ 3.02-3.10 (dd, 1H, $\text{C}_4\text{-H}_\text{A}$), δ 3.84-3.89 (dd, 1H, $\text{C}_4\text{-H}_\text{B}$) and δ 5.50-5.54 (dd, 1H, $\text{C}_5\text{-H}_\text{X}$) confirming the presence of ABX pattern of pyrazoline. Aromatic protons were observed a multiplet at δ 7.12-8.18. The $-\text{OH}$ proton was obtain as singlet at δ 8.84 where as $-\text{NH}$ of benzimidazolyl ring gave a singlet at δ 9.12. The mass spectra (FAB) of compounds (**2**) and (**3**) gave molecular ions peaks corresponding to their molecular masses.

Experimental

All the melting point reported are uncorrected and was taken in open capillary on Buchi 130 melting point apparatus. The purity of products and progress of reaction was checked by TLC using silica gel G as adsorbent and benzene-ethyl acetate as eluent. IR spectra (KBr , ν cm^{-1}) were recorded on Perkin-Elmer 1600 spectrophotometer. ^1H NMR spectra were taken on Brucker DRX-600 spectrophotometer using TMS as internal standard and CDCl_3 or DMSO-d_6 as solvent. Mass spectra were recorded on Jeol-SX-DA 600 mass spectrometer using *m*-nitrobenzyl alcohol as matrix. The matrix peaks were observed at *m/z* 136,137,154,289 and 307. All the transformation was carried out in domestic microwave oven (Samsung 1630N, output 600 watt, 2450 MHz).

General procedure for synthesis of 3, 5-diaryl-2-pyrazoline-1-carbaldehyde hydrazones (2a-f)

3, 5-Diaryl-2-pyrazoline-1-carbaldehyde ($1_{\text{a-f}}$, 0.01 mole) and hydrazine hydrate (0.012 moles) were mixed thoroughly to form a thick paste. It was then subjected to microwave irradiation at 560 watt for 4-6 minutes. After completion of reaction as indicated by TLS the residue was cooled to room temperature and washed with water. The separated solid was recrystallised from ethanol as colorless crystals (Table 1).

General procedure for synthesis of 1-benzimidazolyl-3, 5-diaryl-2-pyrazolines (3a-f)

3, 5-Diaryl-2-pyrazoline-1-carbaldehyde ($1_{\text{a-f}}$, 0.01 moles) and *o*-phenylene diamine (0.012 moles) were taken in DMF (10 mL) and mixed thoroughly to form a homogeneous mixture. It was then subjected to microwave irradiation at 560 watt for 5-7 minutes. After completion of reaction the residue was cooled to room temperature; washed thoroughly with water, dried and crystallized from ethanol as cream coloured crystal of $3_{\text{a-f}}$ (Table 1).

Antibacterial activity

Newly synthesized compounds were screened for their antibacterial activity *in vitro* against *S. aureus*, *S. albus*, *K.pneumoniae*, *P. vulgaris* and *E. coli* at a concentration 250 mg/mL using cup plate diffusion method²¹. Zone inhibition was measured in mm. Standard drugs used were ciproflaxange and fluconazole. The screening results are tabulated in Table 2.

Table 1. Physical data of synthesized compounds (2) & (3).

Compd	Ar	Mol. Formula, M. Wt.	M.p. °C	Yield, %	Rxn time, min	% N	
						Calcd	Found
2a	Phenyl	C ₁₆ H ₁₆ N ₄ O(280)	164	84	5.0	20.0	19.68
2b	4-oMe phenyl	C ₁₇ H ₁₈ N ₄ O ₂ (310)	167	82	5.0	18.6	18.44
2c	3,4-dioMe phenyl	C ₁₈ H ₂₀ N ₄ O ₃ (340)	136	81	4.5	16.47	16.10
2d	4-Cl phenyl	C ₁₆ H ₁₅ N ₄ OCl(314.5)	185	83	5.0	17.80	17.45
2e	4-NMe ₂ phenyl	C ₁₈ H ₂₁ N ₅ O(323)	148	80	5.0	21.67	20.98
2f	2-Furanyl	C ₁₄ H ₁₄ N ₄ O ₂ (270)	105	85	4.5	20.74	20.22
3a	Phenyl	C ₂₂ H ₁₈ N ₄ O(354)	145	86	4.0	15.82	15.41
3b	4-oMe phenyl	C ₂₃ H ₂₀ N ₄ O ₂ (384)	194	85	4.0	14.58	14.30
3c	3,4-dio Me phenyl	C ₂₄ H ₂₂ N ₄ O ₃ (414)	149	85	4.5	13.52	13.23
3d	4-Cl phenyl	C ₂₂ H ₁₇ N ₄ OCl(388.5)	187	88	4.0	14.41	14.09
3e	4-NMe ₂ phenyl	C ₂₄ H ₂₃ N ₅ O(397)	170	85	6.0	17.63	17.51
3f	2-Furanyl	C ₂₀ H ₁₆ N ₄ O ₂ (344)	182	85	6.5	16.28	16.00

Table 2. Biological screening results of compounds (2) & (3) zone of inhibition in mm.

Compd.	<i>S.aureus</i>	<i>S.albus</i>	<i>K.pneumoniae</i>	<i>P.vulgaris</i>	<i>E.coli</i>
2a	09	18	12	10	16
2b	12	14	10	09	12
2c	10	20	18	09	14
2d	10	22	12	11	10
2e	08	16	12	05	09
2f	08	15	10	05	10
3a	12	16	14	09	12
3b	12	13	10	12	12
3c	10	18	10	13	16
3d	12	20	16	13	14
3e	07	15	09	08	10
3f	08	09	10	04	09
Ciproflaxange (std. drug)	14	30	25	15	23
Fluconazole (std. drug)	18	22	16	15	20

Conclusion

All the transformations were carried out using microwave irradiation method under solvent less condition which lead to considerable time saving, better yields and energetically profitable procedure. The solvent less condition diminish the problem of waste disposal and is ecofriendly. Some of the synthesized compounds have shown promising antibacterial activity.

Acknowledgment

The authors are highly grateful to Dr. B. L. Verma (Retd Professor, MLS University, Udaipur) for valuable suggestions, guidance and encouragement. Thanks are also due to the Director SAIF, CDRI Lucknow for spectral results.

References

1. Verma R S, *Green Chemistry*, 1999, **1**, 43.

2. Verma R S, Advance in Green chemistry. Chemical synthesis using microwave irradiation, Astxa-zeneea Research Foundation India, Bangalore, 2002.
3. Caddock S, *Tetrahedron*, 1995, **52**, 10403.
4. Bose A K, Banik B K, Lavlinskati N, Jayaraman M and Manhas M S, *Chemtech.*, 1997, **27**, 18.
5. Preston P N, Benzimidazoles and Carcinogenic Tricyclic Compounds (Interscience Wiley, N.Y) 1980, Part-2, chap.10, p531.
6. Enguidiard C, Renou J C, Allouchi H, Legar J M and Guiffer H, *Chem Pharma Bull.*, 2000, **48**, 938.
7. Hadizadeh F, Burnshad M, Poorsaghat H and Fatehi H M, *Indian J Chem.*, 2000, **44B**, 2343.
8. Gohar H, Khus O, Botkin D and Altanar N, *Bioorg Med Chem.*, 2002, **10**, 2589.
9. Insuasty B, Fernandez F, Qulrong J, Martinez R, Gavino P and Angeles E, *Heterocyclic Commun.*, 2002, **8(1)**, 51.
10. Shaifee A, Rastkari N and Sharifzadeh, *DARU*, 2004, **12**, 81.
11. Auram S, Svad I, Bologo C and Florit M C, *J Cell Mol Med.*, 2003, **7(3)**, 287.
12. Pandey V K, Gupta V D and Tiwari D N, *Indian J Heterocyclic Chem.*, 2005, **14(4)**, 217.
13. Azarifar D and Maseud S, *Molecules*, 2002, **7**, 885.
14. Abid, M. and Azam, A., *Eur J Med Chem.*, 2005, **40**, 935.
15. Chimichi S, Boualini M, Hassan M M M, Viola G, Doll A F and Curini M, *Tetrahedron*, 2006, **62**, 90.
16. Tandon V K, Yadav D B, Chatumvedi A K and Shukla P K, *Bioorg Med Chem Lett.*, 2005, **15**, 3288.
17. Kumar A, Archana, Sharma, S, Malik V, Sharma P, Kaushik K Saxena K K, Srivastava V K, Verma R S, Sharma H, Gupa S C and Agrawal R C, *Indian J Chem.*, 2004, **43B**, 1532.
18. Bhat B A, Dhar K L, Puri S C, Saxena A K, Shanmugoved M and Quazi G N, *Bioorg Med Chem Lett.*, 2005, **15**, 3177.
19. Srivastava Y K, *Rasayan J Chem.*, 2008, **1(4)**, 837.
20. Bajia B and Srivastava Y K, *E Journal of Chemistry*, 2007, **4(2)**, 187.
21. Barry A L, Antimicrobial susceptibility test, Principle and practice, (Illus Lea and Fehninger, Philedelphia, USA) 1976, 93.