

**NOTE****Microwave Assisted Synthesis of 2-Alkyl and 2-Aryl Derivatives of Benzimidazole**

D.D. RISHIPATHAK, S.C. PAL, SUBHASH C. MANDAL<sup>†</sup> and D.P. BELSARE\*  
Department of Pharmaceutical Chemistry, N.D.M.V.P. Samaj's College of Pharmacy  
Gangapur Road, Nashik 422 002, India  
E-mail: drishipathak@rediffmail.com

In the present study, various 2-alkyl and 2-aryl substituted benzimidazole were synthesized under microwave irradiation. This method proved to be advantageous over conventional method with respect to reaction time and yield.

**Key Words:** Microwave induced synthesis, Benzimidazole derivatives.

Microwave induced organic reaction chemistry<sup>1,2</sup> is gaining popularity as a non-conventional technique for rapid organic synthesis. It can be termed as *e-chemistry* because it is easy, effective economic and eco-friendly and is believed to be a step towards green chemistry.

A number of methods are available for synthesis of benzimidazoles<sup>3</sup>. Philips method<sup>4</sup> gave satisfactory results in the preparation of 2-alkyl benzimidazole derivatives but frequently fails or gives poor yields<sup>5</sup> when applied to 2-aryl analogs. By using catalyst polyphosphoric acid, 2-aryl derivatives can be effectively synthesized, but requires at least 0.5 h for their synthesis.

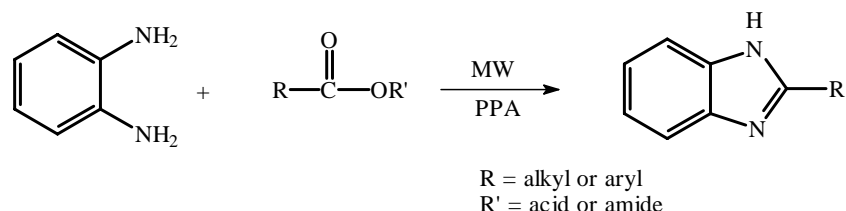
In present investigation, the 2-alkyl and 2-aryl substituted benzimidazole derivatives is synthesized by reacting *o*-phenylenediamine with various carboxylic acids using polyphosphoric acid as catalyst using conventional as well as by irradiation microwave methods.

All melting points were determined in Elico melting point apparatus in open glass capillaries and are uncorrected. TLC, using silica gel-G as an adsorbent, determined the purity of compounds and spots were viewed by exposure to iodine vapours. IR spectra were recorded on a Shimadzu-IR Spectrophotometer-408 in nujol mull or KBr. GC-MS spectra were recorded on Perkin-Elmer auto system excel gas chromatography. PMR spectra were recorded on a FX-90 QFT NMR Spectrophotometer (in  $\delta$  ppm) using TMS

---

<sup>†</sup>Department of Pharmaceutical Technology Jadavpur University, Kolkata-700 001, India.

as internal standard. All microwave reactions were carried on Raga's electromagnetic system with automatic power setting from P-1 to P-10.



**Scheme<sup>6</sup>**

**General procedure for preparation by microwave irradiation:** *o*-Phenylenediamine<sup>7</sup> (1.08 g, 0.01 mol), carboxylic acid (0.01 or 0.02 mol) and polyphosphoric acid<sup>8</sup> (10 g) were properly mixed with glass rod in a beaker. This mixture was irradiated in microwave oven with P-3 for appropriate time (Table-1). After irradiation, the mixture was poured into ice cold water and then slowly neutralized with NaOH to pH 8. The precipitate was collected by filtration, washed with hot water, dried and recrystallized from ethanol.

TABLE-1  
PHYSICAL DATA OF SYNTHESIZED COMPOUND

Benzimidazole derivative	Carboxylic acid or Amide	Reaction time (min)		Yield (%)		m.p. (°C)	
		A	B	A	B	A	B
–	Formic acid	40	0.40	60	93	170	168
2-Methyl	Acetic acid	45	1.00	60	98	176	175
2-Methyl	Acetamide	45	1.00	40	90	176	176
2-Benzyl	Phenyl acetic acid	45	1.00	55	71	191	189
2-Chloro methyl	Chloro-acetic acid	120	1.00	85	85	161	160
2-Pentyl	Hexanoic acid		0.55		96		185
2-Phenyl	Benzoic acid	120	3.00	95	99	294	292
2-Phenyl	Benzamide	240	0.40	99	69	294	294
2-( <i>o</i> -Chloro)phenyl	<i>o</i> -Chloro benzoic acid	240	2.00	90	88	234	230
2- <i>m</i> -Tolyl	<i>m</i> -Toluic acid	210	1.00	99	75	212- 213	211
2-( <i>o</i> -Amino)phenyl	<i>o</i> -Amino benzoic acid	210	1.00	72	73	213	220

A = Conventional, B = Microwave

**Spectral characteristics of synthesized compounds:**

**2-Methylbenzimidazole:** IR ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ) ( $\text{CHCl}_3$ ) 3500-3000 (N-H), 3000 (C-H), 1620 (N-H/C=N), 1600 (Ar C=C), 760 (Ar C-H), 835 (Ar C-H). MS ( $m/z$ ) 132/131 ( $M^+$ ), 104, 90, 76, 63, 41. NMR ( $\text{CDCl}_3$ )  $\delta$  ppm 2.62 (s, 1H), 0.92 (s, 3H), 7.35 (s, 4H).

**2-Chloromethylbenzimidazole:** IR ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ) ( $\text{CHCl}_3$ ) 3500-3000 (N-H), 3000 (C-H), 1620 (N-H/C=N), 1600 (Ar, C=C) 760 (C-Cl), 1260 (C-N). MS (m/z) 166 (M<sup>+</sup>), 132, 104, 90, 76, 63. NMR ( $\text{CDCl}_3$ )  $\delta$  ppm 2.68 (s, 1H), 5.50 (s, 2H), 7.30 (s, 4H).

**2-Chlorobenzimidazole:** IR ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ) ( $\text{CHCl}_3$ ) 3550-3000 (N-H), 3000 (C-H), 1620 (N-H/C=N) 1590 (Ar, C=C), 730 (C-Cl), 1275 (C-N) MS (m/z) 152/154 (M<sup>+</sup>), 117, 105, 90, 63. NMR ( $\text{CDCl}_3$ )  $\delta$  ppm 2.65 (s, 1H), 7.28 (s, 4H).

## REFERENCES

1. S. Caddick, *Tetrahedron*, **51**, 10403 (1995).
2. J. Hamelin, P. Jacquat, A. Loupy, D. Mathe, A. Petit and F.T. Boulet, *Synthesis*, 1213 (1998).
3. P.N. Preston, Benzimidazole and Congeneric Tricyclic Compounds, Part-1, Vol. 41, pp. 5-28 (1981).
4. M.A. Philips, *J. Chem. Soc.*, 2393 (1928).
5. D.W. Hein, R.J. Alheim and J.J. Leavitt, *J. Am. Chem. Soc.*, **79**, 1427 (1957).
6. A. Ben-Alloum, S. Bakkas and M. Soufaoui, *Tetrahedron*, **39**, 4481 (1998).
7. B.S. Furniss, A.J. Hannaford, P.W.G. Smith and A.R. Tatchell, A.I. Vogel's Textbook of Practical Organic Chemistry, ELBS Publication, London, edn. 5, p. 1163 (1989).
8. N. Suzuki, T. Yamabayashi and Y. Izawa, *Bull. Chem. Soc. (Japan)*, **49**, 353 (1976).

(Received: 17 October 2005;

Accepted: 1 February 2007)

AJC-5385