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A micro-wave assisted synthesis of benzimidazole derivatives using solid support

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ABSTRACT

Synthesis of Various benzimidazole derivatives under micro-wave irradiation from simple and substituted ortho phenylenediamines (OPDA) and isonicotinic acid using SiO_2/H_2SO_4 as catalyst is described .The structure of the synthesized compounds have been established on the basis of spectral and analytical data.

Key words: Benzimidazole, isonicotinic acid, H_2SO_4/ SiO_2, microwave irradiation.

INTRODUCTION

Benzimidazoles [1] contains a bicyclic system in which benzene has been fused to the 4 and 5 position of the hetero cycle (imidazole). Literature survey reveals that various substituted benzimidazoles posses antifungal [2] [3], antitubercular [4], antioxidant [5] [6] and antiallergic [7] properties. The classical synthetic protocols for the above substituted benzimadazoles suffer from some disadvantages like prolonged reaction time. In this connection and by knowing the advantages of microwave reaction[8], we felt that the synthesis of the various benzimadazoles using MARS 240/50 Model No. 907510 microwave reactor in the presence of solid support H_2SO_4/ SiO_2, an alternate synthetic methodology.

Hence, we wish to report a convenient and efficient synthesis of various substituted benzimadazoles under microwave irradiation, to improve the efficiency and to reduce the reaction time.

MATERIALS AND METHODS

Melting points are recorded and were obtained in Polmon MP 96. TLC checking was done on plastic sheets coated with silica gel GF-254, supplied by Merck & Co., and spotting was done using Iodine or UV lamp. IR spectra were recorded using Bruker or Satellite 2000 spectrometer

using KBr pellet. ^{1}H NMR spectra were recorded on Brukar avance 300 MHz respectively. An elemental analysis is given as % of C, H & N only for new compounds. Mass spectra were taken on Water-Micromass Quattro-II spectrometer. MARS 240/50, Model No. 907510, Micro-wave reactor is used to carry out these reactions.

Preparation of H_2SO_4- SiO_2

H_2SO_4 (12.5 m.mol) was added to the suspension of silica gel (23.5 g, 230-400 mesh) in diethyl ether. The mixture was concentrated and the residue heated at 100 °C for 72 hours under vacuum to afford H_2SO_4-SiO_2 as a free flowing powder.

General procedure for the Synthesis of simple and substituted benzimidazole derivatives (3a-g):

Ortho phenylene diamine (1.0mmol), Isonicotinic acid (1.1mmol) was adsorbed on H_2SO_4-SiO_2 (2.00mmol) and transferred in to a microwave vial. The vial was sealed and placed in microwave. The reaction was run at 80 °C for 5 min. For the entire experiment, the power setting was held at 100 W. After the completion of reaction, the reaction mixture was cooled to room temperature and purified by SiO_2 gel column chromatography with hexane: EtOAc (90:10%) to get the substituted benzimidazoles.

3a: Yield=90%; m.p= 262-266 °C ; IR (KBr): 3366, 3012, 2888, 2079, 1590, 1416, 1320, 1232 cm^{-1}; ^{1}H-NMR(DMSO-d_6/TMS): δ 7.59(m, 1H), 7.59 (m, 1H), 7.26 (m, 1H), 7.26 (m, 1H), 3.51 (S, 3H), 3.45(m, 1H), 3.32 (m, 2H), 3.08(m, 1H), 2.29 (m, 2H), 2.08 (m, 2H); Mass (ES): m/z 202 [M+H] $^{+\cdot}$Elemental analysis: Calculated for C_{12} $H_{15}N_3$: C, 71.61; H, 7.51; N, 20.88 % Found: C, 71.41; H, 7.45; N, 20.77%.

3b: Yield=85%; m.p >280^{o}C ; IR (KBr): 3382, 3096, 2880, 2100, 1601, 1428, 1357, 1335, 1241cm^{-1} ; ^{1}H-NMR(DMSO-d_6/TMS):δ 7.78(m, 1H), 7.6 (m, 1H), 7.38 (m, 1H), 3.55(m, 1H), 3.4 (m, 2H), 3.08(m, 1H), 2.3 (m, 2H), 2.08 (m, 2H); Mass (ES): m/z 220.1 [M+H] $^+$; Elemental analysis: Calculated for C_{12} $H_{14}FN_3$: C, 65.73; H, 6.44; N,19.16 % Found: C, 65.90; H, 6.31; N: 18.98%.

3c: Yield=80%; m.p>280^{o}C; IR (KBr): 3341, 3091, 2876, 2085, 1436, 1357, 1275, 1241, 678 cm^{-1}; ^{1}H-NMR(DMSO-d_6/TMS): δ 7.68(m, 1H), 7.54 (m, 1H), 7.27 (m, 1H), 3.45(m, 1H), 3.32 (m, 2H), 3.08(m, 1H), 2.29 (m, 2H), 2.08 (m, 2H); Mass (ES): m/z 235.89 [M+H] $^+$; Elemental analysis: Calculated for C_{12} $H_{14}ClN_3$: C, 61.15; H, 5.99; N, 17.83 % Found: C, 61.02; H, 5.83; N: 17.70 %.

3d: Yield=80%; m.p>280^{o}C; IR (KBr): 3318, 3075, 2870, 2088, 1420, 1280, 551 cm^{-1}; ^{1}H-NMR(DMSO-d_6/TMS):δ 7.87(m, 1H), 7.59 (m, 1H), 7.43 (m, 1H), 3.45(m, 1H), 3.32 (m, 2H), 3.08(m, 1H), 2.29 (m, 2H), 2.08 (m, 2H); Mass (ES): m/z 280.96 [M+H] $^+$; Elemental analysis: Calculated for C_{12} $H_{14}BrN_3$: C, 51.44; H, 5.15; N, 15.00 % Found: C, 51.21; H, 5.15; N: 15.20 %.

3e: Yield=65%; m.p>280^{o}C ; IR (KBr): 3338, 3090, 2905, 2101, 1608, 1432, 1347, 1248 cm^{-1}; ^{1}H-NMR (DMSO-d_6/TMS): δ 8.1 (s, 1H), 7.9 (d, 1H), 7.78 (d, 1H), 3.56(m, 1H), 3.4(m, 2H), 3.1(m, 2H), 2.32(m, 2H), 2.1(m, 2H); MS (M+1): 270.3; Mass (ES): m/z 270.3[M+H] $^+$;

Elemental analysis: Calculated for C_{12} $H_{14}F_3N_3$: C, 57.99; H, 5.24; N, 15.61 % Found: C, 58.21; H, 5.16; N: 15.48 %.

3f: Yield=60%; m.p>280^oC ; IR (KBr): 3094, 2882, 2241, 1622, 1418, 1325, 1228 cm^{-1}; ^{1}H-NMR(DMSO-d_6/TMS): δ 8.1 (s, 1H), 7.9 (d, 1H), 7.78 (d, 1H), 3.56(m, 1H), 3.4(m, 2H), 3.1(m, 2H), 2.32(m, 2H), 2.1(m, 2H); Mass (ES): m/z 227.4 $[M+H]^+$; Elemental analysis: Calculated for C_{12} $H_{14}N_4$: C, 69.00; H, 6.24; N, 24.76 % Found: C, 68.81; H, 6.28; N: 24.60 %.

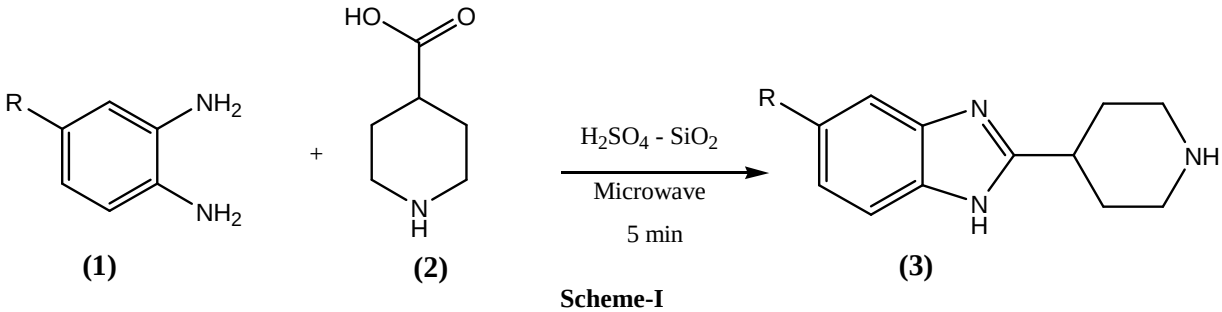
3g: Yield=75%; m.p>280^oC ; IR (KBr): 3352, 3105, 2885, 1592, 1421, 1350, 1237 cm^{-1}; ^{1}H-NMR (DMSO-d_6/TMS): δ 7.59(m, 1H), 7.21 (m, 1H), 7.01 (m, 1H), 3.51 (S, 3H), 3.45(m, 1H), 3.32 (m, 2H), 3.08(m, 1H), 2.29 (m, 2H), 2.08 (m, 2H); Mass (ES): m/z 232.01; $[M+H]^+$Elemental analysis: Calculated for C_{13} $H_{17}N_3O$: C, 67.51; H, 7.41; N, 18.17 % Found: C, 67.35; H, 7.61; N: 17.94 %.

RESULTS AND DISCUSSION

Reaction of substituted OPDA **(1)** with Isonicotinic acid **(2)** in 4N HCl (under Philips condition) on refluxing for about 24 hrs gave **3** in moderate yields. When the same reaction was carried out under micro-wave irradiation in the presence of solid support H_2SO_4/ SiO_2 for 5min, **3** obtained in high yields **(Scheme-I)**.

This method seems to be the best choice among all conventional synthetic methodologies. We carried out the same reaction with various substituted Ortho Phenylene Diamines **(Table-I)**.

In summary, micro-wave assisted synthesis of benzimidazole derivatives in the presence of solid support has been studied. The best results are obtained under micro-wave irradiation technique.



(1) **(2)** **(3)**

Scheme-I

Table-I synthesis of substituted benzimidazoles under microwave irradiation

S. No.	R	Yield (%)
1	*3a = H*	90
2	*3b= Fluoro*	85
3	*3c= Chloro*	80
4	*3d= Bromo*	80
5	*3e= Trifluoro methyl*	65
6	*3f= Cyano*	60
7	*3g= Methoxy*	75

CONCLUSION

We have developed a simple and efficient method for the synthesis of benzimidazole derivatives using H_2SO_4- SiO_2 as catalyst under solvent-free conditions. The notable advantages of this method are the experimental simplicity, inexpensive reagents, short reaction times and easy workup procedure.

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REFERENCES

[1] H. A. Barker, R. D. Smyth, H. Weissbach, J. I. Toohey, J. N. Ladd, and B. E. Volcani (February 1, **1960**).
[2] B. Maxwell, Antifungal activity ofselected benzimidazole compounds. *Appl. Microbiolol*. **1971,** 21, 944-945.
[3] K.A.M.Walker, A.C. Braemer, S. Hitt, R.E. Jones, and T.R. Mathews, *J. med. Chem.* **1978**, 21, 840-842.
[4] O. Gaban, H. Ertepinar and S. Qzden, *pharmazie*. **1996**, 51 (1), 34-36.
[5] *J.Agric. Food chem.*, **1974**, 22 (5), pp 918-918
[6] *J.Enzyme inhib med chem.*, **2006** Apr, 21 (2):241-247
[7] Agents and actions. **1990** Apr:30(1-2):174-177
[8] S. Jubie, et al, *J.Pharma sci. & Res.* **2010,** Vol2 (2), 69-76.