A microwave assisted synthesis of 2-aryl-1-arylmethyl-1*H*-1,3-benzimidazoles in the presences of K-10

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Dedicated to Professor P.T.Narasimhan on the occasion of his 75th birthday
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Abstract
A series of 2-aryl-1-arylmethyl-1*H*-1,3-benzimidazoles were synthesized expeditiously in good yields from *ortho*-phenylenediamine and aromatic aldehydes in the presence of montmorillonite K-10 under microwave irradiation in the absence of solvent.

Keywords: Microwave assisted, synthesis, benzimidazoles, K-10, tandem reactions

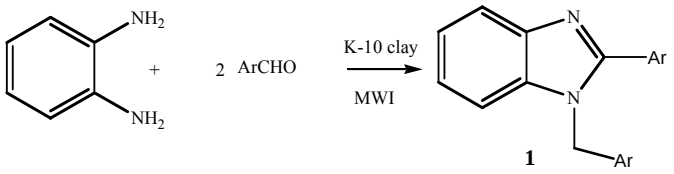
Introduction

Several microwave assisted organic reactions proceed at mild reaction conditions at much enhanced reaction rates relative to thermal reactions.[1] Hence the decomposition of reactants and/or products is diminished in these reactions leading to enhanced yields. Often, microwave assisted organic reactions proceed rapidly in the absence of solvent also. Environmentally benign solid catalysts such as clays and zeolites, instead of mineral acids, are also employed for acid catalyzed microwave assisted synthetic transformations, rendering them eco-friendly.[2] Microwave irradiation has been used to effect organic reactions such as pericyclic,[3] cyclization,[4] aromatic substitution,[5] oxidation,[6] alkylation,[7] decarboxylation,[8] radical reactions,[9] condensation,[10] peptide synthesis,[11] *etc*.

In this study, we have employed microwave irradiation for the synthesis of substituted benzimidazoles in the presence of montmorillonite K-10. This work assumes importance, in view of the fact that benzimidazoles and their derivatives display a number of important biological activities such as local anaesthetic,[12] antipyretic[12] and antihistaminic[13] and hence possess great chemotherapeutic potential.

Results and Discussion

In the present study, all the 2-aryl-1-arylmethyl-1*H*-1,3-benzimidazoles (1) were obtained in good yields by the reaction of *o*-phenylenediamine with various aldehydes in the presence of montmorillonite K-10 under microwave irradiation (Scheme 1) in the absence of solvent.



Scheme 1

The ^{1}H and ^{13}C NMR spectra of the products are in consonance with benzimidazole structures and their m.p. are in agreement with those available in the literature. The yields, m.p. and literature m.p. are given in Table 1. The reaction under microwave condition goes to completion in 10 minutes at the maximum power level and pure product is obtained in most of the cases as evident from ^{1}H NMR. The same reaction under thermal conditions at 130° C, over an oil bath, for the same time duration affords lower yields. The percentage of conversion under thermal conditions was estimated from the intensities of the ^{1}H signals of the CHO in aldehydes and CH_2 in benzimidazoles.

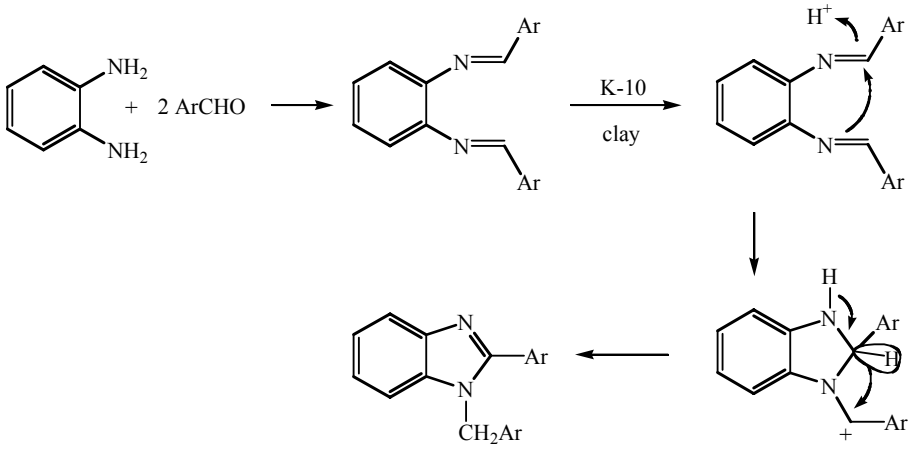
Table 1. Yield, m.p. and literature m.p. of benzimidazoles

Compound 1	Ar	Time (min)	Yield (%) MWI[a]	Thermal[b]	m.p. (° C)	Lit. m.p. (° C)
A	C_6H_5	10	90	20	132	134[15]
B	*p*-$MeOC_6H_4$	10	87	27	131	129-130[16]
C	*p*-MeC_6H_4	10	93	21	126	127-128[17]
D	*p*-ClC_6H_4	10	95	19	137	136[16]
E	*o*-$MeOC_6H_4$	10	92	~9	151	-----[c]
F	*o*-ClC_6H_4	10	96	~2	155	159[16]
G	2-Furyl	10	94	~3	96	95-96[15]
H	*p*-$NO_2C_6H_4$	10	89	9	192	------[c]
I	*o*- $NO_2C_6H_4$	10	78	20	118	120[16]
J	*p*-$(CH_3)_2NC_6H_4$	10	95	45	252	255[16]

[a] Isolated yield. [b] Percentage conversion from ^{1}H NMR data estimated from the intensities of protons of CHO in aldehydes and CH_2 in benzimidazoles. [c] Literature m.p. not available, but ^{1}H and ^{13}C NMR spectra consistent with structure in these cases.

In general, benzimidazoles with *p*-substituted aryl groups are formed in higher yields than the *o*-substituted ones under thermal conditions although in all cases, good yields are obtained under microwave irradiation. This is in accordance with earlier observation that the microwave effect becomes important when steric effects impede a reaction.[14]

The reaction may tentatively be visualized to occur *via* a tandem sequence of reactions depicted in Scheme 2 involving (i) formation of dibenzylidene-*o*-phenylenediamine, (ii) protonation of the dibenzylidene-*o*-phenylenediamine by clay and ring closure leading to a five membered ring in either a sequential or a concerted manner, (iii) 1,3-hydride transfer and (iv) deprotonation. While the aryl groups/nitrogen atom could stabilize the positively charged intermediates involved in the intermediate steps, the aromatic stabilization of the resulting benzimidazoles could provide the impetus for the transformation.



Scheme 2

In the previously reported syntheses of benzimidazoles by (i) the reaction of *ortho*-phenylenediamine with aromatic aldehydes at 120-160 °C[18] and (ii) heating the dry diamine hydrochloride with the aldehyde until evolution of hydrogen chloride ceased, either the yields are not good for all substituted cases or the protocols are not eco-friendly.[18]

Conclusions

The present synthetic protocol for the preparation of 2-aryl-1-arylmethyl-1*H*-1,3-benzimidazoles is advantageous over the previous methods as (i) the reaction could be performed with an environmentally benign clay catalyst, (ii) it provides a good yield of product and (iii) reaction occurs more rapidly.

Experimental Section

General Procedures. All the m.p. reported in this work are uncorrected. The ^{1}H and ^{13}C NMR spectra of the benzimidazoles were measured at 300 MHz and 75 MHz respectively using Bruker (Avance) NMR instrument in $CDCl_3$ and the chemical shifts referenced to tetramethylsilane. An unaltered domestic IFB Microwave oven operating at 230 V and 50 Hz with a consumption of 1000 W with maximum microwave power level of 600 W and microwave frequency of 2450 MHz was employed for the irradiation done in this work.

Typical procedure for preparation of 2-aryl-1-arylmethyl-1*H*-1,3-benzimidazoles (1)
ortho-Phenylenediamine (0.108 g, 1 mmol), freshly distilled benzaldehyde (0.212 g, 2 mmol) and montmorillonite K-10 (0.1 g) was thoroughly mixed in a glass tube which was loosely closed and immersed in a silica gel bath in a beaker and irradiated in the microwave oven for about 10 min. at maximum microwave power level (600 watts) in two 5 min. durations with intermittent cooling. The temperature during irradiations rose to a maximum of about 130° C, as found by measuring the maximum temperature of the silica gel bath immediately after the irradiation was over by gently stirring the silica gel with the thermometer. After the irradiation was over, the reaction mixture was cooled and added into water (5 ml) and extracted with diethyl ether (5 ml). After filtering the clay particles, the ethereal layer was washed with water, dried with anhydrous sodium sulfate and the solvent removed. In most of the cases pure product is obtained and in cases wherein small impurities are formed, a filtration column using hexane-ethyl acetate [95:5 (v/v)] mixture afforded the pure product.

Thermal reaction
The reaction mixture of the same composition as above for microwave irradiation was employed for thermal reaction and heated over an oil bath at 130° C for 10 min. and from the ^{1}H NMR spectrum of the resulting product mixture, the percentage conversion was estimated.
1-Benzyl-2-phenyl-1*H*-1,3-benzimidazole. ^{1}H NMR: δ 7.81 (d, *J* = 8 Hz, 1H) ; 7.62 (dd, *J* = 8 and 2 Hz, 2H) ; 7.40-7.32 (m, 3H) ; 7.26-7.10 (m, 6H) ; 7.00 (dd, *J* = 8 and 2 Hz, 2H) ; 5.34 (s, 2H); ^{13}C NMR: δ 153.7, 142.7, 136.0, 135.6, 129.6(3), 129.6(0), 128.9, 128.7, 128.4, 127.4, 125.6, 122.7, 122.3, 119.5, 110.3, 47.9 ppm.
1-(4-Methoxybenzyl)-2-(4-methoxyphenyl)-1*H*-1,3-benzimidazole. ^{1}H NMR: δ 7.83 (d, *J* = 8 Hz, 1H); 7.62 (d, *J* = 9 Hz, 2H) ; 7.30-7.23 (m, 1H); 7.20 (m, 2H); 7.02 (d, *J* = 9 Hz, 2H) ; 6.94 (d, *J* = 9 Hz, 2H); 6.84 (d, *J* = 8 Hz, 2H); 5.37 (s, 2H); 3.83 (s, 3H); 3.77 (s, 3H); ^{13}C NMR: δ 160.9, 159.1, 154.1, 143.2, 136.1, 130.7, 128.5, 127.2, 122.7, 122.5, 119.7, 114.4, 114.2, 110.4, 55.3(4), 55.2(6), 47.9 ppm.
1-(4-Methylbenzyl)-2-(4-methylphenyl)-1*H*-1,3-benzimidazole. ^{1}H NMR: δ 7.85 (m, 1H); 7.58 (d, *J* = 8 Hz, 2H); 7.28 (m, 1H); 7.24 (d, *J* = 8 Hz, 2H); 7.19 (m, 2H); 7.12 (d, *J* = 8 Hz, 2H); 6.98 (d, *J* = 8 Hz, 2H); 5.39 (s, 2H); 2.39 (s, 3H); 2.32 (s, 3H); ^{13}C NMR: δ 154.3, 143.2,

139.9, 137.4, 136.1, 133.4, 129.6, 129.4, 129.1, 127.2, 125.8, 122.7, 122.5, 119.8, 110.4, 48.1, 21.4, 21.0 ppm.

1-(4-Chlorobenzyl)-2-(4-chlorophenyl)-1*H*-1,3-benzimidazole. ^{1}H NMR: δ 7.86 (d, *J* = 8 Hz, 1H); 7.58 (m, 2H); 7.43 (m, 2H); 7.36–7.24 (m, 4H); 7.19 (d, *J* = 8 Hz, 1H); 7.02 (d, *J* = 9 Hz, 2H); 5.40 (s, 2H); ^{13}C NMR: δ 152.8, 143.0, 136.3, 135.9, 134.6, 133.8, 130.4, 129.3, 129.1, 128.3, 127.2, 123.4, 123.0, 120.1, 110.3, 47.7 ppm.

1-(2-Methoxybenzyl)-2-(2-methoxyphenyl)-1*H*-1,3-benzimidazole. ^{1}H NMR: δ 7.84 (d, *J* = 8 Hz, 1H); 7.53 (dd, *J* = 8 and 2 Hz, 1H); 7.43 (td, *J* = 8 and 2 Hz, 1H); 7.29 - 7.12 (m, 4H); 7.03 (t, *J* = 8 Hz, 1H); 6.93 (d, *J* = 8 Hz, 1H); 6.81 (d, *J* = 8 Hz, 1H); 6.75 (t, *J* = 7 Hz, 1H); 6.69 (dd, *J* = 7 and 1 Hz, 1H); 5.23 (s, 2H); 3.76 (s, 3H); 3.56 (s, 3H); ^{13}C NMR: δ 157.4, 156.3, 152.4, 143.2, 135.4, 132.2, 131.3, 128.3, 127.6, 124.4, 122.3, 121.8, 120.7, 120.3, 119.7, 110.6(9), 110.6(6), 109.8, 55.1, 55.0, 43.3 ppm.

1-(2-Chlorobenzyl)-2-(2-chlorophenyl)-1*H*-1,3-benzimidazole. ^{1}H NMR: δ 7.89 (d, *J* = 8 Hz, 1H); 7.52-7.38 (m, 3H); 7.36-7.12 (m, 6H); 7.05 (td, *J* = 8 and 1 Hz, 1H); 6.62 (dd, *J* = 8 and 1 Hz, 1H); 5.36 (s, 2H); ^{13}C NMR: δ 151.4, 143.0, 134.7, 134.3, 133.2, 132.3, 132.1, 131.4, 129.8, 129.6, 129.5, 128.9, 127.6, 127.0, 126.9, 123.3, 122.6, 120.3, 110.5, 45.7 ppm.

2-(2-Furyl)-1-(2-furylmethyl)-1*H*-1,3-benzimidazole. ^{1}H NMR: δ 7.82-7.75 (m, 1H); 7.62 (dd, *J* = 2 and 1 Hz, 1H); 7.51-7.44 (m, 1H); 7.31-7.25 (m, 3H); 7.20 (dd, *J* = 3 and 1 Hz, 1H); 6.59 (dd, *J* = 4 and 2 Hz, 1H); 6.26 (dd, *J* = 3 and 2 Hz, 1H); 6.21 (dd, *J* = 3 and 1 Hz, 1H); 5.64 (s, 2H); ^{13}C NMR: δ 149.6, 145.4, 143.9, 143.0, 142.6, 135.5, 123.2, 122.9, 119.8, 112.8, 112.0, 110.5, 110.0, 109.7, 108.3, 41.6 ppm.

1-(4-Nitrobenzyl)-2-(4-nitrophenyl)-1*H*-1,3-benzimidazole. ^{1}H NMR: δ 8.33 (d, *J* = 9 Hz, 2H); 8.24 (d, *J* = 8 Hz, 2H); 7.93 (dd, *J* = 8 and 1 Hz, 1H); 7.84 (d, *J* = 9 Hz, 2H); 7.41 (td, *J* = 7 and 1 Hz, 1H); 7.35 (td, *J* = 9 and 1 Hz, 1H); 7.28 (d, *J* = 9 Hz, 2H); 7.19 (dd, *J* = 8 and 1 Hz, 1H); 5.59 (s, 2H); ^{13}C NMR: δ 151.3, 148.5, 147.7, 143.1, 142.8, 135.9, 135.7 130.0, 126.7, 124.6, 124.5, 124.1, 123.7, 120.7 110.2, 47.9 ppm.

1-(2-Nitrobenzyl)-2-(2-nitrophenyl)-1*H*-1,3-benzimidazole. ^{1}H NMR: δ 8.20-8.12 (m, 2H); 7.87 (dd, *J* = 8 and 1 Hz, 1H); 7.73-7.65 (m, 2H); 7.56-7.43 (m, 3H); 7.37 (td, *J* = 8 and 1 Hz, 1H); 7.30 (td, *J* = 8 and 1 Hz, 1H); 7.15 (dd, *J* = 8 and 1 Hz, 1H); 6.95 (dd, *J* = 7 and 1 Hz, 1H); 5.70 (s, 2H); ^{13}C NMR: δ 149.8, 148.9, 146.9, 143.0, 134.8, 134.3, 133.3, 132.0, 131.4, 131.4, 128.9, 128.3, 125.5, 125.2, 125.1, 123.8, 123.1, 120.5, 110.2, 45.7 ppm.

1-(4-Dimethylaminobenzyl)-2-(4-dimethylaminophenyl)-1*H*-1,3-benzimidazole. ^{1}H NMR: δ 7.73 (d, *J* = 8 Hz, 1H); 7.55 (d, *J* = 9 and 2 Hz, 2H); 7.70-7.05 (m, 3H); 6.96 (d, *J* = 9 Hz, 2H), 6.70-6.55 (m, 4H); 2.93 (s, 3H); 2.86 (s, 3H);^{13}C NMR: δ 155.0, 151.2, 149.9, 143.1, 136.3, 130.2, 126.9, 124.2, 122.2, 119.1, 117.1, 112.7, 111.7, 110.4, 48.0, 40.5, 40.1 ppm.

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