Simple And Mild Procedures For Synthesis Of Benzimidazole Derivatives Using Heterogeneous Catalyst Systems

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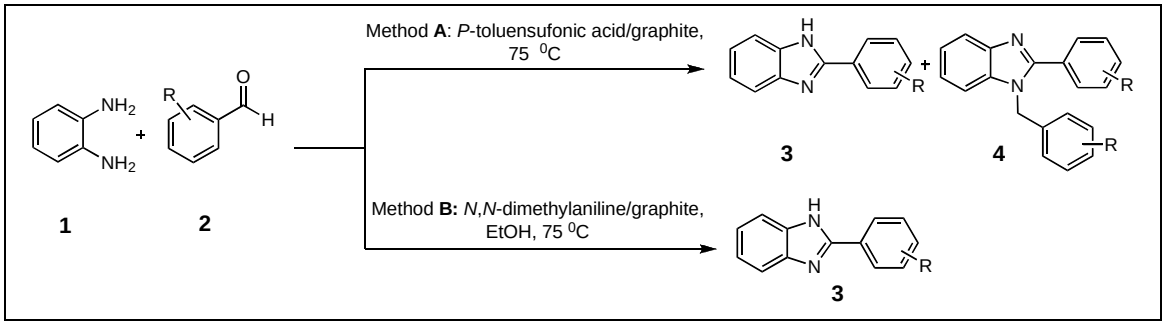

Abstract: TsOH/graphite and *N*,*N*-dimethylaniline/graphite were found to be catalyst systems for condensation reaction of *o*-phenylendiamine with different aldehydes to form benzimidazole derivatives under mild and simple conditions. The graphite was easily recovered by a simple extraction and could be reused without decrease of activity in the presence of fresh TsOH and *N*,*N*-dimethylaniline.

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INTRODUCTION

The benzimidazole ring is an important pharmacophore in modern drug discovery [1]. Attempts for identifying new compounds containing this nucleus have gained importance in recent years because many of these derivatives have shown various spectrum of pharmacological activities such as: antiviral effects [2], antagonistic and inhibitory activities [3], potential antitumor agents [4], antibacterial agents [5], a treatment for interstitial cystitis [6], as anthelmintic agents in veterinarian medicine and in diverse human therapeutic areas such as treatment of ulcers and as antihistaminics [7].

In spite of their importance as a pharmacological incorporated motif, comparatively few methods for the synthesis of benzimidazole derivatives have been reported. The conventional synthesis of benzimidazoles involve the reaction between an *o*-phenylenediamine and a carboxylic acid or its derivatives (nitriles, amidates, orthoesters) under severe dehydrating conditions [8]. Alternatively, a two-step procedure is employed wherein the resulting mono-acylated product is subjected to cyclodehydration under a variety of conditions [9]. However, many of these synthetic protocols reported so far have disadvantages such as a) needing anhydrous conditions b) use of organic solvents c) drastic reaction conditions d) tedious work-up procedures and e) involving more than one step in synthesis of these compounds. Furthermore, the main disadvantage of almost all exiting protocols is that the catalysts are destroyed in the work-up procedure and cannot be recovered or reused.

In continuation with our work to develop new synthetic methodologies [10], we report herein simple and mild methods for the synthesis of 2-aryl-1-arylmethyl-1*H*-1,3-benzimidazole derivatives (*N*-substituted benzimidazoles 4) in the presence of an available and cheap heterogeneous catalyst system, *p*-toluenesulfonic acid/graphite, under solvent-free condition and 2-aryl-1,3-benzimidazole derivatives (benzimidazoles 3) using a second catalyst system, *N*,*N*-dimethylaniline/graphite, in ethanol by condensation of *o*-phenylenediamine with different aldehydes.

RESULTS AND DISCUSSION

The benzimidazoles 3 and 4 obtained inclusively in a solvent-free catalytic condition using graphite/TsOH system at 75 °C as sketched in Scheme I, method A. All reactions conducted within 15-180 minutes. In the second procedure for the selective preparation of 2-aryl-1,3-benzimidazole derivatives, the reaction condition performed in the presence of *N*,*N*-dimethylaniline and ethanol as shown in Scheme I, method B. All reactions led to excellent yield of corresponding benzimidazoles 3 within 3-20 hours.

Initially, we examined several reported reactions, focusing on high efficacy under various catalytic conditions (Table 1, entries 1-5). As can be seen, the

Scheme 1

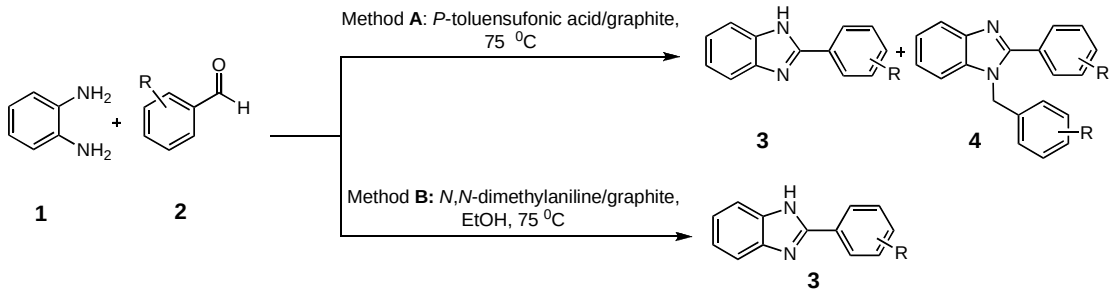


Table 1

The Condensation reaction of *o*-phenylenediamine with benzaldehyde under various reaction conditions

Entry	Condition	Condensing agent	Time (min)	Total Yields (mole ratio) [a]
1	$I_2/KI/K_2CO_3/H_2O$ [11]	PhCHO	45	63% (1:0.7)
2	Silicasulfuric acid, EtOH, rt [12b]	PhCHO	60	73% (1:5.1)
3	Silicasulfuric acid, H_2O, rt [12b]	PhCHO	20	66% (1:5.3)
4	EtOH, H_2O, $NaHSO_3$, 60 °C [13]	PhCHO	60	79% (1:0.3)
5	L-proline, $CHCl_3$, rt [14]	PhCHO	300	91% (1:0.7)
6	TsOH (0.5 g) , 75 °C	PhCHO	120	0.0% (.0:.0)
7	Graphite (0.5 g), 75 °C	PhCHO	140	71% (1:1.8)
8	Graphite (0.5 g), TsOH (0.03 g, 0.19 mmol), 75 °C	PhCHO	65	84% (1:2.6)
9	Graphite (1.0 g), TsOH (0.03 g, 0.19 mmol), 75 °C	PhCHO	40	89% (1:2.9)
10	Graphite (1.0 g), TsOH (0.03 g, 0.19 mmol), EtOH (6 ml), 75 °C	PhCHO	60	81% (1:1.6)
11	Graphite (1.0 g), TsOH (0.03 g, 0.19 mmol), CH_3CN (6 ml), 75 °C	PhCHO	180	65% (1:1.8)
12	Graphite (1.0 g), TsOH (0.03 g, 0.19 mmole), H_2O (6 ml), 75 °C	PhCHO	180	61% (1:2.2)
13	Graphite (1.0 g), TsOH (0.03 g, 0.19 mmole), 75 °C	PhCHO(excess)	40	86% (1:3.0)

a) Isolated yields (mole ratio of products **3**:**4**)

Table 2

Condensation reaction of *o*-phenylenediamine (1 mmol) with different aldehyds (1.6 mmol) using *p*-toluenesulfonic acid/graphite system (1.0 g/0.03 g, 0.19 mmol) at 75 °C

Entry	Aldehyde	Time (min)	Total Yields (mole ratio) [a]	Melthing points (°C)	
				Product **3**	Product **4**
a	C_6H_5CHO	40	89% (1:2.9)	295 (295) [11]	132 (132) [15]
b	4-$MeOC_6H_4CHO$	20	90% (1:3.6)	226 (226-227) [16]	130 (129-130) [12a]
c	4-MeC_6H_4CHO	20	88% (1:1.5)	276-277 (275-276) [16]	130 (128-130) [15]
d	4-ClC_6H_4CHO	45	79% (1:1.9)	302-303 (301) [17]	136 (136) [18]
e	2-ClC_6H_4CHO	15	81% (1:1.7)	233-234 (234) [19]	163 (163) [15]
f	2-Pyridylaldehyde	60	75% (1:2.2)	218 (218) [19]	130 (130) [12a]
g	4-CNC_6H_4CHO	180	79% (1:3.2)	262	221
h	4-$^{i}PrC_6H_4CHO$	10	91% (1:2.4)	250-251	172
i	3-$NO_2C_6H_4CHO$	150	78% (1:2.3)	202-203 (200-202) [20]	169-170
j	2,6-$DiClC_6H_3CHO$	130	85%(1:1.9)	279	177
k	*β*-Naphtaldehyde	50	87% (1:2.0)	217	123
l	2-OHC_6H_4CHO	90	89% (1:2.6)	242 (242) [19]	219

a) Isolated yields (mole ratio of product **3**:**4**)

coincidental production of benzimidazoles 3 and 4 is a common issue in many previously reported papers. In our case when the *o*-phenylenediamine 1 and aromatic aldehydes 2 in the presence of *p*-toluenesulfonic acid/ graphite were allowed to react at 75 °C, both expected products were obtained. Since the resulted proportions showed a dominant trend towards the production of *N*-substituted derivatives 4, several different amounts of graphite and TsOH in the condensation reaction of benzaldehyde with *o*-phenylenediamine were screened for optimization and results are shown in Table 1 (entries 6-13). While no products were obtained in the presence of TsOH alone, a 71% total yield was obtained using graphite (entries 6 and 7). The yields were improved in the best way when 1.0 g of graphite and 0.03 g of TsOH were used (entry 9). The effect of solvents in this reaction

was detrimental since overall yields have decreased in CH_3CN, H_2O and even EtOH solutions (entries 10-12). Using excess amount of benzaldehyde showed no improvement in the yields as shown in Table 1 (entry 13).

Several examples of condensation reaction of *o*-phenylenediamine with aromatic aldehydes containing different electron-withdrawing and electron-donating groups in the presence of a catalytic amount of TsOH and graphite are shown in Table 2.

As can be seen in Table 2, aromatic aldehydes having different substituents such as methoxy, chloro, methyl, etc. were converted to the corresponding benzimidazoles in reasonable yields. All reactions were carried out within 15 to 180 minutes. The time of reactions was depending on the substituents present on the substrates. Reactions with substrates having electron-withdrawing groups such as chloro, cyano, etc. proceeded at slower rates than those with electron-donating groups such as methyl, isopropyl, etc.. From the yield point of view, aldehydes containing electron-donating groups gave products in higher yields than those containing electron-withdrawing groups.

According to our experiments, we found that excellent selectivity towards the production of benzimidazoles 3 can be best achieved when using a basic agent in the reaction media and ethanol as solvent, as shown in Table 3. Based on Table 3, aliphatic bases resulted in lower yields compared to aromatic ones. Since *N*,*N*-dimethylaniline provided the best condition, it was chosen for further study (Table 3, entry 6).

Table 3

The condensation reaction of *o*-phenylenediamine (1 mmol) with 4-Chlorobenzaldehyde (1.05 mmol) in the presence of different basic agents (1.1 mmol), graphite (1.0 g) and ethanol as solvent at 75 °C.

Entry	Base (1.1 mmol)	Time (h)	Yields of **3** (%)[a]
1	$EtNH_2$	45	43
2	Et_2NH	45	39
3	Et_3N	40	45
4	Pyridine	16	79
5	Aniline	15	86
6	*N*,*N*-dimethylaniline	15	91

[a]) Isolated yields

The results of condensation reaction of *o*-phenylenediamine with the same aromatic aldehydes as those used in method A are shown in Table 4. In all cases, the production of *N*-substituted benzimidazoles 4 was trace to a few percents. As can be seen in Table 4, aromatic aldehydes having different substituents such as methyl, hydroxyl, chloro, etc. were converted to the corresponding 2-aryl-1,3-bezimidazoles in excellent yields. All reactions were done within 3 to 20 hours. The time of reactions was depending on the substituents present on the substrates. Reactions with substrates having electron-withdrawing groups such as chloro, cyano, nitro, etc. produced at slower rates than those with electron-donating groups such as methyl, isopropyl, etc.

Table 4

Condensation of o-phenylenediamine (1 mmol) with different aldehydes (1.05 mmol) using heterogeneous *N*,*N*-dimethylaniline/graphite (1.0 mmol/1.0 g) system in ethanol at 75 °C.

Entry	Aldehyde	Time (h)	Yields of **3** (%)[a]
a	C_6H_5CHO	4	67
b	4-$MeOC_6H_4CHO$	6	85
c	4-MeC_6H_4CHO	3	86
d	4-ClC_6H_4CHO	15	91
e	2-ClC_6H_4CHO	13	87
f	2-Pyridylaldehyde	17	79
g	4-CNC_6H_4CHO	16	91
h	4-$^{i}PrC_6H_4CHO$	3	83
i	3-$NO_2C_6H_4CHO$	20	71
j	2,6-$DiClC_6H_3CHO$	17	84
k	*β*-Naphtaldehyde	14	81
l	2-OHC_6H_4CHO	8	93

a) Isolated yields

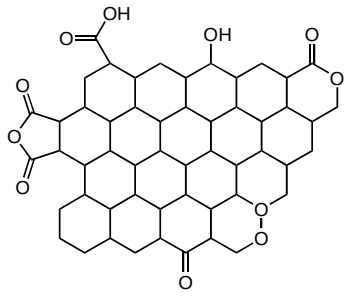
In the case of yields, no significant difference could be found in the products of the condensation reaction of electron rich and electron deficient aldehydes. This is noteworthy that the condensation reaction of *o*-phenylenediamine with benzaldehyde on a 30 mmol scale proceeded just as well as the 1 mmol reaction for both methods A and B.

The mechanism of the reaction is a subject of a further study. As for now, we believe that graphite acts as a dehydration reagent or it serves as a heat conductor surface for benzimidazoles synthesis.

At the edge of the basal planes of carbon atoms in the graphite structure, where bonding in the plane is terminated, are unsaturated carbon atoms. These sites are associated with high concentrations of unpaired electrons and therefore play a significant role in chemisorption.

These carbons may chemisorb oxygen, producing oxygen surface groups which are by far the most important in influencing the surface characteristics and adsorption behavior of graphite [21] (Scheme II).

Scheme II



The surface groups most suggested are carboxyl, phenolic hydroxyl and quinine carbonyl groups. Slightly fewer in number are the reports of ether, peroxide, ester

groups, lactones, carboxylic acid anhydrides and cyclic peroxides [22]. These structures exhibit a high affinity for water [22e, 23]. As described in Scheme III we have formulated a suggested mechanism for the solvent free condensation reaction of *o*-phenylenediamine and aldehyde molecules (method A).

As can be seen, at the initial stage, the aldehyde molecule is protonated, subsequently one of the amine groups attacks to the activated aldehyde then a water molecule is lost to form the iminium intermediate. The intermediate can go through two directions. Firstly, it can be cyclized to form the dihydrobenzimidazole derivatives B, following a subsequent oxidation to form benzimidazoles **3** [11, 24, 25]. Secondly, it may proceed further and attack to the second activated aldehyde molecule to form dibenzylidene-*o*-phenylenediamine derivatives C followed by ring closure [12a, 14]. Finally aromatization takes place *via* deprotonation and 1,3-hydrid transfer.

The role of TsOH as a co-activator seems to be a provider of available proton for different stages of the reaction like, dehydration stage or recovery of the deprotonated carbon surface groups for subsequent catalytic cycles.

Conducting the reaction in the absence of TsOH (with a longer time and lower yield) (Table 1, entry 7) and presence of basic agents (with very longer times and lower yields) (Table 3) may be able to confirm the proton availability role.

So, we believe that *N*,*N*-dimethylaniline as a good base not a nucleophile diminished the presence of available proton, resulted in a good selectivity. Moreover, the reduced number of activated aldehyde molecules, provided the situation in which the attack of the free NH_2 functional groups to the iminium carbon atom instead of the carbonyl group of a second aldehyde molecule led to the formation of benzimidazoles **3** selectively.

Besides availability and cheapness of graphite, another interesting behavior of graphite lies in the fact that it can be reused after a simple washing with EtOH or ethylacetate, thus rendering the process more economic. The yields of the condensation reaction of *o*-phenylenediamine with benzaldehyde in the 2nd, 3rd and 4th use of the graphite for both methods A and B were almost the same as that in the first use (Table 5). It should be noted that after extraction with ethylacetate or ethanol, *p*-toluenesulfonic acid and *N*,*N*-dimethylaniline were not found on the graphite; therefore it is necessary to add them again for the 2nd use of recovered graphite.

Table 5

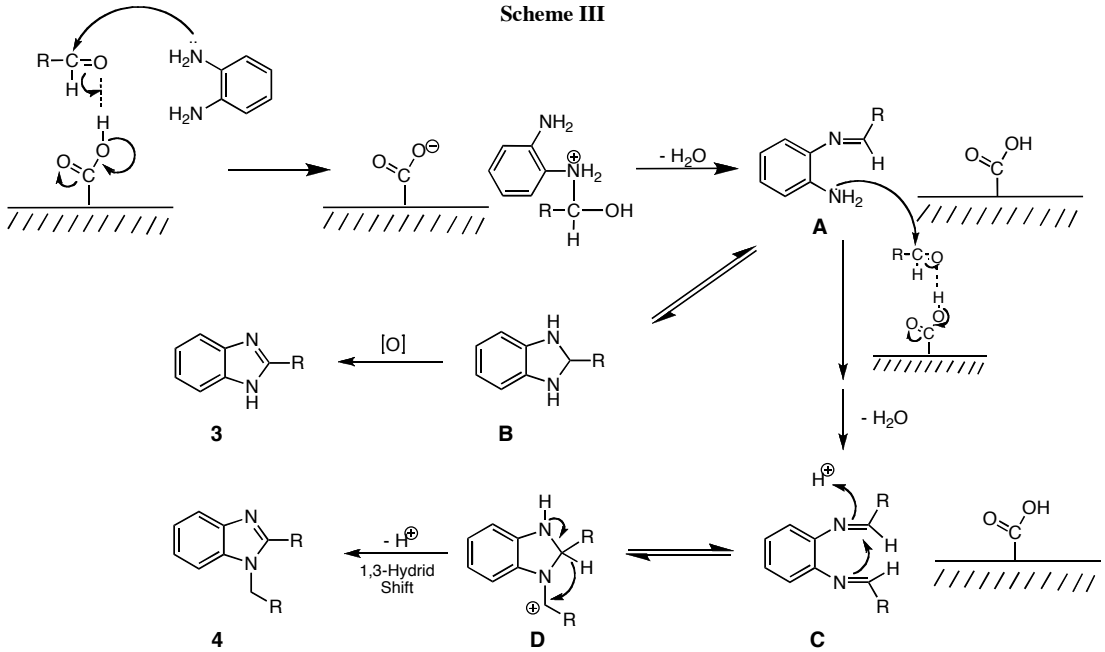
reuse of graphite in the condensation reaction of *o*-phenylendiamine with benzaldehyde for both methods A and B

Number of use	Total Yields (mol ratio **3**:**4** /yield of **3**)[a]	Recovery of graphite (% / %)[a]
1	89% (1:2.9)/67%	98/96
2	86% (1:2.6)/61%	93/93
3	87% (1:2.9)/60%	89/90

a) (method A/method B)

In conclusion, the present synthetic methods are simple, inexpensive and mild procedures for preparation of biologically active benzimidazole derivatives using heterogeneous catalyst systems, TsOH/graphite and *N*,*N*-dimethylaniline/graphite. The advantages of the present reactions are the elimination of organic solvents (method A), toxic reagents, using biologically and environmentally safe solvent, ethanol, (method B) and reusability of graphite.

Scheme III



EXPERIMENTAL

Instrumentation, Analysis and Starting Material. Progress of reactions was monitored by the using silica gel Polygram's SIL G/UV 254 plates. IR spectra were recorded on the Shimadzu FT-IR 8300 spectrophotometer. NMR spectra were recorded on a Bruker DPX 250 MHz instrument and Mass spectra on a Shimadzu QP 1100 EX spectrometer using EI 70 ev modes. Chemical materials were purchased from Fluka, Aldrich and Merck Companies.

General procedure for method A: A mixture of graphite (1.0 g), TsOH (0.03 g, 0.19 mmol), and *o*-phenylenediamine (0.108 g, 1 mmol) was prepared, well mixed and grinded by a mortar and pestle. Then aldehyde (1.6 mmol) was added to the mixture and grinding was continued for another 10 minutes. The mixture was transferred into a quickfit tube, capped and stirred with a magnetic stirrer in an oil bath with a temperature of 75 °C for the time specified in Table 2. Progress of reactions was monitored by TLC using *n*-hexane/ethylacetate (7:1). After reactions were completed, reaction mixtures were washed with hot ethanol or ethylacetate (3 × 30 mL). After evaporating the solvent, the mixtures of products **3** and **4** were obtained either by recrystallization in ethanol or using short silica gel column chromatography using *n*-hexane/ethylacetate (10:1) as eluent.

General procedure for method B. A mixture of *o*-phenylenediamine (1.0 mmol) and graphite (1.0 g) was stirred in ethanol (15 mL) in a quickfit tube. *N*,*N*-Dimethylaniline (1.0 mmol) and aldehydes (1.05) were then added respectively; tubes were loosely capped and stirred with a magnetic stirrer in an oil bath with a temperature of 75 °C for the time specified in Table 4. Progress of reactions was monitored by TLC using *n*-hexane/ethylacetate (7:1). After the reactions were completed, the reaction mixtures were filtered and washed with hot ethanol (3 × 40 mL). The mixtures were concentrated under reduced pressure to give the crude products, which were purified by recrystallization or silica gel column chromatography (for entries **3a** and **3i**, Table 4) using hexane/ethylacetate (10:1) as eluent.

4-(1*H*-1,3-Benzimidazol-2-yl)benzonitrile (3g). This compound was obtained as white crystals; mp: 262 °C; IR (KBr): 3417 (m), 3047 (w), 2912 (w), 2222 (m), 1605 (m), 1454 (m), 1408 (s), 837 (s), 748 (s) cm^{-1}; ^1H NMR (DMSO-d_6, 250 MHz): Δ 7.23-768 (m, 4H), 8.00 (d, 2H, J = 8.1 Hz), 8.32 (d, 2H, J = 8.1 Hz); ^{13}C NMR (DMSO-d_6, 62.9 MHz): Δ 111.7, 111.8, 118.6, 119.3, 122.2, 123.3, 127.0, 132.9, 134.2, 149.3; Mass m/z (%) 220 (M^++1, 14), 219 (M^+, 100), 102 (20); *Anal*. Calcd for $C_{14}H_9N_3$: C, 76.70; H, 4.14. Found: C, 76.53; H, 4.22.

2-(4-IsoPropylphenyl)-1*H*-1,3-benzimidazole (3h). This compound was obtained as white crystals; mp: 250-251 °C; IR (KBr): 3425 (w), 3055 (w), 2873 (m), 2951 (s), 1439 (s), 1273 (m), 741 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz,): Δ 1.19 (d, 6H, J = 6.9 Hz), 2.85 (m, 1H), 7.17-7.26 (m, 4H), 7.57 (m, 2H), 7.96 (d, 2H, J = 8.3 Hz); ^{13}C NMR (DMSO-d_6, 62.9 MHz): Δ 23.6, 33.3, 121.9, 126.4, 127.7, 129.1, 129.4, 134.5, 150.3, 151.3; Mass m/z (%) 237 (M^++1, 17), 236 (M^+, 62), 221 (100), 193 (13), 116 (72); *Anal*. Calcd for $C_{16}H_{16}N_2$: C, 81.32; H, 6.82. Found: C, 81.20; H, 6.74.

2-(3-Nitrophenyl)-1*H*-1,3-benzimidazole (3i). This compound was obtained as pale yellow crystals; mp: 202-203 °C; IR (KBr): 3437 (w), 3078 (w), 1529 (s), 1348 (s), 732 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz): Δ 7.20-7.39 (m, 2H), 7.61-7.67 (m, 3H), 8.25 (d, 1H, J = 8.4 Hz), 8.43 (d, 1H, J = 7.8 Hz), 8.77 (t, 1H, J = 1.8 Hz); ^{13}C NMR (DMSO-d_6, 62.9 MHz): Δ 116.0, 120.8, 122.7, 124.2, 130.6, 131.6, 132.4, 136.9, 148.3, 149.0; Mass m/z (%) 240 (M^++1, 17), 239 (M^+, 100), 193 (67); *Anal*. Calcd for $C_{13}H_9N_3O_2$: C, 65.27; H, 3.79. Found: C, 65.41; H, 3.68.

2-(2,6-Dichlorophenyl)-1*H*-1,3-benzimidazole (3j). This compound was obtained as white crystals; mp: 279 °C; IR (KBr): 3430 (w), 3058 (w), 1553 (w), 1429 (s), 1329 (w), 777 (m), 741 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz): Δ 7.11-7.30 (m, 6H), 7.54 (d, 2H, J = 2.32 Hz); ^{13}C NMR (DMSO-d_6, 62.9 MHz): Δ 115.4, 122.2, 128.3, 130.4, 132.4, 135.0, 137.0, 146.6; Mass m/z (%) 267 (M^++4, 0.1), 265 (M^++2, 7), 263 (100) (M^+), 228 (58), 193 (71); *Anal*. Calcd for $C_{13}H_8C_{12}N_2$: C, 59.34; H, 3.06. Found: C, 59.16; H, 3.15.

2-(2-Naphtyl)-1*H*-1,3-benzimidazole (3k). This compound was obtained as white crystals; mp: 217 °C; IR (MBr): 3425 (w), 3047 (m), 1605 (w), 1447 (m), 1385 (m), 748 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz): Δ 7.19 (dd, 2H, J_1 = 6.0 Hz, J_2 = 3.0 Hz), 7.37-7.40 (m, 2H), 7.59-7.77 (m, 5H), 8.11 (dd, 1H, J_1 = 8.6, J_2 = 1.7), 8.49 (s, 1H); ^{13}C NMR ($CDCl_3$, 62.9 MHz): Δ 115.2, 123.2, 123.6, 126.5, 126.8, 127.2, 127.8,128.5, 129.0, 134.2, 138.1, 145.9, 151.6; Mass m/z (%) 245 (M^++1, 43), 244 (M^+, 100), 153 (58); *Anal*. Calcd for $C_{17}H_{12}N_2$: C, 83.58; H, 4.95. Found: C, 83.40; H, 4.97.

1-(4-Methoxybenzyl)-2-(4-methoxyphenyl)-1*H*-1,3-benzimidazole (4b). This compound was obtained as white Crystals; mp: 130 °C; IR (KBr): 3047 (w), 2931 (m), 1604 (m), 1458 (s), 1245 (s), 1165 (m), 1022 (m), 825 (m), 737 (m) cm^{-1}; ^1H NMR (DMSO-d_6, 250 MHz): Δ 3.65 (S, 3H), 3.81 (S, 3H) , 5.46 (S, 2H), 6.83 (d, 2H, J = 7.7 Hz), 6.92 (d, 2H, J = 7.7 Hz), 7.05 (d, 2H, J = 7.5 Hz), 7.17-7.21 (m, 2H), 7.39-7.21 (m, 2H), 7.5 (d, 2H, J = 7.5 Hz); ^{13}C NMR (DMSO-d_6, 62.9 MHz): Δ 46.8, 55.0, 55.2, 111.0, 114.1, 114.3, 118.9, 122.0, 122.3, 127.4, 128.0, 129.0, 130.4, 135.8, 142.7, 153.1, 158.5, 160.3; Mass m/z (%) 345 (M^++1, 65), 344 (M^+, 100), 224 (83), 133 (25); *Anal*. Calcd for $C_{22}H_{20}N_2O_2$: C, 76.72; H, 5.85. Found: C, 76.59; H, 5.75.

4-(1-(4-Cyanobenzyl)-1*H*-1,3-benzimidazole-2-yl)benzonitrile (4g). This compound was obtained as white crystals; mp: 221 °C; IR (KBr): 3059 (w), 2843 (m), 2642 (w), 2222 (m), 1610 (w), 1431 (s), 837 (m), 748 (m) cm^{-1}; ^1H NMR: (DMSO-d_6, 250 MHz): Δ 5.62 (s, 2H), 7.14 (d, 2H, J = 8.3), 7.27-7.31 (m, 2H), 7.48-7.52 (m, 2H), 7.73-7.79 (m, 2H), 7.88 (d, 2H, J = 8.3), 7.97 (d, 2H, J = 8.1); ^{13}C NMR (DMSO-d_6, 62.9 MHz): Δ 47.2, 110.3, 111.1, 118.3, 118.4, 119.67, 122.8, 123.5, 127.0, 129.8, 132.7, 134.2, 135.9, 142.3, 150.5, 151.8; Mass m/z (%) 335 (40) (M^++1, 40) 334 (M^+, 100), 232 (10), 218 (58), 116 (87); *Anal*. Calcd for $C_{22}H_{14}N_4$: C, 79.02; H, 4.22. Found: C, 78.81; H, 4.34.

1-(4-isopropylbenzyl)-2-(4-isopropylphenyl)-1*H*-1,3-benzimidazole (4h). This compound was obtained as white Crytals; mp: 172 °C; IR (KBr): 3039 (m), 2951 (s), 1462 (s), 829 (m), 741 (m) cm^{-1}; ^1H NMR (DMSO-d_6, 250 MHz): Δ 1.11 (d, 6H, J = 6.6 Hz), 1.21 (d, 6H, J = 6.1 Hz), 2.79 (m, 1H), 2.93 (m, 1H), 5.52 (S, 2H), 6.90 (d, 2H, J = 7.1 Hz), 7.14-7.20 (m, 4H), 7.39-7.50 (m, 4H), 7.63 (d, 2H, J = 7.4 Hz); ^{13}C NMR (DMSO-d_6, 62.9 MHz): Δ 23.6, 23.7, 32.9, 33.2, 47.2, 111.0, 119.1, 122.1, 122.5, 125.9, 126.6, 128.7, 129.0, 133.2, 134.2, 135.8, 142.6, 147.5, 150.2, 153.0; Mass m/z (%) 369 (M^++1, 29), 368 (M+, 100), 325 (9), 235 (14); *Anal*. Calcd for $C_{26}H_{28}N_2$: C, 84.74; H, 7.66. Found: C, 84.85, H, 7.55.

1-(3-Nitrobenzyl)-2-(3-nitrophenyl)-1*H*-1,3-benzimidazole (4i). This compound was obtained as pale yellow crystals; mp: 169-170 °C; IR (KBr): 3178 (w), 1523 (s), 1342 (s), 741 (m)

cm^{-1}. ^1H NMR (DMSO-d_6, 250 MHz): Δ 5.67 (s, 2H), 7.16-7.20 (m, 2H), 7.26 (d, 1H, J = 7.6 Hz), 7.37-7.49 (m, 2H), 7.64- 7.70 (m, 2H), 7.81 (s, 1H), 7.96-8.05 (m, 2H), 8.21 (d, 2H, J = 8.22 Hz), 8.30 (s, 1H); ^{13}C NMR (DMSO-d_6, 62.9 MHz): Δ 46.8, 111.1, 119.7, 121.2, 122.5, 122.8, 123.5, 123.7, 124.5, 130.6, 131.2, 132.7, 135.2, 136.0, 139.0, 142.4, 147.8, 150.9, 156.0; Mass m/z (%) 375 (M^++1, 23), 374 (M^+, 100),328 (2), 282 (12), 239 (5); *Anal*. Calcd for $C_{20}H_{14}N_4O_4$: C, 64.17; H, 3.77. Found: C, 64.01; H, 3.89.

1-(2,6-Dichlorobenzyl)-2-(2,6-dichlorophenyl)-1*H*-1,3-benzimidazole (4j). This compound was obtained as white crystals; mp: 177 °C; IR (KBr): 3059 (w), 2923 (m), 1566 (w), 1423 (s), 779 (s), 737 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz): Δ 5.56 (S, 2H), 7.09-7.20 (m, 1H), 7.26-7.41 (m, 7H), 7.85 (m, 2H); ^{13}C NMR ($CDCl_3$, 62.9 MHz): Δ 44.0, 110.6, 121.0, 122.3, 123.2, 128.0, 128.5, 130.0, 130.65, 131.0, 131.4, 135.3, 137.0, 146.2; Mass m/z (%) 428 (M^++6, 0.06), 426 (M^++4, 0.9), 224 (M^++2, 11), 422 (M^+, 74), 383 (86), 350 (8), 262 (100), 229 (81), 192 (54); *Anal*. Calcd for $C_{20}H_{12}C_{l4}N_2$: C, 56.91; H, 2.87. Found: C, 56.82; H, 2.96.

2-(2-Naphtyl)-1-(2-naphtylmethyl)-1*H*-1,3-benzimidazole (4k). This compound was obtained as white crystals; mp: 123 °C; IR (KBr): 3049 (s), 1604 (w), 1423 (s), 1388, 746 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz): Δ 5.59 (s, 2H), 7.17-7.25 (m, 4H), 7.39- 7.46 (m, 4H), 7.48 (s, 1H), 7.63 (m, 2H), 7.77- 7.89 (m, 6H), 8.13 (s, 1H); ^{13}C NMR ($CDCl_3$, 62.9 MHz): Δ 48.8, 110.6, 120.0, 123.0, 123.3, 124.8, 126.0, 126.3, 126.6, 126.7, 127.3, 127.9, 128.6, 128.6, 129.1, 129.3, 133.9; Mass m/z (%) 384 (M^+, 100), 243 (68), 153 (62), 141 (91); *Anal*. Calcd for $C_{28}H_{20}N_2$: C, 87.47; H, 5.24. Found: C, 87.61; H, 5.31.

2-(1-(2-Hydroxybenzyl)-1*H*-1,3-benzimidazole-2-yl)phenol (4l). This compound was obtained as white crystals; mp: 219 °C; IR (KBr): 3302 (b), 3047 (w), 2932 (w), 1589 (m), 1454 (s), 1389 (m), 1250 (m), 740 (m) cm^{-1}; ^1H NMR (DMSO-d_6, 250 MHz): Δ 5.39 (S, 2H), 6.39 (m, 1H), 6.57 (m, 1H), 6.79-6.87 (m, 2H), 7.01 (m, 2H), 7.20-7.23 (m, 2H), 7.36-7.42 (m, 3H), 7.68 (m, 1H), 10.08 (S, 1H), 10.88 (S.1H); ^{13}C NMR (DMSO-d_6, 62.9 MHz): Δ 43.2, 110.8, 115.0, 116.1, 116.4, 118.7, 118.9, 122.0, 122.6, 126.6, 128.3, 130.2, 131.3. 135.1, 141.8, 152.0, 154.4, 156.3; Mass m/z (%) 316 (M^+, 67), 219 (28), 210 (100); *Anal*. Calcd for $C_{20}H_{16}N_2O_2$: C, 75.93; H, 5.10. Found: C, 76.08; H, 5.00.

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