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Graphical Abstract

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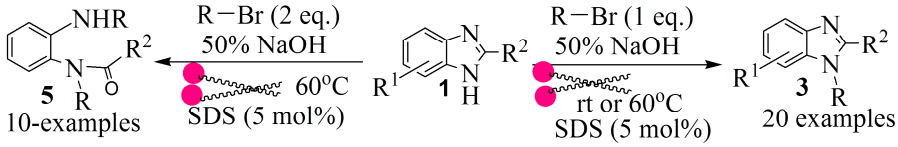

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An efficient strategy for *N*-alkylation of benzimidazoles/ imidazoles in SDS-aqueous basic medium and *N*-alkylation induced ring opening of benzimidazoles

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ABSTRACT

A sustainable route for the *N*-1 alkylation of imidazole and benzimidazole derivatives has been developed under volatile organic solvent free condition in alkaline water-SDS system. Incorporation of SDS in the reaction medium enhances the reaction rate by suppressing the solubility issue that arises for different substrates. This method provides high yield of the alkylated product in a shorter reaction time. For reactive alkyl halides reaction proceeds at ambient temperature whereas in the cases of less reactive alkyl halides require 55-60^{o}C to complete alkylation process. *N*-alkylation induced ring opening of the heterocyclic ring in benzimidazole derivatives to multifunctional aromatic compounds were noticed at 60^{o}C when more than two equivalents of alkyl halide was used.

1. Introduction

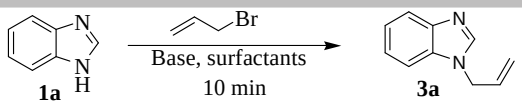
The development of novel synthetic methodologies that are efficient and more compatible with the environment is an intense area of research to facilitate the synthesis of target molecules of specific interest. One of the most desirable approaches to address this challenge is a search for surrogates for commonly employed organic solvents those are used in large quantity due to various health and environmental reasons associated with them. In this regard water would be the perfect solvent to carry out chemical operations due to the fact that it is safe, most non-toxic, and inexpensive. However, often the poor solubility of organic compounds in aqueous medium becomes detrimental and therefore improving the solubility of organic compounds in water has been drastically investigated.[1-7] One of such approach is the incorporation of surface-active agents (surfactants)[8,9] in aqueous media that not only enhance the solubility of organic substrates but also increase the reactivity via the formation of micelles or vesicular cavities.[10-13] In recent years micelle-mediated organic reactions become an area of rapidly growing interest.[14-17] On the other hand, imidazoles/ benzimidazoles are the most abundant and integral scaffolds that occur ubiquitously in a large number of bioactive natural products, synthetic drugs, pharmaceuticals and agro-chemicals.[18,19] Amongst many derivatives of benzimidazoles, an *N*-1 substituted derivative represents an important branch of this family due to their wide spectrum of biological and pharmacological activity.[20] *N*-1 Alkylated benzimidazoles and imidazoles are also important intermediates in the preparation of various ionic liquids.[21-29] Thus, synthesis of *N*-1 alkylated benzimidazole/imidazole derivatives depending on the biological importance or application in the development of new methodologies have become a challenge in organic synthesis and moreover the reaction in aqueous medium is of further importance. Although Singh et al.[30] reported a convenient access of secondary/tertiary amines from primary amine under water-SDS condition but a general approach for N-1 alkylation of benzimidazoles/imidazoles in water are lacking. Despite of such importance only few methods are reported for the synthesis of *N*-alkylated benzimidazoles and imidazoles. Generally *N*-1 alkylation of amines is achieved[31] by reaction with alkyl halide using anhydrous K_2CO_3 or Cs_2CO_3 in different organic solvent like acetone, methanol or DMF. Some other reported methods include a convenient access for the *N*- alkylation of imidazoles and benzimidazoles using powdered KOH in acetone at room temperature with a slight excess of the alkyl halide at room temperature to give the mono alkylated product or using a KOH in the presence of 3-5 mol% of a crown ether, dicyclohexyl-18 crown-6 to afford the *N*-alkylated product.[32] Direct condensation between o-phenylene diamine and various aromatic aldehydes under different reaction conditions such as 'on water' approach or other catalysts also provides direct routes to *N*-1 alkylated 2-aryl substituted benzimidazoles.[33-36] In spite of having tremendous potentiality of these reported methods they suffer from some serious drawbacks[37,38] such as low yields, harsh reaction conditions, prolonged reaction time, selectivity issue, solubility and competitive side reaction, application of hazardous bases and also concomitant formation of quaternary ammonium salts. Moreover, the synthesis of these compounds is usually

carried out in polar solvents such as ethanol, methanol, acetic acid, dimethyl formamide (DMF), and dimethyl sulfoxide (DMSO), leading to complex isolation and recovery products. Thus as a part of our ongoing program to develop a novel methodology for *N*- alkylated benzimidazole or its derivatives we herein report base mediated *N*-1 alkylation of substituted benzimidazoles/imidazoles, followed by alkylation induced ring opening of the benzimidazoles using in excellent yields under surfactants mediated organic solvent free condition. The present method has several advantages that include a mild reaction condition, operational simplicity, very short reaction time, excellent yield of products and no formation of quaternary salt.

2. Results and discussions

Initially we consider *N*-1 alkylation of benzimidazole as model reaction using allyl bromide as alkylating agent. To standardize the condition several attempt were made by variation of different parameter. Stirring of the suspension of benzimidazole **1a** (1 mmol) in 50 % aq. NaOH (1.0 mL) with allyl bromide at room temperature afforded *N*- allylated benzimidazole **3a** in 65% yield (entry 1, Table 1) after 10 min., increasing or decreasing the amount of NaOH or reaction time did not improve the yield. We reasoned that the solubility problem may occur between the organic substrate and the aq. NaOH. As aqueous medium has always been considered as beneficial for carrying out organic reaction and the amount of aqueous solution may not good enough to get soluble the substrates, and hence the reaction did not occur with a satisfactory yield. Thus to improve the yield various surfactants were planned to introduce into the system to increase the solubility of the organic substrates in aqueous phase.[10-13,39] The uses of cationic surfactants (10 mol%) like TBAB or CTAB gave a complex mixture with incomplete conversion of the organic substrate as revealed by TLC (entries 2, Table 1). The neutral surfactant Triton X 100 provides improved yield of **3a** to some extent as compared to non-surfactant mediated reaction (entry 1 vs entry 3, Table 1). Gratifyingly, utilization of anionic surfactant SDS (10 mol%), remaining other reaction conditions being the same, the yield of **3a** was improved drastically to 97% (entry 4, Table 1). On decreasing the amount of SDS to 5 mol% and amount of NaOH (0.5 mL) the yield was again 97% (entries 5-6, Table 1). It was also observed that uses of quaternary ammonium hydroxide (50% aq. Bu_4OH) as base yielded poor yield of the allylated product (entry 7, Table 1). Under the similar reaction condition organic base such as Et_3N provides only trace amount of the product whereas in organic environment no product was traced (entries 8-9, Table 1). Most probably because of high pKa value (pKa of benzimidazole 12.8) Et_3N is unable to abstract N-H proton rather it gets quaternization (as indicated by the formation of white precipitate and TLC) in the presence of reactive allyl bromide. Thus it is assumed that water present in the medium[40, 41] may play pivotal role in the alkylation process through H-bonding that facilitated substrate to get solubilize as additional effect with SDS. Being inspired by the optimization reaction allylation of benzimidazole (Table 1) at the *N*-1 position under aqueous environment we aimed to generalize the procedure using different substituted benzimidazoles and imidazoles. Subsequently, we carried out the

Table 1: Optimization of the reaction condition[a]



1a **3a**

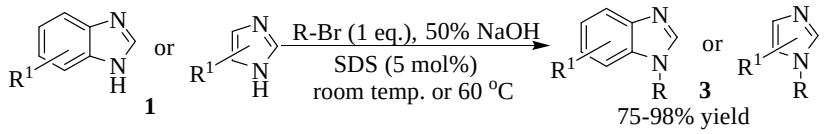
Entry	Base	Surfactant	Yield (%)
1	NaOH	No	65[b]
2	NaOH	TBAB or CTAB (10 mol%)	Mixture[b]
3	NaOH	Triton X 100 (10 mol%	73[b,c]
4	NaOH	SDS (10 mol%)	97[b,c]
5	NaOH	SDS (5 mol%)	97[b,c]
6	NaOH	SDS (10 mol%)	97[c,d]
7	Bu_4OH	SDS (10 mol%)	30[e]
8	Et_3N	SDS (10 mol%)	trace[f]
9	Et_3N	No	NR[g]

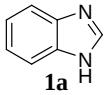
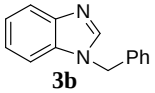
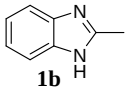
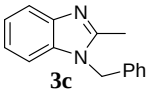
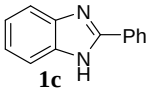
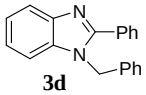
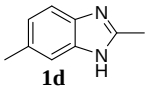
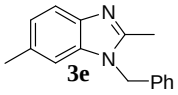
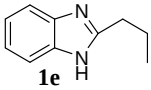
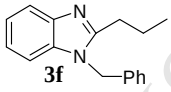
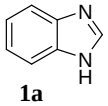
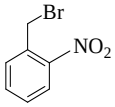
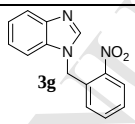
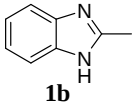
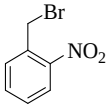
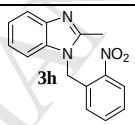
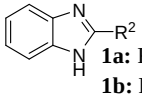
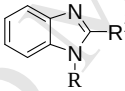
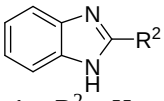
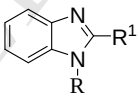
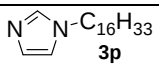
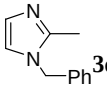
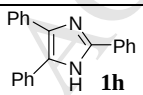
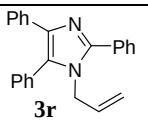
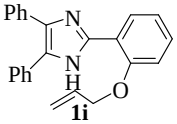
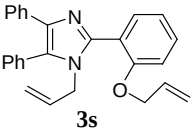
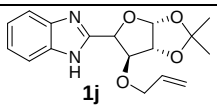
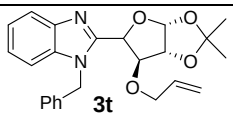
[a] Reaction performed in 1mmol scale; [b] 1mL50% aq. NaOH was used; [c] isolated yield; [d] 0.5 mL of 50 % aq. NaOH was used; [e] 0.5 mL aqueous Bu_4NOH was used; [f] reaction performed in water; [g] reaction performed in dichloromethane

N-1 alkylation of different benzimidazole derivatives according to the standard protocol as described in Table 1. The choice of alkyl halides were made considering reactivity of alkyl halides. Reactive alkyl halide, benzyl bromide underwent alkylation of different benzimidazoles **1a-e** to **3b-f** (entries 1-5 Table 2) in excellent yields in the range of 78-96% and 2-nitrobenzylbromide afforded corresponding alkylated products **3g-h** in 85% yields (entries 6-7, Table 2). The substrate 2, 6-dimethyl benzimidazole (**1d**) undergoes *N*-1 alkylation smoothly in good yields and shorter reaction time but resulted tautomers (equal population) of *N*-1 benzylated benzimidazoles (entry 4, Table 2) as revealed by NMR spectroscopy. In contrast, the less reactive alkyl bromides like butyl or hexyl bromide or long chain alkyl bromides like octyl, or hexadecyl bromide did not produce any alkylated product at room temperature but at the temperature of 60°C a clean transformation to *N*-1 alkylated products (as shown in Table 2) were achieved in excellent yields within a short period of time (entries 8-14, Table 2). Apart from benzimidazoles, we then focused on the *N*-1 alkylation of imidazoles, substituted imidazoles which gratifyingly afforded *N*-1 alkylation in excellent yields and shorter reaction time. The imidazoles when treated with cetyl bromide (entry 15, Table 2) underwent smooth alkylation in excellent yield of **3p** (95%) at 60°C. The other imidazoles like 2-methyl imidazole also gave *N*-1-benzylated (entry 16, Table 2) product **3q** in 93% yield and 2, 4, 5-triphenyl imidazole (**1h**) underwent *N*-1- allylation (entry 17, Table 2) in 20 mins at 60°C and the yield (**3r**) was found to be 80%. The imidazole derivative 2-(2-(allyloxy phenyl)- 4, 5-diphenyl imidazole (**1i**) also afforded *N*-1 allylated product **3s** (entry 18, Table 2) in 20 mins. Another important feature of the present methodology is the alkylation of sugar based chiral benzimidazole (**1j**) [42] to the formation of corresponding *N*-benzyl derivative **3t** in 82% yield (entry 19, Table 2).

The results summarized in Table 2 indicated that in the cases of reactive alkyl halides the alkylation reactions proceed at room temperature whereas elevated temperature is required for alkyl halides of poor reactivities. Then we were curious to observe the effect of temperature on the *N*-allylation or benzylation of benzimidazole under basic SDS medium to complete the reaction even in faster. Accordingly, 2-phenyl

Table 2: *N*-alkylation of Benzimidazoles and Imidazoles in 50% aq. NaOH-SDS medium

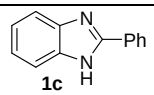
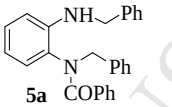
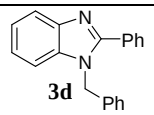
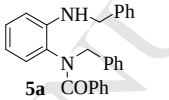
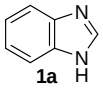
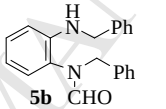
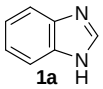
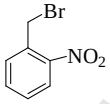
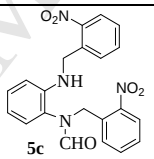
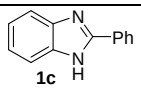
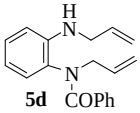
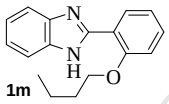
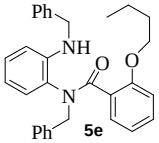
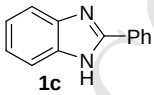
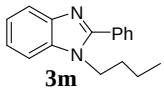
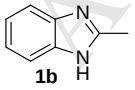
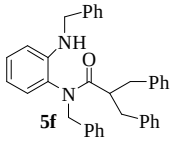
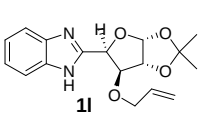
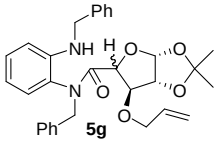


Entry	Substrate (**1**)	RBr (**2**)	Product (**3**)	Time (mins)	Yield (%)
1	 **1a**	$PhCH_2Br$	 **3b**	15	96[a]
2	 **1b**	$PhCH_2Br$	 **3c**	10	90[a]
3	 **1c**	$PhCH_2Br$	 **3d**	20	85[a]
4	 **1d**	$PhCH_2Br$	 **3e**	30	87[b]
5	 **1e**	$PhCH_2Br$	 **3f**	30	88[a]
6	 **1a**		 **3g**	40	85[a]
7	 **1b**		 **3h**	40	85[a]
8 9 10	 **1a:** R^2 = H **1b:** R^2 = Me **1c**: R^2 = Ph	nC_4H_9Br	 **3i**: R^1 = H, R = nC_4H_9 **3j**: R^1 = Me, R = nC_4H_9 **3k**: R^1 = Ph, R = nC_4H_9	15 20 30	89[b] 91[b] 85[b]
11 12 13 14	 **1a:** R^2 = H **1b:** R^2 = Me	$nC_6H_{13}Br$/ $nC_8H_{17}Br$/ $nC_8H_{17}Br$/ $nC_{16}H_{33}Br$	 **3l**: R^1 = H, R = nC_6H_{13} **3m**: R^1 = H, R = nC_8H_{17} **3n**: R^1 = Me, R = nC_8H_{17} **3o**: R^1 = H, R = $nC_{16}H_{33}$	20 20 30 20	97[b] 96[b] 90[b] 98[b]
15	 **1f**	$C_{16}H_{33}Br$	 **3p**	20	95[b]
16	 **1g**	$PhCH_2Br$	 **3q**	20	93[a]
17	 **1h**		 **3r**	20	80[b]
18	 **1i**		 **3s**	20	78[b]
19	 **1j**	$PhCH_2Br$	 **3t**	20	82[a]

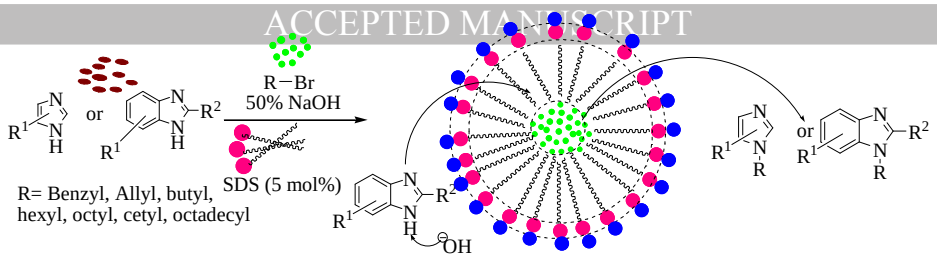
[a] reaction at room temperature, [b] reaction at 60 °C

benzimidazole was heated at 60°C in the presence of one equivalent of benzyl bromide, 5mol% of SDS and 0.5 mL of 50% NaOH for 15 minutes, we observed a mixture of product with incomplete conversion of starting materials and one of the product was detected as *N*-1 alkylated product **3d** and other was completely different. The situation did not improve even heating of the mixture for longer time (3hrs). To our surprise addition of 2 equivalents of benzyl bromide a clean transformation of starting material was detected with the formation of new compound but no *N*-1 alkylated product **3d** was detected in this case. Upon workup and careful purification of the reaction product we found that benzylation of 2-phenyl benzimidazole took place with concomitant opening of heterocyclic ring that produced **5a** (entry 1, Table 3) in excellent yield (90%). The formation of **5a** was confirmed by its ^{1}H and ^{13}C NMR spectra's. The ^{1}H-NMR spectra of **5a** showed the presence of two distinct doublets at δ 4.97 ppm and δ 4.79 ppm for the two protons of –CO-N-CH_2Ph and a multiplet at δ 4.09-3.98 for the other three protons of –NCH_2 and –N*H*. But the later peak upon D_2O exchange appeared as clear two doublets in its ^{1}H NMR spectra (please see SI). In the ^{13}C NMR spectra, a downfield shift at δ 171.5 ppm confirms the presence of carbonyl group, IR band at 1638 cm^{-1} and HRMS data also support the suggested structure of **5a**. Ring opening reaction of *N*-1 alkylated benzimidazole derivative **3d** was also achieved using 1 eq. of benzyl bromide under same reaction condition (entry 2, Table 3). It is important to mention here that heterocyclic ring in benzimidazole moiety is completely survived under the reaction condition if the reaction conducts without benzyl bromide (eq. 1 in Scheme 2).

Table 3 Alkylation induced base mediated imidazole ring opening reaction of substituted benzimidazoles

Entry	Substrate	Alkylating agent	Product (5)	Time (min.)	Yield (%)
1	 **1c**	$PhCH_2Br$	 **5a**	40	90[a]
2	 **3d**	$PhCH_2Br$	 **5a**	40	88[a]
3	 **1a**	$PhCH_2Br$	 **5b**	30	85[a]
4	 **1a**		 **5c**	20	85[a]
5	 **1c**		 **5d**	60	85[a]
6	 **1m**	$PhCH_2Br$	 **5e**	40	86[2]
7	 **1c**	nBuBr	 **3m**	40	82[b]
8	 **1b**	$PhCH_2Br$	 **5f**	40	80[c]
9	 **1i**	$PhCH_2Br$	 **3s**	40	93[b]
10	 **1l**	$PhCH_2Br$	 **5g**	40	81[d]

[a] 2.2 eq. of alkylating agent was used; [b] no ring opening product was observed; [c] 4.5 eq. of benzyl bromide was used;
[d] two diastereomers in equal ratios were detected by NMR due to racemization of α-stereocenter

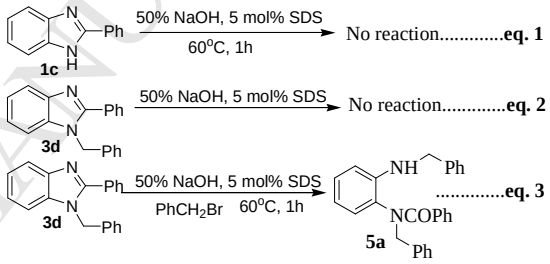


Scheme 1: Micellar aggregation leading to *N*-alkylation of Benzimidazoles/imidazoles

As it was well known that the ring opening reactions[40-44] in different carbocycles or heterocycle provide multifunctional entity offering different levels of practicality for varying applications in medicinal chemistry or drug discovery. Although acylation induced imidazole ring opening reaction in nucleic acid chemistry under different condition was reported long back[48-50] but we reasoned that the ring opening of the imidazole moiety in benzimidazoles under induction of alkyl bromides and aqueous base might open a simple straight forward route to the synthesis of functionalized aromatic core which further undergo ring closing to produce *N*-heterocycles of complex orientations. So being inspired by the incidental formation of **5a** we looked forward for the general application of this alkylation induced ring opening protocol to other benzimidazole substrates. We then carried out a few more reactions using benzimidazole (**1a)** with 2 equivalent of benzyl bromide (entry 3, Table 3) or 2-nitro benzyl bromide (entry 4, Table 3) at 60°C and the yields (**5b** and **5c**) were found 85% in both the cases. Again when 2-phenyl benzimidazole (**1c**) was allowed to react with allyl bromide, we obtained ring opening product **5d** in 85% yield (entry 5, Table 3).

Similar kind of alkylation driven ring opening reaction was also observed in the case of structurally different benzimidazole derivative **1m** to afforded **5e** in 85% yield (entry 6, Table 3). But the reaction of 2-phenyl benzimidazole with less reactive butyl bromide (2 equivalent) did not lead to the alkylation induced ring opening product; rather usual alkylated product *N*-butyl-2-phenyl benzimidazole (**3m**) was obtained in 85% as the sole product (entry 7, Table 3). A different observation was noticed when the reaction was carried out with 2-methyl benzimidazole (**1b**) and excess benzyl bromide (5 equivalent). In this case we found *N*-benzylation induced ring opening as well as *C*-benzylation at the methyl group of benzimidazole (entry 8, Table 3) leading to **5f**. The structure of **5f** was also confirmed by ^{1}H, ^{13}C NMR and mass spectral studies. The formation of **5f** is attributed to the fact that the acidic nature of the methyl group at C-2 enables the formation of the carbanion in the presence of the base followed by reaction with reactive benzyl bromide to form tetra-alkylated **5f** in 80% yield. Then we turned our attention to imidazole derivative such as 2-methyl imidazole using benzyl bromide (2 equivalents) exactly under the same condition as mentioned for benzimidazole derivatives. Unfortunately no ring opening product was formed; only *N*-1-benzylated imidazole derivative **3s** was detected (entry 9, Table 3). The sugar benzimidazole **3l** when subjected to ring opening reaction with 2 equivalent benzyl bromide under identical condition leads to ring opening product **5g** (entry 10, Table 3), however due to basic nature of the reaction medium results complex mixture due to racemization about the chiral center at C-4 of sugar backbone (α to carbonyl).

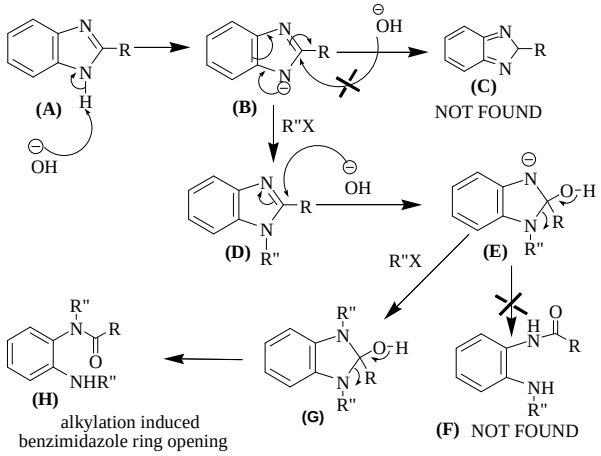
To investigate the course of the reaction further we carried out the reaction using 2-phenyl benzimidazole (**1c**) or 1-benzyl- 2-phenyl benzimidazole (**3d**) with or without benzyl bromide. As expected without alkylating agent the heterocyclic ring of this benzimidazole compound was survived (eq. 2 in Scheme 2) while in the presence of alkylating agent benzyl bromide alkylation induced ring opening reaction proceed smoothly to give **5a** in 88% of yield (Scheme 2). This observation helped us to presume that the reaction proceeds by *N*-alkylation in the first step followed by the second alkylation induced ring opening of the benzimidazoles.



Scheme 2: Control experiments in alkylation process.

The formation of the micelle aggregation by the surfactants is stabilized by the Na^{+} ions at the hydrophilic periphery (shown in Scheme 1). The reaction thus proceeded by the abstraction of the acidic proton of the benzimidazole or imidazole by the base 50% NaOH. The anion generated so reacts with the alkyl bromide present in the medium through the formation of a hydrophobic pocket and finally releases the *N*- alkylated product as shown in Scheme 1. Dynamic light scattering was employed to investigate the micro structural changes taken place within the system. Successive measurements were made within a cell of 3 mL for normalization analysis. The average hydrodynamic size distribution was found in (i) water-SDS system is 190 nm, (ii) Water-SDS-substrate and reagent system at room temperature is 570 nm and (iii) Water-SDS-substrate and reagent system at 60°C temperature is 718 nm (Figure 2). Enhancement of size after addition of substrate and reagent suggested strong interrelations between SDS and substrate during the reaction. Though the exact mechanism of the reaction is not certain we believe that the reaction proceeds first by the abstraction of the –NH proton of 2- substituted benzimidazole (**A**) by the base that formed intermediate (**B**). The reaction with alkyl bromide then forms mono alkylated derivative (**D**). The intermediate (**C**) cannot be formed as nucleophile OH^{-} is unable to attack at C-2 due to more negative charge on this center by delocalization of electrons. As soon as (**D**) is formed, nucleophile OH^{-} can attack at C-2 to form (**E**) under elevated

temperature. Ring opening of (**E**) to (**F**) is quite impossible as it is prevented by negative charge available on neighboring nitrogen atom. Finally (**E**) undergoes simultaneous reaction with second molecule of alkyl bromide on the second nitrogen (**G**) followed by C-N bond cleavage leading to the ring opening product (**H**). Again no formation of the type (**C**) or (**G**) (Scheme 3) was noticed.



Scheme 3: Alkylation induced ring opening of benzimidazoles.

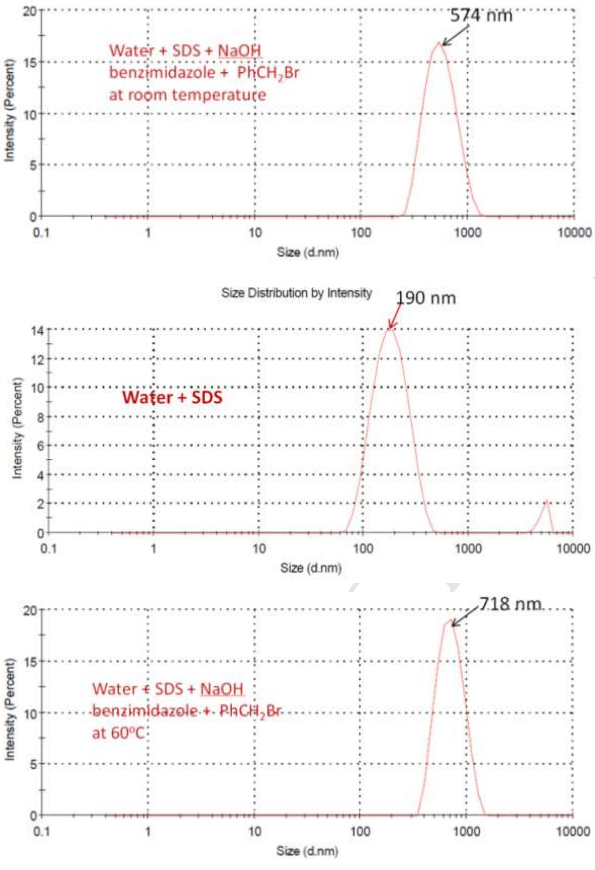


Figure 2: Microstructural changes in the reaction systems

Conclusion

In conclusion, we have developed a robust, environmentally benign, fast and operationally convenient method for *N*-1 alkylation of benzimidazoles/imidazoles in aqueous micellar condition using sodium dodecyl sulphate (SDS) as surfactant with exclusive formation of the mono alkylated product and without any quaternary ammonium salt formation. Simultaneously, we have also developed an operationally convenient method for *N*-alkylation induced temperature mediated imidazolium ring opening of the benzimidazoles by consequent C-N bond cleavage in good yields without the formation of any unwanted side products. Generally, the results open a concise access to rare pharmaceutically promising compounds, which may be used in drug design.

3. Experimental

All reagents were purchased from best-known commercial sources and used without further purification unless otherwise stated. Thin layer chromatography was performed on E-Merck 250 Kieselgel 60 F254 silica gel plates. Silica gel 60-120 or 100-200 mesh size was used for chromatography. The TLC spots were visualized by UV lamp followed by absorption over iodine. Melting points were recorded in open capillaries and were uncorrected. FT-IR spectra were recorded using KBr plates or in neat. ^{1}H and ^{13}C NMR spectroscopic data were recorded at 300/400 and 75/100 MHz respectively. High-resolution mass spectra (HRMS) were recorded on a Q-TOF mass spectrometer using positive electrospray ionization.

General procedure for *N*-alkylation of Benzimidazoles and Imidazoles

To the reaction vessel containing benzimidazole or imidazole (1mmol), alkyl halide (1 mmol), 50% NaOH (0.5 mL) and anionic surfactant sodium dodecyl sulfate (5 mol%) was added and the reaction mixture was vigorously stirred at room temperature or 60 ^{o}C. After the completion of reaction (TLC) followed by standard workup using ethyl acetate as extracting solvent the crude product was purified over silica-gel (60–120 mesh) using ethyl acetate–hexane (3:7) as eluent to afford pure products. Identities of the products were judged by the comparison of melting point, IR data, ^{1}H NMR, ^{13}C NMR and HRMS analyses.

Spectral and analytical data:

1-allyl-benzimidazole(3a):[51] Yield 97%, colorless syrup; IR (KBr) ν_{max} 3392, 2923, 1645, 1615, 1495, 1459 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (s, 1H, -C*H*=N), 7.75-7.72 (m, 1H, *aromatic H*), 7.31-7.28 (m, 1H, *aromatic H*), 7.23-7.20 (m, 1H, *aromatic H*), 5.99-5.86 (m, 1H, *H*C=C), 5.21 (d, *J* = 10.2 Hz, 1H), 5.10 (d, *J* = 17.1 Hz, 1H), 5.14-5.08 (m, 1H), 4.69 (d, *J* = 5.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.8 (-*C*=N), 142.9, 133.8, 131.9, 122.9, 122.1, 120.3, 118.6, 109.9, 47.4 (-NCH_2).

1-benzyl-benzimidazole (3b):[52] Yield 98 %, colorless wax; IR (KBr) ν_{max} 3093, 3031, 2925, 1669, 1614, 1455, 1360 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (s, 1H, -C*H*=N), 7.75 (d, *J* = 7.8 Hz, 1H, *aromatic H*), 7.28-7.19 (m, 5H, *aromatic H*), 7.18-7.07 (m, 3H, *aromatic H*), 5.25 (s, 2H, -CH_2Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.9 (C=N-), 143.1, 135.4, 133.9, 129.0, 128.2, 127.0, 123.0, 122.2, 120.4, 110.0, 48.8 (-*C*H_2Ph).

1-benzyl-2-methyl benzimidazole (3c):[53] Yield 90%, yellowish wax; IR ($CHCl_3$) ν_{max} 3379, 2925, 1616, 1525, 1453, 1402, 1354 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 (δ, *J* = 7.2 Hz, 1H, *aromatic H*), 7.20-7.09 (m, 6H, *aromatic H*), 6.95 (t, *J* = 5.4 Hz,

2H, aromatic H), 5.19 (s, 2H, -NCH_2), 2.45 (s, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.8 (C=N), 142.6, 135.8, 135.5, 129.0, 127.9, 126.2, 122.3, 119.1, 109.3, 47.0 (NCH_2), 13.9.

1-benzyl-2-phenyl benzimidazole (3d):[54] Yield: 87%, colorless solid, m. p. 132-134^{o}C; IR (KBr) ν_{max} 3056, 1640, 1558, 1494, 1482, 1362 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.8 Hz, 1H), 7.62-7.59 (m, 2H), 7.38-7.34 (m, 3H), 7.25-7.13 (m, 6H), 7.02 (d, *J* = 7.2 Hz, 2H), 5.37 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.1, 143.1, 136.4, 136.0, 129.8, 129.2, 129.0, 128.7, 127.7, 125.9, 123.0, 122.6, 119.9, 110.5, 67.7, 48.3.

1-benzyl-2, 6-dimethyl-benzimidazole (3e): Yield 87 %, colorless wax; IR (KBr) ν_{max} 3029, 2923, 1625, 1518, 1452, 1399 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.1 Hz, 1H), 7.48 (s, 1H, *aromatic H*), 7.24 (bs, 6H), 7.05-6.97 (m, 8H), 5.20 (s, 4H, -NCH_2), 2.49 (s, 3H, CH_3), 2.47 (s, 3H), 2.41 (s, 3H, -CH_3), 2.28 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.6, 151.4 (C=N), 142.6, 140.3, 135.8, 135.5, 133.3, 132.1, 131.6, 128.8, 127.7, 126.1, 126.0, 123.6, 123.5, 118.8, 118.5, 109.2, 108.8, 46.9, 46.7(-NCH_2), 21.7, 21.4 (-CH_3), 13.7(-CH_3); HRMS calcd for $C_{16}H_{16}N_2$+H^+ 237.1391 found 237.1402.

1-benzyl-2-propyl-benzimidazole (3f):Yield 88%, colorless wax; IR (KBr) ν_{max} 3033, 2963, 2931, 1614, 1510, 1496, 1330 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.8 Hz,1H, *aromatic H*), 7.21-7.06 (m, 6H, *aromatic H*), 6.95 (t, *J* = 5.7 Hz, 2H, *aromatic H*), 5.24 (s, 2H, -CH_2Ph), 2.72 (t, *J* = 7.8 Hz, 2H), 1.84-1.72 (m, 2H, -CH_2), 0.92 (t, *J* = 7.5 Hz, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.3(*C*=N), 142.6, 136.0, 135.3, 128.9, 127.8, 126.0, 122.2, 121.9, 119.2, 109.5, 46.8 (-NCH_2), 29.4 (-CH_2), 21.0 (-CH_2), 13.4 (-CH_3); HRMS calcd for $C_{17}H_{18}N_2$+ Na^+ 273. 1367 found 273.1368**.**

1-(2-nitrobenzyl)-1*H*-benzimidazole (3g): Yield 85 %, colorless solid, m. p. 118-120 ^{o}C; IR (KBr) ν_{max} 2955, 2932, 2865, 1639, 1524, 1425, 1049 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.21- 8.18 (m, 1H), 7.99 (s, 1H), 7.85 (d, *J* = 8.1 Hz, 1H, *aromatic H*), 7.49-7.45 (m, 2H, *aromatic H*), 7.34-7.18 (m, 3H, *aromatic H*), 6.70-6.67 (m, 1H, *aromatic H*), 5.8 (s, 2H, -NCH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.2, 143.8, 143.6, 134.3, 133.7, 131.9, 129.0, 128.1, 125.6, 123.5, 122.7, 120.6, 109.7, 46.0 (-NCH_2); HRMS calcd for $C_{14}H_{11}N_3O_2$ + H^+ 254.0931 found 254.0932.

1-(2-nitrobenzyl)-2-methyl-benzimidazole (3h): Yield 85 %, colorless solid, m. p. 120-122^{o}C; IR (KBr) ν_{max} 3066, 2960, 2929, 2873, 1610, 1529, 1461, 1447 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17 (t, *J* = 6.9 Hz, 1H), 7.69 (d, *J* = 6.9 Hz, 1H), 7.42-7.34 (m, 2H), 7.23-7.10 (m, 2H), 7.04-7.01 (m, 1H), 6.37 (d, *J* = 6.3 Hz, 1H), 5.68 (s, 2H), 2.46 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.8 (*C*=N), 147.0, 142.6, 135.0, 134.5, 132.0, 128.7, 127.0, 125.6, 122.6, 122.5, 119.3, 109.0, 44.6 (-NCH_2), 13.6 (-CH_3); HRMS calcd for $C_{15}H_{13}N_3O_2$+H^+ 268.1088 found 268.1077.

1-butyl-benzimidazole(3i):[52] Yield 95%, yellow syrup; IR (KBr) ν_{max} 3392, 3091, 2959, 2934, 1615, 1497, 1459, 1364, 1330, 1286 cm^{-1}, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (s, 1H, -C*H*=N), 7.75-7.20 (m, 1H, *aromatic H*), 7.34-7.31 (m, 1H, *aromatic H*), 7.25-7.17 (m, 2H, *aromatic H*), 4.08 (t, *J* = 7.2 Hz, 2H, -NCH_2), 1.83-1.74 (m, 2H, -CH_2), 1.34-1.18 (m, 2H, -CH_2), 0.87 (t, *J* = 7.5 Hz, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.7, 142.9, 134.5, 122.7, 121.9, 120.3, 109.6, 44.8 (-CH_2), 31.8 (-CH_2), 19.9 (-CH_2), 13.5 (-CH_3).

1-butyl-2-methyl-benzimidazole (3j):Yield 95 %, yellow syrup; IR (KBr) ν_{max} 3392, 2934, 1615, 1497, 1459, 1286, 1170 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62-7.59 (m, 1H, *aromatic H*), 7.23-7.13 (m, 3H, *aromatic H*), 4.01 (t, *J* = 7.2 Hz, 2H, -NCH_2), 2.53 (s, 3H, -CH_3), 1.75-1.65 (m, 2H, -CH_2), 1.35-1.27 (m, 2H, -CH_2), 0.91-0.86 (t, *J* = 7.5 Hz, 3H, -CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.3, 141.9, 134.9, 122.1, 122.0, 118.8, 109.3, 43.7 (-NCH_2), 31.8, 20.2, 13.8, 13.7 (-CH_3); HRMS calcd for $C_{12}H_{16}N_2$ + H^+ 189.1393 found 189.1398.

1-butyl-2-phenyl-benzimidazole (3k):Yield 87%, colorless wax; IR (KBr) ν_{max} 3063, 2959, 1614, 1456, 1330, 1133 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77-7.74 (m, 1H, *aromatic H*), 7.65-7.62 (m, 2H, *aromatic H*), 7.48-7.36 (m, 3H, *aromatic H*), 7.35-7.24 (m, 1H, *aromatic H*), 7.23-7.18 (m, 2H, *aromatic H*), 4.15 (t, *J* = 7.8 Hz, 2H, -NCH_2), 1.77-1.67 (m, 2H, -CH_2), 1.26-1.13 (m, 2H, -CH_2), 0.78 (t, *J* = 7.2 Hz, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.6 (*C*=N), 142.9, 135.5, 130.6, 129.6, 129.2, 128.6, 122.5, 122.2, 119.8, 110.2, 44.4(-NCH_2), 31.7(CH_2), 19.8(CH_2), 13.4(CH_3); HRMS calcd for $C_{17}H_{18}N_2$+H^+ 251.1550 found 251.1558.

1-hexyl-benzimidazole (3l): Yield 96 %, colorless syrup; IR (KBr) ν_{max} 3061, 2960, 2930, 2858, 1615, 1496, 1459, 1382 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.8 (s, 1H, -C*H*=N), 7.74-7.19 (m, 1H, *aromatic H*), 7.32 (t, *J* = 8.4 Hz, 1H, *aromatic H*), 7.25-7.17 (m, 2H, *aromatic H*), 4.07 (t, *J* = 7.2 Hz, 2H, -NCH_2), 1.79 (t, *J* = 6.6 Hz, 2H, -CH_2), 1.23 (s, 6H, -CH_2), 0.80 (t, *J* = 6.9 Hz, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.0 (-C=N-),142.9, 133.7, 122.7, 121.9, 120.3, 109.6, 45.0 (-NCH_2), 31.2 (-CH_2), 29.7 (-CH_2), 26.4 (-CH_2), 22.4 (-CH_2), 13.9 (-CH_3); HRMS calcd for $C_{13}H_{18}N_2$ + H^+ 203.1550 found 203. 1558.

1-octyl-benzimidazole (3m): Yield 96 %, yellow syrup; IR (KBr) ν_{max} 3053, 2929, 2857, 1617, 1495, 1459, 1265 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.75-7.72 (m, 1H), 7.33-7.31 (m, 1H, *aromatic H*), 7.25-7.20 (m, 2H, *aromatic H*), 4.07 (t, *J* = 6.3 Hz, 2H, -NCH_2), 1.79 (m, 2H, -CH_2), 1.24 (m, 10H, -CH_2), 0.80 (t, *J* = 1.8 Hz, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.7, 142.8, 133.8, 122.7, 121.9, 120.2, 109.6, 45.0 (-NCH_2), 31.6, 29.7, 29.0, 26.7, 22.5, 14.0 (-CH_3); HRMS calcd for $C_{15}H_{22}N_2$ + H^+ 231.1863 found 231.1871.

2-methyl-1-octyl-benzimidazole (3n): Yield 90%, yellowish oil; IR (KBr) ν_{max} 3389, 2927, 2855, 1616, 1518 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64-7.57 (m, 1H, aromatic *H*), 7.22-7.10 (m, 3H, *aromatic H*), 3.99 (t, *J* = 7.2 Hz, 2H, -NCH_2), 2.51 (s, 3H, -CH_3), 1.72-1.60 (m, 2H, -CH_2), 1.39 -1.17 (m, 10H, -CH_2), 0.78 (t, *J* = 7.2 Hz, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.3 (-C=N), 142.5, 134.9, 130.8, 128.7, 121.7, 121.6, 118.8, 109.0, 65.4, 43.7 (-NCH_2), 31.6, 30.5, 29.6, 29.1, 29.0, 26.8, 22.5, 19.0, 13.9, 13.8 (-CH_3), 13.6(-CH_3); HRMS calcd for $C_{16}H_{24}N_2$ + H^+ 245.2019 found 245.2021.

1-hexadecyl-benzimidazole (3o): Yield 98%, colorless wax: IR (KBr) ν_{max} 3057, 2956, 2853, 1615, 1495, 1459, 1330, 1285 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.75-7.72 (m, 1H), 7.34-7.31 (m, 1H), 7.25-7.19 (m, 2H, *aromatic H*), 4.08 (t, *J* = 7.2 Hz, 2H, -NCH_2), 1.80 (t, *J* = 6.6 Hz, 2H, -CH_2), 1.25-1.18 (m, 26H, -CH_2), 0.87 (t, *J* = 7.5 Hz, 3H, -CH_3); ^{13}C NMR

(75 MHz, $CDCl_3$) δ 142.8, 122.7, 121.9, 120.3, 109.6, 45.1 (-NCH_2), 31.9, 29.8, 29.6, 29.5, 29.4, 29.3, 29.0, 26.8, 22.6 (CH_2), 14.0 (CH_3); HRMS calcd for $C_{23}H_{38}N_2$ + H^+ 343. 3113 found 343. 3117.

1-hexadecyl-imidazole (3p):Yield 96 %, colorless wax; IR (KBr) ν_{max} 3392, 2924, 2853, 1507, 1466, 1283 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 (s, 1H, -C=NH), 6.96 (s, 1H,), 6.81 (s, 1H), 3.83 (t, *J* = 6.9 Hz, 2H, -NCH_2), 1.68 (m, 2H, -CH_2), 1.71 (s, 26H, -CH_2), 0.8 (t, *J* = 6.9 Hz, 3H, -CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.0, 129.2, 118.8, 47.1 (-NCH_2), 31.9, 31.1, 29.7, 29.6, 29.5, 29.4, 29.3, 29.1, 26.5, 22.7 (-CH_2), 14.1 (-CH_3); HRMS calcd for $C_{19}H_{36}N_2$ + H^+ 293. 2958 found 293. 2925.

1-benzyl-2-methyl-imidazole (3q): Yield 93%, yellowish oil; IR (KBr) ν_{max} 3398, 2961, 1641, 1559, 1498, 1283 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31-7.21 (m, 3H), 7.01-6.98 (m, 2H), 6.91 (s, 1H), 6.78 (s, 1H), 4.99 (s, 2H, -NCH_2), 2.29 (s, 3H, -CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.9, 136.2, 129.0, 128.0, 126.9, 126.7, 119.9, 49.8 (-NCH_2), 12.9 (-CH_3); HRMS calcd for $C_{11}H_{12}N_2$+H^+ 173.1080 found 173.1079.

1-allyl-2,4,5-triphenyl-imidazole(3r):Yield 80%, colorless wax; IR (KBr) ν_{max} 3064, 2924, 1648, 1602, 1481, 1453, 1396, 1284, 1256 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68-7.65 (m, 2H), 7.48-7.45 (m, 2H, *aromatic H*), 7.41-7.30 (m, 8H, *aromatic H*), 7.17-7.05 (m, 3H, *aromatic H*), 5.70-5.07 (m, *J* = 6 Hz, 1H), 5.07-5.04 (m, 1H), 4.81-4.40 (t, *J* = 17.1 Hz, 1H, -C*H*=CH_2), 4.38 (t, *J* = 2.1 Hz, 2H, -CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.7, 137.8, 134.5, 133.8, 131.1, 130.9, 129.8, 129.0, 128.8, 128.7, 128.5, 128.0, 126.8, 126.2, 117.0, 116.0, 46.8 (-NCH_2); HRMS calcd for $C_{24}H_{20}N_2$ + H^+ 337.1706 found 337. 1716.

1-allyl-2-(2-(allyloxy) phenyl)-4,5-diphenyl-imidazole (3s): Yield 75 %, yellowish syrup; IR (KBr) ν_{max} 3063, 2932, 1602, 1501, 1479, 1449, 1394, 1326 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50-7.36 (m, 3H, *aromatic H*), 7.35-7.21 (m, 6H, *aromatic H*), 7.17-6.96 (m, 4H, *aromatic H*), 6.88 (d, *J* = 9Hz, 1H, *aromatic H*), 5.97-5.91 (m, 1H), 5.5-5.39 (m, 1H), 5.28-5.12 (q, *J* = 14.7 Hz, 2H, C*H*=CH_2), 4.80-4.76 (d, *J* = 9.9 Hz, 1H), 4.5-4.47 (m, 3H), 4.27-4.20 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.4 (C=N), 145.2, 133.5, 132.9, 132.7, 131.5, 131.0, 130.7, 129.2, 128.8, 128.5, 127.9, 126.7, 126.0, 121.2, 116.9, 116.3, 112.7, 69.1 (-OCH_2), 46.8 (-NCH_2), 29.6 (-CH_2). HRMS calcd for $C_{27}H_{24}N_2O$+H^+ 393.1967 found 393.1967.

1-Benzyl-2-[(2S, 3R, 4R, 5R)-4-allyloxy-tetrahydrofurano] benzi-midazole (3t): Yield 82%, nature yellowish syrup, IR (neat) ν_{max} 3040, 2990, 2936, 1613, 1517, 1463, 1162 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8 Hz, 1H), 7.25- 7.16 (m, 8H), 6.08 (d, *J* = 3.6 Hz, 1H), 5.95 (d, *J* = 12.3 Hz, 1H), 5.82 (d, *J* = 3.2 Hz, 1H), 5.64 -5.55 (m, 1H), 5.30 -5.25 (t, 1H), 5.08 - 4.98 (m, 2H), 4.71 (d, *J* = 4 Hz, 1H), 4.31(d, *J* = 4 Hz, 1H), 3.84-3.79 (m, 1H), 3.67-3.62 (m,1H), 1.58 (s, 3H), 1.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.5, 142.1, 136.9, 136.1, 133.4, 128.6, 127.4, 126.8, 122.8, 122.3, 119.6, 117.8, 112.3, 110.6, 104.9, 84.3, 82.8, 79.3, 71.4, 49.0, 26.8, 26.3; HRMS calcd for $C_{24}H_{26}N_2O_4$ 406.1893 found HRMS calcd for $C_{24}H_{26}N_2O_4$ + H^+ 407.1973 found 407.2111.

General procedure for *N*-alkylation induced ring opening of Benzimidazoles: A mixture of benzimidazole (1mmol), alkyl halide (2 mmol), 50% NaOH (1mL) and anionic surfactant sodium dodecyl sulfate (5 mol%) was vigorously stirred at 60 ^{o}C. After the complete consumption of starting material (TLC) followed by standard workthe crude product was purified over silica-gel (60–120 mesh) using ethyl acetate–hexane as eluent to afford pure products.

***N*-benzyl-*N*-(2-(benzylamino) phenyl)benzamide (5a)**: Yield 90%, colorless solid, m. p. 124-126^{o}C; IR (KBr) ν_{max} 3074, 2923, 1638, 1604, 1517, 1257 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31- 7.14 (m, 11H), 7.08-6.99 (m, 3H, *aromatic H*), 6.91 (t, *J* = 7.5 Hz, 2H, *aromatic H*), 6.57(d, *J* = 7.5 Hz, 1H, *aromatic H*), 6.37 (d, *J* = 5.4 Hz, 2H, *aromatic H*), 4.97(d, *J* = 13.8 Hz, 1H, -CO-NCH_2Ph), 4.79 (d, *J* = 13.8 Hz, 1H, -CO-NCH_2Ph), 4.09-3.98 (m, 3H, -NHCH_2Ph + -N*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.5, 143.8, 138.7, 137.3, 135.6, 130.0,129.7, 129.3, 128.8, 128.5, 128.4, 128.2, 127.8, 127.6, 127.4, 127.1, 127.0, 116.9, 111.5, 52.2 (-CO-NCH_2Ph), 47.5 (-NHCH_2Ph); HRMS calcd for $C_{27}H_{24}N_2O$ + H^+ 393.1969 found 393.1979.

***N*- benzyl- *N*-(2- (benzylamino) phenyl) formamide (5b):** Yield 82%, colorless solid, m.p. 108-110^{o}C; IR (KBr) ν_{max} 3382, 2928, 2858, 1670, 1604, 1456, 1196 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (s, 1H, -C*H*O), 7.50-7.23 (m, 8H), 7.16 (m, 3H), 6.83-6.76 (m, 1H), 6.64-6.59 (m, 2H, *aromatic H*), 4.8 (s, 2H, -NCH_2Ph), 4.18 (t, *J* = 5.4 Hz, 2H, -NHCH_2Ph), 4.04 (d, *J* = 5.1Hz, -N*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.8, 145.0, 138.4, 136.8, 129.8, 129.2, 128.7, 128.6, 127.9, 127.2, 127.0, 125.6, 117.1, 111.8, 48.0 (CO-NCH_2Ph), 47.7 (NHCH_2Ph); HRMS calcd for $C_{21}H_{20}N_2O$ + H^+ 317.1656 found 317.1650.

***N*-(2-nitrobenzyl-*N*-(2-(2-nitrobenzylamino)phenyl) formam- ide (5c):** Yield 70%, yellowish solid, m. p. 140-142^{o}C; IR (KBr) ν_{max} 3384, 2939, 1673, 1606, 1523, 1146 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28 (s, 1H, C*H*O), 8.07- 7.99 (m, 1H,), 7.87-7.85 (d, *J* = 8.1 Hz, 1H), 7.59 - 7.39 (m, 6H), 7.12 (t, *J* = 7.8 Hz, 1H), 6.78 (d, *J* = 7.5 Hz, 1H), 6.45 (d, *J* = 8.1 Hz, 1H), 6.34 (d, *J* = 8.4 Hz, 1H), 5.23 (s, 2H), 4.66 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.0, 149.2, 148.1, 144.2, 134.2, 133.8, 133.3, 131.4, 131.1, 130.2, 129.4, 129.2, 128.7, 128.2, 125.2, 124.8, 124.7, 117.7, 111.9, 45.1, 44.4; HRMS calcd for $C_{21}H_{18}N_4O_5$+H^+ 407.1355 found 407.1347.

***N*-allyl-*N*-(2-(allylamino)phenyl)benzamide (5d)**: Yield 85%, yellowish oil; IR (KBr) ν_{max} 3079, 2925,1634, 1604, 1519 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46- 6.98 (m, 7H), 6.70- 6.67 (d, *J* = 6.6 Hz, 1H), 6.55- 6.52 (d, *J* = 7.8Hz, 1H), 6.43 (t, *J* = 7.2 Hz, 1H), 6.06-6.00 (m, 1H, = C*H*), 5.99- 5.79 (m, 1H, = C*H*), 5.19-5.06 (m, 4H, -NCH_2), 4.56- 4.49 (m, 1H), 4.26 - 4.20(m, 1H), 4.07- 4.00 (m, 1H), 3.78- 3.75 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.5, 143.5, 135.5, 134.7, 132.8, 130.0. 129.9, 128.8, 127.7, 127.5, 118.8, 116.8, 116.5, 111.5, 51.5, 45.9, 45.8; HRMS calcd for $C_{19}H_{20}N_2O$ + H^+ 293. 1654 found 293. 1663.

***N*-Benzyl-N-(2-(benzylamino)phenyl)-2-butoxybenzamide (5e)**: Yield 86%, colourless solid, m.p 128-130^{o}C, IR (KBr) ν_{max} 3063, 2959, 2936, 1644, 1605, 1521, 1324 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53- 7.25 (m, 10H), 7.18- 7.08 (m, 4H), 7.01-6.94 (m, 1H), 6.92-6.38 (m, 3H), 6.37 (d, *J* = 7.2 Hz, 1H),

5.28 (d, *J* = 13.6 Hz, 1H), 4.74 (d, *J* = 14. 4 Hz, 1H), 4.15 (s, 2H), 3.86 (t, *J* = 6.4 Hz, 2H), 1.74-1.58 (m, 2H), 1.50-1.41 (m, 2H), 0.98 (t, *J* = 7.2Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 154.8, 144.0, 138.9, 137.6, 130.6, 129.8, 129.5, 129.2, 128.9, 128.6, 128.5, 128.3, 128.2, 127.6, 127.4, 127.2, 127.0, 126.6, 126.5, 119.5, 116.2, 111.5, 111.1, 68.2, 67.9, 51.0, 47.6, 31.3, 19.2, 13.9; HRMS clcd for for $C_{31}H_{32}N_2O_2+H^+$ 465.2544 found 465.2542.

***N*,2-dibenzyl-*N*-(2-(benzylamino)phenyl)-3-phenylpropan-amide (5f)**:Yield 80%, colorless solid, m. p. 108-110 ^oC; IR (KBr) ν_{max} 3067, 3027, 2922, 2939, 1651, 1602, 1514 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.21- 6.96 (m, 19H, *aromatic H*), 6.86-6.83 (m, 2H, *aromatic H*), 6.43 (d, *J* = 7.5 Hz, 1H, *aromatic H*), 6.36-6.31 (m, 1H), 5.74-5.71 (dd, *J* = 7.8, 1.5 Hz, 1H), 4.87 (d, *J* = 13.8 Hz, 1H, -CO-NC*H*$_2$Ph), 4.49 (d, *J* = 13.5 Hz, 1H, -CO-NC*H*$_2$Ph), 3.84 (t, *J* = 6.3 Hz, 2H, -NHC*H*$_2$Ph), 3.44 (d, *J* = 5.1 Hz, 1H, -N*H*), 3.08-2.91 (m, 2H), 2.75- 2.60 (m, 1H), 2.58-2.51(m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.7, 143.9, 140.0, 139.5, 138.7, 137.4, 129.9, 129.3, 128.5, 128.3, 128.2, 127.4, 127.0, 126.9, 126.6, 116.8, 111.4, 51.1, 47.6, 38.7; HRMS calcd for $C_{36}H_{34}N_2O+H^+$ 511.2749 found 511.2721.

(*3R, 6R, 6R*)-6-(allyloxy)-*N*-benzyl-*N*-(2-(benzylamino)-phenyl)-tetrahydro-2,2-dimethylfuro[2,3-d][1,3]dioxole-5-carboxamide (5g, 1:1 mixture of two epimer): Yield 85%, yellowish syrup, IR (neat) ν_{max} 3063, 2955, 1654, 1603, 1521, 1327, 12471cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.11(m, 14H), 6.69-6.55 (m, 3H), 5.95 (d, *J* = 5.2 Hz,0.5H), 5.86 (d, *J* = 5.2 Hz, 0.5H), 5.17-5.12 (m, 2H), 5.03-5.01 (d, *J* = 6.5 Hz, 0.5H), 4.99-4.98 (d, *J* = 6.4 Hz, 0.5H), 4.71-4.70 (m, 1H), 4.23-4.12 (m, 3H), 1.44- 1.38 (s, 1.5H), 1.36 (s, 1.5H), 1.27 (s, 1.5H), 1.24 (s, 1.5H); ^{13}C NMR(100 MHz, $CDCl_3$) 162.10, 162.07, 152.5, 152.2, 144.5, 144.4, 138.7, 138.6, 136.6, 136.5, 132.9, 129.9, 129.8, 129.7, 129.6, 129.5, 128.7, 128.5, 127.9, 127.3, 127.2, 127.1, 127.0, 126.9, 126.6, 126.4, 117.4, 112.6, 112.5, 111.9, 111.8, 106.0, 105.7, 105.4, 83.2, 77.2, 52.2, 47.7, 44,6, 31.9, 29.7, 29.3, 27.8, 27.7.

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References and notes

1 Breslow R. Acc. Chem. Res. 1991; 24: 159-164.
2 Herrmann WA, Kohlpaintner CW. Angew. Chem. Int. Ed. Engl. 1993; 32: 1524-1544.
3 Li CJ. Chem. Rev. 1993; 93: 2023- 2035.
4 Lindström UM. Chem. Rev. 2002; 102: 2751-2772.
5 Kobayashi S, Manabe K. Acc. Chem. Res. 2002; 35: 209-217.
6 Okuhara T. Chem. Rev. 2002; 102: 3641-3666.
7 Pae AN, Cho YS. Curr. Org. Chem. 2002; 6: 715-737.
8 Holmberg K, Jhonson B, Kronberg B, Lindman B. Surfactants and Polymers in aqueous solution, 2nd Ed., John Wiley and Sons Ltd., UK, 2002.
9 De S, Malik S, Ghosh A, Saha R, Saha B. RSC Adv. 2015; 5: 65757-65767.
10 Handa S, Fennewald JC, Lipshutz BH, Angew. Chem., Int. Ed. 2014; 53: 3432–3435.
11 Chatterjee A, Maiti DK, Bhattacharya PK. Org. Lett., 2003; 5: 3967–3969.
12 Chatterjee N, Pandit P, Halder S, Patra A, Maiti, DK. J. Org. Chem. 2008; 73: 7775–7778.
13 Pandit P, Gayen KS, Khamarui S, Chatterjee N, Maiti DK. Chem. Commun. 2011; 47: 6933–6935.
14 Gawande MB, Bonifacio VDB, Luque R, Branco PS, Verma RS. Chem. Soc. Rev. 2013; 42: 5522–5551.
15 Dallinger D, Kappe CO. Chem. Rev. 2007; 107: 2563–2591.
16 Samai S, Ghosh D, Das UK, Atta S, Manna SK, Maiti DK, Green Chem. 2016; 18: 2961-2965.
17 Li C-J. Chem. Rev. 2005; 105: 3095–3165.
18 Tonelli M, Simone M, Tasso B, Novelli F, BoidoV, Sparatore F, Paglietti G, Pricl S, Blois S, Ibba C, Sanna C. Bioorg. Med. Chem. 2010; 18: 2937-2953.
19 Shaharyar M, Abdullah MM, Bakh, MA, Majeed J. Eur. J. Med. Chem. 2010; 45: 114-119.
20 Dubey PK, Prasada Reddy PVV, Srinivas K. Synth. Comm. 2007; 37: 1675-1681.
21 MacFarlane DR, Forsyth SA, Golding J, Deacon GB. Green Chem. 2002; 4: 444–448.
22 Larsen AS, Holbrey, JD, F. S. Tham FS, Reed CA. J. Am. Chem. Soc. 2000; 122: 7264–7272.
23 Hasan M, Kozhevnikov IV, Siddiqui MRH, Steiner A, Winterton N. Inorg. Chem. 1999; 38: 5637–5641.
24 Deetlefs M, Seddon KR. Green Chem. 2003; 5: 181–186.
25 Lev´ eque JM, Luche, JL, P ˆ etrier C, Roux R, Bonrath W. Green Chem. 2002; 4: 357–360.
26 Varma RS, Namboodiri VV. Pure Appl. Chem. 2001; 73: 1309–1313.
27 Varma RS, Namboodiri, VV. Chem. Commun. 2001; 7: 643–644.
28 Vu PD, Boydston, AJ, Bielawski CW. Green Chem. 2007; 9: 1158–1159.
29 Sawant, AD, Raut, DG, Darvatkar NB, Salunkhe MM. Green Chem. Letts. Rev. 2011; 4: 41–54.
30 Singh CB, Kavala V, Akshaya K. Samal AK, Patel BK.Eur. J. Org. Chem. 2007; 2007:1369–1377.
31 Kikugawa Y, Synthesis 1981; 2: 124-125.
32 Santaniello E, Farachi C, Ponti F. Synthesis 1979; 8: 617-618.
33 Kommi DN, Jadhavar PS, KumarD, Chakraborti AK. Green Chem. 2013; 15: 798-810.
34 Kumar D, Kommi DN, Chebolu R, Sanjeev K, Garg SK, Kumar R, Chakraborti AK. RSC Adv. 2013; 3: 91-98.
35 Kommi DN, Kumar D, Bansal R, Chebolu R, Chakraborti, AK. Green Chem. 2012; 14: 3329-3335.
36 Chebolu R, Kommi DN, Kumar D, Bollineni N, Chakraborti AK. J. Org. Chem. 2012; 77: 10158-10167.
37 Teimouria A, Najafi AJ. Mol. Catal. A: Chem. 2011; 346: 39-45.
38 Davoodnia A, Heravi MM, Safavi-Rad Z, Tavakoli-Hoseini N. Synth. Commun. 2010; 40: 2588-2597.
39 Kumar D, Seth K, Kommi DN, Bhagat S, Chakraborty AK. RSC Adv. 2013; 3: 15157-15168.
40 Kommi DN, KumarD, Seth K, Chakraborti AK. Org. Lett. 2013: 15: 1158-1161.
41 Kommi DN, Kumar D, Chakraborti AK. Green Chem. 2013; 15: 756-767.
42 Majumdar S, Chakraborty M, Pramanik N, Maiti DK. RSC Adv. 2015; 5: 51012-51018.
43 Furimsky E, Massoth FE. Catal. Rev. Sci. Eng. 2005; 47: 297-489.
44 Trofimov BA, Andriyankova LV, Nikitina LP, Belyaeva KV, Mal'kina AG, Afonin AV. Synthesis 2010; 9: 1536-1542.
45 Belyaeva KV, Andriyankova LV, Nikitina LP, Bagryanskaya IY, Afonin AV, Ushakov IA, Mal'kina AG, Trofimov BA. Tetrahedron 2015; 71: 2891-2899.

46 Trofimov BA, Andriyankova LV, Nikitina LP, Belyaeva KV, Mal'kina AG, Sobenina LN, Afonin AV, Ushakov IA. Org. Letts. 2013; 15: 2322-2324.
47 Portillo M, Maxwell MA, Frederich J. H. Org. Letts. 2016; 18: 5142-5145.
48 Pratt RF, Kraus KK. Tett. Letts. 1981; 22: 2431–2434
49 Loosemore MJ, R.F. Pratt RF. FEBS Letts. 1976; 72: 155-158
50 Grace ME, Loosemore MJ, Semmel ML, Pratt RF. J. Am. Chem. Soc. 1980; 102: 6784–6789
51 Stanley LM, Hartwig JF. J. Am. Chem. Soc. 2009; 131: 8971-8983.
52 Hayat S, Rahman A, Choudhary MI, Khan KM, Schumann W, Bayer E. Tetrahedron 2007; 57: 9951-9957.
53 Dubey PK, Kumar R. Ind. J. Heterocycl. Chem. 2006; 16: 131-134.
54 Perumal S, Mariappan S, Selvaraj S. ARKIVOC 2004; 8: 46-51.