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Synthesis of 1,2-disubstituted benzimidazoles through DDQ-oxidized intramolecular dehydrogenative coupling of *N*,N′-dialkyl *o*-phenylenediamines

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ABSTRACT

The synthetic methodology of 1,2-disubstituted benzimidazoles has been developed, which starts from *N*,N′-dialkyl *o*-phenylenediamines via intramolecular dehydrogenative coupling under the oxidation of DDQ with mild conditions. Through detailed optimization of reaction conditions, only DDQ was found essential without any additives to reach to the highest yield of 99%. In the cases of linear aliphatic substituents, the synthesis of 1-alkyl-2-phenylbenzimidazoles showed high selectivities and their structures were identified by 2D NMR COSY correlation analysis. A plausible mechanism was proposed to interpret the observed reactivities and selectivities.

1. Introduction

Benzimidazoles, as a kind of heterocyclic compound, are bioactive molecules widely existing in natural products. Their unique structural characteristics and electron rich atmosphere enable them to combine with many biological targets to produce important activities. Therefore, they are widely used in drug discovery and medicinal chemistry research in recent years [1]. Currently, benzimidazoles with different substituents have been shown to possess antiviral, antibacterial, anti-tumor, anti-hypertension, anti-diabetes, anti-HIV clinical and other biological activity potential [2]. In agriculture, compounds with benzimdazole structures also have fungicidal and plant growth-regulating properties, and are commonly used in agrochemicals [3]. And in the coordination chemistry, benzimidazoles can be used as raw materials for catalyst prepration. For example, 1-(triphenylmethyl)benzimidazole-modified ruthenium-diphosphane precatalysts have been employed to effectively promote enantioselective bifunctional hydrogenation of ketones [4], while 1,3-bis(*N*-alkylbenzimidazole) benzene-based Rh complexes were synthesized and their catalytic activity was studied in the hydrosilylation of phenylacetylene [5], and novel chelating benzimidazole-based Nickel(II) complexes have been utilized to catalyze Kumada coupling reaction [6]. In addition, benzimidazole and its derivatives can also be used as corrosion inhibitors [7], proton exchange membranes [8], photochemical sensors [9], bioenzyme inhibitors [10] and polymer electrolyte membranes [11].

There are two common methods to synthesis benzimidazole and its derivatives. The first one is the reaction of *o*-phenylenediamine and carboxylic acid with or without catalyst. In this method, benzimidazoles were synthesized, involving successive *N*-acylation, addition and cyclization of amino group and carbonyl group [12]. The second method is the reaction of *o*-phenylenediamine and aldehyde. *o*-Phenylenediamine condensed with the carbonyl of aldehyde to form a single or double schiff base, which then underwent nucleophilic addition and dehydrogenation to obtain benzimidazoles [13].

In other synthetic methodologies, the transformation has been concentrated on *N*,N′-dialkyl *o*-phenylenediamines. Recently, in Foss's work, the reactions were executed by heating conditions, catalyzed by $FeCl_3 \cdot 6H_2O$, and the air was a green oxidation source with good substrate compatibility [14]. In our previous work, benzimidazoles had been synthesized with a metal-free method,

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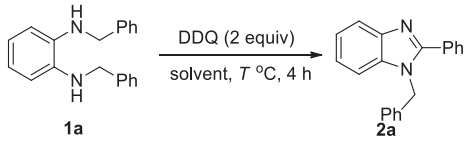
which could effectively avoid metal ion pollution in product, especially facing so strong coordination of benzimidazoles, and the yield was initially in 74% at 80 °C without further detailed optimization of reaction conditions [15]. Hereby, along with our interest in transformations of amines [16], we would like to report our extension studies on by DDQ-oxidized intramolecular cycloaddition of *N*,N′-dialkyl *o*-phenylenediamines towards synthesis of benzimidazoles under optimal and mild conditions with safe profile.

2. Results and discussion

We first investigated the treatment of *N*,N′-dibenzyl *o*-phenylenediamine **1a** and DDQ as model reaction to verify the possibility of conversion of **1a**. The reaction was initially carried out in an oil bath of 30 °C, where 2.0 equivalents of DDQ were reacted with substrate in 2.0 mL of THF to produce **2a** that was afforded in 74% yield (Table 1, entry 1). Then we gradually increased the reaction temperature , finding that product **2a** had an better yield of 80% at 40 °C (Table 1, entries 2 and 3). Under these conditions, the solvent effect was investigated, discovering that solvents with medium to weak polarity such as methylene chloride (CH_2Cl_2), chloroform ($CHCl_3$), diethyl ether (Et_2O), toluene and 1,4-dioxane afforded lower yields, however, the use of ethyl acetate (EtOAc) was slightly lower than THF (Table 1, entries 4–9). While we used strong polar solvents such as *N*,N-dimethyl formamide (DMF), methanol (MeOH) and dimethyl sulfoxide (DMSO), it was found that the yields were all improved, which DMSO provided the best yield in 89% (Table 1, entries 10–12). This is probably due to the high solubility of dimethyl sulfoxide, so that the reactants could be fully dissolved.

The influences of amount of oxidants and additives on the reaction were examined with the results shown in Table 2. When the amount of oxidant was less than the stoichiometric ratio (**1a**:DDQ = 1:2), **1a** was not completely converted to **2a** due to the insufficient amount of DDQ, and the yield was 74% (Table 2, entry 1). When the amount of DDQ increased gradually, the yield of product **2a** increased first and then decreased (Table 2, entries 2–4). When the amount of DDQ was 2.4 times of substrate **1a**, the yield of **2a** reached to 93% (Table 2, entry 3). In order to further increase the yield of the reaction, the trials of additives were

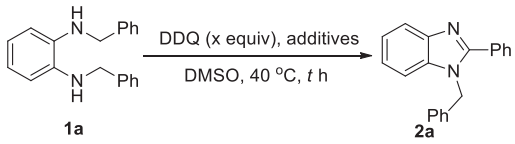
Table 1
Optimizations of solvent and temperature[a].



Entry	Solvent (x mL)	*T* °C	Yield (%)
1	THF (2)	30	74
2	THF (2)	40	80
3	THF (2)	60	70
4	EtOAc (2)	40	78
5	DCM (2)	40	70
6	$CHCl_3$ (2)	40	66
7	Et_2O (2)	40	54
8	Toluene (2)	40	59
9	1,4-dioxane (2)	40	49
10	DMF (2)	40	82
11	MeOH (2)	40	81
12	**DMSO (2)**	**40**	**89**

[a] Reaction conditions: **1a** (0.3 mmol) and DDQ (2.0 equiv) in solvent (2.0 mL) at specified temperature for 4 h.

Table 2
Optimizations of additives, amount of DDQ and DMSO and time[a].



Entry	DDQ (equiv)	DMSO (mL)	Additives	*t* h	Yield (%)
1	1.8	2	–	4	74
2	2.2	2	–	4	90
3	2.4	2	–	4	93
4	2.6	2	–	4	88
5	2.4	2	Na_2SO_4	4	62
6	2.4	2	HOAc	4	63
7	2.4	2	K_2CO_3	4	71
8	2.4	2	TEA	4	84
9	2.4	2	PhCOOH	4	91
10	2.4	2	4 Å MS	4	88
11	2.4	1.5	–	4	93
12	2.4	1	–	4	93
13	2.4	0.5	–	4	85
14	**2.4**	**1**	**-**	**2**	**99**
15	2.4	1	–	1	91

[a] Reaction conditions: **1a** (0.3 mmol) and DDQ (specified) in DMSO (specified) at 40 °C for specified time.

performed. When acidic, basic and neutral substances such as sodium sulfate, acetic acid and potassium carbonate were used as additives, the reaction yields significantly lowered to the range of 62–71% (Table 2, entries 5–7), while triethylamine, benzoic acid and 4 Å molecular sieve resulted in slightly lower yields (Table 2, entries 8–10). In general, these selected additives showed detriments to maintain a high yield.

Furthermore, it was found that when the amount of solvent dimethyl sulfoxide decreased, the yield did not decrease significantly where the best amount of solvent was kept in 1 mL because of 0.5 mL of solvent not enough to dissolve the reactants (Table 2, entries 11–13). Then the reaction time was investigated and as a result for 2 h the yield reached to 99% (Table 2, entry 14). While the reaction time continues to be shortened, the conversion of substrate **1a** was incomplete, resulting in a reduced yield in 91% (Table 2, entry 15). Accordingly, the optimal reaction conditions were acquired as 2.4 equivalents of DDQ stirred in 1.0 mL of dimethyl sulfoxide at 40 °C of oil bath for 2 h.

With the optimal reaction conditions in hand, the substrate scope was then explored with the results summarized in Table 3, The effects of R^1, R^2 and R^3 groups of substrate **1** on the reactivities were studied. The results show that when the 3- and 4-methyl substituted **1a** was employed as substrates, 4- and 6-methyl-1-benzyl-2-phenyl benzimidazoles (**2b** and **2c)** were obtained in yields of 56% and 74%, respectively, where remoter 4-methyl substitution indicated less steric hindrance to this reaction and therefore showed higher yield. 4-Chloro substituted **1a** was used as substrate, 5- and 6-chloro substituted products (**2d** and **2d′**) were obtained simultaneously in total yield of 88% with molar ratio of 1:3. Monobenzyl substituted substrate such as *N*-benzyl-*o*-phenylenediamine was subjected to these conditions, reaction did not take place and no 2-phenyl-1H-benzo[*d*]imidazole (**2e**) was obtained, probably due to weaker basicity of aromatic primary amine. When one benzyl group was substituted by a methyl ester group at the *para* position, the yield of **2f** dropped in 2 h, and prolonging reaction time led to improved yield of 95%. *m*-Bromo substituent gave rise to 1-(3-bromobenzyl)-2-phenyl-1*H*-benzo[*d*]imidazole (**2g**) in good yield of 62% yet. In case of N^1-*n*-octyl substituent, 1-alkyl substituted benzimidazole (**2h**) was produced in high yield

Table 3
Investigation on substrates.

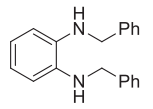
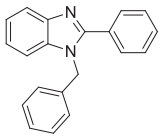
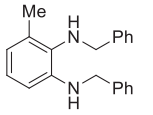
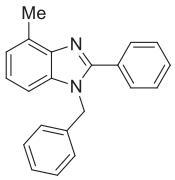
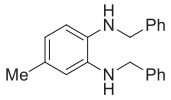
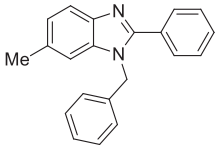
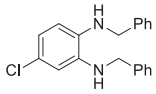
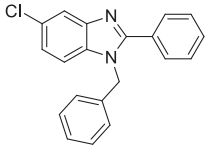
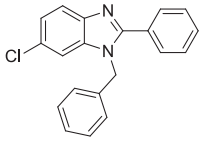
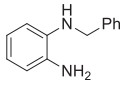
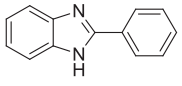
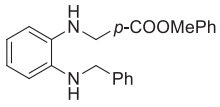
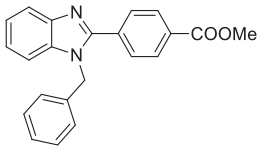
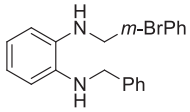
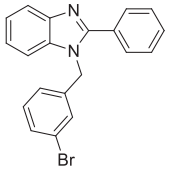
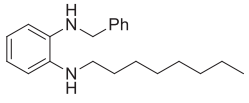
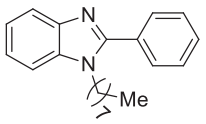
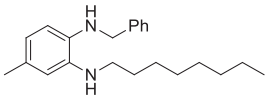
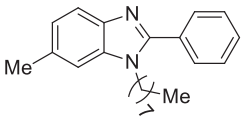
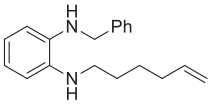
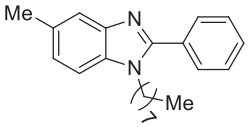
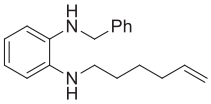
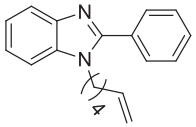
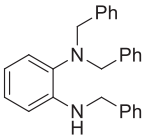
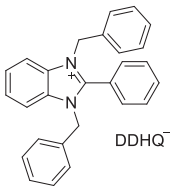
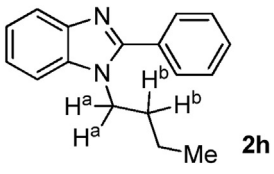
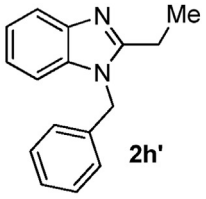
Substrate	Product	Yield (%)[a]
 **1a**	 **2a**	99
 **1b**	 **2b**	56
 **1c**	 **2c**	74
 **1d**	 **2d**	22
	 **2d′**	66
 **1e**	 **2e**	0
 **1f**	 **2f**	95[b]
 **1g**	 **2g**	62
 **1h**	 **2h**	86

Table 3 (*continued*)

Substrate	Product	Yield (%)[a]
 **1i**	 **2i**	30
 **1j**	 **2j**	26
 **1k**	 **2k**	66[b]
 **1l**	 **2l**	0


2h


2h'

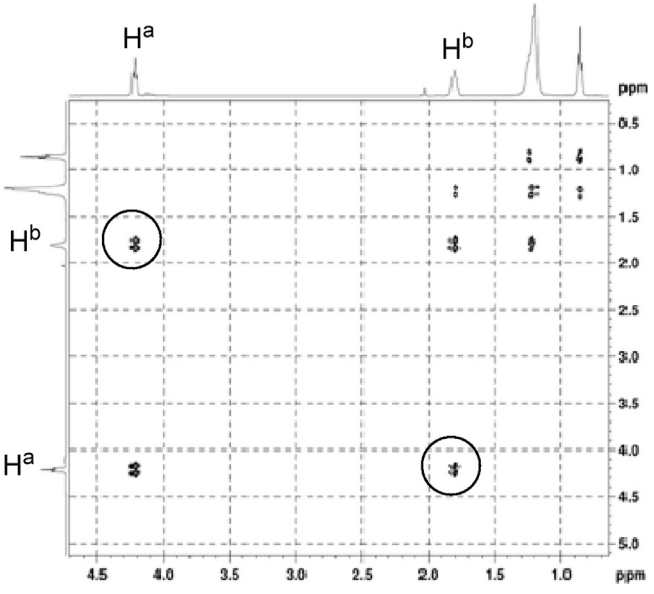


Fig. 1. Key connections determined from 2D NMR 3-bond COSY correlation for **2h**.

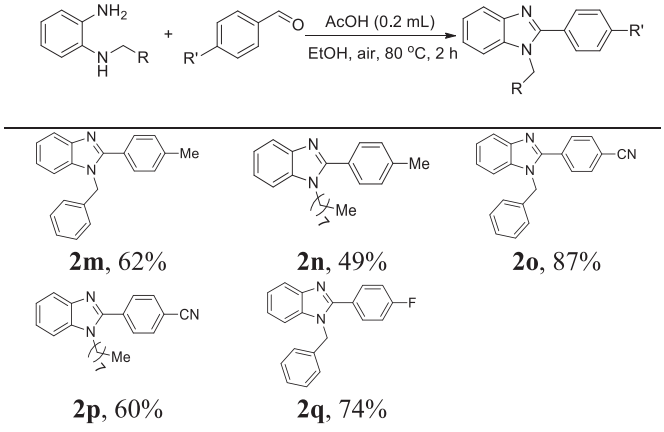
of 86% without the coexistence of isomer **2h′** (Fig. 1). However, the equal mixture of **1i** and **1j** was used as starting materials, in which the 6- and 5-methyl substituted products (**2i** and **2j**) were obtained in total yield of 56% with about 1:1 M ratio. The alkenyl substituted substrate (**1k**) was employed as substrate with coexistence of **1a**, the transformation of **1a** is quantitatively, and assembled benzimidazole (**2k**) was obtained in yield of 66% as well, in which low yield was presumed probably due to the existence of active olefin.

However, in another case, when using N^1,N^1,N^2-tribenzylbenzene-1,2-diamine (**1l**) as substrate, in which one of secondary amines was further substituted by benzyl, the reaction was inhibited and the expected imidazolium salt (**2l**) was not formed.

Although there are two possible isomeric products (**2h** and **2h′**) from unsymmetrical **1h**, only **2h** was obtained with n-octyl substitution on N1, which is readily identified by the 2D NMR H—H COSY correlation (Fig. 1). The triplet signal peak at 4.23 ppm was assigned as H^a in **2h**. The hydrogen H^a at the chemical displacement of 4.23 ppm was observed correlation with the hydrogen H^b at 1.81—1.82 ppm, which implied that there are two neighbouring hydrogens of methylene to H^a. If benzylic methylene was connected to N^1, the benzylic hydrogen would be resonated singlet signal peak and shifted more downfield. Likewise, the structures of **2i-k** were identified as single products like **2h**, respectively.

In the preparation of substrates, it was also found that in the presence of acetic acid, mixing N^1-benzylbenzene-1,2-diamine and p-methylbenzaldehyde generated **2m** in yield of 62% under reflux conditions (Scheme 1.). The yield of **2n** was 49% when N^1-octylbenzene-1,2-diamine reacted with *p*-methylbenzaldehyde for 2 h. While the aldehydes were cyano substituents, the yields of benzimidazoles (**2o** and **2p)** were increased to 87% and 60%, respectively. Higher activities was speculated from the properties of more electron-deficiency of aldehydes. Similarly, the yield of 74% was obtained for **2q**, in which the aldehyde was substituted by strongly electron-withdrawing fluorine.

According to our experimental results, a reasonable mechanism was proposed to explain the formation of benzimidazole through the oxidative coupling of *N*,N′-dibenzyl *o*-phenylenediamine, as shown in Fig. 2. First of all, *N*,N′-dibenzyl *o*-phenylenediamine proceeeds via single electron transfer and dehydrogenation by DDQ oxidation to form an iminium cation [17], which is hard to permit the loss of second electron of another amine, due to the positive charge of iminium intermediate, and intramolecular nuelceophilic addition of amine to iminium generates protonated annulated product benzimidazoline. Through hydrogen absorption of $DDHQ^-$,



Scheme 1. Alternative method to synthesis of benzimidazoles. Reaction conditions: diamine (0.3 mmol) and aldehyde (0.3 mmol) in EtOH (10.0 mL) at 80 °C for 2 h under air.

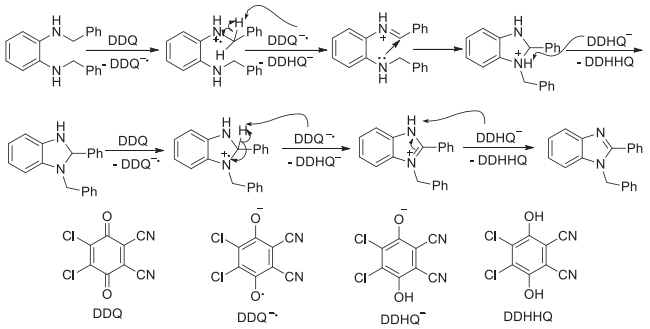


Fig. 2. Plausible reaction mechanism.

free benzimidazoline is released. Repeatedly, by DDQ oxidation, a single electron transfer and H-absorption eventually results in the formation of final product.

In above mechanism, for unsymmetrical starting material **1h-k**, the possible two iminium intermediates, i.e. aromatic and aliphatic iminiums, might be involved and proceed to generate two isomers. The experimental results showed that the aliphatic groups are always connected with N^1. Two simplified corresponding iminium structures from N^1-benzyl-N^2-ethylbenzene-1,2-diamine were therefore calculated to interpret the formation of **2h-k** at the level of B3LYP/6-31G (Fig. 3). The former showed high stability giving 8.7 kcal/mol lower energy than the latter, because of the larger conjugation plane, even if the shortest distance of H···H is 2.39 Å in this structure and is close to the sum of their Van der Waals radius. This delivers the pathways through aromatic iminiums are more preferable in these transformations than aliphatic ones.

3. Conclusion

In summary, we have developed a synthesis of 1,2- substitutive benzimidazoles by DDQ oxidized intramolecular dehydrogenative coupling of *N*,N′-dialkyl *o*-phenylenediamines under optimal conditions. As a particular case, *N*-benzyl *o*-phenylenediamine was able to be cyclized with *para*-cyano benzaldehyde by air oxidation to form benzimidazole. The experimental results showed that *N*, N′-dibenzyl and *N*-benzyl N′-linear aliphatic chain substitutions were compatible in this transformation, which provided an alternative protocol for the synthesis of versatile 1,2-disubstituted benzimidazoles.

4. Experimental section

4.1. General

The product was characterized by ^1H and ^{13}C NMR using 500/125 MHz NMR spectrometer at 20—25 °C , $CDCl_3$ (containing 0.03%

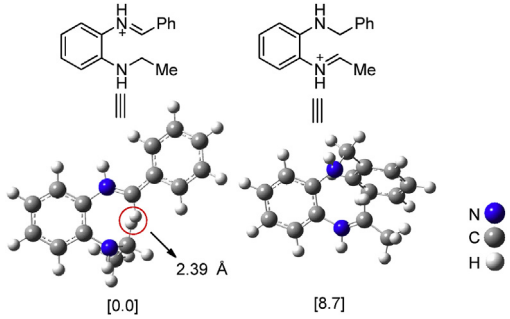


Fig. 3. Energy comparison of aromatic and aliphatic iminiums.

v/v TMS) was used as solvent. ^{1}H NMR spectra was reported in parts per million using tetramethylsilane (TMS, δ = 0.00 ppm) as an internal standard, and ^{13}C NMR was calibrated at 77.2 ppm for the chemical shift of the deuterated chloroform peak. The NMR data are reported as follows: chemical shift (ppm), integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quad, m = multiplicity, br = wide state) and coupling constant (Hz). High resolution mass spectra (HRMS) were obtained with a FT-ICRMS. Thin layer chromatography (TLC) was performed on a glass plate coated with GF254 silica gel and observed under 254 nm UV light, while column chromatography was performed using silica gel HG/T2354-2010. All reagents are analytically pure, purchased from commercial suppliers and used directly unless further purification is indicated otherwise. All reactions were performed at atmospheric pressure and all reagent weighing was performed at room temperature in air.

4.2. General method for the synthesis of benzimidazoles (2a-l)

Compounds **2a-l** were synthesized by adding DDQ (0.72 mmol) to *o*-phenylenediamine derivatives (**1**, 0.3 mmol) in 1.0 mL of dimethyl sulfoxide at 40 °C for 2 h. TLC was employed to monitor the reaction. When *N*,N′-dialkyl *o*-phenylenediamine was converted completely, saturate $Na_2S_2O_3$ was dropped into reaction mixture, and stirring was continued. Then the mixture was extracted and evaporated, and the resulting residue was purified by column chromatography on silica gel column using EtOAc-petroleum ether solution as eluent to afford desired benzimidazole **2**.

4.2.1. 1-Benzyl-2-phenyl-1H-benzo[d]imidazole (**2a**) [18a]

White solid; 99% yield, 84.5 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.0 Hz, 1H), 7.69 (d, *J* = 6.5 Hz, 2H), 7.49–7.44 (m, 3H), 7.35–7.28 (m, 4H), 7.24–7.20 (m, 2H), 7.11 (d, *J* = 7.0 Hz, 2H), 5.46 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.4, 143.4, 136.6, 136.3, 130.3, 130.1, 129.5, 129.2, 128.9, 128.0, 126.2, 123.2, 122.9, 120.2, 110.7, 48.6.

4.2.2. 1-Benzyl-4-methyl-2-phenyl-1H-benzo[d]imidazole (**2b**) [18a]

White solid; 56% yield, 50.1 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, *J* = 6.5 Hz, 2H), 7.44 (d, *J* = 6.5 Hz, 3H), 7.31–7.25 (m, 3H), 7.13–7.07 (m, 4H), 7.04 (d, *J* = 7.5 Hz, 1H), 5.40 (s, 2H), 2.75 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.7, 142.7, 136.7, 135.8, 130.5, 130.3, 129.9, 129.6, 129.2, 128.9, 127.9, 126.2, 123.2, 123.1, 108.2, 48.5, 17.0.

4.2.3. 1-Benzyl-6-methyl-2-phenyl-1H-benzo[d]imidazole (**2c**) [18a]

White solid; 74% yield, 66.2 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, *J* = 6.5 Hz, 1H), 7.67 (s, 2H), 7.45 (s, 3H), 7.34–7.32 (m, 3H), 7.15–7.12 (m, 3H), 7.01 (s, 1H), 5.43 (s, 2H), 2.44 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.9, 141.5, 136.8, 136.6, 133.3, 130.4, 129.9, 129.4, 129.2, 128.9, 127.9, 126.1, 124.5, 119.7, 110.5, 48.4, 22.0.

4.2.4. 1-Benzyl-5-chloro-2-phenyl-1H-benzo[d]imidazole (**2d**) [18a]

Light yellow solid; 22% yield, 21.0 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (s, 1H), 7.68 (d, *J* = 4.0 Hz, 2H), 7.47 (m, 3H), 7.34 (m, 3H), 7.20 (d, *J* = 8.5 Hz, 1H), 7.10 (m, 3H), 5.45 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.6, 144.2, 136.1, 134.8, 130.4, 129.9, 129.4, 129.3, 129.0, 128.5, 128.2, 126.1, 123.6, 120.0, 111.5, 48.7.

4.2.5. 1-Benzyl-6-chloro-2-phenyl-1H-benzo[d]imidazole (**2d'**) [18b]

Light yellow solid; 66% yield, 63.1 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.5 Hz, 1H), 7.67 (d, *J* = 2.0 Hz, 2H), 7.49–7.46 (m, 3H), 7.36–7.32 (m, 3H), 7.27 (d, *J* = 10.0 Hz, 1H), 7.20 (s,1H), 7.09 (d, *J* = 6.5 Hz, 2H), 5.42 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.2, 142.0, 136.9, 136.0, 130.3, 129.8, 129.4, 129.0, 128.9, 128.2, 126.1, 123.6, 121.0, 110.7, 48.7.

4.2.6. Methyl 4-(1-benzyl-1H-benzo[d]imidazole-2-yl)benzoate (**2f**) [18a]

Light yellow viscous liquid; 13% yield, 13.4 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.0 Hz, 2H), 7.89 (d, *J* = 8.5 Hz, 1H), 7.79–7.77 (d, *J* = 7.5 Hz, 2H), 7.34–7.33 (m, 4H), 7.28–7.26 (m, 2H), 7.10 (d, *J* = 7.0 Hz, 2H), 5.47 (s, 2H), 3.94 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.7, 153.1, 143.4, 136.5, 136.3, 134.6, 131.4, 130.1, 129.44, 129.35, 128.1, 126.1, 123.7, 123.2, 120.4, 110.8, 52.5, 48.7.

4.2.7. 1-(3-bromobenzyl)-2-phenyl-1H-benzo[d]imidazole (**2g**)

Light yellow solid; 62% yield, 67.6 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.87 (d, *J* = 6.5 Hz, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.56 (d, *J* = 7.5 Hz, 1H), 7.34–7.30 (m, 4H), 7.27–7.26 (m, 3H), 7.10 (d, *J* = 7.0 Hz, 2H), 5.45 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.6, 143.2, 136.3, 133.1, 132.6, 132.3, 130.4, 129.3, 128.1, 127.7, 126.1, 123.6, 123.09, 123.06, 120.4, 110.7, 48.6; HRMS (FT-ICR) *m/z*: $[M + H]^+$ calcd for $C_{20}H_{15}BrN_2$, 363.0491; found, 363.0480.

4.2.8. 1-Octyl-2-phenyl-1H-benzo[d]imidazole (**2h**) [18c]

Light yellow viscous liquid; 86% yield, 82.7 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, *J* = 5.5 Hz, 1H), 7.71 (dd, *J1* = 4.5 Hz, *J2* = 2.0 Hz, 2H), 7.51 (s, 3H), 7.41 (t, *J* = 3.0 Hz, 1H), 7.32 (s, 2H), 4.22 (t, *J* = 7.0 Hz, 2H), 1.81 (s, 2H), 1.25–1.19 (m, 10H), 0.86 (t, *J* = 6.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.6, 142.7, 135.4, 130.5, 129.9, 129.5, 128.8, 122.9, 122.6, 119.9, 110.3, 44.9, 31.8, 29.8, 29.1, 29.0, 26.8, 22.7, 14.2. HRMS (FT-ICR) *m/z*: $[M + H]^+$ calcd for $C_{21}H_{26}N_2$, 307.2169; found, 307.2159.

4.2.9. 5-Methyl- and 6-methyl-1-octyl-2-phenyl-1H-benzo[d] imidazole (**2i, 2j**)

Light yellow viscous liquid; 56% yield, 56.2 mg; 1H NMR (500 MHz, $CDCl_3$) δ 7.68 (s, 5H), 7.61 (s, 1H), 7.49 (s, 6H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.18 (s, 1H), 7.12 (d, *J* = 7.0 Hz, 2H), 4.17 (s, 4H), 2.53 (s, 3H), 2.50 (s, 3H), 1.79 (s, 4H), 1.25–1.19 (m, 20H), 0.87–0.84 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.8, 153.4, 143.6, 141.4, 136.0, 133.9, 132.7, 132.0, 131.0, 129.7, 129.6, 129.43, 129.42, 128.8, 124.2, 124.0, 119.8, 119.6, 110.1, 109.8, 44.8, 44.7, 31.8, 29.84, 29.81, 29.2, 29.1, 26.8, 22.7, 22.1, 21.7, 14.2. HRMS (FT-ICR) *m/z*: $[M + H]^+$ calcd for $C_{22}H_{28}N_2$, 321.2325; found, 321.2315.

4.2.10. 1-(Hex-5-en-1-yl)-2-phenyl-1H-benzo[d]imidazole (**2k**)

Light yellow viscous liquid; 23% yield, 15.5 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84–7.83 (d, *J* = 7.5 Hz, 1H), 7.70–7.68 (m, 2H), 7.52 (s, 2H), 7.46–7.41 (m, 1H), 7.33–7.32 (m, 2H), 7.26–7.20 (m, 1H), 5.74–5.66 (m, 1H), 4.94 (d, *J* = 13.0 Hz, 2H), 4.24 (t, *J* = 7.0 Hz, 2H), 2.00–1.99 (m, 2H), 1.85–1.82 (m, 2H), 1.37–1.34 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.9, 143.3, 138.0, 135.7, 130.9, 129.9, 129.5, 128.9, 122.5, 115.3, 110.2, 44.7, 33.1, 29.2, 26.0. HRMS (FT-ICR) *m/z*: $[M + H]^+$ calcd for $C_{19}H_{20}N_2$, 277.1699; found, 277.1691.

4.3. Procedure for synthesis of benzimidazole (2m-q)

To a round bottom flask that was equipped with a stirring bar, corresponding monosubstituted *o*-phenylenediamine (0.3 mmol) and ethanol (10.0 mL) were added successively and the resulting mixture was stirred thoroughly for 10 min, followed by addition of acetic acid (0.2 mL) and corresponding aldehydes (0.3 mmol, 1.0 equiv) to the dispersion solution in turn, and refluxed at 80 °C for 2 h. After completion of the reaction, the reaction mixture was cooled to room temperature and monitored by TLC. Then the

solvent was evaporated and the resulting residue was purified by column chromatography on silica gel column using EtOAc-petroleum ether solution as eluent to afford desired benzimidazoles **2m-q**.

*4.3.1. 1-Benzyl-2-(p-tolyl)-1H-benzo[d]imidazole (**2m**) [18a]*

White solid; 62% yield, 55.5 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, J = 7.5 Hz, 1H), 7.58 (d, J = 7.5 Hz, 2H), 7.34–7.29 (m, 4H), 7.25 (d, J = 7.5 Hz, 2H), 7.22–7.19 (m, 2H), 7.11 (d, J = 7.0 Hz, 2H), 5.45 (s, 2H), 2.40 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.5, 143.3, 140.3, 136.7, 136.2, 129.6, 129.3, 129.2, 127.9, 127.2, 126.1, 123.1, 122.8, 120.0, 110.6, 48.5, 21.6.

*4.3.2. 1-Octyl-2-(p-tolyl)-1H-benzo[d]imidazole (**2n**)*

Light yellow solid; 49% yield, 47.1 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83–7.81 (m, 1H), 7.59 (d, J = 7.0 Hz, 2H), 7.39–7.38 (m, 1H), 7.32–7.28 (m, 4H), 4.19 (t, J = 7.0 Hz, 2H), 2.43 (s, 3H), 1.79 (s, 2H), 1.25–1.20 (m, 10H), 0.86 (t, J = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.0, 143.2, 139.8, 135.7, 129.5, 129.3, 127.9, 122.6, 122.3, 119.9, 110.1, 44.8, 31.8, 29.8, 29.2, 29.0, 26.7, 22.7, 21.5, 14.2. HRMS (FT-ICR) m/z: $[M + H]^+$ calcd for $C_{22}H_{28}N_2$, 321.2325; found, 321.2315.

*4.3.3. 4-(1-benzyl-1H-benzo[d]imidazole-2-yl)benzonitrile (**2o**) [18d]*

White solid; 87% yield, 80.7 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.81 (s, 2H), 7.72 (s, 2H), 7.34–7.27 (m, 6H), 7.08 (s, 2H), 5.46 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.9, 143.2, 136.4, 135.9, 134.6, 132.6, 129.9, 129.4, 128.2, 125.9, 124.1, 123.4, 120.5, 118.4, 113.6, 110.8, 48.6.

*4.3.4. 4-(1-octyl-1H-benzo[d]imidazole-2-yl)benzonitrile (**2p**)*

Light yellow solid; 60% yield, 59.7 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88–7.82 (m, 5H), 7.45 (d, J = 6.5 Hz, 1H), 7.38–7.33 (m, 2H), 4.24 (t, J = 7.0 Hz, 2H), 1.82 (s, 2H), 1.25–1.21 (m, 10H), 0.87 (t, J = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.5, 143.1, 135.9, 135.3, 132.7, 130.1, 123.7, 123.1, 120.5, 118.4, 113.6, 110.5, 45.1, 31.8, 30.0, 29.2, 29.1, 26.8, 22.7, 14.2. HRMS (FT-ICR) m/z: $[M + H]^+$ calcd for $C_{22}H_{25}N_3$, 332.2121; found, 332.2111.

*4.3.5. 1-Benzyl-2-(4-fluorophenyl)-1H-benzo[d]imidazole (**2q**) [18a]*

White solid; 74% yield, 56.2 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, J = 8.0 Hz, 1H), 7.67 (t, J = 5.5 Hz, 2H), 7.35–7.31 (m, 4H), 7.26–7.22 (m, 2H), 7.14 (t, J = 8.5 Hz, 2H), 7.09 (d, J = 7.0 Hz, 2H), 5.44 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.9, 162.9, 153.3, 143.2, 136.4, 136.2, 131.5, 131.4, 129.3, 128.1, 126.1, 123.4, 123.0, 120.1, 116.2, 116.0, 110.7, 48.5.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tet.2020.131474.

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