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ORIGINAL ARTICLE

A concise synthesis of benzimidazoles via the microwave-assisted one-pot batch reaction of amino acids up to a 10-g scale

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Abstract An efficient method for the synthesis of aminomethyl benzimidazoles is developed by using a one-pot batch reaction between amino acids and *o*-phenylenediamines. This reaction proceeds smoothly in an unmodified household microwave oven, even though scale-up is to 10 g. A desirable method for the quick synthesis of benzimidazoles, which are used as a kind of important intermediates in drug synthesis, is provided by the scale-up utilization of amino acid resource.

Keywords Benzimidazoles · One-pot synthesis · Amino acids · *o*-Phenylenediamine · Microwave irradiation

Introduction

Benzimidazole compounds have important applications in many fields, such as medicinal chemistry (Narasimhan et al. 2012; Masoud et al. 2013), biochemistry (Wu et al. 2012) and coordination chemistry (Wang et al. 2006), in catalysis (Li et al. 2011), as flame retardant (Xiong et al. 2013), for molecular recognization (Dessingou et al. 2012), and as chemosensor (Guo et al. 2012; Ishida et al. 2013) and liquid crystal material (Wicklein et al. 2010; Zhang et al. 2013). Consequently, the researches on the synthesis of benzimidazoles earn increasing attentions in recent years (Ueda and Buchwald 2012; Xiao et al. 2013a, b; Peng et al. 2013; Baars et al. 2014). Normally, benzimidazole compounds are prepared by a two-step process, amidation and subsequently cyclization, when using available carboxylic acid and *o*-phenylenediamines as starting materials (Renneberg and Dervan 2003; Combs et al. 2006; Sparks et al. 2007; Zhang et al. 2009). If a suitable catalyst is used, a concise one-pot route to construct benzimidazoles can be developed (Wu et al. 2008; Alatorre-Santamaría et al. 2009). Moreover, the reflux time of this one-pot process can be greatly shortened by using the microwave-assisted technology. However, the solvent and catalyst are crucial for the one-pot microwave-assisted reflux method starting from *o*-phenylenediamines and carboxylic acid (Chen et al. 2009; Duan et al. 2012; Peng et al. 2013).

If the one-pot process is carried out in a household microwave oven without solvent, this one-pot microwave-assisted melting method for the synthesis of benzimidazoles will be greener, simpler, and more practical. Especially, the scale-up development of microwave-promoted reactions to the multigram level is important for both industrial production and laboratory synthesis (Barnard et al. 2006; Bowman et al. 2008; Mao et al. 2010). Thus, herein we report the scale-up synthesis of aminomethyl benzimidazole **3** (Scheme 1), which is an important intermediate (Balboni et al. 2008; Gudmundsson et al. 2009; Cherepanova et al. 2011; Masoud et al. 2013) or ligand

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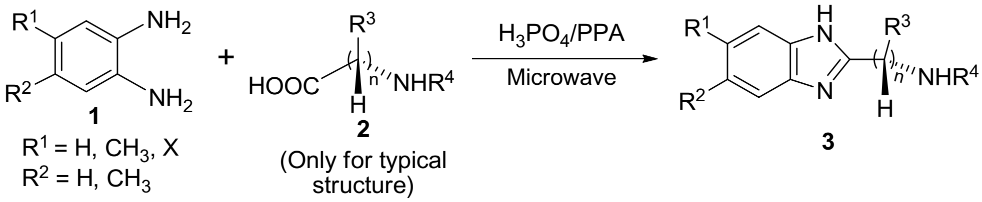
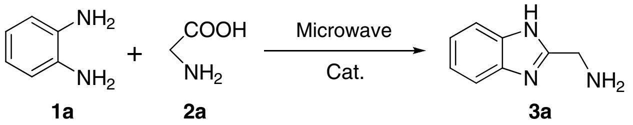
Scheme 1 The synthesis of aminomethyl benzimidazoles



(Li et al. 2009), by using the one-pot microwave-assisted melting method in an unmodified household microwave oven (Mao et al. 2010; Pasha and Nizam 2012) from natural amino acids, a kind of inexpensive functional synthons (Wang et al. 2012; Chaulagain et al. 2013; Tahoori et al. 2014), and *o*-phenylenediamines.

Table 1 Optimization of reaction conditions for the synthesis of benzimidazole **3a**



Entry[a]	Catalyst (dosage)	Power (W)	Time	Yield (%)[b]
1	No catalyst	320 (40 %)	30 s × 25	0
2	$SnCl_2$ (0.175 eq.)	320 (40 %)	30 s × 25	Trace
3	PPA (3 eq.)	320 (40 %)	30 s × 25	Carbonization
4	PPA + Glycol[c]	320 (40 %)	30 s × 25	20
5	PPA + H_3PO_4[d]	320 (40 %)	30 s × 25	78
6	PPA + H_3PO_4[d]	160 (20 %)	30 s × 25	58
7	PPA + H_3PO_4[d]	480 (60 %)	30 s × 25	–[e]
8	PPA + H_3PO_4[d]	640 (80 %)	30 s × 25	Carbonization
9	PPA + H_3PO_4[d]	320 (40 %)	30 s × 10	Trace
10	PPA + H_3PO_4[d]	320 (40 %)	30 s × 20	61
11	PPA + H_3PO_4[d]	320 (40 %)	30 s × 28	79
12	PPA + H_3PO_4[d]	320 (40 %)	30 s × 30	–[e]

[a] Reaction conditions: *o*-phenylenediamine **1a** (30 mmol, 3.242 g), glycine **2a** (30 mmol, 2.251 g), and catalyst dosage based on reactant **1a**

[b] Isolated yield

[c] According to the literature (Chen et al. 2009), 4 mL glycol was added and uniformly mixed with 3 mL polyphosphoric acid (PPA)

[d] According to the literature (Duan et al. 2012), 2 mL PPA was uniformly mixed with 5 mL H_3PO_4

[e] Partial carbonization made the mixture difficult to be separated

Results and discussion

Optimization of reaction conditions

In recent years, the microwave synthesis of benzimidazoles is still an active area of research (Mao et al. 2010; Mukhopadhyay et al. 2011; Pasha and Nizam 2012; Rashid et al. 2012; Kahveci et al. 2013; Xiao et al. 2013a, b). However, there are only a few examples using simple *o*-phenylenediamine and inexpensive natural amino acids as starting materials, and only limited natural amino acids are utilized (Chen et al. 2009; Duan et al. 2012). What is worse, though the one-pot microwave-assisted reflux method can greatly shorten the reaction time from several days or hours to 40 min with an increase of yield from 46 to 83 %, unfortunately a solvent with high boiling point, such as glycol, is necessary (Chen et al. 2009; Peng et al. 2013). Thus, the optimal reaction conditions of the one-pot microwave-assisted melting method are explored before the investigation on the substrate scope for the synthesis of aminomethyl benzimidazoles.

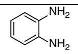
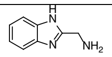
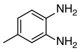
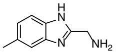
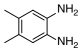
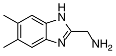
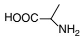
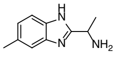
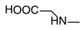
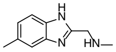
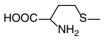
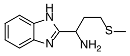
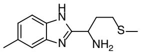
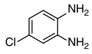
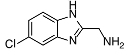
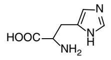
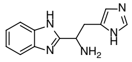
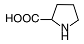
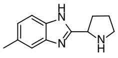
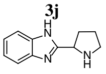
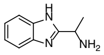
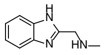
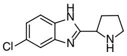
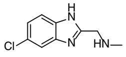
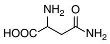
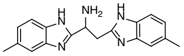
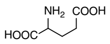
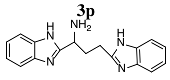
On the basis of our previous research on the one-pot synthesis of aminomethyl benzimidazoles by using the melting method (Chen et al. 2014), the conditions of the reaction are optimized by taking *o*-phenylenediamine **1a** and glycine **2a** as model substrates in an unmodified household microwave oven (Mao et al. 2010; Pasha and Nizam 2012). According to the literature (Mao et al. 2010), the uniformly mixed reactants in an open round-bottom flask were intermittently heated without reflux equipment in a microwave cavity with a pre-adjusted output power (maximum 800 W, 100 %) for 30 s per irradiation. The effects of catalyst, reaction time, and microwave output power on the reaction were evaluated.

As shown in Table 1, the catalyst has a prominent influence on the yield (entries 1–5). Obviously, the composite catalyst of polyphosphoric acid (PPA) and phosphoric acid (H_3PO_4) works very well (Duan et al. 2012) and gives the desired product with a yield of 78 % (entry 5). The microwave power is also important for the reaction (Table 1, entries 5–8), and 320 W proved to be the best (entry 5). The reaction times are screened (Table 1, entries 5, 9–12). As shown, the appropriate reaction time should be 14 min (entry 11) and the separation of product **3a** becomes difficult if the reaction time is prolonged (entry 12).

Scope of reaction substrates

Using the optimized conditions, the substrates' scope is investigated. Different natural amino acids and some

Table 2 The yields of aminomethyl benzimidazoles **3**

Entry [a]	Substrate **1**	Substrate **2**	Product **3**	Yield (%) [b]
1	 **1a**	 **2a**	 **3a**	79 (83)
2	 **1b**	**2a**	 **3b**	83 (84)
3	 **1c**	**2a**	 **3c**	86 (86)
4	**1b**	 **2b**	 **3d**	75 (72)
5	**1b**	 **2c**	 **3e**	88 (82)
6	**1a**	 **2d**	 **3f**	71 (75)
7	**1b**	**2d**	 **3g**	74 (76)
8	 **1d**	**2a**	 **3h**	72 (66)
9	**1a**	 **2e**	 **3i**	72 (70)
10	**1b**	 **2f**	 **3j**	82 (81)
11	**1a**	**2f**	 **3k**	81
12	**1a**	**2b**	 **3l**	71
13	**1a**	**2c**	 **3m**	76
14	**1d**	**2f**	 **3n**	78
15	**1d**	**2c**	 **3o**	76
16 [c]	**1b**	 **2g**	 **3p**	65
17 [c]	**1a**	 **2h**	 **3q**	79

[a] Reaction conditions except for special explanations: *o*-phenylenediamine **1a** (30 mmol, 3.242 g), glycine **2a** (30 mmol, 2.251 g), a composite catalyst of PPA (2 mL) and H_3PO_4 (5 mL), and the total reaction time 30 s × 28 under intermittent irradiation in a microwave cavity with an output power of 320 W

[b] Isolated yield; the latter data in parentheses show the yield of this compound synthesized via the one-pot melting method (Chen et al. 2014)

[c] The molar feed ratio (diamine **1**/amino acid **2**) is 2/1

substituted *o*-phenylenediamines are used as the starting materials, and the effects on the yield of aminomethyl benzimidazoles are summarized in Table 2. Obviously, almost all substrates can give satisfactory yields of the products (basically over 71 %, except for product **3p**, entry 16).

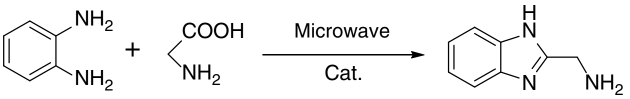
Compared with the previous one-pot melting method (Chen et al. 2014), the yields are basically similar (Table 2, entries 1–10), but the reaction time is greatly shortened from 5 h (Chen et al. 2014) to 14 min. More importantly, for reactions with relatively lower yields, especially below 72 %, the yield is improved efficiently (e.g., entry 8). On the other hand, for the synthesis of some products (e.g., **3a** and **3q**), which was synthesized by using the one-pot microwave-assisted reflux method before (Chen et al. 2009; Peng et al. 2013), the one-pot microwave-assisted melting method developed by us also shows some apparent advantages, such as higher yield, shorter reaction time, less reagent consumption, and simpler reaction equipment.

As shown in Table 2, the yields of aminomethyl benzimidazoles **3** are mainly influenced by the steric hindrance in substrates **2** and the electronic effect in substrates **1**. Compared with other amino acids, glycine **2a** generally gives a higher yield (entries 1 vs. 6, 9, 12) due to its smaller steric hindrance. For similar reasons, there is a higher yield in entry 2 than in entries 4, 7, and 10. As an isomer of alanine **2b**, *N*-methyl glycine **2c** with smaller steric hindrance in the reaction often gives higher yield than alanine **2b** (entries 4 vs. 5, 12 vs. 13).

When the same amino acids were used in the one-pot reaction, substrates **1** containing electron-donating substituent (e.g., methyl) in the *o*-phenylenediamine structure, give products with excellent yields (Table 2, entries 1 vs. 2; 4 vs. 12; 5 vs. 13; 6 vs. 7; 10 vs. 11) and a higher yield is given by substrates **1** with more electron-donating substituent (entries 1–3). On the contrary, when the *o*-phenylenediamine derivative **1c** contains electron-withdrawing substituent chlorine, the corresponding yields can be lower (entries 1 vs. 8; 11 vs. 14). Thus, the factors affecting the yields are similar to those in the melting method (Chen et al. 2014).

Among products **3**, some aminomethyl benzimidazoles have not been synthesized using the melting method before, but the yields of these compounds, especially some novel compounds, are satisfactory (Table 2, entries 11–17). Notably, for the synthesis of bisbenzimidazole **3p** using the novel one-pot microwave-assisted melting method, the reaction time under intermittent irradiation is 14 min, which is too short to eliminate an amino group. In contrast, due to a long time (5 h) in the melting state of the previous melting method, the easy loss of the amino group produced a more stable conjugate bisbenzimidazole structure instead of yielding **3p** (Chen et al. 2014). So the anticipated product can be given by using the improved method. Of course, the combination of the two melting methods (with/without microwave assistance) actually provides a complementary

Table 3 Scale-up for the synthesis of aminomethyl benzimidazole **3a**



1a **2a** **3a**

Entry[a]	Amount of **1a**	Amount of **2a**	Product **3a** (g)	Yield (%)[b]
1	3.242 g (30 mmol)	2.251 g (30 mmol)	3.456	79
2	6.484 g (60 mmol)	4.502 g (60 mmol)	6.894	78
3	9.726 g (90 mmol)	6.753 g (90 mmol)	10.239	78
4	12.968 g (120 mmol)	9.004 g (120 mmol)	13.619	77
5	32.421 g (300 mmol)	22.509 g (300 mmol)	20.389	47

[a] Reaction conditions: controlling the molar feed ratio of **1a/2a** as 1/1; the dosage of composite catalyst is based on reactant **1a** according to the standard that 2 mL PPA is uniformly mixed with 5 mL H_3PO_4 per 30 mmol **1a**. The total reaction time is 30 s × 28 under intermittent irradiation in a microwave cavity with an output power of 320 W

[b] Isolated yield

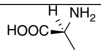
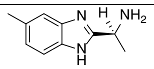
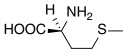
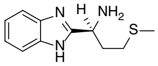
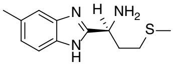
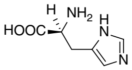
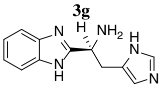
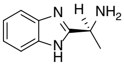
process for the synthesis of bisbenzimidazoles with or without the amino group when the amino acids containing two carboxyl groups are used as the starting materials.

Scale-up of microwave-assisted melting method

As an effective and simple method, the scale-up of the one-pot microwave-assisted melting method has great practical significance for the large-scale preparation of aminomethyl benzimidazoles **3** in the laboratory, and even in the industry. Using *o*-phenylene-diamine **1a** and glycine **2a** as model substrates, we further explored the one-pot microwave-assisted melting reaction in a larger round-bottom flask with the same microwave output power (320 W) for the same reaction time (30 s × 28). The results are shown in Table 3.

With the increase of the amount of reactant from 30 mmol step by step, the yield of product **3a** is gradually decreased. However, when the total weight of the reactants is increased to about 22 g, the yield of **3a** is only decreased slightly (Table 3, entry 4). Even when the amount of reactant is scaled up to ten times (300 mmol), the conversion can still keep a moderate yield (47 %) and the weight of product **3a** is over 20 g (entry 5). Therefore, the quick synthesis of aminomethyl benzimidazoles **3** at the level of tens of grams becomes possible. The one-pot microwave-assisted melting method can be an improved and a concise process obtained for the proper scale-up production of benzimidazole intermediates in many fields, such as drug synthesis, ligand synthesis, and so on.

Table 4 The rotation data of some aminomethyl benzimidazoles **3**

Entry	Amino acid **2**	Product **3**	$[\alpha]^{20}_{D}$ in C_2H_5OH	
1	 **2b**	 **3d**	-21.6°	-20.5° (Chen 2014)
2	 **2d**	 **3f**	-39.6°	---
3	**2d**	 **3g**	-29.9°	-30.5° (Chen 2014)
4	 **2e**	 **3i**	-23.6°	---
5	**2b**	 **3l**	-12.7°	---

Influence of microwave-assisted melting method on stereochemistry

Though there are only a few reports on the rotation data of chiral aminomethyl benzimidazoles (Chen et al. 2014), due to the importance of the stereochemistry of amino acid, the influences of this microwave-assisted melting method on the stereochemistry are investigated by testing the optical activity of the products when some typical L-amino acids are used as substrates (Table 4).

As shown in Table 4, the products synthesized from optically active amino acids and *o*-phenylenediamines are not racemic compounds, and some compounds have similar optical activity as reported (Chen et al. 2014). The stereochemistry of optically active amino acids may be not affected under our mild reaction conditions, which is beneficial for the preparation of optically active aminomethyl benzimidazoles and the utilization of natural L-amino acids.

Conclusions

In summary, a simple, efficient and practical methodology for the synthesis of benzimidazoles in an unmodified household microwave oven without reflux equipment is developed. More importantly, this one-pot microwave-assisted melting process using easily available amino acids as substrates can be successfully implemented up to a 10-g scale with a high yield of 77 %, and it provides a commercially viable and desirable method for the production of aminomethyl benzimidazole intermediates in the field of drug synthesis.

Experimental section

General

All the melting points were determined on an X-5 digital melting point apparatus and were uncorrected. Infrared spectra were recorded on a Bruker Vector 33 FT-IR instrument by the liquid film method in the absorption range of 4,000–400 cm^{-1}. ^{1}H and ^{13}C NMR spectra were obtained in DMSO-d_6 on a Varian DRX-400 MHz spectrometer and tetramethylsilane (TMS) was used as an internal standard. UV absorption peaks were measured by Shimazu UV-2550 ultraviolet absorption detector with dichloromethane as a solvent. Elemental analysis was performed on a Perkin Elmer Series II 2400 elemental analyzer. The mass spectra (MS) were recorded on Thermo LCQ DECA XP MAX mass spectrometer. Optical rotations were determined with an Autopol IV polarimeter in CH_3CH_2OH in a 10 cm cell. An 800-W unmodified household microwave oven (2.45 GHz) was used for microwave heating, and the microwave irradiation was intermittent at the appropriate power. All reagents and solvents were commercially available and used as received.

Typical procedure for the synthesis of compounds 3a–3q

In a 50-mL round-bottom flask, 30 mmol *o*-phenylenediamine **1** and amino acid **2** (1 equiv.) was uniformly mixed and 2 mL PPA and 5 mL H_3PO_4 was added subsequently. The mixture was intermittently irradiated in a microwave cavity with an output at 40 % (320 W) for specified times (30 s per irradiation). After completion of the reaction as indicated by TLC, the mixture was cooled to room temperature and diluted with 30 mL deionized water. Once the pH of the resulting solution was adjusted by the NaOH solution to 8–9, filtration gave the crude product which was purified by recrystallization with ethanol to afford samples **3a**–**3q** for analysis.

All newly synthesized aminomethyl benzimidazoles **3** were well characterized with FT-IR, UV, ^{1}H and ^{13}C NMR, MS, and elemental analysis. All known compounds were also characterized with m.p., ^{1}H NMR, and MS. Among them, the characterization data of products **3a**–**3j** are basically the same as the previous data reported by us (Chen et al. 2014). Therefore, listed are only the characterization data of other known compounds which were not synthesized via the melting method before.

2-(Pyrrolidin-2-yl)-1H-benzo[d]imidazole (Product 3 k)

Yellowish solid, yield 81 %, m.p. 158.4–160.1 °C (159–161 °C) (Maekawa and Ohtania 1976); ^{1}H NMR (400 MHz, DMSO-d_6-TMS), δ, ppm: 1.67–1.80 (2H, *m*, CH_2), 1.92–2.18 (2H, *m*, CH_2), 2.89–2.99 (2H, *m*, CH_2), 3.25 (1H, *b*, NH), 4.33–4.37 (1H, *m*, NCH), 7.08–7.12 (2H, *m*, ArH), 7.45–7.49 (2H, *m*, ArH), 11.82 (1H, *b*, NH); ESI–MS, *m/z* (%): calcd for $C_{11}H_{14}N_3^+$ ($[M + H]^+$): 188.11 (100 %), found: 188.25 (100 %).

1-(1H-benzo[d]imidazol-2-yl)ethanamine (Product 3 l)

Yellowish solid, yield 71 %, m.p. 207.5–209.1 °C (206.8–210.2 °C) (Roeder and Day 1941); ^{1}H NMR (400 MHz, DMSO-d_6-TMS), δ, ppm: 1.42 (3H, *d*, $J = 4.0$ Hz, CH_3), 2.20–2.70 (2H, *m*, NH_2), 4.14–4.19 (1H, *m*, NCH), 7.09–7.13 (2H, *m*, ArH), 7.47–7.56 (2H, *m*, ArH), 12.06 (1H, *b*, NH); ESI–MS, *m/z* (%): calcd for $C_{12}H_{16}N_3^+$ ($[M + H]^+$): 162.10 (100 %), found: 162.24 (100 %).

1-(1H-benzo[d]imidazol-2-yl)-N-methylmethanamine (Product 3 m)

Yellowish solid, yield 76 %, m.p. 126.8–128.5 °C (128 °C) (Kaupp and Dipl-Chem 1990); ^{1}H NMR (400 MHz, DMSO-d_6-TMS), δ, ppm: 2.33 (3H, *s*, NCH_3), 2.81 (1H, *b*, NH), 3.87 (2H, *s*, NCH_2), 7.10–7.14 (2H, *m*, ArH), 7.47–7.50 (2H, *m*, ArH), 11.81 (1H, *b*, NH); ESI–MS, *m/z* (%): calcd for $C_{12}H_{16}N_3^+$ ($[M + H]^+$): 162.10 (100 %), found: 162.11 (100 %).

5-Chloro-2-(pyrrolidin-2-yl)-1H-benzo[d]imidazole (Product 3n)

Yellowish solid, yield 78 %, m.p. 156.2–158.1 °C; UV–vis (CH_3OH), λ_{max}: 282 nm; ^{1}H NMR (400 MHz, DMSO-d_6-TMS), δ, ppm: 1.70–1.79 (2H, *m*, CH_2), 1.91–2.20 (2H, *m*, CH_2), 2.96 (2H, *t*, $J = 8.0$ Hz, NCH_2), 4.07 (1H, *b*, NH), 4.37–4.42 (1H, *m*, NCH), 7.10–7.15 (1H, *m*, ArH), 7.46–7.52 (2H, *m*, ArH), 10.77 (1H, *b*, NH); ^{13}C NMR (100 MHz, DMSO-d_6-TMS), δ, ppm: 25.23, 31.87, 46.40, 55.88, 114.31, 121.28, 125.44, 130.81, 148.69, 157.78, 159.88; IR ($CHCl_3$), ν, cm^{-1}: 3,184, 3,030, 2,970, 2,876, 1,623, 1,538, 1,450, 1,275, 858, 804, 604; ESI–MS, *m/z* (%): calcd for $C_{11}H_{13}ClN_3^+$ ($[M + H]^+$): 222.07 (100 %), found: 222.22 (100 %); anal. calcd for $C_{11}H_{12}ClN_3$: C 59.60, H 5.46, N 18.95, found: C 59.51, H 5.40, N 18.98.

1-(5-Chloro-1H-benzo[d]imidazol-2-yl)-N-methylmethanamine (Product 3o)

Yellowish solid, yield 76 %, m.p. 160.9–162.9 °C; UV–vis (CH_3OH), λ_{max}: 281 nm; ^{1}H NMR (400 MHz, DMSO-d_6-TMS), δ, ppm: 2.32 (3H, *s*, NCH_3), 2.82 (1H, *b*, NH), 3.87 (2H, *s*, NCH_2), 7.11–7.16 (1H, *m*, ArH), 7.48–7.54 (2H, *m*, ArH), 10.76 (1H, *b*, NH); ^{13}C NMR (100 MHz, DMSO-d_6-TMS), δ, ppm: 35.85, 48.93, 114.76, 121.36, 125.54, 136.49, 139.65, 147.00, 155.98; IR ($CHCl_3$), *ν*, cm^{-1}: 3,174, 3,025, 2,970, 2,876, 1,619, 1,538, 1,444, 1,275, 858, 804, 599; ESI–MS, *m/z* (%): calcd for $C_9H_{11}ClN_3^+$ ($[M + H]^+$): 196.06 (100 %), found: 196.19 (100 %); anal. calcd for $C_9H_{10}ClN_3$: C 55.25, H 5.15, N 21.48, found: C 55.30, H 5.09, N 21.44.

1,2-Bis(5-methyl-1H-benzo[d]imidazol-2-yl)ethanamine (Product 3p)

Yellowish solid, yield 65 %, m.p. >320 °C; UV–vis (CH_3OH), λ_{max}: 282 nm; ^1H NMR (400 MHz, DMSO-d_6-TMS), *δ*, ppm: 2.40–2.51 (6H, *m*, $2CH_3$), 3.70–4.62 (4H, *m*, NH_2, CH_2), 4.71–5.77 (1H, *m*, NCH), 6.85–7.02 (2H, *m*, ArH), 7.15–7.42 (4H, *m*, ArH), 12.73 (2H, *b*, 2NH); ^{13}C NMR (100 MHz, DMSO-d_6-TMS), *δ*, ppm: 21.34, 46.11, 55.32, 116.32, 120.88, 122.97, 123.47, 129.74, 131.48, 133.59, 134.91, 135.91, 140.04, 145.35, 151.16, 156.88, 159.52; IR ($CHCl_3$), *ν*, cm^{-1}: 3,148, 3,048, 2,919, 2,879, 1,628, 1,561, 1,485, 1,449, 1,278, 862, 803; ESI–MS, *m/z* (%): calcd for $C_{18}H_{20}N_5^+$ ($[M + H]^+$): 306.16 (100 %), found: 306.36 (100 %); anal. calcd for $C_{18}H_{19}N_5$: C 70.80, H 6.27, N 22.93, found: C 70.91, H 6.22, N 22.87.

1,3-Di(1H-benzo[d]imidazol-2-yl)propan-1-amine (Product 3q)

Yellowish solid, yield 79 %, m.p. 124.6–126.2 °C (124–126 °C) (Duan et al. 2012); ^1H NMR (400 MHz, DMSO-d_6-TMS), *δ*, ppm: 2.17–2.44 (2H, *m*, CH_2), 2.94 (2H, *t*, $J = 8.0$ Hz, CH_2), 3.36–3.48 (2H, *m*, NH_2), 4.12–4.15 (1H, *m*, NCH), 7.09–7.15 (4H, *m*, ArH), 7.45–7.52 (4H, *m*, ArH), 12.18 (2H, *b*, 2NH); ESI–MS, *m/z* (%): calcd for $C_{17}H_{18}N_5^+$ ($[M + H]^+$): 292.15 (100 %), found: 292.33 (100 %).

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Conflict of interest The authors declare no completing financial interest.

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