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Improved and ligand-free copper-catalyzed cyclization for an efficient synthesis of benzimidazoles from *o*-bromoarylamine and nitriles†

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We present an improved copper-catalyzed cyclization for an efficient synthesis of benzimidazoles from *o*-bromoarylamine and nitriles, under mild and ligand-free conditions. The optimal conditions yielded exceptional products of up to 98%, demonstrating the broad applicability of this synthetic strategy in generating a wide range of valuable imidazole derivatives. This methodology enables the efficient synthesis of various substituted benzimidazole derivatives and offers an environmentally friendly alternative to conventional methods. By eliminating the use of harsh reagents and high temperatures associated with traditional synthesis approaches, this method proves to be more efficient and robust. Notably, we successfully applied this synthetic approach to the synthesis of bendazol and thiabendazole, yielding 82% and 78%, respectively, on a 100 gram scale.

Introduction

Benzimidazole (**2**) and its derivatives are crucial nitrogen-containing heterocycles that serve as privileged scaffolds in the pharmaceutical industry.[1] This is primarily due to their prominence in various bioactive compounds and pharmaceutical active ingredients (APIs). These include antihypertensive drugs like telmisartan, bendazol, and candesartan, as well as antihelminthic drugs such as albendazole, thiabendazole, and mebendazole. Additionally, benzimidazoles are utilized in the production of antiviral drugs like enviradine, proton pump inhibitors such as esomeprazole, lansoprazole, and pantoprazole, then as antihistamines like semizole (Fig. 1).[2] Due to the significant biological activities, unique structural features, and wide-ranging industrial applications, the synthesis of benzimidazole-based drugs has garnered considerable attention from chemists, resulting in the development of various strategies.[2] One of the key focal points has been the efficient construction of the essential benzimidazole skeleton.

The conventional method for synthesizing benzimidazoles involves the condensation and cyclization of substituted *o*-phenylenediamines with carboxylic acid derivatives and aldehydes under strong acidic conditions, high temperatures, or with equivalent amounts of oxidants. Additionally, the production of the required substituted *o*-phenylenediamines typically necessitates the incorporation of nitro groups through nitration with nitrosulfuric acid on the substituting aniline, followed by reduction (Scheme 1A). Several alternative approaches have been evaluated to improve the synthesis of benzimidazoles, including the use of aldehydes as substrates and iodine as a catalyst in the presence of hydrogen peroxide,[3] employing metal-catalyzed or oxidative cyclization of amidines (Scheme 1B),[4] and the use of an iridium photocatalyst to generate benzimidazoles from *N*-phenylamidoxime esters (Scheme 1C), and a recently reported approach involving Pd-catalyzed carbonylative cyclization.[5,6] However, certain underlying issues remain unresolved or new drawbacks have emerged, such as the commercial unavailability of viable raw materials, laborious procedures, the need for homogeneous precious-metal catalysts, and high cost. Moreover, these approaches generate significant amounts of stoichiometric waste due to the presence of leaving groups or additives in the substrate. Furthermore, the original synthetic route for

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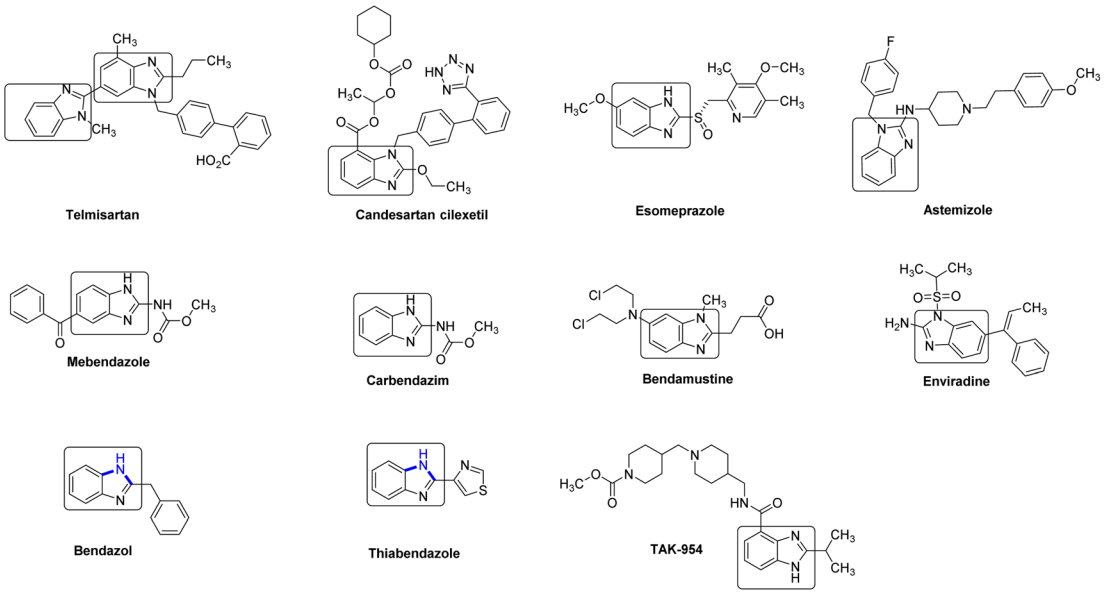

Fig. 1 Selected examples of drugs containing benzimidazole ring unit.

constructing benzimidazole intermediates, which involved nitration and polyphosphoric acid (PPA)-mediated cyclization, resulted in safety issues and the generation of acidic sewage that required treatment.[7]

In prior research, various synthesis methods for benzimidazoles have been reported (Scheme 1A–C), including the copper-catalyzed Ullman-type C–N coupling of *o*-haloanilides with primary amides in a one-pot reaction.[8] It's worth noting that Xiang *et al.*[9] and Yu *et al.*[10] demonstrated the synthesis of benzimidazoles through intermolecular cyclization reactions of 2-iodoanilines with aryl nitriles. Although their approaches offers route to synthesize a range of amides and benzoxazole derivatives, its application in terms of catalytic synthesis of heterocycles is limited. More so, using nitriles as nitrogen nucleophiles, the direct reaction with arylamines through a catalytic cyclization system streamlines the synthesis of benzimidazoles compared to that with amides, and even with ligands.

In light of previous studies and existing knowledge, particularly Xiang *et al.*[9] and Yu *et al.*,[10] we were inspired to investigate the feasibility of employing nitriles as an alternative to amides for the synthesis of benzimidazoles, and expand the substrate scope through the cyclization of anilines with nitriles to generate the desired product (Scheme 1D), and further demonstrate the synthetic application of our approach in a number of benzimidazole-based drugs.

Herein, we present an improved approach for the synthesis of benzimidazoles by cyclization of *o*-bromoarylamine with nitriles. Remarkably, the reaction occurs under mild and ligand-free conditions, using a relatively low catalytic load. This methodology utilizes readily accessible starting materials, thus promoting a safe and efficient synthesis pathway. It is noteworthy that this method exhibits a high tolerance for functional groups on the substrate and enables the efficient construction of structurally diverse benzimidazoles compared to previous approaches. In addition, this method provided an improved approach for making bendazol and thiabenzadole, avoiding the undesired cyclization with polyphosphoric acid, high reaction temperature, and other drawbacks in the existing operations.

Results and discussion

The cyclization reaction conditions for the formation of benzimidazole (**2**) were investigated in this study, with a focus on the reaction between anilines and *n*-butyronitrile (**3**) as our model starting materials. We specifically chose anilines due to their cleaner and more promising alternative to other aromatic amines. Previous reports corroborate that anilines are readily available, cost-effective, and easy to handle.[11] Consequently, we anticipated that the cyclization process with anilines under mild conditions would offer significant advantages by reducing the reliance on harsh reagents and conditions typically associated with traditional methods.

In our investigation, we initially explored the synthesis of benzimidazoles using the cyclization reaction of 2-iodoaniline (**1I**) and arylnitrile, as previously reported by Xiang's[9] and Yu's[10] research group. Building upon this method, we aimed to directly cyclize *o*-bromoaniline (**1Br**) or *o*-chloroaniline (**1Cl**) with *n*-butyronitrile in the absence of copper catalyst and ligand. However, our experimental results indicated that the desired product was only obtained in limited quantities (Table 1, entries 1–3).

Based on the aforementioned observations, we hypothesized that the desired product could be obtained through the cyclization reaction of *o*-bromoaniline (**1Br**) with nitriles under optimized conditions (Table 1, entry 3). Hence, our investigation focused on determining the optimal conditions for this

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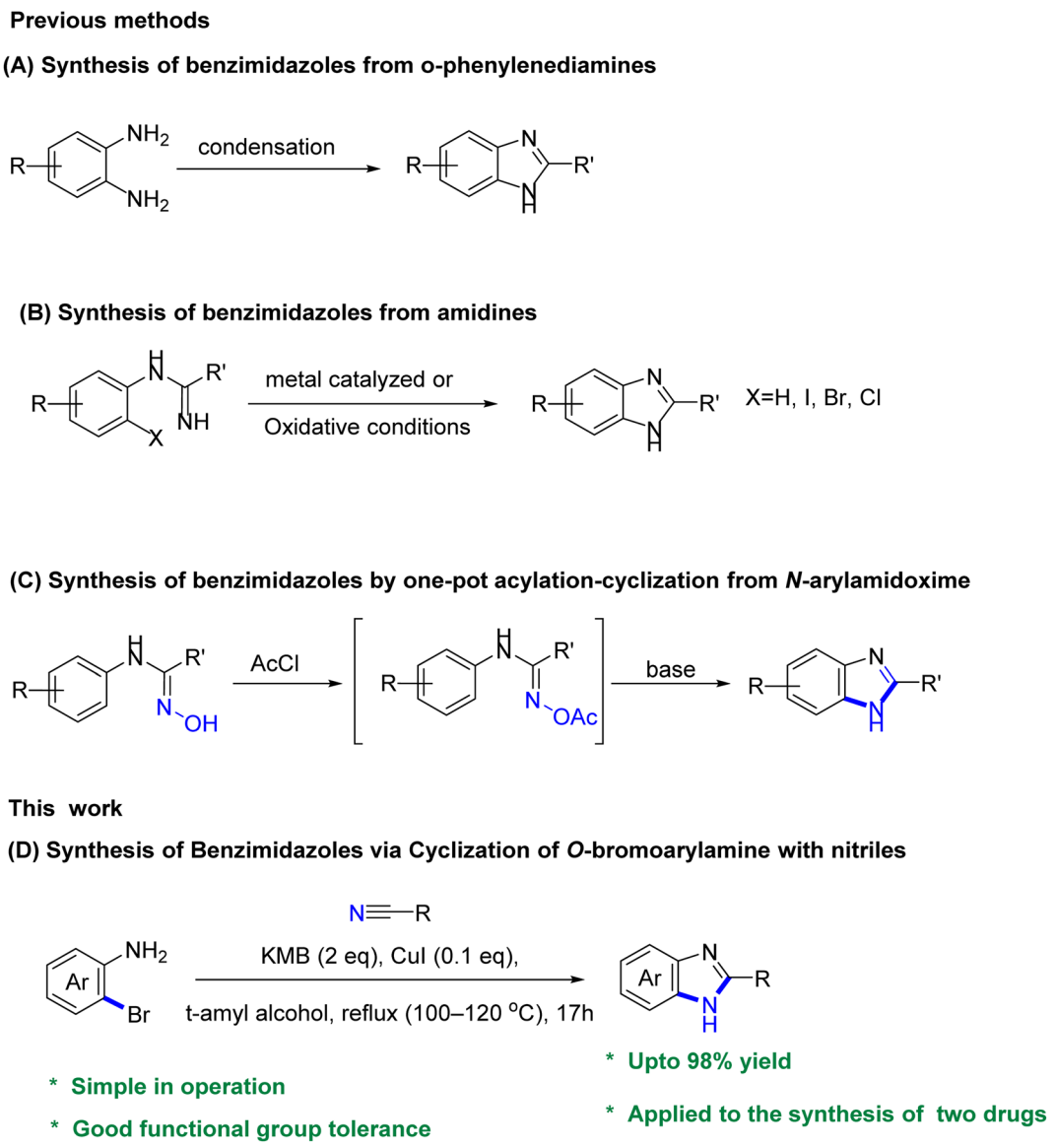

Scheme 1 Previous methods (A–C) for producing benzimidazoles, and our method (D) for the synthesis of benzimidazoles *via* cyclization of *o*-bromoarylamine with nitriles.

cyclization reaction, starting with an evaluation of the base and catalyst's effect.

When the reaction was conducted in the absence of a base, the desired product was not obtained. Moreover, reducing the equivalent of the base resulted in a decreased yield compared to the other case (entry 5 *vs.* 4).

Again, our findings revealed that the inclusion of a copper catalyst was essential, as its absence led to a significant decrease in product yield and a notable unconsumed amount of starting material (Table 1, entries 1–3, *vs.* 4–11). We attempted the addition of different copper catalysts to react in *t*-BuOH as a solvent to coordinate with *o*-bromoaniline. We found that copper(I) bromide (CuBr), a univalent copper catalyst, could afford the desired product in 80% yield (Table 1, entry 4). We also examined the catalytic effects of cuprous chloride (CuCl) and cuprous oxide (Cu_2O). However, it was observed that these catalysts led to a decreased yield compared to CuBr (Table 1, entries 6–7, *vs.* 4). In addition to the previously tested copper catalysts, we also investigated divalent copper catalysts such as copper bromide ($CuBr_2$), copper chloride ($CuCl_2$), and copper acetate ($Cu(OAc)_2$). However, in comparison to the monovalent copper catalysts, these divalent copper catalysts showed lower catalytic efficiency (Table 1, entries 8–10 *vs.* 4, 6 and 7). After screening various copper catalysts, it was determined that copper iodide (CuI) exhibited the best catalytic effect (Table 1, entry 11). The yield of the cyclization product using copper iodide reached 86%.

Several bases were tested as alternatives to potassium *tert*-butoxide (*t*-BuOK) in our study, including potassium hydroxide (KOH), potassium carbonate (K_2CO_3), and potassium phosphate (K_3PO_4). However, the use of these bases (Table 1, entries 12–14) yielded only trace amounts or no detectable cyclization

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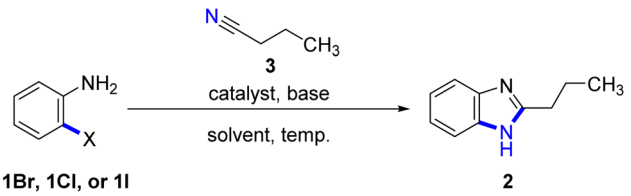
Table 1 Optimization of the cyclization reaction for benzimidazole using *o*-bromoaniline with *n*-butyronitrile[a]



Entry	Starting material	Catalyst	Base	Solvent	Temp. (°C)	Time (h)	Yield[b] (%)
1	2-Iodoaniline	—	*t*-BuOK	*t*-BuOH	84	17	14
2	2-Chloroaniline	—	*t*-BuOK	*t*-BuOH	84	17	Trace
3	*o*-Bromoaniline	—	*t*-BuOK	*t*-BuOH	84	17	26
4	*o*-Bromoaniline	CuBr	*t*-BuOK	*t*-BuOH	84	17	80
5	*o*-Bromoaniline	CuBr	*t*-BuOK	*t*-BuOH	84	17	39[c]
6	*o*-Bromoaniline	CuCl	*t*-BuOK	*t*-BuOH	84	15	68
7	*o*-Bromoaniline	Cu_2O	*t*-BuOK	*t*-BuOH	84	15	71
8	*o*-Bromoaniline	$CuBr_2$	*t*-BuOK	*t*-BuOH	84	16	41
9	*o*-Bromoaniline	$CuCl_2$	*t*-BuOK	*t*-BuOH	84	16	35
10	*o*-Bromoaniline	$Cu(OAc)_2$	*t*-BuOK	*t*-BuOH	84	16	38
11	*o*-Bromoaniline	CuI	*t*-BuOK	*t*-BuOH	84	16	86
12	*o*-Bromoaniline	CuI	KOH	*t*-BuOH	84	16	Trace
13	*o*-Bromoaniline	CuI	K_2CO_3	*t*-BuOH	84	16	Nd[d]
14	*o*-Bromoaniline	CuI	K_3PO_4	*t*-BuOH	84	16	Nd[d]
15	*o*-Bromoaniline	CuI	*t*-BuONa	*t*-BuOH	84	16	64
16	*o*-Bromoaniline	CuI	$(t\text{-BuO})_2Mg$	*t*-BuOH	84	16	55
17	*o*-Bromoaniline	CuI	*t*-BuOLi	*t*-BuOH	84	16	74
18	*o*-Bromoaniline	CuI	KMB	*t*-BuOH	84	18	87
19	*o*-Bromoaniline	CuI	KMB	1,4-Dioxane	100	18	56
20	*o*-Bromoaniline	CuI	KMB	Toluene	110	16	45
21	*o*-Bromoaniline	CuI	KMB	DMF	140	17	50
22	*o*-Bromoaniline	CuI	KMB	NMP	140	18	55
23	*o*-Bromoaniline	CuI	KMB	*t*-Amyl alcohol	120	17	92
24	*o*-Bromoaniline	CuI	KMB	*t*-Amyl alcohol	120	17	93[e]
25	2-Chloroaniline	CuI	KMB	*t*-Amyl alcohol	120	17	20
26	2-Iodoaniline	CuI	KMB	*t*-Amyl alcohol	120	17	85
27	*o*-Bromoaniline	CuI	KMB	*t*-Amyl alcohol	120	17	86[f]
28	*o*-Bromoaniline	CuI	KMB	*t*-Amyl alcohol	120	17	85[f]
29	*o*-Bromoaniline	CuI	KMB	*t*-Amyl alcohol	120	17	Trace[g]
30	*o*-Bromoaniline	CuI	KMB	*t*-Amyl alcohol	120	17	43[c]

[a] Reactions were conducted by dissolving compound **1Br**, **1Cl** or **1I** (1.0 mmol) in solvent (6 ml), then adding *n*-butyronitrile **3** (2 equiv.), catalysts (0.1 equiv.) and a base (2.0 equiv.), followed by stirring at 84–140 °C for 17 h. [b] Isolated yield. [c] With 1 equivalent of base. [d] Not detected. [e] Stirring for 36 h. [f] Addition of ligand. [g] With 0.5 equivalent of base.

product. We also explored the use of other bases such as sodium *tert*-butoxide (*t*-BuONa), magnesium di-*tert*-butoxide ($(t\text{-BuO})_2Mg$), and lithium *tert*-butoxide (*t*-BuOLi), which were found to promote the reaction and generate the desired products. Nevertheless, their efficiency was comparatively lower than that of potassium *tert*-amylate (KMB) (Table 1, entries 15–17 *vs.* 18). We investigated the effect of different solvents on the cyclization reaction. Various solvents, including *tert*-amyl alcohol, ethylene glycol, dioxane, toluene, dimethylformamide (DMF), and *N*-methylpyrrolidone (NMP), were examined. Among these screened solvents, *tert*-amyl alcohol was found to be more effective than other solvents (Table 1, entry 23 *vs.* 19–22). Under the same reaction conditions, the yield did not increase significantly with the extension of reaction time (Table 1, entry 24). It was observed that, under same conditions, the reaction of 2-chloroaniline and 2-iodoaniline resulted in the desired product with yields of 20% and 85% respectively. Nonetheless, it is evident that 2-bromoaniline proves to be the optimal 2-haloaniline derivative for this reaction (Table 1, entry 23 *vs.* 25–26).

Interestingly, when attempting to add *N*,*N*-dimethylethylenediamine or proline as a ligand, the yield rather decreased (Table 1, entries 27–28). The results clearly indicate that maintaining a reaction time of 16–17 hours without the use of ligands is the optimal approach. Therefore, we selected copper iodide as the catalyst, potassium *tert*-amylate (KMB) as the base, and a refluxing (120 °C) cyclization reaction in *tert*-amyl alcohol as the optimal reaction conditions (Table 1, entry 23).

Additional control experiments were conducted under optimized conditions, specifically without a base, resulting in no detectable cyclization product. Using less than 2 equivalent of the base resulted in a trace amount (entry 29) and low yield of

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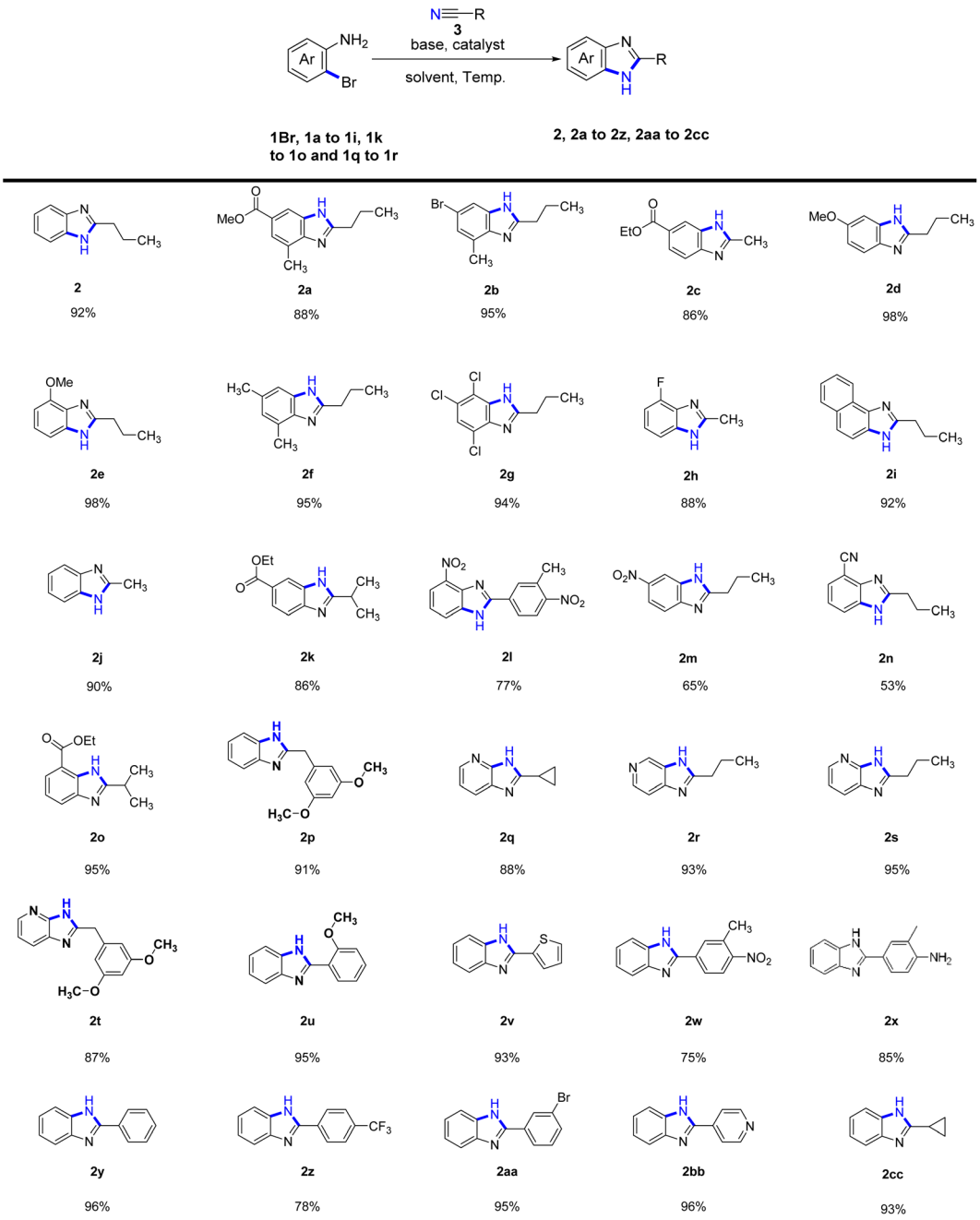
the desired product, indicating a lower catalytic efficiency as compared to other yield (entry 30 *vs.* 23). These results unequivocally demonstrate that copper-catalyzed cyclization reactions require a substantial amount of base, along with a catalytic amount of copper catalyst, to produce the desired benzimidazoles.[12]

Following the establishment of the optimal cyclization reaction conditions, we proceeded to explore the scope and versatility of aliphatic nitrile substrates and *o*-bromoaromatic amines (Table 2). Remarkably, our research revealed that when the benzene ring of the *o*-bromoaromatic amine substrate (**1a–1c**, **1f**, **1k**, **1o**) was substituted with a methyl group or an ester, the reaction proceeded smoothly, leading to the formation of the desired products (**2a–2c**, **2f**, **2k**, **2o**) with yields ranging between 86-95%. We further explored the influence of different substituents on the cyclization reaction by investigating the electronic effects of substituents on the benzene ring of *o*-bromoaromatic amine. Remarkably, the presence of a methoxy

Table 2 Substrate scope of the cyclization reaction for benzimidazoles[a]



[a] The reactions were performed on the scale of 1.0 mmol of **1Br**, **1a–1i**, **1k–1o** and **1q–1r** under the conditions: 2.0 equiv. of nitriles, 2 equiv. of KMB, 0.1 equiv. of CuI catalyst, 6 ml *t*-amyl alcohol solvent, 120 °C for 17 h. The yields were given as isolated yields.

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group in the phenyl substrates (**1d**, **1e**) resulted in efficient cyclization reactions, yielding benzimidazoles (**2d** and **2e**) with a high yield of 98%. Moreover, when the phenyl *o*-bromoaromatic amine substrates (**1g–1h**) contained chlorine or fluorine substituents, the cyclization products (**2g** and **2h**) were obtained in even higher yields of 94% and 88%, respectively.

Furthermore, we successfully investigated the reactivity of the phenyl unsubstituted *o*-bromoaniline substrate (**1Br**) in cyclization reactions with various nitriles, resulting in higher yields of products (**2**, **2j**, **2cc**, **2p**). However, when *o*-bromoaniline substrates with electron-withdrawing groups such as nitro (**1m**) and nitrile (**1n**) substituents were used, the yields of the corresponding products (**2m**, **2n**) were lower, ranging from 53% to 65%. Interestingly, *o*-bromoaromatic amines bearing 1-naphthyl (**1i**) and pyridyl (**1q**, and **1r**) substituents also exhibited reactivity in the intermolecular cyclization reactions, affording products **2i** (92% yield), **2q** (88% yield), **2r** (93% yield), **2s** (95% yield) and **2t** (87% yield).

Again, an investigation was conducted on the scope of aromatic nitrile substrates and *o*-bromoaromatic amines. The results showed that most aromatic nitrile substrates and *o*-bromoarylamine cyclization yielded satisfactory results. However, it was observed that the presence of charge-drawing functional groups, such as 3-methyl-4-nitrobenzonitrile and *p*-trifluoromethylbenzonitrile, led to lower cyclization yields (**2l**, **2w**, and **2z** at 75–78%). Other aromatic nitrile substrates, such as benzonitrile, 2-methoxybenzonitrile, 2-nitrilethiophene, and 3-methyl-4-aminobenzonitrile can all undergo cyclization with *o*-bromoaniline (**1Br**) to afford the desired products with higher yields. Specifically, the desired products **2y**, **2u**, **2v**, and **2x** were obtained with yields of 96%, 95%, 93%, and 85%, respectively. Remarkably, even when 3-bromobenzonitrile was cyclized with *o*-bromoaniline (**1Br**), the reaction exhibited good functional group compatibility as the bromine atom did not participate in the reaction, leading to the formation of the desired product **2aa** with a yield of 95%. Similarly, the reaction of aromatic nitriles with heterocyclic rings, such as 4-nitrilepyridine and *o*-bromoaniline (**1Br**) successfully gave the desired product **2bb** with a yield of 96%.

Post-application for the synthesis of thiabendazole, and bendazol

Subsequently, the applicability of our cyclization approach was demonstrated in a concise synthesis of antihypertensive drug, bendazol, and anthelminthic drug, thiabenzadole.[2] Gram-scale cyclization of 2-bromoaniline with thiazole-4-carbonitrile and potassium-2-methylbutan-2-olate in *tert*-amyl alcohol in the presence of CuI at 120 °C afforded thiabendazole with an impressive isolated yield of 78%, surpassing the reported yield of 64% achieved using a catalyzed-polyphosphoric acid cyclization method.[13] Likewise, this succinct approach was utilized to synthesize the antihypertensive drug, bendazol, yielding a light yellow solid of bendazol in a 82% isolated yield through DCM/hexane re-crystallization, showcasing outstanding functional group compatibility for the cyclization of the benzonitrile substrate as compared to previous report.[14]

Based on the experimental results and relevant literature,[11,13] we propose a reaction mechanism pathway for the synthesis of benzimidazole compounds *via* the cyclization of *o*-bromoaromatic amines and nitrile substrates, as depicted in Fig. 2. Initially, under basic conditions, the amino group of the *o*-bromoaromatic amine undergoes deprotonation, resulting in the formation of intermediate **C** with a negatively charged nitrogen atom. Subsequently, it reacts with the cyano group of the nitrile substrate to produce intermediate amidine **D**. Introducing a copper iodide catalyst leads to the formation of a metal intermediate **E**. Subsequently, intramolecular bromine transmetalation occurs, resulting in the formation of intermediate **F**. Ultimately, through reduction and elimination reactions, the final product, benzimidazole compound, is generated, and the catalyst is released, thereby completing the

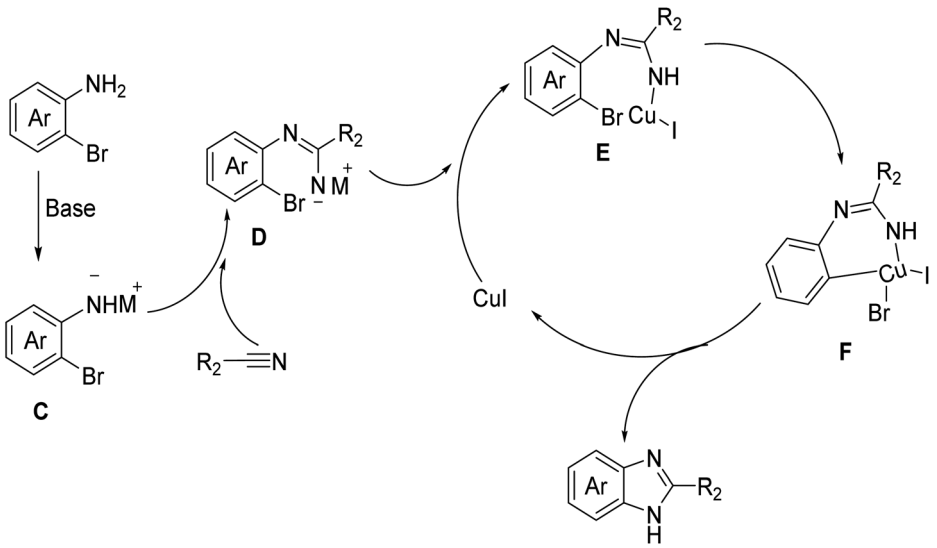

Fig. 2 Proposed mechanism of the cyclization reaction between *o*-bromoaromatic amines and nitrile substrates.

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catalytic cycle. These results demonstrate the efficiency of this synthetic pathway for the synthesis of nitrile-based compounds. The findings further demonstrate the broad applicability of the present synthetic strategy in producing valuable imidazole derivatives.

Conclusions

In this study, we have successfully developed an improved and ligand-free copper-catalyzed cyclization method for the synthesis of benzimidazoles. By utilizing the cyclization of *o*-bromoarylamine with nitriles, we have demonstrated remarkable yields of benzimidazoles, with optimization leading to 30 examples with yields of up to 98%. Our approach builds upon the previous work of Xiang *et al.*[9] and Yu *et al.*,[10] offering significant advantages in terms of simplicity, compatibility with various functional groups, substrate scope, and overall efficiency compared to their methods and other existing methodologies. Additionally, we have validated the applicability of our method in the synthesis of two benzimidazole-based drugs, namely bendazol and thiabenzadole, yielding 82% and 78% respectively on a 100 gram scale. Notably, our method eliminates the need for ligands, nitric acid, sulfuric acid, and polyphosphoric acid, emphasizing its versatility and environmentally friendly nature. An ongoing research at our laboratory explores additional applications of this approach.

Experimental section

General information

^{1}H, ^{19}F and ^{13}C NMR spectra were recorded on a Brucker 500 Hz or 600 Hz instrument. Chemical shifts for ^{1}H NMR are reported in parts per million (ppm), and multiplicities are denoted as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Chemical shifts for ^{13}C NMR are reported as the chemical shift. Electrospray ionization (ESI) mass spectra were measured using a Thermo Fisher FINNIGAN LTQ instrument. All high-resolution mass spectroscopy (HRMS) results were obtained on an Agilent 1290-6545 UHPLC-QTOF LC/MS spectrometer. TLC inspections were performed on silica gel plates (GF-254). All commercially available chemicals and solvents were used without further purification unless otherwise noted.

General procedure

O-Bromoarylamine (1.0 mmol, 1.0 eq.), potassium-2-methylbutan-2-olate (2.0 mmol, 2 eq.), CuI (0.1 mmol, 0.1 eq.), nitriles **3** (2 mmol, 2 eq.), and *tert*-amyl alcohol (6.0 ml) were charged to a Schleck tube that had been purged with nitrogen. After addition, the mixture was then warmed to 110–120 °C and held for 17 h. The reaction was considered complete when the conversion of *o*-bromoarylamine was ≥99%. The reaction mixture was concentrated in vacuum at 40–45 °C to remove most of the solvents to give the residue. The residue was purified by silica-gel column chromatography to give benzimidazoles.

Benzimidazoles 2. Following the general procedure, **2** was obtained from **1** (172 mg, 1.0 mmol). The residue was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 30/1) to give **2** (147 mg, 92%) as a light yellow solid; m.p. 155–157 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (brs, 1H), 7.56 (dd, J = 6.0, 3.2 Hz, 2H), 7.35–7.16 (m, 2H), 2.93 (t, J = 7.6 Hz, 2H), 1.95–1.86 (m, 2H), 1.01 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.6, 138.5, 122.1, 114.6, 31.2, 21.8, 13.8. HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{10}H_{13}N_2$ 161.1073, found 161.1071.

Benzimidazoles 2a. Following the general procedure, **2a** was obtained from **1a** (244 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 20/1) to afford the title compound **2a** (204 mg, 88%) as a white solid; m.p. 143–145 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (brs, 1H), 8.11 (s, 1H), 7.77 (s, 1H), 3.91 (s, 3H), 2.93 (t, J = 7.6 Hz, 2H), 2.57 (s, 3H), 1.94–1.83 (m, 2H), 0.96 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 157.3, 141.8, 137.5, 124.6, 124.2, 124.1, 114.3, 52.1, 31.3, 21.8, 17.1, 13.8. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{13}H_{17}N_2O_2$ 233.1285, found: 233.1281.

Benzimidazoles 2b. Following the general procedure compound **2b** was obtained from **1b** (264 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 20/1) to afford the title compound **2b** (240 mg, 95%) as a white solid; m.p. 125–128 °C; Two sets of ^{1}HNMR data representing two isomers (10 : 9) were observed as indicative of the presence of tautomerism; ^{1}H NMR (400 MHz, DMSO-d_6, major isomer) δ 12.30 (s, 1H), 7.51 (s, 1H), 7.08 (s, 1H), 2.77 (t, J = 7.1 Hz, 2H), 2.45 (s, 3H), 1.78 (dt, J = 14.3, 7.2 Hz, 2H), 0.94 (t, J = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, major isomer) δ 156.78, 144.90, 130.26, 124.78, 118.41, 113.43, 111.35, 30.90, 21.44, 17.09, 14.16; ^{1}HNMR (400 MHz, DMSO-d_6, minor isomer) δ 12.24 (s, 1H), 7.40 (s, 1H), 7.08 (s, 1H), 2.77 (t, J = 7.1 Hz, 2H), 2.48 (s, 3H), 1.78 (dt, J = 14.3, 7.2 Hz, 2H), 0.94 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, DMSO-d_6, minor isomer) δ 156.8, 155.6, 144.9, 142.3, 135.4, 133.6, 130.3, 124.9, 124.2, 123.2, 118.4, 113.8, 113.4, 111.3, 30.1, 30.9, 21.4, 17.1, 16.7, 14.1. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{11}H_{14}BrN_2$ 253.0335, found: 253.0332.

Benzimidazoles 2c. Following the general procedure compound **2c** was obtained from **1c** (244 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 20/1) to afford the title compound **2c** (175 mg, 86%) as a white solid; m.p. 172–174 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (s, 1H), 7.98 (dd, J = 8.5, 1.4 Hz, 1H), 7.58 (d, J = 8.5 Hz, 1H), 4.42 (q, J = 7.1 Hz, 2H), 2.70 (s, 3H), 1.43 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 153.7, 142.4, 138.1, 124.6, 123.9, 114.2, 60.1, 15.1, 14.3. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{11}H_{13}N_2O_2$ 205.0972, found: 205.0969.

Benzimidazoles 2d. Following the general procedure compound **2d** was obtained from **1d** (202 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 20/1) to afford the title compound **2d** (186 mg, 98%) as a white solid; m.p. 82–84 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, J = 8.7 Hz, 1H), 6.97 (d, J =

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1.3 Hz, 1H), 6.83–6.74 (m, 1H), 3.73 (s, 3H), 2.82 (t, J = 7.5 Hz, 2H), 1.86–1.72 (m, 2H), 0.90 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.4, 154.5, 137.9, 132.4, 115.1, 111.8, 97.5, 55.8, 30.9, 21.6, 13.7. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{11}H_{15}N_2O$ 191.1179, found: 191.1177.

Benzimidazoles 2e. Following the general procedure compound **2e** was obtained from **1e** (202 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 20/1) to afford the title compound **2e** (186 mg, 98%) as a white solid; m.p. 130–131 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22–7.07 (m, 2H), 6.67 (dd, J = 7.5, 1.2 Hz, 1H), 3.94 (s, 3H), 2.90 (t, J = 7.4 Hz, 2H), 2.03–1.76 (m, 2H), 0.99 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.0, 148.3, 139.7, 128.6, 122.6, 107.4, 102.6, 55.5, 31.1, 21.7, 13.8. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{11}H_{15}N_2O$ 191.1179, found: 191.1176.

Benzimidazoles 2f. Following the general procedure compound **2f** was obtained from **1f** (200 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 20/1) to afford the title compound **2f** (178 mg, 95%) as a white solid; m.p. 170–171 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 7.34 (s, 1H), 7.20 (s, 1H), 3.16–3.12 (m, 2H), 2.59 (s, 3H), 2.49 (s, 3H), 2.07–1.86 (m, 2H), 1.07 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 153.3, 136.7, 131.0, 128.6, 127.9, 123.6, 110.1, 27.8, 20.6, 20.1, 15.1, 12.3. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{12}H_{17}N_2$ 189.1386, found: 189.1383.

Benzimidazoles 2g. Following the general procedure compound **2g** was obtained from **1g** (275 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 20/1) to afford the title compound **2g** (247 mg, 94%) as a foamy solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.12 (s, 1H), 7.52 (s, 1H), 2.84 (t, J = 7.5 Hz, 2H), 1.87–1.75 (m, 2H), 0.95 (t, J = 7.4 Hz, 3H);

^{13}C NMR (100 MHz, CD_3OD) δ 159.6, 132.6, 131.2, 130.7, 128.1, 119.3, 117.7, 29.65, 22.6, 13.9. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{10}H_{10}Cl_3N_2$ 262.9904, found: 262.9898.

Benzimidazoles 2h. Following the general procedure compound **2h** was obtained from **1h** (190 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 20/1) to afford the title compound **2h** (132 mg, 88%) as a white solid m.p. 194–196 °C; two sets of ^{1}HNMR data representing two isomers (3 : 1) were observed as indicative of the presence of tautomerism; ^{1}H NMR (400 MHz, DMSO-d_6, major isomer) δ 12.47 (s, 1H), 7.24 (d, J = 8.0 Hz, 1H), 7.13–7.03 (m, 1H), 6.99–6.84 (m, 1H), 2.49 (s, 3H). ^{1}HNMR (400 MHz, DMSO-d_6, minor isomer) δ 12.71 (s, 1H), 7.34 (d, J = 7.6 Hz, 1H), 7.13–7.03 (m, 1H), 7.01–6.89 (m, 1H), 2.49 (s, 3H); ^{13}C NMR (101 MHz, DMSO) δ 154.2, 152.3, 151.7, 138.1, 138.0, 132.0, 122.3, 122.2, 107.5, 106.80, 106.6, 15.0; ^{19}F NMR (377 MHz, DMSO) δ −135.23. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_8H_8FN_2$ 151.0666, found: 151.0662.

Benzimidazoles 2i. Following the general procedure compound **2i** was obtained from **1i** (222 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 20/1) to afford the title compound **2i** (193 mg, 92%) as a white solid; m.p. 90–93 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 8.36–8.28 (m, 1H), 8.09–8.01 (m, 1H), 7.97–7.89 (m, 1H), 7.78–7.67 (m, 2H), 7.67–7.60 (m, 1H), 3.22 (t, J = 7.7 Hz, 2H), 2.08–1.95 (m, 2H), 1.11 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 153.1, 132.6, 132.6, 130.3, 129.3, 129.2, 128.6, 127.9, 122.0, 121.9, 113.1, 29.2, 22.1, 13.8. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{14}H_{15}N_2$ 211.1230, found: 211.1226.

Benzimidazoles 2j. Following the general procedure compound **2j** was obtained from **1j** (172 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 20/1) to afford the title compound **2j** (119 mg, 90%) as a light yellow solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.15 (s, 1H), 7.43 (d, J = 3.2 Hz, 2H), 7.09 (dd, J = 5.9, 3.1 Hz, 2H), 2.56–2.21 (m, 3H); ^{13}C NMR (101 MHz, DMSO) δ 151.6, 121.4, 40.6, 40.4, 15.1. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_8H_9N_2$ 133.0760.

Benzimidazoles 2k. Following the general procedure compound **2k** was obtained from **1k** (244 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 20/1) to afford the title compound **2k** (200 mg, 86%) as a foamy solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, J = 0.7 Hz, 1H), 8.26 (dd, J = 8.6, 1.4 Hz, 1H), 7.86 (d, J = 8.6 Hz, 1H), 4.46 (q, J = 7.1 Hz, 2H), 3.59 (dt, J = 14.0, 7.0 Hz, 1H), 1.60 (d, J = 7.0 Hz, 6H), 1.45 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, CD_3OD) δ 166.8, 162.5, 135.2, 132.1, 129.9, 128.2, 116.5, 114.8, 62.8, 29.1, 20.3, 14.6. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{13}H_{17}N_2O_2$ 233.1285, found: 233.1282.

Benzimidazoles 2l. Following the general procedure compound **2l** was obtained from **1l** (217 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 20/1) to afford the title compound **2l** (229 mg, 77%) as a light yellow solid; m.p. 154–156 °C; ^{1}H NMR (400 MHz, ^{1}H NMR (400 MHz, DMSO-d_6)) δ 9.76–9.38 (s, 1H), 8.03–7.94 (m, 2H), 7.71–7.67 (m, 1H), 7.53–7.51 (s, 1H), 7.31–7.24 (m, 1H), 7.03–6.97 (dd, J = 8.1, 1.0 Hz, 1H), 2.24–1.93 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 167.9, 152.8, 150.4, 142.1, 135., 134.5, 134.4, 133.4, 133.4, 128.1, 127.1, 125.8, 125.2, 125.1, 19.7. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{14}H_{14}N_4O_4$ 299.0775, found: 299.0772.

Benzimidazoles 2m. Following the general procedure compound **2m** was obtained from **1m** (217 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 20/1) to afford the title compound **2m** (133 mg, 65%) as a light yellow solid; m.p. 160–162 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 8.66 (d, J = 1.9 Hz, 1H), 8.46 (dd, J = 9.0, 2.1 Hz, 1H), 7.97 (d, J = 9.0 Hz, 1H), 3.28–3.20 (m, 2H), 2.07–1.95 (m, 2H), 1.12 (t, J = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, CD_3OD) δ 158.8, 145.8, 134.8, 130.7, 121.1, 114.3, 110.1, 28.3, 20.1, 12.3. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{10}H_{12}N_3O_2$ 206.0924, found: 206.0921.

Benzimidazoles 2n. Following the general procedure compound **2n** was obtained from **1n** (197 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 20/1) to afford the title compound **2n** (98 mg, 53%) as a light yellow solid; m.p. 168–169 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 8.12 (d, J = 8.3 Hz, 1H), 8.02 (d, J = 7.7 Hz, 1H), 7.75 (t, J = 8.0 Hz, 1H), 3.24 (t, J = 7.7 Hz,

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2H), 2.12–1.93 (m, 2H), 1.13 (t, J = 7.4 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, CD_3OD) δ 157.0, 131.8, 131.6, 130.5, 126.1, 118.7, 113.9, 97.9, 28.1, 20.4, 12.4. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{11}H_{12}N_3$ 186.1026, found: 186.1024.

Benzimidazoles 2o. Following the general procedure compound **2o** was obtained from **1o** (244 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 50/1) to afford compound **2o** (220 mg, 95%) as a foamy solid; For compound **2o** ^{1}H NMR (400 MHz, CD_3OD) δ 8.22 (d, J = 7.7 Hz, 1H), 8.04 (d, J = 8.1 Hz, 1H), 7.76–7.68 (m, 1H), 4.57 (q, J = 7.1 Hz, 1H), 3.72 (dd, J = 14.0, 7.0 Hz, 1H), 1.59 (d, J = 7.0 Hz, 1H), 1.48 (t, J = 7.1 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, CD_3OD) δ 165.8, 162.5, 134.8, 131.8, 128.3, 126.4, 120.4, 117.9, 62.9, 28.8, 21.0, 14.7. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{13}H_{17}N_2O_2$ 233.1285, found: 233.1283.

Benzimidazoles 2p. Following the general procedure compound **2p** was obtained from **1p** (172 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 20/1) to afford the title compound **2p** (244 mg, 91%) as a foamy solid; ^{1}H NMR (400 MHz, chloroform-d) δ 7.52 (s, 2H), 7.21 (dd, J = 6.0, 3.2 Hz, 2H), 6.44 (d, J = 2.1 Hz, 2H), 6.37 (d, J = 2.1 Hz, 1H), 4.21 (s, 6H), 3.73 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.3, 153.0, 138.3, 122.4, 107.1, 99.2, 55.3, 36.2. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{16}H_{17}N_2O_2$ 269.1285.

Benzimidazoles 2q. Following the general procedure compound **2q** was obtained from **1q** (173 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 20/1) to afford the title compound **2q** (140 mg, 88%) as a white solid; ^{1}H NMR (400 MHz, Methanol-d_4) δ 8.24 (d, J = 4.4 Hz, 1H), 7.83 (dd, J = 8.0, 1.3 Hz, 1H), 7.21 (dd, J = 8.0, 4.9 Hz, 1H), 2.19 (s, 0H), 1.43–1.03 (m, 4H); ^{13}C NMR (101 MHz, CD_3OD) δ 160.4, 151.6, 142.4, 130.7, 121.8, 117.5, 9.2, 8.4. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_9H_{10}N_3$ 160.0869.

Benzimidazoles 2r. Following the general procedure compound **2r** was obtained from **1r** (173 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 20/1) to afford the title compound **2r** (150 mg, 93%) as a light yellow solid; ^{1}H NMR (400 MHz, Methanol-d_4) δ 8.62 (dd, J = 5.2, 1.2 Hz, 1H), 8.33 (dd, J = 8.2, 1.3 Hz, 1H), 7.66 (dd, J = 8.2, 5.2 Hz, 1H), 3.16 (t, J = 7.6 Hz, 2H), 1.98 (q, J = 7.5 Hz, 2H), 1.09 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, CD_3OD) δ 164.7, 145.0, 135.1, 134.6, 131.5, 111.2, 29.8, 20.4, 12.5. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_9H_{12}N_3$ 162.1026.

Benzimidazoles 2s. Following the general procedure, compound **2s** and was obtained from **1s** (173 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 80/1 to 50/1) to afford compound **2s** (153 mg, 95%) as a foamy solid; ^{1}H NMR (400 MHz, CD_3OD) δ 8.62 (dd, J = 5.2, 1.2 Hz, 1H), 8.33 (dd, J = 8.2, 1.3 Hz, 1H), 7.66 (dd, J = 8.2, 5.2 Hz, 1H), 3.16 (t, J = 7.6 Hz, 2H), 1.98 (q, J = 7.5 Hz, 2H), 1.09 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, CD_3OD) δ 160.5, 147.0, 144.8, 127.5, 125.6, 121.8, 30.4, 21.7, 13.8. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_9H_{11}N_3$ 235.1077, found: 162.1023.

Benzimidazoles 2t. Following the general procedure compound **2t** was obtained from **1t** (173 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 20/1) to afford the title compound **2t** (234 mg, 87%) as a white solid; ^{1}H NMR (400 MHz, methanol-d_4) δ 8.30 (s, 1H), 7.91 (s, 1H), 7.25 (dd, J = 7.9, 4.9 Hz, 1H), 6.51 (d, J = 1.7 Hz, 2H), 6.37 (s, 1H), 4.86 (s, 3H), 4.19 (s, 2H), 3.74 (s, 6H), 3.31 (s, 3H); ^{13}C NMR (101 MHz, CD_3OD) δ 162.7, 144.5, 139.6, 119.4, 107.9, 100.0, 55.7, 36.6. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{15}H_{16}N_3O_2$ 270.1237.

Benzimidazoles 2u. Following the general procedure compound **2u** was obtained from **1u** (172 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 20/1) to afford the title compound **2u** (213 mg, 95%) as a light yellow solid; ^{1}H NMR (400 MHz, methanol-d_4) δ 8.24 (dd, J = 7.8, 1.7 Hz, 1H), 7.64 (dd, J = 6.0, 3.2 Hz, 2H), 7.47 (ddd, J = 8.7, 7.5, 1.7 Hz, 1H), 7.24 (dd, J = 6.1, 3.2 Hz, 2H), 7.19 (d, J = 8.3 Hz, 1H), 7.15–7.08 (m, 1H), 4.05 (s, 3H); ^{13}C NMR (101 MHz, CD_3OD) δ 157.3, 149.6, 138.1, 131.4, 129.5, 122.2, 120.7, 117.5, 114.4, 111.4, 54.8. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{14}H_{13}N_2O$ 225.1022.

Benzimidazoles 2v. Following the general procedure compound **2v** was obtained from **1v** (172 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 30/1) to give **2v** (186 mg, 93%) as a yellow solid; m.p. 168–169 °C; ^{1}H NMR (400 MHz, methanol-d_4) δ 8.20 (dd, J = 3.9, 1.1 Hz, 1H), 8.11 (dd, J = 5.0, 1.1 Hz, 1H), 7.78 (dt, J = 6.8, 3.4 Hz, 2H), 7.60 (dt, J = 6.2, 3.4 Hz, 2H), 7.43 (dd, J = 4.9, 3.9 Hz, 1H); ^{13}C NMR (101 MHz, CD_3OD) δ 145.8, 135.5, 134.5, 132.7, 130.6, 127.8, 124.9, 114.7. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{11}H_9S_2$ 201.0481.

Benzimidazoles 2w. Following the general procedure, compound **2w** and was obtained from **1w** (172 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 30/1) to give **2w** (190 mg, 75%) as a white solid; m.p. 221–223 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.33 (s, 1H), 8.31 (s, 1H), 8.25–8.16 (m, 2H), 7.66 (dd, J = 5.9, 3.2 Hz, 2H), 7.32–7.23 (m, 2H), 2.64 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 149.4, 149.3, 139.9, 134.7, 134.1, 130.8, 130.7, 125.8, 125.3, 123.2, 115.9, 20.3. HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{14}H_{12}N_3O_2$ 254.0924, found 254.0919.

Benzimidazoles 2x. Following the general procedure compound **2x** was obtained from **1x** (172 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 30/1) to give **2x** (198 mg, 85%) as a yellow solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.40 (s, 1H), 7.81–7.66 (m, 3H), 7.47 (s, 2H), 7.10 (dd, J = 5.9, 3.2 Hz, 2H), 6.69 (d, J = 8.3 Hz, 1H), 5.35 (s, 2H), 2.14 (s, 3H); ^{13}C NMR (101 MHz, DMSO) δ 154.7, 148.7, 143.1, 137.1, 131.6, 128.3, 121.9, 121.9, 121.2, 118.77, 117.6, 113.8, 110.4, 32.2, 17.92. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{14}H_{14}N_3$ 224.1128.

Benzimidazoles 2y. Following the general procedure compound **2y** was obtained from **1y** (172 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 30/1) to give **2y** (186 mg, 96%) as a yellow solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.90 (s, 1H),

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8.30–8.03 (m, 2H), 7.67–7.45 (m, 5H), 7.33–6.96 (m, 2H); ^{13}C NMR (101 MHz, DMSO) δ 151.6, 130.6, 130.3, 129.4, 126.8, 122.5. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{13}H_{11}N_2$ 195.0917.

Benzimidazoles 2z. Following the general procedure compound **2z** was obtained from **1z** (172 mg, 2.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 30/1) to give **2z** (204 mg, 78%) as a yellow solid; ^{1}H NMR (400 MHz, Methanol-d_4) δ 8.36 (d, J = 8.2 Hz, 2H), 8.08 (d, J = 8.3 Hz, 2H), 7.90 (dd, J = 6.2, 3.2 Hz, 2H), 7.68 (dd, J = 6.2, 3.1 Hz, 2H); ^{13}C NMR (101 MHz, CD_3OD) δ 149.3, 135.9, 135.6, 133.2, 130.1, 128.3, 128.1, 128.1, 128.0, 127.9, 127.9, 126.2, 123.5, 115.2; ^{19}F NMR (377 MHz, CD_3OD) δ −63.13, −63.61. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{14}H_{10}F_3N_2$ 263.0791.

Benzimidazoles 2aa. Following the general procedure compound **2aa** was obtained from **1aa** (172 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 30/1) to give **2aa** (259 mg, 95%) as a yellow solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.33–12.82 (s, 1H), 8.42–8.33 (t, J = 1.7 Hz, 1H), 8.22–8.14 (dt, J = 7.8, 1.1 Hz, 1H), 7.74–7.68 (ddd, J = 8.0, 1.9, 0.9 Hz, 1H), 7.66–7.57 (s, 2H), 7.57–7.47 (t, J = 7.9 Hz, 1H), 7.30–7.15 (m, 2H); ^{13}C NMR (101 MHz, DMSO) δ 150.1, 132.9, 132.8, 131.6, 129.3, 125.8, 122.7. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{13}H_{10}BrN_2$ 273.0022.

Benzimidazoles 2bb. Following the general procedure compound **2bb** was obtained from **1bb** (172 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 30/1) to give **2bb** (187 mg, 96%) as a yellow solid; ^{1}H NMR (400 MHz, Methanol-d_4) δ 8.69 (d, J = 5.0 Hz, 2H), 8.12–7.96 (m, 2H), 7.64 (dd, J = 5.9, 3.2 Hz, 2H), 7.40–7.22 (m, 2H); ^{13}C NMR (101 MHz, CD_3OD) δ 151.1, 150.0, 139.2, 124.8, 122.1, 116.6, 112.7. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{12}H_{10}N_3$ 196.0896.

Benzimidazoles 2cc. Following the general procedure compound **2cc** was obtained from **1cc** (172 mg, 1.0 mmol). The crude product was purified by silica-gel column chromatography (DCM/MeOH = 100/1 to 30/1) to give **2cc** (147 mg, 93%) as a yellow solid; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.51 (dd, J = 6.0, 3.2 Hz, 2H), 7.19 (dd, J = 6.0, 3.2 Hz, 2H), 2.16–1.99 (m, 1H), 1.35–1.19 (m, 2H), 1.18–0.97 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.5, 135.5, 122.2, 114.3, 9.6, 8.8, −0.01. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{10}H_{11}N_2$ 159.0917.

Synthesis of bendazol. The reaction mixture, consisting of **1** (1 eq.), potassium-2-methylbutan-2-olate (2 eq.), and 2-phenylacetonitrile 3 (2 eq.) in the presence of CuI (0.1 eq.), was vigorously stirred in a reaction vessel for 17 hours at 110–120 °C. Upon completion, the reaction was cooled to 25 °C and quenched with water. The resulting mixture was then extracted with ethyl acetate, and the organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was subsequently purified by re-crystallization from DCM/hexane, yielding **bendazol** as a light yellow solid (80.9 g, 82%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 15.53 (s, 1H), 7.77 (dt, J = 6.7, 3.4 Hz, 2H), 7.62–7.46 (m, 4H), 7.44–6.86 (m, 3H), 4.57 (s, 2H); ^{13}C NMR (101 MHz, DMSO) δ 152.5, 134.0, 130.7, 129.1, 128.9, 127.6, 125.5, 113.8, 31.8.

Synthesis of thiabendazole. Following the general procedure, this material was obtained as white solid in a yield 93.2 g (78%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.00 (s, 1H), 9.34 (d, J = 2.0 Hz, 1H), 8.47 (d, J = 1.9 Hz, 1H), 7.61 (dd, J = 55.4, 7.1 Hz, 2H), 7.23 (dt, J = 8.6, 4.9 Hz, 2H); ^{13}C NMR (101 MHz, DMSO) δ 155.5, 147.0, 146.9, 143.7, 134.3, 122.5, 121.7, 119.3, 118.7, 111.7.

Conflicts of interest

The authors declare that they have no apparent conflicting financial interests or personal connections that could have appeared to impact the findings presented in this manuscript.

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