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Copper-Catalyzed Inter/Intramolecular *N*-Alkenylation of Benzimidazoles via Tandem Processes Involving Selectively Mild Iodination of sp^3 C-H Bond at *α*-Position of Ester

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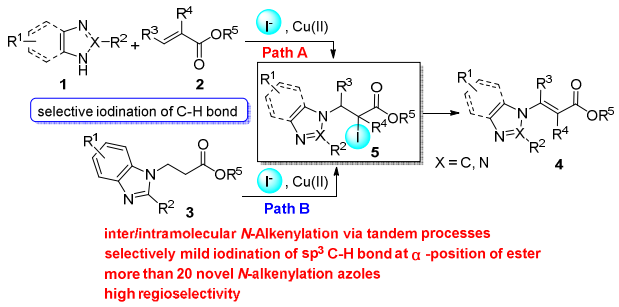
Keywords: sp^3 C-H bond activation; iodination; tandem reactions; *N*-alkenylation azoles; copper

Abstract: Inter/intramolecular approaches to sp^2 C-N bond formation of *N*-alkenyl benzimidazoles have been accomplished in the presence of iodide anion associated with copper catalyst. Both intermolecular and intramolecular reactions included tandem processes, in which selective iodination of sp^3 C-H bond at *α*-position of ester under mild conditions was demonstrated for the first time. Tandem reactions involving sp^3 C-H activation via *α*-iodo ester intermediate under copper catalysis efficiently provided more than 20 novel azole compounds, and free radicals were not involved in this transformation.



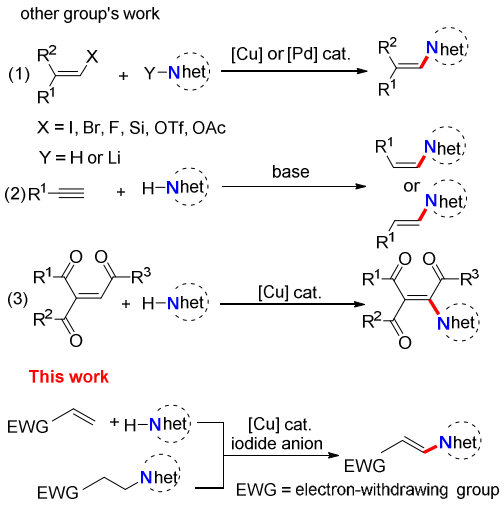
Introduction

Nitrogen-containing heterocycles are important motifs and versatile building blocks, as core intermediates for medicines and other materials.[1,2] Particularly, efficient approaches to sp^2 C-N bond formation of *N*-heterocycles[3] is a topic of vital importance to the pharmaceutical industry and other related industries. Although great achievements of *N*-alkenylation of heterocycles had been obtained,[4,5,6] current methods possessed some limitations such as the lack of atom and step economy as well as the uncontrollable regioselectivity (Scheme 1).

Thus the strategy concerning selective C-H bond activation, namely dual dehydrogenative amination involving sp^2 C-H bond of alkenes and N-H bond of *N*-heterocycles, is desirable to construct sp^2 C-N bond of *N*-heterocycles. As for dual dehydrogenative amination of *N*-alkenyl benzimidazoles,[2] there are mainly two challenges. The first challenge is the cleavage activity of the C-N bond.[7] The second challenge is the polymerization of *α,β*-unsaturated esters[8a] and the homocoupling of benzimidazole[8b] in the presence of copper catalyst. Despite significant progress in the *α,β*-dehydrogenation of carbonyl compounds (such as aldehydes, ketones, amides and esters)[9], a combination of diverse dehydrogenation of esters and benzimidazole functionalizations for highly efficient synthesis of *N*-alkenyl benzimidazoles in one-pot is quite rare (Scheme 1).

Recently, direct C-H amination via a dehydrogenative pathway has bloomed as an elegant strategy to construct various C-N bonds owing to obviating complicated steps associated with prefunctionalized partners.[10] For example, representative palladium(II)-mediated oxidative amination of alkenes with *N*-heterocycles had been developed by Stahl, Miura, Su and Jang, independently.[9b-d,11] Besides, Gold-catalyzed heterogeneous oxidative amination of *α,β*-unsaturated aldehydes and *N*-heterocycles was also demonstrated by Mizuno.[12] Moreover, Ueno and Kuwano reported the *β* amination of ethyl ketones catalyzed by Nickel.[13] The strategy involving copper salt catalyzed dehydrogenative amination has been promoted by Su[14] and Wu[15]. Especially, Wu's work[15] provided an efficient procedure for the preparation of tetrasubstituted 1,4-enedione derivatives, while the special structure of 1,4-enediones limited the scope of this method. Based on the inspiration of the combination of Pd and hypervalent iodine catalyzed the tandem Wacker oxidation-dehydrogenation[16], we report herein iodide anion-initiated and Cu-catalyzed inter/intramolecular *N*-alkenylation of benzimidazoles through tandem processes involving selective iodination of sp^3 C-H bond at *α*-position of ester under mild conditions.

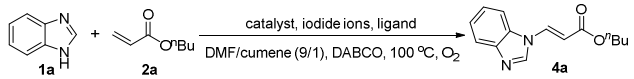
Scheme 1. *N*-Alkenylation of heterocycles.



Results and Discussion

Based on previous work[17], we attempted to develop simple synthetic protocols for the construction of *N*-alkenyl heterocycles through dual dehydrogenative amination. Our investigation started with the dehydrogenation coupling of easily available 1*H*-benzimidazole (**1a**) and butyl acrylate (**2a**) as the model reaction (Table 1). (*E*)-Butyl-3-(1*H*-benzo[*d*]imidazole-1-yl) acrylate (**4a**) was obtained in 75% isolated yield when we submitted 1*H*-benzimidazoles (**1a**) and butyl acrylate (**2a**) in the presence of LiI, $Cu(OAc)_2 \cdot H_2O$ as a catalyst, 2,2'-bipyridine (BPY) as a ligand and DABCO (1,4-diaza bicycle [2.2.2] octane) as an additive with O_2 balloon in DMF at 100 °C for 48 h (Table 1, entry 1). The use of cumene, recently reported for the dehydrogenative amination of phenols[18], resulted in the formation of a trace amount of **4a** (entry 2). The mixture solvents of DMF and cumene were further screened by changing the ratio of DMF/cumene (entries 3-4), and the best results showed that **4a** was obtained in 84% isolated yield at a DMF / cumene ratio of 9:1 (entry 4). Furthermore, various factors were evaluated regarding the optimal condition. **4a** was not isolated in the absence of LiI, while removing $Cu(OAc)_2 \cdot H_2O$ led to a 30% yield of the corresponding product **4a**. Those results showed that the iodide would be critical for dehydrogenation transformation (entries 5-6). Using LiCl in place of LiI did not afford the desired product **4a** to exclude the Lewis acid effect of lithium ion (entry 7). Moreover, replacing LiI with other iodide salts and iodine, respectively, gave unsatisfactory results (entries 9-10). However KI was a suitable replacement (entry 8). Especially, **4a** could not been found in the presence of $PhI(OAc)_2$, which again verified that iodide anion might initiate this process (entry 11). Other copper catalysts such as $CuBr_2$, CuI and CuOAc were also suitable (entries 12-14) with the exception of $Pd(OAc)_2$ that was found to be inferior (entry 15). In addition, other relative factors were evaluated including the ligand, the O_2 atmosphere, the additive as well as the reaction temperature and those results showed above factors affected this transformation, to an extent (entries 16-20). Besides, **4a** was obtained in 51% isolated yield under the optimal condition of path B (entry 21). Certainly, **4a** was not generated under the reaction condition reported by Wu[15] (entry 22). It may be briefly summarized that the reaction was initiated by iodide anion and $Cu(OAc)_2 \cdot H_2O$ as an important catalyst along with other factors together promoted this transformation.

Table 1. Optimization of path A[a].



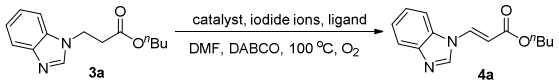
entry	catalyst	iodide/LiCl	solvent	**4a**(%)[b]
1	$Cu(OAc)_2·H_2O$	LiI	DMF	75
2	$Cu(OAc)_2·H_2O$	LiI	cumene	<10
3	$Cu(OAc)_2·H_2O$	LiI	DMF/cumene (5/5)	55
4	$Cu(OAc)_2·H_2O$	LiI	DMF/cumene (9/1)	84
5	$Cu(OAc)_2·H_2O$	-	DMF/cumene (9/1)	NP[c]
6	-	LiI	DMF/cumene (9/1)	30
7	$Cu(OAc)_2·H_2O$	LiCl	DMF/cumene (9/1)	NP[c]
8	$Cu(OAc)_2·H_2O$	KI	DMF/cumene (9/1)	71
9	$Cu(OAc)_2·H_2O$	Bu_4NI	DMF/cumene (9/1)	<10
10	$Cu(OAc)_2·H_2O$	I_2	DMF/cumene (9/1)	25
11	$Cu(OAc)_2·H_2O$	$PhI(OAc)_2$	DMF/cumene (9/1)	NP[c]
12	$CuBr_2$	LiI	DMF/cumene (9/1)	80
13	CuI	LiI	DMF/cumene (9/1)	71
14	CuOAc	LiI	DMF/cumene (9/1)	77
15	$Pd(OAc)_2$	LiI	DMF/cumene (9/1)	33
16[d]	$Cu(OAc)_2·H_2O$	LiI	DMF/cumene (9/1)	78
17[e]	$Cu(OAc)_2·H_2O$	LiI	DMF/cumene (9/1)	50
18[f]	$Cu(OAc)_2·H_2O$	LiI	DMF/cumene (9/1)	58
19[g]	$Cu(OAc)_2·H_2O$	LiI	DMF/cumene (9/1)	37
20[h]	$Cu(OAc)_2·H_2O$	LiI	DMF/cumene (9/1)	62
21[i]	$Cu(OAc)_2·H_2O$	LiI	DMF	51
22[j]	$Cu(OAc)_2·H_2O$	-	DMSO	NP[c]

[a]**1a** (0.25 mmol), **2a** (0.5 mmol), catalyst (0.025 mmol), iodide ions (2.5 mmol), 2,2'-bipyridine (0.025 mmol), DABCO (0.25 mmol) and solvent (1 mL) in a sealed tube under O_2 balloon at 100 °C for 48 h. [b]isolated yields. [c]NP = no desired product.[d]Without 2,2'-bipyridine. [e]Under N_2. [f]Under air. [g]Without DABCO. [h]80 °C. [i]The optimal condition of path B. [j]80 °C in DMSO under air (the condition of wu's work[15]).

Interestingly, we found that **4a** could be obtained coming from benzimidazole ester **3a**. The *α,β*-dehydrogenation of esters was regarded as an unmet challenge[9c], thus we also investigated *α,β*-dehydrogenation of **3a** to optimize the protocol as shown in Table 2. The desired product **4a** was obtained in 51% isolated yield via applying the optimal condition of path A (entry 1). Similarly to path A, **4a** was not generated from **3a** in the absence of LiI (entry 2), which meant iodide anion also initiated this transformation regarding *α,β*-dehydrogenation of **3a**. A decrease in the amount of LiI also led to the poor performance (entry 3). Replacing the mixed solvent with pure cumene gave the unsatisfactory result (entry 4), whereas using pure DMF afforded the desired product **4a** in 70% isolated yield (entry 5). Furthermore, the effect of 2,2'-bipyridine ligand

and $Cu(OAc)_2 \cdot H_2O$ catalyst was also evaluated respectively (entries 6-7), those results showed that the catalyst was necessary for this transformation yet the ligand was unnecessary. Both the O_2 atmosphere and DABCO also played assistant roles as shown in entries 8-9. Owing to the presence of 1*H*-benzimidazole coming from the C-N bond cleavage of benzimidazole ester **3a**, the extra addition of butyl acrylate **2a** could slightly improve this transformation in 79% isolated yield (entry 10).

Table 2. Optimization of path B[a]



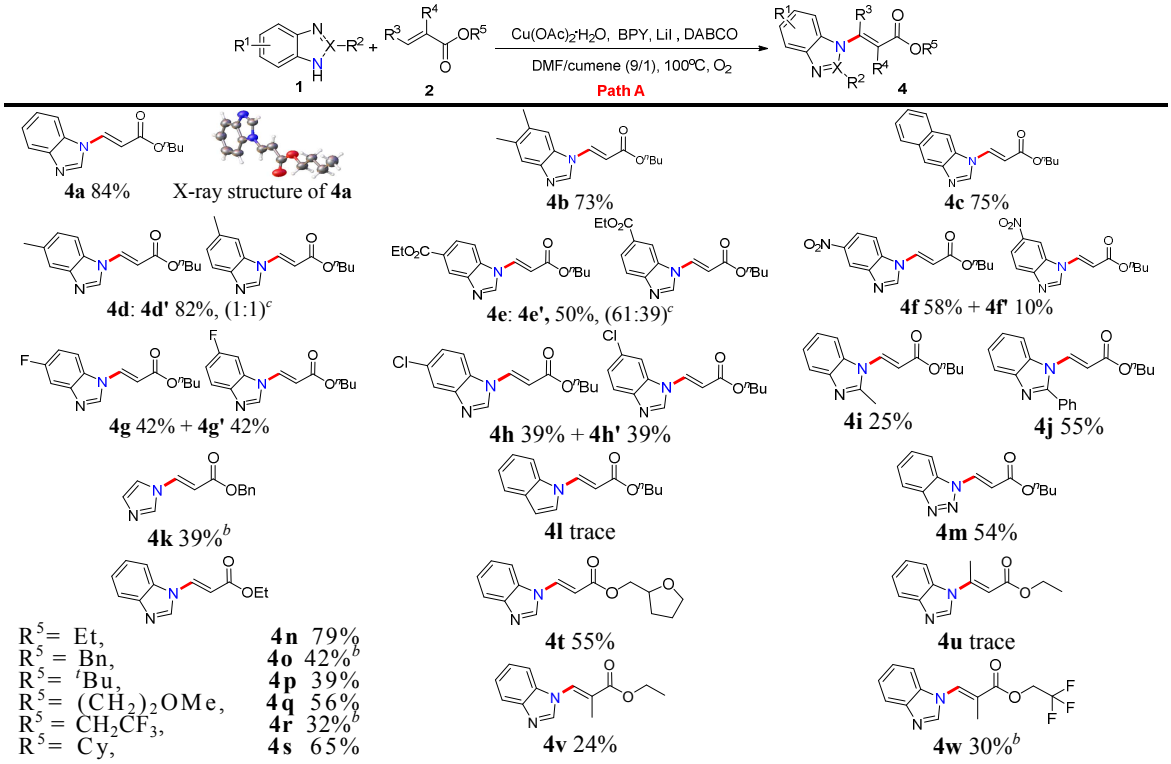
entry	catalyst	iodide	solvent	**4a**(%)[b]
1	$Cu(OAc)_2 \cdot H_2O$	LiI	DMF/cumene (9/1)	51
2	$Cu(OAc)_2 \cdot H_2O$	-	DMF/cumene (9/1)	NP[c]
3	$Cu(OAc)_2 \cdot H_2O$	LiI[d]	DMF/cumene (9/1)	36
4	$Cu(OAc)_2 \cdot H_2O$	LiI	cumene	<10
5	$Cu(OAc)_2 \cdot H_2O$	LiI	DMF	70
6[e]	$Cu(OAc)_2 \cdot H_2O$	LiI	DMF	72
7[e]	-	LiI	DMF	9
8[ef]	$Cu(OAc)_2 \cdot H_2O$	LiI	DMF	15
9[eg]	$Cu(OAc)_2 \cdot H_2O$	LiI	DMF	22
10[eh]	$Cu(OAc)_2 \cdot H_2O$	LiI[h]	DMF	79

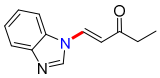
[a]**3a** (0.25 mmol), catalyst (0.025 mmol), LiI (2.5 mmol), 2,2'-bipyridine (0.025 mmol), DABCO (0.25 mmol) and solvent (1 mL) in a sealed tube under O_2 balloon at 100 °C for 48 h. [b]isolated yields. [c]NP = no desired product. [d]LiI (1.25 mmol). [e]Without 2,2'-bipyridine. [f]Under N_2. [g]Without DABCO. [h]Extra *n*-butylacrylate **2a** (0.25 mmol) was added.

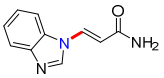
The substrate scope of intermolecular *N*-alkenylation reaction was investigated using a range of benzimidazole derivatives **1** and acrylates **2** under the optimal condition of path A, as shown in Scheme 2. The desired product of **4a** was confirmed by X-ray crystallographic analysis. 5,6-Dimethyl-1*H*-benzo[*d*]imidazole afforded the corresponding product **4b** in 73% isolated yield. 1*H*-Naphtho[2,3-*d*]imidazole also underwent the transformation to give the target product **4c** in 75% isolated yield. Owing to the tautomerism, benzimidazole derivatives bearing the single substituent on the phenyl led to a tautomeric mixture. Benzimidazole derivatives possessing various substituents on the phenyl, such as methyl-, nitryl-, ester and halogen groups were suitable to provide corresponding products **4d(d')-4h(h')** in moderate to good yields, in which each isomer of benzimidazoles (**4f** and **4f'**, **4g** and **4g'**, **4h** and **4h'**) was independently isolated for the first time. The above results showed that the

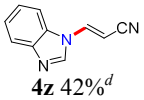
intermolecular *N*-alkenylation reaction , possessing excellent functional group tolerance, was compatible with electron-rich and electron-deficient phenyl rings of benzimidazole derivatives. The 2-substituent of benzimidazole apparently decreased this transformation owing to the steric hindrance effect. For example, the treatment of 2-methylbenzimidazole and 2-phenylbenzimidazole led to corresponding products **4i** and **4j** in 25% and 55% isolated yields, respectively. Moreover, other *N*-containing heterocyclic compounds, such as imidazole, indole and benzotriazole were screened under the suitable condition. Although the result of indole reacting with **2a** was unsatisfactory, imidazole and benzotriazole smoothly transformed into corresponding products **4k** and **4m** in moderate yields without isomers. Subsequently, the scope of *α,β*-unsaturated esters was explored via the treatment of 1*H*-benzimidazole **1a** and various acrylates. Acrylates bearing functional groups, such as ethyl, benzyl, *tert*-butyl, 2-methoxyethyl, trifluoroethyl, cyclohexyl and tetrahydrofurfuryl groups, provided corresponding products (**4n-4t**) in moderate to good yields. The steric hindrance of alkenes obviously reduced this transformation (**4u-4w**). Although target products were obtained in low yields, this approach compensated for limitations of traditional methods, such as **4v** and **4w**, which could not be synthesized through nucleophilic addition of *N*-heterocycles to alkynes. Furthermore, other *α,β*-unsaturated compounds such as ethyl vinyl ketone, acrylamide and acrylonitrile were respectively tested, and the results showed that three compounds were tolerant and acrylonitrile performed good reactivity under suitable conditions (**4x-4z**).

Scheme 2. Scope of Path A[a]




4x <10%

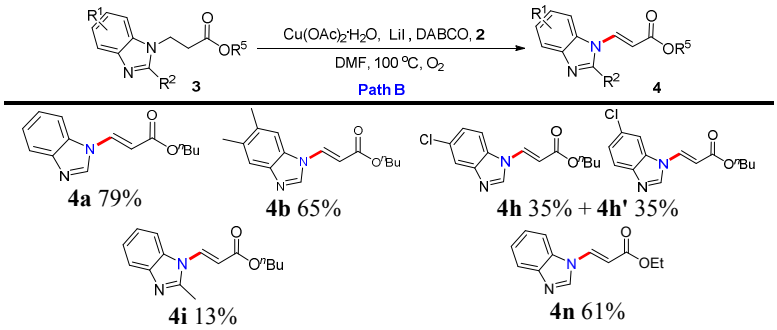

4y <10%


4z 42%[d]

[a]**1** (0.25 mmol), **2** (0.5 mmol), $Cu(OAc)_2 \cdot H_2O$ (0.025 mmol), LiI (2.5 mmol), 2,2'-bipyridine (0.025 mmol), DABCO (0.25 mmol) and solvent (1 mL) in a sealed tube at 100 °C under O_2 balloon for 17 to 48 h with isolated yields; [b]KI (2.5 mmol) instead of LiI (2.5 mmol); [c]The ratio is determined by ^{1}H NMR. [d] Acrylonitrile (1.0 mmol) was added.

Furthermore, the intramolecular *N*-alkenylation reaction was selectively explored under the optimal condition of path B, as shown in Scheme 3. Desired products of **4a** and **4b** were obtained in 79% and 65% isolated yields, respectively. Each isomer of *N*-alkenyl benzimidazole derivatives (**4h** and **4h'**) was independently isolated in moderate yields. Butyl 3-(2-methyl-1*H*-benzo[*d*]imidazol-1-yl) propanoate afforded the corresponding product **4i** in poor yield, which meant that the steric hindrance had obvious inhibitory effect on this transformation. Additionally, (*E*)-ethyl-3-(1*H*-benzo[*d*]imidazol-1-yl) acrylate **4n** was obtained in 61% isolated yield.

Scheme 3. Scope of Path B[a]



[a]**3** (0.25 mmol), corresponding acrylate **2** (0.25 mmol), $Cu(OAc)_2 \cdot H_2O$ (0.025 mmol), LiI (2.5 mmol), DABCO (0.25 mmol) and solvent (1 mL) in a sealed tube at 100 °C under O_2 balloon for 30 to 60 h with isolated yields.

We further had insight into the mechanism besides the correlation between intermolecular reaction and intramolecular reaction under the optimal condition of path A. The reaction progress was monitored by LC, and overall kinetic profiles of intermolecular and intramolecular reaction were presented in Figure 1. Regarding intermolecular reaction (Figure 1a), the rate of reaction of **1a** and **2a** was quite fast, in which **3a** and **4a** were produced in approximate 50 % and 20% LC yields at 4 min. Subsequently, the decrease of **3a** and the increase of **4a** processed simultaneously after one-hour reaction time. Those results illustrated that the intermolecular reaction might mainly undergo tandem aza-Michael addition and *α,β*-dehydrogenation process. Moreover, the result of the intramolecular reaction of **3a** transforming to **4a** also verified the *α,β*-dehydrogenation of benzimidazole ester **3a** as shown in Figure 1b.

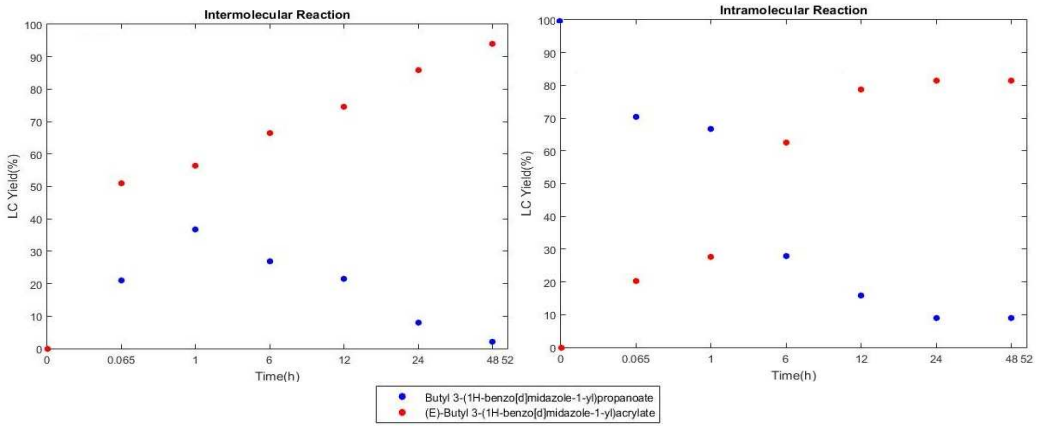
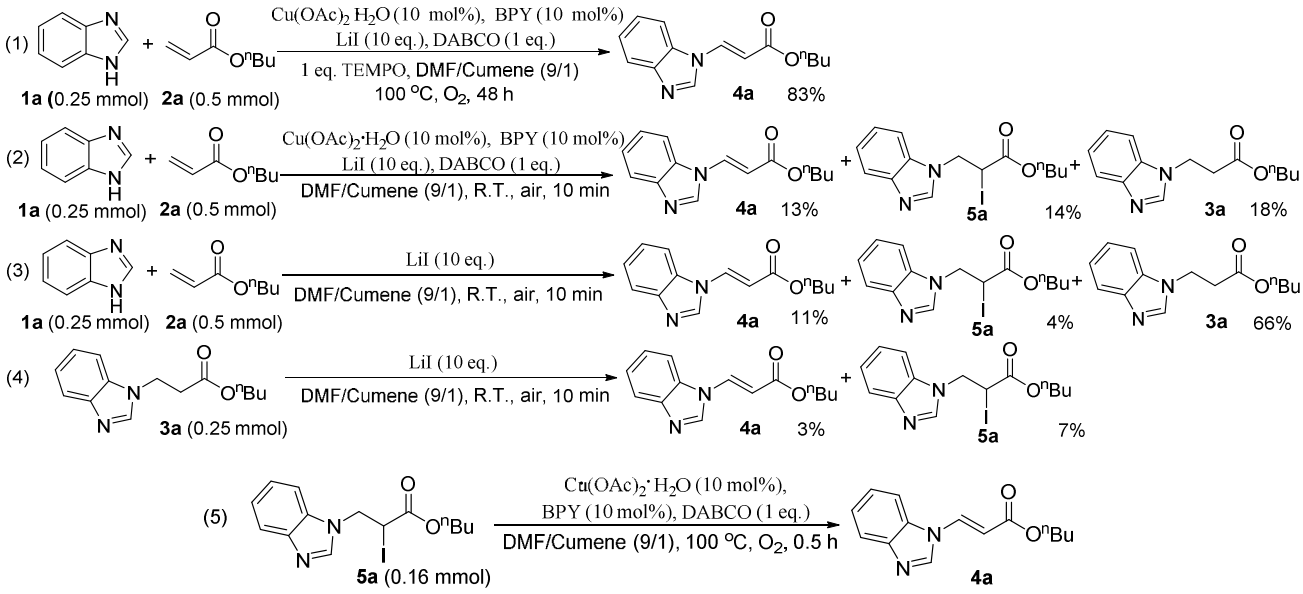


Figure 1. Overall kinetic profiles of intermolecular reaction and intramolecular reaction

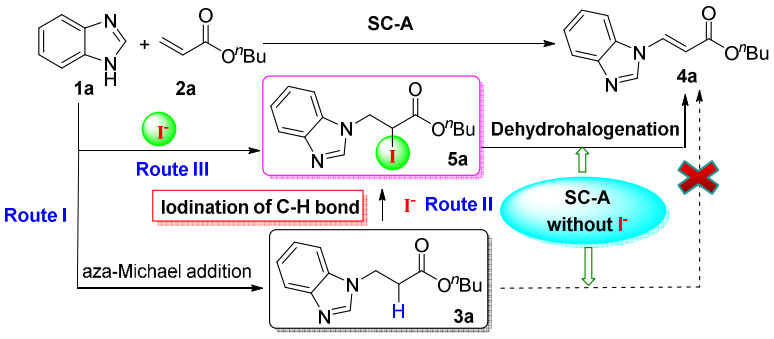


entry	changes from the optimal condition	yield of **4a** (%)
1	none	92
2	R.T.	49
3	without DABCO	20
4	without $Cu(OAc)_2 \cdot H_2O$, BPY	92
5	without $Cu(OAc)_2 \cdot H_2O$, BPY, DABCO	8
6	without $Cu(OAc)_2 \cdot H_2O$, BPY, DABCO, RT	0

Scheme 4. Control experimental results

In addition, various control experiments were conducted to explore the mechanism (Scheme 4). Compared with Lei's work[19], the control experiment of using TEMPO indicated that the transformation was not involved in free radicals (equation 1). We further investigated the *α,β*-dehydrogenation mechanism. When the reaction of **1a** and **2a** was dealt under standard condition at room temperature for 10 minutes, **3a**, **4a** and α-iodo benzimidazole ester **5a** were obtained in 18%, 13%, 14% isolated yields, respectively (equation 2). The treatment of **1a** and **2a** with LiI led to **3a**, **4a** and **5a** in 66%, 11% and 4% isolated yields, respectively (equation 3). Dealing with **3a** in the

presence of LiI gave **4a** and **5a** in 3% and 7% isolated yields, respectively, accompanying with a large amount of substrate **3a** (equation 4). Owing to *α*-iodo ester[20] **5a** isolated from both intermolecular and intramolecular reactions, various control experiments of **5a** were investigated (equation 5). The compound **5a** under the optimal condition of path A without iodide anion smoothly transferred to **4a** with 92% isolated yield, which showed that *α*-iodo benzimidazole ester **5a**, as a vital intermediate participating in this transformation (equation 5, entry1). Control experiments at R.T. and without DABCO performed inferior reactivity (equation 5, entries 2-3), while the control experiment without $Cu(OAc)_2 \cdot H_2O$ and BPY also afforded **4a** with 92% isolated yield (equation 5, entry 4). Those results showed that both DABCO and heating promoted the dehydrohalogenation of *α*-iodo benzimidazole ester **5a**. Owing to the exothermic phenomenon of LiI dissolving in DMF, **4a** was generated by the dehydrohalogenation of **5a** as shown in equations 3 and 4. Besides, other control experiments (equation 5, entries 5-6) illustrated the stability of α-iodo ester **5a** without basic compounds and heating, to an extent. In short, regarding intermolecular reaction, the process would primarily include tandem aza-Michael addition, selective iodination of C-H bond and dehydrohalogenation (Scheme 5, Route I) and an alternative path could not been excluded (Scheme 5, Route III); whereas intramolecular formal *α,β*-dehydrogenation of benzimidazole esters involved selective iodination of C-H bond and dehydrohalogenation (Scheme 5, Route II). Especially, as for the effect of copper catalyst[21], according to the result of screening condition (Table 2, entry 7), the absence of $Cu(OAc)_2 \cdot H_2O$ gave **4a** with 9% isolated yield, which showed preliminarily that copper catalyst could promote selective iodination of sp^3 C-H bond at α-position of benzimidazole ester. The detailed mechanism involving copper catalyst is under investigation in our group.



Scheme 5. The process of *N*-alkenylation of benzimidazoles.

Conclusion

In conclusion, we have demonstrated the C-N bond formation of *N*-alkenyl benzimidazoles *via* intermolecular tandem aza-Michael addition, occurred from iodination of C-H bond and dehydrohalogenation as well as intramolecular formal *α,β*-dehydrogenation of benzimidazole esters initiated by iodide anion under copper catalysis. We believed that this protocol described here would provide a viable methodology for synthesizing a series of potential biologically active *N*-alkenyl azole derivatives. Further studies of functionalizing benzimidazoles and other heterocycles are future goals of our group.

EXPERIMENTAL SECTION

General Information

Reagents and solvents were purchased from commercial sources and were used without further purification. Butyl 3-(1*H*-benzo[*d*]imidazol-1-yl)propanoate (**3a**), butyl 3-(5,6-dimethyl- 1*H*-benzo[d]imidazol-1-yl)propanoate (**3b**), butyl 3-(2-methyl-1*H*-benzo[*d*]imidazol-1-yl)propanoate (**3i**) butyl 3-(5-chloro-1*H*-benzo[*d*]imidazol-1-yl) propanoate (**3g**) and butyl 3-(6-chloro-1*H*-benzo[*d*]imidazol-1-yl)propanoate (**3g'**) ethyl 3-(1*H*-benzo[*d*] imidazol-1-yl)propanoate (**3o**)[17], ethyl 1*H*-benzimidazole-5-carboxylate[22] and 1*H*-naphtho[2,3-*d*]imidazole[23] were prepared according to published procedures. NMR Spectra were recorded on 400 or 600 MHz NMR spectrometers. The chemical shift is given in dimensionless δ values and is frequency referenced relative to TMS in ^{1}H and ^{13}C NMR spectroscopy. Chemical shifts are reported relative to $CDCl_3$ (δ =7.26 ppm) for ^{1}H NMR and relative to $CDCl_3$ (δ =77 ppm) for ^{13}C NMR. Peak multiplicities were recorded as follows: s = singlet, d = doublet, t = triplet, m = multiplet or unresolved, br = broad singlet. FT-IR spectra were tested by using KBr pellets in the 400-4000 cm^{-1} range. High resolution mass spectra were obtained from Q-TOF instrument by electrospray ionization (ESI). A polar-embedded reversed phase stationary phase-column (250*4.6mm, analytical Column) was prepared in HPLC analyses. (Solvent: H_2O (0.1% HCOOH): MeCN (0.1% HCOOH) = 1:1, flow rate = 0.8mL/min, λ = 205 nm, 30 ^{o}C). Unless otherwise stated, all reactions were conducted in sealed tube under an atmosphere of oxygen balloon.

General experiments of path A for the synthesis of compounds 4

Benzimidazole derivatives (0.25 mmol), acrylates (0.5 mmol), 2,2'-bipyridine (0.025 mmol, 10 mol%), $Cu(OAc)_2 \cdot H_2O$ (0.025 mmol, 10 mol%), LiI (2.5 mmol), DABCO (1,4-diazabicyclo[2.2.2]octane) (0.25 mmol), DMF (0.9 mL) and cumene (0.1 mL) as mixed solvent were put into the 10 mL sealed tube under an atmosphere of oxygen balloon. The mixture was stirred at 100 °C for required time. After cooled to room temperature, the mixture was added the appropriate amount of $Na_2S_2O_3$, as monitored by TLC, and the resulting mixture was

partitioned between water and ethyl acetate, and the separated aqueous layer extracted with ethyl acetate (2 mL×3). The combined organic layers were washed with brine (2 mL×3), dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The residue was purified by flash column chromatography on neutral Al_2O_3, eluting with EA/PE (1:15 to 1:5) to afford compounds **4**.

General experiments of path B for the synthesis of compounds 4

3-(1*H*-benzo[*d*]imidazol-1-yl)propanoates (0.25 mmol), corresponding acrylates (0.25 mmol), $Cu(OAc)_2 \cdot H_2O$ (0.025 mmol, 10 mol%), LiI (2.5 mmol) and DABCO (0.25 mmol), and DMF (1 mL) as noted were put into the 10 mL sealed tube under an atmosphere of oxygen balloon. The mixture was stirred at 100 °C for required time. The reaction was added the right amount of $Na_2S_2O_3$, as monitored by TLC, and the resulting mixture was partitioned between water and ethyl acetate, and the separated aqueous layer extracted with ethyl acetate (2 mL×3). The combined organic layers were washed with brine (2 mL×3), dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The residue was purified by flash column chromatography on neutral Al_2O_3, eluting with EA/PE (1:15 to 1:5) to afford compounds **4**.

Synthesis of compound butyl 3-(1*H*-benzo[*d*]imidazol-1-yl)-2-iodopropanoate 5a

1*H*-Benzimidazole (0.25 mmol), butyl acrylate (0.5 mmol), 2,2'-bipyridine (0.025 mmol, 10 mol%), $Cu(OAc)_2 \cdot H_2O$ (0.025 mmol, 10 mol%), LiI (2.5 mmol), DABCO (1,4-diazabicyclo[2.2.2]octane) (0.25 mmol), DMF (0.9 mL) and cumene (0.1 mL) as mixed solvent were put into the 10 mL sealed tube under air. The reaction mixture was stirred at room temperature for 10 minutes. The mixture was added the right amount of $Na_2S_2O_3$, as monitored by TLC, and the resulting mixture was partitioned between water and ethyl acetate, and the separated aqueous layer extracted with ethyl acetate (2 mL×3). The combined organic layers were washed with brine (2 mL×3), dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The residue was purified by flash column chromatography on neutral Al_2O_3, eluting with EA/PE (1:25 to 1:5) to afford intermediate **5a** (yellow oil, 13 mg, 14%). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.08 (s, 1H), 7.84 (d, *J* = 6.4 Hz, 1H), 7.41 (d, *J* = 6.9 Hz, 1H), 7.38-7.28 (m, 2H), 4.93-4.83 (t, *J* = 12Hz, 1H), 4.80-4.50 (m, 2H), 4.20-3.95 (m, 2H), 1.54 (m, 2H), 1.33-1.23 (m, 2H), 0.87 (t, *J* = 6.8 Hz, 3H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 168.8, 142.5, 142.1, 132.1, 122.7, 122.0, 119.5, 108.3, 65.4, 48.2, 29.1, 17.9, 14.1, 12.5 ppm; HRMS (ESI/TOF-Q) m/z Calcd for $C_{14}H_{17}IN_2O_2$ $[M + H]^+$: 373.0407, Found 373.0411.

General experiments from intermediate 5a to compound 4a

Butyl 3-(1*H*-benzo[*d*]imidazol-1-yl)-2-iodopropanoate **5a** (0.16 mmol), $Cu(OAc)_2 \cdot H_2O$ (0.016 mmol, 10 mol%), DABCO (0.16 mmol), DMF (0.576 mL) and cumene (0.064 mL) as mixed solvent were put into the 10 mL sealed

tube under an atmosphere of oxygen balloon. The mixture was stirred at 100 °C for 0.5 h. The reaction was added the right amount of $Na_2S_2O_3$, as monitored by TLC, and the resulting mixture was partitioned between water and ethyl acetate, and the separated aqueous layer extracted with ethyl acetate (2 mL×3). The combined organic layers were washed with brine (2 mL×3), dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The residue was purified by flash column chromatography on neutral Al_2O_3, eluting with EA/PE (1:15 to 1:5) to afford compound **4a**.

(*E*)-Butyl 3-(1*H*-benzo[*d*]imidazol-1-yl) acrylate (4a): The title compound could be prepared according to general procedure A for 48 h. The crude product was purified by column chromatography on neutral Al_2O_3 and eluted with EA/PE (1:15 to 1:5) to afford a white solid (51 mg, 84%).

The reaction also was conducted with modifications to the general procedure B for 48 h. The crude product was purified by column chromatography on neutral Al_2O_3 and eluted with EA/PE (1:15 to 1:5) to afford a white solid (48 mg, 79%).

The third method was butyl 3-(1*H*-benzo[*d*]imidazol-1-yl)-2-iodopropanoate (0.16 mmol) as reactant, $Cu(OAc)_2 \cdot H_2O$ (0.016 mmol, 10 mol%), DABCO (0.16 mmol), DMF (0.576 mL) and cumene (0.064 mL) as mixed solvent were put into the 10 mL sealed tube under an atmosphere of oxygen balloon. The mixture was stirred at 100 °C for 0.5 h. The reaction was added the right amount of $Na_2S_2O_3$, as monitored by TLC, and the resulting mixture was partitioned between water and ethyl acetate, and the separated aqueous layer extracted with ethyl acetate (2 mL×3). The combined organic layers were washed with brine (2 mL×3), dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The residue was purified by flash column chromatography on neutral Al_2O_3, eluting with EA/PE (1:15 to 1:5) to afford a white solid (42 mg, 92%), m.p.: 69-71 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.21 (s, 1H), 8.15 (d, *J* = 14.4 Hz, 1H), 7.84 (d, *J* = 7.8 Hz, 1H), 7.65 (d, *J* = 7.9 Hz, 1H), 7.41 (dt, *J* = 18.0, 7.4 Hz, 2H), 6.32 (d, *J* = 14.4 Hz, 1H), 4.26 (t, *J* = 6.7 Hz, 2H), 1.74-1.68 (m, 2H), 1.49-1.41 (m, 2H), 0.98 (t, *J* = 7.4 Hz, 3H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 166.4, 144.6, 141.6, 135.4, 132.2, 125.0, 124.3, 121.2, 111.1, 106.0, 64.9, 30.8, 19.2, 13.7 ppm; IR (KBr) υ 3088, 3058, 3030, 2956, 2871, 1711, 1649, 1461, 1402, 1269, 1195, 1164, 1111, 742 cm^{-1}; HRMS (ESI/TOF-Q) m/z Calcd for $C_{14}H_{16}N_2O_2$ $[M + Na]^+$: 267.1104, Found: 267.1093.

(*E*)-Butyl 3-(5,6-dimethyl-1*H*-benzo[*d*]imidazol-1-yl) acrylate (4b): The title compound could be prepared according to general procedure A for 48 h. The crude product was purified by column chromatography on neutral Al_2O_3 and eluted with EA/PE (1:15 to 1:5) to afford a white solid (50 mg, 73%).

The reaction also was conducted with modifications to the general procedure B for 60 h. The crude product was

purified by column chromatography on neutral Al_2O_3 and eluted with EA/PE (1:15 to 1:5) to afford a white solid (44 mg, 65%), m.p.: 100-102°C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.22 (s, 1H), 8.09 (d, *J* = 14.4 Hz, 1H), 7.65 (s, 1H), 7.40 (s, 1H), 6.30 (d, *J* = 14.4 Hz, 1H), 4.25 (t, *J* = 6.7 Hz, 2H), 2.41 (s, 3H), 2.36 (s, 3H), 1.75-1.68 (m, 2H), 1.50-1.41 (m, 2H), 0.98 (t, *J* = 7.4 Hz, 3H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 166.4, 142.1, 141.5, 135.5, 134.7, 133.9, 130.5, 120.8, 111.7, 106.2, 64.9, 30.8, 20.6, 20.2, 19.2, 13.7 ppm; IR (KBr) υ 3100, 2958, 2924, 2870, 1702, 1650, 1513, 1200, 1161, 854 cm^{-1}; HRMS (ESI/TOF-Q) m/z Calcd for $C_{16}H_{20}N_2O_2$ $[M + Na]^+$: 295.1417, Found: 295.1415.

(*E*)-Butyl 3-(1*H*-naphtho[2,3-*d*]imidazol-1-yl) acrylate (4c): The title compound could be prepared according to general procedure A for 48 h. The crude product was purified by column chromatography on neutral Al_2O_3 and eluted with EA/PE (1:15 to 1:5) to afford a white solid (55 mg, 75%), m.p.: 141-143 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.27 (d, *J* = 5.6 Hz, 2H), 8.19 (d, *J* = 14.3 Hz, 1H), 7.98 (dd, *J* = 17.9, 7.9 Hz, 3H), 7.54-7.44 (m, 2H), 6.34 (d, *J* = 14.3 Hz, 1H), 4.28 (t, *J* = 6.7 Hz, 2H), 1.78-1.69 (m, 2H), 1.53-1.43 (m, 2H), 1.00 (t, *J* = 7.4 Hz, 3H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 166.6, 145.3, 144.1, 135.5, 132.0, 131.4, 131.0, 128.6, 127.9, 125.7, 124.9, 118.7, 108.2, 104.8, 64.8, 30.9, 19.2, 13.8 ppm; IR (KBr) υ 3123, 3055, 2960, 2871, 1707, 1636, 1517, 1449, 1356, 1272, 1183, 1162, 1111, 985, 751 cm^{-1}; HRMS (ESI/TOF-Q) m/z Calcd for $C_{18}H_{18}N_2O_2$ $[M + H]^+$: 295.1441, Found: 295.1438.

(*E*)-Butyl 3-(5-methyl-1*H*-benzo[*d*]imidazol-1-yl)acrylate (4d) and (*E*)-Butyl 3-(6-methyl-1*H*-benzo [*d*]imidazol-1-yl)acrylate (4d'): The title compounds could be prepared according to general procedure A. 5-Methylbenzimidazole (33 mg, 0.25 mmol), butyl acrylate (64 mg, 72 μL, 0.5 mmol), 2,2'-bipyridine (4 mg, 0.025 mmol, 10 mol%), $Cu(OAc)_2 \cdot H_2O$ (5 mg, 0.025 mmol, 10 mol%), LiI (333 mg, 2.5 mmol), DABCO (28 mg, 0.25 mmol), DMF (0.9 mL) and cumene (0.1 mL) as mixed solvent were put into the 10 mL sealed tube under an atmosphere of oxygen balloon. The reaction mixture was stirred at 100 °C for 48 h. The crude product was purified by column chromatography on neutral Al_2O_3 and eluted with EA/PE (1:15 to 1:5) to afford a white solid (52 mg, 81%, **4d**: **4d' =** 1: 1). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.18 (m, 4H), 7.70 (d, *J* = 8.2 Hz, 1H), 7.62 (s, 1H), 7.52 (d, *J* = 8.3 Hz, 1H), 7.43 (s, 1H), 7.24 (d, *J* = 8.3 Hz, 1H), 7.20 (d, *J* = 8.2 Hz, 1H), 6.32-6.27 (m, 2H), 4.28-4.22 (m, 4H), 2.53 (s, 3H), 2.50 (s, 3H), 1.75-1.68 (m, 4H), 1.50-1.41 (m, 4H), 1.01-0.92 (m, 6H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 166.53, 166.52, 145.0, 142.7, 141.8, 141.1, 135.6, 135.5, 135.3, 134.4, 132.4, 130.2, 126.3, 125.8, 121.0, 120.6, 111.2, 110.8, 105.6, 105.5, 64.83, 64.81, 30.8, 21.9, 21.5, 19.2, 13.7 ppm; IR (KBr) υ 3105, 3051, 2963, 2870, 1708, 1647, 1504, 1354, 1267, 1183, 812 cm^{-1}; HRMS (ESI/TOF-Q) m/z Calcd for $C_{15}H_{18}N_2O_2$ $[M + Na]^+$: 281.1261, Found: 281.1256.

(*E*)-Ethyl 1-(3-butoxy-3-oxoprop-1-en-1-yl)-1*H*-benzimidazole-5-carboxylate (4e) and (*E*)-Ethyl 1-(3-butoxy-3-oxoprop-1-en-1-yl)-1*H*-benzimidazole-6-carboxylate (4e'): The title compound could be prepared according to general procedure A. Ethyl 1*H*-benzimidazole-5-carboxylate (47 mg, 0.25 mmol), butyl acrylate (64 mg, 72 μL, 0.5 mmol), 2,2'-bipyridine (4 mg, 0.025 mmol, 10 mol%), $Cu(OAc)_2 \cdot H_2O$ (5 mg, 0.025 mmol, 10 mol%), LiI (333 mg, 2.5 mmol), DABCO (28 mg, 0.25 mmol), DMF (0.9 mL) and cumene (0.1 mL) as mixed solvent were put into the 10 mL sealed tube under an atmosphere of oxygen balloon. The reaction mixture was stirred at 100 °C for 48 h. After extraction and evaporation, the crude product was purified by column chromatography on neutral Al_2O_3 and eluted with EA/PE (1:15 to 1:5) to afford a white solid (40 mg, 50%, **4e** : **4e'** = 61 : 39). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.54 (s, 1H), 8.37 (d, *J* = 10.3 Hz, 2H), 8.31 (s, 1H), 8.23-8.07 (m, 4H), 7.90-7.60 (m, 2H), 6.40 (d, *J* = 14.4 Hz, 1H), 6.36 (d, *J* = 14.4 Hz, 1H), 4.49-4.39 (m, 4H), 4.27 (d, *J* = 4.0 Hz, 4H), 1.72 (d, *J* = 6.1 Hz, 4H), 1.51-1.40 (m, 10H), 0.99 (d, *J* = 1.4 Hz, 6H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 166.34, 166.32, 166.10, 166.05, 147.6, 144.2, 143.7, 142.7, 135.2, 134.9, 134.8, 132.1, 127.4, 127.0, 126.4, 125.6, 123.2, 120.8, 113.0, 110.7, 107.3, 65.0, 61.4, 61.2, 30.8, 19.2, 14.41, 14.37, 13.7 ppm; IR (KBr) υ 3082, 2961, 2873, 1715, 1652, 1502, 1284, 1191, 1025, 769 cm^{-1}; HRMS (ESI/TOF-Q) m/z Calcd for $C_{17}H_{20}N_2O_4$ [M + Na]$^+$: 339.1315, Found: 339.1305.

(*E*)-Butyl 3-(5-nitro-1*H*-benzo[*d*]imidazol-1-yl) acrylate (4f): The title compound could be prepared according to general procedure A for 48 h. The crude product was purified by column chromatography on neutral Al_2O_3 and eluted with EA/PE (1:25 to 1:7) to afford a yellow solid (42 mg, 58%), m.p.: 137-139 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.74 (d, *J* = 1.4 Hz, 1H), 8.42 (s, 1H), 8.36 (dd, *J* = 8.9, 1.7 Hz, 1H), 8.16 (d, *J* = 14.4 Hz, 1H), 7.75 (d, *J* = 9.0 Hz, 1H), 6.43 (d, *J* = 14.4 Hz, 1H), 4.28 (t, *J* = 6.7 Hz, 2H), 1.76-1.69 (m, 2H), 1.50-1.41 (m, 2H), 0.99 (t, *J* = 7.4 Hz, 3H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 165.6, 145.1, 144.1, 136.2, 134.2, 120.5, 117.6, 111.0, 108.8, 77.3, 77.1, 76.9, 65.3, 30.7, 19.2, 13.7 ppm; IR (KBr) υ 3103, 3042, 2962, 2872, 1708, 1652, 1524, 1347, 1262, 1204, 1166, 952, 736 cm^{-1}; HRMS (ESI/TOF-Q) m/z Calcd for $C_{14}H_{15}N_3O_4$ [M + Na]$^+$: 312.0955 Found: 312.0947.

(*E*)-Butyl 3-(6-nitro-1*H*-benzo[*d*]imidazol-1-yl) acrylate (4f'): The title compound could be prepared according to general procedure A for 48 h. The crude product was purified by column chromatography on neutral Al_2O_3 and eluted with ethyl acetate/petroleum ether (1/25 to 1/5) to afford a yellow solid (7 mg, 10%), m.p.: 119-121 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.61 (s, 1H), 8.43 (s, 1H), 8.32 (d, *J* = 8.2 Hz, 1H), 8.17 (d, *J* = 14.4 Hz, 1H), 7.95 (d, *J* = 8.8 Hz, 1H), 6.43 (d, *J* = 14.4 Hz, 1H), 4.29 (t, *J* = 6.7 Hz, 2H), 1.77-1.70 (m, 2H), 1.51-1.43 (m, 2H), 0.99 (t, *J* = 7.4 Hz, 3H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 165.6, 148.7, 145.6, 145.2, 134.2, 131.8, 121.5, 119.9, 108.7, 107.9, 65.3, 30.7, 19.2, 13.7 ppm; HRMS (ESI/TOF-Q) m/z Calcd for $C_{14}H_{15}N_3O_4$ [M + H]$^+$:

290.1135, Found: 290.1139.

(*E*)-Butyl 3-(5-fluoro-1*H*-benzo[*d*]imidazol-1-yl) acrylate (4g): The title compound could be prepared according to general procedure A for 48 h. The crude product was purified by column chromatography on neutral Al_2O_3 and eluted with EA/PE (1:25 to 1:5) to afford a white solid (27 mg, 42%), m.p.: 87-89 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.25 (s, 1H), 8.11 (d, *J* = 14.4 Hz, 1H), 7.59 (dd, *J* = 8.9, 4.3 Hz, 1H), 7.54 (dd, *J* = 8.7, 2.2 Hz, 1H), 7.18 (td, *J* = 9.0, 2.3 Hz, 1H), 6.32 (d, *J* = 14.4 Hz, 1H), 4.26 (t, *J* = 6.7 Hz, 2H), 1.74-1.68 (m, 2H), 1.49-1.42 (m, 2H), 0.98 (t, *J* = 7.4 Hz, 3H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 166.2, 160.3 (d, J_{C-F} = 241.6 Hz), 145.0, 143.1, 135.1, 128.7, 113.3 (d, J_{C-F} = 27.2Hz), 111.7 (d, J_{C-F} = 10.6 Hz), 107.3 (d, J_{C-F} =24.2 Hz), 106.7, 65.0, 30.8, 19.2, 13.7 ppm; IR (KBr) υ 3125, 3078, 3044, 2961, 2873, 1708, 1650, 1486, 1251, 1213, 1174, 956, 835 cm^{-1}; HRMS (ESI/TOF-Q) m/z Calcd for $C_{14}H_{15}FN_2O_2$ $[M + Na]^+$: 285.1010, Found:. 285.1008.

(*E*)-Butyl 3-(6-fluoro-1*H*-benzo[*d*]imidazol-1-yl) acrylate (4g'): The title compound could be prepared according to general procedure A for 48 h. The crude product was purified by column chromatography on neutral Al_2O_3 and eluted with EA/PE (1:15 to 1:5) to afford a white solid (27 mg, 42%), m.p.: 86-88 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.22 (s, 1H), 8.07 (d, *J* = 14.4 Hz, 1H), 7.80 (dd, *J* = 8.6, 4.7 Hz, 1H), 7.35 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.14 (td, *J* = 9.1, 2.1 Hz, 1H), 6.29 (d, *J* = 14.4 Hz, 1H), 4.26 (t, *J* = 6.7 Hz, 2H), 1.75-1.68 (m, 2H), 1.49-1.42 (m, 2H), 0.98 (t, *J* = 7.4 Hz, 3H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 166.1, 160.8 (d, J_{C-F} = 244.6 Hz), 142.1, 140.6, 134.9, 132.5, 122.0 (d, J_{C-F} = 9.1 Hz), 112.8 (d, J_{C-F} = 25.7 Hz), 107.0, 98.5 (d, J_{C-F} = 28.7 Hz), 65.0, 30.8, 19.2, 13.7 ppm; HRMS (ESI/TOF-Q) m/z Calcd for $C_{14}H_{15}FN_2O_2$ $[M + H]^+$: 263.1190, Found:. 263.1197.

(*E*)-Butyl 3-(5-chloro-1*H*-benzimidazol-1-yl) acrylate (4h)[23]: The title compound could be prepared according to general procedure A 48 h. The crude product was purified by column chromatography on neutral Al_2O_3 and eluted with EA/PE (1:15 to 1:5) to afford a white solid (27 mg, 39%).

The reaction also was conducted with modifications to the general procedure B. The mixture of butyl 3-(5-chloro-1*H*-benzimidazol-1-yl)propanoate and butyl 3-(6-chloro-1*H*-benzoimidazol-1-yl)propanoate (70 mg, 0.25 mmol), butyl acrylate (32 mg, 37 μL, 0.25 mmol), $Cu(OAc)_2 \cdot H_2O$ (5 mg, 0.025 mmol, 10 mol%), LiI (333 mg, 2.5 mmol), DABCO (28 mg, 0.25 mmol), DMF (1 mL) as solvent were put into the 10 mL sealed tube under an atmosphere of oxygen balloon. The reaction mixture was stirred at 100 °C for 30 h. After extraction and evaporation, the crude product was purified by column chromatography on neutral Al_2O_3 and eluted with EA/PE (1:20 to 1:5) to afford a white solid (24 mg, 35%). m.p.: 121-123 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.24 (s, 1H), 8.10 (d, *J* = 14.4 Hz, 1H), 7.84 (s, 1H), 7.56 (d, *J* = 8.6 Hz, 1H), 7.42-7.37 (m, 1H), 6.32 (d, *J* = 14.4 Hz, 1H), 4.26

(t, J = 6.7 Hz, 2H), 1.74-1.68 (m, 2H), 1.50-1.40 (m, 2H), 0.98 (t, J = 7.4 Hz, 3H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 166.1, 145.1, 142.8, 134.9, 130.8, 130.2, 125.5, 121.0, 111.9, 107.1, 65.0, 30.8, 19.2, 13.7 ppm; IR (KBr) υ 3135, 3089, 2959, 2872, 1706, 1650, 1502, 1467, 1399, 1360, 1204, 1167, 1063, 805, 656 cm^{-1}; HRMS (ESI/TOF-Q) m/z Calcd for $C_{14}H_{15}ClN_2O_2$ $[M + H]^+$: 279.0895, Found: 279.0893.

(*E*)-Butyl 3-(6-chloro-1*H*-benzimidazol-1-yl) acrylate (4h')[23]: The title compound could be prepared according to general procedure A for 48 h. The crude product was purified by column chromatography on neutral Al_2O_3 and eluted with EA/PE (1:15 to 1:5) to afford a white solid (27 mg, 39%).

The reaction also was conducted with modifications to the general procedure B. The mixture of butyl 3-(5-chloro-1*H*-benzimidazol-1-yl)propanoate and butyl 3-(6-chloro-1*H*-benzimidazol-1-yl)propanoate (70 mg, 0.25 mmol), butyl acrylate (32 mg, 37 μL, 0.25 mmol), $Cu(OAc)_2 \cdot H_2O$ (5 mg, 0.025 mmol, 10 mol%), LiI (333 mg, 2.5 mmol), DABCO (28 mg, 0.25 mmol), DMF (1 mL) as solvent were put into the 10 mL sealed tube under an atmosphere of oxygen balloon. The reaction mixture was stirred at 100 °C for 30 h. After extraction and evaporation, the crude product was purified by column chromatography on neutral Al_2O_3 and eluted with EA/PE (1:20 to 1:5) to afford a white solid (24 mg, 35%), m.p.: 90-92 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.22 (s, 1H), 8.08 (d, J = 14.4 Hz, 1H), 7.77 (d, J = 8.6 Hz, 1H), 7.65 (s, 1H), 7.38-7.34 (m, 1H), 6.31 (d, J = 14.4 Hz, 1H), 4.26 (t, J = 6.7 Hz, 2H), 1.75-1.68 (m, 2H), 1.51-1.41 (m, 2H), 0.99 (t, J = 7.4 Hz, 3H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 166.0, 142.9, 142.2, 134.8, 132.8, 131.1, 125.1, 121.9, 111.5, 107.1, 65.0, 30.8, 19.2, 13.7 ppm; HRMS (ESI/TOF-Q) m/z Calcd for $C_{14}H_{15}ClN_2O_2$ $[M + H]^+$: 279.0895, Found: 279.0894.

(*E*)-Butyl 3-(2-methyl-1*H*-benzo[*d*]imidazol-1-yl) acrylate (4i): The title compound could be prepared according to general procedure A for 48 h. The crude product was purified by column chromatography on neutral Al_2O_3 and eluted with EA/PE (1:15 to 1:5) to afford a white solid (16 mg, 25%).

The reaction also was conducted with modifications to the general procedure B for 48 h. The crude product was purified by column chromatography on neutral Al_2O_3 and eluted with EA/PE (1:15 to 1:5) to afford a white solid (9 mg, 13%), m.p.: 70-72 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.10 (d, J = 14.3 Hz, 1H), 7.73 (s, 1H), 7.64 (dd, J = 6.0, 2.4 Hz, 1H), 7.36-7.30 (m, 2H), 6.35 (d, J = 14.3 Hz, 1H), 4.26 (t, J = 6.7 Hz, 2H), 2.75 (s, 3H), 1.76-1.68 (m, 2H), 1.50-1.42 (m, 2H), 0.99 (t, J = 7.4 Hz, 3H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 166.8, 152.4, 143.2, 135.9, 133.1, 124.22, 124.18, 120.0, 111.9, 107.0, 64.9, 30.8, 19.2, 14.9, 13.7 ppm; IR (KBr) υ 3061, 2959, 2873, 1715, 1649, 1611, 1553, 1459, 1380, 1276, 1152, 955, 741 cm^{-1}; HRMS (ESI/TOF-Q) m/z Calcd for $C_{15}H_{18}N_2O_2$ $[M + H]^+$: 259.1441, Found: 259.1437.

(*E*)-Butyl 3-(2-phenyl-1*H*-benzo[*d*]imidazol-1-yl) acrylate (4j): The title compound could be prepared according to general procedure A for 48 h. The crude product was purified by column chromatography on neutral Al_2O_3 and eluted with EA/PE (1:15 to 1:5) to afford a white solid (44 mg, 55%), m.p.: 80-82 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.16 (d, *J* = 14.4 Hz, 1H), 7.87 (dd, *J* = 6.2, 2.8 Hz, 1H), 7.75 (ddd, *J* = 9.4, 7.5, 4.0 Hz, 3H), 7.56 (dd, *J* = 6.8, 3.5 Hz, 3H), 7.44-7.39 (m, 2H), 6.41 (d, *J* = 14.4 Hz, 1H), 4.21 (t, *J* = 6.6 Hz, 2H), 1.70-1.63 (m, 2H), 1.48-1.36 (m, 2H), 0.95 (t, *J* = 7.4 Hz, 3H) ppm; ^{13}C NMR (151 MHz, CDCl3) δ = 166.6, 154.3, 144.0, 137.8, 133.5, 130.6, 130.1, 129.1, 129.0, 124.6, 124.5, 120.8, 112.4, 107.8, 64.7, 30.7, 19.2, 13.7 ppm; IR (KBr) υ 3059, 2953, 2869, 1716, 1648, 1541, 1455, 1377, 1283, 1185, 1185, 820, 737, 698 cm^{-1}; HRMS (ESI/TOF-Q) m/z Calcd for $C_{20}H_{20}N_2O_2$ $[M + Na]^+$: 343.1417, Found: 343.1403.

(*E*)-Benzyl 3-(1*H*-imidazol-1-yl) acrylate (4k): The title compound could be prepared according to general procedure A. 1*H*-imidazole (17 mg, 0.25 mmol), benzyl acrylate (81 mg, 75 μL, 0.5 mmol), 2,2'-bipyridine (4 mg, 0.025 mmol, 10 mol%), $Cu(OAc)_2 \cdot H_2O$ (5 mg, 0.025 mmol, 10 mol%), KI (415 mg, 2.5 mmol), DABCO (28 mg, 0.25 mmol), DMF (0.9 mL) and cumene (0.1 mL) as mixed solvent were put into the 10 mL sealed tube under an atmosphere of oxygen balloon. The reaction mixture was stirred at 100 °C for 17 h. After extraction and evaporation, the crude product was purified by column chromatography on neutral Al_2O_3 and eluted with ethyl EA/PE (1:15 to 1:5) to afford a white solid (22 mg, 39%), m.p.: 91-93 °C. H NMR (600 MHz, $CDCl_3$) δ = 7.91 (d, *J* = 14.2 Hz, 1H), 7.77 (s, 1H), 7.42-7.32 (m, 5H), 7.23 (s, 1H), 7.18 (s, 1H), 6.10 (d, *J* = 14.2 Hz, 1H), 5.24 (s, 2H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 165.7, 138.1, 136.9, 135.7, 132.0, 128.7, 128.5, 128.4, 116.4, 106.8, 66.8 ppm; IR (KBr) υ 3144, 3125, 3090, 3061, 2921, 1704, 1652, 1498, 1218, 1168, 1020, 961, 878, 736 cm^{-1}; HRMS (ESI/TOF-Q) m/z Calcd for $C_{13}H_{12}N_2O_2$ $[M + Na]^+$: 251.0791, Found: 251.0802.

(*E*)-Butyl 3-(1*H*-benzo[*d*][1,2,3]triazol-1-yl) acrylate (4m): The title compound could be prepared according to general procedure A for 48 h. The crude product was purified by column chromatography on neutral Al_2O_3 and eluted with EA/PE (1:15 to 1:5) to afford a white solid (33 mg, 54%), m.p.: 65-67°C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.51 (d, *J* = 14.3 Hz, 1H), 8.14 (d, *J* = 8.3 Hz, 1H), 7.75 (d, *J* = 8.3 Hz, 1H), 7.64 (t, *J* = 7.6 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 1H), 6.76 (d, *J* = 14.3 Hz, 1H), 4.28 (t, *J* = 6.7 Hz, 2H), 1.76-1.69 (m, 2H), 1.51-1.43 (m, 2H), 0.99 (t, *J* = 7.4 Hz, 3H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 166.0, 146.7, 135.2, 131.6, 129.4, 125.5, 120.9, 110.2, 108.4, 65.0, 30.8, 19.2, 13.3 ppm; IR (KBr) υ 3096, 3063, 2960, 2929, 2867, 1706, 1657, 1461, 1282, 1161, 959, 754 cm^{-1}; HRMS (ESI/TOF-Q) m/z Calcd for $C_{13}H_{15}N_3O_2$ $[M + Na]^+$: 268.1057, Found: 268.1059.

(*E*)-Ethyl 3-(1*H*-benzimidazol-1-yl) acrylate (4n)[24]: The title compound could be prepared according to general procedure A for 48 h. The crude product was purified by column chromatography on neutral Al_2O_3 and eluted

with EA/PE (1:15 to 1:5) to afford a white solid (43 mg, 79%).

The reaction also was conducted with modifications to the general procedure B for 36 h. The crude product was purified by column chromatography on neutral Al_2O_3 and eluted with EA/PE (1:15 to 1:5) to afford a white solid (33 mg, 61%). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.24 (s, 1H), 8.15 (d, *J* = 14.3 Hz, 1H), 7.86 (d, *J* = 7.7 Hz, 1H), 7.64 (d, *J* = 6.4 Hz, 1H), 7.45-7.36 (m, 2H), 6.33 (d, *J* = 14.4 Hz, 1H), 4.31 (dd, *J* = 8.4, 5.3 Hz, 2H), 1.36 (t, *J* = 6.8 Hz, 3H) ppm.

(*E*)-Benzyl 3-(1*H*-benzimidazol-1-yl) acrylate (4o): The title compound could be prepared according to general procedure A. Benzimidazole (29 mg, 0.25 mmol), benzyl acrylate (81 mg, 75 μL, 0.5 mmol), 2,2'-bipyridine (4 mg, 0.025 mmol, 10 mol%), $Cu(OAc)_2 \cdot H_2O$ (5 mg, 0.025 mmol, 10 mol%), KI (415 mg, 2.5 mmol), DABCO (28 mg, 0.25 mmol), DMF (0.9 mL) and cumene (0.1 mL) as mixed solvent were put into the 10 mL sealed tube under an atmosphere of oxygen balloon. The reaction mixture was stirred at 100 °C for 36 h. After extraction and evaporation, the crude product was purified by column chromatography on neutral Al_2O_3 and eluted with EA/PE (1:15 to 1:5) to afford a white solid (29 mg, 42%), m.p.: 115-117 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.17 (d, *J* = 15.0 Hz, 2H), 7.83 (d, *J* = 7.6 Hz, 1H), 7.62 (d, *J* = 7.8 Hz, 1H), 7.45-7.34 (m, 7H), 6.35 (d, *J* = 14.3 Hz, 1H), 5.28 (s, 2H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 166.2, 144.6, 141.6, 135.9, 135.8, 132.1, 128.7, 128.5, 128.4, 125.0, 124.4, 121.2, 111.2, 105.5, 66.8 ppm; IR (KBr) υ 3080, 3031, 2953, 1715, 1647, 1498, 1464, 1368, 1267, 1152, 998, 742 cm^{-1}; HRMS (ESI/TOF-Q) m/z Calcd for $C_{17}H_{14}N_2O_2$ $[M + Na]^+$: 301.0948, Found: 301.0944.

(*E*)-*tert*-Butyl 3-(1*H*-benzimidazol-1-yl) acrylate (4p): The title compound could be prepared according to general procedure A for 48 h. The crude product was purified by column chromatography on neutral Al_2O_3 and eluted with EA/PE (1:15 to 1:5) to afford a white solid (24 mg, 39%), m.p.: 125-127 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.18 (s, 1H), 8.06 (d, *J* = 14.3 Hz, 1H), 7.84 (d, *J* = 7.8 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.40 (dt, *J* = 21.1, 7.4 Hz, 2H), 6.26 (d, *J* = 14.4 Hz, 1H), 1.56 (s, 9H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 165.5, 144.5, 141.5, 134.6, 132.2, 124.9, 124.2, 121.1, 111.1, 108.0, 81.4, 28.3 ppm; IR (KBr) υ 3087, 3061, 3027, 2974, 2929, 2859, 1715, 1650, 1496, 1460, 1367, 1258, 1147, 955, 861, 765, 700, 554 cm^{-1}; HRMS (ESI/TOF-Q) m/z Calcd for $C_{14}H_{16}N_2O_2$ $[M + Na]^+$: 267.1104, Found: 267.1101.

(*E*)-2-Methoxyethyl 3-(1*H*-benzimidazol-1-yl) acrylate (4q): The title compound could be prepared according to general procedure A for 48 h. The crude product was purified by column chromatography on neutral Al_2O_3 and eluted with EA/PE (1:15 to 1:5) to afford a white solid (34 mg, 56%), m.p.: 80-82 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.18 (dd, *J* = 13.8, 4.5 Hz, 2H), 7.84 (d, *J* = 6.1 Hz, 1H), 7.64 (d, *J* = 6.2 Hz, 1H), 7.44-7.35 (m, 2H), 6.37 (d, *J* = 14.4 Hz, 1H), 4.43-4.39 (m, 2H), 3.71-3.66 (m, 2H), 3.46-3.41 (m, 3H) ppm; ^{13}C NMR (151 MHz,

$CDCl_3$) δ = 166.3, 144.6, 141.7, 135.9, 132.1, 125.0, 124.4, 121.2, 111.2, 105.4, 70.5, 63.9, 59.0 ppm; IR (KBr) υ 3087, 3056, 2983, 2909, 2816, 1721, 1651, 1502, 1459, 1364, 1270, 1205, 1165, 1122, 974, 766 cm^{-1}; HRMS (ESI/TOF-Q) m/z Calcd for $C_{13}H_{14}N_2O_3$ $[M + Na]^+$: 269.0897, Found 269.0907.

(*E*)-Trifluoromethyl 3-(1*H*-benzimidazol-1-yl) acrylate (4r): The title compound could be prepared according to general procedure A. Benzimidazole (29 mg, 0.25 mmol), 2,2,2-trifluoroethyl acrylate (77 mg, 63 μL, 0.5 mmol), 2,2'-bipyridine (4 mg, 0.025 mmol, 10 mol%), $Cu(OAc)_2 \cdot H_2O$ (5 mg, 0.025 mmol, 10 mol%), KI (415 mg, 2.5 mmol), DABCO (28 mg, 0.25 mmol), DMF (0.9 mL) and cumene (0.1 mL) as mixed solvent were put into the 10 mL sealed tube under an atmosphere of oxygen balloon. The reaction mixture was stirred at 100 °C for 36 h. The crude product was purified by column chromatography on neutral Al_2O_3 and eluted with EA/PE (1:7 to 1:5) to afford a white solid (22 mg, 32%), m.p.: 113-115 °C. ^1H NMR (600 MHz, $CDCl_3$) δ = 8.28-8.17 (m, 2H), 7.86 (d, *J* = 7.8 Hz, 1H), 7.66 (d, *J* = 7.9 Hz, 1H), 7.43 (dd, *J* = 14.3, 7.7 Hz, 2H), 6.37 (d, *J* = 14.3 Hz, 1H), 4.64 (q, *J* = 8.4 Hz, 2H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 164.7, 144.6, 141.8, 137.3, 132.1, 125.4, 124.8, 123.0 (q, $J_{C\text{-}F}$ = 277.8 Hz), 121.4, 111.3, 103.5, 60.6 (q, $J_{C\text{-}F}$ = 37.8 Hz) ppm; IR (KBr) υ 3124, 3066, 3050, 2967, 2921, 2851, 1721, 1653, 1502, 1464, 1417, 1368, 1270, 1155, 989, 768 cm^{-1}; HRMS (ESI/TOF-Q) m/z Calcd for $C_{12}H_9F_3N_2O_2$ $[M + Na]^+$: 293.0508, Found 293.0512.

(*E*)-Cyclohexyl 3-(1*H*-benzimidazol-1-yl) acrylate (4s): The title compound could be prepared according to general procedure A for 48 h. The crude product was purified by column chromatography on neutral Al_2O_3 and eluted with EA/PE (1:15 to 1:5) to afford a white solid (44 mg, 65%), m.p.: 120-122 °C. ^1H NMR (600 MHz, $CDCl_3$) δ = 8.19 (s, 1H), 8.14 (d, *J* = 14.4 Hz, 1H), 7.84 (d, *J* = 7.7 Hz, 1H), 7.65 (d, *J* = 7.9 Hz, 1H), 7.40 (dt, *J* = 15.1, 7.1 Hz, 2H), 6.32 (d, *J* = 14.3 Hz, 1H), 4.96-4.88 (m, 1H), 1.98-1.91 (m, 2H), 1.80-1.78 (m, 2H), 1.60-1.58 (m, 1H), 1.54-1.49 (m, 2H), 1.45-1.39 (m, 2H), 1.35-1.25 (m, 1H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 165.8, 144.6, 141.6, 135.2, 132.2, 124.9, 124.3, 121.2, 111.2, 106.6, 73.4, 31.8, 25.4, 23.8 ppm; IR (KBr) υ 3117, 3051, 2939, 2858, 1774, 1643, 1495, 1464, 1360, 1269, 1162, 1018, 716 cm^{-1}; HRMS (ESI/TOF-Q) m/z Calcd for $C_{16}H_{18}N_2O_2$ $[M + Na]^+$: 293.1261, Found 293.1256.

(*E*)-(Tetrahydrofuran-2-yl) methyl 3-(1*H*-benzimidazol-1-yl) acrylate (4t): The title compound could be prepared according to general procedure A for 48 h. The crude product was purified by column chromatography on neutral Al_2O_3 and eluted with EA/PE (1:15 to 1:3) to afford a white solid (38 mg, 55%), m.p.: 70-72 °C. ^1H NMR (600 MHz, $CDCl_3$) δ = 8.19 (t, *J* = 7.1 Hz, 2H), 7.84 (d, *J* = 7.7 Hz, 1H), 7.65 (d, *J* = 7.7 Hz, 1H), 7.44-7.36 (m, 2H), 6.38 (d, *J* = 14.4 Hz, 1H), 4.35 (d, *J* = 11.0 Hz, 1H), 4.25-4.13 (m, 2H), 3.97-3.91 (m, 1H), 3.88-3.81 (m, 1H), 2.12-2.03 (m, 1H), 2.02-1.92 (m, 2H), 1.70-1.61 (m, 1H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ

= 166.3, 144.6, 141.7, 135.9, 132.1, 125.0, 124.4, 121.2, 111.2, 105.4, 76.6, 68.5, 66.9, 28.1, 25.7 ppm; IR (KBr) υ 3092, 2924, 2853, 1718, 1651, 1504, 1461, 1366, 1276, 1193, 1087, 1027, 742 cm^{-1}; HRMS: (ESI/TOF-Q) m/z Calcd for $C_{15}H_{16}N_2O_3$ $[M + Na]^+$: 295.1053, Found 295.1054.

(*E*)-Ethyl 3-(1*H*-benzo[*d*]imidazol-1-yl)-2-methylacrylate (4v)*:* The title compound could be prepared according to general procedure A for 48 h. The crude product was purified by column chromatography on neutral Al_2O_3 and eluted with ethyl EA/PE (1:10 to 1:5) to afford a white solid (14 mg, 24%), m.p.: 120-122 °C. ^1H NMR (600 MHz, $CDCl_3$) δ = 8.30 (s, 1H), 8.02 (s, 1H), 7.89 (d, *J* = 7.2 Hz, 1H), 7.49 (d, *J* = 5.5 Hz, 1H), 7.42-7.36 (m, 2H), 4.34 (q, *J* = 7.1 Hz, 2H), 2.18 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 167.1, 142.6, 142.0, 129.6, 124.5, 124.0, 122.0, 120.6, 110.4, 100.0, 61.5, 14.3, 13.6 ppm; IR (KBr) υ 3127, 3057, 2923, 2853, 1705, 1656, 1495, 1460, 1385, 1363, 1267, 1135, 1088, 887, 774 cm^{-1}; HRMS (ESI/TOF-Q) m/z Calcd for $C_{13}H_{14}N_2O_2$ $[M + Na]^+$: 253.0948, Found 253.0945.

(*E*)-Trifluoroethyl 3-(1*H*-benzimidazol-1-yl)-2-methylacrylate (4w): The title compound could be prepared according to general procedure A. Benzimidazole (29 mg, 0.25 mmol), 2,2,2-trifluoroethyl methacrylate (84 mg, 71 μL, 0.5 mmol), 2,2'-bipyridine (4 mg, 0.025 mmol, 10 mol%), $Cu(OAc)_2 \cdot H_2O$ (5 mg, 0.025 mmol, 10 mol%), KI (415 mg, 2.5 mmol), DABCO (28 mg, 0.25 mmol), DMF (0.9 mL) and cumene (0.1 mL) as mixed solvent were put into the 10 mL sealed tube under an atmosphere of oxygen balloon. The reaction mixture was stirred at 100 °C for 28 h. The crude product was purified by column chromatography on neutral Al_2O_3 and eluted with EA/PE (1/10 - 1/5) to afford a white solid (21 mg, 30%), m.p.: 119-121 °C. ^1H NMR (600 MHz, $CDCl_3$) δ = 8.25 (s, 1H), 8.13 (s, 1H), 7.85 (d, *J* = 7.2 Hz, 1H), 7.48 (d, *J* = 7.3 Hz, 1H), 7.45-7.37 (m, 2H), 4.67 (q, *J* = 8.4 Hz, 2H), 2.29-2.20 (m, 3H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ = 165.7, 143.1, 141.3, 133.5, 131.6, 125.7, 124.6, 124.1, 123.0 (q, $J_{C\text{-}F}$ = 277.8 Hz), 117.9, 110.1, 61.1 (q, $J_{C\text{-}F}$ = 36.2 Hz) 13.6 ppm; IR (KBr) υ 3158, 3054, 1726, 1644, 1489, 1400, 1365, 1315, 1277, 1249, 1164, 957, 741 cm^{-1}; HRMS (ESI/TOF-Q) m/z Calcd for $C_{13}H_{11}F_3N_2O_2$ $[M + H]^+$: 285.0845, Found 285.0847.

(*E*)-3-(1*H*-benzo[*d*]imidazol-1-yl)acrylonitrile (4z)[25]: The title compound could be prepared according to general procedure A. Benzimidazole (29 mg, 0.25 mmol), acrylonitrile (53 mg, 65 μL, 1.0 mmol), 2,2'-bipyridine (4 mg, 0.025 mmol, 10 mol%), $Cu(OAc)_2 \cdot H_2O$ (5 mg, 0.025 mmol, 10 mol%), LiI (333 mg, 2.5 mmol), DABCO (28 mg, 0.25 mmol), DMF (0.9 mL) and cumene (0.1 mL) as mixed solvent were put into the 10 mL sealed tube under an atmosphere of oxygen balloon. The reaction mixture was stirred at 100 °C for 48 h. The crude product was purified by column chromatography on neutral Al_2O_3 and eluted with EA/PE (1:15 to 1:5) to afford a yellow

solid (18 mg, 42%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.13 (s, 1H), 7.86 (m, 1H), 7.82 (d, *J* = 14.8 Hz, 1H), 7.55 (m, 1H), 7.48-7.38 (m, 2H), 5.77 (d, *J* = 14.8 Hz, 1H) ppm.

Associated Content

Supporting Information Available: Copies of ^{1}H and ^{13}C NMR spectra for products; LC-MS spectra of the overall kinetic profiles of intermolecular reaction and intramolecular reaction at 4 minute. Crystal data and structure refinement, important bond lengths, bond angles for **4a**. This material is available free of charge via the Internet at http://pubs.acs.org.

Author Information

Notes

The authors declare no competing financial interest.

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