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Copper-Catalyzed Domino Addition/Double Cyclization: An Approach to Polycyclic Benzimidazole Derivatives

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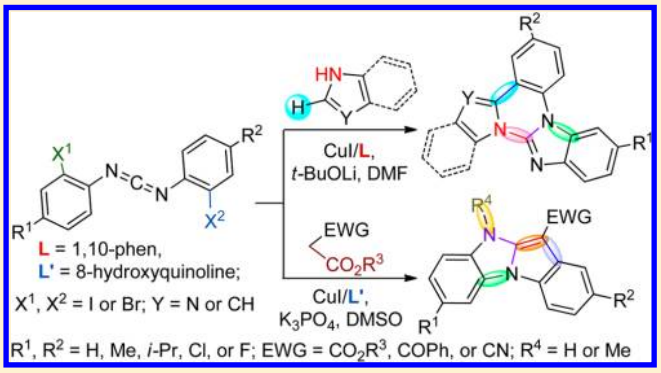
Supporting Information

ABSTRACT: An efficient and versatile method for the assembly of novel polycyclic benzimidazole derivatives has been developed by Cu-catalyzed domino addition/double cyclization reactions. A wide variety of polycyclic benzimidazole derivatives, which might be used as synthetic medicines and functional materials, were successfully assembled from bis(*o*-haloaryl)carbodiimides. Unexpected *N*-methylated benzo[4,5]imidazo[1,2-*a*]indoles can also be selectively assembled. Multibonds and polycyclic moieties were conveniently formed in one pot during these domino processes.



INTRODUCTION

N-Heterocylic moieties widely exist in natural products, pharmaceutical agents, and synthetic materials. Development for efficient synthesis of diverse *N*-heterocylic derivatives is of great interest in the field of organic chemistry.[1] Among the *N*-heterocyles, benzimidazoles are important because of their broad spectrum of biological activities[2] and interesting material applications.[3] The synthesis of polycyclic benzimidazole derivatives has attracted much attention, as is concluded from their applications in the fields of medicinal chemistry[4] and organic material science.[5]

The combination of benzimidazole, quinazoline, and azole moieties leads to the azole-fused benzimidazoquinazolines (Figure 1, I and II). Such heterocycles have aroused considerable interest in the field of organic light-emitting devices (OLEDs).[6] Imidazo[1,2-*c*]quinazoline derivatives are also useful in pharmaceutical areas for their antimicrobial, antitumor, and antipsychotic activities.[7] Benzo[4,5]imidazo[1,2-*a*]indoles (III), which incorporate imidazole and indole frameworks, might be employed as antibiotics and antiviral agents.[8] Although these fused benzimidazoles play important roles in medicinal chemistry and material science, efficient and concise approaches to these molecules have been rarely documented. The limited methods for the assembly of benzo[4,5]imidazo[1,2-*a*]imidazo[1,2-*c*]quinazolines (I) and benzo[4,5]imidazo[1,2-*a*]indoles (III)[9] may suffer from the tedious steps, low efficiency, and/or the narrow scopes, and there is no report about synthesis of benzo[4,5]imidazo[1,2-*a*]indolo[1,2-*c*]quinazolines (II).

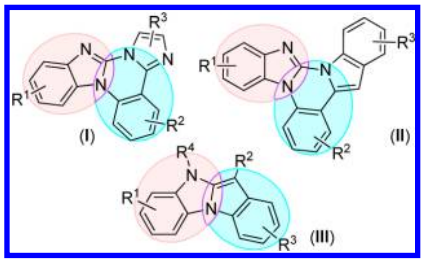


Figure 1. Structures of the target polycyclic benzimidazole derivatives.

Catalytic domino reaction is an efficient and facile strategy for one-step construction of molecular complexity.[10] Because of their high efficiency, low cost, and convenience, Cu-catalyzed domino reactions have emerged as attractive protocols for generating structurally diversified molecules.[11] On the other hand, Cu-mediated C−H functionalization[12] and cross-coupling[13] have been applied as powerful tools for the assembly of heterocycles via domino processes.[11b,c,13a] Notably, although great achievements have been accomplished in the C−H functionalization using transition-metal catalysis, only limited domino approaches to *N*-heterocyles through Cu-catalyzed intramolecular direct sp^2 C−H arylation of azoles have been developed thus far.[14] And to the best of our knowledge, there is no report about the one-pot multibond-forming elaboration of benzo[4,5]imidazo[1,2-*a*]indoles and azole-fused benzo[4,5]-imidazo[1,2-*a*]quinazolines. As part of our ongoing efforts to assemble *N*-heterocycles using Cu-mediated domino protocols,[15] we report on a novel Cu-catalyzed domino synthesis of the

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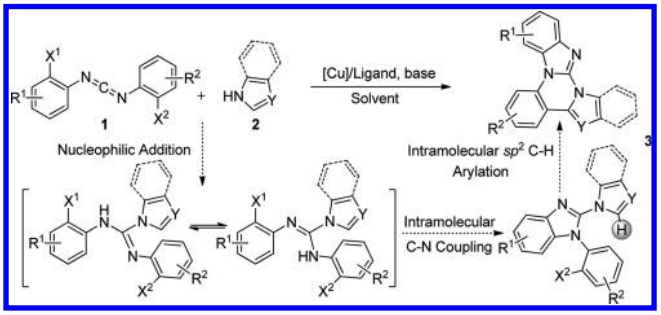
polycyclic benzimidazole derivatives from bis-(*o*-haloaryl)-carbodiimides.[16]

We envisaged that the reaction of bis-(*o*-haloaryl)-carbodiimide **1** with azole **2** might proceed through a nucleophilic addition, an intramolecular C−N coupling, and an intramolecular sp^2 C−H arylation under proper Cu catalysis (Scheme 1). We anticipate that the hypothetic process would be a good vehicle for the direct assembly of benzo[4,5]imidazo[1,2-*a*]quinazoline **3**.

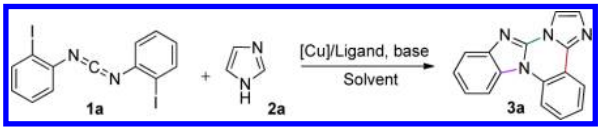
Scheme 1. Proposed Domino Synthesis of Benzo[4,5]imidazo[1,2-*a*]quinazolines



RESULTS AND DISCUSSION

With this hypothesis in mind, we commenced our investigation with the model reaction between bis-(*o*-iodophenyl)-carbodiimide **1a** and imidazole **2a** under Cu(I) catalysis (Table 1, entry 1). The reaction was initially promoted by CuI (5 mol %) and 1,10-phenanthroline (1,10-phen, 10 mol %) with K_2CO_3 (4.0 equiv) as base in dioxane at 110 °C. However, no desired product was detected under these conditions (Table 1, entry 1). K_3PO_4 also failed to show any improvement (entry 2). In light of the previous methods developed for the intermolecular sp^2 C−H arylation of azoles,[17] we also attempted to utilize strong bases to facilitate the present domino transformation. To our delight, when the base was replaced by *t*-BuOLi, the desired product **3a**[6a,18] was obtained in 21% yield (entry 3). Other bases such as *t*-BuOK and mix bases are unsuitable (entries 4 and 5). A higher yield was achieved when DMF was used as the solvent (entry 6). Raising the temperature to 125 °C provided **3a** in 75% yield (entry 7). However, no obvious improvement was observed when heated to 140 °C (entry 8). We examined different Cu catalysts (entries 7, 9, and 10), and CuI proved to be the most efficient. No desired product was observed in a control experiment without the addition of Cu catalyst (entry 11). Other ligands (BtOH, L-proline and 2,2′-bipy) were also screened (entries 12−14), and 1,10-phen showed the best effect (entry 7). We also investigated different organic solvent (entries 3, 7, 15, and 16) and identified DMF as the optimal solvent.[19]

Table 1. Optimization of the Reaction Conditions[a]



entry	cat	ligand	base	solvent	temp (°C)	yield[b] (%)
1	CuI	1,10-phen	K_2CO_3	dioxane	110	nd[c]
2	CuI	1,10-phen	K_3PO_4	dioxane	110	nd
3	CuI	1,10-phen	*t*-BuOLi	dioxane	110	21
4	CuI	1,10-phen	*t*-BuOK	dioxane	110	trace
5	CuI	1,10-phen	K_3PO_4/ *t*-BuOLi[d]	dioxane	110	17
6	CuI	1,10-phen	*t*-BuOLi	DMF	110	28
7	CuI	1,10-phen	*t*-BuOLi	DMF	125	75
8	CuI	1,10-phen	*t*-BuOLi	DMF	140	76
9	CuBr	1,10-phen	*t*-BuOLi	DMF	125	trace
10	CuCl	1,10-phen	*t*-BuOLi	DMF	125	64
11	–	1,10-phen	*t*-BuOLi	DMF	125	nd
12	CuI	BtOH[e]	*t*-BuOLi	DMF	125	trace
13	CuI	L-proline	*t*-BuOLi	DMF	125	nd
14	CuI	2,2′-bipy[f]	*t*-BuOLi	DMF	125	12
15	CuI	1,10-phen	*t*-BuOLi	DMSO	125	69
16	CuI	1,10-phen	*t*-BuOLi	DMAc	125	72

[a]Reaction conditions: bis-(*o*-iodophenyl)carbodiimide **1a** 0.5 mmol (1 equiv), imidazole **2a** 0.55 mmol (1.1 equiv), Cu catalyst 0.05 mmol (10 mol %), ligand 0.10 mmol (20 mol %), and base 2 mmol (4 equiv), in solvent (3 mL), under N_2, 24 h. [b]Isolated yield. [c]nd = not detected. [d]Mole ratio = 1:1. [e]BtOH = 1*H*-benzotriazole-1-methanol. [f]2,2′-bipy = 2,2′-bipyridine.

After the optimized conditions had been established, the scope of the domino synthesis was studied using a series of bis-(*o*-halophenyl)carbodiimides and azoles. As shown in Table 2, a variety of azoles smoothly reacted with bis-(*o*-iodophenyl)-carbodiimides to afford the desired benzo[4,5]imidazo[1,2-*a*]quinazolines in moderate to good yields. Azoles such as imidazole, benzimidazoles, pyrazole, and indoles are compatible with the reaction (entries 1−7).[20,21] Benzimidazoles showed higher efficiency in comparison with other azoles tested (entries 2 and 3). It is noticeable that indoles can also successfully deliver corresponding benzo[4,5]imidazo[1,2-*a*]indolo-[1,2-*c*]-quinazolines via addition/coupling/direct C_2-arylation process (entries 5−7). The bis-(*o*-iodophenyl)carbodiimides bearing electron-donating group (*p*-Me) or electron-withdrawing group (*p*-F) on the aryl rings seemed less reactive and gave moderate yields (entries 8 and 10). Bis-(*o*-iodophenyl)carbodiimides **1c** with branched alkyl groups on the phenyl rings reacted smoothly with benzimidazole **2b** (entry 9). The use of substituted 2-bromo-2′-iodo-diphenylcarbodiimide **1e** successfully delivered the desired product (entry 11), indicating that the intramolecular sp^2 C−H arylation of imidazole with aryl bromide also proceeded smoothly under these conditions.

Having developed a novel domino method for the assembly of benzo[4,5]imidazo[1,2-*a*]quinazolines, we then sought to synthesize benzo[4,5]imidazo[1,2-*a*]indole derivatives by using active methylene compounds as the nucleophiles. Initially, bis-(*o*-iodophenyl)carbodiimide **1a** and diethyl malonate **6a** were used as the starting materials, and the reaction was carried out under the above optimized conditions (at 100 °C). However, no desired product was observed. Shifting the base to K_3PO_4 and replacing the ligand with 8-hydroquinoline gave the desired product **7a** in 21% yield. Other Cu catalysts such as CuCl and CuBr showed less effective. Gratifyingly, with DMSO as the solvent instead of DMF, the yield was remarkably improved (88% yield).

The scope of this domino reaction was then explored under the above modified conditions. As shown in Table 3, a range of bis-(*o*-iodophenyl)carbodiimides and active methylene compounds underwent the domino cyclization smoothly and deliver the desired products **7** in moderate to good yields.[22] Various nucleophiles such as diethyl malonate, dimethyl malonate, ethyl acetoacetate and ethyl cyanoacetate performed well in these domino reactions (Table 3, entries 1−4). Notably, *β*-keto ester

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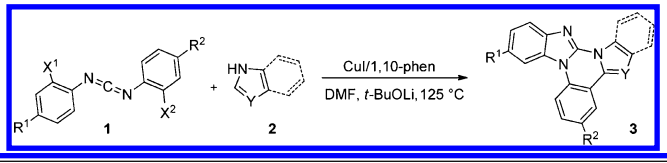
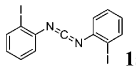
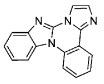
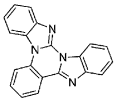
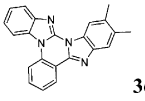
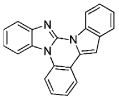
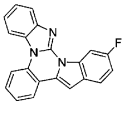
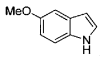
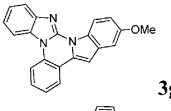
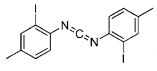
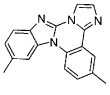
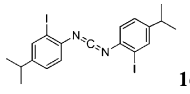
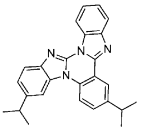
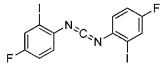
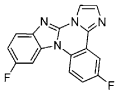
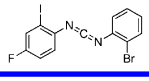
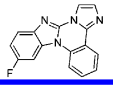
Table 2. Domino Reactions of Bis-(*o*-haloaryl)carbodiimides and Azoles[a]



entry	carbodiimide	azole	product	yield[b]
1	 **1a**	 **2a**	 **3a**	75%
2	**1a**	 **2b**	 **3b**	86%
3	**1a**	 **2c**	 **3c**	87%
4	**1a**	 **2d**	 **3d**	72%
5	**1a**	 **2e**	 **3e**	70%
6	**1a**	 **2f**	 **3f**	66%[c]
7	**1a**	 **2g**	 **3g**	62%[c]
8	 **1b**	 **2a**	 **3h**	57%
9	 **1c**	 **2b**	 **3i**	71%
10	 **1d**	 **2a**	 **3j**	64%
11	 **1e**	 **2a**	 **3k**	54%[c, d]

[a]Reaction conditions: bis-(*o*-haloaryl)carbodiimide 0.5 mmol (1 equiv), azole 0.55 mmol (1.1 equiv), CuI 0.05 mmol (10 mol %), 1,10-phen 0.10 mmol (20 mol %), and *t*-BuOLi 2 mmol (4 equiv), in DMF (3 mL), under N_2, at 125 °C for 24 h. [b]Isolated yield. [c]At 140 °C. [d]*t*-BuOLi 2.5 mmol (5 equiv) was used as the base.

exclusively delivered the deacylation product (entries 3 and 6). An inseparable mixture was obtained when acetylacetone **6e** was utilized, probably because of the special activity of the *β*-diketone and the instability of the product (entry 5). The steric hindrance on the nucleophile might also affect its reactivity. Ethyl 3-oxo-3-phenylpropanoate **6f** afforded the desired product in low yield (entry 6, with small amount of unexpected byproduct **5a**[23]). On the basis of entries 1−3, 5, and 6, it could be concluded that the reactions with malonic diesters gave the decarboxylation products, *β*-keto esters selectively delivered the deacylation products, and the diketones were incompatible with the reaction conditions and afforded a mixture of inseparable components. Both electron-donating and electron-withdrawing groups on the phenyl rings of bis-(*o*-haloaryl)carbodiimides were well tolerated (entries 7−10 and 12−13). The 2-bromo-2′-iodo-diphenylcarbodiimides also efficiently reacted with malonates (entries 11−13). Asymmetric diiodide **1f** gave a mixture of two regioisomers (entry 9), because of the two different cyclization directions of

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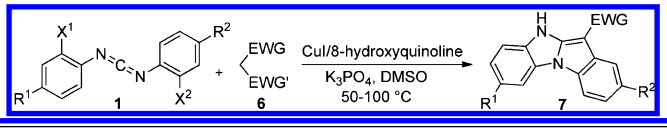
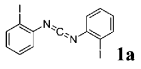
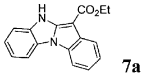
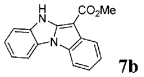
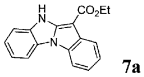
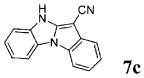
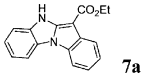
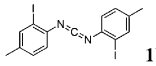
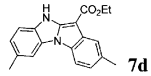
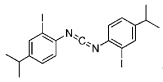
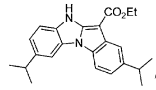
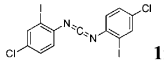
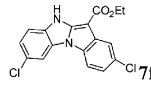
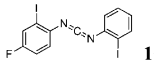
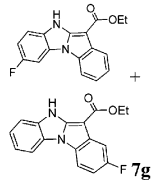
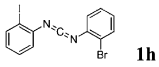
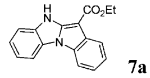
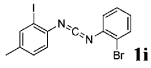
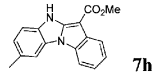
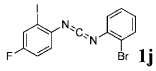
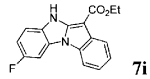
Table 3. Domino Reactions of Bis-(*o*-haloaryl)carbodiimides and Active Methylene Compounds[a]



entry	carbodiimide	*C*-nucleophile	product	yield[b]
1	 **1a**	 **6a**	 **7a**	88%
2	**1a**	 **6b**	 **7b**	80%
3	**1a**	 **6c**	 **7a**	61%
4	**1a**	 **6d**	 **7c**	73%
5	**1a**	 **6e**	-	-[c]
6	**1a**	 **6f**	 **7a**	47% (18%)[d]
7	 **1b**	**6a**	 **7d**	86%
8	 **1c**	**6a**	 **7e**	76%
9	 **1f**	**6a**	 **7f**	70%
10	 **1g**	**6a**	 **7g + 7g'**	71% (69:31)[e]
11	 **1h**	**6a**	 **7a**	81%[f]
12	 **1i**	**6b**	 **7h**	75%[f]
13	 **1j**	**6a**	 **7i**	77%[f]

[a]Reaction conditions: bis-(*o*-haloaryl)carbodiimide 0.5 mmol (1 equiv), active methylene compound 0.55 mmol (1.1 equiv), CuI 0.05 mmol (10 mol %), 8-hydroxyquinoline 0.10 mmol (20 mol %), and K_3PO_4 2 mmol (4 equiv), in DMSO (3 mL), under N_2, prestirred at 50 °C for 3 h, and then stirred at 100 °C for 24 h. [b]Isolated yield. [c]An inseparable complex mixture was obtained. [d]Small amount of unexpected byproduct **5a** was also isolated (its yield is given in parentheses). [e]A mixture of two isomers was obtained (the isomeric ratio in parentheses was approximately determined by ^{1}H NMR). [f]At 110 °C.

the adduct. It is worth noting that sole desired product was isolated when substituted 2-bromo-2′-iodo-diphenylcarbodiimide was used (entries 12 and 13).

To our surprise, when we reduced the amount of base to 3 equiv and raised the temperature to 120 °C for the reaction with dimethyl malonate, an unexpected *N*-methylated product **8a** was isolated in company with the formation of **7b** (Scheme 2, eq 1). The structure of **8a** was ascertained unambigously by the X-ray crystal diffraction analysis (for details, see the Supporting Information). Amazingly, other active methylene species such as **6a** and **6c** did not afford similar *N*-alkylated derivatives, and only **7a** was obtained. The result that **7b** did not react with **6b** to

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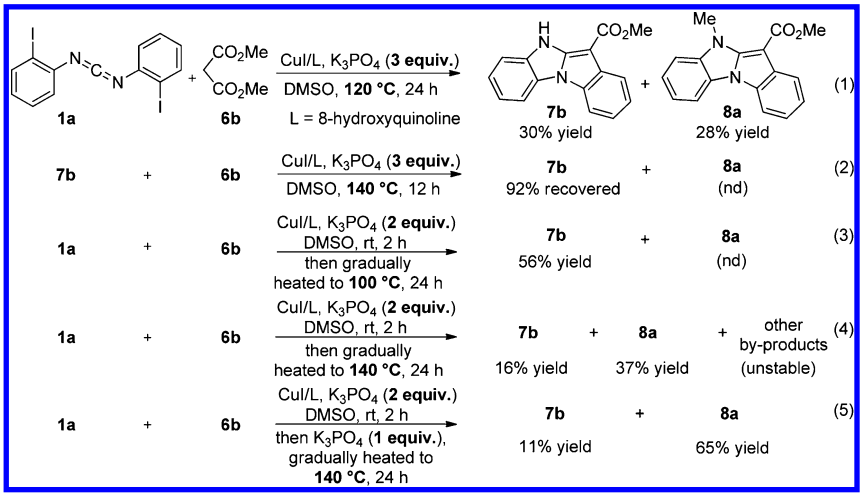
Scheme 2. Initial Attempts to Obtain *N*-Methylated Benzo[4,5]imidazo[1,2-*a*]indoles

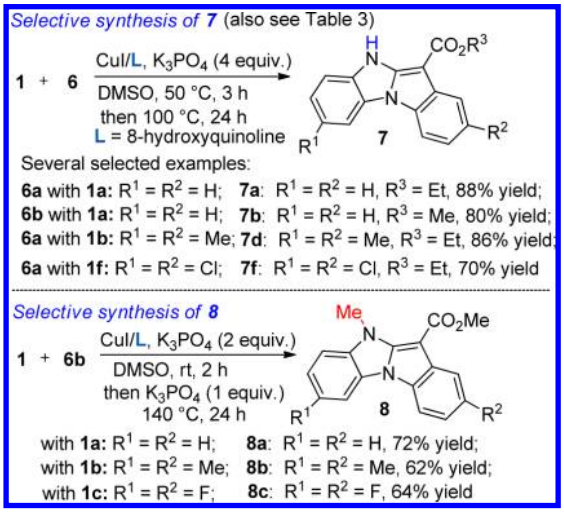


generate **8a** even at 140 °C (Scheme 2, eq 2) indicates that the methylated product should be formed intramolecularly.

Reducing the amount of K_3PO_4 to 2 equiv did not afford any double-cyclized product **8a**. And only a moderate yield of unmethylated product **7b** was isolated (Scheme 2, eq 3), indicating that both adequate amount of base and appropriate temperature might be indispensable for the formation of the methylated product. We also found that when 2 equiv of base was used and the mixture was heated to 140 °C, a complex mixture was obtained (Scheme 2, eq 4; 16% yield of **7b** and 37% yield of **8a**, companied by small amount of other byproducts[24]). Interestingly, when another equivalent of K_3PO_4 was added and the temperature was raised up to 140 °C, **8a** was isolated as the major product (65% yield) accompanied with a small amount of **7b** (11% yield) (Scheme 2, eq 5), indicating that the methylated and unmethylated products might be selectively obtained just by tuning the conditions. Further investigation found that heating process also significantly affected the results. When the mixture was preheated at 50 °C and then stirred at 100 °C, product **7b** was exclusively generated, whereas *N*-methylated derivative **8a** was obtained as almost the sole product when prestirred at rt and then immediately heated to 140 °C. In order to extend the application scope of the method, we carried out representative experiments for tandem synthesis of methylated benzo[4,5]imidazo[1,2-*a*]indoles (Scheme 3). Substrates **1b** and **1c** bearing either electron-donating or electron-withdrawing groups on the phenyl rings also successfully provided the desired *N*-methylated products. Therefore, the selective one-pot assembly of methylated or unalkylated benzo[4,5]imidazo[1,2-*a*]indoles can be facilely and tunably achieved.

Preliminary investigation found that Cu catalyst was indispensable to the domino reaction.[25] In view of above observations and the previous reports,[16,26] possible mechanisms for the domino synthesis of compound **7b** and **8a** was proposed (Scheme 4). The addition of **6b** to carbodiimide **1a** initiates the reaction and gives intermediate **I**, which might proceed through two different routes: (A) an C−N coupling, a C−C coupling, a decarboxylation, and an isomerization, or (B) an intramolecular decarboxylative methylation, a C−C coupling, an isomerization, and a C−N coupling; thus, corresponding products **7b** and **8a** formed, respectively.

Scheme 3. Cu-Catalyzed One-Pot Selective Synthesis of Products 7 and 8



CONCLUSIONS

In summary, we have developed a versatile and efficient approach to various benzo[4,5]imidazo[1,2-*a*]imidazo[1,2-*c*]quinazolines, benzo[4,5]imidazo[1,2-*a*]-indolo[1,2-*c*]quinazolines, and benzo[4,5]imidazo[1,2-*a*]indoles by Cu-catalyzed domino addition/coupling/sp^2 C−H arylation, addition/double coupling/deacylation and addition/decarboxylative methylation/double coupling reactions. Using bis-(*o*-haloaryl)carbodiimides and azoles/active methylene compounds as the substrates, the corresponding polycyclic benzimidazoles could be conveniently assembled in moderate to good yields. Notably, multibonds and polycyclic moieties were conveniently formed in one pot. Furthermore, *N*-methylated and unalkylated benzo[4,5]imidazo-[1,2-*a*]indole derivatives were selectively synthesized. The domino synthesis may be useful for the assembly of various polycyclic *N*-heterocycles of pharmaceutical and material interests.

EXPERIMENTAL SECTION

General Information. All one-pot reactions were carried out in an overdried Schlenk tube equipped with a magnetic stir bar under N_2 atmosphere. 1,4-Dioxane, DMF, DMAc, and DMSO were distilled from CaH_2. Bis-(*o*-haloaryl)carbodiimides **1** were prepared according to the

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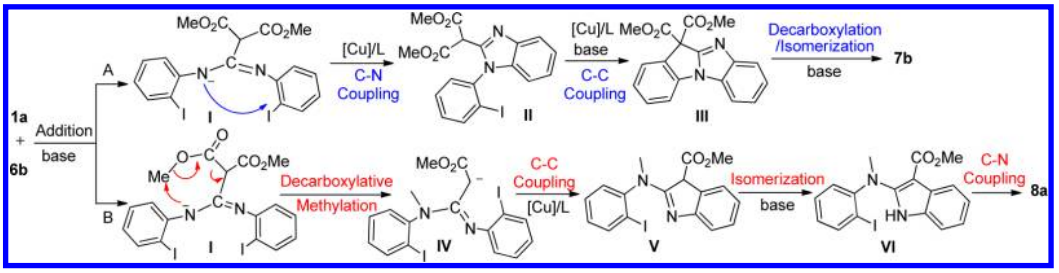
Scheme 4. Possible Mechanisms for the Synthesis of 7b and 8a



known literatures.[27] All other reagents were obtained from commercial sources and used as received, if not stated otherwise. All melting points are uncorrected. The NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 on a 400 or 600 MHz instrument with TMS as internal standard. Chemical shifts (δ) were reported in ppm with respect to TMS. Data are represented as follows: chemical shift, mutiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad), coupling constant (J, Hz) and integration. TLC was carried out with 0.2 mm thick silica gel plates (GF254). Visualization was accomplished by UV light. The columns were hand packed with silica gel 60 (160−200 mesh). Key products were additionally confirmed by high-resolution mass spectra (HRMS) (excepting for the isomeric mixture **7g** + **7g′**). HRMS analyses were carried out using a TOF-MS instrument with an ESI source.

Typical Procedure for the Synthesis of Compound 3. An oven-dried Schlenk tube was charged with imidazole **2** (0.55 mmol, 1.1 equiv), CuI (0.05 mmol), 1,10-phen (0.1 mmol), and *t*-BuOLi (2 mmol). The Schlenk tube was capped and then evacuated and backfilled with N_2 (3 times). Under a positive pressure of N_2, DMF (1.5 mL) was added via syringe, and the mixture was stirred at rt for 10 min. Then a solution of bis-(*o*-iodophenyl)carbodiimide **1** (0.5 mmol, 1.0 equiv) in DMF (1.5 mL) was added dropwise via syringe. The Schlenk tube was sealed and allowed to prestir at rt for 2 h. Then the mixture was stirred at 125 °C for 24 h. After being cooled to rt, 30 mL of EtOAc was added. The mixture was washed with brine (15 mL × 3). The organic phase was dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel using petroleum ether/EtOAc (3:1, v:v) as eluent to afford product **3**.

*Benzo[4,5]imidazo[1,2-a]imidazo[1,2-c]quinazoline (**3a**).*[6b] Yellow solid, 97 mg, 75% yield: R_f = 0.2 (petroleum ether:EtOAc = 1:1, v:v); mp 155−157 °C (recrystallized from EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (d, J = 8.0 Hz, 1H), 8.42 (d, J = 8.4 Hz, 1H), 8.22−8.24 (m, 1H), 8.18 (d, J = 1.2 Hz, 1H), 7.91−7.94 (m, 1H), 7.75−7.80 (m, 1H), 7.64 (d, J = 1.2 Hz, 1H), 7.59 (t, J = 7.6 Hz, 1H), 7.47−7.54 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 141.3, 141.2, 132.8, 132.7, 130.6, 125.6, 125.2, 124.6, 123.4, 120.1, 118.8, 115.1, 113.8, 113.2, 100.0; HRMS (ESI) m/z calcd for $C_{16}H_{11}N_4$ $[M + H]^+$ 259.0978, found 259.0983.

*Benzo[4,5]imidazo[1,2-a]benzo[4,5]imidazo[1,2-c]quinazoline (**3b**).*[6b] Yellow solid, 133 mg, 86% yield: R_f = 0.6 (petroleum ether:EtOAc = 1:1, v:v); mp 231−233 °C (recrystallized from petroleum ether/EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.70−8.73 (m, 1H), 8.65−8.67 (m, 1H), 8.21 (d, J = 8.4 Hz, 1H), 7.99 (d, J = 8.0 Hz, 1H), 7.93−7.96 (m, 1H), 7.82 (d, J = 7.6 Hz, 1H), 7.68−7.71 (m, 1H), 7.52−7.55 (m, 2H), 7.46−7.47 (m, 1H), 7.37−7.39 (m, 1H), 7.32−7.35 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 144.5, 143.8, 142.5, 141.6, 134.1, 132.0, 130.3, 130.0, 126.6, 125.3, 124.4, 124.2, 123.1, 120.0, 119.6, 115.0, 114.9, 114.5, 112.6; HRMS (ESI) m/z calcd for $C_{20}H_{13}N_4$ $[M + H]^+$ 309.1135, found 309.1122.

*2,3-Dimethylbenzo[4,5]imidazo[1,2-a]benzo[4,5]imidazo[1,2-c]-quinazoline (**3c**).* White solid, 146 mg, 87% yield: R_f = 0.5 (petroleum ether:EtOAc = 1:1, v:v); mp 239−241 °C (recrystallized from petroleum ether/EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.63−8.65 (m, 1H), 8.42 (s, 1H), 8.25 (d, J = 8.4 Hz, 1H), 8.04 (d, J = 8.0 Hz, 1H), 7.86 (d, J = 8.0 Hz, 1H), 7.69−7.73 (m, 1H), 7.64 (s, 1H), 7.49 (t, J = 7.5 Hz, 1H), 7.39−7.42 (m, 1H), 7.36−7.38 (m, 1H), 2.50 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 143.8, 142.6, 142.3, 141.8, 134.5, 134.0, 133.9, 131.5, 128.7, 126.4, 125.2, 124.1, 122.9, 119.9, 119.6, 114.9, 114.8, 114.7, 112.6, 20.7, 20.6; HRMS (ESI) m/z calcd for $C_{22}H_{17}N_4$ $[M + H]^+$ 337.1448, found 337.1451.

*Benzo[4,5]imidazo[1,2-a]pyrazolo[1,5-c]quinazoline (**3d**).*[6b] Yellow solid, 93 mg, 72% yield: R_f = 0.2 (petroleum ether:EtOAc = 1:1, v:v); mp 178−180 °C (recrystallized from EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.38 (d, J = 8.4 Hz, 1H), 8.17 (d, J = 8.1 Hz, 1H), 8.14 (d, J = 1.8 Hz, 1H), 8.05−8.07 (m, 1H), 7.97−7.99 (m, 1H), 7.69−7.72 (m, 1H), 7.48−7.51 (m, 2H), 7.45−7.46 (m, 1H), 7.02 (d, J = 1.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 144.4, 137.2, 132.1, 130.9, 130.3, 125.4, 125.2, 124.5, 123.2, 120.7, 115.3, 115.2, 112.9, 110.2, 101.1; HRMS (ESI) m/z calcd for $C_{16}H_{11}N_4$ $[M + H]^+$ 259.0978, found 259.0972.

*Benzo[4,5]imidazo[1,2-a]indolo[1,2-c]quinazoline (**3e**).* Yellow solid, 108 mg, 70% yield: R_f = 0.4 (petroleum ether:EtOAc = 3:1, v:v); mp 237−239 °C (recrystallized from petroleum ether/EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.08 (d, J = 8.4 Hz, 1H), 8.24 (d, J = 8.4 Hz, 1H), 8.07−8.09 (m, 2H), 7.91 (d, J = 7.8 Hz, 1H), 7.79 (d, J = 7.8 Hz, 1H), 7.52−7.56 (m, 2H), 7.42−7.46 (m, 2H), 7.37−7.40 (m, 2H), 7.19 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 142.9, 131.7, 129.5, 129.1, 125.0, 124.7, 123.8, 123.7, 123.4, 122.4, 120.4, 119.5, 117.2, 115.8, 115.0, 112.4, 98.6; HRMS (ESI) m/z calcd for $C_{21}H_{14}N_3$ $[M + H]^+$ 308.1182, found 308.1189.

*13-Fluorobenzo[4,5]imidazo[1,2-a]indolo[1,2-c]quinazoline (**3f**).* Yellow solid, 107 mg, 66% yield: R_f = 0.3 (petroleum ether:EtOAc = 3:1, v:v); mp 235−237 °C (recrystallized from petroleum ether/EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.83 (d, J = 9.6 Hz, 1H), 8.30 (d, J = 7.8 Hz, 1H), 8.10−8.13 (m, 2H), 7.93 (d, J = 7.2 Hz, 1H), 7.70−7.73 (m, 1H), 7.59−7.62 (m, 1H), 7.42−7.48 (m, 3H), 7.20 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 142.9, 131.7, 129.2, 125.1, 124.6, 123.9, 122.6, 119.7, 115.2, 112.5, 112.3, 112.2, 102.9, 102.7, 98.3; HRMS (ESI) m/z calcd for $C_{21}H_{13}FN_3$ $[M + H]^+$ 326.1088, found 326.1093.

*12-Methoxybenzo[4,5]imidazo[1,2-a]indolo[1,2-c]quinazoline (**3g**).* Yellow solid, 105 mg, 62% yield: R_f = 0.2 (petroleum ether:EtOAc = 3:1, v:v); mp 229−231 °C (recrystallized from petroleum ether/EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.97 (d, J = 9.0 Hz, 1H), 8.32 (d, J = 8.4 Hz, 1H), 8.12−8.15 (m, 2H), 7.92 (d, J = 7.8 Hz, 1H), 7.59−7.63 (m, 1H), 7.39−7.47 (m, 3H), 7.23 (d, J = 2.4 Hz, 1H), 7.15−7.18 (m, 2H), 3.96 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 143.4, 143.1, 131.8, 131.7, 130.5, 130.4, 129.0, 125.0, 124.7, 123.8, 122.3, 119.5, 116.6, 115.1, 113.5, 112.5, 102.1, 98.3, 55.7; HRMS (ESI) m/z calcd for $C_{22}H_{16}N_3O$ $[M + H]^+$ 338.1288, found 338.1297.

*5,10-Dimethylbenzo[4,5]imidazo[1,2-a]imidazo[1,2-c]-quinazoline (**3h**).* Yellow solid, 82 mg, 57% yield: R_f = 0.2 (petroleum ether:EtOAc = 1:1, v:v); mp 195−197 °C (recrystallized from EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.41 (s, 1H), 8.26 (d, J = 8.4 Hz, 1H), 8.14 (s, 1H), 7.97 (s, 1H), 7.78 (d, J = 8.2 Hz, 1H), 7.60 (s, 1H), 7.55 (d, J = 8.4 Hz, 1H), 7.32 (d, J = 8.0 Hz, 1H), 2.65 (s, 3H), 2.57 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 141.2, 135.5, 133.3, 132.5, 131.5, 131.0, 130.7, 125.8, 125.1, 120.9, 119.4, 116.7, 114.9 (d, J = 6.0 Hz), 113.7, 113.2, 100.0, 22.2, 21.0; HRMS (ESI) m/z calcd for $C_{18}H_{15}N_4$ $[M + H]^+$ 287.1291, found 287.1309.

*7,12-Diisopropylbenzo[4,5]imidazo[1,2-a]benzo[4,5]imidazo[1,2-c]quinazoline (**3i**).* White solid, 139 mg, 71% yield: R_f = 0.4 (petroleum ether:EtOAc = 3:1, v:v); mp 207−209 °C (recrystallized from petroleum ether/EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.79−8.81 (m, 1H), 8.62 (d, J = 1.8 Hz, 1H), 8.32 (d, J = 8.4 Hz, 1H), 7.97−7.98 (m, 2 H), 7.84 (d, J = 8.4 Hz, 1H). 7.69−7.72 (dd, J^1 = 1.8 Hz, J^2 = 8.4 Hz, 1H), 7.53−7.56 (m, 2H), 7.36 (d, J = 8.4 Hz, 1H), 3.12−3.21 (m,

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2H), 1.40−1.43 (m, 12H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 146.3, 145.0, 144.4, 143.9, 141.6, 140.9, 132.6, 130.7, 130.5, 125.3, 124.3, 124.2, 119.7, 119.6, 115.1, 115.0, 114.5, 110.4, 34.9, 33.9, 24.7, 23.9; HRMS (ESI) m/z calcd for $C_{26}H_{25}N_4$ $[M + H]^+$ 393.2074, found 393.2058.

*5,10-Difluorobenzo[4,5]imidazo[1,2-a]imidazo[1,2-c]quinazoline (**3j**).* Yellow solid, 94 mg, 64% yield: R_f = 0.4 (petroleum ether:EtOAc = 1:1, v:v); mp 202−204 °C (recrystallized from EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.27−8.30 (m, 1H), 8.20−8.23 (m, 1H), 8.14 (d, J = 0.8 Hz, 1H), 7.83−7.87 (m, 2H), 7.64 (d, J = 0.8 Hz, 1H), 7.46−7.50 (m, 1H), 7.26−7.28 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 140.2, 138.2, 133.4, 133.1, 128.7, 120.8 (d, J = 10.2 Hz), 118.2, 118.0, 116.6 (d, J = 8.2 Hz), 114.3, 112.8, 112.7, 111.6, 111.4, 100.5, 100.3; HRMS (ESI) m/z calcd for $C_{16}H_9F_2N_4$ $[M + H]^+$ 295.0790, found 295.0797.

*10-Fluorobenzo[4,5]imidazo[1,2-a]imidazo[1,2-c]quinazoline (**3k**).* White solid, 75 mg, 54% yield: R_f = 0.3 (petroleum ether:EtOAc = 3:1, v:v); mp 193−195 °C (recrystallized from petroleum ether/EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.61 (d, J = 7.2 Hz, 1H), 8.22 (d, J = 8.0 Hz, 1H), 8.12−8.16 (m, 1H), 7.91 (d, J = 8.8 Hz, 1H), 7.82−7.84 (m, 1H), 7.76 (t, J = 7.2 Hz, 1H), 7.63 (m, 1H), 7.58 (t, J = 6.8 Hz, 1H), 7.25−7.27 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 141.0, 138.3, 132.8, 132.2, 130.7, 125.9, 125.3, 120.64, 120.57, 114.7, 113.8, 112.7, 112.5, 100.8, 100.7; HRMS (ESI) m/z calcd for $C_{16}H_{10}FN_4$ $[M + H]^+$ 277.0884, found 277.0895.

*2-(1H-Imidazol-1-yl)-1-(2-iodophenyl)-1H-benzo[d]imidazole (Intermediate **4a**).* White solid, 131 mg, 68% yield (reaction at 75 °C): R_f = 0.4 (petroleum ether:EtOAc = 4:1, v:v); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05−8.08 (m, 1H), 7.82−7.86 (m, 2H), 7.57−7.62 (m, 1H), 7.38−7.46 (m, 2H), 7.28−7.35 (m, 2H), 7.20 (s, 1H), 7.07 (s, 1H), 7.01 (d, J = 8.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 142.6, 140.9, 140.5, 137.5, 135.3, 132.0, 130.3, 129.6, 124.1, 123.9, 119.8, 118.5, 110.7, 98.4; HRMS (ESI) calcd for $C_{16}H_{12}IN_4$ $[M + H]^+$ 387.0101, found 387.0129.

*5-Phenyl-5H-benzo[d]benzo[4,5]imidazo[1,2-a]imidazole (Byproduct **5a**).* White solid: R_f = 0.3 (petroleum ether:EtOAc = 3:1, v:v); mp 142−144 °C (recrystallized from petroleum ether/EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86−7.89 (m, 4H), 7.81 (d, J = 8.0 Hz, 1H), 7.66 (t, J = 7.8 Hz, 2H), 7.59 (d, J = 7.8 Hz, 1H), 7.48 (t, J = 7.5 Hz, 1H), 7.32−7.42 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 152.4, 147.1, 135.22, 135.16, 130.1, 127.6, 124.7, 123.3, 123.2, 122.1, 120.3, 119.0, 110.9, 110.8, 110.2; HRMS (ESI) calcd for $C_{19}H_{14}N_3$ $[M + H]^+$ 284.1182, found 284.1191.

General Procedure for the Synthesis of Compound 7. An oven-dried Schlenk tube was charged with CuI (0.05 mmol), 1,10-phen (0.1 mmol), and K_3PO_4 (2 mmol). The Schlenk tube was capped and then evacuated and backfilled with N_2 (3 times). Under a positive pressure of N_2, a solution of active methylene compound **6** (0.55 mmol, 1.1 equiv) in DMSO (1.5 mL) was added via syringe, and the mixture was stirred at rt for 10 min. Then a solution of bis-(*o*-iodophenyl)carbodiimide **1** (0.5 mmol, 1.0 equiv) in DMSO (1.5 mL) was added dropwise via syringe. The Schlenk tube was sealed and allowed to prestir at 50 °C for 3 h. Then the mixture was stirred at 100 °C for 24 h. After being cooled to rt, 30 mL of EtOAc was added. The mixture was washed with brine (15 mL × 3). The organic phase was dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel using petroleum ether/EtOAc (10:1, v:v) as eluent to afford product **7**.

*Ethyl 10H-benzo[4,5]imidazo[1,2-a]indole-11-carboxylate (**7a**).* White solid, 122 mg, 88% yield (Table 3, entry 1): R_f = 0.6 (petroleum ether:EtOAc = 1:1, v:v); mp 222−224 °C (recrystallized from EtOAc); ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.10 (b, 1H), 8.22 (d, J = 7.8 Hz, 1H), 8.14 (d, J = 7.8 Hz, 1H), 8.00 (d, J = 7.8 Hz, 1H), 7.56 (d, J = 7.8 Hz, 1H), 7.39 (t, J = 7.5 Hz, 1H), 7.34 (dd, J^1 = 8.0 Hz, J^2 = 16.2 Hz, 2H), 7.23 (t, J = 7.5 Hz, 1H), 4.36 (q, J = 7.0 Hz, 2H), 1.41 (t, J = 7.0 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 164.2, 138.4, 136.3, 127.2, 126.4, 124.1, 123.3, 121.9, 120.3, 112.5, 111.8, 100.0, 59.0, 15.4; HRMS (ESI) m/z calcd for $C_{17}H_{15}N_2O_2$ $[M + H]^+$ 279.1128, found 279.1121.

*Methyl 10H-benzo[4,5]imidazo[1,2-a]indole-11-carboxylate (**7b**).* White solid, 106 mg, 80% yield (Table 3, entry 2): R_f = 0.2 (petroleum ether:EtOAc = 3:1, v:v); mp 214−216 °C (recrystallized from petroleum ether/EtOAc); ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.21 (b, 1H), 8.21 (d, J = 7.8 Hz, 1H), 8.13 (d, J = 7.8 Hz, 1H), 7.99 (d, J = 7.2 Hz, 1H), 7.55 (d, J = 7.8 Hz, 1H), 7.37−7.40 (m, 1H), 7.33 (dd, J^1 = 7.2 Hz, J^2 = 14.4 Hz, 2H), 7.22 −7.25 (m, 1H), 3.87 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 164.4, 147.2, 136.3, 136.1, 130.8, 127.3, 126.4 (d, J = 3.6 Hz), 124.1, 123.3, 121.9 (d, J = 1.8 Hz), 120.3 (d, J = 1.2 Hz), 120.1, 112.44, 112.40, 111.8 (d, J = 5.6 Hz), 50.7; HRMS (ESI) m/z calcd for $C_{16}H_{13}N_2O_2$ $[M + H]^+$ 265.0972, found 265.0967.

*10H-Benzo[4,5]imidazo[1,2-a]indole-11-carbonitrile (**7c**).* White solid, 84 mg, 73% yield: R_f = 0.5 (petroleum ether:EtOAc = 1:1, v:v); mp 197−199 °C (recrystallized from petroleum ether/EtOAc); ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.84 (b, 1H), 8.23 (d, J = 7.8 Hz, 1H), 8.19 (d, J = 7.8 Hz, 1H), 7.59 (d, J = 7.8 Hz, 1H), 7.50 (d, J = 7.8 Hz, 1H), 7.39 (t, J = 7.6 Hz, 1H), 7.36 (d, J = 7.2 Hz, 1H), 7.34 (d, J = 7.2 Hz, 1H), 7.27−7.30 (m, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 147.7, 136.1, 131.9, 126.6, 126.2, 124.4, 123.5, 122.0, 120.9, 118.2, 112.3, 112.2, 111.9; HRMS (ESI) m/z calcd for $C_{15}H_{10}N_3$ $[M + H]^+$ 232.0869, found 232.0875.

*Ethyl 2,7-dimethyl-10H-benzo[4,5]imidazo[1,2-a]indole-11-carboxylate (**7d**).* White solid, 132 mg, 86% yield: R_f = 0.5 (petroleum ether:EtOAc = 1:1, v:v); mp 213-215 °C (recrystallized from EtOAc); ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.91 (b, 1H), 8.03 (s, 1H), 8.00 (d, J = 8.1 Hz, 1H), 7.79 (s, 1H), 7.41 (d, J = 8.1 Hz, 1H), 7.17 (d, J = 8.1 Hz, 1H), 7.04 (d, J = 8.2 Hz, 1H), 4.34 (q, J = 7.1 Hz, 2H), 2.52 (s, 3H) (overlapped with the signal of DMSO-d_6), 2.47 (s, 3H), 1.39 (t, J = 7.1 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.2, 145.4, 134.1, 132.1, 131.5, 126.6, 125.5, 124.6, 121.2, 120.3, 112.0, 111.9, 111.4, 100.0, 58.8, 22.0, 21.5, 15.4; HRMS (ESI) m/z calcd for $C_{19}H_{19}N_2O_2$ $[M + H]^+$ 307.1441, found 307.1453.

*Ethyl 2,7-diisopropyl-10H-benzo[4,5]imidazo[1,2-a]indole-11-carboxylate (**7e**).* White solid, 138 mg, 76% yield: R_f = 0.3 (petroleum ether:EtOAc = 3:1, v:v); mp 215−217 °C (recrystallized from petroleum ether/EtOAc); ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.89 (b, 1H), 8.09 (d, J = 8.2 Hz, 1H), 8.01 (s, 1H), 7.89 (s, 1H), 7.45 (d, J = 8.2 Hz, 1H), 7.25 (d, J = 8.2 Hz, 1H), 7.10 (dd, J^1 = 1.2 Hz, J^2 = 8.2 Hz, 1H), 4.36 (q, J = 7.1 Hz, 2H), 3.03−3.13 (m, 2H), 1.41 (t, J = 7.1 Hz, 3H), 1.30−1.35 (m, 12 H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.2, 147.6, 143.5, 142.9, 134.4, 131.0, 126.7, 125.7, 121.9, 118.7, 117.5, 112.1, 111.6, 109.4, 58.8, 34.3, 34.2, 25.0, 24.9, 15.4; HRMS (ESI) m/z calcd for $C_{23}H_{27}N_2O_2$ $[M + H]^+$ 363.2067, found 363.2101.

*Ethyl 2,7-dichloro-10H-benzo[4,5]imidazo[1,2-a]indole-11-carboxylate (**7f**).* Yellow solid, 122 mg, 70% yield: R_f = 0.5 (petroleum ether:EtOAc = 1:1, v:v); mp 231−233 °C (recrystallized from EtOAc); ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.88 (b, 1H), 8.00 (s, 1H), 7.98 (d, J = 8.2 Hz, 1H), 7.78 (s, 1H), 7.41 (d, J = 8.2 Hz, 1H), 7.17 (d, J = 8.2 Hz, 1H), 7.03 (d, J = 8.2 Hz, 1H), 4.33 (q, J = 7.1 Hz, 2H), 1.38 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.5, 147.7, 138.5, 131.5, 128.8, 128.7, 125.9, 125.5, 124.9, 121.2, 120.8, 111.8, 109.7, 100.0, 59.0, 22.0; HRMS (ESI) m/z calcd for $C_{17}H_{13}Cl_2N_2O_2$ $[M + H]^+$ 347.0349, found 347.0356.

*Ethyl 7-fluoro-10H-benzo[4,5]imidazo[1,2-a]indole-11-carboxylate (**7g**) and Ethyl 2-fluoro-10H-benzo[4,5]imidazo[1,2-a]indole-11-carboxylate (**7g′**).* Mole ratio = 69:31 (approximately determined by ^{1}H NMR). Yellow solid, 105 mg, 71% yield (total): R_f = 0.6 (petroleum ether:EtOAc = 1:1, v:v). **Major** (approximate attributions): ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.1 (b, 1H), 8.18−8.21 (m, 2H), 7.99 (t, J = 6.8 Hz, 1H), 7.52−7.56 (m, 1H), 7.30−7.40 (m, 2H), 7.22 (t, J = 7.8 Hz, 1H), 4.35 (q, J = 7.0 Hz, 2H), 1.40 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.2, 136.2, 136.1, 127.2, 126.4, 124.2, 123.6, 122.1, 120.3, 118.6, 112.8, 112.4, 111.8, 107.2, 100.0, 58.9, 15.4. **Minor** (approximate attributions): ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.2 (b, 1H), 8.10−8.15 (m, 2H), 7.62−7.65 (m, 1H), 7.48−7.52 (m, 1H), 7.30−7.40 (m, 2H), 7.00−7.05 (m, 1H), 4.35 (q, J = 7.0 Hz, 2H), 1.40 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.2, 136.6, 135.9, 127.4, 126.2, 124.1, 123.3, 121.9, 120.2, 118.4, 112.8, 112.6, 111.7, 107.4, 100.9, 59.2, 15.3.

*Methyl 7-methyl-10H-benzo[4,5]imidazo[1,2-a]indole-11-carboxylate (**7h**).* Yellow solid, 104 mg, 75% yield: R_f = 0.5 (petroleum ether:EtOAc = 1:1, v:v); mp 209−211 °C (recrystallized from petroleum ether/EtOAc); ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.00 (b, 1H), 7.99−8.02 (m, 2H), 7.68−7.84 (m, 2H), 7.40 (d, J = 7.2 Hz, 1H), 7.17 (d, J = 7.2 Hz, 1H), 7.03 (d, J = 7.2 Hz, 1H), 3.85 (s, 3H), 2.47 (s, 3H); ^{13}C NMR(150 MHz, DMSO-d_6) δ 160.4, 134.1, 132.2, 131.5,

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126.6, 125.5, 124.6, 121.2, 120.1, 112.0, 111.9, 111.4, 50.6, 22.0; HRMS (ESI) m/z calcd for $C_{17}H_{15}N_2O_2$ $[M + H]^+$ 279.1128, found 279.1120.

*Ethyl 7-fluoro-10H-benzo[4,5]imidazo[1,2-a]indole-11-carboxylate (**7i**).* Yellow solid, 114 mg, 77% yield: R_f = 0.6 (petroleum ether:EtOAc = 1:1, v:v); mp 201−203 °C (recrystallized from petroleum ether/EtOAc); ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.11 (b, 1H), 8.13−8.29 (m, 2H), 7.93−8.00 (m, 1H), 7.49−7.56 (m, 1H), 7.29−7.40 (m, 2H), 7.21−7.25 (m, 1H), 4.35 (q, J = 6.9 Hz, 2H), 1.40 (t, J = 6.9 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 164.9, 133.5, 132.8, 127.0, 123.6, 121.9, 120.3, 112.0, 111.8, 111.0, 110.8, 100.0 (d, J = 7.0 Hz), 59.0, 15.4; HRMS (ESI) m/z calcd for $C_{17}H_{14}FN_2O_2$ $[M + H]^+$ 297.1034, found 297.1043.

General Procedure for the Synthesis of Compound 8. An oven-dried Schlenk tube was charged with CuI (0.05 mmol), 1,10-phen (0.1 mmol), and K_3PO_4 (1 mmol). The Schlenk tube was capped and then evacuated and backfilled with N_2 (3 times). Under a positive pressure of N_2, a solution of active methylene compound **6** (0.55 mmol, 1.1 equiv) in DMSO (1.5 mL) was added via syringe, and the mixture was stirred at rt for 10 min. Then a solution of bis-(*o*-iodophenyl)carbodiimide **1** (0.5 mmol, 1.0 equiv) in DMSO (1.5 mL) was added dropwise via syringe. The Schlenk tube was allowed to prestir at rt for about 2 h. Then the mixture was immediately stirred at 140 °C for about 3 h. After being cooled, additional equivalent of K_3PO_4 (0.5 mmol) was added under a positive pressure of N_2. The Schlenk tube was sealed and allowed to continue stir at 140 °C for 21 h. After being cooled to rt, 30 mL of EtOAc was added. The mixture was washed with brine (15 mL × 3). The organic phase was dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel using petroleum ether/EtOAc (10:1, v:v) as eluent to afford product **8**.

*Methyl 10-methyl-10H-benzo[4,5]imidazo[1,2-a]indole-11-carboxylate (**8a**).* Yellow solid, 100 mg, 72% yield (Scheme 3, entry 1): R_f = 0.4 (petroleum ether:EtOAc = 1:1, v:v); mp 204−206 °C (recrystallized from petroleum ether/EtOAc); ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.22 (d, J = 7.8 Hz, 1H), 8.12 (d, J = 7.8 Hz, 1H), 8.07 (d, J = 7.8 Hz, 1H), 7.65 (d, J = 7.8 Hz, 1H), 7.45 (t, J = 7.5 Hz, 1H), 7.39 (t, J = 7.5 Hz, 1H), 7.32 (t, J = 7.5 Hz, 1H), 7.25 (t, J = 7.5 Hz, 1H), 4.23 (s, 3H), 3.86 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 164.7, 137.8, 131.7, 131.2, 126.7, 125.9, 124.1, 123.4, 122.4, 121.2, 120.7, 111.6, 111.4, 110.9, 100.0, 50.9, 32.4; HRMS (ESI) m/z calcd for $C_{17}H_{15}N_2O_2$ $[M + H]^+$ 279.1128, found 279.1131.

Important Crystal Data for 8a. $C_{17}H_{14}N_2O_2$, M = 278.30, monoclinic, space group $P21/n$, a = 11.3450(7) Å, b = 8.1717(6) Å, c = 14.9978(9) Å, V = 1344.91(15) Å^3, Z = 4, T = 170(2) K, 5419 reflections collected, 2451 independent reflections, Final R = 0.0533, wR = 0.0978, GoF = 1.057 for 2451 reflections with $I > 2\sigma(I)$ and 192 parameters. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre: deposition no. CCDC-975905.

*Methyl 2,7,10-trimethyl-10H-benzo[4,5]imidazo[1,2-a]indole-11-carboxylate (**8b**).* Yellow solid, 95 mg, 62% yield: R_f = 0.6 (petroleum ether:EtOAc = 1:1, v:v); mp 195−197 °C (recrystallized from petroleum ether/EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.64 (s, 1H), 7.23 (d, J = 8.2 Hz, 1H), 7.18 (d, J = 8.1 Hz, 1H), 7.08 (d, J = 8.0 Hz, 1H), 4.29 (s, 3H), 3.98 (s, 3H), 2.58 (s, 3H), 2.55 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.6, 135.7, 132.6, 131.7, 125.2, 123.9, 121.5, 121.2, 111.2, 110.0, 109.1, 50.6, 32.1, 21.9, 21.6; HRMS (ESI) m/z calcd for $C_{19}H_{19}N_2O_2$ $[M + H]^+$ 307.1441, found 307.1447.

*Methyl 2,7-difluoro-10-methyl-10H-benzo[4,5]imidazo[1,2-a]-indole-11-carboxylate (**8c**).* Yellow solid, 101 mg, 64% yield: R_f = 0.6 (petroleum ether:EtOAc = 1:1, v:v); mp 174−176 °C (recrystallized from petroleum ether/EtOAc); ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.23−8.26 (m, 1H), 8.18−8.20 (m, 1H), 7.69−7.71 (m, 1H), 7.65−7.66 (m, 1H), 7.28−7.32 (m, 1H), 7.01−7.05 (m, 1H), 4.20 (s, 3H), 3.86 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 164.8, 133.5, 132.8, 127.0, 124.1, 123.6, 123.3, 122.5, 121.9, 120.3, 112.5, 112.0, 111.8, 111.0, 100.0, 59.0, 31.2; HRMS (ESI) calcd for $C_{17}H_{13}F_2N_2O_2$ $[M + H]^+$ 315.0940, found 315.0948.

*Dimethyl 2-(bis((2-iodophenyl)amino)methylene)malonate (Intermediate **9a**).* Yellow solid, 275 mg, 95% yield (reaction at 100 °C): R_f = 0.6 (petroleum ether:EtOAc = 3:1, v:v); mp 160−162 °C (recrystallized from EtOAc/EtOH); ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.25 (b, 2H), 7.57−7.58 (m, 2H), 6.99−7.04 (m, 4H), 6.56−6.59 (m, 2H), 3.85 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.2, 158.7, 139.3, 138.8, 128.2, 126.2, 123.8, 93.6, 80.4, 51.8; HRMS (ESI) calcd for $C_{18}H_{17}I_2N_2O_4$ $[M + H]^+$ 578.9272, found 578.9293.

Procedure for the *N*-Methylation of 7b Using MeI. Compound **7b** (0.3 mmol, 1.0 equiv), K_2CO_3 (0.6 mmol, 2.0 equiv), and a solution of methyl iodide (0.45 mmol, 1.5 equiv) in DMF (20 mL) were successively added to a flask under an N_2 atmosphere. The mixture was heated to 50 °C for 12 h. After being cooled to rt and quenched by aq. sat. Na_2SO_3 (5 mL), 30 mL of EtOAc was added. The organic phase was separated, washed by water (15 mL × 3), and dried over Na_2SO_4. The solvent was removed in vacuo, and the resulting residue was purified by column chromatography on silica gel using petroleum ether/EtOAc (10:1, v:v) as eluent to afford the product as a yellow solid (75 mg, 90% yield). Its spectral data (^{1}H NMR and ^{13}C NMR) are in good accordance with those of product **8a**.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra for the products, X-ray crystal structure of **8a**, and X-ray data for **8a** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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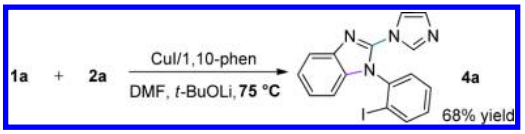
(16) For previous reports about the copper-mediated one-pot synthesis of benzimidazole derivatives from carbodiimides, see the following. (a) Synthesis of 2-aminobenzimidazoles from the reaction of *o*-haloanilines with carbodiimides: Wang, F.; Cai, S. J.; Liao, Q.; Xi, C.-J. *J. Org. Chem.* **2011**, *76*, 3174. (b) Synthesis of 2-aminobenzimidazoles from the reaction of arylcarbodiimides with amines (under O_2): He, H. F.; Wang, Z. J.; Bao, W. L. *Adv. Syn. Catal.* **2010**, *352*, 2905. (c) Synthesis of benzoxazoles and benzimidazoles from the reaction of arylcarbodiimides with *o*-halophenols/*o*-haloanilines: Shen, G. D.; Bao, W. L. *Adv. Synth. Catal.* **2010**, *352*, 981. (d) Synthesis of 2-heterobenzimidazoles from the reaction of *o*-haloaryl carbodiimides with amines/imidazoles/phenols: Lv, X.; Bao, W. L. *J. Org. Chem.* **2009**, *74*, 5618.

(17) We found that better results could be obtained when the reaction was carried out under the conditions similar to those developed by Daugulis et al., which were successfully applied for the intermolecular sp^2 C−H arylations of electron-poor arenas/heteroarenes with aryl halides: (a) Do, H.-Q.; Khan, R. M. K.; Daugulis, O. *J. Am. Chem. Soc.* **2008**, *130*, 15185. (b) Do, H.-Q.; Daugulis, O. *J. Am. Chem. Soc.* **2008**, *130*, 1128.

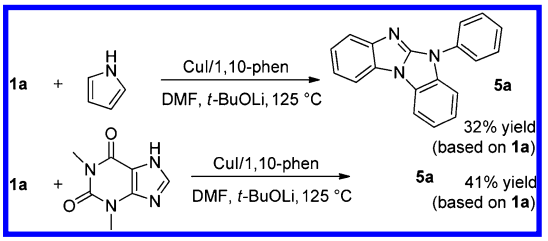
(18) The spectral data of compound **3a** are in good accordance with those in a previous report (ref 6b).

(19) During the preliminary study, we found that monocyclized product **4a** was isolated as the sole product when the reaction was performed at 75 °C, indicating that a higher temperature was necessary for the second cyclization process:



(20) There are rare reports about the Cu-catalyzed domino transformations with intramolecular sp^2 C−H arylation of azoles as the key step; see: ref 14b, c.

(21) We have also attempted to use other azoles such as pyrrole and theophylline as the reagents. Unfortunately, in both cases, no desired double-cyclized product was observed, and moderate yields of unexpected byproduct **5a** were isolated. The pathway to the unexpected byproduct is uncertain, and the mechanism study is currently underway.

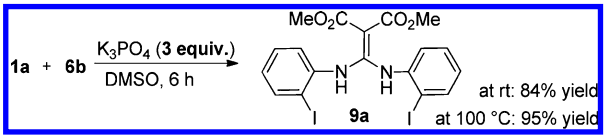


(22) One of the products (**7b**) can be conveniently *N*-methylated using MeI, and the derivative (**8a**) was ascertained by the X-ray crystal diffraction analysis. For details, see the Experimental Section.

(23) The pathway to the unexpected byproduct is uncertain, and the mechanism study is currently underway.

(24) These byproducts were unstable and could not be separated.

(25) The control experiment indicated that without the addition of Cu catalyst, only addition intermediate **9a** was generated and no cyclized product formed:



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