Organic & Biomolecular Chemistry

Cite this: *Org. Biomol. Chem.*, 2012, **10**, 1602

www.rsc.org/obc

PAPER

Copper-catalyzed domino intramolecular cyclization: a facile and efficient approach to polycyclic indole derivatives†

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Received 30th August 2011, Accepted 16th November 2011
DOI: 10.1039/c1ob06488f

A mild and efficient Cu_2O-catalyzed domino intramolecular C–N coupling/C–Y (Y = O, S, N) bond formation was successfully achieved. Thus oxazino[3,2-*a*]indole, thiazino[3,2-*a*]indole and indolo[2,1-*b*]quinazoline derivatives were facilely assembled from readily accessible *gem*-dibromovinyl systems. The protocol is general and practical, affording a variety of the indole-incorporated products in good to excellent yields even under air atmosphere.

Introduction

Indole moiety is a privileged structural motif in many biologically active and medicinally valuable molecules.[1] The indole-incorporated oxazino[3,2-*a*]indole and indolo[2,1-*b*]quinazoline derivatives have been known as important heterocycles in pharmaceutical areas (Fig. 1). For example, SB-207266 and its metabolites **(A)** exhibit 5-HT_4 receptor antagonist activity and are used to control cardiovascular or gastrointestinal disorders;[2] indo[2,1-*b*][1,3]benzoxazines **(B)** are potent drugs for the treatment of atrial arrhythmia and CNS disorders;[3] tryptanthrins and their analogues **(C)**, which possess various biological activities,[4] have aroused great interest as antibacterial,[5] antifungal,[6] and anticancer[4b,7] agents; several indolo[2,1-*b*]quinazoline-12-ones **(D)** show remarkable antileishmanial activity.[8]

Although oxazino[3,2-*a*]indole and indolo[2,1-*b*]quinazoline derivatives play important roles in biological and medicinal areas, few approaches to these compounds have been developed to date. These molecules could be elaborated *via* multiple steps from indole or its derivatives,[2a,2d,4b] but the methods may suffer from tedious procedures, poor precursor scopes, and/or low efficiency.

In the last decade, copper-mediated coupling strategies have drawn much attention for their low cost and high efficiency.[9] And recently, Cu-catalyzed carbon-heteroatom coupling has become a powerful tool for the assembly of various useful heterocyclic compounds *via* one-pot protocols.[10–12]

The readily available *gem*-dihalovinyl systems have been employed for the one-pot synthesis of various 2-substituted indole heterocycles.[13,14] For example, Lautens and co-workers developed a Cu-catalyzed intramolecular double amidation to form imidazoindolones using *gem*-dibromovinyl systems.[13j] Recently, it was reported that certain novel polycyclic indole derivatives were assembled from *gem*-dihalovinyl systems *via* Pd-catalyzed Suzuki–Miyaura coupling/direct arylation,[13d] Pd-catalyzed amination/direct arylation,[13f] Cu-catalyzed coupling/Pd-catalyzed C–H activatioon,[14b] and nucleophilic addition/Cu-catalyzed *N*-arylation/Pd-catalyzed arylation processes.[14c] These strategies provided efficient and facile access to the novel polycyclic indole derivatives.

However, to the best of our knowledge, there is no report for the one-pot synthesis of oxazino[3,2-*a*]indole and indolo[2,1-*b*]quinazoline derivatives, which are of potentially biological and medicinal value. And as far as we know, copper-catalyzed cascade intramolecular C–N coupling/C–Y (Y = O, S) bond formation has not been explored. In addition, although Cu-catalyzed tandem intramolecular amidation/amidation has been reported,[13j] there is no report about Cu-catalyzed domino intramolecular amidation/amination.

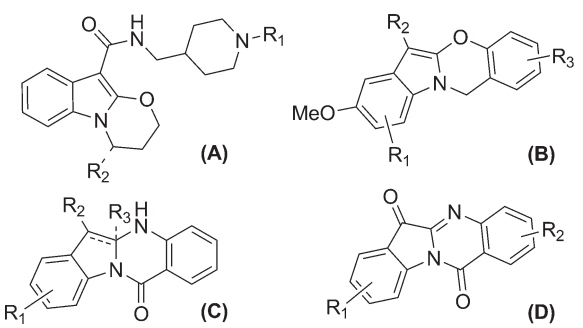

Fig. 1 Several biologically and medicinally valuable oxazino[3,2-*a*]indol-12-ones and indolo[2,1-*b*]quinazolin-12-ones.

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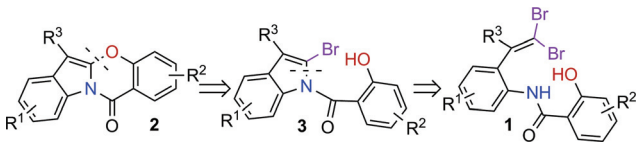
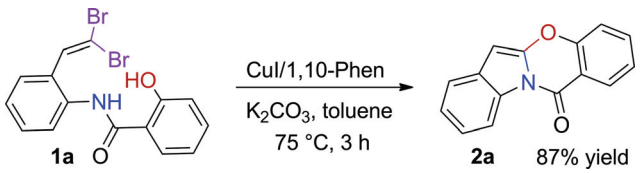
†Electronic supplementary information (ESI) available: characterization data for the substrates, intermediates and by-product, X-ray crystallographic information of product **2a**, and spectra for the compounds. CCDC reference number 832179. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c1ob06488f



Scheme 1 Retrosynthesis of benzoxazino[3,2-*a*]indol-12-ones.



Scheme 2 The first approach to **2a**.

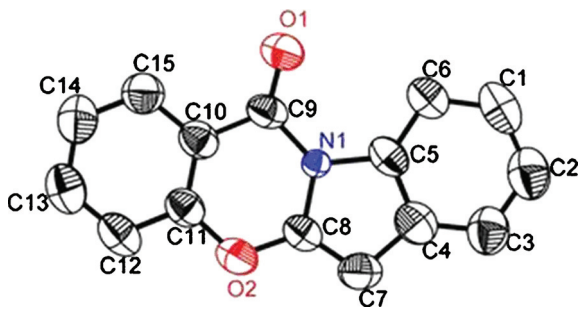


Fig. 2 The X-ray crystal structure of **2a**.

In the context of developing a domino coupling for the assembly of oxazino[3,2-*a*]indole and indolo[2,1-*b*]quinazoline derivatives using readily available *gem*-dibromovinyl substrates, we conceived that benzoxazino[3,2-*a*]indol-12-one **2** might be synthesized from *o*-*gem*-dibromovinyl salicylanilide **1** *via* Cu-catalyzed domino intramolecular C–N coupling/C–O bond formation process (Scheme 1).

Results and discussion

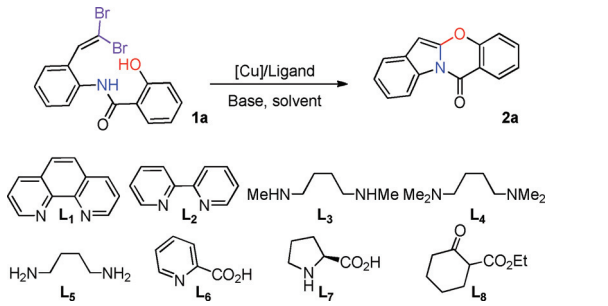
The first approach

During our initial studies, *o*-*gem*-dibromovinyl salicylanilide **1a**, which could be conveniently synthesized from *o*-*gem*-dibromovinylaniline and salicylic acid,[15] was employed as the substrate. The first attempt was carried out using **1a** in the presence of CuI (10 mol%), 1,10-phenanthroline (1,10-Phen, 20 mol%), and K_2CO_3 (4 equiv) in dry toluene under nitrogen atmosphere at 75 °C (Scheme 2). Fortunately, the desired polycyclic product **2a** was successfully isolated after 3 h. The colourless single crystals of **2a** were obtained by recrystallization in ethyl acetate/petroleum ether (1 : 10, v:v) at room temperature. And the structure of **2a** was ascertained unambiguously by the X-ray crystal diffraction analysis (Fig. 2).

Optimization of the reaction

The optimization of the reaction conditions was performed and the results were listed in Table 1. Initially, the reaction temperature was investigated (Entries 1–3). Lowering the temperature from 75 °C to 70 °C did not bring about obvious change in the efficiency (Entry 2), but a further decrease in the temperature to 50 °C caused drastic drop in the yield (47%) and longer reaction time (>24 h) (Entry 3). Considering that the ligand type may influence the domino transformation, a range of ligands were therefore screened (Entries 2 and 4–10, **L_1–L_8**). 1,10-Phenanthroline and 2,2′-bipyridine gave good results, but DMEDA was the optimal ligand (Entry 5 *vs.* Entries 2 and 4). DMEDA gave the cleanest reaction, affording **2a** in excellent yield within 1 h (Entry 5, 95% yield). It should be noted that in the absence of ligand, the desired product was obtained only in 20% yield (Entry 11). The influence of solvents was also investigated (Entries 5 and 12–15). DMF, CH_3CN and 1,2-dimethoxyethane (DME) afforded lower yields. Both dioxane and toluene gave satisfactory yields, and toluene was slightly superior to dioxane (Entry 5 *vs.* Entry 13). Therefore, toluene was chosen as the best solvent. It was found that a Cu-catalyst was essential for the

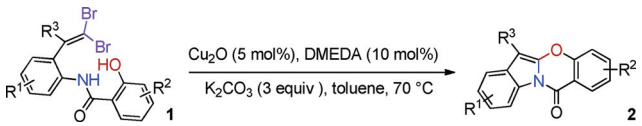
Table 1 Optimization of the reaction conditions



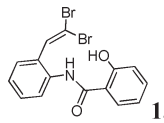
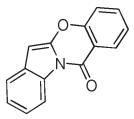
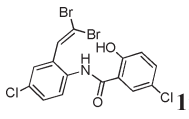
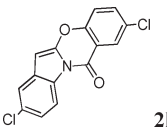
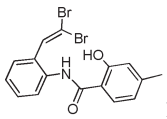
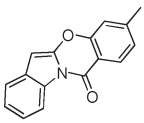
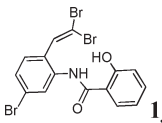
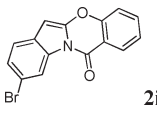
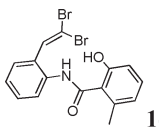
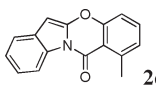
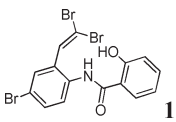
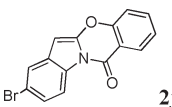
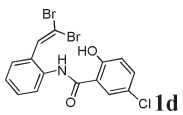
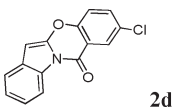
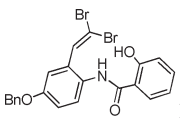
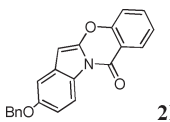
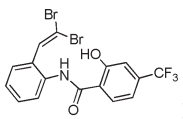
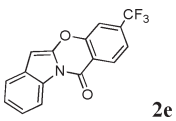
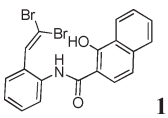
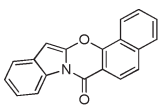
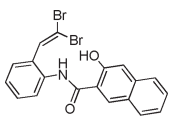
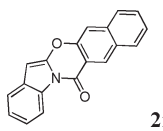
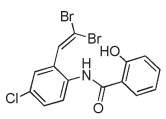
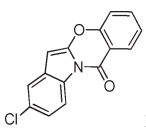
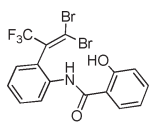
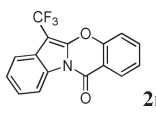
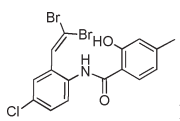
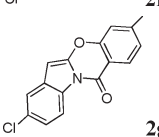
Entry	[Cu]	L	Solvent	*T*/°C	Time (h)	Yield (%)[a,b]
1	CuI	L_1	Toluene	75	3	87
2	CuI	L_1	Toluene	70	3	87
3	CuI	L_1	Toluene	50	24	47
4	CuI	L_2	Toluene	70	3	86
5	CuI	L_3	Toluene	70	1	95
6	CuI	L_4	Toluene	70	24	32
7	CuI	L_5	Toluene	70	24	38
8	CuI	L_6	Toluene	70	24	15
9	CuI	L_7	Toluene	70	24	6
10	CuI	L_8	Toluene	70	24	19
11	CuI	—	Toluene	70	24	20
12	CuI	L_3	DMF	70	1	49
13	CuI	L_3	Dioxane	70	1	92
14	CuI	L_3	CH_3CN	70	15	46
15	CuI	L_3	DME	70	15	61
16	CuBr	L_3	Toluene	70	3	95
17	CuCl	L_3	Toluene	70	1	95
18	Cu_2O	L_3	Toluene	70	1	96
19	$Cu(OAc)_2·H_2O$	L_3	Toluene	70	5	87
20	—	L_3	Toluene	70	30	n.d.[c]
21	Cu_2O	L_3	Toluene	70	1	96[d]
22	Cu_2O	L_3	Toluene	70	1	96[d,e]
23	Cu_2O	L_3	Toluene	70	1	90[d,f]
24	Cu_2O	L_3	Toluene	70	1	91[d,e,g]

[a] Reaction conditions: substrate **1a** (0.5 mmol), copper-catalyst (0.05 mmol, 10 mol%), ligand (0.10 mmol, 20 mol%), K_2CO_3 (4 equiv), in solvent (3 mL), under N_2. [b] Isolated yield. [c] n.d. = not detected. [d] Cu_2O (5 mol%) as the catalyst and DMEDA (10 mol%) as the ligand. [e] K_2CO_3 (3 equiv) was used as the base. [f] K_2CO_3 (2 equiv) was used as the base. [g] Under common conditions: in commercial toluene under air atmosphere.

Table 2 Domino intramolecular C–N/C–O bond formation reactions



1 2

Entry	Substrate	Product	Time, yield[a,b]	Entry	Substrate	Product	Time, yield[a,b]
1	 1a	 2a	1 h, 96% 1 h, 91%[c]	9	 1i	 2h	6 h, 93%
2	 1b	 2b	1 h, 94% 3 h, 91%[c]	10	 1j	 2i	1 h, 96%
3	 1c	 2c	3 h, 90% 0.5 h, 58%[d]	11	 1k	 2j	6 h, 94%
4	 1d	 2d	6 h, 91% 6 h, 88%[c]	12	 1l	 2k	6 h, 81%
5	 1e	 2e	2 h, 96%	13	 1m	 2l	1 h, 94% 1 h, 93%[c]
6	 1f	—	24 h, trace	14	 1n	 2m	1 h, 96%
7	 1g	 2f	5 h, 97% 6 h, 90%[c]	15	 1o	 2n	6 h, 76%
8	 1h	 2g	6 h, 85%				

[a] Reaction conditions: substrate **1** (0.5 mmol), Cu_2O (0.025 mmol, 5 mol%), DMEDA (0.05 mmol, 10 mol%), K_2CO_3 (3 equiv), in toluene (3 mL), under N_2, at 70 °C. [b] Isolated yield. [c] Under common conditions: in commercial toluene under air atmosphere. [d] The intermediate (2-bromo-1*H*-indol-1-yl)(2-hydroxy-6-methylphenyl)methanone **3a** was also isolated (in 33% yield).

tandem cyclization (Entry 20). Different copper sources were also examined. Among the tested Cu-catalysts such as CuI, CuCl, CuBr, $Cu(OAc)_2{\cdot}H_2O$ and Cu_2O (Entries 5 and 16–19), Cu_2O performed the best and gave **2a** in 96% yield (Entry 18). Reducing the amount of the Cu-catalyst and ligand to 5 mol% and 10 mol%, respectively, did not affect the efficiency (Entry 21). We also examined the influence of the base. Different bases including K_2CO_3, K_3PO_4, Na_2CO_3 and Cs_2CO_3 were evaluated during the preliminary investigation. The results showed that K_3PO_4 and Na_2CO_3 were less effective. Both K_2CO_3 and Cs_2CO_3 were equally efficient. With respect to the lower cost, K_2CO_3 was chosen as the optimal base for the reaction. Three equivalents of the base seemed to be suitable for the reaction (Entries 21–23). An additional experiment showed that the reaction could also proceed smoothly under the common conditions (in commercial toluene under air atmosphere, Entry 24).

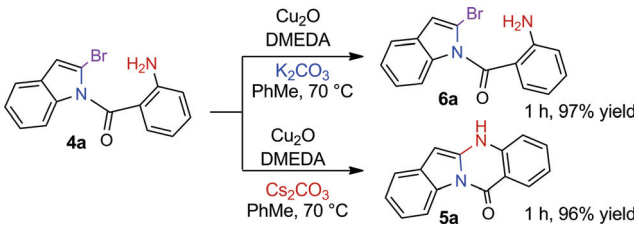
Scope of the reaction

Domino intramolecular C–N coupling/C–O bond formation reactions. After the optimized conditions were established, we then investigated the generality of this Cu-catalyzed domino reaction by using a variety of the substrates (Table 2). Most of the substituted *o-gem*-dibromovinyl substrates reacted smoothly

and afforded the desired polycyclic products in excellent yields within 6 h. As shown in Table 2, both electron-donating groups (Entries 2–3 and 12–14) and electron-withdrawing groups (Entries 4–5, 7–11 and 15) on the indolyl or phenyl ring were well tolerated. However, the *o-gem*-dibromovinyl salicylanilide bearing two strongly electron-withdrawing groups on the phenyl ring gave the desired tetracyclic product only in trace amount (Entry 6), due probably to the weakening of the nucleophilicity of both the NH and OH groups. It was noteworthy that the domino reactions seemed insensitive to the *ortho*-steric hindrance on the aryl ring. 4-Methyl-12*H*-benzo[5,6]-[1,3]oxazino [3,2-*a*]indol-12-one **2c** could be smoothly assembled from the corresponding substrate **1c** (Entry 3). And interestingly, both the *o-gem*-dibromovinyl systems bearing 3-hydroxy-2-naphthoyl and 2-hydroxy-1-naphthoyl could efficiently afford the pentacyclic products within 1 h (Entries 13 and 14). The method was also viable for the synthesis of 6-substituted benzoxazino[3,2-*a*] indol-12-one derivatives (Entry 15).

Intermediates **3** could also be isolated from the reaction mixtures, indicating that the reaction might occur in the desired manner. For example, reducing the reaction time of **1c** to 0.5 h gave a mixture of the desired product **2c** and the intermediate **3a** (in 58% and 33% yield, respectively) (Table 2, Entry 3).

Domino intramolecular C–N coupling/C–N (or C–S) bond formation reactions. Having developed an efficient protocol for the synthesis of benzoxazino[3,2-*a*]indol-12-ones, we then sought to extend the protocol to assemble indolo-[2,1-*b*]quinazolin-12-ones. Initially, compound **4a** was used as the starting material. The first attempt was also carried out under the above optimized conditions. However, no desired double cyclized product **5a** was observed, and the intermediate *N*-anthraniloyl 2-bromoindole **6a** was isolated in 97% yield, indicating that the second cyclization might be more difficult than the first. Increasing the reaction temperature and changing the solvent did not improve the result. Interestingly, when K_2CO_3 was replaced by Cs_2CO_3, the desired polycyclic product **5a** could be obtained in excellent yield within 1 h (Scheme 3). In addition to the stronger basicity of Cs_2CO_3, its good solubility in toluene may play the major role in this case.[9a]

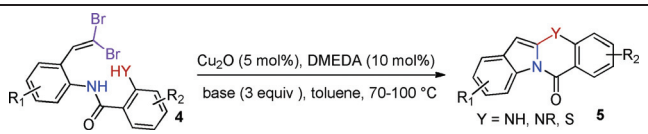


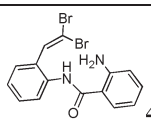
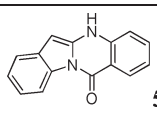
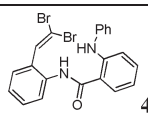
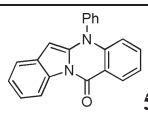
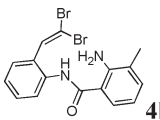
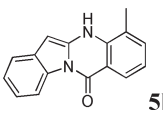
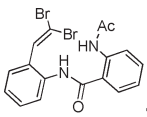
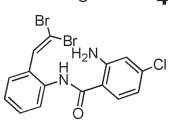
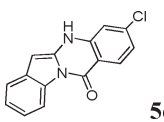
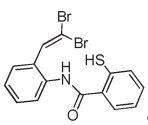
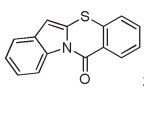
Scheme 3 The reaction of **4a** under different conditions.

Further investigation proved that Cu_2O was the best catalyst and DMEDA was the optimal ligand for this domino process. On the basis of these results, the optimal conditions for the reactions of indolo-[2,1-*b*]quinazolin-12-ones were established as the following: in toluene under N_2 at 70 °C with Cu_2O (5 mol%) as catalyst along with DMEDA (10 mol%) as additive and Cs_2CO_3 (3 equiv) as base.

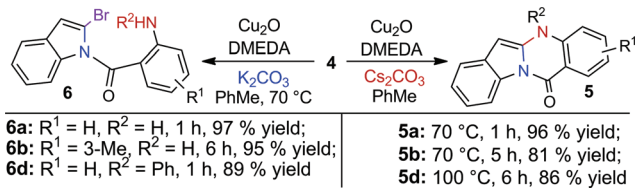
Under the above modified conditions, a series of 2-amino-*N*-(2-(2,2-dibromovinyl)phenyl)-benzamides **4**[16] were utilized to examine the scope of the reaction (Table 3, entries 1–5). Generally, the electron-rich and electron-deficient groups (such as Me, Ph, and Cl) on the aryl was well tolerated (Entries 1–4). However, the double cyclization required longer reaction time and/or higher temperature due to the impact of the steric hindrance (Entries 2 and 4). An *N*-acetyl substrate was also investigated, but an inseparable mixture was obtained because of the instability of the desired product (Entry 5). Under the common conditions, the reactions also proceeded successfully (Entries 1 and 4).

Table 3 Domino intramolecular C–N/C–N (or C–S) bond formation reactions



Entry	Substrate	Product	Time, yield[a,b]	Entry	Substrate	Product	Time, yield[a,b]
1	 **4a**	 **5a**	1 h, 96% 1 h, 90%[d]	4	 **4d**	 **5d**	6 h, 86%[c] 6 h, 82%[c,d]
2	 **4b**	 **5b**	5 h, 81%	5	 **4e**	—[e]	24 h, 95%[f]
3	 **4c**	 **5c**	2 h, 94%	6	 **4f**	 **5e**	18 h, 80%[g]

[a] Reaction conditions: substrate **4** (0.5 mmol), Cu_2O (0.025 mmol, 5 mol%), DMEDA (0.05 mmol, 10 mol%), Cs_2CO_3 (3 equiv), in toluene (3 mL), at 70 °C. [b] Isolated yield. [c] At 100 °C. [d] Under common conditions. [e] An inseparable mixture was obtained. [f] Conversion. [g] Using K_2CO_3 as the base, at 70 °C; the intermediate (2-bromo-1*H*-indol-1-yl) (2-mercaptophenyl)methanone **6e** was also isolated (in 17% yield).



Scheme 4 Selective synthesis of monocyclized and double cyclized products.

In order to further extend our method for the preparation of *S*-containing polycyclic products, the domino reaction of *N*-(2-(2,2-dibromovinyl)phenyl)-2-mercaptobenzamide **4f** was also investigated. To our delight, the protocol was also viable for the assembly of 12*H*-benzo[5,6][1,3]thiazino[3,2-*a*]indol-12-one (Table 3, Entry 6). Thus the cascade C–N coupling/C–S bond formation could also be successfully achieved under the similar reaction conditions (using K_2CO_3 as the base).

Tunable synthesis of different cyclized products

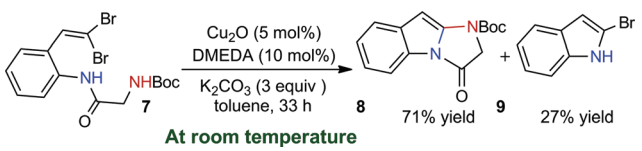
The reactions could proceed at either stage of the cyclization by utilizing different bases. With K_2CO_3 as the base, monocyclized product anthraniloyl 2-bromoindoles **6** were solely obtained in satisfactory yields; while Cs_2CO_3 afforded double cyclized products **5** in good to excellent yields (Scheme 4).

One-pot synthesis of an imidazoindolone derivative

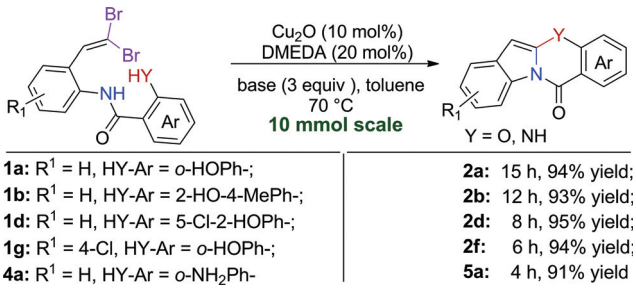
Our catalytic system was also applied successfully to the assembly of an imidazoindolone **8**, which had been synthesized using the tandem intramolecular amidation facilitated by CuI/*trans*-1,2-cyclohexyldiamine (Scheme 5).[13j] Surprisingly, compared with the reported method (at 120 °C), the present protocol could smoothly give the desired product at room temperature. It would be of potential value for the assembly of the chiral indole derivatives owing to its particularly mild conditions.

Synthesis on large scale

Large-scale reactions of several representative substrates (**1a**, **1b**, **1d**, **1g** and **4a**) using the simplified procedures were also investigated (for details, see Experimental section). These domino



Scheme 5 One-pot synthesis of an imidazoindolone derivative.



Scheme 6 Synthesis of double cyclized products on large scale.

reactions proceeded equally well on 10 mmol scale and gave the corresponding double cyclized products in good to excellent yields despite the requirement of more amount of promoters and longer reaction times (Scheme 6).[17]

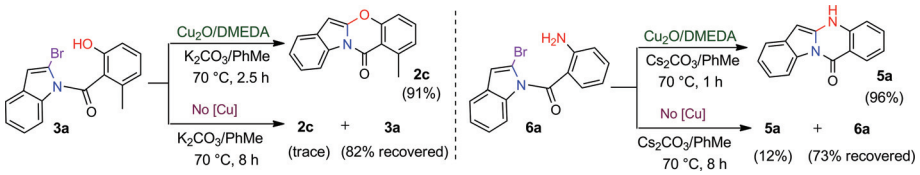
Mechanism

Preliminary investigation found that the copper catalyst was indispensable to the first cyclization.[18] In order to elucidate whether the second step was promoted by copper catalyst or simply by base, control experiments were carried out additionally. As shown in Scheme 7, without a copper catalyst, the double cyclized product (**2c** or **5a**) could be obtained only in poor yield even in longer reaction time. Based on the above experiments, we propose that the second cyclization should also proceed mainly *via* copper-catalyzed intramolecular coupling reaction.

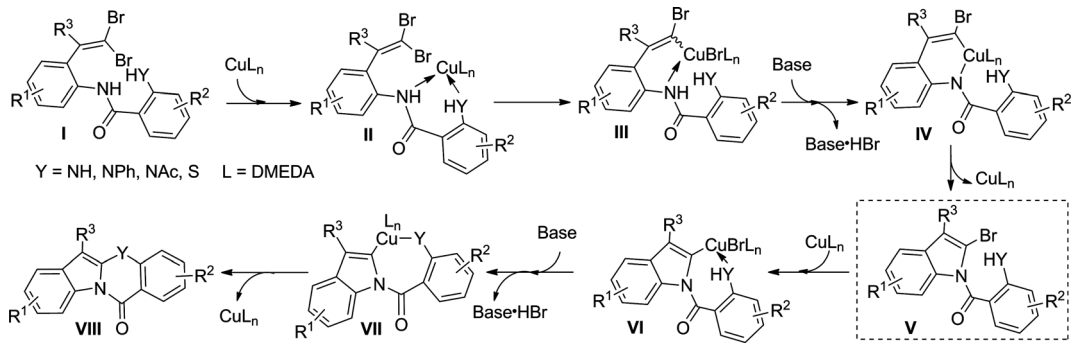
In view of the above observations and the previous reports,[13] a possible mechanism for the copper(I)-catalyzed domino intramolecular cyclization was proposed (Scheme 8). The *o-gem*-dibromovinyl substrate **I**, which might act as a *N*,*Y*-bidentate ligand,[9d,19] chelates with low valent Cu to form complex **II**. Oxidative addition of **II** leads to **III** (the NH on amide may still chelate with Cu). The intramolecular *N*-vinylation gives the monocyclized intermediate **V** (*via* complex **IV**). Finally, the intramolecular C–Y bond formation affords the double cyclized product **VIII** (*via* intermediate **VI** and complex **VII**).

Conclusions

In summary, we have developed a mild and efficient Cu_2O-catalyzed domino intramolecular C–N coupling/C–Y (Y = O, S, N) bond formation process, which has been applied in the assembly of novel fused heterocyclic indole derivatives. Benzo[5,6][1,3]oxazino[3,2-*a*]indol-12-ones, thiazino[3,2-*a*]indol-12-one and indolo[2,1-*b*]quinazolin-12-ones were facilely and rapidly obtained in good to excellent yields from *gem*-dibromovinyl



Scheme 7 The reactions of monocyclized products **3a** and **6a** under different conditions.



Scheme 8 Proposed mechanism for the copper-catalyzed double cyclization process.

systems. The method is particularly practical since the high efficiency was maintained even under air atmosphere. The protocol also enables the facile and efficient synthesis of these polycyclic products in large scale. Additionally, its potential to assemble imidazoindolones under particularly mild conditions opens an attractive entrance toward this valuable molecule class. Therefore, the domino approach may be practical and useful for the synthesis of the polyaromatic indole derivatives in the field of biology and medicine science. Further investigations concerning more synthetic applications of the copper-catalyzed domino coupling strategy are underway.

Experimental

General information

Toluene was distilled from sodium/benzophenone. Phosphorus trichloride (PCl_3) was re-distilled before use. *o-gem*-Dibromovinylaniline[13e,13h] and substrate **7**[13j] were prepared according to the known literatures. All other reagents were obtained from commercial sources and used without further purification, if not stated otherwise. Petrol ether (60–90 °C) was used. All melting points are uncorrected. The IR spectra were recorded on a FT-IR spectrophotometer. The NMR spectra were recorded in $CDCl_3$ or d^6-DMSO on a 400 MHz instrument with TMS as internal standard. Recorded shifts are reported in parts per million (δ) downfield from TMS. Data are represented as follows: Chemical shift, multiplicity (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 (300–400 mesh) or basic alumina (200–300 mesh). Unless otherwise noted, all one-pot reactions were carried out in an oven-dried Schlenk tube equipped with a magnetic stir bar under N_2 atmosphere. Unknown compounds including the typical substrates and all the key products were additionally confirmed by HRMS. Mass spectra were obtained using ESI ionization.

General procedure

General procedure for the synthesis of the substrates (Compounds 1 and 4)

General procedure for the synthesis of substrates 1a–o, 4d and 4f[15]. A mixture of *o-gem*-dibromovinylaniline (10 mmol), *ortho*-hydroxy/phenylamino/mercapto benzoic acid (10 mmol), and dry toluene (50 mL) in an oven-dried two-necked flask was stirred at reflux. PCl_3 (0.4 mL) was added dropwise *via* a syringe. The reaction mixture was stirred at reflux until the reaction completed (monitored by TLC). After being cooled to room temperature, the reaction mixture was diluted by EtOAc/THF (4 : 1, v:v), washed subsequently with *aq.* HCl, and *sat.* $NaHCO_3$. The organic phase was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (300–400 mesh) using petrol/EtOAc (15 : 1 → 8 : 1, v:v) as eluent to afford the corresponding substrate.

General procedure for the synthesis of substrates 4a–c[16]. $SOCl_2$ (8 mL) was added dropwise to a stirred solution of *o*-aminobenzoic acid (10 mmol) in dry $CHCl_3$ (50 mL) at 0 °C, and the mixture was stirred for another 15 min. The reaction mixture was allowed to stir at room temperature for 30 min, and then stir at reflux for 12 h. After removing the solvent and the excess $SOCl_2$ under reduced pressure, the corresponding *o*-aminobenzoyl chloride could be obtained (could be used directly without further purification).

To a stirred solution of *o-gem*-dibromovinylaniline (10 mmol) in dry $CHCl_3$ (50 mL), was added dropwise a solution of the corresponding *o*-aminobenzoyl chloride (10 mmol) in dry $CHCl_3$ (10 mL) at 0 °C, and the mixture was stirred for another 15 min. The reaction mixture was allowed to stir at room temperature for 30 min, and then stirred at reflux until the reaction completed (monitored by TLC). After being cooled to room temperature, the reaction mixture was diluted by EtOAc/THF (4 : 1, v:v), washed subsequently with *sat.* $NaHCO_3$ and brine. The organic phase was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (300–400 mesh) using petrol/EtOAc (15 : 1 → 8 : 1, v:v) as eluent to afford the corresponding substrate.

General procedure for the synthesis of substrates 4e. A mixture of substrate **4a** (1 mmol), TEA (5 mmol), and dry THF (10 mL) in an oven-dried flask was stirred at 0 °C. Acetylchloride (3.0 mmol) was added dropwise *via* a syringe. The reaction mixture was stirred at 0 °C for 10 min, then allowed to stir at room temperature until the reaction completed (monitored by TLC). The reaction mixture was diluted by EtOAc, and washed with *sat.* $NaHCO_3$ and brine. The organic phase was dried over

Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (300–400 mesh) using petrol/EtOAc (15 : 1, v:v) as eluent to afford the corresponding substrate **4e**.

General procedure for the synthesis of the products (double cyclized and monocyclized products)[20]

General procedure for the synthesis of the double cyclized products 2. An oven-dried Schlenk tube was charged with a magnetic stir bar, substrate **1** (0.5 mmol, 1 equiv), Cu_2O (0.025 mmol, 5 mol%), and K_2CO_3 (1.5 mmol, 3 equiv). The Schlenk tube was capped, and then evacuated and backfilled with N_2 (3 times). Under a positive pressure of N_2, DMEDA (0.05 mmol, 10 mol%) and toluene (3 mL) was added *via* syringe. The Schlenk tube was sealed and allowed to stir at 70 °C (monitored by TLC). After being cooled to room temperature, an additional 30 mL of EtOAc was added. The mixture was subsequently washed with *sat.* Na_2CO_3 and brine. The organic phase was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on basic alumina (200–300 mesh) using petrol/EtOAc (15 : 1 → 8 : 1, v:v) as eluent to give the corresponding product **2**.

General procedure for the synthesis of the double cyclized products 5. An oven-dried Schlenk tube was charged with a magnetic stir bar, substrate **4** (0.5 mmol, 1 equiv), Cu_2O (0.025 mmol, 5 mol%), and Cs_2CO_3 (K_2CO_3 for the synthesis of **5e**) (1.5 mmol, 3 equiv). The Schlenk tube was capped, and then evacuated and backfilled with N_2 (3 times). Under a positive pressure of N_2, DMEDA (0.05 mmol, 10 mol%) and toluene (3 mL) was added *via* syringe. The Schlenk tube was sealed and allowed to stir at 70–100 °C (monitored by TLC). After being cooled to room temperature, an additional 30 mL of EtOAc was added. The mixture was subsequently washed with *sat.* Na_2CO_3 and brine. The organic phase was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on basic alumina (200–300 mesh) using petrol/EtOAc (15 : 1 → 8 : 1, v:v) as eluent to give the corresponding product **5**.

General procedure for the synthesis of the monocyclized products 6. An oven-dried Schlenk tube was charged with a magnetic stir bar, substrate **4** (0.5 mmol, 1 equiv), Cu_2O (0.025 mmol, 5 mol%), and K_2CO_3 (1.5 mmol, 3 equiv). The Schlenk tube was capped, and then evacuated and backfilled with N_2 (3 times). Under a positive pressure of N_2, DMEDA (0.05 mmol, 10 mol%) and toluene (3 mL) was added *via* syringe. The Schlenk tube was sealed and allowed to stir at 70 °C (monitored by TLC). After being cooled to room temperature, an additional 30 mL of EtOAc was added. The mixture was subsequently washed with *sat.* Na_2CO_3 and brine. The organic phase was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on basic alumina (200–300 mesh) using petrol/EtOAc (15 : 1 → 8 : 1, v:v) as eluent to give the corresponding product **6**.

Procedure for the synthesis of the imidazoindolone 8. An oven-dried Schlenk tube was charged with a magnetic stir bar, substrate **7** (0.5 mmol, 1 equiv), Cu_2O (0.025 mmol, 5 mol%), and K_2CO_3 (1.5 mmol, 3 equiv). The Schlenk tube was capped, and then evacuated and backfilled with N_2 (3 times). Under a positive pressure of N_2, DMEDA (0.05 mmol, 10 mol%) and toluene (3 mL) was added *via* syringe. The Schlenk tube was sealed and allowed to stir at room temperature (monitored by TLC). An additional 30 mL of EtOAc was added. The mixture was subsequently washed with *sat.* Na_2CO_3 and brine. The organic phase was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (300–400 mesh) using petrol/EtOAc (15 : 1 → 8 : 1, v:v) as eluent to give the corresponding product **8**.

General procedure for the one-pot reactions under common conditions. A Schlenk tube was charged with a magnetic stir bar, *gem*-dibromovinyl substrate (0.5 mmol, 1 equiv), Cu_2O (0.025 mmol, 5 mol%), and K_2CO_3 (1.5 mmol, 3 equiv). Then DMEDA (0.05 mmol, 10 mol%) and commercial toluene (3 mL) was added *via* syringe under air atmosphere. The Schlenk tube was sealed and allowed to stir at the indicated temperature (monitored by TLC). After being cooled to room temperature, an additional 30 mL of EtOAc was added. The mixture was subsequently washed with *sat.* Na_2CO_3 and brine. The organic phase was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on basic alumina (200–300 mesh) using petrol/EtOAc (15 : 1 → 8 : 1, v:v) as eluent to give the corresponding product.

Procedure for the one-pot synthesis on a large scale

General procedure for the one-pot synthesis of 2 on 10 mmol scale. An oven-dried two-necked 100 mL flask was charged with a magnetic stir bar, substrate **1** (10 mmol), Cu_2O (1.0 mmol, 10 mol%), and K_2CO_3 (30 mmol, 3 equiv). The flask was capped, and then evacuated and backfilled with N_2 (3 times). Under a positive pressure of N_2, DMEDA (2 mmol, 20 mol%) and toluene (60 mL) was added immediately *via* syringe. The flask was stirred at 70 °C under N_2 until the substrate was consumed completely (monitored by TLC). After being cooled to room temperature, an additional 500 mL of EtOAc was added. The mixture was subsequently washed with *sat.* Na_2CO_3 (3 × 100 mL) and brine (3 × 100 mL). The organic phase was dried over Na_2SO_4, then flashed through a plug of basic alumina (200–300 mesh), and the plug was washed with additional EtOAc (3 × 50 mL). The combined filtrate was concentrated *in vacuo* to give the corresponding product **2**. The product could be further purified by recrystallization in petrol/THF.

General procedure for the one-pot synthesis of 5 on 10 mmol scale. An oven-dried two-necked 100 mL flask was charged with a magnetic stir bar, substrate **4** (10 mmol), Cu_2O (1.0 mmol, 10 mol%), and Cs_2CO_3 (30 mmol, 3 equiv). The flask was capped, and then evacuated and backfilled with N_2 (3 times). Under a positive pressure of N_2, DMEDA (2 mmol, 20 mol%) and toluene (60 mL) was added immediately *via* syringe. The flask was stirred at 70 °C under N_2 until the substrate was consumed completely (monitored by TLC). After being cooled to room temperature, an additional 500 mL of EtOAc was added. The mixture was subsequently washed with

sat. Na_2CO_3 (3 × 100 mL) and brine (3 × 100 mL). The organic phase was dried over Na_2SO_4, then flashed through a plug of basic alumina (200–300 mesh), and the plug was washed with additional EtOAc (3 × 50 mL). The combined filtrate was concentrated *in vacuo* to give the corresponding product **5**. The product could be further purified by recrystallization in petrol/EtOAc.

Characterization data for the products 2a–2n

12*H*-Benzo[5,6][1,3]oxazino[3,2-*a*]indol-12-one (2a). Pale yellow solid; mp 150–152 °C; IR (KBr): *ν* 3127, 1714, 1702, 1625, 1597, 1576, 1468, 1453, 1367, 1336, 1208, 1101, 875, 753, 646 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* 8.61 (d, *J* = 8.4 Hz, 1H), 8.33 (d, *J* = 8.4 Hz, 1H), 7.71–7.75 (m, 1H), 7.58–7.60 (m, 1H), 7.35–7.40 (m, 4H), 6.18 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 156.7, 153.9, 145.7, 135.5, 129.0, 128.1, 127.8, 124.7, 124.0, 122.6, 119.6, 116.4, 115.9, 114.3, 84.2; HRMS (ESI) calcd. for $C_{15}H_9NO_2$ $[M + H]^+$: 236.0706; found: 236.0703.

3-Methyl-12*H*-benzo[5,6][1,3]oxazino[3,2-*a*]indol-12-one (2b). Pale yellow solid; mp 154–155 °C; IR (KBr): *ν* 3055, 2922, 1703, 1615, 1605, 1577, 1456, 1428, 1384, 1361, 1331, 1165, 763 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* 8.59 (d, *J* = 7.6 Hz, 1H), 8.17 (d, *J* = 8.0 Hz, 1H), 7.57 (d, *J* = 7.2 Hz, 1H), 7.34–7.37 (m, 2H), 7.14–7.18 (m, 2H), 6.14 (s, 1H), 2.50(s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 156.8, 154.0, 147.3, 145.9, 129.0, 127.9, 127.8, 125.4, 124.6, 122.5, 119.5, 116.5, 115.9, 111.8, 84.0, 22.0; HRMS (ESI) calcd. for $C_{16}H_{11}NO_2$ $[M + H]^+$: 250.0863; found: 250.0862.

1-Methyl-12*H*-benzo[5,6][1,3]oxazino[3,2-*a*]indol-12-one (2c). White solid; mp 147–149 °C; IR (KBr): *ν* 3117, 3055, 2922, 1710, 1624, 1598, 1577, 1485, 1470, 1454, 1388, 1371, 1204, 752 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* 8.60 (d, *J* = 8.0 Hz, 1H), 8.15 (d, *J* = 8.0 Hz, 1H), 7.53–7.58 (m, 2H), 7.34–7.37 (m, 2H), 7.25 (t, *J* = 7.2 Hz, 1H), 6.18 (s, 1H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 157.0, 152.2, 145.8, 136.7, 128.9, 127.8, 126.0, 125.7, 124.6, 123.5, 122.5, 119.5, 115.9, 114.0, 84.1, 15.5; HRMS (ESI) calcd. for $C_{16}H_{11}NO_2$ $[M + H]^+$: 250.0863; found: 250.0861.

2-Chloro-12*H*-benzo[5,6][1,3]oxazino[3,2-*a*]indol-12-one (2d). Pale yellow solid; mp 213–214 °C; IR (KBr): *ν* 3127, 3050, 1702, 1629, 1603, 1472, 1453, 1436, 1382, 1360, 1334, 1272, 1200, 823, 790, 768, 743, 694 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* 8.55–8.57 (m, 1H), 8.25–8.26 (m, 1H), 7.65 (dd, J_1 = 8.8 Hz, J_2 = 2.4 Hz, 1H), 7.57 (d, *J* = 6.8 Hz, 1H), 7.30–7.38 (m, 3H), 6.17 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 155.5, 152.3, 145.3, 135.5, 129.6, 128.9, 127.7, 127.5, 125.0, 122.9, 119.7, 118.1, 115.9, 115.4, 84.7; HRMS (ESI) calcd. for $C_{15}H_8ClNO_2$ $[M + H]^+$: 270.0316; found: 270.0326.

3-(Trifluoromethyl)-12*H*-benzo[5,6][1,3]oxazino[3,2-*a*]indol-12-one (2e). Yellow solid; mp 211–213 °C; IR (KBr): *ν* 3134, 1704, 1643, 1623, 1458, 1438, 1401, 1336, 1131, 929, 770, 693 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* 8.56 (d, *J* = 6.8 Hz, 1H), 8.43 (d, *J* = 8.0 Hz, 1H), 7.57–7.63 (m, 3H), 7.38 (m, 2H), 6.21 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 156.1, 155.5, 153.7, 145.1, 129.3, 129.0, 127.6, 125.2, 123.1, 120.51, 120.48, 119.9, 116.0, 114.2, 114.16, 85.2; HRMS (ESI) calcd. for $C_{16}H_8F_3NO_2$ $[M + Na]^+$: 326.0399; found: 326.0398.

8-Chloro-12*H*-benzo[5,6][1,3]oxazino[3,2-*a*]indol-12-one (2f). Pale yellow solid; mp 185–186 °C; IR (KBr): *ν* 3117, 3070, 1705, 1593, 1466, 1448, 1360, 1068, 875, 749, 647 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* 8.47 (d, *J* = 8.4 Hz, 1H), 8.27 (d, *J* = 7.6 Hz, 1H), 7.70–7.73 (m, 1H), 7.50 (s, 1H), 7.33–7.39 (m, 2H), 7.26–7.27 (m, 1H), 6.08 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 156.4, 153.9, 146.5, 135.8, 130.3, 129.1, 128.1, 127.2, 124.3, 122.8, 119.3, 116.9, 116.5, 114.1, 83.7; HRMS (ESI) calcd. for $C_{15}H_8ClNO_2$ $[M + H]^+$: 270.0316; found: 270.0317.

8-Chloro-3-methyl-12*H*-benzo[5,6][1,3]oxazino[3,2-*a*]indol-12-one (2g). White solid; mp 210–212 °C; IR (KBr): *ν* 3070, 2911, 1709, 1594, 1458, 1378, 1355, 1164, 1114, 1065, 910, 806, 759, 730 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* 8.45 (d, *J* = 8.4 Hz, 1H), 8.11 (d, *J* = 8.0 Hz, 1H), 7.47 (s, 1H), 7.23–7.25 (m, 1H), 7.15 (d, *J* = 7.6 Hz, 1H), 7.10 (s, 1H), 6.03 (s, 1H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 156.5, 153.9, 147.5, 146.7, 130.2, 129.1, 127.8, 127.2, 125.6, 122.6, 119.2, 116.8, 116.5, 111.6, 83.5, 22.0; HRMS (ESI) calcd. for $C_{16}H_{10}ClNO_2$ $[M + H]^+$: 284.0473; found: 284.0476.

2,8-Dichloro-12*H*-benzo[5,6][1,3]oxazino[3,2-*a*]indol-12-one (2h). Pale yellow solid; mp 217–219 °C; IR (KBr): *ν* 3120, 1716, 1621, 1597, 1575, 1475, 1431, 1400, 1360, 1069, 918, 862, 771, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* 8.44 (d, *J* = 8.8 Hz, 1H) 8.23 (s, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.51 (s, 1H), 7.26–7.32 (m, 2H), 6.09 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 154.2, 152.3, 145.8, 135.7, 130.7, 129.9, 129.0, 127.5, 123.1, 119.4, 118.1, 116.9, 115.9, 115.2, 84.2; HRMS (ESI) calcd. for $C_{15}H_7Cl_2NO_2$ $[M + Na]^+$: 325.9746; found: 325.9750.

9-Bromo-12*H*-benzo[5,6][1,3]oxazino[3,2-*a*]indol-12-one (2i). Pale yellow solid; mp 201–203 °C; IR (KBr): *ν* 3131, 1708, 1622, 1604, 1594, 1471, 1436, 1401, 1359, 878, 817, 751 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* 8.76 (s, 1H), 8.29 (d, *J* = 7.6 Hz, 1H), 7.73 (t, *J* = 7.6 Hz, 1H), 7.34–7.45 (m, 4H), 6.12 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 156.5, 153.9, 145.8, 135.8, 129.4, 128.2, 127.9, 126.6, 124.3, 120.7, 118.9, 116.5, 115.5, 114.0, 84.0; HRMS (ESI) calcd. for $C_{15}H_8BrNO_2$ $[M + Na]^+$: 335.9631; found: 335.9646.

8-Bromo-12*H*-benzo[5,6][1,3]oxazino[3,2-*a*]indol-12-one (2j). Pale yellow solid; mp 204–206 °C; IR (KBr): *ν* 3130, 1704, 1621, 1592, 1467, 1443, 1401, 875, 771, 749, 646 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): *δ* 8.39 (s, 1H), 8.25 (s, 1H), 7.65–7.71 (m, 2H), 7.34–7.38 (m, 3H), 6.06 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 156.4, 153.8, 146.3, 135.8, 129.5, 128.1, 127.5, 125.4, 124.3, 122.2, 118.1, 117.2, 116.5, 114.1, 83.6; HRMS (ESI) calcd. for $C_{15}H_8BrNO_2$ $[M + Na]^+$: 335.9631; found: 335.9640.

8-(Benzyloxy)-12*H*-benzo[5,6][1,3]oxazino[3,2-*a*]indol-12-one (2k). Pale yellow solid; mp 202–204 °C; ^1H NMR (400 MHz, $CDCl_3$): *δ* 8.48 (d, *J* = 8.8 Hz, 1H), 8.30 (d, *J* = 8.0 Hz, 1H), 7.70 (t, *J* = 7.6 Hz, 1H), 7.47–7.49 (m, 2H), 7.33–7.42 (m, 5H), 7.12–7.13 (m, 1H), 7.03 (d, *J* = 8.0 Hz, 1H), 6.09 (s, 1H), 5.15

(s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.5, 153.7, 146.2, 135.3, 128.9, 128.5, 127.9, 127.8, 127.4, 125.4, 124.0, 123.6, 119.6, 116.7, 116.3, 111.3, 104.2, 84.2, 70.4; HRMS (ESI) calcd. for $C_{22}H_{15}NO_3$ $[M + Na]^+$: 364.0944; found: 364.0956.

7*H*-Naphtho[2′,1′:5,6][1,3]oxazino[3,2-*a*]indol-7-one (2l). Pale yellow solid; mp 222–224 °C; IR (KBr): ν 3127, 1705, 1614, 1596, 1577, 1510, 1453, 1442, 1398, 763 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.64 (d, J = 7.2 Hz, 1H), 8.52 (d, J = 7.2 Hz, 1H), 8.20 (d, J = 8.4 Hz, 1H), 7.91 (d, J = 7.2 Hz, 1H), 7.67–7.74 (m, 3H), 7.61–7.63 (m, 1H), 7.37–7.39 (m, 2H), 6.32 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.0, 151.4, 145.7, 136.9, 129.8, 128.8, 128.0, 127.6, 127.2, 124.6, 123.8, 122.6, 122.5, 121.9, 119.7, 119.6, 115.9, 109.0, 84.3; HRMS (ESI) calcd. for $C_{19}H_{11}NO_2$ $[M + Na]^+$: 308.0682; found: 308.0690.

6*H*-Naphtho[2′,3′:5,6][1,3]oxazino[3,2-*a*]indol-6-one (2m). Pale yellow solid; mp 267–269 °C; IR (KBr): ν 3130, 1699, 1619, 1597, 1477, 1461, 1400, 767, 741 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.92 (s, 1H), 8.61 (d, J = 8.0 Hz, 1H), 8.05 (d, J = 8.4 Hz, 1H), 7.89 (d, J = 8.4 Hz, 1H), 7.72 (s, 1H), 7.62 (t, J = 7.6 Hz, 1H), 7.52–7.57 (m, 2H), 7.35–7.37 (m, 2H), 6.16 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.8, 149.9, 146.0, 136.9, 130.5, 129.7, 129.64, 129.59, 128.0, 127.1, 125.9, 124.8, 122.8, 119.6, 116.0, 114.5, 112.1, 110.0, 84.5; HRMS (ESI) calcd. for $C_{19}H_{11}NO_2$ $[M + Na]^+$: 308.0682; found: 308.0688.

6-(Trifluoromethyl)-12*H*-benzo[5,6][1,3]oxazino[3,2-*a*]indol-12-one (2n). White solid; mp 189–191 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.62 (d, J = 7.2 Hz, 1H), 8.33 (d, J = 7.2 Hz, 1H), 7.79 (t, J = 7.2 Hz, 1H), 7.73 (d, J = 7.2 Hz, 1H), 7.41–7.50 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.1, 153.4, 136.2, 128.2, 128.15, 128.06, 125.6, 125.2, 124.1, 123.7, 121.8, 118.6, 116.9, 116.1, 116.0, 114.1; HRMS (ESI) calcd. for $C_{16}H_8F_3NO_2$ $[M + Na]^+$: 326.0399; found: 326.0407.

Characterization data for the products 5a–5e

Indolo[2,1-*b*]quinazolin-12(5*H*)-one (5a). Yellow solid; mp 180 °C (decomposed); IR (KBr): ν 3126, 1648, 1607, 1582, 1525, 1449, 1401, 1302, 1215, 1165, 757 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (d, J = 8.0 Hz, 1H), 7.34–7.38 (m, 2H), 7.26–7.28 (m, 2H), 7.16–7.20 (m, 1H), 6.70–6.77 (m, 2H), 6.39 (b, 1H), 5.94 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.0, 149.5, 147.5, 137.9, 132.9, 130.9, 129.6, 127.4, 126.2, 121.8, 119.4, 116.52, 116.50, 110.9, 79.7; HRMS (ESI) calcd. for $C_{15}H_{10}N_2O$: $[M + H]^+$: 235.0866; found: 235.0864.

4-Methylindolo[2,1-*b*]quinazolin-12(5*H*)-one (5b). Pale yellow solid; mp 194 °C (decomposed); IR (KBr): ν 3115, 1637, 1606, 1591, 1567, 1463, 1400, 1281, 1238, 1124, 760, 740 cm^{-1}; ^{1}H NMR (400 MHz, d^6-DMSO): δ 7.91 (d, J = 7.6 Hz, 1H), 7.75 (d, J = 7.6 Hz, 1H), 7.44–7.47 (m, 2H), 7.26–7.34 (m, 2H), 7.18–7.19 (m, 1H), 6.67 (s, 1H), 6.59 (t, J = 7.2 Hz, 1H), 2.15 (s, 3H); ^{13}C NMR (100 MHz, d^6-DMSO): δ 155.1, 149.2, 147.1, 137.5, 134.3, 131.8, 128.2, 126.9, 126.2, 123.6, 123.2, 119.2, 115.1, 108.9, 81.8, 18.3; HRMS (ESI) calcd. for $C_{16}H_{12}N_2O$ $[M + H]^+$: 249.1022; found: 249.1018.

3-Chloroindolo[2,1-*b*]quinazolin-12(5*H*)-one (5c). Pale yellow solid; mp 212 °C (decomposed); IR (KBr): ν 3127, 1639, 1614, 1570, 1542, 1485, 1456, 1401, 1287, 1241, 1123, 1090, 753.0, 697 cm^{-1}; ^{1}H NMR (400 MHz, d^6-DMSO): δ 7.94 (d, J = 8.8 Hz, 1H), 7.75 (d, J = 7.6 Hz, 1H), 7.59 (b, 1H), 7.43–7.48 (m, 2H), 7.28–7.31 (m, 1H), 6.92 (s, 1H), 6.65–6.70 (m, 2H); ^{13}C NMR (100 MHz, d^6-DMSO): δ 154.0, 151.7, 147.0, 138.0, 137.4, 131.8, 130.6, 128.4, 126.5, 123.1, 119.3, 115.6, 115.3, 108.0, 82.0; HRMS (ESI) calcd. for $C_{15}H_9ClN_2O$ $[M + H]^+$: 269.0476; found: 269.0481.

5-Phenylindolo[2,1-*b*]quinazolin-12(5*H*)-one (5d). Pale yellow solid; mp 195 °C (decomposed); IR (KBr): ν 3130, 1686, 1608, 1597, 1581, 1572, 1492, 1484, 1475, 1467, 1450, 1401, 1365, 1340, 1314, 867, 753, 698 cm^{-1}; ^{1}H NMR (400 MHz, d^6-DMSO): δ 8.61 (d, J = 6.8 Hz, 1H), 8.28 (d, J = 6.8 Hz, 1H), 7.62–7.74 (m, 6H), 7.43 (s, 1H), 7.22–7.27 (m, 3H), 6.60 (d, J = 7.6 Hz, 1H), 5.31 (s, 1H); ^{13}C NMR (100 MHz, d^6-DMSO): δ 158.9, 142.1, 140.4, 138.2, 135.4, 131.6, 130.4, 130.2, 130.0, 129.7, 128.5, 124.7, 121.3, 120.9, 118.8, 115.9, 114.2, 113.1, 83.8; HRMS (ESI) calcd. for $C_{21}H_{14}N_2O$ $[M + H]^+$: 311.1179; found: 311.1188.

12*H*-Benzo[5,6][1,3]thiazino[3,2-*a*]indol-12-one (5e). Yellow solid; mp 164–166 °C; IR (KBr): ν 3123, 1674, 1520, 1437, 1401, 1371, 1360, 1340, 748 cm^{-1}; ^{1}H NMR (400 MHz, d^6-DMSO): δ 8.67 (m, 1H), 8.44 (d, J = 6.4 Hz, 1H), 7.62–7.70 (m, 3H), 7.51 (m, 1H), 7.36 (m, 2H), 7.01 (s, 1H); ^{13}C NMR (100 MHz, d^6-DMSO): δ 159.7, 135.4, 134.3, 133.3, 131.0, 129.3, 127.0, 126.7, 126.2, 125.1, 123.7, 123.2, 119.8, 116.8, 104.6; HRMS (ESI) calcd. for $C_{15}H_9NOS$ $[M + Na]^+$: 274.0297; found: 274.0302.

Characterization data for the product 8

***tert*-Butyl-3-oxo-2,3-dihydro-1*H*-imidazo[1,2-*a*]indole-1-carboxylate (8)[13j].** White solid; mp 175–177 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (d, J = 6.8 Hz, 1H), 7.41 (d, J = 6.8 Hz, 1H), 7.17–7.26 (m, 2H), 6.17 and 5.86 (s, 1H), 4.53 (s, 2H), 1.63 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.7, 149.8, 135.1, 127.5, 124.9, 122.5, 120.1, 113.2, 86.6, 53.9, 28.2.

Acknowledgements

This work was financially supported by the Zhejiang Provincial Natural Science Foundation (No. Y4110044), the National Natural Science Foundation of China (No. 20802070), and the College Science and Technology Innovation Program of Zhejiang Province (No. 2011R404051).

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18 A blank test of the reaction of **1c** was performed without the copper(I) catalyst, and the monocyclized product **3a** could be obtained only in trace amount after 6 h (**2c** was not detected)

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20 **Special notes for the treatments of the products:** Surprisingly, although all of the cyclized products were stable when they were dry, most of these compounds seemed to be rather sensitive to some solvents such as CH_2Cl_2 and $CHCl_3$. Contact with these solvents would lead to the formation of an unidentified substance with strong polarity. Therefore, once the sample was dissolved in $CDCl_3$, its NMR spectrum should be recorded immediately. These products were also sensitive to silica gel. Basic alumina should be used instead of silica gel when they were purified by column chromatography