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Solvent-Dependent Copper-Catalyzed Indolyl C3-Oxygenation and N1-Cyclization Reactions: Selective Synthesis of 3*H*-Indol-3-ones and Indolo[1,2-*c*]quinazolines

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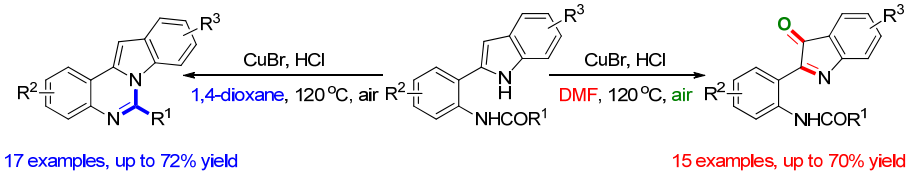


Abstract: A simple and practical procedure for the selective preparation of 3*H*-indol-3-one and indolo[1,2-*c*]quinazoline derivatives through copper-catalyzed aerobic oxygenation and intramolecular cyclization reactions of 2-(2-amidoaryl)-1*H*-indoles in the presence of acid has been disclosed. Interestingly, the reaction outcomes are exclusively dependent on the reaction medium employed. With DMF as the solvent, the amide moiety of indole substrates could act as an auxiliary to enable the indole's oxygenation reaction with molecular oxygen from air as the oxidant to give 3*H*-indol-3-one derivatives in a highly selective manner. On the other hand, when the reactions were performed in 1,4-dioxane, the amide moiety switched to participate in an intramolecular indolyl N1-cyclization to afford indolo[1,2-*c*]quinazolines as the predominating products.

Introduction

3*H*-Indol-3-one derivatives not only are frequently found in naturally occurring alkaloids[1] and natural/artificial colorants,[2] but also exhibit important antiplasmodial, antiproliferative, antimicrobial, and potent CYP1A1 enzyme inhibitory activities.[3] In addition, they have also been extensively utilized as key building blocks for the construction of synthetically valuable indolin-3-one skeletons with a quaternary carbon center at the C2-position through nucleophilic addition[4] and Diels-Alder reactions,[5] exemplified by the synthesis of natural alkaloids (-)-isatisine A[6] and 8-desbromohinckdentine A.[7] Accordingly, much effort has been dedicated to the preparation of 3*H*-indol-3-one derivatives, and several synthetic routes have been documented. For example, 2-substituted-3*H*-indol-3-one derivatives have been prepared via the classical four-step procedure,[7a,8] the oxidation of indoles with different oxidants,[9] and the indium-mediated deoxygenation of indolone-*N*-oxides.[3a,10] However, these existing methods suffer from the disadvantages of multistep processes, low yields, use of stoichiometric oxidants or expensive metal catalysts, and difficult-to-obtain starting materials. Therefore, the development of practical and efficient procedures for the preparation of 3*H*-indol-3-one derivatives in a user-friendly manner remains in high demand in the fields of organic and pharmaceutical chemistry.

Recently, the combination of copper catalyst and molecular oxygen has emerged as an ideal oxygenating reagent for the incorporation of oxygen atom into diverse organic molecules to deliver more complex oxygen-containing organic compounds via selective oxidative C-H bond functionalization.[11] For example, copper-catalyzed oxygenation reactions of indole derivatives with the use of molecular oxygen as a green oxidant and reactant have been successfully utilized in the preparation of various valuable nitrogen-containing heterocyclic

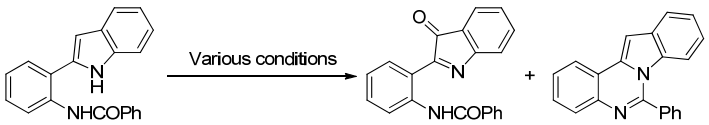
compounds, such as benzoxazinone, 2,2-bis(3'-indolyl)-indoxyl, quinazolinone, and tryptanthrin derivatives.[12] However, literature searching revealed that, to date, 3*H*-indol-3-ones are hardly obtained through copper-catalyzed direct oxygenation of indoles. As a continuation of our studies on copper-catalyzed aerobic synthesis of N-heterocycles, we recently found that 3*H*-indol-3-one derivatives could be successfully obtained through the direct oxygenation reaction of 2-arylindoles featuring an amido group on the 2-position of aryl ring by using copper as catalyst and molecular oxygen from air as oxygen-atom source in acidic conditions. Here, we would like to disclose our preliminary results in this aspect.

Results and Discussion

Initially, *N*-(2-(1*H*-indol-2-yl)phenyl)benzamide (**1a**) was chosen as a model substrate to optimize the reaction parameters with regard to copper catalysts, acids, reaction temperature, and solvents (Table 1). Treatment of **1a** (0.4 mmol) with CuI (10 mol %) and HCl (20 mol %) in DMSO (2 mL) at 120 ^{o}C for 4 h under air could give rise to *N*-(2-(3-oxo-3*H*-indol-2-yl)phenyl)benzamide (**2a**) in 49% yield (entry 1). The structure of **2a** was unambiguously confirmed by X-ray analysis (see the Supporting Information). To improve the efficiency, other copper catalysts including CuBr, CuCl, $CuBr_2$, $CuCl_2$, and $Cu(OAc)_2$ were tested (entries 2-6). Of these catalysts, CuBr showed the highest activity (56%). Then, we also investigated the effect of different acids such as H_2SO_4, CF_3COOH, TsOH, and PivOH on this CuBr-catalyzed oxygenation reaction (entries 7-10). Among them, HCl gave the best result (entries 2 vs. 7-10). Furthermore, the amount of CuBr and HCl was screened, and the use of 10 mol % of CuBr and 20 mol % of HCl proved to be optimal (Table S1, in supporting information). Increasing or decreasing the reaction temperature from 120 ^{o}C resulted in a lower yield of **2a** (entries 11-12). In following studies, three more solvents

including DMF, NMP, and DMA (*N*,*N*-dimethylacetamide) were also tried (entries 13-15), and it turned out that DMF was the best reaction medium for the formation of **2a** (70%, entry 13). It should be noted that, with the use of DMA as solvent, this reaction not only afforded **2a** in 18% yield, but also gave rise to the unexpected 6-phenylindolo[1,2-*c*]quinazoline (**3a**) in 16% yield (entry 15). Moreover, the formation of **2a** was obviously suppressed in the absence of HCl or CuBr (entries 16-17). Finally, it was also observed that under a nitrogen atmosphere, this reaction afforded a trace amount of **2a** along with 77% recovery of **1a** (entry 18). When the reaction was performed under an oxygen atmosphere, **2a** was obtained in 68% yield (entry 19).

Table 1. Optimization of Reaction Conditions for the Synthesis of 2a[a]



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

entry	catalyst	acid	solvent	yield (%)[b]	
				2a	**3a**
1	CuI	HCl (0.5 M)	DMSO	49	nd
2	CuBr	HCl (0.5 M)	DMSO	56	nd
3	CuCl	HCl (0.5 M)	DMSO	35	nd
4	$CuBr_2$	HCl (0.5 M)	DMSO	20	nd
5	$CuCl_2$	HCl (0.5 M)	DMSO	28	nd
6	$Cu(OAc)_2$	HCl (0.5 M)	DMSO	52	nd
7	CuBr	H_2SO_4 (0.5 M)	DMSO	30	nd
8	CuBr	CF_3COOH	DMSO	44	nd
9	CuBr	TsOH	DMSO	41	nd
10	CuBr	PivOH	DMSO	42	nd
11[c]	CuBr	HCl (0.5 M)	DMSO	27	nd
12[d]	CuBr	HCl (0.5 M)	DMSO	14	nd
13	CuBr	HCl (0.5 M)	DMF	70	nd
14	CuBr	HCl (0.5 M)	NMP	29	nd
15	CuBr	HCl (0.5 M)	DMA	18	16
16	CuBr	-	DMF	48	nd

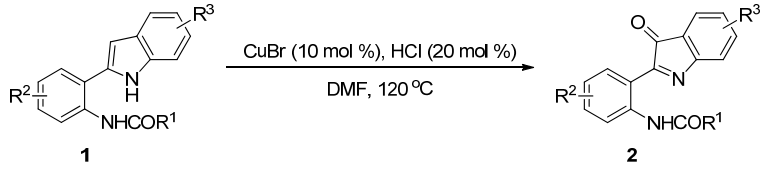
17[e]	-	HCl (0.5 M)	DMF	3	nd
18[f]	CuBr	HCl (0.5 M)	DMF	4	nd
19[g]	CuBr	HCl (0.5 M)	DMF	68	nd

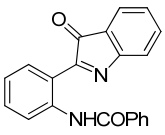
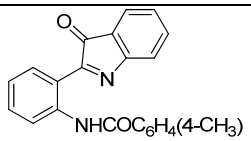
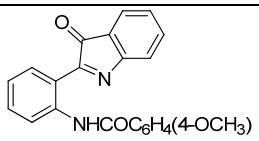
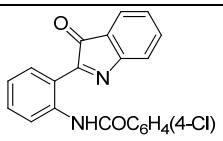
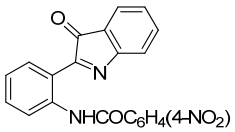
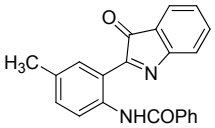
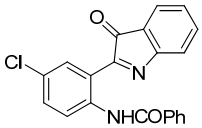
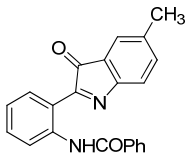
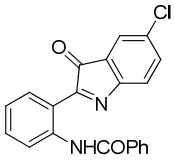
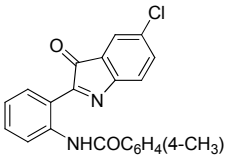
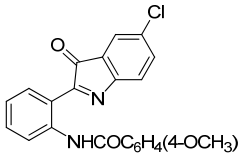
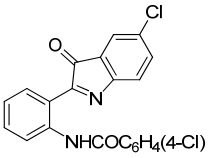
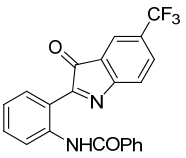
[a]The reactions were run with: **1a** (0.4 mmol), catalyst (0.04 mmol), acid (0.08 mmol), solvent (2 mL), 120 °C, 4 h, air. [b]nd = not detected. [c]The reaction was run at 140 °C. [d]The reaction was run at 100 °C. [e]**1a** (79%) was recovered. [f]The reaction was run under N_2 and **1a** (77%) was recovered. [g]The reaction was run under O_2.

With the optimized reaction conditions (Table 1, entry 13) in hand, we next investigated the scope and limitation of this copper-catalyzed oxygenation reaction leading to 2-aryl-3*H*-indol-3-ones (**2**), and the results are demonstrated in Table 2. First, the effect of different substituents (R^1) was examined. It was found that 1*H*-indoles **1b-1f** bearing both aromatic and aliphatic groups on the amide moiety were all compatible with the optimized reaction conditions to afford the corresponding 3*H*-indol-3-one derivatives **2** in moderate yields. For example, indole substrates with either electron-donating groups (-Me and -OMe) or electron-withdrawing groups (-Cl, and -NO_2) at the *para* position of the phenyl ring (R^1) underwent this oxygenation reaction smoothly to give rise to the desired oxygenated indoles **2b**-**2e** in 43-61% yields. When 2-aryl-1*H*-indole (R^1 = Me) was employed, this reaction could also afford the corresponding 3*H*-indol-3-one **(2f)** in 44% yield. Next, we also studied the effect of the substituents (R^2) attached to the 2-phenyl unit of indoles (**1**) on this oxygenation reaction. The results indicated that indole substrates (**1**) bearing a methyl, chloro, or trifluoromethyl group on the 2-phenyl unit took part in this reaction smoothly to yield **2g-2i** in modest yields. In addition, substrates (**1**) with either electron-donating or electron-withdrawing groups (R^3) on the indole scaffold were well tolerated with the reaction conditions to provide the corresponding products **2j-2o** in 51%-64% yields. To further expand the substrate scope, we also tested the oxygenation reactions of substrates **1p** and **1q**. Unfortunately, the expected oxygenation reactions did not occur possibly due to the low reactivity of **1p** and **1q**. Finally, to demonstrate the practicability of the present protocol, a

gram-scale oxygenation reaction of **1a** (1.56 g) was carried out, and it afforded **2a** in 72% yield.

Table 2. Scope for the Synthesis of 3*H*-Indol-3-one Derivatives (2)[a,b]



 **2a**, 70%/72%[c]	 **2b**, 55%	 **2c**, 60%	 **2d**, 61%
 **2e**, 43%	 **2f**, 44%	 **2g**, 51%	 **2h**, 48%
 **2i**, 47%	 **2j**, 52%	 **2k**, 60%	 **2l**, 60%
 **2m**, 63%	 **2n**, 64%	 **2o**, 51%	 **2p**, not obtained
 **2q**, not obtained			

[a]Reaction conditions: **1** (0.4 mmol), CuBr (0.04 mmol), 0.5 M HCl (0.16 mL), DMF (2 mL), 120 °C, air. [b]Yields. [c] **1a** (1.56 g) was used.

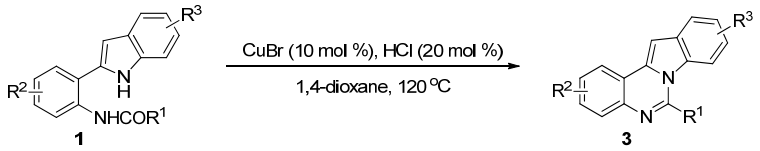
Having established a practical route to 3*H*-indol-3-ones (**2**) through the copper-catalyzed direct oxygenation of indoles (**1**) by using molecular oxygen from air as a green oxidant and

reactant, we turned our attention back to 6-phenylindolo[1,2-*c*]quinazoline (**3a**), which was isolated as an unexpected byproduct in 16% yield (Table 1, entry 15). As we know, indolo[1,2-*c*]quinazolines, as an important class of fused *N*-heterocycles, are frequently encountered in naturally occurring alkaloids and synthetic compounds with a broad spectrum of bioactivities.[13] Although several synthetic routes have been developed,[14] it is still in high demand to develop a new alternative for the synthesis of indolo[1,2-*c*]quinazoline derivatives by using the indoles (**1**) as starting materials. To the best of our knowledge, the N1-cyclization reaction of the indoles (**1**) promoted by the combination of copper and acid leading to indolo[1,2-*c*]quinazolines has not been reported yet.

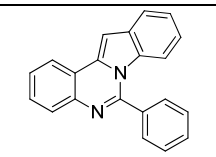
Thus, we undertook an extensive study on the selective synthesis of indolo[1,2-*c*]quinazoline derivatives from the indoles (**1**) by tuning the reaction parameters. After several attempts (Table S2, in supporting information), we found that, with the replacement of DMF by 1,4-dioxane as the reaction medium, indole (**1a**) could be exclusively transformed into the desired 6-phenylindolo[1,2-*c*]quinazoline (**3a**) in 72% yield under the optimal reaction conditions for the preparation of **2a** (Table 1, entry 13), suggesting that reaction medium played a vital role in the selective transformation of **1a** to **2a** or **3a**. With the optimal reaction conditions established, we then tested the substrate scope for the synthesis of indolo[1,2-*c*]quinazolines (**3**) in detail. As shown in Table 3, various indole substrates (**1**) with aromatic and aliphatic substituents (R^1) on the amide unit took part in this N-cyclization reaction to provide the expected indolo[1,2-*c*]quinazolines **3a**-**3f** in moderate to good yields. In addition, both electron-donating and electron-withdrawing functional groups (R^2) attached on the 2-phenyl ring of indoles (**1**) were well compatible with the optimized reaction conditions to yield the corresponding products **3g** and **3h** in 60% and 62% yields, respectively.

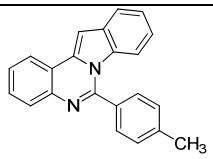
Next, we also found that indoles (**1**) with different functional groups (R^3) on the indole scaffold proved to be good substrates and underwent this reaction smoothly to afford the desired products **3i-3o**. Finally, with **1p** and **1q** as reactants, these cyclization reactions could also generate the desired products **3p** and **3q** in 50% and 65% yields, respectively.

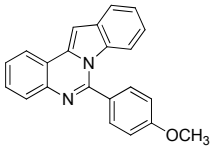
Table 3. Scope for the Synthesis of Indolo[1,2-*c*]quinazoline Derivatives (3)[a,b]

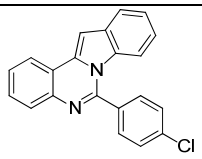


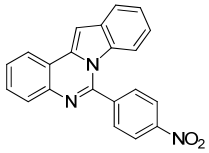
1 **3**

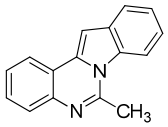

3a, 72%

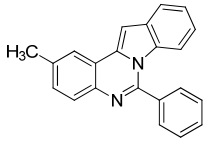

3b, 54%

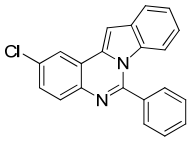

3c, 57%

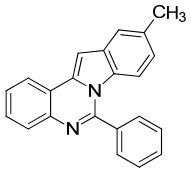

3d, 61%

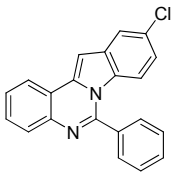

3e, 40%

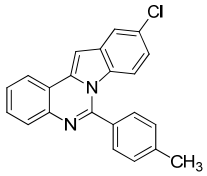

3f, 48%

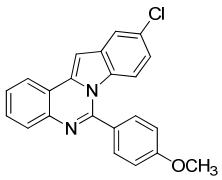

3g, 60%

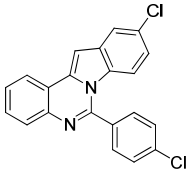

3h, 62%

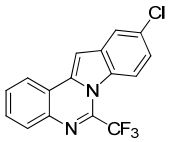

3i, 53%

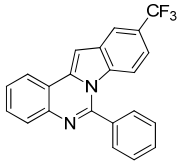

3j, 67%

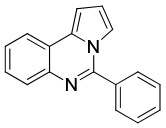

3k, 63%

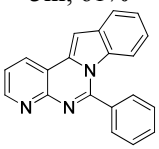

3l, 60%


3m, 61%


3n, 45%


3o, 50%


3p, 50%

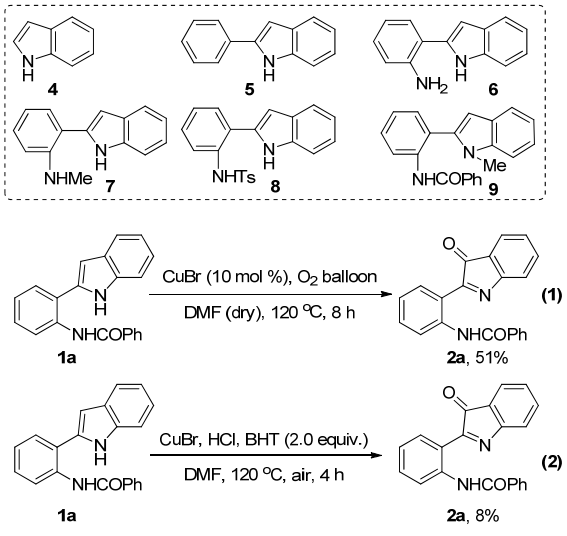

3q, 65%

[a]Reaction conditions: **1** (0.4 mmol), CuBr (0.04 mmol), 0.5 M HCl (0.16 mL), 1,4-dioxane (2 mL), 120 °C, air. [b]Yields.

To gain some insights into the reaction mechanism for the formation of **2a**, several control experiments were carried out as demonstrated in Scheme 1. First, when indole substrates (**4-8**)

and *N*-Me-protected indole (**9**) were subjected to the optimized reaction conditions (Table 1, entry 13), no reaction occurred. These observations suggested that the amide moiety as a key auxiliary and the free *N*-H group of indoles (**1a**) are essential for the copper-catalyzed oxygenation reaction. Second, this oxygenation reaction could only produce a trace amount of **2a** under a nitrogen atmosphere (Table 1, entry 18). Whereas, treatment of **1a** with CuBr in anhydrous DMF under an oxygen atmosphere could afford **2a** in 51% yield (Scheme 1, Eq. 1). These results indicated that the newly introduced oxygen atom of 3*H*-indol-3-one (**2a**) derived from dioxygen (O_2), rather than from water. Third, the addition of BHT (2.0 equiv.) as a radical scavenger into the reaction system inhibited this transformation dramatically to provide **2a** in only 8% yield (Scheme 1, Eq. 2), indicating that radical intermediates might be involved in the oxygenation reaction.

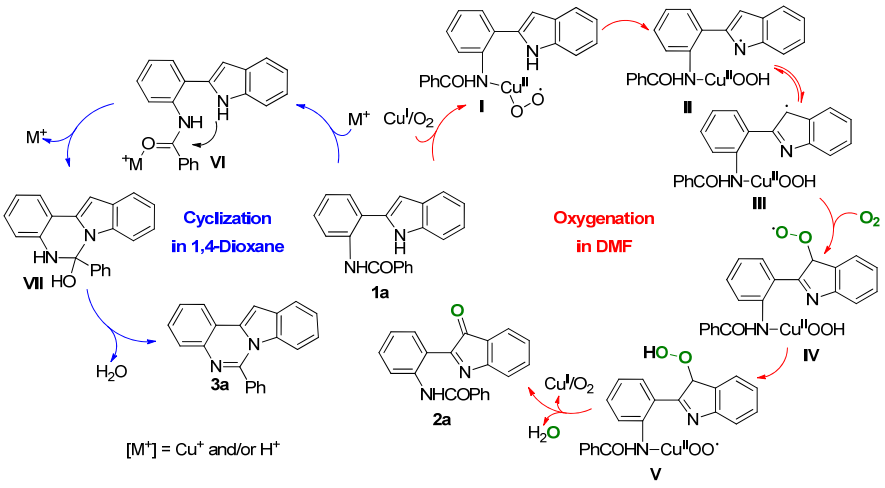
Scheme 1. Control Experiments



On the basis of the above results and the relevant literatures,[15] possible mechanisms for the formation of **2a** and **3a** are shown in Scheme 2. In the oxygenation reaction of **1a**, although the detailed mechanism is unclear now, we believe that, with the use of DMF as a polar solvent and molecular oxygen from air as the oxidant, the chelation assistance of amide

moiety with CuBr facilitates the formation of copper-superoxide complex **I**, which might be more stable in a polar solvent (DMF) than a non-polar one (dioxane). And then, **I** abstracts a hydrogen atom from the indolyl *NH* unit to afford a *N*-centered radical **II**, which then isomerizes to an indolyl C3 radical **III**. Next, the radical **III** would react with molecular oxygen from air to form a peroxy radical **IV**. Subsequently, the peroxy radical (**IV**) undergoes an intramolecular hydrogen abstraction to produce a hydroperoxide intermediate **V**, which then undergoes an acid-promoted elimination of water and a dissociation of the copper catalyst to yield **2a**. As for the formation of **3a**, when 1,4-dioxane is employed as a non-polar reaction medium, the carbonyl group of the amide moiety in **1a** is firstly activated in the presence of copper and HCl to generate intermediate **VI**. Subsequent intramolecular *N*-nucleophilic addition reaction affords intermediate **VII**, which then eliminates water to furnish **3a**.

Scheme 2. Possible Mechanisms for the Formation of 2a and 3a



Conclusion

In summary, we have successfully achieved a practical protocol for the selective synthesis of 3*H*-indol-3-ones and indolo[1,2-*c*]quinazolines via the copper-catalyzed oxygenation by

using molecular oxygen as a sole and green oxygenating reagent and intramolecular N-cyclization reaction under acidic conditions. Notably, the selectivity of the reaction is exclusively dependent on the reaction solvents. With DMF as the reaction solvent, the indole substrates undergo a selective C3-oxygenation reaction to give 3*H*-indol-3-ones as the main products. Whereas, with 1,4-dioxane as the reaction medium, indolo[1,2-*c*]quinazolines are selectively obtained via an intramolecular indolyl N1-cyclization. Further studies on the reactivities of the obtained 3*H*-indol-3-ones and the development of novel copper-catalyzed aerobic oxygenation reaction is currently underway in our laboratory.

Experimental Section

General Methods. Indoles (**1**, **6**, **8**) and pyrrole (**1p**) were prepared according to the previously reported literature.[16] Indole (**9**) was synthesized based on a literature procedure.[17] Unless noted, other commercial reagents and solvents were used without further purification. Melting points were recorded with a micro melting point apparatus and uncorrected. The ^{1}H NMR spectra were recorded at 400 or 600 MHz. The $^{13}C\{^{1}H\}$ NMR spectra were recorded at 100 or 150 MHz. High-resolution mass spectra (HRMS) were collected in ESI mode by using a MicrOTOF mass spectrometer. All reactions were monitored by thin-layer chromatography (TLC) using silica gel plates (silica gel 60 F254 0.25 mm) and components were visualized by observation under UV light (254 and 365 nm).

General Procedure for the Preparation of 3*H*-Indol-3-ones (2). To a mixture of indole **1** (0.4 mmol) in DMF (2 mL) were added CuBr (5.7 mg, 0.04 mmol) and 0.5 M HCl aqueous solution (0.16 mL, 0.08 mmol) under air and then the resulting mixture was stirred at 120 ^{o}C for 4~7 h. After the reactant **1** was consumed completely, water was added into the reaction system, followed by extraction with ethyl acetate. The extract was washed with water and

brine, and then dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography on silica gel to give the corresponding 3*H*-indol-3-one **2**.

***N*-(2-(3-Oxo-3*H*-indol-2-yl)phenyl)benzamide (2a):** Petroleum ether/ethyl acetate (10:1) as eluent; red solid (91 mg, 70%), mp 145-146 ^{o}C. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.13 (t, *J* = 7.8 Hz, 1H), 7.23 (t, *J* = 7.2 Hz, 1H), 7.25 (d, *J* = 7.8 Hz, 1H), 7.48-7.53 (m, 6H), 8.07 (d, *J* = 7.2 Hz, 2H), 8.70 (d, *J* = 7.8 Hz, 1H), 8.93 (d, *J* = 8.4 Hz, 1H), 13.22 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) δ 116.4, 120.4, 121.1, 121.5, 123.1, 125.5, 127.8, 128.7, 128.8, 131.4, 132.0, 133.9, 135.5, 137.0, 142.5, 158.4, 160.4, 166.4, 193.2. HRMS (ESI) calcd for $C_{21}H_{15}N_2O_2$ $[M + H]^+$ 327.1128, found 327.1128.

4-Methyl-*N*-(2-(3-oxo-3*H*-indol-2-yl)phenyl)benzamide (2b): Petroleum ether/ethyl acetate (10:1) as eluent; red solid (75 mg, 55%), mp 176-177 ^{o}C. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 2.44 (s, 3H), 7.13 (t, *J* = 7.8 Hz, 1H), 7.24-7.26 (m, 2H), 7.31 (d, *J* = 7.8 Hz, 2H), 7.50-7.53 (m, 3H), 7.99 (d, *J* = 7.8 Hz, 2H), 8.70 (d, *J* = 7.8 Hz, 1H), 8.94 (d, *J* = 8.4 Hz, 1H), 13.17 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) δ 21.5, 116.3, 120.2, 121.0, 121.4, 122.9, 125.4, 127.8, 128.7, 129.3, 131.3, 132.5, 133.8, 136.9, 142.5, 142.7, 158.3, 160.2, 166.2, 193.2. HRMS (ESI) calcd for $C_{22}H_{17}N_2O_2$ $[M + H]^+$ 341.1285, found 341.1285.

4-Methoxy-*N*-(2-(3-oxo-3*H*-indol-2-yl)phenyl)benzamide (2c): Petroleum ether/ethyl acetate (10:1) as eluent; red solid (85 mg, 60%), mp 163-164 ^{o}C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.89 (s, 3H), 6.98 (d, *J* = 8.8 Hz, 2H), 7.11 (t, *J* = 7.6 Hz, 1H), 7.21-7.25 (m, 2H), 7.47-7.52 (m, 3H), 8.04 (d, *J* = 8.4 Hz, 2H), 8.68 (dd, *J* = 1.2, 8.0 Hz, 1H), 8.91 (d, *J* = 8.4 Hz, 1H), 13.10 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 55.5, 113.8, 116.2, 120.1, 120.9, 121.4,

122.8, 125.3, 127.6, 128.7, 129.7, 131.3, 133.7, 136.9, 142.8, 158.3, 160.2, 162.6, 165.8, 193.1. HRMS (ESI) calcd for $C_{22}H_{17}N_2O_3$ $[M + H]^+$ 357.1234, found 357.1246.

4-Chloro-*N*-(2-(3-oxo-3*H*-indol-2-yl)phenyl)benzamide (2d): Petroleum ether/ethyl acetate (10:1) as eluent; red solid (88 mg, 61%), mp 191-192 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.18-7.22 (m, 1H), 7.28-7.32 (m, 2H), 7.51-7.61 (m, 5H), 8.05-8.08 (m, 2H), 8.76 (dd, *J* = 1.6, 8.4 Hz, 1H), 8.94 (d, *J* = 8.4 Hz, 1H), 13.28 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 116.3, 120.2, 120.9, 121.4, 123.2, 125.5, 128.9, 129.2, 131.4, 133.7, 133.8, 137.0, 138.3, 142.3, 158.1, 160.2, 165.0, 192.9 (one ^{13}C signal was not observed). HRMS (ESI) calcd for $C_{21}H_{14}ClN_2O_2$ $[M + H]^+$ 361.0738, found 361.0745.

4-Nitro-*N*-(2-(3-oxo-3*H*-indol-2-yl)phenyl)benzamide (2e): Petroleum ether/ethyl acetate (20:1) as eluent; red solid (64 mg, 43%), mp 186-188 °C. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.30-7.31 (m, 1H), 7.35-7.40 (m, 2H), 7.63-7.68 (m, 3H), 8.35 (d, *J* = 8.4 Hz, 2H), 8.46 (d, *J* = 8.4 Hz, 2H), 8.86 (d, *J* = 7.8 Hz, 1H), 9.00 (d, *J* = 8.4 Hz, 1H), 13.53 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) δ 116.7, 120.4, 121.0, 121.4, 123.9, 125.7, 128.9, 129.2, 131.6, 134.0, 137.3, 141.0, 141.8, 149.9, 158.1, 160.5, 164.1, 192.9 (one ^{13}C signal was not observed). HRMS (ESI) calcd for $C_{21}H_{14}N_3O_4$ $[M + H]^+$ 372.0979, found 372.1010.

***N*-(2-(3-Oxo-3*H*-indol-2-yl)phenyl)acetamide (2f):** Petroleum ether/ethyl acetate (20:1) as eluent; red solid (46 mg, 44%), mp 178-179 °C. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 2.25 (s, 3H), 7.10 (t, *J* = 7.8 Hz, 1H), 7.23-7.28 (m, 2H), 7.46 (t, *J* = 7.8 Hz, 1H), 7.50-7.53 (m, 2H), 8.64 (d, *J* = 7.8 Hz, 1H), 8.71 (d, *J* = 8.4 Hz, 1H), 12.35 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) δ 25.6, 115.7, 120.1, 121.4, 122.8, 125.3, 128.7, 131.2, 133.6, 136.9, 142.1, 158.4, 160.2, 169.3, 193.2 (one ^{13}C signal was not observed). HRMS (ESI) calcd for $C_{16}H_{12}N_2NaO_2$ $[M + Na]^+$ 287.0791, found 287.0801.

***N*-(4-Methyl-2-(3-oxo-3*H*-indol-2-yl)phenyl)benzamide (2g):** Petroleum ether/dichloromethane (1:1) as eluent; red solid (70 mg, 51%), mp 147-149 ^{o}C. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 2.37 (s, 3H), 7.24-7.26 (m, 2H), 7.32 (dd, *J* = 1.2, 8.4 Hz, 1H), 7.51-7.55 (m, 4H), 7.59 (t, *J* = 7.2 Hz, 1H), 8.10 (d, *J* = 7.2 Hz, 2H), 8.49 (s, 1H), 8.84 (d, *J* = 8.4 Hz, 1H), 13.15 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) δ 20.9, 116.3, 120.2, 120.9, 121.4, 125.3, 127.7, 128.56, 128.61, 131.3, 131.8, 132.5, 134.6, 135.4, 136.9, 140.2, 158.3, 160.2, 166.0, 193.2. HRMS (ESI) calcd for $C_{22}H_{16}N_2NaO_2$ $[M + Na]^+$ 363.1104, found 363.1104.

***N*-(4-Chloro-2-(3-oxo-3*H*-indol-2-yl)phenyl)benzamide (2h):** Petroleum ether/ethyl acetate (10:1) as eluent; red solid (69 mg, 48%), mp 186-188 ^{o}C. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.31-7.34 (m, 2H), 7.48 (dd, *J* = 2.4, 9.0 Hz, 1H), 7.55-7.63 (m, 5H), 8.10 (d, *J* = 7.8 Hz, 2H), 8.74 (d, *J* = 2.4 Hz, 1H), 8.96 (d, *J* = 9.0 Hz, 1H), 13.21 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) δ 117.4, 121.3, 121.5, 125.6, 127.8, 128.2, 128.7, 129.2, 130.5, 132.2, 133.5, 135.0, 137.1, 141.0, 157.9, 159.3, 166.2, 192.4 (one ^{13}C signal was not observed). HRMS (ESI) calcd for $C_{21}H_{14}ClN_2O_2$ $[M + H]^+$ 361.0738, found 361.0760.

***N*-(2-(3-Oxo-3*H*-indol-2-yl)-4-(trifluoromethyl)phenyl)benzamide (2i):** Petroleum ether/ethyl acetate (10:1) as eluent; red solid (74 mg, 47%), mp 162-163 ^{o}C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.33-7.36 (m, 2H), 7.55-7.64 (m, 5H), 7.76-7.79 (m, 1H), 8.12-8.14 (m, 2H), 9.09 (s, 1H), 9.13 (d, *J* = 9.2 Hz, 1H), 13.42 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) δ 116.0, 120.3, 121.3, 121.4, 123.8 (q, *J* = 270.2 Hz, 1C), 125.0 (q, *J* = 32.9 Hz, 1C), 125.8, 127.9, 128.4 (q, *J* = 4.4 Hz, 1C), 128.8, 129.4, 130.2 (q, *J* = 4.4 Hz, 1C), 132.4, 134.8, 137.2, 144.9, 157.8, 159.5, 166.6, 192.4. HRMS (ESI) calcd for $C_{22}H_{14}F_3N_2O_2$ $[M + H]^+$ 395.1002, found 395.1006.

***N*-(2-(5-Methyl-3-oxo-3*H*-indol-2-yl)phenyl)benzamide (2j):** Petroleum ether/ethyl acetate (10:1) as eluent; red solid (71 mg, 52%), mp 162-163 °C. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 2.26 (s, 3H), 7.03 (d, *J* = 7.8 Hz, 1H), 7.06 (t, *J* = 7.2 Hz, 1H), 7.20 (d, *J* = 7.2 Hz, 1H), 7.24 (s, 1H), 7.43-7.46 (m, 3H), 7.50 (t, *J* = 7.2 Hz, 1H), 8.03 (d, *J* = 7.2 Hz, 2H), 8.61 (dd, *J* = 1.2, 8.4 Hz, 1H), 8.88 (d, *J* = 8.4 Hz, 1H), 13.16 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) δ 21.2, 116.5, 120.2, 120.7, 121.6, 123.0, 126.2, 127.8, 128.6, 131.2, 131.9, 133.5, 135.4, 137.1, 139.2, 142.3, 156.0, 159.7, 166.2, 193.4. HRMS (ESI) calcd for $C_{22}H_{17}N_2O_2$ $[M + H]^+$ 341.1285, found 341.1292.

***N*-(2-(5-Chloro-3-oxo-3*H*-indol-2-yl)phenyl)benzamide (2k):** Petroleum ether/ethyl acetate (10:1) as eluent; red solid (86 mg, 60%), mp 194-196 °C. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.13 (t, *J* = 7.2 Hz, 1H), 7.18-7.19 (m, 1H), 7.45-7.54 (m, 6H), 8.04 (d, *J* = 7.2 Hz, 2H), 8.65 (dd, *J* = 1.2, 7.8 Hz, 1H), 8.92 (d, *J* = 8.4 Hz, 1H), 13.07 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) δ 116.1, 120.4, 121.9, 122.7, 123.2, 125.8, 127.8, 128.7, 131.4, 132.1, 134.2, 134.6, 135.4, 136.3, 142.7, 156.6, 160.3, 166.4, 192.2. HRMS (ESI) calcd for $C_{21}H_{14}ClN_2O_2$ $[M + H]^+$ 361.0738, found 361.0746.

***N*-(2-(5-Chloro-3-oxo-3*H*-indol-2-yl)phenyl)-4-methylbenzamide (2l):** Petroleum ether/ethyl acetate (20:1) as eluent; red solid (90 mg, 60%), mp 190-192 °C. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 2.47 (s, 3H), 7.20 (t, *J* = 7.2 Hz, 1H), 7.29 (d, *J* = 8.4 Hz, 1H), 7.36 (d, *J* = 7.2 Hz, 2H), 7.54-7.60 (m, 3H), 8.02 (d, *J* = 7.2 Hz, 2H), 8.73 (d, *J* = 7.8 Hz, 1H), 9.00 (d, *J* = 7.8 Hz, 1H), 13.10 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) δ 21.5, 115.9, 120.3, 121.8, 122.6, 123.0, 125.7, 127.8, 129.3, 131.3, 132.4, 134.1, 134.5, 136.2, 142.6, 142.8, 156.5, 160.2, 166.2, 192.2. HRMS (ESI) calcd for $C_{22}H_{16}ClN_2O_2$ $[M + H]^+$ 375.0895, found 375.0906.

***N*-(2-(5-Chloro-3-oxo-3*H*-indol-2-yl)phenyl)-4-methoxybenzamide (2m):** Petroleum ether/ethyl acetate (20:1) as eluent; red solid (98 mg, 63%), mp 198-199 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.91 (s, 3H), 7.01 (d, *J* = 8.4 Hz, 2H), 7.15 (t, *J* = 7.2 Hz, 1H), 7.23 (d, *J* = 7.2 Hz, 1H), 7.50-7.57 (m, 3H), 8.06 (d, *J* = 8.8 Hz, 2H), 8.69 (d, *J* = 7.2 Hz, 1H), 8.95 (d, *J* = 8.4 Hz, 1H), 13.01 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 55.5, 113.9, 115.9, 120.3, 121.8, 122.6, 122.9, 125.7, 127.6, 129.6, 131.3, 134.2, 134.5, 136.2, 142.9, 156.6, 160.3, 162.7, 165.9, 192.2. HRMS (ESI) calcd for $C_{22}H_{16}ClN_2O_3$ $[M + H]^+$ 391.0844, found 391.0843.

4-Chloro-*N*-(2-(5-chloro-3-oxo-3*H*-indol-2-yl)phenyl)benzamide (2n): Petroleum ether/ethyl acetate (30:1) as eluent; red solid (100 mg, 64%), mp 221-222 °C. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.24 (t, *J* = 7.8 Hz, 1H), 7.27-7.28 (m, 1H), 7.55-7.63 (m, 5H), 8.08 (d, *J* = 8.4 Hz, 2H), 8.76 (d, *J* = 7.8 Hz, 1H), 8.98 (d, *J* = 8.4 Hz, 1H), 13.16 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) δ 116.1, 120.4, 121.9, 122.6, 123.4, 125.9, 129.0, 129.2, 131.5, 133.8, 134.3, 134.8, 136.3, 138.4, 142.4, 156.4, 160.3, 165.2, 192.1. HRMS (ESI) calcd for $C_{21}H_{13}Cl_2N_2O_2$ $[M + H]^+$ 395.0349, found 395.0336.

***N*-(2-(3-Oxo-5-(trifluoromethyl)-3*H*-indol-2-yl)phenyl)benzamide (2o):** Petroleum ether/dichloromethane (1:2) as eluent; red solid (80 mg, 51%), mp 148-150 °C. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.20-7.23 (m, 1H), 7.44 (d, *J* = 7.8 Hz, 1H), 7.56 (t, *J* = 7.2 Hz, 2H), 7.60-7.63 (m, 2H), 7.86-7.88 (m, 2H), 8.11-8.13 (m, 2H), 8.77 (dd, *J* = 1.8, 8.4 Hz, 1H), 9.01 (dd, *J* = 0.6, 8.4 Hz, 1H), 13.14 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) δ 115.9, 120.5, 121.1, 121.8, 122.6 (q, *J* = 3.2 Hz, 1C), 123.35, 123.36 (q, *J* = 271.2 Hz, 1C), 127.8, 128.7, 131.1 (q, *J* = 33.9 Hz, 1C), 131.8, 132.2, 134.3 (q, *J* = 3.3 Hz, 1C), 134.9, 135.4, 143.1, 160.9, 161.9, 166.4, 191.9. HRMS (ESI) calcd for $C_{22}H_{14}F_3N_2O_2$ $[M + H]^+$ 395.1002, found 395.1002.

General Procedure for the Preparation of Indolo[1,2-*c*]quinazolines (3). To a mixture of indole **1** (0.4 mmol) in 1,4-dioxane (2 mL) were added CuBr (5.7 mg, 0.04 mmol) and 0.5 M HCl aqueous solution (0.16 mL, 0.08 mmol) under air and then the resulting mixture was stirred at 120 ^{o}C for 4~10 h. After the reactant **1** was consumed completely, water was added into the reaction system, followed by extraction with ethyl acetate. The extract was washed with water and brine, and then dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography on silica gel to give the corresponding indolo[1,2-*c*]quinazoline **3**.

6-Phenylindolo[1,2-*c*]quinazoline (3a):[14f] Petroleum ether/ethyl acetate (5:1) as eluent; yellow solid (85 mg, 72%), mp 187-188 ^{o}C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.34 (d, *J* = 8.4 Hz, 1H), 6.84-6.88 (m, 1H), 7.12 (s, 1H), 7.18 (t, *J* = 7.6 Hz, 1H), 7.36 (td, *J* = 1.6, 7.6 Hz, 1H), 7.41 (td, *J* = 1.6, 7.6 Hz, 1H), 7.46-7.55 (m, 5H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.72 (dd, *J* = 0.8, 7.6 Hz, 1H), 7.96 (dd, *J* = 0.8, 7.6 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 94.7, 113.8, 119.4, 119.5, 120.4, 121.7, 122.4, 126.3, 126.8, 127.2, 128.0, 128.2, 129.3, 130.6, 134.2, 134.9, 138.2, 148.3 (one ^{13}C signal was not observed). MS (ESI) *m/z* 295 $[M + H]^+$.

6-*p*-Tolylindolo[1,2-*c*]quinazoline (3b):[14f] Petroleum ether/ethyl acetate (5:1) as eluent; yellow solid (67 mg, 54%), mp 154-155 ^{o}C. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 2.51 (s, 3H), 6.56 (d, *J* = 8.4 Hz, 1H), 6.98 (t, *J* = 8.4 Hz, 1H), 7.23 (s, 1H), 7.28 (t, *J* = 7.2 Hz, 1H), 7.39 (d, *J* = 7.2 Hz, 2H), 7.46 (t, *J* = 7.8 Hz, 1H), 7.51 (t, *J* = 7.2 Hz, 1H), 7.54 (d, *J* = 7.8 Hz, 2H), 7.74 (d, *J* = 7.8 Hz, 1H), 7.81 (d, *J* = 7.8 Hz, 1H), 8.07 (d, *J* = 7.2 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) δ 21.7, 95.7, 115.1, 120.5, 120.6, 121.4, 122.7, 123.4, 127.3, 127.9, 128.2, 129.1, 129.9, 130.4, 131.8, 133.2, 135.3, 139.4, 140.5, 149.6. MS (ESI) *m/z* 309 $[M + H]^+$.

6-(4-Methoxyphenyl)indolo[1,2-*c*]quinazoline (3c):[14f] Petroleum ether/ethyl acetate (5:1) as eluent; yellow solid (74 mg, 57%), mp 177-178 °C. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 3.93 (s, 3H), 6.63 (d, *J* = 9.0 Hz, 1H), 7.01 (t, *J* = 7.2 Hz, 1H), 7.11 (d, *J* = 8.4 Hz, 2H), 7.25 (s, 1H), 7.30 (t, *J* = 7.2 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.52 (t, *J* = 7.2 Hz, 1H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.76 (d, *J* = 7.8 Hz, 1H), 7.81 (d, *J* = 7.8 Hz, 1H), 8.08 (d, *J* = 7.8 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) δ 55.5, 95.7, 114.6, 115.1, 120.48, 120.54, 121.4, 122.7, 123.4, 127.3, 127.8, 128.4, 129.1, 129.8, 130.4, 131.8, 135.4, 139.4, 149.3, 161.2. MS (ESI) *m/z* 325 $[M + H]^+$.

6-(4-Chlorophenyl)indolo[1,2-*c*]quinazoline (3d):[14f] Petroleum ether/ethyl acetate (5:1) as eluent; yellow solid (80 mg, 61%), mp 195-196 °C. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.57 (d, *J* = 8.4 Hz, 1H), 7.01-7.03 (m, 1H), 7.23 (s, 1H), 7.30 (t, *J* = 7.8 Hz, 1H), 7.47 (t, *J* = 7.2 Hz, 1H), 7.51 (td, *J* = 7.2, 1.2 Hz, 1H), 7.56-7.61 (m, 4H), 7.75 (d, *J* = 7.8 Hz, 1H), 7.79 (d, *J* = 7.8 Hz, 1H), 8.05 (dd, *J* = 0.6, 7.2 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) δ 96.0, 114.7, 120.6, 120.7, 121.7, 122.8, 123.6, 127.6, 127.9, 129.2, 129.6, 129.9, 130.4, 131.5, 134.4, 135.2, 136.6, 139.1, 148.2. MS (ESI) *m/z* 329 $[M + H]^+$.

6-(4-Nitrophenyl)indolo[1,2-*c*]quinazoline (3e):[15e] Petroleum ether/ethyl acetate (10:1) as eluent; yellow solid (54 mg, 40%), mp 188-189 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.37 (d, *J* = 8.8 Hz, 1H), 6.90-6.94 (m, 1H), 7.15 (s, 1H), 7.23 (t, *J* = 7.2 Hz, 1H), 7.39-7.46 (m, 2H), 7.66-7.70 (m, 2H), 7.75 (d, *J* = 8.8 Hz, 2H), 7.96-7.98 (m, 1H), 8.33 (d, *J* = 8.8 Hz, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 96.3, 114.3, 120.6, 121.0, 121.9, 122.9, 123.9, 124.5, 128.0, 128.1, 129.4, 129.8, 130.5, 131.1, 135.1, 138.8, 141.8, 147.0, 149.0. MS (ESI) *m/z* 340 $[M + H]^+$.

6-Methylindolo[1,2-*c*]quinazoline (3f):[14c,14d] Petroleum ether/ethyl acetate (20:1) as eluent; yellow solid (45 mg, 48%), mp 105-106 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.00 (s, 3H), 7.05 (s, 1H), 7.27-7.31 (m, 1H), 7.34-7.39 (m, 2H), 7.44-7.48 (m, 1H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.95 (d, *J* = 8.4 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 25.3, 95.4, 114.7, 120.2, 120.7, 122.0, 122.6, 123.3, 126.7, 126.9, 128.9, 130.4, 131.7, 134.8, 138.9, 148.5. MS (ESI) *m/z* 233 $[M + H]^+$.

2-Methyl-6-phenylindolo[1,2-*c*]quinazoline (3g): Petroleum ether/ethyl acetate (15:1) as eluent; yellow solid (74 mg, 60%), mp 197-198 °C. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 2.48 (s, 3H), 6.38 (d, *J* = 8.4 Hz, 1H), 6.89 (t, *J* = 7.8 Hz, 1H), 7.19 (s, 1H), 7.22 (t, *J* = 7.2 Hz, 1H), 7.29-7.30 (m, 1H), 7.53-7.61 (m, 5H), 7.66 (d, *J* = 8.4 Hz, 1H), 7.70 (d, *J* = 7.8 Hz, 1H), 7.85 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) δ 21.7, 95.4, 114.9, 120.35, 120.45, 121.4, 122.6, 123.3, 127.7, 128.3, 129.3, 130.3, 130.4, 130.5, 131.7, 135.4, 136.1, 137.2, 137.5, 148.6. HRMS (ESI) calcd for $C_{22}H_{17}N_2$ $[M + H]^+$ 309.1386, found 309.1377.

2-Chloro-6-phenylindolo[1,2-*c*]quinazoline (3h):[14f] Petroleum ether/ethyl acetate (10:1) as eluent; yellow solid (81 mg, 62%), mp 201-202 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.46 (d, *J* = 9.2 Hz, 1H), 6.97-7.02 (m, 1H), 7.24 (s, 1H), 7.29-7.33 (m, 1H), 7.45 (dd, *J* = 2.4, 8.4 Hz, 1H), 7.58-7.67 (m, 5H), 7.73 (d, *J* = 8.4 Hz, 1H), 7.77 (d, *J* = 7.6 Hz, 1H), 8.04 (d, *J* = 2.0 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 96.7, 115.0, 120.8, 121.8, 122.0, 122.3, 123.7, 128.2, 129.28, 129.35, 130.2, 130.6, 131.7, 132.9, 134.0, 135.7, 137.7, 149.5 (one ^{13}C signal was not observed). MS (ESI) *m/z* 329 $[M + H]^+$.

10-Methyl-6-phenylindolo[1,2-*c*]quinazoline (3i):[14c] Petroleum ether/ethyl acetate (10:1) as eluent; yellow solid (65 mg, 53%), mp 178-179 °C. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 2.41 (s, 3H), 6.30 (d, *J* = 9.0 Hz, 1H), 6.77 (d, *J* = 9.0 Hz, 1H), 7.11 (s, 1H), 7.44 (t, *J* = 7.8 Hz, 1H),

7.48-7.50 (m, 2H), 7.55-7.58 (m, 2H), 7.60-7.62 (m, 3H), 7.80 (d, *J* = 8.4 Hz, 1H), 8.02 (d, *J* = 7.8 Hz, 1H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 150 MHz) δ 21.5, 95.4, 114.5, 120.2, 120.7, 122.7, 123.2, 127.3, 127.9, 128.3, 129.0, 129.3, 130.0, 130.4, 130.8, 133.1, 135.4, 136.1, 139.3, 149.3. HRMS (ESI) calcd for $C_{22}H_{17}N_2$ $[M + H]^+$ 309.1386, found 309.1372.

10-Chloro-6-phenylindolo[1,2-*c*]quinazoline (3j):[14f] Petroleum ether/ethyl acetate (10:1) as eluent; yellow solid (88 mg, 67%), mp 231-232 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.31 (d, *J* = 9.2 Hz, 1H), 6.89 (dd, *J* = 2.4, 9.2 Hz, 1H), 7.10 (s, 1H), 7.46 (td, *J* = 7.2, 1.2 Hz, 1H), 7.53 (td, *J* = 7.2, 1.6 Hz, 1H), 7.56-7.63 (m, 5H), 7.65 (d, *J* = 2.0 Hz, 1H), 7.81 (dd, *J* = 0.8, 8.0 Hz, 1H), 8.02 (dd, *J* = 1.2, 8.0 Hz, 1H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz) δ 95.1, 115.8, 119.7, 120.2, 121.7, 122.9, 127.6, 128.0, 128.2, 129.2, 129.4, 129.5, 129.9, 130.6, 131.5, 135.6, 136.5, 139.3, 148.9. MS (ESI) *m/z* 329 $[M + H]^+$.

10-Chloro-6-(*p*-tolyl)indolo[1,2-*c*]quinazoline (3k):[14f] Petroleum ether/ethyl acetate (20:1) as eluent; yellow solid (86 mg, 63%), mp 195-196 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.53 (s, 3H), 6.46 (d, *J* = 9.2 Hz, 1H), 6.94 (dd, *J* = 2.0, 8.8 Hz, 1H), 7.21 (s, 1H), 7.42 (d, *J* = 7.6 Hz, 2H), 7.52-7.57 (m, 4H), 7.73 (d, *J* = 2.0 Hz, 1H), 7.84 (dd, *J* = 1.2, 8.0 Hz, 1H), 8.11 (dd, *J* = 1.2, 7.6 Hz, 1H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz) δ 21.7, 95.0, 116.0, 119.6, 120.2, 121.6, 122.8, 127.5, 128.0, 128.1, 129.2, 129.5, 130.02, 130.04, 131.5, 132.7, 136.6, 139.4, 140.8, 149.1. HRMS (ESI) calcd for $C_{22}H_{16}ClN_2$ $[M + H]^+$ 343.0997, found 343.0992.

10-Chloro-6-(4-methoxyphenyl)indolo[1,2-*c*]quinazoline (3l): Petroleum ether/ethyl acetate (10:1) as eluent; yellow solid (86 mg, 60%), mp 177-178 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.93 (s, 3H), 6.51 (d, *J* = 8.8 Hz, 1H), 6.94 (dd, *J* = 2.4, 9.2 Hz, 1H), 7.10 (dt, *J* = 8.8, 2.4 Hz, 2H), 7.15 (s, 1H), 7.46-7.59 (m, 4H), 7.69 (d, *J* = 2.0 Hz, 1H), 7.81 (dd, *J* = 1.2, 8.0 Hz, 1H), 8.06 (dd, *J* = 1.2, 7.6 Hz, 1H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz) δ 55.5, 95.0, 114.7,

116.0, 119.7, 120.1, 121.6, 122.8, 127.5, 127.91, 127.94, 129.2, 129.5, 129.8, 130.1, 131.5, 136.7, 139.4, 148.9, 161.3. HRMS (ESI) calcd for $C_{22}H_{16}ClN_2O$ $[M + H]^+$ 359.0946, found 359.0933.

10-Chloro-6-(4-chlorophenyl)indolo[1,2-*c*]quinazoline (3m):[14f] Petroleum ether/ethyl acetate (20:1) as eluent; yellow solid (89 mg, 61%), mp 192-193 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.50 (d, *J* = 9.2 Hz, 1H), 6.99 (dd, *J* = 2.0, 8.8 Hz, 1H), 7.22 (s, 1H), 7.52-7.65 (m, 6H), 7.74 (d, *J* = 2.0 Hz, 1H), 7.81-7.83 (m, 1H), 8.10-8.12 (m, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 95.3, 115.6, 119.9, 120.2, 121.9, 122.9, 127.9, 128.0, 129.4, 129.6, 129.7, 129.77, 129.81, 131.5, 134.0, 136.5, 136.8, 139.2, 147.8. HRMS (ESI) calcd for $C_{21}H_{12}Cl_2N_2Na$ $[M + Na]^+$ 385.0270, found 385.0282.

10-Chloro-6-(trifluoromethyl)indolo[1,2-*c*]quinazoline (3n): Petroleum ether/ethyl acetate (20:1) as eluent; yellow solid (58 mg, 45%), mp 175-176 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.29 (s, 1H), 7.38 (dd, *J* = 2.4, 9.2 Hz, 1H), 7.60-7.63 (m, 2H), 7.79 (d, *J* = 2.4 Hz, 1H), 7.89-7.91 (m, 1H), 8.05-8.10 (m, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ 96.9, 115.6 (q, *J* = 7.3 Hz, 1C), 118.8 (q, *J* = 273.5 Hz, 1C), 120.1, 121.3, 122.8, 123.5, 128.4, 129.0, 129.8, 129.9, 130.2, 131.4, 136.2, 136.3 (one ^{13}C signal was not observed). HRMS (ESI) calcd for $C_{16}H_9ClF_3N_2$ $[M + H]^+$ 321.0401, found 321.0393.

6-Phenyl-10-(trifluoromethyl)indolo[1,2-*c*]quinazoline (3o): Petroleum ether/dichloromethane (1:2) as eluent; yellow solid (72 mg, 50%), mp 192-193 °C. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.51 (d, *J* = 9.0 Hz, 1H), 7.20 (dd, *J* = 1.2, 8.4 Hz, 1H), 7.32 (s, 1H), 7.54 (td, *J* = 7.8, 1.2 Hz, 1H), 7.58 (td, *J* = 7.2, 1.2 Hz, 1H), 7.62-7.68 (m, 5H), 7.85 (d, *J* = 7.8 Hz, 1H), 8.05 (s, 1H), 8.12 (dd, *J* = 1.2, 7.8 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz) δ 96.0, 115.2, 117.9 (q, *J* = 4.4 Hz, 1C), 120.2, 123.0, 124.7 (q, *J* = 270.2 Hz, 1C), 125.6 (q, *J* =

31.7 Hz, 1C), 127.9, 128.16, 128.21, 129.5, 129.78, 129.80, 130.7, 132.8, 135.5, 136.8, 139.2, 148.9 (one ^{13}C signal was not observed). HRMS (ESI) calcd for $C_{22}H_{14}F_3N_2$ $[M + H]^+$ 363.1104, found 363.1086.

5-Phenylpyrrolo[1,2-*c*]quinazoline (3p):[16a] Petroleum ether/ethyl acetate (5:1) as eluent; yellow solid (49 mg, 50%), mp 172-173 ^oC. ^1H NMR ($CDCl_3$, 400 MHz) δ 6.68 (t, *J* = 3.6 Hz, 1H), 6.92 (dd, *J* = 1.6, 4.0 Hz, 1H), 7.31 (dd, *J* = 1.2, 2.4 Hz, 1H), 7.36-7.42 (m, 2H), 7.48-7.50 (m, 3H), 7.77-7.79 (m, 3H), 7.90-7.92 (m, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz) δ 101.1, 114.0, 114.8, 121.1, 121.6, 127.3, 127.5, 128.3, 128.6, 129.0, 130.6, 130.8, 134.3, 138.3, 147.7. MS (ESI) *m/z* 245 $[M + H]^+$.

6-Phenylpyrido[2',3':4,5]pyrimido[1,6-*a*]indole (3q): Dichloromethane/ethyl acetate (2:1) as eluent; yellow solid (76.8 mg, 65%), mp 192-193 ^oC. ^1H NMR ($CDCl_3$, 400 MHz) δ 6.54 (d, *J* = 8.8 Hz, 1H), 6.97 (t, *J* = 7.6 Hz, 1H), 7.25-7.28 (m, 2H), 7.34-7.37 (m, 1H), 7.51-7.61 (m, 3H), 7.67 (d, *J* = 7.6 Hz, 2H), 7.72 (d, *J* = 8.0 Hz, 1H), 8.35 (d, *J* = 8.0 Hz, 1H), 8.71 (m, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz) δ 97.8, 115.2, 115.9, 120.7, 122.2, 122.4, 123.9, 128.4, 129.0, 130.5, 130.7, 131.3, 131.7, 134.7, 135.3, 150.6, 150.9, 152.9. HRMS (ESI) calcd for $C_{20}H_{13}N_3Na[M + Na]^+$ 318.1002, found 318.1011.

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Supporting Information

Table Sl, X-ray crystal structure and data of **2a**, Table S2, and ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of compounds **2a-2o** and **3a-3q**. This material is available free of charge via the Internet at .....

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