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Copper-Catalyzed Cascade Synthesis of 1*H*-Indolo[1,2-*c*]quinazoline Derivatives

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A simple, efficient and practical approach to 1*H*-indolo[1,2-*c*]quinazoline derivatives has been developed that uses inexpensive and readily-available catalyst and substrates. The method should provide a new strategy for *N*-fused heterocycles and will show wide application in organic chemistry and medicinal chemistry.

Introduction

Nitrogen-containing heterocycles are widely found in natural products and biologically active molecules.[1] The indole unit acts as a privileged structural motif of both designed medicinal agents and natural products. For example, indole derivatives have been used as neurotransmitter, antihypertensive and antibiotic agents,[2] and some of them are 5-HT3 or 5HT1 receptor antagonists used in the treatment of chemotherapy-induced nausea and vomiting,[3] and cluster headaches.[4] Quinazolines also exhibit a variety of biological functions. For example, quinazoline derivatives have been used as tyrosine kinase and cellular phosphorylation inhibitors,[5] ligands for benzodiazepine and GABA receptors in the central nervous system[6] and DNA binders,[7] and some of them have acted as anticancer,[8] antiviral,[9] and antitubercular agents.[10] *N*-Fused heterocycles of indole and quinazoline frameworks, indoloquinazoline derivatives (Figure 1), are important biological molecules, and they exhibit antibacterial,[11] antifungal and weak cytotoxic activity.[12] However, the methods for synthesis of indoloquinazoline derivatives are very limited. Recently, great achievements have been made in copper-catalyzed cross-couplings[13] and synthesis of *N*-heterocycles by us[14] and other research groups.[15] Herein, we report a new and efficient copper-catalyzed approach to indoloquinazoline derivatives.

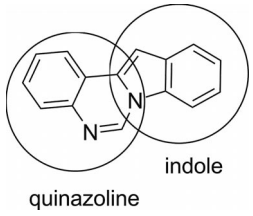

Figure 1. Indoloquinazoline-containing indole and quinazoline frameworks.

Results and Discussion

As shown in Table 1, reaction of 2-(2-bromophenyl)-1*H*-indole (**1a**) with acetamidine hydrochloride (**2a**) was used as the model to optimize catalytic conditions including catalysts, bases, solvents and temperature under a nitrogen atmosphere. Six catalysts were screened by using K_2CO_3 (1.5 equiv.) as the base (relative to **1a**), and DMSO as the solvent at 80 °C (Table 1, Entries 1–6), and CuBr afforded the highest yield (Table 1, Entry 2). Cs_2CO_3 and Na_2CO_3 were used as bases (Table 1, Entries 7 and 8), and K_2CO_3 showed the highest efficiency (Table 1, Entries 2, 7 and 8). DMF and dioxane were trialed as solvents (Table 1, Entries 9 and 10) but were inferior to DMSO (Table 1, Entries 2, 9 and 10). The effect of temperature was also investigated (Table 1, Entries 11–13) and 80 °C was a good choice (Table 1, Entry 2).

The substrate scope of the copper-catalyzed cascade synthesis of 1*H*-indolo[1,2-*c*]quinazoline derivatives was investigated under the optimized conditions [CuBr (10 mol-%) as catalyst, K_2CO_3 (1.5 equiv.) as the base under a nitrogen atmosphere]. As shown in Table 2, most of the tested substrates afforded good to excellent yields. For the substituted 2-(2-halophenyl)-1*H*-indoles, aryl iodide (**1d**) showed slightly higher reactivity than aryl bromide (**1a**; Table 2, Entries 2 and 6), and no evident difference on the electronic effect in the substrates was observed. For the amidines, most of aliphatic amidines provided slightly higher yields

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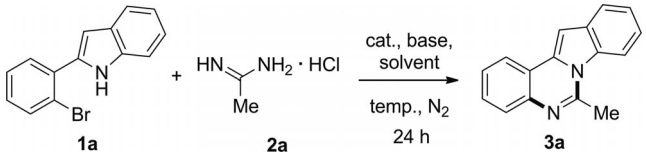
Table 1. Copper-catalyzed cascade synthesis of 6-methyl-1*H*-indolo[1,2-*c*]quinazoline (**3a**) through reaction of 2-(2-bromophenyl)-1*H*-indole (**1a**) with acetamidine hydrochloride (**2a**). Optimization of the reaction conditions.[a]

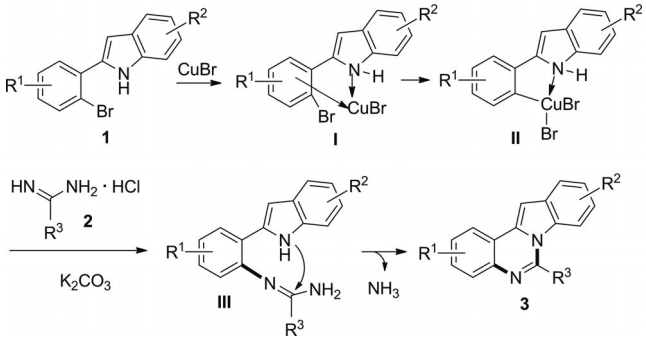


Entry	Cat.	Base	Solvent	Temp.	% Yield[b]
1	CuI	K_2CO_3	DMSO	80	84
2	CuBr	K_2CO_3	DMSO	80	92
3	CuCl	K_2CO_3	DMSO	80	89
4	Cu_2O	K_2CO_3	DMSO	80	90
5	$Cu(OAc)_2$	K_2CO_3	DMSO	80	64
6	$CuBr_2$	K_2CO_3	DMSO	80	82
7	CuBr	Cs_2CO_3	DMSO	80	87
8	CuBr	Na_2CO_3	DMSO	80	29
9	CuBr	K_2CO_3	DMF	80	62
10	CuBr	K_2CO_3	dioxane	80	66
11	CuBr	K_2CO_3	DMSO	r.t.	trace
12	CuBr	K_2CO_3	DMSO	60	69
13	CuBr	K_2CO_3	DMSO	100	79

[a] Reaction conditions: 2-(2-bromophenyl)-1*H*-indole (**1a**, 0.5 mmol), acetamidine hydrochloride (**2a**, 1 mmol), catalyst (0.05 mmol), base (1.5 mmol), solvent (2 mL) under a nitrogen atmosphere, reaction time (24 h). [b] Isolated yield.

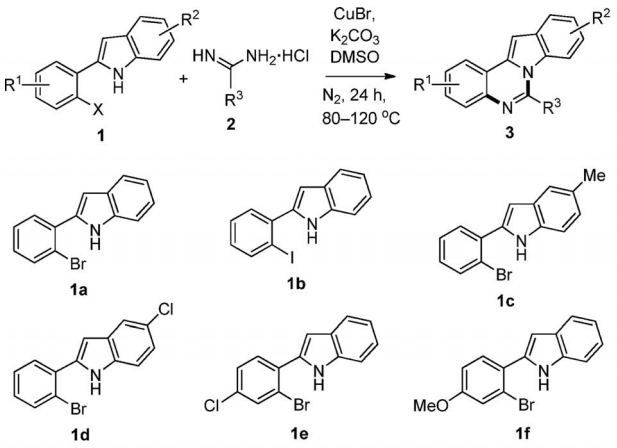
than aromatic ones. The copper-catalyzed cascade reactions could tolerate some functional groups including fluoro (Table 2, Entries 7 and 15), nitro (Table 2, Entries 8 and 16), chloro (Table 2, Entries 17–22) and ether (Table 2, Entry 23). The reactions above did not need addition of any ligand or additive, which demonstrated the *ortho*-substituent effect of the benzimidazole group (see Scheme 1).

According to the results above, a possible mechanism for synthesis of 1*H*-indolo[1,2-*c*]quinazoline derivatives was proposed in Scheme 1. Coordination of substituted 2-(2-bromophenyl)-1*H*-indole with CuBr gives **I**, and oxidative addition of **I** gives **II**. Coupling of **II** with amidine (*N*-arylation) yields intermediate **III**, and the intramolecular nucleophilic attack of the NH of the indole group to the carbon of the amidine provides target product **3** releasing NH_3.[14j]



Scheme 1. Possible copper-catalyzed mechanism for synthesis of 1*H*-indolo[1,2-*c*]quinazoline derivatives.

Table 2. Copper-catalyzed cascade synthesis of 1*H*-indolo[1,2-*c*]quinazoline derivatives.[a]



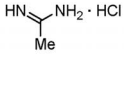
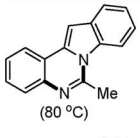
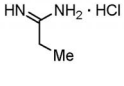
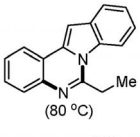
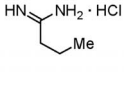
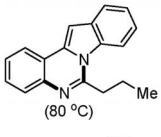
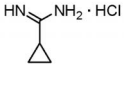
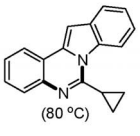
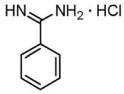
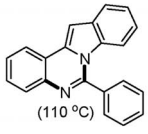
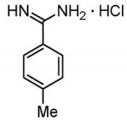
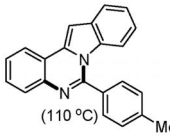
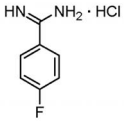
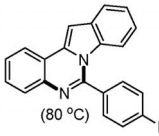
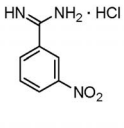
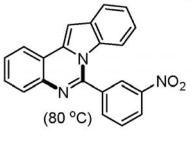
Entry	2	3 (Temp.)	Yield [%][b]
1	 **2a**	 (80 °C) **3a**	87
2	 **2b**	 (80 °C) **3b**	80[c] 89[d]
3	 **2c**	 (80 °C) **3c**	91
4	 **2d**	 (80 °C) **3d**	93
5	 **2e**	 (110 °C) **3e**	74
6	 **2f**	 (110 °C) **3f**	75[c] 78[d]
7	 **2g**	 (80 °C) **3g**	72
8	 **2h**	 (80 °C) **3h**	83

Table 2. *(Continued)*

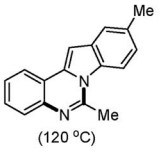
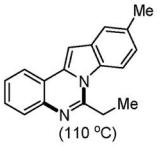
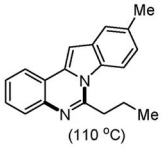
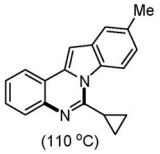
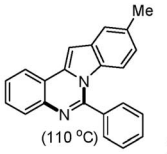
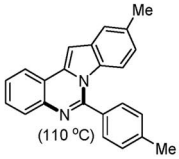
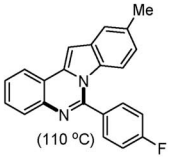
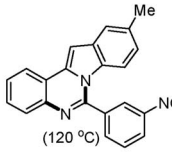
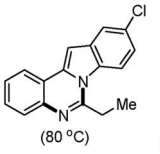
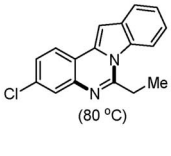
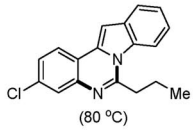
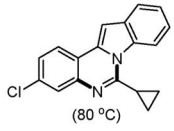
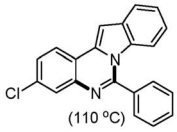
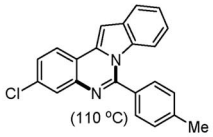
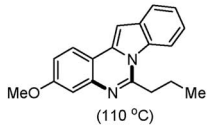
Entry	2	3 (Temp.)	Yield [%][b]
9	2a	 (120 °C) **3i**	68
10	2b	 (110 °C) **3j**	75
11	2c	 (110 °C) **3k**	80
12	2d	 (110 °C) **3l**	84
13	2e	 (110 °C) **3m**	91
14	2f	 (110 °C) **3n**	87
15	2g	 (110 °C) **3o**	66
16	2h	 (120 °C) **3p**	58
17	2b	 (80 °C) **3q**	80
18	2a	 (80 °C) **3r**	61

Table 2. *(Continued)*

Entry	2	3 (Temp.)	Yield [%][b]
19	2b	 (80 °C) **3s**	81
20	2c	 (80 °C) **3t**	89
21	2d	 (110 °C) **3u**	71
22	2e	 (110 °C) **3v**	78
23	2c	 (110 °C) **3w**	74

[a] Reaction conditions: Substituted 2-(2-halophenyl)-1*H*-indole (**1**, 0.5 mmol), amidine hydrochloride (**2**, 1 mmol), CuBr (0.05 mmol), K_2CO_3 (1.5 mmol), DMSO (2 mL) under a nitrogen atmosphere, reaction temperature (80–120 °C), reaction time (24 h). [b] Isolated yield. [c] **1a** as substrate. [d] **1b** as substrate.

Interestingly, high regioselectivity was observed for N-1 cyclization over C-3 cyclization of indoles owing to the higher nucleophilic power of N-1 over C-3 in the indoles.

Conclusions

A simple and efficient copper-catalyzed cascade method for the synthesis of 1*H*-indolo[1,2-*c*]quinazoline derivatives has been developed. The present method uses inexpensive CuBr as the catalyst and readily-available substituted 2-(2-halophenyl)indoles and amidines as starting materials. The copper-catalyzed cascade reactions performed well under mild conditions. Interestingly, no ligand or additive was required. Therefore, the present method provides a practical approach to this kind of *N*-fused heterocycle.

Experimental Section

General: All reactions were carried out under a nitrogen atmosphere. ^{1}H NMR and ^{13}C NMR spectroscopic data were recorded by using tetramethylsilane (TMS) and the remaining $CHCl_3$ in the

$CDCl_3$ solvent as the internal standard (^1H NMR: TMS at δ = 0.00 ppm, $CHCl_3$ at δ = 7.26 ppm. ^{13}C NMR: $CDCl_3$ at δ = 77.4 ppm).

Compounds **1a**–**f** were prepared according to the previous procedures.[16]

General Procedure for Copper-Catalyzed Synthesis of 1*H*-Indolo[1,2-*c*]quinazoline Derivatives (3): A 25 mL Schlenk tube was charged with substituted 2-(2-halophenyl)indole (**1**, 0.5 mmol), amidine hydrochloride (**2**, 1 mmol), and CuBr (0.05 mmol, 7.1 mg), K_2CO_3 (0.75 mmol, 104 mg), and DMSO (2 mL). The tube was sealed and the mixture was allowed to stir at 80–120 °C (see Table 2) under a nitrogen atmosphere for 24 h. The resulting solution was cooled to room temperature, and water (8 mL) was added to the resulting solution. The resulting aqueous solution was extracted with ethyl acetate (3 × 10 mL), the combined organic phase was dried with anhydrous $MgSO_4$ and concentrated with the aid of a rotary evaporator. The residue was purified by column chromatography on silica gel to provide desired product **3**.

6-Methylindolo[1,2-*c*]quinazoline (3a):[17] Eluent: petroleum ether/ethyl acetate (50:1); yield 107 mg (92%), yellow solid, m.p. 119–120 °C. ^1H NMR ($CDCl_3$, 300 MHz): δ = 3.15 (s, 3 H), 7.21 (s, 1 H), 7.36–7.54 (m, 4 H), 7.71–7.73 (d, *J* = 7.56 Hz, 1 H), 7.81–7.84 (d, *J* = 7.56 Hz, 1 H), 8.03–8.06 (d, *J* = 7.92 Hz, 1 H), 8.08–8.11 (d, *J* = 8.25 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 25.5, 95.6, 114.9, 120.3, 120.9, 122.2, 122.7, 123.5, 126.9, 127.0, 129.1, 130.6, 131.8, 135.0, 139.0, 148.6 ppm. MS (ESI): *m*/*z* = 233.2 [M + H]$^+$.

6-Ethylindolo[1,2-*c*]quinazoline (3b): Eluent: petroleum ether/ethyl acetate (50:1); yield 98.9 mg (80%) with 2-(2-bromophenyl)-1*H*-indole as the substrate and 110 mg (89%) with 2-(2-iodophenyl)-1*H*-indole as the substrate, yellow solid, m.p. 90–91 °C. ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.56–1.61 (t, *J* = 7.56 Hz, 3 H), 3.39–3.46 (q, *J* = 7.53 Hz, 2 H), 7.20 (s, 1 H), 7.34–7.54 (m, 4 H), 7.73–7.76 (d, *J* = 8.1 Hz, 1 H), 7.80–7.83 (d, *J* = 6.87 Hz, 1 H), 8.02–8.06 (d, *J* = 7.89 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 10.8, 30.3, 95.5, 115.2, 120.4, 120.8, 122.1, 122.7, 123.3, 126.8, 127.3, 129.0, 130.6, 131.3, 135.3, 139.0, 152.4 ppm. HRMS: calcd. for $C_{17}H_{14}N_2$ [M + H]$^+$ 247.1235; found 247.1225.

6-Propylindolo[1,2-*c*]quinazoline (3c): Eluent: petroleum ether/ethyl acetate (50:1); yield 118 mg (91%), yellow solid, m.p. 108–109 °C. ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.17–1.22 (t, *J* = 7.2 Hz, 3 H), 2.01–2.08 (m, 2 H), 3.29–3.34 (t, *J* = 7.56 Hz, 2 H), 7.15 (s, 1 H), 7.34–7.49 (m, 4 H), 7.70–7.73 (d, *J* = 7.2 Hz, 1 H), 7.77–7.80 (d, *J* = 7.2 Hz, 1 H), 7.93–8.01 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.0, 19.7, 38.9, 95.5, 115.1, 120.4, 120.9, 122.1, 122.7, 123.3, 126.8, 127.3, 129.0, 130.6, 131.3, 135.3, 139.0, 151.4 ppm. HRMS: calcd. for $C_{18}H_{16}N_2$ [M + H]$^+$ 261.1392; found 261.1389.

6-Cyclopropylindolo[1,2-*c*]quinazoline (3d): Eluent: petroleum ether/ethyl acetate (50:1); yield 120 mg (93%), yellow solid, m.p. 120–121 °C. ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.26–1.32 (m, 2 H), 1.46–1.51 (m, 2 H), 2.63–2.68 (m, 1 H), 7.19 (s, 1 H), 7.35–7.48 (m, 4 H), 7.68–7.72 (d, *J* = 7.89 Hz, 1 H), 7.80–7.83 (d, *J* = 7.56 Hz, 1 H), 7.99–8.02 (d, *J* = 7.56 Hz, 1 H), 8.43–8.46 (d, *J* = 8.25 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 8.0, 17.3, 95.4, 115.5, 120.4, 120.7, 121.9, 122.7, 123.4, 126.8, 127.3, 129.0, 130.6, 131.8, 135.3, 139.0, 151.5 ppm. HRMS: calcd. for $C_{18}H_{14}N_2$ [M + H]$^+$ 259.1235; found 259.1230.

6-Phenylindolo[1,2-*c*]quinazoline (3e):[18] Eluent: petroleum ether/ethyl acetate (50:1); yield 109 mg (74%), yellow solid, m.p. 205–206 °C. ^1H NMR ($CDCl_3$, 300 MHz): δ = 6.43–6.46 (d, *J* = 8.58 Hz, 1 H), 6.94–7.00 (t, *J* = 8.58 Hz, 1 H), 7.23–7.31 (m, 2 H), 7.49–7.67 (m, 7 H), 7.74–7.77 (d, *J* = 7.89 Hz, 1 H), 7.82–7.84 (d, *J* = 7.2 Hz, 1 H), 8.08–8.11 (d, *J* = 7.2 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 95.9, 115.0, 120.6, 120.7, 121.6, 122.8, 123.5, 127.5, 128.0, 128.3, 129.2, 129.4, 130.5, 131.7, 135.3, 136.1, 139.3, 149.4 ppm. MS (ESI): *m*/*z* = 295.2 [M + H]$^+$.

6-*p*-Tolylindolo[1,2-*c*]quinazoline (3f): Eluent: petroleum ether/ethyl acetate (50:1); yield 116 mg (75%) with 2-(2-bromophenyl)-1*H*-indole as the substrate and 120 mg (78%) with 2-(2-iodophenyl)-1*H*-indole as the substrate, yellow solid, m.p. 160–161 °C. ^1H NMR ($CDCl_3$, 300 MHz): δ = 2.52 (s, 3 H), 6.55–6.58 (d, *J* = 8.58 Hz, 1 H), 6.96–7.02 (t, *J* = 7.89 Hz, 1 H), 7.24–7.31 (m, 2 H), 7.39–7.57 (m, 6 H), 7.74–7.77 (d, *J* = 7.92 Hz, 1 H), 7.80–7.84 (d, *J* = 7.92 Hz, 1 H), 8.08–8.11 (d, *J* = 7.56 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 20.6, 94.6, 114.0, 119.4, 119.5, 120.3, 121.6, 122.3, 126.2, 126.8, 127.1, 128.0, 128.8, 129.3, 130.7, 132.1, 134.3, 138.3, 139.4, 148.5 ppm. HRMS: calcd. for $C_{22}H_{16}N_2$ [M + H]$^+$ 309.1392; found 309.1389.

6-(4-Fluorophenylindolo[1,2-*c*]quinazoline (3g): Eluent: petroleum ether/ethyl acetate (50:1); yield 112 mg (72%), yellow solid, m.p. 234–235 °C. ^1H NMR ($CDCl_3$, 300 MHz): δ = 6.50–6.53 (d, *J* = 8.58 Hz, 1 H), 6.99–7.04 (t, *J* = 8.22 Hz, 1 H), 7.24–7.33 (m, 4 H), 7.46–7.55 (m, 2 H), 764–7.68 (m, 2 H), 7.75–7.82 (m, 2 H), 8.07–8.09 (d, *J* = 7.56 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 96.0, 114.8, 116.6 (d, *J* = 21.5 Hz), 120.6, 120.7, 121.7, 122.8, 123.7, 127.6, 128.0, 129.3, 130.6, 130.7, 131.6, 132.2, 135.3, 139.2, 148.4, 164.0 (d, *J* = 248.8 Hz) ppm. HRMS: calcd. for $C_{21}H_{13}FN_2$ [M + H]$^+$ 313.1141; found 313.1128.

6-(3-Nitrophenyl)indolo[1,2-*c*]quinazoline (3h): Eluent: petroleum ether/ethyl acetate (50:1); yield 140 mg (83%), yellow solid, m.p. 210–211 °C. ^1H NMR ($CDCl_3$, 300 MHz): δ = 6.48–6.51 (d, *J* = 8.61 Hz, 1 H), 6.99–7.05 (t, *J* = 7.89 Hz, 1 H), 7.32–7.37 (m, 2 H), 7.54–7.61 (m, 2 H), 7.80–7.85 (m, 3 H), 8.04–8.06 (d, *J* = 7.56 Hz, 1 H), 8.13–8.16 (m, 1 H), 8.52–8.55 (d, *J* = 8.25 Hz, 1 H), 8.63 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 96.4, 114.2, 120.7, 121.1, 122.0, 122.9, 123.9, 124.0, 125.3, 128.0,128.1, 129.4, 130.4, 130.6, 131.2, 134.6, 135.2, 137.5, 138.9, 146.7, 148.8 ppm. HRMS: calcd. for $C_{21}H_{13}N_2O_2$ [M + H]$^+$ 340.1086; found 340.1074.

6,10-Dimethylindolo[1,2-*c*]quinazoline (3i): Eluent: petroleum ether/ethyl acetate (50:1); yield 84 mg (68%), yellow solid, m.p. 161–162 °C. ^1H NMR ($CDCl_3$, 300 MHz): δ = 2.46 (s, 3 H), 2.95 (s, 3 H), 6.95 (s, 1 H), 7.05–7.08 (d, *J* = 8.61 Hz, 1 H), 7.33–7.38 (t, *J* = 7.56 Hz, 1 H), 7.42–7.47 (m, 2 H), 7.64–7.67 (d, *J* = 7.92 Hz, 1 H), 7.75–7.79 (m, 1 H), 7.88–7.91 (m, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 20.3, 24.1, 93.9, 113.2, 119.1, 119.2, 121.4, 122.5, 125.4, 125.7, 127.7, 128.9, 129.6, 131.8, 133.8, 137.9, 147.3 ppm. HRMS: calcd. for $C_{17}H_{14}N_2$ [M + H]$^+$ 247.1235; found 247.1227.

6-Ethyl-10-methylindolo[1,2-*c*]quinazoline (3j): Eluent: petroleum ether/ethyl acetate (50:1); yield 98 mg (75%), yellow solid, m.p. 128–129 °C. ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.51–1.57 (t, *J* = 7.23 Hz, 3 H), 2.50 (s, 3 H), 3.30–3.37 (q, *J* = 7.2 Hz, 2 H), 7.06 (s, 1 H), 7.12–7.15 (d, *J* = 8.94 Hz, 1 H), 7.36–7.42 (t, *J* = 7.56 Hz, 1 H), 7.44–7.50 (t, *J* = 7.56 Hz, 1 H), 7.53 (s, 1 H), 7.70–7.73 (d, *J* = 7.89 Hz, 1 H), 7.83–7.86 (d, *J* = 8.58 Hz, 1 H), 7.95–7.98 (d, *J* = 7.56 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 10.7, 21.5, 30.1, 95.1, 114.8, 120.4, 122.6, 123.7, 126.7, 127.2, 128.8, 129.6, 130.9, 132.9, 135.4, 139.1, 152.4 ppm. HRMS: calcd. for $C_{18}H_{16}N_2$ [M + H]$^+$ 261.1392; found 261.1395.

10-Methyl-6-propylindolo[1,2-*c*]quinazoline (3k): Eluent: petroleum ether/ethyl acetate (50:1); yield 110 mg (80%), yellow solid, m.p.

136–137 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.16–1.21 (t, J = 7.56 Hz, 3 H), 1.99–2.06 (m, 2 H), 2.50 (s, 3 H), 3.25–3.30 (t, J = 7.56 Hz, 2 H), 7.06 (s, 1 H), 7.13–7.17 (d, J = 8.58 Hz, 1 H), 7.36–7.42 (t, J = 7.56 Hz, 1 H), 7.45–7.50 (t, J = 7.56 Hz, 1 H), 7.54 (s, 1 H), 7.69–7.72 (d, J = 7.89 Hz, 1 H), 7.77–7.80 (d, J = 8.94 Hz, 1 H), 7.95–7.98 (d, J = 7.89 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.9, 19.5, 21.4, 38.6, 94.9, 114.5, 120.4, 122.5, 123.6, 126.5, 127.1, 128.7, 129.5, 130.8, 132.8, 135.3, 138.9, 151.3 ppm. HRMS: calcd. for $C_{19}H_{18}N_2$ $[M + H]^+$ 275.1548; found 275.1545.

6-Cyclopropyl-10-methylindolo[1,2-*c*]quinazoline (3l): Eluent: petroleum ether/ethyl acetate (50:1); yield 115 mg (84%), yellow solid, m.p. 137–138 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.21–1.27 (m, 2 H), 1.41–1.47 (m, 2 H), 2.51 (s, 3 H), 2.55–2.64 (m, 1 H), 7.06 (s, 1 H), 7.12–7.15 (d, J = 8.58 Hz, 1 H), 7.34–7.39 (t, J = 7.56 Hz, 1 H),42–7.47 (t, J = 7.56 Hz, 1 H), 7.55 (s, 1 H), 7.65–7.68 (d, J = 8.25 Hz, 1 H), 7.94–7.98 (d, J = 7.53 Hz, 1 H), 8.25–8.28 (d, J = 8.58 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 7.9, 17.2, 21.6, 94.9, 115.0, 120.4, 120.5, 122.7, 123.5, 126.6, 127.3, 128.8, 130.1, 130.9, 133.0, 135.4, 139.2, 151.4 ppm. HRMS: calcd. for $C_{19}H_{16}N_2$ $[M + H]^+$ 273.1392; found 273.1384.

10-Methyl-6-phenylindolo[1,2-*c*]quinazoline (3m): Eluent: petroleum ether/ethyl acetate (50:1); yield 141 mg (91%), yellow solid, m.p. 197–198 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.43 (s, 3 H), 6.30–6.33 (d, J = 8.58 Hz, 1 H), 6.78–6.81 (d, J = 8.58 Hz, 1 H), 7.18 (s, 1 H), 7.48–7.53 (m, 3 H), 7.59–7.65 (m, 5 H), 7.81–7.84 (d, J = 7.23 Hz, 1 H), 8.07–8.10 (d, J = 7.56 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 21.4, 95.3, 114.5, 120.1, 120.6, 122.7, 123.1, 127.2, 127.8, 128.2, 128.9, 129.3, 130.0, 130.3, 130.7, 133.1, 135.3, 136.0, 139.3, 149.3 ppm. HRMS: calcd. for $C_{22}H_{16}N_2$ $[M + H]^+$ 309.1392; found 309.1383.

10-Methyl-6-*p*-tolylindolo[1,2-*c*]quinazoline (3n): Eluent: petroleum ether/ethyl acetate (50:1); yield 140 mg (87%), yellow solid, m.p. 171–172 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.44 (s, 3 H), 2.51 (s, 3 H), 6.41–6.44 (d, J = 8.94 Hz, 1 H), 6.80–6.83 (d, J = 8.58 Hz, 1 H), 7.17 (s, 1 H), 7.38–7.41 (d, J = 7.89 Hz, 2 H), 7.44–7.56 (m, 5 H), 7.80–7.82 (d, J = 8.25 Hz, 1 H), 8.06–8.09 (d, J = 7.56 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 21.5, 21.7, 95.3, 114.8, 120.1, 120.7, 122.8, 123.2, 127.3, 127.9, 128.2, 129.0, 130.0, 130.1, 130.8, 133.1, 133.3, 135.5, 139.5, 140.5, 149.6 ppm. HRMS: calcd. for $C_{23}H_{18}N_2$ $[M + H]^+$ 323.1548; found 323.1544.

6-(4-Fluorophenyl)-10-methylindolo[1,2-*c*]quinazoline (3o): Eluent: petroleum ether/ethyl acetate (50:1); yield 108 mg (66%), yellow solid, m.p. 230–231 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.44 (s, 3 H), 6.36–6.39 (d, J = 8.58 Hz, 1 H), 6.82–6.85 (d, J = 8.91 Hz, 1 H), 7.17 (s, 1 H), 7.24–7.32 (m, 2 H), 7.46–7.53 (m, 3 H), 7.63–7.68 (m, 2 H), 7.78–7.81 (d, J = 7.56 Hz, 1 H), 8.05–8.08 (d, J = 7.2 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 21.5, 95.6, 114.4, 116.5 (d, J = 22.2 Hz), 120.4, 120.7, 122.8, 123.3, 127.5, 127.9, 129.1, 129.9, 130.6 (d, J = 8.6 Hz), 130.8, 132.3 (d, J = 3.6 Hz), 133.3, 135.4, 139.3, 148.4, 164.0 (d, J = 248.8 Hz) ppm. HRMS: calcd. for $C_{22}H_{15}FN_2$ $[M + H]^+$ 327.1298; found 327.1292.

10-Methyl-6-(3-nitrophenyl)indolo[1,2-*c*]quinazoline (3p): Eluent: petroleum ether/ethyl acetate (50:1); yield 103 mg (58%), yellow solid, m.p. 247–248 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.45 (s, 3 H), 6.33–6.36 (d, J = 8.94 Hz, 1 H), 6.81–6.84 (d, J = 8.58 Hz, 1 H), 7.21 (s, 1 H), 7.50–7.56 (m, 3 H), 7.77–7.82 (m, 2 H), 8.00–8.03 (d, J = 7.53 Hz, 1 H), 8.07–8.10 (m, 1 H), 8.50–8.52 (d, J = 8.22 Hz, 1 H), 8.60 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 20.4, 94.9, 112.7, 119.5, 119.6, 121.7, 122.5, 122.9, 124.1, 126.9, 128.1, 128.4, 129.3, 129.8, 132.5, 133.4, 134.2, 136.4, 137.8, 145.5, 147.6 ppm. HRMS: calcd. for $C_{22}H_{15}N_3O_2$ $[M + H]^+$ 354.1243; found 354.1234.

10-Chloro-6-ethylindolo[1,2-*c*]quinazoline (3q): Eluent: petroleum ether/ethyl acetate (50:1); yield 112 mg (80%), yellow solid, m.p. 137–138 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.56 (t, J = 7.2 Hz, 3 H), 3.33 (q, J = 7.2 Hz, 2 H), 7.07 (s, 1 H), 7.26–7.30 (m, 1 H), 7.41–7.46 (t, J = 7.2 Hz, 1 H), 7.50–7.55 (t, J = 7.2 Hz, 1 H), 7.72–7.76 (m, 2 H), 7.88–7.92 (d, J = 9.27 Hz, 1 H), 7.97–8.00 (d, J = 7.89 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 10.6, 30.1, 94.8, 116.1, 120.0, 122.2, 122.8, 127.0, 127.4, 129.1, 129.4, 129.5, 131.7, 136.6, 139.0, 151.8 ppm. HRMS: calcd. for $C_{17}H_{14}ClN_2$ $[M + H]^+$ 281.0846; found 281.0841.

3-Chloro-6-ethylindolo[1,2-*c*]quinazoline (3r): Eluent: petroleum ether/ethyl acetate (50:1); yield 85 mg (61%), yellow solid, m.p. 141–142 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.54–1.59 (t, J = 7.56 Hz, 3 H), 3.35–3.43 (q, J = 7.53 Hz, 2 H), 7.16 (s, 1 H), 7.35–7.45 (m, 3 H), 7.72–7.73 (d, J = 2.1 Hz, 1 H), 7.79–7.82 (d, J = 7.2 Hz, 1 H), 7.90–7.93 (d, J = 8.2 Hz, 1 H), 8.01–8.04 (d, J = 8.2 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 10.6, 30.2, 95.9, 115.3, 118.9, 120.9, 122.4, 123.5, 123.8, 127.0, 127.1, 130.5, 131.3, 134.3, 134.5, 140.0, 153.5 ppm. HRMS: calcd. for $C_{17}H_{13}ClN_2$ $[M + H]^+$ 281.0846; found 281.0841.

3-Chloro-6-propylindolo[1,2-*c*]quinazoline (3s): Eluent: petroleum ether/ethyl acetate (50:1); yield 120 mg (81%), yellow solid, m.p. 129–130 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.15–1.20 (t, J = 7.2 Hz, 3 H), 1.97–2.04 (m, 2 H), 3.20–3.25 (t, J = 7.53 Hz, 2 H), 7.05 (s, 1 H), 7.28–7.41 (m, 3 H), 7.66–7.67 (d, J = 2.1 Hz, 1 H), 7.73–7.76 (d, J = 7.23 Hz, 1 H), 7.79–7.82 (d, J = 8.58 Hz, 1 H), 7.88–7.91 (d, J = 7.89 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 12.8, 18.3, 37.6, 94.7, 114.0, 117.7, 119.7, 121.3, 122.3, 122.5, 125.7, 129.3, 130.1, 133.1, 133.1, 133.3, 138.8, 151.2 ppm. HRMS: calcd. for $C_{18}H_{15}ClN_2$ $[M + H]^+$ 295.1002; found 295.0992.

3-Chloro-6-cyclopropylindolo[1,2-*c*]quinazoline (3t): Eluent: petroleum ether/ethyl acetate (50:1); yield 130 mg (89%), yellow solid, m.p. 106–107 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.25 (m, 2 H), 1.43–1.46 (m, 2 H), 2.57–2.61 (m, 1 H), 7.08 (s, 1 H), 7.27–7.41 (m, 3 H), 7.62–7.63 (d, J = 2.07 Hz, 1 H), 7.75–7.78 (d, J = 7.23 Hz, 1 H), 7.81–7.84 (d, J = 8.53 Hz, 1 H), 8.35–8.38 (d, J = 8.61 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 8.1, 17.1, 95.7, 115.4, 118.9, 120.8, 122.2, 123.6, 123.7, 126.9, 130.5, 131.7, 134.2, 134.5, 140.1, 152.5 ppm. HRMS: calcd. for $C_{18}H_{13}ClN_2$ $[M + H]^+$ 293.0846; found 293.0839.

3-Chloro-6-phenylindolo[1,2-*c*]quinazoline (3u): Eluent: petroleum ether/ethyl acetate (50:1); yield 117 mg (71%), yellow solid, m.p. 187–188 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.44–6.47 (d, J = 8.58 Hz, 1 H), 6.96–7.01 (t, J = 8.58 Hz, 1 H), 7.23 (s, 1 H), 7.27–7.32 (t, J = 7.89 Hz, 1 H), 7.42–7.45 (d, J = 8.58 Hz, 1 H), 7.58–7.68 (m, 5 H), 7.74–7.76 (d, J = 8.19 Hz, 1 H), 7.80–7.81 (d, J = 1.38 Hz, 1 H), 7.97–8.00 (d, J = 8.58 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 96.2, 114.9, 119.1, 120.6, 121.8, 123.7, 123.8, 127.5, 127.7, 128.1, 129.3, 130.3, 130.6, 131.6, 134.4, 134.5, 135.6, 140.2, 150.3 ppm. HRMS: calcd. for $C_{21}H_{13}ClN_2$ $[M + H]^+$ 329.0846; found 329.0839.

3-Chloro-6-*p*-tolylindolo[1,2-*c*]quinazoline (3v): Eluent: petroleum ether/ethyl acetate (50:1); yield 133 mg (78%), yellow solid, m.p. 176–177 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.53 (s, 3 H), 6.56–6.59 (d, J = 8.58 Hz, 1 H), 6.98–7.04 (t, J = 8.58 Hz, 1 H), 7.24 (d, J = 0.69 Hz, 1 H), 7.28–7.34 (t, J = 8.22 Hz, 1 H), 7.40–7.46 (m, 3 H), 7.54 (d, J = 2.07 Hz, 1 H), 7.56 (d, J = 1.74 Hz, 1 H), 7.75–7.78 (d, J = 7.89 Hz, 1 H), 7.80–7.81 (d, J = 2.04 Hz, 1 H), 8.00–8.02 (d, J = 8.61 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 21.7, 96.2, 115.2, 119.1, 120.6, 121.8, 123.7, 123.9, 127.5, 127.6, 128.1, 130.0, 130.4, 131.8, 132.9, 134.4, 134.6, 140.4, 140.9,

150.7 ppm. HRMS: calcd. for $C_{22}H_{15}ClN_2$ $[M + H]^+$ 343.1002; found 343.0989.

3-Methoxy-6-propylindolo[1,2-*c*]quinazoline (3w): Eluent: petroleum ether/ethyl acetate (50:1); yield 107 mg (74%), yellow solid, m.p. 158–159 °C. ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.22 (t, J = 7.2 Hz, 3 H), 2.07 (m, 2 H), 3.37 (t, J = 7.89 Hz, 2 H), 3.92 (s, 3 H), 7.04–7.08 (m, 2 H), 7.20–7.21 (d, J = 2.4 Hz, 1 H), 7.31–7.43 (m, 2 H), 7.77–7.80 (d, J = 7.71 Hz, 1 H), 7.93–7.97 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.0, 19.7, 38.9, 55.6, 93.8, 108.9, 113.8, 115.0, 116.3, 120.5, 121.5, 123.3, 123.9, 130.9, 131.0, 135.6, 140.5, 152.0, 160.5 ppm. HRMS: calcd. for $C_{19}H_{18}N_2O$ $[M + H]^+$ 291.1497; found 291.1485.

Supporting Information (see footnote on the first page of this article): Copies of ^1H and ^{13}C NMR spectra of compounds **3a**–**w**.

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