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Copper-Catalyzed Synthesis of 2-Arylquinazolinones from 2-Arylindoles with Amines or Ammoniums

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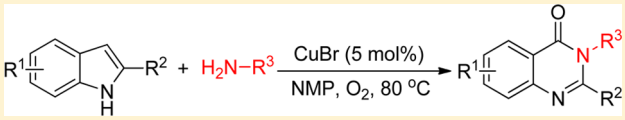
Supporting Information

ABSTRACT: A novel copper-catalyzed synthesis of quinazolinones from easily available 2-arylindoles and amines or ammoniums has been developed, which provided various quinazolinones in up to 99% yields for 43 examples. This strategy features tolerance of a wide range of functional groups, easily available starting materials, simple operation, mild reaction conditions, and environmental friendliness.



INTRODUCTION

Quinazolinone is a ubiquitous and significant heterocycle and widely exists in natural alkaloids and pharmaceuticals.[1] Various quinazolinones have been found to be with bioactivities,[1−9] such as antibacterial,[2] antifungal,[3] antimalarial,[4] anticancer,[5] antihypertensive,[6] antitubercular,[7] and anticonvulsant.[8]

As a result, numerous methods for synthesis of quinazolinone derivatives have been developed.[10] Conventionally, such a structure was synthesized from the condensation of halobenzoic acids, halobenzamides, aminobenzamides, nitrobenzamides with amidines, benzyl alcohols, benzylamine, acid amides or amino acids. Metal-catalyzed insertion of carbon monoxide (CO) or isocyanide has provided an alternative pathway to quinazolinones in moderate yields.[11] Although efficient as documented in the literature, development of a straightforward, mild, economic and environmentally friendly method for the preparation of quinazolinones from easily available substrates is still highly desirable.

Herein, we present a copper-catalyzed expansion reaction of 2-arylindoles with amines or ammoniums, affording both 2-substituted and 2,3-disubstituted quinazolinones, simultaneously. In this catalytic process, molecular oxygen has been significantly used as an oxidant. The corresponding products were obtained in good to excellent yields with H_2O as the sole byproduct. In comparison with the existing methods in the literature, this approach features easy operation, cheap and easily available starting materials, high efficiency, environmentally friendliness, and tolerance of a broad range of substrates. Moreover, it is applied to synthsize both 2-substituted and 2,3-disubstituted quinazolinones. To the best of our knowledge, this is the first example of constructing quinazolinones from easily available 2-arylindoles and amines or ammoniums via Baeyer−Villiger oxidation expansion using O_2 as a clean oxidant, followed by dehydration condensation ingeniously.

RESULTS AND DISCUSSION

At the outset of our studies, 2-phenyl-1*H*-indole (**1a**) and phenethylamine (**2a**) were chosen as model substrates to optimize the reaction conditions. Initially, the reaction was carried out in the presence of $CuBr_2$ (5 mol %) in NMP at 80 °C and afforded a 77% isolated yield of **3aa** (Table 1, entry 1). In the absence of catalysts, the desired product **3aa** could not be detected (Table 1, entry 2). Only a trace amount of the target product **3aa** was observed in the absence of O_2 or using *t*-BuOOH, H_2O_2, or *m*-CPBA as an oxidant under air (Table 1, entries 3−6). Copper salts, such as $Cu(OAc)_2$, CuBr, CuCl, and CuI, were further screened and showed that CuBr favored this transformation, probably due to its stronger electronegativity as well as better ionization power, and the catalytic effect of freshly generated Cu^{2+} is better (Table 1, entries 7−10 vs entry 1). Moreover, 1-methyl-2-pyrrolidinone (NMP) proved to be the best solvent and gave the desired product **3aa** in 96% (Table 1, entry 8 vs entries 11−13). However, only a 58% isolated yield of **3aa** could be afforded using dried NMP. Addition of 10 equiv of H_2O resulted in an 85% yield, which indicated that water in this reaction system plays an important role (Table 1, entries 14−15). The yield of **3aa** decreased with increasing or decreasing reaction temperature (Table 1, entries 16−19 vs entry 8) as well as reducing the reaction time (Table 1, entries 20−21).

With the optimized conditions in hand, the scope of indoles was first investigated. As shown in Scheme 1, a methyl group at the *ortho*-, *meta*-, and *para*-position of 2-phenyl in 2-aryl-1*H*-indole provided the corresponding products **3ab**−**3ad** in 76%, 85%, and 84% yields, respectively, which indicated that the steric effect of 2-aryl groups did not impact this transformation obviously. Halogen groups, such as F, Cl, and Br, were well-tolerated (**3ae**−**3ag**, and **3aj**), which made this reaction particularly attractive for increasing the molecular complexity by various transition-metal-catalyzed cross-coupling

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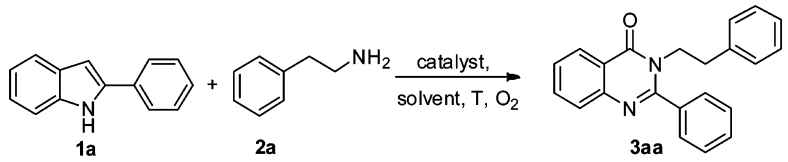
Table 1. Optimization of the Reaction of 1a with 2a[a]



entry	catalyst	solvent	temp (°C)	time (h)	yield[b] (%)
1	$CuBr_2$	NMP	80	24	77
2	–	NMP	80	24	no
3[c]	$CuBr_2$	NMP	80	24	trace
4[d]	$CuBr_2$	NMP	80	24	trace
5[e]	$CuBr_2$	NMP	80	24	trace
6[f]	$CuBr_2$	NMP	80	24	trace
7	$Cu(OAc)_2$	NMP	80	24	69
8	**CuBr**	**NMP**	**80**	**24**	**96**
9	CuCl	NMP	80	24	91
10	CuI	NMP	80	24	73
11	CuBr	DMSO	80	24	47
12	CuBr	THF	80	24	trace
13	CuBr	toluene	80	24	trace
14[g]	CuBr	NMP	80	24	58
15[h]	CuBr	NMP	80	24	85
16	CuBr	NMP	60	24	62
17	CuBr	NMP	70	24	78
18	CuBr	NMP	90	24	84
19	CuBr	NMP	100	24	76
20	CuBr	NMP	80	18	83
21	CuBr	NMP	80	12	55

[a]Reaction conditions: **1a** (0.25 mmol), **2a** (0.5 mmol), catalyst (5 mol %), solvent (2.0 mL), under an O_2 atmosphere (1 atm). [b]Isolated yield. [c]Under air. [d]Under air with *t*-BuOOH (3 equiv). [e]Under air with H_2O_2 (3 equiv). [f]Under air with *m*-CPBA (3 equiv). [g]Using dried NMP. [h]Using dried NMP with H_2O (10 equiv).

reactions. Both 2-(4-methoxyphenyl)-1*H*-indole and 2-(4-trifluoromethylphenyl)-1*H*-indole proceeded well to give the corresponding products **3ah** and **3ai** in 98% and 90% yields, respectively, which suggested the electron density in 2-aryl moieties also did not effect this transformation significantly. Furthermore, 2-naphthylindole was a suitable substrate as well and provided the corresponding product in 51% yield (**3ak**). Moreover, various substituents at the C5 or C6 position of indoles, such as methyl, halo, and isopropyl groups, could give the corresponding products in satisfactory yields (74%−90%) (**3al**−**3ar**).

Thereafter, we investigated a range of differently decorated amines (**2b**−**2i**) (Scheme 2). Benzylamine, benzedrine, ethylamine, *n*-propylamine, and *n*-butylamine could be smoothly converted into the corresponding products in moderate to good yields (60%−89%) (**3bb** and **3be**−**3bh**). The electron density in the phenyl of benzylamine had a slight effect on this conversion. For instance, 4-*tert*-butyl benzylamine and 4-trifluoromethyl benzylamine provided the desired products **3bc** and **3bd** in 82% and 72% yields, respectively. Notably, long-chain dodecylamine could also be converted into corresponding product in 60% yield (**3bi**). However, aniline and amines with large steric hindrance at the N atom, such as *tert*-butylamine, could not be a suitable substrate for this transformation.

To further demonstrate the potential application of this protocol in organic synthesis, we explored this strategy for the preparation of 2-phenylquinazolin-4(3*H*)-ones from indoles and ammoniums (Scheme 3). Various indoles were well-tolerated in this reaction, affording the corresponding products in good to excellent yields. In addition, ammoniums, such as NH_4Cl and NH_4HCO_3, could be used as an efficient nitrogen source as well and give the corresponding product **3ca** in 55% and 78% yield, respectively (Scheme 4). To prove the practicality of this ingenious reaction system, a gram-scale synthesis of the 2-phenylquinazolin-4(3*H*)-one **3ca** was performed. When 0.93 g 2-phenyl-1*H*-indole (**1a**) and 2.0 g NH_3 (aq) (**4**) were loaded, 0.95 g of the corresponding product (**3ca**) was obtained in 86% yield. Easy operation and high efficiency made this reaction possess extensive applications in organic synthesis as well as in the pharmaceutical industry.

Yamashita and Guan's group has reported that 2-arylindole **1** could be converted into lactone via a Baeyer−Villiger oxidation reaction.[12a,b] To gain insight into the reaction mechanism, several control experiments were conducted (Scheme 5). First, lactone **5a** was synthesized from 2-arylindole catalyzed by CuCl under an O_2 atmosphere. Then, **5a** reacted with NH_3(aq) under the standard conditions, and product **3ca** was obtained in almost quantitative yield. On the other hand, when amine **2j** was introduced into the reaction, compound **6j** was afforded as a main product and could not be converted into the desired product **3bj**, possibly due to the large steric hindrance. The parallel experiments were performed using $CuBr_2$ and CuBr as the catalyst for the model reaction under the standard reaction conditions. The reactions were followed by GC. These results revealed that the catalytic activity of CuBr was higher than that of $CuBr_2$

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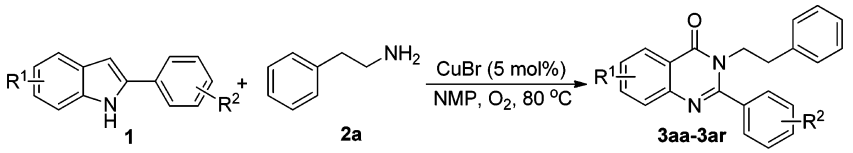
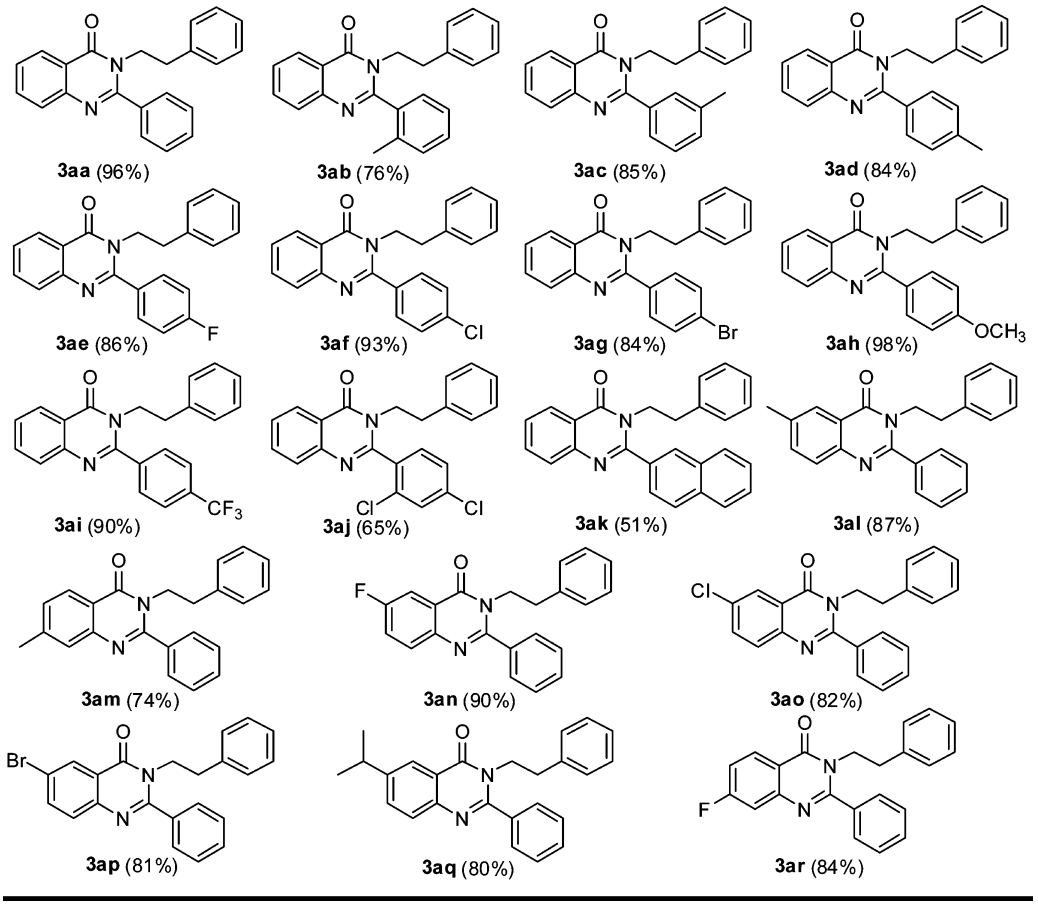
Scheme 1. Scope of Indole[a]





[a]Reaction conditions: **1** (0.25 mmol), **2a** (0.5 mmol), CuBr (5 mol %), NMP (2 mL), under an O_2 atmosphere (1 atm), 80 °C, 24 h.

and both exhibited an induction period (25 min) (see Figure 1 in Supporting Information). CuBr showed higher activity than $CuBr_2$. Based on the above-mentioned results and literature,[12] a possible reaction mechanism was proposed and is shown in Scheme 6. Initially, compound **5** was formed via the copper-catalyzed aerobic Baeyer–Villiger oxidation reaction of **1** mediated by Cu, which was followed by hydrolysis to give carboxylic acid **7**. Subsequently, the amination reaction of carboxylic acid **7** with amine **2** efficiently provided the amide **8**, followed by dehydration condensation to generate corresponding products **3**.

CONCLUSION

In summary, we have developed a simple and efficient copper-catalyzed reaction for the construction of quinazolinones starting from 2-arylindoles. Cheap and easily available CuBr, 2-arylindoles, and amines or ammoniums were used as the catalyst and starting materials, respectively. Moreover, both 2-substituted and 2,3-disubstituted quinazolinones could be afforded; economically and environmentally friendly O_2 was employed as an oxidant in this strategy. In comparison with the existing methods in the literature, the present approach features high efficiency, environmentally friendliness, tolerance of a broad range of substrates, high atomic economy, and easy operation. To the best of our knowledge, this is the first example of constructing quinazolinones from easily available 2-arylindoles and amines or ammoniums via sequential Baeyer–Villiger oxidation expansion under O_2 together with continuous dehydration condensation ingeniously.

EXPERIMENTAL SECTION

General Methods. All commercial materials and solvents were used directly without further purification. Melting points were determined on a melting point apparatus and were uncorrected. ^1H and $^{13}C\{1H\}$ NMR spectra were measured on a 400 MHz spectrometer (^1H 400 MHz, ^{13}C 100 MHz) using $CDCl_3$ or DMSO-d_6 as the solvent with tetramethylsilane (TMS) as the internal standard at room temperature. HRMS ESI spectra were obtained on a Q-TOF spectrometer.

Preparation of Quinazolinones 3. A mixture of 2-arylindoles **1** (0.25 mmol), amine **2** (0.5 mmol) or ammonium **4** (0.10 g), and CuBr (5 mol %) in NMP (2 mL) was stirred at 80 °C under oxygen for 24 h. After cooling to room temperature, the reaction mixture

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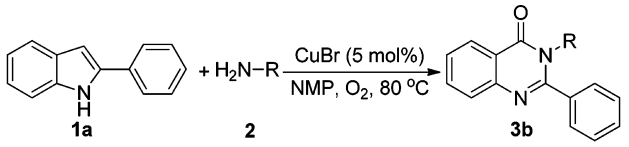
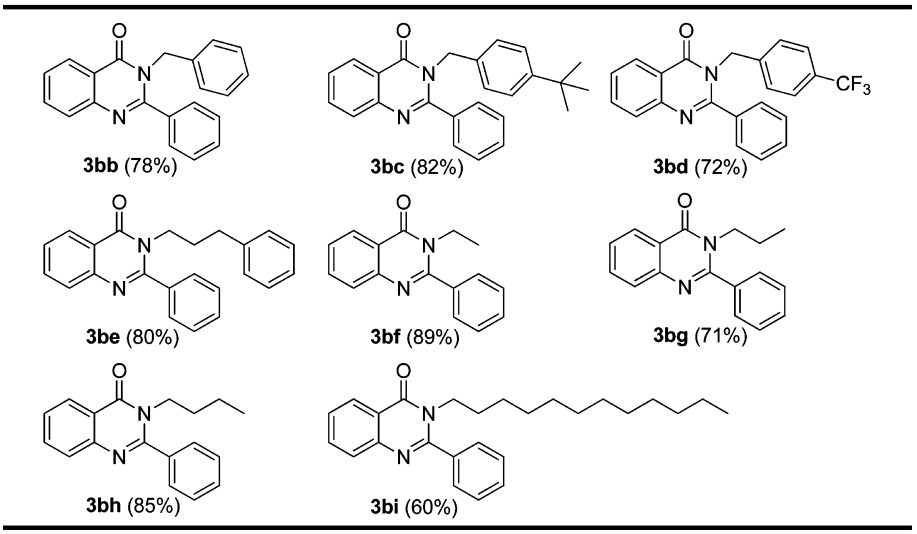
Scheme 2. Scope of Amine[a]





[a]Reaction conditions: **1a** (0.25 mmol), **2b**−**2i** (0.5 mmol), CuBr (5 mol %), NMP (2 mL), under an O_2 atmosphere (1 atm), 80 °C, 24 h.

was poured into water and extracted with EtOAc. The organic layer was washed with brine and dried over $MgSO_4$. Purification by column chromatography on silica gel using petroleum ether/ethyl acetate (10:1 to 5:1) as the eluent delivered the desired products **3**.

3-Phenethyl-2-phenylquinazolin-4(3H)-one (***3aa***).[10w] Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 96% (78 mg); mp 198−200 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.24 (d, J = 8.0 Hz, 1H), 7.94−7.80 (m, 1H), 7.68 (d, J = 8.1 Hz, 1H), 7.63−7.48 (m, 6H), 7.25−7.12 (m, 3H), 6.92−6.72 (m, 2H), 4.1(t, J = 7.8 Hz, 2H), 2.83 (t, J = 7.8 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.1, 155.9, 146.8, 137.8, 135.2, 134.5, 129.6, 128.5, 128.3 (overlapped), 127.9, 127.2, 127.0, 126.5, 126.1, 120.4, 46.9, 33.7.

3-Phenethyl-2-(o-tolyl)quinazolin-4(3H)-one (***3ab***).[10x] Eluent: petroleum ether/ethyl acetate (10:1). Colorless oil. Yield: 76% (65 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, J = 8.0 Hz, 1H), 7.83−7.72 (m, 2H), 7.59−7.52 (m, 1H), 7.44 (t, J = 7.2 Hz, 1H), 7.33 (t, J = 7.6 Hz, 2H), 7.24−7.15 (m, 4H), 6.86 (dd, J = 7.2, 2.0 Hz, 2H), 4.47−4.35 (m, 1H), 3.73−3.59 (m,1H), 3.00−2.89 (m, 1H), 2.85−2.74 (m, 1H), 2.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.0, 155.7, 147.2, 137.7, 135.3, 134.7, 134.4, 130.6, 129.9, 128.7, 128.5, 127.8, 127.5, 127.1, 126.7, 126.6, 126.2, 121.0, 47.2, 34.5, 19.2.

3-Phenethyl-2-(m-tolyl)quinazolin-4(3H)-one (***3ac***).[10x] Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 85% (72 mg); mp 128−130 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, J = 8.0 Hz, 1H), 7.83−7.70 (m, 2H), 7.57−7.49 (m, 1H), 7.38 (t, J = 7.5 Hz, 1H), 7.32 (d, J = 7.7 Hz, 1H), 7.19 (dd, J = 6.8, 3.8 Hz, 4H), 7.13 (s, 1H), 6.89 (dd, J = 6.5, 2.8 Hz, 2H), 4.19 (t, J = 7.8 Hz, 2H), 2.94 (t, J = 7.8 Hz, 2H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 156.4, 147.2, 138.7, 137.8, 135.2, 134.4, 130.5, 128.8, 128.5 (overlapped), 128.3, 127.5, 127.0, 126.7, 126.6, 124.7, 120.9, 47.6, 34.7, 21.4.

3-Phenethyl-2-(p-tolyl)quinazolin-4(3H)-one (***3ad***).[10x] Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 84% (71 mg); mp 168−170 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, J = 8.0 Hz, 1H), 7.84−7.69 (m, 2H), 7.55−7.49 (m, 1H), 7.33−7.27 (m, 4H), 7.23−7.14 (m, 3H), 6.91 (dd, J = 7.1, 2.1 Hz, 2H), 4.21 (t, J = 7.8 Hz, 2H), 2.92 (t, J = 7.8 Hz, 2H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 156.3, 147.2, 139.9, 137.8, 134.3, 132.5, 129.3, 128.8, 128.5, 127.7, 127.5, 126.9, 126.7, 126.6, 120.9, 47.5, 34.7, 21.4.

2-(4-Fluorophenyl)-3-phenethylquinazolin-4(3H)-one (***3ae***).[10x] Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 86% (74 mg); mp 177−178 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, J = 8.0 Hz, 1H), 7.83−7.75 (m, 1H), 7.72 (d, J = 7.9 Hz, 1H), 7.55 (t, J = 7.5 Hz, 1H), 7.35−7.28 (m, 2H), 7.24−7.11 (m, 5H), 6.88 (dd, J = 6.4, 2.8 Hz, 2H), 4.21 (t, J = 7.8 Hz, 2H), 2.92 (t, J = 7.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3 (d, J_{C-F} = 250.0 Hz), 162.1, 155.2, 147.0, 137.6, 134.5, 131.5 (d, J_{C-F} = 3.6 Hz), 130.0(d, J_{C-F} = 8.5 Hz), 128.8, 128.7, 127.5, 127.2, 126.8, 126.7, 120.9, 115.9 (d, J_{C-F} = 22.0 Hz), 47.6, 34.6.

2-(4-Chlorophenyl)-3-phenethylquinazolin-4(3H)-one (***3af***).[10x] Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 93% (84 mg); mp 156−157 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, J = 8.0 Hz, 1H), 7.82−7.75 (m, 1H), 7.71 (d, J = 7.9 Hz, 1H), 7.55 (t, J = 7.5 Hz, 1H), 7.44 (t, J = 5.3 Hz, 2H), 7.26−7.16 (m, 5H), 6.89 (dd, J = 6.4, 2.9 Hz, 2H), 4.21 (t, J = 7.8 Hz, 2H), 2.93 (t, J = 7.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.1, 155.1, 147.0, 137.6, 136.0, 134.5, 133.7, 129.3, 129.0, 128.8, 128.7, 127.5, 127.3, 126.8 (overlapped), 120.9, 47.6, 34.6.

2-(4-Bromophenyl)-3-phenethylquinazolin-4(3H)-one (***3ag***). Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 84% (84 mg); mp 133−134 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, J = 7.9 Hz, 1H), 7.78 (t, J = 7.6 Hz, 1H), 7.71 (d, J = 8.0 Hz, 1H), 7.60 (d, J = 8.2 Hz, 2H), 7.54 (t, J = 7.5 Hz, 1H), 7.24−7.13 (m, 5H), 6.89 (dd, J = 6.2, 2.7 Hz, 2H), 4.25−4.13 (m, 2H), 2.97−2.87 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.0, 155.1, 147.0, 137.6, 134.5, 134.2, 131.9, 129.5, 128.8, 128.7, 127.5, 127.3, 126.8 (overlapped), 124.2, 120.9, 47.6, 34.5; HRMS (ESI) m/z calcd for $C_{22}H_{17}BrN_2O$ $[M + H]^+$ 405.0603, found 405.0597.

2-(4-Methoxyphenyl)-3-phenethylquinazolin-4(3H)-one (***3ah***).[10x] Eluent: petroleum ether/ethyl acetate (5:1). White solid. Yield: 98% (88 mg); mp 129−130 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (dd, J = 8.0, 0.8 Hz, 1H), 7.80−7.70 (m, 2H), 7.55−7.48 (m, 1H), 7.35−7.31 (m, 2H), 7.19 (dd, J = 5.7, 4.2 Hz, 3H), 7.00 (d, J = 8.7 Hz, 2H), 6.93 (dd, J = 7.1, 2.1 Hz, 2H), 4.33−4.19 (m, 2H), 3.89 (s,

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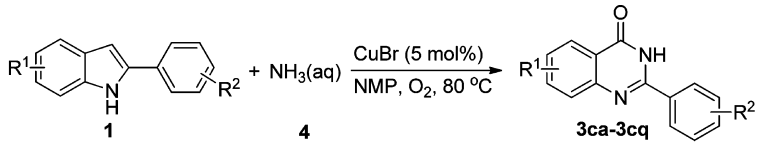
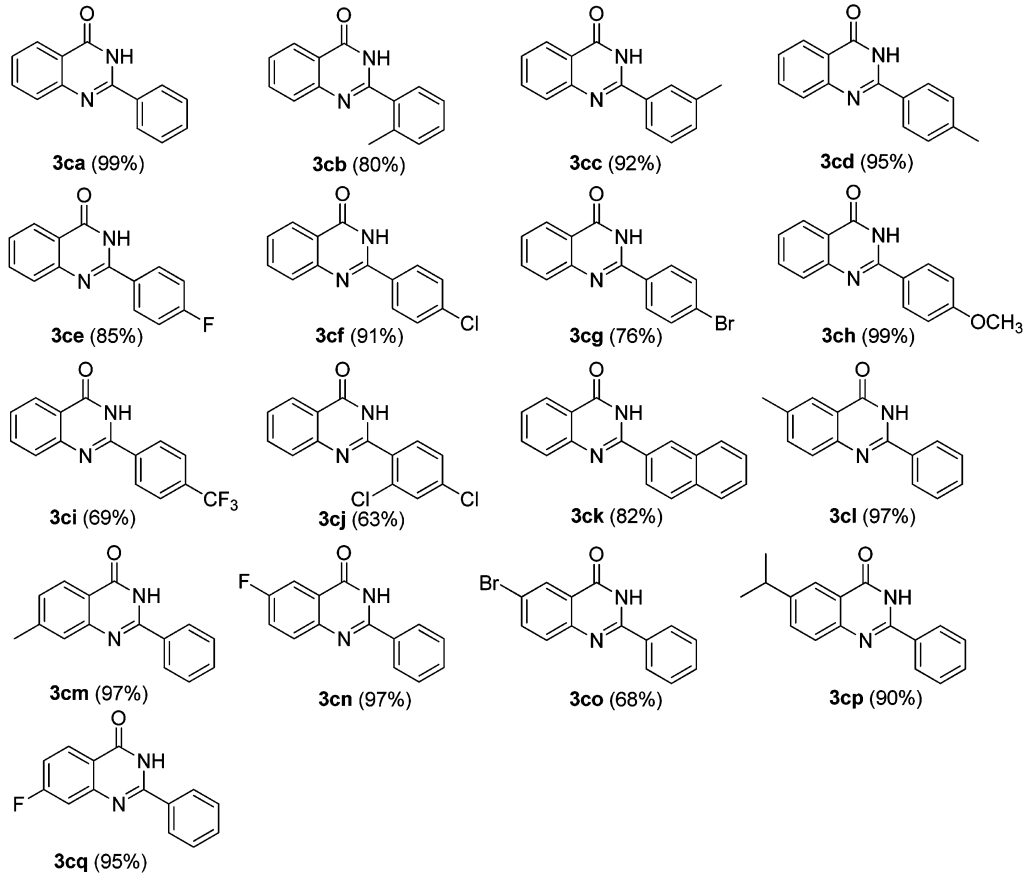
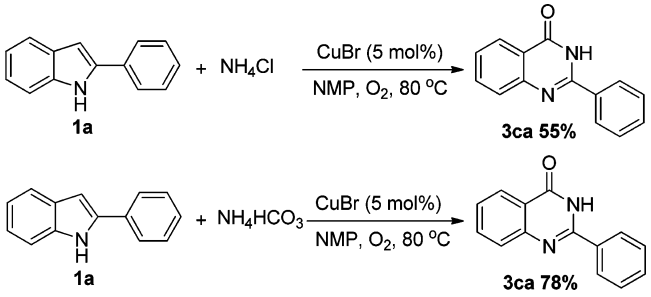
Scheme 3. Reaction of Indoles with Ammonium[a]





[a]Reaction conditions: **1** (0.25 mmol), **4** (0.10 g), CuBr (5 mol %), NMP (2 mL), under an O_2 atmosphere (1 atm), 80 °C, 24 h.

Scheme 4. Reaction of 2-Phenyl-1*H*-Indole (1a) with Ammoniums



3H), 2.95–2.88 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 160.6 156.1, 147.2, 137.8, 134.3, 129.4, 128.8, 128.6, 127.8, 127.5, 126.9, 126.7, 126.6, 120.8, 114.1, 55.5, 47.6, 34.7.

*3-Phenethyl-2-(4-(trifluoromethyl)phenyl)quinazolin-4(3H)-one (**3ai**).* Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 90% (89 mg); mp 164–165 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.25 (d, J = 7.9 Hz, 1H), 7.87 (t, J = 8.0 Hz, 3H), 7.69 (t, J = 8.5 Hz, 3H), 7.61 (t, J = 7.5 Hz, 1H), 7.25–7.07 (m, 3H), 6.86–6.73 (m, 2H), 4.12–3.97 (m, 2H), 2.90–2.77 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.0, 154.7, 146.7, 139.0, 137.8, 134.6, 130.0, 129.6, 129.0, 128.5, 128.4, 127.3, 127.2, 126.5, 126.2, 125.3, 122.6, 120.6, 47.0, 33.6; HRMS (ESI) m/z calcd for $C_{23}H_{17}F_3N_2O$ $[M + H]^+$ 395.1371, found 395.1370.

*2-(2,4-Dichlorophenyl)-3-phenethylquinazolin-4(3H)-one (**3aj**).*[10x] Eluent: petroleumether/ethyl acetate (10:1). Colorless oil. Yield: 65% (64 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, J = 8.0 Hz, 1H), 7.82–7.66 (m, 2H), 7.62–7.45 (m, 2H), 7.28 (dd, J = 8.2, 1.9 Hz, 1H), 7.23–7.16 (m, 3H), 6.93–6.77 (m, 3H), 4.53 (dt, J = 13.5, 6.7 Hz, 1H), 3.63 (dt, J = 13.5, 8.2 Hz, 1H), 2.94 (q, J = 7.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6, 152.5, 147.0, 137.6, 136.4, 134.6, 133.2, 132.7, 130.6, 129.4, 128.8, 128.7, 127.5 (overlapped), 127.5, 126.8, 126.7, 121.1, 47.4, 34.2.

*2-(Naphthalen-2-yl)-3-phenethylquinazolin-4(3H)-one (**3ak**).* Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 51% (48 mg); mp 146–147 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, J = 8.0 Hz, 1H), 7.93 (t, J = 9.5 Hz, 2H), 7.88–7.83 (m, 1H), 7.82–7.71 (m, 3H), 7.65–7.52 (m, 3H), 7.43 (dd, J = 8.4, 1.3 Hz, 1H), 7.20–7.05 (m, 3H), 6.81 (d, J = 7.1 Hz, 2H), 4.34–4.20 (m, 2H), 3.03–2.92 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 156.2, 147.2, 137.7, 134.5, 133.5, 132.8, 132.6, 128.8, 128.6, 128.5 (overlapped), 127.9, 127.8, 127.6, 127.3, 127.1, 127.0, 126.8,

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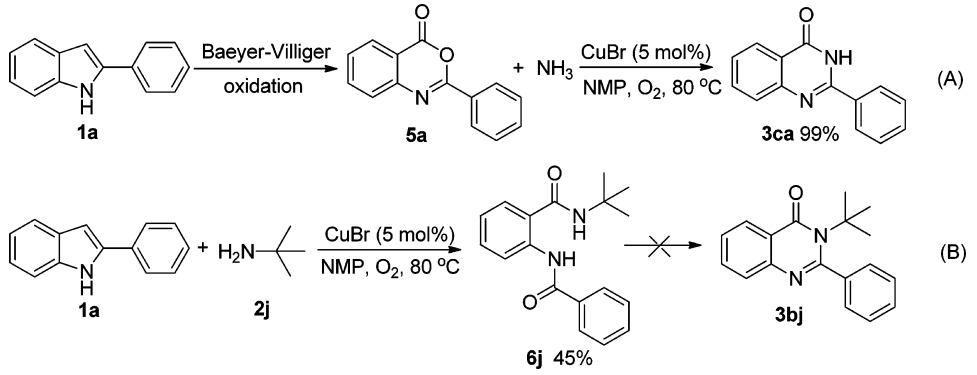
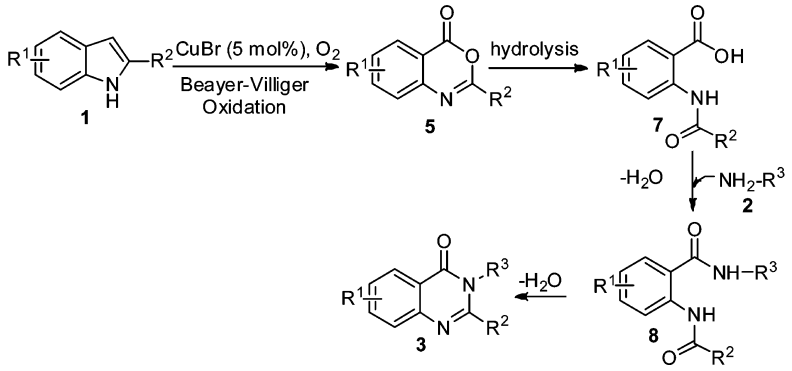
Scheme 5. Control Experiments



Scheme 6. A Plausible Reaction Mechanism



126.6, 124.5, 121.0, 47.7, 34.6; HRMS (ESI) *m*/*z* calcd for $C_{26}H_{20}N_2O$ [M + H]$^+$ 377.1654, found 377.1650.

6-Methyl-3-phenethyl-2-phenylquinazolin-4(3H)-one (***3al***). Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 87% (74 mg); mp 178−179 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.61 (dt, *J* = 8.3, 5.0 Hz, 2H), 7.55−7.45 (m, 3H), 7.37 (dd, *J* = 7.6, 1.2 Hz, 2H), 7.18 (dd, *J* = 4.8, 1.5 Hz, 3H), 6.87 (dd, *J* = 6.4, 2.7 Hz, 2H), 4.23−4.11 (m, 2H), 2.96−2.85 (m, 2H), 2.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.1, 155.3, 145.2, 137.8, 137.3, 135.9, 135.4, 129.7, 128.8, 128.7, 128.6, 127.8, 127.4, 126.6, 126.1, 120.6, 47.5, 34.7, 21.4; HRMS (ESI) *m*/*z* calcd for $C_{23}H_{20}N_2O$ [M + H]$^+$ 341.1654, found 341.1649.

7-Methyl-3-phenethyl-2-phenylquinazolin-4(3H)-one (***3am***). Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 74% (63 mg); mp 171−172 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.1 Hz, 1H), 7.59−7.45 (m, 4H), 7.37 (dd, *J* = 10.7, 4.6 Hz, 3H), 7.23−7.13 (m, 3H), 6.87 (dd, *J* = 6.5, 2.7 Hz, 2H), 4.24−4.10 (m, 2H), 2.96−2.85 (m, 2H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.1, 156.2, 147.3, 145.4, 137.8, 135.5, 129.7, 128.8, 128.7, 128.7, 128.6, 127.8, 127.2, 126.6, 126.5, 118.5, 47.4, 34.7, 21.9; HRMS (ESI) *m*/*z* calcd for $C_{23}H_{20}N_2O$ [M + H]$^+$ 341.1654, found 341.1651.

6-Fluoro-3-phenethyl-2-phenylquinazolin-4(3H)-one (***3an***). Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 90% (78 mg); mp 189−190 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (dd, *J* = 8.5, 3.0 Hz, 1H), 7.74 (dd, *J* = 8.9, 4.9 Hz, 1H), 7.55−7.45 (m, 4H), 7.38 (dt, *J* = 3.7, 2.1 Hz, 2H), 7.22−7.15 (m, 3H), 6.87 (dd, *J* = 6.6, 2.9 Hz, 2H), 4.24−4.14 (m, 2H), 2.94−2.86 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 161.5, 159.8, 155.4, 143.9, 137.6, 135.1, 130.0, 130.0, 129.9, 128.8, 128.7, 128.6, 127.8, 126.7, 123.2, 122.9, 122.2, 122.1, 111.7, 111.4, 47.6, 34.6; HRMS (ESI) *m*/*z* calcd for $C_{22}H_{17}FN_2O$ [M + H]$^+$ 345.1403, found 345.1400.

6-Chloro-3-phenethyl-2-phenylquinazolin-4(3H)-one (***3ao***). Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 82% (74 mg); mp 170−171 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 2.0 Hz, 1H), 7.73−7.64 (m, 2H), 7.57−7.46 (m, 3H), 7.36 (d, *J* = 7.4 Hz, 2H), 7.23−7.11 (m, 3H), 6.93−6.79 (m, 2H), 4.26−4.13 (m, 2H), 2.94−2.84 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 156.4, 145.7, 137.5, 135.0, 134.8, 132.8, 130.0, 129.2, 128.8, 128.7, 128.6, 127.7, 126.7, 126.1, 121.9, 47.7, 34.6; HRMS (ESI) *m*/*z* calcd for $C_{22}H_{17}ClN_2O$ [M + H]$^+$ 361.1108, found 361.1104.

6-Bromo-3-phenethyl-2-phenylquinazolin-4(3H)-one (***3ap***). Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 81% (81 mg); mp 189−190 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, *J* = 2.1 Hz, 1H), 7.84 (dd, *J* = 8.6, 2.1 Hz, 1H), 7.60 (d, *J* = 8.7 Hz, 1H), 7.57−7.45 (m, 3H), 7.35 (d, *J* = 7.4 Hz, 2H), 7.24−7.09 (m, 3H), 6.94−6.81 (m, 2H), 4.27−4.14 (m, 2H), 2.96−2.84 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 156.5, 146.0, 137.6, 137.5, 135.1, 130.0, 129.4, 129.3, 128.8, 128.7, 128.6, 127.7, 126.7, 122.3, 120.6, 47.7, 34.5; HRMS (ESI) *m*/*z* calcd for $C_{22}H_{17}BrN_2O$ [M + H]$^+$ 405.0603, found 405.0598.

6-Isopropyl-3-phenethyl-2-phenylquinazolin-4(3H)-one (***3aq***). Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 80% (73 mg); mp 168−169 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.71−7.64 (m, 2H), 7.54−7.45 (m, 3H), 7.38 (dd, *J* = 7.5, 1.4 Hz, 2H), 7.22−7.15 (m, 3H), 6.89 (dd, *J* = 6.8, 2.4 Hz, 2H), 4.23−4.13 (m, 2H), 3.10 (dt, *J* = 13.8, 6.9 Hz, 1H), 2.96−2.84 (m, 2H), 1.35 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 155.3, 148.2, 145.5, 137.8, 135.4, 133.6, 129.7, 128.8, 128.7, 128.6, 127.8, 127.5, 126.6, 123.4, 120.7, 47.5, 34.7, 34.1, 23.9; HRMS (ESI) *m*/*z* calcd for $C_{25}H_{24}N_2O$ [M + H]$^+$ 369.1967, found 369.1960.

7-Fluoro-3-phenethyl-2-phenylquinazolin-4(3H)-one (***3ar***). Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 84% (72 mg); mp 150−151 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (dd, *J* = 8.9, 6.1 Hz, 1H), 7.59−7.46 (m, 3H), 7.45−7.32 (m, 3H), 7.26−7.22 (m, 1H), 7.22−7.15 (m, 3H), 6.87 (dd, *J* = 6.4, 2.8 Hz, 2H), 4.26−4.13 (m, 2H), 2.97−2.86 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 165.3, 161.4, 157.4, 149.3, 149.2, 137.6, 135.1, 130.0, 129.6, 129.5, 128.8, 128.7, 128.6, 127.7, 126.7, 117.7, 117.7, 116.0, 115.8, 112.9, 112.6, 47.6, 34.6; HRMS (ESI) *m*/*z* calcd for $C_{22}H_{17}FN_2O$ [M + H]$^+$ 345.1403, found 345.1401.

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3-Benzyl-2-phenylquinazolin-4(3H)-one (**3bb**).[10w] Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 78% (61 mg); mp 152−153 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, J = 8.2 Hz, 1H), 7.82−7.73 (m, 2H), 7.53 (ddd, J = 8.2, 6.3, 2.0 Hz, 1H), 7.47 (dd, J = 8.4, 6.1 Hz, 1H), 7.40 (t, J = 7.5 Hz, 2H), 7.34 (d, J = 7.7 Hz, 2H), 7.20 (dd, J = 6.5, 3.7 Hz, 3H), 6.97−6.86 (m, 2H), 5.28 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 156.4, 147.3, 136.6, 135.3, 134.5, 129.9, 128.6, 128.5, 128.0, 127.6, 127.4, 127.1, 127.1, 127.0, 120.9, 48.8.

3-(4-(tert-Butyl)benzyl)-2-phenylquinazolin-4(3H)-one (**3bc**). Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 82% (76 mg); mp 166−167 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, J = 8.1 Hz, 1H), 7.81−7.73 (m, 2H), 7.54−7.37 (m, 6H), 7.22 (d, J = 8.3 Hz, 2H), 6.88 (d, J = 8.2 Hz, 2H), 5.25 (s, 2H), 1.26 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 156.4, 150.4, 147.3, 135.4, 134.5, 133.5, 129.8, 128.6, 128.1, 127.5, 127.1, 126.8 (overlapped), 125.4, 120.9, 48.6, 34.4, 31.3; HRMS (ESI) m/z calcd for $C_{25}H_{24}N_2O$ $[M + H]^+$ 369.1967, found 369.1959.

2-Phenyl-3-(4-(trifluoromethyl)benzyl)quinazolin-4(3H)-one (**3bd**). Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 72% (66 mg); mp 148−149 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, J = 8.1 Hz, 1H), 7.87−7.73 (m, 2H), 7.59−7.52 (m, 1H), 7.49 (t, J = 7.8 Hz, 3H), 7.42 (t, J = 7.5 Hz, 2H), 7.35 (d, J = 7.4 Hz, 2H), 7.07 (d, J = 8.0 Hz, 2H), 5.31 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 156.0, 147.2, 140.6, 135.0, 134.8, 130.1, 128.8, 127.9, 127.7, 127.4, 127.3, 127.1, 125.5, 125.5, 120.7, 48.5; HRMS (ESI) m/z calcd for $C_{22}H_{15}F_3N_2O$ $[M + H]^+$ 381.1215, found 381.1209.

2-Phenyl-3-(3-phenylpropyl)quinazolin-4(3H)-one (**3be**).[11a] Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 80% (68 mg); mp 135−136 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, J = 8.0 Hz, 1H), 7.79−7.69 (m, 2H), 7.54−7.45 (m, 6H), 7.18 (t, J = 7.2 Hz, 2H), 7.12 (dd, J = 8.5, 5.8 Hz, 1H), 6.98 (d, J = 7.2 Hz, 2H), 4.05−3.96 (m, 2H), 2.51 (t, J = 7.6 Hz, 2H), 1.95 (dt, J = 15.5, 7.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 156.1, 147.2, 140.4, 135.3, 134.3, 129.8, 128.8, 128.3, 128.0, 127.6, 127.5, 127.0, 126.7, 125.9, 120.9, 45.5, 32.9, 29.7.

3-Ethyl-2-phenylquinazolin-4(3H)-one (**3bf**).[10y] Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 89% (56 mg); mp 155−156 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39−8.30 (m, 1H), 7.79−7.71 (m, 2H), 7.57−7.47 (m, 6H), 4.04 (q, J = 7.0 Hz, 2H), 1.22 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.0, 156.2, 147.2, 135.6, 134.3, 129.8, 128.8, 127.7, 127.5, 126.9, 126.7, 121.0, 41.2, 14.1.

2-Phenyl-3-propylquinazolin-4(3H)-one (**3bg**).[10z] Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 71% (47 mg); mp 139−140 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, J = 7.8 Hz, 1H), 7.79−7.70 (m, 2H), 7.57−7.47 (m, 6H), 3.94 (dd, J = 8.8, 6.7 Hz, 2H), 1.64 (dd, J = 15.3, 7.6 Hz, 2H), 0.77 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.1, 156.2, 147.2, 135.6, 134.3, 129.8, 128.7, 127.7, 127.4, 126.9, 126.7, 120.9, 47.4, 22.1, 11.1.

3-Butyl-2-phenylquinazolin-4(3H)-one (**3bh**).[11d] Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 85% (59 mg); mp 169−170 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36−8.30 (m, 1H), 7.79−7.71 (m, 2H), 7.54−7.48 (m, 6H), 4.02−3.95 (m, 2H), 1.63−1.55 (m, 2H), 1.17 (dt, J = 14.8, 7.4 Hz, 2H), 0.76 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 156.2, 147.2, 135.6, 134.3, 129.8, 128.7, 127.8, 127.4, 126.9, 126.7, 120.9, 45.7, 30.7, 19.9, 13.4.

3-Dodecyl-2-phenylquinazolin-4(3H)-one (**3bi**). Eluent: petroleum ether/ethyl acetate (10:1). Colorless oil. Yield: 60% (59 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (dd, J = 4.5, 4.0 Hz, 1H), 7.79−7.70 (m, 2H), 7.55−7.48 (m, 6H), 4.02−3.90 (m, 2H), 1.64−1.55 (m, 2H), 1.26−1.09 (m, 18H), 0.88 (t, J = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.1, 156.2, 147.2, 135.6, 134.2, 129.7, 128.7, 127.8, 127.4, 126.9, 126.7, 120.9, 45.9, 31.9, 29.6, 29.5, 29.4, 29.3, 29.3, 28.8, 28.6, 26.6, 22.7, 14.1; HRMS (ESI) m/z calcd for $C_{26}H_{34}N_2O$ $[M + H]^+$ 391.2749, found 391.2744.

2-Phenylquinazolin-4(3H)-one (**3ca**).[11c] Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 99% (55 mg); mp 245−246 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.75 (s, 1H), 8.36−8.24 (m, 3H), 7.88−7.76 (m, 2H), 7.65−7.56 (m, 3H), 7.54−7.45 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 151.8, 149.5, 134.9, 132.8, 131.6, 129.0, 128.0, 127.4, 126.8, 126.4, 120.9.

2-(-Tolyl)quinazolin-4(3H)-one (**3cb**).[11c] Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 80% (47 mg); mp 223−224 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.80 (s, 1H), 8.24 (d, J = 7.8 Hz, 1H), 7.80 (d, J = 3.3 Hz, 2H), 7.64−7.30 (m, 5H), 2.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1, 153.5, 149.1, 136.9, 134.9, 133.6, 131.4, 130.6, 128.8, 127.9, 127.0, 126.4, 126.3, 120.8, 20.1.

2-(m-Tolyl)quinazolin-4(3H)-one (**3cc**).[10j] Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 92% (54 mg); mp 211−212 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.81 (s, 1H), 8.33 (d, J = 7.8 Hz, 1H), 8.18−7.95 (m, 2H), 7.91−7.71 (m, 2H), 7.59−7.31 (m, 3H), 2.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 152.0, 149.6, 138.8, 134.8, 132.7, 132.4, 128.9, 128.1, 128.0, 126.7, 126.3, 124.5, 120.8, 21.5.

2-(p-Tolyl)quinazolin-4(3H)-one (**3 cd**).[11c] Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 95% (56 mg); mp 237−238 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.46 (s, 1H), 8.15 (dd, J = 7.9, 1.2 Hz, 1H), 8.11 (d, J = 8.2 Hz, 2H), 7.86−7.80 (m, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.52 (dd, J = 11.1, 3.9 Hz, 1H), 7.36 (d, J = 8.1 Hz, 2H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.2, 152.2, 148.8, 141.4, 134.5, 129.7, 129.1, 127.6,127.3, 126.3, 125.8, 120.9, 20.9.

2-(4-Fluorophenyl)quinazolin-4(3H)-one (**3ce**).[11c] Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 85% (51 mg); mp 292−293 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.57 (s, 1H), 8.30−8.21 (m, 2H), 8.15 (dd, J = 7.9, 1.3 Hz, 1H), 7.89−7.80 (m, 1H), 7.73 (d, J = 7.9 Hz, 1H), 7.59−7.45 (m, 1H), 7.47−7.32 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.3, 162.8, 162.2, 151.4, 148.6, 134.6, 130.4, 130.3, 129.2, 129.2, 127.5, 126.6, 125.9, 120.9, 115.7, 115.5.

2-(4-Chlorophenyl)quinazolin-4(3H)-one (**3cf**).[11c] Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 91% (58 mg); mp 280−281 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.58 (s, 1H), 8.17 (dd, J = 17.5, 8.2 Hz, 3H), 7.88−7.79 (m, 1H), 7.74 (d, J = 8.1 Hz, 1H), 7.62 (d, J = 8.6 Hz, 2H), 7.53 (t, J = 7.5 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.2, 151.4, 148.6, 136.3, 134.7, 131.6, 129.6, 128.7, 127.5, 126.8, 125.9, 121.0.

2-(4-Bromophenyl)quinazolin-4(3H)-one (**3cg**).[10j] Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 76% (57 mg); mp 297−298 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.61 (s, 1H), 8.22−8.07 (m, 3H), 7.90−7.69 (m, 4H), 7.58−7.48 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.2, 151.5, 148.5, 134.7, 131.9, 131.6, 129.8, 127.5, 126.8, 125.9, 125.2, 121.0.

2-(4-Methoxyphenyl)quinazolin-4(3H)-one (**3ch**).[10j] Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 99% (63 mg); mp 246−247 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.77 (s, 1H), 8.36−8.25 (m, 1H), 8.20−8.05 (m, 2H), 7.84−7.70 (m, 2H), 7.48 (ddd, J = 8.1, 5.6, 2.7 Hz, 1H), 7.15−6.99 (m, 2H), 3.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 162.5, 151.2, 149.6, 134.9, 128.8, 127.8, 126.4, 126.4, 125.0, 120.6, 114.5, 55.5.

2-(4-(Trifluoromethyl)phenyl)quinazolin-4(3H)-one (**3ci**).[11c] Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 69% (50 mg); mp 229−230 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.74 (s, 1H), 8.38 (d, J = 8.2 Hz, 2H), 8.18 (dd, J = 7.9, 1.1 Hz, 1H), 7.93 (d, J = 8.4 Hz, 2H), 7.90−7.83 (m, 1H), 7.78 (d, J = 7.9 Hz, 1H), 7.60−7.52 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.1, 151.2, 148.4, 136.6, 134.7, 131.3, 130.9, 128.7, 127.7, 127.1, 125.9, 125.5, 125.5, 125.4, 125.3, 122.3, 121.2.

2-(2,4-Dichlorophenyl)quinazolin-4(3H)-one (**3cj**).[10j] Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 63% (46 mg); mp 225−226 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.65 (s, 1H), 8.18 (dd, J = 8.0, 1.3 Hz, 1H), 7.90−7.80 (m, 2H), 7.72 (d, J = 8.3 Hz, 2H), 7.63−7.54 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.4, 151.4, 148.4, 135.4, 134.6, 132.7 (overlapped), 132.2, 129.1, 127.5 (overlapped), 127.2, 125.8, 121.2.

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*2-(Naphthalen-2-yl)quinazolin-4(3H)-one (**3ck**).*[11c] Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 82% (56 mg); mp 287−288 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.67 (s, 1H), 8.83 (s, 1H), 8.32 (d, J = 8.6 Hz, 1H), 8.19 (d, J = 7.8 Hz, 1H), 8.11−8.05 (m, 2H), 8.02 (d, J = 8.4 Hz, 1H), 7.87 (t, J = 7.5 Hz, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.69−7.60 (m, 2H), 7.55 (t, J = 7.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.2, 152.2, 148.8, 134.6, 134.1, 132.3, 129.9, 128.9, 128.1, 128.1, 127.9, 127.6, 127.5, 126.9, 126.6, 125.9, 124.5, 121.0.

*6-Methyl-2-phenylquinazolin-4(3H)-one (**3cl**).*[10a] Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 97% (57 mg); mp 240−241 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.46 (s, 1H), 8.17 (d, J = 7.2 Hz, 2H), 7.95 (s, 1H), 7.68−7.62 (m, 2H), 7.61−7.50 (m, 3H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.2, 151.5, 146.7, 136.3, 135.9, 132.8, 131.2, 128.6, 127.6, 127.4, 125.2, 120.7, 20.8.

*7-Methyl-2-phenylquinazolin-4(3H)-one (**3 cm**).*[10m] Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 97% (57 mg); mp 229−230 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.44 (s, 1H), 8.18 (dd, J = 8.0, 1.4 Hz, 2H), 8.05 (d, J = 8.1 Hz, 1H), 7.66−7.50 (m, 4H), 7.35 (dd, J = 8.1, 1.2 Hz, 1H), 2.48 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.1, 152.3, 148.8, 145.0, 132.8, 131.3, 128.5, 128.0, 127.7, 127.1, 125.7, 118.6, 21.3.

*6-Fluoro-2-phenylquinazolin-4(3H)-one (**3cn**).*[10m] Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 97% (58 mg); mp 232−233 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.67 (s, 1H), 8.20−8.13 (m, 2H), 7.85−7.79 (m, 2H), 7.72 (td, J = 8.7, 3.0 Hz, 1H), 7.61−7.50 (m, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 161.7, 161.2, 158.8, 151.9, 145.6, 132.5, 131.4, 130.3, 128.9, 128.6, 127.7, 123.2, 122.9, 122.1, 110.6, 110.4.

*6-Bromo-2-phenylquinazolin-4(3H)-one (**3co**).*[10a] Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 68% (51 mg); mp 285−286 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.70 (s, 1H), 8.30−8.11 (m, 3H), 7.97 (dd, J = 8.7, 2.4 Hz, 1H), 7.71 (t, J = 15.6 Hz, 1H), 7.63−7.49 (m, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.3, 153.1, 147.7, 137.3, 132.6, 131.6, 129.8, 128.6, 128.0, 127.8, 122.6, 118.8.

*6-Isopropyl-2-phenylquinazolin-4(3H)-one (**3 cP**).*[11c] Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 90% (59 mg); mp 225−226 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.47 (s, 1H), 8.18 (d, J = 6.7 Hz, 2H), 7.99 (d, J = 1.8 Hz, 1H), 7.80−7.64 (m, 2H), 7.62−7.45 (m, 3H), 3.07 (dt, J = 13.8, 6.9 Hz, 1H), 1.28 (d, J = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.3, 151.5, 147.0, 133.5, 132.7, 131.2, 128.5, 127.7, 127.6, 127.5, 122.3, 120.7, 33.1, 23.7.

*7-Fluoro-2-phenylquinazolin-4(3H)-one (**3cq**).*[11c] Eluent: petroleum ether/ethyl acetate (10:1). White solid. Yield: 95% (57 mg); mp >300 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.63 (s, 1H), 8.27−8.14 (m, 3H), 7.63−7.47 (m, 4H), 7.37 (td, J = 8.7, 2.5 Hz, 1H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 167.1, 164.6, 161.6, 153.7, 150.9, 150.8, 132.4, 131.7, 129.0, 128.9, 128.6, 127.9, 118.0, 1152, 115.0, 112.5, 112.3.

■ ASSOCIATED CONTENT

Supporting Information

NMR spectra of the compounds. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00957.

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Notes

The authors declare no competing financial interest.

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