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Efficient Synthesis of 2-Aminoquinazoline Derivatives via Acid-Mediated [4+2] Annulation of *N*-Benzyl Cyanamides

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Abstract: The synthesis of 2-aminoquinazoline derivatives is achieved by using hydrochloric acid as a mediator in the [4+2] annulation reaction between *N*-benzyl cyanamides and 2-amino aryl ketones. In addition, 2-amino-4-iminoquinazolines are synthesized by the reaction of 2-aminobenzonitriles, instead of 2-amino aryl ketones, with *N*-benzyl cyanamides. A wide range of substrates can be used and high yields are obtained, demonstrating the practicality of this method for the synthesis of 2-aminoquinazoline derivatives.

Keywords: acid-mediated; [4+2] annulation; *N*-benzyl cyanamides; 2-aminoquinazolines; 2-amino-4-iminoquinazolines

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1. Introduction

Quinazoline is a heterocyclic aromatic scaffold that possesses significant biological and pharmaceutical properties [1,2]. This structure is known for its anti-inflammatory [3,4], antibacterial [5,6], antiviral [7], antimalarial [8,9], and anticancer activities [10–12]. Figure 1 highlights some quinazoline-based drugs that are in clinical use [13–15].

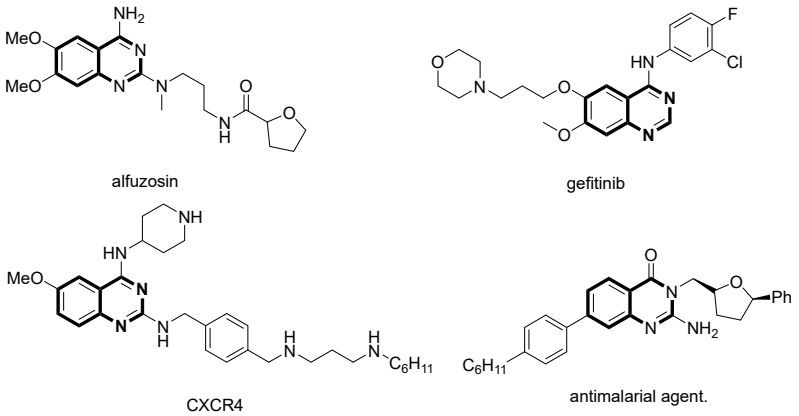
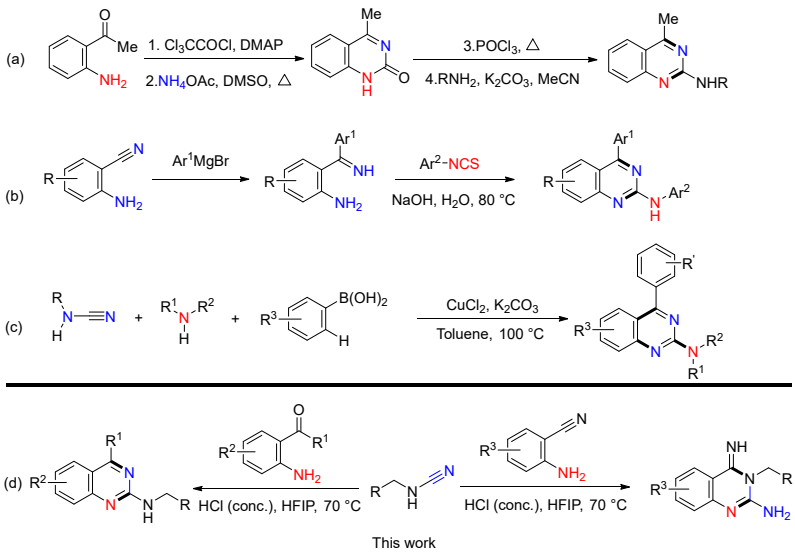


Figure 1. Representative drug molecules containing quinazoline skeleton.

Various methods have been reported for the synthesis of quinazolines [16–21]. Classical synthetic approaches to the quinazoline scaffold include Pd-catalyzed cyclization [22–24], Ru-catalyzed C-H activation/annulation [25–28] and Cu-catalyzed oxidative functionalization reactions; these routes start from amidines, aromatic amines, or nitrile compounds [29–32].

Although there are many routes for the synthesis of quinazoline compounds, methods for the direct synthesis of 2-aminoquinazolines are still relatively rare. Because 2-aminoquinazolines have important medicinal properties, the development of new strategies to obtain 2-aminoquinazoline derivatives is desirable from simple substrates. For example, Dyke and co-workers explored the multi-step preparation of pharmacologically active quinazoline derivatives from 2-aminoacetophenone and trichloroacetyl chloride, albeit with low yields (Scheme 1a) [33]. Subsequently, a two-step method for the synthesis of quinazolines was reported by the Palakodety group. This reaction began with 2-aminobenzonitriles, which underwent a reaction with aryl Grignard reagents to form ortho-Aminoketimines. These intermediates were submitted to alkaline conditions to constructed N,4-disubstituted quinazolines. (Scheme 1b) [34]. In addition, Neuville et al. developed a copper-promoted one-pot three-component domino reaction of 2-aminoquinazolines involving cyanamides, aryl boronic acids, and amines (Scheme 1c) [35]. Inspired by these works and our previous studies [36], herein, we report a hydrochloric acid-mediated [4+2] annulation for the efficient synthesis of 2-aminoquinazoline derivatives from o-aminoaryl ketones and *N*-benzyl cyanamide. Furthermore, 2-amino-4-iminoquinazoline derivatives are formed by the reaction of 2-aminobenzonitriles instead of o-aminoaryl ketones with *N*-benzyl cyanamides (Scheme 1d).



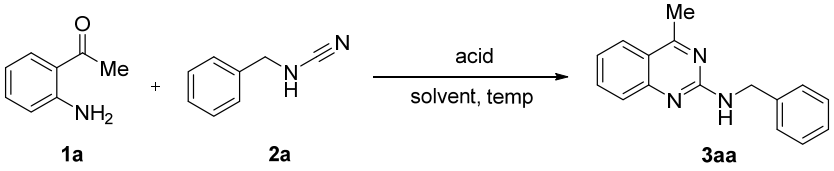
Scheme 1. Strategies for access to 2-aminoquinazolines.

2. Results and Discussion

2-Aminoacetophenone (**1a**) and *N*-benzyl cyanamide (**2a**) were chosen as model substrates to optimize the reaction conditions (Table 1). Fortunately, the desired product N-benzyl-4-methylquinazolin-2-amine (**3aa**) was obtained in a 57% yield with MsOH as an additive in HFIP at 90 °C for 1 h (Entry 1). Encouraged by this result, we sought to optimize the reaction conditions to improve the reaction yield (Table 1). Several additives, solvents, and temperatures were examined, and the results are summarized in Table 1. The yield of **3aa** was increased to 73% when the reaction was carried out in the presence of hydrochloric acid (Entry 13). Various additives were screened (Entries 1–12), and concentrated hydrochloric acid was identified as the optimal mediator. When no additive was introduced, the target product was not obtained (Entry 14); therefore, the additive played an important role in this reaction. Next various solvents were investigated. Although other solvents (EtOAc, ^{i}PrOH, MeOH, CH_3CN, ethanol, H_2O, Et_2O and dioxane) were tested, HFIP was found to be the best solvent for the reaction (Entries 15–22). Temperature screening confirmed that 70 °C was appropriate for this reaction (Entries 23–26). Next, the amount of hydrochloric acid and the reaction time were examined. The reaction proceeded with an 85% yield when only 2.0 equivalents of hydrochloric acid were used (Entries 27–29)),

and the yield of 3aa decreased with increasing reaction time (Entry 30). The information of spectral copies of 1HNMR, and 13CNMR can refer to Supplementary Material.

Table 1. Optimization of the reaction conditions [a].



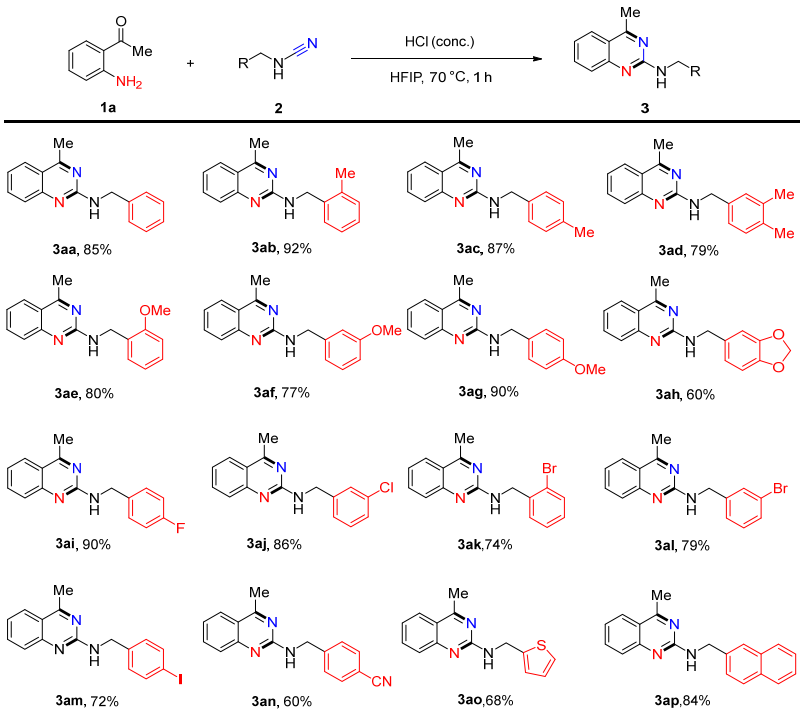
1a **2a** **3aa**

Entry	Solvent	Additive [b]	Temp (°C)	Yield (%) [c]
1	HFIP	MsOH	90	57
2	HFIP	TfOH	90	45
3	HFIP	TFA	90	30
4	HFIP	HCOOH	90	30
5	HFIP	AcOH	90	45
6	HFIP	TsOH	90	60
7	HFIP	H_2SO_4	90	47
8	HFIP	HI	90	55
9	HFIP	HBr	90	50
10	HFIP	$CuBr_2$	90	58
11	HFIP	CuI	90	63
12	HFIP	$FeCl_3$	90	57
13	HFIP	HCl	90	73
14	HFIP	-	90	0
15	EtOAc	HCl	90	20
16	^{i}PrOH	HCl	90	32
17	MeOH	HCl	90	40
18	CH_3CN	HCl	90	60
19	EtOH	HCl	90	42
20	Dioxane	HCl	90	30
21	H_2O	HCl	90	35
22	Et_2O	HCl	90	30
23	HFIP	HCl	70	80
24	HFIP	HCl	80	70
25	HFIP	HCl	60	62
26	HFIP	HCl	50	50
27 [d]	HFIP	HCl (2)	70	85
28 [e]	HFIP	HCl (1)	70	78
29 [f]	HFIP	HCl (0.5)	70	72
30 [g]	HFIP	HCl (2)	70	76

[a] Reactions were carried out with **1a** (1.0 mmol, 1.0 equiv.), **2a** (1.5 mmol, 1.5 equiv.), additive (2.0 mmol, 2.0 equiv.), and HFIP (5 mL) heated to 70 °C in an oil bath for 1 h. HFIP = 1,1,1,3,3,3-Hexafluoroisopropanol. [b] All HCl entries in this table refer to 3.0 equiv. of 12 M HCl. [c] Isolated products. [d] HCl entry in this table refer to 2.0 equiv. of 12 M HCl. [e] HCl entry in this table refer to 1.0 equiv. of 12 M HCl. [f] HCl entry in this table refer to 0.5 equiv. of 12 M HCl. [g] Reaction time of 4 h.

With the optimal reaction conditions for the synthesis of **3aa** at hand, we explored the substrate scope of the *N*-benzyl cyanamide (**2a**), as shown in Scheme 2. It is noteworthy that the electronic properties of the substituents on the aromatic ring system had little effect on the efficiency of this reaction. *N*-benzyl cyanamides with electron-neutral (H), electron-donating (2-Me, 3-Me, 3,4-dimethyl., 2-OMe, 3-OMe, 4-OMe, 3,4-(OCH_2O)-), and halogen-substituted (4-F, 3-Cl, 2-Br, 3-Br, 4-I) groups attached to the benzene ring were smoothly transformed into their corresponding products in good to excellent yields (60–92%; **3aa**–**3am**). The substrate with an electron-withdrawing (4-CN) group on its benzene ring was transformed into the corresponding product in good yield (60%; **3an**). Additionally, moderate to good yields were obtained for heteroaromatic (2-thienyl) group substrates (68%; **3ao**). To our satisfaction, a substrate containing a sterically hindered

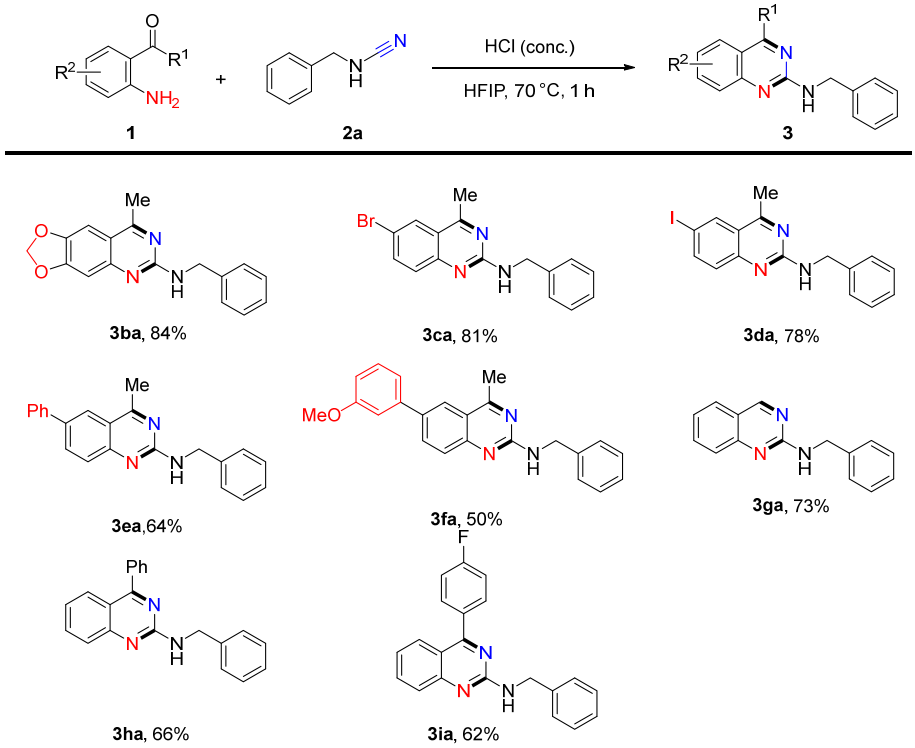
2-naphthyl group was converted into the desired product (**3ap**) in high yield (84%). The structure of **3aa** was identified by single-crystal X-ray diffraction (CCDC:2294005).



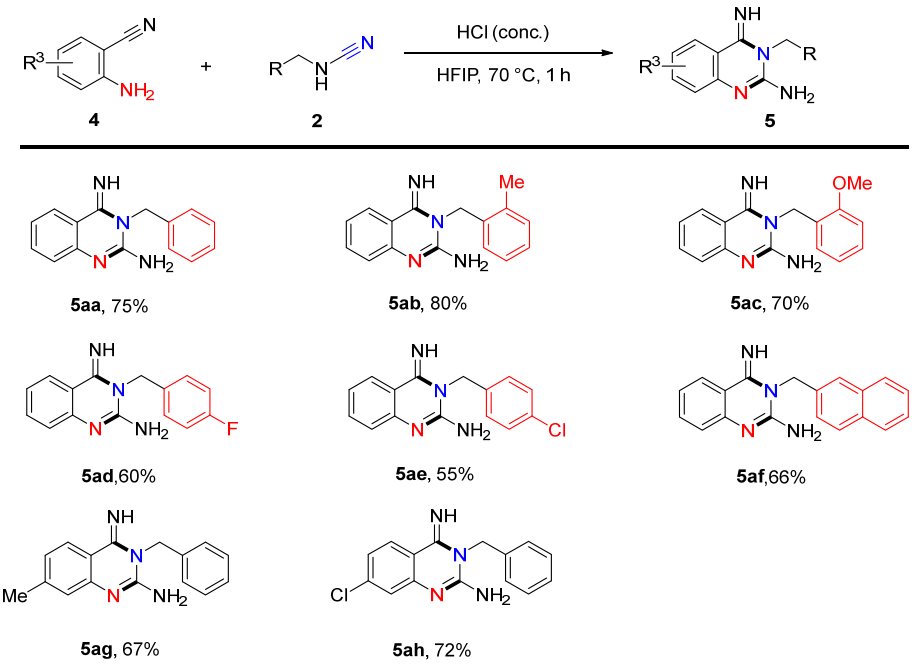
Scheme 2. Scope of *N*-benzyl cyanamides.Reactions were carried out with **1a** (1.0 mmol, 1.0 equiv.), **2** (1.5 mmol, 1.5 equiv.), HCl (2.0 mmol, 2.0 equiv.), and HFIP (5 mL) heated to 70 °C in an oil bath for 1 h. Isolated yields are shown.

Encouraged by these results described above, next, we examined the scope of 2-amino aryl ketones (**1**) (Scheme 3). As expected, Substrate (**1**) substituted at either the 4- or 5-position was effective under the reaction conditions. Substrate (**1**) with electron-donating (1,3-benzodioxole) or electron-withdrawing (6-Br, 6-I, and 6-(3-MeOC_6H_4) groups attached to the benzene ring were transformed into their corresponding products in good to high yields (**3ba**–**3fa**; 50–84%). 2-Aminobenzaldehyde (**1g**), (2-aminophenyl)(phenyl)methanone (**1h**) and (2-aminophenyl)(4-fluorophenyl)methanone (**1i**) substrates were well-tolerated by the reaction, affording the desired products (**3ga**–**3ia**) in 62–77% yields.

To our satisfaction, when 2-aminoacetophenone was accidentally replaced with 2-aminobenzonitrile, 3-benzyl-4-imino-3,4-dihydroquinazolin-2-amine (**5aa**) was obtained. We further investigated the substrate scope of *N*-benzyl cyanamides (Scheme 4). As shown in the table, unsubstituted 2-aminobenzonitrile offered a 75% isolated yield of **5aa**, Substrate (**2**) with electron-donating (2-Me and 2-OMe) and electron-withdrawing (6-F and 6-Cl) groups attached to the benzene ring was transformed smoothly into the corresponding products in good to high yields (**5ab**–**5ae**; 55–80%). Notably, even when the substrate contained a sterically hindered 2-naphthyl group, the desired product (**5af**) was obtained in a 66% yield. For 2-aminobenzonitriles bearing an electron-donating 4-Me group and a 4-Cl group, the reaction performed well, affording the desired products (**5ag**–**5ah**) in 70 and 72% yields, respectively. In addition, the structure of compound **5ab** was determined by X-ray crystallographic analysis (CCDC:2294029) (Tables S1 and S2).



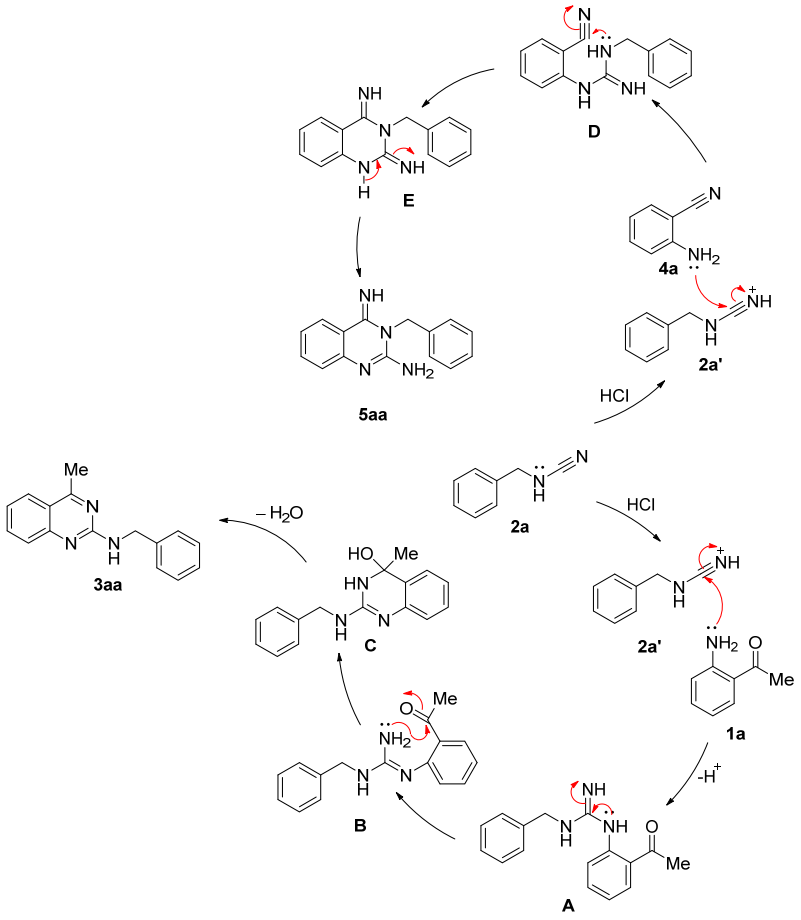
Scheme 3. Scope of 2-amino aryl ketones. Reactions were carried out with **1** (1.0 mmol, 1.0 equiv), **2a** (1.5 mmol, 1.5 equiv), HCl (2.0 mmol, 2.0 equiv), and HFIP (5 mL) heated to 70 °C in an oil bath for 1 h. Isolated yields are shown.



Scheme 4. Scope of *2-aminobenzonitriles*. Reactions were carried out with **4** (1.0 mmol, 1.0 equiv.), **2** (1.5 mmol, 1.5 equiv.), HCl (2.0 mmol, 2.0 equiv.), and HFIP (5 mL) heated to 70 °C in an oil bath for 1 h. Isolated yields are shown.

On the basis of these results, a plausible mechanism was proposed for the formation of 2-aminoquinazolines (Scheme 5). Initially, *N*-benzyl cyanamide (**2a**) was protonated under acidic conditions (forming **2a′**), which increases the electrophilic character of the cyanamide carbon. This allowed the amino group of **1a** the attack on the protonated

cyanogen group, forming the amidine intermediate **A**, which underwent isomerization, leading to intermediate **B**. Intermediate **B** underwent intramolecular cyclization through nucleophilic addition of the amino group to the carbonyl group, transforming into **C**. Finally, intermediate **C** was converted to the desired product, 2-aminoquinazoline **3aa,** through an aromatization reaction with the elimination of H_2O. The mechanism for the preparation of **5aa** from **2a** and 2-aminobenzonitrile (**4a**) differs from the above mechanism. First, the amino group of 2-aminobenzonitrile **4a** attacks the electrophilic carbon of **2a′** to form amidine intermediate **D**. Then, intermediate **D** undergoes intramolecular cyclization into **E** through nucleophilic addition, which transforms into **5aa** by intramolecular isomerization.



Scheme 5. A plausible mechanism.

3. Conclusions

In summary, we developed a hydrochloric acid-mediated [4+2] annulation synthesis of 2-aminoquinazoline derivatives from *N*-benzyl cyanamides and 2-amino aryl ketones. In addition, 2-amino-4-iminoquinazolines were produced from the reaction of *N*-benzyl cyanamides with 2-aminobenzonitriles. These reactions tolerate a wide range of substrates and exhibit good functional group tolerance. Further studies on this method for the synthesis of biologically active compounds are in progress in our laboratory.

4. Experimental Section

General Information. Unless otherwise noted, all commercially available compounds were used as provided without further purification. TLC analysis was performed using precoated glass plates. For column chromatography, a 200–300 mesh silica gel was used. ^{1}H NMR spectra were determined at 25 °C on a 500 or a 600 MHz spectrometer. ^{13}C{1H} NMR spectra were determined at 25 °C on a 125 or a 150 MHz spectrometer (Bruker AVANCE II

500 and Bruker AVANCE III 600, Billerica, MA, USA). Chemical shifts are given in ppm relative to the internal standard of tetramethyl silane (TMS). HRMS were obtained by using UPLC G2-XS QTof MS equipped with an ESI source. Melting points were determined using an XT-4 apparatus and not corrected. ^{1}H NMR chemical shifts were referenced to $CDCl_3$ (TMS, 7.26 ppm). ^{13}C NMR chemical shifts were referenced to $CDCl_3$ (TMS, 77.00 ppm).

General procedure for the synthesis of **3aa**: The mixture of 2-Aminoacetophenone **1a** (135.2 mg, 1.0 mmol), *N*-benzyl cyanamide **2a** (198.3 mg, 1.5 mmol) and hydrochloric acid (72.9 mg, 2.0 mmol) was soluted in HFIP (5 mL). Then, the resulting mixture was stirred at 70 °C for 1 h. The residue was extracted with ethylacetate, the organic layer was washed with brine and dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography. Product **3aa** was obtained in an 85% yield (211.8 mg).

General procedure for the synthesis of **5aa**: The mixture of 2-Aminobenzonitrile **4a** (118.1 mg, 1.0 mmol), *N*-benzyl cyanamide **2a** (198.3 mg, 1.5 mmol) and hydrochloric acid (72.9 mg, 2.0 mmol) was soluted in HFIP (5 mL). Then, the resulting mixture was stirred at 70 °C for 1 h. After the disappearance of the reactant (monitored by TLC), the residue was extracted with ethylacetate 3 times (3 × 50 mL), the organic layer was washed with brine and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography. Product **5aa** was obtained in a 75% yield (188.5 mg).

*4.1. N-Benzyl-4-methylquinazolin-2-amine (**3aa**)*

Yield 85% (211.8 mg); Rf (Pet/EtOAc; 6:1) 0.25; white solid; m.p. 116–118 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.85 (d, J = 8.3 Hz, 1H), 7.66–7.59 (m, 2H), 7.41 (d, J = 7.5 Hz, 2H), 7.33 (t, J = 7.5 Hz, 2H), 7.26 (t, J = 8.5 Hz, 1H), 7.22 (t, J = 8.0 Hz, 1H), 5.48 (s, 1H), 4.77 (d, J = 6 Hz, 2H), 2.76 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ (ppm) 169.5, 158.8, 151.9, 139.4, 133.6, 128.5, 127.7, 127.2, 126.3, 125.3, 122.3, 119.8, 45.6, 21.6; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{16}H_{16}N_3$: 250.1344; found: 250.1343.

*4.2. 4-Methyl-N-(2-methylbenzyl)quinazolin-2-amine (**3ab**)*

Yield 92% (242.1 mg); Rf (Pet/EtOAc; 8:1) 0.25; white solid; m.p. 145–146 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.85 (d, J = 8.0 Hz, 1H), 7.66–7.60 (m, 2H), 7.37 (d, J = 6.5 Hz, 1H), 7.23–7.15 (m, 4H), 5.31 (s, 1H), 4.73 (d, J = 5.5 Hz, 2H), 2.76 (s, 3H), 2.41 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ (ppm) 169.5, 158.7, 151.9, 137.0, 136.5, 133.6, 130.4, 128.4, 127.4, 126.3, 126.1, 125.3, 122.3, 119.8, 43.7, 21.6, 19.1; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{17}H_{18}N_3$: 264.1501; found: 264.1497.

*4.3. 4-Methyl-N-(4-methylbenzyl)quinazolin-2-amine (**3ac**)*

Yield 87% (228.9 mg); Rf (Pet/EtOAc; 8:1) 0.30; white solid; m.p. 119–120 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.84 (d, J = 8.0 Hz, 1H), 7.65–7.59 (m, 2H), 7.29 (d, J = 8.0 Hz, 2H), 7.22 (t, J = 8.0 Hz, 1H), 7.13 (d, J = 7.5 Hz, 2H), 5.44 (s, 1H), 4.72 (d, J = 5.5 Hz, 2H), 2.75 (s, 3H), 2.33 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ (ppm) 169.5, 158.8, 151.9, 136.8, 136.3, 133.6, 129.2, 127.7, 126.3, 125.3, 122.2, 119.8, 45.4, 21.6, 21.1; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{17}H_{18}N_3$: 264.1501; found: 264.1505.

*4.4. N-(3,4-Dimethylbenzyl)-4-methylquinazolin-2-amine (**3ad**)*

Yield 79% (179.5 mg); Rf (Pet/EtOAc; 8:1) 0.30; white solid; m.p. 109–110 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.85 (d, J = 7.7 Hz, 1H), 7.66–7.60 (m, 2H), 7.22 (t, J = 8.0 Hz, 1H), 7.18 (s, 1H), 7.14 (d, J = 7.5 Hz, 1H), 7.09 (d, J = 7.7 Hz, 1H), 5.45 (s, 1H), 4.69 (d, J = 5.7 Hz, 2H), 2.76 (s, 3H), 2.24 (s, 6H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ (ppm) 169.5, 158.8, 151.9, 136.7, 136.7, 135.4, 133.6, 129.8, 129.1, 126.2, 125.3, 125.2, 122.2, 119.8, 45.4, 21.6, 19.7, 19.4; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{18}H_{20}N_3$: 278.1657; found: 278.1659.

*4.5. N-(2-Methoxybenzyl)-4-methylquinazolin-2-amine (***3ae***)*

Yield 80% (223.3 mg); Rf (Pet/EtOAc; 4:1) 0.35; white solid; m.p. 134–135 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.82 (d, J = 8.0 Hz, 1H), 7.64–7.58 (m, 2H), 7.42 (d, J = 7.5 Hz, 1H), 7.26–7.16 (m, 2H), 6.91–6.87 (m, 2H),5.62 (s, 1H), 4.76 (d, J = 6.0 Hz, 2H), 3.87 (s, 3H), 2.74 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ (ppm) 169.3, 158.9, 157.7, 152.0, 133.5, 129.6, 128.4, 127.4, 126.2, 125.2, 122.0, 120.4, 119.7, 110.1, 55.3, 41.1, 21.6; HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{17}H_{18}N_3O$: 280.1450; found: 280.1454.

*4.6. N-(3-Methoxybenzyl)-4-methylquinazolin-2-amine (***3af***)*

Yield 77% (214.9 mg); Rf (Pet/EtOAc; 4:1) 0.30; white solid; m.p. 125–126 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.85 (d, J = 9.0 Hz, 1H), 7.66–7.59 (m, 2H), 7.24–7.20 (m, 2H), 7.00–6.97 (m, 2H), 6.80 (d, J = 8.0 Hz, 1H), 5.47 (s, 1H), 4.75 (d, J = 6.0 Hz, 2H), 3.79 (s, 3H), 2.76 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ (ppm) 169.5, 159.8, 158.8, 151.9, 141.0, 133.6, 129.5, 126.3, 125.3, 122.3, 120.0, 119.9, 113.2, 112.7, 55.3, 45.6, 21.6; HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{17}H_{18}N_3O$: 280.1450; found: 280.1450.

*4.7. N-(4-Methoxybenzyl)-4-methylquinazolin-2-amine (***3ag***)*

Yield 90% (251.2 mg); Rf (Pet/EtOAc; 4:1) 0.25; white solid; m.p. 97–98 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.84 (d, J = 8.0 Hz, 1H), 7.66–7.59 (m, 2H), 7.32 (d, J = 8.5 Hz, 2H), 7.26–7.19 (m, 1H), 6.88–6.84 (m, 2H), 5.46 (s, 1H), 4.68 (d, J = 5.5 Hz, 2H), 3.78 (s, 3H), 2.75 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ (ppm) 169.4, 158.8, 158.7, 151.9, 133.6, 131.4, 129.0, 126.2, 125.3, 122.2, 119.8, 113.9, 55.3, 45.1, 21.5; HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{17}H_{18}N_3O$: 280.1450; found: 280.1452.

*4.8. N-(Benzo[d][1,3]dioxol-5-ylmethyl)-4-methylquinazolin-2-amine (***3ah***)*

Yield 60% (175.9 mg); Rf (Pet/EtOAc; 4:1) 0.30; white solid; m.p. 110–111 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.85 (d, J = 6.5 Hz, 1H), 7.66–7.59 (m, 2H), 7.22 (t, J = 6.5 Hz, 1H), 6.91 (s, 1H), 6.86 (d, J = 6.5 Hz, 1H), 6.76 (d, J = 7.0 Hz, 1H), 5.92 (s, 2H), 5.47 (s, 1H), 4.66 (d, J = 5.0 Hz, 2H),2.76 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ (ppm) 169. 6, 158.6, 151.7, 147.7, 146.7, 133.6, 133.2, 126.2, 125.3, 122.3, 120.9, 119.8, 108.4, 108.2, 100.9, 45.3, 21.6; HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{17}H_{16}N_3O_2$: 294.1243; found: 294.1235.

*4.9. N-(4-Fluorobenzyl)-4-methylquinazolin-2-amine (***3ai***)*

Yield 90% (240.4 mg); Rf (Pet/EtOAc; 5:1) 0.30; white solid; m.p. 109–110 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.86 (d, J = 9.0 Hz, 1H), 7.65 (t, J = 7.5 Hz, 1H), 7.60 (d, J = 8.0 Hz, 1H), 7.39–7.36 (m, 2H), 7.23 (t, J = 8.0 Hz, 1H), 7.00 (t, J = 9.0 Hz, 2H), 5.46 (s, 1H), 4.73 (d, J = 6.0 Hz, 2H), 2.76 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ (ppm) 169.6, 163.0, 161.1, 158.6, 151.8, 135.2, 129.4, 126.3, 125.3, 122.4, 119.9, 115.4, 44.8, 21.6; HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{16}H_{15}N_3F$: 268.1250; found: 268.1254.

*4.10. N-(3-Chlorobenzyl)-4-methylquinazolin-2-amine (***3aj***)*

Yield 86% (243.5 mg); Rf (Pet/EtOAc; 5:1) 0.30; white solid; m.p. 115–116 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.85 (d, J = 8.5 Hz, 1H), 7.66–7.58 (m, 2H), 7.40 (s, 1H), 7.28–7.20 (m, 4H), 5.60 (s, 1H), 4.75 (d, J = 6.0 Hz, 2H), 2.76 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ (ppm) 169.6, 158.6, 151.7, 141.7, 134.3, 133.7, 129.7, 127.7, 127.2, 126.3, 125.7, 125.3, 122.4, 119.9, 44.9, 21.6; HRMS (ESI): m/z [M+H]$^+$ calcd for $C_{16}H_{15}N_3Cl$: 284.0955; found: 284.0952.

*4.11. N-(2-Bromobenzyl)-4-methylquinazolin-2-amine (***3ak***)*

Yield 74% (242.0 mg); Rf (Pet/EtOAc; 8:1) 0.25; white solid; m.p. 141–142 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.84 (d, J = 8.0 Hz, 1H), 7.65–7.53 (m, 4H), 7.26–7.20 (m, 2H), 7.12 (t, J = 7.5 Hz, 1H), 5.67 (s, 1H), 4.84 (d, J = 6.5 Hz, 2H), 2.75 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ (ppm) 169.6, 158.6, 151.8, 138.5, 133.6, 132.7, 130.0, 128.69, 127.4,

126.3, 125.2, 123.8, 122.4, 119.9, 45.6, 21.6; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{16}H_{15}N_3Br$: 328.0449; found: 328.0450.

*4.12. N-(3-Bromobenzyl)-4-methylquinazolin-2-amine (***3al***)*

Yield 79% (258.4 mg); Rf (Pet/EtOAc; 8:1) 0.30; white solid; m.p. 114–115 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.85 (d, J = 9.0 Hz, 1H), 7.67–7.54 (m, 3H), 7.37 (d, J = 8.0 Hz, 1H), 7.32 (d, J = 7.5 Hz, 1H), 7.22 (t, J = 8.5 Hz, 1H), 7.17 (t, J = 7.5 Hz, 1H),5.60 (s, 1H), 4.75 (d, J = 6.5 Hz, 2H), 2.76 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ (ppm) 169.7, 158.6, 151.7, 142.0, 133.7, 130.6, 130.2, 130.0, 126.3, 126.2, 125.3, 122.6, 122.5, 119.9, 44.8, 21.6; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{16}H_{15}N_3Br$: 328.0449; found: 328.0439.

*4.13. N-(4-Iodobenzyl)-4-methylquinazolin-2-amine (***3am***)*

Yield 72% (270.0 mg); Rf (Pet/EtOAc; 8:1) 0.30; white solid; m.p. 177–178 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.85 (d, J = 9.0 Hz, 1H), 7.68–7.55 (m, 4H), 7.25–7.20 (m, 1H), 7.15 (d, J = 8.5 Hz, 2H), 5.52 (s, 1H), 4.71 (d, J = 6.0 Hz, 2H), 2.76 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ (ppm) 169.6, 158.6, 151.7, 139.3, 137.5, 133.7, 129.6, 126.3, 125.3, 122.5, 119.9, 92.4, 44.9, 21.6; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{16}H_{15}N_3I$: 376.0311; found: 376.0314.

*4.14. 4-(((4-Methylquinazolin-2-yl)amino)methyl)benzonitrile (***3an***)*

Yield 60% (164.5 mg); Rf (Pet/EtOAc; 6:1) 0.30; white solid; m.p. 178–179 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.88 (d, J = 7.8 Hz, 1H), 7.67 (t, J = 8.4 Hz, 1H), 7.62–7.56 (m, 3H), 7.51 (d, J = 8.4 Hz, 2H), 7.25 (t, J = 6.0 Hz, 1H), 5.60 (s, 1H), 4.84 (d, J = 6.6 Hz, 2H), 2.78 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ (ppm) 166.6, 161.6, 152.8, 145.3, 133.9, 132.3, 128.0, 125.4, 122.8, 118.9, 110.8, 100.4, 100.0, 45.0, 21.7; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{17}H_{15}N_4$: 275.1297; found: 275.1293.

*4.15. 4-Methyl-N-(thiophen-2-ylmethyl)quinazolin-2-amine (***3ao***)*

Yield 68% (173.5 mg); Rf (Pet/EtOAc; 8:1) 0.35; white solid; m.p. 131–132 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.86 (d, J = 9.0 Hz, 1H), 7.69–7.61 (m, 2H), 7.23 (t, J = 7.5 Hz, 1H), 7.19 (d, J = 5.0 Hz, 1H), 7.05 (d, J = 4.0 Hz, 1H),6.95–6.94 (m, 1H), 5.50 (s, 1H), 4.93 (d, J = 6.0 Hz, 2H), 2.77 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ (ppm) 169.6, 158.3, 151.7, 142.3, 133.7, 126.6, 126.3, 125.5, 125.3, 124.7, 122.5, 119.9, 40.5, 21.6; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{14}H_{14}N_3S$: 256.0908; found: 256.0906.

*4.16. 4-Methyl-N-(naphthalen-2-ylmethyl)quinazolin-2-amine (***3ap***)*

Yield 84% (251.3 mg); Rf (Pet/EtOAc; 4:1) 0.30; white solid; m.p. 150–151 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.87–7.78 (m, 5H), 7.67–7.60 (m, 2H), 7.53 (d, J = 8.5 Hz, 1H), 7.47–7.42 (m, 2H), 7.22 (t, J = 8.0 Hz, 1H), 5.59 (s, 1H), 4.94 (d, J = 6.0 Hz, 2H), 2.77 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ (ppm) 169.6, 158.8, 151.9, 136.9, 133.6, 133.5, 132.7, 128.3, 127.73, 127.65, 126.3, 126.1, 126.0, 126.0, 125.7, 125.3, 122.4, 119.9, 45.7, 21.6; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{20}H_{18}N_3$: 300.1501; found: 300.1500.

*4.17. N-Benzyl-8-methyl-[1,3]dioxolo [4,5-g]quinazolin-6-amine (***3ba***)*

Yield 84% (246.2 mg); Rf (Pet/EtOAc; 10:1) 0.33; white solid; m.p. 157–158 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.39 (d, J = 7.5 Hz, 2H), 7.34–7.28 (m, 2H), 7.27–7.23 (m, 1H), 7.11 (s, 1H), 6.94 (s, 1H), 6.03 (s, 2H), 5.30 (s, 1H), 4.72 (d, J = 6.0 Hz, 2H), 2.64 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ (ppm) 166.6, 158.7, 153.5, 151.2, 144.6, 139.7, 128.5, 127.6, 127.1, 115.2, 103.4, 101.5, 101.0, 45.6, 21.8; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{17}H_{16}N_3O_2$: 294.1243; found: 294.1240.

*4.18. N-Benzyl-6-bromo-4-methylquinazolin-2-amine (***3ca***)*

Yield 81% (264.9 mg); Rf (Pet/EtOAc; 10:1) 0.30; white solid; m.p. 166–167 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.98 (s, 1H), 7.69 (d, J = 9.0 Hz, 1H), 7.47 (d, J = 9.0 Hz,

2H), 7.39 (d, *J* = 7.2 Hz, 2H), 7.34 (t, *J* = 7.2 Hz, 1H), 5.57 (s, 1H), 4.75 (d, *J* = 6.0 Hz, 2H), 2.72 (s, 3H); $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$): *δ* (ppm) 167.8, 158.7, 139.9, 139.0, 136.8, 128.6, 127.7, 127.6, 127.3, 120.9, 114.9, 109.2, 45.5, 21.6; HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{16}H_{15}N_3Br$: 328.0449; found: 328.0446.

*4.19. N-Benzyl-6-iodo-4-methylquinazolin-2-amine (***3da***)*

Yield 78% (292.5 mg); Rf (Pet/EtOAc; 8:1) 0.30; white solid; m.p. 175–176 °C; ^{1}H NMR (500 MHz, $CDCl_3$): *δ* (ppm) 8.18 (d, *J* = 2.0 Hz, 1H), 7.84 (d, *J* = 9.0 Hz, 1H), 7.39 (d, *J* = 7.5 Hz, 2H), 7.33 (t, *J* = 7.5 Hz, 3H), 7.29–7.25 (m, 1H), 5.53 (s, 1H), 4.74 (d, *J* = 5.5 Hz, 2H), 2.71 (s, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): *δ* (ppm) 168.5, 158.8, 151.0, 142.0, 139.1, 134.1, 128.6, 128.2, 127.7, 127.3, 121.8, 85.3, 45.5, 21.6; HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{16}H_{15}N_3I$: 376.0311; found: 376.0315.

*4.20. N-Benzyl-4-methyl-6-phenylquinazolin-2-amine (***3ea***)*

Yield 64% (208.3 mg); Rf (Pet/EtOAc; 8:1) 0.30; white solid; m.p. 148–149 °C; ^{1}H NMR (600 MHz, $CDCl_3$): *δ* (ppm) 8.03 (s, 1H), 7.95 (d, *J* = 8.4 Hz, 1H), 7.70 (d, *J* = 9.0 Hz, 1H), 7.65 (d, *J* = 7.8 Hz, 2H), 7.49 (t, *J* = 7.2 Hz, 2H), 7.43–7.34 (m, 5H), 7.28 (t, *J* = 7.8 Hz, 1H), 5.61 (s, 1H), 4.81 (d, *J* = 6.0 Hz, 2H), 2.84 (s, 3H); $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$): *δ* (ppm) 169.8, 158.6, 151.0, 140.5, 139.2, 135.3, 133.2, 128.9, 128.5, 127.7, 127.3, 127.2, 127.0, 126.5, 123.2, 119.9, 45.5, 21.7; HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{16}H_{15}N_3I$: 326.1657; found: 326.1662.

*4.21. N-Benzyl-6-(3-methoxyphenyl)-4-methylquinazolin-2-amine (***3fa***)*

Yield 50% (177.7 mg); Rf (Pet/EtOAc; 8:1) 0.30; white solid; m.p. 146–147 °C; ^{1}H NMR (600 MHz, $CDCl_3$): *δ* (ppm) 8.02 (s, 1H), 7.92 (d, *J* = 9.0 Hz, 1H), 7.68 (d, *J* = 9.0 Hz, 1H), 7.43–7.34 (m, 3H), 7.34 (t, *J* = 7.2 Hz, 2H), 7.28 (d, *J* = 7.2 Hz, 1H), 7.24 (d, *J* = 7.8 Hz, 1H), 7.18 (s, 1H), 6.93 (d, *J* = 8.4 Hz, 1H), 5.58 (s, 1H), 4.80 (d, *J* = 7.2 Hz, 2H), 3.90 (s, 3H), 2.82 (s, 3H); $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$): *δ* (ppm) 160.1, 148.9, 142.0, 139.1, 133.4, 130.3, 130.0, 128.6, 127.7, 127.3, 123.3, 119.6, 113.1, 112.5, 103.4, 102.9, 95.0, 55.4, 45.6, 21.8; HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{23}H_{22}N_3O$: 356.1763; found: 356.1764.

*4.22. N-Benzylquinazolin-2-amine (***3ga***)*

Yield 73% (171.8 mg); Rf (Pet/EtOAc; 4:1) 0.30; white solid; m.p. 122–123 °C; ^{1}H NMR (500 MHz, $CDCl_3$): *δ* (ppm) 8.71 (s, 1H), 7.67–7.58 (m, 3H), 7.42 (d, *J* = 7.0 Hz, 2H), 7.33 (t, *J* = 7.5 Hz, 2H), 7.29–7.19 (m, 2H), 6.21 (s, 1H), 4.77 (d, *J* = 5.5 Hz, 2H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): *δ* (ppm) 161.9, 159.5, 152.1, 139.2, 134.2, 128.6, 127.8, 127.5, 127.2, 125.6, 122.5, 120.6, 45.7; HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{15}H_{14}N_3$: 236.1188; found: 236.1189.

*4.23. N-Benzyl-4-phenylquinazolin-2-amine (***3ha***)*

Yield 66% (205.5 mg); Rf (Pet/EtOAc; 4:1) 0.25; white solid; m.p. 153–154 °C; ^{1}H NMR (600 MHz, $CDCl_3$): *δ* (ppm) 7.82 (d, *J* = 7.8 Hz, 1H), 7.70–7.65 (m, 4H), 7.53 (s, 3H), 7.43 (d, *J* = 6.0 Hz, 2H), 7.33 (t, *J* = 7.8 Hz, 2H), 7.27 (t, *J* = 7.2 Hz, 1H), 7.17 (t, *J* = 7.8 Hz, 1H), 5.70 (s, 1H), 4.81 (d, *J* = 6.0 Hz, 2H); $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$): *δ* (ppm) 170.1, 158.8, 153.2, 139.3, 137.4, 133.8, 129.7, 129.5, 128.5, 128.4, 127.7, 127.5, 127.2, 126.1, 122.5, 118.6, 45.7; HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{21}H_{18}N_3$: 312.1501; found: 312.1499.

*4.24. N-Benzyl-4-(4-fluorophenyl)quinazolin-2-amine (***3ia***)*

Yield 62% (204.2 mg); Rf (Pet/EtOAc; 4: 1) 0.35; white solid; m.p. 168–170 °C; ^{1}H NMR (600 MHz, $CDCl_3$): *δ* (ppm) 7.79 (d, *J* = 8.4 Hz, 1H), 7.72–7.66 (m, 4H), 7.43 (d, *J* = 7.2 Hz, 2H), 7.34 (t, *J* = 7.2 Hz, 2H), 7.27 (t, *J* = 7.2 Hz, 2H), 7.24–7.18 (m, 3H), 5.66 (s, 1H), 4.81 (d, *J* = 5.4 Hz, 2H); $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$): *δ* (ppm) 168.9, 164.6, 162.9, 158.7, 153.3, 133.9, 131.6, 128.6, 127.7, 127.2, 127.2, 122.6, 118.5, 115.6, 115.5, 45.6, 29.7; HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{21}H_{17}N_3F$: 330.1407; found: 330.1406.

*4.25. 3-Benzyl-4-imino-3,4-dihydroquinazolin-2-amine (***5aa***)*

Yield 75% (188.5 mg); Rf (EtOAc/CH_3OH; 8:1) 0.28; white solid; m.p. 186–187 °C; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.72 (d, J = 7.8 Hz, 1H), 7.49 (t, J = 7.8 Hz, 1H), 7.38 (s, 1H), 7.36 (d, J = 7.2 Hz, 2H), 7.33–7.29 (m, 3H), 7.21 (d, J = 7.2 Hz, 1H), 7.17 (t, J = 7.8 Hz, 1H), 5.49 (s, 2H), 4.79 (s, 2H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ (ppm) 158.7, 151.6, 145.8, 135.4, 132.8, 129.3, 127.9, 126.2, 124.8, 124.2, 122.9, 116.3, 46.9; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{15}H_{14}N_3O$: 252.1137; found: 252.1139.

*4.26. 4-Imino-3-(2-methylbenzyl)-3,4-dihydroquinazolin-2-amine (***5ab***)*

Yield 80% (212.1 mg); Rf (EtOAc/CH_3OH; 10:1) 0.32; white solid; m.p. 221–222 °C; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.72 (d, J = 7.8 Hz, 1H), 7.52 (t, J = 7.8 Hz, 1H), 7.27 (s, 1H), 7.23 (t, J = 7.2 Hz, 2H), 7.22–7.18 (m, 2H), 7.16 (d, J = 9.0 Hz, 1H), 7.03 (d, J = 7.8 Hz, 1H), 5.41 (s, 2H), 4.58 (s, 2H), 2.42 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ (ppm) 158.2, 151.5, 144.8, 135.3, 133.0, 132.2, 130.9, 127.7, 126.9, 124.6, 124.2, 124.1, 123.2, 116.2, 45.1, 19.1; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{16}H_{17}N_{4:}$ 265.1453; found: 265.1458.

*4.27. 4-Imino-3-(2-methoxybenzyl)-3,4-dihydroquinazolin-2-amine (***5ac***)*

Yield 70% (197.0 mg); Rf (EtOAc/CH_3OH; 10:1) 0.35; white solid; m.p. 202–203 °C; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.71 (d, J = 7.8 Hz, 1H), 7.49 (d, J = 7.2 Hz, 1H), 7.46 (t, J = 7.8 Hz, 1H), 7.29 (s, 1H), 7.28 (s, 1H), 7.19 (d, J = 7.8 Hz, 1H), 7.13 (t, J = 7.8 Hz, 1H), 6.94–6.92 (m, 2H), 5.46 (s, 2H), 5.25 (s, 2H), 3.93 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ (ppm) 158.8, 156.3, 151.4, 145.8, 132.7, 129.1, 128.7, 124.5, 124.2, 123.6, 122.5, 121.5, 116.1, 110.5, 55.6, 40.4; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{16}H_{17}N_4O$: 281.1402; found: 281.1397.

*4.28. 3-(4-Fluorobenzyl)-4-imino-3,4-dihydroquinazolin-2-amine (***5ad***)*

Yield 60% (161.6 mg); Rf (EtOAc/CH_3OH; 14:1) 0.30; white solid; m.p. 195–196 °C; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.72 (d, J = 7.8 Hz, 1H), 7.51 (t, J = 7.8 Hz, 1H), 7.32 (t, J = 5.4 Hz, 2H), 7.25 (s, 1H), 7.24 (s, 1H), 7.19 (t, J = 8.4 Hz, 1H), 7.06 (t, J = 8.4 Hz, 2H), 5.45 (s, 2H), 4.64 (s, 2H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ (ppm) 163.2, 161.6, 158.7, 151.4, 145.7, 132.9, 131.2, 128.0, 127.9, 124.8, 123.0, 116.3, 46.3; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{15}H_{14}N_4F$: 269.1202; found: 269.1203.

*4.29. 3-(4-Chlorobenzyl)-4-imino-3,4-dihydroquinazolin-2-amine (***5ae***)*

Yield 55% (157.2 mg); Rf (EtOAc/CH_3OH; 10:1) 0.25; white solid; m.p. 186–187 °C; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.71 (d, J = 7.8 Hz, 1H), 7.51 (t, J = 7.8 Hz, 1H), 7.34 (d, J = 8.4 Hz, 2H), 7.28 (s, 1H), 7.27 (d, J = 9.6 Hz, 2H), 7.24 (d, J = 8.4 Hz, 1H), 7.19 (t, J = 7.8 Hz, 1H), 5.45 (s, 2H), 4.61 (s, 2H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ (ppm) 158.6, 151.4, 145.7, 134.0, 133.8, 132.9, 129.4, 127.6, 124.8, 124.2, 123.0, 116.2, 46.4; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{15}H_{14}N_4Cl$: 285.0907; found: 285.0901.

*4.30. 4-Imino-3-(naphthalen-2-ylmethyl)-3,4-dihydroquinazolin-2-amine (***5af***)*

Yield 66% (198.9 mg); Rf (EtOAc/CH_3OH; 10:1) 0.28; white solid; m.p. 218–219 °C; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 8.06 (d, J = 7.8 Hz, 1H), 7.92 (d, J = 8.4 Hz, 1H), 7.81 (d, J = 8.4 Hz, 1H), 7.61 (t, J = 6.6 Hz, 1H), 7.57 (t, J = 7.2 Hz, 1H), 7.53 (t, J = 8.4 Hz, 1H), 7.41 (t, J = 7.2 Hz, 1H), 7.28 (s, 1H), 7.25 (d, J = 5.4 Hz, 2H), 7.24 (d, J = 7.2 Hz, 1H), 7.20 (t, J = 7.8 Hz, 1H), 5.94 (s, 2H), 4.62 (s, 2H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ (ppm) 161.7, 158.1, 151.6, 149.0, 144.8, 134.0, 133.1, 130.5, 129.3, 129.1, 128.5, 126.7, 126.2, 125.7, 124.3, 123.3, 122.3, 121.9, 44.9; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{19}H_{17}N_{4:}$ 301.1453; found: 301.1453.

*4.31. 3-Benzyl-4-imino-7-methyl-3,4-dihydroquinazolin-2-amine (***5ag***)*

Yield 60% (168.8 mg); Rf (EtOAc/CH_3OH; 12:1) 0.30; white solid; m.p. 189–190 °C; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.60 (d, J = 7.8 Hz, 1H), 7.36 (t, J = 7.8 Hz, 2H), 7.32 (d, J = 7.2 Hz, 2H), 7.30 (s, 1H), 7.29 (s, 1H), 7.03 (s, 1H), 7.00 (d, J = 7.8 Hz, 1H), 5.48 (s, 2H),

4.66 (s, 2H), 2.40 (s, 3H); $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$): δ (ppm) 157.4, 152.2, 144.3, 141.7, 134.7, 129.4, 128.2, 126.2, 125.1, 124.3, 121.8, 112.7, 46.6, 21.6; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{16}H_{17}N_4$: 265.1453; found: 265.1459.

*4.32. 3-Benzyl-7-chloro-4-imino-3,4-dihydroquinazolin-2-amine (***5ah***)*

Yield 65% (185.7 mg); Rf (EtOAc/CH_3OH; 10:1) 0.25; white solid; m.p. 185–186 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.63 (d, J = 8.4 Hz, 1H), 7.39 (s, 1H), 7.37 (d, J = 7.2 Hz, 2H), 7.32–7.31 (m, 3H), 7.21 (d, J = 7.8 Hz, 1H), 7.11 (d, J = 8.4 Hz, 1H), 5.46 (s, 2H), 4.72 (s, 2H); $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$): δ (ppm) 152.3, 147.1, 138.7, 135.1, 129.4, 128.1, 126.1, 125.7, 124.3, 123.2, 114.8, 46.9; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{15}H_{14}N_4Cl$: 285.0907; found: 285.0906.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/catal13111447/s1. Table S1. The crystallographic data of 3aa (CCDC: 2294005); Table S2. The crystallographic data of **5ab** (CCDC: 2294029); spectral copies of ^{1}HNMR, and ^{13}CNMR.

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