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ARTICLE

Metal-Free One-Pot Synthesis of 1,3-Diazaheterocyclic Compounds via I_2-Mediated Oxidative C–N Bond Formation

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A one-pot I_2-mediated annulation reactionof substrates containing diamino groups and aldehydes has been developed via oxidative C–N bond formation. This general and environmentally benign synthetic approach provides a facile access to a variety of 1,3-diazaheterocyclic compounds, including quinazolinones, benzimidazoles, and cyclic amidines.

Introduction

As an eco-friendly reagent, molecular iodine has extensive application in organic synthesis.[1] In particular, I_2-mediated carbon-nitrogen (C–N) bond formation via oxidation of carbon-hydrogen (C–H) and nitrogen-hydrogen (N–H) bonds has received considerable attentions in recent years, and resulted in various new synthetic methods for the preparation of nitrogen-containing compounds.[2] Generally, the reactions were carried out under transition-metal-free conditions, and the C–H bonds in substrates were directly functionalized by NHR groups without preactivation. These features make the synthesis more environmentally friendly and the preparation of substrates more facilitative. Previously, we have reported such an oxidative annulation reaction for pyrazole synthesis.[3] This metal-free one-pot protocol requires no isolation of the less stable condensation products of α,β-unsaturated aldehydes/ketones and hydrazines. Under the I_2-mediated cyclization conditions, the hydrazone intermediates formed in situ were directly transformed into the desired pyrazoles. As a continuous research, in the present work, we further explored this strategy for the synthesis of 1,3-diazaheterocyclic compounds.

1,3-diazaheterocycles, such as quinazolinones, benzimidazoles, and cyclic amidines occur in many natural and synthetic molecules possessing diverse biological activities.[4] For example, Pegamine, isolated from *Peganumharmala*, exhibits cytotoxic activity (Figure 1).[5] Thiabendazole is a fungicide and parasiticide. Clonidine as a α_2 adrenergic agonist is used for the treatment of diseases, such as, high blood pressure, anxiety disorders, and migraine. Manzacidin A is a bioactive marine alkaloid isolated from the Okinawan sponge, *Hymeniacidon* sp.[6] Moreover, cyclic amidines (*e.g.* imidazolines) have also found important applications in organic synthesis as synthetic intermediates, chiral auxiliaries, chiral catalysts, and ligands for asymmetric catalysis.[7] Consequently, a vast number of synthetic methods[4a-4d, 4f, 4h, 8] have been developed for the preparation of these 1,3-diazaheterocycles, respectively. Despite these achievements, the development of simpler and more general protocols that are capable to construct 1,3-diazaheterocyclic frameworks is still highly desirable and will be of great importance to the drug discovery community. Herein, we describe a convenient one-pot methodology for the synthesis of quinazolinones, benzimidazoles, and cyclic amidines via I_2-mediated oxidative C–N bond formation.

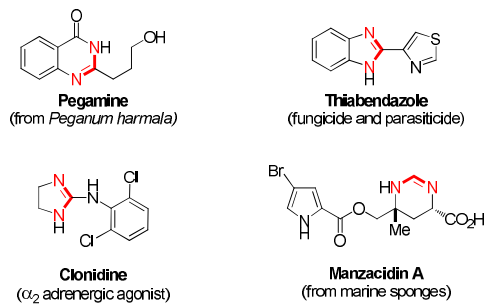

Figure 1. Representing Natural and Synthetic Molecules Containing 1,3-Diaza Moieties

Results and discussion

Initially, we investigated the oxidative cyclization of isolated condensation intermediate **7a**. I_2-mediated oxidation of purified imine **7a** in the presence of base in 1,4-dioxane ga quinazolinone **1a** in moderate yield (Table 1, entry 1). The reaction also worked well with crude **7a**, producing the desired product in even better overall yield (entry 2). Later, we fou that the oxidative cyclization of intermediate **7a** can occur i ethanol in the absence of base (not shown). Based on thi encouraging observation, we continued to optimize the reactio conditions by directly treating a mixture of anthranilamide (**5**

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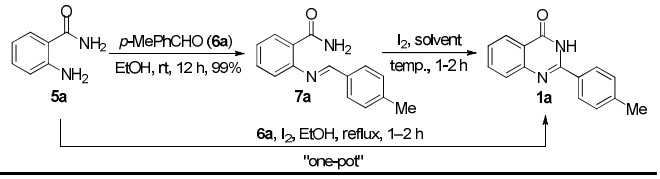
and 4-methylbenzaldehyde (**6a**) in ethanol without pre-condensation of the two substrates. To our delight, the conversion was completed within 1 h and afforded product **1a** in excellent yield (entry 3). Further study demonstrated that 1.1 equivalent of iodine was enough for this oxidative annulation (entry 4). However, substoichiometric amount of the oxidant resulted in decreased yield of quinazolinone **1a** (entry 5). Lowering the reaction temperature slowed down the reaction rate with intermediate **7a** and some unidentified byproducts formed (not shown).

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

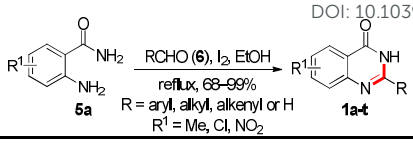


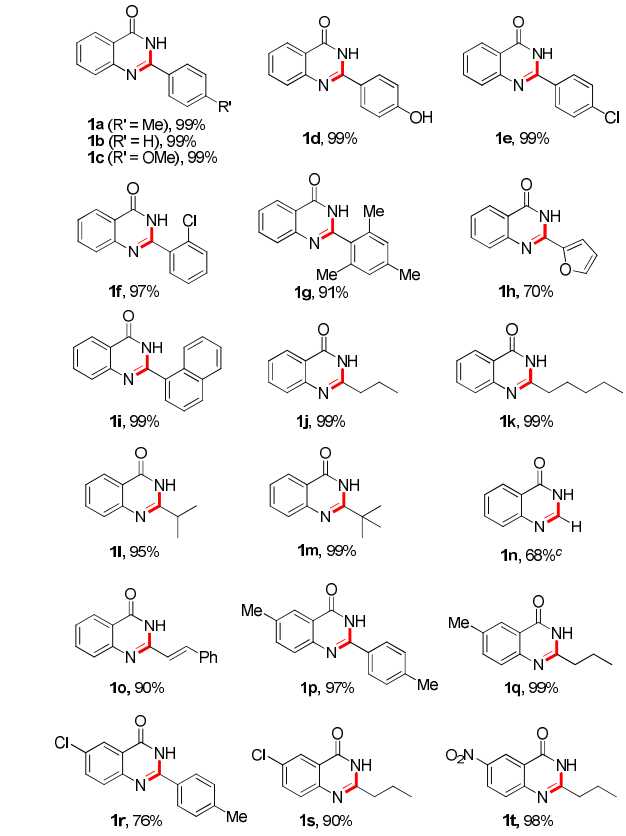
entry	substrates	iodine	solvent	temp.	time	yield[b]
1[c]	**7a**	1.5 equiv.	1,4-dioxane	80 ºC	1 h	63%
2[c]	**7a**[d]	1.5 equiv.	1,4-dioxane	80 ºC	1 h	90%
3	**5a** + **6a**	1.5 equiv.	EtOH	reflux	1 h	99%
4	**5a** + **6a**	1.1 equiv.	EtOH	reflux	1 h	99%
5[e]	**5a** + **6a**	0.9 equiv.	EtOH	reflux	2 h	91%

[a]Optimal reaction conditions (entry 4): **5a** (0.5 mmol), **6a** (0.6 mmol), I_2 (0.55 mmol), EtOH, reflux, 1 h. [b]Isolated yields. [c]The reaction was carried out in the presence of K_2CO_3 (3.2 equiv.). [d]Crude **7a** obtained by evaporation of ethanol was directly dissolved in 1,4-dioxane for the oxidative cyclization. [e]Trace amount of starting material **5a** was left after refluxed for 2 h.

With the optimal reaction conditions in hand (Table 1, entry 4), we began to examine the scope and generality of this synthetic method. Firstly, a variety of substituted aldehydes were subjected to the above one-pot annulation conditions (Table 2). Both aromatic (**6a**–**i**) and aliphatic aldehydes (**6j**–**m**) were smoothly converted to 2-substituted (R) quinazolinones **1a**–**m** in good to excellent yields via the reaction with anthranilamide **5a**. It is worth to mention that the good functional group tolerance allows the preparation of the product bearing a phenolic hydroxyl group (**1d**). The reaction of paraformaldehyde (**6n**) and cinnamaldehyde (**6o**) with **5a** produced quinazolinones **1n** and **1o** in 68% and 90% yields, respectively. In addition, cyclization of anthranilamides bearing electron-donating (*e.g.* Me) and electron-withdrawing groups (*e.g.* Cl and NO_2) on the benzene ring with the corresponding aldehydes also afforded the desired products (**1p**–**t**).

Table 2. One-Pot Synthesis of 2-Substituted Quinazolinones **1**[a,b]

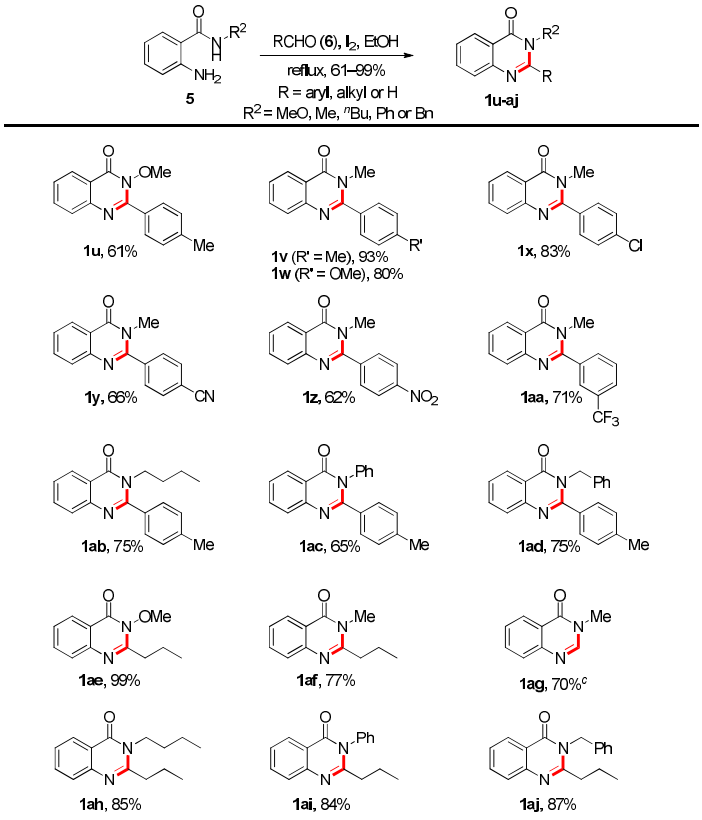




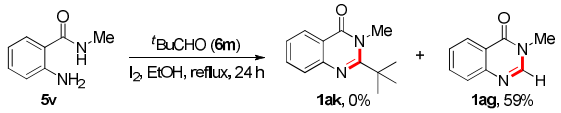
[a]Optimal reaction conditions: **5a** (0.5 mmol), **6** (0.6 mmol), I_2 (0.55 mmol), EtOH, reflux, 1–6 [b]Isolated yields. [c]Paraformaldehyde (**6n**) was used.

In light of these encouraging results, we further examine the substrate scope by incorporating substitutents (R^2), such as methoxy, methyl, *n*-butyl, phenyl, and benzyl groups, to the amide groups of anthranilamides (Table 3). Under the optimal one-pot annulation conditions, all these *N*′-substituted anthranilamides were transformed into the expected 3-substituted quinazolinones **1u**–**aj** by reacting with aromatic or aliphatic aldehydes. Steric effect of the R^2 group was observed in the reactions involving pivalaldehyde (**6m**). Oxidative annulation of anthranilamide **5a** (R^2 = H) with **6m** formed 2-*tert*-butyl quinazolinone **1m** in nearly quantitative yield (Table 2). However, when a methyl group was introduced to the R^2 position, the reaction rate became very slow, and resulted in no expected 2-*tert*-butyl quinazolinone **1ak** but only the de-*tert*-butyl product **1ag** (Scheme 1). This de-*tert*-butylation process might be caused by hydrogen iodide (HI) formed during the reaction.[3]

Table 3. One-Pot Synthesis of 3-Substituted Quinazolinones **1**[a,b]

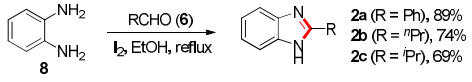


[a]Optimal reaction conditions: **5** (0.5 mmol), **6** (0.6 mmol), I_2 (0.55 mmol), EtOH, reflux, 1–6 h. [b]Isolated yields. [c]Paraformaldehyde (**6n**) was used.

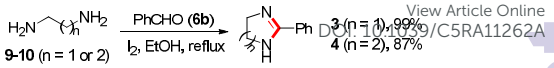


Scheme 1. Formation of the De-*tert*-butyl Product **1ag** in the Reaction of *N'*-Methyl Anthranilamide (**5v**) and Pivalaldehyde (**6m**)

Furthermore, this synthetic strategy can also be utilized to prepare other 1,3-diazaheterocycles, such as benzimidazoles and cyclic amidines. Replacement of anthranilamides with 1,2-diaminobenzene (**8**) afforded benzimidazole derivatives **2a**–**c** (Scheme 2) in satisfactory yields. Oxidative annulation of benzaldehyde (**6b**) with diamines **9** or **10** produced imidazoline **3** or tetrahydropyrimidine **4**, respectively (Scheme 3).



Scheme 2. Synthesis of Benzimidazoles **2**



Scheme 3. Synthesis of Cyclic Amidines **3** and **4**

Experimental

4.1. General Information. ^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz (100 MHz for ^{13}C NMR) spectrometer. Chemical shift values are given in ppm (parts per million) with tetramethylsilane (TMS) as an internal standard. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; sext, sextet; m, multiplet; dd, doublet of doublets; dt, doublet of triplets. The coupling constants (*J*) are reported in Hertz (Hz). Melting points were determined on a micro melting point apparatus without corrections. Flash column chromatography was performed over silica gel 200-300 mesh. High-resolution mass spectra (HRMS-ESI) were obtained on a Q-TOF mass spectrometer.

4.2. Synthesis of Quinazolinones 1. *General Procedure A:* A stirred mixture of anthranilamide **5** (0.5 mmol) and aldehyde **6** (0.6 mmol) in ethanol (5 mL) was treated with iodine (0.55 mmol), and then heated to reflux until the starting material **5** disappeared (monitored by TLC, 1−6 h). After cooling to room temperature, the reaction mixture was quenched with 5% $Na_2S_2O_3$ (1 mL), and concentrated to remove most of the solvent. The resulting residue was redissolved in ethyl acetate (15 mL), followed by the addition of brine (15 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate (15 mL × 2). The combined organic layer was dried over anhydrous Na_2SO_4, concentrated, and purified through silica gel column chromatography using a mixture of ethyl acetate (EtOAc) and petroleum ether (PE) as eluent to afford the corresponding quinazolinone **1**.

*2-Phenylquinazolin-4(3H)-one (**1a**).* Yield: 110 mg, 99%; white solid, mp 238-240 °C (lit.[9] mp 241-242 °C); R_f = 0.25 (EtOAc:PE = 25:75); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.55 (br, s, 1H), 8.23-8.15 (m, 3H), 7.88-7.82 (m, 1H), 7.78-7.74 (m, 1H), 7.63-7.51 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.6, 152.7, 149.2, 135.0, 133.1, 131.8, 129.0, 128.2, 127.9, 127.0, 126.3, 121.4; HRMS (m/z) [M + H]$^+$ calcd for $C_{14}H_{11}N_2O$ 223.0866, found 223.0866.

*2-(p-Tolyl)quinazolin-4(3H)-one (**1b**).* Yield: 117 mg, 99%; white solid, mp 240-242 °C (lit.[10] mp 240-242 °C); R_f = 0.27 (EtOAc:PE = 25:75); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.47 (br, s, 1H), 8.17 (dd, *J* = 8.0, 1.2 Hz, 1H), 8.12 (d, *J* = 8.0 Hz, 2H), 7.86-7.82 (m, 1H), 7.75-7.73 (m, 1H), 7.55-7.49 (m, 1H), 7.36 (d, *J* = 8.4 Hz, 2H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.7, 152.6, 149.2, 141.8, 134.9, 130.3, 129.6, 128.1, 127.8, 126.8, 126.2, 121.3, 21.4; HRMS (m/z) [M + H]$^+$ calcd for $C_{15}H_{13}N_2O$ 237.1022, found 237.1022.

*2-(4-Methoxyphenyl)quinazolin-4(3H)-one (**1c**).* Yield: 125 mg, 99%; white solid, mp 246-247 °C (lit.[11] mp 247-248 °C); R_f = 0.36 (EtOAc:PE = 33:67); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.42 (br, s, 1H), 8.24-8.18 (m, 2H), 8.15 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.86-7.79 (m, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.52-7.46 (m, 1H), 7.13-7.06 (m, 2H), 3.86 (s, 3H); ^{13}C NMR (100 MHz,

DMSO-d_6) δ 162.7, 162.3, 152.3, 149.4, 134.9, 129.9, 127.7, 126.5, 126.2, 125.2, 121.1, 114.4, 55.9; HRMS (m/z) [M + H]$^+$calcd for $C_{15}H_{13}N_2O_2$ 253.0972, found 253.0977.

2-(4-Hydroxyphenyl)quinazolin-4(3H)-one ***(1d)***. Yield: 118 mg, 99%; white solid; mp > 300 °C (lit.[12] mp > 300 °C), R_f = 0.22 (EtOAc:PE = 60:40); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.34 (br, s, 1H), 10.22 (s, 1H), 8.14 (dd, J = 8.0, 1.2 Hz, 1H), 8.13-8.09 (m, 2H), 7.84-7.79 (m, 1H), 7.70 (d, J = 8.0 Hz, 1H), 7.50-7.46 (m, 1H), 6.94-6.91 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.7, 161.0, 152.5, 149.5, 134.9, 130.0, 127.6, 126.3, 126.2, 123.6, 121.0, 115.8; HRMS (m/z) [M + Na]$^+$calcd for $C_{14}H_{10}N_2O_2Na$ 261.0634, found 261.0632.

2-(4-Chlorophenyl)quinazolin-4(3H)-one ***(1e)***. Yield: 127 mg, 99%; white solid, mp > 300 °C (lit.[11] mp > 300 °C); R_f = 0.30 (EtOAc:PE = 25:75); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.61 (br, s, 1H), 8.23-8.19 (m, 2H), 8.17 (dd, J = 8.0, 1.2 Hz, 1H), 7.87-7.83 (m, 1H), 7.76-7.74 (m, 1H), 7.65-7.61 (m, 2H) 7.56-7.52 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.6, 151.7, 149.0, 136.7, 135.1, 132.0, 130.0, 129.1, 127.9, 127.2, 126.3, 121.4; HRMS (m/z) [M + H]$^+$calcd for $C_{14}H_{10}ClN_2O$ 257.0476, found 257.0475.

2-(2-Chlorophenyl)quinazolin-4(3H)-one ***(1f)***.[13] Yield: 125 mg, 97%; white solid, mp 168-170 °C; R_f = 0.20 (EtOAc:PE = 25:75); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.69 (br, s, 1H), 8.26 (d, J = 7.6 Hz, 1H), 7.86-7.78 (m, 3H), 7.55-7.42 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 151.1, 148.9, 134.9, 132.7, 132.0, 131.9, 131.4, 130.5, 127.9, 127.4, 127.3, 126.5, 121.0; HRMS (m/z) [M + H]$^+$ calcd for $C_{14}H_{10}ClN_2O$ 257.0476, found 257.0476.

2-Mesitylquinazolin-4(3H)-one ***(1g)***. Yield: 120 mg, 91%; white solid, mp 191-193 °C; R_f = 0.25 (EtOAc:PE = 25:75); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.62 (br, s, 1H), 8.27 (d, J = 8.4 Hz, 1H), 7.84-7.75 (m, 2H), 7.56-7.49 (m, 1H), 6.95 (s, 2H), 2.33 (s, 3H), 2.23 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 153.5, 149.0, 139.8, 135.9, 134.8, 131.1, 128.7, 127.8, 127.0, 126.4, 120.9, 21.2, 19.4; HRMS (m/z) [M + H]$^+$ calcd for $C_{17}H_{17}N_2O$ 265.1335, found 265.1324.

2-(Furan-2-yl)quinazolin-4(3H)-one ***(1h)***. Yield: 74 mg, 70%; white solid, mp 221-222 °C (lit.[11] mp 219-220 °C); R_f = 0.20 (EtOAc:PE = 33:67); ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.78 (br, s, 1H), 8.31 (ddd, J = 8.0, 1.6, 0.8 Hz, 1H), 7.85-7.73 (m, 2H), 7.69-7.67 (m, 2H), 7.50-7.46 (m, 1H), 6.66 (dd, J = 3.6, 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2, 149.3, 146.2, 145.7, 143.6, 135.0, 127.7, 126.7, 126.4, 120.9, 114.2, 112.7; HRMS (m/z) [M + H]$^+$ calcd for $C_{12}H_9N_2O_2$ 213.0659, found 213.0657.

2-(Naphthalen-1-yl)quinazolin-4(3H)-one ***(1i)***. Yield: 135 mg, 99%; white solid, mp 280-281 °C (lit.[11] mp 278-281 °C); R_f = 0.20 (EtOAc:PE = 25:75); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.69 (br, s, 1H), 8.23 (d, J = 7.6 Hz, 1H), 8.19-8.17 (m, 1H), 8.13 (d, J = 8.0 Hz, 1H), 8.06 (dd, J = 6.0, 2.0 Hz, 1H), 7.91-7.84 (m, 1H), 7.81 (d, J = 6.8 Hz, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.66 (t, J = 8.0 Hz, 1H), 7.63-7.57 (m, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.3, 154.1, 149.1, 134.9, 133.5, 132.1, 130.8, 130.7, 128.8, 128.1, 127.9, 127.5, 127.2, 126.8, 126.3, 125.6, 125.5, 121.6; HRMS (m/z) [M + H]$^+$ calcd for $C_{18}H_{13}N_2O$ 273.1022, found 273.1029.

2-Propylquinazolin-4(3H)-one ***(1j)***. Yield: 93 mg, 99%; white solid, mp 202-203 °C (lit.[14] mp 200-202 °C); R_f = 0.2 (EtOAc:PE = 33:67); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.17 (br, s, 1H), 8.09 (dd, J = 8.0, 1.2 Hz, 1H), 7.80-7.75 (m, 1H), 7.61-7.59 (m, 1H), 7.48-7.44 (m, 1H), 2.59 (t, J = 7.2 Hz, 2H), 1.76 (sext, J = 7.6 Hz, 2H), 0.95 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.2, 157.7, 149.3, 134.7, 127.2, 126.3, 126.1, 121.2, 36.8, 20.6, 13.9; HRMS (m/z) [M + H]$^+$ calcd for $C_{11}H_{13}N_2O$ 189.1022, found 189.1026.

2-Pentylquinazolin-4(3H)-one ***(1k)***.[15] Yield: 107 mg, 99%; white solid, mp 76-77 °C; R_f = 0.25 (EtOAc:PE = 25:75); ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.15 (br, s, 1H), 8.29 (dd, J = 7.6, 1.2 Hz, 1H), 7.80-7.74 (m, 1H), 7.72-7.70 (m, 1H), 7.49-7.45 (m, 1H), 2.81 (t, J = 7.6 Hz, 2H), 1.91 (quint, J = 7.6 Hz, 2H), 1.48-1.38 (m, 4H), 0.93 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 157.1, 149.5, 134.7, 127.2, 126.2, 126.1, 120.4, 35.9, 31.4, 27.2, 22.3, 13.9; HRMS (m/z) [M + H]$^+$ calcd for $C_{13}H_{17}N_2O$ 217.1335, found 217.1340.

2-Isopropylquinazolin-4(3H)-one ***(1l)***. Yield: 89 mg, 95%; white solid, mp 225-226 °C (lit.[14] mp 225-228 °C); R_f = 0.25 (EtOAc:PE = 25:75); ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.75 (br, s, 1H), 8.31 (dd, J = 8.0, 1.2 Hz, 1H), 7.80-7.70 (m, 2H), 7.49-7.45 (m, 1H), 3.07 (heptet, J = 6.8 Hz, 1H), 1.46 (d, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 160.9, 149.4, 134.6, 127.3, 126.3, 126.2, 120.7, 34.9, 20.4; HRMS (m/z) [M + H]$^+$ calcd for $C_{11}H_{13}N_2O$ 189.1022, found 189.1018.

2-(tert-Butyl)quinazolin-4(3H)-one ***(1m)***. Yield: 100 mg, 99%; white solid, mp 181-183 °C (lit.[9] mp 184-186 °C); R_f = 0.47 (EtOAc:PE = 25:75); ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.42 (br, s, 1H), 8.29 (dd, J = 8.0, 0.4 Hz, 1H), 7.77-7.72 (m, 2H), 7.48-7.44 (m, 1H), 1.51 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 162.2, 149.2, 134.4, 127.7, 126.2, 126.1, 120.6, 37.5, 28.3; HRMS (m/z) [M + Na]$^+$ calcd for $C_{12}H_{14}N_2ONa$ 225.0998, found 225.0999.

Quinazolin-4(3H)-one ***(1n)***. Yield: 50 mg, 68%; white solid, mp 208-209 °C (lit.[16] mp 212-214 °C); R_f = 0.25 (EtOAc:PE = 67:33); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.27 (br, s, 1H), 8.21-8.05 (m, 2H), 7.88-7.78 (m, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.54 (t, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.1, 149.2, 145.8, 134.7, 127.6, 127.2, 126.2, 123.0; HRMS (m/z) [M + H]$^+$ calcd for $C_8H_7N_2O$ 147.0553, found 147.0555.

(E)-2-Styrylquinazolin-4(3H)-one ***(1o)***.[17] Yield: 112 mg, 90%; white solid, mp 247-249 °C; R_f = 0.45 (EtOAc:PE = 33:67); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.34 (br, s, 1H), 8.13 (d, J = 8.0 Hz, 1H), 7.97 (d, J = 16.0 Hz, 1H), 7.85-7.78 (m, 1H), 7.73-7.63 (m, 3H), 7.54-7.38 (m, 4H), 7.02 (d, J = 16.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.1, 151.8, 149.4, 138.7, 135.4, 134.9, 130.2, 129.5, 128.1, 127.6, 126.7, 126.3, 121.5; HRMS (m/z) [M + H]$^+$ calcd for $C_{16}H_{13}N_2O$ 249.1022, found 249.1025.

6-methyl-2-(p-tolyl)quinazolin-4(3H)-one ***(1p)***.[18] Yield: 121 mg, 97%; white solid, mp 279-280 °C; R_f = 0.39 (EA/PE 25:75); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.39 (br, s, 1H), 8.09 (d, J = 8.4 Hz, 2H), 7.95 (s, 1H), 7.67-7.62 (m, 2H), 7.35 (d, J = 8.0 Hz, 2H), 2.46 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.7, 151.9, 147.3, 141.7, 136.5, 136.3, 130.4,

129.6, 128.0, 127.7, 125.7, 121.1, 21.4, 21.3; HRMS (m/z) [M + H]$^+$ calcd for $C_{16}H_{15}N_2O$ 251.1179, found 251.1185.

6-methyl-2-propylquinazolin-4(3H)-one ***(1q)***. Yield: 100 mg, 99%; white solid, mp 244-246 °C (lit.[19] mp 244.3-244.8 °C); R_f = 0.30 (EA/PE 25:75); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.09 (br, s, 1H), 7.88 (s, 1H), 7.59 (d, J = 8.0 Hz, 1H), 7.50 (d, J = 8.4 Hz, 1H), 2.57 (t, J = 7.6 Hz, 2H), 2.43 (s, 3H), 1.74 (sext, J = 7.6 Hz, 2H), 0.94 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.2, 156.8, 147.4, 136.0, 135.9, 127.1, 125.5, 121.0, 36.7, 21.2, 20.7, 14.0; HRMS (m/z) [M + H]$^+$ calcd for $C_{12}H_{15}N_2O$ 203.1179, found 203.1179.

6-Chloro-2-(p-tolyl)quinazolin-4(3H)-one ***(1r)***. Yield: 103 mg, 76%; white solid, mp > 300 °C (lit.[11] mp > 300 °C); R_f = 0.30 (EtOAc:PE = 25:75); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.65 (br, s, 1H), 8.10-8.08 (m, 3H), 7.86 (dd, J = 8.4, 2.4 Hz, 1H), 7.75 (d, J = 8.8 Hz, 1H), 7.37 (d, J = 8.0 Hz, 2H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.8, 153.2, 148.1, 142.2, 135.2, 131.0, 130.14, 130.08, 129.7, 128.2, 125.3, 122.6, 21.5; HRMS (m/z) [M + H]$^+$ calcd for $C_{15}H_{12}ClN_2O$ 271.0633, found 271.0637.

6-Chloro-2-propylquinazolin-4(3H)-one ***(1s)***. Yield: 100 mg, 90%; white solid, mp 246-248 °C (lit.[20] mp 248-250 °C); R_f = 0.40 (EtOAc:PE = 25:75); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.35 (br, s, 1H), 8.01 (d, J = 2.0 Hz, 1H), 7.79 (dd, J = 8.8, 2.0 Hz, 1H), 7.62 (d, J = 8.8 Hz, 1H), 2.58 (t, J = 7.6 Hz, 2H), 1.74 (sext, J = 7.6 Hz, 2H), 0.94 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.2, 158.4, 148.1, 134.8, 130.5, 129.5, 125.1, 122.5, 36.8, 20.5, 13.9; HRMS (m/z) [M + H]$^+$ calcd for $C_{11}H_{12}ClN_2O$ 223.0633, found 223.0647.

6-Nitro-2-propylquinazolin-4(3H)-one ***(1t)***. Yield: 114 mg, 98%; light yellow solid, mp 264-266 °C (lit.[20] mp 264-266 °C); R_f = 0.20 (EtOAc:PE = 25:75); ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.66 (br, s, 1H), 8.77 (d, J = 2.8 Hz, 1H), 8.50 (dd, J = 8.8, 2.8 Hz, 1H), 7.78 (d, J = 9.2 Hz, 1H), 2.64 (t, J = 7.2 Hz, 2H), 1.77 (sext, J = 7.6 Hz, 2H), 0.95 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.9, 161.5, 153.6, 144.8, 129.0, 128.7, 122.3, 121.2, 37.0, 20.5, 13.9; HRMS (m/z) [M + H]$^+$ calcd for $C_{11}H_{12}N_3O_3$ 234.0873, found 234.0874.

3-Methoxy-2-(p-tolyl)quinazolin-4(3H)-one ***(1u)***. Yield: 81 mg, 61%; white solid, mp 157-158 °C; R_f = 0.30 (EtOAc:PE = 16:84); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (dt, J = 8.0, 0.8 Hz, 1H), 7.84-7.81 (m, 2H), 7.78-7.76 (m, 2H), 7.53-7.47 (m, 1H), 7.32 (d, J = 8.0 Hz, 2H), 3.77 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.1, 153.2, 146.6, 141.2, 134.4, 129.4, 129.1, 129.0, 127.9, 126.8, 126.7, 122.5, 63.9, 21.5; HRMS (m/z) [M + Na]$^+$ calcd for $C_{16}H_{14}N_2O_2Na$ 289.0947, found 289.0933.

3-Methyl-2-(p-tolyl)quinazolin-4(3H)-one ***(1v)***. Yield: 116 mg, 93%; white solid, mp 137-139 °C (lit.[21] mp 138 °C);R_f = 0.30 (EtOAc:PE = 16:84); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34-8.30 (m, 1H), 7.78-7.68 (m, 2H), 7.53-7.41 (m, 3H), 7.32 (d, J = 8.0 Hz, 2H), 3.50 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 156.2, 147.3, 140.2, 134.2, 132.5, 129.4, 127.9, 127.4, 126.8, 126.6, 120.4, 34.3, 21.4; HRMS (m/z) [M + H]$^+$ calcd for $C_{16}H_{15}N_2O$ 251.1179, found 251.1179.

2-(4-Methoxyphenyl)-3-methylquinazolin-4(3H)-one ***(1w)***. Yield: 107 mg, 80%; white solid, mp 142-143 °C (lit.[21] mp 142 °C); R_f = 0.47 (EtOAc:PE = 25:75); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34-8.28 (m, 1H), 7.79-7.70 (m, 2H), 7.54 (dt, J = 9.6, 2.8 Hz, 2H), 7.51-7.47 (m, 1H), 7.04 (dt, J = 9.6, 2.8 Hz, 2H), 3.88 (s, 3H), 3.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.9, 160.9, 156.0, 147.4, 134.2, 129.7, 127.7, 127.4, 126.8, 126.6, 120.3, 114.2, 55.5, 34.5; HRMS (m/z) [M + H]$^+$ calcd for $C_{16}H_{15}N_2O_2$ 267.1128, found 267.1124.

2-(4-Chlorophenyl)-3-methylquinazolin-4(3H)-one ***(1x)***.[21] Yield: 112 mg, 83%; white solid, mp 166-168 °C; R_f = 0.25 (EtOAc:PE = 16:84); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (dd, J = 8.0, 0.8 Hz, 1H), 7.79-7.71 (m, 2H), 7.56-7.48 (m, 5H), 3.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6, 155.0, 147.1, 136.3, 134.4, 133.7, 129.5, 129.1, 127.5, 127.2, 126.7, 120.5, 34.2; HRMS (m/z) [M + H]$^+$ calcd for $C_{15}H_{12}ClN_2O$ 271.0633, found 271.0632.

4-(3-Methyl-4-oxo-3,4-dihydroquinazolin-2-yl)benzonitrile ***(1y)***. Yield: 86 mg, 66%; white solid, mp 216-218 °C; R_f = 0.4[illegible] (EtOAc:PE = 25:75); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (dd, J = 8.0, 1.2 Hz, 1H), 7.88-7.82 (m, 2H), 7.82-7.76 (m, 1H), 7.76-7.69 (m, 3H), 7.58-7.52 (m, 1H), 3.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 154.1, 147.0, 139.4, 134.6, 132.7, 129.0, 127.62, 127.56, 126.8, 120.6, 117.9, 114.0, 34.1; HRMS (m/z) [M + Na]$^+$ calcd for $C_{16}H_{11}N_3ONa$ 284.0794, found 284.0791.

3-Methyl-2-(4-nitrophenyl)quinazolin-4(3H)-one ***(1z)***. Yield: 87 mg, 62%; white solid, mp 191-192 °C; R_f = 0.30 (EtOAc:PE = 25:75); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43-8.40 (m, 2H), 8.35 (dd, J = 8.0, 0.8 Hz, 1H), 7.82-7.78 (m, 3H), 7.74-7.72 (m, 1H) 7.58-7.54 (m, 1H), 3.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 153.8, 148.6, 146.9, 141.1, 134.6, 129.4, 127.7, 127.6, 126.8, 124.1, 120.6, 34.1; HRMS (m/z) [M + Na]$^+$ calcd for $C_{15}H_{11}N_3O_3Na$ 304.0693, found 304.0687.

3-Methyl-2-(3-(trifluoromethyl)phenyl)quinazolin-4(3H)-one ***(1aa)***. Yield: 108 mg, 71%; white solid, mp 126-127 °C; R_f = 0.25 (EtOAc:PE = 16:84); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (dd, J = 8.0, 0.8 Hz, 1H), 7.89 (s, 1H), 7.82-7.77 (m, 3H), 7.75-7.73 (m, 1H), 7.69 (t, J = 7.6 Hz, 1H), 7.56-7.52 (m, 1H), 3.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 154.5, 147.0, 136.1, 134.5, 131.5 (q, J_{C-F} = 32.8 Hz), 131.4, 129.5, 127.5, 127.4, 126.8 (q, J_{C-F} = 3.7 Hz), 126.7, 125.2 (q, J_{C-F} = 3.9 Hz), 123.5 (d, J_{C-F} = 271.1 Hz), 120.6, 34.2; HRMS (m/z) [M + Na]$^+$ calcd for $C_{16}H_{11}F_3N_2ONa$ 327.0716, found 327.0706.

3-Butyl-2-(p-tolyl)quinazolin-4(3H)-one ***(1ab)***. Yield: 110 mg, 75%; white solid, mp 78-79 °C; R_f = 0.45 (EtOAc:PE = 16:84); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37-8.28 (m, 1H), 7.79-7.69 (m, 2H), 7.53-7.45 (m, 1H), 7.45-7.38 (m, 2H), 7.31 (d, J = 8.0 Hz, 2H), 4.00 (t, J = 8.0 Hz, 2H), 2.44 (s, 3H), 1.64-1.54 (m, 2H), 1.18 (sext, J = 7.6 Hz, 2H), 0.78 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 156.4, 147.2, 139.8, 134.2, 132.7, 129.3, 127.7, 127.4, 126.8, 126.7, 120.8, 45.7, 30.7, 21.4, 19.9, 13.4; HRMS (m/z) [M + H]$^+$ calcd for $C_{19}H_{21}N_2O$ 293.1648, found 293.1648.

3-Phenyl-2-(p-tolyl)quinazolin-4(3H)-one ***(1ac)***. Yield: 102 mg, 65%; white solid, mp 174-176 °C (lit.[22] mp 178 °C); R_f = 0.[illegible]5 (EtOAc:PE = 16:84); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, J = 8.0 Hz, 1H), 7.83-7.77 (m, 2H), 7.54-7.50 (m, 1H), 7.35-7.[illegible]8 (m, 3H), 7.22 (d, J = 8.0 Hz, 2H), 7.17-7.15 (m, 2H), 7.01 (d, J = 8.0 Hz, 2H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ

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162.4, 155.2, 147.6, 139.4, 137.8, 134.6, 132.6, 129.1, 128.95, 128.92, 128.6, 128.3, 127.7, 127.15, 127.08, 120.8, 21.3; HRMS (m/z) $[M + Na]^+$ calcd for $C_{21}H_{16}N_2ONa$ 335.1145, found 335.1155.

*3-Benzyl-2-(p-tolyl)quinazolin-4(3H)-one (**1ad**)*. Yield: 123 mg, 75%; white solid, mp 120-121 °C; R_f = 0.30 (EtOAc:PE = 16:84); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, J = 7.6 Hz, 1H), 7.81-7.71 (m, 2H), 7.55-7.47 (m, 1H), 7.27-7.18 (m, 7H), 7.00-6.92 (m, 2H), 5.28 (s, 2H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 156.5, 147.3, 140.0, 136.7, 134.4, 132.4, 129.2, 128.5, 127.9, 127.5, 127.3, 127.02, 126.98, 126.89, 120.8, 48.9, 21.4; HRMS (m/z) $[M + Na]^+$ calcd for $C_{22}H_{18}N_2ONa$ 349.1311, found 349.1304.

*3-Methoxy-2-propylquinazolin-4(3H)-one (**1ae**)*. Yield: 108 mg, 99%; white solid, mp 50-51 °C; R_f = 0.40 (EtOAc:PE = 16:84); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, J = 8.0 Hz, 1H), 7.75-7.71 (m, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.45 (t, J = 8.0 Hz, 1H), 4.12 (s, 3H), 2.86 (t, J = 8.0 Hz, 2H), 1.90 (sext, J = 7.6 Hz, 2H), 1.08 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.9, 156.1, 146.4, 134.2, 127.2, 126.5, 126.3, 122.4, 64.3, 34.5, 20.1, 13.9; HRMS (m/z) $[M + Na]^+$ calcd for $C_{12}H_{14}N_2O_2Na$ 241.0947, found 241.0934.

*3-Methyl-2-propylquinazolin-4(3H)-one (**1af**)*. Yield: 78 mg, 77%; white solid, mp 76-77 °C (lit.[23] mp 76-77 °C); R_f = 0.20 (EtOAc:PE = 16:84); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (dd, J = 8.0, 1.2 Hz, 1H), 7.73-7.68 (m, 1H), 7.65-7.61 (m, 1H), 7.45-7.40 (m, 1H), 3.63 (s, 3H), 2.81 (t, J = 7.6 Hz, 2H), 1.88 (sext, J = 7.6 Hz, 2H), 1.10 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 156.9, 147.2, 134.0, 126.8, 126.7, 126.2, 120.2, 37.6, 30.5, 20.3, 13.9; HRMS (m/z) $[M + Na]^+$ calcd for $C_{12}H_{14}N_2ONa$ 225.0998, found 225.0982.

*3-Methylquinazolin-4(3H)-one (**1ag**)*. Yields: 56 mg, 70%, from paraformaldehyde; or 49 mg, 59%, from pivalaldehyde (2 equiv.); white solid, mp 96-98 °C (lit.[24] mp 98-100 °C); R_f = 0.37 (CH_3OH:CH_2Cl_2 = 2:98); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, J = 8.0 Hz, 1H), 8.05 (s, 1H), 7.77-7.69 (m, 2H), 7.51 (t, J = 8.0 Hz, 1H), 3.60 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5, 148.2, 146.7, 134.1, 127.4, 127.2, 126.5, 121.9, 34.0; HRMS (m/z) $[M + Na]^+$ calcd for $C_9H_8N_2ONa$ 183.0529, found 183.0535.

*3-Butyl-2-propylquinazolin-4(3H)-one (**1ah**)*. Yield: 104 mg, 85%; colorless oil; R_f = 0.41 (EtOAc:PE = 15:85); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (dd, J = 8.0, 0.8 Hz, 1H), 7.73-7.67 (m, 1H), 7.64-7.60 (m, 1H), 7.45-7.39 (m, 1H), 4.09 (t, J = 8.0 Hz, 2H), 2.80 (t, J = 8.0 Hz, 2H), 1.89 (sext, J = 7.6 Hz, 2H), 1.76-1.68 (m, 2H), 1.47 (sext, J = 7.6 Hz, 2H), 1.10 (t, J = 7.6 Hz, 3H), 1.00 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 156.8, 147.3, 133.9, 126.8, 126.6, 126.2, 120.5, 43.6, 37.0, 31.0, 21.0, 20.3, 13.9, 13.7; HRMS (m/z) $[M + Na]^+$ calcd for $C_{15}H_{20}N_2ONa$ 267.1468, found 267.1468.

*3-Phenyl-2-propylquinazolin-4(3H)-one (**1ai**)*. Yield: 111 mg, 84%; white solid, mp 117-120 °C (lit.[22] mp 120-121 °C);R_f = 0.30 (EtOAc:PE = 16:84); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (dd, J = 8.0, 1.2 Hz, 1H), 7.79-7.74 (m, 1H), 7.73-7.68 (m, 1H), 7.60-7.48 (m, 3H), 7.48-7.42 (m, 1H), 7.29-7.23 (m, 2H), 2.40 (t, J = 7.6 Hz, 2H), 1.72 (sext, J = 7.6 Hz, 2H), 0.87 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 156.8, 147.5, 137.4, 134.4, 129.8, 129.2, 128.3, 127.00, 126.97, 126.5, 120.7, 37.7, 20.5, 13.7; HRMS (m/z) $[M + Na]^+$ calcd for $C_{17}H_{16}N_2ONa$ 287.1155, found 287.1154.

*3-Benzyl-2-propylquinazolin-4(3H)-one (**1aj**)*. Yield: 121 mg, 87%; white solid, mp 87-89 °C; R_f = 0.35 (EtOAc:PE = 16:84); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (dd, J = 7.6, 0.8 Hz, 1H), 7.77-7.71 (m, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.47-7.44 (m, 1H), 7.35-7.23 (m, 3H), 7.18 (d, J = 7.2 Hz, 2H), 5.42 (s, 2H), 2.72 (t, J = 7.6 Hz, 2H), 1.86-1.74 (m, 2H), 0.99 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6, 157.1, 147.4, 136.2, 134.3, 128.9, 127.6, 127.03, 126.95, 126.4, 126.3, 120.3, 46.4, 37.0, 20.7, 13.8; HRMS (m/z) $[M + Na]^+$ calcd for $C_{18}H_{18}N_2ONa$ 301.1311, found 301.1297.

4.3. Synthesis of Benzimidazoles 2. *General Procedure B:* A stirred mixture of 1,2-diaminobenzene (**8**, 0.5 mmol) and aldehyde **6** (0.6 mmol) in ethanol (5 mL) was refluxed for 1 h. The reaction mixture was cooled slightly, followed by the treatment with iodine (0.55 mmol), and then heated to reflux for another 1−2 h. After cooling to room temperature, it was quenched with 5% $Na_2S_2O_3$ (1 mL), concentrated, and directly purified through silica gel column chromatography using a mixture of EtOAc and PE as eluent to afford the corresponding benzimidazole **2**.

*2-Phenyl-1H-benzo[d]imidazole (**2a**)*. Yield: 86 mg, 89%; white solid, mp 282-284 °C (lit.[25] mp 280-282 °C); R_f = 0.27 (EtOAc:PE = 80:20); ^{1}H NMR (400 MHz, CD_3OD) δ 8.08-8.05 (m, 2H), 7.61-7.57 (m, 2H), 7.52-7.44 (m, 3H), 7.25-7.21 (m, 2H); ^{13}C NMR (100 MHz, CD_3OD) δ 151.9, 129.9, 129.6, 128.7, 126.4, 122.5, 114.4; HRMS (m/z) $[M + H]^+$ calcd for $C_{13}H_{11}N_2$ 195.0917, found 195.0913.

*2-Propyl-1H-benzo[d]imidazole (**2b**)*. Yield: 59 mg, 74%; white solid, mp 151-153 °C (lit.[26] mp 153-154 °C); R_f = 0.22 (EtOAc:PE = 25:75); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.97 (br, 1H), 7.60-7.51 (m, 2H), 7.24-7.18 (m, 2H), 2.95 (t, J = 7.2 Hz, 2H), 1.90 (sext, J = 7.6 Hz, 2H), 0.98 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.4, 138.5, 122.1, 114.6, 31.2, 21.7, 13.8; HRMS (m/z) $[M + H]^+$ calcd for $C_{10}H_{13}N_2$ 161.1073, found 161.1071.

*2-Isopropyl-1H-benzo[d]imidazole (**2c**)*.[27] Yield: 55 mg, 69%; white solid, mp 183-185 °C; R_f = 0.20 (EtOAc:PE = 34:66);^{1}H NMR (400 MHz, DMSO-d_6) δ 7.50-7.44 (m, 2H), 7.15-7.08 (m, 2H), 3.15 (hept, J = 6.8 Hz, 1H), 1.35 (d, J = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.2, 138.9, 129.8, 121.5, 114.8, 28.7, 21.8; HRMS (m/z) $[M + H]^+$ calcd for $C_{10}H_{13}N_2$ 161.1073, found 161.1066.

4.4. Synthesis of Cyclic Amidines 3 and 4. *General Procedure C:* A stirred mixture of diamines **9** or **10** (1 mmol) and benzaldehyde (**6b**, 0.5 mmol) in ethanol (5 mL) was refluxed for 1 h. The reaction mixture was cooled slightly, followed by the treatment with iodine (0.75 mmol), and then heated to reflux for another 2 h. After cooling to room temperature, the reaction mixture was quenched with 5% $Na_2S_2O_3$ (1 mL), and concentrated to remove most of the solvent. The resulting residue was redissolved in dichloromethane (15 mL), followed by the addition of 2 N NaOH (15 mL). The organic layer was separated and the aqueous layer was extracted with dichloromethane (15 mL × 2). The combined organic layer was

dried over anhydrous Na_2SO_4, concentrated, and purified through preparative TLC using a mixture of sat. NH_3 in CH_3OH, CH_3OH, and CH_2Cl_2 (2:18:80) as eluent to afford the corresponding cyclic amidine **3** or **4**.

2-Phenyl-4,5-dihydro-1H-imidazole (3). Yield: 73 mg, 99%; white solid, mp 95-96 °C (lit.[28] mp 96-98 °C); R_f = 0.40 (CH_3OH:EtOAc = 5:95); ^1H NMR (400 MHz, $CDCl_3$) δ 7.82-7.76 (m, 2H), 7.48-7.36 (m, 3H), 4.65 (br, s, 1H), 3.77 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 130.8, 129.8, 128.5, 127.1, 49.9; HRMS (m/z) $[M + H]^+$ calcd for $C_9H_{11}N_2$ 147.0917, found 147.0913.

2-Phenyl-1,4,5,6-tetrahydropyrimidine (4). Yield: 70 mg, 87%; white solid, mp 83-85 °C (lit.[29] mp 84-86 °C); R_f = 0.30 (CH_3OH/CH_2Cl_2 = 20:80); ^1H NMR (400 MHz, $CDCl_3$) δ 7.68-7.60 (m, 2H), 7.44-7.31 (m, 3H), 4.49 (br, s, 2H), 3.50-3.40 (m, 4H), 1.87-1.78 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.2, 136.4, 129.9, 128.3, 126.2, 41.9, 29.7, 20.4; HRMS (m/z) $[M + H]^+$ calcd for $C_{10}H_{13}N_2$ 161.1073, found 161.1064.

Conclusions

In summary, a general and facile one-pot method has been established for the synthesis of 1,3-diazaheterocyclic compounds via I_2-mediatedoxidative C−N bond formation. This environmentally benign synthetic process is metal-free and requires no isolation of the condensation intermediates. Under the optimal reaction conditions, a variety of substituted quinazolinones, benzimidazoles, and cyclic amidines were prepared from readily available starting materials.

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