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Imidazolium chloride as an additive for synthesis of 4(3H)-quinazolinones using anthranilamides and DMF derivatives

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ABSTRACT

Imidazolium chloride as an environmentally benign additive efficiently facilitates construction of 4(3H)-quinazolinones using anthranilamides and DMF derivatives. A series of 4(3H)-quinazolinones were prepared in moderate to excellent yields without conventional oxidants, metal catalysts and corrosive acids or other additives.

1. Introduction

4(3H)-quinazolinone as a scaffold in numerous natural products [1,2] and bioactive compounds [3–5] has been widely explored so far. Many drugs containing a sub-structure of 4(3H)-quinazolinone have been commercially available today, such as Albaconazole [6], a potent and long-life term antifungal agent used in both human and animals; Raltitrexed [7], a thymidine synthase inhibitor used in cancer chemotherapy; and Bouchardatine [8], a natural alkaloid used in reducing lipid accumulation without cytotoxicity (Fig. 1).

In recent years, as evidenced by studies on the structure-activity relationship [9–11] of 4(3H)-quinazolinone core, various novel 4(3H)-quinazolinone derivatives exhibited corresponding biological activities such as anticancer [12], antitumor [13], anti-inflammatory [14,15], antibacterial [16,17], antifungal [18,19]. From the view of pharmaceutical value, further unlocking the biological potentials of 4(3H)-quinazolinone derivatives is imperative, which increased the interest of chemists in construction of 4(3H)-quinazolinone core and its derivatives.

Conventional synthesis routes of 4(3H)-quinazolinones via microwave-assisted Niementowski reaction [20–22], Aza-Wittig reaction [23], and cyclocondensation of anthranilic acid [24] have been reported in last decade. Also, palladium [25,26] and other transition metals [27,28] have been employed as catalysts to construct the quinazolinone core. In addition, oxidative heterocyclization [29,30] for 4(3H)-quinazolinones is another alternative. Whereas, drawbacks among these routes such as using corrosive acids, expensive metal catalysts, explosive oxidants and low atom efficiency go against the current trend.

In the light of our previous work in synthesis of benzimidazole [31], benzoxazole and benzothiazole [32], the application of imidazolium chloride should be further extended. In this paper, synthesis of 4(3H)-quinazolinones from anthranilamide using N, N-dimethylformamide (**DMF**) derivatives as carbon source and imidazolium chloride as additive will be described (Scheme 1).

2. Results and discussion

In our preliminary experiments, anthranilamide **1** and DMF catalyzed by imidazolium chloride was carried out as a model reaction. Progress and results are listed in Table 1.

The initial temperature of model reaction was set at 100 °C, imidazolium chloride as additive. Disappointingly, the reaction did not take place in the first 10 h. After prolongation of the reaction time, product **3a** was obtained finally in a trace amount (Table 1, Entry 1). After reaction temperature was elevated to 130 °C with

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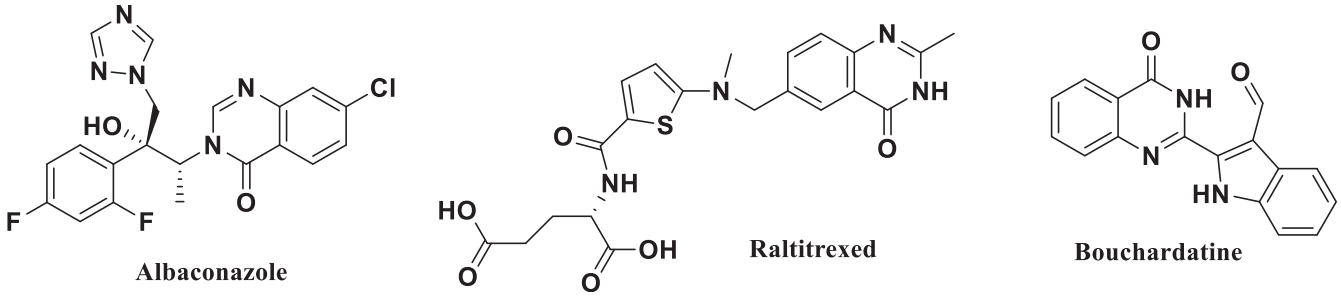
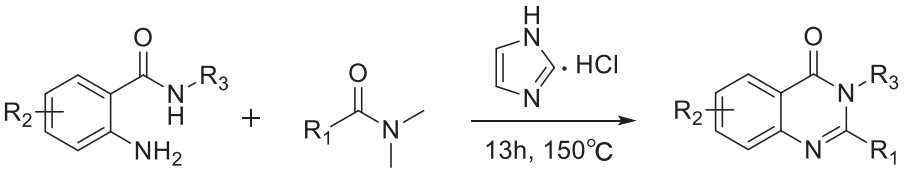


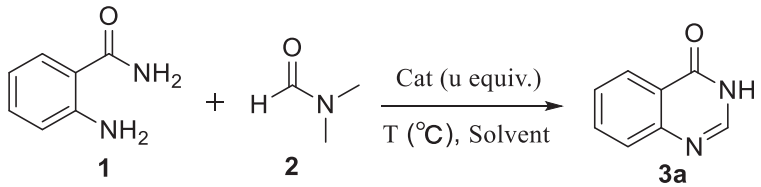
Fig. 1. Bioactive compounds containing 4(3H)-quinazolinone core.



R_1= H, Alkyl, Aryl
R_2= H, CH_3, OCH_3, Cl
R_3= H, CH_3, NH_2

Scheme 1. Synthesis of 4(3)-quinazolinone derivatives.

Table 1
Optimization of reaction condition[a].



Entry	Cat (equiv.)	Solvent	Temperature (°C)	Time (h)	Yield[c] (%)
1	Imidazolium chloride (0.5)	DMF	100	13	Trace
2	Imidazolium chloride (0.5)	DMF	130	13	38
3	Imidazolium chloride (0.5)	DMF	150	13	49
4	Imidazolium chloride (0.5)	DMF	160	13	51
5	Imidazole (0.5)	DMF	150	13	NR[d]
6	Sulfuric Acid (0.5)	DMF	150	13	58
7	Hydrochloride Acid (0.5)	DMF	150	13	46
8	Imidazolium chloride (2)	DMF	150	13	81
9	Imidazolium chloride (2.5)	DMF	150	13	97
10	Imidazolium chloride (3)	DMF	150	12	97
11[b]	Imidazolium chloride (2.5)	1,4-Dioxane	100	13	24
12[b]	Imidazolium chloride (2.5)	Toluene	110	13	29
13[b]	Imidazolium chloride (2.5)	Xylene	135	13	36

[a] Reaction condition: anthranilamide **1a** (3.67 mmol, 1 equiv.), DMF (1 ml), 1,4-Dioxane (2 ml), Toluene (2 ml), Xylene (2 ml). All reactions were performed under reflux.
[b] DMF (1 equiv.) was added.
[c] Isolated yield.
[d] No reaction.

other conditions unchanged, improvement was obtained, which indicated that temperature was the crucial element in the system. Further elevating reaction temperature to 160 °C failed to give the expected yield. Thus, 150 °C was chosen as most suitable temperature for the reaction system (Table 1, Entries 2–4). Meanwhile, reaction was proved not to occur when imidazole was used as catalyst, suggesting that imidazolium chloride is the key to initiate this reaction (Table 1, Entry 5). Inorganic acids HCl and H_2SO_4 could also promote the reaction to afford product **3a** in moderate yield of 46% and 58%, respectively (Table 1, Entries 6, 7). Further investigation evidenced that increasing the amount of imidazolium chloride to 3 equiv. Surprisingly facilitated the reaction to completion with material **1a** completely consumed, whereas not much improvement was found in control experiments catalyzed by

H_2SO_4 or HCl. Interestingly, 2.5 equiv. Imidazolium chloride was later proved sufficient enough to afford an excellent yield of **3a** in 97%, and reaction reached completion faster when extra load of imidazolium chloride 3 equiv. was used (Table 1, Entries 8–10). Next, reaction of equivalent anthranilamide **1a** and DMF was conducted in solvent toluene, xylene and 1,4-dixane respectively. However, owing to the poor solubility of substance **1a** in these solvents and high temperature sensitivity of the reaction itself, all ended up with dissatisfied yields (Table 1, Entries 11–13).

With the optimized condition in hand, substituted anthranilamides **1** with DMF derivatives **2** were used to investigate the scope of the reaction. Results were displayed in Table 2.

Introduction of methyl, ethyl, propyl, butyl, isopropyl and isobutyl groups at the C2 position resulted in 2-alkylsubstituted products **3a-3f** in excellent yields, ranging from 80% to 97%. Decrease in yield possibly reflected that the bulky alkyl group on DMF derivatives hampered the synthesis of product due to steric hindrance. With N,N-dimethyl-2-(p-tolyl)acetamide employed to react with anthranilamide, yield of desired product **3g** decreased dramatically. Subsequently, N,N-Dimethylbenzamide reacted with anthranilamide to afford product **3h** in a good yield of 73%, steric hindrance possibly cause the lower yield. And N,N-Dimethylbenzamides bearing electron-donating substituents such as methyl, methoxy underwent the reaction smoothly to afford target product **3i-3k**. However, decrease in yield was observed while electron-withdrawing substituents such as halo group and trifluoromethyl were attached. Products **3l-3n** were obtained in lower yield ranging from 31% to 56%, which indicated that the electron-withdrawing substituents disfavor the reaction system. To further examine the substrate scope of the reaction, anthranilamides with substituents both on benzene ring and N3 position were employed. All products **3o-3v** were afforded in good to excellent yields followed by the same procedure.

To demonstrate the utility of this method, 2-(4-hydroxybenzyl) quinazolin-4(3H)-one, which exhibits cytotoxicity [33–35], was synthesized followed by two steps in Scheme 2. First, reaction of anthranilamide **1** (1 equiv., 3.67 mmol) and 2-(4-methoxyphenyl)-N,N-dimethylacetamide (1 equiv.) was carried out with imidazolium chloride (2.5 equiv.) to obtain product **3w** in 56% yield. Next, **3w** (20 mmol) was converted to target product 2-(4-hydroxybenzyl)quinazolin-4(3H)-one **3x** in yield of 61% via cleavage of aryl methyl ether, in which aqueous HBr (47%, 4.5 mmol equiv. of **3w**) and Aliquat-336 (10 wt% of **3w**) were employed [36].

Followed by our previous work, a plausible mechanism for the formation of 4(3H)-quinazolinones is depicted in Scheme 3. To start with, imidazolium chloride activates DMF. A tetrahedral intermediate **A** is generated by nucleophilic attack of imidazole on activated DMF. The reactive intermediate **B** [37], N-formyl imidazole, is formed. Amino from anthranilamide launches the second nucleophilic attack on intermediate **B**. Collapse of intermediate **C** precedes the formation of intermediate **D** (UPLC-MS/MS: *m/z* called for $C_8H_8N_2O_2$ $[M+Na]^+$ found at 187.1) which engages in cyclization [38] to form the target product 4(3H)-quinazolinone.

3. Conclusion

In conclusion, this work focuses on imidazolium chloride as an environmentally benign additive, with which 24 examples of 4(3H)-quinazolinones were constructed from anthranilamides and DMF derivatives via a combination of transamidation and intramolecular cyclization. The major advantage is circumvention of oxidants, metal catalysts and other additives. This protocol proceeds with a wide substrate scope and furnishes products in moderate to excellent yields. Further development and researches on this protocol are now under investigation in our laboratory.

4. Materials and methods

4.1. Chemicals and materials

Commercial reagents were purchased from Meyer Reagent Co., Ltd. (Shanghai, China), Macklin Reagent Co., Ltd. (Shanghai, China), Chongqing Chuandong Chemical Co., Ltd. (Chongqing, China), etc., and used as received without further purification. ^1H and ^{13}C NMR spectra were recorded at Bruker Avance-III spectrometer (600 MHz and 151 MHz) using TMS as internal standard. Chemical shifts were reported in ppm and coupling constants (J) in Hz. The multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), multiplet (m), triplet (t) and broad singlet (brs). TLC plates were visualized by exposing UV light or by iodine. Purification of crude compounds and separation of reaction mixtures were carried out by column chromatography using silica gel (200–300 meshes, Shanghai, China). All substrates are known compounds according to the literature.

4.1.1. General procedures for the synthesis of 4(3H)-quinazolinones *3a-3g, 3o-3v*

A mixture of anthranilamide **1** (0.5g, 3.67 mmol, 1 equiv.), DMF (2 ml) and imidazolium chloride (2.5 equiv.) was stirred in a round-bottom flask at 150 °C under reflux for 13h. When the reaction reached completion, reduced the temperature to 80 °C, extra 2 ml DMF was added to dissolve the reaction mixture, then, a saturated solution of NaCl (25 ml) was added. The aqueous phase was extracted with ethyl acetate (4 × 20 mL), and dried over anhydrous Na_2SO_4 and concentrated in vacuum with silica gel added. The residue was purified by flash chromatography (petroleum ether/ethyl acetate) to obtain the product.

4.1.2. General procedures for the synthesis of 4(3H)-quinazolinones *3h-3n, 3w, 3x*

A round-bottom flask was charged with anthranilamide **1** (0.5g, 3.67 mmol, 1 equiv.), N,N-dimethylbenzamide (1 equiv.), and imidazolium chloride (2.5 equiv.). No solvent was used. The mixture was stirred at 150 °C for 13h. When the reaction reached completion, reduced the temperature to 65 °C, methanol (20 ml) was added to dissolve the reaction mixture. Solution was concentrated in vacuum after addition of silica gel. The residue was purified by flash chromatography (petroleum ether/ethyl acetate) to obtain the product.

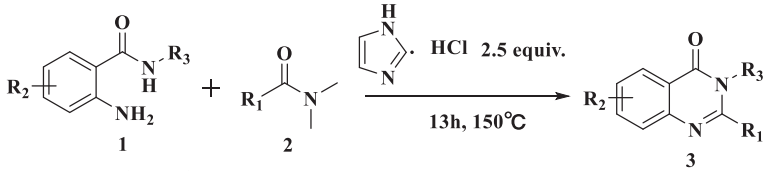
4.1.3. General procedures for the synthesis of 2-(4-hydroxybenzyl) quinazolin-4(3H)-one *3x*

To a solution of 2-(4-methoxybenzyl)quinazolin-4(3H)-one (**3w**) (20 mmol) and aqueous HBr (47%, 4.5 mmol equiv. of **3w**), Alquat-336 (10 wt% of **3w**) was added. The mixture was stirred at 105 °C for 8h under reflux. Reaction was monitored by TLC. When the reaction reached completion, it was cooled to room temperature and quenched by adding water (30 ml). Reaction mixture was then extracted with ethyl acetate (4 × 20 mL), dried over anhydrous Na_2SO_4 and concentrated in vacuum with silica gel added. The residue was purified by flash chromatography (petroleum ether/ethyl acetate) to obtain the product.

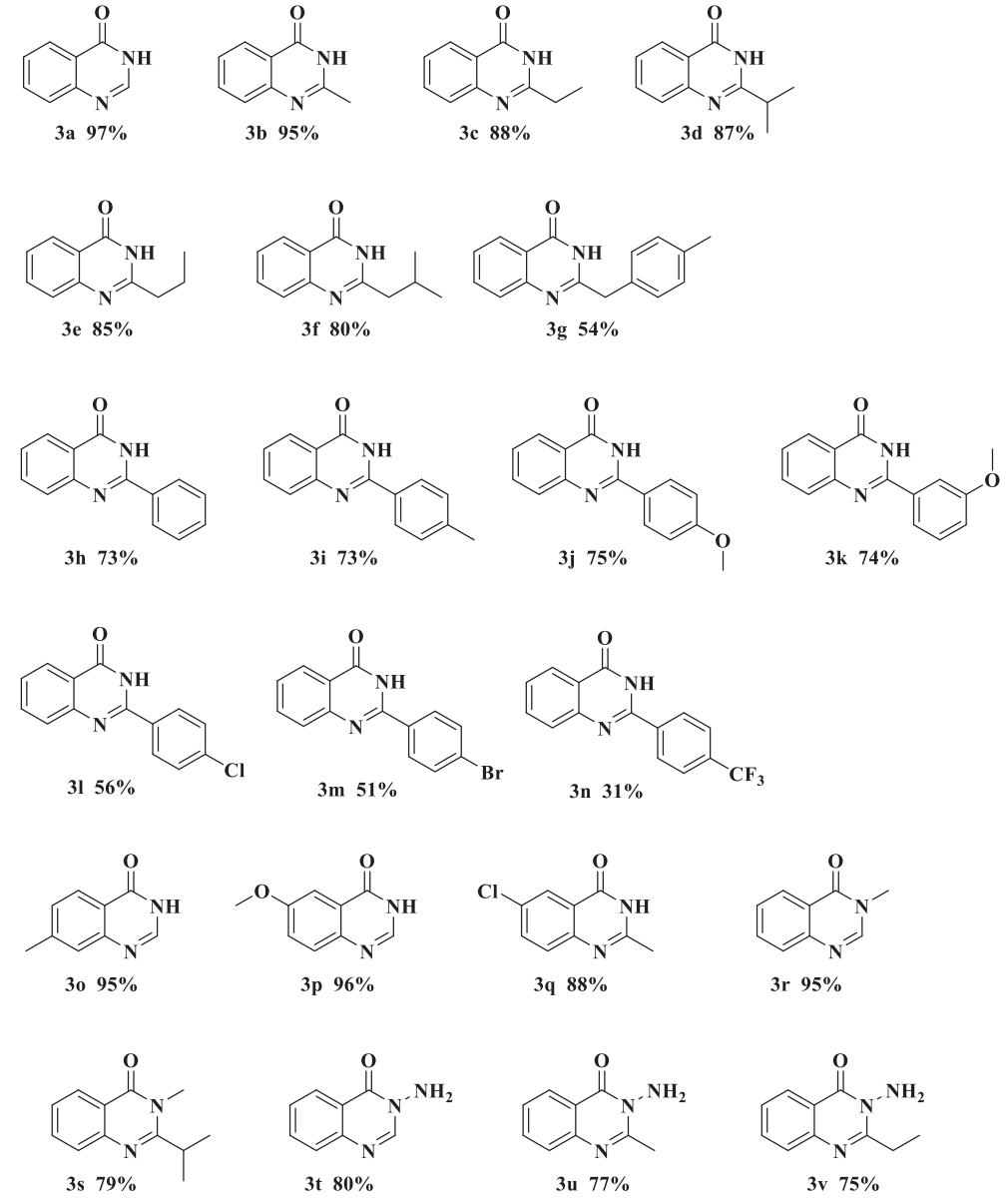
4.2. Product characterization data

Quinazolin-4(3H)-one (**3a**) [39] obtained as white solid in 97% yield; M.P: 212–214 °C. ^1H NMR (600 MHz, DMSO-d6) δ 12.26 (s, 1H), 8.13 (dd, J = 7.9, 1.5 Hz, 1H), 8.10 (d, J = 3.5 Hz, 1H), 7.82 (ddd, J = 8.6, 7.1, 1.5 Hz, 1H), 7.67 (d, J = 8.1 Hz, 1H), 7.57–7.49 (m, 1H). ^{13}C NMR (151 MHz, DMSO-d6) δ 161.1, 149.2, 145.8, 134.8, 127.7, 127.2, 126.3, 123.1.

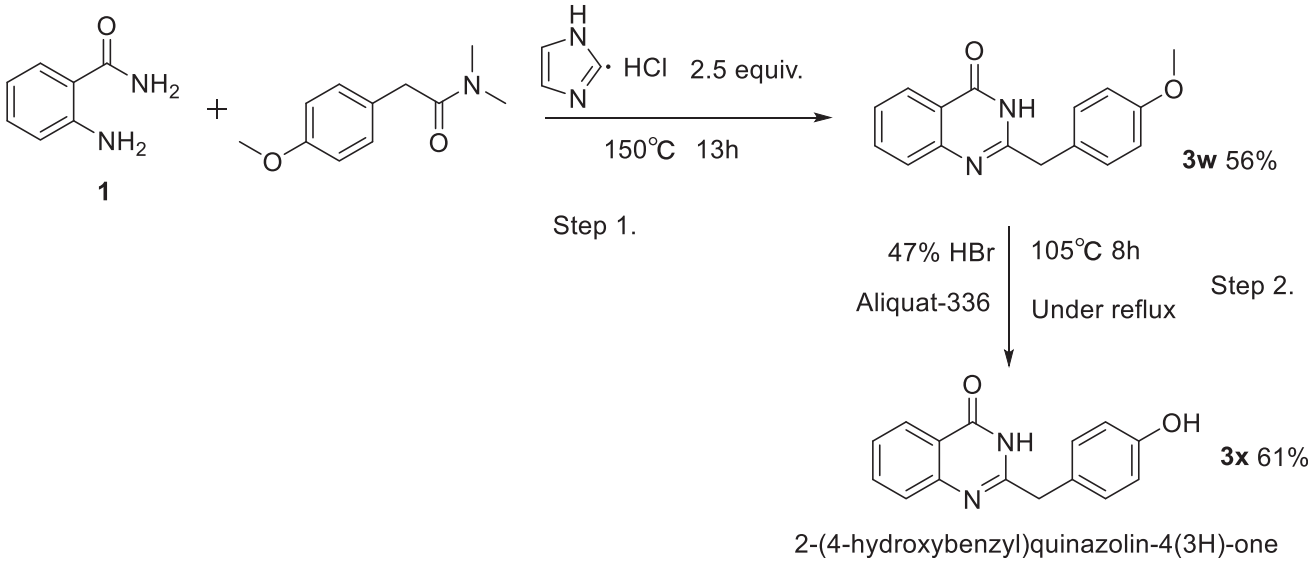
Table 2
Substrate scope with respect to DMF derivatives.[a]



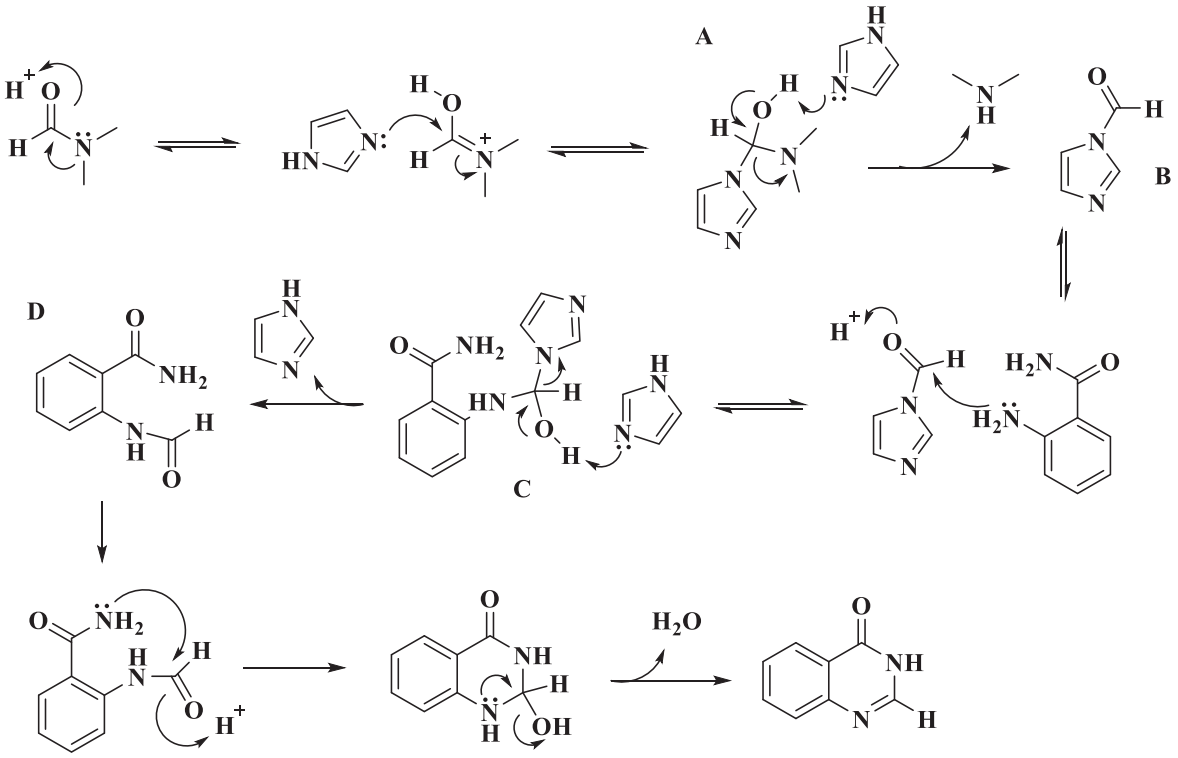
R_1= H, Alkyl, Aryl
R_2= H, Methyl, Chloro, Methoxyl
R_3= H, Methyl, Amino



[a] Reaction conditions: Substituted anthranilamides **1** (1 equiv., 3.67 mmol), DMF derivatives 2 (1 equiv.), imidazolium chloride (2.5 equiv.), solvent-free, 13 h at 150 °C under reflux, yields refer to isolated yield.



Scheme 2. Synthesis of 2-(4-hydroxybenzyl)quinazolin-4(3H)-one **3x**.



Scheme 3. A plausible mechanism for the formation of 4(3H)-quinazolinone.

2-Methylquinazolin-4(3H)-one (**3b**) [40] obtained as white solid in 95% yield; M.P: 238–240 °C. ^{1}H NMR (600 MHz, DMSO-d6) δ 12.18 (s, 1H), 8.06 (dd, J = 7.9, 1.6 Hz, 1H), 7.76 (ddd, J = 8.4, 7.1, 1.6 Hz, 1H), 7.58–7.54 (m, 1H), 7.44 (ddd, J = 8.1, 7.1, 1.2 Hz, 1H), 2.34 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d6) δ 162.1, 154.7, 149.4, 134.7, 127.0, 126.3, 126.1, 121.0, 21.8.

2-Ethylquinazolin-4(3H)-one (**3c**) [40] obtained as white solid in 88% yield; M.P: 228–230 °C. ^{1}H NMR (600 MHz, Chloroform-d) δ 11.31 (s, 1H), 8.30 (dd, J = 8.0, 1.6 Hz, 1H), 7.78 (ddd, J = 8.4, 6.9, 1.6 Hz, 1H), 7.72 (d, J = 8.2 Hz, 1H), 7.51–7.45 (m, 1H), 2.84 (q, J = 7.6 Hz, 2H), 1.51–1.40 (m, 3H). ^{13}C NMR (151 MHz, DMSO- d 6) δ 162.2, 158.8, 149.4, 134.7, 127.2, 126.4, 126.1, 121.2, 28.3, 11.7.

2-Isopropylquinazolin-4(3H)-one (**3d**) [40] obtained as white solid in 87% yield; ^{1}H NMR (600 MHz, Chloroform-d) δ 10.82 (s, 1H), 8.29 (d, J = 7.9 Hz, 1H), 7.78 (t, J = 7.4 Hz, 2H), 7.48 (t, J = 7.6 Hz, 1H), 3.06 (s, 1H), 1.45 (d, J = 7.0 Hz, 6H). ^{13}C NMR (151 MHz, DMSO-d6) δ 162.4, 162.0, 149.3, 134.7, 127.4, 126.4, 126.1, 121.4, 33.7, 20.8.

2-Propylquinazolin-4(3H)-one (**3e**) [40] obtained as white solid

in 85% yield; M.P: 198–200 °C. ^{1}H NMR (600 MHz, Chloroform-d) δ 11.88 (s, 1H), 8.30 (dd, J = 7.9, 1.6 Hz, 1H), 7.78 (ddd, J = 8.3, 7.0, 1.5 Hz, 1H), 7.73 (d, J = 8.2 Hz, 1H), 7.48 (tt, J = 7.0, 1.1 Hz, 1H), 2.80 (t, J = 7.8 Hz, 2H), 1.94 (h, J = 7.7 Hz, 2H), 1.09 (td, J = 7.4, 1.0 Hz, 3H). ^{13}C NMR (151 MHz, Chloroform-d) δ 164.2, 156.8, 149.3, 134.8, 127.1, 126.4, 126.2, 120.4, 37.7, 21.0, 13.7.

2-Isobutylquinazolin-4(3H)-one (**3f**) [41] obtained as white solid in 80 yield; M.P: 193–195 °C. ^{1}H NMR (600 MHz, Chloroform-d) δ 11.93 (s, 1H), 8.30 (d, J = 7.9 Hz, 1H), 7.78 (t, J = 7.6 Hz, 1H), 7.73 (d, J = 8.2 Hz, 1H), 7.48 (t, J = 7.5 Hz, 1H), 2.68 (t, J = 5.6 Hz, 2H), 2.34 (dq, J = 13.2, 6.8 Hz, 1H), 1.08 (dd, J = 6.8, 1.9 Hz, 6H). ^{13}C NMR (151 MHz, Chloroform-d) δ 164.2, 156.2, 149.3, 134.8, 127.2, 126.3, 126.2, 120.4, 44.8, 28.0, 22.3.

2-(4-Methylbenzyl)quinazolin-4(3H)-one (**3g**) [42] obtained as white solid in 54 yield; M.P:231–233 °C. ^{1}H NMR (600 MHz, DMSO-d6) δ 12.39 (s, 1H), 8.08 (dd, J = 8.0, 1.6 Hz, 1H), 7.78 (ddd, J = 8.4, 7.1, 1.6 Hz, 1H), 7.61 (d, J = 8.1 Hz, 1H), 7.50–7.44 (m, 1H), 7.27 (d, J = 7.8 Hz, 2H), 7.13 (d, J = 7.7 Hz, 2H), 3.88 (s, 2H), 2.26 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d6) δ 162.3, 156.6, 149.4, 136.3, 134.8, 133.9, 129.5, 129.2, 127.3, 126.6, 126.1, 121.1, 40.8, 21.1.

2-Phenylquinazolin-4(3H)-one (**3h**) [39] obtained as white solid in 73% yield; M.P:236–237 °C. ^{1}H NMR (600 MHz, Chloroform-d) δ 11.61 (s, 1H), 8.34 (d, J = 7.9 Hz, 1H), 8.30–8.21 (m, 2H), 7.88 (d, J = 8.2 Hz, 1H), 7.82 (t, J = 7.6 Hz, 1H), 7.67–7.57 (m, 3H), 7.52 (t, J = 7.3 Hz, 1H). ^{13}C NMR (151 MHz, Chloroform-d) δ 163.5, 151.6, 149.4, 134.9, 132.7, 131.7, 129.1, 128.0, 127.3, 126.8, 126.3, 120.8.

2-(p-Tolyl)quinazolin-4(3H)-one (**3i**) [39] obtained as white solid in 73% yield; M.P:240–243 °C. ^{1}H NMR (600 MHz, Chloroform-d) δ 11.07 (s, 1H), 8.33 (dd, J = 7.9, 1.5 Hz, 1H), 8.11 (d, J = 7.8 Hz, 2H), 7.86 (d, J = 8.1 Hz, 1H), 7.81 (tt, J = 8.2, 1.4 Hz, 1H), 7.51 (td, J = 7.5, 6.9, 1.2 Hz, 1H), 7.39 (d, J = 7.8 Hz, 2H), 2.47 (s, 3H). ^{13}C NMR (151 MHz, Chloroform-d) δ 165.6, 153.9, 144.8, 137.3, 132.3, 130.4, 129.5, 129.1, 128.9, 123.4, 79.7, 79.5, 79.3, 24.0.

2-(4-Methoxyphenyl)quinazolin-4(3H)-one (**3j**) [39] obtained as white solid in 75% yield; M.P:246–248 °C. ^{1}H NMR (600 MHz, Chloroform-d) δ 10.76 (s, 1H), 8.31 (dd, J = 7.8, 1.5 Hz, 1H), 8.18 (d,J = 8.3 Hz, 2H), 7.90 (s, 1H), 7.81 (t, J = 7.2 Hz, 1H), 7.50 (t, J = 7.5 Hz, 1H), 7.09 (d, J = 8.3 Hz, 2H), 3.92 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d6) δ 162.7, 162.3, 152.3149.4135.0, 129.9, 127.7, 126.6, 126.3, 125.2, 121.1, 114.4, 55.9.

2-(3-Methoxyphenyl)quinazolin-4(3H)-one (**3k**) [43] obtained as white solid in 74% yield; M.P:211–213 °C. ^{1}H NMR (600 MHz, Chloroform-d) δ 10.90 (s, 1H), 8.32 (dd, J = 7.9, 1.5 Hz, 1H), 8.00 (d, J = 8.4 Hz, 1H), 7.87–7.81 (m, 1H), 7.78 (s, 1H), 7.72 (d, J = 7.6 Hz, 1H), 7.52 (dt, J = 24.7, 7.7 Hz, 2H), 7.16 (dd,J = 8.2, 2.3 Hz, 1H), 3.97 (s, 3H). ^{13}C NMR (151 MHz, Chloroform-d) δ 163.8, 160.1, 151.6, 149.4, 134.9, 134.0, 130.1, 128.0, 126.8, 126.3, 119.7, 118.3, 112.1, 55.6.

2-(4-Chlorophenyl)quinazolin-4(3H)-one (**3l**) [39] obtained as pale green solid in 56% yield . ^{1}H NMR (600 MHz, DMSO-d6) δ 12.64 (s, 1H), 8.21 (d, J = 8.4 Hz, 2H), 8.16 (dd, J = 8.0, 1.5 Hz, 1H), 7.85 (td, J = 7.6, 6.9, 1.5 Hz, 1H), 7.75 (d, J = 8.1 Hz, 1H), 7.67–7.60 (m, 2H), 7.54 (t, J = 7.6 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d6) δ 162.6, 151.8, 149.0, 136.7, 135.1, 132.0, 130.1, 129.1, 128.0, 127.2, 126.3, 121.4.

2-(4-Bromophenyl)quinazolin-4(3H)-one (**3m**) [39] obtained as light brown solid in 51% yield; M.P:296–299 °C. ^{1}H NMR (600 MHz, DMSO-d6) δ 12.62 (s, 1H), 8.16 (dd, J = 8.0, 1.5 Hz, 1H), 8.15–8.10 (m, 2H), 7.85 (ddd, J = 8.5, 7.1, 1.6 Hz, 1H), 7.80–7.71 (m, 3H), 7.54 (ddd, J = 8.1, 7.1, 1.2 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d6) δ 162.6, 151.9, 149.0, 135.1, 132.4, 132.1, 130.2, 128.0, 127.2, 126.3, 125.7, 121.5.

2-(4-(Trifluoromethyl)phenyl)quinazolin-4(3H)-one (**3n**) [39] obtained as white solid in 31% yield; M.P: 280–282 °C. ^{1}H NMR (600 MHz, DMSO-d6) δ 12.77 (s, 1H), 8.38 (d, J = 8.2 Hz, 2H), 8.18 (dd, J = 7.9, 1.5 Hz, 1H), 7.94 (d, J = 8.2 Hz, 2H), 7.88 (ddd, J = 8.2, 7.1, 1.6 Hz, 1H), 7.81–7.77 (m, 1H), 7.57 (ddd, J = 7.9, 7.1, 1.2 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d6) δ 162.6, 151.7, 148.9, 137.1, 135.2, 131.6, 131.4, 129.2, 128.1, 127.6, 126.3, 125.9, 125.3, 123.5, 121.6.

7-Methylquinazolin-4(3H)-one (**3o**) [44] obtained as white solid in 95% yield; ^{1}H NMR (600 MHz, DMSO-d6) δ 12.12 (s, 1H), 8.04 (s, 1H), 8.00 (d, J = 8.1 Hz, 1H), 7.47 (s, 1H), 7.34 (dd, J = 8.2, 1.7 Hz, 1H), 2.45 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d6) δ 161.0, 149.3, 145.8, 145.3, 128.6, 127.3, 126.1, 120.6, 21.7.

6-Methoxyquinazolin-4(3H)-one (**3p**) [44] obtained as white solid in 96% yield; M.P: 242–244 °C. ^{1}H NMR (600 MHz, DMSO-d6) δ 12.20 (s, 1H), 7.99 (s, 1H), 7.62 (dd, J = 8.9, 1.8 Hz, 1H), 7.51 (dd, J = 3.1, 1.1 Hz, 1H), 7.42 (dt, J = 9.0, 2.9 Hz, 1H), 3.87 (d, J = 1.0 Hz, 3H). ^{13}C NMR (151 MHz, DMSO-d6) δ 160.9, 158.2, 143.6, 143.5, 129.4, 124.2, 123.9, 106.2, 56.0.

6-Chloro-2-methylquinazolin-4(3H)-one (**3q**) [45] obtained as pale green solid in 93% yield; M.P:286–289 °C. ^{1}H NMR (600 MHz, Chloroform-d) δ 11.07 (s, 1H), 8.25 (s, 1H), 7.72 (d, J = 8.7 Hz, 1H), 7.64 (d, J = 8.7 Hz, 1H), 2.58 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d6) δ 161.2, 155.4, 148.1, 134.8, 130.5, 129.3, 125.1, 122.3, 21.9.

3-Methylquinazolin-4(3H)-one (**3r**) [46] obtained as white solid in 95% yield; M.P: 69–71 °C. ^{1}H NMR (600 MHz, DMSO-d6) δ 8.37 (s, 1H), 8.15 (dd, J = 8.0, 1.6 Hz, 1H), 7.81 (t, J = 6.9 Hz, 1H), 7.67 (d, J = 8.1 Hz, 1H), 7.56–7.52 (m, 1H), 3.50 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d6) δ 161.1, 148.9, 148.5, 134.5, 127.6, 127.4, 126.3, 121.9, 33.9.

2-Isopropyl-3-methylquinazolin-4(3H)-one (**3s**) [40] obtained as white solid in 79% yield; ^{1}H NMR (600 MHz, Chloroform-d) δ 8.24 (dt, J = 8.1, 2.9 Hz, 1H), 7.73–7.62 (m, 2H), 7.41 (dd, J = 9.0, 5.5 Hz, 1H), 3.66 (d, J = 3.4 Hz, 3H), 3.20 (h, J = 6.7 Hz, 1H), 1.38 (dd, J = 6.9, 3.0 Hz, 6H). ^{13}C NMR (151 MHz, Chloroform-d) δ 162.8, 161.1, 147.2, 133.9, 127.0, 126.6, 126.2, 120.1, 32.1, 30.1, 20.8.

3-Aminoquinazolin-4(3H)-one (**3t**) [47] obtained as tan solid in 80% yield; M.P: 205–208 °C. ^{1}H NMR (600 MHz, DMSO-d6) δ 8.26 (s, 1H), 8.07 (ddd, J = 8.0, 1.6, 0.6 Hz, 1H), 7.72 (ddd, J = 8.5, 7.1, 1.6 Hz, 1H), 7.59 (dt, J = 7.9, 0.9 Hz, 1H), 7.45 (ddd, J = 8.1, 7.1, 1.2 Hz, 1H), 5.74 (s, 2H). ^{13}C NMR (151 MHz, DMSO-d6) δ 160.9, 148.8, 147.8, 134.8, 127.6, 127.5, 126.3, 121.6.

3-Amino-2-methylquinazolin-4(3H)-one (**3u**) [47] obtained as tan solid in 77% yield; ^{1}H NMR (600 MHz, DMSO-d6) δ 8.11 (dd, J = 8.0, 1.5 Hz, 1H), 7.79 (ddd, J = 8.4, 7.1, 1.6 Hz, 1H), 7.61 (dd, J = 8.4, 1.1 Hz, 1H), 7.49 (ddd, J = 8.0, 7.0, 1.1 Hz, 1H), 5.81 (s, 2H), 2.59 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d6) δ 160.8, 156.4, 146.7, 134.7, 126.7, 126.3, 119.9, 22.0.

3-Amino-2-ethylquinazolin-4(3H)-one (**3v**) [47] obtained as tan solid in 75% yield; M.P:117–120 °C. ^{1}H NMR (600 MHz, DMSO-d6) δ 8.12 (ddd, J = 8.0, 1.6, 0.6 Hz, 1H), 7.79 (ddd, J = 8.5, 7.1, 1.6 Hz, 1H), 7.64 (dt, J = 8.1, 0.9 Hz, 1H), 7.49 (ddd, J = 8.1, 7.1, 1.2 Hz, 1H), 5.75 (s, 2H), 2.97 (q, J = 7.4 Hz, 2H), 1.28 (t, J = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, DMSO-d6) δ 161.2, 160.1, 146.7, 134.7, 126.9, 126.7, 126.3, 119.9, 27.5, 11.2.

2-(4-methoxybenzyl)quinazolin-4(3H)-one (**3w**) [48] obtained as white solid in 56% yield; M.P: 215–218 °C ^{1}H NMR (600 MHz, DMSO-d6) δ 12.36 (s, 1H), 8.07 (d, J = 9.4 Hz, 1H), 7.77 (t, J = 8.4 Hz, 1H), 7.60 (d, J = 8.0 Hz, 1H), 7.46 (t, J = 8.1 Hz, 1H), 7.31 (d, J = 8.7 Hz, 2H), 6.89 (d, J = 8.7 Hz, 2H), 3.85 (s, 2H), 3.71 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d6) δ 162.40, 158.66, 156.81, 149.19, 135.10, 130.40, 128.72, 127.23, 126.86, 126.17, 120.93, 114.41, 55.49, 40.27.

2-(4-hydroxybenzyl)quinazolin-4(3H)-one (**3x**) [34] obtained as white solid in 61% yield; M.P: 200–203 °C ^{1}H NMR (600 MHz, DMSO-d6) δ 12.32 (s, 1H), 9.30 (s, 1H), 8.07 (d, J = 8.1 Hz, 1H), 7.77 (t, J = 6.9 Hz, 1H), 7.60 (d, J = 8.1 Hz, 1H), 7.46 (t, J = 6.9 Hz, 1H), 7.17 (d, J = 8.5 Hz, 2H), 6.70 (d, J = 8.5 Hz, 2H), 3.80 (s, 2H). ^{13}C NMR (151 MHz, DMSO-d6) δ 162.55, 157.07, 156.34, 149.00, 135.29, 130.38, 130.35, 127.08, 127.02, 126.19, 120.74, 115.71, 114.44, 40.26.

CRediT author contribution statement

Xuetong Wang: Conceptualization, Methodology, Validation, Writing - original draft, Supervision. **Suqin Shang:** Conceptualization, Methodology, Writing - review & editing. **Qingqiang Tian:** Conceptualization, Formal analysis, Supervision. **Yin Wang:** Validation. **Huili Wu:** Validation. **Zhiyao Li:** Investigation. **Shangjun Zhou:** Investigation. **Heng Liu:** Investigation. **Wen Luo:** Formal analysis. **Dan Li:** Formal analysis. **Xin Xiao:** Data curation. **Shuqi Wang:** Data curation. **Jianyong Yuan:** Project administration.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tet.2020.131480.

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