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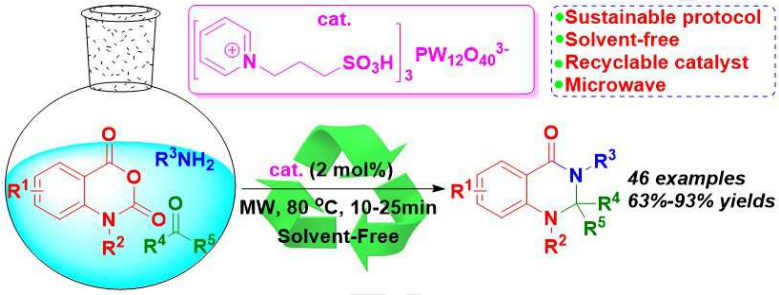

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ABSTRACT

A series of 2,3-dihydroquinazoline-4(1*H*)-one derivatives have been synthesized via one-pot three-component reaction using isatoic anhydrides, amines and aldehydes (or ketones) catalyzed by heteropolyanion-based ionic liquids under solvent-free and microwave-promoted conditions. The practical protocol was found to tolerate a wide range of substrates with different functional groups. Moderate to excellent yields, solvent-free media and operational simplicity are the main highlights. Furthermore, the catalyst can be recovered and reused without evident loss of reactivity. This method provides a green and much improved protocol over the existing methods.

1. Introduction

N-heterocyclic molecules have attracted considerable attention in current synthetic chemistry owing to their immense relevance in wide-ranging areas of medicinal chemistry, pharmaceuticals, agrochemicals, dyes and functional materials.[1–4] 2,3-dihydroquinazolin-4(*1H*)-ones are considered as the privileged heterocyclic skeletons for drug design due to their a broad range of biological and pharmacological activities, such as anti-inflammatory, antiviral, analgesic, antimicrobial and anticancer activity (Fig. 1).[5–8] Additionally, 2,3-dihydroquinazolin-4(*1H*)-one derivatives can easily be oxidized to their quinazolin-4(3*H*)-one analogues, which are also important biologically active heterocycles.[9] Regarding such prominent significance and pharmaceutical utility, various procedures have been focused on the construction of 2,3-dihydroquinazolin-4(*1H*)-one scaffolds as stated in literature.[10–18] Among them, a more attractive and atom-efficient strategy for preparation of these compounds is one-pot three-component condensation of isatoic anhydride, amines and aldehydes, which was firstly reported by Salehi and coworkers in 2005.[19–20] Until now, numerous protocols have been developed recently for the synthesis using catalysts including acidic reagents,[21–29] lewis acids,[30–36] nanoparticles[37–46] and metal complexes.[47–49] These reported methodologies produce good results in many cases, whereas most of those procedures are associated with different negative aspects, such as long reaction times, low yields, harsh acidic conditions, tedious work-up, use of expensive reagents and toxic catalysts. The use of ionic liquids was also reported for this conversion.[50–54] However, the requirement of reaction media and narrow substrates scope limit the practical application in chemical industry. Therefore, the development of a simple, practical, efficient and environmentally benign approach for the preparation of 2,3-dihydroquinazolinones is still favored.

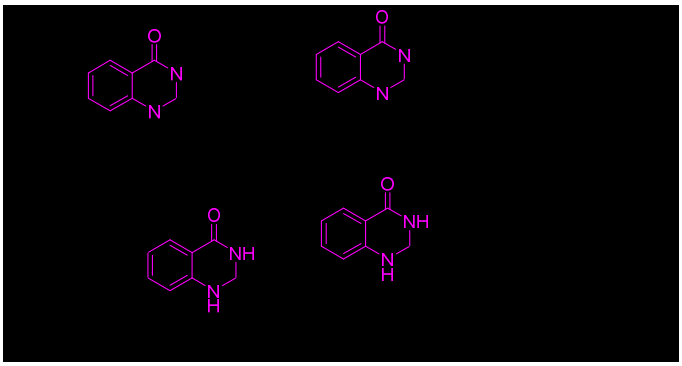

Fig. 1. Structures of pharmacologically active 2,3-dihydroquinazolin-4(1*H*)-ones.

With the growing awareness of green and sustainable chemical process, the use of alternative methods to perform organic

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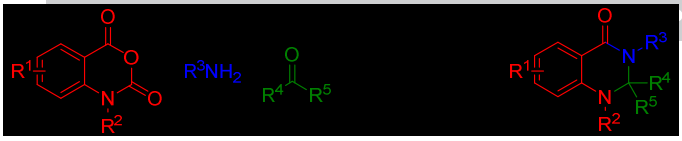


Scheme 1. One-pot three-component synthesis of 2,3-Dihydroquinazolin-4(1*H*)-ones.

synthesis under environmentally benign conditions is in focus.[55] With this perspective, ionic liquids (ILs) have attracted more and more interest as efficient and eco-friendly reaction catalysts and/or media owing to their ease of recovery and reuse.[56-58] In particular, a family of heteropolyanion-based ILs (HPAILs) have been obtained as new species of hybrid materials by combining Keggin heteropolyanions with 'taskspecific' ILs (TSILs) cations containing special functional groups.[59] The distinctive properties of HPAILs are high melting points, negligible vapour pressure, thermal stability and chemical stability due to the large volume and high valence of heteropolyanions and hydrogen bonding networks.[60] So far, HPAILs have made significant contributions to green chemistry and have been used widely as an attractive alternative for traditional reagents[61–63] because of their operational simplicity, no toxicity, easy isolation and reusability. Therefore, HPAILs have been turned out to be a novel candidate for green and sustainable catalysts.

During the last few years, the potential of microwave (MW) energy have been well explored in organic synthesis as a non-classical approach to enhanced yields in significantly short reaction times.[64–65] Actually, MW irradiation enables the use of a wide variety of experimental conditions. However, the focus is now shifted to green and efficient procedure, that is MW irradiation in conjunction with solvent-free conditions, which aim for a straightforward process by simplifying the product recovery, preventing waste generation as well as reducing the operational costs.[66] Following our ongoing efforts to develop novel, efficient and green methods for organic transformations,[67–74] herein we report the synthesis of 2,3-dihydroquinazolin-4(*1H*)-ones through MW-promoted one-pot three-component condensation of isatoic anhydrides, amines and aldehydes (or ketones) using HPAILs as the catalysts under solvent-free conditions (Scheme 1).

2. Results and discussions

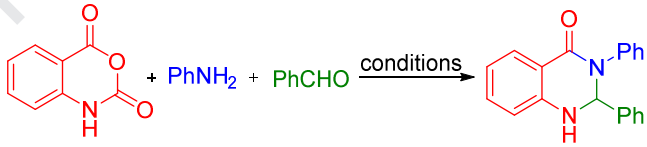
We initiated the investigation by employing the typical N-substituted imidazole, pyridine and triethylamine fused HPAILs (Fig. 2) as potential catalysts for this condensation, which were

Fig. 2. N-substituted imidazole, pyrdine and triethylamine based HPAILs.

readily available based on our previous publications in HPAIL catalyzed organic reactions.[67–74]

At the onset of the research, the reaction of isatoic anhydride, aniline and benzaldehyde was selected as a model reaction and the effect of the different experimental variables related to the isolated yields was investigated to optimize the reaction conditions (Table 1). Firstly, control experiments were performed at room temperature and 60 °C with conventional heating in the absence of any catalyst and additional solvent and, as expected, poor yields were observed even after a prolonged reaction time of 12 h (Table 1, entries 1-2). Whereas addition of 2 mol % amount of $[MIMPS]_3PW_{12}O_{40}$ to the reaction mixture at 60 °C with conventional heating resulted in 2,3-diphenyl-2,3-dihydroquinazolin-4(1*H*)-one with moderate yield (Table 1, entry 3). The results revealed that HPAILs could definitely promote this reaction. In order to improve the yield, some adjustments to the reaction conditions were made. To our delight, when MW heating was utilized at 60 °C, 80 °C and 100 °C, it was shown that the rate and yield of the reaction both increased dramatically with 80 °C as the prefered reaction temperature (Table 1, entries 3-5). In addition, the amount of catalyst is important in the reaction performance. Interestingly, the reaction was found to be equally efficient with 3 mol % amount of $[MIMPS]_3PW_{12}O_{40}$ (Table 1, entry 6), while bringing down the catalyst loading to 1 mol % led

Table 1. Optimization of the reaction conditions for three-component condensation of isatoic anhydride, aniline and benzaldehyde.[a]



1a **2a** **3a** **4a**

Entry	Catalyst [mol %]	Temp (°C)	Time (min)	Yield (%)[b]
1	-	rt	720	trace
2	-	60	720[c]	10[c]
3	$[MIMPS]_3PW_{12}O_{40}$ [2]	60	240[c], 25	56[c], 63
4	$[MIMPS]_3PW_{12}O_{40}$ [2]	80	120[c], 15	75[c], 86
5	$[MIMPS]_3PW_{12}O_{40}$ [2]	100	120[c], 15	73[c], 83
6	$[MIMPS]_3PW_{12}O_{40}$ [3]	80	15	86
7	$[MIMPS]_3PW_{12}O_{40}$ [1]	80	15	65
8	$[MIMPS]_3PW_{12}O_{40}$ [2]	80	15	48[d], 35[e], 28[f], 15[g], 58[h]
9	$[MIMPS]_3PMo_{12}O_{40}$ [2]	80	20	80
10	**$[PyPS]_3PW_{12}O_{40}$ [2]**	**80**	**15**	**90**
11	$[PyPS]_3PMo_{12}O_{40}$ [2]	80	20	82
12	$[TEAPS]_3PW_{12}O_4$ [2]	80	25	75
13	$[TEAPS]_3PMo_{12}O_{40}$ [2]	80	30	68

[a] Unless otherwise specified, all reactions were carried out with isatoic anhydride **1a** (2.0 mmol), aniline **2a** (2.4 mmol), benzaldehyde **3a** (2.4 mmol) and related catalyst under MW (700 W) and solvent-free conditions in a sealed glass pressure tube.
[b] Isolated yields based on isatoic anhydride.
[c] Conventional heating.
[d] C_2H_5OH (1.0 mL) was used as solvent.
[e] CH_3CN (1.0 mL) was used as solvent.
[f] 1,4-Dioxane (1.0 mL) was used as solvent.
[g] Toluene (1.0 mL) was used as solvent.
[h] H_2O (1.0 mL) was used as solvent.

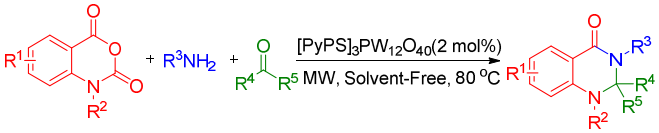
to a reduction in the yield to 65 % (Table 1, entry 7). Next, to compare the solvent-free condition versus solvent condition, various solvents with different polarities such as C_2H_5OH, CH_3CN, 1,4-dioxane, Toluene and H_2O were test in this reactions. As depicted in Table 1 entry 8, an obvious decrease was found in the yield with any solvent in the condensation. Then the catalytic activities of other related HPAILs catalysts prepared earlier were screened (Table 1 entries 9-13), more efficient results were observed by switching the catalyst from MIMPS and TEAPS species to PyPS species. Furthermore, in the case of catalysts combining with different heteropolyanions the results demonstrated that $PW_{12}O_{40}$ was more active than $PMo_{12}O_{40}$ HPAILs. Finally, the optimized condition was shown using 2 mol% of $[PyPS]_3PW_{12}O_{40}$ under MW and solvent-free conditions at 80 ^oC affording 2,3-diphenyl-2,3-dihydroquinazolin-4(*1H*)-one in 90% yield (Table 1, entry 10).

In order to explore the scope and limitation of this three-component process, the reactions of diverse isatoic anhydrides, amines and aldehydes (or ketones) were conducted under the optimized conditions. In general, a wide range of desired dihydroquinazolinones **4a**−**33c** were obtained in moderate to excellent yields in all the cases within 10 to 25 min. Initially, as illustrated in Table 2, when isatoic anhydride and benzaldehyde were employed, reactions of aromatic amines bearing electron-donating groups on the aryl nucleus afforded relatively higher reactivity than those bearing electron-withdrawing counterparts (Table 2, **4a**–**4g**). And the heteroaromatic amines, including pyridin-2-amine, thiazol-2-amine and benzo[*d*]thiazol-2-amine, were found equally competent for the reaction and the desired products were furnished in good yields (Table 2, **4h**–**4j**). Moreover, aliphatic amines and ammonium acetate (ammonia source) were found to be effective substrates and afforded the respective 2,3-dihydroquinazolin-4(*1H*)-one derivatives in excellent yields and short reaction times (Table 2, **4k**–**4n**). The results can be explained that the stronger nucleophilicities of amines could be beneficial for the transformation.

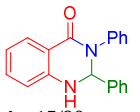
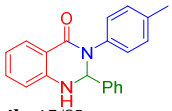
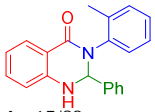
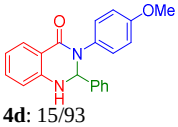
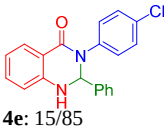
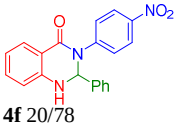
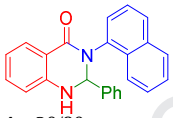
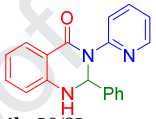
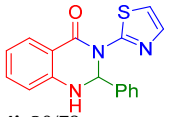
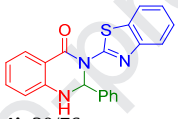
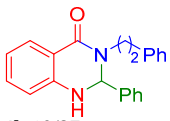
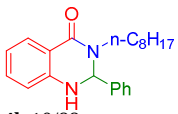
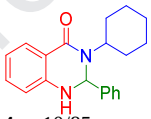
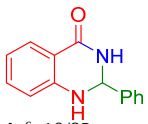
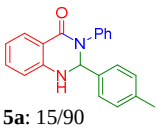
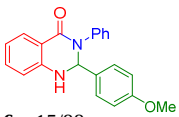
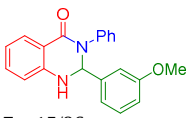
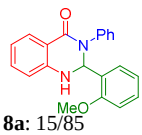
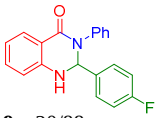
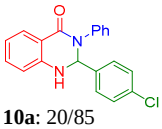
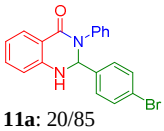
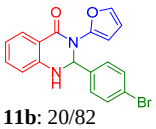
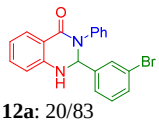
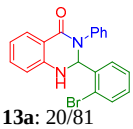
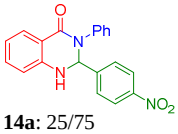
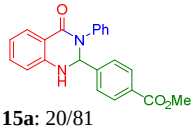
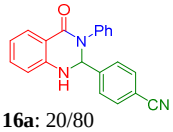
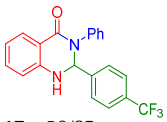
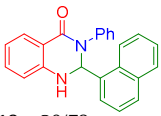
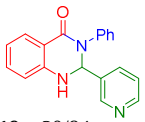
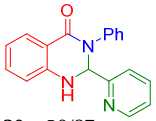
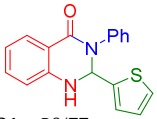
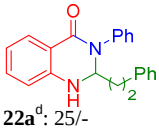
Subsequently, this protocol was surveyed with a variety of aldehydes (or ketones) to further demonstrate its generality. The results shown that the reaction was compatible with a variety of substituents (Me, OMe, F, Cl, Br, NO_2, CO_2Me, CN and CF_3) on the aryl aldehyde moiety, which are very important functional units for post-diversification in pharmaceutical chemistry. It should be noted that the electronic effect and position of the substituents on the phenyl rings seemed to have a certain but not strong influence on this reaction, and reactions of aromatic aldehydes possessing electron-rich substituents afforded little better yields than those possessing the electron-poor substituents (Table 2, entries **5a**–**18a**). Satisfactorily, the reactions of aryl aldehydes containing heteroatom, such as pyridinecarboxaldehyde and thiophenecarboxaldehyde, were well tolerated and furnished the corresponding products in good yields (Table 2, entries **19a**–**21a**). While 3-phenylpropanal as an example of aliphatic aldehydes was checked under our standard conditions, 2-amino-N-phenylbenzamide was the only product (Table 2, **22a**). However, with regard to the reactivities of ketones, lower isolated yields and longer reaction times were achieved as compared to the aldehydes substrates (Table 2, entries **22a**–**23a**).

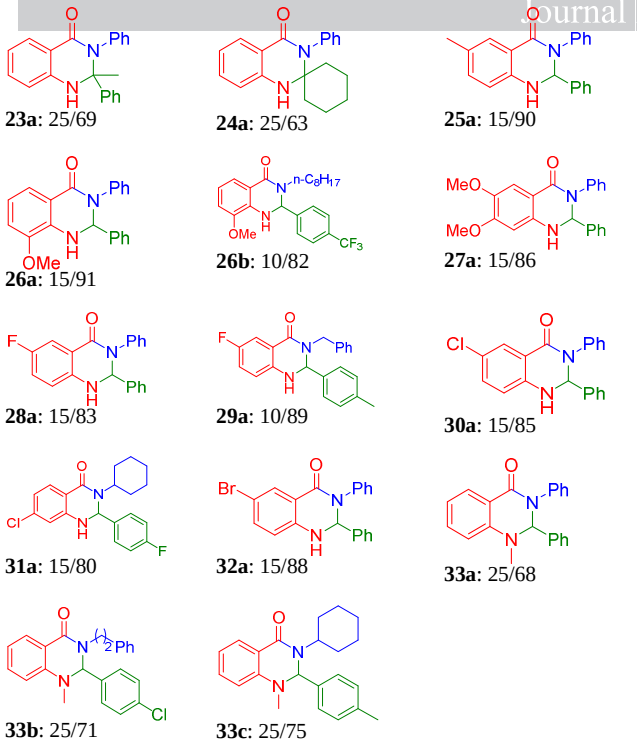
In order to enrich the diversity of the product library, further extension of this transformation to different substituted isatoic

Table 2. HPAIL catalyzed three-component condensation of isatoic anhydrides, amines and aldehydes (or ketones).[a]



1 2 3 4-32

Product: time (min)/yield (%)[b]		
 **4a**: 15/90	 **4b**: 15/92	 **4c**: 15/89
 **4d**: 15/93	 **4e**: 15/85	 **4f** 20/78
 **4g**: 20/80	 **4h**: 20/82	 **4i**: 20/78
 **4j**: 30/76	 **4k**:10/87	 **4l**: 10/88
 **4m**: 10/85	 **4n**[c]: 10/92	 **5a**: 15/90
 **6a**: 15/88	 **7a**: 15/86	 **8a**: 15/85
 **9a**: 20/88	 **10a**: 20/85	 **11a**: 20/85
 **11b**: 20/82	 **12a**: 20/83	 **13a**: 20/81
 **14a**: 25/75	 **15a**: 20/81	 **16a**: 20/80
 **17a**: 20/85	 **18a**: 20/78	 **19a**: 20/84
 **20a**: 20/87	 **21a**: 20/77	 **22a**[d]: 25/-



[a] Unless otherwise specified, all reactions were carried out with isatoic anhydrides **1** (2.0 mmol), amines **2** (2.4 mmol), aldehydes **3** (or ketones) (2.4 mmol) and $[PyPS]_3PW_{12}O_{40}$ (2 mol %) under MW (700 W) and solvent-free conditions at 80 °C in a sealed glass pressure tube.
[b] Isolated yields based on isatoic anhydrides.
[c] Ammonium acetate was used as ammonia source.
[d] 2-Amino-N-phenylbenzamide was the only product.

anhydrides was performed. It is pleased to find that various functional groups (Me, OMe, F, Cl and Br) in different positions of isatoic anhydride could be well tolerated with this protocol, affording the desired products in good yields (Table 2, entries **25a**–**32a**). Additionally, when N-Methylisatoic anhydride was introduced as substrate, the desired 2,3-dihydroquinazolin-4(1*H*)-one derivatives were obtained in moderate yields (Table 2, entries **33a**–**33c**). Finally, the above results proved the generality of this method access to multisubstituted 2,3-dihydroquinazolin-4(*1H*)-one derivatives.

In the view of sustainable chemistry, another distinguishing feature of HPAILs catalyzed process is recovery and reusability, the potential recycling of HPAILs was investigated using the model reaction of isatoic anhydride, aniline and benzaldehyde. Upon accomplishment of the reaction in the frist run, hot EtOAc was added to dissolve the organic products. After vigorous stirring, $[PyPS]_3PW_{12}O_{40}$ can be easily separated from the

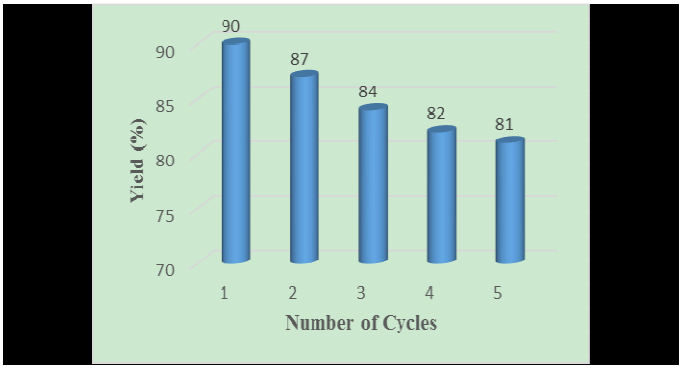
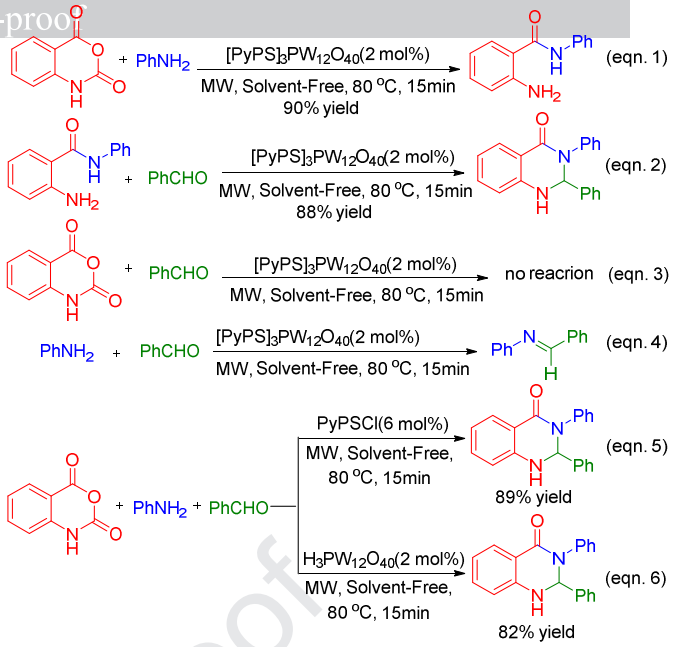


Fig. 3. Reusability studies of the catalyst for the one-pot three-component condensation.



Scheme 2. Control experiments for the mechanism study.

reaction mixture via simple centrifugation or filtration, washed with ethyl acetate to remove traces of the previous reaction mixture and then dried. The recovered catalyst was reused directly for further four runs in the same reaction. As is evident from Fig. 3, the catalyst can be reused without appreciable loss of catalytic efficiency. Furthermore, the recycled $[PyPS]_3PW_{12}O_{40}$ catalyst was characterized and the results indicated the maintaining of the original structure (detailed spectra in Supplementary Material). The slight decrease in the observed yield is probably attributed to inadequate recovery of the catalyst due to the attrition during filtration. Thus, that proved the robustness of HPAILs and their reusability in this reaction.

According to the mechanism suggested by previous reports,[19-49] one of the possible intermediates for the reaction might be 2-aminobenzamide derivatives. In order to elucidate the reaction mechanism of this one-pot three-component condensation, some control experiments were performed. Firstly, 2-amino-N-phenylbenzamide was successfully prepared from the reaction of isatoic anhydride with aniline under the standard condition (Scheme 2, eqn (1)), which is consistent with reports in the literature.[75] Secondly, when 2-amino-N-phenylbenzamide reacted with benzaldehyde, the corresponding 2,3-dihydroquinazolin-4(1*H*)-one product was formed in the presence of $[PyPS]_3PW_{12}O_{40}$ (Scheme 2, eqn (2)). In addition, the reactions of isatoic anhydride with benzaldehyde and aniline with benzaldehyde did not proceed to 2,3-dihydroquinazolin-4(1*H*)-one under the same conditions (Scheme 2, eqn (3) and eqn (4)). Thus, the results revealed that the 2-amino-N-phenylbenzamide should be absolutely the key intermediate. In addition, to further understand the catalytic effect of $[PyPS]_3PW_{12}O_{40}$, the PyPS cation and the $PW_{12}O_{40}$ anion were used respectively as the catalyst under the same conditons. As shown in Scheme 2 eqn (5) and eqn (6), the yields were almost comparable with PyPSCl and $[PyPS]_3PW_{12}O_{40}$, while $H_3PW_{12}O_{40}$ exhibited the relatively lower catalytic activity. It was implied that no significant coordination of cation and anion was observed, and the PyPS cation played an important role in the catalytic reaction as well.

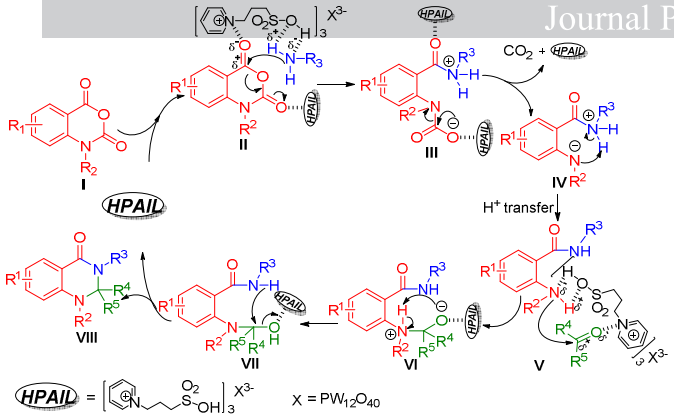


Fig. 4. Plausible mechanism of HPAIL catalyzed one-pot three-component condensation.

On the basis of the points mentioned above, a reasonable mechanism for the preparation of 2,3-dihydroquinazolin-4(*1H*)-one derivatives using HPAILs is proposed in Fig 4. Initially, the activation of carbonyl of isatoic anhydride (I) and N–H bond in amine are achieved via coordination with the aminium cation and sulfonic group in the HPAIL cation respectively to produce a reactive intermediate (**II**). Subsequently, N-nucleophilic primary amine attack on the carbonyl unit and ring opening form a dipolar adduct (**III**), which in turn generates intermediate (**IV**) via decarboxylation. Upon the proton transfer reaction, the key intermediate 2-amino-N-substituted benzamide (**V**) is afforded. Afterwards, the HPAIL cation activate carbonyl of aldehyde (or ketone) and N–H bond in 2-aminobenzamide (**V**) respectively, followed by addition of the amine to the carbonyl carbon to result in the formation of the dipolar adduct (**VI**). Finally, the proton transfer leads to intermediate **VII**, which in turn affords the target product **VIII** by a ring closure via dehydration.

Finally, in order to show the advantages of the present work in comparison with some other reported catalysts, several results for the preparation of 2,3-dihydroquinazolin-4(1*H*)-ones from the model reaction of isatoic anhydride **1a**, aniline **2a** and benzaldehyde **3a** were summarized. As shown in Table 3, the $[PyPS]_3PW_{12}O_{40}$ (Table 3, entry 12) gives better yields or shorter reaction times than other catalysts.

Table 3. Comparison of $[PyPS]_3PW_{12}O_{40}$ with other reported catalysts in the reaction of isatoic anhydride, aniline and benzaldehyde.

Entry	Catalyst	Conditions	Time (min)/Yield (%)	Ref.
1	PTSA-paraformaldehyde copolymer	Ethanol, 80 °C	390/82	22
2	EDDA	H_2O, 100 °C	300/94	23
3	Citric acid	H_2O, 80 °C	90/77	24
4	Starch sulfate	Solvent-free, 100 °C	28/90	29
5	SiO_2-$FeCl_3$	Solvent-free, 80 °C	27/89	32
6	H_3PO_4–Al_2O_3	Solvent-free, 100 °C	30/91	33
7	Fe_3O_4 nanoparticle	H_2O, 100 °C	120/80	37
8	CuO nanoparticle	Aqueous ethanol, reflux	180/85	41
9	Nano-In_2O_3	Aqueous ethanol, 80 °C	240/87	42
10	Aluminum methanesulfonate	Aqueous ethanol, reflux	90/90	48
11	Copper benzenesulfonate	Aqueous ethanol, reflux	90/91	49
12	**$[PyPS]_3PW_{12}O_{40}$**	**Solvent-free, MW, 80 °C**	**15/90**	**This work**

3. Conclusion

In conclusion, the MW-promoted syhthesis of 2,3-dihydroquinazolin-4(*1H*)-one family via one-pot three-component condensation of isatoic anhydrides, amines and aldehydes (or ketones) using HPAILs as catalyst is introduced. Compared to previous reported methodologies, the present procedure offers several advantages, such as simple operations, short reaction times, environmental compatibility, reusability of catalyst and the compatibility with various functional groups. It is expected that this method could find extensive applications in the synthesis of many biologically active derivatives.

4. Experimental section

4.1. General methods

Reagent grade solvents were used for extraction, recrystallization and flash chromatography. All other commercial reagents were used as received without additional purification. The progress of reactions were checked by analytical thin-layer chromatography (TLC, silica gel 60 F-254 plates) (Qingdao Haiyang Chemical Co., Ltd, Qingdao, Shandong, China). The plates were visualized first with UV illumination followed by iodine or phosphomolybdic acid hydrate. Column chromatography was performed using silica gel (200-300 mesh) (Qingdao Haiyang Chemical Co., Ltd, Qingdao, Shandong, China). NMR spectra were obtained using BRUKER AVANCE III instrument. ^{1}H NMR spectra were recorded at 300 MHz or 400 MHz and are reported in parts per million (ppm) on the δ scale relative to tetramethylsilane (TMS) as an internal standard. ^{13}C NMR spectra were recorded at 75 MHz or 100 MHz and are reported in parts per million (ppm) on the δ scale relative to $CDCl_3$ (δ 77.16) and DMSO-d_6 (δ 39.52). Multiplicities are indicated as the following : s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, doubled doublet; td, tripled doublet; br, broad. Coupling constants (*J* values) where noted are quoted in hertz. Mass spectra were obtained using Agilent 1260-6120 (ESI) instrument (Agilent Technologies Co., Ltd, Santa Clara, Calif. USA). MW-promoted heating was obtained using MAS-II instrument manufactured by Shanghai Sineo Microwave Chemistry Technology Co., Ltd. The melting point was uncorrected.

4.2. General Procedure for the Synthesis of HPAILs

To a mixture of toluene (30 mL) and 1,3-propane sulfone (0.10 mol, 12.2 g) in a 100 mL round bottomed flask was added pyridine (0.11 mol, 8.7 g, 8.9 mL). The reaction mixture was stirred for 24 h at 50 °C under a nitrogen atmosphere until a white precipitate (PyPS) was formed. After the completion of reaction, it was cooled to room temperature. After filtration, washing with diethyl ether and drying in a vacuum, PyPS was obtained. Then, PyPS (0.09 mol, 18.1 g) was added to an aqueous solution of $H_3PW_{12}O_{40}$ (0.03 mol, 86.4 g) and then the mixture was stirred at room temperature for 24 h. Finally, the solution was removed in vacuum to give the HPAIL product $[PyPS]_3PW_{12}O_{40}$ as a solid. Thus $[PyPS]_3PMo_{12}O_{40}$, $[MIMPS]_3PW_{12}O_{40}$, $[MIMPS]_3PMo_{12}O_{40}$, $[TEAPS]_3PW_{12}O_{40}$ and $[TEAPS]_3PMo_{12}O_{40}$ were prepared using according starting materials.

*4.2.1. 1-Methyl-3-(3-sulfopropyl)imidazole (**MIMPS**)*

White solid. Mp: 55.5-58.8 °C; IR (KBr) : 3433, 3025, 2944, 1631, 1487, 1328, 1197, 1099, 775, 687, 604, 522, 481 cm^{-1}; ^1H NMR (400 MHz, D_2O) δ 8.71 (s, 1H), 7.48 (s, 1H), 7.41 (s, 1H), 4.32 (t, *J* = 7.2 Hz, 2H), 3.86 (s, 3H), 2.88 (t, *J* = 7.2 Hz, 2H), 2.31-2.24 (m, 2H); ^{13}C NMR (100 MHz, D_2O) δ 136.2, 123.8, 122.2, 47.8, 47.3, 35.8, 25.1; HRMS Calcd for $C_7H_{13}N_2O_3S$ ($M + H^+$): 205.0641; Found: 205.0645.

*4.2.2. 1-(3-Sulfopropyl)pyridine (**PyPS**).*

White solid. Mp: 62.5-64.8 °C; IR (KBr) : 3443, 3159, 3103, 1572, 1459, 1184, 1010, 842, 780, 654, 601, 528 cm^{-1}; ^1H NMR (400 MHz, D_2O) δ 8.86 (d, *J* = 6.0 Hz, 2H), 8.53 (t, *J* = 7.8 Hz, 1H), 8.06 (t, *J* = 7.6 Hz, 2H), 4.75 (t, *J* = 7.2 Hz, 2H), 2.95 (t, *J* = 7.2 Hz, 2H), 2.47-2.40 (m, 2H); ^{13}C NMR (100 MHz, D_2O) δ 146.0, 144.5, 128.5, 60.0, 47.1, 26.2; HRMS Calcd for $C_8H_{12}NO_3S$ ($M + H^+$): 202.0532; Found: 202.0534.

*4.2.3. Triethyl-(3-sulfopropyl)amine (**TEAPS**)*

White solid. Mp: 48.5-49.8 °C; ^1H NMR (400 MHz, D_2O) δ 3.27 (q, *J* = 7.2 Hz, 8H), 2.93 (t, *J* = 7.2 Hz, 2H), 2.10-2.06 (m, 2H), 1.27-1.20 (m, 9H); ^{13}C NMR (100 MHz, D_2O) δ 52.7, 47.3, 46.7, 17.3, 8.3; HRMS Calcd for $C_9H_{22}NO_3S$ ($M + H^+$): 224.1315; Found: 224.1318.

*4.2.4. 1-Methyl-3-(3-sulfopropyl)imidazolium phosphotungstate (**$[MIMPS]_3PW_{12}O_{40}$**)*

White solid. Mp: 119.5-120.8 °C; IR (KBr) : 3417, 3147, 1636, 1571, 1459, 1418, 1173, 1080, 980, 897, 800, 516 cm^{-1}; ^1H NMR (400 MHz, D_2O) δ 8.68 (s, 1H), 7.55 (s, 1H), 7.51 (s, 1H), 4.42 (t, *J* = 7.2 Hz, 2H), 4.02 (s, 3H), 2.91 (t, *J* = 7.2 Hz, 2H), 2.36-2.28 (m, 2H); ^{13}C NMR (100 MHz, D_2O) δ 135.9, 124.2, 122.6, 48.1, 47.4, 36.1, 25.3; HRMS Calcd for $C_7H_{13}N_2O_3S$ ($M + H^+$): 205.0641; Found: 205.0645.

*4.2.5. 1-Methyl-3-(3-sulfopropyl)imidazolium hosphomolybdate (**$[MIMPS]_3PMo_{12}O_{40}$**)*

Green solid. Mp: 105.5-108.8 °C; IR (KBr) : 3422, 3149, 3100, 1630, 1569, 1454, 1405, 1217, 1171, 1059, 963, 882, 796, 610, 504 cm^{-1}; ^1H NMR (400 MHz, D_2O) δ 8.63 (s, 1H), 7.48 (s, 1H), 7.42 (s, 1H), 4.35 (brs, 2H), 3.92 (s, 3H), 2.86 (brs, 2H), 2.26 (brs, 2H); ^{13}C NMR (100 MHz, D_2O) δ 136.3, 124.3, 122.6, 48.2, 47.4, 36.1, 25.3; HRMS Calcd for $C_7H_{13}N_2O_3S$ ($M + H^+$): 205.0641; Found: 205.0643.

*4.2.6. 1-(3-Sulfopropyl)pyridinium phosphotungstate (**$[PyPS]_3PW_{12}O_{40}$**)*

White solid. Mp: 142.5-145.8 °C; IR (KBr) : 3409, 3131, 3068, 1633, 1488, 1220, 1182, 1079, 1042, 978, 896, 805, 681, 595, 521 cm^{-1}; ^1H NMR (400 MHz, D_2O) δ 8.87 (brs, 2H), 8.59 (brs, 1H), 8.11 (brs, 2H), 4.78 (brs, 2H), 2.97 (brs, 2H), 2.46 (brs, 2H); ^{13}C NMR (100 MHz, D_2O) δ 146.3, 144.4, 128.6, 60.2, 47.2, 26.2; HRMS Calcd for $C_8H_{12}NO_3S$ ($M + H^+$): 202.0532; Found: 202.0535.

*4.2.7. 1-(3-Sulfopropyl)pyridinium hosphomolybdate (**$[PyPS]_3PMo_{12}O_{40}$**)*

Green solid. Mp: 142.5-145.8 °C; IR (KBr) : 3421, 3066, 1633, 1488, 1181, 1062, 1044, 957, 880, 795, 680, 609, 505 cm^{-1}; ^1H NMR (400 MHz, D_2O) δ 8.87 (brs, 2H), 8.67 (t, *J* = 7.2 Hz, 1H), 8.20 (t, *J* = 7.2 Hz, 2H), 4.82 (t, *J* = 7.2 Hz, 2H), 2.98 (t, *J* = 7.2 Hz, 2H), 2.51-2.43 (m, 2H); ^{13}C NMR (100 MHz, D_2O) δ 146.4, 144.3, 129.0, 60.3, 47.3, 26.5; HRMS Calcd for $C_8H_{12}NO_3S$ ($M + H^+$): 202.0532; Found: 202.0536.

*4.2.8. Triethyl-(3-sulfopropyl)aminium phosphotungstate (**$[TEAPS]_3PW_{12}O_{40}$**)*

White solid. Mp: 185.5-187.8 °C; IR (KBr) : 3440, 1485, 1460, 1400, 1230, 1170, 1080, 978, 893, 810 cm^{-1}; ^1H NMR (400 MHz, D_2O) δ 3.29-3.28 (m, 8H), 2.98-2.93 (m, 2H), 2.17-2.01 (m, 2H), 1.28-1.25 (m, 9H); ^{13}C NMR (100 MHz, D_2O) δ 60.2, 52.9, 48.0, 24.3, 6.7; HRMS Calcd for $C_9H_{22}NO_3S$ ($M + H^+$): 224.1315; Found: 224.1318.

*4.2.9. Triethyl-(3-sulfopropyl)aminium hosphomolybdate (**$[TEAPS]_3PMo_{12}O_{40}$**)*

Green solid. Mp: 165.5-167.8 °C; ^1H NMR (400 MHz, D_2O) δ 3.37-3.21 (m, 8H), 2.97-2.87 (m, 2H), 2.16-2.06 (m, 2H), 1.28-1.25 (m, 9H); ^{13}C NMR (100 MHz, D_2O) δ 60.2, 52.9, 48.0, 24.3, 6.7; HRMS Calcd for $C_9H_{22}NO_3S$ ($M + H^+$): 224.1315; Found: 224.1318.

4.3. General procedure for the synthesis 2,3-dihydroquinazolin-4(1H)-ones

To a mixture of isatoic anhydride (2 mmol), amine (2.4 mmol) and aldehyde (or ketone) (2.4 mmol) in a 15 mL glass pressure tube was added $[PyPS]_3PW_{12}O_{40}$ (0.14 g, 0.04 mmol). After the pressure tube was closed, the reaction mixture was stirred at 80 °C under MW (700 W). The progress of the reaction could be monitored by TLC. After the reaction is completed, the mixture was diluted with hot ethyl acetate (30 mL) with stirring for 30 min. After filtration, the filtrate was evaporated and the residue was directly purified by recrystallization or column chromatography to give the desired product. And the insoluble $[PyPS]_3PW_{12}O_{40}$ catalyst was recovered. After washing with ethyl acetate (10 mL) to remove traces of the previous reaction mixture and then drying under vacuum, the recovered $[PyPS]_3PW_{12}O_{40}$ catalyst could be used for further runs for the same reaction.

*4.3.1. 2,3-Diphenyl-2,3-dihydroquinazolin-4(1H)-one (**4a**)*

White solid. Mp: 207.3-209.1 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 6.8 Hz, 1H), 7.29-7.24 (m, 2H), 7.21-7.14 (m, 6H), 7.11-7.09 (m, 3H), 6.79 (t, *J* = 6.8 Hz, 1H), 6.53 (d, *J* = 7.6 Hz, 1H), 6.00 (s, 1H), 4.82 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 145.5, 140.7, 140.0, 134.0, 129.2, 129.1, 129.0, 128.8, 127.1, 126.9, 126.8, 119.7, 117.0, 115.0, 74.8; HRMS Calcd for $C_{20}H_{17}N_2O$ ($M + H^+$): 301.1335; Found: 301.1339.

*4.3.2. 2-Phenyl-3-(p-tolyl)-2,3-dihydroquinazolin-4(1H)-one (**4b**)*

White solid. Mp: 214.2-216.2 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.6 Hz, 1H), 7.26-7.25 (m, 2H), 7.21-7.18 (m, 4H), 6.97 (brs, 4H), 6.77 (t, *J* = 7.2 Hz, 1H), 6.51 (d, *J* = 8.0 Hz, 1H), 5.95 (s, 1H), 4.94 (brs, 1H), 2.18 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 145.5, 140.0, 138.0, 136.7, 133.9, 129.6, 129.0, 128.9, 128.7, 126.9, 126.8, 119.4, 116.7, 114.8, 74.7, 21.1; HRMS Calcd for $C_{21}H_{19}N_2O$ ($M + H^+$): 315.1492; Found: 315.1493.

*4.3.3. 2-Phenyl-3-(o-tolyl)-2,3-dihydroquinazolin-4(1H)-one (**4c**)*

White solid. Mp: 216.2-218.2 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 7.2 Hz, 1H), 7.29-7.26 (m, 5H), 7.20-7.12 (m, 3H), 6.99 (t, *J* = 7.6 Hz, 1H), 6.88 (t, *J* = 7.6 Hz, 1H), 6.74 (d, *J* = 7.6 Hz, 1H), 5.59 (d, *J* = 7.6 Hz, 1H), 5.77 (s, 1H), 4.78 (s, 1H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 145.7, 140.3, 139.3, 135.7, 133.9, 131.2, 129.6, 129.3, 128.9, 128.5, 128.0, 126.7, 126.5, 119.5, 116.5, 114.7, 74.6, 18.3; HRMS Calcd for $C_{21}H_{19}N_2O$ ($M + H^+$): 315.1492; Found: 315.1495.

*4.3.4. 3-(4-Methoxyphenyl)-2-phenyl-2,3-dihydroquinazolin-4(1H)-one (**4d**)*

White solid. Mp: 117.3-119.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 7.6 Hz, 1H), 7.36-7.32 (m, 2H), 7.30-7.26 (m, 4H), 7.06 (d, J = 8.8 Hz, 2H), 6.86 (t, J = 7.6 Hz, 1H), 6.77 (d, J = 8.8 Hz, 2H), 6.59 (d, J = 8.0 Hz, 1H), 6.03 (s, 1H), 5.13 (brs, 1H), 3.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 158.3, 145.6, 140.0, 133.9, 133.3, 129.1, 128.8, 128.6, 127.0, 125.1, 119.5, 116.6, 114.8, 114.3, 75.2, 55.5; HRMS Calcd for $C_{21}H_{19}N_2O_2$ (M + H^+): 331.1441; Found: 331.1444.

*4.3.5. 3-(4-Chlorophenyl)-2-phenyl-2,3-dihydroquinazolin-4(1H)-one (**4e**)*

White solid. Mp: 133.3-135.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 7.2 Hz, 1H), 7.39-7.33 (m, 3H), 7.28-7.23 (m, 3H), 7.18-7.16 (m, 2H), 7.05 (d, J = 8.4 Hz, 2H), 6.95 (t, J = 7.6 Hz, 1H), 6.83 (d, J = 8.0 Hz, 1H), 5.77 (s, 1H), 5.08 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 146.5, 138.3, 136.7, 134.3, 129.3, 129.1, 128.8, 128.2, 128.0, 127.5, 126.7, 120.3, 119.5, 115.9, 78.1; HRMS Calcd for $C_{20}H_{16}ClN_2O$ (M + H^+): 335.0946; Found: 335.0948.

*4.3.6. 3-(4-Nitrophenyl)-2-phenyl-2,3-dihydroquinazolin-4(1H)-one (**4f**)*

White solid. Mp: 133.3-135.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, J = 7.2 Hz, 1H), 8.08 (d, J = 8.8 Hz, 2H), 7.62 (t, J = 7.6 Hz, 1H), 7.48 (t, J = 7.6 Hz, 1H), 7.40-7.30 (m, 6H), 6.57 (d, J = 8.8 Hz, 2H), 6.15 (s, 1H), 4.92 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 165.4, 152.2, 146.7, 138.4, 137.5, 133.9, 130.3, 129.3, 129.1, 128.6, 128.0, 127.5, 126.5, 111.5, 77.4; HRMS Calcd for $C_{20}H_{16}N_3O_3$ (M + H^+): 346.1186; Found: 346.1188.

*4.3.7. 3-(Naphthalen-1-yl)-2-phenyl-2,3-dihydroquinazolin-4(1H)-one (**4g**)*

White solid. Mp: 147.3-149.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 8.0 Hz, 1H), 8.06 (d, J = 7.2 Hz, 1H), 7.88 (d, J = 7.6 Hz, 1H), 7.77 (d, J = 8.4 Hz, 1H), 7.56-7.51 (m, 2H), 7.33-7.26 (m, 5H), 7.25-7.23 (m, 2H), 7.05 (d, J = 7.6 Hz, 1H), 6.91 (t, J = 7.6 Hz, 1H), 6.64 (d, J = 8.0 Hz, 1H) 5.94 (s, 1H), 4.86 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1, 145.8, 140.4, 136.5, 134.9, 134.1, 129.3, 128.9, 128.8, 128.5, 128.3, 128.2, 127.9, 127.3, 126.6, 126.4, 125.5, 122.8, 119.6, 116.4, 114.7, 74.8; HRMS Calcd for $C_{24}H_{19}N_2O$ (M + H^+): 351.1492; Found: 351.1494.

*4.3.8. 2-Phenyl-3-(pyridin-2-yl)-2,3-dihydroquinazolin-4(1H)-one (**4h**)*

White solid. Mp: 181.1-183.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 8.20 (d, J = 8.0 Hz, 1H), 7.99 (d, J = 7.2 Hz, 1H), 7.70 (t, J = 7.2 Hz, 1H), 7.36-7.34 (m, 2H), 7.26 (brs, 3H), 7.22-7.20 (m, 2H), 7.04 (s, 1H), 6.85 (t, J = 7.2 Hz, 1H), 6.74 (d, J = 8.0 Hz, 1H), 5.22 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 152.6, 147.8, 145.5, 140.6, 137.6, 134.3, 129.4, 128.5, 128.1, 126.6, 120.2, 119.8, 119.0, 118.2, 115.9, 68.2; HRMS Calcd for $C_{19}H_{16}N_3O$ (M + H^+): 302.1288; Found: 302.1290.

*4.3.9. 2-Phenyl-3-(thiazol-2-yl)-2,3-dihydroquinazolin-4(1H)-one (**4i**)*

White soild. Mp: 148.3-151.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 8.0 Hz, 1H), 7.51 (d, J = 10.8 Hz, 2H), 7.36-7.29 (m, 4H), 7.22 (d, J = 3.6 Hz, 2H) 7.04 (d, J = 3.2 Hz, 1H), 6.90 (t, J = 7.6 Hz, 1H), 6.75 (d, J = 8.0 Hz, 1H), 5.25 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 158.4, 145.1, 139.5, 137.3, 135.0, 130.2, 129.2, 128.8, 128.6, 126.1, 120.3, 116.1, 115.2, 69.0; HRMS Calcd for $C_{17}H_{14}N_3OS$ (M + H^+): 308.0852; Found: 308.0856.

*4.3.10. 3-(Benzo[d]thiazol-2-yl)-2-phenyl-2,3-dihydroquinazolin-4(1H)-one (**4j**)*

White soild. Mp: 158.3-161.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 7.6 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.72 (s, 1H), 7.47 (t, J = 7.6 Hz, 1H), 7.42 (t, J = 7.6 Hz, 1H), 7.37-7.35 (m, 2H), 7.31 (t, J = 7.6 Hz, 1H), 7.22-7.20 (m, 3H), 6.90 (t, J = 7.6 Hz, 1H), 6.80 (t, J = 8.0 Hz, 1H), 5.33 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.1, 158.3, 148.3, 145.4, 139.4, 135.3, 133.5, 130.2, 129.5, 128.8, 128.6, 126.2, 126.1, 124.1, 121.4, 121.3, 120.4, 116.3, 68.9; HRMS Calcd for $C_{21}H_{16}N_3OS$ (M + H^+): 358.1009; Found: 358.1007.

*4.3.11. 3-Phenethyl-2-phenyl-2,3-dihydroquinazolin-4(1H)-one (**4k**)*

White solid. Mp: 178.3-179.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 7.6 Hz, 1H), 7.28 (s, 5H), 7.20-7.17 (m, 4H), 7.04 (d, J = 7.2 Hz, 2H), 6.79 (t, J = 7.6 Hz, 1H), 6.46 (d, J = 8.0 Hz, 1H), 5.48 (s, 1H), 4.39 (brs, 1H), 4.02-3.94 (m, 1H), 2.98-2.85 (m, 2H), 2.75-2.68 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.4, 145.3, 139.6, 139.3, 133.6, 129.6, 129.1, 129.0, 128.6, 128.5, 127.0, 126.5, 119.5, 116.3, 114.5, 73.1, 47.1, 34.3; HRMS Calcd for $C_{22}H_{21}N_2O$ (M + H^+): 329.1648; Found: 329.1649.

*4.3.12. 3-Octyl-2-phenyl-2,3-dihydroquinazolin-4(1H)-one (**4l**)*

White solid. Mp: 148.3-150.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 7.6 Hz, 1H), 7.38-7.33 (m, 5H), 7.22 (t, J = 7.6 Hz, 1H), 6.83 (t, J = 7.6 Hz, 1H), 6.51 (d, J = 8.0 Hz, 1H), 5.74 (s, 1H), 4.56 (s, 1H), 3.98-3.91 (m, 1H), 2.79-2.72 (m, 1H), 1.62-1.49 (m, 2H), 1.22 (s, 10H), 0.86 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2, 145.1, 140.1, 133.4, 129.4, 129.1, 128.6, 126.7, 119.3, 116.5, 114.4, 72.3, 44.9, 31.9, 29.4, 29.3, 27.8, 27.1, 22.8, 14.2; HRMS Calcd for $C_{22}H_{29}N_2O$ (M + H^+): 337.2274; Found: 337.2276.

*4.3.13. 3-Cyclohexyl-2-phenyl-2,3-dihydroquinazolin-4(1H)-one (**4m**)*

White solid. Mp: 124.1-127.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 8.0 Hz, 1H), 7.31-7.29 (m, 2H), 7.26-7.24 (m, 3H), 7.16 (t, J = 7.6 Hz, 1H), 6.81 (t, J = 7.6 Hz, 1H), 6.45 (d, J = 8.0 Hz, 1H), 5.76 (s, 1H), 4.62 (brs, 1H), 4.58 (tt, J = 12.0, 3.2 Hz, 1H), 1.89-1.79 (m, 2H), 1.66-1.54 (m, 4H), 1.46-1.39 (m, 1H), 1.34-1.27 (m, 1H), 1.04-0.97 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 144.2, 142.3, 133.3, 128.8, 128.6, 128.5, 125.8, 119.5, 117.8, 114.9, 67.7, 53.7, 31.2, 31.1, 26.0, 25.9, 25.6; HRMS Calcd for $C_{20}H_{23}N_2O$ (M + H^+): 307.1805; Found: 307.1807.

*4.3.14. 2-Phenyl-2,3-dihydroquinazolin-4(1H)-one (**4n**)*

White solid. Mp: 197.3-199.1 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.26 (brs, 1H), 7.62 (d, J = 7.6 Hz, 1H), 7.50 (d, J = 7.2 Hz, 2H), 7.41-7.42 (m, 3H), 7.24 (t, J = 7.6 Hz, 1H), 7.09 (brs, 1H), 6.76 (d, J = 8.0 Hz, 1H), 6.68 (t, J = 7.6 Hz, 1H), 5.76 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.5, 147.8, 141.6, 133.2, 128.4, 128.3, 127.3, 126.8, 117.1, 114.9, 114.4, 66.5; HRMS Calcd for $C_{14}H_{13}N_2O$ (M + H^+): 225.1022; Found: 225.1020.

*4.3.15. 3-Phenyl-2-(p-tolyl)-2,3-dihydroquinazolin-4(1H)-one (**5a**)*

White solid. Mp: 194.8-196.2 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.72 (d, J = 7.6 Hz, 1H), 7.59 (s, 1H), 7.34-7.31 (m, 2H), 7.27-7.25 (m, 5H), 7.20-7.16 (m, 1H), 7.10 (d, J = 8.0 Hz, 2H), 6.75 (d, J = 8.0 Hz, 1H), 6.71 (t, J = 7.6 Hz, 1H), 6.23 (d, J = 2.4 Hz, 1H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.8, 147.0, 141.4, 138.3, 138.0, 134.2, 129.4, 129.1, 128.4, 127.0, 126.6, 126.4, 117.9, 115.9, 115.3, 72.9, 21.1; HRMS Calcd for $C_{21}H_{19}N_2O$ (M + H^+): 315.1492; Found: 315.1494.

*4.3.16. 2-(4-Methoxyphenyl)-3-phenyl-2,3-dihydroquinazolin-4(1H)-one (**6a**)*

White soild. Mp: 130.3-132.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 7.6 Hz, 1H), 7.53 (d, J = 8.4 Hz, 1H), 7.31-7.27 (m, 4H), 7.17-7.25 (m, 3H), 6.88 (t, J = 7.6 Hz, 1H), 6.76 (d, J = 8.0 Hz, 2H), 6.62 (d, J = 8.0 Hz, 1H), 6.05 (s, 1H), 5.13 (s, 1H), 3.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 160.0, 145.6, 140.6, 134.0, 130.9, 129.1, 129.0, 128.3, 127.3, 126.9, 119.6, 114.9, 114.0, 113.5, 74.4, 55.3; HRMS Calcd for $C_{21}H_{19}N_2O_2$ (M + H^+): 331.1441; Found: 331.1444.

*4.3.17. 2-(3-Methoxyphenyl)-3-phenyl-2,3-dihydroquinazolin-4(1H)-one (**7a**)*

White soild. Mp: 146.3-148.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 7.6 Hz, 1H), 7.32-7.26 (m, 3H), 7.22-7.16 (m, 4H), 6.94-6.87 (m, 3H), 6.80 (d, J = 8.4 Hz, 1H), 6.63 (d, J = 8.0 Hz, 1H), 6.06 (s, 1H), 4.82 (s, 1H), 3.70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2, 159.9, 145.4, 141.5, 140.6, 134.0, 129.9, 129.1, 129.0, 127.1, 127.0, 119.8, 119.2, 116.9, 114.9, 114.5, 112.5, 74.7, 55.4; HRMS Calcd for $C_{21}H_{19}N_2O_2$ (M + H^+): 331.1441; Found: 331.1444.

*4.3.18. 2-(2-Methoxyphenyl)-3-phenyl-2,3-dihydroquinazolin-4(1H)-one (**8a**)*

White soild. Mp: 144.8-146.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 7.6 Hz, 1H), 7.43 (d, J = 7.6 Hz, 1H), 7.35-7.32 (m, 4H), 7.24-7.18 (m, 3H), 6.91-6.86 (m, 2H), 6.81 (t, J = 7.6 Hz, 1H), 6.54 (d, J = 8.0 Hz, 1H), 6.35 (s, 1H), 5.13 (s, 1H), 3.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 155.9, 145.9, 141.3, 133.9, 129.9, 129.1, 128.9, 127.6, 127.5, 126.4, 125.7, 120.8, 119.3, 116.7, 115.0, 110.7, 69.9, 55.6; HRMS Calcd for $C_{21}H_{19}N_2O_2$ (M + H^+): 331.1441; Found: 331.1444.

*4.3.19. 2-(4-Fluorophenyl)-3-phenyl-2,3-dihydroquinazolin-4(1H)-one (**9a**)*

White solid. Mp: 221.8-223.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 7.6 Hz, 1H), 7.47-7.44 (m, 1H), 7.28-7.18 (m, 4H), 7.12-7.04 (m, 3H), 6.88-6.80 (m, 3H), 6.56 (d, J = 8.0 Hz, 1H), 6.02 (s, 1H), 5.05 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 163.3, 161.8, 147.2, 145.4, 140.4, 139.4, 135.3, 134.1, 129.1, 129.0, 127.2, 127.1, 125.1, 119.9, 119.2, 115.9, 115.7, 115.0, 74.1; HRMS Calcd for $C_{20}H_{16}FN_2O$ (M + H^+): 319.1241; Found: 319.1243.

*4.3.20. 2-(4-Chlorophenyl)-3-phenyl-2,3-dihydroquinazolin-4(1H)-one (**10a**)*

White solid. Mp: 201.2-203.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (dd, J = 7.6, 1.2 Hz, 1H), 7.25-7.19 (m, 5H), 7.16-7.08 (m, 5H), 6.82 (t, J = 7.6 Hz, 1H), 6.56 (d, J = 8.0 Hz, 1H), 5.99 (s, 1H), 4.81 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1, 145.2, 140.5, 138.6, 135.0, 134.1, 129.2, 129.1, 128.4, 127.1, 126.9, 123.0, 120.0, 117.1, 115.2, 74.1; HRMS Calcd for $C_{20}H_{16}ClN_2O$ (M + H^+): 335.0946; Found: 335.0948.

*4.3.21. 2-(4-Bromophenyl)-3-phenyl-2,3-dihydroquinazolin-4(1H)-one (**11a**)*

White solid. Mp: 224.3-226.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (dd, J = 8.0, 1.2 Hz, 1H), 7.31-7.29 (m, 2H), 7.25-7.21 (m, 2H), 7.20-7.09 (m, 6H), 6.82 (t, J = 7.6 Hz, 1H), 6.55 (d, J = 8.0 Hz, 1H), 5.97 (s, 1H), 4.84 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1, 145.1, 140.5, 139.1, 134.2, 132.0, 129.2, 129.1, 128.6, 127.1, 126.9, 123.1, 120.0, 117.1, 115.2, 74.1; HRMS Calcd for $C_{20}H_{16}BrN_2O$ (M + H^+): 379.0441; Found: 379.0440.

*4.3.22. 2-(4-Bromophenyl)-3-(furan-2-ylmethyl)-2,3-dihydroquinazolin-4(1H)-one (**11b**)*

White solid. Mp: 183.3-185.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 7.6 Hz, 1H), 7.46-7.44 (m, 2H), 7.30 (s, 1H), 7.25-7.21 (m, 3H), 6.84 (t, J = 7.6 Hz, 1H), 6.53 (d, J = 8.0 Hz, 1H), 6.29-6.28 (m, 1H), 6.20 (d, J = 2.4 Hz, 1H), 5.75 (s, 1H), 5.30 (d, J = 15.6 Hz, 1H), 4.65 (s, 1H), 3.84 (d, J = 15.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1, 150.2, 145.1, 142.4, 138.5, 133.9, 132.2, 128.9, 128.5, 123.5, 119.6, 115.8, 114.6, 110.6, 109.1, 71.2, 40.2; HRMS Calcd for $C_{19}H_{16}BrN_2O_2$ (M + H^+): 383.0390; Found: 383.0394.

*4.3.23. 2-(3-Bromophenyl)-3-phenyl-2,3-dihydroquinazolin-4(1H)-one (**12a**)*

White soild. Mp: 151.3-153.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 7.6 Hz, 1H), 7.51 (s, 1H), 7.40 (d, J = 8.0 Hz, 1H), 7.32-7.30 (m, 4H), 7.23-7.19 (m, 3H), 7.14 (t, J = 8.0 Hz, 1H), 6.92 (t, J = 7.6 Hz, 1H), 6.66 (d, J = 8.0 Hz, 1H), 6.07(s, 1H), 4.82 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0, 144.9, 142.3, 140.5, 134.2, 132.2, 130.5, 130.0, 129.2, 127.1, 126.9, 125.5, 123.0, 120.1, 117.1, 115.2, 74.0; HRMS Calcd for $C_{20}H_{16}BrN_2O$ (M + H^+): 379.0441; Found: 379.0444.

*4.3.24. 2-(2-Bromophenyl)-3-phenyl-2,3-dihydroquinazolin-4(1H)-one (**13a**)*

White soild. Mp: 135.3-137.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 7.6 Hz, 1H), 7.57 (dd, J = 12.0, 8.0 Hz, 2H), 7.36-7.30 (m, 2H), 7.27-7.21 (m, 5H), 7.16 (t, J = 8.0 Hz, 1H), 6.86 (t, J = 7.6 Hz, 1H), 6.58 (d, J = 8.0 Hz, 1H), 6.39 (s, 1H), 5.36 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 144.7, 140.8, 138.2, 134.2, 133.7, 130.5, 129.1, 129.0, 128.5, 128.0, 126.9, 125.9, 121.6, 119.7, 116.6, 115.0, 73.3; HRMS Calcd for $C_{20}H_{16}BrN_2O$ (M + H^+): 379.0441; Found: 379.0443.

*4.3.25. 2-(4-Nitrophenyl)-3-phenyl-2,3-dihydroquinazolin-4(1H)-one (**14a**)*

Yellow soild. Mp: 173.8-177.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 8.4 Hz, 2H), 8.04 (d, J = 7.6 Hz,1H), 7.56 (d, J = 8.4 Hz, 2H), 7.37-7.30 (m, 3H), 7.21-7.19 (m, 2H), 7.01 (d, J = 8.8 Hz, 1H), 6.95 (t, J = 7.6 Hz, 1H), 6.70 (d, J = 8.0 Hz, 1H), 6.22 (s, 1H), 4.85 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 148.3, 146.9, 144.6, 140.4, 137.2, 134.4, 129.4, 128.0, 127.4, 126.7, 124.2, 120.7, 117.4, 115.6, 73.8; HRMS Calcd for $C_{20}H_{16}N_3O_3$ (M + H^+): 346.1184; Found: 346.1186.

*4.3.26. Methyl 4-(4-oxo-3-phenyl-1,2,3,4-tetrahydroquinazolin-2-yl)benzoate (**15a**)*

White solid. Mp: 180.8-182.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 7.6 Hz, 1H), 7.82 (d, J = 8.0 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 7.22-7.17 (m, 3H), 7.10-7.08 (m, 3H), 6.78 (t, J = 7.6 Hz, 1H), 6.53 (d, J = 8.0 Hz, 1H), 6.00 (s, 1H), 5.13 (s, 1H), 3.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 163.1, 145.2, 144.8, 140.5, 134.2, 130.7, 130.1, 129.2, 129.1, 127.1, 126.9, 126.8, 119.8, 116.8, 115.2, 74.1, 52.3; HRMS Calcd for $C_{22}H_{19}N_2O_3$ (M + H^+): 359.1390; Found: 359.1392.

*4.3.27. 4-(4-Oxo-3-phenyl-1,2,3,4-tetrahydroquinazolin-2-yl)benzonitrile (**16a**)*

White solid. Mp: 202.4-204.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 7.6 Hz, 1H), 7.46-7.44 (m, 2H), 7.39-7.38 (m, 2H), 7.24-7.19 (m, 3H), 7.14-7.08 (m, 3H), 6.82 (t, J = 7.2 Hz, 1H), 6.57 (d, J = 8.0 Hz, 1H), 6.03 (s, 1H), 5.17 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.9, 145.0, 144.8, 140.3, 134.3, 132.6, 129.3, 129.0, 127.6, 127.2, 126.6, 120.1, 118.3, 116.8, 115.4, 112.8, 73.7; HRMS Calcd for $C_{12}H_{16}N_3O$ (M + H^+): 326.1288; Found: 326.1285.

*4.3.28. 3-Phenyl-2-(4-(trifluoromethyl)phenyl)-2,3-dihydroquinazolin-4(1H)-one (**17a**)*

White solid. Mp: 213.8-235.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (dd, J = 7.6, 1.2 Hz, 1H), 7.44-7.38 (m, 4H), 7.24-7.18 (m, 3H), 7.13-7.10 (m, 3H), 6.81 (t, J = 7.6 Hz, 1H), 6.55 (d, J = 8.0

Hz, 1H), 6.02 (s, 1H), 5.11 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0, 145.0, 144.0, 140.6, 134.3, 129.3, 129.1, 127.2, 127.1, 126.7, 125.9, 125.8, 125.8, 125.7, 120.0, 117.0, 115.4, 73.9; HRMS Calcd for $C_{21}H_{16}F_3N_2O$ (M + H^+): 369.1209; Found: 369.1206.

*4.3.29. 2-(Naphthalen-1-yl)-3-phenyl-2,3-dihydroquinazolin-4(1H)-one (**18a**)*

White solid. Mp: 221.8-223.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, J = 8.0 Hz, 1H), 8.00 (d, J = 8.0 Hz, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.53 (d, J = 7.2 Hz, 1H), 7.49-7.40 (m, 3H), 7.24 (t, J = 8.0 Hz, 1H), 7.17-7.10 (m, 3H), 7.08-7.04 (m, 1H), 7.00-6.96 (m, 1H), 6.81-6.77 (m, 2H), 6.41 (d, J = 8.0 Hz, 1H), 5.05 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 145.6, 140.5, 135.3, 134.3, 134.1, 133.5, 130.1, 129.9, 129.4, 129.2, 128.8, 126.9, 126.7, 126.2, 126.1, 125.2, 125.1, 119.8, 116.6, 115.2, 72.8; HRMS Calcd for $C_{24}H_{19}N_2O$ (M + H^+): 351.1492; Found: 351.1494.

*4.3.30. 3-Phenyl-2-(pyridin-3-yl)-2,3-dihydroquinazolin-4(1H)-one (**19a**)*

White solid. Mp: 227.5-229.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, J = 2.0 Hz, 1H), 8.44 (dd, J = 4.8, 1.6 Hz, 1H), 7.95 (dd, J = 7.6, 1.2 Hz, 1H), 7.68 (dt, J = 8.0, 1.6 Hz, 1H), 7.28-7.19 (m, 3H), 7.15-7.10 (m, 4H), 6.85 (t, J = 7.6 Hz, 1H), 6.61 (d, J = 8.0 Hz, 1H), 6.10 (s, 1H), 4.91 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0, 150.3, 148.5, 145.0, 140.3, 135.6, 134.6, 134.3, 129.4, 127.3, 127.0, 125.2, 123.8, 120.3, 117.2, 115.4, 72.7; HRMS Calcd for $C_{19}H_{16}N_3O$ (M + H^+): 302.1288; Found: 302.1289.

*4.3.31. 3-Phenyl-2-(pyridin-2-yl)-2,3-dihydroquinazolin-4(1H)-one (**20a**)*

White solid. Mp: 221.8-223.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, J = 4.8 Hz, 1H), 7.91 (d, J = 7.6 Hz, 1H), 7.53 (t, J = 7.6 Hz, 1H), 7.43 (d, J = 8.0 Hz, 1H), 7.28-7.23 (m, 3H), 7.16-7.09 (m, 4H), 6.74 (t, J = 7.6 Hz, 1H), 6.53 (d, J = 8.0 Hz, 1H), 6.00 (s, 1H), 5.05 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0, 159.0, 149.8, 145.6, 141.1, 137.2, 134.0, 129.1, 129.0, 126.5, 125.5, 123.5, 121.2, 119.6, 117.0, 115.3, 74.4; HRMS Calcd for $C_{19}H_{16}N_3O$ (M + H^+): 302.1288; Found: 302.1286.

*4.3.32. 3-Phenyl-2-(thiophen-2-yl)-2,3-dihydroquinazolin-4(1H)-one (**22a**)*

White soild. Mp: 127.3-129.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 7.6 Hz, 1H), 7.34 (t, J = 7.6 Hz, 3H), 7.29-7.24 (m, 3H), 7.15 (d, J = 4.8 Hz, 1H), 6.94 (d, J = 8.0 Hz, 1H), 6.91 (d, J = 3.6 Hz, 1H), 6.82 (t, J = 4.0 Hz, 1H), 6.70 (d, J = 8.0 Hz, 1H), 6.30 (s, 1H), 5.12 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 145.0, 143.7, 140.5, 134.0, 129.2, 129.1, 127.2, 127.0, 126.8, 126.5, 126.1, 120.3, 117.4, 115.6, 71.0; HRMS Calcd for $C_{18}H_{15}N_2OS$ (M + H^+): 307.0900; Found: 307.0903.

*4.3.33. 2-Methyl-2,3-diphenyl-2,3-dihydroquinazolin-4(1H)-one (**23a**)*

White solid. Mp: 161.3-163.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 7.6 Hz, 1H), 7.54 (d, J = 6.4 Hz, 2H), 7.30-7.19 (m, 8H), 7.05 (brs, 2H), 6.84 (t, J = 7.6 Hz, 1H), 6.59 (d, J = 8.0 Hz, 1H), 1.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 145.1, 143.6, 138.9, 133.9, 130.0, 129.2, 128.8, 128.6, 128.4, 127.6, 126.7, 119.4, 116.4, 114.6, 76.6, 27.7; HRMS Calcd for $C_{21}H_{19}N_2O$ (M + H^+): 315.1492; Found: 315.1490.

*4.3.34. 3'-Phenyl-1'H-spiro[cyclohexane-1,2'-quinazolin]-4'(3'H)-one (**24a**)*

Yellow soild. Mp: 111.8-113.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 7.6 Hz, 1H), 7.44-7.31 (m, 4H), 7.23 (d, J = 7.2 Hz, 2H), 6.87 (t, J = 7.6 Hz, 1H), 6.74 (d, J = 8.0 Hz, 1H), 4.75 (brs, 1H), 1.68-1.61 (m, 2H), 1.44-1.40 (m, 2H), 1.28-1.26 (m, 4H), 0.88 (t, J = 6.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 144.5, 138.2, 133.6, 130.5, 129.2, 129.1, 128.1, 119.4, 117.4, 115.3, 73.5, 35.2, 32.1, 29.8, 29.7, 24.5, 22.6, 14.2; HRMS Calcd for $C_{19}H_{21}N_2O$ (M + H^+): 293.1648; Found: 293.1650.

*4.3.35. 6-Methyl-2,3-diphenyl-2,3-dihydroquinazolin-4(1H)-one (**25a**)*

White solid. Mp: 165.1-167.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.26 (brs, 2H), 7.17 (brs, 5H), 7.12-7.01 (m, 3H), 6.81 (t, J = 6.8 Hz, 1H), 6.46 (d, J = 7.6 Hz, 1H), 5.96 (s, 1H), 4.20 (s, 1H), 2.19 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.4, 143.1, 140.9, 140.1, 134.9, 129.0, 129.0, 128.9, 128.8, 126.9, 126.8, 126.7, 117.3, 115.4, 112.8, 74.7, 20.7; HRMS Calcd for $C_{21}H_{19}N_2O$ (M + H^+): 315.1492; Found: 315.1495.

*4.3.36. 8-Methoxy-2,3-diphenyl-2,3-dihydroquinazolin-4(1H)-one (**26a**)*

White solid. Mp: 193.3-197.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 8.0 Hz, 1H), 7.31-7.29 (m, 2H), 7.20-7.19 (m, 5H), 7.12-7.10 (m, 3H), 6.81 (d, J = 7.6 Hz, 1H), 6.74 (t, J = 7.6 Hz, 1H), 6.09 (s, 1H), 5.14 (s, 1H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 146.2, 140.7, 140.1, 136.2, 129.1, 129.0, 128.8, 127.3, 127.0, 126.9, 120.5, 118.4, 116.5, 113.5, 74.9, 55.8; HRMS Calcd for $C_{21}H_{19}N_2O_2$ (M + H^+): 331.1441; Found: 331.1444.

*4.3.37. 8-Methoxy-3-octyl-2-(4-(trifluoromethyl)phenyl)-2,3-dihydroquinazolin-4(1H)-one (**26b**)*

White oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60-7.56 (m, 3H), 7.50-7.48 (m, 2H), 6.83-6.76(m, 2H), 5.85 (s, 1H), 5.04 (s, 1H), 4.07-4.00 (m, 1H), 3.77 (s, 3H), 2.76-2.69 (m, 1H), 1.65-1.52 (m, 2H), 1.23 (s, 10H), 0.86 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0, 146.0, 144.3, 135.0, 126.8, 126.1, 126.1, 126.0, 126.0, 120.0, 118.5, 116.0, 115.4, 113.3, 71.5, 55.8, 45.2, 31.9, 29.4, 29.3, 27.8, 27.0, 22.7, 14.2; HRMS Calcd for $C_{24}H_{30}F_3N_2O_2$ (M + H^+): 435.2254; Found: 435.2256.

*4.3.38. 6,7-Dimethoxy-2,3-diphenyl-2,3-dihydroquinazolin-4(1H)-one (**27a**)*

White solid. Mp: 138.3-140.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (s, 1H), 7.32-7.19 (m, 9H), 6.76 (d, J = 8.0 Hz, 1H), 6.54 (d, J = 8.0 Hz, 1H), 6.04 (s, 1H), 5.41 (brs, 1H), 4.00 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7, 154.4, 146.8, 143.8, 139.5, 130.3, 129.5, 128.9, 128.7, 127.6, 126.5, 112.8, 108.3, 106.1, 99.1, 74.7, 56.5, 56.4; HRMS Calcd for $C_{22}H_{21}N_2O_3$ (M + H^+): 361.1547; Found: 361.1549.

*4.3.39. 6-Fluoro-2,3-diphenyl-2,3-dihydroquinazolin-4(1H)-one (**28a**)*

White solid. Mp: 177.3-179.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (dd, J = 8.8, 2.8 Hz, 1H), 7.35-7.33 (m, 2H), 7.29-7.25 (m, 5H), 7.19-7.15 (m, 3H), 7.00 (td, J = 8.8, 2.8 Hz, 1H), 6.59 (dd, J = 8.8, 4.0 Hz, 1H), 6.05 (s, 1H), 4.91 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 162.4, 158.1, 155.7, 141.7, 141.6, 140.5, 139.6, 129.1, 129.0, 128.8, 127.0, 126.9, 126.8, 121.5, 121.3, 118.5, 118.4, 117.0, 116.9, 114.9, 114.6, 74.7; HRMS Calcd for $C_{20}H_{26}FN_2O$ (M + H^+): 319.1241; Found: 319.1244.

*4.3.40. 3-Benzyl-6-fluoro-2-(p-tolyl)-2,3-dihydroquinazolin-4(1H)-one (**29a**)*

White solid. Mp: 138.3-140.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.4 Hz, 1H), 7.31-7.27 (m, 3H), 7.21-7.19 (m, 2H), 7.15-7.10 (m, 4H), 6.98-6.94 (m, 1H), 6.47 (dd, J = 8.8, 4.0 Hz, 1H), 5.59-5.53 (m, 2H), 4.55 (brs, 1H), 3.66 (d, J = 15.2 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6, 157.8, 157.7,

155.5, 155.4, 141.6, 141.5, 139.4, 136.7, 136.1, 129.7, 128.7, 128.1, 127.6, 126.6, 121.1, 120.9, 117.1, 117.0, 116.9, 116.1, 116.0, 114.7, 114.5, 71.0, 47.1, 21.3; HRMS Calcd for $C_{22}H_{20}FN_2O$ (M + H^+): 347.1554; Found: 347.1557.

*4.3.41. 6-Chloro-2,3-diphenyl-2,3-dihydroquinazolin-4(1H)-one (**30a**)*

White solid. Mp: 193.3-197.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.27-7.23 (m, 2H), 7.20-7.18 (m, 6H), 7.10-7.08 (m, 3H), 6.46 (dd, *J* = 8.4, 4.0 Hz, 1H), 5.96 (s, 1H), 5.04 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 143.9, 140.4, 139.6, 133.9, 129.2, 129.1, 128.9, 128.5, 127.1, 126.9, 126.8, 124.6, 119.0, 116.6, 74.6; HRMS Calcd for $C_{20}H_{16}ClN_2O$ (M + H^+): 335.0946; Found: 335.0949.

*4.3.42. 7-Chloro-3-cyclohexyl-2-(4-fluorophenyl)-2,3-dihydroquinazolin-4(1H)-one (**31a**)*

White soild. Mp: 105.3-107.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.4 Hz, 1H), 7.28-7.25 (m, 2H), 6.96 (t, *J* = 8.4 Hz, 2H), 6.79 (d, *J* = 8.4 Hz, 1H), 6.48 (s, 1H), 5.75 (s, 1H), 4.85 (s, 1H), 4.56-4.50 (m, 1H), 1.83-1.79 (m, 2H), 1.68-1.53 (m, 4H), 1.45-1.38 (m, 1H), 1.31-1.26 (m, 1H), 1.07-0.94 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 161.9, 161.6, 144.9, 139.3, 137.9, 137.8, 130.1, 127.5, 127.4, 120.0, 116.1, 116.0, 115.8, 114.7, 67.0, 53.8, 31.3, 31.1, 26.0, 25.9, 25.5; HRMS Calcd for $C_{20}H_{21}ClFN_2O$ (M + H^+): 359.1321; Found: 359.1325.

*4.3.43. 6-Bromo-2,3-diphenyl-2,3-dihydroquinazolin-4(1H)-one (**32a**)*

White solid. Mp: 228.8-229.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.30-7.19 (m, 9H), 7.13-7.08 (m, 2H), 6.44 (dd, *J* = 8.0, 3.2 Hz, 1H), 5.99 (s, 1H), 4.90 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.0, 144.3, 140.4, 139.6, 136.7, 131.6, 129.3, 129.1, 128.9, 127.1, 126.9, 126.8, 118.4, 116.9, 111.6, 74.6; HRMS Calcd for $C_{20}H_{16}BrN_2O$ (M + H^+): 379.0441; Found: 379.0443.

*4.3.44. 1-Methyl-2,3-diphenyl-2,3-dihydroquinazolin-4(1H)-one (**33a**)*

White solid. Mp: 163.3-167.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 7.6 Hz, 1H), 7.31 (t, *J* = 7.6 Hz, 1H), 7.27-7.21 (m, 2H), 7.19-7.17 (m, 3H), 7.13-711 (m, 5H), 6.82 (t, *J* = 7.6 Hz, 1H), 6.50 (d, *J* = 8.4 Hz, 1H), 5.71 (s, 1H), 2.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 146.5, 140.9, 137.6, 134.3, 129.2, 129.2, 129.1, 128.8, 127.2, 127.0, 126.5, 118.7, 117.3, 112.6, 81.7, 36.5; HRMS Calcd for $C_{21}H_{19}N_2O$ (M + H^+): 315.1492; Found: 315.1494.

*4.3.45. 2-(4-Chlorophenyl)-1-methyl-3-phenethyl-2,3-dihydroquinazolin-4(1H)-one (**33b**)*

White oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.6 Hz, 1H), 7.35-7.19 (m, 8H), 7.03 (d, *J* = 8.4 Hz, 2H), 6.86 (t, *J* = 7.6 Hz, 1H), 6.43 (d, *J* = 8.4 Hz, 1H), 4.91 (s, 1H), 4.29-4.24 (m, 1H), 3.03-2.84 (m, 3H), 2.60 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 145.9, 139.3, 135.8, 135.1, 134.0, 129.1, 128.7, 128.6, 127.8, 126.6, 118.5, 116.7, 112.1, 78.8, 47.3, 35.6, 34.6; HRMS Calcd for $C_{23}H_{22}ClN_2O$ (M + H^+): 377.1415; Found: 377.1417.

*4.3.46. 3-Cyclohexyl-1-methyl-2-(p-tolyl)-2,3-dihydroquinazolin-4(1H)-one (**33c**)*

White soild. Mp: 132.3-134.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.6 Hz, 1H), 7.30-7.26 (m, 1H), 7.09 (d, *J* = 7.6 Hz, 2H), 7.02 (d, *J* = 7.6 Hz, 2H), 6.85 (t, *J* = 7.6 Hz, 1H), 6.39 (d, *J* = 8.0 Hz, 1H), 5.45 (s, 1H), 4.55 (t, *J* = 12.0 Hz, 1H), 2.84 (s, 3H), 2.27 (s, 3H), 1.87-1.80 (m, 2H), 1.74-1.60 (m, 4H), 1.49-1.41 (m, 2H), 1.09-0.92 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 145.6, 138.5, 135.5, 133.5, 129.2, 128.6, 126.3, 118.6, 118.5, 112.6, 74.6, 53.7, 36.1, 31.4, 30.8, 26.1, 25.9, 25.6, 21.2; HRMS Calcd for $C_{22}H_{27}N_2O$ (M + H^+): 335.2118; Found: 335.2119.

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References and notes

1. Vo, C. T.; Bode, J. W. *J. Org. Chem.* **2014**, *79*, 2809-2815.
2. Zhang, B.; Studer, A. *Chem. Soc. Rev.* **2014**, *44*, 3505-3521.
3. Albano, G.; Aronica, L.A. *Eur. J. Org. Chem.* **2017**, *2017*, 7204-7221.
4. Diez-Poza, C.; Barbero, A. *Eur. J. Org. Chem.* **2017**, *2017*, 4651-4665.
5. Noel, R.; Gupta, N.; Pons, V.; Goudet, A.; Garcia-Castillo, M. D.; Michau, A.; Martinez, J.; Buisson, D. A.; Johannes, L.; Gillet, D.; Barbier, J.; Cintrat, J. C. *J. Med. Chem.* **2013**, *56*, 3404-3413.
6. Williams, R.; Niswender, C. M.; Luo, Q.; Le, U.; Conn, P. J.; Lindsley, C.W. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 962-966.
7. Kshirsagar, U. A. *Org. Biomol. Chem.* **2015**, *13*, 9336-9352.
8. Rambabu, D.; Kumar, S. K.; Sreenivas, B. Y.; Sandra, S.; Kandale, A.; Misra, P.; Rao, B.; Manojit Pal, M.V. *Tetrahedron Lett.* **2013**, *54*, 495-501.
9. Atobe, M.; Nagami, T.; Muramatsu, S.; Ohno, T.; Kitagawa, M.; Suzuki, H.; Ishiguro, M.; Watanabe, A.; Kawanishi, M. *J. Med. Chem.* **2019**, *62*, 1468-1483.
10. Safaei, H. R.; Shekouhy, M.; Ghorbanzadeh, S. *Chem. Select* **2018**, **3**, 4750-4759.
11. Zhang, X.; Li, Z.; Ding, Q.; Li, X.; Fan, X.; Zhang, G. *Adv. Synth. Catal.* **2019**, *361*, 976-982.
12. Das, S.; Santra, S.; Jana, S.; Zyryanov, G.; Majee, A.; Hajra, A. *Eur. J. Org. Chem.* **2017**, *33*, 4955-4962.
13. Ayyanar, S.; Vijaya, P.; Mariyappan, M.; Kumar, A.; Sadhasivam, V.; Balkrishnan, S.; Chinnadurai, C.; Murgesan, S. *New J. Chem.* **2017**, *41*, 7980-7986.
14. Zhao, W.; Ma, W.; Xiao, T.; Li, F. *Chem. Select* **2017**, *2*, 3608-3612.
15. Majumdar, B.; Mandani, S.; Bhattacharya, T.; Sarma, D.; Sarma, T. K. *J. Org. Chem.* **2017**, *82*, 2097-2106.
16. Borase, P. N.; Thale, P. B.; Shankarling, G. S. *RSC Adv.* **2016**, *6*, 63078-63083.
17. Yashwantrao, G.; Jejurkar, V. P.; Kshatriya, R.; Saha, S. *ACS Sustainable Chem. Eng.* **2019**, *7*, 13551-13558.
18. Jejurkar, V. P.; Mali, S. N.; Kshatriya, R.; Chaudhari, H. K.; Synthesis, S. S. *Chem. Select* **2019**, *4*, 9470-9475.
19. Salehi, P.; Dabiri, M.; Zolfigol, M. A.; Baghbanzadeh, M. *Synlett* **2005**, *7*, 1155–1157.
20. Dabiri, M.; Salehi, P.; Otokesh, S.; Baghbanzadeh, M.; Kozehgary, G.; Mohammadi, A. A. *Tetrahedron Lett.* **2005**, *46*, 6123-6126.
21. Rostamizadeh, S.; Amani, A. M.; Mahdavinia, G. H.; Sepehrian, H.; Ebrahimi, S. *Synthesis* **2010**, *8*, 1356-1360.
22. Saffar-Teluri, A.; Bolouk, S. *Monatsh. Chem.* **2010**, *141*, 1113-1115.
23. Narasimhulu, M.; Lee, Y. R. *Tetrahedron* **2011**, *67*, 9627-9634.
24. Ghorbani-Choghamarani, A.; Taghipour, T. *Lett. Org. Chem.* **2011**, *8*, 470-476.
25. Niknam, K.; Jafarpour, N.; Niknam, E. *Chin. Chem. Lett.* **2011**, *22*, 69-72.
26. Niknam, K.; Mohammadizadeh, M. R.; Mirzaee, S. *Chin. J. Chem.* **2011**, *29*, 1417-1422.
27. Wang, M.; Zhang, T. T.; Gao, J. J.; Liang, Y. *Chem. Het. Compd.* **2012**, *48*, 897-902.
28. Wu, J.; Du, X.; Ma, J.; Zhang, Y.; Shi, Q.; Luo, L.; Song, B.; Yang, S.; Hu, D. *Green Chem.* **2014**, *16*, 3210-3217.
29. Shaterian, H. R.; Rigi, F. *Res. Chem. Intermed.* **2015**, *41*, 721-738.
30. Shaterian, H. R.; Oveisi, A. R.; Honarmand, M. *Synth. Commun.* **2010**, *40*, 1231-1242.
31. Wang, M.; Zhang, T. T.; Liang, Y.; Gao, J. J. *Chin. Chem. Lett.* **2011**, *22*, 1423-1426.
32. Majid, G.; Kobra, A.; Hamed, M. P.; Reza, S. H. *Chin. J. Chem.* **2011**, *29*, 1617-1623.
33. Shaterian, H. R.; Fahimi, N.; Azizi, K. *Res. Chem. Intermed.* **2014**, *40*, 1879-1898.

34. Chen, B. H.; Li, J. T.; Chen, G. F. *Ultrason. Sonochem.* **2015**, *23*, 59-65.
35. Magyar, Á.; Hell, Z. *Catal. Lett.* **2016**, *146*, 1153-1162.
36. Wu, S. J.; Zhao, Z. Q.; Gao, J. S.; Chen, B. H.; Chen, G. F. *Res. Chem. Intermed.* 2019, 45, 2327-2339.
37. Zhang, Z. H.; Lu, H. Y.; Yang, S. H.; Gao, J. W. *J. Comb. Chem.* **2010**, *12*, 643-646.
38. Kassaee, M. Z.; Rostamizadeh, S.; Shadjou, N.; Motamedi, E.; Esmaeelzadeh, M. *J. Heterocycl. Chem.* **2010**, *47*, 1421-1424.
39. Yavari, I.; Beheshti, S. *J. Iran. Chem. Soc.* **2011**, *8*, 1030-1035.
40. Safari, J.; Gandomi-Ravandi, S. *J. Mol. Catal. A Chem.* **2013**, *371*, 135-140.
41. Ren, D.; Ma, Y.; Wang,W.; Wu, H. *Tetrahedron* **2014**, *70*, 5274-5282.
42. Santra, S.; Rahman, M.; Roy, A.; Majee, A.; Hajra, A. *Cat. Commun.* **2014**, *49*, 52-57.
43. Zhang, J.; Bharathi, A.; Roopan, S. M.; Kajbafvala, A.; Padmaja, R. D.; Darsana, M. S.; Kumari, G. N. *Chin. Chem. Lett.* **2014**, *25*, 324-326.
44. Toosi, F. S.; Khakzadi, M. *Res. Chem. Intermed.* **2015**, *41*, 311-317.
45. Dam, B.; Patil, R. A.; Ma, Y.; Pal, A. K. *New J. Chem.* **2017**, *41*, 6553-6563.
46. Safaei-Ghomi, J.; Teymuri, R. *J. Chin. Chem. Soc.* **2019**, *66*, 1490-1498.
47. Wang, L. M.; Hu, L.; Shao, J. H.; Yu, J. J.; Zhang, L.J. *J. Fluorine Chem.* **2008**, *129*, 1139-1145.
48. Song, Z.; Liu, L.; Wang, Y.; Sun, X. *Res. Chem. Intermed.* **2012**, *38*, 1091-1099.
49. Wang, M.; Zhang, T. T.; Liang, Y.; Gao, J. J. *Monatsh Chem.* **2012**, *143*, 835-839.
50. Chen, J. X.; Su, W. K.; Wu, H. Y.; Liu, M. C.; Jin, C. *Green Chem.* **2007**, *9*, 972-975.
51. Dabiri, M.; Salehi, P.; Baghbanzadeh, M. *Monatsh. Chem.* **2007**, *138*, 1191-1194.
52. Darvatkar, N. B.; Bhilare, S. V.; Deorukhkar, A. R.; Raut, D. G.; Salunkh, M. M. *Green Chem. Lett. Rev.* **2010**, *3*, 301-306.
53. Wang, M.; Zhang, T. T.; Song, Z. G. *Chin. Chem. Lett.* **2011**, *22*, 427-430.
54. Fard, M. A. B.; Mobinikhaledi, A.; Hamidinasab, M. *Synth. React. Inorg. Metal-Org. Nano-Metal Chem.* **2014**, *44*, 567-571.
55. Sheldon, R. A. *Chem. Soc. Rev.* **2012**, *41*, 1437-1451.
56. Petkovic, M.; Seddon, K. R.; Rebelo, L. P. N.; Pereira, C. S. *Chem. Soc. Rev.* **2011**, *40*, 1383-1403.
57. El-Harairy, A.; Yiliqi; Lai, B.; Vaccaro, L.; Li, M.; Gu, Y. *Adv. Synth. Catal.* **2019**, *361*, 3342-3350.
58. Li, M.; Wu, F.; Gu, Y. *Chin. J. Catal.* **2019**, *40*, 1135-1140.
59. Bourlinos, A. B.; Raman, K.; Herrera, R.; Zhang, Q.; Archer, L. A.; Giannelis, E. P. *J. Am. Chem. Soc.* **2004**, *126*, 15358-15359.
60. Rickert, P. G.; Antonio, M. R.; Firestone, M.; Kubatko, A. K. A.; Szreder, T.; Wishart, J. F.; Dietz, M. L. *Dalton Trans.* **2007**, 529-531.
61. Leng, Y.; Wang, J.; Zhu, D.; Ren, X.; Ge, H.; Shen, L. *Angew. Chem.* **2008**, *121*, 174-177; *Angew. Chem. Int. Ed.* **2009**, *48*, 168-171.
62. Leng, Y.; Wang, J.; Zhu, D.; Zhang, M.; Zhao, P; Long, Z.; Huang, J. *Green Chem.* **2011**, *13*, 1636-1639.
63. Leng, Y.; Liu, J.; Jiang, P.; Wang, J. *ACS Sustainable Chem. Eng.* **2015**, *3*, 170-176.
64. Polshettiwar, V.; Varma, R. S. *Acc. Chem. Res.* **2008**, *41*, 629-639.
65. Kappe, C. O.; Stadler, A.; Dallinger, D. *In Microwaves in Organic and Medicinal Chemistry*; Mannhold, R., Kubinyi, H., Folkers, G., Eds.; Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, Germany, 2012.
66. Kappe, C. O. *Chem. Soc. Rev.* **2008**, *37*, 1127-1139.
67. Chen, Z.; Fu, R.; Chai, W.; Zheng, H.; Sun, L.; Lu, Q.; Yuan, R. *Tetrahedron* **2014**, *70*, 2237-2245.
68. Fu, R.; Yang, Y.; Chen, Z.; Lai, W.; Ma, Y.; Wang, Q.; Yuan, R. *Tetrahedron* **2014**, *70*, 9492-9499.
69. Fu, R.; Yang, Y.; Ma, Y.; Yang, F.; Li, J.; Chai, W.; Wang, Q.; Yuan, R. *Tetrahedron Lett.* **2015**, *56*, 4527-4531.
70. Fu, R.; Yang, Y.; Lai, W.; Ma, Y.; Chen, Z.; Zhou, J.; Chai, W.; Wang, Q.; Yuan, R. *Synth. Commun.* **2015**, *5*, 477-487.
71. Fu, R.; Yang, Y.; Zhang, J.; Shao, J.; Xia, X.; Ma, Y.; Yuan, R. *Org. Biomol. Chem.* **2016**, *14*, 1784-1793.
72. Fu, R.; Yang, Y.; Jin, W.; Gu, H.; Zeng, X.; Chai, W.; Ma, Y.; Wang, Q.; Yi, J.; Yuan, R. *RSC Adv.* **2016**, *6*, 107699-107707.
73. Fu, R.; Yang, Y.; Feng, W.; Ge, Q.; Feng, Y.; Zeng, X.; Chai, W.; Yi, J.; Yuan, R. *Tetrahedron* **2016**, *72*, 8319-8326.
74. Fu, R.; Yang, Y.; Ma, X.; Sun, Y.; Li, J.; Gao, H.; Hu, H.; Zeng, X.; Yi, J. *Molecules* **2017**, *22*, 1531-1542.
75. Mahdavi, M.; Foroughi, N.; Saeedi, M.; Karimi, M.; Alinezhad, H.; Foroumadi, A.; Shafiee, A.; Akbarzadeh, T. *Synlett* **2014**, *25*, 385-388.

Supplementary Material

Supplementary data (copies of the ^{1}H and ^{13}C NMR spectra of all products) associated with this article can be found at http://dx.doi.org/XXXXXXXXXXXX.

Microwave-promoted one-pot three-component synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones catalyzed by heteropolyanion-based ionic liquids under solvent-free conditions

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Highlights:

2,3-Dihydroquinazoline-4(1*H*)-one derivatives have been synthesized via one-pot three-component reaction catalyzed by heteropolyanion-based ionic liquids under solvent-free and microwave-promoted conditions. Wide substrate scope, moderate to excellent yields, solvent-free media and operational simplicity are the main highlights. The catalyst can be recovered and reused.

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Declaration of interests

☒ 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.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: