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A rapid, solvent-free synthesis of 2-aryl-2,3-dihydroquinazolin-4(1*H*)-ones catalyzed by bismuth(III) nitrate pentahydrate

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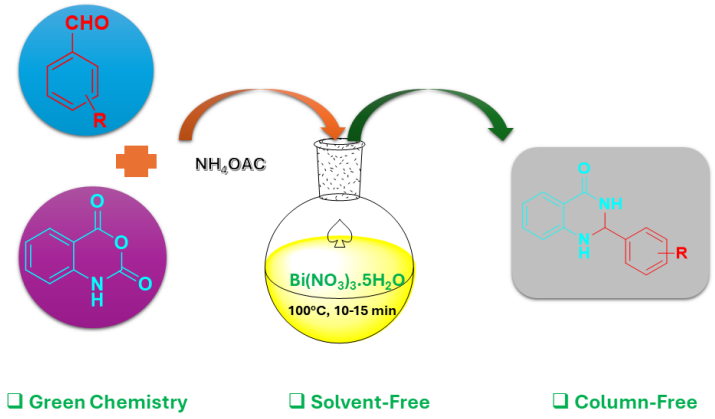
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Abstract

An efficient, solvent-free protocol for the synthesis of 2-aryl-2,3-dihydroquinazolin-4(1*H*)-ones (DHQs) has been developed using bismuth(III) nitrate pentahydrate [$Bi(NO_3)_3{\cdot}5H_2O$] as a catalyst. The method involves a one-pot multicomponent condensation of benzaldehyde, isatoic anhydride, and ammonium acetate under mild reaction conditions. A variety of DHQs were obtained in high to excellent isolated yields, demonstrating the broad substrate scope and functional group tolerance of the catalytic system. The reaction proceeds through imine formation, nucleophilic addition of isatoic anhydride, decarboxylation, and intramolecular cyclization to furnish the DHQ framework. The protocol offers operational simplicity, short reaction times (10-15 min), and good to excellent isolated yields (87-97%) for the investigated aromatic and heteroaromatic aldehydes. In addition, selected green chemistry metrics were calculated and compared with previously reported methods to assess the material efficiency and waste-related characteristics of the present protocol.



Keywords: Quinazoline, $Bi(NO_3)_3.5H_2O$, heterocycles, green synthesis, C-N bond formation, condensation.

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Introduction

Quinazolinones, particularly Dihydroquinazolinones (DHQs), represent a distinguished category of fused nitrogen-containing heterocycles that are prominently featured in biologically active compounds and commercial pharmaceuticals.[1-5] Compounds bearing this scaffold exhibit a wide range of pharmacological effects, such as anticancer, antibacterial, anti-inflammatory, antiviral, and kinase-inhibitory effects. The most important of these is their ability to block the epidermal growth factor receptor (EGFR).[6-8] **Figure 1** represents the Quinazolinone and DHQ-based FDA-approved drugs. Consequently, the development of efficient and sustainable synthetic methodologies for these heterocyclic pharmacophores remains an important objective in heterocyclic and medicinal chemistry.

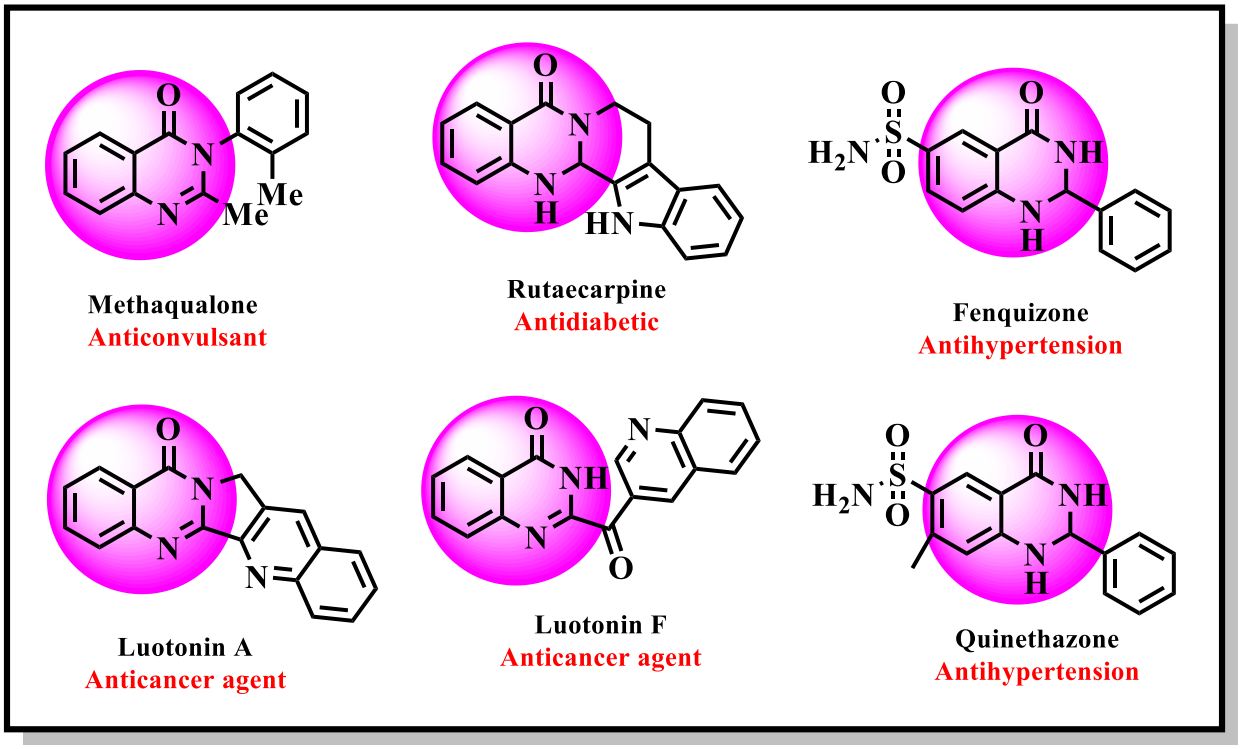


Figure 1. Some FDA-approved drugs bearing quinazolinones/DHQ moieties.

Numerous synthetic methods for DHQ derivatives have been documented, such as multicomponent reactions involving anthranilic acid derivatives, oxidative annulation strategies, and cyclocondensation of 2-aminobenzamides with aldehydes.[9-12] Nevertheless, several of these procedures require transition-metal catalysts like palladium, copper, or ruthenium, high reaction temperatures, stoichiometric oxidants, or severe acidic conditions.[13, 14] These restrictions limit their practical and industrial applicability because they frequently result in poor atom economy, limited substrate tolerance, and environmental concerns.

The development of catalytic systems that reduce solvent consumption, reaction time, and waste generation has attracted considerable attention in organic synthesis. Among the available catalysts, bismuth(III) salts have been widely investigated as Lewis acids in various organic transformations because of their catalytic activity and practical handling characteristics.[15-16] In particular, bismuth(III) nitrate pentahydrate [$Bi(NO_3)_3{\cdot}5H_2O$] has shown exceptional effectiveness in a range of organic transformations, such as heterocycle synthesis, multicomponent reactions, and carbonyl activation.[17-19] [$Bi(NO_3)_3{\cdot}5H_2O$] has been

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employed as a Lewis acid catalyst in various organic transformations, including multicomponent reactions and heterocyclic synthesis. It has also recently been investigated in a variety of transformations, including aromatic iodination,[20] oxidation of alcohols,[21] Michael reactions,[22] aromatic nitration,[23] deprotection of oximes,[24] and conversion of thiocarbonyl compounds into their corresponding carbonyl derivatives.[25] Moreover, many of these reactions were carried out under solvent-free conditions, which is essential for green protocols. This broad range of applications prompted us to further examine its effectiveness in the synthesis of dihydroquinazoline.

A notable contribution in this area was reported by Baltork and co-workers,[26] who developed a Bi-catalyzed synthesis of disubstituted DHQ, which were subsequently oxidised to the corresponding quinazolin-4(3*H*)-ones (**Figure 2**). However, the reported methodology requires primary amines to introduce substituents at the N3 position. Vemula and his team also utilized [$Bi(NO_3)_3{\cdot}5H_2O$] for the synthesis of DHQ *via* a condensation reaction between 2-aminobenzamide and an aldehyde, requiring a reaction time of 12 hours (**Figure 2**).[27] Barebita prepared a bismuth-based catalyst for the synthesis of DHQ.[28] In contrast, the direct synthesis of NH-containing (unsubstituted) DHQ using ammonium acetate as a readily available and inexpensive ammonia source has not been exploited. Moreover, systematic investigations addressing catalyst loading, reaction temperature, solvent effects, catalyst comparison, substrate scope, and quantitative green chemistry metrics for this transformation remain scarce.

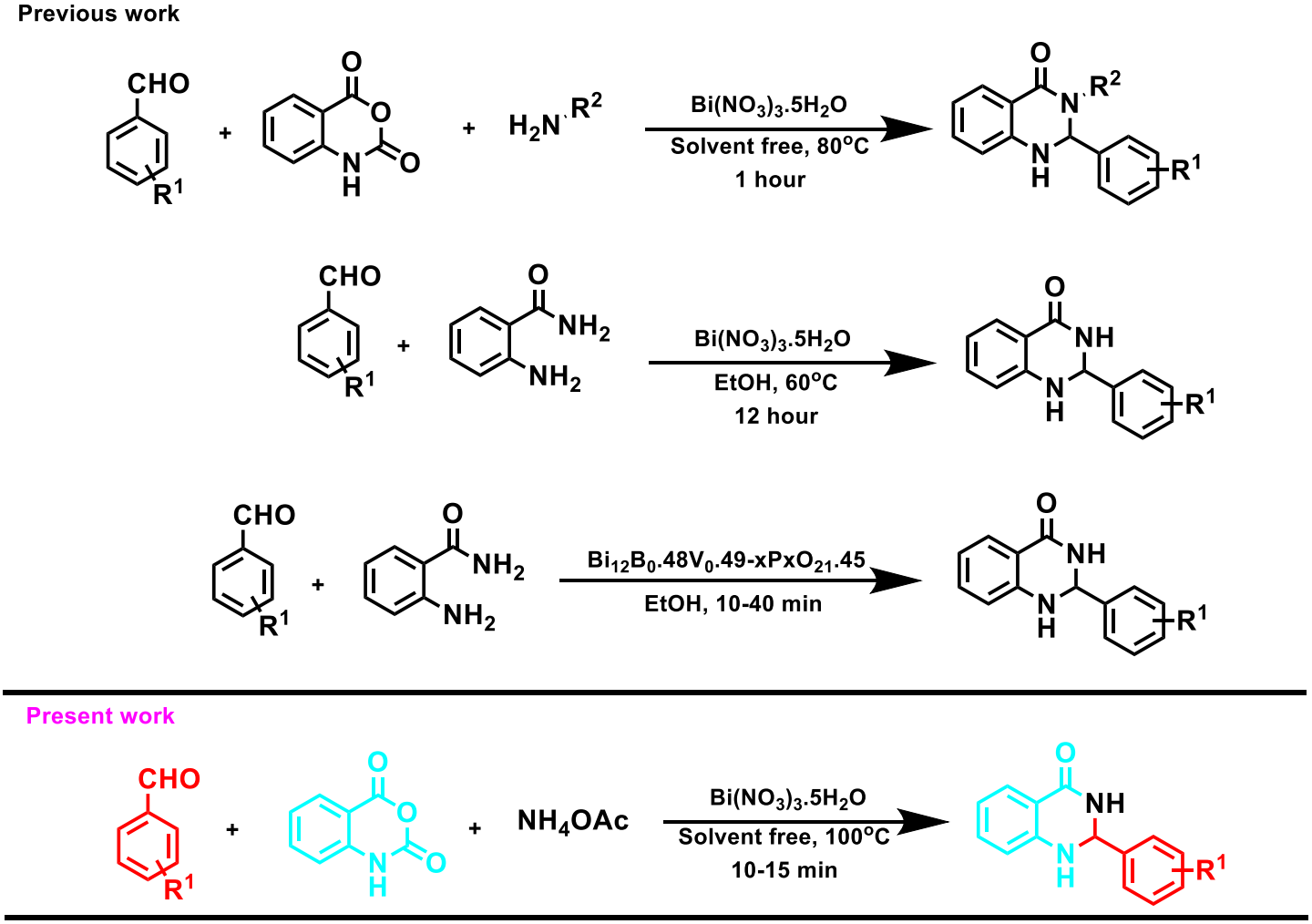


Figure 2. Bismuth-based mediated derivatives of DHQ.

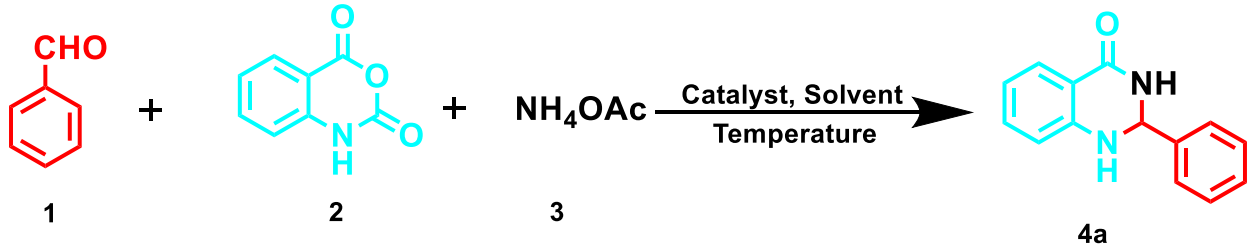
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In the present study, we investigated a one-pot, three-component condensation of isatoic anhydride, aromatic aldehydes, and ammonium acetate using $Bi(NO_3)_3{\cdot}5H_2O$ under solvent-free conditions. Unlike the previously discussed approach involving primary amines to introduce substituents at the N3 position, ammonium acetate serves as an ammonia source for the preparation of NH-containing dihydroquinazolinones. The present protocol employs an inexpensive ammonia source instead of primary amines, affords the desired products within remarkably short reaction times (10-15 min) in excellent isolated yields, and includes comprehensive optimization of catalyst loading, reaction temperature, solvent effects, and catalyst type. In addition, selected green chemistry metrics were calculated and compared with reported methods to evaluate the material efficiency and waste-related characteristics of the developed protocol.

Results and Discussion

The reaction conditions for the synthesis of DHQ were systematically optimized by analysing the effects of different Bi(III) catalysts, catalyst loading, temperature, reaction time, and solvent. As represented in **Scheme 1**, the reaction between benzaldehyde **1**, isatoic anhydride **2**, and ammonium acetate 3 was selected as the model reaction for the synthesis of DHQ derivative (**4a**). The optimization results for the synthesis of DHQ derivatives are summarized in Table 1.

Table 1. Optimization results for the synthesis of DHQ.



Scheme 1.

Entry	Catalyst	Amount of Catalyst (mol%)	Solvent (mL)	Temperature (°C)	Time (min)	Yield[a] (%)
1	-	-	-	100	24h	Trace
2	$Bi(NO_3)_3.5H_2O$	1	-	100	24h	Trace
3	$Bi(NO_3)_3.5H_2O$	2	-	100	12h	35
4	$Bi(NO_3)_3.5H_2O$	3	-	100	30	64
5	$Bi(NO_3)_3.5H_2O$	4	-	100	30	78
6	**$Bi(NO_3)_3.5H_2O$**	**5**	**-**	**100**	**15**	**96**
7	$Bi(NO_3)_3.5H_2O$	6	-	100	15	88
8	$Bi(NO_3)_3.5H_2O$	7	-	100	15	82
9	$Bi(NO_3)_3.5H_2O$	5	-	120	15	80
10	$Bi(NO_3)_3.5H_2O$	5	-	140	15	68
11	$Bi(NO_3)_3.5H_2O$	5	-	80	15	84
12	$Bi(NO_3)_3.5H_2O$	5	-	60	15	72
13	$Bi(NO_3)_3.5H_2O$	5	EtOH	80	60	81
14	$Bi(NO_3)_3.5H_2O$	5	MeOH	65	60	76

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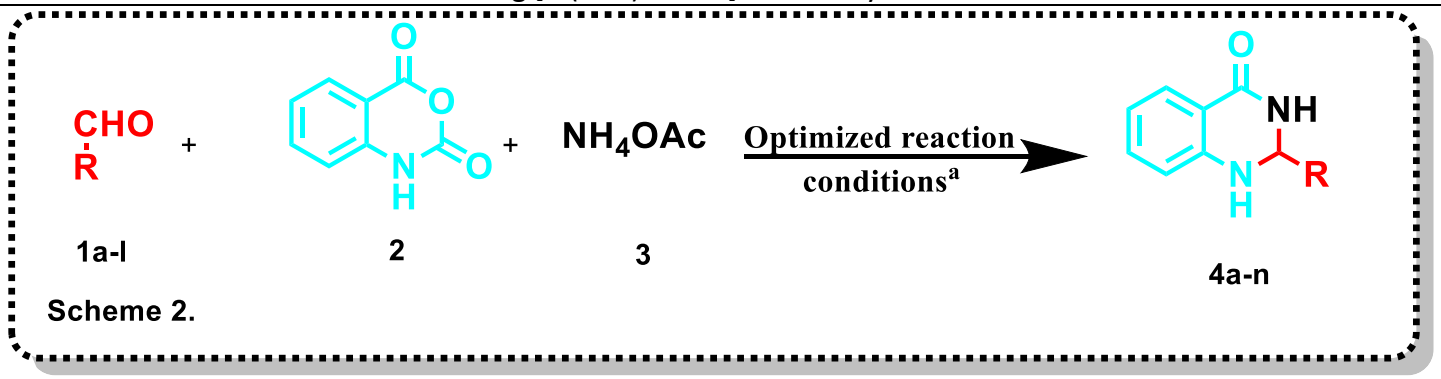
15	$Bi(NO_3)_3.5H_2O$	5	H_2O	100	60	52
16	$Bi(NO_3)_3.5H_2O$	5	ACN	85	60	64
17	$Bi(NO_3)_3.5H_2O$	5	DCM	40	60	28
18	$BiCl_3$	5	-	100	15	72
19	$BiBr_3$	5	-	100	15	60
20	$Bi(OTf)_3$	5	-	100	15	66

[a]Isolated yield; Reaction conditions: benzaldehyde **1a** (1eq.), isatoic anhydride **2** (1eq.), and ammonium acetate **3** (1eq.).

In initial experiments, the absence of any catalyst afforded only trace amounts of product even after prolonged heating (Entry 1). Further studies revealed that lower catalyst loadings (1 to 4 mol%) of $Bi(NO_3)_3.5H_2O$ resulted in poor to moderate yields (trace to 78%) and required longer reaction times (Entry 2-5). However, a gradual increase in the amount of $Bi(NO_3)_3{\cdot}5H_2O$ led to a significant enhancement in product yield, reaching an optimum at 5 mol% under solvent-free conditions at 100 °C, where the desired DHQ was obtained in 96% yield within 15 minutes (Entry 6). It was noted that the aldehydes may also provide media during the reaction. Further increases in catalyst loading caused a noticeable decrease in yield, possibly due to overactivation of reactants, catalyst aggregation, or the formation of side products (Entry 7-8). Temperature screening showed that 100 °C was optimal for this transformation. Both lower and higher temperatures led to diminished yields (Entry 9-12). Solvent screening demonstrated that solvent-free conditions were superior to reactions carried out in common organic solvents, including ethanol (81%), methanol (76%), water (52%), acetonitrile (64%), and dichloromethane (28%) (Entry 13-17). The enhanced efficiency under solvent-free conditions may be attributed to higher effective reactant concentration and improved interaction between the catalyst and substrates. A comparison of different bismuth salts revealed that $Bi(NO_3)_3{\cdot}5H_2O$ afforded a higher yield (96%) than $BiCl_3$ (72%), $BiBr_3$ (60%), and $Bi(OTf)_3$ (66%) under identical reaction conditions (Table 1, entries 6 and 18-20). Previous studies have demonstrated the catalytic utility of $Bi(NO_3)_3{\cdot}5H_2O$ in related dihydroquinazolinone syntheses.[16,26] Nevertheless, the observed differences in catalytic performance do not establish the specific contributions of the nitrate counterion or hydration state, which would require further mechanistic investigation. Overall, the optimized conditions enabled the synthesis of DHQ derivatives within short reaction times and with high isolated yields, without the addition of a reaction solvent.

With the optimized protocol in hand, we further explored the efficacy of the catalyst for the synthesis of different DHQ derivatives using various substituted aldehydes.

Table 2. The derivatization of DHQ using $[Bi(NO_3)_3{\cdot}5H_2O]$ as a catalyst.



Scheme 2.

S. No.	R	Compound	Time (min)	Yield[b] (%)	Melting Point (M. P.)	
					Observed M. P. (°C)	Reported M. P. (°C)

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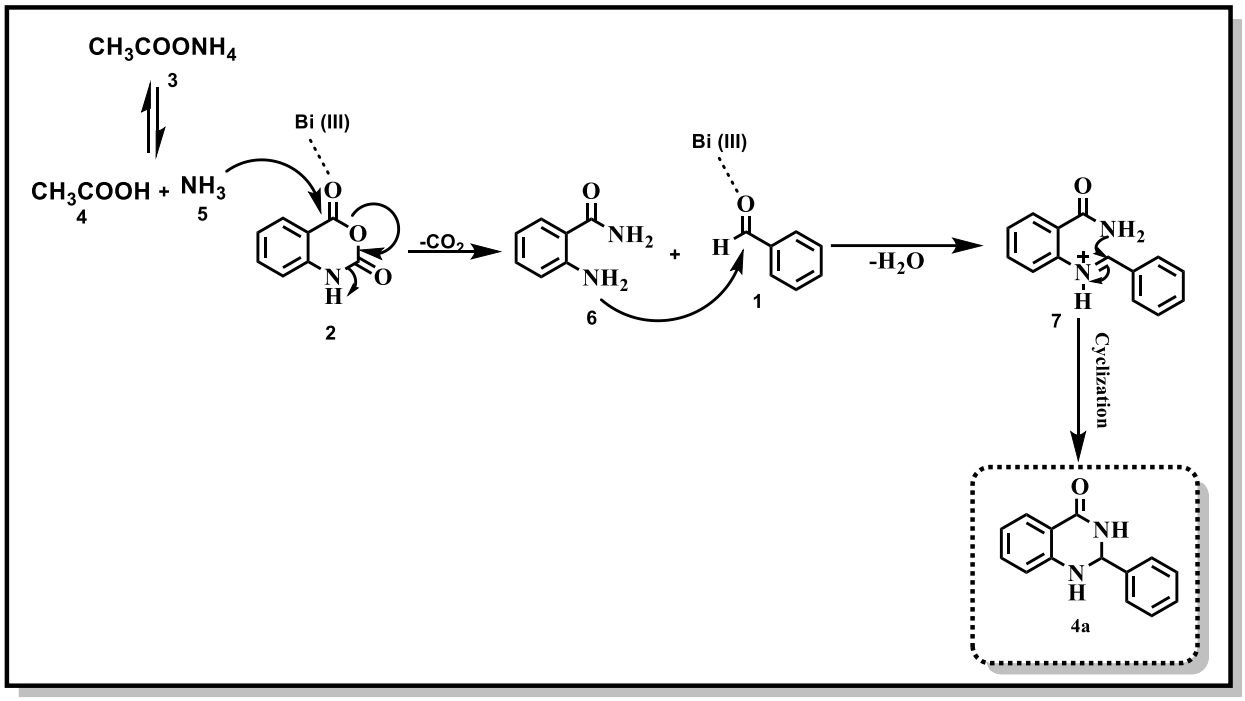
1	C_6H_5	**4a**	15	96	217-219	216-218[15]
2	4-Me-C_6H_4	**4b**	15	88	221-222	224-225[15]
3	4-OMe-C_6H_4	**4c**	14	90	183-185	181-183[15]
4	4-iPr-C_6H_4	**4d**	15	91	161-163	162-163[15]
5	4-F-C_6H_4	**4e**	13	96	201-203	203-204[15]
6	4-Cl-C_6H_4	**4f**	13	95	204-206	205-206[15]
7	4-Br-C_6H_4	**4g**	14	97	195-197	196-198[15]
8	4-CF_3-C_6H_4	**4h**	10	94	193-195	191-193[15]
9	4-NO_2-C_6H_4	**4i**	10	92	196-198	197-198[15]
10	3-F-C_6H_4	**4j**	12	91	263-265	263-266[15]
11	3-Cl-C_6H_4	**4k**	13	90	186-188	185-187[15]
12	3-Br-C_6H_4	**4l**	12	92	224-226	227-228[15]
13	Thiophene	**4m**	15	87	209-211	210-212[15]
14	H	**4n**	60	0	-	-

[a]Reaction conditions: benzaldehyde **1a** (1.0 eq), isatoic anhydride **2** (1.0 eq), and ammonium acetate **3** (1.0 eq). [b]Isolated yield.

Table 2 summarizes the results for the synthesis of DHQ derivatives catalyzed by [$Bi(NO_3)_3{\cdot}5H_2O$] as an efficient Lewis acid catalyst. A series of substituted DHQ compounds **4a**-**4m** was successfully prepared by the one-pot multicomponent reaction of different benzaldehydes **1a**, isatoic anhydride **2**, and ammonium acetate **3** under optimized reaction conditions. The reaction proceeded smoothly for a wide range of substituents, affording the desired DHQ derivatives in excellent isolated yields ranging from 88% to 97%. Compounds **4a**, **4e**, and **4g** showed particularly high yields (96-97%), indicating that the electronic nature of the substituents has minimal adverse effect on the efficiency of the bismuth nitrate-catalyzed protocols. The heterocyclic compound **4m** was also synthesized with good yield (87%), but it does not offer more yield than aromatic compounds. Even substrates bearing electron-withdrawing or electron-donating groups furnished the products in consistently high yields, demonstrating the broad substrate scope and robustness of the catalyst. The substrate scope was further examined using an aliphatic aldehyde under the optimized reaction conditions. However, the corresponding DHQ derivative **4n** was not obtained, even after extending the reaction time to 60 min (Table 2). This result indicates a limitation of the present protocol for the investigated aliphatic substrate. Further experiments would be required to determine the origin of this difference in reactivity.

A plausible reaction pathway for the $Bi(NO_3)_3{\cdot}5H_2O$-catalyzed synthesis of DHQ derivatives is illustrated in **Scheme 3**.[26] Initially, ammonia **5** generated from ammonium acetate **3** may react with isatoic anhydride **2** to form an anthranilamide intermediate **6** through ring opening and subsequent decarboxylation. The amino group of the resulting intermediate may then undergo condensation with the aldehyde, potentially facilitated by Lewis acid activation of the carbonyl group, to generate an imine intermediate **7**. Subsequent intramolecular cyclization and proton transfer would afford the corresponding DHQ derivative **4a**. This pathway is proposed on the basis of the expected reactivity of the starting materials; however, the individual intermediates and the precise catalytic role of $Bi(NO_3)_3{\cdot}5H_2O$ have not been experimentally established.

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Scheme 3. A plausible mechanism for the synthesis of DHQ catalysed by $[Bi(NO_3)_3{\cdot}5H_2O]$.

Table 3 illustrates a comparison of the present work with previously reported work.

Table 3. The previously reported work for the synthesis of DHQ **4a**.

S. No.	Author[R]	Reaction Conditions	Time (hour/min)	Yield (%)
1	Duta et al.[29]	$[\{SiO_2\text{-(acac)}\}_3FeIII]Cl_3/H_2O$, 80 °C	1 hour	98
2	Tamaddon et al.[30]	Starch (alk.)/H_2O, 80 °C	30 min	96
3	Hutait et al.[31]	*N* -Bromosaccharin/H_2O, 100 °C	30 min	95
4	Kumar et al.[32]	2-Chloro-1-methylpyridiniumiodide/MeCN, 110 °C	3 hours	95
5	Gharib et al.[33]	Nano preyssler/H_2O, 100 °C	2 hours	95
6	Wang et al.[34]	732-Resin/EtOH-H_2O, reflux	0.7 hour	95
7	Khaksar et al.[35]	2,2,2-Trifluoroethanol, reflux	3 hours	95
8	Hiwarale et al.[36]	cellulose-supported alumina/EtOH, reflux	30 min	94
9	Agarwal et al.[37]	FeNi-NPs/H_2O, 70 °C	1 hour	94
10	**Present work**	**$Bi(NO_3)_3.5H_2O$, 100 °C**	**15 min**	**96**

[R]References

Green metrics parameter

Green chemistry metrics provide quantitative measures for evaluating the material efficiency and waste generation associated with synthetic processes.[15] In the present study, selected green chemistry metrics were calculated for the synthesis of compound **4a** and compared with those of previously reported methods (Refs. 31 and 37)[31,37], as illustrated in **Figures 3** and **4**. The evaluated parameters include atom economy (AE), atom efficiency (AEf), carbon efficiency (CE), reaction mass efficiency (RME), optimum efficiency (OE), mass

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productivity (MP), process mass intensity (PMI), E-factor, water intensity (WI), and solvent intensity (SI). The corresponding calculations are provided in the Supporting Information.

The calculated metrics were used to compare the material efficiency and waste-related characteristics of the present protocol (Method A) with the selected literature procedures (Methods B[31] and C[37]). The comparison provides an assessment of the relative performance of these methods under the defined calculation conditions. Although the solvent-free reaction conditions and short reaction time are advantageous features of the present protocol, the overall environmental performance also depends on factors such as reagent consumption, catalyst use, energy requirements, and materials used during product isolation and purification. Therefore, the calculated metrics should be interpreted within the boundaries of the assessment rather than as evidence of overall environmental superiority.

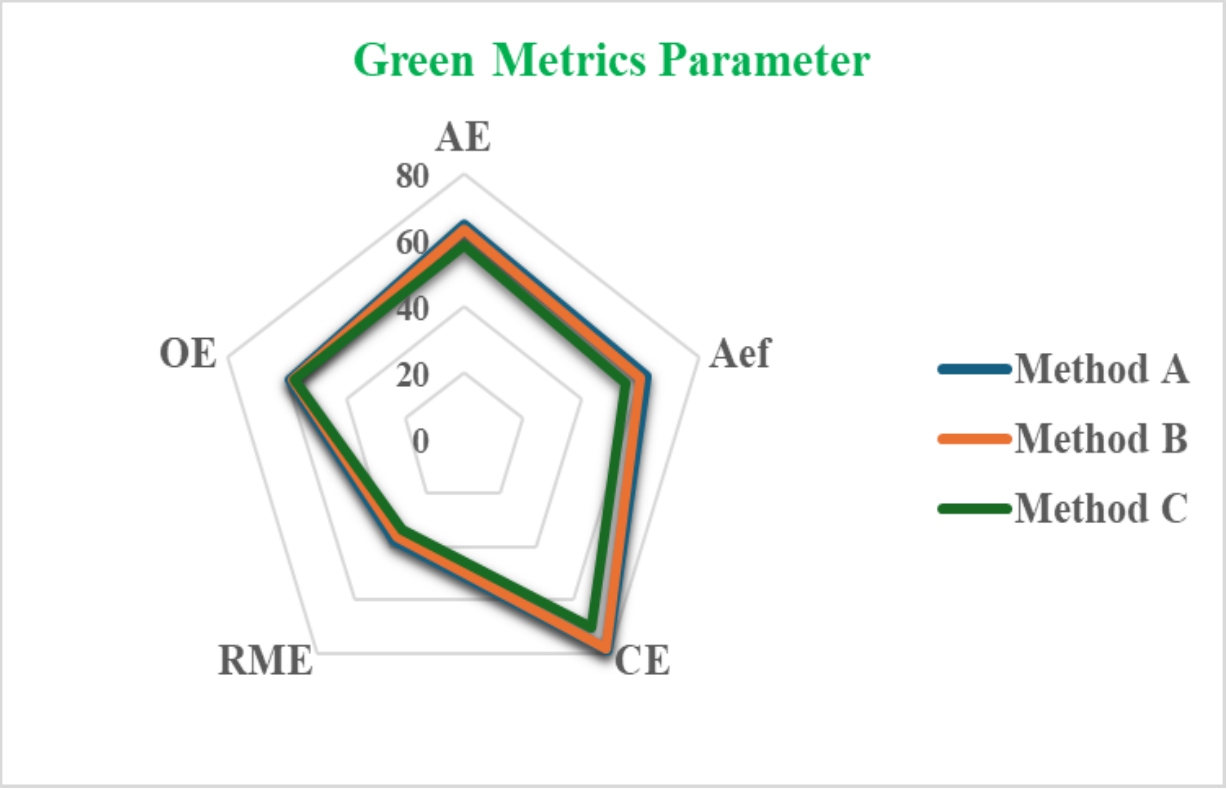


Figure 3. Radar pentagonal diagram representing green metrics parameter AE, AEf, CE, RME, and OE for compound **4a** synthesized by methods A, B, and C.

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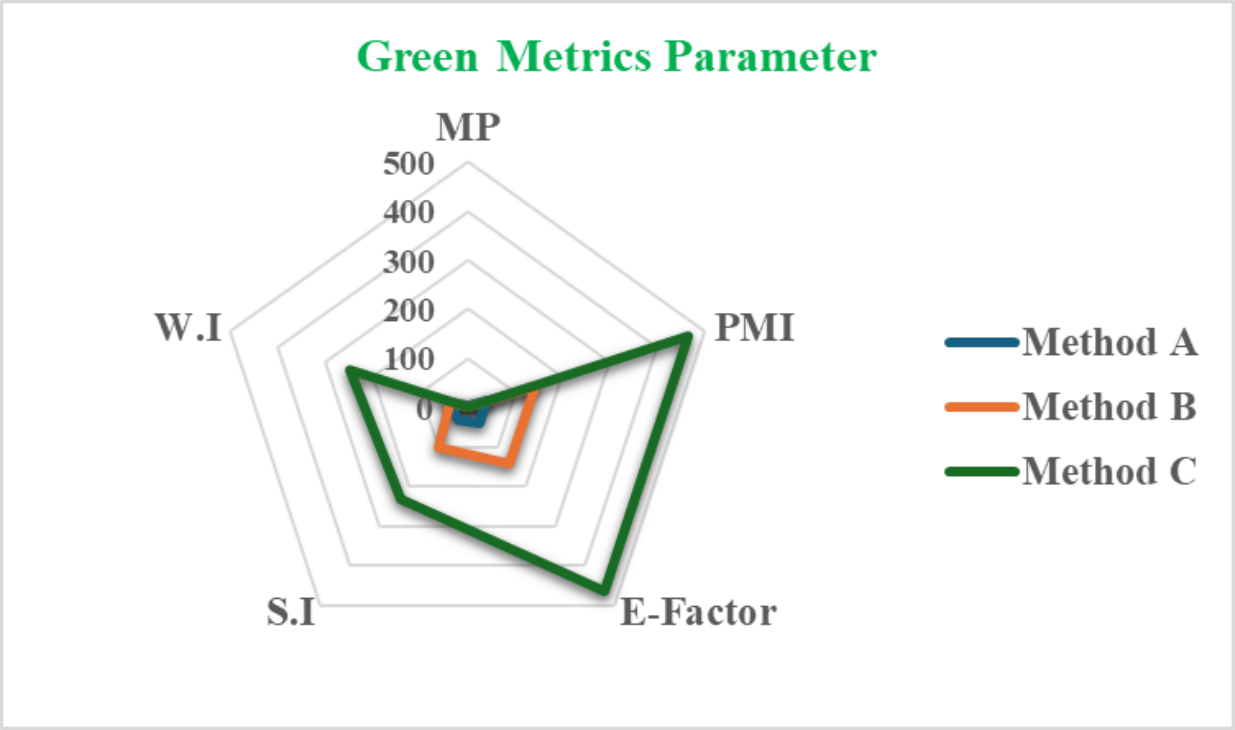


Figure 4. Radar pentagon diagram representing green metrics parameters MP, PMI, E-factor, WI, and SI for compound **4a** synthesized by methods A, B, and C.

Conclusions

A one-pot, three-component synthesis of 2-aryl-2,3-dihydroquinazolin-4(1*H*)-ones was investigated using $Bi(NO_3)_3{\cdot}5H_2O$ as a catalyst under solvent-free conditions. The optimized protocol afforded the desired products in 87-97% isolated yields within 10-15 min at 100 °C. The reaction was applicable to a range of aromatic and heteroaromatic aldehydes, whereas the investigated aliphatic aldehyde did not afford the desired product. Selected green chemistry metrics were also calculated to assess the material efficiency and waste-related characteristics of the protocol in comparison with reported methods.

Experimental Section

General. All chemicals were obtained from commercial suppliers, including Spectrochem, Acros, Aldrich, and Merck, and were used as received without further purification. Reaction progress was monitored by thin-layer chromatography (TLC) on Merck Kieselgel 60 F-254 plates. Melting points of the synthesized compounds were determined using a digital melting point apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded on a Bruker spectrometer operating at 600 MHz, using DMSO-d_6 as the solvent.

General procedure for the synthesis of compounds 4a-4n. An environmentally benign and efficient protocol was employed for the synthesis of compounds **4a-4m**. In a typical reaction, aldehydes (106.12mg, 1.0 mmol), isatoic anhydride (163.13mg, 1.0 mmol), ammonium acetate (77.08mg, 1.0 mmol) and [$Bi(NO_3)_3{\cdot}5H_2O$] (24.25mg, 5.0 mmol) as a catalyst were combined and heated under the optimized reaction conditions. The progress of the reaction was monitored by TLC. After the reaction was complete, the mixture was allowed to cool to room temperature, and water (5mL) was added, resulting in the precipitation of the product. The solid

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was isolated by vacuum filtration and purified by recrystallization from ethanol (5mL) to afford the desired compounds **4a-4m** in good to excellent yields.

The structures of compounds **4a-4m** were confirmed by ^{1}H and ^{13}C NMR spectroscopy and LC-MS.

***2*-Phenyl-*2,3*-dihydroquinazolin-*4*(*1H*)-one (4a)**. ^{1}H NMR (600 MHz, DMSO-d_6): 5.75 (s, 1H), 6.66 (t, *J* 7.5 Hz, 1H), 6.74 (d, *J* 8.0 Hz, 1H), 7.12 (s, 1H), 7.23 (t, *J* 7.1 Hz, 1H), 7.33 (t, *J* 7.3 Hz, 1H), 7.37 (t, *J* 7.6 2H), 7.48 (d, *J* 7.2 Hz, 2H), 7.60 (d, *J* 7.7 Hz, 1H), 8.30 (s, 1H). ^{13}C NMR (150 MHz, DMSO-d_6): 66.9, 114.9, 115.3, 117.6, 127.2, 127.8, 128.8, 128.9, 133.8, 142.1, 148.2, 164.1. MS *m/z* 224.09 (M+1); Anal. Calc. for $C_{14}H_{12}N_2O$: 224.09; found: 225.

***2*-(*p*-Tolyl)-*2,3*-dihydroquinazolin-*4*(*1H*)-one (4b)**. ^{1}H NMR (600 MHz, DMSO-d_6): 2.29 (s, 3H), 5.72 (s, 1H), 6.66 (t, *J* 7.3 Hz, 1H), 6.74 (d, *J* 8.2 Hz, 1H), 7.06 (s, 1H), 7.19 (d, *J* 4.5 Hz, 2H), 7.23 (t, *J* 7.0 Hz, 1H), 7.37 (d, *J* 8.0 Hz, 2H), 7.61 (d, *J* 7.6 Hz, 1H), 8.25 (s, 1H). ^{13}C NMR (150 MHz, DMSO-d_6): 21.2, 66.8, 114.9, 115.5, 117.6, 127.3, 127.8, 129.3, 133.7, 138.2, 139.1, 148.4, 164.1. MS *m/z* 238.11 (M+1); Anal. Calc. for $C_{15}H_{14}N_2O$: 238.11; found: 239.

***2*-(*4*-Methoxyphenyl)-*2,3*-dihydroquinazolin-*4*(*1H*)-one (4c)**. ^{1}H NMR (600 MHz, DMSO-d_6): 3.74 (s, 3H), 5.70 (s, 1H), 6.66 (t, *J* 7.5 Hz, 1H), 6.73 (d, *J* 8.0 Hz, 1H), 7.12 (s, 1H), 6.93 (t, *J* 8.4 Hz, 1H), 7.01 (s, 1H), 7.23 (t, *J* 6.6 Hz, 2H), 7.40 (d, *J* 8.6 Hz, 2H), 7.60 (d, *J* 8.6 Hz, 1H), 8.19 (s, 1H). ^{13}C NMR (150 MHz, DMSO-d_6): 55.6, 66.7, 114.1, 114.9, 115.4, 117.6, 127.8, 128.6, 133.8, 134.0, 148.4, 159.9, 164.2. MS *m/z* 254.10 (M+1); Anal. Calc. for $C_{15}H_{14}N_2O_2$: 254.10; found: 255.

***2*-(*4*-Isopropylphenyl)-*2,3*-dihydroquinazolin-*4*(*1H*)-one (4d)**. ^{1}H NMR (600 MHz, DMSO-d_6): 1.17 (d, *J* 6.9 Hz, 6H), 2.84-2.71 (sept, 1H), 5.71 (s, 1H), 6.66 (t, *J* 6.5 Hz, 1H), 6.72 (t, *J* 8.1 Hz, 1H), 7.06 (s, 1H), 7.22 (d, *J* 8.0, 1H), 7.25 (d, *J* 8.0 Hz, 2H), 7.40 (d, *J* 8.0 Hz, 2H), 7.60 (d, *J* 7.5 Hz, 1H), 8.23 (s, 1H). ^{13}C NMR (150 MHz, DMSO-d_6): 24.3, 33.7, 66.9, 114.9, 115.3, 117.6, 126.7, 127.3, 127.8, 133.8, 139.5, 148.4, 149.3, 164.1. MS *m/z* 266.14 (M+1); Anal. Calc. for $C_{17}H_{18}N_2O$: 266.14; found: 267.

***2*-(*4*-Fluorophenyl)-*2,3*-dihydroquinazolin-*4*(*1H*)-one (4e)**. ^{1}H NMR (600 MHz, DMSO-d_6): 5.77 (s, 1H), 6.68 (t, *J* 8.1 Hz, 1H), 6.74 (d, *J* 8.0 Hz, 1H), 7.09 (s, 1H), 7.20 (t, *J* 8.9 Hz, 2H), 7.24 (d, *J* 7.0 Hz, 1H), 7.52 (dd, *J* 2.6 Hz, *J* 7.4 Hz, 2H), 7.61 (d, *J* 7.9 Hz, 1H), 8.28 (s, 1H). ^{13}C NMR (150 MHz, DMSO-d_6): 66.3, 115.0, 115.3, 115.5, 115.6, 117.8, 127.8, 129.4, 129.4, 133.9, 138.3, 138.3, 148.2, 160.3, 161.8, 163.4, 164.1. (multiple peaks observed due to fluorine coupling). MS *m/z* 242.08 (M+1); Anal. Calc. for $C_{14}H_{11}FN_2O$: 242.08; found: 243.

***2*-(*4*-Chlorophenyl)-*2,3*-dihydroquinazolin-*4*(*1H*)-one (4f)**. ^{1}H NMR (600 MHz, DMSO-d_6): 5.78 (s, 1H), 6.68 (t, *J* 7.1 Hz, 1H), 6.75 (d, *J* 8.1 Hz, 1H), 7.15 (s, 1H), 7.24 (dd, *J* 1.5 Hz, *J* 6.5 Hz, 1H), 7.44 (d, *J* 8.4 Hz, 2H), 7.50 (d, *J* 8.7 Hz, 2H), 7.61 (d, *J* 7.1 Hz, 1H), 8.34 (s, 1H). ^{13}C NMR (150 MHz, DMSO-d_6): 66.2, 115.0, 115.3, 117.8, 127.9, 128.8, 129.1, 133.5, 133.9, 141.1, 148.0, 164.0. MS *m/z* 258.05 (M+1); Anal. Calc. for $C_{14}H_{11}ClN_2O$: 258.05; found: 259.

***2*-(*4*-Bromophenyl)-*2,3*-dihydroquinazolin-*4*(*1H*)-one (4g)**. ^{1}H NMR (600 MHz, DMSO-d_6): 5.76 (s, 1H), 6.68 (t, *J* 7.3 Hz, 1H), 6.75 (d, *J* 8.1 Hz, 1H), 7.15 (s, 1H), 7.24 (dd, *J* 1.4 Hz, *J* 6.5 Hz, 1H), 7.43 (d, *J* 8.5 Hz, 2H), 7.58 (d, *J* 8.7 Hz, 2H), 7.61 (d, *J* 7.1 Hz, 1H), 8.35 (s, 1H). ^{13}C NMR (150 MHz, DMSO-d_6): 66.3, 114.9, 115.3, 117.8, 122.0, 127.8, 129.5, 131.7, 133.9, 141.6, 148.0, 164.0. MS *m/z* 302.00 (M+1); Anal. Calc. for $C_{14}H_{11}BrN_2O$: 302.00; found: 303.

***2*-(*4*-(Trifluoromethyl)phenyl)-*2,3*-dihydroquinazolin-*4*(*1H*)-one (4h)**. ^{1}H NMR (600 MHz, DMSO-d_6): 5.78 (s, 1H), 6.68 (t, *J* 7.5 Hz, 1H), 6.76 (d, *J* 7.8 Hz, 1H), 7.24 (t, *J* 7.4 Hz, 2H), 7.61 (d, *J* 7.3 Hz, 1H), 7.70 (d, *J* 8.1 Hz, 2H), 7.76 (d, *J* 8.3 Hz, 2H), 8.45 (s, 1H). ^{13}C NMR (150 MHz, DMSO-d_6): 66.2, 114.9, 115.4, 117.8, 123.7, 125.7, 125.8, 127.8, 128.1, 133.9, 146.9, 17.9, 160.2, 163.9. (multiple peaks observed due to fluorine coupling). MS *m/z* 292.08 (M+1); Anal. Calc. for $C_{15}H_{11}F_3N_2O$: 292.08; found: 293.

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***2*-(*4*-Nitrophenyl)-*2,3*-dihydroquinazolin-*4*(*1H*)-one (4i)**. ^{1}H NMR (600 MHz, DMSO-d_6): 5.92 (s, 1H), 6.68 (t, *J* 7.6 Hz, 1H), 6.77 (d, *J* 8.1 Hz, 1H), 7.25 (dd, *J* 1.4 Hz, *J* =6.9 Hz, 1H), 7.32 (s, 1H), 7.61 (d, *J* 7.8 Hz, 1H), 7.73 (d, *J* 8.8 Hz, 2H), 8.23 (d, *J* 8.6 Hz, 2H), 8.52 (s, 1H). ^{13}C NMR (150 MHz, DMSO-d_6): 65.8, 115.0, 115.3, 118.0, 124.0, 127.9, 128.4, 134.1, 147.6, 147.9, 149.7, 163.9. MS *m/z* 269.08 (M+1); Anal. Calc. for $C_{14}H_{11}N_3O_3$: 269.08; found: 270.

***2*-(*3*-Fluorophenyl)-*2,3*-dihydroquinazolin-*4*(*1H*)-one (4j)**. ^{1}H NMR (600 MHz, DMSO-d_6): 5.78 (s, 1H), 6.67 (t, *J* 7.5 Hz, 1H), 6.76 (d, *J* 8.2 Hz, 1H), 7.15 (t, *J* 8.2 Hz, 1H), 7.20 (s, 1H), 7.26 (dd, *J* 1.4 Hz, *J* 7.4 Hz, 2H), 7.31 (d, *J* 7.7 Hz, 1H), 7.41 (dd, *J* 7.1 Hz, *J* 14.3 Hz, 1H), 7.60 (d, *J* 7.3 Hz, 1H), 8.38 (s, 1H). ^{13}C NMR (150 MHz, DMSO-d_6): 66.0, 113.9, 114.1, 114.9, 115.5, 115.6, 117.8, 123.2, 123.20, 127.8, 130.8, 130.9, 133.9, 145.3, 145.3, 147.9, 161.7, 163.3, 163.9. (multiple peaks observed due to fluorine coupling). MS *m/z* 242.08 (M+1); Anal. Calc. for $C_{14}H_{11}FN_2O$: 242.08; found: 243.

***2*-(*3*-Chlorophenyl)-*2,3*-dihydroquinazolin-*4*(*1H*)-one (4k)**. ^{1}H NMR (600 MHz, DMSO-d_6): 5.78 (s, 1H), 6.68 (t, *J* 7.4 Hz, 1H), 6.76 (d, *J* 8.1 Hz, 1H), 7.22 (s, 1H), 7.25 (dd, *J* 1.2 Hz, *J* 7.4 Hz, 1H), 7.38-7.45 (m, 3H), 7.52 (s, 1H), 7.61 (d, *J* 7.4 Hz, 1H), 8.40 (s, 1H). ^{13}C NMR (150 MHz, DMSO-d_6): 65.9, 114.9, 115.3, 117.8, 125.7, 127.1, 127.8, 128.7, 130.7, 133.5, 134.0, 144.87, 147.9, 163.9. MS *m/z* 258.05 (M+1); Anal. Calc. for $C_{14}H_{11}FClN_2O$: 258.05; found: 259.

***2*-(*3*-Bromophenyl)-*2,3*-dihydroquinazolin-*4*(*1H*)-one (4l)**. ^{1}H NMR (600 MHz, DMSO-d_6) 5.78 (s, 1H), 6.68 (t, *J* 7.2 Hz, 1H), 6.76 (d, *J* 8.2 Hz, 1H), 7.21 (s, 1H), 7.25 (t, *J* 7.9 Hz 1H), 7.34 (t, *J* 7.8 Hz, 1H), 7.47 (d, *J* 7.4 Hz, 1H), 7.52 (d, *J* 7.8 Hz, 1H), 7.61 (d, *J* 6.4 Hz, 1H), 7.66 (s, 1H), 8.39 (s, 1H). ^{13}C NMR (150 MHz, DMSO-d_6): 65.9, 114.9, 115.3, 117.9, 122.1, 126.2, 127.8, 130.0, 131.1, 131.6, 134.0, 145.12 147.8, 163.9. MS *m/z* 302.00 (M+1); Anal. Calc. for $C_{14}H_{11}BrN_2O$: 302.00; found: 303.

***2*-(Thiophen-*2*-yl)-*2,3*-dihydroquinazolin-*4*(*1H*)-one (4m)**. ^{1}H NMR (600 MHz, DMSO-d_6) 6.00 (t, *J* 1.8 Hz, 1H), 6.7 (dd, *J* 7.6 Hz, *J* 1.6 Hz, 1H), 6.74 (d, *J* 7.9 Hz, 1H), 6.96 (dd, *J* 7.4 Hz, *J* 1.9 Hz, 1H), 7.11 (d, *J* 7.5 Hz, 1H), 7.24 (dd, *J* 7.2 Hz, *J* 1.6 Hz, 2H), 7.43 (dd, *J* 6.4 HZ, *J* 1.8 Hz), 7.60 (dd, *J* 6.7 Hz, *J* 1.9 Hz, 1H), 8.46 (s, 1H). ^{13}C NMR (150 MHz, DMSO-d_6): 62.01 114.2, 114.6, 117.1, 125.2, 125.4, 126.0, 126.9, 132.9, 146.0, 146.7, 162.7. MS *m/z* 230.05 (M+1); Anal. Calc. for $C_{12}H_{10}N_2OS$: 230.05; found: 231.

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Supplementary Material

Spectra and MS data are provided in a separate file.

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