$Yb(OTf)_3$-Catalyzed One-Pot Synthesis of Quinazolin-4(3*H*)-ones from Anthranilic Acid, Amines and Ortho Esters (or Formic Acid) in Solvent-Free Conditions

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Abstract: An efficient synthesis of an array of quinazolin-4(3*H*)-ones from anthranilic acid, ortho esters (or formic acid) and amines using $Yb(OTf)_3$ in one-pot under solvent-free conditions is described. Compared with the classical reaction conditions, this new synthetic method has the advantage of excellent yields (75–99%), shorter reaction time (few minutes) and reusability of the catalyst.

Key words: quinazolin-4(3*H*)-ones, ytterbium triflate, one-pot reaction, anthranilic acid, amine

It has been more than a century since the initial studies on quinazolin-4(3*H*)-ones was published.[1] Quinazolin-4(3*H*)-ones are a class of fused heterocycles that are of considerable interest on account of the diverse range of their biological properties, e.g. anticancer, diuretic, antiinflammatory, anticonvulsant, and antihypertensive activities.[2] For example, febrifugine and isofebriguine were isolated as the active principles[3] of the roots of *Dichroa febrifuga* Lour (Chinese name: Chang Shan) which have been used effectively against malaria fever in China for centuries. Recently a new type of febrifugine derivative has been reported,[4] which showed high activity against *P. falciparum* malaria in vitro and was equally effective against *P. berghei* in vivo as the clinically used drug chloroquine. Similarly, quinazoline containing structures have been known as tyrosine kinase inhibitors,[5] dihydrofolate reductase inhibitors,[6] and tubulin polymerization inhibitors.[7]

In view of the importance of quinazolines and their derivatives, many classical methods for the synthesis of quinazolines were reported in the literature.[8] Usually, 4*H*-3,1-benzoxazin-4-ones are valuable starting materials for the synthesis of a variety of 2,3-disubstituted quinazolin-4(3*H*)-ones.[9] A number of synthetic methods for the preparation of 2-substituted 4*H*-3,1-benzoxazin-4-ones have been described: (a) cyclodehydration of *N*-acylanthranilic acid by acetic anhydride;[10] (b) reaction of anthranilic acid with acid chlorides in pyridine;[11] (c) treatment of methyl *N*-aroylanthranilates or methyl 2-ureidobenzoates with concentrated sulfuric acid;[12] (d) photoisomerization of 2-arylisatogen;[13] and (e) reaction of anthranilic acid with ortho esters under microwave irradiation.[14] Quinazolin-4(3*H*)-ones have been prepared by means of multistep procedures, either by reaction of benzoxazin-4-one carboxylic esters with amines[15] or other methods.[16] Furthermore, anthranilic acid and their derivatives are valuable starting materials for the synthesis of a variety of quinazolin-4(3*H*)-ones which have been prepared by various methods such as carbonylation catalyzed by palladium,[17] coupling *O*-methylbutyrolactim with anthranilic acid,[18] cycloaddition of anthranilic acid iminoketene to methylbutyrolactam (via sulfinamide anhydride),[19] anthranilic acid derivatives together with a wide range of substrates including imidates and iminohalides,[20] the reaction of anthranilic acid and the appropriately substituted imidate in a facile one-pot procedure.[21] A concise and practical synthesis of homochiral quinazolin derivatives is the treatment of anthranilic acid derivatives with 1,3-oxazolidine-2-thiones.[22] Microwaves also could promote the reaction of anthranilic acid with an amine and formic acid (or ortho esters),[23] etc. However, in spite of their potential utility, some of the reported methods suffer from drawbacks like longer reaction time, unsatisfactory yields, cumbersome product isolation procedures and synthesis in multi-step synthetic programs, on the other hand, benzoxazin-4-ones and other derivatives are valuable starting materials for the synthesis of a variety of quinazolin-4(3*H*)-ones[9] that are moisture sensitive, very hygroscopic, and unstable at high temperature.

The increasing attention during the last decades for environmental protection has influenced both modern academic and industrial groups to develop chemical processes with maximum yield and minimum cost whilst using non-toxic reagents, catalysts and solvents, or even better, without solvents. One of the tools to combine economic aspects with the environmental ones is the multicomponent reaction strategy; this process consists of three or more synthetic steps which are carried out without isolation of any intermediate thus reducing time, saving energy and raw materials.[24]

As part of our program aimed at developing new selective and environmentally friendly methodologies for the preparation of fine chemicals, we wish to report herein another remarkable catalytic activity of lanthanide triflates for the

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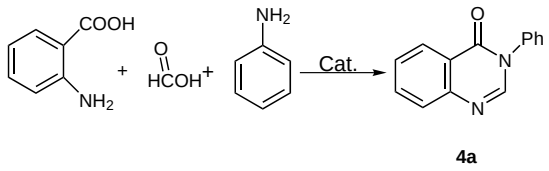
one-pot synthesis of quinazolin-4(3*H*)-ones. Of late, lanthanide triflates have been shown to be a type of Lewis acid that is different from traditional Lewis acids such as $AlCl_3$, $SnCl_4$, $BF_3{\cdot}OEt_2$, etc. Especially, lanthanide triflates are quite stable to water and reusable, as well as highly effective in the cases of many nitrogen-containing compounds such as imines and hydrazones, etc. Therefore, it has emerged as a powerful Lewis acid catalyst imparting high regio- and chemoselectivity in various organic reactions, such as aldol condensations,[25] Fridel–Crafts acylations,[26] glyoxylate-ene reaction,[27] Diels–Alder reaction,[28] and ring-opening Mannich reaction,[29] as well as some other reactions.[30] In continuation of our interest on lanthanide triflates-catalyzed organic reactions,[31] we describe here a novel, efficient and high yielding protocol for the preparation of quinazolin-4(3*H*)-ones through a three-component one-pot reaction of anthranilic acid, amines and ortho esters (or formic acid) in solvent-free conditions employing lanthanide triflates as efficient and mild catalyst.

Recently, organic reactions in water without use of harmful organic solvents and in solvent-free conditions have attracted much attention, because water is a cheap, safe, and environmentally benign solvent. In the course our investigation to develop new synthetic methods in water and in solvent-free conditions, we have recently found that a combination of a water-stable Lewis acid such as lanthanide triflates provides an efficient system for some Lewis acid-catalyzed reaction in water and in solvent-free conditions. As an extension of these studies, first of all, we decided to investigate the use of lanthanide triflates and other Lewis acids as a catalyst for the preparation of quinazolin-4(3*H*)-ones from cyclocondensation of anthranilic acid (**1**), aniline (**3a**) and aqueous formic acid (15%) without using any organic solvent (Scheme 1). The results are summarized in Table 1. The reaction proceeded smoothly to afford the corresponding quinazolin-4(3*H*)-one **4a** in moderate yields. Screening of series of lanthanide triflates catalysts for the reaction of anthranilic acid with aniline and aqueous formic acid revealed that $Yb(OTf)_3$ is better than other lanthanide triflates. In contrast, some traditional Lewis acids such as $ZnCl_2$, $AlCl_3$ and $SnCl_2$ furnish the product in low yields.



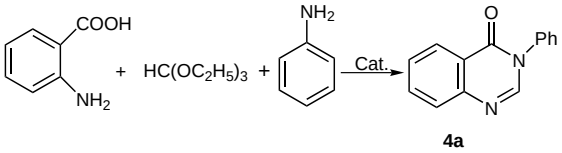
Scheme 1

Although this one-pot reaction under solvent-free conditions in the presence of $Yb(OTf)_3$ afforded the desired corresponding quinazolin-4(3*H*)-one **4a** in moderate yield (80%), it takes much more time. In order to reduce the reaction time and increase the yield, we tried using triethyl orthoformate (**2**, R = Et) instead of aqueous formic acid. This was successfully carried out in the same case, and the model reaction is shown in Scheme 2. Using triethyl orthoformate with a catalytic amount of lanthanide triflates and other Lewis acids instead of formic acid in the above reaction leads to formation of the corresponding quinazolin-4(3*H*)-one **4a** in fair yield, especially the lanthanide triflates-catalyzed reaction proceeded rapidly to give the product in excellent yields (Table 2). The reaction rates and yields are dramatically increased and the yields were significantly raised (94–99% vs for the classical reaction method), and the reaction time was shortened from several hours to few minutes. Note that the amount of $Yb(OTf)_3$ catalyst affects the yield of products, and in the presence of $Yb(OTf)_3$ (>1.3 mol%), the reaction afforded the corresponding quinazolin-4(3*H*)-one **4a** in highest yield (99%).

Table 1 One-Pot Reaction of Anthranilic Acid (**1**), Aqueous Formic Acid (15%), and Aniline (**3a**) Catalyzed by Various Lewis Acids Under Different Reaction Conditions[a] (Scheme 1)

Entry	Catalyst	Amount of Catalyst (mol%)	Time (h)	Yield of **4a** (%)[b]
1	$ZnCl_2$	2.5	10	28
2	$AlCl_3$	2.5	10	31
3	$SnCl_2$	2.5	10	38
4	$LaCl_3$	2.5	10	45
5	$YbCl_3$	2.5	10	50
6	$La(OTf)_3$	2.5	10	76
7	Sm(OTf)	2.5	10	72
8	$Yb(OTf)_3$	2.5	10	80

[a] Refluxed at 60 °C for 10 h under solvent-free conditions.
[b] Isolated yield.



Scheme 2

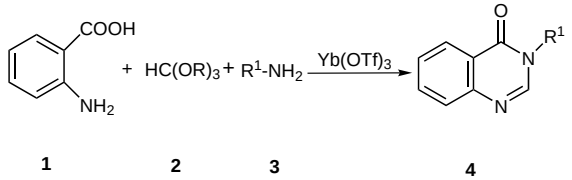
While lanthanide triflates have similar properties, the catalytic activity of $Yb(OTf)_3$ in this case is higher than that of other lanthanide triflates and it could be reused three times without showing any loss of activity (entry 12: yield of product **4a**: 1st run, 97%; 2nd run, 95%; 3rd run, 94%). In addition, it was found that the yield of the reaction by traditional Lewis acids such as $ZnCl_2$, $AlCl_3$ and $SnCl_2$ have also been increased compared to the above reaction with aqueous formic acid (see Scheme 1).

Table 2 One-Pot Reaction of Anthranilic acid (**1**), Triethyl Orthoformate (**2**, R = Et) and Aniline (**3a**) Catalyzed by Various Lewis Acids Under Different Reaction Conditions[a] (Scheme 2)

Entry	Catalyst	Amount of Catalyst (mol%)	Time (min)	Yield of **4a** (%)[b]
1	$ZnCl_2$	2.5	400	38
2	$AlCl_3$	2.5	400	42
3	$SnCl_2$	2.5	400	46
4	$LaCl_3$	2.5	400	58
5	$YbCl_3$	2.5	400	65
6	$Sm(OTf)_3$	1.3	2	92
7	$La(OTf)_3$	1.3	2	95
8	$Yb(OTf)_3$	3	2	99
9	$Yb(OTf)_3$	2.5	2	99
10	$Yb(OTf)_3$	1.3	2	99
11	$Yb(OTf)_3$	0.8	2	97
12	$Yb(OTf)_3$[c]	1.3	2	97, 95, 94

[a] Refluxed at 60 °C at for the time given under solvent-free conditions.
[b] Isolated yield.
[c] Catalyst was reused three times.

A wide range of structurally varied amines **3**, including aromatic amines and benzyl amines, anthranilic acid (**1**), and ortho esters **2** were examined in the presence of a catalytic amount (1.3 mol%) of $Yb(OTf)_3$ under solvent-free conditions (Scheme 3), and the results are summarized in Table 3. In all cases, the three-component reaction proceeded rapidly to afford the corresponding quinazolin-4(3*H*)-ones **4** in excellent yields. In general, electron-donating groups on the aniline system (such as methoxy and methyl) are beneficial for the reaction possibly due to the increased electron density of aromatic system, whereas electron-withdrawing group (such as chloro and nitro) are unfavorable for the transformation. Most importantly, anilines having electron-donating substituents all reacted very well, giving excellent yields in a few minutes. The yield of product was considerably affected by the electronic nature and position of the substituent on aniline. Anilines having electron-withdrawing substituents such as NO_2, Cl gave generally lower yield than anilines having substituents with electron-donating character (OMe, Me). With *ortho* and *meta* electron-withdrawing substituted anilines, the product yield was higher than *para* electron-



Scheme 3

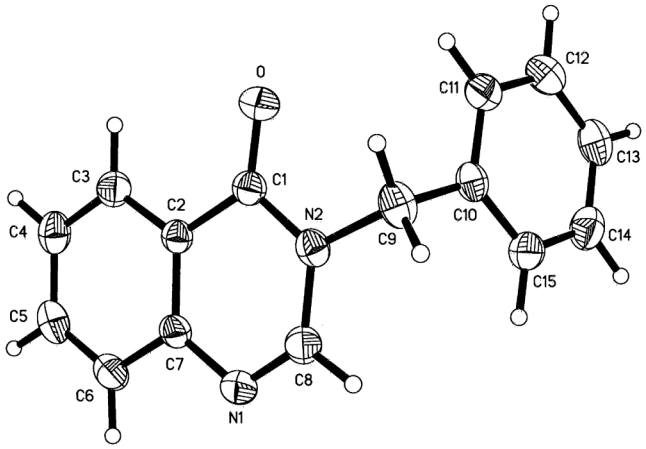


Figure 1 X-ray molecular structure of **4r**

Table 3 One-Pot Synthesis of Different Quinazolin-4(3*H*)-ones by Catalyzed $Yb(OTf)_3$ Under Solvent-Free Condtions[a] (Scheme 3)

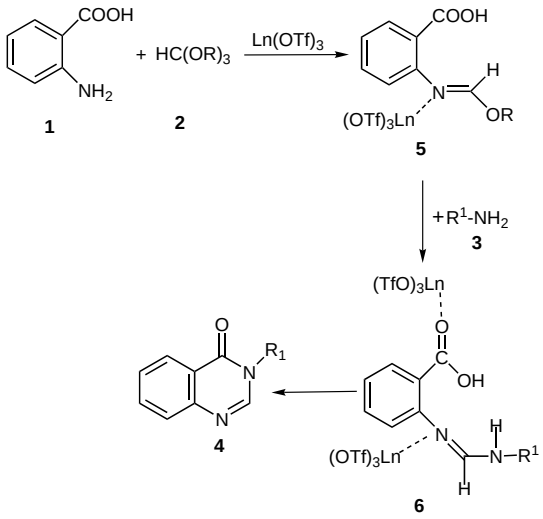
Entry	R^1	R	Time (min)	Product	Yield (%)[b]
1	Ph	Me	2	**4a**	99
2	Ph	Et	2	**4a**	99
3	$2\text{-}MeC_6H_4$	Et	2	**4b**	98
4	$3\text{-}MeC_6H_4$	Et	2	**4c**	95
5	$4\text{-}MeC_6H_4$	Et	2	**4d**	99
6	$3,4\text{-}Me_2C_6H_3$	Et	2	**4e**	99
7	$4\text{-}EtC_6H_4$	Et	2	**4f**	99
8	$3\text{-}MeOC_6H_4$	Et	2	**4g**	98
9	$4\text{-}MeOC_6H_4$	Et	2	**4h**	98
10	$2\text{-}ClC_6H_4$	Et	2	**4i**	97
11	$3\text{-}ClC_6H_4$	Et	2	**4j**	94
12	$4\text{-}ClC_6H_4$	Et	2	**4k**	95
13	$4\text{-}FC_6H_4$	Et	2	**4l**	94
14	$2\text{-}NO_2C_6H_4$	Et	3	**4m**	85[c]
15	$3\text{-}NO_2C_6H_4$	Et	3	**4n**	82[c]
16	$4\text{-}NO_2C_6H_4$	Et	4	**4o**	80[c]
17	$2,4\text{-}(NO_2)_2C_6H_3$	Et	5	**4p**	75[c]
18	$4\text{-}NHAcC_6H_4$	Et	2	**4q**	97
19	$PhCH_2$	Et	2	**4r**	96

[a] Refluxed at 60 °C for the time given under solvent-free conditions.
[b] Isolated yield.
[c] Refluxed at 80 °C for the time given under solvent-free conditions.

withdrawing substituted anilines. In the case of 2,4-dinitroaniline, the product yield decreased and the reaction time was prolonged as compared to monosubstituted nitroaniline. Furthermore, for benzyl amine, the corre-

sponding product could be obtained in 96% yield **4r**. The X-ray crystal structure of compound **4r** is shown in Figure 1.

We propose a mechanism similar to that of Errede[32] and Khajavi,[14] and Rad-Moghadam[23] for the reaction. The first step in this reaction involves the lanthanide-catalyzed formation of imidic ester **5** formed by reaction of the ortho ester with anthranilic acid and stabilized by lanthanide. The imidic ester is very prone to react immediately with amine and to form an amidine intermediate stabilized by lanthanide, which is the key rate-limiting step. Subsequently, the reaction proceeds through the amidine intermediate **6** by intramolecular attack of the nitrogen nucleophile at carbonyl carbon, which is activated by lanthanide to produce the corresponding cyclized product **4** (Scheme 4).



Scheme 4

In summary, it can be concluded that lanthanide triflate is an efficient and excellent in the one-pot reaction of anthranilic acid, an amine and ortho esters (or formic acid) to afford quinazolin-4(3*H*)-ones derivatives in high yields under solvent-free and mild conditions in shorter reaction times. The notable factors of this reaction are: (a) reasonably good yields; (b) fast reaction; (c) mild reaction conditions; (d) choice of appropriate substituents on the aniline; (e) green synthesis avoiding toxic solvents; and (f) the catalyst lanthanide triflates can be easily recovered from the aqueous layer after the reaction is complete and can be reused with no loss of yield. Thus, we believe that our procedure will find important applications in the synthesis of quinazolin-4(3*H*)-ones to cater for the needs of academia as well as pharmaceutical industries.

Melting points were determined on a Kofler hot plate. ^{1}H NMR spectra were recorded at 500 MHz in $CDCl_3$ using TMS as internal standard. ^{13}C NMR spectral measurements were performed at 75 MHz using $CDCl_3$ as an internal standard. IR spectra were obtained as KBr discs on FTS-185 spectrometer. Mass spectra were determined on a Finnigan 8230 mass spectrometer.

Ytterbium Triflate-Catalyzed Synthesis of Different Quinazolin-4(3*H*)-ones Under the Solventless Conditions; General Procedure

Anthranilic acid (**1**; 137 mg, 1 mmol), an ortho ester **2** (1.3 mmol), the appropriate amine **3** (1.2 mmol), and $Yb(OTf)_3$ (7 mg, 0.013 mmol, 1.3 mol%) were heated at 60 °C (or 80 °C) under stirring for a few min (Table 3). Then H_2O was added and the product was extracted with EtOAc. After the organic layer was dried (Na_2SO_4) and evaporated, the residue was recrystallized from EtOAc–hexane to give the product **4**. The catalyst remaining in the aqueous phase can be recovered by removing the H_2O by heating and then drying under reduced pressure at 100 °C for 2 h.

3-Phenylquinazolin-4(3*H*)-one (4a)

Mp 139–140 °C.

IR (KBr): 1699, 1598, 1463 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 8.34 (d, *J* = 7.9 Hz, 1 H), 8.16 (s, 1 H), 7.72–7.78 (m, 2 H), 7.51 (t, *J* = 7.3 Hz, 1 H), 7.28–7.36 (m, 5 H).

^{13}C NMR ($CDCl_3$): δ = 160.7, 147.74, 147.25, 136.36, 135.25, 134.62, 129.91, 128.63, 128.13, 127.61, 127.25, 127.04, 122.64.

GC/MS: *m*/*z* (%) = 222.2 (M^+, 100), 223.2 (M + 1, 15).

Anal. Calcd for $C_{14}H_{10}N_2O$: C, 75.66; H, 4.54; N, 12.60. Found: C, 75.60; H, 4.44; N, 12.52.

3-(2-Methylphenyl)quinazolin-4(3*H*)-one (4b)

Mp 137–138 °C.

IR (KBr): 1692, 1593, 1464 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 8.32 (d, *J* = 7.7 Hz, 1 H), 8.13 (s, 1 H), 7.71–7.73 (m, 2 H), 7.48 (t, *J* = 7.1 Hz, 1 H), 7.23–7.34 (m, 4 H), 2.31 (s, 3 H).

^{13}C NMR ($CDCl_3$): δ = 160.23, 147.73, 147.21, 136.33, 135.22, 134.60, 129.73, 128.73, 128.65, 127.04, 127.16, 127.05, 122.44, 19.34.

GC/MS: *m*/*z* (%) = 236.2 (M^+, 100), 237.2 (M + 1, 16).

Anal. Calcd for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86. Found: C, 76.27; H, 5.11; N, 11.76.

3-(3-Methylphenyl)quinazolin-4(3*H*)-one (4c)

Mp 136–137 °C.

IR (KBr): 1691, 1600, 1458 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 8.31 (d, *J* = 7.7 Hz, 1 H), 8.12 (s, 1 H), 7.70–7.73 (m, 2 H), 7.46 (t, *J* = 7.2 Hz, 1 H), 7.22–7.31 (m, 4 H), 2.28 (s, 3 H).

^{13}C NMR ($CDCl_3$): δ = 159.24, 147.33, 146.21, 134.33, 133.22, 131.60, 128.73, 127.75, 127.05, 126.10, 125.14, 124.12, 122.43, 19.31.

GC/MS: *m*/*z* (%) = 236.2 (M^+, 100), 237.2 (M + 1, 18).

Anal. Calcd for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86. Found: C, 76.21; H, 5.08; N, 11.71.

3-(4-Methylphenyl)quinazolin-4(3*H*)-one (4d)

Mp 146–147 °C.

IR (KBr): 1690, 1603, 1457 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 8.29 (d, *J* = 7.6 Hz, 1 H), 8.11 (s, 1 H), 7.69–7.71 (m, 2 H), 7.40 (t, *J* = 7.2 Hz, 1 H), 7.16 (d, *J* = 7.6 Hz, 2 H), 7.28 (d, *J* = 7.6 Hz, 2 H), 2.26 (s, 3 H).

^{13}C NMR ($CDCl_3$): δ = 159.9, 147.32, 146.20, 134.31, 133.20, 131.58, 128.15, 127.12, 126.23, 125.14, 124.81, 124.13, 122.11, 19.30.

GC/MS: *m*/*z* (%) = 236.2 (M^+, 100), 237.2 (M + 1, 14).

Anal. Calcd for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86. Found: C, 76.28; H, 5.18; N, 11.70

3-(3,4-Dimethylphenyl)quinazolin-4(3*H*)-one (4e)
Mp 134–135 °C.

IR (KBr): 1692, 1600, 1455 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 8.28 (d, *J* = 7.6 Hz, 1 H), 8.11 (s, 1 H), 7.68–7.70 (m, 2 H), 7.40 (t, *J* = 7.1 Hz, 1 H), 7.10 (s, 1 H), 7.27 (m, 2 H), 2.28 (s, 6 H).

^{13}C NMR ($CDCl_3$): δ = 160.1, 147.32, 146.21, 134.28, 133.19, 131.58, 128.13, 127.14, 126.11, 125.24, 124.35, 123.23, 122.14, 19.30, 19.05.

GC/MS: *m*/*z* (%) = 250.2 (M^+, 35), 91 (100).

Anal. Calcd for $C_{16}H_{14}N_2O$: C, 76.78; H, 5.64; N, 11.19. Found: C, 76.72; H, 5.58; N, 11.13.

3-(4-Ethylphenyl)quinazolin-4(3*H*)-one (4f)
Mp 130–131 °C.

IR (KBr): 1692, 1600, 1455 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 8.28 (d, *J* = 7.6 Hz, 1 H), 8.10 (s, 1 H), 7.68–7.71 (m, 2 H), 7.40 (t, *J* = 7.1 Hz, 1 H), 7.15 (d, *J* = 7.5 Hz, 2 H), 7.26 (d, *J* = 7.7 Hz, 2 H), 2.25 (q, *J* = 7.1 Hz, 2 H), 1.01 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR ($CDCl_3$): δ = 160.5, 148.32, 146.21, 134.35, 133.20, 131.57, 128.4, 127.15, 126.12, 125.18, 124.83, 124.14, 122.43, 19.33.

GC/MS: *m*/*z* (%) = 250.2 (M^+, 23), 237.2 (M + 1, 14), 130 (100).

Anal. Calcd for $C_{16}H_{14}N_2O$: C, 76.78; H, 5.64; N, 11.19. Found: C, 76.73; H, 5.55; N, 11.12.

3-(2-Methoxyphenyl)quinazolin-4(3*H*)-one (4g)
Mp 195–196 °C.

IR (KBr): 1692, 1605, 1456 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 8.29 (d, *J* = 7.6 Hz, 1 H), 8.13 (s, 1 H), 7.66–7.73 (m, 2 H), 7.42 (t, *J* = 7.3 Hz, 1 H), 7.23–7.35 (m, 4 H), 3.72 (s, 3 H).

^{13}C NMR ($CDCl_3$): δ = 162.23, 148.34, 146.21, 134.32, 133.21, 131.48, 128.12, 127.11, 126.22, 125.14, 124.81, 124.21, 122.13, 19.35.

Anal. Calcd for $C_{15}H_{12}N_2O$: C, 71.42; H, 4.79; N, 11.10. Found: C, 71.46; H, 4.75; N, 11.13.

3-(4-Methoxyphenyl)quinazolin-4(3*H*)-one (4h)
Mp 193–194 °C.

IR (KBr): 1692, 1598, 1458 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 8.28 (d, *J* = 7.6 Hz, 1 H), 8.12 (s, 1 H), 7.68–7.72 (m, 2 H), 7.42 (t, *J* = 7.3 Hz, 1 H), 7.15 (d, *J* = 7.7 Hz, 2 H), 7.29 (d, *J* = 7.6 Hz, 2 H), 3.71 (s, 3 H).

^{13}C NMR ($CDCl_3$): δ = 161.22, 148.33, 146.20, 134.32, 133.20, 131.56, 128.11, 127.10, 126.22, 125.14, 124.81, 124.21, 122.13, 19.35.

Anal. Calcd for $C_{15}H_{12}N_2O$: C, 71.42; H, 4.79; N, 11.10. Found: C, 71.36; H, 4.71; N, 11.03.

3-(2-Chlorophenyl)quinazolin-4(3*H*)-one(4i)
Mp 180–181 °C.

IR (KBr): 1696, 1600, 1466 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 8.38 (d, *J* = 7.8 Hz, 1 H), 8.18 (s, 1 H), 7.72–7.75 (m, 2 H), 7.53 (t, *J* = 7.3 Hz, 1 H), 7.32–7.38 (m, 4 H).

^{13}C NMR ($CDCl_3$): δ = 162.24, 147.83, 147.61, 136.53, 135.32, 134.60, 131.75, 130.74, 129.63, 128.12, 127.14, 126.15, 122.41.

GC/MS: *m*/*z* (%) = 256.0 (M^+, 100), 258.0 (M + 2, 32), 257.0 (M – 1, 16).

Anal. Calcd for $C_{14}H_9ClN_2O$: C, 65.51; H, 3.53; N, 10.91. Found: C, 65.46; H, 3.49; N, 10.82.

3-(3-Chlorophenyl)quinazolin-4(3*H*)-one(4j)
Mp 178–180 °C.

IR (KBr): 1694, 1599, 1465 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 8.36 (d, *J* = 7.8 Hz, 1 H), 8.16 (s, 1 H), 7.70–7.73 (m, 2 H), 7.48 (t, *J* = 7.3 Hz, 1 H), 7.31–7.30 (m, 4 H).

^{13}C NMR ($CDCl_3$): δ = 161.24, 147.83, 147.61, 136.43, 135.22, 134.60, 131.75, 130.52, 129.34, 127.91, 127.13, 126.10, 122.41.

GC/MS: *m*/*z* (%) = 256.0 (M^+, 18), 130 (100), 257.0 (M – 1, 16).

Anal. Calcd for $C_{14}H_9ClN_2O$: C, 65.51; H, 3.53; N, 10.91. Found: C, 65.56; H, 3.42; N, 10.72.

3-(4-Chlorophenyl)quinazolin-4(3*H*)-one (4k)
Mp 182–183 °C.

IR (KBr): 1696, 1601, 1462 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 8.33 (d, *J* = 7.5 Hz, 1 H), 8.13 (s, 1 H), 7.68–7.71 (m, 2 H), 7.48 (t, *J* = 7.3 Hz, 1 H), 7.38 (d, *J* = 0.6 Hz, 2 H), 7.25 (d, *J* = 8.6 Hz, 2 H).

^{13}C NMR ($CDCl_3$): δ = 160.2, 148.83, 146.61, 136.43, 135.21, 134.61, 132.75, 130.55, 128.33, 127.91, 126.82, 125.14, 122.42.

GC/MS: *m*/*z* (%) = 256.0 (M^+, 18), 130 (100), 258.0 (M + 2, 32).

Anal. Calcd for $C_{14}H_9ClN_2O$: C, 65.51; H, 3.53; N, 10.91. Found: C, 65.50; H, 3.41; N, 10.71.

3-(4-Fluorophenyl)quinazolin-4(3*H*)-one (4l)
Mp 170–171 °C.

IR (KBr): 1695, 1599, 1461 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 8.32 (d, *J* = 7.5 Hz, 1 H), 8.12 (s, 1 H), 7.67–7.70 (m, 2 H), 7.46 (t, *J* = 7.0 Hz, 1 H), 7.35 (m, 4 H).

^{13}C NMR ($CDCl_3$): δ = 160.12, 147.73, 146.64, 136.45, 135.26, 134.66, 132.62, 130.55, 128.33, 127.91, 126.84, 124.14, 122.43.

Anal. Calcd for $C_{14}H_9FN_2O$: C, 69.99; H, 3.78; N, 11.66. Found: C, 69.92; H, 3.73; N, 11.62.

3-(2-Nitrophenyl)quinazolin-4(3*H*)-one (4m)
Mp 156–158 °C.

IR (KBr): 1710, 1620, 1474 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 8.42 (d, *J* = 7.6 Hz, 1 H), 8.18 (s, 1 H), 7.52 (t, *J* = 7.5 Hz, 1 H), 7.70–7.73 (m, 2 H), 7.26–7.96 (m, 4 H).

^{13}C NMR ($CDCl_3$): δ = 165.14, 152.75, 147.64, 144.74, 144.12, 133.55, 127.35, 122.16, 121.33, 123.64.

Anal. Calcd for $C_{14}H_9N_3O_3$: C, 62.92; H, 3.39; N, 15.72. Found: C, 62.88; H, 3.31; N, 15.65.

3-(3-Nitrophenyl)quinazolin-4(3*H*)-one (4n)
Mp 154–156 °C.

IR (KBr): 1708, 1622, 1470 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 8.41 (d, *J* = 7.6 Hz, 1 H), 8.16 (s, 1 H), 7.50 (t, *J* = 7.5 Hz, 1 H), 7.68–7.72 (m, 2 H), 7.38–7.98 (m, 4 H).

^{13}C NMR ($CDCl_3$): δ = 163.18, 152.34, 147.56, 144.63, 143.56, 133.23, 126.45, 123.63, 122.73, 121.35.

Anal. Calcd for $C_{14}H_9N_3O_3$: C, 62.92; H, 3.39; N, 15.72. Found: C, 62.86; H, 3.28; N, 15.61.

3-(4-Nitrophenyl)quinazolin-4(3*H*)-one (4o)
Mp 165–166 °C.

IR (KBr): 1712, 1621, 1478 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 8.41 (d, *J* = 7.6 Hz, 1 H), 8.16 (s, 1 H), 7.71–7.75 (m, 2 H), 7.51 (t, *J* = 7.4 Hz, 1 H), 7.90 (d, *J* = 8.63 Hz, 2 H), 8.0 (d, *J* = 8.7 Hz, 2 H).

^{13}C NMR ($CDCl_3$): δ = 165.28, 152.85, 147.84, 144.84, 144.10, 133.34, 127.15, 122.16, 121.34, 123.81.

GC/MS: *m*/*z* (%) = 267.0 (M^+, 100), 268 (M^+ + 1, 15).

Anal. Calcd for $C_{14}H_9N_3O_3$: C, 62.92; H, 3.39; N, 15.72. Found: C, 62.85; H, 3.31; N, 15.63.

3-(2,4-Dinitrophenyl)quinazolin-4(3*H*)-one (4p)
Mp 150–152 °C.

IR (KBr): 1715, 1625, 1478 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 9.10 (s, 1 H), 8.17–8.56 (m, 4 H), 7.73–7.76 (m, 2 H), 7.51 (t, *J* = 7.4 Hz, 1 H).

^{13}C NMR ($CDCl_3$): δ = 167.21, 152.83, 147.86, 144.84, 144.0, 138.23, 133.3, 128.75, 127.15, 123.83, 122.16, 121.34, 120.43.

Anal. Calcd for $C_{14}H_8N_4O_5$: C, 53.85; H, 2.58; N, 17.94. Found: C, 68.76; H, 4.61; N, 15.01.

***N*-{4-[4-Oxo-3(4*H*)-quinazolinyl]phenyl}acetamide (4q)**
Mp 198–200 °C.

IR (KBr): 1720, 1686, 1601, 1462 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 8.34 (d, *J* = 7.5 Hz, 1 H), 8.12 (s, 1 H), 8.02 (s, 1 H), 7.69–7.72 (m, 2 H), 7.47 (t, *J* = 7.4 Hz, 1 H), 7.36 (d, *J* = 0.7 Hz, 2 H), 7.26 (d, *J* = 8.6 Hz, 2 H), 2.30 (s, 3 H).

^{13}C NMR ($CDCl_3$): δ = 168.25, 161.24, 147.84, 146.74, 136.55, 135.36, 134.65, 132.72, 131.54, 128.36, 127.31, 126.80, 125.15, 122.44, 19.05.

Anal. Calcd for $C_{16}H_{13}N_3O_2$: C, 68.81; H, 4.69; N, 15.05. Found: C, 68.76; H, 4.61; N, 15.01.

3-Benzylquinazolin-4(3*H*)-one (4r)
Mp 118–120 °C.

IR (KBr): 1670, 1600, 1466 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 8.33 (d, *J* = 7.8 Hz, 1 H), 8.15 (s, 1 H), 7.70–7.76 (m, 2 H), 7.49 (t, *J* = 7.2 Hz, 1 H), 7.27–7.35 (m, 5 H), 5.20 (s, 2 H).

^{13}C NMR ($CDCl_3$): δ = 160.94, 147.55, 146.58, 135.63, 134.52, 129.15, 128.91, 128.45 128.18, 127.66, 127.27, 127.12, 122.15, 49.75.

GC/MS: *m*/*z* (%) = 236.1 (M^+, 100), 235.1 (M – 1, 31), 237.1 (M + 1, 11).

Anal. Calcd for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86. Found: C, 76.15; H, 5.02; N, 11.76.

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