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# An efficient, one-pot three components synthesis of [1,2,4] triazoloquinazolinone derivatives using anthranilic acid as green catalyst

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**Abstract** A simple, efficient and convenient approach has been reported for the synthesis of quinazolines by the condensation of 3-amino, 1,2,4-triazole with dimedone and different aromatic aldehydes in the presence of anthranilic acid as a catalyst through a one-pot reaction. The high yield, at low cost, with no need of chromatographic separation, and the environmentally friendly catalyst are the prominent features of this protocol. The zwitterion of anthranilic acid plays an important role in this one-pot reaction.

**Keywords** Quinazolinones · 3-Amino 1,2,4-triazole · Dimedone · Anthranilic acid · Zwitterions

## Introduction

Amino acids, being building blocks of proteins, are found in every part of every cell. Tryptophan is one of the most important essential amino acids and anthranilic acid plays a vital role both in the anabolism and catabolism of tryptophan. In the

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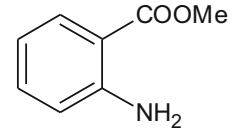
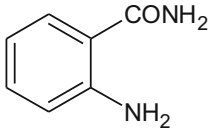
catabolism of tryptophan, one of the intermediates is 3-hydroxy anthranilic acid, which serves as a precursor in the biosynthesis of the vitamin-nicotinic acid. Deficiency of nicotinic acid leads to the disease pellagra in man and black tongue in dogs. Moreover, intermediates in tryptophan catabolism act as the precursors for the biosynthesis of the important biomolecule serotonin, which is a neurotransmitter substance and vasoconstrictor. Anthranilic acid and tryptophan are equally important as biosynthesis of tryptophan occurs through a series of enzymatic reactions from anthranilic acid. In continuation of this text, it is stated that anthranilic acid flows in our veins as a byproduct of many biochemical reactions occurring in cells [1–4].

Major biochemical pathways of bacteria, plants and animals exhibit the importance of anthranilic acid as it acts as the starting material for several other types of compounds in nature. Among these are alkaloids [5] like nicotine, nicotinamide, plant signaling compounds like DIMBOA [6], plant growth hormone indole–3 acetic acid [7, 8], and that the concentration of methyl anthranilate in grapes generally increases on ripening [9], wine, such as Pinot Noir from Burgundy contains ethyl and methyl anthranilate as odorants [10]. A beetle 'black chafer' use anthranilic acid as a pheromone [11]. The presence of *N*-acetylated derivatives of anthranilic acid in oats has been proved [12].

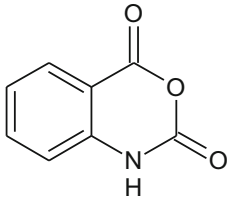
In addition, anthranilic acid and its derivatives are playing a significant role in industry. In perfumes, methyl anthranilate is used as an important ingredient; moreover, it is a flavor additive in soft drinks. The annual production of methyl anthranilate is estimated to be over 1000 tons [13].



methyl anthranilate



anthranilamide



isatonic anhydride

Anthranilamide is also widely applied in numerous synthetic procedures for pharmaceuticals and natural products [14].

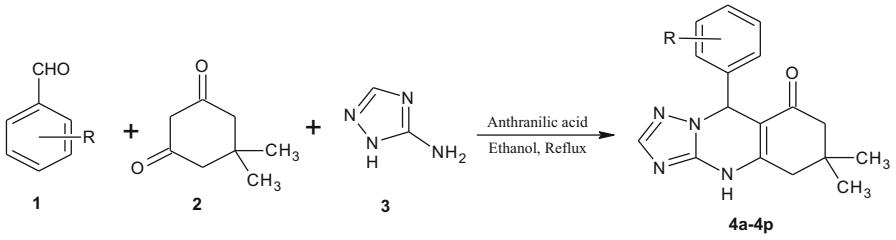
Use of anthranilic acid in stoichiometric amounts in the synthesis of quinazolines, substituted quinazolines, benzodiazepines and benzoxazine-4-ones is well documented in the literature [14]. Rastogi et al. [15] have reported anthranilic acid as a co-catalyst in the synthesis of conjugated nitroalkanes in THF along with the catalyst imidazole via the Morita–Baylis–Hillman reaction. Kassehin et al. [16] proved anthranilic acid as being an innovative green nucleophilic catalyst in the synthesis of antitrypansomal thiosemicarbazones. These reported protocols significantly exhibit the capability of anthranilic acid to act as a catalyst. Moreover, anthranilic acid is non-toxic, inexpensive, readily available, easy to handle and its nucleophilic moiety ($–NH_2$) and acidic moiety (–COOH) are in close vicinity, which leads to the formation of a zwitterion that facilitates the desired transformations.

Quinazolines and condensed quinazolines have been proved to be advantageous to human beings due to their various therapeutic and pharmacological properties like antihypertensives [17, 18], antihistamines, antibacterials [19], analgesics, anti-inflammatories [20], anti-HIV, anti-fungals [21] and anticancer agents [22]. The excellent biological activities and wide applications of quinazolines and condensed quinazolines prompted us to investigate studies on [1,2,4] triazoloquinazolinone derivatives. In recent years, multicomponent reactions are more efficient and are a green alternative [23–25] to conventional bimolecular reactions due to their atom economy, multiple bond forming efficiency, and high selectivity as well as enabling straight forward access to a series of structurally related drug-like compounds. These features made multicomponent reactions (MCR) a powerful tool [26–28] in medicinal, combinatorial and organic chemistry.

It is evident from the literature that the most common methodology for the synthesis of substituted triazolo/benzimidazolo quinazolinones is the one-pot reaction of substituted aldehydes with 3-amino-1,2,4 triazole or 2-aminobenzimidazole with dimedone in the presence of an acid or a basic catalyst. Furthermore, recent reported protocols of the synthesis of 6,6-dimethyl-9-phenyl-5,6,7,9-tetrahydro-[1,2,4] triazolo [5,1-b] quinazolin-8(4H)-one included heating of starting materials in DMF under reflux conditions [29, 30], in the presence of sulfamic acid [31] using acetonitrile as solvents, utilising catalysts like ionic liquids [32], heteropolyacids [33], molecular iodine [34], boric acid [35] and chitosan [36] biopolymers. Despite the potential utility of these strategies, they exhibit various drawbacks such as harsh reaction conditions, use of toxic organic solvents, use of metal catalysts as well as expensive, moisture sensitive, hazardous catalysts, unsatisfactory yields and cumbersome experimental procedures. All these literature facts attracted us to use biodegradable anthranilic acid as a green catalyst in the present protocol.

## Results and discussion

As per our best knowledge, anthranilic acid was herein explored for the first time as a catalyst in the synthesis of 1,2,4 triazoloquinazolines in a one-pot three components coupling of substituted aromatic aldehydes, dimedone and 3-amino-1,2,4-triazole as an amine source in alcohol (Scheme 1).




**Scheme 1** Synthesis of [1,2,4] triazolo [5,1-b] quinazoline-8 (4H)—one derivatives

For the selection of the most appropriate solvent, condensation of dimedone, 4-chlorobenzaldehyde and 3-amino-1,2,4 triazole, as a model reaction, was examined in water, 50% ethanol, ethanol, DMF, and acetonitrile (Table 1). The synthesis of a target product in the ethanol at 80 °C with anthranilic acid as the catalyst was obtained in high yield (Table 1, entry-5). The yields are much lower with other solvents.

Our next task was to optimize the appropriate concentration of the catalyst. We, therefore, carried out a model reaction at various mole percentages, and the results were compared (Table 2).

The highest yield was obtained with 30 mol% anthranilic acid in alcohol as the solvent (Table 2, entry-6). Increase in the concentration of catalyst did not increase the yield. It was noticed that at low concentration of the catalyst, lower yield of the product is encountered, and, of course, without catalyst we did not get any product.

To optimize the reaction time on the yield of the desired product, the model reaction was screened at different time intervals (Table 3).

To our delight, we obtained the maximum yield of the product within 6 h. (Table 3, entry-6) Furthermore, increase in reaction time did not show any effect on

**Table 1** Synthesis of 9-(4-chlorophenyl)-6-6 dimethyl-5,6,7,9-tetrahydro [1,2,4] triazolo [5,1-b] quinazolin-8(4H) one

| Entry | Solvent | Temperature (°C) | Time (h) | Yield[a] (%) |
|---|---|---|---|---|
| 1 | DMF | 100 | 10 | Trace |
| 2 | $CH_3CN$ | 85 | 10 | Trace |
| 3 | Water | 100 | 10 | Trace |
| 4 | 50% EtOH | 90 | 10 | 30 |
| **5** | **EtOH** | **80** | **10** | **80** |

Reagents and reaction conditions—reaction was carried out using dimedone (1 mmol), 4-chlorobenzaldahyde (1 mmol), 3-amino, 1,2,4 triazole and 20 mol% anthranilic acid as a catalyst

Bold values indicate optimized conditions

[a] Isolated yields

**Table 2** Optimization of catalyst

Reagents and reaction conditions—reaction was carried out using dimedone (1 mmol), 4-chlorobenzaldehyde (1 mmol), 3-amino 1,2,4 triazole (1 mmol) and various mol% of anthranilic acid as a catalyst at 80 °C for 10 h under reflux

Bold values indicate optimized conditions

| Entry | Anthranilic acid mol% | Time (h) | Yield[a] (%) |
|---|---|---|---|
| 1 | 5 | 10 | Trace |
| 2 | 10 | 10 | 20 |
| 3 | 15 | 10 | 60 |
| 4 | 20 | 10 | 80 |
| 5 | 25 | 10 | 88 |
| **6** | **30** | **10** | **95** |
| 7 | 35 | 10 | 95 |
| 8 | 40 | 10 | 95 |
| 9 | – | 10 | No reaction |

**Table 3** Optimization of reaction time

| Entry | Time (h) | Yield[a] (%) |
|---|---|---|
| 1 | 1 | Trace[b] |
| 2 | 2 | 12[b] |
| 3 | 3 | 45[b] |
| 4 | 4 | 82[b] |
| 5 | 5 | 92 |
| **6** | **6** | **95** |
| 7 | 7 | 95 |
| 8 | 8 | 95 |

Reagents and reaction conditions—reaction was carried out with dimedone (1 mmol), 4-chlorobenzaldehyde (1 mmol), 3-amino 1,2,4 triazole in 5 ml EtOH using 30 mol % anthranilic acid at 80 °C

Bold values indicate optimized conditions

[a] Isolated yields

[b] Knoevenagel condensation product was obtained as byproduct

the yield of the product. In the present protocol, we initiated our studies by employing a trial reaction in which a mixture of dimedone (1 mmol), 4-chlorobenzaldehyde (1 mmol) and 3-amino-1,2,4 triazole (1 mmol) in the presence of 30 mol% anthranilic acid was refluxed in 5 mL of ethanol at 80 °C for the stipulated period of time. The formation of title compound (**4-a**) was evident from the appearance of >C=O stretching at 1647 $cm^{-1}$, C–Cl stretching at 728 $cm^{-1}$ and N–H stretching at 3089 $cm^{-1}$ in IR, with appearance of the characteristic methine proton as a singlet at d 6.43, and the appearance of $[M + H]^+$ at *m/z* 329 in the mass spectrum (ESI) was in agreement with the proposed structure.

To establish the scope and utility of our catalyst for the synthesis of [1,2,4] triazolo-[5,1-b]-8(4H)-one derivatives, different substituted aromatic aldehydes were reacted with dimedone and 3-amino-1,2,4-triazole in the presence of anthranilic acid and ethanol as the reaction medium at 80 °C (Table 4).

From the analysis of reaction data (Table 4), we noticed that electron withdrawing groups on aromatic aldehydes are favorable for this transformation as they exhibit higher yields with low reaction time. However, electron donating groups on aromatic aldehydes showed slightly lower yield with increased reaction time. All the compounds reported in Table 4 have been characterized by IR, $^1H$, $^{13}C$ NMR, MS and elemental analysis, and data is consistent with their structures.

The implementation of an efficient catalyst and an adequate solvent is thus planned in the context of green chemistry [37, 38]. In chemical research and engineering, the aim of green chemistry is to encourage the design of products and processes that minimize the use and generation of hazardous substances.

To evaluate the present protocol according to green chemistry principles, green metrics such as Mass Intensity (MI), Reaction Mass Efficiency (RME), Carbon Efficiency (CE), and Atom Economy (AE) [39] are the terms which reveal the greenness of the reaction. In an ideal situation, it is expected that MI $\approx$ 1% [40],

**Table 4** Synthesis of (1,2,4) triazoloquinazolone derivatives by using anthranilic acid catalyst

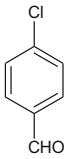
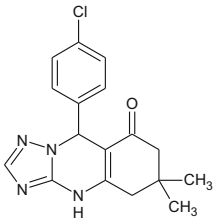
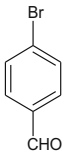
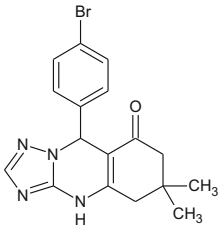
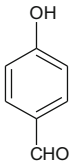
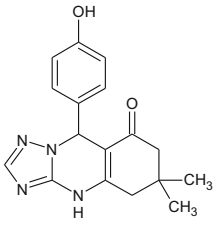
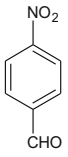
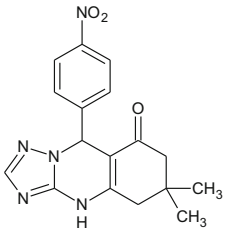
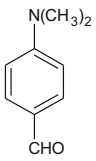
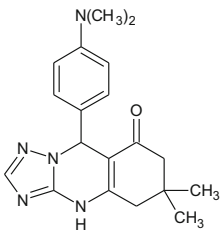
| Entry | Aldehyde [1–3] | Product [6] | Time (h) | Yield[a] (%) | M.P. (°C) | |
|---|---|---|---|---|---|---|
| | | | | | Found | Literature |
| **4a** |  |  | 6 | 95 | 302–304 | 304–306 [34] |
| **4b** |  |  | 6 | 95 | 285–287 | 286–288 [34] |
| **4c** |  |  | 6 | 90 | 302–304 | >300 [34] |
| **4d** |  |  | 6 | 95 | 305–307 | >300 [34] |
| **4e** |  |  | 7 | 87 | 288–300 | 285–287 [35] |

**Table 4** continued

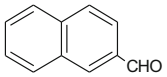
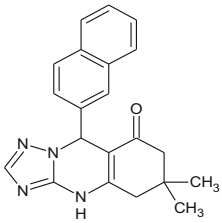
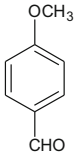
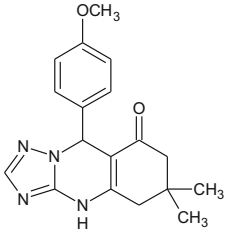
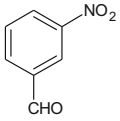
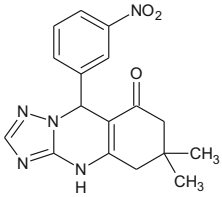
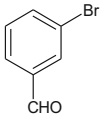
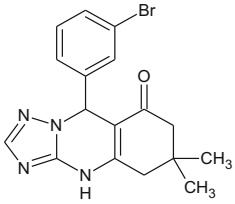
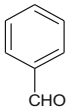
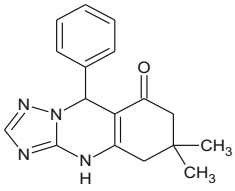
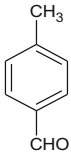
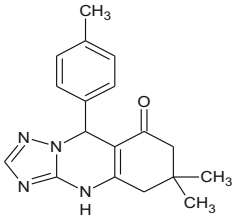
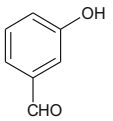
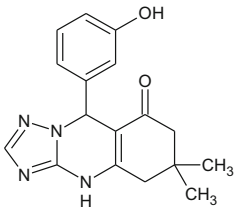
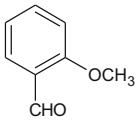
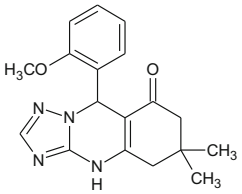
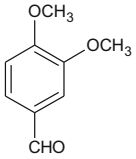
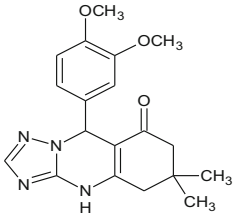
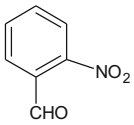
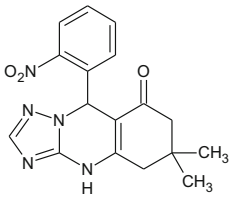
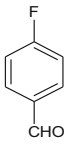
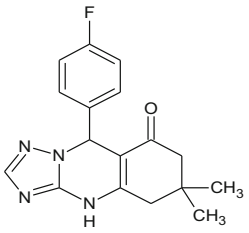
| Entry | Aldehyde [1–3] | Product [6] | Time (h) | Yield[a] (%) | M.P. (°C) | |
|---|---|---|---|---|---|---|
| | | | | | Found | Literature |
| **4f** |  |  | 6 | 91 | 286–288 | 287–290 [31] |
| **4g** |  |  | 7 | 94 | 224–226 | 228–230 [35] |
| **4h** |  |  | 7 | 90 | 268–270 | 266–269 [31] |
| **4i** |  |  | 7 | 92 | 278–280 | 280–282 [32] |
| **4j** |  |  | 6 | 95 | 252–254 | 250–252 [34] |
| **4k** |  |  | 7 | 90 | 265–269 | 266–268 [34] |

**Table 4** continued

| Entry | Aldehyde [1–3] | Product [6] | Time (h) | Yield[a] (%) | M.P. (°C) | |
|---|---|---|---|---|---|---|
| | | | | | Found | Literature |
| **4l** |  |  | 7 | 92 | 288–290 | 289–290 [34] |
| **4m** |  |  | 8 | 92 | 241–243 | 240–243 [34] |
| **4n** |  |  | 8 | 86 | 278–280 | – |
| **4o** |  |  | 6 | 91 | 288–290 | 290–292 [34] |
| **4p** |  |  | 7 | 94 | 306–308 | 301–303 [34] |

[a] Isolated yield

RME ≈ 100%, %CE ≈ 100 and %AE ≈ 100. We have represented the green metrics calculations for all the reactions in Table 5.

The results demonstrate that MI values for all compounds are quite excellent as well as excellent yields produced good values of RME while moderate yield

**Table 5** Green metrics calculations

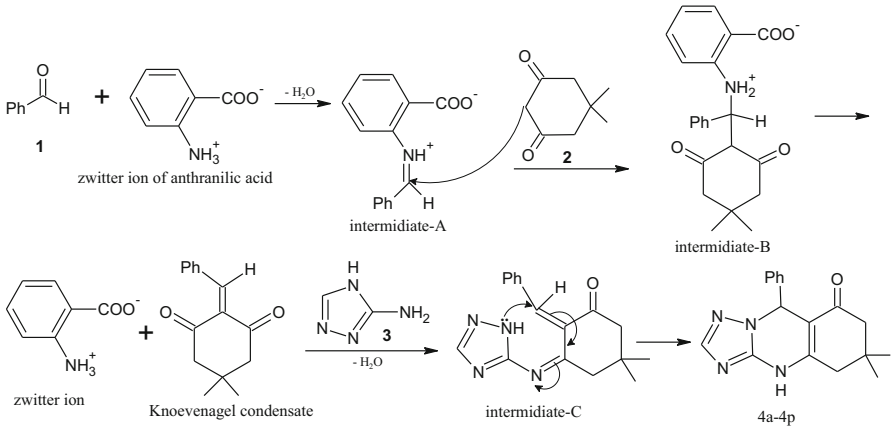
| Entry | Compound code | %Yield | FW (product) | Yield (g) | MI | %RME | %CE | %AE |
|---|---|---|---|---|---|---|---|---|
| 1 | **4a** | 95 | 328.796 | 0.311 | 1.17 | 85.43 | 94.80 | 90.44 |
| 2 | **4b** | 95 | 373.247 | 0.354 | 1.15 | 86.55 | 94.90 | 91.21 |
| 3 | **4c** | 90 | 310.350 | 0.279 | 1.24 | 80.36 | 90.00 | 89.91 |
| 4 | **4d** | 95 | 339.348 | 0.322 | 1.16 | 89.06 | 94.90 | 90.43 |
| 5 | **4e** | 87 | 337.418 | 0.293 | 1.27 | 73.10 | 86.90 | 90.37 |
| 6 | **4f** | 91 | 344.409 | 0.313 | 1.21 | 82.36 | 90.90 | 90.55 |
| 7 | **4g** | 94 | 324.377 | 0.304 | 1.18 | 84.44 | 93.80 | 90.22 |
| 8 | **4h** | 90 | 339.348 | 0.305 | 1.22 | 81.33 | 89.90 | 90.42 |
| 9 | **4i** | 92 | 373.247 | 0.348 | 1.17 | 84.87 | 91.95 | 91.21 |
| 10 | **4j** | 95 | 294.351 | 0.279 | 1.19 | 83.53 | 94.89 | 89.96 |
| 11 | **4k** | 90 | 308.301 | 0.277 | 1.24 | 80.06 | 90.00 | 89.53 |
| 12 | **4l** | 92 | 310.350 | 0.285 | 1.21 | 82.36 | 91.95 | 89.59 |
| 13 | **4m** | 92 | 324.377 | 0.298 | 1.20 | 82.77 | 91.96 | 90.00 |
| 14 | **4n** | 85 | 354.402 | 0.309 | 1.26 | 79.23 | 85.02 | 90.80 |
| 15 | **4o** | 91 | 339.348 | 0.308 | 1.21 | 82.13 | 90.90 | 90.40 |
| 16 | **4p** | 94 | 312.341 | 0.293 | 1.11 | 89.66 | 93.90 | 89.75 |

produced moderate RME values. Moreover, our reactions show excellent CE because all the carbon atoms of the reactants are present in the product. Atom economy values $\approx$90% reveals that the present protocol is of high atom economy. Table 5 clearly exhibited that anthranilic acid is an excellent catalyst for this one pot three components reaction since it gives desired product in good to excellent yields and leads to excellent green metrics.

A plausible reaction mechanism for a three components reaction of dimedone, aromatic aldehydes and 3-amino 1,2,4 trizole catalysed by anthranilic acid is shown in Scheme 2. We believe that the zwitter ionic property of anthranilic acid accelerates the reaction. The free amino group of anthranilic acid attacks the carbonyl group of aldehyde (1) through nucleophilic attack to produce the intermediate-A. Further dimedone (**2**) reacts with intermediate-A through the Knoevenagel type condensation and produces Knoevenagel condensate via formation of intermediate-B and elimination of catalyst, which again participates in the mechanism. The Knoevenagel condensate undergoes nucleophilic attack of the amine moiety of triazole, which is followed by cyclization to afford the target product (**4a**–**4p**).

## Experimental section

Melting points were measured by an open capillary tube method and are uncorrected. IR spectra were recorded on a FTIR Nicolet, iS 10, Thermoscientific, USA, $^{1}$H and $^{13}$C NMR spectra were recorded using a 400 MHz Bruker




**Scheme 2** Plausible mechanism for the synthesis of [1,2,4] triazoloquinazolone derivatives using anthranilic acid

spectrometer in $CDCl_3$/DMSO solvents. Mass spectra were recorded on a Shimadzu Toshvin. All chemicals and reagents were purchased from Aldrich, Alfa Asar and Spetrochem and used without any purification. The progress of the reaction was monitored on readymade silica gel plates (Merck) using the ethyl acetate-pet ether solvent system.

### General procedure for the synthesis of [1,2,4] triazolo [5,1-b] quinazolin–8(4H)-ones

A mixture of aromatic aldehyde (1 mmol), dimedone (1 mmo1), 3-amino 1,2,4 triazole (1 mmol) in the presence of 30 mol % anthranilic acid was refluxed in 5 mL of ethanol at 80 °C for the stipulated period of time. The reaction was monitored by TLC. After completion of the reaction, yellowish white product appeared in the flask. Then the reaction mixture was allowed to cool at room temperature. The solid obtained was filtered and washed with alcohol to afford the title compounds (**4a**–**4p**) in excellent yield with good purity. All the compounds were characterized by using their data in the literature.

## Conclusion

In conclusion, we have developed an environmentally benign protocol for the synthesis of 1,2,4 triazolo-[5,1-b]-quinazolin-8(4H)-one derivatives by using aromatic aldehydes, dimedone and 3-amino-1,2,4 triazole by employing anthranilic acid as a biodegradable green catalyst. This protocol offers several advantages such as mild reaction conditions, low cost, easy operation, high reaction yields, and no need of column chromatography for separation, and it has a simple purification. Moreover, the use of anthranilic acid as a new catalyst proved to be superior on the basis of green metrics.

## Spectral data of synthesized compounds

*9-(4-Chlorophenyl) 6,6-dimethyl-5,6,7,9 tetrahydro-[1,2,4]–triazolo [5,1-b] quinazolin-8(4H)-one* (**4a**) Pale yellow solid, yield—95%, mp-302–304 °C; **IR**: 3089, 2963, 1647, 1575, 1364, 1253, 759 $cm^{-1}$; **$^1$H NMR** (400 MHz, $CDCl_3$)—$\delta$ = 1.11 (s, 3H, $CH_3$), 1.18 (s, 3H, $CH_3$), 2.25–2.35 (q, $J$ = 16.8 Hz, $J$ = 16.8 Hz, 2H, H-5), 2.58 (s, 2H, H-7), 6.43 (s, 1H, H-9), 7.25–7.31 (m, 4H, Ar–H) 7.69 (s, 1H, H-2) 11.20 (s, 1H, NH); **$^{13}$C NMR** (100 MHz, $CDCl_3$) 193.47, 148.90, 148.72, 147.30, 139.01, 134.22, 128.88, 128.55, 107.23, 58.26, 50.35, 40.77, 32.81, 28.98, 27.62; Anal. Calcd (%) C: 62.10, H: 5.17, N: 17.05; $C_{17}H_{17}N_4OCl$; found: (%) C: 62.12, H: 5.14, N: 16.98 MS *m/z* (ESI): 329 $[M + H]^+$.

*9-(4-Bromophenyl)-6,6-dimethyl 5,6,7,9-tetrahydro-[1,2,4]-triazolo-[5,1-b] quinazolin-8 (4H)-one* (**4b**) Pale yellow solid, yield-95%, mp 285–287 °C, **IR**: 3066, 2956, 2919, 1636, 1568, 1363, 1255, 841 $cm^{-1}$ **$^1$H NMR** (400 MHz, DMSO) $\delta$ = 0.96 (s, 3H, $CH_3$), 1.04 (s, 3H, $CH_3$), 2.05–2.19 (q, $J$ = 16.4 Hz, $J$ = 16.4 Hz, 2H, H-5), 2.48–2.50 (m, 2H, H-7), 6.19 (s, 1H, H-9), 7.08–7.35 (m, 4H, Ar–H), 7.49 (s, 1H, H-2), 11.03 (s, 1H, NH); Anal calcd (%): C:54.71, H:4.56, N:15.02, $C_{17}H_{17}N_4OBr$, found (%): C:54.46, H:4.28, N:15.34; MS *m/z* (ESI): 373 $[M]^+$.

*9-(4–Hydroxyphenyl)-6,6-dimethyl-5,6,7,9–tetrahydro-[1,2,4]-triazolo-[5,1-b] quinazolin-8 (4H)-one* (**4c**) Pale yellow solid, yield—90%, mp 302–304 °C; **IR**: 3088, 2964, 1630, 1580, 1363, 1267, 730 $cm^{-1}$; **$^1$H NMR** (400 MHz, DMSO) $\delta$ = 0.95–0.96 (d, 3H, $CH_3$), 1.01–1.03 (d, 3H, $CH_3$), 2.02–2.08 (q, $J$ = 7.2 Hz, $J$ = 7.2 Hz, 2H, H-5), 2.11–2.17 (m, 2H, H-7), 6.08–6.10 (d, 1H, H-9), 6.58–7.47 (m, 5H, Ar–H, H-2), 9.31 (s, 1H, OH), 10.87 (s, 1H, NH); Anal, Calcd (%) C: 65.81, H: 5.81, N: 18.06; $C_{17}H_{18}N_4O_2$, found (%): C: 65.34, H: 5.71, N: 17.90; MS *m/z* (ESI): 311 $[M + H]^+$.

*9-(4-Nitrophenyl)-6,6 dimethyl-5,6,7,9-tetrahydro-[1,2,4]-triazolo-[5,1-b]-quinazolin-8 (4H)-one* (**4d**) Pale yellow solid, yield—95%, mp—305-307 °C; **IR**—2964, 1644, 1577, 1351, 1252, 729 $cm^{-1}$; **$^1$H NMR** (400 MHz, DMSO) $\delta$ = 0.95 (s, 3H, $CH_3$), 1.05 (s, 3H, $CH_3$), 2.05–2.20 (q, $J$ = 16.4 Hz, $J$ = 16.4 Hz, 2H, H-5), 2.50 (s, 2H, H-7), 6.34 (s, 1H, H-9), 7.40–7.42 (d, $J$ = 8.4 Hz, 2H, Ar–H), 8.06–8.09 (d, $J$ = 8.8 Hz, 2H, Ar–H), 7.54 (s, 1H, H-2), 11.19 (s, 1H, NH); **$^{13}$C NMR** (100 MHz, DMSO) $\delta$ = 193.84, 151.27, 150.44, 148.15, 147.29, 128.35, 123.65, 105.49, 58.00, 50.26, 32.57, 28.84, 27.41; Anal calcd (%) C: 60.18, H: 5.015, N: 20.6, $C_{17}H_{17}N_5O_3$; found (%): C: 60.17, H: 5.44, N: 20.61; MS *m/z* (ESI): 353.12.

*9-(4-Dimethylaminophenyl)-6,6-dimethyl-5,6,7,9-tetrahydro-[1,2,4]-triazolo-[5,1-b]quinazolin-8 (4H)-one* (**4e**) Pale yellow solid, yield—87%, mp—288–300 °C; IR—3085, 2961, 1646, 1579, 1366, 1253, 735 $cm^{-1}$; $^1$H NMR (400 MHz, DMSO) $\delta$ = 0.99 (s, 3H, $CH_3$), 1.04 (s, 3H, $CH_3$), 2.04-2.18 (q, $J$ = 16.4 Hz, $J$ = 16.4 Hz, 2H, H-5), 2.46 (s, 2H, H-7), 2.82 (s, 6H, $2NCH_3$ group), 6.11 (s,1H, H-9), 6.50–6.52 (d, $J$ = 8.4 Hz, 2H, Ar–H), 7.00-7.02 (d, $J$ = 8.4 Hz, 2H, Ar–H), 7.44 (s, 1H, H-2) 10.75 (s, 1H, NH); $^{13}$C NMR (100 MHz, DMSO) $\delta$ = 193.81, 150.16, 149.74,

147.04, 129.42, 127.94, 112.11, 106.82, 57.98, 50.47, 32.51, 29.10, 27.38; MS *m/z* (ESI): 337.183 $[M]^+$.

*9-(2-Naphthyl)-6,6 dimethyl-5,6,7,9-tetrahydro-[1,2,4] triazolo-[5,1-b]-quinazolin-8 (4H)-one* (**4f**) Pale yellow solid, yield—91%, mp—286–288 °C; **IR**—3081, 2962, 1651,1573, 1362, 1250, 729 $cm^{-1}$; **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta = 1.11$ (s, 3H, $CH_3$), 1.17 (s, 3H, $CH_3$), 2.24–2.35 (q, $J = 16.4$ Hz, $J = 16.8$ Hz, 2H, H-5), 2.61 (s, 2H, H-7), 6.64 (s, 1H, H-9), 7.37–7.88 (m, 7H, Ar–H), 7.70 (s, 1H, H-2), 11.22 (s, 1H, NH); **$^{13}$C NMR** (100 MHz, $CDCl_3$), $\delta = 193.55$, 150.80, 150.19, 147.29, 138.99, 132.92, 132.89, 128.19, 127.67, 126.49, 126.46, 124.94, 106.12, 58.73, 50.42, 32.58, 29.05, 27.35; Anal calcd (%) C: 73.25, H: 5.81, N: 16.28,$C_{21}H_{20}N_4O$ found (%): C: 71.72, H: 5.92, N: 15.90; MS *m/z* (ESI): 356.102 $[M]^+$.

*9-(4-Methoxyphenyl)-6,6 dimethyl-5,6,7,9 tetrahydro-[1,2,4]-triazolo-[5,1-b]-quinazolin-8 (4H)-one* (**4g**) Pale yellow solid, yield—94%, mp—224–226 °C; **IR**—3093, 2964, 1649, 1576, 1363, 1245, 1174 $cm^{-1}$; **$^1$H NMR** (400 MHz, DMSO) $\delta = 0.98$ (s, 3H, $CH_3$), 1.05 (s, 3H, $CH_3$), 2.04–2.18 (q, $J = 16.4$ Hz, $J = 16.4$ Hz, 2H, H-5), 2.48–2.51 (d, 2H, H-7), 3.67 (s, 3H, $OCH_3$), 6.15–6.16 (d, 1H, H-9), 6.71–7.47 (m, 5H, Ar–H, H-2), 10.90 (s, 1H, NH); **$^{13}$C NMR** (100 MHz, DMSO) $\delta = 193.89$, 159.10, 150.16, 149.92, 147.10, 133.69, 128.27, 113.75, 106.73, 57.97, 55.17, 50.43, 32.52, 28.98, 27.38; MS *m/z* (ESI): 324.175 $[M]^+$.

*9-(3-Nitrophenyl)-6,6 dimethyl-5,6,7,9 tetrahydro-[1,2,4]–triazolo-[5,1-b]-quinazolin-8 (4H)-one* (**4h**) Pale yellow solid, yield—90%, mp—268–270 °C; **IR**—2965, 1646, 1578, 1352, 1254, 731 $cm^{-1}$; **$^1$H NMR** (400 MHz, DMSO) $\delta = 0.98$ (s, 3H, $CH_3$), 1.06 (s, 3H, $CH_3$), 2.07–2.21(q, $J = 16.0$ Hz, $J = 16.4$ Hz, 2H, H-5), 2.52 (s, 2H, H-7), 6.36 (s, 1H, H-9), 7.45–8.03 (m, 5H, Ar–H, H-2), 11.17(s, 1H, NH); **$^{13}$C NMR** (100 MHz, DMSO) $\delta = 193.60$, 151.32, 150.50, 148.09, 147.26, 143.48, 133.68, 129.81, 122.93, 122.11, 105.30, 57.99, 50.29, 32.61, 28.92, 27.44; Anal calcd (%) C: 60.18, H: 5.015, N: 20.65, $C_{17}H_{17}N_5O_3$; found (%): C: 59.94, H: 4.76, N: 20.58; MS *m/z* (ESI): 340 $[M + H]^+$.

*9-(3-Bromophenyl)-6,6 dimethyl-5,6,7,9-tetrahydro-[1,2,4]–triazolo-[5,1-b]-quinazolin-8 (4H)-one* (**4i**) Pale yellow solid, yield-92%, mp—278–280 °C; **IR**—3065, 2964, 1640, 1570, 1364, 1253, 840 $cm^{-1}$; **$^1$H NMR** (400 MHz, DMSO) $\delta = 0.98$ (s, 3H, $CH_3$), 1.05 (s, 3H, $CH_3$), 2.07–2.19 (q, $J = 16.4$ Hz, $J = 16.4$ Hz, 2H, H-5), 2.49 (s, 2H, H-7), 6.19 (s, 1H, H-9), 7.11–7.48 (m, 4H, Ar–H), 7.51 (s, 1H, H-2), 11.03 (s, 1H, NH) ppm; **$^{13}$C NMR** (100 MHz, DMSO) $\delta = 193.60$, 150.92, 150.27, 147.20, 143.83, 130.93, 130.32, 130.28, 126.02, 122.14, 105.75, 58.00, 50.36, 32.59, 28.93, 27.42; Anal calcd (%) C: 54.71, H: 4.56, N: 15.02, $C_{17}H_{17}N_4OBr$, found (%): C: 54.44, H: 4.30, N: 15.22; MS *m/z* (ESI): 373 $[M]^+$.

*9-Phenyl-6,6 dimethyl-5,6,7,9-tetrahydro-[1,2,4]-triazolo-[5,1-b]-quinazolin-8 (4H)-one* (**4j**) Pale yellow solid, yield—95%, mp—252–254 °C; **IR**—3032, 2961, 1647, 1576, 1365, 1253, 727 $cm^{-1}$; **$^1$H NMR** (400 MHz, DMSO) $\delta = 0.97$ (s, 3H, $CH_3$), 1.05 (s, 3H, $CH_3$), 2.04–2.19 (q, $J = 16.4$ Hz, $J = 16.0$ Hz, 2H, H-5), 2.49 (s, 2H, H-7), 6.19 (s, 1H, H-9), 7.14–7.23 (m, 5H, Ar–H), 7.50-7.51 (d, 1H,

H-2), 11.00 (s, 1H, NH); **$^{13}$C NMR**—(100 MHz, DMSO) $\delta = 193.74$, 150.57, 150.00, 147.22, 141.48, 128.42, 127.96, 127.17, 106.45, 58.48, 50.40, 32.54, 29.00, 27.36; MS *m/z* (ESI): 295.150 $[M + H]^+$.

*9-(3, 4-Dimethoxylphenyl)-6, 6 dimethyl–5,6,7,9-tetrahydro-[1,2,4]-triazolo-[5,1-b]-quinazolin-8 (4H)-one* (**4n**) Pale yellow solid, yield—86%, mp—278–280 °C; **IR**—3158, 2952, 1620, 1562, 1360, 1251, 833 $cm^{-1}$; **$^1$H-NMR** (400 MHz, DMSO) $\delta = 1.00$ (s, 3H, $CH_3$), 1.05 (s, 3H, $CH_3$), 2.06–2.20 (q, $J = 16.4$ Hz, $J = 16.4$ Hz, 2H, H-5), 2.48 (s, 2H, H-7), 3.32 (s, 3H, $OCH_3$), 3.72 (s, 3H, $OCH_3$), 6.11 (s, 1H, H-9), 6.52–6.54 (d, $J = 8.0$ Hz 1H, Ar–H), 6.62–6.64 (d, $J = 8.0$ Hz, 1H Ar–H), 6.74 (s, 1H, Ar–H), 7.49 (s, 1H, H-2), 10.90 (s, 1H, NH); **$^{13}$C NMR**—(100 MHz, DMSO) $\delta = 193.52$, 150.36, 147.47, 146.47, 132.98, 119.67, 115.44, 111.44, 106.53, 58.14, 55.88, 50.46, 32.51, 29.20, 27.23.

*9-(4-Fluorophenyl)-6,6-dimethyl-5,6,7,9-tetrahydro-[1,2,4]-triazolo-[5,1-b]-quinazolin-8 (4H)-one* (**4p**) Pale yellow solid, yield—93%, mp—279–280 °C; **IR**—3137, 2962, 2888, 1646, 1577, 1363, 1254, 761 $cm^{-1}$; **$^1$H NMR** (400 Hz, DMSO), $\delta = 0.97$ (s, 3H, $CH_3$), 1.04 (s, 3H, $CH_3$), 2.05–2.19 (q, $J = 16.4$ Hz, $J = 16.4$ Hz, 2H, H-5), 2.49 (s, 2H, H-7), 6.21 (s, 1H, H-9), 6.90–7.50 (m, 5H, Ar–H, H-2), 10.99 (s, 1H, NH); Anal calcd (%) C: 54.70, H: 4.59, N: 15.01, $C_{17}H_{17}N_4OF$, found (%): C: 54.55, H: 4.60, N: 14.96.

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