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A simple, convenient one-pot synthesis of [1,2,4]triazolo/benzimidazolo quinazolinone derivatives by using molecular iodine

Ravinder Goud Puligoundla [b,†], Shuklachary Karnakanti [a,†], Rajashaker Bantu [a,†], Nagaiah Kommu [b,*], Sudhakar Babu Kondra [c,*], Lingaiah Nagarapu [a,†]

[a] Organic Chemistry Division-II, Indian Institute of Chemical Technology, Hyderabad 500 607, India
[b] Organic Chemistry Division-III, Indian Institute of Chemical Technology, Hyderabad 500 607, India
[c] Department of Chemistry, Sri Krishnadevaraya University, Ananthapur 515 037, India

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ABSTRACT

A wide variety of quinazolinone derivatives have been synthesized by condensation of 3-amino-1,2,4-triazole and 2-aminobenzimidazole as amine sources, with aromatic aldehydes and dimedone in the presence of 10 mol % of molecular iodine in acetonitrile under reflux conditions through one-pot reactions. Environmental acceptability, low cost, no need of chromatographic separation, and high yields are the important features of this protocol.

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In the mainstream of current interest, multicomponent processes have recently gained considerable economic and ecological interest as they address fundamental principles of synthetic efficiency and reaction design. Multi-component reactions (MCRs) have been proven to be a very elegant and rapid way to access complex structures in a single synthetic operation from simple building blocks and show high selectivity.[1]

Nitrogen-containing heterocycles have always played a major role in the pharmaceutical and agrochemical industries because of their often potent physiological properties, which have resulted in numerous applications.[2] Triazolo quinazolinone derivatives are an important class of natural products and exhibit a wide range of spectrum of biological activities, such as antihypertensive,[3] antihistaminic,[4] analgesic, anti-inflammatory,[5] anticancer,[6] and anti-HIV activities.[7] Moreover, the triazoles, imidazoles, pyrazoles, and tetrazoles are representing an important structural motif in medicinal chemistry and can be found in the drugs containing aromatic five-membered nitrogen heterocycle, such as cholesterol-reducing atorvastatin, anti-inflammatory celecoxib, anti-ulcerative cimetidine, β-lactamase tazobactam, antifungal fluconazole, and anti-hypertensive losartan (Fig. 1). These derivatives also have a long history of application in agrochemicals and pharmaceutical industry as herbicides and active pharmaceuticals. The prevalence of triazolo quinazolinone cores in biologically active molecules has stimulated the need for elegant and efficient ways to make these heterocyclic lead.

Several different strategies for the synthesis of substituted triazolo/benzimidazolo quinazolinones are known, the most common protocol is the reaction of substituted aldehydes with 3-amino-1,2,4-triazole and 2-aminobenzimidazole as amine sources and dimedone in the presence of acid or basic catalysts. There are literary data about the synthesis of 6,6-dimethyl-9-phen yl-5,6,7,9-tetrahydro-[1,2,4]triazolo[5,1-*b*]quinazolin-8(4*H*)-one and 3,3-dimethyl-12-phenyl-1,2,3,4,5,12-hexatrahydro-[4,5]imidazolo [2,1-*b*]quinaz olin-1-one derivatives by treatment of 3-amino-1,2,4-triazolo or 2-aminobenzimidazole with aldehydes and dimedone.[8] The cyclocondensation was realized by heating of the starting materials in DMF under reflux conditions[8a,b] or in the presence of sulfamic acid using acetonitrile as solvent under reflux conditions[8c] or in the presence of ionic liquids[8d] or in the presence of heteropolyacids.[8e] However, many of these methods are associated with various drawbacks such as use of metal catalysts, harsh reaction conditions, tedious experimental procedures, unsatisfactory yields, long reaction times, and usage of expensive and moisture sensitive catalysts. Hence, there is a need to develop a rapid, efficient, and environmentally benign synthetic protocol for the synthesis of triazolo/benzimidazolo quinazolinone derivatives.

In recent years, the use of molecular iodine in organic synthesis has received considerable attention as an inexpensive, non-toxic, readily available agent affording the corresponding products with

* Corresponding authors. Tel.: +91 40 27191509/10; fax: +91 40 27193382 (K.N.); tel.: +91 40 27191509; fax: +91 40 27193382 (S.B.K.).
E-mail addresses: rajashakerbantu@yahoo.co.in (R. Bantu), nagaiah@iict.res.in (K. Nagaiah), drksbabu@gmail.com (S.B. Kondra).
† Tel.: +91 40 27191509; fax: +91 40 27193382.

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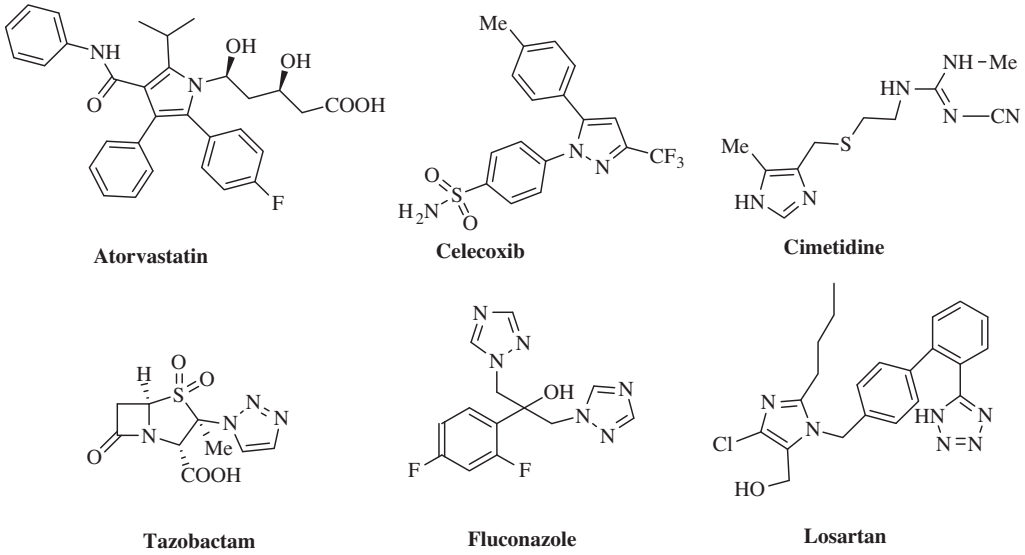


Figure 1.

high selectivity in excellent yields. The mild Lewis acidity associated with iodine enhanced its usage in organic synthesis to perform several organic transformations using stoichiometric levels to catalytic amounts. Owing to advantages associated with this eco-friendly catalyst, molecular iodine has been explored as a powerful reagent in organic synthesis.[9] Recently, we reported the use of iodine for the synthesis of 1,2,3,6-tetrahydropyrimidines.[10] In this Letter, we report the synthesis of [1,2,4]triazolo[5,1-*b*]quinazolin-8(4*H*)-one and 3,3-dimethyl-12-phenyl-3,4,5,12-tetrahydro benzo[4,5]imidazo[2,1-*b*]quinazolin-1(2*H*)-one derivatives by the iodine catalyzed cyclocondensation of 3-amino1,2,4-triazole **1**/2-aminobenzimidazole **5**, aromatic aldehydes **2** and **3** in excellent yields (Scheme 1 and Table 1).

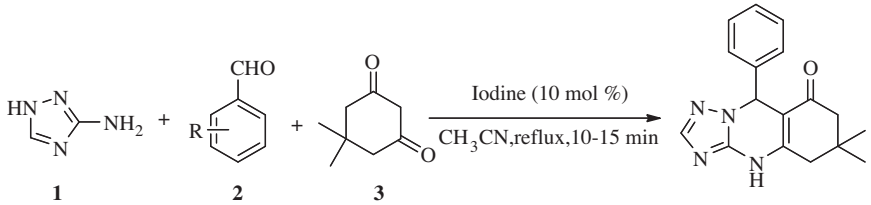
Initially, the reaction of 3-amino-1,2,4 triazole (**1**) with 4-nitro benzaldehyde (**2**) and dimedone (**3**) in the presence of 10 mol % of iodine for 10–15 min. was refluxed in 5 mL of CH_3CN. The reaction mass was cooled to room temperature and filtered. The solid was separated and washed with water, dried at reduced pressure to afford the title compound 6,6-dimethyl-9-(4-nitrophenyl)-5,6,7,9-tetrahydro-[1,2,4]triazolo[5,1-*b*]quinazolin-8(4*H*)-one (**4d**) in 97.1% yield. Interestingly we did not obtain any product when the experiment was done without catalyst under refluxing in acetonitrile. All the [1,2,4]triazolo/benzimidazolo quinazolinone derivatives were obtained in excellent yields with good purity. The isolated products were completely characterized by IR, ^{1}H NMR, and mass spectroscopic analyses. The formation of compound **4d** was evident from the appearance of $[M+H]^+$ peak at *m*/*z* 340 in mass spectrum (ESI), –C=O stretching at 1646 cm^{-1} in IR and the appearance of characteristic methine proton as a singlet at δ 6.35 in ^{1}H NMR and the appearance of carbonyl carbon at δ 170.25 ppm in ^{13}C NMR spectrum was in agreement with the proposed structure.

Table 1
Multicomponent reaction of aromatic aldehydes **2**, 3-amino 1,2,4-triazole **1**, and dimedone **3** for the synthesis of **4a**–**n**

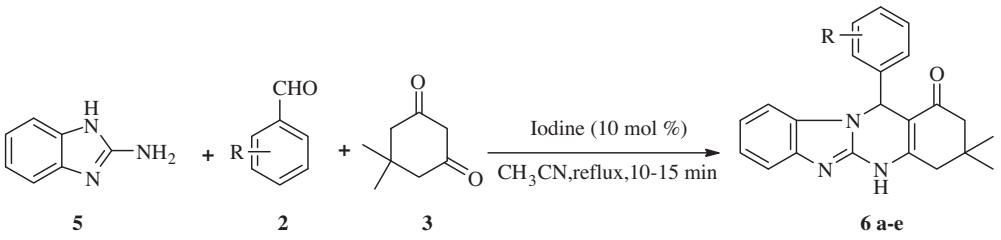
Entry	R	Product	Time (min)	Yield (%)
1	C_6H_5	**4a**	10.0	81.2
2	2,4-diCl-C_6H_3	**4b**	10.0	92.2
3	4-BrC_6H_4	**4c**	10.0	84.4
4	4-$NO_2C_6H_4$	**4d**	10.0	97.1
5	4-FC_6H_4	**4e**	10.0	82.4
6	4-ClC_6H_4	**4f**	10.0	96.1
7	2,4,6-triOMe-C_6H_2	**4g**	15.0	84.3
8	4-$OCH_3C_6H_4$	**4h**	10.0	89.9
9	4-$CH_3C_6H_4$	**4i**	10.0	85.8
10	4-OHC_6H_4	**4j**	15.0	88.5
11	3-OHC_6H_4	**4k**	15.0	83.1
12	2,4-$OMeC_6H_3$	**4l**	15.0	85.7
13	2-$NO_2C_6H_4$	**4m**	15.0	91.0
14	2-$OMeC_6H_4$	**4n**	15.0	88.0

[a] Reaction conditions: benzaldehyde (1.0 mmol), dimedone (1.0 mmol), 3-amino 1,2,4-triazole (1.0 mmol), 10 mol % iodine, 10–15 min reflux.
[b] Isolated yields.

To explore the scope of this reaction for the synthesis of [1,2,4]triazolo[5,1-*b*]quinazolin-8(4*H*)-one derivatives different substituted aldehydes were reacted with 3-amino-1,2,4 triazole and dimedone in the presence of molecular iodine and acetonitrile as the reaction medium (Table 1). In general, all the reactions were very clean, and the 1,2,4-triazolo[5,1-*b*]quinazolin-8(4*H*)-one derivatives were obtained in high yields under these conditions. Aldehyde bearing electron-donating groups (Me, OMe) and



Scheme 1. Molecular iodine mediated synthesis of 1,2,4-triazolo[5,1-*b*]quinolin-8(4*H*)-one derivatives.



Scheme 2. Molecular iodine mediated synthesis of 3,3-dimethyl-12-phenyl-3,4,5,12-tetrahydrobenzo[4,5]imidazo[2,1-*b*]quinazolin-1(2*H*)-one derivatives.

Table 2
Multicomponent reaction of aromatic aldehydes **2**, 2-amino benzimidazole **5**, and dimedone **3** for the synthesis of **6a–6e**

Entry	R	Product	Time (min)	Yield (%)
1	C_6H_5	**6a**	10.0	84.6
2	2,4-diCl-C_6H_3	**6b**	10.0	82.2
3	4-BrC_6H_4	**6c**	10.0	84.4
4	4-$NO_2C_6H_4$	**6d**	10.0	69.1
5	4-ClC_6H_4	**6e**	10.0	72.4

[a] Reaction conditions: benzaldehyde (1.0 mmol), dimedone (1.0 mmol), 2-amino benzimidazole (1.0 mmol), 10 mol % iodine, 10–15 min reflux.
[b] Isolated yields

electron-withdrawing groups (NO_2) gave the desired products in quantitative yields in 10 min (Table 1, entries 4, 7, 8, 12, and 14). Results show that the substituent groups did not play any significant role in the reactivity of the substrate.

In order to explore the generality of the reaction, we extended our study using 2-amino benzimidazole **5** as amino source, reacting with dimedone **3**, iodine as catalyst in the presence of acetonitrile with different substituted aromatic aldehydes to prepare a series of benzimidazole quinazolinone derivatives (Scheme 2 and Table 2). Various aromatic aldehydes containing electron-withdrawing and electron-donating substituents show equal ease toward the product formation in good to high yields.

Molecular iodine showed remarkable reactivity as a 'hard–soft' reagent and considerably accelerated the reactions. On the basis of all our experimental results, together with literature reports we have proposed the plausible mechanism for the formation of [1,2,4]triazolo/benzimidazolo quinazolinone derivatives **3a–n** and **6a–e** in the presence of molecular iodine (Scheme 3). The hypothesis supported the fact that initially the reaction was initiated by iodine, which reacts with benzaldehyde and forms a complex **A**. Further complex **A** reacts with amine sources, giving rise to complex **B** and upon loss of water molecule, proton transformation takes place giving rise to the crucial intermediate **C**. Further complex **C** undergoes intramolecular cyclization by loss of water molecule to give the target products (Scheme 3). The simplicity, together with the use of inexpensive, non-toxic, and environmentally benign natured molecular iodine under acetonitrile media is another remarkable feature of the procedure. The reaction mixture was cooled to room temperature, the precipitate formed was filtered, washed with water and dried to give pure **3a–n** and **6a–e** in excellent yields.

In conclusion, we have developed an efficient and facile method for the synthesis of 1,2,4-triazolo[5,1-*b*]quinazolin-8(4*H*)-one derivatives and 3,3-dimethyl-12-phenyl-3,4,5,12-tetrahydrobenzo [4,5]imidazo[2,1-*b*]quinazolin-1(2*H*)-one derivatives by treatment of the corresponding aldehydes with 3-amino-1,2,4-triazoles or 2-amino benzimidazole and dimedone by using iodine in the presence of acetonitrile at reflux conditions in 10–15 min. The mild reaction conditions, less expensive reaction medium, operational simplicity, and high yields are the advantages of this protocol. Molecular iodine mediated reactions are very useful both from economical and environmental points of view.

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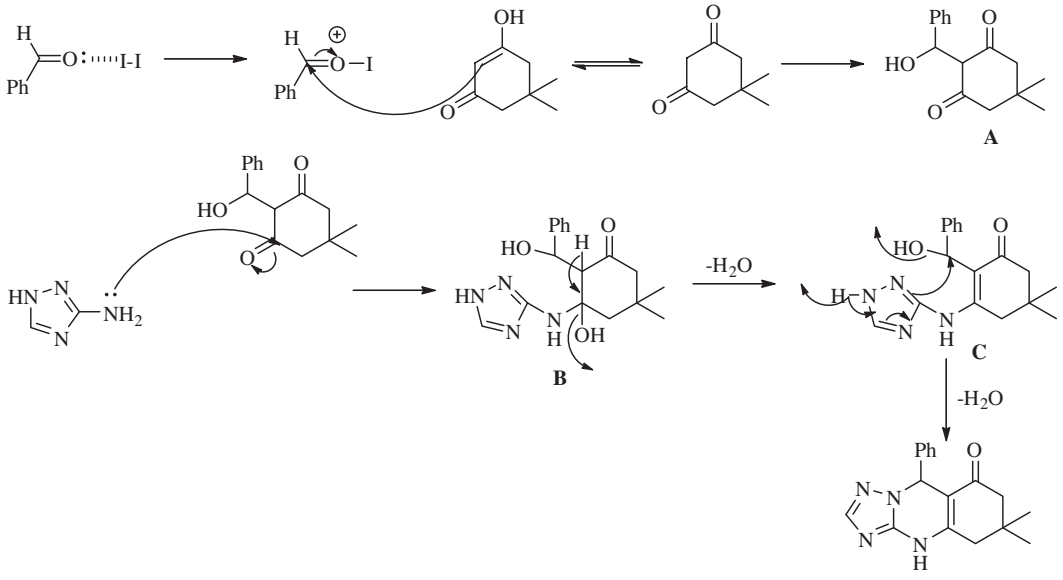

Scheme 3. A plausible mechanism for the synthesis of [1,2,4]triazolo/benzimidazolo quinazolinone derivatives by using molecular iodine.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2013.02.099.

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Further reading

11. *General procedure for the synthesis of [1,2,4]triazolo[5,1-b]quinazolin-8(4H)-ones and hexahydro[4,5]benzimidazolo[2,1-b]quinazolinones by using molecular iodine as the reaction medium:* A mixture of 3-amino-1,2,4-triazole or benzimidazole (1.0 mmol), benzaldehyde (1.0 mmol), dimedone (1.0 mmol), and acetonitrile (5 mL) was taken in a round bottom flask and added iodine (10 mol %) and stirred at 80 °C for 10 min. After completion of the reaction, as monitored by TLC, the reaction mass was cooled to room temperature and the solid separated was filtered and washed with water and dried at reduced pressure.

Data of representative examples: *6,6-Dimethyl-9-phenyl-5,6,7,9-tetrahydro-[1,2,4]triazolo[5,1-b]quinazolin-8(4H)-one* (Table 1, entry 1, **4a**): White solid; Yield 92%; mp 250–252 °C; IR: 3090, 2962, 1650, 1579, 1366, 1254, 729 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 1.05 (s, 3H, CH_3), 1.11 (s, 3H, CH_3), 2.21 (q, J = 10.19, 16.43 Hz, 2H, $-CH_2$), 2.54 (s, 2H, $-CH_2$), 6.33 (s, 1H, –CH), 7.25 (s, 4H, Ar-H), 7.56 (s, 2H, Ar-H), 10.82 (s, 1H, NH); MS m/z (ESI); 295 $[M+H]^+$. 9-(2,4-Dichlorophenyl)-6,6-dimethyl-5,6,7,9-tetrahydro-[1,2,4]triazolo[5,1-b]quinazolin-8(4H)-one (Table 1, *entry 2,* **4b**): Pale yellow solid; Yield 94.61%; mp 323–325 °C; IR: 3089, 2964, 1650, 1585, 1368, 1269, 850 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 1.02 (s, 3H, CH_3), 1.08 (s, 3H, CH_3), 2.14 (q, J = 16.24, 24.36 Hz, 2H, $-CH_2$), 2.53 (s, 2H, $-CH_2$), 6.56 (s, 1H, –CH), 7.26–7.36 (m, 2H, Ar-H), 7.43 (s, 1H, Ar-H), 7.62 (s, 1H, Ar-H), 11.23 (s, 1H, NH); MS m/z (ESI); 364 $[M+H]^+$.9-(4-Bromophenyl)-6,6-dimethyl-5,6,7,9-tetrahydro-[1,2,4]triazo lo[5,1-b]quinazolin-8(4H)-one (Table 1, entry 3, **4c**): Pale yellow solid; Yield 93%; mp 286–288 °C; IR: 3091, 2962, 2919, 1649, 1584, 1367, 1255, 841 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 1.04 (s, 3H, CH_3), 1.12 (s, 3H, CH_3), 2.21 (q, J = 10.38, 16.43 Hz, 2H, $-CH_2$), 2.54 (s, 2H, $-CH_2$), 6.30 (s, 1H, –CH), 7.16 (d, J = 8.30 Hz, 2H, Ar-H), 7.40 (d, J = 8.30 Hz, 2H, Ar-H), 7.58 (s, 1H, Ar-H), 10.94 (s, 1H, NH); MS m/z (ESI); 373 $[M]^+$, 375 $[M+2]^+$. 6,6-Dimethyl-9-(4-nitro phenyl)-5,6,7,9-tetrahydro-[1,2,4]triazolo[5,1-b]quinazolin-8(4H)-one (Table 1, entry 4, **4d**): Pale yellow solid; Yield 93%; mp>300 °C; IR: 2965, 1646, 1579, 1352, 1253, 730 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 1.04 (s, 3H, CH_3), 1.12 (s, 3H, CH_3), 2.22 (q, J = 7.74, 16.99 Hz, 2H, $-CH_2$), 2.54 (s, 2H, $-CH_2$), 6.35 (s, 1H, –CH), 6.95 (t, J = 8.68, 2H, Ar-H), 7.22-7.29 (m, 2H, Ar-H), 7.47 (s, 1H, Ar-H), 10.83 (s, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.25, 159.25, 136.29, 127.46, 122.00, 110.43, 71.79, 64.99, 29.68, 15.72; MS m/z (ESI); 340 $[M+H]^+$. 9-(4-Fluorophenyl)-6,6-dimethyl-5,6,7,9-tetrahydro-[1,2,4]triazolo[5,1-b]qui nazolin-8(4H)-one (Table 1, entry, 5, **4e**): Orange oil liquid; Yield 92%; mp 301–303 °C; IR: 3091, 2962, 1648, 1579, 1365, 1216, 762 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 1.04 (s, 3H, CH_3), 1.12 (s, 3H, CH_3), 2.22 (q, J = 7.74, 16.99 Hz, 2H, $-CH_2$), 2.54 (s, 2H, $-CH_2$), 6.35 (s, 1H, –CH), 6.95 (t, J = 8.68, 2H, Ar-H), 7.22–7.29 (m, 2H, Ar-H), 7.47 (s, 1H, Ar-H), 10.83 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 192.9, 150.4, 150.0, 146.7, 137.7, 129.0, 128.8, 115.1, 114.8, 105.3, 57.2, 49.7, 32.1, 28.3, 26.8; MS m/z (ESI); 313 $[M+H]^+$. 9-(4-Chlorophenyl)-6,6-dimethyl-5,6,7,9-tetrahydro-[1,2,4]triazolo[5,1-b]quinazol in-8(4H)-one (Table 1, entry 6, **4f**): Pale yellow solid; Yield 92%; mp 304–306 °C; IR: 3091, 2963, 1649, 1578, 1366, 1254, 760 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 1.04 (s, 3H, CH_3), 1.12 (s, 3H, CH_3), 2.22 (q, J = 16.82, 17.90 Hz, 2H, $-CH_2$), 2.54 (s, 2H, $-CH_2$), 6.34 (s, 1H, –CH), 7.23 (q, J = 4.88, 8.68, 4H, Ar-H), 7.43 (s, 1H, Ar-H), 10.77 (s, 1H, NH); MS m/z (ESI); 329 $[M+H]^+$. *6,6-Dimethyl-9-(2,4,6-trimethoxyphenyl)-5,6,7,9-tetrahydro-[1,2,4]triazolo[5,1-b]qu inazolin-8(4H)-one* (Table 1, entry7, **4g**): Pale yellow solid; Yield 92%; mp 290–292 °C; IR: 3103, 2966, 1648, 1586, 1336, 1122, 1008 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 1.15 (s, 3H, CH_3), 1.18 (s, 3H, CH_3), 2.31 (s, 2H, $-CH_2$), 2.58 (q, J = 9.44, 16.61 Hz, 2H, $-CH_2$), 3.79 (s, 3H, $-OCH_3$), 3.82 (s, 6H, 2 $\times$ $-OCH_3$), 6.37 (s, 1H, CH), 6.54 (s, 2H, Ar-H), 7.69 (s, 1H, Ar-H), 10.86 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 193.0, 152.6, 150.6, 149.9, 146.6, 137.0, 105.2, 104.4, 59.8, 57.9, 55.7, 49.7, 32.0, 28.6, 26.5; MS m/z (ESI); 385 $[M+H]^+$. *9-(4-Methoxyphenyl)-6,6-dimethyl-5,6,7,9-tetrahydro-[1,2,4]triazolo[5,1-b]quin azolin-8(4H)-one* (Table 1, entry 8, **4h**): Pale yellow solid; Yield 92%; mp 228–230 °C; IR: 3092, 2966, 1647, 1582, 1367, 1248, 1176 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 1.10 (s, 3H, CH_3), 1.17(s, 3H, CH_3), 2.30 (s, 2H, $-CH_2$), 2.56 (s, 2H, $-CH_2$), 3.76 (s, 3H, OCH_3), 6.39 (s, 1H, –CH), 6.82 (d, J = 8.49 Hz, 2H, Ar-H), 7.25 (d, J = 7.55 Hz, 2H, Ar-H), 7.65 (s, 1H, Ar-H), 11.37 (s, 1H, NH); MS m/z (ESI); 325 $[M+H]^+$. 6,6-Dimethyl-9-p-tolyl-5,6,7,9-tetrahydro-[1,2,4]tria zolo[5,1-b]quinazolin-8(4H)-one (Table 1, entry 9, **4i**): Pale yellow solid; Yield 92%; mp 266–268 °C; IR: 3091, 2924, 1649, 1581, 1368, 1253, 756 cm^{-1};^1H NMR (300 MHz, DMSO-d_6): $\delta\delta$ 1.05 (s, 3H, CH_3), 1.12 (s, 3H, CH_3), 2.20 (d, J = 11.52 Hz, 2H, $-CH_2$), 2.27 (s, 3H, $-CH_3$), 2.54 (s, 2H, $-CH_2$), 6.28 (s, 1H, –CH), 7.07 (d, J = 7.93, 2H, Ar-H), 7.15 (d, J = 8.12, 2H, Ar-H), 7.54 (s, 1H, Ar-H), 10.81 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 192.2, 148.9, 148.6, 145.8, 137.3, 136.0, 127.7, 125.7, 105.2, 56.9, 59.1, 31.2, 37.7, 26.0, 19.7; MS m/z (ESI); 309 $[M+H]^+$. *9-(4-Hydroxyphenyl)-6,6-dimethyl-5,6,7,9-tetrahydro-[1,2,4]triazolo[5,1-b]quinazolin-8(4H)-one* (Table 1, entry 10, **4j**): Pale yellow solid; Yield 92%; mp >300 °C; IR: 3225, 2930, 1630, 1585, 1366, 1268, 731 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 1.06 (s, 3H, CH_3), 1.12 (s, 3H, CH_3), 2.14–2.24 (m, 2H, $-CH_2$), 2.52–2.64 (m, 2H, $-CH_2$), 6.26 (s, 1H, –CH, 6.69-6.75 (m, 2H, Ar-H), 7.078 (d, J = 8.49, Hz, 2H, Ar-H), 7.54 (d, J = 10.38 Hz, 1H, Ar-H), 10.70 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.95, 138.61, 130.69, 125.72, 123.92, 112.44, 64.81, 63.18, 16.07, 14.1; MS m/z (ESI); 311 $[M+H]^+$. *9-(3-Hydro xyphenyl)-6,6-dimethyl-5,6,7,9-tetrahydro-[1,2,4]triazolo[5, 1-b]quinazolin-8(4 H)-one* (Table 1, entry 11, **4k**): Pale yellow solid; Yield 92%; mp 289–290 °C; IR: 3090, 2962, 1650, 1579, 1366, 1254, 729 cm^{-1}; IR: 3164, 2955, 1624, 1563, 1362, 1249, 699 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 1.06 (s, 3H, CH_3), 1.11(s, 3H, CH_3), 2.21 (q, J = 6.04, 16.43 Hz, 2H, $-CH_2$), 2.53 (s, 2H, $-CH_2$), 6.25 (s, 1H, –CH), 6.65-6.76 (m, 3H, Ar-H), 7.06 (t, J = 7.93, 8.12 Hz, 1H, Ar-H), 7.57 (d, J = 5.66, 1H, Ar-H), 8.91 (s, 1H, –OH), 10.78 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.95, 138.61, 130.69, 125.72, 123.92, 112.44, 64.81, 63.18, 16.07, 14.1; MS m/z (ESI); 311 [M+H]. *9-(2,4-Dime thoxyphenyl)-6,6-dimethyl-5,6,7,9-tetrahydro-[1,2,4]triazolo[5,1-b]quinazolin-8 (4H)-one* (Table 1, entry 12, **4l**): Pale yellow solid; Yield 92%; mp 210–212 °C; IR: 3092, 2932, 1651, 1580, 1367, 1262, 826 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 1.01 (s, 3H, CH_3), 1.11 (s, 3H, CH_3), 2.16 (q, J = 16.43, 17.94 Hz, 2H, $-CH_2$), 2.50 (d, J = 6.61 Hz, 2H, $-CH_2$), 3.69 (s, 3H, $-OCH_3$), 3.75 (s, 3H, $-OCH_3$), 6.35-6.45 (m, 3H, –CH, Ar-H), 7.26 (d, J = 8.30 Hz, 1H, Ar-H), 7.63 (s, 1H, Ar-H), 10.68 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.95, 138.61, 130.69, 125.72, 123.92, 112.44, 64.81, 63.18, 16.07, 14.1; MS m/z (ESI); 355 $[M+H]^+$. *6,6-Di methyl-9-(2-nitrophenyl)-5,6,7,9-tetrahydro-[1,2,4]triazolo[5,1-b]quinazolin-8(4 H)-one* (Table 1, entry 13, **4m**): Pale yellow solid; Yield 92%; mp 290–292 °C; IR: 3094, 2924, 1645, 1586, 1356, 1264, 735 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 0.99 (s, 3H, CH_3), 1.10 (s, 3H, CH_3), 2.16 (q, J = 11.70, 16.43 Hz, 2H, $-CH_2$), 2.53 (s, 2H, $-CH_2$), 7.15 (s, 1H, –CH), 7.19 (d, J = 7.74 Hz, 1H, Ar-H), 7.34–7.41 (m, 1H, Ar-H), 7.44–7.52 (m, 1H, Ar-H), 7.63 (s, 1H, Ar-H), 7.81 (d, J = 8.12 Hz, 1H, Ar-H), 10.97 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 192.9, 150.7, 150.1, 148.3, 146.9, 135.1, 133.0, 128.7, 123.7, 104.9, 52.7, 49.4, 32.1, 28.1, 26.9; MS m/z (ESI); 340 $[M+H]^+$. *9-(2-Methoxyphenyl)-6,6-dimethyl-5,6,7,9-tetrahydro-[1,2,4] triazolo[5,1-b]quinazolin-8(4H)-one* (Table 1, *entry 14,* **4n**): Pale yellow solid; Yield 92%; mp 240–243 °C; IR: 2930, 2837, 1648, 1583, 1368, 1246, 755 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 1.01 (s, 3H, CH_3), 1.11 (s, 3H, CH_3), 2.18 (q, J = 14.91, 16.43 Hz, 2H, $-CH_2$), 2.51 (s, 2H, $-CH_2$), 3.71 (s, 3H, $-OCH_3$), 6.54 (s, 1H, –CH), 6.79–6.92 (m, 2H, Ar-H), 7.16-7.23 (m, 1H, Ar-H), 7.37 (d, J = 7.36 Hz, 1H, Ar-H), 7.43-7.43 (m, 1H, Ar-H), 10.62 (s, 1H, NH); MS m/z (ESI); 325 $[M+H]^+$.*3,3-Dimethyl-12-phenyl-1,2,3,4,5,12-hexatrahydro-[4,5]imidazolo [2,1-b]quinazolin-1-one* (*Table 2*, entry 6a): White solid; Yield 92%; mp >300 °C; IR: 3365, 2962, 1648, 1577 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 1.01 (s, 3H, CH_3), 1.11 (s, 3H, CH_3), 2.11–2.22 (m, 2H, $-CH_2$), 2.54–2.64 (m, 2H, $-CH_2$), 6.42 (s, 1H, –CH), 6.85–7.25 (m, 9H, Ar-H), 10.84 (s, 1H, NH); MS m/z (ESI); 344 $[M+H]^+$.

12(4-Bromo-phenyl)-3,3-dimethyl-1,2,3,4,5,12-hexahydro benzo[4,5]imidazolo [2,1,b] (Table 2, entry 6c): White solid; Yield 92%; mp >300 °C; IR: 3380, 2945, 1650, 1565 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 1.04 (s, 3H, CH_3), 1.11 (s, 3H, CH_3), 2.10–2.24 (m, 2H, $-CH_2$), 2.58–2.70 (m, 2H, $-CH_2$), 6.44 (s, 1H, –CH), 6.85–7.35 (m, 8H, Ar-H), 10.84 (s, 1H, NH); MS m/z (ESI); 422 $[M]^+$, 424 $[M+2]^+$.