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Research Article

$H_2SO_4 \cdot SiO_2$: AN EFFICIENT AND HETEROGENEOUS CATALYST FOR THE SYNTHESIS OF [1,2,4] TRIAZOLO/BENZIMIDAZOLOQUINAZOLINONE DERIVATIVES

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ABSTRACT

Multi-component condensation of 3-amino-1,2,4-triazole/2-aminobenzimidazole as amine source, with aryl aldehydes and,dimedone in the presence of 10 mol% $H_2SO_4 \cdot SiO_2$ has been accomplished for the synthesis a series of 6,6-dimethyl-9-phen yl-5,6,7,9-tetrahy-dro-[1,2,4]triazolo[5,1-b]quinazolin-8(4H)-one/3,3-dimethyl-12-phenyl-1,2,3,4,5,12-hexatrahydro-[4,5]imidazolo [2,1-b]quinaz olin-1-one derivatives. High yields, environmentally benign, and mild reaction conditions are some of the important features of this protocol.

Keywords: Aryl substituted aldehydes, 3-amino-1,2,4-triazole, 2-aminobenzimidazole.

INTRODUCTION

Multi-component reactions play an important role in pharmaceutical industries. Pharmacies are trying to develop green chemistry reactions. Solvent-free synthesis of complex organic structures as drugs is the dream of every pharmacy. Multi-component reaction as a powerful tool for the rapid introduction of molecular diversity is evident and developed for the generation of heterocycles with receives growing interest.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.[1-3]

MCRs have great contribution in convergent synthesis of complex and important organic molecules from simple and readily available starting materials and have emerged as powerful tools for drug discovery. The quinazolinone derivative is a fertile source of biologically important molecules. Compounds containing quinazolinone derivatives moiety have many pharmacological properties and play important roles in biochemical processes.

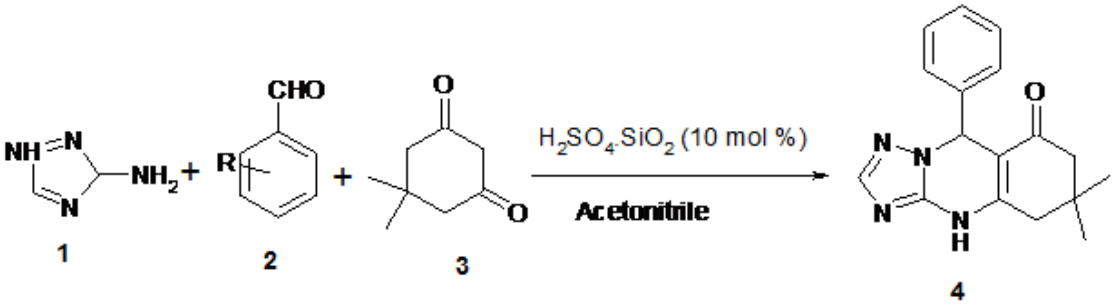
Synthesis of Triazoloquinazolinone and related derivatives are an important class of natural products and exhibit a wide range of spectrum of biological activities, such as antihypertensive,[4] anti-histaminic,[5] analgesic, anti-inflammatory,[6] anticancer,[7] anti-HIV activities[8] and other fused compounds such as triazoles, imidazoles, pyrazoles, and tetrazoles

are representing an important structural motif in medicinal. These derivatives also have a long history of application in agrochemicals and pharmaceutical industry as herbicides and active pharmaceuticals. The prevalence of triazoloquinazolinone cores in biologically active molecules has stimulated the need for elegant and efficient ways to make these heterocyclic lead.

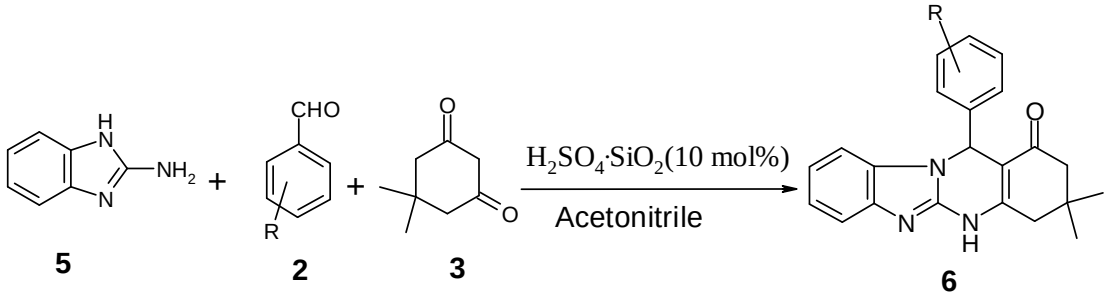
Expeditious synthesis of substituted triazolo and benzimidazoloquinazolinones derivatives from Aryl substituted aldehydes with 3-amino-1,2,4-triazole and 2-aminobenzimidazole as amine sources and dimedone in the presence of acid or basic catalysts, improvements in the synthesis have been sought continuously. Thus, the preparation of this type of heterocyclic nucleus is of much importance. Consequently, a few methods have been reported with different regents such as Silica SBA-15[9], p-TSA[10], sulfamic acid[11], ionic liquids[12] heteropolyacids[13]and molecular Iodine as a catalyst.[14] However, many of existing methods involve expensive reagents, strongly acidic conditions, longer reaction times, high temperatures, unsatisfactory yields, cumbersome product isolation and environmental pollution. Therefore, there is a need for simple and environmentally friendly processes for the synthesis of 6,6-dimethyl-9-phen yl-5,6,7,9-tetrahy-dro-[1,2,4]triazolo[5,1-b]quinazolin-8(4H)-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 derivatives.

RESULT AND DISCUSSION

In continuation of the work on the synthesis of medicinally important molecules under environmentally safe conditions[15–16], it has been found that $H_2SO_4{\cdot}SiO_2$, which is an inexpensive and common chemical, can efficiently catalyze this reaction. Synthesis of triazolo and benzimidazoloquinazolinones using Aryl substituted aldehydes with 3-amino-1,2,4-triazole and 2-aminobenzimidazole and dimedone in the presence of $H_2SO_4{\cdot}SiO_2$ (catalytic amount) using acetonitrile as solvent under at 80°C condition is achieved in good to excellent yield within 20-30 min as shown in **Scheme I** and **Scheme II**.



Scheme. I:



Scheme. II:

Experimental and characterization

Melting points were determined on a Buchi melting point apparatus and are uncorrected. IR, 1H and ^{13}C NMR and GCMS were recorded on Nicolet 400DFT-IR spectrophotometer, 200 MHz Brucker spectrometer and Shimadzu GC-MS QP5050A respectively. 3-Amino-1,2,4-triazole or 2-Amino-benzimidazole, Aromatic aldehyde and dimedone were all commercial products and were used without further purification. All the products are known compounds, which were characterized by IR and 1H NMR spectral data and their melting points were compared with literature reports.

Preparation of the $H_2SO_4{\cdot}SiO_2$ catalyst

To a slurry of silica gel (10g, 230-400 mesh) in dry diethyl ether (50 mL was added concentrated H_2SO_4(3 mL) with shaking for 5 min. The solvent was evaporated under reduced pressure to obtained dry $H_2SO_4{\cdot}SiO_2$ catalyst which was then heated at 120°C for 3hrs.

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 $H_2SO_4{\cdot}SiO_2$ as a catalyst

A mixture of 3-amino-1,2,4-triazole or 2-amino-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 $H_2SO_4{\cdot}SiO_2$ (10 mol %) and stirred at 80°C for 20 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. For further purification it was recrystallized from ethanol 93% afford pure product. All the products prepared by this procedure were characterized by comparison of their IR,NMR spectral and GC-MS spectral analysis with authentic samples.

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[a]	Time (min)	Yield [b] (%)	M.P (°C)	Lit.M.P (°C)[11,14]
1	$C_6H_5$4a	20	93	250-251	250-252
2	4-$NO_2C_6H_4$4b	25	95	304-305	>300
3	4-$FC_6H_4$4c	25	92	298-300	301-303
4	4-BrC_6H_4 4d	25	92	285-286	286-288
5	4-$ClC_6H_4$4e	25	95	305-307	304-306
6	2,4-diCl-C_6H_3 4f	20	92	322-324	323-325
7	3-$OHC_6H_4$4g	25	92	290-292	289-290
8	4-OHC_6H_4 4h	25	95	300-302	>300
9	4-$CH_3C_6H_4$ 4i	25	92	265-267	266-268
10	4-$OCH_3C_6H_4$ 4j	25	95	229-231	228-230
11	2-$NO_2C_6H_4$ 4k	25	92	292-293	290-292
12	2-$OMeC_6H_4$ 4l	30	90	242-244	240-243
13	2,4-$OMeC_6H_3$ 4m	30	94	212-213	210-212
14	2-Naphthyl-	30	92	288-290	287-290

[a]All the products are known, characterized by IR,MS and NMR spectral analysis and compared with the authentic samples.
[b]Isolated yields.

Table 2: Multicomponent reaction of aromatic aldehydes 2,2-aminobenzimidazole5 and dimedone 3 for the synthesis of 6a–6f

Entry R	Product[a]	Time (min)	Yield [b] (%)	M.P (°C)	Lit.M.P (°C)[11,14]
1	$C_6H_5$6a	20	92	302-304	>300
2	4-$NO_2C_6H_4$6b	20	93	>300	-
3	4-$BrC_6H_4$6c	20	92	302-303	>300
4	4-$ClC_6H_4$6d	25	90	>300	-
5	4-OHC_6H_4 6e	25	92	>300	-
6	4-$MeOC_6H_4$ 6f	25	91	>300	

[a]All the products are known, characterized by IR,MS and NMR spectral analysis and compared with the authentic samples.[b]Isolated yields.

Spectral analytical data of all compounds

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; IR (KBr):ν_{max}= 3090, 2962, 1650, 1579, 1366, 1254, 729 cm^{-1}; ^{1}H 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, 6.43 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)ppm; Mass (m/z) (ESI); 295 $[M+H]^+$.

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 2,4b)

Pale yellow solid; IR (KBr):ν_{max}=2965, 1646, 1579,1352, 1253, 730 cm^{-1}; ^{1}H 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)ppm;^{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; Mass (m/z) (ESI); 340 $[M+H]^+$.

9-(4-Fluorophenyl)-6,6-dimethyl-5,6,7,9-tetrahydro-[1,2,4]triazolo[5,1-b]quinazolin-8(4H)-one (Table 1, entry, 3, 4c)

Pale yellow solid; IR (KBr):ν_{max}=3091, 2962, 1648, 1579, 1365, 1216, 762 cm^{-1}; ^{1}H 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)ppm; ^{13}C NMR(75 MHz, $CDCl_3$): δ192.9, 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; Mass m/z (ESI); 313 $[M+H]^+$.

9-(4-Bromophenyl)-6,6-dimethyl-5,6,7,9-tetrahydro-[1,2,4]triazolo[5,1-b] quinazolin-8(4H)-one (Table 1, entry 4, 4d)

Pale yellow solid; IR (KBr):ν_{max}=3091, 2962, 2919, 1649, 1584, 1367, 1255, 841 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ1.04 (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)ppm; Mass (m/z) (ESI); 373 $[M]^+$, 375 $[M+2]^+$.

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 5, 4e)

Pale yellow solid; IR (KBr):ν_{max}=3091, 2963, 1649, 1578, 1366, 1254, 760 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ1.04 (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)ppm; Mass (m/z) (ESI); 329 $[M+H]^+$.

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 6, 4f)

Pale yellow solid; IR (KBr):ν_{max}=3089, 2964, 1650, 1585, 1368, 1269, 850 cm^{-1}; ^{1}H 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)ppm; Mass (m/z) (ESI); 364 $[M+H]^+$

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 7, 4g)

Pale yellow solid; IR (KBr):ν_{max}=3090, 2962, 1650, 1579, 1366, 1254, 729 cm^{-1}; IR: 3164, 2955, 1624, 1563, 1362, 1249, 699 cm ^{1}; ^{1}H 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)ppm; ^{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; Mass (m/z) (ESI); 311 [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 8, 4h)

Pale yellow solid; IR (KBr):ν_{max}=3225, 2930, 1630, 1585, 1366, 1268, 731 cm^{-1}; ^{1}H 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)ppm; ^{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; Mass (m/z) (ESI); 311 $[M+H]^+$.

6,6-Dimethyl-9-p-tolyl-5,6,7,9-tetrahydro-[1,2,4]triazolo[5,1-b]quinazolin-8(4H)-one (Table 1, entry 9, 4i)

Pale yellow solid; IR (KBr):ν_{max}=3091, 2924, 1649, 1581, 1368, 1253, 756 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 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)ppm;^{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; Mass (m/z) (ESI); 309 $[M+H]^+$.

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 10, 4j)

Pale yellow solid; IR (KBr):ν_{max}=3092, 2966, 1647, 1582, 1367, 1248, 1176 cm^{-1}; ^{1}H 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)ppm; Mass (m/z) (ESI); 325 $[M+H]^+$

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 11, 4k)

Pale yellow solid; IR (KBr):ν_{max}=3094, 2924, 1645, 1586, 1356, 1264, 735 cm^{-1}; ^{1}H 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)ppm; ^{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; Mass (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 12,4l)

Pale yellow solid; IR (KBr):ν_{max}=2930, 2837, 1648, 1583, 1368, 1246, 755 cm^{-1}; ^{1}H 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)ppm; Mass (m/z) (ESI); 325 $[M+H]^+$

9-(2,4-Di methoxyphenyl)-6,6-dimethyl-5,6,7,9-tetrahydro-[1,2,4]triazolo[5,1-b]quinazolin-8 (4H)-one (Table 1, entry 13, 4m)

Pale yellow solid; IR (KBr):ν_{max}=3092, 2932, 1651, 1580, 1367, 1262, 826 cm^{-1}; ^{1}H 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)ppm

; ^{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; Mass (m/z) (ESI); 355 $[M+H]^+$.

6,6-Dimethyl-9(2-naphthyl)-5,6,7,9-tetrahydro-1,2,4-triazolo[5,1-b]quinazolin-8(4H)-one.(Table 1 , entry 14 , 4n)

Pale brown solid;IR (KBr):ν_{max}= 2926-3449,1650, 1577 cm^{-1};^{1}H NMR (DMSO-d_6) : *δ* 0.97 (s,3H,CH_3) , 1.05 (s, 3H, CH_3), 2.03 (d,*J*=16.14Hz, 1H , CH_2) , 2.20 (d , *J*=16.26 HZ , 1H, CH_2) , 2.50 (m,2H, CH_2), 6.38 (s,1H,CH) , 7.25-7.91 (m,7H) , 7.69 (s,1H, CH) , 11.21 (s,1H, NH) ppm; Mass (m/z) (ESI); 344$[M+H]^+$.

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; IR (KBr):ν_{max}= 3365, 2962, 1648, 1577 cm^{-1}; ^{1}H 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)ppm; Mass (m/z) (ESI); 344 $[M+H]^+$.

3,3-Dimethyl-12(4-nitro-phenyl)-1,2,3,4,5,12-hexahydrobenzo[4,5]Imidazo[2,1-b]quinazolin-1-one. (Table 2, entry 6b)

Yellow solid;IR (KBr):ν_{max}= 3540,3045,1644,1612,1592,1568 cm^{-1}; ^{1}NMR (DMSO-d_6) : *δ* 0.92(s,3H,CH_3), 1.07(s,3H,CH_3), 2.07 (d, *J*= 20.7H_Z,1H,H-4), 2.28 (d, *J*=15.9 Hz, 1H , H-4), 2.57-2.70 (m,2H,H-2), 6.60(s,1H,H-12), 7.04-8.10(m,8H,Ar-H),11.31(s,1H,NH)ppm;Mass (m/z) (ESI); 388 $[M]^+$, 389$[M+1]^+$.

12(4-Bromo-phenyl)-3,3-dimethyl-1,2,3,4,5,12-hexahydrobenzo[4,5]imidazolo [2,1,b]quinazolin-1-one (Table 2, entry 6c)

White solid; IR (KBr):ν_{max}= 3380, 2945, 1650, 1565 cm^{-1}; ^{1}H 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); Mass (m/z) (ESI); 422 $[M]^+$, 424 $[M+2]^+$.

12(4-chlorophenyl)-3,3-dimethyl-1,2,3,4,5,12-hexahydrobenzo[4,5]imidazo[2,1-b]quinazolin-1-one(Table 2, entry 6d)

White solid;IR (KBr):ν_{max}= 3485, 3045,1645,1613,1590,1566 cm^{-1}; ^{1}NMR

(DMSO-d_6) : δ0.96 (s ,3H,CH_3),1.06(s,3H,CH_3), 2.03-2.25(m,4H,H-2&H-4), 6.56(s,1H, CH), 6.94-7.53(m,8H,Ar-H), 11.23 (s,1H,NH)ppm; Mass (m/z) (ESI); 377 $[M]^+$, 379$[M+2]^+$.

3,3-Dimethyl-12(4-hydroxy-phenyl)-1,2,3,4,5,12-hexahydrobenzo[4,5] imidazo[2,1-b]quinazolin-1-one(Table 2 entry 6e)

Off white solid;IR (KBr):ν_{max}= 3448,2890,1641,1612,1589,1566 cm^{-1}; ^{1}NMR (DMSO-d_6) : δ 0.95 (s,3H,CH_3),1.06 (s,3H,CH_3),2.04(d,*J*=8.94,1H,H-4), 2.24(d,*J*=9.24Hz,1H,H-4'),2.50-2.73 (m,2H,H-2),6.19 (s,1H,H-12),6.60-7.35 (m,8H, Ar-H),9.32 (s,1H,OH),11.01 (s,1H,NH) ppm;Mass (m/z) (ESI); 359 $[M]^+$, 361$[M+2]^+$.

3,3-Dimethyl-12(4-methoxy-phenyl)-1,2,3,4,5,12-hexahydrobenzo[4,5] imidazo[2,1-b]quinazolin-1-one(Table 2, entry 6f)

Pale yellow solid;IR (KBr):ν_{max}= 3435,2890,1641,1612,1589,1566 cm^{-1}; ^{1}NMR (DMSO-d_6) : δ 0.95 (s,3H,CH_3), 1.06 (s,3H,CH_3), 2.06 (d, *J*=16.5Hz, 1H , H-4) , 2.25 (d, *J*=16.25Hz , 1H, H-4') , 2.53-2.68 (m, 2H, H-2), 3.66 (s,3H, OCH_3), 6.35 (s,1H,H-12), 6.73-7.42 (m,8H, Ar-H), 11.01 (s, 1H, NH) ppm;Mass (m/z) (ESI); 373 $[M]^+$, 374$[M+1]^+$.

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