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ARTICLE

Deep eutectic solvent mediated synthesis of quinazolinones and dihydroquinazolinones: synthesis of natural products and drugs

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A mild and greener protocol was developed to synthesize substituted quinazolinones and dihydroquinazolinones *via* deep eutectic solvent (DES) mediated cyclization with a series of aliphatic, aromatic, heteroaromatic aldehydes in good to excellent yields. This greener strategy was further utilised to synthesize various quinazolinone natural products and drugs.

Introduction:

Minimizing the waste and maximizing the sustainability of a reaction would be the breakthrough in the field of synthetic chemistry to favour the human race.[1] Although the achievements are still limited but sustainable chemistry and their applications are the new era in beginning. For chemists to mimic the nature and design an environment friendly chemical synthesis with respect to reagents, solvents and ambient conditions is very challenging. Since, from last decade more efforts were devoted towards the design of environmentally benign solvents that could be easily biodegradable or reusable.[2] In recent years there are green solvents like water,[3] Ionic liquids (ILs),[4] supercritical liquids,[5] Polyethylene glycol (PEG)[6] emerged to outplace many organic solvents, however the use of these solvents are restricted due to their poor solubility and stability of organic compounds. Extensive usage of ILs as solvent was well documented for many organic reactions over a decade but depending on their counterpart, it can be toxic and non biodegradable. Thus, nowadays the use of ILs as solvent is reduced by less than a half.[7] Whereas, deep eutectic solvents (DES) has risen as a green solvent due to their properties like polarity, low toxicity, non-volatility, biodegradability, low-cost, thermal stability, and ready availability from bulk renewable resources without any further modification.[8] Use of DES as a replacement of typical organic solvents in reactions like, Perkin,[9] Diels-Alder,[10] Heck,[11] Suzuki,[12] Biginelli[13] were well documented in literature. Hence, improvisation on the uses of DES in synthesis of organic compounds should be the major aim.

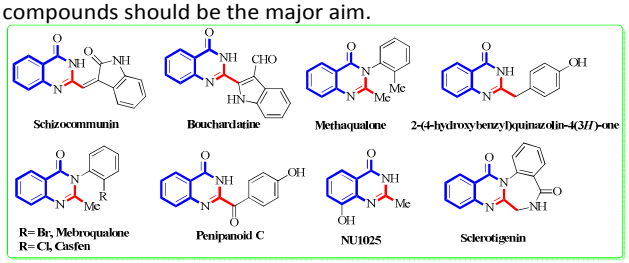

Figure 1. Examples of biologically and pharmaceutically important quinazolinones

Among the nitrogen containing natural products, quinazolinone is one of the most important heterocyclic core that accessorize many naturally occurring alkaloids as well as marketed drugs. Substituted and unsubstituted quinazolinones exhibit broad biological and pharmaceutical properties like protein tyrosine kinase inhibitory, cholecystokinin inhibitory, anti-microbial, anticonvulsant, sedative, hypotensive, anti-depressant, antiinflammatory, and anti-allergy.[14] Certain quinazolionones which is being marketed as drugs, like methqualone (quaalude), mebroqualone, mecloqulaone (Casfen) contains sedative, hypnotic and anxiolytic properties and are used for treatment of insomnia (**Fig. 1**).[15] In 2011, Wang and Che group isolated two alkaloids, penipanoid C and 2-(4-hydroxybenzyl)quinazolin-4(3*H*)-one from the marine sediment-derived fungus *penicillium paneum* SD-44 that exhibits cytotoxicity against the human lung carcinoma cell line A549 and BEL-7402 cell lines with IC_{50} values of 17.5 and 19.8 μM, respectively.[16] Due to this undeniable impression of quinazolione alkaloids over pharmacological industry, there is a continuous interest among the researchers to develop new methods for synthesis of quinazolinone core. Over the years, plenty of protocols have been reported by various scientific groups using metal (Cu, Pd, Ir),[17] Sp^3 carbon oxidation,[18] multi component reaction,[19] microwave condition,[20] gallium(III) triflate,[21] montmorillonite K-10,[22] Zinc(II) perfluorooctanoate,[23] $KAl(SO_4)_2{\cdot}12H_2O$,[24] $Al(H_2PO_4)_3$,[25] Cu-CNTs[26] and MNP-PSA (*N*-

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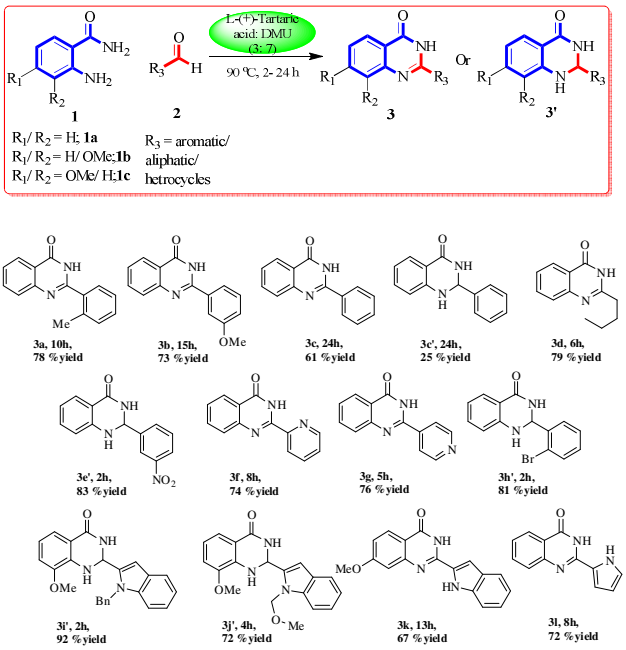
propylsulfamic acid supported onto magnetic Fe_3O_4 nanoparticles)[27] as catalysts. A keen survey of literature also reveals the use of metal free conditions like iodine,[28] amberlyst-15,[29] Bronsted acid,[30] citric acid,[31] ionic liquids,[32] β-cyclodextrin,[33] water-Sodium dodecayl sulfate (SDS),[34] cellulose-SO_3H,[35] CLAY,[36] Propane phosphonic acid anhydride (T3P)[37] for synthesis of quinazoline as well as quinazolinone. Deep eutectic solvents (DES) being more eco-friendly due to their inherent properties (*vide supra*) it is now becoming the choice of solvent over many organic solvents. In 2012, Zhang *et al.* reported a three component synthesis of quinazoline in DES media.[38] Whereas, to the best of our knowledge there was limited report[39] till date for synthesis of quinazolinone using particularly deep eutectic solvents in spite of their aforementioned environmental impact. Furthermore, this DES mediated cyclization can be utilised for synthesis of quinazolinone alkaloids or drugs as a key step. In environmental perspective, use of deep eutectic solvent mediated cyclization as a key step for total synthesis of alkaloids would open new directions for the scientific community. With this outlook to our ongoing research,[40] herein we report a DES mediated cyclization strategy to synthesize substituted/ unsubstituted quinazolinones that has been further utilised for synthesis of various natural products and drugs.

Results & Discussion:

To obtain 2-(*o*-tolyl)quinazolin-4(3*H*)-one (**3a**, **scheme 1**) we started our venture with optimizing few of the deep eutectic solvents mixture like, citric acid–N, N'-Dimethylurea (DMU), D-(−)-fructose–DMU, L-(+)-tartaric acid–DMU and mannose–DMU–NH_4Cl with model substrates anthranilamide (**1a**) (1.0 equiv.) and *o*-tolualdehyde (**2a**) (1.2 equiv). Among them, L-(+)-tartaric acid–DMU (3:7) mixture melt at 90 °C was found to be the most effective to give the maximum yield of compound **3a**. The reaction was carried out in an open air atmosphere to aromatize the initially formed dihydroquinazolinone to quinazolinone product *via* aerobic oxidation. With this optimized conditions, we explored the scope and generality of the reaction using this DES. The initial formation of dihydroquinazolinone can be identified with thin layer chromatography (bright blue long UV active) which was further aromatized to the corresponding quinazolinone *via* aerobic oxidation. An array of aldehydes (aromatic, aliphatic, heterocyclic) (**2a- 2l**) was exposed to these conditions with substituted/ unsubstituted anthranilamides (**1a- 1c**). To our delight, all reactions underwent smoothly to give the corresponding dihydroquinazolinone/ quinazolinone depending on time of the reaction. The electron donating aromatic/ aliphatic aldehydes and anthranilamides were transferred smoothly to the cyclized quinazolinone product within 6-15 h in good yields (**3a, 3b, 3d**), whereas, in case of benzaldehyde we obtained both the quinazolinone (**3c**) and dihydroquinazolinone (**3c'**) product even after 24h also. The electron withdrawing aromatic aldehydes were not converted to the corresponding quinazolinone after 24h also, although we had obtained the corresponding dihydro derivatives within 2h (**3e', 3h'**) of the reaction.

Scheme 1. Synthesis of 2- substituted quinazolinone[a]



[a] Reaction was performed in a scale with 1 (1.0 equiv.), 2 (1.2 equiv.), in L-(+)-Tartaric acid : DMU (3:7) mixture at 90 ^{0}C in an open mouth round bottomed flask.

The same outcome was obtained when we used substituted anthranilamides (**1b, 1c**) with heterocyclic (pyridine, indole, pyrrole) aldehydes. This observation showed that with variation of time, both dihydroquinazolinone product as well as quinazolinone products can be obtained. All the compounds were extracted with ethyl acetate and purified using column chromatography. Once we gained an insight of this DES mediated cyclization, to synthesize various substituted dihydroquinazolinone and quinazolinones, we shifted our focus to apply this protocol for formal synthesis of some biologically important quinazolinone natural products and drugs.

Bouchardatine[41] (**Fig. 1**), is a very well known β-indoloquinazoline alkaloid isolated from *B. neurococca* (Rutaecae), shows wide biological properties like anti-cancer, anti-inflammatory and anti-tuberculosis. Recently it has also been documented as a novel inhibitor of adipogenesis/ lipogenesis in 3T3-L1 adipocytes. Due to these vital properties, it immediately draws the attention and we were eager to apply our DES mediated protocol for synthesizing it. Indole-2-carboxaldehyde (**4**) was obtained in two steps from indole-2-carboxylic acid which on treatment with anthranilamide (**1a**) in L-(+)-tartaric acid-DMU (3:7) melt at 90 °C for 8h gave the 2-(1*H*-indol-2-yl)quinazolin-4(3*H*)-one (**5**) in 81% yield. Formylation of compound **5** with $DMF/POCl_3$ will introduced

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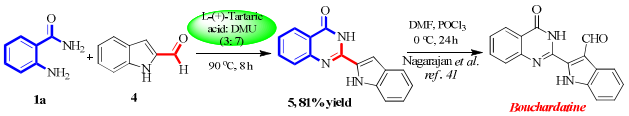
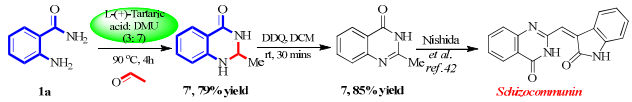
the aldehyde group at indole C3 to give bouchardatine, that has already been reported from our group (**Scheme 2, part A**).[42]

Scheme 2. Formal Synthesis of 2-substitued quinazolinone alkaloids

Part A: Formal Synthesis of Bouchardatine



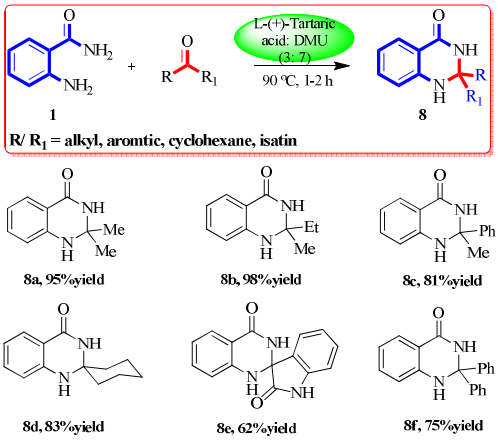
***Part B*:** Formal synthesis of Schizocommunin



In, **part B**; a formal synthesis of schizocommunin was achieved. Schizocommunin was first reported in 1999 from the liquid culture medium of *Schizophyllum commune* by Hosoe *et al.* It shows strong cytotoxic activity against murine lymphoma cells, further biological studies on schizocommunin were prevented because of its scarcity from natural sources, and there had been no reports of the total synthesis for schizocommunin until Nishida *et al.* in 2013 reported the revised structure.[43] Their synthesis of schizocommunin was demonstrated from 2-methyl-4(3*H*)-quinazolinone on refluxing in acetic acid media with istain. Hence, the scarcity of schizocommunin in nature, and high cost of the commercially available 2-methyl-4(3*H*)-quinazolinone attracted us. 2-Methyl-4(3*H*)-quinazolinone could be easily prepared *via* our protocol from cheaper starting material anthranilamide (**1a**). Hence, anthranilamide (1.0 equiv.) was treated with acetaldehyde (3.0 equiv) in the green melt at 90 °C for 2 h to obtain the corresponding dihydroquinazolione (**7'**) which was further treated with 2,3-Dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) in dry DCM at rt to acquire 2-methyl-4(3*H*)-quinazolinone (**7**) in 85% yield (**Scheme 2, part B**). Schizocommunin can be synthesized in one step from compound **7** following Nishida's procedure.

Though 2,2'-disubstituted quinazolinones were not found often in naturally occurring alkaloids but their synthetic versions show wide spectrum of pharmacological activities. Incorporation of a spirocyclohexane, aliphatic or hetrocyclic moiety at C2 of the quinazolinone heterocycles gives anti-inflammatory, analgesic, antileishmanial agents. Some spiroquinazolinones exhibiting anti-amoebic activity in vitro was also tested as central nervous system depressants.[44] Thus we were excited to test our protocol for the synthesis of different 2, 2'-disubstitued quinazolinone. Variety of ketones reacted smoothly over the melt at 90 °C with anthranilamide (**1a**) to furnish the corresponding substituted quinazolinones. A wide range of compounds were (aliphatic-aliphatic, aliphatic-aromatic, aromatic-aromatic, cyclic ketones and isatin) well tolerated in this reaction condition to give excellent yield of products (**Scheme 3**).

Scheme 3: Synthesis of 2, 2'-disubstitued quinazolinones[b]

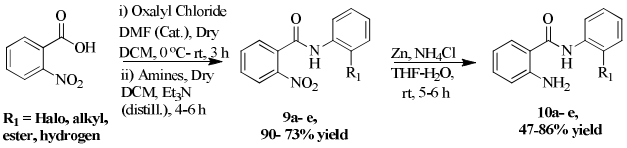


[b] Reaction was performed in a scale with 1a (1.0 equiv.), ketone (1.0 equiv.), in L-(+)-Tartaric acid : DMU (3:7) mixture at 90 ^{0}C in an open mouth round bottomed flask.

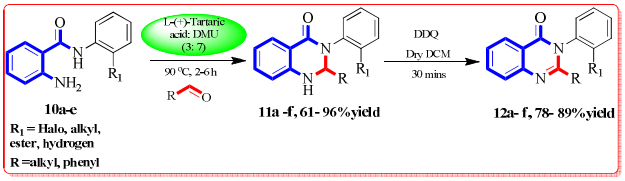
After a successful manifestation of our green protocol over 2-substituted/ 2, 2-disubstituted quinazolinones, we were eager to explore the scope of the reaction on synthesis of 2, 3-disubstitued quinazolinones. Significance of this quinazolinone core was more prominent particularly in respect to their pharmacological properties (*vide supra,* **Fig. 1**).

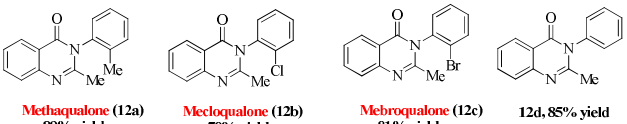
Scheme 4: Synthesis of 2, 3 substituted quinazolinones (Drugs and Natural products)

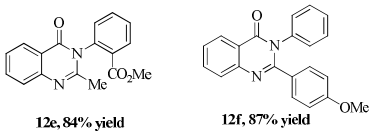
Part A: Preparation of starting materials



Part B: General method for synthesis of 2, 3 substituted quinazolinone drugs and alkaloids







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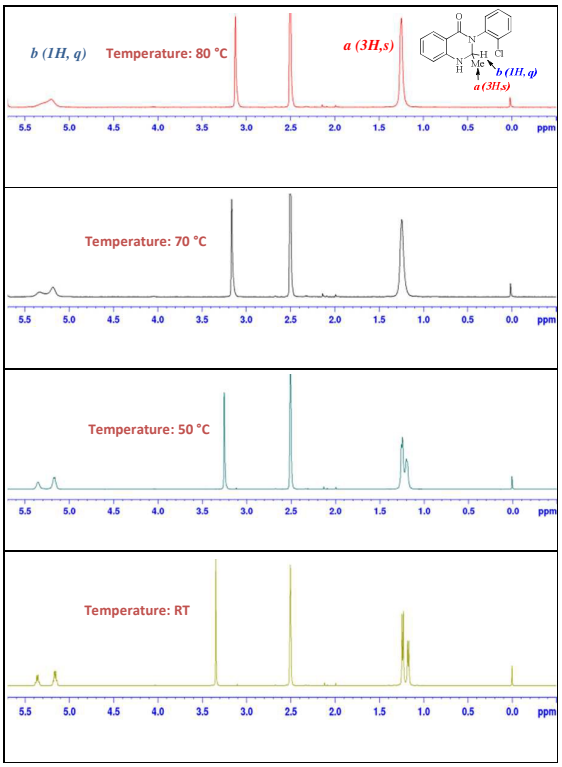
Hence, we selected some of the drugs (methaqualone, mecloqualone, mebroqualone) and alkaloids as our target molecules to validate our protocol.

To synthesize the exact target molecules, we prepared the corresponding starting material 2-amino-*N*-(substituted) benzamide from 2-nitrobenzoic acid in two steps. In the first step 2-nitrobenzoic acid was stirred with oxalyl chloride in dry DCM for 3h at rt, followed by removal of excess solvent and oxalyl chloride under pressure led to the corresponding acid chloride. Next, this acid chloride was added to the mixture of substituted benzamides and triethylamine, and stirred for another 4-6 h at rt to furnish the respective 2-nitro-*N*-(substituted)benzamides (**9a-e**).[45] Nitro group reduction of compound **9a-e** in presence of Zn/NH_4Cl gave 2-amino-*N*-(substituted)benzamides (**10a-e**) in good yields. Pleasingly, all 2-amino-*N*-(substituted)benzamides reacted smoothly with corresponding aldehydes onto the green melt at 90 °C to give corresponding dihydroquinazoliones (**11a-f**) in good to excellent yields.

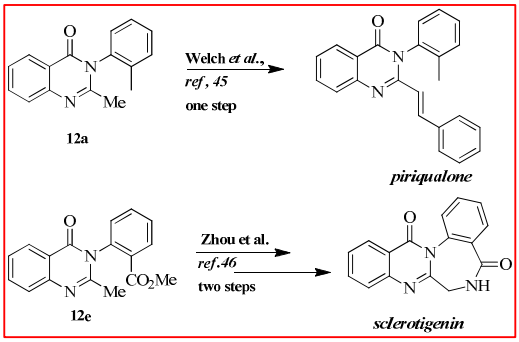
Figure 2: Temperature effect on conformational isomerism **11b**



Although in NMR spectrum, we observed a firm existence of two isomers for compounds **11a, 11b, 11c** and **11e** (see supporting) with different ratios. We presumed that due to the presence of R_1 group in compound **11** restrict the C-C bond rotation and generate conformational isomerism. To prove the existence of rotamers, we carried out temperature variant NMR experiment where spectral changes were measured in DMSO-d_6 solvent over a temperature range of RT-80 ^{0}C. As fig. 2 for the compound **11b** shows, with the increase of temperature the signal spread (Δδ) between signals of ***a (3H, s)*** and ***b (1H, q)*** decreases. At 50 ^{o}C the signals of ***a*** and ***b*** start to coalesce on NMR time scale. Measurement at 70 ^{o}C shows, peaks of both ***a*** and ***b*** merged as both the conformers lost their identity and exhibit a rapidly equilibrating species.

Next, dihydroquinazolinones were aromatized with DDQ to furnish respective quinazolinones in good yields (**12a-f**). We have tested a variety of substitutes on aniline particularly like halo, ester, and alkyl to synthesis the exact drugs and alkaloid. To our delight, all reaction went with ease to give excellent yields of the compounds including 2-(4-methoxyphenyl)-3-phenylquinazolin-4(3*H*)-one (**12f**). Drugs like methaqualone (**12a**), mecloqualone (**12b**), mebroqualone (**12c**) and alkaloid methyl 2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)benzoate (**12e)** was synthesized with good overall yields (**Scheme 4**). Compounds **12a** and **12e** can be further improvise to two more natural products piriqualone and sclerotigenin in one and two steps *via* Welch[46] and Zhou's[47] method (**Scheme 5**).

Scheme 5: Formal syntheses of sclerotigenin and piriqualone



Conclusions

In conclusion, we have developed a greener and cheaper strategy to synthesis substituted and unsubstituted dihydroquinazolinones as well as quinazolinones in good to excellent yields. Numerous aldehydes/ ketones and substituted anthranilamides were well tolerated in this optimized condition. This protocol was further utilized for formal synthesis of many naturally occurring alkaloids and drugs.

Experimental Section

General Information:

^{1}H and ^{13}C-NMR spectra were recorded at 400 and 100 MHz, respectively, or at 500 and 125 MHz, respectively. Chemical shifts were calculated in ppm downfield from TMS (δ = 0) for ^{1}H NMR, and relative to the central $CDCl_3$ resonance (δ =77.0) and DMSO-d_6 (δ = 39.51) for ^{13}C NMR. Data presented in the experimental section are as follows: chemical shift,

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integration, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, dd=doublet doublet), coupling constant in Hertz (Hz). TOF and quadrupole mass analyzer types are used for the HRMS measurements. Mass spectral data was obtained from HRMS (ESI). IR spectra were recorded on a FT-IR spectrometer using KBr pellets or neat. Melting points were measured in open capillary tubes and are uncorrected. All the obtained products were purified by column chromatography using silica gel (100-200 mesh). All reaction solvents used were dried from GR grade solvents. All other commercial reagents were used as received.

General experimental procedure to synthesis dihydroquinazolinone/ quinazolinone:

For 0.100 g starting amide, a total 2g mixture of L-(+)-Tartaric acid and N, N´-Dimethylurea (DMU) in a ratio of 3:7 was taken in an oven dried open mouth round bottomed flask and heated to its eutectic point 70 ^{0}C, where the mixture melted to give a clear solution. Next, aldehyde (1.2/ 1.5 equiv.) and substituted anthraniliamide (1.0 equiv.) was added to this melt and heated at 90 ^{0}C for 2-24h, depending on the desired product. On Completion of the reaction water was (checked by thin layer chromatography technique) added to it. The mixture was extracted with EtOAc, dried over Na_2SO_4 and evaporated in vacuum. The residue was purified by column chromatography on silica gel using ethyl acetate/ hexane mixture to afford the desired dihydroquinazolinone/ quinazolinone.

2-(o-Tolyl)quinazolin-4(3*H*)-one (3a):

This compound was obtained as white solid; yield = (0.135 g/ 0.100 g of **1a**; 78%); m.p. = 232-234 ^{o}C; R_f = 0.45 (EtOAc: hexanes= 3:7); IR (KBr) 3057, 1670, 1601, 1469, 1286, 1264, 765 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.49 (1H, s, br), 8.34 (1H, d, *J* = 7.6 Hz), 8.15 (2H, d, *J* = 8.0 Hz), 7.82 (2H, t, *J* = 8.0 Hz), 7.50 (1H, t, *J* = 8.0 Hz), 7.38 (2H, d, *J* = 2.0 Hz), 2.47 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 151.9, 149.6, 142.1, 134.8, 130.0, 129.7, 127.9, 127.4, 127.3, 126.5, 126.3, 120.8, 21.5; m/z=237 (M+H), positive mode; Anal. Calcd for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86%. Found: C, 76.12; H, 5.18; N, 11.96%.

2-(3-Methoxyphenyl)quinazolin-4(3*H*)-one (3b):
This compound was obtained as white solid; yield = (0.135 g/ 0.100 g of **1a**; 73%); m.p. = 216 ^{o}C; R_f = 0.24 (EtOAc: hexanes= 3:7); IR (KBr) 1678, 1602, 1484, 1264, 834 cm^{-1};^{1}H NMR (500 MHz, DMSO-d_6) δ 12.39 (1H, s, br), 8.19 (2H, d, *J* = 8.5 Hz), 8.13 (1H, d, *J* = 7.0 Hz), 7.81 (1H, t, *J* = 6.5 Hz), 7.70 (1H, d, *J* = 8.0 Hz), 7.48 (1H, t, *J* = 7.0 Hz), 7.09 (2H, d, *J* = 9.0 Hz), 3.85 (3H, s); ^{13}C NMR (125 MHz, DMSO-d_6) δ 162.7, 162.4, 152.3, 149.4, 134.9, 129.9, 127.7, 126.5, 126.3, 125.3, 121.2, 114.5, 55.9; m/z=253 (M+H), positive mode; Anal. Calcd for $C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79; N, 11.10%. Found: C, 71.57; H, 4.71; N, 11.26%.

2-Phenylquinazolin-4(3*H*)-one (3c):
This compound was obtained as yellow solid; yield = (0.099 g/ 0.100 g of **1a**; 61%); m.p. = 236 ^{o}C; R_f = 0.40 (EtOAc: hexanes= 3:7); IR (KBr) 2918, 1666, 1601, 1291, 1265, 768 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$+ DMSO-d_6) δ 11.94 (1H, s), 8.05 (1H, d, *J* = 7.2 Hz), 7.99- 7.98 (2H, m), 7.57- 7.55 (2H, m), 7.32- 7.29 (3H, m), 7.27- 7.21 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$+ DMSO-d_6) δ 163.2, 152.3, 149.2, 134.3, 132.9, 131.2, 129.5, 128.6, 128.1, 127.6, 126.3, 126.0, 121.1; m/z=223 (M+H), positive mode; Anal. Calcd for $C_{14}H_{10}N_2O$: C, 75.66; H, 4.54; N, 12.60%. Found: C, 75.81; H, 4.51; N, 12.53%.

2-Phenyl-2,3-dihydroquinazolin-4(1*H*)-one (3c'):

This compound was obtained as white solid; yield = (0.040 g/ 0.100 g of **1a**; 25%); m.p. = 216 ^{o}C; R_f = 0.41 (EtOAc: hexanes= 3:7); IR (KBr) 3299, 2925, 1651, 1608, 1264 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.29 (1H, s), 7.63 (1H, d, *J* = 7.6 Hz), 7.51 (2H, d, *J* = 7.6 Hz), 7.42- 7.34 (3H, m), 7.26 (1H, t, *J* = 7.2 Hz), 7.12 (1H, s), 6.77 (1H, d, *J* = 8.4 Hz), 6.69 (1H, t, *J* = 7.2 Hz), 5.77 (1H, s); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.1, 148.3, 142.1, 133.8, 128.9, 128.8, 127.8, 127.3, 117.6, 115.4, 114.9, 67.0; m/z=225 (M+H), positive mode; Anal. Calcd for $C_{14}H_{12}N_2O$: C, 74.98; H, 5.39; N, 12.49%. Found: C, 74.82; H, 5.45; N, 12.56%.

2-Butylquinazolin-4(3*H*)-one (3d):
This compound was obtained as white solid; yield = (0.117 g/ 0.100 g of **1a**; 79%); m.p. = 110 ^{o}C; R_f = 0.36 (EtOAc: hexanes= 3:7); IR (KBr) 2919, 1682, 1616, 1467, 1261, 1130 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.02 (1H, s), 8.29 (1H, d, *J* = 8.0 Hz), 7.77 (1H, t, *J* = 8.0 Hz), 7.71 (1H, d, *J* = 8.0 Hz), 7.47 (1H, t, *J* = 8.0 Hz), 2.81 (2H, t, *J* = 8.0 Hz), 1.92- 1.82 (2H, m), 1.51 (2H, q, *J* = 7.4 Hz), 1.00 (3H, t, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.4, 157.0, 149.5, 134.8, 127.2, 126.3, 126.2, 120.5, 35.7, 29.7, 22.4, 13.8; HRMS (ESI-MS) cald. for $C_{12}H_{14}N_2O$ (M+H) 203.1184, found 203.1187.

2-(3-Nitrophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3e'):

This compound was obtained as brown solid; yield = (0.082 g/ 0.050 g of **1a**; 83%); m.p. = 216 ^{o}C; R_f = 0.16 (EtOAc: hexanes= 3:7); IR (KBr) 2920, 1731, 1682, 1616, 1468, 1200, 1145 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.53 (1H, s), 8.35 (1H, s), 8.19 (1H, d, *J* = 8.0 Hz), 7.93 (1H, d, *J* = 7.2 Hz), 7.68 (1H, t, *J* = 8.0 Hz), 7.61 (1H, d, *J* = 7.2 Hz), 7.34 (1H, s), 7.26 (1H, t, *J* = 7.2 Hz), 6.78 (1H, d, *J* = 8.0 Hz), 6.68 (1H, t, *J* = 7.2 Hz), 5.94 (1H, s); ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.8, 148.2, 147.8, 144.7, 134.1, 133.8, 130.5, 127.9, 123.7, 122.0, 118.0, 115.4, 115.1, 65.6; HRMS (ESI-MS) cald. for $C_{14}H_{11}N_3O_3$ (M+H) 270.0878, found 270.0874.

2-(Pyridin-2-yl)quinazolin-4(3*H*)-one (3f):

This compound was obtained as white crystalline solid; yield = (0.061 g/ 0.050 g of **1a**; 74%); m.p. = 166 ^{o}C; R_f = 0.35 (EtOAc: hexanes= 3:7); IR (KBr) 1684, 1607, 1472, 1331, 769 cm^{-1};^{1}H NMR (400 MHz, DMSO-d_6) δ 11.82 (1H, s, br), 8.74 (1H, d, *J* =

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4.4 Hz), 8.43 (1H, d, *J* = 8.0 Hz), 8.17 (1H, d, *J* = 8.0 Hz), 8.06 (1H, t, *J* = 8.0 Hz), 7.86 (1H, t, *J* = 8.0 Hz), 7.79 (1H, d, *J* = 8.0 Hz), 7.65-7.62 (1H, m), 7.56 (1H, t, *J* = 7.6 Hz); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.3, 150.3, 149.5, 149.0, 148.8, 138.5, 135.2, 128.1, 127.8, 127.0, 126.5, 122.6, 122.4 ; m/z=224 (M+H), positive mode; Anal. Calcd for $C_{13}H_9N_3O$: C, 69.95; H, 4.06; N, 18.82%. Found: C, 69.86; H, 4.15; N, 18.75%.

2-(Pyridin-4-yl)quinazolin-4(3*H*)-one (3g):

This compound was obtained as white solid; yield = (0. 125g/ 0.100 g of **1a**; 76%); m.p. = >240 °C; R_f = 0.2 (EtOAc: hexanes= 1:1); IR (KBr) 3358, 2964, 1682, 1561, 1468, 1260, 1030 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.77 (1H, s), 8.79 (2H, d, *J* = 4.0 Hz), 8.18 (1H, d, *J* = 7.6 Hz), 8.12 (2H, d, *J* = 4.5 Hz), 7.88 (1H, t, *J* = 7.5 Hz), 7.79 (1H, d, *J* = 7.9 Hz), 7.58 (1H, t, *J* = 7.2 Hz); ^{13}C NMR (125 MHz, DMSO-d_6) δ 162.5, 151.0, 150.7, 140.4, 135.3, 128.2, 127.9, 126.4, 122.0, 121.9; HRMS (ESI-MS) cald. for $C_{13}H_9N_3O$ (M+H) 224.0824, found 224.0820.

2-(2-Bromophenyl)-2,3-dihydroquinazolin-4(1*H*)-one (3h'):

This compound was obtained as light yellow solid; yield= (0.180 g/ 0.100 g of **1a**; 81%); m.p. = 188 °C; R_f = 0.32 (EtOAc: hexanes= 3:7); IR (KBr) 3220, 1656, 1612, 1486, 1249 cm^{-1};^{1}H NMR (400 MHz, DMSO-d_6) δ 8.21 (1H, s), 7.69- 7.65 (3H, m), 7.44 (1H, t, *J* = 7.2 Hz), 7.32 (1H, t, *J* = 7.6 Hz), 7.27 (1H, t, *J* = 7.6 Hz), 7.00 (1H, s), 6.78 (1H, d, *J* = 8.4 Hz), 6.74 (1H, t, *J* = 7.6 Hz), 6.11 (1H, s); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.2, 148.1, 139.6, 133.9, 133.3, 131.2, 129.5, 128.5, 127.9, 122.6, 118.0, 115.1, 115.0, 66.8; HRMS (ESI-MS) cald. for $C_{14}H_{11}BrN_2O$ (M+Na) 324.9952, found 324.9959.

2-(1-Benzyl-1*H*-indol-2-yl)-8-methoxy-2,3-dihydroquinazolin-4(1*H*)-one (3i'):

This compound was obtained as yellowish brown solid; yield = (0.230 g/ 0.108 g of **1b**; 92%); m.p. = 198- 200 °C; R_f = 0.18 (EtOAc: hexanes= 3:7); IR (KBr) 2920, 1671, 1610, 1457, 1249 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.48 (1H, s), 7.52 (1H, d, *J* = 7.6 Hz), 7.33- 7.28 (5H, m), 7.09- 6.94 (5H, m), 6.69 (1H, t, *J* = 7.6 Hz), 6.43 (1H, s, br), 6.39 (1H, s), 6.05 (1H, s), 5.65 (2H, s), 3.72 (3H, s); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.0, 146.9, 140.5, 138.6, 137.8, 136.5, 129.0, 127.6, 127.0, 126.8, 122.2, 120.9, 120.0, 119.3, 117.4, 116.0, 114.0, 110.8, 101.9, 60.1, 56.0, 46.7:; HRMS (ESI-MS) cald. for $C_{24}H_{21}N_3O_2$ (M+H) 384.1712, found 384.1706.

8-Methoxy-2-(1-(methoxymethyl)-1*H*-indol-2-yl)-2,3-dihydroquinazolin-4(1*H*)-one (3j'):

This compound was obtained as brown solid; yield = (0.290 g/ 0.200 g of **1b**; 72%); m.p. = > 184°C; R_f = 0.37 (EtOAc: hexanes= 3:7); IR (KBr) 3419, 1687, 1605, 1468, 1276, 761cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6) δ 7.57 (1H, s, br), 7.52- 7.43(3H, m), 7.22 (1H, t, *J* = 8.0 Hz), 7.09 (1H, t, *J* = 8.0 Hz), 6.85 (1H, dd, *J* = 1.2 Hz, *J* = 8.0 Hz), 6,74 (1H, t, *J* = 8.0 Hz), 6.63 (1H, s), 6.16 (1H, d, *J* = 2.0 Hz), 5.70 (1H, s, br), 5.66 (1H, d, *J* = 11.2 Hz), 5.55 (1H, d, *J* = 11.6 Hz), 3.79 (3H, s), 3.31 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6) δ 169.5, 151.2, 143.3, 142.7, 141.8, 131.7, 127.8, 125.9, 125.4, 124.2, 122.8, 120.2, 118.3, 114.2, 108.9, 78.9, 66.3, 60.8, 60.4; m/z=338(M+H), positive mode; Anal. Calcd for $C_{19}H_{19}N_3O_3$: C, 67.64; H, 5.68; N, 12.46%. Found: C, 67.49; H, 5.73; N, 12.38%.

2-(1*H*-Indol-2-yl)-7-methoxyquinazolin-4(3*H*)-one (3k):

This compound was obtained as brown solid; yield = (0.065 g/ 0.056 g of **1c**; 67%); m.p. = 244-246 °C; R_f = 0.37 (EtOAc: hexanes= 3:7); IR (KBr) 3484, 2898, 1654, 1600, 1315, 1145 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.48 (1H, s), 11.77 (1H, s), 8.06 (1H, t, *J* = 9.2 Hz), 7.63 (2H, d, *J* = 11.2 Hz), 7.51 (1H, d, *J* = 8.4 Hz), 7.21 (1H, t, *J* = 8.4 Hz), 7.12 (1H, s), 7.09- 7.03 (2H, m), 3.91 (3H, s); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.6, 161.8, 151.4, 147.6, 138.1, 130.5, 128.2, 127.9, 124.5, 122.0, 120.4, 116.1, 115.0, 112.9, 108.6, 105.4, 56.1; HRMS (ESI-MS) cald. for $C_{17}H_{13}N_3O_2$ (M+H) 292.1086, found 292.1086.

2-(1*H*-Pyrrol-2-yl)quinazolin-4(3*H*)-one (3l):

This compound was obtained as brown powder; yield = (0.112 g/ 0.100 g of **1a**; 72%); m.p. = > 240°C; R_f = 0.45 (EtOAc: hexanes= 3:7); IR (KBr) 2919, 1672, 1596, 1496, 1261, 765 cm^{-1};^{1}H NMR (400 MHz, DMSO-d_6) δ 12.18 (1H, s), 11.70 (1H, s), 8.08 (1H, d, *J* = 7.6 Hz), 7.77 (1H, t, *J* = 7.6 Hz), 7.62 (1H, d, *J* = 8.0 Hz), 7.41 (1H, t, *J* = 7.2 Hz), 7.29 (1H, s), 7.05 (1H, s), 6.21 (1H, s) ; ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.4, 149.7, 146.8, 135.0, 126.9, 126.4, 125.7, 124.7, 124.3, 120.9, 112.9, 110.2; m/z=212 (M+H), positive mode; Anal. Calcd for $C_{12}H_9N_3O$: C, 68.24; H, 4.29; N, 19.89%. Found: C, 68.15; H, 4.36; N, 19.78%.

2-(1*H*-Indol-2-yl)quinazolin-4(3*H*)-one (5):

This compound was obtained as yellow solid; yield = (0.154 g/ 0.100 g of **1a**; 81%); m.p. = 268 °C; R_f = 0.24 (EtOAc: hexanes= 1:1); IR (KBr) 3413, 1665, 1589, 1468, 1260, 772 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.62 (1H, s), 11.81 (1H, s), 8.17 (1H, d, *J* = 8.0 Hz); 7.88- 7.85 (1H, m), 7.75 (1H, d, *J* = 8.0 Hz), 7.68 (1H, s), 7.65 (1H, d, *J* = 8.0 Hz), 7.54 (2H, t, *J* = 7.2 Hz), 7.24 (1H, t, *J* = 8.4 Hz), 7.07 (1H, t, *J* = 7.2 Hz); ^{13}C NMR (125 MHz, DMSO-d_6) δ 162.3, 149.2, 147.0, 138.1, 135.2, 130.5, 127.9, 127.4, 126.7, 126.5, 124.5, 122.0, 121.6, 120.4, 112.9, 105.5; HRMS (ESI-MS) cald. for $C_{16}H_{11}N_3O$ (M+H) 262.0980, found 262.0980.

2-Methyl-2,3-dihydroquinazolin-4(1*H*)-one (7'):

This compound was obtained as yellow solid; yield = (0.094g/ 0.100 g of **1a**; 79%); m.p. = 136 °C; R_f = 0.14 (EtOAc: hexanes= 1:1); IR (KBr) 3266, 1668, 1615, 1257, 753 cm^{-1};^{1}H NMR (400 MHz, DMSO-d_6) δ 7.90 (1H, s), 7.59 (1H, d, *J* = 8.0 Hz), 7.23 (1H, t, *J* = 8.0 Hz), 6.68 (2H, d, *J* = 8.0 Hz), 6.60 (1H, s), 4.82 (1H, q, *J* = 5.6 Hz), 1.31 (3H, d, *J* = 5.6 Hz); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.6, 149.2, 133.6, 127.9, 117.6, 115.6, 114.8,

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61.3, 21.7; HRMS (ESI-MS) cald. for $C_9H_{10}N_2O$ (M+H) 163.0871, found 163.0870.

2-Methylquinazolin-4(3*H*)-one (7):

Compound **7'** (0.050g, 0.308 mmol) was taken in to an oven dried round bottom flask, dry DCM (5mL), DDQ (0.350g, 1.54 mmol) was added and stirred at rt for 30 mins. After completion of the (checked by TLC) reaction, reaction mixture was extracted with DCM, dried over Na_2SO_4 and evaporated in vacuum. The residue was purified by column chromatography on silica gel (EtOAc: hexane) to afford a desired product (**7**). This compound was obtained as yellowish brown crystalline; yield = (0.042 g/ 0.050 g of 7'; 85%); m.p. = 228 ^oC; R_f = 0.21 (EtOAc: hexanes= 1:1); IR (KBr) 2915, 1693, 1665, 1610, 1468, 1254 cm^{-1};^{1}H NMR (400 MHz, $CDCl_3$) δ 11.81 (1H, s, br), 8.29 (1H, d, *J* = 8.0 Hz), 7.78 (1H, t, *J* = 8.0 Hz), 7.69 (1H, d, *J* = 8.0 Hz), 7.48 (1H, t, *J* = 8.0 Hz), 2.60 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 153.2, 149.4, 134.9, 127.0, 126.4, 126.2, 120.3, 22.1; HRMS (ESI-MS) cald. for $C_9H_8N_2O$ (M+H) 161.0715, found 161.0710;We followed the same procedure for compound **12a- 12f**.

2,2-Dimethyl-2,3-dihydroquinazolin-4(1*H*)-one (8a):

This compound was obtained as white solid; yield = (0.123g/ 0.100 g of **1a**; 95%); m.p. = 176-178 ^oC; R_f = 0.25 (EtOAc: hexanes= 1:1); IR (KBr) 3255, 1632, 1485, 1270, 1175, 750 cm^{-1};^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (1H, d, *J* = 7.2 Hz), 7.31 (1H, t, *J* = 8.0 Hz), 7.05 (1H, s, br), 6.83 (1H, t, *J* = 7.2 Hz), 6.64 (1H, d, *J* = 7.6 Hz), 4.25 (1H, s, br), 1.58 (6H, s) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 146.0, 133.9, 128.3, 118.7, 114.7, 114.6, 67.6, 29.6; m/z=177(M+H), positive mode. Anal. Calcd for $C_{10}H_{12}N_2O$: C, 68.16; H, 6.86; N, 15.90%. Found: C, 68.26; H, 6.81; N, 15.82%.

2-Ethyl-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (8b):

This compound was obtained as yellowish brown solid; yield = (0.137g/ 0.100 g of **1a**; 98%); m.p. = 164-166 ^oC; R_f = 0.18 (EtOAc: hexanes= 1:1); IR (KBr) 3270, 1638, 1612, 1266, 754 cm^{-1};^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (1H, d, *J* = 7.5 Hz), 7.31 (1H, d, *J* = 8.5 Hz), 6.82 (1H, t, *J* = 7.0 Hz), 6.62 (1H, d, *J* = 8.0 Hz), 6.17 (1H, s, br), 4.13 (1H, s, br), 1.82 (2H, q, *J* = 7.4 Hz), 1.51 (3H, s), 1.01 (3H, t, *J* = 7.4 Hz) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 146.1, 134.1, 128.3, 118.4, 114.5, 114.2, 70.1, 34.8, 27.5, 8.2; m/z=191(M+H), positive mode. Anal. Calcd for $C_{11}H_{14}N_2O$: C, 69.45; H, 7.42; N, 14.73%. Found: C, 69.56; H, 7.35; N, 14.62%.

2-Methyl-2-phenyl-2,3-dihydroquinazolin-4(1*H*)-one (8c):

This compound was obtained as light yellow solid; yield = (0.141g/ 0.100g of **1a**; 81%); m.p. = 220 ^oC; R_f = 0.13 (EtOAc: hexanes= 3:7); IR (KBr) 3402, 1665, 1610, 1501, 1380, 1265 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$+ DMSO-d_6) δ 7.64 (1H, d, *J* = 8.0 Hz), 7.60 (1H, s, br), 7.43 (2H, d, *J* = 8.0 Hz), 7.17 (2H, t, *J* = 8.0 Hz), 7.14- 7.08 (2H, m), 6.64 (1H, d, *J* = 8.0 Hz), 6.59 (1H, t, *J* = 8.0 Hz), 5.98 (1H, s, br), 1.72 (3H, s) ; ^{13}C NMR (100 MHz, $CDCl_3$+ DMSO-d_6) δ 164.8,146.4, 146.0, 133.7, 128.2, 128.0, 127.6, 125.2, 118.1, 115.2, 114.7, 70.7, 30.3; HRMS (ESI-MS) cald. for $C_{15}H_{14}N_2O$ (M+Na) 261.1004, found 261.1003.

1'*H*-Spiro[cyclohexane-1,2'-quinazolin]-4'(3'*H*)-one (8d):

This compound was obtained as yellow crystalline solid; yield = (0.131g/ 0.100g of **1a**; 83%); m.p. = 212-214 ^oC; R_f = 0.13 (EtOAc: hexanes= 3:7); IR (KBr) 3169, 2922, 2852, 1642, 1606, 1479, 1267 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$+ DMSO-d_6) δ 7.62-7.58 (1H, m), 7.06 (1H, d, *J* = 6.8 Hz), 6.89 (1H, s), 6.55- 6.52 (2H, m), 5.21 (1H, s, br), 1.63 (4H, s), 1.41 (4H, s), 1.26 (2H, s); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6) δ 164.3, 146.2, 133.5, 127.8, 117.7, 114.7, 68.2, 37.4, 24.6, 21.6; m/z=217 (M+H), positive mode. Anal. Calcd for $C_{13}H_{16}N_2O$: C, 72.19; H, 7.46; N, 12.95%.Found: C, 72.25; H, 7.41; N, 13.07%.

1'*H*-Spiro[indoline-3,2'-quinazoline]-2,4'(3'*H*)-dione (8e):

This compound was obtained as yellow solid; yield = (0.121g/ 0.100g of **1a**; 62%); m.p. = 214 ^oC; R_f = 0.15 (EtOAc: hexanes= 1:1); IR (KBr) 1726, 1659, 1609, 1585, 1264 cm^{-1};^{1}H NMR (400 MHz, DMSO-d_6) δ 10.31 (1H, s), 8.36 (1H, s), 7.61 (1H, d, *J* = 7.2 Hz), 7.48 (1H, d, *J* = 7.2 Hz), 7.34 (1H, t, *J* = 7.6 Hz), 7.28 (1H, s), 7.24 (1H, t, *J* = 8.0 Hz), 7.07 (1H, t , *J* = 7.6 Hz), 6.87 (1H, d, *J* = 7.6 Hz), 6.69 (1H, t, *J* = 7.6 Hz), 6.62 (1H, d, *J* = 7.6 Hz); ^{13}C NMR (100 MHz, DMSO-d_6) δ 176.5, 164.5, 147.3, 142.5, 133.8, 131.3, 129.8, 127.3, 125.8, 122.8, 117.7, 114.7, 114.3, 110.6, 71.4; m/z=266(M+H), positive mode; Anal. Calcd for $C_{15}H_{11}N_3O_2$: C, 67.92; H, 4.18; N, 15.84%.Found: C, 67.85; H, 4.12; N, 15.76%.

2, 2-Diphenyl-2,3-dihydroquinazolin-4(1*H*)-one (8f):

This compound was obtained as yellowish white solid; yield = (0.165g/ 0.100g of **1a**; 75%); m.p. = 140 ^oC; R_f = 0.26 (EtOAc: hexanes= 3:7); IR (KBr) 3375, 3243, 1649, 1610, 1484, 1375, 1210, 750 cm^{-1};^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (1H, d, *J* = 7.6 Hz), 7.43- 7.40 (4H, m), 7.34- 7.27 (7H, m), 6.78 (1H, t, *J* = 7.6 Hz), 6.73 (2H, d, *J* = 8.0 Hz), 5.36 (1H, s, br); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.3, 145.6, 143.7, 134.2, 128.6, 128.5, 127.3, 119.2, 115.4, 114.9, 76.0; HRMS (ESI-MS) cald. for $C_{20}H_{16}N_2O$ (M+Na) 323.1160, found 323.1163.

Compound 9a- 9e:
These compounds were prepared *via* adopting method from *reference* 44.

2-Amino-*N*-(o-tolyl)benzamide (10a):

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Compound **9a** (0.500, 2.2 mmol) was dissolved in THF-H_2O solution (5:1, 20 mL).To this solution NH_4Cl (0.353 g, 6.6 mmol) and Zn dust (1.15 g, 17.6 mmol) was added. The reaction was stirred at rt for 5-6 h. After the completion of the reaction, reaction mixture was filtered and extracted with ethyl acetate and evaporated to dryness. The residue was purified by column chromatography on silica gel to give compound **10a**. We followed the same procedure for preparation of compound **10b- 10e**. This compound was obtained as yellowish white solid; yield = (0.380g/ 0.500g of **10a**; 86%); m.p. = 104 ^{o}C; R_f = 0.55 (EtOAc: hexanes= 3:7); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (1H, d, *J* = 8.0 Hz), 7.66 (1H, s, br), 7.53 (1H, d, *J* = 8.0 Hz), 7.31- 7.26 (3H, m), 7.15 (1H, t, *J* = 7.2 Hz), 6.76 (2H, d, *J* = 8.0 Hz), 5.56 (2H, s, br), 2.35 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 149.2, 135.7, 132.8, 130.6, 130.0, 127.2, 126.8, 125.5, 123.7, 117.6, 116.8, 116.1, 17.9; HRMS (ESI-MS) cald. for $C_{14}H_{14}N_2O$ (M+Na) 249.1004, found 249.1008.

2-Amino-*N*-(2-chlorophenyl)benzamide (10b):

This compound was obtained as yellowish white solid; yield = (0.345g/ 0.500g of **9b**; 77%); m.p. = 108 ^{o}C; R_f = 0.65 (EtOAc: hexanes= 3:7); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (1H, d, *J* = 8.4 Hz), 8.37 (1H, s, br), 7.57 (1H, d, *J* = 7.6 Hz), 7.44 (1H, d, *J* = 8.0 Hz), 7.37- 7.29 (2H, m), 7.10 (1H, t, *J* = 8.0 Hz), 6.77 (2H, t, *J* = 7.6 Hz), 5.63 (2H, s, br) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 149.4, 134.8, 133.1, 129.1, 127.7, 127.2, 124.6, 123.4, 121.7, 117.7, 116.9, 115.6; HRMS (ESI-MS) cald. for $C_{13}H_{11}ClN_2O$ (M+H) 247.0638, found 247.0636.

2-Amino-*N*-(2-bromophenyl)benzamide (10c):

This compound was obtained as yellowish white solid; yield = (0.375g/ 0.500g of **9c**; 82%); m.p. = 102 ^{o}C; R_f = 0.65 (EtOAc: hexanes= 3:7); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (1H, dd, *J* = 1.6 Hz, *J* = 8.4 Hz), 8.37 (1H, s, br), 7.60 (2H, t, *J* = 7.6 Hz), 7.39 (1H, t, *J* = 7.6 Hz), 7.33- 7.29 (1H, m), 7.03 (1H, dt, *J* = 1.2 Hz, *J* = 7.6 Hz), 6.77 (2H, t, *J* = 8.0 Hz), 5.65 (2H, s, br); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.3, 149.5, 135.9, 133.1, 132.3, 128.4, 127.2, 125.1, 122.0, 117.7, 117.0, 115.5, 114.1; HRMS (ESI-MS) cald. for $C_{13}H_{11}BrN_2O$ (M+H) 291.0133, found 291.0139.

2-Amino-*N*-phenylbenzamide (10d):

This compound was obtained as yellowish white solid; yield = (0.370g/ 0.500g of **9d**; 84%); m.p. = 118 ^{o}C; R_f = 0.55 (EtOAc: hexanes= 3:7); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (1H, s, br), 7.59 (2H, d, *J* = 8.0 Hz), 7.50 (1H, d, *J* = 8.0 Hz), 7.39 (2H, t, *J* = 7.6 Hz), 7.28 (1H, t, *J* = 7.6 Hz), 7.17 (1H, t, *J* = 7.2 Hz), 6.74 (2H, d, *J* = 7.6 Hz), 5.51 (2H, s, br); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 148.9, 137.8, 132.7, 129.1, 127.2, 124.5, 120.6, 117.6, 116.8, 116.3; HRMS (ESI-MS) cald. for $C_{13}H_{12}N_2O$ (M+H) 213.1028, found 213.1026.

Methyl 2-(2-aminobenzamido)benzoate (10e):

This compound was obtained as yellowish white solid; yield = (0.212g/ 0.500g of **9e**; 47%); m.p. = 112 ^{o}C; R_f = 0.65 (EtOAc: hexanes= 3:7); ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.84 (1H, s, br), 8.85 (1H, dd, *J* = 0.8 Hz, *J* = 8.8 Hz), 8.10 (1H, dd, *J* = 1.6 Hz, *J* = 8.0 Hz), 7.76 (1H, dd, *J* = 1.2 Hz, *J* = 8.0 Hz), 7.61 (1H, t, *J* = 7.2 Hz), 7.29 (1H, t, *J* = 8.4 Hz), 7.13 (1H, t, *J* = 8.0 Hz), 6.80 (1H, t, *J* = 8.0 Hz), 6.74 (1H, dd, *J* = 0.8 Hz, *J* = 8.4 Hz), 5.80 (2H, s, br), 4.00 (3H, s) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0, 168.2, 149.8, 141.9, 134.6, 132.9, 131.0, 127.7, 122.3, 120.5, 117.5, 116.9, 115.7, 115.3, 52.5; HRMS (ESI-MS) cald. for $C_{15}H_{14}N_2O_3$ (M+Na) 293.0902, found 293.0907.

2-Methyl-3-(o-tolyl)-2,3-dihydroquinazolin-4(1*H*)-one (11a):

It is probably the steric reason for that these compounds exists as rotamers, the ratio of both isomer is variable depending on the substitution (**11a, 11b, 11c, 11e**). This compound (**11a**) was obtained as white crystalline solid; yield = (0.097g/ 0.100g of **10a**; 87%); m.p. = 176-178 ^{o}C; R_f = 0.42 (EtOAc: hexanes= 3:7); IR (KBr) 3296, 1632, 1612, 1506, 1326, 1263, 758 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.68 (2H, t, *J* = 6.4 Hz), 7.33 (4H, t, *J* = 6.8 Hz), 7.28- 7.24 (5H, m), 7.19 (1H, d, *J* = 6.8 Hz), 6.93 (2H, d, *J* = 8.8 Hz), 6.80 (2H, d, *J* = 8.0 Hz), 6.75 (2H, t, *J* = 7.6 Hz), 5.33 (1H, q, *J* = 5.6 Hz), 4.97 (1H, q, *J* = 5.6 Hz), 2.22 (3H, s), 2.17 (3H, s), 1.28 (3H, d, *J* = 5.6 Hz), 1.13 (3H, d, *J* = 5.6 Hz); ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.5, 162.2, 148.5, 147.9, 139.43, 139.38, 137.3, 136.0, 133.91, 133.86, 131.3, 130.8, 130.6, 128.5, 128.4, 128.3, 128.2, 127.9, 127.3, 126.8, 118.0, 117.9, 115.9, 115.5, 115.3, 114.9, 67.9, 67.1, 20.5, 18.6, 17.9; m/z=253(M+H), positive mode. Anal. Calcd for $C_{16}H_{16}N_2O$: C, 76.16; H, 6.39; N, 11.10%.Found: C, 76.31; H, 6.31; N, 11.18%.

3-(2-Chlorophenyl)-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (11b):

This compound was obtained as brown solid; yield = (0.100g/ 0.100g of **10b**; 91%); m.p. = 162 ^{o}C; R_f = 0.27 (EtOAc: hexanes= 3:7); IR (KBr) 3057, 2915, 1687, 1605, 1468, 1342, 1282, 1068 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (1H, d, *J* = 8.0 Hz), 7.54-7.51 (1H, m), 7.41- 7.31 (4H, m), 6.92 (1H, t, *J* = 7.6 Hz), 6.74 (1H, d, *J* = 8.0 Hz), 5.31 (1H, q, *J* = 5.2 Hz), 4.59- 4.54 (1H, m), 1.38- 1.34 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2, 162.7, 146.6, 146.5, 136.8, 134.5, 133.7, 132.9, 132.3, 130.4, 130.3, 129.9, 129.3, 129.2, 127.9, 127.5, 119.6, 116.6, 115.3, 115.1, 68.4, 66.6, 20.5; m/z=272 (M+), positive mode. Anal. Calcd for $C_{15}H_{13}ClN_2O$: C, 66.06; H, 4.80; N, 10.27%.Found: C, 66.15; H, 4.73; N, 10.36%.

3-(2-Bromophenyl)-2-methyl-2,3-dihydroquinazolin-4(1*H*)-one (11c):

This compound was obtained as brown solid; yield = (0.087g/ 0.086g of **10c**; 93%); m.p. = 120 ^{o}C; R_f = 0.31 (EtOAc: hexanes= 3:7); IR (KBr) 3088, 2349, 1679, 1601, 1567, 1469, 1275, 757 cm^{-1};^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (1.2H, dd, *J* = 0.8 Hz, *J* = 7.6 Hz), 7.73- 7.69 (1.2H, m), 7.43- 7.31 (3.6H, m), 7.27- 7.22

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(1.2H, m), 6.94- 6.90 (1.33H, m), 6.75- 6.72 (1.29H, m), 5.32 (1.4H, q, *J* = 6.0 Hz),4.62- 4.57 (1.36H, m), 1.37- 1.35 (3.6H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0, 162.9, 146.8, 146.5, 139.1, 138.5, 133.75, 133.69, 133.6, 132.4, 129.9, 129.5, 129.3, 129.27, 129.2, 128.6, 128.2, 125.1, 123.2, 119.6, 116.9, 116.6, 115.4, 115.1, 68.2, 66.7, 20.45, 20.42 ; HRMS (ESI-MS) cald. for $C_{15}H_{13}{}^{79}BrN_2O$ (M+Na) 339.0109, found 339.0114; $C_{15}H_{13}{}^{81}BrN_2O$ (M+Na) 341.0088, found 341.0099.

2-Methyl-3-phenyl-2,3-dihydroquinazolin-4(1*H*)-one (11d):

This compound was obtained as yellow solid; yield = (0.108g/ 0.100g of **10d**; 96%); m.p. = 168 °C; R_f = 0.26 (EtOAc: hexanes= 3:7); IR (KBr) 3299, 1634, 1612, 1495, 1263 cm^{-1};^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (1H, d, *J* = 8.0 Hz), 7.44 (2H, t, *J* = 8.0 Hz), 7.36- 7.29 (4H, m), 6,90 (1H, t, *J* = 7.6 Hz), 6.70 (1H, d, *J* = 8.0 Hz), 5.23 (1H, q, *J* = 6.0 Hz), 4.61 (1H, s, br), 1.42 (3H, d, *J* = 6.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO- d_6) δ 162.9, 145.9, 140.2, 133.7, 129.3, 129.1, 127.8, 127.3, 119.4, 116.7, 115.1, 68.5, 20.9; m/z=239 (M+H), positive mode. Anal. Calcd for $C_{15}H_{14}N_2O$: C, 75.61; H, 5.92; N, 11.76%.Found: C, 75.52; H, 6.07; N, 11.65%.

Methyl 2-(2-methyl-4-oxo-1,2-dihydroquinazolin-3(4*H*)-yl)benzoate (11e):

This compound was obtained as white solid and is unstable in NMR solvent media ($CDCl_3$/ DMSO-d_6), thus after several efforts also we were unable to get a very clear 13C spectra. yield = (0.033g/ 0.050g of **10e**; 61%); m.p. = 158 °C; R_f = 0.18 (EtOAc: hexanes= 3:7); IR (KBr) 3304, 2958, 2920, 1726, 1649, 1523, 1260, 958 cm^{-1};^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (1H, s, br), 7.98 (1H, d, *J* = 7.6 Hz), 7.61 (1H, t, *J* = 7.6 Hz), 7.45 (1H, t, *J* = 6.8 Hz), 7.36 (2H, d, *J* = 6.8 Hz), 6.93 (1H, t, *J* = 7.6 Hz), 6.76 (1H, d, *J* = 8.0 Hz), 5.41 (1H, d, *J* = 5.2 Hz), 4.51 (1H, s, br), 3.83 (3H, s), 1.3 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.0, 163.8, 146.5, 139.2, 134.6, 133.5, 132.9, 132.3, 132.1, 131.5, 131.0, 129.1, 128.0, 127.7, 122.4, 120.5, 119.8, 117.5, 115.7, 67.7, 52.3, 20.6; HRMS (ESI-MS) cald. for $C_{17}H_{16}N_2O_3$ (M+Na) 319.1059, found 319.1065.

2-(4-Methoxyphenyl)-3-phenyl-2,3-dihydroquinazolin-4(1*H*)-one (11f):

This compound was obtained as white solid; yield = (0.130g/ 0.100g of **10d**; 84%); m.p. = 194-196 °C; R_f = 0.35 (EtOAc: hexanes= 3:7); IR (KBr) 3294, 1631, 1610, 1507, 1249, 1160, 747 cm^{-1};^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (1H, t, *J* = 7.2 Hz), 7.33- 7.29 (5H, m), 7.22- 7.19 (3H, m), 6.91 (1H, t, *J* = 7.2 Hz), 6,79 (2H, d, *J* = 7.6 Hz), 6.65 (1H, d, *J* = 8.0 Hz), 6.09 (1H, s), 4.77 (1H, s), 3.77 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2, 159.9, 145.5, 140.6, 133.8, 131.9, 129.1, 128.9, 128.2, 127.1, 126.8, 119.5, 116.9, 114.8, 113.9, 74.3, 55.2; m/z=331 (M+H), positive mode. Anal. Calcd for $C_{21}H_{18}N_2O_2$: C, 76.34; H, 5.49; N, 8.48%.Found: C, 76.25; H, 5.41; N, 8.56%.

Methaqualone (12a):

This compound was obtained as yellow solid; yield = (0.044g/ 0.050g of **11a**; 89%); m.p. = 112 °C; R_f = 0.12 (EtOAc: hexanes= 3:7); IR (KBr) 2920, 1678, 1608, 1270, 771 cm^{-1};^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (1H, d, *J* = 8.0 Hz), 7.66 (1H, t, *J* = 8.0 Hz), 7.59 (1H, d, *J* = 8.0 Hz), 7.36 (1H, t, *J* = 7.6 Hz), 7.30- 7.23 (3H, m), 7.05 (1H, d, *J* = 7.2 Hz), 2.08 (3H, s), 2.02 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 153.7, 147.0, 136.2, 134.7, 134.0, 130.9, 128.9, 127.3, 127.0, 126.5, 126.2, 126.0, 120.1, 23.3, 16.8; HRMS (ESI-MS) cald. for $C_{16}H_{14}N_2O$ (M+H) 251.1184, found 251.1181.

Mecloqualone (12b):

This compound was obtained as yellow solid; yield = (0.058g/ 0.075g of **11b**; 78%); m.p. = 98-100 °C; R_f = 0.30 (EtOAc: hexanes= 3:7); IR (KBr) 2917, 1686, 1607, 1472, 1280 cm^{-1};^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (1H, dd, *J* = 1.2 Hz, *J* = 8.0 Hz), 7.83- 7.79 (1H, m), 7.72 (1H, d, *J* = 8.0 Hz), 7.66- 7.62 (1H, m), 7.52- 7.47 (3H, m), 7.38- 7.35 (1H, m), 2.25 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5, 153.7, 147.5, 135.5, 134.8, 132.6, 130.85, 130.81, 129.9, 128.4, 127.2, 126.9, 126.8, 120.6, 23.6; m/z=271 (M+H), positive mode. Anal. Calcd for $C_{15}H_{11}ClN_2O$: C, 66.45; H, 4.10; N, 10.35%.Found: C, 66.42; H, 4.18; N, 10.26%.

Mebroqualone (12c):

This compound was obtained as white solid; yield = (0.040g/ 0.050g of **11c**; 81%); m.p. = 144 °C; R_f = 0.36 (EtOAc: hexanes= 3:7); IR (KBr) 1685, 1605, 1341, 1282, 774 cm^{-1};^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (2H, d, *J* = 7.6 Hz), 7.81 (1H, t, *J* = 8.0 Hz), 7.72 (1H, d, *J* = 7.6 Hz), 7.57- 7.49 (2H, m), 7.42 (1H, t, *J* = 8.0 Hz), 7.38 (1H, d, *J* = 8.0 Hz), 2.25 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 153.6, 147.6, 137.2, 134.8, 134.0, 130.9, 129.9, 129.1, 127.2, 126.9, 126.7, 122.9, 120.6, 23.7; HRMS (ESI-MS) cald. for $C_{15}H_{11}{}^{79}BrN_2O$ (M+H) 315.0133, found 315.0128; $C_{15}H_{11}{}^{81}BrN_2O$ (M+H) 317.0113, found 317.0109.

2-Methyl-3-phenylquinazolin-4(3*H*)-one (12d):

This compound was obtained as brown solid; yield = (0.042g/ 0.050g of **11d**; 85%); m.p. = 130-132 °C; R_f = 0.29 (EtOAc: hexanes= 3:7); IR (KBr) 1682,1607, 1342, 1274, 769 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (1H, dd, *J* = 1.0 Hz, *J* = 7.5 Hz), 7.79- 7.76 (1H, m), 7.70 (1H, d, *J* = 8.0 Hz), 7.59-7.51 (3H, m), 7.49- 7.46 (1H, m), 7.29- 7.27 (2H, m), 2.26 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.3, 154.3, 147.4, 137.8, 134.6, 130.0, 129.3, 128.0, 127.1, 126.75, 126.7, 120.8, 24.4; HRMS (ESI-MS) cald. for $C_{15}H_{12}N_2O$ (M+Na) 259.0848, found 259.0846.

Methyl 2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)benzoate (12e):

This compound was obtained as yellow solid; yield = (0.041g/ 0.050g of **11e**; 84%); m.p. = 136 °C; R_f = 0.14 (EtOAc: hexanes= 3:7); IR (KBr) 3052, 2964, 1600, 1419, 1260, 1095 cm^{-1};^{1}H NMR (400 MHz, DMSO-d_6) δ 8.20 (1H, d, *J* =

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7.6 Hz), 7.91 (2H, t, *J* = 8.0 Hz), 7.78- 7.73 (2H, m), 7.68 (1H, d, *J* = 7.6 Hz), 7.57 (1H, t, *J* = 8.0 Hz), 3.70 (3H, s), 2.15 (3H, s); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.4, 161.3, 154.1, 147.3, 137.7, 134.6, 134.3, 131.3, 130.4, 129.7, 127.3, 126.6, 126.3, 126.2, 120.2, 52.3, 23.6; HRMS (ESI-MS) cald. for $C_{17}H_{14}N_2O_3$ (M+Na) 317.0902, found 317.0899.

2-(4-Methoxyphenyl)-3-phenylquinazolin-4(3*H*)-one (12f):

This compound was obtained as white solid; yield = (0.069g/ 0.050g of **11d**; 87%); m.p. = 146 ^{o}C; R_f = 0.33 (EtOAc: hexanes= 3:7); IR (KBr) 1682, 1606, 1512, 1252, 774 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (1H, d, *J* = 7.6 Hz), 7.84 (2H, s), 7.56- 7.54 (1H, m), 7.39- 7.29 (5H, m), 7.19 (2H, d, *J* = 7.2 Hz), 6.74 (2H, d, *J* = 8.4 Hz), 3.78 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 160.3, 154.9, 147.6, 137.9, 134.7, 130.8, 129.1, 129.0, 128.3, 127.8, 127.6, 127.2, 127.0, 120.8, 113.4, 55.2; m/z=329 (M+H), positive mode; Anal. Calcd for $C_{21}H_{16}N_2O_2$: C, 76.81; H, 4.91; N, 8.53%.Found: C, 76.95; H, 5.07; N, 8.45%.

NMR, CHN, LCMS and HRMS spectra are available in supporting information.

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