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# NIS Mediated Regioselective Amidation of Indole with Quinazolinone and Pyrimidone

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A mild metal free condition was developed for the direct regioselective C2 amidation of indole and pyrrole with quinazolinone and pyrimidone derivatives in intermolecular fashion, which led to novel indolyl/pyrrolyl quinazolinone and pyrimidone derivatives in moderate to good yield.

## Introduction:

Indole[1] and pyrrole[2] structural motifs are considered as 'privileged' skeleton in numerous biologically active natural products. Hence, there is a continual interest among the chemists for direct functionalization of indole and pyrrole in regioselective fashion.[3]A huge number of reports have been displayed by various groups to form C-C bond regioselectively at C2 position of indole[4] as well as pyrrole,[5]however only few reports were available to form C-N bond at the same. In most of the cases, regioselective amination of indole have been achieved via using metal or other harsh condition by different research groups.[6] But reports for C2 amination using mild conditions without metal are scarce. Recently Huang group demonstrated C-N bond formation at indole C2 with azole in presence of iodine.[7]However, regioselective amidation of indole and pyrrole always remained a challenge to the synthetic community. Only very few reports regarding amidation at C2 of indoles[8] and pyrroles[9] are available. Our group also reported the palladium catalysed Buchwald cross coupling reaction at C2 of indole.[10]Very recently, Li group presented direct amidation on indole using CDC process.[11] But still now, reports for metal free direct amidation at indole C2 are limited. In 2008, Baran's group reported a C2 amidation at indole in intramolecular fashion to synthesize psychotrimine.[12] Very recently, Ji and Wang coworkers also reported intramolecular amidation at indole C2 with sulphonamides.[13] Liang group also described iodine mediated intermolecular amidation of N-protected indoles with tosylbenzenamine.[14] To the best of our knowledge,till now there is no report for metal free direct C2 amidation of indole with cyclic amide in intermolecular manner. Numerous biologically active natural products contain C-N amide linkage at C2 position of indole, such as asperazine, chetomin (Fig.1). Most of these natural products contain cyclic amide linkage, but direct amidation with cyclic amide at the C2 position of indole still remain unexposed.

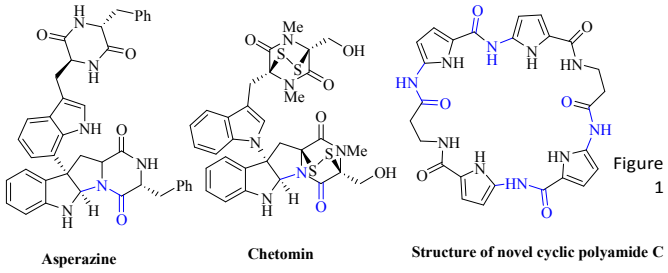


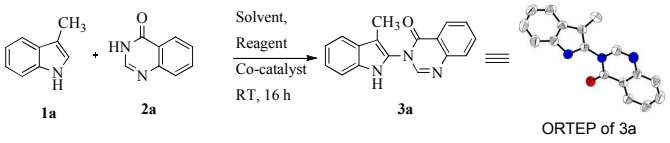

Figure 1 :Naturally occurring indole and pyrrole alkaloids containing C-N amide linkage

Quinazolinone[15] and pyrimidones[16] are very important classes of heterocycle, due to their diverse range of biological properties like anticancer, anti-inflammatory, diuretic, anticonvulsant, and antihypertensive. Study has shown, functionalization of quinazolinone's amide N-H with alkyl, aryl groups increases the activity of quinazolinone motif.[17]In spite of that, till now heterocycles like indole, pyrrole and other cyclic amide have not been explored elaborately as functionality.[18] Thus, indolylquinazolinone product may possess some novel biological activity, which can be furtherexplored. So, in this letter we wish to report, a novel *N*-iodosuccinimide mediated protocol for direct C2 amidation of indole and pyrrole with cyclic amides like pyrimidone /quinazolinone derivatives.

## Results and discussion:

To develop a metal free condition for selective amidation in indole moiety, we began our study with the reaction of 3-methylindole (1a) 1.1 equiv. and quinazolinone (2a) 1.0 equiv. with an iodinating source *N*-iodosuccinimide (NIS) 1.2 equiv. in $CH_3CN$ solvent at room temperature. After 16 h, we were delighted to find the desired product 3-(3-methyl-1*H*-indol-2-yl)-3*H*-quinazolin-4-one (3a) in 30% yield. The relative structure of compound 3a was determined by detailed spectroscopic analysis and X-ray crystallographic study (Table 1). Next, to improve the yield of the desired product 3a, we have screened a variety of both polar and nonpolar solvents (entries 1-12). Polar solvents such as, $CH_3CN$, THF, DMSO, EtOAc (entries 1-4) gave only moderate yields of the desired product. Interestingly, when $CHCl_3$ was used as solvent, which is relatively nonpolar in nature, it gave 70% yield of 3a (entry 5).

Table 1. Screening of reaction parameters.[a]



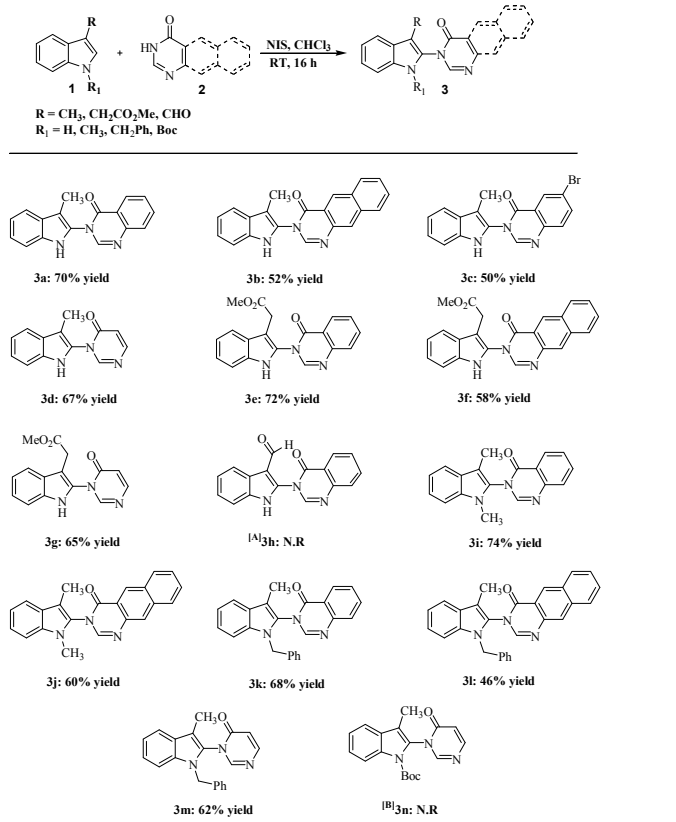

| Entry | Solvent | Reagent/ Catalyst | Co-catalyst [b] | Yields [c] **3** [%] |
|---|---|---|---|---|
| 1 | $CH_3CN$ | NIS | - | 30 |
| 2 | THF | NIS | - | 10 |
| 3 | DMSO | NIS | - | 40 |
| 4 | EtOAc | NIS | - | 58 |
| **5** | **$CHCl_3$** | **NIS** | - | **70** |
| 6 | Toluene | NIS | - | 15 |
| 7 | Benzene | NIS | - | 34 |
| 8 | p- xylene | NIS | - | 20 |
| 9 | DCM | NIS | - | 53 |
| 10 | DCE | NIS | - | 64 |
| 11 | 1,2 DCB | NIS | - | 42 |
| 12 | $H_2O$ | NIS | - | 40 |
| 13 | neat | NIS | - | 33 |
| 14 | $CHCl_3$ | NBS | - | 62 |
| 15 | $CHCl_3$ | $I_2$ | - | 67 |
| 16 | $CHCl_3$ | NIS | CuI | 62 |
| 17 | $CHCl_3$ | NIS | CuBr | 56 |
| 18 | $CHCl_3$ | NIS | DIB | 20 |
| 19 | $CHCl_3$ | NIS | KI | 30 |
| 20[d] | $CHCl_3$ | NIS | - | 70 |
| 21[e] | $CHCl_3$ | NIS | - | 20 |

[a] Unless otherwise specified, reaction was performed on 0.34 mmol scale with 1a (1.1 equiv.), 2 (1.0 equiv.), reagent (1.2 equiv.) and solvent 5 ml. The reaction time was 16 h. [b] Co-catalyst used 10 mol%. [c] Isolated yields. [d] NIS used 2 equiv. [e] NIS used 30 mol%.

As a result, we used nonpolar solvents like toluene, benzene, p-xylene but unfortunately they were inferior to $CHCl_3$ in terms of yields (entries 6-8). We assumed that chlorinated solvents might give a better yield compared to $CHCl_3$. Thus, we varied some chlorine contained solvents like DCM, DCE and 1, 2-dichlorobenzene (entries 9-11). Among them only DCE was able to give a maximum yield of 64%. On water and neat reaction conditions also failed to improve the yield (entries 12-13). Taking $CHCl_3$ as the optimized solvent, we varied other parameters. When *N*-bromosuccinimide (entry 14) was used instead of NIS, yield decreased, whereas in case of iodine (entry 15) yield remained almost unaffected. Further, screening of co-catlaysts like CuI, CuBr, DIB, KI in 10 mol%, led to no improvement of the reaction performance.

To verify the role of NIS, if it was catalytic or stoichiometric, we carried out two reactions, where NIS had been used in 2 equiv. (entry 20), and 30 mol% (entry 21). Use of catalytic amount of NIS decreased the yield of the product. Whereas, higher loading of NIS also failed to furnish more than 70% of the desired product.

**Scheme 1:** Synthesis of indolylquinazolinone derivatives[a]

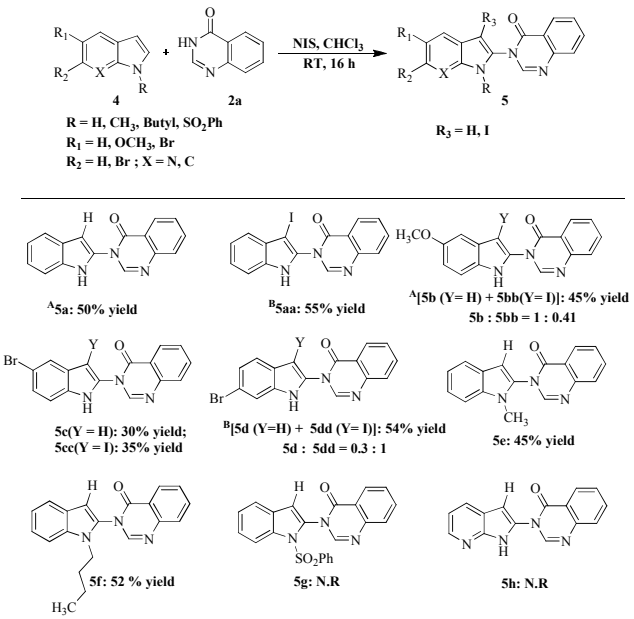



[a]unless otherwise specified, reaction was performed on 0.68 mmol scale with 1 (1.1 equiv.), 2 (1 equiv.), NIS (1.2 equiv.) in solvent 7 ml at RT. [A] Reaction time was 72 h. [B] Reaction time was 48 h. N.R = No Reaction

With the support of summarized results on table 1, reaction of 1.0 equiv. of quinazolinone 2a, with 1.1 equiv. of indole 1a, using NIS 1.2 equiv. in $CHCl_3$ solvent at RT for 16 h was deemed to provide optimum condition (entry 5). With these optimized condition in hand, the generality and scope of the reaction have been explored for a range of 3- substituted indole as well as 1,3 disubstituted indole with quinazolinone derivatives and pyrimidone (Scheme 1). A variety of functional groups such as moderate electron withdrawing and electron

releasing group in substituted indoles were well tolerated to give moderate to good yield of indolylquinazolinone and indolylpyrimidones products (**3a-n**). When electron donating substituents at indole C3 wascoupled with quinazolinone and pyrimidone, a good yield of the corresponding products were obtained (**3a, 3d**). But 6-bromoquinazolinone, benzoquinazolinone which are electron deficient, gave a lower yield of the products (**3b-c**).Whereas, when methyl was substituted with a moderate electron withdrawing group like $CH_2CO_2Me$, yields of the corresponding products remained almost unaffected (**3f-g**).

**Scheme 2:** Synthesis of 3-unsubstitued indolylquinazolinone derivatives[a]




[a]unless otherwise specified reaction was performed on 0.68 mmol scale with 4 (1.1 equiv.), 2a (1 equiv.), NIS (1.2 equiv.) in solvent 7 ml at RT. [A] 1.05 equiv. of NIS used, reaction time 16 h. [B] 1.7 equiv. of NIS used, reaction time 24 h.; N.R = No Reaction.

Surprisingly when aldehyde group was placed at C3 of indole, reaction did not proceed even after 3 days (**3h**). After examining electron donating as well as withdrawing groups in C3 position of indoles, we tested the feasibility of the reaction with 1,3-disubstituted indoles. We found that substituent like methyl, benzyl groups on nitrogen were well tolerated (**3i-m**). It is worth mentioning that, 1,3-dimethylindole gave a better yield with the corresponding indolylquinazolinone product compared to the 3-methylindole. When indole nitrogen was protected with an electron withdrawing group Boc, reaction did not proceed even after 48h (**3n**). It may be due to thelowering of nucleophilicity on the indole nitrogen which plays a vital role in iodination. Subsequently, we expanded the scope of the reaction with C3 unsubstitued indoles. Thus, we applied our optimized condition over plain indole and quinazolinone. The outcome of this reaction was not surprising, which gave the expected product **5a**, but along with that a lower percentage of 3-iodoindolylquinazolinone (**5aa**) was also obtained. We suspected that variation in the amount of NIS may give one of the products specifically. Thus, we took indole and quinazolinone as coupling product and used only 1.05 equiv. of NIS instead of 1.2 equiv. under the same optimized condition. After 16h we obtained 3-(1*H*-indol-2-yl)-3*H*-quinazolin-4-one (**5a**) specifically, whereas, when 1.7 equiv. of NIS was used, reaction gave only 3-(3-iodo-1*H*-indol-2-yl)-3*H*-quinazolin-4-one (**5aa**) specifically.

Furthermore, this reaction also tolerated 5 and 6-bromoindoles and 5-methoxyindole, affording the targeted product along with the undesired iodo substituted product. Yields of both the product were depended on the amount of NIS and time of reaction. The $^1$H NMR clearly showed the yield variation between the desired indolylquinazolinone and undesired 3-iodoindolylquinazolinone products. (See supporting information). Surprisingly, when 1-methylindole and 1-butylindoles was reacted with quinazolinone, we obtained only our desired products (**5f-g**), whereas 1-sulfonylindole and 7-azaindole were not active in this procedure. The reason behind this observation may be again justified by the lowering and increasing of the nucleophilicity of the indole nitrogen depending upon the electron withdrawing/ releasing group.

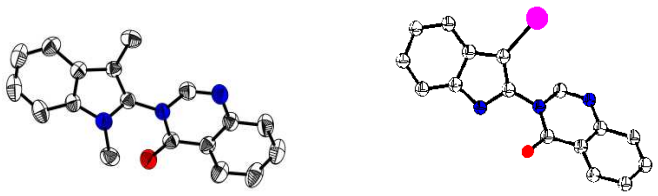
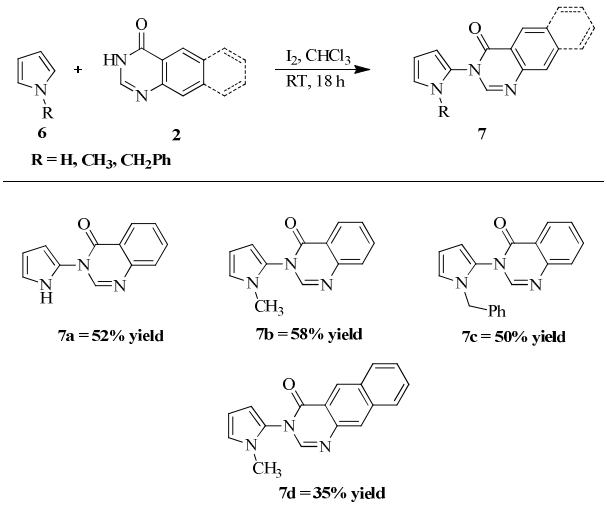


Figure 2. ORTEP of Compound 3i, 5aa (Hydrogens are removed for clarity)

After a successful encounter with indoles, we further extended the scope to pyrrole heterocycle. Since reports for regioselective C-N bond formation at pyrrole C2 were limited, we executed our optimized condition over pyrrole and quinazolinone moiety. Unfortunately, the reaction failed to give the desired pyrrolylquinazolinone product after 48 h of stirring at room temp. Next, we replaced NIS with granular iodine in our optimized condition. To our delight, we obtained 38% of the desired product after 12h.

**Scheme 3:** Synthesis of pyrrolylquinazolinone derivatives[a]

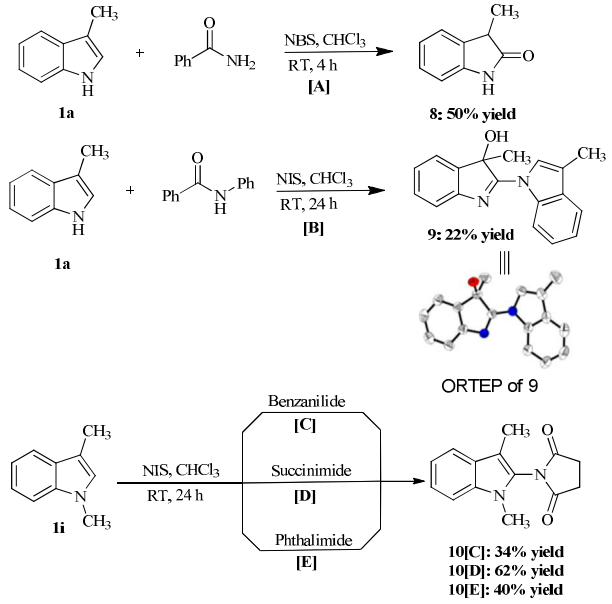



[a] Reaction was performed on 0.68 mmol scale with 6 (1.1 equiv.), 2 (1 equiv.), $I_2$ (1.3 equiv.) in solvent 7 ml at RT.

Hence, again we sought for an optimum condition with Iodine and different solvents, and it was obtained that iodine is the key component for this reaction to occur. The optimized conditions (1.1 equiv. of 6, 1.3 equiv of $I_2$, $CHCl_3$, RT, 18h) were found to be applicable over a range of N-substituted/ unsubstituted pyrrole and quinazolinone derivatives (Scheme 3). *N*-substituted/ unsustitued pyrroles reacted smoothly with quinazolinone derivatives to give corresponding pyrroloquinazolinone products (**7a-d**) in moderate.

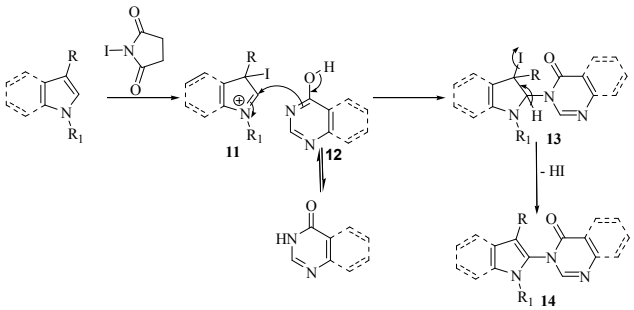
Furthermore, we were eager to see the outcome of the reaction when aliphatic amides/imides were employed as a coupling partner with 3-methylindole. Hence, we took 3-methylindole (1.1 equiv), benzamide (1.0 equiv.), NBS (1.1 equiv.) at room temperature in $CHCl_3$, after 4h an unexpected 3-methyl-1, 3-dihydro-indol-2-one (8) was formed in 50% yield (scheme 4, [A]). Next, 3-methylindole (1.1 equiv.) was treated with benzanilide (1.0 equiv.) and NIS (1.1 equiv.) in $CHCl_3$ again we obtained another undesired 3, 3'-dimethyl-3'*H*-[1, 2'] biindolyl-3'-ol product (**9**) in 22% yield after 24h. This unexpected compound (**9**)was fully characterized with NMR spectral data along with the X-ray crystallographic study. Synthesis of this kind of dimer is already reported in the literature using Co-salen complex in oxygen atmosphere.[19]It might be that indole nitrogen which is more nucleophilic in comparison with the nitrogen of benzanilide, which in turn led to the formation of this unexpected product (9). So we suspected that may be protection of the indole nitrogen would be able to furnish our expected coupled product. Thus we used the same reaction condition with 1,3-dimethylindole. Although this time we got a coupled product, but instead of benzanilide, succinimide coupled to the 1,3-dimethylindole (Scheme 4, [C]). The lower yield for the formation of 1-(1, 3-dimethyl-1*H*-indol-2-yl)-pyrrolidine-2, 5-dione (10) can be justified by the in situ formation of succinimide. Next, when succinimide was used as a starting material, the yield of the coupled product (10) was increased to 62% (Scheme 4, [D]), however use of phthalimide as a starting material also furnished only succinimide coupled product (10) (Scheme 4, [E]). This may be due to the iminol form rather than the amide form which is participating in the reaction as shown in mechanism (Scheme 5).

**Scheme 4:**Reaction between indole and aliphatic amide/imide




[A] 1a (0.98 mmol), benzamide (0.82 mmol) and NBS (0.98 mmol) in solvent at RT for 4 h. [B] 1a (0.51 mmol), benzanilide (0.51 mmol), NIS (0.61 mmol) in solvent at RT for 24 h. [C] 1i (0.35 mmol), benzanilide (0.35 mmol), NIS (0.35 mmol) in solvent at RT for 24 h. [D] 1i (1 mmol), succinimide (1 mmol), NIS (1 mmol) in solvent at RT for 24 h.[E] 1i (0.68 mmol), pthalimide (0.68 mmol), NIS (0.82 mmol) in solvent at RT for 24 h.

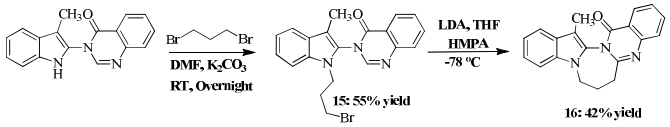
**Scheme 5.** Possible mechanism.




After all these extensive studies with a variety of substrate, and form the outcome we proposed a possible pathway of the reaction in Scheme 5. Iodination on C3 of indole with NIS produces the intermediate 11, which undergoes a immediate nucleophilic substitution with the iminol form (12) to generate

the intermediate 13. Then subsequent elimination of HI led to the expected product (14).

**Scheme 6:** Synthesis of the indolo [1,3]-diazepine skeleton




In the final part of our study, we synthesised an indolo [1,3]-diazepine skeleton fused with quinazolinone. Diazepines are very important class of heterocycles and huge applications are found in pharmaceutical industry. However among them maximum application is found with 1,4-diazepine. Whereas, 1,3-diazepine systems are very rarely known due to their biological activity. Some 1,3-diazepine fused heterocycles show anticancer, anti-AIDS activity and also inhibits HIV protease.[20] Thus, we synthesised a 1,3-diazpine containing novel indolylquinazolinone heterocycle, which may possess some interesting biological properties. We took compound 3a and treated with 1, 3 dibromopropane in presence of $K_2CO_3$ and DMF solvent at room temperature, which led to the 3-[1-(3-bromo-propyl)-3-methyl-1H-indol-2-yl]-3H-quinazolin-4-one (15). Next, treatment of compound 15 with LDA in presence of HMPA at -78 $^oC$ furnished the desired macrocyclic compound 16 in 42% yields.

**Conclusions:**

In summary, we have developed an efficient metal free methodology for direct amidation regioselectively at C2 in indole and pyrrole with quinazolinone and pyrimidone. A series of novel indolylquniazolinone/pyrimidone and pyrrolylquinazolinone were prepared with free or protected indoles and pyrroles. Further we prepared a highly functionalized 1,3-diazepine compound, which may contain useful biological properties.

**Experimental:**

**General experimental procedure for preparation of indolylquinazolinone:**

An oven dried schlenk tube was charged with indole or its derivative (**1,** 0.74 mmol), quinazolinone derivatives (**2**, 0.68 mmol), NIS (0.81 mmol) and distilled $CHCl_3$ (7 ml). The slung tube was then flushed with nitrogen. The reaction mixture was stirred at R.T for 16h.The reaction mixture was diluted with water, and aqueous phase was extracted with DCM (30 ml).The combined organic layer was dried over $Na_2SO_4$ and concentrated using a rotary evaporator under reduced pressure. The resulting residue was purified by column chromatography on silica gel (ethyl acetate/ hexanes = 3:7) to afford the desired product.

**3-(3-Methyl-1*H*-indol-2-yl)-4a, 8a-dihydro-3*H*-quinazolin-4-one (3a):** Compound was obtained as yellow solid (131 mg, 70%); m.p. = 222 $^oC$; IR (KBr) 3274, 2921, 2853, 1708, 1662, 1600, 1257, 1014, 738 $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO- $d_6$ ) δ 11.48 (1H, s), 8.40 (1H, s), 8.24 (1H, d, $J$ = 7.6 Hz), 7.93 (1H, t, $J$ = 7.2 Hz), 7.79 (1H, d, $J$ = 8.0 Hz), 7.64 (1H, t, $J$ = 7.2 Hz), 7.59 (1H, d, $J$ = 7.6 Hz), 7.38 (1H, d, $J$ = 8.0 Hz), 7.20 (1H, t, $J$ = 7.2 Hz), 7.09 (1H, t, $J$ = 7.2 Hz), 2.14 (3H, s); $^{13}C$ NMR (100 MHz, DMSO- $d_6$) δ 160.5, 147.9, 135.6, 134.3, 128.3, 128.0, 127.5, 127.0, 122.9, 122.1, 119.5, 119.5, 111.8, 106.4, 8.1; HRMS (ESI-MS) cald. for $C_{17}H_{13}N_3O$ (M+H) 276.1137, found 276.1139.

**3-(3-Methyl-1*H*-indol-2-yl)-4a, 10a-dihydro-3*H*-benzo[g]quinazolin-4-one (3b):**
Compound was obtained as pale yellow solid (115mg, 52%); m.p. = 228 $^oC$; IR (KBr) 3271, 2920, 1671, 1605, 1265, 739, 706 $cm^{-1}$; $^1H$ NMR (500 MHz, DMSO- $d_6$) δ 11.51 (1H, s), 9.00 (1H, s), 8.39 (1H, s), 8.38 (1H, s), 8.30 (1H, d, $J$ = 8.0 Hz), 8.20 (1H, d, $J$ = 8.5 Hz ), 7.76- 7.73 (1H, m), 7.68- 7.65 (1H, m), 7.61 (1H, d, $J$ = 7.5 Hz), 7.40 (1H, d, $J$ = 8.5 Hz), 7.24- 7.20 (1H, m), 7.13- 7.10 (1H, m), 2.18 (3H, s); $^{13}C$ NMR (125 MHz, DMSO- $d_6$) δ 160.9, 146.9, 143.3, 136.7, 134.3, 131.9, 129.9, 129.5, 128.8, 128.5, 128.2, 127.5, 127.4, 125.8, 122.9, 120.9, 119.5, 119.4, 111.8, 106.4, 8.1; HRMS (ESI-MS) cald. for $C_{21}H_{15}N_3O$ (M+H) 326.1293, found 326.1294.

**6-Bromo-3-(3-methyl-1*H*-indol-2-yl)-4a, 8a-dihydro-3*H*-quinazolin-4-one (3c):**
Compound was obtained as yellow solid (120 mg, 50%); m.p. = 220 $^oC$ ; IR (KBr) 3276, 2958, 1665, 1600, 1265, 832, 739 $cm^{-1}$;$^1H$ NMR (500 MHz, DMSO- $d_6$) δ 11.48 (1H, s), 8.47 (1H, s), 8.33 (1H, d, $J$ = 2.5 Hz ), 8.10 (1H, dd, $J$ = 8.5 Hz, $J$ = 2.5 Hz), 7.76 (1H, d, $J$ = 8.5 Hz), 7.60 (1H, d, $J$ = 8.0 Hz), 7.40 (1H, d, $J$ = 7.8 Hz), 7.23- 7.20 (1H, m), 7.12- 7.09 (1H, m), 2.15 (3H, s); $^{13}C$ NMR (125 MHz, DMSO- $d_6$) δ 159.4, 148.6, 147.0, 138.4, 134.3, 130.5, 129.0, 127.7, 127.4, 123.7, 123.1, 120.8, 119.6, 119.5, 111.9, 106.6, 8.1; HRMS (ESI-MS) cald. for $C_{17}H_{12}Br^{79}N_3O$ (M+H) 354.0242, found 354.0240; $C_{17}H_{12}Br^{81}N_3O$ (M+H) 356.0222, found 354.0219.

**3-(3-Methyl-1*H*-indol-2-yl)-3*H*-pyrimidin-4-one (3d):**
Compound was obtained as grayish solid (102 mg, 67%); m.p. = 138 $^oC$; IR (KBr) 3336, 3063, 1671, 1589, 1221, 991, 750 $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO- $d_6$) δ 11.50 (1H, s), 8.52 (1H, s), 8.04 (1H, dd, $J$ = 6.4 Hz, $J$ = 2.0 Hz), 7.58 (1H, d, $J$ = 8.0 Hz), 7.38 (1H, dd, $J$ = 8.0 Hz, $J$ = 0.8 Hz), 7.22- 7.18 (1H, m), 7.11- 7.07 (1H, m), 6.60 (1H, dd, $J$ = 6.0 Hz, $J$ = 0.8 Hz), 2.11 (3H, s); $^{13}C$ NMR (100 MHz, DMSO- $d_6$) δ 160.3, 154.3, 153.3, 134.3, 127.6, 127.4, 123.1, 119.6, 119.5, 116.2, 111.9, 106.2, 8.0; HRMS (ESI-MS) cald. for $C_{13}H_{11}N_3O$ (M+H) 226.0980, found 226.0980 .

**[2-(4-Oxo-4a, 8a-dihydro-4*H*-quinazolin-3-yl)-1*H*-indol-3-yl]-acetic acid methyl ester (3e):**
Compound was obtained as light yellow solid (163 mg, 72%); m.p = 102 $^oC$; IR (KBr) 3260, 2926, 1731, 1676, 1605, 1276, 975, 739 $cm^{-1}$; $^1H$ NMR (500 MHz, DMSO- $d_6$) δ 11.76 (1H, s), 8.35 (1H, s), 8.25 (1H, dd, $J$ = 8.0 Hz, $J$ = 1.0 Hz), 7.96- 7.92 (1H, m), 7.80 (1H, d, $J$ = 8.0 Hz), 7.67- 7.64 (1H, m), 7.62 (1H, d, $J$ = 8.0 Hz), 7.43 (1H, d, $J$ = 8.5 Hz), 7.26- 7.22 (1H, m), 7.14- 7.11 (1H, m), 3.72 (2H, s), 3.50 (3H, s); $^{13}C$ NMR (125

MHz, DMSO- $d_6$) δ 171.6, 160.4, 147.9, 147.6, 135.6, 134.1, 129.2, 128.3, 128.0, 127.0, 126.8, 123.2, 122.1, 120.0, 119.6, 112.1, 104.2, 52.1, 29.3; HRMS (ESI-MS) cald. for $C_{19}H_{15}N_3O_3$ (M+H) 334.1192, found 334.1187 .

**[2-(4-Oxo-4a, 10a-dihydro-4*H*-benzo[g]quinazolin-3-yl)-1*H*-indol-3-yl]-acetic acid methyl ester (3f):**
Compound was obtained as yellow solid (150 mg, 58%) ; m.p = 106 °C; IR (KBr) 3441, 3046, 1731, 1676, 1276, 745 $cm^{-1}$; 1H NMR (500 MHz, DMSO- $d_6$) δ 11.79 (1H, s), 9.00 (1H, s), 8.38 (1H, s), 8.32 (1H, s), 8.30 (1H, d, *J* = 8.0 Hz), 8.20 (1H, d, *J* = 8.5 Hz), 7.76- 7.73 (1H, m), 7.68- 7.62 (2H, m), 7.44 (1H, d, *J* = 8.0 Hz), 7.26- 7.23 (1H, m), 7.15- 7.12 (1H, m), 3.75 (2H, s), 3.50 (3H, s); $^{13}$C NMR (125 MHz, DMSO- $d_6$) δ 171.6, 160.9, 146.6, 143.2, 136.7, 134.1, 131.9, 129.9, 129.5, 129.4, 128.8, 128.5, 127.4, 126.9, 125.8, 123.1, 120.90, 119.99, 119.6, 112.1, 104.2, 52.1, 29.4; HRMS (ESI-MS) cald. for $C_{23}H_{17}N_3O_3$ (M+H) 384.1348, found 384.1349.

**[2-(6-Oxo-6*H*-pyrimidin-1-yl)-1*H*-indol-3-yl]-acetic acid methyl ester (3g):**
Compound was obtained as red solid (125mg, 65%); m.p.= 92 °C; IR (KBr) 3221, 2947, 1736, 1698, 1600, 1238, 827, 761 $cm^{-1}$; $^1$H NMR (400 MHz, DMSO- $d_6$) δ 11.78 (1H, s), 8.46 (1H, s), 8.03 (1H, dd, *J* = 8.8 Hz, *J* = 2.0 Hz), 7.60 (1H, d, *J* = 7.6 Hz), 7.40 (1H, d, *J* = 8.0 Hz), 7.22 (1H, t, *J* = 8.0 Hz), 7.11 (1H, t, *J* = 8.0 Hz), 6.58 (1H, d, *J* = 6.8 Hz), 3.65 (2H, s), 3.52 (3H, s); $^{13}$C NMR (100 MHz, DMSO- $d_6$) δ 171.5, 160.1, 154.2, 152.9, 134.1, 128.7, 126.7, 123.3, 120.0, 119.6, 116.2, 112.1, 103.9, 52.2, 29.3; HRMS (ESI-MS) cald. for $C_{15}H_{13}N_3O_3$ (M+H) 284.1035, found 284.1031.

**3-(1, 3-Dimethyl-1*H*-indol-2-yl)-4a, 8a-dihydro-3*H*-quinazolin-4-one (3i):**
Compound was obtained as yellow solid (145 mg, 74%); m.p. = 156 °C ; IR (KBr) 3068, 2920, 1693, 1605, 1249, 920, 750 $cm^{-1}$; $^1$H NMR (500 MHz, DMSO- $d_6$) δ 8.37 (1H, s), 8.26 (1H, dd, *J* = 8.0 Hz, *J* = 1.0 Hz), 7.98- 7.94 (1H, m), 7.82 (1H, d, *J* = 8.0 Hz), 7.68- 7.65 (1H, m), 7.64 (1H, d, *J* = 8.0 Hz), 7.52 (1H, d, *J* = 8.5 Hz), 7.31- 7.28 (1H, m), 7.15 (1H, t, *J* = 8.0 Hz), 3.54 (3H, s), 2.14 (3H, s); $^{13}$C NMR (125 MHz, DMSO- $d_6$) δ 160.8, 148.1, 147.9, 135.8, 135.3, 129.4, 128.4, 128.1, 127.1, 126.5, 123.2, 122.0, 119.8, 119.6, 110.4, 106.7, 29.6, 8.1; HRMS (ESI-MS) cald. for $C_{18}H_{15}N_3O$ (M+H) 290.1293 found 290.1291.

**3-(1, 3-Dimethyl-1*H*-indol-2-yl)-4a, 10a-dihydro-3*H*-benzo[g]quinazolin-4-one (3j):**
Compound was obtained as light yellow solid (137 mg, 60%); m.p. = 164 °C; IR (KBr) 3310, 2894, 1682, 1249, 942, 756 $cm^{-1}$; 1H NMR (400 MHz, DMSO- $d_6$) δ 8.99 (1H, s), 8.39 (1H, s), 8.31 (1H, s), 8.27 (1H, d, *J* = 8.4 Hz), 8.18 (1H, d, *J* = 8.4 Hz), 7.73 (1H, t, *J* = 7.6 Hz), 7.66- 7.62 (2H, m), 7.51 (1H, d, *J* = 8.4 Hz), 7.28 (1H, t, *J* = 7.6 Hz), 7.14 (1H, t, *J* = 7.2 Hz), 3.56 (3H, s), 2.16 (3H, s); $^{13}$C NMR (100 MHz, DMSO- $d_6$) δ 161.4, 146.9, 143.4, 136.8, 135.3, 131.9, 129.9, 129.6, 128.9, 128.5, 127.4, 126.5, 125.9, 123.1, 120.8, 119.8, 119.6, 110.4, 106.7, 29.6, 8.2; HRMS (ESI-MS) cald. for $C_{22}H_{17}N_3O$ (M+H) 340.1450, found 340.1450.

**3-(1-Benzyl-3-methyl-1*H*-indol-2-yl)-4a, 8a-dihydro-3*H*-quinazolin-4-one (3k):**
Compound was obtained as light grayish solid (169 mg, 68%); m.p. = 106 °C; IR (KBr) 3364, 3024, 2909, 1687, 1610, 1249, 920, 739 $cm^{-1}$; $^1$H NMR (500 MHz, DMSO- $d_6$) δ 8.23 (1H, d, *J* = 8.0 Hz), 8.14 (1H, s), 7.92 (1H, t, *J* = 7.5 Hz), 7.74 (1H, d, *J* = 8.0 Hz), 7.68 (1H, d, *J* = 8.0 Hz), 7.64 (1H, t, *J* = 7.5 Hz), 7.45 (1H, d, *J* = 8.0 Hz), 7.24 (1H, t, *J* = 7.5 Hz), 7.18- 7.14 (4H, m), 6.96- 6.94 (2H, m), 5.43 (1H, d, *J* = 17 Hz), 5.05 (1H, d, *J* = 17 Hz), 2.15 (3H, m). $^{13}$C NMR (125 MHz, DMSO- $d_6$) δ 160.8, 147.9, 147.7, 137.9, 135.7, 135.1, 129.2, 128.9, 128.4, 128.0, 127.7, 127.1, 126.9, 126.7, 123.5, 121.9, 120.1, 119.9, 110.9, 107.9, 46.6, 8.2; HRMS (ESI-MS) cald. for $C_{24}H_{19}N_3O$ (M+H) 366.1606, found 366.1606.

**3-(1-Benzyl-3-methyl-1*H*-indol-2-yl)-4a, 10a-dihydro-3*H*-benzo[g]quinazolin-4-one (3l):** Compound was obtained as light yellow solid (130 mg, 46%); m.p. = 130 °C; IR (KBr) 3052, 2920, 1687, 1600, 1265, 898, 750 $cm^{-1}$; $^1$H NMR (400 MHz, DMSO- $d_6$) δ 8.96 (1H, s), 8.31 (1H, s), 8.27 (1H, d, *J* = 8.4 Hz), 8.16 (1H, d, *J* = 8.4 Hz), 8.08 (1H, s), 7.72 (1H, t, *J* = 7.2 Hz), 7.68- 7.62 (2H, m), 7.45 (1H, d, *J* = 8.0 Hz), 7.30 (1H, d, *J* = 6.4 Hz), 7.24 (1H, t, *J* = 7.6 Hz), 7.17- 7.14 (3H, m), 6.99- 6.96 (2H, m), 5.45 (1H, d, *J* = 16.8 Hz), 5.09 (1H, d, *J* = 16.8 Hz), 2.17 (3H, s); $^{13}$C NMR (100 MHz, DMSO- $d_6$) δ 161.3, 146.6, 143.2, 138.1, 136.7, 135.1, 131.9, 129.9, 129.5, 129.3, 129.1, 128.9, 128.4, 127.7, 127.6, 127.4, 126.9, 126.8, 125.8, 123.4, 120.7, 120.0, 119.8, 110.9, 107.9, 46.61, 8.2; HRMS (ESI-MS) cald. for $C_{28}H_{21}N_3O$ (M+H) 416.1763, found 416.1764.

**3-(1-Benzyl-3-methyl-1*H*-indol-2-yl)-3*H*-pyrimidin-4-one (3m):**
Compound was obtained as yellow solid (132 mg, 62%); m.p. = 102 °C; IR (KBr) 3079, 2915, 1731, 1698, 1282, 843, 739 $cm^{-1}$; $^1$H NMR (400 MHz, DMSO- $d_6$) δ 8.22 (1H, s), 7.99 (1H, d, *J* = 6.8 Hz), 7.66 (1H, d, *J* = 7.6 Hz), 7.48 (1H, d, *J* = 8.0 Hz), 7.26- 7.13 (5H, m), 6.97-6.95 (2H, m), 6.59 (1H, dd, *J* = 6.8 Hz, *J* = 0.8 Hz), 5.43 (1H, d, *J* = 16.4 Hz), 4.94 (1H, d, *J* = 16.8 Hz), 2.11 (3H, s); $^{13}$C NMR (100 MHz, DMSO- $d_6$) δ 160.5, 154.4, 153.3, 137.8, 135.2, 129.0, 128.8, 127.8, 126.9, 126.6, 123.6, 120.1, 119.9, 116.3, 110.8, 107.7, 46.6, 8.1; HRMS (ESI-MS) cald. for $C_{20}H_{17}N_3O$ (M+H) 316.1450, found 316.1451.

**3-(1*H*-Indol-2-yl)-3*H*-quinazolin-4-one (5a):** Compound was obtained as yellow solid (89 mg, 50%); m.p. = 140 °C; IR (KBr) 3276, 2920, 1660, 1600, 1265, 1008, 734 $cm^{-1}$; $^1$H NMR (400 MHz, DMSO- $d_6$) δ 11.81 (1H, s), 8.49 (1H, s), 8.23 (1H, d, *J* = 8.0 Hz), 7.92- 7.88 (1H, m), 7.77 (1H, d, *J* = 8.0 Hz), 7.63 (2H, t, *J* = 8.0 Hz), 7.46 (1H, d, *J* = 8.0 Hz), 7.20 (1H, t, *J* = 8.0 Hz), 7.09 (1H, t, *J* = 8.0 Hz), 6.69 (1H, s); $^{13}$C NMR (100 MHz, DMSO- $d_6$) δ 160.3, 147.7, 147.4, 135.6, 134.9, 131.9, 128.3, 127.9, 126.9, 122.7, 121.9, 120.9, 120.2, 112.1, 98.1; HRMS (ESI-MS) cald. for $C_{16}H_{11}N_3O$ (M+H) 262.0980, found 262.0981.

**3-(3-Iodo-1*H*-indol-2-yl)-3*H*-quinazolin-4-one (5aa)**
Compound was obtained as bright yellow solid; (144 mg, 55%); m.p. = 205 °C; IR (KBr) 3342, 3063, 1682, 1254, 904, 767 $cm^{-1}$; $^1$H NMR (400 MHz, DMSO- $d_6$) δ 12.34 (1H, s), 8.42 (1H, s), 8.26 (1H, d, *J* = 8.0 Hz), 7.96 (1H, t, *J* = 8.0 Hz), 7.81 (1H, d, *J* = 8.0 Hz), 7.67 (1H, t, *J* = 7.2 Hz), 7.48 (1H, d, *J* = 8.0 Hz), 7.39 (1H, d, *J* = 7.6 Hz), 7.30 (1H, t, *J* = 7.2 Hz), 7.21 (1H, t, *J* = 7.6 Hz); $^{13}$C NMR (100 MHz, DMSO- $d_6$) δ 160.2, 147.9, 147.8, 136.0, 135.3, 133.2, 129.3, 128.6, 128.2, 127.1, 124.2, 121.8, 121.2, 121.1, 112.8, 58.8; HRMS (ESI-MS) cald. for $C_{16}H_{10}IN_3O$ (M+H) 387.9947, found 387.9946.

**3-(5-Methoxy-1*H*-indol-2-yl)-3*H*-quinazolin-4-one (5b)**
**3-(3-Iodo-5-methoxy-1*H*-indol-2-yl)-3*H*-quinazolin-4-one (5bb)**
Compounds were obtained as bright yellow solid mixture with ratio of (5b:5bb = 1:0.41); (overall 108 mg, 45%); IR (KBr) 3358, 3260, 2991, 2926, 1682, 1654, 1254, 1210, 767, 690 $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO- $d_6$) δ 12.20 (0.396H, s), 11.62 (1.00H, s), 8.46 (1.040H, s), 8.38 (0.443H, s), 8.25- 8.23 (1.428H, m), 7.97- 7.89 (1.433H, m), 7.82- 7.76 (1.390H, m), 7.68- 7.61 (1.392H, m), 7.39- 7.32 (1.459H, m), 7.102 (1.063H, s), 6.94- 6.92 (0.446H, m), 6.84- 6.82 (1.387H, m), 6.59 (0.978H, s), 3.81 (1.184H, s), 3.76 (2.961H, s); $^{13}C$ NMR (100 MHz, DMSO- $d_6$) δ 160.3, 155.0, 154.2, 147.7, 147.4, 135.6, 132.1, 129.9, 128.4, 127.9, 127.4, 126.9, 121.9, 113.0, 112.9, 102.5, 97.9, 55.8; HRMS (ESI-MS) cald. for **5b** $C_{17}H_{13}N_3O_2$ (M+H) 292.1086, found 292.1079; for **5bb** $C_{17}H_{12}IN_3O_2$ (M+H) 418.0052, found 418.0051.

**3-(5-Bromo-1*H*-indol-2-yl)-3*H*-quinazolin-4-one (5c):**
Compound was obtained as bright yellow solid (70 mg, 30%); m.p. = 188 $^oC$; IR (KBr) 3221, 2926, 1682, 1654, 904, 772 $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO- $d_6$) δ 12.03 (1H, s), 8.48 (1H, s), 8.25 (1H, d, $J$ = 8.0 Hz), 7.92 (1H, t, $J$ = 7.6 Hz), 7.81 (1H, s), 7.77 (1H, d, $J$ = 8.0 Hz), 7.64 (1H, t, $J$ = 7.6 Hz), 7.42 (1H, d, $J$ = 8.8 Hz), 7.30 (1H, d, $J$ = 8.8 Hz), 6.69 (1H, s); $^{13}C$ NMR (100 MHz, DMSO- $d_6$) δ 160.2, 147.7, 147.2, 135.7, 133.5, 133.2, 128.8, 128.4, 128.0, 126.9, 125.3, 123.2, 121.8, 114.2, 112.6, 97.7; HRMS (ESI-MS) cald. for $C_{16}H_{10}Br^{79}N_3O$ (M+H) 340.0085, found 340.0082; $C_{16}H_{10}Br^{81}N_3O$ (M+H) 342.0065, found 342.0085.
**3-(5-Bromo-3-iodo-1*H*-indol-2-yl)-3*H*-quinazolin-4-one (5cc):** Compound was obtained as bright yellow solid (111 mg, 35%); m.p. = 218 $^0C$; IR (KBr) 3407, 2932, 1675, 1601, 1455, 1008, 938 $cm^{-1}$; $^1H$ NMR (500 MHz, DMSO- $d_6$) δ 12.59 (1H, s), 8.43 (1H, s), 8.26 (1H, dd, $J$ = 8.0 Hz, $J$ = 1.0 Hz), 7.99- 7.95 (1H, m), 7.82 (1H, d, $J$ = 8.0 Hz), 7.68 (1H, t, $J$ = 8.0 Hz), 7.55 (1H, d, $J$ = 1.5 Hz), 7.49 (1H, d, $J$ = 9.0 Hz), 7.43 (1H, dd, $J$ = 8.5 Hz, $J$ = 2.0 Hz); $^{13}C$ NMR (100 MHz, DMSO- $d_6$) δ 160.1, 147.8, 147.5, 136.1, 134.5, 134.1, 131.1, 128.7, 128.2, 127.1, 126.9, 123.2, 121.7, 115.0, 113.6, 58.1; HRMS (ESI-MS) cald. for $C_{16}H_9Br^{79}IN_3O$ (M+H) 465.9052, found 465.9049, $C_{16}H_9Br^{81}IN_3O$ (M+H) 467.9031, found 467.9028.

**3-(6-Bromo-1*H*-indol-2-yl)-3*H*-quinazolin-4-one (5d)**
**3-(6-Bromo-3-iodo-1*H*-indol-2-yl)-3*H*-quinazolin-4-one (5dd):**
Compounds were obtained as bright yellow solid mixture with ratio of (5d: 5dd = 0.3:1); (overall 160 mg, 54%); IR (KBr) 3342, 2915, 1676, 1610, 1413, 1260, 772, 701 $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO- $d_6$) δ 12.48 (1H,s), 11.96 (0.304H, s), 8.49 (0.326H, s), 8.41 (0.994H, s), 8.26-8.24 (1.35H, m), 7.98- 7.90 (1.48H, m), 7.82- 7.76 (1.356H, m), 7.72 (1.048H, s), 7.68- 7.62 (1.672H, m), 7.59- 7.57 (0.334H, m), 7.35 (2.14H, s), 7.22- 7.20 (0.346H, m), 6.73 (0.298H, s); $^{13}C$ NMR (100 MHz, DMSO- $d_6$) δ 160.1, 147.9, 147.5, 147.2, 136.0, 135.9, 135.7, 134.0, 128.6, 128.4, 128.2, 127.9, 127.0, 125.9, 124.2, 123.0, 121.8, 116.8, 115.3, 114.6, 98.2, 59.1; HRMS (ESI-MS) cald. for **5d** $C_{16}H_{10}Br^{79}N_3O$ (M+H) 340.0085, found 340.0075; $C_{16}H_{10}Br^{81}N_3O$ (M+H) 342.0065, found 342.0056, for **5dd** $C_{16}H_9Br^{79}IN_3O$ (M+H) 465.9052, found 465.9049; $C_{16}H_9Br^{81}IN_3O$ (M+H) 467.9031, found 467.9029,

**3-(1-Methyl-1*H*-indol-2-yl)-3*H*-quinazolin-4-one (5e):**
Compound was obtained as red solid (84 mg, 45%); m.p. = 178 $^oC$; IR (KBr) 3106, 2920, 1676, 1600, 1238, 810, 772 $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO- $d_6$) δ 8.37 (1H, s), 8.24 (1H, d, $J$ = 7.6 Hz), 7.93 (1H, t, $J$ = 8.0 Hz), 7.79 (1H, d, $J$ = 8.0 Hz), 7.66-7.63 (2H, m), 7.54 (1H, d, $J$ = 8.4 Hz), 7.28 (1H, t, $J$ = 7.6 Hz), 7.14 (1H, t, $J$ = 7.6 Hz), 6.72 (1H, s), 3.56 (3H, s); $^{13}C$ NMR (100 MHz, DMSO- $d_6$) δ 160.9, 148.1, 147.9, 135.9, 135.7, 133.0, 128.4, 128.0, 127.1, 126.1, 122.9, 121.9, 121.3, 120.4, 110.7, 99.6, 29.8; HRMS (ESI-MS) cald. for $C_{17}H_{13}N_3O$ (M+Na) 298.0956, found 298.0960.

**3-(1-Butyl-1*H*-indol-2-yl)-3*H*-quinazolin-4-one (5f):**
Compound was obtained as red solid; (112 mg, 52%); m.p. = 170 $^oC$; IR (KBr) 3025, 2920, 1670, 1600, 1310, 926, 701 $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO- $d_6$) δ 8.42 (1H, s), 8.24 (1H, d, $J$ = 7.6 Hz), 7.96- 7.92 (1H, m), 7.80 (1H, d, $J$ = 8.0 Hz), 7.67- 7.63 (2H, m), 7.56 (1H, d, $J$ = 8.0 Hz), 7.27 (1H, t, $J$ = 7.2 Hz), 7.13 (1H, t, $J$ = 7.6 Hz), 6.71 (1H, s), 4.06 (1H, s), 3.86 (1H, s), 1.57 (2H, s), 1.13 (2H, s), 0.71 (3H, t, $J$ = 7.6 Hz); $^{13}C$ NMR (100 MHz, DMSO- $d_6$) δ 160.9, 147.9, 135.8, 135.3, 132.4, 128.5, 128.1, 127.1, 126.3, 123.0, 121.9, 121.4, 120.4, 110.9, 100.2, 42.8, 31.9, 19.8, 13.9; HRMS (ESI-MS) cald. for $C_{20}H_{19}N_3O$ (M+H) 318.1606, found 318.1606.

**3-(1*H*-Pyrrol-2-yl)-3*H*-quinazolin-4-one (7a):**
Compound was obtained as yellow semisolid (74 mg, 52%); IR (KBr) 3043, 2934, 1675, 1420, 863 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 10.01 (1H, s), 8.34 (1H, s), 8.29 (1H, d, $J$ = 8.0 Hz), 7.80- 7.72 (2H, m), 7.54- 7.50 (1H, m), 6.84- 6.82 (1H, m), 6.29- 6.27 (1H, m), 6.26- 6.25 (1H, m); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 160.8, 147.0, 144.6, 134.7, 127.9, 127.7, 126.9, 126.4, 121.8, 116.8, 108.1, 100.4; HRMS (ESI-MS) cald. for $C_{12}H_9N_3O$ (M+H) 212.0824, found 212.0830.
**3-(1-Methyl-1*H*-pyrrol-2-yl)-3*H*-quinazolin-4-one (7b)**: Compound was obtained as yellow solid (88 mg, 58%); m.p. = 112 $^oC$; IR (KBr) 3117, 3073, 1687, 1600, 1320, 772 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 8.38 (1H, d, $J$ = 7.6 Hz), 8.10 (1H, s), 7.84- 7.78 (2H, m), 7.58 (1H, t, $J$ = 7.6 Hz), 6.74 (1H, s), 6.232- 6.226 (2H, m), 3.50 (3H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 161.2, 147.7, 147.2, 134.9, 127.9, 127.6, 127.3, 125.3, 122.2, 121.9, 107.4, 106.3, 33.5; HRMS (ESI-MS) cald. for $C_{13}H_{11}N_3O$ (M+H) 226.0980, found 226.0979.

**3-(1-Benzyl-1*H*-pyrrol-2-yl)-3*H*-quinazolin-4-one (7c):**
Compound was obtained as yellow solid (102 mg, 50%); m.p. = 178 $^oC$; IR (KBr) 3603, 2920, 1693, 1610, 1276, 723 $cm^{-1}$ ; $^1H$ NMR (400 MHz, $CDCl_3$) δ 8.36 (1H, d, $J$ = 8.0 Hz), 7.79 (1H, t, $J$ = 7.2 Hz), 7.69 (1H, d, $J$ = 8.0 Hz), 7.65 (1H, s), 7.56 (1H, t, $J$ = 8.0 Hz), 7.22- 7.21 (3H, m), 7.00- 6.96 (2H, m), 6.82 (1H, s), 6.30- 6.28 (1H, m), 6.25- 6.24 (1H, m), 5.00- 4.92 (2H, m); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 161.4, 147.7, 147.1, 136.8, 134.8, 128.8, 128.0, 127.7, 127.6, 127.2, 127.0, 125.2, 122.0, 121.9, 107.7, 107.1, 50.9; HRMS (ESI-MS) cald. for $C_{19}H_{15}N_3O$ (M+H) 302.1293, found 302.1293.

**3-(1-Methyl-1*H*-pyrrol-2-yl)-3*H*-benzo[g]quinazolin-4-one (7d):** Compound was obtained as yellow solid (65 mg, 35%); m.p. = 152 $^oC$; IR (KBr) 2958, 2926, 1682, 1605, 1265, 756 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 8.98 (1H, s), 8.26 (1H, s), 8.10- 8.02 (3H, m), 7.67 (1H, t, $J$ = 6.8 Hz), 7.60 (1H, t, $J$ = 7.2 Hz), 6.76- 6.75 (1H, m), 6.26- 6.24 (2H, m), 3.53 (3H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 161.8, 146.2, 143.0, 136.7, 131.9, 129.5, 129.1, 128.9, 128.2, 126.9, 125.8, 125.5, 122.0, 120.4,

107.4, 106.2, 33.4; HRMS (ESI-MS) cald. for $C_{17}H_{13}N_3O$ (M+H) 276.1137, found 276.1138.

**3-Methyl-1,3-dihydro-indol-2-one (8)** [21] :
This compound was verified by the literature values.

**3, 3'-Dimethyl-3'*H*-[1, 2'] biindolyl-3'-ol (9):**
Compound was obtained as yellow solid (31mg, 22%); m.p. = 174 $^oC$; IR (KBr) 3347, 3052, 1791, 1561, 1205, 942, 745 $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO- $d_6$) δ 8.78 (1H, d, $J$ = 8.0 Hz), 8.06 (1H, s), 7.60 (1H, d, $J$ = 7.6 Hz), 7.44- 7.28 (5H, m), 7.16 (1H, t, $J$ = 7.6 Hz), 6.68 (1H, s), 2.31 (3H, s), 1.65 (3H, s); $^{13}C$ NMR (100 MHz, DMSO- $d_6$) δ 170.9, 151.9, 140.9, 135.9, 130.90, 129.7, 124.9, 124.6, 123.2, 122.1, 119.3, 117.1, 116.6, 81.9, 26.3, 9.9; HRMS (ESI-MS) cald. for $C_{18}H_{16}N_2O$ (M+H) 277.1341, found 277.1344.

**1-(1, 3-Dimethyl-1*H*-indol-2-yl)-pyrrolidine-2, 5-dione (10):**
Compound was obtained as yellow solid; m.p. = 178 $^oC$; IR (KBr) 2926, 2367, 1720, 1479, 1167, 750 $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO- $d_6$) δ 7.54 (1H, d, $J$ = 8.0 Hz), 7.41 (1H, d, $J$ = 8.0 Hz), 7.22 (1H, t, $J$ = 7.2 Hz), 7.08 (1H, t, $J$ = 7.2 Hz), 3.48 (3H, s), 2.94 (4H, s), 2.05 (3H, s); $^{13}C$ NMR (100 MHz, DMSO- $d_6$) δ 177.4, 135.4, 126.6, 124.5, 122.7, 119.5, 119.3, 110.2, 107.2, 29.5, 29.2, 8.4; HRMS (ESI-MS) cald. for $C_{14}H_{14}N_2O_2$ (M+H) 243.1134, found 243.1133.

**3-[1-(3-Bromo-propyl)-3-methyl-1*H*-indol-2-yl]-3*H*-quinazolin-4-one (15):**
In to the reaction mixture of 3-(3-Methyl-1*H*-indol-2-yl)-4a, 8a-dihydro-3*H*-quinazolin-4-one **(3a)** (0.100 g, 0.36 mmol) in dry DMF solvent 5 mL, $K_2CO_3$ (0.100 g, 0.72 mmol) was added and stirred at R.T for 1h. Then 1, 3 dibromopropane (0.109 g, 0.54 mmol) was added to the reaction mixture drop wise and stirred at R.T for another 5 h. Then the reaction mixture was extracted with EtOAc, dried over $Na_2SO_4$ and evaporated in vacuum. The residue was purified by column chromatography on silica gel (EtOAc: hexanes = 1:9) to afford the desired product **(15)** (78 mg; 55% yield).This compound was obtained as yellow sticky semisolid with little inseparable impurities ; IR (KBr) 3052, 2920, 1693, 1610, 1276, 920 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$) δ 8.42 (1H, d, $J$ = 7.5 Hz), 8.025 (1H, s), 7.89-7.84 (2H, m), 7.67 (1H, d, $J$ = 8.0 Hz), 7.63 (1H, t, $J$ = 7.5 Hz), 7.46 (1H, d, $J$ = 8.0 Hz), 7.38- 7.35 (1H, m), 7.24 (1H, t, $J$ = 7.5 Hz), 4.24- 4.10 (2H, m), 3.39- 3.29 (2H, m), 2.33- 2.23 (2H, m), 2.24 (3H, s); $^{13}C$ NMR (125 MHz, $CDCl_3$) δ 161.1, 147.9, 146.6, 135.1, 133.2, 128.1, 127.9, 127.4, 126.9, 123.5, 122.2, 120.0, 119.8, 117.0, 109.8, 108.5, 41.4, 32.4, 30.5, 8.1; HRMS (ESI-MS) cald. for $C_{20}H_{18}Br^{79}N_3O$ (M+H) 396.0711, found 396.0711; $C_{20}H_{18}Br^{81}N_3O$ (M+H) 398.0691, found 398.0693.

**14-methyl-7,8-dihydroindolo[2',1':2,3][1,3]diazepino[7,1-b]quinazolin-16(6*H*)-one (16):**
To a freshly prepared solution of LDA (0.054 g, 0.50 mmol) in anhydrous THF (8 ml) at -78 $^0C$ under nitrogen atmosphere, a solution of 3-[1-(3-Bromo-propyl)-3-methyl-1*H*-indol-2-yl]-3*H*-quinazolin-4-one **(15)** (0.100 g, 0.25 mmol) in THF and HMPA (0.180g, 1.00 mmol) was added dropwise. The reaction mixture was stirred for another 3 h at -78 $^0C$, followed by additional 2 h at R.T. Then the reaction mixture was quenched with saturated solution of $NH_4Cl$ and extracted with EtOAc. The solvent was dried over $Na_2SO_4$ and evaporated in vacuum. The residue was purified by column chromatography on silica gel (EtOAc: hexanes = 3:7) to afford the desired product **16** (55 mg, 42% yield). This compound was obtained as yellow solid; m.p. = 158 $^oC$; IR (KBr) 3046, 2958, 2920, 1693, 1605, 1457, 1260, 739 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$ + DMSO- $d_6$) δ 8.22 (1H, d, $J$ = 8.0 Hz), 7.89 (1H, t, $J$ = 7.2 Hz), 7.72 (1H, d, $J$ = 8.0 Hz), 7.63- 7.56 (3H, m), 7.23 (1H, t, $J$ = 7.6 Hz), 7.11 (1H, t, $J$ = 7.2 Hz), 4.62- 4.57 (1H, m), 4.02- 3.95 (1H, m), 2.78- 2.74 (1H, m), 2.25- 2.17 (3H, m), 2.11 (3H, s); $^{13}C$ NMR (100 MHz, $CDCl_3$ + DMSO- $d_6$) δ 159.6, 156.1, 147.4, 135.4, 133.5, 127.9, 127.6, 127.6, 127.3, 127.0, 122.7, 121.0, 119.8, 119.4, 110.0, 106.2, 39.0, 32.9, 27.6, 9.4; HRMS (ESI-MS) cald. for $C_{20}H_{17}N_3O$ (M+H) 316.1450, found 316.1448.

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## Notes and references

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22. Molecular formula: $C_{17}H_{13}N_3O_1$, unit cell parameters: a=10.830(3), b=12.205(3), c=12.209(3)Å, $\alpha$= 102.677(4)$^o$, $\beta$= 106.686(4)$^o$, $\gamma$= 110.923(4)$^o$ and space group P -1. CCDC 956412 contains the supplementary crystallographic data for compound 3a of this paper. Molecular formula: $C_{18}H_{15}N_3O_1$, unit cell parameters: a=8.3989(18), b=12.9656(14), c=13.6993(18)Å, $\beta$= 101.702(16)$^o$ and space group P 21/n. CCDC 956410 contains the supplementary crystallographic data for compound 3i of this paper. Molecular formula: $C_{16}H_{10}I_1N_3O_1$, unit cell parameters: a=13.0741(18), b=4.2988(4), c=24.974(3)Å, $\beta$= 100.040(11)$^o$ and space group P 21/n. CCDC 956409 contains the supplementary crystallographic data for compound 5aa of this paper. Molecular formula: $C_{18}H_{16}N_2O_1$, unit cell parameters: a=10.8278(7), b=11.3669(8), c=13.0687(6)Å, $\alpha$= 100.716(5)$^o$, $\beta$= 106.227(5)$^o$, $\gamma$= 104.477(6)$^o$ and space group P -1. CCDC 956411 contains the supplementary crystallographic data for compound 9 of this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.