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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 indoles and pyrroles with quinazolinone and pyrimidone derivatives in intermolecular fashion, which led to novel indolyl/pyrrolyl quinazolinone and pyrimidone derivatives in moderate to good yields.

Introduction

Indole[1] and pyrrole[2] structural motifs are considered as 'privileged' skeletons in numerous biologically active natural products. Hence, there is continual interest among chemists for the direct functionalization of indoles and pyrroles in regioselective fashion.[3] A large number of reports by various groups have focused on forming C–C bonds regioselectively at C2 position of indole[4] as well as pyrrole;[5] however, only few reports are available on formation of C–N bond at the C2 position. In most cases, regioselective amination of indole has been achieved by using metal or other harsh conditions by different research groups.[6] However, reports for C2 amination by using mild conditions without metal are scarce. Recently, Huang's group demonstrated C–N bond formation at indole C2 with azole in the presence of iodine.[7] However, regioselective amidation of indole and pyrrole has always remained a challenge to the scientific community. 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 the C2 position of indole.[10] Very recently, Li's group presented direct amidation on indole by using the CDC process.[11] However, to date, reports for metal-free direct amidation at indole C2 are limited. In 2008, Baran's group reported a C2 amidation in indole in an intramolecular fashion to synthesize psychotrimine.[12] Very recently, Ji and coworkers also reported intramolecular amidation at the indole C2 with sulphonamides.[13] Liang's group also described iodine-mediated intermolecular amidation of N-protected indoles with tosylbenzenamine.[14] However, to the best of our knowledge, there is no report for metal-free direct C2 amidation of indole with cyclic amides in an intermolecular manner to date. Numerous biologically active natural products contain C–N amide linkage at the C2 position of indole, such as asperazine and chetomin (Fig. 1). Most of these natural products contain cyclic amide linkage, but direct amidation with cyclic amides at the C2 position of indole still remains unexplored.

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

Results and discussion

To develop a metal-free condition for selective amidation in an indole moiety, we began our study with the reaction of 3-methylindole (**1a**; 1.1 equiv.) and quinazolinone (**2a**; 1.0 equiv.) with an iodination source such as *N*-iodosuccinimide (NIS; 1.2

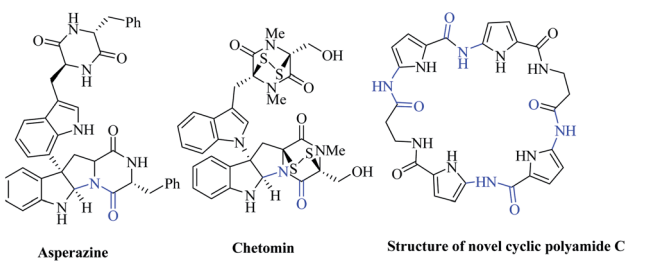

Fig. 1 Naturally occurring indole and pyrrole alkaloids containing C–N amide linkage.

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† Electronic supplementary information (ESI) available: Copies of ^{1}H NMR and ^{13}C NMR spectra and crystal data. CCDC 956409–956412. For ESI and crystallographic data in CIF or other electronic format See DOI: 10.1039/c4ra02417f

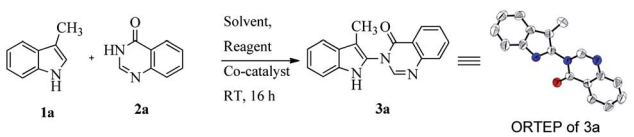
equiv.) in CH_3CN solvent at room temperature. After 16 h, we were delighted to find the desired product 3-(3-methyl-1*H*-indol-2-yl)-3*H*-quinazolin-4-one (**3a**) in 30% yield. The relative structure of compound **3a** was determined by detailed spectroscopic analysis and X-ray crystallographic study (Table 1). Next, to improve the yield of the desired product **3a**, we screened a variety of both polar and nonpolar solvents (entries 1–12). Polar solvents such as CH_3CN, THF, DMSO and EtOAc (entries 1–4) gave only moderate yields of the desired product. Interestingly, when $CHCl_3$ was used as the solvent, which is relatively nonpolar in nature, the yield of **3a** was 70% (entry 5).

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). Therefore, we assumed that chlorinated solvents might give a better yield compared with $CHCl_3$. Thus, we used some chlorine-containing solvents like DCM, DCE and 1,2-dichlorobenzene (entries 9–11); however, among them, only DCE was able to give a maximum yield of 64%. Moreover, using water and neat-reaction conditions also failed to improve the yield (entries 12–13). Thus, considering $CHCl_3$ as the optimized solvent, we varied other parameters. When *N*-bromosuccinimide (entry 14) was used instead of NIS, the yield decreased, whereas in the case of iodine (entry 15), the yield remained almost unaffected. Furthermore, the screening of co-catalysts like CuI, CuBr, DIB, KI in 10 mol%, led to no improvement of the reaction performance.

To verify the role of NIS, *i.e.*, whether it was catalytic or stoichiometric, we carried out two reactions, in which NIS had been used in 2 equiv. (entry 20) and 30 mol% (entry 21). The use of catalytic amounts of NIS decreased the yield of the product, whereas higher loading of NIS failed to furnish more than 70% of the desired product.

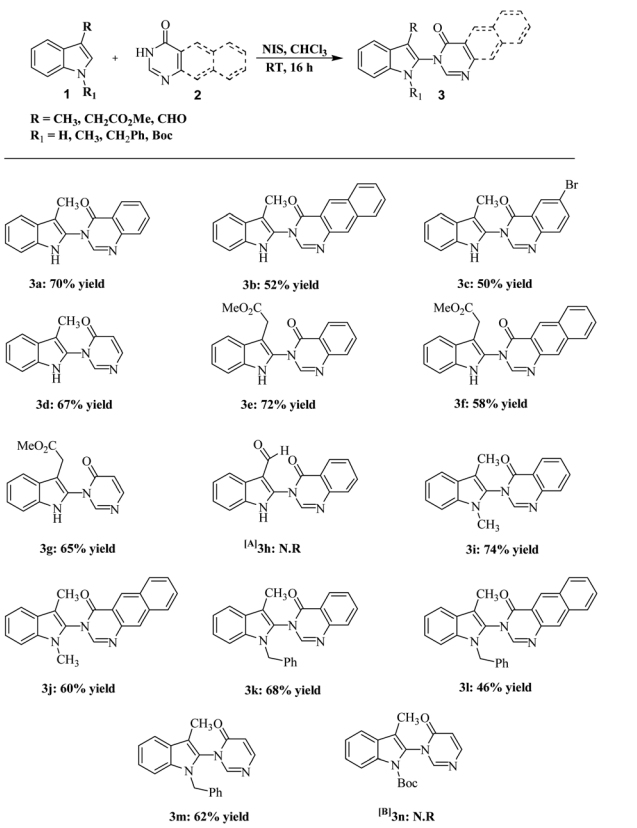
From the summarized results in Table 1, the reaction of 1.0 equiv. of quinazolinone **2a**, with 1.1 equiv. of indole **1a**, using 1.2 equiv. of NIS in $CHCl_3$ solvent at RT for 16 h was deemed to be the optimum condition (entry 5). With these optimized conditions in hand, the generality and scope of the reaction was 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 groups in substituted indoles were well tolerated to give moderate to good yield of indolylquinazolinone and indolylpyrimidone products (**3a–n**). When electron-donating substituents at indole C3 were coupled with quinazolinones and pyrimidones, a good yield of the corresponding products was obtained (**3a,d**). However, 6-bromoquinazolinone and benzoquinazolinone, which are electron deficient, gave a lower yield of the product (**3b–c**), whereas when methyl was substituted with a moderate

Table 1 Screening of reaction parameters[a]



Entry	Solvent	Reagent/catalyst	Co-catalyst[b]	Yields[c] **3a** [%]
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.), **2a** (1.0 equiv.), reagent (1.2 equiv.) and solvent (5 ml) at RT. The reaction time was 16 h. [b] Co-catalyst used 10 mol%. [c] Isolated yields. [d] NIS used was 2 equiv. [e] NIS used was 30 mol%.



Scheme 1 Synthesis of indolylquinazolinone derivatives. Unless otherwise specified, the 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.

electron-withdrawing group like CH_2CO_2Me, the yields of the corresponding products remained almost unaffected (**3f–g**).

Surprisingly, when the aldehyde group was placed at C3 of indoles, the reaction did not proceed even after three days (**3h**). After examining electron-donating as well as electron-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 and 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 with the 3-methylindole. When the indole nitrogen was protected with an electron-withdrawing group, Boc, the reaction did not proceed even after 48 h (**3n**). This may be due to the lowering of nucleophilicity on the indole nitrogen, which plays a vital role in iodination. Subsequently, we expanded the scope of the reaction with the C3 unsubstituted indoles and applied our optimized condition on plain indoles and quinazolinones. The outcome of this reaction, which gave the expected product **5a**, was not surprising; however, along with the product a lower percentage of 3-iodoindolylquinazolinone (**5aa**) was also obtained. We suspected that the variation in the amount of NIS may give one of the products specifically. Thus, we took indoles and quinazolinones as the coupling products and used only 1.05 equiv. of NIS instead of 1.2 equiv. under the same optimized conditions. After 16 h, we obtained 3-(1*H*-indol-2-yl)-3*H*-quinazolin-4-one (**5a**), whereas when 1.7 equiv. of the NIS was used, the reaction gave only 3-(3-iodo-1*H*-indol-2-yl)-3*H*-quinazolin-4-one (**5aa**) specifically (Fig. 2).

Furthermore, this reaction also tolerated 5- and 6-bromoindoles and 5-methoxyindole, as well as afforded the targeted product along with the undesired iodo-substituted product. The yields of both products depended on the amount of the NIS and the time of the reaction. The ^{1}H NMR clearly showed the variation in yield between the desired indolylquinazolinone and the undesired 3-iodoindolylquinazolinone products (see ESI†). Surprisingly, when 1-methylindole and 1-butylindoles reacted with quinazolinone, we obtained only our desired products (**5f–g**), whereas 1-sulfonylindole and 7-azaindole were inactive 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 (Scheme 2).

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

Hence, we again sought for an optimum condition with iodine and different solvents, and it was determined 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, 18 h) were found to be applicable over a range of N-substituted/unsubstituted pyrrole and quinazolinone derivatives (Scheme 3). N-substituted/unsubstituted pyrroles reacted smoothly with quinazolinone derivatives to give corresponding pyrroloquinazolinone products (**7a–d**) in moderate yields (Scheme 3).

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.), and NBS (1.1 equiv.) at room temperature in $CHCl_3$, and an unexpected product, 3-methyl-1,3-dihydro-indol-2-one (**8**), was formed in 50% yield after 4 h (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 product, 3,3′-dimethyl-3′*H*-[1,2′]biindolyl-3′-ol (**9**), in 22% yield after 24 h. 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 the oxygen atmosphere.[19] It

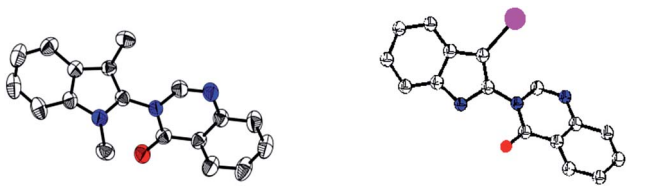
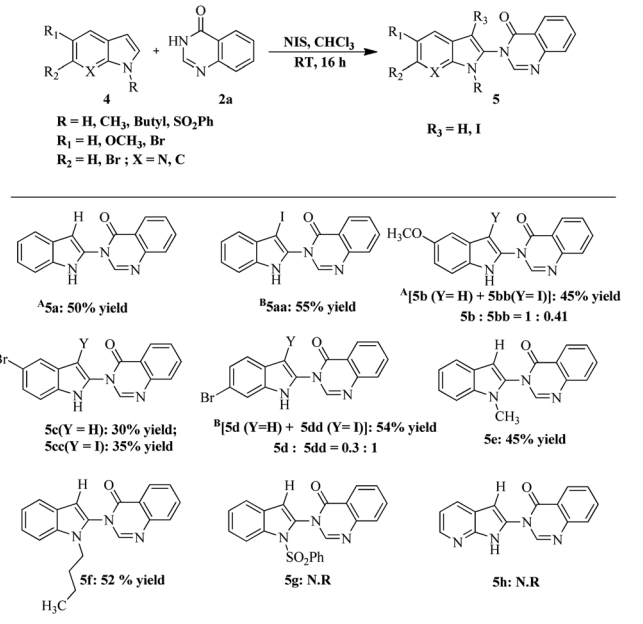
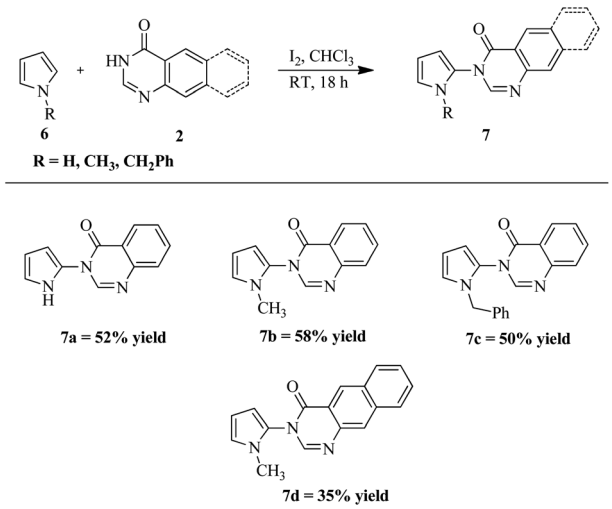


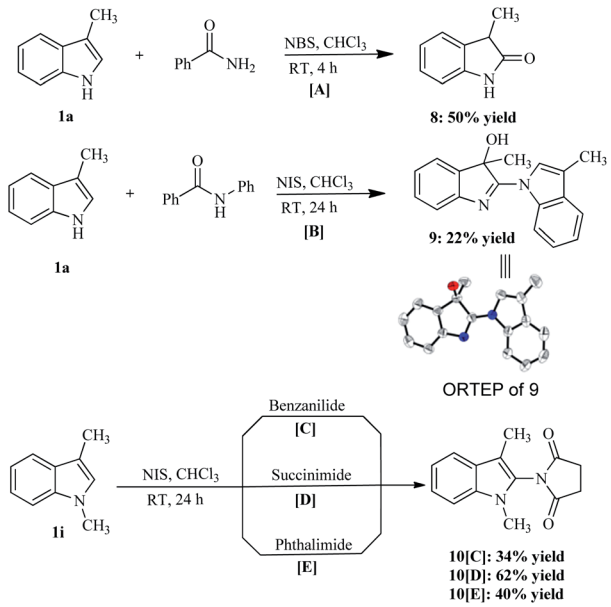
Fig. 2 ORTEP of Compound **3i**, **5aa** (hydrogens are removed for clarity).



Scheme 2 Synthesis of 3-unsubstituted indolylquinazolinone derivatives. Unless otherwise specified, the 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 was used, and reaction time 16 h. [B] 1.7 equiv. of NIS was used, and reaction time was 24 h. N.R. = no reaction.



Scheme 3 Synthesis of pyrrolylquinazolinone derivatives. 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.

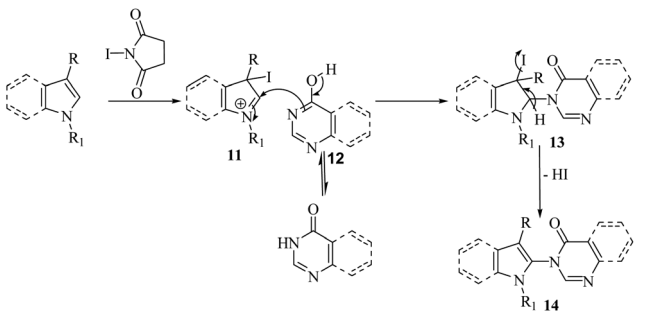


Scheme 4 Reaction between indoles and aliphatic amides/imides. [A] **1a** (0.98 mmol), benzamide (0.82 mmol) and NBS (0.98 mmol) in a solvent at RT for 4 h. [B] **1a** (0.51 mmol), benzanilide (0.51 mmol), NIS (0.61 mmol) in a solvent at RT for 24 h. [C] **1i** (0.35 mmol), benzanilide (0.35 mmol), NIS (0.35 mmol) in a solvent at RT for 24 h. [D] **1i** (1 mmol), succinimide (1 mmol), NIS (1 mmol) in a solvent at RT for 24 h. [E] **1i** (0.68 mmol), phthalimide (0.68 mmol), NIS (0.82 mmol) in a solvent at RT for 24 h.

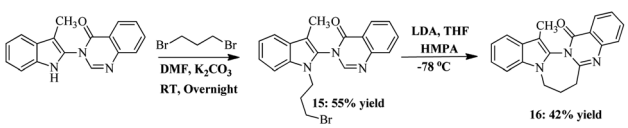
may be that the indole nitrogen is more nucleophilic, in comparison with the nitrogen of benzanilide, which led to the formation of the unexpected product (**9**). Thus, we suspected that protection of the indole nitrogen would be able to furnish our expected coupled product. Therefore, we used the same reaction condition with 1,3-dimethylindole. However, this time we obtained 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**) increased to 62% (Scheme 4[D]); however, the use of phthalimide as a starting material also furnished only a 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).

After all of these extensive studies with a variety of substrates, and from the outcomes we proposed a possible pathway of the reaction as shown in Scheme 5. Iodination on C3 of indole with NIS produces the intermediate **11**, which undergoes an 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 5).

In the final part of our study, we synthesised an indolo [1,3]-diazepine skeleton fused with quinazolinone. Diazepines are a very important class of heterocycles having considerable applications in pharmaceutical industry. However, among them, 1,4-diazepine has the maximum applications, whereas, 1,3-diazepine systems are very rarely known because of their biological activity. Some 1,3-diazepine-fused heterocycles show anticancer and anti-AIDS activity as well as inhibition of HIV protease.[20] Thus, we synthesised a 1,3-diazpine containing a novel indolylquinazolinone heterocycle, which may possess some interesting biological properties. We took compound **3a** and treated with 1,3-dibromopropane in the presence of K_2CO_3 and DMF solvent at room temperature, which led to the formation of 3-[1-(3-bromo-propyl)-3-methyl-1*H*-indol-2-yl]-3*H*-quinazolin-4-one (**15**). Next, the treatment of compound **15** with LDA in presence of HMPA at −78 °C furnished the desired macrocyclic compound 16 in 42% yields (Scheme 6).



Scheme 5 Possible mechanism.



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

Conclusions

In summary, we have developed an efficient, metal-free methodology for direct amidation regioselectively at C2 in indoles and pyrroles with quinazolinones and pyrimidones. A series of novel indolylquniazolinones/pyrimidones and pyrrolylquinazolinones were prepared with free or protected indoles and pyrroles. Further, we prepared a highly functionalized 1,3-diazepine compound, which may have 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 Schlenk tube was then flushed with nitrogen. The reaction mixture was stirred at RT for 16 h. It was then diluted with water, and the 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–hexane = 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 °C; 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) calcd 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 (115 mg, 52%); m.p. = 228 °C; 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) calcd 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 °C; 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) calcd 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 °C; 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) calcd 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 °C; 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) calcd 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) calcd 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 (125 mg, 65%); m.p. = 92 °C; IR (KBr) 3221, 2947, 1736, 1698, 1600, 1238, 827, 761 cm^{-1}; ^1H 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) calcd 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}; ^1H 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) calcd 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) calcd 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}; ^1H 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) calcd 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}; ^1H 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) calcd 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}; ^1H 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) calcd 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}; ^1H 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) calcd 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}; ^1H 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) calcd 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-1H-indol-2-yl)-3H-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) calcd 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 °C; 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) calcd 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-1H-indol-2-yl)-3H-quinazolin-4-one (**5cc**).* Compound was obtained as bright yellow solid (111 mg, 35%); m.p. = 218 °C; 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) calcd 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-1H-indol-2-yl)-3H-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) calcd 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 °C; 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) calcd 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 °C; 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) calcd 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) calcd 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 °C; 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) calcd 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 °C; 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) calcd 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 °C; 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) calcd 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).[22] Compound was obtained as yellow solid (31 mg, 22%); m.p. = 174 °C; 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) calcd 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 °C; 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) calcd 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 the reaction mixture of 3-(3-methyl-1*H*-indol-2-yl)-**4a** and **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 RT for 1 h. Then, 1,3-dibromopropane (0.109 g, 0.54 mmol) was added to the reaction mixture dropwise and stirred at RT 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 : hexane = 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) calcd 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 °C 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 (0.180 g, 1.00 mmol) was added dropwise. The reaction mixture was stirred for another 3 h at −78 °C, followed by additional 2 h at RT. 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 : hexane = 3 : 7) to afford the desired product **16** (55 mg, 42% yield). This compound was obtained as yellow solid; m.p. = 158 °C; 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) calcd for $C_{20}H_{17}N_3O$ (M + H) 316.1450, found 316.1448.

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