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AN EFFICIENT ECOFRIENDLY SYNTHESIS OF 1, 2-DIHYDROQUINAZOLINONES BY USING CLAY AS CATALYST

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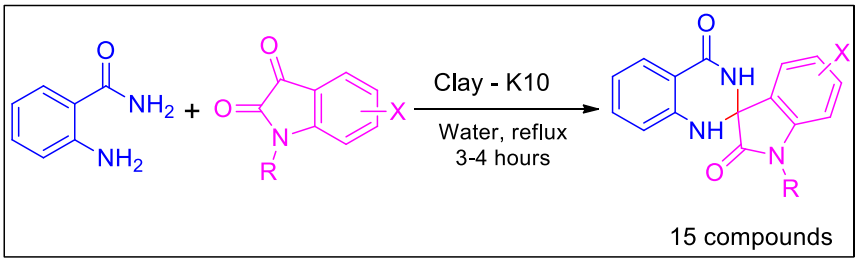
ABSTRACT

A simple, efficient and eco-friendly method for the synthesis of quinazolinones has been developed using water as solvent. This protocol involves one pot reaction of readily available substituted isatins and 2-aminobenzamide with montmorillonite-K-10 as a green and eco-friendly catalyst. This method is carried out in shorter reaction time with operational simplicity, higher yields and selectivity. Using this method, a series of fifteen compounds were synthesized.

Graphical abstract:



KEY WORDS

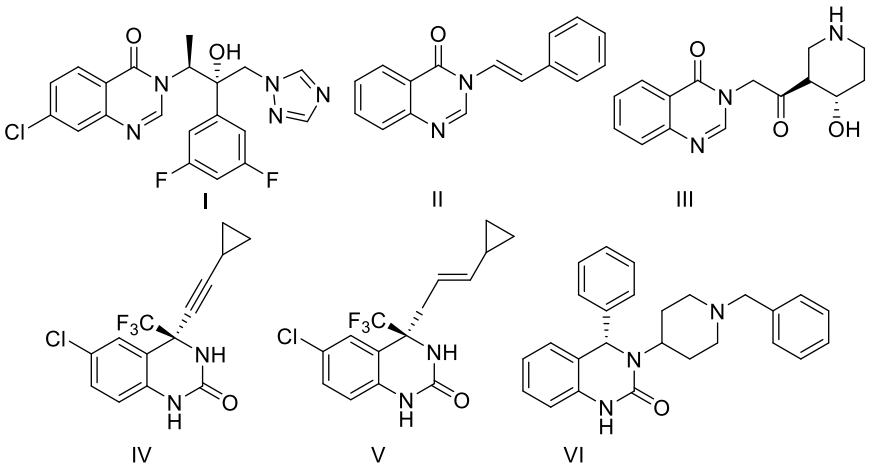
Efficient synthesis. Clay, One pot, Quinazolinones.

INTRODUCTION

Quinazolinone derivatives are important bioactive nitrogen-containing heterocycles and are present in several natural products such as vitamins, alkaloids, etc. Due to their diverse pharmacological and biological activities [1], quinazolinone scaffolds are very important in the synthesis of various biologically active compounds. Recently, these compounds are reported to exhibit as gene associated peptide and vasopressin receptor antagonists [2, 3] Febrifugine (III), a quinazolinone alkaloid was first isolated from the Chinese herb *Dichoria febrifuga*. It has important biological properties such as antimalarial [4], anticancer [5] and anti-inflammatory [6, 7].

Albacanazole (I) in which the quinazolinone ring is fused by triazole moiety and exhibits broad spectrum anti-fungal activity [8, 11]. DPC-961 (IV), DPC-963 (V) and SM-15811 (VI) (Fig. 1) are compounds having quinazolinone ring, have resemblance with the compounds bearing quinazolinone type of scaffold exhibiting 2nd generation HIV activity, ion exchanger properties and also used to treat heart diseases. Considering the importance of quinazolinones from an application perspective, some synthetic methods have been developed. Generally, metal catalysed reductive cyclization of *o*-nitrobenzamides and ketones or aldehydes [12]. Alternative approaches [13, 14] used anthranilic acid and carboxylic acids or acyl chlorides, anthranilamide and ketone, cyclization of *o*-amino

benzonitrile with ketone for the synthesis of substituted quinazolinones. However, the drawbacks of the previous methods are associated with reaction time and conditions, usage of solvents and outputs of the product yields.



I. Albaconzole, II. (E)-Bogorin, III. Febbrifugine, IV. DPC961, V. DPC083, VI. (+) SM-15811

Fig. 1 Biologically important quinazolinones

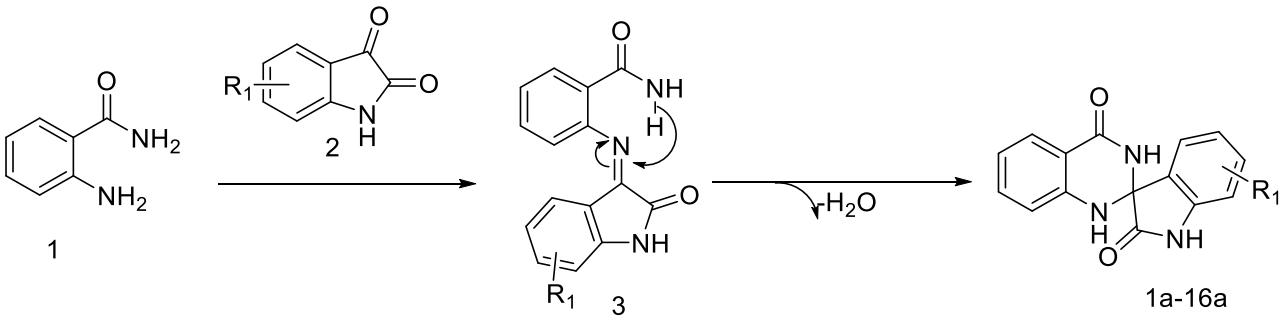
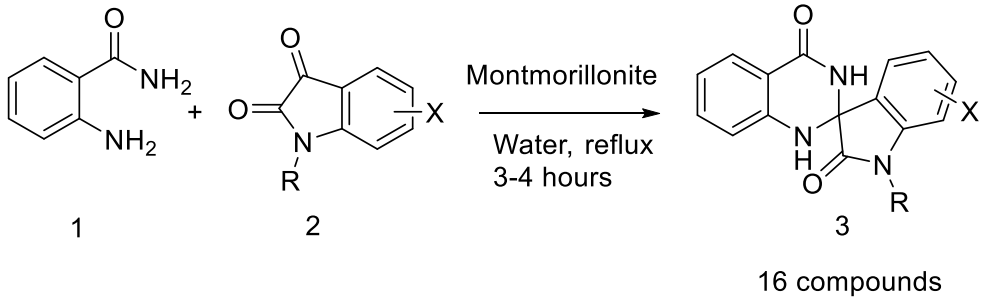


Fig. 2 Plausible mechanism for the formation of Quinazolinone

Scheme Captions

Scheme 1 Synthesis of 1,2-dihydroquinazolinones



Reagents and conditions 1) 2-aminobenziamide, 2) substituted Isatin, Catalyst, Water reflux, 3) Product.

Montmornolite-K-10 is a versatile catalyst having Lewis acid property [15, 18] and is reported to catalyse many important organic reactions [19] such as aldol, Mannich, Michael and Diels–Alder reaction. It is an excellent promoter for the copper-catalysed coupling reactions. From an environmental and economic perspective, montmorillonite-K-10 has several advantages of being metal ion free, easy to handle, experimental simplicity, cost-effective, non-corrosive and has excellent solubility in water and organic solvents. It has been widely used in Multicomponent reactions under liquid and solvent free conditions [20]. In this procedure reaction solvent is water and catalyst are cost effective [21] and non hazardous, it is the

green principle for synthetic organic chemistry. Due to this, the method most beneficial while comparing with previously reported methods, it is the noteworthy route for the developing of quinazolinone derivatives via one pot reaction by involving isatin and 2-amino benzimide.

RESULTS AND DISCUSSION

Chemistry

The reaction optimization conditions to develop the quinazolinone derivatives by using montmorillonite catalyst are found to be the best. Initially the reaction was kept using 2-aminobenzamide and isatin without any catalyst at atmospheric temperature (entry 1, Table 1), in the presence of universal solvent until 6 h, here the reaction was not proceed confirmed by the TLC monitoring. Then the reaction was carried out in the presence of montmorillonite catalyst at the same temperature, product was observed with low yield (entries 6,7). Then the reaction was performed in the reflex condition with catalyst (entries 2-5 & 8-10, Table 1), finally offered the required product in the good to excellent yields in the water medium. Then the reaction was carried out using various concentrations of the catalyst such as 2, 5, 10 and 15 mol % in the 3-6 h time period (Table 2). 2 and 5 mol % of catalyst gives only 52 and 60 % of the required product and if the catalyst concentration is increased more than 10 mol % there is no variations in the yield of the product. The presence of an electron withdrawing group at position 5 of the isatin slowed down the reaction resulting in a comparable increase in the reaction time and lower yields. It is important to note that under the conditions mentioned above, the quinazolinone was formed as an exclusive desired product employing montmorillonite-K-10 as the catalyst. With the optimized conditions a series of compounds (Table 3) were synthesized.

Table 1: Optimization of various solvents at different temperatures for the synthesis of 1, 2-dihydroquinazolinones

Entry	Solvent	Temperature (°C)	Catalyst[b]	Time (hr)	Yield[a] (%)
1	water	RT	--	6	--
2	water	Reflux	--	4	<10
3	ethanol	40	--	5	15
4	methanol	40	--	5	10
5	hexane	50	M-K-10	5	10
6	water	RT	M-K-10	6	20
7	ethanol	RT	M-K-10	4	30
8	methanol	40	M-K-10	4	70
9	ethanol	60	M-K-10	4	80
10	**water**	**100**	**M-K-10**	**3-4**	**87**

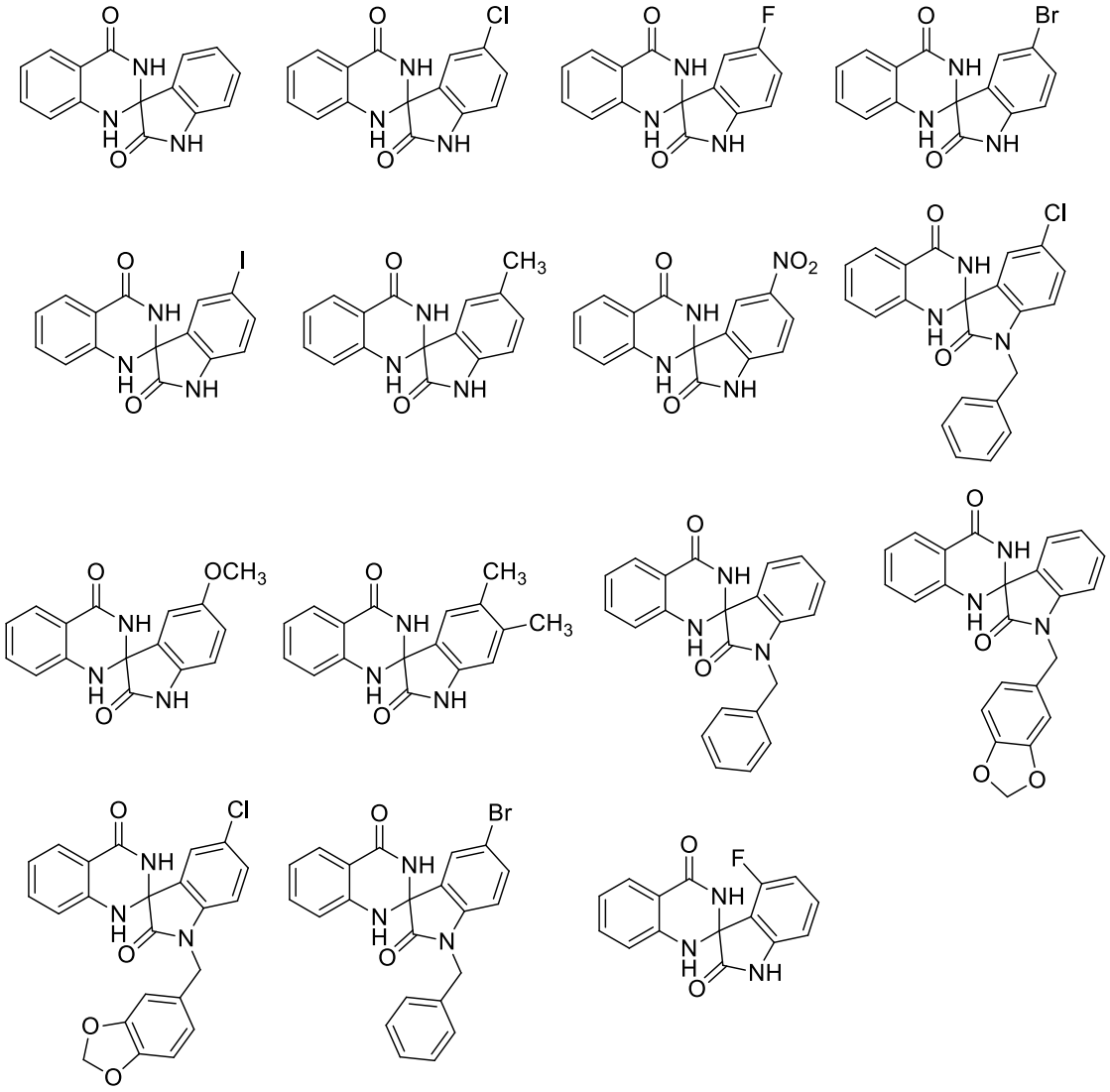
[a] - isolated yields

Table 2: Condensation of isatin and 2-aminobenzamide in water at different concentrations of montmorillonite-K-10

Entry	Catalyst (mole %)	Time (h)	Yield (%) [a]
1	-	6	Nil
2	2	5	52
3	5	5	60
4	**10**	**3.5**	**87**
5	15	5	87

[a] - isolated yields

Table 3 Synthesis of 1, 2-dihydroquinazolinones derivatives.



Plausible mechanism

The plausible mechanism for the formation of quinazolinone ring from isatin and 2-aminobenzamide is outlined in Fig. 2. The reaction is hypothetical to proceed with the formation of a keto imine from 2-aminobenzimide with isatin. Hence, this step was promoted by the catalyst montmorillonite-K-10 and it reacted with the keto group to form an imino derivative with the elimination of water. The imine carbon which is active for a nucleophilic attack was then attacked by the adjacent nitrogen atom to cyclise into a conformationally constructive six membered ring to form the desired product.

CONCLUSION

In conclusion, a simple, efficient and environmentally benign method for the synthesis of 1, 2-dihydroquinazolinones has been developed by employing montmorillonite-K-10 as a catalyst in water. The advantages of this method include its simplicity of operation, clean reactions, higher yields and absence of side products, by using this procedure we synthesized fifteen compounds.

General reaction procedure for the preparation of compounds (1a-16a)

To the solution of 2-aminobenzamide (1 mmol) in water add substituted isatin (1 mmol) and montmorillonite-K-10 (10 mol %), reflux the reaction at 100 °C for 4 h, appearance of solid indicates the product formation and which was also monitored by

the TLC. Then filter the reaction mixture and recrystalised the resulted solid to obtain the respective pure quinazolinones in good to excellent yields.

***1H-spiro[indoline-3,2'-quinazoline]-2,4'(3'H)-dione* (1a)**

Dirty white powder; 87 % yield; mp 290-295 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 9.76 (s, 1H), 7.80 (d, J = Hz, 1H), 7.59 (d, J=Hz, 1H), 7.29-7.21 (m, 2H), 7.03 (t, 2H), 6.85 (d, 1H), 6.76 (t, 1H), 6.67 (d, 1H), 6.15 (bs, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 70.84, 109.96, 113.77, 114.07, 117.05, 121.93, 124.94, 126.73, 129.18, 130.38, 132.98, 141.88, 146.53, 164.14, 175.79; IR (KBr pellets) υ: 3363, 3339, 3179, 3050, 1730, 1706, 1663, 1620, 1509, 1483, 1470, 1359, 1324, 1185, 748 cm^{-1}; ESI-MS : *m/z* = 266 (M+H) $^{+}$; HRMS (ESI) *m/z* for $C_{15}H_{12}O_2N_3$ calculated *m/z*: 266.09240, found *m/z*: 266.09225 (M+H) $^{+}$.

***5-chloro-1H-spiro[indoline-3,2'-quinazoline]-2,4'(3'H)-dione* (2a)**

White powder; 80 % yield; mp 289-294 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.86 (s,1H), 7.56- 7.49 (m, 3H), 6.81-6.62 (m, 4H) 4.79 (s, 1H), 3.82 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 70.02, 119.70, 112.67, 112.83, 112.94, 115.80, 117.40, 126.80, 130.43, 133.09, 137.63, 146.14, 164.10, 175.80; IR (KBr pellets) υ: 3252, 1731, 1660, 1651, 1613, 1514, 1504, 1483, 1440, 1359, 1268, 1190, 753, 694 cm^{-1};ESI-MS: *m/z* = 300 (M+H)$^{+}$; HRMS (ESI) *m/z* for $C_{15}H_{11}O_2N_3Cl$ calculated *m/z*: 300.05343, found *m/z*: 300.05341 (M+H)$^{+}$.

***5-flouoro-1H-spiro[indoline-3,2'-quinazoline]-2,4'(3'H)-dione* (3a)**

White powder; 79 % yield; mp 285-287 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 9.98(s, 1H), 7.78 (m, 2H), 7.23 (bs, 2H), 7.01 (t, *J* =7.36 Hz, 1H), 6.81-6.66 (m, 3H), 6.58 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 71.12, 110.70, 112.67, 113.83, 113.94, 116.80, 117.40, 126.80, 130.43, 133.09, 137.63, 146.14, 164.10, 175.80; IR (KBr pellets) υ: 3282, 1741, 1661, 1632, 1613, 1520, 1185, 1146, 1124, 1042, 817, 758, 710, 693, 636, 616 cm^{-1}; ESI-MS: *m/z* = 284 (M+H)$^{+}$; HRMS (ESI) *m/z* for $C_{15}H_{11}O_2N_3F$ calculated *m/z*: 284.08298, found *m/z*: 284.08315 (M+H)$^{+}$.

***5-bromo-1H-spiro[indoline-3,2'-quinazoline]-2,4'(3'H)-dione* (4a)**

Light red powder; 77 % yield; mp 280-285 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 6.43 (s, 1H), 6.68 (d, *J* = 7.93 Hz, 1H), 6.74-6.78 (m, 2H), 7.24 (dt, *J* = 1.51 & 8.30 Hz, 1H), 7.40 (dd, *J* = 1.88 & 8.30 Hz, 1H), 7.48-7.51 (m, 1H), 7.61 (d, *J* = 1.70 Hz, 1H), 7.79 (d, *J* = 7.55 Hz, 1H), 10.02 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 70.83, 111.67, 113.74, 113.88, 117.32, 126.74, 127.81, 131.17, 132.89, 133.01, 140.91, 146.04, 163.92, 175.28; IR (KBr pellets) υ: 1731, 1660, 1614, 1513, 1482, 1434, 1358, 1302, 1268, 1189, 1145, 1122, 817, 752, 628, 566, 538 cm^{-1}; ESI-MS: *m/z* = 343 (M)$^{+}$; HRMS (ESI) *m/z* for $C_{15}H_{11}O_2N_3Br$ calculated *m/z*: 343.00292, found *m/z*: 343.00306 (M)$^{+}$.

***5-iodo-1H-spiro[indoline-3,2'-quinazoline]-2,4'(3'H)-dione* (5a)**

White powder ; 80 %yield; mp 240-245°C; ^{1}HNMR(300MHz,DMSO-d_6): 10.04 (s,1H), 7.77 (d, *J* = 8.6Hz, 3H), 7.58 (d, *J* = 7.9Hz, 1H),7.25(t, *J* = 7.55Hz, 1H), 6.76-6.64 (m,4H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 70.76, 83.96, 112.42, 113.84, 117.82, 127.05, 130.99, 133.28, 133.55, 139.09, 141.31, 145.72, 164.18, 175.02; IR (KBr pellets) υ: 3282, 1741, 1661, 1613, 1520, 1484, 1425, 1371, 1335, 1299, 1265, 1185, 1146, 1124, 1042, 817, 758, 636, 616 cm-1; ESI-MS: *m/z* = 390 (M)$^{+}$; HRMS (ESI) *m/z* for $C_{15}H_{10}O_2N_3$ calculated *m/z*: 390.90292, found *m/z*: 390.90306 (M)$^{+}$.

***5-methyl-1H-spiro[indoline-3,2-quinazoline]-2,4'(3'H)-dione* (6a)**

White powder; 85 % yield; mp 150-155 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.30 (s, 3H), 6.49 (s, 1H), 6.65-6.80 (m, 3H), 7.07 (d, *J* = 7.55 Hz, 1H), 7.22 (t, *J* = 8.30 & 15.29 Hz, 1H), 7.34 (s, 1H), 7.40 (brs, 1H), 7.75 (d, *J* = 7.17 Hz, 1H), 9.81 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 20.48, 70.92, 109.73, 113.72, 113.97, 117.06, 125.49, 126.75, 129.00, 130.62, 131.16, 132.94, 139.20, 146.40, 164.19, 175.77; IR (KBr pellets) υ: 3314, 2922, 2853, 1706, 1655, 1613, 1513, 1489, 1357, 1329, 1270, 1207, 1154, 811, 751, 698 cm^{-1}; ESI-MS: *m/z* = 280 (M+H); HRMS (ESI) *m/z* for $C_{16}H_{14}O_2N_3$ calculated *m/z*: 280.10805, found *m/z*: 280.10812 (M+H) $^{+}$.

***5-nitro-1H-spiro[indoline-3,2'-quinazoline]-2,4'(3'H)-dione* (7a)**

White powder; 84% yield; mp 230-235°C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 6.67 (d, *J* = 7.93 Hz, 1H), 6.75 (t, *J* = 7.55 & 14.91 Hz, 1H), 7.00 (d, *J* = 8.68 Hz, 1H), 7.14 (s, 1H), 7.24 (t, *J* = 8.49 & 16.61 Hz, 1H), 7.71 (d, *J* = 7.17 Hz, 1H), 8.19-8.40 (m, 3H), 10.85 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 70.56, 109.99, 113.90, 117.62, 120.62, 126.81, 127.10, 130.02, 133.19, 142.41, 145.90, 148.22, 163.82, 176.04; IR (KBr pellets) υ: 3342, 3021, 2860, 1727, 1649, 1616, 1522, 1482, 1405, 1339, 1296, 1252, 1229, 1189, 1143, 1121, 1085, 837, 746, 733, 690, 635, 550 cm^{-1}; ESI-MS: *m/z* = 311 (M+H)$^{+}$;

HRMS (ESI) *m/z* for $C_{15}H_{11}O_4N_4$ calculated *m/z*: 311.07748, found *m/z*: 311.07744 $(M+H)^+$.

1-benzyl-5-chloro-1-H-spiro[indoline-3,2-quinazoline]-2,4(3H)-dione **(8a)**

White powder; 79 % yield; mp 150-155 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ: 8.1 (s, 1H), 7.8 (d, 1H),7.6 (s, 1H), 7.55 (t, 2H, J=8.1Hz), 6.9 (s, 1H) ,6.77 -6.68 (m, 4H), 6.5 (bs, 1H) , 6.0 (bs ,1H), 4.9 (s, 1H), 4.8 (s, 2H,), 3.8 (d, 1H), ^{13}C NMR (75 MHz, DMSO-d_6): δ 145.16, 141.26, 133.8, 133.4, 130.75, 129.4, 126.09, 123.8, 121.6, 116.4, 115.41, 113.70, 107.65, 69.27, 41.89; IR (KBr pellets, υ: 3758, 3713, 3707, 3685, 3644, 3625, 3583, 3270, 2923, 2357, 1737, 1731, 1715, 1666, 1660, 1650, 1644, 1633, 1613, 1514, 1504, 1494, 1485 1434, 1336 cm^{-1}; ESI-MS *m/z*: 389 (M+); HRMS (ESI) *m/z* for $C_{22}H_{16}ClN_3O_2$ calculated *m/z*: 389.08298, found *m/z*: 389.08315 $(M+H)^+$.

5-methoxy-1H-spiro[indoline-3,2'-quinazoline]-2,4'(3'H)-dione **(9a)**

White powder; 85 % yield; mp 270-275 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 9.74 (s, 1H), 7.79 (d, 1H), 7.5 (s, 1H), 7.45 (bs , 1H) ,7.1 (s , 1H) ,6.81 -6.45 (m, 4H) , 6.45 (s, 1H), 3.75 (s, 3H) , 13C NMR60 (DMSO), ppm, 174.8, 163, 154.17, 145.58, 134.01, 131.94, 129.27, 125.71, 116.01, 144.44, 112.76, 110.43, 109.45, 70.23, 54.36; IR (KBr pellets) υ: 3314, 3215, 2924, 1719, 1648, 1609, 1513, 1485, 1440, 1357, 1296, 1270, 1234, 1162, 1043, 1024, 824, 794, 756, 715, 698, 672, 621, 578 cm^{-1}; ESI-MS : *m/z* = 296 $(M+H)^+$; HRMS (ESI) *m/z* for $C_{15}H_{12}O_2N_3$ calculated *m/z* : 296.09240, found *m/z*: 296.09225 $(M+H)^+$.

5,6-dimethyl-1H-spiro[indoline-3,2'-quinazoline]-2,4'(3'H)-dione **(10a)**

White powder; 87 % yield; mp 320-325 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.39 (d, 6H), 6.49 (s, 1H), 6.65-6.80 (m, 3H), 7.07 (d, *J* = 7.55 Hz, 1H), 7.22 (t, *J* = 8.30 & 15.29 Hz, 1H), 7.34 (s, 1H), 7.40 (brs, 1H), 7.75 (d, *J* = 7.17 Hz, 1H), 9.81 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 20.48, 70.92, 109.73, 113.72, 113.97, 117.06, 125.49, 126.75, 129.00, 130.62, 131.16, 132.94, 139.20, 146.40, 164.19, 175.77; IR (KBr pellets) υ: 3311, 3301, 2902, 2833, 1706, 1685, 1623, 1513, 1489, 1357, 1329, 1270, 1207, 1154, 811, 751, 698 cm^{-1}; ESI-MS : *m/z* = 293 $(M+H)^+$; HRMS (ESI) *m/z* for $C_{17}H_{15}O_2N_3$ calculated *m/z*: 293.09240, found *m/z*: 293.133 $(M+H)^+$.

1-benzyl-1'H-spiro[indoline-3,2'-quinazoline]-2,4'(3'H)-dione **(11a)**

White powder; 82 % yield; mp 240-245 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.04 (s, 1H), 7.79 (d, 1H), 7.68 (s, 1H), 7.59 (d, 1H), 7.12 (t, 1H), 6.93-6.84 (m, 3H), 6.77-6.68 (m, 5H), 5.94 (s, 2H), 4.72 (s, 2H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 170.02, 163.28, 145.15, 141.29, 133.88, 132.04, 129.40, 129.4, 127.23, 126.09, 123.08, 121.31, 116.41, 113.86, 112.85, 107.38, 69.62, 41.89; IR (KBr pellets) υ: 3329, 3179, 3054, 2918, 1705, 1667, 1615, 1511, 1489, 1466, 1454, 1362, 1314, 1264, 1175, 1142, 993, 749, 696, 678, 630 cm^{-1}; ESI-MS : *m/z* = 356 $(M+H)^+$; HRMS (ESI) *m/z* for $C_{15}H_{12}O_2N_3$ calculated *m/z*: 356.09240, found *m/z*: 356.09225 $(M+H)^+$.

1-(benzo[d][1,3]dioxol-5-ylmethyl)-1H-spiro[indoline-3,2-quinazoline]2,4(3H)-dione **(12a)**

White powder; 84 % yield; mp 260-265 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.01 (s, 1H), 7.79 (d, 1H), 7.77 (s, 1H), 7.66 (d, *J* = 7.21 Hz, 1H), 7.59(d, *J* = 7.26 Hz, 1H),7.29 -6.75 (m, 7H), 5.94 (s, 2H), 4.72 (s, 2H): ^{13}C NMR (75 MHz, DMSO-d_6): δ 42.67, 70.67, 100.57, 107.41, 107.80, 109.16, 113.84, 114.05, 117.31, 120.31, 122.64, 124.75, 126.79, 128.64, 130.38, 133.03, 142.27, 146.28, 146.47, 147.44, 164.22, 174.05; IR (KBr pellets) υ: 3193, 3059, 1658, 1670, 1615, 1487, 1467, 1444, 1356, 1272, 1244, 1190, 1174, 1143, 1100, 1036, 743, 695 cm^{-1}; ESI-MS: *m/z* = 400 $(M+H)^+$; HRMS (ESI) *m/z* for $C_{23}H_{18}O_4N_3$ calculated *m/z*: 400.12918, found *m/z*: 400.12982 $(M+H)^+$.

1-(benzo[d][1,3]dioxol-5-ylmethyl)-5-chloro-1H-spiro[indoline-3,2-quinazoline]2,4(3H)-dione **(13a)**

White powder; 77% yield; mp 195-200 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.62 (s, 3H), (bs, 1H), 7.55 (bs, 1H), 7.4 (bs, 1H), 7.41-6.79 (m, 4H), 6.54 (s, 1H), 5.96 (s, 2H) 4.89 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 46.7, 70.67, 103.57, 106.41, 107.80, 109.16, 113.84, 114.05, 117.31, 119.31, 120.64, 124.25, 126.79, 128.64, 130.38, 133.03, 142.27, 146.28, 146.47, 147.44, 164.20; IR (KBr pellets) υ: 3270, 1671, 1660, 1650, 1644, 1633, 1613, 1574, 1567, 1556, 1537, 1530, 1514, 1494, 1485, 1471, 1454, 1434, 1416, 1392, 1371, 1336, 1172, 1253, 1123, 1080, 1029, 815, 752 cm^{-1}; ESI-MS: *m/z* = 434 $(M+H)^+$; HRMS (ESI) *m/z* for $C_{23}H_{17}O_4N_3Cl$ calculated *m/z*: 434.09021, found *m/z*: 434.09025 $(M+H)^+$.

1-(benzo[d][1,3]dioxol-5-ylmethyl)-5-bromo-1H-spiro[indoline-3,2-quinazoline]2,4 (3H)-dione **(14a)**

White powder; 76 % yield; mp 160-165 °C; ^{1}H NMR (DMSO-D6, 300 MHz, ppm) δ: 7.53, (t, 3H, *J* = 8.3Hz), 7.3 (bs, 1H), 7.20 (t, 3H , *J* = 8.3Hz), 6.7 (d, 3H , *J* = 7.9Hz), 6.62 (t, 2H, *J* = 7.7Hz), 5.9 (bs, 4H,). ^{13}C NMR (75 MHz, DMSO-d_6): δ 173.47, 170.80, 163.72, 148.75, 1425.60, 141.74, 134.32, 132.48, 131.20, 129.84,

127.68, 124.24, 122.09, 116.85, 115.85, 113.35, 108.43, 70.07, 42034: IR (KBr pellets, υ: 3411, 2923, 2853, 1731, 1650, 1585, 1546, 1487, 1452, 1402, 1315, 1257, 1151, 743 cm^{-1}; ESI-MS *m/z*: 433 (M+). HRMS (ESI) *m/z* for $C_{22}H_{17}O_2N_3$ calculated *m/z*: 433.08298, found *m/z*: 434.08315 $(M+H)^+$.

7-fluoro-1H-spiro[indoline-3,2'-quinazoline]-2,4'(3'H)-dione **(15a)**

light white powder; 79 % yield; mp 310-315 °C; ^1H NMR (300 MHz, DMSO-d_6): δ, 9.96 (s,1H), 7.78 (d, 2H, *J* = 7.5Hz), 7.70 (s, 1H), 7.23 (s,1H) 7.09, 6.99 (t, 1H, *J* = 7.36Hz), 6.81-6.78 (m, 2H) 6.68 (s, 1H, *J* = 7.9Hz) 6.58 (s, 1H) ^{13}C NMR (75 MHz, DMSO-d_6): δ 71.12, 110.70, 112.67, 113.83, 113.94, 116.80, 117.40, 126.80, 130.43, 133.09, 137.63, 146.14, 164.10, 175.80 IR (KBr pellets, υ: 3326, 3177, 1732, 1614, 1588, 1516, 1486, 1370, 1358, 1314, 1272, 1254, 1203, 1152, 1083, 1033, 902, 736, 686, 661, 603, 578, 527 cm^{-1}; ESI-MS: *m/z* = 284 $(M+H)^+$; HRMS (ESI) *m/z* for $C_{15}H_{10}O_2N_3F$ calculated *m/z*: 284.08298, found *m/z*: 284.08315 $(M+H)^+$.

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