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A regioselective three-component reaction for synthesis of novel 1′*H*-spiro[isoindoline-1,2′-quinazoline]-3,4′(3′*H*)-dione derivatives

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ABSTRACT

A ring opening and regioselective three-component reaction of isatoic anhydride, isatins, and aromatic or aliphatic primary amines in the presence of catalytic amount of $KAl(SO_4)_2{\cdot}12H_2O$ (alum) to yield a novel series of 1′*H*-spiro[isoindoline-1,2′-quinazoline]-3,4′(3′*H*)-dione is described.

1. Introduction

Combinatorial chemistry is now routinely applied to find out novel biologically active compounds. In this context, multicomponent reactions (MCRs) are powerful tools in the modern drug discovery process in terms of lead finding and lead optimization.[1–6] However, the range of easily accessible and functionalized small heterocycles is rather limited. The development of new, rapid, and robust routes toward focused libraries of such heterocycles is therefore of great importance.

2,3-Dihydroquinazoline-4(3*H*)-ones and spirooxindole derivatives are important classes of heterocyclic compounds. 2,3-Dihydroquinazolin-4(3*H*)-ones possess a broad spectrum of biological and pharmaceutical activities, such as analgesic, antitumor, anticancer, diuretic, and herbicide activities.[7] In addition, these compounds can easily be oxidized to their quinazolin-4(3*H*)-one analogues,[8] which also include important pharmacologically active compounds.[9] Several methods have been reported for the synthesis of 2,3-dihydroquinazolinones.[10–13]

The heterocyclic spirooxindole ring system is a widely distributed structural framework that is present in a number of pharmaceuticals and natural products,[14] including cytostatic alkaloids like spirotryprostatins A, B, and strychnophylline.[15] The unique structural array and the highly pronounced pharmacological activity displayed by this class of spirooxindole compounds have made them attractive synthetic targets.[16] Oxa and azaspiro derivatives are well-known,[16–18] but the preparation of corresponding quinazolinone analogues has not yet evolved.

2. Results and discussions

We have concentrated most of our recent studies on the preparation of bioactive nitrogen-containing heterocycles, and have already described simple, efficient procedures, and MCRs[19] for preparation of 2,3-dihydroquinazolin-4(3*H*)-one,[20] oxindole,[21] and spirooxindole.[22] We have designed the regioselective three-component one-pot synthesis of 1′*H*-spiro[indoline-3,2′-quinazoline]-2,4′(3′*H*)-diones **4a–m** from isatoic anhydride **1**, isatins **2a–c**, and primary amines **3a–m** using non-toxic and easily available alum as a heterogeneous catalyst (Scheme 1).[23–26]

When a mixture of isatoic anhydride **1**, isatin **2a**, and aniline **3b** in ethanol was stirred and refluxed in the presence of a catalytic amount of alum $KAl(SO_4)_2{\cdot}12H_2O$, the reaction was complete within 8 h. Workup of the reaction mixture showed that 1′*H*-spiro[indoline-3,2′-quinazoline]-2,4′(3′*H*)-dione **4b** was prepared in 88% yield. Interestingly, we have found that this reaction is highly regioselective in the preparation of 1′*H*-spiro[indoline-3,2′-quinazoline]-2,4′(3′*H*)-diones **4**, since there is no evidence for the formation of iminoisatins **5**,[27] 6-arylimino-6*H*-indolo[2,1-

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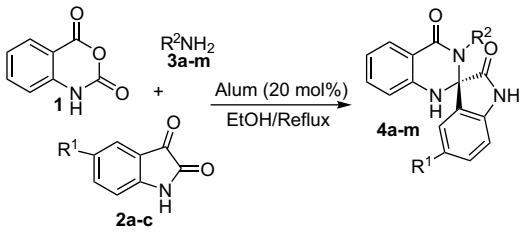
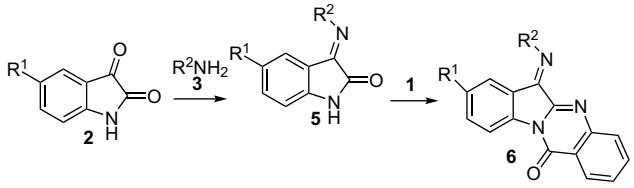
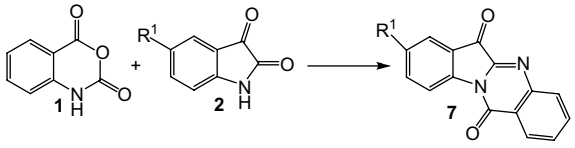
b]quinazolin-12-one **6**[28] or indolo[2,1-*b*]quinazoline-6,12-dione **7**[29] (Schemes 2 and 3).



Scheme 1.



Scheme 2.



Scheme 3.

Encouraged by this success, we extended this reaction of isatoic anhydride with a range of other isatins **2** and amines **3** under similar conditions, furnishing the respective 1′*H*-spiro[indoline-3,2′-quinazoline]-2,4′(3′*H*)-diones **4** in good yields. The optimized results are summarized in Table 1.

It is noticeable that when the isatoic anhydride **1**, isatin **2a**–**m**, and amines **3a**–**m** in the presence of alum were stirred at reflux for within 1.5 h, in all cases the reaction led to the formation of the intermediates **8** that could be isolated and characterized by spectroscopic methods. Furthermore, the continuation of reaction for 4 h led to a mixture of **4a**–**m** and intermediates **8** (monitored by TLC and spectroscopic methods), meanwhile after the times indicated in Table 1, just **4a**–**m** were obtained and the intermediates **8** were not detected in the final mixture.

Notably, imines **5** were not detected in this reaction pathway. According to these results, the reaction can be mechanistically considered to proceed via the initial formation of the intermediates **8** from isatoic anhydride and amines, then intermediates **8** reaction with isatin in the presence of alum gives the intermediate **9**. Once intermediate **9** is formed, a nucleophilic attack takes place by the nitrogen group and the final product is produced (Scheme 4).

The structures of products were characterized by IR, ^{1}H NMR, ^{13}C NMR, MS spectra, and elemental analysis.

Table 1
The synthesis of 1′*H*-spiro[isoindoline-1,2′-quinazoline]-3,4′(3′*H*)-dione **4a**–**m**

Product **4**	R^1	R^2	Time (h)	Yield[a] (%)	Mp (°C)	Lit. mp (°C)
a	H	H	6	92	261–263 dec	—
b	H	Ph	8	91	251–253 dec	—
c	H	*p*-$CH_3C_6H_4$	7	93	271–273 dec	—
d	H	*p*-$CH_3OC_6H_4$	8	92	269–271 dec	—
e	H	*p*-BrC_6H_4	8	86	213–215 dec	—
f	H	*p*-ClC_6H_4	8	85	264–266 dec	—
g	H	$PhCH_2$	7	92	190–192 dec	—
h	Br	*p*-$CH_3C_6H_4$	8	89	150–152 dec	—
i	F	*p*-$CH_3C_6H_4$	9	88	245–247 dec	—
j	H	Et	10	78	274–276 dec	—
k	H	*n*-Pr	10	82	204–206 dec	—
l	H	*n*-Bu	11	84	216–218 dec	—
m	H	*n*-Pen	11	81	237–239 dec	—

[a] Yields of pure isolated product based on isatin.

3. Conclusions

In summary, we have described a successful strategy, an efficient and convenient synthesis for the preparation of 1′*H*-spiro[indoline-3,2′-quinazoline]-2,4′(3′*H*)-diones via a three-component cyclocondensation of isatoic anhydride, isatins, and amines, using the inexpensive, non-toxic, and easily available $KAl(SO_4)_2{\cdot}12H_2O$ catalyst. The method offers several advantages including high yield of products and easy experimental workup procedure. Surprisingly, this reaction is regioselective in the preparation of 1′*H*-spiro[indoline-3,2′-quinazoline]-2,4′(3′*H*)-diones, which makes it a useful process for the synthesis of 1′*H*-spiro[indoline-3,2′-quinazoline]-2,4′(3′*H*)-diones.

4. Experimental

4.1. General methods

Melting points were obtained in open capillary tubes and were measured on an electro-thermal 9200 apparatus. Mass spectra were recorded on a Shimadzu QP 1100 BX mass spectrometer. The IR spectra were recorded on KBr pellets on a Shimadzu IR-470 spectrophotometer. ^{1}H and ^{13}C NMR spectra were determined on a Bruker 300 DRX Avance instrument at 300 and 75 MHz. Elemental analysis for C, H, and N was performed using a Heraus CHN rapid analyzer. The chemical used in this work were purchased from Merck and Fluka, and $KAl(SO_4)_2{\cdot}12H_2O$ was from Merck.

4.2. General experimental procedure for synthesis of 1′*H*-spiro[isoindoline-1,2′-quinazoline]-3,4′(3′*H*)-dione

A mixture of isatoic anhydride **1** (1 mmol), isatin **2** (1 mmol), primary amines **3** (1 mmol), 0.1 g (0.2 mmol) alum, and 10 ml EtOH in a 50 ml flask was stirred at reflux for the time period as indicated in Table 1. After completion of the reaction (monitored by TLC, ethyl acetate/*n*-hexane, 1:1), 25 ml EtOH was added to the reaction mixture, and recrystallized from ethanol to afford pure product.

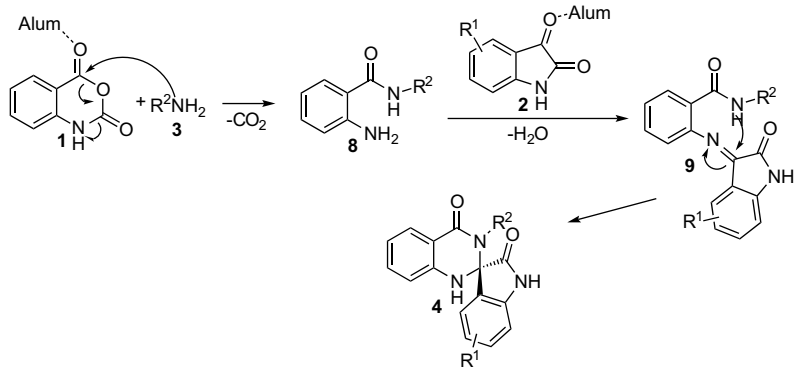
4.3. Typical experimental procedure

*4.3.1. 1′H-Spiro[indoline-3,2′-quinazoline]-2,4′(3′H)-dione (**4a**)*

Cream powder; mp 261–263 °C dec; IR (KBr) (ν_{max}, cm^{-1}): 3491 (NH), 3227(NH), 2964, 1725 (C=O), 1642 (C=O), 1614, 1526; ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 6.60 (d, 1H, *J*=8.0, ArH), 6.68 (t, 1H, *J*=7.4, ArH), 6.84 (d, 1H, *J*=7.7, ArH), 7.05 (t, 1H, *J*=7.4, ArH), 7.22 (t, 1H, *J*=7.2, ArH), 7.28 (s, 1H, NH), 7.33 (t, 1H, *J*=7.8, ArH), 7.47 (d, 1H, *J*=7.3, ArH), 7.59 (d, 1H, *J*=7.4, ArH), 8.36 (s, 1H, NH), 10.30 (s, 1H, NH); ^{13}C NMR (75 MHz, DMSO-d_6): δ_C 71.41, 110.53, 114.31, 114.76, 117.61, 122.73, 125.81, 127.30, 129.89, 131.26, 133.75, 142.58, 147.28, 164.40, 176.47; MS (EI, 70 eV) (*m*/*z*, %): 265 (M^+, 25), 263 (50), 237 (100), 119 (95), 92 (60), 63 (35), 50 (30), 39 (40). Anal. Calcd for $C_{15}H_{11}N_3O_2$: C, 67.92; H, 4.18; N, 15.84. Found: C, 67.80; H, 4.11; N, 15.73.

*4.3.2. 3′-Phenyl-1′H-spiro[indoline-3,2′-quinazoline]-2,4′(3′H)-dione (**4b**)*

Yellow powder; mp 251–253 °C dec; IR (KBr) (ν_{max}, cm^{-1}): 3428 (NH), 3265 (NH), 2916, 1727 (C=O), 1642 (C=O), 1616; ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 6.63 (d, 1H, *J*=7.7, ArH), 6.70–6.78 (m, 2H,



Scheme 4.

ArH), 6.92 (t, 1H, *J*=7.4, ArH), 6.98 (d, 2H, *J*=7.0, ArH), 7.12–7.23 (m, 4H, ArH), 7.30 (t, 1H, *J*=7.0, ArH), 7.53 (d, 1H, *J*=7.3, ArH), 7.63 (s, 1H, NH), 7.66 (d, 1H, *J*=7.0, ArH), 10.42 (s, 1H, NH); ^{13}C NMR (75 MHz, DMSO-d_6): δ_C 76.85, 110.57, 114.57, 115.04, 118.17, 122.59, 126.96, 127.75, 127.90, 128.10, 129.11, 129.74, 131.29, 134.16, 138.55, 142.12, 146.58, 164.08, 175.96; MS (EI, 70 eV) (*m*/*z*, %): 341 (M^+, 5), 313 (100), 269 (15), 249 (15), 221 (25), 194 (25), 167 (15), 120 (60), 92 (30), 77 (80), 63 (35), 51 (50), 39 (40). Anal. Calcd for $C_{21}H_{15}N_3O_2$: C, 73.89; H, 4.43; N, 12.31. Found: C, 73.80; H, 4.32; N, 12.25.

*4.3.3. 3′-p-Tolyl-1′H-spiro[indoline-3,2′-quinazoline]-2,4′(3′H)-dione (**4c**)*

Cream powder; mp 271–273 °C dec; IR (KBr) (ν_{max}, cm^{-1}): 3420 (NH), 3258 (NH), 2964, 1708 (C=O), 1644 (C=O), 1613, 1503; ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 2.17 (s, 3H, CH_3), 6.63–6.77 (m, 3H, ArH), 6.85 (d, 2H, *J*=8.2, ArH), 6.93 (d, 2H, *J*=7.5, ArH), 6.99 (d, 2H, *J*=8.2, ArH), 7.15 (t, 1H, *J*=7.2, ArH), 7.29 (t, 1H, *J*=7.0, ArH), 7.53 (d, 1H, *J*=7.3, ArH), 7.60 (s, 1H, NH), 7.64 (d, 1H, *J*=7.0, ArH), 10.40 (s, 1H, NH); ^{13}C NMR (75 MHz, DMSO-d_6): δ_C 21.00, 76.86, 110.59, 114.51, 115.04, 118.09, 122.60, 126.90, 127.88, 127.96, 129.65, 131.26, 134.08, 135.91, 137.30, 142.10, 146.56, 164.12, 175.96; MS (EI, 70 eV) (*m*/*z*, %): 355 (M^+, 5), 353 (15), 327 (100), 249 (15), 235 (25), 208 (25), 120 (50), 91 (35), 77 (20), 65 (45), 51 (30), 39 (30). Anal. Calcd for $C_{22}H_{17}N_3O_2$: C, 74.35; H, 4.82; N, 11.82. Found: C, 74.24; H, 4.73; N, 11.74.

*4.3.4. 3′-(4-Methoxyphenyl)-1′H-spiro[indoline-3,2′-quinazoline]-2,4′(3′H)-dione (**4d**)*

Cream powder; mp 269–271 °C dec; IR (KBr) (ν_{max}, cm^{-1}): 3426 (NH), 3287(NH), 2964, 1726 (C=O), 1638 (C=O), 1612, 1510; ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 3.64 (s, 3H, OCH_3), 6.67–6.75 (m, 5H, ArH), 6.89–9.91 (m, 3H, ArH), 7.16–7.29 (m, 2H, ArH), 7.55 (s, 1H, NH), 7.59–7.68 (m, 2H, ArH), 10.40 (s, 1H, NH); ^{13}C NMR (75 MHz, DMSO-d_6): δ_C 55.54, 77.03, 110.59, 114.23, 114.50, 115.01, 118.09, 122.63, 126.85, 127.92, 128.08, 131.02, 131.23, 134.08, 142.08, 146.59, 158.61, 164.27, 175.97; MS (EI, 70 eV) (*m*/*z*, %): 371 (M^+, 5), 369 (15), 343 (100), 328 (90), 249 (35), 221 (25), 192 (25), 120 (40), 91 (45), 77 (60), 65 (45), 51 (45), 39 (50). Anal. Calcd for $C_{22}H_{17}N_3O_3$: C, 71.15; H, 4.61; N, 11.31. Found: C, 71.06; H, 4.53; N, 11.20.

*4.3.5. 3′-(4-Bromophenyl)-1′H-spiro[indoline-3,2′-quinazoline]-2,4′(3′H)-dione (**4e**)*

Yellow powder; mp 213–215 °C dec; IR (KBr) (ν_{max}, cm^{-1}): 3429 (NH), 3252 (NH), 2964, 1725 (C=O), 1642 (C=O), 1614; ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 6.67–6.79 (m, 3H, ArH), 6.93–6.97 (m, 3H, ArH), 7.16 (t, 1H, *J*=7.6, ArH), 7.31 (t, 1H, *J*=7.2, ArH), 7.41 (d, 2H, *J*=8.4, ArH), 7.56 (d, 1H, *J*=7.3, ArH), 7.67 (s, 1H, NH), 7.69 (d, 1H, *J*=7.0, ArH), 10.47 (s, 1H, NH); ^{13}C NMR (75 MHz, DMSO-d_6): δ_C 76.81, 110.74, 114.65, 114.75, 118.25, 120.71, 121.24, 126.97, 127.46, 127.93, 131.53, 131.99, 132.21, 134.34, 137.91, 142.13, 146.59, 164.08, 175.77; MS (EI, 70 eV) (*m*/*z*, %): 419 (M^+, 5), 391 (100), 301 (15), 272 (15), 249 (35), 221 (15), 194 (25), 171 (35), 155 (20), 120 (90), 92 (45), 77 (60), 63 (65), 51 (65), 39 (55). Anal. Calcd for $C_{21}H_{14}BrN_3O_2$: C, 60.02; H, 3.36; N, 10.00. Found: C, 59.83; H, 3.26; N, 9.89.

*4.3.6. 3′-(4-Chlorophenyl)-1′H-spiro[indoline-3,2′-quinazoline]-2,4′(3′H)-dione (**4f**)*

Yellow powder; mp 264–266 °C dec; IR (KBr) (ν_{max}, cm^{-1}): 3427 (NH), 3337 (NH), 2964, 1739 (C=O), 1643 (C=O), 1608, 1491; ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 6.66–6.78 (m, 3H, ArH), 6.92–7.02 (m, 3H, ArH), 7.16 (t, 1H, *J*=7.5, ArH), 7.28–7.33 (m, 3H, ArH), 7.56 (d, 1H, *J*=7.3, ArH), 7.63 (d, 1H, *J*=7.3, ArH), 7.66 (s, 1H, NH), 10.46 (s, 1H, NH); ^{13}C NMR (75 MHz, DMSO-d_6): δ_C 76.86, 110.73, 114.65, 114.76, 118.24, 122.75, 126.98, 127.47, 127.93, 129.25, 131.52, 131.66, 132.66, 134.34, 137.47, 142.14, 146.60, 164.13, 175.79; MS (EI, 70 eV) (*m*/*z*, %): 375 (M^+, 5), 347 (100), 249 (35), 228 (15), 192 (25), 166 (25), 120 (70), 92 (35), 75 (60), 63 (65), 51 (60), 39 (60). Anal. Calcd for $C_{21}H_{14}ClN_3O_2$: C, 67.12; H, 3.75; N, 11.18. Found: C, 67.01; H, 3.76; N, 11.09.

*4.3.7. 3′-Benzyl-1′H-spiro[indoline-3,2′-quinazoline]-2,4′(3′H)-dione (**4g**)*

Cream powder; mp 190–192 °C dec; IR (KBr) (ν_{max}, cm^{-1}): 3480 (NH), 3329 (NH), 2924, 1729 (C=O), 1623 (C=O), 1610; ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 4.15–4.20 (d, *J*=15.3, 1H, CH_2), 4.47–4.52 (d, *J*=15.3, 1H, CH_2), 6.67 (d, 1H, *J*=7.9, ArH), 6.76 (t, 1H, *J*=7.4, ArH), 6.81 (d, 1H, *J*=7.6, ArH), 6.90–6.92 (m, 3H, ArH), 7.14–7.16 (t, 2H, ArH), 7.24–7.34 (m, 3H, ArH), 7.48 (s, 1H, NH), 7.73 (d, 1H, *J*=7.5, ArH), 10.36 (s, 1H, NH); ^{13}C NMR (75 MHz, DMSO-d_6): δ_C 46.31, 75.54, 110.91, 114.41, 115.06, 118.12, 122.41, 126.71, 126.76, 127.27, 127.82, 127.87, 128.24, 131.73, 133.86, 137.83, 142.97, 146.47, 164.53, 175.47; MS (EI, 70 eV) (*m*/*z*, %): 355 (M^+, 5), 353 (20), 327 (100), 249 (20), 235 (25), 208 (25), 120 (50), 91 (30), 77 (30), 65 (35), 51 (20), 39 (35). Anal. Calcd for $C_{22}H_{17}N_3O_2$: C, 74.35; H, 4.82; N, 11.82. Found: C, 74.23; H, 4.71; N, 11.70.

*4.3.8. 5-Bromo-3′-p-tolyl-1′H-spiro[indoline-3,2′-quinazoline]-2,4′(3′H)-dione (**4h**)*

Yellow powder; mp 150–152 °C dec; IR (KBr) (ν_{max}, cm^{-1}): 3450 (NH), 3236 (NH), 1736 (C=O), 1645 (C=O), 1613, 1512; ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 2.08 (s, 3H, CH_3), 6.60 (d, 1H, *J*=8.2, ArH), 6.67 (d, 1H, *J*=7.7, ArH), 6.74 (t, 1H, ArH), 6.89 (d, 2H, *J*=6.7, ArH), 7.03 (d, 1H, *J*=7.8, ArH), 7.28–7.35 (m, 2H, ArH), 7.65–7.69 (m, 2H, ArH), 7.76 (s, 1H, NH), 10.55 (s, 1H, NH); ^{13}C NMR (75 MHz, DMSO-d_6): δ_C 21.03, 76.87, 112.66, 114.17, 114.54, 114.98, 118.34, 127.94, 129.68, 129.81, 130.15, 134.03, 134.21, 135.69, 137.61, 141.44, 146.27, 163.91, 175.64; MS (EI, 70 eV) (*m*/*z*, %): 434 (M^+, 10), 405 (95), 327 (25), 286 (35), 250 (15), 209 (15), 192 (25), 166 (25), 146 (20), 120

(100), 91 (85), 77 (60), 65 (95), 51 (60), 39 (70). Anal. Calcd for $C_{22}H_{16}BrN_3O_2$: C, 60.84; H, 3.71; N, 9.68. Found: C, 60.74; H, 3.62; N, 9.57.

4.3.9. 5-Fluoro-3′-p-tolyl-1′H-spiro[indoline-3,2′-quinazoline]-2,4′(3′H)-dione (**4i**)

Cream powder; mp 245–247 °C dec; IR (KBr) (ν_{max}, cm^{-1}): 3440 (NH), 3264 (NH), 1720 (C=O), 1640 (C=O), 1484; ^1H NMR (300 MHz, DMSO-d_6): δ_H 2.18 (s, 3H, CH_3), 6.62–6.67 (m, 2H, ArH), 6.67 (t, 1H, J=7.6, ArH), 6.90 (d, 2H, J=7.5, ArH), 6.97–7.05 (m, 3H, ArH), 7.65 (t, 1H, J=7.7, ArH), 7.50 (d, 1H, J=7.7, ArH), 7.63–7.65 (m, 1H, ArH), 7.67 (s, 1H, NH), 10.45 (s, 1H, NH); ^{13}C NMR (75 MHz, DMSO-d_6): δ_C 21.00, 77.09, 111.54, 111.64, 114.51, 114.67, 114.97, 118.29, 127.91, 129.34, 129.47, 129.78, 134.19, 135.71, 137.56, 138.35, 146.34, 163.99, 176.19; MS (EI, 70 eV) (m/z, %): 373 (M^+, 10), 345 (100), 329 (15), 269 (25), 253 (25), 226 (35), 120 (50), 91 (45), 77 (40), 65 (45), 51 (30), 39 (35). Anal. Calcd for $C_{22}H_{16}FN_3O_2$: C, 70.77; H, 4.32; N, 11.25. Found: C, 70.66; H, 4.22; N, 11.13.

4.3.10. 3′-Ethyl-1′H-spiro[indoline-3,2′-quinazoline]-2,4′(3′H)-dione (**4j**)

Yellowish powder; mp 274–276 °C dec; IR (KBr) (ν_{max}, cm^{-1}): 3294 (NH), 1724 (C=O), 1635 (C=O), 1615; ^1H NMR (300 MHz, DMSO-d_6): δ_H 0.89 (t, 3H, J=6.9, CH_3), 2.81–2.92 (m, 1H, CH_2), 3.13–3.24 (m, 1H, CH_2), 6.60 (d, 1H, J=8.0, ArH), 6.70 (t, 1H, J=7.3, ArH), 6.92 (d, 1H, J=7.7, ArH), 7.10 (t, 1H, J=7.4, ArH), 7.22 (t, 1H, J=7.1, ArH), 7.36–7.41 (m, 1H, ArH, 1H, NH), 7.51 (d, 1H, J=7.3, ArH), 7.63 (d, 1H, J=7.3, ArH), 10.55 (s, 1H, NH); ^{13}C NMR (75 MHz, DMSO-d_6): δ_C 14.01, 38.30, 75.68, 111.14, 114.17, 114.92, 117.97, 122.99, 126.20, 127.51, 127.98, 131.77, 133.65, 142.60, 146.13, 163.66, 175.95; MS (EI, 70 eV) (m/z, %): 264 (M^+−Et, 100), 249 (35), 119 (25), 92 (35), 77 (30), 63 (30), 51 (30), 39 (30). Anal. Calcd for $C_{17}H_{15}N_3O_2$: C, 69.61; H, 5.15; N, 14.33. Found: C, 69.53; H, 5.06; N, 14.22.

4.3.11. 3′-n-Propyl-1′H-spiro[indoline-3,2′-quinazoline]-2,4′(3′H)-dione (**4k**)

Yellow powder; mp 204–206 °C dec; IR (KBr) (ν_{max}, cm^{-1}): 3263 (NH), 1722 (C=O), 1687 (C=O), 1624; ^1H NMR (300 MHz, DMSO-d_6): δ_H 0.61 (t, 3H, J=7.2, CH_3), 1.24–1.34 (m, 1H, CH_2), 1.35–1.40 (m, 1H, CH_2), 2.69–2.79 (m, 1H, CH_2), 3.06–3.16 (m, 1H, CH_2), 6.60 (d, 1H, J=8.0, ArH), 6.70 (t, 1H, J=7.4, ArH), 6.92 (d, 1H, J=7.7, ArH), 7.09 (t, 1H, J=7.4, ArH), 7.22 (t, 1H, J=7.5, ArH), 7.36–7.39 (m, 1H, ArH, 1H, NH), 7.50 (d, 1H, J=7.3, ArH), 7.63 (d, 1H, J=7.5, ArH), 10.31 (s, 1H, NH); ^{13}C NMR (75 MHz, DMSO-d_6): δ_C 11.73, 21.81, 45.07, 75.69, 111.11, 114.20, 114.99, 117.97, 122.91, 126.24, 127.58, 127.88, 131.76, 133.64, 142.61, 146.17, 163.91, 175.84; MS (EI, 70 eV) (m/z, %): 278 (M^+−Et, 100), 263 (45), 237 (70), 119 (55), 92 (45), 79 (30), 65 (30), 51 (30), 39 (35). Anal. Calcd for $C_{18}H_{17}N_3O_2$: C, 70.34; H, 5.58; N, 13.67. Found: C, 70.25; H, 5.49; N, 13.60.

4.3.12. 3′-n-Butyl-1′H-spiro[indoline-3,2′-quinazoline]-2,4′(3′H)-dione (**4l**)

Orange powder; mp 216–218 °C dec; IR (KBr) (ν_{max}, cm^{-1}): 3260 (NH), 1724 (C=O), 1685 (C=O), 1622; ^1H NMR (300 MHz, DMSO-d_6): δ_H 0.64 (t, 3H, J=7.2, CH_3), 0.96–1.07 (m, 1H, CH_2), 1.17–1.25 (m, 1H, CH_2), 1.27–1.36 (m, 1H, CH_2), 2.75–2.85 (m, 1H, CH_2), 3.08–3.18 (m, 1H, CH_2), 6.60 (d, 1H, J=8.0, ArH), 6.70 (t, 1H, J=7.4, ArH), 6.91 (d, 1H, J=7.7, ArH), 7.10 (t, 1H, J=7.5, ArH), 7.22 (t, 1H, J=7.8, ArH), 7.36–7.41 (m, 1H, ArH, 1H, NH), 7.50 (d, 1H, J=7.3, ArH), 7.62 (d, 1H, J=7.6, ArH), 10.55 (s, 1H, NH); ^{13}C NMR (75 MHz, DMSO-d_6): δ_C 13.77, 19.96, 30.41, 43.00, 75.66, 111.06, 114.18, 115.01, 117.95, 122.88, 126.33, 127.55, 127.82, 131.77, 133.61, 142.63, 146.17, 163.82, 175.88; MS (EI, 70 eV) (m/z, %): 292 (M^+−Et, 100), 277 (30), 263 (25), 249 (55), 237 (85), 119 (55), 92 (35), 77 (25), 65 (25), 41 (25). Anal. Calcd for $C_{19}H_{19}N_3O_2$: C, 71.01; H, 5.96; N, 13.08. Found: C, 70.92; H, 5.81; N, 13.00.

4.3.13. 3′-n-Pentyl-1′H-spiro[indoline-3,2′-quinazoline]-2,4′(3′H)-dione (**4m**)

Reddish powder; mp 237–239 °C dec; IR (KBr) (ν_{max}, cm^{-1}): 3284 (NH), 1729 (C=O), 1627 (C=O); ^1H NMR (300 MHz, DMSO-d_6): δ_H 0.70 (t, 3H, J=7.0, CH_3), 1.01–1.08 (m, 4H, $2CH_2$), 1.23–1.28 (m, 1H, CH_2), 1.33–1.42 (m, 1H, CH_2), 2.74–2.86 (m, 1H, CH_2), 3.10–3.19 (m, 1H, CH_2), 6.62 (d, 1H, J=8.0, ArH), 6.71 (t, 1H, J=7.5, ArH), 6.93 (d, 1H, J=7.7, ArH), 7.07 (t, 1H, J=7.5, ArH), 7.22 (t, 1H, J=7.5, ArH), 7.36–7.41 (m, 1H, ArH, 1H, NH), 7.51 (d, 1H, J=7.3, ArH), 7.64 (d, 1H, J=7.6, ArH), 10.56 (s, 1H, NH); ^{13}C NMR (75 MHz, DMSO-d_6): δ_C 14.05, 21.84, 27.79, 28.88, 43.29, 75.68, 111.07, 114.20, 115.03, 117.96, 122.87, 126.29, 127.57, 127.85, 131.74, 133.60, 142.63, 146.18, 163.85, 175.90; MS (EI, 70 eV) (m/z, %): 306 (M^+−Et, 100), 291 (40), 264 (35), 250 (75), 237 (95), 221 (25), 119 (65), 92 (55), 77 (35), 65 (30), 50 (25), 41 (75). Anal. Calcd for $C_{20}H_{21}N_3O_2$: C, 71.62; H, 6.31; N, 12.53. Found: C, 71.51; H, 6.21, N, 12.41.

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