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ORIGINAL PAPER

# A convenient synthesis of spiroindolo[2,1-*b*]quinazoline-6,2′-[1,3,4]oxadiazoles from tryptanthrin and nitrile imines

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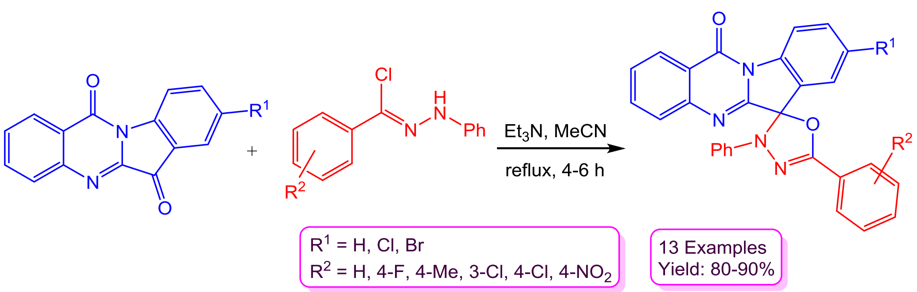
## Abstract

A convenient method for the synthesis of functionalized spiroindolo[2,1-*b*]quinazoline-6,2′-[1,3,4]oxadiazoles from indolo[2,1-*b*]quinazoline-6,12-diones and 13 hydrazonoyl chlorides in refluxing MeCN is described. These transformations are highlighted by inert atmosphere and lack of activator or metal promoters.


### Graphical abstract




**Keywords** Spiro compound · 1,3-Dipolar cycloaddition · Tryptanthrin · 1,3,4-Oxadiazole · Azomethine ylide

## Introduction

Development of heterocyclic synthesis has always been an important area in synthetic organic chemistry [1]. Spiro heterocycles are regarded as a privileged framework because of their rigidity, three-dimensional geometries, and wide distribution in various natural products and synthetic molecules. Currently, these spirans are attracting considerable interest in organic chemistry because of their molecular structure and diverse biological activities [2]. In particular, spiroindoles represent important structural motifs that can be found in many biologically active synthetic compounds and natural products [3, 4].

Synthesis of spirooxindoles is significant in medicinal chemistry due to their biological and pharmacological properties [5, 6]. Spirooxindoles are found in many natural products [7, 8], which often possess antitumor [9], antimicrobial [10], antibacterial [11], antimalarial [12], and anti-inflammatory [13] activities.

Heterocyclic systems containing 1,3,4-oxadiazole moiety are synthetic interest due to their potential biological activities [14]. Beside the numerous applications in medicinal chemistry [15, 16], 1,3,4-oxadiazoles are building blocks in the synthesis of natural products [17]. Furthermore, oxadiazoles have found practical applications as organic light-emitting diodes and liquid crystals [18].

Quinazolines are important nitrogen-containing heterocyclic systems that have been studied because of their presence in different natural products and synthetic drugs [19].

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Quinazoline derivatives are also used in veterinary, agrochemical, and pharmaceutical industries [20].

Natural alkaloid tryptanthrin (indolo[2,1-*b*]quinazoline-6,12-dione) and its analogs are found to exhibit antitubercular activity [21]. Tryptanthrin (Fig. 1) consists of a quinazoline ring fused to an indole moiety with carbonyl groups in the 6 and 12 positions [22]. Various approaches have been explored for efficient construction of this skeleton [23]. The derivatives of tryptanthrin, such as methylisatoid, candidine, ophiuroidine, phaitanthrin A–E, (±)-cruciferane, and cephalanthrine A–B (Fig. 1), have been found in plants and show broad spectrum of biological activities [24–27].

## Results and discussion

Stimulated by the structure and biological significance of tryptanthrin motif, the construction of this type of nucleus has received much attention from the organic chemistry community [28–30]. Reaction between isatoic anhydride and isatin derivatives, in the presence of a base, is a convenient method for the synthesis of tryptanthrin derivatives [19, 31]. The synthesis of tryptanthrins has been previously reported under different reaction conditions [28, 32, 33].

Nitrile imines are easily generated in situ by treatment of hydrazonoyl chlorides [34] with $Et_3N$ [35]. The reaction of these 1,3-dipoles with a carbonyl group constitutes an effective method for the synthesis of structurally complex spiroindolo[2,1-*b*]quinazoline-6,2′-[1,3,4]oxadiazoles from readily available precursors [36]. In continuation of our interest in the synthesis of heterocyclic compounds using nitrile imines [37], we describe an efficient procedure for the synthesis of 5′-aryl-3′-phenyl-3′*H*,12*H*-spiro[indolo[2,1-*b*]quinazoline-6,2′-[1,3,4]oxadiazol]-12-ones **3** from tryptanthrins **1** and hydrazonoyl chlorides **2**. Thus, stirring a mixture of **1a** and **2a** in MeOH in the presence of $Et_3N$ at 60 °C for 4 h led to the formation of **3a** in 10% yield (Table 1, entry 1). Product **3a** was obtained in 40% yield in $CH_2Cl_2$ (Table 1, entry 5). The use of MeCN as solvent led to an improved yield of 53% (Table 1, entry 6). Compound **3a** was obtained in 76% yield in the presence of 1,4-diazabicyclo[2.2.2]octane (DABCO) (Table 1, entry 7). Finally, when the reaction was performed in MeCN at 80 °C in the presence of $Et_3N$, the yield was 85%.

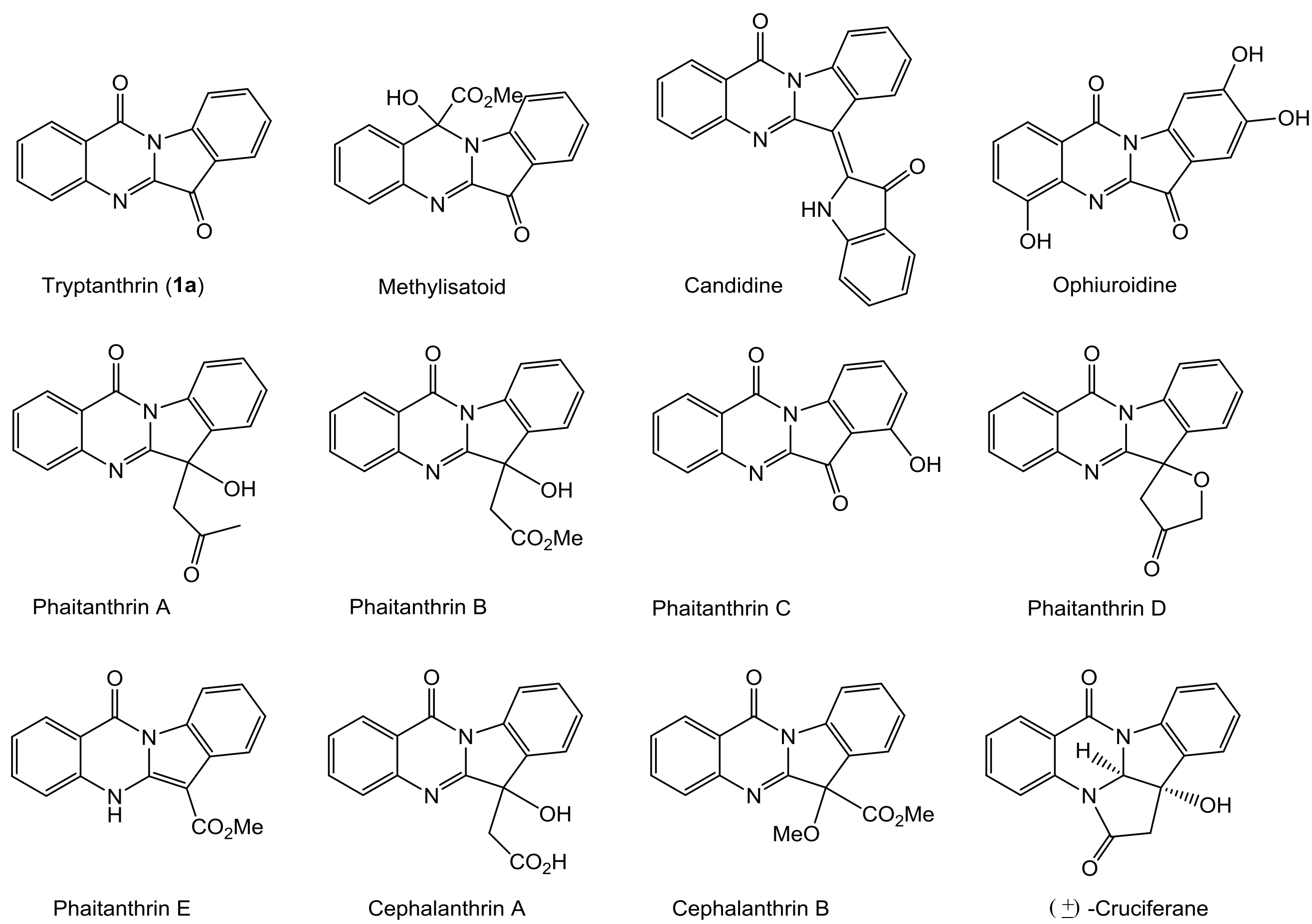
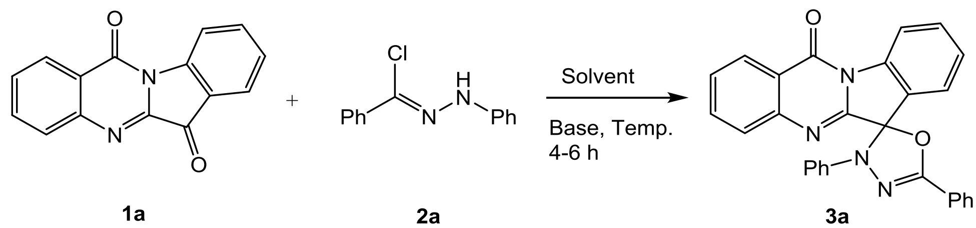



**Fig. 1** Tryptanthrin and related biologically active alkaloids

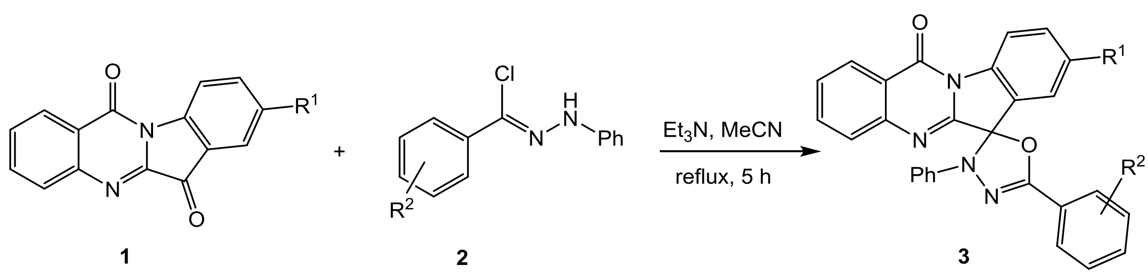
**Table 1** Optimization of the reaction conditions for the formation of spiroindolo[2,1-*b*]quinazoline-6,2′-[1,3,4]oxadiazole **3a**




| Entry | Base | Solvent | Temp./°C | Yield/%[a] |
|---|---|---|---|---|
| 1 | $Et_3N$ | MeOH | 60 | 10 |
| 2 | $Et_3N$ | Toluene | 100 | 5 |
| 3 | $Et_3N$ | DMF | rt | Trace |
| 4 | $Et_3N$ | DMF | 80 | 15 |
| 5 | $Et_3N$ | $CH_2Cl_2$ | rt | 40 |
| 6 | $Et_3N$ | MeCN | rt | 53 |
| 7 | DABCO | MeCN | 80 | 76 |
| 8 | $Et_3N$ | MeCN | 80 | 85 |

[a]Isolated yield

**Table 2** Convenient synthesis of spirooxadiazoles **3**[a]

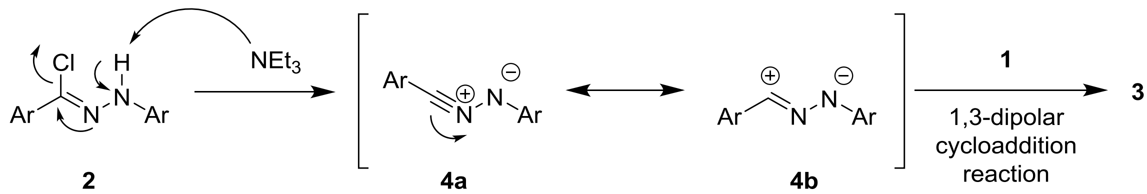



| Entry | $R^1$ | $R^2$ | Product | Yield/%[b] |
|---|---|---|---|---|
| 1 | H | H | **3a** | 85 |
| 2 | H | 4-F | **3b** | 87 |
| 3 | H | 4-Me | **3c** | 80 |
| 4 | H | 3-Cl | **3d** | 86 |
| 5 | H | 4-Cl | **3e** | 90 |
| 6 | H | $4\text{-}NO_2$ | **3f** | 85 |
| 7 | Cl | H | **3g** | 86 |
| 8 | Cl | 4-Me | **3h** | 83 |
| 9 | Cl | 4-Cl | **3i** | 88 |
| 10 | Br | H | **3j** | 85 |
| 11 | Br | 4-F | **3k** | 85 |
| 12 | Br | 3-Cl | **3l** | 87 |
| 13 | Br | 4-Cl | **3m** | 89 |

[a]Reaction conditions: **1** (0.5 mmol), **2** (0.5 mmol), **3** (0.5 mmol), 2 $cm^3$ solvent, reflux

[b]Yield of isolated product

**Scheme 1**




Then, we used the optimized reaction conditions to prepare a series of functionalized spirooxadiazoles **3a**–**3 m** from **1** to **2**. The reactions proceeded smoothly providing the spirooxadiazole derivatives in moderate-to-good yields (Table 2).

The structures of products **3a**–**3 m** were confirmed by their IR, $^{1}$H NMR, and $^{13}$C NMR spectroscopic data. The mass spectra of products **3** displayed the molecular ion peaks at appropriate *m/z* values. The $^{1}$H NMR spectrum of **3a** showed characteristic multiplets for the aromatic protons at 6.75–8.68 ppm. The $^{1}$H-decoupled $^{13}$C NMR spectrum of **3a** showed 24 signals in agreement with the proposed structure.

A plausible mechanism for the formation of product **3** is given in Scheme 1. Presumably, the initial event involves the formation of nitrile imine intermediate **4** from the reaction of hydrazonoyl chloride and $Et_3N$. Then, the 1,3-dipolar cycloaddition reaction of intermediate **4** with the C=O group of tryptanthrin **1** generates product **3** (Scheme 1).

## Conclusion

In summary, we have developed an efficient method for the synthesis of 5′-aryl-3′-phenyl-3′*H*,12*H*-spiro[indolo[2,1-*b*]-quinazoline-6,2′-[1,3,4]oxadiazol]-12-ones from indolo[2,1-*b*]quinazoline-6,12-diones and hydrazonoyl chlorides in refluxing MeCN. This protocol has some advantages such as using available starting materials, relatively short reaction time, neutral reaction conditions, and high yields of product.

## Experimental

All purchased solvents and chemicals were of analytical grade and used without further purification. Melting points and IR spectra of all the compounds were measured on an Electrothermal 9100 apparatus and a Shimadzu IR-460 spectrometer, respectively. The $^{1}$H and $^{13}$C NMR spectra were obtained with a BRUKER DRX-500 AVANCE instrument using $CDCl_3$ as applied solvent and TMS as internal standard at 500.1 and 125.7 MHz, respectively. The abbreviations used for NMR signals: s = singlet, d = doublet, t = triplet, and m = multiplet. Mass spectra were recorded on an FINNIGAN-MAT 8430 mass spectrometer operating at an ionization potential of 70 eV. Elemental analyses for C, H, and N were performed using a Heraeus CHN-O-Rapid analyzer.

### General procedure for the preparation of compounds 3a–3m

A mixture of tryptanthrin **1** (1 mmol), hydrazonoyl chloride **2** (1 mmol), and $Et_3N$ (1 mmol) in 5 $cm^3$ MeCN was stirred in 80 °C for 4–6 h. After completion of the reaction (TLC), the mixture was filtered and the precipitate washed with EtOH to afford the pure products **3**.

**3′,5′-Diphenyl-3′*H*,12*H*-spiro[indolo[2,1-*b*]quinazoline-6,2′-[1,3,4]oxadiazol]-12-one (3a, $C_{28}H_{18}N_4O_2$)** Yellow powder; yield: 0.38 g (85%); m.p.: 235 °C (decomposed); $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta = 6.75$–6.79 (m, 3H, Ar), 7.06 (t, $^{3}J = 7.3$ Hz, 2H, Ar), 7.38 (t, $^{3}J = 7.55$ Hz, 1H, Ar), 7.44–7.76 (m, 8H, Ar), 7.93–7.95 (m, 2H, Ar), 8.43 (d, $^{3}J = 7.9$ Hz, 1H, Ar), 8.68 (d, $^{3}J = 8.4$ Hz, 1H, Ar) ppm; $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta = 98.8$ (C), 114.5 (2 CH), 117.6 (CH), 121.0 (CH), 122.4 (C), 125.0 (C), 125.8 (CH), 126.2 (C), 126.5 (2 CH), 126.9 (CH), 127.5 (CH), 128.3 (CH), 128.5 (2 CH), 128.8 (CH), 129.1 (2 CH), 130.6 (CH), 132.9 (CH), 134.6 (CH), 139.4 (C), 141.9 (C), 146.9 (C), 152.0 (C=N), 153.2 (C=N), 159.3 (C=O) ppm; IR (KBr): $\bar{\nu} = 1696$ (C=O), 1651 (C=N), 1599 (C=N) $cm^{-1}$; MS (70 eV): *m/z* (%) = 442 (59, $M^+$), 346 (8), 322 (54), 294 (5), 279 (8), 248 (69), 220 (22), 194 (100), 167 (17), 149 (22), 121 (11), 105 (57), 91 (89), 77 (47), 57 (18).

**5′-(4-Fluorophenyl)-3′-phenyl-3′*H*,12*H*-spiro[indolo[2,1-*b*]quinazoline-6,2′-[1,3,4]oxadiazol]-12-one (3b, $C_{28}H_{17}FN_4O_2$)** Yellow powder; yield: 0.40 g (87%); m.p.: 235 °C (decomposed); $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta = 6.76$–6.80 (m, 3H, Ar), 7.07 (t, $^{3}J = 7.6$ Hz, 2H, Ar), 7.15 (t, $^{3}J = 8.6$ Hz, 2H, Ar), 7.38 (t, $^{3}J = 7.55$ Hz, 1H, Ar), 7.54–7.57 (m, 1H, Ar), 7.64–7.76 (m, 4H, Ar), 7.92–7.95 (m, 2H, Ar), 8.43 (d, $^{3}J = 7.8$ Hz, 1H, Ar), 8.69 (d, $^{3}J = 8$ Hz, 1H, Ar) ppm; $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta = 98.7$ (C), 114.5 (2 CH), 115.8 (2 CH), 117.6 (CH), 121.1 (C), 121.2 (C), 122.4 (C), 125.7 (CH), 126.0 (CH), 126.9 (CH), 127.5 (CH), 128.4 (CH), 128.6 (2 CH), 128.8 (CH), 129.1 (2 CH), 133.0 (CH), 134.6 (CH), 139.4 (C), 141.8 (C), 146.9 (C), 151.3 (C=N), 153.1 (C=N), 159.3 (C=O), 164.1 (C–F) ppm; IR (KBr): $\bar{\nu}$ = 1692 (C=O), 1663 (C=N), 1593 (C=N) cm$^{-1}$; MS (70 eV): *m/z* (%) = 460 (29, M$^+$), 367 (4), 322 (7), 246 (4), 212 (66), 192 (2), 177 (2), 149 (2), 123 (19), 91 (100), 69 (17), 55 (10).

**3′-Phenyl-5′-(*p*-tolyl)-3′*H*,12*H*-spiro[indolo[2,1-*b*]quinazoline-6,2′-[1,3,4]oxadiazol]-12-one (3c, $C_{29}H_{20}N_4O_2$)** Yellow powder; yield: 0.36 g (80%); m.p.: 220 °C (decomposed); $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ = 2.42 (s, 3H, Ar), 6.75–6.81 (m, 3H, Ar), 7.06 (t, $^3J$ = 7.8 Hz, 2H, Ar), 7.27 (d, $^3J$ = 7.7 Hz, 2H, Ar), 7.37 (t, $^3J$ = 7.5 Hz, 1H, Ar), 7.54–7.76 (m, 5H, Ar), 7.84 (d, $^3J$ = 7.9 Hz, 2H, Ar), 8.43 (d, $^3J$ = 7.8 Hz, 1H, Ar), 8.69 (d, $^3J$ = 8.0 Hz, 1H, Ar) ppm; $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ = 21.62 (Me), 98.4 (C), 114.5 (2 CH), 117.6 (CH), 120.9 (CH), 122.2 (C), 122.4 (C), 125.8 (CH), 126.2 (C), 126.5 (2 CH), 126.9 (CH), 127.5 (CH), 128.3 (CH), 128.8 (CH), 129.0 (2 CH), 129.3 (2 CH), 132.9 (CH), 134.6 (CH), 139.4 (C), 141.0 (C), 142.0 (C), 146.9 (C), 152.3 (C=N), 153.3 (C=N), 159.3 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 1691 (C=O), 1651 (C=N), 1600 (C=N) cm$^{-1}$; MS (70 eV): *m/z* (%) = 456 (60, M$^+$), 363 (7), 322 (2), 246 (5), 208 (100), 181 (4), 119 (15), 91 (57), 64 (5).

**5′-(3-Chlorophenyl)-3′-phenyl-3′*H*,12*H*-spiro[indolo[2,1-*b*]quinazoline-6,2′-[1,3,4]oxadiazol]-12-one (3d, $C_{28}H_{17}ClN_4O_2$)** Yellow powder; yield: 0.41 g (86%); m.p.: 220 °C (decomposed); $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ = 6.77–6.80 (m, 3H, Ar), 7.07 (t, $^3J$ = 7.8 Hz, 2H, Ar), 7.37–7.44 (m, 3H, Ar), 7.55–7.75 (m, 5H, Ar), 7.82 (d, $^3J$ = 7.6 Hz, 1H, Ar), 7.92 (s, 1H, Ar), 8.43 (d, $^3J$ = 7.9 Hz, 1H, Ar), 8.69 (d, $^3J$ = 8.3 Hz, 1H, Ar) ppm; $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ = 98.8 (C), 114.5 (2 CH), 117.6 (CH), 121.3 (C), 122.4 (C), 124.5 (CH), 125.7 (CH), 125.9 (C), 126.4 (CH), 126.7 (CH), 127.0 (CH), 127.5 (CH), 128.4 (CH), 128.8 (CH), 129.1 (2 CH), 129.9 (CH), 130.5 (CH), 133.1 (CH), 134.6 (CH), 134.7 (C), 139.5 (C), 141.6 (C), 146.8 (C), 150.9 (C=N), 152.9 (C=N), 159.3 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 1686 (C=O), 1649 (C=N), 1598 (C=N) cm$^{-1}$; MS (70 eV): *m/z* (%) = 476 (42, M$^+$), 383 (5), 368 (4), 322 (31), 246 (7), 228 (66), 165 (5), 138 (12), 111 (9), 91 (100), 77 (8), 64 (10).

**5′-(4-Chlorophenyl)-3′-phenyl-3′*H*,12*H*-spiro[indolo[2,1-*b*]quinazoline-6,2′-[1,3,4]oxadiazol]-12-one (3e, $C_{28}H_{17}ClN_4O_2$)** Yellow powder; yield: 0.43 g (90%); m.p.: 240 °C (decomposed); $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ = 6.77–6.79 (m, 3H, Ar), 7.07 (t, $^3J$ = 7.8 Hz, 2H, Ar), 7.38 (t, $^3J$ = 7.55 Hz, 1H, Ar), 7.43 (d, $^3J$ = 8.55 Hz, 2H, Ar), 7.54–7.60 (m, 1H, Ar), 7.64–7.67 (m, 2H, Ar), 7.71–7.76 (m, 2H, Ar), 7.86 (d, $^3J$ = 8.5 Hz, 2H, Ar), 8.42 (d, $^3J$ = 7.85 Hz, 1H, Ar), 8.68 (d, $^3J$ = 8.3 Hz, 1H, Ar) ppm; $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ = 98.7 (C), 114.5 (2 CH), 117.6 (CH), 121.2 (CH), 122.4 (C), 123.5 (C), 125.7 (CH), 125.9 (C), 127.0 (CH), 127.5 (CH), 127.7 (2 CH), 128.4 (CH), 128.8 (CH), 128.9 (2 CH), 129.1 (2 CH), 133.0 (CH), 134.6 (CH), 136.6 (C), 139.4 (C), 141.7 (C), 146.8 (C), 151.3 (C=N), 153.0 (C=N), 159.3 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 1690 (C=O), 1652 (C=N), 1601 (C=N) cm$^{-1}$; MS (70 eV): *m/z* (%)=476 (34, M$^+$), 383 (4), 322 (8), 246 (4), 228 (57), 138 (13), 111 (8), 91 (100), 78 (6), 64 (8).

**5′-(4-Nitrophenyl)-3′-phenyl-3′*H*,12*H*-spiro[indolo[2,1-*b*]quinazoline-6,2′-[1,3,4]oxadiazol]-12-one (3f, $C_{28}H_{17}N_5O_4$)** Orange powder; yield: 0.41 g (85%); m.p.: 240 °C (decomposed); $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ = 6.79–6.83 (m, 3H, Ar), 7.09 (t, $^3J$ = 7.0 Hz, 2H, Ar), 7.39-7.73 (m, 6H, Ar), 8.06 (d, $^3J$ = 8.0 Hz, 2H, Ar), 8.30 (d, $^3J$ = 8.15 Hz, 2H, Ar), 8.42 (d, $^3J$ = 7.6 Hz, 1H, Ar), 8.69 (d, $^3J$ = 7.75 Hz, 1H, Ar) ppm; $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ = 99.2 (C), 114.6 (2 CH), 117.7 (CH), 121.8 (C), 122.4 (C), 123.9 (2 CH), 125.4 (C), 125.7 (CH), 126.9 (2 CH), 127.0 (CH), 127.6 (CH), 128.6 (CH), 128.7 (CH), 129.2 (2 CH), 130.8 (CH), 133.3 (CH), 134.7 (CH), 139.5 (C), 141.0 (C), 146.7 (C), 148.5 (C=N), 150.2 (C=N), 152.6 (C), 159.1 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 1692 (C=O), 1651 (C=N), 1597 (C=N) cm$^{-1}$; MS (70 eV): *m/z* (%) = 487 (49, M$^+$), 458 (4), 394 (6), 322 (17), 296 (4), 239 (43), 225 (5), 204 (39), 179 (5), 150 (7), 91 (100), 77 (8), 51 (5).

**8-Chloro-3′,5′-diphenyl-3′*H*,12*H*-spiro[indolo[2,1-*b*]quinazoline-6,2′-[1,3,4]oxadiazol]-12-one (3g, $C_{28}H_{17}ClN_4O_2$)** Yellow powder; yield: 0.41 g (86%); m.p.: 260 °C (decomposed); $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ = 6.78–6.83 (m, 3H, Ar), 7.07–7.12 (m, 2H, Ar), 7.44–7.75 (m, 8H, Ar), 7.92–7.95 (m, 2H, Ar), 8.42 (d, $^3J$ = 7.9 Hz, 1H, Ar), 8.64 (d, $^3J$ = 8.55 Hz, 1H, Ar) ppm; $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ = 98.0 (C), 114.5 (2 CH), 118.7 (CH), 121.3 (CH), 122.2 (C), 124.7 (C), 126.0 (CH), 126.5 (2 CH), 126.9 (C), 128.1 (C), 128.5 (CH), 128.6 (2 CH), 128.9 (CH), 129.2 (2 CH), 130.7 (CH), 133.0 (CH), 133.2 (CH), 134.8 (CH), 137.8 (C), 141.6 (C), 146.8 (C), 152.0 (C=N), 152.7 (C=N), 159.1 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 1697 (C=O), 1650 (C=N), 1599 (C=N) cm$^{-1}$; MS (70 eV): *m/z* (%) = 476 (61, M$^+$), 380 (10), 356 (49), 328 (8), 313 (7), 282 (71), 254 (19), 228 (100), 201 (17), 183 (20), 155 (9), 139 (55), 125 (42), 111 (39), 91 (89), 77 (42), 57 (15).

**8-Chloro-3′-phenyl-5′-(*p*-tolyl)-3′*H*,12*H*-spiro[indolo[2,1-*b*]quinazoline-6,2′-[1,3,4]oxadiazol]-12-one (3h, $C_{29}H_{19}ClN_4O_2$)** Yellow powder; yield: 0.41 g (83%); m.p.: 250 °C (decomposed); $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ = 2.44 (s, 3H, Me), 6.79–6.82 (m, 3H, Ar), 7.08–7.11 (m, 2H, Ar), 7.27.29 (m, 2H, Ar), 7.56–7.76 (m, 5H, Ar), 7.83 (d, $^3J$ = 8.2 Hz, 2H, Ar), 8.42 (d, $^3J$ = 7.95 Hz, 1H, Ar), 8.63 (d, $^3J$ = 8.6 Hz, 1H, Ar) ppm; $^{13}$C NMR (125 MHz, $CDCl_3$):

$\delta$ = 21.63 (Me), 97.9 (C), 114.5 (2 CH), 118.7 (CH), 121.2 (CH), 121.9 (C), 122.2 (C), 126.0 (CH), 126.5 (2 CH), 126.9 (C), 128.2 (C), 128.5 (CH), 128.9 (CH), 129.2 (2 CH), 129.3 (2 CH), 132.9 (CH), 133.1 (CH), 134.7 (CH), 137.7 (CH), 141.2 (C), 141.7 (C), 146.8 (C), 152.2 (C=N), 152.7 (C=N), 159.2 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 1690 (C=O), 1649 (C=N), 1602 (C=N) cm$^{-1}$; MS (70 eV): *m/z* (%) = 490 (50, M$^+$), 397 (12), 356 (8), 280 (11), 242 (100), 215 (9), 153 (25), 125 (21), 91 (65), 64 (8).

**8-Chloro-5′-(4-chlorophenyl)-3′-phenyl-3′*H*,12*H*-spiro-[indolo[2,1-*b*]quinazoline-6,2′-[1,3,4]oxadiazol]-12-one (3i, $C_{28}H_{16}Cl_2N_4O_2$)** Yellow powder; yield: 0.45 g (88%); m.p.: 250 °C (decomposed); $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ = 6.78–6.83 (m, 3H, Ar), 7.10 (t, $^3J$ = 7.8 Hz, 2H, Ar), 7.45 (d, $^3J$ = 8.4 Hz, 2H, Ar), 7.57–7.75 (m, 5H, Ar), 7.86 (d, $^3J$ = 8.4 Hz, 2H, Ar), 8.42 (d, $^3J$ = 7.65 Hz, 1H, Ar), 8.64 (d, $^3J$ = 8.55 Hz, 1H, Ar) ppm; $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ = 98.2 (C), 114.5 (2 CH), 118.7 (CH), 121.5 (CH), 122.2 (C), 123.2 (C), 126.0 (CH), 127.0 (CH), 127.7 (2 CH), 127.9 (C), 128.6 (C), 128.8 (CH), 128.9 (2 CH), 129.2 (2 CH), 133.1 (CH), 133.2 (CH), 134.8 (CH), 136.8 (C), 137.8 (C), 141.4 (C), 146.7 (C), 151.2 (C=N), 152.5 (C=N), 159.1 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 1698 (C=O), 1662 (C=N), 1612 (C=N) cm$^{-1}$; MS (70 eV): *m/z* (%) = 510 (25, M$^+$), 418 (8), 356 (10), 280 (5), 262 (22), 172 (9), 220 (11), 184 (73), 93 (34), 67 (23), 91 (100), 64 (8).

**8-Bromo-3′,5′-diphenyl-3′*H*,12*H*-spiro[indolo[2,1-*b*]quinazoline-6,2′-[1,3,4]oxadiazol]-12-one (3j, $C_{28}H_{17}BrN_4O_2$)** Yellow powder; yield: 0.44 g (85%); m.p.: 255 °C (decomposed); $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ = 6.78–6.81 (m, 3H, Ar), 7.08 (t, $^3J$ = 7.85 Hz, 2H, Ar), 7.44–8.03 (m, 10H, Ar), 8.39 (d, $^3J$ = 8.05 Hz, 1H, Ar), 8.50–8.56 (dd, $^3J$ = 8.55 Hz, 1H, Ar) ppm; $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ = 97.9 (C), 114.5 (2 CH), 119.0 (CH), 119.4 (CH), 120.7 (CH), 121.3 (CH), 122.2 (C), 124.7 (C), 126.5 (2 CH), 126.9 (CH), 127.5 (C), 128.1 (C), 128.6 (2 CH), 129.2 (2 CH), 130.7 (CH), 134.7 (CH), 135.9 (CH), 138.2 (CH), 140.5 (C), 141.6 (C), 146.8 (C), 152.0 (C=N), 152.5 (C=N), 159.1 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 1698 (C=O), 1648 (C=N), 1599 (C=N) cm$^{-1}$; MS (70 eV): *m/z* (%) = 520 (5, M$^+$), 442 (5), 402 (8), 368 (5), 328 (100), 313 (8), 298 (32), 270 (12), 248 (10), 219 (22), 191(57), 164 (35),144 (15), 117(10), 100 (20), 91 (45), 75 (18), 57 (7).

**8-Bromo-5′-(4-fluorophenyl)-3′-phenyl-3′*H*,12*H*-spiro[indolo[2,1-*b*]quinazoline-6,2′-[1,3,4]oxadiazol]-12-one (3k, $C_{28}H_{16}BrFN_4O_2$)** Yellow powder; yield: 0.46 g (85%); m.p.: 255 °C (decomposed); $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ = 6.77–6.82 (m, 3H, Ar), 7.09 (t, $^3J$ = 7.85 Hz, 2H, Ar), 7.15 (t, $^3J$ = 8.4 Hz, 2H, Ar), 7.54–7.58 (m, 1H, Ar), 7.72–7.80 (m, 4H, Ar), 7.91–7.94 (m, 2H, Ar), 8.40 (d, $^3J$ = 8.0 Hz, 1H, Ar), 8.56 (d, $^3J$ = 8.55 Hz, 1H, Ar) ppm; $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ = 98.1 (C), 114.5 (2 CH), 115.9 (2 CH), 119.1 (C), 120.7 (C), 121.02 (C), 121.4 (CH), 122.2 (C), 127.0 (CH), 128.2 (CH), 128.6 (CH), 128.7 (CH), 128.7 (CH), 128.9 (2 CH), 129.2 (2 CH), 134.8 (CH), 136.0 (CH), 138.3 (C), 141.6 (C), 146.8 (C), 151.3 (C=N), 152.4 (C=N), 159.1 (C=O), 164.2 (C–F) ppm; IR (KBr): $\bar{\nu}$ = 1696 (C=O), 1657 (C=N), 1591 (C=N) cm$^{-1}$; MS (70 eV): *m/z* (%) = 538 (10, M$^+$), 445 (4), 402 (6), 326 (10), 308 (12), 212 (93), 123 (57), 91 (100), 77 (8), 64 (8).

**8-Bromo-5′-(3-chlorophenyl)-3′-phenyl-3′*H*,12*H*-spiro[indolo[2,1-*b*]quinazoline-6,2′-[1,3,4]oxadiazol]-12-one (3l, $C_{28}H_{16}BrClN_4O_2$)** Yellow powder; yield: 0.48 g (87%); m.p.: 260 °C (decomposed); $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ = 6.78–6.83 (m, 3H, Ar), 7.10 (t, $^3J$ = 7.9 Hz, 2H, Ar), 7.37–7.56 (m, 3H, Ar), 7.72–7.80 (m, 5H, Ar), 7.90 (s, 1H, Ar), 8.40 (d, $^3J$ = 8.0 Hz, 1H, Ar), 8.56 (d, $^3J$ = 8.6 Hz, 1H, Ar) ppm; $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ = 98.2 (C), 114.5 (2 CH), 119.1 (CH), 120.7 (C), 121.6 (CH), 122.2 (C), 124.5 (C), 126.4 (CH), 127.0 (CH), 127.6 (C), 128.1 (C), 128.6 (CH), 128.8 (CH), 129.3 (2 CH), 129.9 (CH), 130.7 (CH), 134.7 (CH), 134.8 (CH), 136.1 (CH), 138.3 (CH), 139.5 (C), 141.3(C), 146.7 (C), 150.8 (C=N), 152.2 (C=N), 159.1 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 1694 (C=O), 1653 (C=N), 1597 (C=N) cm$^{-1}$; MS (70 eV): *m/z* (%) = 554.01 (25, M$^+$), 461 (5), 401 (10), 324 (12), 306 (12), 262 (8), 227 (93), 203 (5), 165 (8), 138 (35), 109 (10), 91 (100), 64 (9).

**8-Bromo-5′-(4-chlorophenyl)-3′-phenyl-3′*H*,12*H*-spiro[indolo[2,1-*b*]quinazoline-6,2′-[1,3,4]oxadiazol]-12-one (3m, $C_{28}H_{16}BrClN_4O_2$)** Yellow powder; yield: 0.49 g (89%); m.p.: 260 °C (decomposed); $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ = 6.77–6.80 (m, 3H, Ar), 7.08 (t, $^3J$ = 7.85 Hz, 2H, Ar), 7.43 (d, $^3J$ = 6.3 Hz, 2H, Ar), 7.55–7.58 (m, 1H, Ar), 7.64–7.67 (m, 2H, Ar), 7.71–7.76 (m, 2H, Ar), 7.87 (d, $^3J$ = 8.6 Hz, 2H, Ar), 8.43 (d, $^3J$ = 8.1 Hz, 1H, Ar), 8.69 (d, $^3J$ = 8.2 Hz, 1H, Ar) ppm; $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ = 98.1 (C), 114.5 (2 CH), 119.1 (CH), 120.7 (CH), 121.5 (CH), 122.2 (C), 123.2 (C), 127.0 (C), 127.7 (2 CH), 128.1 (C), 128.6 (CH), 128.8 (CH), 128.9 (2 CH), 129.2 (2 CH), 132.7 (CH), 134.8 (CH), 136.0 (CH), 136.8 (C), 138.3 (C), 141.4 (C), 146.7 (C), 151.2 (C=N), 152.3 (C=N), 159.1 (C=O) ppm; IR (KBr): $\bar{\nu}$ = 1699 (C=O), 1659 (C=N), 1610 (C=N) cm$^{-1}$; MS (70 eV): *m/z* (%) = 554 (21, M$^+$), 462 (4), 400 (8), 324 (4), 306 (18), 216 (7), 264 (6), 228 (68), 137 (30), 111 (20), 91 (100), 64(8).

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