# Efficient One-Pot Synthesis of Spirooxindole Derivatives Catalyzed by L-Proline in Aqueous Medium

Yuling Li, Hui Chen, Chunling Shi, Daqing Shi,* and Shunjun Ji

*Key Laboratory of Organic Synthesis of Jiangsu Province, College of Chemistry, Chemical Engineering and Materials Science, Soochow University, Suzhou 215123, P. R. China*

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An efficient one-pot synthesis of spirooxindole derivatives by three-component reaction of isatins, malononitrile (cyanoacetic ester) and 1,3-dicarbonyl compounds in water in the presence of L-proline is reported. This new protocol has the advantages of environmental friendliness, higher yields, shorter reaction times, low cost, and convenient operation.

## 1. Introduction

Multicomponent reactions (MCRs), in which multiple reactions are combined into the synthetic operation have been used extensively to form carbon−carbon bonds in the synthetic chemistry.[1] Such reactions offer a wide range of possibilities for the efficient construction of highly complex molecules in a single procedural step, thus avoiding the complicated purification operations and allowing savings of both solvents and reagents. Thus, they are perfectly amenable to automation for combinatorial synthesis.[2] In the past decade there have been tremendous development in three- and four-component reactions and great efforts continue to be made to develop new MCRs.[3]

The indole nucleus is probably the most well-known heterocycle, a common and important feature of a variety of natural products and medicinal agents.[4] Compounds carrying the indol moiety exhibit antibacterial and antifungal activities.[5] Furthermore, it has been reported that sharing of the indole 3-carbon in the formation of spiroindoline derivatives highly enhances biological activity.[6] The spirooxindole system is the core structure of many pharmacological agents and natural alkaloids.[7]

Small organic molecules like cinchona alkaloids, L-proline, and its derivatives are readily commercially available catalysts and have been used in various transformations with excellent yields.[8] L-Proline has been found to be very effective in enamine based direct catalytic asymmetric aldol,[9] Mannich,[10] Michael,[11] Diels−Alder,[12] α-amination reactions,[13] and Knoevenagel type reaction,[14] and unsymmetric Biginelli reaction.[15] More recently, L-proline and its derivatives have been used in multicomponent reactions.[16]

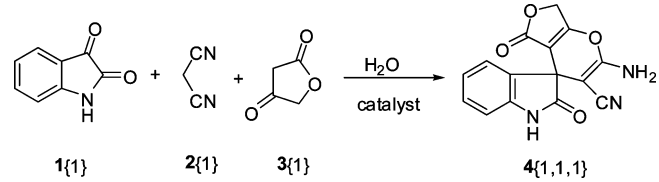
The need to reduce the amount of toxic waste and byproduct arising from chemical process requires increasing emphasis on the use of less toxic and environmentally compatible materials in the design of new synthetic methods. One of the most promising approaches is using water as reaction media. Breslow,[17] who showed that hydrophobic effects could strongly enhance the rate of several organic reactions, rediscovered the use of water as a solvent in organic chemistry in the 1980s. There has been growing recognition that water is an attractive medium for many organic reactions[18] and many MCRs in aqueous medium have been reported.[19] However, to the best of our knowledge,[20] there have been few reports about the synthesis of spirooxindole derivatives in aqueous medium. As a consequence of our interest in the aqueous medium organic synthesis[21] and our continual work on the synthesis of indole derivatives[22] guided by the observation that the presence of two or more different heterocyclic moieties in a single molecule often enhances the biocidal profile remarkably, we investigated an efficient one-pot synthesis spirooxindole derivatives catalyzed by L-proline in aqueous medium.

## 2. Results and Discussion

First, to study the reaction in water, we tested the reaction of isatin **1**{*1*}, malononitrile **2**{*1*}, and tetronic acid **3**{*1*} as a simple model substrate in various additives (Scheme 1). The results are shown in Table 1.

We examined this reaction in the absence and presence of several additives. The results are summarized in Table 1. It was found that when the reaction was carried out without any additives only trace product was detected (Table 1, entry 1). *p*-TSA (*p*-toluenesulfonic acid) could not catalyze this reaction (Table 1, entry 2). Some bases such as $NaHCO_3$, $K_2CO_3$ can catalyze this reaction with moderate yields (Table 1, entries 3−4). When some surfactants, for example, SDS (sodium dodecyl sulfate), TEBA (triethylbenzylammonium chloride), TBAB (tetrabutylammonium bromide), and CTAB (cetyltrimethylammonium bromide) were used in this reac-

**Scheme 1.** Model Reaction




**1**{1} **2**{1} **3**{1} **4**{1,1,1}

* To whom correspondence should be addressed. E-mail: dqshi@suda.edu.cn.

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**Table 1.** Optimization of Reaction Conditions[a]

| entry | additive (mol %) | $T$ (°C) | time (min) | yield[b] (%) |
|---|---|---|---|---|
| 1 | none | 80 | 30 | trace |
| 2 | *p*-TSA (10%) | 80 | 240 | trace |
| 3 | $NaHCO_3$ (10%) | 80 | 120 | 62 |
| 4 | $K_2CO_3$ (10%) | 80 | 120 | 68 |
| 5 | SDS (10%) | 80 | 240 | 72 |
| 6 | TEBA (10%) | 80 | 30 | 77 |
| 7 | TBAB (10%) | 80 | 120 | 77 |
| 8 | CTAB (10%) | 80 | 90 | 83 |
| 9 | L-proline (10%) | 80 | 15 | 92 |
| 10 | L-proline (10%) | 40 | 50 | 66 |
| 11 | L-proline (10%) | 60 | 25 | 74 |
| 12 | L-proline (10%) | 70 | 15 | 79 |
| 13 | L-proline (10%) | 90 | 15 | 90 |
| 14 | L-proline (5%) | 80 | 15 | 73 |
| 15 | L-proline (15%) | 80 | 15 | 90 |
| 16 | L-proline (20%) | 80 | 15 | 91 |
| 17 | L-proline (10%) | 80 | 5 | 51 |
| 18 | L-proline (10%) | 80 | 10 | 78 |
| 19 | L-proline (10%) | 80 | 20 | 92 |
| 20 | L-proline (10%) | 80 | 30 | 91 |
| 21 | L-proline (10%) | 80 | 60 | 92 |

[a] The reaction was carried out with isatin, malononitrile, and tetronic acid in water. [b] Isolated yields.

tion system, the products was obtained in moderate yields (Table 1, entries 5−8). The best result was obtained when L-proline was used according to the yield and the reaction time (Table 1, entry 9). So L-proline was chosen as the catalyst for this reaction.

To optimize the reaction temperature, the reactions were carried out at different temperatures ranging from 40 to 90 °C. We found that the yield of product **4**{*1*,*1*,*1*} was improved and the reaction time was shortened as the temperature was increased to 80 °C. The yield plateau when temperature was further increased to 90 °C (Table 1, entries 10−13). Therefore, the most suitable reaction temperature is 80 °C.

We also evaluated the amount of L-proline required for this reaction. It was found that when increasing the amount of the L-proline from 5 to 10, 15, and 20 mol %, the yields increased from 73 to 92, 90, and 91%, respectively (Table 1, entries 14−16). Using 10 mol % L-proline in water is sufficient to push this reaction forward. More amounts of the additive did not improve the yields.

Finally, we studied the yields according to reaction times. It can be seen from the Table 1 that this reaction was completed within 15 min. (Table 1, entries 17−21).

After optimization of the conditions, to delineate this approach, particularly in regard to library construction, this methodology was evaluated by using different isatins, 1,3-dicarbonyl compounds and malononitrile or cyanoacetic ester. Three substituted isatins **1**{*1*−*3*}, four malononitrile or cyanoacetic esters **2**{*1*−*4*}, and eight 1,3-dicarbonyl compounds **3**{*1*−*8*} were chosen for the library validation (Figure 1). Corresponding spirooxindole derivatives **4** were synthesized by the one-pot, three-component reaction of isatin **1**, malononitrile (cyanoacetic ester) **2** and 1,3-dicarbonyl compound **3** in good yields at 80 °C in water in the presences of L-proline. The results are shown in Table 2. As shown in Table 2, it was found that this method works with a wide variety of substrates. A series of substituted isatins and different 1,3-dicarbonyl compounds were used in this

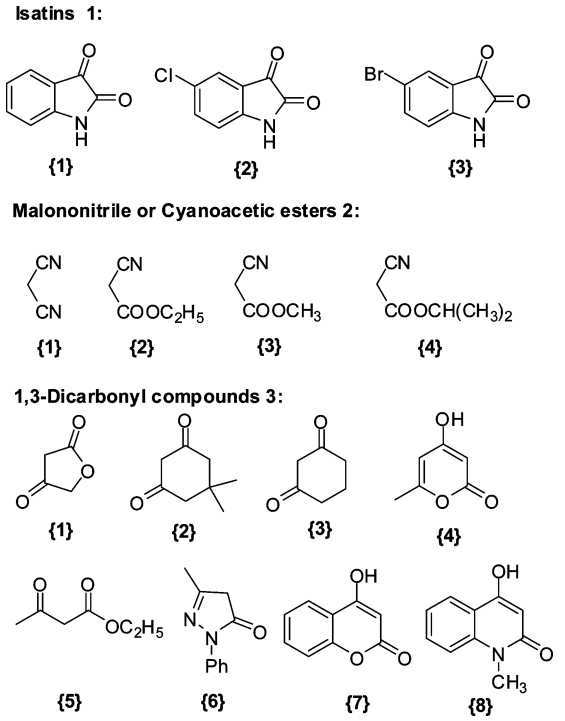
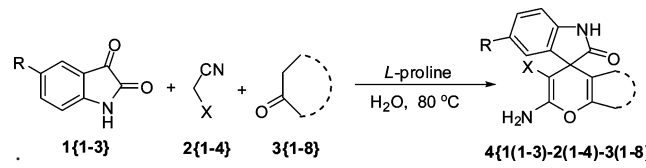



**Figure 1.** Diversity of reagents.

**Table 2.** Synthesis of Spirooxindole Derivatives **4** in Aqueous Medium Catalyzed by L-Proline




| entry | products **4** | time (min) | yield (%) | mp (°C) |
|---|---|---|---|---|
| 1 | **4**{*1*,*1*,*1*} | 15 | 92 | 238−240 |
| 2 | **4**{*1*,*1*,*2*} | 20 | 94 | 290−292 |
| 3 | **4**{*1*,*1*,*3*} | 11 | 93 | 298−299 |
| 4 | **4**{*1*,*1*,*4*} | 38 | 94 | 278−280 |
| 5 | **4**{*1*,*1*,*5*} | 20 | 90 | 258−260 |
| 6 | **4**{*1*,*1*,*6*} | 12 | 95 | 236−237 |
| 7 | **4**{*1*,*1*,*7*} | 15 | 94 | >300 |
| 8 | **4**{*1*,*2*,*2*} | 30 | 81 | 256−258 |
| 9 | **4**{*1*,*2*,*3*} | 45 | 76 | 253−255 |
| 10 | **4**{*1*,*2*,*6*} | 45 | 79 | 235−237 |
| 11 | **4**{*1*,*2*,*7*} | 60 | 83 | 251−253 |
| 12 | **4**{*1*,*2*,*8*} | 60 | 85 | >300 |
| 13 | **4**{*1*,*3*,*2*} | 30 | 78 | 230−232 |
| 14 | **4**{*1*,*4*,*2*} | 30 | 80 | 251−253 |
| 15 | **4**{*2*,*1*,*1*} | 15 | 94 | 252−254 |
| 16 | **4**{*2*,*1*,*2*} | 17 | 95 | >300 |
| 17 | **4**{*2*,*1*,*3*} | 18 | 94 | 294−296 |
| 18 | **4**{*2*,*1*,*4*} | 40 | 94 | >300 |
| 19 | **4**{*2*,*1*,*5*} | 17 | 91 | 256−258 |
| 20 | **4**{*2*,*1*,*6*} | 20 | 94 | 226−228 |
| 21 | **4**{*2*,*1*,*7*} | 24 | 95 | >300 |
| 22 | **4**{*3*,*1*,*1*} | 10 | 94 | 266−268 |
| 23 | **4**{*3*,*1*,*2*} | 11 | 93 | >300 |
| 24 | **4**{*3*,*1*,*3*} | 20 | 93 | 290−292 |
| 25 | **4**{*3*,*1*,*4*} | 42 | 93 | >300 |
| 26 | **4**{*3*,*1*,*5*} | 10 | 90 | 262−264 |
| 27 | **4**{*3*,*1*,*6*} | 17 | 94 | 225−226 |
| 28 | **4**{*3*,*1*,*7*} | 24 | 93 | >300 |

reaction. Additionally, the reaction with malononitrile or cyanoacetic esters also proceeded smoothly; however, the reaction time of cyanoacetic esters with isatins and 1,3-dicarbonyl compounds was longer than those of malononi-

**Table 3.** Studies on the Reuse of Reaction Solution in the Preparation of **4**{*1*,*1*,*1*}

| round | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| yield (%) | 92 | 93 | 92 | 91 | 93 | 92 | 90 | 90 | 91 | 89 | 88 | 84 | 79 |

trile, which is probably due to the lower reactivities of the cyanoacetic esters.

Given the large number of commercially available isatins, malononitrile or cyanoacetic esters, and 1,3-dicarbonyl compounds, the present method should be applicable to synthesis of libraries with high diversity. We expect this method to find extensive application in the filed of combinatorial chemistry and drug discovery.

Apart from the mild conditions of the process and its excellent results, the simplicity of product isolation and the possibility to recover and recycle the L-proline as catalyst offer a significant advantage. Because L-proline is soluble in reaction medium—water and the desired products is less soluble in water, the products can be directly separated by cooling to room temperature and filtering after the reaction was completed. The filtrate containing L-proline can directly be recovered and recycled. Studies using **1**{*1*}, **2**{*1*}, and **3**{*1*} as model substrates showed that the recovered filterate could be successively recycled in subsequent reactions without any decrease of yields (Table 3). It is shown that reaction solution have been recovered nineth rounds, catalytic efficiency of L-proline in reaction solution still be noted that even in the nineth round. While when the filterate was recovered thirteenth the catalyst started to lose effect because of the losing of the catalyst.

Proposed mechanism for the synthesis of spirooxindole derivative **4**{*1*,*1*,*1*} was described in Scheme 2. We suggest that L-proline catalyze the formation of iminium ion **5** in a reversible reaction with isatin **1**{*1*}. The higher reactivity of the iminium ion compared to the carbonyl species could facilitate Knoevenagel condensation between isatin **1**{*1*} and malononitrile **2**{*1*}, via intermediate **6** and after the elimination of L-proline, **7** might be produced as an intermediate. Then, **7** is attacked via Michael addition of tetronic acid **3**{*1*} to give the intermediate **8**, followed by the cycloaddition of hydroxyl group up to the cyano moiety to form the desired produst **4**{*1*,*1*,*1*}.

It is noticed that the compounds obtained are racemic ones. L-Proline plays a key role in this reaction. According to above proposed mechanism L-proline only catalyzes the formation of intermediate **7** and not takes part in the generation of this spiranic stereocenter. So the stereoselection is not achieved.

In this study, all the products were characterized by melting point, IR, and $^1$H NMR spectral data, as well as HRMS.

## 3. Conclusion

In conclusion, we have described an efficient one-pot three-component reaction of isatin, malononitrile (cyanoacetic ester) and 1,3-dicarbonyl compound for the synthesis of spirooxindole derivatives catalyzed by L-proline in aqueous medium. This new method has the advantages of higher yields, mild reaction conditions, shorter reaction time, convenient procedure and environmental friendliness.

## 4. Experimental Section

**Typical Procedure for Preparation of Spirooxindole Derivatives (4{*1*−*2*−*3*}).** A mixture of isatin **1**{*1*−*3*} (1 mmol), malononitrile or cyanoacetic esters **2**{*1*−*4*} (1 mmol), 1,3-dicarbonyl compounds **3**{*1*−*8*} (1 mmol), and L-proline (0.1 mmol) in water (2 mL) was stirred at 80 °C for 15−60 min. After completion of the reaction confirmed by TLC, the reaction mixture was cooled to room temperature. Then, the precipitated product was filtered and washed with water and cooled ethanol to afford the pure **4**{*1*−*2*−*3*}.

**2-Amino-2′,5-dioxo-5,7-dihydrospiro[furo[3,4-*b*]pyran-4,3′-indoline]-3-carbonitrile 4{*1*,*1*,*1*}.** mp: 238−240 °C. IR (KBr) $\nu$: 3341, 3247, 3147, 2198, 1748, 1653, 1619, 1472, 1378, 1030, 918 cm$^{-1}$. $^1$H NMR (DMSO-$d_6$, 400 MHz) $\delta$: 5.10 (d, $J$ = 16.8 Hz, 1H, $CH_2$), 5.20 (d, $J$ = 16.8 Hz, 1H, $CH_2$), 6.88 (d, $J$ = 7.6 Hz, 1H, ArH), 7.01 (d, $J$ = 7.6 Hz, 1H, ArH), 7.20 (d, $J$ = 7.6 Hz, 1H, ArH), 7.26 (t, $J$ = 7.6 Hz, 1H, ArH), 7.70 (s, 2H, $NH_2$), 10.71 (s, 1H, NH). HRMS [Found $m/z$ 295.0609 ($M^+$); Calcd for $C_{15}H_9N_3O_4$ M, 295.0593].

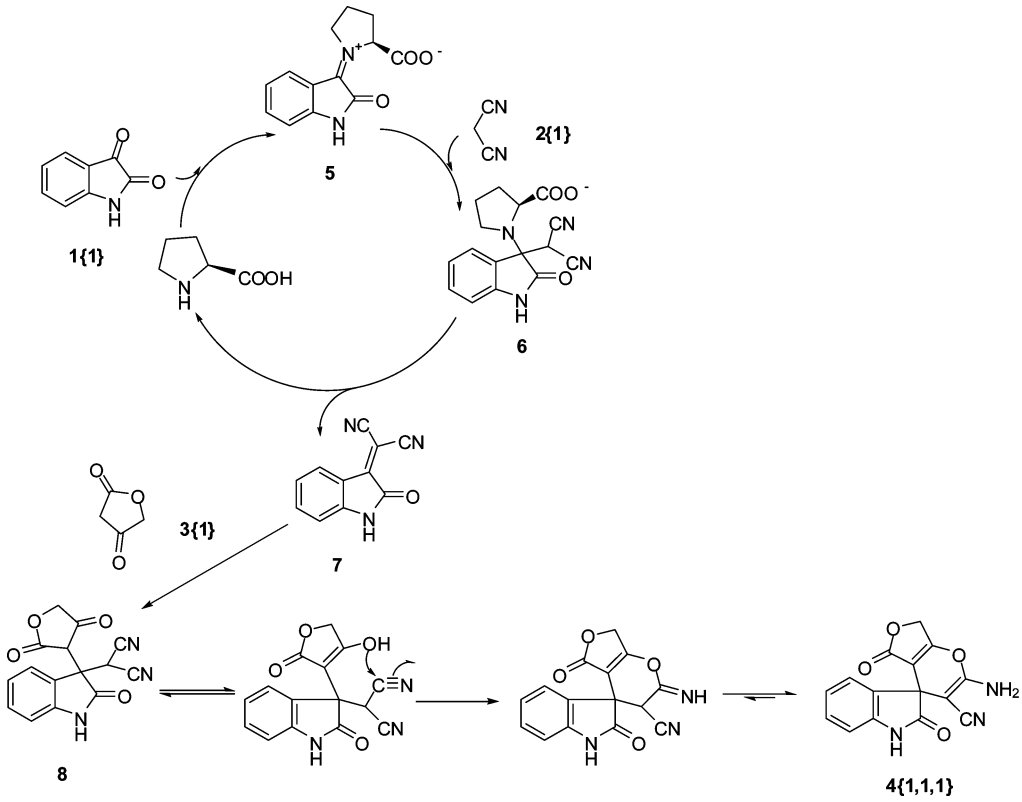
**2-Amino-7,7-dimethyl-2′,5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3′-indoline]-3-carbonitrile 4{*1*,*1*,*2*}.** mp: 290−292 °C. IR (KBr) $\nu$: 3377, 3312, 3144, 2192, 1723, 1683, 1656, 1472, 1348, 1223, 1055 cm$^{-1}$. $^1$H NMR (DMSO-$d_6$, 400 MHz) $\delta$: 1.01 (s, *3*H, $CH_3$), 1.04 (s, 3H, $CH_3$), 2.10 (d, $J$ = 16.0 Hz, 1H, $CH_2$), 2.18 (d, $J$ = 16.0 Hz, 1H, $CH_2$), 2.54 (d, $J$ = 18.0 Hz, 1H, $CH_2$), 2.59 (d, $J$ = 18.0 Hz, 1H, $CH_2$), 6.79 (d, $J$ = 7.6 Hz, 1H, ArH), 6.89 (t, $J$ = 7.2 Hz, 1H, ArH), 6.98 (d, $J$ = 7.2 Hz, 1H, ArH), 7.14 (t, $J$ = 7.6 Hz, 1H, ArH), 7.24 (s, 2H, $NH_2$), 10.40 (s, 1H, NH). HRMS [Found $m/z$ 335.1281 ($M^+$); Calcd for $C_{19}H_{17}N_3O_3$ M, 335.1270].

**2-Amino-2′,5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3′-indoline]-3-carbonitrile 4{*1*,*1*,*3*}.** mp: 298−299 °C. IR (KBr) $\nu$: 3370, 3286, 3134, 2191, 1709, 1679, 1655, 1604, 1471, 1351, 1211, 1076, 1011 cm$^{-1}$. $^1$H NMR (DMSO-$d_6$, 400 MHz) $\delta$: 1.91−1.95 (m, 2H, $CH_2$), 2.20−2.25 (m, 2H, $CH_2$), 2.66 (t, $J$ = 6.0 Hz, 2H, $CH_2$), 6.78 (d, $J$ = 7.6 Hz, 1H, ArH), 6.89 (t, $J$ = 7.6 Hz, 1H, ArH), 7.00 (d, $J$ = 7.2 Hz, 1H, ArH), 7.14 (t, $J$ = 7.6 Hz, 1H, ArH), 7.22 (s, 2H, $NH_2$), 10.40 (s, 1H, NH). $^{13}$C NMR (DMSO-$d_6$, 400 MHz) $\delta$: 20.48, 27.44, 37.07, 47.58, 58.23, 109.84, 112.56, 118.06, 122.35, 123.88, 128.83, 135.22, 142.66, 159.32, 166.74, 178.84, 195.72. HRMS [Found $m/z$ 307.0957 ($M^+$); Calcd for $C_{17}H_{13}N_3O_3$ M, 307.0957].

**2′-Amino-7′-methyl-2,5′-dioxo-5′H-spiro[indoline-3,4′-pyrano[4,3-*b*]pyran]-3′-carbonitrile 4{*1*,*1*,*4*}.** mp: 278−280 °C. IR (KBr) $\nu$: 3378, 3184, 2198, 1743, 1699, 1664, 1612, 1472, 1370, 1170, 1094 cm$^{-1}$. $^1$H NMR (DMSO-$d_6$, 400 MHz) $\delta$: 2.24 (s, 3H, $CH_3$), 6.36 (s, 1H, CH), 6.82 (d, $J$ = 7.6 Hz, 1H, ArH), 6.93 (t, $J$ = 7.2 Hz, 1H, ArH), 7.11 (d, $J$ = 7.6 Hz, 1H, ArH), 7.20 (t, $J$ = 8.0 Hz, 1H, ArH), 7.46 (s, 2H, $NH_2$), 10.59 (s, 1H, NH). HRMS [Found $m/z$ 321.0750 ($M^+$); Calcd for $C_{17}H_{11}N_3O_4$ M, 321.0750].

**Ethyl 2′-Amino-3′-cyano-6′-methyl-2-oxospiro[indoline-3,4′-pyran]-5′-carboxylate 4{*1*,*1*,*5*}.** mp: 258−260 °C. IR (KBr) $\nu$: 3482, 3282, 3159, 2192, 1712, 1619, 1597, 1471, 1382, 1289, 1212, 1073 cm$^{-1}$. $^1$H NMR (DMSO-$d_6$, 400 MHz) $\delta$: 0.78 (t, $J$ = 6.8 Hz, 3H, $CH_3$), 2.32 (s, 3H, $CH_3$),

**Scheme 2.** Plausible Mechanism for the Reaction of Isatin and Malononitrile with Tetronic Acid




3.75−3.79 (m, 2H, $CH_2$), 6.80 (d, $J$ = 7.6 Hz, 1H, ArH), 6.93 (t, $J$ = 7.2 Hz, 1H, ArH), 7.06 (d, $J$ = 7.2 Hz, 1H, ArH), 7.15 (s, 2H, $NH_2$), 7.18 (t, $J$ = 7.6 Hz, 1H, ArH), 10.40 (s, 1H, NH). $^{13}$C NMR (DMSO-$d_6$, 100 MHz) $\delta$: 13.66, 19.24, 49.63, 57.18, 60.94, 105.31, 110.01, 118.18, 122.54, 124.06, 129.23, 135.22, 142.81, 159.21, 159.61, 165.17, 179.28. HRMS [Found *m*/*z* 325.1065 ($M^+$); Calcd for $C_{17}H_{15}N_3O_4$ M, 325.1063].

**6′-Amino-3′-methyl-2-oxo-1′-phenyl-1′*H*-spiro[indoline-3,4′-pyrano[2,3-*c*]pyrazole]-5′-carbonitrile 4{*1*,*1*,*6*}.** mp: 236−237 °C. IR (KBr) $\nu$: 3461, 3274, 3176, 2196, 1703, 1655, 1594, 1469, 1391, 1331, 1220, 1127, 1070 cm$^{-1}$. $^1$H NMR (DMSO-$d_6$, 400 MHz) $\delta$: 1.55 (s, 3H, $CH_3$), 6.95 (d, $J$ = 7.6 Hz, 1H, ArH), 7.04 (t, $J$ = 7.6 Hz, 1H, ArH), 7.19 (d, $J$ = 7.2 Hz, 1H, ArH), 7.29 (t, $J$ = 7.6 Hz, 1H, ArH), 7.36 (t, $J$ = 7.6 Hz, 1H, ArH), 7.53 (t, $J$ = 8.0 Hz, 2H, ArH), 7.59 (s, 2H, $NH_2$), 7.80 (d, $J$ = 7.6 Hz, 2H, ArH), 10.76 (s, 1H, NH). HRMS [Found *m*/*z* 369.1223 ($M^+$); Calcd for $C_{21}H_{15}N_5O_2$ M, 369.1226].

**2′-Amino-2,5′-dioxo-5′*H*-spiro[indoline-3,4′-pyrano[3,2-*c*]chromene]-3′-carbonitrile 4{*1*,*1*,*7*}.** mp: >300 °C. IR (KBr) $\nu$: 3473, 3357, 3117, 2194, 1738, 1681, 1621, 1471, 1366, 1069 cm$^{-1}$. $^1$H NMR (DMSO-$d_6$, 400 MHz) $\delta$: 6.86 (d, $J$ = 7.6 Hz, 1H, ArH), 6.94 (t, $J$ = 7.6 Hz, 1H, ArH), 7.22 (t, $J$ = 7.2 Hz, 2H, ArH), 7.49 (d, $J$ = 8.4 Hz, 1H, ArH), 7.54 (t, $J$ = 8.0 Hz, 1H, ArH), 7.68 (s, 2H, $NH_2$), 7.77 (t, $J$ = 8.0 Hz, 1H, ArH), 7.95 (d, $J$ = 7.6 Hz, 1H, ArH), 10.69 (s, 1H, NH). HRMS [Found *m*/*z* 357.0750 ($M^+$); Calcd for $C_{20}H_{11}N_3O_4$ M, 357.0750].

**Ethyl 2-Amino-7,7-dimethyl-2′,5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3′-indoline]-3-carboxylate 4{*1*,*2*,*2*}.** mp: 256−258 °C. IR (KBr) $\nu$: 3372, 3236, 3181, 2956, 1715, 1688, 1670, 1648, 1617, 1526, 1470, 1347, 1316, 1291, 1222, 1166, 1053, 901, 786, 745, cm$^{-1}$. $^1$H NMR (DMSO-$d_6$, $\delta$, 400 MHz): 0.80 (t, $J$ = 7.2 Hz, 3H, $CH_3$), 0.95 (s, 3H, $CH_3$), 1.02 (s, 3H, $CH_3$), 1.96−2.18 (m, 2H, $CH_2$), 2.46−2.61 (m, 2H, $CH_2$), 3.63−3.73 (m, 2H, $CH_2O$), 6.67 (d, $J$ = 7.6 Hz, 1H, ArH), 6.76 (t, $J$ = 7.2 Hz, 1H, ArH), 6.84 (d, $J$ = 7.2 Hz, 1H, ArH), 7.03−7.07 (m, 1H, ArH), 7.87 (br s, 2H, $NH_2$), 10.15 (s, 1H, NH). $^{13}$C NMR (DMSO-$d_6$, 100 MHz) $\delta$: 13.79, 27.35, 28.47, 32.23, 47.29, 51.32, 59.53, 76.99, 108.81, 113.77, 121.22, 122.91, 127.86, 136.66, 144.71, 159.79, 160.88, 163.09, 168.32, 180.49, 195.34. HRMS (ESI): *m*/*z* calcd for $C_{21}H_{22}N_2O_5$ 405.1426 $[M + Na]^+$; found 405.1430.

**Ethyl 2-Amino-2′,5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3′-indoline]-3-carboxylate 4{*1*,*2*,*3*}.** mp: 253−255 °C. IR (KBr) $\nu$: 3361, 3257, 3188, 2902, 1715, 1692, 1659, 1644, 1524, 1471, 1349, 1294, 1251, 1224, 1133, 1082, 933, 742, 679 cm$^{-1}$. $^1$H NMR (DMSO-$d_6$, $\delta$, 300 MHz): 0.77 (t, $J$ = 7.2 Hz, 2H, $CH_2$), 1.83−1.88 (m, 2H, $CH_2$), 2.13−2.20 (m, 3H, $CH_3$), 2.58−2.64 (m, 2H, $CH_2$), 3.66−3.69 (m, 2H, $CH_2O$), 6.63−6.84 (m, 3H, ArH), 7.00−7.11 (m, 1H, ArH), 7.86 (br s, 2H, $NH_2$), 10.15 (s, 1H, NH). HRMS [Found *m*/*z* 354.1214 ($M^+$); calcd for $C_{19}H_{18}N_2O_5$ M, 354.1216].

**Ethyl 6′-Amino-3′-methyl-2-oxo-1′-phenyl-1′*H*-spiro[indoline-3,4′-pyrano[2,3-*c*]pyrazole]-5′-carboxylate 4{*1*,*2*,*6*}.** mp: 235−237 °C. IR (KBr) $\nu$: 3381, 3233, 3174, 1718, 1692, 1663, 1612, 1534, 1470, 1353, 1283, 1116, 1030, 966, 762, 678 cm$^{-1}$. $^1$H NMR (DMSO-$d_6$, $\delta$, 300 MHz): 0.72 (t, $J$ = 7.2 Hz, 3H, $CH_3$), 1.56 (s, 3H, $CH_3$), 3.70−3.74 (m, 2H, $CH_2O$), 6.82−6.96 (m, 3H, ArH), 7.13−7.18 (m, 1H, ArH), 7.32 (t, $J$ = 7.2 Hz, 1H, ArH), 7.49 (t, $J$ = 7.8 Hz, 2H, ArH), 7.78 (d, $J$ = 7.8 Hz, 2H, ArH), 8.20 (br s, 2H, $NH_2$),

10.50 (s, 1H, NH). HRMS [Found *m/z* 416.1483 ($M^+$); calcd for $C_{23}H_{20}N_4O_4$ M, 416.1485].

**Ethyl 2′-Amino-2,5′-dioxo-5′*H*-spiro[indoline-3,4′-pyrano[3,2-*c*]chromene]-3′-carboxylate 4{*1*,*2*,*7*}.** mp: 251−254 °C. IR (KBr) *ν*: 3358, 3261, 2981, 1696, 1641, 1514, 1491, 1472, 1396, 1380, 1289, 1135, 1074, 929, 747, 684 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$, *δ*, 300 MHz): 0.81 (t, *J* = 7.2 Hz, 3H, $CH_3$), 3.73−3.77 (m, 2H, $CH_2O$), 6.71−6.81 (m, 2H, ArH), 7.00 (d, *J* = 6.9 Hz, 1H, ArH), 7.10 (t, *J* = 7.8 Hz, 1H, ArH), 7.42−7.53 (m, 2H, ArH), 7.73 (t, *J* = 8.1 Hz, 1H, ArH), 8.01 (d, *J* = 8.4 Hz, 1H, ArH), 8.13 (br s, 2H, $NH_2$), 10.42 (s, 1H, NH). HRMS [Found *m/z* 404.1011 ($M^+$); calcd for $C_{22}H_{16}N_2O_6$ M, 404.1008].

**Ethyl 2′-Amino-6′-methyl-2,5′-dioxo-5′,6′-dihydrospiro[indoline-3,4′-pyrano[3,2-*c*]quinoline]-3′-carboxylate 4{*1*,*2*,*8*}.** mp: >300 °C. IR (KBr) *ν*: 3379, 3257, 3200, 2970, 1718, 1701, 1598, 1534, 1483, 1361, 1273, 1160, 1110, 1031, 961, 931, 760, 680 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$, *δ*, 300 MHz): 0.83 (t, *J* = 7.2 Hz, 3H, $CH_3$), 3.43 (s, 3H, $CH_3$), 3.72−3.76 (m, 2H, $CH_2O$), 6.71 (t, *J* = 8.4 Hz, 2H, ArH), 6.83 (t, *J* = 8.4 Hz, 1H, ArH), 7.05 (t, *J* = 7.5 Hz, 1H, ArH), 7.39 (t, *J* = 7.5 Hz, 1H, ArH), 7.52 (d, *J* = 8.4 Hz, 1H, ArH), 7.71 (t, *J* = 7.8 Hz, 1H, ArH), 8.05 (br s, 2H, $NH_2$), 8.13 (d, *J* = 8.1 Hz, 1H, ArH), 10.26 (s, 1H, NH). $^{13}C$ NMR (DMSO-$d_6$, 100 MHz) *δ*: 13.85, 29.81, 48.66, 59.62, 76.70, 108.79, 109.68, 112.87, 115.36, 121.24, 122.84, 123.25, 123.37, 128.03, 132.64, 136.26, 139.09, 145.30, 150.97, 159.34, 159.83, 168.27, 180.37. HRMS (ESI): *m/z* calcd for $C_{23}H_{19}N_3O_5$ 440.1222 $[M + Na]^+$; found 440.1222.

**Methyl 2-Amino-7,7-dimethyl-2′,5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3′-indoline]-3-carboxylate 4{*1*,*3*,*2*}.** mp: 230−232 °C. IR (KBr) *ν*: 3366, 3257, 3195, 2955, 1714, 1692, 1650, 1621, 1472, 1442, 1347, 1313, 1224, 1167, 1138, 1054, 988, 901, 787, 748, 668 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$, *δ*, 300 MHz): 0.92 (s, 3H, $CH_3$), 1.00 (s, 3H, $CH_3$), 1.98 (d, *J* = 15.9 Hz, 1H, CH), 2.14 (d, *J* = 15.9 Hz, 1H, CH), 2.42−2.61 (m, 2H, $CH_2$), 3.23 (s, 3H, $CH_3O$), 6.66 (d, *J* = 7.5 Hz, 1H, ArH), 6.74 (t, *J* = 7.2 Hz, 1H, ArH), 6.81 (d, *J* = 6.9 Hz, 1H, ArH), 7.02 (t, *J* = 7.5 Hz, 1H, ArH), 7.80 (br s, 2H, $NH_2$), 10.14 (s, 1H, NH). HRMS (ESI): *m/z* calcd for $C_{20}H_{20}N_2O_5$ 369.1450 $[M + H]^+$; found 369.1469.

**Isopropyl 2-Amino-7,7-dimethyl-2′,5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3′-indoline]-3-carboxylate 4{*1*,*4*,*2*}.** mp: 251−253 °C. IR (KBr) *ν*: 3388, 3250, 3199, 2985, 1715, 1688, 1672, 1617, 1527, 1471, 1351, 1285, 1103, 1052, 915, 746, 674 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$, *δ*, 300 MHz): 0.53 (d, *J* = 6.0 Hz, 3H, $CH_3$), 0.93−1.00 (m, 9H, 3 × $CH_3$), 2.00 (d, *J* = 15.9 Hz, 1H, CH), 2.13 (d, *J* = 15.9 Hz, 1H, CH), 2.43−2.59 (m, 2H, $CH_2$), 4.55−4.64 (m, 1H, CHO), 6.66 (d, *J* = 4.5 Hz, 1H, ArH), 6.74 (t, *J* = 7.2 Hz, 1H, ArH), 6.81 (d, *J* = 6.9 Hz, 1H, ArH), 7.03 (t, *J* = 7.5 Hz, 1H, ArH), 7.83 (br s, 2H, $NH_2$), 10.09 (s, 1H, NH). HRMS [Found *m/z* 396.1667 ($M^+$); calcd for $C_{22}H_{24}N_2O_5$ M, 396.1685].

**2-Amino-5′-chloro-2′,5-dioxo-5,7-dihydrospiro[furo[3,4-*b*]pyran-4,3′-indoline]-3-carbonitrile 4{*2*,*1*,*1*}.** mp: 252−254 °C. IR (KBr) *ν*: 3374, 3337, 3199, 2203, 1778, 1694, 1597, 1480, 1375, 1027, 824 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$, 400 MHz) *δ*: 5.05 (d, *J* = 16.8 Hz, 1H, $CH_2$), 5.21 (d, *J* = 16.8 Hz, 1H, $CH_2$), 6.89 (d, *J* = 8.4 Hz, 1H, ArH), 7.31 (d, *J* = 8.0 Hz, 1H, ArH), 7.38 (s, 1H, ArH), 7.77 (s, 2H, $NH_2$), 10.85 (s, 1H, NH). HRMS [Found *m/z* 329.0210 ($M^+$); calcd for $C_{15}H_8N_3O_4{}^{35}Cl$ M, 329.0203].

**2-Amino-5′-chloro-7,7-dimethyl-2′,5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3′-indoline]-3-carbonitrile 4{*2*,*1*,*2*}.** mp: >300 °C. IR (KBr) *ν*: 3372, 3290, 3156, 2193, 1726, 1680, 1654, 1602, 1478, 1350, 1225, 1057 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$, 400 MHz) *δ*: 1.02 (s, 6H, 2 × $CH_3$), 2.16 (t, *J* = 16.4 Hz, 2H, $CH_2$), 2.52 (d, *J* = 18.0 Hz, 1H, $CH_2$), 2.59 (d, *J* = 18.0 Hz, 1H, $CH_2$), 6.81 (d, *J* = 8.4 Hz, 1H, ArH), 7.11 (s, 1H, ArH), 7.19 (d, *J* = 8.4 Hz, 1H, ArH), 7.33 (s, 2H, $NH_2$), 10.55 (s, 1H, NH).$^{13}C$ NMR (DMSO-$d_6$, 100 MHz) *δ*: 27.91, 28.19, 32.66, 47.79, 50.63, 57.40, 110.87, 111.34, 117.92, 123.96, 126.33, 128.77, 137.11, 141.71, 141.79, 159.56, 165.30, 178.51, 195.79. HRMS [Found *m/z* 369.0877 ($M^+$); calcd for $C_{19}H_{16}N_3O_3{}^{35}Cl$ M, 369.0880].

**2-Amino-5′-chloro-2′,5-dioxo-5,6,7,8-tetrahydrospiro-[chromene-4,3′-indoline]-3-carbonitrile 4{*2*,*1*,*3*}.** mp: 294−296 °C. IR (KBr) *ν*: 3364, 3247, 3175, 2193, 1719, 1681, 1477, 1350, 1219, 1079, 1011 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$, 400 MHz) *δ*: 1.90−2.00 (m, 2H, $CH_2$), 2.25 (t, *J* = 6.8 Hz, 2H, $CH_2$), 2.65 (t, *J* = 6.4 Hz, 2H, $CH_2$), 6.80 (d, *J* = 8.4 Hz, 1H, ArH), 7.15 (d, *J* = 2.0 Hz, 1H, ArH), 7.19 (dd, $J_1$ = 2.0 Hz, $J_2$ = 8.0 Hz,1H, ArH), 7.31 (s, 2H, $NH_2$), 10.54 (s, 1H, NH). HRMS [Found *m/z* 341.0564 ($M^+$); calcd for $C_{17}H_{12}N_3O_3{}^{35}Cl$ M, 341.0567].

**2′-Amino-5-chloro-7′-methyl-2,5′-dioxo-5′*H*-spiro[indoline-3,4′-pyrano[4,3-*b*]pyran]-3′-carbonitrile 4{*2*,*1*,*4*}.** mp: >300 °C. IR (KBr) *ν*: 3412, 3300, 3184, 2201, 1721, 1670, 1609, 1475, 1367, 1345, 1241, 1174, 1050 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$, 400 MHz) *δ*: 2.25 (s, 3H, $CH_3$), 6.37 (s, 1H, CH), 6.84 (d, *J* = 8.4 Hz, 1H, ArH), 7.25 (d, *J* = 8.4 Hz, 1H, ArH), 7.32 (s, 1H, ArH), 7.55 (s, 2H, $NH_2$), 10.74 (s, 1H, NH). $^{13}C$ NMR (DMSO-$d_6$, 100 MHz) *δ*: 19.97, 47.96, 56.95, 98.50, 98.76, 111.52, 117.75, 124.93, 126.75, 129.37, 135.75, 141.79, 159.46, 160.57, 160.84, 164.58, 177.82. HRMS [Found *m/z* 355.0360 ($M^+$); calcd for $C_{17}H_{10}N_3O_4{}^{35}Cl$ M, 355.0360].

**Ethyl 2′-Amino-5-chloro-3′-cyano-6′-methyl-2-oxospiro[indoline-3,4′-pyran]-5′-carboxylate 4{*2*,*1*,*5*}.** mp: 256−258 °C. IR (KBr) *ν*: 3389, 3300, 3170, 2205, 1716, 1666, 1591, 1476, 1380, 1280, 1221, 1079 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$, 400 MHz) *δ*: 0.83 (t, *J* = 7.2 Hz, 3H, $CH_3$), 2.33 (s, 3H, $CH_3$), 3.76−3.86 (m, 2H, $CH_2O$), 6.81 (d, *J* = 8.4 Hz, 1H, ArH), 7.19 (s, 1H, ArH), 7.23 (d, *J* = 6.8 Hz, 1H, ArH), 7.24 (s, 2H, $NH_2$), 10.55 (s, 1H, NH). HRMS [Found *m/z* 359.0673 ($M^+$); calcd for $C_{17}H_{14}N_3O_4{}^{35}Cl$ M, 359.0673].

**6′-Amino-5-chloro-3′-methyl-2-oxo-1′-phenyl-1′*H*-spiro[indoline-3,4′-pyrano[2,3-*c*]pyrazole]-5′-carbonitrile 4{*2*,*1*,*6*}.** mp: 226−228 °C. IR (KBr) *ν*: 3467, 3305, 3138, 2191, 1736, 1645, 1526, 1476, 1384, 1211, 1072 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$, 400 MHz) *δ*: 1.60 (s, 3H, $CH_3$), 6.96 (d, *J* = 8.4 Hz, 1H, ArH), 7.33−7.36 (m, 3H, ArH), 7.52 (t, *J* = 8.0 Hz, 2H, ArH), 7.64 (s, 2H, $NH_2$), 7.79 (d, *J* = 8.0 Hz, 2H, ArH), 10.89 (s, 1H, NH). $^{13}C$ NMR (DMSO-$d_6$, 100

MHz) $\delta$: 12.45, 48.77, 56.29, 96.40, 105.00, 112.08, 118.64, 120.98, 125.88, 127.33, 127.46, 127.51, 130.12, 135.04, 137.95, 141.12, 144.51, 145.77, 161.81, 163.02, 178.04. HRMS [Found *m/z* 403.0836 ($M^+$); calcd for $C_{21}H_{14}N_5O_2{}^{35}Cl$ M, 403.0836].

**2′-Amino-5-chloro-2,5′-dioxo-5′*H*-spiro[indoline-3,4′-pyrano[3,2-*c*]chromene]-3′-carbonitrile 4{*2*,*1*,*7*}.** mp: >300 °C. IR (KBr) $\nu$: 3319, 3207, 2199, 1741, 1677, 1608, 1475, 1360, 1222, 1090, 972 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$, 400 MHz) $\delta$: 6.87 (d, $J$ = 8.4 Hz, 1H, ArH), 7.25−7.28 (m, 1H, ArH), 7.44 (s, 1H, ArH), 7.50 (d, $J$ = 8.4 Hz, 1H, ArH), 7.55 (t, $J$ = 7.6 Hz, 1H, ArH), 7.74 (s, 2H, $NH_2$), 7.78 (d, $J$ = 8.4 Hz, 1H, ArH), 7.94 (d, $J$ = 7.6 Hz, 1H, ArH), 10.82 (s, 1H, NH). $^{13}C$ NMR (DMSO-$d_6$, 100 MHz) $\delta$: 48.60, 57.11, 101.47, 111.62, 113.24, 117.30, 117.67, 123.42, 125.27, 125.61, 126.86, 129.53, 134.32, 135.73, 141.81, 152.76, 156.13, 159.20, 159.29, 177.78. HRMS [Found *m/z* 391.0376 ($M^+$); calcd for $C_{20}H_{10}N_3O_4{}^{35}Cl$ M, 391.0360].

**2-Amino-5′-bromo-2′,5-dioxo-5,7-dihydrospiro[furo[3,4-*b*]pyran-4,3′-indoline]-3-carbonitrile 4{*3*,*1*,*1*}.** mp: 266−268 °C. IR (KBr) $\nu$: 3339, 3308, 3182, 2201, 1774, 1697, 1634, 1598, 1478, 1373, 1026, 814 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$, 400 MHz) $\delta$: 5.04 (d, $J$ = 16.8 Hz, 1H, $CH_2$), 5.20 (d, $J$ = 16.8 Hz, 1H, $CH_2$), 6.85 (d, $J$ = 8.4 Hz, 1H, ArH), 7.44 (d, $J$ = 8.4 Hz, 1H, ArH), 7.49 (s, 1H, ArH), 7.77 (s, 2H, $NH_2$), 10.86 (s, 1H, NH). $^{13}C$ NMR (DMSO-$d_6$, 100 MHz) $\delta$: 46.99, 56.51, 66.78, 101.50, 112.49, 114.76, 117.87, 128.38, 132.90, 134.04, 141.87, 161.27, 168.78, 170.37, 176.47. HRMS [Found *m/z* 372.9696 ($M^+$); Calcd for $C_{15}H_8N_3O_4{}^{79}Br$ M, 372.9698].

**2-Amino-5′-bromo-7,7-dimethyl-2′,5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3′-indoline]-3-carbonitrile 4{*3*,*1*,*2*}.** mp: >300 °C. IR (KBr) $\nu$: 3365, 3290, 3161, 2957, 2194, 1726, 1681, 1656, 1603, 1475, 1350, 1223, 1056 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$, 400 MHz) $\delta$: 1.02 (s, 6H, 2 × $CH_3$), 2.13 (d, $J$ = 16.8 Hz, 1H, $CH_2$), 2.20 (d, $J$ = 16.8 Hz, 1H, $CH_2$), 2.51 (d, $J$ = 17.6 Hz, 1H, $CH_2$), 2.60 (d, $J$ = 17.6 Hz, 1H, $CH_2$), 6.76 (d, $J$ = 8.4 Hz, 1H, ArH), 7.21 (s, 1H, ArH), 7.32 (d, $J$ = 7.2 Hz, 1H, ArH), 7.33 (s, 2H, $NH_2$), 10.56 (s, 1H, NH). HRMS [Found *m/z* 413.0367 ($M^+$); calcd for $C_{19}H_{16}N_3O_3{}^{79}Br$ M, 413.0375].

**2-Amino-5′-bromo-2′,5-dioxo-5,6,7,8-tetrahydrospiro-[chromene-4,3′-indoline]-3-carbonitrile 4{*3*,*1*,*3*}.** mp: 290−292 °C. IR (KBr) $\nu$: 3359, 3290, 3147, 2194, 1726, 1659, 1603, 1474, 1352, 1217, 1079, 1010 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$, 400 MHz) $\delta$: 1.91−1.98 (m, 2H, $CH_2$), 2.22−2.26 (m, 2H, $CH_2$), 2.73 (t, $J$ = 6.4 Hz, 2H, $CH_2$), 6.75 (d, $J$ = 8.0 Hz, 1H, ArH), 7.22−7.26 (m, 1H, ArH), 7.32 (s, 3H, ArH+$NH_2$), 10.56 (s, 1H, NH). HRMS [Found *m/z* 385.0062 ($M^+$); Calcd for $C_{17}H_{12}N_3O_3{}^{79}Br$ M, 385.0062].

**2′-Amino-5-bromo-7′-methyl-2,5′-dioxo-5′*H*-spiro[indoline-3,4′-pyrano[4,3-*b*]pyran]-3′-carbonitrile 4{*3*,*1*,*4*}.** mp: >300 °C. IR (KBr) $\nu$: 3308, 3189, 2204, 1728, 1667, 1605, 1474, 1376, 1235, 1169, 1049 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$, 400 MHz) $\delta$: 2.26 (s, 3H, $CH_3$), 6.38 (s, 1H, CH), 6.80 (d, $J$ = 7.6 Hz, 1H, ArH), 7.38 (d, $J$ = 8.0 Hz, 1H, ArH), 7.43 (s, 1H, ArH), 7.55 (s, 2H, $NH_2$), 10.75 (s, 1H, NH). HRMS [Found *m/z* 398.9858 ($M^+$); calcd for $C_{17}H_{10}N_3O_4{}^{79}Br$ M, 398.9855].

**Ethyl 2′-Amino-5-bromo-3′-cyano-6′-methyl-2-oxospiro[indoline-3,4′-pyran]-5′-carboxylate 4{*3*,*1*,*5*}.** mp: 262−264 °C. IR (KBr) $\nu$: 3384, 3314, 3190, 2207, 1716, 1661, 1596, 1476, 1417, 1380, 1282, 1222, 1073 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$, 400 MHz) $\delta$: 0.84 (t, $J$ = 6.8 Hz, 3H, $CH_3$), 2.33 (s, 3H, $CH_3$), 3.80−3.84 (m, 2H, $CH_2$), 6.77 (d, $J$ = 8.0 Hz, 1H, ArH), 7.23 (s, 2H, $NH_2$), 7.29 (s, 1H, ArH), 7.36 (d, $J$ = 8.4 Hz, 1H, ArH), 10.55 (s, 1H, NH). HRMS [Found *m/z* 403.0172 ($M^+$); calcd for $C_{17}H_{14}N_3O_4{}^{79}Br$ M, 403.0168].

**6′-Amino-5-bromo-3′-methyl-2-oxo-1′-phenyl-1′*H*-spiro[indoline-3,4′-pyrano[2,3-*c*]pyrazole]-5′-carbonitrile 4{*3*,*1*,*6*}.** mp: 225−226 °C. IR (KBr) $\nu$: 3365, 3189, 2204, 1705, 1659, 1521, 1398, 1220, 1132, 1070 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$, 400 MHz) $\delta$: 1.59 (s, 3H, $CH_3$), 6.92 (d, $J$ = 8.4 Hz, 1H, ArH), 7.36 (t, $J$ = 6.8 Hz, 1H, ArH), 7.46−7.54 (m, 4H, ArH), 7.64 (s, 2H, $NH_2$), 7.79 (d, $J$ = 7.6 Hz, 2H, ArH), 10.90 (s, 1H, NH).

**2′-Amino-5-bromo-2,5′-dioxo-5′*H*-spiro[indoline-3,4′-pyrano[3,2-*c*]chromene]-3′-carbonitrile 4{*3*,*1*,*7*}.** mp: >300 °C. IR (KBr) $\nu$: 3315, 3190, 2200, 1745, 1681, 1614, 1473, 1362, 1084 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$, 400 MHz) $\delta$: 6.83 (d, $J$ = 8.0 Hz, 1H, ArH), 7.40 (d, $J$ = 8.0 Hz, 1H, ArH), 7.50 (d, $J$ = 8.4 Hz, 1H, ArH), 7.55 (t, $J$ = 8.0 Hz, 2H, ArH), 7.75 (s, 2H, $NH_2$), 7.79 (d, $J$ = 7.6 Hz, 1H, ArH), 7.94 (d, $J$ = 8.0 Hz, 1H, ArH), 10.83 (s, 1H, NH). HRMS [Found *m/z* 434.9863 ($M^+$); calcd for $C_{20}H_{10}N_3O_4{}^{79}Br$ M, 434.9855].

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**Supporting Information Available.** Experimental details and spectroscopic characterization for compound **4**. This material is available free of charge via the Internet at http://pubs.acs.org.

## References and Notes

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