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RESEARCH ARTICLE

Three-component cyclization as an approach to a combinatorial library of 2*H*-spiro-[chromeno[2,3-*c*]pyrrole-1,3'-indoline]-2',3,9-triones

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Abstract: A versatile and efficient three-component cyclization of methyl 4-(o-hydroxyphenyl)-2,4-dioxobutanoates **1**, N-substituted isatins **2,** and primary amines **3** was explored to synthesize of 2H-spiro[chromeno[2,3-c]pyrrole-1,3'-indoline]-2',3,9-triones. We obtained a library of 122 derivatives with an indolin-2-one motif as an important structural fragment in natural alkaloids. This method is a practical and useful strategy for constructing dihydrochromeno[2,3-c]pyrrole-3,9-diones. Most of the obtained products also have functional groups for easy and further diversification by classical reactions.

Keywords: isatin, multicomponent reactions, chromenes, combinatorial library.

Introduction

The synthesis of privileged heterocyclic compounds has become one of the prime areas of research in the field of synthetic and medicinal chemistry as most of the compounds with biological activity are derived from heterocyclic structures [1, 2].

Natural products are important privileged scaffolds that serve as important, biologically pre-validated platforms for the design of compound libraries in the search for new drug candidates [3]. The structural motif of indolin-2-ones is an important scaffold for medicinal chemistry and can be found in many naturally occurring compounds related to indole alkaloids [4]. Spirocyclic indolenines have significant therapeutic potential, and these structural motifs are present in a number of biologically active natural products. Examples of such spiro[indoline-3,2'-pyrroles] are Horsfiline [5], Coerulescine [6], and Elacomine [7] as well as polyfused Spirotryptostatin A [8] and Strychnofoline [9] (Figure 1).

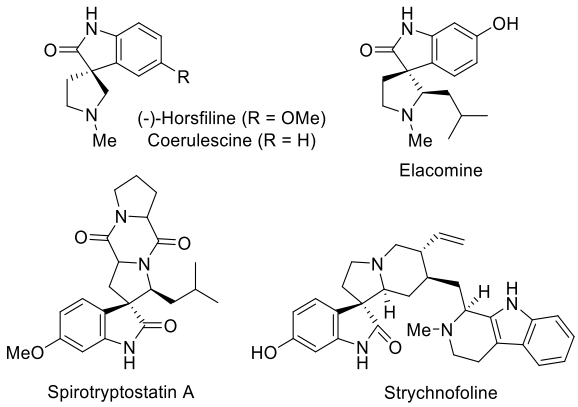

Figure 1. Examples of natural compounds with indolin-2-one motif.

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The most numerous representatives of polyfused indolin-2-ones are spiro[indoline-3,6'-pyrano[3,4-f]indolizins]. The members of this group differ mostly in the configuration of specific asymmetric centers (like alkaloids Mitraphylline, Formosanine, and Pteropodine, Figure 2) and the presence of substituents in the benzol ring (e.g., mono- and dimethoxy derivativs – Vinerine and Elegantissine (Herboxine) [10].

According to the literature, spiro[indoline-3,6'-pyrano-[3,4-*f*]indolizin] alkaloids are widely represented in plants that have long been used in traditional medicine [11, 12]. It is not surprising therefore that according to the recent data, these and similar structures can find practical use in medicine. For example, Pteropodine has manifested antigenotoxic, antioxidant and lymphocyte induction effects [13], while Mitraphylline has shown anti-inflammatory activity [14]. Several synthetic spiroheterocycles containing both indole and pyran heterocycles possess anticonvulsant and analgesic [15], antimicrobial [16], and herbicidal activities [17].

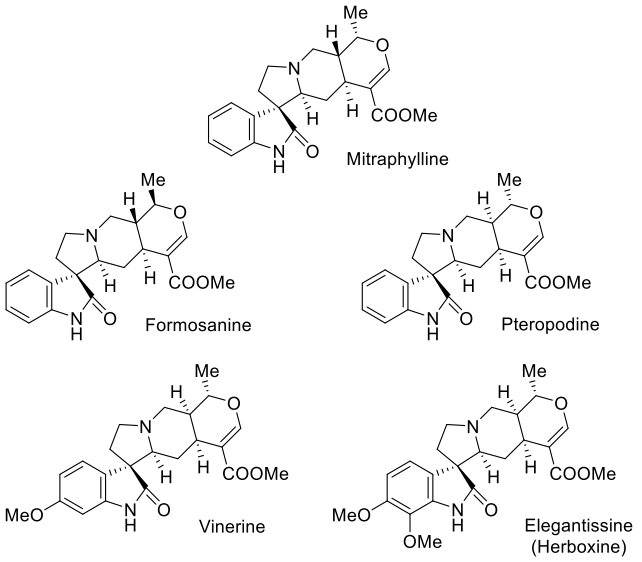
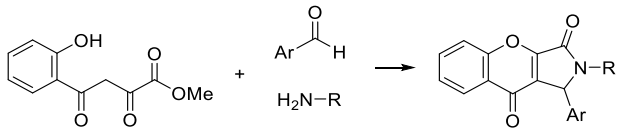


Figure 2. Examples of natural spiro[indoline-3,6'-pyrano[3,4-*f*]-indolizin] alkaloids.

In most cases, the synthesis of these compounds is a challenging task comprising of multiple synthetic steps [18]. One of the main goals of modern synthetic organic chemistry is the rapid construction of target drug-like compound libraries, characterized by several important features, for example, the complexity and variety of molecules, high variability, and easy access from relatively simple and commercially available reagents.

Results and Discussion

In our previous works, several examples of 1,2-dihydrochromeno[2,3-*c*]pyrrole-3,9-diones were obtained in a three-component condensation of methyl 4-(*o*-hydroxy-phenyl)-2,4-dioxobutanoate with aromatic aldehydes and heterocyclic amines [19] or aromatic amines [20], aliphatic amines [21] (Scheme 1). Alternative routes to the synthesis of 2-phenyl-5,6-dihydropyrano[2,3-c]pyrrole-4,7-diones [22] and 1-aryl-2-[2-(dimethylamino)ethyl]-1,2-dihydro-chromeno[2,3-c]pyrrole-3,9-diones [23] were also developed.

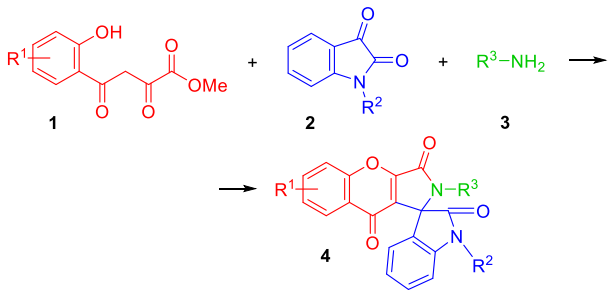


Scheme 1. Synthesis of 1,2-dihydrochromeno[2,3-*c*]pyrrole-3,9-diones (previous work).

Only two examples of 1,2-dihydrochromeno[2,3-*c*]pyrrole-3,9-dione spiro derivatives were obtained in our previous research when *N*-methylisatin was used as the carbonyl component [24].

The goal of the present research was to study a one-pot three-component condensation of methyl 4-(*o*-hydroxy-phenyl)-2,4-dioxobutanoate, *N*-substituted isatins, and primary amines, as well as the applicability of this reaction in the combinatorial synthesis. The utility and scope of this method were tested on a wide range of commercially available substrates.

The substrate scope in this condensation was subsequently explored by employing various methyl 4-(*o*-hydroxyphenyl)-2,4-dioxobutanoates **1**{*1-5*} (5 examples) with *N*-substituted isatins **2**{*1-8*} (8 examples), and primary amines **3**{*1-24*} (24 examples) (Scheme 2). The representative substrates – methyl 4-(*o*-hydroxyphenyl)-2,4-dioxobutanoates (**1**{*1-5*}), *N*-substituted isatins **2**{*1-8*}, and primary amines **3**{*1-24*} are listed in Figure 3.



Scheme 2. The 1-aryl-1,2-dihydrochromeno[2,3-*c*]pyrrole-3,9-dione **4** library generation.

First, the compatibility of different *N*-substituted isatins and primary amines in the present transformation was examined. To our delight, a wide range of alkyl groups in the case of *N*-substituted isatins, including methyl, ethyl, propyl, butyl, allyl, and benzyl, were well compatible in this transformation. It should be mentioned that the substituted primary amines were also suitable for the transformation, and synthesis of 2*H*-spiro[chromeno[2,3-*c*]pyrrole-1,3'-indoline]-2',3,9-triones was conducted in MeOH (for **3**{*1-10, 13-15, 24*}), EtOH (for **3**{*11*}), *i*-PrOH (for **3**{*12*}) at 35-40 °C, or acetic acid (for **3**{*16-23*}) under reflux. Methyl 4-(*o*-hydroxyphenyl)-2,4-dioxobutanoates with methyl, chloro, and fluoro substituents were also tolerated in this one-pot three-component procedure. As the

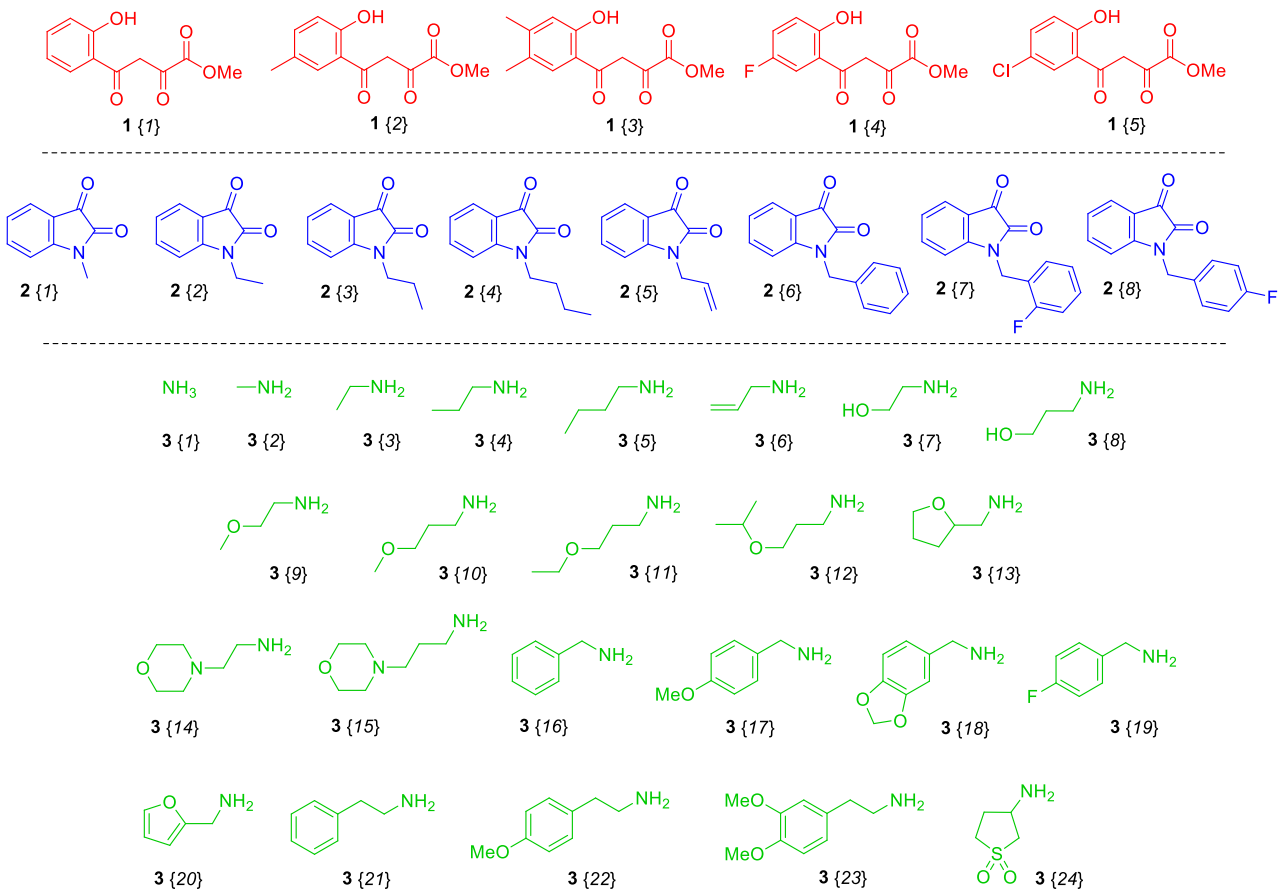


Figure 3. Scope of 4-(2-hydroxyphenyl)-2,4-dioxobutanoates **1**{*1-5*}, isatins **2**{*1-13*} and primary amines **3**{*1-24*}.

result, spiro[chromeno[2,3-*c*]pyrrole-1,3'-indoline]-2',3,9-triones (87% success rate) with good purity (> 95% according MS) (Table 1). In most cases, the yields were in the range of 48-81%, and for more than 50% of the representative set, the yield was over 70%.

^{1}H NMR spectra of products **4** corresponded to the proposed structures. However, because the skeleton of the molecules is complex, ^{13}C NMR spectra were also measured to prove the structure of the compounds, and for several compounds, COSY, HMBS, and HSQC experiments were performed.

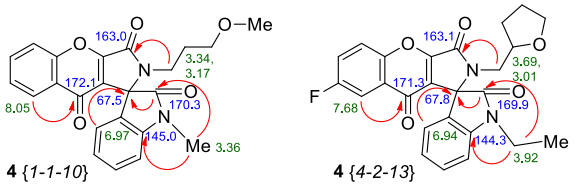


Figure 4. Important HMBC correlations for **4**{*1-1-10*} and **4**{*4-2-13*}.

In ^{13}C NMR spectra of library members **4**{*1-1-10*} and **4**{*4-2-13*}, signals at 163.0-163.1 ppm are attributed to the C-3 atom, signals at 171.3 and 172.1 ppm are attributed to the C-9 atom and signals at 169.9-170.3 ppm are attributed to the C-2' atom. Carbon atom at 67.5, and 67.8 ppm assigned to spirocarbon of pyrrole-1,3'-indoline moiety. Figure 4 shows the assignments and the most important HMBC correlations for **4**{*1-1-10*} and **4**{*4-2-13*} between signals in the ^{13}C NMR spectra (blue) and ^{1}H NMR spectra (green) upon which the assignments were based (red arrow).

The IR spectra of products **4** contain fairly intense absorption bands of carbonyl groups at 1735-1715 cm^{-1} and 1670-1660 cm^{-1}, as well as rather an intensive absorption of the unsaturated fragments conjugated with them, at approximately 1610 cm^{-1}.

Conclusions

In conclusion, we have developed an efficient protocol for the rapid synthesis of 2*H*-spiro[chromeno[2,3-*c*]pyrrole-1,3'-indoline]-2',3,9-triones using *N*-substituted isatins and primary amines in a one-pot three-component cyclo-condensation. This protocol was found to be compatible with a wide range of substituents and paves the way for the practical synthesis of 2*H*-spiro[chromeno[2,3-*c*]pyrrole-1,3'-indoline]-2',3,9-triones with a broad range of substituents under mild conditions.

Table 1. Scope of the products **4**.

4{*1-1-1*}	**4**{*1-1-21*}[a]	**4**{*1-3-5*}	**4**{*1-5-8*}	**4**{*2-1-13*}	**4**{*2-7-10*}	**4**{*3-1-13*}	**4**{*3-5-10*}	**4**{*4-5-9*}
4{*1-1-3*}	**4**{*1-1-22*}	**4**{*1-3-7*}	**4**{*1-5-9*}	**4**{*2-2-13*}	**4**{*2-7-12*}[a]	**4**{*3-2-9*}[a]	**4**{*3-5-12*}	**4**{*4-5-10*}
4{*1-1-4*}	**4**{*1-1-23*}	**4**{*1-3-8*}[a]	**4**{*1-5-10*}	**4**{*2-3-7*}	**4**{*2-7-13*}	**4**{*3-2-10*}	**4**{*3-5-13*}[a]	**4**{*4-5-12*}[a]
4{*1-1-5*}	**4**{*1-2-4*}	**4**{*1-3-9*}	**4**{*1-5-11*}	**4**{*2-3-10*}[a]	**4**{*2-7-17*}	**4**{*3-2-12*}	**4**{*4-1-5*}	**4**{*4-5-21*}
4{*1-1-6*}	**4**{*1-2-5*}	**4**{*1-3-10*}	**4**{*1-5-12*}	**4**{*2-3-9*}	**4**{*2-7-18*}[a]	**4**{*3-2-13*}	**4**{*4-1-10*}	**4**{*5-1-21*}[a]
4{*1-1-7*}	**4**{*1-2-7*}	**4**{*1-3-13*}	**4**{*1-5-13*}	**4**{*2-3-13*}	**4**{*2-7-19*}	**4**{*3-3-7*}[a]	**4**{*4-1-12*}	**4**{*5-2-5*}
4{*1-1-8*}	**4**{*1-2-8*}	**4**{*1-3-11*}	**4**{*1-5-17*}	**4**{*2-3-17*}	**4**{*2-7-20*}[a]	**4**{*3-3-9*}	**4**{*4-2-10*}	**4**{*5-3-17*}[a]
4{*1-1-9*}	**4**{*1-2-9*}	**4**{*1-3-12*}	**4**{*1-6-4*}[a]	**4**{*2-5-7*}	**4**{*2-7-21*}	**4**{*3-3-10*}	**4**{*4-2-12*}	**4**{*5-5-5*}[a]
4{*1-1-10*}[a]	**4**{*1-2-10*}	**4**{*1-3-24*}[a]	**4**{*1-6-11*}	**4**{*2-5-8*}	**4**{*2-7-22*}	**4**{*3-3-12*}	**4**{*4-2-13*}[a]	**4**{*5-5-7*}
4{*1-1-11*}	**4**{*1-2-11*}	**4**{*1-4-11*}	**4**{*1-6-17*}	**4**{*2-5-9*}	**4**{*3-1-7*}	**4**{*3-3-13*}	**4**{*4-3-10*}	**4**{*5-5-19*}
4{*1-1-12*}	**4**{*1-2-12*}	**4**{*1-4-24*}[a]	**4**{*2-1-7*}	**4**{*2-5-10*}	**4**{*3-1-8*}	**4**{*3-3-21*}	**4**{*4-3-12*}	**4**{*5-5-23*}
4{*1-1-13*}	**4**{*1-2-13*}	**4**{*1-5-2*}	**4**{*2-1-8*}	**4**{*2-5-12*}	**4**{*3-1-9*}	**4**{*3-5-8*}	**4**{*4-3-13*}	**4**{*5-6-6*}[a]
4{*1-1-14*}	**4**{*1-2-22*}[a]	**4**{*1-5-5*}	**4**{*2-1-10*}	**4**{*2-5-13*}[a]	**4**{*3-1-10*}[a]	**4**{*3-5-9*}	**4**{*4-3-16*}[a]	**4**{*5-8-10*}[a]
4{*1-1-15*}	**4**{*1-3-4*}	**4**{*1-5-7*}[a]	**4**{*2-1-12*}	**4**{*2-7-9*}				

[a] The method of the synthesis, physicochemical properties, NMR and LCMS spectra are described in the experimental section.

Experimental section

The solvents were purified according to the standard procedures. All starting materials such as substituted methyl 4-(*o*-hydroxyphenyl)-2,4-dioxobutanoates, *N*-substituted isatins, and primary amines were obtained from Enamine, Ltd. All materials were purchased from commercial sources and used without further purification. The success rate was calculated as the number of successful experiments divided by the total number of experiments. ^{1}H NMR spectra were recorded on a Varian VXR-300 spectrometer (300 MHz) or Bruker 170 spectrometer (500 MHz) and ^{13}C NMR spectra were recorded at Bruker 170 spectrometer (125 MHz) spectra in DMSO-d_6 or CF_3CO_2D or $CDCl_3$ solution. Chemical shifts are reported in ppm downfield from TMS as internal standards. Mass spectra were recorded on an LC-MS instrument with chemical ionization (CI). LC-MS data were acquired on an Agilent 1200 HPLC system equipped with DAD/ELSD/LCMS-6120 diode matrix and mass-selective detector. Melting points were measured on a MPA100 OptiMelt automated melting point system. Elemental analyses were performed at the Laboratory of Organic Analysis, Department of Chemistry, Taras Shevchenko National University of Kyiv.

The Experimental Section describes 25 compounds selected in a random manner, which corresponds to generally accepted approaches in combinatorial chemistry (according to ACS standards).

*A representative procedure for the synthesis of 1'-methyl-2-phenethyl-2H-spiro[chromeno[2,3-c]pyrrole-1,3'-indoline]-2',3,9-trione (**4**{1-1-21}).*

To a suspension of 0.01 mol of *N*-methylisatin **2**{*1*} in 15 mL of glacial acetic acid, 0.01 mol of 2-phenylethylamine **3**{*21*} and 0.01 mol of methyl-*o*-hydroxybenzoylpyruvate **1**{*1*} were added. The reaction mixture was refluxed for 1 h, cooled, and evaporated. The residues were purified by crystallization from ethanol. Yield: 335 mg, 77%. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.98 (d, *J* 7.5 Hz, 1H), 7.92-7.82 (m, 2H), 7.56-7.44 (m, 2H), 7.27-7.10 (m, 5H), 7.07-6.96 (m, 3H), 3.35 (s, 3H), 3.33-3.23 (m, 2H), 2.68 (t, *J* 7.3 Hz, 2H). IR (KBr) ν 3063, 3020, 2934, 1729 (vs), 1715 (vs), 1664 (vs), 1611, 1495, 1457, 1385, 1369, 1341, 1283, 1199, 1184, 1128, 1105, 1085, 938, 888, 751, 699, 690. MS (CI) m/z $(M+H)^+$ 437.

*2-(3-Methoxypropyl)-1'-methyl-2H-spiro[chromeno-[2,3-c]pyrrole-1,3'-indoline]-2',3,9-trione (**4**{1-1-10}).*

Yield: 310 mg, 77%. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.97 (d, *J* 7.9 Hz, 1H), 7.94-7.83 (m, 2H), 7.54 (t, *J* 6.6 Hz, 1H), 7.47 (t, *J* 7.7 Hz, 1H), 7.25 (t, *J* 6.6 Hz, 2H), 7.07 (t, *J* 7.5 Hz, 1H), 3.32 (s, 3H), 3.29-3.00 (m, 7H), 1.66-1.45 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.1, 170.3, 163.0, 156.5, 155.7, 145.0, 134.7, 131.3, 126.2, 125.9, 125.9, 125.4, 123.9, 123.6, 121.7, 119.2, 109.6, 69.7, 67.5, 58.4, 39.2, 28.0, 27.3. IR (KBr) ν 2976, 2931, 2894, 2832, 2808, 1735 (vs), 1712 (vs), 1665 (vs), 1611, 1463, 1374, 1304, 1279, 1200, 1106, 943, 873, 755, 692. MS (CI) m/z $(M+H)^+$ 405.

*1'-Ethyl-2-(4-methoxyphenethyl)-2H-spiro[chromeno-[2,3-c]pyrrole-1,3'-indoline]-2',3,9-trione (**4**{1-2-22}).*

Yield: 360 mg, 75%. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.99 (d, *J* 7.9 Hz, 1H), 7.95-7.83 (m, 2H), 7.59-7.51 (m, 1H), 7.47 (t, *J* 7.6 Hz, 1H), 7.30 (d, *J* 7.8 Hz, 1H), 7.18 (d, *J* 7.3 Hz, 1H), 7.03 (t, *J* 7.4 Hz, 1H), 6.89 (d, *J* 8.5 Hz, 2H), 6.74 (d, *J* 8.5 Hz, 2H), 3.90 (q, *J* 6.7 Hz, 2H), 3.69 (s, 3H), 3.35-3.09 (m, 2H), 2.59 (t, *J* 7.9 Hz, 2H), 1.31 (t, *J* 7.0 Hz, 3H). IR (KBr) ν 3073, 3046, 2976, 2932, 2840, 1727 (vs), 1664, 1610, 1513, 1492, 1463, 1365, 1307, 1284, 1245, 1187, 1134, 1026, 884, 833, 757, 688. MS (CI) m/z $(M+H)^+$ 480.

*2-(3-Hydroxypropyl)-1'-propyl-2H-spiro[chromeno[2,3-c]-pyrrole-1,3'-indoline]-2',3,9-trione (**4**{1-3-8}).*

Yield: 305 mg, 73%. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.98 (d, *J* 7.8 Hz, 1H), 7.95-7.83 (m, 2H), 7.59-7.49 (m, 1H), 7.44 (t, *J* 7.7 Hz, 1H), 7.30-7.19 (m, 2H), 7.05 (t, *J* 7.5 Hz, 1H), 4.30 (br s, 1H), 3.86-3.68 (m, 2H), 3.35-2.99 (m, 4H), 1.75 (m, 2H), 1.55-1.38 (m, 2H), 1.00 (t, *J* 7.4 Hz, 3H). IR (KBr) *v* 3512 (vs, br), 3063, 2955, 2934, 2877, 1728 (vs), 1664 (vs), 1610, 1490, 1462, 1361, 1312, 1284, 1191, 1135, 1107, 1069, 942, 871, 759, 690. MS (CI) m/z $(M+H)^+$ 419.

*2-(1,1-Dioxidotetrahydrothiophen-3-yl)-1'-propyl-2H-spiro[chromeno[2,3-c]pyrrole-1,3'-indoline]-2',3,9-trione (**4**{1-3-24}).*

Yield: 349 mg, 73%. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.97 (d, *J* 7.9 Hz, 1H), 7.94-7.83 (m, 2H), 7.53 (ddd, *J* 8.2, 6.0, 2.3 Hz, 1H), 7.47 (t, *J* 7.8 Hz, 1H), 7.39 (t, *J* 8.2 Hz, 1H), 7.27 (d, *J* 7.9 Hz, 1H), 7.06 (t, *J* 7.5 Hz, 1H), 3.92-3.55 (m, 3.5H), 3.49-3.27 (m, 1.5H), 3.17-2.95 (m, 1.5H), 2.92-2.59 (m, 1.5H), 2.28-2.13 (m, 0.4H), 2.13-1.98 (m, 0.6H), 1.85-1.67 (m, 2H), 1.00 (t, *J* 7.3 Hz, 3H). IR (KBr) *v* 3069, 3036, 2963, 2942, 2875, 1732 (vs), 1718 (vs), 1666 (vs), 1610, 1486, 1463, 1414, 1349, 1320, 1287, 1215, 1192, 1127, 1089, 940, 875, 757, 688, 654, 572. MS (CI) m/z $(M+H)^+$ 479.

*1'-Butyl-2-(1,1-dioxidotetrahydrothiophen-3-yl)-2H-spiro[chromeno[2,3-c]pyrrole-1,3'-indoline]-2',3,9-trione (**4**{1-4-24}).*

Yield: 373 mg, 76%. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.98 (d, *J* 8.0 Hz, 1H), 7.94-7.83 (m, 2H), 7.54 (ddd, *J* 8.1, 5.8, 2.4 Hz, 1H), 7.47 (t, *J* 7.7 Hz, 1H), 7.43-7.35 (m, 1H), 7.25 (d, *J* 7.9 Hz, 1H), 7.06 (t, *J* 7.5 Hz, 1H), 3.95-3.55 (m, 3.5H), 3.50-3.25 (m, 1.5H), 3.18-2.94 (m, 1.5H), 2.89-2.59 (m, 1.5H), 2.27-2.13 (m, 0.5H), 2.11-1.97 (m, 0.5H), 1.78-1.64 (m, 2H), 1.51-1.35 (m, 2H), 0.97 (t, *J* 7.3 Hz, 3H). IR (KBr) *v* 3100, 3069, 3038, 3020, 2961, 2936, 2875, 1732 (vs), 1667 (vs), 1610, 1488, 1464, 1411, 1351, 1322, 1306, 1288, 1189, 1126, 1106, 1089, 942, 756, 690, 573. MS (CI) m/z $(M+H)^+$ 493.

*1'-Allyl-2-(2-hydroxyethyl)-2H-spiro[chromeno[2,3-c]-pyrrole-1,3'-indoline]-2',3,9-trione (**4**{1-5-7}).*

Yield: 309 mg, 77%. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.00 (d, *J* 7.8 Hz, 1H), 7.98-7.90 (m, 2H), 7.64-7.54 (m, 1H), 7.46 (t, *J* 7.8 Hz, 1H), 7.36 (d, *J* 7.4 Hz, 1H), 7.17 (d, *J* 7.9 Hz, 1H), 7.08 (t, *J* 7.5 Hz, 1H), 6.00-5.87 (m, 1H), 5.49 (d, *J* 17.4 Hz, 1H), 5.25 (d, *J* 10.4 Hz, 1H), 4.76 (br s, 1H), 4.54 (d, *J* 16.9 Hz, 1H), 4.39 (d, *J* 17.1 Hz, 1H), 3.42-3.07 (m, 4H). IR (KBr) *v* 3477 (s, br), 2966, 2932, 2886, 1725 (vs), 1659 (vs), 1610, 1490, 1459, 1361, 1285, 1178, 1055, 933, 888, 756, 691. MS (CI) m/z $(M+H)^+$ 403.

*1'-Benzyl-2-propyl-2H-spiro[chromeno[2,3-c]pyrrole-1,3'-indoline]-2',3,9-trione (**4**{1-6-4}).*

Yield: 336 mg, 75%. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.98 (d, *J* 7.6 Hz, 1H), 7.94-7.81 (m, 2H), 7.58-7.49 (m, 1H), 7.45 (t, *J* 7.7 Hz, 1H), 7.30-7.19 (m, 2H), 7.05 (t, *J* 7.4 Hz, 1H), 3.94-3.77 (m, 2H), 3.26-3.10 (m, 1H), 2.98 (dt, *J* 14.1, 7.0 Hz, 1H), 1.40-1.21 (m, 2H), 0.77 (t, *J* 7.3 Hz, 3H). IR (KBr) *v* 3095, 3064, 3042, 2963, 2932, 2875, 1720 (vs), 1666 (vs), 1610, 1488, 1467, 1367, 1342, 1286, 1198, 1152, 1135, 1097, 946, 832, 775, 756, 689. MS (CI) m/z $(M+H)^+$ 451.

*2-(3-Methoxypropyl)-7-methyl-1'-propyl-2H-spiro-[chromeno[2,3-c]pyrrole-1,3'-indoline]-2',3,9-trione (**4**{2-3-10}).*

Yield: 343 mg, 77%. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.78-7.72 (m, 2H), 7.68 (dd, *J* 8.8, 2.0 Hz, 1H), 7.44 (td, *J* 7.8, 1.1 Hz, 1H), 7.28-7.21 (m, 2H), 7.04 (t, *J* 7.4 Hz, 1H), 3.87-3.69 (m, 2H), 3.28-3.15 (m, 3H), 3.15-2.99 (m, 4H), 2.42 (s, 3H), 1.83-1.66 (m, 2H), 1.65-1.47 (m, 2H), 1.00 (t, *J* 7.4 Hz, 3H). IR (KBr) *v* 3055, 3029, 2980, 2942, 2888, 2878, 2827, 2745, 1721 (vs), 1664 (vs), 1611, 1479, 1469, 1367, 1321, 1281, 1204, 1113, 1095, 1027, 945, 926, 909, 886, 825, 796, 749, 689, 658. MS (CI) m/z $(M+H)^+$ 447.

*1'-Allyl-7-methyl-2-((tetrahydrofuran-2-yl)methyl)-2H-spiro[chromeno[2,3-c]pyrrole-1,3'-indoline]-2',3,9-trione (**4**{2-5-13}).*

Yield: 351 mg, 77%. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.82 (d, *J* 8.4 Hz, 1H), 7.80-7.71 (m, 2H), 7.43 (t, *J* 7.4 Hz, 1H), 7.29 (t, *J* 7.4 Hz, 1H), 7.15-7.02 (m, 2H), 5.98-5.85 (m, 1H), 5.52 (d, *J* 15.6 Hz, 1H), 5.24 (d, *J* 13.4Hz, 1H), 4.52 (br d, *J* 15.0 Hz), 4.36 (m, 1H), 3.70-3.54 (m, 2H), 5.55-3.37 (m, 2H), 3.00 (dd, *J* 14.4, 4.8 Hz, 0.7H), 2.91 (dd, *J* 14.4, 7.5 Hz, 0.3H), 2.42 (s, 3H), 1.82-1.63 (m, 3H), 1.62-1.35 (m, 1H). IR (KBr) *v* 3075, 3057, 3025, 2981, 2965, 2918, 2869, 1729 (vs), 1664 (vs), 1612, 1479, 1467, 1362, 1282, 1191, 1091, 993, 948, 923, 819, 750, 736. MS (CI) m/z $(M+H)^+$ 457.

*1'-(2-Fluorobenzyl)-2-(3-isopropoxypropyl)-7-methyl-2H-spiro[chromeno[2,3-c]pyrrole-1,3'-indoline]-2',3,9-trione (**4**{2-7-12}).*

Yield: 410 mg, 76%. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.82-7.74 (m, 2H), 7.70 (dd, *J* 8.7, 1.9 Hz, 1H), 7.55 (t, *J* 7.7 Hz, 1H), 7.43-7.32 (m, 2H), 7.29 (d, *J* 6.9 Hz, 1H), 7.26-7.14 (m, 2H), 7.10-7.01 (m, 2H), 5.14 (d, *J* 16.4 Hz, 1H), 5.04 (d, *J* 16.3 Hz, 1H), 3.44-3.02 (m, 5H), 2.45 (s, 3H), 1.56-1.40 (m, 2H), 0.99 (t, *J* 6.3 Hz, 6H). IR (KBr) *v* 3058, 2972, 2932, 2864, 1732 (vs), 1723 (vs), 1662 (vs), 1614, 1491, 1469, 1409, 1360, 1341, 1311, 1284, 1228, 1201, 1172, 1146, 1099, 943, 921, 828, 816, 758, 748, 690. MS (CI) m/z $(M+H)^+$ 541.

*2-(Benzo[d][1,3]dioxol-5-ylmethyl)-1'-(2-fluorobenzyl)-7-methyl-2H-spiro[chromeno[2,3-c]pyrrole-1,3'-indoline]-2',3,9-trione (**4**{2-7-18}).*

Yield: 430 mg, 75%. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.82-7.74 (m, 2H), 7.70 (dd, *J* 8.7, 1.9 Hz, 1H), 7.47 (t, *J* 7.7 Hz, 1H), 7.40-7.26 (m, 2H), 7.24-7.08 (m, 3H), 6.99-6.86 (m, 2H), 6.59 (d, *J* 7.9 Hz, 1H), 6.48 (d, *J* 1.4 Hz, 1H), 6.32 (dd, *J* 7.9, 1.4 Hz, 1H), 5.92 (s, 2H), 4.92 (d, *J* 16.6 Hz, 1H), 4.78 (d, *J* 16.5 Hz, 1H), 4.42 (d, *J* 15.1 Hz, 1H), 4.13 (d, *J* 15.1 Hz, 1H), 2.43 (s, 3H). IR (KBr) *v* 3098, 3060, 3027, 2926, 2890, 2782, 1722 (vs), 1663 (vs), 1611, 1491, 1467, 1448, 1367, 1308, 1285, 1253, 1228, 1187,

1099, 1042, 946, 823, 771, 754, 687. MS (CI) m/z $(M+H)^+$ 575.

*1'-(2-Fluorobenzyl)-2-(furan-2-ylmethyl)-7-methyl-2H-spiro[chromeno[2,3-c]pyrrole-1,3'-indoline]-2',3,9-trione (**4**{2-7-20}).*

Yield: 390 mg, 75%. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.78 (d, *J* 8.5 Hz, 2H), 7.71 (dd, *J* 8.7, 2.0 Hz, 1H), 7.55 (t, *J* 7.2 Hz, 1H), 7.41-7.27 (m, 3H), 7.28-7.13 (m, 3H), 6.98 (t, *J* 7.5 Hz, 1H), 6.92 (d, *J* 7.9 Hz, 1H), 6.17 (dd, *J* 3.0, 1.9 Hz, 1H), 5.87 (d, *J* 3.1 Hz, 1H), 4.96 (d, *J* 16.7 Hz, 1H), 4.81 (d, *J* 16.6 Hz, 1H), 4.62 (d, *J* 15.8 Hz, 1H), 4.20 (d, *J* 15.8 Hz, 1H), 2.44 (s, 3H). IR (KBr) *v* 3048, 2923, 1730 (vs), 1660 (vs), 1612, 1491, 1472, 1424, 1361, 1288, 1229, 1204, 1182, 1146, 1102, 1080, 1010, 942, 828, 767, 753, 733, 689. MS (CI) m/z $(M+H)^+$ 521.

*2-(3-Methoxypropyl)-1',6,7-trimethyl-2H-spiro[chromeno-[2,3-c]pyrrole-1,3'-indoline]-2',3,9-trione (**4**{3-1-10}).*

Yield: 311 mg, 72%. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.66 (s, 1H), 7.61 (s, 1H), 7.45 (td, *J* 8.7, 1.1 Hz, 1H), 7.22 (d, *J* 8.5 Hz, 2H), 7.06 (t, *J* 7.9 Hz, 1H), 3.32 (s, 3H), 3.29-3.15 (m, 3H), 3.13 (s, 3H), 3.11-2.98 (m, 1H), 2.40 (s, 3H), 2.31 (s, 3H), 1.67-1.44 (m, 2H). IR (KBr) *v* 3061, 3047, 3029, 2973, 2928, 2876, 2834, 1733 (vs), 1719 (vs), 1662 (vs), 1611, 1467, 1414, 1367, 1350, 1284, 1195, 1133, 1113, 1084, 1020, 942, 754, 690. MS (CI) m/z $(M-H)^-$ 430.

*1'-Ethyl-2-(2-methoxyethyl)-6,7-dimethyl-2H-spiro-[chromeno[2,3-c]pyrrole-1,3'-indoline]-2',3,9-trione (**4**{3-2-9}).*

Yield: 320 mg, 74%. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.68 (s, 1H), 7.62 (s, 1H), 7.43 (td, *J* 7.8, 1.1 Hz, 1H), 7.21 (d, *J* 7.8 Hz, 1H), 7.18 (d, *J* 6.7 Hz, 1H), 7.03 (t, *J* 7.3 Hz, 1H), 3.98-3.70 (m, 2H), 3.50-3.36 (m, 1H), 3.31-3.09 (m, 6H), 3.03 (s, 3H), 2.40 (s, 3H), 2.31 (s, 3H), 1.30 (t, *J* 7.1 Hz, 3H). IR (KBr) *v* 3060, 3031, 2986, 2935, 2886, 2832, 1727 (vs), 1664 (vs), 1611, 1493, 1467, 1414, 1373, 1303, 1194, 1160, 1123, 1093, 1008, 873, 765, 690. MS (CI) m/z $(M+H)^+$ 433.

*2-(2-Hydroxyethyl)-6,7-dimethyl-1'-propyl-2H-spiro-[chromeno[2,3-c]pyrrole-1,3'-indoline]-2',3,9-trione (**4**{3-3-7}).*

Yield: 311 mg, 72%. ^{1}H NMR (500 MHz, CF_3CO_2D) δ 7.98 (s, 1H), 7.64 (s, 2H), 7.37-7.18 (m, 3H), 4.64-4.39 (m, 1H), 4.15-3.90 (m, 3H), 3.90-3.69 (m, 1.5H), 3.63-3.46 (m, 0.5H), 2.55 (s, 3H), 2.45 (s, 3H), 2.08-1.88 (m, 2H), 1.15 (t, *J* 7.2 Hz, 3H). IR (KBr) *v* 3500 (vs, br), 3052, 2966, 2934, 2876, 1726 (vs), 1667 (vs), 1610 (vs), 1489, 1468, 1410, 1367, 1305, 1285, 1193, 1139, 1095, 1054, 943, 852, 763, 690. MS (CI) m/z $(M+H)^+$ 433.

*1'-Allyl-6,7-dimethyl-2-((tetrahydrofuran-2-yl)methyl)-2H-spiro[chromeno[2,3-c]pyrrole-1,3'-indoline]-2',3,9-trione (**4**{3-5-13}).*

Yield: 357 mg, 76%. ^{1}H NMR (500 MHz, CF_3CO_2D) δ 7.98 (s, 1H), 7.73-7.56 (m, 2H), 7.39-7.18 (m, 3H), 6.16-5.93 (m, 1H), 5.58 (dd, *J* 17.3, 4.9 Hz, 1H), 5.47 (d, *J* 10.4 Hz, 1H), 4.82-4.68 (m, 1H), 4.67-4.50 (m, 1H), 4.43-4.32 (m, 0.6H), 4.32-4.21 (m, 0.4H), 4.11-3.89 (m, 2H), 3.82 (dd, *J* 15.1, 5.3 Hz, 0.6H), 3.66-3.34 (m, 1.4H), 2.56 (s, 3H), 2.45 (s, 3H), 2.26-1.98 (m, 3H), 1.97-1.78 (m, 1H). IR (KBr) *v* 3092, 3056, 2971, 2952, 2924, 2854, 1731 (vs), 1662 (vs), 1609, 1489, 1467, 1436, 1408, 1360, 1303, 1275, 1182, 1132, 1067, 941, 864, 825, 764, 692, 675. MS (CI) m/z $(M+H)^+$ 469.

*1'-Ethyl-7-fluoro-2-((tetrahydrofuran-2-yl)methyl)-2H-spiro[chromeno[2,3-c]pyrrole-1,3'-indoline]-2',3,9-trione (**4**{4-2-13}).*

Yield: 363 mg, 81%. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.07 (dd, *J* 9.3, 4.2 Hz, 1H), 7.91-7.78 (m, 1H), 7.68 (dd, *J* 8.3, 3.1 Hz, 1H), 7.46 (t, *J* 7.8 Hz, 1H), 7.33-7.22 (m, 2H), 7.06 (t, *J* 7.5 Hz, 1H), 3.92-3.71 (m, 2H), 3.71-3.53 (m, 1H), 3.52-3.30 (m, 3H), 3.05 (dd, *J* 14.7, 4.9 Hz, 0.3H), 2.92 (dd, *J* 14.4, 7.4 Hz, 0.7H), 1.85-1.59 (m, 3H), 1.59-1.33 (m, 1H), 1.25 (t, *J* 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ (as a mixture of two diastereomers (1:2.5), signals of the main isomer) 171.3, 169.9, 163.1, 160.0 (d, $J_{C\text{-}F}$ 249.0 Hz), 155.5, 152.6, 144.4, 131.2, 126.7 (d, $J_{C\text{-}F}$ 7.4 Hz), 125.9, 124.1, 123.1, 122.8 (d, $J_{C\text{-}F}$ 25.4 Hz), 121.4, 121.3 (d, $J_{C\text{-}F}$ 8.2 Hz), 111.07 (d, $J_{C\text{-}F}$ 24.1 Hz), 109.5, 76.6, 67.8, 45.1, 35.9, 29.5, 28.3, 25.2, 12.4. IR (KBr) *v* 3068, 2978, 2949, 2876, 1726 (vs), 1670 (vs), 1609, 1475, 1362, 1282, 1258, 1191, 1140, 1110, 1056, 932, 897, 834, 764, 750, 689. MS (CI) m/z $(M+H)^+$ 449.

*2-Benzyl-7-fluoro-1'-propyl-2H-spiro[chromeno[2,3-c]-pyrrole-1,3'-indoline]-2',3,9-trione (**4**{4-3-16}).*

Yield: 355 mg, 76%. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.09 (dd, *J* 9.3, 4.2 Hz, 1H), 7.86 (ddd, *J* 9.2, 8.0, 3.2 Hz, 1H), 7.68 (dd, *J* 8.3, 3.1 Hz, 1H), 7.40 (t, *J* 7.7 Hz, 1H), 7.25-7.11 (m, 5H), 7.00-6.88 (m, 3H), 4.49 (d, *J* 15.4 Hz, 1H), 4.17 (d, *J* 15.4 Hz, 1H), 3.52 (t, *J* 6.9 Hz, 2H), 1.66-1.47 (m, 2H), 0.89 (t, *J* 7.4 Hz, 3H). IR (KBr) *v* 3091, 3056, 3043, 2967, 2935, 2919, 2876, 1727 (vs), 1667, 1609, 1580, 1470, 1376, 1354, 1326, 1285, 1256, 1189, 1140, 1086, 940, 883, 832, 735, 704, 687. MS (CI) m/z $(M+H)^+$ 469.

*1'-Allyl-7-fluoro-2-(3-isopropoxypropyl)-2H-spiro[chromeno[2,3-c]pyrrole-1,3'-indoline]-2',3,9-trione (**4**{4-5-12}).*

Yield: 366 mg, 77%. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.00 (dd, *J* 9.3, 4.2 Hz, 1H), 7.82-7.71 (m, 1H), 7.65 (dd, *J* 8.2, 3.1 Hz, 1H), 7.43 (t, *J* 7.3 Hz, 1H), 7.27 (d, *J* 7.2 Hz, 1H), 7.13 (d, *J* 7.9 Hz, 1H), 7.06 (t, *J* 7.5 Hz, 1H), 5.90 (ddd, *J* 15.1, 10.2, 5.0 Hz, 1H), 5.45 (d, *J* 17.3 Hz, 1H), 5.24 (d, *J* 10.4 Hz, 1H), 4.51 (dd, *J* 16.8, 4.4 Hz, 1H), 4.39 (dd, *J* 16.8, 4.7 Hz, 1H), 3.45-3.01 (m, 5H), 1.60-1.44 (m, 2H), 1.00 (t, *J* 6.2 Hz, 3H). IR (KBr) *v* 3083, 3061, 3044, 3035, 3028, 2974, 2932, 2885, 2843, 1729 (vs), 1660 (vs), 1610, 1471 (vs), 1368, 1335, 1286, 1258, 1189, 1141, 1087, 977, 922, 886, 838, 756, 705, 691, 561. MS (CI) m/z $(M+H)^+$ 477.

*7-Chloro-1'-methyl-2-phenethyl-2H-spiro[chromeno-[2,3-c]pyrrole-1,3'-indoline]-2',3,9-trione (**4**{5-1-21}).*

Yield: 371 mg, 79%. ^{1}H NMR (500 MHz, CF_3CO_2D) δ 8.18 (d, *J* 1.1 Hz, 1H), 7.91 (dd, *J* 9.1, 1.1 Hz, 1H), 7.79 (d,

J 9.1 Hz, 1H), 7.65 (t, *J* 7.8 Hz, 1H), 7.33-7.18 (m, 5H), 7.08-6.97 (m, 3H), 3.74-3.50 (m, 3H), 3.03-2.85 (m, 2H). IR (KBr) *ν* 3074, 3024, 2937, 1730 (vs), 1714 (vs), 1665 (vs), 1609, 1494, 1461, 1367, 1349, 1282, 1177, 1114, 1087, 942, 823, 757, 700, 688, 655. MS (CI) m/z $(M+H)^+$ 471.

*7-Chloro-2-(4-methoxybenzyl)-1'-propyl-2H-spiro[chromeno[2,3-c]pyrrole-1,3'-indoline]-2',3,9-trione (**4**{5-3-17}).*

Yield: 386 mg, 75%. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.99-7.93 (m, 1H), 7.93-7.87 (m, 2H), 7.39 (t, *J* 7.7 Hz, 1H), 7.12 (d, *J* 7.9 Hz, 1H), 7.08 (d, *J* 7.3 Hz, 1H), 6.94 (t, *J* 7.5 Hz, 1H), 6.79 (d, *J* 8.6 Hz, 2H), 6.65 (d, *J* 8.6 Hz, 2H), 4.49 (d, *J* 15.0 Hz, 1H), 4.03 (d, *J* 15.0 Hz, 1H), 3.70 (s, 3H), 3.57-3.38 (m, 2H), 1.69-1.49 (m, 2H), 0.92 (t, *J* 7.4 Hz, 3H). IR (KBr) *ν* 3088, 3076, 2958, 2932, 2873, 2841, 1736 (vs), 1725 (vs), 1668 (vs), 1609 (vs), 1512, 1488, 1463, 1436, 1365, 1313, 1281, 1265, 1247, 1201, 1180, 1139, 1111, 1087, 1024, 942, 902, 825, 765, 687, 656. MS (CI) m/z $(M+H)^+$ 515.

*1'-Allyl-2-butyl-7-chloro-2H-spiro[chromeno[2,3-c]pyrrole-1,3'-indoline]-2',3,9-trione (**4**{5-5-5}).*

Yield: 313 mg, 70%. ^{1}H NMR (500 MHz, CF_3CO_2D) δ 7.98 (s, 1H), 7.69-7.56 (m, 2H), 7.36-7.21 (m, 3H), 6.04 (ddt, *J* 15.9, 10.4, 5.3 Hz, 1H), 5.54 (d, *J* 17.3 Hz, 1H), 5.47 (d, *J* 10.3 Hz, 1H), 4.68 (qd, *J* 16.4, 5.4 Hz, 2H), 3.64-3.45 (m, 1H), 3.45-3.25 (m, 1H), 2.56 (s, 3H), 2.46 (s, 1H), 1.63-1.48 (m, 2H), 1.41-1.23 (m, 2H), 0.87 (t, *J* 7.3 Hz, 3H). IR (KBr) *ν* 3058, 3048, 3029, 2960, 2931, 2874, 2860, 1731 (vs), 1718 (vs), 1663 (vs), 1621, 1610, 1487, 1467, 1438, 1410, 1391, 1360, 1306, 1285, 1192, 1136, 1104, 954, 868, 752, 692. MS (CI) m/z $(M+H)^+$ 449.0.

*2-Allyl-1'-benzyl-7-chloro-2H-spiro[chromeno[2,3-c]pyrrole-1,3'-indoline]-2',3,9-trione (**4**{5-6-6}).*

Yield: 347 mg, 72%. ^{1}H NMR (500 MHz, CF_3CO_2D) δ 8.23 (br s, 1H), 7.94 (br d, *J* 9.1 Hz, 1H), 7.81 (d, *J* 9.1 Hz, 1H), 7.59-7.34 (m, 6H), 7.31-7.18 (m, 3H), 5.76-5.58 (m, 1H), 5.23 (d, *J* 15.4 Hz, 1H), 5.08 (d, *J* 15.4 Hz, 1H), 4.96 (d, *J* 10.1 Hz, 1H), 4.88 (d, *J* 17.0 Hz, 1H), 4.43 (dd, *J* 15.3, 5.4 Hz, 1H), 3.80 (dd, *J* 15.4, 8.0 Hz, 1H). IR (KBr) *ν* 3092, 3073, 3025, 2984, 2932, 2907, 1730 (vs), 1661 (vs), 1608, 1489, 1461, 1368, 1350, 1282, 1256, 1200, 1177, 1114, 944, 928, 829, 756, 698, 657. MS (CI) m/z $(M+H)^+$ 483.

*7-Chloro-1'-(4-fluorobenzyl)-2-(3-methoxypropyl)-2H-spiro[chromeno[2,3-c]pyrrole-1,3'-indoline]-2',3,9-trione (**4**{5-8-10}).*

Yield: 372 mg, 70%. ^{1}H NMR (500 MHz, CF_3CO_2D) δ 8.22 (br s, 1H), 7.94 (br d, *J* 9.1 Hz, 1H), 7.81 (d, *J* 9.1 Hz, 1H), 7.62-7.47 (m, 3H), 7.33-7.23 (m, 3H), 7.13 (t, *J* 8.2 Hz, 2H), 5.27 (d, *J* 15.5 Hz, 1H), 5.16 (d, *J* 15.6 Hz, 1H), 3.63 (t, *J* 5.9 Hz, 2H), 3.59-3.42 (m, 5H), 1.98-1.77 (m, 2H). IR (KBr) *ν* 3071, 2984, 2929, 2868, 2826, 2805, 1728 (vs), 1667 (vs), 1608, 1509, 1489, 1462, 1374, 1360, 1323, 1287, 1258, 1225, 1202, 1174, 1118, 1095, 944, 907, 839, 826, 763, 687, 676, 663. MS (CI) m/z $(M+H)^+$ 533.

Notes

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Трикомпонентна циклізація як підхід до створення комбінаторної бібліотеки 2*H*-спіро[хромено[2,3-*c*]пірол-1,3'-індолін]-2',3,9-трионів

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Резюме: Представлено дослідження трикомпонентної циклізації метилових естерів 4-(*o*-гідроксифеніл)-2,4-діоксобутанових кислот **1**, *N*-заміщених ізатинів **2** та первинних амінів **3**, що веде до утворення 2*H*-спіро[хромено[2,3-*c*]пірол-1,3'-індолін]-2',3,9-трионів. Спіроциклічні індолін-2-они досить широко представлені серед природних біоактивних сполук, зокрема, у складі алкалоїдів, молекули яких містять систему спіро[індолін-3,6'-пірано[3,4-*f*]індолізину]. Зараз є доведеним, що деякі популярні в традиційній медицині лікарські рослини зобов'язані своїм цілющим властивостям саме алкалоїдам цієї групи. Разом із тим, синтез таких похідних досить складний, що обмежує можливості їх використання на практиці. Альтернативною стратегією є високоефективний трикомпонентний одностадійний синтез близьких за будовою структур, зокрема, 2*H*-спіро[хромено[2,3-*c*]пірол-1,3'-індолін]-2',3,9-трионів, з можливістю варіації в широких межах замісників і функціональних груп. В ході досліджень було підтверджено, що вказана трикомпонентна гетероциклізація дійсно є універсальним та ефективним інструментом синтезу 2*H*-спіро[хромено[2,3-*c*]пірол-1,3'-індолін]-2',3,9-трионів. На основі естерів 4-(*o*-гідроксифеніл)-2,4-діоксобутанових кислот, ізатинів із алкільними, алільним та бензильними замісниками в положенні 1, а також широкого набору аліфатичних амінів (в тому числі з активними функціональними групами, ароматичними та гетероциклічними фрагментами) було створено комбінаторну бібліотеку з 122 похідних, причому синтетична ефективність склала 87%, а виходи більш ніж 50% представників бібліотеки перевищували 70%. Синтетична процедура є простою у виконанні, допускає варіацію розчинників і придатна для автоматизації. ЯМР дослідження синтезованих сполук, а саме ^{1}H та ^{13}C спектри ЯМР, а також (для окремих представників) – COSY, HMBS та HSQC, дозволили не лише однозначно підтвердити структуру речовин, але й встановити характеристичні сигнали в спектрах ^{1}H та ^{13}C ЯМР, зокрема сигнал спіроатома карбону – близько 67 м.ч. Сигнали карбонільних груп в ІЧ спектрах виявляються двома широкими та інтенсивними смугами – 1735-1715 та 1670-1660 см$^{-1}$.

Ключові слова: ізатин, трикомпонентна циклізація, 1,2-дигідрохромено[2,3-*c*]пірол-3,9-діони, комбінаторна бібліотека.