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Synthesis of Fused 2′-Amino-3′-R-spiro-[indole-3,4′-pyran]-2(1*H*)-ones

L. A. Shemchuk, V. P. Chernykh, and R. G. Red'kin

Natsional Pharmaceutical University, ul. Pushkinskaya 53, Khar'kov, 61002 Ukraine
e-mail: ruslan_red@ukr.net

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Abstract—An efficient one-pot procedure has been proposed for the synthesis of fused 2′-amino-3′-R-spiro-[indole-3,4′-pyran]-2(1*H*)-ones via base-catalyzed three-component condensation of isatins with the corresponding nitriles and 1,3-diketones.

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The goal of the present study was to synthesize derivatives of 2-oxoindole with a view to obtain new melatonin analogs containing spiro-fused 4*H*-pyran and 2-oxoindole rings and an aminoethyl pharmacophoric group incorporated into the pyran ring. Spirocyclic systems possessing 2-oxoindole and pyran fragments have been found in the nature, in particular as alstonisine alkaloids isolated from *Alstonia* plants, which exhibit mainly cholinolytic and anti-inflammatory effects [1, 2]. Synthetic 4*H*-pyran derivatives, including spirocyclic ones, are widely known as biologically active substances possessing versatile pharmacological activity [3, 4]. Among these, melatonin analogs lacking indole fragment were also found [5].

Spirocyclic systems in which the spiro-carbon atom occupies position *3* in 2-oxoindole and position *4* in 2-amino-4*H*-pyran were poorly studied. Reactions of 2-(2-oxoindol-3-ylidene)malononitrile with dimedone and cyclohexane-1,3-dione were reported [6–8]; however, no systematic studies on such compounds were performed.

Different methods for the synthesis of 2-amino-4*H*-pyran are known [9], but the most important is Michael addition of carbonyl compounds to electron-deficient ethylenes possessing a cyano group [10]. We followed an analogous approach to synthesize 2′-amino-3′-R-spiro[indole-3,4′-pyran]-2(1*H*)-ones.

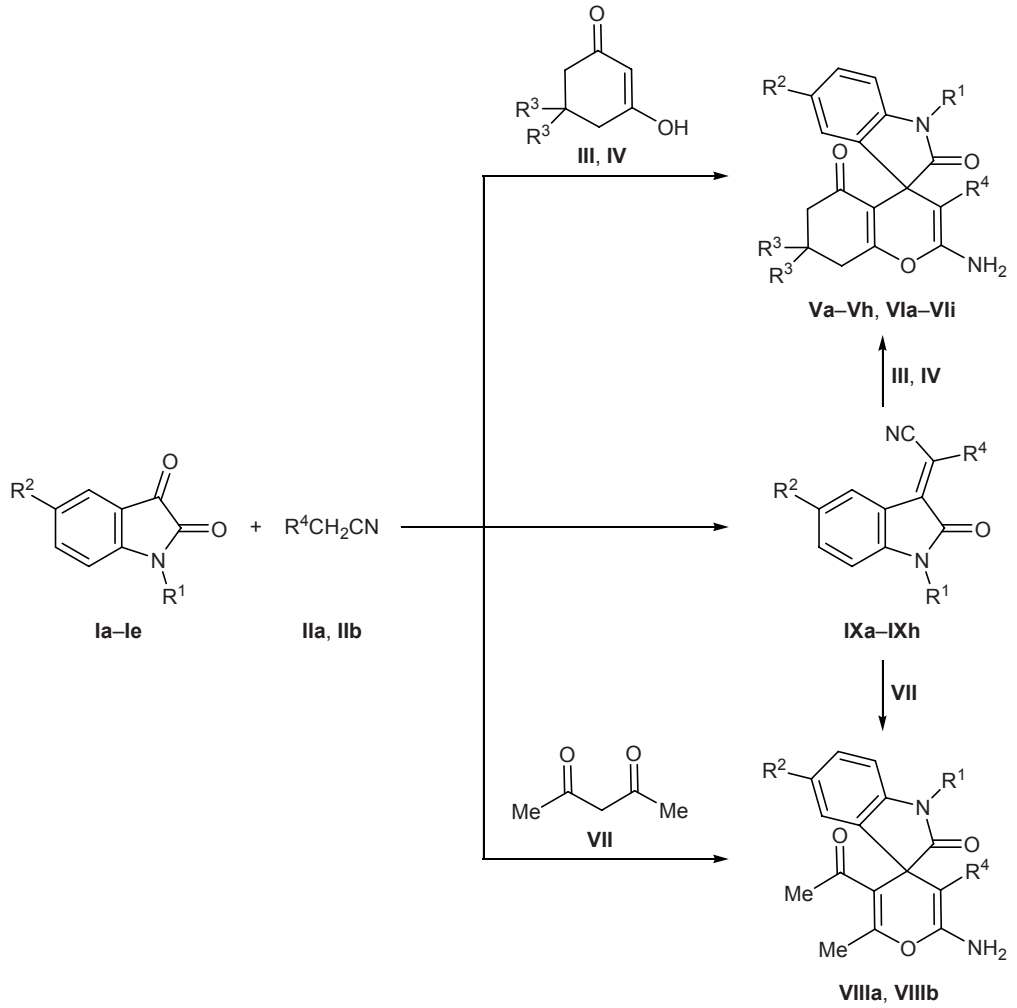
Three-component condensation of isatins **Ia**–**Ie** with malononitrile (**IIa**) or ethyl cyanoacetate (**IIb**) and cyclic 1,3-diketone, cyclohexane-1,3-dione (**III**) or dimedone (**IV**), on heating for a short time in ethanol in the presence of an equimolar amount of tris(2-hydroxyethyl)amine gave the corresponding 2-amino-3-R-5,6,7,8-tetrahydrospiro[chromene-4,3′-indole]-2′,5(1′*H*,4*H*)-diones **Va**–**Vh** or 2-amino-3-R-7,7-dimethyl-5,6,7,8-tetrahydrospiro[chromene-4,3′-indole]-2′,5(1′*H*,4*H*)-diones **VIa**–**VIi** (Scheme 1).

Replacement of cyclic 1,3-diketones by acetylacetone (**VII**) in the condensation with isatin **Ia** and malononitrile (**IIa**) or ethyl cyanoacetate (**IIb**) in the presence of tris(2-hydroxyethyl)amine in ethanol (short heating or reflux for 2 h) also resulted in 2′-amino-2-oxo-3′-R-1,2-dihydrospiro[indole-3,4′-pyran] derivatives **VIIIa** and **VIIIb** (Scheme 1).

When 2-(2-oxoindol-3-ylidene)malononitriles **IXa**–**IXd** or ethyl 2-(2-oxoindol-3-ylidene)cyanoacetate derivatives **IXe**–**IXh** were used as α-cyanoethylene component in the Michael reactions with 1,3-dicarbonyl compounds **III**, **IV**, and **VII** on prolonged heating in boiling ethanol in the presence of a catalytic amount of tris(2-hydroxyethyl)amine, we obtained the same fused 4*H*-pyran derivatives **V**, **VI**, and **VIII**. Obviously, compounds **IX** are key intermediates in the three-component condensation of isatins with CH-active nitriles and 1,3-diketones, which is consistent with the generally accepted mechanism of such reactions.

Compounds **IXa**–**IXd** were synthesized by condensation of isatins **Ia**–**Ie** with malononitrile (**IIa**), and esters **IXe**–**IXh** were obtained by heating isatins **Ia**–**Ie** with ethyl cyanoacetate (**IIb**) in boiling ethanol in the presence of an equimolar amount of tris(2-hydroxyethyl)amine according to the procedure described in [11]. In the three-component condensation of *N*-(morpholinomethyl)isatin (**X**) with cyclic 1,3-diketones **III**

Scheme 1.



I, R^1 = H, R^2 = H (**a**); R^1 = H, R^2 = Me (**b**); R^1 = Me, R^2 = H (**c**); R^1 = $PhCH_2$, R^2 = H (**d**); R^1 = H, R^2 = Br (**e**); **II**, R^4 = CN (**a**), CO_2Et (**b**); **III**, R^3 = H; **IV**, R^3 = Me; **V**, R^1 = R^2 = R^3 = H, R^4 = CN (**a**); R^1 = R^3 = H, R^2 = Me, R^4 = CN (**b**); R^1 = Me, R^2 = R^3 = H, R^4 = CN (**c**); R^1 = $PhCH_2$, R^2 = R^3 = H, R^4 = CN (**d**); R^1 = R^2 = R^3 = H, R^4 = CO_2Et (**e**); R^1 = R^3 = H, R^2 = Me, R^4 = CO_2Et (**f**); R^1 = Me, R^2 = R^3 = H, R^4 = CO_2Et (**g**); R^1 = $PhCH_2$, R^2 = R^3 = H, R^4 = CO_2Et (**h**); **VI**, R^1 = R^2 = H, R^3 = Me, R^4 = CN (**a**); R^1 = H, R^2 = R^3 = Me, R^4 = CN (**b**); R^1 = R^3 = Me, R^2 = Br, R^4 = CN (**c**); R^1 = R^3 = Me, R^2 = H, R^4 = CN (**d**); R^1 = $PhCH_2$, R^2 = H, R^3 = Me, R^4 = CN (**e**); R^1 = R^2 = H, R^3 = Me, R^4 = CO_2Et (**f**); R^1 = H, R^2 = R^3 = Me, R^4 = CO_2Et (**g**); R^1 = R^3 = Me, R^2 = H, R^4 = CO_2Et (**h**); R^1 = $PhCH_2$, R^2 = H, R^3 = Me, R^4 = CO_2Et (**i**); **VIII**, R^1 = R^2 = H, R^4 = CN (**a**); R^1 = R^2 = H, R^4 = CO_2Et (**b**); IX, R^1 = R^2 = H, R^4 = CN (**a**); R^1 = H, R^2 = Me, R^4 = CN (**b**); R^1 = Me, R^2 = H, R^4 = CN (**c**); R^1 = $PhCH_2$, R^2 = H, R^4 = CN (**d**); R^1 = R^2 = H, R^4 = CO_2Et (**e**); R^1 = H, R^2 = Me, R^4 = CO_2Et (**f**); R^1 = Me, R^2 = H, R^4 = CO_2Et (**g**); R^1 = $PhCH_2$, R^2 = H, R^4 = CO_2Et (**h**).

and **IV** or acetylacetone (**VII**), the same products as in the reaction with **Ia** (compounds **Va**, **Ve**, **VIa**, **VIf**, **VIIIa**, and **VIIIb**) were isolated even at room temperature (Scheme 2).

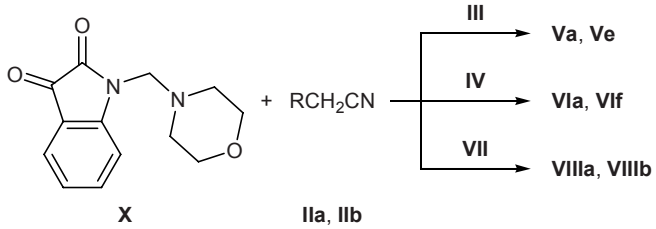
Elimination of the morpholinomethyl residue from isatin **X** which is capable of acting as reactive Mannich base was also observed previously. Compound **X** readily reacts with 1,3-diketones even at room temperature [12]. We failed to isolate the corresponding products, but this assumption is confirmed by the fact that the yield of 4*H*-pyrans decreased from 70–90 to 30–45%.

Thus three-component condensation of isatins with cyanomethylene compounds and 1,3-diketones smoothly occurs under mild conditions in the presence of an equimolar amount of tris(2-hydroxyethyl)amine to give the corresponding fused 2-amino-3′-R-spiro-[indole-3,4′-pyran]-2(1*H*)-ones in high yield.

EXPERIMENTAL

The ^{1}H NMR spectra were measured from solutions in DMSO-d_6 on a Varian M-200 spectrometer (200 MHz) using tetramethylsilane as internal refer-

Scheme 2.



ence. The IR spectra were recorded in KBr on a Bruker Tensor-27 spectrophotometer. The mass spectra (electron impact, 70 eV) were obtained on a Varian 1200L mass spectrometer with direct sample admission into the ion source heated to 50–150°C. The progress of reactions and the purity of products were monitored by TLC on Silufol UV-254 plates.

Initial 2-(2-oxoindol-3-ylidene)malononitriles **IXa**–**IXd** and ethyl 2-(2-oxoindol-3-ylidene)cyanoacetates **IXe**–**IXh** were synthesized according to the procedure described in [11]. Compounds **IXa**, **IXc**, **IXe**, and **IXg** were reported in [13, 14].

2-(5-Methyl-2-oxo-2,3-dihydro-1*H*-indol-3-ylidene)malononitrile (IXb). Yield 89%, mp 185°C (decomp.). IR spectrum, ν, cm^{-1}: 3257, 3108, 2231, 2110, 1731, 1620, 1584, 1466, 1341. ^1H NMR spectrum, δ, ppm: 3.42 s (3H, CH_3), 6.98–7.1 m (3H, H_{arom}), 11.25 s (1H, NH). Found, %: C 68.70; H 3.26; N 20.06. $C_{12}H_7N_3O$. Calculated, %: C 68.89; H 3.37; N 20.09.

2-(1-Benzyl-2-oxo-2,3-dihydro-1*H*-indol-3-ylidene)malononitrile (IXd). Yield 90%, mp 200–203°C (decomp.). IR spectrum, ν, cm^{-1}: 3030, 2227, 1719, 1612, 1592, 1496, 1469. ^1H NMR spectrum, δ, ppm: 4.93 s (2H, CH_2), 7.05–7.95 m (9H, H_{arom}). Found, %: C 75.59; H 3.85; N 14.70. $C_{18}H_{11}N_3O$. Calculated, %: C 75.78; H 3.89; N 14.73.

Ethyl cyano(5-methyl-2-oxo-2,3-dihydro-1*H*-indol-3-ylidene)acetate (IXf). Yield 71%, mp 198°C. IR spectrum, ν, cm^{-1}: 3267, 2988, 2213, 1716, 1622, 1576, 1485. ^1H NMR spectrum, δ, ppm: 1.31 t (3H, CH_3), 2.22 s (3H, CH_3), 2.48 q (2H, CH_2), 6.74 d (1H, H_{arom}), 7.27 d (1H, H_{arom}), 7.90 s (1H, H_{arom}), 10.94 s (1H, NH). Found, %: C 65.44; H 4.70; N 10.98. $C_{14}H_{12}N_2O_3$. Calculated, %: C 65.62; H 4.72; N 10.93.

Ethyl (1-benzyl-2-oxo-2,3-dihydro-1*H*-indol-3-ylidene)cyanoacetate (IXh). Yield 72%, mp 225°C (decomp.). IR spectrum, ν, cm^{-1}: 3028, 2227, 2213, 1719, 1622, 1578, 1469. ^1H NMR spectrum, δ, ppm: 1.35 t (3H, CH_3), 2.52 q (2H, CH_2), 4.90 s (2H, CH_2), 7.10–7.95 m (9H, H_{arom}). Found, %: C 65.44; H 4.70; N 10.98. $C_{20}H_{16}N_2O_3$. Calculated, %: C 65.62; H 4.72; N 10.93.

2-Amino-3′-R-spiro[indole-3,4′-pyran]-2(1*H*)-ones Va–Vh, VIa–VIi, VIIIa, and VIIIb (*general procedure*). *a*. Isatin **Ia**–**Ie**, 1 mmol, was dissolved in 10 ml of ethanol, and 0.066 g (1 mmol) of malononitrile or 0.11 ml (1 mmol) of ethyl cyanoacetate, 1 mmol of 1,3-diketone **III**, **IV**, or **VII**, and 0.13 ml (1 mmol) of tris(2-hydroxyethyl)amine were added. In the condensations with malononitrile, the mixture was stirred, heated to the boiling point, and left to stand at room temperature for crystallization. In the condensations with ethyl cyanoacetate, the mixture was heated for 2 h under reflux and left to stand for 24 h in a refrigerator. The precipitate was filtered off, washed first with boiling hexane and then with ethanol, and dried.

b. A mixture of 1 mmol of 2-(2-oxo-2,3-dihydro-1*H*-indol-3-ylidene)malonitrile **IXa**–**IXd** or ethyl cyano(2-oxo-2,3-dihydro-1*H*-indol-3-ylidene)acetate **IXe**–**IXh**, 1 mmol of the corresponding 1,3-diketone, and 0.13 ml (1 mmol) of tris(2-hydroxyethyl)amine in 15 ml of ethanol was heated for 1 (compounds **IXa**–**IXd**) or 3–4 h (**IXe**–**IXf**) and was then treated as described above in *a*.

2-Amino-2′,5-dioxo-1′,2′,5,6,7,8-hexahydrospiro-[chromene-4,3'-indole]-3-carbonitrile (Va). Yield 0.26 g (84%), mp 290°C (decomp.). ^1H NMR spectrum, δ, ppm: 1.90 t (2H, CH_2), 2.20 m (2H, CH_2), 2.57 t (2H, CH_2), 6.75 d (1H, H_{arom}), 6.85 t (1H, H_{arom}), 7.0 d (1H, H_{arom}), 7.12 t (1H, H_{arom}), 7.21 s (2H, NH_2, D_2O), 10.35 s* (1H, NH, D_2O). Mass spectrum, *m*/*z* (I_{rel}, %): 307 (19.7) $[M]^+$, 281 (7.9) $[M - 26]^+$, 262 (26.6) $[M - 45]^+$, 252 (11.2) $[M - 55]^+$, 251 (100) $[M - 56]^+$, 250 (28.4) $[M - 57]^+$, 236 (7.6) $[M - 71]^+$, 210 (16.0) $[M - 97]^+$, 209 (36.4) $[M - 98]^+$, 195 (30.8) $[M - 109]^+$, 194 (11.4) $[M - 113]^+$, 179 (7.8) $[M - 128]^+$, 151 (8.2) $[M - 156]^+$, 127 (7.0) $[M - 180]^+$. Found, %: C 66.63; H 4.18; N 13.82. $C_{17}H_{13}N_3O_3$. Calculated, %: C 66.44; H 4.26; N 13.67.

* Hereinafter, the position of signals marked with an asterisk may vary.

2-Amino-5′-methyl-2′,5-dioxo-1′,2′,5,6,7,8-hexahydrospiro[chromene-4,3′-indole]-3-carbonitrile (Vb). Yield 0.22 g (69%), mp 287°C (decomp.). ^{1}H NMR spectrum, δ, ppm: 1.85 t (2H, CH_2), 2.25 m (2H, CH_2, CH_3), 2.57 t (2H, CH_2), 6.65 d (1H, H_{arom}), 6.78 s (1H, H_{arom}), 6.92 d (1H, H_{arom}), 7.20 s* (2H, NH_2, D_2O), 10.27 s* (1H, NH, D_2O). Mass spectrum, *m*/*z* (I_{rel}, %): 321 (100) $[M]^+$, 295 (9.9) $[M - 26]^+$, 265 (30.9) $[M - 56]^+$, 264 (8.1) $[M - 57]^+$, 224 (9.2) $[M - 97]^+$, 223 (16.8) $[M - 98]^+$, 208 (5.2) $[M - 113]^+$. Found, %: C 67.03; H 4.68; N 13.12. $C_{18}H_{15}N_3O_3$. Calculated, %: C 67.28; H 4.71; N 13.08.

2-Amino-1′-methyl-2′,5-dioxo-1′,2′,5,6,7,8-hexahydrospiro[chromene-4,3′-indole]-3-carbonitrile (Vc). Yield 0.29 g (92%), mp 250°C (decomp.). ^{1}H NMR spectrum, δ, ppm: 1.75 t (2H, CH_2), 2.45 m (2H, CH_2), 2.57 t (2H, CH_2), 3.35 s (3H, CH_3), 6.90–7.15 m (3H, H_{arom}), 7.25 s* (2H, 1H, H_{arom}, NH_2, D_2O). Mass spectrum, *m*/*z* (I_{rel}, %): 322 (7.1) $[M + 1]^+$, 321 (41.4) $[M]^+$, 295 (7.8) $[M - 26]^+$, 265 (100) $[M - 56]^+$, 255 (15.9) $[M - 66]^+$, 223 (28.7) $[M - 98]^+$, 180 (7.2) $[M - 141]^+$, 154 (6.2) $[M - 167]^+$. Found, %: C 67.11; H 4.81; N 13.14. $C_{18}H_{15}N_3O_3$. Calculated, %: C 67.28; H 4.71; N 13.08.

2-Amino-1′-benzyl-2′,5-dioxo-1′,2′,5,6,7,8-hexahydrospiro[chromene-4,3′-indole]-3-carbonitrile (Vd). Yield 0.37 g (94%), mp 290–292°C. ^{1}H NMR spectrum, δ, ppm: 1.80 t (2H, CH_2), 2.25 m (2H, CH_2), 2.70 t (2H, CH_2), 4.85 s (2H, CH_2), 6.90 t (1H, H_{arom}), 7.10 m (2H, H_{arom}), 7.30 m (5H, H_{arom}), 7.50 s* (2H, 1H, H_{arom}, NH_2, D_2O). Found, %: C 72.47; H 4.53; N 10.72. $C_{24}H_{19}N_3O_3$. Calculated, %: C 72.53; H 4.82; N 10.57.

Ethyl 2-amino-2′,5-dioxo-1′,2′,5,6,7,8-hexahydrospiro[chromene-4,3′-indole]-3-carboxylate (Ve). Yield 0.24 g (67%), mp 230°C (decomp.). ^{1}H NMR spectrum, δ, ppm: 0.75 t (2H, CH_3), 1.80 t (2H, CH_2), 2.20 m (2H, CH_2), 2.60 t (2H, CH_2), 3.75 q (2H, CH_2), 6.60–6.90 m (3H, H_{arom}), 7.10 t (1H, H_{arom}), 7.80 s* (2H, NH_2, D_2O), 10.10 s* (1H, NH, D_2O). Mass spectrum, *m*/*z* (I_{rel}, %): 354 (30.8) $[M]^+$, 299 (9.7) $[M - 55]^+$, 298 (63.5) $[M - 56]^+$, 282 (16.1) $[M - 72]^+$, 281 (100) $[M - 73]^+$, 263 (8.3) $[M - 91]^+$, 253 (21.4) $[M - 101]^+$, 252 (7.3) $[M - 102]^+$, 236 (7.3) $[M - 118]^+$, 225 (5.3) $[M - 129]^+$, 224 (11.7) $[M - 130]^+$. Found, %: C 64.08; H 5.29; N 8.06. $C_{19}H_{18}N_2O_5$. Calculated, %: C 64.40; H 5.12; N 7.91.

Ethyl 2-amino-5′-methyl-2′,5-dioxo-1′,2′,5,6,7,8-hexahydrospiro[chromene-4,3′-indole]-3-carboxylate (Vf). Yield 0.24 g (64%), mp 257°C (decomp.). ^{1}H NMR spectrum, δ, ppm: 0.80 t (2H, CH_3), 1.85 t (2H, CH_2), 2.20 m (5H, CH_2, CH_3), 2.65 t (2H, CH_2), 3.70 q (2H, CH_2), 6.55 d (1H, H_{arom}), 6.65 s (1H, H_{arom}), 6.80 d (1H, H_{arom}), 7.80 s* (2H, NH_2, D_2O), 10.05 s* (1H, NH, D_2O). Mass spectrum, *m*/*z* (I_{rel}, %): 368 (35.5) $[M]^+$, 313 (6.9) $[M - 55]^+$, 312 (35.5) $[M - 56]^+$, 313 (6.9) $[M - 55]^+$, 296 (13.7) $[M - 72]^+$, 295 (100) $[M - 73]^+$, 267 (7.4) $[M - 101]^+$, 238 (6.9) $[M - 130]^+$, 190 (5.3) $[M - 178]^+$. Found, %: C 65.49; H 5.32; N 7.76. $C_{20}H_{20}N_2O_5$. Calculated, %: C 65.21; H 5.47; N 7.60.

Ethyl 2-amino-1′-methyl-2′,5-dioxo-1′,2′,5,6,7,8-hexahydrospiro[chromene-4,3′-indole]-3-carboxylate (Vg). Yield 0.27 g (72%), mp 289–291°C. ^{1}H NMR spectrum, δ, ppm: 0.68 t (2H, CH_3), 1.80 t (2H, CH_2), 2.12 m (2H, CH_2), 2.63 t (2H, CH_2), 3.05 s (3H, CH_3), 3.63 q (2H, CH_2), 6.82 m (3H, H_{arom}), 7.15 t (1H, H_{arom}), 7.89 s* (2H, NH_2, D_2O). Mass spectrum, *m*/*z* (I_{rel}, %): 369 (7.2) $[M + 1]^+$, 368 (29.1) $[M]^+$, 312 (37.8) $[M - 56]^+$, 296 (15.8) $[M - 72]^+$, 295 (100) $[M - 73]^+$, 267 (30.9) $[M - 102]^+$, 253 (16.1) $[M - 115]^+$, 239 (38.3) $[M - 129]^+$, 238 (76.5) $[M - 130]^+$, 296 (15.8) $[M - 72]^+$, 235 (8.2) $[M - 133]^+$, 210 (14.1) $[M - 158]^+$, 181 (12.6) $[M - 187]^+$, 154 (7.6) $[M - 214]^+$. Found, %: C 64.99; H 5.62; N 7.84. $C_{20}H_{20}N_2O_5$. Calculated, %: C 65.21; H 5.47; N 7.60.

Ethyl 2-amino-1′-benzyl-2′,5-dioxo-1′,2′,5,6,7,8-hexahydrospiro[chromene-4,3′-indole]-3-carboxylate (Vh). Yield 0.28 g (65%), mp 247–250°C (decomp.). ^{1}H NMR spectrum, δ, ppm: 0.52 t (2H, CH_3), 1.75 t (2H, CH_2), 2.45 m (2H, CH_2), 2.35 t (2H, CH_2), 3.45 q (2H, CH_2), 4.72 s (2H, CH_2), 6.65 d (1H, H_{arom}), 6.85 t (1H, H_{arom}), 6.95 d (1H, H_{arom}), 7.10 t (1H, H_{arom}), 7.30 m (3H, H_{arom}), 7.60 d (1H, H_{arom}), 7.93 s* (2H, NH_2, D_2O). Mass spectrum, *m*/*z* (I_{rel}, %): 444 (13.4) $[M]^+$, 428 (8.4) $[M - 16]^+$, 400 (28.1) $[M - 44]^+$, 399 (100) $[M - 45]^+$, 388 (28.1) $[M - 56]^+$, 381 (17.2) $[M - 63]^+$, 361 (7.2) $[M - 83]^+$, 335 (7.6) $[M - 109]^+$, 400 (28.1) $[M - 44]^+$, 309 (14.7) $[M - 135]^+$, 280 (9.8) $[M - 164]^+$, 230 (8.9) $[M - 214]^+$, 223 (22.8) $[M - 221]^+$, 204 (9.6) $[M - 240]^+$, 195 (23.3) $[M - 249]^+$, 168 (12.6) $[M - 276]^+$, 128 (9.3) $[M - 316]^+$. Found, %: C 70.37; H 5.52; N 6.41. $C_{26}H_{24}N_2O_5$. Calculated, %: C 70.26; H 5.44; N 6.30.

2-Amino-7,7-dimethyl-2′,5-dioxo-1′,2′,5,6,7,8-hexahydrospiro[chromene-4,3′-indole]-3-carbonitrile (VIa). Yield 0.32 g (95%), mp 285°C (decomp.); published data [7]: mp 285–286°C. ^{1}H NMR spectrum, δ, ppm: 1.02 s [6H, $C(CH_3)_2$], 2.10 s (2H, CH_2), 2.58 s

(2H, CH_2), 6.78 d (1H, H_{arom}), 6.85 t (1H, H_{arom}), 6.98 d (1H, H_{arom}), 7.15 t (1H, H_{arom}), 7.23 s* (2H, NH_2, D_2O), 10.40 s* (1H, NH, D_2O). Found, %: C 68.23; H 5.19; N 12.76. $C_{19}H_{17}N_3O_3$. Calculated, %: C 68.05; H 5.11; N 12.53.

2-Amino-5′,7,7-trimethyl-2′,5-dioxo-1′,2′,5,6,7,8-hexahydrospiro[chromene-4,3′-indole]-3-carbonitrile (VIb). Yield 0.32 g (92%), mp 255°C (decomp.). ^{1}H NMR spectrum, δ, ppm: 1.0 s [6H, $C(CH_3)_2$], 2.10 s (2H, CH_2), 2.50 s (5H, CH_2, CH_3), 6.60 d (1H, H_{arom}), 6.75 s (1H, H_{arom}), 6.90 d (1H, H_{arom}), 7.18 s* (2H, NH_2, D_2O), 10.35 s* (1H, NH, D_2O). Mass spectrum, *m*/*z* (I_{rel}, %): 350 (19.1) $[M]^+$, 349 (100) $[M]^+$, 323 (16.7) $[M - 26]^+$, 304 (33.8) $[M - 45]^+$, 265 (55.6) $[M - 84]^+$, 250 (13.3) $[M - 99]^+$, 223 (37.9) $[M - 126]^+$, 220 (11.4) $[M - 129]^+$, 192 (21.8) $[M - 157]^+$, 177 (7.5) $[M - 172]^+$, 153 (8.2) $[M - 196]^+$. Found, %: C 68.51; H 5.52; N 12.09. $C_{20}H_{19}N_3O_3$. Calculated, %: C 68.75; H 5.48; N 12.03.

2-Amino-5′-bromo-7,7-dimethyl-2′,5-dioxo-1′,2′,5,6,7,8-hexahydrospiro[chromene-4,3′-indole]-3-carbonitrile (VIc). Yield 0.27 g (65%), mp 275°C (decomp.). ^{1}H NMR spectrum, δ, ppm: 1.05 s [6H, $C(CH_3)_2$], 2.20 s (2H, CH_2), 2.57 s (2H, CH_2), 6.70 d (1H, H_{arom}), 6.85 s (1H, H_{arom}), 7.30 m (3H, 1H, H_{arom}, NH_2, D_2O), 10.55 s* (1H, NH, D_2O). Mass spectrum, *m*/*z* (I_{rel}, %): 415 (13.2) $[M + 1]^+$, 414 (8.9) $[M]^+$, 413 (15.8) $[M - 1]^+$, 372 (14.4) $[M - 42]^+$, 371 (19.6) $[M - 43]^+$, 329 (100) $[M - 85]^+$, 328 (15.7) $[M - 86]^+$, 303 (14.3) $[M - 111]^+$, 287 (27.8) $[M - 127]^+$, 261 (8.4) $[M - 153]^+$, 217 (14.5) $[M - 197]^+$, 194 (20.8) $[M - 220]^+$, 165 (20.6) $[M - 249]^+$, 140 (31.2) $[M - 274]^+$, 139 (16.1) $[M - 275]^+$, 127 (8.8) $[M - 287]^+$. Found, %: C 55.31; H 4.09; N 10.22. $C_{19}H_{16}BrN_3O_3$. Calculated, %: C 55.09; H 3.89; N 10.14.

2-Amino-1′,7,7-trimethyl-2′,5-dioxo-1′,2′,5,6,7,8-hexahydrospiro[chromene-4,3′-indole]-3-carbonitrile (VId). Yield 0.26 g (75%), mp 265–267°C. ^{1}H NMR spectrum, δ, ppm: 1.0 d [6H, $C(CH_3)_2$], 2.10 s (2H, CH_2), 2.60 s (2H, CH_2), 3.10 s (3H, CH_3), 6.90–7.10 m (3H, H_{arom}), 7.25 m (2H, 1H, H_{arom}, NH_2, D_2O). Mass spectrum, *m*/*z* (I_{rel}, %): 349 (7.7) $[M]^+$, 323 (10.6) $[M - 26]^+$, 306 (6.0) $[M - 43]^+$, 283 (6.0) $[M - 66]^+$, 283 (6.0) $[M - 66]^+$, 265 (100) $[M - 66]^+$, 264 (24.5) $[M - 85]^+$, 255 (6.0) $[M - 94]^+$, 250 (9.9) $[M - 99]^+$, 283 (6.0) $[M - 66]^+$, 240 (67.8) $[M - 109]^+$, 238 (34.8) $[M - 111]^+$, 237 (59.3) $[M - 112]^+$, 222 (9.0) $[M - 127]^+$, 194 (9.0) $[M - 155]^+$. Found, %: C 68.11; H 5.61; N 12.12. $C_{20}H_{19}N_3O_3$. Calculated, %: C 68.75; H 5.48; N 12.03.

2-Amino-1′-benzyl-7,7-dimethyl-2′,5-dioxo-1′,2′,5,6,7,8-hexahydrospiro[chromene-4,3′-indole]-3-carbonitrile (VIe). Yield 0.36 g (85%), mp 285°C (decomp.). ^{1}H NMR spectrum, δ, ppm: 1.0 d [6H, $C(CH_3)_2$], 2.15 q (2H, CH_2), 2.60 s (2H, CH_2), 4.89 s (2H, CH_2), 6.65 d (1H, H_{arom}), 6.95 t (1H, H_{arom}), 7.12 m (2H, H_{arom}), 7.30 m (5H, 3H, H_{arom}, NH_2, D_2O), 7.50 d (1H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 425 (7.7) $[M]^+$, 397 (14.2) $[M - 28]^+$, 362 (9.0) $[M - 63]^+$, 334 (19.9) $[M - 91]^+$, 316 (13.3) $[M - 109]^+$, 285 (7.6) $[M - 140]^+$, 251 (9.7) $[M - 174]^+$, 238 (23.0) $[M - 187]^+$, 236 (56.5) $[M - 189]^+$, 234 (100) $[M - 191]^+$, 224 (7.2) $[M - 201]^+$, 219 (28.1) $[M - 206]^+$, 206 (14.8) $[M - 219]^+$, 189 (26.8) $[M - 236]^+$, 170 (11.8) $[M - 255]^+$, 139 (11.6) $[M - 286]^+$, 114 (12.4) $[M - 311]^+$. Found, %: C 73.28; H 5.55; N 10.08. $C_{26}H_{23}N_3O_3$. Calculated, %: C 73.39; H 5.45; N 9.88.

Ethyl 2-amino-7,7-dimethyl-2′,5-dioxo-1′,2′,5,6,7,8-hexahydrospiro[chromene-4,3′-indole]-3-carboxylate (VIf). Yield 0.24 g (63%), mp 263°C (decomp.). IR spectrum, ν, cm^{-1}: 3372, 3235, 3181, 3115, 2986, 2959, 2900, 1714, 1689, 1616, 1526, 1472. ^{1}H NMR spectrum, δ, ppm: 0.78 t (3H, $OCH_2C\mathbf{H}_3$), 1.0 d [6H, $C(CH_3)_2$], 2.05 s (2H, CH_2), 2.60 s (2H, CH_2), 3.70 q (2H, OCH_2), 6.65–6.85 m (3H, H_{arom}), 7.05 t (1H, H_{arom}), 7.85 s* (2H, NH_2, D_2O), 10.12 s* (1H, NH, D_2O). Found, %: C 66.16; H 5.94; N 7.51. $C_{21}H_{22}N_2O_5$. Calculated, %: C 65.96; H 5.80; N 7.33.

Ethyl 2-amino-5′,7,7-trimethyl-2′,5-dioxo-1′,2′,5,6,7,8-hexahydrospiro[chromene-4,3′-indole]-3-carboxylate (VIg). Yield 0.27 g (69%), mp 272°C (decomp.). ^{1}H NMR spectrum, δ, ppm: 0.80 t (3H, $OCH_2C\mathbf{H}_3$), 1.0 d [6H, $C(CH_3)_2$], 2.05 s (2H, CH_2), 2.10 s (5H, CH_2, CH_3), 3.70 q (2H, OCH_2), 6.52 d (1H, H_{arom}), 6.65 s (1H, H_{arom}), 6.80 d (1H, H_{arom}), 7.80 s* (2H, NH_2, D_2O), 10.02 s* (1H, NH, D_2O). Found, %: C 66.73; H 6.19; N 7.22. $C_{22}H_{24}N_2O_5$. Calculated, %: C 66.65; H 6.10; N 7.07.

Ethyl 2-amino-1′,7,7-trimethyl-2′,5-dioxo-1′,2′,5,6,7,8-hexahydrospiro[chromene-4,3′-indole]-3-carboxylate (VIh). Yield 0.32 g (82%), mp 205°C (decomp.). ^{1}H NMR spectrum, δ, ppm: 0.68 t (3H, $OCH_2C\mathbf{H}_3$), 0.98 d [6H, $C(CH_3)_2$], 2.05 q (2H, CH_2), 2.65 t (2H, CH_2), 3.05 s (3H, CH_3), 3.65 q (2H, OCH_2), 6.80 m (3H, H_{arom}), 7.13 t (1H, H_{arom}), 7.90 s* (2H, NH_2, D_2O). Mass spectrum, *m*/*z* (I_{rel}, %): 396 (29.0) $[M]^+$, 323 (100) $[M - 73]^+$, 312 (28.3) $[M - 84]^+$, 295 (18.7) $[M - 101]^+$, 283 (6.0) $[M - 66]^+$, 250 (8.6) $[M - 146]^+$, 211 (9.7) $[M - 185]^+$, 168 (6.6) $[M - 228]^+$, 140 (6.9) $[M - 256]^+$. Found, %: C 66.84; H 6.24;

N 7.12. $C_{22}H_{24}N_2O_5$. Calculated, %: C 66.65; H 6.10; N 7.07.

Ethyl 2-amino-1′-benzyl-7,7-dimethyl-2′,5-dioxo-1′,2′,5,6,7,8-hexahydrospiro[chromene-4,3′-indole]-3-carboxylate (VIi). Yield 0.37 g (78%), mp 289°C (decomp.). ^{1}H NMR spectrum, δ, ppm: 0.50 t (3H, $OCH_2C\mathbf{H}_3$), 1.0 d [6H, $C(CH_3)_2$], 2.05 q (2H, CH_2), 2.50 t (2H, CH_2), 3.50 q (2H, OCH_2), 4.80 q (2H, CH_2), 6.65 d (1H, H_{arom}), 6.82 t (1H, H_{arom}), 6.90 d (1H, H_{arom}), 7.15 t (1H, H_{arom}), 7.30 m (3H, H_{arom}), 7.6 d (2H, H_{arom}), 7.80 s* (2H, NH_2, D_2O). Found, %: C 70.97; H 5.91; N 6.01. $C_{28}H_{28}N_2O_5$. Calculated, %: C 71.17; H 5.97; N 5.93.

5′-Acetyl-2′-amino-6′-methyl-2-oxo-1,2-dihydrospiro[indole-3,4′-pyran]-3′-carbonitrile (VIIIa). Yield 0.19 g (64%), mp 240°C (decomp.). ^{1}H NMR spectrum, δ, ppm: 2.05 s (3H, CH_3), 2.25 s (3H, $COCH_3$), 6.65 d (1H, H_{arom}), 6.90 t (1H, H_{arom}), 7.05 d (1H, H_{arom}), 7.15 m (3H, 1H, H_{arom}, NH_2, D_2O), 10.35 s* (1H, NH, D_2O). Mass spectrum, *m*/*z* (I_{rel}, %): 295 (8.9) $[M]^+$, 279 (5.4) $[M-16]^+$, 266 (6.9) $[M-29]^+$, 254 (8.0) $[M-41]^+$, 253 (23.8) $[M-42]^+$, 252 (66.2) $[M-43]^+$, 224 (10.2) $[M-71]^+$, 210 (100) $[M-85]^+$, 207 (15.1) $[M-88]^+$, 194 (6.9) $[M-101]^+$, 179 (10.1) $[M-116]^+$, 154 (8.3) $[M-141]^+$. Found, %: C 65.27; H 4.62; N 14.14. $C_{16}H_{13}N_3O_3$. Calculated, %: C 65.08; H 4.44; N 14.23.

Ethyl 5′-acetyl-2′-amino-6′-methyl-2-oxo-1,2-dihydrospiro[indole-3,4′-pyran]-3′-carboxylate (VIIIb). Yield 0.22 g (65%), mp 235°C (decomp.). ^{1}H NMR spectrum, δ, ppm: 065 t (3H, $OCH_2C\mathbf{H}_3$), 1.80 s (3H, CH_3), 2.05 s (3H, $COCH_3$), 3.65 q (2H, OCH_2), 6.65 d (1H, H_{arom}), 6.80 t (1H, H_{arom}), 6.98 d (1H, H_{arom}), 7.05 t (1H, H_{arom}), 7.72 s* (1H, NH_2, D_2O), 10.25 s* (1H, NH, D_2O). Found, %: C 63.15; H 5.30; N 8.18. $C_{18}H_{18}N_2O_5$. Calculated, %: C 63.15; H 5.30; N 8.18.

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