

'Solvent-free' and 'on-solvent' multicomponent reaction of isatins, malononitrile, and bicyclic CH-acids: a fast and efficient way to a medicinally-privileged spiro-oxindole scaffold

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Dedicated to Professor Gordon Gribble in celebration of his many outstanding contributions
to organic synthesis

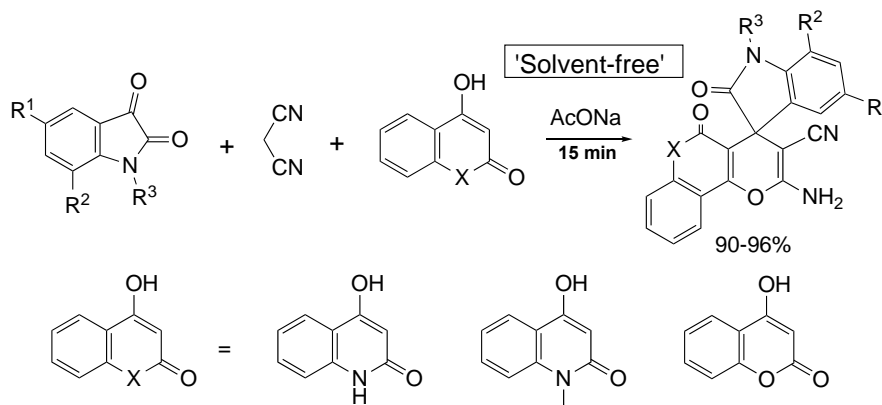
Received 05-28-2018

Accepted 06-20-2018

Published on line 07-13-2018

Abstract

The fast (15 min) PASE-'solvent-free' and 'on-solvent' multicomponent reactions of isatins, malononitrile and bicyclic CH-acids catalyzed by sodium acetate result in efficient formation of substituted spiro-oxindoles in 90–98% yields. These methods are fast multicomponent approaches to the spiro-oxindoles, substances with promising anticancer activities. These new 'solvent-free' and 'on-solvent' techniques reduce solvent use, thereby leading to reduced waste, in connection with a new concept of solvent-assisted domino-reaction strategy.



Keywords: Multicomponent reaction; catalysis, 'on-solvent' synthesis, spiro-oxindole

Introduction

Domino reactions are an up-to-date method to obtain ideal synthesis¹ in one-pot reactions. Domino reaction strategy has substantial advantages over conventional linear-type synthesis due to its flexible, convergent and atom efficient nature.² In this way, domino processes overlap with PASE (Pot, Atom, Step Economic)-strategy,^{3s} which claims pot and step economy, and introduces *atom economy*, meaning that ideally the number of atoms of all reagents should be present in the final compound.

With the advent of domino processes, solvent-free chemistry has emerged as a powerful tool for creating molecular complexity by much greener ways. The use of costly, explosive, toxic and carcinogenic chemicals (catalyst, reagents or solvents) do not qualify them under sustainability metrics as they augment the ecosystem toxicity resulting in socioeconomic burden. Solvent-free methods, in comparison with classic synthesis, produce many advantages such as high efficiency and selectivity and operational simplicity.⁴ However, the solvent assisted ('on-water' and 'on-solvent') methods in comparison with solventless mechano-chemical processes have many more application areas due to greater flexibility, selectivity, and reduced reaction time.⁵

The design of functional organic and hybrid molecular systems has shown outstanding recent growth, and of high priority is the development of new technologies and novel functional materials. In this connection, the concept of 'privileged medicinal structures or scaffolds' has emerged as one of the guiding principles of drug discovery design.⁶ Such privileged scaffolds commonly consist of a rigid heterocyclic ring system that assigns well-defined orientation of appended functionalities for target recognition.

The privileged heterocyclic spiro-oxindole scaffold is a widely distributed structural framework in a number of pharmaceuticals and natural products,⁷ including such cytostatic alkaloids as spirotryprostatins A, B, and strychnophylline.⁸ The unique structural array and the pronounced pharmacological activity displayed by the class of spiro-oxindole compounds have made them attractive synthetic targets.^{9,10}

Among nitrogen-containing heterocyclic systems, functionalized pyranoquinolines have received considerable attention owing to their wide range of diverse pharmacological activity, such as psychotropic, antiallergenic, and estrogenic activity.^{11,12} Functionalized pyranochromenes are also relevant from the medicinal viewpoint because of revealed activity against human breast and human alveolar adenocarcinoma cells.¹³ Fused coumarin derivatives exhibit anti-inflammatory and antiviral activities.¹⁴ For pyranocoumarins anti-cancer activity is known.¹⁵

Thus, a spiro-oxindole fragment connected with a nitrogen-containing heterocyclic system is pharmacologically promising in respect to various biological responses.

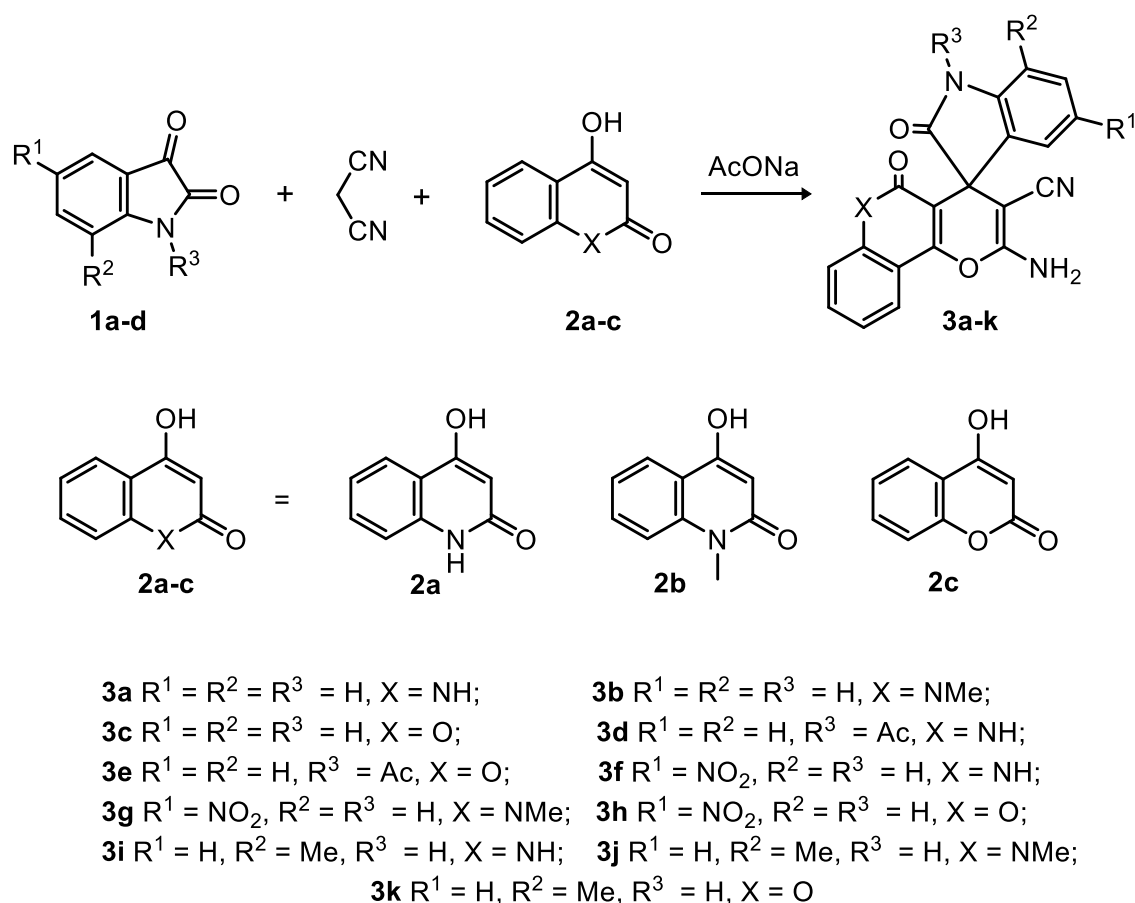
In recent years, multicomponent reactions have been suggested for the synthesis of spiro-oxindole scaffolds assembled from isatin, CH-acids and malononitrile in solution under different conditions. As for spiroindoline-3,4'-pyrano[3,2-c]quinolones, one of these methods utilizes extremely complex catalysts FeNi₃-SiO₂-nanoparticles in PEG as a solvent, which are prepared in multi-step syntheses with non-eco-friendly N₂H₄·H₂O solution.¹⁶ Another method utilized ionic liquid as solvents: 1-butyl-3-methylimidazolium-tetrafluoroborate or DBU acetate, very expensive and hazardous agents.^{17,18} Other known methodologies utilize techniques such as microwave irradiation and sonication with heating, which generally result in insufficient yields of spiroindoline-3,4'-pyrano[3,2-c]quinolones.^{19,20} In regard to spiroindoline-3,4'-pyrano[3,2-c]chromenes, most methods are concerned either with only one or two examples of the synthesis of spiroindoline-3,4'-pyrano[3,2-c]chromenes,^{16,21-24} or suffer from high temperatures, extremely expensive catalysts²⁵⁻²⁷ and also long reaction times (of the order of two days).²⁸

Thus, each of the known procedures for the synthesis of the spiro-oxindole fragments connected with a nitrogen-containing heterocyclic system has its merits; however, a fast and efficient PASE 'solvent-free' and 'on-solvent' method for this process has yet to be developed.

Considering our results on the 'solvent-free' and 'on-solvent' multicomponent transformations of carbonyl compounds and CH-acids,²⁹⁻³³ and also the wide biomedical applications of spiro-oxindoles mentioned above, we were prompted to design a convenient fast and facile PASE solvent-assisted methodology for the efficient and clean multicomponent assembling of isatins, malononitrile and bicyclic CH-acids.

Results and Discussion

In the present study, we report our results on multicomponent 'solvent-free' and 'on-solvent' reactions of isatins **1a-d**, malononitrile and bicyclic CH-acids **2a-c** leading to spiro-oxindoles **3a-k** (Scheme 1, Table 1).



Scheme 1. Multicomponent 'solvent-free' transformation of isatins **1a-d**, malononitrile and bicyclic CH-acids **2a-c** into spiro-oxindoles **3a-k**.

In the first stage of the investigation, the reaction of isatin **1a**, malononitrile and 4-hydroxy-2H-chromen-2-one **2a** was studied. 2'-Amino-2,5'-dioxo-5',6'-dihydrospiro[indoline-3,4'-pyrano[3,2-c]quinoline]-3'-carbonitrile **3a** was obtained under mild 'solvent-free' conditions without any heating within 15 minutes in the presence of 5 mol% of KF as catalyst in 90% yield (entry 1, Table 1).

Table 1. Multicomponent transformation of isatins **1a-d**, malononitrile and CH-acids **2a-c** into spiro-oxindoles **3a-k**^a

Entry	Isatin	R ¹	R ²	R ³	C-H acid	Spiro-oxindole	Additive (mL)	Catalyst, mol%	Time, min	Yield, % ^b
1	1a	H	H	H	2a	3a	neat	KF 5%	15	90
2	1a	H	H	H	2a	3a	neat	KF 10%	15	92
3	1a	H	H	H	2a	3a	neat	AcONa 10%	15	98
4	1a	H	H	H	2b	3b	neat	AcONa 10%	15	94
5	1a	H	H	H	2c	3c	neat	AcONa 10%	15	90
6	1a	H	H	H	2c	3c	H ₂ O (1)	AcONa 10%	15	92
7	1a	H	H	H	2c	3c	H ₂ O (2)	AcONa 10%	15	95
8	1b	H	H	Ac	2a	3d	neat	AcONa 10%	15	83
9	1b	H	H	Ac	2a	3d	H ₂ O (2)	AcONa 10%	15	89
10	1b	H	H	Ac	2a	3d	EtOH (2)	AcONa 10%	15	95
11	1b	H	H	Ac	2c	3e	neat	AcONa 10%	15	78
12	1b	H	H	Ac	2c	3e	H ₂ O (2)	AcONa 10%	15	87
13	1b	H	H	Ac	2c	3e	EtOH (2)	AcONa 10%	15	96
14	1c	NO ₂	H	H	2a	3f	neat	AcONa 10%	15	92
15	1c	NO ₂	H	H	2b	3g	neat	AcONa 10%	15	93
16	1c	NO ₂	H	H	2c	3h	neat	AcONa 10%	15	91
17	1d	H	Me	H	2a	3i	neat	AcONa 10%	15	88
18	1d	H	Me	H	2a	3i	EtOH (2)	AcONa 10%	15	95
19	1d	H	Me	H	2b	3j	EtOH (2)	AcONa 10%	15	93
20	1d	H	Me	H	2c	3k	EtOH (2)	AcONa 10%	15	92

^a Isatin **1a-d** (3 mmol), malononitrile (3 mmol), bicyclic CH-acid **2a-c** (3 mmol) and catalyst (0.3 mmol), neat grinding or grinding with additive using pestle and mortar. ^b Isolated yield.

Use of 10 mol% of KF as a catalyst resulted in 92% yield of spiro[indoline-3,4'-pyrano[3,2-c]quinoline] **3a** (entry 2, Table 1). The replacement of KF by AcONa led to a 98% yield of **3a** within 15 min under optimal 'solvent-free' conditions (entry 3, Table 1).

Under these optimal conditions (AcONa 10%, 15 min, 25 °C, 'solvent-free' grinding) the corresponding spiro-oxindoles **3b** (entry 4, Table 1) and **3c** (entry 5, Table 1) were obtained in 94% and 90% yields respectively. The

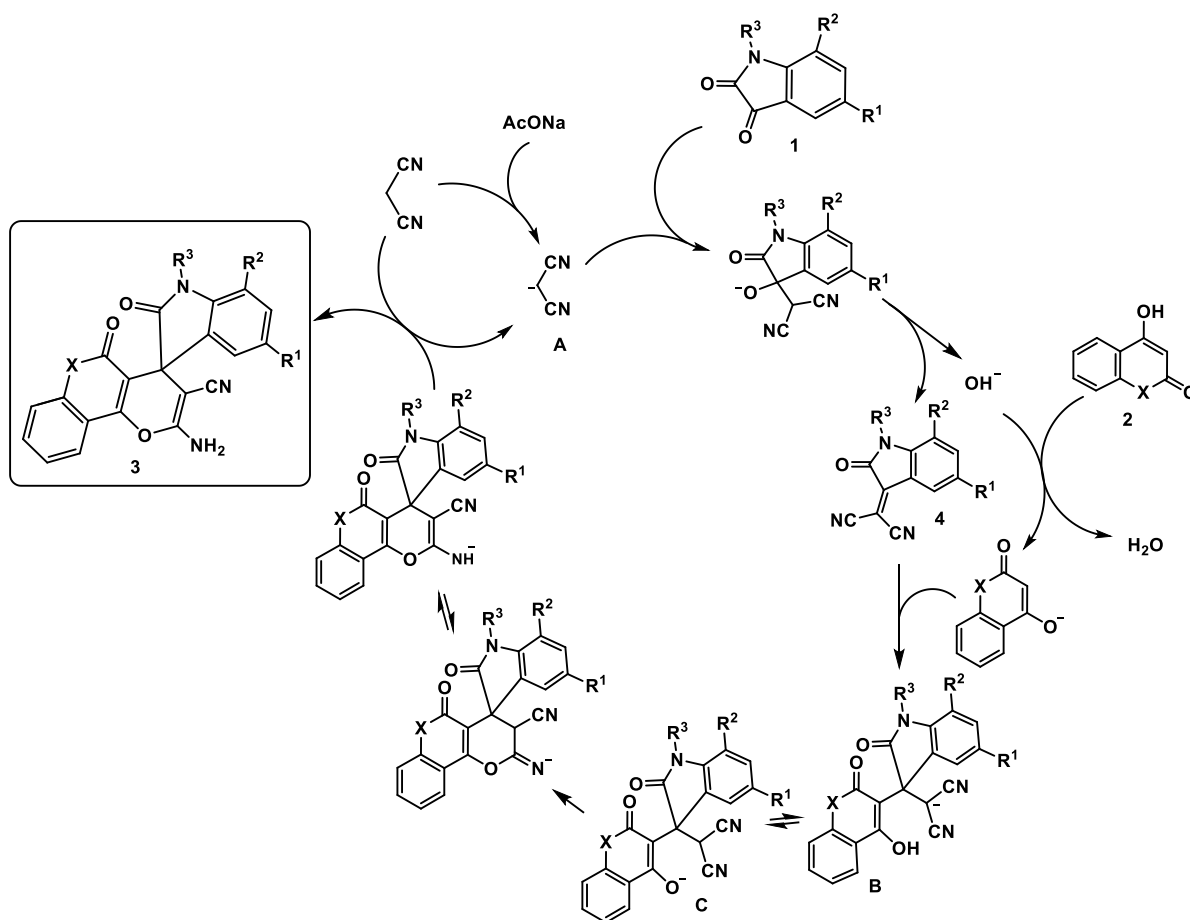
same conditions were also optimal for NO₂-substituted spiro-oxindole **3f**, **3g**, **3h** synthesis with excellent 92%, 93%, 91% yields respectively (entries 14, 15, 16, Table 1).

Recently we have found that small additives of water or alcohols have improved thermal multicomponent processes or assembling initiated by grinding.^{34,35} Thus, the next stage was to carry out experiments with a small addition of water ('on-water' conditions).

Under ambient temperature with 10 mol% of AcONa and addition of 1 or 2 mL of H₂O (optimal 'on-water' conditions) the spiro-oxindole **3c** was obtained in 92% or an excellent 95% yield correspondingly (entries 6 and 7, Table 1), but under these optimal 'on-water' conditions the reaction of isatin **1b**, malononitrile, and 4-hydroxyquinolin-2(1*H*)-one **2a** with 10% AcONa as a catalyst led to 89% yield of spiro-oxindole **3d** (entry 9, Table 1).

Nowadays, solvent assisted ('on-solvent') methods in comparison with solventless mechano-chemical processes have much more application areas due to their greater flexibility, high rates and selectivity, as well as reduced reaction times.³⁶ These 'on-solvent' methodologies^{37,38} have been suggested for cascade and multi-component reactions in a minimum quantity of solvent – in reagent mixtures or emulsions without the complete solution of components to increase the efficiency of the desired complex synthetic organic chemistry processes.

Thus, to improve the yield of spiro-oxindole **3d** the reaction was carried out with addition of 2 ml of EtOH, which resulted in an excellent 95% of **3d** (entry 10, Table 1), determining thereby optimal 'on-solvent' conditions. Under such optimal 'on-solvent' conditions spiro-oxindoles **3e**, **3i**, **3j**, **3k** were obtained in 96%, 95%, 93% and 92% yields respectively (entry 13, 18, 19, 20, Table 1).



Scheme 2. Mechanism of multicomponent transformation of isatins **1**, malononitrile and bicyclic CH-acids **2**.

With the above results and the data on mechanisms of the multicomponent transformation of isatins and CH-acids³⁹⁻⁴¹ the following process for the multicomponent assemblage of isatins **1a-d** malononitrile and bicyclic CH-acids **2a-c** into substituted spiro-oxindoles **3a-k** is proposed (Scheme 2).

The initiation step of the catalytic cycle begins with the sodium acetate-induced deprotonation of a molecule of malononitrile, which leads to malononitrile anion (**A**) formation. Then Knoevenagel condensation of the anion **A** with isatin **1** takes place with the elimination of a hydroxide anion and formation of Knoevenagel adduct **4**.⁴² The subsequent hydroxide-promoted Michael addition of bicyclic CH-acid **2** to electron-deficient Knoevenagel adduct **4** results in formation of the anions **B** and **C**. Further cyclization of anion **C** and protonation with the participation of the next molecule of malononitrile leads to the corresponding spiro-oxindole **3** with the regeneration of malononitrile anion at the last step of the catalytic cycle (Scheme 2).

Conclusions

Under simple and efficient 'solvent-free' and 'on-solvent' conditions sodium acetate as a catalyst can produce, without any heating, a very fast (15 min) and selective multicomponent transformation of isatins, malononitrile and bicyclic CH-acids into substituted spiro-oxindoles in 90-98% yields. This developed multicomponent method is a significant approach to these substituted spiro-oxindoles, pharmacologically important substances with pronounced anticancer activities. The 'solvent-free' and 'on-solvent' green variants of this multicomponent process reduce the quantity of waste, being appealing to chemical industry, and present a new concept of 'on-solvent' domino strategy. It utilizes simple procedures and equipment; it is easy to carry out in the laboratory and to adapt to large-scale processes.

Experimental Section

General. All melting points were measured with a Gallenkamp melting point apparatus. ¹H- and ¹³C-NMR spectra were recorded in DMSO-*d*₆ with a Bruker Avance II 300 spectrometer at ambient temperature. Chemical shifts values are relative to Me₄Si. IR spectra were recorded with a Bruker ALPHA-T FT-IR spectrometer in KBr pellets. Mass-spectra (EI = 70 eV) were obtained directly with a Finningan MAT INCOS 50 spectrometer. HRMS (ESI) was measured on a Bruker microTOF II instrument; external or internal calibration was effected with Electrospray Calibrant Solution (Fluka). All chemicals used in this study are commercially available.

General procedure. Isatin **1** (3 mmol), malononitrile (0.2 g, 3 mmol), bicyclic CH-acid **2** (3 mmol) and sodium acetate (0.025 g, 0.3 mmol) in 'solvent-free' manner or with additive ('on-solvent' manner) were grinded with a pestle and mortar at ambient temperature for 15 minutes. After the reaction was finished, the mixture was air-dried. Then the crude solid was put on filter, rinsed with water (2 mL) and EtOH (2 mL), and then dried with a water pump to isolate the spiro-oxindole **3**.

2'-Amino-2,5'-dioxo-5',6'-dihydrospiro[indoline-3,4'-pyrano[3,2-*c*]quinoline]-3'-carbonitrile (3a). White solid; 1.05 g (98%); mp 300-302 °C (Lit.²⁰ mp > 300 °C). ¹H NMR (300 MHz, DMSO-*d*₆): δ 6.82-6.92 (m, 2H, Ar), 7.03-7.05 (m, 1H, Ar), 7.19 (t, *J* 7.7 Hz, 1H, Ar), 7.32 (m, 2H, Ar), 7.45 (s, 2H, NH₂), 7.64 (t, *J* 7.7 Hz, 1H, Ar) 7.97 (d, *J* 8.0 Hz, 1H, Ar), 10.53 (s, 1H, NH), 11.74 (s, 1H, NH) ppm.

2'-Amino-6'-methyl-2,5'-dioxo-5',6'-dihydrospiro[indoline-3,4'-pyrano[3,2-*c*]quinoline]-3'-carbonitrile (3b). White solid; 1.04 g (94%); mp 302-304 °C (Lit.²⁰ mp > 300 °C). ¹H NMR (300 MHz, DMSO-*d*₆): δ 3.49 (s, 3H, CH₃),

6.83-6.88 (m, 2H, Ar), 7.01-7.04 (m, 1H, Ar), 7.18 (t, *J* 7.6 Hz, 1H, Ar), 7.43-7.46 (m, 1H, Ar), 7.48 (s, 2H, NH₂), 7.58-7.61 (m, 1H, Ar), 7.77 (t, *J* 7.6 Hz, 1H, Ar), 8.08 (d, *J* 7.8 Hz, 1H, Ar), 10.54 (s, 1H, NH) ppm.

2'-Amino-2,5'-dioxo-5'-H-spiro[indoline-3,4'-pyrano[3,2-*c*]chromene]-3'-carbonitrile (3c). White solid; 1.02 g (95%); mp 307-308 °C (Lit.²³ mp 305-307 °C). ¹H NMR (300 MHz, DMSO-*d*₆): δ 6.88 (d, *J* 7.9 Hz, 1H, Ar), 6.94 (t, *J* 7.7 Hz, 1H, Ar), 7.20-7.24 (m, 2H, Ar), 7.47-7.57 (m, 2H, Ar), 7.66 (s, 2H, NH₂), 7.77 (t, *J* 7.7 Hz, 1H, Ar), 7.95 (d, *J* 7.9 Hz, 1H, Ar), 10.67 (s, 1H, NH) ppm.

1-Acetyl-2'-amino-2,5'-dioxo-5',6'-dihydrospiro[indoline-3,4'-pyrano[3,2-*c*]quinoline]-3'-carbonitrile (3d). White solid; 1.14 g (95%); mp 310-312 °C; ¹H NMR (300 MHz, DMSO-*d*₆): δ 2.63 (s, 3H, CH₃), 7.17-7.27 (m, 2H, Ar), 7.35-7.42 (m, 3H, Ar), 7.68 (t, *J* 7.8 Hz, 1H, Ar), 7.74 (s, 2H, NH₂), 8.00 (d, *J* 8.0 Hz, 1H, Ar), 8.13 (d, *J* 8.0 Hz, 1H, Ar), 11.87 (s, 1H, NH) ppm; ¹³C NMR (75 MHz, DMSO-*d*₆): δ 26.5, 49.0, 57.4, 107.2, 112.0, 115.8, 115.9, 116.2, 122.6, 122.7, 123.0, 126.0, 129.3, 132.7, 133.2, 138.5, 140.2, 153.1, 159.5, 160.0, 170.9, 178.3 ppm; IR (KBr): ν 3433, 3321, 2202, 1751, 1720, 1682, 1637, 1366, 1164, 756 cm⁻¹; MS (EI, 70 eV), *m/z* (%): 398 ([M]⁺, 18), 355 (100), 312 (51), 266 (9), 229 (8), 201 (4), 165 (5), 120 (11), 77 (4), 43 (71); HRMS (ESI): 399.1091 [M+H]⁺, calcd for C₂₂H₁₅N₄O₄: 399.1088.

1-Acetyl-2'-amino-2,5'-dioxo-5'-H-spiro[indoline-3,4'-pyrano[3,2-*c*]chromene]-3'-carbonitrile (3e). White solid; 1.15 g (96%); mp 278-280 °C (Lit.⁴³ mp: 276 °C); ¹H NMR (300 MHz, DMSO-*d*₆): δ 2.64 (s, 3H, CH₃), 7.25 (t, *J* 7.5 Hz, 1H, Ar), 7.40-7.62 (m, 4H, Ar), 7.82 (t, *J* 7.5 Hz, 1H, Ar), 7.96-8.01 (m, 3H, Ar+NH₂), 8.13 (d, *J* 8.0 Hz, 1H, Ar) ppm.

2'-Amino-5-nitro-2,5'-dioxo-5',6'-dihydrospiro[indoline-3,4'-pyrano[3,2-*c*]quinoline]-3'-carbonitrile (3f). Yellow solid; 1.22 g (92%); mp 312-313 °C (Lit.²⁰ mp > 300 °C); ¹H NMR (300 MHz, DMSO-*d*₆): δ 7.03 (d, *J* 8.8 Hz, 1H, Ar), 7.30-7.35 (m, 2H, Ar), 7.59-7.64 (m, 3H, Ar + NH₂), 7.94 (d, *J* 7.6 Hz, 1H, Ar), 8.07-8.08 (m, 1H, Ar), 8.15 (dd, *J*¹ 8.8 Hz, *J*² 2.4 Hz, 1H, Ar), 11.23 (s, 1H, NH), 11.76 (s, 1H, NH) ppm.

2'-Amino-1-methyl-5-nitro-2,5'-dioxo-5',6'-dihydrospiro[indoline-3,4'-pyrano[3,2-*c*]quinoline]-3'-carbonitrile (3g). Yellow solid; 1.28 g (93%); mp 318-319 °C (Lit.²⁰ mp > 300 °C); ¹H NMR (300 MHz, DMSO-*d*₆): δ 3.49 (s, 3H, CH₃), 7.06 (d, *J* 8.8 Hz, 1H, Ar), 7.47 (t, *J* 7.4 Hz, 1H, Ar), 7.61 (d, *J* 8.8 Hz, 1H, Ar), 7.68 (m, 2H, NH₂), 7.77-8.18 (m, 4H, Ar), 11.31 (s, 1H, NH) ppm.

2'-Amino-5-nitro-2,5'-dioxo-5'-H-spiro[indoline-3,4'-pyrano[3,2-*c*]chromene]-3'-carbonitrile (3h). White solid; 1.21 g (91%); mp 201-203 °C (Lit.²⁹ mp 200-202 °C); ¹H NMR (300 MHz, DMSO-*d*₆): δ 7.11 (d, *J* 8.6 Hz, 1H, Ar), 7.48 (d, *J* 8.6 Hz, 1H, Ar), 7.54 (t, *J* 7.6 Hz, 1H, Ar), 7.76 (t, *J* 7.6 Hz, 1H, Ar), 7.87 (s, 2H, NH₂), 7.97 (d, *J* 7.9 Hz, 1H, Ar), 8.25-8.38 (m, 2H, Ar), 11.46 (s, 1H, NH) ppm.

2'-Amino-7-methyl-2,5'-dioxo-5',6'-dihydrospiro[indoline-3,4'-pyrano[3,2-*c*]quinoline]-3'-carbonitrile (3i). Cream solid. 1.06 g (95%); mp 305-306 °C; ¹H NMR (300 MHz, DMSO-*d*₆): δ 2.22 (s, 3H, CH₃), 6.74-6.81 (m, 2H, Ar), 6.95-6.97 (m, 1H, Ar), 7.27-7.41 (m, 4H, Ar + NH₂), 7.59 (t, *J* 7.6 Hz, 1H, Ar), 7.92 (d, *J* 7.9 Hz, 1H, Ar), 10.51 (s, 1H, NH), 11.64 (s, 1H, NH) ppm; ¹³C NMR (75 MHz, DMSO-*d*₆): δ 16.9, 48.5, 58.0, 107.7, 112.0, 115.9, 118.0, 121.4, 122.1, 122.4, 122.6, 122.6, 130.2, 132.2, 134.5, 138.3, 141.5, 152.8, 159.4, 159.9, 178.8 ppm; IR (KBr): ν 3288, 3211, 2192, 1715, 1675, 1617, 1370, 1122, 753, 581 cm⁻¹; MS (EI, 70 eV), *m/z* (%): 370 ([M]⁺, 100), 316 (90), 299 (13), 238 (14), 209 (32), 161 (22), 120 (24), 92 (18), 66 (16), 44 (36); HRMS (ESI): 371.1141 [M+H]⁺, calcd for C₂₁H₁₅N₄O₃: 371.1139.

2'-Amino-6',7-dimethyl-2,5'-dioxo-5',6'-dihydrospiro[indoline-3,4'-pyrano[3,2-*c*]quinoline]-3'-carbonitrile (3j). Cream solid; 1.07 g (93%); mp 319-321; ¹H NMR (300 MHz, DMSO-*d*₆): δ 2.23 (s, 3H, CH₃), 3.45 (s, 3H, CH₃), 6.72-6.80 (m, 2H, Ar), 6.95-6.97 (m, 1H, Ar), 7.39-7.43 (m, 3H, Ar + NH₂), 7.56 (d, *J* 8.6 Hz, 1H, Ar), 7.73 (t, *J* 8.3 Hz, 1H, Ar), 8.05 (d, *J* 8.0 Hz, 1H, Ar), 10.52 (s, 1H, NH) ppm; ¹³C NMR (75 MHz, DMSO-*d*₆): δ 17.0, 29.8, 48.9, 56.5, 107.2, 112.8, 115.5, 118.0, 118.8, 121.3, 122.1, 122.9, 130.2, 132.7, 132.8, 134.5, 139.1, 141.6, 151.9, 159.3, 159.4, 178.8 ppm; IR (KBr): ν 3360, 3256, 2200, 1724, 1676, 1625, 1597, 1368, 1162, 753 cm⁻¹; MS (EI, 70

eV), m/z (%): 384 ($[M]^+$, 100), 330 (56), 310 (6), 252 (13), 209 (51), 175 (39), 146 (23), 104 (14), 77 (12), 44 (9); HRMS (ESI): 385.1298 $[M+H]^+$, calcd for $C_{22}H_{17}N_4O_3$: 385.1295.

2'-Amino-7-methyl-2,5'-dioxo-5'H-spiro[indoline-3,4'-pyrano[3,2-c]chromene]-3'-carbonitrile (3k). Cream solid; 1.03 g (92%); mp > 300 °C (Lit.²⁰ mp > 300 °C); 1H NMR (300 MHz, DMSO- d_6): δ 2.32 (s, 3H, CH₃), 6.72-6.70 (m, 3H, Ar), 7.28 (d, J 7.6 Hz, 1H, Ar), 7.38 (m, 1H, Ar), 7.44 (s, 2H, NH₂), 7.75 (m, 1H, Ar), 7.98 (d, J 7.3 Hz, 1H, Ar), 10.35 (s, 1H, NH) ppm.

Acknowledgements

The authors gratefully acknowledge the financial support of the Russian Science Foundation (Grant no. 14-50-00126).

Supplementary Material

The 1H and ^{13}C NMR spectra associated with this article can be found in the online version of the text.

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