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# Synthesis and reactivity of new amide-substituted oxindole derivatives

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ABSTRACT

Oxindole derivatives are of growing importance in organic synthesis and in the synthesis of biologically active compounds, therefore, a very important goal is to develop new ways of modifying such scaffold. In this article we proposed a general approach to synthesis of oxindole-based amide-substituted compounds, which includes usage of protecting group. To stabilize the key-molecule for further modifications – amino-isatin, the carbonyl group in the 3-position of the starting nitro-isatin was protected by ketal synthesis. Next, the reduction of nitro-group and further modification of amino-group was carried out. The proposed strategy allows us to obtain mono- and diamido-substituted isatins. The possibility of their modification in the 3-position for synthesis of potent biologically active compounds is demonstrated.

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## 1. Introduction

The unique synthetic potential of isatins and their availability have made them valuable building blocks in organic synthesis. They undergo electrophilic aromatic substitution at positions C-5 and C-7 of the phenyl ring, N-substitutions, nucleophilic additions onto the C-3 carbonyl group,[1–6] chemoselective reductions,[7,8] oxidations, ring-expansions, and spiro-annulations,[9–11] etc. Synthesis of several heterocyclic frameworks of biological significance such as pyrrolidines, quinolines, indoles, β-lactams, and 2-oxindoles, etc. has been developed with use of isatins as starting materials. Moreover, the stability of these compounds and their derivatives under physiological conditions is another reason for their attractiveness.

Thus, such compounds are of great interest for chemists working in the field of synthesis of drugs for treatment of proliferative diseases. The large potential of 3-benzylidene-substituted oxindole derivatives as well as 3-spiro-oxindoles and other oxindole derivatives has been illustrated using different types of targets,[1] such as cyclin-dependent kinases,[2] receptor tyrosine kinase (RTK),[3–6,12,13] benzimidazole-oxindole conjugates as microtubule-targeting agents,[14,15] cell cycle arrest-based cytotoxic agents,[16,17] etc.

Furthermore, the possibility of using oxindole as the main core for drug design and synthesis and the high biological activity values was clearly demonstrated. For example, oxindole derivatives are proved to be potent antidepressants agents,[18,19] antibacterial agents,[20] HIV-1 non-nucleoside reverse transcriptase inhibitors,[16] antidiabetic agents,[21–27] antimalarials,[28] etc. Our research group had previously revealed a great potential of oxindole-based small molecule agents for treatment of increased intraocular pressure (IOP)-related diseases, such as glaucoma.[29–31] Thus, development of novel methods to functionalize an oxindole nucleus has attracted much attention.[9,32,33]

In commercially available isatins a variety of substituents in the aromatic cycle is limited basically by alkyl, alkoxy, halogen or nitro groups. However, in the search for hit compounds or optimization of the leader compound, it is usually a matter of improving the affinity for the potential drug or optimizing other important properties of drug candidate such as pharmacokinetics and pharmacodynamics, log P and bioavailability, etc. All these properties can be improved by simple replacement the substituents in the main scaffold by isosters or bioisosters.

Thus amino-isatin derivatives are of particular interest because of their reactivity. And their modification allows us to synthesize plurality of compounds containing promising pharmacophore groups such as acylamide, carbamoyl, thiourea, guanidine, etc. In this study we reveal a simple approach to synthesis of a wide range of amido-substituted isatins and oxindole derivatives.

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## 2. Results and discussion

The general approach includes introduction of an amino-group into the 5 and 7 positions of the oxindole core, then modification of the obtained amine by a wide range of available acylating agents and further modification of carbonyl group at position 3 if necessary (Scheme 1).

For the synthesis of amido-substituted oxindole derivatives nitro-isatins were used as starting compounds. At the first stage the introduction of amino-group can be carried out via catalytic reduction procedure as described by Garlich J.R. and co-workers.[30] But because of the presence of amino- and carbonyl-groups in one molecule, amino-isatin is unstable in air and requires specific isolation techniques, inert atmosphere and absolute dry solvents, which is not always convenient. In this study we offer the use of carbonyl group protection with ketal group and further catalytic reduction of obtained nitro-spiro-derivative (Scheme 2).

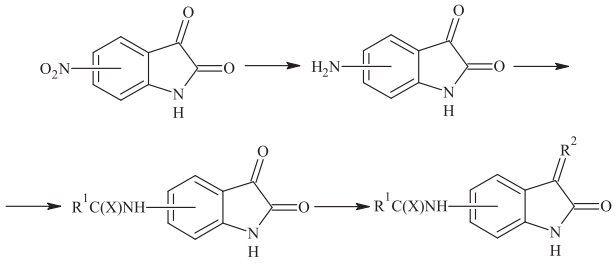
High boiling benzenes such as xylene or toluene can be used as solvents. PTSA was used as a catalyst due to its high water solubility and non-volatile nature. Nitro-substituted spiro-[1,3-dioxolan-2,3′-indol]-2′(1′H)-ones were obtained in good yields and with sufficient purity to carry out the subsequent catalytic reduction reaction of the nitro-group without purification.

Reduction procedure was performed using two different techniques – continuous flow and liquid phase hydrogenation. In both methods palladium based catalysts were used. Amino-isatins were obtained with high yields and purity in both cases. For continuous flow hydrogenation standard cartridge filled with Pd/C was used. For liquid phase hydrogenation commercially available palladium catalyst on the ceramic foam substrate[28] was applied.

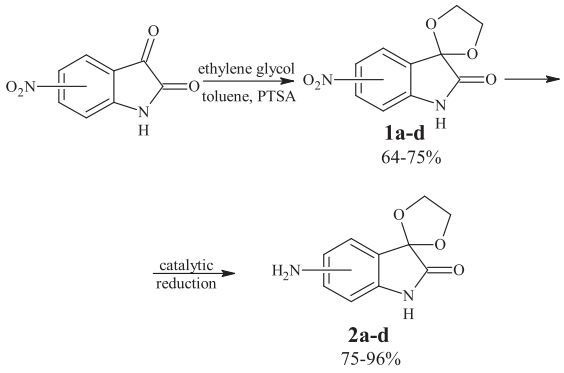
The obtained protected amino-isatins are convenient scaffolds for further modification (acylation, imine production, Michael addiction and others). In the present work acylation was carried out (Scheme 3). The reaction proceeds very rapidly due to the high reactivity of the resulting amino derivative, therefore, the slow addition of the acylating agent and intensive mixing of the reaction mixture are required to avoid the occurrence of poly-acylation side process. According to Scheme 3, amido-substituted spiro-[1,3-dioxolan-2,3′-indol]-2′(1′H)-ones were obtained in good yields and did not require further purification.

The deprotection of modified isatins was carried out via acidic hydrolysis (Scheme 4). The target compounds, i.e. unprotected amido-isatins, were isolated by filtration or extraction from aqueous environment (Table 1).

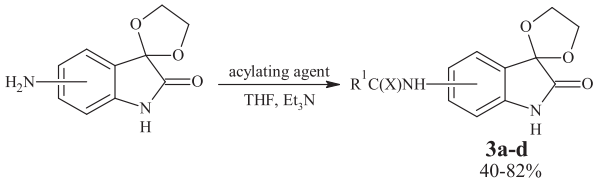
Moreover, all procedures mentioned above can be used to synthesize amide-substituted compounds containing additional substituents in the oxindole fragment. Thus, 5-methoxy-7-amido-substituted isatin was prepared according to the proposed approach, which implies the use of 5-methoxy-7-nitro-isatin as a starting material. However, in case of 5,7-dinitro-isatin derivatives, the mixture of 3-hydroxy-3-hydroxyethoxy- and 3-dihydroxyethoxy-substituted compounds instead of cycle acetal



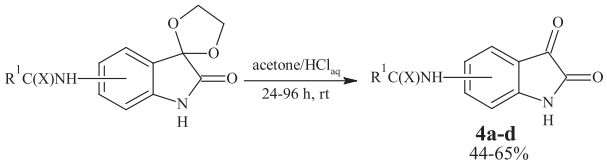
**Scheme 1.** The general approach to amido-substituted oxindole derivatives.




**Scheme 2.** Synthesis of protected amino-isatin.

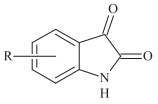



**Scheme 3.** Acylating procedure.




**Scheme 4.** Removing a protecting group.

**Table 1**
The yields of obtained isatins.



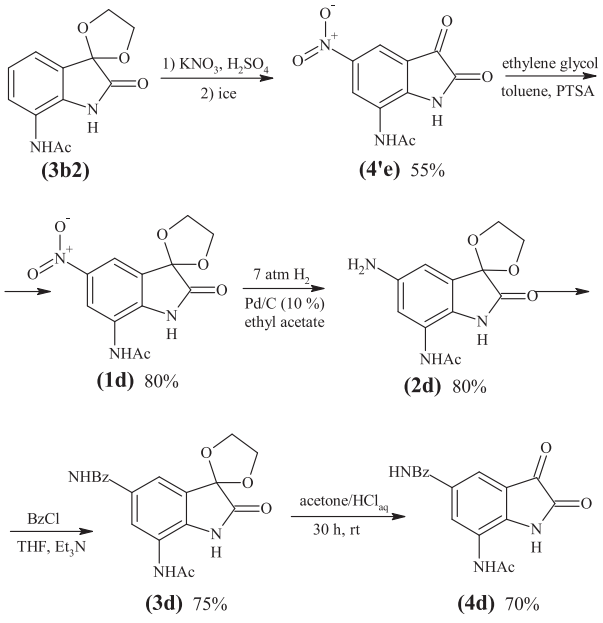
| Compound | R | Yield[a], % |
|---|---|---|
| **4a1** | 5-NHC(O)OMe | 27 |
| **4a2** | 5-NH-(2-Furoyl) | 21 |
| **4a3** | 5-NHBz | 31 |
| **4b1** | 7-NHBz | 34 |
| **4b2** | 7-NHAc | 13 |
| **4b3** | 7-NHC(O)$CH_2$Cl | 16 |
| **4c** | 5-OMe-7-NHAc | 18 |
| **4d** | 5-NHBz-7-NHAc | 34 |

[a] Overall yields from nitro-isatins.

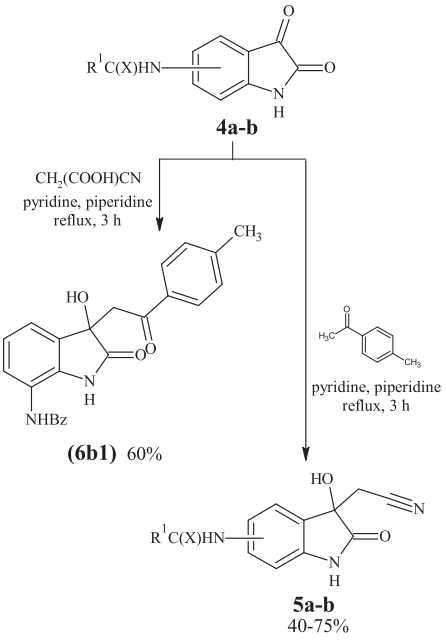
was obtained.

Therefore a sequential procedure for introducing an amide substituent can be carried out. For this purpose after the synthesis of amido-isatin with one amido-substituent the nitration procedure can be carried out. Then whole synthetic procedures described above should be repeated: carbonyl protection, second nitro-group reduction, second amino-group modification and ketal hydrolysis (Scheme 5).

Fortunately if nitration proceeds in acidic environment, removal of the dioxolane group of spiro-[1,3-dioxolan-2,3′-indol]-2′(1′H)-one occurs *in situ*. For example, if spiro-[1,3-dioxolan-7′-amido-




**Scheme 5.** Diamido-substituted isatin synthesis.




**Scheme 6.** Aldol condensation reaction of amido-isatins with CH-acidic compounds.

2,3′-indol]-2′(1′H)-one is subjected to nitration with nitrating mixture then 5-nitro-7-amido-substituted-isatin can be obtained in good yield. Further 3-carbonyl-group protection, nitro-group reduction, acylation and deprotection procedures make it possible to obtain diamido-substituted isatin with different amides in each position.

Other substituents can be introduced into the oxindole core for its further modification, because of high stability of obtained isatins. To illustrate the synthetic opportunities of amido-isatins, the procedures below were applied to synthesize amide-substituted compounds containing additional substituents in the oxindole fragment.

Mostly, all oxindole derivatives are obtained by aldol or crotonic condensation reaction of corresponding isatins with CH-acidic compounds, such as benzaldehydes, acetophenons, malonic acid derivatives, etc. Thus, the reactivity of all obtained compounds and amido-group stability were investigated under classical condensation conditions (Scheme 6). Only the products of aldol condensation reaction were isolated in both cases (Table 2). Moreover, it was found that reaction does not take place in low boiling solvents, such as ethanol.

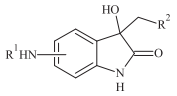
For the synthesis of crotonic condensation products, an additional stage of dehydratation is required. For example, for 5-methoxycarbonylamino-substituted derivative (***5a1***) it was shown that such procedure can be carried out by boiling the aldol condensation product in concentrated hydrochloric acid for several hours (Scheme 7). Despite the severe conditions, no hydrolysis of the carbamoyl group was observed.

In some cases, the presence of a Michael acceptor fragment in the target compound is undesirable, therefore, if necessary, a hydrogenation of the double bond at position 3 can be carried out. Since such reaction proceeds under mild conditions, neither the substituents present in the benzene ring of oxindole, nor amide bond of oxindole ring are affected.

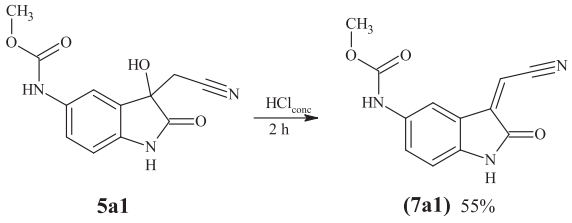
## 3. Conclusion

To sum up, we proposed a simple and effective strategy for the synthesis of various mono- and diamide-substituted isatins. The possibility of their use as reagents for the preparation of a few classes of chemical compounds, which may have biologically activity, was also shown. In addition, the proposed method of synthesis can be automated, which will further widen the range of available isatins for direct synthesis of new classes of compounds, for example, by screening.

**Table 2**
The yields of oxindole derivatives.



| Compound | $R^1$ | $R^2$ | Yield, % |
|---|---|---|---|
| **5a1** | 5-C(O)OMe | CN | 75 |
| **5a2** | 5-(2-Furoyl) | CN | 50 |
| **5a3** | 5-Bz | CN | 65 |
| **5b1** | 7-Bz | CN | 40 |
| **6b1** | 7-Bz | C(O)-(4-MePh) | 60 |




**Scheme 7.** Dehydratation procedure.

## 4. Experimental section

$^1$H, $^{13}$C NMR spectra were recorded on a “Bruker Avance-400” spectrometer (400.1 and 100.6 MHz, respectively). IR spectra were recorded on ThermoNicolet IR-200 (KBr) spectrophotometer. High

resolution mass-spectra were recorded on the quadrupole mass spectrometer Finnigan MAT INCOS 50 (USA). Elemental analyses were performed with a Carlo-Erba CHN analyzer. Melting points were measured with an Electrothermal 9100 apparatus. Reaction completion was controlled by TLC ("Silufol-UV-254").

### 4.1. General procedures

#### 4.1.1. Ketal synthesis (**1**)

In a round bottom flask connected to a Dean-Stark apparatus the solution of nitro-isatin, PTSA (0.06 eq), ethylene glycol (15.5 eq) in toluene was refluxed. After 5 h the crude reaction mixture was cooled to room temperature, and then cold water was added. The product was obtained by filtration, washed with water and diethyl ether. To improve the product yield, water filtrate was extracted with ethyl acetate (3 times); organics were dried with non-aqueous sodium sulfate, and the solvent was evaporated in vacuum. Crude product was washed with diethyl ether.

#### 4.1.2. Catalytic nitro-group reduction (**2**)

*4.1.2.1. Method A.* The solution of nitro-spiro[1,3-dioxolan-2,3′-indol]-2′(1′H)-one in ethyl acetate (2 mg/mL) was hydrogenated using continuous flow reactor H-Cube (ThalesNano Nanotechnology Inc., Hungary) under the following conditions: Pd/C (10%), 3–10 bar $H_2$, 1,0–2,0 mL/min, rt. After the reaction proceeded the solvent was removed in vacuum.

*4.1.2.2. Method B.* Liquid phase hydrogenation was carried out in stainless steel reactor partially filled with block of palladium catalyst on the ceramic foam substrate.[34] Highly porous ceramic material (α-$Al_2O_3$) covered by sol γ-$Al_2O_3$ with pores no less than 70–95% – catalyst carrier, is readily permeable for air and water. This catalyst carrier was impregnated with $Pd(NO_3)_2$ and heated at 450 °C to afford a PdO-coated catalyst. PdO was hydrogenated to metallic Pd by hydrogen at 50–55 °C, yielding the highly porous ceramic catalyst with 2.5–3.0% Pd/6% γ-$Al_2O_3$ (catalysts can be repeatedly regenerated by their heating at 400–450 °C 30 to 40 times without activity loss).

Palladium catalyst on the ceramic foam (2.5–3.0% Pd/6% γ-$Al_2O_3$, 50 mm in diameter, 50 mm heigh, 10 ppi cell, 35.0 g, 70–95% pores, cylinder form) was fixed on the middle of stainless steel cylinder autoclave (50 mm in inner diameter) equipped with thermocouple, hydrogen inlet tube, and electric heating system. The stirring of the reaction mixture was provided by the shaking device (capacity 120–140 $min^{-1}$).[9]

The solution of nitro-spiro[1,3-dioxolan-2,3′-indol]-2′(1′H)-one in ethyl acetate (or THF) was hydrogenated at room temperature for 3–4 h (pressure of 10 bar) using stainless steel autoclave filled with palladium catalyst on ceramic foam substrate (2.5% Pd/6% γ-$Al_2O_3$). Then the reaction mixture was removed from the autoclave and the solvent was evaporated under vacuum; the residue was recrystallized from diethyl ether. If necessary, to improve the yield the filtrate was also evaporated under vacuum, and the residue was purified by dry column vacuum chromatography (hexane-ethyl acetate 3:1 to 1:1).

#### 4.1.3. Acylation typical procedure (**3**)

Acylating agent (1.05 eq) was slowly added to a solution of amino-spiro[1,3-dioxolan-2,3′-indol]-2′(1′H)-one, triethylamine (1.05 eq) in THF at room temperature. After acylating agent was added, the reaction mixture stood for 10 min and then cold water was added. The crude reaction mixture was extracted with ethyl acetate (3 times); the organics were dried under non-aqueous sodium sulfate; and the solvent was removed in vacuum.

#### 4.1.4. Ketal hydrolysis (**4**)

Concentrated hydrochloric acid (12 eq) was added to the solution of 5-amido-spiro[1,3-dioxolan-2,3′-indol]-2′(1′H)-one in aqueous acetone (70%). The reaction mixture was stirred at room temperature for 24–96 h, and then poured into ice. The product was obtained by filtration, washed with cold water and dried on air. If water soluble isatin was obtained, it was isolated by extraction with ethyl acetate.

#### 4.1.5. Nitration procedure (**4′**)

The solution of the corresponding isatin or amido-spiro[1,3-dioxolan-2,3′-indol]-2′(1′H)-one in concentrated sulfuric acid (14.5 eq) was cooled down by ice bath to 0 °C. The potassium nitrate (1 eq) was added portionwise over 2 h maintaining the temperature between 0 and 5 °C. After complete addition the mixture was stirred at room temperature for 0.5 h and poured into ice. The precipitate was collected by vacuum filtration, washed with cold water and dried on air. If the water soluble product was obtained, it was isolated by extraction with ethyl acetate.

#### 4.1.6. Aldol condensation reaction (**5**–**6**)

The solution of isatin and CH-acidic compound (1.05 eq) with piperidine (0.05 eq) in pyridine was refluxed for 3 h. After the reaction completed (TLC monitoring), the reaction mixture was cooled to room temperature, and then the solution of hydrochloric acid in 1,4-dioxane (1 mL) was added to stop the reaction. Next, cold water was slowly added, and the product was obtained by extraction with ethyl acetate. The organics were dried with non-aqueous sodium sulfate and then the solvent was removed in vacuum.

#### 4.1.7. Dehydratation procedure (**7**)

The solution of 3-hydroxy oxindole derivative in concentrated hydrochloric acid was refluxed for 2 h. After the reaction completed (TLC monitoring), the reaction mixture was cooled to room temperature. The precipitate was collected by vacuum filtration, washed with cold water and dried on air. If the water soluble product was obtained, it was isolated by extraction with ethyl acetate from the acidic solution diluted with cold water.

### 4.2. Characterization

*5′-Nitro-spiro[1,3-dioxolan-2,3′-indol]-2′(1′H)-one (**1a**)* was obtained as light yellow powder with yield 71%, m.p. 215°C (lit.m.p. 218°C);[9] $\delta_H$ (400.1 MHz, DMSO-$d_6$) 4.35 (4H, s, –*O*-(C<u>H</u>$_2$)$_2$–*O*–), 7.05 (1H, d, J 8.6, –CH–C–CH–C<u>H</u>–), 8.16 (1H, d, J 2.3, –C<u>H</u>–C–CH–CH–), 8.27 (1H, dd, J 2.3, 8.6, –CH–C–C<u>H</u>–CH–), 11.16 (1H, s, N<u>H</u>); $\delta_C$ (100.6 MHz, DMSO-$d_6$) 66.5, 101.1, 111.5, 121.0, 126.1, 129.0, 143.3, 149.4, 175.1.

*7′-Nitro-spiro[1,3-dioxolan-2,3′-indol]-2′(1′H)-one (**1b**)* was obtained as grey powder with yield 64%, m.p. 207–208 °C [Found C 50.78, H 3.55, N 11.79. $C_{10}H_8N_2O_5$ requires C 50.85, H 3.41, N 11.86%]; $\nu_{max}$ (KBr) 1119, 1322, 1346, 1465, 1528, 1630, 1762, 3219 $cm^{-1}$; $\delta_H$ (400.1 MHz, DMSO-$d_6$) 4.30–4.40 (4H, m, –*O*-(C<u>H</u>$_2$)$_2$–*O*–), 7.24 (1H, dd, J 7.2, 8.6, –CH–C<u>H</u>–CH–C–); 7.77 (1H, dd, J 0.6, 7.2, –C<u>H</u>–CH–CH–C–), 8.12 (1H, dd, J 1.0, 8.6, –CH–CH–C<u>H</u>–C–), 11.17 (1H, s, N<u>H</u>); $\delta_C$ (100.6 MHz, DMSO-$d_6$) 66.4, 123.3, 126.9, 131.6; MS (EI, 70 eV): *m/z* (I, %): 236 (41, M+), 219 (96), 208 (46), 191 (100), 175 (22), 161 (20), 147 (29), 131 (11), 117 (58), 106 (12), 90 (29), 75 (26), 63 (30), 43 (19), 30 (60).

*5′-Methoxy-7′-nitro-spiro[1,3-dioxolan-2,3′-indol]-2′(1′H)-one (**1c**)* was obtained as black powder with yield 75%. m.p. 170–172 °C [Found C 49.60, H 3.85, N 10.49. $C_{11}H_{10}N_2O_6$ requires C 49.63, H 3.79, N 10.52%]; $\nu_{max}$ (KBr) 1272; 1485; 1546; 1770; 2847; 3253 $cm^{-1}$ $\delta_H$ (400.1 MHz, DMSO-$d_6$) 3.83 (3H, s, -O<u>Me</u>), 4.28–4.40

(4H, m, –*O*-(C$\underline{H}_2$)$_2$–*O*–), 7.47 (1H, d, J 2.2, –C$\underline{H}$–C–CH–C–), 7.53 (1H, d, J 2.2, –CH–C–C$\underline{H}$–C–), 11.04 (1H, s, N$\underline{H}$); $\delta_C$ (100.6 MHz, DMSO-$d_6$) 56.8, 66.5, 100.1, 108.9, 120.5, 130.1, 131.9, 133.0, 155.2, 174.9; MS (EI, eV): *m*/*z* (I, %): 222 (83, M+), 205 (68), 194 (41), 175 (58), 164 (38), 147 (37), 132 (21), 104 (65), 93 (47), 76 (35), 62 (32), 50 (31), 30 (100), 15 (70).

*5′-Nitro-7′-acetylamino-spiro[1,3-dioxolan-2,3′-indol]-2′(1′H)-one (**1d**)* was obtained as dark-red powder with yield 80%. m.p. 185–190 °C [Found C, 49.09; H, 3.86; N, 14.30. $C_{12}H_{11}N_3O_6$ requires C, 49.15; H, 3.78; N, 14.33%]; $\nu_{max}$ (KBr) 1120, 1322, 1346, 1465, 1528, 1630, 1736, 1762, 3219 cm$^{-1}$; $\delta_H$ (400.1 MHz, DMSO-$d_6$) 2.08 (3H, s, –C(O)M$\underline{e}$), 4.36 (4H, s, –*O*-(C$\underline{H}_2$)$_2$–*O*–), 8.00 (1H, d, J 1.9, –C$\underline{H}$–C–CH–C–), 8.50 (1H, d, J 1.9, –CH–C–C$\underline{H}$–C–), 9.71 (1H, s, AcN-H–), 10.83 (1H, s, N$\underline{H}$); $\delta_C$ (100.6 MHz, DMSO-$d_6$) 23.9, 66.5, 101.2, 116.8, 121.9, 122.8, 126.5, 141.9, 143.1, 169.4, 174.7.

*5′-Amino-spiro[1,3-dioxolan-2,3′-indol]-2′(1′H)-one (**2a**)* was obtained as light-grey powder with yield 96% (Method A)/89% (Method B) m.p. 203°C [Found C, 58.12; H, 4.96; N, 13.50. $C_{10}H_{10}N_2O_3$ requires C, 58.25; H, 4.89; N, 13.59%]; $\nu_{max}$ (KBr) 1012, 1188, 1291, 1718, 3062, 3335, 3396 cm$^{-1}$;$\delta_H$ (400.1 MHz, DMSO-$d_6$) 4.15–4.25 (2H, m, –*O*–C$\underline{H}_2$–CH$_2$–*O*–), 4.27–4.37 (2H, m, –*O*–CH$_2$–C$\underline{H}_2$–*O*–), 4.83 (2H, br.s., N$\underline{H}_2$), 6.49–6.52 (2H, m, –C$\underline{H}$–C–CH–C$\underline{H}$–), 6.57–6.59 (1H, m, –CH–C–C$\underline{H}$–CH–), 9.96 (1H, s, N$\underline{H}$); $\delta_C$ (100.6 MHz, DMSO-$d_6$) 65.7, 111.2, 112.3, 116.8, 125.6, 132.8, 144.2, 174.7.

*7′-Amino-spiro[1,3-dioxolan-2,3′-indol]-2′(1′H)-one (**2b**)* was obtained grey powder with yield 80% (Method A)/66% (Method B) m.p. 205–210 °C [Found C, 58.16; H, 4.92; N, 13.52. $C_{10}H_{10}N_2O_3$ requires C, 58.25; H, 4.89; N, 13.59%]; $\nu_{max}$ (KBr) 1005, 1193, 1286, 1720, 3062, 3330, 3391 cm$^{-1}$; $\delta_H$ (400.1 MHz, DMSO-$d_6$) 4.16–4.24 (2H, m, –*O*–C$\underline{H}_2$–CH$_2$–*O*–), 4.28–4.36 (2H, m, –*O*–CH$_2$–C$\underline{H}_2$–*O*–), 4.94 (2H, s, N$\underline{H}_2$), 6.66 (1H, d, J 7.7, –C$\underline{H}$–CH–CH–C–), 6.64 (1H, d, J 7.7, –CH–CH–C$\underline{H}$–C–), 6.77 (1H, t, J 7.7, –CH–C$\underline{H}$–CH–C–), 9.95 (1H, s, N$\underline{H}$); $\delta_C$ (100.6 MHz, DMSO-$d_6$) 113.1, 117.7, 123.6, 125.1, 128.1, 132.8, 174.7; MS (EI, eV): *m*/*z* (I, %): 206 (66, M+), 189 (5), 178 (100), 161 (9), 147 (8), 133 (49), 117 (19), 106 (84), 105 (61), 79 (25), 52 (23), 45 (19), 29 (28).

*5-Methoxy-7′-amino-spiro[1,3-dioxolan-2,3′-indol]-2′(1′H)-one (**2c**)* was obtained as dark-red powder with yield 75% m.p. 172–177 °C, [Found C, 55.83; H, 5.25; N, 11.79. $C_{11}H_{12}N_2O_4$ requires C, 55.93; H, 5.12; N, 11.86%]; $\nu_{max}$ (KBr) 1005, 1193, 1287, 1550, 1720, 3062, 3330, 3391 cm$^{-1}$; $\delta_H$ (400.1 MHz, DMSO-$d_6$) 3.63 (3H. s. -OM$\underline{e}$), 4.16–4.36 (4H, m, –*O*-(C$\underline{H}_2$)$_2$–*O*–), 5.00 (2H, br.s, N$\underline{H}_2$), 6.18 (1H, d, J 2.3, –CH–C–C$\underline{H}$–C–), 6.23 (1H, d, J 2.3, –C$\underline{H}$–C–CH–C–), 9.77 (1H, s, N$\underline{H}$); $\delta_C$ (100.6 MHz, DMSO-$d_6$) 54.7, 64.2, 100.4, 103.5, 110.0, 122.3, 127.3, 127.5, 149.6, 168.6.

*5′-Amino-7′-acetylamino-spiro[1,3-dioxolan-2,3′-indol]-2′(1′H)-one (**2d**)* was obtained as yellow powder with yield 80%, m.p. 223–227 °C, [Found C, 54.71; H, 5.13; N, 15.89. $C_{12}H_{13}N_3O_4$ requires C, 54.75; H, 4.98; N, 15.96%]; $\nu_{max}$ (KBr) 1005, 1193, 1286, 1720, 1735, 3062, 3330, 3345, 3391 cm$^{-1}$; $\delta_H$ (400.1 MHz, DMSO-$d_6$) 3.32 (3H, s, –C(O)M$\underline{e}$), 4.24–4.32 (2H, m, –*O*–C$\underline{H}_2$–CH$_2$–*O*–), 4.33–4.41 (2H, m, –*O*–CH$_2$–C$\underline{H}_2$–*O*–), 4.92 (2H, br.s, N$\underline{H}_2$), 6.18 (1H, d, J 2.3, –C$\underline{H}$–C–CH–C–), 6.23 (1H, d, J 2.3, –CH–C–C$\underline{H}$–C–), 9.94 (1H s, AcN$\underline{H}$–), 10.38 (1H, s, N$\underline{H}$). $\delta_C$ (100.6 MHz, DMSO-$d_6$) 23.6, 63.8, 109.1, 110.3, 111.3, 122.9, 123.4, 129.0, 143.3, 167.6, 167.6.

*5′-Methoxycarbonylamino-spiro[1,3-dioxolane-2,3′-indole]-2′(1′H)-one (**3a1**)* was obtained as beige powder with yield 70%, m.p. 115–117 °C [Found C, 54.57; H, 4.70; N, 10.58. $C_{12}H_{12}N_2O_5$ requires C, 54.55; H, 4.58; N, 10.60%]; $\nu_{max}$ (KBr) 1196, 1207, 1665, 1725, 3130, 3280 sm$^{-1}$; $\delta_H$ (400.1 MHz, DMSO-$d_6$) 3.63 (3H, s, -OM$\underline{e}$), 4.14–4.27 (2H, m, –*O*–C$\underline{H}_2$–CH$_2$–*O*–), 4.29–4.40 (2H, m, –*O*–CH$_2$–C$\underline{H}_2$–*O*–), 6.75 (1H, d, J 8.3, –CH–C–CH–C$\underline{H}$–); 7.32 (1H, d, J 8.3, –C$\underline{H}$–C–C$\underline{H}$–CH–), 7.46 (1H, s, –C$\underline{H}$–C–CH–C$\underline{H}$–), 9.56 (1H, s, –N$\underline{H}$C(O)OMe), 10.33 (1H, s, N$\underline{H}$); $\delta_C$ (100.6 MHz, DMSO-$d_6$) 52.1, 65.8, 102.3, 111.1, 111.2, 116.4, 125.1, 134.7, 138.1, 154.6, 174.9.

*5′-(2-Furoyl)amino-spiro[1,3-dioxolan-2,3′-indol]-2′(1′H)-one (**3a2**)* was obtained as beige powder with yield 68%, m.p. 169 °C [Found C, 59.53; H, 4.18; N, 9.29. $C_{15}H_{12}N_2O_5$ requires C, 60.00; H, 4.03; N, 9.33%]; $\nu_{max}$ (KBr) 1200, 1212, 1655, 1736, 3127, 3278 sm$^{-1}$; $\delta_H$ (400.1 MHz, DMSO-$d_6$) 4.20–4.30 (2H, m, –*O*–C$\underline{H}_2$–CH$_2$–*O*–), 4.30–4.40 (2H, m, –*O*–CH$_2$–C$\underline{H}_2$–*O*–), 6.68 (1H, dd, J 1.6, 3.3, –*O*–CH–C$\underline{H}$–CH–), 6.82 (1H, d, J 8.4, –CH–C–CH–C$\underline{H}$–), 7.29 (1H, d, J 3.3, –*O*–CH–CH–C$\underline{H}$–), 7.63 (1H, dd, J 2.0, 8.4, –CH–C–C$\underline{H}$–CH–), 7.77 (1H, d, J 1.6, –*O*–C$\underline{H}$–CH–CH–), 7.91 (1H, d, J 2.0, –C$\underline{H}$–C–CH–CH–), 10.14 (1H, s, –N$\underline{H}$C(O)furoyl), 10.42 (1H, s, N$\underline{H}$); $\delta_C$ (100.6 MHz, DMSO-$d_6$) 65.9, 102.3, 111.0, 112.6, 115.0, 118.4, 124.2, 125.0, 134.0, 139.2, 146.1, 147.9, 156.5, 175.0; MS (EI, 70 eV), *m*/*z* (I, %): 300 (15, M+), 272 (50), 228 (2), 200 (2), 177 (13), 144 (6), 133 (30), 105 (16), 95 (100), 52 (9), 39 (26), 29 (10).

*5′-Benzoylamino-spiro[1,3-dioxolan-2,3′-indol]-2′(1′H)-one (**3a3**)* was obtained as beige powder with yield 70%, m.p. 210 °C [Found C, 65.75; H, 4.59; N, 8.99. $C_{17}H_{14}N_2O_4$ requires C, 65.80; H, 4.55; N, 9.03%]; $\nu_{max}$ (KBr) 1200, 1210, 1490, 1605, 1715, 1735, 3125, 3275 sm$^{-1}$; $\delta_H$ (400.1 MHz, DMSO-$d_6$) 4.23–4.32 (2H, m, –*O*–C$\underline{H}_2$–CH$_2$–*O*–), 4.34–4.42 (2H, m, –*O*–CH$_2$–C$\underline{H}_2$–*O*–), 6.84 (1H, d, J 8.3, –CH–C–CH–C$\underline{H}$–), 7.47–7.60 (3H, m, Ph), 7.67 (1H, dd, J 2.2, 8.3, –CH–C–C$\underline{H}$–CH–), 7.84 (1H, d, J 2.2, –C$\underline{H}$–C–CH–CH–), 7.91–8.00 (2H, m, Ph), 10.21 (1H, s, –N$\underline{H}$Bz), 10.43 (1H, s, N$\underline{H}$); $\delta_C$ (100.6 MHz, DMSO-$d_6$) 65.9, 110.9, 118.5, 124.2, 125.0, 128.0, 128.9, 132.0, 134.7, 135.2, 139.1, 165.7, 175.0; MS (EI, 70 eV), *m*/*z* (I, %): 310 (18, M+), 282 (64), 238 (1), 210 (2), 177 (16), 133 (33), 106 (13), 105 (100), 77 (78), 51 (13), 28 (4).

*7′-Benzoylamino-spiro[1,3-dioxolan-2,3′-indol]-2′(1′H)-one (**3b1**)* was obtained as beige powder with yield 82%, m.p. 240–242 °C [Found C, 65.73; H, 4.61; N, 8.97. $C_{17}H_{14}N_2O_4$ requires C, 65.80; H, 4.55; N, 9.03%]; $\nu_{max}$ (KBr) 1214, 1292, 1672, 1750, 3174, 3351 sm$^{-1}$; $\delta_H$ (400.1 MHz, DMSO-$d_6$) 4.24–4.32 (2H, m, –*O*–C$\underline{H}_2$–CH$_2$–*O*–), 4.33–4.41 (2H, m, –*O*–CH$_2$–C$\underline{H}_2$–*O*–), 7.05 (1H, t, J 7.6, –CH–C$\underline{H}$–CH–C–), 7.22 (1H, d, J 7.6, –C$\underline{H}$–CH–CH–C–), 7.45 (1H, d, J 7.6, –CH–CH–C$\underline{H}$–C–), 7.53 (2H, t, J 7.6, –CH–C$\underline{H}$–CH–C$\underline{H}$–CH–), 7.59 (1H, t, J 7.6, –CH–CH–C$\underline{H}$–CH–CH–), 7.99 (2H, d, J 7.6, –C$\underline{H}$–CH–CH–CH–C$\underline{H}$–), 9.94 (1H, s, –N$\underline{H}$Bz), 10.38 (1H, s, N$\underline{H}$); $\delta_C$ (100.6 MHz, DMSO-$d_6$) 66.0, 102.1, 122.1, 122.3, 122.8, 126.0, 128.4, 128.7, 129.0, 129.7, 132.1, 137.7, 166.0, 174.6; MS (EI, 70 eV), *m*/*z* (I, %): 310 (13, M+), 282 (11), 268 (21), 238 (7), 205 (18), 177 (4), 161 (18), 133 (9), 105 (100), 91 (11), 77 (53), 51 (23), 29 (5).

*7′-Acetylamino-spiro[1,3-dioxolan-2,3′-indol]-2′(1′H)-one (**3b2**)* was obtained as beige powder with yield 40%, m.p. 210–212 °C [Found C, 58.00; H, 5.02; N, 11.25. $C_{12}H_{12}N_2O_4$ requires C, 58.06; H, 4.87; N, 11.29%]; $\nu_{max}$ (KBr) 1120, 1322, 1346, 1465, 1528, 1630, 1736, 1762, 3219 sm$^{-1}$; $\delta_H$ (400.1 MHz, DMSO-$d_6$) 2.05 (3H, s, –NHC(O)M$\underline{e}$), 4.24–4.37 (4H, m, –*O*-(C$\underline{H}_2$)$_2$–*O*–), 7.02 (1H, t, J 7.7, –CH–C$\underline{H}$–CH–C–), 7.21 (1H, d, J 7.7, –C$\underline{H}$–CH–CH–C–), 7.30 (1H, d, J 7.7, –CH–CH–C$\underline{H}$–C–), 9.86 (1H, s, –N$\underline{H}$Ac), 10.21 (1H, s, N$\underline{H}$); $\delta_C$ (100.6 MHz, DMSO-$d_6$) 43.5, 66.0, 102.1, 121.1, 122.7, 123.0, 126.0, 128.2, 137.8, 165.5, 174.5.

*7′-(Chloroacetyl)amino-spiro[1,3-dioxolan-2,3′-indol]-2′(1′H)-one (**3b3**)* was obtained as pale beige powder with yield 61%, m.p. > 340 °C [Found C, 50.86; H, 4.07; Cl, 12.49; N, 9.85. $C_{12}H_{11}ClN_2O_4$ requires C, 50.99; H, 3.92; Cl, 12.54; N, 9.91%]; $\nu_{max}$ (KBr) 1121, 1325, 1343, 1467, 1528, 1630, 1735, 1760, 3225 sm$^{-1}$; $\delta_H$ (400.1 MHz, DMSO-$d_6$) 4.24–4.30 (4H, m, –*O*-(C$\underline{H}_2$)$_2$–O), 4.31–4.37 (2H, m, Cl–C$\underline{H}_2$–C(O)NH–), 7.02 (1H, t, J 7.7, –CH–C$\underline{H}$–CH–C–), 7.21 (1H, d, J 7.7, –C$\underline{H}$–CH–CH–C–), 7.30 (1H, d, J 7.7, –CH–CH–C$\underline{H}$–C–), 9.86 (1H, s, –N$\underline{H}$C(O)CH$_2$Cl), 10.21 (1H, s, N$\underline{H}$); $\delta_C$ (100.6 MHz, DMSO-$d_6$) 43.5, 66.0, 102.1, 121.1, 122.7, 123.0, 126.0, 128.2, 137.8, 165.5, 174.5.

*5′-Methoxy-7′-acetylamino-spiro[1,3-dioxolan-2,3′-indol]-2′(1′H)-one (**3c**)* was obtained as dark-red powder with yield 50%,

m.p. 200–202 °C [Found C, 56.12; H, 5.18; N, 10.05. $C_{13}H_{14}N_2O_5$ requires C, 56.11; H, 5.07; N, 10.07%]; $\nu_{max}$ (KBr) 1135, 1330, 1558, 1655, 1722, 3330 $sm^{-1}$; $\delta_H$ (400.1 MHz, DMSO-$d_6$) 2.05 (3H, s, –NHC(O)Me), 3.15 (3H, s, -OMe), 4.24–4.32 (2H, m, –O–$CH_2$–$CH_2$–O–), 4.33–4.41 (2H, m, –O–$CH_2$–$CH_2$–O–), 6.18 (1H, d, J 2.3, –CH–C–CH–C–), 6.23 (1H, d, J 2.3, –CH–C–CH–C–), 9.94 (1H, s, –NHAc), 10.38 (1H, s, NH); $\delta_C$ (100.6 MHz, DMSO-$d_6$) 23.7, 54.7, 64.4, 104.7, 105.4, 108.4, 126.1, 127.7, 129.5, 153.7, 167.2.

*5′-Benzoylamino-7′-acetylamino-spiro[1,3-dioxolan-2,3′-indol]-2′(1′H)-one (**3d**)* was obtained as beige powder with yield 75%, m.p. 240–242 °C [Found C, 62.07; H, 4.76; N, 11.43. $C_{19}H_{17}N_3O_5$ requires C, 62.12; H, 4.66; N, 11.44%]; $\nu_{max}$ (KBr) 1120, 1220, 1337, 1665, 1718, 1730, 3270 $sm^{-1}$; $\delta_H$ (400.1 MHz, DMSO-$d_6$) 3.32 (3H, s, –NHC(O)Me), 4.24–4.32 (2H, m, –O–$CH_2$–$CH_2$–O–), 4.33–4.41 (2H, m, –O–$CH_2$–$CH_2$–O–), 6.18 (1H, d, J 2.3, –CH–C–CH–C–), 6.23 (1H, d, J 2.3, –CH–C–CH–C–), 7.05–7.15 (1H, m, Ph), 7.22–7.40 (3H, m, Ph), 7.45–7.50 (1H, m, Ph), 9.94 (1H, –NHAc), 10.22 (1H, s, –NHBz), 10.38 (1H, s, NH); $\delta_C$ (100.6 MHz, DMSO-$d_6$) 24.0, 64.9, 109.1, 110.4, 114.1, 125.6, 126.4, 128.4, 128.9, 131.5, 132.3, 132.5, 135.8, 163.9, 166.3.

*5-Methoxycarbonylamino-isatin (**4a1**)* was obtained as dark-purple powder with yield 55%, m.p. 289–291 °C [Found C, 54.47; H, 3.82; N, 12.68. $C_{10}H_8N_2O_4$ requires C, 54.55; H, 3.66; N, 12.72%]; $\nu_{max}$ (KBr) 1187, 1323, 1728, 1700, 1758, 2965, 3233, 3363 $sm^{-1}$; $\delta_H$ (400.1 MHz, DMSO-$d_6$) 3.66 (3H, s, -OMe), 6.85 (1H, d, J 8.1, –CH–C–CH–CH–), 7.50–7.63 (2H, m, –CH–C–CH–CH–), 9.71 (1H, s, –NH–C(O)OMe), 10.92 (1H, s, NH); $\delta_C$ (100.6 MHz, DMSO-$d_6$) 52.2, 113.0, 118.2, 128.4, 128.5, 135.0, 146.2, 154.6, 160.0, 185.1; MS (EI, 70 eV), *m*/*z* (I, %): 220 (55, M+), 192 (100), 164 (27), 132 (62), 105 (36), 78 (14), 59 (21), 52 (21), 29 (11), 15 (21).

*5-(2′-Furoyl)amino-isatin (**4a2**)* was obtained as dark-purple powder with yield 44%, m.p. 297–299°C [Found C, 60.89; H, 3.23; N, 10.89. $C_{13}H_8N_2O_4$ requires C, 60.94; H, 3.15; N, 10.93%]; $\nu_{max}$ (KBr) 1727, 1738, 1768, 3107, 3302 $sm^{-1}$; $\delta_H$ (400.1 MHz, DMSO-$d_6$) 6.70 (1H, s, –CH–C–CH–CH–), 6.01 (1H, d, J 8.1, –CH–C–CH–CH–), 7.32 (1H, d, J 8.1, –CH–C–CH–CH–), 7.80–8.00 (3H, m, furoyl), 10.30 (1H, s, –NH–C(O)furoyl), 11.01 (1H, s, NH); $\delta_C$ (100.6 MHz, DMSO-$d_6$) 112.7, 112.8, 115.4, 117.1, 118.1, 130. 7, 134.2, 146.3, 147.1, 147.7, 156.7, 160.1, 184.9; MS (EI, 70 eV), *m*/*z* (I, %): 256 (86, M+), 228 (99), 200 (9), 171 (20), 144 (18), 112 (17), 95 (100), 79 (6), 39 (29), 29 (9).

*5-Benzoylamino-isatin (**4a3**)* was obtained as purple powder with yield 63%, m.p. 310°C [Found C, 67.62; H, 3.85; N, 10.50. $C_{15}H_{10}N_2O_3$ requires C, 67.67; H, 3.79; N, 10.52%]; $\nu_{max}$ (KBr) 1642, 1733, 1757, 3299, 3372 $sm^{-1}$; $\delta_H$ (400.1 MHz, DMSO-$d_6$) 6.91 (1H, d, J 8.1, –CH–C–CH–CH, 7.45–7.65 (3H, m, –CH–C–CH–CH–, –CH–CH–CH–CH–CH–), 7.82–8.03 (4H, m, 4H, –CH–C–CH–CH–, –CH–CH–CH–CH–CH–), 10.31 (1H, s, –NHBz), 11.00 (1H, s, NH); $\delta_C$ (100.6 MHz, DMSO-$d_6$) 112.7, 117.1, 118.1, 128.1, 128.9, 130.7, 132.2, 134.9, 135.0, 147.0, 160.1, 166.0, 185.0; MS (EI, 70 eV), *m*/*z* (I, %): 266 (19, M+), 238 (13), 210 (1), 181 (0.5), 161 (1), 133 (7), 105 (100), 77 (71), 51 (23), 29 (1.5).

*7-Benzoylamino-isatin (**4b1**)* was obtained as purple powder with yield 64%, m.p. 307°C [Found C, 67.63; H, 3.83; N, 10.51. $C_{15}H_{10}N_2O_3$ requires C, 67.67; H, 3.79; N, 10.52%]; $\nu_{max}$ (KBr) 1621, 1655, 1737, 3255 $sm^{-1}$; $\delta_H$ (400.1 MHz, DMSO-$d_6$) 7.11 (1H, t, J 7.2, –CH–CH–CH–C–), 7.41 (1H, d, J 7.2, –CH–CH–CH–C–), 7.54 (2H, t, J 7.1, –CH–CH–CH–CH–CH–), 7.61 (1H, t, J 7.1, –CH–CH–CH–CH–CH–), 7.73 (1H, d, J 7.2, –CH–CH–CH–C–), 8.01 (2H, d, J 7.1, –CH–CH–CH–CH–CH–), 10.01 (1H, s, –NHBz), 11.03 (1H, s, NH); $\delta_C$ (100.6 MHz, DMSO-$d_6$) 119.15, 122.11, 123.15, 123.45, 128.48, 128.75, 132.27, 134.48, 135.15, 145.21, 159.71, 166.13, 184.84.

*7-Acetylamino-isatin (**4b2**)* was obtained as dark-red powder with yield 65%, m.p. 301–303°C [Found C, 58.79; H, 4.13; N, 13.69. $C_{10}H_8N_2O_3$ requires C, 58.82; H, 3.95; N, 13.72%]; $\nu_{max}$ (KBr) 1665, 1723, 1735, 3274 $sm^{-1}$; $\delta_H$ (400.1 MHz, DMSO-$d_6$) 2.10 (3H, s, –NH–C(O)Me), 7.02 (1H, t, J 7.7, –CH–CH–CH–C–), 7.21 (1H, d, J 7.7, –CH–CH–CH–C–), 7.30 (1H, d, J 7.7, –CH–CH–CH–C–), 9.66 (1H, s, –NHAc), 11.27 (1H, s, NH); $\delta_C$ (100.6 MHz, DMSO-$d_6$) 24.0, 115.4, 118.6, 123.7, 125.4, 142.5, 147.1, 159.2, 169.2, 182.5.

*7-(Chloroacetyl)amino-isatin (**4b3**)* was obtained as red powder with yield 50%, m.p. > 340°C [Found C, 50.28; H, 3.13; Cl, 14.85; N, 11.71. $C_{10}H_7ClN_2O_3$ requires C, 50.33; H, 2.96; Cl, 14.86; N, 11.74%]; $\nu_{max}$ (KBr) 1653, 1708, 1735, 3270 $sm^{-1}$; $\delta_H$ (400.1 MHz, DMSO-$d_6$) 2.55 (2H, s, –NHC(O)–$CH_2$–Cl), 7.05 (1H, t, J 7.7, –CH–CH–CH–C–), 7.22 (1H, d, J 7.7, –CH–CH–CH–C–), 7.30 (1H, d, J 7.7, –CH–CH–CH–C–), 9.66 (1H, s, –NH–C(O)$CH_2$Cl), 11.27 (1H, s, NH); $\delta_C$ (100.6 MHz, DMSO-$d_6$) 24.0, 115.4, 118.6, 123.7, 125.4, 142.5, 147.1, 159.2, 175.1, 182.5.

*5-Methoxy-7-acetamido-isatin (**4c**)* was obtained as dark-violet powder with yield 63%, m.p. 305–308°C [Found C, 56.39; H, 4.35; N, 11.95. $C_{11}H_{10}N_2O_4$ requires C, 56.41; H, 4.30; N, 11.96%]; $\nu_{max}$ (KBr) 1655, 1705, 1732, 3264 $sm^{-1}$; $\delta_H$ (400.1 MHz, DMSO-$d_6$) 2.05 (3H, s, –NHC(O)Me), 3.15 (3H, s, -OMe), 6.18 (1H, d, J 2.3, –CH–C–CH–C–), 6.23 (1H, d, J 2.3, –CH–C–CH–C–), 9.94 (1H, s, –NHAc), 10.38 (1H, s, NH); $\delta_C$ (100.6 MHz, DMSO-$d_6$) 23.7, 54.7, 104.7, 105.4, 108.4, 126.1, 127.7, 129.5, 153.7, 158.9, 167.2.

*5-Benzoyl-7-acetamido-isatin (**4d**)* was obtained as dark-purple powder with yield 70%, m.p. 289–292°C [Found C, 63.15; H, 4.16; N, 12.97. $C_{17}H_{13}N_3O_4$ requires C, 63.16; H, 4.05; N, 13.00%]; $\nu_{max}$ (KBr) 1660, 1685, 1710, 1737, 3225 $sm^{-1}$; $\delta_H$ (400.1 MHz, DMSO-$d_6$) 3.32 (3H, s, –NHC(O)Me), 6.18 (1H, d, J 2.3, –CH–C–CH–C–), 6.23 (1H, d, J 2.3, –CH–C–CH–C–), 7.05–7.15 (2H, m, –CH–CH–CH–CH–CH–), 7.22–7.40 (3H, m, –CH–CH–CH–CH–CH–), 9.94 (1H, s, –NHAc), 10.22 (1H, s, –NHBz), 10.38 (1H, NH); $\delta_C$ (100.6 MHz, DMSO-$d_6$) 24.0, 109.1, 110.4, 114.1, 125.6, 126.4, 128.4, 128.9, 131.5, 132.3, 132.5, 135.8, 159.2, 163.9, 166.3.

*5′-Nitro-7′-acetylamino-isatin (**4′e**)* was obtained as orange powder with yield 55%, m.p. 279–282 °C [Found C, 48.18; H, 2.96; N, 16.84. $C_{10}H_7N_3O_5$ requires C, 48.20; H, 2.83; N, 16.86%]; $\nu_{max}$ (KBr) 1465, 1528, 1715, 1730, 1745, 3330 $sm^{-1}$; $\delta_H$ (400.1 MHz, DMSO-$d_6$) 2.10 (3H, s, –NHC(O)Me), 8.01 (1H, d, J 1.7, –CH–C–CH–C–), 8.74 (1H, d, J 1.7, –CH–C–CH–C–), 9.66 (1H, s, –NHAc), 11.27 (1H, s, NH); $\delta_C$ (100.6 MHz, DMSO-$d_6$) 24.0, 115.6, 118.9, 123.9, 125.4, 142.8, 147.7, 160.0, 169.6, 182.5.

*(5-Methoxycarbonylamino-3-hydroxy-2-oxindole-3-yl)acetonitrile (**5a1**)* was obtained black powder with yield 75%, m.p. 160–165 °C [Found C, 55.13; H, 4.31; N, 16.03. $C_{12}H_{11}N_3O_4$ requires C, 55.17; H, 4.24; N, 16.09%]; $\nu_{max}$ (KBr) 1716, 1726, 2258, 2852, 2925, 2953, 3000–3650 $sm^{-1}$; $\delta_H$ (400.1 MHz, DMSO-$d_6$) 2.91 (1H, d, J 16.6, –$CH^1H^2$–CN), 3.01 (1H, d, J 16.6, –$CH^1H^2$–CN), 3.65 (3H, s, -OMe), 6.61 (1H, s, –OH), 6.79 (1H, d, J 8.3, –CH–C–CH–CH–), 7.33 (1H, dd, J 1.5, 8.3, –CH–C–CH–CH–), 7.63 (1H, d, J 1.5, –CH–C–CH–CH–), 9.56 (1H, s, –NHC(O)OMe), 10.44 (1H, s, NH); $\delta_C$ (100.6 MHz, DMSO-$d_6$) 26.7, 52.0, 72.8, 110.5, 116.0, 117.4, 120.6, 130.6, 134.4, 136.9, 154.6, 177.1; MS (EI, 70 eV), *m*/*z* (I, %): 261 (56, M+), 221 (100), 189 (89), 165 (18), 133 (22), 105 (28), 84 (18), 59 (43), 15 (42).

*(5-(2′-Furoyl)amino-3-hydroxy-2-oxindole-3-yl)acetonitrile (**5a2**)* was obtained as black powder with yield 50%, m.p. 298–300 °C [Found C, 60.55; H, 3.85; N, 14.08. $C_{15}H_{11}N_3O_4$ requires C, 60.61; H, 3.73; N, 14.14%]; $\nu_{max}$ (KBr) 1557, 1724, 2268, 2852, 3240, 3305 $sm^{-1}$; $\delta_H$ (400.1 MHz, DMSO-$d_6$) 2.94 (1H, d, J 16.6, –$CH^1H^2$–CN), 3.03 (1H, d, J 16.6, –$CH^1H^2$–CN), 6.65 (1H, br.s, –OH), 6.68 (1H, dd, J 1.7, 3.4, –O–CH–CH–CH–), 6.84 (1H, d, J 8.4, –CH–C–CH–CH–), 7.31 (1H, d, J 3.4, –O–CH–CH–CH–), 7.64 (1H, dd, J 2.0, 8.4, –CH–C–CH–CH–), 7.87 (1H, d, J 2.0, –CH–C–CH–CH–), 7.91 (1H, d, J 1.7, –O–CH–CH–CH–), 10.20 (1H, s, –NH–C(O)furoyl), 10.53 (1H, s, NH); $\delta_C$ (100.6 MHz, DMSO-$d_6$) 26.6, 72.8, 110.4, 112.6, 114.9, 117.5, 118.0, 122.8, 130.4, 133.6, 137.9, 146.1,

148.0, 156.6, 177.2; MS (EI, 70 eV), *m/z* (I, %): 297 (66, M+), 279 (9), 257 (65), 229 (23), 189 (13), 174 (5), 133 (10), 105 (12), 95 (100), 79 (29), 52 (18), 43 (20), 39 (33), 28 (18).

*(5-Benzoylamino-3-hydroxy-2-oxindole-3-yl)acetonitrile* (***5a3***) was obtained as black powder with yield 61%, m.p. 173–176°C [Found C, 66.43; H, 4.30; N, 13.65. $C_{17}H_{13}N_3O_3$ requires C, 66.44; H, 4.26; N, 13.67%]; $\nu_{max}$ (KBr) 1657, 1724, 2270, 2860, 3000–3650 $sm^{-1}$; $\delta_H$ (400.1 MHz, DMSO-$d_6$) 2.94 (1H, d, J 16.5, –CH$^1$H$^2$–CN), 3.04 (1H, d, J 16.5, –CH$^1$H$^2$–CN), 6.66 (1H, s, –OH), 6.80–6.90 (1H, m, –CH–C–CH–CH–), 7.45–7.60 (3H, m, –CH–C–CH–CH–, –CH–CH–CH–CH–CH–), 7.63–7.74 (1H, m, –CH–C–CH–CH–), 7.85–8.05 (3H, m, –CH–CH–CH–CH–CH–), 10.26 (1H, s, –NHBz), 10.53 (1H, s, NH); $\delta_C$ (100.6 MHz, DMSO-$d_6$) 26.7, 72.8, 110.3, 117.4, 118.0, 122.8, 128.0, 128.8, 130.4, 131.9, 134.4, 135.3, 137.9, 165.7, 177.2.

*(7-Benzoylamino-3-hydroxy-2-oxindole-3-yl)acetonitrile* (***5b1***) was obtained as black powder with yield 40%, m.p. 115–120°C [Found C, 66.42; H, 4.36; N, 13.63. $C_{17}H_{13}N_3O_3$ requires C, 66.44; H, 4.26; N, 13.67%]; $\nu_{max}$ (KBr) 1660, 1728, 2265, 2858, 3000–3650 $sm^{-1}$; $\delta_H$ (400.1 MHz, DMSO-$d_6$) 2.96 (1H, d, J 16.6, –CH$^1$H$^2$–CN), 3.07 (1H, d, J 16.6, –CH$^1$H$^2$–CN), 6.68 (1H, br.s., –OH), 7.06 (1H, t, J 7.3, –CH–CH–CH–CH–CH–), 7.34 (2H, m, –CH–CH–CH–C–), 7.44–7.62 (3H, m, –CH–CH–CH–CH–CH–), 8.00 (2H, d, J 7.3, –CH–CH–CH–CH–CH–), 8.89 (1H, d, J 5.1, –CH–CH–CH–C–), 9.96 (1H, s, –NHBz), 10.53 (1H, s, NH); $\delta_C$ (100.6 MHz, DMSO-$d_6$) 26.7, 72.8, 110.5, 117.8, 118.2, 122.9, 128.0, 128.7, 130.4, 132.0, 134.4, 135.4, 137.9, 165.7, 177.3.

*N-{3-hydroxy-3-[2-(4-methylphenyl)-2-oxoethyl]-2-oxindol-7-yl} benzamide* (***6b1***) was obtained black powder with yield 60%, m.p. 150–155°C [Found C, 71.95; H, 5.15; N, 6.98. $C_{24}H_{20}N_2O_4$ requires C, 71.99; H, 5.03; N, 7.00%]; $\nu_{max}$ (KBr) 1665, 1705, 1737, 2270, 3000–3650 $sm^{-1}$; $\delta_H$ (400.1 MHz, DMSO-$d_6$) 3.50 (1H, d, J 17.4, –CH$^1$H$^2$–C(O)-(4-MePh)), 3.85 (3H, s, 4-MePh-), 3.99 (1H, d, J 17.4, –CH$^1$H$^2$–C(O)-(4-MePh)), 6.02 (1H, br.s, –OH), 6.99 (2H, d, J 8.8, –CH–CH-CMe-CH–CH–), 7.11 (1H, t, J 7.7, –CH–CH–CH–C–), 7.15–7.36 (3H, m, –CH–CH–CH–CH–CH–, –CH–CH–CH–C–), 7.39 (1H, d, J 7.7, –CH–CH–CH–C–), 7.42–7.66 (3H, m, –CH–CH–CH–CH–CH–, CH–CH–CMe–CH–CH–), 7.85 (2H, d, J 8.9, –CH–CH-CMe–CH–CH–), 7, 90–8.05 (2H, m, –CH–CH–CH–CH–CH–), 10.23 (1H, s, –NHBz), 10.33 (1H, s, NH); $\delta_C$ (100.6 MHz, DMSO-$d_6$) 21.4, 44.8, 76.6, 121.0, 122.6, 126.5, 127.5, 127.9, 128.1, 128.8, 129.8, 130.7, 131.9, 134.3, 135.3, 136.1, 145.0, 161.7, 176.9, 198.6.

*(5-Methoxycarbonylamino-2-oxindole-3-yliden)acetonitrile* (***7a1***) was obtained as dark-violet powder with yield 55%, m.p. 180–185 °C [Found C, 59.25; H, 3.80; N, 17.25. $C_{12}H_9N_3O_3$ requires C, 59.26; H, 3.73; N, 17.28%]; $\nu_{max}$ (KBr) 1716, 1726, 2260, 2855, 2927, 2950, 3265 $sm^{-1}$; $\delta_H$ (400.1 MHz, DMSO-$d_6$) 3.64 (3H, s, -OMe), 6.82 (1H, s, –C=CH–CN), 7.28 (1H, d, J 8.9, –CH–C–CH–CH–), 7.61 (1H, d, J 8.9, –CH–C–CH–CH–), 8.29 (1H, s, –CH–C–CH–CH–), 9.73 (1H, s, –NH–C(O)OMe), 11.98 (1H, s, NH); $\delta_C$ (100.6 MHz, DMSO-$d_6$) 52.7, 96.8, 111.7, 112.9, 115.8, 120.7, 124.4, 131.1, 136.2, 146.1, 153.7, 165.5.

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