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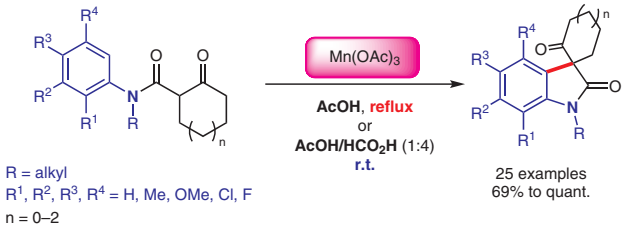
Manganese(III)-Based Oxidative Cyclization of *N*-Aryl-2-oxocycloalkane-1-carboxamides: Synthesis of Spiroindolinones

Shintaro Katayama
Hiroshi Nishino*

Department of Chemistry, Graduate School of Science, Kumamoto University, Kurokami 2-39-1, Chûou-Ku, Kumamoto 860-8555, Japan
nishino@kumamoto-u.ac.jp

This manuscript is dedicated to the late Professor Shô Ito, Professor Emeritus of Tohoku University, Japan, who showed Hiroshi Nishino the way as a chemist.



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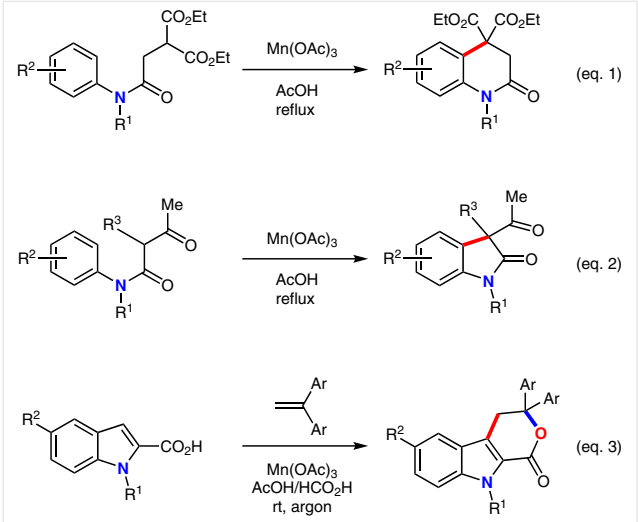
Abstract The Mn(III)-based oxidative cyclization of twenty-five *N*-aryl-2-oxocycloalkane-1-carboxamides is investigated. The reactions progress efficiently to give the desired spiro[cycloalkane-1,3′-indoline]-2,2′-diones in high to quantitative yields. The easy conversion of the carbonyl functional group of one of the indoline products, 1′-methylspiro[cyclohexane-1,3′-indoline]-2,2′-dione, is also demonstrated.

Key words spiro[cycloalkane-1,3′-indoline]-2,2′-diones, oxidative cyclization, 5-*exo* cyclization, radicals, heterocycles, spiro compounds, indolinones

Cyclization is one of the most important techniques to construct complex organic molecules,[1] and can be accomplished via ionic,[2] radical,[3] and concerted techniques,[4] and by ring-closing metathesis.[5] From the standpoint of the cyclization reaction, we have been studying the oxidative radical cyclization using $Mn(OAc)_3$.[6] For example, the oxidation of 2-{2-[alkyl(aryl)amino]-2-oxoethyl}malonates gave 1-alkyl-2-oxo-2,3-dihydroquinoline-4,4(1*H*)-dicarboxylates (Scheme 1, eq. 1),[7] which could be converted into quinolines. A similar reaction of *N*,2-dialkyl-*N*-aryl-3-oxobutanamides produced 3-acetyl-1,3-dialkylindolin-2-ones in quantitative yields (Scheme 1, eq. 2),[8] which could be transformed into indoles. On the other hand, indole-2-carboxylic acids underwent oxidative trapping reactions with alkenes followed by cyclization to give indolelactones (Scheme 1, eq. 3).[9] During the course of these studies, we communicated our preliminary results on the synthesis of spiro[cyclohexane-1,3′-indoline]-2,2′-diones via the oxidation of *N*-aryl-2-oxocyclohexane-1-carboxamides through a formal 5-*exo*-trig cyclization.[10] Although the reaction was very simple and convenient and the product spiroindolinones are important for the total synthesis of some natural products, for example, satavaptan, as a selective vasopressin V_2 receptor antagonist[11a,b] and gelsemine, as a highly toxic plant alkaloid,[11c–e] the yields and the synthetic applications were not high enough. Recently, we developed the activation of $Mn(OAc)_3$ by adding HCO_2H to the reaction and dramatically changed the reaction time and temperature, which improved the product yields.[12] We then attempted to scrutinize the reactions of *N*-aryl-2-oxocycloalkane-1-carboxamides in order to develop the synthesis of spiroindolinone derivatives.

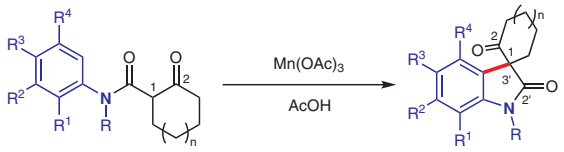


Scheme 1 Synthesis of heterocycles using Mn(III)-based oxidations

N-Aryl-2-oxocycloalkane-1-carboxamides **1a–y** were prepared by the condensation of ethyl 2-oxocycloalkanecarboxylates with the corresponding anilines (see the Supporting Information). The oxidation of *N*-methyl-2-oxo-*N*-phenylcyclohexane-1-carboxamide (**1a**) with $Mn(OAc)_3$ in AcOH gave 1′-methylspiro[cyclohexane-1,3′-indoline]-2,2′-

dione (**2a**) (Table 1, entries 1–3);[10] however, the reaction took a long time in AcOH (2 days at r.t.), giving a low yield of **2a** (entry 1), elevating the temperature (reflux) in AcOH caused the retro-condensation of **1a** (entry 2), and the use of an excess amount of the oxidant led to **2a** in 55% yield (entry 3). Thus, we decided to explore the reaction under milder conditions in the presence of HCO_2H. The reaction in AcOH/HCO_2H (4:1 v/v) at room temperature afforded the spiroindolinone **2a** in 38% yield after 30 hours (entry 4). When the amount of HCO_2H was further increased, the yield of **2a** was higher, and a maximum yield of 88% was achieved using AcOH/HCO_2H (1:4 v/v) (entry 7). However, the use of only HCO_2H as the solvent decreased the yield of **2a**, although the reaction time was shorter (entry 8). We thus considered the reaction conditions in entry 7 to be optimum, and other *N*-alkyl-2-oxo-*N*-phenylcyclohexane-1-carboxamides **1b–e** underwent the reaction to give the desired spiroindolinones **2b–e** in good yields (entries 9–12). These results indicated that the oxidative cyclization was not influenced by the *N*-alkyl group of the carboxamides **1a–e**, although the yield of **2d** was slightly lower than those of the 1′-alkylspiroindolinones **2a–c** and **2e**.

Table 1 Oxidation of *N*-Aryl-2-oxocycloalkane-1-carboxamides **1a–y** with $Mn(OAc)_3$[a,b]



1a–y **2a–y**

Entry		Carboxamide						**1**/$Mn(OAc)_3$[c]	AcOH/HCO_2H	Temp	Time	Product
		R	R^1	R^2	R^3	R^4	n		v/v			(yield)[d]
1	**1a**	Me	H	H	H	H	1	1:2.5	5:0	r.t.	2 d	**2a** (15%)
2	**1a**	Me	H	H	H	H	1	1:2.5	5:0	reflux	4 min	**2a** (69%)[e]
3	**1a**	Me	H	H	H	H	1	1:3	5:0	reflux	5 min	**2a** (55%)
4	**1a**	Me	H	H	H	H	1	1:2.5	4:1	r.t.	30 h	**2a** (38%)
5	**1a**	Me	H	H	H	H	1	1:2.5	3:2	r.t.	24 h	**2a** (60%)
6	**1a**	Me	H	H	H	H	1	1:2.5	2:3	r.t.	24 h	**2a** (68%)
7	**1a**	Me	H	H	H	H	1	1:2.5	1:4	r.t.	24 h	**2a** (88%)
8	**1a**	Me	H	H	H	H	1	1:2.5	0:5	r.t.	18 h	**2a** (67%)
9	**1b**	Et	H	H	H	H	1	1:2.5	1:4	r.t.	24 h	**2b** (83%)
10	**1c**	*n*-Pr	H	H	H	H	1	1:2.5	1:4	r.t.	24 h	**2c** (90%)
11	**1d**	*i*-Pr	H	H	H	H	1	1:2.5	1:4	r.t.	24 h	**2d** (69%)
12	**1e**	*n*-Bu	H	H	H	H	1	1:2.5	1:4	r.t.	24 h	**2e** (87%)
13	**1f**	Me	H	H	Me	H	1	1:2.5	1:4	r.t.	24 h	**2f** (37%)
14	**1f**	Me	H	H	Me	H	1	1:2	5:0	reflux	1 min	**2f** (84%)
15	**1g**	Me	H	H	OMe	H	1	1:2	5:0	reflux	1 min	**2g** (86%)
16	**1h**	Me	H	H	Cl	H	1	1:2.5	5:0	reflux	1 min	**2h** (75%)
17	**1i**	Me	H	H	F	H	1	1:2.5	5:0	reflux	1 min	**2i** (90%)
18	**1j**	Me	Me	H	H	H	1	1:2	5:0	reflux	0.5 min	**2j** (96%)
19	**1k**	Me	OMe	H	H	H	1	1:2.5	5:0	reflux	1 min	**2k** (88%)
20	**1l**	Me	Cl	H	H	H	1	1:2.5	5:0	reflux	0.5 min	**2l** (93%)
21	**1m**	Me	H	Me	H	H	1	1:2.5	5:0	reflux	2 min	**2m** (92%)[f]
22	**1n**	Me	Me	Me	H	H	1	1:2.5	5:0	reflux	1 min	**2n** (95%)
23	**1o**	Me	H	Me	H	Me	1	1:2.5	5:0	reflux	1 min	**2o** (88%)
24	**1p**	Me	H	H	H	H	0	1:2.5	5:0	reflux	1 min	**2p** (87%)
25	**1p**	Me	H	H	H	H	0	1:2.5	1:4	r.t.	0.5 min	**2p** (84%)

Table 1 (continued)

Entry		Carboxamide						**1**/Mn(OAc)$_3$[c]	AcOH/HCO$_2$H	Temp	Time	Product
		R	R^1	R^2	R^3	R^4	n		v/v			(yield)[d]
26	**1q**	Et	H	H	H	H	0	1:2.5	1:4	r.t.	0.5 min	**2q** (quant.)
27	**1r**	*n*-Pr	H	H	H	H	0	1:2.5	1:4	r.t.	0.5 min	**2r** (quant.)
28	**1s**	*i*-Pr	H	H	H	H	0	1:2.5	1:4	r.t.	0.5 min	**2s** (98%)
29	**1t**	*n*-Bu	H	H	H	H	0	1:2.5	1:4	r.t.	0.5 min	**2t** (97%)
30	**1u**	Me	H	H	H	H	2	1:2.5	1:4	r.t.	48 h	**2u** (76%)
31	**1u**	Me	H	H	H	H	2	1:2.5	5:0	reflux	5 min	**2u** (90%)
32	**1v**	Me	H	H	Me	H	2	1:2.5	5:0	reflux	5 min	**2v** (86%)
33	**1w**	Me	H	H	Cl	H	2	1:2.5	5:0	reflux	6 min	**2w** (78%)
34	**1x**	Me	Me	H	H	H	2	1:2.5	5:0	reflux	3 min	**2x** (93%)
35	**1y**	Me	Cl	H	H	H	2	1:2.5	5:0	reflux	3 min	**2y** (74%)

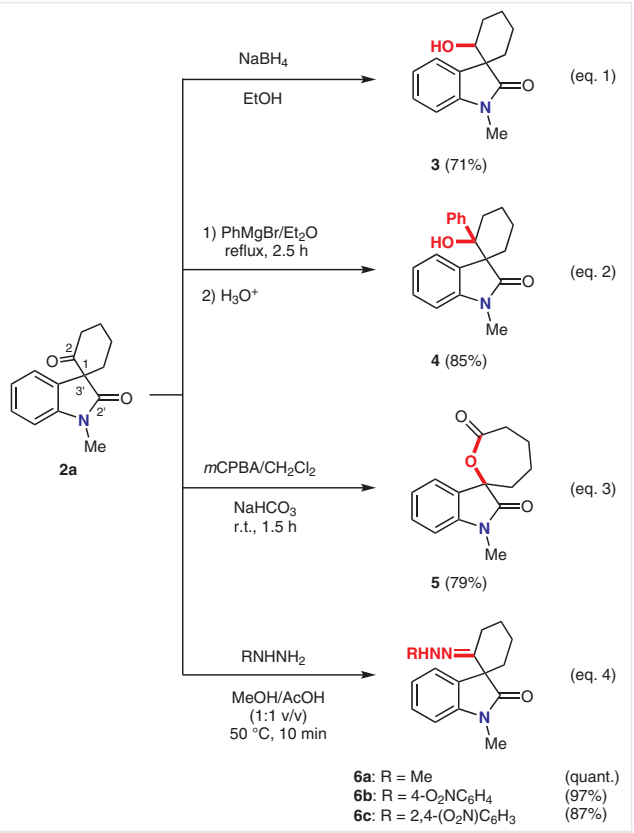
[a] The reactions of carboxamides **1** (0.5 mmol) were carried out in solvent (15 mL) under argon (entries 1–12).
[b] The reactions of carboxamides **1** (0.3 mmol) were carried out in solvent (10 mL) under argon (entries 13–35).
[c] Molar ratio.
[d] Yield of isolated product **2**.
[e] The retro-condensation of **1a** also occurred and no starting **1a** was recovered.
[f] The regioisomers **2m** (R^2 = Me) and **2m′** (R^4 = Me) were produced in a 2:1 regioisomeric ratio.

In order to investigate the influence of a substituent on the phenyl group, the reaction of *N*-4-methylphenylcyclohexane-1-carboxamide **1f** was carried out under the optimized conditions. Contrary to our expectation, the reaction still took 24 hours and the decomposition of **1f** occurred somewhat before the oxidative cyclization, resulting in the formation of product **2f** in a low yield (Table 1, entry 13). It was then necessary to activate the reaction and shorten the reaction time, so that the reaction could be conducted at reflux temperature. Gratifyingly, the reaction was complete within 1 minute and gave the desired spiroindolinone **2f** in 84% yield (entry 14). Methyl-, methoxy-, chloro-, and fluoro-substituted phenylcyclohexane-1-carboxamides **1g–o** also gave very good results under similar conditions (entries 15–23). The reaction of *N*-3-methylphenylcyclohexane-1-carboxamide **1m** produced two regioisomers, **2m** (R^2 = Me) and **2m′** (R^4 = Me) in a 2:1 regioisomeric ratio, probably due to the steric hindrance of the methyl group (entry 21). In any event, the oxidative cyclization was not influenced by electron-donating and halo groups on the phenyl group.

We also compared the reactivity of a 2-oxocyclohexyl group to that of 2-oxocyclopentyl and 2-oxocycloheptyl groups. The oxidation of *N*-methyl-2-oxocyclopentanecarboxamide **1p** in boiling AcOH gave the desired spiroindolinone **2p** in a high yield as expected (Table 1, entry 24). Surprisingly, when a similar reaction was carried out in AcOH/HCO$_2$H (1:4 v/v) at room temperature, the oxidant was consumed in an extremely short reaction time and **2p** was obtained in a similar yield (entry 25). The reaction of other *N*-alkyl-2-oxocyclopentanecarboxamides **1q–t** also led to very good results, producing the corresponding spiroindolinones **2q–t** in excellent to quantitative yields (entries 26–29). On the other hand, the reaction of *N*-methyl-2-oxocycloheptanecarboxamide **1u** at room temperature needed a long reaction time (48 h) to consume the oxidant, affording the corresponding spiroindolinone **2u** in 76% yield (entry 30). However, the reaction in AcOH at reflux temperature was complete within 5 minutes to produce **2u** in 90% yield (entry 31). The reactions of other substituted 2-oxocycloheptanecarboxamides **1v–y** were also carried out in boiling AcOH to give the desired spiroindolinones **2v–y** in high yields (entries 32–35). Accordingly, it was found that the trend in the reactivity decreased in the order: cyclopentanecarboxamides > cyclohexanecarboxamides > cycloheptanecarboxamides based on the reaction conditions described above.

Finally, in order to investigate the synthetic applications, 1′-methylspiro[cyclohexane-1,3′-indoline]-2,2′-dione (**2a**) was subjected to reduction, a Grignard reaction,[13] Baeyer–Villiger oxidation,[14] and to reactions with hydrazines (Scheme 2).[15] The spiroindolinone **2a** underwent reduction with NaBH$_4$ in EtOH to afford the corresponding alcohol **3**, of which the diastereomer **3′** (3:4 dr) could be isolated by chromatographic separation (eq. 1). The Grignard reaction with phenylmagnesium bromide followed by hydrolysis gave 2-hydroxy-1′-methyl-2-phenylspiro[cyclohexane-1,3′-indolin]-2′-one (**4**) in 85% yield (eq. 2). The Baeyer–Villiger oxidation/rearrangement occurred effectively using *m*-chloroperbenzoic acid (*m*CPBA) in the presence of NaHCO$_3$ to produce the corresponding spiro[indoline-3,2′-oxepane]-2,7′-dione **5** in 79% yield (eq. 3). The reactions with methylhydrazine, 4-nitrophenylhydrazine, and 2,4-dinitrophenylhydrazine were carried out in

MeOH/AcOH at 50 °C. The reactions proceeded smoothly and the corresponding hydrazones **6a–c** were obtained in very good yields (eq. 4).



Scheme 2 Several transformations of the spiroindolinone **2a**

In summary, we have demonstrated the facile synthesis of spiroindolinones **2a–y** and subsequent synthetic applications. That is, the oxidation of *N*-alkyl-2-oxo-*N*-phenylcyclohexane-1-carboxamides **1a–e** and *N*-alkyl-2-oxo-*N*-phenylcyclopentane-1-carboxamides **1p–t** proceeded in AcOH/HCO_2H at room temperature, producing the corresponding spiroindolinones **2a–e** and **2p–t** in yields ranging from 69% to quantitative. 2-Oxocyclohexane-1-carboxamides **1f–o**, having substituents on the phenyl group, and the *N*-aryl-2-oxocycloheptane-1-carboxamides **1u–y** underwent the oxidation in boiling AcOH, giving the desired spiroindolinones **2f–o** and **2u–y** in high yields. The synthetic and work-up procedures were very simple and the corresponding spiroindolinones were obtained in high to quantitative yields. In addition, spiroindolinone **2a** was easily transformed into the alcohols **3** and **4**, the ring-expanded lactone **5**, and the hydrazones **6a–c**. The obtained spiroindolinones can be used as convenient starting materials for the synthesis of natural products,[11] and we believe this methodology could be widely used by the chemistry community.

The anilines, 2-oxocycloalkane-1-carboxylates, and solvents were commercially available and used as received. Manganese(III) acetate dihydrate [$Mn(OAc)_3{\cdot}2H_2O$] was synthesized according to our modified method.[8] The *N*-alkyl-*N*-aryl-2-oxocycloalkane-1-carboxamides **1a–y** were prepared by the condensation of *N*-alkylanilines with ethyl 2-oxocycloalkane-1-carboxylates (see the Supporting Information). Melting points were recorded using a MP-J3 Yanagimoto micromelting point apparatus and are uncorrected. IR spectra were measured neat or in $CHCl_3$ using an IRAffinity-1S spectrophotometer with a MIRacle 10 ATR accessory and are expressed in cm^{-1}. NMR spectra were recorded using a JNM ECX 500 spectrometer at 500 MHz for ^1H and at 125 MHz for ^{13}C, with tetramethylsilane as the internal standard. The chemical shifts are reported as δ values (ppm) and the coupling constants in Hz. The following abbreviations are used for the multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. High-resolution mass spectra were recorded using a JEOL JMS-700 MStation and were obtained at the Instrumental Analysis Center, Kumamoto University, Kumamoto, Japan. Elemental analyses were obtained using a J-Science Lab JM10 instrument.

Oxidation of 2-Oxocycloalkane-1-carboxamides 1a–y; General Procedure

The general procedure for the oxidation of 2-oxocycloalkane-1-carboxamides **1a–f** and **1p–u** at room temperature was as follows. To cycloalkanecarboxamide **1** (0.3 mmol) dissolved in glacial AcOH (2 mL)/HCO_2H (8 mL) was added $Mn(OAc)_3{\cdot}2H_2O$ (0.75 mmol), and the resulting mixture was stirred at room temperature under an argon atmosphere until the brown-black color of the solution turned transparent pale yellow. After the Mn(III) oxidant was completely consumed (if needed, the presence of Mn(III) can be monitored using iodine–starch paper), the solvent was removed under reduced pressure. Following removal of the solvent, 2 M HCl (15 mL) was added to dissolve the solid residue and the obtained aqueous mixture was extracted with $CHCl_3$ (3 × 20 mL). The combined extracts were washed with a saturated aqueous solution of $NaHCO_3$ and H_2O, dried over anhydrous $MgSO_4$, then concentrated to dryness. The obtained residue was separated by silica gel column chromatography eluting with EtOAc/hexane (2:8 or 3:7 v/v) to give the desired spiro[cycloalkane-1,3′-indoline]-2,2′-diones **2a–f** and **2p–u** (see Table 1).

The oxidations of the 2-oxocycloalkane-1-carboxamides **1f–p** and **1u–y** at reflux temperature were as follows. To cycloalkanecarboxamide **1** (0.3 mmol) dissolved in glacial AcOH (10 mL) was added $Mn(OAc)_3{\cdot}2H_2O$ (0.75 mmol), and the mixture was quickly heated at reflux temperature using a pre-heated oil bath at 140 °C under an argon atmosphere until the brown color of Mn(III) turned transparent. After work-up as described above, the desired spiro[cycloalkane-1,3′-indoline]-2,2′-diones **2f–p** and **2u–y** were obtained (see Table 1). The solid products were further purified by recrystallization from appropriate solvents to prepare analytical samples. Specific details are given below.

1′-Methylspiro[cyclohexane-1,3′-indoline]-2,2′-dione (2a)[11a]

Yield: 97.8 mg (88%); colorless microcrystals (from EtOH/hexane); mp 97–99 °C (Lit.[16] 92–94 °C); R_f = 0.31 (EtOAc/hexane, 3:7).

IR ($CHCl_3$): 1690 (C=O) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.31–7.28 (m, 2 H, arom H), 7.09 (dt, *J* = 7.6, 1.0 Hz, 1 H, arom H), 6.84 (dd, *J* = 8.0, 0.8 Hz, 1 H, arom H), 3.18 (s, 3 H, =N-Me), 3.05 (ddd, *J* = 14.3, 10.4, 5.6 Hz, 1 H, *H*-CH), 2.59 (dt, *J* =

14.3, 5.6 Hz, 1 H, *H*-CH), 2.45–2.37 (m, 1 H, *H*-CH), 2.26–2.21 (m, 1 H, *H*-CH), 2.20–2.13 (m, 1 H, *H*-CH), 2.09 (ddd, *J* = 14.1, 10.3, 4.1 Hz, 1 H, *H*-CH), 2.02–1.94 (m, 1 H, *H*-CH), 1.89–1.82 (m, 1 H, *H*-CH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 204.9 (C=O), 174.0 (-N-C=O), 143.0 (C-7′a), 129.2 (C-3′a), 128.4, 124.3, 122.4, 108.2 (arom CH), 63.4 (C-1), 39.5, 37.0, 26.7 (CH_2), 26.2 (=N-Me), 20.1 (CH_2).

Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.20; H, 6.87; N, 6.09.

1′-Ethylspiro[cyclohexane-1,3′-indoline]-2,2′-dione (2b)

Yield: 101.5 mg (83%); colorless microcrystals (from EtOH/hexane); mp 64–66 °C; R_f = 0.31 (EtOAc/hexane, 3:7).

IR ($CHCl_3$): 1694 (C=O) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.31–7.27 (m, 2 H, arom H), 7.08 (t, *J* = 7.5 Hz, 1 H, arom H), 6.86 (d, *J* = 7.5 Hz, 1 H, arom H), 3.74 (q, *J* = 7.3 Hz, 2 H, -C*H*$_2$-CH$_3$), 3.06 (ddd, *J* = 16.5, 10.5, 6.0 Hz, 1 H, *H*-CH), 2.85 (dt, *J* = 14.0, 5.3 Hz, 1 H, *H*-CH), 2.49–2.39 (m, 1 H, *H*-CH), 2.25–2.21 (m, 1 H, *H*-CH), 2.19–2.17 (m, 1 H, *H*-CH), 2.11–2.15 (m, 1 H, *H*-CH), 2.02–1.93 (m, 1 H, *H*-CH), 1.89–1.82 (m, 1 H, *H*-CH), 1.24 (t, *J* = 7.25 Hz, 3 H, -CH$_2$-C*H*$_3$).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.1 (C=O), 173.7 (-N-C=O), 142.2 (C-7′a), 129.6 (C-3′a), 128.4, 124.6, 122.3, 108.4 (arom C), 63.4 (C-1), 39.6, 37.2 (CH_2), 34.8 (-*C*H$_2$-CH$_3$), 26.8, 20.2 (CH_2), 12.5 (-CH$_2$-*C*H$_3$).

FAB HRMS (acetone/NBA): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{18}NO_2$: 244.1338; found: 244.1331.

1′-Propylspiro[cyclohexane-1,3′-indoline]-2,2′-dione (2c)

Yield: 109.1 mg (90%); colorless microcrystals (from EtOH/hexane); mp 51–53 °C; R_f = 0.34 (EtOAc/hexane, 3:7).

IR ($CHCl_3$): 1694 (C=O) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.30–7.27 (m, 2 H, arom H), 7.08 (t, *J* = 7.8 Hz, 1 H, arom H), 6.85 (d, *J* = 8.5 Hz, 1 H, arom H), 3.66 (t, *J* = 7.3 Hz, 2 H, -C*H*$_2$-CH$_2$-CH$_3$), 3.06 (ddd, *J* = 16.0, 10.5, 5.5 Hz, 1 H, *H*-CH), 2.59 (dt, *J* = 13.5, 4.8 Hz, 1 H, *H*-CH), 2.46–2.38 (m, 1 H, *H*-CH), 2.26–2.16 (m, 2 H, CH_2), 2.12–2.07 (m, 1 H, *H*-CH), 2.02–1.94 (m, 1 H, *H*-CH), 1.88–1.84 (m, 1 H, *H*-CH), 1.73–1.69 (m, 2 H, -CH$_2$-C*H*$_2$-CH$_3$), 0.94 (t, *J* = 7.5 Hz, 3 H, -CH$_2$-CH$_2$-C*H*$_3$).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.1 (C=O), 174.2 (-N-C=O), 142.6 (C-7′a), 129.5 (C-3′a), 128.4, 124.6, 122.3, 108.6 (arom C), 63.4 (C-1), 41.6 (-*C*H$_2$-CH$_2$-CH$_3$), 39.6, 37.3, 26.7 (CH_2), 20.6 (-CH$_2$-*C*H$_2$-CH$_3$), 20.2 (CH_2), 11.2 (-CH$_2$-CH$_2$-*C*H$_3$).

FAB HRMS (acetone/NBA): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{20}NO_2$ 258.1494; found: 258.1489.

1′-Isopropylspiro[cyclohexane-1,3′-indoline]-2,2′-dione (2d)

Yield: 88.5 mg (69%); yellow oil; R_f = 0.28 (EtOAc/hexane, 3:7).

IR ($CHCl_3$): 1692 C=O) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.28–7.26 (m, 2 H, arom H), 7.07 (t, *J* = 7.8 Hz, 1 H, arom H), 7.01 (d, *J* = 8.5 Hz, 1 H, arom H), 4.60 (hept, *J* = 6.9 Hz, 1 H, -C*H*-(CH$_3$)$_2$), 3.11–3.05 (m, 1 H, *H*-CH), 2.60–2.55 (m, 1 H, *H*-CH), 2.47–2.40 (m, 1 H, *H*-CH), 2.22–2.17 (m, 2 H, CH_2), 2.11–2.05 (m, 1 H, *H*-CH), 1.99–1.92 (m, 1 H, *H*-CH), 1.86–1.82 (m, 1 H, *H*-CH), 1.47 (d, *J* = 7.0 Hz, 6 H, -CH-(C*H*$_3$)$_2$).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.2 (C=O), 173.8 (-N-C=O), 141.8 (C-7′a), 129.9 (C-3′a), 128.2, 124.7, 122.0, 109.9 (arom C), 63.2 (C-1), 43.9 (-*C*H-(CH$_3$)$_2$), 39.7, 37.5, 26.8, 20.2 (CH_2), 19.3 (-CH-(*C*H$_3$)$_2$).

FAB HRMS (acetone/NBA): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{20}NO_2$: 258.1494; found: 258.1489.

1′-Butylspiro[cyclohexane-1,3′-indoline]-2,2′-dione (2e)

Yield: 118.6 mg (87%); yellow oil; R_f = 0.28 (EtOAc/hexane, 3:7).

IR ($CHCl_3$): 1694 (C=O) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.31–7.27 (m, 2 H, arom H), 7.08 (t, *J* = 7.8 Hz, 1 H, arom H), 6.85 (d, *J* = 8.0 Hz, 1 H, arom H), 3.69 (t, *J* = 7.5 Hz, 2 H, -C*H*$_2$-CH$_2$-CH$_2$-CH$_3$), 3.09–3.03 (m, 1 H, *H*-CH), 2.61–2.56 (m, 1 H, *H*-CH), 2.46–2.39 (m, 1 H, *H*-CH), 2.24–2.17 (m, 2 H, CH_2), 2.12–2.07 (m, 1 H, *H*-CH), 2.02–1.95 (m, 1 H, *H*-CH), 1.88–1.84 (m, 1 H, *H*-CH), 1.64 (quint, *J* = 7.5 Hz, 2 H, -CH$_2$-C*H*$_2$-CH$_2$-CH$_3$), 1.36 (sext, *J* = 7.4 Hz, 2 H, -CH$_2$-CH$_2$-C*H*$_2$-CH$_3$), 0.94 (t, *J* = 7.5 Hz, 3 H, -CH$_2$-CH$_2$-CH$_2$-C*H*$_3$).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.1 (C=O), 174.1 (-N-C=O), 142.6 (C-7′a), 129.5 (C-3′a), 128.4, 124.6, 122.3, 108.6 (arom C), 63.4 (C-1), 39.8 (CH_2), 39.6 (-*C*H$_2$-CH$_2$-CH$_2$-CH$_3$), 37.3 (CH_2), 29.3 (-CH$_2$-*C*H$_2$-CH$_2$-CH$_3$), 26.8, 20.2 (CH_2), 19.9 (-CH$_2$-CH$_2$-*C*H$_2$-CH$_3$), 13.6 (-CH$_2$-CH$_2$-CH$_2$-*C*H$_3$).

FAB HRMS (acetone/NBA): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{22}NO_2$: 272.1651; found 272.1654.

1′,5′-Dimethylspiro[cyclohexane-1,3′-indoline]-2,2′-dione (2f)

Yield: 102.5 mg (84%); colorless microcrystals (from EtOH/hexane); mp 125–127 °C; R_f = 0.37 (EtOAc/hexane, 2:8).

IR ($CHCl_3$): 1690 (C=O) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.12–7.10 (m, 2 H, arom H), 6.73 (d, *J* = 8.0 Hz, 1 H, arom H), 3.18 (s, 3 H, =N-Me), 3.07 (ddd, *J* = 16.0, 11.0, 6.0 Hz, 1 H, *H*-CH), 2.59 (dt, *J* = 14.0, 5.0 Hz, 1 H, *H*-CH), 2.44–2.40 (m, 1 H, *H*-CH), 2.36 (s, 3 H, Me), 2.25–2.27 (m, 2 H, *H*-CH), 2.08 (ddd, *J* = 13.5, 10.5, 4.0 Hz, 1 H, *H*-CH), 2.01–1.93 (m, 1 H, *H*-CH), 1.89–1.82 (m, 1 H, *H*-CH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.3 (C=O), 174.1 (-N-C=O), 140.8 (C-7′a), 132.1 (C-5′), 129.4 (C-3′a), 128.9, 125.4, 108.1 (arom CH), 63.7 (C-1), 39.8, 37.3, 26.9 (CH_2), 26.4 (=N-Me), 21.2 (Me), 20.3 (CH_2).

FAB HRMS (acetone/NBA): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{18}NO_2$: 244.1338; found: 244.1321.

5′-Methoxy-1′-methylspiro[cyclohexane-1,3′-indoline]-2,2′-dione (2g)

Yield: 111.0 mg (86%); colorless microcrystals (from EtOH/hexane); mp 111–113 °C; R_f = 0.38 (EtOAc/hexane, 2:8).

IR ($CHCl_3$): 1684 (C=O) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.89 (d, *J* = 2.4 Hz, 1 H, arom H), 6.83 (dd, *J* = 8.5, 2.4 Hz, 1 H, arom H), 6.74 (d, *J* = 8.5 Hz, 1 H, arom H), 3.80 (s, 3 H, MeO), 3.17 (s, 3 H, =N-Me), 3.08 (ddd, *J* = 16.0, 11.0, 6.0 Hz, 1 H, *H*-CH), 2.57 (dt, *J* = 14.0, 5.0 Hz, 1 H, *H*-CH), 2.49–2.40 (m, 1 H, *H*-CH), 2.25–2.17 (m, 2 H, CH_2), 2.08 (ddd, *J* = 14.5, 11.0, 4.0 Hz, 1 H, *H*-CH), 2.01–1.92 (m, 1 H, *H*-CH), 1.87–1.81 (m, 1 H, *H*-CH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.1 (C=O), 173.8 (-N-C=O), 155.9 (C-5′), 136.7 (C-7′a), 130.6 (C-3′a), 112.6, 112.3, 108.6 (arom CH), 64.0 (C-1), 55.8 (MeO), 39.7, 37.5, 26.9 (CH_2), 26.5 (=N-Me), 20.3 (CH_2).

FAB HRMS (acetone/NBA): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{18}NO_3$: 260.1287; found: 260.1296.

5′-Chloro-1′-methylspiro[cyclohexane-1,3′-indoline]-2,2′-dione (2h)

Yield: 58.4 mg (75%); colorless microcrystals (from EtOH/hexane); mp 89–91 °C; R_f = 0.34 (EtOAc/hexane, 2:8).

IR ($CHCl_3$): 1694 (C=O) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.29 (dd, *J* = 8.3, 2.0 Hz, 1 H, arom H), 7.25 (d, *J* = 2.0 Hz, 1 H, arom H), 6.76 (d, *J* = 8.3 Hz, 1 H, arom H), 3.18 (s, 3 H, =N-Me), 3.10 (ddd, *J* = 16.5, 11.5, 6.0 Hz, 1 H, *H*-CH), 2.57 (dt, *J* = 14.0, 5.0 Hz, 1 H, *H*-CH), 2.50–2.42 (m, 1 H, *H*-CH), 2.25–2.19 (m, 2 H, CH_2), 2.08 (ddd, *J* = 15.0, 11.5, 4.0 Hz, 1 H, *H*-CH), 2.00–1.91 (m, 1 H, *H*-CH), 1.86–1.80 (m, 1 H, *H*-CH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 204.4 (C=O), 173.6 (-N-C=O), 141.7 (C-7′a), 130.9 (C-3′a), 128.5 (arom CH), 128.0 (C-5′), 125.2, 109.2 (arom CH), 63.7 (C-1), 39.6, 37.5, 26.9 (CH_2), 26.6 (=N-Me), 20.1 (CH_2).

FAB HRMS (acetone/NBA): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{15}ClNO_2$: 264.0791; found: 264.0784.

5′-Fluoro-1′-methylspiro[cyclohexane-1,3′-indoline]-2,2′-dione (2i)

Yield: 66.4 mg (90%); colorless microcrystals (from EtOH/hexane); mp 76–78 °C; R_f = 0.27 (EtOAc/hexane, 2:8).

IR ($CHCl_3$): 1697 (C=O) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.04–6.99 (m, 2 H, arom H), 6.77–6.75 (m, 1 H, arom H), 3.18 (s, 3 H, =N-Me), 3.12 (ddd, *J* = 17.0, 11.5, 5.5 Hz, 1 H, *H*-CH), 2.56 (dt, *J* = 13.5, 4.5 Hz, 1 H, *H*-CH), 2.52–2.43 (m, 1 H, *H*-CH), 2.25–2.19 (m, 2 H, CH_2), 2.08 (ddd, *J* = 15.5, 11.5, 4.0 Hz, 1 H, *H*-CH), 2.00–1.91 (m, 1 H, *H*-CH), 1.85–1.79 (m, 1 H, *H*-CH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 204.5 (C=O), 173.7 (-N-C=O), 159.0 (d, *J* = 239 Hz, C-5′), 139.0 (d, *J* = 3 Hz, C-7′a), 130.7 (d, *J* = 9 Hz, C-3′a), 114.7 (d, *J* = 23 Hz, C-6′), 112.8 (d, *J* = 23 Hz, C-4′), 108.6 (d, *J* = 9 Hz, C-7′), 63.8 (d, *J* = 1 Hz, C-1), 39.5, 37.5, 26.9 (CH_2), 26.5 (=N-Me), 20.0 (CH_2).

FAB HRMS (acetone/NBA): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{15}FNO_2$: 248.1087; found: 248.1091.

1′,7′-Dimethylspiro[cyclohexane-1,3′-indoline]-2,2′-dione (2j)

Yield: 117.0 mg (96%); colorless microcrystals (from EtOH/hexane); mp 128–130 °C; R_f = 0.33 (EtOAc/hexane, 2:8).

IR ($CHCl_3$): 1684 (C=O) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.09 (d, *J* = 7.2 Hz, 1 H, arom H), 7.03 (d, *J* = 7.6 Hz, 1 H, arom H), 6.99 (t, *J* = 7.6 Hz, 1 H, arom H), 3.47 (s, 3 H, =N-Me), 3.08 (ddd, *J* = 16.5, 11.5, 5.5 Hz, 1 H, *H*-CH), 2.59–2.57 (m, 1 H, *H*-CH), 2.56 (s, 3 H, Me), 2.48–2.41 (m, 1 H, *H*-CH), 2.21–2.18 (m, 2 H, CH_2), 2.07 (ddd, *J* = 14.0, 10.5, 4.0 Hz, 1 H, *H*-CH), 1.99–1.90 (m, 1 H, *H*-CH), 1.86–1.81 (m, 1 H, *H*-CH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.4 (C=O), 174.8 (-N-C=O), 140.9 (C-7′a), 132.3 (arom CH), 130.0 (C-3′a), 122.5 (2 C, arom CH), 119.9 (C-7′), 63.0 (C-1), 39.7, 37.7 (CH_2), 29.8 (=N-Me), 26.9, 20.3 (CH_2), 19.1 (Me).

FAB HRMS (acetone/NBA): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{18}NO_2$: 244.1338; found: 244.1326.

7′-Methoxy-1′-methylspiro[cyclohexane-1,3′-indoline]-2,2′-dione (2k)

Yield: 68.7 mg (88%); colorless microcrystals (from EtOH/hexane); mp 94–96 °C; R_f = 0.33 (EtOAc/hexane, 2:8).

IR ($CHCl_3$): 1684 (C=O) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.04 (t, *J* = 7.9 Hz, 1 H, arom H), 6.88 (s, 1 H, arom H), 6.88 (d, *J* = 8.0 Hz, 1 H, arom H), 3.84 (s, 3 H, MeO), 3.46 (s, 3 H, =N-Me), 3.10 (ddd, *J* = 16.5, 11.0, 6.0 Hz, 1 H, *H*-CH), 2.56 (dt, *J* = 13.5, 4.8 Hz, 1 H, *H*-CH), 2.50–2.41 (m, 1 H, *H*-CH), 2.23–2.19 (m, 2 H, CH_2), 2.07 (ddd, *J* = 14.0, 10.0, 4.0 Hz, 1 H, *H*-CH), 1.98–1.89 (m, 1 H, *H*-CH), 1.85–1.80 (m, 1 H, *H*-CH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.4 (C=O), 174.2 (-N-C=O), 145.3 (C-7′a), 131.1 (C-3′a), 130.9 (C-7′), 123.1, 117.2, 112.4 (arom CH), 63.6 (C-1), 55.9 (MeO), 39.6, 37.6 (CH_2), 29.7 (=N-Me), 26.8, 20.1 (CH_2).

FAB HRMS (acetone/NBA): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{18}NO_3$: 260.1287; found: 260.1277.

7′-Chloro-1′-methylspiro[cyclohexane-1,3′-indoline]-2,2′-dione (2l)

Yield: 72.8 mg (93%); yellow oil; R_f = 0.35 (EtOAc/hexane, 2:8).

IR (neat): 1699 (C=O) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.23 (dd, *J* = 8.2, 1.1 Hz, 1 H, arom H), 7.12 (dd, *J* = 7.4, 1.1 Hz, 1 H, arom H), 7.01 (t, *J* = 7.5 Hz, 1 H, arom H), 3.56 (s, 3 H, =N-Me), 3.13 (ddd, *J* = 18.0, 12.5, 6.0 Hz, 1 H, *H*-CH), 2.55 (dt, *J* = 13.5, 4.3 Hz, 1 H, *H*-CH), 2.52–2.45 (m, 1 H, *H*-CH), 2.25–2.18 (m, 2 H, CH_2), 2.08 (ddd, *J* = 15.5, 11.5, 4.0 Hz, 1 H, *H*-CH), 1.97–1.88 (m, 1 H, *H*-CH), 1.84–1.78 (m, 1 H, *H*-CH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 204.5 (C=O), 174.1 (-N-C=O), 139.0 (C-7′a), 131.9 (C-3′a), 130.8, 123.4, 123.2 (arom CH), 115.5 (C-7′), 63.2 (C-1), 39.5, 37.9 (CH_2), 29.8 (=N-Me), 26.9, 20.0 (CH_2).

FAB HRMS (acetone/NBA): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{15}ClNO_2$: 264.0791; found: 264.0777.

1′,6′-Dimethylspiro[cyclohexane-1,3′-indoline]-2,2′-dione (2m)

Yield: 45.0 mg (61%); colorless microcrystals (from EtOH/hexane); mp 168–170 °C; R_f = (EtOAc/hexane, 2:8).

IR (neat): 1688 (C=O) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.18 (d, *J* = 7.5 Hz, 1 H, arom H), 6.91 (d, *J* = 7.5 Hz, 1 H, arom H), 6.67 (s, 1 H, arom H), 3.17 (s, 3 H, =N-Me), 3.02 (ddd, *J* = 15.5, 9.5, 5.0 Hz, 1 H, *H*-CH), 2.59 (dt, *J* = 13.5, 5.3 Hz, 1 H, *H*-CH), 2.44–2.34 (m, 1 H, *H*-CH), 2.38 (s, 3 H, Me), 2.26–2.21 (m, 1 H, *H*-CH), 2.19–2.15 (m, 1 H, *H*-CH), 2.07 (ddd, *J* = 13.5, 9.5, 3.5 Hz, 1 H, *H*-CH), 2.02–1.94 (m, 1 H, *H*-CH), 1.89–1.83 (m, 1 H, *H*-CH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.3 (C=O), 174.5 (-N-C=O), 143.2 (C-7′a), 138.8 (C-6′), 126.4 (C-3′a), 124.2, 123.1, 109.3 (arom C), 63.4 (C-1), 39.6, 37.1, 26.8 (CH_2), 26.3 (=N-Me), 21.7 (Me), 20.3 (CH_2).

FAB HRMS (acetone/NBA): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{18}NO_2$: 244.1338; found: 244.1320.

1′,4′-Dimethylspiro[cyclohexane-1,3′-indoline]-2,2′-dione (2m′)

Yield: 22.6 mg (31%); colorless microcrystals (from EtOH/hexane); mp 81–83 °C; R_f = (EtOAc/hexane, 2:8).

IR (neat): 1695 (C=O) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.21 (t, *J* = 8.0 Hz, 1 H, arom H), 6.90 (d, *J* = 8.0 Hz, 1 H, arom H), 6.67 (d, *J* = 8.0 Hz, 1 H, arom H), 3.20–3.13 (m, 1 H, *H*-CH), 3.16 (s, 3 H, =N-Me), 2.64–2.55 (m, 2 H, CH_2), 2.40 (dt, *J* = 14.0, 4.0 Hz, 1 H, *H*-CH), 2.28–2.23 (m, 1 H, *H*-CH), 2.22 (s, 3 H, Me), 2.05 (d, *J* = 14.0 Hz, 1 H, *H*-CH), 1.89–1.82 (m, 1 H, *H*-CH), 1.79–1.76 (m, 1 H, *H*-CH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 204.5 (C=O), 173.6 (-N-C=O), 143.3 (C-7′a), 135.0 (C-4′), 128.5 (arom C), 127.7 (C-3′a), 125.4, 105.9 (arom C), 63.5 (C-1), 40.3, 34.8 (CH_2), 26.5 (=N-Me), 26.3, 20.0 (CH_2), 19.2 (Me).

FAB HRMS (acetone/NBA): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{18}NO_2$: 244.1338; found: 244.1333.

1′,6′,7′-Trimethylspiro[cyclohexane-1,3′-indoline]-2,2′-dione (2n)

Yield: 74.2 mg (95%); colorless microcrystals (from EtOH/hexane); mp 132–134 °C; R_f = 0.37 (EtOAc/hexane, 2:8).

IR ($CHCl_3$): 1684 (C=O) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.99 (d, *J* = 7.5 Hz, 1 H, arom H), 6.92 (d, *J* = 7.5 Hz, 1 H, arom H), 3.49 (s, 3 H, =N-Me), 3.07 (ddd, *J* = 16.5, 11.0, 5.5 Hz, 1 H, *H*-CH), 2.56 (dt, *J* = 14.5, 5.0 Hz, 1 H, *H*-CH), 2.47 (s, 3 H, Me-C-7′), 2.45–2.38 (m, 1 H, *H*-CH), 2.30 (s, 3 H, Me-C-6′), 2.21–2.17 (m, 2 H, CH_2), 2.11–2.02 (m, 1 H, *H*-CH), 1.98–1.89 (m, 1 H, *H*-CH), 1.86–1.79 (m, 1 H, *H*-CH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.5 (C=O), 175.2 (-N-C=O), 141.2 (C-7′a), 138.4 (C-6′), 127.9 (C-3′a), 124.2, 121.7 (arom C), 119.1 (C-7′), 62.7 (C-1), 39.6, 37.6 (CH_2), 30.6 (=N-Me), 26.8 (CH_2), 20.8 (*Me*-C-7′a), 20.3 (CH_2), 14.1 (*Me*-C-6′a).

FAB HRMS (acetone/NBA): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{20}NO_2$: 258.1494; found: 258.1505.

1′,4′,6′-Trimethylspiro[cyclohexane-1,3′-indoline]-2,2′-dione (2o)

Yield: 68.4 mg (88%); colorless microcrystals (from EtOH/hexane); mp 164–166 °C; R_f = 0.31 (EtOAc/hexane, 1:9).

IR ($CHCl_3$): 1686 (C=O) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.72 (s, 1 H, arom H), 6.49 (s, 1 H, arom H), 3.19–3.15 (m, 1 H, *H*-CH), 3.13 (s, 3 H, =N-Me), 2.64–2.54 (m, 2 H, CH_2), 2.38 (dt, *J* = 13.8, 4.5 Hz, 1 H, *H*-CH), 2.33 (s, 3 H, Me-C-6′), 2.27–2.22 (m, 1 H, *H*-CH), 2.17 (s, 3 H, Me-C-4′), 2.05–2.01 (m, 1 H, *H*-CH), 1.87–1.79 (m, 1 H, *H*-CH), 1.78–1.74 (m, 1 H, *H*-CH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 204.6 (C=O), 173.8 (-N-C=O), 143.4 (C-7′a), 138.6 (C-6′), 134.6 (C-4′), 125.9 (arom C), 124.7 (C-3′a), 125.9 (arom C), 63.3 (C-1), 40.3, 34.8, 26.4 (CH_2), 26.3 (=N-Me), 21.5 (*Me*-C-6′), 20.0 (CH_2), 19.0 (*Me*-C-4′).

FAB HRMS (acetone/NBA): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{19}NO_2Na$: 280.1313; found: 280.1315.

1′-Methylspiro[cyclopentane-1,3′-indoline]-2,2′-dione (2p)

Yield: 54.4 mg (84%); colorless microcrystals (from EtOH/hexane); mp 123–125 °C; R_f = 0.28 (EtOAc/hexane, 2:8).

IR (neat): 1742 (-C=O), 1694 (-N-C=O) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.21 (dd, *J* = 15.5, 8.0 Hz, 1 H, arom H), 7.02–6.95 (m, 2 H, arom H), 6.77 (d, *J* = 7.5 Hz, 1 H, arom H), 3.12 (s, 3 H, =N-Me), 2.62–2.52 (m, 2 H, CH_2), 2.49–2.39 (m, 2 H, CH_2), 2.29 (dt, *J* = 13.0, 7.5 Hz, 1 H, *H*-CH), 2.17–2.12 (m, 1 H, *H*-CH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 212.7 (C=O), 175.0 (-N-C=O), 144.2 (C-7′a), 130.2 (C-3′a), 128.6, 122.8, 122.3, 108.4 (arom C), 62.8 (C-1), 38.2, 34.0 (CH_2), 26.4 (=N-Me), 20.1 (CH_2).

FAB HRMS (acetone/NBA): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{14}NO_2$: 216.1025; found: 216.1005.

1′-Ethylspiro[cyclopentane-1,3′-indoline]-2,2′-dione (2q)

Yield: 69.9 mg (quant.); colorless microcrystals (from EtOH/hexane); mp 72–74 °C; R_f = 0.28 (EtOAc/hexane, 2:8).

IR (neat): 1747 (-C=O), 1695 (-N-C=O) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.28 (t, *J* = 7.0 Hz, 1 H, arom H), 7.09 (d, *J* = 7.0 Hz, 1 H, arom H), 7.03 (t, *J* = 7.5 Hz, 1 H, arom H), 6.87 (d, 1 H, *J* = 8.0 Hz, arom H), 3.74 (q, *J* = 7.3 Hz, 2 H, -*CH*$_2$-CH$_3$), 2.70–2.59 (m, 2 H, CH_2), 2.55–2.46 (m, 2 H, CH_2), 2.36 (dt, *J* = 14.0, 7.0 Hz, 1 H, *H*-CH), 2.26–2.17 (m, 1 H, *H*-CH), 1.26 (t, *J* = 7.3 Hz, 3 H, -CH$_2$-*CH*$_3$).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 212.6 (C=O), 174.6 (-N-C=O), 143.4 (C-7′a), 130.5 (C-3′a), 128.5, 122.6, 122.5, 108.5 (arom C), 62.8 (C-1), 38.2 (CH_2), 34.9 (-*CH*$_2$-CH$_3$), 34.0, 20.1 (CH_2), 12.5 (-CH$_2$-*CH*$_3$).

FAB HRMS (acetone/NBA): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{16}NO_2$: 230.1181; found: 230.1185.

1′-Propylspiro[cyclopentane-1,3′-indoline]-2,2′-dione (2r)

Yield: 76.0 mg (quant.); colorless microcrystals (from EtOH/hexane); mp 69–71 °C; R_f = 0.32 (EtOAc/hexane, 2:8).

IR (neat): 1748 (-C=O), 1695 (-N-C=O) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.27 (t, *J* = 4.0 Hz, 1 H, arom H), 7.08 (d, *J* = 7.5 Hz, 1 H, arom H), 7.03 (t, *J* = 7.8 Hz, 1 H, arom H), 6.86 (d, *J* = 8.0 Hz, 1 H, arom H), 3.72–3.60 (m, 2 H, -*CH*$_2$-CH$_2$-CH$_3$), 2.70–2.60 (m, 2 H, CH_2), 2.55–2.47 (m, 2 H, CH_2), 2.36 (dt, *J* = 13.0, 7.0 Hz, 1 H, *H*-CH), 2.25–2.19 (m, 1 H, *H*-CH), 1.74–1.69 (m, 2 H, -CH$_2$-*CH*$_2$-CH$_3$), 0.95 (t, *J* = 7.3 Hz, 3 H, -N-CH$_2$-CH$_2$-*CH*$_3$).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 212.7 (C=O), 175.1 (-N-C=O), 143.8 (C-7′a), 130.5 (C-3′a), 128.5, 122.54, 122.49, 108.6 (arom C), 62.8 (C-1), 41.6 (-*CH*$_2$-CH$_2$-CH$_3$), 38.2, 34.0 (CH_2), 20.6 (-CH$_2$-*CH*$_2$-CH$_3$), 20.1 (CH_2), 11.1 (-CH$_2$-CH$_2$-*CH*$_3$).

FAB HRMS (acetone/NBA): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{18}NO_2$: 244.1338; found: 244.1322.

1′-Isopropylspiro[cyclopentane-1,3′-indoline]-2,2′-dione (2s)

Yield: 71.1 mg (98%); colorless microcrystals (from EtOH/hexane); mp 61–63 °C; R_f = 0.36 (EtOAc/hexane, 2:8).

IR (neat): 1749 (-C=O), 1694 (-N-C=O) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.26 (t, *J* = 7.8 Hz, 1 H, arom H), 7.08 (d, *J* = 6.0 Hz, 1 H, arom H), 7.03–7.00 (m, 2 H, arom H), 4.56 (hept, *J* = 7.3 Hz, 1 H, -*CH*-(CH$_3$)$_2$), 2.69–2.59 (m, 2 H, CH_2), 2.54–2.46 (m, 2 H, CH_2), 2.35 (dt, *J* = 14.0, 7.0 Hz, 1 H, *H*-CH), 2.24–2.16 (m, 1 H, *H*-CH), 1.48 (d, *J* = 7.3, 6 H, -CH-(CH$_3$)$_2$).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 212.6 (C=O), 174.8 (-N-C=O), 143.1 (C-7′a), 130.8 (C-3′a), 128.3, 122.6, 122.2, 109.9 (arom C), 62.7 (C-1), 41.2 (-*CH*-(CH$_3$)$_2$), 38.2, 34.0, 20.1 (CH_2), 19.4, 19.2 (-CH-(*CH*$_3$)$_2$).

FAB HRMS (acetone/NBA): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{18}NO_2$: 244.1338; found: 244.1326.

1′-Butylspiro[cyclopentane-1,3′-indoline]-2,2′-dione (2t)

Yield: 75.0 mg (97%); colorless microcrystals (from EtOH/hexane); mp 42–44 °C; R_f = 0.37 (EtOAc/hexane, 2:8).

IR (neat): 1748 (-C=O), 1697 (-N-C=O) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.28 (t, *J* = 7.8 Hz, 1 H, arom H), 7.08 (d, *J* = 7.5 Hz, 1 H, arom H), 7.03 (t, *J* = 7.8 Hz, 1 H, arom H), 6.87 (d, *J* = 8.0 Hz, 1 H, arom H), 3.75–3.63 (m, 2 H, -*CH*$_2$-CH$_2$-CH$_2$-CH$_3$), 2.69–2.60 (m, 2 H, CH_2), 2.55–2.47 (m, 2 H, CH_2), 2.36 (dt, *J* = 13.5, 7.0 Hz, 1 H, *H*-CH), 2.25–2.18 (m, 1 H, *H*-CH), 1.70–1.62 (m, 2 H, -CH$_2$-*CH*$_2$-CH$_2$-CH$_3$), 1.42–1.34 (m, 2 H, -CH$_2$-CH$_2$-*CH*$_2$-CH$_3$), 0.94 (t, *J* = 7.5 Hz, 3 H, -CH$_2$-CH$_2$-CH$_2$-*CH*$_3$).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 212.7 (C=O), 175.0 (-N-C=O), 143.7 (C-7′a), 130.5 (C-3′a), 128.5, 122.52, 122.47, 108.6 (arom C), 62.8 (C-1), 39.8 (-*CH*$_2$-CH$_2$-CH$_2$-CH$_3$), 38.2, 34.0 (CH_2), 29.3 (-CH$_2$-*CH*$_2$-CH$_2$-CH$_3$), 20.1 (CH_2), 19.9 (-CH$_2$-CH$_2$-*CH*$_2$-CH$_3$), 13.6 (-CH$_2$-CH$_2$-CH$_2$-*CH*$_3$).

FAB HRMS (acetone/NBA): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{20}NO_2$: 258.1494; found: 258.1474.

1′-Methylspiro[cycloheptane-1,3′-indoline]-2,2′-dione (2u)

Yield: 65.6 mg (90%); colorless microcrystals (from EtOH/hexane); mp 113–115 °C (Lit.[16] 104–107 °C); R_f = 0.32 (EtOAc/hexane, 2:8).

IR (neat): 1709 (-C=O), 1683 (-N-C=O) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.30 (t, *J* = 7.8 Hz, 1 H, arom H), 7.26 (d, *J* = 7.5 Hz, 1 H, arom H), 7.07 (t, *J* = 7.3 Hz, 1 H, arom H), 6.85 (d, *J* = 8.0 Hz, 1 H, arom H), 3.19 (s, 3 H, =N-Me), 3.06 (t, *J* = 10.5 Hz, 1 H, *H*-CH), 2.73 (t, *J* = 9.3 Hz, 1 H, *H*-CH), 2.32 (dd, *J* = 14.0, 9.0 Hz, 1 H, *H*-CH), 2.16–2.12 (m, 1 H, *H*-CH), 2.02 (dd, *J* = 14.5, 9.5 Hz, 1 H, *H*-CH), 1.92–1.87 (m, 1 H, *H*-CH), 1.83–1.78 (m, 4 H, -CH_2-CH_2).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 207.4 (C=O), 175.1 (-N-C=O), 143.3 (C-7′a), 130.6 (C-3′a), 128.5, 123.4, 122.5, 108.4 (arom C), 65.3 (C-1), 42.1, 34.6, 30.7, 26.6 (CH_2), 26.3 (=N-Me), 25.2 (CH_2).

1′,5′-Dimethylspiro[cycloheptane-1,3′-indoline]-2,2′-dione (2v)

Yield: 65.9 mg (86%); colorless microcrystals (from EtOH/hexane); mp 112–114 °C; R_f = 0.24 (EtOAc/hexane, 2:8).

IR (neat): 1707 (-C=O), 1690 (-N-C=O) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.10 (d, *J* = 7.5 Hz, 1 H, arom H), 7.08 (s, 1 H, arom H), 6.73 (d, *J* = 8.0 Hz, 1 H, arom H), 3.17 (s, 3 H, =N-Me), 3.07 (t, *J* = 10.8 Hz, 1 H, *H*-CH), 2.72 (t, *J* = 9.8 Hz, 1 H, *H*-CH), 2.35 (s, 3 H, Me), 2.32–2.23 (m, 1 H, *H*-CH), 2.17–2.12 (m, 1 H, *H*-CH), 2.04–1.98 (m, 1 H, *H*-CH), 1.93–1.88 (m, 1 H, *H*-CH), 1.84–1.77 (m, 4 H, -CH_2-CH_2).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 207.6 (C=O), 175.1 (-N-C=O), 140.9 (C-7′a), 132.1 (C-3′a), 130.7 (C-5′), 128.8, 124.3, 108.1 (arom C), 65.5 (C-1), 42.2, 34.7, 30.8, 26.6 (CH_2), 26.4 (=N-Me), 25.3 (CH_2), 21.1 (Me).

FAB HRMS (acetone/NBA): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{20}NO_2$: 258.1494; found: 258.1487.

5′-Chloro-1′-methylspiro[cycloheptane-1,3′-indoline]-2,2′-dione (2w)

Yield: 64.9 mg (78%); colorless microcrystals (from EtOH/hexane); mp 125–127 °C; R_f = 0.31 (EtOAc/hexane, 2:8).

IR (neat): 1713 (-C=O), 1688 (-N-C=O) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.27 (d, *J* = 8.0 Hz, 1 H, arom H), 7.24 (s, 1 H, arom H), 6.77 (d, *J* = 8.0 Hz, 1 H, arom H), 3.18 (s, 3 H, =N-Me), 3.12 (t, *J* = 10.8 Hz, 1 H, *H*-CH), 2.67 (t, *J* = 9.3 Hz, 1 H, *H*-CH), 2.33 (dd, *J* = 14.5, 10.0 Hz, 1 H, *H*-CH), 2.18–2.12 (m, 1 H, *H*-CH), 2.00 (dd, *J* = 15.0, 9.0 Hz, 1 H, *H*-CH), 1.96–1.90 (m, 1 H, *H*-CH), 1.86–1.72 (m, 4 H, -CH_2-CH_2).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 206.7 (C=O), 174.4 (-N-C=O), 141.9 (C-7′a), 132.3 (C-3′a), 128.4 (arom C), 127.9 (C-5′), 124.2, 109.3 (arom C), 65.6 (C-1), 42.1, 34.7, 30.7, 26.6 (CH_2), 26.5 (=N-Me), 25.3 (CH_2).Cl

FAB HRMS (acetone/NBA): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{17}ClNO_2$: 278.0948; found: 278.0940.

1′,7′-Dimethylspiro[cycloheptane-1,3′-indoline]-2,2′-dione (2x)

Yield: 71.8 mg (93%); colorless microcrystals (from EtOH/hexane); mp 119–121 °C; R_f = 0.32 (EtOAc/hexane, 2:8).

IR (neat): 1713 (-C=O), 1686 (-N-C=O) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.10 (d, *J* = 7.0 Hz, 1 H, arom H), 7.02 (d, *J* = 8.0 Hz, 1 H, arom H), 6.94 (t, *J* = 7.5 Hz, 1 H, arom H), 3.48 (s, 3 H, =N-Me), 3.02 (t, *J* = 10.3 Hz, 1 H, *H*-CH), 2.73 (t, *J* = 10.3 Hz, 1 H, *H*-CH), 2.55 (s, 3 H, Me), 2.28 (dd, *J* = 14.5, 9.0 Hz, 1 H, *H*-CH), 2.18–2.12 (m, 1 H, *H*-CH), 2.00 (dd, *J* = 14.5, 9.5 Hz, 1 H, *H*-CH), 1.88–1.76 (m, 5 H, *H*-CH-CH_2-CH_2).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 207.6 (C=O), 176.0 (-N-C=O), 141.1 (C-7′a), 132.3 (arom C), 131.1 (C-3′a), 122.4, 121.2 (arom C), 120.0 (C-7′), 64.7 (C-1), 42.3, 35.0, 30.8 (CH_2), 29.7 (=N-Me), 26.6, 25.2 (CH_2), 19.0 (Me).

FAB HRMS (acetone/NBA): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{20}NO_2$: 258.1494; found: 258.1473.

7′-Chloro-1′-methylspiro[cycloheptane-1,3′-indoline]-2,2′-dione (2y)

Yield: 62.4 mg (74%); colorless microcrystals (from EtOH/hexane); mp 116–118 °C; R_f = 0.43 (EtOAc/hexane, 2:8).

IR (neat): 1726 (-C=O), 1688 (-N-C=O) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.22 (t, *J* = 8.0 Hz, 1 H, arom H), 7.13 (d, *J* = 7.0 Hz, 1 H, arom H), 6.98 (t, *J* = 8.0 Hz, 1 H, arom H), 3.56 (s, 3 H, =N-Me), 3.09 (t, *J* = 10.5 Hz, 1 H, *H*-CH), 2.69 (t, *J* = 10.0 Hz, 1 H, *H*-CH), 2.31 (dd, *J* = 14.5, 9.5 Hz, 1 H, *H*-CH), 2.17–2.11 (m, 1 H, *H*-CH), 2.00 (dd, *J* = 15.0, 9.0 Hz, 1 H, *H*-CH), 1.93–1.88 (m, 1 H, *H*-CH), 1.84–1.74 (m, 4 H, -CH_2-CH_2).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 206.8 (C=O), 175.2 (-N-C=O), 139.2 (C-7′a), 133.3 (C-3′a), 130.8, 123.3, 122.1 (arom C), 115.7 (C-7′), 65.0 (C-1), 42.1, 35.0, 30.7 (CH_2), 29.8 (=N-Me), 26.6, 25.2 (CH_2).

FAB HRMS (acetone/NBA): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{17}ClNO_2$: 278.0948; found: 278.0939.

2-Hydroxy-1′-methylspiro[cyclohexane-1,3′-indoline]-2′-one (3) and (3′)

The spiroindolinone **2a** (69 mg, 0.3 mmol) and $NaBH_4$ (14 mg, 0.3 mmol) were dissolved in EtOH (5 mL) and the mixture was stirred at room temperature for 10 min. After removal of the solvent, H_2O (10 mL) was added and the aqueous mixture was extracted with $CHCl_3$ (3 × 10 mL). The combined extracts were washed with a saturated aqueous solution of $NaHCO_3$ and H_2O, dried over anhydrous $MgSO_4$, then concentrated to dryness. The obtained residue was separated by silica gel column chromatography eluting with EtOAc/hexane (1:1 v/v), affording the corresponding alcohol **3** and the diastereomer **3′**.

Compound 3

Yield: 21.0 mg (31%); colorless microcrystals (from EtOH/hexane); mp 145–146 °C; R_f = 0.31 (EtOAc/hexane, 5:5).

IR (neat): 3435 (OH), 1690 (-C=O) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.36 (d, *J* = 7.0 Hz, 1 H, arom H), 7.32–7.29 (t, *J* = 7.8 Hz, 1 H, arom H), 7.09 (t, *J* = 6.5 Hz, 1 H, arom H), 6.86 (d, *J* = 8.0 Hz, 1 H, arom H), 3.85–3.84 (m, 1 H, *H*-C-OH), 3.21 (s, 3 H, =N-Me), 2.78 (s, 1 H, -OH), 2.24–2.17 (m, 1 H, *H*-CH), 2.02–1.96 (m, 3 H, *H*-CH/CH_2), 1.93–1.87 (m, 1 H, *H*-CH), 1.69–1.62 (m, 1 H, *H*-CH), 1.60–1.50 (m, 2 H, *H*-CH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 179.1 (-N-C=O), 143.7 (C-7′a), 132.4 (C-3′a), 128.1, 123.3, 122.3, 108.0 (arom C), 72.3 (C-2), 52.3 (C-1), 31.4, 28.5 (CH_2), 26.0 (=N-Me), 22.1, 20.0 (CH_2).

FAB HRMS (acetone/NBA): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{17}NO_2$: 231.1259; found: 231.1258.

Compound 3′

Yield: 27.8 mg (40%); colorless microcrystals (from EtOH/hexane); mp 153–156 °C; R_f = 0.19 (EtOAc/hexane, 5:5).

IR (neat): 3431 (-OH), 1682 (-C=O) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.57 (d, *J* = 7.0 Hz, 1 H, arom H), 7.34 (t, *J* = 7.8 Hz, 1 H, arom H), 7.07 (t, *J* = 8.0 Hz, 1 H, arom H), 6.89 (d, *J* = 8.0 Hz, 1 H, arom H), 4.07–4.05 (m, 1 H, *H*-C-OH), 3.23 (s, 3 H, =N-Me), 2.06–1.97 (m, 2 H, CH_2), 1.93–1.86 (m, 1 H, *H*-CH), 1.84–1.78 (m, 1 H, *H*-CH), 1.75–1.70 (m, 2 H, CH_2), 1.64–1.58 (m, 2 H, CH_2), 1.25 (s, 1 H, -OH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 179.5 (-N-C=O), 144.4 (C-7′a), 130.2 (C-3′a), 128.2, 125.4, 121.8, 108.2 (arom C), 73.1 (C-2), 54.9 (C-1), 32.7, 30.9 (CH_2), 26.4 (=N-Me), 24.0, 20.5 (CH_2).

FAB HRMS (acetone/NBA): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{17}NO_2$: 231.1259; found: 231.1259.

2-Hydroxy-1′-methyl-2-phenylspiro[cyclohexane-1,3′-indolin]-2′-one (4)

Bromobenzene (393 mg, 2.5 mmol) dissolved in dry Et_2O (2 mL) was added dropwise over 20 min to Mg turnings (61 mg, 2.5 mmol) in dry Et_2O (3 mL) in a 50 mL three-necked flask under an argon atmosphere, then the mixture was heated at 50 °C for 30 min. The spiroindolinone **2a** (112.4 mg, 0.5 mmol) in dry Et_2O (3 mL) was added dropwise over 30 min to the mixture, then the mixture was heated under reflux for 2 h. The reaction was quenched by adding crushed ice and the obtained aqueous solution was acidified with a saturated aqueous solution of NH_4Cl, then extracted with EtOAc (3 × 20 mL). The combined extracts were washed with a saturated aqueous solution of $NaHCO_3$ and H_2O, dried over anhydrous $MgSO_4$, then concentrated to dryness. The obtained residue was separated by silica gel column chromatography, eluting with EtOAc/hexane (2:8 v/v), to give the corresponding alcohol **4**.

Yield: 127.5 mg (85%); colorless microcrystals (from EtOH/hexane); mp 137–139 °C; R_f = 0.26 (EtOAc/hexane, 1:9).

IR (neat): 3350 (OH), 1672 (-C=O) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.83 (d, *J* = 7.5 Hz, 1 H, arom H), 7.20 (t, *J* =7.8 Hz, 1 H, arom H), 7.10 (t, *J* = 7.5 Hz, 1 H, arom H), 6.98–6.93 (m, 5 H, arom H), 6.54 (d, *J* = 7.5 Hz, 1 H, arom H), 6.00 (s, 1 H, -OH), 2.88 (s, 3 H, =N-Me), 2.60–2.52 (m, 2 H, CH_2), 2.34–2.24 (m, 1 H, *H*-CH), 2.06–1.96 (m, 1 H, *H*-CH), 1.90–1.82 (m, 3 H, CH_2/*H*-CH), 1.49–1.46 (m, 1 H, *H*-CH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 180.3 (-N-C=O), 143.7, 143.1, 131.6, 127.9 (arom C), 126.7 (2 C, arom C), 126.4, 125.7 (arom C), 125.5 (2 C, arom C), 122.1, 108.3 (arom C), 74.9 (C-2), 55.7 (C-1), 32.5, 29.8 (CH_2), 25.7 (=N-Me), 20.1, 19.9 (CH_2).

FAB HRMS (acetone/NBA): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{21}NO_2$: 307.1572; found: 307.1591.

1-Methylspiro[indoline-3,2′-oxepane]-2,7′-dione (5)

To the spiroindolinone **2a** (69 mg, 0.3 mmol) in CH_2Cl_2 (4 mL) were added *m*-chloroperbenzoic acid (106 mg, 0.6 mmol) and $NaHCO_3$ (50 mg, 0.6 mmol). The mixture was stirred at room temperature for 1.5 h and the reaction was quenched by adding brine. The organic layer was separated, dried over anhydrous $MgSO_4$, and concentrated to dryness. The obtained residue was separated by silica gel column chromatography, eluting with EtOAc/benzene (1:9 v/v), to give the corresponding lactone **5**.

Yield: 59.8 mg (79%); colorless microcrystals (from EtOH/hexane); mp 167–169 °C; R_f = 0.37 (EtOAc/benzene, 1:9).

IR (neat): 1714 (-C=O) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.37 (d, *J* = 7.5 Hz, 1 H, arom H), 7.32 (t, *J* = 7.8 Hz, 1 H, arom H), 7.09 (t, *J* = 7.5 Hz, 1 H, arom H), 6.81 (d, *J* = 8.0 Hz, 1 H, arom H), 3.86 (m, 1 H, *H*-CH), 3.18 (s, 3 H, =N-Me), 2.86 (dd, *J* = 15.0, 6.5 Hz, 1 H, *H*-CH), 2.36–2.30 (m, 1 H, *H*-CH), 2.29–2.21 (m, 1 H, *H*-CH), 2.15–2.11 (m, 1 H, *H*-CH), 2.00–1.97 (m, 1 H, *H*-CH), 1.88–1.85 (m, 1 H, *H*-CH), 1.76–1.68 (m, 1 H, *H*-CH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 174.8 (-N-C=O), 173.3 (-C=O), 141.6 (C-7′a), 130.7 (C-3′a), 130.0, 123.4, 123.2, 108.4 (arom C), 81.5 (C-1), 37.2, 36.7 (CH_2), 26.3 (=N-Me), 23.0, 22.9 (CH_2).

FAB HRMS (acetone/NBA): *m*/*z* [M]$^+$ calcd for $C_{14}H_{15}NO_3$: 245.1052; found: 245.1062.

1′-Methyl-2-(2-methylhydrazineylidene)spiro[cyclohexane-1,3′-indolin]-2′-one (6a); Typical Procedure

A mixture of the spiroindolinone **2a** (45.9 mg, 0.2 mmol) and methylhydrazine (18.4 mg, 0.4 mmol) was heated at 50 °C in MeOH/AcOH (1:1 v/v, 4 mL) for 10 min. After removal of the solvent, H_2O (10 mL) was added and the aqueous solution was extracted with $CHCl_3$ (3 × 10 mL). The combined extracts were washed with a saturated aqueous solution of $NaHCO_3$ and H_2O, dried over anhydrous $MgSO_4$, then concentrated to dryness. The obtained residue was separated by silica gel column chromatography, eluting with EtOAc/hexane (1:1 v/v), to give the corresponding methylhydrazone **6a**.

Yield: 54.0 mg (quant.); colorless microcrystals (from EtOH/hexane); mp 131–132 °C; R_f = 0.31 (EtOAc/hexane, 6:4).

IR (neat): 1664 (-N-C=O) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.23 (d, *J* = 7.5 Hz, 1 H, arom H), 7.18 (t, *J* = 7.5 Hz, 1 H, arom H), 6.81 (t, *J* = 7.5 Hz, 1 H, arom H), 6.53 (d, *J* = 8.0 Hz, 1 H, arom H), 4.21 (s, 1 H, =NN*H*-CH_3), 3.03 (s, 3 H, =N-CH_3), 2.82 (s, 3 H, =NNH-CH_3), 2.20–2.18 (m, 1 H, *H*-CH), 2.09–2.04 (m, 1 H, *H*-CH), 1.69–1.63 (m, 2 H, CH_2), 1.49–1.29 (m, 4 H, CH_2-CH_2).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 173.3 (-N-C=O), 141.6 (C-7′a), 130.7 (C-3′a), 130.0, 123.4, 123.2, 108.4 (arom C), 81.5 (C-1), 37.2, 36.7 (CH_2), 26.3 (=N-Me), 23.0, 22.9 (CH_2).

Anal. Calcd for $C_{15}H_{19}N_3O$: C, 70.01; H, 7.44; N, 16.33. Found: C, 69.91; H, 7.64; N, 16.20.

1′-Methyl-2-[2-(4-nitrophenyl)hydrazineylidene]spiro[cyclohexane-1,3′-indolin]-2′-one (6b)

The reaction of **2a** (68.6 mg, 0.3 mmol) with 4-nitrophenylhydrazine (91.9 mg, 0.6 mmol) gave 4-nitrophenylhydrazone **6b**.

Yield: 112.6 mg (97%); orange microcrystals (from EtOH/hexane); mp 214–217 °C; R_f = 0.23 (EtOAc/hexane, 3:7).

IR (neat): 1697 (-N-C=O) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.03 (d, *J* = 9.5 Hz, 2 H, arom H), 7.86 (s, 1 H, -N-H), 7.37–7.32 (m, 2 H, arom H), 7.13 (t, *J* = 8.0 Hz, 1 H, arom H), 6.89 (d, *J* = 7.5 Hz, 1 H, arom H), 6.76 (d, *J* = 9.0 Hz, 1 H, arom H), 3.24 (s, 3 H, =N-Me), 2.83–2.77 (m, 1 H, *H*-CH), 2.68–2.63 (m, 1 H, *H*-CH), 2.34–2.26 (m, 1 H, *H*-CH), 2.12–2.09 (m, 1 H, *H*-CH), 2.08–1.94 (m, 2 H, CH_2), 1.86–1.76 (m, 2 H, CH_2), 1.76–1.68 (m, 1 H, *H*-CH).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 177.1 (-N-C=O), 150.5 (C-6), 150.1 (arom C), 142.6 (C-7′a), 139.6 (arom C), 132.3 (C-3′a), 128.0 (arom C), 125.8 (2 C, arom C), 124.5, 122.2 (arom C), 111.5 (2 C, arom C), 108.4 (arom C), 55.8 (C-1), 35.8 (CH_2), 26.3 (=N-Me), 24.7, 23.2, 20.1 (CH_2).

FAB HRMS (MeOH-NBA-NaI): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{20}N_4NaO_3$: 387.1433; found 387.1489.

2-[2-(2,4-Dinitrophenyl)hydrazineylidene]-1′-methylspiro[cyclohexane-1,3′-indolin]-2′-one (6c)

The reaction of **2a** (45.5 mg, 0.2 mmol) with 2,4-dinitrophenylhydrazine (39.8 mg, 0.2 mmol) gave the desired 2,4-dinitrophenylhydrazone **6c**.

Yield: 70.3 mg (87%); orange microcrystals (from EtOH/hexane); mp 86–89 °C; R_f = 0.39 (EtOAc/hexane, 3:7).

IR (neat): 1699 (-N-C=O) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 11.16 (s, 1 H, -N-H), 9.04 (d, *J* = 2.5 Hz, 1 H, arom H), 8.17 (dd, *J* = 10.0, 3.0 Hz, 1 H, arom H), 7.44 (d, *J* = 9.5 Hz, 1 H, arom H), 7.39–7.35 (m, 2 H, arom H), 7.15 (t, *J* = 7.3 Hz, 1 H, arom H), 6.92 (d, *J* = 8.0 Hz, 1 H, arom H), 3.26 (s, 3 H, =N-Me), 3.03–2.97 (m, 1 H, *H*-CH), 2.77 (dt, *J* = 16.5, 5.5 Hz, 1 H, *H*-CH), 2.37–2.30 (m, 1 H, *H*-CH), 2.19–2.08 (m, 2 H, CH_2), 2.05–1.99 (m, 1 H, *H*-CH), 1.94–1.87 (m, 2 H, CH_2).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.1 (-N-C=O), 157.4 (C-6), 145.2 (arom C), 142.8 (C-7′a), 137.9 (arom C), 131.6 (C-3′a), 129.9, 129.2, 128.3, 124.4, 123.2, 122.3, 116.4, 108.5 (arom C), 56.1 (C-1), 36.0 (CH_2), 26.4 (=N-Me), 25.0, 24.6, 20.1 (CH_2).

FAB HRMS (MeOH-NBA-NaI): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{19}N_5NaO_5$: 432.1284; found 432.1278.

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Supporting Information

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