Regio- and stereoselective synthesis of spirooxindole 1’-nitro pyrrolizidines with five concurrent stereocenters under aqueous media and their bioprospection using the zebrafish (*Danio rerio*) embryo model

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ELECTRONIC SUPPORTING INFORMATION

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1. Reagents

Isatin: Was purchased from Aldrich and used as received.
L-Proline: Was purchased from Aldrich and used as received.
2,3,4-Trimethoxybenzaldehyde: Was purchased from Aldrich and used as received.
3,4-Dimethoxybenzaldehyde: Was purchased from Aldrich and used as received.
Piperonal (3,4-Methylenedioxybenzaldehyde): Was purchased from Merck and used as received.
Nitromethane: Was purchased from Merck and used as received.
Silica gel 60 (0.063-0.200 mm) 70-230 mesh: Was purchased from Merck and used as received.
Ethanolamine: Was purchased from Aldrich and used as received.
Methyl iodide: Was purchased from Merck and used as received.
Potassium carbonate: Was purchased from Aldrich and used as received.
Sulfuric acid: Was purchased from Merck and used as received.
Potassium nitrate: Was purchased from Aldrich and used as received.
Trichloroisocyanuric acid: Was purchased from Aldrich and used as received.
trans-4-Hydroxy-L-proline: Was purchased from Aldrich and used as received
Propylene carbonate: Was purchased from Aldrich and used as received.

2. Characterization data of all synthesized spirooxindoles 12a-12t.

1’-Nitro-2’-(3,4,5-trimethoxyphenyl)-1’,2’,5’,6’,7’,7a’-hexahydrospiro[indoline-3,3’-pyrrolizin]-2-one (12a): White solid (846 mg, 1.93 mmol, 77 % yield); Obtained as a mixture of two regioisomers (12a:12a’ = 64:36); Rf [hexane-EtOAc, 2:1] = 0.38; MP 128-130 °C; FT-IR (KBr disk, cm⁻¹): 3301 ν(NH), 2962 ν(=CHAr), 2869 ν(CH₃), 1727 ν(C=O), 1542 ν(C-NO₂), 1373 ν(C-NO₂), 1326 ν(C-N-C), 1249 ν(C-O-C); Spectroscopy NMR data for the major regioisomer 12a: ¹H NMR (400 MHz, CDCl₃), δ(ppm): 8.29 (1H, s, NH), 7.56 (1H, d, J = 7.8, 1.0 Hz, 4-H_Ar), 7.23 (1H, td, J = 7.8, 1.0 Hz, 6-H_Ar), 7.09 (1H, td, J = 7.6, 0.7 Hz, 5-H_Ar), 6.71 (1H, d, J = 7.6 Hz, 7-H_Ar), 6.26 (1H, t, J = 9.9 Hz, CH-NO₂), 6.25 (2H, s, 9’ and 13’-H_Ar), 4.85 (1H, dd, J = 16.9, 8.1 Hz, 7a’-H), 4.43 (1H, d, J = 10.4 Hz, 2’-H), 3.70 (3H, s, OCH₃), 3.59 (6H, s, 2xOCH₃), 3.26 (1H, td, J = 11.0, 5.5 Hz, 5’-H_eq), 2.89 (1H, t, J = 7.3 Hz, 5’-H_ax), 2.13 (1H, dt, J = 14.0, 7.9 Hz, 7’-H_eq), 2.03-1.95 (1H, m, 6’-H_eq), 1.86-1.78 (1H, m, 6’-H_ax), 1.50 (1H, ddt, J = 12.8, 11.1, 7.8 Hz, 7’-H_ax); ¹³C NMR (101 MHz, CDCl₃), δ(ppm): 178.2, 152.9 (2C), 142.3, 137.3, 130.2 (+), 128.0, 126.1 (+), 125.5, 122.3 (+), 110.7 (+), 105.0 (+, 2C), 91.4 (+), 75.3, 64.2 (+), 60.7 (+), 55.9 (+, 2C), 53.4 (+), 51.2 (-), 27.9 (-), 25.7 (-); HRMS (ESI+): m/z: calcd for C₂₃H₂₈N₃O₆ ([M+Na]⁺) 440,1816, found: 440,1820; calcd for C₂₃H₂₅N₃O₆Na ([M+Na]⁺) 462,1636, found: 462,1633.
**1'-Nitro-2'-(3,4-dimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (12b):** White solid (798 mg, 1.95 mmol, 78 % yield); Obtained as a mixture of two regioisomers (12b:12b' = 74:26); 

Rf [hexane-EtOAc, 2:1] = 0.42; 

MP 192-194 °C; 

FT -IR (KBr disk, cm⁻¹): 3286 ν(NH), 2962 ν(=CHAr), 2931 ν(OCH₃), 2869 ν(CH₂), 1727 ν(C=O), 1619 ν(C=CHAr), 1542 ν(C-N-C), 1394 ν(C-NO₂), 1265 ν(O-C); 

Spectroscopy NMR data for the major regioisomer 12b: 

1H NMR (400 MHz, CDCl₃), δ (ppm): 8.37 (1H, s, NH), 7.57 (1H, d, J = 7.5 Hz, 4-HAr), 7.24 (1H, td, J = 7.9, 0.9 Hz, 6-HAr), 7.10 (1H, td, J = 7.8, 0.6 Hz, 5-HAr), 6.72-6.68 (2H, m, 7 and 12'-HAr), 6.61 (1H, d, J = 8.4 Hz, 13'-HAr), 6.45 (1H, d, J = 1.9 Hz, 9'-HAr), 6.27 (1H, t, J = 10.0 Hz, CH-NO₂), 4.84 (1H, dd, J = 16.9, 8.0 Hz, 7a'-H), 4.45 (1H, d, J = 10.6 Hz, 2'-H), 3.72 (3H, s, OCH₃), 3.54 (3H, s, OCH₃), 3.27 (1H, ddd, J = 10.9, 8.7, 5.5 Hz, 5' -Heq), 2.89 (1H, t, J = 7.3 Hz, 5' -Hax), 2.18-2.09 (1H, m, 7' -Heq), 1.99 (1H, dd, J = 11.8, 6.2 Hz, 6' -Hax), 1.85-1.78 (1H, m, 6' -Hax), 1.50 (1H, tt, J = 12.9, 7.7 Hz, 7'-Hax); 

13C NMR (101 MHz, CDCl₃), δ (ppm): 178.5, 148.5, 148.5, 142.2, 130.1 (+), 126.2 (+), 125.5, 124.6, 122.4 (+), 120.0 (+), 111.1 (+), 110.9 (+), 110.6 (+), 91.3 (+), 75.3, 64.2 (+), 55.7 (+), 55.5 (+), 52.9 (+), 51.2 (-), 27.9 (-), 25.7 (-); COSY Correlation [δH/δH]: 7.57/7.10 [4-HAr/5-HAr], 7.24/6.72-6.68 [6-HAr/7-HAr], 7.24/7.10 [6-HAr/5-HAr], 6.72-6.68/6.45 [12'-HAr/9'-HAr], 6.72-6.68/6.61 [12'-HAr/13'-HAr], 6.27/4.45 [CH-NO₂/2'-H], 6.27/4.84 [CH-NO₂/7a'-H], 4.84/1.50 [7a'-H/7'-Hax], 4.84/2.18-2.09 [7a'-H/7'-Hax], 3.27/1.85-1.78 [5'-Heq/6'-Hax], 3.27/1.99 [5'-Heq/6'-Hax], 3.27/2.89 [5'-Heq/5'-Hax], 2.89/1.85-1.78 [5'-Hax/6'-Hax], 2.18-2.09/1.50 [7'-Hax/7'-Hax], 1.99/1.50 [6'-Heq/7'-Hax], 1.99/1.85-1.78 [6'-Heq/6'-Hax], 1.85-1.78/1.50 [6'-Hax/7'-Hax]. 

HSQC Correlation [δH/δC]: 8.37/75.3/125.5/142.2 [NH/C-3'/C-7a/C-3a], 7.57/75.3/130.1/142.2 [4-HAr/C-3'/C-5/C-3a], 7.24/62.6/142.2 [6-HAr/C-5/C-3a], 7.10/110.6/125.5 [5-HAr/C-12'/C-7a], 6.72-6.68/120.0 [7-HAr/C-7], 6.72-6.68/110.6 [12'-HAr/C-13'], 6.61/110.9 [13'-HAr/C-13'], 6.45/111.1 [9'-HAr/C-9'], 6.27/91.3 [CH-NO₂/C-1'], 4.84/64.2 [7a'-H/C-7a'], 4.45/52.9 [2'-H/C-2'], 3.72/55.7 [H-OCH₃/C-OCH₃], 3.54/55.2 [H-OCH₃/C-OCH₃], 3.27/51.2 [5'-Heq/C-5''], 2.89/51.2 [5'-Hax/C-5''], 2.18-2.09/27.9 [7'-Hax/C-7'], 1.99/25.7 [6'-Hax/C-6'], 1.85-1.78/25.7 [6'-Hax/C-6'], 1.50/27.9 [7'-Hax/C-7']. 

HMBC Correlation [δH/δC]: 8.37/75.3/125.5/142.2 [NH/C-3'/C-7a/C-3a], 7.57/75.3/130.1/142.2 [4-HAr/C-3'/C-5/C-3a], 7.24/62.6/142.2 [6-HAr/C-5/C-3a], 7.10/110.6/125.5 [5-HAr/C-12'/C-7a], 6.72-6.68/120.0 [7-HAr/C-7], 6.72-6.68/52.9/110.9/148.5 [12'-HAr/C-13'/C-11'], 6.61/124.6/ 148.5 [13'-HAr/C-8'/C-11'], 6.45/52.9/ 120.0/148.5 [9'-HAr/C-2'/C-7/C-10'], 6.27/27.9 /52.9/64.2/110.9/124.6 [CH-NO₂/C-7'/C-2'/C-7a'/C-13'/C-8'], 4.84/51.2/75.3 [7a'-H/C-5'/C-3'], 4.45/75.3/91.3/110.9/120.0/124.6/ 178.5 [2'-H/C-3'/C-1'/C-13'/C-7/C-8'/C-2], 3.72/55.5/148.5 [H-OCH₃/C-OCH₃/C-10'], 3.54/ 55.7/148.5 [H-OCH₃/C-OCH₃/C-11'], 3.27/25.7/75.3 [5'-Heq/C-6'/C-3'], 2.89/25.7/72.9/ 64.2 [5'-Hax/C-6'/C-7a'], 2.18-2.09/25.7/51.3 [7'-Hax/C-6'/C-5''], 1.99/64.2 [6'-Hax/C-7a'], 1.50/25.7/64.2/91.3 [7'-Hax/C-6'/C-7a'/C-1']. 


1'-Nitro-2'-(3,4-methylenedioxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (12c): White solid (738 mg, 1.88 mmol, 75 % yield); Obtained as a mixture of two regioisomers (12c:12c' = 62:38); \(R_f\) [hexane-EtOAc, 2:1] = 0.45; MP 198-200 °C; FT -IR (KBr disk, cm\(^{-1}\)):

- 3193 \(\nu\) (NH)
- 3085 \(\nu\) (=CHAr)
- 2977 \(\nu\) (OCH\(_2\)O)
- 2885 \(\nu\) (CH\(_2\))
- 1712 \(\nu\) (C=O)
- 1619 \(\nu\) (CAr=CAr)
- 1527 \(\nu\) (C-NO\(_2\))
- 1373 \(\nu\) (C-NO\(_2\))
- 1342 \(\nu\) (C-N-C)
- 1249 \(\nu\) (C-O-C);

Spectroscopy NMR data for the major regioisomer 12c:

- \(^1H\) NMR (400 MHz, CDCl\(_3\), \(\delta\) (ppm): 7.92 (1H, s, \(N\)H), 7.53 (1H, d, \(J = 7.4\) Hz, 4-H\(_{Ar}\)), 7.12-7.07 (1H, m, 6-H\(_{Ar}\)), 6.96-6.87 (1H, m, 5-H\(_{Ar}\)), 6.74 (1H, d, \(J = 8.0\) Hz, 7-H\(_{Ar}\)), 6.63 (1H, d, \(J = 1.0\) Hz, 9'-H\(_{Ar}\)), 6.56 (2H, dt, \(J = 14.1, 4.6\) Hz, 12' and 13'-H\(_{Ar}\)), 6.20 (1H, t, \(J = 10.0\) Hz, CH-NO\(_2\)), 5.83 (2H, s, -OCH\(_2\)O), 4.83 (1H, dd, \(J = 17.0, 7.9\) Hz, 7a'-H), 4.41 (1H, d, \(J = 10.7\) Hz, 2'-H), 3.23 (1H, ddt, \(J = 10.6, 5.6\) Hz, 6'-H\(_{eq}\)), 1.98 (1H, dd, \(J = 10.6, 5.6\) Hz, 6'-H\(_{ax}\)),

13C NMR (101 MHz, CDCl\(_3\), \(\delta\) (ppm): 178.0, 147.8, 147.4, 141.9, 130.2 (+), 126.2, 126.2, 122.6 (+), 122.1 (+), 110.5 (+), 108.5 (+), 108.4 (+), 101.2 (-), 92.1 (+), 75.1, 64.0 (+), 53.0 (+), 51.2 (-), 27.9 (-), 25.7 (-).

HRMS (ESI+): \(m/z\) calcd for C\(_{21}\)H\(_{20}\)N\(_3\)O\(_5\) ([M+H]+) 394.1397, found: 394.1402; Calcd for C\(_{21}\)H\(_{19}\)N\(_3\)O\(_5\)Na ([M+Na]+) 416.1217, found: 416.1221.

1-Methyl-1'-nitro-2'(3,4,5-trimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (12d): White solid (941 mg, 2.08 mmol, 83 % yield); \(R_f\) [hexane-EtOAc, 2:1] = 0.31; MP 174-176 °C; FT -IR (KBr disk, cm\(^{-1}\)):

- 2946 \(\nu\) (=CHAr)
- 2930 \(\nu\) (OCH\(_3\))
- 2838 \(\nu\) (CH\(_2\))
- 1712 \(\nu\) (C=O)
- 1589 \(\nu\) (CAr=CAr)
- 1542 \(\nu\) (C-NO\(_2\))
- 1465 \(\nu\) (CH\(_3\))
- 1373 \(\nu\) (C-NO\(_2\))
- 1342 \(\nu\) (C-N-C)
- 1249 \(\nu\) (C-O-C);

1H NMR (400 MHz, CDCl\(_3\), \(\delta\) (ppm): 7.58 (1H, d, \(J = 7.0\) Hz, 4-H\(_{Ar}\)), 7.29 (1H, td, \(J = 7.7, 1.1\) Hz, 6-H\(_{Ar}\)), 7.11 (1H, td, \(J = 7.6, 0.9\) Hz, 5-H\(_{Ar}\)), 6.65 (1H, d, \(J = 7.6\) Hz, 7-H\(_{Ar}\)), 6.27 (1H, dd, \(J = 10.3, 9.6\) Hz, CH-NO\(_2\)), 6.24 (2H, s, 9' and 13'-H\(_{Ar}\)), 4.90 (1H, dd, \(J = 17.0, 7.9\) Hz, 7a'-H), 4.42 (1H, d, \(J = 10.5\) Hz, 2'-H), 3.71 (3H, s, OCH\(_3\)), 3.62 (6H, s, 2xOCH\(_3\)), 3.27 (1H, ddt, \(J = 10.6, 5.6\) Hz, 6'-H\(_{ax}\)), 1.98 (1H, dd, \(J = 10.6, 5.6\) Hz, 6'-H\(_{eq}\)), 1.82 (1H, ddt, \(J = 15.7, 11.4, 4.8\) Hz, 6'-H\(_{ax}\)), 1.48 (1H, ddt, \(J = 15.8, 13.0, 8.0\) Hz, 7'-H\(_{ax}\));

13C NMR (101 MHz, CDCl\(_3\)), \(\delta\) (ppm): 178.0, 147.8, 147.4, 141.9, 130.2 (+), 126.2 (+), 126.1, 125.2, 122.6 (+), 122.1 (+), 110.5 (+), 108.5 (+), 108.4 (+), 101.2 (-), 92.1 (+), 75.1, 64.0 (+), 53.0 (+), 51.2 (-), 27.9 (-), 25.7 (-);

HRMS (ESI+): \(m/z\) calcd for C\(_{21}\)H\(_{20}\)N\(_3\)O\(_5\) ([M+H]+) 394,1397, found: 394,1402; Calcd for C\(_{21}\)H\(_{19}\)N\(_3\)O\(_5\)Na ([M+Na]+) 416,1217, found: 416,1221.

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4], 7.29/130.2 [6-H$_{Ar}$/C-6], 7.11/122.4 [5-H$_{Ar}$/C-5], 6.65/108.8 [7-H$_{Ar}$/C-7], 6.27/91.9 [CH-NO$_2$/C-1’],

6.24/104.9 [9’ and 13’-HAr/C-9’ and C-13’], 4.90/64.3 [7a’-H/C-7a’], 4.42/53.5 [2’-H/C-2’], 3.71/60.8 [H-OCH3/C-OCH3], 3.62/56.0 [2xH-OCH3/2xC-OCH3], 3.27/51.4 [5’-Heq/C-5’], 2.94/25.7 [H-NCH3/C-NCH3], 2.89/51.4 [5’-Hax/C-5’], 2.16/27.9 [7’-Heq/C-7’], 1.99/25.9 [6’-Heq/C-6’], 1.83/25.9 [6’-Hax/C-6’], 1.49/27.9 [7’-Hax/C-7’].

HMBC Correlation [δH/δC]: 7.58/75.0/108.8/130.2/144.9 [4-HAr/C-3’/C-7/C-6/C-7a], 7.29/108/122.4/125.7/144.9 [6-HAr/C-7/C-5/C-4/C-7a], 7.11/108.8/125.0/130.2/144.9 [5-HAr/C-7/C-3a/C-6/C-7a], 6.65/122.4/125.0/144.9 [7-HAr/C-5/C-3a/C-7a], 6.27/27.9/53.5/64.3/75.0 [CH-N(NO2)/C-7’/C-2’/C-7a’/C-3], 6.24/104.9/125.0/128.1/137.3 /152.9 [9’ and 13’-HAr/C-9’-C-3a/C-8’/C-11’/C-10’ and C-12’], 4.90/25.7/27.9/51.4/75.0 [7a’-H/C-6’/C-7’/C-5’/C-3’], 4.42/75.0/91.9/104.9/125.0/128.1/176.2 [2’-H/C-3’/C-1’/C-9’ and C-13’/C-3a/C-8’/C-2’], 3.71/137.3 [H-OCH3/C-11’], 3.62/104.9/152.9 [2xH-OCH3/C-9’ and -C-13’/C-10’ and C-12’], 1.49/25.7/75.0 [5’-Heq/C-6’/C-3’], 2.94/144.9/176.2 [N-CH3/C-7a/C-2’], 2.89/25.7/27.9/64.3 [5’-Heq/C-6’/C-3’/C-7a], 2.16/25.7/51.4/64.3/91.9 [7’-Hax/C-6’/C-3’/C-7a’/C-3], 1.99/27.9/64.3 [6’-Heq/C-7’/C-7a’/C-1’]; HRMS (ESI+): m/z: caled for C24H26N4O6 ([M+H]+) 454,1973, found: 454,1977; caled for C24H27N4O6Na ([M+Na]+) 476,1792, found: 476,1788.

1-Methyl-1’-nitro-2’-(3,4-dimethoxyphenyl)-1’,2’,5’,6’,7’,7’a-hexahydrospiro
indoline-3,3’-pyrroloidin-2-one (12e): White solid (847 mg, 2.00 mmol, 80 % yield); Rf [hexane-EtOAc, 2:1] = 0.34; MP 103-105 °C; FT-IR (KBr disk, cm−1): 2962 ν(=CHAr), 2931 ν(=CH3), 2838 ν(CH2), 1712 ν(C=O), 1604 ν(C=O), 1542 ν(CH3), 1373 ν(C=NO2), 1342 ν(C-N-C), 1265 ν(C-O-C); 1H NMR (400 MHz, CDCl3), δ (ppm): 7.58 (1H, d, J = 7.5 Hz, 4-HAr), 7.29 (1H, td, J = 7.8, 1.0 Hz, 6-HAr), 7.11 (1H, td, J = 7.8, 0.9 Hz, 5-HAr), 6.67 (1H, dd, J = 8.3, 1.8 Hz, 12’-HAr), 6.63 (1H, d, J = 7.8 Hz, 7’-HAr), 6.60 (1H, d, J = 8.3 Hz, 13’-HAr), 6.46 (1H, d, J = 1.8 Hz, 9’-HAr), 6.28 (1H, t, J = 10.0 Hz, CH-NO2), 4.89 (1H, dd, J = 17.0, 7.9 Hz, 7a’-H), 4.44 (1H, d, J = 10.6 Hz, 2’-H), 3.75 (3H, s, OCH3), 3.59 (3H, s, OCH3), 3.28 (1H, ddd, J = 11.3, 8.4, 5.3 Hz, 5’-Heq), 2.93 (3H, s, NCH3), 2.88 (1H, t, J = 7.4 Hz, 5’-Hax), 2.15 (1H, dt, J = 13.9, 7.9 Hz, 7’-Hax), 1.99 (1H, dd, J = 12.2, 5.7 Hz, 6’-Hax), 1.82 (1H, ddd, J = 16.4, 11.5, 4.2 Hz, 6’-Hax), 1.50 (1H, ddt, J = 13.0, 11.1, 7.7 Hz, 7’-Hax); 13C NMR (101 MHz, CDCl3), δ (ppm): 176.3, 148.5 (2C), 144.9, 130.1 (+), 125.8 (+), 125.1, 124.8, 122.4 (+), 120.3 (+), 110.9 (+), 110.8 (+), 108.7 (+), 91.8 (+), 75.0, 64.3 (+), 55.7 (+), 55.6 (+), 53.0 (+), 51.4 (-), 27.9 (-), 25.9 (-), 25.7 (+); COSY Correlation [δH/δC]: 7.58/7.11 [4-HAr/5-HAr], 7.29/6.63 [6-HAr/7-HAr], 7.29/7.11 [6-HAr/5-HAr], 6.67/6.46 [12’-HAr/9’-HAr], 6.28/4.44 [CH-NO2/2’-H], 6.28/4.89 [CH-NO2/7a’-H], 4.89/1.50 [7a’-H/7’-Hax], 4.89/2.15 [7a’-H/7’-Hax], 3.28/1.82 [5’-Hax/6’-Hax], 3.28/1.99 [5’-Hax/6’-Hax], 3.28/2.88 [5’-Hax/5’-Hax], 2.88/1.82 [5’-Hax/6’-Hax], 2.15/1.50 [7’-Hax/7’-Hax], 1.99/1.50 [6’-Hax/7’-Hax], 1.99/1.82 [6’-Hax/6’-Hax], 1.82/1.50 [6’-Hax/7’-Hax]. HSQC Correlation [δH/δC]: 7.58/125.8 [4-HAr/C-4’], 7.29/130.1 [6-HAr/C-6’], 7.11/122.4 [5-HAr/C-5’], 6.67/108.7

1-Methyl-1’-nitro-2’-(3,4-methylenedioxyphenyl)-1’,2’,5’,6’,7’,7a’-hexahydrospiroindoline-3,3’-pyrrolizin-2-one (12f): White solid (866 mg, 2.13 mmol, 85 % yield); Rf [hexane-EtOAc, 2:1] = 0.38; MP 192-194 °C; FT-IR (KBr disk, cm⁻¹): 2977 ν(OCH2O), 2946 ν(=CHAr), 2885 ν(CH2), 1712 ν(C=O), 1542 ν(C-N-C), 1357 ν(C=O), 1249 ν(C-O-C); 1H NMR (400 MHz, CDCl₃), δ(ppm): 7.52 (1H, d, J = 2.0 Hz, 4’-HAr), 7.27 (1H, dd, J = 8.5, 1.9 Hz, 6’-HAr), 6.62 (1H, s, 5’-HAr), 6.60 (1H, s, 7’-HAr), 6.58 (1H, s, 9’-HAr), 6.55 (2H, d, J = 0.9 Hz, -OCH2O-), 6.16 (1H, t, J = 10.0 Hz, CH-N=O2), 5.84 (2H, dd, J = 4.3, 1.3 Hz, 12’ and 13’-H), 4.85 (1H, dd, J = 17.1, 8.0 Hz, 7a’-H), 4.36 (1H, d, J = 10.5 Hz, 2’-H), 3.17 (1H, ddd, J = 11.3, 8.2, 5.3 Hz, 5’-Hax), 2.98 (3H, s, NCH3), 2.85 (1H, t, J = 7.2 Hz, 5’-Hax), 2.17-2.09 (1H, m, 7’-Hax), 2.03-1.96 (1H, m, 6’-Hax), 1.81 (1H, ddd, J = 16.1, 11.3, 4.2 Hz, 6’-Hax), 1.46 (1H, ddt, J = 12.9, 11.4, 7.8 Hz, 7’-Hax). 13C NMR (101 MHz, CDCl₃), δ(ppm): 175.7, 147.8, 147.4, 143.4, 130.1 (+), 127.9, 126.0 (+), 125.8, 122.2 (+, 2C), 109.6 (+), 108.4 (+, 2C), 101.2 (-), 92.4 (+), 74.7, 64.1 (+), 53.1 (+), 51.3 (-), 27.8 (-), 26.1 (+), 25.7 (-), HRMS (ESI+): m/z: calced for C₂₃H₂₆N₃O₅ ([M+H]+) 424,1871, found: 424,1871; calcd for C₂₃H₂₅N₃O₅Na ([M+Na]+) 446,1670, found: 446,1670.

6’-Hydroxy-1-methyl-1’-nitro-2’-(3,4,5-trimethoxyphenyl)-1’,2’,5’,6’,7’,7a’-hexahydrospiroindoline-3,3’-pyrrolizin-2-one (12g): Beige solid (939 mg, 2.00 mmol, 80 % yield); Rf [hexane-EtOAc, 2:1] = 0.38; MP 192-194 °C; FT-IR (KBr disk, cm⁻¹): 3455 ν(OH), 2985 ν(CH₂), 1712 ν(C=O), 1604 ν(C=O), 1542 ν(C-N-C), 1373 ν(C=O), 1249 ν(C-O-C); 1H NMR (400 MHz, CDCl₃), δ(ppm): 7.52 (1H, d, J = 2.0 Hz, 4’-HAr), 7.27 (1H, dd, J = 8.5, 1.9 Hz, 6’-HAr), 6.62 (1H, s, 5’-HAr), 6.60 (1H, s, 7’-HAr), 6.58 (1H, s, 9’-HAr), 6.55 (2H, d, J = 0.9 Hz, -OCH₂O-), 6.16 (1H, t, J = 10.0 Hz, CH-N=O₂), 5.84 (2H, dd, J = 4.3, 1.3 Hz, 12’ and 13’-H), 4.85 (1H, dd, J = 17.1, 8.0 Hz, 7a’-H), 4.36 (1H, d, J = 10.5 Hz, 2’-H), 3.17 (1H, ddd, J = 11.3, 8.2, 5.3 Hz, 5’-Hax), 2.98 (3H, s, NCH₃), 2.85 (1H, t, J = 7.2 Hz, 5’-Hax), 2.17-2.09 (1H, m, 7’-Hax), 2.03-1.96 (1H, m, 6’-Hax), 1.81 (1H, ddd, J = 16.1, 11.3, 4.2 Hz, 6’-Hax), 1.46 (1H, ddt, J = 12.9, 11.4, 7.8 Hz, 7’-Hax).

= 7.5, 0.7 Hz, 1H, 4-H\textsubscript{Ar}), 7.31 (1H, td, \(J = 7.8, 1.2\) Hz, 6-H\textsubscript{Ar}), 7.11 (1H, td, \(J = 7.6, 1.0\) Hz, 5-H\textsubscript{Ar}), 6.66 (1H, d, \(J = 7.5\) Hz, 7-H\textsubscript{Ar}), 6.26 (1H, t, \(J = 9.9\) Hz, CH-NO\textsubscript{2}), 6.23 (2H,

6'-Hydroxy-1-methyl-1'-nitro-2'- (3,4-dimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (12h): Beige solid (846 mg, 1.93 mmol, 77 % yield); Rt [hexane-EtOAc, 1:1] = 0.30; MP 129-131 °C; FT-IR (KBr disk, cm\(^{-1}\)):

| ν(C=O) | 175.7, 153.0 (2C), 145.0, 137.5, 130.4 (+), 127.9, 125.4 (+), 124.8, 122.5 (+), 108.9 (+), 105.0 (+, 2C), 92.3 (+), 74.8, 72.0 (+), 63.0 (+), 60.8 (+), 58.5 (+), 56.0 (+, 2C), 54.2 (+), 37.1 (+), 25.9 (+); COSY Correlation [δ(H/δ(C)]: 7.52/125.4 [4-HAr/5-HAr], 7.31/6.66 [6-HAr/7-HAr], 7.31/7.11 [6-HAr/5-HAr], 6.26/4.45 [CH-NO2/2'-H], 6.26/5.12 [CH-NO2/7a'-H], 6.23/3.62 [9' and 13'-HAr/H-CH3], 5.12/1.78 [7a'-H/7'-Hax], 5.12/2.21 [7a'-H/7'-Hax], 4.51/1.78 [6'-H/5'-Hax], 3.45/2.93 [5'-Heq/5'-Hax], 2.93/2.21 [5'-Hax/7'-Hax], 2.21/1.78 [7'-Hax/7'-Hax]. HSQC Correlation [δ(H/δ(C)]: 7.52/125.4 [4-HAr/4-C-4], 7.31/130.4 [6-HAr/6-C-6], 7.11/122.5 [5-HAr/5-C-5], 6.66/108.9 [7-HAr/7-C-7], 6.26/92.3 [CH-NO2/C-1'], 6.23/105.0 [9' and 13'-HAr/C-9' and C-13'], 5.12/63.0 [7a'-H/C-7a'], 4.51/72.0 [6'-H/C-6'], 4.45/54.2 [2'-H/C-2'], 3.71/60.8 [H-CH3/C-CH3], 3.62/56.0 [2H-CH3/2H-CH3], 3.45/58.5 [5'-Hax/C-5'], 2.94/25.9 [H-NCH3/C-NCH3], 2.93/58.5 [5'-Hax/C-5'], 2.21/37.1 [7'-Hax/C-7'], 1.78/37.1 [7'-Hax/C-7']. HMBC Correlation [δ(H/δ(C)]: 7.52/74.8/122.5/130.4/145.0 [4-HAr/C-3'/C-6/C-5/C-7a], 7.31/125.4/145.0 [6-HAr/C-4/C-7a], 7.11/108.9/124.8 [5-HAr/C-7/C-3a], 6.66/122.5/124.8 [7-HAr/C-6/C-3a], 6.26/54.1/63.0 [CH-NO2/C-2/C-7a'], 6.23/105.0/127.9/137.5/153.0 [9' and 13'-HAr/C-13' and C-9'/C-8'/C-11'/C-10' and C-12'], 5.12/58.5 [7a'-H/C-7'], 4.45/74.8/92.3/105.0/124.8/127.9/175.0 [2'H/C-3'/C-1'/C-9' and C-13'/C-3a/C-8'/C-2'], 3.71/137.5 [H-CH3/C-11'], 3.62/152.9 [2H-CH3/2H-CH3], 3.45/74.8 [5'-Hax/C-5'], 2.94/145.0/175.0 [N-Ch3/C-7a/C-2], 2.93/37.4/63.0/72.0 [5'-Hax/C-7'/C-7'a/C-6'], 2.21/58.5/72.0/92.3 [7'-Hax/C-5'/C-6'/C-1'], 1.78/63.0/92.3 [7'-Hax/C-7'a/C-1']; HRMS (ESI+): m/z: calcd for C_{24}H_{27}N_3O_7Na ([M+Na]^+) 470,1922, found: 470,1917; calcd for C_{24}H_{27}N_3O_7Na ([M+Na]^+) 492,1741, found: 492,1744.

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-13C NMR (101 MHz, CDCl3), δ (ppm): 175.8, 148.6, 148.5, 144.9, 130.3 (+), 125.5 (+), 124.8, 124.6, 122.5 (+), 120.3 (+), 110.9 (+, 2C), 108.8 (+), 92.3 (+), 74.8, 72.0 (+), 62.9 (+), 58.5 (+), 55.7 (+), 55.6 (+), 53.6 (+), 37.1 (+), 25.9 (+); COSY Correlation [δH/δH]: 7.52/7.12 [4-HAr/5-HAr], 7.31/6.68-6.63 [6-HAr/7-HAr], 7.31/7.12 [6-HAr/5-HAr], 6.68-6.63/6.45 [12'-HAr/9'-HAr], 6.68-6.63/6.61 [12'-HAr/13'-HAr], 6.26/4.47 [CH-NO2/2'-H], 6.26/5.12 [CH-NO2/7a'-H], 5.12/1.79 [7a'-H/7'-Heq], 5.12/2.21 [7a'-H/7'-Hax], 4.51/1.79 [6'-H/7'-Hax], 4.51/3.46 [6'-H/5'-Heq], 3.46/2.93 [5'-Heq/5'-Hax], 2.93/2.21 [5'-Hax/7'-Hax], 2.21/1.89 [7'-Hax/7'-Heq]. HSQC Correlation [δH/δC]: 7.52/125.5 [4-HAr/C-4], 7.31/130.3 [6-HAr/C-6], 7.12/122.5 [5-HAr/C-5], 6.68-6.63/108.8 [12'-HAr/C-12'], 6.68-6.63/120.3 [7-HAr/C-7a], 6.61/110.9 [13'-HAr/C-13'], 6.45/110.9 [9'-HAr/C-9'], 6.26/92.9 [CH-NO2/C-1'], 5.12/62.9 [7a'-H/C-7a'], 4.51/72.0 [6'-H/C-6'], 4.47/53.6 [2'-H/C-2'], 3.75/55.7 [H-OCH3/C-OCH3], 3.59/55.6 [H-OCH3/C-OCH3], 3.46/58.5 [5'-Heq/C-5'], 2.93/25.9 [H-NCH3/C-NCH3], 2.93/58.5 [5'-Hax/C-5'], 2.21/37.1 [7'-Hax/C-7'], 1.79/37.1 [7'-Heq/C-7']. HMBC Correlation [δH/δC]: 7.52/74.8/130.3/144.9 [4-HAr/C-3'/C-6/C-3a], 7.31/125.5/144.9 [6-HAr/C-4/C-3a], 7.12/108.8/124.6 [5-HAr/C-12'/C-7a], 6.68-6.63/53.6/110.9/124.8/148.5/148.6 [12'-HAr/C-2'/C-13' and C-9'/C-10'/C-11'], 6.68-6.63/122.5/124.6 [7-HAr/C-5/C-7a], 6.61/124.6/148.5/148.6 [13'-HAr/C-8'/C-10'/C-11'], 6.45/53.6/120.3/124.8/148.5/148.6 [9'-HAr/C-2'/C-12'/C-8'/C-10'/C-11'], 6.28/36.1/53.6/62.9/110.9/124.8 [CH-NO2/C-7'/C-7a'/C-9' and C-13'-C-8'], 5.12/58.5 [7a'-H/C-9'], 4.47/74.8/92.3/110.9/120.3/124.8/175.8 [2'-H/C-3'/C-1'/C-9' and 13'-C-7/C-8'/C-2], 3.75/148.5 [H-OCH3/C-10'], 3.59/148.6 [H-OCH3/C-11'], 3.46/74.8 [5'-Heq/C-3'], 2.93/144.9/175.8 [N-CH3/C-3a/C-2], 2.93/37.1/62.9/72.0 [5'-Hax/C-7'/C-7a'/C-6'], 2.21/58.5/72.0 [7'-Hax/C-5'/C-6'], 1.79/62.9/72.0/92.3 [7'-Heq/C-7a'/C-6'/C-1']; HRMS (ESI+): m/z: calcd for C23H26N3O6 ([M+H]+) 440.1816, found: 440.1821; calcd for C23H25N3O6Na ([M+Na]+) 462.1636, found: 462.1630.

6'-Hydroxy-1-methyl-1'-nitro-2'-(3,4-methylenedioxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (12i): Beige solid (783 mg, 1.85 mmol, 74% yield); Rf [hexane-EtOAc, 1:1] = 0.33; MP 141-143 °C; FT-IR (KBr disk, cm⁻¹): 3425 ν (-OH), 3054 ν (=CHAr), 2931 ν (CH2), 1712 ν (C=O), 1604 ν (CAr=CAr), 1542 ν (C-NO2), 1496 ν (C-N-C), 1450 ν (CH3), 1373 ν (C-NO2), 1249 ν (C-O-C); 1H NMR (400 MHz, CDCl3), δ (ppm): 7.47 (1H, d, J = 7.5 Hz, 4-HAr), 7.30 (1H, t, J = 7.8 Hz, 6-HAr), 7.11 (1H, t, J = 7.6 Hz, 5-HAr), 6.67 (1H, d, J = 7.8 Hz, 7-HAr), 6.60 (1H, s, 13'-HAr), 6.53 (2H, s, 9' and 12'-HAr), 6.18 (1H, t, J = 9.8 Hz, CH-NO2), 5.84-5.82 (2H, m, -OCH2-O-), 5.08 (1H, dd, J = 16.2, 8.5 Hz, 7a'-H), 4.48 (1H, t, J = 4.1 Hz, 6'-H), 4.42 (1H, d, J = 10.3 Hz, 2'-H), 3.41 (1H, dd, J = 9.6, 3.4 Hz, 5'-Heq), 2.99 (3H, s, NCH3), 2.87 (1H, dd, J = 9.5, 1.6 Hz, 5'-Hax), 2.18 (1H, ddd, J = 14.3, 8.4, 1.7 Hz, 7'-Hax), 1.81 (1H, br.s, -OH), 1.75 (1H, ddd, J = 14.3, 7.0, 5.3 Hz, 7'-Heq). 13C NMR (101 MHz, CDCl3), δ (ppm): 175.8, 147.8, 147.4, 144.8, 130.4 (+), 125.9, 125.4 (+), 124.4, 122.7 (+), 122.1 (+), 108.8 (+), 108.5 (+), 108.3 (+), 101.1 (+), 92.9 (+), 74.6, 71.9 (+), 62.7 (+), 58.4 (-), 53.5 (+), 37.1 (-), 26.0
(+); COSY Correlation $[\delta_H/\delta_H]$:
7.47/7.11 [4-H$_{Ar}$/5-H$_{Ar}$], 7.30/6.67 [6-H$_{Ar}$/7-H$_{Ar}$],
7.30/7.11 [6-H$_{Ar}$/5-H$_{Ar}$], 6.60/6.53 [13’-H$_{Ar}$/9’ and 12’-H$_{Ar}$], 6.18/4.42 [CH-NO$_2$/2’-H],

6.18/5.08 [CH-NO2/7a'-H], 5.08/1.75 [7a'-H/7'-H eq], 5.08/2.18 [7a'-H/7'-H ax], 4.48/1.75 [6'-H/7'-H eq], 4.48/3.41 [6'-H/5'-H eq], 3.41/2.87 [5'-H eq/5'-H ax], 2.87/2.18 [5'-H ax/7'-H ax]. HSQC Correlation [δH/δC]: 7.47/125.4 [4-HAr/C-4], 7.30/130.4 [6-HAr/C-6], 7.11/122.7 [5-HAr/C-5], 6.67/108.8 [7-HAr/C-7], 6.60/108.5 [13'-HAr/C-13'], 6.53/108.3 [9'-HAr/C-9'], 6.53/122.1 [12'-HAr/C-12'], 6.18/92.9 [CH-NO2/C-1'], 5.84-5.82/101.1 [H-OCH2O/C-OCH2O], 5.08/62.7 [7a'-H/C-7a'], 4.48/1.9 [6'-H/C-6'], 4.42/53.5 [2'-H/C-2'], 3.41/58.4 [5'-H eq/C-5'], 2.99/26.0 [H-NCH3/C-NCH3], 2.87/58.4 [5'-H ax/C-5'], 2.18/37.1 [7'-H ax/C-7']. HMBC Correlation [δH/δC]: 7.47/74.6/130.4/144.8 [4-HAr/C-3'/C-6/C-3a], 7.30/125.5/144.8 [6-HAr/C-4/C-3a], 7.11/108.8/124.4 [5-HAr/C-7/C-7a], 6.67/53.5/122.1/124.4/147.4/147.8 [2'-H/C-3'/C-1'/C-9'/C-12'/C-7a/C-8'/C-2].

5-Chloro-1-methyl-1'-nitro-2'-(3,4,5-trimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (12j): White solid (1.02 g, 2.10 mmol, 84% yield); Rf [hexane-EtOAc, 2:1] = 0.60; MP 180-182 °C; FT-IR (KBr disk, cm⁻¹): 3070 ν (=CHAr), 2946 ν (OCH3), 2838 ν (CH2), 1712 ν (C=O), 1589 ν (CAr=CAr), 1542 ν (C-NO2), 1496 ν (CH3), 1357 ν (C-N=O), 1234 ν (C-OC), 817 ν (C=Cl), 1H NMR (400 MHz, CDCl3), δ (ppm): 7.56 (1H, d, J = 1.8 Hz, 4-HAr), 7.28 (1H, dd, J = 8.4, 2.0 Hz, 6-HAr), 6.58 (1H, d, J = 8.3 Hz, 7-HAr), 6.26 (2H, s, 9' and 12'-HAr), 6.24 (1H, t, J = 10 Hz, CH-NO2), 4.88 (1H, dd, J = 17.0, 8.0 Hz, 7a'-H), 4.37 (1H, d, J = 10.6 Hz, 2'-H), 3.72 (3H, s, OCH3), 3.66 (6H, s, 2xOCH3), 3.21 (1H, ddd, J = 11.1, 8.3, 5.4 Hz, 5'-H eq), 2.94 (3H, s, NCH3), 2.91 (1H, t, J = 7.3 Hz, 5'-H ax), 2.20-2.12 (1H, m, 7'-H eq), 2.02 (1H, dt, J = 11.9, 6.1 Hz, 6'-H eq), 1.90-1.77 (1H, m, 6'-H ax), 1.48 (1H, ddt, J = 12.9, 11.4, 7.7 Hz, 7'-H ax); 13C NMR (101 MHz, CDCl3), δ (ppm): 175.8, 153.0 (2C), 143.4, 137.4, 130.1 (+), 127.9, 127.7, 126.7, 126.1 (+), 109.8 (+), 104.9 (+, 2C), 91.6 (+), 74.9, 64.3 (+), 60.8 (+, 2C), 56.0 (+), 53.7 (+), 51.4 (-), 27.9 (-), 26.0 (+), 25.7 (-); HRMS (ESI+): m/z: calcd for C22H22N3O6 ([M+H]+) 424,1503, found: 424,1507; Calcd for C22H21N3O6Na ([M+Na]+) 446,1323, found: 446,1328.

5-Chloro-1-methyl-1'-nitro-2'-(3,4-dimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (12k): White solid (1.00 g, 2.20 mmol, 88% yield); Rf [hexane-EtOAc, 2:1] = 0.60; MP 181-183 °C; FT-IR (KBr disk, cm⁻¹): 3070 ν (=CHAr), 2946 ν (OCH3), 2838 ν (CH2), 1712 ν (C=O), 1604 ν (CAr=CAr), 1542 ν (C-N=O), 1465 ν (CH3), 1357

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v(\text{C-NO}_2), 1265 \text{ } v(\text{C-O-C}), 817 \text{ } v(\text{C-Cl}), \text{ } ^1H \text{ NMR (400 MHz, CDCl}_3), \delta(\text{ppm}): 7.57 (1H, d, J = 1.4 Hz, 4-\text{H}_{\text{Ar}}), 7.27 (1H, dd, J = 8.2, 1.7 Hz, 6-\text{H}_{\text{Ar}}), 6.66 (1H, dd, J = 8.2, 1.5 Hz, 7-\text{H}_{\text{Ar}}), 6.62 (1H, d, J = 8.2 Hz, 12’-\text{H}_{\text{Ar}}), 6.56 (1H, d, J = 8.4 Hz, 13’-\text{H}_{\text{Ar}}), 6.51 (1H, s, 9’-\text{H}_{\text{Ar}}), 6.24 (1H, t, J = 9.9 Hz, \text{CH-NO}_2), 4.88 (1H, dd, J = 16.8, 8.2 Hz, 7a’-\text{H}), 4.40 (1H, d, J = 10.5 Hz, 2’-\text{H}), 3.76 (3H, s, OCH\_3), 3.65 (3H, s, OCH\_3), 3.22 (1H, ddd, J = 11.5, 8.0, 5.3 Hz, 5’-\text{H}_{eq}), 2.92 (3H, s, NCH\_3), 2.89 (1H, t, J = 7.8 Hz, 5’-\text{H}_{ax}), 2.19-2.11 (1H, m, 7’-\text{H}_{eq}), 2.02 (1H, dt, J = 12.2, 6.1 Hz, 6’-\text{H}_{eq}), 1.83 (1H, tdd, J = 18.8, 11.7, 7.1 Hz, 6’-\text{H}_{ax}), 1.53-1.43 (1H, m, 7’-\text{H}_{ax}), \text{C}^{13} \text{NMR (101 MHz, CDCl}_3), \delta(\text{ppm}): 175.8, 148.5, 148.5, 143.3, 129.9 (+), 127.8, 126.7, 126.0 (+), 124.3, 120.3 (+), 110.8 (+), 110.7 (+), 109.5 (+), 91.6 (+), 74.9, 64.2 (+), 55.7 (+), 55.6 (+), 53.1 (+), 51.3 (-), 27.7 (-), 25.9 (+), 25.7 (-); HRMS (ESI+): m/z: calcd for C\text{23}H\text{24}Cl\text{N}_3O\text{5} ([M+Na]^+) 480.1297, found: 480.1294.

5-Chloro-1-methyl-1'-nitro-2'- (3,4-methylenedioxyphenyl)-1,2',5',6',7',7a'-hexahydropyrido[1,2-c]indoline-3,3'-pyrrolizin]-2-one (12l): White solid (1.00 g, 2.28 mmol, 91 % yield); Rf [hexane-EtOAc, 2:1] = 0.63; MP 172-173 °C; FT-IR (KBr disk, cm\(^{-1}\)): 3054 v(=C\_Ar), 2977 v(OCH\_2O), 2915 v(CH\_2), 1697 v(C=O), 1604 v(C\_Ar=C\_Ar), 1542 v(\text{C-NO}_2), 1496 v(C-N-C), 1357 v(C-NO\_2), 1234 v(C-O-C), 817 v(C-Cl); \text{C}^{13} \text{NMR (101 MHz, CDCl}_3), \delta(\text{ppm}): 175.7, 148.7, 147.4, 143.4, 130.1 (+), 127.9, 126.5, 126.0 (+), 125.8, 122.2 (+), 109.6 (+), 108.4 (+, 2C), 101.2 (-), 92.4 (+), 74.7, 64.1 (+), 53.1 (+), 51.3 (-), 27.8 (-), 26.1 (+), 25.7 (-); HRMS (ESI+): m/z: calcd for C\text{22}H\text{21}Cl\text{N}_3O\text{5} ([M+H]^+) 458,1477, found: 458,1481; calcd for C\text{23}H\text{24}Cl\text{N}_3O\text{5}Na ([M+Na]^+) 480,1297, found: 480,1294.

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$^1$H NMR (400 MHz, CDCl$_3$), $\delta$(ppm): 175.3, 153.0 (+, 2C), 143.5, 137.5, 130.2 (+), 127.9, 127.4, 126.4, 125.8 (+), 109.9 (+), 104.9 (+, 2C), 92.0 (+), 74.8, 71.8 (+), 63.1

(+), 60.8 (+), 58.4 (-), 56.0 (+, 2C), 54.2 (+), 37.0 (-), 26.0 (+); COSY Correlation \[\delta_H/\delta_H\]: 7.50/7.29 [4-H\textsubscript{Ar}/6-H\textsubscript{Ar}], 7.29/6.59 [6-H\textsubscript{Ar}/7-H\textsubscript{Ar}], 6.25/3.65 [9' and 13'-H\textsubscript{Ar}/H-OCH\textsubscript{3}], 6.21/4.38 [CH-NO\textsubscript{2}/2'-H], 6.21/5.11 [CH-NO\textsubscript{2}/7a'-H], 5.11/1.76 [7a'-H/7'-H\textsubscript{eq}], 5.11/2.20 [7a'-H/7'-H\textsubscript{ax}], 4.53/1.76 [6'-H/7'-H\textsubscript{eq}], 4.53/3.40 [6'-H/5'-H\textsubscript{eq}], 3.40/2.95-2.89 [5'-H\textsubscript{eq}/5'-H\textsubscript{ax}], 2.95-2.89/2.20 [5'-H\textsubscript{ax}/7'-H\textsubscript{ax}], 2.20/1.76 [7'-H\textsubscript{ax}/7'-H\textsubscript{eq}].

HSQC Correlation \[\delta_H/\delta_C\]: 7.50/125.8 [4-H\textsubscript{Ar}/C-4], 7.29/130.2 [6-H\textsubscript{Ar}/C-6], 6.59/109.9 [7-H\textsubscript{Ar}/C-7], 6.21/92.0 [CH-NO\textsubscript{2}/C-1'], 6.25/104.9 [9' and 13'-H\textsubscript{Ar}/C-9' and C-13'], 5.11/63.1 [7a'-H/C-7a'], 4.53/71.8 [6'-H/C-6'], 4.38/54.2 [2'-H/C-2'], 3.72/60.8 [H-OCH\textsubscript{3}/C-OCH\textsubscript{3}], 3.65/56.0 [2xH-OCH\textsubscript{3}/2xC-OCH\textsubscript{3}], 3.40/58.4 [5'-H\textsubscript{eq}/C-5'], 2.93/26.0 [H-NCH\textsubscript{3}/C-NCH\textsubscript{3}], 2.95-2.89/58.4 [5'-H\textsubscript{ax}/5'-H\textsubscript{eq}], 2.20/37.0 [7'-H\textsubscript{ax}/7'-H\textsubscript{eq}], 1.76/37.0 [7'-H\textsubscript{eq}/7'-H\textsubscript{ax}].

HMBC Correlation \[\delta_H/\delta_C\]: 7.50/74.8/127.9/130.2/143.4 [4-H\textsubscript{Ar}/C-3'/C-5/C-6/C-7a'], 7.29/125.8/127.9/143.5 [6-H\textsubscript{Ar}/C-4/C-5/C-7a'], 6.59/126.4/127.9/143.5 [7-H\textsubscript{Ar}/C-3a/C-5/C-7a'], 6.25/104.9/127.9/143.5 [9' and 13'-H\textsubscript{Ar}/C-9' and C-13'], 5.11/63.1 [7a'-H/C-7a'], 4.53/71.8 [6'-H/C-6'], 4.38/54.2 [2'-H/C-2'], 3.72/60.8 [H-OCH\textsubscript{3}/C-OCH\textsubscript{3}], 3.65/56.0 [2xH-OCH\textsubscript{3}/2xC-OCH\textsubscript{3}], 3.40/58.4 [5'-H\textsubscript{eq}/C-5'], 2.93/26.0 [H-NCH\textsubscript{3}/C-NCH\textsubscript{3}], 2.95-2.89/58.4 [5'-H\textsubscript{ax}/5'-H\textsubscript{eq}], 2.20/37.0 [7'-H\textsubscript{ax}/7'-H\textsubscript{eq}], 1.76/37.0 [7'-H\textsubscript{eq}/7'-H\textsubscript{ax}]; HRMS (ESI+): \[m/z\]: calcd for C\textsubscript{24}H\textsubscript{27}ClN\textsubscript{3}O\textsubscript{7} ([M+H]\textsuperscript{+}) 504.1532, found: 504.1536; calcd for C\textsubscript{24}H\textsubscript{26}ClN\textsubscript{3}O\textsubscript{7}Na ([M+Na]\textsuperscript{+}) 526.1351, found: 526.1356.

5-Chloro-6'-hydroxy-1-methyl-1'-nitro-2'-(3,4-dimethoxy phenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (12n): Beige solid (875 mg, 1.85 mmol, 74 % yield); \[R_f\] [hexane-EtOAc, 1:1] = 0.39; MP 196-198 °C; FT-IR (KBr disk, cm\(^{-1}\)): 3440 \(\nu\) (-OH), 3070 \(\nu\) (=CH\textsubscript{Ar}), 2931 \(\nu\) (OCH\textsubscript{3}), 2838 \(\nu\) (CH\textsubscript{2}), 1712 \(\nu\) (C=O), 1604 \(\nu\) (CAr=CAr), 1542 \(\nu\) (C-NO\textsubscript{2}), 1465 \(\nu\) (CH\textsubscript{3}), 1357 \(\nu\) (C-NO\textsubscript{2}), 1265 \(\nu\) (C-O-C), 1104 \(\nu\) (C=O), 1049 \(\nu\) (C=O).

1H NMR (400 MHz, CDCl\textsubscript{3}), \(\delta\) (ppm): 7.51 (1H, d, \(J = 2.0\) Hz, 4'-H\textsubscript{Ar}), 7.28 (1H, dd, \(J = 8.3, 1.6\) Hz, 6'-H\textsubscript{Ar}), 6.67-6.61 (2H, m, 9' and 13'-H\textsubscript{Ar}), 6.57 (1H, d, \(J = 8.3\) Hz, 12'-H\textsubscript{Ar}), 6.51 (1H, d, \(J = 1.5\) Hz, 7'-H\textsubscript{Ar}), 6.22 (1H, t, \(J = 9.8\) Hz, CH-NO\textsubscript{2}), 5.11 (1H, dd, \(J = 16.3, 8.5\) Hz, 7a'-H), 4.54 (1H, t, \(J = 3.9\) Hz, 6'-H), 4.42 (1H, d, \(J = 10.2\) Hz, 2'-H), 3.76 (3H, s, OCH\textsubscript{3}), 3.66 (3H, s, OCH\textsubscript{3}), 2.93 (3H, s, NCH\textsubscript{3}), 2.21 (1H, dd, \(J = 14.4, 8.4\) Hz, 7'-H\textsubscript{ax}), 1.78 (1H, ddd, \(J = 14.1, 6.9, 5.3\) Hz, 7'-H\textsubscript{eq}), 1.73 (1H, br.s, -OH); 13C NMR (101 MHz, CDCl\textsubscript{3}), \(\delta\) (ppm): 175.4, 148.8, 148.7, 143.5, 130.2 (+), 128.0, 126.5, 125.8 (+), 124.1, 120.5 (+), 111.0 (+), 110.8 (+), 109.7 (+), 92.2 (+), 74.8, 72.0 (+), 63.0 (+), 58.4 (-), 55.8 (+), 55.7 (+), 53.8 (+), 37.1 (-), 26.0 (+); COSY Correlation \[\delta_H/\delta_H\]: 7.51/7.28 [4-H\textsubscript{Ar}/6-H\textsubscript{Ar}], 7.28/6.51 [6-H\textsubscript{Ar}/7-H\textsubscript{Ar}], 6.67-6.61/6.57 [9' and 13'-H\textsubscript{Ar}/12'-H\textsubscript{Ar}], 6.22/4.42 [CH-NO\textsubscript{2}/2'-H], 6.22/5.11 [CH-NO\textsubscript{2}/7a'-H], 5.11/1.78 [7a'-H/7'-H\textsubscript{eq}], 5.11/2.21 [7a'-H/7'-H\textsubscript{ax}], 4.54/1.78 [6'-H/7'-H\textsubscript{eq}], 4.54/3.42 [6'-H/5'-H\textsubscript{eq}], 3.42/2.96-2.90 [5'-H\textsubscript{eq}/5'-H\textsubscript{ax}], 2.93-2.90/2.21 [5'-H\textsubscript{ax}/7'].

Hax], 2.21/1.78 [7’-Hax/7’-Heq]. HSQC Correlation [δ_H/δ_C]: 7.51/125.8 [4-HAr/C-4], 7.28/130.2 [6-HAr/C-6], 6.67-6.61/120.5 [13’-HAr/C-13’], 6.67-6.61/111.0 [9’-HAr/C-9’], 5.11/63.0 [7a’-H/7a’-Hax], 4.54/72.0 [2’-H/C-2’], 3.76/55.8 [H-OCH3/C-OCH3], 3.66/55.7 [H-OCH3/C-OCH3], 3.42/58.4 [5’-Heq/C-5’], 2.93/26.0 [H-NCH3/C-NCH3], 2.21/37.1 [7'-Hax/C-7’], 1.78/37.1 [7’-Heq/C-7’]. HMBC Correlation [δ_H/δ_C]: 7.51/74.8/128.0/130.2/143.5 [4-HAr/C-3’/C-5/C-6/C-3a], 7.28/125.8/128.0/143.5 [6-HAr/C-4/C-5/C-3a], 6.67-6.61/53.8/110.8/124.1/148.7 [9’-HAr/C-2’/C-13’ and C-9’-HAr/C-7a/C-10’/C-11’], 6.57/53.8/120.5/124.1/148.7 [5-HAr/C-6’/C-1’/C-9/C-7/C-8’/C-2], 5.85 (2H, s, -OC2H2O-), 5.10 (1H, dd, J = 16.6, 8.2 Hz, 7a’-H), 4.62 (1H, t, J = 4.0 Hz, 6’-H), 4.45 (1H, d, J = 9.9 Hz, 2’-H), 3.44 (1H, dd, J = 9.1, 3.3 Hz, 5’-Heq), 3.01 (3H, s, NC2H3), 2.86 (1H, dd, J = 9.1, 1.5 Hz, 5’-Hax), 2.23 (1H, ddd, J = 14.6, 8.2, 1.4 Hz, 7’-Hax), 1.87 (1H, br.s, -OH), 1.77 (1H, ddd, J = 14.6, 7.4, 4.9 Hz, 7’-Heq); 13C NMR (101 MHz, CDCl3), δ(ppm): 175.8, 147.9, 147.5, 143.3, 129.3 (+), 128.2, 127.0, 125.7 (+), 124.6, 123.2 (+), 109.8 (+), 109.6 (+), 108.2 (+), 101.3 (-), 92.6 (+), 74.7, 72.0 (+), 62.6 (+), 55.3 (-), 53.4 (+), 36.8 (-), 26.2 (+); HRMS (ESI+): m/z: calcd for C22H25ClN3O6 ([M+H]+) 474,1426, found: 474,1422; calcd for C23H24ClN3O6Na ([M+Na]+) 496,1246, found: 496,1250.

5-Chloro-6'-hydroxy-1-methyl-1'-nitro-2'-(3,4-methylenedioxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (12o): Beige solid (847 mg, 1.85 mmol, 74 % yield); Rf [hexane-EtOAc, 1:1] = 0.43; MP 189-191 °C; FT-IR (KBr disk, cm-1): 3425 ν(-OH), 3070 ν(=CHAr), 2915 ν(CH2), 1712 ν(C=O), 1604 ν(CAr=CAr), 1542 ν(C-NO2), 1496 ν(C-N-C), 1357 ν(C-NO2), 1249 ν(C-O-C), 817 ν(C-C), 1H NMR (400 MHz, CDCl3), δ(ppm): 7.38 (1H, s, 4-HAr), 7.31 (1H, dd, J = 8.3, 1.9 Hz, 6-HAr), 6.83 (1H, d, J = 8.3 Hz, 7-HAr), 6.72 (1H, m, 9’-HAr), 6.67-6.59 (2H, m, 12’ and 13’-HAr), 6.15 (1H, t, J = 9.9 Hz, CH-NO2), 5.85 (2H, s, -OC2H2O-), 5.10 (1H, dd, J = 16.6, 8.2 Hz, 7a’-H), 4.62 (1H, t, J = 4.0 Hz, 6’-H), 4.45 (1H, d, J = 9.9 Hz, 2’-H), 3.44 (1H, dd, J = 9.1, 3.3 Hz, 5’-Heq), 3.01 (3H, s, NC2H3), 2.86 (1H, dd, J = 9.1, 1.5 Hz, 5’-Hax), 2.23 (1H, ddd, J = 14.6, 8.2, 1.4 Hz, 7’-Hax), 1.87 (1H, br.s, -OH), 1.77 (1H, ddd, J = 14.6, 7.4, 4.9 Hz, 7’-Heq); 13C NMR (101 MHz, CDCl3), δ(ppm): 175.8, 147.9, 147.5, 143.3, 129.3 (+), 128.2, 127.0, 125.7 (+), 124.6, 123.2 (+), 109.8 (+), 109.6 (+), 108.2 (+), 101.3 (-), 92.6 (+), 74.7, 72.0 (+), 62.6 (+), 55.3 (-), 53.4 (+), 36.8 (-), 26.2 (+); HRMS (ESI+): m/z: calcd for C23H25ClN3O6 ([M+H]+) 474,1426, found: 474,1422; calcd for C23H24ClN3O6Na ([M+Na]+) 496,1246, found: 496,1250.

1-Methyl-1',5-dinitro-2'-(3,4,5-trimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (12p): Yellow solid (1.15 g, 2.33 mmol, 93 % yield); Rf [hexane-EtOAc, 2:1] = 0.57; MP 161-163 °C; FT-IR (KBr disk, cm-1): 3425 ν(-OH), 2946 ν(OCH3), 2838 ν(CH2), 1712 ν(C=O), 1604 ν(CAr=CAr), 1542 ν(CNO2), 1465 ν(CH3), 1342 ν(CNO2), 1295 ν(C-O-C); 1H NMR (400 MHz, CDCl3), δ(ppm): 8.46 (1H, d, J = 2.2 Hz, 4-

$H_{Ar}$, 8.28 (1H, dd, $J = 8.7$, 2.2 Hz, 6-$H_{Ar}$), 6.77 (1H, d, $J = 8.7$ Hz, 7-$H_{Ar}$), 6.27 (2H, s, 9’ and 13’-$H_{Ar}$), 6.22 (1H, t, $J = 10.0$ Hz, CH-NO$_2$), 4.87 (1H, dd, $J = 17.1$, 8.0 Hz, 7a’-

1-Methyl-1',5-dinitro-2'-(3,4-dimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (12q): Yellow solid (1.01 g, 2.18 mmol, 87 % yield); Rf [hexane-EtOAc, 2:1] = 0.59; MP 179-181 °C; FT-IR (KBr disk, cm⁻¹): 3085 ν (=CHAr), 2946 ν (OCH3), 1727 ν (C=O), 1619 ν (C=N), 1511 ν (C=O), 1450 ν (CH3), 1342 ν (C=O-NO2), 1265 ν (C-O-C); ¹H NMR (400 MHz, CDCl₃), δ (ppm): 8.46 (1H, d, J = 2.0 Hz, 4-HAr), 8.27 (1H, dd, J = 8.6 Hz, 7-HAr), 6.74 (1H, d, J = 8.6 Hz, 7-HAr), 6.63-6.57 (3H, m, 9', 12' and 13' -HAr), 6.22 (1H, t, J = 9.9 Hz, CH-NO2), 4.87 (1H, dd, J = 16.9 Hz, 7a'-H), 4.48 (1H, d, J = 10.5 Hz, 2'-H), 3.74 (3H, s, OC₃H₃), 3.66 (3H, s, OC₂H₂O), 3.27 (1H, ddd, J = 11.8, 8.2, 5.4 Hz, 5' -Heq), 3.03 (3H, s, NC₃H₃), 2.86 (1H, t, J = 7.1 Hz, 5'-Hax), 2.21-2.14 (1H, m, 7' -Hey), 2.07-2.02 (1H, m, 6' -Heq), 1.83 (1H, t, J = 18.8 Hz, 6'-Hax), 1.14 (H, d, J = 12.3 Hz, 7.9 Hz, 7'-Hax); ¹³C NMR (101 MHz, CDCl₃), δ (ppm): 176.5, 150.4, 148.9, 148.8, 143.2, 137.6, 127.3 (+), 127.3, 126.0, 123.8, 121.4 (+), 120.9 (+), 111.1 (+), 110.5 (+), 108.3 (+), 91.7 (+), 74.4, 64.3 (+), 55.8 (+, 2C), 53.2 (+), 51.4 (-), 27.8 (-), 26.0 (+), 25.7 (-); HRMS (ESI+): m/z: calcd for C₂₄H₂₇N₄O₈ ([M+H]+) 499,1823, found: 499,18228; calcd for C₂₄H₂₆N₄O₈Na ([M+Na]+) 521,1643, found: 521,1639.

1-Methyl-1',5-dinitro-2'-(3,4-methylenedioxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (12r): Yellow solid (1.04 g, 2.30 mmol, 92 % yield); Rf [hexane-EtOAc, 2:1] = 0.65; MP 205-207 °C; FT-IR (KBr disk, cm⁻¹): 3085 ν (=CHAr), 2946 ν (OCH3), 2885 ν (CH2), 1727 ν (C=O), 1619 ν (C=N), 1511 ν (C=O), 1450 ν (CH3), 1342 ν (C=O-NO2), 1265 ν (C-O-C); ¹H NMR (400 MHz, CDCl₃), δ (ppm): 8.44 (1H, d, J = 2.0 Hz, 4-HAr), 8.29 (1H, dd, J = 8.7 Hz, 6-HAr), 6.78 (1H, d, J = 8.6 Hz, 7-HAr), 6.63-6.57 (3H, m, 9', 12' and 13' -HAr), 6.22 (1H, t, J = 9.9 Hz, CH-NO2), 5.86-5.83 (2H, m, 12' and 13' -HAr), 4.85 (1H, dd, J = 17.1 Hz, 7a'-H), 4.45 (1H, d, J = 10.5 Hz, 2'-H), 3.27-3.20 (1H, m, 5' -Hax), 3.03 (3H, s, NC₃H₃), 2.83 (1H, t, J = 7.1 Hz, 5'-Hax), 2.20-2.12 (1H, m, 7' -Hey), 2.07-2.01 (1H, m, 6' -Heq), 1.87-1.75 (1H, m, 6' -Hax), 1.55-1.44 (1H, m, 7' -Hey). ¹³C NMR (101 MHz, CDCl₃), δ (ppm): 176.3, 150.4, 148.0, 147.7, 143.3, 127.3 (+), 125.8, 125.2, 122.2 (+), 121.3 (+), 108.6 (+), 108.4 (+), 108.3 (+), 101.3 (+), 92.1 (+), 74.2, 64.1 (+), 53.1 (+), 51.4 (-), 27.8 (-), 26.5 (+), 25.7 (+); HRMS (ESI+): m/z: calcd for C₂₂H₂₁N₄O₇ ([M+H]+) 453,1405, found: 453,1409; Calcd for C₂₂H₂₀N₄O₇Na ([M+Na]+) 475,1224, found: 475,1221.

6'-Hydroxy-1-methyl-1',5-dinitro-2'-(3,4,5-trimethoxyphenyl)-1',2',5',6',7',7'a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one (12s): Beige solid (1.05 g, 2.05 mmol, 82 % yield); $R_f$ [hexane-EtOAc, 1:1] = 0.37; MP 165-168 °C; FT-IR (KBr disk, cm$^{-1}$): 3517 ν(OH), 3085 ν(CH$_2$), 2931 ν(OCH$_3$), 2838 ν(CH$_3$), 1727 ν(C=O), 1604 ν(C$_{Ar}$-C$_{Ar}$), 1542 ν(C$_{NO_2}$), 1465 ν(CH$_3$), 1342 ν(C$_{NO_2}$), 1295 ν(C-O-C); $^1$H NMR (400 MHz, CDCl$_3$), δ/ppm: 8.40 (1H, d, $J = 2.2$ Hz, 4-H$_{Ar}$), 8.29 (1H, dd, $J = 8.7, 2.2$ Hz, 6-H$_{Ar}$), 6.78 (1H, d, $J = 8.7$ Hz, 7-H$_{Ar}$), 6.27 (2H, s, 9' and 13'-H$_{Ar}$), 6.22 (1H, t, $J = 9.8$ Hz, CH$_2$-NO$_2$), 5.11 (1H, dd, $J = 16.6, 8.3$ Hz, 7'-H$_{eq}$), 4.58 (1H, t, $J = 3.2$ Hz, 6'-H$_{eq}$), 4.47 (1H, d, $J = 10.3$ Hz, 2'-H$_{eq}$), 3.71 (3H, s, OCH$_3$), 3.64 (6H, s, 2xOCH$_3$), 3.46 (1H, dd, $J = 9.3, 3.4$ Hz, 5'-H$_{eq}$), 3.05 (3H, s, NCH$_3$), 2.90 (1H, dd, $J = 9.1, 1.1$ Hz, 5'-H$_{ax}$), 2.22 (1H, dd, $J = 14.0, 8.2$ Hz, 7'-H$_{ax}$), 1.83-1.78 (1H, dd, $J = 14.4, 7.1, 5.3$ Hz, 7'-H$_{eq}$), 1.75 (1H, br.s, -OH); $^{13}$C NMR (101 MHz, CDCl$_3$), δ/ppm: 176.0, 153.2 (2C), 150.5, 143.2, 137.8, 127.5 (+), 127.0, 125.6, 121.0 (+), 108.6 (+), 105.0 (+, 2C), 92.1 (+), 74.2, 71.7 (+), 63.1 (+), 60.8 (+), 58.4 (+), 56.1 (+, 2C), 54.1 (+), 37.0 (+), 26.4 (+); COSY Correlation [δ_H/δ_H]: 8.40/8.29 [4-H$_{Ar}$/6-H$_{Ar}$], 8.29/6.78 [6-H$_{Ar}$/7-H$_{Ar}$], 6.22/4.47 [CH$_2$-NO$_2$/2'-H], 6.22/5.11 [CH$_2$-NO$_2$/7a'-H], 5.11/1.83-1.78 [7a'-H'$/7'$-H$_{ax}$], 5.11/2.22 [7a'-H'/7'$-H_{eq}$], 4.58/1.75 [6'H/OH], 4.58/1.83-1.78 [6'H'/7'-H$_{ax}$], 4.58/3.46 [6'H'/5'-H$_{eq}$], 3.46/2.90 [5'-H$_{eq}$/5'-H$_{ax}$], 2.22/1.83-1.78 [7'-H$_{eq}$/7'$-H_{ax}$]. HSQC Correlation [δ_C/δ_H]: 8.40/121.07 [4-H$_{Ar}$/C-4'], 8.29/127.5 [6-H$_{Ar}$/C-6'], 6.78/108.6 [7-H$_{Ar}$/C-7'], 6.22/105.0 [9' and 13'-H$_{Ar}$/C-9' and C-13'], 6.22/92.1 [CH$_2$-NO$_2$/C-1'], 5.10/63.1/4.58/71.7 [6'-H$_{Ar}$/C-6'], 4.47/54.1 [2'-H'/C-2'], 3.71/60.8 [H-OCH$_3$/C-OCH$_3$], 3.64/56.1 [2xH-OCH$_3$/2xC-OCH$_3$], 3.46/58.4 [5'-H$_{eq}$/C-5'], 3.05/26.4 [H-NCH$_3$/C-NCH$_3$], 2.90/58.4 [5'-H$_{ax}$/C-5'], 2.22/30.7 [7'-H$_{eq}$/C-7'], 1.83-1.78/37.0 [7'-H$_{ax}$/C-7']. HMBC Correlation [δ_H/δ_C]: 8.40/74.2/127.5/143.2/150.5 [4-H$_{Ar}$/C-3'/C-6/C-3a/C-5], 8.29/121.0/143.2/150.5 [6-H$_{Ar}$/C-4/C-3a/C-5], 6.78/125.6/143.2 [7-H$_{Ar}$/C-7a/C-3a], 6.27/54.1/105.0/127.0/137.8/153.2 [9' and 13'-H$_{Ar}$/C-9' and C-13'], 6.22/92.1 [CH$_2$-NO$_2$/C-1'], 5.10/63.1/4.58/71.7 [6'-H$_{Ar}$/C-6'], 4.47/54.1 [2'-H'/C-2'], 3.71/60.8 [H-OCH$_3$/C-OCH$_3$], 3.64/56.1 [2xH-OCH$_3$/2xC-OCH$_3$], 3.46/58.4 [5'-H$_{eq}$/C-5'], 3.05/26.4 [H-NCH$_3$/C-NCH$_3$], 2.90/58.4 [5'-H$_{ax}$/C-5'], 2.22/30.7 [7'-H$_{eq}$/C-7'], 1.83-1.78/37.0 [7'-H$_{ax}$/C-7']. HRMS (ESI+): m/z: calcd for C$_{24}$H$_{27}$N$_4$O$_9$ ([M+H]$^+$) 515,1773, found: 515,1776; calcd for C$_{24}$H$_{26}$N$_4$O$_9$Na ([M+Na]$^+$) 537,1592, found: 537,1589.

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8.7 Hz, 7-\textit{H}_{\text{Ar}}), 6.61 (1H, d, \textit{J} = 1.7 Hz, 9'-\textit{H}_{\text{Ar}}), 6.56-6.50 (2H, m, 12' and 13'-\textit{H}_{\text{Ar}}),
6.15 (1H, t,

\[ J = 10.1 \text{ Hz, } CH-NO_2 \], 5.86 (1H, d, J = 1.4 Hz, 14’-H(eq), 5.84 (1H, d, J = 1.4 Hz, 14’-H(ax), 5.08 (1H, dd, J = 16.7, 8.2 Hz, 7a’-H), 4.56 (1H, t, J = 4.1 Hz, 6’-H), 4.47 (1H, d, J = 10.3 Hz, 2’-H), 3.45 (1H, dd, J = 9.3, 3.4 Hz, 5’-H(eq), 3.08 (3H, s, NCH_3), 2.88 (1H, dd, J = 9.3, 1.4 Hz, 5’-H(ax), 2.10 (1H, ddd, J = 14.5, 8.3, 1.1 Hz, 7’-H(ax), 1.83 (1H, br.s, -OH)), 1.79 (1H, ddd, J = 14.4, 7.2, 5.2 Hz, 7’-H(eq); 13C NMR (101 MHz, CDCl_3), \[ \delta_{(ppm)}: 175.9, 150.5, 148.1, 147.8, 143.3, 127.5 (+), 125.5, 124.9, 122.3 (+), 121.0 (+), 108.6 (+), 108.5 (+), 108.2 (+), 101.3 (-), 92.4 (+), 74.0, 71.7 (+), 62.9 (+), 58.4 (-), 53.6 (+), 37.0 (-), 26.5 (+); COSY Correlation \[ \delta_H/\delta_H \]: 8.38/8.29 [4-HAr/6-HAr], 8.29/6.78 [6-HAr/7-HAr], 6.61/6.56-6.50 [9’-HAr/12’ and 13’-HAr], 6.15/4.47 [CH-NO_2/2’-H], 6.15/5.08 [CH-NO_2/7a’-H], 5.08/1.79 [7a’-H/7’-H(eq)], 5.08/2.20 [7a’-H/7’-H(ax)], 4.56/1.79 [6’-H/7’-H(eq)], 4.56/3.45 [6’-H/5’-H(eq)], 3.45/2.88 [5’-H(eq)/5’-H(ax)], 2.88/2.20 [5’-H(ax)/7’-H(ax)], 2.21/1.79 [7’-H(ax)/7’-H(eq)]. HSQC Correlation \[ \delta_H/\delta_C \]: 8.38/121.0 [4-HAr/C-4], 8.29/127.5 [6-HAr/C-6], 6.78/108.5 [7-HAr/C-7], 6.61/108.2 [9’-HAr/C-9’], 6.56-6.50/108.6 [12’-HAr/C-12’], 6.56-6.50/122.3 [13’-HAr/C-13’], 6.15/92.4 [CH-NO_2/C-1’], 5.86/101.3 [14’-H(eq/C-OCH_2O), 5.84/101.3 [14’-H(ax/C-OCH_2O)], 5.08/62.9 [7a’-H/C-7a’], 4.56/71.7 [6’-H/C-6’], 4.47/53.6 [2’-H/C-2’], 3.45/58.4 [5’-H(eq/C-5’), 3.08/26.5 [H-NCH_3/C-NCH_3], 2.88/58.4 [5’-H(ax/C-5’), 2.21/37.0 [7’-H(ax/C-7’), 1.79/37.0 [7’-H(eq/C-7’)], HMBC Correlation \[ \delta_H/\delta_C \]: 8.38/74.0/127.5//143.3/150.5 [4-HAr/C-3’/C-6/C-3a/C-5], 8.29/121.0/143.3/150.5 [6-HAr/C-4/C-3a/C-5], 6.78/125.5/143.3 [7-HAr/C-7a/C-3a], 6.61/53.6/122.3/147.8/148.1 [9’-HAr/C-2’/C-13’/C-10’/C-11’], 6.56-6.50/108.2/124.9/147.8/148.1 [13’-HAr/C-9’/C-8’/C-10’/C-11’], 6.56-6.50/53.6/147.8/148.1 [12’-HAr/C-2’/C-10’/C-11’], 6.15/37.0/53.6/62.9/101.3/124.9 [CH-NO_2/C-7’/C-2’/C-7a’/C-OCH_2O/C-8’], 5.86/147.8/148.1 [14’-H(eq/C-10’/C-11’], 5.84/147.8/148.1 [14’-H(ax/C-10’/C-11’], 5.08/37.0/58.4 [7a’-H/C-7’/C-5’], 4.47/74.0/92.4/108.2/122.3/124.9/125.9/175.9 [2’-H/C-3’/C-1’/C-9’/C-13’/C-8’/C-2’], 3.45/74.0 [5’-H(eq/C-3’], 3.08/150.5/175.9 [NCH_3/C-5/C-2’], 2.88/37.0/62.9/71.7 [5’-H(ax/C-7’/C-7a’/C-6’), 2.20/58.4/71.7/92.4 [7’-H(ax/C-5’/C-6’/C-1’], 1.79/62.7/71.7/92.4 [7’-H(eq/C-7’/C-6’/C-1’]. HRMS (ESI+): m/z: calcd for C_{22}H_{21}N_4O_8 ([M+H]^+) 469,1354, found: 469,1359; Calcd for C_{22}H_{20}N_4O_8Na ([M+Na]^+) 491,1173, found: 491,1189.

3. Copies of 1H NMR, 13C NMR, DEPT-135, COSY, HSQC and HMBC charts of the synthesized spirooxindoles 1’-nitro pyrrolizidines 12a-12t.
Figure ESI1. $^1$H-NMR spectrum of 1'-nitro-2'-(3,4,5-trimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12a

Figure ESI2. $^{13}$C-NMR spectrum of 1'-nitro-2'-(3,4,5-trimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12a
Figure ESI3. DEPT-135 spectrum of 1’-nitro-2’-(3,4,5-trimethoxyphenyl)-1’,2’,5’,6’,7’,7a’-hexahydrospiro[indoline-3,3’-pyrrolizin]-2-one 12a

Figure ESI4. $^1$H-NMR spectrum of 1’-nitro-2’-(3,4-dimethoxyphenyl)-1’,2’,5’,6’,7’,7a’-hexahydrospiro[indoline-3,3’-pyrrolizin]-2-one 12b
Figure ESI5. $^{13}$C-NMR spectrum of 1'-nitro-2'-(3,4-dimethoxyphenyl)-1',2',5',6',7',7a'hexahydropyridine-3,3'-pyrrolizin]-2-one 12b

Figure ESI6. DEPT-135 spectrum of 1'-nitro-2'-(3,4-dimethoxyphenyl)-1',2',5',6',7',7a'hexahydropyridine-3,3'-pyrrolizin]-2-one 12b
Figure ESI7. COSY spectrum of 1'-nitro-2'-(3,4-dimethoxyphenyl)-1',2',5',6',7',7a'-hexahydropyrido[3',2'-indoline]-2'-one 12b

Figure ESI8. HSQC spectrum of 1'-nitro-2'-(3,4-dimethoxyphenyl)-1',2',5',6',7',7a'-hexahydropyrido[3',2'-indoline]-2'-one 12b

Figure ESI9. HMBC spectrum of 1'-nitro-2'(3,4-dimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12b

Figure ESI10. $^1$H-NMR spectrum of 1'-nitro-2'(3,4-methylenedioxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12c
Figure ESI11. $^{13}$C-NMR spectrum of 1'-nitro-2'-(3,4-methylenedioxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12c

Figure ESI12. DEPT-135 spectrum of 1'-nitro-2'-(3,4-methylenedioxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12c
Figure ESI13. $^1$H-NMR spectrum of 1-methyl-1'-nitro-2'- (3,4,5-trimethoxyphenyl)-1',2',5',6',7', 7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12d

Figure ESI14. $^{13}$C-NMR spectrum of 1-methyl-1'-nitro-2'- (3,4,5-trimethoxyphenyl)-1',2',5',6',7', 7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12d
Figure ESI15. DEPT-135 spectrum of 1-methyl-1’-nitro-2’-(3,4,5-trimethoxyphenyl)-1’,2’,5’,6’,7’,
7a’-hexahydrospiro[indoline-3,3’-pyrrolizin]-2-one 12d

Figure ESI16. COSY spectrum of 1-methyl-1’-nitro-2’-(3,4,5-trimethoxyphenyl)-1’,2’,5’,6’,7’,
7a’-hexahydrospiro[indoline-3,3’-pyrrolizin]-2-one 12d

**Figure ESI17.** HSQC spectrum of 1-methyl-1'-nitro-2'-{(3,4,5-trimethoxyphenyl)-1',2',5',6',7', 7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12d

**Figure ESI18.** HMBC spectrum of 1-methyl-1'-nitro-2'-{(3,4,5-trimethoxyphenyl)-1',2',5',6',7', 7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12d
**Figure ESI19.** $^1$H-NMR spectrum of 1-methyl-1'-nitro-2'-(3,4-dimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12e

**Figure ESI20.** $^{13}$C-NMR spectrum of 1-methyl-1'-nitro-2'-(3,4-dimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12e

**Figure ESI21.** DEPT-135 spectrum of 1-methyl-1'-nitro-2'(3,4-dimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12e

![DEPT-135 spectrum of 1-methyl-1'-nitro-2'(3,4-dimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12e](image1)

**Figure ESI22.** COSY spectrum of 1-methyl-1'-nitro-2'(3,4-dimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12e

![COSY spectrum of 1-methyl-1'-nitro-2'(3,4-dimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12e](image2)

Figure ESI23. HSQC spectrum of 1-methyl-1’-nitro-2’-(3,4-dimethoxyphenyl)-1’,2’,5’,6’,7’,7a’-hexahydrospiro[indoline-3,3’-pyrrolizin]-2-one 12e

Figure ESI24. HMBC spectrum of 1-methyl-1’-nitro-2’-(3,4-dimethoxyphenyl)-1’,2’,5’,6’,7’,7a’-hexahydrospiro[indoline-3,3’-pyrrolizin]-2-one 12e

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Figure ESI25. $^1$H-NMR spectrum of 1-methyl-1'-nitro-2'-{(3,4-methylenedioxyphenyl)-1',2',5',6',7', 7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12f

Figure ESI26. $^{13}$C-NMR spectrum of 1-methyl-1'-nitro-2'-{(3,4-methylenedioxyphenyl)-1',2',5',6',7', 7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12f

Figure ESI27. DEPT-135 spectrum of 1-methyl-1'-nitro-2'-3,4-methylenedioxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12f

![DEPT-135 spectrum of 1-methyl-1'-nitro-2'-3,4-methylenedioxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12f](image)

Figure ESI28. 1H-NMR spectrum of 6'-hydroxy-1-methyl-1'-nitro-2'-3,4,5-trimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12g

![1H-NMR spectrum of 6'-hydroxy-1-methyl-1'-nitro-2'-3,4,5-trimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12g](image)
Figure ESI29. $^{13}$C-NMR spectrum of 6'-hydroxy-1-methyl-1'-nitro-2'-(3,4,5-trimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12g

Figure ESI30. DEPT-135 spectrum of 6'-hydroxy-1-methyl-1'-nitro-2'-(3,4,5-trimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12g
Figure ESI31. COSY spectrum of 6'-hydroxy-1-methyl-1'-nitro-2'-(3,4,5-trimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12g

Figure ESI32. HSQC spectrum of 6'-hydroxy-1-methyl-1'-nitro-2'-(3,4,5-trimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12g

**Figure ESI33.** HMBC spectrum of 6'-hydroxy-1-methyl-1'-nitro-2'-(3,4,5-trimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12g

![HMBC spectrum of 6'-hydroxy-1-methyl-1'-nitro-2'-(3,4,5-trimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12g](image)

**Figure ESI34.** 1H-NMR spectrum of 6'-hydroxy-1-methyl-1'-nitro-2'-(3,4-dimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12h

![1H-NMR spectrum of 6'-hydroxy-1-methyl-1'-nitro-2'-(3,4-dimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12h](image)
Figure ESI35. $^{13}$C-NMR spectrum of 6'-hydroxy-1-methyl-1'-nitro-2'-(3,4-dimethoxyphenyl)-1',2',5',6',7,7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12h

Figure ESI36. DEPT-135 spectrum of 6'-hydroxy-1-methyl-1'-nitro-2'-(3,4-dimethoxyphenyl)-1',2',5',6',7,7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12h
Figure ESI37. COSY spectrum of 6’-hydroxy-1-methyl-1’-nitro-2’-(3,4-dimethoxyphenyl)-1’,2’,5’,6’,7’,7a’-hexahydrospiro[indoline-3,3’-pyrrolizin]-2-one 12h

Figure ESI38. HSQC spectrum of 6’-hydroxy-1-methyl-1’-nitro-2’-(3,4-dimethoxyphenyl)-1’,2’,5’,6’,7’,7a’-hexahydrospiro[indoline-3,3’-pyrrolizin]-2-one 12h

Figure ESI39. HMBC spectrum of 6'-hydroxy-1-methyl-1'-nitro-2'-(3,4-dimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12h

Figure ESI40. $^1$H-NMR spectrum of 6'-hydroxy-1-methyl-1'-nitro-2'-(3,4-methylenedioxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12i

**Figure ESI41.** $^{13}$C-NMR spectrum of 6'-hydroxy-1-methyl-1'-nitro-2'- (3,4-methylenedioxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12i

**Figure ESI42.** DEPT-135 spectrum of 6'-hydroxy-1-methyl-1'-nitro-2''-(3,4-methylenedioxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12i

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Figure ESI43. COSY spectrum of 6’-hydroxy-1-methyl-1’-nitro-2’-(3,4-methylenedioxyphenyl)-1’,2’,5’,6’,7’,7a’-hexahydrospiro[indoline-3,3’-pyrrolizin]-2-one 12i

Figure ESI44. HSQC spectrum of 6’-hydroxy-1-methyl-1’-nitro-2’-(3,4-methylenedioxyphenyl)-1’,2’,5’,6’,7’,7a’-hexahydrospiro[indoline-3,3’-pyrrolizin]-2-one 12i

Figure ESI45. HMBC spectrum of 6'-hydroxy-1-methyl-1'-nitro-2'(3,4-methylenedioxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12i

Figure ESI46. ¹H-NMR spectrum of 5-chloro-1-methyl-1'-nitro-2'(3,4,5-trimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12j
Figure ESI47. $^{13}$C-NMR spectrum of 5-chloro-1-methyl-1'-nitro-2'-(3,4,5-trimethoxyphenyl)-1',2',5',6',7,7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12j

Figure ESI48. DEPT-135 spectrum of 5-chloro-1-methyl-1'-nitro-2'-(3,4,5-trimethoxyphenyl)-1',2',5',6',7,7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12j
Figure ESI49. $^1$H-NMR spectrum of 5-chloro-1-methyl-1'-nitro-2'-(3,4-dimethoxyphenyl)-1',2',5',
6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12k

Figure ESI50. $^{13}$C-NMR spectrum of 5-chloro-1-methyl-1'-nitro-2'-(3,4-dimethoxyphenyl)-1',2',5',
6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12k

**Figure ESI51.** DEPT-135 spectrum of 5-chloro-1-methyl-1'-nitro-2'-(3,4-dimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12k

**Figure ESI52.** 1H-NMR spectrum of 5-chloro-1-methyl-1'-nitro-2'-(3,4-methylenedioxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12l

Figure ESI53. $^{13}$C-NMR spectrum of 5-chloro-1-methyl-1’-nitro-2’-(3,4-methylenedioxyphenyl)-1’,2’,5’,6’,7’,7a’-hexahydrospiro[indoline-3,3’-pyrrolizin]-2-one 12l

![13C-NMR spectrum of 5-chloro-1-methyl-1’-nitro-2’-(3,4-methylenedioxyphenyl)-1’,2’,5’,6’,7’,7a’-hexahydrospiro[indoline-3,3’-pyrrolizin]-2-one 12l](image)

Figure ESI54. DEPT-135 spectrum of 5-chloro-1-methyl-1’-nitro-2’-(3,4-methylenedioxyphenyl)-1’,2’,5’,6’,7’,7a’-hexahydrospiro[indoline-3,3’-pyrrolizin]-2-one 12l

![DEPT-135 spectrum of 5-chloro-1-methyl-1’-nitro-2’-(3,4-methylenedioxyphenyl)-1’,2’,5’,6’,7’,7a’-hexahydrospiro[indoline-3,3’-pyrrolizin]-2-one 12l](image)

Figure ESI55. $^1$H-NMR spectrum of 5-chloro-6’-hydroxy-1-methyl-1’-nitro-2’-(3,4,5-trimethoxy phenyl)-1’,2’,5’,6’,7’,7a’-hexahydrospiro[indoline-3,3’-pyrrolizin]-2-one 12m

Figure ESI56. $^{13}$C-NMR spectrum of 5-chloro-6’-hydroxy-1-methyl-1’-nitro-2’-(3,4,5-trimethoxy phenyl)-1’,2’,5’,6’,7’,7a’-hexahydrospiro[indoline-3,3’-pyrrolizin]-2-one 12m

Figure ESI57. DEPT-135 spectrum of 5-chloro-6'-hydroxy-1-methyl-1'-nitro-2'-(3,4,5-trimethoxy phenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12m

Figure ESI58. COSY spectrum of 5-chloro-6'-hydroxy-1-methyl-1'-nitro-2'-(3,4,5-trimethoxy phenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12m

Figure ESI59. HSQC spectrum of 5-chloro-6'-hydroxy-1-methyl-1'-nitro-2'(3,4,5-trimethoxy phenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12m

Figure ESI60. HMBC spectrum of 5-chloro-6'-hydroxy-1-methyl-1'-nitro-2'(3,4,5-trimethoxy phenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12m
Figure ESI61. $^1$H-NMR spectrum of 5-chloro-6'-hydroxy-1-methyl-1'-nitro-2'-(3,4-dimethoxy phenyl)-1',2','5','6','7','7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12n

Figure ESI62. $^{13}$C-NMR spectrum of 5-chloro-6'-hydroxy-1-methyl-1'-nitro-2'-(3,4-dimethoxy phenyl)-1',2','5','6','7','7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12n
Figure ESI63. DEPT-135 spectrum of 5-chloro-6'-hydroxy-1-methyl-1'-nitro-2'-((3,4-dimethoxy phenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12n

Figure ESI64. COSY spectrum of 5-chloro-6'-hydroxy-1-methyl-1'-nitro-2'-((3,4-dimethoxy phenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12n
Regio- and stereoselective synthesis of spirooxindole 1’-nitro pyrrolizidines.

**Figure ESI65.** HSQC spectrum of 5-chloro-6’-hydroxy-1-methyl-1’-nitro-2’-(3,4-dimethoxy phenyl)-1’,2’,5’,6’,7’,7a’-hexahydrospiro[indoline-3,3’-pyrrolizin]-2-one 12n

**Figure ESI66.** HMBC spectrum of 5-chloro-6’-hydroxy-1-methyl-1’-nitro-2’-(3,4-dimethoxy phenyl)-1’,2’,5’,6’,7’,7a’-hexahydrospiro[indoline-3,3’-pyrrolizin]-2-one 12n

**Figure ESI67.** $^1$H-NMR spectrum of 5-chloro-6'-hydroxy-1-methyl-1'-nitro-2'- (3,4-methylene dioxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12o

**Figure ESI68.** $^{13}$C-NMR spectrum of 5-chloro-6'-hydroxy-1-methyl-1'-nitro-2'- (3,4-methylene dioxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12o
**Figure ESI69.** DEPT-135 spectrum of 5-chloro-6'-hydroxy-1-methyl-1'-nitro-2'-(3,4-methylene dioxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12o

**Figure ESI70.** $^1$H-NMR spectrum of 1-methyl-1',5-dinitro-2'-(3,4,5-trimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12p
Figure ESI71. $^{13}$C-NMR spectrum of 1-methyl-1',5-dinitro-2'-(3,4,5-trimethoxyphenyl)-1',2',5',6', 7,7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12p

Figure ESI72. DEPT-135 spectrum of 1-methyl-1',5-dinitro-2'-(3,4,5-trimethoxyphenyl)-1',2',5',6', 7,7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12p
Figure ESI73. $^1$H-NMR spectrum of 1-methyl-1',5-dinitro-2'-(3,4-dimethoxyphenyl)-1',2',5',6',7', 7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12q

Figure ESI74. $^{13}$C-NMR spectrum of 1-methyl-1',5-dinitro-2'-(3,4-dimethoxyphenyl)-1',2',5',6',7', 7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12q

**Figure ESI75.** DEPT-135 spectrum of 1-methyl-1’,5-dinitro-2’-(3,4-dimethoxyphenyl)-1’,2’,5’,6’,7’, 7a’-hexahydrospiro[indoline-3,3’-pyrrolizin]-2-one 12q

![DEPT-135 spectrum of 1-methyl-1’,5-dinitro-2’-(3,4-dimethoxyphenyl)-1’,2’,5’,6’,7’, 7a’-hexahydrospiro[indoline-3,3’-pyrrolizin]-2-one 12q](image)

**Figure ESI76.** $^1$H-NMR spectrum of 1-methyl-1’,5-dinitro-2’-(3,4-methylenedioxyphenyl)-1’,2’,5’, 6’,7’,7a’-hexahydrospiro[indoline-3,3’-pyrrolizin]-2-one 12r

![$^1$H-NMR spectrum of 1-methyl-1’,5-dinitro-2’-(3,4-methylenedioxyphenyl)-1’,2’,5’, 6’,7’,7a’-hexahydrospiro[indoline-3,3’-pyrrolizin]-2-one 12r](image)
Figure ESI77. $^{13}$C-NMR spectrum of 1-methyl-1',5-dinitro-2'-{(3,4-methylenedioxyphenyl)-1',2',5', 6',7',7'a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12r

Figure ESI78. DEPT-135 spectrum of 1-methyl-1',5-dinitro-2'-(3,4-methylenedioxyphenyl)-1',2',5', 6',7',7'a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12r
**Figure ESI79.** $^1$H-NMR spectrum of 6'-hydroxy-1-methyl-1',5-dinitro-2'-(3,4,5-trimethoxyphenyl)-1',2,5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12s

**Figure ESI80.** $^{13}$C-NMR spectrum of 6'-hydroxy-1-methyl-1',5-dinitro-2'-(3,4,5-trimethoxyphenyl)-1',2,5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12s

**Figure ESI81.** DEPT-135 spectrum of 6'-hydroxy-1-methyl-1',5-dinitro-2'-(3,4,5-trimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12s

![DEPT-135 spectrum](image1)

**Figure ESI82.** COSY spectrum of 6'-hydroxy-1-methyl-1',5-dinitro-2'-(3,4,5-trimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12s

![COSY spectrum](image2)
Figure ESI83. HSQC spectrum of 6’-hydroxy-1-methyl-1’,5-dinitro-2’-(3,4,5-trimethoxyphenyl)-1’,2’,5’,6’,7’,7a’-hexahydrospiro[indoline-3,3’-pyrrolizin]-2-one 12s

Figure ESI84. HMBC spectrum of 6’-hydroxy-1-methyl-1’,5-dinitro-2’-(3,4,5-trimethoxyphenyl)-1’,2’,5’,6’,7’,7a’-hexahydrospiro[indoline-3,3’-pyrrolizin]-2-one 12s
Figure ESI85. \( ^1\)H-NMR spectrum of 6'-hydroxy-1-methyl-1',5-dinitro-2'-(3,4-methylenedioxy phenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12t

![1H-NMR spectrum of 6'-hydroxy-1-methyl-1',5-dinitro-2'-(3,4-methylenedioxy phenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12t](image)

Figure ESI86. \( ^{13}\)C-NMR spectrum of 6'-hydroxy-1-methyl-1',5-dinitro-2'-(3,4-methylenedioxy phenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12t

![\( ^{13}\)C-NMR spectrum of 6'-hydroxy-1-methyl-1',5-dinitro-2'-(3,4-methylenedioxy phenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12t](image)
**Figure ESI87.** DEPT-135 spectrum of 6'-hydroxy-1-methyl-1',5-dinitro-2'-(3,4-methylenedioxy phenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12t

**Figure ESI88.** COSY spectrum of 6'-hydroxy-1-methyl-1',5-dinitro-2'-(3,4-methylenedioxy phenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12t

Figure ESI89. HSQC spectrum of 6'-hydroxy-1-methyl-1',5-dinitro-2'- (3,4-methylenedioxy phenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12t

Figure ESI90. HMBC spectrum of 6'-hydroxy-1-methyl-1',5-dinitro-2'- (3,4-methylenedioxy phenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12t
4. Copies of NOESY charts of the synthesized spirooxindoles 1'-nitro pyrrolizidines 12j and 12s.

Figure ESI91. NOESY spectrum of 5-chloro-1-methyl-1'-nitro-2'-(3,4,5-trimethoxyphenyl)-1',2',5',6',7',7a'-hexahydrospiro[indoline-3,3'-pyrrolizin]-2-one 12j.
5. Structural elucidation of spirooxindole 1'-nitropyrrrolizidine 12t through $^1$H, COSY and HMBC experiments.

The $^1$H-NMR experiment for compound 12t showed a general group of characteristic signals for the aromatic protons present in the isatin and the aryl moiety form the respective $\beta$-nitrostyrenes. While the coupling constants of protons from the pyrrolizidine ring, identified as H-1' (t, $J = 10.1$ Hz), H-2' (d, $J = 10.3$ Hz, 1H) and H-7a' (dd, $J = 16.7, 8.2$ Hz, 1H), established the trans- configuration between protons H-1' and H-2' and the cis-configuration within H-1' and H-7a', correlation corroborated by the H-H COSY experiment (Figure 3). Each methylene group in this ring displayed two groups of signals, for example: the protons H-5' presented a two pairs of doublet of doublets at 3.45 ppm ($J = 9.3, 3.4$ Hz, 1H), corresponding to the equatorial H-5', and at 2.88 ppm ($J = 9.3, 1.4$ Hz, 1H) for the axial H-5'. Likewise, the protons H-7' exhibit as well two pairs of doublet of doublets at 2.20 ppm ($J = 14.5, 8.3, 1.1$ Hz, 1H), for the axial proton H-7', and at 1.79 ppm ($J = 14.4, 7.2, 5.2$ Hz, 1H), corresponding to the equatorial proton H-7'. The correlation between these protons and their connectivity with the pyrrolizidine skeleton, as well as their interaction with proton H-6' found at 4.56 ppm (t, $J = 4.1$ Hz, 1H), were determined with H-H COSY and HMBC experiments. Finally, the hydroxyl group (-OH) appeared as a broad signal at 1.83 ppm.

Selected H-H COSY correlation (↔) and HMBC connectivity (→) for the pyrrolizidine core of 12t.

6. Photographic record of the phenotypic changes during the development of the zebrafish embryo treated with compound 12l after 96 hpf.

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<th>Compound</th>
<th>96 hours post-fecundation, concentration in μM</th>
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<tr>
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<tr>
<td>Control</td>
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<td><img src="image8.png" alt="Image" /> 50 <img src="image9.png" alt="Image" /></td>
<td>LC₅₀ (μmol/L ± SEM) 419.59 ± 9.92</td>
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7. Photographic record of the phenotypic changes during the development of the zebrafish embryo treated with compound 12m after 96 hpf.

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<td>LC₅₀ (μmol/L ± SEM) 211.09 ± 8.27</td>
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8. Photographic record of the phenotypic changes during the development of the zebrafish embryo treated with compound 12o after 96 hpf.

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<td>LC₅₀ (μmol/L ± SEM)</td>
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