Construction of tetrahydro-β-carboline skeleton via Brønsted acid activation of imide carbonyl group: Syntheses of indole alkaloids (±)-harmicine and (±)-10-desbromoarborescidine-A

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(A) General Information

Instrumentation. All reactions were performed in oven-dried round bottom flasks. Stainless steel syringes or cannulae were used to transfer air and moisture sensitive liquids. Melting points reported in this paper are uncorrected and were determined using EZ Melt, Stanford Research Systems, USA. Infrared spectra were recorded on Thermo Nicolet 6700 FT-IR Spectrophotometer and are reported in frequency of absorption (cm⁻¹). High resolution mass spectra (HRMS) were recorded on Q-TOF Micro mass spectrometer. ¹H and ¹³C NMR were recorded on Brucker AVANCE 400 spectrometer. NMR spectra for all the samples were measured either in CDCl₃ or DMSO-d₆ or acetone-d₆ a using TMS as an internal standard. The chemical shifts are expressed in δ ppm down field from the signal of internal TMS. Data are represented as follows: chemical shift, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, dd = doublet of doublet, ddd = doublet of doublet of doublet, td = triplet of doublet, dt = doublet of triplet, sep = septet, m = multiplet), coupling constants in Hertz (Hz), and integration. Trifluromethanesulphonic acid, 4-amino-1-butanol, oxalyl chloride, substituted phenyl hydrazine hydrochloride were purchased from Aldrich; remaining from local products and used without further purification. Column chromatography was performed on Merck silica gel 100-200 mesh, neutral alumina 70-230 mesh and TLC analysis was facilitated using phosphomolybdic acid stain in addition to UV light with Merck 60 F₂₅₄ pre-coated silica plates.

Representative Experimental procedures

(B) Synthesis of 6, 7, 8, 9

2-(4-Hydroxybutyl)isoindoline-1,3-dione (6)\(^1\)

A mixture of finely powdered phthalic anhydride (8.308 g, 56.092 mmol) and 4-amino-1-butanol (5.000 g, 56.092 mmol) were heated at 170 °C with vigorous stirring under nitrogen atmosphere. After 6 h the reaction mixture was cooled to 80 °C and it was poured to 100 mL of ice-cold water. The product was extracted with CHCl\(_3\) (4 x 100 mL), and the combined organic layer was washed with 5% NaHCO\(_3\) solution (3 x 100 mL), and with water (3 x 100 mL). Organic layer was dried over anhydrous Na\(_2\)SO\(_4\), filtered and the solvent was removed under vacuum to give the mixture, which was purified through silica gel column chromatography using ethyl acetate : hexane as eluent (2:5) to give 2-(4-hydroxybutyl)isoindoline-1,3-dione in 92% yield (11.314 g) as colorless solid. (m.p. : 45-46 °C, lit.\(^1\) 47-49 °C); IR (KBr, cm\(^{-1}\)) : 3471, 2938, 1771, 1710, 1399; \(^1\)H-NMR (CDCl\(_3\), 400 MHz) : δ 7.84 (dd, \(J = 5.4, 3.0 \text{ Hz}, 2\text{H}\)), 7.71 (dd, \(J = 5.4, 3.0 \text{ Hz}, 2\text{H}\)), 3.74 (t, \(J = 7.2 \text{ Hz}, 2\text{H}\)), 3.69 (t, \(J = 6.4 \text{ Hz}, 2\text{H}\)), 1.82-1.75 (m, 2H), 1.66-1.59 (m, 2H); \(^13\)C-NMR (CDCl\(_3\), 100 MHz): 168.63, 134.06, 132.23, 123.34, 62.43, 37.84, 29.90, 25.23.

2-(3-(1,3-Dioxan-2-yl)propyl)isoindoline-1,3-dione (7)

To a well stirred solution of oxalyl chloride (2.8 mL, 33.56 mmol) in 20 mL of CH\(_2\)Cl\(_2\), a solution of anhydrous (CH\(_3\))\(_2\)SO (5.7 mL, 80.24 mmol) in 20 mL of CH\(_2\)Cl\(_2\) was added under nitrogen atmosphere at -50 °C at such a rate that temperature was maintained
at -50 °C. Stirring was continued for additional 15 min, then a solution of 2-(4-hydroxybutyl)isoindoline-1,3-dione (5.00 g, 22.82 mmol) in 40 mL of CH2Cl2 was added while keeping the temperature at -50 °C. The reaction mixture was stirred for another 1 h at -50 °C, and triethylamine (21.42 mL, 153.56 mmol) was added. The mixture is allowed to warm to room temperature, and 200 mL of water was added and stirred for 30 min. The organic layer was separated and washed with water, dried over anhydrous Na2SO4, filtered and concentrated in vacuo. The crude 4-(1,3-dioxoisindolin-2-yl)butanal was obtained as viscous oil in 98% yield (4.84 g) and was stored under nitrogen atmosphere and used without further purification for the next step.

Propane-1,3-diol (4.2 g, 55.28 mmol) was added to a solution of 4-(1,3-dioxoisindolin-2-yl)butanal (4.0 g, 18.4 mmol) and p-toluenesulphonic acid monohydrate (0.348 g, 0.92 mmol) in toluene (200 mL) at room temperature. The solution was stirred for 12 h, then diluted with ethyl acetate (200 mL) and washed with saturated NaHCO3 (60 mL). The layers were separated and the aqueous layer was extracted with ethyl acetate (4 x 50 mL). The combined organic layers were dried over anhydrous MgSO4 filtered and concentrated under reduced pressure. The residue was purified through column chromatography using silica gel and ethyl acetate : hexane : (1:1) to give 2-(3-(1,3-dioxan-2-yl)propyl)isoindoline-1,3-dione in 84% yield (4.256 g) as colorless solid. (m.p. : 86-87 °C); IR (KBr, cm⁻¹) : 3064, 2949, 2843, 1764, 1715, 1613, 1143; ¹H-NMR (CDCl3, 400 MHz) : 7.82 (dd, J = 5.4, 3.0 Hz, 2H), 7.69 (dd, J = 5.4, 3.0 Hz, 2H), 4.55 (t, J = 5.0 Hz, 1H), 4.07 (dd, J = 5.0, 1.2 Hz, 1H), 4.03 (dd, J = 5.0, 1.2 Hz, 1H), 3.76 (dd, J = 2.4, 1.6 Hz, 1H), 3.73 (d, J = 2.4 Hz, 1H), 3.70 (t, J = 7.2 Hz, 2H), 2.10-1.98 (m, 1H), 1.84-1.76 (m, 2H), 1.65 (d, J = 5.0 Hz, 1H), 1.63-1.61 (m, 1H), 1.30 (d of sep, J = 13.2, 1.2 Hz, 1H); ¹³C-NMR (CDCl3, 100 MHz) : 168.50, 133.97, 132.29, 123.27, 101.69, 66.97, 37.84, 32.49, 25.89, 23.24.

1-(4-Hydroxybutyl)pyrrolidine-2,5-dione (8)

A mixture of finely powdered succinic anhydride (4.491 g, 44.873 mmol) and 4-amino-1-butanol (4.000 g, 44.873 mmol) were heated at 170 °C with vigorous stirring under nitrogen atmosphere. After 6 h the reaction mixture was cooled to room temperature and distilled under reduced pressure to give 1-(4-hydroxybutyl)pyrrolidine-2,5-dione in 70% yield (5.377 g) as
colorless viscous liquid. IR (KBr, cm\(^{-1}\)) : 3448, 2942, 1764, 1695, 1250; \(^1\)H-NMR (CDCl\(_3\), 400 MHz) : \(\delta\) 3.67-3.62 (m, 2H), 3.56-3.51 (m, 2H), 2.69-2.68 (m, 4H), 1.69-1.61 (m, 2H), 1.58-1.51 (m, 2H); \(^1\)C-NMR (CDCl\(_3\), 100 MHz) : 177.44, 62.16, 38.54, 29.69, 28.17, 24.24.

1-(3-(1,3-Dioxan-2-yl)propyl)pyrrolidine-2,5-dione (9)

To a well stirred solution of oxalyl chloride (2.9 mL, 34.36 mmol) in 20 mL of CH\(_2\)Cl\(_2\), a solution of anhydrous (CH\(_3\))\(_2\)SO (5.8 mL, 82.16 mmol) in 20 mL of CH\(_2\)Cl\(_2\) was added under nitrogen atmosphere at -50 °C at such a rate that temperature was maintained at -50 °C. Stirring was continued for additional 15 min, then a solution of 1-(4-hydroxybutyl)pyrrolidine-2,5-dione (4.00 g, 23.37 mmol) in 40 mL of CH\(_2\)Cl\(_2\) was added while keeping the temperature at -50 °C. The reaction mixture was stirred for another 1 h at -50 °C, and triethylamine (21.93 mL, 157.23 mmol) was added. The mixture is allowed to warm to room temperature, and 200 mL of water was added and stirred for 30 min. The organic layer was separated and washed with water, dried over anhydrous Na\(_2\)SO\(_4\), filtered and concentrated in vacuo. The crude 4-(2,5-dioxopyrrolidin-1-yl)butanal was obtained as viscous oil in 98% yield (3.87 g) and was stored under nitrogen atmosphere and used without further purification for the next step.

Propane-1,3-diol (4.73 g, 62.15 mmol) was added to a solution of 4-(2,5-dioxopyrrolidin-1-yl)butanal (3.5 g, 20.69 mmol) and p-toluenesulphonic acid monohydrate (0.196 g, 1.0344 mmol ) in toluene (200 mL) at room temperature. The solution was stirred for 12 h, then diluted with ethyl acetate (200 mL) and washed with saturated NaHCO\(_3\) (60 mL). The layers were separated and the aqueous layer was extracted with ethyl acetate (4 x 50 mL). The combined organic layers were dried over anhydrous MgSO\(_4\), filtered and concentrated under reduced pressure. The residue was purified through column chromatography using silica gel and ethyl acetate : hexane as eluent (1:1) to give 1-(3-(1,3-dioxan-2-yl)propyl)pyrrolidine-2,5-dione in 84% yield (4.256 g) as colorless solid. (m.p. : 112-113 °C); IR (KBr, cm\(^{-1}\)) : 2861, 1763, 1695, 1238, 1145; \(^1\)H-NMR (CDCl\(_3\), 400 MHz) : \(\delta\) 4.51 (t, \(J = 5.0\) Hz, 1H), 4.05 (ddd, \(J = 12.4, 5.0, 1.2\) Hz, 2H), 3.72 (td, \(J = 12.4, 2.4\) Hz, 2H), 3.50 (t, \(J = 7.2\) Hz, 2H), 2.66 (s, 4H), 2.09-1.97 (m, 1H), 1.73-1.64 (m, 2H), 1.56 (dd, \(J = 8.8, 5.0\) Hz, 2H), 1.30 (d of sep, \(J = 13.5, 1.2\) Hz, 1H); \(^1\)C-NMR (CDCl\(_3\), 100 MHz) : 177.17, 101.47, 66.82, 38.50, 32.28, 28.11, 25.72, 22.20.
General procedure for the synthesis of imide derivative of tryptamine

\[
\text{Phthalic anhydride (2.773 g, 18.725 mmol)} + \text{Tryptamine (3.000 g, 18.725 mmol)} \rightarrow \text{2-(2-(1H-Indol-3-yl)ethyl)isoindoline-1,3-dione (1a)}^{2}
\]

A suspension of phthalic anhydride (2.773 g, 18.725 mmol) in toluene in an oven dried round bottom flask fitted with Dean-Stark set up was heated at reflux until complete dissolution of the anhydride and no additional water was removed. To this solution was added tryptamine (3.000 g, 18.725 mmol) and refluxing was continued until the water evolution was completed (12 h). Reaction mixture was concentrated under reduced pressure to give a residue which was purified through neutral alumina column chromatography using ethyl acetate : hexane as eluent (1:4) to give 2-(2-(1H-indol-3-yl)ethyl)isoindoline-1,3-dione in 78% yield (4.240 g) as yellow solid. (m.p. : 166-167 °C, lit.\(^2\) 166-168 °C); IR (KBr, cm\(^{-1}\)) : 3383, 3044, 2942, 2858, 1767, 1703, 1233; \(^1\)H-NMR (CDCl\(_3\), 400 MHz) : δ 8.05 (br s, 1H), 7.83 (dd, \(J = 5.4, 3.0 \text{ Hz}, 2H\)), 7.74 (dt, \(J = 8.0, 0.8 \text{ Hz}, 1H\)), 7.70 (dd, \(J = 5.4, 3.0 \text{ Hz}, 2H\)), 7.34 (dt, \(J = 7.6, 0.8 \text{ Hz}, 1H\)), 7.19 (td, \(J = 7.6, 1.2 \text{ Hz}, 1H\)), 7.13 (td, \(J = 8.0, 1.2 \text{ Hz}, 1H\)), 7.08 (d, \(J = 2.4 \text{ Hz}, 1H\)), 4.04-3.99 (m, 2H), 3.19-3.15 (m, 2H); \(^1\)C-NMR (CDCl\(_3\), 100 MHz) : 168.51, 136.37, 134.00, 132.34, 127.55, 123.31, 122.27, 122.14, 119.66, 119.01, 112.59, 111.24, 38.66, 24.60.

\[
\text{1-(2-(1H-Indol-3-yl)ethyl)pyrrolidine-2,5-dione (1i)}^{3}
\]

A suspension of succinic anhydride (1.874 g, 18.725 mmol) in toluene in an oven dried round bottom flask fitted with Dean-Stark set up was heated at reflux until complete dissolution of the anhydride and no additional water was removed. To this solution was added tryptamine (3.000 g, 18.725 mmol) and refluxing was continued until the water evolution was completed (12 h). Reaction mixture was concentrated under reduced pressure to give a residue which was purified through neutral alumina column chromatography using ethyl acetate : hexane as eluent (1:4) to give 1-(2-(1H-indol-3-yl)ethyl)pyrrolidine-2,5-dione in 71% yield (3.211 g) as tan solid. (m.p. : 166-167 °C, lit.\(^3\) 163-166 °C); IR (KBr, cm\(^{-1}\)) : 3265, 3052, 2925, 1764, 1694, 1401, 1339; \(^1\)H-NMR (CDCl\(_3\), 400 MHz) : δ 8.04 (br s, 1H), 7.66 (d, \(J = 8.0 \text{ Hz}, 1H\), 7.45 (d, \(J = 2.4 \text{ Hz}, 1H\)), 7.40-7.36 (m, 2H), 7.19-7.15 (m, 2H), 7.03 (m, 2H), 4.03-3.97 (m, 2H), 3.20-3.16 (m, 2H); \(^1\)C-NMR (CDCl\(_3\), 100 MHz) : 168.54, 136.37, 134.00, 132.34, 127.55, 123.31, 122.27, 122.14, 119.66, 119.01, 112.59, 111.24, 38.66, 24.60.
S7
7.34 (d, J = 8.0 Hz, 1H), 7.19 (t, J = 7.6 Hz, 1H), 7.13 (t, J = 7.6 Hz, 1H), 7.08 (d, J = 1.9 Hz, 1H), 3.83 (t, J = 7.6 Hz, 2H), 3.06 (t, J = 7.6 Hz, 2H), 2.61 (s, 4H); 13C-NMR (CDCl3, 100 MHz) : 177.38, 136.29, 127.64, 122.27, 122.23, 119.67, 118.77, 112.41, 111.30, 39.65, 28.29, 23.45.

1-(2-(1H-Indol-3-yl)ethyl)piperdine-2,6-dione (1r)

A suspension of glutaric anhydride (2.136 g, 18.725 mmol) in toluene in an oven dried round bottom flask fitted with Dean-Stark set up was heated at reflux until complete dissolution of the anhydride and no additional water was removed. To this solution was added tryptamine (3.000 g, 18.725 mmol) and refluxing was continued until the water evolution was completed (12 h). Reaction mixture was concentrated under reduced pressure to give a residue which was purified through neutral alumina column chromatography using ethyl acetate : hexane as eluent (1:4) to give 1-(2-(1H-indol-3-yl)ethyl)piperdine-2,6-dione in 67% yield (3.215 g) as tan solid. (m.p. : 174-175 °C), IR (KBr, cm⁻¹) : 3333, 2971, 2958, 1718, 1665, 1456, 1354; ¹H-NMR (CDCl3, 400 MHz) : δ 8.02 (br s, 1H), 7.77 (d, J = 7.6 Hz, 1H), 7.34 (d, J = 8.0 Hz, 1H), 7.20-7.12 (m, 2H), 7.06 (d, J = 1.7 Hz, 1H), 4.07 (t, J = 8.0 Hz, 2H), 2.98 (t, J = 8.0 Hz, 2H), 2.61 (t, J = 6.4 Hz, 4H), 1.87 (p, 6.4 Hz, 2H); ¹³C-NMR (CDCl3, 100 MHz) : 172.67, 136.27, 127.78, 122.25, 122.13, 119.56, 119.25, 113.06, 111.17, 40.45, 32.99, 23.84, 17.26.

2-(2-(1H-Indol-3-yl)ethyl)hexahydro-1H-isoindole-1,3(2H)-dione (1q)

A suspension of hexahydrophthalic anhydride (2.887 g, 18.725 mmol) in toluene in an oven dried round bottom flask fitted with Dean-Stark set up was heated at reflux until complete dissolution of the anhydride and no additional water was removed. To this solution was added tryptamine (3.000 g, 18.725 mmol) and refluxing was continued until the water evolution was completed (12 h). Reaction mixture was concentrated under reduced pressure to give a residue which was purified through neutral alumina column chromatography using ethyl acetate : hexane as eluent (1:4) to give 2-(2-(1H-indol-3-yl)ethyl)hexahydro-1H-isoindole-1,3(2H)-dione in 63% yield (3.496 g) as pale orange solid. (m.p. : 145-146 °C); IR (KBr, cm⁻¹) : 3364, 2944, 2860, 1766, 1694, 1401, 1341; ¹H-NMR (CDCl3, 400 MHz) : δ 8.02 (br s, 1H), 7.69 (d, J = 7.6 Hz, 1H), 7.34 (d, J = 8.0 Hz, 1H), 7.18 (t, J = 7.2 Hz, 1H), 7.15-7.11 (m, 1H), 7.07 (d, J = 1.8 Hz, 1H), 3.82 (t, J = 7.6 Hz, 2H), 3.07
(t, J = 7.6 Hz, 2H), 2.78-2.72 (m, 2H), 1.79-1.77 (m, 2H), 1.64-1.61 (m, 2H), 1.42-1.31 (m, 4H); \(^{13}\)C-NMR (CDCl\(_3\), 100 MHz) : 179.98, 136.25, 127.63, 122.28, 122.13, 119.55, 118.93, 112.17, 111.21, 39.73, 39.12, 23.69, 23.37, 21.62.

(D) General procedure for the synthesis of imide derivative of substituted tryptamine

\[ \text{R} \quad \text{N} \quad \text{HCl} \]

\[ \text{O} \quad \text{O} \quad \text{H} \quad \text{O} \quad \text{O} \]

\[ \text{N} \quad \text{H} \quad \text{N} \]

\[ \text{R} = \text{H, OMe, Me} \quad \text{F, Cl, Br} \]

\[ 1b - 1h \quad \text{and} \quad 1j - 1p \]

Where, X = 1,2-C\(_6\)H\(_4\) = 7

X = -CH\(_2\)CH\(_2\) = 9

2-(2-(5-Methoxy-1H-indol-3-yl)ethyl)isoindoline-1,3-dione (1f)

A mixture of (4-methoxyphenyl)hydrazine hydrochloride (349 mg, 1.998 mmol) and 2-(3-(1,3-dioxan-2-yl)propyl)isoindoline-1,3-dione (550 mg, 1.998 mmol) in 100 mL of 4% H\(_2\)SO\(_4\) was heated at reflux for 12 h. The reaction mixture was cooled to room temperature and treated with aqueous NaHCO\(_3\). The tryptamine product was extracted with CH\(_2\)Cl\(_2\) (4 x 50 mL). The combined organic layer was dried over anhydrous Na\(_2\)SO\(_4\), filtered and the solvent was evaporated under reduced pressure. The residue was purified through neutral alumina column chromatography using ethyl acetate : hexane (1:4) as eluent to give 2-(2-(5-methoxy-1H-indol-3-yl)ethyl)isoindoline-1,3-dione in 67% yield (429 mg) as yellow solid. (m.p. : 160-161 °C); IR (KBr, cm\(^{-1}\)) : 3390, 2999, 2939, 2835, 1765, 1704, 1579, 1398, 1211, 1097; \(^1\)H-NMR (CDCl\(_3\), 400 MHz) : δ 7.95 (br s, 1H), 7.83 (dd, J = 5.4, 3.0 Hz, 2H), 7.70 (dd, J = 5.4, 3.0 Hz, 2H), 7.22 (d, J = 8.8 Hz, 1H), 7.16 (d, J = 2.4 Hz, 1H), 7.06 (d, J = 2.4 Hz, 1H), 6.83 (dd, J = 8.8, 2.4 Hz, 1H), 4.02-3.98 (m, 2H), 3.86 (s, 3H), 3.14-3.10 (m, 2H); \(^{13}\)C-NMR (CDCl\(_3\), 100 MHz) : 168.39, 154.08, 133.87, 132.19, 131.30, 127.81, 123.16, 122.74, 112.57, 112.20, 111.89, 100.31, 55.82, 38.44, 24.50.

2-(2-(7-Methyl-1H-indol-3-yl)ethyl)isoindoline-1,3-dione (1g)

A mixture of o-tolylhydrazine hydrochloride (317 mg, 1.998 mmol) and 2-(3-(1,3-dioxan-2-yl)propyl)isoindoline-1,3-dione (550 mg, 1.998 mmol) in 100 mL of 4% H\(_2\)SO\(_4\) was heated at reflux for 12 h. The reaction mixture was cooled to room temperature and treated with aqueous NaHCO\(_3\). The tryptamine product was extracted with
CH$_2$Cl$_2$ (4 x 50 mL). The combined organic layer was dried over anhydrous Na$_2$SO$_4$, filtered and the solvent was evaporated under reduced pressure. The residue was purified through neutral alumina column chromatography using ethyl acetate : hexane (1:4) as eluent to give 2-(2-(7-methyl-1H-indol-3-yl)ethyl)isoindoline-1,3-dione in 64% yield (389 mg) as orange solid. (m.p. : 208-209 °C); IR (KBr, cm$^{-1}$) : 3391, 3045, 2931, 2857, 1760, 1703, 1438, 1072; $^1$H-NMR (CDCl$_3$, 400 MHz) : $\delta$ 7.95 (br s, 1H), 7.83 (dd, $J = 5.4$, 3.0 Hz, 2H), 7.70 (dd, $J = 5.4$, 3.0 Hz, 2H), 7.60 (d, $J = 7.6$ Hz, 1H), 7.11 (d, $J = 2.0$ Hz, 1H), 7.06 (t, $J = 7.6$ Hz, 1H), 6.99 (d, $J = 7.0$ Hz, 1H), 4.03-3.99 (m, 2H), 3.15 (t, $J = 7.6$ Hz, 2H), 2.48 (s, 3H); $^{13}$C-NMR (CDCl$_3$, 100 MHz) : 168.52, 135.97, 134.00, 132.35, 127.08, 123.32, 122.82, 121.86, 120.39, 119.90, 116.76, 113.08, 38.68, 24.75, 16.71.

2-(2-(5,7-Dimethyl-1H-indol-3-yl)ethyl)isoindoline-1,3-dione (1h)

A mixture of (2,4-dimethylphenyl)hydrazine hydrochloride (345 mg, 1.998 mmol) and 2-(3-(1,3-dioxan-2-yl)propyl)isoindoline-1,3-dione (550 mg, 1.998 mmol) in 100 mL of 4% H$_2$SO$_4$ was heated at reflux for 12 h. The reaction mixture was cooled to room temperature and treated with aqueous NaHCO$_3$. The tryptamine product was extracted with CH$_2$Cl$_2$ (4 x 50 mL). The combined organic layer was dried over anhydrous Na$_2$SO$_4$, filtered and the solvent was evaporated under reduced pressure. The residue was purified through neutral alumina column chromatography using ethyl acetate : hexane (1:4) as eluent to give 2-(2-(5,7-dimethyl-1H-indol-3-yl)ethyl)isoindoline-1,3-dione in 59% yield (375 mg) as pale brown solid. (m.p. : 221-222 °C); IR (KBr, cm$^{-1}$) : 3380, 2919, 2856, 1766, 1705, 1608, 1442, 1086; $^1$H-NMR (CDCl$_3$, 400 MHz) : $\delta$ 7.87 (br s, 1H), 7.83 (dd, $J = 5.4$, 3.0 Hz, 2H), 7.70 (dd, $J = 5.4$, 3.0 Hz, 2H), 7.34 (s, 1H), 7.06 (d, $J = 1.7$ Hz, 1H), 6.82 (s, 1H), 3.99 (t, $J = 7.6$ Hz, 2H), 3.12 (t, $J = 7.6$ Hz, 2H), 2.43 (s, 3H), 2.40 (s, 3H); $^{13}$C-NMR (CDCl$_3$, 100 MHz) : 168.53, 134.27, 133.96, 132.35, 129.12, 127.33, 124.54, 123.27, 122.02, 120.05, 116.25, 112.55, 38.79, 24.73, 21.54, 16.64.

2-(2-(5-Fluoro-1H-indol-3-yl)ethyl)isoindoline-1,3-dione (1b)

A mixture of (4-fluorophenyl)hydrazine hydrochloride (325 mg, 1.998 mmol) and 2-(3-(1,3-dioxan-2-yl)propyl)isoindoline-1,3-dione (550 mg, 1.998 mmol) in 100 mL of 4% H$_2$SO$_4$ was heated at reflux for 12 h. The reaction mixture was cooled to room temperature and treated with aqueous NaHCO$_3$. The tryptamine product was extracted with CH$_2$Cl$_2$ (4 x 50 mL). The combined organic layer was dried over anhydrous Na$_2$SO$_4$, filtered and the solvent was evaporated under reduced pressure. The residue was purified through neutral alumina column chromatography using ethyl acetate : hexane (1:4) as eluent to give 2-(2-(5-fluoro-1H-indol-3-yl)ethyl)isoindoline-1,3-dione in 64% yield (389 mg) as orange solid. (m.p. : 208-209 °C); IR (KBr, cm$^{-1}$) : 3391, 3045, 2931, 2857, 1760, 1703, 1438, 1072; $^1$H-NMR (CDCl$_3$, 400 MHz) : $\delta$ 7.95 (br s, 1H), 7.83 (dd, $J = 5.4$, 3.0 Hz, 2H), 7.70 (dd, $J = 5.4$, 3.0 Hz, 2H), 7.60 (d, $J = 7.6$ Hz, 1H), 7.11 (d, $J = 2.0$ Hz, 1H), 7.06 (t, $J = 7.6$ Hz, 1H), 6.99 (d, $J = 7.0$ Hz, 1H), 4.03-3.99 (m, 2H), 3.15 (t, $J = 7.6$ Hz, 2H), 2.48 (s, 3H); $^{13}$C-NMR (CDCl$_3$, 100 MHz) : 168.52, 135.97, 134.00, 132.35, 127.08, 123.32, 122.82, 121.86, 120.39, 119.90, 116.76, 113.08, 38.68, 24.75, 16.71.

Electronic Supplementary Material (ESI) for RSC Advances

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temperature and treated with aqueous NaHCO₃. The tryptamine product was extracted with CH₂Cl₂ (4 x 50 mL). The combined organic layer was dried over anhydrous Na₂SO₄, filtered and the solvent was evaporated under reduced pressure. The residue was purified through neutral alumina column chromatography using ethyl acetate : hexane (1:4) as eluent to give 2-(2-(5-fluoro-1H-indol-3-yl)ethyl)isoindoline-1,3-dione in 75% yield (462 mg) as pale yellow solid. (m.p. : 125-126 °C, lit.⁶ 122-124 °C); IR (KBr, cm⁻¹) : 3390, 3048, 2934, 1766, 1702, 1448, 1402, 1247, 716; ¹H-NMR (CDCl₃, 400 MHz) : δ 8.04 (br s, 1H), 7.83 (dd, J = 5.4, 3.0 Hz, 2H), 7.70 (dd, J = 5.4, 3.0 Hz, 2H), 7.34 (dd, J = 9.6, 2.4 Hz, 1H), 7.24 (t, J = 4.4 Hz, 1H), 7.12 (d, J = 2.0 Hz, 1H), 6.91 (td, J = 9.0, 2.4 Hz, 1H), 3.98 (t, J = 7.6 Hz, 2H), 3.10 (t, J = 7.6 Hz, 2H); ¹³C-NMR (CDCl₃, 100 MHz) : 168.33, 157.81, 133.90, 132.68, 132.12, 127.82, 123.79, 123.19, 112.63, 111.72, 110.52, 103.75, 38.33, 24.33.

2-(2-(5-Chloro-1H-indol-3-yl)ethyl)isoindoline-1,3-dione (1c)

A mixture of (4-chlorophenyl)hydrazine hydrochloride (358 mg, 1.998 mmol) and 2-(3-(1,3-dioxan-2-yl)propyl)isoindoline-1,3-dione (550 mg, 1.998 mmol) in 100 mL of 4% H₂SO₄ was heated at reflux for 12 h. The reaction mixture was cooled to room temperature and treated with aqueous NaHCO₃. The tryptamine product was extracted with CH₂Cl₂ (4 x 50 mL). The combined organic layer was dried over anhydrous Na₂SO₄, filtered and the solvent was evaporated under reduced pressure. The residue was purified through neutral alumina column chromatography using ethyl acetate : hexane (1:4) as eluent to give 2-(2-(5-chloro-1H-indol-3-yl)ethyl)isoindoline-1,3-dione in 62% yield (402 mg) as pale yellow solid. (m.p. : 195-196 °C); IR (KBr, cm⁻¹) : 3340, 1769, 1702, 1610, 1450, 1402, 1238, 721; ¹H-NMR (CDCl₃, 400 MHz) : δ 8.05 (br s, 1H), 7.83 (dd, J = 5.4, 3.0 Hz, 2H), 7.70 (dd, J = 5.4, 3.0 Hz, 2H), 7.64 (d, J = 1.3 Hz, 1H), 7.24 (d, J = 8.0 Hz, 1H), 7.13-7.11 (m, 2H), 3.98 (t, J = 7.6 Hz, 2H), 3.11 (t, J = 7.6 Hz, 2H); ¹³C-NMR (CDCl₃, 100 MHz) : 168.47, 134.67, 134.06, 132.24, 128.70, 125.46, 123.56, 123.79, 123.19, 112.63, 111.72, 110.52, 103.75, 103.75, 38.56, 24.35.

2-(2-(5-Bromo-1H-indol-3-yl)ethyl)isoindoline-1,3-dione (1d)
A mixture of (4-bromophenyl)hydrazine hydrochloride (430 mg, 1.943 mmol) and 2-(3-(1,3-dioxan-2-yl)propyl)isoindoline-1,3-dione (535 mg, 1.943 mmol) in 100 mL of 4% H₂SO₄ was heated at reflux for 12 h. The reaction mixture was cooled to room temperature and treated with aqueous NaHCO₃. The tryptamine product was extracted with CH₂Cl₂ (4 x 50 mL). The combined organic layer was dried over anhydrous Na₂SO₄, filtered and the solvent was evaporated under reduced pressure. The residue was purified through neutral alumina column chromatography using ethyl acetate : hexane (1:4) as eluent to give 2-(2-(5-bromo-1H-indol-3-yl)ethyl)isoindoline-1,3-dione in 72% yield (517 mg) as pale orange solid. (m.p.: 212-213 °C); IR (KBr, cm⁻¹): 3318, 3048, 2934, 2860, 1764, 1695, 1458, 1389, 1230, 719; ¹H-NMR (CDCl₃, 400 MHz): δ 8.05 (br s, 1H), 7.82 (dd, J = 5.4, 3.0 Hz, 2H), 7.79-7.78 (m, 1H), 7.70 (dd, J = 5.4, 3.0 Hz, 2H), 7.23 (dd, J = 8.8, 1.6 Hz, 1H), 7.19 (dd, J = 8.8, 0.4 Hz, 1H), 7.09 (d, J = 2.3 Hz, 1H), 4.00-3.96 (m, 2H), 3.13-3.09 (m, 2H); ¹³C-NMR (DMSO-d₆, 100 MHz): 167.75, 134.82, 134.33, 131.52, 128.90, 124.77, 123.86, 122.95, 113.42, 111.00, 110.53, 38.16, 23.52.

2-(2-(7-Fluoro-1H-indol-3-yl)ethyl)isoindoline-1,3-dione (1e)

A mixture of (2-fluorophenyl)hydrazine hydrochloride (325 mg, 1.998 mmol) and 2-(3-(1,3-dioxan-2-yl)propyl)isoindoline-1,3-dione (550 mg, 1.998 mmol) in 100 mL of 4% H₂SO₄ was heated at reflux for 12 h. The reaction mixture was cooled to room temperature and treated with aqueous NaHCO₃. The tryptamine product was extracted with CH₂Cl₂ (4 x 50 mL). The combined organic layer was dried over anhydrous Na₂SO₄, filtered and the solvent was evaporated under reduced pressure. The residue was purified through neutral alumina column chromatography using ethyl acetate : hexane (1:4) as eluent to give 2-(2-(5-fluoro-1H-indol-3-yl)ethyl)isoindoline-1,3-dione in 68% yield (419 mg) as orange solid. (m.p.: 199-200 °C); IR (KBr, cm⁻¹): 3358, 2944, 1768, 1704, 1429, 1228, 715; ¹H-NMR (CDCl₃, 400 MHz): δ 8.24 (br s, 1H), 7.83 (dd, J = 5.4, 3.0 Hz, 2H), 7.70 (dd, J = 5.4, 3.0 Hz, 2H), 7.47 (d, J = 8.0 Hz, 1H), 7.11 (d, J = 2.4 Hz, 1H), 7.01 (td, J = 8.0, 4.8 Hz, 1H), 6.91-6.86 (m, 1H), 4.02-3.98 (m, 2H), 3.16-3.13 (m, 2H); ¹³C-NMR (CDCl₃, 100 MHz): 168.48, 149.69 (d, J = 242.3 Hz, 1C), 134.05, 132.26, 131.31 (d, J = 5.2 Hz, 1C), 124.68 (d, J = 13.2 Hz, 1C), 123.34, 122.85, 119.90 (d, J = 6.3 Hz, 1C), 114.76 (d, J = 3.5 Hz, 1C), 113.41 (d, J = 2.2 Hz, 1C), 107.08 (d, J = 15.9 Hz, 1C), 38.52, 24.57.
1-(2-(5-Methoxy-1H-indol-3-yl)ethyl)pyrrolidine-2,5-dione (1n)**

A mixture of (4-methoxyphenyl)hydrazine hydrochloride (231 mg, 1.320 mmol) and 1-(3-(1,3-dioxan-2-yl)propyl)pyrrolidine-2,5-dione (300 mg, 1.320 mmol) in 100 mL of 4% H$_2$SO$_4$ was heated at reflux for 12 h. The reaction mixture was cooled to room temperature and treated with aqueous NaHCO$_3$. The tryptamine product was extracted with CH$_2$Cl$_2$ (4 x 50 mL). The combined organic layer was dried over anhydrous Na$_2$SO$_4$, filtered and the solvent was evaporated under reduced pressure. The residue was purified through neutral alumina column chromatography using ethyl acetate : hexane (1:4) as eluent to give 1-(2-(5-methoxy-1H-indol-3-yl)ethyl)pyrrolidine-2,5-dione in 61% yield (219 mg) as pale tan solid. (m.p.: 169-170°C); IR (KBr, cm$^{-1}$): 3424, 2951, 1761, 1696, 1487, 1404, 1227, 1153; $^1$H-NMR (CDCl$_3$, 400 MHz): $\delta$ 7.98 (br s, 1H), 7.28 (d, $J = 6.1$ Hz, 1H), 7.18 (d, $J = 2.4$ Hz, 1H), 7.09 (d, $J = 2.1$ Hz, 1H), 6.89 (dd, $J = 8.8$, 2.4 Hz, 1H), 3.93 (s, 3H), 3.85 (t, $J = 8.0$ Hz, 2H), 3.05 (t, $J = 8.0$ Hz, 2H), 2.67 (s, 4H); $^{13}$C-NMR (CDCl$_3$, 100 MHz): 177.31, 154.08, 131.24, 127.86, 122.49, 112.91, 111.91, 100.24, 55.87, 39.29, 28.18, 23.40.

1-(2-(7-Methyl-1H-indol-3-yl)ethyl)pyrrolidine-2,5-dione (1o)**

A mixture of o-tolylhydrazine hydrochloride (349 mg, 2.200 mmol) and 1-(3-(1,3-dioxan-2-yl)propyl)pyrrolidine-2,5-dione (500 mg, 2.200 mmol) in 100 mL of 4% H$_2$SO$_4$ was heated at reflux for 12 h. The reaction mixture was cooled to room temperature and treated with aqueous NaHCO$_3$. The tryptamine product was extracted with CH$_2$Cl$_2$ (4 x 50 mL). The combined organic layer was dried over anhydrous Na$_2$SO$_4$, filtered and the solvent was evaporated under reduced pressure. The residue was purified through neutral alumina column chromatography using ethyl acetate : hexane (1:4) as eluent to give 1-(2-(7-methyl-1H-indol-3-yl)ethyl)pyrrolidine-2,5-dione in 66% yield (372 mg) as colorless solid. (m.p.: 172-173°C); IR (KBr, cm$^{-1}$): 3272, 1770, 1694, 1405, 1343; $^1$H-NMR (CDCl$_3$, 400 MHz): $\delta$ 7.97 (br s, 1H), 7.51 (d, $J = 8.0$ Hz, 1H), 7.09 (d, $J = 2.2$ Hz, 1H), 7.06 (t, $J = 8.0$ Hz, 1H), 6.99 (d, $J = 7.2$ Hz, 1H), 3.85-3.81 (m, 2H), 3.07-3.03 (m, 2H), 2.62 (s, 4H), 2.47 (s, 3H); $^{13}$C-NMR (CDCl$_3$, 100 MHz): 177.39, 135.88, 127.15, 122.76, 121.96, 120.45, 119.86, 116.47, 112.83, 39.67, 28.27, 23.58, 16.69.

1-(2-(5,7-Dimethyl-1H-indol-3-yl)ethyl)pyrrolidine-2,5-dione (1p)**

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A mixture of (2,4-dimethylphenyl)hydrazine hydrochloride (380 mg, 2.200 mmol) and 1-(3-(1,3-dioxan-2-yl)propyl)pyrrolidine-2,5-dione (500 mg, 2.200 mmol) in 100 mL of 4% H₂SO₄ was heated at reflux for 12 h. The reaction mixture was cooled to room temperature and treated with aqueous NaHCO₃. The tryptamine product was extracted with CH₂Cl₂ (4 x 50 mL). The combined organic layer was dried over anhydrous Na₂SO₄, filtered and the solvent was evaporated under reduced pressure. The residue was purified through neutral alumina column chromatography using ethyl acetate : hexane (1:4) as eluent to give 1-(2-(5,7-dimethyl-1H-indol-3-yl)ethyl)pyrrolidine-2,5-dione in 55% yield (327 mg) as pale yellow solid. (m.p. : 192-193 °C); IR (KBr, cm⁻¹) : 3348, 3125, 2860, 1769, 1691, 1405, 1264; ¹H-NMR (CDCl₃, 400 MHz) : δ 7.84 (br s, 1H), 7.28 (s, 1H), 7.05 (d, J = 2.2 Hz, 1H), 6.83 (s, 1H), 3.83-3.79 (m, 2H), 3.03-3.00 (m, 2H), 2.62 (s, 4H), 2.43 (s, 6H); ¹³C-NMR (CDCl₃, 100 MHz) : 177.26, 134.09, 128.98, 127.27, 124.42, 121.95, 119.97, 115.88, 112.25, 39.58, 28.15, 23.47, 21.45, 16.51.

1-(2-(5-Fluoro-1H-indol-3-yl)ethyl)pyrrolidine-2,5-dione (1j)

A mixture of (4-fluorophenyl)hydrazine hydrochloride (122 mg, 0.748 mmol) and 1-(3-(1,3-dioxan-2-yl)propyl)pyrrolidine-2,5-dione (170 mg, 0.748 mmol) in 100 mL of 4% H₂SO₄ was heated at reflux for 12 h. The reaction mixture was cooled to room temperature and treated with aqueous NaHCO₃. The tryptamine product was extracted with CH₂Cl₂ (4 x 50 mL). The combined organic layer was dried over anhydrous Na₂SO₄, filtered and the solvent was evaporated under reduced pressure. The residue was purified through neutral alumina column chromatography using ethyl acetate : hexane (1:4) as eluent to give 1-(2-(5-fluoro-1H-indol-3-yl)ethyl)pyrrolidine-2,5-dione in 73% yield (142 mg) as tan solid. (m.p. : 136-137 °C); IR (KBr, cm⁻¹) : 3344, 2935, 2860, 1773, 1697, 1486, 1404, 1260, 1152, 805; ¹H-NMR (CDCl₃, 400 MHz) : δ 8.14 (br s, 1H), 7.30-7.23 (m, 2H), 7.10 (d, J = 1.4 Hz, 1H), 6.92 (td, J = 9.0, 2.2 Hz, 1H), 3.79 (t, J = 7.6 Hz, 2H), 2.99 (t, J = 7.6 Hz, 2H), 2.63 (s, 4H); ¹³C-NMR (CDCl₃, 100 MHz) : 177.35, 157.96 (d, J = 234.0 Hz, 1C), 132.77, 128.03 (d, J = 9.0 Hz, 1C), 124.03, 112.60 (d, J = 4.0 Hz, 1C), 111.97 (d, J = 9.0 Hz, 1C), 110.66 (d, J = 27.0 Hz, 1C), 103.64 (d, J = 23.0 Hz, 1C), 39.46, 28.27, 23.38.

1-(2-(5-Chloro-1H-indol-3-yl)ethyl)pyrrolidine-2,5-dione (1k)
A mixture of (4-chlorophenyl)hydrazine hydrochloride (197 mg, 1.100 mmol) and 1-(3-(1,3-dioxan-2-yl)propyl)pyrrolidine-2,5-dione (250 mg, 1.100 mmol) in 100 mL of 4% H$_2$SO$_4$ was heated at reflux for 12 h. The reaction mixture was cooled to room temperature and treated with aqueous NaHCO$_3$. The tryptamine product was extracted with CH$_2$Cl$_2$ (4 x 50 mL). The combined organic layer was dried over anhydrous Na$_2$SO$_4$, filtered and the solvent was evaporated under reduced pressure. The residue was purified through neutral alumina column chromatography using ethyl acetate : hexane (1:4) as eluent to give 1-(2-(5-chloro-1H-indol-3-yl)ethyl)pyrrolidine-2,5-dione in 71% yield (216 mg) as pale yellow solid. (m.p.: 145-146 °C); IR (KBr, cm$^{-1}$): 3420, 2922, 1763, 1686, 1462, 1409, 1267; $^1$H-NMR (CDCl$_3$, 400 MHz): $\delta$ 8.20 (br s, 1H), 7.59 (d, $J = 1.9$ Hz, 1H), 7.28 (d, $J = 0.8$ Hz, 1H), 7.14 (dd, $J = 8.6$, 1.9 Hz, 1H), 7.10 (d, $J = 2.2$ Hz, 1H), 3.82 (t, $J = 7.6$ Hz, 2H), 3.03 (t, $J = 7.6$ Hz, 2H), 2.64 (s, 4H); $^{13}$C-NMR (CDCl$_3$, 100 MHz): 177.39, 134.58, 128.77, 125.38, 123.67, 122.52, 118.14, 112.38, 112.28, 39.59, 28.24, 23.22.

1-(2-(5-Bromo-1H-indol-3-yl)ethyl)pyrrolidine-2,5-dione (1l)

A mixture of (4-bromophenyl)hydrazine hydrochloride (171 mg, 0.770 mmol) and 1-(3-(1,3-dioxan-2-yl)propyl)pyrrolidine-2,5-dione (175 mg, 0.770 mmol) in 100 mL of 4% H$_2$SO$_4$ was heated at reflux for 12 h. The reaction mixture was cooled to room temperature and treated with aqueous NaHCO$_3$. The tryptamine product was extracted with CH$_2$Cl$_2$ (4 x 50 mL). The combined organic layer was dried over anhydrous Na$_2$SO$_4$, filtered and the solvent was evaporated under reduced pressure. The residue was purified through neutral alumina column chromatography using ethyl acetate : hexane (1:4) as eluent to give 1-(2-(5-bromo-1H-indol-3-yl)ethyl)pyrrolidine-2,5-dione in 53% yield (131 mg) as tan solid. (m.p.: 138-139 °C); IR (KBr, cm$^{-1}$): 3318, 2919, 2854, 1767, 1699, 1336, 666; $^1$H-NMR (CDCl$_3$, 400 MHz): $\delta$ 8.28 (br s, 1H), 7.71 (s, 1H), 7.25-7.18 (m, 2H), 7.04 (s, 1H), 3.82 (t, $J = 7.6$ Hz, 2H), 2.99 (t, $J = 7.2$ Hz, 2H), 2.61 (s, 4H); $^{13}$C-NMR (CDCl$_3$, 100 MHz): 177.43, 134.84, 129.42, 124.97, 124.51, 121.15, 112.86, 112.80, 112.13, 39.65, 28.22, 23.17.

1-(2-(7-Fluoro-1H-indol-3-yl)ethyl)pyrrolidine-2,5-dione (1m)

A mixture of (2-fluorophenyl)hydrazine hydrochloride (122 mg, 0.748 mmol) and 1-(3-(1,3-dioxan-2-yl)propyl)pyrrolidine-2,5-dione (170 mg, 0.748 mmol) in 100 mL of 4% H$_2$SO$_4$ was heated at reflux for 12
The reaction mixture was cooled to room temperature and treated with aqueous NaHCO₃. The tryptamine product was extracted with CH₂Cl₂ (4 x 50 mL). The combined organic layer was dried over anhydrous Na₂SO₄, filtered and the solvent was evaporated under reduced pressure. The residue was purified through neutral alumina column chromatography using ethyl acetate : hexane (1:4) as eluent to give 1-(2-(7-fluoro-1H-indol-3-yl)ethyl)pyrrolidine-2,5-dione in 69% yield (98 mg) as pale yellow solid. (m.p. : 170-171 °C); IR (KBr, cm⁻¹) : 3282, 2943, 1770, 1699, 1448, 1336, 796; ¹H-NMR (CDCl₃, 400 MHz) : δ 8.29 (br s, 1H), 7.41 (d, J = 8.0 Hz, 1H), 7.10 (d, J = 2.3 Hz, 1H), 7.03 (td, J = 8.0, 4.8 Hz, 1H), 6.92-6.87 (m, 1H), 3.84-3.80 (m, 2H), 3.06-3.03 (m, 2H), 2.62 (s, 4H); ¹³C-NMR (CDCl₃, 100 MHz) : 177.33, 149.73 (d, J = 243.0 Hz, 1C), 131.39 (d, J = 5.0 Hz, 1C), 124.65 (d, J = 13.0 Hz, 1C), 122.93, 119.97 (d, J = 6.0 Hz, 1C), 114.57 (d, J = 4.0 Hz, 1C), 113.30 (d, J = 2.0 Hz, 1C), 107.08 (d, J = 16.0 Hz, 1C), 39.51, 28.29, 23.46.

(E) General procedure for the synthesis of benzindolizino indolones.

13b-Hydroxy-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2)

A 50 mL two neck round bottom flask fitted with condenser and rubber septum was charged with 2-(2-(1H-indol-3-yl)ethyl)isoindoline-1,3-dione (110 mg, 0.379 mmol), 4Å molecular sieves (50 mg), magnetic stir bar and anhydrous dichloromethane (20 mL) under nitrogen atmosphere. To this mixture was added trifluoromethanesulfonic acid (335 µL, 3.789 mmol) with stirring at room temperature. After 12 h the reaction mixture was quenched with aqueous NaHCO₃. Organic layer was separated and aqueous layer was extracted with ethyl acetate (3 x 50 mL). The combined organic layer was washed with aqueous NaHCO₃, dried over anhydrous Na₂SO₄ and filtered. The solvent was removed under reduced pressure. The crude mixture was purified through neutral alumina column chromatography using ethyl acetate as eluent to give 13b-hydroxy-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one in 81% yield (86 mg) as colorless solid. (m.p. : 163-
164 °C); IR (KBr, cm\(^{-1}\)) : 3350, 3226, 2924, 1682, 1409, 1300; \(^1\)H-NMR (DMSO-\(d_6\), 400 MHz) : \(\delta\) 11.51 (br s, 1H), 8.32 (d, \(J = 7.6\) Hz, 1H), 7.72 (t, \(J = 7.6\) Hz, 1H), 7.68 (d, \(J = 7.6\) Hz, 1H), 7.55 (t, \(J = 7.2\) Hz, 1H), 7.42 (d, \(J = 7.6\) Hz, 1H), 7.36 (d, \(J = 8.4\) Hz, 1H), 7.26 (s, 1H), 7.13-7.09 (m, 1H), 6.98 (t, \(J = 7.2\) Hz, 1H), 4.41 (dd, \(J = 13.0\), 5.6 Hz, 1H), 3.47 (td, \(J = 12.1\), 4.4 Hz, 1H), 2.79 (dd, \(J = 15.6\), 4.4 Hz, 1H), 2.73-2.65 (m, 1H); \(^{13}\)C-NMR (DMSO-\(d_6\), 100 MHz) : 166.70, 147.07, 136.56, 133.14, 132.64, 130.38, 129.76, 125.64, 123.78, 122.92, 122.42, 119.12, 118.99, 111.71, 109.06, 84.23, 35.10, 21.63; HRMS (ESI) (m/z) : [M+Na]\(^+\) 

Found 313.0958; Calculated 313.0953; for C\(_{18}\)H\(_{14}\)N\(_2\)O\(_2\)Na.

\[
\text{NNHH} \quad \text{OO} \\
\quad \text{RR} \\
\begin{array}{c}
\text{11.. TTffOOHH ((1100 eeqquuiivv))} \\
\text{CCHH22CCll22,, 44AA MMSS} \\
\text{22.. NNaaHHCCOO33} \\
\text{33.. NNaaBBHH44//CCFF33CCOOOOHH}
\end{array}
\]

\[
\quad \text{NNHH} \quad \text{RR} \\
\quad \text{NN} \\
\begin{array}{c}
\text{OO} \\
\text{RR == HH,, MMee,, OOMMee,, FF,, CCll,, BBrr}
\end{array}
\]

7,8,13,13b-Tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2a)

A 50 mL two neck round bottom flask fitted with condenser and rubber septum was charged with 2-(2-(1H-indol-3-yl)ethyl)isoindoline-1,3-dione (110 mg, 0.379 mmol), 4Å molecular sieves (50 mg), magnetic stir bar and anhydrous dichloromethane (20 mL) under nitrogen atmosphere. To this mixture was added trifluoromethanesulfonic acid (335 \(\mu\)L, 3.789 mmol) with stirring at room temperature. After 12 h the reaction mixture was neutralized with solid NaHCO\(_3\) (350 mg, 4.168 mmol). After 15 min., to this crude reaction mixture was added NaBH\(_4\) (64 mg, 1.705 mmol) and CF\(_3\)COOH (392 \(\mu\)L, 5.115 mmol) under nitrogen atmosphere with vigorous stirring at room temperature. After 12 h the reaction mixture was quenched with aqueous NaHCO\(_3\). Organic layer was separated and aqueous layer was extracted with ethyl acetate (3 x 50 mL). The combined organic layer was washed with aqueous NaHCO\(_3\), dried over anhydrous Na\(_2\)SO\(_4\) and filtered. The solvent was removed under reduced pressure. The crude mixture was purified through neutral alumina column chromatography using ethyl acetate : hexane (4:1) mixture as eluent to give 7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one in 83% yield (86 mg) as pale yellow solid. (m.p. : 215-216 °C, lit.\(^3\) 212-214 °C); IR (KBr, cm\(^{-1}\)) : 3225, 2932, 2841, 1670, 1461; \(^1\)H-NMR (CDCl\(_3\), 400 MHz) : \(\delta\) 8.51 (br s, 1H), 7.90 (d, \(J = 7.6\) Hz, 1H), 7.84 (d, \(J = 7.6\) Hz, 1H), 7.61 (td, \(J = 7.6\), 1.0 Hz, 1H), 7.49 (t, \(J = 8.0\) Hz, 2H), 7.37 (d, \(J = 8.0\) Hz, 1H), 7.18 (td,
J = 8.0, 1.0 Hz, 1H), 7.10 (td, J = 7.6, 1.0 Hz, 1H), 5.84 (s, 1H), 4.87 (dd, J = 13.2, 5.6 Hz, 1H), 3.41 (ddd, J = 13.2, 11.2, 5.2 Hz, 1H), 3.02-2.93 (m, 1H), 2.87 (dd, J = 15.2, 5.2 Hz, 1H); 13C-NMR (CDCl3, 100 MHz) : 168.36, 143.07, 136.72, 132.68, 132.04, 130.18, 129.04, 126.92, 124.61, 122.75, 122.33, 120.20, 118.82, 111.24, 109.59, 57.22, 38.36, 21.83.

10-Methoxy-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2f)

A 50 mL two neck round bottom flask fitted with condenser and rubber septum was charged with 2-(2-(5-methoxy-1H-indol-3-yl)ethyl)isoindoline-1,3-dione (100 mg, 0.312 mmol), 4Å molecular sieves (50 mg), magnetic stir bar and anhydrous dichloromethane (20 mL) under nitrogen atmosphere. After 15 min to this mixture was added trifluoromethanesulfonic acid (276 µL, 3.121 mmol) with stirring at room temperature. After 12 h the reaction mixture was neutralized with solid NaHCO3 (288 mg, 3.433 mmol). After 15 min., to this crude reaction mixture was added NaBH4 (53 mg, 1.404 mmol) and CF3COOH (323 µL, 4.213 mmol) under nitrogen atmosphere with vigorous stirring at room temperature. After 12 h the reaction mixture was quenched with aqueous NaHCO3. Organic layer was separated and aqueous layer was extracted with ethyl acetate (3 x 50 mL). The combined organic layer was washed with aqueous NaHCO3, dried over anhydrous Na2SO4 and filtered. The solvent was removed under reduced pressure. The crude mixture was purified through neutral alumina column chromatography using ethyl acetate : hexane (4:1) mixture as eluent to give 10-methoxy-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one in 74% yield (70 mg) as pale yellow solid. (m.p. : 230-231 °C); IR (KBr, cm⁻¹) : 3246, 3057, 2838, 1674, 1473, 1405, 1206, 861; 1H-NMR (DMSO-d6, 400 MHz) : δ 11.18 (br s, 1H), 8.27 (dd, J = 7.6, 0.6 Hz, 1H), 7.73 (d, J = 7.6 Hz, 1H), 7.70 (dd, J = 7.6, 1.1 Hz, 1H), 7.55 (t, J = 7.6 Hz, 1H), 7.27 (d, J = 8.7 Hz, 1H), 6.91 (d, J = 2.4 Hz, 1H), 6.73 (dd, J = 8.7, 2.4 Hz, 1H), 6.03 (s, 1H), 4.58 (dd, J = 13.2, 5.6 Hz, 1H), 3.73 (s, 3H), 3.37 (dd, J = 11.6, 4.8 Hz, 1H), 2.80 (dd, J = 15.2, 4.8 Hz, 1H), 2.71-2.64 (m, 1H); 13C-NMR (DMSO-d6, 100 MHz) : 167.05, 153.27, 143.62, 131.81, 131.63, 131.43, 131.40, 128.55, 126.46, 123.71, 123.06, 111.88, 111.36, 106.94, 100.11, 56.61, 55.28, 37.67, 21.42; HRMS (ESI) (m/z) : [M+H]+ Found 305.1302; Calculated 305.1290; for C19H17N2O2.
12-Methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2g)

A 50 mL two neck round bottom flask fitted with condenser and rubber septum was charged with 2-(2-(7-methyl-1H-indol-3-yl)ethyl)isoindoline-1,3-dione (120 mg, 0.394 mmol), 4Å molecular sieves (50 mg), magnetic stir bar and anhydrous dichloromethane (20 mL) under nitrogen atmosphere. To this mixture was added trifluoromethanesulfonic acid (349 µL, 3.943 mmol) with stirring at room temperature. After 12 h the reaction mixture was neutralized with solid NaHCO₃ (364 mg, 4.337 mmol). After 15 min., to this crude reaction mixture was added NaBH₄ (67 mg, 1.774 mmol) and CF₃COOH (408 µL, 5.323 mmol) under nitrogen atmosphere with vigorous stirring at room temperature. After 12 h the reaction mixture was quenched with aqueous NaHCO₃. Organic layer was separated and aqueous layer was extracted with ethyl acetate (3 x 50 mL). The combined organic layer was washed with aqueous NaHCO₃, dried over anhydrous Na₂SO₄ and filtered. The solvent was removed under reduced pressure. The crude mixture was purified through neutral alumina column chromatography using ethyl acetate : hexane (4:1) mixture as eluent to give 12-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one in 66% yield (75 mg) as pale yellow solid. (m.p. : 204-205 °C); IR (KBr, cm⁻¹) : 3266, 3046, 2848, 2788, 1666, 1464, 1407; ¹H-NMR (CDCl₃, 400 MHz) : δ 8.09 (br s, 1H), 7.91 (d, J = 7.6 Hz, 1H), 7.83 (d, J = 7.2 Hz, 1H), 7.64 (t, J = 6.8 Hz, 1H), 7.52 (t, J = 7.6 Hz, 1H), 7.33 (d, J = 7.6 Hz, 1H), 7.04 (t, J = 7.6 Hz, 1H), 7.00 (d, J = 6.8 Hz, 1H), 5.85 (s, 1H), 4.86 (dd, J = 13.2, 5.6 Hz, 1H), 3.42-3.36 (m, 1H), 3.02-2.93 (m, 1H), 2.86 (dd, J = 15.4, 4.8 Hz, 1H), 2.52 (s, 3H); ¹³C-NMR (CDCl₃, 100 MHz) : 168.26, 143.09, 136.23, 132.76, 132.03, 129.93, 129.03, 126.56, 124.70, 123.50, 122.20, 120.53, 120.33, 116.58, 110.39, 57.20, 38.35, 21.93, 16.84; HRMS (ESI) (m/z) : [M+H]^+ Found 289.1355; Calculated 289.1341; for C₁₉H₁₇N₂O.

10,12-Dimethyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2h)

A 50 mL two neck round bottom flask fitted with condenser and rubber septum was charged with 2-(2-(5,7-dimethyl-1H-indol-3-yl)ethyl)isoindoline-1,3-dione (120 mg, 0.394 mmol), 4Å molecular sieves (50 mg), magnetic stir bar and anhydrous dichloromethane (20 mL) under nitrogen atmosphere. To this mixture was added trifluoromethanesulfonic acid (349 µL, 3.943 mmol) with stirring at room temperature. After 12 h the reaction mixture was neutralized with solid NaHCO₃ (364 mg, 4.337 mmol). After 15 min., to this crude reaction mixture was added NaBH₄ (67 mg, 1.774 mmol) and CF₃COOH (408 µL, 5.323 mmol) under nitrogen atmosphere with vigorous stirring at room temperature. After 12 h the reaction mixture was quenched with aqueous NaHCO₃. Organic layer was separated and aqueous layer was extracted with ethyl acetate (3 x 50 mL). The combined organic layer was washed with aqueous NaHCO₃, dried over anhydrous Na₂SO₄ and filtered. The solvent was removed under reduced pressure. The crude mixture was purified through neutral alumina column chromatography using ethyl acetate : hexane (4:1) mixture as eluent to give 10,12-dimethyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one in 66% yield (75 mg) as pale yellow solid. (m.p. : 204-205 °C); IR (KBr, cm⁻¹) : 3266, 3046, 2848, 2788, 1666, 1464, 1407; ¹H-NMR (CDCl₃, 400 MHz) : δ 8.09 (br s, 1H), 7.91 (d, J = 7.6 Hz, 1H), 7.83 (d, J = 7.2 Hz, 1H), 7.64 (t, J = 6.8 Hz, 1H), 7.52 (t, J = 7.6 Hz, 1H), 7.33 (d, J = 7.6 Hz, 1H), 7.04 (t, J = 7.6 Hz, 1H), 7.00 (d, J = 6.8 Hz, 1H), 5.85 (s, 1H), 4.86 (dd, J = 13.2, 5.6 Hz, 1H), 3.42-3.36 (m, 1H), 3.02-2.93 (m, 1H), 2.86 (dd, J = 15.4, 4.8 Hz, 1H), 2.52 (s, 3H); ¹³C-NMR (CDCl₃, 100 MHz) : 168.26, 143.09, 136.23, 132.76, 132.03, 129.93, 129.03, 126.56, 124.70, 123.50, 122.20, 120.53, 120.33, 116.58, 110.39, 57.20, 38.35, 21.93, 16.84; HRMS (ESI) (m/z) : [M+H]^+ Found 289.1355; Calculated 289.1341; for C₁₉H₁₇N₂O.
ethyl)isoindoline-1,3-dione (120 mg, 0.377 mmol), 4Å molecular sieves (50 mg), magnetic stir bar and anhydrous dichloromethane (20 mL) under nitrogen atmosphere. To this mixture was added trifluoromethanesulfonic acid (334 µL, 3.769 mmol) with stirring at room temperature. After 12 h the reaction mixture was neutralized with solid NaHCO₃ (348 mg, 4.146 mmol). After 15 min., to this crude reaction mixture was added NaBH₄ (64 mg, 1.696 mmol) and CF₃COOH (390 µL, 5.088 mmol) under nitrogen atmosphere with vigorous stirring at room temperature. After 12 h the reaction mixture was quenched with aqueous NaHCO₃. Organic layer was separated and aqueous layer was extracted with ethyl acetate (3 x 50 mL). The combined organic layer was washed with aqueous NaHCO₃ and filtered. The solvent was removed under reduced pressure. The crude mixture was purified through neutral alumina column chromatography using ethyl acetate : hexane (4:1) mixture as eluent to give 10,12-dimethyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one in 60% yield (68 mg) as pale yellow solid. (m.p. : 200-201 °C); IR (KBr, cm⁻¹) : 3271, 2851, 1666, 1409; ¹H-NMR (CDCl₃, 400 MHz) : δ 8.03 (br s, 1H), 7.90 (d, J = 7.6 Hz, 1H), 7.83 (d, J = 7.6 Hz, 1H), 7.63 (t, J = 7.4 Hz, 1H), 7.50 (t, J = 7.4 Hz, 1H), 7.12 (s, 1H), 6.84 (s, 1H), 5.83 (s, 1H), 4.85 (dd, J = 13.2, 6.0 Hz, 1H), 3.42-3.34 (m, 1H), 2.98-2.90 (m, 1H), 2.83 (dd, J = 15.4, 4.8 Hz, 1H), 2.48 (s, 3H), 2.39 (s, 3H); ¹³C-NMR (CDCl₃, 100 MHz) : 168.29, 143.20, 134.59, 132.74, 132.00, 130.02, 129.81, 128.96, 126.84, 125.16, 124.61, 122.30, 119.99, 116.20, 109.87, 57.30, 38.39, 21.94, 21.49, 16.78; HRMS (ESI) (m/z) : [M+H]+ Found 303.1498; Calculated 303.1497; for C₂₀H₁₉N₂O.

10-Fluoro-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2b)

A 50 mL two neck round bottom flask fitted with condenser and rubber septum was charged with 2-(2-(5-fluoro-1H-indol-3-yl)ethyl)isoindoline-1,3-dione (125 mg, 0.405 mmol), 4Å molecular sieves (50 mg), magnetic stir bar and anhydrous dichloromethane (20 mL) under nitrogen atmosphere. To this mixture was added trifluoromethanesulfonic acid (359 µL, 4.054 mmol) with stirring at room temperature. After 12 h the reaction mixture was neutralized with solid NaHCO₃ (375 mg, 4.460 mmol). After 15 min., to this crude reaction mixture was added NaBH₄ (69 mg, 1.824 mmol) and CF₃COOH (419 µL, 5.473 mmol) under nitrogen atmosphere with vigorous stirring at room temperature. After 12 h the reaction mixture was quenched with aqueous NaHCO₃. Organic
layer was separated and aqueous layer was extracted with ethyl acetate (3 x 50 mL). The combined organic layer was washed with aqueous NaHCO₃, dried over anhydrous Na₂SO₄ and filtered. The solvent was removed under reduced pressure. The crude mixture was purified through neutral alumina column chromatography using ethyl acetate : hexane (4:1) mixture as eluent to give 10-fluoro-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one in 79% yield (94 mg) as pale yellow solid. (m.p. : 251-252 °C); IR (KBr, cm⁻¹) : 3216, 2949, 1671, 1471, 1419, 727; ¹H-NMR (DMSO-d₆, 400MHz) : δ 11.46 (br s, 1H), 8.27 (d, J = 8.0 Hz, 1H), 7.72 (dd, J = 14.0, 8.0 Hz, 2H), 7.55 (t, J = 8.0 Hz, 1H), 7.38 (dd, J = 10.0, 5.0 Hz, 1H), 7.18 (dd, J = 11.2, 4.0 Hz, 1H), 6.93 (td, J = 10.0, 3.0 Hz, 1H), 6.06 (s, 1H), 4.58 (dd, J = 13.2, 5.0 Hz, 1H), 3.40-3.36 (m, 1H) [to assign this proton the compound was recorded in acetone-d₆, the value obtained was 3.27 (ddd, J = 13.2, 10.8, 5.6 Hz, 1H)], 2.81 (dd, J = 16.0, 4.0 Hz, 1H), 2.71-2.62 (m, 1H); ¹³C-NMR (DMSO-d₆, 100MHz) : 167.03, 156.80 (d, J = 230.4 Hz, 1C), 143.37, 132.98 (d, J = 4.3 Hz, 1C), 131.86, 131.63, 128.63, 126.38 (d, J = 10.0 Hz, 1C), 123.60, 123.09, 112.16 (d, J = 9.7 Hz, 1C), 109.55, 109.29, 107.47 (d, J = 4.6 Hz, 1C), 103.03 (d, J = 23.2 Hz, 1C), 56.52, 37.54, 21.29; HRMS (ESI) (m/z) : [M+H]⁺ Found 293.1099; Calculated 293.1090; for C₁₈H₁₄N₂OF.

10-Chloro-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2c)

A 50 mL two neck round bottom flask fitted with condenser and rubber septum was charged with 2-(2-(5-chloro-1H-indol-3-yl)ethyl)isoindoline-1,3-dione (120 mg, 0.370 mmol), 4Å molecular sieves (50 mg), magnetic stir bar and anhydrous dichloromethane (20 mL) under nitrogen atmosphere. To this mixture was added trifluoromethanesulfonic acid (330 µL, 3.695 mmol) with stirring at room temperature. After 12 h the reaction mixture was neutralized with solid NaHCO₃ (341 mg, 4.065 mmol). After 15 min., to this crude reaction mixture was added NaBH₄ (63 mg, 1.663 mmol) and CF₃COOH (382 µL, 4.988 mmol) under nitrogen atmosphere with vigorous stirring at room temperature. After 12 h the reaction mixture was quenched with aqueous NaHCO₃. Organic layer was separated and aqueous layer was extracted with ethyl acetate (3 x 50 mL). The combined organic layer was washed with aqueous NaHCO₃, dried over anhydrous Na₂SO₄ and filtered. The solvent was removed under reduced pressure. The crude mixture was purified through neutral alumina column chromatography using ethyl
acetate : hexane (4:1) mixture as eluent to give 10-chloro-7,8,13,13b-tetrahydro-5\(H\)-benzo[1,2]indolizino[8,7-\(b\)]indol-5-one in 78% yield (89 mg) as pale yellow solid. (m.p. : 242-243 °C), IR (KBr, cm\(^{-1}\)) : 3220, 2939, 1671, 1468, 1413, 725; \(^1\)H-NMR (DMSO-\(d_6\), 400MHz) : \(\delta\) 11.57 (br s, 1H), 8.27 (d, \(J = 7.6\) Hz, 1H), 7.72 (dd, \(J = 14.4, 7.6\) Hz, 2H), 7.55 (t, \(J = 7.6\) Hz, 1H), 7.47 (d, \(J = 1.6\) Hz, 1H), 7.40 (d, \(J = 8.8\) Hz, 1H), 7.08 (dd, \(J = 8.8, 1.6\) Hz, 1H), 6.07 (s, 1H), 4.58 (dd, \(J = 13.0, 5.6\) Hz, 1H), 3.45-3.39 (m, 1H), [to assign this proton the compound was recorded in acetone-\(d_6\), the value obtained was 3.45 (ddd, \(J = 13.2, 11.2, 5.2\) Hz, 1H)], 2.82 (dd, \(J = 15.2, 4.0\) Hz, 1H), 2.71-2.63 (m, 1H); \(^{13}\)C-NMR (DMSO-\(d_6\), 100 MHz) : 167.12, 146.36, 134.92, 132.78, 131.97, 131.69, 128.75, 127.34, 123.77, 123.53, 123.21, 121.44, 117.58, 112.82, 107.24, 56.54, 37.58, 21.27; HRMS (ESI) : [M+H]\(^{+}\) Found 309.0780; Calculated 309.0795; for C\(_{18}\)H\(_{14}\)N\(_2\)OCl.

10-Bromo-7,8,13,13b-tetrahydro-5\(H\)-benzo[1,2]indolizino[8,7-\(b\)]indol-5-one (2d)

A 50 mL two neck round bottom flask fitted with condenser and rubber septum was charged with 2-(2-(5-bromo-1\(H\)-indol-3-yl)ethyl)isoindoline-1,3-dione (120 mg, 0.389 mmol), 4Å molecular sieves (50 mg), magnetic stir bar and anhydrous dichloromethane (20 mL) under nitrogen atmosphere. To this mixture was added trifluoromethanesulfonic acid (344 \(\mu\)L, 3.892 mmol) with stirring at room temperature. After 12 h the reaction mixture was neutralized with solid NaHCO\(_3\) (360 mg, 4.281 mmol). After 15 min., to this crude reaction mixture was added NaBH\(_4\) (66 mg, 1.751 mmol) and CF\(_3\)COOH (402 \(\mu\)L, 5.254 mmol) under nitrogen atmosphere with vigorous stirring at room temperature. After 12 h the reaction mixture was quenched with aqueous NaHCO\(_3\). Organic layer was separated and aqueous layer was extracted with ethyl acetate (3 x 50 mL). The combined organic layer was washed with aqueous NaHCO\(_3\), dried over anhydrous Na\(_2\)SO\(_4\) and filtered. The solvent was removed under reduced pressure. The crude mixture was purified through neutral alumina column chromatography using ethyl acetate : hexane (4:1) mixture as eluent to give 10-bromo-7,8,13,13b-tetrahydro-5\(H\)-benzo[1,2]indolizino[8,7-\(b\)]indol-5-one in 73% yield (100 mg) as pale brown solid. (m.p. : 238-239 °C); IR (KBr, cm\(^{-1}\)) : 3235, 2844, 1672, 1466, 1413, 725; \(^1\)H-NMR (DMSO-\(d_6\), 400 MHz) : \(\delta\) 11.59 (br s, 1H), 8.27 (d, \(J = 7.6\) Hz, 1H), 7.72 (dd, \(J = 14.5, 7.6\) Hz, 2H), 7.61 (d, \(J = 1.7\) Hz, 1H), 7.55 (t, \(J = 7.6\) Hz, 1H), 7.36 (d, \(J = 8.6\) Hz, 1H), 7.20 (dd, \(J = 8.6, 1.7\) Hz, 1H), 7.14 (d, \(J = 7.6\) Hz, 1H), 7.08 (d, \(J = 1.6\) Hz, 1H), 6.05 (s, 1H), 4.58 (dd, \(J = 13.0, 5.6\) Hz, 1H), 3.48-3.42 (m, 1H), [to assign this proton the compound was recorded in acetone-\(d_6\), the value obtained was 3.45 (ddd, \(J = 13.0, 11.2, 5.2\) Hz, 1H)], 2.82 (dd, \(J = 15.2, 4.0\) Hz, 1H), 2.72-2.64 (d, 1H); \(^{13}\)C-NMR (DMSO-\(d_6\), 100 MHz) : 167.12, 146.36, 134.92, 132.78, 131.97, 131.69, 128.75, 127.34, 123.77, 123.53, 123.21, 121.44, 117.58, 112.82, 107.24, 56.54, 37.58, 21.27; HRMS (ESI) : [M+H]\(^{+}\) Found 309.0780; Calculated 309.0795; for C\(_{18}\)H\(_{14}\)N\(_2\)OCl.
1H), 6.07 (s, 1H), 4.57 (dd, J = 13.1, 6.0 Hz, 1H), 3.40-3.38 (m, 1H), [to assign this proton the compound was recorded again in acetone-d$_6$, the value obtained was 3.36 (ddd, J = 12.8, 11.2, 4.8 Hz)], 2.83 (dd, J = 15.5, 4.0 Hz, 1H), 2.70-2.64 (m, 1H); $^{13}$C-NMR (DMSO-d$_6$, 100 MHz) : 167.11, 143.34, 135.16, 132.60, 131.97, 131.68, 128.75, 128.02, 123.97, 123.76, 123.20, 120.59, 113.29, 111.43, 107.14, 56.50, 37.57, 21.25; HRMS (ESI) (m/z) : [M+H]$^+$ Found 353.0307; Calculated 353.0289; for C$_{18}$H$_{14}$N$_2$OBr.

12-Fluoro-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one (2e)

A 50 mL two neck round bottom flask fitted with condenser and rubber septum was charged with 2-(2-(7-fluoro-1H-indol-3-yl)ethyl)isoindoline-1,3-dione (125 mg, 0.405 mmol), 4Å molecular sieves (50 mg), magnetic stir bar and anhydrous dichloromethane (20 mL) under nitrogen atmosphere. To this mixture was added trifluoromethanesulfonic acid (359 µL, 4.054 mmol) with stirring at room temperature. After 12 h the reaction mixture was neutralized with solid NaHCO$_3$ (375 mg, 4.460 mmol). After 15 min., to this crude reaction mixture was added NaBH$_4$ (69 mg, 1.824 mmol) and CF$_3$COOH (419 µL, 5.473 mmol) under nitrogen atmosphere with vigorous stirring at room temperature. After 12 h the reaction mixture was quenched with aqueous NaHCO$_3$. Organic layer was separated and aqueous layer was extracted with ethyl acetate (3 x 50 mL). The combined organic layer was washed with aqueous NaHCO$_3$, dried over anhydrous Na$_2$SO$_4$ and filtered. The solvent was removed under reduced pressure. The crude mixture was purified through neutral alumina column chromatography using ethyl acetate : hexane (4:1) mixture as eluent to give 12-fluoro-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one in 71% yield (84 mg) as pale yellow solid. (m.p. : 230-231 °C); IR (KBr, cm$^{-1}$) : 3185, 3046, 1674, 1471, 1237, 719; $^1$H-NMR (DMSO-d$_6$, 400 MHz) : δ 11.81 (br s, 1H), 8.45 (dd, J = 7.6, 0.6 Hz, 1H), 7.74 (d, J = 7.6 Hz, 1H), 7.71 (dd, J = 7.6, 1.2 Hz, 1H), 7.55 (t, J = 7.6 Hz, 1H), 7.25 (dd, J = 6.4, 2.0 Hz, 1H), 6.99-6.91 (m, 2H), 6.06 (s, 1H), 4.59 (dd, J = 13.2, 5.6 Hz, 1H), 3.40-3.37 (m, 1H), [to assign this proton the compound was recorded again in acetone-d$_6$, the value obtained was 3.54 (ddd, J = 13.2, 11.2, 5.2 Hz, 1H)], 2.84 (dd, J = 15.6, 4.4 Hz, 1H), 2.74-2.65 (m, 1H); $^{13}$C-NMR (DMSO-d$_6$, 100 MHz) : 167.31, 149.04 (d, J = 241.3 Hz, 1C), 143.50, 132.33, 132.04, 131.62, 130.16 (d, J = 5.9 Hz, 1C), 128.73, 124.11, 123.96, 123.11, 119.39 (d, J = 6.1 Hz, 1C), 114.47 (d, J = 3.0 Hz, 1C), 108.60 (d, J = 2.0 Hz, 1C), 106.63 (d, J = 16.2 Hz, 1C), S22
56.66, 37.68, 21.60; HRMS (ESI) (m/z) : [M+H]+ Found 293.1087; Calculated 293.1090; for C_{18}H_{14}N_{2}OF.

(F) General procedure for the synthesis of indoloindolizinones and indoloquinolinizinones

![Chemical Structure](content)

Where, R = H, F, Cl, Br, OMe, Me
X - X = -CH_{2}CH_{2}-, cyc-1,2-C_{6}H_{10}-, -CH_{2}CH_{2}CH_{2}-

5,6,11,11b-Tetrahydro-1H-indolizino[8,7-b]indol-3(2H)-one (2i)

A 50 mL two neck round bottom flask was charged with 1-(2-(1H-indol-3-yl)ethyl)pyrrolidine-2,5-dione (150 mg, 0.619 mmol), 4Å molecular sieves (50 mg), anhydrous CH_{2}Cl_{2} (20 mL), and a stir bar. The flask was capped with a rubber septum and maintained in nitrogen atmosphere. Trifluoromethanesulfonic acid (548 µL, 6.191 mmol) was added and stirred at room temperature for 12 h. To this reaction mixture was added NaBH₄ (105 mg, 2.786 mmol), methanol (3 mL) and stirred for 0.5 h under nitrogen atmosphere. Then the reaction mixture was quenched with aqueous NaHCO₃. Organic layer was separated and aqueous layer was extracted with ethyl acetate (3 x 50 mL). The combined organic layer was washed with aqueous NaHCO₃, dried over anhydrous Na₂SO₄ and filtered. The solvent was removed under reduced pressure. The crude mixture was purified through neutral alumina column chromatography using ethyl acetate : hexane (4:1) as eluent to give 5,6,11,11b-tetrahydro-1H-indolizino[8,7-b]indol-3(2H)-one in 82% yield (113 mg) as off white solid. (m.p. : 251-252 ℃, lit³ 250 ℃); IR (KBr, cm⁻¹) : 3444, 3076, 2853, 1659, 1450, 1304; ¹H-NMR (CDCl₃, 400 MHz) : δ 8.13 (br s, 1H), 7.49 (d, J = 7.6 Hz, 1H), 7.34 (d, J = 8.0 Hz, 1H), 7.19 (t, J = 7.6 Hz, 1H), 7.13 (t, J = 7.2 Hz, 1H), 4.96-4.92 (m, 1H), 4.57-4.52 (m, 1H), 3.08-3.01 (m, 1H), 2.92-2.80 (m, 2H), 2.65-2.48 (m, 3H), 1.99-1.93 (m, 1H); ¹³C-NMR (CDCl₃, 100 MHz) : 173.33, 136.39, 133.28, 126.92, 122.37, 120.01, 118.57, 111.09, 108.45, 54.38, 37.72, 31.75, 25.81, 21.14.

8-Methoxy-5,6,11,11b-tetrahydro-1H-indolizino[8,7-b]indol-3(2H)-one (2n)
A 50 mL two neck round bottom flask was charged with 1-(2-(5-methoxy-1H-indol-3-yl)ethyl)pyrrolidine-2,5-dione (100 mg, 0.367 mmol), 4Å molecular sieves (50 mg), anhydrous CH₂Cl₂ (20 mL), and a stir bar. The flask was capped with a rubber septum and maintained in nitrogen atmosphere. Trifluoromethanesulfonic acid (325 µL, 3.672 mmol) was added and stirred at room temperature for 12 h. To this reaction mixture was added NaBH₄ (63 mg, 1.653 mmol), methanol (3 mL) and stirred for 0.5 h under nitrogen atmosphere. Then the reaction mixture was quenched with aqueous NaHCO₃. Organic layer was separated and aqueous layer was extracted with ethyl acetate (3 x 50 mL). The combined organic layer was washed with aqueous NaHCO₃, dried over anhydrous Na₂SO₄ and filtered. The solvent was removed under reduced pressure. The crude mixture was purified through neutral alumina column chromatography using ethyl acetate : hexane (4:1) as eluent to give 8-methoxy-5,6,11b-tetrahydro-1H-indolizino[8,7-b]indol-3(2H)-one in 80% yield (75 mg) as off white solid. (m.p. : 220-221 °C); IR (KBr, cm⁻¹) : 3255, 2983, 2909, 2838, 1669, 1441, 1303, 1134; ¹H-NMR (CDCl₃, 400 MHz) : δ 7.91 (br s, 1H), 7.22 (d, J = 8.8 Hz, 1H), 6.94 (d, J = 2.4 Hz, 1H), 6.84 (dd, J = 8.8, 2.4 Hz, 1H), 4.92 (t, J = 7.2 Hz, 1H), 4.56-4.51 (m, 1H), 3.85 (s, 3H), 3.07-3.00 (m, 1H), 2.89-2.75 (m, 2H), 2.67-2.48 (m, 3H), 2.02-1.89 (m, 1H); ¹³C-NMR (CDCl₃, 100 MHz) : 173.37, 154.48, 134.17, 131.42, 127.40, 112.30, 111.84, 108.33, 100.72, 56.07, 54.47, 37.75, 31.77, 25.83, 21.23.

10-Methyl-5,6,11b-tetrahydro-1H-indolizino[8,7-b]indol-3(2H)-one (2o)

A 50 mL two neck round bottom flask was charged with 1-(2-(7-methyl-1H-indol-3-yl)ethyl)pyrrolidine-2,5-dione (125 mg, 0.488 mmol), 4Å molecular sieves (50 mg), anhydrous CH₂Cl₂ (20 mL), and a stir bar. The flask was capped with a rubber septum and maintained in nitrogen atmosphere. Trifluoromethanesulfonic acid (432 µL, 4.877 mmol) was added and stirred at room temperature for 12 h. To this reaction mixture was added NaBH₄ (83 mg, 2.195 mmol), methanol (3 mL) and stirred for 0.5 h under nitrogen atmosphere. Then the reaction mixture was quenched with aqueous NaHCO₃. Organic layer was separated and aqueous layer was extracted with ethyl acetate (3 x 50 mL). The combined organic layer was washed with aqueous NaHCO₃, dried over anhydrous Na₂SO₄ and filtered. The solvent was removed under reduced pressure. The crude mixture was purified through neutral alumina column chromatography using ethyl acetate : hexane (4:1) as eluent to give 10-methyl-5,6,11b-tetrahydro-1H-indolizino[8,7-b]indol-3(2H)-one (2o) in 70% yield (82 mg) as...
A 50 mL two neck round bottom flask was charged with 1-(2-(5,7-dimethyl-1H-indol-3-yl)ethyl)pyrrolidine-2,5-dione (100 mg, 0.370 mmol), 4Å molecular sieves (50 mg), anhydrous CH$_2$Cl$_2$ (20 mL), and a stir bar. The flask was capped with a rubber septum and maintained in nitrogen atmosphere. Trifluoromethanesulfonic acid (327 µL, 3.699 mmol) was added and stirred at room temperature for 12 h. To this reaction mixture was added NaBH$_4$ (63 mg, 1.665 mmol), methanol (3 mL) and stirred for 0.5 h under nitrogen atmosphere. Then the reaction mixture was quenched with aqueous NaHCO$_3$. Organic layer was separated and aqueous layer was extracted with ethyl acetate (3 x 50 mL). The combined organic layer was washed with aqueous NaHCO$_3$, dried over anhydrous Na$_2$SO$_4$ and filtered. The solvent was removed under reduced pressure. The crude mixture was purified through neutral alumina column chromatography using ethyl acetate : hexane (4:1) as eluent to give 8,10-dimethyl-5,6,11,11b-tetrahydro-1H-indolizino[8,7-b]indol-3(2H)-one in 65% yield (61 mg) as pale blue solid. (m.p. : 252-253 °C; IR (KBr, cm$^{-1}$) : 3264, 2907, 2719, 1665, 1431, 1368; $^1$H-NMR (CDCl$_3$, 400 MHz) : δ 7.83 (br s, 1H), 7.13 (s, 1H), 6.84 (s, 1H), 4.96-4.92 (m, 1H), 4.52 (ddd, $J = 12.8, 5.5, 1.6$ Hz, 1H), 3.06-2.98 (m, 1H), 2.84 (ddd, $J = 15.6, 5.5, 1.6$ Hz, 1H), 2.80-2.79 (m, 1H), 2.65-2.57 (m, 2H), 2.54-2.50 (m, 1H), 2.45 (s, 3H), 2.42 (s, 3H), 1.98-1.91 (m, 1H); $^{13}$C-NMR (CDCl$_3$, 100 MHz) : 173.24, 134.09, 133.02, 129.48, 126.65, 124.61, 119.81, 115.83, 108.43, 54.39, 37.66, 31.69, 25.86, 21.36, 21.15, 16.65; HRMS (ESI) : [M+H]$^+$ Found 255.1509; Calculated 255.1497; for C$_{16}$H$_{19}$N$_2$O.

8-Fluoro-5,6,11,11b-tetrahydro-1H-indolizino[8,7-b]indol-3(2H)-one (2j)
A 50 mL two neck round bottom flask was charged with 1-(2-(5-fluoro-1H-indol-3-yl)ethyl)pyrrolidine-2,5-dione (100 mg, 0.384 mmol), 4Å molecular sieves (50 mg), anhydrous CH₂Cl₂ (20 mL), and a stir bar. The flask was capped with a rubber septum and maintained in nitrogen atmosphere. Trifluoromethanesulfonic acid (340 µL, 3.842 mmol) was added and stirred at room temperature for 12 h. To this reaction mixture was added NaBH₄ (65 mg, 1.729 mmol), methanol (3 mL) and stirred for 0.5 h under nitrogen atmosphere. Then the reaction mixture was quenched with aqueous NaHCO₃. Organic layer was separated and aqueous layer was extracted with ethyl acetate (3 x 50 mL). The combined organic layer was washed with aqueous NaHCO₃, dried over anhydrous Na₂SO₄ and filtered. The solvent was removed under reduced pressure. The crude mixture was purified through neutral alumina column chromatography using ethyl acetate : hexane (4:1) as eluent to give 8-fluoro-5,6,11,11b-tetrahydro-1H-indolizino[8,7-b]indol-3(2H)-one in 65% yield (61 mg) as off white solid. (m.p. : 276-277 °C); IR (KBr, cm⁻¹) : 3244, 2978, 2924, 2865, 1658, 1439, 1306, 799; ¹H-NMR (acetone-d₆, 400 MHz) : δ 10.3 (br s, 1H), 7.38 (dd, J = 9.0, 4.4 Hz, 1H), 7.20 (dd, J = 9.6, 2.4 Hz, 1H), 6.91 (td, J = 9.0, 2.4 Hz, 1H), 5.02-4.98 (m, 1H), 4.44 (ddd, J = 12.8, 5.6, 1.2 Hz, 1H), 3.08-3.00 (m, 1H), 2.81-2.70 (m, 2H), 2.69-2.64 (m, 1H), 2.58-2.49 (m, 1H), 2.35 (ddd, J = 16.4, 9.6, 2.4 Hz, 1H), 2.01-1.93 (m, 1H); ¹³C-NMR (DMSO-d₆, 100 MHz) : 172.33, 156.82 (d, J = 230.0 Hz, 1C), 136.82, 132.74, 126.69 (d, J = 9.8 Hz, 1C), 112.00 (d, J = 9.7 Hz, 1C), 108.82 (d, J = 25.7 Hz, 1C), 106.36 (d, J = 4.4 Hz, 1C), 102.79 (d, J = 23.1 Hz, 1C), 53.60, 36.80, 31.00, 25.30, 20.69.

8-Chloro-5,6,11,11b-tetrahydro-1H-indolizino[8,7-b]indol-3(2H)-one (2k)

A 50 mL two neck round bottom flask was charged with 1-(2-(5-chloro-1H-indol-3-yl)ethyl)pyrrolidine-2,5-dione (140 mg, 0.506 mmol), 4Å molecular sieves (50 mg), anhydrous CH₂Cl₂ (20 mL), and a stir bar. The flask was capped with a rubber septum and maintained in nitrogen atmosphere. Trifluoromethanesulfonic acid (448 µL, 5.059 mmol) was added and stirred at room temperature for 12 h. To this reaction mixture was added NaBH₄ (86 mg, 2.277 mmol), methanol (3 mL) and stirred for 0.5 h under nitrogen atmosphere. Then the reaction mixture was quenched with aqueous NaHCO₃. Organic layer was separated and aqueous layer was extracted with ethyl acetate (3 x 50 mL). The combined organic layer was washed with aqueous NaHCO₃, dried over anhydrous Na₂SO₄ and filtered. The solvent was removed under reduced pressure. The crude mixture was...
purified through neutral alumina column chromatography using ethyl acetate : hexane (4:1) as eluent to give 8-chloro-5,6,11b-tetrahydro-1H-indolizino[8,7-b]indol-3(2H)-one in 88% yield (116 mg) as pale brown solid. (m.p. : 241-242 °C); IR (KBr, cm⁻¹) : 3256, 2978, 2913, 2852, 2353, 1659, 1438, 1262, 641; \(^1\)H-NMR (CDCl₃, 400 MHz) : δ 7.88 (br s, 1H), 7.45 (d, \(J = 1.6\) Hz, 1H), 7.14 (dd, \(J = 8.6, 1.6\) Hz, 1H), 4.94-4.90 (m, 1H), 4.53 (dd, \(J = 13.2, 6.0, 1.6\) Hz, 1H), 3.03 (td, \(J = 11.6, 6.0\) Hz, 1H), 2.84 (ddd, \(J = 15.4, 6.0, 2.0\) Hz, 1H), 2.81-2.74 (m, 1H), 2.68-2.49 (m, 3H), 2.04-1.90 (m, 1H); \(^13\)C-NMR (DMSO-d₆, 100 MHz) : 172.38, 136.57, 134.61, 127.63, 123.29, 120.88, 117.26, 112.68, 106.06, 53.55, 36.77, 31.01, 25.26, 20.60; HRMS (ESI) : [M+H]⁺ Found 261.0784; Calculated 261.0795; for C₁₄H₁₄N₂OCl.

8-Bromo-5,6,11b-tetrahydro-1H-indolizino[8,7-b]indol-3(2H)-one (2l)

![Structural formula of 8-Bromo-5,6,11b-tetrahydro-1H-indolizino[8,7-b]indol-3(2H)-one (2l)](image)

A 50 mL two neck round bottom flask was charged with 1-(2-(5-bromo-1H-indol-3-yl)ethyl)pyrrolidine-2,5-dione (80 mg, 0.249 mmol), 4Å molecular sieves (50 mg), anhydrous CH₂Cl₂ (20 mL), and a stir bar. The flask was capped with a rubber septum and maintained in nitrogen atmosphere. Trifluoromethanesulfonic acid (220 µL, 2.491 mmol) was added and stirred at room temperature for 12 h. To this reaction mixture was added NaBH₄ (42 mg, 1.121 mmol), methanol (3 mL) and stirred for 0.5 h under nitrogen atmosphere. Then the reaction mixture was quenched with aqueous NaHCO₃. Organic layer was separated and aqueous layer was extracted with ethyl acetate (3 x 50 mL). The combined organic layer was washed with aqueous NaHCO₃, dried over anhydrous Na₂SO₄ and filtered. The solvent was removed under reduced pressure. The crude mixture was purified through neutral alumina column chromatography using ethyl acetate : hexane (4:1) as eluent to give 8-bromo-5,6,11b-tetrahydro-1H-indolizino[8,7-b]indol-3(2H)-one in 85% yield (65 mg) as off white solid. (m.p. : 260-261 °C); IR (KBr, cm⁻¹) : 3260, 2966, 2844, 1661, 1437, 1304, 793; \(^1\)H-NMR (CDCl₃, 400 MHz) : δ 8.10 (br s, 1H), 7.61 (s, 1H), 4.94-4.90 (m, 1H), 4.52 (dd, \(J = 13.6, 5.6\) Hz, 1H), 3.02 (td, \(J = 11.2, 5.6\) Hz, 1H), 2.83 (ddd, \(J = 16.0, 5.6\) Hz, 1H), 2.79-2.74 (m, 1H), 2.67-2.48 (m, 3H), 1.99-1.89 (m, 1H); \(^13\)C-NMR (DMSO-d₆, 100 MHz) : 172.32, 136.37, 134.83, 128.32, 123.40, 120.27, 113.15, 111.20, 105.96, 53.50, 36.74, 31.00, 25.25, 20.58.

10-Fluoro-5,6,11b-tetrahydro-1H-indolizino[8,7-b]indol-3(2H)-one (2m)

![Structural formula of 10-Fluoro-5,6,11b-tetrahydro-1H-indolizino[8,7-b]indol-3(2H)-one (2m)](image)
A 50 mL two neck round bottom flask was charged with 1-(2-(7-fluoro-1H-indol-3-yl)ethyl)pyrrolidine-2,5-dione (100 mg, 0.384 mmol), 4Å molecular sieves (50 mg), anhydrous CH₂Cl₂ (20 mL), and a stir bar. The flask was capped with a rubber septum and maintained in nitrogen atmosphere. Trifluoromethanesulfonic acid (340 µL, 3.842 mmol) was added and stirred at room temperature for 12 h. To this reaction mixture was added NaBH₄ (65 mg, 1.729 mmol), methanol (3 mL) and stirred for 0.5 h under nitrogen atmosphere. Then the reaction mixture was quenched with aqueous NaHCO₃. Organic layer was separated and aqueous layer was extracted with ethyl acetate (3 x 50 mL). The combined organic layer was washed with aqueous NaHCO₃, dried over anhydrous Na₂SO₄ and filtered. The solvent was removed under reduced pressure. The crude mixture was purified through neutral alumina column chromatography using ethyl acetate : hexane (4:1) as eluent to give 10-fluoro-5,6,11,11b-tetrahydro-1H-indolizino[8,7-b]indol-3(2H)-one in 81% yield (76 mg) as pale brown solid. (m.p. : 219-220 °C); IR (KBr, cm⁻¹) : 3221, 2924, 2855, 1672, 1437, 1352, 726; ¹H-NMR (acetone-d₆, 400 MHz) : δ 10.3 (br s, 1H), 7.13 (d, J = 7.8 Hz, 1H), 6.85 (td, J = 7.8, 4.7 Hz, 1H), 6.73 (dd, J = 11.5, 7.8 Hz, 1H), 4.87-4.83 (m, 1H), 4.27 (ddd, J = 13.0, 5.8, 1.0 Hz, 1H), 2.91-2.83 (m, 1H), 2.65-2.52 (m, 3H), 2.41-2.32 (m, 1H), 2.17 (ddd, J = 16.3, 9.4, 2.4 Hz, 1H), 1.84-1.76 (m, 1H); ¹³C-NMR (DMSO-d₆, 100 MHz) : 172.4, 149.13 (d, J = 239.1 Hz, 1C), 135.95, 130.43, 123.61 (d, J = 12.8 Hz, 1C), 119.07, 114.17, 107.15, 106.08 (d, J = 15.8 Hz, 1C), 53.61, 36.74, 31.04, 25.48, 20.89; HRMS (ESI) (m/z) : [M+H]+ Found 245.1100; Calculated 245.1090; for C₁₄H₁₄N₂OF.

1,2,3,6,7,12b-Hexahydroindolo[2,3-a]quinolinizin-4(12H)-one (2r)⁸

A 50 mL two neck round bottom flask was charged with 1-(2-(1H-indol-3-yl)ethyl)piperidine-2,6-dione (150 mg, 0.585 mmol), 4Å molecular sieves (50 mg), anhydrous CH₂Cl₂ (20 mL), and a stir bar. The flask was capped with a rubber septum and maintained in nitrogen atmosphere. Trifluoromethanesulfonic acid (518 µL, 5.853 mmol) was added and stirred at room temperature for 12 h. To this reaction mixture was added NaBH₄ (100 mg, 2.634 mmol), methanol (3 mL) and stirred for 0.5 h under nitrogen atmosphere. Then the reaction mixture was quenched with aqueous NaHCO₃. Organic layer was separated and aqueous layer was extracted with ethyl acetate (3 x 50 mL). The combined organic layer was washed with aqueous NaHCO₃, dried over anhydrous Na₂SO₄ and filtered. The solvent was removed under reduced pressure. The crude mixture was purified through neutral alumina column
chromatography using ethyl acetate : hexane (4:1) as eluent to give 1,2,3,6,7,12b-hexahydroindolo[2,3-α]quinolinizin-4(12H)-one in 87% yield (122 mg) as off white solid. (m.p. : 239-240 °C, lit.\(^8\) 240-241 °C); IR (KBr, cm\(^{-1}\)) : 3265, 3052, 1596, 1434, 1262; \(^1\)H-NMR (DMSO-\(d_6\), 400 MHz) : δ 10.92 (br s, 1H), 7.39 (d, \(J = 7.6\) Hz, 1H), 7.31 (d, \(J = 8.0\) Hz, 1H), 7.06 (t, \(J = 7.2\) Hz, 1H), 6.97 (t, \(J = 7.2\) Hz, 1H), 4.91 (dd, \(J = 12.4, 4.4\) Hz, 1H), 4.78 (dd, \(J = 10.4, 4.4\) Hz, 1H), 2.78 (td, \(J = 12.0, 4.0\) Hz, 1H), 2.71-2.54 (m, 3H), 2.39-2.22 (m, 2H), 1.82-1.75 (m, 2H), 1.67-1.57 (m, 1H); \(^13\)C-NMR (CDCl\(_3\), 100 MHz) : 169.19, 136.23, 133.32, 126.93, 122.18, 119.87, 118.43, 110.93, 109.67, 54.39, 40.15, 32.45, 29.10, 21.01, 19.42.

2,3,4,4a,7,8,13b,13c-Octahydro-1\(H\)-benzo[1,2]indolizino[8,7-\(b\)]indol-5(13\(H\))-one (2q)

A 50 mL two neck round bottom flask was charged with 2-(2-(1\(H\)-indol-3-yl)ethyl)hexahydro-1\(H\)-isoindole-1,3(2\(H\))-dione (80 mg, 0.270 mmol), 4Å molecular sieves (50 mg), anhydrous CH\(_2\)Cl\(_2\) (20 mL), and a stir bar. The flask was capped with a rubber septum and maintained in nitrogen atmosphere. Trifluoromethanesulfonic acid (239 µL, 2.699 mmol) was added and stirred at room temperature for 12 h. To this reaction mixture was added NaBH\(_4\) (46 mg, 1.215 mmol), methanol (3 mL) and stirred for 0.5 h under nitrogen atmosphere. Then the reaction mixture was quenched with aqueous NaHCO\(_3\). Organic layer was separated and aqueous layer was extracted with ethyl acetate (3 x 50 mL). The combined organic layer was washed with aqueous NaHCO\(_3\), dried over anhydrous Na\(_2\)SO\(_4\) and filtered. The solvent was removed under reduced pressure. The crude mixture was purified through neutral alumina column chromatography using ethyl acetate : hexane (4:1) as eluent to give 2,3,4,4a,7,8,13b,13c-octahydro-1\(H\)-benzo[1,2]indolizino[8,7-\(b\)]indol-5(13\(H\))-one in 62% yield (47 mg) as pale yellow solid. (m.p. : 248-249 °C); IR (KBr, cm\(^{-1}\)) : 3293, 2929, 2851, 1668, 1430, 1250; \(^1\)H-NMR (CDCl\(_3\), 400 MHz) : δ 7.94 (br s, 1H), 7.51 (d, \(J = 8.0\) Hz, 1H), 7.18 (t, \(J = 7.6\) Hz, 1H), 7.13 (t, \(J = 7.6\) Hz, 1H), 4.85 (d, \(J = 4.8\) Hz, 1H), 4.54 (dd, \(J = 12.8, 5.6\) Hz, 1H), 2.98 (td, \(J = 11.6, 4.4\) Hz, 1H), 2.88 (dd, \(J = 15.2, 4.4\) Hz, 1H), 2.84-2.80 (m, 1H), 2.76 (t, \(J = 5.6\) Hz, 1H), 2.68-2.64 (m, 1H), 2.32 (d, \(J = 14.0\) Hz, 1H), 1.56-1.46 (m, 3H), 1.28-1.24 (m, 1H), 1.12-1.01 (m, 2H), 0.83-0.74 (m, 1H); \(^13\)C-NMR (CDCl\(_3\), 100 MHz) : 173.87, 136.53, 130.20, 127.02, 122.27, 119.93, 118.46, 111.02, 110.43,
S30

56.47, 43.13, 38.25, 37.45, 29.84, 23.85, 23.19, 22.77, 21.25; HRMS (ESI) (m/z) : [M+H]^+

Found 281.1652; Calculated 281.1654; for C_{18}H_{21}N_{2}O.

**G** Synthesis of (±)-harmicine

2,3,5,6,11,11b-hexahydro-1H-indolizino[8,7-b]indole (4)^9

Lithium aluminium hydride (252 mg, 6.629 mmol) was weighed into a pre-dried two neck round bottom flask fitted with a condenser under nitrogen atmosphere. 5,6,11,11b-tetrahydro-1H-indolizino[8,7-b]indol-3(2H)-one (100 mg, 0.442 mmol) was added to the reaction flask under nitrogen atmosphere. Anhydrous tetrahydrofuran was added to the reaction mixture at 0 °C and the reaction mixture was stirred at room temperature for 24 h. After checking TLC, tert-butyl methyl ether (25.0 mL) was added and the reaction was quenched by careful addition of saturated aqueous sodium potassium tartrate solution. The mixture was stirred for 1 h before the addition of anhydrous Na$_2$SO$_4$ prior to filtration through celite pad. The filtrate was evaporated under reduced pressure to give of 2,3,5,6,11,11b-hexahydro-1H-indolizino[8,7-b]indole, 73 mg (78%), as colorless solid. (m.p. : 171-172 °C, lit.9 174-175 °C); IR (KBr, cm$^{-1}$) : 3433, 3054, 2940, 2842, 1453, 1305, 743; $^1$H-NMR (CDCl$_3$, 400 MHz) : $\delta$ 7.85 (br s, 1H), 7.48 (d, $J = 7.6$ Hz, 1H), 7.31 (d, $J = 7.8$ Hz, 1H), 7.14 (td, $J = 7.2$, 1.0 Hz, 1H), 7.09 (td, $J = 7.6$, 1.0 Hz, 1H), 4.26-4.23 (m, 1H), 3.33 (ddd, $J = 13.2$, 5.6, 2.4 Hz, 1H), 3.12-3.05 (m, 1H), 2.99-2.87 (m, 3H), 2.69-2.64 (m, 1H), 2.31-2.28 (m, 1H), 1.96-1.83 (m, 3H); $^{13}$C-NMR (CDCl$_3$, 100 MHz) : 136.10, 135.57, 127.52, 121.57, 119.55, 118.27, 110.84, 108.03, 57.09, 49.41, 46.10, 29.55, 23.58, 17.95.

**Synthesis of (±)-10-desbromoarborescidine-A**

1,2,3,4,6,7,12,12b-Octahydroindolo[2,3-a]quinolizine (5)^10

Lithium aluminium hydride (710 mg, 18.727 mmol) was weighed into a pre-dried two neck round bottom flask fitted with a condenser under nitrogen atmosphere. 1,2,3,6,7,12b-hexahydroindolo[2,3-a]quinolizin-4(12H)-one (300 mg, 1.248 mmol) was added to the reaction flask under nitrogen atmosphere. Anhydrous tetrahydrofuran was added to the reaction mixture at 0 °C and the reaction mixture was heated to reflux for 24 h. After checking TLC, tert-butyl methyl ether (25.0 mL) was added and the reaction was quenched by careful addition of
saturated aqueous sodium potassium tartrate solution. The mixture was stirred for 1 h before the addition of anhydrous Na₂SO₄ prior to filtration through celite pad. The filtrate was evaporated under reduced pressure to give 1,2,3,4,6,7,12,12b-octahydroindolo[2,3-a]quinolizine, 178 mg (63%), as colorless solid. (m.p. : 144-145 °C, lit.¹⁰ 146-148 °C); IR (KBr, cm⁻¹) : 3191, 2922, 2848, 1448, 1321, 735; ¹H-NMR (CDCl₃, 400 MHz) : δ 7.72 (br s, 1H), 7.47 (d, J = 7.6 Hz, 1H), 7.30 (d, J = 7.8 Hz, 1H), 7.15-7.07 (m, 2H), 3.24 (d, J = 11.0 Hz, 1H), 3.10-2.98 (m, 3H), 2.75-2.59 (m, 2H), 2.39 (td, J = 11.0, 4.0 Hz, 1H), 2.07 (dd, J = 12.0, 2.4 Hz, 1H), 1.91 (dt, J = 12.0, 3.2 Hz, 1H), 1.80-1.71 (m, 2H), 1.60 (ddd, J = 24.0, 12.0, 3.2 Hz, 1H), 1.55-1.45 (m, 1H); ¹³C-NMR (CDCl₃, 100 MHz) : 136.09, 135.27, 127.64, 121.37, 119.47, 118.23, 110.83, 108.26, 60.37, 55.89, 53.69, 30.13, 25.88, 24.46, 21.73.

(H) Crystal structures

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(1) References


C13CPD CDCl3 {D:\CRR} KOPAL 1
C13CPD CDCl3 {D:\CRR} KOPAL 1

Current Data Parameters
NAME             SMR-PR
EXPNO                 2
PROCNO                1

F2 - Acquisition Parameters
Date_          20120307
Time              11.29
INSTRUM           spect
PROBHD            5 mm BBO BB-1H
PULPROG          zgpg30
TD           65536
SOLVENT           CDCl3
NS                  256
DS                  4
SWR           24038.461 Hz
FTRES          0.366798 Hz
AQ            1.3631988 sec
RG                50.8
DN            20.800 usec
DE             6.00 usec
TE          295.5 K
D1            2.00000000 sec
d11            0.03000000 sec
DELTA            1.89999998 sec
TD0                   1

======== CHANNEL f1 ========
NUC1               13C
P1               9.50 usec
PL1            -0.60 dB
SF01        106.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2         waltz16
NUC2                1H
PCPD2            90.00 usec
PL12            15.60 dB
PL13            15.60 dB
PL2             -0.90 dB
SF02        400.1316005 MHz

F2 - Processing parameters
S1              32768
SF          106.6127546 MHz
WOK              EM
SSB             0
LB          1.60 Hz
GB                  0
PC             1.40

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Current Data Parameters
NAME           SMR-PHIM
EXPNO                 2
PROCNO                1

F2 - Acquisition Parameters
Date_          20101102
Time              13.29
INSTRUM           spect
PROBHD   5 mm BBO BB-1H
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                  106
DS                    4
SWR           24038.461 Hz
T1RES               0.366798 Hz
AQ           1.3631988 sec
RG                  912
DW               20.800 usec
TE           298.0 K
D1       2.00000000 sec
d11      0.03000000 sec
DELTA      1.89999998 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                13C
P1                 9.50 usec
PL1               -0.60 dB
SF01      100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2         waltz16
NUC2                 1H
PCPD2             90.00 usec
PL12               15.60 dB
PL13               15.60 dB
PL2               -0.90 dB
SF02      400.1316005 MHz

F2 - Processing parameters
SI                32768
SF           100.6127547 MHz
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LB               1.00 Hz
GB                  0
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Electronic Supplementary Material (ESI) for RSC Advances
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C13CPD CDC13 {D:\CRR} KOPAL 1

Current Data Parameters
NAME     SMR-1-156-1
EXPNO     2
PROCNO    1

F2 - Acquisition Parameters
Date_      20101229
Time       12.53
INSTRUM    spect
PROBHD     5 mm BBO BB-1H
PULPROG    zgpg30
TD         65536
SOLVENT    CDCl3
NS         63
DS         4
SNR        24038.461 Hz
PDRES      0.366798 Hz
AQ         1.3631988 sec
RG         1440
DN         20.800 usec
DE         6.00 usec
TE         297.6 K
D1         2.00000000 sec
d11        0.03000000 sec
DELTA      1.89999998 sec
TD0        1

======== CHANNEL f1 ========
NUC1       13C
P1         9.50 usec
PL1        -0.60 dB
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2    waltz16
NUC2       1H
P12        90.00 usec
PL12       15.60 dB
PL13       15.60 dB
PL2        -0.90 dB
SFO2       400.1316005 MHz

F2 - Processing parameters
SI         32768
SF         100.6127690 MHz
ROW        EM
SSB        0
LB         1.00 Hz
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PROTON CDCl3 (D:\CRR) KOPAL 1

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#### CHANNEL f1

| NUC1         | 13C                            |
| P1           | 9.50 usec                      |
| PL1          | -8.60 dB                       |
| SFO1         | 100.6228298 MHz                |

#### CHANNEL f2

| NUC2         | 1H                             |
| PCPD2        | 90.00 usec                     |
| PL12         | 15.60 dB                       |
| PL13         | 15.60 dB                       |
| PL2          | -9.90 dB                       |
| SFO2         | 400.1316005 MHz                |

#### F2 - Processing parameters

| S1           | 32748                          |
| SF           | 100.6127561 MHz                |
| RWX          | 10                             |
| SSB          | 0                              |
| LB           | 1.60 Hz                        |
| GB           | 0                              |
| FC           | 1.40                           |
Current Data Parameters
NAME          SMR-Con-A
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameters
Date_          20120130
Time              18.32
INSTRUM           spect
PROBHD   5 mm BBO BB-1H
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                4
SNR                24038.461 Hz
FTRES         0.366798 Hz
AQ             1.3631988 sec
RG                50.8
DW               20.800 usec
DE                 6.00 usec
TE                297.1 K
D1             2.00000000 sec
d11          0.03000000 sec
DELTA        1.89999998 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                13C
P1                 9.50 usec
PL1             -0.60 dB
SF01           100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2         waltz16
NUC2                 1H
PCPD2         90.00 usec
PL12             15.60 dB
PL13             15.60 dB
PL2             -0.90 dB
SF02         400.1316005 MHz

F2 - Processing parameters
SI                32768
SF             100.6228298 MHz
KOM                 EM
SSB                  0
LB                1.00 Hz
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SMR-CHLORO

**EXPNO**  
1

**PROCNO**  
1

**F2 - Acquisition Parameters**

**Date_**  
20111208

**Time**  
11.28

**INSTRUM**  
spect

**PROBHD**  
5 mm BEZ BB-1H

**PULPROG**  
zpg30

**TD**  
65536

**SOLVENT**  
CDCl3

**NS**  
256

**DS**  
4

**SNR**  
24038.461 Hz

**FTRES**  
0.366798 Hz

**AQ**  
1.3631988 sec

**RG**  
1290

**DN**  
20.800 usec

**DE**  
6.00 usec

**TE**  
298.1 K

**D1**  
2.000000000 sec

**d11**  
0.000000000 sec

**DELTA**  
1.89999998 sec

**TDO**  
1

**LU3C**

**F2 - Processing parameters**

**SI**  
32768

**SF**  
100.6127543 MHz

**WDW**  
EM

**SSB**  
0

**LB**  
1.00 Hz

**GB**  
0

**PC**  
1.40
Current Data Parameters
NAME          SMR-con-B
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameters
Date_          20120130
Time              13.53
INSTRUM           spect
PROBHD   5 mm BBO BB-1H
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                 4
SNR              24038.461 Hz
FTIDRES         0.366798 Hz
AQ             1.3631988 sec
RG              1030
INW              20.800 usec
TE               6.00 usec
DK                795.9 K
DK1              2.00000000 sec
d11            0.03000000 sec
DELTA         1.39999998 sec
TDO                   1

======== CHANNEL f1 ========
NUC1                13C
P1                 9.50 usec
PL1                -6.60 dB
SPFO1      100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2         waltz16
NUC2                 1H
PCPD2            90.00 usec
PL12              15.60 dB
PL13              15.60 dB
PL2               -0.90 dB
SPFO2    400.1316005 MHz

F2 - Processing parameters
SI                32768
SF             100.6127546 MHz
KOK                 EM
SSB                 0
LB                1.00 Hz
GB                 0
FC                 1.40
C13CPD CDCl3 {D:\CRR} KOPAL 1

Current Data Parameters
NAME: SMR-I-230-1
EXPNO: 2
PROCNO: 1

F2 - Acquisition Parameters
Date: 20110713
Time: 14.00
INSTRUM: spect
PROBHD: 5 mm BBO BB-1H
PULPROG: zgpg30
TD: 65536
SOLVENT: CDCl3
NS: 269
DS: 4
SWR: 24038.461 Hz
FTDRFS: 0.366798 Hz
AQ: 1.3631988 sec
RG: 50.8
DN: 20.800 usec
DE: 6.00 usec
TE: 295.5 K
D1: 2.00000000 sec
d11: 0.03000000 sec
DELTA: 1.89999998 sec
TD0: 1

====== CHANNEL f1 ======
NUC1: 13C
P1: 9.50 usec
PL1: -0.60 dB
SF01: 100.6228298 MHz

====== CHANNEL f2 ======
CPDPRG2: waltz16
NUC2: 1H
PCPD2: 90.00 usec
PL12: 15.60 dB
PL13: 15.60 dB
PL2: -0.90 dB
SF02: 400.1316005 MHz

F2 - Processing parameters
SI: 32768
SF: 100.6127664 MHz
WOK: EM
SSB: 0
LB: 1.60 Hz
GB: 0
PC: 1.40
Current Data Parameters
NAME          SMR-I-235-2
EXPNO             1
PROCNO            1

F2 - Acquisition Parameters
Date_        20110708
Time            12.15
INSTRUM       spect
PROBHD      5 mm BBO BB-1H
PULPROG   zg30
TD          65536
SOLVENT      CDCl3
NS            16
DS            2
SWH      8223.685 Hz
FIDRES 0.125483 Hz
AQ         3.9846387 sec
RG             228
DW 60.800 usec
DE           6.00 usec
TE        295.7 K
D1   1.000000000 sec
TD0            1

==== CHANNEL f1 =====
NUC1         1H
P1        14.00 usec
PL1      -0.80 dB
SFO1  400.1324710 MHz

F2 - Processing parameters
SI        32768
SF    400.1299888 MHz
WDW      EM
SSB           0
LB          0.30 Hz
GB            0
PC            1.00
C13CPD CDCl3 {D:\CRR} KOPAL 1

Current Data Parameters
NAME        SMR-I-235-2
EXPNO                 3
PROCNO                1

F2 - Acquisition Parameters
Date_          20110713
Time              12.45
INSTRUM           spect
PROBHD   5 mm BBO BB-1H
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           24038.461 Hz
FTPDRES         0.366798 Hz
AQ                 1.3631988 sec
RG                 50.8
DW               20.800 usec
DE                6.00 usec
TE               295.7 K
D1                 2.00000000 sec
d11              0.03000000 sec
DELTA        1.89999998 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                13C
P1                 9.50 usec
PL1              -0.60 dB
SP01          100.6228298 MHz

======== CHANNEL f2 ========
CPDP2G2         waltz16
NUC2                 1H
PCPD2             90.00 usec
PL12              15.60 dB
PL13              15.60 dB
PL2                -0.90 dB
SP02          400.1316005 MHz

F2 - Processing parameters
SI                  32768
SF               100.6127685 MHz
RWW            0 MHz
SSB                   0
LB                1.00 Hz
GB                    0
PC                1.40
PROTON CDCl3 (D:\CRR) KOPAL 1

- Peaks at 7.966, 7.509, 7.093, 7.040, 6.985 ppm
- Peaks at 3.848, 3.829, 3.069, 3.048, 3.031 ppm
- Other peaks at various ppm values

Chemical structure with labels for protons.
Current Data Parameters
NAME       SMR-I-100-10
EXPNO                 2
PROCNO                1

F2 - Acquisition Parameters
Date_          20110802
Time              11.42
INSTRUM           spect
PROBHD   5 mm BBO BB-1H
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                  175
DS                    4
SNR 24038.461 Hz
FTRES        0.366798 Hz
AQ            1.3631988 sec
RG                 50.8
DN      20.800 usec
DE                6.00 usec
TE                297.5 K
D1        2.00000000 sec
d11              0.03000000 sec
DELTA     1.89999998 sec
TD0                   1

==== CHANNEL f1 ========
NUC1                13C
P1                 9.50 usec
PL1               -0.60 dB
SP01            100.6228298 MHz

==== CHANNEL f2 ========
CPDPDG2         waltz16
NUC2                 1H
PCPD2            90.00 usec
PL12             15.60 dB
PL13             15.60 dB
PL2               -0.90 dB
SP02          400.1316000 MHz

F2 - Processing parameters
S1               32768
SF        100.6127564 MHz
KOM            0
SSB               0
LB               1.00 Hz
GB                0
PC                 1.40
C13CPD CDC13 (D:\CRR) KOPAL 1

Current Data Parameters
NAME         SMR-4DS
EXPNO         1
PROCNO        1

F2 - Acquisition Parameters
Date           20120216
Time            18.14
INSTRUM        spect
PROBHD       5 mm BBO BB-1H
PULPROG       zgpg30
TD            65536
SOLVENT       CDCl3
NS             1024
DS             4
SNR        24038.461 Hz
FIDRES      0.366798 Hz
AQ           1.3631988 sec
RG             50.8
DW        20.800 usec
DE             6.00 usec
TE           297.7 K
D1       2.00000000 sec
d11      0.00000000 sec
DELTA    1.89999998 sec
TD0         1

====== CHANNEL f1 ======
NUC1         13C
F1               9.50 usec
PL1            -3.60 dB
SF01 100.6228298 MHz

====== CHANNEL f2 ======
NUC2           1H
PCPD2         90.00 usec
PL12          15.60 dB
PL13          15.60 dB
PL2          -2.90 dB
SP02 400.1316005 MHz

F2 - Processing parameters
S1        32768
SF       100.6127547 MHz
DSW        EM
SSB         0
LB          1.60 Hz
GB            0
PC           1.40
PROTON CDCl3 {D:\CRR} KOPAL 1

Current Data Parameters
NAME        SMR-I-192-2
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameters
Date_          20110324
Time              11.48
INSTRUM           spect
PROBHD   5 mm BBO BB-1H
PULPROG            zg30
TD                65536
SOLVENT           CDCl3
NS                   16
DS                    2
SWH            8223.685 Hz
FIDRES         0.125483 Hz
AQ            3.9846387 sec
RG                  256
DW               60.800 usec
DE                 6.00 usec
TE                294.4 K
D1           1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 1H
P1                14.00 usec
PL1               -0.90 dB
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                32768
SF          400.1299939 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
C13CPD CDCl3 {D:\CRR} KOPAL 1

Current Data Parameters
NAME        SMR-I-192-2
EXPNO                 2
PROCNO                1

F2 - Acquisition Parameters
Date_          20110324
Time              12.04
INSTRUM           spect
PROBHD   5 mm BBO BB-1H
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                  256
DS                4
SMR                    24038.461 Hz
FIDRES         0.366798 Hz
AQ            1.3631988 sec
RG                 1030
DW               20.800 usec
DE                6.00 usec
TE                294.8 K
D1             2.00000000 sec
d11          0.03000000 sec
DELTA        1.89999998 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                13C
P1                 9.50 usec
PL1               -0.60 dB
SP01           100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2         waltz16
NUC2                 1H
PCPD2               90.00 usec
PL12              15.60 dB
PL13              15.60 dB
PL2             -0.90 dB
SP02          400.1316005 MHz

F2 - Processing parameters
SI                32768
SF            100.6127561 MHz
CKW            0
SSB          1.00 Hz
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PC             1.40
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PROTON CDCl₃ \{D:\CRR\} KOPAL 1

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EXPNO: 1
PROCNO: 1

F2 - Acquisition Parameters
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Time: 15.40
INSTRUM: spect
PROBHD: 5 mm BBO BB-1H
PULPROG: zg30
TD: 65536
SOLVENT: CDCl₃
NS: 16
DS: 2
SWH: 8233.685 Hz
FIDRES: 0.125483 Hz
AQ: 3.9846387 sec
RG: 256
DW: 60.800 usec
DE: 6.00 usec
TE: 294.2 K
D1: 1.00000000 sec
TD0: 1

== CHANNEL f1 ==
NUC1: 1H
P1: 14.00 usec
PL1: -0.90 dB
SF01: 400.1324710 MHz

F2 - Processing parameters
SI: 32768
SF: 400.1300034 MHz
WDW: EM
SSB: 0
LB: 0.30 Hz
GB: 0
PC: 1.00
C13CPD CDCl3 \{D:\CRR\} KOPAL 1

---

Current Data Parameters
NAME: SMR-ALPHA
EXPNO: 1
PROCNO: 1

F2 - Acquisition Parameters
Date: 20111221
Time: 11.46
INSTRUM: spect
PROBHD: 5 mm BBO BB-1H
PULPROG: zgpg30
TD: 65536
SOLVENT: CDCl3
NS: 512
DS: 4
SNR: 24038.461 Hz
PTRES: 0.366798 Hz
AQ: 1.3631988 sec
RG: 57
DW: 20.800 usec
DE: 6.00 usec
TE: 297.8 K
D1: 2.00000000 sec
d11: 0.03000000 sec
DELTA: 1.89999998 sec
TD0: 1

====== CHANNEL f1 ======
NUC1: 13C
P1: 9.50 usec
PL1: -0.60 dB
SF01: 100.6228298 MHz

====== CHANNEL f2 ======
CPDPRG2: waltz16
NUC2: 1H
PCPD2: 90.00 usec
PL12: 15.60 dB
PL13: 15.60 dB
PL2: -0.90 dB
SF02: 400.1316005 MHz

F2 - Processing parameters
SI: 32768
SF: 100.6127594 MHz
ROW: EM
SSB: 0
LB: 1.00 Hz
GB: 0
PC: 1.40

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Electronic Supplementary Material (ESI) for RSC Advances
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PROTON CDCl3 {D:\CRR} KOPAL 1
Current Data Parameters
NAME        SMR-I-206-2
EXPNO                 2
PROCNO                1

F2 - Acquisition Parameters
Date_          20110420
Time              12.22
INSTRUM           spect
PROBHD   5 mm BBO BB-1H
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                  512
DS                    4
SWH           24038.461 Hz
FIDRES         0.366798 Hz
AQ            1.3631988 sec
RG                 50.8
DW               20.800 usec
DE                 6.00 usec
TE                295.2 K
D1           2.00000000 sec
d11          0.03000000 sec
DELTA        1.89999998 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                13C
P1                 9.50 usec
PL1              -8.60 dB
SP01  100.6228298 MHz

======== CHANNEL f2 ========
CPDPKG2         waltz16
NUC2                 1H
PCPD2              90.00 usec
PL12             15.60 dB
PL13              15.60 dB
PL2             -0.90 dB
SP02  400.1316005 MHz

F2 - Processing parameters
SI                32768
SF          100.6127538 MHz
NOW             0
SSB              0
LB                1.60 Hz
GB                0
PC                1.40
PROTON DMSO (D:\CRR) crr 1
C13CPD DMSO {D:\CRR} KOPAL 1

Current Data Parameters
NAME    SMR-I-214-2
EXPNO    2
PROCNO   1

F2 - Acquisition Parameters
Date_    20110525
Time      12.02
INSTRUM   spect
PROBHD    5 mm BBO BB-1H
PULPROG   zgpg30
TD        65536
SOLVENT   DMSO
NS        512
DS        4
SNR       24038.461 Hz
FTRES     0.366798 Hz
AQ        1.3631988 sec
RG        50.8
DM        20.800 usec
DE        6.00 usec
TE        296.2 K
D1        2.00000000 sec
d11       0.03000000 sec
DELTA     1.89999998 sec
TD0       1

======== CHANNEL f1 ========
NUC1     13C
P1        9.50 usec
PL1       -8.60 dB
SF01      100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2   waltz16
NUC2     1H
PCPD2     90.00 usec
PL12      15.60 dB
PL13      15.60 dB
PL2       -0.90 dB
SF02      400.1316005 MHz

F2 - Processing parameters
SI        32768
SF        100.6128109 MHz
WOK       SM
SSB       0
LB        1.60 Hz
GB        0
FC        1.40
C13CPD DMSO {D:\CRR} KOPAL 1

Current Data Parameters
NAME                SMR-I-215-2
EXPNO                2
PROCNO               1

F2 - Acquisition Parameters
Date_           20110525
Time                   12.57
INSTRM           spect
PROBHD      5 mm BBO BB-1H
PULPROG          zgpg30
TD               65536
SOLVENT            DMSO
NS                 512
DS                   4
SNR            24038.461 Hz
TR/TRES     0.366798 Hz
AQ            1.3631988 sec
GS                 50.8
DN             20.800 usec
DE               6.00 usec
TE           295.7 K
D1               2.0000000 sec
d11          0.0000000 sec
DELTA          1.8999998 sec
TD0               1

======== CHANNEL f1 ========
NUC1               13C
P1                   9.50 usec
PL1               -8.60 dB
SP01            100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2         waltz16
NUC2               1H
PCPD2             90.00 usec
PL12               15.60 dB
PL13              -15.60 dB
PL2            -0.90 dB
SP02           400.1316005 MHz

F2 - Processing parameters
SI               32768
SF              100.6228298 MHz
WDW                  EM
SSB                   0
LB            1.00 Hz
GB                0
PC                1.40
2-F Pthalimide cyclized
PROTON Acetone
C13CPD DMSO {D:\CRR} KOPAL 1

Current Data Parameters
NAME: SMR-BETCAR
EXPHD: 1
PROCNO: 1

F2 - Acquisition Parameters
Date: 20120112
Time: 9.30
INSTRUM: spect
PROBHD: 5 mm BBO BB-1H
PULPROG: zgpg30
TD: 65536
SOLVENT: DMSO
NS: 17000
DS: 4
SNR: 24038.461 Hz
FTRES: 0.366798 Hz
AQ: 1.3631988 sec
RG: 50.8
DN: 20.800 usec
DE: 6.00 usec
TE: 293.9 K
D1: 2.00000000 sec
d11: 0.03000000 sec
DELTA: 1.89999998 sec
TD0: 1

---------- CHANNEL f1 ----------
NUC1: 13C
P1: 9.50 usec
PL1: -8.60 dB
SP01: 100.6228298 MHz

---------- CHANNEL f2 ----------
CPDPRG2: waltz16
NUC2: 1H
PCPD2: 90.00 usec
PL12: 15.60 dB
PL13: 15.60 dB
PL2: -0.90 dB
SP02: 400.1316005 MHz

F2 - Processing parameters
SI: 32768
SF: 100.6228113 MHz
NOW: 8M
SSB: 0
LB: 1.00 Hz
GB: 0
PC: 1.40
PROTON CDCl3 [D:\CRR] KOPAL 1
4-F Succinimide cyclized
PROTON Acetone
Current Data Parameters
NAME          SMR-I-188
EXPNO                 2
PROCNO                1

F2 - Acquisition Parameters
Date_          20110321
Time              11.02
INSTRUM           spect
PROBHD   5 mm BBO BB-1H
PULPROG          zgpg30
TD                65536
SOLVENT            DMSO
NS                  512
DS                 4
SNR            24038.461 Hz
FT0RES         0.366798 Hz
AQ            1.3631988 sec
RG               1290
DN            20.800000 sec
DE                6.00 usec
TE               295.5 K
D1            2.000000000 sec
d11           0.030000000 sec
DELTA        1.89999998 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                13C
P1                 9.50 usec
PL1              -0.60 dB
SFO1        100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2         waltz16
NUC2                 1H
PCPD2            90.00 usec
PL12              15.60 dB
PL13             15.60 dB
PL2             -0.90 dB
SFO2        400.1316005 MHz

F2 - Processing parameters
SI                32768
SF          100.6128210 MHz
RGB               8M
SSB                0
LB               1.00 Hz
GB                0
PC                1.40
C13CPD CDC13 {D:\CRR} KOPAL 1

Current Data Parameters
NAME     SMR-I-189-2
EXPHD    4
PROCNO   1

F2 - Acquisition Parameters
Date_    20110321
Time_    17.11
INSTRUM  spect
PROBHD   5 mm BBO BB-1H
PULPROG  zgpg30
TD       65536
SOLVENT  CDCl3
NS       123
DS       4
SNR      24038.48 Hz
PT1RES   0.366798 Hz
AQ       1.3631988 sec
RG       912
DN       20.800 usec
DE       6.00 usec
TE       294.6 K
D1       2.00000000 sec
d11      0.03000000 sec
DELTA    1.89999998 sec
TD0      1

======== CHANNEL f1 ========
NUC1     13C
P1       9.50 usec
PL1      -0.60 dB
SFO1     100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2  waltz16
NUC2     1H
PCPD2    90.00 usec
PL12     15.60 dB
PL13     15.60 dB
PL2      -0.90 dB
SFO2     400.1316005 MHz

F2 - Processing parameters
SI       32768
SF       100.6132883 MHz
WOW      EM
SSB      0
LB       1.00 Hz
GB       0
FC       1.40
2F Succinimide cyclized
PROTON Acetone \(D:\text{data} \) nmr 1
C13CPD CDCl3 {D:\CRR} KOPAL 1

Current Data Parameters
NAME          SMR-CON-D
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameters
Date_          20120221
Time              21.37
INSTRUM           spect
PROBHD   5 mm BBO BB-1H
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                13497
DS                4
SNR              24038.461 Hz
FTRES          0.366798 Hz
AQ                 1.3631988 sec
RG                50.8
DN             20.800 usec
DE                6.00 usec
TE                298.1 K
D1            2.00000000 sec
d11            0.00000000 sec
DELTA          1.89999998 sec
TD0           1

======== CHANNEL f1 ========
NUC1                13C
P1                 9.50 usec
PL1            -0.60 dB
FO1            100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2         waltz16
NUC2                1H
PCPD2            90.00 usec
PL12           15.60 dB
PL13           15.60 dB
PL2            -0.90 dB
FO2            400.1316005 MHz

F2 - Processing parameters
SI                32768
SF            100.6127673 MHz
ROW            0
SSB             0
LB             1.60 Hz
GB             0
PC             1.40
Current Data Parameters
NAME            SMR-HEX
EXPNO                 2
PROCNO                1

F2 - Acquisition Parameters
Date_          20110809
Time              14.22
INSTRUM           spect
PROBHD   5 mm BBO BB-1H
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                  346
DS                    4
SNR                  24038.46 Hz
FIDRES         0.366798 Hz
AQ            1.3631988 sec
RG                 1150
DW               20.800 usec
DE                6.00 usec
TE                298.0 K
D1          2.00000000 sec
d11          0.03000000 sec
DELTA        1.89999998 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                13C
P1                 9.50 usec
PL1                -0.60 dB
SPO1           100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2         waltz16
NUC2                 1H
PCPD2            90.00 usec
PL12            15.80 dB
PL13            15.80 dB
PL2             -0.90 dB
SPO2          400.1316005 MHz

F2 - Processing parameters
SI                32768
SF                   100.6127532 MHz
WOK                 SM
SSB                 0
LB                1.00 Hz
GB                0
PC                1.40
C13CPD CDCl3 {D:\CRR} KOPAL 1
Current Data Parameters
NAME            SMR-AL
EXPNO            2
PROCNO            1

F2 - Acquisition Parameters
Date_          20111125
Time              12.10
INSTRUM           spect
PROBHD   5 mm BBO BB-1H
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                  512
DS                4
SWH           24038.461 Hz
FTDRES           0.366798 Hz
AQ            1.3631988 sec
RG                 2050
DW              20.800 usec
DE                6.00 usec
TE            295.8 K
D1           2.00000000 sec
d11        0.00000000 sec
DELTA        1.89999998 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                13C
P1                 9.50 usec
PL1              -8.60 dB
SP01          100.6228298 MHz

======== CHANNEL f2 ========
NUC2                 1H
PCPD2           90.00 usec
PL12              15.60 dB
PL13              15.60 dB
PL2               -0.90 dB
SP02          400.1316005 MHz

F2 - Processing parameters
S1           32768
SF           100.6127541 MHz
ROW            SM
SSB              0
LB             1.00 Hz
GB            0
PC            1.40
C13CPD CDCl3 {D:\CRR} KOPAL 1