

Electronic Supplementary Information

3-(2-Formylphenyl)-4-(5-benzyloxy-1H-indol-3-yl)-1-methyl-1H-pyrrole-2,5-dione (4).

Compound **4** was obtained as an orange solid (79% yield) following the same procedure as previously described for compound **3** (ref 22) starting from **2** (12 mmol). Reaction time 3.5 h. Mp : 92-94 °C ; Rf 0.84 (EtOAc) ; IR (KBr, cm⁻¹) v 3549, 2774, 1760, 1697, 1616, 1385, 743 ; ¹H NMR (DMSO-*d*₆, 250 MHz) δ 3.05 (s, 3H, CH₃), 4.29 (s, 2H, CH₂), 5.80 (d, 1H, H₄, *J* = 2.2 Hz), 6.74 (dd, 1H, H₆, *J* = 8.8 Hz, *J* = 2.2 Hz), 7.23-7.39 (m, 7H, H₇/H₆/H_{φ,a/b/c}), 7.66-7.72 (m, 2H, H₄/H₅), 8.01 (d, 1H, H₃, *J* = 9.0 Hz), 8.11 (s, 1H, H₂), 10.00 (s, 1H, CHO), 11.95 (br s, 1H, NH) ; ¹³C NMR (DMSO-*d*₆, 62.9 MHz) δ 24.2 (CH₃), 69.0 (CH₂), 103.6 (CH), 104.1 (Cq), 113.1 (2CH), 124.4 (Cq), 125.0 (Cq), 127.1 (2CH), 127.6 (CH), 128.4 (2CH), 128.8 (CH), 129.4 (CH), 131.6 (CH+Cq), 132.5 (CH), 133.4 (Cq), 133.8 (CH), 134.5 (Cq), 134.7 (Cq), 136.9 (C), 152.8 (Cq), 170.9 (CO), 171.2 (CO), 191.8 (CO). MS (IS) : 437 (M+H)⁺, 459 (M+Na)⁺.

4,5-Dimethoxy-2-tributylstannylbenzoic acid methyl ester (10).

To a solution of **9** (1.0 g, 3.6 mmol) in dry toluene (30 mL) were successively added Sn₂Bu₆ (2.53 g, 4.3 mmol) and LiCl (75 mg, 1.8 mmol). The solution was degassed by bubbling argon for 20 min. and PdCl₂(PPh₃)₂ (229 mg, 0.36 mmol) was added. The reaction mixture was placed in a pre-heated oil bath and refluxed for 24 h. After cooling, hexane (30 mL) and an aqueous saturated KF solution (30 mL) were added. The salts were removed by filtration over celite and washed with hexane (3x30 mL). The organic layer was concentrated under reduced pressure and the crude residue was purified by flash chromatography on silica gel (petroleum ether then petroleum ether / EtOAc 98/2) to afford compound **10** as colorless oil (959 mg, 54 %). Rf 0.39 (petroleum ether /EtOAc 1/1) ; IR (KBr, cm⁻¹) v 2954, 1703, 1584, 1505, 1268 ; ¹H NMR (DMSO-*d*₆, 250 MHz) δ 0.87 (t, 9H, CH₃, *J* = 7.2 Hz), 1.03 (t, 6H, CH₂-Sn, *J* = 8.2 Hz), 1.23-1.38 (m, 6H, CH₂), 1.44-1.56 (m, 6H, CH₂), 3.88 (s, 3H, CH₃), 3.92 (s, 3H, CH₃), 3.95 (s, 3H, CH₃), 7.08 (s, 1H, H₃), 7.64 (s, 1H, H₆) ; ¹³C NMR (DMSO-*d*₆, 62.9 MHz) δ 11.3 (CH₂), 13.9 (CH₃), 27.6 (CH₂), 29.3 (CH₂), 52.2 (CH₃), 55.9 (CH₃), 56.0 (CH₃), 112.8 (CH), 118.4 (CH), 128.2 (Cq), 139.9 (Cq), 148.6 (Cq), 152.0 (Cq), 168.5 (CO) ; MS (MALDI-TOF) : 486.4 (M+H)⁺.

4,5-Dimethoxy-2-trimethylstannylbenzoic acid methyl ester (11).

This compound was obtained following the same procedure as described for **10** starting from **9** (11 mmol); reaction time 6 h. Compound **11** was isolated as a white solid in 81% yield. Mp : 88-89 °C ; Rf 0.43 (petroleum ether /EtOAc 9/1) ; IR (KBr, cm⁻¹) v 3021, 2953, 1698, 1584, 1506, 1273 ¹H NMR (DMSO-*d*₆, 250 MHz) δ 0.26 (s, 9H, CH₃), 3.90 (s, 3H, CH₃), 3.93 (s, 3H, CH₃), 3.96 (s, 3H, CH₃), 7.11 (s, 1H, H₃), 7.66 (s, 1H, H₆) ; ¹³C NMR (DMSO-*d*₆, 62.9 MHz) δ -7.1 (CH₃), 52.3 (CH₃), 55.9 (CH₃), 56.0 (CH₃), 112.8 (CH), 117.9 (CH), 127.7 (Cq), 140.0 (Cq), 148.9 (Cq), 152.2 (Cq), 168.5 (CO) ; MS (IS) : 357, 358, 359, 361, 363 (M+H)⁺.

2-[4-(1H-Indol-3-yl)-1-methyl-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl]-benzoic acid methyl ester (12).

A solution of **1** (103 mg, 0.33 mmol), **6** (210 mg, 0.49 mmol) and CuI (7 mg, 0.03 mmol) in dry dioxane (10 mL) was degassed by bubbling argon for 30 min. PdCl₂(PPh₃)₂ (42 mg, 0.06 mmol) was added and the reaction mixture was placed in a pre-heated oil bath at 120°C for 6 h. After cooling and filtration over celite, the precipitate was washed with EtOAc (3x10 mL) and the filtrate was concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (petroleum ether / CH₂Cl₂ 1/1 then petroleum ether / EtOAc/ CH₂Cl₂ 2/1/2) and the solid washed with CH₃CN (20 mL) and petroleum ether (2x20 mL) to afford compound **12** as an orange solid (87 mg, 74%). Mp : 99-102 °C ; Rf 0.43 (petroleum ether /EtOAc 9/1) ; IR (KBr, cm⁻¹) v 3357, 3950, 1762, 1700, 1385, 743 ; ¹H NMR (DMSO-*d*₆, 250 MHz) δ 3.03 (s, 3H, CH₃), 3.74 (s, 3H, CH₃), 6.37 (d, 1H, H₇, *J* = 8.6 Hz), 6.65 (t, 1H, H₆, *J* = 7.4 Hz), 7.02 (t, 1H, H₅, *J* = 7.7 Hz), 7.12 (d, 1H, H₆, *J* = 6.4 Hz), 7.39-7.56 (m, 3H, H₄/H₄/H₅), 8.00-8.03 (m, 2H, H₂/H₃), 11.92 (br s, 1H, NH) ; ¹³C NMR (DMSO-*d*₆, 62.9 MHz) δ 24.1 (CH₃), 52.2 (CH₃), 104.01 (Cq), 112.2 (CH), 120.0 (CH), 120.4 (CH), 122.1 (CH), 124.2 (Cq), 129.1 (CH), 129.9 (CH), 130.3 (Cq), 130.7 (Cq), 130.9 (2CH), 131.4 (Cq), 131.6 (Cq), 132.1 (CH), 136.5 (Cq), 167.0 (CO), 170.7 (CO), 171.3 (CO) ; MS (IS) : 360 (M+H)⁺.

4,5-Dimethoxy-2-[4-(1H-indol-3-yl)-N-methyl-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl]benzoic acid methyl ester (13).

This compound was obtained following the same procedure as described for **12**, starting from **1** (0.08 mmol) and **10** (0.12 mmol), reaction time 6 h. Compound **13** was isolated as an orange solid in 78% yield. Mp : 218-220 °C ; Rf 0.33 (petroleum ether /EtOAc 6/4) ; IR (KBr, cm⁻¹) v 3261, 1761, 1710, 1688, 1434, 750 ; ¹H NMR (DMSO-*d*₆, 250 MHz) δ 3.03 (s, 3H, CH₃), 3.24 (s, 3H, CH₃), 3.72 (s, 3H, CH₃), 3.87 (s, 3H, CH₃), 6.48 (d, 1H, H₄, *J* = 8.0 Hz), 6.62 (s, 1H, H₆), 6.71 (t, 1H, H₅, *J* = 7.3 Hz), 7.05 (t, 1H, H₆, *J* = 7.5 Hz), 7.42 (d, 1H, H₇, *J* = 8.2 Hz), 7.52 (s, 1H, H₃), 7.98 (d,

1H, H₂, *J* = 2.3 Hz), 11.87 (br s, 1H, NH) ; ¹³C NMR (DMSO-*d*₆, 62.9 MHz) δ 24.0 (CH₃), 52.0 (CH₃), 55.4 (CH₃), 55.7 (CH₃), 104.2 (Cq), 112.1 (CH), 112.7 (CH), 113.8 (CH), 119.9 (CH), 120.7 (CH), 122.1 (CH), 123.1 (Cq), 124.3 (Cq), 125.1 (Cq), 130.5 (Cq), 130.8 (CH), 130.9 (Cq), 136.4 (Cq), 148.6 (Cq), 151.1 (Cq), 166.5 (CO), 170.6 (CO), 171.4 (CO) ; MS (MALDI-TOF) : 443.5 (M+Na)⁺.

2-[4-(5-Benzyloxy-1H-indol-3-yl)-1-methyl-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl]benzoic acid methyl ester (14).

This compound was obtained following the same procedure as described for **12**, starting from **2** (0.28 mmol) and **6** (0.41 mmol), reaction time 3 h 45. Compound **14** was isolated as an ochre solid in 75% yield. Mp : 175-177 °C ; Rf 0.67 (petroleum ether /EtOAc 6/4) ; IR (KBr, cm⁻¹) ν 3315, 1762, 1696, 1625, 1435, 1280, 1075, 727 ; ¹H NMR (DMSO-*d*₆, 250 MHz) δ 3.02 (s, 3H, CH₃), 3.71 (s, 3H, OCH₃), 4.33 (s, 2H, CH₂), 5.94 (d, 1H, H₄, *J* = 2.5 Hz), 6.74 (dd, 1H, H₆, *J* = 8.7 Hz, *J* = 2.5 Hz), 7.14 (dd, 1H, H₆, *J* = 7.7 Hz, *J* = 1.1 Hz), 7.21 (d, 2H, H_{φ,b}, *J* = 7.1 Hz), 7.28-7.37 (m, 4H), 7.51 (dt, 1H, H₅, *J* = 7.6 Hz, *J* = 1.3 Hz), 7.57 (dt, 1H, H₄, *J* = 7.7 Hz, *J* = 1.2 Hz), 8.03-8.05 (m, 2H, H₂/H₃), 11.84 (br s, 1H, NH) ; ¹³C NMR (DMSO-*d*₆, 62.9 MHz) δ 24.0 (CH₃), 52.1 (CH₃), 68.9 (CH₂), 103.6 (CH), 103.9 (Cq), 112.9 (CH), 113.0 (CH), 124.6 (Cq), 126.9 (2CH), 127.5 (CH), 128.3 (2CH), 129.1 (CH), 129.2 (Cq), 129.9 (CH), 130.6 (Cq), 131.1 (CH), 134.6 (Cq), 131.3 (Cq), 131.4 (CH), 131.5 (Cq), 131.9 (Cq), 132.2 (CH), 137.0 (C), 152.7 (Cq), 166.9 (CO), 170.7 (CO), 171.1 (CO) ; MS (IS) : 467.5 (M+H)⁺, 489.5 (M+Na)⁺.

2-[4-(5-Benzyloxy-1H-indol-3-yl)-1-methyl-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl]benzoic acid (16).

This compound was obtained following the same procedure as described in ref. 22 for **15**, starting from **4** (0.46 mmol), temperature 2°C. Compound **16** was isolated as a red solid in 83% yield. Mp : 118-121 °C ; Rf 0.48 (EtOAc) ; IR (KBr, cm⁻¹) ν 3378, 1761, 1696, 1624, 1439, 1385, 738 ; ¹H NMR (DMSO-*d*₆, 250 MHz) δ 3.02 (s, 3H, CH₃), 4.22 (d, 1H, CH₂, *J* = 11.9 Hz), 4.40 (d, 1H, CH₂, *J* = 11.9 Hz), 6.06 (s, 1H, H₄), 6.71 (dd, 1H, H₆, *J* = 8.7 Hz, *J* = 2.0 Hz), 7.08 (d, 1H, H₆, *J* = 7.8 Hz), 7.24-7.56 (m, 8H), 7.99 (d, 1H, H₂, *J* = 3.0 Hz), 8.09 (d, 1H, H₃, *J* = 7.0 Hz), 11.80 (br s, 1H, NH) ; ¹³C NMR (DMSO-*d*₆, 62.9 MHz) δ 24.0 (CH₃), 69.1 (CH₂), 103.6 (CH), 104.0 (Cq), 112.8 (CH), 112.9 (CH), 124.8 (Cq), 127.2 (2CH), 127.7 (CH), 128.4 (2CH), 129.0 (CH), 130.1 (CH+C), 130.6 (Cq), 130.9 (CH), 131.0 (CH), 131.5 (Cq), 131.8 (CH+C), 132.3 (Cq), 136.9 (C), 152.6 (Cq), 168.2 (CO), 170.7 (CO), 171.6 (CO) ; MS (IS) : 453.5 (M+H)⁺, 470.5 (M+NH₄)⁺.

2-[4-(1H-Indol-3-yl)-2,5-dioxo-2,5-dihydrofuran-3-yl]benzoic acid (17).

Compound **17** was obtained from **12** or **15** following a similar procedure. A solution of compound **12** (120 mg, 0.31 mmol) in acetone (2 mL) and KOH (702 mg, 12.53 mmol) was stirred at room temperature for 5 h. Water (10 mL) was added and acetone was evaporated under reduced pressure. A solution of conc. HCl (2 mL) was added and after 8 h, the precipitate was filtered and dissolved in EtOAc (30 mL). The organic layers were washed with water (3x30 mL) then with brine (30 mL), dried over MgSO₄, filtered and concentrated under reduced pressure to afford compound **17** as a orange solid (103 mg, quantitative). Mp : 104-106 °C ; Rf 0.59 (EtOAc) ; IR (KBr, cm⁻¹) ν 3380, 3017, 1758, 1705, 743 ; ¹H NMR (DMSO-*d*₆, 250 MHz) δ 6.33 (d, 1H, H₇, *J* = 8.0 Hz), 6.70 (t, 1H, H₆, *J* = 7.3 Hz), 7.07 (t, 1H, H₅, *J* = 7.7 Hz), 7.19 (d, 1H, H₆, *J* = 7.0 Hz), 7.42-7.53 (m, 2H, H₄/H₅), 7.61 (t, 1H, H₄, *J* = 7.0 Hz), 8.09 (d, 1H, H₂, *J* = 3.0 Hz), 8.13 (d, 1H, H₃, *J* = 7.6 Hz), 12.15 (br s, 1H, NH) ; ¹³C NMR (DMSO-*d*₆, 62.9 MHz) δ 103.7 (Cq), 112.6 (CH), 120.5 (CH), 120.6 (CH), 122.7 (CH), 124.0 (Cq), 130.0 (CH), 130.6 (CH), 130.7 (Cq), 130.8 (CH), 131.5 (Cq), 131.7 (Cq), 132.2 (CH), 132.5 (CH), 133.5 (Cq), 136.8 (Cq), 165.2 (CO), 166.2 (CO), 167.7 (CO) ; MS (IS) : 332 (M-H)⁻.

4,5-Dimethoxy-2-[4-(1H-indol-3-yl)-2,5-dioxo-2,5-dihydro furan-3-yl]benzoic acid (18).

This compound was obtained following the same procedure as described for compound **17**, starting from **13** (0.12 mmol). Reaction time: 2 h in basic medium at reflux and overnight at room temperature in acidic medium. Compound **18** was isolated as an orange solid in a quantitative yield. Mp : 120-122 °C ; Rf 0.54 (EtOAc) ; IR (KBr, cm⁻¹) ν 3356, 1826, 1758, 1702, 1625, 1501, 746 ; ¹H NMR (DMSO-*d*₆, 250 MHz) δ 3.34 (s, 3H, CH₃), 3.89 (s, 3H, CH₃), 6.48 (d, 1H, H₄, *J* = 8.1 Hz), 6.74 (s, 1H, H₆), 6.78 (t, 1H, H₅, *J* = 7.7 Hz), 7.10 (t, 1H, H₆, *J* = 7.6 Hz), 7.45 (d, 1H, H₇, *J* = 8.3 Hz), 7.63 (s, 1H, H₃), 8.06 (d, 1H, H₂, *J* = 2.9 Hz), 12.10 (br s, 1H, NH) ; ¹³C NMR (DMSO-*d*₆, 62.9 MHz) δ 55.6 (CH₃), 55.7 (CH₃), 103.8 (Cq), 112.4 (CH), 113.3 (CH), 113.6 (CH), 120.5 (CH), 120.6 (CH), 122.6 (CH), 123.8 (Cq), 124.0 (Cq), 124.1 (Cq), 131.7 (Cq), 132.2 (CH), 133.1 (C), 136.6 (Cq), 149.2 (Cq), 151.2 (Cq), 165.0 (CO), 166.2 (CO), 167.0 (CO) ; MS (IS) : 392 (M-H)⁻.

2-[4-(5-Benzyloxy-1H-indol-3-yl)-2,5-dioxo-2,5-dihydro furan-3-yl]benzoic acid (19).

Compound **19** was obtained from **14** (0.73 mmol) or **16** (0.09 mmol) following the same procedure as described for compound **17**. Reaction time: 7 h (for **14**) or 24 h (for **16**) in basic media and overnight (for **14**) or 24 h (for **16**) in acidic media. Compound **19** was isolated from **14** in a 48% yield and from **16** in a 95% yield as an orange solid. Mp : 180-184 °C ; Rf 0.65 (EtOAc) ; IR (KBr, cm⁻¹) ν 3386, 1826, 1753, 1686, 1612, 1261, 736 ; ¹H NMR (DMSO-*d*₆, 250 MHz) δ 4.29 (d, 1H, CH₂, *J* = 11.2 Hz), 4.41 (d, 1H, CH₂, *J* = 11.0 Hz), 5.95 (d, 1H, H₄, *J* = 2.3 Hz), 6.78 (dd, 1H, H₆, *J* = 8.8 Hz, *J* = 2.4 Hz), 7.21 (d, 1H, H₇, *J* = 7.7 Hz), 7.26 (d, 2H, *J* = 7.1 Hz), 7.29-7.32 (m, 1H), 7.34-7.39 (m, 3H),

7.57 (dt, 1H, H₅, *J* = 7.4 Hz, *J* = 1.0 Hz), 7.64 (dt, 1H, H₄, *J* = 7.7 Hz, *J* = 1.1 Hz), 8.13 (d, 1H, H₂, *J* = 3.1 Hz), 8.18 (dd, 1H, H₃, *J* = 7.8 Hz, *J* = 1.0 Hz), 12.11 (br s, 1H, NH); ¹³C NMR (DMSO-*d*₆, 62.9 MHz) δ 69.0 (CH₂); 103.6 (Cq), 103.7 (CH), 113.3 (CH), 113.5 (CH), 124.6 (Cq), 127.1 (2CH), 127.7 (CH), 128.4 (2CH), 130.0 (CH), 130.6 (CH), 130.6 (Cq), 131.0 (CH), 131.1 (Cq), 131.4 (Cq), 131.7 (Cq), 132.3 (CH), 132.8 (CH), 133.3 (Cq), 136.8 (C), 153.0 (Cq), 165.1 (C=O), 166.2 (C=O), 167.6 (C=O); (IS): 438 (M-H)⁻.

2-[4-(5-Benzyloxy-1H-indol-3-yl)-1-methyl-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl]benzoic acid methyl ester (20).

To a solution of **14** (154 mg, 0.33 mmol) dissolved in dry CH₂Cl₂ (10 mL) was dropwise added a solution of BBr₃ (1M in CH₂Cl₂, 826 μL, 0.82 mmol) under vigorous stirring at 0°C. The mixture was then stirred for 5 min at room temperature; ice (40 g) and EtOAc (40 mL) were added. The aqueous layer was extracted with EtOAc (3x30 mL) and the combined organic layers were concentrated to dryness to afford compound **20** as an orange solid (106 mg, 86%). Mp: 110-112 °C; Rf 0.76 (EtOAc); IR (KBr, cm⁻¹) ν 3269, 2924, 1670, 1697, 1626, 1435, 750; ¹H NMR (DMSO-*d*₆, 250 MHz) δ 3.01 (s, 3H, CH₃), 3.74 (s, 3H, OCH₃), 5.80 (d, 1H, H₄, *J* = 2.1 Hz), 6.55 (dd, 1H, H₆, *J* = 8.7 Hz, *J* = 2.3 Hz), 7.08 (d, 1H, H₆, *J* = 7.7 Hz), 7.18 (d, 1H, H₇, *J* = 8.7 Hz), 7.42 (dt, 1H, H₅, *J* = 7.6 Hz, *J* = 1.3 Hz), 7.51 (dt, 1H, H₄, *J* = 7.7 Hz, *J* = 1.3 Hz), 7.85 (d, 1H, H₂, *J* = 2.9 Hz), 7.99 (dd, 1H, H₃, *J* = 7.9 Hz, *J* = 1.2 Hz), 8.49 (s, 1H, OH), 11.84 (br s, 1H, NH); ¹³C NMR (DMSO-*d*₆, 62.9 MHz) δ 24.0 (CH₃), 52.0 (CH₃), 103.5 (Cq), 105.5 (CH), 112.1 (CH), 112.2 (CH), 125.4 (Cq), 128.9 (CH), 129.4 (Cq), 130.1 (CH), 130.6 (Cq), 130.7 (CH+C), 130.9 (CH), 131.6 (2C), 131.9 (CH), 151.3 (C), 167.0 (C=O), 170.7 (C=O), 171.4 (C=O); (IS): 377 (M+H)⁺, 394 (M+NH₄)⁺, 399 (M+Na)⁺.

2-[4-(5-Hydroxy-1H-indol-3-yl)-1-methyl-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl]benzoic acid (21).

Compound **21** was obtained from **16** (0.10 mmol) following the same procedure as described for compound **20** as an orange solid in a 83% yield. Mp: 160-163 °C; Rf 0.42 (EtOAc); IR (KBr, cm⁻¹) ν 3398, 1762, 1693, 1388, 762; ¹H NMR (DMSO-*d*₆, 500 MHz) δ 3.00 (s, 3H, CH₃), 5.91 (s, 1H, H₄), 6.55 (dd, 1H, H₆, *J* = 8.7 Hz, *J* = 2.2 Hz), 7.01 (d, 1H, H₆, *J* = 5.6 Hz), 7.17 (d, 1H, H₇, *J* = 8.8 Hz), 7.36 (t, 1H, H₅, *J* = 7.7 Hz), 7.47 (t, 1H, H₄, *J* = 7.4 Hz), 7.77 (d, 1H, H₂, *J* = 2.6 Hz), 8.03 (d, 1H, H₃, *J* = 7.8 Hz), 8.51 (s, 1H, OH, exchangeable D₂O), 11.58 (br s, 1H, NH); ¹³C NMR (DMSO-*d*₆, 125.8 MHz) δ 24.4 (CH₃), 104.0 (Cq), 105.9 (CH), 112.5 (CH), 112.6 (CH), 126.0 (Cq), 129.3 (CH), 130.7 (CH), 130.9 (CH+CH), 131.0 (Cq), 131.2 (Cq), 131.8 (CH), 131.9 (Cq), 132.3 (Cq), 133.1 (Cq), 151.4 (Cq), 168.9 (CO), 171.4 (CO), 172.3 (CO); (IS): 363.5 (M+H)⁺, 385.5 (M+Na)⁺.

2-[4-(5-Hydroxy-1H-indol-3-yl)-2,5-dioxo-2,5-dihydrofuran-3-yl]benzoic acid (22).

Compound **22** was obtained following the same procedure as described for compound **17** starting from **21** (0.14 mmol) after 25 h in basic media and 3 days in acidic media as a red solid in a 94% yield or from compound **19** (0.08 mmol) following the same procedure as described for compound **20** in a quantitative yield. Mp: 193-195 °C; Rf 0.54 (petroleum ether / EtOAc 2/8); IR (KBr, cm⁻¹) ν 3384, 1831, 1761, 1700, 1627, 1262, 744; ¹H NMR (DMSO-*d*₆, 250 MHz) δ 5.78 (d, 1H, H₄, *J* = 2.2 Hz); 6.60 (dd, 1H, H₆, *J* = 8.7 Hz, *J* = 2.3 Hz), 7.15 (d, 1H, H₆, *J* = 7.7 Hz), 7.22 (d, 1H, H₇, *J* = 8.6 Hz), 7.49 (d, 1H, H₅, *J* = 7.5 Hz), 7.59 (t, 1H, H₄, *J* = 7.6 Hz), 7.98 (d, 1H, H₂, *J* = 1.5 Hz), 8.11 (d, 1H, H₃, *J* = 7.0 Hz), 8.65 (s, 1H, OH), 11.99 (br s, 1H, NH); ¹³C NMR (DMSO-*d*₆, 125.8 MHz) δ 103.2 (Cq), 105.7 (CH), 112.6 (CH), 112.7 (CH), 125.2 (Cq), 129.8 (CH), 130.3 (Cq), 130.5 (CH), 130.6 (Cq), 130.7 (CH), 130.8 (Cq), 131.2 (Cq), 132.0 (CH), 132.4 (CH), 133.6 (Cq), 151.9 (Cq), 165.2 (CO), 166.3 (CO), 167.6 (CO); (IS): 348 (M-H)⁻.

General procedure for electrophilic cyclization: synthesis of compounds 23-26, 28.

To a stirred solution of starting material in dichloroethane (0.025 mol.L⁻¹), BF₃.Et₂O (40 eq.) was dropwise added at room temperature and the reaction mixture was then refluxed for the desired time. After cooling to 0°C, cold water was added and the aqueous layer was washed three times with EtOAc. The combined organic layers were dried over MgSO₄, filtered and concentrated under reduced pressure to give the desired products.

1H-Benzo-[5,6]pyrrolo[3',4'-3,4]cyclohept[1,2-*b*]-12-hydroxy-2-methylindole-1,3,8 (2H, 9H) trione (24).

Compound **24** was obtained from **21** after 2 h as a red solid in a 60% yield. Mp: 109-112 °C; Rf 0.58 (EtOAc); IR (KBr, cm⁻¹) ν 3263, 1761, 1698, 1586, 1442, 1385; ¹H NMR (DMSO-*d*₆, 250 MHz) δ 3.07 (s, 3H, CH₃), 7.06 (dd, 1H, H₁₁, *J* = 8.9 Hz, *J* = 2.3 Hz), 7.50 (d, 1H, H₁₀, *J* = 8.9 Hz), 7.79 (t, 1H, H₆, *J* = 7.9 Hz), 7.88 (t, 1H, H₅, *J* = 7.5 Hz), 8.16 (d, 1H, H₁₃, *J* = 1.9 Hz), 8.43 (d, 1H, H₇, *J* = 7.9 Hz), 8.82 (d, 1H, H₄, *J* = 8.1 Hz), 9.33 (s, 1H, OH), 12.84 (br s, 1H, NH); ¹³C NMR (DMSO-*d*₆, 62.9 MHz) δ 24.2 (CH₃), 109.6 (CH), 110.9 (Cq), 113.4 (CH), 118.3 (CH), 124.2 (Cq), 125.1 (Cq), 128.5 (Cq), 129.3 (CH), 130.0 (CH), 130.2 (CH), 131.6 (Cq), 131.7 (CH), 132.6 (Cq), 137.0 (Cq), 141.3 (Cq), 152.9 (Cq), 169.2 (CO), 170.4 (CO), 179.8 (CO); HRMS calcd for. (C₂₀H₁₂N₂O₄) (M⁺) 344.07971; found 344.0788.

5,6-Dimethoxybenzo[5,6]furo[3',4':3,4]cyclohept[1,2-*b*]indole-1,3,8-(9H)-trione (26).

Compound **26** was obtained from **18** (0.51 mmol) after 5.5 h as a red solid in a 32% yield. Mp: 178-180 °C; Rf 0.36 (petroleum ether / EtOAc 2/8); IR (KBr, cm⁻¹) ν 3282, 2900, 1828, 1745, 1573, 1505, 1390; ¹H NMR (DMSO-*d*₆, 250

MHz) δ 4.03 (s, 3H, CH₃), 4.06 (s, 3H, CH₃), 7.40 (t, 1H, H₁₂, J = 7.7 Hz), 7.57 (t, 1H, H₁₁, J = 7.6 Hz), 7.77 (d, 1H, H₁₀, J = 8.3 Hz), 8.20 (s, 1H, H₇), 8.65 (s, 1H, H₄), 8.83 (d, 1H, H₁₃, J = 8.4 Hz), 13.10 (br s, 1H, NH) ; ¹³C NMR (DMSO-*d*₆, 62.9 MHz) δ 55.7 (CH₃), 55.8 (CH₃), 110.9 (CH), 111.4 (CH), 113.0 (CH), 122.1 (CH), 125.7 (CH), 127.1 (CH) ; HRMS calcd for. C₂₁H₁₃NO₆ (M⁺) 375.07429; found 375.0738. .

5,6-Dihydroxybenzo[5,6]furo[3',4':3,4]cyclohept[1,2-*b*]indole-1,3,8-(9*H*)-trione (27).

Compound **27** was obtained from **18** (0.22 mmol) following the same procedure as described for compound **20** (reaction time 47 h) ; **27** was isolated as a brown solid in a 88% yield. Mp : 195-197 °C ; Rf 0.40 (petroleum ether / EtOAc 2/8) ; IR (KBr, cm⁻¹) ν 3382, 3118, 1828, 1753, 1740, 1557, 1490 ; ¹H NMR (DMSO-*d*₆, 250 MHz) δ 7.35 (t, 1H, H₁₂, J = 7.7 Hz), 7.52 (t, 1H, H₁₁, J = 7.6 Hz), 7.70 (d, 1H, H₁₀, J = 8.3 Hz), 8.13 (s, 1H, H₇), 8.52 (s, 1H, H₄), 8.77 (d, 1H, H₁₃, J = 8.5 Hz), 10.75 (br s, 2H, OH), 13.09 (br s, 1H, NH) ; ¹³C NMR (DMSO-*d*₆, 62.9 MHz) δ 110.2 (Cq), 113.1 (CH), 115.6 (CH), 115.8 (CH), 122.1 (CH), 122.2 (Cq), 123.6 (Cq), 125.9 (CH), 126.0 (Cq), 127.1 (CH), 129.0 (Cq), 132.0 (Cq), 137.4 (Cq), 141.0 (Cq), 150.0 (Cq), 150.7 (Cq), 164.4 (CO), 165.6 (CO), 177.1 (CO) ; HRMS calcd for. C₁₉H₉NO₆ (M⁺) 347.04299; found 347.0435.

12-Hydroxybenzo[5,6]furo[3',4':3,4]cyclohept[1,2-*b*]indole-1,3,8 (9*H*)-trione (28).

Compound **28** was obtained from **22** (0.07 mmol) after 19 h as a red solid in a 60% yield or alternatively from **24** (0.29 mmol) following the same procedure as described for compound **17** after 3 days in basic medium and 2 days in acidic medium in a 92% yield. Mp : 200-203 °C ; Rf 0.32 (petroleum ether / EtOAc 6/4) ; IR (KBr, cm⁻¹) ν 3288, 1820, 1759, 1700, 1580, 1480, 1264, 767 ; ¹H NMR (DMSO-*d*₆, 250 MHz) δ 7.09 (dd, 1H, H₁₁, J = 8.8 Hz, J = 2.1 Hz), 7.55 (d, 1H, H₁₀, J = 8.7 Hz), 7.91 (t, 1H, H₆, J = 7.6 Hz), 8.00 (t, 1H, H₅, J = 7.7 Hz), 8.10 (d, 1H, H₁₃, J = 2.1 Hz), 8.55 (dd, 1H, H₇, J = 8.0 Hz, J = 1.4 Hz), 8.84 (d, 1H, H₄, J = 8.3 Hz), 9.50 (s, 1H, OH), 13.18 (br s, 1H, NH) ; ¹³C NMR (DMSO-*d*₆, 125.8 MHz) δ 108.9 (CH), 109.8 (Cq), 113.9 (CH), 118.6 (CH), 125.0 (Cq), 125.2 (Cq), 127.7 (Cq), 129.8 (CH), 129.9 (CH), 131.2 (CH), 132.4 (CH), 132.5 (Cq), 132.8 (Cq), 137.1 (Cq), 141.6 (Cq), 153.5 (Cq), 164.2 (CO), 165.1 (CO), 179.5 (CO) ; HRMS calcd for. C₁₉H₉NO₅ (M⁺) 331.04807; found 331.0482.

1*H*-Benzo[5,6]pyrrolo[3',4'-3,4]cyclohept[1,2-*b*]-2-dimethylaminoethyl-12-hydroxyindole-1,3,8 (2*H*, 9*H*) trione (32).

In a sealed tube, a mixture of compound **28** (41 mg, 0.12 mmol), dimethylaminoethylamine (70 μ L, 0.61 mmol) and silica gel (65 mg) was placed under microwave irradiation at 150°C for 15 min. After cooling to room temperature, a mixture of CH₂Cl₂ and MeOH (20 mL, 1/1) was added and the mixture filtered. The filtrate was concentrated under reduced pressure and the crude residue was purified by flash chromatography on silica gel to afford compound **32** as a red solid (24 mg, 48%). Mp : 235-237 °C ; Rf 0.54 (CH₂Cl₂ / MeOH ; 9/1) ; IR (KBr, cm⁻¹) ν 3265, 2781, 1761, 1695, 1581, 1481, 1236, 770 ; ¹H NMR (DMSO-*d*₆, 500 MHz) δ 2.21 (s, 6H, CH₃), 2.56 (t, 2H, CH₂, J = 6.6 Hz), 3.75 (t, 2H, CH₂, J = 6.6 Hz), 7.06 (dd, 1H, H₁₁, J = 8.8 Hz, J = 2.4 Hz), 7.51 (d, 1H, H₁₀, J = 8.9 Hz), 7.84 (t, 1H, H₆, J = 7.1 Hz), 7.92 (t, 1H, H₅, J = 7.7 Hz), 8.18 (d, 1H, H₁₃, J = 2.3 Hz), 8.51 (dd, 1H, H₇, J = 8.1 Hz, J = 1.3 Hz), 8.88 (d, 1H, H₄, J = 8.1 Hz), 9.33 (s, 1H, OH), 12.91 (br s, 1H, NH) ; ¹³C NMR (DMSO-*d*₆, 125.8 MHz) δ 36.0 (CH₂), 45.1 (2CH₃), 56.4 (CH₂), 109.5 (CH), 110.8 (Cq), 113.4 (CH), 118.3 (CH), 124.0 (Cq), 125.1 (Cq), 128.5 (Cq), 129.4 (CH), 130.2 (CH+CH), 131.5 (Cq), 131.8 (CH), 132.6 (Cq), 137.1 (Cq), 141.4 (Cq), 152.9 (Cq), 169.0 (CO), 170.2 (CO), 179.8 (CO) ; HRMS calcd for. C₂₃H₁₉N₃O₄ (M⁺) 402.14538; found 402.1457.

1*H*-Benzo[5,6]pyrrolo[3',4'-3,4]cyclohept[1,2-*b*]-5-hydroxy-2-(dimethylaminoethyl)-indole-1,3 (2*H*, 9*H*) dione (33).

This compound was obtained during the purification of **32** in a 17% yield as a red solid. Mp : 163-165 °C ; Rf 0.47 (CH₂Cl₂ / MeOH ; 9/1) ; IR (KBr, cm⁻¹) ν 3374, 2922, 1758, 1696, 1594, 1459, 767 ; ¹H NMR (DMSO-*d*₆, 500 MHz) δ 2.26 (s, 6H, CH₃), 2.59 (s, 2H, CH₂), 3.72 (t, 2H, CH₂, J = 6.5 Hz), 3.88 (s, 2H, CH₂), 6.65 (dd, 1H, H₁₁, J = 8.7 Hz, J = 2.5 Hz), 7.22 (d, 1H, H₁₀, J = 8.7 Hz), 7.35-7.38 (m, 2H, H₅/H₇), 7.48-7.49 (m, 2H, H₆/H₁₃), 7.85 (dd, 1H, H₄, J = 8.3 Hz, J = 1.3 Hz), 8.90 (s, 1H, OH), 11.91 (br s, 1H, NH) ; ¹³C NMR (DMSO-*d*₆, 125.8 MHz) δ 33.6 (CH₂), 35.4 (CH₂), 45.0 (2CH₃), 56.6 (CH₂), 104.5 (Cq), 105.9 (CH), 112.1 (CH+CH), 125.6 (Cq), 125.7 (Cq), 126.1 (CH), 128.6 (CH+CH), 129.2 (Cq), 130.3 (CH), 130.8 (Cq), 135.0 (Cq), 135.3 (Cq), 141.4 (Cq), 152.1 (Cq), 170.1 (CO), 170.6 (CO) ; HRMS calcd for. C₂₃H₂₁N₃O₃ (M+ H⁺) 388.16612; found 388.1659.

5,6-Dihydroxy-1*H*-benzo[5,6]pyrrolo[3',4'-3,4]cyclohept [1,2-*b*]indole-1,3,8 (2*H*, 9*H*) trione (35).

A mixture of compound **27** (153 mg, 0.44 mmol) and NH₄OAc (4.00 g, 51.94 mmol) was heated at 130°C for 3h30. After cooling at room temperature, water (30 mL) was added and the aqueous layer was acidified to pH = 1 with a concentrated solution of hydrochloric acid. The precipitate was filtered and washed with EtOAc (3x50 mL). The combined organic layers were washed with water (30 mL), dried over MgSO₄, filtered and evaporated under reduced pressure to afford compound **35** as a red solid (99 mg, 65%). Mp : 239-241 °C ; Rf 0.10 (petroleum ether / EtOAc 1/1) ; IR (KBr, cm⁻¹) ν 3242, 1758, 1716, 1558, 1505 ; ¹H NMR (DMSO-*d*₆, 250 MHz) δ 7.29 (t, 1H, H₁₂, J = 7.8 Hz), 7.47 (t, 1H, H₁₁, J = 7.7 Hz), 7.65 (d, 1H, H₁₀, J = 8.3 Hz), 8.07 (s, 1H, H₇), 8.55 (s, 1H, H₄), 8.79 (d, 1H, H₁₃, J = 8.3 Hz),

10.51 (s, 1H, OH), 10.55 (s, 1H, OH), 11.37 (br s, 1H, NH_{mal}), 12.84 (br s, 1H, NH_{ind}) ; ¹³C NMR (DMSO-*d*₆, 62.9 MHz) □ 111.3 (Cq), 112.7 (CH), 115.1 (CH), 116.3 (CH), 121.4 (CH), 123.2 (Cq), 123.9 (Cq), 125.7 (Cq), 126.7 (2CH), 128.7 (Cq), 132.1 (Cq), 137.9 (Cq), 140.7 (Cq), 149.1 (Cq), 150.1 (Cq), 170.7 (CO), 172.2 (CO), 177.7 (CO) ; HRMS calcd for. C₁₉H₁₀N₂O₅ (M⁺) 346.05897; found 346.0557.

12-Hydroxy-1*H*-benzo[5,6]pyrrolo[3',4'-3,4]cyclohept[1,2-*b*]indole-1,3,8 (2*H*, 9*H*) trione (36).

Compound **36** was obtained following the same procedure as described for compound **35** starting from **28** (0.24 mmol) as an orange solid in a 73% yield. Mp : 212-214 °C ; Rf 0.21 (petroleum ether / EtOAc 6/4) ; IR (KBr, cm⁻¹) ν 3258, 1763, 1715, 1582, 1481, 679 ; ¹H NMR (DMSO-*d*₆, 500 MHz) δ 7.05 (dd, 1H, H₁₁, *J* = 8.9 Hz, *J* = 2.3 Hz), 7.49 (d, 1H, H₁₀, *J* = 8.9 Hz), 7.83 (dt, 1H, H₆, *J* = 7.6 Hz, *J* = 1.2 Hz), 7.91 (dt, 1H, H₅, *J* = 7.6 Hz, *J* = 1.5 Hz), 8.13 (d, 1H, H₁₃, *J* = 2.3 Hz), 8.49 (dd, 1H, H₇, *J* = 8.2 Hz, *J* = 1.4 Hz), 8.86 (dd, 1H, H₄, *J* = 8.1 Hz, *J* = 1.1 Hz), 9.31 (s, 1H, OH), 12.87 (br s, 1H, NH) ; ¹³C NMR (DMSO-*d*₆, 125.8 MHz) δ 109.6 (CH), 110.9 (Cq), 113.4 (CH), 118.2 (CH), 125.0 (Cq), 125.2 (Cq), 128.6 (Cq), 129.3 (CH), 130.1 (CH), 130.4 (CH), 131.7 (CH), 132.1 (Cq), 132.6 (Cq), 137.3 (Cq), 141.4 (Cq), 152.8 (Cq), 170.4 (CO), 171.7 (CO), 180.0 (CO) ; HRMS calcd for. C₁₉H₁₀N₂O₄ (M⁺) 330.06406 found 330.0638.