SUPPORTING INFORMATION

The synthesis and evaluation of 3-aryloxymethyl-1,2-dimethylindole-4,7-diones as mechanism-based inhibitors of NAD(P)H:quinone oxidoreductase 1 (NQO1) activity

Marie A. Colucci, Philip Reigan, David Siegel, Aurélie Chilloux, David Ross and Christopher J. Moody

Contents

Methyl 2-azido-3-(2-benzyloxy-4-methoxyphenyl)propenoate 31

Sodium (4.76 g, 207 mmol) was added to a stirred solution of dry methanol (110 mL). A solution of methyl azidoacetate (23.80 g, 207 mmol)**,** 2-benzyloxy-4-methoxybenzaldehyde **30** (12.53g, 52 mmol) in dry methanol (14 mL) was slowly added over 1 h to the above solution cooled to -12 °C. The reaction mixture was stirred between -10 °C and 0 °C for 4 h and then at 4 °C for 15 h. The reaction mixture was diluted with water (30 mL), extracted into ethyl acetate (3 × 100 mL) and the combined organic layers washed with water (2 × 50 mL), brine (50 mL), dried ($MgSO_4$), filtered and the filtrate evaporated *in vacuo* to give the *title compound* (13.94 g, 79%) as a pale yellow crystalline solid; mp 91 – 93 °C (from ethyl acetate); IR ($CHCl_3$/cm^{-1}) 2434, 2927, 2126, 1701, 1604, 1570, 1503, 1476, 1436, 1425, 1384, 1283, 1206, 1116, 1038; ^{1}H NMR (300 MHz; $CDCl_3$) δ 8.25 (1 H, d, *J* 8.8, 6-H), 7.46 (1 H, s, ArC<u>H</u>=), 7.46 – 7.30 (5 H, m, ArH), 6.54 (1 H, dd, *J* 8.8, 2.4, 5-H), 6.47 (1 H, d, *J* 2.4, 3-H), 5.12 (2 H, s, CH_2), 3.87 (3 H, s, OMe), 3.80 (3 H, s, OMe); ^{13}C NMR (75 MHz; $CDCl_3$) δ 164.9 (C), 162.3 (C), 158.8 (C), 137.0 (C), 132.3 (CH), 129.0 (CH), 128.4 (CH), 127.4 (CH), 123.2 (C), 120.1 (CH), 116.1 (C), 105.6 (CH), 100.1 (CH), 70.9 (CH_2), 55.8 (Me), 53.1 (Me); MS (CI) 312 (MH^+ - N_2, 100%); Found: MH^+ - N_2, 312.1224. $C_{18}H_{17}N_3O_4$ - N_2 + H requires 312.1236.

Methyl 4-benzyloxy-6-methoxyindole-2-carboxylate 32

A solution of methyl 2-azido-3-(2-benzyloxy-4-methoxyphenyl)propenoate **31** (13.90 g, 41 mmol) in dry xylene (300 mL) was introduced dropwise by means of a pressure equalising dropping funnel to refluxing dry xylene (1000 mL). After complete addition the solution was heated under reflux for a further 3 h. The solvent was removed *in vacuo* and the crude product was purified by chromatography (gradient elution with 10 – 20% ethyl acetate/light petroleum) to give the *title compound* (11.48 g, 90%) as a pale yellow crystalline solid; mp 187 – 188 °C (from ethyl acetate); IR (KBr/cm^{-1}) 1324, 1692, 1634, 1587, 1523, 1356, 1281, 1212, 1204; ^{1}H NMR (300 MHz; $CDCl_3$) δ 8.90 (1 H, bs, NH), 7.49 – 7.47 (2 H, m, ArH), 7.43 – 7.31 (4 H, m, ArH), 6.44 (1 H, m, ArH), 6.26 (1 H, d, *J* 1.8, ArH), 5.16 (2 H, s, CH_2), 3.91 (3 H, s, OMe), 3.82 (3 H, s, OMe); ^{13}C NMR (75 MHz; $CDCl_3$) δ 162.8 (C), 160.6 (C), 154.5 (C), 139.1 (C), 137.2 (C), 129.0 (CH), 128.3 (CH), 127.8 (CH), 125.0 (C), 114.5 (C), 107.6 (CH), 94.3 (CH), 86.8 (CH), 70.3 (CH_2), 56.0 (Me), 52.2 (Me); MS (CI) 312 (MH^+, 100%); Found: MH^+, 312.1248.

$C_{18}H_{17}NO_4$ + H requires 312.1236. (Found C, 68.76; H, 5.49; N, 4.62. $C_{18}H_{17}NO_4$ requires C, 69.44; H, 5.50; N, 4.50%).

4-Benzyloxy-6-methoxy-2-methylindole 33

A solution of methyl 4-benzyloxy-6-methoxyindole-2-carboxylate **32** (0.91 g, 2.9 mmol) in dry dioxane (8 mL) was added dropwise with stirring to an ice cooled suspension of lithium aluminium hydride (1.11 g, 29.3 mmol) in dry dioxane (39 mL). The reaction mixture was then heated under reflux for 20 h. The reaction mixture was cooled to 0 °C and quenched by the addition of water (1 mL) and sodium hydroxide (2 M; 1 mL). The reaction mixture was stirred at room temperature for 30 min and then water (3 mL) was added and the granular precipitate formed was filtered through a pad of Celite and the filtrate evaporated *in vacuo.* The crude product was purified by chromatography (gradient elution with 10 – 20% ethyl acetate/light petroleum) to give the *title compound* (469 mg, 60%) as a colorless crystalline solid; mp 113 – 114 °C (chloroform/light petroleum); IR (KBr/cm^{-1}) 3414, 2915, 1629, 1599, 1555, 1509, 1451, 1384, 1369, 1333, 1240, 1160, 1116; ^{1}H NMR (400 MHz; $CDCl_3$) 7.74 (1 H, bs, NH), 7.51 – 7.49 (2 H, m, ArH), 7.42 – 7.33 (3 H, m, ArH), 6.40 (1 H, m, ArH), 6.30 – 6.29 (2 H, m, ArH), 5.18 (2 H, s, CH_2), 3.80 (3 H, s, OMe), 2.37 (3 H, s, Me); ^{13}C NMR (100 MHz; $CDCl_3$) 159.6 (C), 152.0 (C), 137.5 (C), 137.3 (C), 132.0 (C), 128.5 (CH), 127.8 (CH), 127.4 (CH), 114.0 (C), 97.5 (CH), 92.8 (CH), 87.2 (CH), 69.9 (CH_2), 55.7 (Me), 13.6 (Me); MS (EI) 267 (M^+, 52%), 176 (100), 91 (22), 133 (20); Found: M^+, 267.1267. $C_{17}H_{17}NO_2$ requires 267.1259.

4-Benzyloxy-6-methoxy-2-methylindole-3-carbaldehyde 34

To a stirred solution of 4-benzyloxy-6-methoxy-2-methylindole **33** (0.90 g, 3.4 mmol) in DMF (1 mL) at -5 °C in a salt/ice bath was added dropwise an ice-cold solution of phosphoryl chloride (314 l, 3.4 mmol) in DMF (0.85 mL). The reaction mixture was stirred between -5 °C and 0 °C for 1 h and then allowed to warm to room temperature. The mixture was dissolved in ice/water (10 mL) and the solution made strongly alkaline with sodium hydroxide (10%). After stirring for 30 min at room temperature, the precipitate formed was extracted into ethyl acetate (3 50 mL). The combined ethyl acetate layers were washed with water (25 mL), brine (20 mL), dried ($MgSO_4$) and filtered. The solvent was removed *in vacuo* to give the *title compound* (0.89 g, 90 %) as a colorless crystalline solid; mp 227 – 228 °C (from ethyl acetate); IR (KBr/cm^{-1}) 3437,

3188, 1628, 1588, 1542, 1458, 1384, 1371, 1333, 1303, 1201, 1190, 1150; ^{1}H NMR (300 MHz; $CDCl_3$) 10.48 (1 H, s, CHO), 8.49 (1 H, br s, NH), 7.48 – 7.45 (2 H, m, ArH), 7.42 – 7.31 (3 H, m, ArH), 6.50 (1 H, d, *J* 1.8, ArH), 6.45 (1 H, d, *J* 1.8, ArH), 5.20 (2 H, s, CH_2), 3.82 (3 H, s, OMe), 2.74 (3 H, s, Me); ^{13}C NMR (100 MHz; DMSO-*d*) 186.8 (CH), 156.7 (C), 152.4 (C), 141.7 (C), 137.0 (C), 136.3 (C), 128.5 (CH), 127.8 (CH), 127.5 (CH), 113.6 (C), 110.9 (C), 94.6 (CH), 87.9 (CH), 69.4 (CH_2), 55.3 (Me), 13.8 (Me); MS (EI) 295 (M^+, 27%), 204 (100), 91 (87); Found: M^+, 295.1216. $C_{18}H_{17}NO_3$ requires 295.1208. (Found C, 72.81; H, 5.78; N, 4.72. $C_{18}H_{17}NO_3$ requires C, 73.20; H, 5.80; N, 4.74%).

4-Benzyloxy-6-methoxy-1,2-dimethylindole-3-carbaldehyde 35

To a stirred suspension of potassium hydride (30% in oil; 169 mg, 4.2 mmol) in dry DMF (5.5 mL) at 0 °C was added dropwise a solution of 4-benzyloxy-6-methoxy-2-methylindole-3-carbaldehyde **34** (830 mg, 2.8 mmol) in dry DMF (3.60 mL). The reaction mixture was stirred at room temperature for 45 min. Iodomethane (0.20 mL, 3.2 mmol) was added dropwise at 0 °C and the mixture allowed to warm to room temperature for 18 h. The reaction mixture was quenched with saturated ammonium chloride solution (20 mL), extracted into ethyl acetate (3 50 mL). The combined organic layers were washed with water (2 25 mL), dried ($MgSO_4$), filtered and the filtrate evaporated *in vacuo* to give the *title compound* (812 mg, 93%) as a beige crystalline solid; mp 160 – 162 °C (from ethyl acetate); IR (KBr/cm^{-1}) 3436, 1649, 1618, 1525, 1467, 1442, 1395, 1377, 1151; ^{1}H NMR (300 MHz; $CDCl_3$) 10.56 (1 H, s, CHO), 7.48 – 7.45 (2 H, m, ArH), 7.42 – 7.33 (3 H, m, ArH), 6.47 (1 H, d, *J* 1.8, ArH), 6.44 (1 H, d, *J* 1.8, ArH), 5.20 (2 H, s, CH_2), 3.87 (3 H, s, Me), 3.65 (3 H, s, Me), 2.78 (3 H, s, Me); ^{13}C NMR (75 MHz; $CDCl_3$) 189.4 (CH), 157.8 (C), 153.8 (C), 143.0 (C), 138.7 (C), 137.0 (C), 129.1 (CH), 128.5 (CH), 127.9 (CH), 114.9 (C), 111.6 (C), 95.3 (CH), 86.7 (CH), 70.7 (CH_2), 56.2 (Me), 30.0 (Me), 12.7 (Me); MS (CI) 310 (MH^+, 100%), 38 (282), 27 (219); Found: MH^+, 310.1441, $C_{19}H_{19}NO_3$+ H requires 310.1443.

4-Hydroxy-6-methoxy-1,2-dimethylindole-3-carbaldehyde 36

To a solution of 4-benzyloxy-6-methoxy-1,2-dimethylindole-3-carbaldehyde **35** (0.60 g, 1.9 mmol) in THF (30 mL) was added palladium on carbon (10%; 0.06 g). The mixture was stirred under a hydrogen atmosphere for 48 h. The reaction mixture was filtered through Celite and the

filtrate evaporated *in vacuo*. The crude product was purified by chromatography (50% ethyl acetate/light petroleum) to give the *title compound* (0.42 g, 80%) as a yellow crystalline solid; mp 135 – 137 °C (from ethyl acetate/hexane); IR (KBr/cm^{-1}) 3436, 2923, 2848, 1642, 1609, 1475, 1443, 1406, 1372, 1346, 1250, 1203, 1133; ^{1}H NMR (300 MHz; $CDCl_3$) 11.06 (1 H, s, OH), 9.63 (1 H, s, CHO), 6.39 (1 H, d, *J* 2.0, ArH), 6.26 (1 H, d, *J* 2.0, ArH), 3.83 (3 H, s, Me), 3.61 (3 H, s, Me), 2.63 (3 H, s, Me); ^{13}C NMR (75 MHz; $CDCl_3$) 184.4 (CH), 160.0 (C), 152.8 (C), 149.1 (C), 140.1 (C), 116.0 (C), 108.8 (CH), 97.1 (CH), 86.2 (CH), 56.1 (Me), 30.5 (Me), 11.2 (Me); MS (CI) 220 (MH^+, 100%); Found: MH^+, 220.0965. $C_{12}H_{13}NO_3$ + H requires 220.0974.

3-Hydroxymethyl-6-methoxy-1,2-dimethylindole-4,7-dione 37

N,N-Bis(salicylidene)ethyleneiminocobalt(II) (0.12 g, 0.37 mmol) was added to a stirred solution of 6-methoxy-1,2-dimethylindole-3-carbaldehyde **36** (0.08 g, 0.37 mmol) in DMF (19 mL). The reaction mixture was stirred for 2 h at room temperature. The solvent was removed *in vacuo* and the crude product dissolved in dichloromethane (100 mL), washed with water (2 20 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. The crude product was taken through to the next step without further purification.

Sodium borohydride (0.087 g, 2.30 mmol), was added to a stirred solution of the above 3-formyl-6-methoxy-1-methylindole-4,7-dione in anhydrous methanol (19 mL). The solution was stirred under nitrogen at room temperature for 2 h. Acetone (0.9 mL) followed by aqueous $FeCl_3$ (1 M; 0.45 mL) in HCl (0.1 M; 0.45 mL) was added. The reaction mixture was immediately extracted with dichloromethane (3 50 mL). The combined extracts were washed with water (20 mL), brine (20 mL), dried ($MgSO_4$), filtered and the filtrate evaporated *in vacuo*. The crude product was purified by chromatography (elution with 50% ethyl acetate/light petroleum) to give the *title compound* (0.05 g, 58%) as a red crystalline solid; mp 197 – 199 °C (from dichloromethane/light petroleum); UV (MeCN/nm) λ_{max} 228 (log 4.14), 287 (4.13), 295 (4.11), 353 (3.61), 456 (3.16); IR (KBr/cm^{-1}) 3378, 3046, 2944, 1662, 1638, 1621, 1597, 1502, 1487, 1464, 1339, 1216; ^{1}H NMR (300 MHz; MeOH-*d*) 5.74 (1 H, s, 5-H), 4.71 (2 H, s, CH_2), 3.93 (3 H, s, Me), 3.84 (3 H, s, Me), 2.32 (3 H, s, Me); ^{13}C NMR (75 MHz; $CDCl_3$) 185.6 (C), 170.9 (C), 160.5 (C), 136.7 (C), 127.4 (C), 124.8 (C), 123.3 (C), 106.0 (CH), 56.7 (Me), 56.0 (CH_2), 32.6 (Me), 9.8 (Me);

MS (FI) 235 (M^+, 100%); Found: M^+, 235.0847. $C_{12}H_{13}NO_4$ requires 235.0845; (Found C, 60.96; H, 5.54; N, 5.93. $C_{12}H_{13}NO_4$ requires C, 61.27; H, 5.57; N, 5.95%).

CHN Microanalytical data on compounds for biological evaluation

Compound	
1	known compound
5	known compound
6	See HPLC
7	See HPLC
8	known compound
9	known compound
10	Found: C, 58.98; H, 3.72; N, 3.65. $C_{18}H_{14}F_3NO_4$ requires C, 59.18; H, 3.86; N, 3.83%
11	See HPLC data
12	See HPLC data
13	See HPLC data
14	known compound
15	Found: C, 60.11; H, 4.57; N, 7.57. $C_{18}H_{16}N_2O_6$ requires C, 60.67; H, 4.53; N, 7.86% See HPLC data
16	See HPLC data
17	See HPLC data
18	Found: C, 59.99; H, 4.53; N, 7.57. $C_{18}H_{16}N_2O_6$ requires C, 60.67; H, 4.53; N, 7.86% See HPLC data
19	Found: C, 60.07; H, 4.43; N, 7.81. $C_{18}H_{16}N_2O_6$ requires C, 60.67; H, 4.53; N, 7.86% See HPLC data
20	Found: C, 53.43; H, 4.00; N, 9.75. $C_{18}H_{15}N_3O_8$ requires C, 53.87; H, 3.77; N, 10.47% See HPLC data
21	Found: C, 57.45; H, 4.15; N, 6.92. $C_{18}H_{17}FN_2O_6$ requires C, 57.46; H, 4.15; N, 7.44% See HPLC data
22	Found: C, 66.67; H, 4.81; N, 8.00. $C_{19}H_{16}N_2O_4$ requires C, 67.85; H, 4.79; N, 8.33% See HPLC data
23	Found: C, 59.98; H, 4.29; N, 3.69. $C_{19}H_{16}F_3NO_4$ requires C, 60.16; H, 4.25; N, 3.69%
24	See HPLC data
25	Found: C, 62.02; H, 4.35; N, 4.01. $C_{18}H_{15}F_2NO_4$ requires C, 62.25; H, 4.35; N, 4.03%
26	Found: C, 59.09; H, 3.87; N, 3.77. $C_{18}H_{14}F_3NO_4$ requires C, 59.18; H, 3.86; N, 3.83%
27	Found: C, 62.00; H, 5.08; N, 8.64. $C_{17}H_{16}N_2O_4$ requires C, 65.38; H, 5.16; N, 8.97% See HPLC data
28	See HPLC data
29	See HPLC data

5-Methoxy-1,2-dimethyl-3-(3-nitrophenoxymethyl)indole-4,7-dione 6

mp 219 – 227 °C; UV (MeCN/nm) λ_{max} 223 (log ε 3.54), 280 (3.43), 290 (3.42), 333 (2.84), 448 (2.33); IR ($CHCl_3$/cm^{-1}) 2962, 2357, 1674, 1640, 1457, 1352, 1094; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.82 (2 H, m, ArH), 7.43 (1 H, t, *J* 8.4, ArH), 7.29 (1 H, m, ArH), 5.64 (1 H, s, 6-H), 5.36 (2 H, s, CH_2), 3.91 (3 H, s, Me), 3.82 (3 H, s, Me), 2.32 (3 H, s, Me); ^{13}C NMR (100 MHz; $CDCl_3$) δ 178.8 (C), 178.2 (C), 160.0 (C), 159.1 (C), 149.2 (C), 138.0 (C), 130.0 (CH), 129.0 (C), 121.6 (CH), 121.4 (C), 115.9 (overlapping CH and C), 109.9 (CH), 106.8 (CH), 61.1 (CH_2), 56.5 (Me), 32.4 (Me), 9.9 (Me); MS (ESI) 379 (M+Na^+, 100%), 218 (71); Found: M+Na^+, 379.0902. $C_{18}H_{16}N_2O_6$ + Na requires 379.0906.

5-Methoxy-1,2-dimethyl-3-(2-nitrophenoxymethyl)indole-4,7-dione 7

mp 204 – 205 °C; UV (MeCN/nm) λ_{max} 218 (log ε 4.52), 281 (4.37), 290 (4.38), 331 (3.82), 450 (3.32); IR ($CHCl_3$/cm^{-1}) 2978, 2957, 2413, 1641, 1446, 1250, 1095, 999; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.78 (1 H, dd, *J* 1.6, 8.0, ArH); 7.50 (1 H, dt, *J* 1.2, 8.4, ArH), 7.41 (1 H, dd, *J* 0.6, 8.4, ArH), 7.00 (1 H, dt, *J* 0.6, 8.0, ArH), 5.63 (1 H, s, 6-H), 5.50 (2 H, s, CH_2), 3.89 (3 H, s, Me), 3.82 (3 H, s, Me), 2.26 (3 H, s, Me); ^{13}C NMR (100 MHz; $CDCl_3$) δ 178.6 (C), 178.5 (C), 159.5 (C), 151.6 (C), 140.5 (C), 139.0 (C), 134.2 (CH), 128.7 (C), 125.4 (CH), 121.2 (C), 120.7 (CH), 116.4 (CH), 115.9 (C), 106.8 (CH), 62.1 (CH_2), 56.2 (Me), 32.4 (Me), 9.9 (Me); MS (ESI) 379 (M+Na^+, 100); Found: M+Na^+, 379.0883. $C_{18}H_{16}N_2O_6$ + Na requires 379.0906.

5-Methoxy-1,2-dimethyl-3-(2,4,6-trifluorophenoxymethyl)indole-4,7-dione 10

mp 201 – 202 °C; UV (MeCN/nm) λ_{max} 223 (log ε 4.49), 281 (4.29), 289 (4.28), 338 (3.52), 451 (3.22); IR ($CHCl_3$/cm^{-1}) 2961, 1638, 1463, 1262, 1092, 869; ^{1}H NMR (400 MHz; $CDCl_3$) δ 6.67 (2 H, t, *J* 8.0, ArH), 5.62 (1 H, s, 6-H), 5.33 (2 H, s, CH_2), 3.93 (3 H, s, Me), 3.81 (3 H, s, Me), 2.35 (3 H, s, Me); ^{13}C NMR (100 MHz; $CDCl_3$) δ 177.8 (C), 176.7 (C), 156.3 (dt, J_{CF} 245, 14, CF), 155.5 (ddd, J_{CF} 250, 14, 8, CF), 155.0 (C), 137.9 (C), 130.8 (td, J_{CF} 14, 6, C), 127.7 (C), 120.5 (C), 115.2 (C), 105.6 (C), 99.5 (ddd, J_{CF} 27, 27, 8, CH), 64.9 (CH_2), 55.4 (Me), 31.4 (Me), 8.5 (Me); MS (ESI) 388 (M+Na^+, 100%), 363 (4); Found: M+Na^+, 388.0773. $C_{18}H_{14}F_3NO_4$ + Na requires 388.0773.

5-Methoxy-1,2-dimethyl-3-(pyridin-2-yloxymethyl)indole-4,7-dione 11

mp 138 – 140 °C; UV (MeCN/nm) λ_{max} 220 (log ε 4.32), 280 (4.25), 290 (4.24), 332 (3.49), 450 (3.21); IR ($CHCl_3$/cm^{-1}) 2963, 1736, 1675, 1639, 1463, 1263, 1096; ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.18 (1 H, ddd, *J* 0.8, 2.0, 5.2, PyrH), 7.54 (1 H, ddd, *J* 2.0, 7.2, 8.4, PyrH), 6.86 (1 H, ddd, *J* 0.8, 5.2, 6.8, PyrH), 6.72 (1 H, dt, *J* 0.8, 8.4, PyrH), 5.61 (1 H, s, 6-H), 5.51 (2 H, s, CH_2), 3.90 (3 H, s, Me), 3.81 (3 H, s, Me), 2.32 (3 H, s, Me); ^{13}C NMR (100 MHz; $CDCl_3$) δ 178.9 (C), 177.7 (C), 163.7 (C), 159.8 (C), 146.8 (C), 138.5 (CH), 138.0 (CH), 121.9 (C), 117.2 (2 C), 116.8 (CH), 111.2 (CH), 106.6 (CH), 58.0 (CH_2), 56.4 (Me), 32.4 (Me), 9.7 (Me); MS (ESI) 335 ($M+Na^+$, 100%), 218 (82); Found: $M+Na^+$, 335.1002. $C_{17}H_{16}N_2O_4$ + Na requires 335.1008.

5-methoxy-1,2-dimethyl-3-(2-pyridon-1-ylmethyl)indole-4,7-dione

mp 226 – 232 °C; UV (MeCN/nm) λ_{max} 229 (log ε 4.13), 283 (4.04), 291 (4.07), 456 (3.00); IR ($CHCl_3$/cm^{-1}) 2963, 1656, 1640, 1583, 1461, 1263, 1096; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.95 (1 H, dd, *J* 2.0, 6.8, PyrH), 7.26 (1 H, ddd, *J* 2.0, 6.4, 8.8, PyrH), 6.50 (1 H, d, *J* 8.8, PyrH), 6.10 (1 H, td, *J* 1.2, 6.8, PyrH), 5.62 (1 H, s, 6-H), 5.22 (2 H, s, CH_2), 3.88 (3 H, s, Me), 3.82 (3 H, s, Me), 2.47 (3 H, s, Me); ^{13}C NMR (100 MHz; $CDCl_3$) δ 177.5 (2 C), 158.5 (C), 138.6 (CH), 138.4 (C), 138.3 (CH), 131.2 (C), 128.1 (C), 120.4 (CH), 119.5 (C), 115.2 (C), 105.8 (CH), 104.9 (CH), 55.5 (Me), 41.4 (CH_2), 31.6 (Me), 9.1 (Me); MS (ESI) 335 ($M+Na^+$, 100%), 218 (50); Found: $M+Na^+$, 335.1006. $C_{17}H_{16}N_2O_4$ + Na requires 335.1008.

5-Methoxy-1,2-dimethyl-3-(3-pyridyloxymethyl)indole-4,7-dione 12

mp 158 – 162 °C; UV (MeCN/nm) λ_{max} 223 (log ε 4.27), 280 (4.21), 288 (4.17), 337 (3.45); IR ($CHCl_3$/cm^{-1}) 2963, 1673, 1640, 1576, 1463, 1092; ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.38 (1 H, bs, PyrH), 8.25 (1 H, d, *J* 0.8, PyrH), 7.45 (1 H, dd, *J* 2.0, 8.4, PyrH), 7.30 (1 H, dd, *J* 4.0, 8.4, PyrH), 5.66 (1 H, s, 6-H), 5.39 (2 H, s, CH_2), 3.93 (3 H, s, Me), 3.84 (3 H, s, Me), 2.34 (3 H, s, Me); ^{13}C NMR (100 MHz; $CDCl_3$) δ 178.7 (C), 178.2 (C), 159.6 (C), 154.8 (C), 141.9 (CH), 138.4 (CH), 138.1 (C), 128.9 (C), 124.1 (CH), 121.8 (CH), 121.3 (C), 116.3 (C), 106.8 (CH), 60.8 (CH_2), 56.5 (Me), 32.4 (Me), 9.9 (Me); MS (ESI) 313 (MH^+, 100%), 218 (76); Found: MH^+, 313.1174. $C_{17}H_{16}N_2O_4$ + H requires 313.1188.

5-Methoxy-1,2-dimethyl-3-(pyridin-4-yloxymethyl)indole-4,7-dione 13

mp 195 – 201 °C; UV (MeCN/nm) λ_{max} 221 (log ε 4.12), 281 (3.98), 290 (4.00), 339 (3.25), 446 (3.01); IR ($CHCl_3$/cm^{-1}) 2962, 1673, 1640, 1594, 1463, 1000; ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.40 (2 H, br s, PyrH), 6.89 (2 H, d, *J* 4.8, PyrH), 5.62 (1 H, s, 6-H), 5.34 (2 H, s, CH_2), 3.89 (3 H, s, Me), 3.80 (3 H, s, Me), 2.29 (3 H, s, Me); ^{13}C NMR (100 MHz; $CDCl_3$) δ 178.7 (C), 178.3 (C), 164.5 (C), 159.6 (C), 151.1 (CH), 138.1 (C), 128.9 (C), 121.2 (C), 115.9 (C), 110.6 (CH), 106.8 (CH), 60.1 (CH_2), 56.5 (Me), 32.4 (Me), 9.9 (Me); MS (ESI) 218 (MH^+, 100%), 313 (9); Found: MH^+, 313.1190. $C_{17}H_{16}N_2O_4$ + H requires 313.1188.

s

6-Methoxy-1,2-dimethyl-3-(4-nitrophenoxymethyl)indole-4,7-dione 15

mp 213 – 215 °C (decomp) (from methanol); UV (MeCN/nm) λ_{max} 228 (log ε 4.18), 286 (4.16), 295 (4.21), 313 (4.03), 442 (3.05); IR (KBr/cm^{-1}) 3436, 2923, 1668, 1649, 1593, 1509, 1493, 1465, 1343, 1264, 1172; ^{1}H NMR (300 MHz; $CDCl_3$) δ 8.19 (2 H, d, *J* 9.3, ArH), 7.06 (2 H, d, *J* 9.3, ArH), 5.68 (1 H, s, 5-H), 5.43 (2 H, s, CH_2), 3.92 (3 H, s, Me), 3.83 (3 H, s, Me), 2.34 (3 H, s, Me); ^{13}C NMR (75 MHz; $CDCl_3$) δ 184.9 (C), 171.8 (C), 163.9 (C), 160.4 (C), 142.0 (C), 140.8 (C), 127.5 (C), 126.3 (CH), 124.3 (C), 116.4 (C), 115.3 (CH), 107.1 (CH), 61.3 (CH_2), 57.1 (Me), 33.1 (Me), 10.6 (Me); MS (FI) 356 (M^+, 10%), 219 (28), 139 (100); Found: M^+, 356.1006. $C_{18}H_{16}N_2O_6$ requires 356.1008.

6-Methoxy-1,2-dimethyl-3-(phenoxymethyl)indole-4,7-dione 16

mp 173 – 175 °C (decomp) (from ethyl acetate/light petroleum); UV (MeCN/nm) λ_{max} 224 (log ε 4.10), 284 (3.92), 293 (3.91), 341 (3.36), 447 (2.83); IR ($CHCl_3$/cm^{-1}) 2928, 1662, 1642, 1604, 1495, 1467, 1379, 1339, 1170, 1058; ^{1}H NMR (500 MHz; DMSO-*d*) δ 7.29 (2 H, m, ArH), 6.99 (2 H, m, ArH), 6.94 (1 H, m, ArH), 5.77 (1 H, s, 5-H), 5.20 (2 H, s, CH_2) 3.87 (3 H, s, Me), 3.78 (3 H, s, Me), 2.29 (3 H, s, Me); ^{13}C NMR (125 MHz; DMSO-*d*) δ 184.4 (C), 171.0 (C), 160.3 (C), 158.9 (C), 141.5 (C), 129.9 (CH), 126.9 (C), 123.7 (C), 121.0 (CH), 116.7 (C), 115.0 (CH), 106.9 (CH), 59.9 (CH_2), 57.1 (Me), 32.9 (Me), 10.0 (Me); MS (ES) 334 (M+Na^+, 100%), 218 (11); Found: M+Na^+, 334.1056. $C_{18}H_{17}NO_4$ + Na requires 334.1055.

3-(4-Aminophenoxymethyl)-6-methoxy-1,2-dimethylindole-4,7-dione 17

mp 211 – 213 °C (from MeCN/hexane); UV (MeCN/nm) λ_{max} 231 (log ε 4.17), 285 (4.08), 293 (4.07), 339 (3.58), 443 (3.20); IR ($CHCl_3$/cm^{-1}) 3361, 2929, 1654, 1629, 1600, 1509, 1487, 1471,

1339, 1240, 1216, 1174, 1057; ^{1}H NMR (400 MHz; $CDCl_3$) δ 6.86 – 6.82 (2 H, m, ArH), 6.65 – 6.62 (2 H, m, ArH), 5.64 (1 H, s, 5-H), 5.23 (2 H, s, CH_2), 3.90 (3 H, s, Me), 3.81 (3 H, s, Me), 3.42 (2 H, bs, NH_2), 2.31 (3 H, s, Me); ^{13}C NMR (125 MHz; $CDCl_3$) δ 184.4 (C), 171.3 (C), 159.8 (C), 151.6 (C), 140.4 (C), 140.2 (C), 126.9 (C), 124.0 (C), 118.1 (C), 116.3 (CH), 116.2 (CH), 106.7 (CH), 61.0 (CH_2), 56.5 (Me), 32.6 (Me), 10.2 (Me); MS (ES) 349 ($M+Na^+$, 100%), 327 (45); Found: $M+Na^+$, 349.1156. $C_{18}H_{18}N_2O_4$ + Na requires 349.1164.

6-Methoxy-1,2-dimethyl-3-(3-nitrophenoxymethyl)indole-4,7-dione 18

mp 203 – 205 °C (from ethyl acetate/light petroleum); UV (MeCN/nm) λ_{max} 228 (log ε 4.41), 283 (4.27), 291 (4.23), 335 (3.82), 446 (3.16); IR ($CHCl_3$/cm^{-1}) 1664, 1642, 1604, 1467, 1352, 1058; ^{1}H NMR (500 MHz; DMSO-*d*) δ 7.82 – 7.79 (2 H, m, ArH), 7.58 (1 H, t, *J* 8.0, ArH), 7.44 (1 H, ddd, *J* 8.0, 2.5, 1.5, ArH), 5.76 (1 H, s, 5-H), 5.32 (2 H, s, CH_2) 3.86 (3 H, s, Me), 3.77 (3 H, s, Me), 2.30 (3 H, s, Me); ^{13}C NMR (125 MHz; DMSO-*d*) δ 183.8 (C), 170.6 (C), 159.8 (C), 159.0 (C), 148.8 (C), 141.1 (C), 130.7 (C), 126.6 (C), 123.3 (C), 122.2 (CH), 115.6 (CH), 115.2 (C), 108.8 (CH), 106.4 (CH), 60.5 (CH_2), 56.7 (Me), 32.5 (Me), 9.5 (CH_3); MS (ES) 379 ($M+Na^+$, 100%), 218 (16); Found: $M+Na^+$, 379.0906. $C_{18}H_{16}N_2O_6$ + Na requires 379.0901.

6-Methoxy-1,2-dimethyl-3-(2-nitrophenoxymethyl)indole-4,7-dione 19

mp 222 – 224 °C (from ethyl acetate); UV (MeCN/nm) λ_{max} 217 (log ε 4.32), 284 (4.13), 293 (4.12), 322 (3.67), 334 (3.69), 446 (2.92); IR ($CHCl_3$/cm^{-1}) 3468, 3123, 2784, 1685, 1656, 1575, 1522, 1466, 1399; ^{1}H NMR (500 MHz; $CDCl_3$) δ 7.78 (1 H, dd, *J* 8.1, 1.7, ArH), 7.49 (1 H, ddd, *J* 8.5, 7.4, 1.7, ArH), 7.39 (1 H, dd, *J* 8.5, 0.9, ArH), 7.00, (1 H, m, ArH), 5.66 (1 H, s, 5-H), 5.53 (2 H, s, CH_2), 3.91 (3 H, s, Me), 3.82 (3 H, s, Me), 2.38 (3 H, s, Me); ^{13}C NMR (100 MHz; $CDCl_3$) δ 185.1 (C), 171.6 (C), 160.4 (C), 151.9 (C), 141.6 (C), 140.7 (C), 134.5 (CH), 127.3 (C), 125.7 (CH), 124.1 (C), 120.9 (CH), 116.6 (C), 116.3 (CH), 106.9 (CH), 62.1 (CH_2), 57.0 (Me), 33.0 (Me), 10.6 (Me); MS (ES) 379 ($M+Na^+$, 100%); Found: $M+Na^+$, 379.0901. $C_{18}H_{16}N_2O_6$ + Na requires 379.0906.

6-Methoxy-1,2-dimethyl-3-(2,4-dinitrophenoxymethyl)indole-4,7-dione 20

mp 184 – 186 °C (from ethyl acetate/light petroleum); UV (MeCN/nm) λ_{max} 221 (log ε 4.40), 287 (4.40), 294 (4.43), 444 (3.20); IR ($CHCl_3$/cm^{-1}) 1666, 1637, 1605, 1466, 1345, 1057; ^{1}H NMR

(400 MHz; DMSO-*d*) □ 8.68 (1 H, d, *J* 2.8, ArH), 8.37 (1 H, dd, *J* 2.8, 9.2, ArH), 7.60 (1 H, d, *J* 9.2, ArH), 5.69 (1 H, s, 5-H), 5.67 (2 H, s, CH_2) 3.91 (3 H, s, Me), 3.84 (3 H, s, Me), 2.38 (3 H, s, Me); ^{13}C NMR (100 MHz; $CDCl_3$) □ 184.9 (C), 171.3 (C), 160.1 (C), 156.0 (C), 141.4 (C), 140.1 (C), 139.3 (C), 129.0 (CH), 127.0 (C), 123.6 (C), 121.7 (CH), 115.9 (CH), 114.7 (C), 106.6 (CH), 62.5 (CH_2), 56.8 (Me), 32.8 (Me), 10.3 (Me); MS (ES) 424 (M+Na^+, 100%); Found: M+Na^+, 424.0735. $C_{18}H_{15}N_3O_8$ + Na requires 424.0756.

3-(2-Fluoro-4-nitrophenoxymethyl)-6-methoxy-1,2-dimethylindole-4,7-dione 21

mp 229 – 231 °C (from chloroform/hexane); UV (MeCN/nm) □$_{max}$ 226 (log □4.41), 287 (4.39), 294 (4.19), 316 (4.19), 435 (3.41); IR ($CHCl_3$/cm^{-1}) 1665, 1641, 1604, 1466, 1347, 1278, 1076, 1057; ^{1}H NMR (400 MHz; $CDCl_3$) □ 8.04 (1 H, ddd, *J* 8.8, 2.8, 1.6, ArH), 7.96 (1 H, dd, *J* 10.8, 2.8, ArH), 7.34 (1 H, dd, *J* 8.8, 8.4, ArH), 5.68 (1 H, s, 5-H), 5.53 (2 H, s, CH_2) 3.92 (3 H, s, Me), 3.83 (3 H, s, Me), 2.36 (3 H, s, Me); ^{13}C NMR (100 MHz; $CDCl_3$) □ 184.6 (C), 171.4 (C), 160.0 (C), 151.5 (d, J_{CF} 249, CF), 152.2 (d, J_{CF} 11.3, C), 140.9 (C), 140.7 (C), 127.2 (C), 123.9 (C), 121.0 (d, J_{CF} 3.8, CH), 115.6 (C), 114.1 (CH), 112.3 (d, J_{CF} 23.8, CH), 106.7 (CH), 61.8 (CH_2), 56.7 (Me), 32.7 (Me), 10.2 (Me); MS (ES) 397 (M+Na^+, 79%), 218 (100); Found: M+Na^+, 397.0788. $C_{18}H_{15}FN_2O_6$ + Na requires 397.0812.

3-(4-Cyanophenoxymethyl)-6-methoxy-1,2-dimethylindole-4,7-dione 22

mp 184 °C (from ethyl acetate); UV (MeCN/nm) □$_{max}$ 235 (log □4.35), 249 (4.34), 284 (4.23), 293 (4.21), 339 (3.70), 444 (3.19); IR ($CHCl_3$/cm^{-1}) 2939, 1666, 1645, 1606, 1507, 1441, 1338, 1241, 1173, 1120, 1058; ^{1}H NMR (400 MHz; $CDCl_3$) □ 7.57 (2 H, dd, *J* 7.0, 1.8, ArH), 7.05 (2 H, dd, *J* 7.0, 1.8, ArH), 5.67 (1 H, s, 5-H), 5.38 (2 H, s, CH_2), 3.92 (3 H, s, Me), 3.83 (3 H, s, Me), 2.32 (3 H, s, Me); ^{13}C NMR (100 MHz; $CDCl_3$) □ 184.4 (C), 171.4 (C), 161.7 (C), 159.9 (C), 140.3 (C), 134.0 (CH), 127.1 (C), 123.9 (C), 119.2 (C), 116.2 (C), 115.6 (CH), 106.7 (CH), 104.1 (C), 60.5 (CH_2), 56.6 (Me), 32.7 (Me), 10.2 (Me); MS (ES) 359 (M+Na^+, 80%), 218 (100); Found: M+Na^+, 359.1017. $C_{19}H_{16}N_2O_4$ + Na requires 359.1007.

6-Methoxy-1,2-dimethyl-3-[4-(trifluoromethyl)phenoxymethyl]indole-4,7-dione 23

mp 150 °C (from ethyl acetate/hexane); UV (MeCN/nm) □$_{max}$ 229 (log □4.41), 284 (4.17), 293 (4.15), 337 (3.65), 441 (3.16); IR ($CHCl_3$/cm^{-1}) 2939, 1167, 1614, 1590, 1518, 1439, 1424, 1324,

1248, 1182, 1127, 1057; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.52 (2 H, d, *J* 8.8, ArH), 7.05 (2 H, d, *J* 8.8, ArH), 5.66 (1 H, s, 5-H), 5.37 (2 H, s, CH_2), 3.91 (3 H, s, Me), 3.82 (3 H, s, Me), 2.32 (3 H, s, Me); ^{13}C NMR (100 MHz; $CDCl_3$) δ 184.4 (C), 171.4 (C), 160.9 (C), 159.9 (C), 140.3 (C), 127.1 (C), 126.8 (q, J_{CF} 3.7, CH), 124.4 (q, J_{CF} 271, CF_3), 123.0 (q, J_{CF} 32.7, C), 123.9 (C), 116.7 (C), 114.8 (CH), 106.7 (CH), 60.4 (CH_2), 56.6 (Me), 32.6 (Me), 10.2 (Me); MS (ES) 402 ($M+Na^+$, 49%), 218 (100); Found: $M+Na^+$, 402.0930. $C_{19}H_{16}F_3NO_4$ + Na requires 402.0929.

3-(4-Fluorophenoxymethyl)-6-methoxy-1,2-dimethylindole-4,7-dione 24

mp 171 °C (from ethyl acetate); UV (MeCN/nm) λ_{max} 221 (log ε 4.14), 283 (4.06), 291 (4.02), 340 (3.49), 448 (3.01); IR ($CHCl_3$/cm^{-1}) 3693, 2939, 1665, 1643, 1604, 1506, 1338, 1238, 1222, 1209, 1180, 1057; ^{1}H NMR (400 MHz; $CDCl_3$) δ 6.96 – 6.93 (4 H, m, ArH), 5.65 (1 H, s, 5-H), 5.28 (2 H, s, CH_2), 3.91 (3 H, s, Me), 3.82 (3 H, s, Me), 2.32 (3 H, s, Me); ^{13}C NMR (100 MHz; $CDCl_3$) δ 184.4 (C), 171.4 (C), 159.9 (C), 157.4 (d, J_{CF} 238, CF), 154.6 (C), 140.3 (C), 127.0 (C), 124.0 (C), 117.4 (C), 116.0 (d, J_{CF} 8.1, CH), 115.8 (d, J_{CF} 23.0, CH), 106.7 (CH), 60.9 (CH_2), 56.6 (Me), 32.6 (Me), 10.2 (Me); MS (ES) 352 ($M+Na^+$, 100%), 218 (56); Found: $M+Na^+$, 352.0959. $C_{18}H_{16}FNO_4$ + Na requires 352.0961.

3-(2,4-Difluorophenoxymethyl)-6-methoxy-1,2-dimethylindole-4,7-dione 25

mp 173 °C (from ethyl acetate); UV (MeCN/nm) λ_{max} 220 (log ε 4.29), 284 (4.24), 293 (4.20), 339 (3.70); IR ($CHCl_3$/cm^{-1}) 3020, 2939, 1685, 1643, 1604, 1513, 1436, 1338, 1258, 1224, 1212, 1180, 1057; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.11 (1 H, td, *J* 9.2, 5.4, ArH), 6.82 (1 H, ddd, *J* 11.2, 8.3, 2.8, ArH), 6.79 – 6.73 (1 H, m, ArH), 5.65 (1 H, s, 5-H), 5.34 (2 H, s, CH_2), 3.91 (3 H, s, Me), 3.81 (3 H, s, Me), 2.35 (3 H, s, Me); ^{13}C NMR (100 MHz; $CDCl_3$) δ 184.4 (C), 171.4 (C), 159.9 (C), 156.7 (dd, J_{CF} 242, 10.3, CF), 152.9 (dd, J_{CF} 249, 12.1, CF), 142.8 (dd, J_{CF} 10.8, 3.3, C), 140.7 (C), 127.0 (C), 124.0 (C), 117.0 (dd, J_{CF} 9.5, 2.9, CH), 116.9 (C), 110.4 (dd, J_{CF} 22.4, 3.8, CH), 106.6 (CH), 104.7 (dd, ^{2}J 26.7, ^{2}J 22.3, CH), 62.3 (CH_2), 56.6 (Me), 32.6 (Me), 10.1 (Me); MS (ES) 370 ($M+Na^+$, 80%), 218 (100); Found: $M+Na^+$, 370.0863. $C_{18}H_{15}F_2NO_4$ + Na requires 370.0867.

6-Methoxy-1,2-dimethyl-3-(2,4,6-trifluorophenoxymethyl)indole-4,7-dione 26

mp 221 °C (from ethyl acetate/hexane); UV (MeCN/nm) λ_{max} 219 (log ε 4.25), 285 (4.21), 292 (4.20), 338 (3.70), 438 (3.21); IR ($CHCl_3$/cm^{-1}) 2939, 1166, 1645, 1606, 1548, 1508, 1440, 1338, 1240, 1174, 1120, 1058; ^{1}H NMR (400 MHz; $CDCl_3$) δ 6.67 (2 H, t, *J* 8.2, ArH), 5.60 (1 H, s, 5-H), 5.32 (2 H, s, CH_2), 3.92 (3 H, s, Me), 3.79 (3 H, s, Me), 2.35 (3 H, s, Me); ^{13}C NMR (100 MHz; $CDCl_3$) δ 183.9 (C), 171.5 (C), 159.7 (C), 157.3 (dt, J_{CF} 246, 14.3, CF), 156.5 (ddd, J_{CF} 250, 14.8, 7.7, CF), 141.0 (C), 131.9 (dd, J_{CF} 15.3, 5.0, C), 127.0 (C), 124.2 (C), 116.5, (C), 106.6 (CH), 100.6 (t, J_{CF} 26.7, CH), 65.9 (CH_2), 56.5 (Me), 32.6 (Me), 9.7 (Me); MS (ES) 388 ($M+Na^+$, 57%), 218 (100); Found: $M+Na^+$, 388.0766. $C_{18}H_{14}F_3NO_4$ + Na requires 388.0773.

6-Methoxy-1,2-dimethyl-3-(pyridin-2-yloxymethyl)indole-4,7-dione 27

mp 178 – 180 °C (from ethyl acetate/light petroleum); UV (MeCN/nm) λ_{max} 218 (log ε 4.35), 282 (4.24), 292 (4.20), 341 (3.70), 446 (3.22); IR ($CHCl_3$/cm^{-1}) 2940, 1644, 1605, 1570, 1466, 1359, 1340, 1311, 1287, 1057; ^{1}H NMR (500 MHz; $CDCl_3$) δ 8.19 (1 H, dd, *J* 5.0, 1.5, ArH), 7.57 – 7.54 (1 H, m, ArH), 6.88 (1H, ddd, *J* 7.0, 5.0, 1.0, ArH), 6.74 (1 H, d, *J* 8.5, ArH) 5.66 (1 H, s, 5-H), 5.54 (2 H, s, CH_2), 3.92 (3 H, s, Me), 3.81 (3 H, s, Me), 2.35 (3 H, s, Me); ^{13}C NMR (100 MHz; $CDCl_3$) δ 183.9 (C), 171.5 (C), 163.6 (C), 159.7 (C), 146.8 (CH), 140.3 (C), 138.5 (CH), 127.3 (C), 124.5 (C), 117.5 (C), 116.8 (CH), 111.1 (CH), 106.8 (CH), 57.9 (CH_2), 56.5 (Me), 32.6 (Me), 10.0 (Me); MS (ES) 335 ($M+Na^+$, 72%), 218 (100%); Found: $M+Na^+$, 335.1006. $C_{17}H_{16}N_2O_4$ + Na requires 335.1007.

3-Methoxy-1,2-dimethyl-3-(3-pyridyloxymethyl)indole-4,7-dione 28

mp 179 – 181 °C (from ethyl acetate/light petroleum); UV (MeCN/nm) λ_{max} 221 (log ε 4.22), 284 (4.12), 340 (3.55), 444 (3.05); IR ($CHCl_3$/cm^{-1}) 2940, 1664, 1604, 1576, 1488, 1466, 1379, 1340, 1057; ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.36 (1 H, bs, ArH), 8.21 (1 H, apparent bd, ArH), 7.36 (1H, ddd, *J* 8.4, 1.6, 1.2, ArH), 7.22 (1 H, dd, *J* 8.4, 4.8, ArH) 5.67 (1 H, s, 5-H), 5.38 (2 H, s, CH_2), 3.92 (3 H, s, Me), 3.82 (3 H, s, Me), 2.33 (3 H, s, Me); ^{13}C NMR (100 MHz; $CDCl_3$) δ 184.4 (C), 171.4 (C), 159.9 (C), 154.7 (C), 142.1 (CH), 140.4 (C), 138.6 (CH), 127.1 (C), 124.0 (C), 123.9 (CH), 121.4 (CH), 116.6 (C), 106.7 (CH), 60.5 (CH_2), 56.6 (Me), 32.6 (Me), 10.2 (Me); MS (EI) 313 (MH^+, 100%); Found: MH^+, 313.1178. $C_{17}H_{16}N_2O_4$ + H requires 313.1188.

6-Methoxy-1,2-dimethyl-3-(pyridin-4-yloxymethyl)indole-4,7-dione 29

mp 161 – 163 °C (from ethanol/light petroleum); UV (MeCN/nm) λ_{max} 222 (log ε 4.34), 285 (4.18), 293 (4.17), 337 (3.68), 441 (3.18); IR ($CHCl_3$/cm^{-1}) 3438, 2939, 1664, 1641, 1604, 1594, 1571, 1465, 1340, 1282, 1057; ^{1}H NMR (400 MHz; $CDCl_3$) δ 8.42 (2 H, d, *J* 5.0, ArH), 6.92 (2 H, d, *J* 5.0, ArH), 5.67 (1 H, s, 5-H), 5.39 (2 H, s, CH_2), 3.92 (3 H, s, Me), 3.83 (3 H, s, Me), 2.32 (3 H, s, Me); ^{13}C NMR (100 MHz; $CDCl_3$) δ 184.5 (C), 171.4 (C), 164.7 (C), 160.0 (C), 150.8 (CH), 140.4 (C), 127.2 (C), 123.9 (C), 116.1 (C), 110.7 (CH), 106.7 (CH), 60.2 (CH_2), 56.6 (Me), 32.7 (Me), 10.2 (Me); MS (ES) 313 (MH^+, 17%), 218 (100); Found: MH^+, 313.1177. $C_{17}H_{16}N_2O_4$ + H requires 313.1188.

HPLC Analysis of test compounds

HPLC: VARIAN ProStar Model 701

Column: VARIAN Polaris 5 C18-A 250x4.6 mm

UV Detection: 295 nm

Solvent system: A = Water

B = Acetonitrile

Volume of injection: 20 □L

Sequence:

Time [min]	Flow [mL/min]	% A	% B
Prerun	1.000	75.0	25.0
2.000	1.000	75.0	25.0
12.000	1.000	30.0	70.0
15.000	1.000	0.0	100.0
17.000	1.000	0.0	100.0
19.000	1.000	75.0	25.0

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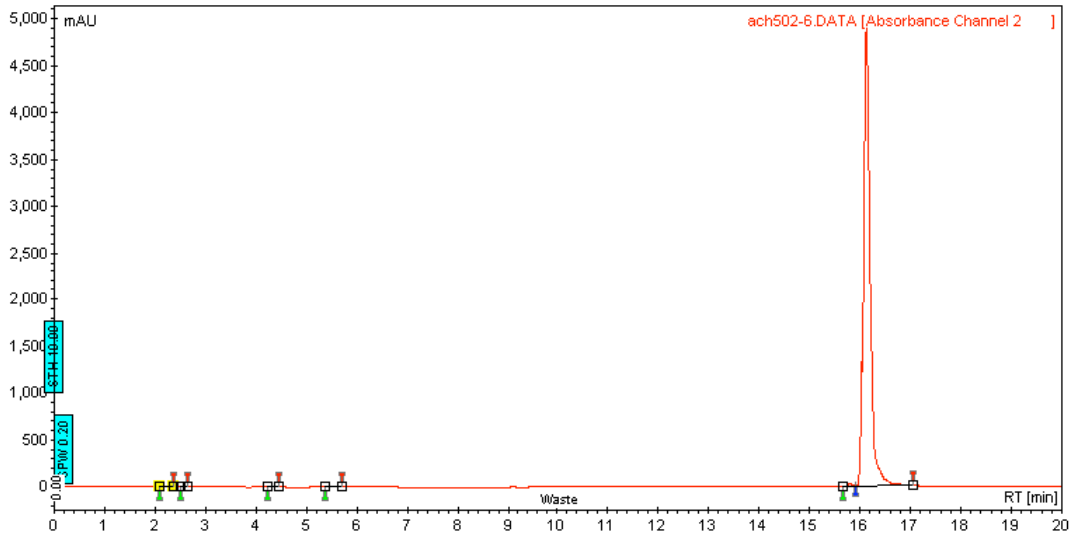
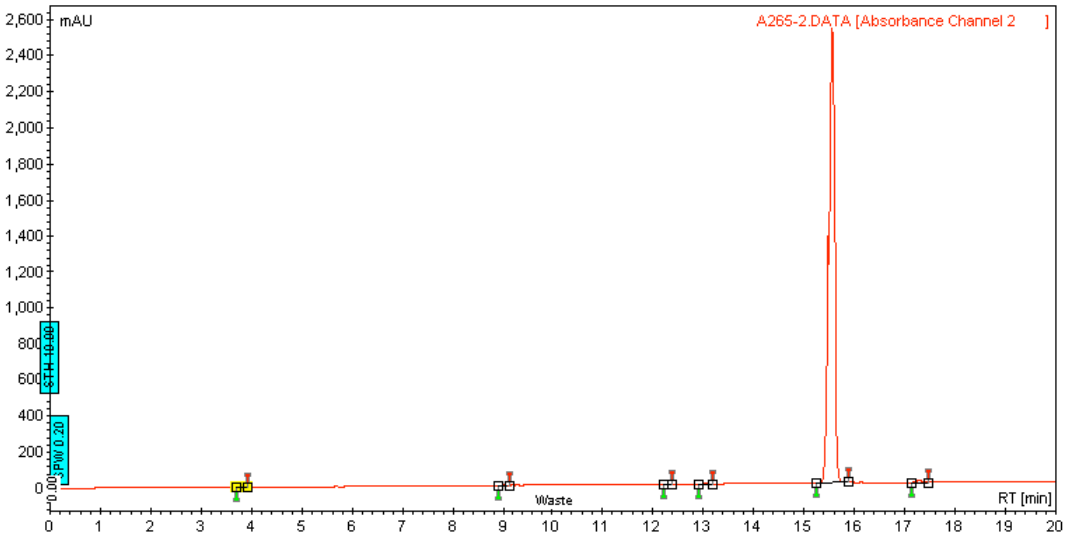
- **Compound 6**



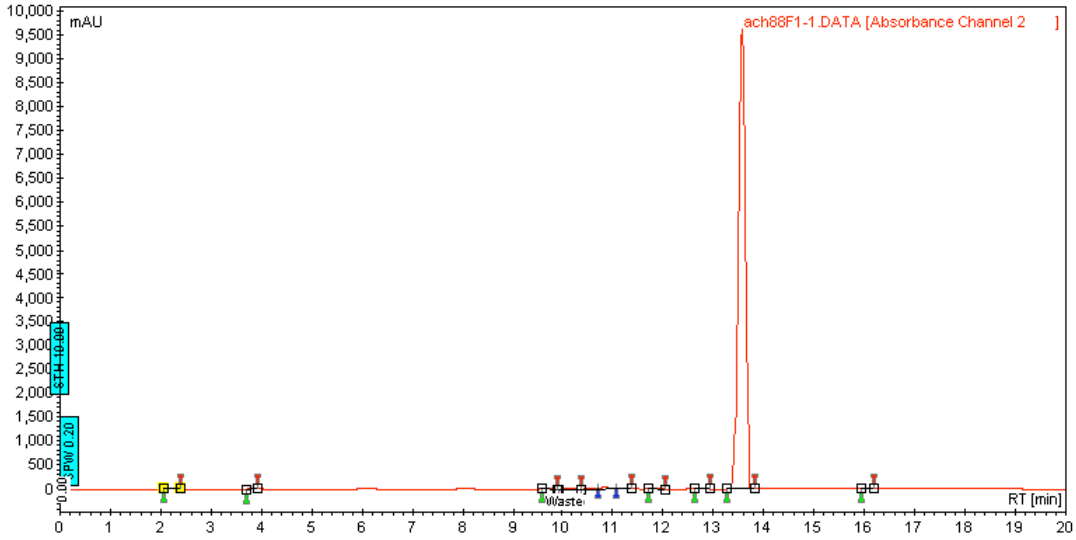
Index	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	2.25	0.08	3.9	0.6	0.076
2	2.56	0.04	4.3	0.3	0.037
3	4.33	0.04	2.7	0.3	0.041
4	5.52	0.11	4.9	0.8	0.111
5	15.80	0.50	35.0	3.7	0.499
6	16.13	99.24	4885.9	742.4	99.237
Total		100.00	4936.8	748.1	100.000

- **Compound 7**



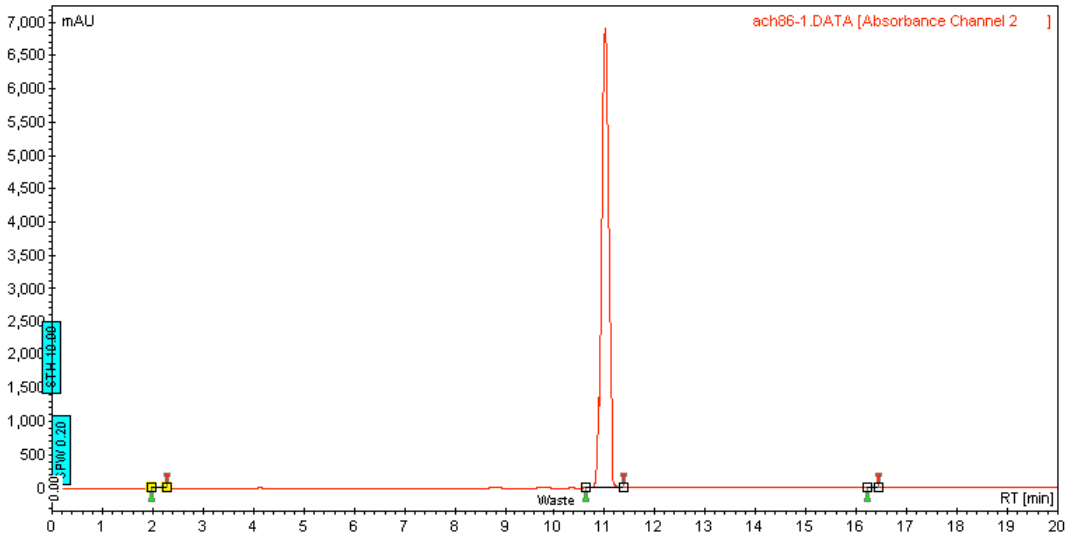
Index	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	3.83	0.04	1.4	0.1	0.044
2	9.00	0.06	1.8	0.2	0.058
3	12.28	0.02	0.9	0.1	0.025
4	13.04	0.09	2.0	0.3	0.085
5	15.56	99.37	2517.8	341.4	99.372
6	17.28	0.42	13.4	1.4	0.417
Total		100.00	2537.4	343.6	100.000

- **Compound 11**



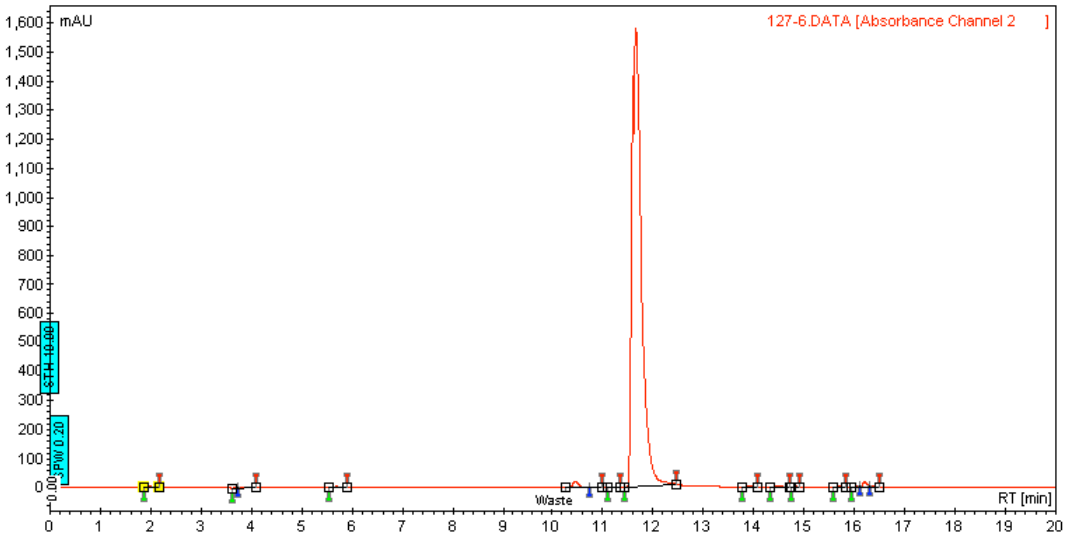
Index	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	2.20	0.20	25.5	3.2	0.202
2	3.79	0.09	12.5	1.4	0.088
3	9.69	0.08	8.1	1.3	0.082
4	10.14	0.15	14.7	2.4	0.152
5	10.57	0.14	14.6	2.2	0.143
6	10.86	0.42	42.0	6.6	0.421
7	11.24	0.07	7.5	1.1	0.067
8	11.86	0.11	13.2	1.8	0.113
9	12.76	0.10	12.6	1.6	0.100
10	13.57	98.57	9585.3	1542.7	98.569
11	16.04	0.06	9.2	1.0	0.064
Total		100.00	9745.0	1565.1	100.000

- **Compound 12**



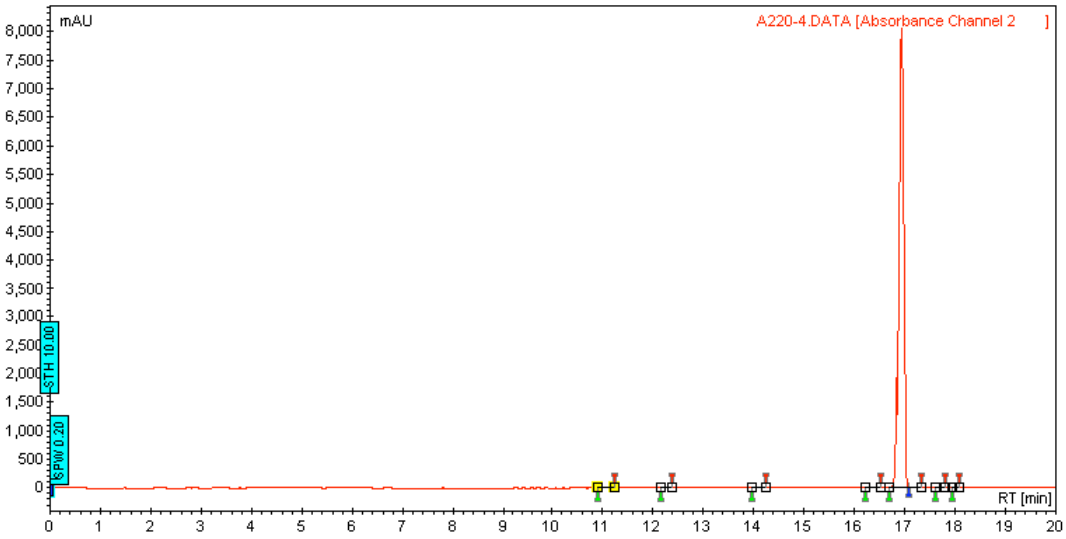
Index	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	2.12	0.10	9.7	1.2	0.102
2	11.01	99.85	6891.1	1156.6	99.851
3	16.32	0.05	5.3	0.5	0.047
Total		100.00	6906.1	1158.4	100.000

- **Compound 13**



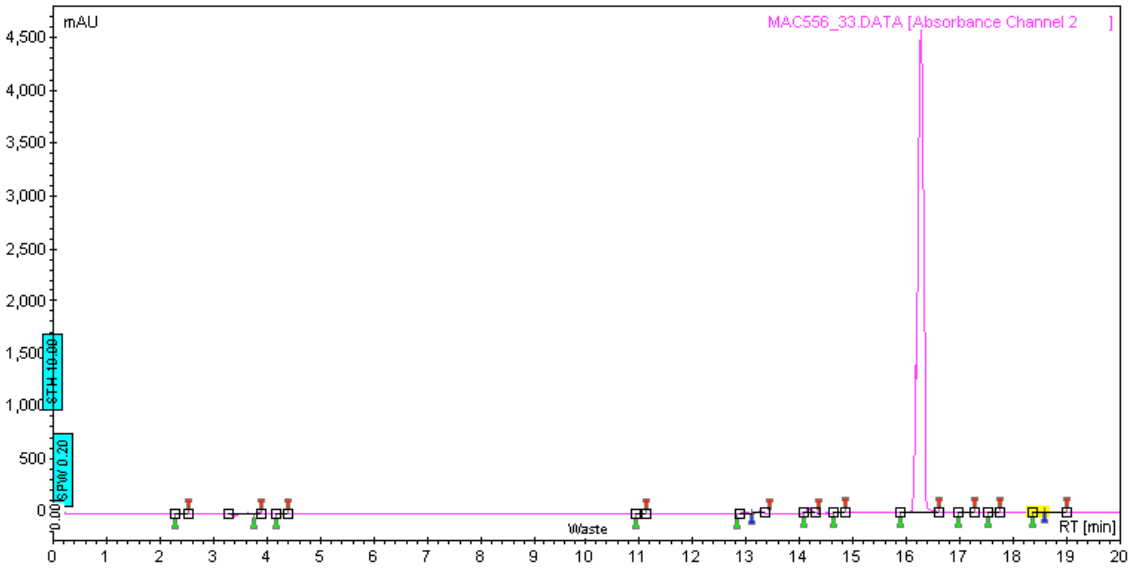
Index	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	1.98	0.13	4.0	0.5	0.135
2	3.69	0.02	0.8	0.1	0.016
3	3.87	0.17	3.4	0.6	0.169
4	5.70	0.14	2.9	0.5	0.139
5	10.46	0.76	20.5	2.7	0.764
6	10.85	0.05	1.3	0.2	0.047
7	11.23	0.05	1.5	0.2	0.054
8	11.66	97.73	1573.6	340.5	97.727
9	13.91	0.11	3.5	0.4	0.110
10	14.50	0.13	2.6	0.4	0.129
11	14.82	0.03	1.1	0.1	0.026
12	15.70	0.04	1.5	0.2	0.044
13	16.07	0.07	2.7	0.2	0.069
14	16.21	0.44	16.1	1.5	0.440
15	16.34	0.13	5.2	0.5	0.132
Total		100.00	1640.7	348.4	100.000

- **Compound 15**



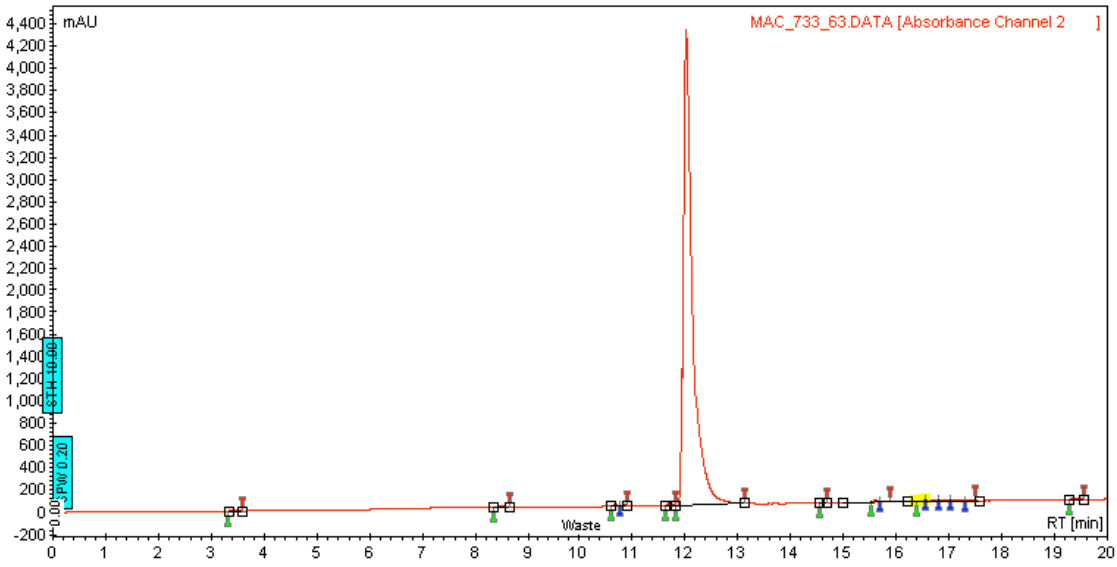
Index	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	11.06	0.15	8.6	1.4	0.150
2	12.22	0.07	5.3	0.6	0.069
3	14.10	0.10	8.4	0.9	0.099
4	16.41	0.17	8.4	1.6	0.171
5	16.94	99.33	8029.3	910.7	99.330
6	17.13	0.09	5.4	0.8	0.089
7	17.71	0.06	6.0	0.5	0.056
8	18.01	0.04	4.5	0.3	0.035
Total		100.00	8076.0	916.9	100.000

- **Compound 16**



Index	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	2.39	0.05	3.2	0.3	0.049
2	3.83	0.12	11.0	0.7	0.116
3	4.26	0.10	6.1	0.6	0.098
4	11.02	0.04	2.5	0.3	0.042
5	12.97	0.14	10.4	0.9	0.143
6	13.25	0.20	15.4	1.2	0.197
7	14.18	0.72	42.7	4.4	0.718
8	14.75	0.04	2.6	0.3	0.042
9	16.27	98.07	4576.0	595.4	98.074
10	17.14	0.12	4.8	0.7	0.121
11	17.64	0.05	2.8	0.3	0.046
12	18.52	0.31	11.7	1.9	0.306
13	18.60	0.05	2.9	0.3	0.048
Total		100.00	4691.9	607.1	100.000

- **Compound 17**



Index	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	3.36	0.08	5.6	0.7	0.083
2	8.51	0.26	13.3	2.3	0.261
3	10.68	0.09	8.3	0.8	0.091
4	10.85	0.03	3.7	0.3	0.035
5	11.72	0.22	19.5	1.9	0.223
6	12.02	97.22	4271.7	845.9	97.217
7	14.63	0.06	6.2	0.5	0.058
8	15.60	0.24	20.5	2.1	0.242
9	15.82	0.15	10.3	1.3	0.148
10	16.49	0.36	29.1	3.1	0.360
11	16.55	0.39	19.0	3.4	0.393
12	16.90	0.28	14.3	2.4	0.278
13	17.16	0.26	12.8	2.3	0.265
14	17.43	0.14	10.4	1.2	0.137
15	19.37	0.21	13.9	1.8	0.211
Total		100.00	4458.5	870.1	100.000

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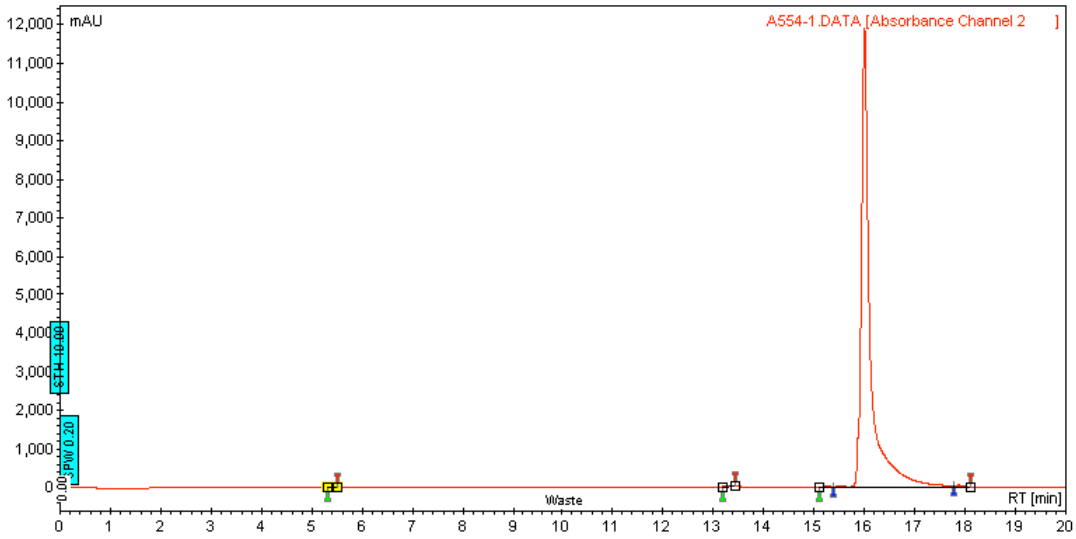
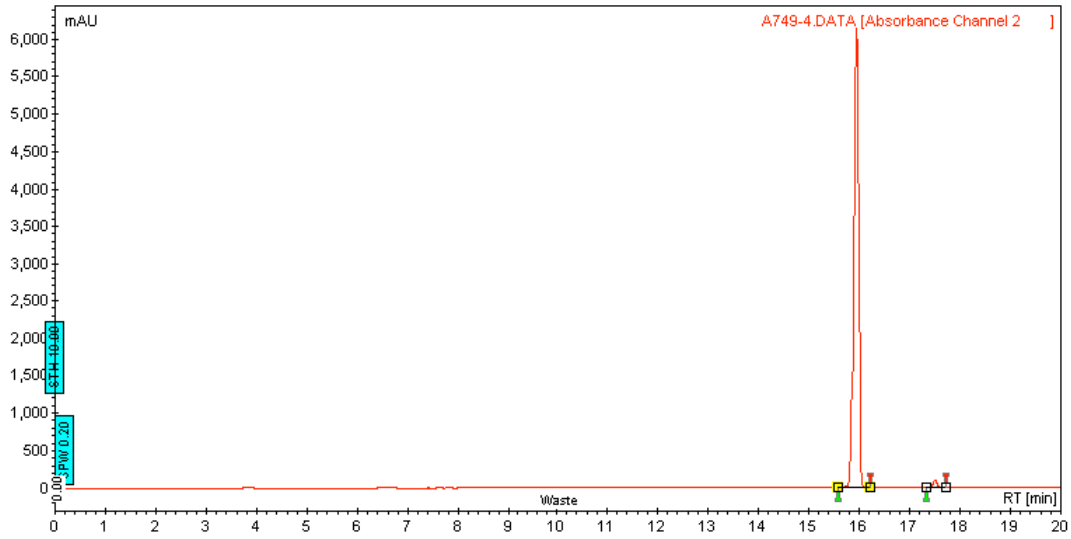
- **Compound 18**



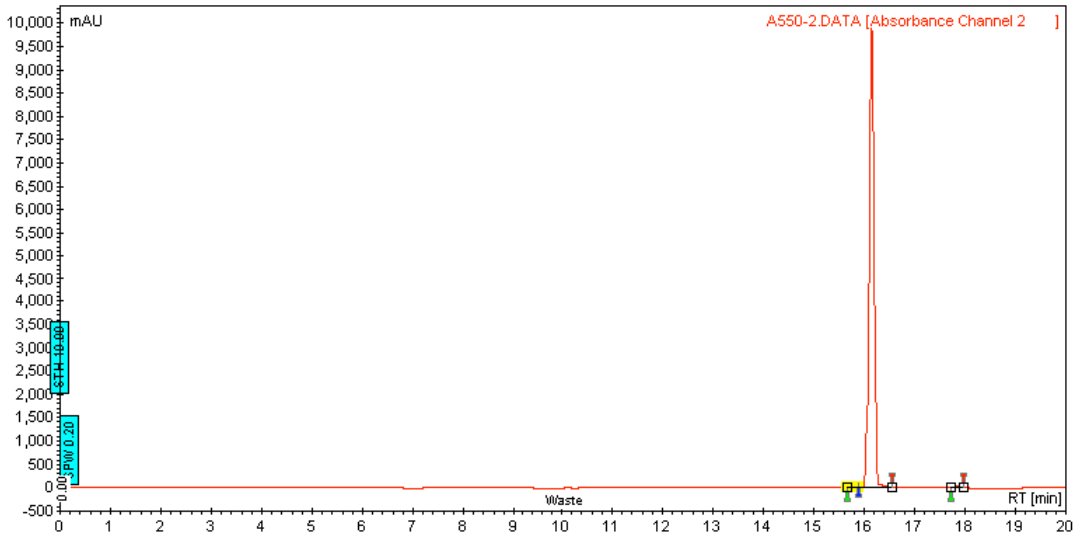
Index	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	5.38	0.05	11.8	1.3	0.055
2	13.30	0.04	9.8	1.1	0.044
3	15.25	0.12	24.3	2.9	0.122
4	16.00	99.51	11866.4	2411.4	99.507
5	17.87	0.27	44.4	6.6	0.273
Total		100.00	11956.7	2423.3	100.000

- **Compound 19**



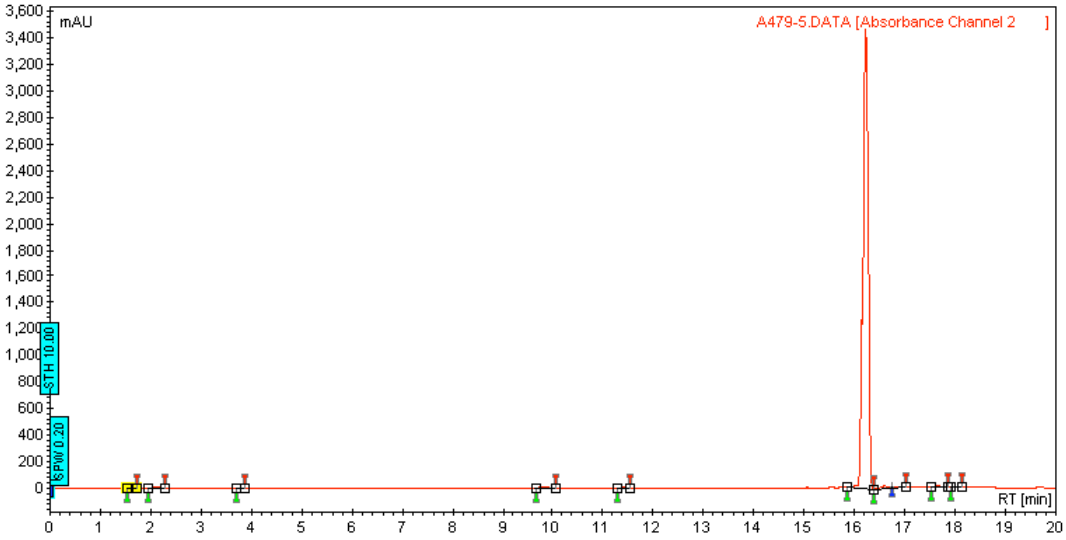
Index	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	15.94	98.65	6122.9	696.5	98.649
2	17.50	1.35	98.0	9.5	1.351
Total		100.00	6220.9	706.0	100.000

- **Compound 20**



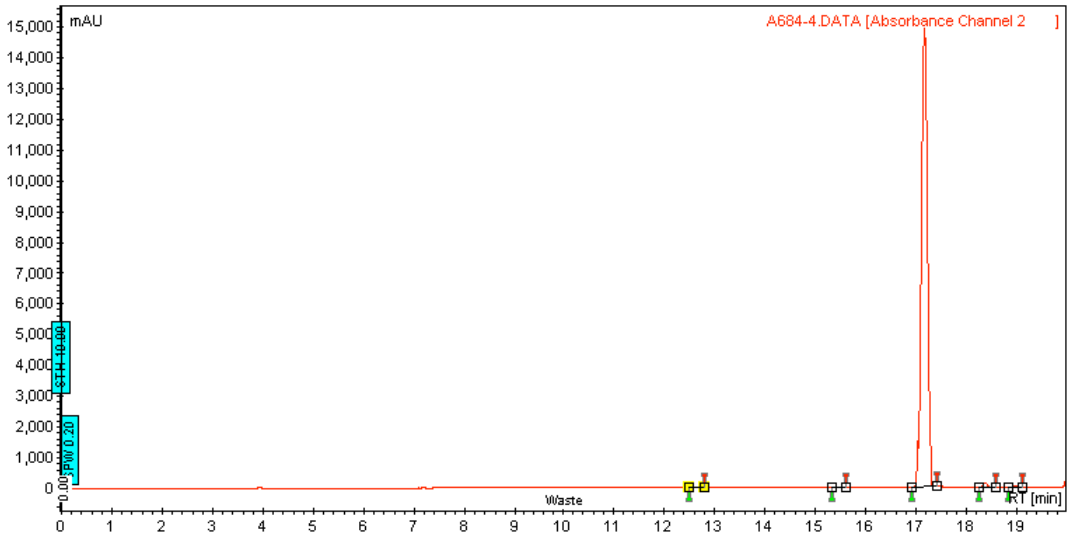
Index	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	15.78	0.14	18.3	1.6	0.145
2	16.15	99.45	9873.1	1107.1	99.450
3	17.84	0.41	53.3	4.5	0.405
Total		100.00	9944.7	1113.3	100.000

- **Compound 21**



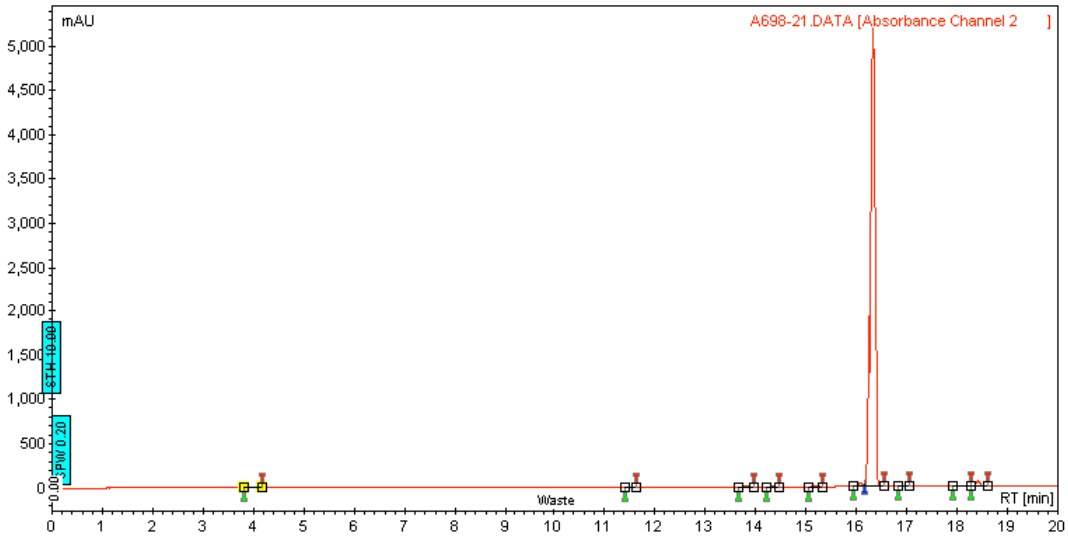
Index	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	1.61	0.03	1.4	0.1	0.031
2	2.10	0.17	6.4	0.7	0.173
3	3.80	0.02	1.2	0.1	0.021
4	9.85	0.28	6.5	1.2	0.284
5	11.42	0.07	2.5	0.3	0.071
6	16.22	97.80	3468.3	417.1	97.801
7	16.60	0.77	18.2	3.3	0.774
8	16.86	0.28	7.9	1.2	0.279
9	17.65	0.50	19.9	2.1	0.497
10	18.02	0.70	3.0	0.3	0.069
Total		100.00	3535.2	426.5	100.000

- **Compound 22**



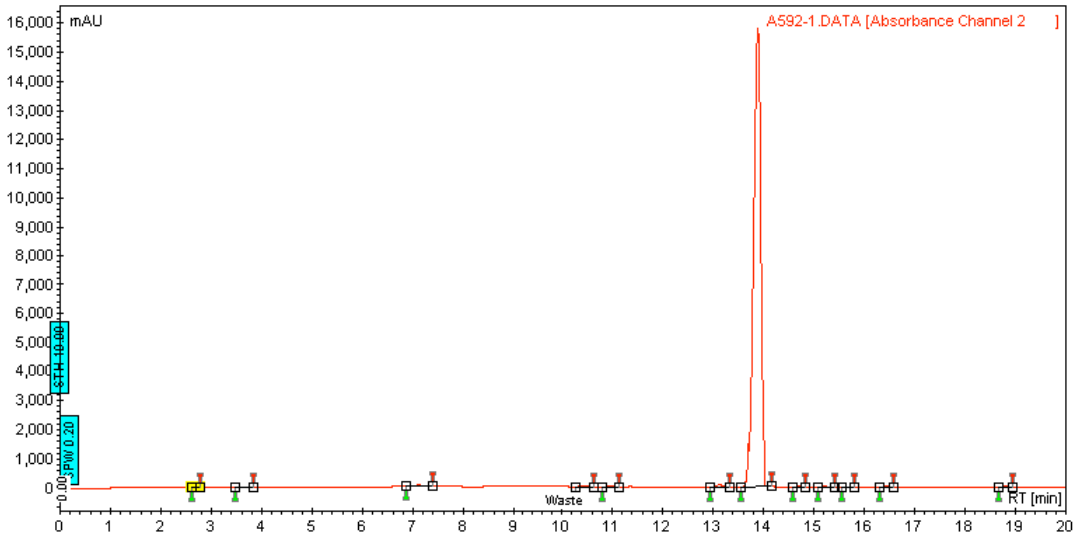
Index	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	12.62	0.13	22.9	2.8	0.132
2	15.44	0.08	14.7	1.6	0.076
3	17.17	98.85	14884.6	2069.8	98.847
4	18.37	0.73	160.8	15.2	0.728
5	18.97	0.22	45.3	4.5	0.216
Total		100.00	15128.2	2093.9	100.000

- **Compound 24**



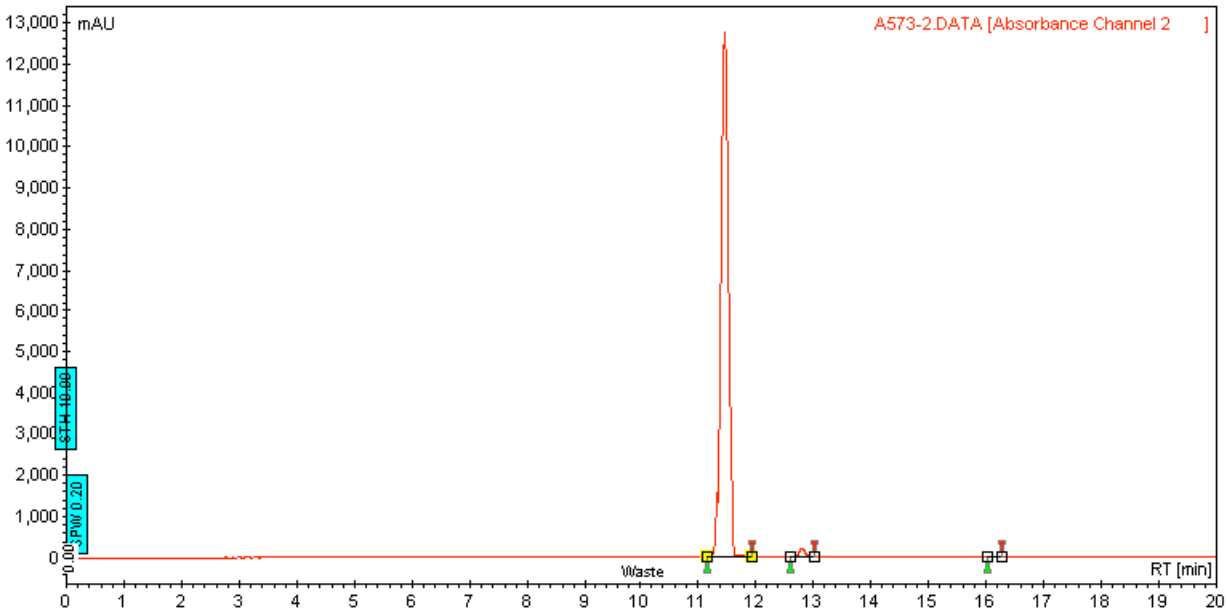
Index	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	3.92	0.15	4.3	0.9	0.146
2	11.50	0.05	3.0	0.3	0.054
3	13.81	0.13	7.0	0.8	0.129
4	14.34	0.07	3.8	0.4	0.069
5	15.17	0.17	9.7	1.0	0.166
6	16.08	0.71	39.5	4.2	0.714
7	16.33	97.34	5168.8	569.1	97.337
8	16.93	0.12	8.1	0.7	0.120
9	18.06	0.25	13.6	1.5	0.248
10	18.41	1.02	63.8	6.0	1.018
Total		100.00	5321.7	584.6	100.000

- **Compound 27**



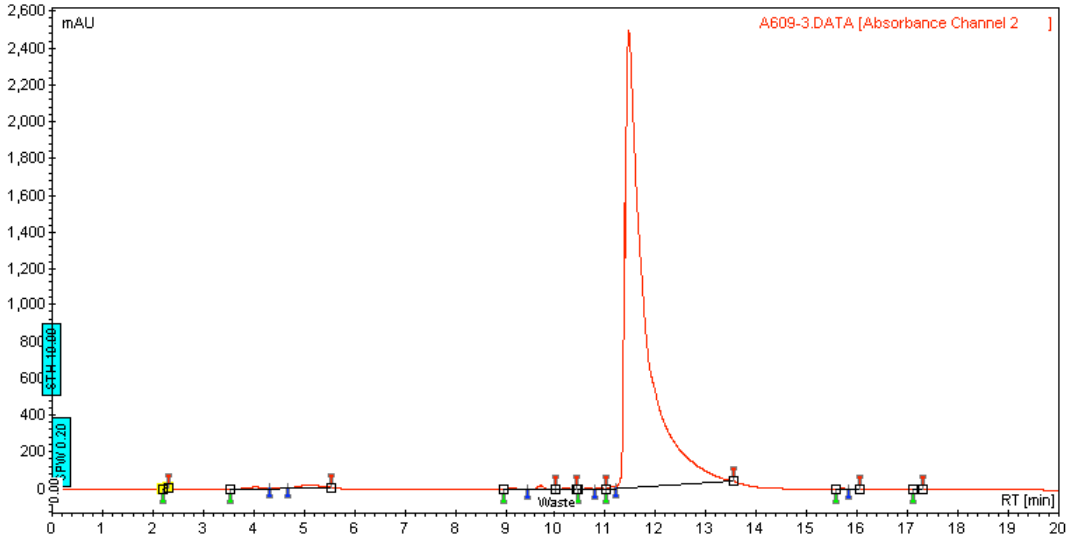
Index	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	2.68	0.02	6.8	0.5	0.019
2	3.62	0.15	24.7	3.9	0.147
3	7.13	0.37	42.6	9.9	0.368
4	10.44	0.16	30.5	4.3	0.162
5	10.97	0.15	28.8	3.9	0.147
6	13.13	0.37	76.0	9.9	0.368
7	13.89	98.24	15759.3	2631.8	98.245
8	14.69	0.08	21.4	2.2	0.082
9	15.20	0.13	25.3	3.5	0.130
10	15.67	0.07	18.4	1.8	0.067
11	16.45	0.17	47.2	4.5	0.169
12	18.80	0.09	24.9	2.5	0.095
Total		100.00	16105.9	2678.9	100.000

- **Compound 28**



Index	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	11.46	98.67	12744.7	1967.4	98.669
2	12.80	1.21	208.9	24.1	1.208
3	16.15	0.12	24.8	2.5	0.124
Total		100.00	12978.5	1993.9	100.000

- **Compound 29**



Index	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	2.26	0.01	1.9	0.1	0.011
2	4.03	0.30	10.3	3.4	0.305
3	4.51	0.09	4.7	1.1	0.094
4	5.10	0.61	14.7	6.9	0.610
5	9.16	0.11	7.6	1.2	0.109
6	9.72	0.27	19.9	3.0	0.270
7	10.23	0.11	8.6	1.2	0.106
8	10.67	0.08	6.1	0.8	0.076
9	10.90	0.07	7.6	0.8	0.072
10	11.13	0.11	12.5	1.3	0.111
11	11.47	98.11	2487.1	1102.4	98.106
12	15.71	0.08	9.4	0.9	0.083
13	17.92	0.03	3.5	0.4	0.033
14	17.20	0.01	1.8	0.2	0.014
Total		100.00	2595.7	1123.7	100.000

Growth Inhibition (MTT) Data for Indolequinone Leaving Groups

Compound	IC_{50} (nM) in MIA PaCa-2 Cells	
	4 h	72 h
Phenol	16535±46	16045±31
4-Nitrophenol	10994±26	12994±23
3-Nitrophenol	7126±21	13856±37
2-Nitrophenol	6084±37	16358±36
2,4-Dinitrophenol	15851±70	22101±48
2-Fluoro-4-nitrophenol	14290±51	19198±65
4-Hydroxypyridine	43203±47	17796±41
3-Hydroxypyridine	56480±39	73100±45
2-Hydroxypyridine	68137±35	68804±58
4-Fluorophenol	12385±45	13164±54
2,4-Difluorophenol	14758±60	20772±57
2,4,6-Trifluorophenol	36360±68	38058±57
4-Trifluoromethylphenol	13053±82	32926±59
4-Cyanophenol	56830±49	73339±57
4-Aminophenol	41979±56	42250±69

Substituted phenol induced growth inhibition in MIA PaCa-2 cells.

Growth inhibition was measured using the MTT growth inhibition assay. Cells were treated with drug in complete media continuously for (A) 4 h and (B) 72 h. Results are expressed as mean of 3 independent experiments.