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Novel synthesised flavone derivatives provide significant insight into the structural features required for enhanced anti-proliferative activity

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1 Synthesis

1.1 Synthesis of methoxy and hydroxy substituted flavonoids

General procedure A: Synthesis of Aryl benzoates (Step i) (1a-19a)

The methoxy substituted 2-hydroxy acetophenone (1.0 mmol, 1.0 eq.) was dissolved in pyridine (2 mL) and heated to 50 ^{o}C. DBU (1 % v/v of pyridine) was added and the mixture was stirred at 50 ^{o}C for 30 min. The corresponding acid chloride (1.5 eq.) was added slowly over 15 min, the mixture was heated to 75 ^{o}C and stirred for 1 h. The reaction was cooled to room temperature, acidified to pH 5 with 2 M HCl and extracted with EtOAc (2 x 5 mL). The organic layers were combined, dried over anhydrous $MgSO_4$ and concentrated *in vacuo* to yield the aryl benzoates. The pure aryl benzoates were obtained by column chromatography.

General procedure B: Synthesis of 1, 3-diketones (Step ii) (1b-19b)

The phenyl benzoate ester (1.0 mmol, 1.0 eq.) was dissolved in pyridine (6 mL) and heated to 50 ^{o}C for 1 h. Anhydrous KOH [powdered] (2 eq.) was added and the reaction was heated to 75 ^{o}C. After 1 h, the reaction mixture was cooled to room temperature, acidified to pH 5 with 2M HCl and extracted with EtOAc (2 x 5 mL). The organic layers were combined dried over anhydrous $MgSO_4$ and concentrated *in vacuo* to yield the crude 1,3-diketones. The crude 1,3-diketones were washed with acetic acid to remove any excess pyridine present and were used for the next step without further purification.

General procedure C: Synthesis of methoxy flavones (Step iii) (1c-19c)

The crude 1,3-diketone (1.0 mmol, 1.0 eq.) was dissolved in acetic acid (3 mL) and heated to 90 ^{o}C for 1 h. Concentrated. H_2SO_4 (1% v/v of acetic acid) was added and heated at 110 ^{o}C for 1 h. The reaction mixture was cooled to room temperature, diluted with water (10 mL) and the aqueous layer was extracted with EtOAc (2 x 5 mL). The organic layers were combined, dried over anhydrous $MgSO_4$ and concentrated *in vacuo* to obtain the crude methoxy flavones. The pure methoxy flavones were obtained by column chromatography.

General procedure D: Synthesis of hydroxy flavones (Step iv) (1d-19d)

The methoxy flavone (0.1 mmol, 1.0 eq.) was dissolved in anhydrous DCM (0.6 mL). BBr_3 (1.25 eq. per –OMe group) was added and the reaction was stirred at room temperature for 4 h for *O*-methoxy flavones or at 40 ^{o}C, overnight, for *m*-methoxy flavones. The reaction mixture was diluted with water (1 mL) and the pH was adjusted to 6 with 5% NaH_2PO_4. The aqueous layer was extracted with EtOAc (2 x 2.5 mL). The organic layers were combined, dried over anhydrous $MgSO_4$ and concentrated *in vacuo* to obtain the crude hydroxy flavones. The pure hydroxy flavones were obtained by column chromatography.

1.2 Synthesis of thioflavones

General procedure E: Synthesis of methoxy 4-thioflavones (Step v) (1e-19e)

The methoxy flavone was dissolved in anhydrous toluene (1 mL). Lawesson's reagent (0.6 eq.) was added and the reaction was heated to 110 ^{o}C for 4 h. The reaction mixture was

cooled to room temperature and concentrated *in vacuo*. The residue was purified by column chromatography to obtain the pure methoxy 4-thioflavones.

General procedure F: Synthesis of hydroxy 4-thioflavones (Step vi) (1f-19f)

The methoxy 4-thioflavone (0.1 mmol, 1.0 eq.) was dissolved in anhydrous DCM (0.6 mL). BBr_3 (1.25 eq. per –OMe group) was added and the reaction was stirred at room temperature for 4 h for *O*-methoxy flavones or at 40 ^{o}C, overnight, for *m*-methoxy flavones. The reaction mixture was diluted with water (1 mL) and the pH was adjusted to 6 with 5% NaH_2PO_4. The aqueous layer was extracted with EtOAc (2 x 2.5 mL). The organic layers were combined, dried over anhydrous $MgSO_4$ and concentrated *in vacuo* to obtain the crude hydroxy 4-thioflavones. The pure hydroxy 4-thioflavones were obtained by column chromatography.

1.3 Experimental section (*-indicates novel compounds)

1.3.1 Synthesis of 6-acetyl- 2, 3-dimethoxyphenyl benzoate (1a)

The titled compound was synthesised according to the general procedure-**A** using gallacetophenone dimethyl ether [1-(2-hydroxy-3, 4-dimethoxyphenyl) ethanone] (1.0 g, 5.09 mmol) and benzoyl chloride (1.07 g, 0.88 mL, 7.64 mmol). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**1a** as a white solid (1.3 g, 87%).

m.p: 102-03 ^{o}C (lit[1]-103-4 ^{o}C); **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 2.49 (3H, s, -C**H$_3$**), 3.82 (3H, s, -OC**H$_3$**), 3.96 (3H, s, -OC**H$_3$**), 6.90 (1H, d, *J* = 9.0 Hz, H-4), 7.54 (2H, app. t, *J* = 7.5 Hz, H-3',5'), 7.64-7.70 (1H, m, H-4**'**), 7.70 (1H, d, *J* = 9.0 Hz, H-5), 8.25 (2H, dd, *J* = 8.0, 4.0 Hz, H-2',6'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 29.81 (**C**H_3), 56.18 (-O**C**H_3), 60.97 (-O**C**H_3), 109.17 (C4), 124.60 (C6), 125.98 (C5), 128.70 (C5', C6'), 129.00 (C1'), 130.40 (C2', C3'), 133.74 (C4'), 141.70 (C2), 144.70 (C3), 157.25 (C1), 164.74 (**C**OO-Ar), 195.78 (**C**OCH_3); **IR ν_{max} [cm^{-1}]:** 1731 (C=O, ν, m), 1088 (O-C=O, ν, m), 1675 (C=O, ν, m), 1265 (-OCH_3, ν, s); ***m/z* (FTMS+ESI):** M+H ($C_{17}H_{17}O_5$) requires 301.1071, found 301.1068.

1.3.2 Synthesis of 1-(2-hydroxy-3,4-dimethoxyphenyl)-3-phenylpropane-1,3-dione (1b)

The titled compound was synthesised according to the general procedure-**B** using 6-acetyl-2,3-dimethoxyphenyl benzoate (**1a**) (1.0 g, 3.33 mmol). The crude product was washed with acetic acid to obtain compound-**1b** as a yellow solid (0.85 g, 85%). The product formation was confirmed by ^{1}H NMR spectroscopic analysis.

^{1}H NMR: ($CDCl_3$, 400 MHz) [The compound exists as a mixture of keto-enol tautomers] δ 3.87 (2H, s, -C**H$_2$**), 3.92 (3H, s, -OC**H$_3$**), 3.94 (3H, s, -OC**H$_3$**), 6.52 (1H, d, *J* = 8.0 Hz, H-6), 6.74 (1H, s, =C**H** of enol form), 7.45-7.61 (4H, m, H-5,3',4',5'), 7.92 (2H, dd, *J* = 7.0, 1.4 Hz, H-2',6'), 12.21 (1H, s, OH), 12.29 (1H, s, OH of enol form).

1.3.3 Synthesis of 7,8-dimethoxy-2-phenyl-4*H*-chomen-4-one (1c)

The titled compound was synthesised according to the general procedure-**C** using 1-(2-hydroxy-3,4-dimethoxyphenyl)-3-phenylpropane-1,3-dione (**1b**) (0.8 g, 2.66 mmol). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**1c** as a white solid (0.60 g, 80%).

m.p: 151-52 ^{o}C (lit[1]-151-52 ^{o}C); **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 4.01 (3H, s, -OC**H$_3$**), 4.05 (3H, s, -OC**H$_3$**), 6.78 (1H, s, H-3), 7.06 (1H, d, *J* = 9.0 Hz, H-6), 7.55-7.60 (3H, m, H-3',4',5'), 7.96-7.98 (3H, m, H-5,2',6'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 56.61 (-O**C**H$_3$), 61.98 (-O**C**H$_3$), 106.94 (C3), 110.08 (C6), 118.59 (C10), 121.19 (C5), 126.25 (C3',4',5'), 129.10 (C2', C6'), 131.55 (C1'), 137.20 (C8), 150.79 (C9), 156.71 (C7), 163.18 (C2), 178.35 (**C**=O); **IR ν_{max} [cm^{-1}]:** 1644 (C=O, ν, s), 1290 (-OCH3, ν, s) 1098 (C-O, ν, m); ***m/z* (FTMS+ESI):** M+H ($C_{17}H_{15}O_4$) requires 283.0965, found 283.0967. **HPLC purity:** 98.6%, RT-12.6 min at 258 nm.

1.3.4 Synthesis of 7,8-dihydroxy-2-phenyl-4*H*-chomen-4-one (1d)

e titled compound was synthesised according to the general procedure-**D** using 7,8-dimethoxy-2-phenyl-4*H*-chomen-4-one (**1c**) (0.050 g, 0.178 mmol). Purification was achieved by column chromatography with EtOAc (100%) to yield the compound-**1d** as a pale yellow solid (0.030 g, 67%).

m.p: 242-43 ^{o}C (lit[1]-242-43 ^{o}C); **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 6.88 (1H, s, H-3), 6.95 (1H, d, *J* = 9.0 Hz, H-6), 7.39 (1H, d, *J* = 9.0 Hz, H-5), 7.55-7.58 (3H, m, H-3',4',5'), 8.14 (2H, dd, *J* = 5.0, 4 Hz, H-2',6'), 9.52 (1H, s, OH), 10.32 (1H, s, OH); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 105.99 (C3), 114.01 (C6), 115.08 (C9), 116.90 (C5), 126.30 (C2', C4', C6'), 128.97 (C3', C5'), 131.45 (C1'), 133.06 (C8), 146.67 (C10), 150.52 (C7), 161.68 (C2), 176.86 (**C**=O); **IR ν_{max} [cm^{-1}]:** 1699 (C=O, ν, s), 1194 (C-O, ν, m), 3164 (OH, w, b), ***m/z* (FTMS+ESI):** M+H ($C_{15}H_{11}O_4$) requires 255.0652, found 255.0652. **HPLC purity:** 98.7%, RT-9.9 min at 258 nm.

1.3.5 Synthesis of 7,8-dimethoxy-2-phenyl-4*H*-chromene-4-thione (1e)

The titled compound was synthesised according to the general procedure-**E** using 7,8-dimethoxy-2-phenyl-4*H*-chomen-4-one (**1c**) (0.2 g, 0.7 mmol). Purification was achieved by column chromatography with $CHCl_3$ (100%) to yield the compound-**1e** as an orange solid (0.17 g, 80 %).

m.p: 170-71 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 4.02 (3H, s, -OC**H$_3$**), 4.05 (3H, s, -OC**H$_3$**), 7.01 (1H, d, *J* = 9.0 Hz, H-6), 7.53-7.58 (3H, m, H-3',4',5'), 8.03 (2H, dd, *J* = 7.0, 1.5 Hz, H-2', 6'), 8.36 (1H, d, *J* = 9.0 Hz, H-5); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 56.61 (-O**C**H$_3$), 61.98 (-O**C**H$_3$), 111.01 (C6), 119.33 (C3), 124.33 (C5), 126.55 (C2', C4', C6'), 129.14 (C3', C5'), 131.18 (C1'), 132.10 (C8), 146.35 (C9), 153.93 (C7), 157.26 (C2), 201.48 (**C**=S); **IR ν_{max} [cm^{-1}]:** 1287 (C=S, ν, s), 1233 (-OCH_3, ν, m) 1094 (C-O, ν, m); ***m/z* (FTMS+ESI):** M+H ($C_{17}H_{15}O_3S$) requires 299.0736, found 299.0737. **HPLC purity:** 95.3%, RT-14.2 min at 270 nm.

1.3.6 Synthesis of 7,8-dihydroxy-2-phenyl-4*H*-chromene-4-thione (1f)

The titled compound was synthesised according to the general procedure-**F** using 7,8-dimethoxy-2-phenyl-4*H*-chromene-4-thione (**1e**) (0.15 g, 0.5 mmol). Purification was achieved by column chromatography with EtOAc (100%) to yield the compound-**1f** as an orange red solid (0.08 g, 59 %).

m.p: 210-11 ^{o}C; **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 7.05 (1H, d, *J* = 9.0 Hz, H-6), 7.57 (3H, app.t, *J* = 7.5 Hz, H-3',4',5'), 7.74 (1H, s, H-3), 7.86 (1H, d, *J* = 9.0 Hz, H-5), 8.21 (2H, dd, *J* = 7.0, 4.0 Hz, H-2',6'), 9.82 (1H, s, OH), 10.85 (1H, s, OH); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 115.74 (C6), 117.69 (C3), 118.85 (C5), 124.3 (C10), 127.02 (C2', C6'), 129.55 (C3', C4', C5'), 132.08 (C1'), 133.25 (C8), 142.59 (C9), 153.48 (C7), 151.73 (C2), 199.97 (**C**=S); **IR ν_{max} [cm^{-1}]:** 1282 (C=S, ν, s), 1102 (C-O, ν, m), 3495 (OH, w, s); ***m/z* (FTMS+ESI):** M+H ($C_{15}H_{11}O_3S$) requires 271.0423, found 271.0424. **HPLC purity:** 98.3%, RT-9.8 min at 260 nm.

1.3.7 Synthesis of 2-acetyl- 3,5-dimethoxyphenyl benzoate (2a)

The titled compound was synthesised according to the general procedure-**A** using phloroacetophenone dimethylether [1-(2-hydroxy-4, 6-dimethoxyphenyl) ethanone] (1g, 5.09 mmol) and benzoyl chloride (1.07 g, 0.88 mL). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**2a** as a white solid (1.1 g, 73%).

m.p: 93-94 ^{o}C (lit[2]-91 ^{o}C); **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 2.47 (3H, s, -C**H$_3$**), 3.82 (3H, s, -OC**H$_3$**), 3.86 (3H, s, -OC**H$_3$**), 6.37 (1H, s, H-4), 6.41 (1H, s, H-6), 7.47 (2H, app.t, *J* = 7.0 Hz, H-3',5'), 7.61 (1H, app.t, *J* = 7.0 Hz, H-4'), 8.14 (2H, dd, *J* = 7.5 Hz, 1.5 Hz, H-2',6'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 31.95 (-**C**H$_3$), 55.66 (-O**C**H$_3$), 55.94 (-O**C**H$_3$), 96.68 (C4), 100.10 (C6), 117.42 (C2), 128.57 (C3', C5'), 129.22 (C1'), 130.29 (C2', C6'), 133.65 (C4'), 150.10 (C1), 159.16 (C5), 162.22 (C3), 165.06 (**C**OO-Ar), 199.21 (**C**OCH$_3$); **IR ν_{max} [cm^{-1}]:** 1732 (C=O, ν, m), 1153 (O-C=O, ν, m), 1679 (C=O, ν, m), 1246 (-OCH$_3$, ν, s); ***m/z* (FTMS+ESI):** M+H ($C_{17}H_{17}O_5$) requires 301.1071, found 301.1071.

1.3.8 Synthesis of 1-(2-hydroxy-4, 6-dimethoxyphenyl)-3-phenylpropane-1, 3-dione (2b)

The titled compound was synthesised according to the general procedure-**B** using 2-acetyl-3, 5-dimethoxyphenyl benzoate (**2a**) (1.0 g, 3.33 mmol). The crude product was washed with acetic acid to obtain compound-**2b** as a yellow solid (0.75 g, 75%). The product formation was confirmed by ^{1}H NMR.

^{1}H NMR: ($CDCl_3$, 400 MHz) [The compound exists as a mixture of keto-enol tautomers] δ 3.82 (C**H$_2$**), 3.89 (3H, s, -OCH$_3$), 3.92 (3H, s, -OCH$_3$), 6.09 (1H, s, H-5), 6.11 (1H, s, H-3), 7.33 (1H, s, =C**H** of enol form), 7.48 (2H, app.t. *J* = 8.0 Hz, H-3', 5'), 7.58 (1H, d, *J* = 7.5 Hz, H-4'), 7.88 (1H, d, *J* = 7.0 Hz, H-2'), 7.96 (1H, d, *J* = 7.0 Hz, H-6'), 13.43 (1H, s, OH), 13.72 (1H, s, OH of enol form).

1.3.9 Synthesis of 5,7-dimethoxy-2-phenyl-4*H*-chomen-4-one (2c)

The titled compound was synthesised according to the general procedure-**C** using 1-(2-hydroxy-4,6-dimethoxyphenyl)-3-phenylpropane-1,3-dione (**2b**) (0.7 g, 2.33 mmol). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**2c** as a white solid (0.40 g, 60%).

m.p: 146-47 ^{o}C (lit[3]-143-45 ^{o}C); **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 3.84(3H, s, -OC**H$_3$**), 3.89 (3H, s,-OC**H$_3$**), 6.31 (1H, s, H-6), 6.51 (1H, s, H-3), 6.62 (1H, s, H-8), 7.43 (3H, app.t, *J* = 8.0 Hz, H-3',4',5'), 7.80 (2H, dd, *J* = 4.0 Hz, 1.5 Hz, H-2',6'); **^{13}C NMR:** ($CDCl_3$, 400 MHz) δ 53.87 (-O**C**H_3), 54.59 (-O**C**H_3), 90.87 (C8), 94.41 (C6), 107.28 (C3), 107.38 (C10), 126.25 (C2', C6'), 127.01 (C3', C5'), 129.25 (C4'), 129.59 (C1'), 158.01 (C9), 158.82 (C5), 159.06 (C2), 162.22 (C7), 176.15 (**C=**O); **IR ν_{max} [cm^{-1}]:** 1645(C=O, ν, s), 1345 (-OCH_3, ν, s), 1118 (C-O, ν, m); ***m/z* (FTMS+ESI):** M+H ($C_{17}H_{15}O_4$) requires 283.0965, found 283.0963. **HPLC purity:** 99.9%, RT-12.3 min at 258 nm.

1.3.10 Synthesis of 5, 7-dihydroxy-2-phenyl-4*H*-chomen-4-one (2d)

The titled compound was synthesised according to the general procedure-**D** using 5,7-dimethoxy-2-phenyl-4*H*-chomen-4-one (**2c**) (50 mg, 0.178 mmol). Purification was achieved by column chromatography with EtOAc (100%) to yield the compound-**2d** as a as a yellow solid (0.030 g, 67%)

m.p: 284-85 ^{o}C (lit[3]-285-88 ^{o}C); **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 6.22 (1H, s, H-6), 6.52 (1H, s, H-8), 6.95 (1H, s, H-3), 7.57-7.61 (3H, m, H-3',4',5'), 8.06 (2H, dd, *J* = 8.0 Hz, 1.5 Hz, H-2',6'), 10.91 (1H, s, OH), 12.81 (1H, s, OH); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 93.90 (C8), 99.17 (C6), 104.08 (C10), 105.35 (C3), 126.42 (C2', C6'), 129.32 (C3', C5'), 130.59 (C1'), 132.05 (C4'), 157.48 (C9), 161.29 (C5), 162.93 (C2), 164.56 (C7), 181.82 (**C=**O); **IR ν_{max} [cm^{-1}]:** 1610 (C=O, ν, s), 1167 (C-O, ν, m), 2922 (OH, w, b); ***m/z* (FTMS+ESI):** M+H ($C_{15}H_{11}O_4$) requires 255.0652, found 255.0651. **HPLC purity:** 99.9%, RT- 12.4 min at 258 nm.

1.3.11 Synthesis of 5,7-dimethoxy-2-phenyl-4*H*-chromene-4-thione (2e)

The titled compound was synthesised according to the general procedure-**E** using 5,7-dimethoxy-2-phenyl-4*H*-chomen-4-one (**2c**) (0.25 g, 0.88 mmol). Purification was achieved by column chromatography with $CHCl_3$ (100%) to yield the compound-**2e** as a green solid (0.15 g, 57%).

m.p: 184-85 ^{o}C (lit[4]-184 ^{o}C); **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 3.93 (6H, s, 2 x -OC**H$_3$**), 6.43 (1H, s, H-6), 6.59 (1H, s, H-8), 7.46-7.53 (3H, m, H-3', 4', 5'), 7.57 (1H, s, H-3), 7.92 (2H, dd, *J* = 2.0, 1.5 Hz, H-2', 6'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 55.83 (-O**C**H_3), 56.61 (-O**C**H_3), 92.79 (C8), 96.68 (C6), 126.25 (C2', C6'), 128.97 (C3', C4', C5'), 129.94 (C10), 130.91 (C3), 131.89 (C1'), 139.0 (C2), 149.78 (C9), 160.09 (C7), 161.02 (C5), 177.77 (**C**=S); **IR ν_{max} [cm^{-1}]:** 1348 (C=S, ν, m), 1220 (-OCH_3, ν, m) 1144 (C-O, ν, m). ***m/z* (FTMS+ESI):** M+H ($C_{17}H_{15}O_3S$) requires 299.0736, found 299.0738. **HPLC purity:** 95.4%, RT-13.7 min at 270 nm.

1.3.12 Synthesis of 5,7-dihydroxy-2-phenyl-4*H*-chromene-4-thione (2f)

The titled compound was synthesised according to the general procedure-**F** using 5,7-dimethoxy-2-phenyl-4*H*-chromene-4-thione (**2e**) (0.15 g, 0.5 mmol). Purification was achieved by column chromatography with EtOAc (100%) to yield the compound-**2f** as a brown solid (0.07 g, 52%).

m.p: 216-17 ^{o}C (lit[5]-218 ^{o}C); **^{1}H NMR:** (DMSO-d6, 400 MHz) 6.32 (1H, s, H-6), 6.59 (1H, s, H-8), 7.56-7.63 (4H, m, H-3, 3',4',5'), 8.11 (2H, dd, *J* = 7.0 Hz, 1.5 Hz, H-2', 6'), 11.41 (1H, s, OH), 13.62 (1H, s, OH); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 94.81 (C8), 100.99 (C6), 112.77 (C10), 117.41 (C3), 126.68 (C2', C6'), 129.38 (C3', C4', C5'), 132.28 (C1'), 153 (C2), 154.29 (C9), 162.01 (C7), 164.72 (C5), 195.81 (**C**=S); **IR ν_{max} [cm^{-1}]:** 1144 (C=S, ν, m), 1144 (C-O, ν, m), 3170 (OH, w, b); ***m/z* (FTMS+ESI):** M+H ($C_{15}H_{11}O_5S$) requires 271.0423, found 271.0424. **HPLC purity:** 99.8%, RT-9.9 min at 258 nm.

1.3.13 Synthesis of 6-acetyl-2, 3-dimethoxyphenyl- 3',4'-dimethoxybenzoate (3a)

The titled compound was synthesised according to the general procedure-**A** using the gallacetophenone dimethyl ether [1-(2-hydroxy-3,4-dimethoxyphenyl) ethanone] (1 g, 5.09 mmol) and 3,4-dimethoxy benzoyl chloride (1.53 g, 7.63 mmol). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**3a** as a white solid (1.2 g, 80%).

m.p: 140-41 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 2.44 (3H, s, -C**H$_3$**) 3.69 (3H, s, -OC**H$_3$**), 3.84 (3H,s, -OC**H$_3$**), 3.88 (3H, s, -OC**H$_3$**), 3.94 (3H, s, -OC**H$_3$**), 7.13 (1H, d, *J* = 9.0 Hz, H-5), 7.16 (1H, d, *J* = 9.0 Hz, H-6), 7.58 (1H, s, H-2'), 7.79 (1H, d, *J* = 7.4 Hz, H-5'), 7.78 (1H, d, *J* = 7.5 Hz, H-6'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 29.42 (-**C**H$_3$), 56.06 (-O**C**H$_3$), 60.31 (-O**C**H$_3$), 109.71 (C4), 111.12 (C5'), 112.12 (C2'), 120.63 (C6), 124.33 (C5, C6'), 126.18 (C1'), 140.98 (C2), 143.57 (C3'), 153.56 (C3), 156.71 (C4'), 163.74 (**C**OO-Ar), 195.56 (**C**OCH$_3$); **IR ν_{max} [cm^{-1}]:** 1735 (C=O, ν, m), 1091 (O-C=O, ν, m), 1679 (C=O, ν, m), 1268 (-OCH$_3$, ν, s); ***m/z* (FTMS+ESI):** M+Na ($C_{19}H_{20}O_7Na$) requires 383.1101, found 383.1099.

1.3.14 Synthesis of 1-(3,4-dimethoxyphenyl)-3-(2-hydroxy-3,4-dimethoxyphenyl) propane-1,3-dione (3b)

The titled compound was synthesised according to the general procedure-**B** using 6-acetyl-2,3-dimethoxyphenyl 3',4'-dimethoxybenzoate (**3a**) (1.0 g, 2.7 mmol). The crude product was washed with acetic acid to obtain compound-**3b** as a yellow solid (0.80 g, 80%). The product formation was confirmed by ^{1}H NMR spectroscopic analysis.

^{1}H NMR: ($CDCl_3$, 400 MHz) [The compound exists as a mixture of keto-enol tautomers] δ 3.82 (C**H$_2$**), 3.87-3.97 (12H, 4 x -OC**H$_3$**), 6.52 (1H, d, *J* = 9.0 Hz, H-5), 6.67 (1H, s, =C**H** of enol form), 6.93 (1H, d, *J* = 8.5 Hz, H-5'), 7,45 (1H, d, *J* = 8.5 Hz, H-6), 7.55 (1H, s, H-2') 7.57 (1H, d, *J* = 7.0 Hz, H-6'), 12.35 (1H, s, OH), 12.52 (1H, s, OH of enol form).

1.3.15 Synthesis of 2-(3, 4-dimethoxyphenyl)-7,8-dimethoxy-4*H*-chomen-4-one (3c)

The titled compound was synthesised according to the general procedure-**C** using 1-(3, 4-dimethoxyphenyl)-3-(2-hydroxy-3,4-dimethoxyphenyl) propane-1,3-dione (**3b**) (0.75 g, 2.08 mmol). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**3c** as a white solid (0.50 g, 70 %).

m.p: 202-04 ^{o}C (lit[6]-203-4 ^{o}C); **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 3.84-3.95 (12H, 4 x -OC**H$_3$**), 6.97 (1H, s, H-3), 7.16 (1H, d, *J* = 8.0 Hz, H-6), 7.26 (1H, d, *J* = 9.0 Hz, H-6'), 7.57 (1H, s, H-2'), 7.68 (1H, d, *J* = 8.0 Hz, H-5), 7.75 (1H, d, *J* = 9.0 Hz, H-5'); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 55.76 (-O**C**H$_3$), 56.67 (-O**C**H$_3$), 61.21 (-O**C**H$_3$), 105.17 (C3), 108.98 (C2'), 110.61 (C5'), 112.0 (C6), 118 (C10), 120.06 (C6'), 123.33 (C5), 123.89 (C1'), 136.22 (C8), 149.12 (C9), 149.98 (C3'), 152.12 (C4'), 156.57 (C7), 162.43 (C2), 176.55 (**C=**O); **IR ν_{max} [cm^{-1}]:** 1630 (C=O, ν, s), 1288, 1262 (-OCH$_3$, ν, s), 1095 (C-O, ν, m); ***m/z* (FTMS+ESI):** M+H ($C_{19}H_{19}O_6$) requires 343.1176, found 343.1179. **HPLC purity:** 97.4%, RT-11.9 min at 258 nm.

1.3.16 Synthesis of 2-(3, 4-dihydroxyphenyl)-7,8-dihydroxy-4*H*-chomen-4-one (3d)

The titled compound was synthesised according to the general procedure-**D** using 2-(3,4-dimethoxyphenyl)-7,8-dimethoxy-4*H*-chomen-4-one (**3c**) (0.05 g, 0.146 mmol) and BBr_3 (164 mg, 0.063 mL, 0.657 mmol, 4.5 eq., d=2.60 g/mL). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**3d** as a yellowish brown solid (0.025 g, 59 %).

m.p: 308-09 ^{o}C (lit[6]-309-310 ^{o}C); **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 6.56 (1H, s, H-3), 6.86 (1H, d, *J* = 8.0 Hz, H-6), 6.89 (1H, d, *J* = 9.0 Hz, 1.5 Hz, H-6'), 7.32 (1H, d, *J* = 6.0 Hz, H5), 7.46 (1H, d, *J* = 7.0 Hz, H5'), 7.48 (1H, s, H2'); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 104.4 (C3), 113.93 (C2'), 116.47 (C5'), 117.37 (C6), 119.24 (C10), 122.91 (5), 123.32 (C6'), 123.80 (C1'), 133.92 (C8), 146.24 (C3'), 147.02 (C9), 153.95 (C7), 162.97 (C2), 177.33 (**C=**O); **IR ν_{max} [cm^{-1}]:** 1558 (C=O, ν, s), 1186 (C-O, ν, w), 3080 (OH, m, b); ***m/z* (FTMS+ESI):** M+H ($C_{15}H_{11}O_4$) requires 287.0550, found 287.0554. **HPLC purity:** 99.1%, RT-7.5 min at 258 nm.

1.3.17 Synthesis of 2-(3, 4-dimethoxyphenyl)-7, 8-dimethoxy-4*H*-chromene-4-thione (3e)*

The titled compound was synthesised according to the general procedure-**E** using 2-(3,4-dimethoxyphenyl)-7,8-dimethoxy-4*H*-chomen-4-one (**3c**) (0.2 g, 0.584 mmol). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**3e** as an orange solid (0.16 g, 76%).

m.p: 201-02 ^{o}C; **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 3.86 (3H, s, -OC**H$_3$**) 3.89 (3H, s, -OC**H$_3$**), 3.96 (3H, s, -OC**H$_3$**), 3.97 (3H, s, -OC**H$_3$**), 7.2 (1H, d, *J* = 8.0 Hz, H-6), 7.35 (1H, d, *J* = 9.0 Hz, H-5), 7.64 (1H, s, H-2'), 7.77 (1H, d, *J* = 8.0 Hz, H-5'), 7.84 (1H, s, H-3), 8.17 (1H, dd, *J* = 9.0 Hz, 1.5 Hz, H-6'); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 55.76 (2 x -O**C**H$_3$), 56.67 (-O**C**H$_3$), 61.21 (-O**C**H$_3$), 109.52 (C6), 111.70 (C2'), 117.34 (C5'), 120.60 (C3), 122.60 (C1'), 123.33 (C6'), 124.24 (C5, C10), 136.22 (C8), 149.12 (C9, C3'), 152.39 (C4'), 153.84 (C7), 157.11 (C2), 199.62 (**C**=S); **IR**

ν_{max} [cm^{-1}]: 1282 (C=S, ν, s), 1259 (-OCH_3, ν, m) 1147 (C-O, ν, m). ***m/z*** **(FTMS+ESI):** M+H ($C_{19}H_{19}O_5S$) requires 359.0948, found 359.0948. **HPLC purity:** 97.3%, RT-13.7 min at 258 nm.

1.3.18 Synthesis of 2-(3,4-dihydroxyphenyl)-7,8-dihydroxy-4*H*-chromene-4-thione (3f)*

The titled compound was synthesised according to the general procedure-**F** using 2-(3,4-dimethoxyphenyl)-7,8-dimethoxy-4*H*-chromene-4-thione (**3e**) (0.15 g, 0.418 mmol). Purification was achieved by column chromatography with EtOAc (100%) to yield the compound-**3f** as a brown solid (0.07 g, 55%).

m.p: 260-61 ^{o}C; **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 6.92 (1H, d, *J* = 9.0 Hz, H-6), 7.01 (1H, d, *J* = 9.0 Hz, H-5), 7.52 (1H, s, H-3), 7.56 (2H, d, *J* = 7.5 Hz, H-5'), 7.58 (1H, s, H-2'), 7.83 (1H, dd, *J* = 9.0 Hz, 1.5 Hz, H-6'), 9.52 (1H, s, OH), 9.97 (1H, s, OH), 10.62 (1H, s, OH), 12.62 (1H, s, OH); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 113.67 (C6), 116.15 (C2'), 116.20 (C5'), 118.47 (C3), 119.51 (C6'), 121.3 (C1'), 123.43 (C5, C10), 132.97 (C8), 142.33 (C3'), 145.81 (C9), 151.15 (C7), 154.18 (C2), 198.42 (**C=**S); **IR ν_{max} [cm^{-1}]:** 1285 (C=S, ν, m), 1187 (C-O, ν, m), 3064 (OH, w, b); ***m/z*** **(FTMS+ESI):** M+H ($C_{15}H_{11}O_5S$) requires 303.0322, found 303.0323. **HPLC purity:** 99.7%, RT-9.9 min at 258 nm.

1.3.19 Synthesis of 2-acetyl-3,5-dimethoxyphenyl 3,4-dimethoxybenzoate (4a)

The titled compound was synthesised according to the general procedure-**A** outlined using phloroacetophenone dimethylether [1-(2-hydroxy-4, 6-dimethoxyphenyl) ethanone] (1 g, 5.09 mmol) and 3,4-dimethoxybenzoyl chloride (1.53 g, 7.63 mmol). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**4a** as a white solid (1.1 g, 60%).

m.p: 151-53 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 2.47 (3H, s, -C**H_3**) 3.82 (3H, s, -OC**H_3**), 3.84 (3H, s, -OC**H_3**), 3.86 (3H, s, -OC**H_3**), 3.96 (3H, s, -OC**H_3**), 6.37 (1H, s, H-4), 6.40 (1H, s, H-6), 6.91 (1H, dd, *J* = 8.0 Hz, 1.0 Hz, H-6'), 7.61 (1H, s, H-2'), 7.80 (1H, d, *J* = 7.0 Hz, H-5'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 29.42 (CH_3), 56.06 (-O**C**H_3), 60.31 (-O**C**H_3), 109.71 (C4), 111.12 (C5'), 112.12 (C2'), 120.63 (C6), 124.33 (C5, C6'), 126.18 (C1'), 140.98 (C2), 143.57 (C3'), 153.56 (C3), 156.71 (C4'), 163.74 (**C**OO-Ar), 195.56 (**C**OCH_3); **IR ν_{max} [cm^{-1}]:** 1713 (C=O, ν, m), 1102 (O-C=O, ν, m), 1689 (C=O, ν, m), 1246 (-OCH_3, ν, s); ***m/z*** **(FTMS+ESI):** M+Na ($C_{19}H_{20}O_7Na$) requires 383.1101, found 383.1102.

1.3.20 Synthesis of 1-(3,4-dimethoxyphenyl)-3-(2-hydroxy-4,6-dimethoxyphenyl) propane-1, 3-dione (4b)

The titled compound was synthesised according to the general procedure-**B** using 2-acetyl-3,5-dimethoxyphenyl 3,4-dimethoxybenzoate (**4a**) (1.0 g, 2.7 mmol). The crude product was washed with acetic acid to obtain compound-**4b** as a yellow solid (0.80 g, 80%). The product formation was confirmed by ^{1}H NMR spectroscopic analysis.

^{1}H NMR: ($CDCl_3$, 400 MHz) [The compound exists as a mixture of keto-enol tautomers] δ 3.78 (2H, s, -C**H$_2$**), 3.89-3.98 (12H, 4 x -OC**H$_3$**), 5.98 (1 H, s, H-5), 5.99 (1 H, s, H-3), 6.02 (1H, s, =C**H** of enol form), 6.93 (1H, dd, *J* = 8.5 Hz, 1.0 Hz, H-6'), 7.27 (1H, d, *J* = 7.0 Hz, H-5'), 7.44 (1H, s, H-2'), 13.44 (1H, s, OH), 13.72 (1H, s, OH of enol form).

1.3.21 Synthesis of 2-(3,4-dimethoxyphenyl)-5,7-dimethoxy-4*H*-chomen-4-one (4c)

The titled compound was synthesised according to the general procedure-**C** using 1-(3,4-dimethoxyphenyl)-3-(2-hydroxy-4,6-dimethoxyphenyl) propane-1,3-dione (**4b**) (0.75g, 2.08 mmol). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**4c** as a white solid (0.50 g, 70%).

m.p: 192-93 ^{o}C (lit[7]-190-94 ^{o}C); **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 3.82 (3H, s, -OC**H$_3$**) 3.83 (3H, s, -OC**H$_3$**), 3.87 (3H, s, -OC**H$_3$**), 3.89 (3H, s, -OC**H$_3$**), 6.49 (1H, s, H-3), 6.76 (1H, s, H-6), 6.86 (1H, s, H-8), 7.01 (1H, dd, *J* = 8.5 Hz, 1.0 Hz, H-6'), 7.52 (1H, s, H-2'), 7.63 (1H, d, *J* = 8.0 Hz, H-5'); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 55.94 (-O**C**H$_3$), 93.42 (C8), 96.38 (C6), 107.08 (C3'), 107.95 (C10), 108.75 (C6'), 111.51 (C3'), 119.27 (C2'), 122.96 (C1'), 149.18 (C4'), 151.58 (C5'), 159.02 (C9), 159.33 (C5), 160.44 (C2), 163.95 (C7), 175.77 (**C**=O); **IR ν_{max} [cm^{-1}]:** 1644 (C=O, v, m), 1252 (-OCH_3, v, m) 1138 (C-O, v, m); ***m/z* (FTMS+ESI):** M+H ($C_{19}H_{19}O_6$) requires 343.1176, found 343.1176. **HPLC purity:** 99.5%, RT-11.5 min at 258 nm.

1.3.22 Synthesis of 2-(3,4-dihydroxyphenyl)-5, 7-dihydroxy-4*H*-chomen-4-one (4d)

The titled compound was synthesised according to the general procedure-**D** using 2-(3,4-dimethoxyphenyl)-5,7-dimethoxy-4*H*-chomen-4-one (**4c**) (0.1 g, 0.292 mmol) and BBr_3 (164 mg, 0.063 mL, 0.657 mmol, 4.5 eq., d=2.60 g/mL). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**4d** as a pale yellow solid (0.50 g, 59%).

m.p: 328-29 ^{o}C (lit[8]-326-28 ^{o}C); **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 6.25 (1H, s, H-3), 6.50 (1H, s, H-6), 6.72 (1H, s, H-8), 6.95 (1H, dd, *J* = 8.0 Hz, 1.5 Hz, H-6'), 7.45 (1H, s, H-2'), 7.46 (1H, d, *J* = 8.0 Hz, H-5'), 9.48 (1H, s, OH), 9.98 (1H, s, OH), 10.90 (1H, s, OH), 13.02 (1H, s, OH) ; **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 93.72 (C8), 98.81 (C6), 102.62 (C3), 103.64 (C10), 113.29 (C2'), 115.96 (C5'), 118.95 (C6'), 121.44 (C1'), 145.68 (C3'), 149.65 (C4'), 157.24 (C9), 161.41 (C5), 163.84 (C2), (164.04, C7), 181.62 (**C**=O); **IR ν_{max} [cm^{-1}]:** 1600 (C=O, v, s), 1160 (C-O, v, m), 3236 (OH, w, b); ***m/z* (FTMS+ESI):** M+H ($C_{15}H_{11}O_6$) requires 287.0550, found 287.0551. **HPLC purity:** 99.4%, RT-10.0 min at 258 nm.

1.3.23 Synthesis of 2-(3,4-dimethoxyphenyl)-5,7-dimethoxy-4*H*-chromene-4-thione (4e)

The titled compound was synthesised according to the general procedure-**E** using 2-(3,4-dimethoxyphenyl)-5,7-dimethoxy-4*H*-chomen-4-one (**4c**) (0.25 g, 0.73 mmol). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**4e** as a green solid (0.16 g, 61%).

m.p: 204-05 ^{o}C (lit[9]-203 ^{o}C); **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 3.82 (3H, s, -OC**H$_3$**) 3.86 (3H, s, -OC**H$_3$**), 3.90 (3H, s, -OC**H$_3$**), 3.94 (3H, s, -OC**H$_3$**), 6.58 (1H, s, H-2'), 6.94 (1H, s, H-8), 7.13 (1H, d, *J* = 8.0 Hz, H-5'), 7.53 (1H, s, H-3), 7.55 (1H, s, H-6), 7.69 (1H, dd, *J* = 8.0 Hz, 1.0 Hz, H-6'); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 53.66 (-O**C**H$_3$), 53.72 (-O**C**H$_3$), 53.81 (-O**C**H$_3$), 54.08 (-O**C**H$_3$), 91.29 (C8), 94.84 (C6), 107.01 (C2'), 109.81 (C5'), 114.35 (C10), 117.86 (C3), 118.14 (C6'), 120.21 (C1'), 147.08 (C4'), 147.29 (C3'), 149.79 (C2), 152.95 (C9), 158.79 (C7), 161.49 (C5), 196.78 (**C**=S); **IR ν_{max} [cm^{-1}]:** 1316 (C=S, ν, m), 1254 (-OCH$_3$, ν, m) 1140 (C-O, ν, m); ***m/z* (FTMS+ESI):** M+H ($C_{19}H_{19}O_5S$) requires 359.0948, found 359.0948. **HPLC purity:** 98.3%, RT-11.5 min at 270 nm.

1.3.24 Synthesis of 2-(3, 4-dihydroxyphenyl)-5, 7-dihydroxy-4*H*-chromene-4-thione (4f)*

The titled compound was synthesised according to the general procedure-**F** using 2-(3,4-dimethoxyphenyl)-5,7-dimethoxy-4*H*-chromene-4-thione (**4e**) (0.15 g, 0.418 mmol). Purification was achieved by column chromatography with EtOAc (100%) to yield the compound-**4f** as a brown solid (0.07 g, 55%).

m.p: 270-72 ^{o}C; **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 6.29 (1H, s, H-2'), 6.51 (1H, s, H-8), 6.89 (1H, d, *J* = 8.0 Hz, H-5'), 7.31 (1H, s, H-3), 7.43 (1H, s, H-6), 7.49 (1H, d, *J* = 8.0 Hz, 1.5 Hz, H-6'), 9.80 (1H, s, OH), 10.12 (1H, s, OH), 11.20 (1H, s, OH), 13.67 (1H, s, OH); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 94.43 (C8), 100.55 (C6), 111.68 (C10), 113.56 (C2'), 115.74 (C5'), 116.25 (C3), 119.77 (C1'), 120.13 (C6'), 145.94 (C3'), 150.36 (C4'), 153.98 (C2), 155.18 (C9), 161.70 (C7), 164.06 (C5), 194.54 (**C**=S); **IR ν_{max} [cm^{-1}]:** 1444 (C=S, ν, m), 1146 (C-O, ν, m), 3293 (OH, w, b); ***m/z* (FTMS+ESI):** M+H ($C_{15}H_{11}O_5S$) requires 303.0322, found 303.0326. **HPLC purity:** 99.3%, RT-11.8 min at 258 nm.

1.3.25 Synthesis of 2-(3,4-dimethoxyphenyl)-3,5,7-trimethoxy-4*H*-chromen-4-one (5c)

Quercetin (**5d**) (1g, 3.30 mmol) was dissolved in KOH (15%, 10 mL) at ambient temperature. Dimethyl sulfate (2.29 g, 1.7 mL, 18.15 mmol, 5.5 eq., d=1.33 g/mL) was added slowly over 10 min and stirred at ambient temperature for 1 h. After 1 h, further dimethyl sulfate (5.5 eq.) and KOH (15%, 10 mL) was added and heated to 90 ^{o}C. After 3 h, further dimethyl sulfate (5.5 eq.) and KOH (15%, 10 mL) was added and stirred overnight at 90 ^{o}C. The reaction was cooled to room temperature and acidified to pH 5 with 2 M HCl (20 mL). The precipitated product was filtered and washed with water. The 2-(3,4-dimethoxyphenyl)-3,5,7-trimethoxy-4*H*-chromen-4-one (**5c**) was obtained in pure form as an off white solid (0.74 g, 60%) by column chromatography [Solvent system: EtOAc (100%)].

m.p: 155-57 ^{o}C (lit[10]-150-52 ^{o}C); **^{1}H NMR:** (DMSO-d6,400 MHz) δ 3.88, 3.90, 3.96 (15H, s, 5 x -OC**H$_3$**), 6.34 (1H, s, H-6), 6.50 (1H, s, H-8), 6.97 (1H, d, *J* = 8.0 Hz, H-5'), 7.69 (1H, dd, *J* = 8.0 Hz, 1.0 Hz, H- 6'), 7.71 (1H, s, H-2'); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 56.37 (4 x-O**C**H$_3$), 59.98 (-O**C**H$_3$), 92.36 (C8), 95.81 (C6), 109.45 (C10), 110.76 (C2'), 111.58 (C5'), 121.61 (C6'), 123.74 (C1'), 141.33 (C3), 148.89 (C4'), 150.86 (C3'), 152.67 (C2), 158.91 (C9), 161.38 (C5), 164.17 (C7), 174.03 (**C**=O); **IR ν_{max} [cm^{-1}]:** 1651(C=O, ν, s), 1291 (-OCH$_3$, ν, s), 1097 (C-O, ν, m); ***m/z***

(FTMS+ESI): M+H ($C_{20}H_{21}O_7$) requires 373.1282, found 373.1277. **HPLC purity:** 96.1%, RT-11.9 min at 258 nm.

1.3.26 Synthesis of 2-(3,4-dimethoxyphenyl)-3,5,7-trimethoxy-4*H*-chromene-4-thione (5e)

The titled compound was synthesised according to the general procedure-**E** using 2-(3,4-dimethoxyphenyl)-3,5,7-trimethoxy-4*H*-chromen-4-one (**5c**) (0.20 g, 0.53 mmol). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**5e** as a brown solid (0.13 g, 65%).

m.p: 168-70 ^{o}C (lit[9]-170 ^{o}C); **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 3.72 (3H, s, OC**H$_3$**), 3.95, 3.93, 3.07, 4.03 (12H, s, 4 x -OC**H$_3$**), 6.42 (1H, s, H-6), 6.54 (1H, s, H-8), 7.00 (1H, d, *J* = 8.5 Hz, H-5'), 7.78 (1H, dd, *J* = 8.5 Hz, 1.0 Hz, H-6'), 7.86 (1H, s, H-2'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 56.00 (-O**C**H$_3$), 58.70 (-O**C**H$_3$), 92.30 (C8), 96.75 (C6), 110.65 (C2'), 111.61 (C5'), 116.83 (C10), 122.04 (C6'), 123.20 (C1'), 146.37 (C3), 148.69 (C4'), 149.66 (C3'), 151.20 (C2), 154.48 (C9), 161.63 (C7), 163.56 (C5), 194.07 (**C**=S); **IR ν_{max} [cm^{-1}]:** 1351 (C=S, v, m), 1220 (-OCH_3, v, m) 1143 (C-O, v, m); ***m/z* (FTMS+ESI):** M+H ($C_{20}H_{21}O_6S$) requires 389.1053, found 389.1055. **HPLC purity:** 96.1%, RT-13.3 min at 258 nm.

1.3.27 Synthesis of 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy-4*H*-chromene-4-thione (5f)

The titled compound was synthesised according to the general procedure-**F** using 2-(3,4-dimethoxyphenyl)-3,5,7-trimethoxy-4*H*-chromene-4-thione (**5e**) (0.10 g, 0.257 mmol) and BBr_3 (0.35 g, 0.135 mL, 1.413 mmol, 5.5 eq., d=2.60 g/mL) at 40 ^{o}C overnight. Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**5f** as a bright red solid (0.45 g, 55%).

m.p: 270 ^{o}C (decomposed); **^{1}H NMR:** (DMSO-d6, 400 MHz) 6.34 (1H, s, H-6), 6.54 (1H, s, H-8), 6.92 (1H, d, *J* = 8.5 Hz, H-5'), 7.71 (1H, dd, *J* = 8.5 Hz, 1.5 Hz, H-6'), 7.76 (1H, s, H-2'), 8.66 (1H, s, OH), 9.44 (1H, s, OH), 9.91 (1H, s, OH), 11.07 (1H, s, OH), 13.06 (1H, s, OH); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 93.82 (C8), 100.43 (C6), 111.31 (C10), 115.79 (5'), 115.85 (C2'), 120.71 (C6'), 121.65 (C1'), 142.40 (C3'), 142.70 (C4'), 145.32 (C9), 149.10 (C7), 152.52 (C2), 160.17 (C5), 163.51 (C3), 181.69 (**C**=S); **IR ν_{max} [cm^{-1}]:** 1267 (C=S, v, m), 1147 (C-O, v, m), 3084 (OH, w, b); ***m/z* (FTMS+ESI):** M+H ($C_{15}H_{11}O_6S$) requires 319.0271, found 319.0266. **HPLC purity:** 99.4%, RT-12.3 at 258 nm.

1.3.28 Synthesis of 6-acetyl-2,3-dimethoxyphenyl thiophene-2-carboxylate (6a)

The titled compound was synthesised according to the general procedure-**A** using gallacetophenone dimethyl ether [1-(2-hydroxy-3,4-dimethoxyphenyl) ethanone] (1 g, 5.09 mmol) and 2-thiophenecarbonyl chloride (1.12 g, 0.82 mL, 7.64 mmol). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**6a** as a white solid (1.4 g, 90%).

m.p: 85-86 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 2.49 (3H, s, -C**H$_3$**), 3.83 (3H, s, -OC**H$_3$**), 3.91 (3H, s, -OC**H$_3$**), 6.88 (1H, d, *J* = 9.0 Hz, H-4), 7.18 (1H, t, *J* = 4.0 Hz, H-4'), 7.66 (1H, d, *J* = 9.0 Hz, H-5), 7.68 (1H, d, *J* = 5.0 Hz, H-3'), 8.01 (1H, d, *J* = 4.0 Hz, H-5'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 29.83 (**C**H_3), 56.17 (-O**C**H_3), 60.95 (-O**C**H_3), 109.38 (C5), 124.59 (C6), 125.98 (C5), 128.22 (C4'), 132.23 (C3'), 133.91 (C5'), 135.12 (C2'), 141.55 (C2), 143.86 (C1), 157.23 (C3), 159.91 (**C**OO-HetAr), 195.72 (**C**OCH_3); **IRν_{max} [cm^{-1}]:** 1720 (C=O, ν, m), 1086 (O-C=O, ν, m), 1669 (C=O, ν, m), 975 (=C-S, ν, m), 1251, 1266 (-OCH_3, ν, s); ***m/z* (FTMS+ESI):** M+H ($C_{15}H_{15}O_5S$) requires 307.0635, found 307.0632.

1.3.29 Synthesis of 1-(2-hydroxy-3,4-dimethoxyphenyl)-3-(thiophen-2-yl) propane-1,3-dione (6b)

The titled compound was synthesised according to the general procedure-**B** using 6-acetyl-2,3-dimethoxyphenyl thiophene-2-carboxylate (**6a**) (1.0 g, 3.26 mmol). The crude product was washed with acetic acid to obtain compound-**6b** as a yellow solid (0.85 g, 85%). The product formation was confirmed by ^{1}H NMR spectroscopic analysis.

^{1}H NMR: ($CDCl_3$, 400 MHz) [The compound exists as a mixture of keto-enol tautomers] δ 3.84 (C**H$_2$**), 3.91 (3H, s, -OC**H$_3$**), 3.93 (3H, s, -OC**H$_3$**), 6.51 (1H, d, *J* = 9.0 Hz, H-5), 6.61 (1H, s, =C**H** of enol form), 7.18 (1H, t, *J* = 4.0 Hz, H-4'), 7.51 (1H, d, *J* = 9.0 Hz, H-6) 7.57 (1H, d, *J* = 5.0 Hz, H-3'), 7.87 (1H, d, *J* = 4.0 Hz, H-5'), 12.15 (1H, s, OH), 12.56 (1H, s, OH of enol form).

1.3.30 Synthesis of 7, 8-dimethoxy-2-(thiophen-2-yl)-4*H*-chomen-4-one (6c)

The titled compound was synthesised according to the general procedure-**C** using 1-(2-hydroxy-3,4-dimethoxyphenyl)-3-(thiophen-2-yl)-1,3-dione (**6b**) (0.8 g, 2.61 mmol). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**6c** as a white solid (0.65 g, 86%).

m.p: 143-44 ^{o}C (lit[11]-140-41 ^{o}C); **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 4.00 (3H, s, -OC**H$_3$**), 4.05 (3H, s, -OC**H$_3$**), 6.64 (1H, s, H-3), 7.03 (1H, d, *J* = 9.0 Hz, H-6), 7.19 (1H, t, *J* = 4.5 Hz, H-4'), 7.56 (1H, d, *J* = 5.0 Hz, H-3'), 7.76 (1H, d, *J* = 4.0 Hz, H-5'), 7.93 (1H, d, *J* = 9.0 Hz, H-5); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 56.47 (-O**C**H_3), 61.68 (-O**C**H_3), 105.60 (C3), 109.83 (C6), 118.72 (C10), 120.99 (C5), 128.33 (C4'), 128.51 (C3'), 130.11 (C5'), 135.34 (C2'), 136.78 (C9), 150.33 (C7), 156.84 (C8), 158.95 (C2), 177.60 (**C=**O); **IR ν_{max} [cm^{-1}]:** 1649 (C=O, ν, s), 1285 (-OCH_3, ν, s) 1090 (C-O, ν, m), 998 (=C-S, ν, m); ***m/z* (FTMS+ESI):** M+H ($C_{15}H_{13}O_4S$) requires 289.0529, found 289.0523. **HPLC purity:** 98.3%, RT-12.4 min at 258 nm.

1.3.31 Synthesis of 7, 8-dihydroxy-2-(thiophen-2-yl)-4*H*-chomen-4-one (6d)*

The titled compound was synthesised according to the general procedure-**D** using 7,8-dimethoxy-2-(thiophen-2-yl)-4*H*-chomen-4-one (**6c**) (0.050 g, 0.173 mmol). Purification was achieved by column chromatography with EtOAc (100%) to yield the compound-**6d** as a yellow solid (0.035 g, 77%).

m.p: 277-78 ^{o}C; **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 6.67 (1H, s, H-3), 6.93 (1H, d, *J* = 9.0 Hz, H-6), 7.27 (1H, t, *J* = 4.0 Hz, H-4'), 7.37 (1H, d, *J* = 9.0 Hz, H-5), 7.90 (1H, d, *J* = 4.0 Hz, H-3'), 8.03 (1H, d, *J* = 6.0 Hz, H-5'), 9.51 (1H, s, OH), 10.48 (1H, s, OH); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 104.37 (C3), 113.90 (C10), 115.10 (C6), 116.82 (C5), 128.81 (C3'), 129.38 (C4'), 131.50 (C5'), 133.05 (C8), 134.40 (C2'), 146.37 (C9), 150.62 (C7), 158.15 (C2), 176.88 (**C=**O); **IR ν_{max} [cm^{-1}]:** 1578 (C=O, v, s), 1165 (C-O, v, m), 1007 (=C-S, v, m), 3068 (OH, w, b), ***m/z* (FTMS+ESI):** M+H ($C_{13}H_9O_4S$) requires 261.0216, found 261.0209. **HPLC purity:** 99.9%, RT-9.5 min at 258 nm.

1.3.32 Synthesis of 7,8-dimethoxy-2-(thiophen-2-yl)-4*H*-chromene-4-thione (6e)*

The titled compound was synthesised according to the general procedure-**E** using 7,8-dimethoxy-2-(thiophen-2-yl)-4*H*-chomen-4-one (**6c**) (0.20 g, 0.69 mmol). Purification was achieved by column chromatography with $CHCl_3$ (100%) to yield the compound-**6e** as an orange solid (0.16 g, 76%).

m.p: 212-13 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 4.01 (3H, s, -OC**H$_3$**), 4.05 (3H, s, -OC**H$_3$**), 7.06 (1H, d, *J* = 9.0 Hz, H-6), 7.21 (1H, t, *J* = 4.0 Hz, H-4'), 7.56 (1H, s, H-3), 7.63 (1H, d, *J* = 4.0 Hz, H-3'), 7.81 (1H, d, *J* = 4.0 Hz, H-5'), 8.33 (1H, d, *J* = 9.0 Hz, H-5); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 56.59 (-O**C**H$_3$), 61.89 (-O**C**H$_3$), 110.89 (C3), 118.04 (C6), 124.15 (C5), 125.24 (C10), 128.99 (C3'), 129.15 (C4'), 130.93 (C5'), 134.79 (C2'), 136.72 (C8),145.79 (C9), 150.04 (C7), 157.19 (C2), 200.64 (**C**=S); **IR ν_{max} [cm^{-1}]:** 1280 (C=S, v, s), 1022 (-OCH$_3$, v, m) 1094 (C-O, v, m),1050 (=C-S, v, m);***m/z* (FTMS+ESI):** M+H ($C_{15}H_{13}O_3S_2$) requires 305.0301, found 305.0296. **HPLC purity:** 98.6%, RT-14.1 min at 258 nm.

1.3.33 Synthesis of 7,8-dihydroxy-2-(thiophen-2-yl)-4*H*-chromene-4-thione (6f)*

The titled compound was synthesised according to the general procedure-**F** using 7,8-dimethoxy-2-(thiophen-2-yl)-4*H*-chromene-4-thione (**6e**) (0.15 g, 0.49 mmol). Purification was achieved by column chromatography with EtOAc (100%) to yield the compound-**6f** as an orange red solid (0.07 g, 50%).

m.p: 260-62 ^{o}C; **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 6.96 (1H, d, *J* = 9.0 Hz, H-6), 7.26 (1H, t, *J* = 4.5 Hz, H-4'), 7.53 (1H, s, H-3), 7.76 (1H, d, *J* = 9.0 Hz, H-5), 7.96 (1H, d, *J* = 5.0 Hz, H-3'), 8.14 (1H, d, *J* = 4.0 Hz, H-5'), 9.50 (1H, s, OH), 10.61 (1H, s, OH); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 115.22 (C6), 116.34 (C3), 118.39 (C5), 123.51(C10), 129.32 (C4'), 130.56 (C3'), 132.67 (C2'), 132.96 (C5'), 134.02 (C9), 141.90 (C8), 149.83 (C7), 151.65 (C2), 198.95 (**C=**S); **IR ν_{max} [cm^{-1}]:** 1270 (C=S, v, s), 1112 (C-O, v, m), 1058 (=C-S, v, m), 3070 (OH, w, s); ***m/z* (FTMS+ESI):** M+H ($C_{13}H_9O_3S_2$) requires 276.9988, found 276.9988. **HPLC purity:** 97.9%, RT-12.2 min at 258 nm.

1.3.34 Synthesis of 2-acetyl-3, 5-dimethoxyphenyl thiophene-2-carboxylate (7a)

The titled compound was synthesised according to the general procedure-**A** using phloroacetophenone dimethylether [1-(2-hydroxy-4,6-dimethoxyphenyl)ethanone] (1 g, 5.09 mmol) and 2-thiophenecarbonyl chloride (1.12 g, 0.82 mL, 7.64 mmol). Purification was

achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**7a** as a white solid (1.3 g, 85%).

m.p: 114-16 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 2.38 (3H, s, -C**H$_3$**), 3.69 (3H, s, -OC**H$_3$**), 3.74 (3H, s, -OC**H$_3$**), 6.27 (1H, s, H-4), 6.41 (1H, s, H-6), 7.03 (1H, t, *J* = 4.5 Hz, H-4'), 7.54 (1H, d, *J* = 5.0 Hz, H- 3'), 7.82 (1H, d, *J* = 4.0 Hz, H- 5'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 31.96 (-**C**H$_3$), 55.66 (-O**C**H$_3$), 55.95 (-O**C**H$_3$), 96.68 (C6), 100.22 (C4), 117.16 (C2), 128.09(C4'), 132.32 (C2'), 133.83 (C3'), 134.97 (C5'), 149.32 (C1), 159.17 (**C**OO- HetAr), 160.28 (C5), 162.23 (C3), 199.16 (**C**OCH$_3$); **IR ν_{max} [cm^{-1}]:** 1720 (C=O, ν, m), 1153 (O-C=O, ν, m), 1677 (C=O, ν, m), 1222 (-OCH$_3$, ν, s), 1098 (=C-S, ν, m);***m/z*** **(FTMS+ESI):** M+H ($C_{15}H_{15}O_5S$) requires 307.0635, found 307.0630.

1.3.35 Synthesis of 1-(2-hydroxy-4,6-dimethoxyphenyl)-3-(thiophen-2-yl)propane-1,3-dione (7b)

The titled compound was synthesised according to the general procedure-**B** using 2-acetyl-3,5-dimethoxyphenyl thiophene-2-carboxylate (**7a**) (1.0 g, 3.26 mmol). The crude product was washed with acetic acid to obtain compound-**7b** as a yellow solid (0.80 g, 80%). The product formation was confirmed by ^{1}H NMR spectroscopic analysis.

^{1}H NMR: ($CDCl_3$, 400 MHz) [The compound exists as a mixture of keto-enol tautomers] δ 3.52 (3H, s, -OCH$_3$), 3.82 (3H, s, -OCH$_3$), 4.48 (C**H$_2$**), 5.83 (1H, s. H-5), 5.97 (1H, s, =C**H** of enol form) 6.08 (1H, s, H-3), 7.16 (1H, t, *J* = 4.0 Hz, H-4'), 7.67 (1H, d, *J* = 5.0 Hz, H-3'), 7.73 (1H, d, *J* = 4.0 Hz, H-5'), 13.35 (1H, s, OH), 13.66 (1H, s, OH of enol form).

1.3.36 Synthesis of 5,7-dimethoxy-2-(thiophen-2-yl)-4*H*-chromen-4-one (7c)*

The titled compound was synthesised according to the general procedure-**C** using 1-(2-hydroxy-4,6-dimethoxyphenyl)-3-(thiophen-2-yl)propane-1,3-dione (**7b**) (0.75, 2.45 mmol). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**7b** as a white solid (0.49 g, 70%).

m.p: 165-70 ^{o}C; **^{1}H NMR:** ($CDCl_3$,400 MHz) δ 3.91 (3H, s, -OC**H$_3$**), 3.95 (3H, s,-OC**H$_3$**), 6.37 (1H, s, H-6), 6.52 (1H, s, H-8), 6.55 (1H, s, H-3), 7.15 (1H, t, *J* = 6.0 Hz, H-4'), 7.52 (1H, d, *J* = 5.0 Hz, H-3'), 7.64 (1H, d, *J* = 4.5 Hz, H-5'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 55.80 (-O**C**H$_3$), 56.46 (-O**C**H$_3$), 92.82 (C8), 96.25 (C6), 107.77 (C3), 109.26 (C10), 127.69 (C3'), 128.33 (C4'), 129.47 (C5'), 134.96 (C2'), 156.54 (C9), 159.63 (C5), 160.91 (C7), 164.00 (C2), 177.24 (**C=**O); **IR ν_{max} [cm^{-1}]:** 1641(C=O, ν, s), 1323 (-OCH$_3$, ν, s), 1161 (C-O, ν, m), 1112 (=C-S, ν, m); ***m/z*** **(FTMS+ESI):**M+H ($C_{15}H_{13}O_5S$) requires 289.0529, found 289.0522. **HPLC purity:** 99.6%, RT-12.0 min at 258 nm.

1.3.37 Synthesis of 5,7-dihydroxy-2-(thiophen-2-yl)-4*H*-chromen-4-one (7d)*

The titled compound was synthesised according to the general procedure-**D** using 5,7-dimethoxy-2-(thiophen-2-yl)-4*H*-chomen-4-one (**7c**) (0.05 g, 0.173 mmol) at 40 ^{o}C.

Purification was achieved by column chromatography with EtOAc (100%) to yield the compound-**7d** as a pale yellow solid (0.027 g, 60%).

m.p: 300-02 ^{o}C; **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 6.20 (1H, s, H-6), 6.42 (1H, s, H-8), 6.84 (1H, s, H-3), 7.29 (1H, t, *J* = 4.5 Hz, H- 4'), 7.98 (1H, d, *J* = 5.0 Hz, H-3'), 8.04 (1H, d, *J* = 3.0 Hz, H-5'), 10.91 (1H, s, OH), 12.83 (1H, s, OH); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 93.92 (C8), 98.98 (C6), 103.36 (C3), 103.94 (C10), 129.11 (C3'), 129.97 (C4'), 132.21 (C5'), 133.69 (C2'), 156.91 (C9), 159.10 (C5), 161.48 (C7), 164.34 (C2), 181.36 (**C=**O); **IR ν_{max} [cm^{-1}]:** 1649 (C=O, v, s), 1166 (C-O, v, m), 1078 (=C-S, v, m), 3315 (OH, w, b); ***m/z* (FTMS+ESI):** M+H ($C_{13}H_9O_4S$) requires 261.0216, found 261.0210. **HPLC purity:** 95.9%, RT-12.3 min at 258 nm.

1.3.38 Synthesis of 5,7- dimethoxy-2-(thiophen-2-yl)-4*H*-chromene-4-thione (7e)*

The titled compound was synthesised according to the general procedure-**E** using 5,7-dimethoxy-2-(thiophen-2-yl)-4*H*-chomen-4-one (**7c**) (0.20 g, 0.69 mmol). Purification was achieved by column chromatography with $CHCl_3$ (100%) to yield the compound-**7e** as a green solid (0.13 g, 60%).

m.p: 180-81 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 3.91 (6H, s, 2 x -OC**H$_3$**), 6.41 (1H, s, H-6), 6.53 (1H, s, H-8), 7.16 (1H, t, *J* = 4.5 Hz, H-4'), 7.42 (1H, s, H-3), 7.56 (1H, d, *J* = 5.0 Hz, H-3'), 7.67 (1H, d, *J* = 3.0 Hz, H-5'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ56.07 (-O**C**H$_3$), 92.88 (C8), 96.92 (C6), 117.54 (C10), 121.25 (C3), 128.21 (C4'), 128.74 (C3'), 130.43 (C5'), 134.63 (C2'), 146.12 (C9), 155.51 (C7), 161.67 (C5), 163.85 (C2), 199.85 (**C**=S); **IR ν_{max} [cm^{-1}]:** 1289 (C=S, v, m), 1289 (-OCH_3, v, m) 1108 (C-O, v, m); ***m/z* (FTMS+ESI):** M+H ($C_{15}H_{13}O_3S_2$) requires 305.0301, found 305.0296. **HPLC purity:** 96.8%, RT-13.7 min at 258 nm.

1.3.39 Synthesis of 5,7-dihydroxy-2-(thiophen-2-yl)-4*H*-chromene-4-thione (7f)*

The titled compound was synthesised according to the general procedure-**F** using 5,7-dimethoxy-2-(thiophen-2-yl)-4*H*-chromene-4-thione (**7e**) (0.15 g, 0.49 mmol). Purification was achieved by column chromatography with EtOAc (100%) to yield the compound-**7f** as a brown solid (0.05 g, 55%).

m.p: 281-82 ^{o}C; **^{1}H NMR:** (DMSO-d6, 400 MHz) 6.30 (1H, s, H-6), 6.47 (1H, s, H-8), 7.31 (1H, t, , *J* = 4.5 Hz, H- 4'), 7.43 (1H, s, H-3), 8.03 (1H, d, *J* = 5.0 Hz, H-3'), 8.14 (1H, d, *J* = 4.0 Hz, H-5'), 13.59 (s, OH); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 94.57 (C8), 100.79 (C6), 112.00 (C10), 115.84 (C3), 129.44 (C3'), 131.07 (C4'), 132.89 (C5'), 133.37 (C2'), 150.71 (C9), 153.58 (C7), 161.82 (C5), 164.60 (C2), 194.88 (**C**=S); **IR ν_{max} [cm^{-1}]:** 1293 (C=S, v, m), 1144 (C-O, v, m), 3083 (OH, w, b). ***m/z* (FTMS+ESI):** M+H ($C_{13}H_9O_3S_2$) requires 276.9988, found 276.9988. **HPLC purity:** 95.9%, RT-13.6 min at 258 nm.

1.3.40 Synthesis of 6-acetyl-2,3-dimethoxyphenyl furan-2-carboxylate (8a)

The titled compound was synthesised according to the general procedure-**A** using gallacetophenone dimethyl ether [1-(2-hydroxy-3, 4-dimethoxyphenyl) ethanone] (1 g, 5.09

mmol) and 2-furoyl chloride (0.99 g, 0.75 mL, 7.64 mmol). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**8a** as a white solid (1.35 g, 90%).

m.p: 101-02 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 2.50 (3H, s, -C**H$_3$**), 3.84 (3H, s, -OC**H$_3$**), 3.93 (3H, s, -OC**H$_3$**), 6.62 (1H, dd, *J* = 2.0 Hz, 2.0 Hz, H-4'), 6.89 (1H, d, *J* = 9.0 Hz, H-4), 7.44 (1H, d, *J* = 3.5 Hz, H-3**'**), 7.67 (1H, d, *J* = 9.0 Hz, H-5), 7.7 (1H, d, *J* = 2.0 Hz, H-5'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 29.73 (**C**H$_3$), 56.18 (-O**C**H$_3$), 60.97 (-O**C**H$_3$), 109.32 (C4), 112.51 (C4'), 119.94 (C3'), 124.59 (C6), 125.98 (C5), 141.60 (C2), 143.39 (C1), 143.79 (C2'), 147.42 (C5'), 156.24 (C3), 157.21 (**C**OO- HetAr), 195.69 (**C**OCH$_3$); **IR ν_{max} [cm^{-1}]:** 1731 (C=O, ν, m), 1094 (O-C=O, ν, m), 1673 (C=O, ν, m), 1269 (-OCH$_3$, ν, s); ***m/z* (FTMS+ESI):** M+Na ($C_{15}H_{14}O_6Na$) requires 313.0682, found 313.0683.

1.3.41 Synthesis of 1-(furan-2-yl)-3-(2-hydroxy-3,4-dimethoxyphenyl)propane-1,3-dione (8b)

The titled compound was synthesised according to the general procedure-**B** using 6-acetyl-2,3-dimethoxyphenyl furan-2-carboxylate (**8a**) (1.0 g, 3.44 mmol). The crude product was washed with acetic acid to obtain compound-**8b** as a yellow solid (0.80 g, 80%). The product formation was confirmed by ^{1}H NMR spectroscopic analysis.

^{1}H NMR: ($CDCl_3$, 400 MHz) [The compound exists as a mixture of keto-enol tautomers] δ 3.87 (C**H$_2$**), 3.93 (3H, s, -OC**H$_3$**), 3.94 (3H, s, -OC**H$_3$**), 4.43 (1H, s, =C**H** of enol form), 6.47 (1H, dd, *J* = 5.0 Hz, 5.0 Hz, H-4'), 6.57 (1H, d, *J* = 9.0 Hz, H-5), 6.86 (1H, d, *J* = 9.0 Hz, H-6), 7.14 (1H, d, *J* = 3.5 Hz, H-3**'**), 7.44 (1H, d, *J* = 3.0 Hz, H-5'), 12.14 (1H, s, OH), 12.33 (1H, s, OH of enol form).

1.3.42 Synthesis of 2-(furan-2-yl)-7,8-dimethoxy-4*H*-chromen-4-one (8c)*

The titled compound was synthesised according to the general procedure-**C** using 1-(furan-2-yl)-3-(2-hydroxy-3,4-dimethoxyphenyl)propane-1,3-dione (**8b**) (0.75 g, 2.26 mmol). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**8c** as a white solid (0.52 g, 84%).

m.p: 178-79 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 4.00 (3H, s, -OC**H$_3$**), 4.03 (3H, s, -OC**H$_3$**), 6.61 (1H, dd, *J* = 2.0 Hz, 2.0 Hz, H-4'), 6.67 (1H, s, H-3), 7.03 (1H, d, *J* = 9.0 Hz, H-6), 7.18 (1H, d, *J* = 3.0 Hz, H-3'), 7.6 (1H, *J* = 1.0 Hz, H-5'), 7.94 (1H, d, *J* = 9.0 Hz, H-5); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 56.44 (-O**C**H$_3$), 61.51 (-O**C**H$_3$), 104.96 (C3), 109.78 (C6), 112.51 (C4'), 113.13 (C3'), 119.07 (C10), 121.05 (C5), 136.77 (C8), 145.80 (C5'), 146.54 (C2'), 150.13 (C9), 154.84 (C7), 156.57 (C2), 177.49 (**C=**O); **IR ν_{max} [cm^{-1}]:** 1600 (C=O, ν, s), 1285 (-OCH3, ν, s) 1104 (C-O, ν, m); ***m/z* (FTMS+ESI):** M+H ($C_{15}H_{13}O_5$) requires 273.0757, found 273.0757. **HPLC purity:** 98.5%, RT-11.9 min at 258 nm.

1.3.43 Synthesis of 2-(furan-2-yl)-7,8-dihydroxy-4*H*-chromen-4-one (8d)*

The titled compound was synthesised according to the general procedure-**D** using 2-(furan-2-yl)-7,8-dimethoxy-4*H*-chromen-4-one (**8c**) (0.050 g, 0.183 mmol). Purification was achieved by column chromatography with EtOAc (100%) to yield the compound-**8d** as a yellow solid (0.033 g, 75%).

m.p: 247-48 ^{o}C; **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 6.47 (1H, s, H-3), 6.79 (1H, dd, *J* = 2.0 Hz, 2.0 Hz, H-4'), 6.92 (1H, d, *J* = 9.0 Hz, H-6), 7.36 (1H, d, *J* = 9.0 Hz, H-5), 7.54 (1H, d, *J* = 3.0 Hz, H-3'), 8.01 (1H, d, *J* = 1.0 Hz, H-5'); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 103.67 (C3), 112.76 (C3'), 113.87 (C4'), 115.08 (C6), 117.02 (C10), 133.07 (C8), 145.02 (C9), 145.80 (C2'), 146.76 (C5'), 150.51 (C7), 153.96 (C2), 176.20 (**C=**O); **IR ν_{max} [cm^{-1}]:** 1569 (C=O, ν, s), 1166 (C-O, ν, m), 3119 (OH, w, b), ***m/z* (FTMS+ESI):** M+H ($C_{13}H_9O_5$) requires 245.0444, found 245.0445. **HPLC purity:** 99.6%, RT-8.8 min at 258 nm.

1.3.44 Synthesis of 2-(furan-2-yl)-7,8-dimethoxy-4*H*-chromene-4-thione (8e)*

The titled compound was synthesised according to the general procedure-**E** using 2-(furan-2-yl)-7,8-dimethoxy-4*H*-chromen-4-one (**8c**) (0.20 g, 0.81 mmol). Purification was achieved by column chromatography with $CHCl_3$ (100%) to yield the compound-**8e** as an orange solid (0.16 g, 76%).

m.p: 210-12 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 4.01 (3H, s, -OC**H$_3$**), 4.04 (3H, s, -OC**H$_3$**), 6.64 (1H, dd, *J* = 2.0 Hz, 2.0 Hz, H-4'), 7.05 (1H, d, *J* = 9.0 Hz, H-6), 7.27 (1H, d, *J* = 3.0 Hz, H-3'), 7.58 (1H, s, H-3), 7.68 (1H, d, *J* = 1.0 Hz, H-5'), 8.33 (1H, d, *J* = 9.0 Hz, H-5); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 56.56 (-O**C**H$_3$), 61.86 (-O**C**H$_3$), 110.71 (C6), 112.88 (C3'), 114.36 (C4'), 117.42 (C5), 124.18 (C3), 125.47 (C10), 136.76 (C7, C8), 145.57 (C2'), 145.78 (C9), 146.30 (C10), 146.59 (C5'), 157.15 (C2), 200.49 (**C**=S); **IR ν_{max} [cm^{-1}]:** 1287 (C=S, ν, s), 1223 (-OCH$_3$, ν, m) 1093 (C-O, ν, m). ***m/z* (FTMS+ESI):** M+H ($C_{15}H_{13}O_4S$) requires 289.0529, found 289.0530. **HPLC purity:** 98.1%, RT-13.9 min at 258 nm.

1.3.45 Synthesis of 2-(furan-2-yl)-7,8-dihydroxy-4*H*-chromene-4-thione (8f)*

The titled compound was synthesised according to the general procedure-**F** using 2-(furan-2-yl)-7,8-dimethoxy-4*H*-chromene-4-thione (**8e**) (0.15 g, 0.52 mmol). Purification was achieved by column chromatography with EtOAc (100%) to yield the compound-**8f** as an orange red solid (0.06 g, 47%).

m.p: 235-37 ^{o}C; **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 6.83 (1H, dd, *J* = 2.0 Hz, 2.0 Hz, H-4'), 7.01 (1H, d, *J* = 9.0 Hz, H-6), 7.36 (1H, s, H-3), 7.69 (1H, d, *J* = 3.0 Hz, H-3'), 7.80 (1H, d, *J* = 9.0 Hz, H-5), 8.09 (1H, d, *J* = 1.0 Hz, H-5'); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 113.52 (C3'), 115.40 (C5, C10, C6), 118.40 (C3), 123.65 (C8), 133.22 (C4'), 141.48 (C5'), 145.42 (C7, C8), 145.52 (C9), 147.86 (C2'), 151.80 (C2), 198.89 (**C=**S); **IR ν_{max} [cm^{-1}]:** 1293 (C=S, ν, s), 1117 (C-O, ν, m), 3083 (OH, w, s); ***m/z* (FTMS+ESI):** M+H ($C_{13}H_9O_4S$) requires 261.0216, found 261.0216. **HPLC purity:** 95.5%, RT-11.9 min at 258 nm.

1.3.46 Synthesis of 2-acetyl-3,5-dimethoxyphenyl furan-2-carboxylate (9a)

The titled compound was synthesised according to the general procedure-**A** using phloroacetophenone dimethylether [1-(2-hydroxy-4, 6-dimethoxyphenyl) ethanone] (1.0 g, 5.09 mmol) and 2-furoyl chloride (0.99 g, 0.75 mL, 7.64 mmol). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**9a** as a white solid (1.3 g, 90%).

m.p: 143-44 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 2.49 (3H, s, -C**H$_3$**), 3.82 (3H, s, -OC**H$_3$**), 3.86 (3H, s, -OC**H$_3$**), 6.35 (1H, d, *J* = 2.0 Hz, H-4), 6.40 (1H, d, *J* = 2.0 Hz, H-6), 6.57 (1H, dd, *J* = 2.0 Hz, 2.0 Hz, H-4'), 7.35 (1H, d, *J* = 3.5 Hz, H- 3'), 7.65 (1H, d, *J* = 1.0 Hz, H-5'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 31.95 (-**C**H$_3$), 55.66 (-O**C**H$_3$), 55.94 (-O**C**H$_3$), 96.81 (C6), 100.07 (C4), 112.24 (C4'), 117.20 (C1), 119.87 (C3'), 143.68 (C2'), 147.30 (C5'), 148.99 (C1), 156.58 (C5), 159.22 (C3), 162.25 (**C**OO- HetAr), 199.14 (**C**OCH$_3$); **IR ν_{max} [cm^{-1}]:** 1720 (C=O, v, m), 1152 (O-C=O, v, m), 1672 (C=O, v, m), 1251 (-OCH$_3$, v, s); ***m/z* (FTMS+ESI):** M+Na ($C_{15}H_{14}O_6Na$) requires 313.0683, found 313.0682.

1.3.47 Synthesis of 1-(furan-2-yl)-3-(2-hydroxy-4,6-dimethoxyphenyl)propane-1,3-dione (9b)

The titled compound was synthesised according to the general procedure-**B** using 6-acetyl-2,3-dimethoxyphenyl furan-2-carboxylate (**9a**) (1.0 g, 3.44 mmol). The crude product was washed with acetic acid to obtain compound-**9b** as a yellow solid (0.80 g, 80%). The product formation was confirmed by ^{1}H NMR spectroscopic analysis.

^{1}H NMR: ($CDCl_3$, 400 MHz) [The compound exists as a mixture of keto-enol tautomers] δ 3.56 (C**H$_2$**), 3.81 (3H, s, -OC**H$_3$**), 3.83 (3H, s, -OC**H$_3$**), 4.42 (1H, s, =C**H** of enol form), 5.85 (1H, d, *J* = 2.0 Hz, H-3), 6.08 (1H, d, *J* = 2.0 Hz, H-5), 6.57 (1H, dd, *J* = 2.0 Hz, *J* = 2.0 Hz, H-4'), 7.25 (1H, d, *J* = 3.0 Hz, H-3'), 7.60 (1H, d, *J* = 1.0 Hz, H-5'), 13.43 (1H, s, OH), 13.63 (1H, s, OH of enol form).

1.3.48 Synthesis of 2-(furan-2-yl)-5,7-dimethoxy-4*H*-chromen-4-one (9c)*

The titled compound was synthesised according to the general procedure-**C** using 1-(furan-2-yl)-3-(2-hydroxy-4,6-dimethoxyphenyl)propane-1,3-dione (**9b**) (0.80 g, 2.75 mmol). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**9c** as a white solid (0.55 g, 73%).

m.p: 112-14 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 3.90 (3H, s, -OC**H$_3$**), 3.95 (3H, s, -OC**H$_3$**), 6.36 (1H, d, *J* = 2.0 Hz, H-6), 6.50 (1H, d, *J* = 2.0 Hz, H-8), 6.57 (1H, dd, *J* = 2.0 Hz, 2.0 Hz, H-4'), 7.25 (1H, d, *J* = 3.0 Hz, H-3'), 7.60 (1H, d, *J* = 1.0 Hz, H-5'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 55.76 (-O**C**H$_3$), 56.44 (-O**C**H$_3$), 92.81 (C8), 96.16 (C6), 107.13 (C10), 109.68 (C3'), 112.06 (C4'), 112.27 (C3), 145.32 (C5'), 146.24 (C2'), 152.93 (C9), 159.61 (C5), 160.94 (C7), 163.98 (C2), 177.05 (**C=**O); **IR ν_{max} [cm^{-1}]:** 1606 (C=O, v, s), 1216 (-OCH$_3$, v, s) 1095 (C-O, v, m); ***m/z* (FTMS+ESI):**

M+H ($C_{15}H_{13}O_5$) requires 273.0757, found 273.0759. **HPLC purity:** 99.8%, RT-11.5 min at 258 nm.

1.3.49 Synthesis of 2-(furan-2-yl)-5,7-dihydroxy-4*H*-chromen-4-one (9d)

The titled compound was synthesised according to the general procedure-**D** using 2-(furan-2-yl)-5,7-dimethoxy-4*H*-chromen-4-one (**9c**) (0.05 g, 0.183 mmol). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**9d** as a pale yellow solid (0.024 g, 55%).

m.p: 275-76 ^{o}C; **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 6.20 (1H, d, *J* = 2.0 Hz, H-6), 6.42 (1H, d, *J* = 2.0 Hz, H-8), 6.59 (1H, s, H-3), 6.57 (1H, dd, *J* = 2.0 Hz, 2.0 Hz, H-4'), 7.44 (1H, d, *J* = 3.0 Hz, H-3'), 8.05 (1H, d, *J* = 1.0 Hz, H-5'); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 93.90 (C8), 99.24 (C6), 102.61 (C3'), 103.86 (C10), 113.46 (C4'), 114.89 (C3), 144.94 (C2'), 147.43 (C5'), 155.08 (C9), 157.03 (C5), 161.48 (C7), 164.50 (C2), 181.40 (**C=**O); **IR ν_{max} [cm^{-1}]:** 1623 (C=O, v, s), 1166 (C-O, v, m), 3127 (OH, w, b); ***m/z* (FTMS+ESI):** M+H (C_{13} H_9O_5) requires 245.0444, found 245.0445. **HPLC purity:** 99.8%, RT-11.9 min at 258 nm.

1.3.50 Synthesis of 2-(furan-2-yl)-5,7-dimethoxy-4*H*-chromene-4-thione (9e)*

The titled compound was synthesised according to the general procedure-**E** using 2-(furan-2-yl)-5,7-dimethoxy-4*H*-chromen-4-one (**9c**) (0.20 g, 0.73 mmol). Purification was achieved by column chromatography with $CHCl_3$ (100%) to yield the compound-**9e** as a green solid (0.18 g, 86%).

m.p: 214-15 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 3.92 (6H, s, 2 x -OC**H$_3$**), 6.40 (1H, d, *J* = 2.0 Hz, H-6), 6.52 (1H, d, *J* = 2.0 Hz, H-8), 6.58 (1H, dd, *J* = 2.0 Hz, 2.0 Hz, H-4'), 7.08 (1H, d, *J* = 3.0 Hz, H-3'), 7.44 (1H, s, H-3), 7.62 (1H, s, H-5'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 54.83 (-O**C**H$_3$), 55.00 (-O**C**H$_3$), 91.88 (C8), 95.94 (C6), 111.78 (C3'), 112.24 (C4'), 116.78 (C10), 119.72 (C3), 141.26 (C2'), 144.92 (C5'), 145.19 (C9), 154.17 (C7), 160.72 (C5), 162.99 (C2), 199.06 (**C**=S); **IR ν_{max} [cm^{-1}]:** 1293 (C=S, v, m), 1220 (-OCH$_3$, v, m) 1147 (C-O, v, m). ***m/z* (FTMS+ESI):** M+H (C_{15} $H_{13}O_4S$) requires 289.0529, found 289.0529. **HPLC purity:** 95.1%, RT-13.4 min at 258 nm.

1.3.51 Synthesis of 2-(furan-2-yl)-5,7-dihydroxy-4*H*-chromene-4-thione (9f)*

The titled compound was synthesised according to the general procedure-**F** using 2-(furan-2-yl)-5,7-dimethoxy-4*H*-chromene-4-thione (**9e**) (0.15 g, 0.52 mmol). Purification was achieved by column chromatography with EtOAc (100%) to yield the compound-**9f** as a brownish red solid (0.07 g, 59%).

m.p: 280-82 ^{o}C; **^{1}H NMR:** (DMSO-d6, 400 MHz) 6.38 (1H, d, *J* = 2.0 Hz, H-6), 6.56 (1H, d, *J* = 2.0 Hz, H-8), 6.90 (1H, dd, *J* = 2.0 Hz, 2.0 Hz, H-4'), 7.28 (1H, s, H-3), 7.66 (1H, d, *J* = 3.0 Hz, H-3'), 8.18 (1H, d, *J* = 1.0 Hz, H-5'), 13.63 (s, OH); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 94.69 (C8), 100.84 (C6), 112.21 (C10), 113.64 (C3'), 115.28 (C4'), 116.21 (C3), 144.39 (C5'), 146.39 (C2'), 148.25 (C10), 153.40 (C7), 161.91 (C5), 164.56 (C2), 195.07 (**C**=S); **IR ν_{max} [cm^{-1}]:** 1268 (C=S, v,

m), 1148 (C-O, v, m), 3137 (OH, w, b). ***m/z* (FTMS+ESI):** M+H ($C_{13}H_9O_4S$) requires 261.0216, found 261.0216. **HPLC purity:** 96.6%, RT-13.5 min at 258 nm.

1.3.52 Synthesis of 6-acetyl-2,3-dimethoxyphenyl nicotinate (10a)

The titled compound was synthesised according to the general procedure-**A** using gallacetophenone dimethyl ether [1-(2-hydroxy-3,4-dimethoxyphenyl)ethanone] (1.0 g, 5.09 mmol) and nicotinoyl chloride hydrochloride (1.36 g, 7.64 mmol). Purification was achieved by column chromatography with $CHCl_3$: Hexane: EtOAc (8:1:1 v/v/v) to yield the compound-**10a** as a white solid (1.3 g, 81%).

m.p: 122-23 ^oC (lit[12]-118-119 ^oC); **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 2.50 (3H, s, -C**H$_3$**), 3.84 (3H, s, -OC**H$_3$**), 3.97 (3H, s, -OC**H$_3$**), 6.91 (1H, d, *J* = 9.0 Hz, H-4), 7.50 (1H, t, *J* = 6.0 Hz, H-5'), 7.70 (1H, d, *J* = 9.0 Hz, H-5), 8.49 (1H, d, *J* = 8.0 Hz, H-4'), 8.87 (1H, d, *J* = 4.0 Hz, H-6'), 9.42 (1H, s, H-2'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 29.28 (**C**H_3), 56.23 (-O**C**H_3), 61.10 (-O**C**H_3), 109.27 (C4), 123.61 (C5), 124.10 (C6), 125.51 (C3'), 126.36 (C5'), 137.88 (C4'), 141.70 (C2), 143.79 (C1), 151.50 (C2'), 153.97 (C6'), 157.33 (C3), 163.57 (**C**OO- HetAr), 195.64 (**C**OCH_3); **IR ν_{max} [cm^{-1}]:** 1747 (C=O, v, m), 1670 (C=O, v, m), 1089 (O-C=O, v, m), 1268 (C=N, v, m), 1215 (-OCH_3, v, s); ***m/z* (FTMS+ESI):** M+H ($C_{16}H_{16}O_5N$) requires 302.1023, found 302.1023.

1.3.53 Synthesis of 1-(2-hydroxy-3,4-dimethoxyphenyl)-3-(pyridin-3-yl)propane-1,3-dione (10b)

The titled compound was synthesised according to the general procedure-**B** using 6-acetyl-2,3-dimethoxyphenyl nicotinate (**10a**) (1.0 g, 3.13 mmol). The crude product (compound-**10b**) was obtained as a yellow solid (0.75 g, 75%). The product formation was confirmed by ^{1}H NMR spectroscopic analysis.

^{1}H NMR: ($CDCl_3$, 400 MHz) [The compound exists as a mixture of keto-enol tautomer] δ 3.83 (C**H$_2$**), 3.95 (3H, s, -OC**H$_3$**), 3.97 (3H, s, -OC**H$_3$**), 6.91 (1H, d, *J* = 9.0 Hz, H-5), 6.77 (1H, s, =C**H** of enol form), 7.49 (1H, t, *J* = 6.0 Hz, H-5'), 7.69 (1H, d, *J* = 9.0 Hz, H-6), 8.48 (1H, d, *J* = 8.0 Hz, H-4'), 8.87 (1H, d, *J* = 5.0 Hz, H-6'), 9.42 (1H, s, H-2'), 12.17 (1H, s, OH) 12.17 (1H, s, OH of enol form).

1.3.54 Synthesis of 7,8-dimethoxy-2-(pyridin-3-yl)-4*H*-chromen-4-one (10c)

1-(2-Hydroxy-3,4-dimethoxyphenyl)-3-(pyridin-3-yl)propane-1,3-dione (**10b**) (0.70 g, 2.32 mmol) was dissolved in $CHCl_3$ (7 mL), the reaction mixture was cooled to 0 ^oC and concentrated H_2SO_4 (2 mL) was added slowly under constant stirring. The reaction mixture was stirred at room temperature for 30 minutes and then quenched with water. The reaction mixture was extracted with EtOAc (2 x 10 mL), the organic layers were combined, dried over anhydrous $MgSO_4$ and concentrated *in vacuo* to obtain the crude product. Purification was achieved by column chromatography with $CHCl_3$: Hexane: EtOAc (8:1:1 v/v/v) to yield the compound-**10c** as a white solid (0.45 g, 69%).

m.p: 172-74 ^{o}C (lit[12]-170-72 ^{o}C); **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 4.02 (3H, s, -OC**H$_3$**), 4.05 (3H, s, -OC**H$_3$**), 6.80 (1H, s, H-3), 7.70 (1H, d, *J* = 10.0 Hz, H-6), 7.49 (1H, t, *J* = 4.5 Hz, H-5'), 7.97 (1H, d, *J* = 8.0 Hz, H-5), 8.23 (1H, d, *J* = 10.0 Hz, H-4'), 7.93 (1H, d, *J* = 5.0 Hz, H-6'), 9.23 (1H, s, H-2'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 56.47 (-O**C**H$_3$), 61.68 (-O**C**H$_3$), 105.60 (C3), 109.83 (C6), 118.72 (C10), 120.99 (C5), 128.33 (C4'), 128.51 (C3'), 130.11 (C5'), 135.34 (C2'), 136.78 (C9), 150.33 (C7), 156.84 (C8), 158.95 (C2), 177.60 (**C=**O); **IR ν_{max} [cm^{-1}]:** 1631 (C=O, ν, m), 1289 (C=N, ν, m), 1215 (-OCH$_3$, ν, s), 1180 (C-O, ν, m); ***m/z* (FTMS+ESI):** M+H ($C_{16}H_{14}O_4N$) requires 284.917, found 284.919. **HPLC purity:** 99.9%, RT-9.8 min at 258 nm.

1.3.55 Synthesis of 7,8- dihydroxy-2-(pyridin-3-yl)-4*H*-chromen-4-one.HBr (10d)

The titled compound was synthesised according to the general procedure-**D** using 7,8-dimethoxy-2-(pyridin-3-yl)-4*H*-chromen-4-one (**10c**) (0.20 g, 0.70 mmol). The crude compound was recrystallised using 9:1 methanol/water to yield the pure compound-**10d** as a yellow solid (0.12 g, 65%).

m.p: 314-15 ^{o}C (lit[12]-313-14 ^{o}C); **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 6.97 (1H, d, *J* = 8.0 Hz, H-6), 7.09 (1H, s, H-3), 7.41 (1H, d, *J* = 9.0 Hz, H-5), 7.82 (1H, t, *J* = 7.0 Hz, H-5'), 8.75 (1H, d, *J* = 9.0 Hz, H-4'), 8.85 (1H, d, *J* = 4.0 Hz, H-6'), 9.45 (1H, s, H-2'); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 104.37 (C3), 113.90 (C10), 115.10 (C6), 116.82 (C5), 128.81 (C3'), 129.38 (C4'), 131.50 (C5'), 133.05 (C8), 134.40 (C2'), 146.37 (C9), 150.62 (C7), 158.15 (C2), 176.88 (**C=**O); **IR ν_{max} [cm^{-1}]:** 3046.38 (OH, b), 1614 (C=O, ν, m), 1297 (C=N, ν, m), 1184 (C-O, ν, m); ***m/z* (FTMS+ESI):** M+H ($C_{14}H_{10}O_4N$) requires 256.0604, found 256.0605; **Elemental analysis:** Calculated: C-50.07%; H-2.97%, N-4.17%, Br-23.77%, found: C-49.98%; H-3.03%, N-4.12%, Br-23.70%. **HPLC purity:** 97.4 %, RT-7.0 min at 258 nm.

1.3.56 Synthesis of 7,8-dimethoxy-2-(pyridin-3-yl)-4*H*-chromene-4-thione (10e)*

The titled compound was synthesised according to the general procedure-**E** using 7,8-dimethoxy-2-(pyridin-3-yl)-4*H*-chromen-4-one (**10c**) (0.20 g, 0.70 mmol). Purification was achieved by column chromatography with $CHCl_3$: Hexane: EtOAc (8:1:1 v/v/v) to yield the compound-**10e** as an orange solid (0.18 g, 86%).

m.p: 240-41 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 4.03, 4.04 (6H, 2 x s, 2 x -OC**H$_3$**), 7.09 (1H, d, *J* = 9.0 Hz, H-6), 7.49 (1H, dd, *J* = 5.0 Hz, H-5'), 7.67 (1H, s, H-3), 8.28 (1H, d, *J* = 8.0 Hz, H-4'), 8.33 (1H, d, *J* = 9.0 Hz, H-5), 8.78 (1H, d, *J* = 5.0 Hz, H-6'), 9.28 (1H, d, *J* = 2.0 Hz, H-2'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 56.85 (-O**C**H$_3$), 61.52 (-O**C**H$_3$), 111.16 (C6), 119.73 (C5'), 123.88 (C3), 124.22 (C5), 125.76 (C10), 127.71 (C3'), 133.75 (C4'), 146.01 (C9), 147.76 (C6'), 151.07 (C7), 152.24 (C2'), 157.69 (C2), 201.50 (**C**=S); **IR ν_{max} [cm^{-1}]:** 1341 (C-O, ν, m), 1285 (C=N, ν, m), 1096 (C=S, ν, m), 1027 (-OCH$_3$, ν, m); ***m/z* (FTMS+ESI):** M+H ($C_{16}H_{14}O_3NS$) requires 300.0689, found 300.0689. **HPLC purity:** 97.5%, RT-12.7 min at 258 nm.

1.3.57 Synthesis of 7,8-dihydroxy-2-(pyridin-3-yl)-4*H*-chromene-4-thione.HBr (10f)*

The titled compound was synthesised according to the general procedure-**F** using 7,8-dimethoxy-2-(pyridin-3-yl)-4*H*-chromene-4-thione (**10e**) (0.10 g, 0.33 mmol). Purification was achieved by recrystallisation using warm methanol to obtain the pure compound-**10f** as a yellowish orange solid (0.07 g, 60%).

m.p: 260-62 ^{o}C; **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 7.04 (1H, d, *J* = 9.0 Hz, H-6), 7.64 (1H, dd, *J* = 5.0 Hz, 4.5 Hz, H-5'), 7.82 (1H, s, H-3), 7.84 (1H, d, *J* = 9.0 Hz, H-5), 8.63 (1H, d, *J* = 8.0 Hz, H-4'), 8.78 (1H, d, *J* = 4.0 Hz, H-6'), 9.42 (1H, d, *J* = 2.0 Hz, H-2'), 9.8 (1H, s, OH), 10.7 (1H, s, OH); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 115.83 (C6), 118.29 (C3), 118.57 (C5'), 124.09 (C8), 127.14 (C10), 132.98 (C5), 134.60 (C7), 142.38 (C3', 4'), 147.58 (C6'), 151.23 (C9), 151.66 (C2), 151.91 (C2), 200.19 (**C=**S); **IR ν_{max} [cm^{-1}]:** 1283 (C=N, ν, s), 1186 (C-O, ν, m), 1123 (C=S, ν, m), 3083 (OH, w, s); ***m/z* (FTMS+ESI):** M+H (C_{14} $H_{10}O_3NS$) requires 272.0376, found 272.0377; **Elemental analysis:** Calculated: C-47.74%; H-2.86%, N-3.98%, S-9.10%, Br-22.69%, found: C-47.71%; H-2.84%, N-3.97%, S-9.04%, Br-22.68%. **HPLC purity:** 95.8%, RT-10.0 min at 258 nm.

1.3.58 Synthesis of 2-acetyl-3,5-dimethoxyphenyl nicotinate (11a)

The titled compound was synthesised according to the general procedure-**A** using phloroacetophenone dimethylether [1-(2-hydroxy-4,6-dimethoxyphenyl)ethanone] (1.0 g, 5.09 mmol) and nicotinoyl chloride hydrochloride (1.36 g, 7.64 mmol). Purification was achieved by column chromatography with $CHCl_3$: Hexane: EtOAc (8:1:1 v/v/v) to yield the compound-**11a** as a white solid (1.2 g, 78%).

m.p: 125-27 ^{o}C (lit[12]-123-24^{o}C); **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 2.49 (3H, s, -C**H$_3$**), 3.84 (3H, s, -OC**H$_3$**), 3.88 (3H, s, -OC**H$_3$**), 6.36 (1H, d, *J* = 2.0 Hz, H-4), 6.43 (1H, *J* = 2.0 Hz, H-6), 7.44 (1H, dd, *J* = 5.0 Hz, 5.0 Hz, H-5'), 8.39 (1H, d, *J* = 8.0 Hz, H-4'), 8.83 (1H, dd, 4.0 Hz, 1.0 Hz, H-6'), 9.31 (1H, d, *J* = 2.0 Hz, H-2'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 32.05 (-**C**H_3), 55.95 (2 x -O**C**H_3), 97.02 (C6), 100.21 (C4), 116.85 (C2), 123.40 (C5'), 125.35 (C3'), 137.74 (C4'), 149.78 (C1), 151.55 (C6'), 154.03 (C2'), 159.70 (C5), 162.53 (C3), 163.95 (**C**OO-HetAr), 199.00 (**C**OCH_3); **IR ν_{max} [cm^{-1}]:** 1736 (C=O, ν, m), 1653 (C=O, ν, m), 1105 (O-C=O, ν, m), 1248 (C=N, ν, m), 1225 (-OCH_3, ν, s); ***m/z* (FTMS+ESI):** M+H ($C_{16}H_{16}O_5N$) requires 302.1023, found 302.1021.

1.3.59 Synthesis of 1-(2-hydroxy-4,6-dimethoxyphenyl)-3-(pyridin-3-yl)propane-1,3-dione (11b)

The titled compound was synthesised according to the general procedure-**B** using 2-acetyl-3,5-dimethoxyphenyl nicotinate (**11a**) (1.0 g, 3.32 mmol). The crude product (compound **11b**) was obtained as a yellow solid (0.78 g, 78%). The product formation was confirmed by ^{1}H NMR spectroscopic analysis.

^{1}H NMR: ($CDCl_3$, 400 MHz) [The compound exists as a mixture of keto-enol tautomers] δ 3.53 (3H, s, -OCH_3), 3.82 (3H, s, -OCH_3), 3.92 (C**H_2**), 5.90 (1H, d, *J* = 2.0 Hz, H-5), 6.11 (1H, d, *J* = 2.0 Hz, H-3), 7.41 (1H, s, =C**H** of enol form), 7.44 (1H, dd, *J* = 5.0 Hz, *J* = 5.0 Hz, H-5'), 8.17 (1H, dd, *J* = 2.0 Hz, 1.5 Hz, H-4'), 9.09 (1H, d, *J* = 2.0 Hz, H-6'), 9.18 (1H, s, H-2'), 13.36 (1H, s, OH), 13.60 (1H, s, OH of enol form).

1.3.60 Synthesis of 5,7-dimethoxy-2-(pyridin-3-yl)-4*H*-chromen-4-one (11c)

1-(2-Hydroxy-4,6-dimethoxyphenyl)-3-(pyridin-3-yl)propane-1,3-dione (**11b**) (0.70 g, 2.32 mmol) was dissolved in $CHCl_3$ (7 mL), the reaction mixture was cooled to 0 ^oC and concentrated H_2SO_4 (2 mL) was added slowly under constant stirring. The reaction mixture was stirred at room temperature for 30 minutes and then quenched with water. The reaction mixture was extracted with EtOAc (2 x 10 mL), the organic layers were combined, dried over anhydrous $MgSO_4$ and concentrated *in vacuo* to obtain the crude product. Purification was achieved by column chromatography with $CHCl_3$: Hexane: EtOAc (8:1:1 v/v/v) to yield the compound-**11c** as a white solid (0.45 g, 68%).

m.p: 161-63 ^oC (lit[12]-161-62 ^oC); **^{1}H NMR:** ($CDCl_3$,400 MHz) δ 3.93, 3.97 (3H, 2 x s, 2 x-OC**H_3**), 6.41 (1H, d, *J* = 2.0 Hz, H-6), 6.59 (1H, d, *J* = 2.0 Hz, H-8), 6.70 (1H, s, H-3), 6.55 (1H, dd, *J* = 5.0 Hz, 5.0 Hz, H-5'), 8.16 (1H, d, *J* = 4.0 Hz, H-4'), 8.74 (1H, d, *J* = 4.0 Hz, H-6'), 9.13 (1H, s, H-2'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 55.86 (-O**C**H_3), 56.49 (-O**C**H_3), 93.16 (C8), 96.82 (C6), 109.39 (C10), 109.94 (C3), 123.75 (C5'), 127.75 (C3'), 133.32 (C4'), 147.35 (C2'), 151.91 (C6'), 158.39 (C9), 159.82 (C5), 161.08 (C2), 164.47 (C7), 176.89 (**C=**O); **IR ν_{max} [cm^{-1}]:** 1610 (C=O, ν, m), 1227 (C=N, ν, m), 1189 (-OCH_3, ν, s), 1109 (C-O, ν, m); ***m/z* (FTMS+ESI):** M+H ($C_{16}H_{14}O_4N$) requires 284.917, found 284.917. **HPLC purity:** 99.8%, RT-9.3 min at 258 nm.

1.3.61 Synthesis of 5,7-dihydroxy-2-(pyridin-3-yl)-4*H*-chromen-4-one.HBr (11d)

The titled compound was synthesised according to the general procedure-**D** using 5,7-dimethoxy-2-(pyridin-3-yl)-4*H*-chromen-4-one (**11c**) (0.15 g, 0.59 mmol). The crude compound was recrystallised using 9:1 methanol/water to yield the pure compound-**11d** as a pale yellow soild (0.095 g, 53%).

m.p: 323-24 ^oC (lit[12]-324 ^oC); **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 6.23 (1H, d, *J* = 2.0 Hz, H-6), 6.56 (1H, d, *J* = 2.0 Hz, H-8), 7.11 (1H, s, H-3), 7.60 (1H, dd, *J* = 4.0 Hz, *J* = 3.5 Hz, H-5'), 8.45 (1H, d, *J* = 8.0 Hz, H-4'), 8.77 (1H, d, *J* = 8.0 Hz, H-6'), 9.27 (1H, s, H-2'), 10.96 (1H, s, -OH), 12.74 (1H, s, -OH); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 94.28 (C8), 98.99 (C6), 104.28 (C10), 106.04 (C3), 124.03 (C5'), 126.85 (C3'), 134.02 (C4'), 147.66 (C6'), 152.48 (C2'), 157.61 (C9), 161.54 (C2. C5), 164.66 (C7), 181.64 (**C=**O); **IR ν_{max} [cm^{-1}]:** 1650 (C=O, ν, m), 1200 (C=N, ν, m), 1099 (C-O, ν, m), 3067 (OH, w, s); ***m/z* (FTMS+ESI):** M+H ($C_{14}H_{10}O_4N$) requires 256.0604, found 256.0605; **Elemental analysis:** Calculated: C-50.02%; H-3.00%, N-4.17%, Br-23.77%, found: C-49.98%; H-3.03%, N-4.15%, Br-23.79%. **HPLC purity:** 95.5%, RT-11.5 min at 258 nm.

1.3.62 Synthesis of 5,7-dimethoxy-2-(pyridin-3-yl)-4*H*-chromene-4-thione (11e)*

The titled compound was synthesised according to the general procedure-**E** using 5,7-dimethoxy-2-(pyridin-3-yl)-4*H*-chromen-4-one (**11c**) (0.20 g, 0.70 mmol). Purification was achieved by column chromatography with $CHCl_3$: Hexane: EtOAc (8:1:1 v/v/v) to yield the compound-**11e** as a dark green solid (0.18 g, 85%).

m.p: 204-05 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 3.93, 3.94 (3H, 2 x s, 2 x-OC**H$_3$**), 6.44 (1H, d, *J* = 2.0 Hz, H-6), 6.59 (1H, d, *J* = 2.0 Hz, H-8), 6.55 (1H, dd, *J* = 4.5 Hz, *J* = 4.0 Hz, H-5'), 7.52 (1H, s, H-3), 8.16 (1H, d, *J* = 8.0 Hz, H-4'), 8.74 (1H, d, *J* = 4.0 Hz, H-6'), 9.17 (1H, s, H-2'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 56.36 (2 x -O**C**H$_3$), 93.13 (C8), 97.05 (C6), 118.37 (C10), 122.94 (C3), 124.03 (C4'), 127.29 (C3'), 133.82 (C5'), 147.31 (C6'), 151.88 (C9), 156.02 (C2'), 162.11 (C5, C7), 164.28 (C2), 200.52 (**C=**S); 1320 (C=N, v, s), 1184 (C-O, v, m), 1120 (C=S, v, m); ***m/z* (FTMS+ESI):** M+H ($C_{16}H_{14}O_3NS$) requires 300.0689, found 300.0689. **HPLC purity:** 95.9%, RT-12.1 min at 258 nm.

1.3.63 Synthesis of 5,7-dihydroxy-2-(pyridin-3-yl)-4*H*-chromene-4-thione.HBr (11f)*

The titled compound was synthesised according to the general procedure-**F** using 5,7-dimethoxy-2-(pyridin-3-yl)-4*H*-chromene-4-thione (**11e**) (0.10 g, 0.33 mmol). Purification was achieved by column chromatography with $CHCl_3$: Hexane: EtOAc (8:1:1 v/v/v) to yield the compound-**11f** as a pale green solid (0.05 g, 51%).

m.p: 320-22^{o}C; **^{1}H NMR:** (DMSO-d6, 400 MHz) 6.33 (1H, s, H-6), 6.63 (1H, s, H-8), 7.31 (1H, dd, *J* = 7.0 Hz, 5.0 Hz, H- 5'), 7.68 (1H, s, H-3), 8.51 (1H, d, *J* = 8.0 Hz, H-4'), 8.77 (1H, d, *J* = 4.0 Hz, H-6'), 9.31 (1H, s, H-2'), 11.31 (1H, s, OH), 13.58 (1H, s, OH); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 95.09 (C8), 101.18 (C6), 112.93 (C10), 117.94 (C5'), 122.25 (C3), 126.21 (C3'), 134.26 (C4'), 147.75 (C6'), 152.32 (C2'), 154.06 (C9), 161.89 (C7), 164.60 (C2, C5), 196.27 (**C**=S);); **IR ν_{max} [cm^{-1}]:** 1203 (C=N, v, m), 1104 (C-O, v, m), 1080 (C=S, v, m), 3066 (OH, w, s); ***m/z* (FTMS+ESI):** M+H ($C_{14}H_{10}O_3NS$) requires 272.0376, found 272.0376; **Elemental analysis:** Calculated: C-47.74%; H-2.86%, N-3.98%, S-9.10%, Br-22.69%, found: C-47.80%; H-2.79%, N-3.94%, S-9.07%, Br-22.61%. **HPLC purity:** 98.6%, RT-12.2 min at 258 nm.

1.3.64 Synthesis of 6-acetyl-2,3-dimethoxyphenyl 4-fluorobenzoate (12a)

The titled compound was synthesised according to the general procedure-**A** using gallacetophenone dimethyl ether [1-(2-hydroxy-3, 4-dimethoxyphenyl) ethanone] (1.0 g, 5.09 mmol) and 4-fluorobenzoyl chloride (1.21 g, 0.79 mL, 7.64 mmol). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**12a** as a white solid (1.35 g, 90%).

m.p: 88-89 °C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 2.49 (3H, s, -C**H$_3$**), 3.82 (3H, s, -OC**H$_3$**), 3.96 (3H, s, -OC**H$_3$**), 6.90 (1H, d, *J* = 9.0 Hz, H-4), 7.20 (2H, app. t, *J* = 8.5 Hz, H-3',5'), 7.68 (1H, d, *J* = 9.0 Hz, H-5), 8.25 (2H, dd, *J* = 6.0 Hz, H-2',6'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 29.81 (**C**H$_3$), 56.14 (-O**C**H$_3$), 61.10 (-O**C**H$_3$), 109.14 (C4), 115.80 (C3', C5'), 116.33 (C5), 124.68 (C6), 125.52 (C1'),

126.23 (C2', C6'), 133.03 (C1'), 141.58 (C1), 144.10 (C3), 163.91 (**C**OO-Ar), 166.14 (C4', $J_{C\text{-}F}$ = 253 Hz), 195.76 (**C**OCH_3); **IR ν_{max} [cm^{-1}]:** 1731 (C=O, ν, m), 1087 (O-C=O, ν, m), 1678 (C=O, ν, m), 1265 (-OCH_3, ν, s); ***m/z* (FTMS+ESI):** M+H ($C_{17}H_{16}O_5F$) requires 301.0976, found 301.0976.

1.3.65 Synthesis of 1-(4-fluorophenyl)-3-(2-hydroxy-3,4-dimethoxyphenyl) propa-ne-1,3-dione (12b)

The titled compound was synthesised according to the general procedure-**B** using 6-acetyl-2,3-dimethoxyphenyl 4-fluorobenzoate (**12a**) (1.0 g, 3.14 mmol). The crude product was washed with acetic acid to obtain compound-**12b** as a yellow solid (0.78 g, 78%). The product formation was confirmed by ^{1}H NMR spectroscopic analysis.

^{1}H NMR: ($CDCl_3$, 400 MHz) [The compound exists as a mixture of keto-enol tautomers] δ 3.91 (3H, s, -OC**H_3**), 3.93 (3H, s, -OC**H_3**), 4.5 (C**H_2**), 6.52 (1H, d, *J* = 9.0 Hz, H-5), 6.69 (1H, =C**H** of enol form), 7.20 (2H, app.t, *J* = 8.0 Hz, H-3',5'), 7.54 (1H, d, *J* = 9.0 Hz, H-6), 8.25 (2H, dd, *J* = 5.5 Hz, 5.0 Hz, H-2',6'), 12.21 (1H, s, OH), 12.27 (1H, s, OH of enol form).

1.3.66 Synthesis of 2-(4-fluorophenyl)-7,8-dimethoxy-4*H*-chromen-4-one (12c)

The titled compound was synthesised according to the general procedure-**C** using 1-(4-fluorophenyl)-3-(2-hydroxy-3,4-dimethoxyphenyl)propane-1,3-dione (**12b**) (0.75 g, 2.35 mmol). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**12c** as a white solid (0.59 g, 83%).

m.p: 207-08 °C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 4.01 (3H, s, -OC**H_3**), 4.05 (3H, s, -OC**H_3**), 6.71 (1H, s, H-3), 7.06 (1H, d, *J* = 9.0 Hz, H-6), 7.23 (2H, app.t, *J* = 8.0 Hz, H-3',5'), 7.96 (2H, d, *J* = 9.0 Hz, H-2',6'), 7.97 (1H, d, *J* = 8.0 Hz, H-5); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 56.51 (-O**C**H_3), 61.56 (-O**C**H_3), 106.81 (C3), 110.31 (C6), 116.52 (C3', C5'), 118.66 (C10), 121.18 (C5), 128.37 (C2', C6', C1'), 137.30 (C8), 150.90 (C9), 156.72 (C7), 162.36 (C2), 165.24 (C4', $J_{C\text{-}F}$ = 245 Hz), 177.89 (**C=**O, C4); **IR ν_{max} [cm^{-1}]:** 1634 (C=O, ν, s), 1293 (-OCH_3, ν, s) 1110 (C-O, ν, m); ***m/z* (FTMS+ESI):** M+H ($C_{17}H_{14}O_4F$) requires 301.0871, found 301.0872. **HPLC purity:** 99.9%, RT-12.9 min at 258 nm.

1.3.67 Synthesis of 2-(4-fluorophenyl)-7,8-dihydroxy-4*H*-chromen-4-one (12d)

The titled compound was synthesised according to the general procedure-**D** using 2-(4-fluorophenyl)-7,8-dimethoxy-4*H*-chromen-4-one (**12c**) (0.15 g, 0.50 mmol). Purification was achieved by column chromatography with EtOAc (100%) to yield the compound-**12d** as a pale yellow solid (0.09 g, 66%).

m.p: 280-81 °C; **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 6.88 (1H, s, H-3), 6.94 (1H, d, *J* = 9.0 Hz, H-6), 7.40 (2H, app.t, *J* = 9.0 Hz, H-3',5'), 7.43 (1H, d, *J* = 8.0 Hz, H-5), 8.23 (2H, dd, *J* = 6.0 Hz, 5.5 Hz, H-2',6'), 9.51 (1H, s, OH), 10.32 (1H, s, OH); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 106.10 (C3), 115.10 (C5), 115.97, 116.16 (C3', C5'), 116.79 (C10), 124.72 (C1'), 127.98 (C2'), 128.92

(C6'), 132.97 (C8), 146.55 (C9), 150.47 (C7), 162.33 (C4', J_{C-F} = 235 Hz), 176.95 (C2), 187.79 (**C=**O); **IR ν_{max} [cm^{-1}]:** 1618 (C=O, v, s), 1069 (C-O, v, m), 3260 (OH, w, b); ***m/z* (FTMS+ESI):** M+H ($C_{15}H_{10}O_4F$) requires 273.0558, found 273.0558. **HPLC purity:** 97.9%, RT-10.4 min at 258 nm.

1.3.68 Synthesis of 2-(4-fluorophenyl)-7,8-dimethoxy-4*H*-chromene-4-thione (12e)*

The titled compound was synthesised according to the general procedure-**E** using 2-(4-fluorophenyl)-7,8-dimethoxy-4*H*-chromen-4-one (**12c**) (0.15 g, 0.50 mmol). Purification was achieved by column chromatography with $CHCl_3$ (100%) to yield the compound-**12e** as a pale orange solid (0.13 g, 82%).

m.p: 216-18 °C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 4.02 (6H, s, 2 x -OC**H$_3$**), 7.01 (1H, d, *J* = 9.0 Hz, H-6), 7.22 (2H, app.t, *J* = 8.5 Hz, H-3',5'), 7.64 (1H, s, H-3), 8.03 (2H, dd, *J* = 5.0 Hz, 5.0 Hz, H-2',6'), 8.35 (2H, d, *J* = 9.0 Hz, H-5); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 56.41 (-O**C**H$_3$), 61.49 (-O**C**H$_3$), 111.09 (C6), 116.50, 116.70 (C3', C5'), 118.85 (C3), 124.24 (C5, C10), 125.46 (C1'), 128.83 (C2', C6'), 136.92 (C9), 146.37 (C7), 154.18 (C4', J_{C-F} = 231 Hz), 157.43 (C2), 201.41 (**C**=S); **IR ν_{max} [cm^{-1}]:** 1290 (C=S, v, s), 1108 (-OCH$_3$, v, m) 1095 (C-O, v, m); ***m/z* (FTMS+ESI):** M+H ($C_{17}H_{14}O_3FS$) requires 317.0642, found 317.0644. **HPLC purity:** 97.6%, RT-14.4 min at 258 nm.

1.3.69 Synthesis of 2-(4-fluorophenyl)-7,8-dihydroxy-4*H*-chromene-4-thione (12f)*

The titled compound was synthesised according to the general procedure-**F** using 2-(4-fluorophenyl)-7,8-dimethoxy-4*H*-chromene-4-thione (**12e**) (0.10 g, 0.31 mmol). Purification was achieved by column chromatography with $CHCl_3$: Hexane: EtOAc (8:1:1 v/v/v) to yield the compound-**12f** as an orange red solid (0.065 g, 86%).

m.p: 253-55 °C; **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 7.03 (1H, d, *J* = 9.0 Hz, H-6), 7.57 (2H, app.t, *J* = 9.0 Hz, H-3',5'), 7.73 (1H, s, H-3), 7.83 (1H, d, *J* = 9.0 Hz, H-5), 8.21 (2H, dd, *J* = 6.0 Hz, 5.5 Hz, H-2',6'); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 115.57 (C6), 116.16, 116.48 (C5'), 117.47 (C3), 118.53 (C3'), 123.74 (C1'), 127.31 (C10), 129.46, 133.02 (C2', C6'), 142.35 (C5), 151.69 (C7, C9), 152.39 (C2), 164.20 (C4', J_{C-F} = 252 Hz), 199.64 (**C=**S); **IR ν_{max} [cm^{-1}]:** 1296 (C=S, v, s), 1123 (C-O, v, m), 3500 (OH, w, s); ***m/z* (FTMS+ESI):** M+H ($C_{15}H_{10}O_3FS$) requires 289.0329, found 289.0331. **HPLC purity:** 96.5%, RT-12.9 min at 258 nm.

1.3.70 Synthesis of 2-acetyl-3,5-dimethoxyphenyl 4-fluorobenzoate (13a)

The titled compound was synthesised according to the general procedure-**A** using phloroacetophenone dimethylether [1-(2-hydroxy-4,6-dimethoxyphenyl)ethanone] (1.0 g, 5.09 mmol) and 4-fluorobenzoyl chloride (1.21 g, 0.79 mL, 7.64 mmol). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**13a** as a white solid (1.42 g, 87%).

m.p: 132-34 °C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 2.47 (3H, s, -C**H$_3$**), 3.82 (3H, s, -OC**H$_3$**), 3.87 (3H, s, -OC**H$_3$**), 6.36 (1H, s, H-4), 6.41 (1H, d, *J* = 1.0 Hz, H-6), 7.15 (2H, app.t, *J* = 8.5 Hz, H-3',5'), 8.15 (2H, dd, *J* = 6.0 Hz, 5.5 Hz, H- 2',6'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 31.96 (-**C**H$_3$), 55.68 (-O**C**H$_3$), 55.95 (-O**C**H$_3$), 96.72 (C6), 115.69, 115.91 (C3', C5'), 117.12 (C2), 125.55 (C1'), 132.89 (C2', C6'), 132.99 (C1), 149.80 (C5), 159.33 (C3), 162.32 (**C**OO-Ar), 166.32 (C4', $J_{C\text{-}F}$ = 245 Hz), 199.23 (**C**OCH$_3$); **IR ν_{max} [cm^{-1}]:** 1684 (C=O, ν, m), 1146 (O-C=O, ν, m), 1603 (C=O, ν, m), 1252 (-OCH$_3$, ν, s); ***m/z* (FTMS+ESI):** M+H ($C_{17}H_{16}O_5F$) requires 319.0976, found 319.0974.

1.3.71 Synthesis of 1-(4-fluorophenyl)-3-(2-hydroxy-4,6-dimethoxyphenyl)pro pane-1,3-dione (13b)

The titled compound was synthesised according to the general procedure-**B** using 2-acetyl-3,5-dimethoxyphenyl 4-fluorobenzoate (**13a**) (1.0 g, 3.14 mmol). The crude product was washed with acetic acid to obtain compound-**13b** as a yellow solid (0.75 g, 75%). The product formation was confirmed by ^{1}H NMR spectroscopic analysis.

^{1}H NMR: ($CDCl_3$, 400 MHz) [The compound exists as a mixture of keto-enol tautomers] δ 3.41 (3H, s, -OCH$_3$), 3.81 (3H, s, -OCH$_3$), 4.52 (C**H$_2$**), 5.84 (1H, s. H-5), 6.09 (1H, s, H-3), 7.15 (2H, app.t, *J* = 8.5 Hz, H-3',5'), 7.27 (1H, =C**H** of enol form), 7.90 (2H, dd, *J* = 6.0 Hz, 5.0 Hz, H-2',6'), 13.38 (1H, s, OH), 13.67 (1H, s, OH of enol form).

1.3.72 Synthesis of 2-(4-fluorophenyl)-5,7-dimethoxy-4*H*-chromen-4-one (13c)

The titled compound was synthesised according to the general procedure-**C** using 1-(4-fluorophenyl)-3-(2-hydroxy-4,6-dimethoxyphenyl)propane-1,3-dione (**13b**) (0.70 g, 2.19 mmol). Purification was achieved by column chromatography with $CHCl_3$: Hexane: EtOAc (8:1:1 v/v/v) to yield the compound-**13c** as a white solid (0.50 g, 76%).

m.p: 200-01 °C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 3.91 (3H, s, -OC**H$_3$**), 3.96 (3H, s,-OC**H$_3$**), 6.38 (1H, d, *J* = 1.5 Hz, H-6), 6.56 (1H, d, *J* = 1.5 Hz, H-8), 6.62 (1H, s, H-3), 7.18 (2H, app.t, *J* = 8.5 Hz, H-3',5'), 7.86 (2H, d, *J* = 5.0 Hz, H-2',6'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 55.79 (-O**C**H$_3$), 56.46 (-O**C**H$_3$), 92.81 (C8), 96.24 (C6), 108.86 (C3), 109.24 (C10), 116.06, 116.28 (C3', C5'), 127.75 (C1'), 128.07, 128.16 (C2', C6'), 159.70, 159.99 (C7, C8), 161.02 (C5), 164.54 (C4', $J_{C\text{-}F}$ = 245 Hz), 164.19 (C2), 177.59 (**C=**O); **IR ν_{max} [cm^{-1}]:** 1647 (C=O, ν, s), 1215 (-OCH$_3$, ν, s), 1116 (C-O, ν, m); ***m/z* (FTMS+ESI):** M+H ($C_{17}H_{14}O_4F$) requires 301.0871, found 301.0872. **HPLC purity:** 99.8%, RT-12.6 min at 258 nm.

1.3.73 Synthesis of 2-(4-fluorophenyl)-5,7-dihydroxy-4*H*-chromen-4-one (13d)

The titled compound was synthesised according to the general procedure-**D** using 2-(4-fluorophenyl)-5,7-dimethoxy-4*H*-chromen-4-one (**13c**) (0.15 g, 0.50 mmol). Purification was achieved by column chromatography with EtOAc (100%) to yield the compound-**13d** as a white solid (0.08 g, 61%).

m.p: 275-76 °C; **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 6.21 (1H, s, H-6), 6.52 (1H, s, H-8), 6.97 (1H, s, H-3), 7.58 (2H, app.t, *J* = 9.0 Hz, H-3',5'), 8.06 (2H, d, *J* = 5.5 Hz, H-2',6'), 10.92 (1H, s, OH), 12.80 (1H, s, OH); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 94.27 (C8), 99.05 (C6), 103.97 (C10), 105.27 (C3), 116.12, 116.33 (C3', C5'), 127.43 (C1), 129.08, 129.16 (C2', C6'), 157.55 (C9), 161.60 (C5), 162.32 (C2), 164.28 (C4', $J_{C\text{-}F}$ = 238 Hz), 164.50 (C7), 182.02 (**C**=O); **IR ν_{max} [cm^{-1}]:** 1603 (C=O, ν, s), 1162 (C-O, ν, m), 3116 (OH, w, b); ***m/z* (FTMS+ESI):** M+H ($C_{15}H_{10}O_4F$) requires 273.0558, found 273.0558. **HPLC purity:** 99.6%, RT-12.7 min at 258 nm.

1.3.74 Synthesis of 2-(4-fluorophenyl)-5,7-dimethoxy-4*H*-chromene-4-thione (13e)*

The titled compound was synthesised according to the general procedure-**E** using 2-(4-fluorophenyl)-5,7-dimethoxy-4*H*-chromen-4-one (**13c**) (0.30, 1.00 mmol). Purification was achieved by column chromatography with $CHCl_3$ (100%) to yield the compound-**13e** as a bluish green solid (0.27 g, 85%).

m.p: 189-90 °C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 3.93 (6H, s, 2 x -OC**H$_3$**), 6.43 (1H, d, *J* = 1.0 Hz, H-6), 6.57 (1H, d, *J* = 1.0 Hz, H-8), 7.18 (2H, app.t, *J* = 8.0 Hz, H-3',5'), 7.49 (1H, s, H-3), 7.92 (2H, d, *J* = 5.0 Hz, H-2',6'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 55.93 (2 x -O**C**H$_3$), 92.83 (C8), 97.10 (C6), 116.13 (C3', C5'), 117.69 (C10), 122.54 (C3), 127.20 (C1'), 128.17 (C2', C6'), 148.76 (C2), 155.75 (C9), 161.58 (C7), 164.52 (C4', $J_{C\text{-}F}$ = 253 Hz), 164.30 (C5), 200.81 (**C**=S); **IR ν_{max} [cm^{-1}]:** 1297 (C=S, ν, m), 1220 (-OCH_3, ν, m) 1100 (C-O, ν, m); ***m/z* (FTMS+ESI):** M+H ($C_{17}H_{14}O_3FS$) requires 317.0642, found 317.0643. **HPLC purity:** 99.2%, RT-14.3 min at 258 nm.

1.3.75 Synthesis of 2-(4-fluorophenyl)-5,7-dihydroxy-4*H*-chromene-4-thione (13f)*

The titled compound was synthesised according to the general procedure-**F** using 2-(4-fluorophenyl)-5,7-dimethoxy-4*H*-chromene-4-thione (**13e**) (0.10 g, 0.32 mmol). Purification was achieved by column chromatography with $CHCl_3$: Hexane: EtOAc (8:1:1 v/v/v) to yield the compound-**13f** as a yellow solid (0.07 g, 77%).

m.p: 258-59 °C; **^{1}H NMR:** (DMSO-d6, 400 MHz) 6.32 (1H, s, H-6), 6.61 (1H, s, H-8), 7.42 (2H, app.t, *J* = 8.0 Hz, H-3',5'), 7.58 (1H, s, H-3), 8.23 (2H, d, *J* = 6.0 Hz, H-2',6'), 11.30 (1H, s, OH), 13.62 (1H, s, OH); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 94.82 (C8), 100.76 (C6), 112.39 (C10), 116.35, 116.55 (C3', C5'), 117.20 (C3), 126.30 (C1'), 129.59, 129.70 (C2', C6'), 153.36 (C2), 154.14 (C9), 161.77 (C7), 164.33 (C4', $J_{C\text{-}F}$ = 240 Hz), 164.49 (C5), 195.95 (**C**=S); **IR ν_{max} [cm^{-1}]:** 1156 (C=S, ν, m), 1148 (C-O, ν, m), 3280 (OH, w, b); ***m/z* (FTMS+ESI):** M+H ($C_{15}H_{10}O_3FS$) requires 289.0329, found 289.0330. **HPLC purity:** 97.3%, RT-13.8 min at 258 nm.

1.3.76 Synthesis of 6-acetyl-2,3-dimethoxyphenyl 4-chlorobenzoate (14a)

The titled compound was synthesised according to the general procedure-**A** using gallacetophenone dimethyl ether [1-(2-hydroxy-3, 4-dimethoxyphenyl) ethanone] (1.0 g, 5.09 mmol) and 4-chlorobenzoyl chloride (1.34 g, 0.98 mL, 7.64 mmol). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**14a** as a white solid (1.55 g, 91%).

m.p: 104-05 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 2.48 (3H, s, -C**H$_3$**), 3.81 (3H, s, -OC**H$_3$**), 3.95 (3H, s, -OC**H$_3$**), 6.90 (1H, d, *J* = 9.0 Hz, H-4), 7.50 (2H, d, *J* = 8.5 Hz, H-3',5'), 7.68 (1H, d, *J* = 9.0 Hz, H-5), 8.17 (2H, d, *J* = 8.5 Hz, H-2',6'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 29.54 (**C**H_3), 56.20 (-O**C**H_3), 61.02 (-O**C**H_3), 109.17 (C4), 124.40 (C6), 126.16 (C5), 127.72 (C1'), 129.07 (C3', C5'), 131.77 (C2', C6'), 140.36 (C4'), 141.71 (C2), 144.26 (C1), 157.27 (C3), 164.12 (**C**OO-Ar), 195.68 (**C**OCH_3); **IR ν_{max} [cm^{-1}]:** 1734 (C=O, ν, m), 1088 (O-C=O, ν, m), 1673 (C=O, ν, m), 1264 (-OCH_3, ν, s); ***m/z* (FTMS+ESI):** M+H ($C_{17}H_{16}O_5Cl$) requires 335.0681, found 335.0677.

1.3.77 Synthesis of 1-(4-chlorophenyl)-3-(2-hydroxy-3,4-dimethoxyphenyl) propa-ne-1,3-dione (14b)

The titled compound was synthesised according to the general procedure-**B** using 6-acetyl-2,3-dimethoxyphenyl 4-chlorobenzoate (**14a**) (1.0 g, 2.99 mmol). The crude product was washed with acetic acid to obtain compound-**14b** as a yellow solid (0.80 g, 80%). The product formation was confirmed by ^{1}H NMR spectroscopic analysis.

^{1}H NMR: ($CDCl_3$, 400 MHz) [The compound exists as a mixture of keto-enol tautomers] δ 3.82-3.95 (8H, 2 x -OC**H$_3$**, C**H$_2$**), 6.52 (1H, d, *J* = 9.0 Hz, H-5), 6.71 (1H, =C**H** of enol form), 7.46 (1H, d, *J* = 8.0 Hz, H-6), 7.86 (2H, d, *J* = 8.0 Hz, H-3',5'), 8.18 (2H, d, *J* = 8.0 Hz, H-2',6'), 12.22 (1H, s, OH), 12.27 (1H, s, OH of enol form).

1.3.78 Synthesis of 2-(4-chlorophenyl)-7,8-dimethoxy-4*H*-chromen-4-one (14c)*

The titled compound was synthesised according to the general procedure-**C** using 1-(4-chlorophenyl)-3-(2-hydroxy-3,4-dimethoxyphenyl)propane-1,3-dione (**14b**) (0.75 g, 2.24 mmol). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**14c** as a pale white solid (0.62 g, 87%).

m.p: 203-06 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 4.01 (3H, s, -OC**H$_3$**), 4.04 (3H, s, -OC**H$_3$**), 6.74 (1H, s, H-3), 7.06 (1H, d, *J* = 9.0 Hz, H-6), 7.51 (2H, d, *J* = 8.0 Hz, H-2',6'), 7.90 (2H, d, *J* = 8.0 Hz, H-3',5'), 7.96 (1H, d, *J* = 9.0 Hz, H-5); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 56.56 (-O**C**H_3), 61.74 (-O**C**H_3), 107.09 (C3), 110.04 (C6), 118.62 (C10), 121.13 (C5), 127.53 (C3'), 129.47 (C5'), 130.36 (C1'), 136.96 (C4'), 137.89 (C8), 150.70 (C9), 156.72 (C7), 162.97 (C2), 178.09 (**C=**O, C4); **IR ν_{max} [cm^{-1}]:** 1641 (C=O, ν, s), 1288 (-OCH_3, ν, s) 1089 (C-O, ν, m); ***m/z* (FTMS+ESI):** M+H ($C_{17}H_{14}O_4Cl$) requires 317.0575, found 317.0575. **HPLC purity:** 100%, RT-13.6 min at 258 nm.

1.3.79 Synthesis of 2-(4-chlorophenyl)-7,8-dihydroxy-4*H*-chromen-4-one (14d)*

The titled compound was synthesised according to the general procedure-**D** using 2-(4-chlorophenyl)-7,8-dimethoxy-4*H*-chromen-4-one (**14c**) (0.15 g, 0.47 mmol). Purification was achieved by column chromatography with EtOAc (100%) to yield the compound-**14d** as a pale yellow solid (0.12 g, 87%).

m.p: 272-76 ^{o}C; **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 6.92 (1H, s, H-3), 6.95 (1H, d, *J* = 9.0 Hz, H-6), 7.39 (1H, d, *J* = 8.0 Hz, H-5), 7.64 (2H, d, *J* = 8.0 Hz, H-2',6'), 8.18 (2H, d, *J* = 8.0 Hz, H-

2',6'), 9.60 (1H, s, OH), 10.35 (1H, s, OH); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 114.11 (C3), 115.08 (C10), 116.85 (C6), 128.15 (C5), 129.07 (C3'), 130.31 (C5'), 133.33 (C1'), 136.33 (C8), 146.82 (C4'), 150.70 (C9), 160.61 (C7), 176.92 (C2), 187.60 (**C**=O); **IR ν_{max} [cm^{-1}]:** 1619 (C=O, ν, s), 1092 (C-O, ν, m), 3406 (OH, w, b); ***m/z* (FTMS+ESI):** M+H ($C_{15}H_{10}O_4Cl$) requires 289.0262, found 289.0263. **HPLC purity:** 98.0%, RT-11.5 min at 258 nm.

1.3.80 Synthesis of 2-(4-chlorophenyl)-7,8-dimethoxy-4*H*-chromene-4-thione (14e)*

The titled compound was synthesised according to the general procedure-**E** using 2-(4-chlorophenyl)-7,8-dimethoxy-4*H*-chromen-4-one (**14c**) (0.30 g, 0.95 mmol). Purification was achieved by column chromatography with $CHCl_3$ (100%) to yield the compound-**14e** as a pale green solid (0.26 g, 83%).

m.p: 245-46 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 4.02, 4.03 (6H, s, 2 x -OC**H$_3$**), 7.08 (1H, d, *J* = 9.0 Hz, H-6), 7.51 (2H, d, *J* = 8.0 Hz, H-2',6'), 7.65 (1H, s, H-3), 7.95 (2H, d, *J* = 9.0 Hz, H-3',5'), 8.35 (2H, d, *J* = 9.0 Hz, H-5); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 56.54 (-O**C**H$_3$), 61.72 (-O**C**H$_3$), 111.15 (C6), 119.09 (C3), 124.17 (C5), 125.50 (C10), 127.73 (C3', C5'), 129.61 (C2', C6'), 129.80 (C1'), 136.92 (C4'), 138.09 (C8), 146.13 (C9), 152.55 (C7), 157.35 (C2), 201.29 (**C**=S); **IR ν_{max} [cm^{-1}]:** 1289 (C=S, ν, s), 1085 (-OCH_3, ν, m) 1042 (C-O, ν, m); ***m/z* (FTMS+ESI):** M+H ($C_{17}H_{14}O_3ClS$) requires 333.0347, found 333.0347. **HPLC purity:** 98.0%, RT-15.2 min at 258 nm.

1.3.81 Synthesis of 2-(4-chlorophenyl)-7,8-dihydroxy-4*H*-chromene-4-thione (14f)*

The titled compound was synthesised according to the general procedure-**F** using 2-(4-chlorophenyl)-7,8-dimethoxy-4*H*-chromene-4-thione (**14e**) (0.10 g, 0.30 mmol). Purification was achieved by column chromatography with $CHCl_3$: Hexane: EtOAc (8:1:1 v/v/v) to yield the compound-**14f** as an orange red solid (0.070 g, 77%).

m.p: 229-32 ^{o}C; **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 7.05 (1H, d, *J* = 9.0 Hz, H-6), 7.57 (2H, d, *J* = 9.0 Hz, H-2',6'), 7.76 (1H, s, H-3), 7.85 (1H, d, *J* = 9.0 Hz, H-5), 8.28 (2H, d, *J* = 8.0 Hz, H-3',5'), 9.68 (1H, s, OH), 10.64 (1H, s, OH); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 115.73 (C5), 117.78 (C6), 118.50 (C3), 123.91 (C10), 128.58 (C3', C5'), 129.27 (C2', C6'), 129.67 (C1'), 132.98 (C8), 136.64 (C4'), 142.36 (C9), 151.77 (C7), 152.09 (C2), 199.85 (**C**=S); **IR ν_{max} [cm^{-1}]:** 1282 (C=S, ν, s), 1190 (C-O, ν, m), 3504 (OH, w, s); ***m/z* (FTMS+ESI):** M+H ($C_{15}H_{10}O_3ClS$) requires 305.0034, found 305.0035. **HPLC purity:** 95.9%, RT-13.4 min at 258 nm.

1.3.82 Synthesis of 2-acetyl-3,5-dimethoxyphenyl 4-chlorobenzoate (15a)

The titled compound was synthesised according to the general procedure-**A** using phloroacetophenone dimethylether [1-(2-hydroxy-4,6-dimethoxyphenyl)ethanone] (1.0 g, 5.09 mmol) and 4-chlorobenzoyl chloride (1.34 g, 0.98 mL, 7.64 mmol). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**15a** as a white solid (1.56 g, 91%).

m.p: 124-26 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 2.47 (3H, s, C**H$_3$**), 3.83 (3H, s, -OC**H$_3$**), 3.87 (3H, s, -OC**H$_3$**), 6.35 (1H, d, *J* = 2.0 Hz, H-4), 6.41 (1H, d, *J* = 2.0 Hz, H-6), 7.46 (2H, d, *J* = 8.5 Hz, H-3',5'), 8.15 (2H, d, *J* = 8.5 Hz, H- 2',6'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 31.61 (-**C**H$_3$), 55.68 (-O**C**H$_3$), 55.96 (-O**C**H$_3$), 96.67 (C6), 100.30 (C4), 117.06 (C2), 127.81 (C1'), 128.95 (C3', C5'), 131.67 (C2', C6'), 140.35 (C4'), 149.78 (C1), 159.44 (C5), 162.55 (C3), 164.49 (**C**OO-Ar), 199.45 (**C**OCH$_3$); **IR ν_{max} [cm^{-1}]:** 1679 (C=O, ν, m), 1116 (O-C=O, ν, m), 1606 (C=O, ν, m), 1250 (-OCH$_3$, ν, s); ***m/z* (FTMS+ESI):** M+H ($C_{17}H_{16}O_5Cl$) requires 335.0681, found 335.0680.

1.3.83 Synthesis of 1-(4-chlorophenyl)-3-(2-hydroxy-4,6-dimethoxyphenyl)pro pane-1,3-dione (15b)

The titled compound was synthesised according to the general procedure-**B** using 2-acetyl-3,5-dimethoxyphenyl 4-chlorobenzoate (**15a**) (1.0 g, 2.98 mmol). The crude product was washed with acetic acid to obtain compound-**15b** as a yellow solid (0.85 g, 85%). The product formation was confirmed by ^{1}H NMR spectroscopic analysis.

^{1}H NMR: ($CDCl_3$, 400 MHz) [The compound exists as a mixture of keto-enol tautomers] δ 3.48 (3H, s, -OCH$_3$), 3.81 (3H, s, -OCH$_3$), 4.51 (C**H$_2$**), 5.84 (1H, s. H-5), 5.99 (1H, s, H-3), 7.29 (1H, s, -C**H** of enol form), 7.43 (2H, d, *J* = 8.0 Hz, H-3',5'), 7.81 (2H, d, *J* = 8.0 Hz, H- 2',6'), 13.38 (1H, s, OH), 13.66 (1H, s, OH of enol form).

1.3.84 Synthesis of 2-(4-chlorophenyl)-5,7-dimethoxy-4*H*-chromen-4-one (15c)

The titled compound was synthesised according to the general procedure-**C** using 1-(4-chlorophenyl)-3-(2-hydroxy-4,6-dimethoxyphenyl)propane-1,3-dione (**15b**) (0.70 g, 2.09 mmol). Purification was achieved by column chromatography with $CHCl_3$: Hexane: EtOAc (8:1:1 v/v/v) to yield the compound-**15c** as a white solid (0.56 g, 66%).

m.p: 188-92 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 3.92 (3H, s, -OC**H$_3$**), 3.96 (3H, s,-OC**H$_3$**), 6.39 (1H, s, H-6), 6.56 (1H, s, H-8), 6.65 (1H, s, H-3), 7.47 (2H, d, *J* = 8.0 Hz, H-2',6'), 7.86 (2H, d, *J* = 8.0 Hz, H-3',5'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 55.80 (-O**C**H$_3$), 56.48 (-O**C**H$_3$), 92.81 (C8), 96.29 (C6), 109.22 (C3), 127.21 (C3',5',1'), 129.27 (C2', C6'), 130.05 (C10), 137.39 (C4'), 159.52 (C9), 159.83 (C5), 160.96 (C2), 164.18 (C7), 177.41 (**C=**O); **IR ν_{max} [cm^{-1}]:** 1645 (C=O, ν, s), 11955 (-OCH$_3$, ν, s), 1118 (C-O, ν, m); ***m/z* (FTMS+ESI):** M+H ($C_{17}H_{14}O_4Cl$) requires 317.0575, found 317.0575. **HPLC purity:** 99.8%, RT-13.4 min at 258 nm.

1.3.85 Synthesis of 2-(4-chlorophenyl)-5,7-dihydroxy-4*H*-chromen-4-one (15d)

The titled compound was synthesised according to the general procedure-**D** using 2-(4-fluorophenyl)-5,7-dimethoxy-4*H*-chromen-4-one (**15c**) (0.15 g, 0.50 mmol). Purification was achieved by column chromatography with EtOAc (100%) to yield the compound-**15d** as a white solid (0.08 g, 61%).

m.p: 294-96 ^{o}C; **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 6.21 (1H, s, H-6), 6.52 (1H, s, H-8), 7.01 (1H, s, H-3), 7.64 (2H, d, *J* = 8.0 Hz, H-2',6'), 8.10 (2H, d, *J* = 8.0 Hz, H-3',5'), 10.93 (1H, s, OH),

12.76 (1H, s, OH); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 94.04 (C8), 99.16 (C6), 105.55 (C3, C10), 128.27 (C3', C5'), 129.35 (C2', C6'), 129.57 (C1'), 136.93 (C4'), 157.39 (C9), 161.32 (C5), 162.11 (C2), 164.47 (C7), 181.88 (**C**=O); **IR ν_{max} [cm^{-1}]:** 1652 (C=O, v, s), 1184 (C-O, v, m), 3348 (OH, w, b); ***m/z* (FTMS+ESI):** M+H ($C_{15}H_{10}O_4Cl$) requires 289.0262, found 289.0264. **HPLC purity:** 98.3%, RT-13.5 min at 258 nm.

1.3.86 Synthesis of 2-(4-chlorophenyl)-5,7-dimethoxy-4*H*-chromene-4-thione (15e)*

The titled compound was synthesised according to the general procedure-**E** using 2-(4-chlorophenyl)-5,7-dimethoxy-4*H*-chromen-4-one (**15c**) (0.30 g, 0.90 mmol). Purification was achieved by column chromatography with $CHCl_3$ (100%) to yield the compound-**15e** as a bluish green solid (0.26 g, 83%).

m.p: 170-72 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 3.93 (6H, s, 2 x -OC**H$_3$**), 6.43 (1H, d, *J* = 2.0 Hz, H-6), 6.57 (1H, d, *J* = 3.0 Hz, H-8), 7.46 (2H, d, *J* = 9.0 Hz, H-3',5'), 7.50 (1H, s, H-3), 7.84 (2H, d, *J* = 9.0 Hz, H-2',6'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 55.88, 55.90 (2 x -O**C**H$_3$), 92.73 (C8), 96.91 (C6), 117.87 (C10), 122.35 (C3), 127.33 (C3', C5'), 129.38 (C2', C6'), 129.52 (C1'), 137.45 (C4'), 148.54 (C2), 155.63 (C10), 161.60 (C7), 163.95 (C5), 200.41 (**C**=S); **IR ν_{max} [cm^{-1}]:** 1263 (C=S, v, m), 1200 (-OCH_3, v, m) 1107 (C-O, v, m); ***m/z* (FTMS+ESI):** M+H ($C_{17}H_{14}O_3ClS$) requires 333.0347, found 333.0339. **HPLC purity:** 95.4%, RT-14.8 min at 258 nm.

1.3.87 Synthesis of 2-(4-chlorophenyl)-5,7-dihydroxy-4*H*-chromene-4-thione (15f)*

The titled compound was synthesised according to the general procedure-**F** using 2-(4-chlorophenyl)-5,7-dimethoxy-4*H*-chromene-4-thione (**15e**) (0.10 g, 0.32 mmol). Purification was achieved by column chromatography with $CHCl_3$: Hexane: EtOAc (8:1:1 v/v/v) to yield the compound-**15f** as a bright yellow solid (0.07 g, 77%).

m.p: 249-52 ^{o}C; **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 6.32 (1H, s, H-6), 6.60 (1H, s, H-8), 7.59 (1H, s, H-3), 7.62 (2H, d, *J* = 8.0 Hz, H-2',6'), 8.16 (2H, d, *J* = 8.0 Hz, H-3',5'), 11.29 (1H, s, OH), 13.59 (1H, s, OH); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 94.62 (C8), 100.77 (C6), 112.54 (C10), 117.35 (C3), 128.62 (C3', C5', C1'), 129.44 (C2', C6'), 137.12 (C4'), 153.09 (C2), 154.01 (C9), 161.90 (C7), 164.66 (C5), 196.00 (**C**=S); **IR ν_{max} [cm^{-1}]:** 1189 (C=S, v, m), 1150 (C-O, v, m), 3356 (OH, w, b); ***m/z* (FTMS+ESI):** M+H ($C_{15}H_{10}O_3ClS$) requires 305.0034, found 305.0034. **HPLC purity:** 98.7%, RT-14.6 min at 258 nm.

1.3.88 Synthesis of 6-acetyl-2,3-dimethoxyphenyl 4-bromobenzoate (16a)

The titled compound was synthesised according to the general procedure-**A** using gallacetophenone dimethyl ether [1-(2-hydroxy-3, 4-dimethoxyphenyl) ethanone] (1.0 g, 5.09 mmol) and 4-bromobenzoyl chloride (1.68 g, 7.64 mmol). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**16a** as a white solid (1.70 g, 88%).

m.p: 117-19 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 2.48 (3H, s, -C**H$_3$**), 3.81 (3H, s, -OC**H$_3$**), 3.96 (3H, s, -OC**H$_3$**), 6.90 (1H, d, *J* = 8.9 Hz, H-4), 7.67 (2H, d, *J* = 8.0 Hz, H-3',5',5), 8.09 (2H, d, *J* = 8.1 Hz, H-2',6'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 29.53 (**C**H_3), 56.20 (-O**C**H_3), 61.02 (-O**C**H_3), 109.18 (C4), 124.37 (C6), 126.17 (C5), 128.18 (C4'), 129.00 (C1'), 131.88 (C3', C5'), 132.07 (C2', C6'), 141.58 (C2), 144.14 (C1), 157.27 (C3), 164.11(**C**OO-Ar), 195.65 (**C**OCH_3); **IR ν_{max} [cm^{-1}]:** 1727 (C=O, v, m), 1087 (O-C=O, v, m), 1669 (C=O, v, m), 1263 (-OCH_3, v, s); ***m/z* (FTMS+ESI):** M+H ($C_{17}H_{16}O_5Br$) requires 379.0176, found 379.0177.

1.3.89 Synthesis of 1-(4-bromophenyl)-3-(2-hydroxy-3,4-dimethoxyphenyl) prop ane-1,3-dione (16b)

The titled compound was synthesised according to the general procedure-**B** using 6-acetyl-2,3-dimethoxyphenyl 4-bromobenzoate (**16a**) (1.0 g, 2.63 mmol). The crude product was washed with acetic acid to obtain compound-**16b** as a yellow solid (0.85 g, 85%). The product formation was confirmed by ^{1}H NMR spectroscopic analysis.

^{1}H NMR: ($CDCl_3$, 400 MHz) [The compound exists as a mixture of keto-enol tautomers] δ 3.81-3.95 (8H, 2 x -OC**H$_3$**, C**H$_2$**), 6.53 (1H, d, *J* = 9.0 Hz, H-5), 6.71 (1H, =C**H** of enol form), 6.90 (1H, d, *J* = 9.0 Hz, H-6), 7.78 (2H, d, *J* = 8.0 Hz, H-3',5'), 8.00 (1H, d, *J* = 9.0 Hz, H-2',6'), 12.21 (1H, s, OH), 12.27 (1H, s, OH of enol form).

1.3.90 Synthesis of 2-(4-bromophenyl)-7,8-dimethoxy-4*H*-chromen-4-one (16c)*

The titled compound was synthesised according to the general procedure-**C** using 1-(4-bromophenyl)-3-(2-hydroxy-3,4-dimethoxyphenyl)propane-1,3-dione (**16b**) (0.75 g, 1.97 mmol). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**16c** as a pale white solid (0.55 g, 90%).

m.p: 197-99 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 4.01 (3H, s, -OC**H$_3$**), 4.04 (3H, s, -OC**H$_3$**), 6.75 (1H, s, H-3), 7.06 (1H, d, *J* = 9.0 Hz, H-6), 7.67 (2H, d, *J* = 8.0 Hz, H-2',6'), 7.83 (2H, d, *J* = 8.0 Hz, H-3',5'), 7.96 (1H, d, *J* = 9.0 Hz, H-5); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 56.64 (-O**C**H_3), 61.83 (-O**C**H_3), 107.08 (C3), 110.07 (C6), 118.73 (C10), 121.19 (C5), 126.27 (C4'), 126.27 (C2', C6'), 130.90 (C1), 132.47 (C3', C5'), 137.10 (C8), 150.62 (C9), 156.81 (C7), 161.97 (C2), 177.95 (**C=**O, C4); **IR ν_{max} [cm^{-1}]:** 1652 (C=O, v, s), 1289 (-OCH_3, v, s) 1094 (C-O, v, m); ***m/z* (FTMS+ESI):** M+H ($C_{17}H_{14}O_4Br$) requires 361.0070, found 361.0072. **HPLC purity:** 99.7%, RT-14.3 min at 258 nm.

1.3.91 Synthesis of 2-(4-bromophenyl)-7,8-dihydroxy-4*H*-chromen-4-one (16d)*

The titled compound was synthesised according to the general procedure-**D** using 2-(4-bromophenyl)-7,8-dimethoxy-4*H*-chromen-4-one (**16c**) (0.15 g, 0.42 mmol). Purification was achieved by column chromatography with EtOAc (100%) to yield the compound-**16d** as a pale yellow solid (0.08 g, 58%).

m.p: 285-90 ^{o}C; **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 6.87 (1H, s, H-3), 6.95 (1H, d, *J* = 6.0 Hz, H-6), 7.40 (1H, d, *J* = 10.5 Hz, H-5), 7.76 (2H, d, *J* = 7.0 Hz, H-2',6'), 8.06 (1H, d, *J* = 10.5 Hz, H-3',5'); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 106.22 (C3), 114.17 (C6), 115.36 (C5), 116.64 (C10), 125.41 (C4'), 128.25 (C2', C6'), 130.53 (C1'), 132.00 (C3', C5'), 133.18 (C8), 146.62 (C9), 150.73 (C7), 160.88 (C2), 177.15 (**C=**O); **IR ν_{max} [cm^{-1}]:** 1618 (C=O, ν, s), 1066 (C-O, ν, m), 3407 (OH, w, b); ***m/z* (FTMS+ESI):** M+H ($C_{15}H_{10}O_4Br$) requires 332.9757, found 332.9759. **HPLC purity:** 98.8%, RT-11.9 min at 258 nm.

1.3.92 Synthesis of 2-(4-bromophenyl)-7,8-dimethoxy-4*H*-chromene-4-thione (16e)*

The titled compound was synthesised according to the general procedure-**E** using 2-(4-bromophenyl)-7,8-dimethoxy-4*H*-chromen-4-one (**16c**) (0.30 g, 0.83 mmol). Purification was achieved by column chromatography with $CHCl_3$ (100%) to yield the compound-**16e** as a pale green solid (0.26 g, 82%).

m.p: 216-18 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 4.03 (6H, s, 2 x -OC**H$_3$**), 7.08 (1H, d, *J* = 9.0 Hz, H-6), 7.66 (1H, s, H-3), 7.68 (2H, d, *J* = 10.5 Hz, H-2',6'), 7.88 (2H, d, *J* = 8.0 Hz, H-3',5'), 8.34 (2H, d, *J* = 9.0 Hz, H-5); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 56.62 (-O**C**H$_3$), 61.77 (-O**C**H$_3$), 111.33 (C6), 119.15 (C3), 124.10 (C5), 125.44 (C4'), 126.58 (C2', C6'), 127.92 (C1'), 130.39 (C3', C5'), 137.26 (C8). 146.22 (C9), 152.51 (C7), 157.27 (C2), 201.50 (**C**=S); **IR ν_{max} [cm^{-1}]:** 1289 (C=S, ν, s), 1091 (-OCH_3, ν, m) 1041 (C-O, ν, m); ***m/z* (FTMS+ESI):** M+H ($C_{17}H_{14}O_3BrS$) requires 378.9821, found 378.9819. **HPLC purity:** 97.8%, RT-15.8 min at 258 nm.

1.3.93 Synthesis of 2-(4-bromophenyl)-7,8-dihydroxy-4*H*-chromene-4-thione (16f)*

The titled compound was synthesised according to the general procedure-**F** using 2-(4-bromophenyl)-7,8-dimethoxy-4*H*-chromene-4-thione (**16e**) (0.10 g, 0.27 mmol). Purification was achieved by column chromatography with $CHCl_3$: Hexane: EtOAc (8:1:1 v/v/v) to yield the compound-**16f** as an orange solid (0.063 g, 68%).

m.p: 235-37 ^{o}C; **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 7.03 (1H, d, *J* = 10.0 Hz, H-6), 7.74 (s, H3), 7.79 (2H, d, *J* = 9.0 Hz, H-2',6'), 7.83 (1H, d, *J* = 10.0 Hz, H-5), 8.17 (2H, d, *J* = 9.0 Hz, H-3',5'), 9.7 (1H, s, OH), 10.66 (1H, s, OH); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 115.83 (C6), 117.65 (C4'), 118.52 (C3), 123.98 (C5), 125.63 (C10), 128.75 (C2', C6'), 129.96 (C1'), 132.22 (C3', C5'), 142.36 (C7), 151.78 (C9), 152.23 (C2), 206.53 (**C=**S); **IR ν_{max} [cm^{-1}]:** 1281 (C=S, ν, s), 1118 (C-O, ν, m), 3503 (OH, w, s); ***m/z* (FTMS+ESI):** M+H ($C_{15}H_{10}O_3BrS$) requires 350.9508, found 350.9507. **HPLC purity:** 95.0%, RT-13.7 min at 258 nm.

1.3.94 Synthesis of 2-acetyl-3,5-dimethoxyphenyl 4-bromobenzoate (17a)

The titled compound was synthesised according to the general procedure-**A** using phloroacetophenone dimethylether [1-(2-hydroxy-4,6-dimethoxyphenyl)ethanone] (1.0 g, 5.09 mmol) and 4-bromobenzoyl chloride (1.68 g, 7.64 mmol). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**17a** as a white solid (1.62 g, 85%).

m.p: 127-28 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 2.47 (3H, s, -C**H$_3$**), 3.82 (3H, s, -OC**H$_3$**), 3.87 (3H, s, -OC**H$_3$**), 6.35 (1H, s, H-4), 6.41 (1H, s, H-6), 7.63 (2H, d, *J* = 8.0 Hz, H-3',5'), 7.99 (2H, d, *J* = 8.0 Hz, H- 2',6'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 31.97 (-**C**H$_3$), 55.68 (-O**C**H$_3$), 55.94 (-O**C**H$_3$), 96.75 (C6), 100.11 (C4), 116.97 (C2), 128.17 (C4'), 128.90 (C1'), 131.76 (C3', C5'), 131.94 (C2', C6'), 149.78 (C1), 159.39 (C5), 162.34 (C3), 164.41 (**C**OO-Ar), 199.10 (**C**OCH$_3$); **IR ν_{max} [cm^{-1}]:** 1728 (C=O, ν, m), 1103 (O-C=O, ν, m), 1606 (C=O, ν, m), 1250 (-OCH$_3$, ν, s); ***m/z* (FTMS+ESI):** M+H ($C_{17}H_{16}O_5Br$) requires 379.0176, found 379.0177.

1.3.95 Synthesis of 1-(4-bromophenyl)-3-(2-hydroxy-4,6-dimethoxyphenyl)pro pane-1,3-dione (17b)

The titled compound was synthesised according to the general procedure-**B** using 2-acetyl-3,5-dimethoxyphenyl 4-bromobenzoate (**17a**) (1.0 g, 3.14 mmol). The crude product was washed with acetic acid to obtain compound-**17b** as a yellow solid (0.75 g, 75%). The product formation was confirmed by ^{1}H NMR spectroscopic analysis.

^{1}H NMR: ($CDCl_3$, 400 MHz) [The compound exists as a mixture of keto-enol tautomers] δ 3.81-3.92 (8H, 2 x -OCH$_3$, C**H$_2$**), 5.84 (1H, =C**H** of enol form), 5.98 (1H, s. H-3), 6.09 (1H, s, H-5), 7.59 (2H, d, *J* = 8.0 Hz, H-3', 5'), 7.74 (2H, d, *J* = 8.0 Hz, H- 2', 6'), 13.38 (1H, s, OH), 13.66 (1H, s, OH of enol form).

1.3.96 Synthesis of 2-(4-bromophenyl)-5,7-dimethoxy-4*H*-chromen-4-one (17c)

The titled compound was synthesised according to the general procedure-**C** using 1-(4-bromophenyl)-3-(2-hydroxy-4,6-dimethoxyphenyl)propane-1,3-dione (**17b**) (0.70 g, 1.84 mmol). Purification was achieved by column chromatography with $CHCl_3$: Hexane: EtOAc (8:1:1 v/v/v) to yield the compound-**17c** as a white solid (0.55 g, 82%).

m.p: 198-201 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 3.91 (3H, s, -OC**H$_3$**), 3.96 (3H, s,-OC**H$_3$**), 6.38 (1H, s, H-6), 6.56 (1H, s, H-8), 6.65 (1H, s, H-3), 7.63 (2H, d, *J* = 8.0 Hz, H-2',6'), 7.73 (2H, d, *J* = 8.0 Hz, H-3',5'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 55.86 (-O**C**H$_3$), 56.62 (-O**C**H$_3$), 92.69 (C8), 96.39 (C6), 109.29 (C3), 125.89 (C4'), 127.50 (C2', C6'), 130.57 (C10), 132.27 (C3', C5', C1'), 159.60 (C9), 159.84 (C5), 160.97 (C2), 164.19 (C2), 165.77 (C7), 177.38 (**C=**O); **IR ν_{max} [cm^{-1}]:** 1638 (C=O, ν, s), 1217 (-OCH$_3$, ν, s), 1103 (C-O, ν, m); ***m/z* (FTMS+ESI):** M+H ($C_{17}H_{14}O_4Br$) requires 361.0070, found 361.0064. **HPLC purity:** 99.4%, RT-13.9 min at 258 nm.

1.3.97 Synthesis of 2-(4-bromophenyl)-5,7-dihydroxy-4*H*-chromen-4-one (17d)

The titled compound was synthesised according to the general procedure-**D** using 2-(4-bromophenyl)-5,7-dimethoxy-4*H*-chromen-4-one (**17c**) (0.15 g, 0.41 mmol). Purification was achieved by column chromatography with EtOAc (100%) to yield the compound-**17d** as a white solid (0.11 g, 80%).

m.p: 265-67 ^{o}C; **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 6.21 (1H, s, H-6), 6.51 (1H, s, H-8), 7.01 (1H, s, H-3), 7.58 (2H, d, *J* = 9.0 Hz, H-2',6'), 8.01 (2H, d, *J* = 8.0 Hz, H-3',5'), 10.96 (1H, s, OH),

12.78 (1H, s, OH) ; **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 94.23 (C8), 99.14 (C6), 103.93 (C10), 105.61 (C3), 125.81 (C4'), 128.36 (C2', C6'), 130.04 (C1'), 132.11 (C3', C5'), 157.31 (C9), 161.35 (C5), 162.10 (C2), 164.44 (C7), 181.79 (**C**=O); **IR ν_{max} [cm^{-1}]:** 1651 (C=O, ν, s), 1163 (C-O, ν, m), 3350 (OH, w, b); ***m/z* (FTMS+ESI):** M+H ($C_{15}H_{10}O_4Br$) requires 332.9757, found 332.9759. **HPLC purity:** 96.5%, RT-13.8 min at 258 nm.

1.3.98 Synthesis of 2-(4-bromophenyl)-5,7-dimethoxy-4*H*-chromene-4-thione (17e)*

The titled compound was synthesised according to the general procedure-**E** using 2-(4-bromophenyl)-5,7-dimethoxy-4*H*-chromen-4-one (**17c**) (0.30 g, 0.83 mmol). Purification was achieved by column chromatography with $CHCl_3$ (100%) to yield the compound-**17e** as a pale green solid (0.25 g, 80%).

m.p: 165-68 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 3.93 (6H, s, 2 x -OC**H$_3$**), 6.43 (1H, s, H-6), 6.57 (1H, s, H-8), 7.51 (1H, s, H-3), 7.63 (2H, d, *J* = 7.0 Hz, H-2',6'), 7.78 (2H, d, *J* = 7.0 Hz, H-3',5'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 55.86 (2 x -O**C**H$_3$), 92.84 (C6, C8), 96.84 (C10), 122.39 (C3), 125.82 (C4'), 127.54 (C2', C6'), 130.20 (C1'), 132.49 (C3', C5'), 148.50 (C2), 155.94 (C9), 161.66 (C7), 163.95 (C5), 200.55 (**C**=S); **IR ν_{max} [cm^{-1}]:** 1265 (C=S, ν, m), 1207 (-OCH_3, ν, m) 1044 (C-O, ν, m); ***m/z* (FTMS+ESI):** M+H ($C_{17}H_{14}O_3BrS$) requires 378.9821, found 378.9814. **HPLC purity:** 95.2%, RT-15.1 min at 258 nm.

1.3.99 Synthesis of 2-(4-bromophenyl)-5,7-dihydroxy-4*H*-chromene-4-thione (17f)*

The titled compound was synthesised according to the general procedure-**F** using 2-(4-bromophenyl)-5,7-dimethoxy-4*H*-chromene-4-thione (**17e**) (0.10 g, 0.27 mmol). Purification was achieved by column chromatography with $CHCl_3$: Hexane: EtOAc (8:1:1 v/v/v) to yield the compound-**17f** as a yellow solid (0.07 g, 78%).

m.p: 250-52 ^{o}C; **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 6.33 (1H, s, H-6), 6.61 (1H, s, H-8), 7.60 (1H, s, H-3), 7.78 (2H, d, *J* = 10.0 Hz, H-2',6'), 8.09 (2H, d, *J* = 13.0 Hz, H-3',5'), 11.30 (1H, s, OH), 13.59 (1H, s, OH); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 94.83 (C8), 100.84 (C6), 112.39 (C10), 117.55 (C3), 126.19 (C4'), 128.70 (C2', C6'), 128.70 (C1'), 132.30 (C3', C5'), 153.24 (C2), 154.03 (C9), 161.85 (C7), 164.90 (C5), 206.65 (**C**=S); **IR ν_{max} [cm^{-1}]:** 1298 (C=S, ν, m), 1166 (C-O, ν, m), 3321 (OH, w, b); ***m/z* (FTMS+ESI):** M+H ($C_{15}H_{10}O_3BrS$) requires 350.9508, found 350.9508. **HPLC purity:** 97.7%, RT-14.9 min at 258 nm.

1.3.100 Synthesis of 6-acetyl-2,3-dimethoxyphenyl 4-cyanobenzoate (18a)

The titled compound was synthesised according to the general procedure-**A** using gallacetophenone dimethyl ether [1-(2-hydroxy-3, 4-dimethoxyphenyl) ethanone] (1.0 g, 5.09 mmol) and 4-cyanobenzoyl chloride (1.27 g, 7.64 mmol). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**18a** as a white solid (1.40 g, 85%).

m.p: 129-30 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 2.49 (3H, s, -C**H$_3$**), 3.82 (3H, s, -OC**H$_3$**), 3.96 (3H, s, -OC**H$_3$**), 6.91 (1H, d, *J* = 9.0 Hz, H-4), 7.68 (1H, d, *J* = 9.0 Hz, H-5), 7.83 (2H, d, *J* = 8.0 Hz, H-3',5'), 8.33 (2H, d, *J* = 8.0 Hz, H-2',6'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 29.81 (**C**H_3), 56.24 (-O**C**H_3), 61.11 (-O**C**H_3), 109.22 (C4), 116.94 (C4'), 118.00 (CN), 123.81 (C6), 126.46 (C5), 130.85 (C2', C6'), 132.45 (C3', C5'), 133.28 (C1'), 142.01 (C2), 144.58 (C1), 157.35 (C3), 163.91 (**C**OO-Ar), 195.56 (**C**OCH_3); **IR ν_{max} [cm^{-1}]:** 2232 (C≡N, m, s), 1736 (C=O, ν, m), 1084 (O-C=O, ν, m), 1672 (C=O, ν, m), 1261 (-OCH_3, ν, s); ***m/z* (FTMS+ESI):** M+H ($C_{18}H_{16}O_5N$) requires 326.1023, found 326.1023.

1.3.101 Synthesis of 4-(3-(2-hydroxy-3,4-dimethoxyphenyl)-3-oxopropanoyl) benzonitrile (18b)

The titled compound was synthesised according to the general procedure-**B** using 6-acetyl-2,3-dimethoxyphenyl 4-cyanobenzoate (**18a**) (1.0 g, 3.07 mmol). The crude product was washed with acetic acid to obtain compound-**18b** as a yellow solid (0.81 g, 81%). The product formation was confirmed by ^{1}H NMR spectroscopic analysis.

^{1}H NMR: ($CDCl_3$, 400 MHz) [The compound exists as a mixture of keto-enol tautomers] δ 3.91 (3H, s, -OC**H$_3$**), 3.96 (3H, s, -OC**H$_3$**), 4.5 (C**H$_2$**), 6.54 (1H, d, *J* = 9.0 Hz, H-5), 6.77 (1H, =C**H** of enol form), 7.55 (1H, d, *J* = 9.0 Hz, H-6), 7.77 (2H, d, *J* = 8.0 Hz, H-3',5'), 8.01 (2H, d, *J* = 8.0 Hz, H-2',6'), 12.12 (OH of enol form).

1.3.102 Synthesis of 4-(7,8-dimethoxy-4-oxo-4*H*-chromen-2-yl)benzonitrile (18c)*

4-(3-(2-Hydroxy-3,4-dimethoxyphenyl)-3-oxopropanoyl)benzonitrile (**18b**) (0.75 g, 2.30 mmol) was dissolved in $CHCl_3$ (7 mL), the reaction mixture was cooled to 0 ^{o}C and concentrated H_2SO_4 (2 mL) was added slowly under constant stirring. The reaction mixture was stirred at room temperature for 30 minutes and then quenched with water. The reaction mixture was extracted with EtOAc (2 x 10 mL), the organic layers were combined, dried over anhydrous $MgSO_4$ and concentrated *in vacuo* to obtain the crude product. Purification was achieved by column chromatography with $CHCl_3$: Hexane: EtOAc (8:1:1 v/v/v) to yield the compound-**18c** as a white solid (0.60 g, 85%).

m.p: 260-63 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 4.03 (3H, s, -OC**H$_3$**), 4.04 (3H, s, -OC**H$_3$**), 6.81 (1H, s, H-3), 7.09 (1H, d, *J* = 9.0 Hz, H-6), 7.84 (2H, d, *J* = 8.0 Hz, H-2',6'), 7.97 (1H, d, *J* = 9.0 Hz, H-5), 7.23 (2H, d, *J* = 8.0 Hz, H-3',5'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 56.51 (-O**C**H_3), 61.76 (-O**C**H_3), 108.56 (C3), 110.50 (C6), 114.97 (C4'), 118.03 (C10), 118.66 (C5), 126.70 (C2', C6'), 132.84 (C3', C5'), 135.94 (C1'), 137.11 (C8), 150.70 (C9), 157.31 (C7), 160.80 (C2), 177.70 (**C=**O, C4); **IR ν_{max} [cm^{-1}]:** 2228 (C≡N, m, s), 1638 (C=O, ν, s), 1291 (-OCH_3, ν, s) 1098 (C-O, ν, m); ***m/z* (FTMS+ESI):** M+H ($C_{18}H_{14}O_4N$) requires 308.0917, found 308.0918. **HPLC purity:** 99.5%, RT-12.8 min at 258 nm.

1.3.103 Synthesis of 4-(7,8-dihydroxy-4-oxo-4*H*-chromen-2-yl)benzonitrile (18d)

The titled compound was synthesised according to the general procedure-**D** using 4-(7,8-dimethoxy-4-oxo-4*H*-chromen-2-yl)benzonitrile (**18c**) (0.15 g, 0.48 mmol). Purification was achieved by column chromatography with EtOAc (100%) to yield the compound-**18d** as a pale yellow solid (0.09 g, 66%).

m.p: 319-21 ^{o}C; **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 6.97 (1H, d, *J* = 8.0 Hz, H-6), 7.03 (1H, s, H-3), 7.40 (1H, d, *J* = 8.0 Hz, H-5), 7.40 (2H, d, *J* = 8.0 Hz, H-2',6'), 8.33 (2H, d, *J* = 8.0 Hz, H-2',6'); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 107.82 (C3), 113.45 (C4'), 114.41 (C6), 115.20 (C5), 116.81 (CN), 118.36 (C10), 127.05 (C2', C6'), 132.88 (C3', C5'), 133.14 (C8), 135.75 (C1'), 146.82 (C9), 150.70 (C7), 159.64 (C2), 176.92 (**C=**O); **IR ν_{max} [cm^{-1}]:** 2233 (C≡N, m, s), 1607 (C=O, ν, s), 1159 (C-O, ν, m), 3400 (OH, w, b); ***m/z* (FTMS+ESI):** M+H ($C_{16}H_{10}O_4N$) requires 280.0604, found 280.0605. **HPLC purity:** 97.9%, RT-10.0 min at 258 nm.

1.3.104 Synthesis of 4-(7,8-dimethoxy-4-thioxo-4*H*-chromen-2-yl)benzonitrile (18e)*

The titled compound was synthesised according to the general procedure-**E** using 4-(7,8-dimethoxy-4-oxo-4*H*-chromen-2-yl)benzonitrile (**18c**) (0.30 g, 0.96 mmol). Purification was achieved by column chromatography with $CHCl_3$ (100%) to yield the compound-**18e** as a pale green solid (0.24 g, 76%).

m.p: 290-95 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 4.02 (3H, s, 2 x -OC**H$_3$**), 7.01 (1H, d, *J* = 9.0 Hz, H-6), 7.22 (2H, app.t, *J* = 8.5 Hz, H-3',5'), 7.64 (1H, s, H-3), 8.03 (2H, dd, *J* = 5.0 Hz, 5.0 Hz, H-2',6'), 8.35 (2H, d, *J* = 9.0 Hz, H-5); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 56.41 (-O**C**H$_3$), 61.49 (-O**C**H$_3$), 111.09 (C6), 116.50, 116.70 (C3', C5'), 118.85 (C3), 124.24 (C5, C10), 125.46 (C1'), 128.83 (C2', C6'), 136.92 (C9), 146.37 (C7), 152.98 (C2), 157.43 (C4'), 201.41 (**C**=S); **IR ν_{max} [cm^{-1}]:** 2226 (C≡N, m, s), 1290 (C=S, ν, s), 1177 (-OCH$_3$, ν, m) 1094 (C-O, ν, m); ***m/z* (FTMS+ESI):** M+H ($C_{18}H_{14}O_3NS$) requires 324.0689, found 324.0690. **HPLC purity:** 97.6%, RT-14.2 min at 258 nm.

1.3.105 Synthesis of 4-(7,8-dihydroxy-4-thioxo-4*H*-chromen-2-yl)benzonitrile (18f)*

The titled compound was synthesised according to the general procedure-**F** using 4-(7,8-dimethoxy-4-thioxo-4*H*-chromen-2-yl)benzonitrile (**18e**) (0.10 g, 0.31 mmol). Purification was achieved by column chromatography with $CHCl_3$: Hexane: EtOAc (8:1:1 v/v/v) to yield the compound-**18f** as a white solid (0.066 g, 72%).

m.p: 275-80 ^{o}C; **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 7.03 (1H, d, *J* = 10.0 Hz, H-6), 7.74 (s, H3), 7.79 (2H, d, *J* = 9.0 Hz, H-2',6'), 7.83 (1H, d, *J* = 10.0 Hz, H-5), 8.15 (2H, d, *J* = 9.0 Hz, H-3',5'); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 115.80 (C6), 117.78 (C4'), 118.55 (C3), 123.97 (CN) , 125.69 (C5), 127.1 (C10), 128.75 (C2', C6'), 130.08 (C8), 132.23 (C3', C5'), 133.09 (C1'), 142.16 (C9), 151.85 (C7), 152.36 (C2), 199.85 (**C=**S); **IR ν_{max} [cm^{-1}]:** 2226 (C≡N, m, s), 1298 (C=S, ν, s), 1177 (C-O, ν, m), 3334 (OH, w, s); ***m/z* (FTMS+ESI):** M+H ($C_{16}H_{10}O_3NS$) requires 296.0376, found 296.0378. **HPLC purity:** 95.6%, RT-12.5 min at 258 nm.

1.3.106 Synthesis of 2-acetyl-3,5-dimethoxyphenyl 4-cyanobenzoate (19a)

The titled compound was synthesised according to the general procedure-**A** using phloroacetophenone dimethylether [1-(2-hydroxy-4,6-dimethoxyphenyl)ethanone] (1.0 g, 5.09 mmol) and 4-cyanobenzoyl chloride (1.27 g, 7.64 mmol). Purification was achieved by column chromatography with Hexane: $CHCl_3$: EtOAc (3:6:1 v/v/v) to yield the compound-**19a** as a white solid (1.38 g, 84%).

m.p: 180-83 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 2.48 (3H, s, -C**H$_3$**), 3.84 (3H, s, -OC**H$_3$**), 3.89 (3H, s, -OC**H$_3$**), 6.35 (1H, s, H-4), 6.43 (1H, s, H-6), 7.79 (2H, d, *J* = 7.0 Hz, H-2',6'), 8.23 (2H, d, *J* = 7.0 Hz, H-3',5'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 32.06 (-**C**H$_3$), 55.72 (-O**C**H$_3$), 55.98 (-O**C**H$_3$), 96.91 (C6), 100.18 (C4), 116.50 (C2), 117.05 (C4'), 117.81 (CN), 130.75 (C2', C6'), 132.37 (C3', C5'), 133.25 (C1'), 149.84 (C1), 159.94 (C5), 162.61 (C3), 163.76 (**C**OO-Ar), 198.83 (**C**OCH$_3$); **IR ν_{max} [cm^{-1}]:** 2232 (C≡N, m, s), 1744 (C=O, v, m), 1064 (O-C=O, v, m), 1603 (C=O, v, m), 1249 (-OCH$_3$, v, s); ***m/z* (FTMS+ESI):** M+H ($C_{18}H_{16}O_5N$) requires 326.1023, found 326.1024.

1.3.107 Synthesis of 4-(3-(2-hydroxy-4,6-dimethoxyphenyl)-3-oxopropanoyl) benzonitrile (19b)

The titled compound was synthesised according to the general procedure-**B** using 2-acetyl-3,5-dimethoxyphenyl 4-cyanobenzoate (**19a**) (1.0 g, 3.10 mmol). The crude product was washed with acetic acid to obtain compound-**19b** as a yellow solid (0.74 g, 74%). The product formation was confirmed by ^{1}H NMR spectroscopic analysis.

^{1}H NMR: ($CDCl_3$, 400 MHz) [The compound was in its keto form] δ 3.82-3.93 (8H, s, 2 x -OCH$_3$, C**H$_2$**), 6.36 (1H, s, H-3), 6.43 (1H, s, H-5), 7.79 (2H, d, *J* = 7.0 Hz, H-3', 5'), 7.64 (2H, d, *J* = 6.0 Hz, 4.7 Hz, H- 2, 6'), 13.30 (1H, s, OH).

1.3.108 Synthesis of 4-(5,7-dimethoxy-4-oxo-4*H*-chromen-2-yl)benzonitrile (19c)*

4-(3-(2-Hydroxy-4,6-dimethoxyphenyl)-3-oxopropanoyl)benzonitrile (**19b**) (0.70 g, 2.15 mmol) was dissolved in $CHCl_3$ (7 mL), the reaction mixture was cooled to 0 ^{o}C and concentrated H_2SO_4 (2 mL) was added slowly under constant stirring. The reaction mixture was stirred at room temperature for 30 minutes and then quenched with water. The reaction mixture was extracted with EtOAc (2 x 10 mL), the organic layers were combined, dried over anhydrous $MgSO_4$ and concentrated *in vacuo* to obtain the crude product. Purification was achieved by column chromatography with $CHCl_3$: Hexane: EtOAc (8:1:1 v/v/v) to yield the compound-**19c** as a white solid (0.53 g, 80%).

m.p: 263-66 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 3.93 (3H, s, -OC**H$_3$**), 3.97 (3H, s,-OC**H$_3$**), 6.41 (1H, s, H-6), 6.58 (1H, s, H-8), 6.73 (1H, s, H-3), 7.80 (2H, d, *J* = 8.0 Hz, H-2',6'), 7.99 (2H, d, *J* = 8.0 Hz, H-3',5'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 55.74 (-O**C**H$_3$), 56.71 (-O**C**H$_3$), 92.64 (C8), 96.52 (C6), 109.14 (C10), 110.70 (C3), 114.19 (C4'), 118.08 (C4'), 126.43 (C2', 6'), 132.70 (C3', C5'), 135.75 (C1'), 158.47 (C9), 159.83 (C5), 161.38 (C2), 164.49 (C7), 177.12 (**C=**O); **IR ν_{max} [cm^{-1}]:**

1647 (C=O, ν, s), 1215 (-OCH_3, ν, s), 1116 (C-O, ν, m); ***m/z* (FTMS+ESI):** M+H ($C_{18}H_{14}O_4N$) requires 308.0917, found 308.0915. **HPLC purity:** 99.8%, RT-12.3 min at 258 nm.

1.3.109 Synthesis of 4-(5,7-dihydroxy-4-oxo-4*H*-chromen-2-yl)benzonitrile (19d)

The titled compound was synthesised according to the general procedure-**D** using 4-(5,7-dimethoxy-4-oxo-4*H*-chromen-2-yl)benzonitrile (**19c**) (0.15 g, 0.54 mmol). Purification was achieved by column chromatography with EtOAc (100%) to yield the compound-**19d** as a white solid (0.07 g, 55%).

m.p: 308-10 ^{o}C; **^{1}H NMR:** (DMSO-d6, 400 MHz) δ 6.22 (1H, s, H-6), 6.53 (1H, s, H-8), 7.05 (1H, s, H-3), 8.00 (2H, d, *J* = 8.0 Hz, H-3',5'), 8.21 (2H, d, *J* = 8.0 Hz, H-2',6'), 12.63 (1H, s, OH); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 94.46 (C8), 99.42 (C6), 104.13 (C10), 107.23 (C3), 113.80 (C4'), 118.27 (CN), 127.32 (C2', C6'), 133.02 (C3', C5'), 135.00 (C1'), 157.40 (C9), 161.09 (C5), 161.38 (C2), 164.88 (C7), 181.78 (**C=**O); **IR ν_{max} [cm^{-1}]:** 2236 (C≡N), 1659 (C=O, ν, s), 1162 (C-O, ν, m), 3352 (OH, w, b); ***m/z* (FTMS+ESI):** M+H ($C_{16}H_{10}O_4N$) requires 280.0604, found 280.0605. **HPLC purity:** 98.5%, RT-12.6 min at 258 nm.

1.3.110 Synthesis of 4-(5,7-dimethoxy-4-thioxo-4*H*-chromen-2-yl)benzonitrile (19e)*

The titled compound was synthesised according to the general procedure-**E** using 4-(5,7-dimethoxy-4-oxo-4*H*-chromen-2-yl)benzonitrile (**19c**) (0.30 g, 0.97 mmol). Purification was achieved by column chromatography with $CHCl_3$ (100%) to yield the compound-**19e** as a bluish green solid (0.25 g, 81%).

m.p: 247-48 ^{o}C; **^{1}H NMR:** ($CDCl_3$, 400 MHz) δ 3.93 (6H, s, 2 x -OC**H$_3$**), 6.45 (1H, s, H-6), 6.58 (1H, s, H-6), 7.53 (1H, s, H-3), 7.79 (2H, d, *J* = 8.0 Hz, H-2',6'), 8.02 (2H, d, *J* = 8.0 Hz, H-3',5'); **^{13}C NMR:** ($CDCl_3$, 100 MHz) δ 56.20 (2 x -O**C**H_3), 92.83 (C8), 97.09 (C6), 114.53 (C10), 118.22 (C4', CN), 117.69 (C10), 123.45 (C3), 126.55 (C2', C6'), 132.75 (C3', C5'), 135.66 (C1'), 147.09 (C2), 155.81 (C9), 161.82 (C7), 164.34 (C5), 200.78 (**C**=S); **IR ν_{max} [cm^{-1}]:** 2225 (C≡N), 1298 (C=S, ν, m), 1220 (-OCH_3, ν, m) 1113 (C-O, ν, m); ***m/z* (FTMS+ESI):** M+H ($C_{18}H_{14}O_3NS$) requires 324.0689, found 324.0688. **HPLC purity:** 96.5%, RT-13.8 min at 258 nm.

1.3.111 Synthesis of 4-(5,7-dihydroxy-4-thioxo-4*H*-chromen-2-yl)benzonitrile (19f)*

The titled compound was synthesised according to the general procedure-**F** using 4-(5,7-dimethoxy-4-thioxo-4*H*-chromen-2-yl)benzonitrile (**19e**) (0.10 g, 0.31 mmol). Purification was achieved by column chromatography with $CHCl_3$: Hexane: EtOAc (8:1:1 v/v/v) to yield the compound-**19f** as a yellow solid (0.06 g, 66%).

m.p: 258-59 ^{o}C; **^{1}H NMR:** (DMSO-d6, 400 MHz) 6.34 (1H, s, H-6), 6.63 (1H, s, H-8), 7.67 1H, s, H-3), 8.01 (2H, d, *J* = 4.0 Hz, H-2',6'), 8.30 (2H, d, *J* = 8.0 Hz, H-3',5'), 13.54 (1H, s, OH); **^{13}C NMR:** (DMSO-d6, 100 MHz) δ 94.86 (C8), 100.87 (C6), 113.07 (C10), 114.02 (C4'), 118.21 (CN), 118.68 (C3), 127.48 (C2', C6'), 132.98 (C3', C5'), 134.06 (C1'), 152.13 (C2), 153.99 (C9), 161.95 (C5), 164.80 (C7), 196.32 (**C**=S); **IR ν_{max} [cm^{-1}]:** 2240 (C≡N), 1280 (C=S, ν, m), 1148 (C-

O, v, m), 3301 (OH, w, b); ***m/z*** **(FTMS+ESI):** M+H ($C_{16}H_{10}O_3NS$) requires 296.0376, found 296.0376. **HPLC purity:** 96.2%, RT-13.8 min at 258 nm.

2 Anti-proliferative data

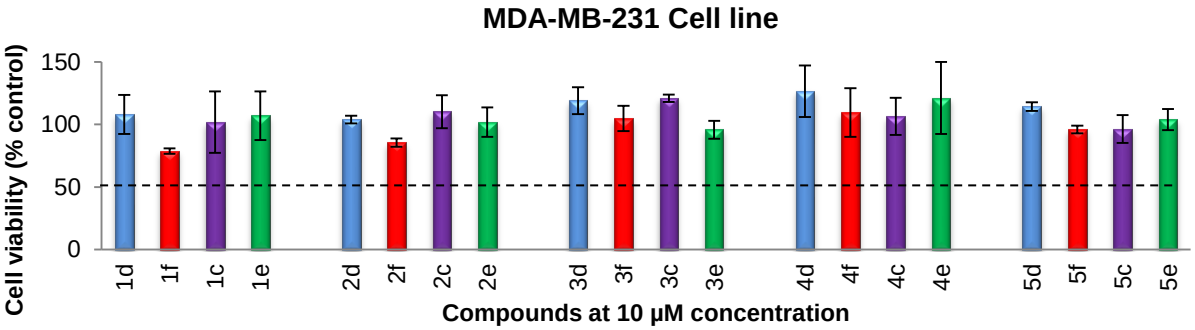
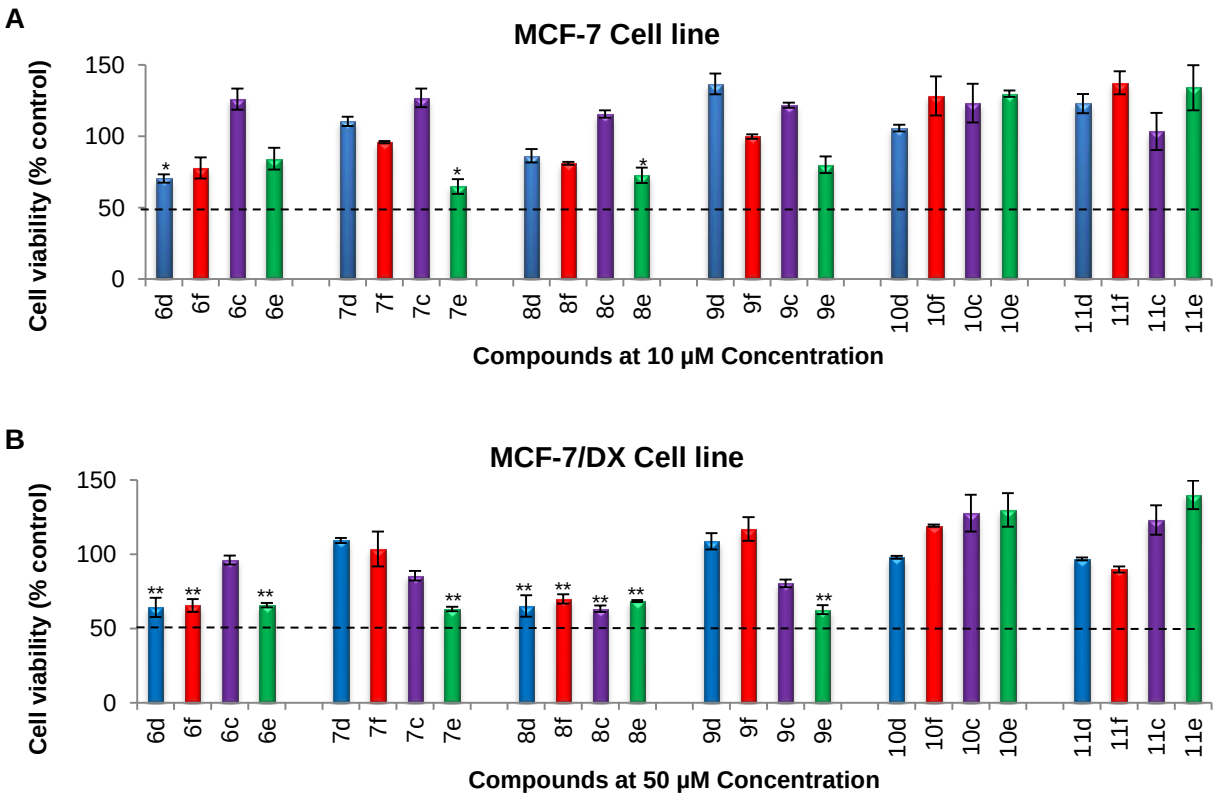


Figure-S1. Anti-proliferative activities of compounds **1c-f to 5c-f** against the MDA-MB-231 cell line. Cell viability was determined using the MTT assay in the presence of compounds **1c-f to 5c-f** at 10 µM concentration. Data are expressed as the mean ± standard error of the mean (SEM) (n = 3). Cells without treatment serve as control. Statistical significance was estimated, with respect to the control, by one-way ANOVA, followed by Bonferroni's *post hoc* test and found non-significant. Dashed line corresponds to 50% cell viability. Colour coding: blue-hydroxy flavone (-OH, 4-C=O), red-hydroxy 4-thioflavone (-OH, 4-C=S), purple-methoxy flavone (-OMe, 4-C=O) and green-methoxy 4-thioflavone (-OMe, 4-C=S).



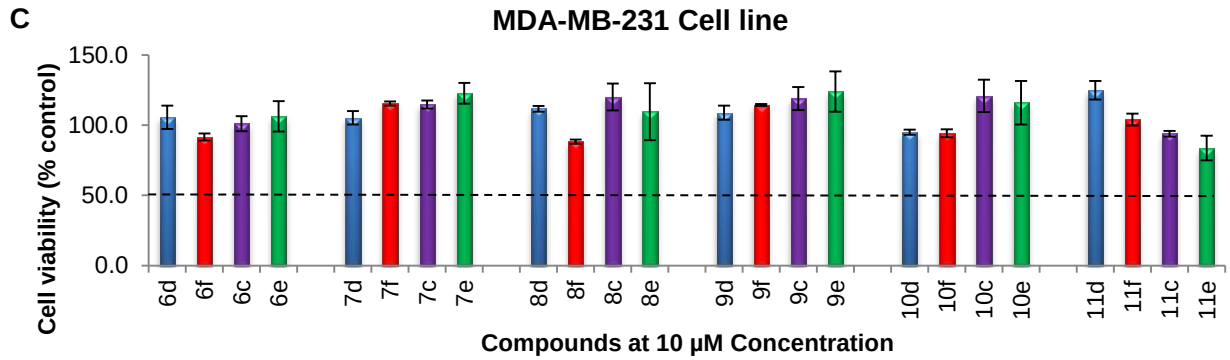


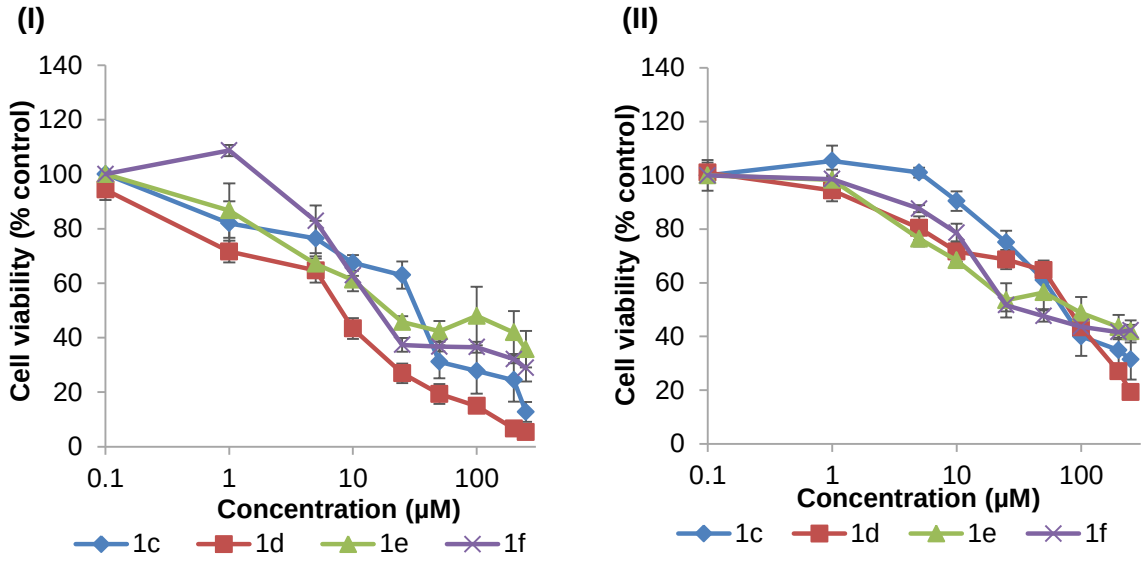
Figure-S2. Anti-proliferative activities of compounds **6c-f to 11c-f** against (A) MCF-7 cell line (B) MCF-7/DX cell line (C) MDA-MB-231 cell line. Cell viability was determined using MTT assay in the presence of compounds **6c-f to 11c-f** at 10 µM concentration against the MCF-7 cell line and the MDA-MB-231 cell line, and 50 µM concentration against the MCF-7/DX cell line. Data are expressed as the mean ± standard error of the mean (SEM) (n = 3). Cells without treatment serve as control. Statistical significance was estimated with respect to the control by one-way ANOVA, followed by Bonferroni's *post hoc* test (*$p < 0.05$ and **$p < 0.01$). Dashed line corresponds to 50% cell viability and those compounds showing < 50% cell viability were considered as active. Colour coding: blue-hydroxy flavone (-OH, 4-C=O), red-hydroxy 4-thioflavone (-OH, 4-C=S), purple-methoxy flavone (-OMe, 4-C=O) and green-methoxy 4-thioflavone (-OMe, 4-C=S).

3 Dose response curves

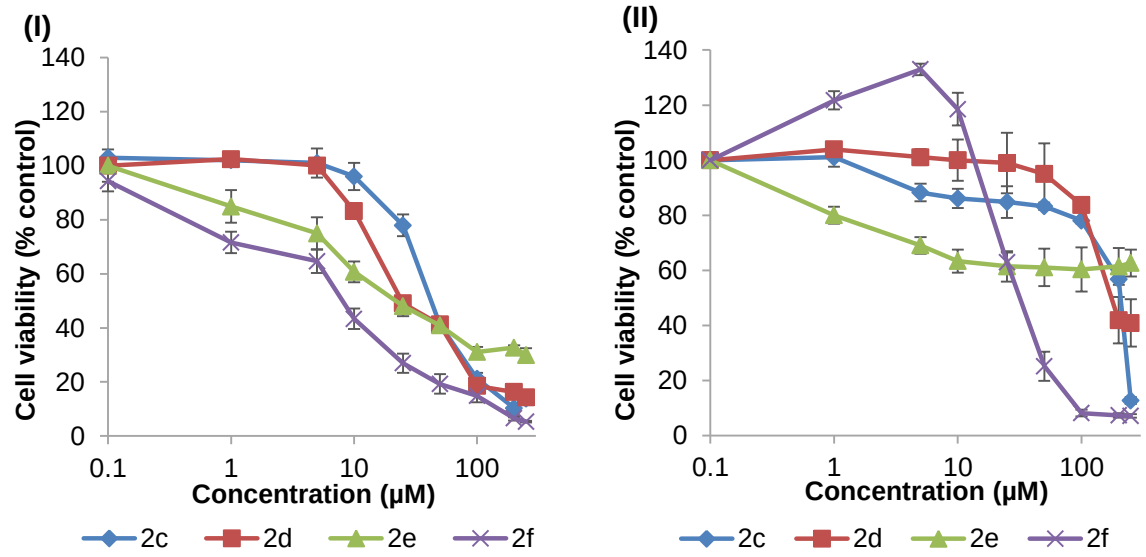
(Data are expressed as the mean ± standard error of the mean (SEM) (n = 3). X-axis is logarithmic. Errors bars when not visible are hidden by the symbol).

3.1 Dose response curves for compounds a) 1c-f, b) 2c-f, c) 3c-f, d) 4c-f and e) 5c-f against (I) MCF-7 and (II) MCF-7/DX

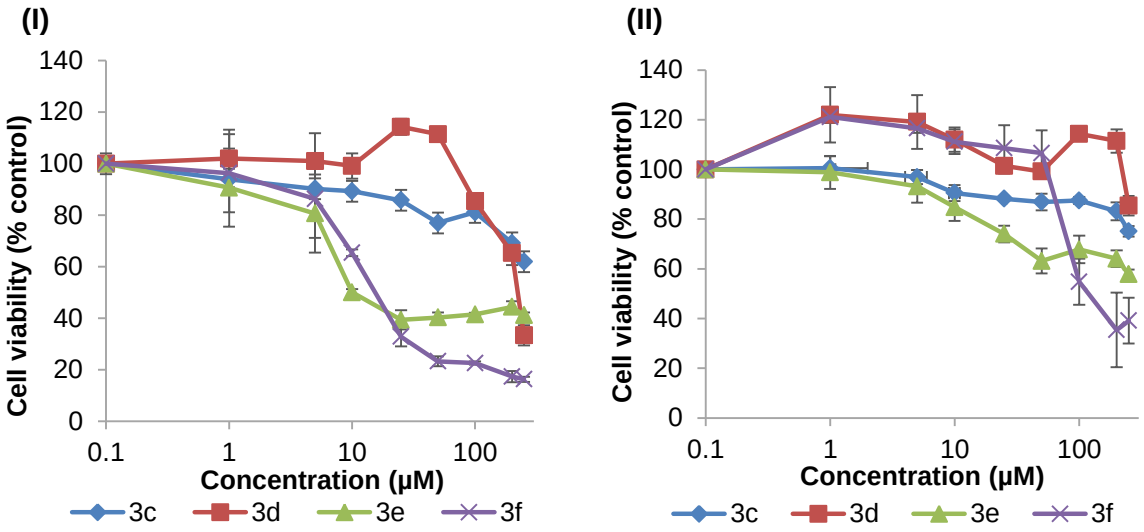
a) 8c-f



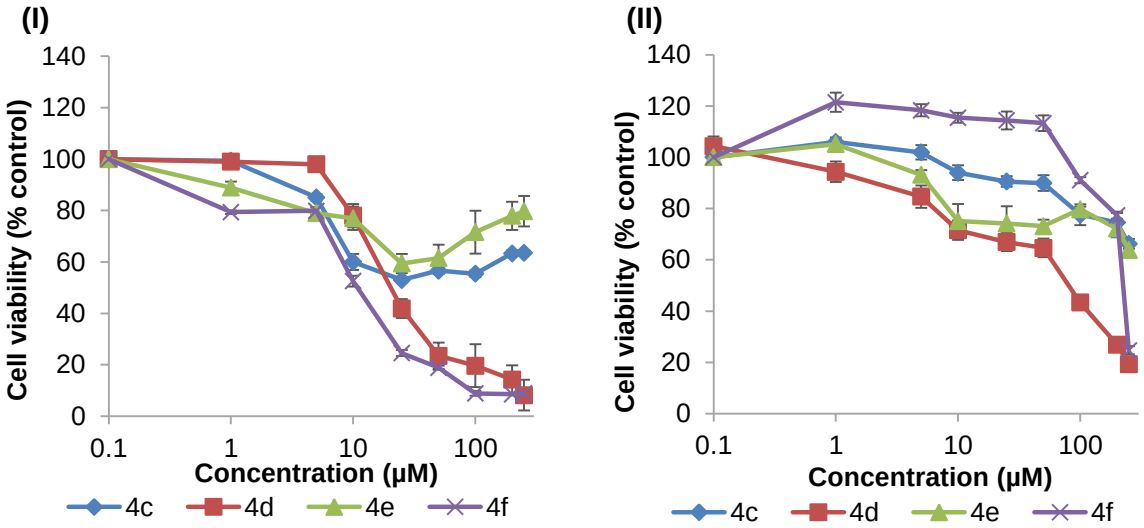
b) 9c-d



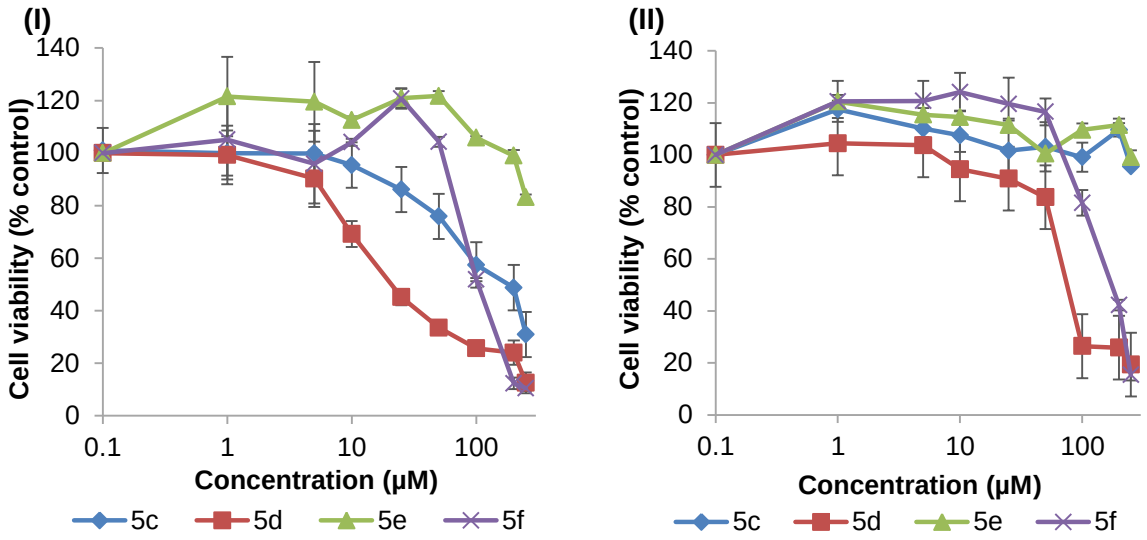
c) 9c-d


(I)
Cell viability (% control)
140
120
100
80
60
40
20
0
0.1
1
10
100
Concentration (μM)
3c
3d
3e
3f
(II)
Cell viability (% control)
140
120
100
80
60
40
20
0
0.1
1
10
100
Concentration (μM)
3c
3d
3e
3f

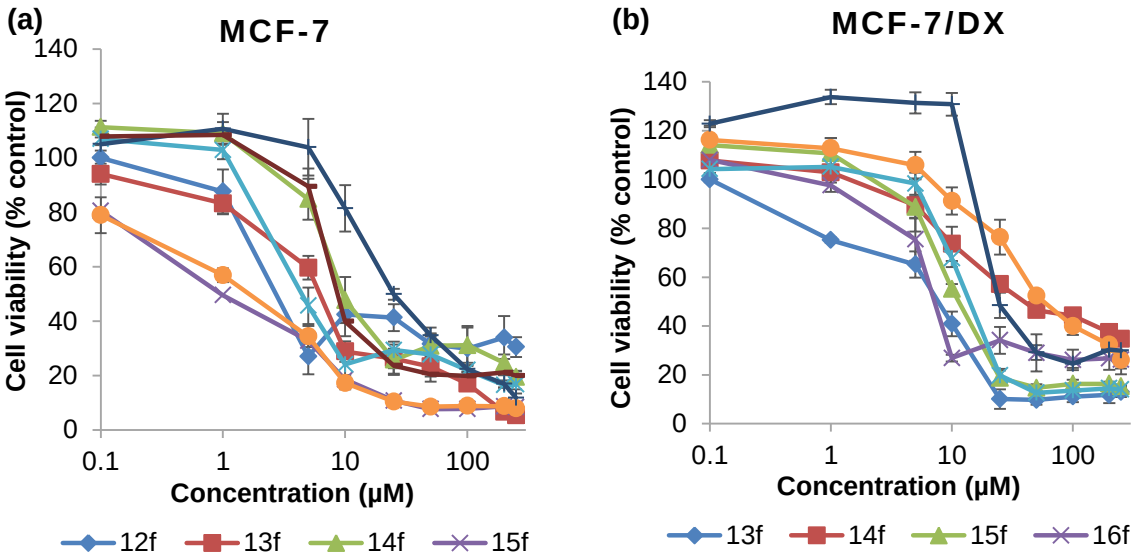
d) 9c-d

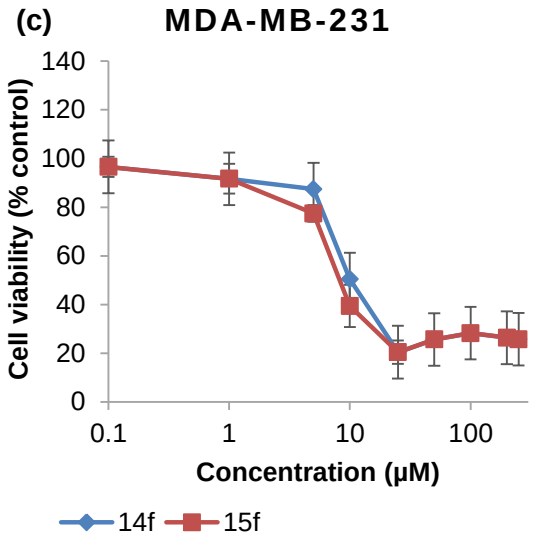

(I)
Cell viability (% control)
140
120
100
80
60
40
20
0
0.1
1
10
100
Concentration (μM)
4c
4d
4e
4f
(II)
Cell viability (% control)
140
120
100
80
60
40
20
0
0.1
1
10
100
Concentration (μM)
4c
4d
4e
4f

e) 9c-d



3.2 Dose response curves for compounds 12f to 19f against MCF-7 (a) and MCF-7/DX (b) and for compounds 14f and 16f against MDA-MB-231 (c) cell lines.



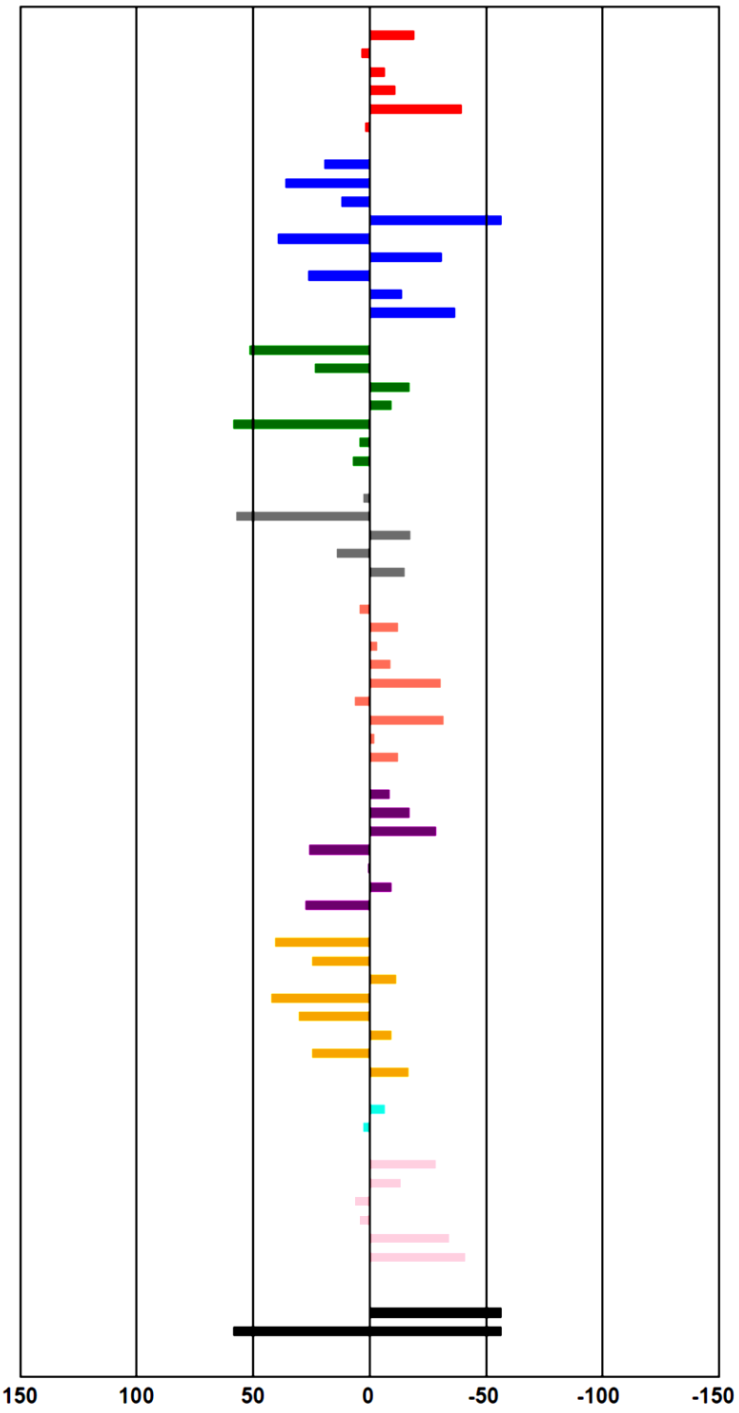

(c)
MDA-MB-231
Cell viability (% control)
140
120
100
80
60
40
20
0
0.1
1
10
100
Concentration (μM)
14f
15f

4 NCI/DTP screening

4.1 One dose mean graph

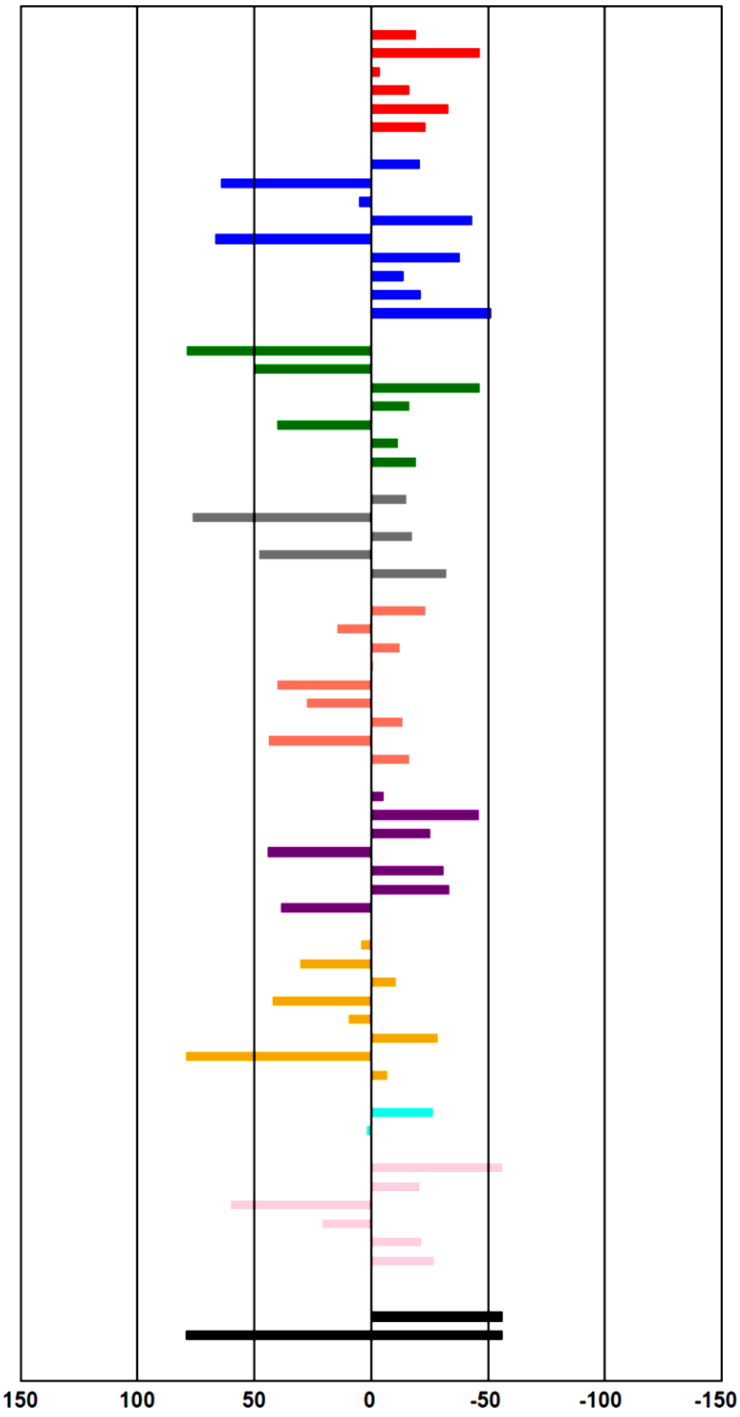
a. Compound-**15f**

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	15.80
HL-60(TB)	37.62
K-562	28.18
MOLT-4	24.06
RPMI-8226	-4.71
SR	36.10
Non-Small Cell Lung Cancer	
A549/ATCC	53.55
EKVX	70.17
HOP-62	46.43
HOP-92	-21.86
NCI-H226	73.64
NCI-H23	4.05
NCI-H322M	60.36
NCI-H460	21.00
NCI-H522	-1.71
Colon Cancer	
COLO 205	85.85
HCC-2998	57.66
HCT-116	17.62
HCT-15	25.44
HT29	92.85
KM12	38.69
SW-620	41.48
CNS Cancer	
SF-268	36.80
SF-295	91.42
SNB-19	17.51
SNB-75	48.27
U251	19.60
Melanoma	
LOX IMVI	38.63
MALME-3M	22.68
M14	31.41
MDA-MB-435	25.89
SK-MEL-2	4.40
SK-MEL-28	40.50
SK-MEL-5	3.09
UACC-257	32.92
UACC-62	22.57
Ovarian Cancer	
IGROV1	26.12
OVCAR-3	17.56
OVCAR-4	6.46
OVCAR-5	60.32
OVCAR-8	34.98
NCI/ADR-RES	25.50
SK-OV-3	61.79
Renal Cancer	
786-0	74.65
A498	59.11
ACHN	23.56
CAKI-1	76.46
RXF 393	64.58
SN12C	25.55
TK-10	58.91
UO-31	18.01
Prostate Cancer	
PC-3	28.37
DU-145	36.90
Breast Cancer	
MCF7	6.22
MDA-MB-231/ATCC	21.58
HS 578T	40.46
BT-549	38.37
T-47D	0.61
MDA-MB-468	-6.34
Mean	34.54
Delta	56.40
Range	114.71



b. Compound-**16f**

Panel/Cell Line	Growth Percent
Leukemia	
CCRF-CEM	5.37
HL-60(TB)	-21.96
K-562	20.73
MOLT-4	7.88
RPMI-8226	-8.44
SR	1.21
Non-Small Cell Lung Cancer	
A549/ATCC	3.47
EKVX	87.89
HOP-62	28.71
HOP-92	-18.88
NCI-H226	90.52
NCI-H23	-13.72
NCI-H322M	10.45
NCI-H460	3.24
NCI-H522	-26.97
Colon Cancer	
COLO 205	102.52
HCC-2998	73.80
HCT-116	-22.02
HCT-15	8.03
HT29	63.88
KM12	12.89
SW-620	5.25
CNS Cancer	
SF-268	9.40
SF-295	100.04
SNB-19	6.80
SNB-75	71.44
U251	-7.83
Melanoma	
LOX IMVI	1.22
MALME-3M	38.30
M14	12.29
MDA-MB-435	23.34
SK-MEL-2	63.77
SK-MEL-28	51.36
SK-MEL-5	10.86
UACC-257	67.54
UACC-62	8.09
Ovarian Cancer	
IGROV1	19.03
OVCAR-3	-21.74
OVCAR-4	-1.04
OVCAR-5	67.90
OVCAR-8	-6.62
NCI/ADR-RES	-8.87
SK-OV-3	62.33
Renal Cancer	
786-0	28.09
A498	53.91
ACHN	13.92
CAKI-1	65.84
RXF 393	33.36
SN12C	-4.08
TK-10	103.14
UO-31	17.42
Prostate Cancer	
PC-3	-2.05
DU-145	25.49
Breast Cancer	
MCF7	-31.90
MDA-MB-231/ATCC	3.73
HS 578T	84.03
BT-549	44.61
T-47D	2.92
MDA-MB-468	-2.50
Mean	24.02
Delta	55.92
Range	135.04



4.2 Five dose graphs

Compound-15f

National Cancer Institute Developmental Therapeutics Program
In-Vitro Testing Results

NSC : D - 783090 / 1	Experiment ID : 1502NS30	Test Type : 08	Units : Molar
Report Date : April 05, 2015	Test Date : February 09, 2015	QNS :	MC :
COMI : TF-16	Stain Reagent : SRB Dual-Pass Related	SSPL : 0ZHF	

			Log10 Concentration												
	Time		Mean Optical Densities					Percent Growth							
Panel/Cell Line	Zero	Ctrl	-8.0	-7.0	-6.0	-5.0	-4.0	-8.0	-7.0	-6.0	-5.0	-4.0	GI50	TGI	LC50
Leukemia															
CCRF-CEM	0.724	2.545	2.706	2.723	2.580	1.045	0.639	109	110	102	18	-12	4.13E-6	3.98E-5	> 1.00E-4
HL-60(TB)	0.790	2.750	2.694	2.581	2.584	0.871	0.710	97	91	92	4	-10	2.99E-6	1.95E-5	> 1.00E-4
K-562	0.215	1.776	1.735	1.702	1.694	0.375	0.168	97	95	95	10	-22	3.39E-6	2.07E-5	> 1.00E-4
MOLT-4	0.864	3.075	3.022	3.049	2.991	1.274	0.730	98	99	96	19	-16	3.93E-6	3.50E-5	> 1.00E-4
RPMI-8226	0.945	2.470	2.413	2.443	2.384	0.945	0.876	96	98	94	.	-7	2.95E-6	1.00E-5	> 1.00E-4
SR	0.441	1.918	1.910	1.821	1.891	0.702	0.359	99	93	98	18	-19	3.97E-6	3.06E-5	> 1.00E-4
Non-Small Cell Lung Cancer															
A549/ATCC	0.445	1.854	1.842	1.861	1.903	1.121	0.375	99	100	103	48	-16	9.20E-6	5.66E-5	> 1.00E-4
EKVX	0.986	2.108	1.983	1.966	1.874	1.812	0.734	89	87	79	74	-26	1.73E-5	5.52E-5	> 1.00E-4
HOP-62	0.558	1.579	1.355	1.383	1.266	0.583	0.288	78	81	69	2	-48	1.95E-6	1.11E-5	> 1.00E-4
HOP-92	1.344	1.792	1.700	1.713	1.682	0.965	0.776	79	82	75	-28	-42	1.76E-6	5.34E-6	> 1.00E-4
NCI-H226	1.011	2.132	2.050	1.971	1.906	1.750	0.699	93	86	80	66	-31	1.46E-5	4.80E-5	> 1.00E-4
NCI-H23	0.799	2.154	1.905	1.816	1.823	0.698	0.327	82	75	76	-13	-59	1.95E-6	7.18E-6	6.36E-5
NCI-H322M	1.014	2.237	2.086	1.978	1.905	1.104	0.646	88	79	73	7	-36	2.23E-6	1.47E-5	> 1.00E-4
NCI-H460	0.194	2.203	2.275	2.158	2.016	0.347	0.077	104	98	91	8	-60	3.09E-6	1.29E-5	7.05E-5
NCI-H522	1.220	2.359	2.374	2.350	2.301	1.045	0.566	101	99	95	-14	-54	2.57E-6	7.39E-6	8.09E-5
Colon Cancer															
COLO 205	0.436	1.341	1.272	1.304	1.278	1.197	0.142	92	96	93	84	-68	1.68E-5	3.58E-5	7.66E-5
HCC-2998	0.849	2.567	2.399	2.267	1.854	1.247	0.160	90	82	58	23	-81	1.74E-6	1.67E-5	5.03E-5
HCT-116	0.324	2.275	2.008	2.258	2.053	0.357	0.007	86	99	89	2	-98	2.78E-6	1.04E-5	3.30E-5
HCT-15	0.267	1.917	1.743	1.375	0.961	0.371	0.089	89	67	42	6	-67	4.82E-7	1.22E-5	5.91E-5
HT29	0.281	1.598	1.549	1.559	1.508	1.506	0.121	96	97	93	93	-57	1.94E-5	4.17E-5	8.99E-5
KM12	0.490	3.075	2.913	2.658	2.320	0.727	0.065	94	84	71	9	-87	2.17E-6	1.25E-5	4.13E-5
SW-620	0.299	2.484	2.469	2.442	2.302	0.748	0.110	99	98	92	21	-63	3.85E-6	1.76E-5	6.93E-5
CNS Cancer															
SF-268	0.653	2.276	2.183	2.129	2.072	0.975	0.490	94	91	87	20	-25	3.57E-6	2.76E-5	> 1.00E-4
SF-295	0.722	2.580	2.299	2.423	2.518	1.608	0.370	85	92	97	48	-49	8.97E-6	3.12E-5	> 1.00E-4
SF-539	0.869	2.568	2.391	2.429	2.365	1.170	0.460	90	92	88	18	-47	3.48E-6	1.88E-5	> 1.00E-4
SNB-19	0.608	1.960	1.928	1.953	1.945	0.816	0.341	98	99	99	15	-44	3.85E-6	1.82E-5	> 1.00E-4
SNB-75	0.968	2.199	1.804	1.785	1.796	1.338	0.611	68	66	67	30	-37	2.91E-6	2.81E-5	> 1.00E-4
U251	0.582	1.962	1.981	1.994	1.985	0.632	0.140	101	102	102	4	-76	3.36E-6	1.11E-5	4.72E-5
Melanoma															
LOX IMVI	0.254	1.858	1.764	1.704	1.700	0.416	0.019	94	90	90	10	-93	3.17E-6	1.25E-5	3.85E-5
MALME-3M	1.060	2.005	1.921	1.849	1.781	0.787	0.413	91	83	76	-26	-61	1.81E-6	5.59E-6	4.85E-5
M14	0.496	1.911	1.764	1.772	1.728	0.704	0.120	90	90	87	15	-76	3.25E-6	1.45E-5	5.18E-5
MDA-MB-435	0.512	2.762	2.652	2.599	2.599	0.816	0.250	95	93	93	13	-51	3.46E-6	1.62E-5	9.59E-5
SK-MEL-2	1.203	2.088	2.050	2.035	2.074	1.031	0.603	96	94	98	-14	-50	2.69E-6	7.46E-6	> 1.00E-4
SK-MEL-28	0.682	2.092	1.979	2.104	1.984	1.092	0.241	92	101	92	29	-65	4.67E-6	2.04E-5	6.96E-5
SK-MEL-5	0.811	2.728	2.564	2.578	2.440	0.591	0.065	91	92	85	-27	-92	2.05E-6	5.73E-6	2.25E-5
UACC-257	1.067	2.062	2.060	2.083	2.052	1.004	0.793	100	102	99	-6	-26	2.93E-6	8.78E-6	> 1.00E-4
UACC-62	1.007	2.646	2.443	2.520	2.487	1.205	0.330	88	92	90	12	-67	3.27E-6	1.42E-5	6.06E-5
Ovarian Cancer															
IGROV1	0.937	2.259	2.079	1.919	1.627	1.110	0.687	86	74	52	13	-27	1.14E-6	2.13E-5	> 1.00E-4
OVCAR-3	0.584	2.129	1.998	1.867	1.654	0.638	0.260	91	83	69	3	-55	1.96E-6	1.15E-5	8.07E-5
OVCAR-4	0.814	1.915	1.735	1.619	1.282	0.901	0.876	84	73	43	8	6	5.70E-7	> 1.00E-4	> 1.00E-4
OVCAR-5	0.842	2.204	1.995	2.072	1.972	1.646	0.422	85	90	83	59	-50	1.21E-5	3.48E-5	> 1.00E-4
OVCAR-8	0.559	2.133	2.065	2.127	2.117	0.645	0.441	96	100	99	5	-21	3.34E-6	1.60E-5	> 1.00E-4
NCI/ADR-RES	0.764	2.384	2.364	2.261	2.223	0.784	0.485	99	92	90	1	-37	2.82E-6	1.08E-5	> 1.00E-4
SK-OV-3	0.948	1.555	1.389	1.439	1.413	1.123	0.806	73	81	77	29	-15	3.61E-6	4.55E-5	> 1.00E-4
Renal Cancer															
786-0	0.854	2.756	2.729	2.745	2.708	1.666	0.187	99	99	97	43	-78	7.35E-6	2.26E-5	5.85E-5
A498	1.213	1.836	1.623	1.588	1.550	1.254	0.153	66	60	54	7	-87	1.22E-6	1.17E-5	4.00E-5
ACHN	0.581	2.364	2.125	2.180	2.045	0.627	0.428	87	90	82	3	-26	2.53E-6	1.23E-5	> 1.00E-4
CAKI-1	0.603	2.188	1.775	1.819	1.785	0.998	0.448	74	77	75	25	-26	3.12E-6	3.10E-5	> 1.00E-4
RXF 393	0.791	1.282	1.302	1.277	1.308	0.874	0.438	104	99	105	17	-45	4.22E-6	1.88E-5	> 1.00E-4
SN12C	0.767	2.300	2.220	2.226	2.104	0.843	0.306	95	95	87	5	-60	2.83E-6	1.19E-5	6.98E-5
TK-10	0.840	1.788	1.910	1.878	1.741	1.097	0.495	113	109	95	27	-41	4.60E-6	2.50E-5	> 1.00E-4
UO-31	0.875	2.454	1.947	1.874	1.776	0.796	0.288	68	63	57	-9	-67	1.28E-6	7.29E-6	5.07E-5
Prostate Cancer															
PC-3	0.487	1.942	1.827	1.874	1.842	0.603	0.145	92	95	93	8	-70	3.21E-6	1.26E-5	5.50E-5
DU-145	0.473	2.002	2.034	1.994	1.950	0.819	0.461	102	99	97	23	-3	4.26E-6	7.93E-5	> 1.00E-4
Breast Cancer															
MCF7	0.597	2.806	2.362	1.948	1.040	0.597	0.541	80	61	20	.	-9	1.87E-7	9.90E-6	> 1.00E-4
MDA-MB-231/ATCC	0.719	1.758	1.576	1.604	1.603	0.596	0.326	82	85	85	-17	-55	2.20E-6	6.79E-6	7.51E-5
HS 578T	0.943	2.168	2.045	2.115	2.038	1.369	0.932	90	96	89	35	-1	5.26E-6	9.28E-5	> 1.00E-4
BT-549	1.326	2.658	2.545	2.612	2.575	1.479	0.251	91	97	94	11	-81	3.40E-6	1.33E-5	4.62E-5
T-47D	0.822	1.517	1.285	1.020	0.699	0.649	0.642	67	29	-15	-21	-22	2.73E-8	4.52E-7	> 1.00E-4
MDA-MB-468	0.696	1.283	1.293	1.257	0.860	0.639	0.530	102	95	28	-8	-24	4.70E-7	5.91E-6	> 1.00E-4

Compound-**16f**

National Cancer Institute Developmental Therapeutics Program
In-Vitro Testing Results

NSC : D - 783091 / 1	Experiment ID : 1502NS30	Test Type : 08	Units : Molar
Report Date : April 05, 2015	Test Date : February 09, 2015	QNS :	MC :
COMI : TF-17	Stain Reagent : SRB Dual-Pass Related	SSPL : 0ZHF	

			Log10 Concentration												
	Time		Mean Optical Densities					Percent Growth							
Panel/Cell Line	Zero	Ctrl	-8.0	-7.0	-6.0	-5.0	-4.0	-8.0	-7.0	-6.0	-5.0	-4.0	GI50	TGI	LC50
Leukemia															
CCRF-CEM	0.724	2.704	2.862	2.884	2.507	0.656	0.550	108	109	90	-9	-24	2.53E-6	8.03E-6	> 1.00E-4
HL-60(TB)	0.790	2.762	2.694	2.541	2.155	0.649	0.700	97	89	69	-18	-11	1.66E-6	6.24E-6	> 1.00E-4
K-562	0.215	1.719	1.776	1.843	1.403	0.294	0.255	104	108	79	5	3	2.47E-6	> 1.00E-4	> 1.00E-4
MOLT-4	0.864	2.990	3.069	3.000	2.643	0.717	0.782	104	100	84	-17	-10	2.16E-6	6.77E-6	> 1.00E-4
RPMI-8226	0.945	2.569	2.602	2.521	1.859	1.008	0.842	102	97	56	4	-11	1.32E-6	1.83E-5	> 1.00E-4
SR	0.441	1.785	1.851	1.737	1.501	0.543	0.417	105	96	79	8	-5	2.54E-6	3.81E-5	> 1.00E-4
Non-Small Cell Lung Cancer															
A549/ATCC	0.445	1.919	1.912	1.934	1.958	0.445	0.318	99	101	103	.	-29	3.26E-6	1.00E-5	> 1.00E-4
EKVX	0.986	2.160	2.038	2.052	2.010	1.870	0.742	90	91	87	75	-25	1.79E-5	5.66E-5	> 1.00E-4
HOP-62	0.558	1.616	1.328	1.352	1.230	0.485	0.378	73	75	64	-13	-32	1.50E-6	6.73E-6	> 1.00E-4
HOP-92	1.344	1.866	1.779	1.820	1.712	1.086	0.964	83	91	71	-19	-28	1.69E-6	6.11E-6	> 1.00E-4
NCI-H226	1.011	2.213	2.157	2.121	2.101	1.532	0.714	95	92	91	43	-29	7.22E-6	3.94E-5	> 1.00E-4
NCI-H23	0.799	2.225	2.015	1.934	1.720	0.674	0.458	85	80	65	-16	-43	1.52E-6	6.38E-6	> 1.00E-4
NCI-H322M	1.014	2.295	2.137	2.114	1.990	0.826	1.007	88	86	76	-19	-1	1.89E-6	6.37E-6	> 1.00E-4
NCI-H460	0.194	2.374	2.382	2.346	1.271	0.268	0.177	100	99	49	3	-9	9.73E-7	1.90E-5	> 1.00E-4
NCI-H522	1.220	2.552	2.366	2.464	1.966	0.743	0.753	86	93	56	-39	-38	1.16E-6	3.88E-6	> 1.00E-4
Colon Cancer															
COLO 205	0.436	1.413	1.351	1.391	1.408	0.964	0.068	94	98	99	54	-85	1.07E-5	2.45E-5	5.63E-5
HCC-2998	0.849	2.648	2.557	2.579	2.408	0.716	0.392	95	96	87	-16	-54	2.28E-6	7.03E-6	7.94E-5
HCT-116	0.324	2.521	2.462	2.483	2.017	0.321	0.078	97	98	77	-1	-76	2.22E-6	9.73E-6	4.51E-5
HCT-15	0.267	1.950	1.855	1.841	1.054	0.383	0.064	94	94	47	7	-76	8.53E-7	1.21E-5	4.85E-5
HT29	0.281	1.626	1.630	1.664	1.641	0.599	0.187	100	103	101	24	-33	4.56E-6	2.59E-5	> 1.00E-4
KM12	0.490	3.029	2.996	2.981	2.855	0.770	0.412	99	98	93	11	-16	3.35E-6	2.56E-5	> 1.00E-4
SW-620	0.299	2.546	2.521	2.541	2.067	0.513	0.243	99	100	79	10	-19	2.60E-6	2.16E-5	> 1.00E-4
CNS Cancer															
SF-268	0.653	2.260	2.182	2.154	1.816	0.757	0.705	95	93	72	6	3	2.18E-6	> 1.00E-4	> 1.00E-4
SF-295	0.722	2.670	2.462	2.583	2.544	1.139	0.551	89	96	94	21	-24	4.01E-6	2.98E-5	> 1.00E-4
SF-539	0.869	2.548	2.406	2.423	2.149	0.763	0.588	92	93	76	-12	-32	1.98E-6	7.28E-6	> 1.00E-4
SNB-19	0.608	1.914	1.934	1.972	1.731	0.731	0.617	102	104	86	9	1	2.95E-6	> 1.00E-4	> 1.00E-4
SNB-75	0.968	2.162	1.766	1.850	1.820	1.433	0.987	67	74	71	39	2	4.55E-6	> 1.00E-4	> 1.00E-4
U251	0.582	2.042	2.072	2.027	1.815	0.557	0.458	102	99	84	-4	-21	2.44E-6	8.93E-6	> 1.00E-4
Melanoma															
LOX IMVI	0.254	1.901	1.798	1.747	1.193	0.153	0.127	94	91	57	-40	-50	1.18E-6	3.87E-6	9.57E-5
MALME-3M	1.060	2.029	1.945	1.906	1.802	0.835	0.459	91	87	77	-21	-57	1.87E-6	6.07E-6	6.47E-5
M14	0.496	2.097	1.922	1.930	1.766	0.408	0.330	89	90	79	-18	-33	2.01E-6	6.57E-6	> 1.00E-4
MDA-MB-435	0.512	2.756	2.651	2.722	2.485	0.689	0.523	95	98	88	8	.	2.98E-6	> 1.00E-4	> 1.00E-4
SK-MEL-2	1.203	2.226	2.155	2.159	2.099	0.987	0.911	93	93	88	-18	-24	2.27E-6	6.76E-6	> 1.00E-4
SK-MEL-28	0.682	2.131	2.030	2.072	1.901	0.845	0.592	93	96	84	11	-13	2.94E-6	2.87E-5	> 1.00E-4
SK-MEL-5	0.811	2.875	2.801	2.760	2.608	0.333	0.038	96	94	87	-59	-95	1.79E-6	3.95E-6	8.68E-6
UACC-257	1.067	2.027	2.005	2.092	2.030	0.970	0.855	98	107	100	-9	-20	2.88E-6	8.25E-6	> 1.00E-4
UACC-62	1.007	2.651	2.486	2.588	2.553	0.573	0.512	90	96	94	-43	-49	2.09E-6	4.85E-6	> 1.00E-4
Ovarian Cancer															
IGROV1	0.937	2.359	2.330	2.275	2.141	0.936	0.874	98	94	85	.	-7	2.56E-6	9.96E-6	> 1.00E-4
OVCAR-3	0.584	2.022	2.018	1.932	1.456	0.251	0.532	100	94	61	-57	-9	1.23E-6	3.27E-6	.
OVCAR-4	0.814	1.971	1.861	1.869	1.633	0.852	0.912	90	91	71	3	8	2.03E-6	> 1.00E-4	> 1.00E-4
OVCAR-5	0.842	2.228	2.012	2.083	2.088	1.366	0.804	84	89	90	38	-5	5.83E-6	7.80E-5	> 1.00E-4
OVCAR-8	0.559	2.165	2.233	2.183	1.848	0.536	0.486	104	101	80	-4	-13	2.28E-6	8.92E-6	> 1.00E-4
NCI/ADR-RES	0.764	2.405	2.343	2.260	1.788	0.631	0.608	96	91	62	-17	-20	1.43E-6	6.05E-6	> 1.00E-4
SK-OV-3	0.948	1.613	1.455	1.521	1.549	0.883	0.777	76	86	90	-7	-18	2.60E-6	8.50E-6	> 1.00E-4
Renal Cancer															
786-0	0.854	2.758	2.688	2.778	2.608	0.868	0.731	96	101	92	1	-14	2.89E-6	1.11E-5	> 1.00E-4
A498	1.213	1.890	1.684	1.704	1.760	1.070	0.868	70	73	81	-12	-28	2.15E-6	7.46E-6	> 1.00E-4
ACHN	0.581	2.329	2.136	2.226	1.959	0.600	0.502	89	94	79	1	-14	2.35E-6	1.18E-5	> 1.00E-4
CAKI-1	0.603	2.230	1.973	1.964	1.979	0.651	0.529	84	84	85	3	-12	2.65E-6	1.55E-5	> 1.00E-4
RXF 393	0.791	1.335	1.343	1.377	1.263	0.750	0.597	102	108	87	-5	-25	2.51E-6	8.78E-6	> 1.00E-4
SN12C	0.767	2.359	2.350	2.231	2.107	0.804	0.585	99	92	84	2	-24	2.61E-6	1.23E-5	> 1.00E-4
TK-10	0.840	1.874	1.930	2.011	2.168	0.858	0.770	105	113	128	2	-8	4.16E-6	1.47E-5	> 1.00E-4
UO-31	0.875	2.468	1.971	1.894	1.681	0.780	0.299	69	64	51	-11	-66	1.02E-6	6.66E-6	5.15E-5
Prostate Cancer															
PC-3	0.487	2.025	1.994	1.998	1.783	0.649	0.318	98	98	84	11	-35	2.92E-6	1.71E-5	> 1.00E-4
DU-145	0.473	2.004	2.069	1.969	1.723	0.587	0.512	104	98	82	7	3	2.67E-6	> 1.00E-4	> 1.00E-4
Breast Cancer															
MCF7	0.597	2.856	2.607	2.515	2.178	0.289	0.495	89	85	70	-52	-17	1.46E-6	3.76E-6	.
MDA-MB-231/ATCC	0.719	1.799	1.774	1.692	1.469	0.678	0.656	98	90	69	-6	-9	1.81E-6	8.40E-6	> 1.00E-4
HS 578T	0.943	2.254	2.241	2.308	2.183	1.475	1.167	99	104	95	41	17	6.69E-6	> 1.00E-4	> 1.00E-4
BT-549	1.326	2.707	2.578	2.655	2.355	1.358	1.174	91	96	75	2	-12	2.19E-6	1.46E-5	> 1.00E-4
T-47D	0.822	1.676	1.518	1.549	1.321	0.628	0.745	81	85	58	-24	-9	1.27E-6	5.15E-6	> 1.00E-4
MDA-MB-468	0.696	1.294	1.325	1.328	1.187	0.565	0.458	105	106	82	-19	-34	2.08E-6	6.50E-6	> 1.00E-4

5 Interaction of compound-3e with ERα-molecular docking study

As mentioned in the manuscript, only compound-**3e** showed higher binding affinity towards the ERα receptor [(docking score of 10.02, versus the native ligand docking score of 13.0. It was found to interact in a similar fashion to that of the native ligand by forming one hydrogen bond with the key active site residue Asp 351 [**3e**-7 (O)…Asp 351 (OD1) 3.21 Å and native ligand-NH…Asp 351 (OD1) 3.26 Å] (Figure-S3). This hydrogen bonding with the Asp-351 residue is considered to be a highly significant interaction for antiestrogenic activity as it displaces helix-12 in the binding pocket of ERα leaving the receptor in the open conformation. The open conformation of ERα is believed to prevent the recruitment of the crucial co-activators and hence inhibits the estrogen signal transduction pathway[13,14]. This may explain the greater anti-proliferative activity observed for **3e** compared with the other derivatives (IC_{50} = 11.8 ± 1.79 µM).

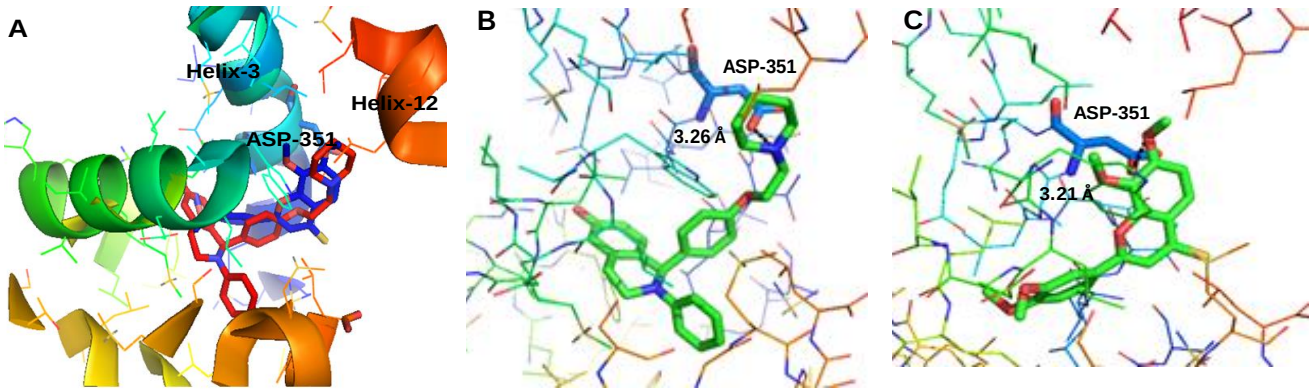


Figure-S3. Molecular docking analysis of compound-**3e** with ERα receptor. (A) Superimposed cartoon representations of the binding modes of the native ligand and the compound-**3e** in complex with ERα. Docking modes of (B) native ligand (2-phenyl-1-[4-(2-piperidin-1-yl-ethoxy)-phenyl]-1,2,3,4-tetrahydro-isoquinolin-6-ol) and (C) compound-**3e**, highlighting a key hydrogen bond interaction with Asp 351.

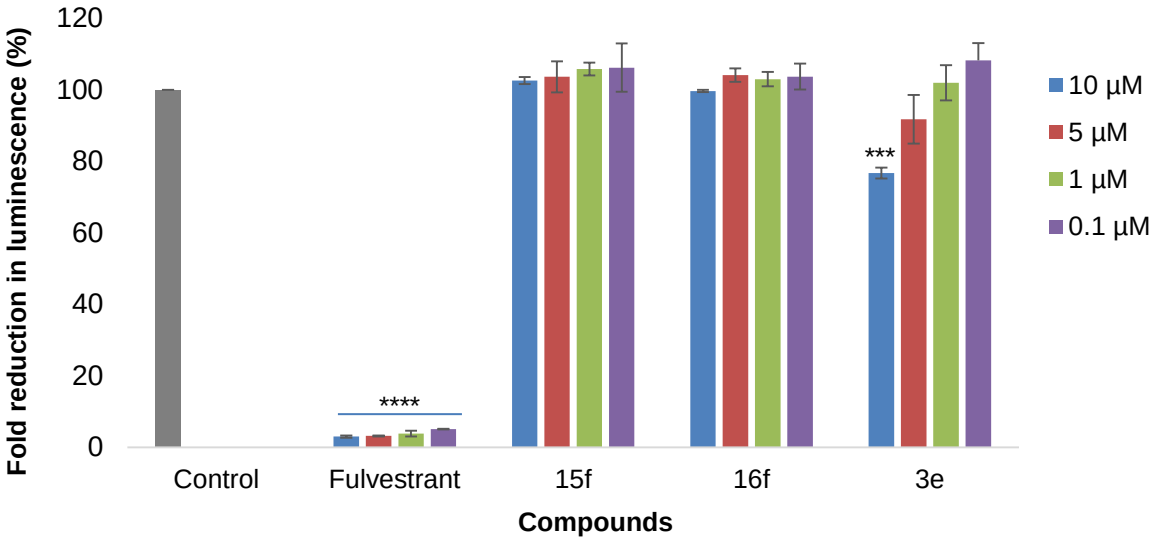


Figure-S4. ERα antagonist assay. Bar chart represents the quantification of the fold reduction in the luminescence intensity upon the treatment of ERα reporter cells for 24 h with compounds 15f, 16f, 3e and fulvestrant (positive control) at different concentrations (10, 5, 1 and 0.1 µM) in the presence of a constant concentration of 17β-estradiol (3.2 nM, EC_{75} as suggested in the manufacture's manual). Cells in the presence of 17β-estradiol (3.2 nM) without treatment was considered as control. Data are expressed as the mean ± standard error of the mean (SEM) (n = 3). Statistical significance was estimated with respect to the control by one-way ANOVA, followed by Bonferroni's post hoc test (, ***$p < 0.001$ and ****$p < 0.0001$).

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