

Design, synthesis, and biological and docking studies of novel epipodophyllotoxin-chalcone hybrids as potential anticancer agents

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Supporting information:

Spectral Data of all the compounds:

6a. 9-[4-(4-Acetyl-phenoxy)methyl]-[1,2,3]triazol-1-yl]-5-(3,4,5-trimethoxy-phenyl)-5,8,8a,9-tetrahydro-5aH-furo[3',4':6,7]naphtho[2,3-d][1,3]dioxol-6-one: White solid; mp: 135-137 °C; $[\alpha]_D^{25}$ - 51 (0.75, CHCl₃); ¹H NMR (400 MHz, CDCl₃): 2.48 (s, 3H), 3.04 (m, 1H), 3.24 (m, 2H), 3.72 (s, 6H), 3.82 (s, 3H), 4.31 (t, *J* = 7.6, 1H), 4.65 (d, *J* = 4.8, 1H), 5.15 (s, 2H), 5.92 (d, *J* = 5.94, 2H), 6.07 (d, *J* = 3.67, 1H), 6.24 (s, 2H), 6.56 (d, *J* = 5.68, 2H), 6.96 (d, *J* = 7.21, 2H), 7.37 (s, 1H), 7.84 (d, *J* = 7.47, 2H); ¹³C NMR (400 MHz, CDCl₃): δ 29.4, 37.0, 41.4, 43.4, 55.9, 58.8, 60.8, 62.4, 67.5, 105.3, 111.3, 111.5, 112.0, 113.8, 113.9, 117.9, 118.0, 127.1, 134.1, 146.7, 150.4, 150.5, 151.5, 152.7, 177.3, 202.2; IR (KBr): 3346.3, 1771.6, 1731.2, 1598.5, 1516.3, 1477.1, 1338.0, 1016.6, 756.7 cm⁻¹; ESI-MS: 636.2 (M + Na). Anal. Calc. for C₃₃H₃₁N₃O₉: C, 64.59; H, 5.09; N, 6.85 Found: C, 64.54; H, 5.03; N, 6.90.

6b. 5-(3,4,5-Trimethoxy-phenyl)-9-{4-[4-(3-oxo-but-1-enyl)-phenoxy)methyl] -[1,2,3]triazol-1-yl]-5,8,8a,9-tetrahydro-5aH-furo[3',4':6,7]naphtho[2,3-d][1,3]-6-one : White solid; mp: 129-131 °C; $[\alpha]_D^{25}$ - 23.3 (0.75, CHCl₃); ¹H NMR (400 MHz, CDCl₃): 2.35 (s, 3H), 3.05 (m, 1H), 3.27 (m, 2H), 3.78 (s, 6H), 3.81 (s, 3H), 4.40 (t, *J* = 7.6, 1H), 4.75 (d, *J* = 4.8, 1H), 5.20 (s, 2H), 5.48 (s, 1H), 6.02 (d, *J* = 4.19, 2H), 6.11 (d, *J* = 4.0, 1H), 6.33 (s, 2H), 6.62 (m, 2H), 7.02 (d, *J* = 8.72, 2H), 7.28 (m, 2H), 7.53 (d, *J* = 8.78, 2H); ¹³C NMR (400 MHz, CDCl₃): δ 25.3, 27.4, 29.7, 35.0, 41.7, 43.5, 56.5, 58.8, 60.87, 62.0, 67.4, 82.5, 84.4, 102.0, 107.8, 108.8, 110.6, 115.2, 123.1, 124.4, 125.4, 127.8, 129.6, 130.0, 133.4, 134.4, 142.9, 143.8, 146.6, 148.1, 150.5, 159.9, 172.1, 198.4; IR (KBr): 3362.9, 1771.6, 1595.5, 1505.3, 1485.2, 1238.0, 1013.6, 764.8

cm⁻¹; ESIMS: 662.2 (M + Na⁺). Anal. Calc. for C₃₅H₃₃N₃O₉: C, 65.72; H, 5.20; N, 6.57 Found: C, 65.80; H, 5.24; N, 6.67.

6c. 5-(3,4,5-Trimethoxy-phenyl)-9-{4-[2-methoxy-4-(3-oxo-but-1-enyl)-phenoxy-methyl]-[1,2,3]triazol-1-yl}-5,8,8a,9-tetrahydro-5aH-furo[3',4':6,7]naphtho [2,3-d][1,3]dioxol-6-one:

White solid; mp: 124-126 °C; $[\alpha]_D^{25} - 34.6$ (0.70, CHCl₃); ¹H NMR (400 MHz, CDCl₃): 2.33 (s, 3H), 3.05 (m, 1H), 3.27 (m, 2H), 3.72 (s, 6H), 3.76 (s, 3H), 3.80 (s, 3H), 4.40 (t, *J* = 7.6, 1H), 4.79 (d, *J* = 4.8, 1H), 5.22 (s, 2H), 5.40 (s, 1H), 6.02 (d, *J* = 3.67, 2H), 6.25 (s, 1H), 6.53 (m, 1H), 6.69 (m, 2H), 7.01 (s, 2H), 7.28-7.48 (m, 2H), 7.53 (d, *J* = 8.78, 2H); ¹³C NMR (400 MHz, CDCl₃): δ 24.3, 27.4, 29.7, 37.0, 41.6, 43.4, 55.9, 56.5, 58.8, 60.6, 62.0, 67.4, 82.5, 84.4, 102.0, 107.8, 108.9, 110.5, 115.2, 122.7, 123.4, 125.8, 127.8, 129.6, 130.0, 133.4, 134.4, 142.9, 143.8, 146.6, 148.1, 149.5, 159.9, 173.1, 196.8; IR (KBr): 3364.6, 1775.2, 1598.2, 1507.1, 1485.2, 1239.2, 1004.6, 755.7 cm⁻¹; ESI-MS: 6792.2 (M + Na). Anal. Calc. for C₃₆H₃₅N₃O₁₀: C, 64.57; H, 5.27; N, 6.27 Found: C, 64.54; H, 5.24; N, 6.34.

6d. 5-(3,4,5-Trimethoxy-phenyl)-9-{4-[4-(3-oxo-3-phenyl-propenyl)-phenoxy-methyl]-[1,2,3]triazol-1-yl}-5,8,8a,9-tetrahydro-5aH-furo[3',4':6,7]naphtho[2,3-d] [1,3]dioxol-6-one:

White solid; mp: 145-147 °C; $[\alpha]_D^{25} - 41$ (0.75, CHCl₃); ¹H NMR (400 MHz, CDCl₃): 3.04 (m, 1H), 3.28 (m, 2H), 3.78 (s, 6H), 3.83 (s, 3H), 4.41 (t, *J* = 7.6, 1H), 4.76 (d, *J* = 4.6, 1H), 5.26 (s, 2H), 5.47 (s, 1H), 6.01 (d, *J* = 3.7, 2H), 6.12 (d, *J* = 4.0, 1H), 6.32 (s, 2H), 6.63 (d, *J* = 7.7, 2H), 7.05 (d, *J* = 8.6, 2H), 7.28-7.54 (m, 3H), 7.57-7.79 (m, 4H), 8.04 (d, *J* = 8.78, 2H); ¹³C NMR (400 MHz, CDCl₃): δ 29.6, 37.1, 41.7, 43.5, 56.6, 58.9, 60.8, 62.1, 67.4, 102.1, 107.9, 108.8, 110.6, 114.7, 121.8, 123.3, 124.5, 128.4, 129.0, 129.7, 130.5, 130.9, 131.8, 134.5, 135.0, 144.3, 146.7, 148.2, 149.5, 186.7; IR (KBr): 3365.7, 1778.6, 1598.5, 1504.3, 1485.2, 1233.4, 1005.3, 758.3 cm⁻¹; ESI-MS: 724.2 (M + Na). Anal. Calc. for C₄₀H₃₅N₃O₉: C, 68.46; H, 5.03; N, 5.99 Found: C, 68.50; H, 5.04; N, 5.93.

6e. 5-(3,4,5-Trimethoxy-phenyl)-9-{4-[4-(3-phenyl-acryloyl)-phenoxy methyl]-[1,2,3]triazol-1-yl}-5,8,8a,9-tetrahydro-5aH-furo[3',4':6,7]naphtho[2,3-d] [1,3]dioxol-6-one:

White solid; mp: 137-138 °C; $[\alpha]_D^{25} - 48.8$ (0.50, CHCl₃); ¹H NMR (400 MHz, CDCl₃): 3.06 (m, 1H), 3.25 (m, 2H), 3.79 (s, 6H), 3.82 (s, 3H), 4.39 (t, *J* = 7.6, 1H), 4.76 (d, *J* = 4.5, 1H), 5.22 (s, 2H), 5.46 (s, 1H), 6.03 (d, *J* = 3.65, 2H), 6.14 (d, *J* = 3.65, 1H), 6.32 (s, 2H), 6.64 (d, *J* = 8.2, 2H), 7.02 (d, *J* = 8.6, 2H), 7.24-7.32 (m, 2H), 7.34-7.54 (m, 3H), 7.56-7.77 (m, 2H), 8.04 (d, *J* = 8.57, 2H); ¹³C NMR (400 MHz, CDCl₃): δ 29.5, 37.2, 41.7, 43.5, 56.6, 58.9, 60.8, 62.1, 67.4, 102.1, 107.9,

108.8, 110.6, 114.7, 121.8, 124.3, 124.5, 128.5, 129.0, 129.7, 130.5, 132.9, 131.8, 134.5, 135.0, 144.3, 146.7, 147.8, 150.4, 186.6; IR (KBr): 3342.1, 1777.7, 1587.2, 1598.3, 1485.2, 1287.0, 1001.6, 758.5 cm^{-1} ; ESIMS: 724.2 ($\text{M} + \text{Na}$). Anal. Calc. for $\text{C}_{40}\text{H}_{35}\text{N}_3\text{O}_9$: C, 68.46; H, 5.03; N, 5.99 Found: C, 68.51; H, 5.03; N, 5.95.

6f. **9-(4-{4-[3-(4-Fluoro-phenyl)-acryloyl]-phenoxy-methyl}-[1,2,3]triazol-1-yl)-5-(3,4,5-trimethoxy-phenyl)-5,8,8a,9-tetrahydro-5aH-furo[3',4':6,7]naphtho [2,3-d] [1,3] dioxol-6-one:** White solid; mp: 154-156 $^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{25} - 33$ (0.75, CHCl_3); ^1H NMR (400 MHz, CDCl_3): 3.05 (m, 1H), 3.26 (m, 2H), 3.79 (s, 6H), 3.82 (s, 3H), 4.42 (t, $J = 7.6$, 1H), 4.75 (d, $J = 4.7$, 1H), 5.26 (s, 2H), 5.50 (s, 1H), 6.03 (d, $J = 3.88$, 2H), 6.12 (d, $J = 4.2$, 1H), 6.32 (s, 2H), 6.64 (d, $J = 7.5$, 2H), 7.05-7.24 (m, 5H), 7.66-7.80 (m, 3H), 8.03 (d, $J = 8.77$, 2H); ^{13}C NMR (400 MHz, CDCl_3): δ 35.9, 42.1, 56.9, 59.27, 60.8, 62.3, 66.2, 67.8, 67.7, 102.41, 106.8, 107.8, 109.6, 113.9, 120.7, 122.4, 124.4, 126.4, 128.3, 129.4, 129.8, 131.8, 132.0, 132.5, 133.5, 138.3, 157.6, 160.8, 162.0, 189.6; IR (KBr): 3407.1, 1776.6, 1598.5, 1505.3, 1485.2, 1238.0, 1012.6, 758.8 cm^{-1} ; ESI-MS: 720 ($\text{M} + \text{H}$). Anal. Calc. for $\text{C}_{40}\text{H}_{34}\text{FN}_3\text{O}_9$: C, 66.75; H, 4.76; N, 5.84 Found: C, 66.79; H, 4.74; N, 5.80.

6g. **9-(4-{4-[3-(3-Fluoro-phenyl)-acryloyl]-phenoxy-methyl}-[1,2,3]triazol-1-yl)-5-(3,4,5-trimethoxy-phenyl)-5,8,8a,9-tetrahydro-5aH-furo[3',4':6,7]naphtho [2,3-d] [1,3] dioxol-6-one:** White solid; mp: 165-167 $^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{25} - 58.3$ (0.65, CHCl_3); ^1H NMR (400 MHz, CDCl_3): 3.07 (m, 1H), 3.26 (m, 2H), 3.79 (s, 6H), 3.82 (s, 3H), 4.43 (t, $J = 7.6$, 1H), 4.76 (d, $J = 4.5$, 1H), 5.27 (s, 2H), 5.51 (s, 1H), 6.02 (d, $J = 4.1$, 2H), 6.16 (d, $J = 4.1$, 1H), 6.33 (s, 2H), 6.65 (d, $J = 4.1$, 2H), 7.08 (m, 3H), 7.22-7.35 (m, 3H), 7.54-7.73 (m, 2H), 8.06 (d, $J = 8.44$, 2H); ^{13}C NMR (400 MHz, CDCl_3): δ 37.3, 42.1, 43.8, 56.9, 59.3, 60.8, 62.2, 67.8, 102.4, 108.3, 109.1, 110.9, 114.5, 115.0, 117.4, 117.8, 123.3, 123.6, 124.9, 129.9, 130.8, 131.3, 131.8, 133.8, 143.2, 147.1, 148.5, 149.9, 162.3, 173.7, 190.2; IR (KBr): 3363.6, 1775.6, 1598.5, 1505.3, 1485.2, 1238.0, 1002.6, 753.9 cm^{-1} ; ESI-MS: 720.2 ($\text{M} + \text{H}$). Anal. Calc. for $\text{C}_{40}\text{H}_{34}\text{FN}_3\text{O}_9$: C, 66.75; H, 4.76; N, 5.84 Found: C, 66.78; H, 4.73; N, 5.82.

6h. **9-(4-{4-[3-(2-Fluoro-phenyl)-acryloyl]-phenoxy-methyl}-[1,2,3]triazol-1-yl)-5-(3,4,5-trimethoxy-phenyl)-5,8,8a,9-tetrahydro-5aH-furo[3',4':6,7]naphtho [2,3-d] [1,3] dioxol-6-one:** White solid; mp: 137-138 $^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{25} - 69.4$ (0.75, CHCl_3); ^1H NMR (400 MHz, CDCl_3): 3.06 (m, 1H), 3.29 (m, 2H), 3.79 (s, 6H), 3.82 (s, 3H), 4.42 (t, $J = 7.5$, 1H), 4.76 (d, $J = 4.7$, 1H), 5.26 (s, 2H), 5.49 (s, 1H), 6.03 (d, $J = 3.88$, 2H), 6.13 (d, $J = 4.2$, 1H), 6.33 (s, 2H), 6.64 (d, $J =$

7.5, 2H), 7.05-7.33 (*m*, 5H), 7.65-7.83 (*m*, 3H), 8.04 (*d*, $J = 8.76$, 2H); ^{13}C NMR (400 MHz, CDCl_3): δ 37.2, 42.1, 56.9, 59.27, 60.8, 66.2, 67.8, 67.7, 102.41, 106.8, 107.8, 109.6, 113.9, 120.7, 122.2, 123.4, 127.4, 128.3, 129.4, 129.8, 130.8, 132.0, 131.8, 133.5, 137.2, 156.6, 160.8, 163.0, 188.3; IR (KBr): 3415.3, 1786.5, 1587.4, 1505.1, 1485.2, 1262.0, 1062.6, 738.9 cm^{-1} ; ES-IMS: 720.2 ($\text{M} + \text{H}$). Anal. Calc. for $\text{C}_{40}\text{H}_{34}\text{FN}_3\text{O}_9$: C, 66.75; H, 4.76; N, 5.84 Found: C, 66.77; H, 4.75; N, 5.80.

6i. 5-(3,4,5-Trimethoxy-phenyl)-9-{4-[4-(3-m-tolyl-acryloyl)-phenoxy methyl]-[1,2,3]triazol-1-yl}-5,8,8a,9-tetrahydro-5aH-furo[3',4':6,7]naphtho[2,3-d] [1,3]dioxol-6-one: White solid; mp: 122-123 $^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{25} - 42$ (0.70, CHCl_3); ^1H NMR (400 MHz, CDCl_3): 2.41 (*s*, 3H), 3.06 (*m*, 1H), 3.26 (*m*, 2H), 3.80 (*s*, 6H), 3.83 (*s*, 3H), 4.41 (*t*, $J = 7.6$, 1H), 4.75 (*d*, $J = 4.5$, 1H), 5.26 (*s*, 2H), 5.45 (*s*, 1H), 6.02 (*d*, $J = 3.65$, 2H), 6.13 (*d*, $J = 3.65$, 1H), 6.33 (*s*, 2H), 6.64 (*d*, $J = 8.2$, 2H), 7.08 (*d*, $J = 8.8$, 2H), 7.24-7.29 (*m*, 4H), 7.57-7.79 (*m*, 2H), 8.04 (*d*, $J = 8.57$, 2H); ^{13}C NMR (400 MHz, CDCl_3): δ 18.6, 36.0, 40.7, 42.5, 55.3, 57.9, 60.7, 61.0, 66.4, 101.0, 106.9, 107.8, 109.6, 113.6, 120.5, 122.2, 123.4, 124.8, 127.8, 128.6, 129.8, 130.3, 131.2, 132.5, 133.5, 133.9, 137.6, 143.4, 145.6, 147.1, 148.5, 160.7, 172.1, 186.7; IR (KBr): 3425, 2915, 1775, 1747, 1599, 1455, 1240, 1114, 1037, 763 cm^{-1} ; ESI-MS: 716.3 ($\text{M} + \text{H}$). Anal. Calc. for $\text{C}_{41}\text{H}_{37}\text{N}_3\text{O}_9$: C, 68.80; H, 5.21; N, 5.87 Found: C, 68.85; H, 5.14; N, 5.89.

6j. 5-(3,4,5-Trimethoxy-phenyl)-9-(4-{4-[3-(4-methoxy-phenyl)-acryloyl]-phenoxy methyl}-[1,2,3]triazol-1-yl)-5,8,8a,9-tetrahydro-5aH-furo[3',4':6,7] naphtho [2,3-d][1,3]dioxol-6-one: White solid; mp: 145-147 $^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{25} - 38.5$ (0.75, CHCl_3); ^1H NMR (400 MHz, CDCl_3): 3.08 (*m*, 1H), 3.26 (*m*, 2H), 3.79 (*s*, 9H), 3.82 (*s*, 3H), 4.41 (*t*, $J = 7.6$, 1H), 4.76 (*d*, $J = 4.5$, 1H), 5.26 (*s*, 2H), 5.47 (*s*, 1H), 6.03 (*d*, $J = 3.83$, 2H), 6.13 (*d*, $J = 4.1$, 1H), 6.33 (*s*, 2H), 6.64 (*d*, $J = 7.59$, 2H), 7.07 (*d*, $J = 7.59$, 2H), 7.24-7.41 (*m*, 4H), 7.66-7.67 (*m*, 2H), 8.06 (*d*, $J = 8.78$, 2H); ^{13}C NMR (400 MHz, CDCl_3): δ 36.2, 41.2, 42.5, 55.8, 58.1, 60.7, 61.0, 65.0, 66.4, 70.2, 101.0, 106.8, 106.8, 109.6, 113.9, 120.7, 122.2, 124.4, 127.4, 128.3, 129.4, 129.8, 130.8, 132.0, 132.5, 133.5, 134.0, 143.1, 145.8, 147.1, 148.2, 156.6, 160.8, 172.1, 191.7; IR (KBr): 3386.3, 1778.6, 1597.3, 1507.2, 1485.2, 1237.0, 1001.5, 733.3 cm^{-1} ; ESI-MS: 732.3 ($\text{M} + \text{H}$). Anal. Calc. for $\text{C}_{41}\text{H}_{37}\text{N}_3\text{O}_{10}$: C, 67.30; H, 5.10; N, 5.74 Found: C, 67.35; H, 5.04; N, 5.77.

7a. 9-[4-(4-Acetyl-phenoxy)methyl]-[1,2,3]triazol-1-yl]-5-(4-hydroxy-3,5-dimethoxy-phenyl)-5,8,8a,9-tetrahydro-5aH-furo[3',4':6,7]naphtho[2,3-d][1,3]dioxol-6-one: White solid; mp: 143-145 °C; $[\alpha]_D^{25}$ - 45 (0.75, CHCl₃); ¹H NMR (400 MHz, CDCl₃): 2.49 (s, 3H), 3.05 (m, 1H), 3.26 (m, 2H), 3.74 (s, 6H), 4.33 (t, *J* = 7.6, 1H), 4.65 (d, *J* = 4.8, 1H), 5.15 (s, 2H), 5.92 (d, *J* = 5.94, 2H), 6.06 (d, *J* = 3.67, 1H), 6.24 (s, 2H), 6.56 (d, *J* = 5.68, 2H), 6.96 (d, *J* = 7.21, 2H), 7.37 (s, 1H), 7.85 (d, *J* = 7.47, 2H); ¹³C NMR (400 MHz, CDCl₃): δ 29.5, 37.0, 41.4, 43.4, 55.9, 58.8, 62.2, 67.5, 105.3, 111.3, 111.5, 112.0, 113.8, 113.9, 117.9, 118.0, 127.1, 134.1, 146.7, 150.4, 150.5, 151.5, 152.8, 177.1, 201.2; IR (KBr): 3385.3, 1773.6, 1731.2, 1598.5, 1515.3, 1477.2, 1338.0, 1016.6, 759.7 cm⁻¹; ESI-MS: 622 (M + Na⁺). Anal. Calc. for C₃₂H₂₉N₃O₉: C, 64.10; H, 4.88; N, 7.01 Found: C, 64.24; H, 5.01; N, 6.92.

7b. 5-(4-Hydroxy-3,5-dimethoxy-phenyl)-9-{4-[4-(3-oxo-but-1-enyl)-phenoxy)methyl]-[1,2,3]triazol-1-yl}-5,8,8a,9-tetrahydro-5aH-furo[3',4':6,7]naphtho[2,3-d][1,3]-6-one : White solid; mp: 139-141 °C; $[\alpha]_D^{25}$ - 16.3 (0.760, CHCl₃); ¹H NMR (400 MHz, CDCl₃): 2.36 (s, 3H), 3.06 (m, 1H), 3.26 (m, 2H), 3.80 (s, 6H), 4.40 (t, *J* = 7.6, 1H), 4.75 (d, *J* = 4.8, 1H), 5.20 (s, 2H), 5.47 (s, 1H), 6.02 (d, *J* = 4.19, 2H), 6.11 (d, *J* = 4.0, 1H), 6.33 (s, 2H), 6.62 (m, 2H), 7.00 (d, *J* = 8.72, 2H), 7.28 (m, 2H), 7.52 (d, *J* = 8.78, 2H); ¹³C NMR (400 MHz, CDCl₃): δ 24.1, 27.4, 29.7, 37.0, 41.7, 43.5, 56.5, 58.8, 62.0, 67.4, 82.5, 84.4, 102.0, 107.8, 108.8, 110.6, 115.2, 123.1, 124.4, 125.4, 127.8, 129.6, 130.0, 133.4, 134.4, 142.9, 143.8, 146.6, 148.1, 149.5, 159.9, 173.1, 198.4; IR (KBr): 3389.9, 1778.6, 1598.5, 1505.3, 1485.2, 1238.0, 1011.6, 774.7 cm⁻¹; ESI-MS: 648 (M + Na⁺). Anal. Calc. for C₃₄H₃₁N₃O₉: C, 65.27; H, 4.99; N, 6.72 Found: C, 65.10; H, 4.84; N, 6.79.

7c. 5-(4-Hydroxy-3,5-dimethoxy-phenyl)-9-{4-[2-methoxy-4-(3-oxo-but-1-enyl)-phenoxy)methyl]-[1,2,3]triazol-1-yl}-5,8,8a,9-tetrahydro-5aH-furo[3',4':6,7]naphtho [2,3-d][1,3]dioxol-6-one: White solid; mp: 136-138 °C; $[\alpha]_D^{25}$ - 25.6 (0.75, CHCl₃); ¹H NMR (400 MHz, CDCl₃): 2.31 (s, 3H), 3.05 (m, 1H), 3.26 (m, 2H), 3.73 (s, 6H), 3.77 (s, 3H), 4.40 (t, *J* = 7.6, 1H), 4.79 (d, *J* = 4.8, 1H), 5.22 (s, 2H), 5.40 (s, 1H), 6.02 (d, *J* = 3.67, 2H), 6.25 (s, 1H), 6.53 (m, 1H), 6.69 (m, 2H), 7.01 (s, 2H), 7.28-7.48 (m, 2H), 7.52 (d, *J* = 8.78, 2H); ¹³C NMR (400 MHz, CDCl₃): δ 24.1, 27.4, 29.7, 37.0, 41.6, 43.4, 55.9, 56.5, 58.8, 62.0, 67.4, 82.5, 84.4, 102.0, 107.8, 108.9, 110.5, 115.2, 122.7, 123.4, 125.8, 127.8, 129.6, 130.0, 133.4, 134.4, 142.9, 143.8, 146.6, 148.1, 149.5, 159.9, 173.1, 197.9; IR (KBr): 3388.6, 1775.2, 1598.2, 1507.1,

1485.2, 1239.2, 1002.6, 754.7 cm^{-1} ; ESI-MS: 678 ($\text{M} + \text{Na}$). Anal. Calc. for $\text{C}_{34}\text{H}_{33}\text{N}_3\text{O}_9$: C, 64.12; H, 5.07; N, 6.41 Found: C, 64.24; H, 5.16; N, 6.53.

7d. 5-(4-Hydroxy-3,5-dimethoxy-phenyl)-9-{4-[4-(3-oxo-3-phenyl-propenyl)-phenoxy-methyl]-[1,2,3]triazol-1-yl}-5,8,8a,9-tetrahydro-5aH-furo[3',4':6,7]naphtho[2,3-d]

[1,3]dioxol-6-one: White solid; mp: 151-153 $^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{25} - 37$ (0.75, CHCl_3); ^1H NMR (400 MHz, CDCl_3): 3.06 (m, 1H), 3.29 (m, 2H), 3.80 (s, 6H), 4.41 (t, $J = 7.6$, 1H), 4.76 (d, $J = 4.6$, 1H), 5.26 (s, 2H), 5.47 (s, 1H), 6.01 (d, $J = 3.7$, 2H), 6.12 (d, $J = 4.0$, 1H), 6.33 (s, 2H), 6.64 (d, $J = 7.7$, 2H), 7.05 (d, $J = 8.6$, 2H), 7.24-7.54 (m, 3H), 7.57-7.79 (m, 4H), 8.05 (d, $J = 8.78$, 2H); ^{13}C NMR (400 MHz, CDCl_3): δ 29.7, 37.1, 41.7, 43.5, 56.6, 58.9, 62.1, 67.4, 102.1, 107.9, 108.8, 110.6, 114.7, 121.8, 123.3, 124.5, 128.4, 129.0, 129.7, 130.5, 130.9, 131.8, 134.5, 135.0, 144.3, 146.7, 148.2, 149.5, 186.7; IR (KBr): 3382.7, 1778.6, 1598.5, 1505.3, 1485.2, 1233.4, 1005.3, 769.3 cm^{-1} ; ESI-MS: 710 ($\text{M} + \text{Na}$). Anal. Calc. for $\text{C}_{39}\text{H}_{33}\text{N}_3\text{O}_9$: C, 68.11; H, 4.84; N, 6.11 Found: C, 68.20; H, 4.94; N, 6.02.

7e. 5-(4-Hydroxy-3,5-dimethoxy-phenyl)-9-{4-[4-(3-phenyl-acryloyl)-phenoxy methyl]-[1,2,3]triazol-1-yl}-5,8,8a,9-tetrahydro-5aH-furo[3',4':6,7]naphtho[2,3-d] [1,3]dioxol-6-one:

White solid; mp: 145-148 $^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{25} - 44.4$ (0.60, CHCl_3); ^1H NMR (400 MHz, CDCl_3): 3.06 (m, 1H), 3.26 (m, 2H), 3.80 (s, 6H), 4.39 (t, $J = 7.6$, 1H), 4.75 (d, $J = 4.5$, 1H), 5.23 (s, 2H), 5.46 (s, 1H), 6.02 (d, $J = 3.65$, 2H), 6.14 (d, $J = 3.65$, 1H), 6.33 (s, 2H), 6.64 (d, $J = 8.2$, 2H), 7.02 (d, $J = 8.6$, 2H), 7.24-7.32 (m, 2H), 7.34-7.54 (m, 3H), 7.57-7.79 (m, 2H), 8.05 (d, $J = 8.57$, 2H); ^{13}C NMR (400 MHz, CDCl_3): δ 29.6, 37.1, 41.7, 43.5, 56.6, 58.9, 62.1, 67.4, 101.1, 107.9, 108.8, 110.6, 114.7, 121.8, 124.3, 124.5, 128.4, 129.0, 129.7, 130.5, 132.9, 131.8, 134.5, 135.0, 144.3, 146.7, 148.2, 150.5, 186.7; IR (KBr): 3347.1, 1777.7, 1587.2, 1598.3, 1485.2, 1287.0, 1002.6, 738.6 cm^{-1} ; ESI-MS: 710 ($\text{M} + \text{Na}$). Anal. Calc. for $\text{C}_{39}\text{H}_{33}\text{N}_3\text{O}_9$: C, 68.11; H, 4.84; N, 6.11 Found: C, 68.21; H, 4.72; N, 6.23.

7f. 9-(4-{4-[3-(4-Fluoro-phenyl)-acryloyl]-phenoxy-methyl}-[1,2,3]triazol-1-yl)-5-(4-hydroxy-3,5-dimethoxy-phenyl)-5,8,8a,9-tetrahydro-5aH-furo[3',4':6,7]naphtho [2,3-d] [1,3]

dioxol-6-one: White solid; mp: 162-164 $^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{25} - 28$ (0.75, CHCl_3); ^1H NMR (400 MHz, CDCl_3): 3.06 (m, 1H), 3.26 (m, 2H), 3.81 (s, 6H), 4.41 (t, $J = 7.6$, 1H), 4.76 (d, $J = 4.7$, 1H), 5.26 (s, 2H), 5.50 (s, 1H), 6.02 (d, $J = 3.88$, 2H), 6.12 (d, $J = 4.2$, 1H), 6.33 (s, 2H), 6.64 (d, $J = 7.5$, 2H), 7.05-7.23 (m, 5H), 7.65-7.82 (m, 3H), 8.04 (d, $J = 8.77$, 2H); ^{13}C NMR (400 MHz, CDCl_3): δ 36.4, 42.1, 56.9, 59.27, 60.6, 66.2, 67.8, 67.7, 102.41, 106.8, 107.8, 109.6, 113.9,

120.7, 122.2, 124.4, 126.4, 128.3, 129.4, 129.8, 131.8, 132.0, 132.5, 133.5, 138.3, 157.6, 160.8, 161.0, 189.4; IR (KBr): 3409.1, 1778.6, 1598.5, 1505.3, 1485.2, 1238.0, 1012.6, 756.8 cm^{-1} ; ESI-MS: 706 ($M + H$). Anal. Calc. for $\text{C}_{39}\text{H}_{32}\text{FN}_3\text{O}_9$: C, 66.38; H, 4.57; N, 5.95 Found: C, 66.29; H, 4.64; N, 5.83.

7g. 9-(4-{4-[3-(3-Fluoro-phenyl)-acryloyl]-phenoxy-methyl}-[1,2,3]triazol-1-yl)-5-(4-hydroxy-3,5-dimethoxy-phenyl)-5,8,8a,9-tetrahydro-5aH-furo[3',4':6,7]naphtho [2,3-d] [1,3]dioxol-6-one: White solid; mp: 173-175 $^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{25} - 53.3$ (0.55, CHCl_3); ^1H NMR (400 MHz, CDCl_3): 3.08 (m, 1H), 3.28 (m, 2H), 3.80 (s, 6H), 4.42 (t, $J = 7.6$, 1H), 4.76 (d, $J = 4.5$, 1H), 5.28 (s, 2H), 5.51 (s, 1H), 6.02 (d, $J = 4.1$, 2H), 6.15 (d, $J = 4.1$, 1H), 6.33 (s, 2H), 6.64 (d, $J = 4.1$, 2H), 7.08 (m, 3H), 7.22-7.36 (m, 3H), 7.54-7.72 (m, 2H), 8.05 (d, $J = 8.44$, 2H); ^{13}C NMR (400 MHz, CDCl_3): δ 37.4, 42.1, 43.8, 56.9, 59.3, 62.3, 67.8, 102.4, 108.3, 109.1, 110.9, 114.5, 115.0, 117.4, 117.8, 123.3, 123.6, 124.9, 129.9, 130.8, 131.3, 131.8, 133.8, 143.2, 147.1, 148.5, 149.9, 162.3, 173.7, 191.2; IR (KBr): 3378.6, 1778.6, 1598.5, 1505.3, 1485.2, 1238.0, 1002.6, 754.9 cm^{-1} ; ESI-MS: 706 ($M + H$). Anal. Calc. for $\text{C}_{39}\text{H}_{32}\text{FN}_3\text{O}_9$: C, 66.38; H, 4.57; N, 5.95 Found: C, 66.47; H, 4.68; N, 5.87.

7h. 9-(4-{4-[3-(2-Fluoro-phenyl)-acryloyl]-phenoxy-methyl}-[1,2,3]triazol-1-yl)-5-(4-hydroxy-3,5-dimethoxy-phenyl)-5,8,8a,9-tetrahydro-5aH-furo[3',4':6,7]naphtho [2,3-d] [1,3]dioxol-6-one: White solid; mp: 142-146 $^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{25} - 62.4$ (0.75, CHCl_3); ^1H NMR (400 MHz, CDCl_3): 3.06 (m, 1H), 3.29 (m, 2H), 3.80 (s, 6H), 4.41 (t, $J = 7.5$, 1H), 4.76 (d, $J = 4.7$, 1H), 5.26 (s, 2H), 5.49 (s, 1H), 6.02 (d, $J = 3.88$, 2H), 6.13 (d, $J = 4.2$, 1H), 6.33 (s, 2H), 6.64 (d, $J = 7.5$, 2H), 7.05-7.33 (m, 5H), 7.65-7.82 (m, 3H), 8.05 (d, $J = 8.77$, 2H); ^{13}C NMR (400 MHz, CDCl_3): δ 37.4, 42.1, 56.9, 59.27, 60.6, 66.2, 67.8, 67.7, 102.41, 106.8, 107.8, 109.6, 113.9, 120.7, 122.2, 123.4, 127.4, 128.3, 129.4, 129.8, 130.8, 132.0, 132.5, 133.5, 137.3, 156.6, 160.8, 163.0, 188.4; IR (KBr): 3405.3, 1789.5, 1587.4, 1505.1, 1485.2, 1262.0, 1063.6, 736.9 cm^{-1} ; ESI-MS: 706 ($M + H$). Anal. Calc. for $\text{C}_{39}\text{H}_{32}\text{FN}_3\text{O}_9$: C, 66.38; H, 4.69; N, 5.95 Found: C, 66.29; H, 4.60; N, 5.87.

7i. 5-(4-Hydroxy-3,5-dimethoxy-phenyl)-9-{4-[4-(3-m-tolyl-acryloyl)-phenoxy methyl]-[1,2,3]triazol-1-yl}-5,8,8a,9-tetrahydro-5aH-furo[3',4':6,7]naphtho[2,3-d] [1,3]dioxol-6-one: White solid; mp: 129-132 $^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{25} - 35$ (0.70, CHCl_3); ^1H NMR (400 MHz, CDCl_3): 2.40 (s, 3H), 3.06 (m, 1H), 3.28 (m, 2H), 3.80 (s, 6H), 4.41 (t, $J = 7.6$, 1H), 4.76 (d, $J = 4.5$, 1H), 5.26 (s, 2H), 5.46 (s, 1H), 6.02 (d, $J = 3.65$, 2H), 6.15 (d, $J = 3.65$, 1H), 6.33 (s, 2H), 6.64 (d, $J = 8.2$,

2H), 7.07 (*d*, *J* = 8.8, 2H) , 7.24-7.29 (*m*, 4H), 7.57-7.79 (*m*, 2H), 8.05 (*d*, *J* = 8.57, 2H); ¹³C NMR (400 MHz, CDCl₃): δ 18.3, 36.0, 40.7, 42.5, 55.5, 57.9, 61.0, 66.4, 101.0, 106.9, 107.8, 109.6, 113.6, 120.5, 122.2, 123.4, 124.6, 127.8, 128.6, 129.8, 130.3, 130.9, 132.5, 133.5, 133.9, 137.6, 143.4, 145.6, 147.1, 148.5, 160.7, 172.1, 187.7; IR (KBr): 3408, 2925, 1775, 1747, 1599, 1457, 1240, 1114, 1037, 760 cm⁻¹; ESI-MS:702 (M + H). Anal. Calc. for C₄₀H₃₅N₃O₉: C, 68.46; H, 5.03; N, 5.99 Found: C, 68.35; H, 5.14; N, 5.87.

7j. 5-(4-Hydroxy-3,5-dimethoxy-phenyl)-9-(4-{4-[3-(4-methoxy-phenyl)-acryloyl]-phenoxy-methyl}-[1,2,3]triazol-1-yl)-5,8,8a,9-tetrahydro-5aH-furo[3',4':6,7] naphtho [2,3-d][1,3]dioxol-6-one: White solid; mp: 152-154 °C; [α]_D²⁵ – 33.2 (0.70, CHCl₃) ; ¹H NMR (400 MHz, CDCl₃): 3.06 (*m*, 1H), 3.27 (*m*, 2H), 3.80 (*s*, 9H), 4.41 (*t*, *J* = 7.6, 1H), 4.76 (*d*, *J* = 4.5, 1H), 5.26 (*s*, 2H), 5.48 (*s*, 1H), 6.02 (*d*, *J* = 3.83, 2H), 6.13 (*d*, *J* = 4.1 , 1H), 6.33 (*s*, 2H), 6.64 (*d*, *J* = 7.59, 2H), 7.07 (*d*, *J* = 7.59, 2H) , 7.22-7.42 (*m*, 4H), 7.64-7.66 (*m*, 2H), 8.05 (*d*, *J* = 8.78, 2H); ¹³C NMR (400 MHz, CDCl₃): δ 36.0, 41.2, 42.5, 55.6, 58.1, 61.0, 65.0, 66.4, 70.2, 101.0, 106.8, 107.8, 109.6, 113.9, 120.7, 122.2, 123.4, 127.4, 128.3, 129.4, 129.8, 130.8, 132.0, 132.5, 133.5, 134.0, 143.3, 145.6, 147.1, 148.2, 156.6, 160.8, 172.1, 191.9; IR (KBr): 3388.3, 1778.6, 1596.4, 1507.3, 1485.2, 1238.0, 1002.6, 732.3 cm⁻¹; ESI-MS:718 (M + H). Anal. Calc. for C₄₀H₃₅N₃O₁₀: C, 66.94; H, 4.92; N, 5.85 Found: C, 66.79; H, 5.04; N, 5.97.