



SUPPLEMENTARY MATERIAL TO
**Novel hybrids of oxoisoaporphine–tryptamine as inhibitors of
acetylcholinesterase-induced β -amyloid aggregation with
improved antioxidant properties**

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CHARACTERIZATION DATA FOR THE SYNTHESIZED COMPOUNDS

4-Oxo-4-[(7-oxo-7H-dibenzo[de,h]quinolin-9-yl)amino](2Z)-but-2-enoic acid (4a). From compound **3** (0.74 g, 3 mmol) and maleic anhydride (2.9 g, 30 mmol), a yellow powder maleic acid derivative **4a** (0.57 g, 55 % yield) was obtained from toluene; $^1\text{H-NMR}$ (500 MHz, $\text{DMSO-}d_6$, δ / ppm): 6.38 (1H, *d*, J = 12.2 Hz), 6.54 (1H, *d*, J = 12.2 Hz), 7.98 (1H, *d*, J = 5.5 Hz), 8.03 (1H, *t*, J = 7.9 Hz), 8.11 (1H, *d*, J = 7.3 Hz), 8.41 (1H, *d*, J = 8.5 Hz), 8.53–8.56 (2H, *m*), 8.75 (1H, *d*, J = 9.2 Hz), 8.77 (1H, *d*, J = 5.5 Hz), 10.83 (1H, *s*); ESI-MS (m/z): 343 $[\text{M-H}]^-$.

4-Oxo-4-[(7-oxo-7H-dibenzo[de,h]quinolin-9-yl)amino]butanoic acid (4b). From compound **3** (0.74 g, 3 mmol) and succinic anhydride (2.9 g, 30 mmol), a yellow powder succinic acid derivative **4b** (0.76 g, 73 % yield) was obtained from toluene; $^1\text{H-NMR}$ (500 MHz, $\text{DMSO-}d_6$, δ / ppm): 2.58 (2H, *t*, J = 6.7 Hz), 2.66 (2H, *t*, J = 6.7 Hz), 8.00 (1H, *d*, J = 5.5 Hz), 8.05 (1H, *dd*, J_1 = 7.3 Hz, J_2 = 7.9 Hz), 8.09 (1H, *d*, J = 8.5 Hz), 8.43 (1H, *d*, J = 8.5 Hz), 8.55–8.57 (2H, *m*), 8.76 (1H, *d*, J = 8.5 Hz), 8.79 (1H, *d*, J = 5.5 Hz), 10.46 (1H, *s*), 12.17 (1H, *brs*); ESI-MS (m/z): 345 $[\text{M-H}]^-$.

5-Oxo-5-[(7-oxo-7H-dibenzo[de,h]quinolin-9-yl)amino]pentanoic acid (4c). From compound **3** (0.74 g, 3 mmol) and glutaric anhydride (3.4 g, 30 mmol), a yellow powder glutaric acid derivative **4c** (0.73 g, 68 % yield) was obtained from toluene; $^1\text{H-NMR}$ (500 MHz, $\text{DMSO-}d_6$, δ / ppm): 1.83–1.89 (2H, *m*), 2.33 (2H, *t*, J = 7.3 Hz), 2.44 (2H, *t*, J = 7.3 Hz), 7.97 (1H, *d*, J = 5.5 Hz), 8.03 (1H, *dd*, J_1 = 7.9 Hz, J_2 = 7.3 Hz), 8.09 (1H, *d*, J = 8.5 Hz), 8.40 (1H, *d*, J = 8.5 Hz),

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8.52–8.55 (2H, *m*), 8.72 (1H, *d*, *J* = 9.2 Hz), 8.76 (1H, *d*, *J* = 5.5 Hz), 10.38 (1H, *s*); ESI-MS (*m/z*): 359 [M–H][–].

N¹-(2-(5-Methoxy-1H-indol-3-yl)ethyl)-N⁴-(7-oxo-7H-dibenzo[de,h]quinolin-9-yl)-(2*Z*)-2-butenediamide (**5a**). Yield: 0.62 g, 60 %; orange solid; Anal. Calcd. for C₃₁H₂₄N₄O₄·2H₂O: C, 67.38; H, 5.11; N, 10.14 %. Found: C, 67.19; H, 5.37; N, 10.41 %; ¹H-NMR (500 MHz, DMSO-*d*₆, δ / ppm): 2.87 (2H, *t*, *J* = 7.1 Hz), 3.46–3.49 (2H, *m*), 3.76 (3H, *s*), 6.72 (1H, *d*, *J* = 8.5 Hz), 7.04–7.14 (4H, *m*), 7.23 (1H, *d*, *J* = 8.6 Hz), 8.02 (1H, *d*, *J* = 5.5 Hz), 8.06 (1H, *dd*, *J*₁ = 7.6 Hz, *J*₂ = 7.7 Hz), 8.16 (1H, *d*, *J* = 7.3 Hz), 8.44 (1H, *d*, *J* = 8.6 Hz), 8.58 (1H, *d*, *J* = 7.0 Hz), 8.65 (1H, *s*), 8.70 (1H, *t*, *J* = 5.2 Hz), 8.78–8.80 (2H, *m*), 10.68 (1H, *s*), 10.93 (1H, *s*); ¹³C-NMR (125 MHz, DMSO-*d*₆, δ / ppm): 24.9, 45.3, 55.2, 100.0, 111.4, 111.9, 116.5, 120.6, 121.4, 123.3, 124.5, 125.9, 127.4, 128.0, 129.6, 130.7, 131.3, 131.4, 132.2, 132.3, 134.0, 134.6, 134.7, 140.8, 143.8, 147.2, 152.9, 162.7, 163.2, 169.4, 181.9; ESI-MS (*m/z*): 517 [M+H]⁺.

N¹-(2-(5-Methoxy-1H-indol-3-yl)ethyl)-N⁴-(7-oxo-7H-dibenzo[de,h]quinolin-9-yl)butanediamide (**5b**). Yield: 0.67 g, 65 %; orange solid; Anal. Calcd. for C₃₁H₂₆N₄O₄·H₂O: C, 69.39; H, 5.26; N, 10.44 %. Found: C, 69.12; H, 5.21; N, 10.07 %; ¹H-NMR (500 MHz, DMSO-*d*₆, δ / ppm): 2.47–2.50 (2H, *m*), 2.66 (2H, *t*, *J* = 7.1 Hz), 2.79 (2H, *t*, *J* = 7.7 Hz), 3.32–3.36 (2H, *m*), 3.75 (3H, *s*), 6.7 (1H, *dd*, *J*₁ = 2.3 Hz, *J*₂ = 8.3 Hz), 7.02 (1H, *d*, *J* = 2.1 Hz), 7.12 (1H, *s*), 7.22 (1H, *d*, *J* = 8.7 Hz), 7.97 (1H, *d*, *J* = 5.6 Hz), 8.01–8.08 (3H, *m*), 8.40 (1H, *d*, *J* = 8.1 Hz), 8.54 (2H, *d*, *J* = 7.9 Hz), 8.72 (1H, *d*, *J* = 8.6 Hz), 8.76 (2H, *d*, *J* = 5.6 Hz), 10.46 (1H, *s*), 10.64 (1H, *s*); ¹³C-NMR (125 MHz, DMSO-*d*₆, δ / ppm): 25.2, 30.2, 31.7, 45.3, 55.2, 100.1, 110.9, 111.6, 111.9, 116.0, 120.4, 121.2, 123.2, 124.1, 125.7, 127.4, 128.0, 129.4, 130.6, 130.7, 131.3, 132.3, 134.0, 134.5, 141.4, 143.9, 147.5, 152.9, 170.9, 171.0, 182.0; ESI-MS (*m/z*): 519 [M+H]⁺.

N¹-(2-(5-Methoxy-1H-indol-3-yl)ethyl)-N⁵-(7-oxo-7H-dibenzo[de,h]quinolin-9-yl)pentanediamide (**5c**). Yield: 0.65 g, 61 %; orange solid; Anal. Calcd. for C₃₂H₂₈N₄O₄·2H₂O: C, 67.59; H, 5.67; N, 9.85 %. Found: C, 67.65; H, 5.91; N, 9.62 %; ¹H-NMR (500 MHz, DMSO-*d*₆, δ / ppm): 1.83–1.89 (2H, *m*), 2.17 (2H, *t*, *J* = 7.2 Hz), 2.39 (2H, *t*, *J*₁ = 7.1 Hz, *J*₂ = 7.2 Hz), 2.78 (2H, *t*, *J* = 7.0 Hz), 3.30–3.34 (2H, *m*), 3.73 (3H, *s*), 6.69 (1H, *d*, *J* = 8.9 Hz), 7.03 (1H, *s*), 7.12 (1H, *s*), 7.21 (1H, *d*, *J* = 8.7 Hz), 7.94 (1H, *d*, *J* = 5.5 Hz), 7.99–8.04 (3H, *m*), 8.37 (1H, *d*, *J* = 8.1 Hz), 8.51 (2H, *d*, *J* = 7.3 Hz), 8.57 (1H, *d*, *J* = 8.7 Hz), 8.73 (1H, *d*, *J* = 5.5 Hz), 10.42 (1H, *s*), 10.61 (1H, *s*); ¹³C-NMR (125 MHz, DMSO-*d*₆, δ / ppm): 22.9, 25.2, 34.6, 35.8, 45.4, 55.3, 100.1, 110.9, 111.6, 111.9, 116.2, 120.7, 121.4, 123.1, 124.4, 126.0, 127.5, 128.2, 129.7, 130.9, 131.0, 131.3, 132.4, 134.1, 134.7, 141.4, 144.0, 147.5, 152.9, 171.4, 171.5, 182.2; ESI-MS (*m/z*): 533 [M+H]⁺.

N¹-(2-(5-Methyl-1H-indol-3-yl)ethyl)-N⁴-(7-oxo-7H-dibenzo[de,h]quinolin-9-yl)-(2*Z*)-2-butenediamide (**5d**). Yield: 0.52 g, 52 %; orange solid; Anal. Calcd.

for $C_{31}H_{24}N_4O_3 \cdot H_2O$: C, 71.80; H, 5.05; N, 10.80 %. Found: C, 71.42; H, 5.22; N, 10.71 %; 1H -NMR (500 MHz, $DMSO-d_6$, δ / ppm): 2.63 (3H, s), 3.01 (2H, t, $J = 6.9$ Hz), 3.58–3.61 (2H, m), 7.02 (1H, d, $J = 8.4$ Hz), 7.20 (1H, s), 7.25 (1H, d, $J = 8.2$ Hz), 7.36 (1H, d, $J = 8.5$ Hz), 7.45 (1H, s), 8.13 (1H, d, $J = 5.5$ Hz), 8.19 (1H, dd, $J_1 = 7.5$ Hz, $J_2 = 8.0$ Hz), 8.29 (1H, d, $J = 8.6$ Hz), 8.56 (1H, d, $J = 8.2$ Hz), 8.70 (1H, d, $J = 7.2$ Hz), 8.77 (1H, s), 8.82 (1H, dd, $J_1 = 4.4$ Hz, $J_2 = 4.9$ Hz), 8.89–8.93 (2H, m), 10.84 (1H, s), 11.08 (1H, s); ^{13}C -NMR (125 MHz, $DMSO-d_6$, δ / ppm): 21.2, 24.9, 45.3, 110.9, 111.1, 116.5, 117.7, 120.6, 121.4, 123.2, 124.6, 125.9, 126.9, 127.3, 128.1, 129.6, 130.8, 131.5, 132.2, 132.3, 134.0, 134.5, 134.6, 134.7, 140.9, 143.9, 147.3, 162.7, 163.3, 169.5, 182.0; ESI-MS (m/z): 501 $[M+H]^+$.

N^1 -(2-(5-Methyl-1H-indol-3-yl)ethyl)- N^4 -(7-oxo-7H-dibenzo[de,h]quinolin-9-yl)butanediamide (**5e**). Yield: 0.55 g, 55 %; orange solid; Anal. Calcd. for $C_{31}H_{26}N_4O_3$: C, 74.09; H, 5.21; N, 11.15 %. Found: C, 74.45; H, 5.47; N, 10.86 %; 1H -NMR (500 MHz, $DMSO-d_6$, δ / ppm): 2.35 (3H, s), 2.49 (2H, t, $J = 7.0$ Hz), 2.66 (2H, t, $J = 6.9$ Hz), 2.79 (2H, t, $J = 7.5$ Hz), 3.32–3.38 (2H, m), 6.88 (1H, d, $J = 8.2$ Hz), 7.10 (1H, s), 7.22 (1H, d, $J = 8.2$ Hz), 7.29 (1H, s), 7.97 (1H, d, $J = 5.4$ Hz), 8.01–8.08 (2H, m), 8.41 (1H, d, $J = 8.1$ Hz), 8.53–8.54 (2H, m), 8.72 (1H, d, $J = 8.5$ Hz), 8.76 (1H, d, $J = 5.4$ Hz), 10.46 (1H, s), 10.67 (1H, s); ^{13}C -NMR (125 MHz, $DMSO-d_6$, δ / ppm): 21.2, 25.2, 30.1, 31.7, 45.4, 110.9, 111.2, 116.0, 117.7, 120.5, 121.3, 122.4, 122.6, 124.2, 125.8, 126.4, 127.4, 128.1, 129.5, 130.6, 130.7, 132.2, 134.0, 134.5, 134.6, 141.4, 143.8, 147.4, 170.9, 171.1, 182.0. ESI-MS (m/z): 503 $[M+H]^+$.

N^1 -(2-(5-Methyl-1H-indol-3-yl)ethyl)- N^5 -(7-oxo-7H-dibenzo[de,h]quinolin-9-yl)pentanediamide (**5f**). Yield: 0.44 g, 43 %; orange solid; Anal. Calcd. for $C_{32}H_{28}N_4O_3 \cdot H_2O$: C, 71.89; H, 5.66; N, 10.48 %. Found: C, 71.77; H, 5.92; N, 10.26 %; 1H -NMR (500 MHz, $DMSO-d_6$, δ / ppm): 1.86–1.91 (2H, m), 2.18 (2H, t, $J = 7.3$ Hz), 2.36 (3H, s), 2.43 (2H, t, $J = 7.2$ Hz), 2.78 (2H, t, $J_1 = 7.7$ Hz), 3.30–3.34 (2H, m), 6.86 (1H, d, $J = 8.2$ Hz), 7.09 (1H, s), 7.20 (1H, d, $J = 8.2$ Hz), 7.29 (1H, s), 7.98–8.01 (2H, m), 8.05 (1H, dd, $J_1 = 8.0$ Hz, $J_2 = 7.4$ Hz), 8.11 (1H, d, $J = 8.7$ Hz), 8.43 (1H, d, $J = 8.2$ Hz), 8.55–8.58 (2H, m), 8.74 (1H, d, $J = 8.6$ Hz), 8.77 (1H, d, $J = 5.5$ Hz), 10.50 (1H, s), 10.69 (1H, s); ^{13}C -NMR (125 MHz, $DMSO-d_6$, δ / ppm): 21.1, 21.2, 25.2, 34.6, 35.8, 45.5, 110.9, 111.3, 116.1, 117.7, 120.5, 121.3, 122.3, 122.5, 124.3, 125.8, 126.4, 127.4, 128.1, 129.5, 130.7, 130.8, 132.2, 134.0, 134.5, 134.6, 141.4, 143.8, 147.4, 171.4, 171.5, 182.1; ESI-MS (m/z): 517 $[M+H]^+$.

N^1 -(2-(5-Fluoro-1H-indol-3-yl)ethyl)- N^4 -(7-oxo-7H-dibenzo[de,h]quinolin-9-yl)-(2Z)-2-butanediamide (**5g**). Yield: 0.57 g, 57 %; orange solid; Anal. Calcd. for $C_{30}H_{21}FN_4O_3 \cdot H_2O$: C, 68.96; H, 4.44; N, 10.72 %. Found: C, 69.23; H, 4.72; N, 10.51 %; 1H -NMR (500 MHz, $DMSO-d_6$, δ / ppm): 2.88 (2H, t, $J_1 = 7.0$ Hz), 3.45–3.49 (2H, m), 6.91 (1H, t, $J_1 = 9.2$ Hz, $J_2 = 9.0$ Hz), 7.04–7.14 (2H,

m), 7.27–7.35 (2H, *m*), 7.99 (1H, *d*, *J* = 5.5 Hz), 8.03 (1H, *dd*, *J*₁ = 7.6 Hz, *J*₂ = 8.2 Hz), 8.14 (1H, *d*, *J* = 8.0 Hz), 8.42 (1H, *d*, *J* = 8.1 Hz), 8.55 (1H, *d*, *J* = 7.1 Hz), 8.62 (1H, *s*), 8.69 (1H, *d*, *J* = 5.3 Hz), 8.74–8.78 (2H, *m*), 10.94 (1H, *s*), 10.97 (1H, *s*); ¹³C-NMR (125 MHz, DMSO-*d*₆, δ / ppm): 24.7, 45.3, 102.9, 111.9, 112.2, 116.5, 120.7, 121.4, 123.3, 124.6, 125.9, 127.4, 128.1, 129.6, 130.8, 131.5, 132.3, 132.4, 132.8, 134.0, 134.6, 134.7, 140.8, 143.9, 147.3, 157.5, 162.7, 163.3, 169.3, 181.9. ESI-MS (*m/z*): 505 [M+H]⁺.

N¹-(2-(5-Fluoro-1H-indol-3-yl)ethyl)-N⁴-(7-oxo-7H-dibenzo[de,h]quinolin-9-yl)butanediamide (**5h**). Yield: 0.49 g, 48 %; orange solid; Anal. Calcd. for C₃₀H₂₃FN₄O₃: C, 71.14; H, 4.58; N, 11.06 %. Found: C, 70.86; H, 4.84; N, 10.74 %; ¹H-NMR (500 MHz, DMSO-*d*₆, δ / ppm): 2.47 (2H, *t*, *J* = 7.2 Hz), 2.66 (2H, *t*, *J* = 7.1 Hz), 2.79 (2H, *t*, *J* = 7.4 Hz), 3.32 (2H, *t*, *J* = 7.2 Hz), 6.87 (1H, *t*, *J* = 9.2 Hz), 7.24 (1H, *s*), 7.26–7.33 (2H, *m*), 7.98 (1H, *d*, *J* = 5.6 Hz), 8.03 (1H, *t*, *J* = 7.7 Hz), 8.07 (1H, *d*, *J* = 8.5 Hz), 8.41 (1H, *d*, *J* = 8.1 Hz), 8.53–8.55 (2H, *m*), 8.72 (1H, *d*, *J* = 8.6 Hz), 8.77 (1H, *d*, *J* = 5.6 Hz), 10.48 (1H, *s*), 10.93 (1H, *s*); ¹³C-NMR (125 MHz, DMSO-*d*₆, δ / ppm): 25.0, 30.1, 31.7, 45.4, 102.9, 111.9, 112.2, 116.3, 120.5, 121.4, 124.2, 124.7, 125.9, 127.3, 127.4, 128.1, 129.6, 130.8, 132.2, 132.7, 134.0, 134.6, 141.4, 143.9, 147.3, 155.6, 157.5, 170.9, 171.0, 182.1; ESI-MS (*m/z*): 507 [M+H]⁺.

N¹-(2-(5-Fluoro-1H-indol-3-yl)ethyl)-N⁵-(7-oxo-7H-dibenzo[de,h]quinolin-9-yl)pentanediamide (**5i**). Yield: 0.42 g, 40 %; orange solid; Anal. Calcd. for C₃₁H₂₅FN₄O₃: C, 71.53; H, 4.84; N, 10.76 %. Found: C, 71.77; H, 5.15; N, 10.57 %; ¹H-NMR (500 MHz, DMSO-*d*₆, δ / ppm): 1.85–1.91 (2H, *m*), 2.18 (2H, *t*, *J* = 7.3 Hz), 2.42 (2H, *t*, *J* = 7.3 Hz), 2.79 (2H, *t*, *J* = 7.5 Hz), 3.30–3.33 (2H, *m*), 6.89 (1H, *t*, *J* = 9.1 Hz), 7.23 (1H, *s*), 7.27–7.33 (2H, *m*), 7.97 (1H, *d*, *J* = 5.6 Hz), 8.03 (1H, *t*, *J* = 7.9 Hz), 8.09 (1H, *d*, *J* = 8.6 Hz), 8.40 (1H, *d*, *J* = 8.2 Hz), 8.53–8.56 (2H, *m*), 8.71 (1H, *d*, *J* = 8.6 Hz), 8.76 (1H, *d*, *J* = 5.6 Hz), 10.43 (1H, *s*), 10.93 (1H, *s*); ¹³C-NMR (125 MHz, DMSO-*d*₆, δ / ppm): 21.3, 25.0, 34.5, 35.7, 45.4, 102.9, 112.1, 116.1, 120.5, 121.3, 124.3, 124.6, 125.8, 127.3, 127.4, 128.1, 129.6, 130.8, 130.9, 132.2, 132.7, 134.0, 134.6, 141.4, 143.8, 147.4, 155.6, 157.4, 171.4, 171.5, 182.1. ESI-MS (*m/z*): 521 [M+H]⁺.