



SUPPLEMENTARY MATERIAL TO
**Synthesis, characterisation and antimicrobial activity of
(5-bromo-5-nitro-2-oxido-1,3,2-dioxaphosphinan-2-yl)
amino acid esters**

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ANALYTICAL AND SPECTRAL DATA OF THE TITLE COMPOUNDS

Methyl [(5-bromo-5-nitro-2-oxido-1,3,2-dioxaphosphinan-2-yl)amino]acetate (3a). Yield: 75 %; m.p.: 177–179 °C; Anal. Calcd. for: C₆H₁₀BrN₂O₇P (FW 332): C, 21.64; H, 3.03; N, 8.41 %. Found: C, 21.60; H, 3.98; N, 8.38 %. IR (KBr, cm⁻¹): 3418 (–N–H, secondary amine), 1745 (–C=O, ester), 1555 (–NO₂), 1255 (–P=O, phosphinan), 552 (–C–Br). ¹H-NMR (400 MHz, DMSO-*d*₆, δ / ppm): 4.14–4.25 (4H, *m*, –CH₂ (C₄ and 6)), 8.22 (1H, *brs*, NH, D₂O exchangeable), 3.42 (3H, *s*, –OCH₃), 4.13 (2H, *s*, –NCH₂). ¹³C-NMR (100 MHz, DMSO-*d*₆, δ / ppm): 54.6 (C₄ and 6), 70.7 (C₅), 170.1 (COO), 37.2 (NCH₂), 53.4 (–OCH₃). ³¹P-NMR (161.7 MHz, DMSO-*d*₆, δ / ppm): 13.2. MS (*m/z*, relative abundance, %): 334 (M+2, 31.6), 332 (M⁺, 32.5).

Methyl 2-[(5-bromo-5-nitro-2-oxido-1,3,2-dioxaphosphinan-2-yl)amino]propanoate (3b). Yield: 71 %; m.p.: 123–124 °C; Anal. Calcd. for: C₇H₁₂BrN₂O₇P (FW 346): C, 24.23; H, 3.49; N, 8.07 %. Found C, 24.18; H, 3.45; N, 8.01 %. IR (KBr, cm⁻¹): 3419 (–N–H, secondary amine), 1745 (–C=O, ester), 1558 (–NO₂), 1254 (–P=O, phosphinan), 553 (–C–Br). ¹H-NMR (400 MHz, DMSO-*d*₆, δ / ppm): 4.17–4.42 (4H, *m*, –CH₂ (C₄ and 6)), 8.42 (1H, *brs*, NH, D₂O exchangeable), 3.48 (1H, *s*, –NCH), 3.45 (3H, *s*, –OCH₃), 1.45 (3H, *d*, *J* = 6.2 Hz, CH₃). ¹³C-NMR (100 MHz, DMSO-*d*₆, δ / ppm): 53.2 (C₄ and 6), 68.4 (C₅), 168.4 (COO), 38.4 (NCH), 52.7 (–OCH₃), 26.3 (CH₃). ³¹P-NMR (161.7 MHz, DMSO-

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d_6 , δ / ppm): 9.02. MS (m/z , relative abundance, %): 348 ($M+2$, 28.6), 346 (M^+ , 30.5).

Ethyl 2-[(5-bromo-5-nitro-2-oxido-1,3,2-dioxaphosphinan-2-yl)amino]propanoate (3c). Yield: 69 %; m.p.: 160–162 °C; Anal. Calcd. for $C_8H_{14}BrN_2O_7P$ (FW 360): C, 26.61; H, 3.91; N, 7.76 %. Found C, 26.58; H, 3.87; N, 7.71 %. IR (KBr, cm^{-1}): 3432 (–N–H, secondary amine), 1743 (–C=O, ester), 1561 (–NO₂), 1258 (–P=O, phosphinan), 557 (–C–Br). ¹H-NMR (400 MHz, DMSO- d_6 , δ / ppm): 4.14–4.42 (4H, *m*, –CH₂ (C₄ and 6)), 8.08 (1H, *brs*, –NH, D₂O exchangeable), 4.13 (2H, *q*, $J = 5.8$ Hz, –OCH₂), 3.49 (1H, *q*, $J = 5.7$ Hz, –NCH), 1.26 (6H, *m*, 2 \times –CH₃). ³¹P-NMR (161.7 MHz, DMSO- d_6 , δ / ppm): 7.24.

Methyl 2-[(5-bromo-5-nitro-2-oxido-1,3,2-dioxaphosphinan-2-yl)amino]-3-methyl butanoate (3d). Yield: 71 %; m.p.: 190–192 °C; Anal. Calcd. for: $C_9H_{16}N_2O_7P$ (FW 374): C, 28.82; H, 4.30; N, 7.47 %. Found C, 28.79; H, 4.28; N, 7.44 %. IR (KBr, cm^{-1}): 3420 (–N–H, secondary amine), 1742 (–C=O, ester), 1561 (–NO₂), 1256 (–P=O, phosphinan), 557 (–C–Br). ¹H-NMR (400 MHz, DMSO- d_6 , δ / ppm): 4.20–4.52 (4H, *m*, –CH₂ (C₄ and 6)), 8.02 (1H, *brs*, –NH, D₂O exchangeable), 3.47 (3H, *s*, –OCH₃), 3.45 (1H, *d*, $J = 5.6$ Hz, –NCH), 1.35 (1H, *m*, –CH), 1.03 (6H, *d*, $J = 6.4$ Hz, 2CH₃). ¹³C-NMR (100 MHz, DMSO- d_6 , δ / ppm): 55.2 (C₄ and 6), 71.1 (C₅), 169.3 (COO), 37.9 (–NCH), 53.8 (–OCH₃), 21.6 (2 \times –CH₂), 18.7 (CH₃). ³¹P-NMR (161.7 MHz, DMSO- d_6 , δ / ppm): 8.52.

Methyl 2-[(5-bromo-5-nitro-2-oxido-1,3,2-dioxaphosphinan-2-yl)amino]pentanoate (3e). Yield: 74 %; m.p.: 189–191 °C; Anal. Calcd. for: $C_9H_{16}N_2O_7P$ (FW 374): C, 28.82; H, 4.30; N, 7.47 %. Found C, 28.79; H, 4.28; N, 7.44 %. IR (KBr, cm^{-1}): 3435 (–N–H secondary amine), 1745 (–C=O, ester), 1560 (–NO₂), 1258 (–P=O, phosphinan), 560 (–C–Br). ¹H-NMR (400 MHz, DMSO- d_6 , δ / ppm): 4.17–4.52 (4H, *m*, CH₂ (C₄ and 6)), 8.68 (1H, *brs*, NH, D₂O exchangeable), 3.56 (1H, *t*, $J = 5.7$ Hz, N–CH), 3.58 (3H, *s*, OCH₃), 1.12–1.58 (4H, *m*, 2 \times CH₂), 1.22 (3H, *t*, $J = 6.8$ Hz, –CH₃). ¹³C-NMR (100 MHz, DMSO- d_6 , δ / ppm): 56.3 (C₄ and 6), 72.3 (C₅), 170.3 (COO), 38.4 (–NCH), 54.4 (–OCH₃), 22.4 (2 \times –CH₂), 17.3 (CH₃). ³¹P-NMR (161.7 MHz, DMSO- d_6 , δ / ppm): 10.41.

Ethyl 2-[(5-bromo-5-nitro-2-oxido-1,3,2-dioxaphosphinan-2-yl)amino]pentanoate (3f). Yield: 74 %; m.p.: 128–130 °C; Anal. Calcd. for: $C_{10}H_{18}BrN_2O_7P$ (FW 388): C, 30.86; H, 4.66; N, 7.20 %. Found C, 30.81; H, 4.62; N, 7.18 %. IR (KBr, cm^{-1}): 3432 (–N–H, secondary amine), 1748 (–C=O, ester), 1561 (–NO₂), 1249 (–P=O, phosphinan), 560 (–C–Br). ¹H-NMR (400 MHz, DMSO- d_6 , δ / ppm): 4.17–4.50 (4H, *m*, –CH₂ (C₄&6)), 8.66 (1H, *brs*, NH, D₂O exchangeable), 3.47 (1H, *m*, –NCH), 4.10 (2H, *q*, $J = 5.7$ Hz, –OCH₂), 1.26 (3H, *t*, $J = 3.2$ Hz, –CH₃), 1.23–1.58 (4H, *m*, 2 \times –CH₂), 1.12 (3H, *t*, $J = 3.3$ Hz, –CH₃). ¹³C-NMR (100 MHz, DMSO- d_6 , δ / ppm): 56.8 (C₄ and 6), 72.6 (C₅), 169.8 (COO), 37.7 (–NCH), 54.2 (–OCH₂), 22.4 (2 \times –CH₂), 17.3 (–CH₃), 19.6 (–CH₃). ³¹P-

-NMR (161.7 MHz, DMSO- d_6 , δ / ppm): 11.7. MS (m/z , relative abundance, %): 390 (M+2, 23.2), 388 (M⁺, 24.6).

Methyl 1-(5-bromo-5-nitro-2-oxido-1,3,2-dioxaphosphinan-2-yl)pyrrolidine-2-carboxylate (3g). Yield: 75 %; m.p.: 177–179 °C; Anal. Calcd. for: C₉H₁₄BrN₂O₇P (FW 372): C, 28.97; H, 3.78; N, 7.51 %. Found C, 28.95; H, 3.75; N, 7.48 %. IR (KBr, cm⁻¹): 1739 (–C=O, ester), 1564 (–NO₂), 1251 (–P=O, phosphinan), 563 (–C–Br). ¹H-NMR (400 MHz, DMSO- d_6 , δ / ppm): 4.15–4.48 (4H, *m*, –CH₂ (C₄ and 6)), 3.19 (1H, *t*, *J* = 5.8 Hz, –NCH), 1.65–2.31 (6H, *m*, 3×–CH₂), 3.54 (3H, *s*, –OCH₃). ³¹P-NMR (161.7 MHz, DMSO- d_6 , δ / ppm): 10.5.

Methyl 2-[(5-bromo-5-nitro-2-oxido-1,3,2-dioxaphosphinan-2-yl)amino]-3-(1H-imidazol-4-yl)propanoate (3h). Yield: 72 %; m.p.: 135–137 °C; Anal. Calcd. for C₁₀H₁₄BrN₄O₇P (FW 412): C, 29.07; H, 3.42; N, 13.56 %. Found C, 29.02; H, 3.39; N, 13.53 %. IR (KBr, cm⁻¹): 3430 (–N–H, secondary amine), 1740 (–C=O, ester), 1554 (–NO₂), 1254 (–P=O, phosphinan), 554 (–C–Br). ¹H-NMR (400 MHz, DMSO- d_6 , δ / ppm): 6.75–7.25 (2H, *m*, Ar–H), 4.15–4.43 (4H, *m*, –CH₂ (C₄ and 6)), 8.72 (2H, *brs*, NH, D₂O exchangeable), 3.45 (1H, *m*, –NCH), 3.59 (3H, *s*, OCH₃), 2.81 (2H, *m*, Ar–CH₂). ³¹P-NMR (161.7 MHz, DMSO- d_6 , δ / ppm): 11.5; MS (m/z , (relative abundance, %): 414 (M+2, 17.3), 412 (M⁺, 18.9).

Methyl 2-[(5-bromo-5-nitro-2-oxido-1,3,2-dioxaphosphinan-2-yl)amino]-3-phenylpropanoate (3i). Yield: 70 %; m.p.: 138–140 °C; Anal. Calcd. for C₁₃H₁₆BrN₂O₇P (FW 421): C, 36.90; H, 3.81; N, 6.62 %. Found C, 36.86; H, 3.78; N, 6.59 %. IR (KBr, cm⁻¹): 3441 (–N–H, secondary amine), 1743 (–C=O, ester), 1555 (–NO₂), 1248 (–P=O, phosphinan), 555 (–C–Br). ¹H-NMR (400 MHz, DMSO- d_6 , δ / ppm): 6.78–7.20 (5H, *m*, Ar–H), 4.35–4.52 (4H, *m*, –CH₂ (C₄ and 6)), 8.59 (1H, *s*, –N–H, D₂O exchangeable), 3.91 (2H, *m*, Ar–CH₂), 3.64 (3H, *s*, –OCH₃), 3.51 (1H, *m*, –NCH). ³¹P-NMR (161.7 MHz, DMSO- d_6 , δ / ppm): 11.5.

Ethyl 2-[(5-bromo-5-nitro-2-oxido-1,3,2-dioxaphosphinan-2-yl)amino]-3-phenylpropanoate (3j). Yield: 68 %; m.p.: 115–117 °C; Anal. Calcd. for C₁₄H₁₈BrN₂O₇P (FW 436): C, 38.46; H, 4.15; N, 6.41 %. Found C, 38.43; H, 4.12; N, 6.38 %. IR (KBr, cm⁻¹): 3439 (–N–H, secondary amine), 1748 (–C=O, ester), 1558 (NO₂), 1250 (–P=O, phosphinan), 561 (–C–Br). ¹H-NMR (400 MHz, DMSO- d_6 , δ / ppm): 6.76–7.21 (6H, *m*, Ar–H), 4.28–4.42 (4H, *m*, –CH₂ (C₄ and 6)), 8.58 (1H, *s*, –N–H, D₂O exchangeable), 3.87 (2H, *m*, Ar–CH₂), 4.12 (2H, *q*, *J* = 5.7 Hz, –OCH₂), 3.54 (1H, *m*, –NCH), 1.25 (3H, *t*, *J* = 6.8 Hz, –CH₃). ¹³C-NMR (100 MHz, DMSO- d_6 , δ / ppm): 168.2 (COO), 123.2–143.7 (C_{aromatic}), 56.8 (NCH), 56.1 (OCH₂), 43.2 (Ar–CH₂), 19.8 (CH₃). ³¹P-NMR (161.7 MHz, DMSO- d_6 , δ / ppm): 12.2. MS (m/z , relative abundance, %): 438 (M+2, 31.2), 436 (M⁺, 35.6).

Methyl 2-[(5-bromo-5-nitro-2-oxido-1,3,2-dioxaphosphinan-2-yl)amino]-3-(1H-indol-3-yl)propanoate (3k). Yield: 72 %; m.p.: 108–110 °C; Anal. Calcd. for: C₁₅H₁₇BrN₃O₇PS (FW 461): C, 39.98; H, 3.71; N, 9.09 %. Found C, 39.96; H, 3.68; N, 9.05 %. IR (KBr, cm⁻¹): 3433 (–N–H, secondary amine), 1742 (C=O, ester), 1558 (–NO₂), 1255 (–P=O, phosphinan), 561 (–C–Br). ¹H-NMR (400 MHz, DMSO-*d*₆, δ / ppm): 6.78–7.29 (5H, *m*, Ar–H), 4.29–4.52 (4H, *m*, –CH₂ (C₄ and 6)), 8.75 (2H, *brs*, –N–H, D₂O exchangeable), 3.62 (3H, *s*, –OCH₃), 3.63 (1H, *m*, –NCH), 6.81–7.36 (2H, *m*, Ar–CH₂). ¹³C-NMR (100 MHz, DMSO-*d*₆, δ / ppm): 58.2 (C₄ and 6), 72.4 (C₅), 170.2 (COO), 37.2 (N–CH), 54.5 (OCH₃), 35.2 (C₃'), 112.5 (C₄'), 126.8 (C₅'), 117.6 (C₁₀'), 131.2 (C_{10a}'), 141.2 (C_{6a}'), 108.3 (C₇'), 125.3 (C₈'), 121.2 (C₉'). ³¹P-NMR (161.7 MHz, DMSO-*d*₆, δ / ppm): 10.9. MS (*m/z*, (relative abundance), %): 463 (M+2, 23.2), 461 (M⁺, 25.3).

Ethyl 1-(5-bromo-5-nitro-2-oxido-1,3,2-dioxaphosphinan-2-yl)-1H-indole-2-carboxylate (3l). Yield: 69 %; m.p.: 104–106 °C; Anal. Calcd. for: C₁₄H₁₄BrN₂O₇P (FW 432): C, 38.82; H, 3.26; N, 6.47 %. Found C, 38.79; H, 3.22; N, 6.43 %. IR (KBr, cm⁻¹): 1742 (–C=O, ester), 1558 (–NO₂), 1253 (–P=O, phosphinan), 561 (–C–Br). ¹H-NMR (400 MHz, DMSO-*d*₆, δ / ppm): 6.77–7.26 (5H, *m*, Ar–H), 4.23–4.52 (4H, *m*, –CH₂ (C₄&6)), 4.14 (2H, *q*, *J* = 5.6 Hz, –OCH₂), 1.22 (3H, *t*, *J* = 6.7 Hz, –CH₃). ¹³C-NMR (100 MHz, DMSO-*d*₆, δ / ppm): 58.4 (C₄ and 6), 72.1 (C₅), 169.5 (COO), 54.6 (OCH₂), 18.9 (–CH₃), 133.3 (C₂'), 104.6 (C₃'), 131.5 (C_{3a}'), 122.2 (C₄'), 117.6 (C₅'), 124.6 (C₆'), 114.6 (C₇'), 145.6 (C_{7a}'). ³¹P-NMR (161.7 MHz, DMSO-*d*₆, δ / ppm): 11.2.