Supporting Information

Synthesis of novel 2-alkoxy-3-amino-3-arylpropan-1-ols and 5-alkoxy-4-aryl-1,3-oxazinanes with antimalarial activity

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Recrystallization from absolute EtOH. Mp = 102.4 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.86 and 0.87 (6H, 2 × d, *J* = 6.6 Hz); 1.72-1.85 (1H, m); 2.39 (3H, s); 2.66 and 3.27 (2H, 2 × (d × d), *J* = 13.9, 8.3, 6.3 Hz); 4.20 and 4.28 (2H, 2 × d, *J* = 11.6 Hz); 4.71 (1H, d, *J* = 4.1 Hz); 4.87 (1H, d, *J* = 4.1 Hz); 6.94-6.97 and 7.19-7.26 (9H, 2 × m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.3, 20.4, 21.2, 27.1, 47.5, 62.5, 72.1, 83.3, 127.8, 128.15, 128.18, 128.5, 129.2, 130.8, 136.5, 138.5, 167.5. IR (NaCl, cm^{-1}): $\nu_{C=O}$ = 1739. MS (70eV): m/z (%) 324 (M^++1, 100). Anal. Calcd for $C_{21}H_{25}NO_2$: C 77.98, H 7.79, N 4.33. Found: C 78.17, H 7.99, N 4.21. Purity > 95% (GC).

***cis*-1-Cyclohexyl-3-methoxy-4-(3-methoxyphenyl)azetidin-2-one 2c**

R_f = 0.075 (hexane/EtOAc 4/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.82-1.30, 1.47-1.80 and 1.90-1.96 (10H, 3 × m); 3.08 (3H, s); 3.39-3.51 (1H, m); 3.82 (3H, s); 4.59 (1H, d, *J* = 4.4 Hz); 4.72 (1H, d, *J* = 4.4 Hz); 6.87-6.99 and 7.26-7.31 (4H, 2 × m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.98, 25.02, 25.2, 30.4, 31.5, 52.5, 55.3, 58.1, 60.7, 84.7, 113.95, 114.01, 120.9, 129.2, 136.9, 159.4, 166.7. IR (NaCl, cm^{-1}): $\nu_{C=O}$ = 1745. MS (70eV): m/z (%) 290 (M^++1, 100). Anal. Calcd for $C_{17}H_{23}NO_3$: C 70.56, H 8.01, N 4.84. Found: C 70.41, H 8.13, N 4.94. Purity > 95% (GC).

***cis*-3-Benzyloxy-4-(4-chlorophenyl)-1-phenylazetidin-2-one 2d**

Recrystallization from absolute EtOH. Mp = 101.7 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.32 and 4.45 (2H, 2 × d, *J* = 11.3 Hz); 5.00 (1H, d, *J* = 4.7 Hz); 5.17 (1H, d, *J* = 4.7 Hz); 6.98-7.10 and 7.22-7.37 (14H, 2 × m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 61.3, 72.8, 82.7, 117.4, 124.6, 128.1, 128.4, 128.9, 129.2, 129.5, 132.1, 134.6, 136.2, 136.9, 164.1. IR (NaCl, cm^{-1}): $\nu_{C=O}$ = 1734. MS (70eV): m/z (%) 364/6 (M^++1, 100). Anal. Calcd for $C_{22}H_{18}ClNO_2$: C 72.62, H 4.99, N 3.85. Found: C 72.71, H 5.13, N 3.95. Purity > 95% (GC).

***cis*-1-*tert*-Butyl-3-methoxy-4-(4-methylphenyl)azetidin-2-one 2e**

Recrystallization from absolute EtOH. Mp = 102.4 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.26 (9H, s); 2.36 (3H, s); 3.04 (3H, d, *J* = 1.1 Hz); 4.50 (1H, d, *J* = 4.4 Hz); 4.74 (1H, d, *J* = 4.4 Hz); 7.17 and 7.29 (4H, 2 × d, *J* = 7.7 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.2, 28.2, 54.4, 57.9, 60.9, 83.6, 128.5, 128.9, 132.9, 138.1, 166.7. IR (NaCl, cm^{-1}): $\nu_{C=O}$ = 1732. MS (70eV): m/z (%) 248 (M^++1, 100). Anal. Calcd for $C_{15}H_{21}NO_2$: C 72.84, H 8.56, N 5.66. Found: C 72.71, H 8.76, N 5.75. Purity > 95% (GC).

***cis*-1-Benzyl-3-benzyloxy-4-(2-bromophenyl)azetidin-2-one 2f**

Recrystallization from absolute EtOH. Mp = 102.5 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.93 (1H, d, *J* = 14.9 Hz); 4.28 and 4.34 (2 × 1H, 2 × d, *J* = 11.6 Hz); 4.86 (1H, d, *J* = 14.9 Hz); 4.90 (1H, d, *J* = 4.4 Hz); 5.05 (1H, d, *J* = 4.4 Hz); 6.94-6.97, 7.14-7.42 and 7.57-7.59 (14H, 3 × m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 44.6, 60.8, 72.5, 83.6, 123.9, 127.4, 127.9, 128.0, 128.2, 128.7, 128.9, 129.5, 129.7, 132.9, 133.3, 134.7, 136.3, 166.7. IR (NaCl, cm^{-1}): $\nu_{C=O}$ = 1754. MS (70eV): m/z (%) 422/4 (M^++1, 100). Anal. Calcd for $C_{23}H_{20}BrNO_2$: C 65.41, H 4.77, N 3.32. Found: C 65.48, H 4.84, N 3.35. Purity > 95% (GC).

***cis*-1-Benzyl-4-(2-fluorophenyl)-3-phenoxyazetidin-2-one 2g**

Recrystallization from absolute EtOH. Mp = 101.8 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.94 and 4.89 (2 × 1H, 2 × d, *J* = 14.6 Hz); 5.18 (1H, d, *J* = 4.4 Hz); 5.42 (1H, d, *J* = 4.4 Hz); 6.73 (2H, d, *J* = 7.7 Hz); 6.84-6.94 and 7.08-7.41 (12H, 2 × m). ^{19}F NMR (282 MHz, $CDCl_3$): δ (-118.93) – (-118.85) (m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 44.6, 54.4 (d, *J* = 4.6 Hz), 82.0, 115.3 (d, *J* = 20.8 Hz), 115.3, 120.2 (d, *J* = 11.5 Hz), 122.1, 124.0 (d, *J* = 3.4 Hz), 128.2, 128.7, 129.0, 129.3, 129.4 (d, *J* = 2.3 Hz), 130.2 (d, *J* = 8.1 Hz), 134.6, 156.8, 161.3 (d, *J* = 248.1 Hz), 165.5. IR (NaCl, cm^{-1}): $\nu_{C=O}$ = 1747. MS (70eV): m/z (%) 348 (M^++1, 100). Anal. Calcd for $C_{22}H_{18}FNO_2$: C 76.06, H 5.22, N 4.03. Found: C 76.28, H 5.50, N 3.89. Purity > 95% (GC).

***cis*-4-(4-Methylphenyl)-3-phenoxy-1-propylazetidin-2-one 2i**

Recrystallization from absolute EtOH. Mp = 102.0 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.90 (3H, t, *J* = 7.5 Hz); 1.38-1.57 (2H, m); 2.30 (3H, s); 2.88-2.97 and 3.40-3.50 (2 × 1H, 2 × m); 4.90 (1H, d, *J* = 4.2 Hz); 5.40 (1H, d, *J* = 4.2 Hz); 6.73-6.76, 6.85-6.90, 7.09-7.15 and 7.21-7.26 (9H, 4 × m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.6, 20.8, 21.2, 42.1, 62.1, 81.9, 115.7, 121.9, 128.6, 129.0, 129.2, 130.1, 138.5, 157.1, 166.1. IR (NaCl, cm^{-1}): $\nu_{C=O}$ = 1748. MS (70eV): m/z (%) 296 (M^++1, 100). Anal. Calcd for $C_{19}H_{21}NO_2$: C 77.26, H 7.17, N 4.74. Found: C 77.07, H 7.28, N 4.64. Purity > 95% (GC).

***cis*-4-(4-Methoxyphenyl)-3-phenoxy-1-propylazetidin-2-one 2j**

Recrystallization from absolute EtOH. Mp = 92.4 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.90 (3H, t, *J* = 7.4 Hz); 1.42-1.57 (2H, m); 2.92 (1H, d × d × d, *J* = 14.0, 7.7, 6.1 Hz); 3.43 (1H, d × d × d, *J* = 14.0, 7.7, 7.7 Hz); 3.76 (3H, s); 4.89 (1H, d, *J* = 4.2 Hz); 5.40 (1H, d, *J* = 4.2 Hz);

6.73-6.76, 6.79-6.89, 7.09-7.15 and 7.24-7.29 (9H, 4 × m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.7, 20.9, 42.1, 55.3, 61.9, 81.9, 113.8, 115.6, 122.0, 125.1, 129.3, 130.0, 157.1, 159.9, 166.1. IR (NaCl, cm^{-1}): $\nu_{C=O}$ = 1742. MS (70eV): m/z (%) 312 (M^++1, 100). Anal. Calcd for $C_{19}H_{21}NO_3$: C 73.29, H 6.80, N 4.50. Found: C 73.36, H 6.88, N 4.43. Purity > 95% (GC).

***cis*-4-(3-Methoxyphenyl)-3-phenoxy-1-propylazetidin-2-one 2k**

Recrystallization from absolute EtOH. Mp = 92.4 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.91 (3H, t, *J* = 7.4 Hz); 1.42-1.63 (2H, m); 2.96 (1H, d × d × d, *J* = 13.9, 7.7, 6.1 Hz); 3.47 (1H, d × d × d, *J* = 13.9, 7.7, 7.7 Hz); 3.75 (3H, s); 4.91 (1H, d, *J* = 4.4 Hz); 5.43 (1H, d, *J* = 4.4 Hz); 6.74-6.92 and 7.10-7.25 (9H, 2 × m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.7, 20.9, 42.3, 55.4, 62.2, 81.9, 114.0, 114.4, 115.7, 121.1, 122.0, 129.27, 129.35, 135.0, 157.1, 159.6, 166.1. IR (NaCl, cm^{-1}): $\nu_{C=O}$ = 1753. MS (70eV): m/z (%) 312 (M^++1, 100). Anal. Calcd for $C_{19}H_{21}NO_3$: C 73.29, H 6.80, N 4.50. Found: C 73.38, H 6.91, N 4.37. Purity > 95% (GC).

***syn*-2-Benzyloxy-3-isobutylamino-3-(4-methylphenyl)propan-1-ol 3b**

R_f = 0.16 (hexane/EtOAc 4/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.86 and 0.87 (6H, 2 × d, *J* = 6.8 Hz); 1.60-1.74 (1H, m); 2.18 and 2.26 (2H, 2 × (d × d), *J* = 11.1, 6.9, 6.5 Hz); 2.36 (3H, s); 3.46-3.50 (1H, m); 3.71 (1H, d × d, *J* = 11.7, 2.5 Hz); 3.85 (1H, d, *J* = 3.9 Hz); 3.92 (1H, d × d, *J* = 11.7, 3.3 Hz); 4.42 and 4.63 (2H, 2 × d, *J* = 11.8 Hz); 7.14-7.35 (9H, m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.6, 20.8, 21.2, 28.6, 55.2, 63.2, 65.9, 71.9, 81.5, 127.7, 127.9, 128.4, 129.1, 137.0, 137.5, 138.2. IR (NaCl, cm^{-1}): $\nu_{NH,OH}$ = 3337. MS (70eV): m/z (%) 328 (M^++1, 100). Anal. Calcd for $C_{21}H_{29}NO_2$: C 77.02, H 8.93, N 4.28. Found: C 77.18, H 9.15, N 4.40. Purity > 95% (GC).

***syn*-3-Cyclohexylamino-2-methoxy-3-(3-methoxyphenyl)propan-1-ol 3c**

R_f = 0.22 (EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.05-1.31, 1.52-1.75 and 1.91-2.23 (10H, 3 × m); 2.44-2.53 (1H, m); 3.22-3.25 (1H, m); 3.33 (3H, s); 3.73 (1H, d × d, *J* = 13.8, 1.9 Hz); 3.82 (1H, d, *J* = 3.3 Hz); 3.82 (3H, s); 3.99 (1H, d × d, *J* = 13.8, 3.1 Hz); 6.53-6.96 and 7.21-7.31 (4H, 2 × m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.4, 24.9, 26.1, 32.1, 34.6, 52.6, 55.2, 57.5, 62.3, 63.1, 83.1, 112.5, 113.3, 120.0, 129.4, 142.9, 159.8. IR (NaCl, cm^{-1}): $\nu_{NH,OH}$ = 3323. MS (70eV): m/z (%) 294 (M^++1, 100). Anal. Calcd for $C_{17}H_{27}NO_3$: C 69.59, H 9.28, N 4.77. Found: C 69.64, H 9.37, N 4.85. Purity > 95% (GC).

***syn*-2-Benzyloxy-3-(4-chlorophenyl)-3-phenylaminopropan-1-ol 3d**

Recrystallization from CH_3CN. Mp = 105.4 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.63-3.84 (3H, m); 4.33 and 4.47 (2H, 2 × d, *J* = 11.6 Hz); 4.55-4.59 (1H, m); 4.74-4.76 (1H, m); 6.46-6.48, 6.52-6.74 and 7.04-7.38 (14H, 3 × m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 57.6, 61.9, 73.1, 82.8, 113.7, 117.8, 128.0, 128.5, 128.6, 128.7, 129.1, 132.9, 137.4, 139.8, 146.8. IR (NaCl, cm^{-1}): $\nu_{NH,OH}$ = 3391. MS (70eV): m/z (%) 368/70 (M^++1, 100). Anal. Calcd for $C_{22}H_{22}ClNO_2$: C 71.83, H 6.03, N 3.81. Found: C 71.64, H 6.17, N 3.68. Purity > 95% (GC).

***syn*-3-*tert*-Butylamino-2-methoxy-3-(4-methylphenyl)propan-1-ol 3e**

R_f = 0.17 (hexane/EtOAc 2/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.98 (9H, s); 2.33 (3H, s); 3.11-3.14 (1H, m); 3.32 (3H, s); 3.69 and 3.94 (2H, 2 × (d × d), *J* = 11.7, 3.9, 1.9 Hz); 4.01 (1H, d, *J* = 3.3 Hz); 7.12 and 7.23 (2 × 2H, 2 × d, *J* = 8.3 Hz). ^{13}C NMR (75 MHz, ref = $CDCl_3$): δ 21.2, 30.3, 51.4, 57.6, 60.6, 62.6, 83.5, 127.5, 129.0, 136.7, 140.8. IR (NaCl, cm^{-1}): $\nu_{NH,OH}$ = 3329. MS (70eV): m/z (%) 252 (M^++1, 100). Anal. Calcd for $C_{15}H_{25}NO_2$: C 71.67, H 10.02, N 5.57. Found: C 71.60, H 10.16, N 5.62. Purity > 95% (GC).

***syn*-3-Benzylamino-2-benzyloxy-3-(2-bromophenyl)propan-1-ol 3f**

R_f = 0.20 (hexane/EtOAc 4/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.50 (1H, d, *J* = 12.7 Hz); 3.54-3.56 (1H, m); 3.64 (1H, d, *J* = 12.7 Hz); 3.86 and 4.01 (2 × 1H, 2 × (d × d), *J* = 12.1, 2.8, 2.7 Hz); 4.26 (1H, d, *J* = 11.6 Hz); 4.50 (1H, d, *J* = 2.2 Hz); 4.56 (1H, d, *J* = 11.6 Hz); 7.07-7.12, 7.16-7.47 and 7.56-7.59 (14H, 3 × m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 50.7, 63.3, 63.8, 71.7, 79.2, 124.5, 127.3, 127.4, 127.6, 127.8, 128.3, 128.4, 128.5, 128.9, 133.2, 137.8, 138.5, 139.0. IR (NaCl, cm^{-1}): $\nu_{NH,OH}$ = 3333. MS (70eV): m/z (%) 426/8 (M^++1, 100). Anal. Calcd for $C_{23}H_{24}BrNO_2$: C 64.79, H 5.67, N 3.29. Found: C 64.91, H 5.87, N 3.14. Purity > 95% (GC).

***syn*-3-Benzylamino-3-(2-fluorophenyl)-2-phenoxypropan-1-ol 3g**

R_f = 0.09 (hexane/EtOAc 9/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.60 and 3.73 (2 × 1H, 2 × d, *J* = 12.7 Hz); 3.86 and 3.98 (2 × 1H, 2 × (d × d), *J* = 12.1, 3.3, 2.8 Hz); 4.35-4.38 (1H, m); 4.55 (1H, d, *J* = 3.3 Hz); 6.81-6.84, 6.90-6.95, 7.05-7.36 and 7.48-7.53 (14H, 4 × m). ^{19}F NMR (282 MHz, $CDCl_3$): δ (-118.82) – (-118.74) (m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 51.1, 57.1, 63.5, 80.7, 115.6 (d, *J* = 23.1 Hz), 116.9, 121.8, 124.5 (d, *J* = 3.5 Hz), 126.5 (d, *J* = 13.9 Hz), 127.3, 128.4, 128.6, 128.7, 129.2 (d, *J* = 8.0 Hz), 129.5, 139.2, 157.9, 161.1 (d, *J* = 244.6 Hz).

IR (NaCl, cm^{-1}): $\nu_{NH,OH}$ = 3296. MS (70eV): m/z (%) 352 (M^++1, 100). Anal. Calcd for $C_{22}H_{22}FNO_2$: C 75.19, H 6.31, N 3.99. Found: C 75.33, H 6.57, N 3.82. Purity > 95% (GC).

***cis*-5-Benzyloxy-3-isobutyl-4-(4-methylphenyl)-1,3-oxazinane 4b**

R_f = 0.35 (hexane/EtOAc 10/1). ^1H NMR (300 MHz, $CDCl_3$): δ 0.76 and 0.93 (6H, 2 × d, *J* = 6.6 Hz); 1.66-1.80 (1H, m); 1.98 (1H, d × d, *J* = 13.1, 5.2 Hz); 2.38 (3H, s); 2.36 (1H, d × d, *J* = 13.1, 9.4 Hz); 3.49-3.52 (1H, m); 3.58 (1H, d, *J* = 2.8 Hz); 3.67 (1H, d × d, *J* = 11.6, 1.9 Hz); 3.85 (1H, d, *J* = 8.8 Hz); 4.13 (1H, d × d, *J* = 11.6, 3.3 Hz); 4.33 (2H, s); 4.70 (1H, d, *J* = 8.8 Hz); 7.03-7.25 and 7.41-7.44 (9H, 2 × m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.8, 21.1, 21.2, 26.2, 58.8, 67.5, 68.8, 71.6, 73.7, 84.3, 127.4, 127.8, 128.1, 128.6, 129.2, 136.3, 136.6, 138.1. IR (NaCl, cm^{-1}): ν_{max} = 2953, 2867, 1454, 1164, 1087, 1054, 1068, 1028, 734, 696. MS (70eV): m/z (%) 340 (M^++1, 100). Anal. Calcd for $C_{22}H_{29}NO_2$: C 77.84, H 8.61, N 4.13. Found: C 78.04, H 8.89, N 3.98. Purity > 95% (GC).

***cis*-3-Cyclohexyl-5-methoxy-4-(3-methoxyphenyl)-1,3-oxazinane 4c**

R_f = 0.10 (EtOAc). ^1H NMR (300 MHz, $CDCl_3$): δ 0.86-1.98 (10H, m); 2.45-2.59 (1H, m); 3.15 (3H, s); 3.26-3.33 (1H, m); 3.69 (1H, d × d, *J* = 11.8, 1.6 Hz); 3.81 (3H, s); 3.99 (1H, d, *J* = 3.3 Hz); 4.11 (1H, d × d, *J* = 11.8, 3.9 Hz); 4.21 and 4.66 (2H, 2 × d, *J* = 8.8 Hz); 6.76-6.91 and 7.06-7.26 (4H, 2 × m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.0, 26.2, 26.9, 31.9, 33.5, 55.3, 57.3, 57.9, 64.2, 68.1, 77.3, 79.7, 112.9, 114.5, 121.4, 128.7, 141.2, 159.3. IR (NaCl, cm^{-1}): ν_{max} = 2926, 2852, 1600, 1585, 1486, 1464, 1450, 1257, 1151, 1107, 1084, 1050, 695. MS (70eV): m/z (%) 306 (M^++1, 100). Anal. Calcd for $C_{18}H_{27}NO_3$: C 70.79, H 8.91, N 4.59. Found: C 70.92, H 9.08, N 4.49. Purity > 95% (GC).

***cis*-5-Benzyloxy-4-(4-chlorophenyl)-3-phenyl-1,3-oxazinane 4d**

R_f = 0.28 (hexane/EtOAc 6/1). ^1H NMR (300 MHz, $CDCl_3$): δ 3.93-3.99 (2H, m); 4.12-4.19 (1H, m); 4.46 and 4.52 (2H, 2 × d, *J* = 12.1 Hz); 4.69-4.93 (3H, m); 6.99-7.17, 7.24-7.44 and 7.63-7.66 (14H, 3 × m). ^{13}C NMR (75 MHz, ref = $CDCl_3$): δ 63.6, 66.9, 71.9, 73.7, 79.3, 119.9, 122.0, 128.0, 128.5, 128.6, 129.4, 130.2, 133.0, 137.6, 137.7, 148.8. IR (NaCl, cm^{-1}): ν_{max} = 2869, 1599, 1491, 1264, 1089, 1058, 733, 696. MS (70eV): m/z (%) 380/2 (M^++1, 100). Anal. Calcd for $C_{23}H_{22}ClNO_2$: C 72.72, H 5.84, N 3.69. Found: C 72.83, H 5.97, N 3.77. Purity > 95% (GC).

***cis*-3-*tert*-Butyl-5-methoxy-4-(4-methylphenyl)-1,3-oxazinane 4e**

R_f = 0.06 (hexane/EtOAc 4/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.23 (9H, s); 2.33 (3H, s); 3.26 (3H, s); 3.80-3.94 (3H, m); 4.46-4.52 (2H, m); 4.68 (1H, d, *J* = 11.6 Hz); 7.11 and 7.47 (2 × 2H, d, *J* = 8.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.1, 29.8, 54.7, 55.7, 57.1, 65.0, 74.4, 76.8, 128.5, 128.6, 135.8, 138.7. IR (NaCl, cm^{-1}): ν_{max} = 2968, 2924, 2868, 1363, 1210, 1200, 1107, 1064, 972, 892, 853, 830. MS (70eV): m/z (%) 264 (M^++1, 100). Anal. Calcd for $C_{16}H_{25}NO_2$: C 72.96, H 9.57, N 5.32. Found: C 73.10, H 9.80, N 5.44. Purity > 95% (GC).

***cis*-3-Benzyl-5-benzyloxy-4-(2-bromophenyl)-1,3-oxazinane 4f**

R_f = 0.16 (hexane/EtOAc 8/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.06 (1H, d, *J* = 14.3 Hz); 3.54-3.62 (2H, m); 3.76-3.80 (2H, m); 4.03 (1H, s); 4.11-4.22 (3H, m); 4.62 (1H, d, *J* = 8.3 Hz); 6.86-6.89, 7.14-7.27, 7.35-7.40, 7.51-7.54 and 8.05-8.07 (14H, 5 × m). ^{13}C NMR (75 MHz, ref = $CDCl_3$): δ 54.8, 67.2, 69.7, 71.2, 72.2, 85.0, 123.9, 127.2, 127.4, 127.6, 128.2, 128.3, 128.4, 128.9, 132.8, 137.0, 137.3, 137.7. IR (NaCl, cm^{-1}): ν_{max} = 2843, 1453, 1346, 1176, 1104, 1083, 1063, 1026, 1017, 909, 752, 696. MS (70eV): m/z (%) 438/40 (M^++1, 100). Anal. Calcd for $C_{24}H_{24}BrNO_2$: C 65.76, H 5.52, N 3.20. Found: C 65.59, H 5.48, N 3.14. Purity > 95% (GC).

***cis*-3-Benzyl-4-(2-fluorophenyl)-5-phenoxy-1,3-oxazinane 4g**

R_f = 0.26 (hexane/EtOAc 9/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.23 (1H, d, *J* = 14.3 Hz); 3.83 (1H, d, *J* = 12.1 Hz); 3.93 (1H, d, *J* = 14.3 Hz); 3.97 (1H, d, *J* = 8.8 Hz); 4.28-4.36 (3H, m); 4.70 (1H, d, *J* = 8.8 Hz); 6.70 (2H, d, *J* = 7.7 Hz); 6.85-6.89, 7.00-7.31 and 7.98-8.03 (12H, 3 × m). ^{19}F NMR (282 MHz, $CDCl_3$): δ (-119.57) – (-119.48) (m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 54.2, 60.1, 69.4, 73.3, 84.7, 115.1 (d, *J* = 21.9 Hz), 116.2, 121.3, 124.0 (d, *J* = 3.4 Hz), 125.1 (d, *J* = 11.5 Hz), 127.2, 128.3, 128.8, 129.0 (d, *J* = 9.3 Hz), 129.4, 131.5 (d, *J* = 3.5 Hz), 137.3, 158.0, 160.7 (d, *J* = 245.8 Hz). IR (NaCl, cm^{-1}): ν_{max} = 2846, 1491, 1454, 1226, 1174, 1048, 751, 736, 692. MS (70eV): m/z (%) 364 (M^++1, 100). Anal. Calcd for $C_{23}H_{22}FNO_2$: C 76.01, H 6.10, N 3.85. Found: C 76.11, H 6.27, N 3.98. Purity > 95% (GC).

***cis*-5-Phenoxy-4-phenyl-3-propyl-1,3-oxazinane 4h**

R_f = 0.19 (hexane/EtOAc 6/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.79 (3H, t, *J* = 7.3 Hz); 1.36-1.59 (2H, m); 2.20 (1H, d × d × d, *J* = 13.3, 9.0, 6.1 Hz); 2.68 (1H, d × d × d, *J* = 13.3, 9.3, 6.4 Hz); 3.80-3.87 (2H, m); 4.08 (1H, d, *J* = 8.8 Hz); 4.31-4.34 (2H, m); 4.85 (1H, d, *J* = 8.8 Hz); 6.68-6.71, 6.85-6.90, 7.08-7.33 and 7.51-7.53 (10H, 4 × m). ^{13}C NMR (75 MHz, ref =

$CDCl_3$): δ 12.0, 20.5, 51.6, 67.7, 69.2, 74.0, 84.6, 116.5, 121.3, 127.5, 128.2, 128.9, 129.5, 138.7, 158.1. IR (NaCl, cm^{-1}): ν_{max} = 2970, 2923, 2860, 1599, 1585, 1488, 1234, 1057, 1035, 754, 691. MS (70eV): m/z (%) 298 (M^++1, 100). Anal. Calcd for $C_{19}H_{23}NO_2$: C 76.73, H 7.80, N 4.71. Found: C 76.76, H 7.89, N 4.62. Purity > 95% (GC).

***cis*-4-(4-Methylphenyl)-5-phenoxy-3-propyl-1,3-oxazinane 4i**

R_f = 0.23 (hexane/EtOAc 8/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.78 (3H, t, *J* = 7.3 Hz); 1.32-1.60 (2H, m); 2.20 (1H, d × d × d, *J* = 13.3, 8.9, 6.0 Hz); 2.30 (3H, s); 2.69 (1H, d × d × d, *J* = 13.3, 9.5, 6.4 Hz); 3.78-3.84 (2H, m); 4.08 (1H, d, *J* = 9.0 Hz); 4.30-4.34 (2H, m); 4.84 (1H, d, *J* = 9.0 Hz); 6.70-6.76, 6.82-6.90, 7.03-7.24 and 7.39-7.42 (9H, 4 × m). ^{13}C NMR (75 MHz, ref = $CDCl_3$): δ 12.0, 20.5, 21.2, 51.5, 67.4, 69.2, 73.9, 84.6, 116.5, 121.3, 128.8, 128.9, 129.5, 135.6, 137.1, 157.8. IR (NaCl, cm^{-1}): ν_{max} = 2962, 2929, 2871, 1598, 1586, 1494, 1237, 1041, 752, 692. MS (70eV): m/z (%) 312 (M^++1, 100). Anal. Calcd for $C_{20}H_{25}NO_2$: C 77.14, H 8.09, N 4.50. Found: C 77.29, H 8.31, N 4.63. Purity > 95% (GC).

***cis*-4-(4-Methoxyphenyl)-5-phenoxy-3-propyl-1,3-oxazinane 4j**

R_f = 0.14 (hexane/EtOAc 6/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.78 (3H, t, *J* = 7.4 Hz); 1.38-1.52 (2H, m); 2.14-2.23 (1H, m); 2.66 (1H, d × d × d, *J* = 13.3, 9.2, 6.6 Hz); 3.78 (3H, s); 3.79-3.83 (2H, m); 4.07 (1H, d, *J* = 8.8 Hz); 4.29-4.33 (2H, m); 4.83 (1H, d, *J* = 8.8 Hz); 6.71-6.77, 6.82-6.91, 7.15-7.21 and 7.43-7.46 (9H, 4 × m). ^{13}C NMR (75 MHz, ref = $CDCl_3$): δ 12.0, 20.4, 51.4, 55.3, 67.1, 69.2, 74.1, 84.7, 113.6, 116.5, 121.3, 129.5, 130.1, 130.7, 158.1, 158.9. IR (NaCl, cm^{-1}): ν_{max} = 2961, 2931, 2871, 1598, 1586, 1513, 1494, 1246, 1175, 1036, 753, 693. MS (70eV): m/z (%) 328 (M^++1, 100). Anal. Calcd for $C_{20}H_{25}NO_3$: C 73.37, H 7.70, N 4.28. Found: C 73.47, H 7.92, N 4.14. Purity > 95% (GC).

***cis*-4-(3-Methoxyphenyl)-5-phenoxy-3-propyl-1,3-oxazinane 4k**

R_f = 0.13 (hexane/EtOAc 8/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.80 (3H, t, *J* = 7.3 Hz); 1.39-1.57 (2H, m); 2.19 (1H, d × d × d, *J* = 13.3, 8.6, 6.2 Hz); 2.68 (1H, d × d × d, *J* = 13.3, 9.3, 6.6 Hz); 3.73 (3H, s); 3.78-3.83 (2H, m); 4.05 (1H, d, *J* = 8.8 Hz); 4.29-4.33 (2H, m); 4.85 (1H, d, *J* = 8.8 Hz); 6.69-6.72, 6.76-6.80, 6.85-6.90, 7.04-7.06 and 7.11-7.22 (9H, 5 × m). ^{13}C NMR (75 MHz, ref = $CDCl_3$): δ 12.0, 20.5, 51.6, 55.3, 67.8, 69.3, 73.9, 84.7, 113.8, 114.1, 116.4, 121.2, 121.3, 129.1, 129.5, 140.3, 158.1, 159.6. IR (NaCl, cm^{-1}): ν_{max} = 2960, 2930, 2871, 1598, 1586, 1493, 1236, 1195, 1155, 1045, 753, 692. MS (70eV): m/z (%) 328 (M^++1,

100). Anal. Calcd for $C_{20}H_{25}NO_3$: C 73.37, H 7.70, N 4.28. Found: C 73.44, H 7.87, N 4.21. Purity > 95% (GC).

Table – Scheme 1. Synthesis of 4-aryl-β-lactams **2** and 3-aminopropan-1-ols **3**

Entry	R^1	R^2	R^3	β-Lactams 2 (Yield)[a]	Aminoalcohols 3 (Yield)[b]
1	iPr	H	Bn	**2a** (85%)	**3a** (42%)
2	iBu	4-Me	Bn	**2b** (89%)	**3b** (58%)
3	cHex	3-OMe	Me	**2c** (58%)	**3c** (49%)
4	Ph	4-Cl	Bn	**2d** (87%)	**3d** (75%)
5	tBu	4-Me	Me	**2e** (55%)	**3e** (32%)
6	Bn	2-Br	Bn	**2f** (72%)	**3f** (66%)
7	Bn	2-F	Ph	**2g** (57%)	**3g** (73%)
8	nPr	H	Ph	**2h** (86%)[c]	**3h** (71%)[8r]
9	nPr	4-Me	Ph	**2i** (57%)	**3i** (42%)[8r]
10	nPr	4-OMe	Ph	**2j** (78%)	**3j** (55%)[8r]
11	nPr	3-OMe	Ph	**2k** (77%)	**3k** (70%)[8r]

[a] Yields obtained after column chromatography (SiO_2) or recrystallization – Crude yields: 72-99%

[b] Yields obtained after column chromatography (SiO_2) or recrystallization – Crude yields: 61-86%

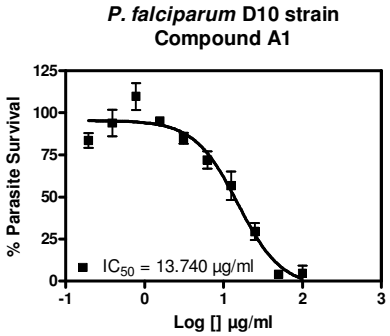
[c] Bose, A. K.; Dayal, B.; Chawla, H. P. S.; Manhas, M. S. Lactams. XVII. Stereospecific synthesis of cis-beta-lactams. *Tetrahedron Lett.* **1972**, *13*, 2823.

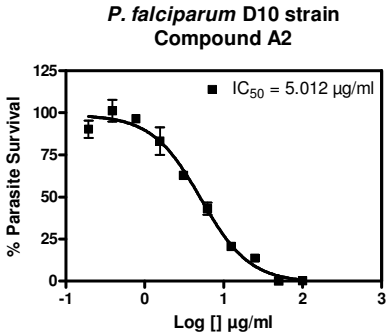
Table – Scheme 2. Synthesis of *cis*-4-aryl-1,3-oxazinanes **4**

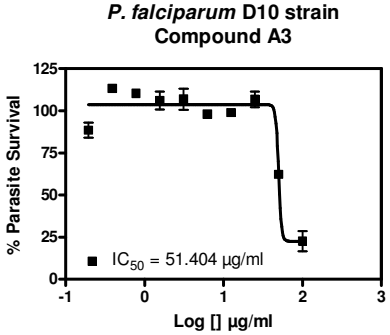
Entry	R^1	R^2	R^3	1,3-Oxazinanes 4 (Yield)[a]
1	iPr	H	Bn	**4a** (65%)
2	iBu	4-Me	Bn	**4b** (74%)
3	cHex	3-OMe	Me	**4c** (50%)
4	Ph	4-Cl	Bn	**4d** (66%)
5	tBu	4-Me	Me	**4e** (53%)
6	Bn	2-Br	Bn	**4f** (53%)
7	Bn	2-F	Ph	**4g** (60%)
8	nPr	H	Ph	**4h** (61%)
9	nPr	4-Me	Ph	**4i** (65%)
10	nPr	4-OMe	Ph	**4j** (57%)
11	nPr	3-OMe	Ph	**4k** (58%)

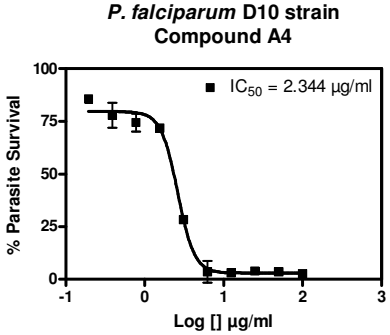
[a] Yields obtained after column chromatography (SiO_2) – Crude yields: 85-98%

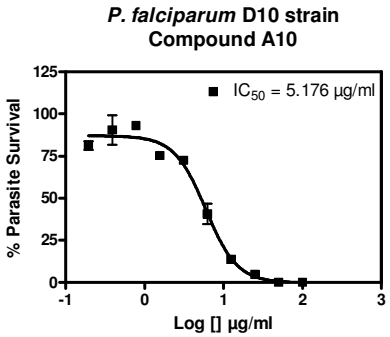
Antimalarial assay

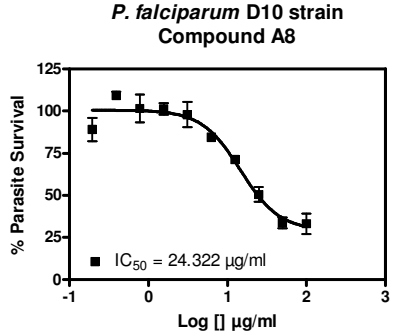


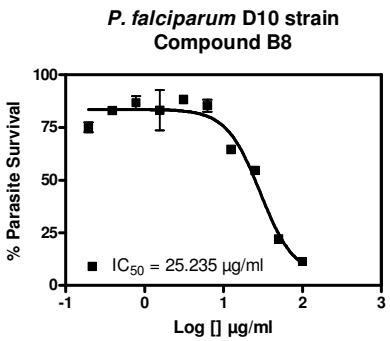


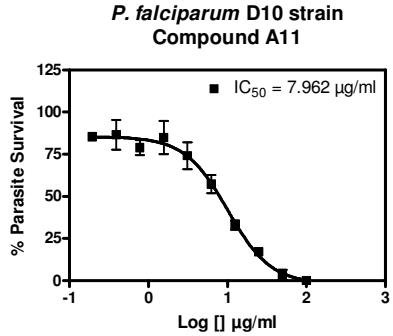






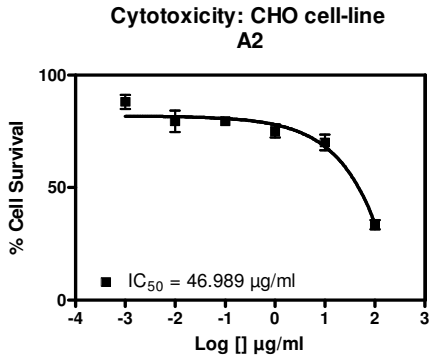


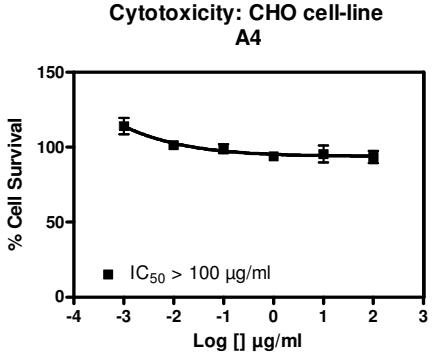


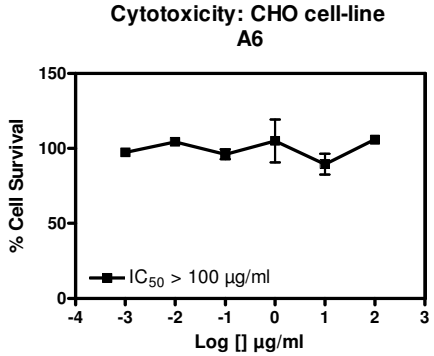


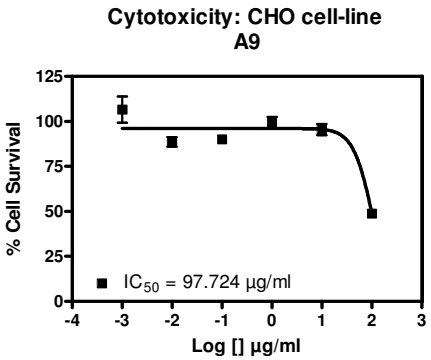
Legend: A1 = **3a**, A2 = **3b**, A3 = **3c**, A4 = **3d**, A5 = **3e**, A6 = **3f**, A7 = **3g**, A8 = **3h**, A9 = **3i**, A10 = **3j**, A11 = **3k**, B1 = **4a**, B2 = **4b**, B3 = **4c**, B4 = **4d**, B5 = **4e**, B6 = **4f**, B7 = **4g**, B8 = **4h**, B9 = **4i**, B10 = **4j**, B11 = **4k**

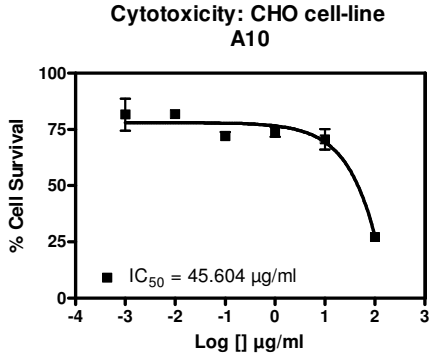
Cytotoxicity assay

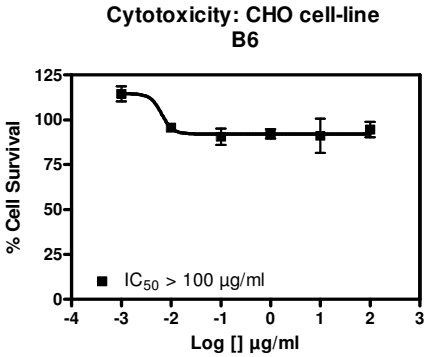


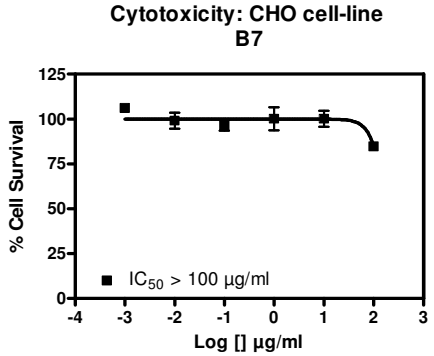












Legend: A1 = **3a**, A2 = **3b**, A3 = **3c**, A4 = **3d**, A5 = **3e**, A6 = **3f**, A7 = **3g**, A8 = **3h**, A9 = **3i**, A10 = **3j**, A11 = **3k**, B1 = **4a**, B2 = **4b**, B3 = **4c**, B4 = **4d**, B5 = **4e**, B6 = **4f**, B7 = **4g**, B8 = **4h**, B9 = **4i**, B10 = **4j**, B11 = **4k**