Supplementary information

Biotransformations of azaarene substrates 2A, 3A and 5A

(7S,8R)-2-Chloro-7,8-dihydroquinoline-7,8-diol 2b: A fermenter scale (100 litre) biotransformation of 2-chloroquinoline 2A (75 g) was carried out, using Pseudomonas putida UV4, following our reported general procedure for this and other substrates. 2b cis-(7S,8R)-2-Chloro-7,8-dihydroquinoline-7,8-diol 2b (27 g, 30%) and cis-(5R,6S)-2-chloro-5,6-dihydroquinoline-5,6-diol 2c (6 g, 8%) were obtained, after separation by column chromatography and further purification.2b

(7S,8R)-2-Chloro-7,8-dihydro-3-methylquinoline-7,8-diol 3B and (5R,6S)-2-Chloro-5,6-dihydro-3-methylquinoline-5,6-diol 3C: Biotransformation of 2-chloro-3-methylquinoline 3A (10 g, 0.056 mol) by Sphingomonas yanoikuyae B8/36 was carried out, using the conditions reported earlier for 2-chloroquinoline 2A.2b The aqueous culture medium was concentrated under reduced pressure (40 °C), extracted with EtOAc, dried (Na2SO4) and the solvent removal under reduced pressure. The residue was purified by flash chromatography (50% EtOAc/hexane) and the purified mixture of bioproducts obtained was separated by preparative PLC (5% MeOH/CHCl3) into two new metabolites, cis-(7S,8R)-2-chloro-7,8-dihydro-3-methylquinoline-7,8-diol 3B (4.17 g, 35%) and cis-(5R,6S)-2-chloro-5,6-dihydro-3-methylquinoline-5,6-diol 3C (2.98 g, 25%).

(7S,8R)-2-Chloro-7,8-dihydro-3-methylquinoline-7,8-diol 3B: Colourless crystalline solid; mp 114-116 ºC (from EtOAc/hexane); [α]D +184 (c 1.01, MeOH); (Found: C, 56.6; H, 4.5; N, 6.6; C10H10ClNO2 requires C, 56.75; H, 4.8; N, 6.6); δH (300 MHz, CDCl3) 2.36 (3 H, s, ArCH3), 4.45 (1 H, dd, J7,6 5.0, J7,8 5.0, H-7), 4.72 (1 H, d, J8,7 5.0, H-8), 6.27 (1 H, dd, J6,5 9.6, J6,7 5.0, H-6), 6.60 (1 H, d, J5,6 9.6, H-5), 7.31 (1 H, s, H-4); δC (125 MHz, CD3OD) 19.72, 69.58, 72.47, 126.57, 129.16, 133.35, 133.69, 138.90, 150.21, 155.49; m/z (EI) 211 (M+, 35Cl, 28%), 213 (M+, 37Cl, 10%), 182 (100), 164 (65), 193 (30), 154 (24), 128 (26), 102 (16); νmax 3288.2 (O-H); CD (CH3CN) Δε -0.86 (308 nm), Δε -0.82 (301 nm), Δε +6.0 (250 nm), Δε +6.0 (218 nm), Δε -1.53 (203 nm).

(5R,6S)-2-Chloro-5,6-dihydro-3-methylquinoline-5,6-diol 3C: Colourless crystalline solid; mp 138-139 ºC (from EtOAc/hexane); [α]D +172 (c 0.58, MeOH); (Found: C, 56.9; H, 4.8; N, 6.6; C10H10ClNO2 requires C, 56.75; H, 4.8; N, 6.6); δH (300 MHz, CDCl3) 2.32 (3 H, s, ArCH3), 4.29 (1 H, dd, J6,5 5.0, J6,7 5.0, H-6), 4.69 (1 H, d, J5,6 5.0, H-5), 6.42 (1 H, dd, J7,6 5.0, J7,8 9.9, H-7), 6.57 (1 H, d, J8,7 9.9, H-8), 7.74 (1H, s, H-4); δC (125 MHz, CD3OD) 20.00, 68.05, 71.00, 129.54, 132.98, 134.13, 136.42, 140.20, 150.61, 151.51; m/z 211 (M+, 35Cl, 15%), 213 (M+, 37Cl, 5%), 193 (100), 182 (43), 156 (40), 130 (28), 103 (20); νmax 3302.4 (O-H); CD: (CH3CN) Δε -2.0 (307 nm), Δε +6.4 (261 nm), Δε +10.1 (221 nm), Δε -5.5 (197 nm).

(1S,2R)-3-(6-Chloro-pyridin-2-yl)cyclohexa-3,5-diene-1,2-diol 5B: Biotransformation of 2-chloro-6-phenyl-pyridine 5A (31 g, 0.16 mol) was carried out using Sphingomonas yanoikuyae B8/36 under the reported conditions for other substrates.2b Ethyl acetate extraction and purification by column chromatography (5% MeOH:CHCl3) yielded (1S,2R)-3-(6-chloro-pyridin-2-yl)cyclohexa-3,5-diene-1,2-diol 5B (5.0 g, 14% yield); colourless crystals, mp 108-110 ºC (from EtOAc); [α]D +171 (c 0.52, CHCl3); (Found: C, 59.2; H,
4.5;N, 6.2 C11H10ClNO2 requires C, 59.1; H, 4.5; N, 6.3); δH (500 MHz; CDCl3) 4.58 (1 H, m, H-1), 4.82 (1 H, d, J= 6.2, H-2), 6.14 (2 H, m, H-6, H-5), 6.75 (1 H, d, J= 5.4, H-4), 7.19 (1H, d, J= 7.9, H-5'), 7.51 (1 H, d, J= 7.8, H-3'), 7.62 (1 H, t, J= 7.5, J= 7.5, H-4'); δC (125MHz; CDCl3) 67.98, 69.16, 118.56, 122.90, 124.20, 125.73, 134.04, 136.03, 139.65, 151.09,157.98; m/z 223 (M+, 35Cl, 15%); CD: Δε +6.99 (323nm) , Δε -11.37 (219nm).

Partial hydrogenations of cis-dihydrodiols 2B, 3B and 5B
A solution of 2B, 3B or 5B (5-10 mmol) in EtOAc (ca. 25 cm3) was stirred at ambient temperature, under an atmosphere of hydrogen (6 h, 4 bar), in the presence of PtO2 catalyst (8 mol %). The catalyst was filtered off and the filtrate concentrated to give the crude hydrogenated product. Purification by column chromatography afforded the pure hydrogenated products 2D or 3D (40% EtOAc/hexane) or 5D (5% MeOH/CHCl3).

(7S,8R)-2-Chloro-5,6,7,8-tetrahydroquinoline-7,8-diol 2D: Low melting solid (1.98 g, 99%); [α]D +74 (c 0.5, CHCl3); (Found: M+ 199.0390, C9H10ClNO2 requires 199.0400); δH (300 MHz, CDCl3) 1.89 (1 H, m, H-6), 2.21 (1 H, m, H-6'), 2.69 (1 H, ddd, J= 6.5, J= 5.5, J= 5.5, H-5), 3.04 (1 H, ddd, J= 5.5, J= 6.5, J= 11.3, H-5'), 4.34 (1 H, m, H-7), 4.62 (1 H, d, J= 3.3, H-8), 7.17 (1 H, d, J= 8.0, H-3), 7.41 (1 H, d, J= 8.0, H-4); δC (125 MHz, CDCl3) 23.42, 25.69, 66.92, 70.73, 123.60, 130.59, 139.78, 149.03, 156.36; m/z 199 (M+, 35Cl, 15%), 127 (100).

(7S,8R)-2-Chloro-3-methyl-5,6,7,8-tetrahydroquinoline-7,8-diol 3D: White solid (0.97 g, 96%); mp 134 °C (from EtOAc/hexane); [α]D -21 (c 0.91, CHCl3); (Found: M+ 213.0557, C10H12ClNO2 requires 213.0557); δH (300 MHz, CDCl3) 1.90 (1 H, m, H-6), 2.1 (1 H, m, H-6'), 2.3 (3 H, s, ArCH3), 2.68 (1 H, ddd, J= 6.5, J= 3.3, J= 3.3, H-5), 3.05 (1 H, ddd, J= 6.5, J= 10.8, J= 10.8, H-5'), 4.32 (1 H, m, H-7), 4.61 (1 H, d, J= 8.2, H-8), 7.32 (1 H, s, H-4); δC (125 MHz, CDCl3) 19.56, 23.31, 25.73, 67.04, 70.49, 130.69, 131.75, 140.36, 149.16, 153.60; m/z 213 (M+, 35Cl, 6%), 215 (M+, 37Cl, 2%), 141 (100), 184 (68), 166 (70), 130(18), 105 (29), 91 (8), 77 (25).

(1S,2R)-3-(6-Chloro-pyridin-2-yl)cyclohex-3-ene-1,2-diol 5D: White solid (0.5 g, 99%); mp 92-94 oC; [α]D -14 (c 0.4, CHCl3); (Found: M+ 225.0566, C11H12ClNO2 requires 225.0557); δH (500 MHz; CDCl3) 1.81 (1 H, m, H-6a), 1.92 (1 H, m, H-6b), 2.28 (1 H, m, H-5a), 2.51 (1 H, m, H-5b), 3.94 (1 H, m, H-1), 4.72 (1 H, d, J= 4.0, H-2), 6.67 (1 H, m, H-4), 7.19 (1 H, d, J= 7.8, H-5), 7.45 (1 H, d, J= 7.8, H-3'), 7.62 (1 H, t, J= 7.8, H-4'); δC (125 MHz, CDCl3) 24.74, 25.86, 67.33, 68.92, 118.31, 122.60, 133.34, 136.11, 139.62, 150.60, 159.16; m/z 225 (M+, 35Cl, 17%), 154 (100).

Synthesis of acetals 2E, 3E and 5E-8E
(a) cis-Tetrahydrodiol 2D or 3D (5 mmol) were dissolved in a mixture of acetone (10 cm3) and 2,2'-dimethoxypropane (DMP) (10 cm3). To this solution, a catalytic amount of trifluoroacetic acid (0.2 cm3) was added at 0 ºC. The reaction mixture was left stirring at ice temperature for 20 min and then at room temperature until the starting material had reacted completely (ca. 4 h, TLC analysis). The solvent was removed under reduced pressure, the residue extracted with EtOAc, the extract dried (NazSO4), concentrated and the residue purified by flash chromatography (20% EtOAc/hexane) to yield acetonide 2E or 3E.

(b) A mixture of cis-diol 5D or 6D or 7D or 8D (1 mmol), p-toluenesulfonic acid monohydrate (0.050 g, 0.26 mmol), appropriate ketone (2.5 equiv.) in benzene (25cm3) was heated at reflux in a Dean-Stark trap for 20 h. The reaction mixture was allowed to
cool to room temperature, a saturated aqueous solution of Na₂CO₃ (5 cm³) was added and the mixture extracted with EtOAc. The extract was dried (Na₂SO₄), the solvent removed under reduce pressure, and the crude acetal purified by column chromatography (20% EtOAc/hexane) to give pure samples of acetal 5E-8E.

(3aS,9bR)-8-Chloro-2,2-diethyl-3a,4,5,9b-tetrahydro-[1,3]dioxolo[4,5h]quinoline 2E: Colourless crystalline solid (0.97 g, 81%); mp 48 ºC (from EtOAc/hexane); [α]D +164 (c 0.8, CHCl₃); (Found: M+ 239.0715, C₁₂H₁₄ClNO₂ requires 239.0713); δH (500 MHz, CDCl₃) 1.37 (3 H, s, CH₃), 1.45 (3 H, s, CH₃), 1.75 (1 H, m, H-4'), 2.14 (1 H, m, H-4'), 2.53 (1 H, ddd, J₅,₄ 4.4, J₅,₅ 15.6, H-5), 2.89 (1 H, ddd, J₅',₄.5 3.5, J₅',₅ 11.4, J₅₅ 15.6, H-5'), 4.66 (1 H, m, H-3a), 5.14 (1 H, d, J₆b,₃a 7.0, H-9b), 7.19 (1 H, d, J₇₆ 8.0, H-7), 7.41 (1 H, d, J₆₇ 8.0, H-6); δC (125 MHz, CDCl₃) 23.28, 24.70, 26.83, 27.74, 73.45, 75.33, 108.74, 123.76, 132.85, 139.12, 149.37, 154.33; m/z 239 (M+, 35Cl, 31%), 117 (100).

(3aS,9bR)-8-Chloro-3a,4,5,9b-tetrahydro-2,2,7-trimethyl-[1,3]dioxolo[4,5h]quinoline 3E: Colourless solid (0.2 g, 87%); mp 68-69 ºC (from hexane); [α]D +139 (c 0.52, CHCl₃); (Found: MH+ 254.0944, C₁₃H₁₄ClNO₂ requires 254.0942); δH (300 MHz, CDCl₃) 1.29 (3 H, s, CH₃), 1.37 (3 H, s, CH₃), 1.66 (1 H, m, H-4), 2.03 (1 H, m, H-4'), 2.26 (3 H, s, ArCH₃), 2.44 (1 H, ddd, J₅,₄ 4.4, J₅,₅ 15.5, H-5), 2.89 (1 H, ddd, J₅',₄ 4.0, J₅',₅ 11.4, J₅₅ 15.5, H-5'), 4.58 (1 H, m, H-3a), 5.04 (1 H, d, J₆b,₃a 6.7, H-9b), 7.25 (1 H, s, H-6); δC (125 MHz, CDCl₃) 19.58, 23.50, 25.28, 27.24, 28.13, 74.24, 75.66, 108.96, 132.28, 133.35, 139.94, 149.91, 152.04; m/z 254 (MH+, 35Cl, 100%), 256 (M+H, 37Cl, 38%), 220 (20), 196 (6), 180 (9), 238 (4), 146 (52), 58 (8).

2-Chloro-6-[(3aR,7aS)-2,2-diethyl-3a,6,7,7a-tetrahydrobenzo[1,3]dioxol-4-yl]-pyridine 5E: Using pentan-2-one colourless oil; [α]D +60 (c 0.9, CHCl₃); (Found: MH+ 294.1255, C₁₆H₂₀ClNO₂ requires 294.1260); δH (500 MHz, CDCl₃) 0.78 (3 H, t, J 7.5, CH₃), 0.93 (3 H, t, J 7.5, CH₃), 1.62 (2 H, m, CH₂), 1.72 (2 H, m, CH₂), 1.79 (1 H, m, H-7), 2.05 (1 H, m, H-7'), 2.18 (1 H, m, H-6), 2.44 (1 H, m, H-6'), 4.51 (1 H, dt, J₇₆,₃a 5.6, J₇₆,₇₆ 3.2, H-7a), 5.01 (1 H, d, J₃₇₆₃₉,₉ 5.9, H-3a), 7.07 (1 H, ddd, J₆₅,₅ 3.3, J₆₅,₆ 5.5, H-5), 7.17 (1 H, d, J₆₅,₅ 7.8, H-5), 7.49 (1 H, m, H-2), 7.61 (1 H, t, J 7.8, H-4'); δC (125 MHz, CDCl₃) 8.42, 9.06, 21.48, 26.01, 30.36, 30.47, 72.28, 74.01, 112.84, 119.25, 122.64, 133.83, 134.74, 139.56, 151.08, 157.87; m/z 294 (MH+, 35Cl, 35%), 190 (45).

(3aS,9bR)-8-Chloro-2,2-diethyl-3a,4,5,9b-tetrahydro-[1,3]dioxolo[4,5h]quinoline 6E: With pentan-2-one white crystalline solid (0.16 g, 60%); mp 37 ºC (from EtOAc/hexane); [α]D +170 (c 0.98, CHCl₃); (Found: MH+ 268.1106, C₁₄H₁₆ClNO₂ requires 268.1104); δH (300 MHz, CDCl₃) 0.72 (3 H, t, J 7.5, CH₂CH₃), 0.96 (3 H, t, J 7.5, CH₂CH₃), 1.59 (2 H, q, J 7.3, CH₂CH₃), 1.72-1.80 (3 H, m, CH₂CH₃, H-4), 2.24 (1 H, m, H-4'), 2.55 (1 H, ddd, J₅',₄ 3.9, J₅,₄ 3.9, J₅₅ 15.6, H-5), 2.99 (1 H, ddd, J₅',₄ 3.9, J₅',₅ 12.6, J₅₅ 15.6, H-5'), 4.70 (1 H, m, H-3a), 5.14 (1 H, d, J₆b,₃a 6.9, H-9b), 7.19 (1 H, d, J₇₆ 8.0, H-7), 7.42 (1 H, d, J₆₇ 8.0, H-6); δC (125 MHz, CDCl₃) 14.61, 21.46, 25.81, 26.43, 59.06, 60.79, 68.57, 77.60, 80.01, 124.19, 131.30, 140.08, 148.89, 155.12; m/z 268 (MH+, 100%).

(3aS,9bR)-8-Chloro-3a,4,5,9b-tetrahydrospiro[1,3]dioxolo[4,5h]quinoline-2,1'-cyclohexane 7E: With cyclohexanone white crystalline solid (0.2 g, 72%); mp 88-89 ºC (from EtOAc/hexane); [α]D +124 (c 1.2, CHCl₃); (Found: M+ 279.1049, C₁₅H₁₈ClNO₂ requires 279.1026); δH (300 MHz, CDCl₃) 1.26-1.61 (11 H, m, (CH₂)₂), 2.05 (1 H, m, H-4'), 2.53 (1 H, ddd, J₅',₄ 4.2, J₅,₄ 4.2, J₅₅ 15.9, H-5), 2.94 (1 H, ddd, J₅',₄ 3.9, J₅',₅ 95.10, 25.7, 107.3, 123.76, 132.85, 139.12, 149.37, 154.33; m/z 239 (M+, 35Cl, 31%), 117 (100).
12.0, J_{5',5} 15.9, H-5'), 4.66 (1 H, m, H-3a), 5.13 (1 H, d, J_{9b,3a} 6.6, H-9b), 7.18 (1 H, d, J_{7,6} 8.1, H-7), 7.42 (1 H, d, J_{6,7} 8.1, H-6); δ (125 MHz, CDCl$_3$) 23.64, 24.07, 24.40, 25.56, 28.37, 34.51, 36.90, 73.41, 75.51, 109.60, 133.38, 139.39, 149.61, 155.03; m/z 279 (M+, 35Cl, 43%), 281 (M+, 37Cl, 16%), 236 (100), 182 (88), 128 (38), 117 (10), 55 (13).

(2S,3aS,9bR)-2-tert-Butyl-8-chloro-3a,4,5,9b-tetrahydro-2-methyl-[1,3]-dioxolo[4,5h] quinoline 8E: (With t-butylmethyl ketone) acetal 8E was obtained as a 9:1 mixture of diastereoisomers. The major diastereoisomer 8E was separated by multi-elution PLC (6% EtOAc/hexane) or by partial crystallization. White crystalline solid (0.19 g, 70%); mp 134 ºC (from EtOAc/hexane); [α]$_D$ +159 (c 1.0, CHCl$_3$); (Found: C, 64.1; H, 7.4; N, 4.85; C$_{15}$H$_{20}$ClNO$_2$ requires C, 63.9; H, 7.15; N, 5.0); δ$_H$ (300 MHz, CDCl$_3$) 0.86 (9 H, s, CMe$_3$), 1.38 (3 H, s, CH$_3$), 1.76 (1 H, m, H-4), 2.29 (1 H, m, H-4'), 2.51 (1 H, ddd, J$_{5',4'}$ 3.5, J$_{5',4}$ 3.5, J$_{5,5'}$ 16.0, H-5), 2.98 (1 H, ddd, J$_{5',4'}$ 3.7, J$_{5',4}$ 3.7, J$_{9b,3a}$ 12.6, J$_{9b,3a}$ 16.0, H-9b), 4.73 (1 H, m, H-3a), 5.14 (1 H, d, J$_{9b,3a}$ 6.6, H-9b), 7.17 (1 H, d, J$_{7,6}$ 8.0, H-7), 7.39 (1 H, d, J$_{6,7}$ 8.0, H-6); δ$_C$ (125 MHz, CDCl$_3$) 18.08, 23.49, 25.59, 27.73, 38.42, 72.99, 75.42, 113.81, 123.74, 132.76, 139.35, 149.62, 155.05; m/z 224 [M+-C(CH$_3$)$_3$, 35Cl, 56%], 226 [M+-C(CH$_3$)$_3$, 37Cl, 18%], 182 (100), 128 (10), 117 (4).

The minor diastereoisomer 8E' was only identified by NMR spectroscopy : δ$_H$ (300 MHz; CDCl$_3$) 1.01 (9 H, s, C(CH$_3$)$_3$), 1.04 (3 H, s, CH$_3$), 1.80 (1 H, m, H-4), 2.30 (1 H, m, H-4'), 2.56 (1 H, ddd, J$_{5',4'}$ 3.5, J$_{5',4}$ 3.5, J$_{5,5'}$ 16.0, H-5), 3.03 (1 H, ddd, J$_{5',4'}$ 3.7, J$_{5',4}$ 3.7, J$_{9b,3a}$ 12.7, J$_{9b,3a}$ 16.0, H-9b), 4.68 (1 H, m, H-3a), 5.15 (1 H, d, J$_{9b,3a}$ 6.3, H-9b), 7.18 (1 H, d, J$_{7,6}$ 8.0, H-7), 7.40 (1 H, d, J$_{6,7}$ 8.0, H-6); δ$_C$ (125 MHz, CDCl$_3$) 22.59, 23.15, 26.00, 27.46, 40.89, 75.94, 115.89, 123.84, 132.22, 139.49, 149.97, 156.17.

Homocoupling of acetals 2E, 3E, 6E-8E

Zinc powder (0.34 g, 5.2 mmol) was added to a stirred solution of nickel (II) chloride hexahydrate (0.5 g, 2.1 mmol) and PPh$_3$ (1.82 g, 6.9 mmol) in dry degassed DMF (10 cm$_3$). The reaction mixture was heated at 60 ºC until the colour of the solution changed to red (ca. 1 h). A solution of appropriate acetal (1.7 mmol), in dry degassed DMF (10 cm$_3$), was then added and the reaction mixture heated at 60 ºC for 5 h, allowed to cool to room temperature and poured into an aqueous solution of NH$_4$OH (10% w/w, 20 cm$_3$). The resultant mixture was extracted with CH$_2$Cl$_2$, the extract washed with brine, dried (Na$_2$SO$_4$), and the solution concentrated to afford the crude product. Purification by column chromatography (50% EtOAc/hexane) gave a pure sample of the corresponding 2,2'-bipyridine.

(3aS,9bR,3a'S,9b'R)-2,2,2',2'-Tetramethyl-3a,4,5,9b,3a',4',5',9b'-octahydro-(8,8')-bi([1,3]-dioxolo[4,5h]quinolinyl) 2F: White crystalline solid (0.31 g, 89%); mp 233 ºC (from EtOAc/hexane); [α]$_D$ +273 (c 1.0, CHCl$_3$); (Found: C, 70.7; H, 6.9; N, 6.7; C$_{24}$H$_{28}$N$_2$O$_4$ requires C, 70.6; H, 6.9; N, 6.9); δ$_H$ (300 MHz, CDCl$_3$) 1.39 (6 H, s, 2 x CH$_3$), 1.50 (6 H, s, 2 x CH$_3$), 1.75 (2 H, m, H-4, H-4'), 2.21 (2 H, m, H-4", H-4"'), 2.63 (2 H, ddd, J$_{5',4''}$ 4.0, J$_{5',4}$ 4.0, J$_{5,5''}$ 15.6, H-5, H-5'), 3.04 (2 H, ddd, J$_{5',4''}$ 3.9, J$_{5',4}$ 12.7, J$_{5,5''}$ 16.0, H-5, H-5'), 4.68 (1 H, m, H-3a), 5.15 (1 H, d, J$_{9b,3a}$ 6.3, H-9b), 7.18 (1 H, d, J$_{7,6}$ 8.0, H-7), 7.40 (1 H, d, J$_{6,7}$ 8.0, H-6); δ$_C$ (125 MHz, CDCl$_3$) 23.82, 24.73, 26.77, 28.39, 73.87, 76.56, 108.28, 120.78, 134.25, 136.86, 152.91, 154.64; m/z 408 (M+, 35Cl, 16%), 293 (100).

(3aS,9bR,3a'S,9b'R)-2,2,7,2',2',7'-Hexamethyl-3a,4,5,9b,3a',4',5',9b'-octahydro-(8,8')-bi([1,3]-dioxolo[4,5h]quinolinyl) 3F: White crystalline solid (0.12 g, 34%); mp 100-162 ºC (from hexane); [α]$_D$ +241 (c 1.1, CHCl$_3$); (Found: MH+, 437.2440, C$_{26}$H$_{33}$N$_2$O$_4$ requires 437.2435); δ$_H$ (300 MHz, CDCl$_3$) 1.37 (6 H, s, 2 x CH$_3$), 1.42 (6 H,
s, 2 x CH₃), 1.75 (2 H, m, H-4, H-4'), 2.15 (8 H, m, 2 x ArCH₃, H-4", H-4"'), 2.56 (2 H, ddd, J₅α,₄,0, J₅α,₄ 4.0, J₅α,₅ 15.4, H-5, H-5'), 2.96 (2 H, ddd, J₅α,₄,3, J₅α,₅ 12.6, J₅α,₅ 15.4, H-5", H-5''), 4.67 (2 H, m, H-3'a, H-3'a'), 5.21 (2 H, d, J₆b,₃a 6.8, H-9b, H-9b'), 7.46 (2 H, s, H-6, H-6'); δc (125 MHz, CDCl₃) 18.84, 24.36, 25.28, 26.96, 28.80, 73.70, 74.47, 108.79, 131.93, 133.77, 138.67, 150.93, 156.60; m/z 436 (M⁺, 44%), 361 (100), 321 (31), 303 (48), 287 (22), 275 (15), 59 (42).

6,6'-bis-[(3aR,7aS)-2,2-Diethyl-3a,6,7,7a-tetrahydro-benzo[1,3]dioxolo[4,4-yl]-[2,2']bipyridinyl 5F: Colourless oil (0.25 g, 66 % yield); [α]D +225 (c 0.1, CHCl₃); (Found: C, 73.45; H, 7.5; N, 5.5; C₃₀H₄₀N₂O₄ requires C, 73.7; H, 8.2; N, 5.7).

(3aS,9bR,3a'S,9b'R)-2,2',2'-Tetraethyl-3a,4,5,9b,3a',4',5',9b'-octahydro-[8,8']bicyclo-[1,3]-dioxolo[4,5-h][quinolinyl] 6F: White crystalline compound (0.38 g, 96 %); mp 187-189 °C (from EtOAc/hexane); [α]D +281 (c 1.0, CHCl₃); (Found: C, 73.2; H, 7.7; N, 5.5; C₃₀H₃₆N₂O₄ requires C, 73.7; H, 8.2; N, 5.7).

(3aS,9bR,3a'S,9b'R)-8,8'-bis-(Spiro[1,3]dioxolo[4,5-h][quinolinyl]-2',1'-cyclohexene) 7F: White crystalline solid (0.29 g, 68 %); mp 245-247 °C (from EtOAc/hexane); [α]D +246 (c 0.55, CHCl₃); (Found: C, 73.45; H, 7.5; N, 5.5; C₃₀H₃₈N₂O₄ requires C, 73.7; H, 7.4; N, 5.7).

(2S,3aS,9bR,2'S,3a'S,9b'R)-2,2'-di-tert-Butyl-3a,4,5,9b,3a',4',5',9b'-octahydro-2,2'-dimethyl-[8,8']bi-[1,3]-dioxolo[4,5-h][quinolinyl] 8F: White crystalline solid (0.4 g, 93 %); mp 252-254 °C (from EtOAc/hexane); [α]D +225 (c 0.93, CHCl₃); (Found: C, 73.2; H, 7.75; N, 5.6; C₃₀H₄₀N₂O₄ requires C, 73.1; H, 8.2; N, 5.7).

Di-(3aS,9bR,3a'S,9b'R)-2,2',2'-tetramethyl-3a,4,5,9b,3a',4',5',9b'-octahydro-[8,8']bi-[1,3]dioxolo[4,5-h][quinolinyl] copper (I) perchlorate 2G: A mixture of 2.2'-bipyridine 2F (0.1 g, 0.25 mmol) and Cu(MeCN)₄ClO₄ (0.04 g, 0.125 mmol) was stirred
in MeOH solution (3 cm³) for 30 min. The deep red solution, when allowed to evaporate slowly at room temperature, yielded red crystals of Cu(I) complex 2G (0.10 g, 72 %); mp 256-257 ºC (from MeOH); (Found: M+ 879.3390 C₄₈H₅₆N₄O₈Cu requires 879.3394); λmax(MeCN)/nm 460 (ε/dm³ mol⁻¹ cm⁻¹ 32000); δH (500 MHz; CDCl₃): 1.72 (2 H, m, H-4, H-4'), 2.01 (2 H, m, H-4", H-4'"), 2.72 (2 H, ddd, J₅,₄ 4.0, J₅,₄" 4.0, J₅,⁵" 15.2, H-5', H-5'"), 2.96 (2 H, ddd, J₅",₄" 3.6, J₅",₄ 10.5, J₅",⁵ 15.2, H-5", H-5"'), 4.35 (2 H, ddd, J₃ₐ,₄ 4.2, J₃ₐ,₄" 4.2, J₃ₐ,⁹b 6.6, H-3a, H-3'a), 4.77 (2 H, d, J₉b,₃ₐ 6.6, H-9b, H-9'b), 7.88 (2 H, d, J₆,₇ 8.2, H-6, H-6'), 8.25 (2 H, d, J₇,₆ 8.2, H-7, H-7'); δC (125 MHz; CDCl₃) 23.74, 24.29, 26.50, 28.12, 73.47, 75.68, 108.13, 120.86, 137.44, 137.76, 150.91, 152.82; m/z 879 (M+, 81%), 471 (100), 355 (40).

Copper (I)-catalysed enantioselective allylic oxidation reaction of alkenes 9 and 11

The ligand (0.06 mmol) and Cu(OTf)₂ (0.018g, 0.05 mmol) were dissolved in acetone (4 cm³) and the yellow solution stirred (1 h) at room temperature under nitrogen atmosphere. Phenylhydrazine (5.9 µl, 0.06 mmol) was added to the stirring reaction mixture; the colour of the solution changed to red. After 10 min, the alkene 9 or 11 (5 mmol) was added, at a temperature listed in Table 4.1, followed by dropwise addition of tert-butyl peroxybenzoate (0.2 cm³, 1.0 mmol). The progress of the reaction was monitored by TLC (10% EtOAc/hexane). When all the oxidant had been consumed (starch and KI solution test), the solvent was removed in vacuo and the residue dissolved in CH₂Cl₂ (15 cm³). The solution was washed successively with aqueous NaHCO₃, brine, water, and then dried (MgSO₄). Purification of the crude product, obtained after removal of CH₂Cl₂, by PLC (10% EtOAc/hexane) gave allylic benzoate 10 or 12.

(S)-2-Cyclohexenyl benzoate 10: Obtained from cyclohexene 9 (0.5cm³, 5 mmol) as a colourless liquid (0.18 g, 91%); 90% ee, [α]D -164 (c 0.96, CHCl₃); [lit.10 71% ee, [α]D -118 (c 0.45, CHCl₃)]; δH (300 MHz, CDCl₃) 1.75-1.80 (1 H, m), 1.84-1.99 (3 H, m), 2.05-2.12 (2 H, m), 5.51 (1 H, m), 5.84 (1 H, m), 6.01 (1 H, m), 7.42 (2 H, m, ArH), 7.54 (1 H, m, ArH), 8.05 (2 H, m, ArH). The other spectral data were also identical to those reported in literature. The enantiopurity was determined by chiral GC using a Supelco β-Dex 225 chiral column (120 min at 100 ºC, then 5 ºC/min to 200 ºC, tr=133.468 min, ts=133.127 min).

(S)-2-Cycloheptenyl benzoate 12: Obtained from cycloheptene 11 (0.58 ml, 5 mmol) as a colourless liquid (0.19 g, 89%); 97% ee, [α]D -52 (c 0.85, CHCl₃); [lit.10 82% ee, [α]D -38 (c 1.0, CHCl₃)]; δH (300 MHz, CDCl₃) 1.43-1.50 (1 H, m), 1.71-1.90 (3 H, m), 1.97-2.01 (2 H, m), 2.15-2.24 (2 H, m), 5.65 (1 H, m), 5.81-5.90 (2 H, m), 7.44 (2 H, m ArH), 7.54 (1 H, m, ArH), 8.06 (2 H, m, ArH). The other spectral data were also identical to that reported in literature. The enantiopurity was determined by chiral stationary phase GC using a Supelco β-Dex 225 chiral column (210 min at 100 ºC, then 5 ºC/min to 200 ºC, tr=225.818 min, ts=225.988 min).

Copper (I)-catalysed enantioselective cyclopropanation reaction of alkenes 13 and 14:

To a solution of Cu(OTf)₂ (0.009g, 0.025 mmol) in CH₂Cl₂ (4 cm³) was added the ligand (0.03 mmol) and the mixture stirred under nitrogen atmosphere at 20 ºC for 1 h. Phenylhydrazine (3 µl, 0.03 mmol) and alkene 13 or 14 (4.37 mmol) was added to the reaction mixture. A solution of diazoacetate (2 mmol) in CH₂Cl₂ (3 cm³) was then added, dropwise over a period of 3 h, using a syringe pump. After the addition, the mixture was stirred for an additional 3 h and then concentrated under reduced pressure. The crude product mixture obtained was analysed by ¹H NMR spectroscopy. Chiral stationary phase GC was employed to determine the ratio of trans and cis isomers and enantiomer composition. Separation of the mixture by PLC (5% EtOAc/hexane) afforded pure
sample of the major trans-cyclopropane 15 or 16 and was stereochemically assigned. The corresponding minor cis-cyclopropane 17 or 18 was only identified by comparison of its 1H-NMR spectrum with the literature data.

\[(1R,2R)\text{-}2\text{-Phenyl-cyclopropane-1-carboxylic acid } t\text{-butyl ester 15 :}\]

Obtained from \(t\)-butyl diazoacetate (0.27 ml, 2 mmol) and styrene 13 (0.49 cm\(^3\), 4.37 mmol) as a colourless oil (0.25 g, 58\%); 92\% ee, \([\alpha]_D - 225 (c 0.98, CHCl_3)\); \([\text{lit.11}] 92\% \text{ ee, } [\alpha]_D - 237 (c 0.92, CHCl_3)\]; \(\delta^H (300 \text{ MHz, CDCl}_3) 1.25 (1 \text{ H, m, } CHH), 1.47 (9 \text{ H, s, } C(CH_3)_3), 1.50-1.56 (1 \text{ H, m, } CHH), 1.86 (1 \text{ H, m, } CHCO_2Et), 2.48 (1 \text{ H, m, } CHPh), 7.07-7.13 (2 \text{ H, m, ArH}), 7.16-7.23 (1 \text{ H, m, ArH}), 7.24-7.32 (2 \text{ H, m, ArH}).\) The 1H-NMR spectrum of the minor cis-cyclopropane 17 was found to be identical to that reported in the literature.11 The enantiopurity of compound 15 was determined by chiral stationary phase GC, using a Supelco \(\beta\)-Dex 325 chiral column (90 min at 100 °C, then 5 °C/min to 200 °C, hold for 10 min, \(t_{R,R}=104.306 \text{ min, } t_{S,S}=104.477 \text{ min}).\)

\[(1R,2R)\text{-}2\text{-}(4-Fluorophenyl)cyclopropane-1-carboxylic acid } t\text{-butyl ester 16:}\]

Obtained from \(t\)-butyl diazoacetate (0.27 cm\(^3\), 2 mmol) and \(p\)-fluorostyrene 14 (0.52 cm\(^3\), 4.37 mmol) as a colourless oil (0.33 g, 71\%); 95\% ee, \([\alpha]_D - 180 (c 1.04, CHCl_3)\); \([\text{lit.11}] 99\% \text{ ee, } [\alpha]_D - 182 (c 0.64, CHCl_3)\]; \(\delta^H (300 \text{ MHz, CDCl}_3) 1.19 (1 \text{ H, m, } CHH), 1.47 (9 \text{ H, s, } t\text{-Bu}, 1.48-1.53 (1 \text{ H, m, } CHH), 1.76 (1 \text{ H, m, } CHCO_2Et), 2.42 (1 \text{ H, m, } CHPh), 6.93-6.987 (2 \text{ H, m, ArH}), 7.02-7.07 (2 \text{ H, m, ArH}).\) The NMR data for the minor isomer 18 was found to be identical to that reported in the literature.11 The enantiopurity of the major isomer 16 was determined by chiral stationary phase GC analysis of its trans-esterification product (ethyl ester, 86\% yield) using a Supelco \(\beta\)-Dex 325 chiral column (90 min at 100 °C, then 5 °C/min to 200 °C, hold for 10 min, \(t_{R,R}=104.447 \text{ min, } t_{S,S}=104.637 \text{ min}).\)