Supplementary information

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

(7*S*,8*R*)-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]

(7*S*,8*R*)-2-Chloro-7,8-dihydro-3-methylquinoline-7,8-diol 3B and (5*R*,6*S*)-2-Chloro-5,6-dihydro-3-methyquinoline-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 (Na_2SO_4) 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/$CHCl_3$) into two new metabolites, *cis*-(7*S*,8*R*)-2-chloro-7,8-dihydro-3-methylquinoline-7,8-diol **3B** (4.17 g, 35%) and *cis*-(5*R*,6*S*)-2-chloro-5,6-dihydro-3-methylquinoline-5,6-diol **3C** (2.98 g, 25%).

(7*S*,8*R*)-2-Chloro-7,8-dihydro-3-methyquinoline-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; $C_{10}H_{10}ClNO_2$ requires C, 56.75; H, 4.8; N, 6.6); δ_H (300 MHz, $CDCl_3$) 2.36 (3 H, s, Ar*CH*$_3$), 4.45 (1 H, dd, $J_{7,6}$ 5.0, $J_{7,8}$ 5.0, H-7), 4.72 (1 H, d, $J_{8,7}$ 5.0, H-8), 6.27 (1 H, dd, $J_{6,5}$ 9.6, $J_{6,7}$ 5.0, H-6), 6.60 (1 H, d, $J_{5,6}$ 9.6, H-5), 7.31 (1 H, s, H-4); δ_C (125 MHz, CD_3OD) 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^+, ^{35}Cl, 28%), 213 (M^+, ^{37}Cl, 10%), 182 (100), 164 (65), 193 (30), 154 (24), 128 (26), 102 (16); ν_{max} 3288.2 (O-H); CD (CH_3CN) $\Delta\varepsilon$ -0.86 (308 nm), $\Delta\varepsilon$ -0.82 (301 nm), $\Delta\varepsilon$ +6.0 (250 nm), $\Delta\varepsilon$ +6.0 (218 nm), $\Delta\varepsilon$ -1.53 (203 nm).

(5*R*,6*S*)-2-Chloro-5,6-dihydro-3-methyquinoline-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; $C_{10}H_{10}ClNO_2$ requires C, 56.75; H, 4.8; N, 6.6); δ_H (300 MHz, $CDCl_3$) 2.32 (3 H, s, Ar*CH*$_3$), 4.29 (1 H, dd, $J_{6,5}$ 5.0, $J_{6,7}$ 5.0, H-6), 4.69 (1 H, d, $J_{5,6}$ 5.0, H-5), 6.42 (1 H, dd, $J_{7,6}$ 5.0, $J_{7,8}$ 9.9, H-7), 6.57 (1 H, d, $J_{8,7}$ 9.9, H-8), 7.74 (1H, s, H-4); δ_C (125 MHz, CD_3OD) 20.00, 68.05, 71.00, 129.54, 132.98, 134.13, 136.42, 140.20, 150.61, 151.51; *m/z* 211 (M^+, ^{35}Cl, 15%), 213 (M^+, ^{37}Cl, 5%), 193 (100), 182 (43), 156 (40), 130 (28), 103 (20); ν_{max} 3302.4 (O-H);CD: (CH_3CN) $\Delta\varepsilon$ -2.0 (307 nm), $\Delta\varepsilon$ +6.4 (261 nm), $\Delta\varepsilon$ +10.1 (221 nm), $\Delta\varepsilon$ -5.5 (197 nm).

(1*S*,2*R*)-3-(6-Chloro-pyridin-2-yl)cyclohexa-3,5-diene-1,2-diol 5B: Biotransformation of 2-chloro-6-phenyl-pyridine **5A** (31 g, 0.16mol) 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:$CHCl_3$) yielded (1*S*,2*R*)-
3-(6-chloro-pyridin-2-yl)cyclohexa-3,5-diene-1,2-diol **5B** (5.0 g, 14% yield); colourless crystals, mp 108-110 ^{o}C (from EtOAc); **[**α**]**$_D$ +171 (*c* 0.52, $CHCl_3$); (Found: C, 59.2; H,

4.5;N, 6.2 $C_{11}H_{10}ClNO_2$ requires C, 59.1; H, 4.5; N, 6.3); δ_H (500 MHz; $CDCl_3$) 4.58 (1 H, m,H-1), 4,82 (1 H, d, $J_{2,1}$ 6.4, H-2), 6.14 (2 H, m, H-6, H-5), 6.75 (1 H, d, $J_{4,5}$ 5.4, H-4), 7.19 (1H, d, $J_{5',4'}$ 7.9, H-5'), 7.51 (1 H, d, $J_{3',4'}$ 7.8, H-3'), 7.62 (1 H, t, $J_{4',3'}$ 7.5, $J_{4',5'}$ 7.5, H-4'); δ_C (125MHz; $CDCl_3$) 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^+, ^{35}Cl, 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 cm^3) was stirred at ambient temperature, under an atmosphere of hydrogen (6 h, 4 bar), in the presence of PtO_2 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/$CHCl_3$).

(7*S*,8*R*)-2-Chloro-5,6,7,8-tetrahydroquinoline-7,8-diol 2D: Low melting solid **(**1.98 g, 99%); **[**α**]**$_D$ +74 (*c* 0.5, $CHCl_3$); (Found: M^+ 199.0390, $C_9H_{10}ClNO_2$ requires 199.0400); δ_H (300 MHz, $CDCl_3$) 1.89 (1 H, m, H-6), 2.21 (1 H, m, H-6'), 2.69 (1 H, ddd, $J_{5,6'}$ 3.2, $J_{5,6}$ 6.5, $J_{5,5'}$ 17.2, H-5), 3.04 (1 H, ddd, $J_{5',6}$ 6.5, $J_{5',6'}$ 11.3, $J_{5',5}$ 17.2, H-5'), 4.34 (1 H, m , H-7), 4.62 (1 H, d, $J_{8,7}$ 3.3, H-8), 7.17 (1 H, d, $J_{3,4}$ 8.0, H-3), 7.41 (1 H, d, $J_{4,3}$ 8.0, H-4); δ_C (125 MHz, $CDCl_3$) 23.42, 25.69, 66.92, 70.73, 123.60, 130.59, 139.78, 149.03, 156.36; *m/z* 199 (M^+, ^{35}Cl, 15%), 127 (100).

(7*S*,8*R*)-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, $CHCl_3$); (Found: M^+ 213.0555, $C_{10}H_{12}ClNO_2$ requires 213.0557); δ_H (300 MHz, $CDCl_3$) 1.90 (1 H, m, H-6), 2.21 (1 H, m, H-6'), 2.34 (3 H, s, Ar*CH*$_3$), 2.68 (1 H, ddd, $J_{5,6'}$ 3.3, $J_{5,6}$ 6.5, $J_{5,5'}$ 17.2, H-5), 3.05 (1 H, ddd, $J_{5',6}$ 6.5, $J_{5',6'}$ 10.8, $J_{5',5}$ 17.2, H-5'), 4.32 (1 H, m, H-7), 4.61 (1 H, d, $J_{8,7}$ 2.8, H-8), 7.32 (1 H, s, H-4); δ_C (125 MHz, $CDCl_3$) 19.56, 23.31, 25.73, 67.04, 70.49, 130.69, 131.75, 140.36, 149.16, 153.60; *m/z* 213 (M^+, ^{35}Cl, 6%), 215 (M^+, ^{37}Cl, 2%), 141 (100), 184 (68), 166 (70), 130(18), 105 (29), 91 (8), 77 (25).

(1*S*,2*R*)-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, $CHCl_3$); (Found; M^+ 225.0566, $C_{11}H_{12}ClNO_2$ requires 225.0557); δ_H (500 MHz; $CDCl_3$) 1.81 (1 H, m, H-6$_a$), 1.92 (1 H, m, H-6$_b$), 2.28 (1 H, m, H-5$_a$), 2.51 (1 H, m, H-5$_b$), 3.94 (1 H, m, H-1), 4,72 (1 H, d, $J_{2,1}$ 4.0, H-2), 6.67 (1 H, m, H-4),7.19 (1 H, d, $J_{5',4'}$ 7.80, H-5'), 7.45 (1 H, d, $J_{3',4'}$ 7.83, H-3'), 7.62 (1 H, t, *J* 7.80, H-4'); δ_C (125 MHz; $CDCl_3$) 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^+, ^{35}Cl, 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 cm^3) and 2,2'-dimethoxypropane (DMP) (10 cm^3). To this solution, a catalytic amount of trifluoroacetic acid (0.2 cm^3) 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 (Na_2SO_4), 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 (25cm^3) 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 Na_2CO_3 (5 cm_3) was added and the mixture extracted with EtOAc. The extract was dried (Na_2SO_4), 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**.

(3a*S*,9b*R*)-8-Chloro-2,2-dimethyl-3a,4,5,9b-tetrahydro-[1,3]dioxolo[4,5*h*]quinoline 2E: Colourless crystalline solid (0.97 g, 81%); mp 48 ºC (from EtOAc/hexane); **[**α**]**$_D$ +164 (*c* 0.8, $CHCl_3$); (Found: M^+ 239.0715, $C_{12}H_{14}ClNO_2$ requires 239.0713); δ_H (500 MHz, $CDCl_3$) 1.37 (3 H, s, CH_3), 1.45 (3 H, s, CH_3), 1.75 (1 H, m, H-4), 2.14 (1 H, m, H-4'), 2.53 (1 H, ddd, $J_{5,4'}$ 4.4, $J_{5,4}$ 4.4, $J_{5,5'}$ 15.6, H-5), 2.89 (1 H, ddd, $J_{5',4}$ 3.5, $J_{5',4'}$ 11.4, $J_{5',5}$ 15.6, H-5'), 4.66 (1 H, m, H-3a), 5.14 (1 H, d, $J_{9b,3a}$ 7.0, H-9b), 7.19 (1 H, d, $J_{7,6}$ 8.0, H-7), 7.41 (1 H, d, $J_{6,7}$ 8.0, H-6); δ_C (125 MHz, $CDCl_3$) 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^+, ^{35}Cl, 31%), 117 (100).

(3a*S*,9b*R*)-8-Chloro-3a,4,5,9b-tetrahydro-2,2,7-trimethyl-[1,3]dioxolo[4,5*h*]quinoline 3E: Colourless crystalline solid (0.2 g, 87%); mp 68-69 ºC (from hexane); **[**α**]**$_D$ +139 (*c* 0.52, $CHCl_3$); (Found: MH^+ 254.0944, $C_{13}H_{17}ClNO_2$ requires 254.0942); δ_H (300 MHz, $CDCl_3$) 1.29 (3 H, s, CH_3), 1.37 (3 H, s, CH_3), 1.66 (1 H, m, H-4), 2.03 (1 H, m, H-4'), 2.26 (3 H, s, Ar*CH*$_3$), 2.44 (1 H, ddd, $J_{5,4'}$ 4.4, $J_{5,4}$ 4.4, $J_{5,5'}$ 15.5, H-5), 2.89 (1 H, ddd, $J_{5',4}$ 4.0, $J_{5',4'}$ 11.4, $J_{5',5}$ 15.5, H-5'), 4.58 (1 H, m , H-3a), 5.04 (1 H, d, $J_{9b,3a}$ 6.7, H-9b), 7.25 (1 H, s, H-6); δ_C (125 MHz, $CDCl_3$) 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^+, ^{35}Cl, 100%), 256 (M^++H, ^{37}Cl, 38%), 220 (20), 196 (6), 180 (9), 238 (4), 146 (52), 58 (8).

5

2-Chloro-6-[(3a*R*,7a*S*)-2,2-diethyl-3a,6,7,7a-tetrahydro-benzo[1,3]dioxol-4-yl-pyridine

5E: (Using pentan-2-one) colourless oil; **[**α**]D** +60 (*c* 0.9, $CHCl_3$); (Found: MH^+ 294.1255, $C_{16}H_{20}ClNO_2$ requires 294.1260); δ_H(500 MHz; $CDCl_3$) 0.78 (3 H, t, *J* 7.5, CH_3), 0.95 (3 H, t, *J* 7.5, CH_3), 1.62 (2 H, m, CH_2), 1.72 (2 H, m, CH_2), 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, $J_{7a,3a}$ 5.6, $J_{7a,7}$ 3.2, $J_{7a,7'}$ 3.2, H-7$_a$), 5.01 (1 H, d, $J_{3a,7a}$ 5.9, H-3$_a$), 7.07 (1 H, dd, $J_{5,6}$ 3.3, $J_{5,6''}$ 5.5, H-5), 7.17(1 H, d, $J_{5',4'}$ 7.8, H-5'), 7.49 (1 H, d, $J_{3',4'}$ 7.7 H-3'), 7.61 (1 H, t, *J* 7.8, H-4'); δ_C(125 MHz; $CDCl_3$) 8.42, 9.06, 21.48, 26.01, 30.26, 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^+, ^{35}Cl, 35%), 190 (45).

(3a*S*,9b*R*)-8-Chloro-2,2-diethyl-3a,4,5,9b-tetrahydro-[1,3]-dioxolo[4,5*h*]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, $CHCl_3$); (Found; MH^+ 268.1106, $C_{14}H_{19}O_2N^{35}Cl$ requires 268.1104); δ_H (300 MHz, $CDCl_3$) 0.72 (3 H, t, *J* 7.5, CH_2*CH*$_3$), 0.96 (3 H, t, *J* 7.5, CH_2*CH*$_3$), 1.59 (2 H, q, *J* 7.3, *CH*$_2$$CH_3$), 1.72-1.80 (3 H, m, *CH*$_2$$CH_3$, H-4), 2.24 (1 H, m, H-4'), 2.55 (1 H, ddd, $J_{5,4'}$ 3.9, $J_{5,4}$ 3.9, $J_{5,5'}$ 15.6, H-5), 2.99 (1 H, ddd, $J_{5',4}$ 3.9, $J_{5',4'}$ 12.6, $J_{5',5}$ 15.6, H-5'), 4.70 (1 H, m, H-3a), 5.14 (1 H, d, $J_{9b,3a}$ 6.9, H-9b), 7.19 (1 H, d, $J_{7,6}$ 8.0, H-7), 7.42 (1 H, d, $J_{6,7}$ 8.0, H-6); δ_C (125 MHz; $CDCl_3$) 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 %).

(3a*S*,9b*R*)-8-Chloro-3a,4,5,9b-tetrahydrospiro{[1,3]dioxolo[4,5*h*]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, $CHCl_3$); (Found: M^+ 279.1049, $C_{15}H_{18}ClNO_2$ requires 279.1026); δ_H (300 MHz, $CDCl_3$) 1.26-1.61 (11 H, m, $(CH_2)_5$, H-4), 2.05 (1 H, m, H-4'), 2.53 (1 H, ddd, $J_{5,4'}$ 4.2, $J_{5,4}$ 4.2, $J_{5,5'}$ 15.9, H-5), 2.94 (1 H, ddd, $J_{5',4}$ 3.9, $J_{5',4'}$

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_C (125 MHz, $CDCl_3$) 23.64, 24.07, 24.40, 25.56, 28.37, 34.51, 36.90, 73.41, 75.51, 109.60, 124.01, 133.38, 139.39, 149.61, 155.03; *m/z* 279 (M^+, ^{35}Cl, 43%), 281 (M^+, ^{37}Cl, 16%), 236 (100), 182 (88), 128 (38), 117 (10), 55 (13).

(2*S*,3a*S*,9b*R*)-2-*tert*-Butyl-8-chloro-3a,4,5,9b-tetrahydro-2-methyl-[1,3]-dioxolo[4,5*h*]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, $J_{5',4'}$ 12.6, $J_{5',5}$ 16.0, H-5'), 4.73 (1 H, m , H-3a), 5.14 (1 H, d, $J_{9b,3a}$ 7.0, 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^+-$C(CH_3)_3$, ^{35}Cl, 56%], 226 [M^+-$C(CH_3)_3$, ^{37}Cl, 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, $J_{5',4}$ 3.9, $J_{5',4'}$ 12.7, $J_{5',5}$ 16.0, 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, $CDCl_3$) 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, 5E and 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 thenadded 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_4OH (10% w/w, 20 cm^3). The resultant mixture was extracted with CH_2Cl_2, the extract washed with brine, dried (Na_2SO_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.

(3a*S*,9b*R*,3a'*S*,9b'*R*)-2,2,2',2'-Tetramethyl-3a,4,5,9b,3a',4',5',9b'-octahydro-(8,8')-bi([1,3]-dioxolo[4,5*h*]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 $C_{24}H_{28}N_2O_4$ 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, $J_{5",4}$ 3.5, $J_{5",4"}$ 11.9, $J_{5",5}$ 15.6, H-5", H-5'"), 4.77 (2 H, m, H-3a, H-3a'), 5.32 (2 H, d, $J_{9b,3a}$ 6.8, H-9b, H-9b'), 7.59 (2 H, d, $J_{6,7}$ 8.0, H-6, H-6'), 8.42 (2 H, d, $J_{7,6}$ 8.0, H-7, H-7'); 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^+, ^{35}Cl, 16%), 293 (100).

(3a*S*,9b*R*,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[4,5*h*]quinolinyl) 3F: White crystalline solid (0.12 g, 34 %); mp 160-162 ºC (from hexane); **[**α**]**$_D$ +241 (*c* 1.1, $CHCl_3$); (Found: MH^+, 437.2440, $C_{26}H_{33}N_2O_4$ 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 CH_3), 1.75 (2 H, m, H-4, H-4'), 2.15 (8 H, m, 2 x Ar*CH*$_3$, H-4", H-4'"), 2.56 (2 H, ddd, $J_{5,4"}$ 4.0, $J_{5,4}$ 4.0, $J_{5,5"}$ 15.4, H-5, H-5'), 2.96 (2 H, ddd, $J_{5",4}$ 3.7, $J_{5",4"}$ 12.6, $J_{5",5}$ 15.4, H-5", H-5'"), 4.67 (2 H, m, H-3a, H-3a'), 5.21 (2 H, d, $J_{9b,3a}$ 6.8, H-9b, H-9b'), 7.46 (2 H, s, H-6, H-6'); δ_C (125 MHz, $CDCl_3$) 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-{(3a*R*,7a*S*)-2,2-Diethyl-3a,6,7,7a-tetrahydro-benzo[1,3]dioxol-4-yl}-[2,2'] bipyridinyl 5F: Colourless oil (0.25 g, 66 % yield); **[**α**]**$_D$ +80 (*c* 0.1, $CHCl_3$); (Found: MH^+517.3064, $C_{32}H_{40}N_2O_4$ requires 517.3066); δ_H (500 MHz, $CDCl_3$) 0.81 (3 H, t, *J* 7.5, CH_3),0.98 (3 H, t, *J* 7.5, CH_3), 1.65 (2 H, m, CH_2), 1.75 (2 H, q, *J* 7.5, CH_2), 1.85 (1 H, m, H-7),2.05 (1 H, m, H-7'), 2.22 (1 H, m, H-6), 2.50 (1 H, m, H-6"), 4.51(1 H, dt, $J_{7a,3a}$ 5.9, $J_{7a,7}$ 3.4, $J_{7a,7'}$ 3.4, H-7a), 5.24 (1 H, d, $J_{3a,7a}$ 5.9, H-3a), 7.14 (1 H, dd, $J_{5,6}$ 3.6, $J_{5,6"}$ 5.2, H-5), 7.57(1 H, d, $J_{5',4'}$ 7.8, H-5'), 7.76 (1 H, t, *J* 7.8, H-4'), 8.37 (1 H, d, $J_{3',4'}$ 7.8, H-3'); δ_C (125 MHz,$CDCl_3$) 8.49, 9.13, 21.87, 26.36, 30.21, 30.55, 72.25, 74.05, 112.64, 119.68, 120.72, 132.13, 136.05, 137.68, 155.80, 156.08; *m/z* 517 (MH^+, 100%).

(3a*S*,9b*R*,3a'*S*,9b'*R*)-2,2,2',2'-Tetraethyl-3a,4,5,9b,3a',4',5',9b'-octahydro-[8,8'] bi-([1,3]-dioxolo[4,5*h*]quinolinyl) 6F: White crystalline compound (0.38 g, 96%); mp 187-189 ºC(from EtOAc/hexane); **[**α**]**$_D$ +281 (*c* 1.0, $CHCl_3$); (Found: M^+ 464.2667 $C_{28}H_{36}O_4N_2$ requires464.2675); δ_H (300 MHz, $CDCl_3$) 0.76 (6 H, t, *J* 7.5, 2x CH_2*CH*$_3$), 1.02 (6 H, t, *J* 7.5, 2 xCH_2*CH*$_3$) 1.62 (4 H, q, *J* 7.3, 2 x *CH*$_2$$CH_3$), 1.67-1.83 (6 H, m, 2 x *CH*$_2$$CH_3$, H-4, H-4'), 2.31 (4 H, m, H-4", H-4'"), 2.62 (2 H, ddd, $J_{5,4"}$ 3.7, $J_{5,4}$ 3.7, $J_{5,5"}$ 15.6, H-5, H-5'), 3.11 (2 H, ddd, $J_{5",4}$ 3.6, $J_{5",4"}$ 12.6, $J_{5",5}$ 15.6, H-5", H-5'"), 4.77 (2 H, m, H-3a, H-3a'), 5.32 (2 H, d, $J_{9b,3a}$ 6.6, H-9b, H-9b'), 7.56 (2 H, d, $J_{6,7}$ 7.8, H-6, H-6'), 8.40 (2 H, d, $J_{7,6}$ 7.8, H-7, H-7'); δ_C (125 MHz; $CDCl_3$) 14.61, 21.46, 25.81, 26.43, 59.06, 60.79, 68.57, 77.60, 80.01, 124.19, 131.

(3a*S*,9b*R*,3a'*S*,9b'*R*)-8,8'-*bis*-(Spiro[1,3]dioxolo[4,5*h*]quinoline-2,1'-cyclohexane]) 7F: White crystalline solid (0.29 g, 68%); mp 245-247 ºC (from EtOAc/hexane); **[**α**]**$_D$ +246 (*c* 0.55, $CHCl_3$); (Found: C, 73.45; H, 7.5; N, 5.5; $C_{30}H_{36}N_2O_4$ requires C, 73.7; H, 7.4; N, 5.7); δ_H (300 MHz, $CDCl_3$) 1.53-1.78 [22 H, m, 2 x $(CH_2)_5$, 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, $J_{5",4}$ 3.6, $J_{5",4"}$ 12.0, $J_{5",5}$ 15.6, H-5", H-5'"), 4.74 (2 H, m , H-3a, H-3a'), 5.32 (2 H, d, $J_{9b,3a}$ 6.6, H-9b, H-9b'), 7.57 (2 H, d, $J_{6,7}$ 8.1, H-6, H-6'), 8.37 (2 H, d, $J_{7,6}$ 8.1, H-7, H-7'); δ_C (125 MHz, $CDCl_3$) 24.47, 25.68, 28.81, 32.28, 35.06, 36.79, 73.94, 76.82, 109.35, 121.50, 134.86, 137.47, 153.78, 155.17; *m/z* 488 (M^+, 49%), 445 (36), 391 (47), 375 (94), 347 (14), 293 (100), 277 (47), 201 (7), 149 (28).

(2*S*,3a*S*,9b*R*,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 ºC (from EtOAc/hexane); **[**α**]**$_D$ +225 (*c* 0.93, $CHCl_3$); (Found: C, 73.2; H, 7.75; N, 5.6; $C_{30}H_{40}N_2O_4$ requires C, 73.1; H, 8.2; N, 5.7); δ_H (300 MHz, $CDCl_3$) 0.86 [18 H, s, 2 x $C(CH_3)_3$], 1.44 (6 H, s, 2 x CH_3), 1.79 (2 H, m, H-4, H-4'), 2.32 (2 H, m, H 4", H-4'"), 2.54 (2 H, ddd, $J_{5,4"}$ 3.7, $J_{5,4}$ 3.7, $J_{5,5"}$ 15.5, H-5, H-5'), 3.04 (2 H, ddd, $J_{5",4}$ 3.9, $J_{5",4"}$ 12.6, $J_{5",5}$ 15.5, H-5", H-5'"), 4.79 (2 H, m , H-3a, H-3a'), 5.28 (2 H, d, $J_{9b,3a}$ 7.3, H-9b, H-9b'), 7.51 (2 H, d, $J_{6,7}$ 8.0, H-6, H-6'), 8.35 (2 H, d, $J_{7,6}$ 8.0, H-7, H-7'); δ_C (125 MHz, $CDCl_3$) 18.38, 24.27, 25.66, 28.26, 38.67, 73.52, 76.30, 113.58, 121.04, 134.21, 137.16, 153.64, 155.20; *m/z* 493 (MH^+, 100 %).

Di-(3a*S*,9b*R*,3a'*S*,9b'*R*)-2,2,2'2'-tetramethyl-3a,4,5,9b,3'a,4',5',9'b-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 $Cu(MeCN)_4ClO_4$ (0.04 g, 0.125 mmol) was stirred

in MeOH solution (3 cm^3) 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 $C_{48}H_{56}N_4O_8Cu$ requires 879.3394); λ_{max}(MeCN)/nm 460 (ε/dm^3 mol^{-1} cm^{-1} 32000); δ_H (500 MHz; $CDCl_3$): 1.72 (2 H, m, H-4, H-4'), 2.01 (2 H, m, H-4", H-4'"), 2.72 (2 H, ddd, $J_{5,4}$ 4.0, $J_{5,4"}$ 4.0, $J_{5,5"}$ 15.2, H-5', H-5'), 2.96 (2 H, ddd, $J_{5",4"}$ 3.6, $J_{5",4}$ 10.5, $J_{5",5}$ 15.2, H-5", H-5'"), 4.35 (2 H, ddd, $J_{3a,4}$ 4.2, $J_{3a,4"}$ 4.2, $J_{3a,9b}$ 6.6, H-3a, H-3'a), 4.77 (2 H, d, $J_{9b,3a}$ 6.6, H-9b, H-9'b), 7.88 (2 H, d, $J_{6,7}$ 8.2, H-6, H-6'), 8.25 (2 H, d, $J_{7,6}$ 8.2, H-7, H-7'); δ_C (125 MHz; $CDCl_3$) 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 cm^3) 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 cm^3, 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 CH_2Cl_2 (15 cm^3). The solution was washed successively with aqueous $NaHCO_3$, brine, water, and then dried ($MgSO_4$). Purification of the crude product, obtained after removal of CH_2Cl_2, by PLC (10% EtOAc/hexane) gave allylic benzoate **10** or **12**.

(*S*)-2-Cyclohexenyl benzoate 10: Obtained from cyclohexene **9** (0.5cm^3, 5 mmol) as a colourless liquid (0.18 g, 91%); 90% *ee*, **[**α**]**$_D$ -164 (*c* 0.96, $CHCl_3$); [lit.[10] 71% *ee*, [α]$_D$ -118 (*c* 0.45, $CHCl_3$)]; δ_H (300 MHz, $CDCl_3$) 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, Ar*H*), 7.54 (1 H, m, Ar*H*), 8.05 (2 H, m, Ar*H*). The spectral and analytical data were identical to those reported in literature.[10] 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, t_R=133.468 min, t_S=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, $CHCl_3$); [lit.[10] 82% *ee*, [α]$_D$ -38 (*c* 1.0, $CHCl_3$)]; δ_H (300 MHz, $CDCl_3$) 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 Ar*H*), 7.54 (1 H, m, Ar*H*), 8.06 (2 H, m, Ar*H*). The other spectral data were also identical to that reported in literature.[10] 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, t_R=225.818 min, t_S=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 CH_2Cl_2 (4 cm^3) 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 CH_2Cl_2 (3 cm^3) 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 ^{1}H-NMR spectrum with the literature data.

(1*R*,2*R*)-*trans*-2-Phenyl-cyclopropane-1-carboxylic acid *t*-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, $CHCl_3$); [lit.[11] 92% *ee*, $[\alpha]_D$ – 237 (*c* 0.92, $CHCl_3$)]; δ_H (300 MHz, $CDCl_3$) 1.25 (1 H, m, C*H*H), 1.47 (9 H, s, $C(CH_3)_3$), 1.50-1.56 (1 H, m, CH*H*), 1.86 (1 H, m, C*H*CO_2Et), 2.48 (1 H, m, C*H*Ph), 7.07-7.13 (2 H, m, Ar*H*), 7.16-7.23 (1 H, m, Ar*H*), 7.24-7.32 (2 H, m, Ar*H*). The ^{1}H-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 *β*-Dex 325 chiral column (90 min at 100 ºC, then 5 ºC/min to 200 ºC, hold for 10 min, $t_{R,R}$=104.306 min, $t_{S,S}$=104.477 min).

(1*R*,2*R*)-*trans*-2-(4-Fluorophenyl)cyclopropane-1-carboxylic acid *t*-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*, **[**α**]**$_D$ – 180 (*c* 1.04, $CHCl_3$); [lit.[11] 99% *ee*, $[\alpha]_D$ – 182 (*c* 0.64, $CHCl_3$)]; δ_H (300 MHz, $CDCl_3$) 1.19 (1 H, m, C*H*H), 1.47 (9 H, s, *t*-Bu), 1.48-1.53 (1 H, m, CH*H*), 1.76 (1 H, m, C*H*CO_2Et), 2.42 (1 H, m, C*H*Ph), 6.93-6.987 (2 H, m, Ar*H*), 7.02-7.07 (2 H, m, Ar*H*). 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 *β*-Dex 325 chiral column(90 min at 100 ºC, then 5 ºC/min to 200 ºC, hold for 10 min, $t_{R,R}$=104.447 min, $t_{S,S}$=104.637 min).