Supplementary Material (ESI) for Chemical Communications

Palladium-Catalysed *N*-Annulation Routes to Indoles: The Synthesis of Indoles with Sterically Demanding *N*-Substituents, Including Demethylasterriquinone A1

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Electronic Supplementary Information

General Information: All reactions were performed under an inert atmosphere of nitrogen, in oven or flame dried glassware unless otherwise stated. Nitrogen was passed through a Drierite® filled drying tube before use.

Analytical thin layer chromatography was carried out using pre-coated aluminium-backed silica plates (Merck Kieselgel $60F_{254}$) and pre-coated plastic backed silica plates (Polygram® Sil G/UV_{254}). Plates were visualised under ultraviolet light (254 nm) or by staining with $KMnO_4$ and vanillin. Flash column chromatography was carried out using Merck Kieselgel 60H silica. Pressure was applied at the column head *via* hand bellows.

Melting points were determined using a Büchi 535 melting point apparatus and a Leica Galen III and are reported uncorrected. Infrared measurements were carried out as liquid films on NaCl discs or as a KBr disc using a Perkin-Elmer 1600 series FTIR spectrometer and Bruker Tensor 27 FT-IR with internal calibration in the range 4000-500 cm^{-1}. Mass spectrometry was carried out on a Micromass Quattro II and Finnegan MAT 95XP by the EPSRC mass spectrometry service at the University of Wales, Swansea.

^{1}H, ^{13}C and ^{19}F nuclear magnetic resonance experiments were carried out using a Bruker AC-200 MHz, AC-250 MHz, AC-300 MHz, AC-400 MHz or AC-500 MHz NMR spectrometers. Chemical shifts were reported in parts per million from tetramethylsilane for ^{1}H and ^{13}C experiments. The residual solvent peak was used as an internal standard. The multiplicities of the spectra are reported as follows: singlet (s), doublet (d), triplet (t), quartet (q) and multiplet (m). Sometimes apparent multiplicities (app.) were observed. Coupling constants (*J*) are given in Hz.

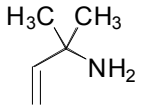
The solvents used in the reactions were obtained by passing through anhydrous alumina columns using an Innovative Technology Inc. PS-400-7 solvent purification system. In addition,

tetrahydrofuran was distilled from sodium/benzophenone. Acetone was distilled from self-indicating Drierite®. Dichloromethane (DCM) was distilled over phosphorus pentoxide.

All chemicals were purchased from Acros, Aldrich, Alfa Aesar or Strem chemical companies and used without further purification.

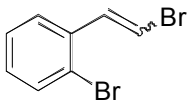
Compounds **3**,[1] **4a**,[2] **4b**[2] and those in **table 2**, **entries 1**,[3] **2**,[4] **5**,[5] **6**,[6] **7**,[7] **10**[8] and natural product **2**[10] prepared in this paper are known compounds and displayed identical spectroscopic data.

2-Methylbut-3-en-2-amine, structure 3.[1]



2,2,2-trichloro-*N*-(2-methylbut-3-en-2-yl)acetamide (33.96 g, 147.5 mmol) was placed in 6 M sodium hydroxide (370 cm^3) in a 1L round bottomed flask fitted with a reflux condenser. The mixture was then heated to 60 ºC for 3 days. After allowing to cool to ambient temperature the aqueous mixture was extracted with diethyl ether (3 x 100 cm^3), dried over anhydrous magnesium sulfate, filtered and concentrated *in vacuo*. The crude oil was then distilled to yield the title compound as a colourless liquid (7.12 g, 57 %). b.p. 73 ºC (Lit. 74-76 ºC). δ_H (300 MHz, $CDCl_3$); 5.95 (1H, dd, *J* 17.2, 10.6, C*H*=CH_2), 5.06 (1H, d, *J* 17.2, CH*H*=CH), 4.90 (1H, d, *J* 10.6, C*H*H=CH), 1.44 (2H, br s, NH_2) and 1.19 (6H, s, CH_3). δ_C (75.5 MHz, $CDCl_3$); 148.8, 109.7, 51.4 and 30.5. ν_{max}/cm^{-1} (Thin film): 3414 (NH_2), 2970 (CH), 1644 (C=C), 1468, 1415, 1380, 1240, 1187 and 916 (fingerprint).

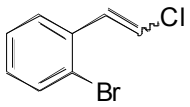
1-Bromo-2-(2-bromovinyl)benzene, structure 4a.[2] **General procedure for the preparation of vinylhalo-bromostyrenes:**



To an oven-dried flask was added bromomethyltriphenylphosphonium bromide (2.83 g, 6.49 mmol) and THF (40 cm^3). To this was added sodium hydride (60 % dispersion in mineral oil) (0.26 g, 6.49 mmol) at 0 ºC and left to stir for 1.5 h. To the reaction mixture was then added 2-bromobenzaldehyde (1.00g, 5.41 mmol) and the mixture left to stir for 12 h. Light petroleum (200 cm^3) was then added and the phosphine oxide by-product was removed by filtering through a plug of celite. The organic solvent was removed *in vacuo* and the residue purified further by silica gel

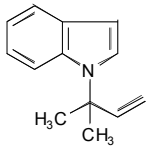
column chromatography using an eluent system of light petroleum. This yielded the title compound as a colourless oil. (1.26 g, 90 %). 4.5:1 ratio of unseparable *Z*/*E* alkene isomers.

1-Bromo-2-(2-chlorovinyl)benzene, structure 4b.[2]



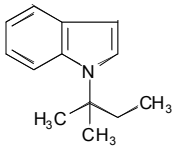
The general procedure for the preparation of halostyrenes was followed using 2-bromo-benzaldehyde (6.513 g, 35.205 mmol), potassium *tert*-butoxide (4.741 g, 42.246 mmol), chloromethyltriphenylphosphonium chloride (14.669 g, 42.246 mmol) and THF (200 cm^3). This gave the title compound as a colourless oil (7.098 g, 93 %), 4.3:1 ratio of inseparable *Z*/*E* alkene isomers.

1-(2-Methylbut-3-en-2-yl)-1*H*-indole, table 2, entry 1, structure 8.[3] General method for the preparation of indoles:



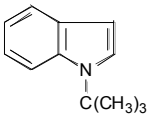
To an oven-dried sealable tube was added 1-bromo-2-(2-chlorovinyl)benzene **4b** (873 mg, 4.014 mmol), palladium acetate (45 mg, 0.200 mmol), tri-*t*-butylphosphonium tetrafluoroborate (140 mg, 0.481 mmol) and sodium *tert*-butoxide (964 mg, 10.035 mmol). The vessel was evacuated and purged with argon 3 times. To the reaction flask was then added reverse-prenylamine **3** (1.367 g, 16.056 mmol) and toluene (8.5 cm^3) and the reaction flask sealed and heated to 130 ºC for 4 h. The reaction mixture was allowed to cool before filtering through a plug of celite and concentrating under reduced pressure. The residue was then further purified by flash silica column chromotagaphy using an eluent system of 1% diethyl ether in petroleum ether. This yielded (508 mg, 68 %) of the title compound as a yellow oil. δ_H (300 MHz, $CDCl_3$); 7.65-7.61 (1H, m, aryl H), 7.55-7.52 (1H, m, aryl H), 7.32 (1H, d, *J* 3.6, H-2), 7.15-7.05 (2H, m, aryl H), 6.49 (1H, dd, *J* 3.6, 0.6, H-3), 6.17 (1H, dd, *J* 17.4, 10.5, C*H*=CH_2), 5.25-5.14 (2H, m, CH_2=CH) and 1.77 (6H, s, CH_3). δ_C (75.5 MHz, $CDCl_3$); 144.1, 135.2, 129.9, 124.9, 120.8, 120.5, 119.0, 113.7, 113.4, 100.5, 58.9 and 27.8. ν_{max}/cm^{-1} (Thin film); 3145, 3049, 2981, 2937, 2877 (CH), 1603 (C=C), 1512, 1456, 1316, 1229, 1209 and 922 (fingerprint).

1-*Tert*-pentyl-1*H*-indole, table 2, entry 2.[4]



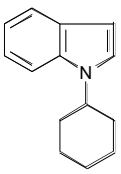
The general procedure for the preparation of indoles was followed using 1-bromo-2-(2-chlorovinyl)benzene (170 mg, 0.782 mmol), palladium acetate (8.8 mg, 0.039 mmol), tri-*tert*-butylphosphonium tetrafluoroborate (27.2 mg, 0.094 mmol), sodium *tert*-butoxide (188 mg, 1.955 mmol), *tert*-amylamine (204 mg, 2.345 mmol) and toluene (1.5 cm^3). This yielded (94 mg, 64 %) of the title compound as a yellow oil.

1-*Tert*-butyl-1*H*-indole, table 2, entry 3.



The general procedure for the preparation of indoles was followed using 1-bromo-2-(2-chlorovinyl)benzene (146 mg, 0.671 mmol), palladium acetate (7.5 mg, 0.034 mmol), tri-*tert*-butylphosphonium tetrafluoroborate (23.4 mg, 0.081 mmol), sodium *tert*-butoxide (161 mg, 1.678 mmol), *tert*-butylamine (0.21 cm^3, 2.014 mmol) and toluene (1.5 cm^3). This yielded (76 mg, 65 %) of the title compound as a colourless oil. δ_H (300 MHz, $CDCl_3$); 7.57-7.52 (2H, m, aryl H), 7.16 (1H, d, *J* 3.3, H-2), 7.09-6.96 (2H, m, aryl H), 6.35 (1H, d, *J* 3.3, H-3) and 1.61 (9H, s, CH_3). δ_C (75.5 MHz, $CDCl_3$); 134.8, 130.2, 125.1, 121.0, 120.5, 118.7, 113.2, 100.0, 55.6 and 29.7. *HRMS* (ESI+ve) [M+H] $C_{12}H_{16}N$, requires: 174.1277, found: 174.1274. *m/z* (CI) 174.1 (100 %, M+H), 162.1 (3), 144.1 (3), 118.2 (11) and 58.1 (10). ν_{max}/cm^{-1} (Thin film); 3048, 2978, 2936, 2874 (CH), 1608, 1512, 1454, 1316, 1293, 1224, 1084, 1019 and 853 (fingerprint).

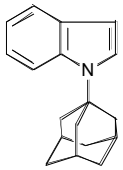
1-Cylohexyl-1*H*-indole, table 2, entry 4.



The general procedure for the preparation of indoles was followed using 1-bromo-2-(2-chlorovinyl)benzene (157 mg, 0.722 mmol), palladium acetate (8.1 mg, 0.036 mmol), tri-*t*-

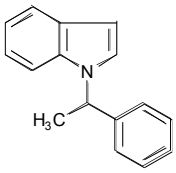
butylphosphonium tetrafluoroborate (25.1 mg, 0.087 mmol), sodium *tert*-butoxide (173 mg, 1.805 mmol), cyclohexylamine (0.24 cm^3, 2.166 mmol) and toluene (1.5 cm^3). This yielded (88 mg, 61 %) of the title compound as a yellow oil. δ_H (300 MHz, $CDCl_3$); 7.65-7.62 (1H, m, aryl H), 7.38 (1H, dd, *J* 8.4, 7.8, aryl H), 7.21 (1H, d, *J* 3.6, H-2), 7.19 (1H, ddd, *J* 8.0, 7.0, 1.2, aryl H), 7.09 (1H, ddd, *J* 8.0, 7.0, 1.2, aryl H), 6.51 (1H, dd, *J* 3.6, 0.9, H-3), 4.21 (1H, app. tt, *J* 11.7, 3.6, CHN), 2.16-2.11 (2H, m, Cy-H), 1.96-1.90 (2H, m, Cy-H), 1.82-1.63 (2H, m, Cy-H) and 1.56-1.20 (4H, m, Cy-H). δ_C (75.5 MHz, $CDCl_3$); 135.4, 128.4, 123.9, 121.0, 120.8, 119.1, 109.3, 100.9, 55.0, 33.4, 25.9, 25.6. *HRMS* (ESI+ve) [M+H] $C_{14}H_{18}N$, requires: 200.1434, found: 200.1433. *m/z* (EI) 199.2 (100 %, M^+), 156.1 (55), 143.1 (12), 130.1 (13), 117.1 (97), 89.0 (20), 55.2 (32) and 41.2 (56). ν_{max}/cm^{-1} (Thin film); 3050, 3038, 2931, 2854 (CH), 1610, 1573, 1508, 1476, 1408, 1312, 1213, 1186, 1013 and 994 (fingerprint).

1-Adamantyl-1*H*-indole, table 2, entry 5.[5]



The general procedure for the preparation of indoles was followed using 1-bromo-2-(2-chlorovinyl)benzene (142 mg, 0.653 mmol), palladium acetate (7.3 mg, 0.033 mmol), tri-*tert*-butylphosphonium tetrafluoroborate (22.7 mg, 0.078 mmol), sodium *tert*-butoxide (157 mg, 1.633 mmol), 1-amino-adamantane (296 mg, 1.959 mmol) and toluene (1.5 cm^3). This yielded (104 mg, 66 %) of the title compound as a white solid.

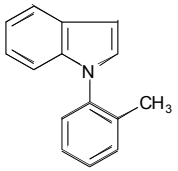
1-(1-Phenylethyl)-1*H*-indole, table 2, entry 6.[6]



The general procedure for the preparation of indoles was followed using 1-bromo-2-(2-chlorovinyl)benzene (179 mg, 0.823 mmol), palladium acetate (9.2 mg, 0.041 mmol), tri-*tert*-butylphosphonium tetrafluoroborate (28.6 mg, 0.099 mmol), sodium *tert*-butoxide (198 mg, 2.058

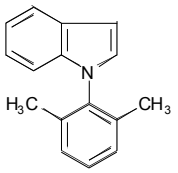
mmol), (*rac*)-α-methylbenzylamine (0.31 cm^3, 2.469 mmol) and toluene (1.5 cm^3). This yielded (140 mg, 77 %) of the title compound as a yellow oil.

1-*o*-Tolyl-1*H*-indole, table 2, entry 7.[7]



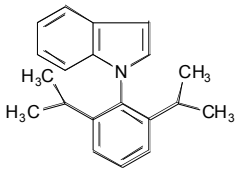
The general procedure for the preparation of indoles was followed using 1-bromo-2-(2-chlorovinyl)benzene (151 mg, 0.694 mmol), palladium acetate (7.8 mg, 0.035 mmol), tri-*t*-butylphosphonium tetrafluoroborate (24.2 mg, 0.083 mmol), sodium *tert*-butoxide (167 mg, 1.735 mmol), 2-toluidine (0.25 cm^3, 2.083 mmol) and toluene (1.5 cm^3). This yielded (123 mg, 85 %) of the title compound as a colourless oil

1-(2,6-Dimethylphenyl)-1*H*-indole, table 2, entry 8.



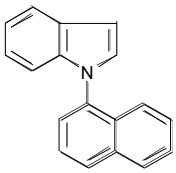
The general procedure for the preparation of indoles was followed using 1-bromo-2-(2-chlorovinyl)benzene (189 mg, 0.869 mmol), palladium acetate (9.8 mg, 0.044 mmol), tri-*t*-butylphosphonium tetrafluoroborate (30.2 mg, 0.104 mmol), sodium *tert*-butoxide (209 mg, 2.173 mmol), 2,6-dimethylaniline (0.32 cm^3, 2.607 mmol) and toluene (1.5 cm^3). This yielded (159 mg, 83 %) of the title compound as a white solid. mp: 57-59 ºC. δ_H (300 MHz, $CDCl_3$); 7.73-7.67 (1H, m, aryl H), 7.27 (1H, dd, *J* 8.7, 6.3, aryl H), 7.19-7.11 (4H, m, aryl H), 7.05 (1H, d, *J* 3.2, H-2), 6.91-6.86 (1H, m, aryl H), 6.70 (1H, dd, *J* 3.2, 0.6, H-3), 1.92 (6H, s, CH_3). δ_C (75.5 MHz, $CDCl_3$); 137.2, 137.0, 136.2, 128.3, 128.2, 128.0, 127.9, 121.9, 120.7, 119.6, 110.0, 102.4 and 17.3. *HRMS* (ESI+ve) [M+H] $C_{16}H_{16}N$, requires: 222.1277, found: 222.1276. *m/z* (EI) 221.2 (100 %, M^+), 206.2 (49), 101.9 (25), 89.1 (27), 77.1 (26) and 63.1 (26). ν_{max}/cm^{-1} (Thin film); 3051, 3017, 2955, 2921, 2857 (CH), 1510, 1483, 1458, 1327, 1226, 1137, 1009 and 951 (fingerprint).

1-(2,6-Di*iso*propylphenyl)-1*H*-indole, table 2, entry 9.



The general procedure for the preparation of indoles was followed using 1-bromo-2-(2-chlorovinyl)benzene (137 mg, 0.630 mmol), palladium acetate (7.1 mg, 0.032 mmol), tri-*t*-butylphosphonium tetrafluoroborate (21.9 mg, 0.075 mmol), sodium *tert*-butoxide (151 mg, 1.575 mmol), 2,6-di*iso*propylaniline (0.24 cm^3, 1.890 mmol) and toluene (1.5 cm^3). This yielded (127 mg, 73 %) of the title compound as a yellow oil. δ_H (250 MHz, $CDCl_3$); 7.67-7.64 (1H, m, aryl H), 7.40 (1H, dd, *J* 8.4, 7.2, aryl H), 7.25 (2H, d, *J* 7.8, aryl H), 7.11-7.02 (2H, m, aryl H), 7.02 (1H, dd, *J* 3.2, H-2), 6.86-6.83 (1H, m, aryl H), 6.65 (1H, dd, *J* 3.2, 0.9, H-3), 2.22 (2H, sept, *J* 6.8, C*H*$(CH_3)_2$), 1.04 (6H, d, *J* 6.8, CH_3) and 0.96 (6H, d, *J* 6.8, CH_3). δ_C (75.5 MHz, $CDCl_3$); 148.0, 138.0, 134.2, 129.36, 129.33, 127.7, 123.8, 122.0, 120.6, 119.7, 110.4, 102.0, 28.1, 24.8 and 23.9. HRMS (ESI+ve) [M+H] $C_{20}H_{24}N$, requires: 278.1903, found: 278.1901. *m/z* (EI) 277.2 (100 %, M^+), 262.2 (42), 220.2 (18), 204.1 (13), 115.0 (11), 91.1 (11), 77.1 (8) and 41.2 (68). ν_{max}/cm^{-1} (Thin film); 3054, 2963, 2927, 2868 (CH), 1508, 1476, 1362, 1336, 1220, 1136 and 1058 (fingerprint).

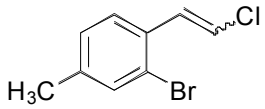
1-(Naphthalen-1-yl)-1*H*-indole, table 2, entry 10.[8]



The general procedure for the preparation of indoles was followed using 1-bromo-2-(2-chlorovinyl)benzene (188 mg, 0.864 mmol), palladium acetate (9.7 mg, 0.043 mmol), tri-*t*-butylphosphonium tetrafluoroborate (30.0 mg, 0.104 mmol), sodium *tert*-butoxide (208 mg, 2.16 mmol), 1-naphthylamine (371 mg, 2.593 mmol) and toluene (1.5 cm^3). This yielded (163 mg, 78 %) of the title compound as a white solid. mp: 77-78 ºC (Lit. mp: 76-78 ºC). δ_H (300 MHz, $CDCl_3$); 7.97-7.92 (2H, m, aryl H), 7.76-7.73 (1H, m, aryl H), 7.58-7.37 (5H, m, aryl H), 7.34 (1H, d, *J* 3.3, H-2), 7.20-7.01 (3H, m, aryl H) and 6.76 (1H, dd, *J* 3.3, 0.9, H-3). δ_C (75.5 MHz, $CDCl_3$); 137.9, 136.0, 134.4, 130.5, 129.7, 128.4, 128.2, 126.9, 126.6, 125.4, 125.0, 123.3, 122.1, 120.8,

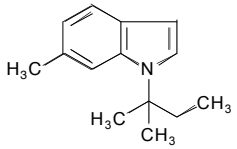
120.0, 110.7 and 102.8 (1 signal missing – peak coincidence). *HRMS* (ESI+ve) [M+H] $C_{18}H_{14}N$, requires: 244.1121, found: 244.1121. *m/z* (EI) 243.2 (91 %, M^+), 215.1 (6), 120.8 (100), 106.5 (10), 89.1 (16), 75.1 (12) and 63.1 (11). ν_{max}/cm^{-1} (Thin film); 3121, 3102, 3051 (CH), 1595, 1510, 1454, 1404, 1327, 1235, 1214, 1142, 1010 and 932 (fingerprint).

2-Bromo-1-(2-chlorovinyl)-4-methylbenzene, table 3, entry 1, substrate.



The general procedure for the preparation of chlorostyrenes was followed using 2-bromo-4-methylbenzaldehyde (2.008 g, 10.088 mmol), potassium *tert*-butoxide (1.358 g, 12.106 mmol), chloromethyltriphenylphosphonium chloride (4.204 g, 12.106 mmol) and THF (50 cm^3). This gave the title compound as a colourless oil (2.065 g, 88 %), 3.3:1 ratio of inseparable *Z*/*E* alkene isomers. δ_H (300 MHz, $CDCl_3$); 7.74 (1H, d, *J* 8.1, aryl H), 7.45-7.42 (1H, m, aryl H), 7.41-7-39 (1H, m, aryl H), 7.28 (1H, d, *J* 8.1, aryl H), 7.28 (3H, m, aryl H and vinyl CH, *E*), 6.83 (1H, d, *J* 8.4, vinyl CH, *Z*), 6.57 (1H, d, *J* 13.5, vinyl CH, *E*), 6.36 (1H, d, *J* 8.4, vinyl CH, *Z*), 2.34 (3H, s, CH_3, *Z*) and 2.31 (3H, s, CH_3, *E*). δ_C (75.5 MHz, $CDCl_3$); 139.8, 133.4, 133.0, 132.1, 130.9, 130.2, 129.9, 129.8, 128.7, 128.2, 127.7, 126.6, 123.7, 122.7, 120.2, 119.1, 20.9 and 20.7. *HRMS* (EI) [M^+] $C_9H_8{}^{79}Br\ {}^{35}Cl$, requires: 229.9492, found: 229.9495. *m/z* (EI) 232.0 (57 %, M^+), 195.0 (16), 151.0 (19), 115.0 (100), 89.1 (28), 63.1 (33) and 49.1 (23). ν_{max}/cm^{-1} (Thin film); 3072, 3030, 2921 (CH), 1601 (C=C), 1482, 1447, 1392, 1343, 1041, 930 and 834 (fingerprint).

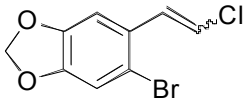
6-Methyl-1-*tert*-pentyl-1*H*-indole, table 3, entry 1, product.



The general procedure for the preparation of indoles was followed using 2-bromo-1-(2-chlorovinyl)-4-methylbenzene (148 mg, 0.640 mmol), palladium acetate (7.2 mg, 0.032 mmol), tri-*t*-butylphosphonium tetrafluoroborate (22.3 mg, 0.077 mmol), sodium *tert*-butoxide (153 mg, 1.600 mmol), *tert*-amylamine (0.22 cm^3, 1.92 mmol) and toluene (1.5 cm^3). This yielded (98 mg, 76 %) of the title compound as a pale yellow oil. δ_H (300 MHz, $CDCl_3$); 7.51 (1H, d, *J* 8.5, aryl H), 7.41 (1H, s, aryl H), 7.17 (1H, d, *J* 3.8, H-2), 6.92 (1H, dd, *J* 8.5, 0.8, aryl H), 6.38 (1H, dd, *J* 3.8, 0.8,

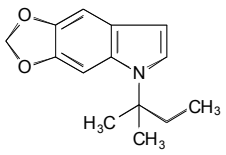
H-3), 2.48 (3H, s, CH_3), 2.10 (2H, q, *J* 7.2, CH_2), 1.68 (6H, s, CH_3) and 0.63 (3H, t, *J* 7.2, CH_3). δ_C (75.5 MHz, $CDCl_3$); 135.3, 130.0, 128.1, 125.5, 120.6, 120.5, 113.2, 99.6, 58.6, 33.3, 27.8, 22.1 and 8.2. *HRMS* (ESI+ve) [M+H] $C_{14}H_{20}N$, requires: 202.1590, found: 202.1589. *m/z* (EI) 201.2 (31 %, M^+), 172.1 (11), 131.1 (100), 103.1 (16), 77.1 (34) and 43.2 (53). ν_{max}/cm^{-1} (Thin film); 2971 (CH), 1615, 1510, 1460, 1317, 1238, 1204 and 801 (fingerprint).

5-Bromo-6-(2-chlorovinyl)benzo[d][1,3]dioxole, table 3, entry 2, substrate.



The general procedure for the preparation of chlorostyrenes was followed using 6-bromopiperonal (2.00 g, 8.73 mmol), potassium *tert*-butoxide (1.176 g, 10.478 mmol), chloromethyltriphenylphosphonium chloride (3.638 g, 10.478 mmol) and THF (100 cm^3). This gave a white solid of the title compound as an inseparable mixture of isomers (2.16 g, 95 %, 1.8:1 *Z*/*E*). m.p. 75-77 ºC. δ_H (300 MHz, $CDCl_3$); 7.39 (1H, s, aryl H, *E*), 7.08 (1H, d, *J* 13.5, vinyl CH, *E*), 7.04 (1H, s, aryl H, *E*), 7.00 (1H, s, aryl H, *Z*), 6.84 (1H, s, aryl H, *Z*), 6.77 (1H, d, *J* 7.8, vinyl CH, *Z*), 6.47 (1H, d, *J* 13.5, vinyl CH, *E*), 6.30 (1H, d, *J* 7.8, vinyl CH, *Z*), 6.00 (2H, s, CH_2O, *E*) and 5.98 (2H, s, CH_2O, *Z*). δ_C (75.5 MHz, $CDCl_3$); 148.3, 148.1, 147.7, 146.8, 132.1, 128.5, 126.9, 119.6, 118.6, 115.3, 114.2, 112.8, 112.6, 109.9, 106.0, 101.94 and 101.90 (1 quat. C, minor isomer not seen). *HRMS* (EI) [M^+] $C_9H_6{}^{79}Br\ {}^{35}ClO_2$, requires: 259.9234, found: 259.9235. *m/z* 262.0 (100 %, M^+), 260.0 (78), 224.9 (9), 181.0 (15), 123.0 (44), 83.9 (92) and 49.1 (98). ν_{max}/cm^{-1} (Thin film); 3072, 3003, 2977, 2897 (CH), 1610, 1475, 1412, 1345, 1231, 1110 and 1039 (fingerprint).

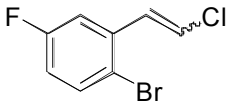
5-*Tert*-pentyl-5*H*-[1,3]dioxolo[4,5-*f*]indole, table 3, entry 2, product.



The general procedure for the preparation of indoles was followed using 5-bromo-6-(2-chlorovinyl)benzo[d][1,3]dioxole (172 mg, 0.658 mmol), palladium acetate (7.4 mg, 0.033 mmol), tri-*t*-butylphosphonium tetrafluoroborate (22.9 mg, 0.079 mmol), sodium *tert*-butoxide (158 mg, 1.645 mmol), *tert*-amylamine (0.23 cm^3, 1.974 mmol) and toluene (1.5 cm^3). This yielded (97 mg,

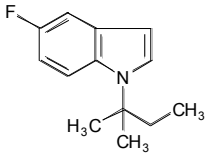
64 %) of the title compound as a pale yellow oil. δ_H (300 MHz, $CDCl_3$); 7.13 (2H, s, aryl H), 7.02 (1H, s, H-2), 6.33 (1H, br s, H-3), 5.94 (2H, s, CH_2O), 2.07 (2H, q, *J* 7.3, CH_2), 1.67 (6H, s, CH_3) and 0.64 (3H, t, *J* 7.3, CH_3). δ_C (75.5 MHz, $CDCl_3$); 143.8, 142.0, 129.6, 124.7, 124.1, 100.4, 100.0, 99.2, 94.1, 58.5, 33.2, 27.7 and 8.1. *HRMS* (ESI+ve) [M+H] $C_{14}H_{17}NO_2$, requires: 232.1322, found: 232.1331. *m/z* (EI) 232.3 (7 %, $M+H^+$), 231.1 (59, M^+), 161.1 (100), 104.1 (16), 76.2 (13), 71.1 (20), 41.2 (26). ν_{max}/cm^{-1} (Thin film); 2971, 2934, 2877, 2768 (CH), 1501, 1466, 1383, 1297, 1225, 1171, 1039 and 946 (selected fingerprint).

1-Bromo-2-(2-chlorovinyl)-4-fluorobenzene, table 3, entry 3, substrate.



The general procedure for the preparation of chlorostyrenes was followed using 5-fluoro-2-bromobenzaldehyde (2.00 g, 9.85 mmol), potassium *tert*-butoxide (1.327 g, 11.82 mmol), chloromethyltriphenylphosphonium chloride (4.10 g, 11.82 mmol) and THF (70 cm^3). This yielded a yellow oil of the title compound as an inseparable mixture of isomers (606 mg, 26 %, 1:2 *E*/*Z*). δ_H (200 MHz, $CDCl_3$); 7.64-7.47 (3H, m, aryl H and vinyl H, *E*), 7.15-7.07 (1H, m, aryl H), 6.96-6.85 (3H, m, aryl H), 6.81 (1H, d, *J* 8.2, vinyl H, *Z*), 6.64 (1H, d, *J* 13.6, vinyl H, *E*) and 6.44 (1H, d, *J* 8.2, vinyl H, *Z*). δ_C (100 MHz, $CDCl_3$); 163.1, 162.5, 160.7, 160.1, 136.5, 135.4, 135.4, 135.3, 134.4, 134.3, 133.8, 133.7, 131.7, 131.6, 128.07, 128.05, 122.6, 120.9, 118.23, 118.20, 117.7, 117.5, 117.1, 116.8, 116.6, 113.8 and 113.6 (3 peaks not seen – complicated by the *E*/*Z* isomers and C-F couplings). *HRMS* (EI) [M^+] $C_8H_5{}^{79}Br^{35}ClF$, requires: 233.9242, found: 233.9242. *m/z* 235.9 (62 %, M^+), 200.9 (23), 155.0 (22), 120.1, 99.1 (54), 94.1 (26) and 74.1 (38). ν_{max}/cm^{-1} (Thin film); 3076, 3034, 2953, 2926, 2853 (CH), 1606, 1574, 1460, 1411, 1274, 1224, 1150 and 1032 (fingerprint).

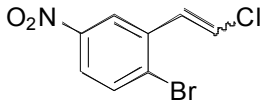
5-Fluoro-1-*tert*-pentyl-1*H*-indole, table 3, entry 3, product.



The general procedure for the preparation of indoles was followed using 1-bromo-4-fluoro-2-(2-chlorovinyl)benzene (178 mg, 0.756 mmol), palladium acetate (8.4 mg, 0.038 mmol), tri-*tert*-

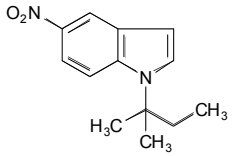
butylphosphonium tetrafluoroborate (26.3 mg, 0.091 mmol), sodium *tert*-butoxide (182 mg, 1.890 mmol), *tert*-amylamine (265 mg, 2.268 mmol) and toluene (1.5 cm^3). This yielded (101 mg, 65 %) of the title compound as a yellow oil. δ_H (300 MHz, $CDCl_3$); 7.56 (1H, dd, *J* 8.9, 3.7 aryl H), 7.31 (1H, d, *J* 3.7, H-2), 7.28 (1H, d, *J* 2.6, aryl H), 6.93 (1H, dt, *J* 8.9, 2.6, aryl H), 6.44 (1H, dd, *J* 3.7, 0.9, H-3), 2.11 (2H, q, *J* 7.6, CH_2), 1.71 (6H, s, CH_3) and 0.64 (3H, t, *J* 7.6, CH_3). δ_C (75.5 MHz, $CDCl_3$); 157.2 (d, $^1J_{CF}$ 234), 131.5, 130.6 (d, $^3J_{CF}$ 10.2), 127.8, 113.6 (d, $^3J_{CF}$ 9.0), 108.8 (d, $^2J_{CF}$ 26.0), 105.4 (d, $^4J_{CF}$ 5.0), 99.9 (d, $^4J_{CF}$ 5.0), 58.8, 33.4, 27.8 and 8.1. *HRMS* (ESI+ve) [M+H] $C_{13}H_{17}FN$, requires: 206.1340, found: 206.1343. *m/z* (EI) 205.2 (18 %, M^+), 176.1 (18), 135.0 (100), 107.1 (19), 71.1 (14), 55.1 (14) and 43.2 (39). ν_{max}/cm^{-1} (Thin film); 2975, 2937, 2880 (CH), 1618 (C=C), 1574, 1479, 1224, 1148, 1114 and 952 (fingerprint).

1-Bromo-2-(2-chlorovinyl)-4-nitrobenzene, table 3, entry 4, substrate.



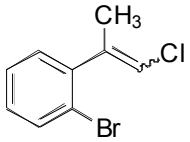
The general procedure for the preparation of chlorostyrenes was followed using 2-bromo-5-nitrobenzaldehyde (1.00 g, 4.349 mmol), sodium hydride (60 % dispersion in mineral oil) (0.209 g, 5.219 mmol), chloromethyltriphenylphosphonium chloride (1.812 g, 5.219 mmol) and THF (70 cm^3). This gave the title compound as a colourless oil (1.140 g, 99 %), 1.4:1 ratio of unseparable *Z*/*E* alkene isomers. δ_H (300 MHz, $CDCl_3$); 8.61 (1H, d, *J* 2.9, aryl H), 8.18 (1H, d, *J* 2.9, aryl H), 7.93 (2H, app. ddd, *J* 11.7, 8.4, 2.4, aryl H), 7.72 (1H, d, *J* 9.3, aryl H), 7.68 (1H, d, *J* 8.4, aryl H), 7.10 (1H, d, *J* 13.8, vinyl H, *E*), 6.78 (1H, d, *J* 8.2, vinyl H, *Z*), 6.75 (1H, d, *J* 13.8, vinyl H, *E*) and 6.51 (1H, d, *J* 8.2, vinyl H, *Z*). δ_C (75.5 MHz, $CDCl_3$); 136.4, 135.4, 134.1, 133.6, 130.9, 130.7, 129.7, 127.2, 125.3, 124.5, 123.7, 123.4, 122.6 and 121.5 (2 signals not seen). *HRMS* (EI) [M^+] $C_8H_5{}^{79}Br{}^{35}ClNO_2$, requires: 260.9187, found: 260.9188. *m/z* 262.9 (62%, M^+), 204.9 (12), 135.9 (73), 101.1 (44), 89.1 (27), 74.1 (100) and 50.1 (53). ν_{max}/cm^{-1} (Thin film); 2922 (CH), 1600, 1564, 1517, 1339, 1034, 930 and 825 (fingerprint).

5-Nitro-1-*tert*-pentyl-1*H*-indole, table 3, entry 4, product.



The general procedure for the preparation of indoles was followed using 1-bromo-4-nitro-2-(2-chlorovinyl)benzene (147 mg, 0.560 mmol), palladium acetate (6.3 mg, 0.038 mmol), tri-*tert*-butylphosphonium tetrafluoroborate (19.5 mg, 0.067 mmol), sodium *tert*-butoxide (135 mg, 1.400 mmol), *tert*-amylamine (146 mg, 1.680 mmol) and toluene (1.5 cm^3). This yielded (44 mg, 34 %) of the title compound as a yellow oil. δ_H (300 MHz, $CDCl_3$); 8.56 (1H, d, *J,* 1.8, aryl H), 8.03 (1H, dd, *J* 7.5, 1.8, aryl H), 7.64 (1H, d, *J* 7.5, aryl H), 7.39 (1H, d, *J* 2.9, H-2), 6.62 (1H, dd, *J* 2.9, 0.5, H-3), 2.11 (2H, q, *J* 6.3, CH_2), 1.72 (6H, s, CH_3) and 0.63 (3H, t, *J* 6.3, CH_3). δ_C (75.5 MHz, $CDCl_3$); 140.9, 137.7, 129.5, 129.4, 118.0, 116.1, 112.7, 102.9, 59.8, 33.6, 27.8 and 8.1. *HRMS* (ESI+ve) [M+H] $C_{13}H_{17}N_2O_2$, requires: 233.1285, found: 233.1282. *m/z* (EI) 232.2 (45 %, M^+), 203.0 (15), 162.0 (52), 132.0 (20), 116.1 (41), 89.1 (34), 71.1 (82) and 43.1 (100). ν_{max}/cm^{-1} (Thin film); 2973 (CH), 1607, 1512, 1461, 1386, 1316, 1074 and 782 (fingerprint).

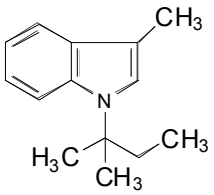
1-Bromo-2-(1-chloroprop-1-en-2-yl)benzene, table 3, entry 5, substrate.



The general procedure for the preparation of chlorostyrenes was followed using 2'-bromoacetophenone (1.38 cm^3, 10.217 mmol), sodium hydride (60 % dispersion in mineral oil)(0.490 g, 12.259 mmol), chloromethyltriphenylphosphonium chloride (4,257 g, 12.259 mmol) and THF (100 cm^3). This gave a yellow oil of the title compound as an inseparable mixture of isomers (1.497 g, 63 %, 1.4:1 *E/Z*, determined by n.O.e). δ_H (200 MHz, $CDCl_3$); 7.68-7.60 (2H, m, aryl H), 7.43-7.16 (6H, m, aryl H), 6.21 (1H, q, *J* 1.6, vinyl CH, *E*), 6.10 (1H, q *J* 1.6, vinyl CH, *Z*), 2.19 (3H, d, *J* 1.6, CH_3, *Z*) and 2.11 (3H, d, *J* 1.6, *E*). δ_C (100.5 MHz, $CDCl_3$); 142.0, 140.3, 139.4, 132.9, 132.7, 130.1, 129.4, 129.1, 128.9, 127.5, 127.3, 122.3, 121.6, 118.0, 115.1, 22.4 and 18.4 (1 signal not seen). *HRMS* (EI) [M^+] $C_9H_8{}^{79}Br^{35}Cl$, requires: 229.9498, found: 229.9512. *m/z* 229.9

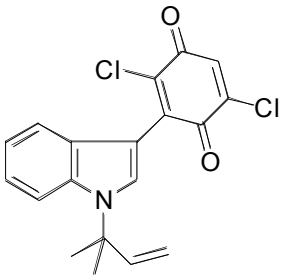
(23 %, M^+), 194.9 (10), 115.0 (100), 103.0 (16) and 75.0 (12). ν_{max}/cm^{-1} (Thin film); 3069, 2923, 2853 (CH), 1634 (C=C), 1569, 1468, 1428, 1028, 808 and 751 (fingerprint).

3-Methyl-1-*tert*-pentyl-1*H*-indole, table 3, entry 5, product.



The general procedure for the preparation of indoles was followed using 1-bromo-2-(1-chloroprop-1-en-2-yl)benzene (143 mg, 0.618 mmol), palladium acetate (6.9 mg, 0.031 mmol), tri-*tert*-butylphosphonium tetrafluoroborate (21.5 mg, 0.074 mmol), sodium *tert*-butoxide (148 mg, 1.545 mmol), *tert*-amylamine (0.22 cm^3, 1.854 mmol) and toluene (1.5 cm^3). This yielded (82 mg, 66 %) of the title compound as a pale yellow oil. δ_H (300 MHz, $CDCl_3$); 7.57-7.54 (2H, m, aryl H), 7.15-7.04 (2H, m, aryl H), 7.00 (1H, m, H-2), 2.30 (3H, d, *J* 0.9, CH_3), 2.05 (2H, q, *J* 7.6, CH_2), 1.64 (6H, s, CH_3) and 0.61 (3H, t, *J* 7.6, CH_3). δ_C (75.5 MHz, $CDCl_3$); 135.1, 130.2, 123.9, 120.4, 118.9, 118.0, 112.9, 108.5, 58.3, 33.4, 27.8, 9.5 and 8.2. *HRMS* (ESI+ve) [M+Na] $C_{13}H_{17}NNa$, requires: 224.1415, found: 224.1410. ν_{max}/cm^{-1} (Thin film); 3048, 2971, 2930, 2880 (CH), 1610, 1453, 1338, 1201, 1052 and 762 (fingerprint).

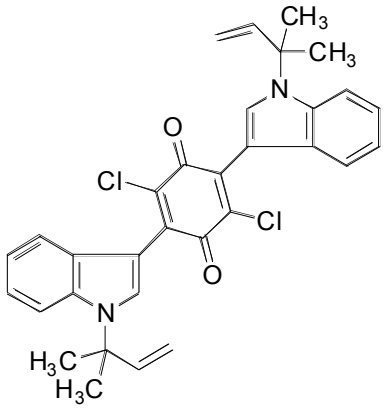
2,5-Dichloro-3-(1-(2-methylbut-3-en-2-yl)-1*H*-indol-3-yl)cyclohexa-2,5-diene-1,4-dione, structure 9.



N-reverse prenyl indole **8**[3] (0.420 g, 2.267 mmol), 2,5-dichloro-1,4-benzoquinone[9] (0.802 g, 4.534 mmol) and THF (14 cm^3) were placed in a 50 cm^3 round bottomed flask and stirred under nitrogen. To this was added conc. hydrochloric acid (10.2 N)(0.27 cm^3, 2.720 mmol) was added dropwise. The reaction mixture was then stirred for 16 h at room temperature. To this was added 2,3-dicloro-5,6-dicyanobenzoquinone (1.029 g, 4.534 mmol) and stirred for a further 3 h. The reaction mixture

was then diluted with ethyl acetate (150 cm^3) and washed with saturated aqueous $NaHCO_3$ (3 x 100 cm^3). The organic fraction was then dried over anhydrous magnesium sulfate, filtered and concentrated *in vacuo*. The crude residue was then purified using silica gel column chromatography with an eluent system of light petroleum:ethyl acetate. This yielded the title compound as a dark blue solid (0.530 g, 65 %). m.p. 100-103ºC. δ_H (300 MHz, $CDCl_3$); 7.59 (1H, s, CH), 7.54-7.49 (1H, m, aryl H), 7.31-7.26 (1H, m, aryl H), 7.13-7.06 (3H, m, aryl H), 6.10 (1H, dd, *J* 17.7, 10.5, vinyl CH), 5.21 (1H, d, *J* 10.5, vinyl CH), 5.16 (1H, d, *J* 17.7, vinyl CH) and 1.74 (6H, s, CH_3). δ_C (75.5 MHz, $CDCl_3$); 177.8, 143.7, 143.1, 138.3, 135.7, 135.4, 133.3, 132.9, 131.1, 127.1, 122.0, 121.6, 120.4, 114.5, 114.3, 104.9, 60.9 and 27.8. *HRMS* (ESI+ve) [M+Na] $C_{19}H_{15}Cl_2NO_2Na$, Requires: 382.0378, Found: 382.0372. ν_{max}/cm^{-1} (Thin film); 3157, 2983, 2879 (CH), 1677 (CO), 1559, 1509, 1457, 1246, 1183, 1111 and 1029 (fingerprint).

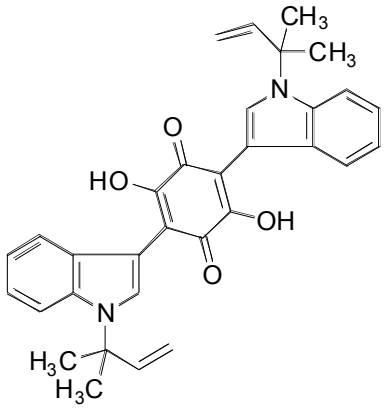
2,5-Dichloro-3,6-bis(2-methylbut-3-en-2-yl)-1*H*-indol-3-yl)cyclohexa-2,5-diene-1,4-dione, structure 10.



To a pre-dried flask was added 2,5-dichloro-3-(1-(2-methylbut-3-en-2-yl)-1*H*-indol-3-yl)cyclohexa-2,5-diene-1,4-dione **9** (99 mg, 0.275 mmol), *N*-reverse prenyl indole **8**[3] (20.6 mg, 0.082 mmol), zinc bis-trifluoromethanesulfonate (74 mg, 0.204 mmol) and THF (3 cm^3). The reaction mixture was then heated to reflux for 16 h . The reaction was then allowed to cool and 2,3-dicloro-5,6-dicyanobenzoquinone (46 mg, 0.204 mmol) was added and left to stir for a further 3 h. The reaction mixture then diluted with ethyl acetate (30 cm^3) and washed 3 times with saturated aqueous sodium hydrogen carbonate and once with brine. The organic fraction was dried over magnesium sulfate, filtered and concentrated *in vacuo*. The crude residue was further purified using flash silica column chromatography with an eluent system of ethyl acetate:light petroleum.

This yielded (28 mg, 64 %) of the title compound as a dark blue solid. m.p. 210-212 ºC. δ_H (500 MHz, $CDCl_3$); 7.80 (2H, s, H-2), 7.66-7.62 (2H, m, aryl H), 7.52-7.48 (2H, m, aryl H), 7.23-7.20 (4H, m, aryl H), 6.23 (2H, dd, *J* 10.9, *J'* 17.3, C*H*=CH_2), 5.32 (2H, d, *J* 10.9, CH=*H*H), 5.29 (2H, d, *J* 17.3, CH=CH*H*) and 1.87 (12H, s, CH_3). δ_C (125.8 MHz, $CDCl_3$); 178.5, 143.2, 138.3, 135.5, 135.4, 131.1, 127.3, 122.3, 121.5, 120.3, 114.4, 114.2, 105.2, 60.1 and 27.9. *HRMS* (ESI+ve) [M+Na] $C_{32}H_{28}Cl_2N_2O_2Na$, requires: 565.1426, found: 565.1420. ν_{max}/cm^{-1} (Thin film); 3049, 2925, 2854 (CH), 1666 (C=O), 1561, 1510, 1457, 1155 and 1113 (fingerprint).

2,5-Dihydroxy-3,6-bis(1-(2-methylbut-3-en-2-yl)-1*H*-indol-3-yl)cyclohexa-2,5-diene-1,4-dione {Asterriquinone A1}, structure 2.[10]



2,5-Dichloro-3,6-bis(2-methylbut-3-en-2-yl)-1*H*-indol-3-yl)cyclohexa-2,5-diene-1,4-dione **10** (53 mg, 0.098 mmol) was dissolved in methanol (6 cm^3) and refluxed for 10 min. To the reaction was then added 10 % aqueous sodium hydroxide (3 cm^3) with the result of the reaction mixture turning from an intense blue to a brown colour. The mixture was refluxed for a further 30 min. and allowed to cool. 3M HCl was then added to acidify to pH 1 and the mixture extracted 3 times with ethyl acetate. The combined organic fractions were then dried over $MgSO_4$ filtered and concentrated *in vacuo*. The crude residue was then columned on pre-treated oxalic acid coated silica gel using an eluent of 7:1 petroleum ether:ethyl acetate to yield the title compound as a red solid (49 mg, 99 %). m.p. 205-207 ºC (decomp.) (Lit. m.p. 218-220 ºC {decomp.}). δ_H (500 MHz, $CDCl_3$); 8.15 (2H, br s, OH), 7.76 (2H, s, H-2), 7.67-7.59 (4H, m, aryl H), 7.21-7.16 (4H, m, aryl H), 6.23 (2H, dd, *J* 17.7, 10.7, C*H*=CH_2), 5.30 (2H, d, *J* 10.7, CH=CH*H*), 5.28 (2H, d, *J* 17.7, CH=C*H*H) and 1.85 (12H, s, CH_3). δ_C (125.8 MHz, $CDCl_3$); 143.7, 135.3, 128.2, 127.9, 121.9, 121.1, 119.6, 114.0, 113.8, 110.8, 102.3, 59.6 and 27.9 (C=O and C-OH quat. C's not seen).

HRMS (ESI-ve) [M-H] $C_{32}H_{29}N_2O_4$, requires: 505.2127, found: 505.2122. ν_{max}/cm^{-1} (Thin film); 3316 (OH), 2980, 2924, 2853 (CH), 1693 (C=O), 1629 (C=C), 1457, 1315, 1280, 1187, 997 and 759 (fingerprint).

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