Synthetic ansamycins prepared by a ring-expanding Claisen rearrangement. Synthesis and biological evaluation of ring and conformational analogues of the Hsp90 molecular chaperone inhibitor geldanamycin

Christopher S. P. McErlean, Nicolas Proisy, Christopher J. Davis, Nicola A. Boland, Swee Y. Sharp, Kathy Boxall, Alexandra M. Z. Slawin, Paul Workman
and Christopher J. Moody

Electronic Supplementary Information (ESI)

5-Methoxy-2-nitrophenol

A solution of 3-hydroxyanisole (4.4 mL, 40 mmol) in propionic acid containing 1% v/v propionic anhydride (50 mL) was cooled to -10 °C. Sodium nitrite (3.0 g, 44 mmol) was added to the stirred mixture in a portionwise manner over a period of 15 min. After the addition was complete the reaction was allowed to stir for a further hour before water (50 mL) was added and the precipitate was collected on the sinter. The solid was washed with water (4 × 25 mL), air dried and then dried *in vacuo*. The product was collected as a green powder (3.5 g, 58%) and used immediately in the next reaction.

The nitroso compound (3.5 g, 23 mmol) was then suspended in propionic acid (45 mL) and cooled to -10 °C. Concentrated HNO_3 (70%; 2.9 mL, 46 mmol) was dropwise added and the solution was left to stir for 2 h. After being diluted with water (50 mL), the precipitate was collected on the sinter and washed with water (4 × 25 mL). The crude material was then dried *in* *vacuo* overnight and the product was collected as a yellow solid (3.1 g, 80%), mp 92-95 °C (lit.,[1] mp 92-93 °C); (Found: M^+, 169.0373. $C_7H_7NO_4$ requires 169.0375); □$_{max}$ ($CHCl_3$)/cm^{-1} 3020, 1622, 1592, 1285, 1256, 1192; □$_H$ (300 MHz; $CDCl_3$) 11.05 (1 H, s, OH), 8.02 (1 H, dd, *J* 9.0, 3.0, H-3), 6.53-6.49 (2 H, m, ArH), 3.87 (3 H, s, OMe); □$_C$ (75 MHz; $CDCl_3$) 167.4 (C), 158.4 (C), 128.1 (C), 127.3 (CH), 109.9 (CH), 101.7 (CH), 56.5 (Me); *m/z* (EI) 169 (100%), 139 (58), 111 (71), 85 (53), 83 (93).

(*E*)-Ethyl 2-methyl-2,4-pentadienoate

To a stirred solution of (carboethoxyethylidene)triphenylphosphorane (1.26 g, 3.5 mmol) in dry dichloromethane (20 mL) was added acrolein (0.26 mL, 0.20 g, 3.5 mmol) dropwise. The reaction mixture was then heated under reflux for 2 h under a nitrogen atmosphere. Most of the solvent was removed *in vacuo*, and light petroleum was added to precipitate triphenylphosphine oxide. The mixture was filtered and the solids washed with light petroleum. The combined petroleum extracts were evaporated *in vacuo* and the crude product was purified by flash chromatography on silica, eluting with ethyl acetate and light petroleum (1 : 9) to give the *title compound* (0.388g, 79%) as an opaque oil, (lit.,[2] oil); □$_{max}$ (film)/cm^{-1} 3091, 2981, 2933, 1709, 1633, 1597; □$_H$ (300 MHz; $CDCl_3$) 7.15 (1 H, d, *J* 1.4, =CHCH=C), 6.69-6.57 (1 H, m, H_2C=CHCH), 5.55 (1 H, d, *J* 17.0, H_2C=CH), 5.41 (1 H, d, *J* 10.0, H_2C=CH), 4.19 (2 H, q, *J* 7.0, OCH_2Me), 1.92 (3 H, s, Me), 1.28 (3 H, t, *J* 7.0, OCH_2Me); □$_C$ (100 MHz; $CDCl_3$) 168.2 (C), 138.1 (CH), 132.2 (CH), 128.1 (C), 123.8 (CH_2), 60.5 (CH_2), 14.2 (Me), 12.5 (Me).

(*E*)-2-Methyl-2,4-pentadienoic acid

(*E*)-Ethyl 2-methyl-2,4-pentadienoate (0.330 g, 2.14 mmol) was dissolved in THF (4 mL) and water (10 mL), then NaOH (2 M; 4 mL) was added. The solution was stirred at room temperature for 24 h, then acidified with HCl (2 M) and extracted with ether (3 × 10 mL). The combined organic extracts were washed with brine (20 mL), dried ($MgSO_4$), filtered and evaporated *in vacuo*. The crude product was purified by flash chromatography on silica, eluting with ethyl acetate and light petroleum (2 : 3) to give the *title compound* as a colourless crystalline solid (0.219 g, 91%); mp 65-67 °C (from light petroleum-ether) (lit.,[3] mp 63.8-65 °C); δ_H (400 MHz; $CDCl_3$) 7.29 (1 H, d, *J* 11.4, =CHC$\underline{H}$=C), 6.68 (1 H, ddd, *J* 16.8, 11.4, 10.0, H_2C=C$\underline{H}$CH), 5.58 (2 H, dd, *J* 16.8, 10.0, $\underline{H}_2C$=CH), 1.97 (3 H, s, Me); δ_C (100 MHz; $CDCl_3$) 173.9 (C), 140.6 (CH), 132.1 (CH), 127.2 (C), 125.4 (CH_2), 12.3 (Me).

9-Decenal

Method A: Powdered molecular sieves (4 Å, 500 mg/mmol, 15.00 g) were added to a solution of 9-decen-1-ol (5.54 mL, 4.69 g, 30 mmol) and *N*-methylmorpholine *N*-oxide (6.08 g, 45 mmol) in dry dichloromethane (2 mL/mmol, 60 mL). Tetra-*n*-propylammonium perruthenate (TPAP) (0.53 g, 1.5 mmol, 5 mol%) was added slowly while stirring at 0 °C under a nitrogen atmosphere. Once added, the reaction mixture was stirred at 0 °C for a further 5 min before allowing to warm to room temperature for 1 h. The product was filtered through Celite, the filtrate evaporated *in vacuo* and purified by flash chromatography on silica, eluting with ethyl acetate and light petroleum (2 : 3) to give the *title compound* (3.67 g, 79%) as a colourless oil (lit.,[4] bp not given) ν_{max} (film)/cm^{-1} 2925, 2848, 2710, 1726, 1465; δ_H (300 MHz; $CDCl_3$) 9.76 (1 H, t, *J* 1.9, $CH_2C\underline{H}O$), 5.79 (1 H, ddt, *J* 17.0, 10.2, 6.8, $C\underline{H}$=CH_2), 4.96-4.84 (2 H, m, CH=$C\underline{H}_2$), 2.41 (2 H, td, *J* 7.2, 1.9, $C\underline{H}_2CHO$), 2.00-1.93 (2 H, m, $C\underline{H}_2CH$=CH_2), 1.58-1.53 (2 H, m, $C\underline{H}_2CH_2CHO$), 1.35-1.27 (8 H, m, 4 □ CH_2); □$_C$ (100 MHz; $CDCl_3$) 203.0 (CH), 139.0 (CH), 114.2 (CH_2), 43.9 (CH_2), 33.7 (CH_2), 29.0 (CH_2), 28.98 (CH_2), 28.85 (CH_2), 28.8 (CH_2), 22.0 (CH_2).

Method B: Oxalyl chloride (9.3 mL, 13.6 g, 0.107 mol) was added to dry dichloromethane (220 mL). The solution was stirred and cooled to between -50 and -60 °C as dimethyl sulfoxide (15.2 mL, 16.7 g, 0.214 mol) in dry dichloromethane (43 mL) was added dropwise at a rapid rate. After 5 min, 9-decen-1-ol (15.4 mL, 13.9, 0.089 mol) was added dropwise over 10 min while maintaining the temperature at -50 °C to -60 °C. After a further 15 min, triethylamine (61.6 mL, 45.9 g, 0.454 mol) was added dropwise and the reaction mixture was allowed to stir for a further 5 min before warming to room temperature and water (250 mL) was added. The aqueous layer was separated and extracted with dichloromethane (2 □ 200 mL). The combined organic layers were dried ($MgSO_4$), filtered and evaporated *in vacuo*. The crude product was purified by flash chromatography, eluting with ethyl acetate and light petroleum (1 : 4) to give the *title compound* as a colourless oil (14.6 g ~100%), data as above.

2-Methyldodeca-1,11-dien-3-ol 8

9-Decenal (3.51 g, 22.6 mmol) in dry THF (15 mL) was added to a solution of isopropenylmagnesium bromide (0.5 M in THF; 58.8 mL, 29.4 mmol) dropwise over 10 min at 0 °C under a nitrogen atmosphere. The reaction mixture was stirred for a further 1.5 h at 0 °C. Saturated ammonium chloride solution (100 mL) was added to quench the reaction and the resulting solution was extracted with ether (3 □ 30 mL), washed with water (3 □ 30 mL), brine (30 mL), dried ($MgSO_4$), filtered and evaporated *in vacuo*. The crude product was purified by flash chromatography on silica, eluting with ethyl acetate and light petroleum (3: 22) to give the *title compound* as a pale yellow oil (2.41 g, 55%); (Found: M+NH_4^+, 214.2175. $C_{13}H_{24}O$ + NH_4 requires 214.2171); ν_{max} (film)/cm^{-1} 3371, 3076, 2927, 2856, 1641; δ_H (300 MHz; $CDCl_3$) 5.81 (1 H, ddt, *J* 16.8,10.2, 6.6, $C\underline{H}=CH_2$), 5.03-4.82 (4 H, m, $CH=C\underline{H}_2$, $MeC=C\underline{H}_2$), 4.06 (1 H, t, *J* 6.5, $C\underline{H}OH$), 2.04 (2 H, q, *J* 7.0, $C\underline{H}_2CH=CH_2$), 1.72 (3 H, s, Me), 1.55-1.50 (2 H, m, $CHOHC\underline{H}_2$), 1.39-1.30 (10 H, m, 5 × CH_2); OH not observed; δ_C (100 MHz; $CDCl_3$) 147.7 (C), 139.2 (CH), 114.1 (CH_2), 110.8 (CH_2), 76.0 (CH), 35.0 (CH_2), 33.8 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.0 (CH_2), 28.9 (CH_2), 25.6 (CH_2), 17.5 (Me); *m/z* (CI) 214 (M+NH_4^+, 60%), 196 (100), 179 (30).

2-Methyl-3-(2-nitrophenoxy)dodeca-1,11-diene 9a

A solution of diethyl azodicarboxylate (1.56 mL, 1.73 g, 9.95 mmol) was added dropwise to a solution of triphenylphosphine (2.61 g, 9.95 mmol), 2-nitrophenol (1.06 g, 7.65 mmol), and 2-methyldodeca-1,11-dien-3-ol **8** (1.50 g, 7.65 mmol) in dry toluene (30 mL) while stirring at 0 °C. The solution was allowed to warm to room temperature and then stirred for 72 h. The mixture was diluted with ethyl acetate (50 mL) and basified with NaOH (2 M), washed with water (3 × 30 mL), brine (30 mL), dried ($MgSO_4$), filtered and evaporated *in vacuo*. The crude product was purified by flash chromatography on silica, eluting with ethyl acetate and light petroleum (1 : 19) to give the *title compound* as a yellow oil (1.43 g, 59%); (Found: M+NH_4^+, 335.2336. $C_{19}H_{27}NO_3$ + NH_4 requires 335.2335); ν_{max} (film)/cm^{-1} 3075, 2927, 2856, 1606, 1583, 1527, 1485, 1356; δ_H (300 MHz; $CDCl_3$) 7.77 (1 H, dd, *J* 6.3, 1.8, ArH), 7.43 (1 H, td, *J* 7.4, 1.8, ArH), 7.03-6.95 (2 H, m, ArH), 5.81 (1 H, ddt, *J* 16.9, 10.2, 6.8, $C\underline{H}=CH_2$), 5.03-4.91 (4 H, m, $HC=C\underline{H}_2$, $MeC=C\underline{H}_2$), 4.65 (1 H, t, *J* 6.6, $ArOC\underline{H}CH_2$), 2.04 (2 H, q, *J* 6.6, $C\underline{H}_2CH=CH_2$), 1.88-1.84 (1 H, m, $ArOCHC\underline{H}H$), 1.75-1.71 (4 H, m, Me, $ArOCHCH\underline{H}$), 1.38-1.28 (10 H, m, 5

× CH_2); δ_C (100 MHz; $CDCl_3$) 151.4 (C), 143.2 (C), 140.5 (C), 139.2 (CH), 133.4 (CH), 125.2 (CH), 119.9 (CH), 115.9 (CH), 114.1 (CH_2), 113.9 (CH_2), 83.6 (CH), 33.8 (CH_2), 33.7 (CH_2), 29.3 (CH_2), 29.0 (CH_2), 28.9 (2 × CH_2), 25.4 (CH_2), 17.2 (Me); *m/z* (CI) 335 ($M+NH_4^+$, 40%), 288 (100), 196 (30), 179 (20), 110 (80).

2-(2-Methyldodeca-1,11-dien-3-yloxy)aniline 10a

2-Methyl-3-(2-nitrophenoxy)dodeca-1,11-diene **9a** (1.08 g, 3.40 mmol) was dissolved in methanol (30 mL). Finely powdered indium (3.56 g, 31 mmol) and saturated ammonium chloride solution (20 mL) were added to the mixture. The reaction was heated under reflux for 24 h. The resulting product was washed through Celite with ethyl acetate (40 mL) and deionized water (30 mL). The filtrate was then basified by the addition of NaOH (2 M) and then extracted with ethyl acetate (2 × 20 mL), the extracts washed with deionized water (3 × 30 mL), brine (2 × 30 mL) and dried ($MgSO_4$), filtered and evaporated *in vacuo* to give the crude *title compound* as a dark red oil (0.730g, 75%); (Found: MH^+, 288.2323. $C_{19}H_{29}NO$ + H requires 288.2327); ν_{max} (film)/cm^{-1} 3481, 3377, 3074, 2927, 2856, 1612, 1593, 1502; δ_H (300 MHz; $CDCl_3$) 6.78-6.63 (4 H, m, ArH), 5.82 (1 H, ddt, *J* 16.9, 10.3, 6.7, $C\underline{H}=CH_2$), 5.02-4.52 (4 H, m, $HC=C\underline{H}_2$, $MeC=C\underline{H}_2$), 4.54 (1 H, t, *J* 6.6, $ArOC\underline{H}CH_2$), 3.70 (2 H, br s, NH_2), 2.08-2.01 (2 H, m, $C\underline{H}_2CH=CH_2$), 1.84-1.81 (1 H, m, $ArOCHC\underline{H}H$), 1.78-1.72 (4 H, m, Me, $ArOCHCH\underline{H}$), 1.38-1.21 (10 H, m, 5 x CH_2); δ_C (100 MHz; $CDCl_3$) 145.9 (C), 144.4 (C), 139.2 (CH), 136.1 (C), 120.9 (CH), 118.5 (CH), 115.4 (CH), 114.2 (CH_2), 113.3 (CH), 112.9 (CH_2), 82.0 (CH), 34.1 (CH_2), 33.8 (CH_2), 29.44 (CH_2), 29.40 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 25.7 (CH_2), 17.3 (Me); *m/z* (CI) 288 (MH^+, 100%), 242 (69), 198 (47), 193 (34), 110 (53).

***N*-[2-(2-Methyldodeca-1,11-dien-3-yloxy)phenyl] pent-4-enamide 11a**

2-(2-Methyldodeca-1,11-dien-3-yloxy)aniline **10a** (0.679 g, 2.37 mmol) was dissolved in dichloromethane (10 mL) and 4-pentenoic acid (0.314 mL, 0.308 g, 3.08 mmol) and DCC (0.735 g, 3.56 mmol) were added. The reaction mixture was stirred at room temperature under an atmosphere of nitrogen for 19 h. The mixture was diluted with dichloromethane (10 mL) and filtered through a short pad of Celite, washed through with dichloromethane (20 mL). The filtrate was then washed with NaOH (2 M) until basic, HCl (2 M) until acidic, water (3 × 10 mL), brine (10 mL), dried ($MgSO_4$), filtered and evaporated *in vacuo*. The crude product was purified by flash chromatography on silica, eluting with ethyl acetate and light petroleum (1 : 19) to give the *title compound* as a colourless oil (0.680 g, 78%); (Found: C, 78.2; H, 9.9; N 3.7. $C_{24}H_{35}NO_2$ requires C, 78.0; H, 9.6; N, 3.8%); (Found: M^+, 369.2665. $C_{24}H_{35}NO_2$ requires 369.2668); ν_{max} (film)/cm^{-1} 3421, 3073, 2971, 2925, 2848, 1690, 1634, 1598, 1521; δ_H (400 MHz; $CDCl_3$) 8.37 (1 H, dd, *J* 7.5, 2.1, ArH), 7.86 (1 H, br, NH), 6.98-6.89 (2 H, m, ArH), 6.85 (1 H, dd, *J* 7.5, 2.1, ArH), 5.96-5.76 (2 H, m, 2 × $\mathrm{C\underline{H}{=}CH_2}$), 5.17-4.93 (6 H, m, 2 × $\mathrm{CH{=}C\underline{H}_2}$, $\mathrm{MeC{=}C\underline{H}_2}$), 4.57 (1 H, t, *J* 6.6, $\mathrm{ArOC\underline{H}}$), 2.51 (4 H, d, *J* 2.8, $\mathrm{COC\underline{H}_2C\underline{H}_2}$), 2.07-2.02 (2 H, m, $\mathrm{C\underline{H}_2CH{=}CH_2}$), 1.87-1.83 (1 H, m, $\mathrm{ArOCHC\underline{H}H}$), 1.75-1.70 (4 H, m, Me, $\mathrm{ArOCHCH\underline{H}}$), 1.47-1.40 (10 H, m, 5 × CH_2); δ_C (100 MHz; $CDCl_3$) 170.2 (C), 146.3 (C), 143.6 (C), 139.1 (CH), 136.8 (CH), 128.1 (C), 123.4 (CH), 121.1 (CH), 119.7 (CH), 115.8 (CH_2), 114.2 (CH_2), 113.5 (CH_2), 112.8 (CH), 82.8 (CH), 37.3 (CH_2), 34.0 (CH_2), 33.8 (CH_2), 29.5 (CH_2), 29.44 (CH_2), 29.43 (CH_2), 29.0 (CH_2), 28.9 (CH_2), 25.8 (CH_2), 17.3 (Me); *m/z* (CI) 369 (MH^+, 5%), 351 (10), 240 (14), 191 (65), 109 (100).

Lactam 12a

To a solution of *N*-[2-(2-methyldodeca-1,11-dien-3-yloxy)phenyl] pent-4-enamide **11a** (0.642 g, 1.74 mmol) in dry dichloromethane (500 mL) was added benzylidene bis(tricyclohexylphosphine)dichlororuthenium (Grubbs catalyst) (0.428 g, 0.52 mmol, 30 mol%) in dry dichloromethane (77 mL). The reaction mixture was heated under reflux under an argon atmosphere for 24 h. The solvent was removed *in vacuo* and the crude product purified by flash chromatography on silica, eluting with ethyl acetate and light petroleum (1 : 19) to give the *title compound* as a colourless solid (0.470 g, 79%) as a mixture of isomers; (Found: M$^+$, 341.2362. $C_{22}H_{31}NO_2$ requires 341.2355); □$_{max}$ (film)/cm^{-1} 3421, 2919, 2843, 1685, 1593, 1521, 1450, 1245, 743; □$_H$ (400 MHz; $CDCl_3$) *major isomer* 8.48-8.42 (1 H, m, ArH), 7.92 (1 H, br, NH), 6.96-6.92 (2 H, m, ArH), 6.86-6.82 (1 H, m, ArH), 5.45-5.38 (2 H, m, CH=CH), 5.02-4.96 (2 H, m, MeC=CH_2), 4.49 (1 H, dd, *J* 10.1, 2.6, ArOCH), 2.73-2.47 (4 H, m, 2 □ CH_2), 2.26-2.05 (4 H, m, 2 □ CH_2), 1.90-1.69 (5 H, m, Me, CH_2), 1.40-1.23 (8 H, m, 4 □ CH_2); *minor isomer* 8.48-8.42 (1 H, m, ArH), 7.99 (1 H, br, NH), 6.96-6.92 (2 H, m, ArH), 6.86-6.82 (1 H, m, ArH), 5.45-5.38 (2 H, m, CH=CH), 5.02-4.96 (2 H, m, MeC=CH_2), 4.40 (1 H, dd, *J* 9.2, 2.8, ArOCH), 2.73-2.47 (4 H, m, 2 □ CH_2), 2.26-2.05 (4 H, m, 2 □ CH_2), 1.90-1.69 (5 H, m, Me, CH_2), 1.40-1.23 (8 H, m, 4 □ CH_2); □$_C$ (100 MHz; $CDCl_3$) *both isomers* 170.6 (C), 170.4 (C), 146.7 (C), 146.65 (C), 145.0 (C), 144.8 (C), 131.8 (CH), 131.4 (CH), 129.4 (CH), 128.03 (C), 128.00 (C), 127.96 (CH), 123.4 (CH), 123.3 (CH), 121.0 (CH), 120.96 (CH), 119.5 (CH), 119.1 (CH), 112.6 (CH), 112.4 (CH), 111.7 (CH_2), 111.5 (CH_2), 83.2 (CH), 82.3 (CH), 39.5 (CH_2), 39.3 (CH_2), 35.6 (CH_2), 35.0 (CH_2), 31.6 (CH_2), 28.8 (CH_2), 28.5 (CH_2), 28.3 (CH_2), 28.1 (CH_2), 28.09 (CH_2), 27.5 (CH_2), 27.4 (CH_2), 26.8 (CH_2), 25.0 (CH_2), 23.9 (CH_2), 18.1 (Me), 18.06 (Me); *m/z* (EI), 341 (M$^+$, 8%), 323 (25), 294 (6), 109 (100).

Hydrogenation of lactam 12a

Lactam **12a** (0.071 g, 0.021 mmol) in ethyl acetate (4 mL) was added to Pd/C (10%; 0.007 g) in ethyl acetate (3 mL). The flask was flushed twice with hydrogen and the mixture stirred under an atmosphere of hydrogen overnight (17 h). The mixture was then filtered through Celite, washed through with ethyl acetate (15 mL), and the filtrate evaporated *in vacuo*. The crude product was purified by flash chromatography on silica, eluting with ethyl acetate and light petroleum (1 : 19) to give the *reduced lactam* **13a** as a colourless solid (0.066 g, 92%), mp 61.5-63 °C (from ethyl acetate and light petroleum); (Found: C, 76.5; H, 10.6; N, 3.9. $C_{22}H_{35}NO_2$ requires C, 76.5, H, 10.2; N, 4.1%); (Found: M^+, 345.2649. $C_{22}H_{35}NO_2$ requires 345.2667); □$_{max}$ (film)/cm^{-1} 3350, 2930, 2858, 1664, 1593, 1525; □$_H$ (400 MHz; $CDCl_3$) 8.47 (1 H, dd, *J* 7.7, 1.6, ArH), 7.96 (1 H, s, NH), 6.98 (1 H, td, *J* 7.7, 1.6, ArH), 6.91 (1 H, t, *J* 7.7, ArH), 6.84 (1 H, *J* 7.7, ArH), 4.17-4.14 (1 H, m, ArOC$\underline{\text{H}}$), 2.52-2.27 (2 H, m, CH_2), 2.18-1.85 (2 H, m, CH_2), 1.65-1.59 (4 H, m, COC$\underline{\text{H}}_2$C$\underline{\text{H}}_2$), 1.40-1.28 (15 H, m, 7 □ CH_2, C$\underline{\text{H}}$Me$_2$), 0.98 (3 H, d, *J* 6.9, CH$\underline{\text{Me}}$Me), 0.95 (3 H, d, *J* 6.9, CHMe$\underline{\text{Me}}$); □$_C$ (100 MHz; $CDCl_3$) 171.2 (C), 146.4(C), 128.5 (C), 123.2 (CH), 120.5 (CH), 119.5 (CH), 111.7 (CH), 83.3 (CH), 38.0 (CH_2), 30.3 (CH), 29.6 (CH_2), 28.1 (CH_2), 27.3 (CH_2), 26.9 (CH_2), 26.89 (CH_2), 26.8 (CH_2), 26.5 (CH_2), 26.2 (CH_2), 25.2 (CH_2), 24.5 (CH_2), 18.8 (Me), 17.4 (Me); *m/z* (CI) 345 (MH^+, 21%), 321 (100), 305 (75), 263 (57), 235 (36).

Claisen rearrangement of lactam 12a to ansa-lactam 14a

To a solution of lactam **12a** (0.30 g, 0.88 mmol) in xylene (3 mL) was added sodium carbonate (0.09 g, 0.88 mmol). The reaction mixture was heated under reflux for 19 h while under a nitrogen atmosphere. The mixture was diluted with ethyl acetate (10 mL) and acidified with HCl (2 M), washed with water (2 □ 5 mL), dried ($MgSO_4$), filtered and evaporated *in vacuo*. The crude product was purified by flash chromatography on silica, eluting with ethyl acetate and light petroleum (1 : 9) to give the *title compound* as a powder (0.20 g, 66%) as a mixture of two isomers (2.5 : 1); (Found: M$^+$, 341.2342. $C_{22}H_{31}NO_2$ requires 341.2355); □$_{max}$ (film)/cm^{-1} 3263, 3150, 3078, 2986, 2858, 2919, 1629, 1588, 1537; □$_H$ (400 MHz; $CDCl_3$) *major isomer* 7.68-7.66 (1 H, m, ArH), 6.92-6.80 (2 H, m, ArH), 5.64-5.45 (2 H, m, C$\underline{H}$=C$\underline{H}$), 5.25-5.22 (1 H, m, MeC=C$\underline{H}$), 3.36 (2 H, s, ArC$\underline{H}_2$), 2.58-2.40 (4 H, m, 2 □ CH_2), 2.11-2.05 (2 H, m, CH_2), 1.96 (2 H, q, *J* 6.6, CH_2), 1.62 (3 H, s, Me), 1.40-1.19 (10 H, m, 5 □ CH_2); OH/NH not observed; *minor isomer* 7.48-7.43 (1 H, m, ArH), 6.92-6.80 (2 H, m, ArH), 5.64-5.45 (2 H, m, C$\underline{H}$=C$\underline{H}$), 5.25-5.22 (1 H, m, MeC=C$\underline{H}$), 3.36 (2 H, s, ArC$\underline{H}_2$), 2.58-2.40 (4 H, m, 2 □ CH_2), 2.11-2.05 (2 H, m, CH_2), 1.96 (2 H, q, *J* 6.6, CH_2), 1.62 (3 H, s, Me), 1.40-1.19 (10 H, m, 5 □ CH_2); □$_C$ (100 MHz; $CDCl_3$) *both isomers* 171.8 (C), 145.8 (C), 134.5 (C), 133.5 (CH), 133.4 (CH), 127.5 (CH), 127.4 (CH), 127.2 (CH), 127.0 (C), 126.9 (CH), 126.8 (CH), 126.3 (C), 120.2 (CH), 120.1 (CH), 119.85 (CH), 119.80 (CH), 42.1-23.3 (18 □ CH_2), 16.34 (Me), 16.30 (Me); *m/z* (EI) 341 (M$^+$, 51%), 323 (98), 294 (42), 280 (32), 149 (100), 85 (42), 71 (57), 57 (83).

Oxidation of ansa-lactam 14a to ansa-quinone 16a

Ansa-lactam **14a** (0.161 g, 0.47 mmol) was dissolved in acetone (32 mL). Fremy's salt (0.504 g, 1.88 mmol) in saturated sodium dihydrogen phosphate buffer (16 mL) was added and the reaction mixture stirred at room temperature for 1 h. The solution was concentrated *in vacuo* and extracted with dichloromethane (3 □ 10 mL), the organic extracts combined and washed with water (10 mL), brine (10 mL), dried ($MgSO_4$), filtered and evaporated *in vacuo*. The crude product was purified by flash chromatography on silica, eluting with ethyl acetate and light petroleum (3 : 7) to give the *title compound* as an orange, sticky oil (0.115 g, 69%) as a mixture of four isomers (ratio 12 : 10 : 6 : 3); (Found: M$^+$, 355.2140. $C_{22}H_{29}NO_3$ requires 355.2147); □$_{max}$ (film)/cm^{-1} 3304, 2925, 2853, 1690, 1665, 1644, 1598, 1501, 1450, 1350, 1310, 1280, 1220, 950, 900, 730; □$_H$ (400 MHz; $CDCl_3$) *major isomer* 8.16-8.14 (1 H, m, NH), 7.59-7.55 (1 H, m, quinone-H), 6.58-6.51 (1 H, m, H-5), 5.68-5.36 (2 H, m, $CH_2C\underline{H}=C\underline{H}CH_2$), 5.27-5.11 (1 H, m, $MeC=C\underline{H}CH_2$), 3.15 (2 H, s, $ArCH_2$), 2.58-2.40 (4 H, m, 2 □ CH_2), 2.10-1.92 (4 H, m, 2 □ CH_2), 1.74 (3 H, s, Me), 1.31-0.98 (10 H, m, 5 □ CH_2); *other isomers* 8.33-8.29 (1 H, m, NH), 7.59-7.55 (1 H, m, quinone-H), 6.58-6.51 (1 H, m, quinone-H), 5.68-5.36 (2 H, m, $C\underline{H}=C\underline{H}$), 5.27-5.11 (1 H, m, $MeC=C\underline{H}$), 3.06 (2 H, s, $ArCH_2$), 2.58-2.40 (4 H, m, 2 □ CH_2), 2.10-1.92 (4 H, m, 2 □ CH_2), 1.65 (3 H, s, Me), 1.31-0.98 (10 H, m, 5 □ CH_2); □$_C$ (100 MHz; $CDCl_3$) *all isomers* 188.4 (C), 188.3 (C), 182.7 (C), 182.69 (C), 172.4 (C), 172.37 (C), 172.3 (C), 144.2 (C), 143.7 (C), 143.6 (C), 138.5 (C), 138.3 (C), 138.1 (C), 135.0 (CH), 134.9 (CH), 134.8 (CH), 134.4 (CH), 134.3 (CH), 133.7 (CH), 133.5 (CH), 130.4 (C), 130.3 (C), 130.0 (CH), 129.8 (CH), 129.3 (C), 129.0 (C), 128.6 (CH), 128.4 (CH), 127.1 (CH), 127.0 (CH), 126.5 (CH), 126.4 (CH), 114.7 (CH), 114.5 (CH), 114.4 (CH), 39.1 (CH_2), 39.0 (CH_2), 38.8 (CH_2), 38.43 (CH_2), 38.41 (CH_2), 32.2 (CH_2), 32.0 (CH_2), 31.8 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 29.0 (CH_2), 28.9 (CH_2), 28.8 (CH_2), 28.7 (CH_2), 28.6 (CH_2), 28.54 (CH_2), 28.51 (CH_2), 28.4 (CH_2), 28.3 (CH_2), 28.2 (CH_2), 28.1 (CH_2), 28.0 (CH_2), 27.9 (CH_2), 27.87 (CH_2), 27.7 (CH_2), 27.5 (CH_2), 27.4 (CH_2), 27.3 (CH_2), 27.2 (CH_2), 24.3 (Me), 24.0 (Me), 23.5 (CH_2), 23.0 (CH_2), 16.7 (Me), 16.66 (Me); *m/z* (EI), 355 (M$^+$, 47%), 341 (100), 323 (90), 294 (41), 176 (46), 160 (43).

3-(5-Methoxy-2-nitrophenoxy)-2-methyldodeca-1,11-diene 9b

A solution of diethyl azodicarboxylate (0.25 g, 1.41 mmol) was added dropwise to a solution of triphenylphosphine (0.37 g, 1.41 mmol), 5-methoxy-2-nitrophenol (0.18 g, 1.08 mmol), and 2-

methyldodeca-1,11-dien-3-ol **8** (0.21 g, 1.08 mmol) in toluene (5 mL) while stirring at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for a further 80 h. The product was diluted with ethyl acetate (30 mL), basified with NaOH (2 M), washed with water (2 □ 30 mL), brine (30 mL), dried ($MgSO_4$), filtered and evaporated *in vacuo*. The crude oil was purified by flash chromatography on silica, eluting with ethyl acetate and light petroleum (1 : 9) to give the *title compound* as a yellowish oil (0.25 g, 67%); (Found: C, 69.3; H, 8.6; N, 3.9. $C_{20}H_{29}NO_4$ requires C, 69.1; H, 8.4; N, 4.0%); (Found: MH^+, 348.2177 $C_{20}H_{29}NO_4 + H$ requires 348.2175) □$_{max}$ (film)/cm^{-1} 3076, 2927, 2856, 1641, 1606, 1593, 1514; □$_H$ (400 MHz; $CDCl_3$) 7.93 (1 H, d, *J* 9.0, ArH), 6.52 (1 H, d, *J* 2.5, ArH), 6.48-6.45 (1 H, dd, *J* 9.0, 2.5, ArH), 5.86-5.76 (1 H, m, C$\underline{H}$=CH$_2$), 5.04-4.91 (4 H, m, CH=C$\underline{H_2}$, MeC=C$\underline{H_2}$), 4.63 (1 H, t, *J* 7.0, ArOC$\underline{H}$), 3.83 (3 H, s, Me), 2.04 (2 H, q, *J* 7.0, C$\underline{H_2}$CH=CH$_2$), 1.93-1.89 (1 H, m, ArOCHC$\underline{H}$H), 1.73 (3 H, s, Me), 1.49-1.46 (1 H, m, ArOCHCH$\underline{H}$), 1.33 (10 H, br, 5 □ CH$_2$); □$_C$ (100 MHz; $CDCl_3$) 164.1 (C), 154.2 (C), 143.4 (C), 139.2 (CH), 133.5 (C), 128.0 (CH), 114.1 (CH$_2$), 113.9 (CH$_2$), 104.8 (CH), 101.6 (CH), 83.7 (CH), 55.7 (Me), 33.8 (CH$_2$), 33.7 (CH$_2$), 29.3 (CH$_2$), 29.3 (CH$_2$), 29.0 (CH$_2$), 28.9 (CH$_2$), 25.4 (CH$_2$), 17.2 (Me); *m/z* (CI) 348 (MH^+, 4%), 317 (7), 302 (4), 198 (85), 170 (100), 152 (56), 123 (27), 109 (14).

4-Methoxy-2-(2-methyldodeca-1,11-dien-3-yloxy)aniline 10b

To 3-(5-methoxy-2-nitrophenoxy)-2-methyldodeca-1,11-diene **9b** (0.797 g, 2.30 mmol) in methanol (23 mL) was added tin powder (1.36 g) and hydrochloric acid (3 M; 15 mL). The solution was stirred at room temperature for 2 h, then decanted from the excess tin powder, basified with NaOH (2 M) and then filtered through a short pad of Celite, washed through with ethyl acetate (2 □ 20 mL). The mixture was extracted with ethyl acetate (3 □ 20 mL), the organic extracts combined and washed with water (3 × 30 mL), brine (30 mL), dried ($MgSO_4$), filtered and evaporated *in vacuo* to give the crude *title compound* as a red oil (1.152 g, 79%); (Found: MH^+, 318.2440. $C_{20}H_{31}NO_2 + H$ requires 318.2433); ν_{max} (film)/cm^{-1} 3452, 3370, 2925, 2848, 1593, 1506; δ_H (400 MHz; $CDCl_3$) 6.65 (1 H, d, *J* 6.4, ArH), 6.46 (1 H, d, *J* 2.1, ArH), 6.34 (1 H, dd, *J* 6.4, 2.1, ArH), 5.83 (1 H, ddt, *J* 7.7, 5.0, $C\underline{H}{=}CH_2$), 4.96-4.93 (4 H, m, $MeC{=}C\underline{H}_2$, $CH{=}C\underline{H}_2$), 4.52 (1 H, t, *J* 4.9, $ArOC\underline{H}CH_2$), 3.72 (3 H, s, Me), 3.52-3.46 (2 H, br, NH_2), 2.08-2.03 (2 H. m, CH_2), 1.88-1.81 (1 H, m, $ArOCHC\underline{H}H$), 1.73-1.67 (4 H, m, Me, $ArOCHCH\underline{H}$), 1.49-1.33 (10 H, m, 5 × CH_2); δ_C (100 MHz; $CDCl_3$) 152.7 (C), 146.8 (C), 144.3 (C), 139.2 (CH), 130.2 (C), 115.3 (CH), 114.2 (CH_2), 113.0 (CH_2), 104.3 (CH), 101.8 (CH), 82.2 (CH), 55.6 (Me), 34.1 (CH_2), 33.8 (CH_2), 29.43 (CH_2), 29.4 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 25.7 (CH_2), 17.3 (Me); *m/z* (CI) 318 (MH^+, 100%), 317 (62), 249 (29).

N-[4-Methoxy-2-(2-methyldodeca-1,11-dien-3-yloxy)phenyl]pent-4-enamide 11b

To 4-methoxy-2-(2-methyldodeca-1,11-dien-3-yloxy)aniline **10b** (0.697 g, 2.20 mmol) in dichloromethane (10 mL) was added 4-pentenoic acid (0.286 g, 0.29 mL, 2.86 mmol) and DCC (0.680 g, 3.30 mmol). The reaction mixture was stirred under a nitrogen atmosphere at room temperature overnight (19 h). The mixture was diluted with dichloromethane (30 mL) then filtered through a short pad of Celite, the filtrate washed with NaOH (2 M), HCl (2 M), water (3 × 10 mL), brine (10 mL), dried ($MgSO_4$), filtered and evaporated *in vacuo*. The crude product was purified by flash chromatography on silica, eluting with ethyl acetate and light petroleum (1 : 19) to give the *title compound* as a colourless oil (0.590 g, 67%); (Found: M^+, 399.2763. $C_{25}H_{37}NO_3$ requires 399.2773); ν_{max} (film)/cm^{-1} 3421, 3078, 2925, 2848, 1696, 1639, 1614, 1600, 1527; δ_H (400 MHz; $CDCl_3$) 8.23 (1 H, d, *J* 8.6, ArH), 7.64 (1 H, s, NH), 6.47-6.42 (2 H, m, ArH), 5.93-5.75 (2 H, m, 2 × $\mathrm{C\underline{H}{=}CH_2}$), 5.15-4.91 (6 H, m, $\mathrm{MeC{=}CH_2}$, 2 × $\mathrm{CH_2CH{=}C\underline{H_2}}$), 4.53 (1 H, t, *J* 6.6, $\mathrm{ArOC\underline{H}}$), 3.74 (3 H, s, OMe), 2.48 (4 H, s, $\mathrm{COC\underline{H_2}C\underline{H_2}}$), 2.04 (2 H, q, *J* 6.7, $\mathrm{CH_2}$), 1.87-1.80 (1 H, m, $\mathrm{ArOCHC\underline{H}H}$), 1.75-1.70 (4 H, m, Me, $\mathrm{ArOCHCH\underline{H}}$), 1.45-1.30 (10 H, m, 5 × $\mathrm{CH_2}$); δ_C (100 MHz; $\mathrm{CDCl_3}$) 169.8 (C), 155.9 (C), 147.7 (C), 143.5 (C), 139.1 (CH), 136.8 (CH), 121.6 (C), 120.6 (CH), 115.8 ($\mathrm{CH_2}$), 114.2 ($\mathrm{CH_2}$), 113.5 ($\mathrm{CH_2}$), 103.9 (CH), 101.1 (CH), 82.8 (CH), 55.4 (Me), 37.1 ($\mathrm{CH_2}$), 34.0 ($\mathrm{CH_2}$), 33.7 ($\mathrm{CH_2}$), 29.6 ($\mathrm{CH_2}$), 29.4 ($\mathrm{CH_2}$), 29.4 ($\mathrm{CH_2}$), 29.0 ($\mathrm{CH_2}$), 28.9 ($\mathrm{CH_2}$), 25.7 ($\mathrm{CH_2}$), 17.3 (Me); *m/z* (EI) 399 ($\mathrm{M^+}$, 17%), 381 (47), 221 (30), 216 (52), 162 (33), 139 (100).

Lactam 12b

To *N*-[4-methoxy-2-(2-methyldodeca-1,11-dien-3-yloxy)phenyl] pent-4-enamide **11b** (0.24 g, 0.60 mmol) in dichloromethane was added Grubbs' catalyst (0.15 g, 0.18 mmol, 30 mol%). The reaction mixture was heated under reflux under a nitrogen atmosphere for 19 h. The solvent was removed *in vacuo* and the crude product was purified by flash chromatography on silica, eluting with ethyl acetate and light petroleum (1 : 19) to give the *title compound* as a colourless oil (0.20 g, 90%) as a mixture of two isomers (1.5 : 1); (Found: $\mathrm{MH^+}$, 372.2553. $\mathrm{C_{23}H_{33}NO_3}$ + H requires 372.2539); ν_{max} (KBr)/$\mathrm{cm^{-1}}$ 3288, 2919, 2848, 1675, 1650, 1609, 1537, 1496; δ_H (400 MHz; $\mathrm{CDCl_3}$) *major isomer* 8.35 (1 H, d, *J* 9.0, ArH), 7.70 (1 H, br, NH), 6.48-6.45 (2 H, m, ArH), 5.56-5.37 (2 H, m, $\mathrm{C\underline{H}{=}C\underline{H}}$), 5.03-4.96 (2 H, m, $\mathrm{MeC{=}C\underline{H_2}}$), 4.47 (1 H, dd, *J* 10.1, 2.6, $\mathrm{ArOC\underline{H}}$), 3.75 (3 H, s, OMe), 2.72-2.64 (2 H, m, $\mathrm{CH_2}$), 2.61-2.41 (2 H, m, $\mathrm{CH_2}$), 2.27-2.00 (4 H, m, 2 × $\mathrm{CH_2}$), 1.93-1.79 (2 H, m, $\mathrm{CH_2}$), 1.71 (3 H, s, Me), 1.71-1.60 (2 H, m, $\mathrm{CH_2}$), 1.55-1.50 (2 H, m, $\mathrm{CH_2}$), 1.38-1.26 (4 H, m, 2 × $\mathrm{CH_2}$); *minor isomer* 8.31 (1 H, d, *J* 9.0, ArH), 7.77 (1 H, br, NH), 6.48-6.45 (2 H, m, ArH), 5.56-5.37 (2 H, m, $\mathrm{C\underline{H}{=}C\underline{H}}$), 5.03-4.96 (2 H, m, $\mathrm{MeC{=}C\underline{H_2}}$), 4.38 (1 H, dd, *J* 10.1, 2.6, ArOC$\underline{H}$), 3.75 (3 H, s, OMe), 2.72-2.64 (2 H, m, CH_2), 2.61-2.41 (2 H, m, CH_2), 2.27-2.00 (4 H, m, 2 □ CH_2), 1.93-1.79 (2 H, m, CH_2), 1.71 (3 H, s, Me), 1.71-1.60 (2 H, m, CH_2), 1.55-1.50 (2 H, m, CH_2), 1.38-1.26 (4 H, m, 2 □ CH_2); □$_C$ (100 MHz; $CDCl_3$) *both isomers* 170.1 (C), 170.0 (C), 155.9 (C), 155.8 (C), 148.0 (C), 147.9 (C), 144.9 (C), 144.7 (C), 131.7 (CH), 131.3 (CH), 129.4 (CH), 128.0 (CH), 121.8 (C), 121.7 (C), 120.1 (CH), 119.7 (CH), 111.9 (CH_2), 111.7 (CH_2), 103.9 (CH), 103.8 (CH), 101.0 (CH), 100.8 (CH), 83.4 (CH), 82.5 (CH), 55.4 (Me), 39.3 (CH_2), 39.2 (CH_2), 35.6 (CH_2), 35.0 (CH_2), 31.6 (CH_2), 28.7 (CH_2), 28.5 (CH_2), 28.3 (CH_2), 28.1 (CH_2), 28.1 (CH_2), 27.5 (CH_2), 27.4 (CH_2), 26.8 (CH_2), 25.0 (CH_2), 23.9 (CH_2), 18.0 (Me), 18.0 (Me); *m/z* (CI) 372 (MH^+, 100%), 371 (30), 370 (12), 354 (17).

Hydrogenation of lactam 12b

A solution of lactam **12b** (0.275 g, 0.74 mmol) in ethyl acetate (4 mL) was added to Pd/C (0.028 g, 10% wt) in ethyl acetate (2 mL). The reaction mixture was then stirred under an atmosphere of hydrogen at room temperature for 12 h. The mixture was filtered through a short pad of Celite, washed through with ethyl acetate (10 mL) and the solvent evaporated *in vacuo*. The crude product was purified by flash chromatography on silica, eluting with ethyl acetate and light petroleum (1 : 9) to give the *reduced lactam* **13b** as a colourless oil (0.098 g, 35%); (Found: MH^+, 376.2856. $C_{23}H_{37}NO_3$ + H requires 376.2852); □$_{max}$ (film)/cm^{-1} 3432, 2930, 2863, 1680, 1614, 1598, 1516, 1485; □$_H$ (300 MHz; $CDCl_3$) 8.35 (1 H, dd, *J* 6.3, 3.2, ArH), 7.74 (1 H, s, NH), 6.44-6.42 (2 H, m, ArH), 4.10 (1 H, q, *J* 5.3, ArOC$\underline{H}$), 3.77 (3 H, s, OMe), 2.49-2.23 (2 H, m, CH_2), 2.14-2.10 (1 H, m, C$\underline{H}$$Me_2$), 1.92-1.55 (2 H, m, CH_2), 1.62-1.55 (2 H, m, CH_2), 1.37-1.26 (16 H, m, 8 □ CH_2), 0.99 (3 H, d, *J* 6.8, CH$\underline{Me}$Me), 0.94 (3 H, d, *J* 6.8, CHMe$\underline{Me}$); □$_C$ (100 MHz; $CDCl_3$) 170.8 (C), 155.9 (C), 147.7 (C), 122.2 (C), 120.1 (CH), 103.1 (CH), 100.3 (CH), 83.5 (CH), 55.5 (Me), 37.9 (CH_2), 30.3 (CH), 29.6 (CH_2), 28.0 (CH_2), 27.3 (2 × CH_2), 26.9 (CH_2), 26.8 (CH_2), 26.5 (CH_2), 26.2 (CH_2), 25.2 (CH_2), 24.4 (CH_2), 18.8 (Me), 17.3 (Me); *m/z* (CI) 376 (MH^+, 100%), 139 (5).

Claisen rearrangement of lactam 12b to ansa-lactam 14b

Lactam **12b** (0.400g, 1.1 mmol) was dissolved in xylene (7 mL) and was heated under reflux under an argon atmosphere for 17 h. The crude product was purified by flash chromatography on silica, eluting with ethyl acetate and light petroleum (3 : 7) to give the *title compound* as a colourless, sticky oil (0.246 g, 62%) as a mixture of two isomers; (Found: M^+, 371.2446. $C_{23}H_{33}NO_3$ requires 371.2460); ν_{max} (film)/cm^{-1} 3284, 2926, 2851, 1629, 1604, 1538, 1528; δ_H (300 MHz; $CDCl_3$) *major isomer* 7.54 (1 H, d, *J* 9.0, ArH), 6.47 (1 H, d, *J* 9.0, ArH), 5.67-5.39 (2 H, m, $C\underline{H}=C\underline{H}$), 5.16-5.12 (1 H, m, $MeC=C\underline{H}$), 3.79 (3 H, s, OMe), 3.43 (2 H, s, $ArC\underline{H_2}$), 2.53-2.40 (4 H, m, $COC\underline{H_2}C\underline{H_2}$), 2.08-2.04 (2 H, m, CH_2), 1.95 (2 H, q, *J* 6.6, $CHC\underline{H_2}CH_2$), 1.66-1.57 (5 H, m, Me, CH_2), 1.35-1.19 (8 H, m, 4 × CH_2); NH/OH not observed; *minor isomer* 7.54 (1 H, d, *J* 9.0, ArH), 6.45 (1 H, d, *J* 9.0, ArH), 5.67-5.39 (2 H, m, $C\underline{H}=C\underline{H}$), 5.16-5.12 (1 H, m, $MeC=C\underline{H}$), 3.79 (3 H, s, OMe), 3.43 (2 H, s, $ArC\underline{H_2}$), 2.53-2.40 (4 H, m, $COC\underline{H_2}C\underline{H_2}$), 2.08-2.04 (2 H, m, CH_2), 1.95 (2 H, q, *J* 6.6, $CHC\underline{H_2}CH_2$), 1.66-1.57 (5 H, m, Me, CH_2), 1.35-1.19 (8 H, m, 4 × CH_2); δ_C (100 MHz; $CDCl_3$) *both isomer*s 171.9 (C), 155.7 (C), 155.5 (C), 147.8 (C), 147.7 (C,), 134.3 (C), 133.9 (C), 133.4 (CH), 133.2 (CH), 127.3 (CH), 126.9 (CH), 125.3 (CH), 125.2 (CH), 120.2 (C), 120.0 (C), 119.8 (CH), 119.7 (CH), 116.0 (C), 102.5 (CH), 56.0 (Me), 55.8 (Me), 37.4-23.4 (20 × CH_2), 16.50 (Me), 16.46 (Me); *m/z* (EI) 371 (M^+, 100%), 353 (49), 151 (13).

Oxidation of ansa-lactam 14b to ansa-quinone 16b

Ansa-lactam **14b** (0.22 g, 0.60 mmol) was dissolved in acetonitrile (15 mL) and salcomine (0.039 g, 0.12 mmol, 20 mol%) was added. Oxygen was bubbled through the solution for 15 min and then the solution was stirred under an oxygen atmosphere overnight (17 h). The mixture was concentrated *in vacuo* and ethyl acetate (15 mL) was added before filtering through a short pad of Celite, then washed through with ethyl acetate (15 mL). The solvent was evaporated *in vacuo* to leave the crude product. The crude product was purified by flash chromatography on silica, eluting with ethyl acetate and light petroleum (1 : 9) to give the *title compound* as an orange oil (0.14 g, 61%) as a mixture of two isomers; (Found: C, 71.6; H, 8.5; N, 3.5. $C_{23}H_{31}NO_4$ requires C, 71.7; H, 8.1; N, 3.6%); (Found: MH^+, 386.2312. $C_{23}H_{31}NO_4$ + H requires 386.2331); $□_{max}$ (MeCN)/nm 393 (□419) and 296 (9692); $□_{max}$ (KBr)/cm^{-1} 3288, 3100, 2918, 2848, 1701, 1659, 1632, 1603, 1503; $□_H$ (400 MHz; $CDCl_3$) *major isomer* 8.25 (1 H, s, NH), 7.43 (1 H, s, quinone-H), 5.61-5.54 (1 H, m, $MeC{=}C\underline{H}$), 5.60-5.32 (2 H, m, $C\underline{H}{=}C\underline{H}$), 4.10 (3 H, s, OMe), 3.10 (2 H, s, $C\underline{H}_2CMe{=}CH$), 2.49-2.39 (4 H, m, $COC\underline{H}_2C\underline{H}_2$), 2.05-1.99 (2 H, m, CH_2), 1.94 (2 H, q, *J* 6.7, CH_2), 1.65 (3 H, s, Me), 1.34-1.00 (10 H, m, 5 □ CH_2); *minor isomer* 8.43 (1 H, s, NH), 7.40 (1 H, s, quinone-H), 5.69-5.63 (1 H, m, $MeC{=}C\underline{H}$), 5.50-5.32 (2 H, m, $CH_2C\underline{H}{=}C\underline{H}CH_2$), 4.09 (3 H, s, OMe), 3.18 (2 H, s, $C\underline{H}_2CMe{=}CH$), 2.49-2.39 (4 H, m, $COC\underline{H}_2C\underline{H}_2\,CH{=}CH$), 2.59-2.53 (2 H, m, CH_2), 1.94 (2 H, q, *J* 6.7, CH_2), 1.61 (3 H, s, Me), 1.34-1.00 (10 H, m, 5 □ CH_2); $□_C$ (100 MHz; $CDCl_3$) *both isomers* 184.5 (C), 183.0 (C), 172.4 (C), 172.3 (C), 156.4 (C), 137.6 (C), 134.5 (CH), 133.8 (CH), 131.3 (C), 126.8 (CH), 126.4 (CH), 126.37 (CH), 126.1 (CH), 126.0 (CH), 112.90 (CH), 112.89 (CH), 61.5 (Me), 38.5 (CH_2), 38.2 (CH_2), 32.1 (CH_2), 32.0 (CH_2), 29.1 (CH_2), 29.0 (CH_2), 28.7 (CH_2), 28.65 (CH_2), 28.6 (CH_2), 28.5 (CH_2), 28.3 (CH_2), 28.2

(CH_2), 28.0 (CH_2), 27.5 (CH_2), 27.4 (CH_2), 27.2 (CH_2), 27.1 (CH_2), 23.1 (CH_2), 17.1 (Me); *m/z* (CI), 386 (MH^+, 71%), 370 (17), 257 (23), 173 (17), 141 (11), 113 (19).

References

1. R. J. Maleski, *Synth. Commun.*, 1993, **23**, 343.
2. E. Piers, G. L. Jung and E. H. Ruediger, *Can. J. Chem.*, 1987, **65**, 670.
3. H. O. House and G. H. Rasmusson, *J. Org. Chem.*, 1961, **26**, 4278.
4. X. D. Qin, T. Tzvetkov, X. Liu, D. C. Lee, L. P. Yu and D. C. Jacobs, *J. Am. Chem. Soc.*, 2004, **126**, 13232.

7,7-Dimethoxyheptanal 17

Cycloheptene (5.0 mL, 42 mmol) was dissolved in a mixture of dichloromethane (185 mL) and methanol (37 mL) in a 3-necked flask and the solution was cooled to -78 °C. Ozone was then bubbled through the solution until a persistent blue colour was observed. The reaction was then purged of excess ozone by bubbling nitrogen through the solution. 4-Toluenesulfonic acid (0.40 g, 2.1 mmol, 5 mol%) was added and the reaction was stirred for 1 h while gently warming to room temperature. Solid sodium hydrogen carbonate (1.40 g, 6.8 mmol) was added and the mixture was stirred for 30 min. Dimethyl sulfide (7.70 mL, 105 mmol) was then added and the reaction was stirred at room temperature for 3.75 h before being transferred to a round bottomed flask where the solvent was evaporated. Flash chromatography using ether and light petroleum (1 : 3) containing triethylamine (0.5% v/v) gave the title compound as a clear oil (6.8 g, 93%); (lit.,[87] bp 78-80 °C at high vacuum); ν_{max} ($CHCl_3$)/cm^{-1} 2947, 1709, 1206, 1127, 1051; δ_H (300 MHz; $CDCl_3$) 9.72 (1 H, dt, *J* 2.1, 1.7, $CH_2C\underline{H}O$), 4.31 (1 H, dd, *J* 5.8, 5.7, $(MeO)_2C\underline{H}$), 3.27 (6 H, s, OMe), 2.40 (1 H, td, *J* 7.0, 1.7, $C\underline{H_2}CHO$), 2.38 (1 H, ddd, *J* 7.4, 7.2, 1.7, $C\underline{H_2}CHO$), 1.64-1.52 (4 H, m, 2 × CH_2), 1.38-1.30 (4 H, m, 2 × CH_2); δ_C (75 MHz; $CDCl_3$) 203.1 (CH), 104.8 (CH), 53.0 (Me), 44.0 (CH_2), 32.7 (CH_2), 29.3 (CH_2), 24.8 (CH_2), 22.3 (CH_2).

10,10-Dimethoxydecen-4-ol 18

To a solution of 7,7-dimethoxyheptanal **17** (7.44 g, 42.8 mmol) in anhydrous THF (111 mL) at between -10 °C and 0 °C was slowly added allylmagnesium chloride (2 M in THF; 27.8 mL, 55.6 mmol) over 15-20 min under a nitrogen atmosphere. The reaction mixture was stirred at 0 °C for 2.5 h before being quenched by the addition of water (150 mL). The aqueous layer was extracted with ethyl acetate (3 × 125 mL), the organic layers combined, washed with water (2 × 100 mL), brine (100 mL), dried ($MgSO_4$), filtered and evaporated *in* *vacuo*. The crude product was purified by flash chromatography on silica, eluting with ethyl acetate and light petroleum (1 : 4) to give the *title compound* as a colourless oil (5.94 g, 64%); (Found: C, 66.5; H, 11.6. $C_{12}H_{24}O_3$ requires C, 66.6; H, 11.2%); (Found: M^+, 216.1721. $C_{12}H_{24}O_3$ requires 216.1725); ν_{max} (film)/cm^{-1} 3447, 2940, 2858, 1639; δ_H (300 MHz; $CDCl_3$) 5.87-5.73 (1 H, m, $C\underline{H}=CH_2$), 5.13-5.07 (2 H, m, $CH=C\underline{H}_2$), 4.33 (1 H, t, *J* 5.7, $(MeO)_2C\underline{H}$), 3.65-3.57 (1 H, m, $C\underline{H}OH$), 3.28 (6 H, s, OMe), 2.30-2.06 (2 H, m, $C\underline{H}_2CH=CH_2$), 1.82 (1 H, br, OH), 1.60-1.54 (2 H, m, CH_2), 1.44-1.32 (8 H, m, 4 × CH_2); δ_C (75 MHz; $CDCl_3$) 135.2 (CH), 118.5 (CH_2), 104.8 (CH), 70.9 (CH), 53.0 (Me), 42.3 (CH_2), 37.0 (CH_2), 32.8 (CH_2), 29.8 (CH_2), 25.9 (CH_2), 24.9 (CH_2); *m/z* (EI) 216 (M^+, 4%), 185 (29), 153 (23), 143 (80), 125 (65), 111 (95), 97 (55), 93 (94), 83 (75), 75 (100).

4-(*tert*-Butyldiphenylsiloxy)-10,10-dimethoxydecene 19a

To a solution of 10,10-dimethoxydecen-4-ol **18** (0.200 g, 0.92 mmol) in anhydrous DMF (3 mL) was added imidazole (0.157 g, 2.30 mmol) and *tert*-butyldiphenylchlorosilane (0.24 mL, 0.25 g, 0.92 mmol). The reaction mixture was stirred at room temperature for 24 h, diluted with ethyl acetate (15 mL), washed with water (6 × 10 mL), brine (10 mL), dried ($MgSO_4$), filtered and evaporated *in vacuo*. The crude product was purified by flash chromatography on silica, eluting with ethyl acetate and light petroleum (1 : 19) to give the *title compound* as a colourless oil (0.360 g, 86%); (Found: MH^+, 455.2962. $C_{28}H_{42}O_3Si$ + H requires 455.2981); ν_{max} (film)/cm^{-1} 3068, 2930, 2858, 1653, 1639, 1589, 1106; δ_H (300 MHz; $CDCl_3$) 7.71-7.68 (4 H, m, ArH), 7.44-7.35 (6 H, m, ArH), 5.74 (1 H, ddt, *J* 17.3, 10.2, 7.2, $C\underline{H}=CH_2$), 5.00-4.91 (2 H, m, $CH=C\underline{H}_2$), 4.34 (1 H, t, *J* 5.7, $(MeO)_2C\underline{H}$), 3.77 (1 H, quintet, *J* 5.5, $C\underline{H}OTBDPS$), 3.32 (6 H, s, OMe), 2.24-2.17 (2 H, m, $C\underline{H}_2CH=CH_2$), 1.57-1.40 (4 H, m, 2 × CH_2), 1.30-1.13 (6 H, m, 3 × CH_2), 1.08 (9 H, *t*-Bu); δ_C (75 MHz; $CDCl_3$) 136.4 (CH), 135.4 (CH), 134.9 (C), 129.9 (CH), 127.8 (CH), 117.1 (CH_2), 104.9 (CH), 73.1 (CH), 52.9

(Me), 41.4 (CH_2), 36.3 (CH_2), 32.8 (CH_2), 29.9 (CH_2), 27.5 (Me), 25.1 (CH_2), 24.9 (CH_2), 19.8 (C); *m/z* (CI) 455 (MH^+, 14%), 423 (100), 381 (94), 365 (31), 345 (12), 167 (48), 135 (83).

9-(*tert*-Butyldiphenylsiloxy)-2-methyldodeca-1,11-dien-3-ol 20a

(a) To a solution of 4-(*tert*-butyldiphenylsiloxy)-10,10-dimethoxydecene **19a** (0.100 g, 0.22 mmol) in chloroform (0.6 mL) was added 50% aqueous trifluoroacetic acid (0.6 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 2 h. The mixture was diluted with ethyl acetate (15 mL), washed with water (3 × 15 mL), brine (15 mL), dried ($MgSO_4$), filtered and evaporated *in vacuo* to give 7-(*tert*-butyldiphenylsiloxy)dec-9-enal as a colourless oil (0.078 g, 87%) used without purification; ν_{max} (film)/cm^{-1} 3072, 2929, 2853, 1725, 1653, 1558, 1109; δ_H (300 MHz; $CDCl_3$) 9.61 (1 H, t, *J* 1.8, $CH_2C\underline{H}O$), 7.63-7.56 (4 H, m, ArH), 7.32-7.16 (6 H, m, ArH), 5.71-5.57 (1 H, m, $C\underline{H}=CH_2$), 4.89-4.79 (2 H, m, $CH=C\underline{H}_2$), 3.65 (1 H, quintet, *J* 5.5, $C\underline{H}OTBDPS$), 2.22 (2 H, td, *J* 7.4, 1.8, $C\underline{H}_2CH_2CHO$), 2.13-2.06 (2 H, m, CH_2), 1.47-1.45 (2 H, m, CH_2), 1.43-1.38 (2 H, m, CH_2), 1.19-1.00 (4 H, m, 2 × CH_2), 0.96 (9 H, s, *t*-Bu).

(b) To a solution of 7-(*tert*-butyldiphenylsiloxy)dec-9-enal (20.78 g, 50.9 mmol) in anhydrous THF (100 mL) at between -10 °C to 0 °C was added isopropenylmagnesium bromide (0.5 M in THF; 122.2 mL, 61.1 mmol) slowly over 10-20 min. The reaction mixture was stirred at 0 °C for 2.5 h then quenched by the addition of saturated ammonium chloride solution (100 mL). The mixture was extracted with ethyl acetate (3 × 100 mL), the organic layers combined, washed with water (3 × 100 mL), brine (100 mL), dried ($MgSO_4$), filtered and evaporated *in vacuo*. The crude product was purified by flash chromatography on silica, eluting with ethyl acetate and light petroleum (1 : 9) to give the *title compound* as a colourless oil (11.47 g, 50%) as a mixture of diastereoisomers; (Found: MH^+, 451.2993.

$C_{29}H_{42}O_2Si$ + H requires 451.3032); ν_{max} (film)/cm^{-1} 3396, 3073, 3048, 2930, 2848, 2884, 1653, 1641, 1588, 1106; δ_H (300 MHz; $CDCl_3$) *mixture of diastereoisomers* 7.75-7.69 (4 H, m, ArH), 7.44-7.38 (6 H, m, ArH), 5.75-5.71 (1 H, m, $CH_2C\underline{H}{=}CH_2$), 5.00-4.84 (4 H, m, $CH{=}C\underline{H}_2$, $MeC{=}C\underline{H}_2$), 4.02 (1 H, t, *J* 4.9, $C\underline{H}OH$), 3.77 (1 H, quintet, *J* 4.2, $C\underline{H}OTBDPS$), 2.28-2.14 (2 H, m, CH_2), 1.72 (3 H, s, Me), 1.49-1.15 (10 H, m, 5 × CH_2), 1.08-1.06 (9 H, s, *t*-Bu); OH not observed; δ_C (75 MHz; $CDCl_3$) *both diastereoisomers* 147.6 (C), 136.0 (CH), 135.9 (CH), 135.2 (C), 135.1 (CH), 134.8 (CH), 134.6 (CH), 129.7 (CH), 129.5 (CH), 127.7 (CH), 127.5 (CH), 116.7 (CH_2), 111.0 (CH_2), 76.0 (CH), 72.8 (CH), 41.0 (CH_2), 35.9 (CH_2), 34.8 (CH_2), 29.5 (CH_2), 27.1 (Me), 26.6 (Me), 25.5 (CH_2), 24.7 (CH_2), 19.4 (C), 19.0 (C), 17.5 (Me); *m/z* (EI) 451 (M^+, 3%), 449 (5), 433 (49), 392 (27), 375 (100).

9-*tert*-Butyldiphenylsiloxy-3-(5-methoxy-2-nitrophenoxy)-2-methyldodeca-1,11-diene 21a

To a solution of 5-methoxy-2-nitrophenol[108] (1.88 g, 11.10 mmol), 9-(*tert*-butyldiphenylsiloxy)-2-methyldodeca-1,11-dien-3-ol (5.00 g, 11.10 mmol) and triphenylphosphine (4.37 g, 16.65 mmol) in anhydrous toluene (35 mL) at 0 °C was slowly added diisopropyl azodicarboxylate (DIAD) (3.28 mL, 3.37 g, 16.65 mmol). The reaction mixture was stirred at room temperature for 24 h. The mixture was concentrated to half the original volume by evaporating *in vacuo*, light petroleum was added to precipitate triphenylphosphine oxide. The precipitate was removed by filtration and washed with light petroleum (3 × 10 mL). The filtrate was then concentrated *in vacuo* and dissolved in ethyl acetate (50 mL), washed with NaOH (2 M; 3 × 30 mL), water (3 × 30 mL), brine (30 mL), dried ($MgSO_4$), filtered and evaporated *in vacuo*. The crude product was purified by flash chromatography on silica, eluting with ethyl acetate and light petroleum (1 : 9) to give the *title compound* as a yellow/orange oil (3.52 g, 55%) as a mixture of diastereoisomers;

(Found: MH$^+$, 602.3287. $C_{36}H_{47}NO_5Si$ + H requires 602.3302.); ν_{max} (film)/cm^{-1} 3073, 2930, 2853, 1607, 1589, 1513, 1033; δ_H (300 MHz; $CDCl_3$) *mixture of diastereoisomers* 7.95 (1 H, d, *J* 9.1, ArH), 7.70 (2 H, d, *J* 1.6, ArH), 7.67 (2 H, d, *J* 1.6, ArH), 7.43-7.35 (6 H, m, ArH), 6.51 (1 H, d, *J* 2.5, ArH), 6.47 (1 H, dd, *J* 9.1, 2.5, ArH), 5.66 (1 H, ddt, *J* 17.1, 10.2, 7.2, $C\underline{H}=CH_2$), 5.03-4.91 (4 H, m, $MeC=C\underline{H}_2$, $CH=C\underline{H}_2$), 4.58 (1 H, t, *J* 6.4, $ArOC\underline{H}$), 3.84 (3 H, s, OMe), 3.76 (1 H, quintet, *J* 5.5, $C\underline{H}OTBDPS$), 2.28-2.12 (2 H, m, CH_2), 1.90-1.78 (1 H, m, CH_2), 1.72 (3 H, s, Me), 1.68-1.60 (1 H, m, CH_2), 1.48-1.38 (2 H, m, CH_2), 1.30-1.14 (6 H, m, $3 \times CH_2$), 0.97 (9 H, s, *t*-Bu); δ_C (75 MHz; $CDCl_3$) *both diastereoisomers* 164.5 (C), 154.5 (C), 143.8 (C), 136.3 (CH), 135.4 (CH), 134.9 (C), 133.9 (C), 129.8 (CH), 128.4 (CH), 127.8 (CH), 117.1 (CH_2), 114.2 (CH_2), 105.1 (CH), 102.0 (CH), 84.0 (CH), 73.1 (CH), 56.1 (Me), 41.4 (CH_2), 36.3 (CH_2), 34.0 (CH_2), 29.6 (CH_2), 27.4 (Me), 25.7 (CH_2), 22.5 (CH_2), 19.8 (Me), 17.5 (C); *m/z* (CI) 602 (MH$^+$, 5%), 544 (100), 433 (57), 391 (66), 375 (66), 355 (27), 350 (60), 346 (60), 333 (19), 309 (29), 199 (47), 177 (33).

2-(9-*tert*-Butyldiphenylsiloxy-2-methyldodeca-1,11-dien-3-yloxy)-4-methoxyaniline 22a

9-*tert*-Butyldiphenylsiloxy-3-(5-methoxy-2-nitrophenoxy)-2-methyldodeca-1,11-diene **21a** (0.43 g, 0.72 mmol) was dissolved in THF (15 mL) and glacial acetic acid (0.23 mL, 3.58 mmol). Indium powder (0.822 g, 7.16 mmol) was added and the mixture heated under reflux for 17 h. The mixture was cooled to room temperature before being diluted with ethyl acetate (40 mL) and filtered through a pad of Celite. The filtrate was washed with water (3 × 20 mL), brine (20 mL), dried ($MgSO_4$), and evaporated *in vacuo* to give the crude *title compound* as an oil (0.31 g, 76%) as a mixture of diastereoisomers; (Found: MH$^+$, 572.3552. $C_{36}H_{49}NO_3Si$ + H requires 572.3560.); ν_{max} (film)/cm^{-1} 3457, 3370, 3083, 2925, 2858, 1593, 1506, 1465, 1040; δ_H (300 MHz; $CDCl_3$) 7.73 (4 H, d, *J* 7.0, ArH), 7.46-7.37 (6 H, m, ArH), 6.69 (1 H, dd, *J* 8.5, 1.3, ArH), 6.48 (1 H, d, *J* 2.5, ArH), 6.37 (1 H, dd, *J* 8.5, 2.5, ArH), 5.79 (1 H, ddt, *J* 16.3, 10.2, 7.3, CH=CH$_2$), 5.02-4.94 (4 H, m, MeC=CH$_2$, CH=CH$_2$), 4.50 (1 H, t, *J* 6.6, ArOCH), 3.80 (1 H, quintet, *J* 5.6, CHOTBDPS), 3.75 (3 H, s, OMe), 3.41 (2 H, br, NH$_2$), 2.33-2.21 (2 H, m, CH$_2$), 1.79-1.59 (5 H, m, CH$_2$, Me), 1.49-1.18 (8 H, m, 4 × CH$_2$), 1.11 (9 H, s, *t*-Bu); δ_C (75 MHz; CDCl$_3$) 153.2 (C), 147.2 (C), 144.6 (C), 136.4 (CH), 135.9 (CH), 134.9 (C), 130.5 (C), 129.9 (CH), 127.9 (CH), 117.2 (CH$_2$), 115.7 (CH), 113.4 (CH$_2$), 104.7 (CH), 102.2 (CH), 82.5 (CH), 73.2 (CH), 56.0 (Me), 41.5 (CH$_2$), 36.3 (CH$_2$), 34.4 (CH$_2$), 29.8 (CH$_2$), 27.5 (Me), 26.0 (CH$_2$), 25.1 (CH$_2$), 19.8 (Me), 17.7 (C); *m/z* (CI) 572 (MH$^+$, 9%), 494 (5), 377 (11), 323 (13), 301 (28), 267 (12), 259 (18), 239 (27), 231 (16), 199 (27), 179 (27), 140 (100).

***N*-[2-(9-*tert*-Butyldiphenylsiloxy-2-methyldodeca-1,11-dien-3-yloxy)-4-methoxyphenyl]-2-methylpenta-2,4-dienamide 23a**

2-(9-*tert*-Butyldiphenylsiloxy-2-methyldodeca-1,11-dien-3-yloxy)-4-methoxyaniline **22a** (2.84 g, 4.98 mmol) was dissolved in anhydrous dichloromethane (20 mL) and triethylamine (1.05 mL, 0.76 g, 7.47 mmol). The mixture was cooled on an ice bath before (*E*)-2-methylpenta-2,4-dienoyl chloride (0.65 g, 4.98 mmol) was added. The mixture was allowed to warm to room temperature and stirred for 3 days. The mixture was partitioned between water (30 mL) and dichloromethane (30 mL). The aqueous phase was extracted further with dichloromethane (2 × 30 mL), combined and washed with brine (30 mL), dried (MgSO$_4$), filtered and evaporated *in vacuo*. The crude product was purified by flash chromatography on silica, eluting with ethyl acetate and light petroleum (1 : 9) to give the *title compound* as a colourless, sticky oil (2.19 g, 66%) as a mixture of diastereoisomers; (Found: MH$^+$, 666.3970. $C_{42}H_{55}NO_4Si$ + H requires 666.3979.); ν_{max} (film)/cm^{-1} 3432, 3073, 2945, 2858, 1670, 1617, 1600, 1531, 1490; δ_H (400 MHz; CDCl$_3$) *mixture of diastereomers* 8.38 (1 H, dd, *J* 9.2, 1.2, ArH), 8.19 (1 H, s, NH), 7.69-7.67 (4 H, m, ArH), 7.43-7.35 (6 H, m, ArH), 7.05

(1 H, d, *J* 11.1, CMe=C$\underline{H}$CH=CH$_2$), 6.73-6.63 (1 H, m, CMe=CHC$\underline{H}$=CH$_2$), 6.51-6.49 (2 H, m, ArH), 5.74 (1 H, ddt, *J* 17.0, 10.1, 7.2, CH$_2$C$\underline{H}$=CH$_2$), 5.54 (1 H, d, *J* 17.0, CHCH=C$\underline{H_2}$), 5.43 (1 H, d, *J* 10.1, CHCH=C$\underline{H_2}$), 5.00-4.91 (4 H, m, CH$_2$CH=C$\underline{H_2}$, MeC=C$\underline{H_2}$), 4.54 (1 H, t, *J* 6.3, ArOC$\underline{H}$), 3.78 (3 H, s, OMe), 3.77-3.74 (1 H, m, C$\underline{H}$OTBDPS), 2.25-2.13 (2 H, m, CH$_2$), 2.08 (3 H, s, Me), 1.80-1.74 (1 H, m, CH$_2$), 1.71 (3 H, s, Me), 1.68-1.62 (1 H, m, CH$_2$), 1.44-1.15 (8 H, m, 4 × CH$_2$), 1.06 (9 H, br, *t*-Bu); δ_C (100 MHz; CDCl$_3$) *mixture of diastereomers* 166.0 (C), 156.0 (C), 147.7 (C), 143.3 (C), 136.0 (CH), 135.9 (CH), 135.0 (CH), 134.5 (CH), 132.1 (CH), 131.3 (CH), 131.28 (C), 129.28 (C), 129.5 (CH), 127.5 (CH), 123.2 (CH$_2$), 121.9 (C), 120.2 (CH), 116.8 (CH$_2$), 113.6 (CH$_2$), 103.9 (CH), 101.0 (CH), 82.62 (CH$_2$), 82.60 (CH), 72.7 (CH), 55.5 (Me), 41.1 (CH$_2$), 35.9 (CH$_2$), 33.9 (CH$_2$), 29.5 (CH$_2$), 27.1 (Me), 25.54 (CH$_2$), 25.51 (CH$_2$), 24.7 (CH$_2$), 19.4 (C), 17.3 (Me), 13.0 (Me); *m/z* (CI) 666 (MH$^+$, 1%), 626 (16), 600 (8), 572 (51), 540 (100), 520 (82), 494 (19), 470 (17), 416 (27), 370 (45), 342 (90), 316 (62), 300 (38), 260 (25), 246 (27), 206 (43), 194 (47), 178 (69), 166 (40).

(*S*)-10,10-Dimethoxydecen-4-ol (*S*)-18

A solution of (+)-DIPCl™ (8.7 g, 27 mmol) in THF (160 mL) was cooled to -78 °C. Allylmagnesium bromide (1.0 M in ether; 25 mL, 25 mmol) was added in a dropwise manner and the mixture was stirred for 30 min, then warmed to room temperature and stirred for a further 1 h. After being re-cooled to -78 °C a solution of 7,7-dimethoxyheptanal **17** (3.2 g, 18 mmol) in THF (20 mL) was added very slowly in order to minimize temperature disruption. The reaction was allowed to proceed at -78 °C for 4 h before being warmed to room temperature, at which time a premixed solution of H_2O_2 (30%; 10 mL, 5eq.) and NaOH (2 M; 45 mL, 5 eq.) was added. After stirring overnight the layers were separated and the aqueous phase was extracted with ethyl acetate (3 × 50 mL) before the combined organics were washed with saturated brine (25 mL), dried (Na_2SO_4) and the solvent was removed. Flash chromatography using ether and light petroleum (1 : 4) followed by ether and light petroleum (1 : 1) gave the *title compound* as a clear oil (3.25 g, 82%); $[\alpha]_D^{32}$- 6.03 (*c* 1.16, $CHCl_3$); spectroscopic data as for racemate.

4-Benzoyloxy-10,10-dimethoxydec-1-ene

Potassium hydride (30% w/w in mineral oils; 0.19 g, 1.5 mmol) was twice washed with THF (2 mL) and then suspended in THF (2 mL). A solution of the racemic 10,10-dimethoxydecen-4-ol **18** (80 mg, 0.37 mmol) was added and the reaction was stirred for 30 min. Then benzoyl chloride (51 μL, 0.44 mmol) was added and the solution was stirred for 4 h before being quenched by the careful addition of water (10 mL). The mixture was extracted with ether (3 × 10 mL) before the combined organics were dried (Na_2SO_4) and the solvent was removed. Flash chromatography using ether and light petroleum (1 : 9) gave the racemic ester as a clear oil (83 mg, 70%); ν_{max} ($CHCl_3$)/cm^{-1} 2938, 2861, 1697, 1317, 1287, 1116, 1070; δ_H (300 MHz; $CDCl_3$) 7.96 (2 H, d, *J* 7.5, ArH), 7.48 (1 H, d, *J* 7.4, ArH), 7.36 (2 H, dd, *J* 7.5, 7.4, ArH), 5.79-5.70 (1 H, m, $C\underline{H}=CH_2$), 5.12-4.96 (3 H, m, $CH=C\underline{H}_2$, $C\underline{H}OBz$), 4.26 (1 H, t, *J* 5.8, $(MeO)_2C\underline{H}$), 3.22 (6 H, s, OMe), 2.37 (2 H, dd, *J* 7.0, 6.0, $C\underline{H}_2CH=CH_2$), 1.68-1.18 (10 H, m, 5 × CH_2); δ_C (75 MHz; $CDCl_3$) 166.6 (C), 134.0 (CH), 133.1 (CH), 131.0 (C), 129.9 (CH), 128.7 (CH), 118.2 (CH_2), 104.8 (CH), 74.3 (CH), 53.0 (Me), 39.1 (CH_2), 33.9 (CH_2), 32.7 (CH_2), 29.7 (CH_2), 25.6 (CH_2), 24.8 (CH_2); HPLC analysis Chiralpak OD, 0.2% IPA in hexane, 1.2 mL min^{-1}, R_t 11.43 and 15.37 min, ratio 1 : 1.

(*S*)-4-Benzoyloxy-10,10-dimethoxydec-1-ene

A solution of (*S*)-10,10-dimethoxydecen-4-ol **(*S*)-18** (50 mg, 0.23 mmol) was dissolved in THF (1 mL) and cooled to 0 °C. LHMDS (1 M in THF; 460 µL, 0.46 mmol) was added and the mixture was allowed to stir for 0.5 h before benzoyl chloride (80 µL, 0.69 mmol) was added. After a further 2 h at room temperature, the reaction was quenched by the addition of water (10 mL), and the mixture was extracted with ether (3 × 10 mL) before the combined organics were dried (Na_2SO_4) and the solvent was evaporated. Flash chromatography using ether and light petroleum (1 : 9) gave the ester as a colourless solid (61 mg, 83%); mp 66-70 °C; $[\alpha]_D^{32}$ - 10.7 (*c* 0.99, $CHCl_3$); (Found: M+Na$^+$, 343.1881. $C_{19}H_{28}O_4$ + Na requires 343.1885); ν_{max} ($CHCl_3$)/cm^{-1} 2938, 2861, 1697, 1317, 1287, 1116, 1070; δ_H (300 MHz; $CDCl_3$) 7.96 (2 H, d, *J* 7.5, ArH), 7.48 (1 H, d, *J* 7.4, ArH), 7.36 (2 H, dd, *J* 7.5, 7.4, ArH), 5.79-5.70 (1 H, m, C$\underline{H}$=CH_2), 5.12-4.96 (3 H, m, CH=C$\underline{H}_2$, C$\underline{H}$OBz), 4.26 (1 H, t, *J* 5.8, $(MeO)_2$C$\underline{H}$), 3.22 (6 H, s, OMe), 2.37 (2 H, dd, *J* 7.0, 6.0, C$\underline{H}_2$CH=CH_2), 1.68-1.18 (10 H, m, 5 × CH_2); δ_C (75 MHz; $CDCl_3$) 166.6 (C), 134.0 (CH), 133.1 (CH), 131.0 (C), 129.9 (CH), 128.7 (CH), 118.2 (CH_2), 104.8 (CH), 74.3 (CH), 53.0 (Me), 39.1 (CH_2), 33.9 (CH_2), 32.7 (CH_2), 29.7 (CH_2), 25.6 (CH_2), 24.8 (CH_2); HPLC analysis Chiralpak OD, 0.2% IPA in hexane, 1.2 mL min^{-1}, R_t 11.99 and 15.75 min, ratio 28.52 : 1.

(*S*)-4-(*tert*-Butyldimethylsiloxy)-10,10-dimethoxydec-1-ene (*S*)-19b

(*S*)-10,10-Dimethoxydecen-4-ol **(*S*)-18** (3.00 g, 13.8 mmol) was dissolved in DMF (10 mL) and then imidazole (2.80 g, 41.0 mmol), and *tert*-butyldimethylchlorosilane (3.10 g, 21.0 mmol) were sequentially added. The mixture was stirred overnight at room temperature, the solvent evaporated and the residue subjected to flash chromatography using ether and light petroleum (1 : 9). The *title compound* was collected as a clear oil (3.60 g, 79%); $[\alpha]_D^{32}$ - 14.7 (*c* 1.36, $CHCl_3$); (Found: M+Na$^+$, 353.2503. $C_{18}H_{38}O_3Si$ + Na requires 353.2488); ν_{max} ($CHCl_3$)/cm^{-1} 2931, 2857, 1471, 1463, 1125, 1050; δ_H (300 MHz; $CDCl_3$) 5.79-5.75 (1 H, m, C<u>H</u>=CH$_2$), 4.99 (1 H, d, *J* 18.0, CH=CH<u>H</u>), 4.97 (1 H, d, *J* 9.0, CH=C<u>H</u>H), 4.32 (1 H, t, *J* 6.0, (MeO)$_2$C<u>H</u>), 3.66-3.60 (1 H, m, C<u>H</u>OTBS), 3.27 (6 H, s, OMe), 2.16 (2 H, t, 6.0, C<u>H</u>$_2$CH=CH$_2$), 1.59-1.51 (2 H, m, CH$_2$), 1.39-1.28 (8 H, m, 4 × CH$_2$), 0.89 (9 H, s, *t*-Bu), 0.00 (6 H, s, Me); δ_C (75 MHz; CDCl$_3$) 135.8 (CH), 116.9 (CH$_2$), 104.9 (CH), 72.3 (CH), 53.0 (Me), 42.3 (CH$_2$), 37.1 (CH$_2$), 32.8 (CH$_2$), 30.1 (CH$_2$), 26.3 (Me), 25.2 (CH$_2$), 25.0 (CH$_2$), 18.5 (C), -4.0 (Me); *m/z* (EI) 299 (M^+-OMe, 38%), 257 (51), 225 (28), 185 (32), 135 (59), 125 (32), 115 (31), 107 (100), 99 (55), 93 (70), 81 (49).

(3*R*,9*S*)- and (3*S*,9*S*)-9-*tert*-Butyldimethylsiloxydodeca-1,11-dien-3-ol 20b

(a) (*S*)-4-(*tert*-Butyldimethylsiloxy)-10,10-dimethoxydec-1-ene **19b** (900 mg, 2.72 mmol) was dissolved in acetone (27 mL) and 4-toluenesulfonic acid (25 mg, 0.13 mmol) was added and the reaction was stirred for 4 h. The reaction was then neutralized by the addition of solid NaHCO$_3$ (~ 3 g) to the vigorously stirred solution. After 10 min, the mixture was filtered and the solvent was removed to leave crude (*S*)-7-*tert*-butyldimethylsiloxydec-9-enal (750 mg, 97%), which was immediately utilized in the next reaction.

(b) The above crude aldehyde (700 mg, 2.46 mmol) was dissolved in THF (25 mL) and the solution was cooled to 0 °C. Vinylmagnesium chloride (1.6 M in THF; 3.1 mL, 5 mmol) was added dropwise and the mixture was left to stir overnight. Saturated ammonium chloride (20 mL) was then added and the mixture was extracted with ether (3 × 25 mL). The combined organics were washed with saturated brine (10 mL), dried (Na$_2$SO$_4$) and the solvent was evaporated. Flash chromatography using ether and light petroleum (1 : 9) gave the *title compound* as a clear oil (570 mg, 74%); $[\alpha]_D^{32}$- 135 (*c* 0.960, CHCl$_3$); (Found: M+Na$^+$, 335.2400. $C_{18}H_{36}O_2Si$ + Na requires 335.2382); ν_{max} (CHCl$_3$)/cm^{-1} 2932, 2857, 1471, 1255, 1057; δ_H (300 MHz; CDCl$_3$) 5.83-5.77 (2 H, m, 2 × C<u>H</u>=CH$_2$), 5.18 (1 H, d, *J* 18.0, CH=CH<u>H</u>), 5.07 (1 H, d, *J* 12.0, CH=C<u>H</u>H), 4.99 (1 H, d, *J* 15.0, CH=CH<u>H</u>), 4.98 (1 H, d, *J*

12.0, CH=C$\underline{H}$H), 4.09-4.02 (1 H, m, C$\underline{H}$OH), 3.66-3.60 (1 H, m, C$\underline{H}$OTBS), 2.16 (1 H, t, *J* 6.0, C$\underline{H}_2$CH=CH$_2$), 1.51-1.22 (12 H, m, 6 × CH$_2$), 0.85 (9 H, s, *t*-Bu), 0.00 (6 H, s, Me); δ_C (75 MHz; CDCl$_3$) 141.6 (CH), 135.8 (CH), 117.0 (CH$_2$), 115.0 (CH$_2$), 73.6 (CH), 72.3 (CH), 42.3 (CH$_2$), 37.8 (CH$_2$), 37.1 (CH$_2$), 30.1 (CH$_2$), 26.3 (Me), 25.74 (CH$_2$), 25.70 (CH$_2$), 18.5 (C), -4.0 (Me); *m/z* (EI) 271 (30%), 253 (49), 185 (39), 145 (56), 121 (62), 95 (80), 75 (100).

(3*R*,9*S*)- and (3*S*,9*S*)-3-(5-Methoxy-2-nitrophenoxy)-9-(*tert*-butyldimethylsiloxy)dodeca-1,11-diene 21b

(3*R*,9*S*)- and (3*S*,9*S*)-9-*tert*-Butyldimethylsiloxydodeca-1,11-dien-3-ol **20b** (510 mg, 1.63 mmol) was dissolved in toluene (16 mL). Triphenylphosphine (0.65 g, 2.5 mmol) and 5-methoxy-2-nitrophenol (0.42 g, 2.5 mmol) were added and the mixture was cooled to 0 °C. DEAD (390 µl, 2.50 mmol) was added dropwise and then the reaction mixture was allowed to stir at room temperature overnight. The mixture was extracted with NaOH (2 M; 2 × 30 mL) that was subsequently extracted with ether (3 × 25 mL). The combined organics were dried (Na$_2$SO$_4$) and the solvent was evaporated. Flash chromatography using ether and light petroleum (1 : 39) gave the *title compound* as a yellow oil (563 mg, 75%); $[\alpha]_D^{32}$ - 5.7 (*c* 0.81, CHCl$_3$); (Found: M+Na$^+$, 486.2634. C$_{25}$H$_{41}$NO$_5$Si + Na requires 486.2652); ν_{max} (CHCl$_3$)/cm^{-1} 2930, 1608, 1592, 1582, 1349, 1291, 1097; δ_H (300 MHz; CDCl$_3$) 7.90 (1 H, d, *J* 6.0, ArH), 6.48 (1 H, d, *J* 1.0, ArH), 6.43 (1 H, dd, *J* 6.0, 1.0, ArH), 5.83-5.72 (2 H, m, 2 × C$\underline{H}$=CH$_2$), 5.29-5.21 (2 H, m, CH=C$\underline{H}_2$), 4.99 (1 H, d, *J* 15.0, ArOCHCH=CH$\underline{H}$), 4.97 (1 H, d, *J* 9.0, ArOCHCH=C$\underline{H}$H), 4.64 (1 H, q, *J* 6.0, ArOC$\underline{H}$), 3.80 (3 H, s, OMe), 3.66-3.60 (1 H, m, C$\underline{H}$OTBS), 2.18-2.14 (2 H, m, CH$_2$), 1.90-1.60 (2 H, m, CH$_2$), 1.43-1.21 (8 H, m, 4 × CH$_2$), 0.84 (9 H, s, *t*-Bu), 0.00 (6 H, s, Me); δ_C (75 MHz; CDCl$_3$)164.5 (C), 154.6 (C), 137.3 (CH), 135.8 (CH), 134.1 (C), 128.4 (CH), 117.8 (CH$_2$), 117.0 (CH$_2$), 105.3 (CH), 102.7 (CH), 81.6

(CH), 72.3 (CH), 56.1 (Me), 42.3 (CH_2), 37.0 (CH_2), 35.7 (CH_2), 29.9 (CH_2), 26.3 (Me), 25.6 (CH_2), 25.3 (CH_2), 18.5 (C), -4.0 (Me).

(3*R*,9*S*)- and (3*S*,9*S*)-*N*-[2-(9-(*tert*-Butyldimethylsiloxydodeca-1,11-dien-3-yloxy)-4-methoxyphenyl]-2-methylpenta-2,4-dienamide 23b

(3*R*,9*S*)- and (3*S*,9*S*)-3-(5-Methoxy-2-nitrophenoxy)-9-(*tert*-butyldimethylsiloxy)dodeca-1,11-diene **21b** (500 mg, 1.08 mmol) was dissolved in a mixture of ethanol (43 mL) and water (20 mL). Solid ammonium chloride (35 mg, 0.65 mmol) and iron powder (302 mg, 5.40 mmol) were added and the mixture was heated under reflux for 2 h. After cooling to room temperature the mixture was filtered through Celite, which was washed with ethyl acetate (2 × 30 mL). The layers were separated and the organic phase was dried (Na_2SO_4) and the solvent was evaporated. The crude aniline **22b** was dried *in vacuo* and then dissolved in DMF (5 mL). Hünig's base (0.75 mL, 4.3 mmol) and 2-methyl-2,4-pentadienoic acid (180 mg, 1.60 mmol) were added, followed by the dropwise addition of a solution of pyBOP (1.14g, 2.20 mmol) in DMF (5 mL). The mixture was stirred overnight, diluted with water (75 mL) and extracted with ethyl acetate (2 × 30 mL). The organic phase was dried (Na_2SO_4) and the solvent was evaporated. Flash chromatography of the residue using ether and light petroleum (1 : 3) gave the *title compound* as a brown oil (378 mg, 66%); $[\alpha]_D^{32}$+ 6.71 (*c* 2.83, $CHCl_3$); (Found: MH^+, 528.3468. $C_{31}H_{49}NO_4Si$ + H requires 528.3509); ν_{max} ($CHCl_3$)/cm^{-1} 3438, 3022, 2932, 1663, 1616, 1525; δ_H (300 MHz; $CDCl_3$) *mixture of isomers* 8.31 (1 H, d, *J* 6.0, ArH), 8.12 (1 H, br s, NH), 7.00 (1 H, d, *J* 12.0, CMe=C$\underline{H}$CH=CH_2), 6.67-6.61 (1 H, m, CMe=CHC$\underline{H}$=CH_2), 6.46-6.42 (2 H, m, ArH), 5.82-5.71 (2 H, m, 2 × C$\underline{H}$=CH_2), 5.50 (1 H, d, *J* 18.0, CMe=CHCH=CH$\underline{H}$), 5.40 (1 H, d, *J* 9.0, CMe=CHCH=C$\underline{H}$H), 5.23 (1 H, d, *J* 18.0, CH_2CH=CH$\underline{H}$), 5.21 (1 H, d, *J* 6.0, CH_2CH=C$\underline{H}$H), 4.99 (1 H, d, *J* 15.0, ArOCHCH=C$\underline{H}$H), 4.97 (1 H, d, *J* 6.0, ArOCHCH=CH$\underline{H}$), 4.59 (1 H, q, *J* 6.0, ArOC$\underline{H}$), 3.73 (3 H, s, OMe), 3.64-

3.61 (1 H, m, $\mathrm{C\underline{H}OTBS}$), 2.17-2.14 (2 H, m, CH_2), 2.04 (3 H, s, Me), 1.82-1.60 (2 H, m, $\mathrm{C\underline{H}_2CH{=}CH_2}$), 1.42-1.21 (8 H, m, 4 × CH_2), 0.84 (9 H, s, *t*-Bu), 0.00 (6 H, s, Me); δ_C (75 MHz; $CDCl_3$) *mixture of isomers* 166.4 (C) 164.5 (C), 156.3 (C), 148.2 (C), 144.4 (C), 143.9 (C), 137.6 (CH), 135.7 (CH), 134.8 (CH), 132.4 (CH), 131.8 (C), 131.7 (C), 129.1 (C), 129.0 (CH), 128.8 (CH), 125.1 (CH), 123.5 (CH_2), 123.2 (CH_2), 122.5 (C), 120.9 (CH), 120.7 (CH), 117.5 (CH_2), 117.0 (CH_2), 116.9 (CH_2), 108.7 (CH_2), 104.5 (CH), 101.8 (CH), 80.4 (CH), 72.4 (CH), 72.2 (CH), 55.8 (Me), 42.3 (CH_2), 37.0 (CH_2), 35.9 (CH_2), 30.1 (CH_2), 26.3 (Me), 25.6 (CH_2), 18.5 (C), 13.3 (Me), 13.2 (Me), -4.0 (Me).

6,6-Dimethoxyhexanal 28

A solution of cyclohexene (15.20 mL, 12.30 g, 150.0 mmol) in anhydrous dichloromethane (500 mL) and anhydrous methanol (100 mL) was cooled to -78 °C. Ozone was bubbled through the solution with stirring until the solution turned blue. The ozone addition was stopped and oxygen then nitrogen was bubbled through until the blue colour had discharged. 4-Toluenesulfonic acid (2.55 g, 14.8 mmol, 10% w/w) was added and the solution allowed to warm to room temperature as it stirred under a nitrogen atmosphere for 90 min. Anhydrous sodium hydrogen carbonate (20.16 g, 324 mmol) was added and the mixture stirred for 14 h. The mixture was concentrated to approximately 150 mL by evaporating *in vacuo*, dichloromethane (250 mL) was added and the mixture washed with water (150 mL). The aqueous layer was extracted with dichloromethane (2 × 250 mL), the organic layers combined, washed with water (150 mL), brine (150 mL), dried ($MgSO_4$), filtered and evaporated *in vacuo*. The crude product was purified by flash chromatography on silica, eluting with ethyl acetate and light petroleum (1 : 4), to give the *title compound* as a colourless oil (17.16 g, 71%) (lit.,[105] bp 80-82 °C at 1.75 mmHg); ν_{max} (film)/cm^{-1} 2947, 2831, 1735; δ_H (300 MHz; $CDCl_3$) 9.77 (1 H, t, *J* 0.8, $CH_2C\underline{H}O$), 4.36 (1 H, t, *J* 5.6, $(MeO)_2C\underline{H}$), 3.31 (6 H, s, OMe), 2.36 (2 H, t, *J* 7.3, $C\underline{H}_2CHO$), 1.64-1.30 (6 H, m, 3 × CH_2); δ_C (75 MHz; $CDCl_3$) 202.8 (CH), 104.7 (CH), 53.1 (Me), 44.1 (CH_2), 32.7 (CH_2), 24.7 (CH_2), 22.4 (CH_2).

9,9-Dimethoxynonen-4-ol 29a

To a solution of 6,6-dimethoxyhexanal **28** (8.01 g, 50 mmol) in anhydrous THF (130 mL) at between -15 °C and 0 °C was slowly added allylmagnesium chloride (2 M in THF; 37.5 mL, 75 mmol) over 30 min under a nitrogen atmosphere. The reaction mixture was stirred at between -10 °C and -5 °C for 3 h before being quenched by the addition of water (175 mL). The aqueous layer was extracted with ethyl acetate (3 × 150 mL), the organic layers combined, washed with water (2 × 120 mL), brine (120 mL), dried ($MgSO_4$), filtered and evaporated *in vacuo*. The crude product was purified by flash chromatography on silica, eluting with ethyl acetate and light petroleum (1 : 4) to give the *title compound* as a colourless oil (5.78 g, 57%) (lit.,[109] bp not given); (Found: MH^+, 203.1646. $C_{11}H_{22}O_3$ + H requires 203.1647); ν_{max} (film)/cm^{-1} 3432, 3075, 2939, 2860, 1640, 1129, 912; δ_H (300 MHz; $CDCl_3$) 5.67-5.53 (1 H, m, $C\underline{H}{=}CH_2$), 5.00-4.94 (2 H, m, $CH{=}C\underline{H}_2$), 4.20 (1 H, t, *J* 5.6, $(MeO)_2C\underline{H}$), 3.51-3.46 (1 H, m, $C\underline{H}OH$), 3.15 (6 H, s, OMe), 2.11-1.19 (10 H, m, 5 × CH_2), 1.47 (1 H, s, OH); δ_C (75 MHz; $CDCl_3$) 135.3 (CH), 118.3 (CH_2), 104.7 (CH), 70.8 (CH), 53.0 (Me), 42.3 (CH_2), 36.8 (CH_2), 32.8 (CH_2), 25.8 (CH_2), 24.9 (CH_2); *m/z* (CI) 203 (MH^+, 72%), 201 (99), 197 (28), 196 (11), 191 (7), 171 (100).

4-tert-Butyldiphenylsiloxy-9,9-dimethoxynonene 30a

To a solution of 9,9-dimethoxynonen-4-ol **29a** (5.56 g, 27.7 mmol) in anhydrous DMF (90 mL) was added imidazole (4.71 g, 69.2 mmol) and *tert*-butyldiphenylchlorosilane (7.20 mL, 7.60 g, 27.7 mmol). The reaction mixture was stirred at room temperature for 24 h, then diluted with ethyl acetate (700 mL), washed with water (6 × 700 mL), brine (700 mL), dried ($MgSO_4$), filtered and evaporated *in vacuo*. The crude product was purified by flash chromatography on silica, eluting with ethyl acetate and light petroleum (1 : 19) to give the *title compound* as a colourless oil (11.00 g, 90%); (Found: MH^+, 441.2825. $C_{27}H_{40}O_3Si + H$ requires 441.2825); ν_{max} (film)/cm^{-1} 3071, 2932, 2899, 1639, 1588, 1111, 702; δ_H (300 MHz; $CDCl_3$) 7.69-7.65 (4 H, m, ArH), 7.41-7.43 (6 H, m, ArH), 5.68-5.73 (1 H, m, $C\underline{H}=CH_2$), 4.96-4.89 (2 H, m, $CH=C\underline{H}_2$), 4.27 (1 H, t, *J* 8.7, $(MeO)_2C\underline{H}$), 3.76 (1 H, q, *J* 5.7, $C\underline{H}OTBDPS$), 3.26 (6 H, s, OMe), 2.20-2.15 (2 H, m, $C\underline{H}_2CH=CH_2$), 1.17-1.51 (8 H, m, 4 × CH_2), 1.04 (9 H, s, *t*-Bu); δ_C (75 MHz; $CDCl_3$) 135.9 (CH), 134.5 (C), 134.4 (CH), 129.5 (CH), 127.4 (CH), 116.9 (CH), 104.4 (CH), 72.7 (CH), 52.5 (Me), 41.0 (CH_2), 35.5 (CH_2), 32.3 (CH_2), 27.0 (Me), 26.5 (CH_2), 24.6 (CH_2), 19.4 (C); *m/z* (CI) 441 (MH^+, 7%), 437 (100), 423 (56).

8-(*tert*-Butyldiphenylsiloxy)-2-methylundeca-1,10-dien-3-ol 31a

(a) To a solution of *4-tert*-butyldiphenylsiloxy-9,9-dimethoxynonene **29a** (0.442 g, 1.00 mmol) in chloroform (2.7 mL) was added aqueous trifluoroacetic acid (50%; 2.70 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 2 h. The mixture was diluted with ethyl acetate (68 mL), washed with water (3 × 70 mL), brine (70 mL), dried ($MgSO_4$), filtered and evaporated *in vacuo* to give 6-(*tert*-butyldiphenylsiloxy)non-8-enal ss a colourless oil (0.400 g, 99%); (Found: MH^+, 395.2401. $C_{25}H_{34}O_2Si + H$ requires 395.2406); ν_{max} (film)/cm^{-1} 3071, 2931, 2858, 1726, 1634, 1577, 1111, 702; δ_H (300 MHz; $CDCl_3$) 9.67 (1 H, t, *J* 1.7, $CH_2C\underline{H}O$), 7.70-7.65 (4 H, m, ArH), 7.41-7.33 (6 H, m, ArH), 5.74-5.6 (1 H, m, $C\underline{H}=CH_2$), 4.98-4.89 (2 H, m, $CH=C\underline{H}_2$), 3.76 (1 H, q, *J* 6.0, $C\underline{H}OTBDPS$), 2.30-2.16 (4 H, m, 2 × CH_2), 1.46-1.22 (6 H, m, 3 × CH_2), 1.05 (9

H, s, *t*-Bu); δ_C (75 MHz; CDCl$_3$) 202.0 (CH), 135.1 (CH), 134.0 (C), 133.6 (CH) 128.9 (CH), 126.7 (CH), 116.1 (CH$_2$) 71.6 (CH), 42.9 (CH$_2$), 40.2 (CH$_2$), 34.8 (CH$_2$), 26.2 (Me), 23.5 (CH$_2$), 21.2 (CH$_2$), 18.2 (C); *m/z* (CI) 395 (MH$^+$, 12%), 353 (29), 317 (100), 257 (24), 139 (81).

(b) To a solution of 6-(*tert*-butyldiphenylsiloxy)non-8-enal (5.29 g, 13.4 mmol) in anhydrous THF (26 mL) at between -10 °C to 0 °C was added isopropenylmagnesium bromide (0.5 M in THF; 32.20 mL, 16.1 mmol) slowly over 30 min. The reaction mixture was stirred at between -10 °C to 0 °C for 3 h then quenched by the addition of saturated ammonium chloride solution (26 mL). The mixture was extracted with ethyl acetate (3 × 25 mL), the organic layers combined, washed with water (3 × 25 mL), brine (25 mL) dried (MgSO$_4$), filtered and evaporated *in vacuo*. The crude product was purified by flash chromatography on silica, eluting with ethyl acetate and light petroleum (1 : 19) to give the *title compound* as a colourless oil (2.39 g, 41%) as a mixture of diastereoisomers; (Found: MH$^+$, 437.2879. $C_{28}H_{40}O_2Si$ + H requires 437.2876); ν_{max} (film)/cm^{-1} 3378, 3071, 3042, 2932, 2857, 1639, 1588, 1111; δ_H (300 MHz; CDCl$_3$) 7.69-7.66 (4 H, m, ArH), 7.41-7.32 (6 H, m, ArH), 5.74-5.72 (1 H, m, C$\underline{\text{H}}$=CH$_2$), 4.97-4.80 (4 H, m, CH=C$\underline{\text{H}}_2$, MeC=C$\underline{\text{H}}_2$), 3.95 (1 H, t, *J* 6.2, C$\underline{\text{H}}$OH), 3.75 (1 H, q, *J* 5.5, C$\underline{\text{H}}$OTBDPS), 2.22-2.15 (2 H, m, C$\underline{\text{H}}_2$CH=CH$_2$), 1.67 (3 H, s, Me), 1.51 (1 H, s, OH), 1.45-1.08 (8 H, m, 4 × CH$_2$), 1.05 (9 H, s, *t*-Bu); δ_C (75 MHz; CDCl$_3$) 147.9 (C), 136.4 (CH), 135.4 (CH), 134.0 (C), 129.9 (CH), 127.8 (CH), 117.2 (CH$_2$), 111.4 (CH$_2$), 76.3 (CH), 73.1 (CH), 41.5 (CH$_2$), 36.3 (CH$_2$), 35.2 (CH$_2$), 27.5 (Me), 25.9 (CH$_2$), 25.1 (CH$_2$), 17.9 (Me), 14.6 (C); *m/z* (CI) 437 (MH$^+$, 24%), 317 (26), 163 (100).

8-*tert*-Butyldiphenylsiloxy-3-(5-methoxy-2-nitrophenoxy)-2-methylundeca-1,10-diene 32a

To a solution of 5-methoxy-2-nitrophenol (0.93 g, 5.48 mmol), 8-(*tert*-butyldiphenylsiloxy)-2-methylundeca-1,10-dien-3-ol **31a** (2.39 g, 5.48 mmol) and triphenylphosphine (2.15 g, 8.22 mmol) in anhydrous toluene (17 mL) at 0 °C was slowly added diisopropyl azodicarboxylate (1.60 mL, 1.66 g, 8.22 mmol). The reaction mixture was then stirred at room temperature for 24 h. The mixture was concentrated to half the original volume by evaporating *in vacuo*, followed by addition of light petroleum to precipitate triphenylphosphine oxide as a white precipitate. The precipitate was removed by filtration and washed with light petroleum (3 × 5 mL). The filtrate was then concentrated *in vacuo* and dissolved in ethyl acetate (25 mL), washed with NaOH (2 M; 3 × 15 mL), water (3 × 15 mL), brine (15 mL), dried ($MgSO_4$), filtered and evaporated *in vacuo*. The crude product was purified by flash chromatography on silica, eluting with ethyl acetate and light petroleum (1 : 9) to give the *title compound* as a yellow oil (2.12 g, 67%) as a mixture of diastereoisomers; (Found: MH^+, 588.3130. $C_{35}H_{45}NO_5Si$ + H requires 588.3145); ν_{max} (film)/cm^{-1} 3071, 2932, 1607, 1581, 1513, 1347, 1111, 702; δ_H (300 MHz; $CDCl_3$) 7.92 (1 H, d, *J* 9.0, ArH), 7.72-7.66 (4 H, m, ArH), 7.42-7.33 (6 H, m, ArH), 6.45-6.42 (2 H, m, ArH), 5.74-5.68 (1 H, m, $C\underline{H}{=}CH_2$), 4.98-4.89 (4 H, m, $CH{=}C\underline{H}_2$, $MeC{=}C\underline{H}_2$), 4.54 (1 H, t, *J* 6.4, $ArOC\underline{H}$), 3.83 (3 H, s, OMe), 3.83-3.74 (1 H, m, $C\underline{H}OTBDPS$), 2.22-2.16 (2 H, m, $C\underline{H}_2CH{=}CH_2$), 1.68 (3 H, s, Me), 2.10-1.06 (8 H, m, 4 × CH_2), 1.04 (9 H, s, *t*-Bu); δ_C (75 MHz; $CDCl_3$) 164.8 (C), 154.8 (C), 144.0 (C), 136.6 (CH), 135.5 (CH), 135.1 (C), 134.1 (C), 130.2 (CH), 128.6 (CH), 128.1 (CH), 117.5 (CH_2), 114.6 (CH_2), 105.4 (CH), 102.3 (CH), 84.2 (CH), 73.3 (CH), 56.4 (Me), 41.7 (CH_2), 36.5 (CH_2), 34.2 (CH_2), 27.7 (Me), 26.0 (CH_2), 25.1 (CH_2), 20.1 (C), 17.8 (Me); some peaks are ‘doubled’ due to the presence of diastereomers; *m/z* (CI) 588 (MH^+, 3%), 530 (37), 419 (24), 163 (100).

2-(8-*tert*-Butyldiphenylsiloxy-2-methylundeca-1,10-dien-3-yloxy)-4-methoxyaniline 33a

8-*tert*-Butyldiphenylsiloxy-3-(5-methoxy-2-nitrophenoxy)-2-methylundeca-1,10-diene **32a** (2.10 g, 3.56 mmol) was dissolved in THF (75 mL) and glacial acetic acid (1.01 mL, 17.8 mmol). Indium powder (4.08 g, 35.6 mmol) was then added and the mixture heated under reflux overnight. The mixture was then cooled to room temperature before being diluted with ethyl acetate (200 mL) and filtered through a pad of Celite. The filtered mixture was then washed with water (3 × 100 mL), brine (100 mL), dried ($MgSO_4$), filtered and evaporated *in vacuo* to give the crude *title compound* as a dark oil (1.96 g, 98%) as a mixture of diastereoisomers; (Found: MH^+, 558.3404. $C_{35}H_{47}NO_3Si$ + H requires 558.3403); ν_{max} (film)/cm^{-1} 3451, 3365, 3071, 2933, 2857, 1595, 1512, 1465, 1111, 703; δ_H (300 MHz; $CDCl_3$) 7.68-7.65 (4 H, m, ArH), 7.43-7.32 (6 H, m, ArH), 6.65-6.62 (1 H, m, ArH), 6.41-6.30 (2 H, m, ArH), 5.73-5.68 (1 H, m, $C\underline{H}=CH_2$), 4.97-4.89 (4 H, m, $CH=C\underline{H}_2$, $MeC=C\underline{H}_2$), 4.21 (1 H, t, *J* 6.6, $ArOC\underline{H}$), 3.77-3.70 (4 H, m, $C\underline{H}OTBDPS$, OMe), 3.47 (2 H, s, NH_2), 2.21-2.15 (2 H, m, $C\underline{H}_2CH=CH_2$), 1.69 (3 H, s, Me), 1.70-1.06 (8 H, m, 4 × CH_2), 1.04 (9 H, s, *t*-Bu); δ_C (75 MHz; $CDCl_3$) 152.8 (C), 146.7 (C), 144.1 (C), 135.9 (CH), 135.8 (CH), 134.9 (CH), 134.4 (C), 129.5 (CH), 127.4 (CH), 116.8 (CH_2), 115.4 (C), 113.1 (CH_2), 104.2 (CH), 101.8 (CH), 82.0 (CH), 72.7 (CH), 55.6 (Me), 41.1 (CH_2), 35.8 (CH_2), 33.9 (CH_2), 27.0 (Me), 25.7 (CH_2), 24.6 (CH_2), 19.4 (C), 17.2 (Me); *m/z* (CI) 558 (MH^+, 100%), 480 (35), 302 (30), 140 (97).

N-[2-(8-*tert*-Butyldiphenylsiloxy-2-methylundeca-1,10-dien-3-yloxy)-4-methoxyphenyl]-2-methylpenta-2,4-dienamide 34a

A solution of 2-(8-*tert*-butyldiphenylsiloxy-2-methylundeca-1,10-dien-3-yloxy)-4-methoxyaniline **33a** (0.415 g, 0.74 mmol), diisopropylethylamine (0.288 g, 2.23 mmol) in DMF (8 mL) was slowly added to a solution of 2-methylpenta-2,4-dienoic acid (0.083 g, 0.74 mmol) in DMF (8 mL). A solution of PyBop (0.541 g, 1.04 mmol) in DMF (8 mL) was added and the reaction mixture was stirred at room temperature for 20 h. Water (20 mL) was added and the product was extracted with ethyl acetate (2 × 30 mL). The organic layers were combined, washed with water (2 × 30 mL), brine (30 mL) and dried ($MgSO_4$). Solvent was evaporated *in vacuo*. The crude product was purified by flash chromatography on silica, eluting with ethyl acetate and light petroleum (1 : 9) to give the *title compound* as a brown yellow oil (0.403 g, 83%) as a mixture of diastereoisomers; (Found: MH^+, 652.3815. $C_{41}H_{53}NO_4Si + H$ requires 652.3822); ν_{max} (film)/cm^{-1} 3439, 3071, 2932, 2857, 1669, 1616, 1520, 1112, 703; δ_H (300 MHz; $CDCl_3$) 8.30-8.27 (1 H, d, *J* 8.7, ArH), 8.07 (1 H, s, NH), 7.60-7.57 (4 H, m, ArH), 7.33-7.25 (6 H, m, ArH), 6.96 (1 H, d, *J* 10.7, $CMe=C\underline{H}CH=CH_2$), 6.62-6.56 (1 H, m, $CMe=CHC\underline{H}=CH_2$), 6.42-6.36 (2 H, m, ArH), 5.66-5.60 (1 H, m, $CH_2C\underline{H}=CH_2$), 5.46 (1 H, d, *J* 16.5, $CMe=CHCH=CH\underline{H}$), 5.34 (1 H, d, *J* 10.2, $CMe=CHCH=C\underline{H}H$), 4.90-4.81 (4 H, m, $CH_2CH=C\underline{H_2}$, $MeC=C\underline{H_2}$), 4.43 (1 H, t, *J* 6.2, $ArOC\underline{H}$), 3.69-3.66 (4 H, m, $C\underline{H}OTBDPS$, OMe), 2.15-2.08 (2 H, m, $C\underline{H_2}CH=CH_2$), 1.97 (3 H, s, Me), 1.59 (3 H, s, Me), 0.97 (9 H, s, *t*-Bu), 1.64-0.97 (8 H, m, 4 × CH_2); δ_C (75 MHz; $CDCl_3$) 166.3 (C), 156.3 (C), 148.1 (C), 143.6 (C), 136.3 (CH), 135.2 (CH), 134.9 (CH), 134.7 (CH), 132.4 (CH), 131.7 (C), 129.9 (CH), 127.9 (CH), 123.6 (CH_2), 122.3 (C), 120.6 (CH_2), 117.3 (CH), 114.1 (CH_2), 104.3 (CH), 101.4 (CH), 82.9 (CH), 72.9 (CH), 55.8 (Me), 41.4 (CH_2), 36.2 (CH_2), 34.3 (CH_2), 27.4 (Me), 26.0 (CH_2), 25.0 (CH_2), 19.8 (C), 17.7 (Me), 13.3 (Me); some peaks are 'doubled' due to the presence of diastereomers; *m/z* (CI) 652 (MH^+, 16%), 634 (21), 396 (29), 120 (100).

10,10-Dimethoxydecen-5-ol 29b

To a solution of 6,6-dimethoxyhexanal **28** (0.69 g, 4.33 mmol) in anhydrous THF (11 mL) at between -15 °C and 0 °C was slowly added 3-butenylmagnesium bromide (0.5 M in THF;

11.2 mL, 5.63 mmol) over 30 min under a nitrogen atmosphere. The reaction mixture was stirred at between -10 °C and -5 °C for 3 h before being quenched by the addition of water (15 mL). The aqueous layer was extracted with ethyl acetate (3 × 12 mL), the organic layers combined, washed with water (2 × 10 mL), brine (10 mL), dried ($MgSO_4$), filtered and evaporated *in vacuo*. The crude product was purified by flash chromatography on silica, eluting with ethyl acetate and light petroleum (1 : 4) to give the *title compound* as a colourless oil (0.68 g, 73%); (Found: MH^+, 217.1800. $C_{12}H_{24}O_3$ + H requires 217.1804); ν_{max} (film)/cm^{-1} 3470, 3076, 2938, 2861, 1640, 1128, 910; δ_H (300 MHz; $CDCl_3$) 5.79-5.85 (1 H, m, C$\underline{H}$=CH_2), 4.95-5.08 (2 H, m, CH=C$\underline{H}_2$), 4.36 (1 H, t, *J* 5.7, $(MeO)_2C\underline{H}$), 3.64-3.60 (1 H, m, C$\underline{H}$OH), 3.31 (6 H, s, OMe), 2.17-2.13 (2 H, m, CH(OH)C$\underline{H}_2$) 1.35-1.62 (11 H, m, OH, 5 × CH_2); δ_C (75 MHz; $CDCl_3$) 138.6 (CH), 114.7 (CH_2), 104.4 (CH), 71.3 (CH), 52.6 (Me), 37.4 (CH_2), 36.4 (CH_2), 32.4 (CH_2), 30.0 (CH_2), 25.4 (CH_2), 24.5 (CH_2); *m/z* (CI) 217 (MH^+, 56%), 153 (100).

5-*tert*-Butyldiphenylsiloxy-10,10-dimethoxydecene 30b

To a solution of 10,10-dimethoxydecen-5-ol **29b** (3.85 g, 17.9 mmol) in anhydrous DMF (56 mL) was added imidazole (3.04 g, 44.7 mmol) and *tert*-butyldiphenylchlorosilane (4.65 mL, 17.9 mmol). The reaction mixture was stirred at room temperature for 24 h, diluted with ethyl acetate (300 mL), washed with water (6 × 200 mL), brine (200 mL), dried ($MgSO_4$), filtered and evaporated *in vacuo*. The crude product was purified by flash chromatography on silica, eluting with ethyl acetate and light petroleum (1 : 19) to give the *title compound* as a colourless oil (7.60 g, 100%); (Found: MH^+, 455.2073. $C_{28}H_{42}O_3Si$ + H requires 455.2981); ν_{max} (film)/cm^{-1} 3070, 2932, 2857, 1639, 1111, 702; δ_H (300 MHz; $CDCl_3$) 7.72-7.65 (4 H, m, ArH), 7.41-7.33 (6 H, m, ArH), 5.68-5.60 (1 H, m, C$\underline{H}$=CH_2), 4.91-4.83 (2 H, m, CH=C$\underline{H}_2$), 4.27 (1 H, t, *J* 5.7, $(MeO)_2C\underline{H}$), 3.72 (1 H, q, *J* 11.2, C$\underline{H}$OTBDPS), 3.28 (6 H, s, OMe), 2.02-

1.99 (2 H, m, C<u>H</u>$_2$CH=CH$_2$), 1.54-1.07 (10 H, m, 5 × CH$_2$), 1.04 (9 H, s, *t*-Bu); δ_C (75 MHz; CDCl$_3$) 139.2 (CH), 136.3 (C), 135.0 (CH), 129.8 (CH), 127.8 (CH), 114.5 (CH), 104.8 (CH), 73.0 (CH), 52.9 (Me), 36.5 (CH$_2$), 35.9 (CH$_2$), 32.7 (CH$_2$), 29.6 (CH$_2$), 27.4 (Me), 21.4 (CH$_2$), 19.8 (CH$_2$), 14.6 (C); *m/z* (CI) 455 (MH$^+$, 24%), 453 (100), 451 (69), 397 (22).

8-(*tert*-Butyldiphenylsiloxy)-2-methyldodeca-1,11-dien-3-ol 31b

(a) To a solution of 5-*tert*-butyldiphenylsiloxy-10,10-dimethoxydecene **30b** (6.68 g, 14.7 mmol) in chloroform (40 mL) was added aqueous trifluoroacetic acid (50%; 40 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 2 h. The mixture was diluted with ethyl acetate (750 mL), washed with water (3 × 500 mL), brine (500 mL), dried (MgSO$_4$), filtered and evaporated *in vacuo* to give 6-(*tert*-butyldiphenylsiloxy)dec-9-enal as a colourless oil (6.00, 99%); (Found: MH$^+$, 409.2558. $C_{26}H_{36}O_2Si$ + H requires 409.2563); ν_{max} (film)/cm^{-1} 3071, 3047, 2714, 1725, 1640, 1111, 702; δ_H (300 MHz; CDCl$_3$) 9.65 (1 H, t, *J* 0.5, CH$_2$C<u>H</u>O), 7.73-7.68 (4 H, m, ArH), 7.44-7.36 (6 H, m, ArH), 5.73-5.59 (1 H, m, C<u>H</u>=CH$_2$), 4.92-4.84 (2 H, m, CH=C<u>H</u>$_2$), 3.74 (1 H, q, *J* 5.6, C<u>H</u>OTBDPS), 2.26 (2 H, dt, *J* 7.2, 1.8, C<u>H</u>$_2$CHO), 2.02 (2 H, q, *J* 7.0, C<u>H</u>$_2$CH=CH$_2$), 1.59-1.18 (8 H, m, 4 × CH$_2$), 1.05 (9 H, s, *t*-Bu); δ_C (75 MHz; CDCl$_3$) 203.1 (CH), 139.0 (CH), 136.3 (C), 135.0 (CH), 130.0 (CH), 127.8 (CH), 114.6 (CH$_2$) 72.0 (CH), 44.1 (CH$_2$), 36.2 (CH$_2$), 35.9 (CH$_2$), 29.6 (CH$_2$), 26.9 (Me), 24.7 (CH$_2$), 22.4 (CH$_2$), 19.4 (C); *m/z* (CI) 409 (MH$^+$, 10%), 351 (88), 331 (100), 257 (25), 135 (80).

(b) To a solution 6-(*tert*-butyldiphenylsiloxy)dec-9-enal (1.00 g, 2.45 mmol) in anhydrous THF (4.8 mL) at between -10 °C to 0 °C was added isopropenylmagnesium bromide (0.5 M in THF; 5.8 mL, 2.94 mmol) slowly over 30 min. The reaction mixture was stirred at between -10 °C to 0 °C for 3 h then quenched by the addition of saturated ammonium chloride solution (5 mL). The mixture was extracted with ethyl acetate (3 × 10 mL), the organic layers combined, washed with water (3 × 10 mL), brine (10 mL) dried ($MgSO_4$), filtered and evaporated *in vacuo*. The crude product was purified by flash chromatography on silica, eluting with ethyl acetate and light petroleum (1 : 19) to give the *title compound* as a colourless oil (0.70 g, 64%); (Found: MH^+, 451.3033. $C_{29}H_{42}O_2Si + H$ requires 451.3032); ν_{max} (film)/cm^{-1} 3373, 3071, 3047, 2932, 2857, 1639, 1588, 1111; δ_H (300 MHz $CDCl_3$) 7.69-7.65 (4 H, m, ArH), 7.43-7.32 (6 H, m, ArH), 5.66-5.61 (1 H, m, $C\underline{H}{=}CH_2$), 4.91-4.80 (4 H, m, $CH{=}C\underline{H_2}$, $MeC{=}C\underline{H_2}$), 3.95 (1 H, t, *J* 6.4, CHOH), 3.73 (1 H, q, *J* 5.6, $C\underline{H}OTBDPS$), 2.01 (2 H, q, *J* 8.4, $C\underline{H_2}CH{=}CH_2$), 1.67 (3 H, s, Me), 1.54-1.07 (11 H, m, OH, 5 × CH_2) (9 H, s, *t*-Bu); δ_C (75 MHz; $CDCl_3$) 147.9 (C), 139.4 (CH), 136.5 (CH), 135.0 (C), 129.8 (CH), 127.8 (CH), 114.5 (CH_2), 111.3 (CH_2), 76.2 (CH), 73.0 (CH), 36.5 (CH_2), 35.9 (CH_2), 35.2 (CH_2), 29.6 (CH_2), 27.5 (Me), 26.0 (CH_2), 25.2 (CH_2), 19.8 (Me), 17.8 (C); *m/z* (CI) 451 (MH^+, 4%), 433 (27), 317 (20), 239 (13), 177 (100).

8-*tert*-Butyldiphenylsiloxy-3-(5-methoxy-2-nitrophenoxy)-2-methyldodeca-1,11-diene 32b

To a solution of 5-methoxy-2-nitrophenol (0.124 g, 0.93 mmol), 8-(*tert*-butyldiphenylsiloxy)-2-methyldodeca-1,11-dien-3-ol **31b** (0.331 g, 0.73 mmol) and triphenylphosphine (0.288 g, 1.10 mmol) in anhydrous toluene (2.30 mL) at 0 °C was slowly added diisopropyl azodicarboxylate (DIAD) (0.22 mL, 1.10 mmol). The reaction mixture was stirred at room temperature for 24 h. The mixture was then concentrated to half the original volume by evaporating in vacuo, then addition of light petroleum precipitated triphenylphosphine oxide as a colourless precipitate. The precipitate was removed by filtration and washed with light petroleum (3 × 5 mL). The filtrate was then concentrated *in vacuo* and dissolved in ethyl acetate (5 mL), washed with NaOH (2 M; 3 × 2 mL), water (3 × 2 mL), brine (3 mL), dried ($MgSO_4$), filtered and evaporated *in vacuo*. The crude product was purified by flash chromatography on silica, eluting with ethyl acetate and light petroleum (1 : 9) to give the *title compound* as a yellow oil (0.295 g, 66%) as a mixture of isomers; (Found: MH$^+$, 602.3303. $C_{36}H_{47}NO_5Si$ + H requires 602.3302.); ν_{max} (film)/cm^{-1} 3071, 2933, 1607, 1590, 1513, 1347, 1110, 703; δ_H (300 MHz; $CDCl_3$) 7.92 (1 H, d, *J* 8.6, ArH), 7.74-7.65 (4 H, m, ArH), 7.42-7.32 (6 H, m, ArH), 6.47-6.43 (2 H, m, ArH), 5.66-5.60 (1 H, m, $C\underline{H}=CH_2$), 4.98-4.83 (4 H, m, $CH=C\underline{H}_2$, $CMe=C\underline{H}_2$), 4.53 (1 H, t, *J* 6.2, $ArOC\underline{H}$), 3.81 (3 H, s, OMe), 3.73 (1 H, q, *J* 5.6, $C\underline{H}$OTBDPS), 2.00 (2 H, q, *J* 5.6, $C\underline{H}_2CH=CH_2$), 1.68 (3 H, s, Me), 1.59-1.04 (10 H, m, 5 × CH_2), 1.03 (9 H, s, *t*-Bu); δ_C (75 MHz; $CDCl_3$) 163.1 (C), 153.1 (C), 142.3 (C), 134.9 (CH), 133.9 (CH), 133.5 (C), 128.4 (C), 127.0 (C), 126.7 (CH), 126.4 (CH), 117.5 (CH_2), 113.1 (CH_2), 103.7 (CH), 100.6 (CH), 82.5 (CH), 71.6 (CH), 54.7 (Me), 35.0 (CH_2), 34.5 (CH_2), 32.6 (CH_2), 28.2 (CH_2), 26.0 (Me), 24.4 (CH_2), 23.5 (CH_2), 18.4 (C), 16.1 (Me); some peaks are 'doubled' due to the presence of diastereomers; *m/z* (CI) 602 (MH$^+$, 11%), 544 (70), 524 (63), 346 (100), 182 (98).

2-(8-*tert*-Butyldiphenylsiloxy-2-methyldodeca-1,11-dien-3-yloxy)-4-methoxyaniline 33b

8-*tert*-Butyldiphenylsiloxy-3-(5-methoxy-2-nitrophenoxy)-2-methyldodeca-1,11-diene **32b** (0.269 g, 0.44 mmol) was dissolved in THF (9.5 mL) and glacial acetic acid (0.130 mL, 2.23 mmol). Indium powder (0.512 g, 4.46 mmol) was added and the mixture heated under reflux overnight. The mixture was cooled to room temperature before being diluted with ethyl acetate (25 mL) and filtered through a pad of Celite. The filtered mixture was washed with water (3 × 15 mL), brine (15 mL), dried ($MgSO_4$), filtered and evaporated *in vacuo* to give the crude *title compound* as a dark oil (0.254 g, 99%); (Found: MH$^+$, 572.3558. $C_{36}H_{49}NO_3Si$ + H requires 572.3560.); ν_{max} (film)/cm^{-1} 3457, 3365, 3070, 2932, 2856, 1634, 1511, 1463, 1111, 703; δ_H (300 MHz; $CDCl_3$) 7.61-7.58 (4 H, m, ArH), 7.33-7.27 (6 H, m, ArH), 6.58-6.56 (1 H, m, ArH), 6.34-6.23 (2 H, m, ArH), 5.68-5.50 (1 H, m, $C\underline{H}=CH_2$), 4.86-4.76 (4 H, m, CH=C$\underline{H}_2$, CMe=C$\underline{H}_2$), 4.34 (1 H, t, *J* 6.2, ArOC$\underline{H}$), 3.68-3.63 (4 H, m, C$\underline{H}$OTBDPS, OMe), 3.25 (2 H, s, NH_2), 1.97-1.89 (2 H, m, C$\underline{H}_2$CH=CH_2), 1.59 (3 H, s, Me), 1.73-0.77 (10 H, m, 5 × CH_2), 0.97 (9 H, s, *t*-Bu); δ_C (75 MHz; $CDCl_3$) 153.4 (C), 147.2 (C), 144.4 (C), 139.2 (CH), 136.3 (CH), 135.0 (C), 134.9 (C), 129.8 (CH), 127.8 (CH), 115.9 (CH), 114.5 (CH_2), 113.5 (CH_2), 104.6 (CH), 102.1 (CH), 82.4 (CH), 73.0 (CH), 56.0 (Me), 36.5 (CH_2), 35.9 (CH_2), 34.3 (CH_2), 29.6 (CH_2), 27.4 (Me), 26.1 (CH_2), 25.1 (CH_2), 19.8 (C), 17.6 (Me); *m/z* (CI) 572 (MH^+, 31%), 494 (8), 140 (100).

N-[2-(8-*tert*-Butyldiphenylsiloxy-2-methyldodeca-1,11-dien-3-yloxy)-4-methoxyphenyl]-2-methylpenta-2,4-dienamide 34b

2-(8-*tert*-Butyldiphenylsiloxy-2-methyldodeca-1,11-dien-3-yloxy)-4-methoxyaniline **33b** (0.078 g, 0.13 mmol) was dissolved in acetonitrile (0.26 mL) followed by addition of 2-methylpenta-2,4-dienoic acid (0.015 g, 0.13 mmol) and triethylamine (0.097 mL, 0.40 mmol). The mixture was stirred 5 min and HBTU (0.077 g, 0.20 mmol) was added. The reaction mixture was then stirred at room temperature for 48 h. Brine (1 mL) was added and the mixture was extracted with ethyl acetate (2 × 2 mL), washed with NaOH (2 M; 3 mL), water (3 mL), aqueous sodium hydrogen carbonate (5%; 53 mL), water (3 mL), dried ($MgSO_4$), filtered and evaporated *in vacuo* to give the crude *title compound* as a dark oil (0.087 g, 95%); (Found: MH^+, 666.3970. $C_{42}H_{55}NO_4Si$ + H requires 666.3978); ν_{max} (film)/cm^{-1} 3439, 3071, 2933, 2857, 1669, 1617, 1525, 1111, 703; δ_H (300 MHz; $CDCl_3$) 8.36 (1 H, d, *J* 8.5, ArH), 8.14 (1 H, s, NH), 7.67-7.64 (4 H, m, ArH), 7.39-7.31 (6 H, m, ArH), 7.05-7.01 (1 H, m, CMe=C$\underline{H}$CH=CH_2), 6.69-6.63 (1 H, m, CMe=CHC$\underline{H}$=CH_2), 6.48-6.43 (2 H, m, ArH), 5.66-5.60 (1 H, m, CH_2CH=C$\underline{H}$), 5.53-5.40 (2 H, d, *J* 16.8, CHCH=C$\underline{H}_2$), 4.96-4.84 (4 H, m, CH_2CH=C$\underline{H}_2$, C=C$\underline{H}_2$), 4.41 (1 H, t, *J* 6.6, ArOC$\underline{H}$), 3.76-3.71 (4 H, m, C$\underline{H}$OTBDPS, OMe), 2.04 (3 H, s, Me), 1.59 (3 H, s, Me), 1.04 (9 H, s, *t*-Bu), 2.06-1.13 (12 H, m, 6 × CH_2); δ_C (75

MHz; $CDCl_3$) 165.8 (C), 155.9 (C), 147.6 (C), 143.1 (C), 138.6 (CH), 135.5 (CH), 134.8 (CH), 134.3 (C), 132.0 (CH), 131.1 (C), 129.4 (CH), 127.4 (CH), 123.4 (CH_2), 123.1 (C), 120.1 (CH), 114.21 (CH_2), 113.6 (CH_2), 103.9 (CH), 100.9 (CH), 82.4 (CH), 72.4 (CH), 55.3 (Me), 36.0 (CH_2), 35.4 (CH_2), 33.8 (CH_2), 27.0 (Me), 25.5 (CH_2), 24.6 (CH_2), 22.6 (CH_2), 19.3 (C), 17.2 (Me), 12.7 (Me); *m/z* (CI) 666 (MH^+, 16%), 610 (21), 572 (29), 410 (100).