Supporting Information

The Conjugate Addition/Peterson Olefination Reaction for the Preparation of Cross-Conjugated Cyclopentenone, PPAR-γ Ligands

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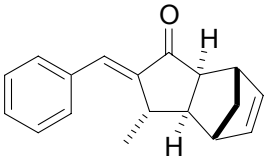
General

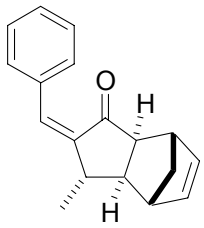
All starting materials were purchased from Aldrich and were used without purification unless otherwise stated. Melting points were measured using a Gallenkamp melting point apparatus. Microanalyses were determined using a Carlo Elba elemental analyser instrument. Nominal and accurate mass spectra were recorded on VG7070E, CIPOS, Kratos Profile HV3 and TRIO1000 machines. Optical rotations were measured at ambient temperature, using a 1 cm^3 cell with 0.1 dm path length, on an Optical Activity Ltd. AA-1000 polarimeter, operating at 589 nm corresponding to the sodium D line, and are recorded in units of $10^{-1}degcm^2g^{-1}$ (concentrations are quoted in g/100 cm^3). Infrared spectra were recorded on a Perkin Elmer 881 infrared spectrophotometer, over the range 4000-800 cm^{-1}. ^1H NMR spectra were recorded on a Bruker AC200 (200 MHz), Bruker AC250 (250 MHz), Varian 300 Gemini 2000 (300 MHz), or a Bruker 400 Avance (400 MHz) instrument. ^{13}C NMR spectra were recorded on a Varian 300 Gemini 2000 (75.5 MHz) or a Bruker 400 Avance (100 MHz) instrument. Analytical HPLC measurements were performed on a Gilson analytical HPLC machine using a Chiralpak AS column (COL-HP-17), under conditions described in the experimental section. THF and Et_2O were distilled from the sodium-benzophenone ketyl radical and DCM was distilled from CaH_2. All reactions were carried out under an atmosphere of nitrogen, in dried glassware. Reactions were monitored by thin layer chromatography (TLC), performed on aluminium backed silica gel Merck 60F-254 plates in a variety of solvents as stated. The plates were visualised by UV light (254 nm), *p*-anisaldehyde, or potassium permanganate. Column chromatography was conducted with Merck Kieselgel 60: 230-400 mesh for flash chromatography under bellows pressure. Hex refers to *n*-hexane and *c*-Hex refers to cyclohexane.

General Procedure for the Conjugate addition—Peterson olefination reactions: Synthesis of adducts 14a to 14q.

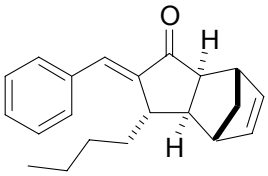


3-Methyl-2-[1-phenylmeth-(*E*)-ylidene]-2,3,3a,4,7,7a-hexahydro-4,7-methano-inden-1-one, *E*-14a. At -78ºC under nitrogen a slurry of CuI (509 mg, 2.67 mmol, 1.2 eq.) in Et_2O (25 cm^3) was treated dropwise with a 1.6 M solution of MeLi in hexanes (3.36 cm^3, 5.37 mmol, 2.4 eq.). The reaction was warmed to -10ºC over a period of 2 h. This solution was cooled to -20ºC before a pre-cooled (-20ºC) solution of the enone ***exo*-12** (485 mg, 2.23 mmol, 1 eq.) in Et_2O (25 cm^3) was added in a dropwise fashion. The flask containing ***exo*-12** was washed with Et_2O (5 cm^3) and this was also transferred to the reaction mixture. Stirring was continued for 1.5 h during which time the temperature rose to -10ºC. Upon cooling to -78ºC, benzaldehyde (0.35 cm^3, 3.44 mmol, 1.5 eq.) was added. The reaction was stirred for 3 h and warmed from -78ºC to 10ºC. A saturated solution of NH_4Cl (25 cm^3) was added and the resultant aqueous phase was further extracted with Et_2O (3 x 25 cm^3). The combined organic extracts were dried over $MgSO_4$, filtered and the solvent removed *in vacuo*. The crude product was then purified by flash column chromatography (Hex-Et_2O; 19:1) affording ***E*-14a** as a colourless solid (520 mg, 93%). Recrystallisation from *n*-hexane gave crystals of ***E*-14a** suitable for X-ray crystallography; M.pt. 82ºC (Hex); R_f 0.15 (Hex-Et_2O; 19:1); υ_{max} (neat/cm^{-1}) 2934, 1694, 1609, 1494, 1448, 1332, 1236, 1183; δ_H (400 MHz, $CDCl_3$) 1.25 (3H, d, *J* 7.0 Hz, CH_3), 1.28 (1H, dt, *J* 1.5, 9.5 Hz, CH_2), 1.36 (1H, d, *J* 9.5 Hz, CH_2), 1.93 (1H, d, *J* 7.5 Hz, CH), 2.48 (1H, d, *J* 7.5 Hz, CH), 2.86 (1H, s, CH), 3.12 (1H, s, CH), 3.19 (1H, q, *J* 7.0 Hz,

CH), 6.18-6.26 (2H, m, CH), 7.28 (1H, d, *J* 2.0 Hz, CH), 7.34-7.44 (3H, m, ArH), 7.57 (2H, d, *J* 7.5 Hz, ArH); δ_C (100 MHz, $CDCl_3$) 21.2, 38.9, 43.2, 48.5, 49.2, 49.5, 53.3, 128.8, 129.4, 130.7, 133.4, 135.9, 137.6, 139.0, 145.1, 209.0; m/z (EI) 250 (M^+, 25%), 183 (100%), 156 (50%), 141 (50%), 128 (40%), 115 (70%), 91 (50%), 66 (90%); Found C, 85.95; H, 7.42%, $C_{18}H_{18}O$ requires C, 86.36; H, 7.25%.

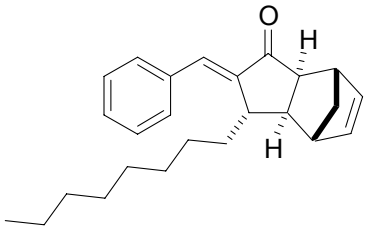


3-Methyl-2-[1-phenylmeth-(*Z*)-ylidene]-2,3,3a,4,7,7a-hexahydro-4,7-methano-inden-1-one, *Z*-14a. Under nitrogen a suspension of CuI (125 mg, 0.66 mmol, 0.1 eq.) in Et_2O (75 cm^3) was cooled to –78°C before treatment with a 1.0 M solution of methylmagnesium bromide in Et_2O (9.0 cm^3, 9.0 mmol, 1.5 eq.). This solution was stirred for 1.5 h during which time the temperature gradually rose to –25°C. The reaction vessel was re-cooled to –45°C and the enone ***exo*-12** (1.308 g, 6.0 mmol, 1 eq.) in Et_2O (15 cm^3) was added. Over 1 h the temperature rose to –5°C and TLC analysis (Hex-EtOAc; 9:1) indicated consumption of enone. The temperature was reduced to –78°C and benzaldehyde (964 mg, 9.0 mmol, 1.5 eq.) was added. The reaction was allowed to warm to room temperature overnight. Saturated NH_4Cl (50 cm^3) was added and the resultant mixture was extracted with Et_2O (5 x 50 cm^3). The combined organic extracts were dried over $MgSO_4$, filtered and the solvent removed *in vacuo*. Purification by flash column chromatography (Hex-EtOAc; 19:1) afforded initially the *cis*-isomer ***Z*-14a** (323 mg, 22%) as a yellow coloured oil followed by the *trans*-isomer ***E*-14a** (970 mg, 65%). Data for ***Z*-14a**: R_f 0.30 (Hex-EtOAc; 9:1); υ_{max} (neat/cm^{-1}) 3063, 2935, 1695, 1610, 1490, 1449, 1332, 1236, 1183; δ_H (250 MHz, $CDCl_3$) 1.28-1.38 (1H, m, CH_2), 1.33 (3H, d, *J* 7.0 Hz, CH_3), 1.45 (1H, d, *J* 9.5 Hz, CH_2), 1.82 (1H, d, *J* 8.0 Hz, CH), 2.44 (1H, d, *J* 8.0 Hz, CH), 2.54 (1H, m, CH), 2.84 (1H, s, CH), 3.12 (1H, s, CH), 6.13-6.25 (2H, m, CH), 6.60 (1H, d, *J* 2.0 Hz, CH), 7.26-7.40 (3H, m, ArH), 7.77-7.87 (2H, m, ArH); m/z (CI) 268 (MNH_4^+, 45%), 251 (MH^+, 50%), 185 (100%); Found 251.14359, $C_{18}H_{19}O$ requires 251.14360; (+0.1 ppm).

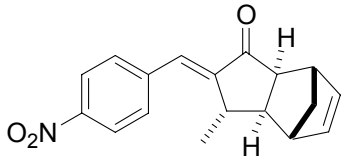


3-Butyl-2-[1-phenylmeth-(*E*)-ylidene]-2,3,3a,4,7,7a-hexahydro-4,7-methanoinden-1-one, 14b. Following the procedure described above (synthesis of ***E*-14a**), ***exo*-12** (1.308 g, 6.0 mmol, 1 eq.) in Et_2O (30 cm^3) was treated with Bu_2CuLi in Et_2O (35 cm^3) generated from CuI (1.37 g, 7.2 mmol, 1.2 eq.) and a 2.5 M solution of *n*-BuLi in Et_2O (5.76 cm^3, 14.4 mmol, 2.4 eq.). After TLC indicated formation of the conjugate adduct, benzaldehyde (967 mg, 9.03 mmol, 1.5 eq.) was added at once at -78ºC to the above solution. Standard work-up as above followed by flash column chromatography (Hex-Et_2O; 9:1) afforded adduct ***E*-14b** (1.600 g, 91%) as a viscous yellow oil. R_f 0.25 (Hex-Et_2O; 9:1); υ_{max} (neat/cm^{-1}) 3059, 3026, 2958, 2872, 1703, 1613, 1574, 1493, 1448, 1378, 1326, 1288; δ_H (400 MHz, $CDCl_3$) 0.87 (3H, t, *J* 7.5 Hz, CH_3), 1.22-1.46 (7H, m, CH_2), 1.63-1.73 (1H, m, CH_2), 2.05 (1H, d, *J* 7.75 Hz, CH), 2.45 (1H, d, *J* 7.75 Hz, CH), 2.81 (1H, s (br), CH), 3.02-3.09 (1H, m, CH), 3.11 (1H, s (br), CH), 6.24 (1H, dd, *J* 2.5, 5.5 Hz, CH), 6.28 (1H, dd, *J* 3.0, 5.5 Hz, CH), 7.29 (1H, d, *J* 2.25 Hz,

CH), 7.32-7.44 (3H, m, ArH), 7.53-7.57 (2H, m, ArH); δ_C (100 MHz, $CDCl_3$) 14.0, 22.7, 29.1, 34.4, 43.2, 44.3, 46.5, 48.4, 49.8, 53.7, 128.7, 129.4, 130.7, 133.4, 135.0, 137.6, 138.9, 144.2, 209.1; m/z (CI) 293 (MH^+, 100%) found 293.19001, $C_{21}H_2O$ requires 293.19052 (-1.9 ppm).

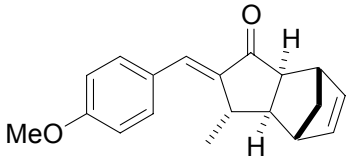


3-Octyl-2-[1-phenylmeth-(*E*)-ylidene]-2,3,3a,4,7,7a-hexahydro-4,7-methano-inden-1-one, 14c. Under N_2 a 1.7 M solution of *tert*-butyllithium in pentane (4.9 cm^3, 8.33 mmol, 4 eq.) was added dropwise to a solution of octyl iodide (0.75 cm^3, 4.15 mmol, 2 eq.) in a mixture of pentane (17 cm^3) and Et_2O (10 cm^3) at -78°C. Stirring was continued at -78°C for 0.25 h before warming to room temperature over 1 h. This solution of octyl lithium was cooled to -78°C and added to a slurry of CuI (395 mg, 2.07 mmol, 1 eq.) in Et_2O (10 cm^3) at -78°C *via* a cannula. The mixture was warmed to -20°C over 1 h. The resultant cuprate was cooled to -40°C and a solution of the enone ***exo*-12** (452 mg, 2.07 mmol, 1 eq.) in Et_2O (5 cm^3) was added dropwise [washed in with Et_2O (2 cm^3)]. After stirring for 1 h, during which time the temperature reached -20°C, TLC analysis indicated loss of enone and formation of a faster moving spot (Hex-EtOAc; 9:1). Benzaldehyde (0.42 cm^3, 4.13 mmol, 1 eq.) was added and the reaction was stirred for 18 h during which period the reaction mixture reached room temperature. Saturated NH_4Cl (25 cm^3) and EtOAc (25 cm^3) were added and the resultant aqueous layer was further extracted with EtOAc (3 x 25 cm^3). The combined organic extracts were dried over $MgSO_4$. Filtration followed by solvent removal *in vacuo* and flash column chromatography (Hex-EtOAc; 19:1) afforded the title compound **14c** (604 mg, 84%) as a viscous yellow liquid. R_f 0.25 (Hex-EtOAc; 19:1); δ_H (400 MHz, $CDCl_3$) 0.88 (3H, t, *J* 6.5 Hz, CH_3), 1.18-1.52 (15H, m, CH_2), 1.64-1.73 (1H, m, CH_2), 2.05 (1H, d, *J* 7.5 Hz, CH), 2.47 (1H, d, *J* 7.5 Hz, CH), 2.82 (1H, s, CH), 3.01-3.09 (1H, m, CH), 3.12 (1H, s, CH), 6.23 (1H, dd, *J* 2.75, 5.5 Hz, CH), 6.28 (1H, dd, *J* 3.0, 5.5 Hz, CH), 7.30 (1H, d, *J* 2.0 Hz, CH), 7.34-7.44 (3H, m, ArH), 7.56 (2H, d, *J* 7.0 Hz, ArH); δ_C (100 MHz, $CDCl_3$) 14.1, 22.6, 26.9, 29.2, 29.5, 29.6, 31.8, 34.7, 43.3, 44.4, 46.5, 48.4, 49.8, 53.7, 128.7, 129.4, 130.7, 133.4, 135.0, 137.6, 138.9, 144.3, 209.2; m/z (CI) 349 (MH^+, 10%), 283 (MH-$C_5H_6^+$, 100%); Found 349.25394, $C_{25}H_{33}O$ requires 349.25314 (+2.5 ppm); Found C, 85.9; H, 9.4%, $C_{25}H_{32}O$ requires C, 86.2; H, 9.2%.

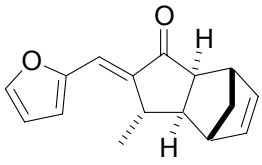


3-Methyl-2-[1-(4-nitrophenyl)meth-(*E*)-ylidene]-2,3,3a,4,7,7a-hexahydro-4,7-methanoinden-1-one, 14d. Following the procedure described above, ***exo*-12** (485 mg, 2.22 mmol, 1 eq.) in Et_2O (10 cm^3) was treated with a Me_2CuLi in Et_2O (25 cm^3) generated from CuI (509 mg, 2.67 mmol, 1.2 eq.) and a 1.6 M solution of MeLi in Et_2O (3.36 cm^3, 5.37 mmol, 2.4 eq.). 4-Nitrobenzaldehyde (504 mg, 3.33 mmol, 1.5 eq.) in benzene (5 cm^3) was added [washed in with THF (5 cm^3)]. Standard work-up as above followed by flash column chromatography (Hex-EtOAc; 3:1) afforded adduct ***E*-14d** (600 mg, 92%) as a yellow crystalline solid. Analytically pure **14d** was obtained on recrystallisation from EtOAc, M.pt. 120ºC (EtOAc); R_f 0.35 (Hex-EtOAc; 3:1); υ_{max} (neat/cm^{-1}) 3062, 2968, 2873, 2451, 1708,

1620, 1596, 1493, 1456, 1415, 1380, 1345, 1297; δ_H (400 MHz, $CDCl_3$) 1.24 (3H, d, *J* 7.0 Hz, CH_3), 1.30-1.35 (2H, m, CH_2), 2.01 (1H, d, *J* 7.5 Hz, CH), 2.54 (1H, d, *J* 7.5 Hz, CH), 2.92 (1H, s (br), CH), 3.14 (1H, s (br), CH), 3.22 (1H, q, *J* 7.0 Hz, CH), 6.23 (1H, dd, *J* 2.5, 5.5 Hz, CH), 6.28 (1H, dd, *J* 3.0, 5.5 Hz, CH), 7.28 (1H, d, *J* 2.25 Hz, CH), 7.72 (2H, d, *J* 8.5 Hz, ArH), 8.27 (2H, d, *J* 8.5 Hz, ArH); δ_C (100 MHz, $CDCl_3$) 21.1, 38.9, 43.5, 48.6, 49.2, 49.4, 53.3, 123.9, 130.2, 130.9, 137.5, 139.0, 141.3, 147.5, 148.8, 208.6; m/z (CI) 313 (MNH_4^+, 80%), 296 (MH^+, 35%), 266 (90%), 247 (65%), 230 ($MH\text{-}C_5H_6^+$, 100%); Found 296.12835, $C_{18}H_{18}NO_3$ requires 296.12866; Found C, 72.73; H, 5.75; N, 4.52%, $C_{18}H_{17}NO_3$ requires C, 73.21; H, 5.80; N, 4.74%.

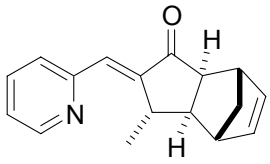


2-[1-(4-Methoxyphenyl)meth-(*E*)-ylidene]-3-methyl-2,3,3a,4,7,7a-hexahydro-4,7-methano-inden-1-one, 14e. Following the general procedure outlined above, a solution of Me_2CuLi in Et_2O (25 cm^3), prepared from CuI (509 mg, 2.67 mmol, 1.2 eq.) and a 1.6 M solution of MeLi in hexanes (3.36 cm^3, 5.37 mmol, 2.4 eq), was treated with ***exo*-12** (485 mg, 2.22 mmol, 1 eq.). On formation of the conjugate adduct (judged by TLC analysis) *p*-methoxybenzaldehyde (455 mg, 3.34 mmol, 1.5 eq.) was added. Following standard work-up described above and purification by flash column chromatography (Hex-EtOAc; 3:1) the adduct ***E*-14e** (281 mg, 45%) was isolated as a colourless solid. M.pt. 94ºC; R_f 0.35 (Hex-EtOAc; 3:1); υ_{max} (neat/cm^{-1}) 3080, 2964, 2900, 2880, 1697, 1596, 1570, 1511, 1460, 1423, 1326, 1307; δ_H (400 MHz, $CDCl_3$) 1.25 (3H, d, *J* 7.25 Hz, CH_3), 1.23-1.28 (1H, m, CH_2), 1.94 (1H, d, *J* 7.5 Hz, CH), 7.48 (1H, d, *J* 7.5 Hz, CH), 2.85 (1H, s, CH), 3.09-3.18 (2H, m, CH), 3.86 (3H, s, CH_3), 6.20 (1H, dd, *J* 3.0, 5.5 Hz, CH), 6.23 (1H, dd, *J* 3.0, 5.5 Hz, ArH), 6.95 (2H, d, *J* 8.5 Hz, ArH), 7.28 (1H, s, CH), 7.54 (2H, d, *J* 8.5 Hz, ArH); δ_C (100 MHz, $CDCl_3$) 21.1, 38.3, 43.1, 48.3, 49.0, 49.5, 53.3, 55.4, 114.3, 127.3, 132.7, 133.3, 137.5, 138.9, 142.6, 160.6, 209.0; m/z (CI) 281 (MNH_4^+, 70%), 215 ($MH\text{-}C_5H_6^+$, 100%); Found 281.15390, $C_{19}H_{21}O_2$ requires 281.15414, (-0.9 ppm); Found C, 81.60; H, 7.31%, $C_{19}H_{20}O_2$ requires C, 81.43; H, 7.14%.

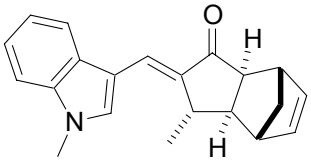


2-[1-Furan-2-ylmeth-(*E*)-ylidene]-3-methyl-2,3,3a,4,7,7a-hexahydro-4,7-methano-inden-1-one, 14f. Following the procedure described above, ***exo*-12** (436 mg, 2.0 mmol, 1 eq.) in Et_2O (10 cm^3) was treated with a Me_2CuLi in Et_2O (25 cm^3) generated from CuI (457 mg, 2.4 mmol, 1.2 eq.) and a 1.6 M solution of MeLi in Et_2O (3.0 cm^3, 4.8 mmol, 2.4 eq.). After TLC indicated formation of the conjugate adduct, furan-2-carbaldehyde (288 mg, 3.0 mmol, 1.5 eq.) was added. Standard work-up as above followed by flash column chromatography (Hex-Et_2O, 9:1) afforded adduct ***E*-14f** (450 mg, 94%) as a yellow amorphous solid. M.pt. 120ºC; R_f 0.2 (Hex-Et_2O; 9:1); υ_{max} (neat/cm^{-1}) 3154, 2972, 2253, 1794, 1690, 1613, 1552, 1474, 1390; δ_H (400 MHz, $CDCl_3$) 1.26-1.34 (5H, m, CH_2, CH_3), 1.90 (1H, d, *J* 7.5 Hz, CH), 2.48 (1H, d, *J* 7.5 Hz, CH), 2.83 (1H, s, CH), 3.09 (1H, s, CH), 3.13 (1H, q, *J* 7.5 Hz, CH), 6.17-6.24 (2H, m, CH), 6.50-6.52 (1H, dd, *J* 1.75, 3.5 Hz, CH), 6.68 (1H, d, *J* 3.5 Hz, CH), 7.06 (1H, d, *J* 2.0 Hz, CH), 7.58 (1H, d, *J* 1.75 Hz, CH); δ_C (100 MHz, $CDCl_3$) 22.6, 39.2, 43.1, 48.3, 49.1, 49.3, 53.7, 112.6, 117.0, 119.2, 137.4, 139.0, 142.6, 145.1, 151.7, 208.7; m/z

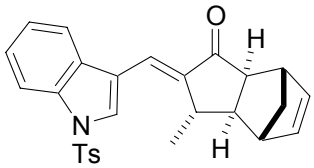
(CI) 241(MH^+, 30%), (175, 100%); Found 241.12319, $C_{16}H_{27}O_2$ requires 241.12286 (+1.5 ppm).



3-Methyl-2-[1-pyridin-2-ylmeth-(*E*)-ylidene]-2,3,3a,4,7,7a-hexahydro-4,7-methano inden-1-one, 14g. Following the procedure described above, ***exo*-12** (436 mg, 2.0 mmol, 1 eq.) in Et_2O (10 cm^3) was treated with a Me_2CuLi in Et_2O (25 cm^3) generated from CuI (381 mg, 2.0 mmol, 1 eq.) and a 1.6 M solution of MeLi in Et_2O (3.0 cm^3, 4.8 mmol, 2.4 eq.). After TLC indicated formation of the conjugate adduct, picolinaldehyde (321 mg, 3.0 mmol, 1.5 eq.) was added. Standard work-up, as above, followed by flash column chromatography (Hex-EtOAc; 9:1 $\rightarrow$ 1:1) afforded adduct ***E*-14g** (226 mg, 45%) as a yellow oil. R_f 0.3 (Hex-EtOAc; 1:1); δ_H (400 MHz, $CDCl_3$) 1.27 (3H, d, *J* 7.0 Hz, CH_2, CH_3), 1.37 (1H, d, *J* 9.0 Hz, CH_2), 1.95 (1H, d, *J* 7.5 Hz, CH), 2.49 (1H, d, *J* 7.5 Hz, CH), 2.89 (1H, s, CH), 3.10 (1H, s, CH), 3.64 (1H, q, *J* 7.0 Hz, CH), 6.20 (1H, dd, *J* 3.0, 5.5 Hz, CH), 6.25 (1H, dd, *J* 3.0, 5.5 Hz, CH), 7.16-7.21 (2H, m, CH, ArH), 7.43 (1H, d, *J* 7.5 Hz, ArH), 7.67 (1H, td, *J* 1.5, 7.5 Hz, ArH), 8.71 (1H, d, *J* 4.5 Hz, ArH); δ_C (100 MHz, $CDCl_3$) 22.1, 39.3, 43.2, 48.6, 49.1, 49.3, 53.5, 122.7, 127.5, 130.4, 136.2, 137.3, 139.2, 149.6, 149.9, 154.5, 210.1; m/z (CI) 252 (MH^+, 100%); Found 252.13876, $C_{17}H_{18}NO$ requires 252.13884 (-0.3 ppm).

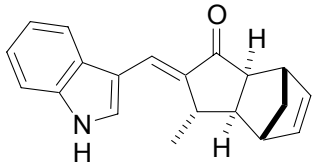


3-Methyl-2-[1-(1-methyl-1*H*-indol-3-yl)meth-(*E*)-ylidene]-2,3,3a,4,7,7a-hexahydro-4,7- methano-inden-1-one, 14h. Following the procedure described above, ***exo*-12** (436 mg, 2.0 mmol, 1 eq.) in Et_2O (10 cm^3) was treated with a Me_2CuLi in Et_2O (25 cm^3) generated from CuI (381 mg, 2 mmol, 1 eq.) and a 1.6 M solution of MeLi in Et_2O (3.0 cm^3, 4.8 mmol, 2.4 eq.). 1-Methyl-1*H*-indole-3-carbaldehyde[1] (477 mg, 3.0 mmol, 1.5 eq.) was then added. Standard work-up as above followed by flash column chromatography (Hex-Et_2O; 9:1) afforded adduct ***E*-14h** (79 mg, 13%) as a viscous yellow oil. R_f 0.45 (Hex-EtOAc; 1:1); δ_H (400 MHz, $CDCl_3$) 1.10-1.15 (H, m, CH_2), 1.21 (3H, d, *J* 7.0 Hz, CH_3), 1.23-1.27 (H, m, CH_2), 1.82 (1H, d, *J* 7.5 Hz, CH), 2.40 (1H, d, *J* 7.5 Hz, CH), 2.73 (1H, s, CH), 2.82 (1H, q, *J* 7.0 Hz, CH), 3.01 (1H, d, *J* 1.0 Hz, CH), 3.77 (3H, s, CH_3), 6.08 (1H, dd, *J* 3.0, 5.5 Hz, CH), 6.12 (1H, dd, *J* 3.0, 5.5 Hz, CH), 7.10-7.15 (1H, m, ArH), 7.16-7.25 (2H, m, ArH), 7.32 (1H, s, CH), 7.63 (1H, d, *J* 1.75 Hz, ArH), 7.75 (1H, d, *J* 7.5 Hz, ArH); δ_C (100 MHz, $CDCl_3$) 19.7, 33.5, 39.6, 43.0, 48.1, 48.7, 49.4, 53.7, 109.6, 111.0, 119.1, 121.0, 123.0, 124.4, 128.8, 130.8, 136.7, 137.5, 138.7, 139.6, 208.0; m/z (CI) 304 (MH^+, 100%); Found 304.17073, $C_{21}H_{22}NO$ requires 304.17014 (+2.2 ppm).

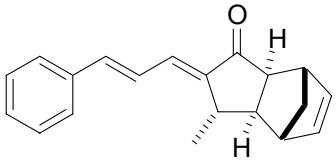


3-Methyl-2-[1-[1-(toluene-4-sulfonyl)-1*H*-indol-3-yl]meth-(*E*)-ylidene]-2,3,3a,4,7, 7a-hexahydro-4,7-methanoinden-1-one, 14i. Following the general procedure outlined, a solution of Me_2CuLi in Et_2O (75 cm^3), prepared from CuI (1.371 g, 7.2 mmol, 1.2 eq.) and a

1.6 M solution of MeLi in hexanes (9.0 cm^3, 14.4 mmol, 2.4 eq.), was treated with ***exo*-12** (1.308 g, 6.0 mmol, 1 eq.). On formation of the conjugate adduct (judged by TLC analysis), a solution of 1-toluene-4-sulfonyl-1*H*-indole-3-carbaldehyde[1] (2.70 g, 9.0 mmol, 1.5 eq.) in a 2:1 mixture of Et_2O and THF (20 cm^3) was added. Following standard work-up, as described above, purification by flash column chromatography (Hex-EtOAc; 1:1) afforded initially ***E*-14i** (2.200 g, 83%) as a yellow amorphous solid. M.pt. 92ºC; R_f 0.45 (Hex-EtOAc, 1:1); υ_{max} (neat/cm^{-1}) 3148, 3074, 2966, 1697, 1614, 1536, 1493, 1447, 1375; δ_H (400 MHz, $CDCl_3$) 1.13-1.17 (5H, m, CH_2, CH_3), 1.83 (1H, d, *J* 7.75 Hz, CH), 2.20 (3H, s, CH_3), 2.37 (1H, d, *J* 7.75 Hz, CH), 2.77 (H, s, CH), 2.86 (1H, q, *J* 7.0 Hz, CH), 2.98 (1H, s, CH), 6.07 (1H, dd, *J* 3.0, 5.5 Hz, CH), 6.12 (1H, dd, *J* 3.0, 5.5 Hz, CH), 7.10 (2H, d, *J* 8.5 Hz, ArH), 7.15 (1H, ddd, *J* 1.0, 7.0, 7.75 Hz, ArH), 7.21 (1H, ddd, *J* 1.0, 7.0, 8.0 Hz, ArH), 7.32 (1H, d, *J* 2.0 Hz, CH), 7.57 (1H, d, *J* 7.75 Hz, ArH), 7.64 (2H, d, *J* 8.5 Hz, ArH), 7.69 (1H, s, CH), 7.82 (1H, d, *J* 8.0 Hz, ArH); δ_C (100 MHz, $CDCl_3$) 19.5, 21.6, 39.5, 43.2, 48.4, 49.1, 49.4, 53.7, 113.6, 117.1, 119.5, 121.4, 123.9, 125.6, 126.2, 126.9, 130.1, 130.6, 134.5, 134.9, 137.5, 139.0, 145.4, 145.5, 208.1; m/z (EI) 466, (MNa^+, 100%), 400 (50%); Found 466.1439, $C_{27}H_{25}O_3NaS$ requires 466.1453 (-3.0 ppm).

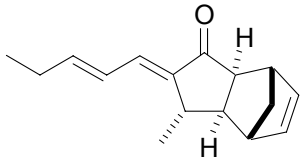


Further elution afforded the corresponding de-tosylated adduct (220 mg, 8%) as a yellow solid. M.pt. 97-99ºC; R_f 0.3 (Hex-EtOAc, 1:1); υ_{max} (neat/cm^{-1}) 3251, 3057, 2965, 2870, 1673, 1590, 1574, 1516, 1492, 1459, 1381, 1367, 1327, 1238; δ_H (400 MHz, $CDCl_3$) 1.17 (1H, dd, *J* 1.0, 8.5 Hz, CH_2), 1.24 (3H, d, *J* 7.0 Hz, CH_3), 1.30 (H, d, *J* 8.5 Hz, CH_2), 1.87 (1H, d, *J* 7.5 Hz, CH), 2.45 (1H, d, *J* 7.5 Hz, CH), 2.77 (1H, s, CH), 2.87 (1H, q, *J* 7.0 Hz, CH), 3.07 (1H, d, *J* 1.0 Hz, CH), 6.14 (1H, dd, *J* 2.75, 5.5 Hz, CH), 6.16 (1H, dd, *J* 2.75, 5.5 Hz, CH), 7.16 (1H, ddd, *J* 1.0, 7.0, 7.5 Hz, ArH), 7.20 (1H, ddd, *J* 1.0, 7.0, 7.5 Hz, ArH), 7.35 (1H, dd, *J* 1.0, 7.5 Hz, ArH), 7.52 (1H, d, *J* 2.0 Hz, ArH), 7.69 (1H, d, *J* 2.0 Hz, CH), 7.79 (1H, d, *J* 7.5 Hz, ArH), 8.70 (1H, s, NH); δ_C (100 MHz, $CDCl_3$) 19.8, 39.7, 43.1, 48.2, 48.9, 49.5, 53.8, 111.4, 112.6, 119.1, 121.3, 123.4, 124.5, 126.3, 128.1, 135.7, 137.6, 138.8, 140.7, 208.2; m/z (CI) 290 (MH^+, 100%); Found 290.15473, $C_{20}H_{20}NO$ requires 290.15449 (+2.0 ppm).



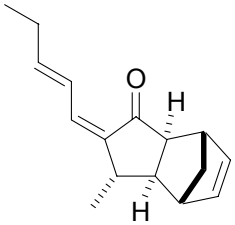
2-[2-Methyl-2-[(*E*)-3-phenylprop-2-en-(*E*)-ylidene]-2,3,3a,4,7,7a-hexahydro-4,7-methanoinden-1-one, 14j. Following the general procedure outlined above, a solution of Me_2CuLi in Et_2O (25 cm^3), prepared from CuI (1.371 g, 7.2 mmol, 1.2 eq.) and a 1.6 M solution of MeLi in hexanes (9.0 cm^3, 13.2 mmol, 2.4 eq.), was treated with ***exo*-12** (1.308 g, 6.0 mmol, 1 eq.). On formation of the conjugate adduct (judged by TLC analysis), a solution of cinnamaldehyde (1.13 cm^3, 8.58 mmol, 1.5 eq.) was added. Following standard work-up, purification by flash column chromatography (Hex-Et_2O; 9:1) afforded adduct ***E,E*-14j** (1.126 g, 68%) as a yellow viscous oil; R_f 0.2 (Hex-Et_2O; 9:1); υ_{max} (neat/cm^{-1}) 3058, 2967, 2873, 1695, 1602, 1589, 1494, 1449, 1421; δ_H (400 MHz, $CDCl_3$) 1.27-1.31 (5H, m, CH_3, CH_2), 1.85 (H, d, *J* 7.5 Hz, CH), 2.48 (H, d, *J* 7.5 Hz, CH), 2.84 (1H, s, CH), 2.90 (1H, q, *J* 7.5 Hz, CH), 3.10 (1H, s, CH), 6.17-6.24 (2H, m, CH), 6.93 (1H, m, CH), 6.95 (1H, m, CH), 7.02-7.06 (1H, m, CH), 7.25-7.38 (3H, m, ArH), 7.46-7.51 (2H, m, ArH); δ_C (100 MHz, $CDCl_3$) 24.0, 38.3, 43.1, 48.2, 49.0, 49.3, 54.5, 121.1, 127.2, 128.8, 129.1, 132.7, 136.4, 137.5, 138.8, 142.0,

146.0, 208.2; m/z (CI) 276 (MH^+, 100%); Found 277.15954, $C_{20}H_{21}O$ requires 277.15924 (+1.2 ppm).

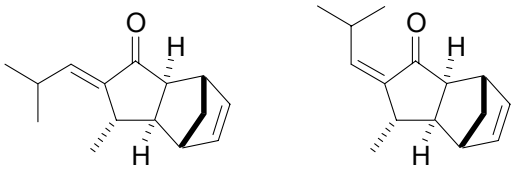


3-Methyl-2-[(*E*)-pent-2-en-(*E*)-ylidene]-2,3,3a,4,7,7a-hexahydro-4,7-methano-inden-1-one, 14k. Following the general procedure outlined above, a solution of Me_2CuLi in Et_2O (25 cm^3); prepared from CuI (457 mg, 2.4 mmol, 1.2 eq.) and a 1.6 M solution of MeLi in hexanes (3.0 cm^3, 4.8 mmol, 2.4 eq), was treated with ***exo*-12** (436 mg, 2.0 mmol, 1 eq.). On formation of the conjugate adduct (judged by TLC analysis), *E*-pent-2-enal (0.3 cm^3, 3.0 mmol, 1.5 eq.) was added. Following the standard work-up as described above, purification by flash column chromatography (Hex-Et_2O; 9:1) afforded initially ***Z,E*-14k** (50 mg, 11%) as a yellow viscous oil followed by ***E,E*-14k** (350 mg, 77%) as a viscous yellow oil; R_f 0.2 (Hex-Et_2O; 9:1); υ_{max} (neat/cm^{-1}) 3060, 2966, 2875, 2360, 1702, 1627, 1600, 1459, 1377, 1327, 1277, 1244, 1210; δ_H (400 MHz, $CDCl_3$) 1.00 (3H, t, *J* 7.5 Hz, CH_3), 1.15 (3H, d, *J* 7.5 Hz, CH_3), 1.18-1.22 (2H, m, CH_2), 1.74 (1H, d, *J* 7.5 Hz, CH), 2.12-2.21 (2H, m, CH_2), 2.36 (1H, d, *J* 7.5 Hz, CH), 2.70 (1H, q, *J* 7.5 Hz, CH), 2.73 (1H, s, CH), 2.99 (1H, d, *J* 1.0 Hz, CH), 6.09-6.18 (4H, m, CH), 6.76-6.81 (1H, m, CH); δ_C (100 MHz, $CDCl_3$) 12.9, 23.6, 26.5, 38.0, 43.1, 48.1, 48.9, 49.3, 54.4, 125.3, 133.3, 137.5, 138.8, 143.8, 148.1, 208.5; m/z (CI) 229 (MH^+, 100%), found 229.15899, $C_{16}H_{21}O$ requires 229.15924 (-1.1 ppm).

Data for ***Z,E*-14k**: R_f 0.35 (Hex-Et_2O; 9:1); δ_H (400 MHz, $CDCl_3$) 1.06 (3H, t, *J* 7.5 Hz, CH_3), 1.22 (3H, d, *J* 7.25 Hz, CH_3), 1.25-1.29 (1H, m, CH_2), 1.31-1.35 (1H, m, CH_2), 1.76 (1H, dd, *J* 3.0, 8.25 Hz, CH), 2.17-2.28 (1H, m, CH_2), 2.36 (1H, d, *J* 8.25 Hz, CH), 2.42-2.52 (1H, m, CH), 2.78 (1H, s, CH), 3.10 (1H, s, CH), 6.06 (1H, dt, *J* 6.5, 15.0 Hz, CH), 6.16-6.21 (2H, m, CH), 6.25 (1H, dd, *J* 1.5, 11.0 Hz, CH), 7.54 (1H, ddt, *J* 1.5, 11.0, 15.0 Hz, CH); δ_C (100 MHz, $CDCl_3$) 13.1, 24.0, 26.1, 40.8, 43.4, 47.7, 48.1, 48.9, 55.6, 126.1, 137.4, 137.7, 138.5, 146.5, 148.1, 208.5; m/z (CI) 229 (MH^+, 100%); Found 229.15921, $C_{16}H_{21}O$ requires 229.15924 (-0.1 ppm).



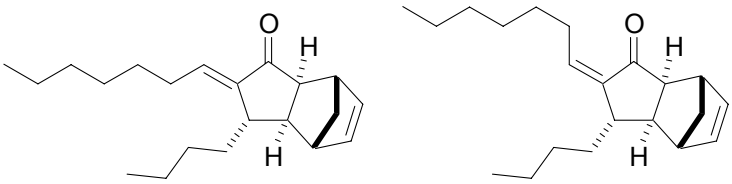
3-Methyl-2-[(*E*)-pent-2-en-(*Z*)-ylidene]-2,3,3a,4,7,7a-hexahydro-4,7-methano-inden-1-one, 14k. Following the general procedure described above, a solution of enone ***exo*-12** (1.308 g, 6.0 mmol, 1 eq.) in Et_2O (25 cm^3) was treated with a 1M solution of methyl magnesium bromide in Et_2O (9.0 cm^3, 9.0 mmol, 1.5 eq.) that had been pre-mixed with CuI (125 mg, 0.66 mmol, 0.1 eq.) in Et_2O (50 cm^3). After the formation of conjugate adduct, *E*-pent-2-enal (0.9 cm^3, 9.0 mmol, 1.5 eq.) was added at -78ºC. Following standard work-up, purification by flash column chromatography (Hex-Et_2O; 9:1) initially ***Z,E*-14k** (240 mg, 14%) was isolated as a yellow viscous oil followed by ***E,E*-14k** (1.130 g, 83%) as a yellow oil. Data as given above.



3-Methyl-2-[2-methyl-prop-(*E*/*Z*)-ylidene]-2,3,3a,4,7,7a-hexahydro-4,7-methano-inden-1-one, 14l. Following the procedure described above, a solution of Me_2CuLi in Et_2O (75 cm^3), prepared from CuI (1.371 g, 7.2 mmol, 1.2 eq.) and a 1.6 M solution of MeLi in hexanes (9.0 cm^3, 14.4 mmol, 2.4 eq.), was treated with ***exo*-12** (1.308 g, 6.0 mmol, 1 eq.). After the formation of conjugate adduct, isobutyraldehyde (662 mg, 9.0 mmol, 1.5 eq.) was added at -78ºC. Following standard work-up, purification by flash column chromatography (Hex-Et_2O; 9:1) afforded initially ***Z*-14l** (261 mg, 20%) followed by ***E*-14l** (531 mg, 41%) both as a yellow oil. R_f 0.25 (Hex-Et_2O; 9:1); υ_{max} (neat/cm^{-1}) 3065, 2960, 2869, 1710, 1640, 1568, 1460; δ_H (400 MHz, $CDCl_3$) 1.01 (3H, d, *J* 7.0 Hz, CH_3), 1.05 (3H, d, *J* 7.0 Hz, CH_3), 1.18 (3H, d, *J* 7.0 Hz, CH_3), 1.23-1.31 (2H, m, CH_2), 1.78 (1H, d, *J* 7.5 Hz, CH), 2.40 (1H, d, *J* 7.5 Hz, CH), 2.48-2.60 (1H, m, CH), 2.67 (1H, m, CH), 2.80 (1H, s, CH), 3.03 (1H, d, *J* 1.5 Hz, CH), 6.14-6.21 (2H, m, CH), 6.28 (1H, dd, *J* 2.0, 11.0 Hz, CH), δ_C (100 MHz, $CDCl_3$) 21.9, 22.1, 23.7, 28.5, 37.6, 42.9, 47.9, 48.7, 49.3, 54.2, 137.4, 138.7, 143.7, 144.1, 208.7; m/z (CI) 217 (MH^+, 100%); Found 217.15904, $C_{15}H_{21}O$ requires 217.15924 (-0.9 ppm). Data for ***Z*-14l**: R_f 0.35 (Hex-Et_2O, 9:1); υ_{max} (neat/cm^{-1}) 3064, 2959, 2870, 1711, 1640, 1568, 1460; δ_H (400 MHz, $CDCl_3$) 0.94 (3H, d, *J* 7.0 Hz, CH_3), 0.96 (3H, d, *J* 7.0 Hz, CH_3), 1.17 (3H, d, *J* 7.0 Hz, CH_3), 1.29-1.33 (2H, m, CH_2), 1.73 (1H, dd, *J* 3.5, 8.0 Hz, CH), 2.30 (1H, d, *J* 8.0 Hz, CH), 2.31-2.43 (1H, m, CH), 2.76 (1H, s, CH), 3.01-3.09 (1H, m, CH), 3.63-3.77 (1H, m, CH), 5.64 (1H, dd, *J* 2.0, 10.0 Hz, CH), 6.14-6.21 (2H, m, CH); δ_C (100 MHz, $CDCl_3$) 22.4, 22.5, 24.1, 26.2, 40.4, 43.4, 47.5, 48.0, 48.8, 55.2, 137.6, 138.5, 143.0, 148.3, 208.9; m/z (CI) 217 (MH^+, 100%), found 217.15904, $C_{15}H_{21}O$ requires 217.15924 (-0.9 ppm).

3-Methyl-2-[2-methyl-prop-(*Z*/*E*)-ylidene]-2,3,3a,4,7,7a-hexahydro-4,7-methano-inden-1-one, 14l. Following the procedure described above, a solution of enone ***exo*-12** (1.308 g, 6.0 mmol, 1 eq.) in Et_2O (25 cm^3) was treated with a 1M solution of methyl magnesium bromide in Et_2O (9.0 cm^3, 9.0 mmol, 1.5 eq.) that was pre-mixed with CuI (125 mg, 0.66 mmol, 0.1 eq.) in Et_2O (50 cm^3). Following formation of conjugate adduct, isobutyraldehyde (662 mg, 9.0 mmol, 1.5 eq.) was added at -78ºC. Standard work-up, as described above, and purification by flash column chromatography (Hex-Et_2O; 9:1) afforded initially the ***Z*-14l** (752 mg, 58%) and then ***E*-14l** (326 mg, 25%) both as a yellow oil, with consistent spectroscopic data (as above).

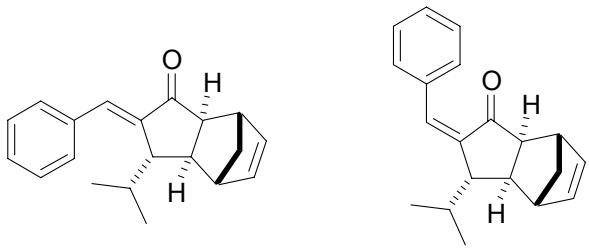
3-Methyl-2-[2-methyl-prop-(*Z*/*E*)-ylidene]-2,3,3a,4,7,7a-hexahydro-4,7-methano-inden-1-one, 14l. A solution of Me_2CuLi in Et_2O (75 cm^3), prepared from CuI (1.371 g, 7.2 mmol, 1.2 eq.) and a 1.6 M solution of MeLi in hexanes (9.0 cm^3, 14.4 mmol, 2.4 eq.), was treated with ***exo*-12** (1.308 g, 6.0 mmol, 1 eq.). After the formation of conjugate adduct, a solution of $ZnCl_2$ in Et_2O (12 cm^3, 12 mmol, 2.0 eq.) was added at -78ºC, which followed the addition of isobutyraldehyde (662 mg, 9.0 mmol, 1.5 eq.). The reaction was allowed to warm under stirring to room temperature over 6 h. Following standard work-up, purification by flash column chromatography (Hex-Et_2O; 9:1) afforded initially ***Z*-14l** (301 mg, 23%) followed by ***E*-14l** (76 mg, 6%) with consistent spectroscopic data (as above).



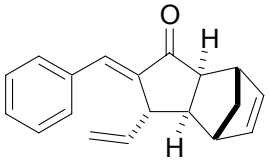
3-Butyl-2-hept-(*E/Z*)-ylidene-2,3,3a,4,7,7a-hexahydro-4,7-methanoinden-1-one, 14m. As described, under N_2 a slurry of copper(I) iodide (17.4 mg, 0.09 mmol, 0.1 eq.) in Et_2O (20 cm^3) was cooled to -78˚C and 2 M BuMgCl in Et_2O (0.69 cm^3, 1.37 mmol, 1.5 eq.) was added dropwise. The reaction vessel was allowed to warm to -20˚C over 1 hour, before ***exo*-12** (200 mg, 0.92 mmol, 1 eq.) dissolved in Et_2O (15 cm^3), was added. The reaction vessel was kept between -20˚C and -5˚C for 1 hour before being re-cooled to -78˚C and heptanal (0.19 cm^3, 1.37 mmol, 1.5 eq.) was added. The reaction vessel was allowed to warm to room temperature and stir for 12 hours. Aqueous ammonium chloride (30 cm^3) and Et_2O (30 cm^3) were then added and the resultant aqueous layer was further extracted with Et_2O (3 x 30 cm^3). The combined organic phases were then dried with $MgSO_4$ filtered and reduced *in vacuo* to yield the crude products as a yellow oil (228 mg, 83%, *Z*:*E*; 70:30). Purification by flash column chromatography (*c*-Hex-EtOAc; 98:2) led to partial separation of the products. ***Z*-14m**: R_f 0.4 (*c*-Hex-EtOAc; 19:1); υ_{max} (cm^{-1}/neat) 2956, 2925, 2856, 1734, 1709, 1637, 1459, 1378, 1327; δ_H (400 MHz, $CDCl_3$) 0.78-0.84 (6H, m, CH_3), 1.16-1.31 (16H, m, CH_2), 1.75 (1H, d, *J* 8.0 Hz, CH), 2.18-2.26 (2H, m, CH), 2.55-2.62 (2H, m, CH_2), 2.65 (1H, s, CH), 2.98 (1H, s, CH), 5.82 (1H, dt, *J* 1.5, 7.5 Hz, CH), 6.09-6.15 (2H, m, CH); δ_C (100 MHz, $CDCl_3$) 14.0, 22.6, 22.9, 28.1, 28.6, 29.0, 29.4, 31.6, 38.5, 36.6, 43.3, 45.8, 47.7, 47.8, 49.4, 55.5, 137.6, 138.5, 142.5, 148.3, 200.1; m/z (CI) 301 (MH^+, 100%); Found 301.25390, $C_{21}H_{33}O$ requires 301.25314 (+2.6 ppm); Data for ***E*-14m**: R_f 0.35 (*c*-Hex-EtOAc; 19:1); υ_{max} (cm^{-1}/neat) 3061, 2957, 2856, 1710, 1638, 1459, 1378, 1260, 714; δ_H (400 MHz, $CDCl_3$) 0.88-0.90 (6H, m, CH_3), 1.28-1.49 (16H, m, CH_2), 1.90 (1H, d, *J* 7.5 Hz, CH), 2.14-2.20 (2H, m, CH_2), 2.36 (1H, d, *J* 7.5 Hz, CH), 2.58-2.62 (1H, m, CH), 2.75 (1H, s, CH), 3.03 (1H, s, CH), 6.16-6.24 (2H, m, CH), 6.50 (1H, dt, *J* 1.5, 7.5 Hz, CH); δ_C (100 MHz, $CDCl_3$) 14.0, 22.8, 26.9, 28.6, 29.1, 29.3, 31.6, 31.9, 36.6, 42.9, 43.1, 46.0, 46.6, 48.0, 49.6, 54.4, 137.4, 138.3, 143.7, 144.1, 195.7; m/z (CI) 301 (MH^+, 100%), found 301.25361, $C_{21}H_{33}O$ requires 301.25314 (+1.6 ppm).

3-Butyl-2-hept-(*E*)-ylidene-2,3,3a,4,7,7a-hexahydro-4,7-methanoinden-1-one

14m: Under N_2, a slurry of copper(I) iodide (0.21 g, 1.10 mmol, 1.2 eq.) in THF (20 cm^3). was cooled to -78˚C and 1.6 M butyl lithium in THF (1.4 cm^3, 2.21 mmol, 2.4 eq.) was added drop-wise. The reaction vessel was allowed to warm up to -10˚C over 1 hour before being re-cooled to -20˚C. A solution of ***exo*-12** (0.20 g, 0.92 mmol, 1 eq.) in THF (10 cm^3) was added dropwise. The reaction was warmed to -5˚C over 1 hour before being re-cooled to -78˚C and heptanal (0.15 cm^3, 1.10 mmol, 1.2 eq.) was added dropwise. The reaction was stirred for 15 hours while gradually warming to room temperature. Aqueous ammonium chloride (30 cm^3) and Et_2O (30 cm^3) were added to the reaction mixture and the aqueous layer was further extracted with Et_2O (2 x 30 cm^3) and the combined organic layers were dried with $MgSO_4$ and concentrated *in vacuo*. Purification by flash column chromatography (*c*-Hex-EtOAc; 19:1) afforded the product (226 mg, 82%) as a yellow oil with consistent data as given above.

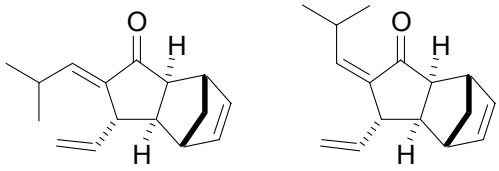


3-Isopropyl-2-[1-phenylmeth-(*E/Z*)-ylidene]-2,3,3a,4,7,7a-hexahydro-4,7-methano-inden-1-one, 14n. At -78ºC under nitrogen a slurry of CuI (45.7 mg, 0.24 mmol, 0.1 eq.) in Et_2O (25 cm^3) was treated dropwise with a 2 M solution of isopropyl magnesium chloride in THF (1.4 cm^3, 2.8 mmol, 1.4 eq.). The reaction was warmed to -20ºC over a period of 1 h. This solution was cooled to -45ºC before a solution of the enone ***exo*-12** (436 mg, 2.0 mmol, 1.0 eq.) in Et_2O (10 cm^3) was added dropwise over a period of 2 min. The reaction was warmed to 0ºC over a period of 1.5 h. Upon cooling to -78ºC, benzaldehyde (0.31 cm^3, 3.00 mmol, 1.5 eq.) was added. The reaction was stirred overnight and allowed to warm from -78ºC to 10ºC. Saturated aqueous NH_4Cl (25 cm^3) was added and the resultant aqueous phase was further extracted with Et_2O (5 x 25 cm^3). The combined organic extracts were dried over $MgSO_4$, filtered and the solvent removed *in vacuo*. The crude product was purified by flash column chromatography (Hex-Et_2O; 19:1) affording initially ***Z*-14n** (187 mg 34%) as a viscous yellow oil followed by ***E*-14n** (260 mg 47%) as a colourless solid. M.pt. 101ºC, R_f 0.15 (Hex-EtOAc; 19:1); υ_{max} (neat/cm^{-1}) 3060, 2959, 2926, 2872, 1704, 1613, 1574, 1494, 1462, 1448, 1368, 1327, 1287; δ_H (400 MHz, $CDCl_3$) 0.67 (3H, d, *J* 7.0 Hz, CH_3), 1.07 (3H, d, *J* 7.0 Hz, CH_3), 1.28 (1H, dt, *J* 1.5, 9.0 Hz, CH_2), 1.39 (1H, d, *J* 9.0 Hz, CH_2), 2.10 (1H, d, *J* 7.5 Hz, CH), 2.17-2.25 (1H, m, CH), 2.36 (1H, d, *J* 7.5 Hz, CH), 2.74 (1H, s, CH), 3.08-3.14 (2H, m, CH), 6.21-6.30 (2H, m, CH), 7.33 (1H, d, *J* 2.5 Hz, CH), 7.34-7.43 (3H, m, ArH), 7.56 (2H, d, *J* 7.5 Hz, ArH); δ_C (100 MHz, $CDCl_3$) 16.8, 20.7, 30.3, 40.6, 43.4, 48.6, 49.9, 50.1, 54.2, 128.8, 129.3, 130.6, 133.7, 135.1, 137.6, 139.0, 143.9, 209.2; m/z (CI) 279 (MH^+, 100%); Found 279.17397, $C_{20}H_{23}O$ requires 279.17487 (-3.3 ppm); Data for ***Z*-14n**: R_f 0.25 (Hex-EtOAc; 19:1); υ_{max} (neat/cm^{-1}) 3060, 2959, 2926, 2872, 1704, 1613, 1574, 1494, 1462, 1448, 1368, 1327, 1287; δ_H (400 MHz, $CDCl_3$) 0.88 (3H, d, *J* 7.0 Hz, CH_3), 1.01 (3H, d, *J* 7.0 Hz, CH_3), 1.29 (1H, ddd, *J* 1.25, 1.5, 9.0 Hz, CH_2), 1.52 (1H, d, *J* 9.0 Hz, CH_2), 1.92-2.02 (2H, m, CH), 2.34 (1H, dd, *J* 0.5, 8.0 Hz, CH), 2.48-2.52 (1H, m, CH), 2.73 (1H, s, CH), 3.05 (1H, s, CH), 6.17-6.26 (2H, m, CH), 6.63 (1H, d, *J* 2.0 Hz, CH), 7.29-7.38 (3H, m, ArH), 7.81-7.85 (2H, m, ArH); δ_C (100 MHz, $CDCl_3$) 16.4, 19.8, 35.6, 41.4, 43.4, 48.3, 49.8, 54.1, 56.1, 127.9, 129.3, 130.4, 135.0, , 137.5, 137.7, 137.9, 138.7, 138.8, 143.3, 221.2; m/z (CI) 279 (MH+, 100%); Found 279.17391, $C_{20}H_{23}O$ requires 279.17487 (-2.5 ppm).

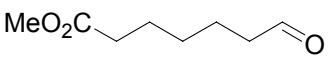


2-[1-Phenylmeth-(*E*)-ylidene]-3-vinyl-2,3,3a,4,7,7a-hexahydro-4,7-methanoinden-1-one, 14o. Following the procedure described above, at -78°C, CuI (45.7 mg, 0.24 mmol, 0.1 eq.) in Et_2O (25 cm^3) was treated dropwise with a 1 M solution of vinyl magnesium bromide in Et_2O (4.2 cm^3, 4.2 mmol, 1.4 eq.). The reaction was warmed to -20ºC over a period of 1 h. This solution was cooled to -45ºC before a solution of the enone ***exo*-12** (654 mg, 3.0 mmol, 1.0 eq.) in Et_2O (10 cm^3) was added dropwise over a period of 3 min. The reaction was warmed to 0ºC over a period of 1.5 h. Upon cooling to -78ºC, benzaldehyde (0.50 cm^3, 4.5 mmol, 1.5 eq.) was added. Standard work-up as above followed by flash column chromatography afforded initially ***Z*-14o** (52 mg, 7%) as a viscous yellow oil then ***E*-14o** (687

mg, 87%) as a viscous yellow oil. R_f 0.15 (Hex-EtOAc; 19:1); υ_{max} (neat/cm^{-1}) 3059, 2967, 2875, 1705, 1614, 1574, 1493, 1449, 1406, 1327, 1289, 1238; δ_H (400 MHz, $CDCl_3$) 1.22 (1H, dt, *J* 1.5, 9.0 Hz, CH_2), 1.30 (1H, d, *J* 9.0 Hz, CH_2), 2.07 (1H, d, *J* 7.75 Hz, CH), 2.40 (1H, d, *J* 7.75 Hz, CH), 2.83 (1H, s, CH), 3.05 (1H, s, CH), 3.55 (1H, d, *J* 6.0 Hz, CH), 4.89-4.97 (2H, m, CH_2), 5.88 (1H, ddd, *J* 6.0, 10.5, 16.75 CH), 6.12-6.20 (2H, m, CH), 7.24-7.33 (3H, m, ArH), 7.41 (1H, d, *J* 2.0 Hz), 7.47-7.52 (2H, m, ArH); δ_C (100 MHz, $CDCl_3$) 43.1, 47.9, 48.0, 48.3, 49.4, 52.7, 114.4, 128.5, 129.7, 131.3, 134.4, 135.6, 137.6, 138.7, 138.8, 140.4, 208.5; m/z (CI) 263, (MH^+, 100%); Found 263.14430, $C_{19}H_{19}O$ requires 263.14359 (+4.4 ppm).

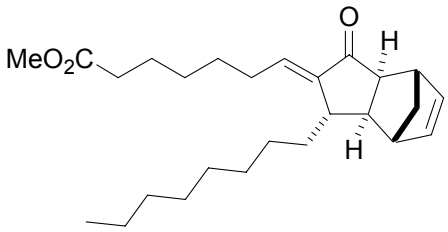


2-[2-Methylprop-(*E*/*Z*)-ylidene]-3-vinyl-2,3,3a,4,7,7a-hexahydro-4,7-methano-inden-1-one, 14p. Following the procedure described above, a solution of enone ***exo*-12** (654 mg, 3.0 mmol, 1 eq.) in Et_2O (25 cm^3) was treated with a 1M solution of vinyl magnesium bromide in Et_2O (4.2 cm^3, 4.2 mmol, 1.4 eq.) that had been pre-mixed with CuI (5.7 mg, 0.03 mmol, 0.01 eq.). After the formation of conjugate adduct, isobutyraldehyde (0.4 cm^3, 4.5 mmol, 1.5 eq.) was added at -78ºC. Following standard work-up, purification by flash column chromatography (Hex-Et_2O, 9:1) afforded initially ***Z*-14p** (289 mg, 48%) as a yellow oil followed by ***E*-14p** (314 mg, 52%) as a yellow oil. R_f 0.2 (Hex-Et_2O; 9:1); υ_{max} (neat/cm^{-1}) 3060, 2964, 2869, 1710, 1636, 1568, 1460, 1382, 1361, 1327, 1287, 1215; δ_H (400 MHz, $CDCl_3$) 0.98 (3H, d, *J* 6.5 Hz, CH_3), 0.99 (3H, d, *J* 6.5 Hz, CH_3), 1.31-1.45 (2H, m, CH_2), 1.97 (1H, dd, *J* 1.5, 8.0 Hz, CH), 2.39 (1H, d, *J* 8.0 Hz, CH), 2.50-2.64 (1H, m, CH), 2.86 (1H, d, *J* 1.0 Hz, CH), 3.07 (1H, d, *J* 1.0 Hz, CH), 3.19 (1H, d, *J* 8.0 Hz, CH), 4.97 (1H, ddd, *J* 1.0, 1.25, 10.0 Hz, CH_2), 5.02 (1H, ddd, *J* 1.0, 1.25, 17.0 Hz, CH_2), 5.83 (1H, ddd, *J* 8.0, 10.0, 17.0 Hz, CH), 6.16-6.22 (2H, m, CH), 6.44 (1H, dd, *J* 2.5, 10.5 Hz, CH); δ_C (100 MHz, $CDCl_3$) 21.4, 21.6, 28.1, 43.1, 47.1, 47.5, 48.0, 49.3, 54.1, 113.1, 137.8, 138.5, 139.8, 141.2, 146.7, 207.8; m/z (CI) 246 MNH_4^+, 25%), 229 (MH^+, 100%); Found 229.15909, $C_{16}H_{21}O$ requires 229.15924 (-0.7 ppm). Data for ***Z*-14p**: R_f 0.4 (Hex-Et_2O; 9:1); υ_{max} (neat/cm^{-1}) 3062, 2964, 2870, 1715, 1638, 1566, 1464, 1382, 1361, 1327, 1287, 1216; δ_H (400 MHz, $CDCl_3$) 0.96 (3H, d, *J* 6.5 Hz, CH_3), 0.98 (3H, d, *J* 6.5 Hz, CH_3), 1.32-1.40 (2H, m, CH_2), 1.97 (1H, dd, *J* 3.5, 8.5 Hz, CH), 2.32 (1H, d, *J* 8.5 Hz, CH), 2.83 (1H, s, CH), 2.89-2.95 (1H, m, CH), 3.12 (1H, d, *J* 1.0 Hz, CH), 3.67-3.80 (1H, m, CH), 5.00-5.06 (2H, m, CH_2), 5.65 (1H, dd, *J* 2.2, 10.0 Hz, CH), 5.70-5.80 (1H, m, CH), 6.17-6.22 (2H, m, CH); δ_C (100 MHz, $CDCl_3$) 22.4, 22.5, 26.3, 43.6, 46.1, 47.5, 48.5, 50.8, 55.3, 114.2, 137.9, 138.3, 140.0, 142.1, 150.9, 208.1; m/z (CI) 246 (NH_4^+, 25%), 163 (MH^+, 100%); Found 229.15943, $C_{16}H_{21}O$ requires 229.15924 (+0.9 ppm).

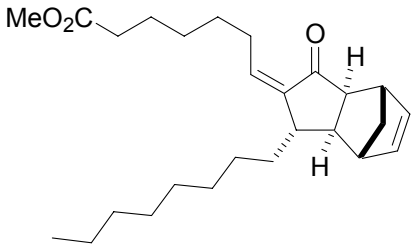


Methyl 6-formylhexanoate.[2] At 0°C cycloheptanone (5.0 cm^3, 42.61 mmol, 1 eq.), trimethyl orthoformate (5.2 cm^3, 46.88 mmol, 1.1 eq.) and anhydrous TsOH (40 mg, 0.213 mmol, 0.05 eq.) were allowed to warm to room temperature and left to stand for 2 d. ^{1}H-NMR spectroscopy of the crude product indicated formation of the intermediate ketal. Distillation, initially at atmospheric pressure, then at water aspirator pressure (*ca.* 15 mmHg) afforded 1-methoxycycloheptene (3.82 g, 71%) as a colourless liquid. B.pt. 130-140°C (15 mmHg); δ_H (250 MHz, $CDCl_3$) 1.35-1.55 (4H, m, CH_2), 1.59-1.74 (2H, m, CH_2), 1.97-2.08 (2H, m, CH_2), 2.12-2.25 (2H, m, CH_2), 3.39 (3H, s, CH_3), 4.67 (1H, t, *J* 7.0 Hz, CH); m/z (CI) 127 (MH^+, 100%). A solution of 1-methoxycycloheptene (4.68 g, 0.037 mol, 1 eq.) in DCM (50 cm^3) was cooled to –78°C and treated with a stream of ozone for 4 h. During this period the temperature

rose to –20°C. Dimethylsulfide (15 cm^3, 0.204 mol, 5.5 eq.) was added and the reaction was left to stir at room temperature for 48 h. Under reduced pressure the DCM and excess dimethylsulfide were removed before purification by flash column chromatography (Hex-EtOAc; 1:1), followed by distillation to afford methyl 6-formylhexanoate (1.52 g, 26%) as a colourless liquid. B.pt. 95-105°C (15 mmHg); R_f 0.1 (streak) (Hex-EtOAc; 1:1); δ_H (400 MHz, $CDCl_3$) 1.33-1.42 (2H, m, CH_2), 1.65 (4H, pent, *J* 7.5 Hz, CH_2), 2.32 (2H, t, *J* 7.5 Hz, CH_2), 2.45 (2H, dt, *J* 1.5, 7.5 Hz, CH_2), 3.64 (3H, s, CH_3), 9.79 (1H, m, CHO); δ_C (100 MHz, $CDCl_3$) 21.6, 24.5, 28.5, 33.7, 43.5, 51.3, 173.8, 202.2; m/z (CI) 176 (MNH_4^+, 100%), 159 (MH^+, 70%).

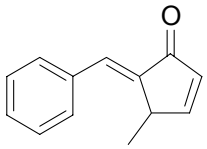


(±)-7-[1-Octyl-3-oxo-1,3,3a,4,7,7a-hexahydro-4,7-methanoinden-(2*E*)-ylidene] heptanoic acid methyl ester, *E*-14q. Under nitrogen at -78°C a solution of octyl iodide (0.63 cm^3, 3.49 mmol, 2 eq.) in a mixture of pentane (15 cm^3) and Et_2O (7.5 cm^3) was treated dropwise with a 1.7 M solution of *tert*-butyllithium in pentane (4.1 cm^3, 6.97 mmol, 4 eq.). After stirring at -78°C for 0.25 h the reaction was warmed to room temperature over 1.5 h. The cloudy white solution was re-cooled to -78°C and then added *via* cannula to a -78°C slurry of CuI (333 mg, 1.75 mmol, 1 eq.) in Et_2O (10 cm^3). The resultant black/brown octyl cuprate solution was warmed from -78°C to -20°C over a period of 1 h. The cuprate was then cooled to -40°C before enone ***exo*-12** (381 mg, 1.75 mmol, 1 eq.) in Et_2O (5 cm^3, washed with 2 cm^3) was added dropwise. Over 1.25 h the temperature rose to –10°C and TLC analysis (Hex-EtOAc; 19:1) indicated consumption of enone. The resulting enolate was re-cooled to –78°C and methyl 6-formylhexanoate (415 mg, 2.63 mmol, 1.5 eq.) was added dropwise. Stirring was continued for 5 h. During this time the temperature rose from –78°C to –10°C. Saturated NH_4Cl (50 cm^3) was added and the resultant mixture was extracted with EtOAc (3 x 50 cm^3). The combined organic extracts were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. Purification by flash column chromatography (Hex-EtOAc; 9:1) afforded the *title compound* **14q** (567 mg, 81%) as a colourless liquid. R_f 0.15 (Hex-EtOAc; 9:1); υ_{max} (neat/cm^{-1}) 2926, 2860, 1738, 1710, 1640, 1461; δ_H (400 MHz, $CDCl_3$) 0.88 (3H, t, *J* 6.5 Hz, CH_3), 1.21-1.43 (18H, m, CH_2), 1.49 (2H, pent, *J* 7.5 Hz, CH_2), 1.65 (2H, pent, *J* 7.5 Hz, CH_2), 1.90 (1H, d, *J* 7.75 Hz, CH), 2.13-2.20 (2H, m, CH_2), 2.30 (2H, t, *J* 7.5 Hz, CH_2), 2.36 (1H, d, *J* 7.75 Hz, CH), 2.57 (1H, d (br), *J* 7.5 Hz, CH), 2.74 (1H, s (br), CH), 3.04 (1H, s (br), CH), 3.67 (3H, s, CH_3), 6.17 (1H, dd, *J* 3.0, 5.5 Hz, CH), 6.23 (1H, dd, *J* 3.0, 5.5 Hz, CH), 6.47 (1H, dt, *J* 2.0, 8.0 Hz, CH); δ_C (100 MHz, $CDCl_3$) 14.0, 22.59, 24.7, 26.4, 28.3, 28.9, 29.1, 29.2, 29.5, 29.8, 31.8, 33.9, 36.9, 42.9, 43.0, 46.0, 48.0, 49.6, 51.4, 54.4, 137.4, 137.5, 138.8, 145.5, 173.9, 208.2; m/z (CI) 418 (MNH_4^+, 5%), 401 (MH^+, 10%), 335 ($M\text{-}C_5H_6^+$, 100%); Found 401.30622, $C_{26}H_{41}O_3$ requires 401.30557 (+1.8 ppm).



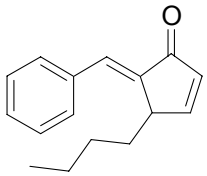
(±)-7-[1-Octyl-3-oxo-1,3,3a,4,7,7a-hexahydro-4,7-methanoinden-(2*Z*)-ylidene] heptanoic acid methyl ester, *Z*-14q. Under nitrogen a slurry of CuI (51 mg, 0.27 mmol, 0.1 eq.) in Et_2O (30 cm^3) was treated with a 2.0 M solution of octyl magnesium bromide in Et_2O (1.33 cm^3, 2.66 mmol, 1.5 eq.) at –78°C. This solution was stirred for 1.5 h during which time the temperature gradually rose to –25°C. The reaction vessel was re-cooled to –45°C and ***exo*-12** (388 mg, 1.78 mmol, 1 eq.) in Et_2O (10 cm^3) was added. Over 1 h the temperature rose to –5°C. TLC analysis (Hex-EtOAc; 9:1) indicated consumption of enone. The temperature was reduced to –78°C and methyl 6-formylhexanoate (422 mg, 2.67 mmol, 1.5 eq.) was added. The reaction was allowed to warm to room temperature over 4 h. Saturated NH_4Cl (50 cm^3) was added and the resultant mixture was extracted with Et_2O (3 x 50 cm^3). The combined organic extracts were dried over $MgSO_4$, filtered and the solvent removed *in vacuo*. Purification by flash column chromatography (Hex-EtOAc; 19:1) afforded initially ***Z*-14q** (266 mg, 37%) as a colourless liquid. R_f = 0.3 (Hex-EtOAc; 9:1); δ_H (400 MHz, $CDCl_3$) 0.89 (3H, t, *J* 6.5 Hz, CH_3), 1.24-1.52 (20H, m, CH_2), 1.63 (2H, pent, *J* 7.5 Hz, CH_2), 1.83 (1H, d (br), *J* 8.0 Hz, CH), 2.30 (2H, t, *J* 7.5 Hz, CH_2), 2.13-2.20 (2H, m, CH_2), 2.29-2.35 (2H, m, CH), 2.72 (1H, s (br), CH), 3.05 (1H, s (br), CH), 3.66 (3H, s, CH_3), 5.85 (1H, dt, *J* 2.0, 7.5 Hz, CH), 6.17 (1H, dd, *J* 2.75, 5.5 Hz, CH), 6.21 (1H, dd, *J* 2.75, 5.5 Hz, CH); δ_C (100 MHz, $CDCl_3$) 14.1, 22.6, 24.8, 26.4, 27.8, 28.8, 29.0, 29.3, 29.6, 29.8, 31.8, 34.0, 38.7, 43.3, 45.8, 45.85, 47.7, 49.4, 51.4, 55.5, 137.5, 138.6, 141.7, 143.9, 174.1, 209.5; m/z (CI) 418 (MNH_4^+, 15%), 401 (MH^+, 15%), 335 ($M-C_5H_6^+$, 100%); Found 401.30659, $C_{26}H_{41}O_3$ requires 401.30557 (+2.8 ppm); further elutions gave ***E*-14q** (140 mg, 20%) whose data was in accord to that reported above.

General Procedure for the* retro-*Diels-Alder reactions: Synthesis of adducts 15a to 15q.

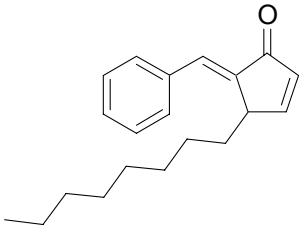


4-Methyl-5-[1-phenylmeth-(*E*)-ylidene]cyclopent-2-enone, 15a. Under nitrogen a solution of ***E*-14a** (250 mg, 1.0 mmol, 1.0 eq.) and maleic anhydride (490 mg, 5.0 mmol, 5.0 eq.) in DCM (10 cm^3) was treated with a 1.0 M solution of $MeAlCl_2$ in hexane (1.1 cm^3, 1.1 mmol, 1.1 eq.). This mixture was heated to reflux for 6 h. On cooling silica (*ca*. 2.5 g) was added and the solvent was removed under reduced pressure. Flash column chromatography (Hex-EtOAc; 3:1) gave the *title compound* ***E*-15a** (138 mg, 75%) as a colourless solid. M.pt. 64-66ºC; R_f 0.25 (Hex-EtOAc; 3:1); υ_{max} (neat/cm^{-1}) 3077, 2983, 2944, 2886, 2340, 1680, 1623, 1580, 1446, 1380; δ_H (400 MHz, $CDCl_3$) 1.22 (3H, d, *J* 7.0 Hz, CH_3), 3.84-4.00 (1H, m, CH), 6.40 (1H, dd, *J* 1.75, 5.75 Hz, CH), 7.39-7.44 (4H, ArH), 7.54 (2H, d, *J* 7.0 Hz, ArH), 7.60 (1H, ddd, *J* 1.0, 2.5, 5.75 Hz, CH); δ_C (100 MHz, $CDCl_3$) 16.3, 38.8, 128.7, 129.3, 130.6, 131.7, 133.6, 134.8, 138.3, 163.9, 197.4; m/z (CI) 202 (NH_4^+, 20%), 185 (MH^+, 100%); Found 185.09654, $C_{13}H_{13}O$ requires 185.09665, (-0.6 ppm); Found C, 84.66; H, 6.60%, $C_{13}H_{12}O$ requires C, 84.78; H, 6.57%.

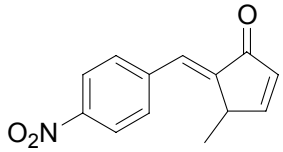
4-Methyl-5-[1-phenylmeth-(*E*)-ylidene]cyclopent-2-enone, 15a. Under nitrogen a solution of ***Z*-14a** (250 mg, 1.0 mmol, 1.0 eq.) and maleic anhydride (490 mg, 5.0 mmol, 5.0 eq.) in DCM (10 cm^3) was treated with a 1.0 M solution of $MeAlCl_2$ in hexane (1.1 cm^3, 1.1 mmol, 1.1 eq.). This mixture was heated to reflux for 3 h. On cooling silica (*ca*. 2.5 g) was added and the solvent was removed under reduced pressure. Flash column chromatography (Hex-EtOAc; 3:1) gave initially isomerized starting material ***E*-14a** (50 mg, 20%) followed by the *title compound* **15a** (118 mg, 64%) as a colourless solid whose data matched that given above.



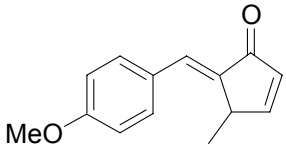
4-Butyl-5-[1-phenylmeth-(*E*)-ylidene]cyclopent-2-enone, 15b. Following the standard *retro*-Diels-Alder procedure described above, a solution of ***E*-14b** (700 mg, 2.4 mmol, 1 eq.) and maleic anhydride (1175 mg, 12 mmol, 5 eq.) in DCM (30 cm^3) was treated with a 1.0 M solution of $MeAlCl_2$ in hexane (2.4 cm^3, 2.4 mmol, 1.0 eq.). This mixture was heated to reflux for 6 h. On cooling silica (*ca*. 2.5 g) was added and the solvent was removed under reduced pressure. Flash column chromatography (Hex-EtOAc; 3:1) gave the *title compound* **15b** (138 mg, 75%) as a yellow coloured thick oil. R_f 0.35 (Hex-EtOAc; 3:1); υ_{max} (neat/cm^{-1}) 3058, 3026, 2956, 2930, 2860, 1698, 1631, 1582, 1495, 1449, 1379, 1338; δ_H (400 MHz, $CDCl_3$) 0.76-0.86 (3H, m, CH_3), 1.14-1.29 (4H, m, CH_2), 1.32-1.44 (1H, m, CH_2), 1.80-1.90 (1H, m, CH_2), 3.88-3.96 (1H, m, CH), 6.45 (1H, dd, *J* 2.0, 6.0, Hz, CH), 7.33-7.44 (4H, m, CH, ArH), 7.52 (2H, d, *J* 7.5 Hz, ArH), 7.70 (1H, ddd *J* 1.0, 2.5, 6.0 Hz, CH); δ_C (100 MHz, $CDCl_3$) 13.8, 22.5, 28.3, 29.9, 43.8, 128.6, 128.7, 129.2, 130.4, 131.5, 134.4, 134.8, 137.2, 162.4, 197.5; m/z (CI) 244 (NH_4^+, 35%), 227 (MH^+, 100%); Found 227.14345, $C_{16}H_{19}O$ requires 227.14359, (-0.6 ppm).



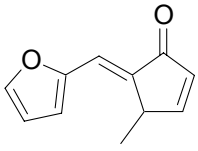
4-Octyl-5-[1-phenylmeth-(*E*)-ylidene]cyclopent-2-enone, 15c. Under N_2 a mixture of ***E*-14c** (541 mg, 1.55 mmol, 1 eq.) and maleic anhydride (762 mg, 7.77 mmol, 5 eq.) in DCM (33 cm^3) was treated with a 1.0 M solution of $MeAlCl_2$ in hexane (1.95 cm^3, 1.95 mmol, 1.25 eq.). The reaction mixture was heated to reflux (*ca.* 40ºC) for 6 h. The mixture was cooled and silica (*ca.* 5 g) was added before the solvent was removed *in vacuo*. Purification by flash column chromatography (Hex-EtOAc; 9:1) afforded the *title compound* **15c** (334 mg, 76%) as a pale yellow liquid. R_f 0.25 (Hex-EtOAc; 9:1); υ_{max} (neat/cm^{-1}) 3058, 2926, 2855, 1698, 1633, 1583, 1495; δ_H (400 MHz, $CDCl_3$) 0.86 (3H, t, *J* 6.5 Hz, CH_3), 1.13-1.30 (12H, m, CH_2), 1.33-1.44 (1H, m, CH_2), 1.78-1.89 (1H, m, CH_2), 3.90-3.96 (1H, m, CH), 6.44 (1H, dd, *J* 1.75, 6.0 Hz, CH), 7.35-7.45 (3H, m, ArH), 7.39 (1H, s, CH), 7.52 (2H, d, *J* 7.5 Hz, ArH), 7.70 (1H, dd, *J* 2.5, 6.0 Hz, CH); δ_C (100 MHz, $CDCl_3$) 14.0, 22.6, 26.0, 29.1, 29.2, 29.4, 30.1, 31.7, 43.9, 128.6, 129.2, 130.4, 131.6, 134.4, 134.8, 137.2, 162.4, 197.5; m/z (CI) 283 (MH^+, 100%); Found 283.20650, $C_{20}H_{27}O$ requires 283.20618 (+1.2 ppm).



4-Methyl-5-[1-(4-nitrophenyl)meth-(*E*)-ylidene]cyclopent-2-enone, 15d. Following the standard *retro*-Diels-Alder procedure described above, a solution of ***E*-14d** (220 mg, 0.746 mmol, 1 eq.) and maleic anhydride (365 mg, 3.72 mmol, 5 eq.) in DCM (20 cm^3) was treated with a 1.0 M solution of $MeAlCl_2$ in hexane (0.75 cm^3, 0.75 mmol, 1 eq.) and heated to reflux for 3.5 h. The reaction was cooled before Et_2O (50 cm^3) and 0.5 M NaOH (50 cm^3) were added. The resultant aqueous layer was extracted with Et_2O (2 x 50 cm^3) and the combined organic extracts were dried over $MgSO_4$. Filtration, pre-absorption onto silica (*ca*. 5 g) and purification by flash column chromatography (Hex-EtOAc; 3:1) afforded **15d** (145 mg, 85%) as a pale yellow solid. M.pt. 76-78ºC; R_f 0.3 (Hex-EtOAc; 3:1); δ_H (400 MHz, $CDCl_3$) 1.20 (3H, d, *J* 7.5 Hz, CH_3), 3.93-4.01 (1H, m, CH), 6.47 (1H, dd, *J* 1.75, 6.0 Hz, CH), 7.42 (1H, s, CH), 7.66 (1H, dd, *J* 2.5, 6.0 Hz, CH), 7.68 (2H, d, *J* 8.5 Hz, ArH), 8.28 (2H, d, *J* 8.5 Hz, ArH); δ_C (100 MHz, $CDCl_3$) 16.4, 38.6, 123.9, 128.8, 130.8, 131.2, 133.6, 141.2, 141.6, 164.3, 196.6; m/z (CI) 247 (MNH_4^+, 5%), 230 (MH^+, 10%), 200 (100%); Found 230.08171, $C_{13}H_{12}NO_3$ requires 230.08164, (-0.3 ppm); Found C, 68.93; H, 4.85; N, 6.10%, $C_{13}H_{11}NO_3$ requires C, 69.09; H, 4.84; N, 6.11%.

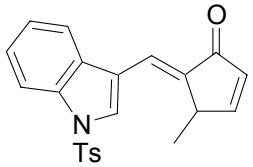


5-[1-(4-Methoxyphenyl)meth-(*E*)-ylidene]-4-methylcyclopent-2-enone, 15e. Following the standard *retro*-Diels-Alder procedure described above, a solution of ***E*-14e** (350 mg, 1.25 mmol, 1 eq.) and maleic anhydride (613 mg, 6.26 mmol, 5 eq.) in DCM (25 cm^3) was treated with a 1.0 M solution of $MeAlCl_2$ in hexane (1.25 cm^3, 1.25 mmol, 1 eq.) and heated to reflux for 35 h. Et_2O (50 cm^3) and 0.5 M NaOH (50 cm^3) were added. The resultant aqueous layer was extracted with Et_2O (2 x 50 cm^3) and the combined organic extracts were dried over $MgSO_4$. Filtration, pre-absorption onto silica (*ca*. 5 g) and purification by flash column chromatography (Hex-EtOAc; 3:1) afforded **15e** (182 mg, 68%) as a colourless solid. M.pt. 56-58ºC; R_f 0.25 (Hex-EtOAc; 3:1); υ_{max} (neat/cm^{-1}) 3080, 2964, 2928, 2880, 1691, 1626, 1600, 1512, 1462, 1423, 1337, 1305; δ_H (400 MHz, $CDCl_3$) 1.21 (3H, d, *J* 7.5 Hz, CH_3), 3.83-3.92 (1H, m, CH), 3.85 (3H, s, CH_3), 6.38 (1H, dd, *J* 2.0, 6.0 Hz, CH), 6.90 (2H, d, *J* 8.5 Hz, ArH), 7.34 (1H, s, CH), 7.49 (2H, d, *J* 8.5 Hz, ArH), 7.57 (1H, ddd, *J* 1.0, 2.5, 6.0 Hz, ArH); δ_C (100 MHz, $CDCl_3$) 16.3, 38.8, 55.3, 114.2, 127.1, 131.4, 133.5, 136.1 160.5, 163.4, 197.5; m/z (CI) 214 (MH^+, 100%), 186 (75%), 171 (100%); Found 214.09934, $C_{14}H_{14}O_2$ requires 214.09937, (-0.1 ppm).



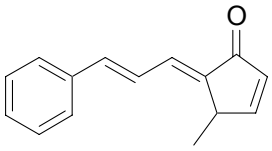
5-[1-Furan-2-ylmeth-(*E*)-ylidene]-4-methylcyclopent-2-enone, 15f. Following the standard *retro*-Diels-Alder procedure described above, a solution of ***E*-14f** (400 mg, 1.66 mmol, 1 eq.) and maleic anhydride (813 mg, 8.3 mmol, 5 eq.) in DCM (25 cm^3) was treated with a 1.0 M solution of $MeAlCl_2$ in hexane (1.66 cm^3, 1.66 mmol, 1.0 eq.). This mixture was heated to reflux for 8 h. On cooling silica (*ca*. 2.5 g) was added and the solvent was removed

under reduced pressure. Flash column chromatography (Hex-EtOAc; 3:1) gave initially starting material **15f** (120 mg, 30%) and then the *title compound* **15f** (185 mg, 64%) as a colourless solid. M.pt. 103-105ºC; R_f 0.25 (Hex-EtOAc; 3:1); δ_H (400 MHz, $CDCl_3$) 1.35 (3H, d, *J* 7.0 Hz, CH_3), 3.02 (1H, s, CH), 3.81-3.89 (1H, m, CH), 6.34 (1H, dd, *J* 1.75, 6.0 Hz, CH), 6.52 (1H, dd, *J* 1.75, 3.5 Hz, CH), 6.70 (1H, d, *J* 3.5 Hz, CH), 7.14 (1H, s, CH), 7.56 (1H, ddd, *J* 1.0, 2.75, 6.0 Hz, CH), 7.60 (1H, d, *J* 1.75 Hz, CH); δ_C (100 MHz, $CDCl_3$) 18.1, 39.6, 112.5, 117.0, 117.5, 133.4, 135.9, 145.2, 151.4, 163.8, 197.3; m/z (CI) 175, (MH^+, 100%), Found 175.07659, $C_{11}H_{11}O_2$ requires 175.07590 (+4.5 ppm).



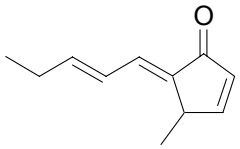
4-Methyl-5-[1-[1-(toluene-4-sulfonyl)-1*H*-indol-3-yl]meth-(*E*)-ylidene]cyclopent-2-enone, 15i. Following the standard *retro*-Diels-Alder procedure described above, a solution of ***E*-14i** (222 mg, 0.5 mmol, 1 eq.) and *N*-methyl maleimide (278 mg, 2.5 mmol, 5.0 eq.) in DCM (10 cm^3) was treated with a 1.0 M solution of $MeAlCl_2$ in hexane (0.5 cm^3, 0.5 mmol, 1 eq.). Following the standard workup, purification by flash column chromatography gave initially **14i** (80 mg, 36%) followed by the *title compound* **15i** (53 mg, 28%) as an amorphous yellow coloured solid. M.pt. 72-74ºC; R_f 0.25 (Hex-EtOAc; 2:1); υ_{max} (neat/cm^{-1}) 3149, 3074, 2965, 1698, 1614, 1536, 1493, 1447, 1375; δ_H (400 MHz, $CDCl_3$) 1.29 (3H, d, *J* 7.5 Hz, CH_3), 2.34 (3H, s, CH_3), 3.76-3.84 (1H, m, CH), 6.43 (1H, dd, *J* 1.75, 6.0 Hz, CH), 7.24 (2H, d, *J* 8.0 Hz, ArH), 7.32 (1H, dd, *J* 7.0, 7.5 Hz, ArH), 7.39 (1H, dd, *J* 7.0, 8.0 Hz, ArH), 7.55 (1H, s, ArH), 7.62 (1H, dd, *J* 2.5, 6.0 Hz, CH), 7.74 (1H, d, *J* 7.5 Hz, ArH), 7.75 (1H, s, ArH), 7.79 (2H, d, *J* 8.0 Hz, CH, ArH), 8.00 (1H, d, *J* 8.0 Hz, ArH); δ_C (100 MHz, $CDCl_3$) 15.3, 21.6, 39.1, 113.6, 117.1, 119.7, 120.1, 123.9, 125.6, 126.5, 126.9, 129.9, 130.1, 130.4, 134.0, 134.6, 134.9, 138.8, 145.5, 163.2, 196.6; m/z (ES) 400, (MNa^+, 100%); Found 400.0971, $C_{22}H_{19}NO_3SNa$ requires 400.0983, (-3.1 ppm).

4-Methyl-5-[1-[1-(toluene-4-sulfonyl)-1H-indol-3-yl]-meth-(*E*)-ylidene]cyclopent-2-enone, 15i. Under N_2, a solution of ***E*-14i** (221.6 mg, 0.5 mmol, 1 eq.) and *N*-methyl maleimide (278 mg, 2.5 mmol, 5.0 eq.) in DCM (10 cm^3) was treated with a 1.0 M solution of $MeAlCl_2$ in hexane (0.5 cm^3, 0.5 mmol, 1 eq.). The solution was then split into two dry microwavable vials. Each vial was irradiated (Smith Creator, 300 Watts) at 70°C for 1500 sec. On cooling the mixtures were combined, silica (*ca*. 2.5 g) added, the solvent was removed *in vacuo* and the product purified using flash column chromatography (Hex-EtOAc; 4:1 → 1:1) to give **15i** (161 mg, 85%) as an amorphous yellow coloured solid, with consistent data (see above).



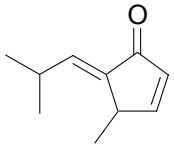
4-Methyl-5-[(*E*)-3-phenylprop-2-en-(*E*)-ylidene]cyclopent-2-enone, 14j. Following the standard *retro*-Diels-Alder procedure described above, a solution of ***E*-14j** (552 mg, 2.0 mmol, 1 eq.) and maleic anhydride (980 mg, 10.0 mmol, 5 eq.) in DCM (25 cm^3) was treated with a 1.0 M solution of $MeAlCl_2$ in hexane (2.0 cm^3, 2.0mmol, 1 eq.) and heated to reflux for 6 h. Et_2O (50 cm^3) and 0.5 M NaOH (50 cm^3) were added. The resultant aqueous layer was extracted with Et_2O (5 x 50 cm^3) and the combined organic extracts were dried over $MgSO_4$.

Filtration, pre-absorption onto silica (*ca*. 5 g) and purification by flash column chromatography (Hex-EtOAc; 3:1) afforded initially ***Z,E*-15j** (26 mg, 6%) as a yellow coloured oil followed by ***E,E*-15j** (300 mg, 72%) as a yellow coloured amorphous solid. M.pt. 98-100ºC; R_f 0.3 (Hex-EtOAc; 3:1); υ_{max} (neat/cm^{-1}) 3055, 3020, 2940, 2860, 1685, 1617, 1578, 1448, 1336,1282; δ_H (400 MHz, $CDCl_3$) 1.39 (3H, d, *J* 7.5 Hz, CH_3), 3.63-3.71 (1H, m, CH), 6.35 (1H, dd, *J* 2.0, 6.0 Hz, CH), 6.94-7.05 (2H, m, CH), 7.12 (1H, ddd, 1.0, 1.5, 9.5 Hz, CH), 7.29-7.40 (3H, m, ArH), 7.46-7.52 (3H, m, CH, ArH); δ_C (100 MHz, $CDCl_3$), 19.1, 38.6, 123.6, 127.2, 128.8, 129.1, 130.8, 134.4, 136.4, 139.1, 141.7, 162.5, 196.9; m/z (EI) 210 (M^+, 10%), 167 (100%), 165 (80%), 115, (55%); Found 210.10473, $C_{15}H_{14}O$ requires 210.10446 (+1.3 ppm). Data for ***Z,E*-15j**: R_f 0.35 (Hex-EtOAc; 3:1); υ_{max} (neat/cm^{-1}) 3058, 3022, 2940, 2860, 1685, 1618, 1576, 1448, 1336,1282; δ_H (400 MHz, $CDCl_3$) 1.30 (3H, d, *J* 7.5 Hz, CH_3), 3.41-3.48 (1H, m, CH), 6.30 (1H, dd, *J* 2.0, 6.0 Hz, CH), 6.58 (1H, d, *J* 11.5 Hz, CH), 6.82 (1H, d, *J* 15.5 Hz, CH), 7.23-7.41 (4H, m, CH, ArH), 7.53-7.57 (2H, m, ArH), 8.44 (1H, dd, *J* 11.5, 15.5 Hz, CH); δ_C (100 MHz, $CDCl_3$) 18.8, 40.1, 123.6, 127.5, 128.6, 128.7, 130.8, 134.4, 135.3, 135.9, 141.0, 161.5, 197.0; m/z (EI) 210 (M+, 15%), 167, (100%); Found 210.10473, $C_{15}H_{14}O$ requires 210.10446 (+1.3 ppm).



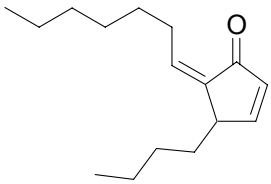
4-Methyl-5-[(*E*)-pent-2-en-(*E*)-ylidene]cyclopent-2-enone, 15k. Following the standard *retro*-Diels-Alder procedure described above, a solution of ***E,E*-14k** (700 mg, 3.06 mmol, 1 eq.) and maleic anhydride (1.50 g, 15.3 mmol, 5.0 eq.) in DCM (25 cm^3) was treated with a 1.0 M solution of $MeAlCl_2$ in hexane (3.06 cm^3, 3.06 mmol, 1.01 eq.). The solution was heated to reflux for 6 h. Following the standard workup, purification by flash column chromatography afforded initially ***Z,E*-15k** (6 mg, 1%) as a yellow coloured oil and then ***E,E*-15k** (58 mg, 12%) as a colourless oil R_f 0.3 (Hex-EtOAc; 3:1). υ_{max} (neat/cm^{-1}) 3051, 2969, 2932, 2874, 2252, 1687, 1629, 1580, 1453; δ_H (400 MHz, $CDCl_3$) 1.08 (3H, t, *J* 7.5 Hz, CH_3), 1.31 (3H, d, *J* 7.3 Hz, CH_3), 2.21-2.30 (2H, m, CH_2), 3.50-3.59 (1H, m, CH), 6.20-6.35 (3H, m, CH), 6.93 (1H, d, *J* 10.3 Hz, CH), 7.44 (1H, ddd, *J* 1.0, 2.5, 5.9 Hz, CH); δ_C (100 MHz, $CDCl_3$) 13.0, 18.7, 26.5, 38.4, 124.8, 131.2, 134.3, 137.0, 147.6, 162.5, 197.3; m/z (CI) 164 (163, 100%), found 163.11273, $C_{11}H_{15}O$ requires 163.11229 (+2.9 ppm); Data for ***Z,E*-15k**: R_f 0.35 (Hex-EtOAc; 3:1); δ_H (400 MHz, $CDCl_3$) 1.07 (3H, t, *J* 7.5 Hz, CH_3), 1.51 (3H, d, *J* 7.5 Hz, CH_3), 2.21-2.32 (2H, m, CH_2), 3.28-3.34 (1H, m, CH), 6.10 (1H, dt, *J* 6.5, 15.5 Hz, CH), 6.28 (1H, dd, *J* 1.5, 6.0 Hz, CH), 6.38 (1H, d, *J* 11.0 Hz, CH), 7.42(1H, dd, *J* 2.5, 6.0 Hz, CH), 7.67 (1H, ddt, *J* 1.5, 11.0, 15.5 Hz, CH).

4-Methyl-5-[(*E*)-pent-2-en-(*E*)-ylidene]cyclopent-2-enone, 15k. Under N_2, a solution of ***E,E*-14k** (700 mg, 3.06 mmol, 1 eq.) and maleic anhydride (4.50 g, 45.9 mmol, 15.0 eq.) in DCM (25 cm^3) was treated with a 1.0 M solution of $MeAlCl_2$ in hexane (4.59 cm^3, 4.59 mmol, 1.5 eq.). The solution was homogenized under stirring and then split into six dry microwavable vials under a nitrogen atmosphere. Each vial was irradiated (Smith Creator, 300 Watts) up to 120°C for 50 sec. As the temperature reached 120ºC each vial was cooled immediately and poured into a 5% aqueous sodium hydrogencarbonate solution (75 cm^3). The suspension was stirred vigorously for 10 min before extraction with Et_2O (8 x 30 cm^3). The combined organic fractions were dried over $MgSO_4$. After filtration the solvent was removed *in vacuo* and the combined crude product purified by flash column chromatography (Hex-EtOAc; 9:1 $\rightarrow$ 4:1 $\rightarrow$ 3:1) to afford initially ***Z,E*-15k** (20 mg, 4%) as a yellow coloured oil followed by ***E,E*-15k** (437 mg, 88%) as a colourless oil. Data corresponded with that reported above.

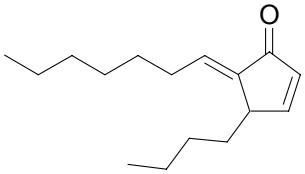


4-Methyl-5-[2-methylprop-(*E*)-ylidene]cyclopent-2-enone, 15l. Following the standard *retro*-Diels-Alder procedure described above, a solution of ***E*-14l** (650 mg, 3.15 mmol, 1 eq.) and maleic anhydride (1.543 g, 15.7 mmol, 5 eq.) in DCM (30 cm^3) was treated with a 1.0 M solution of $MeAlCl_2$ in hexane (3.15 cm^3, 3.15 mmol, 1.0 eq.). This mixture was heated to reflux for 8 h. Silica (*ca*. 2.5 g) was added and the solvent was removed under reduced pressure. Flash column chromatography (Hex-EtOAc; 4:1) gave initially ***Z*-15l** (30 mg, 7%) as yellow coloured liquid followed by ***E*-15l** (300 mg, 75%) as a colourless liquid. R_f 0.35 (Hex-EtOAc; 4:1); δ_H (400 MHz, $CDCl_3$) 1.07 (3H, d, *J* 6.5 Hz, CH_3), 1.09 (3H, d, *J* 6.5 Hz, CH_3), 1.28 (3H, d, *J* 7.5 Hz, CH_3), 2.61-2.75 (1H, m, CH), 3.45-3.55 (1H, m, CH), 6.27 (H, dd, *J* 2.0, 6.0 Hz, CH), 6.35 (H, dd, *J* 1.0, 10.5 Hz, CH), 7.45 (H, ddd, *J* 1.0, 2.0, 6.0 Hz, CH), δ_C (100 MHz, $CDCl_3$) 18.6, 21.8, 21.9, 28.4, 38.0, 133.8, 136.6, 141.6, 163.3, 196.9; m/z (EI) 150 (MH^+, 10%); Found 150.2175, $C_{10}H_{14}O$ requires 150.2176. Data for ***Z*-15l** δ_H (250 MHz, $CDCl_3$)) 1.01 (3H, d, *J* 7.0 Hz, CH_3), 1.05 (3H, d, *J* 7.0 Hz, CH_3), 1.27 (3H, d, *J* 7.5 Hz, CH_3), 3.24-3.28 (1H, m, CH), 3.80-3.85 (1H, m, CH), 6.00 (1H, dd, *J* 2.0, 10.0 Hz, CH), 6.26 (1H, dd, *J* 2.0, 6.0 Hz, CH), 7.44 (H, dd, *J* 2.0, 6.0 Hz, CH). m/z (CI) 151 (MH^+, 10%); Found 150.2175, $C_{10}H_{14}O$ requires 150.2170.

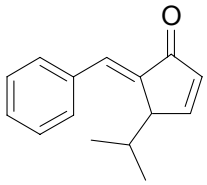
4-Methyl-5-[2-methylprop-(*E*)-ylidene]cyclopent-2-enone, 15l. Following the standard *retro*-Diels-Alder procedure described above, a solution of ***Z*-14l** (580 mg, 2.68 mmol, 1 eq.) and maleic anhydride (1.316 g, 13.4 mmol, 5 eq.) in DCM (25 cm^3) was treated with a 1.0 M solution of $MeAlCl_2$ in hexane (2.68 cm^3, 2.68 mmol, 1.0 eq.). This mixture was heated to reflux for 3 h. On cooling silica (*ca*. 2.5 g) was added and the solvent was removed under reduced pressure. Flash column chromatography (Hex-EtOAc; 4:1) gave initially the isomerized starting material ***E*-14l** (140 mg, 21%) followed by ***Z*-15l** (36 mg, 8%) as a yellow coloured liquid. R_f 0.4 (Hex-EtOAc; 4:1). Further elution gave ***E*-15l** (265 mg, 59%) with consistent data that reported above.



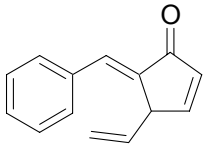
4-Butyl-5-hept-(*Z*)-ylidenecyclopent-2-enone, *Z*-15m: Under N_2 ***Z*-14m** (0.20 g, 0.67 mmol, 1 eq.) was dissolved in distilled DCM (10 cm^3). Maleic anhydride (0.33 g, 3.33 mmol, 5 eq.) was added and the mixture was stirred to effect dissolution. 1 M Methyl aluminium chloride in hexane (0.87 cm^3, 0.87 mmol, 1.3 eq.) was then added and the mixture was heated to reflux for 30 minutes. After cooling, flash silica (*ca.* 2 g) was added to the vessel and the solvent was reduced *in vacuo*. Purification by flash column chromatography (*c*-Hex-EtOAc; 98:2) afforded the product (19 mg, 12%) as a yellow oil. R_f 0.7 (*c*-Hex-EtOAc; 9:1); υ_{max} (cm^{-1}/neat) 2956, 2929, 2858, 2359, 2339, 1736, 1709, 1655, 1466, 1377, 1174; δ_H (400 MHz, $CDCl_3$) 0.79-0.85 (6H, m, CH_3), 1.19-1.29 (10H, m, CH_2), 1.34-1.42 (3H, m, CH_2), 1.61-1.68 (1H, m, CH_2), 2.73 (2H, q, *J* 7.5 Hz, CH_2), 3.19-3.20 (1H, m, CH), 5.96 (1H, t, *J* 7.5 Hz, CH), 6.20 (1H, dd, *J* 1.5, 6.0 Hz, CH), 7.35 (1H, dd, *J* 2.75, 6.0 Hz, CH); δ_C (100 MHz, $CDCl_3$) 14.2, 14.3, 22.8, 23.1, 27.5, 28.7, 29.2, 29.6, 31.9, 33.5, 45.7, 136.6, 137.1, 140.7, 160.5, 198.5; m/z (ESI^+) 234 (MH^+, 100%); Found 235.2062, $C_{16}H_{27}O$ requires 235.2070 (+3.4 ppm). ***E*-14m** (97 mg, 62%) and ***E*-15m** (33 mg, 21%) were also isolated.



4-Butyl-5-hept-(*E*)-ylidenecyclopent-2-enone, *E*-15m: Under N_2 ***E*-14m** (90 mg, 0.30 mmol, 1 eq.) was dissolved in distilled DCM (5 cm^3). Maleic anhydride (0.15 g, 1.50 mmol, 5 eq.) was added to the reaction mixture before 1 M methyl aluminum chloride in hexane (0.42 cm^3, 0.42 mmol, 1.4 eq.) was added dropwise and the vessel was heated to reflux for 5 hours. After cooling, silica (*ca.* 1 g) was added to the vessel and the DCM was reduced *in vacuo*. Purification by flash column chromatography (*c*-Hex-EtOAc; 19:1) afforded ***E*-15m** (59 mg, 84%) as a yellow oil. R_f 0.55 (*c*-Hex-EtOAc; 9:1); υ_{max} (neat/cm^{-1}) 2956, 2929, 2858, 1705, 1655, 1581, 1466, 1230, 833; δ_H (400 MHz, $CDCl_3$) 0.86-0.88 (6H, m, CH_3), 1.26-1.30 (10H, m, CH_2), 1.44-1.56 (3H, m, CH_2), 1.79-1.86 (1H, m, CH_2), 2.19-2.29 (2H, m, CH_2), 3.46-3.47 (1H, m, CH), 6.31 (1H, d, *J* 6.0 Hz, CH), 6.54 (1H, t, *J* 7.25 Hz, CH), 7.53-7.55 (1H, m, CH); δ_C (100 MHz, $CDCl_3$) 14.1, 14.3, 22.7, 23.1, 28.2, 28.9, 29.3, 31.9, 32.3, 43.5, 135.0, 136.0, 138.1, 162.1, 197.2; m/z (ES^+) 234 (MH^+, 100%), found 235.2062, $C_{16}H_{27}O$, requires 235.2056 (+3.2 ppm).

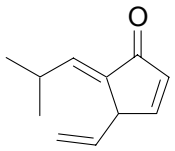


4-Isopropyl-5-[1-phenylmeth-(*E*)-ylidene]cyclopent-2-enone, 15n. Following the standard *retro*-Diels-Alder procedure described above (Section 6.3.1), a solution of ***E*-14n** (200 mg, 0.72 mmol, 1 eq.) and maleic anhydride (353 mg, 3.6 mmol, 5 eq.) in DCM (20 cm^3) was treated with a 1.0 M solution of $MeAlCl_2$ in hexane (0.72 cm^3, 0.72 mmol, 1.0 eq.). This mixture was heated to reflux for 6 h. Silica (*ca*. 2.5 g) was added and the solvent was removed under reduced pressure. Flash column chromatography (Hex-EtOAc; 3:1) gave the *title compound* **15n** (132 mg, 87%) as a colourless solid. M.pt. 103-105ºC; R_f 0.25 (Hex-EtOAc; 3:1); υ_{max} (neat/cm^{-1}) 3061, 2959, 29260, 2885, 1697, 1630, 1582, 1448, 1369; δ_H (400 MHz, $CDCl_3$) 0.52 (3H, d, *J* 7.0 Hz, CH_3), 1.14 (3H, d, *J* 7.0 Hz, CH_3), 2.27-2.32 (1H, m, CH), 3.59-4.00 (1H, m, CH), 6.53 (1H, dd, *J* 2.0, 6.0 Hz, CH), 7.32-7.44 (4H, m, CH, ArH), 7.50-7.54 (2H, m, CH), 7.66 (1H, ddd, *J* 1.0, 2.5, 6.0 Hz, CH); δ_C (100 MHz, $CDCl_3$) 16.8, 21.3, 27.2, 49.9, 128.7, 129.2, 130.3, 131.5, 134.9, 136.0, 136.8, 159.4, 197.5; m/z (CI) 213 (MH^+, 100%); Found 213.12839, $C_{15}H_{17}O$ requires 213.12794, (-2.3 ppm); Found C, 85.00; H, 7.65%, $C_{15}H_{16}O$ requires C, 84.85; H, 7.60%.

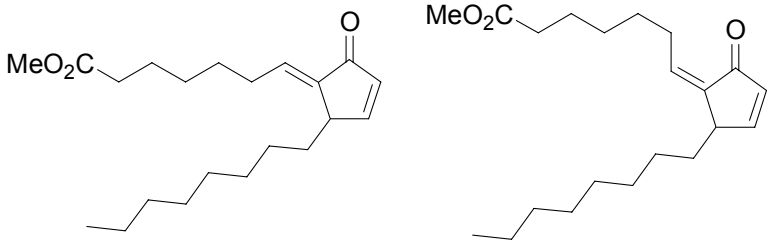


5-[1-Phenylmeth-(*E*)-ylidene]-4-vinylcyclopent-2-enone, 15o. Following the standard *retro*-Diels-Alder procedure described above, a solution of ***E*-14o** (570 mg, 2.17 mmol, 1 eq.) and maleic anhydride (1.063 g, 10.84 mmol, 5 eq.) in DCM (25 cm^3) was treated with a 1.0 M solution of $MeAlCl_2$ in hexane (2.17 cm^3, 2.17 mmol, 1.0 eq.). This mixture was heated to reflux for 8 h. Silica (*ca*. 2.5 g) was added and the solvent was removed under reduced pressure. Flash column chromatography (Hex-EtOAc; 3:1) gave the *title compound* **15o** (310 mg, 73%) as a yellow coloured oil. R_f 0.25 (Hex-EtOAc; 3:1); υ_{max} (neat/cm^{-1}) 3053,

2985, 2305, 2253, 1696, 1630, 1582, 1494, 1449, 1421, 1265; δ_H (400 MHz, $CDCl_3$) 4.43-4.48 (1H, m, CH), 5.16 (1H, dt, *J* 1.0, 10.0 Hz, CH_2), 5.25 (1H, dt, *J* 1.0, 17.0 Hz, CH_2), 5.64 (1H, ddd, *J* 7.0, 10.0, 17.0 Hz, CH), 6.45 (1H, dd, *J* 2.0, 6.0 Hz, CH), 7.33-7.43 (3H, m, ArH), 7.50 (1H, s, CH), 7.53 (1H, ddd, *J* 1.0, 2.5, 6.0 Hz, CH), 7.56-7.60 (2H, m, ArH); δ_C (100 MHz, $CDCl_3$) 48.3, 118.1, 128.5, 129.5, 131.3, 133.2, 133.9, 134.1, 134.3, 134.9, 160.4, 197.3; m/z (CI) 197 (MH^+, 100%); Found 197.09684, $C_{14}H_{13}O$ requires 197.09665, (+1.0 ppm).

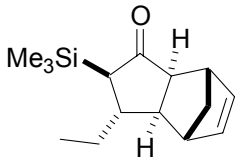


***5*-[2-Methylprop-(*E*)-ylidene]-4-vinylcyclopent-2-enone, 15p.** Following the standard *retro*-Diels-Alder procedure described above, a solution of ***E*-14p** (160 mg, 0.70 mmol, 1 eq.) and maleic anhydride (343 mg, 3.50 mmol, 5 eq.) in DCM (25 cm^3) was treated with a 1.0 M solution of $MeAlCl_2$ in hexane (0.70 cm^3, 0.70 mmol, 1.0 eq.). This mixture was heated to reflux for 8 h. The reaction was quenched with 5% aqueous sodium hydrogencarbonate solution (50 cm^3). The suspension was extracted with Et_2O (8 x 25 cm^3) and the combined organic fractions were dried over $MgSO_4$. The solvent was removed *in vacuo* and the product purified by flash column chromatography (Hex-EtOAc; 4:1) to afford, initially unreacted starting material ***E*-14p** (17 mg, 11%) followed by ***Z*-15p** (14 mg, 12%) as yellow coloured liquid and finally the *title compound* ***E*-15p** (83 mg, 73%) as a yellow coloured oil. R_f 0.35 (Hex-EtOAc; 4:1); δ_H (400 MHz, $CDCl_3$) 0.95 (3H, d, *J* 6.5 Hz, CH_3), 0.97 (3H, d, *J* 6.5 Hz, CH_3), 2.57-2.70 (1H, m, CH), 3.99 (1H, ddd, *J* 0.5, 2.0, 8.5 Hz, CH), 5.09 (1H, dd, *J* 0.5, 10.0 Hz, CH_2), 5.19 (1H, d, *J* 17.0 Hz, CH_2), 5.56 (1H, ddd, *J* 8.5, 10.0, 17.0 Hz, CH), 6.28 (H, dd, *J* 2.0, 6.0 Hz, CH), 6.37 (H, d, *J* 10.5 Hz, CH), 7.28 (H, ddd, *J* 0.5, 2.0, 6.0 Hz, CH); δ_C (100 MHz, $CDCl_3$) 21.6, 21.9, 28.2, 48.1, 116.9, 133.9, 134.9, 136.4, 143.7, 160.0, 196.8; m/z (EI) 163 (M^+, 10%); Found 163.11212, $C_{11}H_{14}O$ requires 163.11229 (-1.1 ppm).

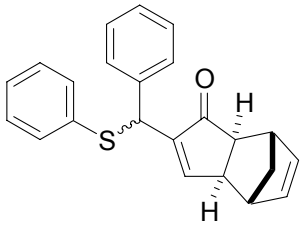


7-[2-Octyl-5-oxocyclopent-3-en-(*E*)-ylidene]heptanoic acid methyl ester, 15q.[3] Under nitrogen in oven dried glassware a mixture of ***E*-14q** (200 mg, 0.50 mmol, 1 eq.) and maleic anhydride (245 mg, 2.50 mmol, 5 eq.) in DCM (20 cm^3) was treated with a 1 M solution of $MeAlCl_2$ in hexanes (0.50 cm^3, 0.50 mmol, 1 eq.) and heated to 50°C (oil bath temperature) for 6 h. The reaction mixture was cooled to room temperature and silica (*ca.* 2 g) was added. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography (Hex-EtOAc; 4:1) affording initially ***Z*-15q** (28 mg, 17%) and finally ***E*-15q** (115 mg, 69%) both as clear liquids. R_f 0.2 (Hex-EtOAc; 3:1); δ_H (400 MHz, $CDCl_3$) 0.88 (3H, t, *J* 6.5 Hz, CH_3), 1.21-1.34 (12H, m, CH_2), 1.34-1.42 (2H, m, CH_2), 1.46-1.54 (1H, m, CH), 1.52 (2H, pent, *J* 7.5 Hz, CH_2), 1.65 (2H, pent, *J* 7.5 Hz, CH_2), 1.76-1.86 (1H, m, CH), 2.18-2.32 (2H, m, CH_2), 2.31 (2H, t, *J* 7.5 Hz, CH_2), 3.44-3.49 (1H, m, CH), 3.66 (3H, s, CH_3), 6.32 (1H, dd, *J* 2.0, 6.0 Hz, CH), 6.53 (1H, t, *J* 7.5 Hz, CH), 7.50-7.57 (1H, m, CH); δ_C (100 MHz, $CDCl_3$) 14.0, 22.6, 24.7, 25.9, 28.3, 28.85, 28.9, 29.2, 29.4, 29.7, 31.8, 32.5, 33.9, 43.3, 51.4, 134.8, 135.1, 138.1, 164.9, 174.0, 196.9; m/z (CI) 352 (MNH_4^+, 5%),

335 (MH^+, 100%); Found C, 75.33; H, 10.35%, $C_{21}H_{34}O_3$ requires C, 75.40; H, 10.26%. Data for ***Z*-15q**: R_f 0.25 (Hex-EtOAc; 3:1); δ_H (400 MHz, $CDCl_3$) 0.88 (3H, t, *J* 6.5 Hz, CH_3), 1.19-1.32 (20H, m, CH_2), 2.29 (2H, t, *J* 7.5 Hz, CH_2), 2.80 (2H, q, *J* 7.5 Hz, CH_2), 3.23-3.28 (1H, m, CH), 3.67 (3H, s, CH_3), 5.99 (1H, t, *J* 7.5 Hz, CH), 6.26 (1H, dd, *J* 2.0, 6.0 Hz, CH), 7.42 (1H, dd, *J* 2.5, 6.0 Hz, CH); δ_C (100 MHz, $CDCl_3$) 14.1, 22.6, 24.8, 26.4, 27.0, 28.8, 29.0, 29.2, 29.4, 29.8, 31.8, 33.6, 34.0, 45.5, 51.4, 136.3, 137.1, 139.8, 160.3, 174.1, 198.2; m/z (CI) 352 (MNH_4^+, 10%), 335 (MH^+, 100%).

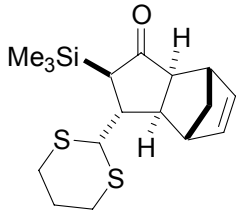


3-Ethyl-2-trimethylsilanyl-2,3,3a,4,7,7a-hexahydro-4,7-methanoindene-1-one, 21. Under N_2 a mixture of CuCN (*ca.* 2 mg, 0.022 mmol, 0.5 mol%) and benzene sulfonamide (*ca.* 4 mg, 0.016 mmol, 0.5 mol%) in Et_2O (5 cm^3) were stirred at 0ºC. A 1 M solution of diethylzinc in heptane (3.1 cm^3 , 3.1 mmol, 1.0 eq.) was then added. After 10 min the resultant mixture was treated with a solution of ***exo*-12** (676 mg, 3.10 mmol, 1 eq.) in Et_2O (10 cm^3). The reaction was allowed to warm to room temperature and stirred for two days. Following standard work-up and purification by flash column chromatography (Hex-Et_2O, 9:1) **21** (308 mg, 40%) was obtained as a colourless viscous oil. R_f 0.4 (Hex-Et_2O, 9:1); υ_{max} (neat/cm^{-1}) 3056, 2961, 2875, 2305, 1725, 1703, 1570, 1461; δ_H (400 MHz, $CDCl_3$) 0.10 (9H, s, CH_3), 1.01 (3H, t, *J* 7.0 Hz, CH_3), 1.19 (1H, d, *J* 9.0 Hz, CH_2), 1.28-1.35 (1H, m, CH), 1.39-1.44 (1H, m, CH_2), 1.59-1.67 (2H, m, CH_2), 1.96 (1H, dd, *J* 2.0, 9.0 Hz, CH), 2.01 (1H, q, *J* 5.0 Hz, CH), 2.33 (1H, d, *J* 9.0 Hz, CH), 2.73 (1H, s, CH), 3.05 (1H, s, CH), 6.15 (1H, dd, *J* 2.75, 5.5 Hz, CH), 6.16 (1H, dd, *J* 2.75, 5.5 Hz, CH); δ_C (100 MHz, $CDCl_3$) -1.5, 11.7, 31.4, 44.1, 44.5, 46.2, 49.5, 49.9, 52.4, 57.7, 138.0, 138.5, 220.8; m/z (EI) 248 (M^+, 5%), 182 (100%); Found 248.15980 requires $C_{15}H_{24}OSi$ 248.15964 (+1.5 ppm).

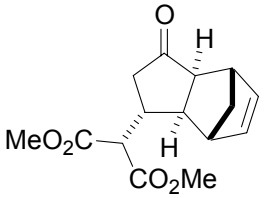


(3a,4,7,7a)-2-[(Phenylsulfanyl)phenylmethyl]-3a,4,7,7a-tetrahydro-4,7-methano-inden-1-one, 22. Under N_2 at room temperature a solution of benzaldehyde (0.17 cm^3, 1.64 mmol, 1.5 eq.) and ***exo*-12** (238 mg, 1.09 mmol, 1 eq.) in dry THF (15 cm^3) was treated dropwise with a 1.0 M solution of lithium thiophenolate in THF (1.20 cm^3, 1.20 mmol, 1.1 eq.). The reaction was stirred at room temperature for 15 h before silica (*ca*. 5 g) was added and the solvent removed under reduced pressure. Purification by flash column chromatography (Hex-EtOAc; 9:1) afforded the *title compound* **22** (360 mg, 96%) as a clear oil containing an inseparable mixture (60:40) of diastereomers. R_f 0.3 (Hex-EtOAc; 9:1); υ_{max} (neat/cm^{-1}) 3438, 2932, 2857, 2286, 2223, 1737, 1437; δ_H (400 MHz, $CDCl_3$) 0.75 (1H, d, *J* 9.5 Hz, CH_2), 0.83 (1H, d, *J* 9.5 Hz, CH_2), 1.61-1.14 (1H, m, CH_2), 2.10 (1H, d, *J* 5.0 Hz, CH), 2.17 (1H, d, *J* 6.0 Hz, CH), 2.46 (1H, s, CH), 2.51 (1H, s, CH), 2.51-2.55 (1H, m, CH), 2.58-2.61 (1H, s, CH), 2.68 (1H, s, CH), 2.72 (1H, s, CH), 5.05 (1H, s, CH), 5.14 (1H, s, CH), 5.98-6.03 (1H, m, CH), 6.07-6.13 (1H, m, CH), 6.98-7.36 (10H, m, ArH); δ_C (100 MHz, $CDCl_3$) 41.1, 41.2, 43.2, 43.8, 43.9, 47.0, 47.4, 47.7, 47.8, 52.7, 52.8, 127.0, 127.05, 127.4, 127.5, 128.1, 128.2, 128.5, 128.8, 131.0, 131.2, 135.1, 135.3, 137.1, 137.2, 138.45, 138.5, 139.0, 139.2, 149.6, 149.8, 161.0,

161.6, 206.8, 206.9; m/z (CI) 345 (MH^+, 30%), 235 (M^+-PhS, 100%); Found 345.13200, $C_{25}H_{20}OSH$ requires 345.13132 (+2.2 ppm).

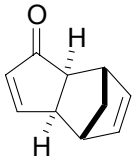


3-[1,3]-Dithian-2-yl-2-trimethylsilanyl-2,3,4,4a,7,7a-hexahydro-4,7-methanoinden-1-one, 23. 1,3-Dithiane (143 mg, 1.19 mmol, 1.3 eq.) was stirred in THF (20 cm^3) under nitrogen. This was cooled to -78˚C and 1.6 M butyl lithium in THF (0.75 cm^3, 1.19 mmol, 1.3 eq.) was added dropwise. Dry DMPU (0.29 cm^3, 2.39 mmol, 2.6 eq.) was then added. The reaction vessel was allowed to warm to -5˚C over 1 h before being re-cooled to -20˚C. A solution of **12** (0.20 g, 0.92 mmol, 1 eq.) in THF (15 cm^3) was added. The reaction vessel was kept between -20˚C and -5˚C for 1 h before aqueous ammonium chloride (30 cm^3) and Et_2O (30 cm^3) were added. The resultant aqueous layer was further extracted with Et_2O (2 x 30 cm^3). The combined organic layers were then dried with $MgSO_4$ and reduced *in vacuo*. Purification was carried out *via* flash column chromatography (Hex-EtOAc; 19:1) affording **23** (130 mg, 42%) as yellow oil. R_f 0.3 (Hex- Et_2O; 9:1); υ_{max} (neat/cm^{-1}) 2949, 2897, 2360, 2342, 1706, 1458, 1422, 1342, 1248, 858, 489; δ_H (400 MHz, $CDCl_3$) 0.15 (9H, s, CH_3), 1.14 (1H, d, *J* 9.0 Hz, CH_2), 1.42 (1H, d, *J* 9.0 Hz, CH_2), 1.81-1.89 (1H, m, CH), 2.14-2.25 (2H, m, CH), 2.36 (1H, d, *J* 9.0 Hz, CH), 2.57-2.60 (1H, m, CH_2), 2.75-2.80 (6H, m, CH_2, CH), 3.07 (1H, s, CH), 4.19 (1H, d, *J* 4.0 Hz, CH), 6.13-6.16 (1H, m, CH), 6.22-6.24 (1H, m, CH); δ_C (100 MHz, $CDCl_3$) -1.84, 25.7, 30.1, 43.9, 46.0, 46.3, 46.8, 48.0, 49.3, 52.9, 54.9, 57.3, 137.4, 138.2, 218.8; m/z (CI) 339 (MH^+, 100%), found 339.12799, $C_{17}H_{27}OS_2Si$ requires 339.12726 (+2.3 ppm).

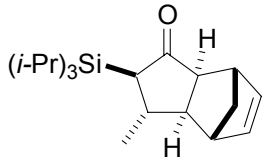


2-(3-Oxo-2,3,3a,4,7,7a-hexahydro-1*H*-4,7-methanoinden-1-yl)malonic acid dimethyl ester, 24. Under nitrogen sodium hydride [60% w/w in mineral oil] (28 mg, 0.69 mmol, 1.5 eq.) was added to a mixture of hexane (10 cm^3) and methanol (10 cm^3) at room temperature. The reaction mixture was allowed stir for 15 min until hydrogen evolution had ceased. Dimethylmalonate (0.08 cm^3, 0.69 mmol, 1.5 eq.) was added dropwise to the methoxide solution and after 15 minutes the reaction vessel was then cooled to -5˚ C. A solution of **12** (100 mg, 0.46 mmol, 1 eq.) in hexane (5 cm^3) was then added. The reaction vessel was kept at -5˚ C for 4 h, after which it was allowed to warm up to room temperature and stir for 8 h. Aqueous ammonium chloride (20 cm^3) and Et_2O (20 cm^3) were added and the aqueous layer was further extracted with Et_2O (2 x 20 cm^3). The combined organic phases were dried over $MgSO_4$ and were reduced *in vacuo*. Purification by flash column chromatography (Hex-EtOAc; 9:1) afforded the product **24** (90 mg, 71%) as colourless oil. R_f 0.15 (Hex-EtOAc; 9:1); υ_{max} (neat/cm^{-1}) 2957, 2925, 2852, 1737, 1634, 1438, 1339, 1275; δ_H (400 MHz, $CDCl_3$) 1.27 (1H, d, *J* 9.5 Hz, CH), 1.46 (1H, d, *J* 9.5 Hz, CH), 2.18 (1H, d, *J* 8.5 Hz, CH), 2.39 (1H, d, *J* 8.5 Hz, CH), 2.69-2.74 (3H, m, CH_2, CH), 2.84 (1H, s (br), CH_2), 3.12 (1H, s (br), CH), 3.55 (1H, d, *J* 8.0 Hz, CH), 3.75 (3H, s, CH_3), 3.78 (3H, s, CH_3), 6.17 (2H, s (br), CH); δ_C (100 MHz, $CDCl_3$) 23.8, 29.3, 37.7, 43.9, 45.6, 46.5, 47.3, 48.1, 49.5,

52.2, 137.3, 137.7, 168.2, 168.3, 216.7; m/z (CI) 296 (MNH_4^+, 100%), found 296.14911, $C_{15}H_{22}O_5N$ requires 296.14981 (-2.6ppm).



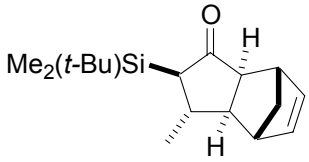
3a,4,7,7a-Tetrahydro-4,7-methanoinden-1-one, 25.[4] Sodium hydride [60% w/w in mineral oil] (95 mg, 2.39 mmol, 2.6 eq.) was stirred under N_2 in a 1:1 mixture of methanol (15 cm^3) and hexane (15 cm^3). This was cooled to -5˚C and a solution of **12** (200 mg, 0.92 mmol, 1 eq.) in hexane (10 cm^3) was added. The reaction vessel was kept at -5˚C over 4 h before being allowed to warm to room temperature and being stirred for 12 h. Aqueous ammonium chloride (30 cm^3) and Et_2O (30 cm^3) were added, the resultant aqueous layer was further extracted with Et_2O (2 x 30 cm^3). The combined organic layers were then dried with $MgSO_4$ and reduced *in vacuo* to yield the product **25** (122 mg, 91%) as a colourless oil. R_f 0.25 (Hex-EtOAc; 9:1); υ_{max} (cm^{-1}/neat) 3062, 2924, 2854, 1702, 1580, 1570, 1458, 1342, 1180; δ_H (400 MHz, $CDCl_3$) 1.25-1.31 (1H, m, CH_2), 1.40-1.42 (1H, m, CH_2), 2.26-2.28 (1H, m, CH), 2.72 (1H, s, CH), 2.86-2.87 (1H, m, CH), 2.92 (1H, s, CH) 6.20-6.25 (1H, m, CH), 6.26-6.30 (2H, m, CH), 7.56-7.60 (1H, m, CH); δ_C (100 MHz, $CDCl_3$) 42.0, 42.6, 43.5, 50.4, 51.9, 137.1, 138.2, 138.3, 165.9, 210.3.



3-Methyl-2-triisopropylsilanyl-2,3,3a,4,7,7a-hexahydro-4,7-methanoinden-1-one, 30. A suspension of CuI (19 mg, 0.1 mmol, 0.1 eq.) in Et_2O (10 cm^3) was treated dropwise with a 1 M solution of methylmagnesium bromide in Et_2O (1.5 cm^3, 1.5 mmol, 1.5 eq.) at -78ºC. The reaction was warmed to -20ºC over a period of 1 h. This solution was cooled to -35ºC before a solution of ***exo*-26** (302 mg, 1.0 mmol, 1.0 eq.) in Et_2O (5 cm^3) was added dropwise over a period of 2 min. Upon cooling to -78ºC, benzaldehyde (160 mg, 1.5 mmol, 1.5 eq.) was added. In a separate experiment *E*-pent-2-enal (126 mg, 1.5 mmol, 1.5 eq.) was also used. Neither of these aldehydes produced the required Peterson olefination adducts. Standard work-up, followed by flash column chromatography, afforded only **30** (320 mg, 97%) as a viscous yellow oil. R_f 0.3 (Hex-EtOAc; 4:1); δ_H (400 MHz, $CDCl_3$) 1.01-1.09 (21H, m, CH_3, CH), 1.16 (1H, d, *J* 6.5 Hz, CH_2), 1.20 (3H, d, *J* 6.5 Hz, CH_3), 1.35-1.42 (1H, m, CH_2), 1.58-1.66 (1H, m, CH), 1.70 (1H, d, *J* 8.5 Hz, CH), 2.42 (1H, d, *J* 8.5 Hz, CH), 2.71 (1H, s, CH), 3.12 (1H, d, *J* 1.0 Hz, CH), 6.14-6.18 (2H, m, CH); δ_C (100 MHz, $CDCl_3$) 16.3, 17.6, 21.5, 22.0, 22.4, 28.3, 40.5, 45.9, 46.7, 48.2, 135.9, 136.0, 210.9; m/z (EI) 318 (M^+, 5%), 252 (100%); Found 318.23776 $C_{20}H_{34}OSi$ requires 318.23789 (+1.5 ppm).

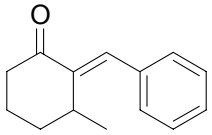
3-Methyl-2-triisopropylsilanyl-2,3,3a,4,7,7a-hexahydro-4,7-methanoinden-1-one, 30. Following the general procedure outlined, a solution of Me_2CuLi in Et_2O (25 cm^3), prepared from CuI (457 mg, 2.4 mmol, 1.2 eq.) and a 1.6 M solution of MeLi in hexanes (3.0 cm^3, 4.8 mmol, 2.4 eq), was treated with a solution of **26** (604 mg, 2.0 mmol, 1.0 eq.) in Et_2O (10 cm^3) at -78ºC. At -78ºC, benzaldehyde (320 mg, 3 mmol, 1.5 eq.) was added. In a separate experiment *E*-pent-2-enal (252 mg, 3 mmol, 1.5 eq.) was also used. As above, neither of these aldehydes formed theproducts of Peterson olefination. Standard work-up, followed by flash

column chromatography afforded only conjugate adduct **30** (625 mg, 98%) as viscous yellow oil.

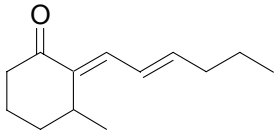


2-(*tert*-Butyldimethylsilanyl)-3-methyl-2,3,3a,4,7,7a-hexahydro-4,7-methanoinden-1-one, 31. Following the procedure described, CuI (3.8 mg, 0.02 mmol, 0.01 eq.) in Et_2O (10 cm^3) was treated dropwise with a 1 M solution of methylmagnesium bromide in Et_2O (2.8 cm^3, 2.8 mmol, 1.4 eq.) at -78ºC. The reaction was warmed to -20ºC over a period of 0.5 h. This solution was cooled to -35ºC before a solution of **27** (520 mg, 2.0 mmol, 1.0 eq.) in Et_2O (5 cm^3) was added. Upon re-cooling to -78ºC, *E*-pent-2-enal (0.3 cm^3, 3.0 mmol, 1.5 eq.) was added. Standard work-up followed by flash column chromatography (Hex-Et_2O, 9:1) afforded initially ***Z,E*-14k** (90 mg, 20%) as a yellow viscous oil followed by **31** (210 mg, 38%) as a viscous colourless oil R_f 0.25 (Hex-Et_2O, 9:1); υ_{max} (neat/cm^{-1}) 3060, 2954, 2928, 2856, 2253, 1711, 1570, 1463; δ_H (400 MHz, $CDCl_3$) -0.01 (3H, s, CH_3), 0.01 (3H, s, CH_3), 0.92 (9H, s, CH_3), 1.15-1.19 (1H, m, CH_2), 1.18 (3H, d, *J* 6.5 Hz, CH_3), 1.38-1.43 (1H, m, CH_2), 1.80-1.88 (1H, m, CH), 1.89-1.95 (1H, m, CH), 1.98 (1H, dd, *J* 2.0, 9.0 Hz, CH), 2.33 (1H, dd, *J* 1.0, 9.0 Hz, CH), 2.75 (1H, s, CH), 3.03 (1H, d, *J* 1.0 Hz, CH), 6.11-6.17 (2H, m, CH); δ_C (100 MHz, $CDCl_3$) -6.3, -5.5, 16.8., 24.5, 26.8, 26.9, 37.9, 44.6, 46.4, 48.6, 51.4, 52.4, 57.7, 138.0, 138.5, 220.0; m/z (CI) 277 (MH^+, 20%), 211 (100%); Found 277.19950 $C_{17}H_{29}OSi$ requires 277.19876 (+2.7 ppm). Further elution gave finally ***E,E*-14k** (95 mg, 21%) as a yellow oil.

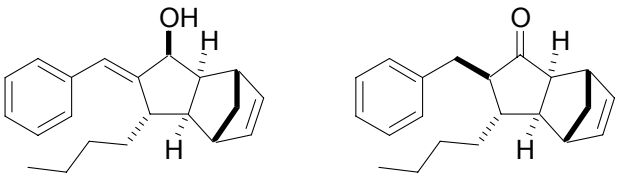
2-(*tert*-Butyldimethylsilanyl)-3-methyl-2,3,3a,4,7,7a-hexahydro-4,7-methanoinden-1-one, 31. Following the general procedure outlined, a solution of Me_2CuLi in Et_2O (25 cm^3), prepared from CuI (457 mg, 2.4 mmol, 1.2 eq.) and a 1.6 M solution of MeLi in hexanes (3.0 cm^3, 4.8 mmol, 2.4 eq), was treated with a solution of ***exo*-27** (520 mg, 2.0 mmol, 1.0 eq.) in Et_2O (5 cm^3) at -78ºC. Benzaldehyde (320 mg, 3 mmol, 1.5 eq.) was then added. Standard work-up, followed by flash column chromatography (Hex-Et_2O, 9:1) afforded only conjugate adduct **31** (520 mg, 94%).



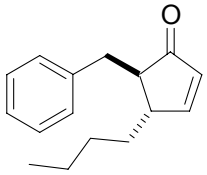
(*E*)-2-Benzylidene-3-methylcyclohexanone, 38.[5] Following the general procedure outlined, a solution of Me_2CuLi in Et_2O (25 cm^3), prepared from CuI (457 mg, 2.4 mmol, 1.2 eq.) and a 1.6 M solution of MeLi in hexanes (3.0 cm^3, 4.8 mmol, 2.4 eq.), was treated with 2-(trimethylsilyl)cyclohex-2-enone **36** (0.368 mg, 2.0 mmol, 1 eq.). On formation of the conjugate adduct (judged by TLC analysis) benzaldehyde (0.31 cm^3, 3.00 mmol, 1.5 eq.) was added at -78ºC. The solution was allowed to warm slowly to 0ºC over 6 h. Following standard work-up, purification by flash column chromatography (Hex-Et_2O, 9:1) afforded adduct **38** (184 mg, 46%) as a colourless viscous oil; R_f 0.15 (Hex-Et_2O, 9:1); δ_H (400 MHz, $CDCl_3$), 1.11 (3H, d, *J* 7.5 Hz, CH_3), 1.17 (1H, m, CH_2), 1.35-1.45 (3H, m, CH_2), 2.34 (1H, m, CH), 2.92-2.96 (2H, m, CH_2), 7.25 (1H, s, CH), 7.33-7.40 (3H, m, ArH), 7.60 (2H, d, *J* 7.5 Hz, ArH); δ_C (100 MHz, $CDCl_3$) 18.7, 22.2, 26.5, 35.5, 39.3, 127.9, 128.5, 128.6, 135.2, 135.4, 135.6, 200.2; m/z (CI) 201(MH^+, 100%); Found 201.13260, $C_{14}H_{17}O$ requires 201.13255 (+1.0 ppm); Found C, 83.80; H, 8.11%, $C_{14}H_{17}O$ requires C, 83.96; H, 8.05%.



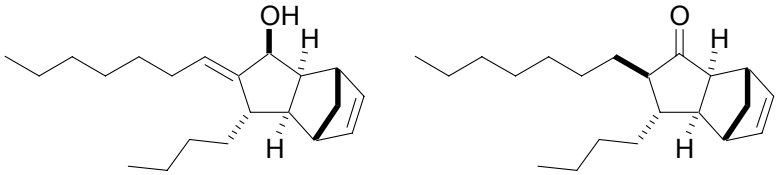
(*E*)-2-[(*E*)-Hex-2-enylidene]-3-methylcyclohexanone, 39. Following the general procedure outlined above, a solution of Me_2CuLi in Et_2O (25 cm^3), prepared from CuI (457 mg, 2.4 mmol, 1.2 eq.) and a 1.6 M solution of MeLi in hexanes (3.0 cm^3, 4.8 mmol, 2.4 eq.), was treated with **36** (0.368 mg, 2.0 mmol, 1 eq.). On formation of the conjugate adduct *E*-hex-2-enal (0.35 cm^3, 3.0 mmol, 1.5 eq.) was added at -78ºC. The solution was allowed to warm slowly to 0ºC over 5 h. Following standard work-up, purification by flash column chromatography (Hex-Et_2O; 9:1) afforded adduct **39** (361 mg, 94%) as a yellow viscous oil. R_f 0.15 (Hex-Et_2O, 9:1); υ_{max} (neat/cm^{-1}) 3055, 2970, 2932, 2874, 1687, 1629, 1580, 1453; δ_H (400 MHz, $CDCl_3$) 0.92 (3H, t, *J* 7.5 Hz, CH_3), 1.11 (3H, d, *J* 7.5 Hz, CH_3), 1.47 (2H, qt, *J* 7.5, 7.5 Hz, CH_2), 1.62-1.70 (1H, m, CH_2), 1.75-2.02 (3H, m, CH_2), 2.18 (2H, m, CH_2), 2.25-2.35 (1H, m, CH_2), 2.47-2.56 (1H, m, CH_2), 3.16-3.25 (1H, m, CH), 6.10-6.20 (H, m, CH), 6.30 (1H, ddt, *J* 1.0, 11.5, 15.0 Hz, CH), 6.95 (1H, d, *J* 11.5 Hz, CH); δ_C (100 MHz, $CDCl_3$) 13.6, 18.6, 21.2, 22.1, 30.3, 30.4, 35.5, 40.1, 125.1, 135.5, 138.6, 145.1, 201.6; m/z (CI) 193 (MH^+, 100%); Found 193.15940, $C_{13}H_{21}O$ requires 193.15924 (+0.2 ppm).



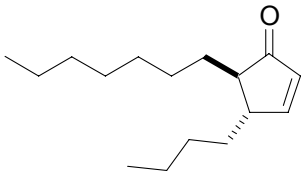
2-Benz-(*E*)-ylidene-3-butyl-2,3,3a,4,7,7a-hexahydro-1*H*-4,7-methanoinden-1-ol, 40b and 2-benzyl-3-butyl-2,3,3a,4,7,7a-hexahydro-4,7-methanoinden-1-one, 41b. Under N_2 ***E*-14b** (50 mg, 0.17 mmol, 1 eq.) was stirred in THF (10 cm^3) at -78˚C before a 1 M solution of lithium-tri-*tert*-butoxy aluminium hydride in THF (0.21 cm^3, 0.21 mmol, 1.2 eq.) was added. The reaction vessel was warmed to room temperature and stirring was continued for 12 h. Aqueous ammonium chloride (10 cm^3) and Et_2O (10 cm^3) were added to the reaction vessel. The aqueous layer was further extracted with Et_2O (2 x 30 cm^3). The combined organic phases were then dried with $MgSO_4$ and concentrated *in vacuo*. Purification by flash column chromatography (Hex-Et_2O; 19:1) gave the products of 1,4-reduction **41b** (32 mg, 64%) and 1,2-reduction **40b** (15 mg, 30%) as pale yellow oils: Data for **41b**: R_f 0.45 (Hex-Et_2O; 9:1); υ_{max} (cm^{-1}/neat) 3062, 2957, 2925, 1855, 1732, 1604, 1496, 1455, 701; δ_H (400 MHz, $CDCl_3$) 0.78-0.80 (1H, m, CH_2), 0.88-0.92 (3H, m, CH_3), 1.23-1.39 (5H, m, CH_2), 1.45-1.51 (2H, m, CH_2, CH), 1.60 (1H, s, CH), 1.87-1.91 (1H, m, CH), 2.30-2.34 (1H, m, CH), 2.52-2.55 (1H, m, CH), 2.65 (1H, s, CH), 2.82 (1H, dd, *J* 5.0, 14.0 Hz, CH_2), 2.99 (1H, dd, *J* 6.0, 14.0 Hz, CH_2), 3.14 (1H, s, CH), 6.14 (1H, dd, *J* 3.0, 7.0 Hz, CH), 6.19 (1H, dd, *J* 3.0, 7.0 Hz, CH), 7.19-7.28 (5H, m, CH); δ_C (100 MHz, $CDCl_3$) 13.6, 22.4, 28.9, 33.2, 35.5, 43.7, 44.2, 44.5, 46.5, 47.9, 53.8, 60.4, 125.6, 127.8, 128.3, 136.9, 137.9, 139.4, 217.6; m/z (CI) 312 (MNH_4^+, 100%); Found 312.23169, $C_{21}H_{30}ON$ requires 312.23273 (-3.8 ppm): Data for **40b**: R_f 0.25 (Hex-Et_2O; 9:1); υ_{max} (cm^{-1}/neat) 3367, 3057, 2956, 2958, 2857, 1599, 1494, 1458, 1328, 1107, 693; δ_H (400 MHz, $CDCl_3$) 0.90-0.93 (3H, m, CH_3), 1.10 (1H, d, *J* 8.5 Hz, CH_2), 1.28-1.43 (6H, m, CH_2), 1.46 (1H, d, *J* 8.5 Hz, CH_2), 1.87 (1H, d, *J* 7.5 Hz, CH), 2.21 (1H, t, *J* 7.5, CH), 2.62 (1H, s, CH), 2.66 (1H, s (br), CH), 2.97 (1H, s, CH), 4.86-4.90 (1H, m, CH), 6.16-6.21 (2H, m, CH), 6.38 (1H, s (br), CH), 7.26-7.40 (5H, m, CH); δ_C (100 MHz, $CDCl_3$) 13.7, 22.3, 29.4, 35.7, 40.8, 41.9, 43.6, 45.9, 47.3, 48.9, 74.4, 118.4, 125.9, 127.1, 128.0, 137.1, 137.5, 138.1, 153.8; m/z (CI) 295 (MH^+, 100%); Found 295.20600, $C_{21}H_{27}O$ requires 295.20618 (-0.6 ppm).



5-Benzyl-4-butylcyclopent-2-enone, 42b. Under N_2 **41b** (65 mg, 0.22 mmol, 1 eq.) was dissolved in DCM (5 cm^3). Maleic anhydride (120 mg, 1.11 mmol, 5 eq.) was added and the reaction mixture was stirred to dissolve the solid. A solution of 1 M methyl aluminium chloride in hexane (0.33 cm^3, 0.33 mmol, 1.5 eq.) was added dropwise and the reaction was heated to reflux for 5 h. After cooling, silica (*ca.* 2 g) was added and the DCM was reduced *in vacuo*. Flash column chromatography (*c*-Hex;EtOAc; 19:1) afforded the product **42b** (49 mg, 97%) as a brown oil. R_f 0.3 (*c*-Hex-EtOAc;19:1); δ_H (400 MHz, $CDCl_3$) 0.70 (3H, t, *J* 7.0 Hz, CH_3), 1.04-1.22 (5H, m, CH_2, CH), 1.23-1.41 (1H, m, CH_2), 2.15-2.19 (1H, m, CH), 2.54-2.63 (2H, m, CH_2, CH), 3.05-3.09 (1H, m, CH_2), 6.03 (1H, dd, *J* 2.0, 6.0 Hz, CH), 7.10-7.22 (5H, m, CH), 7.46-7.48 (1H, dd, *J* 2.0, 6.0 Hz, CH); δ_C (100 MHz, $CDCl_3$) 12.8, 21.5, 28.2, 32.7, 35.8, 45.6, 52.3, 125.3, 127.4, 128.1, 131.5, 138.3, 166.6, 210.3; m/z (ESI^+) 228 (MH^+, 100%); Found 229.1592, $C_{16}H_{21}O$, requires 229.1603 (+4.6 ppm).

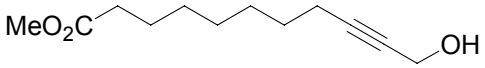


3-Butyl-2-hept-(*E*)-ylidene-2,3,3a,4,7,7a-hexahydro-1H-4,7-methanoinden-1-ol, 40m and 3-butyl-2-heptyl-2,3,3a,4,7,7a-hexahydro-4,7-methanoinden-1-one, 41m. Under N_2 ***E*-14m** (200 mg, 0.67 mmol, 1 eq.) was stirred in THF (10 cm^3) at –78°C and a 1.0 M solution of lithium tri-*tert*-butoxy aluminium hydride in THF (0.80 cm^3, 0.80 mmol, 1.2 eq.) was added dropwise. The reaction mixture was stirred for 12 h during which time room temperature was reached. Aqueous ammonium chloride (10 cm^3) and Et_2O (10 cm^3) were then added to the reaction and the aqueous layer was further extracted with Et_2O (2 x 10 cm^3). The combined organic phases were then dried with $MgSO_4$ and reduced *in vacuo*. Purification by flash column chromatography (*c*-Hex-EtOAc; 19:1) gave **41m** (166 mg, 82%) that co-ran with several minor, unknown impurities. Further elution gave the product of 1,2-reduction **40m** (22 mg, 11%) which was isolated as a clear oil. R_f 0.45 (*c*-Hex-EtOAc; 19:1); υ_{max} (neat/cm^{-1}) 3423, 3060, 2954, 2927, 2872, 2856, 2360, 2341, 1732, 1645, 1533, 1088; δ_H (400 MHz, $CDCl_3$) 0.77-0.80 (6H, m, CH_3), 0.98-1.01 (1H, m, CH_2), 1.16-1.24 (14H, m, CH_2), 1.38-1.40 (1H, m, CH_2), 1.60 (1H, d, *J* 7.25 Hz, CH), 1.90-1.96 (2H, m, CH_2), 2.00-2.07 (1H, m, CH), 2.19 (1H, s, CH), 2.50 (1H, s, CH), 2.80 (1H, s, CH), 4.55 (1H, d, *J* 9.0 Hz, CH), 5.15-5.20 (1H, m, CH), 6.01-6.07 (2H, m, CH); δ_C (100 MHz, $CDCl_3$) 14.1, 22.7, 22.8, 28.6, 29.7, 29.8, 31.8, 36.9, 41.3, 42.3, 43.7, 47.6, 47.7, 49.4, 73.7, 121.1, 139.6, 140.21, 152.7.

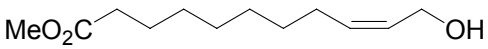


4-Butyl-5-heptylcyclopent-2-enone, 42m. Under N_2 an impure sample of **41m** (355 mg, *ca.* 1.18 mmol, 1 eq.) was dissolved in DCM (10 cm^3). Maleic anhydride (580 mg, 5.88 mmol, 5 eq.) was added to the reaction mixture before a 1.0 M solution of methyl aluminium chloride in hexane (1.42 cm^3, 1.42 mmol, 1.2 eq.) was added and the vessel was heated to reflux for 5 hours. After cooling silica (*ca.* 3 g) was added to the vessel and the DCM was

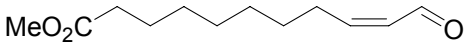
removed *in vacuo*. Purification by flash column chromatography (*c*-Hex-EtOAc; 19:1) afforded **42m** (223 mg, 80%) as a yellow oil. R_f 0.5 (*c*-Hex-EtOAc; 19:1); υ_{max} (neat/cm^{-1}) 2956, 2926, 2856, 1709, 1589, 1525, 1465, 1379, 1350, 1178; δ_H (400 MHz, $CDCl_3$) 0.78-0.87 (6H, m, CH_3), 1.19-1.45 (17H, m, CH_2, CH), 1.60-1.66 (1H, m, CH_2), 1.85-1.89 (1H, m, CH), 2.49-2.54 (1H, m, CH), 6.02 (1H, dd, *J* 2.0, 5.5 Hz, CH), 7.53 (1H, dd, *J* 2.5, 5.5 Hz, CH); δ_C (100 MHz, $CDCl_3$) 14.1, 14.3, 22.8, 23.0, 27.3, 29.3, 29.8, 29.9, 31.5, 32.0, 34.5, 48.2, 51.9, 133.0, 167.4, 212.7; m/z (CI) 237 (MH^+, 100%); Found 237.2218, $C_{16}H_{29}O$ requires 237.2207 (-4.8 ppm).



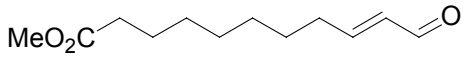
11-Hydroxyundec-9-ynoic acid methyl ester.[6] Liquid ammonia (*ca.* 1000 cm^3) was condensed at -40ºC in a 3 dm^3 3-neck flask, fitted with an overhead stirrer. The solution stirred vigorously and 5 finely divided pieces of lithium (from 1.10 g, 158.5 mmol, 3.53 eq.) were added a blue colour immediately appeared and then ferric nitrate (30 mg) was added. The reaction mixture was stirred for 5 min before the remaining lithium was gradually added. After 10 min the colour of the suspension turned from dark blue to grey. A solution of propargyl alcohol **48** (3.00 g, 53.57 mmol, 1.2 eq.) in THF (10 cm^3) was added dropwise over 5 min and the reaction was stirred at -35ºC for 2 h. 8-Bromooctanoic acid (10.00 g, 44.82 mmol, 1.0 eq.) in THF (50 cm^3) was then added dropwise with vigorous stirring and the reaction was refluxed at -30ºC for 7 h. The ammonia was then allowed to evaporate overnight before the solution was acidified with 2 M HCl (*p*H *ca.* 4.0). The solution was extracted with Et_2O (5 x 100 cm^3) and the combined organic layers were dried over $MgSO_4$. Filtration followed by solvent evaporation under reduced pressure gave crude 11-hydroxy-9-undecanoic acid which was purified (4.80 g, 54%) by crystallization from *n*-hexane. The resultant product (4.50 g, 24.22 mmol, 1.0 eq.) was dissolved in dry MeOH (30 cm^3) and $BF_3{\cdot}Et_2O$ (0.92 cm^3, 7.26 mmol, 0.3 eq.) was added and the reaction mixture was heated to reflux for 10-15 min. The solvent was removed under reduced pressure and the crude product was washed with water (100 cm^3) before extraction with Et_2O (5 x 100 cm^3). Flash column chromatography (DCM-MeOH; 98:2) afforded 11-hydroxyundec-9-ynoic acid methyl ester (4.2 g, 88%) as a colourless oil. R_f 0.3 (DCM-MeOH; 98:2); υ_{max} (neat/cm^{-1}) 3438, 2932, 2857, 2286, 2223, 1737, 1437; δ_H (400 MHz, $CDCl_3$) 1.27-1.43 (6H, m, CH_2), 1.50 (2H, pent, *J* 7.5 Hz, CH_2), 1.63 (2H, pent, *J* 7.5 Hz, CH_2), 2.21 (2H, tt, *J* 2.25, 7.0 Hz, CH_2), 2.31 (2H, t, *J* 7.5 Hz, CH_2), 3.67 (3H, s, CH_3), 4.25 (2H, t, *J* 2.25 Hz, CH_2); δ_H (400 MHz, $CDCl_3$) 18.6, 27.7, 28.4, 28.4, 28.6, 28.8, 34.0, 51.2, 51.4, 78.5, 86.2, 174.3; m/z (CI) 213 (MH^+, 100%); Found 213.14907, $C_{12}H_{21}O_3$ requires 213.14906 (+0.01 ppm).



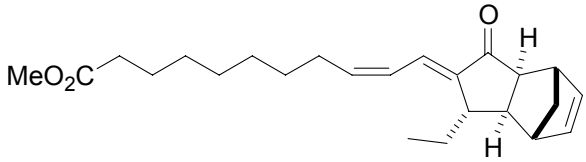
(*Z*)-Methyl 11-hydroxyundec-9-enoate. To a solution of 11-hydroxyundec-9-ynoic acid methyl ester (950 mg, 4.48 mmol, 1.0 eq.) in ethyl acetate (30 cm^3) was added quinoline (100 mg, 0.77 mmol, 0.17 eq.) followed by Lindlar's catalyst (300 mg). This solution was stirred under a balloon of hydrogen for 2.5 h. The reaction mixture was filtered through a plug of silica and the solvent removed in *vacuo*; purification by flash column chromatography yielded (*Z*)-methyl 11-hydroxyundec-9-enoate (868 mg, 90%) as a colourless oil. R_f 0.30 (DCM-MeOH; 99:1); υ_{max} (neat/cm^{-1}) 3422, 3013, 2927, 2854, 1735, 1437; δ_H (400 MHz, $CDCl_3$) 1.27-1.39 (8H, m, CH_2), 1.62 (2H, pent, *J* 7.5 Hz, CH_2), 1.86 (1H, s, OH), 2.06 (2H, q, *J* 7.0 Hz, CH_2), 2.30 (2H, t, *J* 7.5 Hz, CH_2), 3.66 (3H, s, CH_3), 4.19 (2H, dd, *J* 1.0, 6.5 Hz, CH_2), 5.47-5.68 (2H, m, CH); δ_C (100 MHz, $CDCl_3$) 24.8, 27.3, 28.8, 28.9, 9.4, 34.0, 51.3, 58.4, 128.5, 132.7, 174.2; m/z (CI) 232 (MNH_4^+, 20%), 214 (MH^+, 20%), 197 (100%); Found 232.19150, $C_{12}H_{26}O_3N$ requires 232.19150.



(*Z*)-Methyl 11-oxoundec-9-enoate, *Z*-49. To a solution of (*Z*)-methyl 11-hydroxyundec-9-enoate (1.00 g, 4.66 mmol, 1.0 eq.) in DCM (30 cm^3) was added Dess-Martin's periodinane (2.75 g, 6.058 mmol, 1.3 eq.) and the reaction was stirred at room temperature for 1 h. The reaction was quenched by the addition of Et_2O (60 cm^3) and water (60 cm^3) followed by saturated aqueous Na_2SO_3 solution (100 cm^3) and saturated aqueous sodium hydrogencarbonate (100 cm^3) solution. The organic and aqueous phases were separated and the resultant aqueous layer was extracted with Et_2O (5 x 50 cm^3). The combined organic fractions were dried over $MgSO_4$. Filtration and solvent removal *in vacuo* gave ***Z*-49** (929 mg, 94%) as a colourless oil. R_f 0.35 (Hex-EtOAc; 3:1); υ_{max} (neat/cm^{-1}) 2931, 2856, 1737, 1680, 437; δ_H (400 MHz $CDCl_3$) 1.28-1.40 (6H, m, CH_2), 1.51 (2H, pent, *J* 7.5 Hz, CH_2), 1.63 (2H, pent, *J* 7.5 Hz, CH_2), 2.30 (2H, t, *J* 7.5 Hz, CH_2), 2.57-2.64 (2H, tdd *J* 1.5, 7.5, 8.0 Hz, CH_2), 3.66 (3H, s, CH_3), 5.96 (1H, ddt, *J* 1.5, 8.0, 11.0 Hz, CH), 6.62 (1H, dt *J* 8.0, 11.0 Hz, CH), 10.08 (1H, d, *J* 8.0 Hz, CH); δ_C (100 MHz $CDCl_3$) 15.2, 24.8, 27.9, 28.8, 28.9, 29.0, 33.9, 51.3, 130.1, 153.1, 174.0, 190.7; m/z (CI) 230 (MNH_4^+, 100%), 213 (MH^+, 40%); Found 213.14887, $C_{12}H_{21}O_3$ requires 213.14906 (-1.0 ppm).

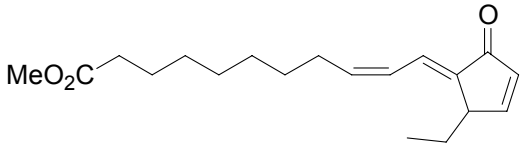


(*E*)-Methyl 11-oxoundec-9-enoate, *E*-49. A solution of ***Z*-49** (1.00 g, 4.66 mmol, 1.0 eq.) in chloroform (50 cm^3) was mixed with *p*-toluene sulfonic acid (100 mg, 0.53 mmol, 0.11 eq.) and stirred at 50ºC for 20 min. After cooling the solution was washed with distilled water (2 x 50 cm^3) and dried over $MgSO_4$. The solvent was removed under reduced pressure and the product purified by flash column chromatography which afforded ***E*-49** (840 mg, 85%) as a yellow oil. R_f 0.35 (Hex-EtOAc; 3:1); υ_{max} (neat/cm^{-1}) 2931, 2857, 1738, 1691, 1638, 1436; δ_H (400 MHz, $CDCl_3$) 1.29-1.38 (6H, m, CH_2), 1.51 (2H, pent, *J* 7.5 Hz, CH_2), 1.63 (2H, pent, *J* 7.5 Hz, CH_2), 2.31 (2H, t, *J* 7.5 Hz, CH_2), 2.33 (2H, qd, *J* 1.5, 7.0 Hz, CH_2), 3.68 (3H, s, CH_3), 6.11 (1H, ddt, *J* 1.5, 7.5, 15.5 Hz, CH), 6.84 (1H, dt, *J* 7.0, 15.5 Hz, CH), 9.50 (1H, d, *J* 7.5 Hz, CH); δ_C (100 MHz, $CDCl_3$) 24.8, 27.7, 28.8, 28.9, 32.6, 34.0, 51.4, 133.0, 158.6, 174.1, 193.9; m/z (CI) 230 (MNH_4^+, 100%), 213 (H^+, 25%); Found 213.14946, $C_{12}H_{21}O_3$ requires 213.14906 (+2.0 ppm).

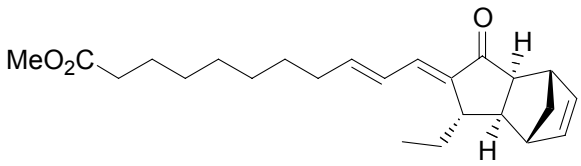


(±)-*Z*-11-[1-Ethyl-3-oxo-1,3,3a,4,7,7a-hexahydro-4,7-methanoinden-2-(*Z*)-ylidene] undec-9-enoic acid methyl ester, (±)-*E,Z*-50. Under N_2 copper(I) iodide (480 mg, 2.52 mmol, 1.2 eq.) was suspended in Et_2O (30 cm^3) at -78ºC. A 0.5 M solution of ethyllithium in cyclohexane-benzene (10.08 cm^3, 5.04 mmol, 2.4 eq.) was added dropwise and the temperature was allowed to increase to -10ºC over 1 h before being reduced to -40ºC. Following dropwise addition of ***exo*-12** (462 mg, 2.10 mmol, 1.0 eq.) in Et_2O (10 cm^3) the reaction was allowed to warm to -5ºC over 30 min and stirred at this temperature for 1.5 h. The temperature of the reaction was decreased to -78ºC and aldehyde ***Z*-49** (900 mg, 4.20 mmol, 2.0 eq.) was added. Following addition the temperature was allowed to warm to 0ºC over 15 h. The reaction was quenched with saturated aqueous NH_4Cl solution (50 cm^3) and the resultant aqueous layer was extracted with Et_2O (5 x 50 cm^3). The combined organic fractions were dried over $MgSO_4$. On filtration and solvent removal the crude product was purified by flash column chromatography (Hex-Et_2O; 95:5 → 90:10 → Hex-EtOAc; 4:1) affording initially **(±)-*E,Z*-50** (500 mg, 64%) as a colourless oil and finally aldehyde ***E*-49** (400 mg). R_f 0.35 (Hex-EtOAc; 4:1); υ_{max} (neat/cm^{-}

[1]) 3058, 2931, 2855, 2348, 1739, 1700, 1625, 1601, 1460, 1435; δ_H (400 MHz $CDCl_3$) 0.93 (3H, t, *J* 7.5 Hz, CH_3), 1.26-1.35 (6H, m, CH_2), 1.37-1.54 (4H, m, CH_2), 1.59-1.67 (4H, m, CH_2), 1.93 (1H, d, *J* 7.75 Hz, CH), 2.29 (2H, t, *J* 7.5 Hz, CH_2), 2.31 (2H, dt, *J* 7.5, 7.75 Hz, CH_2), 2.40 (1H, d, *J* 7.5 Hz, CH), 2.63-2.67 (1H, m (br), CH), 2.76 (1H, s, CH), 3.06 (1H, s, CH), 3.66 (3H, s, CH_3), 5.94-6.01 (1H, dt, *J* 7.75, 10.5 Hz, CH), 6.12-6.25 (3H, m, CH), 7.21 (1H, ddd, *J* 1.0, 2.0, 12.25 Hz, CH); δ_C (100 MHz $CDCl_3$) 10.8, 24.9, 28.2, 29.0, 29.3, 30.1, 34.0, 43.2, 44.6, 45.9, 48.2, 49.6, 51.4, 54.6, 124.4, 127.7, 137.5, 138.8, 143.3, 144.1, 174.2, 209.0; m/z (CI) 371 (MH^+, 20%), (305, 100%); Found 371.25769, $C_{24}H_{35}O_3$ requires 371.25861 (-2.9 ppm).

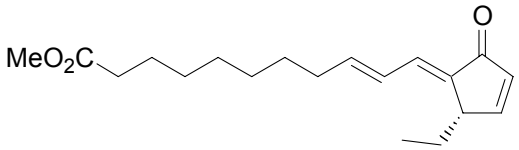


(*Z*)-11-[2-Ethyl-5-oxocyclopent-3-en-(*E*)-ylidene]undec-9-enoic acid methyl ester, (±)-*E,Z*-51. A solution of **(±)-*E,Z*-50** (150 mg, 0.40 mmol, 1.0 eq.) and maleic anhydride (588 mg, 6.00 mmol, 15 eq.) in DCM (10 cm^3) was treated with a 1 M solution of $MeAlCl_2$ in hexane (0.6 cm^3, 0.60 mmol, 1.5 eq.). The reaction mixture was split into two microwavable vials (5 cm^3) and irradiated to 110ºC for 65 seconds. The reaction mixtures from both tubes were quenched in saturated sodium hydrogencarbonate solution (50 cm^3) and stirred for 10 min before extraction with Et_2O (10 x 25 cm^3). The combined organic fractions were then dried over $MgSO_4$ and solvent removed *in vacuo*. Purification by flash column chromatography (Hex-EtOAc; 3:1), yielded initially **(±)-*E,Z*-51** (90 mg, 74%) as a colourless oil. R_f 0.25 (Hex-EtOAc; 3:1); υ_{max} (neat/cm^{-1}) 2929, 2855, 2348, 1737, 1693, 1628, 1579, 1460, 1435; δ_H (400 MHz $CDCl_3$) 0.93 (3H, t, *J* 7.5 Hz, CH_3), 1.26-1.35 (6H, m, CH_2), 1.39-1.46 (2H, m, CH_2), 1.58-1.68 (3H, m, CH_2), 1.87-1.98 (1H, m, CH_2), 2.30 (2H, t, *J* 7.5 Hz, CH_2), 2.35 (2H, dt, *J* 7.25, 7.5 Hz, CH_2), 3.51-3.56 (1H, m (br), CH), 3.66 (3H, s, CH_3), 5.98 (1H, dtd, *J* 0.75, 7.75, 10.5 Hz, CH), 6.21-6.29 (1H, ddt *J* 1.5, 10. 5, 12.25 Hz, CH), 6.38 (1H, dd *J* 1.75, 6.0 Hz, CH), 7.27 (1H, dd, *J* 1.0, 12.25 Hz, CH), 7.52 (1H, ddd, *J* 0.75, 2.5, 6.0 Hz, CH); δ_C (100 MHz $CDCl_3$) 10.0, 24.9, 25.6, 28.0, 29.0, 29.1, 29.1, 29.3, 34.0, 44.5, 51.4, 54.6, 123.7, 125.6, 135.3, 137.1, 142.9, 160.9, 174.2, 197.6; ; m/z (CI) 305, (305, 100%), found (MH^+) 305.21247, $C_{19}H_{28}O_3$ requires 305.21167 (+2.9 ppm). Further elution gave **(±)-*E,E*-51** (15 mg, 12%).



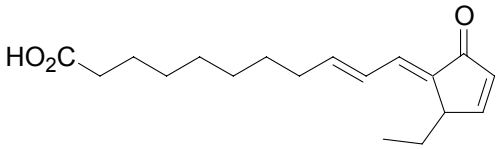
(+)-(*E*)-11-[(1*S*,3a*S*,4*S*,7*R*,7a*S*)-1-ethyl-3-oxo-1,3,3a,4,7,7a-hexahydro-4,7-methano inden-(2*E*)-ylidene]undec-9-enoic acid methyl ester, (+)-*E,E*-50. Under N_2, a 1.5 M solution of *tert*-butyllithium in pentane (1.22 cm^3, 1.83 mmol, 4.0 eq.) was added dropwise to a solution of iodoethane (143 mg, 0.91 mmol, 2.0 eq.) in a mixture of pentane (8.2 cm^3) and ether (4.8 cm^3) at -78°C. Stirring was continued at -78°C for 0.25 h before warming to room temperature over 1 h. The solution was re-cooled to –20°C and added to a pre-cooled (-78ºC) slurry of CuI (308 mg, 1.62 mmol, 1.0 eq.) in Et_2O (10 cm^3) *via* cannula. The combined solution was warmed to -10°C over 1 h and stirred for 30 min between -5°C and –10°C. The resultant cuprate was re-cooled to –78°C before the enone **(+)-*exo*-12** (100 mg, 0.46 mmol, 1.0 eq.) in Et_2O (5 cm^3) was added dropwise. The reaction was allowed to warm to –5°C over 1 h and stirred for 15 min between -5°C and –10°C. Freshly purified aldehyde ***E*-49** (291 mg, 1.37 mmol, 3.0 eq.) was added at –78°C and the solution was allowed to warm to -10ºC over 3 h

and stirred at -5ºC for 2 h. The reaction was then warmed to room temperature and stirred for 10 min. before quenching with a saturated solution of NH_4Cl (20 cm^3). Extraction with Et_2O (6 x 20 cm^3) and drying of the combined organic extracts over $MgSO_4$ gave the crude adduct following filtration and solvent removal. Purification by flash column chromatography (Hex-EtOAc; 19:1 → 4:1) afforded initially the **(+)-*Z,E*-50** (5 mg, 3%) followed by **(+)-*E,E*-50** (115 mg, 68%) as a yellow coloured oil. R_f 0.20 (Hex-EtOAc; 4:1), $[\alpha]_D$ +273 (*c* = 1.00, $CHCl_3$); υ_{max} (neat/cm^{-1}) 3058, 2931, 2855, 2348, 1739, 1700, 1625, 1601, 1460, 1435; δ_H (400 MHz, $CDCl_3$) 0.93 (3H, t, *J* 7.5 Hz, CH_3), 1.23-1.35 (8H, m, CH_2), 1.39-1.48 (2H, m, CH_2), 1.48-1.55 (1H, m, CH_2), 1.58-1.69 (3H, m, CH_2), 1.93 (1H, s, CH), 2.17-2.23 (2H, m, CH_2), 2.30 (2H, t, *J* 7.5 Hz, CH_2), 2.38 (1H, d, *J* 7.5 Hz, CH), 2.62-2.67 (1H, m (br), CH), 2.76 (1H, s, CH), 3.06 (1H, s, CH), 3.66 (3H, s, CH_3), 6.16-6.25 (4H, m, CH), 6.85-6.90 (1H, m, CH); δ_C (100 MHz, $CDCl_3$) 10.7, 24.9, 28.7, 28.9, 29.0, 30.2, 33.4, 34.0, 43.2, 44.6, 45.9, 48.2, 49.6, 51.4, 54.6, 126.4, 133.5, 137.5, 138.8, 142.3, 146.7, 174.2, 208.8; m/z (CI) 371 (MH^+, 15%), 305 (100%); Found 371.25769, $C_{24}H_{35}O_3$ required 371.25861 (-2.9 ppm). Data for **(+)-*Z,E*-50**: R_f 0.25 (Hex-EtOAc; 4:1), υ_{max} (neat/cm^{-1}) 3058, 2930, 2855, 2348, 1740, 1692, 1625, 1591, 1460, 1436; δ_H (400 MHz, $CDCl_3$) 0.95 (3H, t, *J* 7.5 Hz, CH_3), 1.25-1.38 (8H, m, CH_2), 1.39-1.53 (3H, m, CH_2), 1.57-1.68 (3H, m, CH_2), 1.85 (1H, d, *J* 8.0 Hz, CH), 2.18 (2H, q, *J* 7.5 Hz, CH_2), 2.30 (2H, t, *J* 7.5 Hz, CH_2), 2.30-2.36 (2H, m, CH), 2.72 (1H, s, CH), 3.07 (1H, d, *J* 1.0 Hz, CH), 3.66 (3H, s, CH_3), 6.00 (1H, dt, *J* 7.0, 15.0 Hz, CH), 6.16-6.22 (2H, m, CH), 6.25 (1H, dd, *J* 1.0, 11.25 Hz, CH), 7.54 (1H, ddt, *J* 1.5, 11.25, 15.0 Hz, CH); δ_C (100 MHz, $CDCl_3$) 10.8, 24.9, 28.9, 29.0, 29.1, 31.1, 33.0, 34.1, 43.3, 45.3, 47.5, 47.9, 49.4, 51.4, 55.8, 127.0, 137.6, 137.8, 138.6, 140.4, 145.1, 174.2, 208.7; m/z (CI) 393 (MNa^+, 25%), 371 (MH^+, 10%), 305 (100%); Found 393.2392, $C_{24}H_{34}O_3Na$ required 393.2406 (-3.6 ppm).

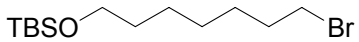


(+)-(*E*)-11-[(S)-2-Ethyl-5-oxocyclopent-3-en-(*E*)-ylidene]undec-9-enoic acid methyl ester, (+)-*E,E*-51. Under N_2, a solution of **(+)-*E,E*-50** (85 mg, 0.23 mmol, 1.0 eq.) in DCM (4 cm^3) was added to a solution of maleic anhydride (338 mg, 3.45 mmol, 15 eq.) in DCM (4 cm^3). The solution was homogenised by stirring before being split into two microwavable vials (Smith Process vial, 2-5 cm^3). A 1.0 M solution of $MeAlCl_2$ in hexane (0.17 cm^3, 0.17 mmol, 1.5 eq.) was added dropwise to each vial before both vials were irradiated (Smith Creator, 300 Watts) up to 110°C over a period of 50 sec. The reaction mixture was quenched immediately on pouring into a rapidly stirred 2% solution of $NaHCO_3$ (20 cm^3) and the mixture was stirred for 4 min before extraction with Et_2O (10 x 25 cm^3). The combined organic extracts were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. Purification by flash column chromatography (Hex-EtOAc; 9:1 → 3:1) gave, initially, starting material **(+)-*E,E*-50** (5 mg, 6%) followed by ***Z,E*-51** (3 mg, 4%) and finally **(+)-*E,E*-51** (58 mg, 83%) as a yellow coloured viscous oil. R_f 0.20 (Hex-EtOAc; 3:1); $[\alpha]_D$ +90 (*c* = 1.00, $CHCl_3$); υ_{max} (neat/cm^{-1}) 3058, 2928, 2854, 2348, 1737, 1693, 1633, 1579, 1460, 1435; δ_H (400 MHz $CDCl_3$) 0.88 (3H, t, *J* 7.5 Hz, CH_3), 1.25-1.36 (6H, m, CH_2), 1.41-1.47 (2H, m, CH_2), 1.58-1.70 (3H, m, CH_2), 1.86-1.98 (1H, m, CH_2), 2.22 (2H, q, *J* 7.0 Hz, CH_2), 2.30 (2H, t, *J* 7.5 Hz, CH_2), 3.51-3.56 (1H, m (br), CH), 3.66 (3H, s, CH_3), 6.15-6.33 (2H, m, CH), 6.37 (1H, dd *J* 1.75, 6.0 Hz, CH), 6.95 (1H, d, *J* 11.0, CH), 7.50 (1H, ddd, *J* 0.75, 2.5, 6.0 Hz, CH); δ_C (100 MHz $CDCl_3$) 10.0, 24.9, 25.7, 28.7, 28.9, 29.0, 29.1, 29.1, 33.4, 34.0, 44.6, 51.4, 125.7, 131.3, 135.3, 135.4, 146.2, 160.7, 174.2, 197.6; m/z (CI) 305 (MH^+, 100%); Found 305.21220, $C_{19}H_{29}O_3$ required 305.21167 (+1.9 ppm); HPLC separation using AS column (COL-HP-17), solvent mixture

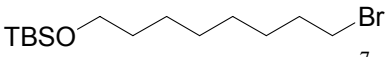
Hex-IPA, 90:10, 254 nm, 0.5 cm^3/min. and sample amount 2 µl gave >99% enantiomeric excess of the *title compound*. Data for ***Z,E*-51**: R_f 0.30 (Hex-EtOAc; 4:1); υ_{max} (neat/cm^{-1}) 3058, 2929, 2856, 1738, 1687, 1630, 1608, 1582, 1436; δ_H (400 MHz $CDCl_3$) 0.92 (3H, t, *J* 7.5 Hz, CH_3), 1.27-1.37 (6H, m, CH_2), 1.40-1.50 (2H, m, CH_2), 1.53-1.68 (3H, m, CH_2), 1.77-1.87 (1H, m, CH_2), 2.22 (2H, qd, *J* 1.25, 7.0 Hz, CH_2), 2.30 (2H, t, *J* 7.5 Hz, CH_2), 3.25-3.33 (1H, m (br), CH), 3.67 (3H, s, CH_3), 6.05 (1H, dt, *J* 7.0, 15.0 Hz, CH), 6.30 (1H, dd, *J* 1.75, 6.0 Hz, CH), 6.38 (1H, d, *J* 11.0 Hz, CH), 7.42 (1H, dd *J* 2.5, 6.0 Hz, CH), 7.67 (1H, ddt, *J* 1.25, 11.0, 15.0 Hz, CH); δ_C (100 MHz $CDCl_3$) 10.4, 24.9, 26.1, 28.9, 29.0, 33.0, 34.1, 46.8, 51.4, 126.4, 133.9, 135.7, 136.7, 145.3, 159.5, 174.2, 197.6; m/z (CI) 305 (MH^+, 100%); Found 305.21247, $C_{19}H_{29}O_3$ requires 305.21167 (+2.9 ppm).



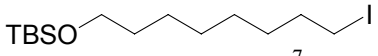
(±)-*E*-11-[2-Ethyl-5-oxocyclopent-3-en-(*E*)-ylidene]undec-9-enoic acid, (±)-52. Commercially available hog liver esterase solution (1.0 cm^3) in 3.2 M ammonium sulfate was added to a solution of **(±)-*E,E*-51** (100 mg, 0.33 mmol) in acetone (3.0 cm^3) and phosphate buffer solution (30 cm^3, *p*H 7.0). The mixture was stirred at room temperature overnight before acidification with acetic acid (2 cm^3) and extraction with Et_2O (5 x 10 cm^3). The combined organic extracts were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. The crude acid was purified by flash column chromatography (Hex-EtOAc; 3:1, containing 1% AcOH) affording acid **(±)-*E,E*-52** (95 mg, 85%) as a viscous yellow oil. R_f 0.20 (Hex-EtOAc; 3:1 with 1% AcOH); υ_{max} (neat/cm^{-1}) 3058, 2929, 2854, 2348, 1737, 1692, 1627, 1579, 1460; δ_H (400 MHz $CDCl_3$) 0.88 (3H, t, *J* 7.5 Hz, CH_3), 1.29-1.37 (6H, m, CH_2), 1.40-1.49 (2H, m, CH_2), 1.59-1.70 (3H, m, CH_2), 1.88-1.99 (1H, m, CH_2), 2.22 (2H, q, *J* 7.0 Hz, CH_2), 2.35 (2H, t, *J* 7.5 Hz, CH_2), 3.51-3.57 (1H, m (br), CH), 6.16-6.34 (2H, m, CH), 6.39 (1H, dd *J* 2.0, 6.0 Hz, CH), 6.95 (1H, d, *J* 11.0, CH), 7.52 (1H, ddd, *J* 1.0, 2.5, 6.0 Hz, CH); (100 MHz $CDCl_3$) 10.0, 24.6, 25.6, 28.7, 28.9, 29.0, 33.4, 33.9, 44.5, 125.7, 131.5, 135.26, 135.28, 135.32, 146.4, 161.0, 179.4, 197.9; m/z (CI) 291 (MH^+, 100%); Found 291.19642, $C_{18}H_{27}O_3$ required 291.19601 (+1.5 ppm).



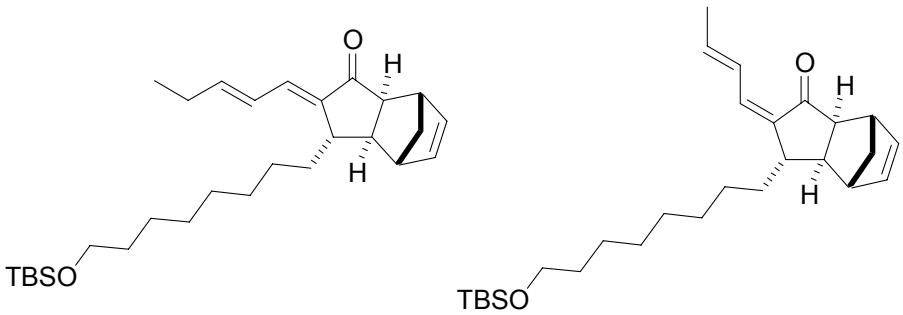
1-*tert*-Butyldimethylsilyloxy-7-bromoheptane, 53.[7] A solution of 7-bromoheptanol (3.48 g, 17.8 mmol, 1 eq.) in DCM (50 cm^3) was cooled to 0°C and treated with TBSCl (2.96 g, 19.6 mmol, 1.1 eq.) and TEA (3.1 cm^3, 22.2 mmol, 1.25 eq.). A catalytic amount of DMAP (*ca.* 10 mg) was added and stirring was continued for 15 h during which period room temperature was reached. The solvent was removed *in vacuo* before Et_2O (50 cm^3) and H_2O (50 cm^3) were added. The resultant aqueous phase was further extracted with Et_2O (3 x 50 cm^3) and the combined organic extracts were dried over $MgSO_4$. Filtration followed by solvent removal under reduced pressure and purification by flash column chromatography (Hex-Et_2O; 19:1) gave **53** (4.30 g, 78%) as a colourless liquid. R_f 0.6 (Hex-Et_2O; 19:1); δ_H (400 MHz, $CDCl_3$) 0.04 (6H, s, CH_3), 0.90 (9H, s, CH_3), 1.28-1.37 (4H, m, CH_2), 1.39-1.45 (2H, m, CH_2), 1.46-1.55 (2H, m, CH_2), 1.85 (2H, pent, *J* 7.5 Hz, CH_2), 3.41 (2H, t, *J* 7.0 Hz, CH_2), 3.62 (2H, t, *J* 6.5 Hz, CH_2); δ_C (100 MHz, $CDCl_3$) -5.3, 18.4, 25.6, 26.0, 28.2, 28.6, 32.8, 34.0, 63.1; m/z (CI) 311 (MH^+, 100%, ^{81}Br), 309 (MH^+, 100%, ^{79}Br).



1-*tert*-Butyldimethylsilyloxy-8-bromooctane, 54.[7] A stirred solution of 8-bromooctanol (6.60 g, 31.56 mmol, 1.0 eq.) in DCM (40 cm^3) was cooled to -10°C and a solution of TBSCl (5.80 g, 38.48 mmol, 1.2 eq.) dissolved in DCM (10 cm^3) and imidazole (2.62 g, 38.48 mmol, 1.2 eq.) in DCM (50 cm^3), containing a catalytic amount of DMAP (50 mg, 0.4 mmol), was added. The reaction was warmed to room temperature and stirred for 24 h. The solvent was removed under reduced pressure and water (100 cm^3) and Et_2O (50 cm^3) were added. The aqueous layer was further extracted with Et_2O (2 x 50 cm^3) and the combined organic extracts were dried over $MgSO_4$. Filtration followed by solvent removal under reduced pressure and purification by flash column chromatography (Hex-Et_2O; 98:2) gave **54** (9.40 g, 93%) as a colourless liquid. R_f 0.25 (Hex-Et_2O; 98:2); δ_H (400 MHz, $CDCl_3$) 0.04 (6H, s, CH_3), 0.90 (9H, s, CH_3), 1.29-1.36 (6H, m, CH_2), 1.39-1.45 (2H, m, CH_2), 1.47-1.55 (2H, m, CH_2), 1.86 (2H, pent, *J* 7.0, Hz, CH_2), 3.41 (2H, t, *J* 7.0, CH_2), 3.60 (2H, t, *J* 6.5, CH_2); δ_C (100 MHz, $CDCl_3$) -5.3, 18.3, 25.7, 25.9, 28.1, 28.7, 29.2, 32.8, 32.85, 33.8, 63.2.



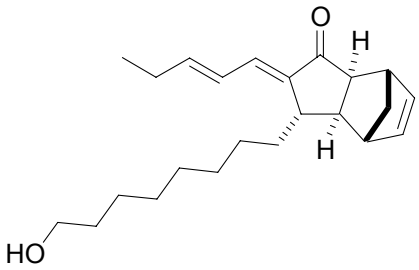
1-*tert*-Butyldimethylsilyloxy-8-iodooctane, 56.[7] A solution of 1-*tert*-butyldimethylsilyloxy-8-bromooctane **54** (5.00 g, 15.46 mmol, 1.0 eq.) in acetone (50 cm^3) was treated with potassium iodide (12.83 g, 77.3 mmol, 5.0 eq.) and heated to reflux for 16 h. The solvent was removed under reduced pressure and water (50 cm^3) and Et_2O (50 cm^3) were added. The organic fraction was separated and aqueous layer was further extracted with Et_2O (2 x 50 cm^3) and the combined organic fractions were dried over $MgSO_4$. Filtration, followed by solvent removal under reduced pressure and flash column chromatography (Hex-Et_2O; 98:2) gave 1-*tert*-butyldimethylsilyloxy-8-iodooctane **56** (5.71g, 99%) as a colourless liquid. R_f = 0.25 (Hex-Et_2O; 98:2); δ_H (400 MHz, $CDCl_3$) 0.05 (6H, s, CH_3), 0.91 (9H, s, CH_3), 1.28-1.35 (6H, m, CH_2), 1.36-1.45 (2H, m, CH_2), 1.48-1.57 (2H, m, CH_2), 1.82 (2H, pent, *J* 7.0, Hz, CH_2), 3.18 (2H, t, *J* 7.0, CH_2), 3.61 (2H, t, *J* 6.5, CH_2); δ_C (100 MHz, $CDCl_3$) -5.3, 7.1, 18.4, 25.7, 26.0, 28.5, 29.2, 30.4, 32.8, 33.6, 63.2.



(±)-3-[8-(*tert*-Butyldimethylsilyloxy)octyl]-2-[*E*-pent-2-en-*Z*/*E*-ylidene]-2,3,3a,4,7,7a-hexahydro-4,7-methanoinden-1-on, 62. Under N_2, at room temperature 1-*tert*-butyldimethylsilyloxy-8-bromooctane **54** (1.00 g, 3.09 mmol, 2 eq.) was added dropwise over 20 min to a rapidly stirred mixture of magnesium (150 mg, 6.17 mmol, 2.0 eq.) in Et_2O (6 cm^3). After the addition the reaction mixture was heated to reflux for 2 h. The resultant Grignard reagent was allowed to cool and added *via* cannula to a slurry of copper(I) iodide (59 mg, 0.31 mmol, 0.1 eq.) at -78°C in Et_2O (10 cm^3) [washed with Et_2O (5 cm^3)]. The mixture was stirred for 1 h and allowed to warm to -5°C. The temperature was reduced to -40°C and a solution of ***exo*-12** (327 mg, 1.50 mmol, 1.0 eq.) in Et_2O (5 cm^3) was added dropwise. Stirring was continued and the reaction was allowed to warm to 0°C over 1.5 h. The temperature was reduced to -78°C and freshly distilled *E*-pent-2-enal (189 mg, 2.25 mmol, 1.5 eq.) was added and the reaction mixture was stirred for 5 h at -78°C and then allowed to warm to room

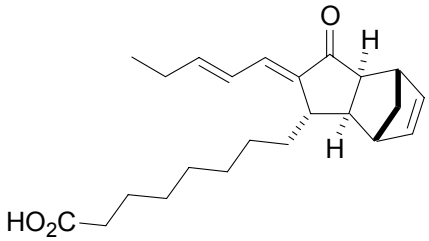
temperature over 3 h. A saturated solution of NH_4Cl (50 cm^3) was added and the *p*H was adjusted to 7.0 with conc. NH_3 before extraction with Et_2O (5 x 30 cm^3). The combined organic extracts were dried over $MgSO_4$. Filtration and solvent removal followed by flash column chromatography (Hex-Et_2O; 19:1 → 9:1 Hex-Et_2O) afforded initially ***Z,E*-62** (190 mg, 28%) and then ***E,E*-62** (380 mg, 56%) both as viscous yellow oils. R_f 0.25 (Hex-Et_2O; 9:1); υ_{max} (neat/cm^{-1}) 3060, 2928, 2855, 1702, 1628, 1602, 1462; δ_H (400 MHz, $CDCl_3$) 0.04 (6H, s, CH_3), 0.89 (9H, s, CH_3), 1.07 (3H, t, *J* 7.5 Hz, CH_3), 1.23-1.37 (13H, m, CH_2), 1.40-1.60 (3H, m, CH_2), 1.92 (1H, d, *J* 7.75 Hz, CH), 2.24 (2H, pent, *J* 7.5 Hz, CH_2), 2.37 (1H, d, *J* 7.75 Hz, CH), 2.65-2.71 (1H, m (br), CH), 2.74 (1H, s, CH), 3.04 (1H, s, CH), 3.59 (2H, t, *J* 6.5 Hz, CH_2), 6.15-6.24 (4H, m, CH), 6.87 (1H, dd, *J* 2.0, 10.5 Hz, CH); δ_C (100 MHz, $CDCl_3$) -5.3, 12.9, 18.4, 25.8, 26.0, 26.5, 29.4, 29.6, 29.7, 32.9, 37.5, 43.2, 43.3, 46.4, 48.1, 49.6, 54.6, 63.3, 125.4, 133.3, 137.5, 138.8, 142.8, 147.0, 207.8; m/z (ESI^+) 479 (MNa^+, 100%); Found 479.3300, $C_{29}H_{48}O_2SiNa$ requires 479.3321 (-4.4 ppm). Data for ***Z,E*-62**: R_f 0.35 (Hex-Et_2O; 9:1) δ_H (400 MHz, $CDCl_3$) 0.10 (6H, s, CH_3), 0.90 (9H, s, CH_3), 1.06 (3H, t, *J* 7.5 Hz, CH_3), 1.19 (1H, d, *J* 9.0 Hz, CH_2), 1.27-1.36 (10H, m, CH_2), 1.40 (1H, dt, *J* 1.5, 9.0 Hz, CH_2), 1.48-1.57 (2H, m, CH_2), 1.85 (1H, d, *J* 8.5 Hz, CH), 2.22 (2H, pent, *J* 7.5 Hz, CH_2), 2.33 (1H, d, *J* 8.5 Hz, CH), 2.34-2.40 (1H, m, CH), 2.71 (1H, s, CH), 3.04 (1H, s, CH), 3.61 (2H, t, *J* 6.5 Hz, CH_2), 6.04 (1H, dt, *J* 6.5, 15.5 Hz, CH), 6.15-6.23 (2H, m, CH) 6.25 (1H, dd, *J* 1.5, 11.5 Hz, CH), 7.55 (1H, ddt, *J* 1.5, 11.5, 15.5 Hz, CH).

(±)-3-[8-(*tert*-Butyldimethylsilyloxy)octyl]-2-[*E*-pent-2-en-*E*-ylidene]-2,3,3a,4,7,7a-hexahydro-4,7-methanoinden-1-one, *E,E*-62. Under N_2, a 1.5 M solution of *tert*-butyllithium in pentane (2.66 cm^3, 4.00 mmol, 4.0 eq.) was added dropwise to a solution of 1-*tert*-butyldimethylsilyloxy-8-iodooctane **56** (740 mg, 2.00 mmol, 2.0 eq.) in a mixture of pentane (8 cm^3) and ether (4.5 cm^3) at -78°C. Stirring was continued at -78°C for 0.25 h before warming to room temperature over 1 h. The solution was re-cooled to -78°C and added to a slurry of copper(I) iodide (190 mg, 1.00 mmol, 1.0 eq.) in Et_2O (10 cm^3) *via* cannula. The solution was then warmed to -10°C over 1 h and further stirred for 20 min between -10°C and -5°C. The resultant cuprate reagent was re-cooled to -60°C before ***exo*-12** (218 mg, 1.00 mmol, 1.0 eq.) solution in Et_2O (7 cm^3) was added dropwise. The reaction was further stirred and allowed to warm to -5°C for 1 h. On re-cooling to -78°C, freshly distilled *E*-pent-2-enal (126 mg, 1.50 mmol, 1.5 eq.) was added and the solution was warmed to room temperature over a period of 5 h. A saturated solution of NH_4Cl (50 cm^3) was added and the *p*H was adjusted to 7.0 with conc. NH_3. The resultant mixture was extracted with Et_2O (5 x 30 cm^3) and the combined organic extracts were dried over $MgSO_4$. Filtration, followed by solvent removal and purification by flash column chromatography (Hex-Et_2O; 19:1 → 9:1) afforded ***E,E*-62** (330 mg, 72%) as a colourless oil, whose data were in agreement to that reported above.

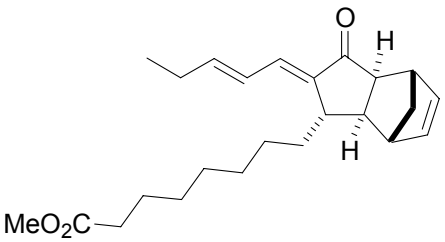


(±)-3-(8-Hydroxyoctyl)-2-[*E*-pent-2-en-*E*-ylidene]-2,3,3a,4,7,7a-hexahydro-4,7-methanoinden-1-one. A solution of ***E,E*-62** (440 mg, 0.96 mmol) in THF (2.0 cm^3) at 0°C was added dropwise to a mixture of acetic acid (12 cm^3) and water (6 cm^3) under vigorous stirring. The reaction was warmed to room temperature and further stirred for 4 h. Ethyl acetate (30 cm^3) and water (10 cm^3) were added followed by dropwise addition of saturated $NaHCO_3$

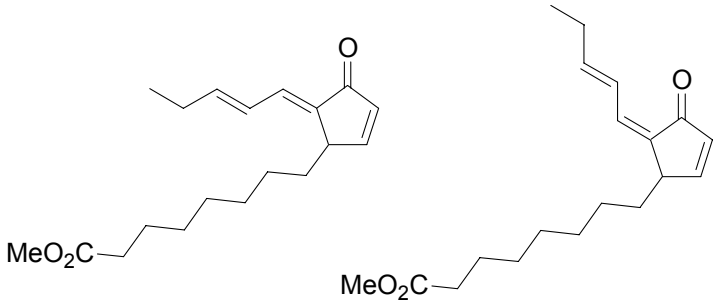
solution (200 cm^3). The resultant organic fraction was separated and the aqueous layer was further extracted with ethyl acetate (5 x 25 cm^3). The combined organic fractions were dried over $MgSO_4$. Filtration followed the evaporation of solvent under reduced pressure and purification by flash column chromatography (Hex-EtOAc; 9:1 → 3:1) afforded the deprotected alcohol (320 mg, 97%) as a colourless viscous oil. R_f 0.25 (Hex-EtOAc; 3:1); υ_{max} (neat/cm^{-1}) 3425, 3058, 2963, 2928, 2854, 1699, 1626, 1600, 1460; δ_H (400 MHz, $CDCl_3$) 1.07 (3H, t, *J* 7.5 Hz, CH_3), 1.23-1.40 (13H, m, CH_2), 1.41-1.49 (1H, m, CH_2), 1.57 (2H, pent, *J* 7.0 Hz, CH_2), 1.90 (1H, d, *J* 7.75 Hz, CH), 2.24 (2H, pent, *J* 7.5 Hz, CH_2), 2.39 (1H, d, *J* 7.75 Hz, CH), 2.68-2.72 (1H, m (br), CH), 2.74 (1H, s, CH), 3.04 (1H, s, CH), 3.63 (2H, t, *J* 6.5 Hz, CH_2), 6.14-6.25 (4H, m, CH), 6.87 (1H, dd, *J* 2.0, 10.5 Hz, CH); δ_C (100 MHz, $CDCl_3$) 12.9, 25.7, 26.5, 26.55, 29.4, 29.5, 29.7, 32.8, 37.5, 43.2, 43.3, 46.4, 48.1, 49.6, 54.6, 63.0, 125.4, 133.4, 137.5, 138.8, 142.7, 148.1, 208.9; m/z (ES) 365 (MNa^+, 100%); Found 365.2448, $C_{23}H_{34}O_2Na$ requires 365.2457 (-2.3 ppm).



(±)-8-{3-Oxo-2-[*E*-pent-2-en-*E*-ylidene]-2,3,3a,4,7,7a-hexahydro-4,7-methanoinden-1-yl}octanoic acid. A solution of the above alcohol (300 mg, 0.87 mmol, 1 eq.) in DCM (20 cm^3) was added dropwise to a suspension of Dess-Martin's periodinane (448 mg, 1.14 mmol, 1.3 eq.) in DCM (10 cm^3) at 0°C. The reaction was warmed to room temperature and stirred for 1.5 h. The reaction was quenched by addition of Et_2O (30 cm^3), water (30 cm^3), a saturated aqueous solution of Na_2SO_3 (30 cm^3) and saturated aqueous solution of sodium hydrogencarbonate (30 cm^3). The resultant aqueous phase was further extracted with Et_2O (5 x 25 cm^3) and the combined organic fractions were dried over $MgSO_4$. Filtration and solvent removal *in vacuo* gave the aldehyde [R_f 0.4 (Hex-EtOAc; 4:1)]. The crude aldehyde (*ca.* 0.87 mmol) was dissolved in a mixture of *t*-BuOH (17 cm^3) and 2,3-dimethylbut-2-ene (6 cm^3) and a solution of 80% w/w sodium chlorite (650 mg, 5,75 mmol, 6.6 eq.) and NaH_2PO_4 (753 mg, 6.27 mmol, 7.2 eq.) in H_2O (8.4 cm^3) was added dropwise at 10°C over 0.25 h. The reaction was stirred for 10 min before removal of the volatile components under reduced pressure. Water (5 cm^3) was added and the mixture was extracted with EtOAc (7 x 25 cm^3). The combined organic fractions were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. The crude product, after purification by flash column chromatography (Hex-EtOAc; 4:1, 1% AcOH), afforded the *title compound* (272 mg, 87%) as a colourless oil. R_f 0.2 (Hex-EtOAc; 3:1, 1% AcOH); υ_{max} (neat/cm^{-1}) 3050, 2929, 2854, 1704, 1625, 1598, 1459; δ_H (400 MHz, $CDCl_3$) 1.07 (3H, t, *J* 7.5 Hz, CH_3), 1.24-1.68 (12H, m, CH_2), 1.91 (1H, d, *J* 7.75 Hz, CH), 2.24 (2H, pent, *J* 7.5 Hz, CH_2), 2.35 (2H, t, *J* 7.5 Hz, CH_2), 2.38 (1H, d, *J* 7.75 Hz, CH), 2.65-2.70 (1H, m(br), CH), 2.75 (1H, s, CH), 3.04 (1H, s, CH), 6.13-6.28 (4H, m, CH), 6.87 (1H, dd, *J* 2.0, 10.5 Hz, CH); δ_C (100 MHz, $CDCl_3$) 12.9, 24.9, 26.4, 26.5, 29.0, 29.2, 29.5, 33.9, 37.5, 43.2, 43.3, 46.4, 48.1, 49.6, 54.6, 125.4, 133.5, 137.5, 138.8, 142.7, 148.2, 179.1, 208.8; m/z (CI) 357 (MH^+, 100%); Found 357.24435, $C_{23}H_{33}O_3$ requires 357.24298 (+4.4 ppm).

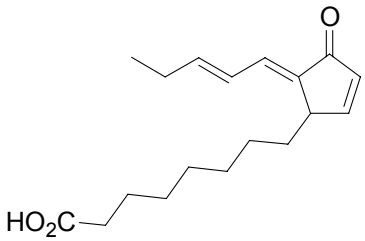


(±)-8-{3-Oxo-2-[*E*-pent-2-en-*E*-ylidene]-2,3,3a,4,7,7a-hexahydro-4,7-methanoinden -1-yl}octanoic acid methyl ester. As described above a solution of the alcohol (160 mg, 0.467 mmol, 1.0 eq.) was converted into the corresponding carboxylic acid on sequential treatment with Dess-Martin's periodinane (258 mg, 0.60 mmol, 1.3 eq.) followed by a solution of 80% w/w sodium chlorite (350 mg, 2.65 mmol, 5.7 eq.). The crude acid (*ca*. 0.467 mmol, 1.0 eq.) was dissolved in a mixture of benzene (27 cm^3) and MeOH (8 cm^3) and at 5°C a 2.0 M solution of (trimethylsilyl)diazomethane in hexane (0.27 cm^3, 0.57 mmol, 1.2 eq.) was added dropwise over 5 min. After 1 h the solvent was removed *in vacuo* and crude product was purified by flash column chromatography (Hex-EtOAc; 4:1) affording the corresponding ester (141 mg, 81%) as a colourless oil. R_f 0.45 (Hex-EtOAc; 4:1); υ_{max} (neat/cm^{-1}) 2932, 2855, 1739, 1701, 1627, 1601, 1459, 1437; δ_H (400 MHz, $CDCl_3$) 1.08 (3H, t, *J* 7.5 Hz, CH_3), 1.25-1.65 (12H, m, CH_2), 1.91 (1H, d, *J* 7.75 Hz, CH), 2.23 (2H, pent, *J* 7.5 Hz, CH_2), 2.29 (2H, t, *J* 7.5 Hz, CH_2), 2.38 (1H, d, *J* 7.75 Hz, CH), 2.65-2.70 (1H, m (br), CH), 2.79 (1H, s, CH), 3.04 (1H, s, CH), 3.66 (3H, s, CH_3), 6.13-6.25 (4H, m, CH), 6.87 (1H, dd, *J* 2.0, 10.5 Hz, CH); δ_C (100 MHz, $CDCl_3$) 12.9, 24.9, 26.4, 26.5, 29.1, 29.2, 29.5, 34.0, 37.5, 43.2, 43.3, 46.3, 48.1, 49.6, 51.4, 54.6, 125.4, 133.3, 137.5, 138.8, 142.7, 148.1, 174.2, 208.8; m/z (ES) 393 (MNa^+, 100%), 371 (MH^+, 5%); found 371.2583, $C_{24}H_{35}O_3$ requires 371.2586 (-0.9 ppm).



(±)-8-{4-Oxo-5-[*E*-pent-2-en-*E*/*Z*-ylidene]cyclopent-2-enyl}octanoic acid methyl ester *Z,E*- and *E,E*-65.[8] Under N_2, a solution of the above ester (110 mg, 0.290 mmol, 1.0 eq.) in DCM (4 cm^3) was added to a solution of maleic anhydride (436 mg, 4.44 mmol, 15 eq.) in DCM (4 cm^3). The solution was homogenised on stirring before being split into two microwavable vials (Smith Process vial, 2-5 cm^3). A 1.0 M solution of $MeAlCl_2$ in hexane (0.15 cm^3, 0.15 mmol, 1.0 eq.) was added dropwise to each vial before both vials were irradiated (Smith Creator, 300 Watts) up to 110°C over a period of 70 sec. The combined reaction mixtures were quenched immediately on pouring into a rapidly stirred saturated solution of $NaHCO_3$ (25 cm^3) and the mixture was stirred for 20 min before extraction with Et_2O (10 x 25 cm^3). The organic extracts were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. Purification by flash column chromatography (Hex-EtOAc; 9:1 → 3:1) gave, initially, recovered starting material (24 mg, 22%) followed by ***Z,E*-65** (4 mg, 4%) and finally ***E,E*-65** (62 mg, 69%) both as yellow viscous oil. R_f 0.4 (Hex-EtOAc; 3:1); υ_{max} (neat/cm^{-1}) 2931, 2850, 1735, 1692, 1632, 1437; δ_H (400 MHz, $CDCl_3$) 1.07 (3H, t, *J* 7.5 Hz, H-18), 1.23-1.32 (8H, m, H-4 - H-7), 1.51-1.65 (3H, m, H-3, H-8), 1.81-1.90 (1H, m, H-8), 2.22-2.28 (2H, m, H-17), 2.29 (2H, t, *J* 7.5 Hz, H-2), 3.53-3.57 (1H, m, H-9), 3.66 (3H, s, CH_3), 6.24-6.30 (2H, m, H-15, H-16), 6.35 (1H, dd, *J* 1.75, 6.0 Hz, H-11), 6.92 (1H, d, *J*

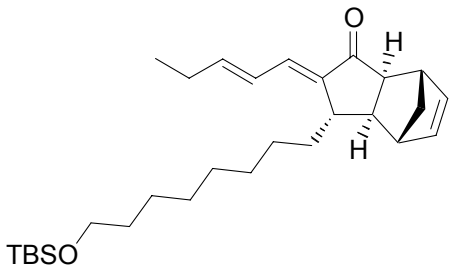
10.0 Hz, H-14), 7.52 (1H, ddd, *J* 0.75, 2.5, 6.0 Hz, H-10); δ_C (100 MHz, $CDCl_3$) 13.0, 24.8, 25.9, 26.5, 29.0, 29.1, 29.5, 32.9, 34.0, 43.5, 51.4, 124.7, 131.3, 135.1, 135.7, 147.7, 161.1, 174.2, 197.6; δ_H (400 MHz, C_6D_6) 0.79 (3H, t, *J* 7.25 Hz, H-18), 0.95-1.12 (8H, m, H-4 - H-7), 1.28-1.64 (4H, m, H-3, H-8), 1.87 (2H, pent, *J* 7.25 Hz, H-17), 2.09 (2H, t, *J* 7.0 Hz, H-2), 3.11-3.16 (1H, m, H-9), 3.26 (3H, s, CH_3), 5.81 (1H, dt, *J* 6.5, 15.0 Hz, H-16), 6.19 (1H, m, H-15), 6.25 (1H, d, *J* 6.0 Hz, H-11), 6.84-6.86 (1H, m, H-10), 7.22 (1H, d, *J* 11.5 Hz, H-14); δ_C (100 MHz, C_6D_6) 13.1, 25.2, 26.0, 26.6, 29.2, 29.3, 29.7, 33.2, 34.0, 43.4, 50.9, 125.1, 130.6, 135.5, 136.5, 146.7, 159.8, 173.3, 196.0; m/z (CI) 305 (MH^+, 100%); Found 305.21247, $C_{19}H_{29}O_3$ requires 305.21167 (+2.9 ppm). Data for ***Z,E*-65**: R_f 0.5 (Hex-EtOAc; 3:1); υ_{max} (neat/cm^{-1}) 2928, 2850, 1736, 1686, 1631, 1437; δ_H (400 MHz, $CDCl_3$) 1.07 (3H, t, *J* 7.5 Hz, CH_3), 1.24-1.37 (8H, m, CH_2), 1.45-1.54 (1H, m, CH_2), 1.62 (2H, pent, *J* 7.5 Hz, CH_2), 1.68-1.77 (1H, m, CH_2), 2.21-2.28 (2H, m, CH_2), 2.30 (2H, t, *J* 7.5 Hz, CH_2), 3.28-3.34 (1H, m, CH), 3.66 (3H, s, CH_3), 6.10 (1H, dt, *J* 6.5, 15.5 Hz, CH), 6.28 (1H, dd, *J* 1.5, 6.0 Hz, CH), 6.38 (1H, d, *J* 11.0 Hz, CH), 7.42(1H, dd, *J* 2.5, 6.0 Hz, CH), 7.67 (1H, ddt, *J* 1.5, 11.0, 15.5 Hz, CH); δ_C (100 MHz, $CDCl_3$) 13.2, 24.8, 26.1, 26.2, 29.0, 29.5, 33.3, 34.0, 45.6, 51.4 125.5, 134.3, 135.7, 136.4, 146.7, 159.8, 174.2, 197.5.



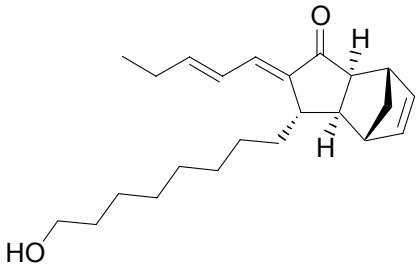
(±)-8-{4-Oxo-5-[*E*-pent-2-en-*E*-ylidene]cyclopent-2-enyl}octanoic acid, *E,E*-6. Under N_2, a solution of the above carboxylic acid (356 mg, 1.00 mmol, 1.0 eq.) in DCM (10 cm^3) was added to a solution of fumaronitrile (1.170 g, 15.00 mmol, 15 eq.) in DCM (15 cm^3). The solution was split into five microwavable vials (Smith Process vial, 2-5 cm^3) and a 1.0 M solution of $MeAlCl_2$ in hexane (0.3 cm^3, 0.30 mmol, 1.5 eq.) was added dropwise to each vial before the vials were irradiated (Smith Creator, 300 Watts) up to 110°C over a period of 90 sec. The combined reaction mixtures were pre-absorbed onto silica (*ca.* 5 g) and purified by flash column chromatography (Hex-EtOAc; 9:1 → 3:1, containing 1% AcOH) affording initially unreacted starting material (50 mg, 14%) followed by ***Z,E*-6** (20 mg, 7%) [R_f 0.3 (Hex-EtOAc; 3:1 with 1% AcOH)] and finally ***E,E*-6** (180 mg, 62%) as a viscous pale yellow oil. R_f 0.25 (Hex-EtOAc; 3:1 with 1% AcOH); υ_{max} (neat/cm^{-1}) 3050, 2930, 2856, 1708, 1694, 1630, 1578, 1461; δ_H (400 MHz, $CDCl_3$) 1.08 (3H, t, *J* 7.5 Hz, H-18), 1.24-1.38 (8H, m, H-4 - H-7), 1.51-1.67 (3H, m, H-3, H-8), 1.81-1.91 (1H, m, H-8), 2.22-2.30 (2H, m, H-17), 2.34 (2H, t, *J* 7.5 Hz, H-2), 3.52-3.57 (1H, m, H-9), 6.21-6.31 (2H, m, H-15, H-16), 6.36 (1H, dd, *J* 1.75, 6.0 Hz, H-11), 6.94 (1H, d, *J* 10.0 Hz, H-14), 7.52 (1H, ddd, *J* 1.0, 2.5, 6.0 Hz, H-10); δ_C (100 MHz, $CDCl_3$) 13.0, 24.6, 25.8, 26.4, 28.9, 29.0, 29.4, 32.8, 33.9, 43.5, 124.7, 131.4, 135.1, 135.7, 147.8, 161.2, 179.3, 197.7; m/z (CI) 291 (MH^+, 100%); Found 291.19615, $C_{18}H_{27}O_3$ requires 291.19601 (+0.5 ppm).

A mixture of commercially available hog liver esterase solution (0.2 cm^3) in 3.2 M ammonium sulfate was added to a solution of ***E,E*-65** (20 mg, 0.065 mmol) in acetone (0.6 cm^3) and phosphate buffer solution (6 cm^3, *p*H 7.0). The mixture was stirred at room temperature for 24 h before acidification with 1 M HCl solution (*p*H 5.5) and extraction with Et_2O (5 x 10 cm^3). The combined organic extracts were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. The crude acid was purified by flash column

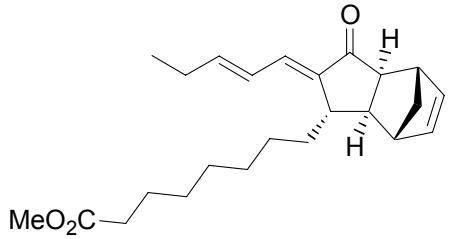
chromatography (Hex-EtOAc; 3:1, containing 1% AcOH) affording the ***E,E*-6** (16 mg, 84%) as a viscous oil whose data was in agreement with that reported above.



(+)-(3*S*,3a*S*,4*R*,7*S*,7a*S*)-3-[8-(*tert*-Butyldimethylsilyloxy)octyl]-2-[*E*-pent-2-en-*E*-ylidene]-2,3,3a,4,7,7a-hexahydro-4,7-methanoinden-1-one, (+)-*E,E*-62. Under N_2, a 1.5 M solution of *tert*-butyllithium in pentane (1.22 cm^3, 1.83 mmol, 4.0 eq.) was added dropwise to a solution of **56** (340 mg, 0.91 mmol, 2.0 eq.) in a mixture of pentane (8 cm^3) and ether (5 cm^3) at -78°C. Stirring was continued at -78°C for 0.25 h before warming to room temperature over 1 h. The solution was re-cooled to -78°C and added to a slurry of copper(I) iodide (87 mg, 0.45 mmol, 1.0 eq.) in Et_2O (5 cm^3) *via* cannula. The solution was warmed to -10°C over 1 h and stirred for 20 min. The cuprate thus formed was cooled to -60°C before **(+)-*exo*-12** (100 mg, 0.45 mmol, 1.0 eq.) in Et_2O (5 cm^3) was added dropwise. The reaction was stirred and allowed to warm to -5°C over 1 h. Freshly distilled *E*-pent-2-enal (77 mg, 0.91 mmol, 1.5 eq.) was added at -78°C and the solution was warmed to room temperature over 6 h. A saturated solution of NH_4Cl (25 cm^3) was added and the *p*H was adjusted to 7 with conc. NH_3 solution. Extraction with Et_2O (5 x 30 cm^3), drying over $MgSO_4$, filtration and solvent removal under reduced pressure afforded the crude product. Purification by flash column chromatography (Hex-Et_2O; 19:1 → 9:1) gave (+)-***E,E*-62** (162 mg, 78%) as a colourless viscous oil. $[\alpha]_D$ +355 (*c* = 1.00, $CHCl_3$) with data in agreement to that reported above.

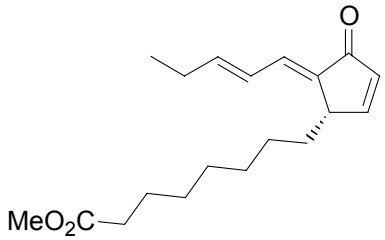


(+)-(3*S*,3a*S*,4*R*,7*S*,7a*S*)-(8-Hydroxyoctyl)-2-[*E*-pent-2-en-*E*-ylidene]-2,3,3a,4,7,7a-hexahydro-4,7-methanoinden-1-one. As described above (+)-***E,E*-62** (160 mg, 0.35 mmol) was converted into the corresponding alcohol (104 mg, 87%) on treatment of a THF (1.5 cm^3) solution with acetic acid (6 cm^3) and water (3 cm^3) at 0°C. $[\alpha]_D$ +288 (*c* = 1.00, $CHCl_3$) with spectroscopic data in accord with that recorded for the corresponding racemic material.

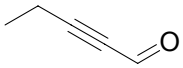


(+)-(3*S*,3a*S*,4*R*,7*S*,7a*S*)-{3-Oxo-2-[*E*-pent-2-en-*E*-ylidene]-2,3,3a,4,7,7a-hexahydro-4,7-methanoinden-1-yl}octanoic acid methyl ester. A solution of the (+)-alcohol (104 mg, 0.30 mmol, 1.0 eq.) was converted into the corresponding methyl ester (80 mg, 72%) over

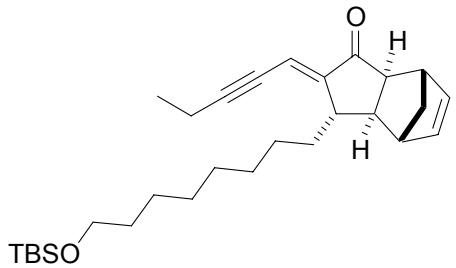
three-steps on treatment with Dess-Martin's periodinane (162 mg, 0.38 mmol, 1.3 eq.), 80% w/w sodium chlorite (250 mg, 2.21 mmol, 7.4 eq.) followed by a 2.0 M solution of (trimethylsilyl)diazomethane in hexane (0.18 cm^3, 0.36 mmol, 1.2 eq.) generated *title compound* as viscous oil. $[\alpha]_D$ +341 (*c* = 1.00, $CHCl_3$) with NMR data identical to that reported above.



(+)-(8*R*)-{4-Oxo-5-[*E*-pent-2-en-*E*-ylidene]cyclopent-2-enyl}octanoic acid methyl ester, (+)-*E,E*-65. Under N_2, (+)-methyl ester (80 mg, 0.216 mmol, 1.0 eq.) in DCM (4 cm^3) was added to a solution of maleic anhydride (326 mg, 3.32 mmol, 15 eq.) in DCM (4 cm^3) in two microwavable vials (Smith Process vial, 2-5 cm^3). The solution was stirred to achieve homogenisation before a 1.0 M solution of $MeAlCl_2$ in hexane (0.3 cm^3, 0.30 mmol, 1.4 eq.) was added to each vial. Both vials were irradiated (Smith Creator, 300 Watts) up to 110°C for 1.5 min and the reaction mixture was quenched immediately by pouring into a rapidly stirred saturated aqueous solution of sodium hydrogencarbonate (25 cm^3). The solution was stirred for 20 min and extracted with Et_2O (10 x 25 cm^3). The combined organic extracts were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. Purification by flash column chromatography (Hex-EtOAc; Hex, 9:1 → 3:1) gave **(+)-*E,E*-63** (61 mg, 93%) as a colourless oil. $[\alpha]_D$ +144 (*c* = 1.00, $CHCl_3$). HPLC separation using an AS column (COL-HP-17), solvent mixture Hex-IPA, 90:10, 254 nm, 0.5 cm^3/min. and sample amount (2 μl) gave 94% enantiomeric excess of the *title compound*. Additional spectroscopic data as stated above.

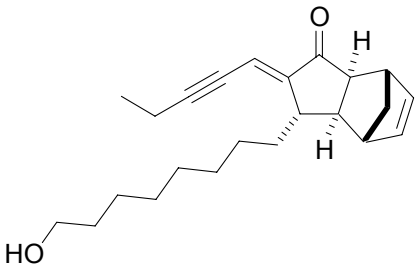


2-Pentynal.[9] A solution of 2-pentyn-1-ol (5.0 g, 59.4 mmol, 1.0 eq.) in a pentane-toluene mixture (60 cm^3, 2:1) was stirred for 15 h with activated MnO_2 (51.7 g, 594 mmol, 10 eq.) at room temperature. 2-Pentynal was collected by distillation following filtration through Celite and was approximately quantified using ^{1}H-NMR spectroscopy. The *aldehyde* (*ca*. 4 g) was dissolved in pentane/toluene (60 cm^3) and was used in the next step as such.

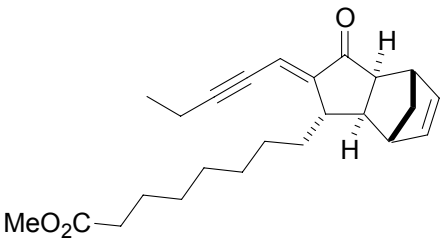


(±)-2-Pent-2-yn-(*E*)-ylidene-3-[8-(*tert*-Butyldimethylsilyloxy)octyl]-2,3,3a,4, 7,7a-hexahydro-4,7-methano-inden-1-one, 63. Under N_2, a 1.5 M solution of *tert*-butyllithium in pentane (4.32 cm^3, 6.48 mmol, 4.0 eq.) was added dropwise to a solution of 1-*tert*-butyldimethylsilyloxy-8-iodooctane (1.200 g, 3.24 mmol, 2.0 eq.) in a mixture of pentane (16 cm^3) and ether (9 cm^3) at -78°C. Stirring was continued at -78°C for 0.25 h before warming to room temperature over 1 h. The solution was re-cooled to –78°C and added to a slurry of CuI (308 mg, 1.62 mmol, 1.0 eq.) in Et_2O (10 cm^3) *via* cannula. The solution was warmed to -

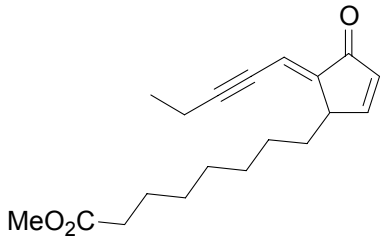
10°C over 1 h and further stirred for 20 min. between -5°C and –10°C. The resultant cuprate was re-cooled to –60°C before ***exo*-12** (353 mg, 1.62 mmol, 1.0 eq.) solution in Et_2O (10 cm^3) was added dropwise. The reaction was stirred and allowed to warm to –5°C for 1 h. Freshly distilled 2-pentynal (*ca.* 266 mg, 3.24 mmol, 2.0 eq.) in 5 cm^3 of pentane/toluene (mixture) was added at –78°C and the solution was stirred overnight at -78ºC and warmed to 0ºC before quenched with saturated solution of NH_4Cl (50 cm^3). The resultant mixture was extracted with Et_2O (5 x 30cm^3) and combined organic extracts were dried over $MgSO_4$. Filtration followed by solvent removal and purification by flash column chromatography (Hex-Et_2O; 19:1 → 9:1) afforded **63** (551 mg, 75%) as a colourless oil. R_f 0.35 (Hex-Et_2O; 9:1). υ_{max} (neat/cm^{-1}) 3059, 2931, 2855 2212, 1705, 1603, 1462, 1387; δ_H (400 MHz, $CDCl_3$) 0.04 (6H, s, CH_3), 0.89 (9H, s, CH_3), 1.22 (3H, t, *J* 7.5 Hz, CH_3), 1.26-1.38 (12, m, CH_2), 1.46-1.56 (3, m, CH_2), 1.80-1.89 (1H, m, CH_2), 1.94 (1H, d, *J* 7.75 Hz, CH), 2.40 (1H, d, *J* 8.25 Hz, CH), 2.45 (2H, qd, *J* 2.25, 7.5 Hz, CH_2), 2.67-2.73 (1H, m, CH), 2.77 (1H, s, CH), 3.07 (1H, s, CH), 3.61 (2H, t, *J* 6.75 Hz, CH_2), 6.17-6.26 (2H, m, CH), 6.37 (1H, dt, *J* 2.25, 2.5 Hz, CH); δ_C (100 MHz $CDCl_3$) -5.3, 13.6, 13.8, 15.3, 25.8, 26.0, 26.6, 29.5, 29.6, 29.7, 32.9, 35.2, 43.4, 44.7, 46.1, 48.2, 49.5, 54.6, 63.3, 77.9, 106.5, 114.7, 137.5, 138.9, 154.3, 207.2; m/z (CI) 477 (MNa^+, 100%); Found, 477.3176 $C_{29}H_{46}O_2NaSi$ requires 477.3165 (+2.3 ppm).



(±)-3-(8-Hydroxy-octyl)-2-pent-2-yn-(*E*)-ylidene-2,3,3a,4,7,7a-hexahydro-4,7-methanoinden-1-one. As described previously, a solution of **63** (500 mg, 1.099 mmol) in THF (2.0 cm^3) at 0°C was added dropwise a mixture of acetic acid (8 cm^3) and water (4 cm^3) with vigorous stirring. The reaction was warmed to room temperature and stirred for 5 h. Ethyl acetate (30 cm^3) and water (10 cm^3) were added followed by dropwise addition of saturated sodium hydrogencarbonate solution (200 cm^3). The resultant organic fraction was separated and the aqueous layer was extracted with ethyl acetate (5 x 25 cm^3). The combined organic fractions were dried over $MgSO_4$. Filtration followed by evaporation of solvent under reduced pressure and purification by flash column chromatography (Hex-EtOAc; 9:1 → 3:1) afforded the alcohol (359 mg, 96%) as a colourless viscous oil. R_f 0.10 (Hex-EtOAc; 3:1); υ_{max} (neat/cm^{-1}) 3399, 3060, 2929, 2855, 2360, 2209, 1703, 1602, 1460; δ_H (400 MHz, $CDCl_3$) 2.30 (3H, t, *J* 7.5 Hz, CH_3), 1.30-1.42 (12H, m, CH_2), 1.54-1.60 (3H, m, CH_2), 1.80-1.86 (1H, m, CH), 1.95 (1H, d, *J* 7.75 Hz, CH), 2.39 (1H, dd, *J* 0.75, 7.75 Hz, CH), 2.44 (2H, qdd, *J* 0.75, 2.5, 7.5 Hz, CH_2), 2.68-2.72 (1H, m, CH), 2.77 (1H, s, CH), 3.07 (1H, s, CH), 3.64 (2H, t, *J* 6.75 Hz, CH_2), 6.17-6.25 (2H, m, CH), 6.36 (1H, dt, *J* 2.25, 2.5 Hz, CH); δ_C (100 MHz, $CDCl_3$) 14.0, 14.2, 26.1, 26.9, 29.8, 29.9, 30.0, 33.2, 35.6, 43.8, 45.1, 46.4, 48.6, 49.9, 55.0, 63.3, 78.3, 106.9, 115.2, 137.9, 139.2, 154.6, 207.6; m/z (CI) 341 (MH^+, 20%), 275 (100%); Found 341.24924 $C_{23}H_{33}O_2$ requires 341.24808 (+4.1 ppm).

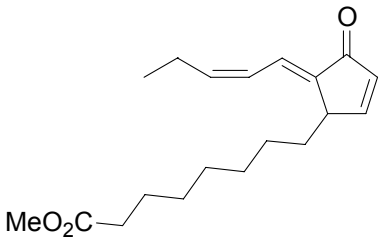


(±)-8-(3-Oxo-2-pent-2-yn-(*E*)-ylidene-2,3,3a,4,7,7a-hexahydro-1H-4,7-methano-inden-1-yl)-octanoic acid methyl ester. A solution of the above alcohol (150 mg, 0.44 mmol, 1.0 eq.) in DCM (5 cm^3) was added dropwise to a suspension of Dess-Martin's periodinane (235 mg, 0.55 mmol, 1.2 eq.) in DCM (5 cm^3) at room temperature. The reaction was stirred for 1.5 h. TLC analysis confirmed complete reaction of the alcohol. The reaction was quenched by the addition of Et_2O (16 cm^3) and water (16 cm^3) followed by saturated aqueous Na_2SO_3 solution (16 cm^3) and sodium hydrogencarbonate solution (16 cm^3). The resultant aqueous phase was extracted with Et_2O (5 x 25 cm^3) and the combined organic fractions were dried over $MgSO_4$. Filtration and solvent removal *in vacuo* gave the aldehyde [R_f 0.4 (Hex-EtOAc; 4:1)]. The crude aldehyde (*ca*. 0.44 mmol, 1.0 eq.) was dissolved in a mixture of *t*-BuOH (8 cm^3) and 2,3-dimethylbut-2-ene (5 cm^3) and a solution of 80% w/w sodium chlorite (300 mg) and NaH_2PO_4 (290 mg) in H_2O (5 cm^3) was added dropwise at 10°C over 15 min. The reaction was stirred for 30 min before water (5 cm^3) was added and the mixture was extracted with EtOAc (7 x 15 cm^3). The combined organic fractions were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. Under N_2 the crude acid (*ca*. 0.44 mmol, 1.0 eq.) was then dissolved in a mixture of toluene (15 cm^3) and MeOH (5 cm^3) and a 2.0 M solution of (trimethylsilyl)diazomethane in hexane (0.28 cm^3, 0.59 mmol, 1.2 eq.) was added dropwise over 5 min. After 1 h the solvent was removed *in vacuo* and crude product was purified by flash column chromatography (Hex-EtOAc; 4:1) affording the ester (132 mg, 81%) as a colourless oil. R_f 0.35 (Hex-EtOAc; 3:1); υ_{max} (neat/cm^{-1}) 3060, 2934, 2855, 2210, 1739, 1703, 1602, 1460, 1436; δ_H (400 MHz, $CDCl_3$) 1.21 (3H, t, *J* 7.5 Hz, CH_3), 1.28-1.38 (12H, m, CH_2), 1.48-1.56 (1H, m, CH_2), 1.57-1.66 (2H, m, CH_2), 1.79-1.88 (1H, m, CH_2), 1.93 (1H, d, *J* 7.75 Hz, CH), 2.67-2.72 (1H, m, CH), 2.76 (1H, s CH), 3.06 (1H, s, CH), 3.66 (3H, s, CH_3), 2.30 (2H, t, *J* 7.5 Hz, CH_2), 2.39 (1H, d, *J* 7.75 Hz, CH), 2.44 (2H, qd, *J* 2.0, 7.5 Hz, CH_2), 6.16-6.25 (2H, m, CH), 6.36 (1H, dt, *J* 2.25, 2.5, Hz, CH); δ_C (100 MHz $CDCl_3$) 13.6, 13.8, 24.9, 26.4, 29.0, 29.1, 29.5, 34.0, 35.1, 43.4, 44.7, 46.0, 48.2, 49.5, 51.4, 54.6, 77.9, 106.5, 114.7, 137.5, 138.8, 154.2, 174.2, 207.2; m/z (CI) 369 (MH^+, 15%), 303 (100%); Found 369.24385 $C_{23}H_{33}O_2$ requires 369.24298 (+2.8 ppm).



(±)-8-[4-Oxo-5-pent-2-yn-(*E*)-ylidenecyclopent-2-enyl]octanoic acid methyl ester, 66. Under N_2, a solution of the above methyl ester (80 mg, 0.217 mmol, 1.0 eq.) in DCM (4 cm^3) was added to a solution of maleic anhydride (319 mg, 3.26 mmol, 15 eq.) in DCM (4 cm^3). The solution was homogenised by stirring before being split into two microwavable vials (Smith Process vial, 2-5 cm^3). A 1.0 M solution of $MeAlCl_2$ in hexane (0.16 cm^3, 0.16 mmol, 1.5 eq.) was added dropwise to each vial before both vials were irradiated (Smith Creator, 300 Watts) up to 110°C over a period of 65 sec. The reaction mixture was quenched immediately on pouring into a rapidly stirred saturated solution of $NaHCO_3$ (20 cm^3) and the mixture was

stirred for 10 min before extraction with Et_2O (10 x 25 cm^3). The combined organic extracts were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. Purification by flash column chromatography (Hex-EtOAc; 9:1 → 3:1) gave **66** (50 mg, 76%) as a colourless viscous oil. R_f 0.25 (Hex-EtOAc; 3:1); υ_{max} (neat/cm^{-1}) 2976, 2933, 2856, 2211, 1738, 1696, 1626, 1575, 1454, 1436; δ_H (400 MHz, $CDCl_3$) 1.22 (1H, t, *J* 7.5 Hz, CH_3), 1.27-1.34 (9H, m, CH_2), 1.57-1.65 (2H, m, CH_2), 1.67-1.75 (1H, m, CH_2), 2.00-2.10 (1H, m, CH), 2.30 (2H, t, *J* 7.5 Hz, CH_2), 2.45 (2H, qd, *J* 2.5, 7.5 Hz, CH_2), 3.52-3.57 (1H, m, CH), 3.67 (3H, s, CH_3), 6.33 (1H, dd, *J* 2.0, 6.0 Hz, CH), 6.44-6.47 (1H, m, CH), 7.56 (1H, ddd, *J* 1.0, 2.5, 6.0 Hz); δ_C (100 MHz $CDCl_3$) 13.6, 13.7, 24.8, 25.8, 29.0, 29.5, 30.7, 34.0, 44.5, 51.4, 77.3, 105.6, 112.7, 134.6, 146.6, 162.0, 174.1, 195.7; m/z (CI) 325 (MNa^+, 100%); Found 325.1792 $C_{19}H_{26}O_3Na$ requires 325.1780 (+3.8 ppm).



(±)-8-{4-Oxo-5-[*Z*-pent-2-en-*E*-ylidene]cyclopent-2-enyl}octanoic acid methyl ester, *E,Z*-67. One drop of quinoline was added to a solution of **66** (38 mg, 0.132 mmol, 1.0 eq.) in EtOAc (10 cm^3). Then Lindlar's catalyst (10 mg) was added and the reaction was stirred at room temperature under a hydrogen atmosphere (1 atm.) for 3 h. The solution was filtered through a silica plug (EtOAc) and the solvent was removed in *vacuo*. Purification by flash column chromatography (Hex-EtOAc; 19:1 → 9:1 → 4:1) gave initially, recovered starting material **66** (5 mg, 13%) and then product ***E,Z*-65** (28 mg, 73%) as a colourless viscous oil. R_f 0.2 (Hex-EtOAc; 3:1); υ_{max} (neat/cm^{-1}) 3060, 2932, 2856, 2300, 1737, 1692, 1628, 1579, 1454, 1437; δ_H (400 MHz, $CDCl_3$) 1.05 (3H, t, *J* 7.5 Hz CH_3), 1.24-1.35 (8H, m, CH_2), 1.50-1.65 (3H, m, CH_2), 1.80-1.90 (1H, m, CH_2), 2.29 (2H, t, *J* 7.5 Hz, CH_2), 2.34-2.40 (2H, m, CH_2), 3.50-3.58 (1H, m, CH), 3.68 (3H, s, CH_3), 5.99 (1H, dtd, *J* 1.0, 7.75, 10.5 Hz, CH), 6.18-6.28 (1H, m, CH), 6.36 (1H, dd, *J* 2.0, 6.0 Hz, CH), 7.27 (1H, dd, *J* 1.0, 12.25 Hz, CH), 7.53 (1H, ddd, *J* 1.0, 2.5, 6.0 Hz, CH); δ_C (100 MHz $CDCl_3$) 13.9, 21.4, 24.8, 25.9, 28.9, 29.0, 29.5, 32.9, 34.0, 43.4, 51.4, 123.1, 125.4, 135.1, 137.4, 144.4, 161.2, 174.1, 197.5; m/z (CI) 327 (MNa^+, 100%); Found 327.1922 $C_{19}H_{28}O_3Na$ requires 327.1936 (-4.3 ppm).

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Determination of biological activity:

Materials - The thiazolidenedione PPAR-γ ligand, Rosiglitazone **68**·maleate was obtained from Alexis Corporation (San Diego, CA, USA) and the prostaglandin PPAR-γ ligand $\Delta^{12,14}$-15-deoxy-PGJ_2 **4** was obtained from Cayman Chemicals Co., Inc. (Ann Arbor, MI, USA). The following were obtained from Invitrogen (Carlsbad, CA, USA): Dulbecco's modified Eagle's medium-Hi glucose (DMEM), Dulbecco's phosphate buffered saline (PBS), Serum-free Opti-MEM I, foetal bovine serum (FBS), trypsin-EDTA (0.05%), l-glutamine (200 mM) and Lipofectamine-2000. Tissue culture plates (145 mm) and 96-well flat bottom plates were from Greiner Bio-one (Frickenhausen, Germany). The Steady-Glo luciferase assay reporter was supplied by Promega (Madison,WI, USA). Sodium pyruvate (100 mM), poly-D-lysine (Mol. Wt. 70,000-150,000, PDL) and dimethylsulphoxide (DMSO) were purchased from Sigma-Aldrich (St Louis, MO, USA). Stericup-GP filter units (500 mL) were sourced from Millipore (Billerica, MA, USA) and Chromalux white luminescence detection microplates were obtained from Dynex (Chantilly, VA, USA).

DNA constructs - The effect of the compounds on the activity of the PPAR-γ transcription factor was determined in a gene reporter assay. Two plasmids were used in this study: pPPAR-γ contained the ligand binding domain of murine PPAR-γ fused with the DNA binding domain of the yeast transcription factor Gal4 under the control of the SV40 promoter The plasmid pluc encoded five Gal4 binding sites upstream of the UAS-firefly luciferase reporter.

Cell culture and transactivation assay - Human embryonic kidney cells, HEK293T (ATCC, CRL-1573) were cultured in DMEM containing 10% FBS supplemented with 1 mM sodium pyruvate and 2 mM L-glutamine at 5% CO_2/37^oC. All culture media were filtered before use. The 96-well plates were coated with 100 µl of 50 µg/ml poly-D-lysine in PBS overnight at 4^oC. The solution was then removed gently and each well rinsed twice with 100 µL PBS immediately before use. Transfections were performed using Lipofectamine 2000 and cells at 70-80% confluence. For each well, 50 ng of each of PPAR-γ and luciferase vector were added to Opti-MEM I medium to a final volume of 5 µL. Subsequently 0.4 mL of Lipofectamine 2000 per well was mixed with 4.6 µL serum-free Opti-MEM I and allowed to sit at room temperature for 5 minutes. DNA and Lipofectamine were then mixed and allowed to sit at room temperature for a further 20 minutes. This complex was mixed with approximately 6 x 10^4 cells to give a total volume of 100 µL and used to seed each well. After 5 hours, the medium was removed from the cells and replaced with fresh DMEM containing drug at varying concentrations diluted with DMEM. The cells were then allowed to grow for a further 24 hours before the medium was aspirated and 100 µL/well of a (1:1) Steady-Glo: DMEM solution were added. After cell lysis, all contents were transferred to a white 96-well plate and luminescence was then measured on a Wallac 1420-011 Victor 2 Multilabel Counter. All drugs tested were stored at –20^oC as 20 mM stock solutions (DMSO) and thawed immediately before performing dilutions into DMEM. All experiments were carried out three times, each time in triplicate. The concentrations of the compounds that caused 50% activation in this assay (EC_{50}) were calculated by the Prism program.