Supporting Information

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

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S2-S42 Experimental Directions
S43 Determination of Biological Activity
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 cm³ 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 10⁻¹degcm²g⁻¹ (concentrations are quoted in g/100 cm³). 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 Varian 300 Gemini 2000 (300 MHz), or a Bruker 400 Avance (400 MHz) instrument. ¹³C 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 Et₂O were distilled from the sodium-benzophenone ketyl radical and DCM was distilled from CaH₂. 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.**

![Chemical structure of 3-Methyl-2-[1-phenylmeth-\(\text{(E)}\)-ylidene]-2,3,3a,4,7,7a-hexahydro-4,7-methano-inden-1-one, \(\text{E-14a}\).](image)

3-Methyl-2-[1-phenylmeth-(\(\text{E}\))-ylidene]-2,3,3a,4,7,7a-hexahydro-4,7-methano-inden-1-one, \(\text{E-14a}\). At ‑78°C under nitrogen a slurry of CuI (509 mg, 2.67 mmol, 1.2 eq.) in Et₂O (25 cm³) was treated dropwise with a 1.6 M solution of MeLi in hexanes (3.36 cm³, 5.37 mmol, 2.4 eq.). The reaction was warmed to -10°C over a period of 2 h. This solution was cooled to -20°C before a pre-cooled (-20°C) solution of the enone \(\text{exo-12}\) (485 mg, 2.23 mmol, 1 eq.) in Et₂O (25 cm³) was added in a dropwise fashion. The flask containing \(\text{exo-12}\) was washed with Et₂O (5 cm³) and this was also transferred to the reaction mixture. Stirring was continued for 1.5 h during which time the temperature rose to -10°C. Upon cooling to -78°C, benzaldehyde (0.35 cm³, 3.44 mmol, 1.5 eq.) was added. The reaction was stirred for 3 h and warmed from -78°C to 10°C. A saturated solution of NH₄Cl (25 cm³) was added and the resultant aqueous phase was further extracted with Et₂O (3 x 25 cm³). The combined organic extracts were dried over MgSO₄, filtered and the solvent removed in vacuo. The crude product was then purified by flash column chromatography (Hex-Et₂O; 19:1) affording \(\text{E-14a}\) as a colourless solid (520 mg, 93%). Recrystallisation from n-hexane gave crystals of \(\text{E-14a}\) suitable for X-ray crystallography; M.pt. 82°C (Hex); \(R_f\) 0.15 (Hex-Et₂O; 19:1); \(\nu_{\text{max}}\) (neat/cm⁻¹) 2934, 1694, 1609, 1494, 1448, 1332, 1236, 1183; \(\delta_{\text{H}}\) (400 MHz, CDCl₃) 1.25 (3H, d, \(J\ 7.0\ Hz\), CH₃), 1.28 (1H, dt, \(J\ 1.5, 9.5\ Hz\), CH₂), 1.36 (1H, d, \(J\ 9.5\ Hz\), CH₂), 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)
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); δC (100 MHz, CDCl3) 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-methanoinden-1-one, Z-14a. Under nitrogen a suspension of CuI (125 mg, 0.66 mmol, 0.1 eq.) in Et2O (75 cm³) was cooled to −78°C before treatment with a 1.0 M solution of methylmagnesium bromide in Et2O (9.0 cm³, 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 Et2O (15 cm³) 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 NH4Cl (50 cm³) was added and the resultant mixture was extracted with Et2O (5 x 50 cm³). 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: Rf 0.30 (Hex-EtOAc; 9:1); νmax (neat/cm⁻¹) 3063, 2935, 1695, 1610, 1490, 1449, 1332, 1236, 1183; δH (250 MHz, CDCl3) 1.28-1.38 (1H, m, CH2), 1.33 (3H, d, J 7.0 Hz, CH3), 1.45 (1H, d, J 9.5 Hz, CH2), 1.82 (1H, d, J 8.0 Hz, CH), 2.44 (1H, d, J 8.0 Hz, CH2), 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 (MNH4⁺, 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, E-14b. Following the procedure described above (synthesis of E-14a), exo-12 (1.308 g, 6.0 mmol, 1 eq.) in Et2O (30 cm³) was treated with Bu₂CuLi in Et2O (35 cm³) generated from CuI (1.37 g, 7.2 mmol, 1.2 eq.) and a 2.5 M solution of n-BuLi in Et2O (5.76 cm³, 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-Et2O; 9:1) afforded adduct E-14b (1.600 g, 91%) as a viscous yellow oil. Rf 0.25 (Hex-Et2O; 9:1); νmax (neat/cm⁻¹) 3059, 3026, 2958, 2872, 1703, 1613, 1574, 1493, 1448, 1378, 1326, 1288; δH (400 MHz, CDCl3) 0.87 (3H, t, J 7.5 Hz, CH3), 1.22-1.46 (7H, m, CH2), 1.63-1.73 (1H, m, CH2), 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,
3-Octyl-2-[1-phenylmethyl-(E)-ylidene]-2,3,3a,4,7,7a-hexahydro-4,7-methanoinden-1-one, 14c. Under N\textsubscript{2} a 1.7 M solution of tert-butyl lithium in pentane (4.9 cm\textsuperscript{3}, 8.33 mmol, 4 eq.) was added dropwise to a solution of octyl iodide (0.75 cm\textsuperscript{3}, 4.15 mmol, 2 eq.) in a mixture of pentane (17 cm\textsuperscript{3}) and Et\textsubscript{2}O (10 cm\textsuperscript{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\textsubscript{2}O (10 cm\textsuperscript{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\textsubscript{2}O (5 cm\textsuperscript{3}) was added dropwise [washed in with Et\textsubscript{2}O (2 cm\textsuperscript{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\textsuperscript{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\textsubscript{4}Cl (25 cm\textsuperscript{3}) and EtOAc (25 cm\textsuperscript{3}) were added and the resultant aqueous layer was further extracted with EtOAc (3 x 25 cm\textsuperscript{3}). The combined organic extracts were dried over MgSO\textsubscript{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); \( \delta \text{H} \) (400 MHz, CDCl\textsubscript{3}) 0.88 (3H, t, \( J \) 6.5 Hz, CH\textsubscript{3}), 1.18-1.52 (15H, m, CH\textsubscript{2}), 1.64-1.73 (1H, m, CH\textsubscript{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); \( \delta \text{C} \) (100 MHz, CDCl\textsubscript{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; \textit{m/z} (CI) 349 (MH\textsuperscript{+}, 10%), 283 (MH-C\textsubscript{5}H\textsubscript{6}\textsuperscript{+}, 100%); Found 349.25394, C\textsubscript{25}H\textsubscript{33}O requires C, 86.2%; H, 9.2%.

3-Methyl-2-[1-(4-nitrophenyl)methyl-(E)-ylidene]-2,3,3a,4,7,7a-hexahydro-4,7-methanoinden-1-one, 14d. Following the procedure described above, \textit{exo}-12 (485 mg, 2.22 mmol, 1 eq.) in Et\textsubscript{2}O (10 cm\textsuperscript{3}) was treated with a Me\textsubscript{2}CuLi in Et\textsubscript{2}O (25 cm\textsuperscript{3}) generated from Cul (509 mg, 2.67 mmol, 1.2 eq.) and a 1.6 M solution of MeLi in Et\textsubscript{2}O (3.36 cm\textsuperscript{3}, 5.37 mmol, 2.4 eq.). 4-Nitrobenzaldehyde (504 mg, 3.33 mmol, 1.5 eq.) in benzene (5 cm\textsuperscript{3}) was added [washed in with THF (5 cm\textsuperscript{3})]. Standard work-up as above followed by flash column chromatography (Hex-EtOAc; 3:1) afforded adduct \textit{E}-14d (600 mg, 92%) as a yellow crystalline solid. Analytically pure 14d was obtained on recrystallisation from EtOAc, M.pt. 120°C (EtOAc); \( R_f \) 0.35 (Hex-EtOAc; 3:1); \( \nu \text{max} \) (neat/cm\textsuperscript{-1}) 3062, 2968, 2873, 2451, 1708, 1708.
δH (400 MHz, CDCl3) 1.24 (3H, d, J 7.0 Hz, CH3), 1.30-1.35 (2H, m, CH2), 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, 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); δC (100 MHz, CDCl3) 21.1, 38.9, 43.5, 48.6, 49.2, 49.4, 53.3, 123.9, 130.2, 130.9, 137.5, 141.3, 147.5, 148.8, 208.6; m/z (CI) 313 (MNH4+, 80%), 296 (MH+, 35%), 266 (90%), 247 (65%), 230 (MH-C5H6+, 100%); Found 296.12835, C18H18NO3 requires 296.12866; Found C, 72.73; H, 5.75; N, 4.52%, C18H17NO3 requires C, 73.21; H, 5.80; N, 4.74%.

Following the general procedure outlined above, a solution of Me2CuLi in Et2O (25 cm3), prepared from CuI (509 mg, 2.67 mmol, 1.2 eq.) and a 1.6 M solution of MeLi in hexanes (3.36 cm3, 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; Rf 0.35 (Hex-EtOAc; 3:1); υmax (neat/cm−1) 3080, 2964, 2900, 2880, 1697, 1596, 1570, 1511, 1460, 1423, 1326, 1307; δH (400 MHz, CDCl3) 1.25 (3H, d, J 7.25 Hz, CH3), 1.23-1.28 (1H, m, CH2), 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, CH3), 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); δC (100 MHz, CDCl3) 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 (MNH4+, 70%), 215 (MH-C5H6+, 100%); Found 281.15390, C19H21O2 requires 281.15414, (-0.9 ppm); Found C, 81.60; H, 7.31%, C19H20O2 requires C, 81.43; H, 7.14%.

Following the procedure described above, exo-12 (436 mg, 2.0 mmol, 1 eq.) in Et2O (10 cm3) was treated with a Me2CuLi in Et2O (25 cm3) generated from CuI (457 mg, 2.4 mmol, 1.2 eq.) and a 1.6 M solution of MeLi in Et2O (3.0 cm3, 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. After standard work-up as above followed by flash column chromatography (Hex-Et2O; 9:1) afforded adduct E-14f (450 mg, 94%) as a yellow amorphous solid. M.pt. 120ºC; Rf 0.2 (Hex-Et2O; 9:1); υmax (neat/cm−1) 3154, 2972, 2253, 1794, 1690, 1613, 1552, 1474, 1390; δH (400 MHz, CDCl3) 1.26-1.34 (5H, m, CH2, CH3), 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); δC (100 MHz, CDCl3) 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
3-Methyl-2-[1-pyrindin-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 Et₂O (10 cm³) was treated with a Me₂CuLi in Et₂O (25 cm³) generated from Cul (381 mg, 2.0 mmol, 1 eq.) and a 1.6 M solution of MeLi in Et₂O (3.0 cm³, 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 → 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, CDCl₃) 1.27 (3H, d, J 7.0 Hz, CH₂, CH₃), 1.37 (1H, d, J 9.0 Hz, CH), 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, CDCl₃) 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, C₁₇H₁₈NO requires 252.13884 (-0.3 ppm).

3-Methyl-2-[1-(1-methyl-1H-indol-3-yl)methyl-(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 Et₂O (10 cm³) was treated with a Me₂CuLi in Et₂O (25 cm³) generated from Cul (381 mg, 2.0 mmol, 1 eq.) and a 1.6 M solution of MeLi in Et₂O (3.0 cm³, 4.8 mmol, 2.4 eq.). 1-Methyl-1H-indole-3-carbaldehyde¹ (477 mg, 3.0 mmol, 1.5 eq.) was then added. Standard work-up as above followed by flash column chromatography (Hex-EtOAc; 9:1) afforded adduct E-14h (79 mg, 13%) as a viscous yellow oil. R_f 0.3 (Hex-EtOAc; 1:1); δ_H (400 MHz, CDCl₃) 1.00-1.15 (H, m, CH₂), 1.21 (3H, d, J 7.0 Hz, CH₃), 1.23-1.27 (H, m, CH₂), 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, CH₃), 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, CDCl₃) 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, C₂₁H₂₂NO requires 304.17014 (+2.2 ppm).

3-Methyl-2-[1-[1-(toluene-4-sulfonyl)-1H-indol-3-yl)methyl-(E)-ylidene]-2,3,3a,4,7,7a-hexahydro-4,7-methano inden-1-one, 14i. Following the general procedure outlined, a solution of Me₂CuLi in Et₂O (75 cm³), prepared from Cul (1.371 g, 7.2 mmol, 1.2 eq.) and a
1.6 M solution of MeLi in hexanes (9.0 cm³, 14.4 mmol, 2.4 eq.), was treated with \textit{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-1H-indole-3-carbaldehyde \textsuperscript{1} (2.70 g, 9.0 mmol, 1.5 eq.) in a 2:1 mixture of Et\textsubscript{2}O and THF (20 cm³) was added. Following standard work-up, as described above, purification by flash column chromatography (Hex-EtOAc: 1:1) afforded initially \textbf{E-14i} (2.200 g, 83\%) as a yellow amorphous solid. M.pt. 92ºC; \(R_f\) 0.45 (Hex-EtOAc, 1:1); \(\nu_{\text{max}}\) (neat/cm\textsuperscript{-1}) 3148, 3074, 2966, 1697, 1614, 1536, 1493, 1447, 1375; \(\delta\textsubscript{H}\) (400 MHz, CDCl\textsubscript{3}) 1.13-1.17 (5H, m, CH\textsubscript{2}, CH\textsubscript{3}), 1.83 (1H, d, \(J\) 7.75 Hz, CH), 2.20 (3H, s, CH\textsubscript{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), 7.69 (1H, s, CH), 7.82 (1H, d, \(J\) 8.0 Hz, ArH); \(\delta\textsubscript{C}\) (100 MHz, CDCl\textsubscript{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 \textsuperscript{+}, 100%), 400 (50%); Found 466.1439, C\textsubscript{27}H\textsubscript{25}O\textsubscript{3}NaS 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); \(\nu_{\text{max}}\) (neat/cm\textsuperscript{-1}) 3251, 3057, 2965, 2870, 1673, 1590, 1574, 1516, 1492, 1459, 1381, 1367, 1327, 1238; \(\delta\textsubscript{H}\) (400 MHz, CDCl\textsubscript{3}) 1.17 (1H, dd, \(J\) 1.0, 8.5 Hz, CH\textsubscript{2}), 1.24 (3H, s, CH\textsubscript{3}), 1.30 (H, d, \(J\) 8.5 Hz, CH\textsubscript{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, \(J\) 7.5 Hz, CH), 6.14 (1H, dd, \(J\) 2.75, 5.5 Hz, CH), 6.16 (1H, dd, \(J\) 2.75, 5.5 Hz, CH), 6.17-6.24 (2H, m, CH), 6.93 (1 H, m, CH), 6.95 (1H, m, CH), 7.02-7.06 (1H, m, CH), 7.25-7.38 (3H, m, Ar H), 7.46-7.51 (2H, m, ArH); \(\delta\textsubscript{C}\) (100 MHz, CDCl\textsubscript{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\textsuperscript{+}, 100%); Found 290.15473, C\textsubscript{20}H\textsubscript{20}NO requires 290.15449 (+2.0 ppm).

**2-[2-Methyl-2-[\textit{(E)}]-3-phenylprop-2-en-(\textit{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\textsubscript{2}CuLi in Et\textsubscript{2}O (25 cm³), prepared from CuI (1.371 g, 7.2 mmol, 1.2 eq.) and a 1.6 M solution of MeLi in hexanes (9.0 cm³, 13.2 mmol, 2.4 eq.), was treated with \textit{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 cm³, 8.58 mmol, 1.5 eq.) was added. Following standard work-up, as described above, purification by flash column chromatography (Hex-EtOAc: 1:1) afforded initially \textbf{E,E-14j} (1.126 g, 68\%) as a yellow viscous oil; \(R_f\) 0.2 (Hex-EtOAc: 9:1); \(\nu_{\text{max}}\) (neat/cm\textsuperscript{-1}) 3251, 3057, 2965, 2870, 1673, 1695, 1602, 1589, 1494, 1449, 1421; \(\delta\textsubscript{H}\) (400 MHz, CDCl\textsubscript{3}) 1.27-1.31 (5H, m, CH\textsubscript{3}, CH\textsubscript{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); \(\delta\textsubscript{C}\) (100 MHz, CDCl\textsubscript{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, 150.0.
146.0, 208.2; m/z (CI) 276 (MH⁺, 100%); Found 277.15954, C₅₀H₂₁O requires 277.15924 (+1.2 ppm).

3-Methyl-2-[(E)-pent-2-en-(E)-ylidene]-2,3,3a,4,7,7a-hexahydro-4,7-methanoindene-1-one, 14k. Following the general procedure outlined above, a solution of Me₂CuLi in Et₂O (25 cm³); prepared from CuI (457 mg, 2.4 mmol, 1.2 eq.) and a 1.6 M solution of MeLi in hexanes (3.0 cm³, 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 cm³, 3.0 mmol, 1.5 eq.) was added. Following the standard work-up as described above, purification by flash column chromatography (Hex-Et₂O; 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; Rf 0.2 (Hex-Et₂O; 9:1); υmax (neat/cm⁻¹) 3060, 2966, 2875, 2360, 1702, 1627, 1600, 1459, 1377, 1327, 1277, 1244, 1210; δH (400 MHz, CDCl₃) 1.00 (3H, t, J 7.5 Hz, CH₃), 1.15 (3H, d, J 7.5 Hz, CH₃), 1.18-1.22 (2H, m, CH₂), 1.74 (1H, d, J 7.5 Hz, CH), 2.12-2.21 (2H, m, CH₂), 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); δC (100 MHz, CDCl₃) 12.9, 23.6, 26.5, 38.0, 43.1, 48.1, 48.9, 49.3, 54.4, 125.3, 133.3, 137.5, 137.7, 138.5, 146.5, 148.1, 208.5; m/z (CI) 229 (MH⁺, 100%), found 229.15921, C₁₆H₂₁O requires 229.15924 (-0.1 ppm).

Data for Z,E-14k: Rf 0.35 (Hex-Et₂O; 9:1); δH (400 MHz, CDCl₃) 1.06 (3H, t, J 7.5 Hz, CH₃), 1.22 (3H, d, J 7.25 Hz, CH₃), 1.25-1.29 (1H, m, CH₂), 1.31-1.35 (1H, m, CH₂), 1.76 (1H, dd, J 3.0, 8.25 Hz, CH), 2.17-2.28 (1H, m, CH₂), 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); δC (100 MHz, CDCl₃) 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, C₁₆H₂₁O requires 229.15924 (-0.1 ppm).

3-Methyl-2-[(E)-pent-2-en-(Z)-ylidene]-2,3,3a,4,7,7a-hexahydro-4,7-methanoindene-1-one, 14k. Following the general procedure described above, a solution of enone exo-12 (1.308 g, 6.0 mmol, 1 eq.) in Et₂O (25 cm³) was treated with a 1M solution of methyl magnesium bromide in Et₂O (9.0 cm³, 9.0 mmol, 1.5 eq.) that had been pre-mixed with CuI (125 mg, 0.66 mmol, 0.1 eq.) in Et₂O (50 cm³). After the formation of conjugate adduct, E-pent-2-enal (0.9 cm³, 9.0 mmol, 1.5 eq.) was added at -78°C. Following standard work-up, purification by flash column chromatography (Hex-Et₂O; 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$_2$CuLi in Et$_2$O (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 -78°C. Following standard work-up, purification by flash column chromatography (Hex-Et$_2$O; 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$_2$O; 9:1); $\nu_{\text{max}}$ (neat/cm$^{-1}$) 3065, 2960, 2869, 1710, 1640, 1568, 1460; $\delta$$_H$ (400 MHz, CDCl$_3$) 1.01 (3H, d, $J$ 7.0 Hz, CH$_3$), 1.05 (3H, d, $J$ 7.0 Hz, CH$_3$), 1.18 (3H, d, $J$ 7.0 Hz, CH$_3$), 1.23-1.31 (2H, m, CH$_2$), 1.78 (1H, d, $J$ 7.5 Hz, CH), 2.40 (1H, d, $J$ 7.5 Hz, CH), 2.48-2.60 (1H, m, CH), 2.67 (1H, m, CH), 2.80 (1H, s, CH), 3.03 (1H, d, $J$ 1.5 Hz, CH), 6.14-6.21 (2H, m, CH), 6.28 (1H, dd, $J$ 2.0, 11.0 Hz, CH), $\delta$$_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$_2$O, 9:1); $\nu_{\text{max}}$ (neat/cm$^{-1}$) 3064, 2959, 2870, 1711, 1640, 1568, 1640; $\delta$$_H$ (400 MHz, CDCl$_3$) 0.94 (3H, d, $J$ 7.0 Hz, CH$_3$), 0.96 (3H, d, $J$ 7.0 Hz, CH$_3$), 1.17 (3H, d, $J$ 7.0 Hz, CH$_3$), 1.29-1.33 (2H, m, CH$_2$), 1.73 (1H, dd, $J$ 3.5, 8.0 Hz, CH), 2.30 (1H, d, $J$ 8.0 Hz, CH), 2.31-2.43 (1H, m, CH), 2.76 (1H, s, CH), 3.01-3.09 (1H, m, CH), 3.63-3.77 (1H, m, CH), 5.64 (1H, dd, $J$ 2.0, 10.0 Hz, CH), 6.14-6.21 (2H, m, CH); $\delta$$_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$_{13}$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. A solution of Me$_2$CuLi in Et$_2$O (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$_2$O (12 cm$^3$, 12 mmol, 2.0 eq.) was added at -78°C, which followed the addition of isobutyraldehyde (662 mg, 9.0 mmol, 1.5 eq.) was added at -78°C. Standard work-up, as described above, and purification by flash column chromatography (Hex-Et$_2$O; 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).

Supplementary Material (ESI) for Organic & Biomolecular Chemistry
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3-Butyl-2-hept-(E/Z)-ylidene-2,3,3a,4,7,7a-hexahydro-4,7-methanoinden-1-one, 14m. As described, under N2 a slurry of copper(I) iodide (17.4 mg, 0.09 mmol, 0.1 eq.) in Et2O (20 cm3) was cooled to -78°C and 2 M BuMgCl in Et2O (0.69 cm3, 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 Et2O (15 cm3), 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 cm3, 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 cm3) and Et2O (30 cm3) were then added and the resultant aqueous layer was further extracted with Et2O (3 x 30 cm3). The combined organic phases were then dried with MgSO4 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:** Rf 0.4 (c-Hex-EtOAc; 19:1); νmax (cm⁻¹/neat) 2956, 2925, 2856, 1734, 1709, 1637, 1459, 1376, 1327; δH (400 MHz, CDCl3) 0.78-0.84 (6H, m, CH3), 1.16-1.31 (16H, m, CH2), 1.75 (1H, d, J 8.0 Hz, CH), 2.18-2.26 (2H, m, CH), 2.55-2.62 (2H, m, CH2), 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); δC (100 MHz, CDCl3) 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 (Cl) 301 (MH⁺, 100%); Found 301.25390, C21H33O requires 301.25314 (+2.6 ppm); Data for **E-14m:** Rf 0.35 (c-Hex-EtOAc; 19:1); νmax (cm⁻¹/neat) 3061, 2957, 1710, 1638, 1459, 1378, 1260, 714; δH (400 MHz, CDCl3) 0.88-0.90 (6H, m, CH3), 1.28-1.49 (16H, m, CH2), 1.90 (1H, d, J 7.5 Hz, CH), 2.14-2.20 (2H, m, CH2), 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); δC (100 MHz, CDCl3) 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 (Cl) 301 (MH⁺, 100%); Found 301.25361, C21H33O 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 N2, a slurry of copper(I) iodide (0.21 g, 1.10 mmol, 1.2 eq.) in THF (20 cm³) was cooled to -78°C and 1.6 M butyl lithium in THF (1.4 cm³, 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 cm³) was added dropwise. The reaction was warmed to -5°C over 1 hour before being re-cooled to -78°C and heptanal (0.15 cm³, 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 cm³) and Et2O (30 cm³) were added to the reaction mixture and the aqueous layer was further extracted with Et2O (2 x 30 cm³) and the combined organic layers were dried with MgSO4 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-methanoinden-1-one, 14n. At -78ºC under nitrogen a slurry of CuI (45.7 mg, 0.24 mmol, 0.1 eq.) in Et₂O (25 cm³) was treated dropwise with a 2 M solution of isopropyl magnesium chloride in THF (1.4 cm³, 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 \(\text{exo-12}\) (436 mg, 2.0 mmol, 1.0 eq.) in Et₂O (10 cm³) 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 cm³, 3.00 mmol, 1.5 eq.) was added. The reaction was stirred overnight and allowed to warm from -78ºC to 10ºC. Saturated aqueous NH₄Cl (25 cm³) was added and the resultant aqueous phase was further extracted with Et₂O (5 x 25 cm³). The combined organic extracts were dried over MgSO₄, filtered and the solvent removed \textit{in vacuo}. The crude product was purified by flash column chromatography (Hex-Et₂O; 19:1) affording initially \(\text{Z-14n}\) (187 mg, 34%) as a viscous yellow oil followed by \(\text{E-14n}\) (260 mg, 47%) as a colourless solid. M.pt. 101ºC, \(R_f\) 0.15 (Hex-EtOAc; 19:1); \(\nu\)max (neat/cm\(^{-1}\)) 3060, 2959, 2926, 2872, 1704, 1613, 1574, 1494, 1462, 1448, 1368, 1327, 1287; \(\delta\)\(\text{H}\) (400 MHz, CDCl₃) 0.67 (3H, d, \(J\) 7.0 Hz, CH₃), 1.07 (3H, d, \(J\) 7.0 Hz, CH₃), 1.28 (1H, dt, \(J\) 1.5, 9.0 Hz, CH₂), 1.39 (1H, d, \(J\) 9.0 Hz, CH₂), 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); \(\delta\)\(\text{C}\) (100 MHz, CDCl₃) 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, C₂₀H₂₃O requires 279.17487 (-3.3 ppm); Data for \(\text{Z-14n}\): \(R_f\) 0.25 (Hex-EtOAc; 19:1); \(\nu\)max (neat/cm\(^{-1}\)) 3060, 2959, 2926, 2872, 1704, 1613, 1574, 1494, 1462, 1448, 1368, 1327, 1287; \(\delta\)\(\text{H}\) (400 MHz, CDCl₃) 0.88 (3H, d, \(J\) 7.0 Hz, CH₃), 1.01 (3H, d, \(J\) 7.0 Hz, CH₃), 1.29 (1H, ddd, \(J\) 1.25, 1.5, 9.0 Hz, CH₂), 1.52 (1H, d, \(J\) 9.0 Hz, CH₂), 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); \(\delta\)\(\text{C}\) (100 MHz, CDCl₃) 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, C₂₀H₂₃O 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 -78ºC, CuI (45.7 mg, 0.24 mmol, 0.1 eq.) in Et₂O (25 cm³) was treated dropwise with a 1 M solution of vinyl magnesium bromide in Et₂O (4.2 cm³, 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 \(\text{exo-12}\) (654 mg, 3.0 mmol, 1.0 eq.) in Et₂O (10 cm³) 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 cm³, 4.5 mmol, 1.5 eq.) was added. Standard work-up as above followed by flash column chromatography afforded initially \(\text{Z-14o}\) (52 mg, 7%) as a viscous yellow oil then \(\text{E-14o}\) (687
mg, 87%) as a viscous yellow oil. \( R_f 0.15 \) (Hex-EtOAc; 19:1); \( \nu_{\text{max}} \) (neat/cm\(^{-1}\)) 3059, 2967, 2875, 1705, 1614, 1574, 1493, 1449, 1406, 1327, 1289, 1238; \( \delta_{\text{H}} \) (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), 5.88 (1H, ddd, \( J_{6.0, 10.5, 16.75} \) CH), 6.12-6.20 (2H, m, CH), 7.14 (1H, d, \( J_{2.0} \) Hz), 7.47-7.52 (2H, m, ArH); \( \delta_{\text{C}} \) (100 MHz, CDCl\(_3\)) 43.1, 47.9, 48.0, 48.3, 49.4, 52.7, 114.4, 128.5, 129.7, 131.3, 133.4, 133.6, 133.7, 133.8, 133.8, 134.0, 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-methanoinden-1-one, 14p. Following the procedure described above, a solution of enone exo-12 (654 mg, 3.0 mmol, 1 eq.) in Et\(_2\)O (25 cm\(^3\)) was treated with a 1M solution of vinyl magnesium bromide in Et\(_2\)O (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\(_2\)O, 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\(_2\)O; 9:1); \( \nu_{\text{max}} \) (neat/cm\(^{-1}\)) 3060, 2964, 2869, 1710, 1638, 1566, 1464, 1382, 1361, 1327, 1287, 1216, 4.5 mmol, 1.5 eq.) was added at -78ºC. Following standard work-up, purification by flash column chromatography (Hex-Et\(_2\)O, 1:9) 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\(_2\)O; 9:1); \( \nu_{\text{max}} \) (neat/cm\(^{-1}\)) 3060, 2964, 2869, 1710, 1638, 1566, 1464, 1382, 1361, 1327, 1287, 1215; \( \delta_{\text{H}} \) (400 MHz, CDCl\(_3\)) 0.98 (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, \( J_{1.0, 1.25, 17.0} \) 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); \( \delta_{\text{C}} \) (100 MHz, CDCl\(_3\)) 21.4, 21.6, 21.6, 28.1, 43.1, 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 (+0.9 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); \( \delta_{\text{H}} \) (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\(_2\)), 2.32-2.40 (1H, d, \( J_{8.5} \) Hz, CH), 2.83 (1H, s, CH), 3.12 (1H, d, \( J_{1.0} \) Hz, CH), 3.67-3.80 (1H, m, CH); 5.00-5.06 (2H, m, CH\(_2\)), 5.35 (1H, d, \( J_{2.2, 10.0} \) Hz, CH), 5.70-5.80 (1H, m, CH), 6.17-6.22 (2H, m, CH); \( \delta_{\text{C}} \) (100 MHz, CDCl\(_3\)) 22.4, 22.5, 26.3, 43.6, 46.1, 47.5, 48.5, 50.8, 55.3, 114.2, 137.4, 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).

\[
\text{MeO}_2\text{C}=0
\]
rose to -20°C. Dimethylsulfide (15 cm³, 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); Rf 0.1 (streak) (Hex-EtOAc; 1:1); δH (400 MHz, CDCl3) 1.33-1.42 (2H, m, CH₂), 1.65 (4H, pent, J 7.5 Hz, CH₂), 2.32 (2H, t, J 7.5 Hz, CH₂), 2.45 (2H, dt, J 1.5, 7.5 Hz, CH₂), 3.64 (3H, s, CH₃), 9.79 (1H, m, CHO); δC (100 MHz, CDCl3) 21.6, 24.5, 28.5, 33.7, 43.5, 51.3, 173.8, 202.2; m/z (CI) 176 (MNH₄⁺, 100%), 159 (MH⁺, 70%).

(±)-7-[1-Octyl-3-oxo-1,3,3a,4,7,7a-hexahydro-4,7-methanoinden-(2E)-ylidene] heptanoic acid methyl ester, E-14q. Under nitrogen at -78°C a solution of octyl iodide (0.63 cm³, 3.49 mmol, 2 eq.) in a mixture of pentane (15 cm³) and Et₂O (7.5 cm³) was treated dropwise with a 1.7 M solution of tert-butyllithium in pentane (4.1 cm³, 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 Cul (333 mg, 1.75 mmol, 1 eq.) in Et₂O (10 cm³). 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 Et₂O (5 cm³, washed with 2 cm³) 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 NH₄Cl (50 cm³) was added and the resultant mixture was extracted with EtOAc (3 x 50 cm³). The combined organic extracts were dried over MgSO₄, 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. Rf 0.15 (Hex-EtOAc; 9:1); νmax (neat/cm⁻¹) 2926, 2860, 1738, 1710, 1640, 1461; δH (400 MHz, CDCl3) 0.88 (3H, t, J 6.5 Hz, CH₃), 1.21-1.43 (18H, m, CH₂), 1.49 (2H, pent, J 7.5 Hz, CH₂), 1.65 (2H, pent, J 7.5 Hz, CH₂), 1.90 (1H, d, J 7.75 Hz, CH), 2.13-2.20 (2H, m, CH₂), 2.30 (2H, t, J 7.5 Hz, CH₂), 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, CH₃), 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); δC (100 MHz, CDCl3) 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 (MNH₄⁺, 5%), 401 (MH⁺, 10%), 335 (M-C₃H₆⁺, 100%); Found 401.30622, C₂₈H₄₁O₃ requires 401.30557 (+1.8 ppm).
(±)-7-[1-Octyl-3-oxo-1,3,3a,4,7,7a-hexahydro-4,7-methanoinden-(2Z)-ylidene] heptanoic acid methyl ester, Z-14q. Under nitrogen a slurry of CuI (51 mg, 0.27 mmol, 0.1 eq.) in Et₂O (30 cm³) was treated with a 2.0 M solution of octyl magnesium bromide in Et₂O (1.33 cm³, 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 Et₂O (10 cm³) 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 NH₄Cl (50 cm³) was added and the resultant mixture was extracted with Et₂O (3 x 50 cm³). The combined organic extracts were dried over MgSO₄, 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. Rₚ = 0.3 (Hex-EtOAc; 9:1); δ H (400 MHz, CDCl₃) 0.89 (3H, t, J 6.5 Hz, CH₃), 1.24-1.52 (20H, m, CH₂), 1.63 (2H, pent, J 7.5 Hz, CH₂), 1.83 (1H, d (br), J 8.0 Hz, CH), 2.30 (2H, t, J 7.5 Hz, CH₂), 3.05 (1H, s (br), CH), 3.66 (3H, s, CH₃), 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, CDCl₃) 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 (MNH₄⁺, 15%), 401 (MH⁺, 15%), 335 (M-C₅H₆⁺, 100%); Found 401.30659, C₂₆H₄₁O₃ 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 mol, 5.0 eq.) in DCM (10 cm³) was treated with a 1.0 M solution of MeAlCl₂ in hexane (1.1 cm³, 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. 64-66°C; Rₚ 0.25 (Hex-EtOAc; 3:1); δ H (400 MHz, CDCl₃) 1.22 (3H, d, J 7.0 Hz, CH₃), 3.84-4.00 (1H, m, CH), 6.40 (1H, dd, J 1.75, 5.75 Hz, CH), 7.39-7.44 (4H, ArH), 7.50 (2H, d, J 7.0 Hz, ArH), 7.60 (1H, dd, J 1.0, 2.5, 5.75 Hz, CH); δ C (100 MHz, CDCl₃) 16.3, 38.8, 128.7, 129.3, 130.6, 131.7, 133.6, 134.8, 136.3, 163.9, 197.4; m/z (CI) 202 (NH₄⁺, 20%), 185 (M⁺, 100%); Found 185.09654, C₁₃H₁₂O requires 185.09665, (-0.6 ppm); Found C, 84.66; H, 6.60%, C₁₃H₁₂O 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.

![Image of 15a structure]

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. \(R_t\) 0.35 (Hex-EtOAc; 3:1); \(\nu_{\text{max}}\) (neat/cm\(^{-1}\)) 3058, 3026, 2956, 2930, 2860, 1698, 1633, 1583, 1495, 1449, 1379, 1338; \(\delta_H\) (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); \(\delta_C\) (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).

![Image of 15b structure]

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 \((ca. 40^\circ C)\) 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. \(R_t\) 0.25 (Hex-EtOAc; 9:1); \(\nu_{\text{max}}\) (neat/cm\(^{-1}\)) 3058, 2926, 2855, 1698, 1633, 1583, 1495; \(\delta_H\) (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); \(\delta_C\) (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).

![Image of 15c structure]
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 cm³) was treated with a 1.0 M solution of MeAlCl₂ in hexane (0.75 cm³, 0.75 mmol, 1 eq.) and heated to reflux for 3.5 h. The reaction was cooled before Et₂O (50 cm³) and 0.5 M NaOH (50 cm³) were added. The resultant aqueous layer was extracted with Et₂O (2 x 50 cm³) and the combined organic extracts were dried over MgSO₄. 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, CDCl₃) 1.20 (3H, d, J 7.5 Hz, CH₃), 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, CDCl₃) 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 (MNH₄⁺, 5%), 230 (MH⁺, 10%), 200 (100%); Found 230.08171, C₁₃H₁₂NO₃ requires 230.08164, (-0.3 ppm); Found C, 68.93; H, 4.85; N, 6.10%, C₁₃H₁₁NO₃ 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 cm³) was treated with a 1.0 M solution of MeAlCl₂ in hexane (1.25 cm³, 1.25 mmol, 1 eq.) and heated to reflux for 35 h. Et₂O (50 cm³) and 0.5 M NaOH (50 cm³) were added. The resultant aqueous layer was extracted with Et₂O (2 x 50 cm³) and the combined organic extracts were dried over MgSO₄. 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); δ_max (neat/cm⁻¹) 3080, 2964, 2928, 2880, 1691, 1626, 1600, 1512, 1462, 1423, 1337, 1305; δ_H (400 MHz, CDCl₃) 1.21 (3H, d, J 7.5 Hz, CH₃), 3.83-3.92 (1H, m, CH), 3.85 (3H, s, CH₃), 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, CDCl₃) 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, C₁₃H₁₄O₂ 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 cm³) was treated with a 1.0 M solution of MeAlCl₂ in hexane (1.66 cm³, 1.66 mmol, 1 eq.). This mixture was heated to reflux for 8 h. On cooling silica (ca. 2.5 g) was added and the solvent was removed

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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; Rf 0.25 (Hex-EtOAc; 3:1); δH (400 MHz, CDCl3) 1.35 (3H, d, J7.0 Hz, CH3), 3.02 (1H, s, CH), 3.81-3.89 (1H, m, CH), 6.34 (1H, dd, J1.75, 6.0 Hz, CH), 6.52 (1H, dd, J1.75, 3.5 Hz, CH), 6.70 (1H, d, J3.5 Hz, CH), 7.14 (1H, s, CH), 7.56 (1H, ddd, J1.75, 3.5 Hz, CH), 7.70 (1H, d, J3.5 Hz, CH), 8.00 (1H, d, J8.0 Hz, ArH); δC (100 MHz, CDCl3) 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, C11H11O2 requires 175.07690 (+4.5 ppm).

4-Methyl-5-[1-[1-(toluene-4-sulfonyl)-1H-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 cm³) was treated with a 1.0 M solution of MeAlCl2 in hexane (0.5 cm³, 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; Rf 0.25 (Hex-EtOAc; 2:1); υmax (neat/cm⁻¹) 3149, 3074, 2965, 1698, 1614, 1536, 1493, 1447, 1375; δH (400 MHz, CDCl3) 1.29 (3H, d, J7.5 Hz, CH3), 2.34 (3H, s, CH3), 3.76-3.84 (1H, m, CH), 6.43 (1H, dd, J1.75, 6.0 Hz, CH), 7.24 (2H, d, J8.0 Hz, ArH), 7.32 (1H, dd, J7.0, 7.5 Hz, ArH), 7.39 (1H, dd, J7.0, 8.0 Hz, ArH), 7.55 (1H, s, ArH), 7.62 (1H, dd, J2.5, 6.0 Hz, CH), 7.74 (1H, d, J7.5 Hz, ArH), 7.75 (1H, s, ArH), 7.79 (2H, d, J8.0 Hz, CH, ArH), 8.00 (1H, d, J8.0 Hz, ArH); δC (100 MHz, CDCl3) 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, C22H19NO3SNa 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 N2, 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 cm³) was treated with a 1.0 M solution of MeAlCl2 in hexane (0.5 cm³, 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 cm³) was treated with a 1.0 M solution of MeAlCl2 in hexane (0.5 cm³, 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).
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. 98-100°C; **R** 0.3 (Hex-EtOAc; 3:1); **υ**\(_{\max}\) (neat/cm\(^{-1}\)) 3055, 3020, 2940, 2860, 1685, 1617, 1578, 1448, 1336, 1282; \(\delta\)\(_H\) (400 MHz, CDCl\(_3\)) 1.39 (3H, d, \(J\) 7.5 Hz, CH\(_3\)), 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); \(\delta\)\(_C\) (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); \(\nu_{\max}\) (neat/cm\(^{-1}\)) 3058, 3022, 2940, 2860, 1685, 1618, 1576, 1448, 1336, 1282; \(\delta\)\(_H\) (400 MHz, CDCl\(_3\)) 1.30 (3H, d, \(J\) 7.5 Hz, CH\(_3\)), 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); \(\delta\)\(_C\) (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 (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); \(\delta\)\(_H\) (400 MHz, CDCl\(_3\)) 1.07 (3H, t, \(J\) 7.5 Hz, CH), 1.51 (3H, d, \(J\) 7.5 Hz, CH), 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, dt, \(J\) 1.5, 11.0, 15.5 Hz, CH).

**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 (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 120°C 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\(_2\)O (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 → 4:1 → 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); \(\delta_H\) (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), \(\delta_C\) (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 \(Z-15l\) \(\delta_H\) (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); \(\upsilon_{max}\) (cm\(^{-1}\)/neat) 2956, 2929, 2858, 2359, 2339, 1736, 1709, 1655, 1466, 1377, 1174; \(\delta_H\) (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); \(\delta_C\) (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)-ylidencyclopent-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); \( \nu_{\text{max}} \) (neat/cm\(^{-1}\)) 2956, 2929, 2858, 1705, 1655, 1581, 1466, 1230, 833; \( \delta_{\text{H}} \) (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); \( \delta_{\text{C}} \) (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); \( \nu_{\text{max}} \) (neat/cm\(^{-1}\)) 3061, 2959, 2926, 2885, 1697, 1630, 1582, 1448, 1369; \( \delta_{\text{H}} \) (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), 7.56 (1H, ddd, \( J \) 1.0, 2.5, 6.0 Hz, CH), \( \delta_{\text{C}} \) (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-Phenylmethyl-(E)-ylidene]-4-vinyleclopent-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); \( \nu_{\text{max}} \) (neat/cm\(^{-1}\)) 3053,
2985, 2305, 2253, 1696, 1449, 1421, 1265; δH (400 MHz, CDCl3) 4.43-4.48 (1H, m, CH), 5.16 (1H, dt, J 1.0, 10.0 Hz, CH2), 5.25 (1H, dt, J 1.0, 17.0 Hz, CH2), 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); δC (100 MHz, CDCl3) 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, C14H13O 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 cm³) was treated with a 1.0 M solution of MeAlCl2 in hexane (0.70 cm³, 0.70 mmol, 1.0 eq.). This mixture was heated to reflux for 8 h. The reaction was quenched with 5% aqueous sodium hydrgencarbonate solution (50 cm³). The suspension was extracted with Et2O (8 x 25 cm³) and the combined organic fractions were dried over MgSO4. 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. Rf 0.35 (Hex-EtOAc; 4:1); δH (400 MHz, CDCl3) 0.95 (3H, d, J 6.5 Hz, CH3), 0.97 (3H, d, J 6.5 Hz, CH3), 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), 5.19 (1H, d, J 17.0 Hz, CH2), 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); δC (100 MHz, CDCl3) 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, C11H14O 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 cm³) was treated with a 1 M solution of MeAlCl2 in hexanes (0.50 cm³, 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. Rf 0.2 (Hex-EtOAc; 3:1); δH (400 MHz, CDCl3) 0.88 (3H, t, J 6.5 Hz, CH3), 1.21-1.34 (12H, m, CH2), 1.34-1.42 (2H, m, CH2), 1.46-1.54 (1H, m, CH), 1.52 (2H, pent, J 7.5 Hz, CH2), 1.65 (2H, pent, J 7.5 Hz, CH2), 1.76-1.86 (1H, m, CH), 2.18-2.32 (2H, m, CH2), 2.31 (2H, t, J 7.5 Hz, CH2), 3.44-3.49 (1H, m, CH), 3.66 (3H, s, CH3), 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); δC (100 MHz, CDCl3) 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 (MNH3+, 5%),...
335 (MH⁺, 100%); Found C, 75.33; H, 10.35%, C₂₁H₃₄O₃ requires C, 75.40; H, 10.26%. Data for Z-15q: \( R_f \) 0.25 (Hex-EtOAc; 3:1); \( \delta_H \) (400 MHz, CDCl₃) 0.88 (3H, t, \( J \) 6.5 Hz, CH₃), 1.19-1.32 (20H, m, CH₂), 2.29 (2H, t, \( J \) 7.5 Hz, CH₂), 2.80 (2H, q, \( J \) 7.5 Hz, CH₂), 3.23-3.28 (1H, m, CH), 3.67 (3H, s, CH₃), 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); \( \delta_C \) (100 MHz, CDCl₃) 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 (MNH₄⁺, 10%), 335 (MH⁺, 100%).

![Chemical Structure](image)

3-Ethyl-2-trimethylsilyl-2,3,3a,4,7,7a-hexahydro-4,7-methanoindene-1-one, 21. Under N₂ 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 Et₂O (5 cm³) were stirred at 0°C. A 1 M solution of diethylzinc in heptane (3.1 cm³, 3.1 mmol, 1.0 eq.) was then added. After 10 min the resultant mixture was treated with a solution of \( \text{exo-12} \) (676 mg, 3.10 mmol, 1 eq.) in Et₂O (10 cm³). 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-EtO, 9:1) 21 (308 mg, 40%) was obtained as a colourless viscous oil. \( R_f \) 0.4 (Hex-EtO, 9:1); \( \nu_{max} \) (neat/cm⁻¹) 3056, 2961, 2875, 2305, 1725, 1703, 1570, 1461; \( \delta_H \) (400 MHz, CDCl₃) 0.10 (9H, s, CH₃), 1.01 (3H, t, \( J \) 7.0 Hz, CH₃), 1.19 (1H, d, \( J \) 9.0 Hz, CH₂), 1.28-1.35 (1H, m, CH), 1.39-1.44 (1H, m, CH₂), 1.59-1.67 (2H, m, CH₂), 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); \( \delta_C \) (100 MHz, CDCl₃) -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 C₁₅H₂₄O₃Si 248.15964 (+1.5 ppm).

(3a,4,7,7a)-2-[(Phenylsulfanyl)phenylmethyl]-3a,4,7,7a-tetrahydro-4,7-methanoinden-1-one, 22. Under N₂ at room temperature a solution of benzaldehyde (0.17 cm³, 1.64 mmol, 1.5 eq.) and \( \text{exo-12} \) (238 mg, 1.09 mmol, 1 eq.) in dry THF (15 cm³) was treated dropwise with a 1.0 M solution of lithium thiophenolate in THF (1.20 cm³, 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-EtO Ac; 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); \( \nu_{max} \) (neat/cm⁻¹) 3438, 2932, 2857, 2286, 2223, 1737, 1437; \( \delta_H \) (400 MHz, CDCl₃) 0.75 (1H, d, \( J \) 9.5 Hz, CH₂), 0.83 (1H, d, \( J \) 9.5 Hz, CH₂), 1.61-1.14 (1H, m, CH₂), 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); \( \delta_C \) (100 MHz, CDCl₃) 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, C₂₅H₂₀OSH 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 cm³) under nitrogen. This was cooled to -78°C and 1.6 M butyl lithium in THF (0.75 cm³, 1.19 mmol, 1.3 eq.) was added dropwise. Dry DMPU (0.29 cm³, 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 cm³) was added. The reaction vessel was kept between -20°C and -5°C for 1 h before aqueous ammonium chloride (30 cm³) and Et₂O (30 cm³) were added. The resultant aqueous layer was further extracted with Et₂O (2 x 30 cm³). The combined organic layers were then dried with MgSO₄ and reduced in vacuo. Purification was carried out via flash column chromatography (Hex-EtOAc; 19:1) affording 23 (130 mg, 42%) as yellow oil. Rf 0.3 (Hex- Et₂O; 9:1); νmax (neat/cm⁻¹) 2949, 2897, 2360, 2342, 1706, 1458, 1422, 1248, 858, 489; δH (400 MHz, CDCl₃) 0.15 (9H, s, CH₃), 1.14 (1H, d, J 9.0 Hz, CH₂), 1.42 (1H, d, J 9.0 Hz, CH₂), 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, CH₂), 2.75-2.80 (6H, m, CH₂, 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); δC (100 MHz, CDCl₃) -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, C₁₇H₂₇OS₂Si requires 339.12726 (+2.3 ppm).

2-(3-Oxo-2,3,3a,4,7,7a-hexahydro-1H-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 cm³) and methanol (10 cm³) at room temperature. The reaction mixture was allowed stir for 15 min until hydrogen evolution had ceased. Dimethylmalonate (0.08 cm³, 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 cm³) 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 cm³) and Et₂O (20 cm³) were added and the aqueous layer was further extracted with Et₂O (2 x 20 cm³). The combined organic phases were dried over MgSO₄ and were reduced in vacuo. Purification by flash column chromatography (Hex-EtOAc; 9:1) afforded the product 24 (90 mg, 71%) as colourless oil. Rf 0.15 (Hex-EtOAc; 9:1); νmax (neat/cm⁻¹) 2957, 2925, 2852, 1737, 1634, 1438, 1339, 1275; δH (400 MHz, CDCl₃) 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, CH₂, CH), 2.84 (1H, s (br), CH₂), 3.12 (1H, s (br), CH), 3.55 (1H, d, J 8.0 Hz, CH), 3.75 (3H, s, CH₃), 3.78 (3H, s, CH₃), 6.17 (2H, s (br), CH); δC (100 MHz, CDCl₃) 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\textsuperscript{+}, 100%), found 296.14911, C\textsubscript{15}H\textsubscript{22}O\textsubscript{5}N requires 296.14981 (-2.6ppm).

\begin{center}
\includegraphics[width=0.2\textwidth]{structure.png}
\end{center}

3a,4,7,7a-Tetrahydro-4,7-methanoinden-1-one, 25.\textsuperscript{4} Sodium hydride [60% w/w in mineral oil] (95 mg, 2.39 mmol, 2.6 eq.) was stirred under N\textsubscript{2} in a 1:1 mixture of methanol (15 cm\textsuperscript{3}) and hexane (15 cm\textsuperscript{3}). This was cooled to -5°C and a solution of 12 (200 mg, 0.92 mmol, 1 eq.) in hexane (10 cm\textsuperscript{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\textsuperscript{3}) and Et\textsubscript{2}O (30 cm\textsuperscript{3}) were added, the resultant aqueous layer was further extracted with Et\textsubscript{2}O (2 x 30 cm\textsuperscript{3}). The combined organic layers were then dried with MgSO\textsubscript{4} and reduced \textit{in vacuo} to yield the product 25 (122 mg, 91%) as a colourless oil. R\textsubscript{f} 0.25 (Hex-EtOAc; 9:1); \textit{v}\textsubscript{max} (cm\textsuperscript{-1}/neat) 3062, 2924, 2854, 1702, 1580, 1570, 1458, 1342, 1180; \textit{δ}\textsubscript{H} (400 MHz, CDCl\textsubscript{3}) 1.25-1.31 (1H, m, CH\textsubscript{2}), 1.40-1.42 (1H, m, CH\textsubscript{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); \textit{δ}\textsubscript{C} (100 MHz, CDCl\textsubscript{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\textsubscript{2}O (10 cm\textsuperscript{3}) was treated dropwise with a 1 M solution of methylmagnesium bromide in Et\textsubscript{2}O (1.5 cm\textsuperscript{3}) at -78ºC. The reaction was warmed to -20°C over a period of 1 h. This solution was cooled to -35°C before a solution of exo-26 (302 mg, 1.0 mmol, 1.0 eq.) in Et\textsubscript{2}O (5 cm\textsuperscript{3}) was added dropwise over a period of 2 min. Upon cooling to -78°C, 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 formed 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\textsubscript{f} 0.3 (Hex-EtOAc; 4:1); \textit{δ}\textsubscript{H} (400 MHz, CDCl\textsubscript{3}) 1.01-1.09 (21H, m, CH\textsubscript{3}, CH), 1.16 (1H, d, J 6.5 Hz, CH\textsubscript{2}), 1.20 (3H, d, J 6.5 Hz, CH\textsubscript{3}), 1.35-1.42 (1H, m, CH\textsubscript{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); \textit{δ}\textsubscript{C} (100 MHz, CDCl\textsubscript{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 (El) 318 (M\textsuperscript{+}, 5%), 252 (100%); Found 318.23776 C\textsubscript{20}H\textsubscript{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\textsubscript{2}CuLi in Et\textsubscript{2}O (25 cm\textsuperscript{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\textsuperscript{3}, 4.8 mmol, 2.4 eq.), was treated with a solution of 26 (604 mg, 2.0 mmol, 1.0 eq.) in Et\textsubscript{2}O (10 cm\textsuperscript{3}) at -78°C. At -78°C, 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 the products 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, Cul (3.8 mg, 0.02 mmol, 0.01 eq.) in Et₂O (10 cm³) was treated dropwise with a 1 M solution of methylmagnesium bromide in Et₂O (2.8 cm³, 2.8 mmol, 1.4 eq.) at -78°C. The reaction was warmed to -20°C over a period of 0.5 h. This solution was cooled to -35°C before a solution of 27 (520 mg, 2.0 mmol, 1.0 eq.) in Et₂O (5 cm³) was added. Upon re-cooling to -78°C, E-pent-2-enal (0.3 cm³, 3.0 mmol, 1.5 eq.) was added. Standard work-up followed by flash column chromatography (Hex-Et₂O, 9:1) afforded initially \( Z,E-\text{14k} \) (90 mg, 20%) as a yellow viscous oil followed by 31 (210 mg, 38%) as a viscous colourless oil \( R_f 0.25 \text{ (Hex-Et}_2\text{O, 9:1); } \nu_{\text{max}} \text{ (neat/cm}^{-1}) 3060, 2954, 2928, 2856, 2253, 1711, 1570, 1463; \delta_H \text{ (400 MHz, CDCl}_3) -0.01 \text{ (3H, s, CH}_3) 0.01 \text{ (3H, s, CH}_3) 0.92 \text{ (9H, s, CH}_3), 1.15-1.19 \text{ (1H, m, CH}_2), 1.18 \text{ (3H, d, J 6.5 Hz, CH}_3), 1.38-1.43 \text{ (1H, m, CH}_2), 1.80-1.88 \text{ (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); \delta_C \text{ (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 \text{ (CI) 277 (MH}^+ 20%), 211 (100%); Found 277.19950 \text{ C}_{17}\text{H}_{29}\text{O} \text{Si requires 277.19876 (+2.7 ppm). Further elution gave finally } E,E-\text{14k} \text{ (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 Me₂CuLi in Et₂O (25 cm³), prepared from CuI (457 mg, 2.4 mmol, 1.2 eq.) and a 1.6 M solution of MeLi in hexanes (3.0 cm³, 4.8 mmol, 2.4 eq.), was treated with a solution of \( \text{exo-27} \) (520 mg, 2.0 mmol, 1.0 eq.) in Et₂O (5 cm³) at -78°C. Benzaldehyde (320 mg, 3 mmo l, 1.5 eq.) was then added. Standard work-up, followed by flash column chromatography (Hex-Et₂O, 9:1) afforded only conjugate adduct 31 (520 mg, 94%).

(E)-2-Benzylidene-3-methylcyclohexanone, 38. Following the general procedure outlined, a solution of Me₂CuLi in Et₂O (25 cm³), prepared from Cul (457 mg, 2.4 mmol, 1.2 eq.) and a 1.6 M solution of MeLi in hexanes (3.0 cm³, 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 cm³, 3.00 mmol, 1.5 eq.) was added. Standard work-up, followed by flash column chromatography (Hex-Et₂O, 9:1) afforded only conjugate adduct 31 (520 mg, 94%).
(E)-2-[(E)-Hex-2-enyldiene]-3-methylcyclohexanone, 39. Following the general procedure outlined above, a solution of Me₂CuLi in Et₂O (25 cm³), prepared from CuI (457 mg, 2.4 mmol, 1.2 eq.) and a 1.6 M solution of MeLi in hexanes (3.0 cm³, 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 cm³, 3.0 mmol, 1.5 eq.) was added at -78°C. The solution was allowed to warm slowly to 0°C over 5 h. Following standard work-up, purification by flash column chromatography (Hex-Et₂O; 9:1) afforded adduct 39 (361 mg, 94%) as a yellow viscous oil. \( R_f 0.15 \) (Hex-Et₂O, 9:1); \( \nu_{\text{max}} \) (neat/cm⁻¹) 3055, 2970, 2932, 2874, 1687, 1617, 1587, 1453; \( \delta_H \) (400 MHz, CDCl₃) 0.92 (3H, t, \( J = 7.5 \) Hz, CH₃), 1.11 (3H, d, \( J = 7.5 \) Hz, CH₃), 1.47 (2H, qt, \( J = 7.5 \), 7.5 Hz, CH₂), 1.62-1.70 (1H, m, CH₂), 1.75-2.02 (3H, m, CH₂), 2.18 (2H, m, CH₂), 2.25-2.35 (1H, m, CH₂), 2.47-2.56 (1H, m, CH₂), 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); \( \delta_C \) (100 MHz, CDCl₃) 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, C₁₃H₂₁O requires 193.15924 (+0.2 ppm).

2-Benz-(E)-ylidene-3-butyl-2,3,3a,4,7,7a-hexahydro-1H-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 N₂ E-14b (50 mg, 0.17 mmol, 1 eq.) was stirred in THF (10 cm³) at -78°C before a 1 M solution of lithium-tri-tert-butoxy aluminium hydride in THF (0.21 cm³, 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 cm³) and Et₂O (10 cm³) were added to the reaction vessel. The aqueous layer was further extracted with Et₂O (2 x 30 cm³). The combined organic phases were then dried with MgSO₄ and concentrated in vacuo. Purification by flash column chromatography (Hex-Et₂O; 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-Et₂O; 9:1); \( \nu_{\text{max}} \) (cm⁻¹/neat) 3062, 2957, 2925, 1855, 1732, 1604, 1496, 1455, 701; \( \delta_H \) (400 MHz, CDCl₃) 0.78-0.80 (1H, m, CH₂), 0.88-0.92 (3H, m, CH₃), 1.23-1.39 (5H, m, CH₂), 1.45-1.51 (2H, m, CH₂, 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, CH₂), 2.99 (1H, dd, \( J = 6.0, 14.0 \) Hz, CH₂), 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); \( \delta_C \) (100 MHz, CDCl₃) 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 (MNH₄⁺, 100%); Found 312.23169, C₂₁H₃₀ON requires 312.23273 (-3.8 ppm): Data for 40b: \( R_f 0.25 \) (Hex-Et₂O; 9:1); \( \nu_{\text{max}} \) (cm⁻¹/neat) 3367, 3057, 2956, 2958, 2857, 1599, 1494, 1458, 1328, 1107, 693; \( \delta_H \) (400 MHz, CDCl₃) 0.90-0.93 (3H, m, CH₃), 1.10 (1H, d, \( J = 8.5 \) Hz, CH₂), 1.28-1.43 (6H, m, CH₂), 1.46 (1H, d, \( J = 8.5 \) Hz, CH₂), 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); \( \delta_C \) (100 MHz, CDCl₃) 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, C₂₁H₂₇O requires 295.20618 (+0.2 ppm).
5-Benzyl-4-butylcyclopent-2-enone, 42b. Under N₂ 41b (65 mg, 0.22 mmol, 1 eq.) was dissolved in DCM (5 cm³). 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 cm³, 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. Rf 0.3 (c-Hex-EtOAc; 19:1); δH (400 MHz, CDCl₃) 0.70 (3H, t, J 7.0 Hz, CH₃), 1.04-1.22 (5H, m, CH₂, CH), 1.23-1.41 (1H, m, CH), 2.15-2.19 (1H, m, CH), 2.54-2.63 (2H, m, CH₂, CH), 3.05-3.09 (1H, m, CH₂), 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); δC (100 MHz, CDCl₃) 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, C₁₆H₂₁O, 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 N₂ E-14m (200 mg, 0.67 mmol, 1 eq.) was stirred in THF (10 cm³) at –78°C and a 1.0 M solution of lithium tri-tert-butoxy aluminium hydride in THF (0.80 cm³, 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 cm³) and Et₂O (10 cm³) were then added to the reaction and the aqueous layer was further extracted with Et₂O (2 x 10 cm³). The combined organic phases were then dried with MgSO₄ 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. Rf 0.45 (c-Hex-EtOAc; 19:1); vmax (neat/cm⁻¹) 3423, 3060, 2954, 2927, 2872, 2856, 2360, 2341, 1732, 1645, 1533, 1088; δH (400 MHz, CDCl₃) 0.77-0.80 (6H, m, CH₃), 0.98-1.01 (1H, m, CH₂), 1.16-1.24 (14H, m, CH₂), 1.38-1.40 (1H, m, CH₂), 1.60 (1H, d, J 7.25 Hz, CH), 1.90-1.96 (2H, m, CH₂), 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); δC (100 MHz, CDCl₃) 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 N₂ an impure sample of 41m (355 mg, ca. 1.18 mmol, 1 eq.) was dissolved in DCM (10 cm³). 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 cm³, 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. 

Rf 0.5 (c-Hex-EtOAc; 19:1); \( \delta_{\text{H}} \) (400 MHz, CDCl3) 0.78-0.87 (6H, m, CH3), 1.19-1.45 (17H, m, CH2, CH), 1.60-1.66 (1H, m, CH2), 1.85-1.89 (1H, m, CH); \( \delta_{\text{C}} \) (100 MHz, CDCl3) 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 (Cl) 237 (MH+, 100%); Found 237.2218, C16H29O requires 237.2207 (-4.8 ppm).

11-Hydroxyundec-9-ynoic acid methyl ester. Liquid ammonia (ca. 1000 cm³) was condensed at -40ºC in a 3 dm³ 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 cm³) 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 cm³) 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 (pH ca. 4.0). The solution was extracted with Et2O (5 x 100 cm³) and the combined organic layers were dried over MgSO4. 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 cm³) and BF3·Et2O (0.92 cm³, 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 cm³) before extraction with Et2O (5 x 100 cm³). Flash column chromatography (DCM-MeOH; 98:2) afforded 11-hydroxyundec-9-ynoic acid methyl ester (4.2 g, 88%) as a colourless oil.

(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 cm³) 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. 

Rf 0.3 (DCM-MeOH; 98:2); \( \delta_{\text{H}} \) (400 MHz, CDCl3) 1.27-1.43 (6H, m, CH2), 1.50 (2H, pent, J 7.5 Hz, CH2), 1.63 (2H, pent, J 7.5 Hz, CH2), 2.21 (2H, tt, J 2.25, 7.0 Hz, CH2), 2.31 (2H, t, J 7.5 Hz, CH2), 3.67 (3H, s, CH3), 4.25 (2H, t, J 2.25 Hz, CH2); \( \delta_{\text{C}} \) (100 MHz, CDCl3) 18.6, 27.7, 28.4, 28.9, 28.6, 28.8, 34.0, 51.2, 51.4, 78.5, 86.2, 174.3; m/z (Cl) 213 (MH+, 100%); Found 213.14907, C12H26O3N requires 213.14906 (+0.01 ppm).
(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 cm³) 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 Et₂O (60 cm³) and water (60 cm³) followed by saturated aqueous Na₂SO₃ solution (100 cm³) and saturated aqueous sodium hydrogencarbonate (100 cm³) solution. The organic and aqueous phases were separated and the resultant aqueous layer was extracted with Et₂O (5 x 50 cm³). The combined organic fractions were dried over MgSO₄. Filtration and solvent removal in vacuo gave Z-49 (929 mg, 94%) as a colourless oil. Rf 0.35 (Hex-EtOAc; 3:1); υ max (neat/cm⁻¹) 2931, 2856, 1737, 1680, 437; δH (400 MHz CDCl₃) 1.28-1.40 (6H, m, CH₂), 1.51 (2H, pent, J 7.5 Hz, CH₂), 1.63 (2H, pent, J 7.5 Hz, CH₂), 2.30 (2H, t, J 7.5 Hz, CH₂), 2.57-2.64 (2H, tdd J 1.5, 7.5, 8.0 Hz, CH₂), 3.66 (3H, s, CH₃), 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); δC (100 MHz CDCl₃) 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 (MNH₄⁺, 100%), 213 (MH⁺, 40%); Found 213.14887, C₁₂H₂₁O₃ 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 cm³) 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 cm³) and dried over MgSO₄. 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. Rf 0.35 (Hex-EtOAc; 3:1); υ max (neat/cm⁻¹) 2931, 2857, 1738, 1691, 1638, 1436; δH (400 MHz, CDCl₃) 1.29-1.38 (6H, m, CH₂), 1.51 (2H, pent, J 7.5 Hz, CH₂), 1.63 (2H, pent, J 7.5 Hz, CH₂), 2.31 (2H, t, J 7.5 Hz, CH₂), 2.33 (2H, qd, J 1.5, 7.0 Hz, CH₂), 3.68 (3H, s, CH₃), 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); δC (100 MHz, CDCl₃) 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 (MNH₄⁺, 100%), 213 (MH⁺, 40%); Found 213.14887, C₁₂H₂₁O₃ 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 N₂ copper(I) iodide (480 mg, 2.52 mmol, 1.2 eq.) was suspended in Et₂O (30 cm³) at -78ºC. A 0.5 M solution of ethyllithium in cyclohexane-benzene (10.08 cm³, 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 Et₂O (10 cm³) 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 NH₄Cl solution (50 cm³) and the resultant aqueous layer was extracted with Et₂O (5 x 50 cm³). The combined organic fractions were dried over MgSO₄. On filtration and solvent removal the crude product was purified by flash column chromatography (Hex-EtO; 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). Rf 0.35 (Hex-EtOAc; 4:1); υ max (neat/cm⁻¹
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); ν_{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, ddt, 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, ddd J 0.75, 6.0 Hz, CH), 7.27 (1H, ddd, 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, 29.3, 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%).
and stirred at -5°C for 2 h. The reaction was then warmed to room temperature and stirred for 10 min. before quenching with a saturated solution of NH4Cl (20 cm³). Extraction with Et2O (6 x 20 cm³) and drying of the combined organic extracts over MgSO4 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, CHCl3); \( \nu \)max (neat/cm⁻¹) 3058, 2931, 2348, 1739, 1700, 1652, 1460, 1435; \( \delta \)H (400 MHz, CDCl3) 0.93 (3H, t, \( J \) 7.5 Hz, CH3), 1.23-1.35 (8H, m, CH2), 1.39-1.48 (2H, m, CH2), 1.48-1.55 (1H, m, CH2), 1.58-1.69 (3H, m, CH2), 1.93 (1H, s, CH), 2.17-2.23 (2H, m, CH2), 2.30 (2H, t, \( J \) 7.5 Hz, CH2), 2.38 (1H, d, \( J \) 7.5 Hz, CH), 2.62-2.67 (1H, m (br), CH), 2.76 (1H, s, CH), 3.06 (3H, s, CH3), 6.16-6.25 (4H, m, CH), 6.85-6.90 (1H, m, CH); \( \delta \)C (100 MHz, CDCl3) 10.7, 24.9, 28.7, 28.9, 29.0, 29.2, 30.1, 33.4, 34.0, 43.2, 44.6, 45.9, 49.1, 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, C24H35O3 required 371.25861 (-2.9 ppm).

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MeO2C

(+)-(E)-11-[(S)-2-Ethyl-5-oxocyclopent-3-en-(E)-ylidene]undec-9-enoic acid methyl ester, (+)-E,E-51. Under N2, a solution of (+)-E,E-50 (85 mg, 0.23 mmol, 1.0 eq.) in DCM (4 cm³) was added to a solution of maleic anhydride (338 mg, 3.45 mmol, 15 eq.) in DCM (4 cm³). The solution was homogenised by stirring before being split into two microwave vials (Smith Process vial, 2-5 cm³). A 1.0 M solution of MeAlCl2 in hexane (0.17 cm³, 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 NaHCO3 (20 cm³) and the mixture was stirred for 4 min before extraction with Et2O (10 x 25 cm³). The combined organic extracts were dried over MgSO4, 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, CHCl3); \( \nu \)max (neat/cm⁻¹) 3058, 2928, 2854, 2348, 1737, 1693, 1633, 1579, 1460, 1435; \( \delta \)H (400 MHz CDCl3) 0.88 (3H, t, \( J \) 7.5 Hz, CH3), 1.25-1.36 (6H, m, CH2), 1.41-1.47 (2H, m, CH2), 1.58-1.70 (3H, m, CH2), 1.86-1.98 (1H, m, CH2), 2.22 (2H, q, \( J \) 7.0 Hz, CH2), 2.30 (2H, t, \( J \) 7.5 Hz, CH2), 3.51-3.56 (1H, m (br), CH), 3.66 (3H, s, CH3), 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); \( \delta \)C (100 MHz CDCl3) 10.0, 24.9, 25.7, 28.7, 28.9, 29.0, 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, C19H29O3Na required 305.21220 (-0.6 ppm).
Hex-IPA, 90:10, 254 nm, 0.5 cm³/min. and sample amount 2 µl gave >99% enantiomeric excess of the title compound. Data for Z,E-51: \( R_e 0.30 \) (Hex-EtOAc; 4:1); \( \nu_{\text{max}} \) (neat/cm⁻¹) 3058, 2929, 2856, 1738, 1687, 1630, 1608, 1582, 1436; \( \delta_{\text{H}} \) (400 MHz CDCl₃) 0.92 (3H, t, \( J 7.5 \) Hz, CH₃), 1.27-1.37 (6H, m, CH₂), 1.40-1.50 (2H, m, CH₂), 1.53-1.68 (3H, m, CH₂), 1.77-1.87 (1H, m, CH₂), 2.22 (2H, q, \( J 7.12, 7.0 \) Hz, CH₂), 2.30 (2H, t, \( J 7.5 \) Hz, CH₂), 3.25-3.33 (1H, m (br), CH), 3.67 (3H, s, CH₃), 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, \( J 1.0, 11.0, 15.0 \) Hz, CH); \( \delta_{\text{C}} \) (100 MHz CDCl₃) 10.4, 24.9, 26.1, 28.9, 29.0, 33.0, 34.1, 46.8, 51.4, 126.4, 133.9, 135.7, 145.3, 159.5, 174.2, 197.6; m/z (CI) 305 (MH⁺, 100%); Found 305.21247, C₁₉H₂₉O₃ requires 305.21167 (+2.9 ppm).

HO2C

(±)-E-11-[2-Ethyl-5-oxocyclopent-3-en-(E)-ylidene]undec-9-enoic acid, (±)-52. Commercially available hog liver esterase solution (1.0 cm³) in 3.2 M ammonium sulfate was added to a solution of (±)-E,E-51 (100 mg, 0.33 mmol) in acetone (3.0 cm³) and phosphate buffer solution (30 cm³, \( pH 7.0 \)). The mixture was stirred at room temperature overnight before acidification with acetic acid (2 cm³) and extraction with Et₂O (5 x 10 cm³). The combined organic extracts were dried over MgSO₄, 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.

1-tert-Butyldimethylsilyloxy-7-bromoheptane, 53. A solution of 7-bromoheptanol (3.48 g, 17.8 mmol, 1 eq.) in DCM (50 cm³) was cooled to 0°C and treated with TBSCI (2.96 g, 19.6 mmol, 1.1 eq.) and TEA (3.1 cm³, 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 Et₂O (50 cm³) and H₂O (50 cm³) were added. The resultant aqueous phase was further extracted with Et₂O (3 x 50 cm³) and the combined organic extracts were dried over MgSO₄. Filtration followed by solvent removal under reduced pressure and purification by flash column chromatography (Hex-Et₂O; 19:1) gave 53 (4.30 g, 78%) as a colourless liquid. \( R_f 0.6 \) (Hex-Et₂O; 19:1); \( \delta_{\text{H}} \) (400 MHz, CDCl₃) 0.04 (6H, s, CH₃), 0.90 (9H, s, CH₃), 1.28-1.37 (4H, m, CH₂), 1.39-1.45 (2H, m, CH₂), 1.46-1.55 (2H, m, CH₂), 1.85 (2H, pent, \( J 7.5 \) Hz, CH₂), 3.41 (2H, t, \( J 7.0 \) Hz, CH₂), 3.62 (2H, t, \( J 6.5 \) Hz, CH₂); \( \delta_{\text{C}} \) (100 MHz, CDCl₃) -5.3, 18.4, 25.6, 26.0, 28.2, 28.6, 32.8, 34.0, 63.1; m/z (CI) 311 (MH⁺, 100%, \(^{81\text{Br}}\)), 309 (MH⁺, 100%, \(^{79\text{Br}}\)).
1-tert-Butyldimethylsilyloxy-8-bromo-octane, 54. A stirred solution of 8-bromo-octanol (6.60 g, 31.56 mmol, 1.0 eq.) in DCM (40 cm³) was cooled to -10°C and a solution of TBSCl (5.80 g, 38.48 mmol, 1.2 eq.) dissolved in DCM (10 cm³) and imidazole (2.62 g, 38.48 mmol, 1.2 eq.) in DCM (50 cm³), 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 cm³) and Et₂O (50 cm³) were added. The aqueous layer was further extracted with Et₂O (2 x 50 cm³) and the combined organic extracts were dried over MgSO₄. Filtration followed by solvent removal under reduced pressure and purification by flash column chromatography (Hex-Et₂O; 98:2) gave 54 (9.40 g, 93%) as a colourless liquid. 

Rₙ = 0.25 (Hex-Et₂O; 98:2); δₜ (400 MHz, CDCl₃) 0.04 (6H, s, CH₃), 0.90 (9H, s, CH₃), 1.29-1.36 (6H, m, CH₂), 1.39-1.45 (2H, m, CH₂), 1.47-1.55 (2H, m, CH₂), 1.86 (2H, pent, J 7.0, Hz, CH₂), 3.41 (2H, t, J 7.0, CH₂), 3.60 (2H, t, J 6.5, CH₂); δ_c (100 MHz, CDCl₃) -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. A solution of 1-tert-butyldimethylsilyloxy-8-bromo-octane 54 (5.00 g, 15.46 mmol, 1.0 eq.) in acetone (50 cm³) 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 cm³) and Et₂O (50 cm³) were added. The organic fraction was separated and aqueous layer was further extracted with Et₂O (2 x 50 cm³) and the combined organic fractions were dried over MgSO₄. Filtration, followed by solvent removal under reduced pressure and flash column chromatography (Hex-Et₂O; 98:2) gave 1-tert-butyldimethylsilyloxy-8-iodooctane 56 (5.71 g, 99%) as a colourless liquid.

Rₙ = 0.25 (Hex-Et₂O; 98:2); δₜ (400 MHz, CDCl₃) 0.05 (6H, s, CH₃), 0.91 (9H, s, CH₃), 1.28-1.35 (6H, m, CH₂), 1.36-1.45 (2H, m, CH₂), 1.48-1.57 (2H, m, CH₂), 1.82 (2H, pent, J 7.0, Hz, CH₂), 3.18 (2H, t, J 7.0, CH₂), 3.61 (2H, t, J 6.5, CH₂); δ_c (100 MHz, CDCl₃) -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-one, 62. Under N₂, at room temperature 1-tert-butyldimethylsilyloxy-8-bromo-octane 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 Et₂O (6 cm³). 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 Et₂O (10 cm³) [washed with Et₂O (5 cm³)]. 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 Et₂O (5 cm³) 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 NH₄Cl (50 cm³) was added and the pH was adjusted to 7.0 with conc. NH₃ before extraction with Et₂O (5 x 30 cm³). The combined organic extracts were dried over MgSO₄. Filtration and solvent removal followed by flash column chromatography (Hex-Et₂O; 19:1 → 9:1 Hex-Et₂O) afforded initially Z,E-62 (190 mg, 28%) and then E,E-62 (380 mg, 56%) both as viscous yellow oils. Rf 0.25 (Hex-Et₂O; 9:1); υmax (neat/cm⁻¹) 3060, 2928, 2855, 1702, 1628, 1602, 1462; δH (400 MHz, CDCl₃) 0.04 (6H, s, CH₃), 0.89 (9H, s, CH₃), 1.07 (3H, t, J 7.5 Hz, CH₃), 1.23-1.37 (13H, m, CH₂), 1.40-1.60 (3H, m, CH₂), 1.92 (1H, d, J 7.75 Hz, CH), 2.24 (2H, pent, J 7.5 Hz, CH₂), 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, CH₂), 6.15-6.24 (4H, m, CH), 6.87 (1H, dd, J 2.0, 10.5 Hz, CH); δC (100 MHz, CDCl₃) -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, C₂₉H₄₈O₂SiNa requires 479.3321 (-4.4 ppm). Data for Z,E-62: Rf 0.35 (Hex-Et₂O; 9:1) δH (400 MHz, CDCl₃) 0.10 (6H, s, CH₃), 0.90 (9H, s, CH₃), 1.06 (3H, t, J 7.5 Hz, CH₃), 1.19 (1H, d, J 9.0 Hz, CH₂), 1.27-1.36 (10H, m, CH₂), 1.40 (1H, dt, J 1.5, 9.0 Hz, CH₂), 1.48-1.57 (2H, m, CH₂), 1.85 (1H, d, J 8.5 Hz, CH), 2.22 (2H, pent, J 7.5 Hz, CH₂), 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, CH₂), 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 N₂, a 1.5 M solution of tert-butyllithium in pentane (2.66 cm³, 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 cm³) and ether (4.5 cm³) 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 Et₂O (10 cm³) 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 Et₂O (7 cm³) 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 NH₄Cl (50 cm³) was added and the pH was adjusted to 7.0 with conc. NH₃. The resultant mixture was extracted with Et₂O (5 x 30 cm³) and the combined organic extracts were dried over MgSO₄. Filtration, followed by solvent removal and purification by flash column chromatography (Hex-Et₂O; 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 cm³) at 0°C was added dropwise to a mixture of acetic acid (12 cm³) and water (6 cm³) under vigorous stirring. The reaction was warmed to room temperature and further stirred for 4 h. Ethyl acetate (30 cm³) and water (10 cm³) were added followed by dropwise addition of saturated NaHCO₃.
solution (200 cm³). The resultant organic fraction was separated and the aqueous layer was further extracted with ethyl acetate (5 x 25 cm³). The combined organic fractions were dried over MgSO₄. 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. 

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(±)-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 cm³) was added dropwise to a suspension of Dess-Martin’s periodinane (448 mg, 1.14 mmol, 1.3 eq.) in DCM (10 cm³) at 0°C. The reaction was warmed to room temperature and stirred for 1.5 h. The reaction was quenched by addition of Et₂O (30 cm³), water (30 cm³), a saturated aqueous solution of Na₂SO₃ (30 cm³) and saturated aqueous solution of sodium hydrogen carbonate (30 cm³). The resultant aqueous phase was further extracted with Et₂O (5 x 25 cm³) and the combined organic fractions were dried over MgSO₄. Filtration and solvent removal in vacuo gave the aldehyde \[ [\text{R} \text{f} 0.4 \text{(Hex-EtOAc; 4:1)}] \]. The crude aldehyde (ca. 0.87 mmol) was dissolved in a mixture of t-BuOH (17 cm³) and 2,3-dimethylbut-2-ene (6 cm³) and a solution of 80% w/w sodium chlorite (650 mg, 5.75 mmol, 6.6 eq.) and NaH₂PO₄ (753 mg, 6.27 mmol, 7.2 eq.) in H₂O (8.4 cm³) 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 cm³) was added and the mixture was extracted with EtOAc (7 x 25 cm³). The combined organic fractions were dried over MgSO₄, 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. 

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(±)-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 cm³) was added dropwise to a suspension of Dess-Martin’s periodinane (448 mg, 1.14 mmol, 1.3 eq.) in DCM (10 cm³) at 0°C. The reaction was warmed to room temperature and stirred for 1.5 h. The reaction was quenched by addition of Et₂O (30 cm³), water (30 cm³), a saturated aqueous solution of Na₂SO₃ (30 cm³) and saturated aqueous solution of sodium hydrogen carbonate (30 cm³). The resultant aqueous phase was further extracted with Et₂O (5 x 25 cm³) and the combined organic fractions were dried over MgSO₄. Filtration and solvent removal in vacuo gave the aldehyde \[ [\text{R} \text{f} 0.4 \text{(Hex-EtOAc; 4:1)}] \]. The crude aldehyde (ca. 0.87 mmol) was dissolved in a mixture of t-BuOH (17 cm³) and 2,3-dimethylbut-2-ene (6 cm³) and a solution of 80% w/w sodium chlorite (650 mg, 5.75 mmol, 6.6 eq.) and NaH₂PO₄ (753 mg, 6.27 mmol, 7.2 eq.) in H₂O (8.4 cm³) 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 cm³) was added and the mixture was extracted with EtOAc (7 x 25 cm³). The combined organic fractions were dried over MgSO₄, 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. 

\[ \text{R} \]

\[ \text{O} \]

\[ \text{HO}_2\text{C} \]

(±)-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 cm³) was added dropwise to a suspension of Dess-Martin’s periodinane (448 mg, 1.14 mmol, 1.3 eq.) in DCM (10 cm³) at 0°C. The reaction was warmed to room temperature and stirred for 1.5 h. The reaction was quenched by addition of Et₂O (30 cm³), water (30 cm³), a saturated aqueous solution of Na₂SO₃ (30 cm³) and saturated aqueous solution of sodium hydrogen carbonate (30 cm³). The resultant aqueous phase was further extracted with Et₂O (5 x 25 cm³) and the combined organic fractions were dried over MgSO₄. Filtration and solvent removal in vacuo gave the aldehyde \[ [\text{R} \text{f} 0.4 \text{(Hex-EtOAc; 4:1)}] \]. The crude aldehyde (ca. 0.87 mmol) was dissolved in a mixture of t-BuOH (17 cm³) and 2,3-dimethylbut-2-ene (6 cm³) and a solution of 80% w/w sodium chlorite (650 mg, 5.75 mmol, 6.6 eq.) and NaH₂PO₄ (753 mg, 6.27 mmol, 7.2 eq.) in H₂O (8.4 cm³) 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 cm³) was added and the mixture was extracted with EtOAc (7 x 25 cm³). The combined organic fractions were dried over MgSO₄, 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.
(±)-8-[3-Oxo-2-[E-pent-2-en-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 cm³) and MeOH (8 cm³) and at 5°C a 2.0 M solution of (trimethylsilyl)diazomethane in hexane (0.27 cm³, 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. Rf 0.45 (Hex-EtOAc; 4:1); vmax (neat/cm⁻¹) 2932, 2855, 1739, 1701, 1627, 1619, 1459, 1437; δH (400 MHz, CDCl₃) 1.08 (3H, t, J 7.5 Hz, CH₃), 1.25-1.65 (12H, m, CH₂), 1.91 (1H, d, J 7.75 Hz, CH), 2.23 (2H, pent, J 7.75 Hz, CH₂), 2.29 (2H, t, J 7.75 Hz, CH₂), 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, CH₃), 6.13-6.25 (4H, m, CH), 6.87 (1H, dd, J 2.0, 10.5 Hz, CH); δC (100 MHz, CDCl₃) 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 (M⁺, 5%); found 371.2583, C₂₄H₃₅O₃ requires 371.2586 (-0.9 ppm).

(±)-8-[4-Oxo-5-[E-pent-2-en-1/E,Z-ylidene]cyclopent-2-enyl]octanoic acid methyl ester Z,E- and E,E-65. Under N₂, a solution of the above ester (110 mg, 0.290 mmol, 1.0 eq.) in DCM (4 cm³) was added to a solution of maleic anhydride (436 mg, 4.44 mmol, 15 eq.) in DCM (4 cm³). The solution was homogenised on stirring before being split into two microwavable vials (Smith Process vial, 2-5 cm³). A 1.0 M solution of MeAlCl₂ in hexane (0.15 cm³, 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 NaHCO₃ (25 cm³) and the mixture was stirred for 20 min before extraction with Et₂O (10 x 25 cm³). The organic extracts were dried over MgSO₄, filtered and the solvent removed under reduced pressure. Purification by flash column chromatography (Hex-EtOAc; 9:1 → 3:1; vmax (neat/cm⁻¹) 2931, 2850, 1735, 1692, 1632, 1437; δH (400 MHz, CDCl₃) 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, CH₃), 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 7.5 Hz, H-18).
10.0 Hz, H-14), 7.52 (1H, ddd, J 0.75, 2.5, 6.0 Hz, H-10); δc (100 MHz, CDCl3) 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; δH (400 MHz, C6D6) 0.79 (3H, t, J 7.25 Hz, H-18), 0.95-1.12 (8H, m, H-4 - H-7), 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, CH3), 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); δc (100 MHz, C6D6) 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, 196.0; m/z (CI) 305 (MH+, 100%); Found 305.21247, C19H29O3 requires 305.21167 (+2.9 ppm). Data for Z,E-65: Rp 0.5 (Hex-EtOAc; 3:1); υmax (neat/cm-1) 2928, 2850, 1736, 1686, 1631, 1437; δH (400 MHz, CDCl3) 1.07 (3H, t, J 7.5 Hz, CH3), 1.24-1.37 (8H, m, CH2), 1.45-1.54 (1H, m, CH2), 1.62 (2H, pent, J 7.5 Hz, CH2), 1.68-1.77 (1H, m, CH2), 2.21-2.28 (2H, m, CH2), 2.30 (2H, t, J 7.5 Hz, CH2), 3.28-3.34 (1H, m, CH), 3.66 (3H, s, CH3), 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); δc (100 MHz, CDCl3) 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, 197.2, 197.5.

(±)-8-{4-Oxo-5-[E-pent-2-en-E-yldene]cyclopent-2-enyl}octanoic acid, E,E-6. Under N2, a solution of the above carboxylic acid (356 mg, 1.00 mmol, 1.0 eq.) in DCM (10 cm3) was added to a solution of fumaronitrile (1.170 g, 15.00 mmol, 15 eq.) in DCM (15 cm3). The solution was split into five microwavable vials (Smith Process vial, 2-5 cm3) and a 1.0 M solution of MeAlCl2 in hexane (0.3 cm3, 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%) [Rf 0.3 (Hex-EtOAc; 3:1 with 1% AcOH)] and finally E,E-6 (180 mg, 62%) as a viscous pale yellow oil. Rp 0.25 (Hex-EtOAc; 3:1 with 1% AcOH); υmax (neat/cm-1) 3050, 2930, 2856, 1708, 1694, 1630, 1578, 1461; δH (400 MHz, CDCl3) 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); δc (100 MHz, CDCl3) 13.0, 24.6, 25.8, 26.4, 28.9, 29.0, 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, C18H27O3 requires 291.19601 (+0.5 ppm).

A mixture of commercially available hog liver esterase solution (0.2 cm3) in 3.2 M ammonium sulfate was added to a solution of E,E-65 (20 mg, 0.065 mmol) in acetone (0.6 cm3) and phosphate buffer solution (6 cm3, pH 7.0). The mixture was stirred at room temperature for 24 h before acidification with 1 M HCl solution (pH 5.5) and extraction with Et2O (5 x 10 cm3). The combined organic extracts were dried over MgSO4, 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.

(+)-(3S,3aS,4R,7S,7aS)-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$_2$O (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$_2$O (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$_4$Cl (25 cm$^3$) was added and the pH was adjusted to 7 with conc. NH$_3$ solution. Extraction with Et$_2$O (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$_2$O; 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.

(+)-(3S,3aS,4R,7S,7aS)-(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.

(+)-(3S,3aS,4R,7S,7aS)-(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 cm³, 0.36 mmol, 1.2 eq.) generated title compound as viscous oil. [α]D +341 (c = 1.00, CHCl3) with NMR data identical to that reported above.

(+)-(8R)-{4-Oxo-5-[E-pent-2-en-E-ylidene]cyclopent-2-enyl}octanoic acid methyl ester, (+)-E,E-65. Under N2, (+)-methyl ester (80 mg, 0.216 mmol, 1.0 eq.) in DCM (4 cm³) was added to a solution of maleic anhydride (326 mg, 3.32 mmol, 15 eq.) in DCM (4 cm³) in two microwavable vials (Smith Process vial, 2-5 cm³). The solution was stirred to achieve homogenisation before a 1.0 M solution of MeAlCl₂ in hexane (0.3 cm³, 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 cm³). The solution was stirred for 20 min and extracted with Et₂O (10 x 25 cm³). The combined organic extracts were dried over MgSO₄, 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. [α]D +144 (c = 1.00, CHCl₃). HPLC separation using an AS column (COL-HP-17), solvent mixture Hex-IPA, 90:10, 254 nm, 0.5 cm³/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 cm³, 2:1) was stirred for 15 h with activated MnO₂ (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 ¹H-NMR spectroscopy. The aldehyde (ca. 4 g) was dissolved in pentane/toluene (60 cm³) 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 N₂, a 1.5 M solution of tert-butyllithium in pentane (4.32 cm³, 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 cm³) and ether (9 cm³) 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 Et₂O (10 cm³) 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 Et₂O (10 cm³) was added dropwise. The reaction was stirred and allowed to warm to -5°C for 1 h. Freshly distilled 2-pentyal (ca. 266 mg, 3.24 mmol, 2.0 eq.) in 5 cm³ of pentane/toluene (mixture) was added at -78°C and the solution was stirred overnight at -78°C and warmed to 0°C before quenched with saturated solution of NH₄Cl (50 cm³). The resultant mixture was extracted with Et₂O (5 x 30 cm³) and combined organic extracts were dried over MgSO₄. Filtration followed by solvent removal and purification by flash column chromatography (Hex-Et₂O; 19:1 → 9:1) afforded 63 (551 mg, 75%) as a colourless oil. Rf 0.35 (Hex-Et₂O; 9:1). ʋmax (neat/cm⁻¹) 3059, 2931, 2855, 2212, 1705, 1603, 1462, 1387; δH (400 MHz, CDCl₃) 0.04 (6H, s, CH₃), 0.89 (9H, s, CH₃), 1.22 (3H, t, J 7.5 Hz, CH₃), 1.26-1.38 (12, m, CH₂), 1.46-1.56 (3, m, CH₂), 1.80-1.89 (1H, m, CH₂), 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, CH₂), 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, CH₂), 6.17-6.26 (2H, m, CH), 6.37 (1H, dt, J 2.25, 2.5 Hz, CH); δC (100 MHz, CDCl₃) -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 C₂₉H₄₆O₂NaSi 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 cm³) at 0°C was added dropwise a mixture of acetic acid (8 cm³) and water (4 cm³) with vigorous stirring. The reaction was warmed to room temperature and stirred for 5 h. Ethyl acetate (30 cm³) and water (10 cm³) were added followed by dropwise addition of saturated sodium hydrogen carbonate solution (200 cm³). The resultant organic fraction was separated and the aqueous layer was extracted with ethyl acetate (5 x 25 cm³). The combined organic fractions were dried over MgSO₄. Filtration followed by evaporation of solvent under reduced pressure and purification by flash column chromatography (Hex-EtOAc; 3:1) afforded the alcohol (359 mg, 96%) as a colourless viscous oil. Rf 0.10 (Hex-EtOAc; 3:1); ʋmax (neat/cm⁻¹) 3399, 3060, 2929, 2855, 2360, 2209, 1703, 1602, 1460; δH (400 MHz, CDCl₃) 2.30 (3H, t, J 7.5 Hz, CH₃), 1.30-1.42 (12H, m, CH₂), 1.54-1.60 (3H, m, CH₂), 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, CH₂), 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, CH₂), 6.17-6.25 (2H, m, CH), 6.36 (1H, dt, J 2.25, 2.5 Hz, CH); δC (100 MHz, CDCl₃) 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 C₂₃H₃₃O₂ requires 341.24808 (+4.1 ppm).
(±)-8-(3-Oxo-2-pent-2-yn-(E)-yldene-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 cm³) was added dropwise to a suspension of Dess-Martin’s periodinane (235 mg, 0.55 mmol, 1.2 eq.) in DCM (5 cm³) 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 Et₂O (16 cm³) and water (16 cm³) followed by saturated aqueous Na₂SO₃ solution (16 cm³) and sodium hydrogencarbonate solution (16 cm³). The resultant aqueous phase was extracted with Et₂O (5 x 25 cm³) and the combined organic fractions were dried over MgSO₄. Filtration and solvent removal in vacuo gave the aldehyde \([R_f 0.4 \text{ (Hex-EtOAc; 4:1)}]\). The crude aldehyde (ca. 0.44 mmol, 1.0 eq.) was dissolved in a mixture of t-BuOH (8 cm³) and 2,3-dimethylbut-2-ene (5 cm³) and a solution of 80% w/w sodium chlorite (300 mg) and NaH₂PO₄ (290 mg) in H₂O (5 cm³) was added dropwise at 10°C over 15 min. The reaction was stirred for 30 min before water (5 cm³) was added and the mixture was extracted with EtOAc (7 x 15 cm³). The combined organic fractions were dried over MgSO₄, filtered and the solvent removed under reduced pressure. Under N₂ the crude acid (ca. 0.44 mmol, 1.0 eq.) was then dissolved in a mixture of toluene (15 cm³) and MeOH (5 cm³) and a 2.0 M solution of (trimethylsilyl)diazomethane in hexane (0.28 cm³, 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 \text{ (Hex-EtOAc; 3:1)}; \nu_{\text{max}} (\text{neat/cm}^{-1}) 3060, 2934, 2855, 2210, 1739, 1703, 1602, 1460, 1436; \delta_{\text{H}} (400 MHz, CDCl₃) 1.21 (3H, t, \(J 7.5 \text{ Hz, CH₃}\)), 1.28-1.38 (12H, m, CH₂), 1.48-1.56 (1H, m, CH₂), 1.57-1.66 (2H, m, CH₂), 1.79-1.88 (1H, m, CH₂), 1.93 (1H, d, \(J 7.75 \text{ Hz, CH}\), 2.67-2.72 (1H, m, CH), 2.76 (1H, s CH), 3.06 (1H, s, CH), 3.66 (3H, s, CH), 2.30 (2H, t, \(J 7.5 \text{ Hz, CH₂}\)), 2.39 (1H, d, \(J 7.75 \text{ Hz, CH}\)), 2.44 (2H, qd, \(J 2.0, 7.5 \text{ Hz, CH₂}\)), 6.16-6.25 (2H, m, CH), 6.36 (1H, dt, \(J 2.25, 2.5, 7.5 \text{ Hz, CH}\)); \delta_{\text{C}} (100 MHz CDCl₃) 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 C₂₃H₃₃O₂ requires 369.24298 (+2.8 ppm).

(±)-8-[4-Oxo-5-pent-2-yn-(E)-yldenedicyclopent-2-enyl]octanoic acid methyl ester, 66. Under N₂, a solution of the above methyl ester (80 mg, 0.217 mmol, 1.0 eq.) in DCM (4 cm³) was added to a solution of maleic anhydride (319 mg, 3.26 mmol, 15 eq.) in DCM (4 cm³). The solution was homogenised by stirring before being split into two microwavable vials (Smith Process vial, 2-5 cm³). A 1.0 M solution of MeAlCl₂ in hexane (0.16 cm³, 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 NaHCO₃ (20 cm³) and the mixture was
stirred for 10 min before extraction with Et₂O (10 x 25 cm³). The combined organic extracts were dried over MgSO₄, 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); \( \nu_{\text{max}} \) (neat/cm⁻¹) 2976, 2933, 2856, 2211, 1738, 1735, 1454, 1436; \( \delta_{\text{H}} \) (400 MHz, CDCl₃) 1.22 (1H, t, \( J = 7.5 \) Hz, CH₃), 1.27-1.34 (9H, m, CH₂), 1.57-1.65 (2H, m, CH₂), 1.67-1.75 (1H, m, CH₃), 2.00-2.10 (1H, m, CH), 2.30 (2H, t, \( J = 7.5 \) Hz, CH₂), 2.45 (2H, qd, \( J = 2.5, 7.5 \) Hz, CH₂), 3.52-3.57 (1H, m, CH), 3.67 (3H, s, CH₃), 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); \( \delta_{\text{C}} \) (100 MHz CDCl₃) 13.6, 13.7, 24.8, 25.8, 29.0, 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 C₁₉H₂₆O₃Na requires 325.1780 (+3.8 ppm).

One drop of quinoline was added to a solution of 66 (38 mg, 0.132 mmol, 1.0 eq.) in EtOAc (10 cm³). 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); \( \nu_{\text{max}} \) (neat/cm⁻¹) 3060, 2932, 2856, 2300, 1737, 1692, 1628, 1579, 1454, 1437; \( \delta_{\text{H}} \) (400 MHz, CDCl₃) 1.05 (3H, t, \( J = 7.5 \) Hz CH₃), 1.24-1.35 (8H, m, CH₂), 1.50-1.65 (3H, m, CH₂), 1.80-1.90 (1H, m, CH₂), 2.29 (2H, t, \( J = 7.5 \) Hz, CH₂), 2.34-2.40 (2H, m, CH₂), 3.50-3.58 (1H, m, CH), 3.68 (3H, s, CH₃), 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); \( \delta_{\text{C}} \) (100 MHz CDCl₃) 13.9, 21.4, 24.8, 25.9, 28.9, 29.0, 29.5, 32.9, 34.0, 43.4, 51.4, 77.3, 105.6, 112.7, 134.6, 146.6, 162.0, 174.1, 197.5; m/z (CI) 327 (MNa⁺, 100%); Found 327.1922 C₁₉H₂₈O₃Na requires 327.1936 (-4.3 ppm).

References:
Determination of biological activity:

**Materials** - The thiazolidinedione PPAR-γ ligand, Rosiglitazone 68·maleate was obtained from Alexis Corporation (San Diego, CA, USA) and the prostaglandin PPAR-γ ligand Δ^{12,14}-15-deoxy-PGJ\textsubscript{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 Chromalu x 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\textsubscript{2}/37°C. 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°C. 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 10⁴ 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°C 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\textsubscript{50}) were calculated by the Prism program.