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Tandem cyclisations involving α-ketenyl alkyl radicals. New syntheses of the natural triquinanes pentalenene and modhephene

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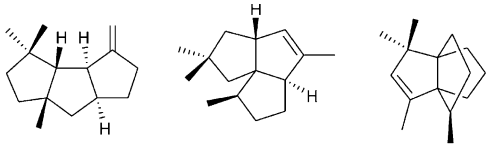
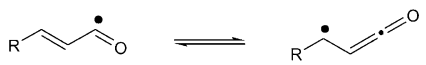
New synthetic approaches to the angular and propellane sesquiterpene triquinanes (±)-pentalenene **2** and (±)-modhephene **3**, respectively, are described. The syntheses are based on tandem cyclisations involving α-ketene alkyl radical intermediates produced from α,β-unsaturated acyl radical species, as highlighted in Schemes 2 and 4.

Introduction

The linear, angular and propellane triquinanes capnellene **1**, pentalenene **2** and modhephene **3** respectively, and their various oxygenated congeners are biologically important sesquiterpenoids,[1] whose interesting structures have captured the attention of synthetic chemists for almost two decades.[2] Prominent among the synthetic approaches that have been developed towards these triquinanes are those based on tandem radical-mediated cyclisation processes[3], arene–alkene photocycloadditions[4] and electrophilic transannulation reactions.[5] In the immediately preceding papers we highlighted the propensity for α,β-unsaturated acyl radical intermediates **4** to react with alkene electrophores *via* their corresponding α-ketenyl alkyl radical counterparts **5**, leading to useful syntheses of ring systems, including diquinanes (Scheme 1).[6] In this paper we now describe the scope for 2,7-diene acyl radicals and their ketene alkyl radical counterparts in tandem radical transannulation and cyclisation reactions leading to concise syntheses of (±)-pentalenene **2** and (±)-modhephene **3**.[7]



1 **2** **3**



4 **5**

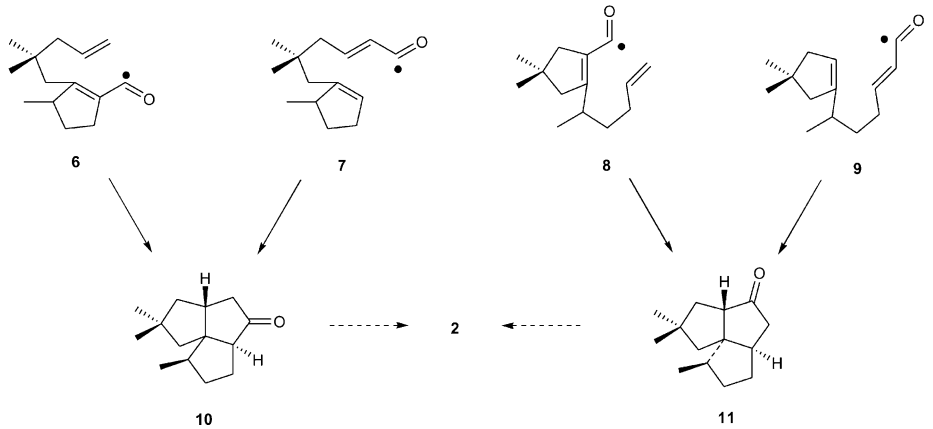
Scheme 1

Results and discussion

Based on our earlier studies leading to diquinanes (Scheme 1),[5] any of the cyclopentene containing α,β-unsaturated acyl radical species **6–9** would be predicted to undergo tandem cyclisations *via* their ketene alkyl counterparts, leading to tricyclic intermediates, *viz.* **10** and **11**, suitable for elaboration to (±)-pentalenene **2** (Scheme 2). After a brief inspection of the alternatives we decided to study the tandem cyclisation from the cyclopentene-substituted α,β-unsaturated acyl radical **9**.

The feasibility of this approach was swiftly demonstrated by elaborating the known carboxylic acid **12a**[8] to the model selenyl ester **12b** and then treating the ester with Bu_3SnH–AIBN in hot benzene. To our satisfaction work up and chromatography gave the anticipated tricyclic ketone **13** in 26% yield; the aldehyde **12c**, resulting from *in situ* reduction of the selenyl ester **12b** under the reaction conditions, was also isolated.

The trimethyl-substituted analogue of **12b**, *i.e.* the α,β-unsaturated phenyl selenyl ester **19**, was then prepared starting from the cyclopentylidene acetic acid ester **14**, as outlined in Scheme 3. Thus, based on precedent,[9] deprotonation of **14** using lithium 2,2,6,6-tetramethylpiperidinamide and DMPU[10] at −90 °C, followed by trapping of the resulting enolate anion with the TBDMS ether of 3-iodo-1-propanol, first gave the β,γ-unsaturated ester **15** in 49% overall yield. Reduction of the ester **15**, using DIBAL, next gave the alcohol **16a**, which, in three straightforward steps, was then converted into the alcohol **17**. A

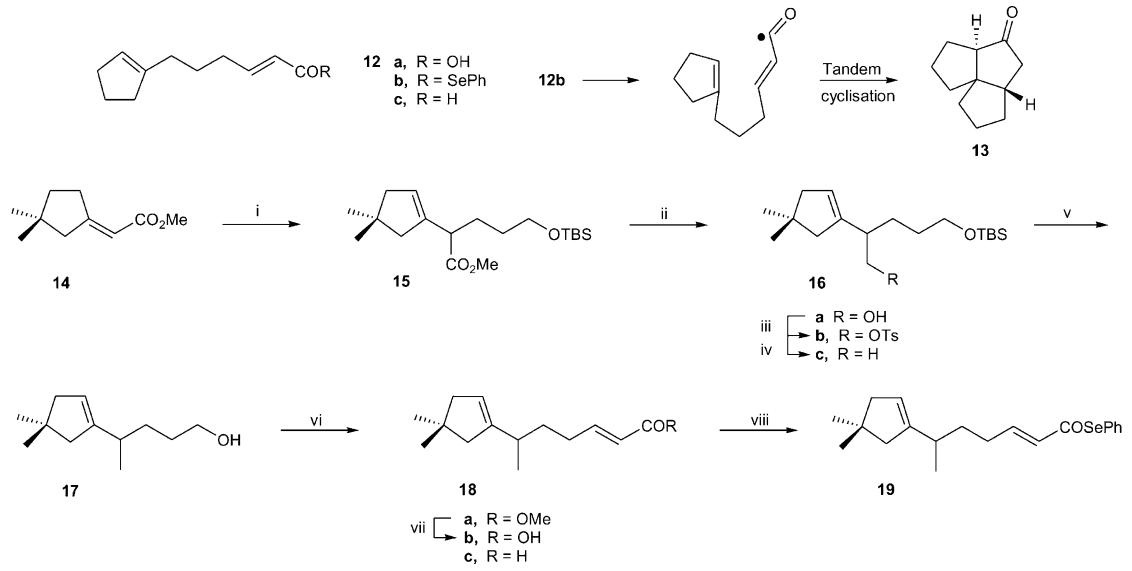


6 **7** **8** **9**

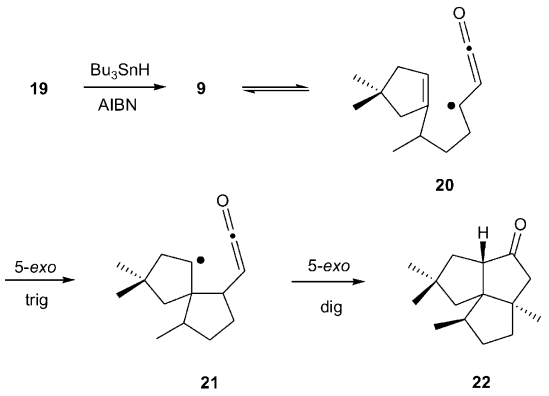
10 **2** **11**

Scheme 2

DOI: 10.1039/b413817c

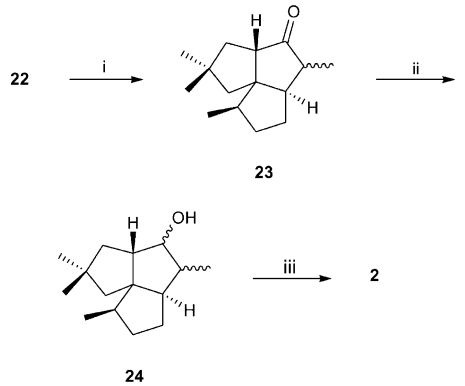


Scheme 3 *Reagents*: i, LiTMP, DMPU, $I(CH_2)_3OTBS$, THF, −90 °C, 49%; ii, DIBAL, toluene, −78 °C, 98%; iii, TsCl, DMAP, Et_3N, CH_2Cl_2, 88%; iv, $LiEt_3BH$, THF, 97%; v, AcOH, H_2O, THF, 93%; vi, $(COCl)_2$, DMSO, CH_2Cl_2, Et_3N, then $Ph_3P{=}CHCO_2Me$, 80%; vii, $LiOH{\cdot}H_2O$, THF, H_2O, 98%; viii, NPSP, $^nBu_3P$, CH_2Cl_2, −30 °C, 57%.



one-pot Swern–Wittig procedure[11] then elaborated **17** to the *E*-α,β-unsaturated ester **18a** in 80% yield. Finally, saponification of the ester **18a** and treatment of the resulting carboxylic acid with *N*-(phenylseleno)phthalimide (NPSP) in the presence of Bu_3P led to the key phenyl selenyl ester **19**.

When a solution of the selenyl ester **19** in benzene was treated with Bu_3SnH–AIBN it underwent tandem radical cyclisation *via* the α-ketene alkyl species **20** and the cyclopentyl radical **21**, leading to the tricyclic ketone **22** as a 5 : 1 mixture of β- and α-methyl epimers in a combined yield of approximately 50% (Scheme 4). Varying amounts (>25%) of the aldehyde **18c** resulting from reduction of the selenyl ester functionality

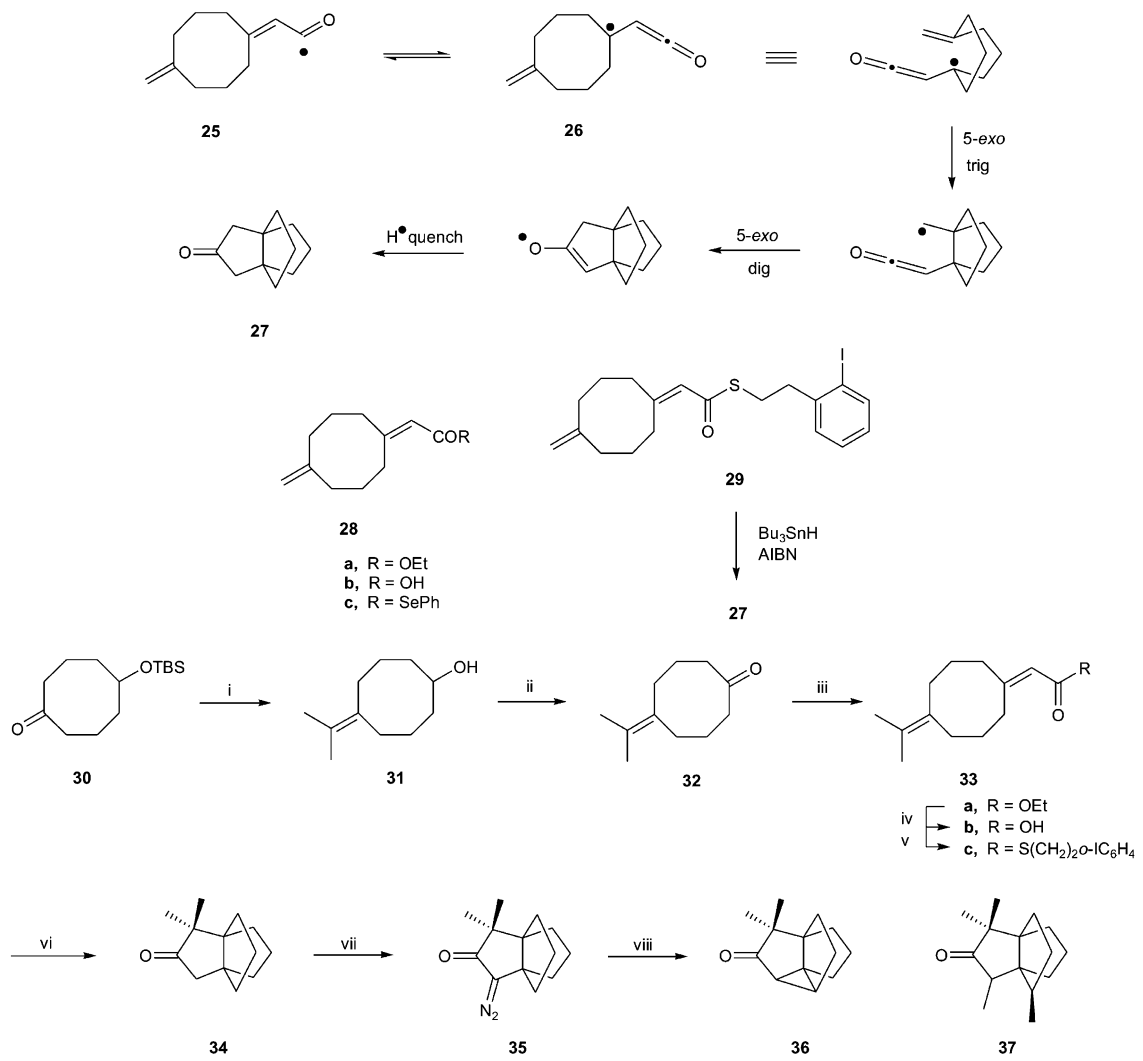


Scheme 4 Reagents: i, LDA, MeI, 37%; ii, $NaBH_4$, MeOH, 53%; iii, *p*-TsOH, benzene, Δ, 70%.

in **19** were also isolated by chromatography. The relative stereochemistry of the major diastereoisomer of the triquinane, *i.e.* **22**, followed conclusively from comparison of its ^1H NMR and ^{13}C NMR spectroscopic data with those described in the literature by Burnell *et al.*[12] for the same compound prepared by an independent route.

The stage was now set to complete a synthesis of (±)-pentalenene from the tricyclic ketone **22** based on three straightforward functional group manipulations. Thus, deprotonation of **22**, using LDA, followed by treatment with methyl iodide first gave the α-methyl derivative **23** as a mixture of epimers in modest yield. Reduction of **23** using $NaBH_4$ in MeOH at 0 °C next led to alcohol **24**, seemingly as a single diastereoisomer, which then underwent dehydration in the presence of *p*-toluenesulfonic acid, leading to pentalenene **2**. The synthetic (±)-pentalenene displayed spectroscopic data which were identical to those reported in the literature, and superimposable on those obtained from an earlier synthesis developed in our laboratory.[13]

We next examined a synthesis of the 3,3,3-propellane ring system, *i.e.* **27**, in the natural sesquiterpene modhephene **3** based on a tandem transannulation–cyclisation sequence from the unsaturated radical species **25** and **26** containing a cyclooctane ring. Thus, a Peterson olefination between 5-methylenecyclooctanone[14] and ethyl trimethylsilylacetate in the presence of LDA at −78 °C first gave the α,β-unsaturated ester **28a**, which was then saponified to the corresponding carboxylic acid **28b**. To our surprise, treatment of **28b** with *N*-(phenylselenyl)phthalimide and PPh_3 failed to produce any of the corresponding selenyl ester **28c**. We therefore prepared **29**, the 2-(*o*-iodophenyl)ethyl thioester of **28b**. Crich and Yao[15] have shown such thioesters to be equally useful precursors to acyl radical intermediates. When a solution of the thioester **29** was treated with Bu_3SnH–AIBN in refluxing benzene it did indeed undergo the anticipated tandem transannulation–cyclisation sequence and produced the known tricyclo[3.3.3.$0^{1,5}$]undecan-3-one **27**[16] in 53% yield. Although we could have elaborated the undecan-3-one **27** to the corresponding *gem*-dimethyl-substituted derivative **34** *en route* to modhephene **3**, instead we next synthesized the *gem*-dimethyl-substituted carbethoxymethylene cyclooctane **33c** and examined its separate radical chemistry. Thus, an intermolecular McMurry coupling reaction[17] between the cyclooctanone **30**[18] and acetone first led to the alkene **31**, which was then converted into the corresponding cyclooctanone **32**, in two straightforward steps (Scheme 5). A Peterson olefination between **32** and ethyl trimethylsilylacetate,



Scheme 5 *Reagents*: i, Li, $TiCl_3$, $AlCl_3$, Me_2CO, 38%; ii, DMSO, $(COCl)_2$, 69%; iii, $Me_3SiCH_2CO_2Et$, LDA, THF, 65%; iv, $NaOH{\cdot}H_2O$, 55%; v, $IC_6H_4CH_2CH_2SH$, DCC, DMAP, 84%; vi, Bu_3SnH, AIBN, 60%; vii, NaH, MeOCHO, then TsN_3, Et_2NH, 38%; viii, $CuSO_4$, toluene, 36%.

followed by saponification of the resulting α,β-unsaturated ester **33a** and treatment of the carboxylic acid product **33b** with 2-(*o*-iodophenyl)ethane thiol, next gave the thioester **33c**. When this thioester was treated with Bu_3SnH–AIBN in hot benzene for 5 h, work up and chromatography produced the tricyclic ketone **34** in a satisfying 60% yield. Finally, the tricyclic ketone **34** was converted into the tricyclo[3.3.3.$0^{1,5}$.$0^{2,8}$]undecan-3-one **36** *via* the corresponding α-diazo derivative **35**, which has been converted previously into modhephene *via* **37** in three steps by Cook and his colleagues.[18] Our concise synthesis of the tricyclic ketone **34** based on tandem transannulation–cyclisation from an α-ketenyl alkyl radical intermediate of type **26** derived from a substituted analogue of **25**, thereby constitutes a new and unusual formal synthesis of (±)-modhephene, and complements the earlier described synthesis of (±)-pentalenene using similar interesting radical cascade chemistry.

Experimental

For general experimental details see the first paper in this series.[6a]

Se-Phenyl 6-cyclopent-1-enylhex-2*E*-eneselenoate 12b

Tri-*n*-butylphosphine (1.20 ml, 4.82 mmol) was added dropwise over 5 min to a stirred solution of (*E*)-6-cyclopent-1-enylhex-2-enoic acid **12a**[8] and its exocyclic double bond regioisomer (*endo* : *exo*, 10 : 1; 586 mg, 3.25 mmol) in dry CH_2Cl_2 (13 ml) at −30 °C under a nitrogen atmosphere. The mixture was stirred at −30 °C for 10 min, then NPSP (1.44 g, 4.77 mmol) was added and the resulting bright yellow mixture was stirred at −30 °C for a further 15 min. Ether (25 ml) was added and the solution was then washed with water (2 × 10 ml), followed by brine, and dried. The solvents were evaporated to leave an oily residue. Repeated chromatography on silica using graduated 0–1% petroleum ether–diethyl ether as eluent gave the *selenyl ester* and its corresponding exocyclic double bond regioisomer (*endo* : *exo*, 10 : 1; 430 mg, 41%) as a yellow oil. No satisfactory microanalytical data could be obtained. ν_{max}(film)/cm^{-1} 1697, 1625, 1579; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.58–1.71 (2H, m, CH_2CH$_2$CH=CH), 1.82–1.92 (2H, m, CH_2CH$_2$CH=CCH_2), 2.08–2.36 (8H, m), 5.32–5.40 (1H, m, CH$_2$C=CHCH$_2$), 6.19 (1H, dt, *J* 15.4, 1.5 Hz, CH$_2$CH=CH), 6.95 (1H, dt, *J* 15.4, 6.9 Hz, CH$_2$CH=CH), 7.34–7.44 (3H, m, 3 × ArH), 7.50–7.58 (2H, m, 2 × ArH); ^{13}C NMR δ 23.4 (t), 25.8 (t), 30.5 (t), 32.0 (t), 32.4 (t), 34.9 (t), 124.1 (d), 126.1 (s), 128.8 (d), 129.3 (2 × d), 130.3 (d), 135.9 (2 × d), 143.7 (s), 146.8 (d), 190.9 (s); *m*/*z* (EI) found 163.1121 (M^+ − SePh), $C_{17}H_{20}$OSe requires 163.1123.

Octahydrocyclopenta[*c*]pentalen-4-one 13

A solution of tributyltin hydride (0.24 ml, 0.89 mmol) and AIBN (12 mg, 0.073 mmol) in dry, degassed benzene (5 ml) was added dropwise over 4.25 h *via* syringe pump to a stirred, refluxing solution of the selenyl ester **12b** and its exocyclic double bond regioisomer (*endo* : *exo*, 10 : 1; 236 mg, 0.74 mmol) and AIBN (13 mg, 0.079 mmol) in dry, degassed benzene (235 ml) under an argon atmosphere. The mixture was heated under reflux for

a further 45 min, then allowed to cool to room temperature, and the solvent was evaporated. The residue was purified by chromatography on silica using petroleum ether–diethyl ether as eluent to give: (i), the *tricyclic ketone* (32 mg, 26%) as a colourless oil; ν_{max}(film)/cm^{-1} 1725; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.36–1.49 (2H, m), 1.60–2.05 (10H, m), 2.13 (1H, ddd, *J* 18.0, 5.9 and 1.8 Hz, CH*H*CO), 2.17–2.38 (2H, m), 2.55 (1H, dd *J* 18.0 and 8.8 Hz, CH*H*CO); ^{13}C NMR δ 25.8 (t), 26.8 (t), 30.9 (t), 34.5 (t), 40.8 (t), 42.0 (t), 44.8 (d), 46.5 (d), 58.6 (s), 59.5 (d), 223.8 (s); and (ii), the corresponding aldehyde **12c** (25 mg, 21%) as an oil; ν_{max}(film)/cm^{-1} 1693, 1637; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.62–1.72 (2H, m, CH_2CH$_2$CH=CH), 1.81–1.91 (2H, m, CH_2CH$_2$CH=CCH$_2$), 2.07–2.39 (8H, m), 5.31–5.38 (1H, m, CH$_2$C=C*H*CH$_2$), 6.13 (1H, ddt, *J* 15.6, 7.9, 1.5 Hz, CH$_2$CH=C*H*), 6.86 (1H, dt, *J* 15.6, 6.8 Hz, CH$_2$C*H*=CH), 9.51 (1H, d, *J* 7.9 Hz, C*H*O); ^{13}C NMR δ 23.4 (t), 25.8 (t), 30.5 (t), 32.4 (2 × t), 34.9 (t), 124.1 (d), 133.1 (d), 143.6 (s), 158.7 (d), 194.1 (s); *m/z* (EI) found 164.1207 (M$^+$), $C_{11}H_{16}O$ requires 164.1201.

Methyl 5-(*t*-Butyldimethylsilanyloxy)-2-(4,4-dimethylcyclopent-1-enyl)pentanoate 15

A solution of *t*-butyldimethylsilyl chloride (24.5 g, 163 mmol) in dry CH_2Cl_2 (40 ml) was added slowly over 10 min to a stirred mixture of triethylamine (19.0 ml, 136 mmol), DMAP (1.88 g, 15.4 mmol) and 3-bromopropan-1-ol (10.5 ml, 116 mmol) in dry CH_2Cl_2 (100 ml) at 0 °C under a nitrogen atmosphere. The resulting heterogeneous mixture was stirred at 0 °C for 20 min, then water was added, followed by ether and 2 N HCl. The organic phase was separated and washed successively with 2 N HCl, saturated, aqueous NH_4Cl and brine, then dried. The solvents were evaporated and the residue was quickly passed through a silica column (eluent: 2% diethyl ether–petroleum ether) to give *t*-butyl-(3-bromopropoxy)dimethylsilane (32 g) as an oil; ν_{max}(film)/cm^{-1} 1472, 1256, 1103; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.07 (6H, s, Si(CH_3)$_2$), 0.90 (9H, s, SiC(CH_3)$_3$), 2.04 (2H, tt, *J* 6.5, 5.7, CH_2CH$_2$Br), 3.52 (2H, t, *J* 6.5, CH_2Br), 3.74 (2H, t, *J* 5.7, CH_2OTBS); ^{13}C NMR δ −5.4 (Si(*C*H$_3$)$_2$), 18.3 (Si*C*Me$_3$), 25.9 (SiC(*C*H$_3$)$_3$), 30.7 (CH$_2$), 35.5 (CH$_2$), 60.4 (*C*H$_2$OTBS).

The bromide was taken up in acetone (520 ml) and heated under reflux with sodium iodide (71.9 g, 480 mmol) for 7 h. The acetone was evaporated, then water and ether were added and the organic layer was washed with brine and dried. The solvents were evaporated to leave the corresponding iodide (32.6 g, 94%) as an oil, which was dried *in vacuo* and used without purification in the next reaction. ν_{max}(film)/cm^{-1} 1471, 1256, 1101; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.07 (6H, s, Si(CH_3)$_2$), 0.91 (9H, s, SiC(CH_3)$_3$, 2.00 (2H, tt, *J* 6.7, 5.7, CH_2CH$_2$I), 3.29 (2H, t, *J* 6.7, CH_2I), 3.68 (2H, t, *J* 5.7, CH_2OTBS); ^{13}C NMR δ −5.3 (Si(*C*H$_3$)$_2$), 3.7 (*C*H$_2$I), 18.3 (Si*C*Me$_3$), 25.9 (SiC(*C*H$_3$)$_3$), 36.1 (CH$_2$), 62.1 (*C*H$_2$OTBS).

n-Butyllithium (2.5 M in hexanes; 19.5 ml, 48.8 mmol) was added over 10 min to a stirred solution of 2,2,6,6-tetramethylpiperidine (8.6 ml, 50.7 mmol) in dry THF (65 ml) at 0 °C under a nitrogen atmosphere. The mixture was stirred at 0 °C for 30 min, then between −60 and −90 °C for 25 min. DMPU (35 ml) was added at −90 °C, and the resulting homogeneous mixture was stirred for 30 min, while the temperature of the cooling bath was maintained between −85 and −100 °C. A solution of methyl (3,3-dimethylcyclopentylidene)acetate **14**[9] (3.97 g, 23.6 mmol) in dry THF (25 ml) was added dropwise *via* cannula at the same temperature as the reaction mixture (−100 °C). The resulting mixture was stirred at −100 °C for 40 min, before it was added rapidly *via* cannula to a solution of *t*-butyl(3-iodopropoxy)dimethylsilane (32.6 g, 109 mmol) in dry THF (70 ml) at −100 °C. After 5 min, the reaction was quenched with water. 2 N HCl was added, and the mixture was extracted with ether. The combined ether extracts were washed with 2 N HCl, then with saturated aqueous NH_4Cl and brine, and dried. The residue was purified by chromatography on silica using petroleum ether as eluent to give the *cyclopentene ester* (4 g, 49%) as a colourless oil; ν_{max}(film)/cm^{-1} 1740, 1646; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.04 (6H, s, Si(CH_3)$_2$), 0.90 (9H, s, SiC(CH_3)$_3$), 1.06 (6H, s, 2 × CH$_3$), 1.45–1.52 (2H, m, CH_2CH$_2$OTBS), 1.60–1.71 (1H, m, CH*H*CHCO$_2$Me), 1.75–1.85 (1H, m, CH*H*CHCO$_2$Me), 2.09 (2H, br. s, CH$_2$), 2.13 (2H, br. s, CH$_2$), 3.14 (1H, br. t, *J* 7.6 Hz, C*H*CO$_2$Me), 3.56–3.66, (2H, m, CH_2OTBS), 3.68 (3H, s, CO$_2$CH_3), 5.42 (1H, br. s, =C*H*); ^{13}C NMR δ −5.3 (q), 18.3 (s), 25.9 (q), 26.6 (t), 29.6 (q), 29.7 (q), 30.6 (t), 38.4 (s), 47.3 (t), 47.6 (d), 47.8 (t), 51.6 (q), 62.8 (t), 126.0 (d), 139.7 (s), 174.3 (s); *m/z* (ES) found 363.2343 (M$^+$ + Na), $C_{19}H_{36}O_3Si$ requires 363.2331.

5-(*t*-Butyldimethylsilanyloxy)-2-(4,4-dimethyl-1-cyclopent-1-enyl)pentan-1-ol 16a

DIBAl-H (1.5 M in toluene; 36 ml, 54 mmol) was added over 10 min to a stirred solution of the ester **15** (4 g) in toluene (90 ml) at −78 °C under a nitrogen atmosphere and the mixture was stirred for 20 min and then quenched at −78 °C with a saturated solution of Rochelle's salt. The mixture was allowed to warm to room temperature and then it was extracted with ether. The combined ether extracts were washed with water and brine, then dried. The solvents were evaporated and the residue was purified by chromatography on silica using petroleum ether–diethyl ether (1 : 9) as eluent to give the *alcohol* (3.62 g, 98%) as a colourless oil; (found, C, 16.2%; H, 11.7%; $C_{18}H_{36}O_2Si$ requires C, 16.2%; H, 11.6%); ν_{max}(film)/cm^{-1} 3358 (br); ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.05 (6H, s, Si(CH_3)$_2$), 0.90 (9H, s, SiC(CH_3)$_3$), 1.08 (6H, s, 2 × CH$_3$), 1.30–1.58 (4H, m, (CH_2)$_2$CH$_2$OTBS), 1.98–2.10 (2H, m, Me$_2$CCH_2), 2.13–2.17 (2H, m, Me$_2$CCH_2), 2.33–2.41 (1H, m, C*H*CH$_2$OH), 3.46 (1H, dd, *J* 10.4, 8.2, CH*H*OH), 3.52 (1H, dd, *J* 10.4, 5.3, CH*H*OH), 3.55–3.65 (2H, m, CH_2OTBS), 5.41 (1H, br. s, =C*H*); ^{13}C NMR δ −5.3 (q), 18.3 (s), 25.6 (t), 26.0 (q), 29.9 (2 × q), 30.5 (t), 38.2 (s), 44.1 (d), 46.6 (t), 47.3 (t), 63.1 (t), 64.2 (t), 126.4 (d), 142.9 (s); *m/z* (EI) found 255.1776 (M$^+$ − C$_4$H$_9$), $C_{18}H_{36}O_2Si$ requires 255.1780.

5-(*t*-Butyldimethylsilanyloxy)-2-(4,4-dimethylcyclopent -1-enyl)pentyl toluene-4-sulfonate 16b

A solution of the alcohol **16a** in dry CH_2Cl_2 (25 ml) was stirred with *p*-toluenesulfonyl chloride (770 mg, 4.04 mmol), DMAP (48 mg, 0.39 mmol) and triethylamine (0.76 ml, 5.45 mmol) at room temperature under a nitrogen atmosphere for 22 h. Water was added and the mixture was stirred for 10 min, and then extracted with ether. The extracts were washed with 2 N HCl, then brine, and dried. The solvents were evaporated and the residue was passed through a silica column (eluent: CH_2Cl_2) to give the *tosylate* (1.47 g, 88%) as a colourless solid; (found, C, 64.2%; H, 9.1%; $C_{25}H_{42}O_4SiS$ requires C, 64.3%; H, 9.1%); ν_{max}(Nujol)/cm^{-1} 1596; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.03 (6H, s, Si(CH_3)$_2$, 0.88 (9H, s, SiC(C*H*)$_3$), 1.02 (6H, s, 2 × CH$_3$), 1.26–1.48 (4H, m, (CH_2)$_2$CH$_2$OTBS), 1.87 (1H, dq, *J* 15.6, 1.9 Hz, Me$_2$CCH*H*), 1.94 (1H, dq, *J* 15.6, 1.8 Hz, Me$_2$CCH*H*), 2.04–2.09 (2H, m, Me$_2$CCH_2), 2.45 (3H, s, ArCH_3), 2.45–2.53 (1H, m, C*H*CH$_2$OTs), 3.49–3.60 (2H, m, CH_2OTBS), 3.89–3.97 (2H, m, CH_2OTs), 5.27 (1H, br. s, =C*H*), 7.34 (2H, d, *J* 8.2 Hz, 2 × Ar*H*), 7.78 (2H, d, *J* 8.2 Hz, 2 × Ar*H*); ^{13}C NMR δ −5.3 (q), 18.3 (s), 21.6 (q), 25.6 (t), 25.9 (q), 29.7 (2 × q), 29.9 (t), 38.2 (s), 40.3 (d), 47.0 (t), 47.2 (t), 62.8 (t), 72.1 (t), 126.1 (d), 127.9 (2 × d), 129.7 (2 × d), 133.1 (s), 140.7 (s), 144.6 (s); *m/z* (FAB) found 467.2650 (M$^+$ + H), $C_{25}H_{42}O_4SiS$ requires 467.2651.

t-Butyl[4-(4,4-dimethylcyclopent-1-enyl)pentyloxy]dimethylsilane 16c

Super-Hydride (1.0 M in THF; 8.8 ml, 8.8 mmol) was added slowly over 5 min to a stirred solution of the tosylate **16b** (1.87 g,

4.01 mmol) in THF (15 ml) at 0 °C under a nitrogen atmosphere. The mixture was stirred at room temperature for 2.75 h before it was again cooled in ice, and 2 M NaOH (15 ml) and then hydrogen peroxide (5 ml) were carefully added. The resulting mixture was heated under reflux for 1.25 h, then allowed to cool, and extracted with ether. The combined ether extracts were washed with 2 N HCl, then brine, and dried. The solvents were evaporated under reduced pressure to leave a residue which was purified by chromatography on silica using petroleum ether–diethyl ether (2 : 98) as eluent to give the *cyclopentene* (1.15 g, 97%) as a colourless oil; (found, C, 73.3%; H, 12.4%; $C_{18}H_{36}OSi$ requires C, 72.9%; H, 12.2%); ν_{max}(film)/cm^{-1} 1647; ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.05 (6H, s, Si(CH_3)$_2$), 0.90 (9H, s, SiC(CH_3)$_3$), 0.99 (3H, d, *J* 6.9 Hz, CHCH_3), 1.07 (6H, s, 2 × CH_3), 1.21–1.51 (4H, m, (CH_2)$_2$$CH_2$OTBS), 1.99 (1H, dq, *J* 15.6, 1.8 Hz, Me_2CCH*H*), 2.06 (1H, dq, *J* 15.6, 1.8 Hz, Me_2CCH*H*), 2.07–2.12 (2H, m, Me_2CCH_2), 2.16–2.25 (1H, m, C*H*Me), 3.59 (2H, t, *J* 6.5 Hz, CH_2OTBS), 5.19 (1H, br. s, =C*H*); ^{13}C NMR δ −5.3 (q), 18.4 (s), 19.4 (q), 26.0 (q), 29.8 (q), 29.9 (q), 30.7 (t), 31.2 (t), 35.1 (d), 38.1 (s), 47.1 (t), 47.3 (t), 63.5 (t), 121.2 (d, 147.9 (s); *m*/*z* (EI) found 239.1823 (M$^+$ − C_4H_9), $C_{18}H_{36}OSi$ requires 239.1831.

4-(4,4-Dimethylcyclopent-1-enyl)pentan-1-ol 17

A solution of the silyl ether **16c** (1.15 g, 3.88 mmol) in acetic acid–water–THF (1 : 1 : 2; 32 ml) was stirred at 45 °C for 14 h. The mixture was cooled in ice and neutralised with saturated aqueous $NaHCO_3$, then extracted with ether. The extracts were washed with brine, dried and concentrated under reduced pressure to leave an oil. Purification by chromatography on silica using petroleum ether–diethyl ether as eluent gave the *alcohol* (657 mg, 93%) as a colourless oil; (found, C, 78.8%; H, 12.1%; $C_{12}H_{22}O$ requires C, 79.1%; H, 12.2%); ν_{max}(film)/cm^{-1} 3330 (br), 1646;^{1}H NMR (360 MHz, $CDCl_3$) δ 1.00 (3H, d, *J* 6.9 Hz, CHCH_3), 1.06 (3H, s, CH_3), 1.07 (3H, s, CH_3), 1.23–1.57 (4H, m, (CH_2)$_2$$CH_2$OH), 1.99 (1H, dq, *J* 15.6, 1.6 Hz, Me_2CCH*H*), 2.06 (1H, dq, *J* 15.6, 1.7 Hz, Me_2CCH*H*), 2.09–2.11 (2H, m, Me_2CCH_2), 2.18–2.88 (1H, m, C*H*Me), 3.63 (2H, t, *J* 6.5 Hz, CH_2OH), 5.20 (1H, br. s, =C*H*); ^{13}C NMR δ 19.4 (q), 29.8 (q), 29.9 (q), 30.6 (t), 31.1 (t), 35.1 (d), 38.1 (s), 47.1 (t), 47.2 (t), 63.2 (t), 121.4 (d) 147.6 (s); *m*/*z* (EI) found 182.1673 (M$^+$), $C_{12}H_{22}O$ requires 182.1671.

Methyl 6-(4,4-dimethylcyclopent-1-enyl)hept-2*E*-enoate 18a

Dimethyl sulfoxide (0.81 ml, 11.4 mmol) was added dropwise over 10 min to a stirred solution of oxalyl chloride (0.5 ml, 5.73 mmol) in dry CH_2Cl_2 (18 ml) at −60 °C under a nitrogen atmosphere. The mixture was stirred at −60 °C for 40 min and then a solution of the alcohol **17** (863 mg, 4.73 mmol) in CH_2Cl_2 (8 ml) was added. The mixture was stirred at −60 °C, for a further 15 min, then triethylamine (3.3 ml, 23.7 mmol) was added and the resulting opaque, viscous mixture was warmed to 0 °C. Further CH_2Cl_2 (4 ml) was added, and the mixture was stirred at 0 °C for 1.75 h. A solution of methyl (triphenylphosphoranylidene)acetate (3.17 g, 9.48 mmol) in CH_2Cl_2 (18 ml) was added, and the mixture was then warmed and stirred at room temperature for 17 h. Water was added and the mixture was extracted twice with ether. The combined ether extracts were washed with 2 N HCl and brine, dried and concentrated under reduced pressure. The residue was purified by chromatography on silica using petroleum ether–diethyl ether (2 : 98) as eluent to give the *E*-α,β-unsaturated ester (890 mg, 80%) (the corresponding *Z*-isomer was also isolated in 7% yield) as a colourless liquid; (found, C, 76.3%; H, 10.4%; $C_{15}H_{24}O_2$ requires C, 76.2%; H, 10.2%); ν_{max}(film)/cm^{-1} 1728, 1657; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.00 (3H, d, *J* 6.9 Hz, CHCH_3), 1.06 (3H, s, CH_3), 1.07 (3H, s, CH_3), 1.37–1.58 (2H, m, =$CHCH_2CH_2$), 1.98 (1H, dq, *J* 15.5, 1.7 Hz, Me_2CCH*H*), 2.05 (1H, dq, *J* 15.5, 1.7 Hz, Me_2CCH*H*), 2.08–2.19 (4H, m, Me_2CCH_2, =$CHCH_2CH_2$), 2.25 (1H, app. sx, *J* 6.9 Hz, C*H*CH_3), 3.73 (3H, s, CO_2CH_3), 5.21 (1H, br. s, =C*H*), 5.81 (1H, dt, *J* 15.6, 1.6 Hz, =C*H*CO_2Me), 6.97 (1H, dt, *J* 15.6, 7.0 Hz, C*H*=$CHCO_2$Me); ^{13}C NMR δ 19.3 (q), 29.8 (q), 29.9 (q), 30.1 (t), 33.2 (t), 34.8 (d), 38.2 (s), 47.0 (t), 47.3 (t), 51.4 (q), 120.7 (d), 122.0 (d), 146.9 (s), 149.9 (d), 167.2 (s); *m*/*z* (EI) found 236.1776 (M$^+$), $C_{15}H_{24}O_2$ requires 236.1776.

6-(4,4-Dimethylcyclopent-1-enyl)hept-2*E*-enoic acid 18b

A solution of the methyl ester **18a** (852 mg, 3.60 mmol) in THF–water (3 : 1; 24 ml) was heated under reflux in the presence of lithium hydroxide (331 mg, 7.89 mmol) for 21 h. 2 N HCl was added to acidify the mixture, which was then extracted with ether, and the combined extracts were washed with brine and dried. The solvents were evaporated to leave the *carboxylic acid* (782 mg, 98%) as a pale yellow oil; (found, C, 75.7%; H, 10.1%; $C_{14}H_{22}O_2$ requires C, 75.6%, H, 10.0%); ν_{max}(film)/cm^{-1} 3400–2400 (br), 1697, 1650; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.01 (3H, d, *J* 6.9 Hz, CHCH_3), 1.07 (3H, s, CH_3), 1.08 (3H, s, CH_3), 1.39–1.60 (2H, m, =$CHCH_2CH_2$), 1.98 (1H, dq, *J* 15.5, 1.7 Hz, Me_2CCH*H*), 2.06 (1H, dq, *J* 15.5, 1.8 Hz, Me_2CCH*H*), 2.09–2.13 (2H, m, Me_2CCH_2), 2.14–2.31 (3H, m, =$CHCH_2CH_2$, C*H*Me), 5.23 (1H, br. s, =C*H*), 5.82 (1H, dt, *J* 15.6, 1.5 Hz, =C*H*CO_2H), 7.09 (1H, dt, *J* 15.6, 7.0 Hz, C*H*=$CHCO_2$H); ^{13}C NMR δ 19.3 (q), 29.8 (q), 29.9 (q), 30.2 (t), 33.0 (t), 34.9 (d), 38.2 (s), 46.9 (t), 47.2 (t), 120.5 (d), 122.1 (d), 146.8 (s), 152.6 (d), 172.6 (s); *m*/*z* (EI) found 222.1626 (M$^+$), $C_{14}H_{22}O_2$ requires 222.1620.

Se-Phenyl 6-(4,4-Dimethylcyclopent-1-enyl)hept-2*E*-eneselenoate 19

Tri-*n*-butylphosphine (940 µl, 3.77 mmol) was added dropwise over 3 min to a stirred solution of the acid **18b** (540 mg, 2.43 mmol) in dry CH_2Cl_2 (20 ml) at −30 °C under a nitrogen atmosphere and the mixture was stirred at −30 °C for 15 min. NPSP (1.11 g, 3.67 mmol) was added and the resulting mixture was stirred at −30 °C for a further 10 min, then diluted with ether. The ether extracts were washed with water and brine, dried and evaporated *in vacuo*. The residue was purified by chromatography on silica using petroleum ether–diethyl ether as eluent to give the *phenyl selenyl ester* (500 mg, 57%) as a yellow oil; ν_{max}(film)/cm^{-1} 1698, 1626, 1580; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.02 (3H, d, *J* 6.9 Hz, CHCH_3), 1.08 (3H, s, CH_3), 1.09 (3H, s, CH_3), 1.40–1.63 (2H, m, =$CHCH_2CH_2$), 1.99 (1H, dqd, *J* 15.5, 1.9, 0.5 Hz, Me_2CCH*H*), 2.06 (1H, dqd, *J* 15.5, 1.9, 0.5 Hz, Me_2CCH*H*), 2.10–2.32 (5H, m, Me_2CCH_2, CH_2CH=CH, C*H*CH_3), 5.21–5.25 (1H, m, =C*H*), 6.16 (1H, dt, *J* 15.4, 1.5 Hz, =C*H*COSePh), 6.94 (1H, dt, *J* 15.4, 6.9 Hz, C*H*=CHCOSePh), 7.37–7.42 (3H, m, 3 × Ar*H*), 7.52–7.56 (2H, m, 2 × Ar*H*); ^{13}C NMR δ 19.3 (q), 29.8 (q), 29.9 (q), 30.3 (t), 33.0 (t), 34.9 (d), 38.2 (s), 46.9 (t), 47.3 (t), 122.2 (d), 126.2 (s), 128.8 (d), 129.3 (2 × d), 130.0 (d), 135.9 (2 × d), 146.7 (s), 147.2 (d), 190.9 (s); *m*/*z* (ES) found 363.1204 (M$^+$ + H), $C_{20}H_{26}OSe$ requires 363.1227.

2,2,8-Trimethyloctahydrocyclopenta[*c*]pentalen-4-one 22

A solution of tributyltin hydride (180 µl, 0.67 mmol) and AIBN (12.5 mg, 0.08 mmol) in dry, degassed benzene (5 ml) was added over 7.5 h *via* syringe pump to a stirred, refluxing solution of the phenyl selenyl ester **19** (163 mg, 0.45 mmol) and AIBN (6.8 mg, 0.04 mmol) in dry, degassed benzene (190 ml), under an argon atmosphere. The mixture was heated under reflux for a further 1 h, then allowed to cool to room temperature. The solvent was removed under reduced pressure, and the residue was purified by chromatography on silica using petroleum ether–diethyl ether as eluent to give a 5 : 1 mixture of the diastereomeric triquinanes (31 mg, 33%) along with the aldehyde **18c** (25 mg, 27%). **22**: ν_{max}(film)/cm^{-1} 1737; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.97 (3H,

d, *J* 6.9 Hz, CHC*H*$_3$), 0.99 (3H, s, CH$_3$), 1.01 (3H, s, CH$_3$), 1.30–1.38 (3H, m, 3 × CH*H*), 1.63 (1H, dd, *J* 12.9, 7.0 Hz, CH*H*CHCO), 1.72 (1H, dd, *J* 12.9, 9.5 Hz, CH*H*CHCO), 1.79–1.86 (2H, m, 2 × CH*H*), 1.86–1.95 (1H, m, C*H*Me), 2.07–2.14 (2H, m, CH*H*, CH*H*CO), 2.40–2.47 (2H, m, C*H*CO, CH$_2$C*H*CH$_2$), 2.78 (1H, dd, *J* 18.6, 9.2 Hz, CH*H*CO); ^{13}C NMR δ 15.5 (q), 29.2 (q), 29.5 (q), 31.3 (t), 34.4 (t), 41.2 (s), 42.9 (d), 44.6 (t), 45.8 (d), 46.8 (t), 47.9 (t), 59.4 (d), 62.7 (s), 222.9 (s); *m/z* (EI$^+$) found 206.1678 (M$^+$), $C_{14}H_{22}O$ requires M$^+$, 206.1671. **18c**: (found, C, 81.4%; H, 10.9%; $C_{14}H_{22}O$ requires C, 81.5%; H, 10.8%); ν_{max}(film)/cm^{-1} 1695, 1638; ^{1}H NMR (360 MHz, CDCl$_3$) δ 1.02 (3H, d, *J* 6.9 Hz, CHC*H*$_3$), 1.067 (3H, s, C*H*$_3$), 1.074 (3H, s, CH$_3$), 1.42–1.64 (2H, m, =CHCH$_2$C*H*$_2$), 1.98 (1H, dq, *J* 15.6, 1.9 Hz, Me$_2$CCH*H*), 2.06 (1H, dq, *J* 15.6, 1.9 Hz, Me$_2$CCH*H*), 2.09–2.12 (2H, m, Me$_2$CC*H*$_2$), 2.23–2.33 (3H, m, =CHC*H*$_2$C*H*$_2$, C*H*Me), 5.23 (1H, br. s, =C*H*), 6.12 (1H, ddt, *J* 15.6, 7.9, 1.5 Hz, =C*H*CHO), 6.86 (1H, dt, *J* 15.6, 6.8 Hz, C*H*=CHCHO), 9.50 (1H, d, *J* 7.9 Hz, C*H*O); ^{13}C NMR δ 19.3 (q), 29.7 (q), 29.9 (q), 30.6 (t), 33.0 (t), 34.9 (d), 38.2 (s), 46.9 (t), 47.2 (t), 122.3 (d), 132.9 (d), 146.6 (s), 159.1 (d), 194.1 (s); *m/z* (EI) found 206.1663 (M$^+$), $C_{14}H_{22}O$ requires 206.1671.

2,2,5,8-Tetramethyloctahydrocyclopenta[*c*]pentalen-4-one 23

A solution of a mixture of the diastereoisomeric ketones **22** (51 mg, 0.25 mmol) in THF (1 ml) was added *via* cannula to a stirred solution of freshly prepared LDA (1.0 M; 0.32 ml, 0.32 mmol) in THF (1 ml) at −78 °C. The stirred mixture was allowed to warm to −20 °C over 1.25 h, then methyl iodide (0.05 ml, 0.80 mmol) was added, and the resulting mixture was stirred at 0 °C for 1.5 h. The mixture was quenched with NH_4Cl and then ether and water were added. The separated organic extracts were washed with brine and dried. Evaporation of the solvents left a residue which was purified by chromatography on silica using petroleum ether–diethyl ether (1 : 99) as eluent to give the *methylated ketone* (20 mg, 37%), along with unreacted starting material (8 mg, 16%) as a colourless oil; ν_{max}(film)/cm^{-1} 1736; ^{1}H NMR (360 MHz, CDCl$_3$) δ 0.85 (3H, s, C*H*$_3$), 0.98 (3H, d, *J* 6.6 Hz, CH$_2$CHC*H*$_3$), 1.00 (3H, s, CH$_3$), 1.09 (3H, d, *J* 6.8 Hz, C*H*$_3$CHCO), 1.19 (1H, d, *J* 13.2 Hz, Me$_2$CCH*H*C$_{quat.}$), 1.30–1.39 (1H, m, CH$_3$CHCH*H*), 1.41–1.50 (1H, m, CH$_3$CHCH$_2$CH*H*), 1.61 (1H, dd, *J* 12.9, 9.8 Hz, CH*H*CHCO), 1.69 (1H, d, *J* 13.2 Hz, Me$_2$CCH*H*C$_{quat.}$), 1.75 (1H, ddd, *J* 12.9, 4.8, 1.0 Hz, CH*H*CHCO), 1.80–2.17 (5H, m), 2.52 (1H, ddd, *J* 9.8, 4.8, 1.7 Hz, CH$_2$C*H*CO); ^{13}C NMR δ 13.5 (q), 14.5 (q), 28.8 (q), 29.8 (q), 29.9 (t), 35.0 (t), 40.8 (s), 43.1 (d), 43.5 (t), 46.7 (t), 53.2 (d), 55.3 (d), 58.0 (d), 59.5 (s), 222.7 (s).

2,2,5,8-Tetramethyldecahydrocyclopenta[*c*]pentalen-4-ol 24

A solution of the ketone **23** (17 mg, 0.077 mmol) in methanol (1 ml) was stirred with sodium borohydride (9 mg, 0.24 mmol) at 0 °C for 1.25 h. Water was added, and most of the methanol was then evaporated. The residue was extracted with ether, and the extracts were then washed with brine and dried. The solvents were evaporated, and the residue was redissolved in methanol (1 ml) and cooled to 0 °C. More sodium borohydride (9 mg, 0.24 mmol) was added, and the mixture was stirred at this temperature for 1.75 h. The reaction was quenched by the addition of water, and most of the methanol was then removed under reduced pressure. The residue was again extracted with ether, and the combined extracts were washed with brine, then dried, and concentrated. The residue was purified by chromatography on silica using petroleum ether–diethyl ether (1 : 99) as eluent to give the alcohol[12] (9 mg, 53%) as a colourless oil; ν_{max}(film)/cm^{-1} 3490 (br); ^{1}H NMR (360 MHz, CDCl$_3$) δ 0.88 (3H, d, *J* 7.0 Hz, CH$_3$), 1.02 (3H, s, CH$_3$), 1.04 (3H, d, *J* 7.0 Hz, CH$_3$), 1.09 (3H, s, CH$_3$), 1.17–1.39 (3H, m), 1.44–1.55 (2H, m), 1.65–1.88 (6H, m), 2.25–2.33 (1H, m, C*H*CHOH), 3.95 (1H, app. t, *J* 5.2 Hz, C*H*OH); ^{13}C NMR δ 14.2 (q), 17.3 (q), 28.4 (t), 30.7 (q), 30.9 (q), 33.8 (t), 40.2 (t), 41.2 (s), 42.5 (d), 48.4 (d), 48.7 (t), 57.2 (d), 58.1 (d), 65.7 (s), 78.2 (d).

(±)-Pentalenene 2

A solution of the alcohol **24** (3 mg, 0.014 mmol) and *p*-toluenesulfonic acid (1 mg, 5 μmol) in dry benzene (0.5 ml) was stirred and heated under reflux under a nitrogen atmosphere for 6 h, and then poured into saturated, aqueous $NaHCO_3$, and extracted with ether. The combined ether extracts were washed with brine, dried and concentrated under reduced pressure. The residue was purified by chromatography on silica using petroleum ether–diethyl ether as eluent to give (±)-pentalenene (2 mg, 70%) as a colourless oil; ^{1}H NMR (500 MHz) δ 0.91 (3H, d, *J* 7.0 Hz, CHC*H*$_3$), 0.99 (2 × 3H, 2 × s, 2 × CH$_3$), 1.18 (1H, dd, *J* 12.5, 5.1 Hz), 1.25–1.34 (3H, m), 1.36 (1H, d, *J* 13.0 Hz), 1.58–1.65 (1H, m), 1.62 (3H, br. s, =CC*H*$_3$), 1.74 (1H, d, *J* 13.0 Hz), 1.74–1.87 (2H, m), 2.55 (1H, d, *J* 9.2 Hz), 2.64–2.70 (1H, m), 5.16 (1H, br. s); ^{13}C NMR (125 MHz) δ 15.5, 17.0, 27.6, 29.1, 29.9, 33.5, 40.5, 44.6, 46.8, 48.9, 59.4, 62.1, 64.7, 129.5, 140.6.

Ethyl (5-methylenecyclooctylmethylene)acetate 28a

A solution of LDA in THF (2.3 ml 2 M, 4.5 mmol) was added over 5 min to a stirred solution of ethyl trimethylsilylacetate (728 mg, 4.5 mmol) in THF (50 ml), and the mixture was stirred at −78 °C for 0.25 h. 5-Methylenecyclooctanone[14] (316 mg, 2.27 mmol) was added dropwise over 15 min, and the pale yellow solution was stirred at −78 °C for a further 1 h and then allowed to warm to room temperature over 2 h. Water (20 ml) was added and the mixture was extracted with ether (4 × 50 ml). The combined organic extracts were dried and then evaporated under reduced pressure. The residue was purified by chromatorgraphy on silica using petroleum ether–diethyl either (9 : 1) as eluent to give the *ethyl ester* (0.26 g, 54%) as a yellow oil; (found: C, 75.3%, H, 10.1%; $C_{13}H_{20}O_2$ requires C, 75.0%, H, 9.7%); ν_{max}(film)/cm^{-1} 1712, 1636; ^{1}H NMR (360 MHz, CDCl$_3$) δ 1.24 (3H, t, *J* 7.1 Hz, CO$_2$CH$_2$C*H*$_3$), 1.80–2.00 (4H, m, CH$_2$C*H*$_2$C*H*$_2$), 2.07–2.22 (4H, m, C*H*$_2$C=C*H*$_2$), 2.30 (2H, app. dd, *J* ~5.6 Hz, C*H*$_2$C=CHCO$_2$Et), 2.72 (2H, app. dd, *J* ~6.1 Hz, C*H*$_2$C=CHCO$_2$Et), 4.10 (2H, q, *J* 7.1 Hz, CO$_2$C*H*$_2$CH$_3$), 4.71 (2H, s, C=C*H*$_2$), 5.60 (1H, s, C=C*H*CO$_2$Et); ^{13}C NMR δ 14.3 (q), 25.3 (t), 29.0 (t), 30.6 (t), 34.1 (t), 36.2 (t), 38.9 (t), 59.2 (t), 113.1 (t), 116.5 (d), 149.4 (s), 166.1 (2 × s); *m/z* (EI) found 208.1470 (M$^+$), $C_{13}H_{20}O_2$ requires 208.1463.

(5-Methylenecyclooctylmethylene)acetic acid 28b

A solution of the ester **28a** (180 mg, 0.86 mmol) in aqueous sodium hydroxide (20 ml, 1 M) was heated under reflux for 10 h, then cooled and extracted with ether. The separated aqueous layer was acidified with dilute HCl (to pH 3) and then extracted with ether (3 × 100 ml). The combined ether extracts were dried and then evaporated under reduced pressure to leave a 7 : 3 mixture of (5-methylenecyclooctylmethylene)acetic acid and its positional isomer, (5-methylenecycloocten-1-yl)acetic acid (0.15 g, 96%), as a colourless solid; ν_{max}(film)/cm^{-1} 3484, 1714; ^{1}H NMR (360 MHz, CDCl$_3$) δ 1.45–2.17 (6H, m, C*H*$_2$C*H*$_2$C*H*$_2$), 2.27 (1.25H, app. dd, *J* ~5.7 Hz, C*H*HC=CCO$_2$H), 2.66 (1.25H, app. dd, *J* ~5.8 Hz, CH*H*C=CCO$_2$H), 2.95 (0.5H, s, C*H*$_2$CO$_2$H), 4.66 (1.5H, s, C=C*H*$_2$ major isomer), 4.70 (0.5H, s, C=C*H*$_2$ minor isomer), 5.56 (1H, br. s, C=C*H*CO$_2$H and CH$_2$C*H*=C), 11.60 (1H, br. s, CO$_2$*H*); ^{13}C NMR major isomer: δ 25.08 (t), 28.95 (t), 30.67 (t), 34.00 (t), 36.17 (t), 39.12 (t), 113.42 (t), 116.05 (d), 149.02 (s), 169.77 (s), 171.78 (s); minor isomer: 26.7 (t), 27.8 (t), 28.4 (t), 32.7 (t), 39.7 (t), 42.5 (2 × t), 112.7 (t), 129.4 (d), 133.4 (s), 150.7 (s), 178.9 (s); *m/z* (EI) found 180.1148 (M$^+$), $C_{11}H_{16}O_2$ requires 180.1150.

The thioester 29

A mixture of the acid **28b** and its positional isomer (84 mg, 0.46 mmol), was treated with 2-(*o*-iodophenyl)ethanethiol (147.3 mg, 0.55 mmol), as described previously,[15] and gave a 7 : 3 mixture of the corresponding conjugated and non-conjugated thioesters (109 mg, 55%) as a colourless oil; ν_{max}(film)/cm^{-1} 1669, 1608, ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.55–1.62 (1H, m, CH_2), 1.88–2.00 (2H, m, CH_2), 2.07 (2H, dd, *J* 6.2, 6.2 Hz, CH_2), 2.15–2.28 (4.5H, m, CH_2), 2.32 (1H, dd, *J* 6.0, 6.2 Hz, CH_2C=CCO), 2.74 (1H, dd, *J* 6.2, 6.0 Hz, CH_2C=CCO), 3.00 (1H, t, *J* 8.6 Hz, SCH_2CH_2Ar), 3.02 (1H, t, *J* 8.6 Hz, SCH_2CH$_2$Ar), 3.1–3.2 (2H, m, ArCH$_2$), 3.24 (1H, s, CH_2CO, minor isomer), 4.77 (1.5H, s, C=CH_2, major isomer), 4.81 and 4.82 (0.25H, s, C=C*H*H and C=CH*H*, minor isomer), 5.66 (0.5H, m, CH$_2$C*H*=CCH$_2$CO), 5.96 (0.5H, s, =C*H*CO), 6.91–6.98 (1H, m, arom. C*H*), 7.27–7.35 (2H, m, arom. C*H*), 7.84 (1H, d, *J* 7.7 Hz, arom. C*H*); ^{13}C NMR (both isomers) δ 25.2 (t), 26.9 (t), 27.9 (t), 28.5 (t), 28.7 (t), 28.9 (t), 29.0 (t), 31.6 (t), 32.8 (t), 34.1 (t), 36.3 (t), 38.6 (t), 39.7 (t), 40.5 (t), 40.7 (t), 52.1 (t), 100.7, 100.8 (arom. *C*I), 112.8 (t), 113.4 (t), 123.7 (d), 128.3 (d), 128.4 (d), 129.9 (d), 130.0 (d), 130.3 (d), 133.8 (s), 139.5 (d), 139.5 (d), 142.6, (s), 149.2, 151.0 (s), 163.7 (s), 187.7 (s), 197.9 (s); *m*/*z* (EI) found 426.0512 (M$^+$), $C_{19}H_{23}OSI$ requires 426.0514.

Tricyclo[3.3.3.0^{1,5}]undecane-3-one 27

A 7 : 3 mixture of the thioester **29** and its positional isomer (70 mg, 0.16 mmol) was heated with tributyltin hydride (62 mg, 0.21 mmol) and AIBN (2.7 mg, 0.01 mmol) in argon-degassed benzene (60 ml) under reflux for 1.5 h, as described previously, and gave the tricycloundecane-3-one[16] (14.2 mg, 53%), whose spectroscopic data were identical to those described in the literature.

5-(Isopropylidene)cyclooctanol 31

THF (1.5 l) was degassed with argon and then added slowly *via* cannula to $TiCl_3$·$AlCl_3$ (100 g, 390 mmol).[17] Slices of lithium metal (8.1 g, 1.2 mmol) were added portionwise and the mixture was stirred at room temperature for 12 h under an argon atmosphere. A solution of 5-(*tert*-butyldimethylsilanyloxy)cyclooctanone **30**[14] (6.7 g, 26 mmol) in acetone (23 ml, 312 mmol) was added dropwise *via* syringe pump over 5 h at room temperature, and the mixture was stirred at room temperature for 14 h and then under reflux for 10 h. Water (50 ml) was added slowly (exothermic) to the cooled mixture which was then extracted with ether, dried and evaporated *in vacuo*. The residue was purified by chromatography on silica using petroleum ether–diethyl ether (1 : 1) as eluent to give the *cyclooctanol* (1.7 g, 38%); as a colourless oil; ν_{max}(film)/cm^{-1} 3342; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.45 (1H, br. s, CHO*H*), 1.60–1.90 (8H, m, CHOHCH_2CH_2), 1.75 (6H, s, CH_3), 2.10–2.40 (4H, m, CH_2C=), 3.91 (1H, br. s, C*H*OH); ^{13}C NMR δ 20.3 (q), 22.9 (t), 31.7, 35.8 (t), 71.4 (d), 126.2 (s), 131.9 (s); *m*/*z* (EI) found 149.1328 (M$^+$ − H_3O), $C_{11}H_{17}$ requires 149.1330.

Ethyl [5-(isopropylidene)cyclooctylmethylene]acetate 33a

The cyclooctanol **31** was oxidized using DMSO–$(COCl)_2$ as described previously for the synthesis of **18a** to give 5-(isopropylidene)cyclooctanone **32** (69%) as a colourless oil, which crystallised slowly; ν_{max}(film)/cm^{-1} 1698; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.64 (6H, s, CH_3), 1.95–2.10 (4H, m, CH$_2$CH_2CH$_2$), 2.26 (4H, app. t, *J* 6.2 Hz, CH_2C=), 2.35 (4H, m, CH_2C=O); ^{13}C NMR δ 20.5 (q), 24.8 (t), 31.8 (t), 41.6 (t), 128.9 (s), 130.8 (s), 215.4 (s).

Ethyl trimethylsilylacetate (110 μl, 0.6 mmol) was added dropwise over 5 min to a stirred solution of LDA (2 M; 300 μl, 0.6 mmol) in THF (10 ml) at −78 °C and the mixture was then stirred at −78 °C for 30 min. A solution of the cyclooctanone **32** (50 mg, 0.3 mmol) in THF (2 ml) was added dropwise over 10 min at −78 °C, and the pale yellow solution was stirred at −78 °C for 1 h and then at room temperature for 4 h. Water was added and the mixure was extracted with ether. The dried ether extracts were evaporated under reduced pressure to leave a residue which was purified by chromatography on silica using petroleum ether–diethyl ether (95 : 5) as eluent to give the *alkene* (46 mg, 65%) as a colourless oil; ν_{max}(film)/cm^{-1} 1712, 1632; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.28 (3H, t, *J* 7.1 Hz, $CO_2CH_2CH_3$), 1.53 (3H, s, =CCH_3), 1.57 (3H, s, =CCH_3), 1.84–1.93 (2H, m, CH_2CH_2CH_2), 1.94–2.00 (2H, m, CH$_2$CH_2CH$_2$), 2.19 (4H, br. t, *J*∼6.1 Hz, CH_2C=C(CH_3)2), 2.24 (2H, ddd, *J* 6.1, 6.2, 1.0 Hz, CH_2C=CCO$_2$Et), 2.73 (2H, dd, *J* 6.1, 6.2 Hz, CH_2C=CCO$_2$Et), 4.13 (2H, q, *J* 7.1 Hz, $CO_2CH_2CH_3$), 5.59 (1H, s, C=C*H*CO$_2$Et); ^{13}C NMR δ 14.3 (q), 20.31 (s), 20.8 (q), 24.9 (t), 26.5 (t), 30.7 (t), 31.0 (t), 32.0 (t), 39.0 (t), 76.5 (t), 113.7 (d), 127.1 (s), 130.8 (s), 166.3 (s), 167.0 (s); *m*/*z* (EI) found 236.1767 (M$^+$), $C_{15}H_{24}O_2$ requires 236.1776.

[5-(Isopropylidene)cyclooctylmethylene]acetic acid 33b

Ethyl (5-(isopropylidene)cyclooctylmethylene)acetate **33a** was saponified with NaOH as described earlier in the synthesis of **28b** to give a 4 : 1 mixture of 5-(isopropylidene)cyclooctylmethylene)acetic acid and its positional isomer 5-(isopropylidene)-cycloocten-1-ylacetic acid (22 mg, 55%) as a colourless solid; ν_{max}(film)/cm^{-1} 3188, 1692, 1626; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.45, 1.48 (2.4H each, s, CH_3, major isomer), 1.56, 1.57 (0.6H each, s, CH_3, minor isomer), 1.68–1.91 (4H, m, CH_2), 2.02–2.20 (6H, m, CH_2 and CH_2C=CHCO$_2$H, major isomer), 2.64 (1.6H, dd, *J* 6.1, 6.2 Hz, CH_2C=CHCO$_2$H, major isomer), 2.94 (0.4H, s, CH_2CO$_2$H, minor isomer), 5.53 (0.8H, s, =C*H*CO$_2$H, major isomer), 5.57 (0.2H, m, =C*H*CH$_2$, minor isomer); ^{13}C NMR δ 20.3 (q), 20.6 (q), 24.9 (t), 26.6 (t), 28.7 (t), 30.8 (t), 31.0 (t), 32.0 (t), 34.6 (t), 39.2 (t), 42.6 (t), 113.0 (d), 126.5 (s), 127.7 (s), 129.78 (s), 130.7 (d), 131.9 (s), 133.1 (s), 171.0 (s), 171.8 (s), 178.5 (s); *m*/*z* (EI) found 208.1464 (M$^+$), $C_{13}H_{20}O_2$ requires 208.1463.

The thioester 33c

Following the general procedure,[15] a 4 : 1 mixture of the acid **33b** and its positional isomer was converted into a mixture of the corresponding conjugated and non-conjugated thioesters (41 mg, 84%), which was obtained as a colourless oil; ν_{max}(film)/cm^{-1} 2923, 1667, 1605; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.44, 1.50, 1.56 (6H, s, 2 × CH_3), 1.79–1.92 (4H, m, CH_2), 2.02–2.14 (6H, m, CH_2), 2.63 (1.4H, dd, *J* 5.9, 6.3 Hz, CH_2C=CHCOS, major isomer), 2.86–2.98 (2H, m, ArCH$_2$CH_2S), 2.99–3.07 (2H, m, ArCH_2CH_2S), 3.12 (0.6H, s, CH$_2$COS, minor isomer), 5.58 (0.3H, m, CH_2C*H*=CCH_2COS, minor isomer), 5.86 (0.7H, br. s, =C*H*COS, major isomer), 6.80–6.86 (1H, m, arom. C*H*), 7.18–7.23 (3H, m, arom. C*H*), 7.73 (1H, d, *J* 8.2 Hz, arom. C*H*); ^{13}C NMR δ 20.0 (q), 20.4 (q), 20.5 (q), 20.8 (q), 24.8 (t), 25.0 (t), 26.5 (t), 26.8 (t), 28.6 (t), 29.0 (t), 31.0 (t), 31.1 (t), 31.7 (t), 32.0 (t), 34.7 (t), 38.8 (t), 40.5 (t), 40.8 (t), 52.1 (t), 100.4 (s), 121.1 (d), 126.5 (s), 128.0 (d), 128.3 (d), 128.4 (d), 128.5 (d), 128.6 (d), 130.0 (d), 130.6 (d), 131.9 (s), 132.3 (s), 133.6 (s), 139.5 (d), 139.4 (d), 142.9 (s), 143.8 (s), 165.0 (s), 187.4 (s), 197.8 (s).

2,2-Dimethyltricyclo[3.3.3.0^{1,5}]undecane-3-one 34

The thioester **33c** was treated with Bu_3SnH–AIBN, according to the general procedure and gave the tricyclo[3.3.3.0^{1,5}]undecane-3-one (60%) as colourless crystals which melted just above room temperature; ν_{max}(film)/cm^{-1} 1735; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.0 (6H, s, CH_3), 1.33–1.54 (4H, m, CH_2), 1.56–1.66 (4H, m, CH_2), 1.66–1.85 (4H, m, CH_2), 2.37 (2H, s, CH_2C=O); ^{13}C NMR δ 22.8 (q), 26.1 (t), 36.5 (t), 43.3 (t), 50.3 (t), 51.1 (s), 53.6 (s), 63.2 (s), 223.4 (s); *m*/*z* (EI) found 192.1514 (M$^+$), $C_{13}H_{20}O$ requires 192.1514.

4,4-Dimethyltetracyclo[3.3.3.0^{1,5}.0^{2,8}]undecane-3-one 35

Following the procedures described by Cook *et al.*,[18] the tricyclo[3.3.3.0^{1,5}]undecane-3-one **34** (215.9 mg) was first converted into 2,2-dimethyltricyclo[3.3.3.0^{1,5}]4-diazaundecane-3-one (78 mg, 32%); ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.08 (6H, s, CH_3), 1.42 (2H, dd, J 12.5, 6.3 Hz, CH_2), 1.66–1.93 (10H, m, CH_2); ^{13}C NMR δ 24.1 (q), 26.5 (t), 36.1 (t), 39.6 (t), 42.4 (s), 51.1 (s), 59.2 (s), 64.8 (s), 205.0 (s), and then into the tetracyclo[3.3.3.0^{1,5}.0^{2,8}]-undecane-3-one (25 mg, 36%); ν_{max}(film)/cm^{-1} 1712; ^{1}H NMR δ 0.84 (3H, s, CH_3), 1.01 (3H, s, CH_3), 1.25–1.4 (1H, m, cyclopropyl CH), 1.5–1.6 (1H, m, cyclopropyl CH), 1.75–1.98 (6H, m, CH_2), 2.01–2.16 (4H, m, CH_2); ^{13}C NMR δ 17.7 (q), 25.9 (q), 27.3 (t), 28.6 (t), 28.7 (t), 30.4 (t), 35.6 (d), 39.5 (d), 41.6 (t), 52.5 (s), 54.7 (s), 63.1 (s), 220.8 (s).

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