Synthesis of the Taxane Ring System using an Intramolecular Diels–Alder Reaction of a 2-Substituted Diene

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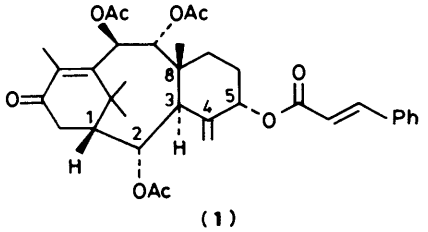
A synthesis of (1*R*/*S*,3*R*/*S*,8*S*/*R*)-8-methyltricyclo[9.3.1.0^{3,8}]pentadec-11-en-2-one, which is the ring system of the taxane natural products and contains 3 chiral centres having the required relative configuration, is described.

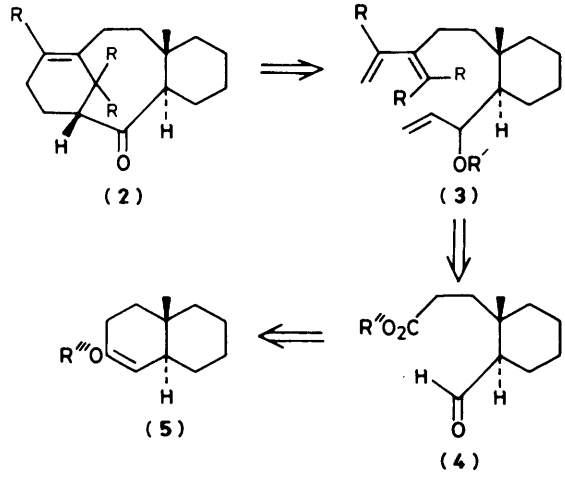
The structures of the taxane group of natural products isolated from the yew tree *Taxus baccata* and *T. cuspidata* were elucidated by the elegant degradative studies of Lythgoe and Nakanishi.[1] The compounds consist of a diterpenoid tricyclic ring system which occurs in nature as an ester of β-dimethylamino-β-phenylpropionic acid, but they are best isolated as the cinnamate esters, *e.g.* taxinine (**1**). Several compounds with



(**1**)

more complicated structures have also been isolated,[2] some of which contain an oxetane ring; antileukaemic and tumour-inhibiting activity has been reported for two of these compounds.[3] Synthetic approaches to the taxane structure have been stimulated by this observation of biological activity and many approaches have been published[4] since we began our studies, although no complete synthesis of a taxane natural product has yet been achieved.

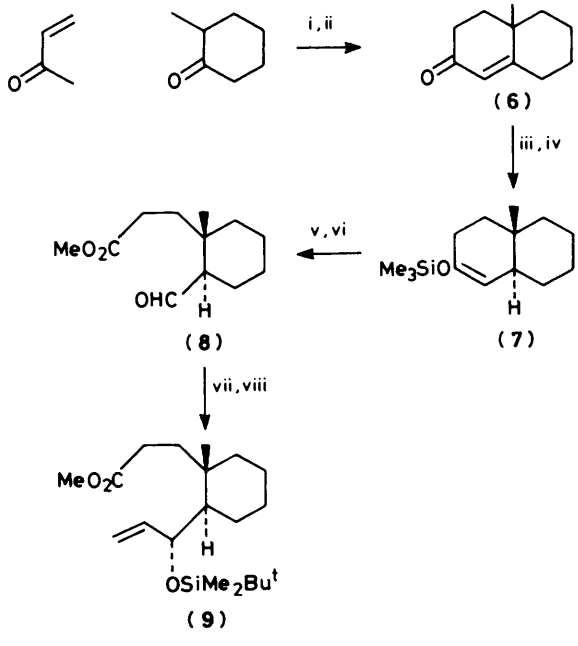
Our approach[5,†] to the taxane ring system is outlined in the retrosynthetic analysis shown in Scheme 1. The key stage is the intramolecular Diels–Alder reaction to construct both the A and the B rings in model system (**2**) which leads back to the precursor (**3**). The intramolecular Diels–Alder reaction of 2-substituted dienes to give bridgehead olefins has been extensively studied by Shea.[6] Suitable methods for diene and olefin construction will then be required, a convenient substrate being (**4**) where the two carbonyl groups are distinguished and can react separately. The 1,6-dicarbonyl reconnection leads to the decalin (**5**) which would be readily cleaved by ozonolysis according to literature precedent. The decalin (**5**) is the product of known chemistry as shown below. One point to note at this planning stage is that a new chiral centre is created in the conversion of triene (**3**) into tricycle (**2**); clearly, only one diastereoisomer is required.



Scheme 1.

Results and Discussion

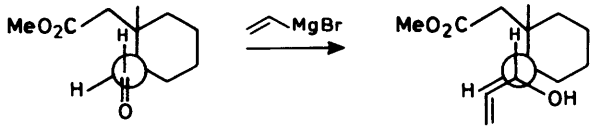
The starting point of the synthesis is the Robinson annelation reaction between 2-methylcyclohexanone and methyl vinyl ketone which leads to enone (**6**);[7] although the Li–NH_3 reduction of enone (**6**) had been extensively studied by Stork,[8] our attempts to reproduce the published procedure, which



Scheme 2. *Reagents and conditions:* i, NaOEt (catalytic), −10 °C, 12 h; ii, KOH, water, steam distil; iii, Li (2.2 equiv.), NH_3 (liquid), THF, 15 min; destroy excess of Li, remove NH_3, add THF, cool to −10 °C; iv, Me_3SiCl (2 equiv.), Et_3N (2 equiv.); v, O_3, CH_2Cl_2, MeOH, Sudan Red III; vi, CH_2N_2; vii, CH_2=$CHMgBr$ (1 equiv.), THF, −78 °C; viii, $Bu^tMe_2SiOSO_2CF_3$ (1.5 equiv.), 2,6-lutidine (2.0 equiv.), CH_2Cl_2, room temp.

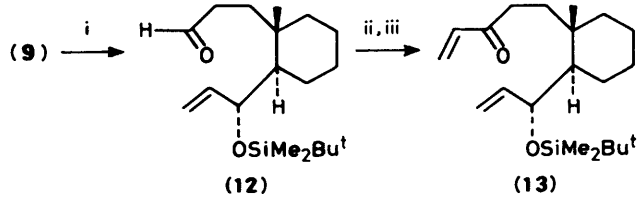
† After completion of most of this work a Diels–Alder approach to a C-aromatic taxane skeleton was independently reported (K. J. Shea and P. D. Davis, *Angew. Chem., Int. Ed. Engl.*, 1983, **22**, 419).

involves reduction with an excess of lithium in liquid ammonia and 0.8 equiv. of Bu^{t}OH followed by trapping with Me_3Si-Cl–Et_3N, resulted in net reduction of the double bond of enone (**6**). After considerable experimentation we obtained a 70% yield of compound (**7**) along with starting materials (~20%) when we used 3 equiv. of lithium in liquid ammonia without Bu^{t}OH and a reaction time of 30 min; the ammonia was then removed and the excess of lithium was destroyed with isoprene before the enolate was trapped with Me_3SiCl–Et_3N (1:1) in tetrahydrofuran (THF). Ozonolysis of the silyl enol ether (**7**) followed by work-up with dimethyl sulphide and esterification with diazomethane provided the ester aldehyde (**8**) as a single diastereoisomer in 78% yield. Highly efficient 1,2-asymmetric induction occurred in the reaction of aldehyde (**8**) to give a single diastereoisomer of compound (**9**) after protection (Scheme 2). Attempts to prepare crystalline derivatives of ester (**9**) suitable for *X*-ray analysis were unsuccessful and our assignment of the relative stereochemistry of the new chiral centre in compound (**9**) is based on the open-chain model for Cram's Rule of steric control in asymmetric induction.[9] The normal reactive conformation for this explanation is structure (**10**) where the quaternary centre is *anti* to the carbonyl oxygen; attack of vinyl Grignard reagent from the least hindered side leads to alcohol (**11**) where the chirality at the new centre is defined.



(**10**) (**11**)

The next problem in the route was the conversion of the ester group in compound (**9**) into a diene fragment. Di-isobutylaluminium hydride (DIBAH) reduction of ester (**9**) to aldehyde (**12**) was readily achieved at −78 °C in 67% yield. Subsequent reaction with vinylmagnesium bromide (60% yield) and oxidation with pyridinium chlorochromate (PCC) (81% yield) furnished the enone (**13**) (Scheme 3). However, enone (**13**) was completely unreactive towards methylenetriphenylphosphorane in dimethyl sulphoxide[10] (DMSO) and trimethylsilylmethylmagnesium chloride.[11]



(**12**) (**13**)

Scheme 3. *Reagents and conditions:* i, DIBAH in hexane (1 equiv.), PhMe, −78 °C; ii, CH_2=CHMgBr (1 equiv.), THF, −40 °C; iii, PCC, CH_2Cl_2

More success was obtained using essentially these steps but in a different order* as shown in Scheme 4. Aldehyde (**12**) was heated under reflux with trimethylsilylmethylmagnesium chloride in ether for 1 h to give the β-hydroxy silane (**14**) in 64% yield after chromatography. Rapid *in situ* Collins oxidation[12] to a β-keto silane was followed by addition of vinylmagnesium bromide at 25 °C. The crude product (**15**) was treated with a saturated solution of sodium acetate in glacial acetic acid[13] to effect the Peterson elimination, and this led to the diene (**16**) in 51% yield from alcohol (**14**) and 41% yield from aldehyde (**12**). High-field n.m.r. spectra of the diene (**16**) showed no trace of any regioisomeric diene products; clearly, nucleophilic attack at a silicon in the cationic intermediate is more favourable than nucleophilic attack at a proton which is in line with a clearly expressed generalisation of this phenomenon.[14] The deprotection of compound (**16**)[15] would only work in glass apparatus and was followed directly by *in situ* Collins oxidation[12] to give the enone (**17**) in 71% overall yield. Diels–Alder cyclisation catalysed by diethylaluminium chloride[16] occurred smoothly at room temperature to give ketone (**18**) as a white crystalline, single isomer, m.p. 84—85 °C in 72% yield.

The next problem to be addressed was to determine the relative stereochemistry at C-1, the new chiral centre in the tricyclic product (**18**). Considerations of Dreiding models and the preference for the formation of '*meta*' products in this type of intramolecular Diels–Alder reaction[6] leads to the definition of two possible modes of cyclisation for enone (**17**). The first is shown in Scheme 5. The eight-membered ring is formed in a twist chair-boat conformation; the energy of this conformation has been estimated by Hendrickson[17] to be 2 kcal† higher than the most stable conformation in cyclo-octane. Clearly our molecule is much more complicated than cyclo-octane, but Scheme 5 indicates that this mode of cyclisation leading to diastereoisomer (**19**) will be higher in energy than that indicated in Scheme 6.

Extensive studies on the conformation of medium-ring compounds indicate that the preferred conformation of cyclo-octane is the chair-boat.[17,18] Consequently it would appear to be a reasonable prediction that, in Scheme 6, as the eight-membered ring in both the transition state and product defines a chair-boat conformation, then this mode of cyclisation will be preferred over that shown in Scheme 5. The first evidence in favour of structure (**20**) came from n.O.e. studies; irradiation of 3-H at δ_H 3.19 produced a 5% n.O.e. of 12 H at δ_H 5.77 showing that these two protons are in close proximity, which is not possible in structure (**19**).

Finally, a crystal of compound (**18**) suitable for *X*-ray analysis was obtained and the result is shown in the Figure which confirms the structure as conformer (**20**). Clearly the remarkable conformational control in the cyclisation to give conformer (**20**) shown in Scheme 6 may have applications to other cases of remote asymmetric induction in the formation of medium-ring compounds and we are at present studying examples of this.

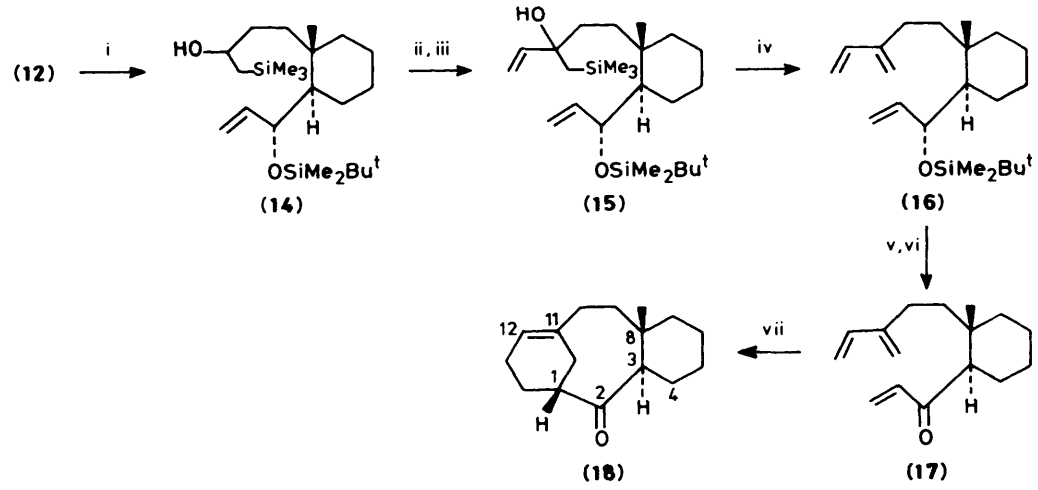
In conclusion the tricycloketone (**18**) is produced with the same relative configuration as the taxane natural product taxinine (**1**).

Experimental

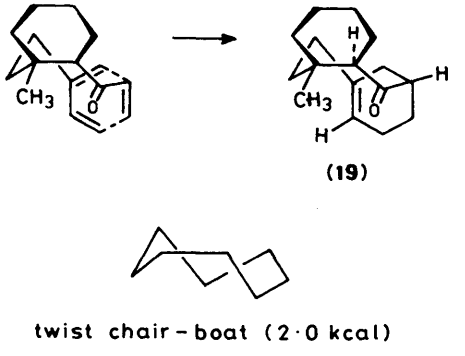
All 90 MHz ^{1}H n.m.r. spectra were recorded using Me_4Si as internal standard on a Varian EM390 spectrometer and all 15 MHz ^{13}C n.m.r. spectra were recorded on a JOEL JNM-FX60 Fourier Transform spectrometer. High-field ^{1}H n.m.r. (400 MHz) and ^{13}C n.m.r. (10 MHz) spectra were recorded using the high-field n.m.r. service at Warwick University. I.r. spectra were recorded on a Perkin-Elmer 298 spectrometer and mass spectra on a Micromass 16B spectrometer. Accurate mass measurments were made at PCMU Harwell and elemental analysis was carried out by CHN analysis, Wigston. M.p.s were determined on a Kofler hot-stage and are uncorrected. Flash chromatography was carried out according to the method of Still[19] using silica gel manufactured by Merck and Co., Kieselgel 60, 230—240 mesh (ASTM). Preparative layer chromatography (p.l.c.)

* Full details of the scope and limitations of this diene synthesis will be submitted for publication separately.

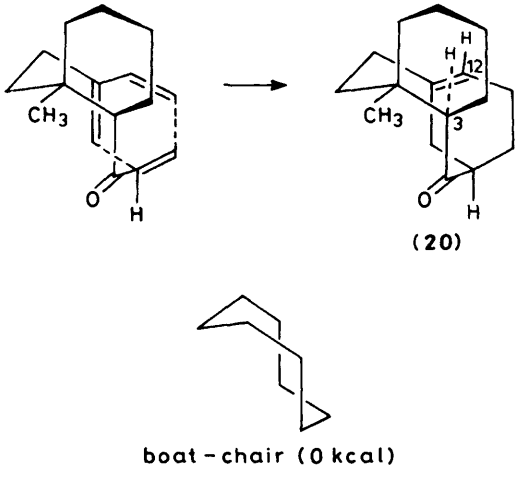
† 1 kcal = 4.185 kJ.



Scheme 4. *Reagents and conditions:* i, Me_3SiCH_2MgCl, Et_2O, reflux, 1 h; ii, CrO_3 (6 equiv.), pyridine (12 equiv.), CH_2Cl_2, room temp., 30 s; iii, CH_2=CHMgBr (1 equiv.), THF, room temp., 1 h; iv, $MeCO_2H$, $MeCO_2Na{\cdot}3H_2O$; v, HF (15%), water, MeCN, room temp., 1.5 h; vi, as ii, room temp., 5 min; vii, Et_2AlCl in hexane (1 equiv.), CH_2Cl_2, room temp., 1.5 h



Scheme 5. Cyclisation *via* the twist chair-boat conformation of the eight-membered ring



Scheme 6. Cyclisation *via* the boat-chair conformation of the eight-membered ring

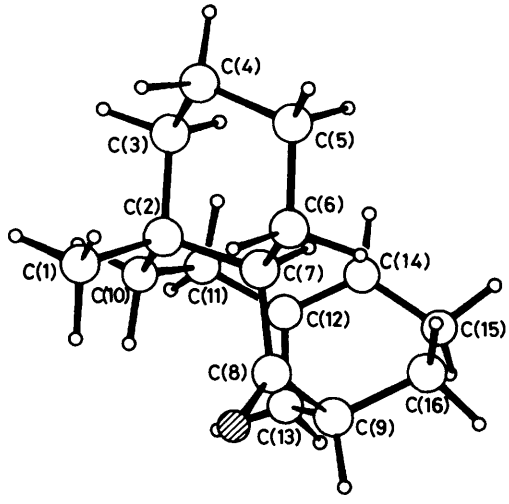


Figure. A view of the *X*-ray molecular structure of compound (**18**). Atoms are represented by circles of arbitary radius. The shaded atom is oxygen, the large circle is carbon, and the small circle is hydrogen. The crystallographic numbering scheme is shown

conducted on precoated glass plates (60F-254) manufactured by Merck and Co. The concentration of butyl-lithium and methyl-lithium–lithium bromide was determined by back-titration with 0.1M-HCl from solution in dibromomethane and water, using phenolphthalein as indicator. All solvents were dried by standard procedures. Light petroleum refers to that fraction boiling in the range 40—60 °C.

trans-1,2,3,4,4a,5,6,8a-*Octahydro*-4a-*methyl*-7-*trimethylsiloxynaphthalene* (**7**).—A degassed solution of 4,4a,5,6,7,8-hexahydro-4a-methylnaphthalen-2(3*H*)-one (**6**) (8.4138 g, 51 mmol) in dry THF (205 ml) was added to a solution of freshly extruded lithium wire in dry distilled ammonia (~400 ml) under nitrogen. The blue solution was stirred for 30 min and then the blue colour was discharged by the addition of isoprene (2.5 ml), leaving a white solution. The ammonia was then removed by flushing with nitrogen, followed by evaporation at reduced pressure (5 mmHg at 40 °C). A further aliquot of THF (160 ml) was added and the solution was cooled to −10 °C. A mixture of trimethylsilyl chloride (13.02 ml, 102 mmol) and triethylamine (14.30 ml, 102 mmol) was added and the solution was stirred for 30 min. Light petroleum (300 ml) was then added, followed by cold saturated brine (300 ml). The organic layer was separated,

washed with brine (300 ml), and dried ($MgSO_4$). After removal of the solvent under reduced pressure and flash chromatography (1% ether–light petroleum), *trans*-1,2,3,4,4a,5,6,8a-octahydro-4a-methyl-7-trimethylsiloxynaphthalene (**7**) was obtained as an oil (8.5691 g, 70%), R_F 0.72 (1% ether–light petroleum; I_2 visualizer); $\nu_{max.}$(film) 2 960s, 2 920s, 2 850s, 1 660s (C=C), 1 260s, 1 250s, 1 195s, 1 115s, 930s, and 905s cm^{-1}; δ_H (90 MHz; $CDCl_3$) 0.2 (9 H, s, Me_3Si), 0.86 (3 H, s, Me), and 1.15—2.15 (13 H, m), 4.55 (1 H, br s, 1-H); g.l.c. (3% OV17; temp. 180 °C) R_t 2.2 min.

Methyl trans-3-(2′-*Formyl*-1′-*methylcyclohexyl*)*propionate* (**8**).—A solution of *trans*-1,2,3,4,4a,5,6,8a-octahydro-4a-methyl-7-trimethylsiloxynaphthalene (**7**) (500 g, 2.1 mmol) in methanol (5 ml)–dichloromethane (4 ml) was ozonised at −78 °C. The reaction was monitored by t.l.c. (light petroleum; I_2); alternatively Sudan Red III was used as indicator.[20] Once starting material had disappeared or the red colour of Sudan Red III had discharged, dimethyl sulphide (0.5 ml) was added and the solution was allowed to warm to room temperature. The solvent was removed under reduced pressure to leave a viscous pale yellow oil, $\nu_{max.}$(film) 3 660—2 450br (OH of acid), 2 920s, 2 860s, 1 715br s (C=O), and 1 015 cm^{-1}.

The yellow oil was then dissolved in ether (5 ml), and an ethereal solution of diazomethane was added until a yellow colour persisted. The excesses of diazomethane and ether were then evaporated off with a stream of nitrogen. The remaining oil was redissolved in ether (10 ml), and the solution was washed with saturated aqueous NH_4Cl (10 ml) and dried ($MgSO_4$). After removal of the solvent under reduced pressure and flash chromatography, methyl *trans*-3-(2′-formyl-1′-methylcyclohexyl)propionate (**8**) was obtained as an oil (281 mg, 64%), R_F 0.3 [(4:1) light petroleum–ether]; $\nu_{max.}$(film) 2 930s, 1 735s (C=O, ester) 1 715sh (C=O, aldehyde), 1 445m, 1 250m, and 1 170s cm^{-1}; δ_H (90 MHz; $CDCl_3$) 1.02 (3 H, s, 1′-Me), 1.20—1.95 (10 H, m, 5 × CH_2), 2.00—2.45 (3 H, m, 2-H_2 and 2′-H), 3.65 (3 H, s, OMe), and 9.72 (1 H, d, $J_{2',CHO}$ 3 Hz, CHO); *m/z* 212 (M^+, 4%), 125 (20), 109 (38), 97 (56), 96 (42), 95 (41), 88 (30), 87 (100), and 81 (50); g.l.c. (3% OV17; temp. 196 °C) R_t 3.9 min. Samples sent for high-field n.m.r. and microanalysis decomposed in transit. Conversion of the aldehyde (**8**) (50 mg, 0.23 mmol) into its 2,4-dinitrophenylhydrazone was carried out by the standard method and after two recrystallisations from ethanol gave *methyl* trans-3-[2′-(2″,4″-*dinitrophenylhydrazonomethyl*)-1′-*methylcyclohexyl*]*propionate* as yellow needles (21 mg, 23%), m.p. 103.5—104.5 °C (Found: C, 54.95; H, 6.2; N, 14.2. $C_{18}H_{24}N_4O_6$ requires C, 55.09; H, 6.16; N, 14.28%); δ_H (400 MHz; $CDCl_3$) 0.96 (3 H, s, 1′-Me), 1.22—1.82 (10 H, m), 2.25—2.45 (3 H, m, 2-H_2 and 2′-H), 3.65 (3 H, s, OMe), 7.44 (1 H, d, *J* 7.2 Hz, CH=N), 7.90 (1 H, d, *J* 9.6 Hz, 6″-H), 8.27 (1 H, ddd, *J* 9.6, 2.5, and 0.5 Hz, 5″-H), 9.05 (1 H, d, *J* 2.5 Hz, 3″-H), and 10.99 (1 H, br s, NH); δ_C (100 MHz; $CDCl_3$) 19.03 (q, 1′-CH_3), 21 31 (t), 25.10 (t), 25.95 (t), 28 19 (t), 35.55 (s, C-1′), 36.44 (t), 37.53 (t), 47.92 (d, C-2′), 51.57 (q, OCH_3), 116.49 (d), 123.31 (d), 128.78 (s), 129.79 (d), 137.75 (s), 144.96 (s), 153.98 (d, NC=N), and 174.24 (s, C-1); *m/z* 392 (M^+, 1%), 357 (21), 135 (34), 134 (26), 123 (26), 109 (30), 95 (86), 93 (52), 91 (46), 74 (46), 67 (82), and 55 (100).

Methyl trans-3-[2′-(1″-*Hydroxyprop*-2″-*enyl*)-1′-*methylcyclohexyl*]*propionate*.—A 1M solution of vinylmagnesium bromide (17.4 ml, 17.4 mmol) in THF was added dropwise to a solution of methyl *trans*-3-(2′-formyl-1′-methylcyclohexyl)-propionate (**8**) (3.7 g, 17 mmol) in dry THF (38 ml) at −78 °C under nitrogen. After 20 min no starting material was visible on t.l.c. The reaction mixture was quenched with 1M-HCl (100 ml) and extracted with ether (3 × 100 ml). Each extract was washed with saturated brine (50 ml) and the combined extracts were dried ($MgSO_4$). After removal of the solvent under reduced pressure and flash chromatography [(3:1 light petroleum–ether], methyl *trans*-3-[2′-(1″-hydroxyprop-2″-enyl)-1′-methylcyclohexyl]propionate was obtained as an oil (2.9487 g, 71%), R_F 0.39 [(3:1) light petroleum–ether]; $\nu_{max.}$(film) 3 520br (OH), 2 920s, 2 860s, 1 735s (C=O, ester), 1 640w (C=C), 1 435s, 1 195s, and 1 175s cm^{-1}; δ_H (90 MHz; $CDCl_3$) 1.00 (3 H, s, 1′-Me), 1.12—1.90 (12 H, m, 5 × CH_2, 2′-H, and OH), 2.20—2.36 (2 H, m, 2-H_2), 3.60 (3 H, s, OMe), 4.44 (1 H, br s, 1″-H), 5.00—5.28 (2 H, m, 3″-H_2), and 5.86 (1 H, ddd, $J_{2'',3'' trans}$ 17, $J_{2'',2'' cis}$ 10, $J_{1'',2''}$ 4 Hz, 2″-H); *m/z* 222 (M^+ − 18, 5%), 184 (26), 183 (42), 152 (63), 151 (73), 135 (47), 133 (45), 123 (21), 110 (26), 109 (100), 97 (84), 96 (42), 95 (47), 93 (40), 88 (39), 81 (63), 79 (31), 67 (73), and 55 (84). The compound was characterised further as its dinitrobenzoate derivative described below.

Methyl trans-3-{2′-[1″-(3‴,5‴-*Dinitrobenzoyloxy*)*prop*-2″-*enyl*]-1′-*methylcyclohexyl*}*propionate*.—A solution of methyl *trans*-3-[2′-(1″-hydroxyprop-2″-enyl)-1′-methylcyclohexyl]-propionate (70 mg, 291 μmol) and 3,5-dinitrobenzoyl chloride (70 mg, 232 μmol) in dry pyridine (1.0 ml) was stirred at room temperature for 1 h. The mixture was then diluted with ether (50 ml), washed successively with 2M-HCl (2 × 30 ml) and saturated aqueous sodium hydrogen carbonate, and dried ($MgSO_4$). Removal of the solvent under reduced pressure left a yellow oil which crystallised upon trituration with hexane (external cooling). The solid was recrystallised twice from hexane–ether (2:1) to give *methyl* trans-3-{2′-[1″-(3‴,5‴-*dinitrobenzoyloxy*)*prop*-2″-*enyl*]-1′-*methylcyclohexyl*}*propionate* as white hexagonal platelets (49 mg, 39%), m.p. 88—89 °C (Found: C, 57.95; H, 6.0; N, 6.4. $C_{21}H_{26}N_2O_8$ requires C, 58.05; H, 6.03; N, 6.54%); $\nu_{max.}$(CH_2Cl_2) 2 940m, 1 735s (C=O, esters), 1 630 (C=C), 1 550s, 1 345s, 1 265s, and 1 170s cm^{-1}; δ_H (90 MHz; $CDCl_3$) 0.84 (3 H, s, 1′-Me), 1.05—2.10 (11 H, m, 5 × CH_2 and 2′-H), 2.15—2.38 (2 H, m, 2-H_2), 3.64 (3 H, s, OMe), 5.05—6.10 (4 H, m, 1″- and 2″-H, and 3″-H_2), and 9.05—9.20 (3 H, m, ArH); *m/z* 434 (M^+, ~1%), 222 (25), 183 (81), 151 (84), 135 (100), 133 (40), 109 (40), 107 (31), 93 (30), 89 (46), and 79 (19).

Methyl trans-3-{2′-[1″-(*Dimethyl*-*t*-*butylsiloxy*)*prop*-2″-*enyl*]-1′-*methylcyclohexyl*}*propionate* (**9**).—t-Butyltrimethylsilyltrifluoromethanesulphonate[21] (4.23 ml, 18 mmol) was added dropwise to a solution of methyl *trans*-3-[2′-(1″-hydroxyprop-2″-enyl)-1′-methylcyclohexyl]propionate (2.9487 g, 12 mmol) and dry 2,6-dimethylpyridine (2.86 ml, 24 mmol) in dichloromethane (13 ml) at room temperature under nitrogen. After t.l.c. showed the disappearance of starting material, dichloromethane (50 ml) was added. The mixture was washed with water (3 × 50 ml) and dried ($MgSO_4$). The solvent was removed under reduced pressure and flash chromatography (5% ether in light petroleum) gave *methyl* trans-3-{2′-[1″-(*dimethyl*-*t*-*butylsiloxy*)*prop*-2″-*enyl*]-1′-*methylcyclohexyl*}-*propionate* (**9**) as a single diastereoisomer (3.2247 g, 75%), R_F 0.44 (5% ether in light petroleum) (Found: C, 67.9; H, 10.7. $C_{20}H_{38}O_3Si$ requires C, 67.74; H, 10.80%); $\nu_{max.}$(film) 2 925s, 2 850s, 1 742s (C=O, ester), 1 254s, 1 170s, 1 095s, 1 076s, 1 032s, 1 006s, 921s, 838s, and 775s cm^{-1}; δ_H (400 MHz; $CDCl_3$) −0.04 (3 H, s MeSi), 0.02 (3 H, s, MeSi), 0.85 (9 H, s, SiBu^t), 0.91 (3 H, s, 1′-Me), 1.04—1.76 (11 H, m), 2.24 (2 H, m, 2-H_2), 3.64 (3 H, s, OMe), 4.31 (1 H, br d, $J_{1',2'}$ 7.2 Hz, 1″-H), 4.95 (1 H, ddd, $J_{2'',3'' cis}$ 10.3, $J_{3'',3''}$ 1.5, $J_{1'',3''}$ 1.0 Hz, 3″-H), 5.03 (1 H ddd, $J_{2'',3'' trans}$ 17.4, $J_{3'',3''}$ 1.5, $J_{1'',3''}$ 1.3 Hz, 3″-H), and 5.86 (1 H, ddd, *J* 17.4, 10.3, and 7.2 Hz, 2″-H); δ_C (100 MHz; $CDCl_3$) −3.66 (q, CH_3Si), −2.23 (q, CH_3Si), 19.01 (s, Me_3CSi), 21.21 (q, 1′-CH_3), 22.06 (t), 22.97 (t), 26.89 (q, Me_3CSi), 27.51 (t), 29.37 (t), 36.54 (s, C-1′), 38.29 (t), 39.26 (t), 51.68 (d, C-2′), 52.35 (q, OCH_3), 73.85 (d, C-1″), 114.26 (t, C-3″), 143.62 (d, C-2″), and 175.73 (s, C=O); *m/z* 354 (M^+, ~1%), 300 (22), 299 (70), 172

(45), 171 (100), 151 (19), 115 (60), 109 (36), 99 (35), 95 (28), 93 (27), 91 (20), 81 (42), 73 (63), 67 (44), and 55 (56).

trans-3-{2′-[1″-(*Dimethyl-t-butylsiloxy*)*prop*-2″-*enyl*]-1′-*methylcyclohexyl*}*propionaldehyde* (**12**).—A 1M solution of DIBAH in toluene (2.8 ml, 2.8 mmol) was added dropwise to a solution of methyl *trans*-3-{2′-[1″-(dimethyl-t-butylsiloxy)-prop-2″-enyl]-1′-methylcyclohexyl}propionate (**9**) (1 g, 2.8 mmol) in dry toluene (40 ml) at −78 °C under nitrogen. After the disappearance of starting material (t.l.c.) the reaction mixture was quenched with 1M-HCl (150 ml), and extracted with ether (3 × 100 ml), and each extract was washed with saturated brine (100 ml) and the combined extracts were dried ($MgSO_4$). After removal of solvent under reduced pressure and flash chromatography *trans*-3-{2′-[1″-(dimethylbutylsiloxy)-prop-2″-enyl]-1′-methylcyclohexyl}propionaldehyde (**12**) was obtained as an oil (607 mg, 67%), R_F 0.35 (5% ether in light petroleum); $\nu_{max.}$(film) 2 930s, 2 860s, 1 725s (C=O, aldehyde), 1 640w (C=C), 1 255s, 1 095s, 920s, 840s, and 775s cm^{-1}; δ_H (90 MHz; $CDCl_3$) −0.02 (3 H, s, MeSi), 0.02 (3 H, MeSi), 0.84 (9 H, s SiBu^t), 0.92 (3 H, s, 1′-Me), 1.02—1.90 (11 H, m, 5 × CH_2 and 2′-H), 2.26—2.48 (2 H, m, 2-H_2), 4.32 (1 H, br d, $J_{1′,2′}$ 7 Hz, 1″-H), 4.92—5.12 (2 H, m, 3″-H_2), 5.90 (1 H, ddd, $J_{2″,3″\ trans}$ 17, $J_{2″,3″\ cis}$ 10, $J_{1″,2″}$ 7 Hz, 2″-H), and 9.74 (1 H, t, $J_{1,2}$ 2 Hz, CHO). Conversion of the aldehyde (**12**) (91.5 mg, 0.282 mmol) into its 2,4-dinitrophenylhydrazone was carried out by the standard method and after two recrystallisations from ethanol gave trans-2-[1′-(*dimethyl-t-butylsiloxy*)*prop*-2′-*enyl*]-1-[3″-2‴,4‴-*dinitrophenylhydrazono*) *propyl*]-1-*methylcyclohexane* as yellow needles (57 mg, 40%), m.p. 116.5—117.5 °C (Found: C, 59.5; H, 8.0; N, 11.1. $C_{25}H_{40}N_4O_5Si$ requires C, 59.49; H, 7.99; N, 11.10%); $\nu_{max.}$(CH_2Cl_2) 3 310 (NH) 2 930s, 2 860s, 1 620s (C=N), 1 595 (C=C), 1 520s, 1 340s, 1 310s, 1 095s, and 835s cm^{-1}; δ_H (90 MHz; $CDCl_3$) −0.02 (3 H, s, MeSi), 0.02 (3 H, s, MeSi), 0.82 (9 H, s, SiBu^t), 0.94 (3 H, s, 1-Me), 1.05—1.85 (11 H, m, 5 × CH_2 and 2-H), 2.22—2.48 (2 H, m, 2″-H_2), 4.28 (1 H, br d, *J* 7 Hz, 1′-H), 4.90—5.10 (2 H, m, 3′-H_2), 4.70—6.08 (1 H, m, 2′-H), 7.48 (1 H, br t, *J* 5 Hz, CH=N), 7.85 (1 H, d, *J* 10 Hz, 6‴-H), 8.22 (1 H, dd, *J* 10, and 3 Hz, 5‴-H), 9.05 (1 H, d, *J* 3 Hz, 3‴-H), and 10.88 (1 H, br s, NH).

trans-5-{2-[1″-(*Dimethyl-t-butylsiloxy*)*prop*-2″-*enyl*]-1′-*methylcyclohexyl*}*pent*-1-*en*-3-*ol*.—A 1M solution of vinylmagnesium bromide in THF (2.5 ml, 2.5 mmol) was added dropwise to a stirred solution of *trans*-3-{2-[1″-(dimethyl-t-butylsiloxy)prop-2″-enyl]-1′-methylcyclohexyl}propionaldehyde (**12**) (651 mg, 2 mmol) in THF (20 ml) under nitrogen at −40 °C. After 10 min, t.l.c. still showed starting material and so a further aliquot of vinylmagnesium bromide (500 µl, 0.5 mmol) was added. After a further 10 min the reaction was quenched with 1M-HCl (150 ml) and the mixture was extracted with ether (3 × 100 ml). Each extract was washed with saturated brine and the combined extracts were dried ($MgSO_4$). After removal of the solvent under reduced pressure and flash chromatography (15% ether–light petroleum), *trans*-5-{2′-[1″-(dimethyl-t-butylsiloxy)prop-2″-enyl]-1′-methylcyclohexyl}-pent-1-en-3-ol was obtained as an oil (418 mg, 60%), R_F 0.43 and 0.36 (15% ether–light petroleum); $\nu_{max.}$(film) 3 360br (OH) 2 950s, 2 930s, 2 860s, 1 250s, 1 090s, 920s, 840s, and 770s cm^{-1}; δ_H (90 MHz; $CDCl_3$) −0.02 (3 H, s, MeSi), 0.04 (3 H, s, MeSi), 0.85 (9 H, s, SiBu^t), 0.92 (3 H, s, Me), 1.05—1.92 (14 H, m, 6 × CH_2, 2′-H, and OH), 4.02 (1 H, br s, 3-H), 4.32 (1 H, br d, $J_{1′,2′}$ 7 Hz, 1″-H), 4.90—5.32 (4 H, m, 1- and 3″-H_2), and 5.70—6.08 (2 H, m, 2- and 2″-H). T.l.c. suggested a mixture of diastereoisomers about the new chiral centre (C-3), which was not noticeable from the ^1H n.m.r. spectrum.

trans-5-{2′-[1″-(*Dimethyl-t-butylsiloxy*)*prop*-2″-*enyl*]-1′-*methylcyclohexyl*}*pent*-1-*en*-3-*one* (**13**).—A solution of *trans*-5-{2′-[1″-dimethyl-t-butylsiloxy)prop-2″-enyl]-1′-methylcyclohexyl}pent-1-en-3-ol (120 mg, 350 µmol) in dichloromethane (2 ml) was added in one portion to a suspension of PCC (113 mg, 526 µmol) in dichloromethane (2 ml) at room temperature. After 1 h the brown solution was diluted with ether (5 ml) and filtered through a short silica column. The residues were washed with ether (20 ml). Removal of the solvent gave *trans*-5-{2′-[1″-(dimethyl-t-butylsiloxy)prop-2″-enyl]-1′-methylcyclohexyl}-pent-1-en-3-one (**13**) as a pale yellow oil (100 mg, 81%), R_F 0.61 (10% ether–light petroleum); $\nu_{max.}$(film) 2 930s, 2 860s, 1685m (C=O), 1 620w (C=C), 1 250s, 1 090s, 970s, 840s, and 775s cm^{-1}; δ_H (400 MHz; $CDCl_3$) −0.03 (3 H, s, MeSi), 0.02 (3 H, s, MeSi), 0.86 (9 H, s, SiBu^t), 0.94 (3 H, s, Me), 1.07—1.74 (11 H, m, 5 × CH_2 and 2′-H), 2.47—2.54 (2 H, m, 4-H_2), 4.32 (1 H, br d, $J_{1′,2′}$ 7.2 Hz, 1″-H), 4.96 (1 H, ddd, $J_{2″,3″\ cis}$ 10.3, $J_{3″,3″}$ 1.6, $J_{1″,3″}$ 1.0 Hz, 3″-H), 5.02 (1 H, ddd, $J_{2″,3″\ trans}$ 17.4, $J_{3″,3″}$ 1.6, $J_{1″,3″}$ 1.3 Hz, 3″-H), 5.79 (1 H, dd, $J_{1,2\ cis}$ 10.3, $J_{1,1}$ 1.2 Hz, 1-H), 5.88 (1 H, ddd, *J* 17.4, 10.3, and 7.2 Hz, 2″-H), 6.20 (1 H, dd, $J_{1,2\ trans}$ 17.6, $J_{1,1}$ 1.2 Hz, 1-H), and 6.36 (1 H, dd, *J* 17.6 and 10.3 Hz, 2-H); δ_C (100 MHz; $CDCl_3$) −4.70 (q, CH_2Si), −3.28 (q, CH_3Si), 20.33 (t), 21.05 (q), 21.98 (t), 25.87 [q, $(CH_3)_3CSi$], 26.51 (t), 33.91 (t), 35.58 (s, C-1′), 36.26 (t), 38.50 (t), 50.81 (d, C-2′), 72.86 (d, C-1″), 113.32 (t), 127 (t), 136.59 (d), 142.83 (d), and 212.02 (s, C=O); $\lambda_{max.}$(MeOH) 210 nm (ε 8 450).

trans-4-{2′-[1″-(*Dimethyl-t-butylsiloxy*)*prop*-2″-*enyl*]-1′-*methylcyclohexyl*}-1-*trimethylsilylbutan*-2-*ol* (**14**).—A 1.6M solution of trimethylsilylmethylmagnesium chloride in ether (3 ml, 4.8 mmol) was added dropwise to a solution of *trans*-3-{2′-[1″-(dimethyl-t-butylsiloxy)prop-2″-enyl]-1′-methylcyclohexyl}propionaldehyde (**12**) (1.0034 g, 3.09 mmol) in ether (70 ml) at room temperature under nitrogen, and the mixture was then heated under reflux for 1 h. The mixture was then cooled, poured into saturated aqueous NH_4Cl (100 ml), and extracted with ether (3 × 100 ml). Each extract was washed with saturated brine (50 ml), the combined brine extracts were back-extracted (50 ml), and the combined organic layers were dried ($MgSO_4$). After removal of the solvent under reduced pressure and flash chromatography (5% ether–light petroleum), *trans*-4-{2′-[1″-(dimethyl-t-butylsiloxy)prop-2″-enyl]-1′-methylcyclohexyl}-1-trimethylsilylbutan-2-ol (**14**) was obtained as an oil (816 mg, 64%), R_F 0.30 (5% ether–light petroleum); $\nu_{max.}$(film) 3 420br (OH), 2 960s, 2 930s, 2 860s, 1 250s, 1 095s, 930, 860s, 840s, and 775s cm^{-1}; δ_H (90 MHz; $CDCl_3$) −0.02 (3 H, s, MeSi), 0.04 (12 H, s, SiMe and $SiMe_3$), 0.86 (9 H, s, SiBu^t), 0.92 (3 H, s, Me), 1.10—1.76 (16 H, m, 7 × CH_2, 2′-H, and OH), 3.69 (1 H, br, 2-H), 4.32 (1 H, br d, $J_{1′,2′}$ 7 Hz, 1″-H), 4.86—5.06 (2 H, m, 3″-H_2), and 5.84 (1 H, ddd, $J_{2″,3″\ trans}$ 17, $J_{2″,3″\ cis}$ 10, $J_{1″,2″}$ 7 Hz, 2″-H).

trans-4-{2′-[1″-(*Dimethyl-t-butylsiloxy*)*prop*-2″-*enyl*]-1′-*methylcyclohexyl*}-1-*trimethylsilylbutan*-2-*one*.—Chromium-(VI) oxide (1.5 g, 15 mmol) was added to a stirred solution of pyridine (2.43 ml, 30 mmol) in dry dichloromethane (40 ml). The resulting red solution was stirred at room temperature for 30 min and then a solution of *trans*-4-{2′-[1″-(dimethyl-t-butylsiloxy)prop-2″-enyl]-1′-methylcyclohexyl}-1-trimethylsilylbutan-2-ol (**14**) (816 mg, 2.5 mmol) in dichloromethane (5 ml) was added in one portion. After 30 s, t.l.c. showed no trace of starting material and so the brown solution was filtered through a short silica column. The residues were washed with ether (2 × 50 ml). The combined organic solution was then washed with aqueous sodium hydrogen carbonate (75 ml) and dried ($MgSO_4$). After removal of the solvent under reduced pressure, *trans*-4-{2′-[1″-(dimethyl-t-butylsiloxy)prop-2″-enyl]-1′-methylcyclohexyl}-1-trimethylsilylbutan-2-one was

obtained as a pale yellow oil (810 mg), R_F 0.44 (5% ether–light petroleum); $\nu_{max.}$(film) 2 950s, 2 920s, 2 850s, 1 690s (C=O), 1 250s, 1 090s, 920s, 855s, 840s, 770s, and 700s cm^{-1}; δ_H (90 MHz; $CDCl_3$) −0.02 (3 H, s, MeSi), 0.03 (3 H, s, MeSi), 0.1 (9 H, s, Me_3Si), 0.84 (9 H, s, SiBu^t), 0.90 (3 H, s, Me), 1.10—1.73 [14 H (should be 11 H), m], 2.10—2.35 (4 H, m, 1- and 3-H_2), 4.30 (1 H, br d, $J_{1',2'}$ 7 Hz, 1″-H), 4.86—5.08 (2 H, m, 3″-H_2), and 5.84 (1 H, ddd, $J_{2',3'\ trans}$ 17, $J_{2',3'\ cis}$ 10, $J_{1',2'}$ 7 Hz, 2″-H).

trans-5-{2′-[1″-(*Dimethyl-t-butylsiloxy*]*prop-2″-enyl*]-1′-*methylcyclohexyl*}-3-*trimethylsilylmethylpent*-1-*en*-3-*ol* (**15**).—A 1M solution of vinylmagnesium bromide in THF (3.8 ml, 3.8 mmol) was added dropwise to a solution of *trans*-4-{2′-[1″-(dimethyl-t-butylsiloxy)prop-2″-enyl)-1′-methylcyclohexyl}-1-trimethylsilylbutan-2-one (810 mg, 2.5 mmol) in THF (40 ml) at room temperature under nitrogen. After 1 h t.l.c. showed disappearance of starting material and so the mixture was poured into saturated aqueous NH_4Cl (100 ml) containing 2M-HCl (2 ml) and extracted with ether (3 × 75 ml). Each extract was washed with saturated brine (75 ml) and the combined extracts were dried ($MgSO_4$). After removal of the solvent under reduced pressure, *trans*-5-{2′-[1″-(dimethyl-t-butylsiloxy)prop-2″-enyl]-1′-methylcyclohexyl}-3-trimethylsilylmethylpent-1-en-3-ol (**15**) was obtained as an oil (674 mg), R_F 0.60 (5% ether–light petroleum); $\nu_{max.}$(film) 3 460br (OH), 2 960s, 2 930s, 2 900s, 2 860s, 1 250s, 1 090s, 1 000s, 920s, 840s, and 770s cm^{-1}; δ_H (90 MHz; $CDCl_3$) −0.02 (3 H, s, MeSi), 0.02 (12 H, s, $SiMe_3$ and SiMe), 0.86 (9 H, s, SiBu^t), 0.90 (3 H, s, Me), 1.03—1.82 [18 H (should be 16 H for 7 × CH_2, 2′-H, and OH), m], 4.28 (1 H, br d, $J_{1',2'}$ 7, Hz, 1″-H), 4.86—5.23 (4 H, m, 1- and 3″-H_2), and 5.67—6.03 (2 H, m, 2- and 2″-H).

trans-2-[1″-(*Dimethyl-t-butylsiloxy*)*prop-2″-enyl*]-1-*methyl*-1-(3′-*methylenepent-4′-enyl*)*cyclohexane* (**16**).—A saturated solution of sodium acetate in glacial acetic acid (10 ml) was added to *trans*-5-{2′[1″-(dimethyl-t-butylsiloxy)prop-2″-enyl]-1′-methylcyclohexyl}-3-trimethylsilylmethylpent-1-en-3-ol (**15**) (617 mg) and the mixture was stirred at 50 °C for 45 min, after which no starting material was visible on t.l.c. The mixture was then poured into water (100 ml), neutralised with solid sodium hydrogen carbonate, and extracted with ether (2 × 100 ml). Each extract was washed with aqueous sodium hydrogen carbonate (50 ml) and the combined extracts were dried ($MgSO_4$). After removal of the solvent under reduced pressure and flash chromatography (light petroleum), trans-2-[1″-(*dimethyl-t-butylsiloxy*)*prop-2″-enyl*]-1-*methyl*-1-(3′-*methylenepent-4′-enyl*)*cyclohexane* (**16**) was obtained as an oil [444 mg, 51% overall yield from (**14**)], R_F 0.50 (light petroleum) (Found: C, 76.05; H, 11.5. $C_{22}H_{40}OSi$ requires C, 75.79; H, 11.57%); $\nu_{max.}$(film) 2 930s, 2 860s, 1 595m (C=C), 920s, 840s, and 770s cm^{-1}; δ_H (400 MHz; $CDCl_3$) −0.02 (3 H, s, MeSi), 0.03 (3 H, s, MeSi), 0.87 (9 H, s, SiBu^t), 0.96 (3 H, s, Me), 1.19—1.60 [10 H (should be 9 H for 3-, 4-, 5-, and 6-H_2 and 2-H), m], 1.74 (2 H, m, 1′-H_2), 2.15 (2 H, m, 2′-H_2), 4.30 (1 H, br d, $J_{1',2'}$ 7.2 Hz, 1″-H), 4.96 (1 H, ddd, $J_{2',3'\ cis}$ 10.1, $J_{3',3'}$ 1.5, $J_{1',3'}$ 1 Hz, 3″-H), 4.99 (2 H, br, s, 3′-CH_2), 5.03 (1 H, ddd, $J_{2',3'\ trans}$ 17.6, $J_{3',3'}$ 1.5, $J_{1',3'}$ 1.5 Hz, 3″-H), 5.05 (1 H, ddd, $J_{4',5'\ cis}$ 10.7, J 2.0, $J_{5',5'}$ 1 Hz, 5′-H), 5.23 (1 H, dd, $J_{4',5'\ trans}$ 17.6, $J_{5',5'}$ 1.0 Hz, 5′-H), 5.89 (1 H, ddd, J 17.6, 10.1, and 7.2 Hz, 2″-H), and 6.36 (1 H, dd, J 17.6 and 10.7 Hz, 4′-H); δ_C (100 MHz; $CDCl_3$) −4.64 (q, MeSi), −3.12 (q, MeSi), 18.06 (s, $SiCMe_3$), 20.63 (q, 1-CH_3), 20.90 (t), 22.16 (t), 25.02 (t), 25.96 (q, $SiCMe_3$), 26.69 (t), 29.62 (s), 36.03 (s, C-1), 38.56 (t), 41.73 (t), 50.67 (d, C-2), 72.74 (d, C-1″), 112.93, 113.06, 115.31, 138.89, 142.93, and 147.44 (s, C-3′). Some of the ^{13}C off-resonance signals did not show coupling; this was due to the position of the decoupling frequency: *m/z* 348 (M^+, 3%), 291 (33), 171 (100), 115 (30), 91 (5), 75 (51), and 73 (56); $\lambda_{max.}$(hexane) 224.5 nm (ε 18 300).

trans-1-[2′-*Methyl*-2′-(3″-*methylenepent*-4″-*enyl*)*cyclohexyl*]-*prop*-2-*enol*.—A solution of 40% aqueous hydrofluoric acid (1.5 ml) was added *via* an Eppendorf syringe to a stirred solution of *trans*-2-[1″-(dimethyl-t-butylsiloxy)prop-2″-enyl]-1-methyl-1-(3′-methylenepent-4′-enyl)cyclohexane (**16**) (250 mg, 717 µl) in acetonitrile (8.5 ml) in a glass round-bottomed flask. The reaction was monitored by t.l.c. After 1.5 h, starting material had disappeared and so the reaction mixture was diluted with water (2 ml), neutralised with solid sodium hydrogen carbonate, and extracted with ether (3 × 5 ml). Each extract was washed with water (2 ml) and then the aqueous washings were back-extracted with ether (2 ml). The combined organic extracts were dried ($MgSO_4$) and then the solvent was removed under reduced pressure to give *trans*-1-[2′-methyl-2′-(3″-methylenepent-4″-enyl)cyclohexyl]prop-2-enol as an oil (168 mg) which was used in the next stage without purification, R_F 0.37 (20% ether–light petroleum); $\nu_{max.}$(film) 3 420br (OH), 2 980s, 2 940s, 2 920s, 2 860s, 1 590s (C=C), 990s, 925s, and 980s cm^{-1}; δ_H (90 MHz; $CDCl_3$) 1.00 (3 H, s, Me), 1.15—1.96 (12 H, m, 1′-H, 3′-, 4′-, 5′-, 6′-, and 1″-H_2, and OH), 2.05—2.23 (2 H, m, 2″-H_2), 4.42 (1 H, br t, J 5 Hz, 1-H), 4.92 (2 H, s, 3″-CH_2), 4.96—5.39 (4 H, m, 3- and 5″-H_2), 5.85 (1 H, ddd, $J_{2,3\ trans}$ 17, $J_{2,3\ cis}$ 10, $J_{1,2}$ 4 Hz, 2-H), and 6.32 (1 H, dd, $J_{4',5'\ trans}$ 17, $J_{4',5'\ cis}$ 10 Hz, 4″-H).

trans-2-*Methyl*-2-(3′-*methylenepent*-4′-*enyl*)*cyclohexyl Vinyl Ketone* (**17**).—Chromium(VI) oxide (430 mg, 4.3 mmol) was added to a stirred solution of pyridine (695 µl, 8.6 mmol) in dry dichloromethane (20 ml) and the mixture was stirred for a further 30 min. A solution of *trans*-1-[2′-methyl-2′-(3″-methylenepent-4″-enyl)cyclohexyl]prop-2-enol (168 mg, 717 µmol) in dichloromethane (1 ml) was then added. After 5 min, t.l.c. showed no starting material, so the mixture was filtered through a short silica column and the residues were washed with ether (2 × 50 ml). After removal of the solvent from the eluate, and flash chromatography of the residue *trans*-2-methyl-2-(3′-methylenepent-4′-enyl)cyclohexyl vinyl ketone (**17**) was obtained as an oil [118 mg, 71% overall yield from (**16**)], R_F 0.62 (20% ether–light petroleum); $\nu_{max.}$(film) 2 930s, 2 860s, 1 690s (C=O), 1 670m (C=C, enone), 1 610m (C=C, diene), 1 595m (C=C diene), 1 400s, and 895 cm^{-1}; δ_H (90 MHz; $CDCl_3$) 1.02 (3 H, s, Me), 1.16—1.98 (10 H, m, 1′-, 3-, 4-, 5-, and 6-H_2), 2.05—2.26 (2 H, m, 2′-H_2), 2.65 (1 H, dd, $J_{1,6\ ax.}$ 9, $J_{1,6\ eq.}$ 6 Hz, 1-H), 4.92 (2 H, br s, 3′-CH_2), 4.98 (1 H, d, $J_{4',5'\ cis}$ 10 Hz, 5′-H), 5.15 (1 H, d, $J_{4',5'\ trans}$ 18 Hz, 5′-H), 5.60 (dd, $J_{2',3'\ cis}$ 10, $J_{3',3'}$ 3 Hz, COCH=C*H*H), and 6.02—6.54 (3 H, m, 4′-H and COC*H*=CH*H*).

(1R/S,3R/S,8S/R)-8-*Methyltricyclo*[9.3.1.0^{3,8}]*pentadec*-11-*en*-2-*one* (**18**).—A 1M solution of diethylaluminium chloride in hexane (344 µl, 344 µmol) was added dropwise to a stirred solution of *trans*-2-methyl-2-(3′-methylenepent-4′-enyl)cyclohexyl vinyl ketone (**17**) (80 mg, 344 µmol) in dry dichloromethane (2 ml) at room temperature under nitrogen. After 2 h, t.l.c. showed no starting material and so the mixture was poured into saturated aqueous NH_4Cl (5 ml) containing 1M-HCl (0.5 ml). The mixture was extracted with dichloromethane (3 × 5 ml) and the combined extracts were dried ($MgSO_4$). After removal of the solvent under reduced pressure and preparative layer chromatography (10% ether–light petroleum), (1R/S,3R/S,8S/R)-8-*methyltricyclo*[9.3.1.0^{3,8}]*pentadec*-11-*en*-2-*one* (**18**) was obtained as a white crystalline solid (58 mg, 72%), m.p. 84—85 °C; R_F 0.44 (10% ether–light petroleum) (Found: C, 82.6; H, 10.4. $C_{16}H_{24}O$ requires C, 82.70; H, 10.41%); $\nu_{max.}$(CH_2Cl_2) 2 930s, 1 688s (C=O), 1 095s, 1 080s, and 1 040s, cm^{-1}; δ_H (400 MHz; $CDCl_3$) 0.87 (3 H, s, Me), 1.02—1.30 (5 H, m), 1.43—1.70 (6 H, m), 1.82—1.93 (3 H, m), 2.15—2.26 (2 H, m), 2.34 (1 H, ddd, J 13.7, 1.8, and 1.8 Hz), 2.46 (1 H, td, J 14.4 and 2.8 Hz), 2.78 (1 H, m, 1-H), 3.19 (1 H, dd, $J_{3,4\ ax.}$ 12.3,

Table. Final atomic postional parameters for conformer (**20**) of compound (**18**), with estimated standard deviations in parentheses. Crystallographic numbering scheme

	x	*y*	*z*
C(1)	0.198 9(18)	0.129 7(11)	0.369(2)
C(2)	0.317 0(17)	0.160 1(11)	0.247(2)
C(3)	0.215 5(15)	0.120 4(10)	0.015(2)
C(4)	0.076 8(16)	0.176 8(10)	−0.069(2)
C(5)	0.150 4(16)	0.297 4(10)	−0.038(2)
C(6)	0.252 0(16)	0.338 2(10)	0.189(2)
C(7)	0.392 7(15)	0.282 2(10)	0.253(2)
C(8)	0.512(2)	0.334 8(14)	0.465(3)
C(9)	0.704 7(16)	0.381 8(10)	0.487(2)
C(10)	0.460 1(17)	0.102 2(11)	0.311(2)
C(11)	0.607 9(16)	0.119 7(10)	0.207(3)
C(12)	0.719 6(15)	0.229 9(10)	0.248(2)
C(13)	0.782 1(17)	0.286 6(11)	0.471(2)
C(14)	0.748 7(15)	0.294 3(11)	0.095(2)
C(15)	0.829 5(16)	0.410 2(10)	0.161(2)
C(16)	0.741 0(16)	0.454 5(10)	0.311(2)
H(11)	0.098 3(18)	0.168 7(11)	0.356(2)
H(12)	0.273 3(18)	0.154 5(11)	0.556(2)
H(13)	0.143 0(18)	0.044 8(11)	0.380(2)
H(31)	0.155 7(15)	0.036 1(10)	0.006(2)
H(32)	0.304 3(15)	0.135 7(10)	−0.081(2)
H(41)	−0.021 2(16)	0.153 4(10)	0.013(2)
H(42)	0.021 0(16)	0.153 6(10)	−0.234(2)
H(51)	0.234 5(16)	0.321 2(10)	−0.138(2)
H(52)	0.045 9(16)	0.332 9(10)	−0.082(2)
H(61)	0.168 1(16)	0.320 9(10)	0.290(2)
H(62)	0.308 9(16)	0.422 9(10)	0.198(2)
H(71)	0.468 4(15)	0.291 1(10)	0.142(2)
H(91)	0.761 3(16)	0.429 4(10)	0.634(2)
H(101)	0.395 5(17)	0.018 3(11)	0.286(2)
H(102)	0.518 9(17)	0.123 6(11)	0.476(2)
H(111)	0.554 7(16)	0.102 2(10)	0.040(3)
H(112)	0.684 1(16)	0.066 7(10)	0.266(3)
H(131)	0.744 0(17)	0.230 1(11)	0.579(2)
H(132)	0.920 1(17)	0.316 1(11)	0.513(2)
H(141)	0.715 2(15)	0.263 7(11)	−0.066(2)
H(151)	0.962 8(16)	0.421 8(10)	0.241(2)
H(152)	0.819 6(16)	0.453 8(10)	0.023(2)
H(161)	0.620 7(16)	0.463 9(10)	0.219(2)
H(162)	0.823 8(16)	0.530 8(10)	0.383(2)
O	0.462 2(12)	0.345 9(9)	0.620(2)

$J_{3,4\,eq.}$ 3 Hz, 3-H), and 5.77 (1 H, m, 12-H); a 5% n.O.e. was observed between 3-H (δ 3.19) and 2 H (δ 5.77), and a 1.5% n.O.e. in the opposite direction; δ_C (100 MHz; $CDCl_3$) 21.66 (t), 22.11 (q, CH_3), 22.27 (t), 23.02 (t), 25.37 (t), 25.61 (t), 27.22 (t), 30.96 (t), 37.36 (t), 38.09 (s, C-8), 38.46 (t), 48.85 (d, C-3), 50.35 (d, C-1), 124.53 (d, C-12), 141.68 (s, C-11), and 218.13 (s, C-2); *m/z* 232 (M^+, 96%), 217 (35), 189 (33), 135 (28), 134 (25), 123 (35), 109 (46), 108 (71), 107 (30), 94 (68), 91 (33), 81 (37), 79 (100), and 67 (50) cm^{-1}; $\lambda_{max.}$(MeOH) 218 nm (ε 15 800).

A crystal for *X*-ray analysis was obtained by dissolving the compound in the minimum amount of hexane and cooling the solution in the freezer overnight.

Crystal Data for Compound (**18**).—$C_{16}H_{24}O$, M = 232.19, triclinic, space group $P\bar{1}$ No. 2, a = 8.412(8), b = 13.125(12), c = 6.645(10) Å, α = 90.5(1), β = 104.9(2), γ = 105.5(2)°, V = 681.08 Å, Z = 2, λ(Mo-K_α) = 0.7107 Å. The intensities of 1 700 unique reflections with 2θ < 45° were measured using a Stoe STADI-2 Weissenberg diffractometer; of these, 537 reflections had $|F_o| > 5\sigma(|F_o|)$. The structure was solved by direct methods and refined to R 0.1079, R_w 0.0972. Hydrogen atoms were included in calculated positions for structure-factor calculations. Final atomic positional parameters are listed in the Table; bond lengths, bond angles, and thermal parameters have been deposited as a Supplementary Publication [SUP No. 56522 (4 pp.)].* The structure factors are available from the Editorial office on request.

* For details of the Supplementary Publications scheme, see Instructions for Authors (1986), *J. Chem. Soc., Perkin Trans. 1*, 1986, Issue 1.

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Received 24th October 1985; *Paper* 5/1851