An Enantioselective Total Synthesis of (+)-Atisirene by Intramolecular Double Michael Reaction

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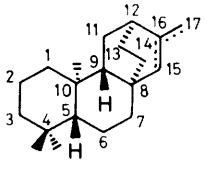
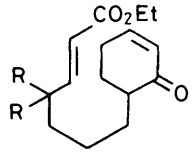
1,6-Conjugate addition of 2-methoxybenzylmagnesium bromide to 4-methylene-3,5,5-trimethylcyclohex-2-enone (**7**), followed by hydrocyanation, gave (±)-(1*RS*,2*SR*)-2-[2-(2-methoxyphenyl)ethyl]-1,3,3-trimethyl-5-oxocyclohexanecarbonitrile (**9**), which was converted into the (*E*)-α,β-unsaturated enone ester (**22**). Intramolecular double Michael reaction of compound (**22**) produced the A/B-*cis* tetracyclic compound (**23**) in 17% yield. On the other hand, Wieland–Miescher ketone(+)-(**27**) was selectively transformed into the (*E*)-α,β-unsaturated enone ester (**46**), whose intramolecular double Michael reaction furnished the A/B-*trans* compound (**48**) in 92% yield. (+)-15-Norisoatisirene (**52**), which had previously been transformed into (+)-atisirene (**53**), was synthesized from keto ester (**48**).

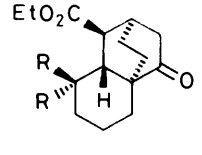
(−)-Atisirene (**1a**) and (−)-isoatisirene (**1b**), first isolated from *Erythroxylon monogynum*, are structurally related to diterpene alkaloids of the atisine group.[1] The first total synthesis of the (±)-forms of both compounds had been accomplished by Ireland and his co-workers[2] before the discovery of the natural products, and (+)-atisirene (**53**) was synthesized starting from abietic acid.[3] Partial syntheses of (−)-atisirene (**1a**) and (−)-isoatisirene (**1b**) were also performed starting from (−)-kaurene[4] and isosteviol.[5] However, a challenging problem for the stereocontrolled construction of the bicyclo[2.2.2]octane part in the skeleton remains to be solved. In our previous paper, we disclosed a highly stereoselective synthesis of tricyclo-[6.2.2.0^{1,6}]dodecanes by the novel intramolecular double Michael reaction, in which the desired stereoisomer (**4**) was formed as the sole product *via* the lithium-chelated intermediate (**3**).[6] Applying this strategy, we have planned a new route to atisirene (**1a**) *via* the tetracyclic keto ester (**5**) which could be obtained by the annelation of the (*E*)-α,β-unsaturated enone ester (**6**) (Scheme 1). Here we report a formal enantioselective total synthesis of (+)-atisirene (**53**).[7]



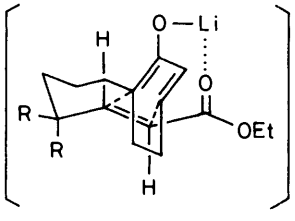
(1a) 16,17-unsaturated
(1b) 15,16-unsaturated



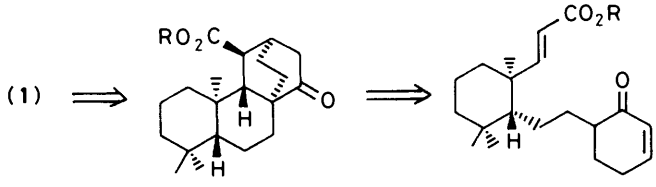
(**2**) R = Me and/or H



(**4**)



(**3**)



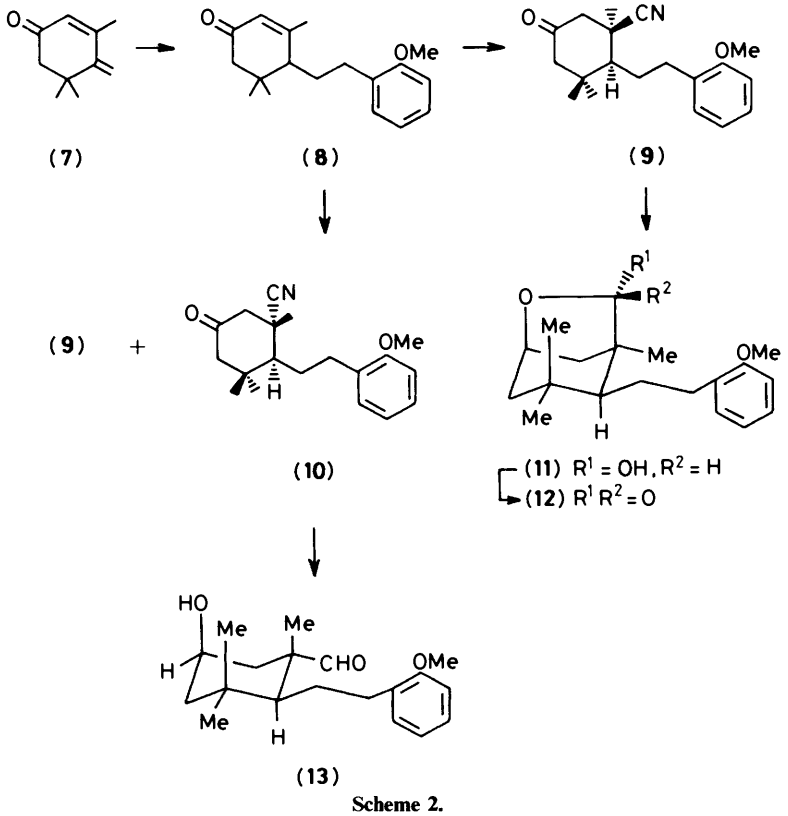
(**5**) (**6**)

Scheme 1.

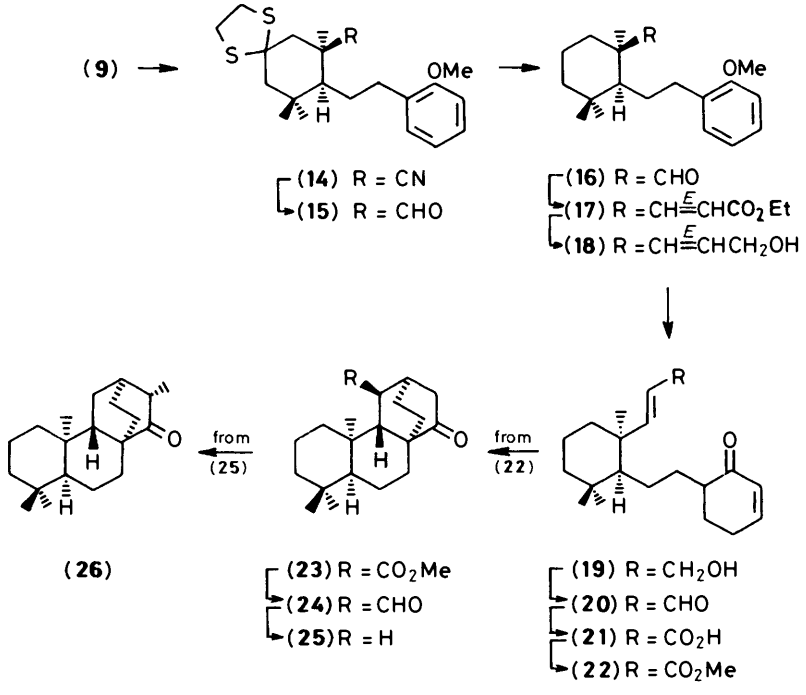
First we examined the preparation of the substrate (**6**) by means of an intramolecular double Michael reaction from the dienone (**7**). According to Davis' procedure,[8] the dienone (**7**) was treated with 2-methoxybenzylmagnesium bromide in the presence of copper(I) bromide and the resulting 1,6-conjugate adduct was isomerised with acid to give the enone (**8**) in 65% yield. Introduction of carbon units at the C-3-position of compound (**8**) was a difficult problem mainly due to the steric effect of the dimethyl groups at C-5. After numerous attempts, a one-carbon unit could be introduced by hydrocyanation.[9] Under thermodynamically controlled conditions using potassium cyanide–ammonium chloride in dimethylformamide (DMF),[10] potassium cyanide–acetone cyanohydrin–18-crown-6,[11] and diethylaluminium cyanide,[12] only one isomer (**9**) was obtained, in 75—78% yield. On the other hand, kinetically controlled conditions with hydrogen cyanide and triethylaluminium[13] gave the above product (**9**) in 71% yield along with the stereoisomer (**10**) in 4.5% yield. It was expected that compound (**9**) would be a thermodynamically stable isomer since a cyano group is less bulky than a methyl group. The structure of compounds (**9**) and (**10**) was determined by the following reactions. Reduction of isomer (**9**) with di-isobutylaluminium hydride (DIBAL) followed by acidic treatment afforded in 65% yield the cyclic hemiacetal (**11**), m.p. 88—89 °C, while isomer (**10**) was converted into the formyl alcohol (**13**) in 66% yield under the same reaction conditions. Oxidation of the cyclic hemiacetal (**11**) with silver carbonate on Celite[14] produced the lactone (**12**) in 80% yield (Scheme 2). Furthermore one of the methyl groups of the aldehyde (**16**), which was synthesized from compound (**9**) by dithioacetalisation in 92% yield, followed by reduction with DIBAL in 85% yield and desulphurisation with Raney nickel in 60% yield,

resonated at highfield, δ_H 0.73, in the ^1H n.m.r. spectrum; the value indicated that one of the methyl groups at C-5 was shielded by the axially oriented formyl group. It was therefore revealed that the main product obtained by the hydrocyanation was the wrong precursor for the synthesis of atisirene. However, we carried on with this isomer in order to examine the validity of the intramolecular double Michael reaction for the assembly of the highly crowded compound.

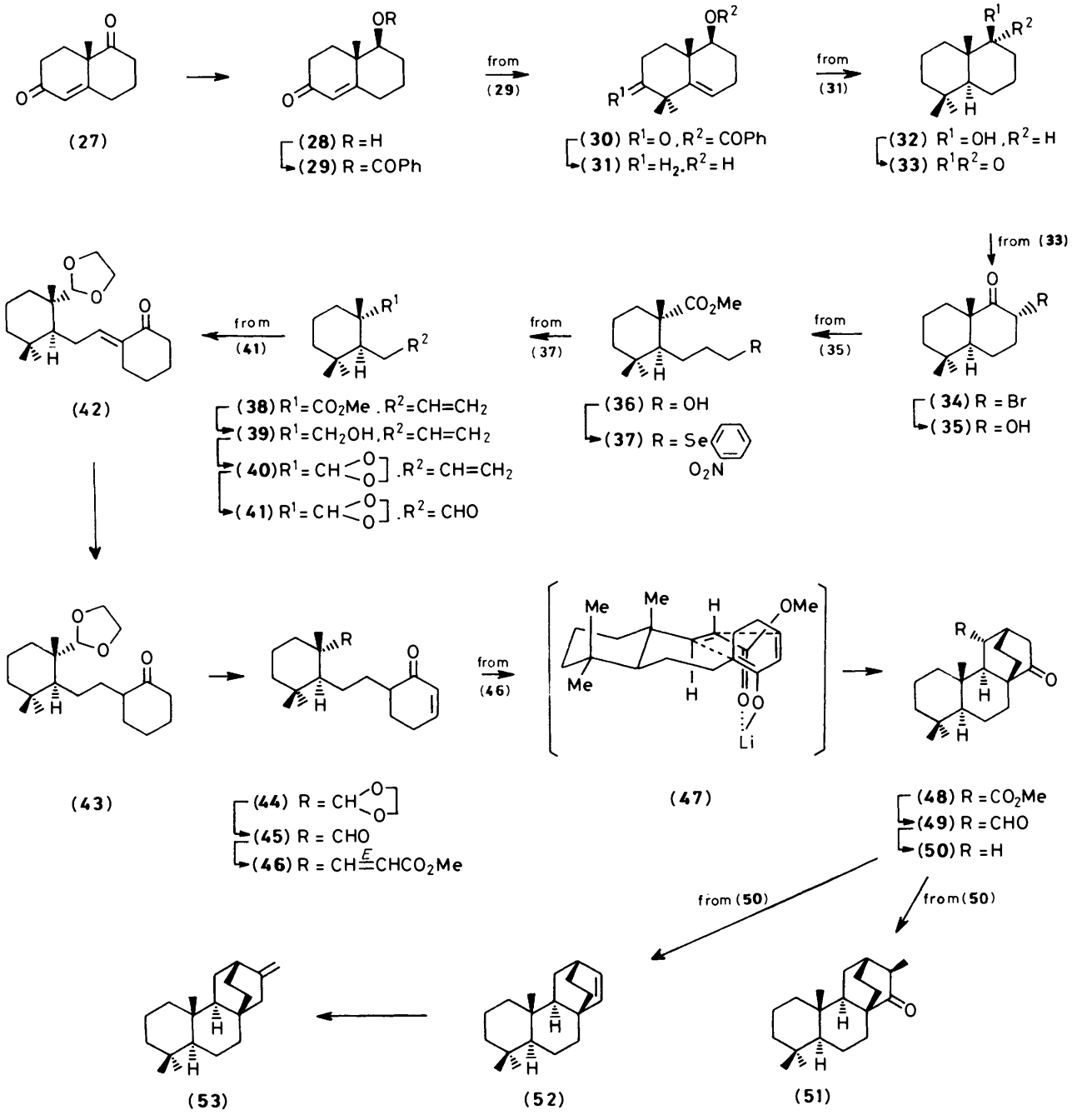
Emmons reaction[15] of the aldehyde (**16**) produced the (*E*)-α,β-unsaturated ester (**17**) in 95% yield as a single product. Reduction of ester (**17**) with DIBAL in diethyl ether gave, in 94% yield, the allylic alcohol (**18**), which was treated with sodium hydride to protect the hydroxy group from hydrogenolysis, and then subjected to Birch reduction carried out using lithium in the presence of t-butyl alcohol in liquid ammonia. After treatment of the crude product with hydro-



Scheme 2.



Scheme 3.



Scheme 4.

chloric acid, the enone (**19**) was obtained in 50% yield based on consumed aryl ether (**18**). Oxidation with pyridinium chlorochromate (PCC) in the presence of Florisil, followed by further oxidation of the resulting aldehyde (**20**), obtained in 83% yield, with sodium chlorite in the presence of sulphamic acid in aqueous t-butyl alcohol,[16] and esterification of the acid (**21**) with methanolic sulphuric acid furnished the α,β-unsaturated enone ester (**22**) in 72% yield. The intramolecular double Michael reaction of compound (**22**) was carried out with lithium hexamethyldisilazide (LiHMDS) in a mixture of n-hexane and diethyl ether (8:1, v/v) for 2 h at −78 °C and then for 4 h at room temperature. After chromatographic separation, one isomer (**23**) of the possible tetracyclic compound was isolated in 17% yield and no formation of other isomers was observed on careful inspection. The stereostructure (**23**) of the product was tentatively assigned on the basis of mechanistic considerations according to previous results.[6] It is noteworthy that the cyclised product was obtained in spite of a crowded intermediate.

The ester moiety of compound (**23**) was removed by the following three steps; reduction of (**23**) with DIBAL in diethyl ether followed by oxidation of the resulting diol with pyridinium dichromate (PDC) in DMF to the keto aldehyde (**24**), m.p. 121—123 °C, obtained in 55% yield from (**23**), and then decarbonylation with tris(triphenylphosphine)rhodium(I) chloride (TTPRCl)[17] to give ketone (**25**) in 28% yield. Methylation of the ketone (**25**), m.p. 80—82 °C, with methyl

iodide in the presence of lithium di-isopropylamide (LDA) at −78 to 0 °C afforded the tetramethylated compound (**26**) as a single isomer (Scheme 3). It was assumed on the basis of CPK molecular model considerations that the kinetically controlled alkylation would occur from the less hindered α-side. The signals due to one of the quaternary methyl groups of compounds (**25**) and (**26**) were observed at lower field, δ_H 1.14, which would support the proposed structures.[18]

Now our attention focussed on the stereoselective construction of the A/B-*trans* isomer. We considered that the proper substrate (**46**) of the intramolecular double Michael reaction could be prepared from a *trans*-octahydronaphthalen-1(2*H*)-one derivative. Thus the easily available Wieland–Miescher ketone (+)-(**27**)[19] was selectively converted into the ketone (**33**) by a modification of Sondheimer's method.[20] Bromination of ketone (**33**) with pyridinium bromide perbromide (PBB) in acetic acid gave the α-bromo ketone (**34**), m.p. 126—128 °C, in 97% yield. In the n.m.r. spectrum of compound (**34**), 2-H was observed as double doublet with *J* 5.7 and 11.4 Hz at δ_H 4.94; this indicated the presence of the equatorially oriented bromine atom. Treatment of compound (**34**) with sodium hydroxide in aqueous DMF[21] at room temperature afforded, in 97% yield, the α-hydroxy ketone (**35**), which was subjected to oxidative cleavage with lead tetra-acetate (LTA) in methanol followed by reduction of the resulting aldehyde, obtained in 90% yield, with sodium borohydride to furnish the alcohol (**36**) in 97% yield. The primary alcohol function of compound (**36**) was, on the action of 2-nitrophenyl selenocyanate and tributylphosphine,[22] converted into the selenide (**37**) in 98% yield, oxidation of which with 30% hydrogen peroxide gave the olefin (**38**) in 91% yield. The ester group of compound (**38**) was reduced with lithium aluminium hydride to give the alcohol (**39**) in 95% yield. After oxidation of compound (**39**) with PCC in the presence of Florisil, the aldehyde, obtained in 88% yield, was protected as the ethylene acetal. The olefinic acetal (**40**), obtained in 98% yield, was oxidatively cleaved with osmium tetraoxide and sodium periodate[23] to provide the unstable aldehyde (**41**) in 78% yield. Aldol condensation of compound (**41**) with cyclohexanone in the presence of LDA, carried out at between −78 °C and room temperature in tetrahydrofuran (THF), gave the (*E*)-enone (**42**), m.p. 52—53 °C; $[\alpha]_D^{17}$ −10.0° ($CHCl_3$), in 62% yield. Catalytic hydrogenation of enone (**42**) in the presence of 10% palladium–charcoal led quantitatively to the ketone (**43**), which was silylated under kinetically controlled conditions. Oxidation of the corresponding silyl enol ether with palladium(II) acetate in the presence of *p*-benzoquinone[24] furnished the enone (**44**) in 85% yield. Deprotection of compound (**44**) with 10% perchloric acid in THF, followed by Emmons reaction[15] of the aldehyde (**45**), obtained in 83% yield, using trimethyl phosphonoacetate [methyl (dimethoxyphosphoryl)acetate] in the presence of sodium hydride provided the (*E*)-α,β-unsaturated enone ester (**46**) in 47% yield. The intramolecular double Michael reaction was conducted using (LiHMDS) in a mixture of n-hexane and diethyl ether during 2.5 h at between −78 °C and room temperature. The desired tetracyclic compound (**48**) was obtained as crystals, 145—148 °C; $[\alpha]_D^{25}$ −9.3° (*c* 0.29 in $CHCl_3$); in 92% yield. The highly stereocontrolled formation of compound (**48**) in such excellent yield can be ascribed to the lithium-chelated intermediate (**47**) having no strong non-bonding interaction. The structure of compound (**48**) was determined by its conversion into the known compounds (**50**)—(**52**). In the same manner as previously, reduction of ester (**48**) with DIBAL followed by oxidation of the corresponding diol with PDC and decarbonylation of the aldehyde (**49**), obtained in 59% from ester (**48**), using TTPRCl[17] gave, in 28% yield, the (+)-ketone (**50**), m.p. 147—149 °C (lit.,[3] 146—148 °C); $[\alpha]_D^{25}$ +19.5° (*c* 0.021 in MeOH) {lit.,[3] $[\alpha]_D$ +19.6° (*c* 0.05 in MeOH)}, whose spectral data were similar to reported ones.[3] Methylation of compound (**50**) with methyl iodide in the presence of LDA provided, in 38% yield, atisiran-15-one (**51**), whose n.m.r. data were consistent with those of the authentic compound.[25,26] The transformation of the ketone (**50**) into the olefin (**52**) was accomplished in the following three steps in 70% overall yield; bromination of compound (**50**) with bromine and LDA, sodium borohydride reduction of the resulting bromo ketone, and reduction of the resulting bromohydrin with zinc in ethanol.[27] The n.m.r. spectral data of (+)-15-norisoatisirene (**52**), m.p. 83—84 °C (lit.,[3] 82—83 °C), $[\alpha]_D^{24}$ +16.4° (*c* 0.134 in MeOH), agreed well with those reported.[3] Since compound (**52**) had been converted into (+)-atisirene (**53**) in three steps,[3] its formal enantioselective synthesis has been achieved (Scheme 4).

Experimental

General Methods.—M.p.s are uncorrected. I.r. spectra were recorded on a Hitachi 260—10 spectrophotometer for solutions in $CHCl_3$. N.m.r. spectra were measured on a JEOL JNM-PMX-60 or a JEOL-PS-100 spectrometer for solutions in $CDCl_3$ unless otherwise stated. Chemical shifts are reported as δ_H values relative to internal $SiMe_4$. Ordinary mass spectra were taken on a Hitachi M-52G machine, and accurate mass spectra with a JEOL-JMS-01SG-2 spectrometer. All new compounds described in the Experimental section were homogeneous on t.l.c. Magnesium sulphate was used to dry extracts. High-pressure liquid chromatography was carried out using a Hitachi 635 instrument monitored by u.v. absorption and refractive-index measurements. Optical rotations were measured on a JASCO-PIP-SL polarimeter for solutions in $CHCl_3$ unless otherwise stated.

4-[2-(2-*Methoxyphenyl*)*ethyl*]-3,5,5-*trimethylcyclohex*-2-*enone* (**8**).—A solution of the Grignard reagent prepared from 2-methoxybenzyl bromide (26.8 g, 0.13 mol) and magnesium (4.2 g, 0.17 mol) in dry THF (80 ml) was slowly added to a stirred mixture of the dienone (**7**) (10 g, 66 mmol) and copper(I) bromide (1 g, 3.5 mmol) in dry diethyl ether (80 ml) at 0 °C. The mixture was allowed to warm to room temperature, stirred for 0.5 h at the same temperature under nitrogen, and then poured into saturated aqueous ammonium chloride (200 ml). The resulting mixture was extracted with diethyl ether. The extract was concentrated to give a residue, which was taken up into THF (50 ml). To the mixture was added 10% hydrochloric acid (50 ml) and the resulting mixture was refluxed for 2 h under nitrogen. Extraction of the mixture with diethyl ether, followed by drying and evaporation of the extract, gave a residue, which was purified by chromatography on silica gel with n-hexane–acetone (50:1, v/v) as eluant to afford the *enone* (**8**) (11.8 g, 65%) as an oil (Found: C, 79.3; H, 8.75. $C_{18}H_{24}O_2$ requires C, 79.35; H, 8.9%); $\nu_{max.}$ 1 650 cm^{-1} (C=O); $\delta_H(CCl_4)$ 1.00 and 1.10 (each 3 H, each s, 2 × Me), 1.90 (3 H, s, 3-Me), 3.80 (3 H, s, OMe), 5.63 (1 H, br s, 2-H), and 6.57—7.23 (4 H, m, ArH); *m/z* 272 (M^+).

(±)-(1RS,2SR)- *and* (1RR,2RR)-2-[2-(2-*Methoxyphenyl*)-*ethyl*]-1,3,3-*trimethyl*-5-*oxocyclohexanecarbonitrile* (**9**) *and* (**10**).—Method A. To a stirred solution of triethylaluminium (255 mg, 2.24 mmol) in dry THF (4 ml) at 0 °C was added a dry THF solution (2 ml) of hydrogen cyanide (40 mg, 1.48 mmol) and the enone (**8**) (200 mg, 0.74 mmol). The mixture was allowed to warm to room temperature, stirred for 22 h under argon, and then poured into a vigorously stirred mixture of 2M-sodium hydroxide and ice. The resulting solution was extracted with diethyl ether and the extract was washed successively with water, 2M-hydrochloric acid, and water, dried, and evaporated to afford a crude product, which was subjected to column chromatography on silica gel. Elution

with n-hexane–ethyl acetate (10:1, v/v) gave the *nitrile* (**10**) (10 mg, 4.5%) as an oil, $\nu_{max.}$ 2 225 (CN) and 1 720 cm^{-1} (C=O); δ_H 0.90, 1.16, and 1.27 (each 3 H, each s, 3 × Me), 1.40—3.20 (9 H, m, 4 × CH_2 and CH), 3.83 (3 H, s, OMe), and 6.66—7.23 (4 H, m, ArH); *m/z* 299 (M^+) (Found: M^+, 299.1885. $C_{19}H_{25}NO_2$ requires *M*, 299.1886).

Further elution gave the *isomer* (**9**) (157 mg, 71%) as an oil, $\nu_{max.}$ 2 225 (CN) and 1 720 cm^{-1} (C=O); δ_H 1.04, 1.07, and 1.54 (each 3 H, each s, 3 × Me), 1.42—2.85 (9 H, m, 4 × CH_2 and CH), 3.83 (3 H, s, OMe), and 6.57—7.27 (4 H, m, ArH); *m/z* 299 (M^+) (Found: M^+, 299.1893).

Method B. To a mixture of the enone (**8**) (1 g, 3.7 mmol), DMF (40 ml), and water (6.3 ml) were added potassium cyanide (480 mg, 7.4 mmol) and ammonium chloride (300 mg, 5.6 mmol). The resulting mixture was stirred and heated at 100 °C for 72 h. After evaporation of the solvent, the resulting residue was taken up into diethyl ether, and the extract was washed with saturated aqueous ammonium chloride and dried. Evaporation of the solvent gave a crude oil, which was chromatographed on silica gel. Elution with n-hexane–ethyl acetate (10:3 v/v) afforded the starting material (**8**) (136 mg) and the nitrile (**9**) [722 mg, 76% based on consumed (**8**)], whose spectral data and t.l.c. behaviour were identical with those of the sample prepared by method A.

Method C. To a stirred solution of the enone (**8**) (5 g, 0.018 mol) in acetonitrile (50 ml) were added potassium cyanide (1.2 g, 0.018 mol), acetone cyanohydrin (1.57 g, 0.018 mol), and 18-crown-6 (4.8 g, 0.018 mol) at ambient temperature. The mixture was refluxed for 120 h. Removal of the solvent under reduced pressure afforded a residue, which was purified by silica gel column chromatography with n-hexane–ethyl acetate (10:3, v/v) as eluant to afford the starting material (**8**) (790 mg) and the nitrile (**9**) [3.5 g, 75.6% based on consumed (**8**)], whose spectral data and t.l.c. behaviour were identical with those of the sample prepared by method A.

Method D. To a mixture of the enone (**8**) (120 mg, 0.44 mmol) in dry benzene (5 ml) and dry toluene (3 ml) at 0 °C under argon was added dropwise diethylaluminium cyanide (294 mg, 2.6 mmol). After being stirred for 0.5 h, the resulting mixture was poured into 4% aqueous sodium hydroxide (50 ml) at 0 °C. The mixture was extracted with chloroform. The extract was dried and then evaporated to afford a residue, which was purified by chromatography on silica gel, with n-hexane–diethyl ether (10:3), v/v) as eluant, to afford the nitrile (**9**) (103 mg, 78%), whose spectral data and t.l.c. behaviour were identical with those of the sample prepared by method A.

(±)-(1RS,2RS,5SR)-5-*Hydroxy*-2-[2-(2-*methoxyphenyl*)-*ethyl*]-1,3,3-*trimethylcyclohexanecarbaldehyde* (**13**).—To a stirred solution of the nitrile (**10**) (3 mg, 0.01 mmol) in dry 1,2-dimethoxyethane (DME) (2 ml) at −78 °C under argon was added dropwise DIBAL (4.3 mg, 0.03 mmol). The mixture was allowed to warm to room temperature during 0.5 h and was then refluxed for 1 h. To the mixture was added slowly 10% hydrochloric acid (3 ml), and the resulting mixture was heated under reflux for 1 h. After cooling to room temperature, the mixture was extracted with diethyl ether. The extract was washed with saturated aqueous sodium chloride, dried, and evaporated to afford a residue, which was subjected to column chromatography on silica gel. Elution with n-hexane–ethyl acetate (10:1, v/v) gave the hydroxy aldehyde (**13**) (2 mg, 66%) as an oil, $\nu_{max.}$ 3 600 (OH) and 1 723 cm^{-1} (C=O); δ_H 0.87, 1.03, and 1.07 (each 3 H, each s, 3 × Me), 1.20—2.75 (9 H, m, 4 × CH_2 and CH), 3.80 (3 H, s, OMe), 3.98—4.20 (1 H, m, 5-H), 6.69—7.37 (4 H, m, ArH), and 9.40 (1 H, s, CHO); *m/z* 304 (M^+).

(±)-(1RS,2SR,5RS,7SR)-2-[2-(2-*Methoxyphenyl*)*ethyl*]-1,3,3-*trimethyl*-6-*oxabicyclo*[3.2.1]*octan*-7-*ol* (**11**).—To a stirred solution of the nitrile (**9**) (26 mg, 0.087 mmol) in dry DME (3 ml) at −78 °C under argon was added dropwise DIBAL (37 mg, 0.26 mmol). The mixture was allowed to warm to room temperature during 0.5 h, and was then refluxed for 1 h. To the mixture was added slowly 10% hydrochloric acid (3 ml), and the resulting mixture was heated under reflux for 1 h. After cooling to room temperature, the mixture was extracted with diethyl ether. The extract was washed with saturated aqueous sodium chloride, dried, and evaporated to afford a residue, which was subjected to column chromatography on silica gel. Elution with n-hexane–ethyl acetate (5:1, v/v) gave the *cyclic hemiacetal* (**11**) (17 mg, 65%) as needles, m.p. 88—89 °C; δ_H 0.91, 1.03, and 1.23 (each 3 H, each s, 3 × Me), 3.81 (3 H, s, OMe), 4.43 (1 H, br t, *J* 5.7 Hz, 5-H), 5.10 (1 H, br s, 7-H), and 6.71—7.36 (4 H, m, ArH); *m/z* 304 (M^+) (Found: M^+, 304.2036. $C_{19}H_{28}O_3$ requires *M*, 304.1995).

(±)-(1RS,2SR,5RS)-2-[2-(2-*Methoxyphenyl*)*ethyl*]-1,3,3-*trimethyl*-6-*oxabicyclo*[3.2.1]*octan*-7-*one* (**12**).—To a solution of compound (**11**) (5 mg, 0.016 mmol) in dry benzene was added silver carbonate on Celite (80 mg, 0.29 mmol) and the mixture was refluxed for 2 h. After cooling to room temperature, the mixture was filtered through Celite. Evaporation of the filtrate gave a residue, which was chromatographed on silica gel. Elution with n-hexane–ethyl acetate (10:1, v/v) gave the *lactone* (**12**) (4 mg, 80%) as an oil, $\nu_{max.}$ 1 760 cm^{-1} (C=O); δ_H 0.93, 0.99, and 1.21 (each 3 H, each s, 3 × Me), 1.20—2.95 (9 H, m, 4 × CH_2 and CH), 3.81 (3 H, s, OMe), 5.66 (1 H, br t, *J* 5.7 Hz, 5-H), and 6.70—7.31 (4 H, m, ArH); *m/z* 302 (M^+) (Found: M^+, 302.1882. $C_{19}H_{26}O_3$ requires *M*, 302.1882).

(±)-(1RS,2SR)-5,5-*Ethylenedithio*-2-[2-(2-*methoxyphenyl*)-*ethyl*]-1,3,3-*trimethylcyclohexanecarbonitrile* (**14**).—To a stirred solution of the ketone (**9**) (1.13 g, 3.77 mmol) and ethane-1,2-dithiol (710 mg, 7.55 mmol) in dry methylene dichloride (15 ml) was added dropwise boron trifluoride–diethyl ether (43 mg, 0.377 mmol) at room temperature. After being stirred for 5 h at room temperature, the mixture was treated with saturated sodium chloride (10 ml), and the resulting mixture was extracted several times with methylene dichloride. The combined extract was dried and evaporated to afford a powder, which was recrystallised from benzene–n-hexane (2:5, v/v) to give the *thioacetal* (**14**) (1.30 g, 92%) as needles, m.p. 163—164 °C (Found: C, 66.8; H, 7.6; N, 3.6; S, 16.9. $C_{12}H_{29}NOS_2$ requires C, 67.15; H, 7.8; N, 3.75; S, 17.05%); $\nu_{max.}$ 2 220 cm^{-1} (C≡N); δ_H 0.94, 1.28, and 1.45 (each 3 H, each s, 3 × Me), 1.50—2.90 (9 H, m, 4 × CH_2 and CH), 3.17—3.57 (4 H, m, SCH_2CH_2S), 3.80 (3 H, s, OMe), and 6.63—7.34 (4 H, m, ArH); *m/z* 375 (M^+).

(±)-(1RS,2SR)-5,5-*Ethylenedithio*-2-[2-(2-*methoxyphenyl*)-*ethyl*]-1,3,3-*trimethylcyclohexanecarbaldehyde* (**15**).—To a stirred solution of the nitrile (**14**) (3.0 g, 8 mmol) in dry DME (30 ml) under argon was added dropwise DIBAL (2.27 g, 16 mmol) at ambient temperature, and the mixture was refluxed for 2 h. To the resulting mixture was added slowly 10% hydrochloric acid (50 ml) and the mixture was heated under reflux for 2 h. After cooling to room temperature, the mixture was extracted with diethyl ether. The extract was washed with saturated aqueous sodium chloride, dried, and evaporated to afford a residue, which was purified by silica gel column chromatography. Elution with n-hexane–diethyl ether (2:1, v/v) afforded the *aldehyde* (**15**) (2.57 g, 85%) as an oil, $\nu_{max.}$ 1 710 cm^{-1} (C=O); δ_H 1.05 (6 H, s, 2 × Me), 1.08 (3 H, s, Me), 3.18—3.35 (4 H, m, SCH_2CH_2S), 3.78 (3 H, s, OMe), 6.63—7.30 (4 H, m, ArH), and 9.77 (1 H, s, CHO); *m/z* 378 (M^+) (Found: M^+, 378.1688. $C_{21}H_{30}O_2S_2$ requires *M*, 378.1706).

(±)-(1RS,2SR)-2-[2-(2-*Methoxyphenyl*)*ethyl*]-1,3,3-*trimethylcyclohexanecarbaldehyde* (**16**).—A mixture of the thioacetal (**15**) (50 mg, 0.13 mmol) and W_1-Raney nickel (3 g) in acetone (7 ml) was stirred for 0.5 h at room temperature and then filtered through Celite. After evaporation of the filtrate, the residue was purified by column chromatography on silica gel. Elution with n-hexane–ethyl acetate (10:1, v/v) yielded the *aldehyde* (**16**) (23 mg, 60%) as an oil (Found: C, 78.8; H, 10.0. $C_{19}H_{28}O_2$ requires C, 79.1; H, 9.8%); $\nu_{max.}$ 1 710 cm^{-1} (C=O); $\delta_H(CCl_4)$ 0.73, 0.99, and 1.02 (each 3 H, each s, 3 × Me), 0.95—2.85 (11 H, m, 5 × CH_2 and CH), 3.80 (3 H, s, OMe), 6.58—7.23 (4 H, m, ArH), and 9.67 (1 H, s, CHO); *m/z* 288 (M^+).

Ethyl (±)-(1′RS,2′RS)-3-{-2′-[2-(2-*Methoxyphenyl*)*ethyl*]-1′,3′,3′-*trimethylcyclohexyl*}*prop*-2(E)-*enoate* (**17**).—To a stirred suspension of 60% sodium hydride (28 mg, 0.69 mmol) in dry DME (3 ml) was added dropwise triethyl phosphonoacetate [ethyl (diethoxyphosphoryl)acetate] (156 mg, 0.69 mmol) at room temperature. After being stirred for 0.5 h, the mixture was treated dropwise a solution of the aldehyde (**16**) (100 mg, 0.35 mmol) in dry DME (2 ml). The resulting mixture was heated for 4 h under reflux. After addition of large amount of water at 0 °C, the mixture was extracted with diethyl ether. The extract was dried and evaporated to give a residue, which was chromatographed on silica gel. Elution with n-hexane–diethyl ether (20:1, v/v) afforded the α,β-*unsaturated ester* (**17**) (116 mg, 95%) as an oil (Found: C, 77.2; H, 9.3. $C_{23}H_{34}O_3$ requires C, 77.05; H, 9.55%); $\nu_{max.}$ 1 700 cm^{-1} (C=O); $\delta_H(CCl_4)$ 0.77, 0.93, and 1.05 (each 3 H, each s, 3 × Me), 1.23 (3 H, t, *J* 7 Hz, CH_2Me), 3.82 (3 H, s, OMe), 4.12 (2 H, q, *J* 7 Hz, CH_2Me), 5.68 (1 H, d, *J* 16 Hz, =$CHCO_2Et$), and 6.63—7.35 (5 H, m, ArH and olefinic H); *m/z* 358 (M^+).

(±)-(1′RS,2′RS)-3-{2′-[2-(2-*Methoxyphenyl*)*ethyl*]-1′,3′,3′-*trimethylcyclohexyl*}*prop*-2(E)-*enol* (**18**).—To a stirred solution of the ester (**17**) (3.0 g, 8.38 mmol) in dry diethyl ether (30 ml) at −78 °C was added dropwise DIBAL (2.38 g, 16.76 mmol). After 1 h, the mixture was allowed to warm to room temperature and was then stirred for 1 h at the same temperature. To the stirred solution was added water (2.4 ml) at 0 °C, and the mixture was stirred for 0.5 h. The resulting mixture was filtered through Celite and the filtrate was evaporated to give a residue, which was chromatographed on silica gel. Elution with n-hexane–ethyl acetate (10:1, v/v) gave the *allylic alcohol* (**18**) (2.5 g, 94%) as an oil (Found: C, 80.1; H, 10.4. $C_{21}H_{32}O_2$ requires C, 79.7; H, 10.2%); $\nu_{max.}$ 3 600 cm^{-1} (OH); $\delta_H(CCl_4)$ 0.77, 0.93, and 1.00 (each 3 H, each s, 3 × Me), 0.90—2.85 (11 H, m, 5 × CH_2 and CH), 3.80 (3 H, s, OMe), 3.97 (2 H, br d, *J* 4 Hz, CH_2OH), 5.30—5.73 (1 H, m, =$CHCH_2$), 5.87 (1 H, d, *J* 16 Hz, CH=$CHCH_2$), and 6.62—7.30 (4 H, m, ArH); *m/z* 316 (M^+).

(±)-(1″RS,2″RS)-6-{2-[3-*Hydroxyprop*-1(E)-*enyl*]-2″,6″,6″-*trimethylcyclohexylethyl*}*cyclohex*-2-*enone* (**19**).—To a solution of the alcohol (**18**) (43 mg, 0.14 mmol) in dry THF (3 ml) was added 60% sodium hydride (8 mg, 0.2 mmol) and the mixture was stirred for 30 min at room temperature. Liquid ammonia (6 ml), t-butyl alcohol (3 ml), and lithium (30 mg, 4.3 mmol) were added to the above mixture, and the resulting mixture was stirred for 2 h under nitrogen. After evaporation of the solvents, followed by addition of saturated aqueous ammonium chloride, the mixture was extracted with diethyl ether. The extract was dried and evaporated to give an oil, which was dissolved in methylene dichloride (2.5 ml). After addition of 10% hydrochloric acid (2.5 ml), the mixture was stirred for 15 h under reflux. The mixture was extracted with methylene dichloride, and the extract was washed with saturated aqueous sodium chloride, dried, and evaporated to give a residue, which was purified by silica gel chromatography. Elution with n-hexane–ethyl acetate (10:1, v/v) gave the starting material (**18**) (10 mg) and the *enone* (**19**) [17 mg, 50% based on consumed (**18**)] as an oil, $\nu_{max.}$ 3 600 (OH) and 1 670 cm^{-1} (C=O); $\delta_H(CCl_4)$ 0.77, 0.86, and 0.95 (each 3 H, each s, 3 × Me), 4.03 (2 H, d, *J* 4 Hz, CH_2OH), 5.30—5.86 (2 H, m, =$CHCH_2OH$ and =CHCO), 5.87 (1 H, br d, *J* 16 Hz, CH=$CHCH_2$), and 6.65—7.00 (1 H, m, CH=CHCO); *m/z* 304 (M^+) (Found: M^+, 304.2403. $C_{20}H_{32}O_2$ requires *M*, 304.2405).

(±)-(1′RS,2′RS)-(E)-3-{1′,3′,3′-*Trimethyl*-2′-[2-(2-*oxocyclohex*-3-*enyl*)*ethyl*]*cyclohexyl*}*acrylaldehyde* (**20**).—To a solution of the alcohol (**19**) (134 mg, 0.44 mmol) in dry methylene dichloride (5 ml) were added Florisil (190 mg) and PCC (190 mg, 0.88 mmol), and the mixture was stirred for 3 h at room temperature. Filtration, followed by evaporation of the filtrate, gave a residue, which was chromatographed on silica gel. Elution with n-hexane–ethyl acetate (10:2, v/v) afforded the *aldehyde* (**20**) (110 mg, 83%) as an oil, $\nu_{max.}$ 1 670 cm^{-1} (C=O); $\delta_H(CCl_4)$ 0.75, 0.90, and 1.07 (each 3 H, each s, 3 × Me), 0.95—2.50 (15 H, m, 7 × CH_2 and CH), 5.73—6.23 (2 H, m, =$CHCHO$ and =CHCO), 6.67—7.03 (1 H, m, CH=CHCO), 6.97 (1 H, d, *J* 16 Hz, CH=CHCHO), and 9.47 (1 H, d, *J* 7 Hz, CHO); *m/z* 302 (M^+) (Found: M^+, 302.2247. $C_{20}H_{30}O_2$ requires *M*, 302.2278).

(±)-(1′RS,2′RS)-3-{1′,3′,3′-*Trimethyl*-2′-[2-(2-*oxocyclohex*-3-*enyl*)*ethyl*]*cyclohexyl*}*prop*-2(E)-*enoic Acid* (**21**).—To a stirred mixture of the aldehyde (**20**) (100 mg, 0.3 mmol), t-butyl alcohol (0.5 ml), and water (4 ml) were added sulphamic acid (400 mg, 4.1 mmol) and sodium chlorite (400 mg, 4.4 mmol), and the mixture was stirred for 1 h at room temperature. After addition of water (4 ml), the mixture was extracted with diethyl ether. The extract was washed with water, dried, and evaporated to give a residue, which was subjected to silica gel column chromatography. Elution with n-hexane–diethyl ether (1:2, v/v) gave the *carboxylic acid* (**21**) (74 mg, 70%) as a syrup, $\nu_{max.}$ 1 690 and 1 670 cm^{-1} (C=O); $\delta_H(CCl_4)$ 0.73, 0.90, and 1.05 (each 3 H, each s, 3 × Me), 0.98—2.55 (15 H, m, 7 × CH_2 and CH), 5.70 (1 H, d, *J* 16 Hz, =$CHCO_2H$), 5.93 (1 H, br d, *J* 10 Hz, =CHCO), 6.62—7.03 (1 H, m, CH_2CH=), 7.28 (1 H, d, *J* 16 Hz, CH=$CHCO_2H$), and 10.90 (1 H, br s, CO_2H); *m/z* 318 (M^+) (Found: M^+, 318.2193. $C_{20}H_{30}O_3$ requires *M*, 318.2165).

Methyl (±)-(1′RS,2′RS)-3-{1′,3′,3′-*Trimethyl*-2′-[2-(2-*oxocyclohex*-3-*enyl*)*ethyl*]*cyclohexyl*}*prop*-2(E)-*enoate* (**22**).—To a solution of the acid (**21**) (10 mg, 0.03 mmol) in anhydrous methanol (1 ml) at 0 °C was slowly added conc. sulphuric acid (0.05 ml), and the mixture was stirred for 1 h at room temperature. After addition of water (5 ml), the mixture was extracted with diethyl ether. The extract was washed with saturated aqueous sodium hydrogen carbonate, dried, and evaporated to give a residue, which was purified by silica gel column chromatography. Elution with n-hexane–diethyl ether (10:1, v/v) afforded the *ester* (**22**) (7.5 mg, 72%) as an oil, $\nu_{max.}$ 1 710 and 1 670 cm^{-1} (C=O); δ_H 0.74, 0.89, and 1.01 (each 3 H, each s, 3 × Me), 1.05—2.50 (15 H, m, 7 × CH_2 and CH), 3.73 (3 H, s, OMe), 5.77 (1 H, d, *J* 16 Hz, =$CHCO_2Me$), 5.97 (1 H, dt, *J* 2 and 10 Hz, CH_2CH=CH=), 6.91 (1 H, m, CH_2CH=), and 7.19 (1 H, d, *J* 16 Hz, CH=$CHCO_2Me$); *m/z* 332 (M^+) (Found: M^+, 332.2350. $C_{21}H_{32}O_3$ requires *M*, 332.2349).

(±)-(3RS,4SR,4aSR,4bRS,8aSR,10aSR)-1,2,3,4,4a,4b,5,6,7,8,8a,9,10,10a-*Tetradecahydro*-4b,8,8-*trimethyl*-1-*oxo*-3,10a-*ethanophenanthrene*-4-*carboxylate* (**23**).—To a stirred solution of LiMHDS, prepared from 1,1,1,3,3,3-hexamethyldisilazane (19 mg, 0.12 mmol) and butyl-lithium (7.5 mg, 0.12 mmol), in dry n-hexane (4 ml) at −78 °C under argon was added a

solution of the ester (**22**) (30 mg, 0.09 mmol) in dry diethyl ether (0.5 ml), and the mixture was stirred for 2 h at −78 °C, and for 4 h at ambient temperature. After the reaction mixture had been poured into saturated aqueous ammonium chloride (3 ml), the mixture was extracted with diethyl ether. The extract was dried and evaporated to give a residue, which was chromatographed on silica gel. Elution with n-hexane–ethyl acetate (10:1, v/v) afforded the *tetracyclic compound* (**23**) (5 mg, 17%) as needles, m.p. 123—125 °C; $\nu_{max.}$ 1 730 and 1 715 cm^{-1} (C=O); δ_H 0.93, 1.06, and 1.13 (each 3 H, each s, 3 × Me), 0.90—2.57 (19 H, m, 8 × CH_2 and 3 × CH), and 3.69 (3 H, s, OMe); *m/z* 332 (M^+) (Found: M^+, 332.2352. $C_{21}H_{32}O_3$ requires *M*, 332.2349).

(±)-(3RS,4aRS,4bSR,8aRS,10aRS)-3,4,4a,4b,5,6,7,8,8a,9,10,-10a-*Dodecahydro*-4b,8,8-*trimethyl*-3,10a-*ethanophenanthren*-1(2H)-*one* (**25**).—To a solution of the keto ester (**23**) (8 mg, 0.024 mmol) in dry diethyl ether (1 ml) at −78 °C was slowly added DIBAL (13.6 mg, 0.096 mmol). After attaining room temperature, the mixture was stirred for 2 h at the same temperature. After addition of water (0.05 ml), the mixture was further stirred for 30 min at room temperature and then filtered through Celite. Evaporation of the filtrate gave a residue, which was dissolved in DMF (1.5 ml). After addition of PDC (22 mg, 0.06 mmol), the mixture was stirred for 2 h at room temperature and then diluted with water (5 ml). The mixture was extracted with benzene and the extract was washed with water, dried, and evaporated. Purification of the product by silica gel column chromatography with n-hexane–ethyl acetate (10:1, v/v) as eluant yielded the aldehyde (**24**) (4 mg, 55%) as needles, m.p. 121—123 °C; $\nu_{max.}$ 1 720 cm^{-1} (C=O); $\delta_H(CCl_4)$ 0.95, 1.07, and 1.13 (each 3 H, each s, 3 × Me) and 9.73 (1 H, br s, CHO); *m/z* 302 (M^+).

To a solution of the above product (**24**) (4 mg, 0.013 mmol) in dry xylene (1 ml) was added TTPRCl (15 mg, 0.016 mmol) and the mixture was stirred and heated for 1 h at 140 °C. After evaporation of the solvent, the residue was taken up into diethyl ether and the solution was filtered through Celite. Evaporation of the filtrate afforded a residue, which was chromatographed on silica gel. Elution with n-hexane–ethyl acetate (10:1, v/v) gave the *ketone* (**25**) (1 mg, 28%) as needles, m.p. 80—82 °C; $\nu_{max.}$ 1 710 cm^{-1} (C=O); δ_H 0.91, 0.97, and 1.14 (each 3 H, each s, 3 × Me) and 1.10—2.40 (21 H, m, 9 × CH_2 and 3 × CH); *m/z* 274 (M^+) (Found: M^+, 274.2296. $C_{19}H_{30}O$ requires *M*, 274.2301).

(±)-(2RS,3RS,4aRS,4bSR,8aRS,10RS)-3,4,4a,4b,5,6,7,8,8a,-9,10,10a-*Dodecahydro*-2,4b,8,8-*tetramethyl*-3,10a-*ethano-phenanthren*-1(2H)-*one* (**26**).—To a stirred solution of LDA, prepared from di-isopropylamine (3.6 mg, 0.036 mmol) and butyl-lithium (2.3 mg, 0.036 mmol), in dry THF (0.5 ml) at −78 °C was added a solution of the ketone (**25**) (2 mg, 0.007 mmol) in dry THF (0.5 ml), and the mixture was stirred for 2 h at −78 °C under argon. After addition of methyl iodide (7.2 mg, 0.05 mmol), the mixture was allowed to attain 0 °C and was then stirred for 3 h at this temperature. After addition of saturated aqueous ammonium chloride (1 ml), followed by extraction with diethyl ether, the extract was dried and evaporated to give a residue, which was purified by h.p.l.c. [LiChrosorb SI 60 (4 × 250 mm); n-hexane–ethyl acetate (100:3, v/v) flow rate 2.0 ml min^{-1}] to afford the *tetramethyl compound* (**26**) (1.4 mg, 67%) as an oil, $\nu_{max.}$ 1 710 cm^{-1} (C=O); δ_H 0.91, 0.99, and 1.14 (each 3 H, each s, 3 × Me) and 1.17 (3 H, d, *J* 7 Hz, 2-Me); *m/z* 288 (M^+) (Found: M^+, 288.2451. $C_{20}H_{32}O$ requires *M*, 288.2450).

(+)-(4aS,5S)-4,4a,5,6,7,8-*Hexahydro*-5-*hydroxy*-4a-*methyl-naphthalen*-2(3H)-*one* (**28**).—To a solution of the enone (**27**) (47 g, 0.264 mol) in ethanol (1 l) at 0 °C was added portionwise sodium borohydride (3.3 g, 0.087 mmol) and the mixture was stirred for 2 min at 0 °C, then treated with acetic acid (30 ml), stirring for another 5 min at 0 °C and then evaporated. The residue was partitioned between methylene dichloride and saturated aqueous sodium chloride. The organic layer was dried and evaporated to give a residue, which was subjected to silica gel column chromatography. Elution with n-hexane–ethyl acetate (1:1, v/v) afforded the *alcohol* (**28**) (45.15 g, 95%) as an oil, $[\alpha]_D^{15}$ +122.2° (*c* 0.18) (Found: C, 73.4; H, 9.25. $C_{11}H_{16}O_2$ requires C, 73.3; H, 8.95%); $\nu_{max.}$ 3 600 (OH) and 1 660 cm^{-1} (C=O); δ_H 1.13 (3 H, s, Me), 1.25—2.50 (10 H, m, 5 × CH_2), 3.05 (1 H, br s, OH), 3.06—3.65 (1 H, m, 5-H), and 5.63 (1 H, br s, 1-H); *m/z* 180 (M^+).

(+)-(4aS,5S)-5-*Benzoyloxy*-4,4a,5,6,7,8-*hexahydro*-4a-*methylnaphthalen*-2(3H)-*one* (**29**).—To a solution of the alcohol (**28**) (55.0 g, 0.306 mol) in pyridine (26 ml, 0.322 mol) at 0 °C was added benzoyl chloride (37 ml, 0.322 mol), and the mixture was stirred for 10 h at room temperature. After filtration, the filtrate was diluted with water and then extracted with diethyl ether. The extract was washed with water, dried, and evaporated to give a residue, which was purified by silica gel column chromatography. Elution with n-hexane–ethyl acetate (5:1, v/v) yielded the *benzoate* (**29**) (83.31 g, 96%) as an oil, $[\alpha]_D^{15}$ +158.9° (*c* 0.18) (Found: C, 76.2; H, 7.2. $C_{18}H_{20}O_3$ requires C, 76.05; H, 7.1%); $\nu_{max.}$ 1 715 and 1 660 cm^{-1} (C=O); δ_H 1.43 (3 H, s, Me), 1.40—2.50 (10 H, m, 5 × CH_2), 4.89 (1 H, dd, *J* 4.3 and 10 Hz, 5-H), 5.83 (1 H, br s, 1-H), 7.31—7.60 (3 H, m, ArH), and 8.91—9.07 (2 H, m, ArH); *m/z* 284 (M^+).

(+)-(4aS,5S)-5-*Benzoyloxy*-3,4,4a,5,6,7-*hexahydro*-1,1,4a-*tri-methylnaphthalen*-2(1H)-*one* (**30**).—To a stirred solution of potassium t-butoxide in t-butyl alcohol, prepared from potassium (570 mg, 21.1 mmol) and t-butyl alcohol (30 ml), was added a solution of the enone (**29**) (2.01 g, 7.1 mmol) in t-butyl alcohol (10 ml), and the mixture was stirred for 15 min at room temperature. After addition of methyl iodide (1.54 ml, 24.9 mmol), the resulting mixture was further stirred for 45 min at ambient temperature and was then neutralised at 0 °C by careful addition of 10% hydrochloric acid. The mixture was extracted with diethyl ether and the extract was washed with saturated aqueous sodium chloride, and dried. Evaporation of the solvent gave a residue, which was chromatographed on silica gel. Elution with n-hexane–ethyl acetate (100:3, v/v) afforded the *ketone* (**30**) (1.86 g, 84%) as an oil, $[\alpha]_D^{15}$ +22.4° (*c* 0.17) (Found: C, 77.05; H, 7.5. $C_{20}H_{24}O_3$ requires C, 76.9; H, 7.75%); $\nu_{max.}$ 1 710 cm^{-1} (C=O); δ_H 1.19, 1.27, and 1.29 (each 3 H, each s, 3 × Me), 1.30—2.60 (8 H, m, 4 × CH_2), 5.04 (1 H, dd, *J* 5.7 and 10.8 Hz, 5-H), 5.60 (1 H, t, *J* 4.3 Hz, 8-H), 7.29—7.64 (3 H, m, ArH), and 7.71—8.13 (2 H, m, ArH); *m/z* 312 (M^+).

(−)-(1S,8aS)-1,2,3,5,6,7,8,8a-*Octahydro*-5,5,8a-*trimethyl-naphthalen*-1-*ol* (**31**).—A mixture of the ketone (**30**) (1.8 g, 5.8 mmol), potassium hydroxide (3.0 g, 46 mmol), and hydrazine hydrate (3.3 ml, 68 mmol) in diethylene glycol (33 ml) was refluxed for 2 h, and then the excess of hydrazine hydrate was evaporated off. The reaction mixture was further refluxed for 4 h, diluted with water (100 ml), and then extracted with diethyl ether. The extract was dried and evaporated to give a residue, which was purified by silica gel column chromatography. Elution with n-hexane–ethyl acetate (5:1, v/v), followed by recrystallisation of the product from n-hexane afforded the *alcohol* (**31**) (1.052 g, 93%) as needles, m.p. 82—83 °C; $[\alpha]_D^{15}$ −58.8° (*c* 0.16) (Found: C, 80.3; H, 11.35. $C_{13}H_{22}O$ requires C, 80.35; H, 11.4%); $\nu_{max.}$ 3 600 cm^{-1}(OH); δ_H 1.06 (3 H, s, Me), 1.11 (6 H, s, 2 × Me), 1.20—2.25 (10 H, m, 5 × CH_2), 3.41 (1 H, dd, *J* 7.1 and 8.6 Hz, 1-H), and 5.37 (1 H, t, *J* 3.6 Hz, 4-H); *m/z* 194 (M^+).

(+)-(1S,4aS,8aS)-1,2,3,4,4a,5,6,7,8,8a-*Decahydro*-5,5,8a-*trimethylnaphthalen*-1-*ol* (**32**).—A mixture of the olefin (**31**) (820 mg, 4.18 mmol) and Adams' catalyst (120 mg) in acetic acid (10 ml) was stirred under an atmosphere of hydrogen until absorption of hydrogen had ceased. After filtration, followed by addition of water (20 ml), the mixture was extracted with diethyl ether. The extract was washed with saturated aqueous sodium hydrogen carbonate, dried, and evaporated to give a residue, which was chromatographed on silica gel. Elution with n-hexane–ethyl acetate, followed by recrystallisation from n-hexane, afforded the *alcohol* (**32**) (792 mg, 95%) as needles, m.p. 88—89 °C; $[\alpha]_D^{17}$ +1.50° (*c* 0.40) (Found: C, 79.45; H, 12.45. $C_{13}H_{24}O$ requires C, 79.55; H, 12.3%); $\nu_{max.}$ 3 610 cm^{-1} (OH); δ_H 0.84, 0.86, and 0.89 (each 3 H, each s, 3 × Me), 0.80—1.90 (13 H, m, 6 × CH_2 and CH), and 3.14 (1 H, dd, *J* 4.3 and 10 Hz, 1-H); *m/z* 196 (M^+).

(−)-(4aS,8aS)-3,4,4a,5,6,7,8,8a-*Octahydro*-5,5,8a-*trimethylnaphthalen*-1(2H)-*one* (**33**).—To a solution of the alchohol (**32**) (792 mg, 4 mmol) in methylene dichloride (20 ml) were added Florisil (1.3 g) and PCC (1.3 g, 6 mmol), and the mixture was stirred for 2 h at room temperature. After filtration through Celite, followed by evaporation of the filtrate, the residue was subjected to silica gel column chromatography. Elution with n-hexane–ethyl acetate (100:5, v/v) yielded the *ketone* (**33**) (706 mg, 90%) as an oil,$[\alpha]_D^{17}$ −39.1° (*c* 0.44); $\nu_{max.}$ 1 700 cm^{-1} (C=O); δ_H 0.89, 0.96, and 1.15 (each 3 H, each s, 3 × Me); *m/z* 194 (M^+) (Found: M^+, 194.1668. $C_{13}H_{22}O$ requires *M*, 194.1667).

(−)-(2R,4aS,8aS)-2-*Bromo*-3,4,4a,5,6,7,8,8a-*octahydro*-5,5,8a-*trimethylnaphthalen*-1(2H)-*one* (**34**).—To a solution of the ketone (**33**) (62 mg, 0.32 mmol) in acetic acid (5 ml) was added PBB (101 mg, 0.32 mmol), and the mixture was stirred for 2 h at room temperature. After addition of water (10 ml), the resulting mixture was extracted with diethyl ether. The extract was washed with saturated aqueous sodium hydrogen carbonate, dried, and evaporated to give a residue, which was chromatographed on silica gel and eluted with n-hexane–ethyl acetate (100:2, v/v). Recrystallisation of the product from n-hexane afforded the *bromide* (**34**) (84 mg, 97%) as needles, m.p. 126—128 °C; $[\alpha]_D^{17}$ −22.0° (*c* 0.30) (Found: C, 57.15; H, 7.55; Br, 29.3. $C_{13}H_{21}BrO$ requires C, 57.15; H, 7.7; Br, 29.3%); $\nu_{max.}$ 1 720 cm^{-1} (C=O); δ_H 0.90, 0.91, and 1.17 (each 3 H, each s, 3 × Me), 1.15—2.80 (11 H, m, 5 × CH_2 and CH), and 4.94 (1 H, dd, *J* 5.7 and 11.4 Hz, 2-H); *m/z* 272 (M^+).

(−)-(4aS,8aS)-3,4,4a,5,6,7,8,8a-*Octahydro*-2-*hydroxy*-5,5,8-*trimethylnaphthalen*-1(2H)-*one* (**35**).—To a solution of the bromide (**34**) (40 mg, 0.15 mmol) in DMF (3 ml) at room temperature was slowly added 0.74% aqueous sodium hydroxide (1 ml), and the mixture was stirred for 30 min at the same temperature before being neutralised at 0 °C by addition of 1% hydrochloric acid. The mixture was extracted with diethyl ether, the extract was washed with saturated aqueous sodium chloride and dried, and evaporation of the solvent afforded a residue, which was chromatographed on silica gel. Elution with n-hexane–ethyl acetate (10:1, v/v) yielded the *acyloin* (**35**) (30 mg, 97%) as an oil, $[\alpha]_D^{17}$ −28.9° (*c* 0.28) (Found: C, 74.2; H, 10.4. $C_{13}H_{22}O_2$ requires C, 74.25; H, 10.55%); $\nu_{max.}$ 3 470 (OH) and 1 700 cm^{-1} (C=O); δ_H 0.91, 0.93, and 1.16 (each 3 H, each s, 3 × Me), 1.05—2.58 (11 H, m, 5 × CH_2 and CH), 4.60 (1 H, d, *J* 3.4 Hz, OH), and 4.38 (1 H, ddd, *J* 3.4, 7.1, and 11.4 Hz, 2-H); *m/z* 210 (M^+).

(−)-(1S,2S)-2-(3-*Hydroxypropyl*)-1,3,3-*trimethylcyclohexanecarboxylate* (**36**).—To a solution of the acyloin (**35**) (125 mg, 0.6 mmol) in a mixture of methanol (1 ml) and benzene (3 ml) at 0 °C was added LTA (293 mg, 0.6 mmol), and the mixture was stirred for 10 min at room temperature. After addition of saturated aqueous sodium hydrogen carbonate, followed by filtration through Celite, the filtrate was extracted with benzene. The extract was dried and evaporated to give the crude aldehyde (128 mg, 90%), which was used in the next reaction without further purification.

To a solution of the above product (40 mg, 0.17 mmol) in methanol at 0 °C was added sodium borohydride (6 mg, 0.17 mmol), and the mixture was stirred for 20 min at room temperature. After evaporation of the solvent, the residue was partitioned between saturated aqueous sodium chloride and methylene dichloride. The organic layer was dried and evaporated to give a residue, which was subjected to silica gel column chromatography. Elution with n-hexane–ethyl acetate (10:4, v/v) afforded the *alcohol* (**36**) (39 mg, 97%) as an oil, $[\alpha]_D^{17}$ −5.70° (*c* 0.14); $\nu_{max.}$ 3 600 (OH) and 1 715 cm^{-1} (C=O); δ_H 0.89, 0.93, and 1.19 (each 3 H, each s, 3 × Me), 1.10—1.85 (11 H, m, 5 × CH_2 and CH), 3.56 (2 H, br t, *J* 5.7 Hz, CH_2O), and 3.64 (3 H, s, OMe); *m/z* 242 (M^+) (Found: M^+, 242.1882. $C_{14}H_{26}O_3$ requires *M*, 242.1884).

(−)-(1S,2S)-1,3,3-*Trimethyl*-2-[3-(2-*nitrophenylseleno*)-*propyl*]*cyclohexanecarboxylate* (**37**).—To a stirred solution of the alcohol (**36**) (25 mg, 0.1 mmol) and 2-nitrophenylselenocyanate (47 mg, 0.2 mmol) in dry THF (3 ml) was added tributylphosphine (0.05 ml, 0.2 mmol) at room temperature, and the mixture was stirred for 20 min at the same temperature. Evaporation of the solvent, followed by purification of the residue by silica gel chromatography with n-hexane–ethyl acetate (100:5, v/v) as eluant, gave the *selenide* (**37**) (48 mg, 98%) as a yellow oil, $[\alpha]_D^{17}$ −3.30° (*c* 0.18); $\nu_{max.}$ 1 710 cm^{-1} (C=O); δ_H 0.91 (6 H, s, 2 × Me), 1.19 (3 H, s, Me), 1.25—2.10 (11 H, m, 5 × CH_2 and CH), 2.85 (2 H, br t, *J* 6 Hz, CH_2Se), 3.57 (3 H, s, OMe), 7.15—7.57 (3 H, m, ArH), and 8.22 (1 H, br d, *J* 7 Hz, ArH); *m/z* 425 (M^+) and 427 ($M^+ + 2$) [Found: M^+, 425.1269 and $(M + 2)^+$ 427.1262. $C_{20}H_{29}NO_4Se$ requires *M*, 425.1304 and (*M* + 2), 427.1280].

Methyl (+)-(1S,2S)-2-*Allyl*-1,3,3-*trimethylcyclohexanecarboxylate* (**38**).—To a stirred solution of the selenide (**37**) (40 mg), 0.094 mmol) in THF (3 ml) at 0 °C was added 30% aqueous hydrogen peroxide (0.1 ml), and the mixture was stirred for 10 h at room temperature. After addition of water (5 ml), the mixture was extracted with diethyl ether. The extract was washed with saturated aqueous sodium chloride, dried, and evaporated to give a residue, which was purified by chromatography on silica gel. Elution with n-hexane–ethyl acetate (100:5, v/v) afforded the *olefin* (**38**) (19 mg, 91%) as an oil, $[\alpha]_D^{17}$ +22.9° (*c* 0.28); $\nu_{max.}$ 1 710 and 1 640 cm^{-1} (C=O); δ_H 0.89, 0.94, and 1.20 (each 3 H, each s, 3 × Me), 1.20—2.30 (9 H, m, 4 × CH_2 and CH), 3.54 (3 H, s, OMe), 4.77 (1 H, br d, *J* 10 Hz, CH=C*H*H), 4.82 (1 H, br d, *J* 16 Hz, CH=CH*H*), and 5.40—5.87 (1 H, m, C*H*=CH_2); *m/z* 224 (M^+) (Found: M^+, 224.1777. $C_{14}H_{24}O_2$ requires *M*, 244.1777).

(+)-(1S,2S)-(2-*Allyl*-1,3,3-*trimethylcyclohexyl*)*methanol* (**39**).—To a stirred mixture of lithium aluminium hydride (34 mg, 0.89 mmol) in dry diethyl ether (5 ml) at 0 °C was added dropwise a solution of the ester (**38**) (100 mg, 0.45 mmol) in dry diethyl ether (1 ml), and the mixture was stirred for 30 min at room temperature. After successive addition of water (0.03 ml), 15% aqueous sodium hydroxide (0.03 ml), and water (0.09 ml), followed by stirring for 30 min, the mixture was filtered through Celite and washed with diethyl ether. Evaporation of the combined filtrate and washings gave a residue, which was chromatographed on silica gel. Elution with n-hexane–ethyl acetate (10:1, v/v) afforded a solid, which was recrystallised

from n-hexane to yield the *alcohol* (**39**) (83 mg, 95%) as needles, m.p. 30—31 °C; $[\alpha]_D^{17}$ +5.0° (*c* 0.24); $\nu_{max.}$ 3 550 (OH) and 1 620 cm^{-1} (C=C); δ_H 0.80, 0.89, and 0.93 (each 3 H, each s, 3 × Me), 1.15—1.60 (7 H, m, 3 × CH_2 and CH), 1.91—2.14 (2 H, m, CH_2CH=), 2.97 and 3.43 (each 1 H, each br d, *J* 11.4 Hz, CH_2OH), 4.83 (1 H, br d, *J* 10 Hz, CH=C*H*H), 4.95 (1 H, br d, *J* 16 Hz, CH=CH*H*), and 5.47—6.20 (1 H, m, C*H*=CH_2); *m/z* 196 (M^+) (Found: M^+, 196.1827. $C_{13}H_{24}O$ requires *M*, 196.1829).

(+)-(1S,2S)-2-*Allyl*-1,3,3-*trimethylcyclohexanecarbaldehyde Ethylene Acetal* (**40**).—To a stirred solution of the alcohol (**39**) (100 mg, 0.51 mmol) in dry methylene dichloride (3 ml) were added Florisil (220 mg) and PCC (220 mg, 1.0 mmol) at room temperature, and the mixture was stirred for 1 h at the same temperature. After filtration through Celite, followed by evaporation of the filtrate, the residue was chromatographed on silica gel. Elution with n-hexane–ethyl acetate (100:3, v/v) gave the corresponding aldehyde (87 mg, 88%) as an oil, $\nu_{max.}$ 1 710 cm^{-1} (C=O); $\delta_H(CCl_4)$ 0.93, 1.00, and 1.10 (each 3 H, each s, 3 × Me), 4.87 (1 H, br d, *J* 16 Hz, CH=C*H*H), 4.88 (1 H, br d, *J* 10 Hz, CH=CH*H*), 5.35—5.90 (1 H, m, C*H*=CH_2), and 9.07 (1 H, s, CHO); *m/z* 194 (M^+).

A mixture of the above aldehyde (30 mg, 0.15 mmol), ethylene glycol (0.013 ml, 0.23 mmol), and toluene-*p*-sulphonic acid (3 mg) in dry benzene (5 ml) was refluxed for 20 min in a Dean–Stark apparatus. After dilution with benzene, the mixture was washed successively with saturated aqueous sodium hydrogen carbonate and water, dried, and evaporated. Purification of the crude product by silica gel column chromatography with n-hexane–ethyl acetate (40:1, v/v) as eluant yielded the *acetal* (**40**) (36 mg, 98%) as an oil, $[\alpha]_D^{17}$ +5.0° (*c* 0.08); $\nu_{max.}$ 1 630 cm^{-1} (C=O); $\delta_H(CCl_4)$ 0.87 (6 H, s, 2 × Me), 0.90 (3 H, s, Me), 1.10—1.50 (7 H, m, 3 × CH_2 and CH), 2.00—2.40 (2 H, m, CH_2CH=), 3.63—3.90 (4 H, m, OCH_2CH_2O), 4.50 (1 H, s, OCHO), 4.73 (1 H, br d, *J* 10 Hz, CH=C*H*H), 4.82 (1 H, br d, *J* 16 Hz, CH=C*H*H), and 5.40—6.10 (1 H, m, C*H*=CH_2); *m/z* 238 (M^+) (Found: M^+, 238.1931. $C_{15}H_{26}O_2$ requires *M*, 238.1914).

(−)-(1″S,2″S)-(*E*)-2-{2′-[2″-(*Dioxolan*-2-*yl*)-2″,6″,6″-*trimethylcyclohexyl*]*ethylidene*}*cyclohexanone* (**42**).—A mixture of the olefin (**40**) (159 mg, 0.67 mmol), osmium tetraoxide (8 mg, 0.003 mmol), diethyl ether (6 ml), and water (6 ml) was stirred for 5 min at room temperature, sodium periodate (4.29 g, 20 mmol) was addded, and the mixture was stirred for 10 h at the same temperature and then extracted with diethyl ether. The extract was washed with saturated aqueous sodium chloride, dried, and evaporated to give a residue, which was subjected to chromatography on silica gel. Elution with n-hexane–ethyl acetate (10:1, v/v) afforded the corresponding aldehyde (**41**) (125 mg, 78%) as an oil, $\nu_{max.}$ 1 720 cm^{-1} (C=O); $\delta_H(CCl_4)$ 0.82, 0.85, and 0.90 (each 3 H, each s, 3 × Me), 3.60—3.90 (4 H, m OCH_2CH_2O), 4.20 (1 H, s, OCHO), and 9.52 (1 H, t, *J* 1 Hz, CHO); *m/z* 240 (M^+).

To a stirred solution of LDA, prepared from di-isopropylamine (37 mg, 0.37 mmol) and butyl-lithium (23 mg, 0.37 mmol), in dry THF (3 ml) at −78 °C was slowly added cyclohexanone (55 mg, 0.23 mmol), and the mixture was stirred for 1 h at this temperature. After slow addition, at −78 °C, of a solution of the above aldehyde (**41**) (55 mg, 0.23 mmol) in dry THF (1 ml), the mixture was allowed to warm to room temperature and was stirred for 1 h at the same temperature. After addition, at 0 °C, of saturated aqueous ammonium chloride, the mixture was extracted with diethyl ether. The extract was dried and evaporated to give a residue, which was chromatographed on silica gel. Elution with n-hexane–ethyl acetate (25:2, v/v) afforded a solid, which was recrystallised from n-hexane to afford the *enone* (**42**) (45 mg, 62%) as needles, m.p. 52—53 °C; $[\alpha]_D^{17}$ −10.0° (*c* 0.08); $\nu_{max.}$ 1 670 cm^{-1} (C=O); δ_H 0.84, 0.90, and 0.97 (each 3 H, each s, 3 × Me), 1.05—2.60 (17 H, m, 8 × CH_2 and CH), 3.66—3.91 (4 H, m, OCH_2CH_2O), 4.43 (1 H, s, OCHO), and 6.69 (1 H, tt, *J* 1.4 and 6.6 Hz, olefinic H); *m/z* 320 (M^+) (Found: M^+, 320.2349. $C_{20}H_{32}O_3$ requires *M*, 320.2349).

Methyl (1′S,2′S)-3-{1′,3′,3′-*Trimethyl*-2′-[2-(2-*oxocyclohex*-3-*enyl*)*ethyl*]*cyclohexyl*}*prop*-2(E)-*enoate* (**46**).—A mixture of the enone (**42**) (120 mg, 0.37 mmol) and 10% palladium–charcoal (50 mg) in ethanol (10 ml) was stirred under an atmosphere of hydrogen until absorption of hydrogen had ceased. After filtration, the filtrate was evaporated and the residue was chromatographed on silica gel. Elution with n-hexane–ethyl acetate (100:8, v/v) yielded the ketone (**43**) (120 mg, 98%) as an oil, $\nu_{max.}$ 1 700 cm^{-1} (C=O); $\delta_H(CCl_4)$ 0.87 (6 H, s, 2 × Me), 0.90 (3 H, s, 3 × Me), 3.68—3.80 (4 H, m, OCH_2CH_2O), and 4.43 and 4.56 [1 H (1:2), each s, OCHO]; *m/z* 322 (M^+).

To a stirred solution of LDA, prepared from di-isopropylamine (16 mg, 0.186 mmol) and butyl-lithium (10 mg, 0.186 mmol), in dry THF (1 ml) at −78 °C under argon was added a solution of the ketone (**43**) (50 mg, 0.155 mmol) in dry THF (0.5 ml). After being stirred for 1 h at −78 °C, the mixture was treated slowly with a solution of trimethylsilyl chloride (34 mg, 0.31 mmol) and triethylamine (7 mg, 0.07 mmol) in dry THF (0.5 ml). The resulting mixture was allowed to warm to room temperature and was then stirred for a further 1 h. After addition, at 0 °C, saturated aqueous sodium hydrogen carbonate (3 ml), the mixture was extracted with diethyl ether. The extract was dried and evaporated to give a residue, which was dissolved in acetonitrile (3 ml). After addition of palladium(II) acetate (52 mg, 0.23 mmol) and *p*-benzoquinone (17 mg, 0.155 mmol), the resulting mixture was stirred overnight at room temperature under nitrogen. After evaporation of the solvents, the residue was taken up into benzene and the solution was filtered. Concentration of the filtrate afforded a residue, which was chromatographed on silica gel. Elution with n-hexane–ethyl acetate (100:5, v/v) yielded the enone (**44**) (42 mg, 85%) as an oil, $\nu_{max.}$ 1 670 cm^{-1} (C=O); $\delta_H(CCl_4)$ 0.88 (3 H, s, Me), 0.90 (6 H, s, 2 × Me), 3.73—3.95 (4 H, m, OCH_2CH_2O), 4.31 and 4.35 [1 H (1:2), each s, OCHO], 5.85 (1 H, br d, *J* 10 Hz, COCH=), and 6.55—6.97 (1 H, m, =C*H*CH_2); *m/z* 320 (M^+).

A mixture of the enone (**44**) (42 mg, 0.13 mmol) and 10% perchloric acid (3 ml) in THF (3 ml) was stirred for 1 h at room temperature. After addition of saturated aqueous sodium hydrogen carbonate, the mixture was extracted with diethyl ether. The extract was washed with water, dried, and evaporated to give a residue, which was subjected to silica gel column chromatography. Elution with n-hexane–ethyl acetate (10:1, v/v) gave the aldehyde (**45**) (30 mg, 83%) as an oil, $\nu_{max.}$ 1 710 and 1 665 cm^{-1} (C=O); $\delta_H(CCl_4)$ 0.92, 1.00, and 1.05 (each 3 H, each s, 3 × Me), 5.83 (1 H, br d, *J* 10 Hz, COCH=), 6.57—6.98 (1 H, m, CH_2CH=), and 9.18 (1 H, s, CHO); *m/z* 276 (M^+).

To a solution of the Emmons reagent, prepared from 60% sodium hydride (13 mg, 0.326 mmol) and methyl (dimethoxyphosphoryl)acetate (59 mg, 0.326 mmol) in dry DME (2 ml), was added a solution of the above aldehyde (**45**) (30 mg, 0.109 mmol) in dry DME (0.5 ml), and the mixture was stirred for 72 h at room temperature under argon. After addition of water, the mixture was extracted with diethyl ether. The extract was dried and evaporated to give a residue, which was purified by silica gel column chromatography. Elution with n-hexane–ethyl acetate (10:1, v/v) afforded the α,β-*unsaturated ester* (**46**) (17 mg, 47%) as an oil (Found: C, 75.7; H, 9.6. $C_{21}H_{32}O_3$ requires C, 75.85; H, 9.7%); $\nu_{max.}$ 1 710 and 1 670 cm^{-1} (C=O); $\delta_H(CCl_4)$ 0.92, 0.95, and 1.05 (each 3 H, each s, 3 × Me), 1.05—2.45 (16 H, m, 7 × CH_2 and 2 × CH), 3.67 (3 H, s, OMe), 5.53 (1 H, d, *J* 16 Hz, =C*H*CO_2Me), 5.78 (1 H, br d, *J* 10 Hz, COCH=), 6.53—6.95 (1

H, m, CH_2CH=), and 6.72 (1 H, d, *J* 16 Hz, C*H*=CHCO$_2$Me); *m/z* 332 (M^+) (Found: M^+, 332.2351. $C_{21}H_{32}O_3$ requires *M*, 332.2349).

Methyl (−)-(3S,4R,4aR,4bS,8aS,10aR)-1,2,3,4,4a,4b,5,6,7,8,8a,9,10,10a-*Tetradecahydro*-4b,8,8-*trimethyl*-1-*oxo*-3,10a-*ethanophenanthrene*-4-*carboxylate* (**48**).—To a stirred solution of LiHMDS, prepared from 1,1,1,3,3,3-hexamethyldisilazane (160 mg, 0.991 mmol) and butyl-lithium (63 mg, 0.991 mmol), in dry n-hexane (20 ml) at −78 °C under argon was added a solution of the α,β-unsaturated ester (**46**) (250 mg, 0.762 mmol) in dry diethyl ether (3.3 ml). After being stirred for 1 h at −78 °C, the mixture was allowed to warm to room temperature during 30 min, and was then stirred for 1 h. The reaction mixture was poured onto silica gel (50 g) at room temperature and diethyl ether (100 ml) was added. The resulting mixture was filtered and the filtrate was evaporated to give a solid, which was purified by silica gel column chromatography. Elution with n-hexane–ethyl acetate (20:3, v/v) afforded the *tetracyclic compound* (**48**) (230 mg, 92%) as needles, m.p. 145—148 °C; $[\alpha]_D^{25}$ −9.3° (*c* 0.29) (Found: C, 75.8; H, 9.6. $C_{21}H_{32}O_3$ requires C, 75.85; H, 9.7%); $\nu_{max.}$ 1 725 and 1 715 cm^{-1} (C=O); δ_H 0.82, 0.88, and 1.02 (each 3 H, each s, 3 × Me), 0.90—2.65 (19 H, m, 8 × CH_2 and 3 × CH), and 3.61 (3 H, s, OMe); *m/z* 332 (M^+) (Found: M^+, 332.2350. $C_{21}H_{32}O_3$ requires *M*, 332.2349).

(−)-(3S,4R,4aR,4bS,8aS,10aR)-1,2,3,4,4a,4b,5,6,7,8,8a,9,10,10a-*Tetradecahydro*-4b,8,8-*trimethyl*-1-*oxo*-3,10a-*ethanophenanthrene*-4-*carbaldehyde* (**49**).—To a solution of the ester (**48**) (100 mg, 0.30 mmol) in dry methylene dichloride (7 ml) at −78 °C under argon was added DIBAL (214 mg, 1.5 mmol); the mixture was allowed to warm to room temperature and was then stirred for 0.5 h. After dropwise addition of water (2.0 ml) to the stirred mixture at 0 °C, the resulting mixture was filtered through Celite and the filter was washed with methylene chloride. The combined filtrate and washings were washed with 2% hydrochloric acid, dried, and evaporated to give the *diol* (92 mg, 100%) as a solid, *m/z* 306 (M^+) (Found: M^+, 306.2558. $C_{20}H_{34}O_2$ requires *M*, 306.2558).

A mixture of the above diol (92 mg, 0.30 mmol) and PDC (256 mg, 0.68 mmol) in dry DMF (5 ml) was stirred for 3 h at room temperature, and was then treated with water (20 ml). The resulting mixture was extracted with benzene, and the extract was washed with saturated aqueous sodium chloride, and dried. Evaporation of the solvent afforded a residue, which was chromatographed on silica gel. Elution with n-hexane–ethyl acetate (10:1, v/v) gave the *aldehyde* (**49**) (53.5 mg, 59%) as needles, m.p. 150—151 °C; $\nu_{max.}$ 1 715 cm^{-1} (C=O); δ_H(CCl_4) 0.78, 0.85, and 0.98 (each 3 H, each s, 3 × Me), 1.05—2.50 (19 H, m, 8 × CH_2 and 3 × CH), and 9.55 (1 H, s, CHO); *m/z* 302 (M^+) (Found: M^+, 302.2246. $C_{20}H_{30}O_2$ requires *M*, 302.2262).

(+)-(3R,4aR,4bS,8aS,10aR)-3,4,4a,4b,5,6,7,8,8a,9,10,10a-*Dodecahydro*-4b,8,8-*trimethyl*-3,10a-*ethanophenanthren*-1(2H)-*one* (**50**).—To a stirred solution of the aldehyde (**49**) (28 mg, 0.09 mmol) in dry toluene (3 ml) under reflux was dropwise added a solution of TTPRCl (172 mg, 0.186 mmol) in dry toluene (3 ml). The mixture was refluxed for 2.5 h, then the solvent was evaporated off to give a residue, which was subjected to chromatography on silica gel. Elution with benzene gave the ketone (**50**) (7 mg, 28%) as a solid, which on recrystallisation from benzene–n-hexane afforded crystals, m.p. 147—149 °C (lit.,[3] 146—148 °C); $[\alpha]_D^{25}$ +19.5° (*c* 0.021 in MeOH) {lit.,[3] $[\alpha]_D$ +19.6° (*c* 0.05 in MeOH)}; $\nu_{max.}$ 1 710 cm^{-1} (C=O); δ_H 0.83, 0.86, and 1.05 (each 3 H, each s, 3 × Me) and 1.18—2.65 (21 H, m, 9 × CH_2 and 3 × CH); *m/z* 274 (M^+) (Found: M^+, 274.2297. Calc. for $C_{19}H_{30}O$: *M*, 274.2310); the spectral data were consistent with those reported.[3]

(2R,3R,4aR,4bS,8aS,10aR)-3,4,4a,4b,5,6,7,8,8a,9,10,10a-*Dodecahydro*-2,4b,8,8-*tetramethyl*-3,10-*ethanophenanthren*-1(2H)-*one* (**51**).—To a solution of LDA, prepared from di-isopropylamine (1.8 mg, 0.018 mmol) and butyl-lithium (1.2 mg, 0.018 mmol) in dry THF (0.5 ml), at −78 °C was slowly added a solution of the ketone (**50**) (1 mg, 0.0036 mmol) in dry THF (0.5 ml), and the mixture was stirred for 2 h at this temperature. After addition of methyl iodide (3.6 mg, 0.025 mmol), the mixture was allowed to warm to 0 °C and was then stirred for 30 min at this temperature. After addition of saturated aqueous ammonium chloride (1 ml), the mixture was extracted with diethyl ether. The extract was dried and evaporated to give a residue, which was purified by h.p.l.c. [LiChrosorb SI 60 (4 × 250 mm); n-hexane–ethyl acetate (100:3, v/v), flow rate 1.5 ml min^{-1}] to afford the tetramethyl compound (**51**) (0.4 mg, 38%) as a solid, δ_H 0.83, 0.86, and 1.05 (each 3 H, each s, 3 × Me) and 1.09 (3 H, d, *J* 7 Hz, 2-Me); *m/z* 288 (M^+) (Found: M^+, 288.2452. Calc. for $C_{20}H_{32}O$ *M*, 288.2450), whose n.m.r. spectral data were consistent with those reported.[25,26]

(+)-(3R,4aR,4bS,8aS,10aS)-3,4,4a,4b,5,6,7,8,8a,9,10,10a-*Dodecahydro*-4b,8,8-*trimethyl*-3,10a-*ethanophenanthrene* (**52**).—To a stirred solution of LDA, prepared from di-isopropylamine (5.6 mg, 0.055 mmol) and butyl-lithium (3.5 mg, 0.055 mmol) in dry THF (2 ml), at −78 °C under argon was added dropwise a solution of the ketone (**50**) (3 mg, 0.011 mmol) in dry THF, and the mixture was then stirred for 1 h. After addition of two drops of bromine at −78 °C, the mixture was further stirred for 0.5 h at this temperature. The mixture was allowed to warm to 0 °C and was treated with water (3 ml) and extracted with diethyl ether. The extract was washed successively with water and 5% aqueous sodium thiosulphate, dried, and evaporated to give the bromide (3.9 mg, 100%) as an oil, $\nu_{max.}$ 1 725 cm^{-1} (C=O); *m/z* 353 (M^+) and 355 (M^+ + 2).

To a stirred solution of the above bromide (3.9 mg) in ethanol (1 ml) was added sodium borohydride (1 mg). After evaporation of the solvent, the residue was partitioned between saturated aqueous sodium chloride and methylene dichloride. The organic layer was dried and evaporated to give the crude α-bromo alcohol, which was used in the next reaction without purification.

A mixture of the above product and zinc (12 mg) in ethanol (1 ml) was refluxed for 1 h, and then the solvent was evaporated off. The residue was taken up into diethyl ether and the solution was filtered through Celite. Evaporation of the filtrate, followed by purification of the residue by h.p.l.c. [LiChrosorb. SI 60 (4 × 250 mm); n-hexane, flow rate 1.5 ml min^{-1}] afforded the olefin (**52**) [1.98 mg, 70% from (**50**)] as prisms, m.p. 83—84 °C (lit.[3] 82—83 °C); $[\alpha]_D^{24}$ +16.4° (*c* 0.134 in MeOH); δ_H 0.81, 0.86, and 0.95 (each 3 H, each s, 3 × Me), 1.00—2.45 (19 H, m, 8 × CH_2 and 3 × CH), and 5.91—6.02 (2 H, m, 1- and 2-H).

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