Stereocontrolled Synthesis of the CDF Part of *Aconitum* Alkaloids *via* Intramolecular Double Michael Reaction

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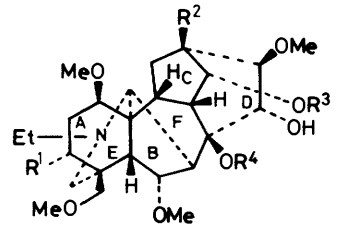
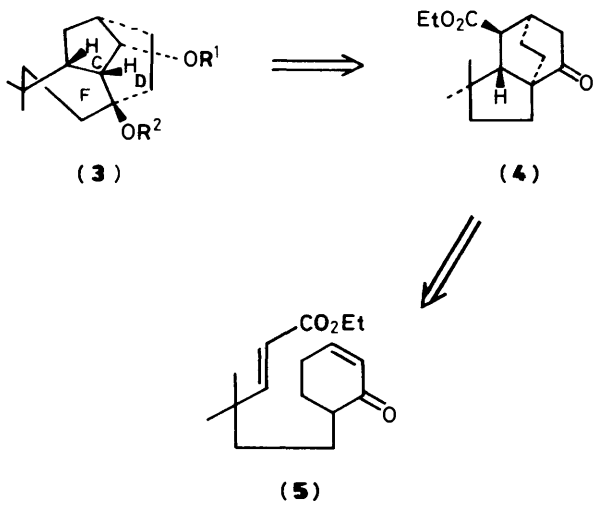
Intramolecular double Michael reaction of the α,β-unsaturated enone ester (**5**) using lithium hexamethyldisilazide produced the tricyclo[5.2.2.$0^{1,5}$]undecane derivative (**4**) in a highly stereoselective manner. The annulation of (**5**) was further investigated under various conditions. The tricyclic compound (**4**) was converted into the tetracyclo[7.3.1.$0^{4,12}$.$0^{5,13}$]tridecane derivative (**31**), the CDF part of *Aconitum* alkaloids, *via* a Wagner–Meerwein-type rearrangement.

Aconitum alkaloids, represented by aconitine (**1**), possessing potent physiological properties and an extremely complex ring system substituted by a number of oxygen functionalities, have elicited substantial interest as targets for organic synthesis. The great efforts by Wiesner and his co-workers led to the successful total synthesis of (±)-chasmanine (**2**).[1] Recently we have



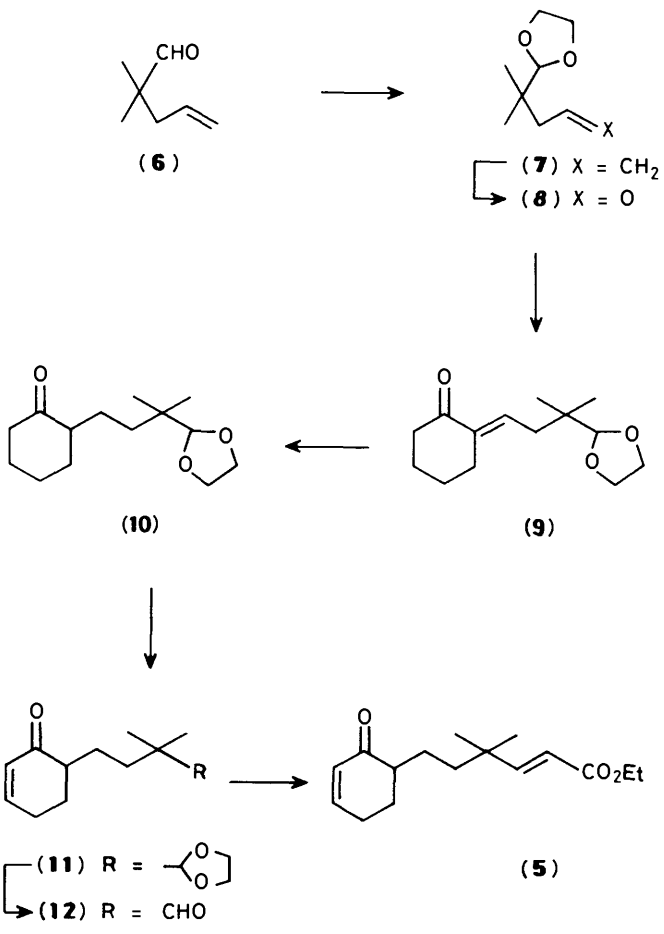
(**1**) $R^1 = R^2 = OH$, $R^3 = COPh$, $R^4 = Ac$
(**2**) $R^1 = R^2 = R^3 = R^4 = H$

developed a stereoselective construction of spiro-fused bicyclo[2.2.2]octane systems by the intramolecular double Michael reaction.[2,3] Utilising this method, we investigated the synthesis of the CDF part of the lycoctonine skeleton as a model study toward a total synthesis of *Aconitum* alkaloids and now report a highly stereocontrolled approach according to the plan shown in Scheme 1.[4]



Scheme. 1

Preparation of the Substrate of Intramolecular Double Michael Reaction.—Refluxing 2,2-dimethylpent-4-enal (**6**)[5] and ethylene glycol in the presence of toluene-*p*-sulphonic acid (PTSA) in benzene in a Dean–Stark apparatus for 40 h gave the acetal (**7**) in 95% yield. Treatment of the acetal (**7**) with osmium tetraoxide and sodium metaperiodate[6] in a mixture of diethyl ether and water (1:1 v/v) afforded the aldehyde (**8**), which was subjected to condensation reaction with cyclohexanone carried out in the presence of potassium hydroxide in refluxing water to produce the enone (**9**) in 67% overall yield from the acetal (**7**). Hydrogenation of the enone (**9**) using 10%



Scheme 2.

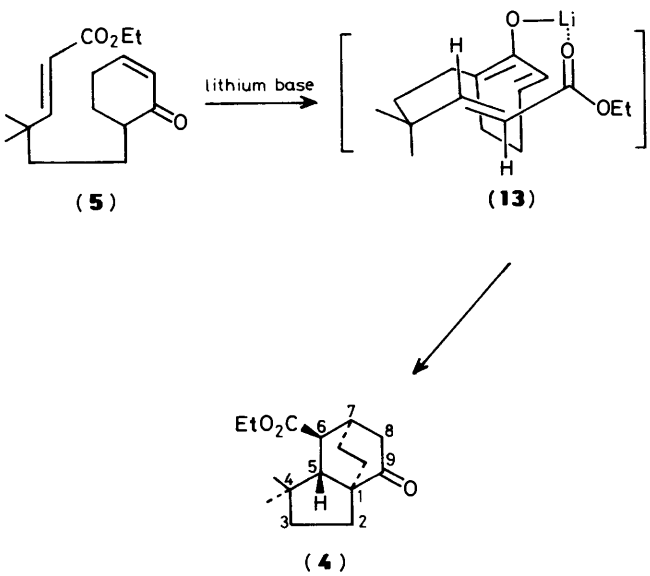
Table. Intramolecular double Michael reaction of compound (**5**), using lithium bases at −78—18 °C

Lithium base	Solvent	Time (h)	Yield of (**4**) (%)
LHMDS[a]	hexane–ether	2.5	64
LHMDS	hexane	3	53
LDA[b]	THF	3	57
LICA[c]	THF	6	26
$LiNEt_2$	THF	4.5	30

[a] Lithium hexamethyldisilazide. [b] Lithium di-isopropylamide. [c] Lithium isopropylcyclohexylamide.

palladium–carbon gave in 81% yield the ketone (**10**), whose enolate anion, prepared by the reaction with lithium di-isopropylamide (LDA) under kinetically controlled conditions, was treated with a mixture of chlorotrimethylsilane and triethylamine. The silyl enol ether formed was oxidised with palladium(II) acetate and *p*-benzoquinone[7] in acetonitrile to afford the enone (**11**) in 90% yield. The substrate (**5**) of the intramolecular double Michael reaction was obtained in 77% yield from the enone (**11**) in two steps (Scheme 2); deblocking using dilute perchloric acid in tetrahydrofuran (THF) and the subsequent Wadsworth–Emmons reaction[8] of the aldehyde (**12**) utilising triethyl phosphonoacetate [ethyl (diethoxyphosphoryl)acetate] and sodium hydride in 1,2-dimethoxyethane (DME). The i.r. spectrum (chloroform) of the α,β-unsaturated ester (**5**) displayed the characteristic absorptions at 1 670 and 1 705 cm^{-1} due to the conjugated enone and the α,β-unsaturated ester. In the n.m.r. spectrum, the *E* olefinic hydrogens were observed at δ_H 5.70 and 6.87 with coupling constant *J* 16.0 Hz, and two hydrogens of the enone moiety resonated at δ_H 5.91 and 6.87, respectively.

Intramolecular Double Michael Reaction.—The annulation of the α,β-unsaturated ester (**5**) was first examined using various lithium bases. Although the tricyclic compound (**4**) was obtained as a single pair of racemic stereoisomers (Scheme 3) the yields were considerably dependent on the lithium base and the solvent used. Some results are summarised in the Table. A solution of the substrate (**5**) in the solvent was slowly added to the lithium base in the solvent at −78 °C and after the mixture had been stirred for several hours, the temperature was gradually raised to ambient. The reaction was quenched by pouring the mixture onto silica gel. The crude product, obtained by filtration followed by evaporation of the filtrate and washings, was purified by silica gel column chromatography. The best yield, 64%, was attained when lithium hexamethyldisilazide (LHMDS) was used as a base in a mixture of hexane and diethyl ether. When the reaction was carried out in the presence of magnesium bromide, the desired product was not formed.

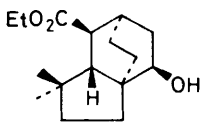


Scheme 3.

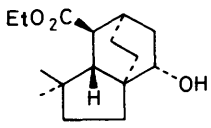
The planar structure of the tricyclic compound (**4**) was suggested from the spectral data; the appearance of an absorption due to the six-membered cyclohexanone and the saturated ester group at 1 720 cm^{-1} and the disappearance of the absorptions due to conjugated carbonyl groups in the i.r. spectrum, and no olefinic hydrogen signal in the n.m.r. spectrum. Two methyl groups were observed, at δ_H 1.00 and 1.11, each as a singlet. On reduction of the tricyclic compound (**4**) with sodium borohydride, a mixture of two epimeric alcohols (**14**) and (**15**) was obtained in a ratio of *ca.* 1 : 1, while the reduction of (**4**) with L-Selectride ($LiBHBu^s_3$) in THF at 0 °C furnished only the alcohol (**14**), in 100% yield. The stereochemistry of compound (**14**) was deduced by the coupling constant of the hydrogen geminal to the hydroxy group and by the assumption that the reagent would attack from the less hindered α face. Since the chemical shifts of the two methyl groups of the tricyclic compound (**4**) were not considerably changed by the above reductions, the relative configuration of the angular hydrogen and the ethano-bridge containing the carbonyl group of (**4**) was assigned as *cis*. The highly selective formation of compound (**4**) when utilising lithium bases could be explained by participation of the intermediate (**13**) chelated with lithium cation.

The annulation of the α,β-unsaturated ester (**5**) was further examined under other conditions. Among numerous conditions tested, the following reactions produced the desired annulation products but with poor stereoselectivity. Thus heating a mixture of the ester (**5**) together with an excess of chlorotrimethylsilane, triethylamine, and zinc chloride[9,10] in toluene in a sealed tube at 180 °C formed the tricyclic ketones (**4**) and (**16**), which were then transformed into their silyl enol ethers. After heating for 100 h, the reaction mixture was treated with dilute hydrochloric acid and the crude product was purified by silica gel column chromatography to afford the tricyclic ketone (**4**) and its isomer (**16**) in 50 and 12.5% yield, respectively. One of the methyl groups of the ketone (**16**) was observed at high field, δ_H 0.63, in the n.m.r. spectrum, because the methyl group would be shielded by the carbonyl group. On the other hand, reaction of the α,β-unsaturated ester (**5**) with tin(II) trifluoromethanesulphonate in the presence of *N*-ethylpiperidine[11] in dichloromethane gave the two tricyclic ketones (**4**) and (**16**) in 18 and 6% yield, respectively, along with the β,γ-enone (**17**) in 16% yield. Interestingly, treatment of compound (**5**) with dimethyl-t-butylsilyl trifluoromethanesulphonate in the presence of triethylamine[12] in dichloromethane at room temperature for 10 min provided the tricyclic silyl enol ethers (**18**) as a mixture of two stereoisomers in 37% yield together with the through-conjugated silyl dienol ether (**19**) in 45% yield. The mixture of the tricyclic silyl enol ethers (**18**) was hydrolysed on treatment with 10% perchloric acid in THF to afford the two ketones (**4**) and (**16**) in 55 and 33% yield, respectively. When the above reaction was carried out using di-isopropylethylamine instead of triethylamine, the through-conjugated silyl dienol ether (**19**) was obtained in 91% yield. Reaction of (**19**) with boron trifluoride–diethyl ether formed the α,β-enone (**5**) and the β,γ-enone (**17**) in 54 and 45% yield, respectively. On the other hand,

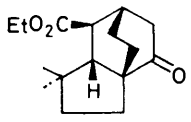
treatment of compound (**5**) with dimethyl-t-butylsilyl trifluoromethanesulphonate in the presence of trimethylamine instead of triethylamine at −78 °C produced the cross-conjugated silyl dienol ether (**20**) in 37% yield without the formation of the through-conjugated enol ether (**19**). Even if this triene (**20**) was treated with dimethyl-t-butylsilyl trifluoromethanesulphonate and triethylamine at room temperature, no tricyclic compound was obtained. On reaction of the triene (**20**) with boron trifluoride–diethyl ether, two tricyclic ketones (**4**) and (**16**) formed in poor yield. We therefore consider that the annulation reaction using dimethyl-t-butylsilyl trifluoromethanesulphonate and triethylamine is the direct tandem conjugate addition and not the intramolecular Diels–Alder reaction of the cross-conjugated dienol ether (**20**).



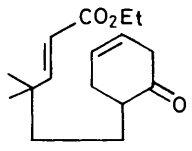
(**14**)



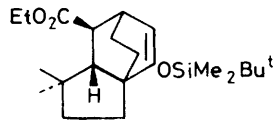
(**15**)



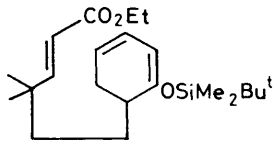
(**16**)



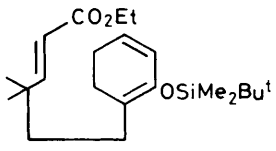
(**17**)



(**18**)



(**19**)



(**20**)

Stereoselective Construction of the CDF *Part of the Lycoctonine Skeleton.*—Next, the transformation of the tricyclic ketone (**4**), highly stereoselectively prepared by the above intramolecular double Michael reaction using LHDMS, into the CDF part of lycoctonine skeleton was studied as a model experiment toward a total synthesis of *aconitum* alkaloids. In order to perform the Wagner–Meerwein rearrangement,[1,13] the inversion of the hydroxy group of the alcohol (**14**) was examined, but all efforts resulted in failure. Next we focussed on rearrangement *via* an epoxide. Selective construction of the epoxide from the α-side of the tricyclic compound should be a requirement to achieve the desired conversion. Therefore the ethoxycarbonyl group of compound (**4**) was first transformed into a bulkier group. Thus the keto ester (**4**) was reduced with di-isobutylaluminium hydride (DIBAL) to provide in 99% yield the corresponding epimeric alcohols (**21**), whose secondary hydroxy group was selectively oxidised with sodium bromate in the presence of cerium(IV) ammonium nitrate (CAN)[14] to give the hydroxy ketone (**22**) in 80% yield. The primary alcohol group of (**22**) was protected as the methoxymethyl (MOM) ether using methoxymethyl chloride and di-isopropylethylamine in 83% yield. The ether (**23**) was then treated with *p*-toluenesulphonohydrazide in the presence of boron trifluoride–diethyl ether and the hydrazone formed was subsequently treated with butyl-lithium[15] to give the olefin (**24**) in 53% yield. The structure (**24**) was supported by the absence of an absorption due to a carbonyl group in the i.r. spectrum, and the presence of two olefinic hydrogen signals at δ_H 5.83 (dd, *J* 8.0 and 6.0 Hz) and δ_H 6.11 (br d, *J* 8.0 Hz), respectively. Oxidation of the olefin (**24**) with *m*-chloroperbenzoic acid (MCPBA) in dichloromethane afforded the expected epoxide (**25**) as a single pair of racemic stereoisomers in 65% yield along with a 4% yield of the tetrahydrofuran (**26**).[16] The structure of the epoxide (**25**) was determined on the basis of the spectroscopic data. The i.r. spectrum showed the absorptions due to epoxide at 910 and 850 cm^{-1}, while two hydrogens attached to the epoxide ring resonated at δ_H 3.22 (dd, *J* 5.0 and 4.0 Hz) and δ_H 3.00 (d, *J* 5.0 Hz), respectively.

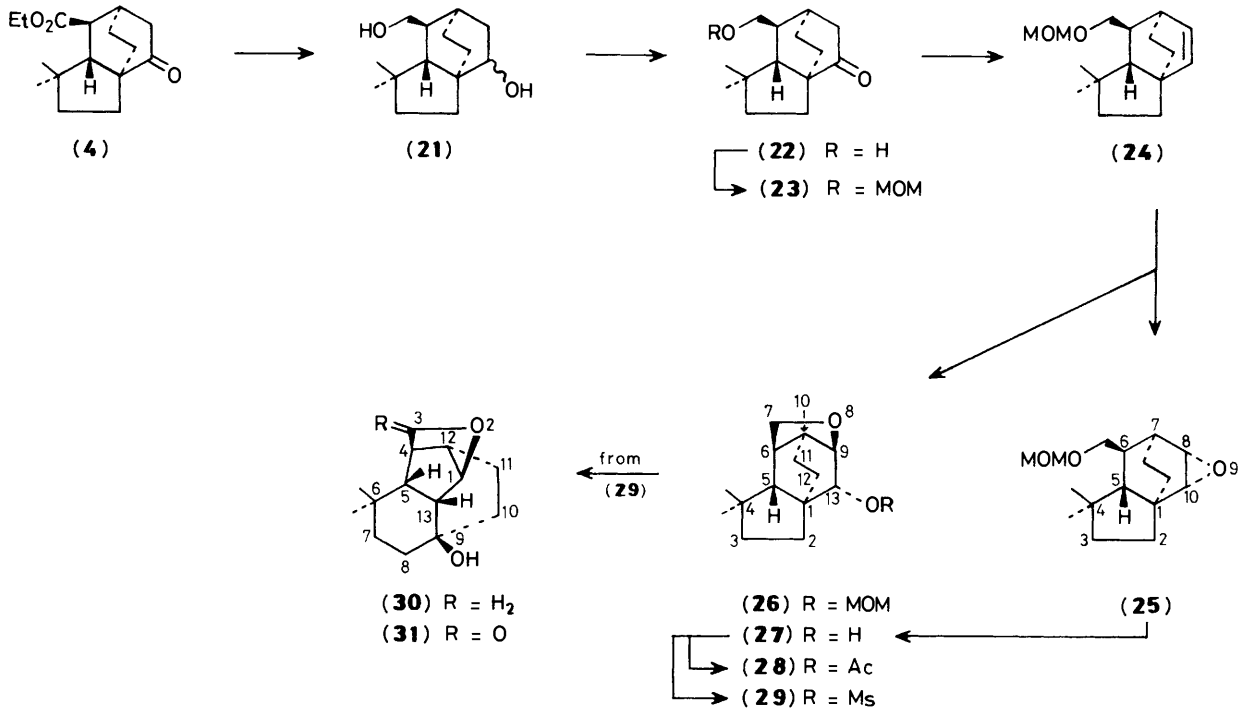
Hoping to perform the rearrangement, we subjected the epoxide (**25**) to the following two acidic treatments. Reaction with 10% perchloric acid in THF gave the alcoholic tetrahydrofuran (**27**) in 71% yield instead of the rearranged product. Similarly, treatment of compound (**25**) with boron trifluoride–diethyl ether in dichloromethane also provided the alcohol (**27**) in 32% yield along with its methoxymethyl ether (**26**) in 36% yield. Deprotection of (**26**) with hydrochloric acid gave the alcohol (**27**). Acetylation of the alcohol (**27**) using acetic anhydride and triethylamine in the presence of 4-(dimethylamino)pyridine (DMAP) gave in 66% yield the acetate (**28**), whose n.m.r. spectrum showed the methine hydrogen at the C-13 position at δ_H 4.30 as a singlet, indicating the presence of an α-oriented acetoxy group. Although the rearrangement of the epoxide (**25**) failed, it was anticipated that the tetracyclic alcohol (**27**) would possess ideal characteristics for the rearrangement: the correct stereochemistry of the hydroxy group and the limitation of rearranged products were due to the existence of the tetrahydrofuran ring.

On the basis of the above considerations, the alcohol (**27**) was treated with methanesulphonyl chloride and triethylamine. Heating of the mesyl ester (**29**), obtained in 66% yield, in a mixture of acetone and water (2:1 v/v) at 70 °C for 15 h gave the desired rearranged compound (**30**) in 65% yield. The i.r. spectrum in chloroform exhibited the tertiary hydroxy group absorption at 3 600 cm^{-1} as a strong peak. In the 360 MHz two-dimensional correlated ^1H n.m.r. spectrum, the methylene hydrogens of the ethereal bridge were observed at δ_H 3.41 (d, *J* 6.3 Hz) and δ_H 3.66 (dd, *J* 6.3 and 1.4 Hz). The methine hydrogen neighbouring the oxygen atom resonates at δ_H 4.44 as broad singlet; the deshielded value can be accounted for by the anisotropy of the tertiary hydroxy group. The structure (**30**) was assigned on the basis of the above observations as well as the ^{13}C n.m.r. spectrum. Furthermore the tertiary alcohol (**30**) was oxidised using ruthenium trichloride and sodium metaperiodiate[17] in a mixture of tetrachloromethane, acetonitrile, and water (2:2:3 v/v/v) (Scheme 4). The lactone (**31**), obtained in 39% yield, showed the carbonyl absorption at 1 780 cm^{-1} in the i.r. spectrum in chloroform.

Thus a highly stereocontrolled construction of the CDF part of the lycoctonine skeleton was achieved.

Experimental

General Procedures.—I.r. spectra were measured with a Hitachi 260-10 spectrophotometer, and n.m.r. spectra with



Scheme 4.

JEOL-PMX-60, JEOL-PS-100, and Nicolet NT-360 spectrometers. Ordinary mass spectra were taken with a Hitachi M-52G spectrometer, and accurate mass spectra with JEOL-JMS-01SG-2 and JEOL-DX-300 spectrometers. All new compounds described in the Experimental section were homogeneous on t.l.c. A solution of butyl-lithium in hexane was titrated before use.

2-(1,1-*Dimethylbut*-3-*enyl*)-1,3-*dioxolane* (**7**).—A solution of the aldehyde (**6**)[5] (34.5 g, 0.27 mol) in dry benzene (350 ml) was refluxed with ethylene glycol (22.8 ml, 0.36 mol) and PTSA (1.4 g, 0.007 mol) for 40 min with removal of water by means of a Dean–Stark apparatus. The organic solution was washed with saturated aqueous sodium hydrogen carbonate, dried ($MgSO_4$), and evaporated to afford a residue, which was purified by distillation to give the *acetal* (**7**) (40.4 g, 95%), b.p. 165—175 °C (760 mmHg); $\nu_{max.}(CHCl_3)$ 1 110 cm^{-1} (C–O–C); $\delta_H(CCl_4)$ 0.83 (6 H, s, 2 × Me), 2.02 (2 H, d, *J* 7.0 Hz, $CH_2CH{=}CH$), 3.80 (4 H, s, OCH_2CH_2O), 4.40 (1 H, s, OCHO), 4.70—5.13 (2 H, m, $H_2C{=}CH$), and 5.33—6.00 (1 H, m, $H_2C{=}CH$); *m/z* 156 (M^+) (Found: M^+, 156.1090. $C_9H_{16}O_2$ requires *M*, 156.1148).

2-[3-(1,3-*Dioxolan*-2-*yl*)-3-*methylbutylidene*]*cyclohexanone* (**9**).—To a stirred solution of the acetal (**7**) (6.0 g, 0.039 mol) and osmium tetraoxide (487 mg, 2 mmol) in diethyl ether–water (1 : 1 v/v, 480 ml) was added sodium metaperiodate (105.2 g, 0.49 mol) during 1 h. After the reaction mixture had been stirred for 2.5 h, it was extracted with ethyl acetate. The extract was washed with brine, dried ($MgSO_4$), and evaporated to give a crude aldehyde (**8**); $\nu_{max.}(CHCl_3)$ 1 715 cm^{-1} (CO); $\delta_H(CCl_4)$ 1.06 (6 H, s, 2 × Me), 2.16 (2 H, d, *J* 3.5 Hz, CH_2CHO), 3.86 (4 H, s, OCH_2CH_2O), 4.46 (1 H, s, OCHO), and 9.63 (1 H, t, *J* 3.5 Hz, CHO), which was used in the following reaction without further purification.

A solution of the above aldehyde (**8**) (6.1 g, 0.039 mol), cyclohexanone (7.6 ml, 0.07 mmol), and 85% potassium hydroxide (1.97 g, 0.03 mol) in water (130 ml) was heated under reflux for 2 h. After the reaction mixture had been extracted with diethyl ether, the extract was washed successively with saturated aqueous ammonium chloride and brine, dried ($MgSO_4$), and evaporated to give a residue. This crude product was purified by chromatography on silica gel with hexane–ethyl acetate (9 : 1 v/v) as eluant to afford the *enone* (**9**) (6.17 g, 67%) as an oil (Found: C, 70.6; H, 9.5. $C_{14}H_{22}O_3$ requires C, 70.55; H, 9.3%); $\nu_{max.}(CHCl_3)$ 1 680 (CO) and 1 110 cm^{-1} (C–O–C); $\delta_H(CCl_4)$ 0.93 (6 H, s, 2 × Me), 1.25—2.67 (10 H, m, 5 × CH_2), 3.82 (4 H, br s, OCH_2CH_2O), 4.42 (1 H, s, OCHO), and 6.55 (1 H, br t, *J* 8.0 Hz, =CH); *m/z* 238 (M^+).

2-[3-(1,3-*Dioxolan*-2-*yl*)-3-*methylbutyl*]*cyclohexanone* (**10**).—A suspension of the enone (**9**) (1.25 g, 5.3 mmol) and 10% palladium–carbon (200 mg) in ethanol (15 ml) was stirred under hydrogen (1 atm) at ambient temperature for 3 h. The suspension was filtered through Celite and the concentrated filtrate was purified by chromatography on silica gel. Elution with hexane–ethyl acetate (9 : 1 v/v) afforded the *ketone* (**10**) (1.05 g, 81%) as an oil (Found: C, 69.95; H, 10.15. $C_{14}H_{24}O_3$ requires C, 69.95; H, 10.05%); $\nu_{max.}(CHCl_3)$ 1 700 cm^{-1} (CO); $\delta_H(CCl_4)$ 0.85 (6 H, s, 2 × Me), 0.95—2.50 (13 H, m, 6 × CH_2 and CH), 3.81 (4 H, s, OCH_2CH_2O), and 4.43 (1 H, br s, OCHO); *m/z* 240 (M^+).

6-[3-(1,3-*Dioxolan*-2-*yl*)-3-*methylbutyl*]*cyclohex*-2-*enone* (**11**).—A stirred solution of dry di-isopropylamine (1.4 ml, 7.5 mmol) in dry THF (10 ml) was cooled to −78 °C and treated with 15% butyl-lithium in hexane solution (6 ml, 7.5 mmol) during several min. After the mixture had been stirred for an additional 20 min at −78 °C, a solution of the ketone (**10**) (1.0 g, 4.2 mmol) in dry THF (10 ml) was added dropwise. After an additional 1 h, a solution of chlorotrimethylsilane (1.1 ml, 8.3 mmol) and triethylamine (0.3 ml, 2.2 mmol) in dry THF (5 ml) was added rapidly to the mixture and the cooling bath was then removed. The reaction mixture was allowed to warm to room temperature. After being stirred for 1 h at ambient temperature, the mixture was then poured into cold saturated aqueous sodium hydrogen carbonate. The aqueous solution was

extracted with diethyl ether and the extract was dried ($MgSO_4$) and concentrated to give an oil, which was used in the following reaction without further purification.

The mixture of the silyl enol ether, palladium(II) acetate (980 mg, 4.2 mmol), and *p*-benzoquinone (462 mg, 4.2 mmol) in dry acetonitrile (40 ml) was stirred at room temperature for 18 h under nitrogen. After evaporation of the solvent, the residue was taken up into benzene. The suspension was filtered through Celite and the concentrated filtrate was purified by chromatography on silica gel. Elution with hexane–ethyl acetate (9:1 v/v) afforded the *enone* (**11**) (903 mg, 90%) as a pale yellow oil (Found: C, 70.9; H, 9.15. $C_{14}H_{22}O_3$ requires C, 70.55; H, 9.3%); $\nu_{max.}(CHCl_3)$ 1 670 cm^{-1} (CO); $\delta_H(CCl_4)$ 0.87 (6 H, s, 2 × Me), 1.01—2.50 (9 H, m, 4 × CH_2 and CH), 3.80 (4 H, br s, OCH_2CH_2O), 4.40 (1 H, s, OCHO), 5.81 (1 H, dt, *J* 10.0 and 2.0 Hz, CH=C*H*CO), and 6.73 (1 H, dt, *J* 10.0 and 4.0 Hz, C*H*=CHCO); *m/z* 238 (M^+).

Ethyl (E)-4,4-*Dimethyl*-6-(2-*oxocyclohex*-3-*enyl*)*hex*-2-*enoate* (**5**).—A solution of the acetal (**11**) (1.43 g, 6.0 mmol) in a mixture of 10% aqueous perchloric acid and THF (1:1 v/v, 50 ml) was stirred at room temperature for 3 h under nitrogen. The aqueous solution was extracted with diethyl ether and the extract was washed successively with saturated aqueous sodium hydrogen carbonate and brine, dried ($MgSO_4$), and evaporated to give the aldehyde (**12**); $\nu_{max.}(CHCl_3)$ 1 721 and 1 670 cm^{-1} (CO); $\delta_H(CCl_4)$ 1.02 (6 H, s, 2 × Me), 1.20—2.60 (9 H, m, 4 × CH_2 and CH), 5.83 (1 H, dt, *J* 10.0 and 2.0 Hz, CH=C*H*CO), 6.81 (1 H, dt, *J* 10.0 and 4.0 Hz, C*H*=CHCO), and 9.45 (1 H, s, CHO), which was used directly in the following reaction.

To a stirred slurry of 60% sodium hydride (240 mg, 7.2 mmol) in dry DME (20 ml) at room temperature was added dropwise 'triethyl phosphonoacetate' [ethyl (diethoxyphosphoryl)-acetate] (1.43 ml, 7.2 mmol). After the mixture had been stirred for 30 min, a solution of the aldehyde (**12**) (1.16 g, 6.0 mmol) in dry DME (10 ml) was added dropwise. After the mixture had been stirred for 1.5 h, it was diluted with a large amount of water. The mixture was extracted with diethyl ether and the extract was washed with brine, dried ($MgSO_4$), and evaporated to give a residue, which was chromatographed on silica gel. Elution with hexane–ethyl acetate (9:1 v/v) afforded the *enone* (**5**) (1.21 g, 77%) as an oil (Found: C, 72.5; H, 9.25. $C_{16}H_{24}O_3$ requires C, 72.7; H, 9.15%); $\nu_{max.}(CHCl_3)$ 1 710 (CO) and 1 670 cm^{-1} (CO); $\delta_H(CDCl_3)$ 1.06 (6 H, s, 2 × Me), 1.28 (3 H, t, *J* 7.0 Hz, CH_2Me), 1.25—2.55 (9 H, m, 4 × CH_2 and CH), 4.16 (2 H, q, *J* 7.0 Hz, CH_2Me), 5.70 (1 H, d, *J* 16.0 Hz, CH=C*H*CO_2Et), 5.91 (1 H, dt, *J* 10.8 and 2.0 Hz, CH=C*H*CO), 6.87 (1 H, d, *J* 16.0 Hz, C*H*=CHCO_2Et), and 6.87 (1 H, dt, *J* 10.8 and 4.0 Hz, C*H*=CHCO); *m/z* 264 (M^+).

(±)-*Ethyl* (1SR,5SR,6SR,7RS)-4,4-*Dimethyl*-9-*oxotricyclo*[5.2.2.0^{1,5}]*undecane*-6-*carboxylate* (**4**).—To a stirred solution of lithium disilazide [prepared from 1,1,1,3,3,3-hexamethyldisilazane (0.057 ml, 0.27 mmol) and 15% butyl-lithium in dry hexane (0.2 ml, 0.27 mmol)] at −78 °C was added a solution of the enone (**5**) (55 mg, 0.21 mmol) in dry diethyl ether (1 ml) dropwise under nitrogen. After the mixture had been stirred for 2 h at the same temperature, it was allowed to warm to ambient temperature during 45 min. The mixture was poured onto silica gel (10 g), filtered, and washed with diethyl ether. The filtrate was concentrated and the residue was chromatographed on silica gel. Elution with hexane–ethyl acetate (92:8 v/v) gave the *keto ester* (**4**) (35 mg, 64%) as an oil (Found: C, 72.5; H, 9.25. $C_{16}H_{24}O_3$ requires C, 72.7; H, 9.15%); $\nu_{max.}(CHCl_3)$ 1 720 cm^{-1} (CO); $\delta_H(CDCl_3)$ 1.00 (3 H, s, Me), 1.11 (3 H, s, Me), 1.26 (3 H, t, *J* 7.0 Hz, CH_2Me), 1.30—2.18 (10 H, m, 4 × CH_2 and 2 × CH), 2.29—2.83 (3 H, m, C*H*CO_2Et and CH_2CO), and 4.14 (2 H, q, *J* 7.0 Hz, CH_2Me); *m/z* 264 (M^+).

(±)-*Ethyl* (1SR,5SR,6SR,7RS,9RS)-9-*Hydroxy*-4,4-*dimethyltricyclo*[5.2.2.0^{1,5}]*undecane*-6-*carboxylate* (**14**).—To a stirred solution of the ketone (**4**) (10 mg, 0.04 mmol) in dry THF (2 ml) at 0 °C was added a 1M solution of L-Selectride in THF (0.06 ml, 0.06 mmol) under nitrogen. After the reaction mixture had been stirred for 10 min, diethyl ether and water were added. The aqueous layer was thoroughly extracted with diethyl ether and the combined extracts were washed successively with 10% hydrochloric acid, saturated aqueous sodium hydrogen carbonate, and brine. The ethereal solution was then dried ($MgSO_4$) and evaporated to give a residue, which was purified by chromatography on silica gel. Elution with hexane–ethyl acetate (9:1 v/v) afforded the *alcohol* (**14**) (10.1 mg, 100%) as an oil; $\nu_{max.}(CHCl_3)$ 3 580 (OH) and 1 720 cm^{-1} (CO); $\delta_H(CDCl_3)$ 1.02 (6 H, s, 2 × Me), 1.26 (3 H, t, *J* 6.4 Hz, CH_2Me), 1.35—2.50 (13 H, m, 5 × CH_2 and 3 × CH), 3.65 (1 H, dd, *J* 8.6 and 5.7 Hz, C*H*OH), and 4.14 (2 H, q, *J* 6.4 Hz, CH_2Me); *m/z* 266 (M^+) (Found: M^+, 266.1882. $C_{16}H_{26}O_3$ requires *M*, 266.1882).

(±)-*Ethyl* (1SR,5SR,6SR,7RS,9RS)- *and* (1SR,5SR,6SR,7RS,9SR)-9-*Hydroxy*-4,4-*dimethyltricyclo*[5.2.2.0^{1,5}]*undecane*-6-*carboxylate* (**14**) *and* (**15**).—Sodium borohydride (2 mg, 0.08 mmol) was added to a solution of the ketone (**4**) (18.2 mg, 0.07 mmol) in ethanol (2 ml) at 0 °C. After the mixture had been stirred at the same temperature for 20 min, the solvent was evaporated off to give a residue, which was purified by silica gel chromatography, with hexane–ethyl acetate (9:1 v/v) as eluant to afford the alcohols (**14**) and (**15**) (17.2 mg, 93%) as a 1:1 mixture; $\nu_{max.}(CHCl_3)$ 3 600 (OH) and 1 720 cm^{-1} (CO); $\delta_H(CDCl_3)$ 1.02 (3 H, s, Me), 1.06 (3 H, s, Me), 1.26 (3 H, t, *J* 7.0 Hz, CH_2Me), 1.35—2.50 (13 H, m, 5 × CH_2 and 3 × CH), 3.64 (1 H, m, C*H*OH), and 4.11 and 4.13 [2 × 1 H (1:1), each d, each *J* 7.0 Hz, CH_2Me]; *m/z* 266 (M^+) (Found: M^+, 266.1855. $C_{16}H_{26}O_3$ requires *M*, 266.1800).

(±)-*Ethyl* (1SR,5SR,6SR,7RS)- *and* (1RS,5SR,6SR,7SR)-4,4-*Dimethyl*-9-*oxotricyclo*[5.2.2.0^{1,5}]*undecane*-6-*carboxylate* (**4**) *and* (**16**) *and Ethyl* (E)-4,4-*Dimethyl*-6-(6-*oxocyclohex*-3-*enyl*)-*hex*-2-*enoate* (**17**).—(A) A mixture of the enone ester (**5**) (24 mg, 0.11 mmol), zinc chloride (0.8 mg, 0.006 mmol), chlorotrimethylsilane (0.027 ml, 0.19 mmol), and triethylamine (0.031 ml, 0.24 mmol) in dry toluene (2 ml) was heated at 180 °C in a sealed tube for 100 h. After addition of benzene, the organic mixture was washed with 0.5M hydrochloric acid, dried ($MgSO_4$), and evaporated to give a residue, which was subjected to silica gel column chromatography with hexane–ethyl acetate (92:8 v/v) as eluant to give the *keto ester* (**16**) (3 mg, 12.5%) as an oil; $\nu_{max.}(CHCl_3)$ 1 730 (CO) and 1 720 cm^{-1} (CO); $\delta_H(CDCl_3)$ 0.63 (3 H, s, Me), 0.94 (3 H, s, Me), 1.29 (3 H, t, *J* 7.0 Hz, CH_2Me), 1.10—2.10 (10 H, m, 4 × CH_2 and 2 × CH), 2.20—2.51 (3 H, m, C*H*CO_2Et and CH_2CO), and 4.16 (2 H, q, *J* 7.0 Hz, CH_2Me); *m/z* 264 (M^+) (Found: M^+, 264.1680. $C_{16}H_{24}O_3$ requires *M*, 264.1725).

Further elution with the same solvent system afforded the ketone (**4**) (12 mg, 50%) as an oil, which displayed identical spectral properties with those of the sample prepared above.

(B) To a solution of tin(II) trifluoromethanesulphonate (104 mg, 0.25 mmol) and *N*-ethylpiperidine (0.034 ml, 0.25 mmol) in dry dichloromethane (2 ml) at −78 °C was added a solution of the enone ester (**5**) (22 mg, 0.083 mmol) in dry dichloromethane (1 ml) under argon. The mixture was stirred at the same temperature for 3 h and then at 0 °C for 3.5 h. After addition of pH 7 phosphate buffer, the organic layer was separated. The resulting aqueous layer was extracted with dichloromethane and the combined extract was washed with brine, dried

($MgSO_4$), and evaporated to give a residue. Chromatography of the product on silica gel with hexane–ethyl acetate (92:8 v/v) gave the *β,γ-enone ester* (**17**) (3.6 mg, 16%) as an oil; $\nu_{max.}(CHCl_3)$ 1 715—1 708 cm^{-1} (CO); $\delta_H(CCl_4)$ 1.10 (6 H, s, 2 × Me), 1.30 (3 H, t, *J* 6.5 Hz, CH_2Me), 2.33 (4 H, m, 2 × CH_2), 2.80 (2 H, br s, $=CHCH_2CO$), 4.05 (2 H, q, *J* 6.5 Hz, CH_2Me), 5.75 (1 H, d, *J* 15.0 Hz, $=CHCO_2Et$), 5.70 (2 H, br s, $CH=CHCH_2CO$), and 6.90 (1 H, d, *J* 15.0 Hz, $CH=CHCO_2Et$); *m/z* 264 (M^+) (Found: M^+, 264.1701. $C_{16}H_{24}O_3$ requires *M*, 264.1724).

Further elution with the same solvent system afforded the keto ester (**16**) (1.4 mg, 6%) as an oil and the keto ester (**4**) (4.0 mg, 18%) as an oil. Their spectral data were identical with those of the compounds (**16**) and (**4**), prepared as above, respectively.

Ethyl (E)-6-[2-(*Dimethyl-t-butylsiloxy*)*cyclohexa*-2,4-*dienyl*]-4,4-*dimethylhex*-2-*enoate* (**19**) *and* (±)-*Ethyl* (5SR,6SR)-9-(*Dimethyl-t-butylsiloxy*)-4,4-*dimethyltricyclo*[5.2.2.0^{1,5}]*undec*-8-*ene*-6-*carboxylate* (**18**).—To a stirred solution of the enone (**5**) (30 mg, 0.11 mmol) and triethylamine (0.024 ml, 0.17 mmol) in dry dichloromethane (2 ml) was added dropwise dimethyl-t-butylsilyl trifluoromethanesulphonate (0.033 ml, 0.13 mmol) under nitrogen, and the mixture was stirred for 10 min. The reaction mixture was diluted with dichloromethane and the organic phase was washed successively with saturated aqueous sodium hydrogen carbonate and brine, dried ($MgSO_4$), and concentrated to give a crude product, which was subjected to medium-pressure liquid chromatography (m.p.l.c.). Elution with hexane–ethyl acetate (99:1 v/v) afforded an oily mixture of two *silyl enol ethers* (**18**) (16 mg, 37%) in the ratio 5:3; $\nu_{max.}(CHCl_3)$ 1 720 (CO) and 1 625 cm^{-1} (C=C); $\delta_H(CCl_4)$ 0.10 (6 H, s, $SiMe_2$), 0.90 (9 H, s, Bu^t), 1.00 (6 H, s, 2 × Me), 3.95 and 4.03 [2 H (5:3), each q, each *J* 7.0 Hz, CH_2Me], and 4.70 and 4.90 [1 H (5:3), each d, each *J* 6.0 Hz, CH=COSi]; *m/z* 378 (M^+) (Found: M^+, 378.2580. $C_{22}H_{38}O_3Si$ requires *M*, 378.2590).

Further elution with the same solvent gave the *silyl dienol ether* (**19**) (19 mg, 45%) as an oil; $\nu_{max.}(CHCl_3)$ 1 700 (CO) and 1 640 cm^{-1} (C=C); $\delta_H(CCl_4)$ 0.10 (6 H, s, $SiMe_2$), 0.86 (9 H, s, Bu^t), 0.96 (6 H, s, 2 × Me), 1.45—2.20 (7 H, m, 3 × CH_2 and CH), 1.15 (3 H, t, *J* 7.0 Hz, CH_2Me), 4.00 (2 H, q, *J* 7.0 Hz, CH_2Me), 4.85 (1 H, d, *J* 6.0 Hz, CH=COSi), 5.32 and 5.75 (each 1 H, each m, $CH=CHCH_2$), 5.70 (1 H, d, *J* 16.0 Hz, $=CHCO_2Et$), and 6.87 (1 H, d, *J* 16.0 Hz, $CH=CHCO_2Et$); *m/z* 378 (M^+) (Found: M^+, 378.2568. $C_{22}H_{38}O_3Si$ requires *M*, 378.2588).

Ethyl (E)-6-[2-(*Dimethyl-t-butylsiloxy*)*cyclohexa*-2,4-*dienyl*]-4,4-*dimethylhex*-2-*enoate* (**19**).—The enone (**5**) (20 mg, 0.08 mmol) was treated with dimethyl-t-butylsilyl trifluoromethanesulphonate (0.022 ml, 0.09 mmol) in the presence of diisopropylethylamine (0.02 ml, 0.12 mmol) in dichloromethane (2 ml) and the mixture was then worked up as above. Purification by m.p.l.c. gave the silyl dienol ether (**19**) (26 mg, 91%) as an oil, which was identical with the above sample in all respects.

Treatment of the Diene (**19**) *with Boron Trifluoride–Diethyl Ether*.—To a stirred solution of the diene (**19**) (16 mg, 0.04 mmol) in dry dichloromethane (1 ml) was added boron trifluoride–diethyl ether (1 drop) and the mixture was stirred at room temperature under nitrogen. After addition of water, the resulting aqueous solution was extracted with dichloromethane. The extract was washed successively with saturated aqueous sodium hydrogen carbonate and brine, dried ($MgSO_4$), and evaporated to give a residue, which was purified by column chromatography on silica gel. Elution with hexane–ethyl acetate (92:8 v/v) gave the ester (**17**) (5 mg, 45%) and the ester (**5**) (6 mg, 54%) as an oil. Their spectral data were identical with those of authentic samples.

Acidic Treatment of the Tricyclic Silyl Enol Ether (**18**).—A mixture of the silyl enol ether (**18**) (13 mg, 0.03 mmol) in 10% perchloric acid–THF (1:1 v/v, 2 ml) was stirred for 1 h. After neutralisation with saturated aqueous sodium hydrogen carbonate, the aqueous solution was thoroughly extracted with diethyl ether. The extract was dried ($MgSO_4$) and evaporated to give a residue, which was chromatographed on silica gel with hexane–ethyl acetate (92:8 v/v) to afford the ketone (**16**) (3 mg, 33%) and the ketone (**4**) (5 mg, 55%) as an oil. They were identical with the above specimens in all respects.

Ethyl (E)-6-[2-(*Dimethyl-t-butylsiloxy*)*cyclohexa*-1,3-*dienyl*]-4,4-*dimethylhex*-2-*enoate* (**20**).—To a solution of the ester (**5**) (30 mg, 0.11 mmol) and trimethylamine (0.1 ml) in dry dichloromethane (2 ml) at −78 °C was added dimethyl-t-butylsilyl trifluoromethanesulphonate (0.06 ml, 0.23 mmol) under nitrogen. The reaction mixture was stirred at the same temperature for 3 h and at room temperature for 20 h. The mixture was diluted with dichloromethane and the organic solution was washed successively with saturated aqueous sodium hydrogen carbonate and brine, dried ($MgSO_4$), and evaporated. The resulting product was purified by silica gel column chromatography with hexane–ethyl acetate (99:1 v/v) as eluant to give the *silyl enol ether* (**20**) (16 mg, 37%) as an oil; $\nu_{max.}(CHCl_3)$ 1 710 (CO) and 1 645 cm^{-1} (C=C); $\delta_H(CCl_4)$ 0.10 (6 H, s, $SiMe_2$), 0.96 (9 H, s, Bu^t), 1.10 (6 H, s, 2 × Me), 1.32 (3 H, t, *J* 7.0 Hz, CH_2Me), 1.40—2.23 (8 H, m, 4 × CH_2), 4.13 (2 H, q, *J* 7.0 Hz, CH_2Me), 5.60 (1 H, d, *J* 16.0 Hz, $=CHCO_2Et$), 5.62 (2 H, br s, $CH=CHCH_2$), and 6.80 (1 H, d, *J* 16.0 Hz, $CH=CHCO_2Et$); *m/z* 378 (M^+) (Found: M^+, 378.2572. $C_{22}H_{38}O_3Si$ requires *M*, 378.2590).

Further elution with hexane–ethyl acetate (9:1 v/v) afforded the starting ester (**5**) (9 mg, 30%).

Reaction of the Siloxydiene (**20**) *with Boron Trifluoride–Diethyl Ether*.—Boron trifluoride–diethyl ether (0.007 ml, 0.04 mmol) was added to a solution of the silyl dienol ether (**20**) (13 mg, 0.03 mmol) in dry dichloromethane (1 ml) at −78 °C under nitrogen and the mixture was stirred at the same temperature for 1.5 h and at room temperature for 10 h. After addition of water, the aqueous solution was extracted with dichloromethane. The organic extract was washed successively with saturated aqueous sodium hydrogen carbonate and brine, dried ($MgSO_4$), and evaporated to give a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (92:8 v/v) gave the ketone (**16**) (1 mg, 11%), the ketone (**4**) (2 mg, 22%), and the enone (**5**) (3 mg, 33%) as an oil. These products were identical with the authentic compounds in all respects.

(±)-(1SR,5SR,6SR,7RS)-6-*Hydroxymethyl*-4,4-*dimethyltricyclo*[5.2.2.0^{1,5}]*undecan*-9-*ol* (**21**).—To a stirred solution of the keto ester (**4**) (500 mg, 1.9 mmol) in dry diethyl ether (15 ml) at −78 °C was added dropwise a 1M solution of DIBAL in toluene (5.7 ml, 5.7 mmol). The mixture was allowed to warm to room temperature during 30 min and was then quenched by addition of water (5.7 ml) whilst being stirred and cooled. The resulting granular precipitate was filtered off on Celite. The concentrated filtrate was chromatographed on silica gel with hexane–ethyl acetate (1:1 v/v) as eluant to give the *diol* (**21**) (420 mg, 99%) as a viscous oil; $\nu_{max.}(CHCl_3)$ 3 600 cm^{-1} (OH); $\delta_H(CCl_4)$ 1.00 (3 H, s, Me), 1.06 (3 H s, Me), 1.15—2.25 (15 H, m, 5 × CH_2, 3 × CH, and 2 × OH), 3.40 (1 H, d, *J* 10.0 Hz, CHOH), 3.53 (1 H, m, CHOH), and 3.73 (1 H, dd, *J* 10.0 and 6.0 Hz, CHOH); *m/z* 206 ($M^+ - H_2O$) [Found: $(M - H_2O)^+$, 206.1650. $C_{14}H_{22}O$ requires *m/z* 206.1670].

(±)-(1SR,5SR,6SR,7RS)-6-*Hydroxymethyl*-4,4-*dimethyltricyclo*[5.2.2.0^{1,5}]*undecan*-9-*one* (**22**).—To a stirred solution of

the diol (**21**) (35 mg, 0.16 mmol) in acetonitrile–water (7:3 v/v, 3 ml) were added sodium bromate (23.6 mg, 0.16 mmol) and CAN (8.6 mg, 0.016 mmol) and the mixture was then refluxed for 30 min under nitrogen. The reaction mixture was thoroughly extracted with diethyl ether. The combined extracts were washed with brine, dried ($MgSO_4$), and evaporated to give a residue, which was chromatographed on silica gel with hexane–ethyl acetate (1:1 v/v) as eluant to give the *ketone* (**22**) (27.6 mg, 80%) as a viscous oil; $\nu_{max.}(CHCl_3)$ 3 600 (OH) and 1 710 cm^{-1} (CO); $\delta_H(CDCl_3)$ 1.05 (3 H, s, Me), 1.16 (3 H, s, Me), 1.20—2.65 (14 H, m, 5 × CH_2, 3 × CH, and OH), 3.33 (1 H, d, *J* 10.0 Hz, C*H*HOH), and 3.53 (1 H, dd, *J* 10.0 and 5.0 Hz, CH*H*OH); *m/z* 222 (M^+) (Found: M^+, 222.1628. $C_{14}H_{22}O_2$ requires *M*, 222.1620).

(±)-(1SR,5SR,6SR,7RS)-6-*Methoxymethoxymethyl*-4,4-*dimethyltricyclo*[5.2.2.0^{1,5}]*undecan*-9-*one* (**23**).—MOMCl (0.5 ml, 6.6 mmol) was added dropwise to a stirred mixture of the ketone (**22**) (290 mg, 1.31 mmol) and di-isopropylethylamine (0.28 ml, 1.6 mmol) in dry dichloromethane (5 ml) at 0 °C under nitrogen and the mixture was stirred at room temperature for 3 h. After addition of water, the resulting mixture was extracted with dichloromethane. The extract was washed with brine, dried ($MgSO_4$), and evaporated to give a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (4:1 v/v) gave the *methoxymethyl ether* (**23**) (287 mg, 83%) as a pale yellow oil; $\nu_{max.}(CHCl_3)$ 1 710 (CO) and 1 110 cm^{-1} (C–O–C); $\delta_H(CCl_4)$ 1.03 (3 H, s, Me), 1.12 (3 H, s, Me), 1.16—2.30 (13 H, m, 5 × CH_2 and 3 × CH), 3.29 (3 H, s, OMe), 3.37 (2 H, d, *J* 6.0 Hz, CH_2OMOM), and 4.50 (2 H, s, OCH_2OMe); *m/z* 266 (M^+) (Found: M^+, 266.1882. $C_{16}H_{26}O_3$ requires *M*, 266.1882).

(±)-(1SR,5SR,6SR,7RS)-6-*Methoxymethoxymethyl*-4,4-*dimethyltricyclo*[5.2.2.0^{1,5}]*undec*-8-*ene* (**24**).—A mixture of the methoxymethyl ether (**23**) (85 mg, 0.32 mmol), *p*-toluenesulphonohydrazide (715 mg, 0.38 mmol), and boron trifluoride–diethyl ether (1 drop) in dry dichloromethane (3 ml) was stirred for 18.5 h. The reaction mixture was diluted with water and extracted with dichloromethane. The extract was washed successively with saturated aqueous sodium hydrogen carbonate and brine, dried ($MgSO_4$), and evaporated to give a residue, which was chromatographed on silica gel. Elution with hexane–ethyl acetate (4:1 v/v) afforded the hydrazone (132 mg) as a yellow solid; $\nu_{max.}(CHCl_3)$ 3 370 and 1 360 cm^{-1} (SO_2NH); $\delta_H(CCl_4)$ 0.94 (3 H, s, Me), 1.05 (3 H, s, Me), 1.15—2.50 (13 H, m, 5 × CH_2 and 3 × CH), 2.41 (3 H, s, Ar*Me*), 3.25 (2 H, d, *J* 6.0 Hz, CH_2OMOM), 3.28 (3 H, s, OMe), 4.53 (2 H, s, OCH_2OMe), and 7.15—7.82 (4 H, m, ArH); *m/z* 434 (M^+).

To a stirred solution of the above hydrazone (131 mg, 0.3 mmol) in dry THF–*N*,*N*,*N*′,*N*′-tetramethylethylenediamine (1:1 v/v, 3 ml) at −78 °C was added 15% butyl-lithium in hexane solution (4.3 ml, 9 mmol) under nitrogen and the mixture was allowed to warm to room temperature during 2 h. The reaction mixture was then cooled, quenched with saturated aqueous ammonium chloride, and extracted with diethyl ether. The extract was washed with brine, dried ($MgSO_4$), and evaporated. The residue was purified by chromatography with hexane–ethyl acetate (99:1 v/v) as eluant to afford the *olefin* (**24**) (42 mg, 50%) as a pale yellow oil; $\delta_H(CDCl_3)$ 1.02 (3 H, s, Me), 1.06 (3 H, s, Me), 1.15—1.92 (11 H, m, 4 × CH_2 and 3 × CH), 3.03 (2 H, d, *J* 7.0 Hz, CH_2OMOM), 3.27 (3 H, s, OMe), 4.45 (2 H, s, OCH_2OMe), 5.83 (1 H, dd, *J* 8.0 and 6.0 Hz, CH=C*H*CH), and 6.11 (1 H, br d, *J* 8.0 Hz, C*H*=CHCH); *m/z* 205 (M^+ − CH_2OMe) [Found: (M − CH_2OMe)$^+$, 205.1585. $C_{14}H_{21}O$ requires *m/z* 205.1590].

(±)-(1SR,5SR,6RS,7SR,8SR,9RS)-8,9-*Epoxy*-6-*methoxymethoxymethyl*-4,4-*dimethyltricyclo*[5.2.2.0^{1,5}]*undecane** (**25**) *and* (±)-(1SR,5SR,6RS,9RS,10SR,13RS)-13-*Methoxymethoxy*-4,4-*dimethyl*-8-*oxatetracyclo*[7.3.1.0^{1,5}.0^{6,10}]*tridecane* (**26**).—After a solution of the olefin (**24**) (109.8 mg, 0.44 mmol) and MCPBA (130 mg, 0.53 mmol) in dry dichloromethane (3 ml) had been stirred at 0 °C for 1 h, the mixture was allowed to warm to room temperature and was stirred at the same temperature for a further 6 h. To the cooled reaction mixture was added saturated aqueous sodium hydrogen carbonate and the mixture was extracted with dichloromethane. The extract was washed successively with saturated aqueous potassium carbonate and brine, dried ($MgSO_4$), and evaporated. The residue was subjected to column chromatography on silica gel with hexane–ethyl acetate (92:8 v/v) as eluant to give the *epoxide* (**25**) (73.2 mg, 63%) as an oil; $\nu_{max.}(CHCl_3)$ 910 and 850 cm^{-1} (C–C); $\delta_H(CDCl_3)$ 1.03 (3 H, s, Me), 1.05 (3 H, s, Me), 1.20—2.35 (11 H, m, 4 × CH_2 and 3 × CH), 3.00 (1 H, d, *J* 5.0 Hz, >CHC*H*–C*H*), 3.22 (1 H, dd, *J* 5.0 and 4.0 Hz, >CHC*H*–CH), 3.36 (3 H, s, OMe), 3.38 (2 H, d, *J* 6.0 Hz, CH_2OMOM), and 4.60 (2 H, s, OCH_2OMe); *m/z* 221 (M^+ − CH_2OMe) [Found: (M − CH_2OMe)$^+$, 221.1551. $C_{14}H_{21}O_2$ requires *m/z* 221.1541].

Further elution with the same solvent system afforded the *methoxymethyl ether* (**26**) (4.7 mg, 4%) as an oil; $\nu_{max.}(CHCl_3)$ 1 110 cm^{-1} (C–O–C); $\delta_H(CDCl_3)$ 1.03 (3 H, s, Me), 1.08 (3 H, s, Me), 1.23—2.15 (11 H, m, 4 × CH_2 and 3 × CH), 3.11 (1 H, s, C*H*OMOM), 3.34 (1 H, d, *J* 6.0 Hz, 9-H), 3.35 (3 H, s, OMe), 3.67 (1 H, dd, *J* 6.0 and 2.0 Hz, OC*H*HCH<), 3.77 (1 H, d, *J* 6.0 Hz, OCH*H*CH<), 4.59 (1 H, d, *J* 6.0 Hz, OC*H*HO), and 4.74 (1 H, d, *J* 6.0 Hz, OCH*H*O); *m/z* 266 (M^+) (Found: M^+, 266.1877. $C_{16}H_{26}O_3$ requires *M*, 266.1880).

(±)-(1SR,5SR,6RS,9RS,10SR,13RS)-4,4-*Dimethyl*-8-*oxatetracyclo*[7.3.1.0^{1,5}.0^{6,10}]*tridecan*-13-*ol* (**27**).—(A) A solution of the above epoxide (**25**) (24.0 mg, 0.09 mmol) in 10% aqueous perchloric acid–THF (1:1 v/v, 8 ml) was stirred at room temperature for 1.5 h. After neutralisation of the cooled mixture with saturated aqueous sodium hydrogen carbonate, the aqueous solution was extracted with diethyl ether. The extract was dried ($MgSO_4$) and evaporated to give a crude product, which was purified by h.p.l.c. [LiChrosorb SI-60; 4 × 250 mm] with hexane–ethyl acetate (4:1 v/v) as eluant to give the *alcohol* (**27**) (14.3 mg, 71%) as a solid. Recrystallisation from hexane afforded *prisms*, m.p. 93—94 °C; $\nu_{max.}(CHCl_3)$ 3 600 cm^{-1} (OH); $\delta_H(CDCl_3)$ 1.03 (3 H, s, Me), 1.09 (3 H, s, Me), 1.19—2.05 (12 H, m, 4 × CH_2, 3 × CH, and OH), 3.19 (1 H, s, C*H*OH), 3.33 (1 H, d, *J* 6.0 Hz, 9-H), 3.63 (1 H, d, *J* 2.0 Hz, OC*H*HCH<), and 3.69 (1 H, dd, *J* 2.0 and 1.0 Hz, OCH*H*CH<); *m/z* 222 (M^+) (Found: M^+, 222.1636. $C_{14}H_{22}O_2$ requires *M*, 222.1621).

(B) To a solution of the epoxide (**25**) (36.5 mg, 0.13 mmol) in dry dichloromethane (2 ml) was added boron trifluoride–diethyl ether (0.002 ml, 0.0065 mmol) and the mixture was stirred at room temperature for 6 h under nitrogen. The mixture was diluted with water and extracted with dichloromethane. The extract was washed successively with saturated aqueous sodium hydrogen carbonate and brine, dried ($MgSO_4$), and concentrated to give a residue, which was chromatographed on silica gel. Elution with hexane–ethyl acetate (19:1 v/v) afforded the methoxymethyl ether (**26**) (13.3 mg, 36%) as an oil,

* *Systematic name:* (+)-(1*SR*,5*SR*,6*RS*,7*SR*,8*SR*,10*RS*)-6-Methoxymethoxymethyl-4,4-dimethyl-9-oxatetracyclo[5.3.2.0^{1,5}.0^{8,10}]-dodecane.

which was identical with the above specimen in all respects. The product from further elution was purified by h.p.l.c. [LiChrosorb SI-60; 4 × 250 mm] with hexane–ethyl acetate (4:1 v/v) as eluant to give the alcohol (**27**) (9.6 mg, 32%) as a solid, whose spectral data were identical with those of the above sample prepared by method A.

(C) A stirred mixture of the methoxymethyl ether (**26**) (10.8 mg, 0.04 mmol) and conc. hydrochloric acid (2 drops) in methanol (2 ml) was heated at 60 °C for 5 h. After evaporation of the solvent, diethyl ether was added to the residue. The ethereal solution was washed with saturated aqueous sodium hydrogen carbonate, and the aqueous layer was thoroughly extracted with diethyl ether. The combined extracts were washed with brine, dried ($MgSO_4$), and concentrated to give a crude product, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (7:3 v/v) gave the alcohol (**27**) (5.5 mg, 61%) as a solid, which was identical with the compound prepared by method A.

(±)-(1SR,5SR,6RS,9RS,10SR,13RS)-4,4-*Dimethyl*-8-*oxatetracyclo*[7.3.1.$0^{1,5}$.$0^{6,10}$]*tridecan*-13-*yl Acetate* (**28**).—A solution of the alcohol (**27**) (2.3 mg, 0.01 mmol), acetic anhydride (0.004 ml, 0.04 mmol), triethylamine (0.006 ml, 0.06 mmol), and DMAP (0.06 mg, 0.005 mmol) in dry dichloromethane (2 ml) was stirred for 1.5 h at room temperature under nitrogen. The diluted dichloromethane solution was washed with 10% hydrochloric acid, dried ($MgSO_4$), and evaporated to give a residue, which was purified by silica gel column chromatography. Elution with hexane–ethyl acetate (9:1 v/v) as eluant afforded the *acetate* (**28**) (2 mg, 66%) as an oil; $\nu_{max.}$($CHCl_3$) 1 730 cm^{-1} (CO); δ_H($CDCl_3$) 1.05 (3 H, s, Me), 1.09 (3 H, s, Me), 1.10—2.05 (11 H, m, 4 × CH_2, and 3 H), 2.06 (3 H, s, COMe), 3.39 (1 H, d, *J* 6.0 Hz, 9-H), 3.66 (1 H, d, *J* 2.0 Hz, OC*H*HCH<), 3.74 (1 H, d, *J* 2.0 Hz, OCH*H*CH<), and 4.30 (1 H, s, C*H*OAc); *m/z* 264 (M^+) (Found: M^+, 264.1723. $C_{16}H_{24}O_3$ requires *M*, 264.1724).

(±)-(1SR,5SR,6RS,9RS,10SR,13RS)-4,4-*Dimethyl*-8-*oxatetracyclo*[7.3.1.$0^{1,5}$.$0^{6,10}$]*tridecan*-13-*yl Methanesulphonate* (**29**).—To a solution of the alcohol (**27**) (27 mg, 0.12 mmol) and triethylamine (0.05 ml, 0.36 mmol) in dry dichloromethane (2 ml) at 0 °C was added methanesulphonyl chloride (0.024 ml, 0.30 mmol) dropwise under nitrogen. The reaction mixture was stirred at the same temperature for 1.5 h. After being washed successively with 3% hydrochloric acid and brine, the dichloromethane solution was dried ($MgSO_4$) and concentrated to afford a residue, which was chromatographed on silica gel. Elution with hexane–ethyl acetate (9:1 v/v) afforded the *mesyl ester* (**29**) (24.0 mg, 66%) as a viscous oil; $\nu_{max.}$($CHCl_3$) 1 360 and 1 175 cm^{-1} (SO_2); δ_H($CDCl_3$) 1.06 (3 H, s, Me), 1.07 (3 H, s, Me), 1.25—2.15 (11 H, m, 4 × CH_2 and 3 × CH), 3.00 (3 H, s, SO_2Me), 3.39 (1 H, d, *J* 6.0 Hz, 9-H), 3.70 (1 H, dd, *J* 4.5 and 1.0 Hz, OC*H*HCH<), 3.96 (1 H, d, *J* 4.5 Hz, OCH*H*CH<), and 4.10 (1 H, s, C*H*OSO_2Me); *m/z* 300 (M^+) (Found: M^+, 300.1372. $C_{15}H_{24}O_4S$ requires *M*, 300.1394).

(±)-(1RS,4RS,5RS,9SR,12SR,13RS)-6,6-*Dimethyl*-2-*oxatetracyclo*[7.3.1.$0^{4,12}$.$0^{5,13}$]*tridecan*-9-*ol* (**30**).—A solution of the mesyl ester (**29**) (9 mg, 0.03 mmol) in acetone–water (2:1 v/v, 2 ml) was heated at 70 °C and stirred under nitrogen for 15 h. After evaporation of acetone, the aqueous solution was thoroughly extracted with dichloromethane. The extract was dried ($MgSO_4$) and evaporated to give a residue, which was purified by h.p.l.c. [LiChrosorb SI-60; 4 × 250 mm] with hexane–ethyl acetate (3:2 v/v) as eluant to give the *alcohol* (**30**) (4.3 mg, 65%) as a viscous oil; $\nu_{max.}$($CHCl_3$) 3 600 cm^{-1} (OH); δ_H($CDCl_3$) (360 MHz; 2D) 1.03 (3 H, s, Me), 1.10 (3 H, s, Me), 1.31—1.73 (8 H, 11-H, 3 × CH_2, and OH), 1.78 (1 H, d, *J* 8.3 Hz, 5-H), 1.9—2.0 (1 H, m, 12-H), 2.20 (1 H, d, *J* 10.0 Hz, 11-H), 2.22 (1 H, d, *J* 10.0 Hz, 4-H), 2.28 (1 H, s, 13-H), 3.41 (1 H, d, *J* 6.3 Hz, OC*H*HCH<), 3.66 (1 H, dd, *J* 6.3 and 1.4 Hz, OCH*H*CH<), and 4.44 (1 H, br s, 1-H); δ_C($CDCl_3$) (INEPT) 22.04 (CH_2), 29.41 (C), 30.34 (Me), 33.33 (Me), 34.56 (CH_2), 35.34 (CH_2), 37.86 (CH_2), 41.02 (CH), 44.50 (CH), 51.49 (CH), 52.98 (CH), 73.55 (C), 77.99 (CH_2), and 78.14 (CH); *m/z* 222 (M^+) (Found: M^+, 222.1611. $C_{14}H_{22}O_2$ requires *M*, 222.1619).

(±)-(1RS,4RS,5SR,9SR,12SR,13RS)-9-*Hydroxy*-6,6-*dimethyl*-2-*oxatetracyclo*[7.3.1.$0^{4,12}$.$0^{5,13}$]*tridecan*-3-*one* (**31**).—To a mixture of the alcohol (**30**) (12 mg, 0.05 mmol) and sodium metaperiodate (35 mg, 0.16 mmol) in tetrachloromethane–acetonitrile–water (2:2:3 v/v/v, 2.1 ml) was added ruthenium(III) trichloride (0.3 mg, 0.001 mmol) and the reaction mixture was stirred for 20 h. The mixture was extracted with dichloromethane. The extract was washed with saturated aqueous sodium chloride, dried ($MgSO_4$), and evaporated. The residue was taken up into diethyl ether and the mixture was filtered. The concentrated filtrate was subjected to silica gel column chromatography with hexane–ethyl acetate (3:7 v/v) as eluant to afford the *lactone* (**31**) (5 mg, 39%) as an oil; $\nu_{max.}$($CHCl_3$) 3 580 (OH) and 1 780 cm^{-1} (CO); δ_H($CDCl_3$) 1.05 (3 H, s, Me), 1.12 (3 H, s, Me), 1.35—2.60 (12 H, m, 4 × CH_2, 3 × CH, and OH), 2.68 (1 H, m, 2-H), and 4.95 (1 H, dd, *J* 2.9 and 1.4 Hz, 1-H); *m/z* 192 ($M^+ - CO_2$) [Found: $(M - CO_2)^+$, 192.1533. $C_{13}H_{20}O$ requires *m/z* 192.1514].

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