Synthesis based on cyclohexadienes. Part 17.[1] Total synthesis of the sesquiterpenes of *Eremophila georgei* Diels

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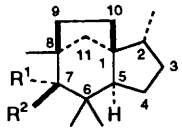
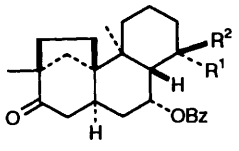
The first stereoselective total synthesis of the novel sesquiterpenes **1** and **2** is described. The preparation of the key intermediate **27** involved a rearrangement of a bicyclo[3.2.1]octane framework to an isomeric bicyclo[3.2.1]octene skeleton *via* a bicyclo[2.2.2]octane derivative.

A number of natural products possess the novel bicyclo-[3.2.1]octane framework with a bridgehead methyl group. These are represented by the complex tricyclic sesquiterpenes **1** and **2**, isolated from *Eremophila georgei* Diels,[2] and the tetracyclic diterpenes scopadulciol **3** and scopadulcic acids A **4** and B **5**, reported from *Scoparia dulcis*.[3] The presence of a unique tricyclic ring system in conjunction with the bridgehead methyl group in these molecules makes them synthetically challenging targets.



1 $R^1 = H, R^2 = OH$
2 $R^1R^2 = O$



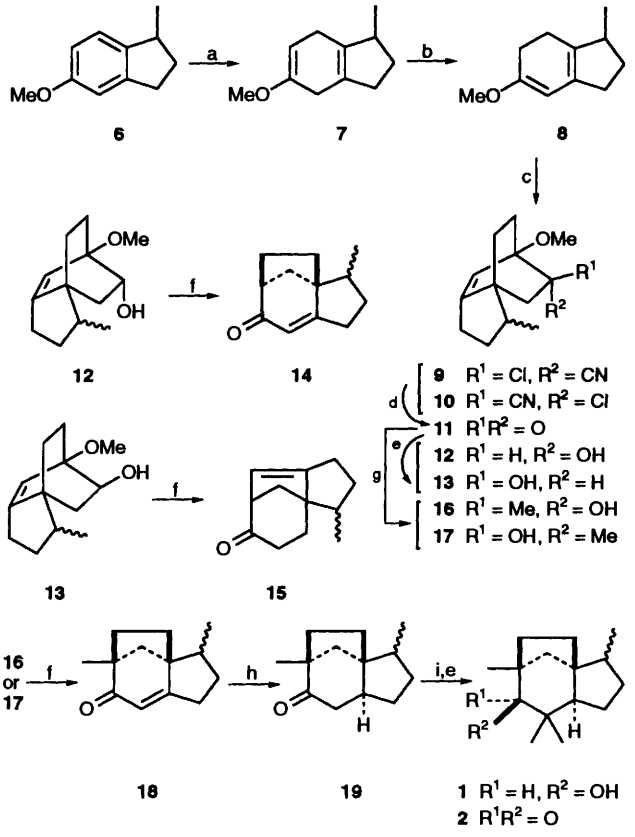
3 $R^1 = Me, R^2 = CH_2OH$
4 $R^1 = CO_2H, R^2 = CH_2OH$
5 $R^1 = Me, R^2 = CO_2H$

The structures of the sesquiterpenes **1** and **2** were established by chemical and spectral methods and confirmed by X-ray crystal studies by Ghisalberti and co-workers.[2] The biogenetic origin of these sesquiterpenes was also proposed by these workers. We describe herein our results[4] in the construction of this unique tricyclic ring system using a Diels–Alder strategy which culminated in the first stereoselective total synthesis of the sesquiterpenes **1** and **2**.[5a]

Results and discussion

Birch reduction of the indane **6**[5b] afforded the diene **7** in quantitative yield (Scheme 1). Treatment of the diene **7** with KNH_2–NH_3 gave the conjugated diene **8**. Regiospecific cycloaddition of the diene **8** with α-chloroacrylonitrile afforded a mixture of the adducts **9** and **10**, which were inseparable by column chromatography. However, hydrolysis of the adducts **9** and **10** with aq. KOH in dimethyl sulfoxide (DMSO)[6] at 55 °C for 48 h furnished the tricyclic ketone **11** (mixture of methyl epimers) in 50% yield.

Reduction of the tricyclic ketone **11** with $NaBH_4$ gave a 2:1 mixture of *endo* and *exo* alcohols **12** and **13** respectively, which were separable by column chromatography. Solvolysis of the *endo* alcohol **12** with BF_3·OEt_2 afforded the enone **14**. The *exo* alcohol **13** yielded the ketone **15** under identical conditions. The IR spectrum of the enone **14** had absorptions at 1680 and 1630 cm^{-1}, while the ^1H NMR spectrum showed signals at δ 0.94 and 1.0 (3 H, 2 d, J 6.5) for the secondary methyl group, indicating that the tricyclic enone **14** is a mixture of diastereoisomers at C-2. On the other hand, the ketone **15** had IR absorptions at 1715 and 1625 cm^{-1} for the saturated



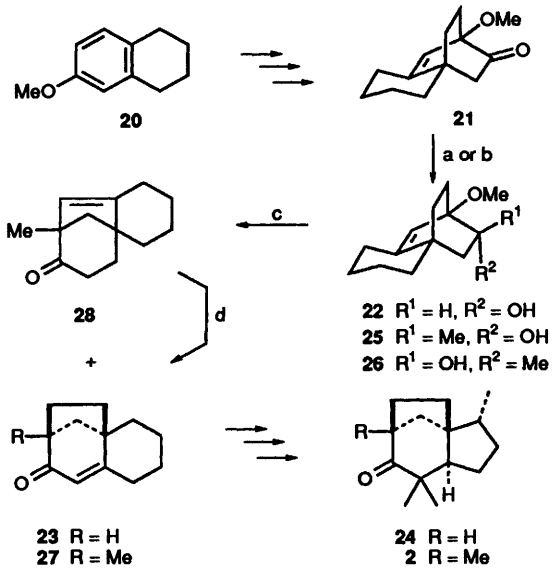
Scheme 1 *Reagents and conditions:* (a) Na, liq. NH_3; (b) KNH_2, NH_3; (c) CH_2=C(Cl)CN, 90 °C, 48 h; (d) aq. KOH, DMSO, 55 °C, 48 h; (e) $NaBH_4$, EtOH; (f) BF_3·OEt_2, PhH, 48 h, reflux; (g) MeMgI, 0 °C to reflux; (h) H_2, 10% Pd/C, EtOH; (i) NaH, MeI, DME, room temp. to 60 °C

carbonyl group and the double bond, respectively. The secondary methyl group appeared as two doublets at δ 0.93 and 0.94 in its ^1H NMR spectrum. The enone **14** has the basic tricyclic ring system present in the sesquiterpenes **1** and **2** except for the bridgehead methyl group, and is accessible in six steps from the indane **6**. A similar methodology for the preparation of the analogous enone **18**, which has the bridgehead methyl group (and can therefore be transformed into the natural sesquiterpenes **1** and **2**) was then examined.

Since the *endo* alcohol **12** was rearranged to the enone **14** under acidic conditions, similar treatment of the tertiary alcohol **16**, available from the ketone **11**, should lead to the enone **18** upon exposure to acid. Reaction of the ketone **11** with MeMgI afforded a 2:1 mixture of the *endo* and *exo* alcohols **16** and **17**, respectively. The skeletal rearrangement was carried out under

mild conditions. Thus, exposure of the *endo* alcohol **16** to a catalytic amount of BF_3·Et_2O in dry benzene at room temp. afforded the enone **18** in good yield. Under identical conditions, the *exo* alcohol **17** also gave the enone **18** in good yield. The ^1H NMR spectrum of the enone **18** showed a pair of doublets at δ 0.92 and 1.04 integrating for the three protons of the C-2 methyl group, indicating the epimeric nature of that centre. Attempted separation of these epimers was not successful.

Catalytic hydrogenation of the enone **18** over 10% Pd/C afforded the saturated ketone **19**. The appearance of only two singlets, at δ 1.1 and 1.14, for the bridgehead methyl group and the presence of two doublets at δ 0.91 and 0.94 for the secondary methyl group in its ^1H NMR spectrum clearly established that the hydrogenation had taken place stereoselectively, presumably from the α face of the molecule as the β face is blocked by the ethano bridge. Alkylation of the ketone **19** with NaH and excess of MeI [7] yielded the sesquiterpene ketone **2**, which upon reduction with $NaBH_4$ gave the sesquiterpene alcohol **1** in good yield. The spectral and analytical data of the synthetic compounds **1** and **2** were in agreement with the data reported for the natural products, thus establishing their gross structure. Although the above synthesis of the tricyclic compounds **1** and **2** was achieved by a short (eight steps), efficient and straightforward route, the stereochemistry of the C-2 methyl group could not be controlled by this method. Hence an alternative strategy for the stereoselective synthesis of the natural products **1** and **2**, involving a stereoselective introduction of the C-2 methyl group, was conceived. The method envisaged is similar to the synthesis [8] of norprezizanone **24** prepared from the enone **23**, which was readily available from the alcohol **22** by an acid-catalysed skeletal rearrangement. The alcohol **22** was obtained from 6-methoxytetralin **20** through the ketone **21**. The key step in these transformations is the stereoselective introduction of the C-2 methyl group. Similar transformations on the alcohol **25**, also available from the ketone **21**, should result in the stereoselective total synthesis of the sesquiterpenes **1** and **2** and hence the preparation of the enone **25** was undertaken.



Scheme 2 *Reagents and conditions:* (a) $NaBH_4$, EtOH; (b) MeLi, Et_2O, −78 °C to room temp.; (c) BF_3·OEt_2, PhH, room temp.; (d) BF_3·OEt_2, PhMe, reflux

Preparation of the enone 27

Treatment of the ketone **21** [8] with MeLi afforded a 1:1 mixture of the tertiary alcohols **25** and **26**, which was easily separated by column chromatography (Scheme 2). Examination of the ^1H NMR spectrum of these alcohols revealed that the methyl protons appeared at δ 1.04 in the less polar alcohol while in the more polar alcohol they appeared at δ 1.24. The shielding of the methyl protons in the less polar alcohol is attributed to the double-bond anisotropy and hence its structure is assigned to be that of the *exo* alcohol **26**.

Reaction of the *exo* alcohol **26** with BF_3·OEt_2 in benzene at room temp. for 30 min afforded a mixture of the ketone **28** and the enone **27** in the ratio 4:1. Under identical conditions, the *endo* alcohol **25** also rearranged to a mixture of the enone **27** and the ketone **28** in the ratio 4:1. The IR spectrum of the enone **27** showed absorptions at 1677 and 1614 cm^{-1} due to the α,β-unsaturated carbonyl group. The appearance of the olefinic proton at δ 5.64 as a broad singlet in the ^1H NMR spectrum confirmed its structure. The ketone **28** showed a carbonyl absorption at 1700 cm^{-1} and the olefinic proton appeared at δ 5.2, in accord with the structure. It is interesting to note that the generation of a stable tertiary carbocation appears to be the rationale behind the formation of the mixture of compounds **27** and **28**.

Since the enone **27** is required for the synthesis of the sesquiterpenes **1** and **2**, and is predominantly formed upon rearrangement of the *endo* alcohol **25**, several experiments were carried out to obtain the *endo* alcohol **25** exclusively from the ketone **21**. Reaction of the ketone **21** with MeLi–$LiClO_4$,[9] Me_2CuLi [10] and Me_3CuLi_2 [11] was investigated. With reagents MeLi–$LiClO_4$ and Me_3CuLi_2, only a mixture of the alcohols was obtained, with the *exo* alcohol **26** predominating. In the case of Me_2CuLi, reaction occurred only partially, even after a prolonged period.

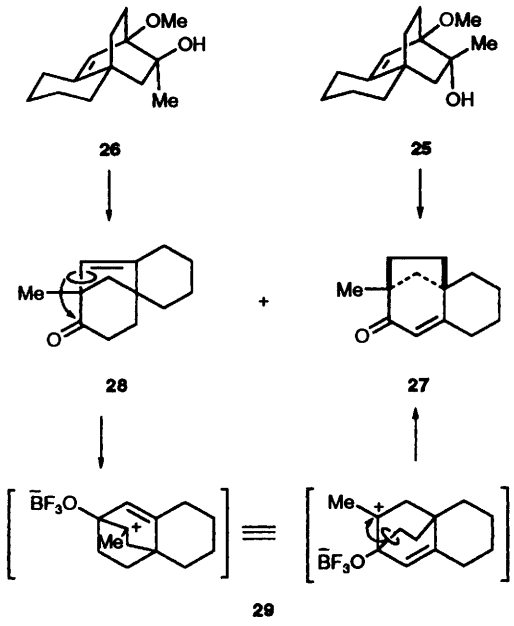
Since all our efforts to increase the yield of the *endo* alcohol **25** from the ketone **21** were in vain, the acid-catalysed rearrangement of the alcohols **25** and **26** was examined in detail with a view to improving the yield of the enone **27**. Upon changing the acid from BF_3·OEt_2 to either $HClO_4$, toluene-*p*-sulfonic acid (PTSA) or formic acid, no improvement in the yield was observed. However, when the rearrangement was performed in refluxing benzene, a significant change was noticed in the ratio of the ketone **28** to the enone **27**. When the *exo* alcohol **26** was refluxed with BF_3·OEt_2 in benzene for 16 h, the ratio of the ketone **28** to enone **27** was found to be 11:9 (unlike the 4:1 mixture formed during the reaction at room temp.) due to the equilibration of the ketone **28** to the enone **27** under refluxing conditions.

To confirm this equilibration process, the ketone **28** was refluxed in benzene in the presence of BF_3·OEt_2 (cat.) and at various intervals of time an aliquot of the reaction mixture was analysed. After 10 h of reflux, a 4:1 mixture of the ketone **28** and the enone **27** was obtained. The transformation was considerably faster for the first 24 h as the ratio reached a 1:1 mixture, but slowed down after 24 h. After a prolonged period (68 h) the ratio became 1:19, thus the ketone **28** isomerizes to the enone **27** in 92% yield.

A probable mechanism of the conversion of the ketone **28** into the enone **27** is depicted in Scheme 3. The enone appears to be thermodynamically more stable than the ketone. When the rearrangement of the alcohols **25** and **26** was carried out at room temp., the kinetic product **28** was also observed. However, under refluxing conditions, it isomerizes to the enone **27**, wherein formation of the stable tertiary carbocation **29** appears to be the driving force for this rearrangement.

Since the energy to overcome the activation barrier is supplied in the form of heat, the rearrangement should be faster if carried out in a higher boiling solvent. This was indeed the case, since a 19:1 ratio of the enone **27** to the ketone **28** was obtained in refluxing toluene.

Having achieved the preparation of the enone **27** in good



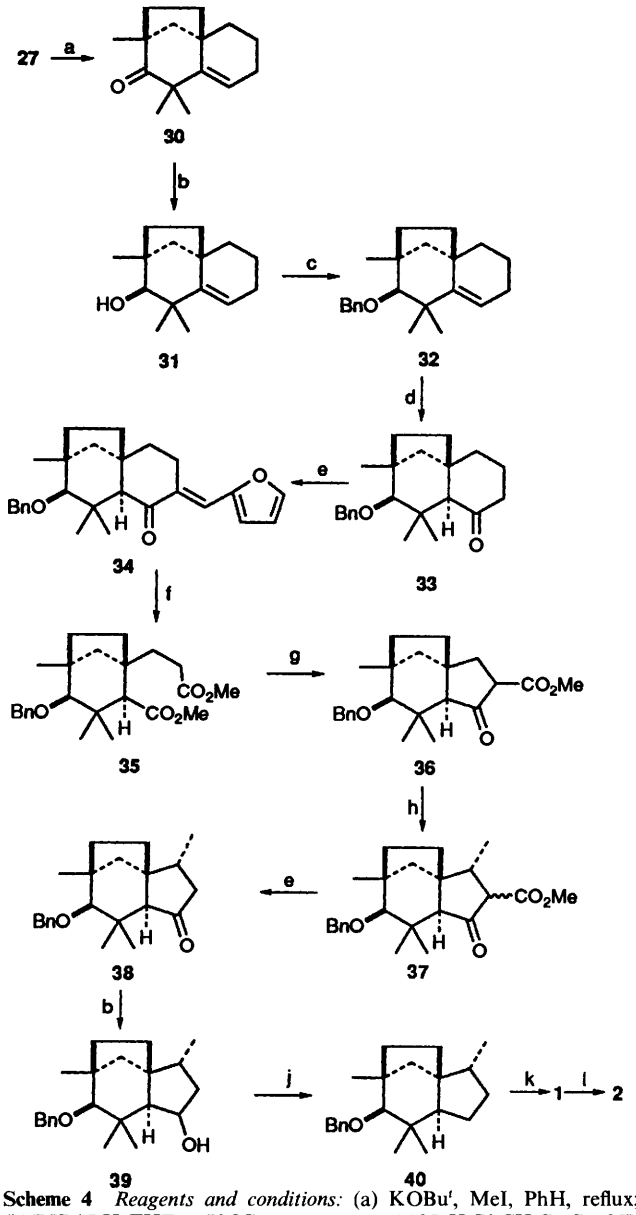
Scheme 3 Probable mechanism for the conversion **28** ⟶ **27**

yield, total synthesis of the natural sesquiterpenes **1** and **2** was undertaken by adopting essentially our earlier strategy[8] with slight modifications as outlined in Scheme 4.

Synthesis of the sesquiterpenes 1 and 2

The enone **27** was treated with KOBu^t in Bu^{t}OH and MeI to obtain the ketone **30** in good yield. The ketone displayed the carbonyl absorption at 1700 cm^{-1} in its IR spectrum and the ^{1}H NMR spectrum exhibited the olefinic proton at δ 5.48 as a triplet. The carbonyl group in compound **30** was protected as the benzyl ether of the corresponding alcohol since the final deprotection of the benzyl ether would regenerate the alcohol functionality leading to the natural products. Reduction of the ketone **30** was found to be sluggish when $NaBH_4$ and lithium aluminium hydride (LAH) were used, presumably due to the steric hindrance. However, the keto group was smoothly reduced to the alcohol **31** with diisobutylaluminium hydride (DIBALH), where the stereochemistry of the OH group was assumed to be 'β' equatorial. Benzylation of the alcohol **31** was sluggish with NaH and benzyl bromide in tetrahydrofuran (THF) with a catalytic amount of tetrabutylammonium iodide (TBAI), even under refluxing conditions. However, the benzyl ether **32** was obtained in quantitative yield when 1,2-dimethoxyethane (DME) was used in place of THF. The ^{1}H NMR spectrum of the benzyl ether exhibited peaks corresponding to the benzylic protons at δ 4.72 as a singlet and at δ 7.3 for the aromatic protons.

Hydroboration of the ether **32** with BH_3·THF complex furnished the alcohol, which was oxidized to the ketone **33** with pyridinium chlorochromate (PCC) in good yield. Aldol condensation of the ketone **33** with furfural afforded the furfurylidene derivative **34**, which was subjected to ozonolysis followed by oxidative work-up to the corresponding diacid.[12] The diacid was esterified with diazomethane to the diester **35**, whose IR spectrum showed an absorption at 1725 cm^{-1} for the ester groups, and the methoxycarbonyl protons appeared as two singlets at δ 3.70 and 3.72 in the ^{1}H NMR spectrum. Dieckmann condensation of diester **35** with 1.2 mol equiv. KOBu^t resulted in the β-keto ester **36** in good yield. The β-keto ester showed two absorptions in the IR spectrum at 1740 and 1720 cm^{-1} for the keto and the ester groups, respectively. In addition, the ^{1}H NMR spectrum exhibited only one peak for the methoxycarbonyl group, at δ 3.76, and a peak for the C-3 proton at δ 3.26 as a doublet of doublets. The β-keto ester **36** possesses the basic tricyclo[6.2.1.0^{1,5}]undecane skeleton with a bridgehead methyl group which is required for the natural products **1** and **2**.



Scheme 4 *Reagents and conditions:* (a) KOBu^t, MeI, PhH, reflux; (b) DIBALH, THF, −78 °C to room temp.; (c) NaH, $PhCH_2Br$, Bu_4NI, DME, reflux; (d) (i) BH_3·THF, THF, 0 °C to room temp., then aq. NaOH, 30% H_2O_2; (ii) PCC, CH_2Cl_2; (e) NaOH, furfural (2-furaldehyde), EtOH, 0 °C to room temp.; (f) (i) O_3, EtOAc, −78 °C; then 30% H_2O_2, AcOH; (ii) CH_2N_2, Et_2O; (g) KOBu^t, PhH, reflux; (h) (i) NaH, PhSeCl, aq. H_2O_2; (ii) Me_2CuLi, −100 °C; (i) DABCO, *o*-xylene, 85 °C; (j) (i) NaH, CS_2, MeI, THF, reflux; (ii) TBTH, AIBN, PhMe, reflux; (k) H_2, 10% Pd/C, EtOH; (l) PDC, CH_2Cl_2

Treatment of the keto ester **36** with NaH and PhSeCl followed by oxidation of the resultant phenylseleno compound[13] gave the unstable unsaturated keto ester, which was immediately treated with 1 mol equiv. of Me_2CuLi at −100 °C affording the β-keto ester **37** as a mixture of diastereoisomers. Based on our earlier experience,[8] the conjugate addition reaction was assumed to have taken place stereoselectively, resulting in an epimeric mixture only at C-3 having the methoxycarbonyl group. This was confirmed by decarboxyl-

ation of the keto ester **37** with 1,4-diazabicyclo[2.2.2]octane (DABCO) in *o*-xylene[14] which afforded the ketone **38** as a single isomer, as evidenced from its ^{1}H NMR spectrum which showed a lone doublet at δ 0.96 for the C-2 methyl group.

Having prepared the ketone **38** as a single isomer, the deoxygenation at C-4 was achieved by the use of Barton's protocol.[15] Reduction of the ketone **38** to the alcohol **39** was accomplished with excess of DIBALH. The xanthate of the resultant alcohol **39** was obtained in nearly quantitative yield with NaH–CS_2–MeI in refluxing THF, which was reduced by successive addition of tributyltin hydride (TBTH) in refluxing toluene to afford the benzyl ether **40** as a single diastereoisomer as evidenced from its ^{1}H NMR spectrum which exhibited peaks at δ 1.01, 1.05 and 1.13 for the protons of the three methyl groups, and the C-2 methyl protons appeared at δ 0.86 as a doublet. Hydrogenolysis of the benzyl ether **40** with 10% Pd on charcoal afforded the sesquiterpene alcohol **1**, which upon oxidation with pyridinium dichromate (PDC) furnished the sesquiterpene ketone **2** in high yield.

The IR and ^{1}H NMR spectra of the synthetic ketone **2** and the alcohol **1** were identical with those of an authentic sample provided by Professor Ghisalberti. This constitutes the first total synthesis of these complex tricyclic sesquiterpenes.

In conclusion, the first stereoselective total synthesis of the sesquiterpenes **1** and **2** is reported from a readily available cyclohexadiene based on a new and general methodology for the construction of a tricyclo[6.2.1.0^{1,5}]undecane skeleton. The synthesis involved a novel rearrangement of a bicyclo-[3.2.1]octene derivative **28** to an isomeric bicyclo[3.2.1]octene derivative **27** through the intermediacy of a bicyclo[2.2.2]system **29**. The enone **27** formed the BCD ring core present in the tetracyclic diterpenes scopadulcic acids **3**–**5**. With proper appendages, this new methodology can be extended to their total synthesis.

Experimental

Mps were measured on a Mettler FP1 instrument and are uncorrected. IR spectra were recorded on a Perkin-Elmer 781 spectrometer as either neat samples or solutions in $CHCl_3$. ^{1}H NMR and ^{13}C NMR spectra were recorded as solutions in $CDCl_3$ (unless otherwise stated) with $SiMe_4$ as internal standard using Hitachi R-1500 FT 60, JEOL FX-90Q, Bruker ACF-200, Bruker WH-270 and Bruker AMX 400 spectrometers. Chemical shifts are reported in δ-units, and *J*-values are in Hz. The usual work-up involved dilution of the reaction mixture with water, extraction with diethyl ether, washing of the organic extract with (successively) water and brine, followed by drying over Na_2SO_4, and evaporation at aspirator pressure. Column chromatography was performed on silica gel (60–120 mesh) by elution with a light petroleum (distillation range 60–80 °C)–ethyl acetate mixture (9:1). Liquid ammonia was distilled over sodium amide. Sodium hydride was 60% in oil, and was used after being washed with light petroleum.

5-Methoxy-1-methyl-4,7-dihydroindane 7

A solution of 5-methoxy-1-methylindane **6**[5b] (8.1 g, 50 mmol) in dry THF (10 cm^3)–*tert*-butyl alcohol (20 cm^3) was added to stirred distilled ammonia (350 cm^3). Sodium (2.3 g, 0.1 mol) was added and the resulting blue solution was stirred for 3 h. Excess of sodium was destroyed by adding solid NH_4Cl. Ammonia was allowed to evaporate off, and the residue was extracted with light petroleum. The organic layer was washed with water and dried. Removal of the solvent gave the diene **7** as a liquid, ν_{max}/cm^{-1} 1690 and 1660; δ_H(60 MHz; CCl_4) 1.0 (3 H, d, *J* 7, Me), 1.65 (2 H, m), 2.2 (3 H, br m, allylic), 2.65 (4 H, br s, doubly allylic), 3.5 (3 H, s, OMe) and 4.6 (1 H, br s, olefinic).

5-Methoxy-1-methyl-6,7-dihydroindane 8

To a solution of potassium amide [formed by the addition of potassium (1 g) to distilled ammonia (250 cm^3) followed by $FeCl_3$ (cat.)] in ammonia was added a solution of the above diene **7** in dry diethyl ether (10 cm^3). The resultant dark red solution was stirred for 45 min before being quenched with solid NH_4Cl until the red colour disappeared. Ammonia was allowed to evaporate off and the reaction mixture was worked up with light petroleum to give the diene **8**, which was used immediately in the next step, ν_{max}/cm^{-1} 1660 and 1610.

8-Chloro-7-methoxy-2-methyltricyclo[5.2.2.0^{1,5}]undec-5-ene-8-carbonitrile 9 and 10

A mixture of the above diene **8**, α-chloroacrylonitrile (11.8 cm^3, 0.15 mol) and hydroquinone (10 mg) was sealed in a tube under nitrogen and heated at 90 °C for 48 h. All the volatiles were removed under reduced pressure and the residue obtained was purified by chromatography to furnish a mixture of *adducts* **9** and **10** (8.05 g, 64%), ν_{max}/cm^{-1} 2220; δ_H(60 MHz; CCl_4) 0.95 (3 H, d, *J* 7, Me), 1.1–2.6 (11 H, m), 3.45 (3 H, s, OMe), 5.81 and 5.98 (1 H, two br s, olefinic) (Found: C, 66.6; H, 7.1. $C_{14}H_{18}ClNO$ requires C, 66.8, H, 7.15%).

7-Methoxy-2-methyltricyclo[5.2.2.0^{1,5}]undec-5-en-8-one 11

A solution of the adducts **9** and **10** (6.29 g, 25 mmol), 50% aq. KOH (5.6 cm^3, 50 mmol) in DMSO (25 cm^3) was stirred at 55 °C for 48 h. The residue obtained after the usual work-up was chromatographed to give the *ketone* **11** (2.58 g, 50%), ν_{max}/cm^{-1} 1725; δ_H(270 MHz) 0.98 and 1.05 (3 H, 2 d, *J* 6.6, Me), 1.3–2.55 (11 H, m), 3.50 and 3.52 (3 H, 2 s, OMe) and 5.88 (1 H, br s, olefinic) (Found: C, 75.6; H, 8.9. $C_{13}H_{18}O_2$ requires C, 75.7; H, 8.8%).

7-Methoxy-2-methyltricyclo[5.2.2.0^{1,5}]undec-5-en-8-ol 12 and 13

To a stirred solution of the ketone **11** (1.03 g, 5 mmol) in methyl alcohol (25 cm^3) was added $NaBH_4$ (95 mg, 2.5 mmol) at room temp. After 2 h, methyl alcohol was removed under reduced pressure from the reaction mixture and the residue was worked up to afford a viscous liquid which showed two closely separated spots on TLC. The mixture was chromatographed: elution with light petroleum–ethyl acetate (9:1) gave the *exo* alcohol **13** (322 mg), ν_{max}/cm^{-1} 3440; δ_H(90 MHz) 0.94 (3 H, d, *J* 6.2, Me), 1.0–2.45 (12 H, m), 3.36 (3 H, s, OMe), 3.84 (1 H, br m, C*H*OH) and 5.84 (1 H, br s, olefinic). Further elution with light petroleum–ethyl acetate (4:1) afforded the endo *alcohol* **12** (645 mg, 93% total yield, *exo*:*endo* ratio 1:2), ν_{max}/cm^{-1} 3460; δ_H(90 MHz) 0.94 (3 H, d, *J* 6.2, Me), 1.0–2.45 (12 H, m), 3.39 (3 H, s, OMe), 3.87 (1 H, br m, C*H*OH) and 5.76 (1 H, br s, olefinic) (Found: C, 74.9; H, 9.8. $C_{13}H_{20}O_2$ requires C, 75.0; H, 9.7%).

2-Methyltricyclo[6.2.1.0^{1,5}]undec-5-en-7-one 14

A solution of the *endo* alcohol **12** (416 mg, 2 mmol) in dry benzene (20 cm^3) with BF_3·OEt_2 (0.5 cm^3) was stirred under reflux for 48 h. The reaction mixture was diluted with benzene, washed successively with water, aq. $NaHCO_3$, and water, and dried. The crude product obtained was purified by chromatography to furnish the *enone* **14** (253 mg, 72%), ν_{max}/cm^{-1} 1680 and 1630; δ_H(270 MHz) 0.94 and 1.0 (3 H, 2 d, *J* 6.5, Me), 1.1–2.3 (9 H, m), 2.6 (2 H, m, allylic protons), 2.9 (1 H, m, bridgehead proton) and 5.74 (1 H, m, olefinic) (Found: C, 81.6; H, 9.0. $C_{12}H_{16}O$ requires C, 81.8; H, 9.15%).

2-Methyltricyclo[5.3.1.0^{1,5}]undec-5-en-8-one 15

When the *exo* alcohol **13** (208 mg, 1 mmol) in dry benzene (15 cm^3) was treated with BF_3·OEt_2 (cat.) as described above, the *ketone* **15** was obtained (120 mg, 68%), ν_{max}/cm^{-1} 1715 and 1625; δ_H(270 MHz) 0.93 and 0.94 (3 H, 2 d, *J* 6.8, Me), 1.1–2.4 (11 H, m), 2.72 (1 H, m, bridgehead proton) and 5.42 (1 H, m, olefinic) (Found: C, 81.6; H, 9.1%).

7-Methoxy-8-methyltricyclo[5.2.2.0^{1,5}]undec-5-en-8-ol 16 and 17

A solution of the ketone **11** (1.24 g, 6 mmol) in dry diethyl ether (10 cm^3) was added during 10 min to a solution of MeMgI [prepared from magnesium (292 mg, 12 mmol)] in diethyl ether (10 cm^3) at 0 °C under nitrogen. The reaction mixture was warmed to room temp. and refluxed for 6 h before being worked up. The residue obtained was chromatographed as above for the compounds **12** and **13** to give the *exo* alcohol **17** (390 mg), ν_{max}/cm^{-1} 3460; δ_H(90 MHz) 0.93 (3 H, d, *J* 6.6, Me), 1.10 (3 H, s, Me), 1.25–2.45 (12 H, m), 3.35 (3 H, s, OMe), 5.89 (1 H, br, olefinic) and *endo* alcohol **16** (781 mg, 88% total yield, *exo*:*endo* ratio 1:2), ν_{max}/cm^{-1} 3500; δ_H(90 MHz) 0.94 (3 H, d, *J* 6.6, Me), 1.21 (3 H, s, Me), 1.26–2.40 (12 H, m), 3.42 (3 H, s, OMe) and 5.96 (1 H, br, olefinic).

2,8-Dimethyltricyclo[6.2.1.0^{1,5}]undec-5-en-7-one 18

A solution of the *endo* alcohol **16** (488 mg, 2.2 mmol) in dry benzene (30 cm^3) was treated with BF_3·OEt_2 (0.5 cm^3) as mentioned above for the compound **14** to furnish the pure *enone* **18** (284 mg, 68%), ν_{max}/cm^{-1} 1680 and 1450; δ_H(90 MHz) 0.92 and 1.04 (3 H, 2 d, *J* 7, Me), 1.23 (3 H, s, Me), 1.4–2.1 (9 H, m), 2.56 (2 H, m, allylic protons) and 5.75 (1 H, m, olefinic) (Found: C, 82.0; H, 9.4. $C_{13}H_{18}O$ requires C, 82.1; H, 9.5%).

Similar treatment of the *exo* alcohol **17** also gave the enone **18**.

2,8-Dimethyltricyclo[6.2.1.0^{1,5}]undecan-7-one 19

A solution of the enone **18** (209 mg, 1.1 mmol) in absolute ethyl alcohol (10 cm^3) was stirred with 10% Pd/C (10 mg) under H_2. After 4 h the catalyst was filtered off on a pad of Celite and silica gel, and the filtrate was chromatographed to furnish the *ketone* **19** (207 mg, 98%), ν_{max}/cm^{-1} 1710; δ_H(270 MHz) 0.91 and 0.94 (3 H, 2 d, *J* 6.6, Me), 1.1 and 1.14 (3 H, 2 s, Me) and 1.3–2.6 (14 H, m) (Found: C, 81.1; H, 10.5. $C_{13}H_{20}O$ requires C, 81.2; H, 10.5%).

2,6,6,8-Tetramethyltricyclo[6.2.1.0^{1,5}]undecan-7-one 2

To a stirred suspension of NaH (120 mg, 3 mmol) in dry DME (16 cm^3) at room temp. was added a solution of the ketone **19** (192 mg, 1 mmol) and MeI (0.6 cm^3, 9.6 mmol) in DME (3 cm^3). The reaction mixture was heated to 60 °C for 2 h before being quenched with water (1 cm^3). The residue obtained after the usual work-up was chromatographed to give *compound* **2** as a liquid (143 mg, 65%), ν_{max}/cm^{-1} 1705; δ_H(90 MHz) 0.90 and 0.94 (3 H, 2 d, *J* 6.5, Me), 1.12 (3 H, s, Me), 1.16 (6 H, s, 2 × Me) and 1.4–2.0 (12 H, m) (Found: C, 81.8; H, 10.9. $C_{15}H_{24}O$ requires C, 81.8; H, 11.0%) [lit.,[2] ν_{max}/cm^{-1} 1700; δ_H(90 MHz) 0.92 (3 H, d, *J* 7, Me), 1.12 (6 H, s, 2 × Me), 1.16 (3 H, s, Me)].

2,6,6,8-Tetramethyltricyclo[6.2.1.0^{1,5}]undecan-7-ol 1

To a solution of the ketone **2** (88 mg, 0.4 mmol) in ethyl alcohol (10 cm^3) was added $NaBH_4$ (15 mg, 0.4 mmol) at room temp. After being stirred for 2 h, the reaction mixture was concentrated under reduced pressure and was poured into aq. NH_4Cl (25 cm^3). The usual work-up followed by chromatography furnished the *alcohol* **1** (83 mg, 93%) as a viscous liquid, ν_{max}/cm^{-1} 3460; δ_H(90 MHz) 0.88 and 0.90 (3 H, 2 d, *J* 6.8, Me), 0.98 (3 H, s, Me), 1.03 (3 H, s, Me), 1.06 (3 H, s, Me), 1.24–2.08 (13 H, m) and 3.23 and 3.26 (1 H, 2 br s, C*H*OH) (Found: M$^+$, 222.1989. $C_{15}H_{26}O$ requires M, 222.1984) [lit.,[2] ν_{max}/cm^{-1} 3640; δ_H(90 MHz) 0.86 (3 H, *J* 7, d, Me), 0.92, 1.03, 1.07 (s, 3 × Me), 3.18 (1 H, s, 7α-H).

8-Methoxy-9-methyltricyclo[6.2.2.0^{1,6}]dodec-6-en-9-ol 25 and 26

Reaction of the ketone 21 with MeLi at −78 °C. A 1.0 mol dm^{-3} solution of MeLi in diethyl ether (12 cm^3, 12 mmol) was added to a solution of ketone **21**[8] (2.06 g, 10 mmol) in dry diethyl ether (100 cm^3) dropwise over a period of 5 min at −78 °C under argon. After 1 h, the reaction mixture was warmed to room temp. over a period of 15 min for 2 h. The product mixture was added into aq. NH_4Cl and extracted with diethyl ether. The organic layer was washed successively with water, aq. sodium thiosulfate, water and brine, and dried. The residue obtained after the removal of solvent showed two well separable components on TLC. The mixture was chromatographed as mentioned above for compounds **12** and **13** to afford the *exo* alcohol **26** (910 mg), ν_{max}/cm^{-1} 3466; δ_H(60 MHz; CCl_4) 1.04 (3 H, s, Me), 1.20–2.50 (15 H, m), 3.33 (3 H, s, OMe) and 5.80 (1 H, br s, olefinic); δ_C(22.5 MHz) 19.0 (t), 21.2 (t), 22.8 (t), 26.8 (t), 27.3 (q), 31.8 (t), 32.2 (t), 37.0 (t), 49.1 (t), 51.1 (q), 76.5 (t), 83.0 (s), 123.0 (d) and 145.0 (s) and the *endo* alcohol **25** (910 mg, 82% total yield, *exo*:*endo* ratio 1:1), ν_{max}/cm^{-1} 3472; δ_H(60 MHz; CCl_4) 1.24 (3 H, s, Me), 1.28–2.54 (15 H, m), 3.40 (3 H, s, OMe) and 5.85 (1 H, br s, olefinic); δ_C-(22.5 MHz) 18.5 (t), 21.0 (t), 24.2 (t), 25.0 (q), 26.3 (t), 31.5 (t, 2 × C), 37.0 (s), 51.0 (q), 51.8 (t), 75.8 (s), 82.0 (s), 122.1 (d) and 145.0 (s).

Reaction of the ketone 21 with various reagents. (a) *With* $LiClO_4$ *and* MeLi.—Lithium perchlorate (321 mg, 2 mmol) was heated to 100 °C under reduced pressure (0.1 mmHg) for 6 h to obtain a fine powder of anhydrous $LiClO_4$, which was dissolved in anhydrous diethyl ether (10 cm^3) and the temperature was brought to −78 °C under argon. To this homogeneous solution were added successively a solution of the ketone **21** (412 mg, 2 mmol) in dry diethyl ether (10 cm^3) and a 1 mol dm^{-3} solution of MeLi (4 cm^3, 4 mmol) in diethyl ether, and the reaction mixture was warmed to room temp. after 1 h. After 30 min at room temp., the reaction mixture was worked up and chromatographed as above to afford the *exo* alcohol **26** (229 mg) and *endo* alcohol **25** (108 mg) (76% total yield, *exo*:*endo* ratio 68:32).

(b) *With excess of* Me_2CuLi.—To a stirred suspension of CuI (2.285 g, 12 mmol) in anhydrous diethyl ether (20 cm^3) at 0 °C under argon was added dropwise a 1 mol dm^{-3} solution of MeLi (24 cm^3, 24 mmol) in diethyl ether. After 5 min, a solution of the ketone **21** (618 mg, 3 mmol) in dry diethyl ether (10 cm^3) was added and the resultant mixture was brought to room temp. and stirred overnight. The reaction mixture was worked up and chromatographed as above. The first component was the *exo* alcohol **26** (107 mg) followed by the unchanged starting material **21** (371 mg, 60% recovered). The last component was the *endo* alcohol **25** (71 mg) (72% on the basis of consumed starting material, *exo*:*endo* ratio 60:40).

(c) *With* Me_3CuLi_2.—To a suspension of CuI (1.714 g, 9 mmol) in anhydrous diethyl ether (20 cm^3) at 0 °C under argon was added a 1 mol dm^{-3} solution of MeLi (27 cm^3, 27 mmol) in diethyl ether slowly over a period of 5 min. After the mixture had been stirred for 5 min, a solution of ketone **21** (618 mg, 3 mmol) in dry diethyl ether (10 cm^3) was added at the same temperature. The resultant mixture was left to warm to room temp. after 1 h and was stirred for a further 3 h. The reaction mixture was worked up and chromatographed as above to afford the *exo* alcohol **26** (359 mg) and the *endo* alcohol **25** (220 mg) (87% total yield, *exo*:*endo* ratio 62:38).

9-Methyltricyclo[7.2.1.0^{1,6}]dodec-6-en-8-one 27 and 8-methyltricyclo[6.3.1.0^{1,6}]dodec-6-en-9-one 28 (R = Me)

Reactions of various substrates with BF_3·OEt_2. (a) exo *Alcohol* **26** *at room temp.*—A solution of the *exo* alcohol **26** (1.11 g, 5 mmol) in dry benzene (35 cm^3) with BF_3·OEt_2 (cat.) was stirred at room temp. for 30 min. The reaction mixture showed two spots different from starting material on TLC. The reaction mixture was worked up with diethyl ether and the residue obtained was chromatographed. Elution with light petroleum–ethyl acetate (9:1) afforded the *ketone* **28** (R = Me) (700 mg), ν_{max}/cm^{-1} 1700; δ_H(90 MHz) 1.12 (3 H, s, Me), 1.20–2.64 (14 H, m) and 5.2 (1 H, d, *J* 2, olefinic); δ_C(22.5 MHz) 17.30 (q), 22.37 (t), 26.01 (t), 26.66 (t), 29.26 (t), 34.86 (t), 36.81 (t), 46.43 (s), 55.79 (t), 56.58 (s), 127.59 (d), 149.96 (s) and 211.60 (s) (Found: M$^+$, 190.1352. $C_{13}H_{18}O$ requires M, 190.1358).

Further elution with light petroleum–ethyl acetate (4:1) gave the *enone* **27** (174 mg, 92% total yield, ketone:enone ratio 4:1), ν_{max}/cm^{-1} 1677 and 1614; δ_H(90 MHz) 1.23 (3 H, s, Me), 1.36–1.96 (12 H, m), 2.4 (2 H, br, C-5) and 5.64 (1 H, br s, olefinic); δ_C(22.5 MHz) 19.32 (q), 22.32 (t), 24.27 (t), 30.38 (t), 34.54 (t, 2 × C), 35.97 (t), 47.16 (s), 50.93 (s), 52.62 (t), 122.20 (d), 169.41 (s) and 203.49 (s) (Found: M$^+$, 190.1370).

(b) endo *Alcohol* **25** *at room temp.*—When *endo* alcohol **25** (888 mg, 4 mmol) was subjected to the rearrangement in benzene (30 cm^3) as described above, there were obtained the ketone **28** (134 mg) and the enone **27** (553 mg, 88% total yield, ketone:enone ratio 1:4).

(c) exo *Alcohol* **26** *in refluxing benzene.*—A solution of the *exo* alcohol **26** (1.465 g, 6.6 mmol) in benzene (40 cm^3) with BF_3·OEt_2 (cat.) was refluxed for 16 h. The reaction mixture was worked up as above to afford the ketone **28** (276 mg) and the enone **27** (225 mg, ketone:enone ratio 11:9).

(d) *Ketone* **28** *in refluxing benzene.*—A mixture of the ketone **28** (1.90 g, 10 mmol), benzene (50 cm^3) and BF_3·OEt_2 (cat.) was refluxed. An aliquot was removed at different intervals of time and worked up as described above. After 10 h of reflux, the ratio of ketone **28** to enone **27** was 4:1, while the same was a 1:1 mixture after 24 h. After 68 h of reflux, the ratio of ketone to enone reached 1:19.

(e) *Ketone* **28** *in refluxing toluene.*—When the ketone **28** (444 mg, 2 mmol) was refluxed with BF_3·OEt_2 (cat.) for 7 h in toluene (20 cm^3) as above, there were obtained the ketone **28** (14 mg) and the enone **27** (336 mg) (92%, ketone:enone ratio 1:19).

7,7,9-Trimethyltricyclo[7.2.1.0^{1,6}]dodec-5-en-8-one 30

To a stirred slurry of KOBu^t in *tert*-butyl alcohol, prepared from potassium (1.17 g, 30 mmol) and dry *tert*-butyl alcohol (25 cm^3), was added a solution of the enone **27** (1.90 g, 10 mmol) in dry benzene (50 cm^3). After 30 min, MeI (6.22 cm^3, 0.1 mol) was added rapidly and the mixture was refluxed for 2 h. The reaction mixture was brought to room temp. and a further quantity of MeI (2 cm^3) was added. The resulting solution was stirred for 6 h and the usual work-up followed by chromatography afforded the *ketone* **30** (1.679 g, 77%), ν_{max}/cm^{-1} 1700; δ_H(60 MHz) 1.18 (3 H, s, Me), 1.22 (3 H, s, Me), 1.28 (3 H, s, Me), 1.40–2.40 (12 H, m) and 5.48 (1 H, t, *J* 4, olefinic); δ_C(22.5 MHz) 19.87 (t), 20.78 (t), 25.34 (t), 30.54 (q), 31.71 (q), 35.61 (t), 36.13 (q), 38.21 (t), 44.59 (s), 46.54 (s), 46.93 (t), 52.52 (s), 118.59 (d), 149.28 (s) and 218.21 (s) (Found: M$^+$, 218.1671. $C_{15}H_{22}O$ requires M, 218.1642).

8-Benzyloxy-7,7,9-trimethyltricyclo[7.2.1.0^{1,6}]dodec-5-ene 32

A 20% solution of DIBALH (13.2 cm^3, 12.25 mmol) in hexane was added to a solution of the ketone **30** (1.526 g, 7 mmol) in dry THF (50 cm^3) under Ar at −78 °C. After being stirred for 1 h, the reaction mixture was warmed to room temp. for 2 h. The resultant solution was quenched with MeOH (4 cm^3) and poured into saturated aq. sodium potassium tartrate (125 cm^3). The clear solution obtained was worked up, and this was followed by chromatography to afford the alcohol **31**, ν_{max}/cm^{-1} 3420; δ_H(60 MHz) 1.12 (3 H, s, Me), 1.14 (3 H, s, Me), 1.19 (3 H, s, Me), 1.20–2.12 (13 H, m), 3.22 (1 H, br d, C*H*OH, becomes singlet with D_2O) and 5.46 (1 H, t, *J* 3.6, olefinic).

A solution of the above alcohol **31** and benzyl bromide (0.83 cm^3, 7 mmol) in dry DME (20 cm^3) was added to a suspension of NaH (560 mg, 14 mmol) and TBAI (cat.) in dry DME (30 cm^3) at room temp. under argon. The reaction mixture was refluxed for 24 h followed by the usual work-up and chromatography (light petroleum) to yield the *ether* **32** as an oil (2.04 g, 94%), ν_{max}/cm^{-1} 1450; δ_H(60 MHz) 1.16 (3 H, s, Me), 1.20 (6 H, s, 2 × Me), 1.24–2.24 (12 H, m), 3.08 (1 H, s, 8-H), 4.72 (2 H, s, OCH_2Ph), 5.44 (1 H, t, *J* 3.6, olefinic) and 7.24–7.48 (5 H, m, Ph); δ_C(50 MHz) 20.64, 25.63, 26.19, 27.80, 30.29, 31.60, 37.49, 38.62, 41.40, 44.90, 46.33, 51.67, 76.44, 93.69, 116.85, 126.88 and 128.00 (5 × ArC), 139.45 and 151.77 (Found: M$^+$, 310.2283. $C_{22}H_{30}O$ requires M, 310.2297).

8-Benzyloxy-7,7,9-trimethyltricyclo[7.2.1.0^{1,6}]dodecan-5-one 33

To a stirred solution of the ether **32** (1.86 g, 6 mmol), in dry THF (50 cm^3) was added 0.6 mol dm^{-3} BH_3·THF (22.6 cm^3, 12 mmol) dropwise at 0 °C under argon. The resultant mixture was brought to room temp. and stirred for a further 5 h. The reaction mixture was quenched with water and was treated successively with 20% aq. NaOH (1.8 cm^3, 9 mmol) and 30% aq. H_2O_2 (1.4 cm^3, 18 mmol). After 3 h, the usual work-up and chromatography afforded the corresponding C-5 alcohol (1.614 g, 82%), ν_{max}/cm^{-1} 3440; δ_H(60 MHz) 1.10 (3 H, s, Me), 1.20 (3 H, s, Me), 1.32 (3 H, s, Me), 1.20–2.20 (14 H, m), 3.02 (1 H, s, 8-H), 3.80 (1 H, br, 5-H), 4.72 (2 H, s, OCH_2Ph) and 7.22–7.46 (5 H, m, Ph).

A mixture of the above alcohol (1.574 g, 4.8 mmol), PCC (1.293 g, 6 mmol) and silica gel (1.5 g) in dry CH_2Cl_2 (40 cm^3) was stirred at room temp. for 30 min. The solvent was removed, the resultant powder was dissolved in diethyl ether, and the solution was filtered through a pad of Celite. The filtrate was evaporated and the residue was purified by chromatography to afford the *ketone* **33** (1.471 g, 94%). An analytical sample was obtained by recrystallization in light petroleum, mp 78 °C; ν_{max}/cm^{-1} 1700; δ_H(60 MHz) 1.16 (3 H, s, Me), 1.28 (3 H, s, Me), 1.32 (3 H, s, Me), 1.30–2.40 (13 H, m), 2.96 (1 H, s, 8-H), 4.70 (2 H, s, OCH_2Ph) and 7.24–7.50 (5 H, m, Ph); δ_C(22.5 MHz) 16.26 (q), 22.63 (t), 24.97 (q), 31.73 (q), 32.90 (t), 33.42 (t), 38.76 (t), 39.67 (s), 43.05 (t), 46.04 (s), 48.90 (s), 55.01 (t), 65.16 (d), 76.60 (t), 93.90 (d), 127.07 and 128.11 (2 d, 5 × ArC), 139.29 (s) and 209.78 (s) (Found: C, 81.0; H, 9.5%; M$^+$, 326.2232. $C_{22}H_{30}O_2$ requires C, 80.9; H, 9.3%; M, 326.2245).

Methyl 4-benzyloxy-1-[2-(methoxycarbonyl)ethyl]-3,3,5-trimethylbicyclo[3.2.1]octane-2-carboxylate 35

To a stirred solution of the ketone **33** (1.467 g, 4.5 mmol) in ethyl alcohol (40 cm^3) at 0 °C under argon was added dropwise 20% aq. NaOH (0.9 cm^3, 4.5 mmol). After 30 min a solution of furfural (2-furaldehyde) (0.37 cm^3, 4.5 mmol) in ethyl alcohol (1 cm^3) was added, and the reaction mixture was warmed to room temp. After 7 h, the usual work-up gave the furfurylidene derivative **34** as a yellow solid which was used directly in the next step without purification.

A solution of compound **34** in ethyl acetate (50 cm^3) was ozonized at −78 °C until TLC indicated the disappearance of starting material. The solvent was evaporated off and the residue was treated with acetic acid (30 cm^3), 30% aq. H_2O_2 (10 cm^3) and dil. H_2SO_4 (0.5 cm^3). The mixture was stirred overnight and concentrated at 40 °C under reduced pressure.

The residue was dissolved in diethyl ether (300 cm^3), the solution was washed with brine, and the solvent was evaporated off to give the corresponding dicarboxylic acid.

A solution of the above acid in dry diethyl ether (100 cm^3) was esterified with ethereal diazomethane. The residue obtained after removal of the solvent was purified by chromatography to obtain the *diester* **35** (1.23 g, 68%), which was recrystallized from light petroleum, mp 63 °C; ν_{max}/cm^{-1} 1725; δ_H(60 MHz) 1.12 (3 H, s, Me), 1.16 (3 H, s, Me), 1.20 (3 H, s, Me), 1.20–2.60 (11 H, m), 3.06 (1 H, s, 4-H), 3.70 (3 H, s, CO_2Me), 3.72 (3 H, s, CO_2Me), 4.70 (2 H, s, OCH_2Ph) and 7.28–7.48 (5 H, m, Ph); δ_C(22.5 MHz) 19.45 (q), 25.41 (q), 30.06 (t), 31.26 (t), 31.91 (q), 33.75 (t, 2 × C), 39.17 (s), 46.21 (s), 46.64 (s), 50.33 (q), 50.76 (q), 51.52 (t), 59.54 (d), 76.76 (t), 93.01 (d), 127.14 and 128.23 (2 d, 5 × ArC), 139.06 (s), 172.87 (s) and 174.06 (s) (Found: C, 72.0; H, 8.7%; M^+, 402.2387. $C_{24}H_{34}O_5$ requires C, 71.6; H, 8.5%; M, 402.2406).

Methyl 7-benzyloxy-6,6,8-trimethyl-4-oxotricyclo[6.2.1.0^{1,5}]-undecane-3-carboxylate 36

To a solution of KOBu^t in *tert*-butyl alcohol [prepared from potassium (111 mg, 3 mmol) and dry *tert*-butyl alcohol (5 cm^3)] was added a solution of the diester **35** (1.005 g, 2.5 mmol) in dry benzene (50 cm^3) under argon. The reaction mixture was refluxed for 6 h and then added to aq. NH_4Cl. Work-up with ethyl acetate followed by chromatography afforded the β-*keto ester* **36** as an oil (722 mg, 78%), ν_{max}/cm^{-1} 1740 and 1720; δ_H(90 MHz) 1.20 (6 H, s, 2 × Me), 1.30 (3 H, s, Me), 1.32–2.44 (9 H, m), 3.04 (1 H, s, 7-H), 3.26 (1 H, dd, *J* 9 and 10.8, 3-H), 3.76 (3 H, s, CO_2Me), 4.70 (2 H, s, OCH_2Ph) and 7.28–7.48 (5 H, m, Ph); δ_C(22.5 MHz) 15.97 (q), 24.94 (q), 30.80 (q), 32.75 (t), 33.01 (t), 35.48 (t), 38.60 (s), 44.58 (s), 47.06 (s), 50.70 (d), 52.26 (q), 54.99 (d), 66.57 (d), 76.71 (t), 93.61 (d), 127.04 and 128.08 (2 d, 5 × ArC), 139.01 (s), 169.76 (s) and 208.33 (s) (Found: C, 74.6; H, 8.35. $C_{23}H_{30}O_4$ requires C, 74.7; H, 8.2%).

7-Benzyloxy-2,6,6,8-tetramethyltricyclo[6.2.1.0^{1,5}]undecan-4-one 38

A solution of the β-keto ester **36** (370 mg, 1 mmol) in dry THF (3 cm^3) was added to a stirred suspension of NaH (44 mg, 1.1 mmol) in dry THF (7 cm^3) over a period of 10 min at 0 °C under argon. After 15 min, PhSeCl (211 mg, 1.1 mmol) in THF (3 cm^3) was added rapidly. The reaction mixture was poured into a mixture of diethyl ether (50 cm^3) and saturated aq. $NaHCO_3$ (50 cm^3), and worked up as usual to obtain the selenide.

To a stirred solution of the above crude selenide in CH_2Cl_2 (8 cm^3) was added 30% aq. H_2O_2 (0.22 cm^3, 1.95 mmol) dropwise at 5 °C. After 10 min, the reaction mixture was diluted with CH_2Cl_2, washed with water and dried to give a residue, which was chromatographed to afford the corresponding unsaturated keto ester as an unstable oil (331 mg, 90%), ν_{max}/cm^{-1} 1719.

A solution of the above unsaturated keto ester (331 mg, 0.9 mmol) in dry diethyl ether (10 cm^3) was added to a solution of Me_2CuLi [prepared by the addition of a 1 mol dm^{-3} solution of MeLi (1.8 cm^3, 1.8 mmol) in diethyl ether into a suspension of CuI (171 mg, 0.9 mmol) in dry diethyl ether (10 cm^3) at 0 °C] under argon at −100 °C. The reaction mixture was stirred for 30 min and quenched with aq. NH_4Cl. The usual work-up followed by chromatography yielded the β-keto ester **37** as an oil (304 mg, 88%), ν_{max}/cm^{-1} 1725; δ_H(200 MHz) 1.00 (3 H, d, *J* 7, 2-Me), 1.12–2.48 (20 H, m), 2.95–3.01 and 3.38–3.42 (2 H, m), 3.71 and 3.73 (3 H, 2 s, CO_2Me), 4.68 (2 H, br, OCH_2Ph) and 7.26–7.40 (5 H, m, Ph).

A mixture of the β-keto ester **37** (288 mg, 0.75 mmol), DABCO (841 mg, 7.5 mmol) and *o*-xylene (5 cm^3) was heated to 85 °C under argon for 7 h. The reaction mixture was acidified with 0.5 mol dm^{-3} HCl and worked up to obtain the *ketone* **38** (200 mg, 82%) after chromatography. An analytical sample was obtained by recrystallization from light petroleum, mp 116 °C; ν_{max}/cm^{-1} 1735; δ_H(90 MHz) 0.96 (3 H, d, *J* 7.2, 2-Me), 1.10 (6 H, s, 2 × Me), 1.24 (3 H, s, Me), 1.28–2.60 (10 H, m), 2.92 (1 H, s, 7-H), 4.60 (2 H, s, OCH_2Ph) and 7.26 (5 H, br s, Ph); δ_C(75 MHz) 16.26, 17.57, 25.07, 30.67, 33.41, 35.18, 35.88, 38.22, 46.40, 47.59 (2 × C), 52.13, 61.03, 76.54, 93.81, 126.98 and 128.04 (5 × ArC), 139.06 and 216.57 (Found: C, 80.65; H, 9.2. $C_{22}H_{30}O_2$ requires C, 80.9; H, 9.3%).

7-Benzyloxy-2,6,6,8-tetramethyltricyclo[6.2.1.0^{1,5}]undecane 40

A 20% solution of DIBALH in hexane (1.08 cm^3, 1 mmol) was added to a stirred mixture of ketone **38** (163 mg, 0.50 mmol) in dry THF (6 cm^3) under argon at −78 °C. After 1 h, a further quantity of DIBALH (1.08 cm^3, 1 mmol) was added and the mixture was stirred for a further 1 h before being warmed to room temp. for another 1 h. The mixture was worked up as for the compound **31** and chromatography afforded the alcohol **39** (148 mg, 90%), ν_{max}/cm^{-1} 3442; δ_H(90 MHz) 0.92 (3 H, d, *J* 7, 2-Me), 1.20 (6 H, s, 2 × Me), 1.36 (3 H, s, Me), 1.36–2.60 (10 H, m), 3.00 (1 H, br, 7-H), 4.40 (1 H, t, *J* 3.6, 4-H), 4.70 (2 H, br, OCH_2Ph) and 7.26–7.48 (5 H, m, Ph); δ_C(22.5 MHz) 18.5, 19.0, 26.0, 30.5, 34.0, 37.5, 38.0, 40.5, 46.0, 48.0, 50.0, 52.0, 60.8, 73.5, 76.5, 94.0, 127.0 and 128.0 (5 × ArC) and 139.5.

To a suspension of NaH (64 mg, 1.6 mmol) and imidazole (cat.) in dry THF (3 cm^3) was added a solution of the alcohol **39** (131 mg, 0.4 mmol) in dry THF (2 cm^3) under argon, and the mixture was refluxed for 2 h. It was then cooled, a solution of CS_2 (0.24 cm^3, 4 mmol) in THF (1 cm^3) was added, and reflux was resumed for a further 45 min. The reaction mixture was cooled, a solution of MeI (0.25 cm^3, 4 mmol) in THF (1 cm^3) was added, and the mixture was refluxed for 30 min. After the usual work-up, the residue obtained upon filtration through a column of silica gel (light petroleum) was worked up to yield the corresponding xanthate as a yellow oil (157 mg, 94%).

A mixture of the above xanthate (154 mg, 0.37 mmol) and azoisobutyronitrile (AIBN) (cat.) in dry toluene (2 cm^3) was added to a refluxing solution of TBTH (0.20 cm^3, 0.74 mmol) in toluene (5 cm^3) under argon. After 6 h, a further quantity of TBTH (0.20 cm^3, 0.74 mmol) with AIBN (cat.) in toluene (1 cm^3) was added during reflux. Reflux was continued for an additional 5 h and all volatiles were then removed under reduced pressure. The residue obtained upon chromatography on neutral alumina (light petroleum) yielded the *benzyl ether* **40** (108 mg, 94%), ν_{max}/cm^{-1} 1452; δ_H(200 MHz) 0.86 (3 H, d, *J* 7, 2-Me), 1.01 (3 H, s, Me), 1.05 (3 H, s, Me), 1.13 (3 H, s, Me), 1.07–2.00 (12 H, m), 3.03 (1 H, s, 7-H), 4.68 (2 H, dd, OCH_2Ph) and 7.26–7.41 (5 H, m, Ph); δ_C(100 MHz) 17.48, 19.83, 23.01, 25.65, 30.38, 32.15, 34.32, 34.83, 38.90, 40.36, 47.35, 47.92, 53.67, 54.10, 76.53, 94.44, 127.11, 127.19, 128.17 (5 × ArC) and 139.71 (Found: C, 84.6; H, 10.4. $C_{22}H_{32}O$ requires C, 84.6; H, 10.3%).

2,6,6,8-Tetramethyltricyclo[6.2.1.0^{1,5}]undecan-7-ol 1

A solution of the benzyl ether **40** (94 mg, 0.3 mmol) in absolute ethyl alcohol (6 cm^3) was stirred with 10% Pd/C (10 mg) under H_2. After 2 h, the reaction mixture was worked up as for compound **19** to give the alcohol **1** (63 mg, 94%), ν_{max}/cm^{-1} 3440; δ_H(200 MHz) 0.85 (3 H, d, *J* 7.1, 2-Me), 0.91 (3 H, s, Me), 1.03 (3 H, s, Me), 1.06 (3 H, s, Me), 1.11–1.92 (13 H, m) and 3.18 (1 H, s, 7-H); δ_C(100 MHz) 16.22, 19.82, 23.31, 24.98, 29.29, 32.22, 33.59, 34.74, 37.85, 40.43, 46.25, 47.79, 53.71, 54.14 and 85.41.

2,6,6,8-Tetramethyltricyclo[6.2.1.0^{1,5}]undecan-7-one 2

A mixture of the alcohol **1** (44 mg, 0.2 mmol), PDC (150 mg, 0.4 mmol) and silica gel (200 mg) in dry CH_2Cl_2 (5 cm^3) was

stirred for 2 h. The reaction mixture was worked up as for compound **33** to obtain the ketone **2** (41 mg, 93%), ν_{max}/cm^{-1} 1698; δ_H(200 MHz) 0.90 (3 H, d, *J* 7.2, 2-Me), 1.10 (6 H, s), 1.13 (3 H, s) and 1.16–2.15 (12 H, m); δ_C(75 MHz) 19.62, 21.49, 22.64, 24.46, 29.17, 31.39, 33.22, 35.00, 40.06, 45.04, 45.41, 53.19, 53.71, 54.01 and 219.64.

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