Cascade radical mediated macrocyclisation–transannulation reactions leading to ring-fused bicycles

Gerald Pattenden,*,[a] Allison J. Smithies,[a] David Tapolczay[b] and Daryl S. Walter[a]

[a] *Department of Chemistry, Nottingham University, Nottingham NG7 2RD, UK*

[b] *Glaxo Research and Development Ltd, Stevenage, Herts SG1 2NY, UK*

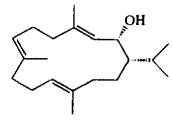
The scope for tandem radical mediated macrocyclisation–transannulation processes in the elaboration of ring-fused carbocycles has been examined. Thus, a range of *E*-iodo dienones *viz.* 21, 30b, 40, 42 and 44 were first prepared using synthetic sequences based on sound literature precedent. Treatment of the iodo dienone 21 with Bu_3SnH–AIBN led to a 3:2 mixture of *trans*-and *cis*-isomers of 1-decalone, 35 and 36, respectively, in a combined yield of 72%, whereas the positional isomer 30b of 21 underwent 10-*endo* macrocyclisation and transannulation to a 1:1 mixture of *trans*-1-decalone 35 and *cis*-octahydroazulen-1-one 39 (combined yield 68%), resulting from competitive 6-*exo*/5-*exo* transannular cyclisation from the intermediate cyclodecenone radical 38.

In further investigations of the scope for sequential radical macrocyclisation–transannulations in the synthesis of bicyclic systems, the iodo dienone 40 was found to undergo regioselective cyclisation to the *cis*-tetralone 41 (50%), whereas the iodo dienone 42 produced only (*Z*)-cyclooct-3-enone 54 and none of the expected bicyclo[3.3.0]octanone 43 on treatment with Bu_3SnH–AIBN. Only the 4-cyclopentylcyclohexanone 61, and none of the hoped for 7,6-bicyclic ketone 45, was produced from radical cyclisation of the iodo dienone 44.

The differing reaction pathways followed by the iodo dienones 21, 30b, 40 and 42 have been rationalised in terms of the conformational preferences of the macrocyclic α-keto radical intermediates, *e.g.* 32, 38 and 52 involved in the various cyclisations supported by some preliminary MM2 studies and calculations.

Free radical reactions have played a dominant and determining role in the development of synthetic organic chemistry during the past 2 decades.[1] Nowhere has this been seen more strikingly than in their applications to ring constructions. Carbon-centred radical additions to carbon-to-carbon multiple bonds, particularly when they are effected in an intramolecular and tandem (cascade, domino, sequential) fashion, have led to many beautiful, and sometimes quite esoteric, syntheses of a whole range of carbon and heteropolycyclic ring structures.[1] Examples of the scope of these powerful methods abound in the contemporary literature. In earlier investigations, from our own laboratory, we have developed facile syntheses of macrocyclic natural products, *e.g.* cembrenes **1**[2] and zearalenone **2**,[3] based on intramolecular *endo*-additions of allylic radical centres to electron-deficient alkenes. We have also illustrated the scope for the carbon-to-cobalt bond in triggering cascade ring forming reactions,[4] and in an approach to the β-lactam thienamycin **3**.[5] In other studies, we have highlighted the use of intramolecular *endo*-cyclisations from unsaturated acyl radicals in the construction of furan-cembrane structures, *e.g.* lophotoxin **4**,[6] and described an approach to the taxane ring system found in taxol **5** using a 12-*endo* macrocyclisation in tandem with a 8-*endo*/6-*exo* radical transannulation process.[7] The elaboration of ring-fused carbocycles based on tandem radical cyclisation processes and/or radical macrocyclisation–transannular processes (Scheme 1) would seem to offer a unique opportunity for the rapid, stereocontrolled synthesis of a wide range of highly functionalised polycyclic natural products, *e.g.* diterpenes, steroids and alkaloids, under mild conditions.

Nature, of course, elaborates polycyclic terpenes and steroids by way of a beautifully controlled series of enzymic reactions triggered by carbonium ion intermediate formation, *e.g.* farnesyl pyrophosphate **6** to pentalenene **8** *via* humulene **7**, and squalene epoxide **9** to progesterone **11** *via* intermediate **10**



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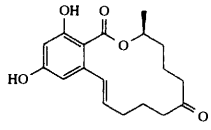

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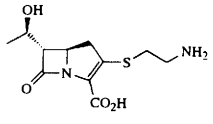

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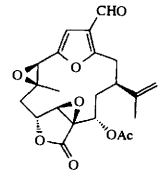

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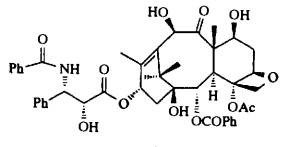

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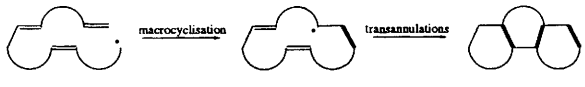
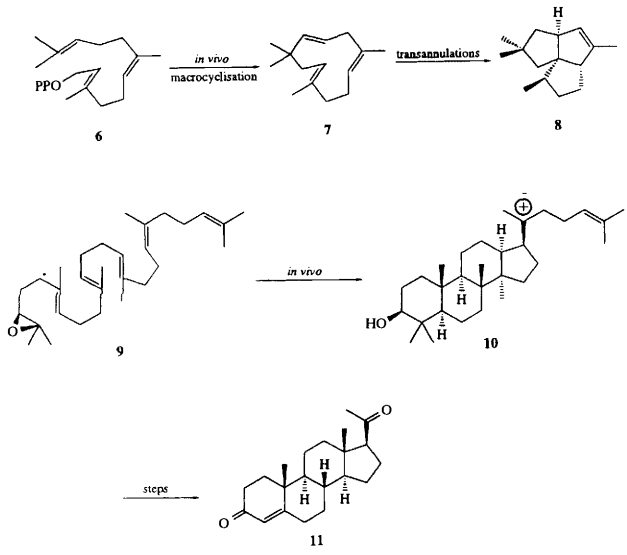


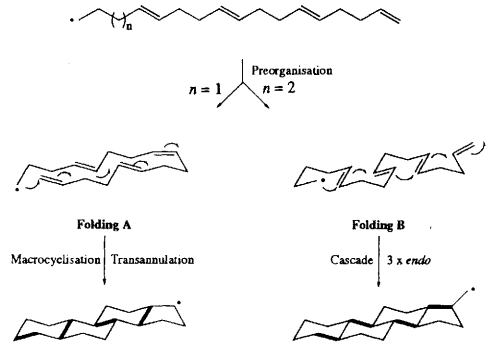
Scheme 1



Scheme 2

(Scheme 2).[8] Many of these carbonium ion initiated transformations can be mimicked in the laboratory, *e.g.* Johnson's biomimetic synthesis of steroidal compounds[9] and our own synthesis of (±)-pentalenene.[10]

Among other questions we have put to ourselves are the following. Can we use radical intermediates and mimic the polycycle constructions found in nature? Is it possible to take a polyene-based radical system–preorganise the chain and 'discipline'† any radical cyclisation to elaborate polycycles either *via* a macrocyclisation–transannulation manifold (folding A) or by sequential *endo*-cyclisations (folding B) (see Scheme 3).

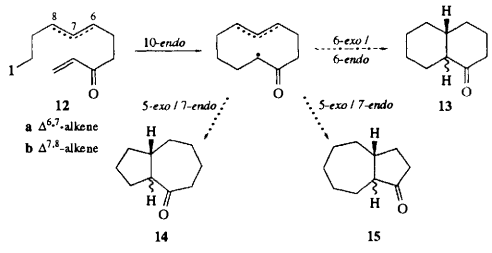


Scheme 3

Is it possible to engineer syntheses of polycycles using radical intermediates in a manner similar to the way nature does *via* carbocation intermediates? Of course we are referring to the selectivity of certain radicals for certain double bonds and, in the case of folding B protocol, we are going against some of the principles (*i.e.* 6-*endo*-*vs*-5-*exo*) of ring closure enunciated by Baldwin,[12] and Beckwith[13] and by others.

In the present series of papers we have collected together our earliest results in investigating and probing the scope for the two strategies, summarised in Scheme 3 towards polycycle constructions. Thus, in this paper we summarise the scope for tandem radical macrocyclisation–transannulation reactions (folding A) as a strategy in the synthesis of linear 5,5-, 5,6-, 5,7- and 6,6- ring fused carbocycles.[14] In the immediately accompanying paper we show how this overall strategy can be extended to the elaboration of tricyclic molecules from appropriate triene alkyl radical precursors.[15] Finally, in papers three and four of this series we show how serial *endo- endo* cyclisations (folding B, Scheme 3) initiated from *acyl* radical intermediates can be applied in the facile synthesis of linear and angular fused 6,6- systems, including steroid constructions.[16]

We began our investigations by first examining the tandem macrocyclisation–transannulation sequences involving the radical intermediates produced from the isomeric iodo dienones **12a** and **12b**. We selected these substrates for our initial studies since, in principle, either diene could lead to decalone **13** or to octahydroazulenone products **14**/**15** (Scheme 4), whose

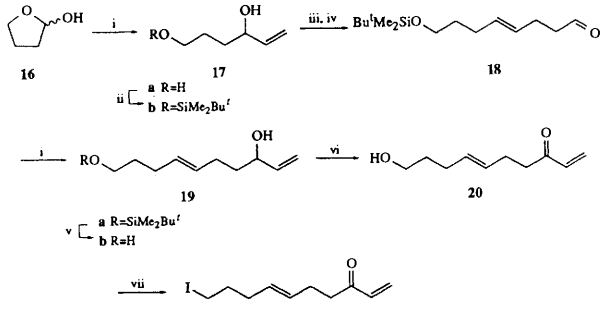


Scheme 4

structures and stereochemistries were well established in the literature.[17]‡ In addition, transannulation reactions from cyclodecadiene rings, under electrophilic conditions, are well documented, and comparisons could be made.[19]

Our earlier work,[1,2,20] based firmly on the principles established by Porter and his colleagues,[21] had demonstrated the need for an electron-deficient alkene electrophore, *e.g.* conjugated enone, to promote macrocyclisations with nucleophilic carbon centres, and the iodides **12a** and **12b** (rather than the corresponding bromides) were selected because of their enhanced reactivity.

The (*E*)-iodo dienone **12a** (≡ **21**) was synthesised as summarised in Scheme 5. Thus, addition of vinylmagnesium



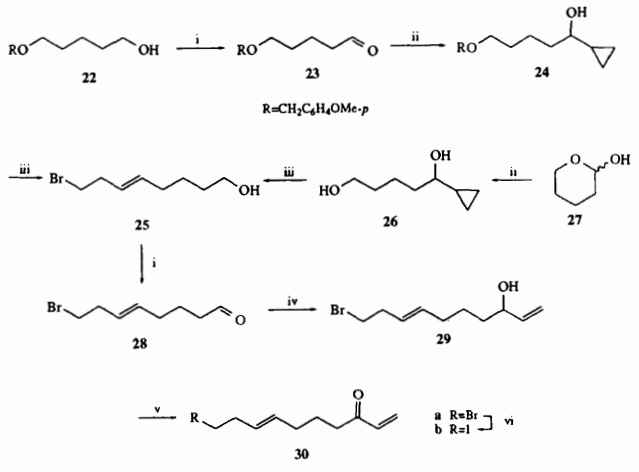
Scheme 5 *Reagents and conditions:* i, CH_2=CHMgCl, THF, 0 °C; ii, Bu^tMe_2SiCl, Im; iii, $Hg(OCOCF_3)_2$, CH_2=CHOEt; iv, heat, C_6H_6; v, TBAF, THF, 0 °C; vi, MnO_2, CH_2Cl_2, 25 °C; vii, $Me(PhO)_3P^+I^-$, DMF, 25 °C

chloride to the γ-butyrolactol **16**[22] followed by selective protection of the primary alcohol group in the resulting bis alcohol **17a** as its TBDMS (Bu^tMe_2Si) ether, first led to the allylic alcohol **17b**. A Claisen rearrangement[23] next converted the allylic alcohol **17b** into the *E*-unsaturated aldehyde **18** which was then elaborated to the secondary alcohol **19a** by a further reaction with vinylmagnesium chloride. After deprotection of the primary alcohol group in **19a**, the resulting diol **19b** was oxidised to the dienone **20** using MnO_2, which, after treatment with methyl(triphenyloxy)phosphonium iodide[24] gave rise to the target iodo dienone **21**.

The positional isomer of **21**, *i.e.* **30b**, was synthesised from

† The use of the word 'discipline' in association with the selectivities of free radical reactions, is attributed to D. H. R. Barton, and is much used by him in his many publications and presentations in this area of research.[11]

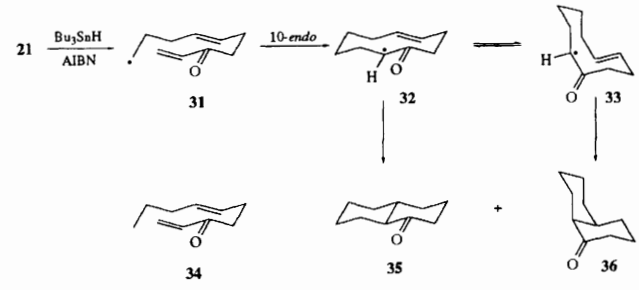
‡ *cis*-Perhydroazulene, δ_C(67.8 MHz, $CDCl_3$) 24.4 (t), 25.4 (t), 26.2 (t), 27.7 (t), 32.5 (t), 35.32 (t), 40.4 (d), 43.2 (t), 54.6 (d) and 212.5 (s).[18]



Scheme 6 *Reagents and conditions:* i, DMSO, $(COCl)_2$, Et_3N; ii, cyclopropylMgBr, Et_2O, 25 °C; iii, $MgBr_2$–$ZnBr_2$; iv, CH_2=CHMgCl, THF, 0 °C; v, MnO_2, CH_2Cl_2, 25 °C; vi, NaI, Me_2CO

pentane-1,5-diol or from δ-valerolactol **27** according to Scheme 6. Thus, addition of cyclopropylmagnesium bromide to the aldehyde **23** produced from oxidation of the mono-4-methoxybenzyl ether **22** of pentane-1,5-diol, first produced the cyclopropylmethanol **24** as a colourless oil (81%). Treatment of **24** with $ZnBr_2$ and $MgBr_2$[25] effected simultaneous ring opening of the cyclopropane ring in **24** and deprotection of the benzyl ether, leading to the (*E*)-bromo alcohol **25**. A less circuitous route to the bromo alcohol **25** involved addition of cyclopropylmagnesium bromide to δ-valerolactol **27**, producing **26**, which was then elaborated to **25** following treatment with $MgBr_2$–$ZnBr_2$. Oxidation of **25** using Swern conditions, followed by treatment of the resulting aldehyde **28** with vinylmagnesium chloride next led to the allylic alcohol **29**. Further oxidation, using MnO_2, then converted the alcohol **29** into the corresponding enone **30a**, which was smoothly transformed into the iodide **30b** under Finkelstein conditions.

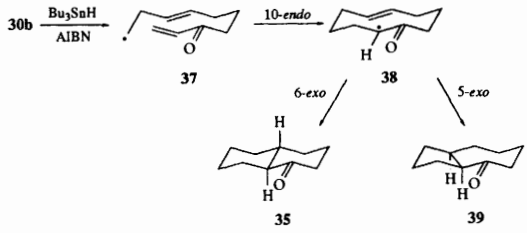
When a 3 mmol dm^{-3} solution of the iodo dienone **21** in dry degassed benzene was heated in the presence of 1.1 equiv. of Bu_3SnH and a catalytic amount of azoisobutyronitrile (AIBN) for 0.5 h, work-up and chromatography, gave a 3:2 mixture of *trans*- and *cis*-isomers of 1-decalone, **35** and **36**, respectively, in a combined yield of 72% (Scheme 7). The formation of **35** and



Scheme 7

36 was accompanied by the product **34** (*ca.* 10%) of reduction of the starting material, but we obtained no evidence for the co-formation of any cyclodec-4-enone, resulting from H-quenching at the macrocyclisation step in the reaction, or to alternative bicyclic products, *e.g.* octahydroazulenones, produced by competitive transannular cyclisations. Treatment of the 3:2 mixture of *trans*- and *cis*-1-decalones **35** and **36** with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) at room temperature for 24 h, resulted in epimerisation at the ring junction centre α- to the carbonyl function, and allowed the isolation of pure *trans*-1-decalone in essentially quantitative yield. The *cis*- and *trans*-1-decalones **35**/**36** produced in this work exhibited NMR spectroscopic data which were identical with those described in the literature.[17]

We next examined the reaction between Bu_3SnH–AIBN and the positional isomer **30b** of the iodo dienone **21**. To our initial surprise, this macrocyclisation–transannulation sequence led to a 1:1 mixture of *trans*-1-decalone **35** and *cis*-octahydroazulen-1-one **39**, in a combined yield of 68%, resulting from competitive 6-*exo*/5-*exo* transannular cyclisation from the intermediate cyclodec-5-enone radical **38** (Scheme 8). The bicyclic ketones **35** and **39** were separated by

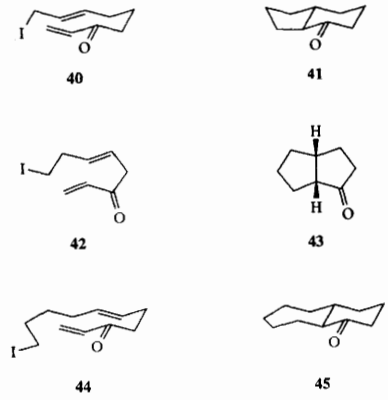


Scheme 8

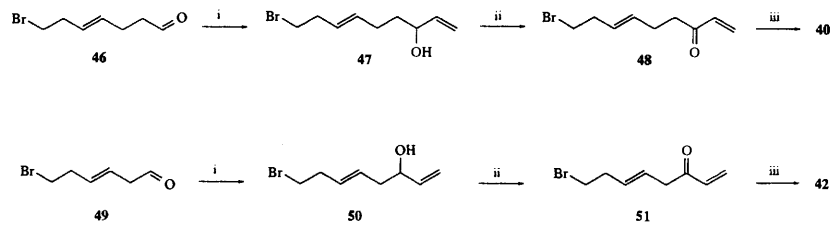
chromatography, and each displayed spectroscopic data which were identical with those described in the literature.[18]

The differing reaction pathways followed by the radicals **31** and **37** produced from the iodo dienones **21** and **30b**, respectively, is interesting and they most likely have their origins in the conformational preferences of the 10-membered α-keto radical intermediates, *viz.* **32** and **38**, involved in the two cyclisations (Schemes 7 and 8). Thus, the α-keto radical **32** derived from **31**, located in a chair-chair 10-membered intermediate would be expected to cyclise in an 6-*endo*/*exo* fashion leading to the *trans*-decalone **35**, whereas the same radical in a chair-boat-chair conformation, *viz.* **33**, would be expected to cyclise to the corresponding *cis*-decalone **36** (Scheme 7). In neither of the conformations **32** and **33** should it be possible for the α-keto radical intermediate to undergo competing 5-*exo* cyclisations, and indeed no octahydroazulen-1-one product was observed from the tandem cyclisation of **21**.

By contrast to the regioselective 6-*endo*/*exo* transannular cyclisation observed for the α-keto radical **32**/**33**, transannular cyclisation from the α-keto radical intermediate **38**, in the lowest energy chair-chair 10-ring conformation should be facile in either a 5-*exo* or a 6-*exo* sense, with the opportunity of producing either a *cis*-7,5- or a *trans*-6,6-bicyclic product, as indeed we observe, *viz.* **39** and **35**.

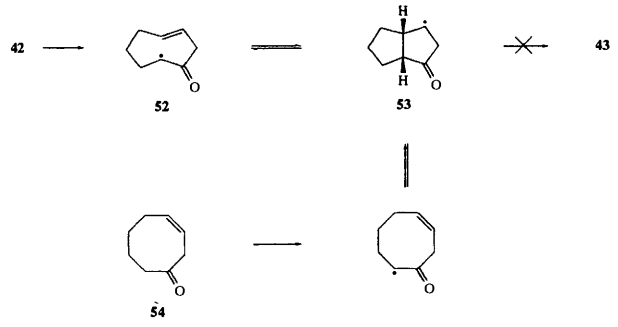


The above rationale for the differing reaction pathways followed by **21** and **30b**, is simplistic and crude in its conception. Accordingly, we have carried out some preliminary MM2 studies relating to these and to other radical macrocyclisation–transannulation reactions. Before these MM2 studies are discussed, however, it would be appropriate to summarise the additional radical reactions we have examined with the iodo dienones **40**, **42** and **44**, designed to access the linear bicyclic



Scheme 9 *Reagents and conditions:* i, CH_2=CHMgCl, THF, 0 °C; ii, periodinane, CH_2Cl_2, 25 °C; iii, NaI, Me_2CO, reflux

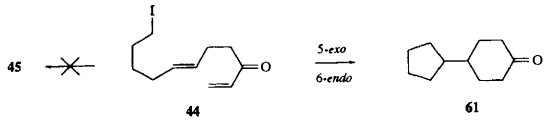
systems **41**, **43** and **45** respectively *via* our macrocyclisation–transannulation protocol. Thus, each of the iodo dienones **40**, **42** and **44** was first prepared, using sequences similar to those used earlier for the synthesis of the analogues **21** and **30b**. These procedures are summarised in Schemes 9 and 11.



Scheme 10

It was instructive to find that although the iodononadienone **40** underwent tandem 9-*endo*-5-*exo* cyclisation producing the *cis*-tetralone **41** in reasonable yield (~ 50%),[26] the corresponding (*E*)-iodooctadienone **42** on treatment with Bu_3SnH–AIBN led only to the (*Z*)-cyclooctenone **54** (40%),§ together with recovered starting material. None of the expected bicyclo[3.3.0]octanone **43** was obtained amongst the reaction products. The isolation of only (*Z*)-cyclooct-3-enone **54** from cyclisation of the *E*-dienone **42** was somewhat surprising, and interesting for a number of reasons. Thus, the outcome either indicates that the transannulation step in this reaction *viz.* **52**→**53** is reversible, or (more likely) that the transannulation does not occur at all, and **54**[27] is produced from **52** [or (*E*)-cyclooct-3-enone], by reversible addition of $Bu_3\dot{S}n$ to the *E*-disubstituted double bond (Scheme 10).

The result of treatment of the iodo dienone **44** with Bu_3SnH–AIBN was interesting since it leads only to 4-cyclopentylcyclohexanone **61** in quantitative yield. None of the hoped for 7,6-bicyclic ketone **45** resulting from sequential 11-*endo*, 6-*exo* cyclisation was produced in this reaction (Scheme 12). This observation reflects once again, the dominance of, and

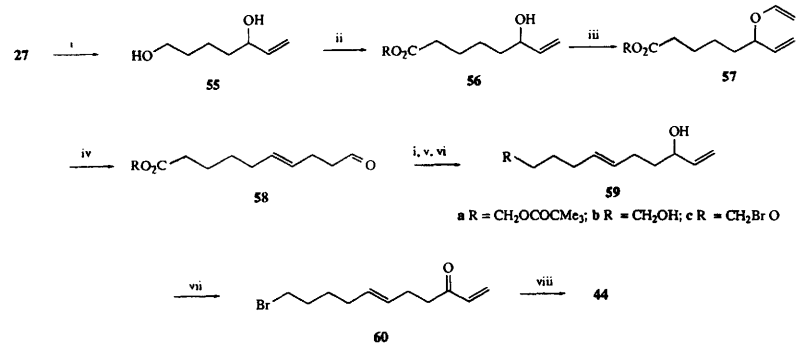


Scheme 12

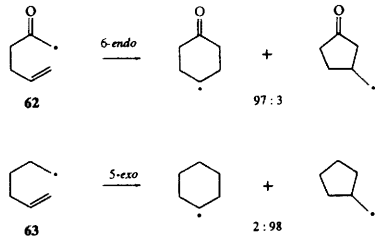
propensity for, hexenyl radicals to undergo 5-*exo*-trigonal cyclisation at the expense of all other modes of cyclisation when given half a chance.

We now return to some preliminary MM2 studies we have carried out relating to the aforementioned macrocyclisation–transannulation reactions. In early investigations, both Beckwith[28] and Houk[29] have independently used different *ab initio* techniques to derive geometrical parameters, for use with Allinger's MM2 force-field,[30] to model radical additions to alkenes by means of molecular mechanics. In our studies, we have made use of the MM2 modifications suggested by Houk and as implemented in the macromodel (version 4.0) program developed by W. C. Still.[31] This method works well for straightforward radical additions to alkenes, and our simple preliminary calculations showed good agreement with published data.[28,29] Furthermore, Houk has published further parameters which constitute a useful MM2 model for the intramolecular additions of α-keto radicals to alkenes.[32] Thus, this latter model, for example, effectively accounts for the 6-*endo*-regioselectivity observed in the cyclisation of the 2-oxohex-5-enyl radical **62**, which is of course opposite to the predominantly 5-*exo* selectivity found in cyclisation of the corresponding hex-5-enyl radical **63** (Scheme 13).[33] The reversal of selectivity in these two reactions is attributed to the energetic constraints on transition-state geometries imposed by limited rotation about the bond between the radical centre and the carbonyl group in the case of the 2-oxohex-5-enyl radical. Thus, Houk's re-parameterised MM2 force-field[32] incorporates an appropriate torsional energy barrier which reflects this delocalisation of the radical species in question. In an attempt to mimic this feature in the Macromodel program we have modelled α-keto-substituted radicals using the parameters for alkyl radicals,[29,31] but imposed the geometric constraint of Ø = 0° (see Fig. 1) to simulate the desired radical. This method showed good qualitative, and reasonable quantitative, agreement with Houk's calculations,[32] and Fig. 1 illustrates the results obtained for cyclisation of the 2-oxohex-5-enyl radical.

§ When stored, the β,γ-enone **54** was found to isomerise largely to the corresponding α,β-cyclooctenone.



Scheme 11 *Reagents and conditions:* i, CH_2=CHMgCl, THF, 0 °C; ii, Me_3CCOCl, py, 0 °C; iii, $Hg(OCOCF_3)_2$, CH_2=CHOEt; iv, heat, C_6H_6; v, DIBAL, −78 °C; vi, NBS, PPh_3; vii, periodinane; viii, NaI, Me_2CO



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Scheme 13

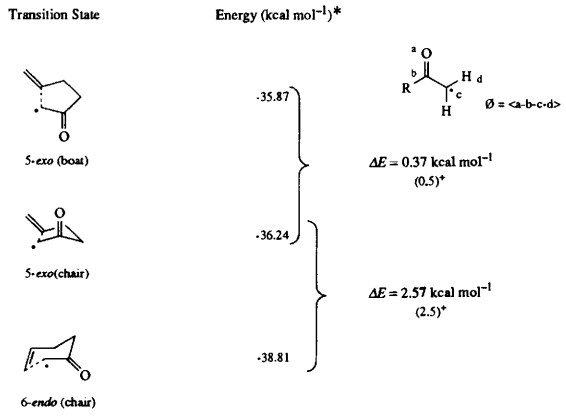


Fig. 1 Transition state energies for cyclisation of the 2-oxohex-5-enyl radical. * The sign and absolute values shown should not be construed as being particularly meaningful. The relative energies are more important. † The values in parentheses refer to the values of ΔE reported by Houk.[32]

The low-energy conformers were established using Monte–Carlo methods and the PRCG minimisation algorithm.

It should be noted that although good agreement was observed in these simple systems, Houk has found that the value of the torsional restraint imposed was crucial to obtaining a good fit with the experimental data. Consequently, although our simpler model is probably qualitatively sound, this factor should be borne in mind when considering apparently small energy differences, or in cases where such constraints would illicit an unreasonable energy penalty. Additionally, one should remember that the assumptions made in this modelling study do not necessarily apply to all the systems examined.

In our work, as well as attempting to determine favoured modes of cyclisation in radical sequential macrocyclisation–transannulation reactions, we also hoped to use the experimental results in tandem with calculations to construct guidelines as to the likelihood of success in a given reaction system. Accordingly, we carried out energy calculations for the transition states in each of the transannulation reactions leading from the iodo dienones **21**, **30b** and **42** to the bicyclic ketones **35**, **39** and **41**, respectively. In all these cases, the energy values for the corresponding initial macrocyclisations were found to be sufficiently low and do not warrant further discussion here.

We first examined the system **42**→**52**→**53** which failed to yield the desired bicyclic ketone **43**, and instead gave only the (*Z*)-cyclooctenone **54**. The transition state energy for the 5-*exo* transannulation in this reaction was found to be relatively high (E^* = −8.71 kcal mol^{-1}), and by analogy to the values we obtained for the system **64** described by Porter *et al.* (*i.e.* 6-*endo* −6.13; 5-*exo* −13.1 kcal mol^{-1})[21b] which also failed to cyclise (*cf.* systems **65** and **66**), we would expect that formation of the bicycle **43** would be highly disfavoured, as observed in the laboratory.

In the case of cyclisation of the iodo dienone **40** to the *cis*-tetralone **41**, the 5-*exo* transannular cyclisation is clearly kinetically preferred and, also quite a favourable process (see

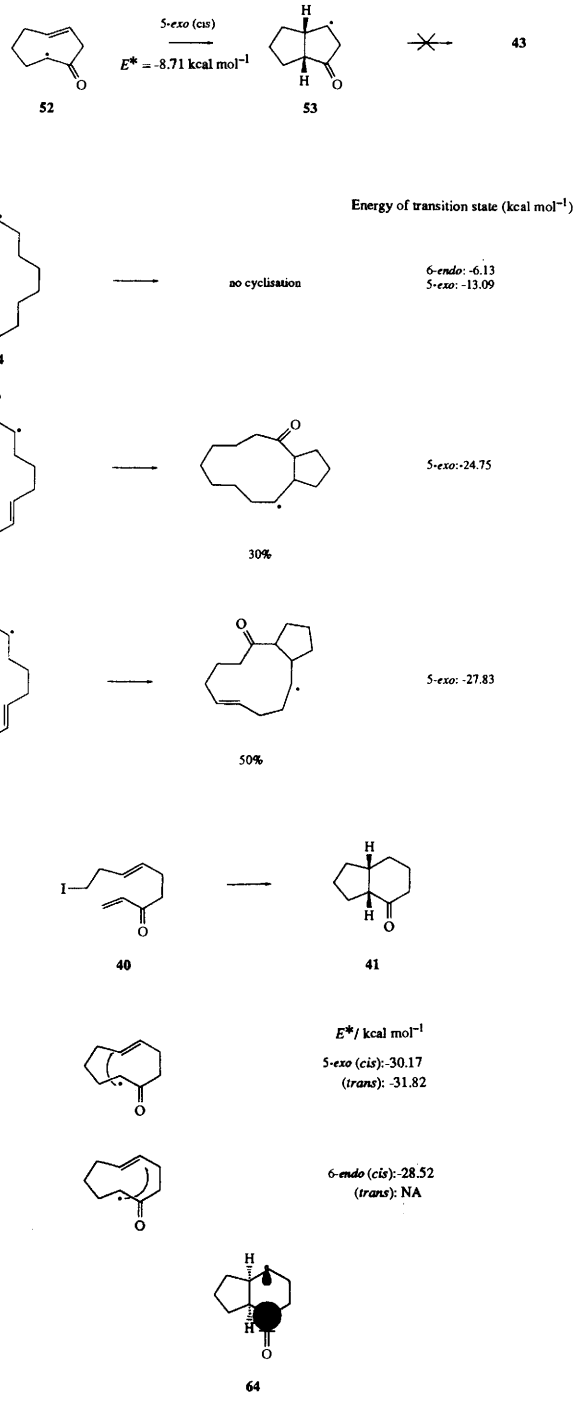


Fig. 2

E^* values on Fig. 2). The fact that only the *cis*-tetralone is isolated is more difficult to rationalise. The transition-state energy values cannot account for this outcome (in fact the *trans*-product would be preferred) and the energy difference (0.38 kcal mol^{-1}) between the two bicyclic radical products is insufficient to favour the single product thermodynamically. However, the *cisoid* transition-state in the transannulation could conceivably accommodate overlap between the developing product radical centre and the LUMO of the carbonyl group (see diagram **64** Fig. 2). Such an interaction could lower the energy of the transition-state and hence favour the formation of the product observed. Although molecular mechanics calculations cannot quantify such effects, preliminary semi-empirical calculations (AM1 as implemented in the Spartan program[34]) seem to support this line of reasoning.

The calculated values obtained for the formation of the 1-decalones **35** and **36** from cyclisation of the iodo dienone **21**

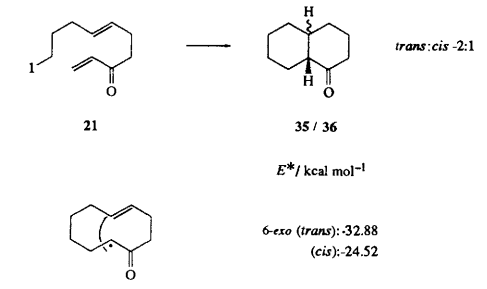


Fig. 3

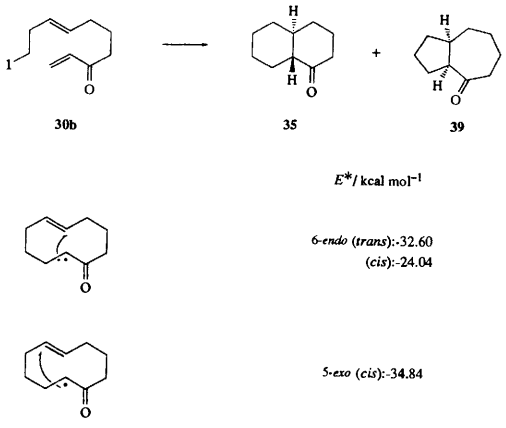
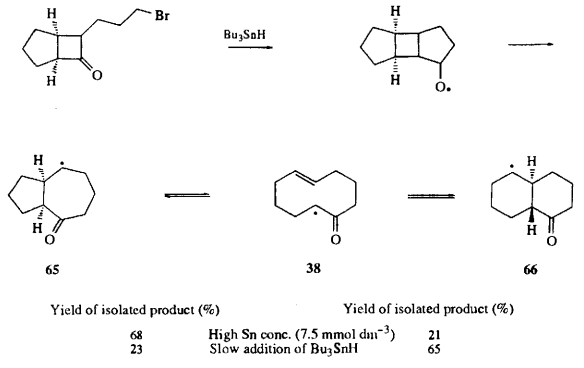


Fig. 4

again confirm the observed propensity for successful reaction (Fig. 3). Furthermore, the relative energies of the transition states leading to isomeric products confirm the formation of the *trans* adduct **35** in preference to its diastereoisomer. The energy difference (*ca.* 8 kcal) is perhaps a little on the large side for one to observe formation of the *cis*-isomer, but in addition to the comments we made earlier regarding quantitative comparisons, an orbital overlap effect as described above could again be in operation (again preliminary AM1 calculations would appear to support this argument).

Of the likely reaction pathways available in the macrocyclisation–transannulation sequence leading from the iodo dienone **30b** to the 6,6- and 7,5-bicycles **35** and **39**, respectively, the transannulations, *i.e.* 5-*exo* (*cis*), 6-*endo* (*trans*), that give the desired products are clearly favoured kinetically (see E^* values on Fig. 4) and although a reasonably even product mixture would be expected, and was observed, the energy difference of the product radicals (ΔE 8.01 kcal mol^{-1} in favour of the 6,6-product) would suggest that the 6,6-product should be favoured under thermodynamic conditions. In an interesting study, Dowd *et al.*[35] have indeed shown this to be the case by generating the same radical intermediates *viz.* **65** and **66** under different conditions (Scheme 14).

The aforementioned MM2 studies have provided a reasonably satisfactory rationale for the outcome of many of the macrocyclisation–transannulation reactions described earlier. Some necessary caution must be exercised however, since the modelling studies only deal with kinetic effects, and the conditions used to produce the products in our studies (*i.e.* refluxing benzene, low concentration of Bu_3SnH) may, in fact, favour the thermodynamic product in some cases. In the accompanying paper we describe the extension to these experimental and associated MM2 studies to the elaboration of tricyclic molecules from appropriate triene alkyl radical precursors.



Scheme 14

Experimental

General details

All melting points were determined on a Köfler hot-stage apparatus and are uncorrected. IR spectra were obtained as either liquid films or as dilute solutions in spectroscopic grade chloroform using a Perkin-Elmer 1600 series FT-IR instrument. ^{1}H NMR spectra were recorded on either a Bruker WM 250 (250 MHz), a Bruker AM 400 (400 MHz) or a JEOL EX-270 (270 MHz) spectrometer as dilute solutions in deuteriochloroform unless stated otherwise. The chemical shifts are recorded relative to an internal tetramethylsilane standard and the multiplicity of a signal is designated by one of the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, quin. = quintet, br = broad and m = multiplet. All coupling constants, *J*, are reported in Hz. ^{13}C NMR spectra were recorded on either a Bruker AM 400 (100 MHz) or JEOL EX-270 (67.8 MHz) instrument. The spectra were recorded as dilute solutions in deuteriochloroform unless stated otherwise with chemical shifts reported relative to internal chloroform standard on a broad band decoupled mode, and the multiplicities obtained using a DEPT sequence. The following symbols are used for the multiplicities in ^{13}C NMR spectra: q = primary methyl, t = secondary methylene, d = tertiary methine and s = quaternary.

Mass spectra were recorded on a AE1 MS-902 or a MM-701CF spectrometer using electron ionisation (EI) or fast atom bombardment (FAB) techniques. Microanalytical data were obtained on a Perkin-Elmer 240B elemental analyser.

Flash chromatography was performed on Merck silica gel 60 as the stationary phase and all solvents were redistilled before use. All chemical reactions were monitored by thin layer chromatography using Merck silica gel 60 F_{254} precoated aluminium plates which were visualised with UV light and then with either acidic alcoholic vanillin solution or basic potassium permanganate solution.

Routinely, dry organic solvents were stored under nitrogen. Benzene, diethyl ether (referred to as ether), toluene and xylenes were dried over sodium wire. Other organic solvents were dried by distillation from the following: tetrahydrofuran (sodium benzophenone ketyl) and dichloromethane (calcium hydride). Other organic solvents and reagents were purified by the accepted literature procedures. Organic extracts were dried over anhydrous magnesium sulphate and filtered under gravity. Solvents were removed on a Büchi rotary evaporator. Where necessary, reactions requiring anhydrous conditions were performed in flame- or oven-dried apparatus under a nitrogen or argon atmosphere. A Büchi GKR-50 Kugelrohr apparatus was used for bulb-to-bulb distillations.

Molecular mechanics calculations were performed with macromodel (version 4.0)[34] and results of AM1 calculations were obtained using Spartan.[33]

Hex-5-ene-1,4-diol 17a

Vinylmagnesium chloride (1.7 mol dm^{-3} solution; 73.5 cm^3, 0.125 mol) was added dropwise over 15 min to a stirred solution of tetrahydrofuran-2-ol **16** (5 g, 0.06 mol)[22] in tetrahydrofuran

(250 cm^3) at 0 °C under a nitrogen atmosphere. The solution was then warmed over 15 min to room temperature at which it was stirred for 2 h; it was then cooled to 0 °C and quenched by the addition of saturated aqueous ammonium chloride (100 cm^3) and ether (100 cm^3). The separated aqueous layer was extracted with ether (2 × 100 cm^3) and the combined extracts were dried and evaporated under reduced pressure to leave a yellow oil. This was purified by column chromatography on silica using ether as eluent to give the *diol* (6.26 g, 95%) as a colourless oil;[36] ν_{max}(film)/cm^{-1} 3334, 2931, 2871, 1670, 1644, 1427, 1052, 993 and 757; δ_H(250 MHz; $CDCl_3$) 1.59–1.71 (4 H, m, 2 × CH_2), 1.80–2.20 (1 H, br s, OH), 2.60–3.0 (1 H, br s, OH), 3.65–3.74 (2 H, m, CH_2OH), 4.14–4.16 (1 H, m, CHOH), 5.11 (1 H, dd, *J* 10.2 and 1.3 Hz, CH=CH_2), 5.24 (1 H, dd, *J* 17.2 and 1.3, CH=CH_2), 5.88 (1 H, dq, *J* 17.2, 10.2, 5.9 and 1.0, CH=CH_2); δ_C(67.8 MHz; $CDCl_3$) 28.5 (t), 34.0 (t), 62.4 (t), 72.6 (d), 114.4 (t) and 140.9 (d); *m/z* (EI) 98.0731 ($M^+ - H_2O$, $C_6H_{10}O$ requires 98.0732), 97 (13%), 74 (3%), 72 (18%) and 57 (100%).

6-*tert*-Butyldimethylsiloxyhex-1-en-3-ol 17b

Imidazole (7.0 g, 0.1 mol) and *tert*-butyldimethylsilyl chloride (7.8 g, 0.052 mmol) were added, each in one portion, to a stirred solution of hex-5-ene-1,4-diol (6 g, 0.052 mol) in dimethylformamide (15 cm^3) under a nitrogen atmosphere. The mixture was stirred at room temperature for 24 h after which it was diluted with ether (30 cm^3) and water (30 cm^3) and the separated aqueous layer was extracted with ether (3 × 30 cm^3). The combined organic extracts were dried and evaporated under reduced pressure to leave a yellow oil which was purified by column chromatography on silica using dichloromethane as eluent to give the *silyl ether* (5.7 g, 49%) as a colourless oil (Found: C, 62.8; H, 11.7. $C_{12}H_{26}O_2Si$ requires C, 62.6; H, 11.4%); ν_{max}(film)/cm^{-1} 3379, 2954, 2886, 2859, 1644, 1472, 1256, 1101, 992, 836 and 759; δ_H(270 MHz; $CDCl_3$) 0.06 (6 H, s, 2 × CH_3), 0.90 [9 H, s, $C(CH_3)_3$], 1.59–1.66 (4 H, m, 2 × CH_2), 2.74 (1 H, br s, OH), 3.66 (2 H, t, *J* 5.6, CH_2O), 4.13 (1 H, m, CHOH), 5.09 (1 H, dt, *J* 10.2, 1.65 and 1.3, CH=CH_2), 5.23 (1 H, dt, *J* 17.2, 1.65 and 1.3, CH=CH_2) and 5.87 (1 H, ddd, *J* 17.2, 10.2 and 5.9, CH=CH_2); δ_C(67.8 MHz; $CDCl_3$) −5.6 (2 × q), 18.1 (s), 25.7 (3 × q), 28.5 (t), 34.2 (t), 63.2 (t), 72.4 (d), 114.1 (t) and 141.0 (d); *m/z* (EI) 173.1010 [$M^+ - C(CH_3)_3$. $C_8H_{17}O_2Si$ requires 173.0998], 127 (3%), 105 (17%) and 81 (100%).

(*E*)-8-*tert*-Butyldimethylsiloxyoct-4-enal 18

Mercuric acetate (693 mg, 2.17 mmol) and mercuric trifluoroacetate (927 mg, 2.17 mmol) were added, each in one portion, to a stirred solution of compound **17b** (5 g, 0.022 mol) in ethyl vinyl ether (250 cm^3), and the mixture was then heated under reflux for 2 days. After the mixture had been allowed to cool to room temperature it was evaporated under reduced pressure to leave a residue which was purified by column chromatography on silica using light petroleum–dichloromethane (4:1) as eluent to give 6-*tert*-butyldimethylsiloxy-3-vinyloxyhex-1-ene (4.6 g, 82%) as a pale yellow oil; ν_{max}(film)/cm^{-1} 2955, 2886, 1635, 1612, 1472, 1256, 1099, 834 and 776; δ_H(270 MHz; $CDCl_3$) 0.05 (6 H, s, 2 × CH_3), 0.90 [9 H, s, $C(CH_3)_3$], 1.62–1.70 (4 H, m, 2 × CH_2), 3.63 (2 H, t, *J* 6.3 Hz, CH_2O), 4.0 (1 H, dd, *J* 6.6 and 1.5, OCH=CH_2), 4.17 (1 H, m, CHO), 4.30 (1 H, dd, *J* 14.2 and 1.5, OCH=CH_2), 5.21 (1 H, dd, *J* 10.6 and 1.0, CHCH=CH_2), 5.22 (1 H, dt, *J* 17.5 and 1.0, CHCH=CH_2), 5.76 (1 H, ddd, *J* 17.5, 10.6 and 6.6, CHCH=CH_2) and 6.33 (1 H, dd, *J* 14.2 and 6.6, OCH=CH_2); δ_C(67.8 MHz; $CDCl_3$) −5.3 (2 × q), 18.3 (s), 26.0 (3 × q), 28.3 (t), 31.4 (t), 62.8 (t), 80.6 (d), 88.6 (t), 116.7 (t), 137.9 (d) and 150.7 (d); *m/z* (EI) 199.1136 [$M^+ - C(CH_3)_3$. $C_{10}H_{19}O_2Si$ requires 199.1154], 155 (22%), 151 (11%), 127 (11%), 113 (10%), 101 (29%) and 81 (100%).

A solution of the preceding product (4.5 g, 0.018 mmol) in benzene (2 cm^3) was heated in a sealed tube at 120 °C for 24 h after which it was allowed to cool to room temperature. Evaporation of the mixture under reduced pressure left the *title aldehyde* **18** (4.5 g, 100%) as a pale yellow oil; ν_{max}(film)/cm^{-1} 2954, 2930, 2857, 2714, 1730, 1472, 1102, 837 and 776; δ_H(270 MHz; $CDCl_3$) 0.05 (6 H, s, 2 × CH_3), 0.90 [9 H, s, $C(CH_3)_3$], 1.58 (2 H, m, CH_2), 2.03–2.08 (2 H, m, CH_2), 2.33–2.37 (2 H, app q), 2.50 (2 H, t, *J* 7.5, CH_2CHO), 3.60 (2 H, t, *J* 6.3, CH_2O), 5.42–5.48 (2 H, m, CH=CH) and 9.77 (1 H, t, *J* 1.8, CHO); δ_C(67.8 MHz; $CDCl_3$) −5.3 (2 × q), 18.3 (s), 25.1 (t), 25.9 (3 × q), 28.7 (t), 32.4 (t), 43.5 (t), 62.4 (t), 128.0 (d), 131.4 (d) and 202.3 (d); *m/z* (EI) 199.1205 [$M^+ - C(CH_3)_3$. $C_{10}H_{19}O_2Si$ requires 199.1154], 171 (5%), 163 (5%), 151 (6%), 101 (30%) and 81 (100%), which was used without further purification.

(*E*)-10-*tert*-Butyldimethylsiloxydeca-1,6-dien-3-ol 19a

Vinylmagnesium chloride (1.7 mol dm^{-3} solution; 13.8 cm^3, 0.023 mmol) was added dropwise over 10 min to a stirred solution of compound **18** (4 g, 0.016 mol) in tetrahydrofuran (100 cm^3) at 0 °C under a nitrogen atmosphere, and the solution was then allowed to warm to room temperature over 15 min. The solution was stirred at room temperature for 2 h after which it was cooled to 0 °C and quenched by the addition of saturated aqueous ammonium chloride (50 cm^3) and ether (50 cm^3). The separated aqueous layer was extracted with ether (2 × 50 cm^3), and the combined organic extracts were then dried and evaporated under reduced pressure. The residue was purified by column chromatography on silica using dichloromethane–light petroleum (2:1) as eluent to give the *allylic alcohol* (3.46 g, 78%) as a colourless oil; ν_{max}(film)/cm^{-1} 3386, 2929, 2857, 1644, 1472, 1255, 1102, 968, 836 and 775; δ_H(250 MHz; $CDCl_3$) 0.05 (6 H, s, 2 × CH_3), 0.89 [9 H, s, $C(CH_3)_3$], 1.18–1.35 (2 H, m, CH_2), 1.51–1.63 (2 H, app q, *J* 7.5, CH_2CH=CH), 2.0–2.12 (4 H, m), 3.60 (2 H, t, *J* 6.3, CH_2O), 4.12 (1 H, app q, *J* 6.0, CHOH), 5.11 (1 H, dd, *J* 10.4 and 1.3, CH=CH_2), 5.23 (1 H, dd, *J* 17.2 and 1.3, CH=CH_2), 5.42–5.46 (2 H, m, CH=CH) and 5.87 (1 H, ddd, *J* 17.2, 10.4 and 6.1, CH:CH_2); δ_C(67.8 MHz; $CDCl_3$) −5.3 (2 × q), 18.3 (s), 25.9 (3 × q), 28.4 (t), 28.8 (t), 32.6 (t), 36.7 (t), 62.6 (t), 72.6 (d), 114.6 (t), 129.8 (d), 130.5 (d) and 141.1 (d); *m/z* (EI) 227.1467 [$M^+ - C(CH_3)_3$. $C_{12}H_{23}O_2Si$ requires 227.1467], 209 (4%), 173 (2%), 135 (20%), 105 (19%) and 81 (100%).

(*E*)-Deca-4,9-diene-1,8-diol 19b

Tetrabutylammonium fluoride (a 1.0 mol dm^{-3} solution; 2.1 cm^3; 2.1 mmol) was added dropwise over 5 min to a stirred solution of compound **19a** (0.5 g, 1.76 mmol) in tetrahydrofuran (920 cm^3) at 0 °C. After the solution had been allowed to warm to room temperature it was stirred for 2 h and then diluted with water (10 cm^3) and ether (20 cm^3). The separated aqueous layer was extracted with ether (4 × 15 cm^3), and the combined organic extracts were then dried and evaporated under reduced pressure. The residue was purified by column chromatography on silica using ether as eluent to give the *diol* (165 mg, 55%) as a colourless oil; ν_{max}(film)/cm^{-1} 3350, 3080, 2933, 1644, 1442, 1320, 1058, 991 and 921; δ_H(250 MHz; $CDCl_3$) 1.50–1.64 (4 H, m, 2 × CH_2), 2.02–2.09 (4 H, m, 2 × CH_2), 2.61 (2 H, br s, 2 × OH), 3.58 (2 H, t, *J* 6.5, CH_2OH), 4.07 (1 H, app q, *J* 6.4, CHOH), 5.07 (1 H, dt, *J* 10.4 and 1.3 Hz, CH=CH_2), 5.18 (1 H, dt, *J* 17.2 and 1.3, CH=CH_2), 5.40–5.45 (2 H, m, CH=CH), 5.82 (1 H, ddd, *J* 17.2, 10.4 and 6.2, CH=CH_2); δ_C(67.8 MHz; $CDCl_3$) 28.3 (t), 28.8 (t), 32.2 (t), 36.5 (t), 62.1 (t), 72.4 (d), 114.4 (t), 130.1 (2 × d) and 141.0 (d); *m/z* (EI) 153.1224 (M^+ − OH. $C_{10}H_{17}O$ requires 153.1279), 152 (6%), 136 (12%), 134 (14%), 133 (15%), 123 (20%) and 105 (50%).

(*E*)-10-Hydroxydeca-1,6-dien-3-one 20

Manganese(IV) oxide (1.55 g, 0.018 mol) was added in one portion to a stirred solution of the diol **19b** (150 mg, 0.88 mmol) in dichloromethane (10 cm^3) at room temperature under a nitrogen atmosphere and the solution was then stirred at room temperature for 2 days. The mixture was filtered through Kieselguhr and the residue was then washed with dichloromethane (200 cm^3). The combined washings were evaporated under reduced pressure to leave a yellow oil which was purified by column chromatography on silica using light petroleum–ether (1:1) as eluent to give the *enone* (108 mg, 73%) as a colourless oil; ν_{max}(film)/cm^{-1} 3417, 2930, 1681, 1615, 1442, 1404, 1059, 969 and 756; δ_H(250 MHz; $CDCl_3$) 1.59–1.67 (2 H, m, CH_2), 2.03–2.11 (2 H, app q, CH_2CH=CH), 2.28–2.36 (2 H, app q, CH_2CH=CH), 2.66 (2 H, t, *J* 7.4, CH_2CO), 3.64 (2 H, t, *J* 6.5, CH_2OH), 5.44–5.48 (2 H, m, CH=CH), 5.84 (1 H, dt, *J* 10.1 and 1.5, CH=CH_2), 6.22 (1 H, dd, *J* 17.7 and 1.5, CH=CH_2) and 6.36 (1 H, dd, *J* 17.7 and 10.1, CH=CH_2); δ_C(67.8 MHz; $CDCl_3$) 26.8 (t), 28.8 (t), 32.2 (t), 39.3 (t), 62.4 (t), 128.1 (t), 129.0 (d), 130.7 (d), 136.5 (d) and 201.2 (s); *m/z* (EI) 168.1158 (M^+. $C_{10}H_{16}O$ requires 168.1150), 150 (17%), 123 (15%), 109 (23%), 95 (28%) and 55 (100%).

(*E*)-10-Iododeca-1,6-dien-3-one 21

Methyltriphenoxyphosphonium iodide (394 mg, 0.7 mmol) in dimethylformamide (1 cm^3) was added dropwise over 2 min to a stirred solution of the dienone **20** (100 mg, 0.60 mmol) in dimethylformamide (2 cm^3) at 0 °C. The solution was allowed to warm to room temperature over 15 min at which temperature it was stirred for 15 min. The solution was poured onto saturated aqueous sodium thiosulphate (10 cm^3), and the aqueous solution was separated and extracted with ether (4 × 10 cm^3). The combined organic extracts were washed with water (20 cm^3), dried and evaporated under reduced pressure. The residue was purified by column chromatography on silica using light petroleum–dichloromethane (1:1) as eluent to give the *iodide* **21** (126 mg, 76%) as a pale yellow oil; ν_{max}(film)/cm^{-1} 2927, 1700, 1681, 1615, 1401, 1217, 1097 and 968 cm^{-1}; δ_H(270 MHz; $CDCl_3$) 1.79 (2 H, quin., *J* 6.9, $CH_2CH_2CH_2$), 2.02 (2 H, app q, CH_2CH=CH), 2.25 (2 H, app q, CH_2CH=CH), 2.59 (2 H, t, *J* 7.3, CH_2CO), 3.09 (2 H, t, *J* 6.5, CH_2I), 5.26–5.48 (2 H, m, CH=CH), 5.77 (1 H, dd, *J* 9.9 and 1.32, CH=CH_2), 6.15 (1 H, dd, *J* 17.8 and 1.32, CH=CH_2) and 6.29 (1 H, dd, *J* 17.8 and 9.9, CH=CH_2); δ_C(67.8 MHz; $CDCl_3$) 6.5 (t), 26.8 (t), 32.8 (t), 32.9 (t), 39.2 (t), 128.1 (t), 128.9 (d), 130.0 (d), 136.5 (d) and 200.1 (s); *m/z* (EI) 278.0150 (M^+. $C_{10}H_{15}IO$ requires 278.0168), 151 (5%), 109 (11%), 81 (28%) and 55 (100%).

5-(4-Methoxybenzyl)pentanal 23

Sodium hydride (60% dispersion in oil; 1.34 g, 34 mmol) was added to a stirred solution of pentane-1,5-diol (7.5 cm^3, 70 mmol) in dry benzene (10 cm^3), and the mixture was then stirred and heated under reflux in a nitrogen atmosphere for 3 h. 4-Methoxybenzyl chloride (5.3 g, 34 mmol) was added dropwise over 30 min to the mixture which was then stirred and heated under reflux for a further 18 h. The mixture was cooled to room temperature, poured into water (50 cm^3) and extracted with dichloromethane (3 × 50 cm^3). The separated organic extracts were combined, dried and evaporated under reduced pressure to leave a brown oil, distillation of which gave 5-(4-methoxybenzyl)pentanol **22** (5.36 g, 71%) as a colourless liquid, bp 187 °C at 4 mmHg; δ_H 7.25 (2 H, d, *J* 8.5, ArH), 6.85 (2 H, d, *J* 8.5, ArH), 4.42 (2 H, s, $ArCH_2O$), 3.80 (3 H, s, MeO), 3.65 (2 H, t, *J* 7, CH_2CH_2O), 3.45 (2 H, t, *J* 7, CH_2CH_2O), 2.05 (1 H, br s, OH) and 1.7–1.35 (m, 6 H, CH_2 × 3). Dimethyl sulfoxide (2.53 cm^3, 35.6 mmol) was added dropwise over 5 min to a stirred solution of oxalyl chloride (1.55 cm^3, 17.8 mmol) in dichloromethane (20 cm^3) at −78 °C under a nitrogen atmosphere. The solution was stirred at −78 °C for 15 min after which a solution of compound **22** (2.0 g, 8.9 mmol) in dichloromethane (2.5 cm^3) was added over 2 min. The mixture was stirred at −78 °C for 2 h, and then triethylamine (6.3 cm^3, 45 mmol) was added dropwise over 2 min. The resulting solution was warmed to room temperature over 1 h and then partitioned between dichloromethane (20 cm^3) and water (30 cm^3). The separated aqueous layer was extracted with dichloromethane (3 × 30 cm^3) and the combined organic extracts were then dried and evaporated under reduced pressure. The residue was purified by column chromatography using light petroleum–dichloromethane (8:1) as eluent to give the *aldehyde* **23** (1.59 g, 80%) as a colourless oil; ν_{max}(film)/cm^{-1} 3006, 2937, 2860, 2723, 1723, 1613, 1513, 1248, 1095 and 754; δ_H(250 MHz; $CDCl_3$) 1.59–1.72 (4 H, m, 2 × CH_2), 2.43 (2 H, dt, *J* 7.0 and 1.4, CH_2CHO), 3.44 (2 H, t, *J* 6.1, CH_2O), 3.78 (3 H, s, OCH_3), 4.41 (2 H, s, OCH_2Ar), 6.86 (2 H, d, *J* 8.6, ArH), 7.24 (2 H, d, *J* 8.6, ArH) and 9.73 (1 H, d, *J* 1.4, CHO); δ_C(67.8 MHz; $CDCl_3$) 18.7 (t), 28.9 (t), 43.3 (t), 55.0 (q), 69.2 (t), 72.3 (t), 113.5 (2 × d), 129.0 (2 × d), 130.3 (s), 158.9 (s) and 202.3 (d); *m/z* (EI) 222.1244 (M^+. $C_{13}H_{18}O_3$ requires 222.1256), 137 (27%) and 121 (100%).

1-Cyclopropyl-5-(4-methoxybenzyloxy)pentan-1-ol 24

Cyclopropyl bromide (0.57 cm^3, 7.09 mmol) was added dropwise to a stirred suspension of magnesium (178 mg, 7.43 mmol) in ether (30 cm^3) at such a rate as to maintain gentle reflux. The solution was heated under reflux in a nitrogen atmosphere for 1 h and then cooled to 0 °C and treated dropwise over 2 min with a solution of the pentanal **23** (1.5 g, 6.76 mmol) in ether (5 cm^3). The mixture was stirred at room temperature for 1 h and then saturated aqueous ammonium chloride (15 cm^3) was added slowly over 5 min. The resulting mixture was partitioned between ether (20 cm^3) and water (20 cm^3), and the aqueous layer was separated and extracted with ether (3 × 30 cm^3). The combined organic extracts were dried and evaporated under reduced pressure to leave a residue which was then purified by column chromatography using dichloromethane–ether (5:1) as eluent to give the title compound **24** (1.44 g, 81%) as a colourless oil; ν_{max}(film)/cm^{-1} 3418, 3001, 2936, 2861, 1613, 1586, 1463, 1302 and 821; δ_H(270 MHz; $CDCl_3$) 0.12–0.29 [2 H, m, CH(OH)CHCH_2], 0.41–0.54 [2 H, m, CH(OH)CHCH_2], 0.8–0.98 [1 H, m, CH(OH)C*H*], 1.47–1.65 (6 H, m), 2.05 (1 H, br s, OH), 2.79–2.86 (1 H, m, C*H*OH), 3.44 (2 H, t, *J* 6.1, CH_2O), 3.78 (3 H, s, OCH_3), 4.42 (2 H, s, OCH_2Ar), 6.87 (2 H, d, *J* 8.6, ArH) and 7.25 (2 H, d, *J* 8.6, ArH); δ_C(67.8 MHz; $CDCl_3$) 2.8 (t), 3.0 (t), 18.2 (d), 22.7 (t), 30.1 (t), 37.3 (t), 55.6 (q), 70.3 (t), 72.8 (t), 76.9 (d), 114.1 (2 × d), 129.6 (2 × d), 131.0 (s) and 159.4 (s); *m/z* (EI) 246.1617 ($M^+ - H_2O$. $C_{16}H_{22}O_2$ requires 246.1619), 189 (1.5%), 137 (19%) and 121 (100%).

(*E*)-8-Bromooct-5-en-1-ol 25

Magnesium bromide–diethyl ether (1.37 g, 5.3 mmol) and zinc bromide (1.19 g, 5.3 mmol) were added, each in one portion, to a stirred solution of the pentanol **24** (1.4 g, 5.3 mmol) in ether (40 cm^3), at room temperature under a nitrogen atmosphere. The solution was heated under reflux for 6 h and then cooled and diluted with ether (40 cm^3). The solution was washed with water (40 cm^3) and the separated aqueous layer was then extracted with ether (3 × 30 cm^3). The combined organic extracts were dried and evaporated under reduced pressure to leave a residue which was purified by column chromatography using light petroleum–ether (2:1) as eluent to give the bromo alcohol **25** (0.66 g, 60%) as a pale yellow oil; ν_{max}(film)/cm^{-1} 3353, 2932, 1612, 1512, 1436, 1249, 970 and 757; δ_H(250 MHz; $CDCl_3$) 1.38–1.59 (4 H, m), 1.82 (1 H, br s, OH), 2.03 (2 H, app q, CH=CHCH_2), 2.53 (2 H, app q,

CH=CHCH_2CH_2Br), 3.35 (2 H, t, J 7.0, CH_2Br), 3.62 (2 H, t, J 6.3, CH_2OH) and 5.3–5.52 (2 H, m, CH=CH); δ_C(67.8 MHz; $CDCl_3$) 25.3 (t), 32.0 (t), 32.1 (t), 32.9 (t), 35.9 (t), 62.6 (t), 126.8 (d) and 133.4 (d); m/z (EI) 188.0186 ($M^+ - H_2O$. $C_8H_{13}Br$ requires 188.0201), 160 (31%), 109 (47%) and 81 (100%).

The same bromo octenol was also obtained from the tetrahydropyran-1-ol **27**[22] following its reaction with cyclopropylmagnesium bromide (Et_2O, 25 °C, 2 h) leading to 5-cyclopropylpentane-1,5-diol (75%) as an oil [ν_{max}/cm^{-1} 3357, 3079, 3002, 2935, 1431, 1138, 1020, 916 and 822; δ_H 0.2–0.3 (2 H, m, cyclopropyl CH_2), 0.43–0.54 (2 H, m, cyclopropyl CH_2), 0.84–0.92 (1 H, m, cyclopropyl H), 1.42–1.76 (6 H, m, 3 × CH_2), 2.05–2.4 (2 H, br s, OH), 2.82–2.88 (1 H, m, CH-OH) and 3.63 (2 H, t, J 6.4, CH_2OH)] and reaction of this with $MgBr_2$–$ZnBr_2$ as described above.

(*E*)-8-Bromooct-5-enal 28

Dimethyl sulfoxide (0.491 cm^3, 6.92 mmol) was added dropwise over 5 min to a stirred solution of oxalyl chloride (0.302 cm^3, 3.46 mmol) in dichloromethane (10 cm^3) at −78 °C under a nitrogen atmosphere. The solution was stirred at −78 °C for 15 min, after which a solution of (E)-8-bromooct-5-enol (0.6 g, 2.88 mmol) in dichloromethane (1.5 cm^3) was added over 2 min. The mixture was stirred at −78 °C for 1.5 h, after which triethylamine (2.1 cm^3, 14.4 mmol) was added dropwise over 2 min. The resulting solution was warmed to room temperature over 0.5 h and then partitioned between dichloromethane (10 cm^3) and water (20 cm^3). The aqueous layer was separated and extracted with dichloromethane (3 × 20 cm^3) and the combined organic extracts were then dried and evaporated under reduced pressure. The residue was purified by column chromatography using light petroleum–ether (4:1) as eluent to give the *aldehyde* **28** (0.446 g, 75%) as a pale yellow oil; ν_{max}(film)/cm^{-1} 2933, 2857, 2722, 1724, 1440, 1266, 1209, 1069, 971 and 738; δ_H(250 MHz; $CDCl_3$) 1.70 (2 H, quin., J 7.2, CH_2CH_2CHO), 2.05 (2 H, app q, CH_2CH=CH), 2.44 (2 H, dt, J 7.3 and 1.7, CH_2CHO), 2.54 (2 H, app q, BrCH$_2$CH_2CH=CH), 3.36 (2 H, t, J 7.0, CH_2Br), 5.42–5.49 (2 H, m, CH=CH) and 9.76 (1 H, t, J 1.7, CHO); δ_C(67.8 MHz; $CDCl_3$) 21.8 (t), 32.0 (t), 33.2 (t), 36.1 (t), 43.3 (t), 128.1 (d), 132.7 (d), 202.7 (d); m/z (EI) 186.0059 ($M^+ - H_2O$. $C_8H_{11}Br$ requires 186.0044), 186 (4.0%), 162 (44%), 160 (45%), 98 (34%) and 81 (100%).

(*E*)-10-Bromodeca-1,7-dien-3-ol 29

Vinylmagnesium bromide (1 mol dm^{-3} solution; 2.13 cm^3, 2.13 mmol) was added dropwise over 5 min to a stirred solution of the enal **28** (0.4 g, 1.94 mmol) in tetrahydrofuran (30 cm^3) at 0 °C under a nitrogen atmosphere. The solution was allowed to warm to room temperature over 15 min after which it was stirred at room temp. for 1 h and then treated with saturated aqueous ammonium chloride (4 cm^3), added slowly over 5 min. The resulting mixture was partitioned between ether (20 cm^3) and water (30 cm^3), and the aqueous layer was then separated and extracted with ether (3 × 30 cm^3). The combined organic extracts were dried and evaporated under reduced pressure to leave a residue which was purified by column chromatography using dichloromethane–light petroleum (2:1) as eluent to give the secondary *alcohol* **29** (0.373 g, 82%) as a colourless oil; ν_{max}(film)/cm^{-1} 3373, 2932, 2858, 1642, 1424, 1315, 1265, 990, 970, 923 and 758; δ_H(270 MHz; $CDCl_3$) 1.3–1.7 (4 H, m), 2.04 (2 H, app q, CH_2CH=CH), 2.54 (2 H, app q, BrCH$_2$CH_2CH=CH), 3.36 (2 H, t, J 7.3, CH_2Br), 4.10 (1 H, app q, CHOH), 5.10 (1 H, dd, J 10.2 and 1.3, CH_2=CH), 5.22 (1 H, dd, J 17.2 and 1.3, CH_2=CH), 5.33–5.58 (2 H, m, CH=CH), 5.80–5.92 (1 H, ddd, J 17.2, 10.2 and 6.3, CH=CH$_2$); δ_C(67.8 MHz; $CDCl_3$) 24.8 (t), 32.2 (t), 32.8 (t), 35.9 (t), 36.2 (t), 72.8 (d), 114.4 (t), 126.7 (d), 133.3 (d) and 141.1 (d); m/z (EI) 159.9887 [M^+ − CH$_2$CH(OH)CHCH$_2$. C_6H_9Br requires 159.9888], 162 (25.8%), 135 (3.2%), 83 (25.2%), 81 (68.6%) and 57 (100%).

(*E*)-10-Bromodeca-1,7-dien-3-one 30a

Manganese(IV) oxide (2.26 g, 26 mmol) was added in one portion to a stirred solution of the dienol **29** (0.3 g, 1.28 mmol) in dichloromethane (30 cm^3) and the mixture was stirred at room temperature for 48 h. It was then filtered and the residue washed with dichloromethane (200 cm^3). The combined washings were then evaporated under reduced pressure to leave a yellow oil which was purified by column chromatography using light petroleum–dichloromethane (2:1) as eluent to give the *enone* **30a** (0.137 g, 46%) as a colourless oil; ν_{max}(film)/cm^{-1} 2930, 2854, 1699, 1681, 1615, 1438, 1402, 1265, 1208 and 969; δ_H(250 MHz; $CDCl_3$) 1.67 (2 H, quin., J 7.2, CH$_2$CH_2CH$_2$), 2.02 (2 H, app q, CH_2CH=CH), 2.47–2.59 (4 H, m), 3.34 (2 H, t, J 7.3, CH_2Br), 5.33–5.50 (2 H, m, CH=CH), 5.79 (1 H, dd, J 10.0 and 1.6, CH=CH_2), 6.18 (1 H, dd, J 17.7 and 1.6, CH=CH_2), 6.32 (1 H, dd, J 17.7 and 10.0, CH=CH$_2$); δ_C(67.8 MHz; $CDCl_3$) 23.4 (t), 32.0 (t), 33.1 (t), 36.0 (t), 38.8 (t), 127.7 (d), 128.2 (t), 133.0 (d), 136.7 (d) and 200.9 (s); m/z (EI) 150.1041 (M^+ − HBr. $C_{10}H_{14}O$ requires 150.1045), 135 (4.29%), 121 (6.25%), 96 (11.1%), 95 (17.7%), 81 (43.9%), 80 (83.2%), 79 (70.0%) and 55 (100%).

(*E*)-10-Iododeca-1,7-dien-3-one 30b

Sodium iodide (71.3 mg, 0.476 mmol) was added in one portion to a stirred solution of the dienone **30a** (100 mg, 0.433 mmol) in acetone (30 cm^3) and the solution was then heated under reflux for 2 h. The mixture was cooled and evaporated under reduced pressure and the residue dissolved in ether (30 cm^3). The resulting solution was washed with aqueous sodium thiosulfate (10%; 30 cm^3), dried and evaporated under reduced pressure to give the *iodide* **30b** (115 mg, 96%); ν_{max}(film)/cm^{-1} 2930, 2851, 1700, 1680, 1615, 1042, 1242, 1169, 1100 and 968; δ_H(250 MHz; $CDCl_3$) 1.70 (2 H, quin., J 7.2, CH$_2$CH_2CH$_2$), 2.03 (2 H, app q, CH_2CH=CH), 2.49–2.62 (4 H, m), 3.13 (2 H, t, J 7.3, CH_2I), 5.32–5.51 (2 H, m, CH=CH), 5.80 (1 H, dd, J 10.0 and 1.6, CH_2=CH), 6.20 (1 H, dd, J 17.7 and 1.6, CH_2=CH) and 6.36 (1 H, dd, J 17.7 and 10.0, CH$_2$=CH); δ_C(67.8 MHz; $CDCl_3$) 6.2 (t), 23.2 (t), 31.8 (t), 36.5 (t), 38.7 (t), 128.0 (t), 129.3 (d), 132.4 (d), 136.6 (d) and 200.8 (s); m/z (EI) 207.9754 (M^+ − CH$_2$COCHCH$_2$. C_6H_9I requires 207.9749), 151 (6.9%), 133 (12.1%), 107 (11.5%) and 81 (100%). This was used without further purification.

cis- and *trans*-Decahydronaphthalen-1-one (1-decalone) 36 and 35

Tributyltin hydride (79 mm^3, 0.30 mmol) ¶ was added dropwise over 5 min to a stirred solution of the dienone **30b** (74.5 mg, 0.27 mmol) and AIBN (10 mg) in degassed benzene (75 cm^3) under reflux in a nitrogen atmosphere. The solution was heated under reflux for a further 30 min, and then cooled to room temperature. Saturated aqueous potassium fluoride (75 cm^3) was added to the mixture which was then stirred vigorously for 18 h. After this the mixture was partitioned between pentane (30 cm^3) and water (30 cm^3), and the aqueous layer was separated and extracted with pentane (2 × 30 cm^3). The combined organic extracts were dried and evaporated under reduced pressure to leave a residue which was purified by column chromatography on silica using pentane–dichloromethane (2:1) as eluent to give (i) (*E*)-deca-1,6-dien-3-one **34** (4 mg, 9.7%) as a colourless oil; ν_{max}($CHCl_3$)/cm^{-1} 2959, 2927, 2873, 1682, 1616, 1402, 1378, 1095, 968 and 789; δ_H(400 MHz; $CDCl_3$) 0.87 (3 H, t, J 7.4, CH$_2$CH_3), 1.34 (2 H, m, CH_2CH$_3$),

¶ 1 mm^3 = 1 μl.

1.94 (2 H, app q, CH_2CH=CH), 2.30 (2 H, app q, CH_2CH=CH), 2.64 (2 H, t, J 7.4, CH_2CO), 5.39–5.44 (2 H, m, CH=CH), 5.82 (1 H, dd, J 10.2 and 1.7, CH=CH_2), 6.20 (1 H, dd, J 17.8 and 1.7, CH=CH_2) and 6.35 (1 H, dd, J 17.8 and 10.2, CH=CH_2); δ_C(67.8 MHz; $CDCl_3$) 13.6 (q), 22.5 (t), 26.9 (t), 34.5 (t), 39.5 (t), 128.0 (t), 128.4 (d), 131.3 (d), 136.5 (d) and 200.3 (s); m/z (EI) 152.1533 (M^+. $C_{10}H_{16}O$ requires 152.1201), 85 (89%), 71 (100%); and (ii) a mixture of the *cis* and *trans* isomers of the 1-decalone (29.3 mg, 72%) as a colourless oil; ν_{max}(film)/cm^{-1} 2926, 2853, 1708, 1448, 1216 and 1102; δ_H(400 MHz; $CDCl_3$) 1.17–1.25 (4 H, m), 1.34–1.49 (2 H, m), 1.61–1.80 (5 H, m), 1.89–1.97 (2 H, m), 2.02–2.08 (1 H, m) and 2.27–2.40 (2 H, m); δ_C(67.8 MHz; $CDCl_3$) *trans* isomer **35**, 25.1 (t), 25.4 (t), 25.7 (t), 26.5 (t), 33.0 (t), 34.3 (t), 41.8 (t), 44.9 (d), 55.0 (d) and 213.7 (s); *cis* isomer **36**, 23.1 (t), 23.5 (t), 24.5 (t), 25.2 (t), 28.9 (t), 29.1 (t), 39.1 (d), 40.6 (t), 50.7 (d) and 212.9 (s); m/z (EI) 152.1195 (M^+. $C_{10}H_{16}O$ requires 152.1201), 134 (15%), 123 (19%), 110 (50%) and 109 (100%).

1,8-Diazabicyclo[5.4.0]undec-7-ene (21 mm^3) was added to a stirred solution of a mixture of the decalones **35** and **36** (20 mg) in dichloromethane (3 cm^3), and stirring continued at room temperature for 24 h. The solution was then washed with water (2 × 5 cm^3), dried and evaporated under reduced pressure to leave the *trans*-decalone **35** (20 mg, 99%) as a colourless oil. The compound showed spectroscopic data identical with those described in the literature.[17]

1-Decalone 35 and octahydroazulen-1-one 39

Tributyltin hydride (64 mm^3, 0.24 mmol) was added dropwise over 5 min to a stirred refluxing solution of the dienone **30b** (60.3 mg, 0.22 mmol) and AIBN (10 mg) in degassed benzene (60 cm^3) under a nitrogen atmosphere. The solution was heated under reflux for 30 min and then cooled to room temperature. Saturated aqueous potassium fluoride (60 cm^3) was added to the benzene solution, and the mixture was then stirred vigorously for 18 h. The resulting mixture was partitioned between pentane (20 cm^3) and water (20 cm^3), and the aqueous layer was then separated and extracted with pentane (2 × 30 cm^3). The combined organic extracts were dried and evaporated under reduced pressure to leave a residue which was purified by column chromatography on silica using pentane–dichloromethane (2:1) as eluent to give a 1:1 mixture of the cyclic ketones (22.4 mg, 68%) as a colourless oil. Further, repeated chromatography on silica using pentane–dichloromethane (4:1) as eluent then gave: (i) *trans*-1-decalone;[17] ν_{max}(film)/cm $^{-1}$ 2925, 2853, 1711, 1448, 1200, 1040, 905 and 831; δ_H(400 MHz; $CDCl_3$) 1.17–1.25 (4 H, m), 1.34–1.49 (2 H, m), 1.61–1.80 (5 H, m), 1.89–1.97 (2 H, m), 2.02–2.08 (1 H, m) and 2.27–2.40 (2 H, m); δ_C(67.8 MHz; $CDCl_3$) 25.1 (t), 25.4 (t), 25.7 (t), 26.5 (t), 33.0 (t), 34.3 (t), 41.8 (t), 44.9 (d), 55.0 (d) and 213.7 (s); and (ii) *cis*-octahydroazulen-1-one;[18] ν_{max}(film)/cm^{-1} 2929, 2856, 1702, 1455, 1445, 1342, 1162, 941 and 856; δ_H(250 MHz; $CDCl_3$) 1.07–1.20 (4 H, m), 1.21–1.43 (2 H, m), 1.45–1.8 (5 H, m), 1.8–2.15 (2 H, m), 2.23–2.56 (2 H, m) and 3.12 (1 H, dt, J 10.6 and 8.3, CH_2CHCO); δ_C(67.8 MHz; $CDCl_3$) 24.4 (t), 25.4 (t), 26.2 (t), 27.7 (t), 32.5 (t), 35.2 (t), 40.4 (d), 43.2 (t), 54.6 (d) and 212.5 (s).

(*E*)-9-Bromonona-1,6-dien-3-ol 47

A solution of vinylmagnesium chloride in THF (1.7 mol dm^{-3} solution; 0.81 cm^3, 1.3 mmol) was added dropwise over 5 min to a stirred solution of 7-bromohept-4-enal **46** (240 mg, 1.26 mmol) in dry THF (5 cm^3) at 0 °C under a nitrogen atmosphere, and the solution was then allowed to warm to room temperature over 10 min. After the solution had been stirred at room temperature for 2 h, it was cooled to 0 °C and quenched with saturated aqueous ammonium chloride and extracted with ether. The combined ether extracts were dried and evaporated under reduced pressure and the residue was purified by chromatography on silica using 5% ethyl acetate in light petroleum as eluent to give the *allylic alcohol* **47** (0.19 g, 69%) as a clear oil; ν_{max}(film)/cm^{-1} 3392, 2933, 1738, 1426, 1258, 1048, 991, 970 and 923; δ_H(250 MHz; $CDCl_3$) 1.40 (2 H, m, CH_2CHOH), 1.91 (2 H, m allylic), 2.34 (2 H, m, app q, J 7, allylic), 2.90 (1 H, br s, OH), 3.17 (2 H, t, J 7.1, CH_2Br), 3.89 (1 H, m, CHOH), 4.86 (1 H dt, J 10.4 and 1.5, CH=CHH), 5.01 (1 H, dt, J 17.3 and 1.5, CH=CHH), 5.30 (2 H, m, vinylic) and 5.58–5.72 (1 H, m, C$H$$CH_2$); δ_C(67.8 MHz; $CDCl_3$) 141.0 (d), 132.7 (d), 126.5 (d), 113.6 (t), 71.6 (d), 36.0 (t), 35.5 (t), 32.2 (t) and 27.9 (t); m/z (EI) 139.1111 (M^+ − Br. $C_9H_{15}O$ requires 139.1123), 139 (7%), 121 (16%), 97 (14%), 93 (53%), 81 (32%) and 57 (100%).

(*E*)-9-Bromonona-1,6-dien-3-one 48

Dess–Martin periodinane (740 mg, 1.74 mmol) was added in one portion to a stirred solution of the dienol **47** (190 mg, 0.87 mmol) in dichloromethane (7 cm^3) at room temperature and the stirring continued at room temperature under a nitrogen atmosphere for 2 h. The mixture was poured into a stirred 1:1 mixture of ether and 10% aqueous sodium thiosulfate in saturated aqueous sodium hydrogen carbonate and stirring continued. The ether layer was then separated and the aqueous layer was washed with ether; the combined ether extracts were then evaporated under reduced pressure. The residue was purified by chromatography on silica using 10% ethyl acetate in light petroleum as eluent to give the *enone* **48** (185 mg, 98%) as a colourless oil; ν_{max}(film)/cm^{-1} 2919, 1682, 1614, 1402 and 967; δ_H(250 MHz; $CDCl_3$) 2.29 (2 H, app q, J 7, allylic), 2.49 (2 H, app q, J 7, allylic), 2.64 (2 H, t, J 7.1, CH_2CO), 3.31 (2 H, t, J 7, CH_2Br) 5.46 (2 H, m, vinylic), 5.80 (1 H, dd, J 10.1 and 1.6, CH=CHH), 6.18 (1 H, dd, J 17.7 and 1.6, CH=CHH), 6.32 (1 H, dd, J 17.7 and 10.1 CH=CH_2); δ_C(67.8 MHz; $CDCl_3$) 199.9 (s), 136.3 (d), 131.7 (d), 128.1 (t), 127.5 (d), 38.9 (t), 35.7 (t), 32.5 (t) and 26.5 (t); m/z (EI) 137.0973 (M^+ − Br. $C_9H_{13}O$ requires 137.0966), 137 (15%), 109 (21%), 95 (14%), 81 (16%), 67 (21%) and 55 (100%).

(*E*)-9-Iodonona-1,6-dien-3-one 40

The iodide was prepared from the corresponding bromide in 76% yield, using a procedure identical with that described for the preparation of the dienone **30b**. The iodide was obtained as a pale yellow oil; ν_{max}(film)/cm^{-1} 2922, 1680, 1615, 1401 and 967; δ_H(250 MHz; $CDCl_3$) 2.30 (2 H, app q, J 7, allylic), 2.51 (2 H, app q, J 7, allylic), 2.66 (2 H, t, J 7.5, CH_2CO), 3.11 (2 H, t, J 7.2, CH_2I), 5.45 (2 H, m, vinylic), 5.82 (1 H, dd, J 10.1 and 1.5, CH=CHH), 6.20 (1 H, dd, J 17.6 and 1.6, CH=CHH) and 6.34 (1 H, dd, J 17.7 and 10.1, CH=CH_2); δ_C(67.8 MHz; $CDCl_3$) 199.7 (s), 136.3 (d), 131.3 (d), 129.3 (d), 128.0 (t), 38.9 (t), 36.3 (t), 26.5 (t) and 5.8 (t); m/z (EI) 137.0950 (M^+ − I. $C_9H_{13}O$ requires 137.0966), 137 (34%), 109 (17%), 95 (15%), 81 (16%), 67 (54%) and 55 (100%), which was used without further purification.

cis-Bicyclo[4.3.0]nonan-1-one 41

Treatment of a solution of the dienone **41** (52 mg) in benzene (66 cm^3) with Bu_3SnH (57 mm^3)–AIBN (3 mg), according to the procedure described for the synthesis of *cis*/*trans*-1-decalone gave the nonanone **41** (15 mg, 52%) as a colourless oil; ν_{max}(film)/cm^{-1} 2928, 2855, 1700, 1102 and 1002; δ_H(270 MHz; $CDCl_3$) 1.1–2.7 (14 H, m); δ_C(67.8 MHz; $CDCl_3$) 214.2 (s), 53.2 (d), 43.0 (d), 39.7 (t), 31.1 (t), 27.4 (t), 26.8 (t), 23.9 (t) and 23.2 (t); these data were identical with those recorded in the literature for authentic material.[26]

(*E*)-8-Bromoocta-1,5-dien-3-ol 50

The bromo dienol was prepared from 6-bromohex-3-enal **49** and vinylmagnesium chloride, in 73% yield, using a procedure

identical with that described for the synthesis of the dienol **47**. Purification by chromatography gave the bromo dienol as a colourless oil, ν_{max}(film)/cm^{-1} 3374br, 2928, 1425, 1266, 971 and 924; δ_H(250 MHz; $CDCl_3$) 2.25 (2 H, m, allylic), 2.56 (2 H, m, allylic), 3.38 (2 H, t, *J* 6.9, CH_2Br), 4.12 (1 H, m, C*H*OH), 5.10 (1 H, dt, *J* 10.4 and 1.5, CH=CH*H*), 5.22 (1 H, dt, *J* 17.2 and 1.5, CH=C*H*H), 5.51 (2 H, m, vinylic) and 5.78–5.92 (1 H, ddd, *J* 17.2, 10.4 and 6, C*H*=CH_2); δ_C(67.8 MHz; $CDCl_3$) 140.1 (d), 130.4 (d), 128.8 (d), 114.6 (t), 71.7 (d), 40.2 (t), 35.7 (t) and 32.8 (t); *m*/*z* (EI) 188.0056 ($M^+ - H_2O$. $C_8H_{11}Br$ requires 186.0044), 69 (60%) and 57 (100%).

(*E*)-8-Bromoocta-1,5-dien-3-one 51

The enone, prepared from the dienol **50**, by oxidation with Dess–Martin periodinone, using a procedure identical with that described for the synthesis of the dienone **48**, was obtained as a colourless oil (98%); ν_{max}(film)/cm^{-1} 2963, 1682, 1615, 1400 and 969; δ_H(250 MHz; $CDCl_3$) 2.59 (2 H, app q, *J* 7, allylic), 3.32 (2 H, m, $COCH_2C$=), 3.37 (2 H, t, *J* 7.0, CH_2Br), 5.64 (2 H, m, vinylic), 5.83 (1 H, dd, *J* 10.0 and 1.6, CH=CH*H*), 6.22 (1 H, dd, *J* 17.6 and 1.7, CH=C*H*H) and 6.36 (1 H, dd, *J* 17.6 and 10.0, C*H*=CH_2); δ_C(67.8 MHz; $CDCl_3$) 198.3 (s), 135.7 (d), 131.1 (d), 128.7 (t), 125.1 (d), 43.3 (t), 35.7 (t) and 32.3 (t); *m*/*z* (EI) 123.0824 (M^+ − Br. $C_8H_{11}O$ requires 123.0810), 123 (25%), 68 (14%), 67 (22%) and 55 (100%).

(*E*)-8-Iodoocta-1,5-dien-3-one 42

The iodide, prepared from the corresponding bromide **51**, in 60% yield, using a procedure identical with that described for the synthesis of the dienone **30b**, was obtained as a pale yellow oil; ν_{max}(film)/cm^{-1} 2958, 1699, 1682, 1614, 1400 and 968; δ_H(250 MHz; $CDCl_3$) 2.58 (2 H, app q, *J* 7, allylic), 3.13 (2 H, t, *J* 7.2, CH_2I), 3.30 (2 H, dd, *J* 6.5 and 2.0, $COCH_2C$=), 5.57 (2 H, m, vinylic), 5.98 (1 H, dd, *J* 9.9 and 1.6, CH=CH*H*), 6.21 (1 H, dd, *J* 17.6 and 1.6, CH=C*H*H) and 6.32 (1 H, dd, *J* 17.6 and 9.9, CH=CH_2); δ_C(67.8 MHz; $CDCl_3$) 198.2 (s), 135.7 (d), 132.9 (d), 128.8 (t), 124.6 (d), 43.3 (t), 36.4 (t) and 5.2 (t); *m*/*z* (EI) 123.0808 (M^+ − I. $C_8H_{11}O$ requires 123.0810), 123 (27%), 95 (10%), 68 (7%) and 55 (100%). This compound was used without further purification.

(*Z*)-Cyclooct-3-enone 54

Treatment of a solution of the dienone **42** (87 mg) in benzene (116 cm^3) with Bu_3SnH (101 mm^3, 0.38 mmol)–AIBN (6 mg), according to the procedure described for the preparation of *cis*/*trans*-decalone, gave the cyclooctenone (40%, or 56% based on recovered starting material) as a colourless oil. The octenone displayed spectroscopic data [ν_{max}(film)/cm^{-1} 2930, 2857, 1695, 1462, 1103 and 1002; δ_H(250 MHz; $CDCl_3$) 1.60 (2 H, m, CH_2), 1.88 (2 H, m, CH_2), 2.11 (2 H, m, allylic), 2.49 (2 H, m, CH_2CH_2CO), 3.15 (2 H, d, *J* 6, $COCH_2C$=), 5.60 (1 H, m, vinylic) and 5.73 (1 H, m, vinylic); δ_C(67.8 MHz; $CDCl_3$) 213.9 (s), 131.6 (d), 124.3 (d), 44.4 (t), 42.3 (t), 27.2 (t), 25.8 (t) and 24.8 (t)] which were superimposable on those reported in the literature for authentic material.[27]

5-Hydroxyhept-6-ene-1,5-diol 55

Vinylmagnesium chloride (1.7 mol dm^{-3} solution; 115 cm^3, 0.196 mol) was added dropwise over 30 min to a stirred solution of the tetrahydropyran-1-ol **27** (10 g, 98 mmol) in tetrahydrofuran (250 cm^3) at 0 °C under a nitrogen atmosphere, and the solution was then allowed to warm to room temperature. After being stirred at room temperature for 3 h, the solution was cooled to 0 °C and quenched by the addition of saturated aqueous ammonium chloride (150 cm^3) and ether (150 cm^3). The aqueous layer was separated and extracted with ether (2 × 150 cm^3), and the combined organic extracts were dried and evaporated under reduced pressure to leave a yellow oil. This was purified by column chromatography on silica using ethyl acetate as eluent to give the *diol* (6.8 g, 53%) as a colourless oil (Found: C, 64.4; H, 11.2. $C_7H_{14}O_2$ requires C, 64.6; H, 10.8%); ν_{max}(film)/cm^{-1} 3334, 3082, 2938, 2864, 1644, 1456, 1074, 992, 923 and 757; δ_H(250 MHz; $CDCl_3$) 1.3–1.7 (6 H, m), 2.80 (2 H, s, OH), 3.61 (2 H, t, *J* 6.1, CH_2OH), 4.09 (1 H, m, C*H*OH), 5.07 (1 H, dt, *J* 10.4 and 1.36, CH=CH_2), 5.20 (1 H, dt, *J* 17.2 and 1.36, CH=CH_2), 5.84 (1 H, ddd, *J* 17.2, 10.4 and 6.1, CH=CH_2); δ_C(67.8 MHz; $CDCl_3$) 21.4 (t), 32.1 (t), 36.4 (t), 62.0 (t), 72.6 (d), 114.3 (t) and 141.1 (d); *m*/*z* (EI) 96.0856 (M^+ − 2OH. C_7H_{12} requires 96.0939), 111 (3%), 86 (6%), 85 (100%) and 67 (15%).

5-Hydroxyhept-6-enyl 2,2-dimethylpropanoate 56

Dichloromethane (50 cm^3) was added to a stirred solution of the alcohol **55** (5.5 g, 42 mmol) in pyridine (50 cm^3), and the mixture was then cooled to 0 °C. 2,2-Dimethylpropanoyl chloride (5.21 cm^3, 42 mmol) was added dropwise over 10 min to the solution which was then warmed to room temperature and stirred at room temperature for 5 min. Hydrochloric acid (2 mol dm^{-3}; 100 cm^3) was added to the reaction mixture after which the aqueous layer was separated and extracted with dichloromethane (4 × 50 cm^3). The combined extracts were washed with hydrochloric acid (2 mol dm^{-3}; 4 × 50 cm^3), dried and evaporated under reduced pressure to leave a yellow liquid. This was purified by column chromatography on silica using dichloromethane–ether (10 : 1) as eluent to give the *ester* (9.05 g, quant.) as a colourless liquid (Found: C, 66.8; H, 10.4. $C_{12}H_{22}O_3$ requires C, 67.3; H, 10.4%); ν_{max}(film)/cm^3 3440, 2974, 2872, 1728, 1644, 1481, 1287, 1162, 1034 and 757; δ_H(250 MHz; $CDCl_3$) 1.24 [9 H, s, $C(CH_3)_3$], 1.3–1.7 (6 H, m), 2.4 (1 H, br s, OH), 4.11 (2 H, t, *J* 6.5, CH_2O), 4.13 (1 H, m, C*H*OH), 5.16 (1 H, dt, *J* 10.4 and 1.2, CH=CH_2), 5.27 (1 H, dt, *J* 17.2 and 1.2, CH=CH_2) and 5.91 (1 H, ddd, *J* 17.2, 10.4 and 6.2, C*H*=CH_2); δ_C(67.8 MHz; $CDCl_3$) 21.6 (t), 27.0 (3 × q), 28.4 (t), 36.3 (t), 38.6 (s), 64.1 (t), 72.7 (d), 114.5 (t), 141.0 (d) and 178.5 (s); *m*/*z* (EI) 112.0880 [$M^+ - (CH_3)_3CCO_2H$. $C_7H_{12}O$ requires 112.0888], 103 (29%), 101 (31%), 95 (24%), 85 (37%) and 57 (100%).

5-Vinyloxyhept-6-enyl 2,2-dimethylpropanoate 57

Mercuric trifluoroacetate (847 mg, 1.99 mmol) was added in one portion to a stirred solution of the ester **56** (8.5 g, 0.04 mol) in ethylvinyl ether (125 cm^3), and the solution was then heated under reflux for 15 h. The solution was allowed to cool to room temperature after which it was evaporated under reduced pressure. The residue was purified by column chromatography on silica using light petroleum–dichloromethane (3 : 1) as eluent to give the *vinyl ether* **57** (6.5 g, 68%) as a pale yellow oil; ν_{max}(film)/cm^{-1} 2958, 2871, 1728, 1634, 1615, 1481, 1461, 1160 and 1040; δ_H(250 MHz; $CDCl_3$) 1.15 [9 H, s, $C(CH_3)_3$], 1.3–1.5 (2 H, m), 1.5–1.68 (4 H, m), 3.94 (1 H, dd, *J* 6.5 and 1.5, OCH=CH_2), 4.01 (2 H, t, *J* 6.4, CH_2O), 4.09 (1 H, app q, *J* 6.2, C*H*OCH=CH_2), 4.24 (1 H, dd, *J* 14.1 and 1.5, OCHCH_2), 5.15 (1 H, dd, *J* 10.0 and 1.0, CHCH=CH_2), 5.16 (1 H, dd, *J* 17.5 and 1.0, CHCH=CH_2), 5.69 (1 H, ddd, *J* 17.5, 10.0 and 6.7, CHC*H*=CH_2) and 6.26 (1 H, dd, *J* 14.1 and 6.5, OC*H*=CH_2); δ_C(67.8 MHz; $CDCl_3$) 21.4 (t), 27.0 (3 × q), 28.3 (t), 34.4 (t), 38.6 (s), 63.9 (t), 80.3 (d), 88.6 (t), 116.5 (t), 137.7 (d), 150.5 (d) and 178.3 (s); *m*/*z* (EI) 197.1540 (M^+ − OCH=CH_2. $C_{12}H_{21}O_2$ requires 197.1541), 103 (6.4%), 96 (8.4%), 95 (100%) and 85 (23%).

(*E*)-9-Oxonon-5-enyl 2,2-dimethylpropanoate 58

A solution of the ester **57** (6.2 g, 26 mmol) in benzene (0.5 cm^3) was heated in a sealed tube at 120 °C for 13 h after which it was allowed to cool to room temperature. It was then evaporated

under reduced pressure to leave a yellow oil which was purified by column chromatography using light petroleum–dichloromethane (1:1) as eluent to give the *ester* **58** (5.12 g, 83%) as a colourless oil (Found: C, 69.6; H, 10.2. $C_{14}H_{24}O_3$ requires C, 70.0; H, 10.1%); ν_{max}(film)/cm^{-1} 2959, 2935, 2721, 1727, 1481, 1286, 1159, 971 and 738; δ_H(250 MHz; $CDCl_3$) 1.16 [9 H, s, $C(CH_3)_3$], 1.39 (2 H, m), 1.58 (2 H, m), 1.98 (2 H, app q, CH_2CH=CH), 2.31 (2 H, app q, CH_2CH=CH), 2.47 (2 H, t, *J* 6.9, CH_2CHO), 4.0 (2 H, t, *J* 6.4, CH_2O), 5.38–5.43 (2 H, m, CH=CH) and 9.72 (1 H, t, *J* 1.6, CHO); δ_C(67.8 MHz; $CDCl_3$) 25.0 (t), 25.5 (t), 27.0 (3 × q), 27.9 (t), 31.8 (t), 38.6 (s), 43.3 (t), 64.0 (t), 128.2 (d), 131.1 (d), 178.4 (s) and 202.0 (d); *m/z* (EI) 138.1002 [$M^+ - (CH_3)_3CCO_2 - H$. $C_9H_{14}O$ requires 138.1045], 120 (8.7%), 110 (8.7%) and 97 (6.2%).

(*E*)-9-Hydroxyundeca-5,10-dienyl 2,2-dimethylpropanoate 59a

Vinylmagnesium chloride (1.7 mol dm^{-3} solution; 1.84 cm^3, 3.13 mmol) was added dropwise over 5 min to a stirred solution of the ester **58** (0.5 g, 2.08 mmol) in tetrahydrofuran (20 cm^3) at 0 °C under a nitrogen atmosphere. The solution was then allowed to warm to room temperature over 15 min after which it was stirred at the same temperature for 2 h. The mixture was then cooled to 0 °C and quenched by the addition of saturated aqueous ammonium chloride (10 cm^3) and ether (10 cm^3). The aqueous layer was separated and extracted with ether (4 × 10 cm^3) and the combined extracts were dried and evaporated under reduced pressure. The residue was purified by column chromatography on silica using dichloromethane as eluent to give the *ester* **59a** (327 mg, 58%) as a colourless oil; ν_{max}(film)/cm^{-1} 3438, 2934, 2871, 1728, 1644, 1481, 1399, 1286, 1159, 969 and 736; δ_H(250 MHz; $CDCl_3$) 1.20 [9 H, s, $C(CH_3)_3$], 1.36–1.47 (2 H, m), 1.55–1.66 (4 H, m), 2.02–2.14 (4 H, m, CH_2CH=CH), 4.05 (2 H, t, *J* 6.4, CH_2O), 4.13 (1 H, app q, CHOH), 5.12 (1 H, dt, *J* 10.4 and 1.2, CH=CH_2), 5.23 (1 H, dt, *J* 17.2 and 1.2, CH=CH_2), 5.44 (2 H, m, CH=CH) and 5.87 (1 H, ddd, *J* 17.2, 10.4 and 6.1, C*H*=CH_2); δ_C(67.8 MHz; $CDCl_3$) 25.6 (t), 27.0 (3 × q), 27.9 (t), 28.3 (t), 31.9 (t), 36.6 (t), 38.6 (s), 64.2 (t), 72.4 (d), 114.4 (t), 130.0 (d), 130.2 (d), 141.0 (d) and 178.6 (s); *m/z* (EI) 250.1968 ($M^+ - H_2O$. $C_{16}H_{26}O_2$ requires 250.1933), 148 (9%), 120 (11%), 105 (11%) and 94 (100%).

(*E*)-Undeca-5,10-diene-1,9-diol 59b

Diisobutylaluminium hydride (1 mol dm^{-3} solution; 3.12 cm^3, 3.12 mmol) was added dropwise over 5 min to a stirred solution of the ester **59a** (300 mg, 1.12 mmol) in dichloromethane (10 cm^3) under a nitrogen atmosphere at −78 °C. The solution was allowed to warm to room temperature at which temperature it was stirred for 1 h before being cooled to 0 °C. The mixture was quenched by careful addition of hydrochloric acid (2 mol dm^{-3}; 5 cm^3), after which the aqueous layer was separated and extracted with dichloromethane (3 × 5 cm^3). The combined extracts were dried and evaporated under reduced pressure to leave a colourless oil which was purified by column chromatography on silica using dichloromethane as eluent to give the *diol* (168 mg, 82%) as a colourless oil; ν_{max}(film)/cm^{-1} 3508, 3217, 2913, 2692, 2606, 1953, 1778, 1688, 1352, 1121 and 992; δ_H(250 MHz; $CDCl_3$) 1.36–1.50 (2 H, m), 1.50–1.63 (4 H, m), 1.91 (2 H, br s, OH), 2.01–2.20 (4 H, m, CH_2CH=CH), 3.64 (2 H, t, *J* 6.4, CH_2OH), 4.12 (1 H, app q, CHOH), 5.11 (1 H, d, *J* 10.4, CH=CH_2), 5.22 (1 H, d, *J* 17.2, CH=CH_2), 5.44 (2 H, m, CH=CH) and 5.86 (1 H, ddd, *J* 17.2, 10.4 and 6.2); δ_C(67.8 MHz; $CDCl_3$) 25.5 (t), 28.3 (t), 31.9 (t), 32.1 (t), 36.5 (t), 62.5 (t), 72.5 (d), 114.5 (t), 129.8 (d), 130.6 (d) and 140.9 (d); *m/z* (FAB) 185 (MH^+, 9%), 167 (13%) and 149 (25%).

(*E*)-11-Bromoundeca-1,6-dien-3-ol 59c

N-Bromosuccinimide (172 mg, 0.96 mmol) and triphenylphosphine (277 mg, 1.06 mmol) were added, each in one portion, to a stirred solution of the diol **59b** (150 mg, 0.96 mmol) in dichloromethane (30 cm^3) under a nitrogen atmosphere at −30 °C. After the solution had been allowed to warm to room temperature it was stirred at the same temperature for 6 h and then evaporated to leave a semi-solid which was purified by column chromatography on silica using dichloromethane as eluent to give the *bromo alcohol* **59c** (112 mg, 53%) as a colourless oil; ν_{max}(film)/cm^{-1} 3362, 2933, 2854, 1644, 1438, 1250, 990, 969, 923 and 644; δ_H(250 MHz; $CDCl_3$) 1.51 (2 H, app q), 1.59 (2 H, app q), 1.70 (1 H, br s, OH), 1.85 (2 H, app q), 1.99–2.13 (4 H, m, CH_2CH=CH), 3.40 (2 H, t, *J* 6.8, CH_2Br), 4.12 (1 H, app q, *J* 6.3, CHOH), 5.11 (1 H, dt, *J* 10.4 and 1.3, CH=CH_2), 5.22 (1 H, dt, *J* 17.2 and 1.3, CH=CH_2), 5.43 (2 H, m, CH=CH) and 5.86 (1 H, ddd, *J* 17.2, 10.4 and 6.2, C*H*=CH_2); δ_C(67.8 MHz; $CDCl_3$) 27.9 (t), 28.4 (t), 31.6 (t), 32.2 (t), 33.8 (t), 36.6 (t), 72.6 (d), 114.6 (t), 130.1 (d), 130.2 (d) and 141.0 (d); *m/z* (EI) 149.1268 ($M^+ - Br - H_2O$. $C_{11}H_{17}$ requires 149.1330), 176 (9%), 174 (11%), 151 (10%), 111 (12%), 107 (17%), 95 (26%) and 79 (100%).

(*E*)-11-Bromoundeca-1,6-dien-3-one 60

Periodinane (282 mg, 0.75 mmol) was added in one portion to a stirred solution of the dienol **59c** (110 mg, 0.5 mmol) in dichloromethane (5 cm^3) at room temperature, and the solution was then stirred at room temperature under a nitrogen atmosphere for 2 h. The mixture was then poured onto a stirred 10% solution of sodium thiosulphate in saturated aqueous sodium hydrogen carbonate (5 cm^3) and stirred vigorously for 15 min. The aqueous layer was separated and extracted with dichloromethane (4 × 5 cm^3), and the combined extracts were then dried and evaporated under reduced pressure to leave a yellow semi-solid. This was purified by column chromatography on silica using light petroleum–dichloromethane (1:1) as eluent to give the *enone* **60** (83 mg, 76%) as a colourless oil; ν_{max}(film)/cm^{-1} 2934, 2856, 1681, 1616, 1458, 1402, 1361, 1298, 1102 and 969; δ_H(250 MHz; $CDCl_3$) 1.48 (2 H, app quin., *J* 7.5), 1.84 (2 H, app quin., *J* 7.0), 1.97–2.04 (2 H, m), 2.31–2.40 (2 H, m), 2.65 (2 H, t, *J* 7.5, CH_2CO), 3.40 (2 H, t, *J* 6.8, CH_2Br), 5.38–5.50 (2 H, m, CH=CH), 5.83 (1 H, dd, *J* 10.1 and 1.32, CH=CH_2), 6.21 (1 H, d, *J* 17.6, CH–CH_2) and 6.36 (1 H, dd, *J* 17.6 and 10.1, C*H*=CH_2); δ_C(67.8 MHz; $CDCl_3$) 26.8 (t), 27.8 (t), 31.5 (t), 32.1 (t), 33.7 (t), 39.3 (t), 128.1 (t), 129.1 (d), 130.6 (d), 136.5 (d) and 200.3 (s); *m/z* (EI) 165.1283 ($M^+ - Br$. $C_{11}H_{17}O$ requires 165.1279), 176 (14%), 174 (14%), 109 (26%) and 55 (100%).

(*E*)-11-Iodoundeca-1,6-dien-3-one 44

Sodium iodide (114 mg, 0.76 mmol) was added in one portion to a stirred solution of the dienone **60** (83 mg, 0.38 mmol) in acetone (12 cm^3) at room temperature after which the mixture was heated under reflux in a nitrogen atmosphere for 3 h. The mixture was then cooled and evaporated under reduced pressure. The residue was dissolved in ether (12 cm^3), and the solution was then washed with aqueous sodium thiosulphate (10%; 10 cm^3). The aqueous layer was then back-extracted with ether (3 × 10 cm^3) after which the combined organic extracts were dried and evaporated under reduced pressure to leave the *iodide* **44** (98 mg, 98%) as a liquid; ν_{max}(film)/cm^{-1} 2936, 2857, 1677, 1490, 1457, 1383, 1352, 1300, 1111 and 642; δ_H(250 MHz; $CDCl_3$) 1.46 (2 H, app quin., *J* 7.2), 1.81 (2 H, app quin., *J* 7.5), 1.97–2.04 (2 H, m), 2.28–2.35 (2 H, m), 2.66 (2 H, t, *J* 7.5, CH_2CO), 3.18 (2 H, t, *J* 7.0, CH_2I), 5.41–5.45 (2 H, m, CH=CH), 5.84 (1 H, dd, *J* 10.1 and 1.7, CH=CH_2), 6.22 (1 H, dd, *J* 17.7 and 1.7, CH=CH_2) and 6.36 (1 H, dd, *J* 17.7 and 10.1, C*H*=CH_2); δ_C(67.8 MHz; $CDCl_3$) 6.92 (t), 26.7 (t), 30.1 (t), 31.2 (t), 32.8 (t), 39.3 (t), 128.0 (t), 129.0 (d), 130.5 (d), 136.4 (d) and 200.1 (s); *m/z* (EI) 292.0312 (M^+. $C_{11}H_{17}IO$ requires 292.0324),

165 (13%), 147 (8%), 109 (21%), 95 (34%) and 55 (100%). The product was used without further purification.

4-Cyclopentylcyclohexanone 61

Tributyltin hydride (100 mm^3, 0.38 mmol) was added dropwise over 5 min to a stirred solution of the iodide **44** (100 mg, 0.34 mmol) and AIBN (10 mg) in degassed benzene (90 cm^3) under a nitrogen atmosphere. The solution was heated under reflux for 5 min and then cooled to room temperature. Saturated aqueous potassium fluoride (20 cm^3) was added to the benzene solution, and the mixture was then stirred vigourously for 10 h. The organic layer was separated, dried and evaporated under reduced pressure to leave a residue which was purified by column chromatography on silica using pentane–dichloromethane (1 : 1) as eluent to give the cyclohexanone (57 mg, 99%) as a yellow oil; ν_{max}(film)/cm^{-1} 2951, 2865, 1717, 1450, 1329, 1245, 1171, 1114, 930, 756 and 669; δ_H(400 MHz; $CDCl_3$) 1.17–1.26 (2 H, m), 1.44–1.65 (8 H, m), 1.74–1.85 (2 H, m), 2.05–2.15 (2 H, m) and 2.31–2.38 (4 H, m, CH_2CO); δ_C(100 MHz; $CDCl_3$) 25.4 (2 × t), 31.0 (2 × t), 31.9 (2 × t), 41.0 (2 × t), 42.0 (d), 45.0 (d) and 212.7 (s); *m/z* (EI) 166.1333 (M^+. $C_{11}H_{18}O$ requires 166.1358), 137 (37%), 125 (100%), 110 (42%), 97 (18%) and 69 (74%).

Acknowledgements

We thank Fisons Pharmaceuticals for a Research Scholarship (to A. J. S.) and Glaxo Group Research Ltd, for a Research Fellowship (to D. S. W.). We also thank Drs J. Dixon (Fisons Pharmaceuticals) and R. F. Newton (Glaxo Group Research Ltd) for their interest.

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Paper 5/03363B
Received 14*th June* 1995
Accepted 2*nd August* 1995