# Acyl Radical Cyclizations in Synthesis. Part 4. Tandem Processes: The 7-*endo*/5-*exo* Serial Cyclization Approach to Enantiomerically Pure Bicyclo[5.3.0]decan-2-ones

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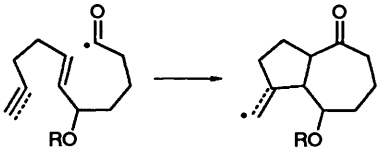
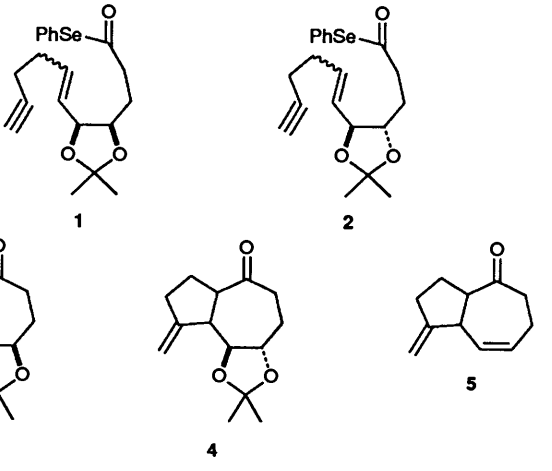
Two diastereoisomeric phenylselenoesters of 4,5-dihydroxyhept-6-enoic acid were prepared as their acetonide derivatives from the chiral pool. On treatment with tributyltin hydride and azoisobutyronitrile the *erythro* isomer cyclized to give *meso*-4,5-dihydroxycycloheptanone, as its acetonide, in moderate yield whereas under the same conditions the *threo*-isomer gave a much lower yield of the corresponding $C_2$-symmetric ketone. In the *erythro*-series an alkyl group at C-7 of the heptenoyl system was found to retard significantly the direct *endo*-mode cyclisation; however, the cycloheptanone could still be obtained by a rearrangement when the tin hydride concentration was kept to a minimum. A tandem 7-*endo*/5-*exo* cyclization system was then constructed and tested, resulting in the formation of all four possible diastereoisomeric bicyclo[5.3.0]decanones. Further model studies were conducted on the effect of alkyl and alkoxy substituents at C-5 of the heptenoyl radical system on the mode of cyclisation. Alkyl substituents exert a steric effect whilst alkoxy substituents also have a stereoelectronic effect.

Parts 1, 2 and 3 of this series describe our investigations into the synthesis of the A-ring of 1α,25-dihydroxyvitamin $D_3$ by acyl radical cyclization methodology. Specifically, Parts 1 and 2[1] outline the strategy and discuss model studies with particular focus on the influence of alkoxy groups at positions 3 and/or 5 on the mode and efficiency of hept-6-enoyl radical cyclizations, whilst Part 3[2] describes the channelling of this body of information into a successful, efficient synthesis of the A-ring ketone. Subsequently we,[3] and others,[4] have used this acyl radical cyclization route as a basis for palladium-mediated asymmetric partial syntheses of 1α,25-dihydroxyvitamin $D_3$. In this paper we describe the application of observations made in the course of our initial studies[1] to some tandem processes as well as further investigations into the directing effect of allylic ethers on acyl radical cyclizations. A part of this work has appeared as a preliminary communication.[5]




**Scheme 1**

Since the elegant pioneering work of Julia,[6] Stork[7] and Curran[8] the serial coupling of two radical cyclizations into what has come to be known as a tandem cyclization approach to bi- and tri-cyclic systems has been extensively exploited in synthesis.[9] With the notable exception of the Porter macrocyclizations[10] the vast majority of these tandem processes couple two 5-*exo*-mode cyclizations and only occasionally include a 6-membered-ring formation.[11] Our earlier observation that hept-6-enoyl radicals bearing either an alkoxy group or a spiro-fused 1,3-dioxolanyl group, *i.e.* two alkoxy groups, at the 5(allylic)-position underwent cyclization to give the *endo*-mode product with little or no formation of the *exo*-mode product led us to propose that a suitably functionalized homologue of a 5-alkoxyhept-6-enoyl radical would undergo tandem 7-*endo*/5-*exo* cyclization enabling formation of [5.3.0] fused bicyclodecanones in a single step (Scheme 1). Consideration of the perhydroazulene class of sesquiterpenoids led us to select the selenoesters **1** and **2** as cyclization precursors. After cyclization these would provide tricycles **3** and **4** which ultimately, by cleavage of the acetal and deoxygenation, would provide the azulenone **5**, an ideal precursor to the pseudoguaianolides and other sesquiterpenoids.[12] Retrosynthetically, precursor selenoesters **1** and **2** could be constructed from erythrose and threose, respectively, by chain elongation at both termini, enabling the eventual preparation of intermediates **3** and **4** as enantiomerically pure substances. This approach to a tandem *endo*/*exo* cyclization sequence differs fundamentally from that of Boger, also initiated with an acyl radical, that appeared whilst this work was in progress.[13,14] In the present approach the initial cyclization was to be directed to the *endo* mode by the allylic oxygen whilst in the Boger approach preferential closure in the *endo* mode was achieved more traditionally by substitution at the internal olefin position.




**1** **2** **3** **4** **5**

Before proceeding with the preparation of selenoesters **1** and/or **2** we decided to conduct a number of model experiments in order to determine which of the two possible stereochemis-

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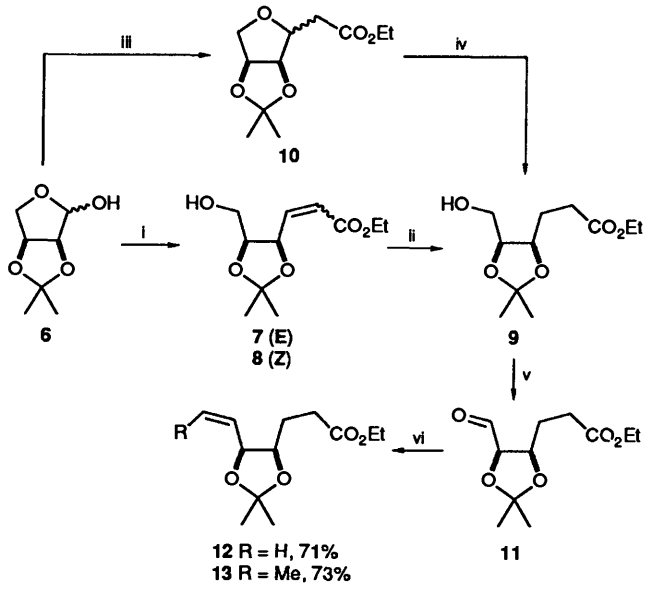
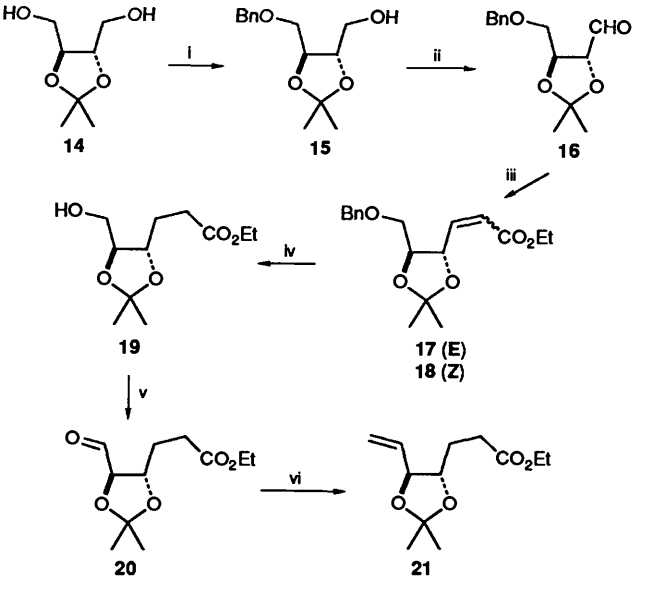
tries, *erythro* or *threo*, would be most suited to the required *endo*-mode cyclization. Also it was necessary to determine the effect of substituents at C-7 of the hept-6-enoyl system on the rate of the *endo* cyclization.




**Scheme 2** *Reagents, conditions and yields:* i, $Ph_3PCHCO_2Et$, $PhCO_2H$, heat (89%); ii, $H_2$, Pd/C, EtOH (91%); iii, $(EtO)_2P(O)CH_2CO_2Et$; iv, $H_2$, Pd/C, NaOEt, EtOH; v, PCC, NaOAc (93%); vi, $Ph_3PCHR$

In the *erythro* series (Scheme 2) we began with 2,3-*O*-isopropylidene-L-*erythro*-furanose **6**, which was prepared from L-rhamnose, by the method of Baxter,[15] in 71% overall yield.[16] Reaction of hemiacetal **6** with ethyl triphenylphosphoranylideneacetate and a catalytic quantity of benzoic acid in benzene at reflux, under conditions described by Corey for pyranose sugars,[17] gave the separable *E*- and *Z*-Wittig products **7** and **8** in 51 and 38% yield, respectively. Hydrogenation of a mixture of compounds **7** and **8** gave ester **9** in 91% yield. Attempted homologation of hemiacetal **6** with triethoxyphosphorylacetate gave not compounds **7** and **8** but the ring-closed tautomer **10** in 86% yield as a 1.4:1 mixture of anomers. The tetrahydrofuran **10** could be reduced to ring-opened compound **9** with hydrogen and palladium/charcoal in ethanol in the presence of sodium ethoxide but the reaction was slow and overall the Wittig procedure was simplest. The alcohol **9** was oxidized to the corresponding aldehyde **11** with sodium acetate-buffered pyridinium chlorochromate (PCC) in chloroform in the presence of 4 Å molecular sieves in excellent yield. A number of other oxidation conditions were surveyed, including unbuffered PCC, Swern oxidation, and Moffat oxidation, but in each case migration of the isopropylidene group to the 5,6-site was a problem. The aldehyde **11** was somewhat unstable and so bulk quantities of material were stored as the alcohol **9** and only converted into aldehyde **11** when necessary. Reaction of aldehyde **11** with methylenetriphenylphosphorane gave the ethyl heptenoate derivative **12** in 71% yield, whilst reaction with ethylidenetriphenylphosphorane gave the homologue **13** in 73% yield. The $^3J$ coupling constant ($\sim$10.9 Hz) between 6-H and 7-H in compound **13** was at the upper limit for *Z*-alkenes but the *Z* geometry of the double bond was evident from the observation of a nuclear Overhauser enhancement (NOE) effect between 5-H and 8-H.

In the *threo* series (Scheme 3) 2,3-*O*-isopropylidenethreitol **14**[18] was monobenzylated in 54% yield with sodium hydride and benzyl bromide in dimethyl sulfoxide (DMSO) to give




**Scheme 3** *Reagents, conditions and yields:* i, NaH, DMSO, BnCl (54%); ii, PCC, NaOAc, 4 Å sieves (87%); iii, $Ph_3PCHCO_2Et$ (71%); iv, $H_2$, Pd/C, EtOH (91%); v, PCC, NaOAc (92%); vi, $Ph_3PCH_2$ (52%)

compound **15**.* Oxidation of the alcohol **15** under the buffered PCC conditions gave the aldehyde **16** in 87% yield.† Wittig reaction then gave the adducts **17** and **18** in 71% combined yield as an approximately 1:1 mixture of separable geometrical isomers. Stirring of this mixture in ethanol under hydrogen with 5% palladium on charcoal effected reduction of the double bond and cleavage of the benzyl ether to give the alcohol **19** in 91% yield. Transformation of alcohol **19** into alkene **21** *via* aldehyde **20** (Scheme 3) followed the method described above for the *erythro* series.

Each of the esters **12**, **13** and **21** was saponified to the corresponding acid **22**, **25** and **28**, respectively, which was then converted into the respective selenoester **23**, **26** and **29** by reaction of the corresponding triethylammonium salt with benzeneselenenyl chloride and tributylphosphine according to a general protocol developed in our laboratory.[21]

Turning to the acyl radical cyclizations, treatment of the *erythro*-selenoester **23**, approx. 0.05 mol $dm^{-3}$ in benzene at reflux, dropwise with tributyltin hydride during 25–30 min followed by a further 1 h at reflux gave the expected four products: the aldehyde **24**, the cyclohexanones **31**, and the *meso*-cycloheptanone **32** in 7, 41 and 51% yield, respectively (Table 1, entry 1). Gratifyingly, under these conditions, which mimicked closely those used in our original studies, the cycloheptanone was the major product. The cyclohexanones **31** were obtained as an approximately 2:1 mixture of diastereoisomers from which the major isomer was obtained pure by careful chromatography on silica gel. It was not possible to obtain a pure sample of the minor isomer. From the closely related $^1H$ chemical shifts of the 2-Me group in both diastereoisomers ($\delta$ 1.15 and 1.16) and from the corresponding $^{13}C$ chemical shift[22] in the major isomer ($\delta_C$ 12.52) it can safely be assumed that both epimers have the 2-Me group in the more stable[23] pseudo-equatorial position. Examination of the $^1H$ chemical shifts of the isopropylidene Me groups in both epimers (major: $\delta$ 1.35 and 1.48; minor: $\delta$ 1.32 and 1.37) led us to the conclusion that the minor epimer has the all-*cis* geometry, as depicted in Fig. 1, whereas the major isomer has the C-2 Me group *trans* to the isopropylidene group. The *endo* isopropylidene Me group in the

* Seebach reports an 80% yield for this monobenzylation, but in DMF.[19]
† Mukaiyama reports an 85% yield for this oxidation under Swern conditions.[20]

**Table 1** Acyl radical cyclizations

| Entry | Substrate | Tin hydride addition time ($t$/h) | Products (% yield) |
|---|---|---|---|
| 1 | **23** | 0.5 | **24** (7), **31** (41), **32** (51) |
| 2 | **29** | 0.5 | **30** (44), **33** (19), **34** (10) |
| 3 | **29** | 11 | **33** (29), **34** (23) |
| 4 | **26** | 0.5 | **27** (7), **35** (91), **36** (3) |
| 5 | **26** | 8 | **27** (18), **35** (42), **36** (21) |
| 6 | **1** | 24 | **39** (20), **40** (13), **41** (4), **42**(8), **43** (20) |

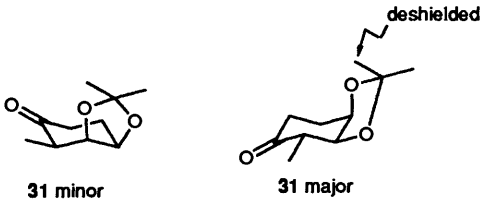
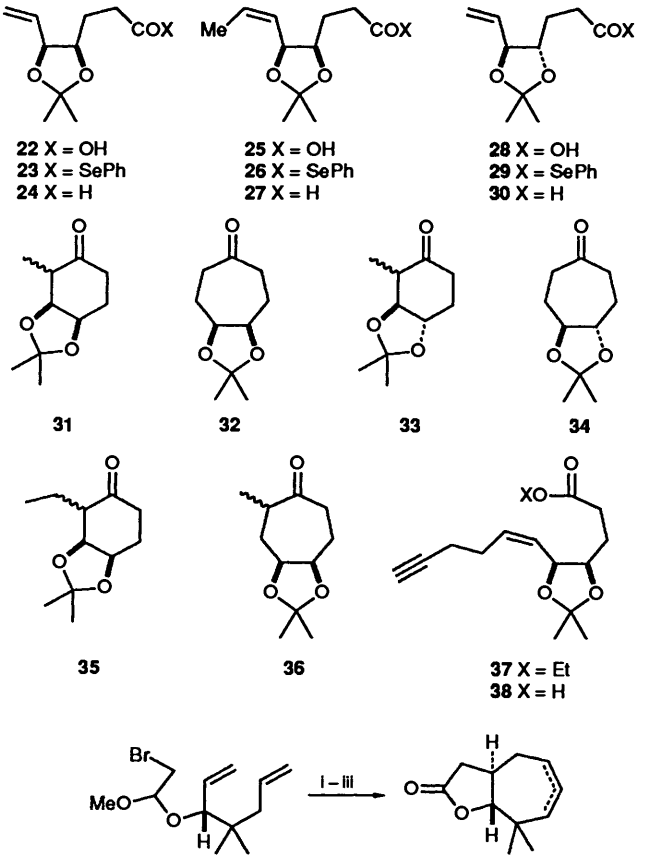



**Fig. 1**

major diastereoisomer is then deshielded by proximity to the deshielding cone of the carbonyl carbon, an interpretation that is borne out by inspection of Dreiding models. When the same reaction was carried out on the *threo*-seleno ester **29** the results were dramatically different (Table 1, entry 2) with the aldehyde **30** being isolated in 44% yield together with only 19% of an approximately 1.1:1 mixture of the cyclohexanones **33**, and a disappointing 10% of the $C_2$-symmetric ketone **34**. In view of the high yield of the aldehyde **30**, representative of a relatively slow cyclization, the reaction was repeated but with dropwise addition of the stannane over a period of 11 h (Table 1, entry 3). Although the yields of products **33** and **34** were thus improved to 29 and 23%, respectively, they were still less than those obtained in the *erythro*-series and hence no further investigations were carried out with compound **29**. Our examination of the *threo*-series selenoester **29** had been prompted by the knowledge that acetals of cyclohexane-1,2-diols form much more readily in the *cis* than the *trans* series,[24] whereas acetals of cycloheptane-1,2-diols are apparently formed with equal ease in either the *cis* or *trans* series.[25,*] In fact, force field calculations with COSMIC[27] indicate that the $C_2$-symmetric cycloheptanone **34** should be 1.0 kcal mol$^{-1}$ † lower in energy than its *meso*-counterpart **32**. The preference of 1,2-acetonides to be *cis*-fused to pyranose rings is well appreciated in carbohydrate chemistry[28] and has even been observed to result in the reversal of the usual propensity of alkoxyglycosyl radicals to undergo axial quenching.[29] We had therefore expected that in the *threo* series the cyclohexanone product would be destabilized and that a greater proportion of the cycloheptanone would be formed. It is evident from the results obtained that this is not the case and that these arguments, based on thermodynamic stabilities, cannot be extended to the early transition states of kinetically controlled radical cyclizations. In contrast, Pattenden has recently reported several examples of the type outlined in Scheme 4 in which the *trans*-fused [5.3.0]-system was formed exclusively to the detriment of the *trans*-fused [4.3.0]-system.[30] The evident differences between this system and the present one are the fusion of the larger onto the smaller ring and the removal of the radical process from the ring junction by one methylene group.

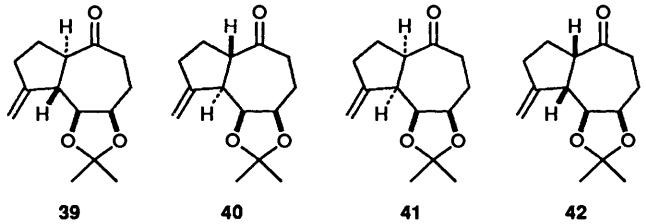
* Equilibration experiments by Allinger on bicyclo[5.3.0]decane itself indicate that the *cis*- and *trans*-form have virtually identical energies.[26]

† 1 cal = 4.184 J.




**Scheme 4** *Reagents and conditions:* i, Co[I]; ii, *hv*; iii, Jones oxidation

We next investigated the effect of a simple methyl group at C-7 on the heptenoyl cyclization. Treatment of the selenoester **26** with tributyltin hydride under the standard conditions gave 7% of the aldehyde **27**, 90% of a 2:1 mixture of cyclohexanones **35** and only 3% of the cycloheptanones **36** (Table 1, entry 4). Clearly, the internal nature of the alkene in substrate **26** very significantly retards direct *endo*-mode cyclization. From the spectral data available no firm conclusions could be drawn as to the relative stereochemistry of the two cyclohexanones **35** or of the cycloheptanones **36**, although, by analogy with compound **31**, we assign the minor epimer of **35** as being all-*cis*. The reaction was repeated but with addition of the stannane during 8 h, and this resulted in an increase in the yield of cycloheptanones to 21% (2:1 ratio of epimers) (Table 1, entry 5). This latter result is evidently due to ring expansion of the *exo*-mode cyclized radical, a point to which we will return below. Interestingly, the minor isomer of the cycloheptanone **36** in the rapid addition of tin hydride was the major isomer in the slow addition, perhaps suggesting that one isomer of compound **36** was formed by direct 7-*endo* cyclization and the other by the rearrangement mechanism.




Secure in the knowledge that C-7-substituted heptenoyl radicals could be induced to form cycloheptanones, by the *exo*-cyclization ring-expansion route, if not by direct *endo*-cycli-

**Table 2** $^1$H NMR parameters for stereoisomers **39–42**

| Compound | δ C=C$H_2$ | δ 5-H | δ 6-H | $J_{5,6}$ (Hz) | $J_{6,7}$ (Hz) | δ C$Me_2$ | Energy (kcal mol$^{-1}$)[a] | % Yield |
|---|---|---|---|---|---|---|---|---|
| **39** | 5.00, 5.23 | 4.40 | 4.25 | 6.5 | 9.0 | 1.38, 1.48, | −16.8 | 20 |
| **40** | 4.90, 5.08 | 4.55 | 4.65 | 8.0 | 2.1 | 1.41, 1.55 | −14.5 | 13 |
| **41** | 4.90, 5.06 | 4.47 | 4.60 | 7.6 | 0 | 1.30, 1.40 | −12.4 | 4 |
| **42** | 4.58, 6.09 | 4.05 | 3.85 | 5.4 | 10.8 | 1.32, 1.35 | −15.5 | 8 |

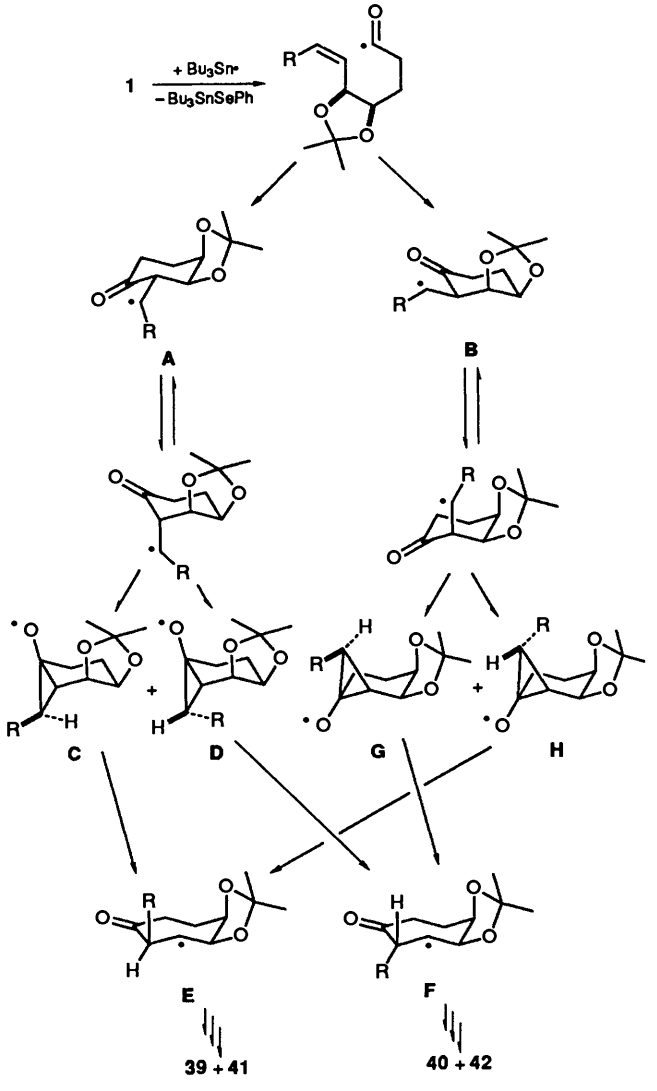
[a] 1 cal = 4.184 J.

zation, we turned to the preparation of the tandem cyclization precursor **1**. This was readily achieved by Wittig homologation of the aldehyde **11** with pent-4-ynylidenetriphenylphosphorane * to give the ester **37** in 66% yield. Saponification to the acid **38** and subsequent conversion into compound **1** in the usual manner was achieved in 76% overall yield. Treatment of compound **1** with tributyltin hydride during 30 min led to a complex reaction mixture containing only traces of the various stereoisomers of tricycle **3** as identified by the presence of signals corresponding to the exocyclic methylene protons in the $^1$H NMR spectrum. When the stannane was added over a period of 8 h a significant increase in the yield of compound **3** was observed from the $^1$H NMR spectrum of the crude reaction mixture. Ultimately (Table 1, entry 6) dropwise addition of the stannane during 24 h to a dilute solution of substrate **1** in benzene gave an isolated yield of approximately 45% of the combined stereoisomers of compound **3**. Separation of the isomers **39–42** was difficult and only one isomer (**41**) was obtained pure. However, from the various mixtures obtained from silica gel chromatography the salient $^1$H NMR features of each diastereoisomer were identified and configurational assignments ultimately made. The main spectroscopic features of each diastereoisomer are grouped in Table 2 together with their global energies as calculated with the COSMIC force field by Dr J. W. Davies of SmithKline Beecham Pharmaceuticals, Chemistry Support Group, whom we thank for his assistance with this problem.†[31] The cyclohexanones **43** were also identified in this reaction mixture in approximately 20% yield and an approximate ratio of 1:1. That compounds **39** and **42** form a pair of epimers differing only in configuration at C-1 is evident from the close similarity of their $J_{5,6}$ and $J_{6,7}$ coupling constants. Similarly, it can be seen that isomers **40** and **41** are a second pair of epimers, again differing in configuration at C-1. Further support for the epimeric nature of structure pairs **39** and **42**, and of **40** and **41**, at C-1 was obtained by base-catalysed epimerization. Storage of a mixture of isomers **39** and **42** in methanol with lithium hydroxide for 48 h caused complete conversion into **39**, confirming both the epimeric nature of these two compounds and the greater stability of isomer **39**. Likewise, a mixture of compounds **40** and **41** was enriched in isomer **40** under the same conditions. Moreover, the large value of $J_{6,7}$ in compounds **39** and **42** leads to the conclusion that the torsion angle H(6)–C(6)–C(7)–H(7) is approaching 180° in this pair of epimers and so to the indicated assignment of configuration at C-7. Unfortunately, neither 1-H, nor 7-H, was sufficiently resolved to enable unambiguous measurement of $J_{1,7}$ and so the *cis*- or *trans*-fused nature of the two carbocyclic rings in any diastereoisomer, hence this distinction was made on the basis of comparison of the calculated and observed relative stabilities of the products. On the basis that the formation of isomers **39–42** is occurring *via* a 6-*exo-trig* process followed by a ring expansion to the formal 7-*endo* product, and finally a 5-*exo-dig* cyclization it is reasonable to assume that the stereochemistry at C-1 is determined in the course of the initial 6-*exo* cyclization and the ring-expansion process. This being the case, and by analogy with the cyclization of selenoester **23** to compound **31** where the *exo*-Me isomer is the major product, we suggest that the acyl radical derived from compound **1** undergoes preferential 6-*exo* cyclization to the *exo*-Me stereoisomer **A**, together with a lesser amount of the all-*cis* diastereoisomer **B** (Scheme 5). The radical **A** may then react, by either of its two diastereotopic faces, with the carbonyl bond to give radicals **C** and **D**, which ultimately lead to carbon-centred radicals **E** and **F**, respectively, after fragmentation of the alkoxyl radical. It is in this step (**A** → **C** and **D**) that any selectivity probably occurs for clearly oxyl radical **D**, and the transition state leading to it, are much more sterically hindered than are its epimer **C** and the corresponding transition state. On this basis the major product is predicted to be the 1α-compound **39** or **41**. In agreement with this model, compound **39** is found to be the major product. On the other hand compound **41** is the least abundant of the four products formed. The molecular mechanics calculations, and simple Dreiding models, reveal that *cis*-isomer **41** is substantially strained and presumably this strain manifests itself in the second ring closure (**E** → **39** and **41**) and reduces isomer **41** to the status of minor product. The second most abundant product is isomer **40**. The two most abundant products, **39** and **40**, have the *trans*-fused bicyclo[5.3.0]heptanone skeleton which the calculations indicate is also the most stable. The formation of mixtures of *cis*-and *trans*-fused bicyclo[5.3.0]heptane skeletons in closely related systems has previously been observed by Clive but configurations were unfortunately not assigned.[32] Evidently a multitude of pathways is available (Scheme 5) for formation of the bicyclodecanone skeleton, resulting in a complex mixture of diastereoisomers. Nevertheless, the ability to equilibrate pairs of epimers at C-1 under basic conditions, and presumably to do so with alkylation, means that a relatively straightforward entry into the two *trans*-fused systems is at hand.

Returning to the question of direct *endo*-mode cyclizations and the influence of allylic oxygen groups, it is evident from the above studies that in systems unsubstituted at the alkene terminus and bearing allylic ether functionality (**23** → **32** and **44** → **45**) that *endo*-mode cyclization occurs directly, whereas when a substituent is introduced at C-7 the *endo*-mode product is formed *via* 6-*exo* cyclization and subsequent ring expansion as outlined in Scheme 5. The question to be answered is how does the allylic oxygen functionality direct cyclization to the *endo*-mode in compounds **23** and **44**? Is a stereoelectronic effect or a simple steric effect involved? To this end we elected to prepare the 5,5-dimethylselenoheptenoate **46** and to investigate its cyclization with tributyltin hydride. Reaction of 3-methylcyclohex-2-enone with lithium dimethylcuprate in the presence

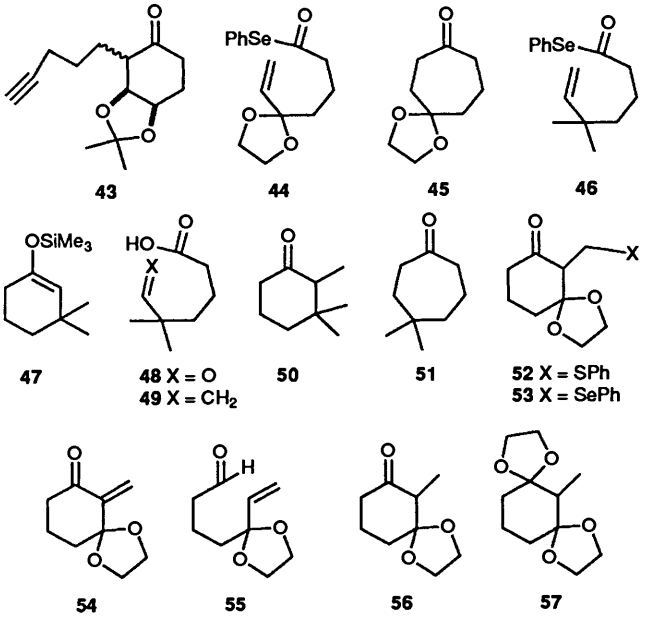
* We thank Dr P. J. Garratt, UCL, for donation of pent-4-ynyl(triphenyl)phosphonium iodide.

† MM-2 calculations by House on *cis*- and *trans*-bicyclo[5.3.0]decan-2-one indicate that the *trans* isomer is very slightly more stable than the *cis*; however, this was subsequently disputed by Peterson whose calculations found the *cis* isomer to be the more stable. Experimentally, House found that equilibration in benzene–methanol at 25 °C gave an 87:13 ratio of *trans*:*cis*.[31]




Scheme 5

of trimethylsilyl chloride and hexamethylphosphoric triamide (HMPA)[33] gave the silyl enol ether **47**[34] almost quantitatively. Ozonolysis of compound **47** in methanol–methylene dichloride followed by reductive work-up with dimethyl sulfide gave the acid **48** which was immediately converted into the hept-6-enoic acid **49** by the Wittig reaction. The unoptimized yield for these two steps was a disappointing 19% but nevertheless sufficient material was available to enable us to probe the radical cyclization. Transformation of acid **49** into its selenoester **46** was effected with benzeneselenenyl chloride and tributylphosphine in 76% yield in the usual manner. Treatment of ester **46** with tributyltin hydride under conditions as close as possible to those used for compounds **23** and **44** resulted in isolation of the cyclohexanone **50**[35] and the cycloheptanone **51**[36] in 20 and 30% yield, respectively. The identities of the two products were confirmed by comparison of spectral data with literature values. Comparison of this result with the cyclization of ester **44**[1] where no cyclohexanone formation was observed clearly indicates that the effect of the allylic oxygen moiety is not simply steric. In view of this result further verification that the cyclization of compound **44** → **45**[1] did indeed occur directly in the 7-*endo* mode was sought. Therefore, the (phenylthiomethyl)cyclohexanone **52**, itself inert towards tin hydride and AIBN for all practical purposes,[1] was stirred with magnesium monoperoxyphthalate in aq. ethanol at room temperature and the so-obtained crude sulfoxides were added, in toluene, to toluene at reflux, enabling us to isolate the labile α-methylenecyclohexanone **54** in 81% yield. More typical, gradual warming of a solution of the sulfoxides of **52** in toluene resulted in a much lower yield of compound **54**. Treatment of compound **54** with sodium triethoxy(phenylseleno)borate[37] in ethanol gave the phenylseleno adduct **53** in 25% yield after chromatography on silica gel. The selenide **53** is a white crystalline solid but is extremely susceptible to elimination and the low yield is largely due to decomposition during the chromatographic purification. Treatment of compound **53** with tributyltin hydride and AIBN in benzene at 80 °C did not result in the formation of **45**[1] nor in that of the aldehyde **55**,[1] but only in that of the cyclohexanone **56** whose identity was confirmed by comparison with an authentic sample prepared by controlled hydrolysis of its ketal **57**, suggesting that under the typical reaction conditions compound **45** was formed from selenoester **44** by direct *endo*-mode cyclization and also that acyl radical cyclizations are not reversible.




Turning to the reasons underlying the *endo*-directing effect of the allylic oxygen in esters **23** and **44** and related systems, we have previously suggested[1] that the answer is to be found in the reactive conformation of the allylic ether moiety. RajanBabu has suggested,[38] in the course of his investigation into the *cis–trans* selectivity of carbohydrate-derived hex-5-enyl radicals, that the allylic ether moiety probably adopts a conformation in which the carbon–oxygen bond is perpendicular to the plane of the π-system and that radical attack takes place antiperiplanar to this carbon–oxygen bond, and it is conceivable that this might be one of the factors operating here. Whatever the underlying reason the effect is clearly small and easily overridden by substitution at the alkene terminus (**29** → **33** and **34**, Table 1, entry 2) and by other bulky substituents in the carbon chain that accelerate the *exo*-mode cyclization.[2]

This ability of exocyclic allylic ethers to direct radical cyclizations to the *endo*-mode should not be restricted to the hept-6-enoyl radical cyclizations as studied here but should also exist in simple alkyl radical cyclizations. Indeed, perusal of the literature reveals examples of simple 4-alkoxy-substituted hex-5-enyl radicals and 5-alkoxy-substituted hept-6-enyl radicals which have been observed to cyclize preferentially in the *endo*-mode.[39] However, these examples are more the exception than the rule[35] for 4-alkoxyhex-5-enyl cyclizations. This is because the vast majority of such cyclization precursors are constructed from carbohydrates and are extensively substituted.

The combined effect of substituents at the 2-, 3- and 4-position of the hex-5-enyl radical, acceleration of the *exo*-mode cyclization,[40] is sufficient to overcome any regiodirecting influence of the allylic oxygen.

## Experimental

*General.*—M.p.s are uncorrected and were determined with a Kofler hot-stage microscope. Optical rotations were measured either with an Optical Activity AA-10 or a Perkin-Elmer 241 polarimeter; $[\alpha]_D$-values are given in units of $10^{-1}$ deg cm$^2$ g$^{-1}$. IR spectra were recorded with either a Perkin-Elmer 983 or 1605 spectrophotometer. $^1$H NMR spectra were recorded at 200, 300 or 400 MHz with either Varian XL 200, Bruker WM 200, Bruker AC 300, Varian VXR 400 or Bruker WM 400 instruments. $^{13}$C NMR spectra were recorded at 50,75 or 100 MHz with the same instruments operating in the $^{13}$C mode. Chemical shifts ($\delta$) are in ppm downfield from tetramethylsilane as internal standard, *J*-values are given in Hz. EIMS (70 eV) mass spectra were recorded with either a VG 7070H or an AEI MS-30 mass spectrometer. Microanalyses were performed by the UCL microanalytical laboratory or by Midwest Microanalytical, Indianapolis. All solvents were dried and distilled by standard techniques. Tetrahydrofuran (THF) was distilled under nitrogen from sodium benzophenone ketyl before use. Ether refers to diethyl ether and light petroleum to the fraction boiling in the range 40–60 °C.

(−)-*Ethyl* (2E,4R,5S)-4,5-*Isopropylidenedioxy*-6-*hydroxyhex*-2-*enoate* **7** *and* (−)-*Ethyl* (2Z,4R,5S)-4,5-*Isopropylidenedioxy*-6-*hydroxyhex*-2-*enoate* **8**.—2,3-*O*-Isopropylidene-L-erythrose **6** (1.11 g, 6.9 mmol), ethyl triphenylphosphoranylideneacetate (2.90 g, 8.32 mmol) and benzoic acid (40 mg, 0.4 mmol) were heated to reflux in dry benzene (80 cm$^3$) under nitrogen for 4 h. The mixture was allowed to cool to room temperature before the solvent was evaporated off under reduced pressure to give an off-white solid. This solid was extracted with cold ether (5 × 10 cm$^3$) and the ether was evaporated off to furnish a green oil which, on chromatography on silica gel [eluent ether–light petroleum (2:1)], yielded first the Z-*alkene* **8** (0.61 g, 38%) and subsequently the E-*alkene* **7** (0.82 g, 51%). The *Z*-alkene **8** was an oil with $[\alpha]_D^{23}$ −111.3 (*c* 1.5, EtOH); $\delta_H$(200 MHz) 1.30 (3 H, t, *J* 7.1, $CH_2Me$), 1.41 (3 H, $CMe_2$), 1.54 (3 H, $CMe_2$), 2.26 (1 H, br t, *J* 5.6, OH), 3.38–3.66 (2 H, m, 6-$H_2$), 4.18 (2 H, q, *J* 7.1, $CH_2$Me), 4.58 (1 H, m, 5-H), 5.60 (1 H, dt, $J_{2,4}$ 1.7, $J_{3,4} = J_{4,5}$ = 7.2, 4-H), 5.94 (1 H, dd, $J_{2,4}$ 1.7, $J_{2,3}$ 11.6, 2-H) and 6.39 (1 H, dd, $J_{2,3}$ 11.6, $J_{3,4}$ 7.2, 3-H); $\delta_C$(100 MHz) 14.14, 24.76, 27.41, 60.53, 61.55, 74.81, 78.92, 108.88, 121.12, 147.00 and 165.91; $\nu_{max}$(film)/cm$^{-1}$ 3479, 1709 and 1644 (Found: C, 57.4; H, 7.9. $C_{11}H_{18}O_5$ requires C, 57.38; H, 7.88%). The *E*-alkene **7**, an oil, had $[\alpha]_D^{22}$ −6.6 (*c* 1.7, EtOH); $\delta_H$(200 MHz) 1.30 (3 H, t, *J* 7.1, $CH_2Me$), 1.40 (3 H, $CMe_2$), 1.53 (3 H, $CMe_2$), 2.56 (1 H, br s, OH), 3.57 (2 H, br d, $J_{5,6}$ 5.7, 6-$H_2$), 4.21 (2 H, q, *J* 7.1, $CH_2$Me), 4.38 (1 H, dt, $J_{4,5} = J_{5,6}$ = 5.7, 5-H), 4.82 (1 H, dt, $J_{2,4}$ 1.6, $J_{3,4} = J_{4,5}$ = 5.7, 4-H), 6.14 (1 H, dd, $J_{2,4}$ 1.6, $J_{2,3}$ 15.6, 2-H) and 6.91 (1 H, dd, $J_{2,3}$ 15.6, $J_{3,4}$ 5.7, 3-H); $\nu_{max}$(film)/cm$^{-1}$ 3473, 1716 and 1657 (Found: C, 57.8; H, 8.1. $C_{11}H_{18}O_5$ requires C, 57.38; H, 7.88%).

(+)-*Ethyl* (4R,5S)-4,5-*Isopropylidenedioxy*-6-*hydroxyhexanoate* **9**.—A mixture of the unsaturated esters **7** and **8** (450 mg, 1.95 mmol) was stirred in ethanol (25 cm$^3$) with 5% palladium on charcoal (40 mg) under an atmosphere of hydrogen (balloon) for 2 h. The catalyst was removed by filtration on Celite, the solvent was evaporated off, and the residue was filtered on silica gel [eluent ether–light petroleum (4:1)] to give the *title compound* as a liquid (410 mg, 91%) with $[\alpha]_D^{22}$ +22.5 (*c* 2, EtOH); $\delta_H$(200 MHz) 1.26 (3 H, t, *J* 7.2, $CH_2Me$), 1.35 (3 H, $CMe_2$), 1.46 (3 H, $CMe_2$), 1.83 (2 H, m, 3-$H_2$), 2.30–2.65 (3 H, m, OH + 2-$H_2$), 3.66 (2 H, br d, $J_{5,6}$ 4.8, 6-$H_2$) and 4.1 (4 H, m, $CH_2$Me + 4- + 5-H); $\delta_C$(100 MHz) 13.88, 24.42, 25.17, 27.81, 30.79, 60.14, 60.96, 75.72, 77.59, 107.90 and 173.05; $\nu_{max}$($CHCl_3$)/cm$^{-1}$ 3577 and 1723 (Found: C, 56.9; H, 8.9. $C_{11}H_{20}O_5$ requires C, 56.88; H, 8.68%).

*Ethyl* [(3R,4S)-3,4-*Isopropylidenedioxytetrahydrofuran*-2-*yl*]-*acetate* **10**.—Under a dry nitrogen atmosphere potassium hydride (35%; 1.07 g, 9.4 mmol) was washed with light petroleum and then suspended in THF (20 cm$^3$). Ethyl diethoxyphosphonylacetate (2.30 g, 10.6 mmol) was then added dropwise and, after 30 min at room temperature, the mixture was treated with a solution of compound **6** (1.00 g, 6.2 mmol) in THF (10 cm$^3$). The reaction mixture was then brought to reflux for 1 h, cooled, and poured into a mixture of water (50 cm$^3$) and ether (50 cm$^3$). The aqueous layer was extracted further with ether (2 × 25 cm$^3$) and the combined ether phases were washed successively with water (20 cm$^3$) and brine (20 cm$^3$), dried ($MgSO_4$), and evaporated to yield an oil which, after chromatography on silica gel [eluent ether–light petroleum (2:1)], gave the *title compound* as an oil (1.24 g, 86%), as a 1.4:1 mixture of stereoisomers at C-2. The major isomer, which could be obtained almost pure on equilibration with sodium ethoxide in ethanol, was assigned the 2*R* configuration (*exo*-$CH_2CO_2Et$) on the basis of its greater thermodynamic stability and NOE data, was characterized by $\delta_H$(200 MHz) 1.28 (3 H, t, *J* 7.2, $CH_2Me$), 1.33 (3 H, $CMe_2$), 1.48 (3 H, $CMe_2$), 2.79 (2 H, d, *J* 6.7, $CH_2CO_2Et$), 3.50 (1 H, ddd, $J_{gem}$ 9.8, $J_{4,5}$ 3.4, $J_{3,5}$ 1.0, 5*exo*-H), 3.85 (1 H, m, 2-H), 4.02 (1 H, d, $J_{gem}$ 9.8, 5*endo*-H), 4.18 (2 H, q, *J* 7.2, $CH_2$Me) and 4.7 (2 H, m, 3- + 4-H). The minor isomer had salient features $\delta_H$(200 MHz) 1.45 (3 H, s), 1.51 (3 H, s), 2.48 (2 H, d, *J* 7.1), 3.5 (1 H, m), 4.18 (2 H, q), 4.46 (1 H, m) and 4.48 (1 H, m). A mixture of the two isomers had $\nu_{max}$(film)/cm$^{-1}$ 1735; *m/z* 215.0925 (M − Me$^+$) ($C_{10}H_{15}O_5$ requires *m/z*, 215.0937).

*Preparation of* (+)-*Ethyl* (4R,5S)-4,5-*Isopropylidenedioxy*-6-*hydroxyhexanoate* **9** *by Reduction of Bicycles* **10**.—To a stirred solution of the isomeric tetrahydrofurans **10** (250 mg, 1.1 mmol) in ethanol (20 cm$^3$) was added an ethanolic solution of sodium ethoxide (1 mol dm$^{-3}$; 0.11 cm$^3$, 0.11 mmol). After 5 min 5% palladium on charcoal (25 mg) was added and the reaction mixture was subsequently maintained under an atmosphere of hydrogen (balloon) and stirred for 7 days. The catalyst was then removed by filtration on Celite and the filtrate was concentrated under reduced pressure and purified by chromatography on silica gel [eluent ether–light petroleum (2:1)] to give, first, the recovered starting material as the more stable 2*R*-isomer (32 mg, 15%) and then the ester **9** (94 mg, 36%), identical in all respects with the sample described above.

*Ethyl* (4R,5R)-5-*Formyl*-4,5-*isopropylidenedioxypentanoate* **11**: *Typical Procedure for Buffered PCC Oxidations.*—To a stirred slurry of PCC (1.74 g, 8.1 mmol), sodium acetate (66 mg, 0.8 mmol) and powdered 4 Å molecular sieves (~0.75 g) in methylene dichloride (40 cm$^3$) under nitrogen at room temperature was added slowly a solution of the hydroxy ester **9** (750 mg, 3.23 mmol) in methylene dichloride (8 cm$^3$). After being stirred for 2.5 h at room temperature the reaction mixture was filtered on silica gel with elution by ether. Evaporation of the solvents under reduced pressure than gave the title aldehyde as a pale green oil (680 mg, 92%), which was used in the next step without further purification. The spectral characteristics were $\delta_H$(200 MHz) 1.21 (3 H, t, *J* 7.2, $CH_2Me$), 1.36 (3 H, $CMe_2$), 1.53 (3 H, $CMe_2$), 1.75 (1 H, m, 3-H), 1.85 (1 H, m, 3-H), 2.4 (2 H, m, 2-$H_2$), 4.09 (2 H, q, *J* 7.2, $CH_2$Me), 4.30 (2 H, m, 4- + 5-H) and 9.63 (1 H, dd, *J* 2.2 and 0.6, CHO); $\nu_{max}$(film)/cm$^{-1}$ 1736.

(+)-*Ethyl* (4R,5S)-*Isopropylidenedioxyhept-6-enoate* **12**.—Methyl(triphenyl)phosphonium bromide (0.84 g, 2.4 mmol) was slurried in THF (20 $cm^3$) at −20 °C under nitrogen and treated with butyllithium (2.33 mol $dm^{-3}$; 0.60 $cm^3$, 1.4 mmol), and the mixture was warmed to room temperature. After being stirred for a further 40 min at room temperature the reaction mixture was recooled to −20 °C and a solution of the aldehyde **11** (0.27 g, 1.2 mmol) in THF (3 $cm^3$) was added dropwise. The reaction mixture was maintained at −20 °C for 30 min then was allowed to warm to room temperature and was stirred for a further 2 h before being poured into ether (100 $cm^3$). After being stirred for 5 min the ether was filtered on Celite and evaporated to dryness under reduced pressure. Chromatography on silica gel [eluent light petroleum–ether (2:1)] gave the *title alkene* as a liquid (0.19 g, 71%) with $[\alpha]_D^{23}$ +20.7 (*c* 1.5, EtOH); $\delta_H$(200 MHz) 1.26 (3 H, t, *J* 7.1, $CH_2Me$), 1.36 (3 H, s, $CMe_2$), 1.48 (3 H, s, $CMe_2$), 1.75 (2 H, m, 3-$H_2$), 2.4 (2 H, m, 2-$H_2$), 4.15 (3 H, m, 4-H + $CH_2Me$), 4.52 (1 H, dd, $J_{4,5} = J_{5,6}$ = 6.3, 5-H), 5.25 (2 H, m, 7-$H_2$) and 5.8 (1 H, m, 6-H); $\nu_{max}$(film)/$cm^{-1}$ 1732 and 1644 (Found: C, 63.2; H, 8.9. $C_{12}H_{20}O_4$ requires C, 63.14; H, 8.76%).

*Ethyl* (4R,5S,6Z)-4,5-*Isopropylidenedioxyoct-6-enoate* **13**.—This substance was prepared in 73% yield analogously to the lower homologue **12** above from hydroxy ester **9** with the difference that ethyl(triphenyl)phosphonium iodide replaced methyl(triphenyl)phosphonium bromide. It was a *liquid* isolated by chromatography on silica gel [eluent light petroleum–ether (1:1)] and had $\delta_H$(200 MHz) 1.26 (3 H, t, *J* 7.3, $CH_2Me$), 1.36 (3 H, s, $CMe_2$), 1.46 (3 H, s, $CMe_2$), 1.70 (3 H, dd, $J_{7,8}$ 6.7, $J_{6,8}$ 1.3, 8-$H_3$), 1.75 (2 H, m, 3-$H_2$), 2.39 (2 H, m, 2-$H_2$), 4.10 (3 H, m, 4-H + $CH_2Me$), 4.96 (1 H, dd, $J_{4,5}$ 6.2, $J_{5,6}$ 8.9, 5-H), 5.47 (1 H, ddq, $J_{5,6}$ 8.9, $J_{6,7}$ 10.9, $J_{6,8}$ 1.3, 6-H) and 5.74 (1 H, dq, $J_{6,7}$ 10.9, $J_{7,8}$ 6.7, 7-H); $\delta_C$(100 MHz) 13.41, 14.24, 25.72, 25.98, 28.33, 30.83, 60.37, 73.61, 77.13, 108.06, 126.11, 128.98 and 173.39; $\nu_{max}$(film)/$cm^{-1}$ 1733 (Found: C, 64.2; H, 9.0. $C_{13}H_{22}O_4$ requires C, 64.44; H, 9.15%).

1-O-*Benzyl*-2,3-O-*isopropylidene*-L-*threitol* **15**.—Sodium hydride (60%; 136 mg, 3.39 mmol) was stirred in dry DMSO (5 $cm^3$) under nitrogen at room temperature for 30 min. A solution of 2,3-*O*-isopropylidene-L-threitol **14** (500 mg, 3.08 mmol) in DMSO (2 $cm^3$) was then added dropwise and the reaction mixture was stirred for a further 30 min before benzyl chloride (410 mg, 3.24 mmol) was added. The reaction mixture was stirred for 1.5 h at room temperature and was then poured into ice–water (25 $cm^3$) and extracted with ether (3 × 15 $cm^3$). The combined extracts were washed successively with water (5 $cm^3$) and brine (5 $cm^3$), dried ($MgSO_4$), and concentrated under reduced pressure. The resulting oil was purified by chromatography on silica gel [eluent light petroleum–ether (1:1)] to give the *title alcohol* as an oil (424 mg, 54%) with $[\alpha]_D^{23}$ +8.3 (*c* 2.9, $CHCl_3$); $\delta_H$(200 MHz) 1.40 (6 H, s, $CMe_2$), 2.50 (1 H, m, OH), 3.6 (4 H, m, 1- + 4-$H_2$), 3.95 (2 H, m, 2- + 3-H), 4.57 (2 H, s, $CH_2Ph$) and 7.32 (5 H, br s, Ph); $\nu_{max}$(film)/$cm^{-1}$ 3452 (Found: C, 66.5; H, 8.2. $C_{14}H_{20}O_4$ requires C, 66.65; H, 7.99%).

4-O-*Benzyl*-2,3-O-*isopropylidene*-L-*threose* **16**.—The threitol **15** (400 mg, 1.59 mmol) was oxidized with PCC (853 mg, 3.96 mmol) and sodium acetate (33 mg, 0.40 mmol) in methylene dichloride (24 $cm^3$) according to the typical procedure above. Filtration of the reaction mixture on silica gel and elution with ether gave the title compound as an oil (347 mg, 87%); $\delta_H$(200 MHz) 1.41 (3 H, s, $CMe_2$), 1.49 (3 H, s, $CMe_2$), 3.67 (2 H, d, $J_{3,4}$ 4.0, 4-$H_2$), 4.25 (2 H, m, 2- + 3-H), 4.60 (2 H, s, $CH_2Ph$) 7.33 (5 H, s, Ph) and 9.75 (1 H, d, $J_{1,2}$ 1.4, 1-H); $\nu_{max}$(film)/$cm^{-1}$ 1731.

*Ethyl* (2E,4S,5S)-6-*Benzyloxy*-4,5-*isopropylidenedioxyhex*-2-*enoate* **17** *and* (−)-*Ethyl* (2Z,4S,5S)-6-*Benzyloxy*-4,5-*isopropylidenedioxyhex*-2-*enoate* **18**.—Reaction of aldehyde **16** (1.00 g, 4.0 mmol) with ethyl triphenylphosphoranylideneacetate (2.09 g, 8.0 mmol) and benzoic acid (25 mg, 0.2 mmol) in benzene (100 $cm^3$) at reflux for 4 h as described above for the preparation of stereoisomers **7** and **8** gave, after chromatography on silica gel [eluent light petroleum–ether (5:1)], first the *Z*-alkene **18** as an oil (0.43 g, 36%) and then the E-*isomer* **17** (0.42 g, 35%) also as an oil. The *Z*-isomer **18** was characterized by $[\alpha]_D$ −13.4 (*c* 2.1, $CHCl_3$); $\delta_H$(200 MHz) 1.23 (3 H, t, *J* 7.1, $CH_2Me$), 1.44 (6 H, s, $CMe_2$), 3.66 (2 H, m, 6-$H_2$), 3.95 (1 H, m, 5-H), 4.12 (2 H, q, *J* 7.1, $CH_2Me$), 4.55 (1 H, d, $J_{gem}$ 12.0, $CH_2Ph$), 4.61 (1 H, d, $J_{gem}$ 12.0, $CH_2Ph$), 5.38 (1 H, ddd, $J_{3,4} = J_{4,5}$ = 8.3, $J_{2,4}$ 1.0, 4-H), 5.92 (1 H, dd, $J_{2,4}$ 1.0, $J_{2,3}$ 10.6, 2-H), 6.18 (1 H, dd, $J_{2,3}$ 10.6, $J_{3,4}$ 8.3, 3-H) and 7.31 (5 H, br s, Ph); $\nu_{max}$(film)/$cm^{-1}$ 1716 and 1652. The E-*isomer* **17** had $\delta_H$(200 MHz) 1.27 (3 H, t, *J* 7.1, $CH_2Me$), 1.42 (3 H, s, $CMe_2$), 1.44 (3 H, s, $CMe_2$), 3.62 (2 H, d, $J_{5,6}$ 4.7, 6-$H_2$), 3.94 (1 H, dt, $J_{4,5}$ 9.4, $J_{5,6}$ 4.7, 5-H), 4.18 (2 H, q, *J* 7.1, $CH_2Me$), 4.41 (1 H, ddd, $J_{2,4}$ 1.3, $J_{3,4}$ 5.5, $J_{4,5}$ 9.4, 4-H), 4.58 (2 H, s, $CH_2Ph$), 6.08 (1 H, dd, $J_{2,4}$ 1.3, $J_{2,3}$ 15.6, 2-H), 6.88 (1 H, dd, $J_{2,3}$ 15.6, $J_{3,4}$ 5.5, 3-H) and 7.32 (5 H, br s, Ph); $\nu_{max}$(film)/$cm^{-1}$ 1718 and 1661; *m/z* 305.1425 ($M - Me^+$) ($C_{17}H_{21}O_5$ requires *m/z*, 305.1389).

(−)-*Ethyl* (4S,5S)-6-*Hydroxy*-4,5-*isopropylidenedioxyhexanoate* **19**.—A mixture of enoates **17** and **18** (0.76 g, 2.4 mmol) was stirred under hydrogen (balloon) in ethanol (20 $cm^3$) with 5% palladium on charcoal (40 mg) for 6 h. Filtration on Celite, evaporation, and filtration on silica gel and elution with ether gave the *title ester* **19** as an oil (0.51 g, 91%) with $[\alpha]_D^{23}$ −24.1 (*c* 2.6, $CHCl_3$); $\delta_H$(400 MHz) 1.20 (3 H, t, *J* 7.1, $CH_2Me$), 1.34 (3 H, s, $CMe_2$), 1.35 (3 H, s, $CMe_2$), 1.80 (1 H, m, 3-H), 1.90 (1 H, m, 3-H), 2.4 (3 H, m, 2-$H_2$ + OH), 3.60 (1 H, m), 3.70 (2 H, m), 3.85 (1 H, m) and 4.10 (2 H, q, *J* 7.1, $CH_2Me$); $\delta_C$(100 MHz) 14.11, 26.94, 27.19, 27.88, 30.57, 60.45, 61.82, 76.09, 80.98, 108.82 and 173.22; $\nu_{max}$(film)/$cm^{-1}$ 3488 and 1721 (Found: C, 56.9; H, 8.9. $C_{11}H_{20}O_5$ requires C, 56.88; H, 8.68%).

*Ethyl* (4S,5R)-5-*Formyl*-4,5-*isopropylidenedioxypentanoate* **20**.—Buffered PCC oxidation of the alcohol **19** (440 mg, 1.89 mmol) as described for compound **11** above, gave the title aldehyde as an oil (0.40 g, 92%) with $\delta_H$(200 MHz) 1.20 (3 H, t, *J* 7.2, $CH_2Me$), 1.34 (3 H, s, $CMe_2$), 1.36 (3 H, s, $CMe_2$), 1.80 (2 H, m, 3-$H_2$), 2.40 (2 H, m, 2-$H_2$), 3.80 (2 H, m, 4- + 5-H), 4.09 (2 H, q, *J* 7.1, $CH_2Me$) and 9.63 (1 H, d, $J_{5,6}$ 2.2, CHO); $\nu_{max}$(film)/$cm^{-1}$ 1738.

*Ethyl* (4S,5S)-4,5-*Isopropylidenedioxyhept-6-enoate* **21**.—Reaction of the aldehyde **20** (330 mg, 1.43 mmol) with methyl(triphenyl)phosphonium bromide (1.40 g, 3.9 mmol) and butyllithium (2.33 mol $dm^{-3}$; 1.01 $cm^3$, 2.35 mmol) essentially as described for compound **12** above gave the title compound as an oil (172 mg, 52%) after chromatography on silica gel [eluent ether–light petroleum (1:1)]. It had $[\alpha]_D$ 0 (*c* 0.9, $CHCl_3$); $\delta_H$(200 MHz) 1.23 (3 H, t, *J* 7.1, $CH_2Me$), 1.38 (6 H, s, $CMe_2$), 1.85 (1 H, m, 3-H), 1.90 (1 H, m, 3-H), 2.45 (2 H, m, 2-$H_2$), 3.68 (1 H, ddd, $J_{3a,4} = J_{4,5}$ = 7.4, $J_{3b,4}$ 3.8, 4-H), 3.99 (1 H, dd, $J_{4,5} = J_{5,6}$ = 7.4, 5-H), 4.11 (2 H, q, *J* 7.1, $CH_2Me$) 5.20 (1 H, d, *J* 12, 7-H), 5.38 (1 H, d, *J* 16, 7-H) and 5.40 (1 H, ddd, *J* 16, 12, 7.4, 6-H); $\delta_C$(100 MHz) 14.20, 26.79, 26.92, 27.18, 30.67, 60.43, 79.53, 82.41, 108.80, 119.20, 134.99 and 173.12; $\nu_{max}$($CHCl_3$)/$cm^{-1}$ 1724.

(+)-(4R,5S)-4,5-*Isopropylidenedioxyhept-6-enoic Acid* **22**.—The ester **13** (200 mg, 0.88 mmol) was stirred at room temperature in THF–methanol (1:1; 10 $cm^3$) and treated with a solution of potassium hydroxide (0.30 g) in water (2.5 $cm^3$).

After being stirred overnight the reaction mixture was poured into a mixture of ether (100 $cm^3$) and water (100 $cm^3$) and was then acidified to pH 4 with 2 mol $dm^{-3}$ hydrochloric acid (~3 $cm^3$). The aqueous layer was extracted with ether (3 × 25 $cm^3$) and the combined organic phases were washed successively with water (2 × 40 $cm^3$) and brine (40 $cm^3$), and dried ($Na_2SO_4$). Evaporation of the solvent under reduced pressure and filtration on silica gel with ether as eluent gave the *title acid* as an oil (151 mg, 86%) with $[\alpha]_D^{22}$ +14.2 (*c* 1.9, $CHCl_3$); $\delta_H$(200 MHz) 1.34 (3 H, s, $CMe_2$), 1.45 (3 H, s, $CMe_2$), 1.72 (2 H, m, 3-$H_2$), 2.50 (2 H, m, 2-$H_2$), 4.15 (1 H, dt, $J_{3,4} = J_{4,5}$ = 7.8, 4-H), 4.54 (1 H, dd, $J_{4,5} = J_{5,6}$ = 7.8, 5-H), 5.25 (1 H, d, $J_{6,7}$ 10.3, 7-H), 5.34 (1 H, d, $J_{6,7}$ 18.1, 7-H) and 5.80 (1 H, ddd, $J_{5,6}$ 7.8, $J_{6,7}$ 10.3 and 18.1, 6-H); $\nu_{max}$(film)/$cm^{-1}$ 3426 and 1708; *m/z* 185.0834 (M − $Me^+$) ($C_9H_{13}O_4$ requires *m/z*, 185.0814).

(+)-Se-*Phenyl* (4R,5S)-4,5-(*Isopropylidenedioxy*)*selenohept*-6-*enoate* **23**: *Typical Procedure for Preparation of Selenoesters.*—The acid **22** (150 mg, 0.75 mmol) was dissolved in methylene dichloride (5 $cm^3$) under nitrogen and treated at room temperature with a solution of triethylamine (76 mg, 0.75 mmol) in methylene dichloride (2 $cm^3$). After 5 min the solvent was removed under reduced pressure to give a viscous oil, which was taken up in THF (5 $cm^3$) and added to a stirred solution of benzeneselenenyl chloride (172 mg, 0.90 mmol) and tributylphosphine (220 $mm^3$, 0.90 mmol) in THF (10 $cm^3$) under nitrogen at room temperature. After 45 min at room temperature the reaction mixture was poured into a mixture of ether (75 $cm^3$) and water (50 $cm^3$) and the aqueous layer was extracted with ether (2 × 20 $cm^3$). The combined organic phases were washed successively with water (25 $cm^3$) and brine (25 $cm^3$), dried ($MgSO_4$), and concentrated under reduced pressure to yield a green oil which, after chromatography on silica gel [eluent light petroleum–ether (10:1)] gave the *title selenoester* as an oil (183 mg, 72%) with $[\alpha]_D$ +25.5 (*c* 2.0, $CHCl_3$); $\delta_H$(200 MHz) 1.36 (3 H, s, $CMe_2$), 1.48 (3 H, s, $CMe_2$), 1.80 (2 H, m, 3-$H_2$), 2.90 (2 H, m, 2-$H_2$), 4.15 (1 H, dd, $J_{3,4} = J_{4,5}$ = 6.3, 4-H), 5.52 (1 H, dd, $J_{4,5} = J_{5,6}$ = 6.3, 5-H), 5.28 (1 H, d, $J_{6,7}$ 9.7, 7-H), 5.31 (1 H, d, $J_{6,7}$ 16.7, 7-H), 5.75 (1 H, ddd, $J_{5,6}$ 6.3, $J_{6,7}$ 9.7 and 16.7), 7.39 (3 H, m, Ph) and 7.52 (2 H, m, Ph); $\nu_{max}$(film)/$cm^{-1}$ 3072, 3056, 1722 and 1644 (Found: C, 56.9; C, 6.2. $C_{16}H_{20}O_3Se$ requires C, 56.64; H, 5.94%).

(+)-(4R,5S,6Z)-4,5-*Isopropylidenedioxyoct*-6-*enoic Acid* **25**.—The ester **13** (450 mg, 1.86 mmol) was saponified, essentially as described for the formation of **22** above, to give the *title acid* as a liquid (330 mg, 83%) with $[\alpha]_D^{23}$ +24.6 (*c* 2, $CHCl_3$); $\delta_H$(200 MHz) 1.38 (3 H, s, $CMe_2$), 1.48 (3 H, s, $CMe_2$), 1.70 (3 H, dd, $J_{6,8}$ 1.7, $J_{7,8}$ 5.3, 8-$H_3$), 1.80 (2 H, 3-$H_2$), 2.50 (2 H, m, 2-$H_2$), 4.16 (1 H, m, 4-H), 4.97 (1 H, dd, $J_{4,5}$ 6.1, $J_{5,6}$ 8.9, 5-H), 5.49 (1 H, dd, $J_{5,6} = J_{6,7}$ = 8.9, 6-H), 5.77 (1 H, dq, $J_{6,7}$ 8.9, $J_{7,8}$ 5.3, 7-H) and 10.2 (1 H, br s, $CO_2H$); $\nu_{max}$(film)/$cm^{-1}$ 3090 and 1707; *m/z* 214.1232 ($M^+$, $C_{11}H_{18}O_4$ requires *M*, 214.1205).

(+)-Se-*Phenyl* (4R,5S,6Z)-4,5-(*Isopropylidenedioxy*)*selenooct*-6-*enoate* **26**.—The acid **25** (300 mg, 1.40 mmol) was converted into the *selenoester* **26** according to the general protocol described above for the preparation of analogue **23**. It was an oil with $[\alpha]_D^{24}$ +50.4 (*c* 2.4, $CHCl_3$); $\delta_H$(200 MHz) 1.37 (3 H, s, $CMe_2$), 1.47 (3 H, s, $CMe_2$), 1.68 (3 H, dd, $J_{6,8}$ 1.7, $J_{7,8}$ 6.9, 8-$H_3$), 1.80 (2 H, m, 3-$H_2$), 2.92 (2 H, m, 2-$H_2$), 4.14 (1 H, dt, $J_{3,4} = J_{4,5}$ = 6.5, 4-H), 4.92 (1 H, dd, $J_{4,5}$ 6.5, $J_{5,6}$ 6.1, 5-H), 5.44 (1 H, dd, $J_{5,6}$ 6.1, $J_{6,7}$ 10.2, 6-H), 5.75 (1 H, dq, $J_{6,7}$ 10.2, $J_{7,8}$ 6.9, 7-H), 7.35 (3 H, m, Ph) and 7.55 (2 H, m, Ph); $\nu_{max}$(film)/$cm^{-1}$ 1721; *m/z* 339.0496 (M − $Me^+$) ($C_{16}H_{19}O_3Se$ requires *m/z*, 339.0499).

(+)-(4S,5S)-4,5-*Isopropylidenedioxyhept*-6-*enoic Acid* **28**.—The ester **21** (150 mg, 0.66 mmol) was saponified as described for the preparation of acid **22** above to give the title acid as an oil (107 mg, 82%), with $[\alpha]_D^{24}$ +6.8 (*c* 0.59, $CHCl_3$); $\delta_H$(200 MHz) 1.39 (6 H, s, $CMe_2$), 1.90 (2 H, m, 3-$H_2$), 2.50 (2 H, m, 2-$H_2$), 3.69 (1 H, dt, $J_{3a,4} = J_{4,5}$ = 8.2, $J_{3b,4}$ 3.8, 4-H), 4.00 (1 H, dd, $J_{4,5} = J_{5,6}$ = 8.2, 5-H), 5.25 (1 H, d, $J_{6,7}$ 10.2, 7-H), 5.38 (1 H, d, $J_{6,7}$ 16.7, 7-H) and 5.75 (1 H, ddd, $J_{5,6}$ 8.2, $J_{6,7}$ 10.2, 16.7, 6-H); $\nu_{max}$(film)/$cm^{-1}$ 3146, 1709 and 1644; *m/z* 185.0835 (M − $Me^+$) ($C_9H_{13}O_4$ requires *m/z*, 185.0814).

(−)-Se-*Phenyl* (4S,5S)-4,5-(*Isopropylidenedioxy*)*selenohept*-6-*enoate* **29**.—Application of the standard procedure for formation of selenoesters to acid **28** (90 mg, 0.45 mmol) gave the *title selenoester* **29** (89 mg, 60%) as an oil with $[\alpha]_D^{24}$ −9.5 (*c* 1.8, $CHCl_3$); $\delta_H$(200 MHz) 1.40 (6 H, s, $CMe_2$), 1.90 (2 H, m, 3-$H_2$), 2.90 (2 H, m, 2-$H_2$), 3.69 (1 H, ddd, $J_{3a,4} = J_{4,5}$ =8.8, $J_{3b,4}$ 4.4, 4-H), 3.98 (1 H, dd, $J_{4,5} = J_{5,6}$ = 8.8, 5-H), 5.23 (1 H, d, $J_{6,7}$ 10.2, 7-H), 5.40 (1 H, d, $J_{6,7}$ 16.7, 7-H), 5.75 (1 H, ddd, $J_{5,6}$ 8.8, $J_{6,7}$ 10.2, 16.7, 6-H), 7.35 (3 H, m, Ph) and 7.50 (2 H, m, Ph); $\nu_{max}$($CHCl_3$)/$cm^{-1}$ 1716 and 1644 (Found: C, 56.9; H, 6.3. $C_{16}H_{20}O_3Se$ requires C, 56.64; H, 5.94%).

*Reaction of Selenoester* **23** *with Tributyltin Hydride: Formation of Products* **24**, **31** *and* **32**.—The selenoester **23** (100 mg, 0.29 mmol) was heated to reflux under nitrogen in benzene (5 $cm^3$) and a solution of tributyltin hydride (94 mg, 0.32 mmol) and AIBN (~5 mg) in benzene (2 $cm^3$) was added during 25 min. Reflux was continued for 1 h after the addition was complete and then the solvents were removed under reduced pressure, and the residue was subjected to chromatography on silica gel. Elution with light petroleum–ether (5:1) gave (4*R*,5*S*)-4,5-isopropylidenedioxyhept-6-enal **24** as an unstable solid (5 mg, 7%) with $\delta_H$(200 MHz) 1.53 (3 H, s, $CMe_2$), 1.71 (3 H, s, $CMe_2$), 1.75 (2 H, m, 3-$H_2$), 2.60 (2 H, m, 2-$H_2$), 4.13 (1 H, dt, $J_{3,4} = J_{4,5}$ = 7, 4-H), 4.54 (1 H, dd, $J_{4,5} = J_{5,6}$ = 7, 5-H), 5.25 (1 H, d, $J_{6,7}$ 11, 7-H), 5.33 (1 H, d, $J_{6,7}$ 17, 7-H), 5.75 (1 H, m, 6-H) and 9.79 (1 H, t, $J_{1,2}$ 1.3, 1-H); $\nu_{max}$($CHCl_3$)/$cm^{-1}$ 1719.

Further elution with the same solvent gave the *cyclohexanones* **31** (22 mg, 41%). The ratio of the isomers of compound **31** was 2:1. A sample of the major isomer was obtained pure; it was assigned the 2*S*,3*S*,4*R*-configuration (see text) and had $[\alpha]_D^{23}$ +24.4 (*c* 0.9, $CHCl_3$); $\delta_H$(200 MHz) 1.15 (3 H, d, $J_{2,7}$ 7.1, 2-Me), 1.35 (3 H, s, $CMe_2$), 1.48 (3 H, s, $CMe_2$), 2.1 (3 H, m, 5-$H_2$ + 6-$H_{eq}$), 2.60 (2 H, m, 2-H + 6-$H_{ax}$), 4.05 (1 H, dd, $J_{2,3} = J_{3,4}$ = 6.8, 3-H) and 4.40 (1 H, m, 4-H); $\delta_C$(100 MHz) 12.52, 24.46, 25.17, 27.05, 34.12, 46.79, 72.20, 78.85, 108.67 and 211.61; $\nu_{max}$($CHCl_3$)/$cm^{-1}$ 1710; *m/z* 169.0889 (M − $Me^+$) ($C_9H_{13}O_3$ requires *m/z*, 169.0865). From a mixture of the two isomers the minor (2*R*)-isomer was found to have the following salient features: $\delta_H$(200 MHz) 1.16 (3 H, d, $J_{2,7}$ 6.8, 2-Me), 1.32 (3 H, s, $CMe_2$), 1.37 (3 H, s, $CMe_2$), 4.55 (1 H, dd, $J_{2,3}$ 3.2, $J_{3,4}$ 7.2, 3-H) and 4.58 (1 H, m, 4-H).

Yet further elution with the same solvent gave the *meso-cycloheptanone* **32** as an oil (28 mg, 51%) with $\delta_H$(400 MHz) 1.36 (3 H, s, $CMe_2$), 1.48 (3 H, s, $CMe_2$), 1.83 (2 H, m, 3- + 6-H), 2.10 (2 H, m, 3- + 6-H), 2.28 (2 H, ddd, *J* 16, 10, 2, 2- + 7-H), 2.71 (2 H, ddd, *J* 16, 11, 2.5, 2- + 7-H) and 4.37 (2 H, virtual multiplet, $w_{\frac{1}{2}}$ 9.3, 4- + 5-H); $\delta_C$(100 MHz) 24.81, 24.85, 27.20, 37.69, 76.11, 107.41 and 211.53; $\nu_{max}$($CHCl_3$)/$cm^{-1}$ 1698; *m/z* 169.0874 (M − $Me^+$) ($C_9H_{13}O_3$ requires *m/z*, 169.0865).

*Reaction of Selenoester* **29** *with Tributyltin Hydride: Formation of Products* **30**, **33** *and* **34**.—Tributyltin hydride (75 mg, 0.26 mmol) and AIBN (~1 mg) dissolved in benzene (1 $cm^3$) were added with a motor-driven syringe pump during 11 h to a solution of the selenoester **29** (75 mg, 0.22 mmol) in benzene (5 $cm^3$) at reflux under nitrogen. After cooling and removal of

solvent under reduced pressure the residue was chromatographed on silica gel [eluent light petroleum–ether (1:1)] to give, first, the aldehyde **30** as an oil (5.9 mg, 14%) with $\delta_H$(200 MHz) 1.39 (6 H, s, $CMe_2$), 1.90 (2 H, m, 3-$H_2$), 2.65 (2 H, m, 2-$H_2$), 3.67 (1 H, ddd, $J_{3a,4} = J_{4,5} = 8.3$, $J_{3b,4}$ 3.7, 4-H), 3.99 (1 H, dd, $J_{4,5} = J_{5,6} = 8.3$, 5-H), 5.25 (1 H, d, $J_{6,7}$ 10.2, 7-H), 5.38 (1 H, d, $J_{6,7}$ 17, 7-H), 5.80 (1 H, m, 6-H) and 9.79 (1 H, t, $J_{1,2}$ 1.3, 1-H); $\nu_{max}$(film)/$cm^{-1}$ 1711.

Further elution with the same solvent gave the *cyclohexanones* **33** as an approximately 1.1:1 mixture in the form of an oil (11.8 mg, 29%). The major isomer was characterised by $\delta_H$(400 MHz) 1.17 (3 H, d, $J_{2,7}$ 6.5, 2-Me), 1.45 (3 H, s, $CMe_2$), 1.51 (3 H, s, $CMe_2$), 3.25 (1 H, dd, $J_{2,3}$ 8.0, $J_{3,4}$ 12, 3-H) and 3.91 (1 H, ddd, $J_{3,4}$ 12, $J_{4,5}$ 9, 4, 4-H). Similarly the minor isomer had $\delta_H$(400 MHz) 1.20 (3 H, d, $J_{2,7}$ 8.0, 2-Me), 1.47 (3 H, s, $CMe_2$), 1.475 (3 H, s, $CMe_2$), 3.74 (1 H, dd, $J_{2,3}$ 6.0, $J_{3,4}$ 9.5, 3-H) and 4.05 (1 H, ddd, $J_{3,4}$ 9.5, $J_{4,5}$ 12, 4, 4-H). The mixture had *m/z* 169.0879 ($M - Me^+$) ($C_9H_{13}O_3$ requires *m/z* 196.0865).

Continued elution with the same solvent finally gave the 4S,5S-*cycloheptanone* **34**, also as an oil (9.4 mg, 24%), with $\delta_H$(400 MHz) 1.40 (6 H, s, $CMe_2$), 1.75 (2 H, m, 3- + 6-H), 2.22 (2 H, m, 3- + 6-H), 2.50 (4 H, m, 2- + 7-$H_2$) and 3.50 (2 H, m, 4- + 5-H); $\delta_C$(100 MHz) 25.36, 26.94, 39.27, 81.65, 108.38 and 212.12; $\nu_{max}$($CHCl_3$)/$cm^{-1}$ 1698; *m/z* 169.0856 ($M - Me^+$) ($C_9H_{13}O_3$ requires *m/z*, 196.0865).

*Reaction of Selenoester* **26** *with Tributyltin Hydride: Formation of Products* **27**, **35** *and* **36**.—The selenoester **26** (300 mg, 0.85 mmol) was heated to reflux in benzene (18 $cm^3$) under nitrogen and a solution of tributyltin hydride (272 mg, 0.93 mmol) and AIBN (5 mg) in benzene (5 $cm^3$) was added dropwise during 30 min. The reaction mixture was maintained at reflux for a further 1 h, then was cooled, and concentrated under reduced pressure to give a viscous oil, which was chromatographed on silica gel [eluent light petroleum–ether (5:1)] to give the unstable aldehyde **27** (11 mg, 6.5%) followed by a single isomer of the cyclohexanones **35** (70 mg, 42%). This isomer was identified as the *exo*-Et-(2*S*)-isomer. The configurations of the isomers of **35** were assigned by comparison of spectral data with those of the two isomers of the lower homologue **31**: the chemical shifts of the isopropylidene methyl groups and of 3- and 4-H were especially revealing in this respect. The major isomer of compound **35** was an oil with $[\alpha]_D^{24}$ +12.7 (*c* 1.6, $CHCl_3$); $\delta_H$(400 MHz) 0.94 (3 H, t, *J* 7.4, $CH_2Me$), 1.32 (3 H, s, $CMe_2$), 1.43 (3 H, s, $CMe_2$), 1.55 (1 H, m, $CH_2Me$), 1.60 (1 H, m, $CH_2Me$), 2.05 (2 H, m, 5-$H_2$), 2.15 (1 H, dt, $J_{gem}$ 15, $J_{5,6}$ 5, 6-$H_{eq}$), 2.45 (2 H, m, 2-H + 6-$H_{ax}$), 4.21 (1 H, dd, $J_{2,3}$ 5.1, $J_{3,4}$ 6.9, 3-H) and 4.39 (1 H, dt, $J_{3,4}$, 6.9, $J_{4,5}$ 4.6, 4-H); $\delta_C$(100 MHz) 12.22, 21.20, 24.38, 25.05, 26.85, 53.55, 71.85, 77.20, 108.24 and 211.34; $\nu_{max}$($CHCl_3$)/$cm^{-1}$ 1707; *m/z* 198.1286 ($M^+$) ($C_{11}H_{18}O_3$ requires *m/z*, 198.1256).

Further elution with the same solvent gave a 1:1 mixture (70 mg, 42%) of the isomeric cyclohexanones **35**. Yet further elution with the same solvent gave a 3:1 mixture (12 mg, 7%) of the minor isomer of **35** and the cycloheptanones **36**. From this latter mixture the main spectral features of the second isomer of compound **35** were determined to be $\delta_H$(400 MHz) 0.97 (3 H, t, *J* 7.4, $CH_2Me$), 1.34 (3 H, s, $CMe_2$), 1.37 (3 H, s, $CMe_2$), 1.45 (1 H, m), 2.0 (3 H, m), 2.25 (2 H, m), 2.45 (1 H, m), 4.55 (1 H, dt, $J_{3,4}$ 7.5, $J_{4,5}$ 2, 4-H) and 4.60 (1 H, dd, $J_{2,3}$ 3.1, $J_{3,4}$ 7.5, 3-H).

Similarly, from this latter mixture, the cycloheptanone **36** was seen to consist of an approximately 6:1 mixture of isomers at C-2. The major isomer of compound **36** had $\delta_H$(400 MHz) 1.05 (3 H, d, *J* 6.9, 2-*Me*), 1.38 (3 H, s, $CMe_2$), 1.53 (3 H, s, $CMe_2$), 1.66 (2 H, m), 2.30 (2 H, m), 2.69 (2 H, m), 3.00 (1 H, m), 4.35 (1 H, m) and 4.41 (1 H, m). The minor isomer of compound **36** was characterized by $\delta_H$(400 MHz) 1.09 (d, *J* 7, 2-Me). Overall the approximate yields of the cyclized products were calculated to be: **35** (major 63%; minor 26%); **36** (major 1.5%; minor 0.25%). When the tin hydride was added over a period of 8 h by means of a motor-driven syringe pump the yields of the cyclized products were found to be approximately as follows: **35** (major 30%; minor 12%); **36** (major 15%; minor 6%).

*Ethyl* (4R,5S,6Z)-4,5-*Isopropylidenedioxyundec*-6-*en*-10-*ynoate* **37**.—To a slurry of pent-4-ynyl(triphenyl)phosphonium iodide (1.88 g, 4.1 mmol) in THF (40 $cm^3$) at 0 °C under nitrogen was added butyllithium in hexanes (2.5 mol $dm^{-3}$; 1.65 $cm^3$, 4.1 mmol). This mixture was stirred for 20 min before a solution of freshly prepared aldehyde **11** (900 mg, 3.9 mmol) in THF (10 $cm^3$) was added. The mixture was stirred for a further 2 h during which time the reaction mixture was allowed to warm to room temperature before it was poured into ether (100 $cm^3$). Filtration on Celite, concentration, and chromatography on silica gel [eluent light petroleum–ether (5:1)] gave the *title ester* **37** as an oil (731 mg, 66%) with $\delta_H$(200 MHz) 1.15 (3 H, t, *J* 7, $CH_2Me$), 1.24 (3 H, s, $CMe_2$), 1.35 (3 H, s, $CMe_2$), 1.66 (2 H, dt, $J_{2,3} = J_{3,4} = 7.4$, 3-$H_2$), 1.91 (1 H, br s, 11-H), 2.2 (6 H, m, 2-, 8- + 9-$H_2$), 4.0 (3 H, m, $CH_2Me$ + 4-H), 4.81 (1 H, dd, $J_{4,5}$ 6.2, $J_{5,6}$ 9.0, 5-H), 5.44 (1 H, dd, $J_{5,6}$ 9.0, $J_{6,7}$ 10.9, 6-H) and 5.58 (1 H, m, 7-H); $\delta_H$(50 MHz) 14.10, 18.55, 25.55, 26.09, 26.81, 30.82, 60.06, 68.96, 73.89, 77.34, 83.23, 108.09, 127.10, 131.95 and 172.93; $\nu_{max}$(film)/$cm^{-1}$ 3292, 2118 and 1734 (Found: C, 68.2; H, 8.7. $C_{16}H_{24}O_4$ requires C, 68.54; H, 8.63%).

(4R,5S,6Z)-4,5-*Isopropylidenedioxyundec*-6-*en*-10-*ynoic Acid* **38**.—The ester **37** (700 mg, 2.5 mmol) was saponified essentially as described for the preparation of acid **22** above to give the acid **38** as an oil (628 mg, 99%) with $\delta_H$(200 MHz) 1.37 (3 H, s, $CMe_2$), 1.48 (3 H, s, $CMe_2$), 1.78 (2 H, m, 3-$H_2$), 1.98 (1 H, br s, 11-H), 2.35 (6 H, m, 2-, 8- + 9-$H_2$), 4.15 (1 H dt, $J_{3,4}$ + $J_{4,5}$ 6.7, 4-H), 4.93 (1 H, dd, $J_{4,5}$ 6.7, $J_{5,6}$ 9.0, 5-H), 5.56 (1 H, dd, $J_{5,6}$ 9.0, $J_{6,7}$ 10.9, 6-H) and 5.75 (1 H, m, 7-H); $\delta_C$(50 MHz) 18.65, 25.66, 25.99, 26.92, 28.34, 30.66, 60.08, 73.98, 77.33, 83.43, 108.45, 126.95, 132.37 and 178.55; $\nu_{max}$(film)/$cm^{-1}$ 3295, 2118 and 1711.

Se-*Phenyl* (4R,5S,6Z)-4,5-(*Isopropylidenedioxy*)*selenoundec*-6-*en*-10-*ynoate* **1**.—The acid **38** (337 mg, 1.3 mmol) was subjected to the typical procedure for the preparation of selenoesters, as described above for selenoester **23** to give, after chromatography on silica gel [eluent light petroleum–ether (10:1)], the *title selenoester* **1** as an oil (398 mg, 76%) with $\delta_H$(400 MHz) 1.38 (3 H, s, $CMe_2$), 1.48 (3 H, s, $CMe_2$), 1.80 (2 H, m, 3-$H_2$), 1.98 (1 H, t, $J_{9,11}$ 1.1, 11-H), 2.30 (4 H, m, 8- + 9-$H_2$), 2.78 (1 H, ddd, $J_{gem}$ 16.0, $J_{2,3}$ 8.4, 7.2, 2-H), 2.88 (1 H, ddd, $J_{gem}$ 16.0, $J_{2,3}$ 8.4, 6.0, 2-H), 4.13 (1 H, ddd, $J_{3,4}$ 9.6, 4.4, $J_{4,5}$ 6.4, 4-H), 4.89 (1 H, dd, $J_{4,5}$ 6.4, $J_{5,6}$ 8.8, 5-H), 5.50 (1 H, dd, $J_{5,6}$ 8.8, $J_{6,7}$ 10.8, 6-H), 5.67 (1 H, m, 7-H), 7.38 (3 H, m) and 7.50 (2 H, m); $\delta_C$(100 MHz) 18.87, 25.93, 26.68, 27.08, 28.57, 44.39, 69.40, 74.05, 77.21, 83.62, 108.65, 126.67, 126.98, 129.14, 129.60, 132.70, 136.01 and 200.07; $\nu_{max}$(film)/$cm^{-1}$ 3294, 2118 and 1723 (Found: C, 61.0; H, 6.2. $C_{20}H_{24}O_3Se$ requires C, 61.38; H, 6.18%).

*Tandem Cyclization Reaction*.—To a solution of the selenoester **1** (700 mg, 1.8 mmol) in benzene (150 $cm^3$) under nitrogen was added a solution of tributyltin hydride (625 mg, 2.2 mmol) and AIBN (10 mg) in benzene (10 $cm^3$) during 24 h by means of a motor-driven syringe pump, after which a further solution of AIBN (20 mg) in benzene (10 $cm^3$) was again added during 24 h to give a total reaction time of 48 h. The reaction mixture was cooled to room temperature and the solvent was removed under reduced pressure. Filtration on silica gel [eluent light petroleum–ether (5:1)] gave, first, the corresponding aldehyde (~40 mg, 9%) with $\delta_H$(400 MHz) 1.32 (3 H, s, $CMe_2$), 1.48 (3 H,

s, $CMe_2$), 1.97 (1 H, t, 11-H), 4.39 (1 H, m, 4-H), 4.87 (1 H, dd, *J* 6.7 + 2.2, 5-H), 5.48 (1 H, dd, *J* 8.9 + 2.2, 6-H), 5.67 (1 H, m, 7-H) and 9.77 (1 H, t, *J* 1.7, 1-H). Further elution gave an approximately 1:1:4 mixture (282 mg, 65%) of the isomeric cyclohexanones **43a** and **43b** and the bicyclodecanones **3** (**39**–**42**). Chromatography of this mixture on silica gel eluting with light petroleum–ether (10:1) gave a number of fractions of various enriched combinations of compounds **39**–**43** from which the most prominent spectral features of each were obtained and these, together with approximate yields, are presented in Table 2. Ultimately a pure sample (5 mg) of one diastereoisomer (**41**) was obtained by preparative TLC [silica gel; developer light petroleum–ether (10:1)] and then recrystallization from light petroleum–ether. This substance had m.p. 124–126 °C; $\delta_H$(400 MHz) 1.30 (3 H, s, $CMe_2$), 1.40 (3 H, s, $CMe_2$), 1.80 (1 H, m), 2.00 (2 H, m), 2.20 (2 H, m), 2.40 (2 H, m), 2.78 (1 H, ddd, *J* 16, 12, 5), 3.10 (2 H, m), 4.47 (1 H, ddd, $J_{5,6}$ 7.6, $J_{4,5}$ 1.8 and > 1, 5-H), 4.60 (1 H, d, $J_{5,6}$ 7.6, 6-H), 4.88 (1 H, br s, =C*H*H) and 5.06 (1 H, br s, =CH*H*); $\delta_C$(75 MHz) 24.30, 25.41, 26.61, 32.75, 38.05, 42.16, 51.72, 74.85, 80.35, 105.50, 108.22, 153.64 and 204.92; $\nu_{max}(CHCl_3)/cm^{-1}$ 1701 and 1601.

A pure sample of the all-*cis*-diastereoisomer of the cyclohexanone **43**, an oil, was also obtained by PTLC [developer light petroleum–ether (10:1)]: it had $\delta_H$(300 MHz) 1.34 (3 H, s, $CMe_2$), 1.38 (3 H, s, $CMe_2$), 1.6 (4 H, m), 1.96 (1 H, t, *J* 2.8, CCH), 2.05 (3 H, m), 2.22 (1 H, dd, *J* 7.0 and 2.6), 2.27 (1 H, ddd, *J* 12, 5.0 and 2.0), 2.36 (1 H, t, *J* 6.7), 2.47 (1 H, ddd, 18, 12 and 5.3) and 4.58 (2 H, br s, $w_{\frac{1}{2}}$ 12, 4- + 5-H); $\delta_C$(75 MHz) 18.55, 24.64, 24.77, 25.77, 26.23, 33.37, 49.31, 68.41, 72.21, 76.05, 84.21, 107.69 and 210.12.

The other diastereoisomer of compound **43**, which was not obtained completely pure, was characterized by $\delta_H$(400 MHz) 1.36 (3 H, s, $CMe_2$), 1.49 (3 H, s, $CMe_2$), 1.95 (1 H, t, CCH), 4.22 (1 H, m) and 4.41 (1 H, m). Assignment of configuration of the diastereoisomers of compound **43** was by comparison with the spectral data of the isomers of compound **31**.

3,3-*Dimethyl*-1-(*trimethylsiloxy*)*cyclohexene* **47**.—To a stirred solution of copper(I) bromide–dimethyl sulfide complex (3.73 g, 18.2 mmol) in ether (50 $cm^3$) under nitrogen at 0 °C was added dropwise a solution of methyllithium in hexanes (1.4 mol $dm^{-3}$; 23.3 $cm^3$, 32.6 mmol). To the resulting clear solution was added dropwise a solution of 3-methylcyclohex-2-enone (1.00 g, 9.1 mmol) and trimethylsilyl chloride (2.96 g, 27.2 mmol) in ether (10 $cm^3$). After the mixture had been stirred for a further 15 min at 0 °C triethylamine (3.8 $cm^3$) and HMPA (1.9 $cm^3$) were added sequentially. The mixture was stirred at 0 °C for 1 h and then at room temperature for 1 h before being poured into hexanes (100 $cm^3$) and then rapidly washed successively with dil. hydrochloric acid (1 mol $dm^{-3}$; 2 × 25 $cm^3$) and aq. sodium hydrogen carbonate (2 × 25 $cm^3$), dried ($MgSO_4$), and evaporated to yield the title siloxy compound as an oil (1.74 g, 99%) whose spectral data were in accord with the literature values[34] and which was used without further purification in the next step.

5,5-*Dimethylhept*-6-*enoic Acid* **49**.—A solution of the siloxy compound **47** (1.87 g, 9.7 mmol) at −78 °C in a 1:1 mixture of methylene dichloride and methanol (20 $cm^3$) was saturated with ozone. The reaction was quenched by addition of dimethyl sulfide (1 $cm^3$), then was allowed to warm to room temperature before the solvents were evaporated off under reduced pressure. The residue was taken up in hexane (30 $cm^3$) and extracted with 5% aq. sodium hydrogen carbonate (4 × 10 $cm^3$). After acidification with dil. hydrochloric acid (4 × 25 $cm^3$) the aqueous phase was extracted with ether (4 × 25 $cm^3$) and the extracts were washed with brine (25 $cm^3$), dried ($MgSO_4$), filtered, and evaporated to yield the crude aldehydo acid **48** as an oil (627 mg, 44%) with $\delta_H$(300 MHz) 0.85 (6 H, s), 1.52 (4 H, m), 2.32 (2 H, t, *J* 6.9) and 9.42 (1 H, s); $\delta_C$(75 MHz) 19.40, 21.12, 34.16, 36.18, 45.60, 179.09 and 206.01; $\nu_{max}$(film)/$cm^{-1}$ 3088 and 1720.

Without further purification, a solution of this aldehyde (600 mg, 3.8 mmol) in DMSO (10 $cm^3$) was added dropwise at room temperature under nitrogen to a solution of methylene(triphenyl)phosphorane in DMSO (40 $cm^3$) formed by dissolution of sodium hydride (80%; 569 mg, 19 mmol) in DMSO (40 $cm^3$) at 70 °C under nitrogen for 40 min followed by cooling to room temperature and treatment with methyl(triphenyl)phosphonium bromide (3.39 g, 9.5 mmol) and then stirring of the mixture for 30 min. After being stirred for 2 h at room temperature the red final reaction mixture was poured into a mixture of light petroleum (50 $cm^3$) and water (100 $cm^3$) and the aqueous layer was separated, acidified with dil. hydrochloric acid, and extracted with ether (4 × 25 $cm^3$). The combined extracts were washed with brine (30 $cm^3$), dried ($MgSO_4$), evaporated, and chromatographed on silica gel [eluent light petroleum–ether (5:1)] to give the title acid **49** as an oil (110 mg, 19%) with $\delta_H$(300 MHz) 0.98 (6 H, s), 1.28 (2 H, m), 1.54 (2 H, m), 2.29 (2 H, t, *J* 7.5), 4.88 (1 H, d, *J* 8.7), 4.90 (1 H, d, *J* 17.1) and 5.73 (1 H, m); $\delta_C$(75 MHz) 14.92, 26.52, 34.56, 36.37, 41.88, 110.56, 147.87 and 179.43; $\nu_{max}$(film)/$cm^{-1}$ 3086, 1712 and 1639; *m*/*z* 156 ($M^+$).

Se-*Phenyl* 5,5-*Dimethyl*(*selenohept*-6-*enoate*) **46**.—The acid **49** (80 mg, 0.51 mmol) was subjected to the typical procedure for selenoester formation, as described for compound **23** above, to give, after chromatography on silica gel [eluent light petroleum–ether (5:1)], the *title selenoester* **46** as an oil (114 mg, 76%) with $\delta_H$(300 MHz) 1.00 (6 H, s), 1.33 (2 H, m), 1.62 (2 H, m), 2.68 (2 H, t, *J* 7.3), 4.91 (1 H, d, *J* 8.8), 4.95 (1 H, d, *J* 17.0), 5.75 (1 H, dd, *J* 17.2, 11), 7.38 (3 H, m) and 7.52 (2 H, m); $\delta_C$(75 MHz) 20.68, 26.56, 36.45, 41.61, 48.00, 110.76, 126.50, 128.72, 129.24, 135.72, 147.72 and 200.16; $\nu_{max}$(film)/$cm^{-1}$ 1726 and 1640; *m*/*z* 296.0686 ($M^+$) ($C_{15}H_{20}OSe$ requires *m*/*z*, 296.0679).

*Reaction of Selenoester* **46** *with Tributyltin Hydride: Formation of Ketones* **50** *and* **51**.—To a solution of the selenoester **46** (50 mg, 0.17 mmol) in benzene (5.0 $cm^3$) at reflux under nitrogen was added dropwise a solution of tributyltin hydride (59 mg, 0.20 mmol) and AIBN (1 mg) in benzene (1.0 $cm^3$) during 15 min. The solution was heated to reflux for a further 1 h, cooled to room temperature, and concentrated under reduced pressure. Subsequent chromatography on silica gel [eluent light petroleum–ether (10:1)] afforded 2,3,3-trimethylcyclohexanone **50** as an oil (5 mg, 20%) with $\delta_H$(300 MHz) 0.76 (3 H, s), 0.96 (3 H, d, *J* 7.2), 1.04 (3 H, s), 1.65 (3 H, m), 1.85 (2 H, m) and 2.25 (2 H, m); $\delta_C$(75 MHz) 9.57, 14.22, 20.84, 22.62, 29.56, 39.57, 40.83 and 54.56; $\nu_{max}(CHCl_3)/cm^{-1}$ 1701. The literature data[35] for this compound are $\delta_H$(60 MHz; $CCl_4$) 0.73 (3 H, s), 0.87 (3 H, d, *J* 7), 1.03 (3 H, m) and 1.45–2.50 (7 H, m).

Further elution with the same solvent system yielded 4,4-dimethylcycloheptanone **51** as an oil (7 mg, 30%) with $\delta_H$(300 MHz) 0.95 (6 H, s), 1.30 (4 H, m), 1.60 (2 H, m) and 2.45 (4 H, m); $\delta_C$(75 MHz) 19.82, 28.68, 33.27, 36.21, 39.35, 43.19 and 43.73; $\nu_{max}(CHCl_3)/cm^{-1}$ 1709. The literature data[36] for this compound are $\delta_H$(60 MHz) 0.9 (s), 1.3–1.7 (m) and 2.1–2.25 (m); $\delta_C$ 19.0, 27.7, 32.4, 35.4, 38.2, 42.5 and 210.9 (the $\delta_C$ data were originally quoted for $CS_2$ as internal standard and have been converted to $SiMe_4$ scale by using $\delta$ $CS_2$ = 192.3).

3,3-*Ethylenedioxy*-2-*methylenecyclohexanone* **54**.—To a stirred solution of the 2-(phenylthiomethyl)cyclohexanone **52**[1] (115 mg, 0.41 mmol) in ethanol (5 $cm^3$) at room temperature under nitrogen was added a solution of magnesium monoperoxyphthalate (80%; 123 mg, 0.25 mmol) in water (1.5 $cm^3$)

dropwise during 20 min. The reaction mixture was stirred for a further 30 min, then was poured into chloroform (25 $cm^3$), washed successively with 5% aq. sodium hydrogen carbonate (2 × 15 $cm^3$) and brine (15 $cm^3$), dried ($MgSO_4$), and evaporated to give the crude sulfoxides as an oil (139 mg). This mixture of sulfoxides was taken up in toluene (0.5 $cm^3$) and added dropwise to toluene (10 $cm^3$) at reflux under nitrogen. Reflux was continued for 1 h before the reaction mixture was allowed to cool to room temperature; the mixture was then concentrated, and purified by chromatography on silica gel [eluent light petroleum–ether (2:1)] to afford the title α-methylenecyclohexanone as an oil (56 mg, 81%) with $\delta_H$(200 MHz) 1.95 (4 H, m), 2.46 (2 H, t, *J* 5.8), 3.90 (4 H, m), 5.56 (1 H, d, $J_{gem}$ 1.9) and 5.89 (1 H, d, $J_{gem}$ 1.9); $\delta_C$(50 MHz) 18.20, 34.41, 34.69, 64.67, 108.09, 119.42, 147.37 and 200.56; $\nu_{max}$-($CHCl_3$)/$cm^{-1}$ 1692 and 1627; *m/z* 168 ($M^+$).

3,3-*Ethylenedioxy*-2-(*phenylselenomethyl*)*cyclohexanone* **53**.—To a stirred solution of diphenyl diselenide (100 mg, 0.32 mmol) in dry THF (3.0 $cm^3$) under nitrogen at room temperature was added sodium borohydride (24 mg, 0.64 mmol). Ethanol (0.15 $cm^3$) was added dropwise and the reaction mixture was stirred for 5 min before a solution of the α-methylenecyclohexanone **54** (55 mg, 0.33 mmol) in THF (0.5 $cm^3$) was added. The mixture was then stirred for 18 h before being poured into ether (50 $cm^3$) and washed successively with water (2 × 15 $cm^3$) and brine (15 $cm^3$), dried ($MgSO_4$), concentrated under reduced pressure, and purified by silica gel chromatography [eluent light petroleum–ether (3:2)] to give the title selenide as a crystalline solid (26 mg, 25%) with m.p. 62 °C; $\delta_H$(200 MHz) 1.8 (4 H, m), 2.30 (1 H, m), 2.45 (1 H, m), 3.02 (1 H, dd, $J_{gem}$ 10.2, $J_{1,7}$ 2.7, C*H*H), 3.23 (2 H, m, CH*H* + 1-H), 4.0 (4 H, m), 7.25 (3 H, m) and 7.50 (2 H, m); $\delta_C$(50 MHz) 19.99, 34.04, 40.19, 61.39, 65.16, 65.38, 112.14, 126.43, 128.96, 131.77 and 206.07; $\nu_{max}$($CHCl_3$)/$cm^{-1}$ 1716.

3,3-*Ethylenedioxy*-2-*methylcyclohexanone* **56**: *Preparation of an Authentic Sample*.—2-Methylcyclohexane-1,3-dione (500 mg, 4.0 mmol), ethylene glycol (984 mg, 16 mmol) and camphor-10-sulfonic acid (46 mg, 0.02 mmol) were heated to reflux in benzene under a Dean–Stark water separator for 2.5 h. After cooling to room temperature the solvent was evaporated off under reduced pressure, the residue was taken up in ether (100 $cm^3$), and the solution was washed successively with water (2 × 25 $cm^3$) and brine (25 $cm^3$), dried ($MgSO_4$), and evaporated to dryness under reduced pressure to give 1,1;3,3-bis(ethylenedioxy)-2-methylcyclohexane **57** as an oil (542 mg, 64%) with $\delta_H$(200 MHz) 0.86 (3 H, d, *J* 6.7), 1.28 (2 H, m), 1.50 (2 H, m), 1.72 (2 H, m), 2.00 (1 H, q, *J* 6.7, 2-H) and 3.8 (8 H, m); $\delta_C$(50 MHz) 6.36, 19.32, 46.82, 64.39, 65.48 and 110.76.

Without further purification compound **57** (400 mg, 1.9 mmol) was stirred in methylene dichloride (5 $cm^3$) and treated with silica gel (800 mg) and sulfuric acid (15%; 0.1 $cm^3$). The reaction mixture was stirred for 2.5 h, then filtered, and the filtrate was washed with saturated aq. sodium hydrogen carbonate (20 $cm^3$), dried ($MgSO_4$), and evaporated to dryness. Chromatography of the crude product on silica gel [eluent light petroleum–ether (1:1)] gave the target ketone as an oil (228 mg, 72%) with $\delta_H$(400 MHz) 1.01 (3 H, d, *J* 6.7), 1.75 (3 H, m), 1.95 (1 H, m), 2.25 (1 H, m), 2.40 (1 H, m), 2.70 (1 H, q, *J* 6.7, 2-H) and 3.90 (4 H, m); $\delta_C$(100 MHz) 9.72, 20.03, 33.98, 39.83, 54.50, 65.27, 65.63, 112.01 and 209.00; $\nu_{max}$(film)/$cm^{-1}$ 1714.

*Reaction of Selenide* **53** *with Tributyltin Hydride*.—A solution of the selenide **53** (5.5 mg, 0.017 mmol) was heated to reflux in benzene (0.85 $cm^3$) under nitrogen and treated dropwise during 20 min with a solution of tributyltin hydride (4.9 mg, 0.016 mmol) and AIBN (1 mg) in benzene (0.85 $cm^3$). The reaction mixture was then heated to reflux for a further 6 h with periodic additions of AIBN before it was cooled to room temperature and evaporated to dryness. The reaction mixture was then taken up in deuteriochloroform and examined by 400 MHz $^1H$ NMR spectroscopy. The only reduction product formed was the cyclohexanone **56**; there was no evidence to suggest formation of the aldehyde **55** or the cycloheptanone **45** as determined by comparison with spectra[1] of authentic samples. Similar reactions were carried out with higher, and lower, concentrations of the tin hydride with the same result.

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## References

1 Part 1: D. Crich and S. M. Fortt, *Tetrahedron*, 1989, **45**, 6581; Part 2: D. Crich, K. A. Eustace, S. M. Fortt and T. J. Ritchie, *Tetrahedron*, 1990, **46**, 2135.
2 Part 3: D. Batty, D. Crich and S. M. Fortt, *J. Chem. Soc., Perkin Trans. 1*, 1990, 2875; also see: D. Batty and D. Crich, *J. Chem. Soc., Perkin Trans. 1*, 1991, 2894.
3 C. Chen and D. Crich, *Tetrahedron Lett.*, 1992, **33**, 1945.
4 K. Nagasawa, Y. Zako, H. Ishihara and I. Shimizu, *Tetrahedron Lett.*, 1991, **32**, 4937; B. M. Trost and J. Dumas, *J. Am. Chem. Soc.*, 1992, **114**, 1924.
5 D. Batty and D. Crich, *Tetrahedron Lett.*, 1992, **33**, 875.
6 M. Julia, F. Le Goffic and L. Katz, *Bull. Soc. Chim. Fr.*, 1964, 1116.
7 G. Stork and R. Mook, *J. Am. Chem. Soc.*, 1983, **105**, 3720.
8 D. P. Curran and D. M. Rakiewicz, *J. Am. Chem. Soc.*, 1985, **107**, 1448; *Tetrahedron*, 1985, **41**, 3943.
9 For examples see: A. L. J. Beckwith, D. H. Roberts, C. H. Schiesser and A. Wallner, *Tetrahedron Lett.*, 1985, **26**, 3349; D. P. Curran and S. C. Kuo, *J. Am. Chem. Soc.*, 1986, **108**, 1106; P. J. Parsons, P. A. Willis and S. C. Eyley, *J. Chem. Soc., Chem. Commun.*, 1988, 283; J. D. Winkler and V. Sridar, *J. Am. Chem. Soc.*, 1986, **108**, 1708; D. H. R. Barton and E. da Silva, *J. Chem. Soc., Chem. Commun.*, 1988, 285; B. B. Snider and M. A. Dombroski, *J. Org. Chem.*, 1987, **52**, 5487; T. L. Fevig, R. L. Elliott and D. P. Curran, *J. Am. Chem. Soc.*, 1988, **110**, 5064; Y. K. Rao and M. Nagarajan, *J. Org. Chem.*, 1989, **54**, 5678; H. Pak, I. I. Canalda and B. Fraser-Reid, *J. Org. Chem.*, 1990, **55**, 3009; H. Cristl, H. Henneberger and S. Freund, *Chem. Ber.*, 1988, **121**, 1675.
10 N. A. Porter, V. H.-T. Chang, D. R. Magnin and B. T. Wright, *J. Am. Chem. Soc.*, 1988, **110**, 3554.
11 K. A. Parker, D. M. Spero and J. Van Epp, *J. Org. Chem.*, 1988, **53**, 4628.
12 For a recent review of the synthesis of this class of terpenoid see: M. G. Banwell, *Aust. J. Chem.*, 1991, **44**, 1.
13 D. L. Boger and R. J. Mathvink, *J. Am. Chem. Soc.*, 1990, **112**, 4003; *J. Org. Chem.*, 1990, **55**, 5442; 1992, **57**, 1429.
14 For a further acyl radical-initiated tandem cyclization see: C. E. Schwartz and D. P. Curran, *J. Am. Chem. Soc.*, 1990, **112**, 9272.
15 J. N. Baxter and A. S. Perlin, *Can. J. Chem.*, 1960, **38**, 2217.
16 For alternative preparations of compound **6** or its enantiomer see: C. S. Wilcox and L. M. Thomasco, *J. Org. Chem.*, 1985, **50**, 546; T. Hudlicky, H. Luna, J. D. Price and F. Rulin, *J. Org. Chem.*, 1990, **55**, 4683; R. Schaffer, *J. Res. Natl. Bur. Stand. A. Phys. Chem.*, 1961, **65**, 507; C. E. Ballou, *J. Am. Chem. Soc.*, 1957, **79**, 165.
17 E. J. Corey, D. A. Clark, G. Goto, A. Marfat, C. Mioskowski, B. Samuelson and S. Hammarstrom, *J. Am. Chem. Soc.*, 1980, **102**, 1436; also see: T. J. RajanBabu, T. Fukunaga and G. S. Reddy, *J. Am. Chem. Soc.*, 1989, **111**, 1759.
18 B. A. Murrer, J. M. Brown, P. A. Chaloner, P. N. Nicholson and D. Parker, *Synthesis*, 1979, 350.
19 E. Hungerbühler and D. Seebach, *Helv. Chim. Acta*, 1981, **64**, 687.
20 T. Mukaiyama, K. Suzuki, T. Yamada and F. Tabusa, *Tetrahedron*, 1990, **46**, 265.
21 D. Batty and D. Crich, *Synthesis*, 1990, 273.
22 J. B. Stothers and C. T. Tan, *Can. J. Chem.*, 1974, **52**, 308.
23 N. L. Allinger and H. M. Blatter, *J. Am. Chem. Soc.*, 1961, **83**, 994.
24 R. I. T. Cromartie and Y. K. Hamied, *J. Chem. Soc.*, 1961, 3622.
25 A. C. Cope, T. A. Liss and G. W. Wood, *J. Am. Chem. Soc.*, 1957, **79**, 6287.

26 N. L. Allinger and Z. B. Zalkow, *J. Am. Chem. Soc.*, 1961, **83**, 1144.
27 J. G. Vinter, A. Davis and M. R. Saunders, *J. Comput. Aided Molec. Design*, 1987, **1**, 31.
28 J. A. Mills, *Adv. Carbohydr. Chem.*, 1955, **10**, 1; A. N. Debelder, *Adv. Carbohydr. Chem. Biochem.*, 1977, **34**, 179.
29 D. Crich and L. B. L. Lim, *J. Chem. Soc., Perkin Trans. 1*, 1991, 2209.
30 A. Ali, D. C. Harrowven and G. Pattenden, *Tetrahedron Lett.*, 1992, **33**, 2851.
31 H. O. House, P. C. Cox and D. VanDerveer, *J. Org. Chem.*, 1983, **48**, 1661; P. E. Peterson, R. L. B. Leffew and B. L. Jensen, *J. Org. Chem.*, 1986, **51**, 1948.
32 A. Y. Mohammed and D. L. J. Clive, *J. Chem. Soc., Chem. Commun.*, 1986, 588; D. L. J. Clive and D. R. Cheshire, *J. Chem. Soc., Chem. Commun.*, 1987, 1520.
33 E. S. Binkley and C. H. Heathcock, *J. Org. Chem.*, 1975, **40**, 2156.
34 J. Plamondon and P. Canonne, *Tetrahedron Lett.*, 1991, **32**, 589.
35 W. G. Dauben, L. Schutte and E. J. Deviny. *J. Org. Chem.*, 1972, **37**, 2047.
36 M. Cristl and J. D. Roberts, *J. Org. Chem.*, 1972, **37**, 3443.
37 M. Miyashita, H. Hoshino and A. Yoshikoshi, *Tetrahedron Lett.*, 1988, **29**, 347.
38 T. V. RajanBabu, *Acc. Chem. Res.*, 1991, **24**, 139.
39 T. Morikawa, T. Nishiwaki and Y. Kobayashi, *Tetrahedron Lett.*, 1989, **30**, 2407; A. V. R. Rao, J. S. Yadav, C. S. Rao and S. Chandrasekar, *J. Chem. Soc., Perkin Trans. 1*, 1990, 1211.
40 A. L. J. Beckwith and C. H. Schiesser, *Tetrahedron*, 1985, **41**, 3925.

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