A Total Synthesis of Allamcin. An Approach to Antileukaemic Iridoid Lactones and Formal Syntheses of Plumericin and Allamandin

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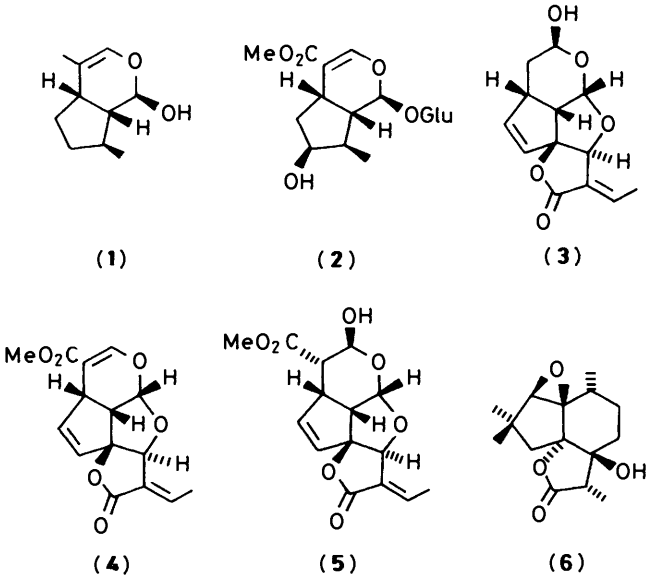
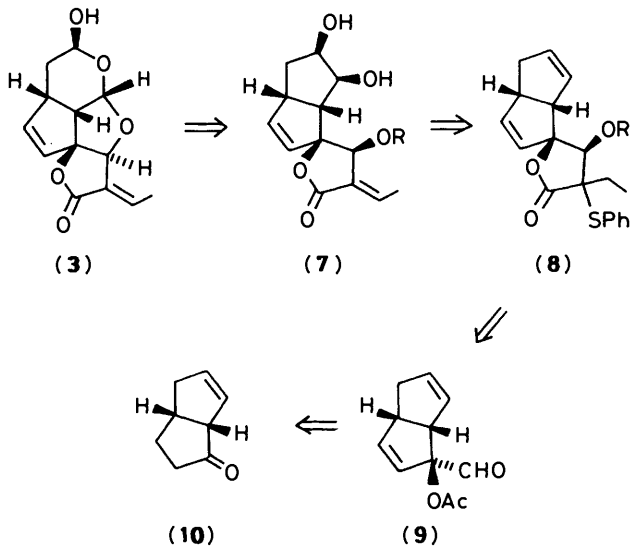
A total synthesis of the iridoid lactone (±)-allamcin (**3**) found in *Allamanda neriifolia* is described. Starting from the readily available bicyclo[3.3.0]octenone (**10**), the synthesis uses a strategy based on: (i) elaboration of the key acetoxy-aldehyde intermediate (**9**) through epoxidative rearrangement of the enol acetate (**71**) derived from (**10**) *via* the unsaturated aldehyde (**57**), (ii) fusion of the β-oxy-γ-butyrolactone ring system on to (**9**) using the dianion (**20**) derived from 2-phenylthiobutanoic acid, (iii) chemo-selective *vic*-bishydroxylation of the ring B carbon-to-carbon double bond in (**75**), using osmium tetraoxide, leading to (**76**), (iv) *in situ* oxidation and elimination of phenylsulphenic acid from (**76**) producing the (*E*)-ethylidenefuranone (**78**), and (v) oxidative-cleavage and cyclisation from the 1,2-diol (**78**) in the presence of sodium metaperiodate. Allamcin was also produced when the allylic transposed intermediate (**84**) derived from compound (**83**) ($MeOH–K_2CO_3$) was treated with periodic acid. Since allamcin has previously been converted into plumericin (**4**) and allamandin (**5**), the synthesis of compound (**3**) also constitutes formal syntheses of (±)-(**4**) and (±)-(**5**).

The 'iridoids,' exemplified by iridodial (**1**) and loganin (**2**), are a large family of structurally diverse natural cyclopentanopyran monoterpenes that show a wide range of biological activities, *e.g.*, anti-tumoral, antibiotic, anti-feedant, anti-leukaemic, antimicrobial.[1] Allamcin (**3**) is a recently isolated iridoid from *Allamanda neriifolia*,[2] where it co-occurs with the structurally related plumericin (**4**) and allamandin (**5**).[3] The structure of allamcin (**3**), together with those of (**4**) and (**5**), features an interesting cyclic hemi-acetal ring portion, which also makes up part of a cyclic acetal, one 'ether' residue of which constitutes the β-oxygen of a spiro-fused α-ethylidene-β-oxy-γ-butyrolactone ring system. Although β-oxy-γ-butyrolactones are found only rarely in Nature, one such member, alliacolide (**6**) from the fungus *Marasmius alliaceus*, has been at the focus of our recent



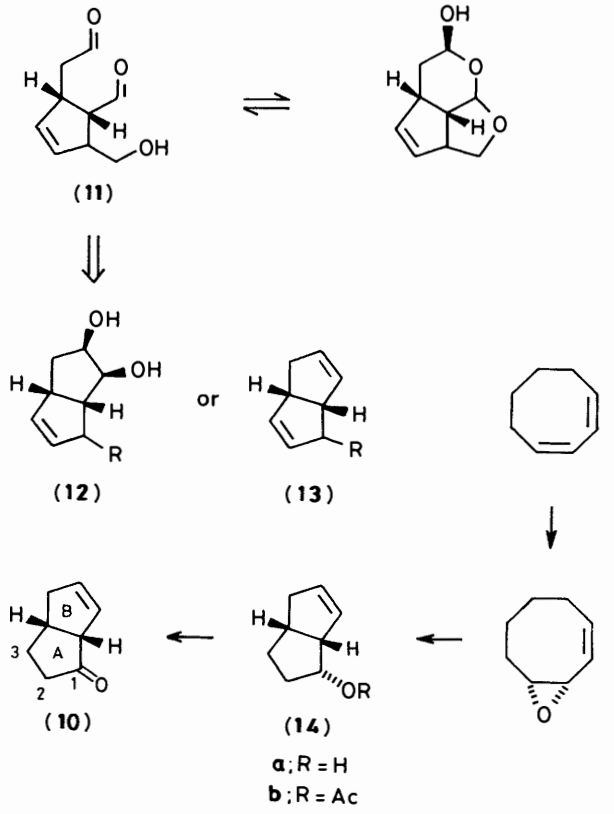
synthesis endeavours, and in the immediately preceding paper we described a total synthesis of this unusual molecule.[4] The afore-mentioned structural features found in allamcin (**3**), densely packed as they are in a molecule accommodating six chiral centres, have combined to make the compound a particularly intriguing and challenging target for synthesis. In this paper we describe a total synthesis of (±)-allamcin which uses the general strategy shown in Scheme 1.[5]



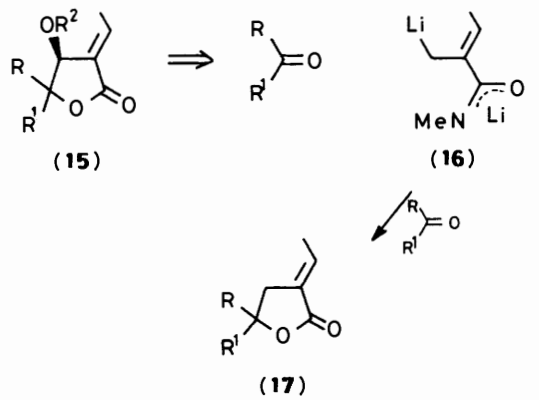
Scheme 1.

Recognition of the angular fused cyclic hemi-acetal–cyclic acetal–cyclopentane ring system in allamcin (**3**) as a tautomer of the hydroxy-dial (**11**), led us to the mono-substituted bicyclo[3.3.0]octene (**13**) or the corresponding *vic*-diol (**12**) as starting materials for our projected synthesis. The substituted bicyclo-octene systems (**12**) and (**13**) not only 'hold' the important *cis*-stereochemistry at their ring junction, to be translated to (**3**), but the differing functionality in the five-membered rings allows each ring to be elaborated independently of the other. Another important benefit of the bicyclo[3.3.0]-octane carbon framework in synthesis, recognised by many researchers,[6,7] is that the ring system in the form of the ketone (**10**) is extremely easily and cheaply available in three steps from cyclo-octa-1,3-diene.[7] With this general protocol in mind, our

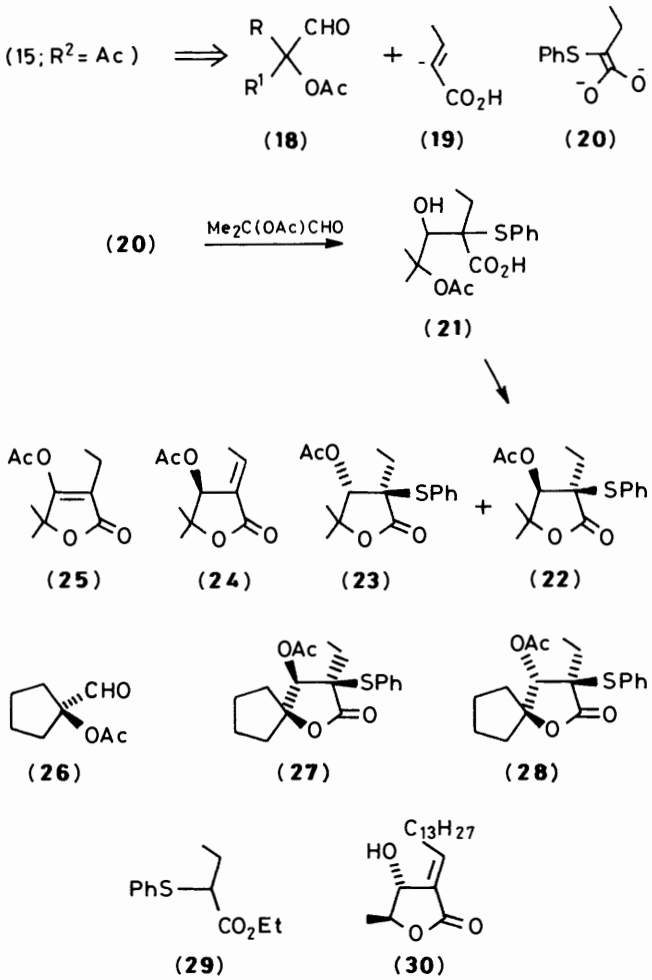
projected synthesis of allamcin, then required a procedure for the spiro-annulation of a substituted γ-butyrolactone unit onto ring A of (**10**), with simultaneous introduction of the correct stereochemistry at C-1, and possibly in concert with incorporation of the additional C=C double bond at C-2, C-3 in ring A.



We first addressed the problem of spiroannulation of an α-ethylidene-β-oxy-γ-butyrolactone onto a ketone group to elaborate the ring system (**15**) present in allamcin (**3**). We had hoped to achieve this objective by modification of our earlier described 'one-pot' synthesis of spiro-(*E*)-α-ethylidene-γ-butyrolactone (**17**) using the dianion (**16**) derived from (*E*)-*N*,2-dimethylbut-2-enamide,[8] but this strategy proved to be impractical when using oxy-substituted butenamides. We decided therefore to examine the possibility of synthesis of (**15**) through condensation of a suitably protected α-hydroxy aldehyde [*viz.* (**18**)] and a synthetic equivalent to the crotonic acid vinyl anion (**19**). The synthetic equivalent to (**19**) which we elected to use was the dianion (**20**) derived *via* deprotonation of 2-phenylthiobutanoic[9] acid using two equivalents of lithium di-isopropylamide. Gratifyingly, and

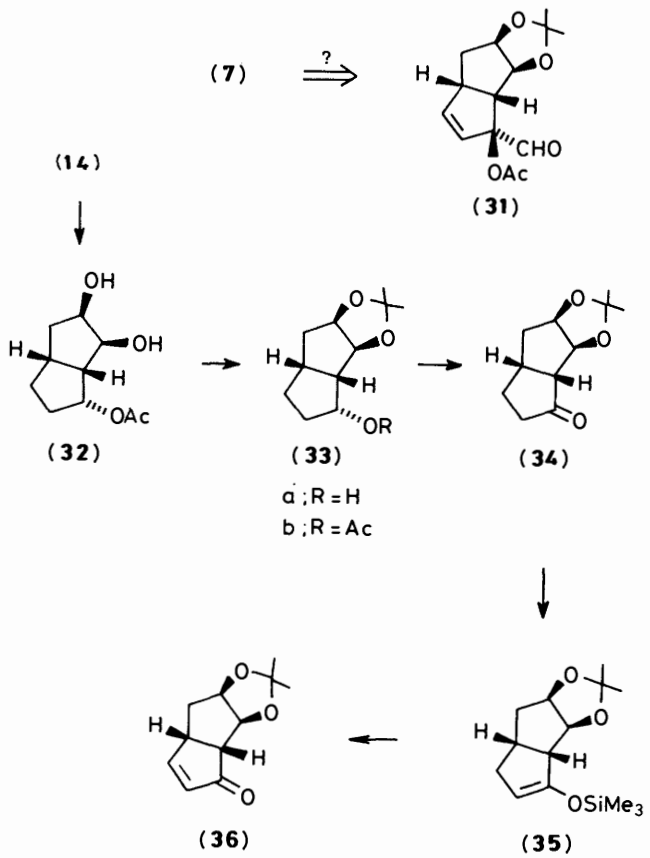


in a model study, we were able to show that the dianion (**20**) condensed with 2-acetoxy-2-methylpropanal to produce a 2:1 mixture of the diastereoisomers, (**22**) and (**23**), of the acetoxybutyrolactone product, in a combined yield of 61%. In a similar manner, the acetoxy-aldehyde (**26**) condensed with (**20**) leading to the crystalline diastereoisomers (**27**) and (**28**), also in a 2:1 ratio. The relative stereochemistries assigned to the adducts (**22**), (**23**), (**27**), and (**28**) followed from comparative chemical shift data in their ^{1}H n.m.r. spectra [δ *ca.* 2.2 (OAc), *syn* OAc-SPh isomers (**22**) and (**27**); δ *ca.* 2.12 (OAc), *anti* OAc-SPh isomers (**23**) and (**28**)], together with the observation of an n.O.e. effect of 7.5% at δ 7.3—7.68 (SPh) by irradiation at δ 5.26 (C*H*OAc) in the *anti*-isomer (**23**), and also from the constitutions of the products resulting from their oxidations with *m*-chloroperbenzoic acid. Thus, treatment of the sulphide (**22**) with *m*-chloroperbenzoic acid resulted in oxidation and simultaneous elimination of phenylsulphenic acid producing the anticipated *exo*-ethylidene butyrolactone (**24**), containing none of the *endo*-isomer (**25**). By contrast, oxidation and elimination from (**23**), which contains *syn*-orientated C–H bonds at both the α- and α′-centres to that containing the phenylsulphide residue, led to a mixture of the *endo*- and *exo*-isomers (**25**) and (**24**) respectively. A small amount of the *Z*-isomer (<5%) corresponding to compound (**24**) was produced concurrently during the oxidative elimination from (**22**). The *E*-stereochemistry assigned to (**24**) followed from comparative shift data in the ^{1}H n.m.r. spectrum [δ 1.98 (*E*=C*Me*); δ 1.91 (*Z*=C*Me*)], together with observations from n.O.e. difference spectra (see Experimental section). During the course of our investigations, Benezra *et al*[10]



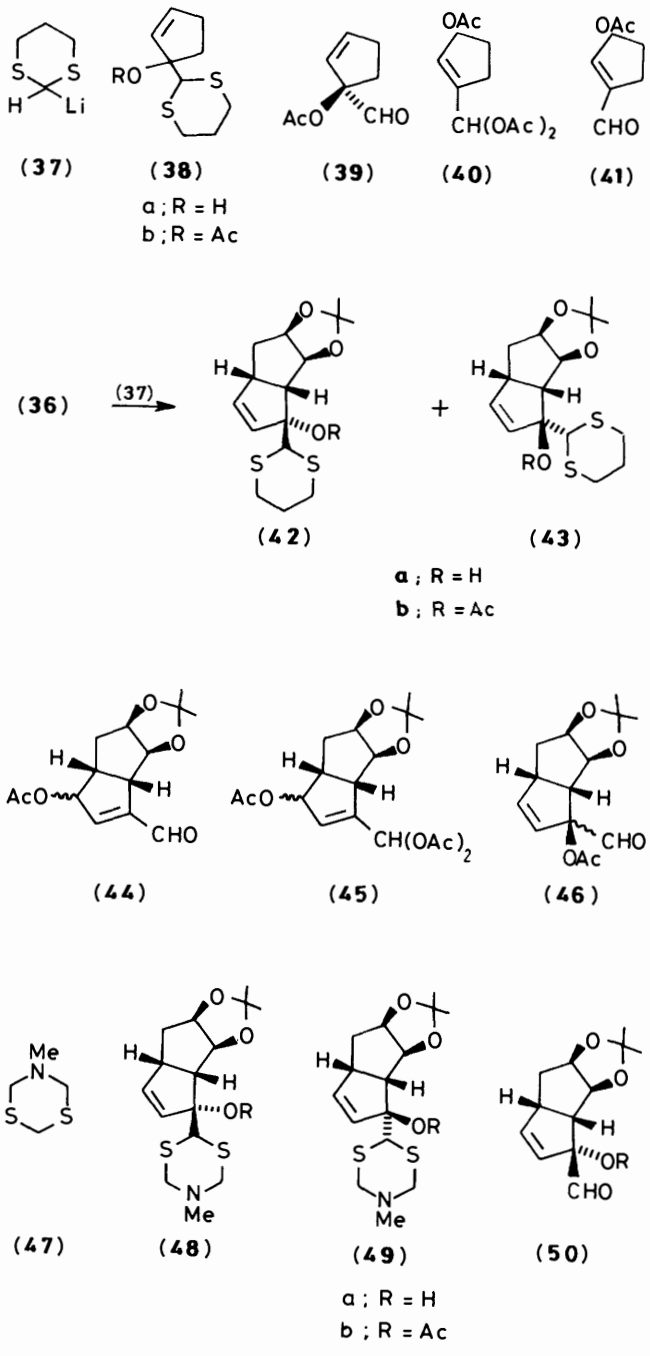
independently described a closely similar approach to the β-oxy-γ-butyrolactone ring system (**24**), which was based on the use of the monoanion derived from substituted ethyl 2-phenylthiobutanoate (**29**) instead of (**20**). The stereochemical outcome of the reactions studied by Benezra *et al.* agrees closely with our own results, and furthermore, these authors later applied their methodology in a useful synthesis of the natural litsenolides, *e.g.*, (**30**).

With the establishment of a procedure for elaborating the α-*E*-ethylidene-β-oxy-γ-butyrolactone ring system in allamcin (**3**), we turned next to the problem of synthesizing a C-1 α-acetoxyaldehyde substituted bicyclo[3.3.0]octane intermediate [*viz.* (**31**)], containing differentiated five-membered rings and with the correct (β-OAc) stereochemistry at C-1. As shown earlier, the bicyclo[3.3.0]octene (**14**) is readily available in two steps from cyclo-octa-1,3-diene, and the acetal-enone (**36**) was an attractive relay compound to examine a number of procedures for the synthesis of (**31**) from (**14**). Thus, conversion



of (**14a**) into the corresponding acetate (**14b**) followed by *vic*-bishydroxylation using osmium tetraoxide in the presence of hydrogen peroxide and t-butanol first led to the crystalline diol (**32**) in 90% yield. After protection of compound (**32**) as the corresponding acetonide (**33a**), saponification, followed by oxidation of the resulting acetal (**33b**) then produced the cyclopentanone (**34**). The cyclopentanone (**34**) was finally converted into the enone (**36**) using the method of Saegusa *et al.*[11] involving oxidation of the corresponding trimethylsilyl ether (**35**) in the presence of palladium(II) acetate and *p*-benzoquinone.

Initially, we examined the possibility of using a formyl anion equivalent to add (α-)stereoselectively and (1,2-)chemoselectively to the enone (**36**) leading to a derivative of the aldehyde (**31**). This was an ambitious proposal however, since (*a*) only a few formyl anion equivalents are known which add in a 1,2-sense to conjugated enones,[12] and (*b*) we would expect most nucleophiles to add preferentially from the least hindered (convex) face of (**36**) leading ultimately to largely the 'wrong' geometry at C-1 in compound (**31**)! We were encouraged when model studies, using lithium dithiane (**37**) and cyclopentenone, led only to the product (**38a**) of 1,2-addition, which could then be converted into the corresponding acetate (**38b**). Discouraging however was the fact that all attempts to unmask the aldehyde



function from (**38b**),[13] producing (**39**), instead led only to the products (**40**) and (**41**) resulting from allylic transposition. The addition of lithium dithiane to the bicyclo[3.3.0]octenone (**36**)

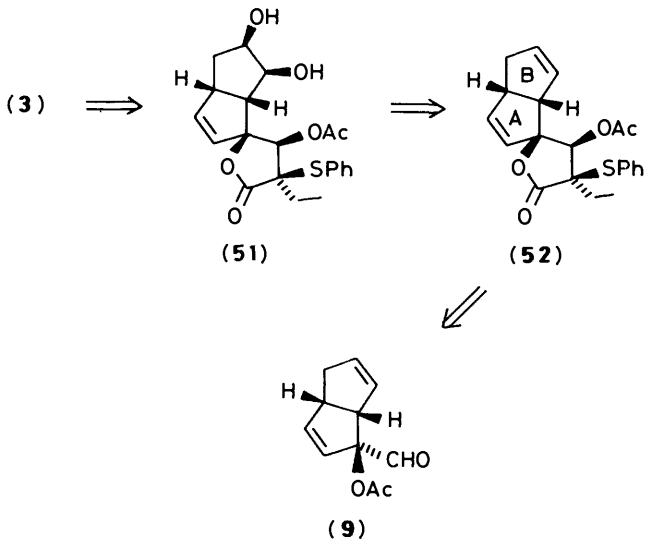
was likewise (1,2-)chemoselective, and led to a 3:2 mixture of the crystalline diastereoisomeric adducts (**42a**) and (**43a**), (87% combined), which were cleanly resolved by chromatography. Each of the acetoxy dithianes (**42b**) and (**43b**) could then be derived from the alcohols (**42a**) and (**43a**) respectively, following treatment with acetic anhydride in triethylamine. All attempts however to deprotect the acetoxy dithianes (**42b**) and (**43b**) to the corresponding acetoxy-aldehyde (**46**) under a wide range of reaction conditions,[13] met with total failure. Only those products resulting from allylic transposition were isolated *viz.* (**44**) and (**45**), together with complex mixtures of products which clearly resulted from decomposition of the acetonide moiety in (**42**)/(**43**).

When the anion from the dithiazine (**47**)[14] was used in place of (**37**), its addition to (**36**) also led to a 2:1 mixture of α-OH and β-OH diastereoisomeric adducts (**48a**) and (**49a**) respectively. Interestingly, after chromatographic separation, the major diastereoisomer (**48a**) could then be converted into the labile α-hydroxyaldehyde (**50a**) following treatment with a suspension of mercury(II) chloride and calcium carbonate in dichloromethane. All attempts to convert (**50a**) into the corresponding α-acetoxy-aldehyde (**50b**) however were unsuccessful. Peculiarly, when the addition between (**47**) and (**36**) was worked up with acetic anhydride, *only* the α-acetoxydithiazine (**48b**) was produced, and this was smoothly converted into the ('wrong') acetoxy-aldehyde (**50b**) in essentially quantitative yield using mercury(II) chloride and calcium carbonate in acetonitrile.

The α-OAc stereochemistry assigned to the diastereoisomer (**48b**) was based on the anticipated addition of the anion derived from (**47**) to the least hindered (convex) face of (**36**), together with data from n.O.e. experiments. Thus, irradiation at δ 5.64 (C*H*S_2) in the ^{1}H n.m.r. spectrum of compound (**48b**) enhanced the peak at δ 3.35 (C*H*COAc) by 2.2%, and irradiation at δ 2.02 (OAc) enhanced the signal at δ 4.99 (CHC*H*O) by 1%. The ^{1}H n.m.r. data for the hydrogen atoms associated with the bicyclo-octane ring portion in the major dithiane adduct (**42b**) derived from (**36**), were almost superimposable on the corresponding resonances found in (**48b**) (See Experimental section). An *X*-ray crystal structure determination on the α-acetoxydithiazine (**48b**) has confirmed the stereochemistry assigned to the molecule.*

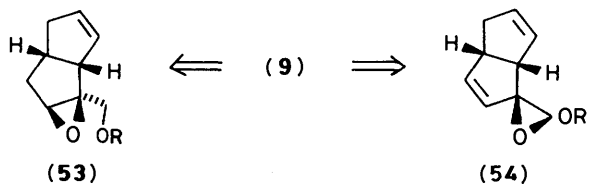
The failure of the formyl anion equivalent (*i.e.* dithiane) approach to provide the key β-acetoxy-aldehyde intermediate (**31**) cleanly or with the correct stereochemistry, together with the obvious sensitivity of the acetonide residue in (**36**) to reaction and work-up conditions necessitated a complete re-appraisal of our synthetic design. In the event, we decided to abandon the use of the acetonide-ketone (**36**), and instead to make the spiro-annulated bicyclo-octadiene (**52**) our new central intermediate towards allamcin (**3**). Mindful of the rate data published by Henbest *et al.*[15] for the epoxidation of substituted cyclohexenes together with the steric encumberance offered by the adjacent spiro-centre, we felt that the ring A (allylic ester) double bond in (**52**) would be *vic*-bishydroxylated at a substantially slower rate than that of the corresponding ring B double bond, thereby allowing us access to the *vic*-diol (**51**) from (**52**) in a chemoselective manner, and furthermore, late in the synthesis design (Scheme 2).

The new strategy towards allamcin required a synthesis of the bicyclic β-acetoxy-aldehyde (**9**), and the easily available enone (**10**) was an obvious starting material. With the problems encountered earlier in adding a nucleophilic *carbon* centre to the 'hindered' (concave) face of bicyclo[3.3.0]octanes, we were now attracted to the possibility of transferring electrophilic *oxygen*, *via* an epoxide intermediate to the unhindered (convex) face of



Scheme 2.

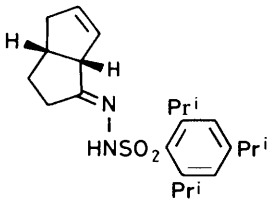
an appropriate bicyclo[3.3.0]octane, and then to cleave the intact epoxide ring in both chemo- and stereo-selective fashion. Thus, both the *endo*-epoxide (**53**) and the *exo*-epoxide (**54**) became attractive molecules to access in order to examine this new possibility.



Conversion of the cyclopentanone (**10**) to the corresponding trisylhydrazone (**55**), followed by treatment with butyl-lithium and quenching the resulting vinyl-anion (**56**) with dimethyl-formamide,[16] first provided an expeditious route to the unsaturated aldehyde intermediate (**57**). Reduction of (**57**) using lithium aluminium hydride, then led to the alcohol (**58**) which was smoothly oxidised with t-butylhydroperoxide in the presence of vanadyl acetonylacetonate[17] to produce largely the required β-epoxide (**59**) (< 15% of the α-epoxide was produced concurrently). Although treatment of the epoxide (**59**) with lithium di-isopropylamide in benzene provided the *vic*-diol (**60**),[18] which could then be converted into the tertiary acetate (**61**), all our attempts to oxidise (**61**) to the key acetoxy-aldehyde intermediate (**9**) met with total failure. Furthermore, although oxidation of the unsaturated aldehyde (**57**) in the presence of buffered hydrogen peroxide gave rise to the epoxide (**62**), we were unable to convert this intermediate to the α-hydroxy-aldehyde (**63**) using a range of conditions, and hence into compound (**9**).

Frustrated with the outcome of our attempts to synthesize the acetoxy-aldehyde (**9**) from either of the *endo*-epoxides (**59**) or (**62**), we next examined the use of the enol ether (**66**) and the enol acetate (**71**) in a synthesis of compound (**9**) *via* the corresponding *exo*-epoxide intermediate (**54**). A 2:1 mixture of *Z*- and *E*-isomers of the enol ether (**66**) was easily prepared from (**64**) following a Wittig-Horner condensation with the phosphine oxide anion (**65**). Interestingly, (and as if the bizarre chemistry of bicyclo[3.3.0]octenones required even further

* We thank Dr. M. J. Begley for this information which will be published separately.



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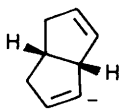

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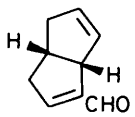

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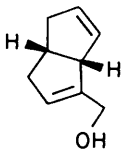

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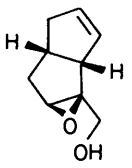

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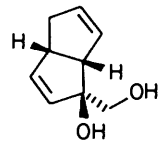

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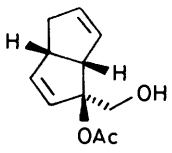

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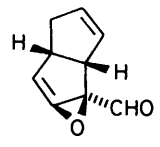

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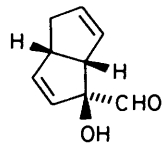


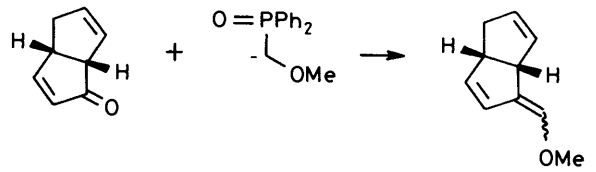
(63)

emphasis!) the condensation between (**64**) and the *P*-ylide (**67**) instead led exclusively to the cyclopropane (**68**). When an ice-cold solution of the enol ether (**66**) in dry methanol was treated with *m*-chloroperbenzoic acid, work-up, and chromatography led directly to a 2:1 mixture of the diastereoisomeric hydroxy-acetals (**70a**) and (**69a**) in a combined yield of 46%. The stereochemistry assigned to the major product (**70a**) followed from an n.O.e. experiment, where irradiation at δ 4.23 [C*H*(OMe)$_2$] was found to enhance the signal δ 3.42 [=CHC*H*C(OH)] by 5.2%. The poor stereoselectivity observed in this reaction was disappointing, and presumably reflects little control in the initial epoxidation step, rather than in the subsequent step involving acid-catalysed epoxide ring cleavage.[19] Separate treatment of the diastereoisomeric alcohols (**69a**) and (**70a**) with acetic anhydride in pyridine then led to the corresponding acetates (**69b**) and (**70b**) respectively, but all attempts to hydrolyse the isomer (**69b**) to the acetoxy-aldehyde (**9**) again met with failure.

Success in elaborating the key acetoxy-aldehyde (**9**) from the enone (**10**) was ultimately achieved when we examined the epoxidation of the enol acetate (**71**). The *Z*-enol acetate (**71**) was smoothly obtained from the enone (**10**) following conversion into the enal (**57**) and treatment of the latter with isopropenyl acetate in the presence of toluene-*p*-sulphonic acid. The outcome of a study of the epoxidation of (**71**) using a range of reagents under differing conditions is shown in the Table. Thus, whereas *m*-chloroperbenzoic acid was found to produce, in one step, a 1:1 mixture of the acetoxy-aldehydes (**9**) and (**72**), use of peracetic acid led largely to the 'required' (β-OAc orientated) material (**9**), and molybdenum pentaoxide–hexamethylphosphoramide complex[20] gave almost exclusively the 'wrong' (α-OAc orientated) acetoxy-aldehyde (**72**). The stereochemistries assigned to (**9**) and (**72**) were established from n.O.e. difference spectra on the two isomers. Thus, irradiation at δ 9.50 (C*H*O) in the ^{1}H n.m.r. spectrum of the β-CHO orientated isomer (**72**) enhanced the angular (β-orientated) C–H signal at δ 4.01 by 3%. A similar enhancement (at δ 3.60) in the corresponding α-CHO orientated isomer (**9**) (by irradiation at δ 9.56) was not observed. Although the rearrangement of

Table. Epoxidation-rearrangement of (**71**) to the acetoxy-aldehydes (**9**) and (**72**).

Reagent	Ratio (**9**):(**72**)	Yield (%)
$MeCO_3H$	4:1	35
m-$ClC_6H_4CO_3H$	1:1	67
MoO_5·HMPA	1:8	37



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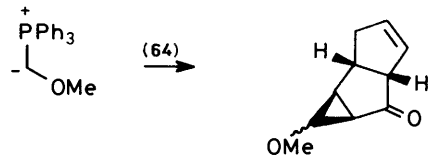

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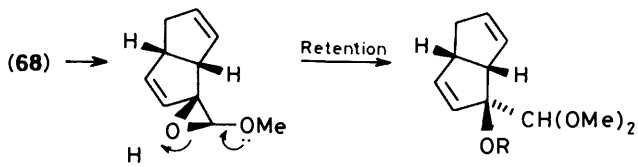
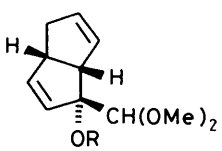


(69)
a ; R = H
b ; R = Ac



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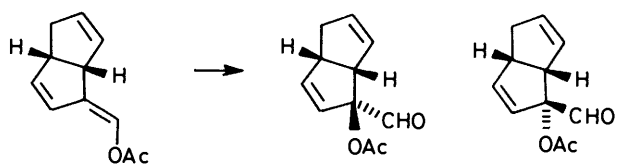
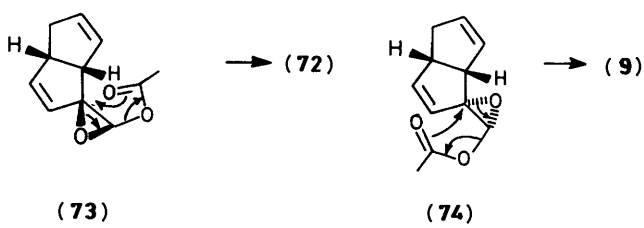


(71) (9) (72)

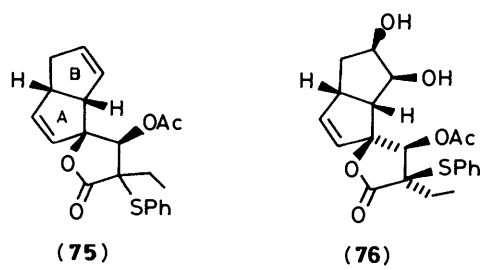


(73) (74)

acetoxy epoxides to α-acetoxy-aldehydes is a well documented process and known to proceed in an intramolecular fashion,[21] the literature contains many conflicting reports concerning the stereochemical outcome of the rearrangement.[22] We believe that the results of the epoxidation of (**71**), summarised in the Table, are best accommodated by a mechanism whereby intramolecular rearrangement of the intermediate acetoxy epoxide occurs with inversion. This proposal is plausible if it is also accepted that the larger molybdenum pentaoxide reagent adds to the less hindered β-face of the enol acetate [leading to (**73**)], and that the smaller peracetic acid molecule preferentially adds to the more hindered α-face of (**71**), leading largely to (**74**).

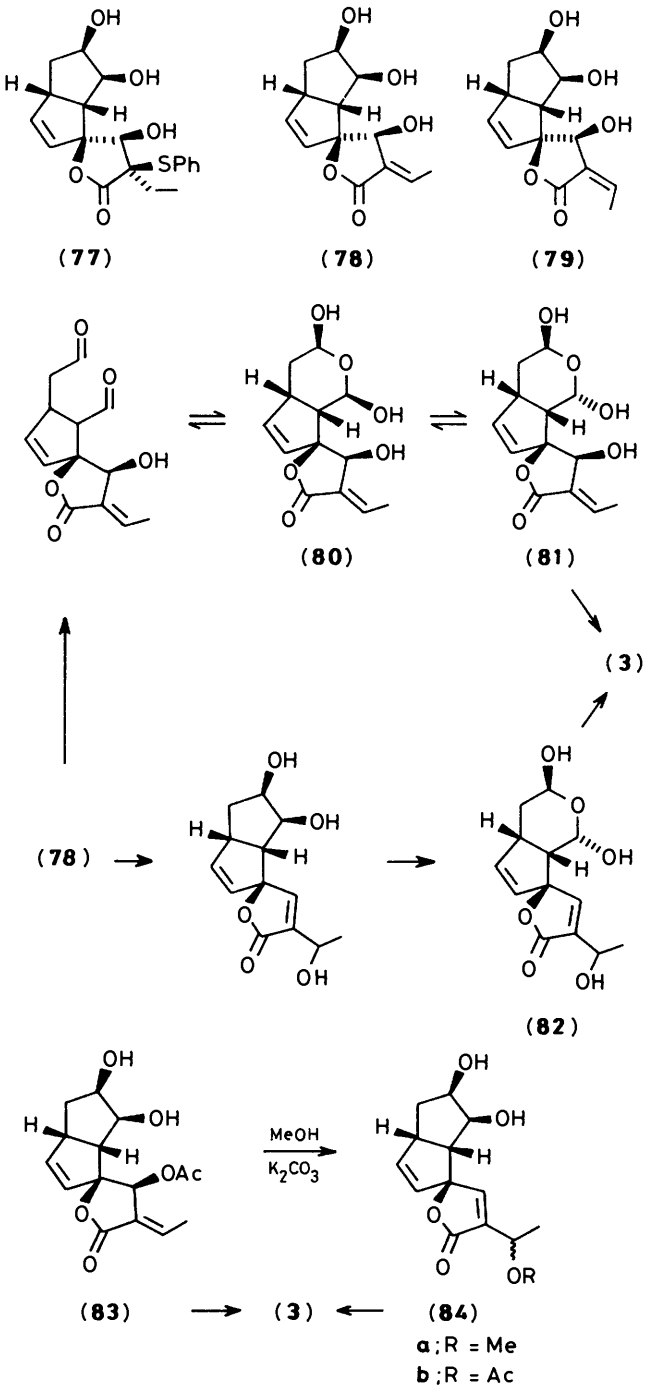
Having secured a viable route to the key acetoxy-aldehyde intermediate (**9**) in just four steps from the bicyclo-octenone (**10**), we were now in a position to elaborate the spirofuranone (**75**). Addition of compound (**9**) to a solution of the dianion (**20**) in tetrahydrofuran at −80 °C, followed by warming to 0 °C, an acid work-up, and chromatography produced a mixture of four diastereoisomers of the spirofuranone (**75**) in a combined yield of 52%. Although partial separation of the mixture of diastereoisomers was possible by laborious chromatography, this could not be achieved on a preparative scale without substantial loss of material. In any event, for our purposes the assignment of stereochemistry to the diastereoisomers (**75**) was largely irrelevant, and we therefore proceeded straightaway to examine the selectivity of *vic*-bishydroxylation of the C=C double bond in ring B of (**75**). Here we were most fortunate, since when a solution of the diastereoisomeric furanones (**75**) in a tetrahydrofuran and aqueous phosphate buffer was treated with a stoicheiometric amount of osmium tetraoxide, chromatography led to the separation of essentially one pure diastereoisomer of the anticipated diol, resulting from chemoselective attack of the C=C double bond in ring B in 24% yield. The compound, a mobile oil, was shown to be a single diastereoisomer using ^{1}H- and ^{13}C-n.m.r. spectroscopy. The chemoselectivity of the oxidation of compound (**75**) was established by inspection and comparison of the olefinic proton signals in the ^{1}H n.m.r. spectra of (**75**) and the resulting diol *i.e.*, retention of the resonances at δ 5.4 and 5.98 (ring A olefinics) and loss of the resonances at δ 5.62—5.8 (ring B olefinics) in (**75**). The (β-)stereoselectivity of the vicinal bishydroxylation of (**75**) followed from the chemical shifts and multiplicities of resonances associated with the C*H*OH hydrogen atoms (δ 4.13; δ 4.25) in the diol (**76**), in comparison with model compounds *e.g.*, (**32**). A *syn*-orientation between the acetoxy and phenylsulphide groups in the single diastereoisomer followed from its facile oxidative-elimination in the presence of *m*-chloroperbenzoic acid to the ethylidene-derivative (**83**). Taken together the above data led us to assign the tentative stereochemistry shown in (**76**) to the major diastereoisomer produced by oxidation of (**75**) with osmium tetraoxide. In addition to the single diastereoisomer (**76**), a mixture of largely two alternative diastereoisomers (20%) was separated by chromatography.

The synthesis of allamcin from the diol (**76**) was achieved by several methods. Thus, saponification of compound (**76**) with potassium carbonate in methanol, followed by *in situ* oxidation and elimination of phenylsulphenic acid from the resulting triol sulphide (**77**) in the presence of *m*-chloroperbenzoic acid, first led to the *E*-ethylidenefuranone triol (**78**), which contained approximately 8% of the corresponding *Z*-isomer (**79**) (δ 2.05, =CH*Me*, *E*-isomer; δ 2.28, =CH*Me*, *Z*-isomer). After much experimentation, and examining of a multitude of reaction conditions, treatment of compound (**78**) with sodium metaperiodate in aqueous ether at 5—10 °C in the presence of sodium acetate then led to (±)-allamcin (**3**), m.p. 189—195 °C, containing 8% of the corresponding *Z*-isomer (δ 2.29, =CH*Me*), which showed spectral characteristics (m.s., ^{1}H n.m.r.) and t.l.c. behaviour identical with an authentic sample. The somewhat



(**75**)

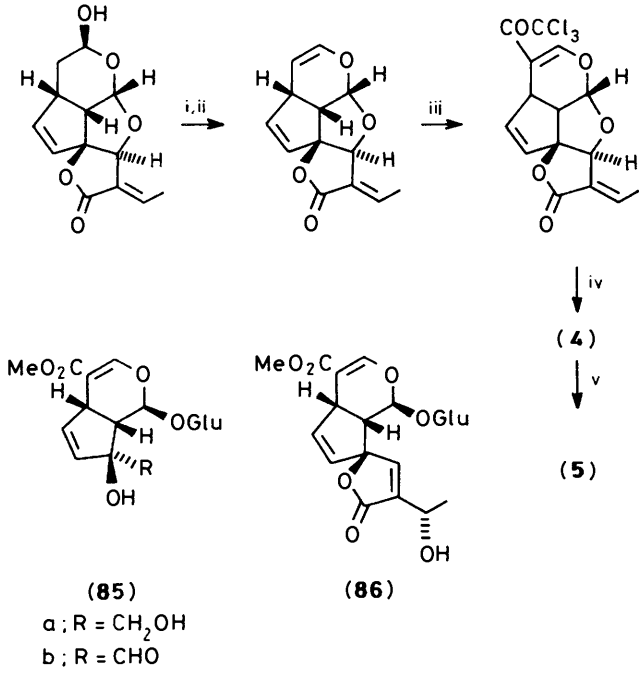
(**76**)



precarious nature of the periodate cleavage-cyclisation of (**78**) to (**3**), no doubt reflects the difficulty in adjusting reaction conditions to increase the proportion of the α-C(1) anomer (**81**) of the intermediate (**80**) in the cleavage step. It might also reflect the fact that the cyclisation step proceeds by way of Michael type reaction involving the transposed alcohol (**82**), which will need time and favourable conditions to form, rather than *via* the intermediate (**81**) (see below).

In an alternative procedure, (±)-allamcin was produced from the acetoxy-sulphide (**75**), following *in situ* oxidation and elimination of benzenesulphenic acid to the ethylidenebutyrolactone (**83**) and treatment of (**83**) with sodium periodate in the presence of sodium acetate. Finally, when the acetate (**83**) was suspended in methanol containing potassium carbonate at room temperature for 16 h, it was converted quantitatively into a 1:1 mixture of methoxy epimers of the transposed ether (**84a**). Treatment of the mixture of methyl ethers (**84**) with periodic acid in aqueous ether then also led to (±)-allamcin (**3**). Due to the limited amounts of material to hand, we only had the opportunity to do some of the final reactions with (**78**), (**83**), and (**84**) on small scale and in the event the yields of (±)-allamcin were not good.

In contemporaneous studies, Trost *et al*,[23] described an alternative synthesis of (±)-allamcin which however also used the spiro-butenolide structure (**84b**) [*cf.* (**84a**)] as a key intermediate. Furthermore, these same workers have used allamcin as an intermediate in neat total syntheses of both (±)-plumericin (**4**) and (±)-allamandin (**5**) (Scheme 3). Our own



Scheme 3. *Reagents:* i, Ac_2O; ii, Flash vacuum thermolysis, 500 °C, 0.005 mm; iii, CCl_3COCl; iv, $Mg(OMe)_2$, MeOH; v, $HClO_4$

synthesis of allamcin, which uses only seven steps from the easily available bicyclo[3.3.0]octenone (**10**), thus constitutes formal syntheses of both (±)-plumericin and (±)-allamandin.

Allamcin (**3**), plumericin (**4**), and allamandin (**5**) co-occur in *Allamanda neriifolia*, together with the biogenetically significant metabolites gardenoside (**85a**), dehydrogardenoside (**85b**) and plumieride (**86**). Furthermore, a biomimetic transformation of dehydrogardenoside (**85b**) into plumieride (**86**) has been described.[24] The structural resemblance between compounds (**85**) and (**9**), and between (**86**) and (**84**), demonstrates an interesting similarity in the synthetic strategy we have used to elaborate allamcin from (**10**), *i.e.*, (**10**)→(**9**)→(**7**)→(**84**)→(**3**), and the probable biosynthetic pathway to allamandin from mevalonic acid (MVA), *i.e.*, MVA→(**85b**)→(**86**)→(**4**)→(**5**).[25]

Experimental

For general experimental details see ref. 26.

2-*Phenylthiobutanoic Acid.*—The thioacid was prepared from thiophenylacetic acid by the method of Uda *et al*,[9] and showed $\nu_{max.}$(film) 2 970 and 1 704 cm^{-1}; $\delta_H(CDCl_3)$ 1.09 (t, *J* 7 Hz, CH_2Me), 1.87 (dq, *J* 9 and 7 Hz, $CHCH_2Me$), 3.6 (t, *J* 9 Hz, CH), 7.3—7.44 (m, 3 H), 7.5—7.64 (m, 2 H), and 11.46 (CO_2H) (Found: C, 61.4; H, 6.5%; *m/z* 196.0481. Calc. for $C_{10}H_{12}O_2S$: C, 61.2; H, 6.2%; *M*, 196.0557).

1-*Acetoxycyclopentanecarbaldehyde* (**26**).—Glycidic ester condensation between cyclopentanone and ethyl chloroacetate in the presence of potassium t-butoxide first gave ethyl oxaspiroheptanecarboxylate (75%),[27] as a colourless oil, b.p. 112—114 °C at 16 mmHg, $\nu_{max.}$(film) 2 960 and 1 750 cm^{-1}; $\delta_H(CDCl_3)$ 1.30 (t, *J* 7 Hz, $MeCH_2$), 1.5—2.3 (m, 4 × CH_2), 3.52 ($CHCO_2$) and 4.26 (q, *J* 7 Hz, $MeCH_2$) (Found: *m/z* 170.0940. $C_9H_{14}O_3$ requires *M*, 170.0943). Saponification of the ester in ethanol containing sodium ethoxide then led (89%) to the corresponding sodium glycidate, m.p. 238 °C (decomp.), $\nu_{max.}$(KBr) 2 950 and 1 670 cm^{-1}; $\delta_H(D_2O)$ 1.5—2.1 (m, 4 × CH_2) and 3.55 ($CHCO_2$).

A mixture of the sodium glycidate (4.3 g) pyridine (4.1 g), lead(IV) acetate (23 g) and benzene (195 ml) was stirred at 25 °C under nitrogen for 0.5 h, and then heated under reflux for 4 h.[27] Ethylene glycol (1 ml) was added, and the resulting suspension was then washed successively with water (100 ml), dilute hydrochloric acid (100 ml), and water (100 ml). Evaporation of the dried benzene extract and distillation of the residue gave the acetoxy-aldehyde (1.5 g, 37%) as a colourless oil, b.p. 110—116 °C at 40 mmHg, $\nu_{max.}$(film) 1 768 and 1 712 cm^{-1}; δ_H1.5—2.3 (4 × CH_2), 2.13 (MeCO), and 9.6 (CHO); [Found: *m/z* 142.0620. $C_7H_{10}O_3$ (*M* − CH_2) requires 142.0630].

Preparation of 4-*Acetoxy*-3-*ethyl*-3-*phenylthio*-4,5-*dihydrofuran*-2(3H)-*ones. General Procedure.*—A solution of 2-phenylthiobutanoic acid (2.2 mmol) in dry tetrahydrofuran (THF) (1.5 ml) was added to a stirred solution of lithium di-isopropylamide (LDA) [prepared from di-isopropylamine (0.48 g) and butyllithium (1.7M) in hexane (2.6 ml)] in dry THF (4.5 ml) at 0 °C under nitrogen. The yellow solution of the enolate dianion (**20**) was stirred at 0 °C for 1 h, and then cooled to −78 °C where a solution of the acetoxy-aldehyde (2.0 mmol) in dry THF (1 ml) was added over 5 min. The mixture was stirred at −78 °C for 1 h, allowed to warm to room temperature, then an excess of 1M-sulphuric acid (10 ml) was added and the mixture was stirred at room temperature overnight. The resulting aqueous suspension was separated, extracted with ether (3 × 50 ml), and the combined ether extracts washed with aqueous sodium hydrogen carbonate (2 × 25 ml), dried, and evaporated. Chromatography on silica, using 1:1 diethyl ether–light petroleum (b.p. 40—60 °C) then produced the diastereoisomeric butyrolactones.

4-*Acetoxy*-3-*ethyl*-5,5-*dimethyl*-3-*phenylthio*-4,5-*dihydrofuran*-2(3H)-*one* [(**22**) and (**23**)].—By the general procedure, condensation between 2-acetoxy-2-methylpropanal[10] and the dianion (**20**), followed by chromatography gave: (i) the 4β-acetoxy isomer (**22**) (36%) $\nu_{max.}$(film) 1 760 cm^{-1}; δ_H 0.95 (t, *J* 7 Hz, $MeCH_2$), 1.45 (Me), 1.55 (Me), 1.5—1.96 (m, CH_2Me), 2.2

(OCOMe), 5.39 (C*H*OCOMe), and 7.26—7.65 (m, 5 × =CH), and (ii) the 4α-acetoxy isomer (**23**) (25%), $\nu_{max.}$(film) 1 760 cm^{-1}; δ_H 1.06 (t, *J* 7 Hz, *Me*CH_2), 1.23 (Me), 1.38 (Me), 1.5—1.96 (m, CH_2Me), 2.1 (OCOMe), 5.26 (C*H*OCOMe), and 7.3—7.68 (m, 5 × =CH). Double irradiation at δ 5.26 gave an n.O.e. enhancement of 7.5% at δ 7.3—7.68; *m/z* 308 (100), 205 (18), 180 (6), 157 (6), 149 (7), 139 (8), 113 (72), and 99(22) (Found: *m/z* 308.1081. $C_{16}H_{20}O_4S$ requires *M*, 308.1082).

4-*Acetoxy*-3-*ethyl*-3-*phenylthio*-1-*oxaspiro*[4.4]*nonan*-2-*one* [(**27**) and (**28**)] (A. G. Smith).[29]—By the general procedure, condensation between 1-acetoxycyclopentanecarbaldehyde (**26**) and the dianion (**20**), followed by chromatography gave: (i) the 4β-acetoxy isomer (**27**) (40%) which crystallised from ether as colourless plates, m.p. 70—71 °C; $\nu_{max.}$(KBr) 1 762 cm^{-1}; δ_H 0.99 (t, *J* 7 Hz, *Me*CH_2), 1.48—2.3 (m, 5 × CH_2), 2.21 (OCO*Me*), 5.7 (C*H*OCOMe), and 7.2—7.68 (m, 5 × =C*H*) (Found: C, 64.1; H, 6.9%; *m/z* 334.1186. $C_{18}H_{22}O_4S$ requires C, 64.6; H, 6.6%; *M*, 334.1238) and (ii) the 4α-acetoxy isomer (**29**) (20%) which crystallised from ether as colourless plates, m.p. 64—65 °C; $\nu_{max.}$(KBr) 1 757 cm^{-1}; δ_H 1.07 (t, *J* 7 Hz, *Me*CH_2), 1.48—2.37 (m, 5 × CH_2), 2.13 (OCOMe), 5.49 (C*H*OCOMe), 7.33—7.68 (m, 5 × =CH_2) (Found: C, 64.3; H, 6.9%; *m/z* 334.1174. $C_{18}H_{22}O_4S$ requires C, 64.6; H, 6.6%; *M*, 334.1174).

(E)-4-*Acetoxy*-3-*ethylidene*-5,5-*dimethyl*-4,5-*dihydrofuran*-2(3H)-*one* (**24**) *and* 4-*Acetoxy*-3-*ethyl*-5,5-*dimethylfuran*-(5H)-*one* (**25**).—A solution of *m*-chloroperoxybenzoic acid (92 mg; 85%, 0.45 mmol) in dichloromethane (5 ml) was added dropwise to a solution of the sulphide (**22**) (139 mg) in dichloromethane (5 ml) at −5 °C under nitrogen. The mixture was allowed to warm to 25 °C and then poured into saturated sodium hydrogen carbonate solution. The aqueous phase was separated and extracted with diethyl ether then the combined organic extracts were dried and evaporated, and the residue heated under reflux in carbon tetrachloride (10 ml) in the presence of calcium carbonate (0.2 g) for 3 h. The cooled mixture was filtered through Celite and the filtrate and washings were then evaporated to dryness. Chromatography of the residue on silica using ether as eluant gave the butyrolactone (74 mg, 68%) as an oil; δ_H 1.38 (Me), 1.43 (Me), 1.98 (d, *J* 7 Hz, =CH*Me*), 2.16 (OCO*Me*), 5.78 (C*H*OCOMe), and 7.2 (dq, *J* 1 and 7 Hz, =C*H*Me). Double irradiation at δ 2.16 gave an n.O.e. enhancement of 3.3% at δ 1.98 p.p.m.

Treatment of the diastereoisomeric acetoxy-sulphide (**23**) with *m*-chloroperoxybenzoic acid in a similar manner, led to a 3:2 mixture of compounds (**24**) and (**25**), as a liquid; $\nu_{max.}$(film) 1 790, 1 765, and 1 690 cm^{-1}; δ_H 1.06 (t, *J* 7 Hz, CH_2*Me*), 1.4 (2 × Me), 2.08 (q, *J* 7 Hz, CH_2Me), and 2.3 (OCOMe); *m/z* 198 (5), 162 (6), 156 (70), 141 (26), 123 (9), 113 (8), and 98 (21) (Found: *m/z* 198.0852. $C_{10}H_{14}O_4$ requires *M*, 198.0892).

(E)-4-*Acetoxy*-3-*ethylidene*-1-*oxaspiro*[4.4]*nonan*-2-*one and* 4-*Acetoxy*-3-*ethyl*-1-*oxaspiro*[4.4]*non*-3-*en*-2-*one* (*N. A. Pegg*).—Oxidative elimination of the diastereoisomeric acetoxy-sulphide (**27**) in the presence of *m*-chloroperbenzoic acid, according to the procedure described for the synthesis of compound (**24**) gave (*E*)-4-acetoxy-3-ethylidene-1-oxaspiro[4.4]nonan-2-one (60%) as an oil; $\nu_{max.}$($CHCl_3$) 1 758, 1 738, and 1 685 cm^{-1}; δ_H 1.6—2.0 (m, 8 H), 1.94 (d, *J* 7 Hz, =CH*Me*), 2.08 (OCOMe), 5.93 (C*H*OCOMe), 7.0 (dq, *J* 7 and 1 Hz, =C*H*Me) [Found: *m/z* 182.0936. $C_{10}H_{12}O_3$ (*M* − C_2H_2O) requires 182.0942]. Treatment of the diastereoisomeric acetoxy-sulphide (**28**) with *m*-chloroperbenzoic acid, in a similar manner, led to a 3:2 mixture of the aforementioned ethylidenenonanone and 4-acetoxy-3-ethyl-1-oxaspiro-[4.4]non-3-en-2-one, as an oil; $\nu_{max.}$($CHCl_3$) 1 786, 1 750, and 1 690 cm^{-1}; δ_H 1.09 (d, *J* 7 Hz, CH_2*Me*), 1.7—2.0 (m, 8 H), 2.18 (q, *J* 7 Hz, CH_2Me), and 2.3 (OCOMe) (Found: *m/z* 224.1036. $C_{12}H_{16}O_4$ requires *M*, 224.1047). A small amount (< 5%) of the *Z*-ethylidene isomer corresponding to the title compound, δ_H 1.6—2.0 (m, 8 H), 2.07 (OCOMe), 2.21 (dd, *J* 7 and 1 Hz, =CH*Me*), 5.6 (t, *J* 1 Hz, C*H*OCOMe), and 6.73 (dq, *J* 7 and 1 Hz, =C*H*Me), was produced concurrently in the oxidative eliminations.

(1β,5β)-2α-*Acetoxybicyclo*[3.3.0]*oct*-7-*ene* (**14b**).—A solution of bicyclo[3.3.0]oct-7-en-2-ol (**14a**) (31 g, 0.25 mol) (prepared by the method of Crandall *et al.*[7]) and 4-dimethylaminopyridine (100 mg), in acetic anhydride (50 g) and triethylamine (27 g) was stirred at room temperature for 24 h. Saturated aqueous sodium hydrogen carbonate (500 ml) was added and the mixture was stirred for 1 h, and then extracted with ether (5 × 50 ml). The combined extracts were washed with dilute hydrochloric acid (2 × 50 ml) and saturated aqueous sodium hydrogen carbonate solution (3 × 50 ml). Evaporation of the dried ether extracts followed by distillation gave the *acetate* (39 g, 95%) as a colourless oil, b.p. 94 °C at 12 mmHg, $\nu_{max.}$(film) 3 055 (m), 2 955 (s), 2 875 (m), 1 740 (s), 1 660 (w), 1 380 (s), 1 260 (s), 1 130 (s), 1 060 (s), 900 (m), and 720 (m) cm^{-1}; δ_H($CDCl_3$) 1.30—2.30 (m, 2 × CH_2 plus CH), 2.03 (MeCO), 2.48—2.85 (m, CH_2CH=), 3.25—3.52 (m, C*H*CH=), 5.00—5.28 (m, AcOC*H*), 5.41—5.59 (m, =CH), and 5.61—5.87 (m, =C*H*); δ_C($CDCl_3$) 21.0 (q), 30.8 (t), 31.0 (t), 39.3 (d), 41.6 (t), 53.7 (d), 77.5 (d), 128.5 (d), 132.3 (d), and 170.6 p.p.m.; *m/z* 166(1), 123 (5), 122 (4), 106 (100), 105 (10), 91 (27), 79 (85), 78 (24), 77 (15), 67 (19), 59 (23), and 45 (100) (Found: C, 72.3; H, 8.5%; *m/z* 166.0997. $C_{10}H_{14}O_2$ requires C, 72.2; H, 8.6%; *M*, 166.0994).

2α-*Acetoxybicyclo*[3.3.0]*octane*-7β,8β-*diol* (**32**).—A solution of osmium(VIII) oxide (40 mg) in t-butyl alcohol (46 ml) was added to an ice-cooled solution of the acetate (**14b**) (38.0 g, 0.23 mol) and 30% hydrogen peroxide (105 ml, 0.23 mol) in t-butyl alcohol (50 ml). The mixture was stirred at room temperature for 24 h, and the solvent removed under reduced pressure. The residue was dissolved in chloroform (20 ml), and the solution dried and evaporated to give the diol (45 g, 98%) which recrystallised from chloroform as colourless needles, m.p. 92—95 °C; $\nu_{max.}$($CHCl_3$) 3 750 (s), 2 590 (s), 2 880 (m), 1 730 (s), 1 380 (s), 1 250 (br s), 1 105 (m), and 1 045 (s) cm^{-1}; δ_H($CDCl_3$) 1.30—3.00 (m, 3 × CH_2 plus 2 × CH), 2.03 (MeCO), 2.90 (br, 2 × OH), 3.99 (dd, *J* 6.1 and 3.8 Hz, C*H*OH), 4.17 (dd, *J* 6 and 3 Hz, C*H*OH), and 5.07 (dd, *J* 6 and 1.2 Hz, C*H*OAc); δ_C($CDCl_3$) 21.0 (q), 30.8 (t), 31.0 (t), 39.3 (d), 41.6 (t), 53.7 (d), 77.5 (d), 128.5 (d), 132.3 (d), and 170.6 p.p.m.; *m/z* 182 (3), 156 (9), 138 (24), 122 (63), 110 (39), 97 (45), 95 (52), 81 (63), 80 (64), 79 (44), 67 (10), and 66 (87) (Found: M^+ − H_2O 182.0943. $C_{10}H_{14}O_3$ requires 182.0943).

(1β,2α,6α,8β)-11α-*Acetoxy*-4,4-*dimethyl*-3,5-*dioxatricyclo*-[6.3.0.$0^{2,6}$]*undecane* (**33b**).—A solution of the diol (**32**) (36 g, 0.18 mol) in 2,2-dimethoxypropane (260 ml) was stirred at room temperature in the presence of toluene-*p*-sulphonic acid (0.1 g) for 18 h. Chloroform (1l) was added, and the mixture was washed with 5% sodium hydrogen carbonate solution (3 × 100 ml), dried and evaporated to give the *dioxatricycloundecane* (43 g, 99%) which was used without further purification; $\nu_{max.}$(film) 2 940 (s), 2 880 (m), 1 740 (s), 1 375 (s), 1 240 (s), 1 055 (s), and 1 030 (m) cm^{-1}; δ_H($CDCl_3$) 1.29 (Me), 1.45 (Me), 1.50—2.20 (m, 3 × CH_2), 2.04 (Ac), 2.58 (dd, *J* ~ 7.5 Hz, C*H*CHOAc), 2.91 (m, CH_2C*H*CH_2), 4.57 (d, *J* 5.3 Hz, CHC*H*O), 4.69 (dd, *J* 5.3 and 5.3 Hz, CH_2C*H*O), and 5.23 (m, C*H*OAc); δ_C($CDCl_3$) 21.3 (q), 24.6 (q), 27.1 (q), 28.6 (t), 33.6 (t), 40.3 (t), 41.3 (d), 55.2 (d), 76.8 (d), 81.8 (d), 83.3 (d), 109.6, and 170.2 p.p.m.; *m/z* 225 (13), 165 (8), 123 (23), 105 (26), 79 (27), 67 (34), 66 (21), 55 (16), and

43 (100); (Found: M^+ − Me 225.1131. $C_{12}H_{17}O_4$ requires 225.1127).

(1β,2α,6α,8β)-4,4-*Dimethyl*-3,5-*dioxatricyclo*[6.3.0.0^{2,6}]*undecan*-11α-*ol* (**33a**).—A solution of the acetate (**33b**) (38 g), 0.16 mol) in ethanol (530 ml) was added over 15 min to a stirred, ice-cooled solution of potassium hydroxide (27 g, 0.47 mol) in water (106 ml). The mixture was stirred at room temperature for 3 h and the ethanol evaporated under reduced pressure. The resulting aqueous solution was extracted with ether (4 × 100 ml), and the extracts were then combined, dried and evaporated. Chromatography of the residue on silica (diethyl ether) gave the *alcohol* (27 g, 86%) as a colourless waxy solid, m.p. 42—43 °C, $\nu_{max.}$(film) 3 470 (br s), 2 980 (s), 2 945 (s), 1 460 (m), 1 385 (s), 1 370 (s), 1 225 (s), 1 210 (s), 1 065 (s), 1 050 (s), 875 (m), and 860 (m) cm^{-1}; δ_H($CDCl_3$) 1.31 (Me), 1.46 (Me), 1.45—1.88 (m, 2 × CH_2 plus *H*CHCHOH), 1.91 (OH), 2.14 (dd, *J* 14.1 and 8.5 Hz, *H*CHCHO), 2.42 (dd, *J* 8.8 and 6.3 Hz, C*H*CHO), 2.85 (m, CH_2CHCH_2), 4.30 (m, C*H*OH), 4.70 (dd, *J* 5.5 and 5 Hz, CH_2CHO), and 4.80 (d, *J* 5.5 Hz, CHC*H*O); δ_C($CDCl_3$) 24.8 (q), 27.2 (q), 28.8 (t), 36.2 (2), 40.6 (t), 41.3 (d), 56.6 (d), 73.4 (d), 81.7 (d), 84.2 (d), and 109.4 p.p.m.; *m/z* 183 (4), 140 (16), 138 (24), 122 (62), 110 (38), 97 (44), 96 (56), 94 (33), 83 (33), 81 (62), 80 (64), 79 (44), 67 (100), 66 (87), 43 (100), and 41 (40) (Found: C, 66.1, H, 9.3%; M^+ − Me 183.1016. $C_{11}H_{18}O_3$ requires C, 66.5, H, 9.2%; $C_{10}H_{15}O_3$ requires 183.1021).

(1β,2α,6α,8β)-4,4-*Dimethyl*-3,5-*dioxatricyclo*[6.3.0.0^{2,6}]*undecan*-11-*one* (**34**).—A solution of the alcohol (**33a**) (18 g, 0.09 mol) in dichloromethane (240 ml) was added over 10 min to an ice-cooled suspension of pyridinium chlorochromate (39 g, 0.18 mol) sodium acetate (3.8 g, 0.05 mol) and Celite (39 g) in dichloromethane (240 ml). The mixture was stirred at 0 °C for 1 h, then at room temperature for 3 h, after which it was diluted with ether (2 l). The mixture was kept at 25 °C for 0.5 h and then filtered through a Celite pad. Evaporation of the solvent and recrystallisation of the residue from chloroform gave the *ketone* (16 g, 89%) as colourless plates, m.p. 84—85 °C, $\nu_{max.}$(KBr) 2 990 (s), 2 945 (s), 1 740 (s), 1 385 (s), 1 370 (s), 1 265 (s), 1 225 (s), 1 210 (s), 1 055 (s), and 960 (s) cm^{-1}; δ_H($CDCl_3$) 1.28 (Me), 1.44 (Me), 1.17—2.42 (m, 3 × CH_2), 2.62 (d, *J* 7.8 Hz, C*H*C=O), 3.13 (m, CH_2CHCH_2), 4.64 (dd, *J* 5.4 and 5 Hz, CH_2CHO), and 4.73 (d, *J* 5.4 Hz, CHC*H*O); δ_C($CDCl_3$) 22.7 (t), 24.2 (q), 26.6 (q), 35.1 (t), 36.5 (t), 38.7 (d), 61.0 (d), 82.1 (d), 83.3 (d), 110.0, and 218.4 p.p.m.; *m/z* 181 (100), 139 (80), 121 (66), 93 (46), 79 (67), 55 (38), 53 (28), 43 (100), and 41 (36) (Found: C, 67.2; H, 8.3%; M^+ − Me 181.0857. $C_{11}H_{16}O_3$ requires C, 67.3; H, 8.2%; $C_{10}H_{13}O_3$ requires 181.0865).

(1β,2α,6α,8β)-4,4-*Dimethyl*-11-*trimethylsilyloxy*-3,5-*dioxatricyclo*[6.3.0.0^{2,6}]*undec*-10-*ene* (**35**).—A solution of the ketone (**34**) (1.0 g, 5.1 mol) in THF (10 ml) was added over 10 min to a stirred solution of LDA [prepared from di-isopropylamine (0.55 g, 5.4 mmol) and butyl-lithium (1.55M solution in hexane, 3.5 mol, 5.4 mmol)] in THF (38 ml) at −80 °C under nitrogen. After 0.5 h chlorotrimethylsilane (737 mg, 6.8 mmol) was added, and the solution was stirred at −80 °C for 1 h, and then at room temperature for a further 2 h. The solvent was evaporated under reduced pressure, and the residue was then suspended in dry ether (100 ml). After filtration and evaporation, distillation gave the *silyl enol ether* (1.48 g, 98%) as a colourless oil, b.p. 83—87 °C at 0.1 mmHg; $\nu_{max.}$(film) 2 960 (s), 1 650 (s), 1 380 (s), 1 340 (s), 1 260 (s), 1 220 (s), 1 060 (s), and 855 (s) cm^{-1}; δ_H($CDCl_3$) 0.2 (3 × MeSi), 1.31 (Me), 1.44 (Me), 1.48 (dd, *J* 12.7 and 4.9 Hz, *H*CHCHO), 1.86 (app. dm, *J* 12.7 and 2.4 Hz, *H*CHCHO), 2.17 (dd, *J* 14.3 and 7.4 Hz, *H*CHCH=), 2.42 (dm, *J* ~ 14.3 Hz *H*CHCH=), 2.79—2.92 (m, CH_2CHCH_2), 2.95 (m, C*H*COSi), 4.47 (dd, *J* 4.5 and 2.2 Hz, CH_2CHO), 4.59 (d, *J* 4.5 Hz, CHC*H*O), and 4.61 (C*H*=); δ_C($CDCl_3$) −0.2 (3 × q), 24.2 (q), 26.9 (q), 32.6 (t), 37.6 (d), 38.6 (t), 58.2 (d), 81.8 (d), 82.4 (d), 100.4 (d), 109.4, and 153.2 p.p.m. (Found: C, 62.4; H, 9.2%. $C_{14}H_{24}O_3Si$ requires C, 62.6; H, 9.0%).

(1β,2α,6α,8β)-4,4-*Dimethyl*-3,5-*dioxatricyclo*[6.3.0.0^{2,6}]*undec*-9-*en*-11-*one* (**36**).—A solution of the trimethylsilyl enol ether (**35**) (7.8 g, 29 mmol) in dry acetonitrile (30 ml) was added to a stirred suspension of palladium(II) acetate (3.8 g, 17 mmol) and *p*-benzoquinone (1.5 g, 14 mmol) in dry acetonitrile (103 ml). The mixture was stirred at room temperature under nitrogen for 90 h, and the solvent evaporated *in vacuo*. Chromatography of the residue on silica (1:1 ether–light petroleum) gave the *enone* (3.0 g, 59%), which recrystallised from chloroform as colourless plates, m.p. 51—53 °C, $\lambda_{max.}$(EtOH) 225 nm; $\nu_{max.}$(film) 3 000 (w), 2 950 (w), 1 710 (s), 1 390 (m), 1 230 (s), 1 080 (s), and 1 060 (s) cm^{-1}; δ_H($CDCl_3$) 1.31 (Me), 1.50 (Me), 1.59—1.71 (app. dt, *J* 14 and 6 Hz, *H*CH), 2.27 (ddd, *J* 14.0, 9.1, and 2.8 Hz, *H*CH), 2.95 (d, *J* 6.5 Hz, C*H*C=O), 3.64—3.75 (m, C*H*CH=CH), 4.63 (m, 2 × C*H*O), 6.02 (dd, *J* 5.6 and 1.5 Hz, CHCH=C*H*), and 7.68 (dd, *J* 5.6 and 3.0 Hz, CHC*H*=CH); δ_C($CDCl_3$) 25.3 (q), 27.7 (q), 36.3 (t), 45.8 (d), 47.9 (d), 81.9 (d), 83.2 (d), 111.0, 132.1 (d), 167.1 (d), and 208.3 p.p.m.; *m/z* 179 (92), 137 (13), 119 (100), 107 (11), and 91 (10); (Found: C, 67.9; H, 7.2%; M^+ − Me 179.0707. $C_{11}H_{14}O_3$ requires C, 68.0%; H, 7.3%; $C_{10}H_{11}O_3$ requires 179.0708).

1-(1,3-*Dithian*-2-*yl*)*cyclopent*-2-*en*-1-*ol* (**38a**).—By the general procedure described for the synthesis of the tricyclo[6.3.0.0^{2,6}]-undecenol (**42a**), addition of lithium dithiane (**37**) to cyclopentenone, followed by chromatography (alumina; CH_2Cl_2) gave the cyclopentenol (82%) as a colourless oil; $\nu_{max.}$(film) 3 450 and 2 920 cm^{-1}; δ_H 1.68—2.78 (m, 3 × CH_2 plus O*H*), 2.9 (m, 2 × SCH_2CH$_2$), 4.4 (SCHS), 5.86 (m, C*H*), and 6.08 (m, =C*H*) (Found: C, 54.0; H, 7.3%; *m/z* 202.0502. $C_9H_{14}OS_2$ requires C, 53.5; H, 7.0%; *M*, 202.0486).

1-*Acetoxy*-1-(1,3-*dithian*-2-*yl*)*cyclopent*-2-*ene* (**38b**).—By the general procedure described for the synthesis of the acetoxytricyclo[6.3.0.0^{2,6}]undecene (**42b**), acetylation of the alcohol (**38a**) gave the acetate (98%) as colourless plates m.p. 59 °C (diethyl ether); $\nu_{max.}$ 2 980, 1 734, and 1 237 cm^{-1}; δ_H 1.6—2.7 (m, 3 × CH_2), 2.03 (OCOMe), 2.84 (m, 2 × SCH_2), 5.27 (SCHS), and 5.99—6.26 (m, 2 × C*H*) (Found: C, 54.1; H, 6.9%; *m/z* 244.0584. $C_{11}H_{16}O_2S_2$ requires C, 54.2; H, 6.6%; *M*, 244.0592).

1-(*Bisacetoxymethyl*)-3-*acetoxycyclopent*-1-*ene* (**40**) *and* 3-*Acetoxycyclopent*-1-*enecarbaldehyde* (**41**).—Attempts to convert the acetoxydithiane (**38b**) into the corresponding acetoxyaldehyde (**39**) in the presence of lead(IV) oxide and boron trifluoride[30] instead led to a mixture of the diacetate (**40**); δ_H 1.62—3.0 (m, 2 × CH_2), 1.98 (OCOMe), 2.0 (2 × OCOMe), 5.65 (m, CHO), 5.92 (m, =CH), and 7.18 [m, C*H*(OAc)$_2$]; and the aldehyde (**41**); $\nu_{max.}$(film) 2 930, 1 760, 1 730 cm^{-1}; δ_H 1.62—3.0 (m, 2 × CH_2), 2.1 (OCOMe), 5.88 (m, C*H*OCOMe), 6.94 (m, =CH), and 9.96 (CHO) (Found: *m/z* 154.0634. $C_8H_{10}O_3$ requires *M*, 154.0630).

(1β,2α,6α,8β)-11α,(β)-(1,3-*Dithian*-2-*yl*)-4,4-*dimethyl*-3,5-*dioxatricyclo*[6.3.0.0^{2,6}]*undec*-9-*en*-11-*ol* [(**42a**) and (**43a**)].—Butyl-lithium (1.54M solution in hexane, 4.1 ml, 6.3 mmol) was added over 10 min to a stirred solution of 1,3-dithiane (0.96 g, 7.2 mmol) in dry THF (16 ml) at −78 °C under nitrogen. The solution was maintained at −20 °C for 1 h, and then re-cooled to −78 °C, when a solution of the enone (**36**) (310 mg, 1.60 mmol) in THF (13 ml) was added over 10 min. After 1 h the mixture was allowed to warm to room temperature, and then

poured into saturated aqueous ammonium chloride solution. The layers were separated, and the aqueous phase was extracted with ether (3 × 30 ml), and the organic layers combined, dried, and evaporated. Very careful chromatography on alumina (hexane, then chloroform) allowed separation of the isomers to give: (i) the 11α-*hydroxy diastereoisomer* (**42a**) (301 mg, 60%) which recrystallised from isopropyl alcohol as colourless needles, m.p. 110—112 °C; $\delta_H(CDCl_3)$ 1.33 (Me), 1.50 (Me), 1.6 (app. dt, *J* 14 and 6 Hz, *H*CH), 1.80—1.98 (m, $CH_2CH_2CH_2$), 2.1 (m, C*H*CHO), 2.14 (app. t, *J* 14 and 9 Hz, HC*H*), 2.42 (OH), 2.81—2.98 (m, 2 × SCH_2), 3.36—3.50 (m, =CHC*H*), 4.35 (SCHS), 4.77 (dd, *J* 5 and 5 Hz, CH_2CHO), 4.92 (d, *J* 5 Hz, CHC*H*O), 5.73 (dd, *J* 5.6 and 1.1 Hz, =C*H*CO), and 6.09 (dd, *J* 5.6 and 2.7 Hz, CHC*H*=); double irradiation of the peak at δ 3.43 leads to simplification of the multiplets at δ 1.52—1.70 and δ 2.14—2.23, and a loss of the fine coupling to the signals at δ 5.73 and δ 6.09; $\delta_C(CDCl_3)$ 24.8 (q), 25.6 (t), 27.3 (q), 30.2 (t), 30.4 (t), 39.5 (t), 49.1 (d), 54.4 (d), 58.5 (d), 81.7 (d), 84.6 (d), 85.9, 109.7, 132.3 (d), and 139.7 (d) p.p.m. (Found: *m*/*z* 314.1022. $C_{15}H_{22}O_3S_2$ requires *M*, 314.1010); (ii) the 11β-*hydroxy diastereoisomer* (**43a**) (186 mg, 37%) which recrystallised from isopropyl alcohol as colourless needles, m.p. 115—117 °C, $\delta_H(CDCl_3)$, 1.33 (Me), 1.50 (Me), 1.42—1.63 (m, *H*CH), 1.80—1.99 (m, $CH_2CH_2CH_2$), 1.99—2.05 (m, C*H*CHO), 2.08—2.20 (m, *H*CH), 2.68 (OH), 2.85—2.99 (m, 2 × SCH_2), 3.60—3.70 (m, =CHC*H*), 4.45 (SCHS), 4.77 (ddd, *J* 5, 5, and 5 Hz, CH_2CHO), 4.90 (dd, *J* 5.0 and 2.0 Hz, CHC*H*O), 5.81 (dd, *J* 5.6 and 1.1 Hz, =C*H*COH), and 5.92 (dd, *J* 5.6 and 2.2 Hz, CHC*H*=); double irradiation of the peak at δ 3.65 leads to a simplification of the multiplets at δ 1.80—1.99 and 1.99—2.05, and a loss of the fine coupling to the signals at δ 5.81 and 5.92; $\delta_C(CDCl_3)$ 25.4 (q), 25.7 (t), 27.8 (q), 30.4 (t), 30.6 (t), 36.7 (t), 49.4 (d), 55.6 (d), 61.3 (d), 82.4 (d), 82.8 (d), 88.0, 110.3, 132.6 (d), and 139.3 (d) p.p.m. (Found: C, 57.2; H, 7.2%; $C_{15}H_{22}O_3S_2$ requires C, 57.3; H, 7.05%).

(1β,2α,6α,8β)-11α(β)-*Acetoxy*-11β(α)-(1,3-*dithian*-2-*yl*)-4,4-*dimethyl*-3,5-*dioxatricyclo*[6.3.0.0^{2,6}]*undec*-9-*ene* [(**42b**) *and* (**43b**)].—A solution of a 3:2 mixture of the diastereoisomeric dithiane alcohols (**42a**) and (**43a**) (2.7 g, 8.66 mmol) and 4-dimethylaminopyridine (44 mg) in acetic anhydride (3.5 g, 34 mmol) and triethylamine (2.8 g, 27 mmol), was stirred at room temperature for 5 days. Ether (220 ml) was added, and the solution was then washed successively with saturated ammonium chloride solution (50 ml), saturated sodium hydrogen carbonate solution (3 × 100 ml) and brine (100 ml). Activated charcoal (0.25 g) was added, and the mixture was then stirred for 15 min, filtered, dried, and evaporated to leave a 3:2 mixture of the diastereoisomeric acetates (2.8 g, 92%) as an off-white solid. Chromatography on silica using diethyl ether–hexane (1:1) as eluant gave: (i) the α-acetate (**42b**) (eluted first) which crystallised from ether as colourless plates, m.p. 133—134 °C; $\nu_{max.}$(KBr) 2 925 and 1 735 cm^{-1}; δ_H 1.34 (Me), 1.4—1.55 (α-*H*CH), 1.51 (Me), 1.73—1.96 (m, $CH_2CH_2CH_2$), 2.02 (OCOMe), 2.16 (dd, *J* 14 and 8 Hz, β-HC*H*), 2.8—3.0 (m, 2 × SCH_2), 3.24 (d, *J* 7 Hz, *H*CCHO), 3.43 (dd, *J* ~ 7 Hz, =CHC*H*), 4.81 (dd, *J* 5 and 5 Hz, CH_2CHO), 4.97 (d, *J* 5 Hz, CHC*H*O), 5.41 (SCHS), and 6.08—6.2 (m, 2 × =C*H*); δ_C 21.4 (q), 24.8 (q), 25.5 (t), 27.1 (q), 30.2 (t), 30.7 (t), 39.5 (t), 45.8 (d), 49.4 (d), 57.3 (d), 81.5 (d), 84.7 (d), 93.3, 109.3, 130.9 (d), 140.9 (d), and 169.0 p.p.m. (Found: C, 57.0; H, 6.8%; *m*/*z* 356.1132. $C_{17}H_{24}O_4S_2$ requires C, 57.3; H, 6.8%; *M*, 356.1116), and (ii) the β-acetate (**43b**) (eluted second) which crystallised from ether as colourless plates, m.p. 144—145 °C; $\nu_{max.}$(KBr) 2 910 and 1 735 cm^{-1}; δ_H 1.34 (Me), 1.4—1.55 (β-*H*CH), 1.47 (Me), 1.73—1.96 (m, $CH_2CH_2CH_2$), 2.06 (OCOMe), 2.04—2.2 (m, α-*H*CH), 2.8—3.0 (m, 2 × SCH_2), 3.02 (d, *J* 7 Hz, *H*CCHO), 3.67 (m, =CHC*H*), 4.81 (dd, *J* 5 and 5 Hz, CH_2CHO), 5.58 (d, *J* 5 Hz, CHCHO), 5.26 (SCHS), 5.78 (d, *J* 5.5 Hz, C*H*=CHCH), and 6.15 (m, CH=C*H*CH); δ_C 21.5 (q), 25.3 (q), 25.7 (t), 27.4 (q), 30.4 (t), 31.3 (t), 37.7 (t), 48.4 (d), 52.6 (d), 61.9 (d), 82.4 (d), 84.6 (d),95.1, 109.5, 129.1 (d), 140.6 (d), and 169.9; *m*/*z* 356 (28), 341 (14), 338 (10), 297 (47), 296 (100), 239 (17), 238 (14), 209 (25), and 182 (88) (Found: C, 57.0; H, 6.8%; *m*/*z* 356.1122. $C_{17}H_{24}O_4S_2$ requires C, 57.3; H, 6.8%; *M*, 356.1116).

(1β,2α,6α,8β)-9-(*Acetoxy*-4,4-*dimethyl*-3,5-*dioxatricyclo*-[6.3.0.0^{2,6}]*undec*-9-*ene*-11-*carbaldehyde* (**44**) *and* (1β,2α,6α,8β)-9-α,β-*Acetoxy*-11-(*bisacetoxymethyl*)-4,4-*dimethyl*-3,5-*dioxatricyclo*[6.3.0.0.^{2,6}]*undec*-9-*ene* (**45**).—Attempts to convert the 3:1 mixture of acetoxy-dithianes (**42b**) and (**43b**) into the corresponding acetoxy-aldehydes (**46**) in the presence of PbO_2–BF_3·OEt_2 in acetic acid led to a mixture of the diacetate (**45**), a colourless oil, $\nu_{max.}$ 3 020 and 1 775 cm^{-1}; δ_H 1.3 (Me), 1.56 (Me), 1.6—2.5 (m, CH_2), 2.03 (OCOMe), 2.13 (2 × OCOMe), 2.7—3.18 (m, *H*CH_2), 3.3—3.5 (m, C*H*CHO), 4.55—4.83 (m, C*H*OC*H*O), 5.28 (m, C*H*OCOMe), 5.88 (m, =C*H*), and 7.4 [C*H*(OCOMe)$_2$], and the unsaturated aldehyde (**44**) as a mixture of OAc-epimers; $\nu_{max.}$ 1 754 and 1 736 cm^{-1}; δ_H (major diastereoisomer) 1.3 (Me), 1.48 (Me), 1.3—1.5 (m, α-*H*CH), 2.07 (OCOMe), 2.34 (dd, *J* 14.4 and 8.0 Hz, β-*H*CH), 3.07 (m, CH_2CHCHOCOMe), 3.54 [d, *J* 6.3 Hz, =C(CHO)C*H*], 4.59 (dd, *J* 4.7 and 4.3 Hz, CH_2CHOCHO), 4.66 (d, *J* 4.3 Hz, CH_2CHOCHO), 5.45 (br, C*H*OCOMe), 6.7 (m, =C*H*), and 9.63 (CHO); δ_H(minor diastereoisomer) 1.3 (Me), 1.47 (Me), 1.3—1.5 (m, β-*H*CH), 1.98 (dd, *J* 12 and 8 Hz, α-*H*CH), 2.04 (OCOMe), 2.98 (m, $CH_2C_2CHOCOMe$), 3.3 (m, =CCHOC*H*), 4.61 (m, CH_2CHOCHO), 4.78 (d, *J* 6.3 Hz, CH_2CHOCHO), 5.8 (m, C*H*OCOMe), 6.64 (m, =CH), and 9.69 (CHO) [Found: *m*/*z* 251.0888. $C_{13}H_{15}O_5$ (*M* − Me) requires 251.0859].

(1β,2α,6α,8β)-4,4-*Dimethyl*-11α(β)-(5-*methylperhydro*-1,3,5-*dithiazin*-2-*yl*)-3,5-*dioxatricyclo*[6.3.0.0^{2,6}]*undec*-9-*en*-11-*ol* [(**48a**) *and* (**49a**)].—Butyl-lithium (1.89M solution in hexane, 2.6 ml, 4.9 mmol) was added dropwise to a solution of 5-methylperhydro-1,3,5-dithiazine (0.66 g, 4.9 mol) in THF (20 ml) at −80 °C under nitrogen. After 10 min the mixture was allowed to warm to −30 °C for 0.5 h, then recooled to −80 °C when a solution of the enone (**36**) (0.75 g, 4.1 mmol) in THF (10 ml) was added. The mixture was stirred for 1 h, then allowed to warm to room temperature and poured into saturated aqueous ammonium chloride (50 ml). The layers were separated, the aqueous phase was extracted with ether (4 × 25 ml), and the organic layers were combined, dried, and evaporated. Chromatography on alumina (1:1 ether–petroleum) gave: (i) the α-*hydroxy epimer* (**48a**) (0.39 g, 29%); $\delta_H(CCl_4)$ 1.18 (Me), 1.33 (Me) 1.65—2.25 (m, CH_2), 2.45 (MeN), 2.72—2.90 (m, C*H*CHO), 2.95—3.45 (m, C*H*CH_2), 3.95 (d, *J* 12 Hz, 2 × equatorial SCHN), 4.45 (d, *J* 12 Hz, 2 × axial SCHN), 4.35—4.85 (m, C*H*OC*H*O), 5.42 (d, *J* 6 Hz, CC*H*=), 5.78 (dd, *J* 6 and 3 Hz, CH=C*H*CH); and (ii) a mixture of the α- and β-*hydroxy epimers* (0.36 g, 27%), $\delta_H(CCl_4)$, 1.25 (Me), 1.40 (Me), 1.50—2.23 (m, CH_2), 2.56 (MeN), 2.70—3.10 (m, C*H*CHO), 3.18—3.75 (m, CHCH_2), 4.05—4.30 (m, CHCH_2), 4.05—4.30 (m, equatorial SCHN), 4.40—5.0 (m, axial SCHN, and C*H*OC*H*O), and 5.62—6.08 (m, C*H*=C*H*).

(1β,2α,6α,8β)-11α-*Hydroxy*-4,4-*dimethyl*-3,5-*dioxatricyclo*-[6.3.0.0^{2,6}]*undec*-9-*en*-11β-*carbaldehyde* (**50a**).—A solution of the alcohol (**48a**) (100 mg, 0.3 mmol) in dichloromethane (5 ml) was added to a well stirred suspension of mercury(II) chloride (182 mg, 0.67 mol) and calcium carbonate (67 mg, 0.67 mol) in dichloromethane (5 ml) and water (300 μl). After the mixture had been stirred at room temperature for 100 h, it was filtered through Celite. The filter cake was washed well with ether, and the organic layers were then combined, washed with brine (10

ml), dried, and evaporated to give the *aldehyde* (60 mg, 88%), $\delta_H(CCl_4)$ 1.20 (Me), 1.40 (Me), 1.45—1.80 (m, *H*CH), 2.27 (ddd, *J* 14, 8, and 2 Hz, *H*CH), 2.80 (d, *J* 8 Hz, *H*CCHO), 3.34—3.75 (m, C*H*CH_2 and OH), 4.60—4.80 (m, C*H*OCHCO), 5.34 (dd, *J* 6 and 2 Hz, CC*H*=), 6.26 (dd, *J* 6 and 3 Hz, =C*H*CH), and 9.40 (CHO). The product was found to be highly unstable. Purification of samples by chromatography was not possible, nor could the aldehyde be stored for more than a few days.

(1β,2α,6α,8β)-11α-*Acetoxy*-4,4-*dimethyl*-11β-(5-*methylperhydro*-1,3,5-dithiazin-2-*yl*)-3,5-*dioxatricyclo*[6.3.0.$0^{2,6}$]*undec*-9-*ene* (**48b**).—Butyl-lithium (2.04M solution in hexane, 5.8 ml, 11.8 mmol) was added dropwise to a solution of 5-methylperhydro-1,3,5-dithiazine (1.62 g, 12 mmol) in THF (50 ml) at −80 °C under nitrogen. After 10 min the mixture was allowed to warm to −30 °C for 0.5 h then recooled to −80 °C when a solution of the enone (**36**) (2.0 g, 10.3 mmol) in THF (10 ml) was added. After 1 h the mixture was allowed to warm to room temperature, acetic anhydride was added (1.42 g, 14 mmol), and stirring was continued overnight (16 h). The mixture was poured into saturated sodium hydrogen carbonate solution (50 ml), and the separated aqueous phase was then extracted with ether (3 × 25 ml). The organic layers were combined, then washed with saturated aqueous sodium hydrogen carbonate (20 ml), dried, and evaporated. Chromatography on silica (3:1 petroleum–ether) gave the acetate (1.84 g, 48%), $\delta_H(CDCl_3)$ 1.35 (Me), 1.43—1.58 (m, α-*H*CH), 1.52 (Me), 2.02 (Ac), 2.17 (dd, *J* 14.0 and 7.8 Hz, β-*H*CH), 2.58 (MeN), 3.35 (d, *J* 7 Hz, *H*CCHO), 3.45 (dd, *J* ~ 7 Hz, C*H*CH=), 4.05 (dd, *J* 13.7 and 1.5, equatorial SCHN), 4.10 (dd, *J* 13.7 and 1.4 Hz, equatorial SCHN), 4.67 (d, *J* 13.7 Hz, axial SCHN), 4.73 (d, *J* 13.7 Hz, axial SCHN), 4.79 (dd, *J* 5.7 and 5.7 Hz, CH_2CHO), 4.99 (d, *J* 5.3 Hz, CHC*H*O), 5.64 (SCHS), 6.07 (dd, *J* 5.7 and 0.8 Hz, CC*H*=CH), and 6.19 (dd, *J* 5.7 and 2.7 Hz, CCH=C*H*); double irradiation at δ 4.10 led to simplification of the doublets at δ 4.67 and δ 4.73 to singlets, at δ 3.35 to simplification of the peak δ 1.43—1.58, and caused the double doublets at δ 2.17, δ 6.07 and δ 6.19 to collapse to doublets. Irradiation at δ 5.64 gave an n.O.e. enhancement at δ 6.07, δ 4.67/4.73, and δ 3.35 of 6.6%, 11%, and 2.2% respectively, and irradiation at δ 2.02 gave an enhancement at δ 4.99 of 0.9%; $\delta_C(CDCl_3)$ 21.6 (q), 24.7 (q), 27.3 (q), 37.6 (q), 39.6 (d), 48.6 (d), 55.7 (d), 57.4 (d), 60.3 (t), 60.8 (t), 81.5 (d), 84.7 (d), 93.9, 109.5, 130.3 (d), 141.7 (d), and 169.2 p.p.m.; (Found: C, 54.3; H, 6.9; N, 3.4%; *m/z* 371.1229. $C_{17}H_{25}O_4S_2N$ requires C, 54.9; H, 6.8; N, 3.8%; *M*, 371.1225).

(1β,2α,6α,8β)-11α-*Acetoxy*-4,4-*dimethyl*-3,5-*dioxatricyclo*-[6.3.0.$0^{2,6}$]*undec*-9-*ene*-11β-*carbaldehyde* (**50b**).—A solution of the acetate (**48b**) (300 mg, 0.81 mol) in acetonitrile (5 ml) was added to a well stirred suspension of mercury(II) chloride (486 mg, 1.8 mmol) and calcium carbonate (180 mg, 1.80 mol) in acetonitrile (10 ml) and water (1 ml), and the resulting mixture was stirred at room temperature for 24 h. Ether (30 ml) was added, and the mixture was then filtered through Celite, washed with brine (10 ml), dried, and evaporated to give the *aldehyde* (216 mg, 98%), $\delta_H(CCl_4)$ 1.23 (Me), 1.42 (Me), 1.50—2.24 (m, CH_2), 2.04 (Ac), 2.97 (dd, *J* 8 and 1 Hz, C*H*CHO), 3.33—3.60 (m, C*H*CH_2), 4.45—4.75 (m, C*H*OC*H*O), 5.83 (dd, *J* 6 and 2 Hz, CC*H*=), 6.19 (dd, *J* 6 and 3 Hz, =C*H*CH), and 9.50 (CHO). The product was found to be highly unstable and storage of samples for more than a few days, or further purification by chromatography, was not possible.

(1β,5β)-*Bicyclo*[3.3.0]*oct*-7-*en*-2-*one* 2,4,6-*Tri-isopropylbenzenesulphonylhydrazone* (**55**).—Concentrated hydrochloric acid (2 ml) was added to an ice-cooled suspension of 2,4,6-tri-isopropyl benzenesulphonylhydrazone (17.70 g, 60 mmol) and the ketone (**10**) (7.26 g, 60 mmol), and the mixture was stirred between 0 °C and 4 °C for 24 h. The precipitate was filtered off, then washed with aqueous methanol (1:1, 30 ml) and dried over silica gel under reduced pressure, to give the *hydrazone* (20.45 g, 85%), m.p. 140—141 °C. $\delta_H(CDCl_3)$ 1.26 (d, *J* 7.5 Hz, 2 × CH*Me*$_2$), 1.28 (d, *J* 7.5 Hz, CH*Me*$_2$), 1.85—2.70 (m, 3 × CH_2 plus 2 × CH), 2.90 (sept, *J* 7 Hz, Me_2CH), 4.26 (sept, *J* 7 Hz, 2 × Me_2CH), 5.58 (m, *H*C=C*H*), and 7.18 (2 × Ar*H*); $\delta_C(CDCl_3)$ 23.5 (2 × q), 24.8 (4 × q), 27.5 (t), 29.9 (d), 30.6 (t), 34.1 (d), 39.4 (d), 39.5 (t), 56.0 (d), 123.7 (d), 130.3 (d), 130.8 (d), 151.4, 151.5, 153.0, and 166.1 p.p.m; *m/z* 402 (8), 359 (4), 323 (5), 282 (53), 267 (18), 204 (19), 203 (17), 189 (43), 161 (27), 136 (52), 135 (72), 106 (53), 105 (52), 91 (100), 79 (58), 78 (54), and 77 (27); (Found: C, 68.9; H, 8.8; N, 7.2%; *m/z* 402.2319. $C_{23}H_{34}N_2SO_2$ requires C, 68.6; H, 8.5; N, 7.0%; *M*, 402.2340).

(1β,5β)-*Bicyclo*[3.3.0]*octa*-2,7-*diene*-2-*carbaldehyde* (**57**).—Butyl-lithium (2.0M) solution in hexane (14 ml, 28 mmol) was added dropwise over 0.5 h to a well stirred suspension of the trisylhydrazone (**55**) (3.70 g, 9.2 mmol) in tetramethylethylenediamine (40 ml) and pentane (150 ml) held at −80 °C under nitrogen. After 0.5 h the mixture had acquired a deep red colour, and it was then allowed to warm to 0 °C and stirred at 0 °C for 0.5 h, during which time it effervesced and became clear and yellow. The mixture was recooled to −80 °C, and dimethylformamide (4 ml) was then added. When the reaction mixture had rewarmed to room temperature it was poured into water (200 ml). The separated aqueous layer was extracted with ether (3 × 100 ml), and the organic layers were then combined, and washed with dilute hydrochloric acid until the washing remained acidic. Evaporation of the dried organic extracts followed by chromatography on silica (4:1 petroleum–ether) gave the *aldehyde* (1.13 g, 90%), as a liquid; $\nu_{max.}$(film) 3 070 (m), 2 950 (s), 2 750 (m), 1 690 (s), 1 620 (s), 1 460 (s), 1 360 (s), 1 180 (s), and 950 (s) cm^{-1}; $\delta_H(CCl_4)$ 1.90—3.25 (m, 2 × CH_2 plus C*H*), 3.90 (m, =CC*H*CH=), 5.60 (m, CH=), 5.83 (m, CH=), 6.74 (m, C*H*=CC=), and 9.80 (CHO); $\delta_C(CDCl_3)$ 39.2 (d), 40.6 (t), 41.7 (t), 55.3 (d), 129.7 (d), 130.9 (d), 148.9, 151.9 (d), and 189.7 (d) p.p.m.; *m/z* 134 (54), 105 (31), 91 (29), 79 (21), 77 (20), 74 (72), 59 (100), and 45 (79) (Found: *m/z* 134.0739. $C_9H_{10}O$ requires *M*, 134.0731).

(1β,4α,6β)-3-*Oxatricyclo*[4.3.0.$0^{2,4}$]*non*-8-*ene*-2α-*carbaldehyde* (**62**).—Hydrogen peroxide solution (2.0 ml, 30%) was added to an ice-cooled solution of the enal (**57**) (0.90 g, 6.7 mmol) and sodium hydrogen carbonate (1.35 g, 16 mmol) in methanol (50 ml) and water (5 ml), and the mixture was then heated on an oil bath between 40 and 50 °C for 2 h. After being allowed to cool to room temperature, the mixture was poured into brine (100 ml), and then extracted with ether (3 × 30 ml). The combined ether extracts were washed with iron(II) sulphate solution, then dried and evaporated. Chromatography on silica (6:1 petroleum–ether) gave recovered enal (166 mg, 18%), and the *epoxy aldehyde* (535 mg, 54%; 64% based on recovered starting material), as a liquid; $\delta_H(CCl_4)$ 1.1—1.7 (m, *H*CH), 2.0—2.8 (m, CH_2, CH, and *H*CH), 3.30 (m, *H*CCH=), 3.60 (HCO), 5.60 (m, HC=), 5.90 (m, HC=), and 8.95 (C*H*O); $\delta_C(CDCl_3)$ 35.1 (t), 36.6 (d), 38.0 (t), 52.0 (d), 63.4 (d), 70.5, 128.1 (d), 132.2 (d), and 196 (d) p.p.m.

(1β,5β)-2-*Hydroxymethylbicyclo*[3.3.0]*octa*-2,7-*diene* (**58**).—A solution of the aldehyde (**57**) (1.40 g, 10.5 mmol) in dry ether (15 ml) was added dropwise to a well stirred suspension of lithium tetrahydridoaluminate (203 mg, 5.34 mmol) in dry ether (35 ml). The mixture was stirred under nitrogen for 15 min, then water (1 ml), aqueous sodium hydroxide (1 ml), and water (1.5 ml) were added successively. Evaporation of the dried ether extract gave the *alcohol* (1.21 g, 93%), as a liquid which was used without further purification; $\nu_{max.}$(film) 3 350 (br s), 2 880 (m),

2 960 (s), 2 880 (s), 1 465 (m), 1 360 (m), 1 050 (s), 1 020 (s), 850 (m), and 820 (m) cm^{-1}; $\delta_H(CCl_4)$ 1.95—3.2 (m, CH_2CHCH_2), 3.40 (br, OH), 3.67 (m, CCHCH=), 4.10 (br, CH_2O), 5.40 (m, HC=CCH_2O), 5.55—5.70 (m, HC=CH), 5.70—5.88 (m, HC=CH); a D_2O shake removed the peak at δ 3.40; $\delta_C(CDCl_3)$ 39.6 (d), 40.3 (t), 41.0 (t); 58.3 (d), 61.2 (t), 124.2 (d), 130.0 (d), 131.1 (d), and 145.4 p.p.m.

(1β,4α,6β)-2α-*Hydroxymethyl*-3-*oxatricyclo*[4.3.0.$0^{2,4}$]*non*-8-*ene* (**59**).—t-Butyl hydroperoxide (70% aqueous solution, 1.20 ml, 10.4 mmol) was added to a solution of the alcohol (**58**) (1.21 g, 8.9 mol) in benzene (120 ml) containing vanadyl acetylacetonate (100 mg, 0.37 mmol). After 2 h the dark red-brown solution, which had turned straw-coloured, was washed with aqueous sodium sulphite solution (3 × 15 ml), then dried and evaporated to give the *epoxide* (1.09 g, 81%) which was used without purification, $\delta_H(CCl_4)$ 1.25 (m, CH_2CHCH_2), 1.93—2.75 (m, 2 × CH_2), 3.07 (br, OH), 3.41 (m, CHO and CHC=), 3.70 (d, *J* 12.5 Hz, HCHOH), 4.05 (d, *J* 12.5 Hz, HCHOH), and 5.78 (m, HC=CH); $\delta_C(CDCl_3)$, 35.7 (t), 36.7 (d), 39.2 (t), 53.8 (d), 62.5 (t), 70.8, 128.0 (d), and 132.4 (d). The ^{13}C n.m.r. spectrum also reveals the presence of about 15% of the (1β,4β,6β)-2β-hydroxymethyl isomer; $\delta_C(CDCl_3)$ 33.7 (t), 41.2 (d), 41.3 (t), 52.5 (d), 61.2 (t), 65.9 (d), 72.0, 127.0 (d), and 132.6 (d).

(1β,5β)-2α-*Hydroxymethylbicyclo*[3.3.0]*octa*-3,7-*dien*-2β-*ol* (**60**).—A solution of the epoxy alcohol (**59**) (250 mg, 1.64 mmol) in dry benzene (10 ml) was added to a solution of LDA (prepared from butyl-lithium 2.0M solution in hexane, 4.0 ml, 8 mmol and di-isopropylamine, 1.4 ml, 10 mmol) in benzene (20 ml)* at 0 °C, and the mixture heated under reflux in a nitrogen atmosphere for 1.5 h. After being cooled to room temperature, the solution was poured into water (20 ml), and the separated aqueous phase was extracted with ether (3 × 15 ml). The organic fractions were combined, dried, (1:1, K_2CO_3–$MgSO_4$) and evaporated to give, after chromatography on silica (ether), the *diol* (60 mg, 24%), as an oil; $\delta_H(CDCl_3)$ 2.12 (m, HCH), 2.46 (m, HCH), 3.62 (m, 2 × CH), 3.88 (d, *J* 12.0 Hz, HCHOH), 3.98 (d, *J* 12.0 Hz, HCHOH), 4.44 (m, 2 × OH), 5.63 (m, HC=), 5.77 (dd, *J* 8 and 2.0 Hz, CCH=), 5.88 (dd, *J* 8 and 2.1 Hz, CCH=CH), and 6.00 (m, HC=); $\delta_C(CDCl_3)$ 36.8 (t), 47.0 (d), 60.6 (d), 67.2 (t), 87.6, 129.7 (d), 130.5 (d), 131.8 (d), and 139.5 (d).

(1β,5β)-2β-*Acetoxy*-2α-*hydroxymethylbicyclo*[3.3.0]*octa*-3,7-*diene* (**61**).—Acetic anhydride (22 mg, 0.22 mmol) was added to a solution of the diol (**60**) (30 mg, 0.2 mmol), 4-dimethylaminopyridine (5 mg) and triethylamine (50 mg, 0.5 mmol) in dichloromethane (2.5 ml). After being stirred under nitrogen at room temperature for 24 h, the mixture was poured into saturated aqueous sodium hydrogen carbonate (10 ml), the layers separated, and the aqueous phase extracted with ether (3 × 10 ml). The organic phases were combined, washed with aqueous copper sulphate (3 × 10 ml), dried, and evaporated. Chromatography on silica (1:1 ether–petroleum) gave the *acetate* (11 mg, 28%); $\delta_H(CDCl_3)$ 1.66 (Ac), 1.88 (dm, *J* ~ 14 Hz, HCHCH=), 2.02 (br, OH), 2.12—2.25 (m, HCHCH=), 3.29 (m, 2 × CH), 4.15 (d, *J* 12 Hz, HCHOH), 4.23 (d, *J* 12 Hz, HCHOH), 5.36—5.53 (m, 4 × HC=). Double irradiation at δ 1.66 gave n.O.e. enhancements of 0.4% and 0.3% at δ 5.36—5.53 and δ 3.29. Double irradiation at δ 3.29 led to simplification of the multiplets at δ 1.81—1.91, δ 2.12—2.25, and δ 5.36—5.53, at δ 5.44 of the multiplets at δ 3.29, δ 1.81—1.91, and δ 2.11—2.25.

(1β,5β)-2-*Trimethylsilyloxybicyclo*[3.3.0]*octa*-2,7-*diene*.—A solution of bicyclo[3.3.0]oct-7-en-2-one, prepared by the method of Crandall *et al*.[7] (2.55 g, 21 mmol) in THF (10 ml) was added dropwise to a solution of LDA [prepared from di-isopropylamine (2.6 g, 25.5 mmol) and butyl-lithium (1.38M solution in hexane, 18.5 ml, 25.5 mol)] in THF (50 ml) held at −80 °C under an atmosphere of nitrogen. After 1 h chlorotrimethylsilane (3.1 g, 29 mmol) was added, and the mixture was stirred for 15 min and then allowed to warm to room temperature. The solvent was evaporated under reduced pressure, and the residue was then taken up in dry ether (100 ml), filtered, and re-concentrated. Distillation gave the *silyl enol ether* (3.07 g, 75%), as a liquid, b.p. 82—88 °C at 10 mmHg, $\delta_H(CDCl_3)$ 0.3 (Me_3Si), 1.0—3.4 (m, 2 × CH_2, 2 × CH), 4.25 (m, HC=CO), and 5.55 (m, HC=CH). The silyl enol ether was used directly in the next stage without any further purification.

(1β,5β)-*Bicyclo*[3.3.0]*octa*-3,7-*dien*-2-*one* (**64**).—A solution of the silyl enol ether derived from bicyclo[3.3.0]oct-7-en-2-one (10.35 g, 53 mmol) in acetonitrile (40 ml) was added to a well stirred suspension of palladium(II) acetate (6.25 g, 28 mmol) and *p*-benzoquinone (3.0 g, 28 mmol) in dry acetonitrile (230 ml), and the resulting mixture was stirred at room temperature under nitrogen for 50 h. The solvent was evaporated, and the residue was then taken up in ether (500 ml), filtered, and re-evaporated. Chromatography on silica (10:1 petroleum–ether) gave (1β,5β)-bicyclo[3.3.0]oct-7-en-2-one (0.57 g, 9%), and the conjugated *enone* (3.52 g, 55%) as a liquid; $\nu_{max.}$(film) 2 970 (w), 1 735 (s), 1 610 (w), 1 365 (w), 1 280 (w), 1 210 (w), 870 (m), 845 (m), and 810 (m) cm^{-1}; $\delta_H(CCl_4)$ 1.85—3.60 (m, CH_2 and 2 × CH), 5.56 (m, CH_2CH=CH), 5.88 (dd, *J* 5.6 and 2.0, =CHC=O), and 7.47 (dd, *J* 5.6 and 2.8 Hz, CH=CHC=O); $\delta_C(CDCl_3)$ 35.6 (t), 43.6 (d), 58.1 (d), 128.5 (d), 131. 0 (d), 131.4 (d), 166.7 (d), and 209.1 p.p.m.; (Found: *m/z* 120.0569. C_8H_8O requires *M*, 120.0574).

(1β,3α,5α,6β)-4-α(β)-*Methoxytricyclo*[4.3.0.$0^{3,5}$]*non*-8-*en*-2-*one* (**68**).—Butyl-lithium (1.35M solution in hexane, 1.64 ml, 2.2 mmol) was added dropwise to a well stirred suspension of methoxymethyltriphenylphosphonium chloride (760 mg, 2.2 mmol) in THF (30 ml) at −50 °C under nitrogen. After 1.5 h the mixture became a clear orange-red, and a solution of the dienone (**64**) (240 mg, 2 mmol) in THF (5 ml) was then added. The mixture was stirred at −50 °C for 1 h, then allowed to warm to room temperature and poured into saturated sodium hydrogen carbonate solution (50 ml). The layers were separated and the aqueous phase extracted with ether (3 × 10 ml). Evaporation of the dried ether extracts followed by chromatography of the residue on silica (2:1 petroleum–ether) gave the *tricyclononenone* (166 mg, 50%) as an oil; $\nu_{max.}$(film) 2 940 (m), 1 720 (s), 1 460 (w), 1 400 (w), 1 230 (w), and 1 060 (w) cm^{-1}; $\delta_H(CCl_4)$ 1.75—2.07 (m, 2 × cyclopropyl H), 2.25—3.25 (m, CH_2 plus 2 × CH), 3.36 (MeOCH), 3.39 (Me), 3.66 (t, *J* 7.5 Hz, MeOCH), and 5.47—5.88 (m, HC=CH); $\delta_C(C_6D_6)$ 32.9 (d), 34.0 (d), 34.6 (d), 35.6 (d), 36.6 (d), 39.0 (d), 40.0 (t), 58.0 (q), 58.8 (d), 62.2 (d), 64.0 (d), 66.2 (d), 127.4 (d), 127.6 (d), 131.6 (d), 131.8 (d), 209.0, and 210.2 p.p.m.; the ^{13}C n.m.r. spectrum shows the product to be a 1:1 mixture of epimers at C-4; *m/z* 164 (3), 151 (2), 136 (2), 132 (3), 119 (6), 98 (9), 84 (100), 82 (11), 56 (29), 54 (24), 52 (15), and 42 (12) (Found: *m/z* 164.0833. $C_{10}H_{12}O_2$ requires *M*, 164.0838).

(1β,5β)-2-*Methoxymethylenebicyclo*[3.3.0]*octa*-3,7-*diene* (**66**).—A solution of methoxymethyldiphenylphosphine oxide (2.12 g, 7.6 mmol) in THF (10 ml) was added slowly to a solution of LDA [prepared from butyl-lithium solution in hexane (1.04M, 7.3 ml, 7.6 mmol) and di-isopropylamine (0.77 g, 7.6 mmol)] in THF (50 ml). After 10 min the orange-red solution was cooled to −80 °C, and a solution of the enone (**64**) (0.825 g, 6.9 mmol) in THF (10 ml) was added. The mixture was

* The use of benzene in this reaction, rather than ether or THF, is critical for its success.

stirred at room temperature for 0.5 h, after which it was poured into saturated aqueous ammonium chloride (100 ml). The separated aqueous phase was extracted with ether (3 × 30 ml), and the ether extracts were combined, dried, and evaporated to leave the β-hydroxy-phosphine oxide intermediate which was added directly as a solution in THF (10 ml) to a suspension of sodium hydride (a washed 50% dispersion in oil, 0.384 g, 8.00 mmol) in THF (50 ml) and stirred under nitrogen at room temperature for 16 h. The mixture was filtered through Celite, and the filter cake washed with ether (50 ml). Evaporation of the dried filtrate, followed by chromatography of the residue on silica (20:1, petroleum–ether), gave the *methyl ether* (0.65 g, 68%) as an oil, $\nu_{max.}$(film) 3 050 (m), 2 830 (s), 1 680 (s), 1 465 (m), 1 370 (m), 1 240 (m), 1 195 (m), and 1 140 (m) cm^{-1}; $\delta_H(CCl_4)$ 2.00—2.30 (m, *H*CH), 2.38—2.80 (m, *H*CH), 3.35—3.70 (m, *H*CCH$_2$), 3.83, 4.04 (m, *H*CC=CO), 3.57 (Me, minor isomer), 3.61 (Me, major isomer), and 5.38—6.30 (m, 5 × CH=); $\delta_C(CDCl_3)$, major isomer 36.9 (t), 47.2 (d), 50.9 (d), 59.6 (q), 128.1 (d, 2 × C), 129.1, 131.9 (d), 136.5 (d), and 139.6 (d); minor isomer, 36.9 (t), 47.0 (d), 50.6 (d), 59.6 (q), 126.3 (d, 2 × C), 127.2, 134.0 (d), 137.2 (d), and 138.1 (d) p.p.m.; comparison of corresponding peaks in the ^{13}C n.m.r. spectrum gave a double bond isomer ratio of 2:1; *m/z* 148 (100), 147 (33), 133 (15), 121 (24), 117 (85), 105 (40), 79 (21), 77 (38), 57 (20), and 51 (19) (Found: *m/z* 148.0896. $C_{10}H_{12}O$ requires *M*, 148.0888).

(1β,5β)-2-α(β)-*Dimethoxymethylbicyclo*[3.3.0]*octa*-3,7-*dien*-2-*ol*[(**69**)*and*(**70a**)].—A solution of *m*-chloroperoxybenzoic acid (200 mg, 85% remainder *m*-chlorobenzoic acid, 1 mmol) in dry methanol (5 ml) was added dropwise to an ice-cooled solution of the vinyl ether (**66**) (148 mg, 1.0 mmol) in methanol (5 ml) and ether (5 ml) under nitrogen. After 1.5 h, the mixture was poured into sodium sulphite solution and the separated aqueous phase extracted with ether (4 × 10 ml). The ether extracts were combined, then washed with sodium carbonate solution, dried, and evaporated. Chromatography on silica gave: (i) the 2β-*dimethoxymethyl epimer* (**70a**) (50 mg, 25%), $\delta_H(CDCl_3)$ 2.15—2.22 (m, *H*CH), 2.49—2.63 (m, *H*CH), 3.3 (m, HC), 3.42 (m, HCCOH), 3.53 (MeO), 3.55 (MeO), 4.23 (OCHO), 5.51 (dd, *J* 5.7 and 2.1 Hz, CC*H*=), 5.69 (m, CH$_2$C*H*=C*H*), and 5.85 (dd, *J* 5.7 and 2.1 Hz, CCH=C*H*); double irradiation of the peak at δ 4.23 gave n.O.e. enhancements of 2.3%, 11.9%, and 5.2% at δ 5.51, δ 3.53—3.55, and δ 3.42; $\delta_C(CDCl_3)$ 38.1 (t), 47.2 (d), 54.3 (d), 57.4 (q), 57.7 (q), 88.0, 109.4 (d), 129.4 (d), 130.1 (d), 130.9 (d), and 139.0 (d); and, (ii) the 2α-*dimethoxymethyl epimer* (**69a**) (21 mg, 11%); $\nu_{max.}$(film) 3 470 (br), 3 060 (m), 2 920 (s), 2 850 (m), 1 450 (w), 1 350 (w), 1 080 (s), 975 (m), 950 (m), 785 (m), and 705 (m) cm^{-1}; $\delta_H(CDCl_3)$ 2.13—2.24 (m, *H*CH), 2.48—2.61 (m, *H*CH), 3.18—3.27 (m, *H*CCH$_2$), 3.55 (MeO), 3.56 (MeO), 3.55—3.63 (m, *H*CCOH), 4.19 (OCHO), 5.61 (dd, *J* 5.7 and 2.4 Hz, CC*H*=), 5.62 (m, CH$_2$C*H*=C*H*), 5.90 (dd, *J* 5.7 and 2.1 Hz, CCH=C*H*); double irradiation of the ^1H n.m.r. spectrum: (*a*) at δ 3.23 gave simplification of the multiplets at δ 2.48—2.61, δ 3.18—3.27, and δ 3.55—3.63; (*b*) at δ 2.55 simplification of the multiplets at δ 2.13—2.24, δ 3.18—3.27, and δ 3.55—3.63; and, (*c*) at δ 3.59 simplification of the multiplets at δ 2.13—2.24 (to dd, *J* 16.9 and 2.3 Hz), δ 2.48—2.61 (to dd, *J* 7.0 and 8.6 Hz), and δ 3.55—3.63; $\delta_C(CDCl_3)$ 36.5 (t), 46.8 (d), 55.7 (q), 57.2 (q), 68.9 (d), 88.7, 107.2 (d), 129.5 (d), 130.3 (d), 130.7 (d), and 140.5 (d); *m/z* 196 (0.3), 179 (3), 165 (11), 164 (7), 133 (34), 131 (18), 121 (52), 105 (58), 103 (33), 91 (51), 77 (59), 76 (52), 75 (100), 65 (26), and 55 (100) (Found: *m/z* 196.1084. $C_{11}H_{16}O_3$ requires *M*, 196.1098).

(1β,5β)-2β-*Acetoxy*-2α-*dimethoxymethylbicyclo*[3.3.0]*octa*-3,7-*diene* (**69b**).—Acetic anhydride (300 μl) was added to an ice-cooled solution of the alcohol (**69a**) (34 mg, 0.17 mmol) and 4-dimethylaminopyridine (5 mg) in triethylamine (3 ml), and the mixture stirred at room temperature for 24 h, then poured into saturated aqueous sodium carbonate (10 ml). The separated aqueous layer was extracted with ether (4 × 5 ml), and the combined ether extracts were washed with copper sulphate solution (5 × 5 ml) and water (5 ml), then dried and evaporated to give the *acetate* (42 mg, 98%), as a liquid which was used without any purification; $\delta_H(CDCl_3)$ 2.04 (Ac), 2.16—2.28 (m, *H*CH), 2.46—2.60 (m, *H*CH), 3.47—3.57 (m, 2 × CH), 3.49 (MeO), 3.51 (MeO), 4.85 (OCHO), 5.58—5.63 (m, *H*C=CHCH$_2$), 5.75—5.81 (m, CH$_2$*H*C=), 5.89 (dd, *J* 5.6 and 1.9 Hz, CC*H*), 6.02 (dd, *J* 5.6 and 1.4 Hz, CCH=C*H*); double irradiation of the spectrum: (*a*) at δ 2.22 leads to simplification of the multiplets at δ 2.46—2.60, δ 3.47—3.57, δ 5.58—5.63, and δ 5.75—5.81, and (*b*) at δ 5.60 to simplification of the multiplets at δ 3.47—3.57 and δ 5.75—5.81. In addition, in a separate experiment no n.O.e. enhancements were observed on irradiation at δ 2.04, but a 12.6% enhancement of the peaks at δ 3.49 and δ 3.51 was observed on irradiation at δ 4.85; [Found: *m/z* 178.0991. $C_{11}H_{14}O_2$ (*M* − MeCO$_2$H) requires 178.0994].

(1β,5β)-2α-*Acetoxy*-2β-*dimethoxymethylbicyclo*[3.3.0]*octa*-3,7-*diene* (**70b**).—The acetate was prepared from the alcohol (**70a**) (70 mg, 0.36 mmol) in an exactly analogous fashion to the 2β-acetoxy-2α-dimethoxymethyl isomer, except that the reaction time was extended to 6 days. Chromatography of the product on silica (3:1, petroleum–ether) gave recovered alcohol (12 mg, 17%), and the *acetate* (30 mg, 33%; or 40% based on recovered starting material); $\delta_H(CDCl_3)$ 2.05 (Ac), 2.15—2.60 (m, CH$_2$), 3.15—3.83 (m, 2 × CH), 3.47 (MeO), 3.52 (MeO), 5.13 (OCHO), 5.45—5.75 (m, CH$_2$C*H*=C*H*), and 5.78—6.00 (m, C*H*=C*H*COAc) [Found: *m/z* 178.0988. $C_{11}H_{14}O_2$ (*M* − CH$_3$CO$_2$H) requires 178.0994].

(1β,5β)-2-*Acetoxymethylenebicyclo*[3.3.0]*octa*-3,7-*diene* (**71**).—A solution of the aldehyde (**57**) (12.0 g, 90 mmol) in freshly distilled isopropenyl acetate (300 ml), was heated at reflux under an argon atmosphere in the presence of toluene-*p*-sulphonic acid (10 mg) for 60 h. The mixture was allowed to cool to room temperature, after which it was washed with saturated aqueous sodium hydrogen carbonate solution (2 × 40 ml). The washings were back-extracted with ether (3 × 40 ml), and the organic extracts were then combined, dried, and concentrated under reduced pressure. Chromatography of the residue on silica (light petroleum) gave the *enol acetate* (10.43 g, 66%), as a colourless liquid; $\nu_{max.}$(film), 2 920 (m), 1 755 (s), 1 680 (w), 1 370 (m), 1 220 (s), 1 105 (s), 1 090 (s), 905 (w), 820 (w), 735 (w), and 705 (w) cm^{-1}; $\delta_H(CDCl_3)$ 2.18 ($MeCO_2$), 2.14—2.28 (m, β-*H*CH), 2.65 (ddq, *J* 16.7, 9.7, and 2.2 Hz, *H*CH), 3.57 (m, C*H*CH$_2$), 4.06 (m, =CC*H*CH=), 5.65 (dq, *J* 5.6 and 2.0 Hz, CHCH=), 5.70 (dq, *J* 5.6 and 2.2 Hz, CH$_2$C*H*=), 5.89 (dd, *J* 5.7 and 2.5 Hz, =CCH=C*H*), 5.98 (dd, *J* 5.7 and 2.0 Hz, =CC*H*=CH), and 7.22 (d, *J* 1.9 Hz, =C*H*OAc). Double irradiation of the proton spectrum at δ 7.22 gave an n.O.e. enhancement of 5.2% at δ 5.98, and similar irradiation at δ 4.06 gave enhancements of 1.7%, 5.4%, and 7% at δ 5.98, δ 5.70, and δ 3.57 respectively. In a separate experiment, irradiation at δ 4.06 led to simplification of the multiplets at δ 5.70, δ 5.65, δ 3.57, and δ 2.65; $\delta_C(CDCl_3)$, 20.6 (q), 37.4 (t), 47.4 (d), 51.3 (d), 127.6 (d, 2 × C), 128.9 (d), 131.1 (d), 134.9, 141.1 (d), and 167.6 p.p.m.; *m/z* 176 (22), 163 (10), 156 (13), 134 (100), 133 (29), 121 (38), 119 (31), 105 (30), 91 (20), 79 (17), and 77 (19) (Found: *m/z* 176.0839. $C_{11}H_{12}O_2$ requires *M*, 176.0840).

(1β,5β)-2β-*Acetoxybicyclo*[3.3.0]*octa*-3,7-*diene*-2α-*carbaldehyde* (**9**).—Dry peracetic acid solution (31.8 ml of a 0.43M solution in dichloromethane; 13.6 mmol) was added to a solution of the enol acetate (**71**) (2.40 g, 13.6 mmol) in dichloromethane (100 ml), containing suspended sodium carbonate (3.0

g, 30 mmol), held at −80 °C under a nitrogen atmosphere. The mixture was stirred for 1 h at −80 °C and then allowed to warm to room temperature over 16 h, when it was poured into water (100 ml). The layers were separated and the aqueous phase extracted with ether (3 × 30 ml). Evaporation of the dried organic extracts, followed by chromatography of the residue on silica (10:1 light petroleum–ether) gave: (i) recovered enol acetate (0.12 g, 5%), (ii) bicyclo[3.3.0]octa-3,7-dien-2-one (0.61 g, 38%), and (iii) the acetoxy-aldehyde (0.91 g, 35%), as a labile liquid; $\nu_{max.}$(film) 3 050 (w), 2 920 (m), 2 850 (w), 1 725 (s), 1 370 (m), 1 240 (s), and 1 020 (m) cm^{-1}; $\delta_H(CDCl_3)$ 2.12 (OCOMe), 2.27 (m, *H*CH), 2.68 (m, *H*CH), 3.6 (m, 2 × C*H*), 5.32 (m, =C*H*), 5.73 (m, =CH), 5.86 (dd, *J* 5.6 and 1 Hz, CCH=C*H*), 6.16 (dd, *J* 5.6 and 1 Hz, C*H*=), and 9.56 (C*H*O); δ_C 20.8 (q), 36.2 (t), 47.2 (d), 58.7 (d), 96.0, 126.2 (d), 127.1 (d), 131.5 (d), 145.7 (d), 170.5, and 197.3; *m/z* 163 (7), 162 (5), 136 (10), 121 (31), 120 (100), 91 (100), 79 (29), and 43 (48) [Found: *m/z* 163.0757. $C_{10}H_{11}O_2$ (*M* − CHO) requires 163.0755]. Integration of the ^1H n.m.r. and ^{13}C n.m.r. spectral data showed that the acetoxy-aldehyde was contaminated by *ca.* 22% of the corresponding epimer (**72**). Attempts to separate the diastereoisomers by chromatography resulted in extensive losses of material.

(1β,5β)-2α-*Acetoxybicyclo*[3.3.0]*octa*-3,7-*diene*-2β-*carbaldehyde* (**72**).—A solution of molybdenum pentaoxide–HMPA complex (203 mg, 0.57 mmol) in dry dichloromethane (4 ml) was added dropwise to a cooled (ice-water) solution of the enol acetate (**71**) (100 mg, 0.57 mol) in dry dichloromethane (3 ml) under nitrogen, and the mixture was then allowed to warm to room temperature and stirred at 25 °C for 1.2 h. The mixture was poured into water, the separated aqueous layer extracted with ether (3 × 5 ml), and the combined dichloromethane and ether extracts washed with brine, then dried and evaporated to dryness under reduced pressure. Chromatography of the residue on silica (10:1 petroleum–ether) gave the acetoxy-aldehyde (40 mg, 38%); δ_H 2.18 (OCOMe), 2.33 (m, *H*CH), 2.62 (m, HC*H*), 3.52 (bt, *J* ~ 5 Hz, C*H*), 4.0 (m, C*H*COAc), 5.35 (m, =C*H*), 5.56 (dd, *J* 5.6 and 2 Hz, CCH=C*H*), 5.78 (m, =CH), 6.06 (dd, *J* 5.6 and 2 Hz, CC*H*=), and 9.51 (CHO). Double irradiation at δ 9.51 gave an n.O.e. enhancement of 3% at δ 4.0, and integration of the ^1H n.m.r. spectrum showed that the acetoxy-aldehyde was contaminated by *ca.* 14% of the corresponding epimer (**9**). δ_C 20.5 (q), 37.9 (t), 47.7 (d), 53.8 (d), 96.4, 124.9 (d), 128.0 (d), 131.5 (d), 131.5 (d), 143.1 (d), 170.7, and 195.7 p.p.m. [Found: *m/z* 163.0757. $C_{10}H_{11}O_2$ (*M* − CHO) requires 163.0755].

Treatment of the enol acetate (**71**) with *m*-chloroperbenzoic acid (CH_2Cl_2, 0 °C, 1.5 h) led to a 1:1 mixture of the acetoxy-aldehydes (**9**) and (**72**) in a combined yield of 67%.

(1RS,2RS,5RS)-3′-*Acetoxy*-4′-*ethyl*-4′-*phenylthio*-3′,4′-*dihydrobicyclo*[3.3.0]*octa*-3,7-*diene*-2-*spiro*-2′-*furan*-5′-(2′H)-*one* (**75**).—A solution of 2-phenylthiobutanoic acid (216 mg, 1.1 mmol) in THF (3ml) was added dropwise to a solution of LDA (prepared from 1.68M butyl-lithium solution in hexane (1.3 ml, 2.2 mmol) and di-isopropylamine (222 mg, 2.2 mmol) in THF (8 ml) at 0 °C under nitrogen. After 1 h the mixture was cooled to −80 °C, and a solution of the acetoxy-aldehyde (**9**) (192 mg, 1 mmol) in THF (3 ml) was then added. The mixture was stirred at −80 °C for 1 h and then allowed to warm to room temperature, an excess of aqueous sulphuric acid (10 ml) was added, and the mixture was stirred for 16 h. The layers were separated, and the aqueous phase was then extracted with ether (3 × 5 ml). The organic layers were combined, washed with saturated aqueous sodium carbonate (2 × 10 ml), dried, and evaporated. Chromatography on silica (5:1, petroleum–ether) gave the *spirofuranone* (194 mg, 52%) as a liquid mixture of four diastereoisomers; $\nu_{max.}(CCl_4)$, 3 060 (w), 2 920 (s), 2 850 (s), 1 755 (s), 1 460 (m), 1 440 (m), 1 370 (m), 1 210 (s), 1 025 (s), and 690 (s) cm^{-1}; $\delta_H(CDCl_3)$ 0.97—1.18 (m, *Me*CH_2), 1.66—1.99 (m, MeC*H*$_2$), 2.07 (Ac), 2.12 (Ac), 2.13 (Ac), 2.18 (Ac), 2.19—2.33 (m, *H*CHCH=), 2.49—2.70 (m, *H*CHCH=), 3.20—4.03 (m, 2 × HC), 5.38—6.35 (m, 4 × =CH and C*H*OAc), 7.31—7.47 (m, *m*-and *p*-Ar*H*), and 7.49—7.62 (m, *o*-Ar*H*); *m/z* 370 (18), 267 (5), 243 (7), 201 (33), 180 (26), 175 (100), 149 (51), 120 (19), 110 (25), 109 (22), 99 (27), 91 (22), 69 (25), 57 (44), 55 (28), and 43 (23) (Found: *m/z* 370.1254. $C_{21}H_{22}O_4S$ requires *M*, 370.1239).

Several attempts to completely separate the diastereoisomers of the spirolactone were unsuccessful, although a minor isomer which we have assigned the 1*RS*, 2*RS*, 5*RS*, 3′*SR*, 4′*SR*, stereochemistry could be separated by chromatography: $\delta_H(CDCl_3)$ 1.06 (t, *J* 7.3 Hz, *Me*CH_2), 1.68 (dq, *J* 14.9 and 7.4 Hz, MeCH*H*), 1.84 (dq, *J* 14.9 and 7.2 Hz, MeCH*H*), 2.08 (Ac), 2.21—2.34 (m, *H*CHCH=), 2.56—2.70 (m, *H*CHCH=), 3.40—3.50 (m, *H*CCH$_2$), 3.79—3.86 (m, *H*CCHCH$_2$), 5.39 (C*H*OAc), 5.40 (dd, *J* 5.6 and 2.2 Hz, *H*C=CHCH), 5.67—5.80 (m, CH$_2$C*H*=CH), 5.94 (dd, *J* 5.6 and 2.0 Hz,HC=C*H*CH), 7.33—7.50 (m, *m*- and *p*-Ar*H*), and 7.52—7.62 (m, *o*-Ar*H*); double irradiation at δ 3.83 gave n.O.e. enhancements of 16.7% and 9.4% at δ 5.39 and δ 3.40—3.50 and irradiation at δ 5.39 gave enhancements of 3.5% and 7.3% at δ 5.94 and δ 3.79—3.86.

(1RS,2RS,5RS,7SR,8RS)-3′-*Acetoxy*-4′-*ethyl*-7,8-*dihydroxy*-4′-*phenylthio*-3′,4′-*dihydrobicyclo*[3.3.0]*oct*-3-*ene*-2-*spiro*-2-*furan*-5′(2′H)-*one* (**76**).—A solution of osmium(VIII) oxide (173 mg, 0.68 mmol) THF (10 ml) was added to an ice-cooled solution of the spirofuranone (**75**) (259 mg, 0.70 mmol) in THF (10 ml) and pH 7 aqueous phosphate buffer (10 ml), and the mixture stirred at room temperature for 3 days. Saturated aqueous sodium dithionite (20 ml) was added and the mixture was then stirred for 30 min, after which it was filtered through Celite, and the THF evaporated. The resulting aqueous solution was extracted with dichloromethane (6 × 10 ml), and the dichloromethane extracts were dried and evaporated. Careful chromatography on silica (ether) gave: (i) essentially a single major diastereoisomer (68 mg, 24%); $\nu_{max.}(CCl_4)$ 3 470 (s), 3 060 (w), 2 970 (m), 2 935 (m), 1 755 (s), 1 440 (m), 1 372 (m), 1 215 (s), 1 083 (m), 1 027 (m), 910 (s), and 692 (s) cm^{-1}; $\delta_H(CDCl_3)$, 1.06 (t, *J* 7.3 Hz, MeCH$_2$), 1.55—2.15 (m, 2 × CH$_2$), 2.07 (Ac), 3.20 (dd, *J* 7.1 and 5.8 Hz, C*H*CHOH), 3.37—3.52 (m, C*H*CH$_2$), 3.71 (br, 2 × OH), 4.13 (dd, *J* 6 and 3.5 Hz, C*H*OH), 4.25 (dd, *J* 6 and 4 Hz, C*H*OH), 5.36 (C*H*OAc), 5.40 (dd, *J* 5.6 and 2 Hz, *H*C=CHCH), 5.98 (dd, *J* 5.7 and 2.0 Hz, HC=C*H*CH), and 7.26—7.58 (m, Ph); $\delta_C(CDCl_3)$ 8.3 (q), 20.3 (q), 22.5 (t), 34.6 (t), 46.8 (d), 55.2 (d), 58.5, 74.8 (d, 2 × C), 80.0 (d), 96.2, 126.9 (d), 127.8, 129.1 (d, 2 × C), 130.5 (d), 137.2 (d), 142.6 (d), 168.8, and 173.5 p.p.m.; *m/z* 404 (32), 295 (5), 209 (42), 196 (50), 191 (69), 180, (27), 151 (77), 141 (46), 135 (30), 110 (100), 109 (62), and 99 (78) (Found: *m/z* 404.1300. $C_{21}H_{24}O_6S$ requires *M*, 404.1293), and (ii) a mixture containing largely two minor diastereoisomers (57 mg, 20%); $\nu_{max.}(CCl_4)$ 3 420 (s), 3 060 (w), 2 975 (s), 2 935 (s), 1 750 (s), 1 438 (m), 1 373 (s), 1 215 (s), 1 080 (s), 910 (s), and 692 (s) cm^{-1}; $\delta_H(CDCl_3)$ 0.90—1.35 (m, *Me*CH_2), 1.40—2.25 (m, 2 × CH$_2$), 2.03 (Ac), 2.06 (Ac), 2.80—3.50 (m, 2 × CH and 2 × OH), 4.05—4.30 (m, *H*COH*H*COH), 5.37 (C*H*OAc), 5.65 (C*H*OAc), 5.83—6.25 (m, *H*C=C*H* and C*H*OAc), and 7.20—7.53 (m, Ph).

(1RS,2RS,5RS,7SR,8RS)-4′-*Ethyl*-3′,7,8-*trihydroxy*-4′-*phenylthio*-3′,4′-*dihydrobicyclo*[3.3.0]*oct*-3-*ene*-2-*spiro*-2′-*furan*-5′-(2′H)-*one* (**77**).—A solution of the diastereoisomer of the diol (**76**) (68 mg, 168 μmol), and potassium carbonate (25 mg, 180 μmol) in methanol (10 ml) was stirred at room temperature for 16 h. The mixture was acidified with dilute sulphuric acid, and the methanol evaporated to leave a residue which was diluted with water (3 ml). The mixture was extracted with dichloro-

methane (6 × 2 ml), and the combined extracts dried and evaporated. Chromatography of the residue (silica; ether), gave essentially one diastereoisomer of the *triol* (43 mg, 73%), as a liquid; $\delta_H(CDCl_3)$ 1.16 (t, *J* 7.2 Hz, Me), 1.45—1.70 (m, 2 × *H*CH), 1.80—2.08 (m, 2 × *H*CH), 3.03 (dd, *J* 7.9 and 5.4 Hz, *H*CCHOH), 3.37 (br, 3 × OH and *H*CCH$_2$), 4.07 (SCC*H*OH), 4.13 (dd, *J* 6 and 3 Hz, C*H*OH), 4.24 (dd, *J* 6 and 3 Hz, *C*HOH), 5.63 (dd, *J* 5.5 and 1.8 Hz, *H*C=CHCH), 6.00 (dd), *J* 5.5 and 2.1 Hz, HC=C*H*CH), 7.28—7.46 (m, *m*- and *p*- Ar*H*), and 7.50—7.59 (m, *o*-Ar*H*); *m/z* 362 (19), 209 (12), 196 (81), 180 (39), 155 (46), 151 (100), 137 (36), 123 (21), 110 (64), 109 (54), and 99 (64) (Found: *m/z* 362. 1178. $C_{19}H_{22}O_5S$ requires *M*, 362.1188).

(1RS,2RS,5RS,7SR,8RS)-(E)-4′-*Ethylidene*-3′,7,8-*trihydroxy*-3′,4′-*dihydrobicyclo*[3.3.0]*oct*-3-*ene*-2-*spiro*-2′-*furan*-5′(2′H)-*one* (**78**).—A solution of *m*-chloroperoxybenzoic acid (84%, remainder *m*-chlorobenzoic acid 24 mg, 116 μmol) in dichloromethane (3 ml) was added dropwise to a solution of the sulphide (**77**) (43 mg, 116 μmol) in dichloromethane (10 ml) at −80 °C under nitrogen. After 1 h the mixture was allowed to warm to room temperature and then poured into saturated aqueous sodium hydrogen carbonate (15 ml) and the layers separated. The aqueous phase was extracted with dichloromethane (6 × 5 ml), and the organic layers were then combined, dried, and evaporated. The resulting pale yellow oil was dissolved in carbon tetrachloride (10 ml) and chloroform (2 ml) containing suspended calcium carbonate (50 mg, 500 μmol), and the mixture was heated under reflux in an atmosphere of nitrogen for 3 h, then filtered through Celite, and evaporated to dryness. Chromatography (silica; ethyl acetate) gave the E-*ethylidenefuranone* (5 mg, 17%) as a liquid, $\delta_H(CDCl_3)$ 1.68 (br, 3 × OH), 2.05 (d, *J* 7 Hz, MeCH=), 1.80—2.35 (m, C*H*$_2$ and C*H*CHOH), 3.23—3.50 (m, =CHC*H*), 4.04—4.35 (m, *H*COH*H*-COH), 4.45—4.68 (m, =CC*H*OH), 5.36 (dd, *J* 5.5 and 1.3 Hz, C*H*=CHCH), 5.94 (dd, *J* 5.5 and 1.5 Hz, =C*H*CH), and 7.06 (dq, *J* 1.3 and 7 Hz, MeC*H*=); *m/z* 252 (4), 234 (5), 165 (13), 155 (100), 137 (80), 119 (23), 70 (32), and 57 (42) (Found: *m/z* 252.1010. $C_{13}H_{16}O_5$ requires *M*, 252,0998), containing *ca.* 8% of the corresponding *Z*-isomer (**79**) [δ 2.28 (d, *J* 7 Hz, MeCH=)].

(±)-*Allamcin* (**3**).—A solution of sodium metaperiodate (5 mg, 23 μmol) in water (1.5 ml) was added to an ice-cooled solution of the triol (**78**) (3 mg, 12 μmol) in ether (4 ml). After 30 min, solid sodium acetate trihydrate (15 mg, 120 μmol) was added, and the mixture was then allowed to warm to room temperature when it was stirred for 4 h. The two layers were separated and the aqueous phase was extracted with dichloromethane (6 × 2 ml). Evaporation of the dried organic extracts, followed by chromatography on silica (ether) and recrystallisation (ether) gave (±)-allamcin (0.3 mg) as a microcrystalline solid, m.p. 189—195 °C with some premelting at 160 °C; $\delta_H(CDCl_3)$ 1.69—1.75 (m, *H*CH), 2.07 (dd, *J* 7.2 and 1.0 Hz, Me), 2.14—2.19 (m, *H*CH), 3.03 (dd, *J* 8.5 and 4.9 Hz, *H*CCHO$_2$), 3.35—3.40 (m, O*H* and *H*CCH$_2$), 51.2 (br, CC*H*), 5.24 (dd, *J* 8.0 and 5.8 Hz, H$_2$CC*H*O$_2$), 5.69 (d, *J* 4.9 Hz, HCC*H*O$_2$), 5.78 (dd, *J* 5.4 and 2.1 Hz, HCC*H*=), 6.02 (dd, *J* 5.4 and 2.0 Hz, HCCH=C*H*), and 7.13 (dq, *J* 7.2 and 1.8 Hz, =C*H*Me); *m/z* 250 (1), 232 (11), 211 (5), 203 (9), 175 (13), 160 (13), 153 (96), 136 (36), 135 (25), 107 (20), 98 (65), 97 (63), 81 (31), and 59 (100) (Found: *m/z* 250.0869. $C_{13}H_{14}O_5$ requires *M*, 250.0839); which did not separate from naturally derived allamcin in t.l.c., and showed ^{1}H n.m.r. and mass spectroscopic data identical with the natural product.

(±)-Allamcin was also produced when the acetate-diol (**83**) was treated in a similar manner to that described for compound (**78**), and also when the methyl ether (**84**) was treated with aqueous periodic acid.

(1RS,2RS,5RS,7SR,8RS)-3′-*Acetoxy*-4′-*ethylidene*-7,8-*dihydroxy*-3′,4′-*dihydrobicyclo*[3.3.0]*oct*-3-*ene*-2-*spiro*-2′-*furan*-5′(2′H)-*one* (**83**).—A solution of *m*-chloroperoxybenzoic acid (84% remainder *m*-chlorobenzoic acid, 33 mg, 160 μmol) in dichloromethane (5 ml) was added dropwise to a solution of the mixture of diastereoisomers of the sulphide (**76**) (66 mg, 160 μmol) in dichloromethane (10 ml) at −80 °C under nitrogen. After 1 h, the mixture was allowed to warm to room temperature, where it was stirred for 1 h and then poured into saturated aqueous sodium hydrogen carbonate (10 ml). The layers were separated, and the aqueous phase extracted with dichloromethane (6 × 10 ml). Evaporation of the dried dichloromethane extracts left a pale yellow oil which was dissolved in carbon tetrachloride (10 ml) and chloroform (3 ml) containing suspended calcium carbonate (150 mg, 1.5 mol). The mixture was heated under reflux in an atmosphere of nitrogen for 3 h, then filtered through Celite, and evaporated to dryness. Chromatography (silica; ether) gave: (i) recovered starting material (5 mg, 7.5%); (ii) a single diastereoisomer of the *acetate* (28 mg, 60%), as a liquid; $\delta_H(CDCl_3)$ 1.54—1.67 (m, *H*CH), 1.98 (dd, *J* 7.3 and 0.4 Hz, *Me*CH=), 2.0—2.13 (m, obs., *H*CH), 2.06 (Ac), 2.74 (dd, *J* 7 and 7 Hz, *H*CCHOH), 3.36—3.49 (m, =CHC*H*), 4.07—4.23 (m, C*H*OC*H*O), 5.55 (dd, *J* 5.6 and 2.1 Hz, *H*C=CH), 5.86 (br, C*H*OAc), 6.00 (dd, *J* 5.6 and 2.1 Hz, *H*C=CH), and 7.11 (dq, *J* 1.5 and 7.3 Hz, MeC*H*=); $\delta_C(CDCl_3)$ 16.0 (q), 20.6 (q), 34.9 (t), 46.1 (d), 54.6 (d), 73.2 (d), 74.6 (d), 75.4 (d), 96.0, 126.5 (d), 127.3, 142.6 (d), 144.6 (d), 169.0, and 169.6 p.p.m.; *m/z* 294 (1), 251 (2), 197 (7), 155 (13), 140 (10), 137 (40), 98 (58), 97 (20), and 60 (15) (Found: *m/z* 294.1085. $C_{15}H_{18}O_6$ requires *M*, 294.1103); and (iii) a sample of the acetate contaminated with a second diastereoisomer (12 mg, 25%) which gave closely similar ^{1}H n.m.r. and m.s. data.

(1RS,2RS,5RS,7SR,8RS)-7,8-*Dihydroxy*-4′-(1-*methoxyethyl*)-*bicyclo*[3.3.0]*oct*-3-*ene*-2-*spiro*-2′-*furan*-5′(2′H)-*one* (**84a**).—A solution of the acetate (**83**) (11 mg, 37.4 μmol) and potassium carbonate (10 mg, 72.5 μmol) in methanol (5 ml) was stirred at room temperature under nitrogen for 16 h. The mixture was acidified with 1M sulphuric acid, and the methanol was then evaporated under reduced pressure. The resulting aqueous solution was extracted with dichloromethane (6 × 2 ml), and the extracts were combined, dried, and evaporated to give the *methyl ether* (10 mg, 98%) as a mixture of OMe-epimers (at 1″), $\delta_H(CDCl_3)$ 1.40 (d, *J* 6.5 Hz, *Me*CHO), 1.41 (d, *J* 6.6 Hz, *Me*CHO), 1.65—1.78 (m, *H*CH), 2.02—2.15 (m, *H*CH), 2.59 (br, 2 × OH), 2.85—2.94 (m, *H*CCHOH), 3.36 (MeO), 3.38 (MeO), 3.43—3.54 (m, *H*CCH$_2$), 4.16 (dq, *J* 6.5 and 0.5 Hz C*H*OMe), 4.17 (dq, *J* 6.5 and 0.5 Hz, C*H*OMe), 4.20—4.28 (m, *H*COH*H*COH), 5.27—5.34 (m, *H*C=CH), 6.04 (dd, *J* 5.4 and 2 Hz, HC=C*H*CH), 7.09 (app. d, *J* 0.5 Hz, CH=CC=O). Integration of the ^{1}H n.m.r. spectrum gave a diastereoisomer ratio of 3:4; irradiation of δ 7.09 failed to give any n.O.e. enhancement of signals in the rest of the spectrum; *m/z* 266 (1), 251 (6), 236 (10), 234 (16), 218 (18), 216 (12), 208 (23), 190 (13), 176 (13), 175 (12), 174 (12), 162 (19), 161 (17), 117 (22), 99 (34), 91 (22), 81 (20), 77 (22), and 59 (100) (Found: *m/z* 266.1144. $C_{14}H_{18}O_5$ requires *M*, 266.1154).

Acknowledgements

We thank the S.E.R.C. for a Fellowship (to K. E. B. P.) and Professor Yamauchi for a sample of natural (+)-allamcin. We also thank Anthony G. Smith for some preliminary studies, particularly on the use of the dianion (**20**) in the elaboration of α-ethylidene-β-oxy-γ-butyrolactones.[29]

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Received 6th March 1987; *Paper* 7/423