Studies on the Functionalisation of *cis*-Bicyclo[3.3.0]oct-7-en-2-ol—Approaches to the Synthesis of Specionin[1]

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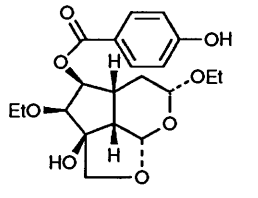
During studies aimed at finding a synthetic route to specionin, methods have been developed for selective functionalisation of each ring of *cis*-bicyclo[3.3.0]oct-7-en-2-ol. Various *exo*-7,8-*cis*-dihydroxy *cis*-bicyclo[3.3.0]octan-2-ol derivatives **9a–c** were prepared and a 'one-pot' conversion into 9-hydroxy 2,4-diethoxy-3-oxa-*cis*-bicyclo[4.3.0]nonane derivatives **10a**, **b** was developed. Acetonide, bis-*tert*-butyldimethylsilyl, and dibenzyl-protected 7,8-diol derivatives **13a–c** were prepared and converted into the corresponding 7-*exo*,8-*exo*-dihydroxy-*cis*-bicyclo[3.3.0]octan-2-one derivatives **12a–c**. Protected 7,8-dihydroxy-*cis*-bicyclo[3.3.0]oct-3-en-2-ones **17a–c** were prepared in moderate yield from ketones **12a–c**. A Wittig–ene reaction sequence was developed whereby ketones **12a–c** were converted into enals **22a–c** and **23a–c**, which were then converted into alcohols **28a–c** and **29a–c**.

Stereoisomers of *exo*,*exo*-6,7-bis(benzyloxy)-4-(hydroxymethyl)-*cis*-bicyclo[3.3.0]oct-2-ene, **28c** and **29c** were distinguished by ^{1}H NMR NOE studies, while a model reaction sequence for completion of the left-hand ring of specionin was developed using a mixture of acetonides **28a** and **29a**, leading to epoxide **35** as a mixture of stereoisomers.

Specionin **1** is an interesting polyhydroxylated iridoid, isolated from the leaves of *Catalpa speciosa* Warder, from North American fir and spruce forests. It was shown to be a powerful insect antifeedant, especially against the Eastern spruce budworm, and its structure was originally assigned as **2** by Nakanishi using spectroscopic data.[2] Specionin is relatively simple compared with some other compounds that have similar activity, but it is a highly functionalised, highly oxygenated molecule, with three oxygen substituents on the same face of the cyclopentane ring, and all but two carbon atoms (in the main skeleton) are asymmetric. These structural and biological features first triggered our interest in specionin, but shortly after our synthetic efforts began, Vandewalle reported a synthesis of compound **2** and concluded that it was not the same as the natural product.[3] He proposed, and later confirmed by synthesis,[4] that the structure of specionin is in fact **1**.† Since Vandewalle's original report, several other groups have synthesized specionin.[1,5] The structure bears a very close relationship to that of catalposide **3**, which has been isolated from the same source. Reaction of catalposide with ethanol could, in principle, lead to specionin and this raises the possibility that specionin could either be biosynthesized from catalposide or could simply be an artifact of it produced during isolation, although attempts to convert catalposide into specionin have not been successful.[6]



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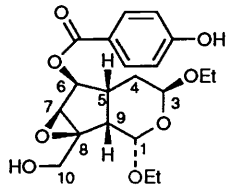
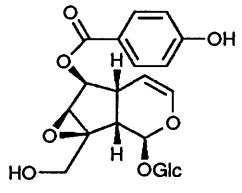


Specionin **1**



Catalposide **3**

Results and Discussion

cis-Bicyclo[3.3.0]oct-7-en-2-ol **4** is readily prepared in racemic form by the well established method of Crandall and Chang,[7] and several methods are available for resolving it.[8,9a] The structural and stereochemical features of *cis*-bicyclo-[3.3.0]oct-7-en-2-ol together with its ease of preparation make it an attractive starting material for the synthesis of iridoids and several other groups have also recognised this.[9]

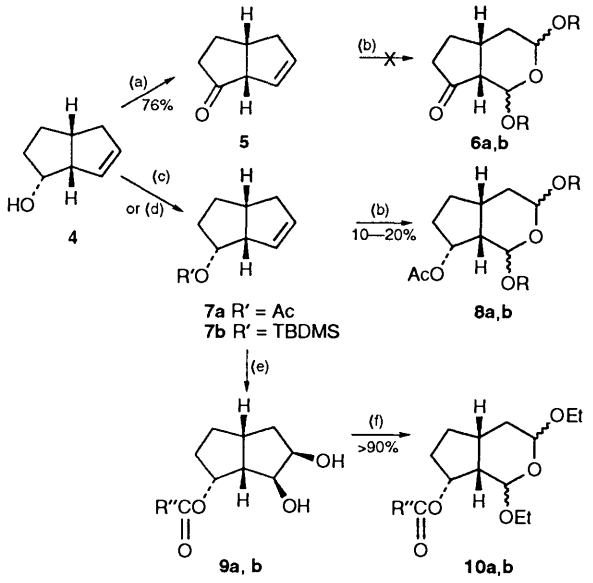
Initially we wanted to investigate the selective functionalisation of each ring of *cis*-bicyclo[3.3.0]oct-7-en-2-ol, and in terms of devising the most effective synthetic strategy we wanted to determine which ring to functionalise first.

Cleavage of the Right-hand Ring Prior to Functionalisation of the Left-hand Ring.—First of all we explored methods for cleaving the alkene bond of the bicycle to a bis-aldehyde, which in alcohol we hoped would cyclise spontaneously to give a bis-acetal, with one diastereoisomer predominating. Before cleaving the alkene we needed to remove the secondary alcohol, and we first thought it would be useful to convert it into a ketone, which we would require later. Oxidation of alcohol **4** to ketone **5** is described in the literature, but we found the yield to be rather disappointing with chromium reagents, and the ketone to be somewhat unstable. A range of oxidising agents were therefore tried and the Swern method proved to be the best in our hands.[10]

Ozonolysis of ketone **5** was carried out in various alcoholic solvents, under a variety of conditions, with or without the addition of an acid to catalyse acetalisation, but none of the required bis-acetals **6** were isolated from very messy reaction products. Performing ozonolysis on acetate **7a** was somewhat more productive, benzyl acetal **8b** being isolated in ~10% yield and methyl acetal **8a** in ~20% yield,

† The numbering system shown for specionin **1** will be used throughout the text for all compounds.

both as diastereoisomer mixtures. At this point we decided to abandon this general strategy and instead to try to functionalise the left-hand ring of *cis*-bicyclo[3.3.0]oct-7-en-2-ol, but in later studies we did find an efficient method for formation of bis-acetals **10a** and **10b**. Alkenes **7a** or **7b** were efficiently converted into *cis*-diols **9a** and **9c** which could then be converted into other esters such as **9b** (see below). Upon periodate cleavage in ethanol diols **9a** and **9b** were each converted into bis-acetals, **10a** and **10b**, in >90% yield (Scheme 1). The discovery that this

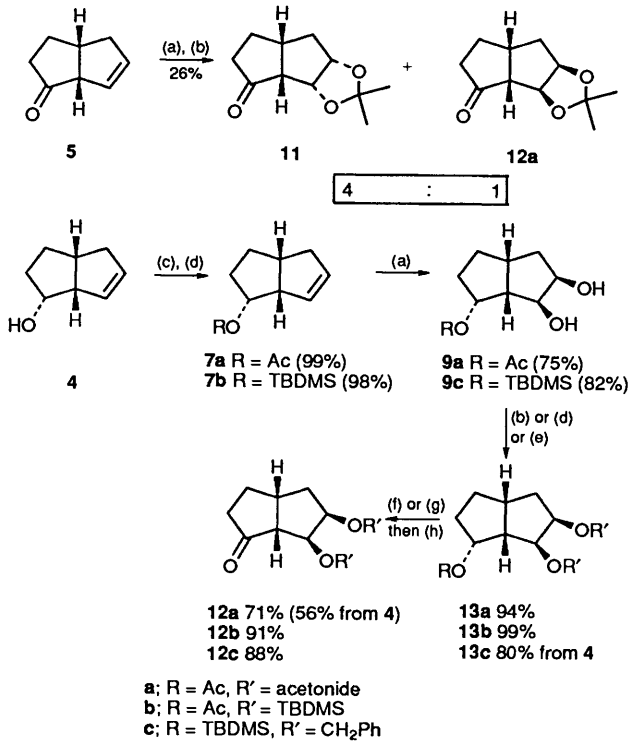


Scheme 1 *Reagents and conditions:* (a) DMSO, $(COCl)_2$, CH_2Cl_2, Et_3N; (b) (i) O_3, MeOH, 78 °C; (ii) Me_2S; (iii) CF_3CO_2H, room temp.; (c) Ac_2O, Et_3N, CH_2Cl_2; (d) TBDMSCl, imidazole, DMF; (e) OsO_4, NMMNO, THF, Bu'OH, water; (f) $NaIO_4$, EtOH, 18 h; (ii) TsOH, 24 h

type of transformation is highly efficient was of great use to us in devising an effective synthesis of specionin. A key step in our revised synthetic strategy (see following paper) was a diol cleavage–bis-acetal cyclisation sequence and as this was to be one of the last steps, it was reassuring that this model reaction proceeded very efficiently.

Conversion of the Alkene Bond of cis-*Bicyclo*[3.3.0]*oct-7-en-2-ol to Protected* cis-*Diols.*—Our revised synthetic strategy for specionin involved early functionalisation of the left-hand ring, but we decided to convert the alkene bond into a protected *cis*-diol first. Ketone **5** was first treated with osmium tetraoxide under catalytic conditions,[11] followed by acetonide protection of the hydroxy groups. The yield of this process was low and some decomposition occurred, but we were surprised to discover that the major product was the *endo* protected diol **11**. It was a rather unstable compound and we think that the low yield may have been due to its decomposition during the reaction sequence. Hydroxylation is apparently occurring predominantly from the concave face of the system, and the carbonyl group may be directing the reaction.

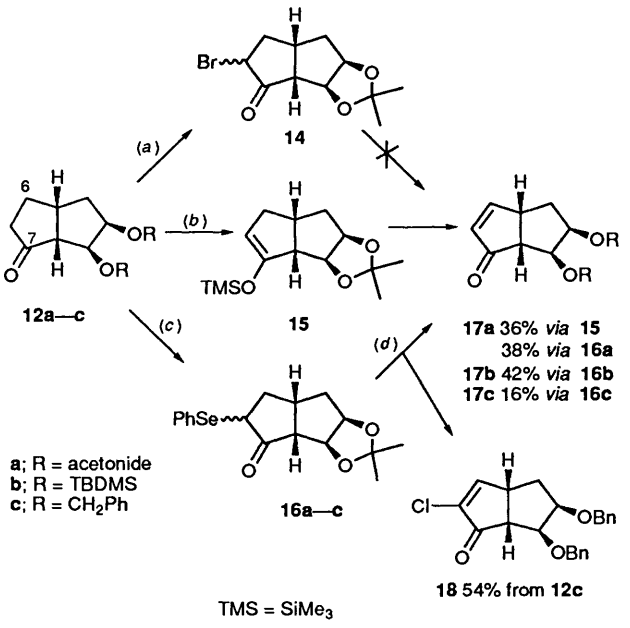
cis-Hydroxylation of protected alcohols **7a** and **7b** was high yielding and, as expected, the hydroxy groups were installed on the convex face of the molecule, providing acetate **9a** or silyl ether **9c**. The alcohols were readily protected in various ways. For our early studies an acetonide protecting group was installed, but this is very difficult to remove and we found silyl ether protection or benzylation to be more useful. With any of these protecting groups installed, the other hydroxy group could be oxidised in very high yield under Swern conditions (Scheme 2).



Scheme 2 *Reagents:* (a) OsO_4, NMMNO, THF, Bu'OH, water; (b) $(MeO)_2CMe_2$, CH_2Cl_2, TsOH; (c) Ac_2O, Et_3N, CH_2Cl_2; (d) TBDMSCl, imidazole, DMF; (e) (i) NaH, THF; (ii) $PhCH_2Br$; (f) MeOH, NaOMe (cat.); (g) Bu_4NF, THF; (h) $(COCl)_2$, CH_2Cl_2, DMSO, Et_3N

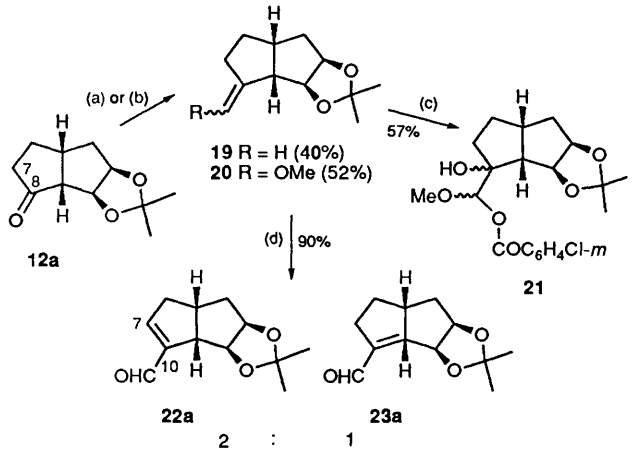
Oxidation of the C-8 *Ketone to an Enone.*—We thought an enone in the left-hand ring would be useful to us, but we were only able to achieve oxidation of the ketones **12** in modest yield. Bromo ketone **14** could be prepared from compound **12a** only in low yield and could not be converted into an enone.[12] The trimethylsilyl (TMS) enol ether **15**, from ketone **12a**, could be prepared and various palladium-catalysed oxidation methods were investigated for converting it into enone **17a**, but the highest yield was 36%.[13,14] The Sharpless seleniation–oxidation method, involving phenyl selenides **16a–c**, was simple to carry out and gave enone **17a** in 38% yield from ketone **12a**.[15] Ketone **12b** was also oxidised to the equivalent enone **17b** in modest yield, but attempted oxidation of compound **12c** *via* seleniation gave a surprising result. Two enones were formed, but the minor product was enone **17c** and the major product was chloro enone **18**. It is not entirely clear how chloride **18** was formed, but an excess of benzeneselenenyl chloride was used and initial bis-seleniation of substrate **12c** might be responsible. Alternatively, some residual selenyl chloride may have reacted with enone **17c** after the oxidation step, as it is known that this can lead to chloro enone formation (Scheme 3).[16]

Introduction of C-10 *as an Enal: Development of a Wittig–Ene Procedure.*—Because the yields of enones **17a–c**, obtained from the equivalent ketones, were low we decided to explore the possibility of introducing the required extra carbon (C-10) prior to functionalisation of C-6/C-7. Introducing the extra carbon as part of an exocyclic spiro-epoxide might have been useful, but we were unable to get ketone **12a** to react with dimethylsulfonium methylide. As an alternative we tried to achieve reaction between ketone **12a** and Wittig reagents, but only



Scheme 3 *Reagents:* (a) pyridinium perbromide, THF; (b) LDA, THF, TMSCl; (c) PhSeCl, EtOAc; (d) 30% H_2O_2

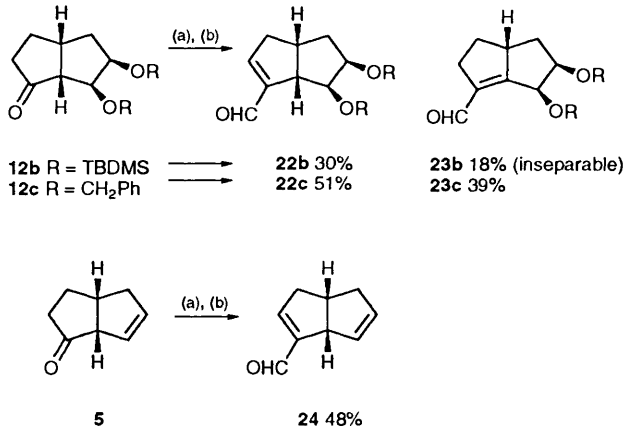
starting material was recovered when Wittig reagents, derived by deprotonation of phosphonium salts with lithium bases, were used. Although the ylide is in principle a neutral reagent, we thought that enolisation of the ketone might be occurring and that this might be counterion dependent. This indeed seems to be the case, since methylene and methoxymethylene ylides reacted in reasonable yield when formed from sodium hexanemethyldisilazide [$NaN(TMS)_2$] (Scheme 4).



Scheme 4 *Reagents and conditions:* (a) $Ph_3{=}CH_2$ [formed from $Ph_3\overset{+}{P}MeBr^-$ + $NaN(TMS)_2$], THF, 0 °C; (b) $Ph_3P{=}CHOMe$ [formed from $Ph_3\overset{+}{P}CH_2OMeCl^-$ + $NaN(TMS)_2$], THF, 0 °C; (c) MCPBA, CH_2Cl_2; (d) $^1O_2$, benzene

Next, we wanted to oxidise enol ether **20** to an enal. Bromination gave very messy products, but treatment with *m*-chloroperbenzoic acid (MCPBA) gave an unusual addition product **21**, as a mixture of two separable diastereoisomers, in 57% yield. We thought that this might be useful to us, but all attempts to hydrolyse the ester led to decomposition. The singlet oxygen ene reaction is an alternative method for the direct conversion of enol ethers into enals.[17] Singlet oxygen is usually generated by irradiation of an oxygenated reaction mixture in the presence of a sensitiser. In our case enol ether **20** was not very stable to the heat generated by the lamps but we were able to design a simple water-cooled reaction flask to overcome this problem. A solution of the enol ether was then allowed to react by passage of a stream of oxygen through it, in the presence of a sensitising dye, whilst the mixture was illuminated with two 150 W tungsten lamps. Experiments were performed with Methylene Blue and *meso*-tetraphenylporphine (MTPP) as sensitisers, in a range of solvents. In all cases enals **22a** and **23a** were obtained in a 2:1 ratio, but MTPP in benzene gave the highest yield of 90%. For simple enol ethers the ene reaction occurs with abstraction of a proton *syn* to the methoxy group,[17b] but in the cases we explored (see below also) the enol ether starting materials were ~ 1:1 mixtures of geometrical isomers, but always gave the least substituted alkene predominantly. It could be that some isomerisation of the alkene occurs under the reaction conditions; on the other hand there could simply be a statistical preference for abstraction of a methylene rather than a methine hydrogen. In any case the preference was pleasing from a synthetic point of view and provided the key functionality required for completion of the left-hand ring of specionin (Scheme 4).

In later work the Wittig–ene procedure was extended to other bicyclic ketones and it was found that the process was more effective if the crude Wittig product (which was not very stable, and was generally difficult to purify) was subjected directly to the ene reaction. The enal products were generally easier to purify and were separated readily from residual triphenylphosphine oxide (Scheme 5). The yield of silyl ethers **22b** and

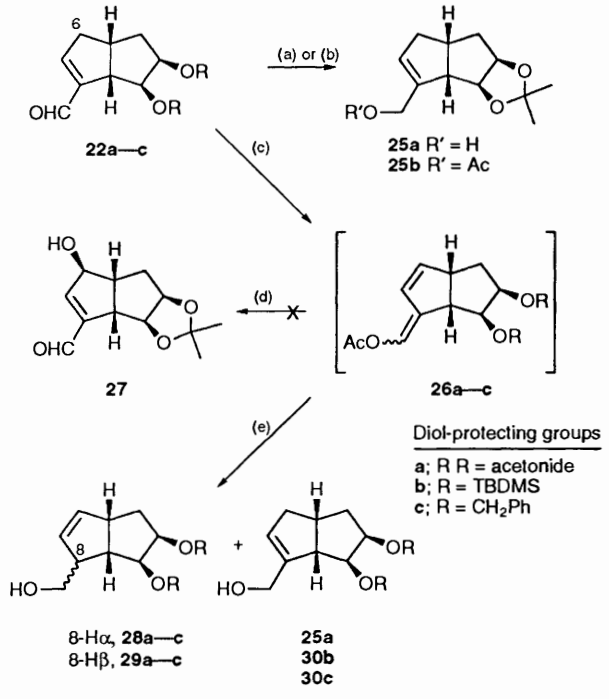


Scheme 5 *Reagents and conditions:* (a) $Ph_3P{=}CHOMe$ [formed from $Ph_3\overset{+}{P}CH_2OMeCl^-$ + $NaN(TMS)_2$], THF, 0 °C; (b) $^1O_2$, benzene

23b was quite low and they were inseparable from one another which compromised their usefulness. When alkene **5** was subjected to the process, enal **24** was the only regioisomer isolated, but the yield was only 48% and it may be that the other isomer had decomposed. Pattenden has used a Shapiro process to convert alkene **5** into enal **24**.[9c] Bis-benzyl ether **12c** was converted into enals in high yield, the regioisomers were readily separated and enal **22c** was eventually our chosen intermediate for the synthesis of specionin.

Functionalisation of the C-6 *Position.*—We needed to find a way to install a hydroxy group at the C-6 position and our initial aim was to introduce some functionality that would facilitate this. When we tried to deconjugate the enal in compound **22a**, by treatment with lithium diisopropylamide–tetrahydrofuran (LDA–THF) followed by protonation, the reduced product **25a** was obtained in a moderate (30%) yield. Although no acid was isolated, we presume that a Cannizzaro-type process is occurring. When the LDA reaction was quenched with acetic anhydride the acetate **25b** was the main product. Changing the base to KOBu^t–THF was productive

though and provided enol acetate **26a** in moderate yield from enal **22a**, on quenching with acetic anhydride. The bis-benzyl ether **22c** was also converted into an enol acetate reasonably cleanly (yield ~60%), but the product from silyl ether **22b** was messy because the enal is inseparable from its regioisomer. The enol acetates were not very stable and were generally allowed to react further without purification. Our original plan was to oxidise the enol acetate from the convex face with MCPBA to produce hydroxy enal **27**. Kirk has used this type of reaction to produce β-hydroxy enones from dienol acetates,[18] but in our case a complex mixture was obtained when acetate **26a** was treated with MCPBA. We had intended to investigate this process with other oxidising agents but the instability of enol acetates **26** made this difficult. We chose instead to take a somewhat longer route to introduction of the OH group, starting with sodium borohydride reduction of the enol acetates to provide a mixture of homoallylic alcohols **28** and **29** and allylic alcohol **25a**/**30**. Our initial study using the acetonide **22a** gave an inseparable mixture of the three alcohols **28a**, **29a** and **25a** in 35% yield. When the same process was carried out with the inseparable silyl-protected compounds **22b** and **23b**, a very low yield of alcohols was obtained. However, in later studies the bis-benzyl ether **22c** was converted into a mixture of the three alcohols **28c**, **29c** and **30c** in a respectable 56% yield. Significantly, the alcohols were separable by preparative HPLC and the required homoallylic alcohols predominated, the proportions being 3:3:2, for **28c**, **29c** and **30c** respectively (Scheme 6).



Scheme 6 *Reagents and conditions:* (a) (i) LDA, THF; (ii) sat. aq. NH_4Cl; (b) (i) LDA, THF; (ii) Ac_2O; (c) (i) KOBu^t, THF, 0 °C; (ii) Ac_2O; (d) MCPBA, CH_2Cl_2; (e) $NaBH_4$, EtOH

There was a good deal of signal overlap in the ^1H NMR spectra of alcohols **28c** and **29c**, but the spectra of their acetates **31** and **32** were well resolved, allowing us to carry out detailed NOE studies to distinguish between the diastereoisomers. Of particular importance for the 8α-H compound **31**, there was a strong positive effect between 1-H and 8-H and a small indirect negative effect between 1-H and the 10-H methylene protons. In contrast there was a large positive effect between 1-H and the 10-H methylene protons for the 8β-H compound **32** and a small indirect negative effect between 1-H and 5-H (Fig. 1).

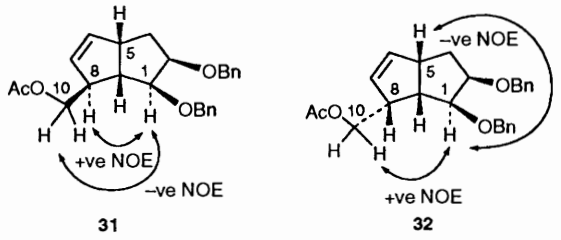
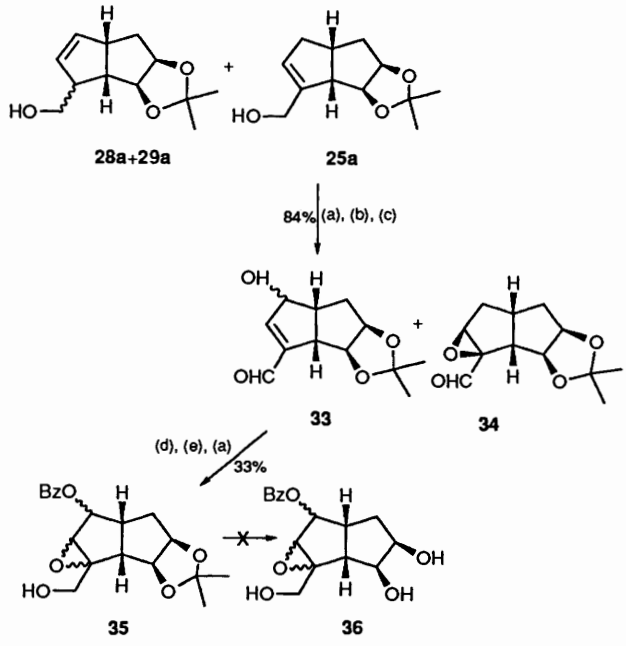


Fig. 1 Nuclear Overhauser effects (NOEs) in compounds **31** and **32**. Specionin numbering scheme.

Model Study for the Introduction of the C-6 *Hydroxy Group.*— All our early synthetic work was in the acetonide-protected diol series and after the previous sequence of reactions we had an inseparable mixture of allylic alcohols **28a**, **29a** and **30a**. Although a completion of the specionin synthesis *via* this route was not practical, we decided to carry out an initial sequence of trial reactions on the alcohol mixture; to test the overall viability of completing the left-hand ring from this type of intermediate and to test whether or not removal of an acetonide protecting group would be viable once the left-hand ring was complete. Thus, the alcohol mixture was sequentially epoxidised with MCPBA, the alcohols were then oxidised under Swern conditions, and the mixture was finally treated with 1,8-diazobicyclo[5.4.0]undec-7-ene (DBU) to cause opening of the β-epoxy aldehydes. This sequence gave a pleasing 84% yield of products, epoxide **34** being the major component, in the ratio 2:1 with an inseparable mixture of α-hydroxy enals **33** (Scheme 7). In another sequential set of reactions the hydroxy enal



Scheme 7 *Reagents:* (a) MCPBA, CH_2Cl_2; (b) $(COCl)_2$, CH_2Cl_2, DMSO, Et_3N; (c) DBU, CH_2Cl_2; (d) PhCOCl, CH_2Cl_2, Et_3N; (e) $NaBH_4$, CeCl, MeOH

mixture **33** was converted into a mixture of only two separable epoxides **35** (stereochemistry not assigned). The essential features of the left-hand ring of specionin are present in compound **35** and our intention was to use it as a model to test the viability of removal of acetonide groups, followed by cleavage of the diol **36** and cyclisation of the right-hand ring. In the event we were unable to remove the acetonide protecting group from compound **35** with retention of the other functionality, even though several methods were tried, including palladium-catalysed methods.[19] More recently Hudlicky *et al.*

have been able to remove an acetonide protecting group from a compound similar to **35** during their work on specionin, but in their case the primary alcohol was acetylated and this may be important.[5d]

Although the sequence described in Scheme 7 was not productive in a synthetic sense, we had gained valuable knowledge by carrying it out. Most importantly we had established that the sequence of epoxidation–alcohol oxidation–epoxide opening, on an intermediate such as **28** or **29** was a highly efficient process for installing the key functionality required in the left-hand ring of specionin. We had also discovered that the acetonide group was unsuitable for protecting the C-1/C-2 diol and with this knowledge we were able to redesign our strategy and complete the synthesis, as described in the following paper.

Experimental

M.p.s were determined on an electrothermal apparatus and were recorded uncorrected. IR absorption spectra were run either neat (for liquids) or as Nujol mulls (for solids) on a Perkin-Elmer 1710 FT-IR instrument or a Perkin-Elmer 297 grating spectrophotometer. ^{1}H NMR spectra were recorded at 60 MHz on a Varian EM360 instrument, at 90 MHz on a Perkin-Elmer R-32 instrument, at 300 MHz on a Bruker AC-300 instrument, or at 400 MHz on a Bruker WH-400 instrument, as solutions in deuteriochloroform, unless stated otherwise. Chemical shifts are referenced to tetramethylsilane (except where stated otherwise) and *J* values are rounded to the nearest 0.5 Hz. Mass spectra were recorded at low resolution on a VG 12-553 instrument or a Finnigan 4500 instrument and at high resolution on a VG ZAB-E instrument or a Kratos Concept 1-S instrument. Mass spectra were recorded under electron-impact (EI) conditions, or chemical-ionisation (CI) conditions using either methane or ammonia as specified. After aqueous work-up of reaction mixtures, organic solutions were routinely dried with anhydrous magnesium sulfate, and 'evaporation' or 'evaporated' refers to removal of solvent on a rotary evaporator. TLC was carried out on Merck Kieselgel 60 F_{254} glass-backed plates. The plates were visualised by the use of a UV lamp, or by dipping in a solution of vanillin in ethanolic sulfuric acid, followed by heating. Silica gel 60 (particle sizes 40–63 μ) supplied by Merck was employed for flash chromatography.[20] Light petroleum refers to the fraction boiling in the range 40–60 °C. Note that compounds are named and numbered in a systematic manner in this Experimental section and this does not correspond to the specionin numbering system used in the Results and Discussion section.

(±)-cis-*Bicyclo*[3.3.0]*oct*-7-*en*-2-*one* **5**.—To a stirred solution of oxalyl dichloride (0.75 cm^3, 8.2 mmol) in dichloromethane (25 cm^3) at −78 °C was added a solution of dimethyl sulfoxide (DMSO) (1.3 cm^3, 16.3 mmol) in dichloromethane (3 cm^3) dropwise. After 2 min a solution of the alcohol **4** (500 mg, 4.0 mmol) in dichloromethane (2 cm^3) was added dropwise, and after a further 15 min triethylamine (5.3 cm^3, 37.4 mmol) was added. After a further 5 min at −78 °C the mixture was allowed to warm to room temperature, then was poured into 1 mol dm^{-3} HCl (30 cm^3) and extracted with dichloromethane (2 × 30 cm^3). The organic layer was washed with saturated aq. $NaHCO_3$ (25 cm^3), dried, and evaporated. Purification by flash chromatography [light petroleum–ethyl acetate (20:1)] provided starting material **4** (25 mg, 5% recovery) and ketone **5** (375 mg, 76%); ν_{max}/cm^{-1} 3050 and 1730; δ_H(60 MHz) 1.0–3.5 (8 H, m) and 5.75 (2 H, m, 7- and 8-H); *m/z* (CI, NH_3) 140 ([M + NH_4], 100%) and 123 ([M + H], 20) (Found: [M + NH_4]$^+$, 140.1072. $C_8H_{10}O{\cdot}NH_4$ requires *m/z*, 140.1075).

(±)-endo-9-*Acetoxy*-2,4-*dimethoxy*-3-*oxa*-cis-*bicyclo*[4.3.0]-*nonane* **8a**.—Ozone was bubbled through a solution of acetoxy-*cis*-bicyclo[3.3.0]oct-7-en-2-ol ester **7a** (200 mg, 1.20 mmol) in dry methanol (30 cm^3) at −78 °C until no more starting material remained, as indicated by TLC. Then dimethyl sulfide (0.15 g, 3.20 mmol) was added and the reaction mixture was allowed to warm to room temperature, after which trifluoroacetic acid (TFA) (1 drop) was added and the mixture was left for *ca.* 20 h. Most of the methanol was removed on a rotary evaporator and the residue was dissolved in dichloromethane (30 cm^3), and the solution was washed with saturated aq. $NaHCO_3$ (20 cm^3), dried, and evaporated. Purification by flash chromatography provided compound **8a** as a mixture of diastereoisomeric bis-acetals (60 mg, 20%); ν_{max}/cm^{-1} 1730 and 1100; δ_H(60 MHz) 1.5–2.5 (8 H, m), 2.0 (3 H, s, Ac), 3.5 (6 H, s, MeO × 2), 4.7 (2 H, m) and 5.25 (1 H, m); *m/z* (EI) 244 (M^+, 3.0%), 213 ([M − OMe^-], 32), 181 (8), 153 (20), 121 (11), 58 (100) and 43 (85).

(±)-endo-9-*Acetoxy*-2,4-*bis*(*benzyloxy*)-3-*oxa*-cis-*bicyclo*-[4.3.0]*nonane* **8b**.—Ozonolysis of the ester **7a** (85 mg, 0.51 mmol) was carried out in dichloromethane (15 cm^3) at −78 °C. After complete reaction (as indicated by TLC), dimethyl sulfide (1 cm^3) was added and the mixture was allowed to warm to room temperature. The solvents were then evaporated off and a solution of the residue in dry benzene (10 cm^3), containing benzyl alcohol (120 mg, 1.12 mmol) and toluene-*p*-sulfonic acid (PTSA) (5 mg), was azeotroped in a Dean–Stark trap for 5 h. After the solvent had been evaporated off, flash chromatography [light petroleum–ethyl acetate (6:1)] gave a mixture of diastereoisomers of compound **8b** (21 mg, 10%) as the only identifiable product; ν_{max}/cm^{-1} 3050, 3025, 1730 and 1670; δ_H(90 MHz) 1.5–3.0 (8 H, m), 2.0 (3 H, s, Ac), 4.6 (4 H, m), 4.9–5.2 (3 H, m) and 7.3 (10 H, m); *m/z* (EI) 396 (M^+, 0.3%), 289 ([M − $PhCH_2O^-$, 20), 229 (18), 181 (30), 91 (100) and 43 (62).

(±)-endo-9-*Acetoxy*-2,4-*diethoxy*-3-*oxa*-cis-*bicyclo*[4.3.0]-*nonanes* **10a**.—A suspension of diol **9a** (see below for preparation) (100 mg, 0.5 mmol) and sodium metaperiodate (220 mg, 1.03 mmol) in absolute ethanol (6 cm^3) was stirred for 24 h. PTSA (~10 mg) was then added, and after 24 h, the bulk of the solvent was removed, dichloromethane (30 cm^3) was added, and the mixture was washed with saturated aq. $NaHCO_3$ (20 cm^3), dried, and evaporated. Flash chromatography [light petroleum–ethyl acetate (8:1, then 4:1)], provided bis-acetals **10a** (125 mg, 92%), as a clear liquid, ν_{max}/cm^{-1} 1740 and 1440; δ_H(60 MHz) 1.15 (6 H, t, *J* 7.0, OCH_2Me × 2), 1.5–2.6 (8 H, m) 2.05 (3 H, s, Ac), 3.2–4.1 (4 H, m, OCH_2Me × 2), 4.6–5.05 (2 H, m, 2- and 4-H) and 5.25 (1 H, m, 9-H); *m/z* (CI, NH_4) 290 ([M + NH_3]$^+$, 40%), 273 ([M + H]$^+$, 1%) and 227 (100) (Found: [M + NH_4]$^+$, 290.1966. $C_{14}H_{28}NO_5$ requires *m/z*, 290.1967).

(±)-2,4-*Diethoxy*-endo-9-(p-*hydroxybenzoyloxy*)-3-*oxa*-cis-*bicyclo*[4.3.0]*nonanes* **10b**.—A stirred solution of (±)-*exo*,*exo*-7,8-dibenzyloxy-*endo*-*cis*-bicyclo[3.3.0]octan-2-ol (see below for preparation) (110 mg, 0.030 mmol), 4-(dimethylamino)pyridine (DMAP) (150 mg, 1.23 mmol) and *p*-benzyloxybenzoyl chloride (200 mg, 0.81 mmol) in dichloromethane (10 cm^3) was stirred for 15 h. The mixture was then diluted with dichloromethane (30 cm^3) and washed successively with 1 mol dm^{-3} HCl (25 cm^3) and then with saturated aq. $NaHCO_3$ (25 cm^3). After drying of the solution, the solvent was evaporated off and flash chromatography [light petroleum–ethyl acetate (10:1, then 4:1)] of the residue provided (±)-*endo*-2-(*p*-benzyloxybenzoyloxy)-*exo*,*exo*-7,8-bis(benzyloxy)-*cis*-bicyclo-[3.3.0]octane (140 mg, 86%), ν_{max}/cm^{-1} 3075, 3050, 1710, 1610, 1590 and 705; δ_H(60 MHz) 1.0–2.5 (6 H, m), 2.85 (2 H, m), 4.0 (2 H, m, 7- and 8-H), 4.45 (2 H, ~s, CH_2Ph), 4.55 (2 H, ~s,

CH_2Ph), 5.05 (2 H, ~ s, $ArOCH_2Ph$), 5.2 (1 H, m, 2-H), 6.9 (2 H, d, *J* 9.0), 7.1–7.4 (15 H, m) and 7.95 (2 H, d, *J* 9.0).

A stirred suspension of the above ester (70 mg, 0.13 mmol) and palladium (5%) on carbon (~ 15 mg) in absolute ethanol (5 cm^3) was hydrogenated at 1 atm for 8 h. The mixture was then filtered through Celite and to the filtrate was added sodium metaperiodate (56 mg, 0.26 mmol). The suspension was stirred for 24 h, then pyridinium toluene-*p*-sulfonate (~ 10 mg) was added and the mixture was stirred for a further 48 h. The bulk of the ethanol was then evaporated off, dichloromethane (20 cm^3) was added, and the mixture was washed with water (15 cm^3), dried, and the solvent was evaporated off. Purification by flash chromatography [light petroleum–ethyl acetate (5:1)], provided bis-acetals **10b** (40 mg, 89%), ν_{max}/cm^{-1} 3400, 3075, 1700, 1610, 1590 and 740; δ_H(300 MHz) 1.00–1.30 (6 H, m, OCH_2Me × 2), 1.5–2.0 (6 H, m), 2.20–2.60 (2 H, m, 1- and 5-H), 3.30–3.60 (2 H, m, OCH_2Me), 3.75–3.98 (2 H, m, OCH_2Me), 4.90 (1 H, m, 4-H), 5.08 (1 H, d, *J* 4.5, 2-H), 5.50 (1 H, m, 9-H), 6.81 (2 H, 2 × d, *J* 8.5, ArH) and 7.88 (2 H, 2 × d, *J* 8.5, ArH); *m/z* (CI, NH_3) 368 ($[M + NH_4]^+$, 5%), 351 ($[M + H]^+$, 1) and 305 (100) (Found: $[M + NH_4]^+$, 368.2090. $C_{19}H_{30}NO_6$ requires *m/z*, 368.2073).

(±)-exo,exo-7,8-(*Isopropylidenedioxy*)-cis-*bicyclo*[3.3.0]-*octan-2-one* **12a**.—A solution of *cis*-bicyclo[3.3.0]oct-7-en-2-ol **4** (5.0 g, 40.3 mmol), acetic anhydride (10 cm^3, 106 mmol) and DMAP (7.4 g, 60.7 mmol) in dichloromethane (150 cm^3), was heated at reflux for 10 h. After cooling, the mixture was washed successively with 1 mol dm^{-3} HCl (100 cm^3) and saturated aq. $NaHCO_3$ (100 cm^3), then was dried, and the solvent was evaporated off. The crude acetate **7a** (6.6 g, 99%) could be purified by flash chromatography [light petroleum–ethyl acetate (30:1)] but was sufficiently pure to use in subsequent reactions; ν_{max}/cm^{-1} 3050, 1730 and 1240; δ_H(60 MHz) 1.2–2.3 (5 H, m), 2.0 (3 H, s, Ac), 2.5–3.6 (3 H, m), 5.0 (1 H, m, 2-H) and 5.35–5.8 (2 H, m, 7- and 8-H).

A mixture of the above crude ester **7a** (6.6 g, 39.8 mmol), *N*-methylmorpholine *N*-oxide (NMMNO) (7.9 g, 58.5 mmol), *tert*-butyl alcohol (50 cm^3), THF (30 cm^3), water (25 cm^3) and osmium tetraoxide (20 drops of a 4% aq. solution) was stirred vigorously for 20 h. The mixture was then poured into dichloromethane (150 cm^3)–10% aq. Na_2S (100 cm^3), and after separation the aqueous layer was extracted with dichloromethane (3 × 75 cm^3). The combined organic layers were washed successively with 2 mol dm^{-3} HCl (100 cm^3), and with saturated aq. $NaHCO_3$, dried, and evaporated. (±)-*endo*-9-acetoxy-*cis*-bicyclo[3.3.0]octa-*cis*,*exo*-2,3-diol **9a** (6 g, 75%) was crystallised from methanol, m.p. 111–112 °C (crystals); ν_{max}(Nujol)/cm^{-1} 3400, 1700 and 1260; δ_H(60 MHz) 1.0–2.2 (6 H, m), 2.1 (3 H, s, Ac), 2.5–2.9 (4 H, m), 4.1 (2 H, m, 7- and 8-H) and 5.0 (1 H, m, 2-H); *m/z* (NH_3, CI) 218 ($[M + NH_4]^+$, 100%) and 201 ($[M + H]^+$, 5) (Found: $[M + NH_4]^+$, 218.1393. $C_{10}H_{20}N_4O$ requires *m/z*, 218.1392).

A solution of the diol **9a** (6 g, 30.0 mmol), 2,2-dimethoxypropane (10 cm^3, 81.3 mmol) and PTSA (200 mg, 1.05 mmol) in dichloromethane (100 cm^3) was stirred at room temperature for 24 h. The mixture was then washed with saturated aq. $NaHCO_3$ (100 cm^3), dried, and evaporated. The crude product **13a** (6.8 g, 94%), ν_{max}/cm^{-1} 2950–2850, 1730 and 1100; δ_H(60 MHz)* 1.25 (3 H, s), 1.45 (3 H, s), 2.1 (3 H, s, AcO), 1.2–3.0 (8 H, m), 4.6 (2 H, m, 7- and 8-H) and 5.25 (1 H, m, 2-H), was sufficiently pure to use in the next step of the sequence.

To a solution of crude acetate **13a** (6.8 g, 28.3 mmol) in methanol (80 cm^3) was added a small piece of sodium metal. After 30 min at room temperature, the mixture was treated with a small piece of solid carbon dioxide and was then evaporated. The residue was taken up in dichloromethane (100 cm^3), and the solution was washed with saturated aq. $NaHCO_3$ (75 cm^3), dried, and evaporated to give a free alcohol, which was oxidised directly.

To a stirred solution of oxalyl dichloride (4.9 cm^3, 53.8 mmol) in dichloromethane (100 cm^3), at −78 °C, under Ar, was added dropwise a solution of DMSO (8.3 cm^3, 107.4 mmol) in dichloromethane (8 cm^3). After 5 min the above alcohol (5.3 g, 26.8 mmol) as a solution in dichloromethane (6 cm^3) was added dropwise, and, after a further 20 min, triethylamine (21.0 cm^3, 150.0 mmol) was added. After 10 min at −78 °C the mixture was allowed to warm to room temperature and was partitioned between 2 mol dm^3 HCl (100 cm^3), and dichloromethane (2 × 75 cm^3). The organic phase was washed with saturated aq. $NaHCO_3$ (100 cm^3), dried, and evaporated. Crystallisation from light petroleum–ethyl acetate provided the bulk of the product, but more was obtained after flash chromatography [light petroleum–ethyl acetate (6:1)] of the mother liquors. The total yield of *ketone* **12a** was 56% from alcohol **4**; m.p. 85–86 °C (crystals); ν_{max}(Nujol)/cm^{-1} 1730, 1200 and 1040; δ_H(400 MHz) 1.24 (1 H, ddd+, $J_{6\alpha,6b}$ 15, $J_{6\alpha,5}$ 11.5, $J_{6\alpha,7}$ 5.0, 6α-H), 1.29 (3 H, s, Me), 1.45 (3 H, s, Me), 1.86 (1 H, ddd+, $J_{4\alpha,4\beta}$ 13.5, $J_{4\alpha,3\alpha}$ 9.0, $J_{4\alpha,3\beta}$ 2.5, $J_{4\alpha,5}$ ~ 1, 4α-H), 2.05–2.18 (2 H, m, 4β- and 6β-H), 2.22 (1 H, dd, $J_{3\alpha,3\beta}$ 19, $J_{3\alpha,4\alpha}$ 9.0, 3α-H), 2.35 (1 H, ddd+, $J_{3\alpha,3\beta}$ 19, $J_{3\beta,4\beta}$ 10.0, $J_{3\beta,4\alpha}$ 2.5, $J_{1,3\beta}$ 1.5, $J_{3\beta,5}$ 1.0, 3β-H), 2.62 (1 H, ~ br d, $J_{1,5}$ 8.0, $J_{1,8}$ ~ 1, 1-H), 3.14 (1 H, m, 5-H), 4.64 (1 H, ~ t $J_{7,8}$ 5.5, $J_{6\alpha,7}$ 5.0, 7-H) and 4.73 (1 H, ~ d, $J_{7,8}$ 5.5, 8-H); δ_C(100 MHz) 22.5, 24.0, 26.4, 34.9, 36.3, 38.5, 60.8, 81.9, 83.0, 109.8 and 218.4; *m/z* (NH_3, CI) 214 ($[M + NH_4]^+$, 100%), 197 ($[M + H]^+$, 5) and 181 (7) (Found: C, 67.5; H, 8.15. $C_{11}H_{16}O_3$ requires C, 67.3; H, 8.2%).

Attempted Preparation of Compound **12a** via *Osmylation of Ketone* **5**.—A mixture of ketone **5** (100 mg, 0.82 mmol), NMMNO (170 mg, 1.26 mmol), *tert*-butyl alcohol (2.5 cm^3), THF (1 cm^3), water (0.6 cm^3) and osmium tetraoxide (4 drops of a 4% aq. solution) was stirred vigorously for 20 h. The solution was then partitioned between dichloromethane (15 cm^3) and 10% aq. Na_2S (10 cm^3) and the aqueous layer was extracted with dichloromethane (3 × 20 cm^3). The combined organic layers were washed successively with 2 mol dm^{-3} HCl (40 cm^3), and saturated aq. $NaHCO_3$ (30 cm^3), dried, and evaporated. The residue was taken up in dichloromethane (10 cm^3), 2,2-dimethoxypropane (2 cm^3, 16.26 mmol) and PTSA (5 mg, 0.03 mmol) were added, and the mixture was left at room temperature for 10 h. The solution was then washed with saturated aq. $NaHCO_3$ (10 cm^3), dried, and evaporated. TLC examination of the crude product indicated the presence of two components, which were separated by flash chromatography [light petroleum–ethyl acetate (4:1, then 2:1)]. The less polar component (8 mg, 5% from ketone **5**) was ketone **12a** and the major component was the isomeric ketone **11** (33 mg, 21% from ketone **5**); for *ketone* **11**; m.p. 77–78 °C (crystals); ν_{max}(Nujol)/cm^{-1} 1740 and 1100; δ_H(400 MHz) 1.26 (3 H, s, Me), 1.45 (3 H, s, Me), 1.99–2.20 (4 H, m), 2.21–2.28 (1 H, m, 3α-H), 2.40 (1 H, m, 3β-H), 2.72 (1 H, ~ t+, $J_{1,8}$ 7.5, $J_{1,5}$ 7.5, 1-H), 2.79 (1 H, m, 5-H), 4.80 (1 H, ~ dt, $J_{7,8}$ 5.5, $J_{6,7}$ 5.5, $J_{6,7}$ 2.0, $J_{5,7}$ 1.0, 7-H) and 4.87 (1 H, dd, $J_{1,8}$ 7.5, $J_{7,8}$ 5.5, $J_{5,8}$ ~ 1, 8-H); positive NOEs were observed between 1-H and 8-H and between 7-H and 5-H; *m/z* (CH_4, CI) 197 ($[M + H]^+$, 100%), 196 (3.2) and 181 (22) (Found: $[M + H]^+$, 197.1183. $C_{11}H_{17}O_3$ requires *m/z*, 197.1177. Found: C, 67.6; H, 8.05. $C_{11}H_{16}O_3$ requires C, 67.3; H, 8.2%).

If, in the above preparation, the reaction to form the acetonide was left for a prolonged period (3 days), then in addition to ketones **11** and **12a** a third product was isolated,

* Numbering follows that of the ketone **12a**.

which was assigned as the dimethyl acetal of ketone **11**, (±)-exo,exo-7,8-(*isopropylidenedioxy*)-2,2-*dimethoxy*-cis-*bicyclo*-[3.3.0]*octane*; ν_{max}/cm^{-1} 2950–2850 and 1050; δ_H(60 MHz) 1.25 (3 H, s), 1.45 (3 H, s), 1.5–3.0 (8 H, m), 3.25 (6 H, s, MeO × 2) and 5.75 (2 H, m, 7- and 8-H); *m/z* (CH_4, CI) 243 ($[M + H]^+$, 3%), 227 (29), 211 (100), 167 (30) and 153 (68) [Found: (EI) M^+, 242.1498. $C_{13}H_{22}O_4$ requires M, 242.1518].

(±)-exo,exo-7,8-*Bis*(tert-*butyldimethylsiloxy*)-cis-*bicyclo*-[3.3.0]*octan-2-one* **12b**.—A solution of the diol **9a** (1.0 g, 5.0 mmol), imidazole (1.4 g, 20.6 mmol) and *tert*-butyldimethylsilyl chloride (TBDMSCl) (2.3 g, 15.3 mmol), in dry dimethylformamide (DMF) (40 cm^3) was stirred at room temperature for 24 h. The mixture was then extracted with pentane (2 × 50 cm^3) and the extracts were dried, and concentrated by rotary evaporation. The crude silyl ether **13b** (2.1 g, 98%) was sufficiently pure to be used in the next step, ν_{max}/cm^{-1} 1740 and 1380; δ_H(60 MHz; standard Me_2SiBu^t) 0.0 (12 H, s), 0.9 (18 H, s), 2.0 (3 H, s, Ac), 1.0–2.4 (6 H, m), 2.4–2.7 (2 H, m), 3.7–4.2 (2 H, m, 7- and 8-H) and 5.15 (1 H, m, 2-H); *m/z* (CH_4, CI) 429 ($[M + H]^+$, 16%), 413 (36), 371 (70), 369 (35), 297 (95) and 237 (100).

To a solution of crude silyl ether **13b** from above (2.1 g, 4.91 mmol) in methanol (80 cm^3) was added a small piece of sodium metal. After the mixture had been kept for 30 min at room temperature, a small piece of solid carbon dioxide was added and the mixture was then evaporated. The residue was taken up in dichloromethane (100 cm^3), and the solution was washed with saturated aq. $NaHCO_3$ (75 cm^3), dried, and the solvent was evaporated off to give a free alcohol (1.85 g, 98%), which was oxidised directly.

To a stirred solution of oxalyl dichloride (1.2 cm^3, 13.2 mmol) in dry dichloromethane (35 cm^3) at −78 °C was added a solution of DMSO (2.0 cm^3, 25.9 mmol) in dichloromethane (2 cm^3) dropwise. After 5 min a solution of the above crude alcohol (1.85 g, 4.8 mmol) in dichloromethane (4 cm^3) was added dropwise and, after a further 20 min, triethylamine (4.0 cm^3, 28.6 mmol) was added. After 10 min at −78 °C the mixture was allowed to warm to room temperature and was then partitioned between 2 mol dm^{-3} HCl (50 cm^3) and dichloromethane (2 × 50 cm^3). The organic layer was washed with saturated aq. $NaHCO_3$ (100 cm^3), dried, and the solvent was evaporated off. Purification by flash chromatography [light petroleum–ethyl acetate (25:1)] provided ketone **12b** (1.75 g, 91% from the diol **9a**), ν_{max}/cm^{-1} 1740 and 1260; δ_H(60 MHz; Me_2SiBu^t) 0.0 (6 H, s), 0.05 (6 H, s), 0.8 (18 H, s), 1.3–2.5 (7 H, m), 2.7–3.3 (1 H, m), 3.70 (1 H, m, 7-H) and 4.00 (1 H, m, 8-H); *m/z* (CH_4, CI) 385 ($[M + H]^+$, 14%), 369 (M − 15, 42), 327 (58) and 253 (100) {Found: (EI) $[M - CH_3]^+$, 369.2300. $C_{19}H_{37}O_3Si_2$ requires *m/z*, 369.2281}.

(±)-exo,exo-2,3-*Bis*(*benzyloxy*)-endo-8-(tert-*butyldimethylsiloxy*)-cis-*bicyclo*[3.3.0]*octane* **13c**.—A solution of *cis*-bicyclo-[3.3.0]oct-7-en-2-ol **4** (1.0 g, 8.06 mmol), imidazole (1.1 g, 16.16 mmol) and TBDMSCl (1.82 g, 12.07 mmol) in dry DMF (35 cm^3) was stirred at room temperature for 24 h. The mixture was then extracted with pentane (2 × 40 cm^3), the organic layers were dried, and the solvent was evaporated off. The crude silyl ether **7b** (1.91 g, quantitative), a clear liquid, was used directly in the next step; ν_{max}/cm^{-1} 3050, 1460 and 1250; δ_H(60 MHz; standard Me_2SiBu^t) 0.0 (6 H, s), 0.85 (9 H, s), 1.3–2.25 (4 H, m), 2.25–3.25 (4 H, m), 4.10 (1 H, m, 2-H) and 5.3–5.8 (2 H, m, 7- and 8-H).

A mixture of crude silyl ether **7b** from above (1.91 g, 8.03 mmol), NMMNO (1.60 g, 11.84 mmol), *tert*-butyl alcohol (10 cm^3), THF (3 cm^3), water (2.5 cm^3) and osmium tetraoxide (20 drops of a 4% aq. solution) was stirred vigorously for 20 h. The solution was then partitioned between dichloromethane (3 × 50 cm^3) and 10% aq. Na_2S solution (40 cm^3) and the combined organic layers were washed successively with 2 mol dm^{-3} HCl (50 cm^3) and aq. Na_2CO_3, dried, and evaporated. The crude diol (±)-*endo*-8-(*tert*-butyldimethylsiloxy)-*cis*-bicyclo[3.3.0]octane-*cis*,*exo*-2,3-diol **9c** (1.8 g, 82%), was clean enough to be used in the next step; ν_{max}/cm^{-1} 3400 and 1260; δ_H(60 MHz; standard Me_2SiBu^t) 0.0 (6 H, s), 0.85 (9 H, s), 1.3–2.0 (5 H, m), 2.0–3.0 (5 H, m) and 3.9–4.35 (3 H, m, 2-, 3- and 8-H).

To a stirred suspension of sodium hydride (60% in mineral oil; 1.2 g, 30.0 mmol) in dry THF (50 cm^3) at room temperature was added dropwise a solution of the crude diol **9c** (1.8 g, 6.62 mmol), in THF (10 cm^3). After evolution of gas had ceased (1 h), benzyl bromide (2.9 cm^3, 24.4 mmol) was added and the mixture was stirred for 15 h. Water was then added cautiously until the mixture became homogeneous and the bulk of the solvent was then evaporated off. The residue was taken up in dichloromethane (100 cm^3), and the solution was washed with saturated aq. $NaHCO_3$ (60 cm^3), dried, and evaporated. Purification by flash chromatography [light petroleum–ethyl acetate (50:1, then 19:1)] provided *bis-benzyl ether* **13c** (2.93 g, 80% from the alcohol **4**), ν_{max}/cm^{-1} 3075, 3050, 1460 and 700; δ_H(60 MHz; standard Me_2SiBu^t) 0.0 (3 H, s), 0.05 (3 H, s), 0.85 (9 H, s), 1.3–2.5 (6 H, m), 2.5–2.9 (2 H, m), 3.8–4.35 (3 H, m), 4.55 (4 H, m, $PhCH_2O$ × 2) and 7.3 (10 H, m, 2 × Ph); *m/z* (CH_4, CI) 453 ($[M + H]^+$, 2%), 345 (10), 237 (6), 239 (12) and 91 (100) (Found: $[M + H]^+$, 453.2828. $C_{28}H_{41}O_3Si$ requires *m/z*, 453.2825).

(±)-exo,exo-7,8-*Bis*(*benzyloxy*)-cis-*bicyclo*[3.3.0]*octan*-2-*one* **12c**.—A solution of the bis-benzyl ether **13c** (2.93 g, 6.48 mmol) and tetrabutylammonium fluoride (1 mol dm^{-3} in THF; 16.0 cm^3, 16.0 mmol) in dry THF (40 cm^3) at room temperature was stirred for 15 h and the solvent was then evaporated off. The residue was taken up in dichloromethane (80 cm^3), and the solution was washed with saturated aq. $NaHCO_3$ (60 cm^3), dried, and the solvent was evaporated off. The residue was dissolved in diethyl ether and passed through a small pad of silica gel, to give a crude alcohol (2.15 g, 98%), which was oxidised without further purification; ν_{max}/cm^{-1} 3600–3150, 3075, 3050, 1460 and 700; δ_H(60 MHz) 1.3–2.5 (7 H, m), 2.5–2.8 (2 H, m), 3.9–4.3 (3 H, m, 2-, 7- and 8-H), 4.45 (4 H, br s, $PhCH_2O$ × 2) and 7.25 (10 H, m, 2 × Ph); *m/z* (NH_3, CI) 356 ($[M + NH_4]^+$, 100%), 339 ($[M + H]^+$, 5), 108 (25) and 91 (18) (Found: $[M + NH_4]^+$, 356.2230. $C_{22}H_{30}NO_3$ requires *m/z*, 356.2226).

To a stirred solution of oxalyl dichloride (1.2 cm^3, 13.2 mmol) in dry dichloromethane (40 cm^3) at −78 °C was added a solution of DMSO (2.0 cm^3, 25.9 mmol) in dichloromethane (2 cm^3) dropwise. After 5 min a solution of the above alcohol (2.15 g, 6.36 mmol) in dichloromethane (4 cm^3) was added dropwise and, after a further 20 min, triethylamine (4.0 cm^3, 28.6 mmol) was added. After 10 min at −78 °C the mixture was allowed to warm to room temperature, then was partitioned between 2 mol dm^{-3} HCl (50 cm^3) and dichloromethane (2 × 50 cm^3). The organic layer was washed with saturated aq. $NaHCO_3$ (100 cm^3), dried, and evaporated. Purification by flash chromatography [light petroleum–ethyl acetate (9:1)] provided ketone **12c** (1.94 g, 90% from the bis-benzyl ether **13c**), ν_{max}/cm^{-1} 3075, 3050, 1740 and 700; δ_H(300 MHz) 1.53–1.64 (2 H, m), 2.05–2.32 (4 H, m), 2.86 (1 H, dd, $J_{1,5}$ 9.5, $J_{1,8}$ 3.0, 1-H), 3.06 (1 H, m, 5-H), 3.78 (1 H, m, 7-H), 3.95 (1 H, ~t, *J* 3.5, 3.0, 8-H), 4.49 (1 H, d, *J* 12.0, CH_2Ph), 4.58 (1 H, d, *J* 12.0, CH_2Ph), 4.62 (1 H, d, *J* 12.0, CH_2Ph), 4.70 (1 H, d, *J* 12.0, CH_2Ph) and 7.23–7.40 (10 H, m, 2 × Ph); δ_C(75 MHz) 26.7, 36.0, 36.2, 37.8, 55.8, 71.5, 71.7, 80.6, 82.1, 127.4, 127.5, 127.7, 128.2, 138.3, 138.4 and 219.3; *m/z* (NH_3, CI), 354 ($[M + NH_4]^+$, 100%), 337 ($[M + H]^+$, 8.3), 245 (20), 198 (13) and 91 (30)

(Found: $[M + NH_4]^+$, 354.2061. $C_{22}H_{28}NO_3$ requires *m/z*, 354.2069).

(±)-exo,exo-7,8-(*Isopropylidenedioxy*)-cis-*bicyclo*[3.3.0]*oct*-3-*en*-2-*one* **17a**.—*Method A*. A solution of the ketone **12a** (40 mg, 0.20 mmol) and benzeneselenenyl chloride (47 mg, 0.24 mmol) in ethyl acetate (5 cm^3) was stirred at room temperature until no starting material remained (TLC). The solution was then extracted with water (5 cm^3), the organic layer was diluted with THF (3 cm^3), and the solution was stirred vigorously with 30% hydrogen peroxide (0.57 mmol) while cooled with ice. After 4 h, saturated aq. $Na_2S_2O_5$ (10 cm^3) was added and the mixture was extracted with ethyl acetate (2 × 10 cm^3). The extract was washed with saturated aq. $NaHCO_3$ (10 cm^3), dried, and evaporated. Flash chromatography [light petroleum–ethyl acetate (5:1)] provided enone **17a** (15 mg, 38%), m.p. 56–57 °C (crystals); ν_{max}(Nujol)/cm^{-1} 1700 and 1575; δ_H(400 MHz) 1.31 (3 H, s, Me), 1.50 (3 H, s, Me), 1.67 (1 H, m, 6α-H), 2.28 (1 H, ddd, $J_{6\alpha,6\beta}$ 14.0, $J_{5,6\beta}$ 9.0, $J_{6\beta,7}$ 3.0, 6β-H), 2.96 (1 H, dd, $J_{1,5}$ 6.5, $J_{1,8}$ < 1.0, 1-H), 3.70 (1 H, m, 5-H), 4.61–4.66 (2 H, m, 8- and 7-H), 6.02 (1 H, dd, $J_{3,4}$ 6.0, $J_{3,5}$ 2.0, 3-H) and 7.67 (1 H, dd, $J_{3,4}$ 6.0, $J_{4,5}$ 3.0, 4-H); *m/z* 212 (NH_3, CI) ($[M + NH_4]^+$, 100) and 195 ($[M + H]^+$, 14) (Found: $[M + NH_4]^+$, 212.1284. $C_{11}H_{18}NO_3$ requires *m/z*, 211.1287).

Method B. To a stirred solution of diisopropylamine (170 mm^3, 1.2 mmol) in dry THF (15 cm^3) at −78 °C was added butyllithium (1.60 mol dm^{-3} in hexane; 700 mm^3, 1.12 mmol) and, after 15 min, ketone **12a** (145 mg, 0.74 mmol) was also added. After 30 min, freshly distilled trimethylsilyl chloride (158 mm^3, 1.24 mmol) was added and, after a further 15 min, the mixture was allowed to warm to room temperature, was evaporated, and the residue was taken up in dichloromethane (30 cm^3). After the solution had been washed with saturated aq. $NaHCO_3$ (20 cm^3), dried and evaporated, silyl ether **15** (190 mg) was obtained and was used without purification in the next stage.

A solution of palladium(II) acetate (80 mg, 0.35 mmol), *p*-benzoquinone (38 mg, 0.35 mmol) and the above silyl ether **15** in dry acetonitrile (4 cm^3) was stirred at room temperature. After 3 h very little reaction had occurred (TLC) and more palladium(II) acetate (10 mg, 0.04 mmol) was added. The mixture was then heated at reflux for 14 h, the solvent then evaporated off, and purification by flash chromatography [light petroleum–ethyl acetate (9:1, then 4:1)] provided the enone **17a** (52 mg, 36%) and ketone **12a** (42 mg, 29% recovery).

(±)-exo,exo-7,8-*Bis*-(tert-*butyldimethylsiloxy*)-cis-*bicyclo*-[3.3.0]*oct*-3-*en*-2-*one* **17b**.—The method was the same as that described for preparation of compound **17a** (Method A) above. Ketone **12b** (85 mg, 0.22 mmol) reacted with benzeneselenenyl chloride (51 mg, 0.27 mmol), followed by oxidation with 30% hydrogen peroxide (0.60 mmol), to provide enone **17b** (36 mg, 42%), ν_{max}/cm^{-1} 2950, 1700, 1580 and 1260; δ_H(300 MHz) 0.03 (6 H, s, 2 × SiMe), 0.08 (3 H, s, SiMe), 0.11 (3 H, s, SiMe), 0.83 (9 H, s, $SiCMe_3$), 0.88 (9 H, s, $SiCMe_3$), 1.57 (1 H, m, 6α-H), 2.09 (1 H, ~q, $J_{6\alpha,6\beta}$ 11.0, $J_{6\beta,5}$ 10.0, $J_{6\beta,7}$ 10.0, 6β-H), 2.61 (1 H, d, $J_{1,5}$ 6.0, 1-H), 3.34 (1 H, m, 5-H), 3.59 (1 H, ddd, $J_{6\beta,7}$ 10.0, $J_{6\alpha,7}$ 6.0, $J_{7,8}$ 3.5, 7-H), 4.05 (1 H, d, $J_{7,8}$ 3.5, 8-H), 6.07 (1 H, dd, $J_{3,4}$ 5.5, $J_{3,5}$ 1.5, 3-H) and 5.99 (1 H, dd, $J_{3,4}$ 5.5, $J_{4,5}$ 3.0, 4-H); *m/z* (NH_3, CI) 400 ($[M + NH_4]^+$, 60%), 383 ($[M + H]^+$, 100) and 298 (20) (Found: $[M + H]^+$, 383.2438. $C_{20}H_{39}O_3Si_2$ requires *m/z*, 383.2438).

(±)-exo,exo-7,8-*Bis*(*benzyloxy*)-cis-*bicyclo*[3.3.0]*oct*-3-*en*-2-*one* **17c**.—A solution of the ketone **12c** (110 mg, 0.33 mmol) and benzeneselenenyl chloride (70 mg, 0.37 mmol), in ethyl acetate (8 cm^3) was stirred at room temperature. TLC examination after 1 h showed ~ 50% conversion, and more benzeneselenenyl chloride (65 mg, 0.34 mmol) was added. After a further 2 h the solvent was evaporated off and the residue was taken up in dichloromethane (8 cm^3). MCPBA (85%; 165 mg, 0.81 mmol) was added at 0 °C, and after being stirred for 30 min at 0 °C, then for 1 h at room temperature, the mixture was diluted with dichloromethane (30 cm^3), washed successively with saturated aq. $Na_2S_2O_5$ (20 cm^3), and saturated aq. $NaHCO_3$ (20 cm^3), dried, and evaporated. Purification by flash chromatography [light petroleum–ethyl acetate (15:1, then 7:1)] provided enone **17c** (17 mg, 16%), ν_{max}/cm^{-1} 3075, 3050, 1710, 1595 and 700; δ_H(300 MHz) 1.82 (1 H, ddd, $J_{6\alpha,6\beta}$ 12.5, $J_{6\alpha,7}$ 6.0, $J_{6\alpha,5}$ 2.0, 6α-H), 2.30 (1 H, ~q, $J_{6\alpha,6\beta}$ 12.5, $J_{6\beta,5}$ 10.5, $J_{6\beta,7}$ 10.0, 6β-H), 2.93 (1 H, dd, $J_{1,5}$ 6.0, $J_{1,8}$ 1.5, 1-H), 3.44 (1 H, m, 5-H), 3.59 (1 H, ddd, $J_{6\beta,7}$ 10.0, $J_{6\alpha,7}$ 6.0, $J_{7,8}$ 4.0, 7-H), 4.02 (1 H, dd, $J_{7,8}$ 4.0, $J_{1,8}$ 1.5, 8-H), 4.37 (d, *J* 12.0, CH_2Ph), 4.49 (d, *J* 12.0, CH_2Ph), 4.67 (d, *J* 12.0, CH_2Ph), 4.73 (d, *J* 12.0, CH_2Ph), 6.08 (1 H, dd, $J_{3,4}$ 5.5, $J_{3,5}$ 1.5, 3-H), 7.20–7.45 (10 H, m, 2 × Ph) and 7.60 (1 H, dd, $J_{3,4}$ 5.5, $J_{4,5}$ 3.0, 4-H); *m/z* (NH_3, CI) 352 ($[M + NH_4]^+$, 100%), 335 ($[M + H]^+$, 38), 108 (14) and 91 (20) (Found: $[M + NH_4]^+$, 352.1910. $C_{22}H_{26}NO_3$ requires *m/z*, 352.1912) and chloro enone **18** (65 mg, 54%), ν_{max}/cm^{-1} 3070, 3050, 1725, 1595 and 700; δ_H(90 MHz) 1.55–1.90 (1 H, ddd, *J* 13, 6, 3, 6α-H), 2.05–2.50 (1 H, dt, *J* 13, 10, 6β-H), 3.05 (1 H, dd, *J* 6, 2, 1-H), 3.35 (1 H, m, 5-H), 3.65 (1 H, m, 7-H), 4.05 (1 H, dd, *J* 4, 2, 8-H), 4.45–4.7 (4 H, m, 2 × CH_2Ph), 7.25 (10 H, m, 2 × Ph) and 7.44 (1 H, d, $J_{4,5}$ 3, 4-H); *m/z* (NH_3, CI) 388 {$[M(^{37}Cl) + NH_4]^+$, 19%}, 386 {$[M(^{35}Cl) + NH_4]^+$, 52}, 108 (48) and 91 (100) (Found: $[M + NH_4^+]$, 386.1521. $C_{22}H_{25}{}^{35}ClNO_3$ requires *m/z*, 386.1523).

(±)-exo,exo-2,3-(*Isopropylidenedioxy*)-8-*methylene*-cis-*bicyclo*[3.3.0]*octane* **19**.—To a suspension of methyltriphenylphosphonium bromide (140 mg, 0.39 mmol) in dry THF (10 cm^3) at 0 °C was added sodium bis(trimethylsilyl)amide (1 mol dm^{-3} in THF; 0.37 cm^{-3}, 0.37 mmol). The mixture was stirred for 20 min, by which time a yellow-orange solution was observed, and a solution of ketone **12a** (50 mg, 0.26 mmol) in THF (1 cm^3) was then added dropwise. After 30 min the mixture was allowed to warm to room temperature for a further 1.5 h, by which time the colour of the mixture had changed to orange and sodium bromide had been deposited. After dilution with dichloromethane (40 cm^3), the mixture was washed with water (20 cm^3), dried, and evaporated (water-bath temperature < 30 °C). *Alkene* **19** (20 mg, 40%) was isolated by flash chromatography [light petroleum–ethyl acetate (49:1 then 30:1)], ν_{max}/cm^{-1} 3075, 1650 and 1440; δ_H(60 MHz) 1.25 (3 H, s, Me), 1.4 (3 H, s, Me), 1.0–2.8 (6 H, m), 2.95 (2 H, m), 4.4–4.7 (2 H, m, 2- and 3-H) and 5.0 (2 H, m, =CH_2); *m/z* (NH_3, CI) 212 ($[M + NH_4]^+$, 22%) and 195 ($[M + H]^+$, 100) (Found: $[M + H]^+$, 195.1380. $C_{12}H_{19}O_2$ requires *m/z*, 194.1385).

(±)-exo,exo-2,3-(*Isopropylidenedioxy*)-8-(*methoxymethylene*)-cis-*bicyclo*[3.3.0]*octane* **20**.—To a stirred suspension of (methoxymethyl)triphenylphosphonium chloride (1.05 g, 3.06 mmol) in dry THF (30 cm^3) at 0 °C was added sodium bis(trimethylsilyl)amide (1 mol dm^{-3} in THF; 2.85 cm^3, 2.85 mmol). After 10 min the mixture was warmed to room temperature for 10 min, then was re-cooled to 0 °C. A solution of ketone **12a** (317 mg, 1.62 mmol) in THF (2 cm^3) was then added dropwise to the deep red ylide and after 30 min at 0 °C the mixture was warmed to room temperature for 1.5 h. After filtration, the filtrate was diluted with dichloromethane (150 cm^3), washed with water (80 cm^3), dried, and evaporated (water-bath temperature < 30 °C). Flash chromatography [light petroleum–ethyl acetate (30:1, then 5:1)] provided starting ketone **12a** (16 mg, 5% recovery) and *enol ether* **20** (290 mg, 52%), ν_{max}/cm^{-1} 3050, 1690 and 1380; δ_H(400 MHz) 1.29 (3 H/2, s, Me), 1.30 (3 H/2, s, Me), 1.32–1.42 (1 H, m), 1.46 (3 H/2, s,

Me), 1.47 (3 H/2, s, Me), 1.50–1.75 (1 H, m) 1.95 (1 H, m,), 2.15–2.40 (3 H, m), 2.8–3.05 (2 H, m, 1- and 5-H), 3.59 (3 H, 2 × s, MeO), 4.43 (H/2, d, *J* 5.5, 2-H), 4.63–4.71 (3 H/2, m, 3-H and 2-H), 5.95 (H/2, q, *J* 2.5, =C*H*OMe) and 5.98 (H/2, m, =C*H*OMe); *m/z* (NH_3, CI) 242 ($[M + NH_4]^+$, 15%) and 225 ($[M + H]^+$, 100) (Found: $[M + H]^+$, 225.1490. $C_{13}H_{21}O_3$ requires *m/z*, 225.1491).

Oxidation of the Enol Ether **20** *with MCPBA.*—A suspension of the enol ether **20** (47 mg, 0.21 mmol), sodium carbonate (60 mg, 0.57 mmol) and MCPBA (85%; 60 mg, 0.29 mmol) in dichloromethane (10 cm^3) was stirred for 1 h. The mixture was then diluted with dichloromethane (30 cm^3), washed successively with saturated aq $Na_2S_2O_5$ (30 cm^3) and saturated aq. $NaHCO_3$ (30 cm^3), dried, and evaporated. Purification by flash chromatography [light petroleum–ethyl acetate (9:1)] provided ester **21** as two separable isomers; less polar component (34 mg, 41%), ν_{max}/cm^{-1} 3600–3300, 3075, 1725 and 1600; δ_H(60 MHz) 1.2 (3 H, s, Me), 1.4 (3 H, s, Me), 1.3–3.25 (9 H, m), 3.55 (3 H, s, MeO), 4.7 (2 H, m), 5.95 [1 H, s, C*H*(OMe)OCOAr], 7.4 (2 H, m) and 8.05 (2 H, m); more polar component (14 mg, 17%), ν_{max}/cm^{-1} 3600–3300, 3050, 1720 and 1580; δ_H(60 MHz) 1.2 (3 H, s, Me), 1.3 (3 H, s, Me), 1.3–3.2 (9 H, m), 3.5 (3 H, s, MeO), 4.55 (2 H, m), 6.1 [1 H, s, C*H*(OMe)OCOAr], 7.45 (2 H, m) and 8.05 (2 H, m).

(±)-exo,exo-7,8-(*Isopropylidenedioxy*)-cis-*bicyclo*[3.3.0]*oct*-2-*ene*-2-*carbaldehyde* **22a** *and* (±)-exo,exo-7,8-(*Isopropylidenedioxy*)*bicyclo*[3.3.0]*oct*-1-*ene*-2-*carbaldehyde* **23a**.—A water-cooled solution of enol ether **20** (190 mg, 0.85 mmol), MTPP (~5 mg) and pyridine (1 drop) in dry benzene (10 cm^3) was irradiated with a tungsten-filament lamp (150 W, 240 V), while oxygen was bubbled through, until no starting material remained, as indicated by TLC. Triphenylphosphine (224 mg, 0.85 mmol) was then added and the mixture was stirred at room temperature for 30 min. The solvent was evaporated off and two isomeric compounds were separated by flash chromatography [light petroleum–ethyl acetate (30:1, 10:1, then 6:1); compound **22a** (104 mg, 59%), ν_{max}/cm^{-1} 3050, 2725, 1680, 1610 and 1380; δ_H(400 MHz) 1.30 (3 H, s, Me), 1.36 (1 H, m, 6α-H), 1.47 (3 H, s, Me), 2.23 (1 H, dd, $J_{6\alpha,6\beta}$ 15.0, $J_{5,6\beta}$ 7.5, 6β-H), 2.37 (1 H, ~t, $J_{4\alpha,4\beta}$ 19.5, $J_{3,4\alpha}$ 2.5, $J_{4\alpha,5}$ 2.5, 4α-H), 2.71 (1 H, dddd, $J_{4\alpha,4\beta}$ 19.5, $J_{5,4\beta}$ 7.5, $J_{3,4\beta}$ 2.5, 4β-H), 3.12 (1 H, m, 5-H), 3.35 (1 H, m, 1-H), 4.56 (1 H, ~t, $J_{7,8}$ 5.0, $J_{6\alpha,7}$ 5.0, 7-H), 4.79 (1 H, ~d, $J_{7,8}$ 5.0, 8-H), 6.77 (1 H, ~q, $J_{3,4\alpha}$ 2.5, $J_{3,4\beta}$ 2.5, $J_{3,1}$ 2.5, 3-H) and 9.83 (1 H, s, CHO); *m/z* (NH_3, CI) 226 ($[M + NH_4]$, 100%) and 209 ($[M + H]^+$, 10); and compound **23a** (53 mg, 30%), ν_{max}/cm^{-1} 2720, 1680 and 1380; δ_H(90 MHz) 1.32 (3 H, s, Me), 1.43 (3 H, s, Me), 1.30–3.50 (6 H, m), 4.64 (1 H, m), 4.95 (1 H, m), 5.10 (1 H, m) and 9.80 (1 H, m, CHO); *m/z* (NH_3, CI) 236 ($[M + NH_4]^+$, 100%) and 209 ($[M + H]^+$, 10).

Attempted Deconjugation of the Enal **22a**.—To a stirred solution of diisopropylamine (73 mm^3, 0.52 mmol) in dry THF (15 cm^3) at −78 °C was added butyllithium (1.32 mol dm^{-3} in hexane; 0.3 cm^3, 0.40 mmol) and, after 10 min, a solution of enal **22a** (80 mg, 0.38 mmol) in THF (2 cm^3) was added. After a further 50 min at −78 °C, the mixture was treated with saturated aq. NH_4Cl (1 cm^3) and was then allowed to warm to room temperature. The bulk of the solvent was evaporated off, the mixture was diluted with dichloromethane (20 cm^3), and the solution was washed successively with 1 mol dm^{-3} HCl (15 cm^3) and saturated aq. $NaHCO_3$ (15 cm^3). After the solution had been dried and evaporated flash chromatography [light petroleum–ethyl acetate (6:1, then 2:1)] provided starting enal **22a** (28 mg, 35% recovery) and the alcohol **25a** (24 mg, 30%), ν_{max}/cm^{-1} 3050–3200, 3050 and 1440; δ_H(60 MHz) 1.3 (3 H, s, Me), 1.5 (3 H, s, Me), 1.55–2.5 (5 H, m), 3.1 (2 H, m), 4.3 (2 H, m, CH_2OH), 4.75 (2 H, m, 7- and 8-H) and 5.25 (1 H, m, 3-H); *m/z* (EI) 210 (M^+, 3.3%), 195 (42) and 96 (100) (Found: M^+, 210.1279. $C_{12}H_{18}O_3$ requires M, 210.1256).

Conversion of Enal **22a** *to a Mixture of Alcohols* **28a**, **29a** *and* **25a**.—To a stirred solution of the enal **22a** (800 mg, 3.85 mmol) in dry THF (70 cm^3) at 0 °C was added potassium *tert*-butoxide (1.1 mol dm^{-3} in Bu^{t}OH; 8.7 cm^3, 9.57 mmol). After 30 min the mixture was allowed to reach room temperature. After 2.5 h it was re-cooled to 0 °C before acetic anhydride (1.5 cm^3, 15.90 mmol) was added. After 15 min, the mixture was allowed to warm to room temperature, the solvent was evaporated off, and the residue was diluted with dichloromethane (100 cm^3). The resultant solution was washed with saturated aq. $NaHCO_3$ (70 cm^3), dried, and evaporated. Enol acetate **26a** was not very stable and was used without further purification in the next step; δ_H(60 MHz) 1.3 (3 H, s, Me), 1.5 (3 H, s, Me), 1.5–2.25 (2 H, m), 2.15 (3 H, s, AcO), 3.5 (2 H, m, 1- and 5-H), 4.5 (2 H, m, 7- and 8-H), 5.9 (2 H, br s, 3- and 4-H) and 7.2 (1 H br s, =C*H*OAc).

To a stirred solution of the crude enol acetate **26a** in ethanol (60 cm^3) was added sodium borohydride (700 mg, 18.50 mmol). When no starting material remained (TLC) the solvent was evaporated off, the residue was taken up in dichloromethane (60 cm^3), and the mixture was washed successively with 2 mol dm^{-3} HCl (40 cm^3) and saturated aq. $NaHCO_3$ (40 cm^3), dried, and evaporated. Purification by flash chromatography [light petroleum–ethyl acetate (6:1, then 2:1)] provided ester **25b** (35 mg, 4% from enal **22a**) and an inseparable mixture of allylic and homoallylic alcohols **28a**, **29a** and **25a** (280 mg, 35% from enal **22a**), ν_{max}/cm^{-1} 3600–3200, 3050, 1380 and 1370; δ_H(90 MHz) 1.3 (3 H, s, Me), 1.5 (3 H, s, Me), 3.2 (1 H, m), 3.7 (1 H, m), 4.25 (2 H, m, CH_2OH) and 5.5–5.9 (>2 H, m, =CH) (2 H, m); *m/z* (CH_4, CI) 211 ($[M + H]^+$, 55%), 192 (45), 153 (60) and 135 (100) [Found: (EI) M^+, 210.1279. $C_{12}H_{18}O_3$ requires M, 210.1259]. The three isomeric alcohols were separated by GC–MS (BPI column, 50–200 °C, ramp 10 °C min^{-1}).

Epoxidation and Oxidation of Unsaturated Alcohols **28a**, **29a** *and* **25a** *followed by Base-mediated Epoxide Opening.*—A suspension of the mixture of alcohols **18a**, **29a** and **25a** (200 mg, 0.95 mmol), sodium hydrogen carbonate (350 mg, 4.17 mmol) and MCPBA (85%; 390 mg, 1.92 mmol) in dichloromethane (30 cm^3), was stirred for 4 h. The mixture was then diluted with dichloromethane (20 cm^3), washed successively with saturated aq. $Na_2S_2O_5$ (40 cm^3) and saturated aq. $NaHCO_3$ (40 cm^3), dried, and evaporated. The crude epoxide mixture thus produced was oxidised without further purification.

To a stirred solution of oxalyl dichloride (200 mm^3, 2.20 mmol) in dry dichloromethane (25 cm^3) at −78 °C was added dropwise a solution of DMSO (340 mm^3, 4.40 mmol) in dichloromethane (2 cm^3). After 5 min, a solution of the above epoxide mixture in dichloromethane (2 cm^3) was added and, after a further 20 min, triethylamine (1.4 cm^3, 10.0 mmol was added). After 10 min at −78 °C the mixture was allowed to warm to room temperature, then was partioned between 2 mol dm^{-3} HCl (35 cm^3) and dichloromethane (2 × 25 cm^3). The organic phase was washed with saturated aq. $NaHCO_3$ (35 cm^3), dried, and evaporated. A solution of the crude mixture from above and 1,5-diazabicyclo[5.4.0]undec-7-ene (240 mg, 1.58 mmol) in dichloromethane (25 cm^3) was stirred at room temperature for 2 h. It was then washed successively with 2 mol dm^{-3} HCl (35 cm^3) and saturated aq. $NaHCO_3$ (35 cm^3), dried, and evaporated. Purification by flash chromatography [light petroleum–ethyl acetate (6:1, then 1:2)] provided (±)-*exo*-2,3-epoxy-*exo*,*exo*-7,8-(isopropylidenedioxy)-*cis*-bicyclo[3.3.0]-octane-2-carbaldehyde **34** (108 mg, 51%), ν_{max}/cm^{-1} 1720 and

1430; δ_H(90 MHz) 1.26 (3 H, s, Me), 1.43 (3 H, s, Me), 1.6–2.2 (4 H, m), 2.8–3.2 (2 H, m), 3.86 (1 H, br s, 3-H), 4.65 (2 H, m, 7- and 8-H) and 9.2 (1 H, s, CHO); *m/z* (CH_4, CI) 225 ([M + H]$^+$, 93%), 209 (46), 195 (29), 167 (100) and 149 (74) {Found: (EI) [M − CH_3]$^+$, 209.0816. $C_{11}H_{13}O_4$ requires *m/z*, 209.0814}; and a mixture of the 4-*endo* and 4-*exo* alcohols **33** (with **27**) (71 mg, 33%), ν_{max}/cm^{-1} 3600–3200, 3050, 2800, 2710, 1680, 1610 and 1200; δ_H(90 MHz) 1.27 (3 H, s, Me), 1.45 (3 H, s, Me), 1.5–2.4 (3 H, m), 2.9–3.6 (2 H, m), 4.63 (2 H, m), 5.2–4.8 (1 H, m), 6.7 (1 H, m, 3-H) 9.82 ($\frac{1}{3}$ H, s, CHO) and 9.90 ($\frac{2}{3}$ H, s, CHO); *m/z* (CH_4, CI) 225 ([M + H]$^+$, 70%), 209 (28), 207 (59) and 59 (100) {Found: (EI) [M − CH_3]$^+$ 209.0793. $C_{11}H_{13}O_4$ requires *m/z*, 209.0814}.

(±)-4-(*Benzoyloxy*)-2,3-*epoxy*-2-(*hydroxymethyl*)-exo,exo-7,8-(*isopropylidenedioxy*)-cis-*bicyclo*[3.3.0]*octanes* **35**.—A mixture of the hydroxy enals **33** (18 mg, 0.08 mmol), DMAP (20 mg, 0.16 mmol) and benzoyl chloride (20 mm^3, 0.17 mmol) in dichloromethane (5 cm^3) was stirred for 24 h. The solution was then diluted with dichloromethane (20 cm^3) and washed successively with 1 mol dm^{-3} HCl (15 cm^3) and saturated aq. $NaHCO_3$ (15 cm^3), then was dried and evaporated.

To a solution of the above crude esters in methanol (5 cm^3) was added cerium(III) chloride (0.4 mol dm^{-3} in methanol; 0.2 cm^3, 0.08 mmol), followed by sodium borohydride (10 mg, 0.26 mmol). After 30 min the mixture was evaporated to low bulk, diluted with dichloromethane (20 cm^3), and the solution was washed successively with 1 mol dm^{-3} HCl (15 cm^3) and saturated aq. $NaHCO_3$ (15 cm^3), dried, and evaporated.

A stirred mixture of the above crude alcohols and sodium hydrogen carbonate (60 mg, 0.71 mmol) in dichloromethane (5 cm^3) was treated with MCPBA (85%; 25 mg, 0.12 mmol). After 5 h the mixture was diluted with dichloromethane (20 cm^3), washed successively with saturated aq. $Na_2S_2O_5$ (15 cm^3) and saturated aq. $NaHCO_3$ (15 cm^3), dried, and evaporated. Purification by flash chromatography [light petroleum–ethyl acetate (1:1)] provided epoxides **35** as two separable isomers (stereochemistry unidentified): the less polar isomer **35a** (6 mg, 22%) and the more polar isomer **35b** (3 mg, 11%). Data for isomer **35a**: ν_{max}/cm^{-1} 3600–3200, 3060, 1710 and 1600; δ_H(90 MHz) 1.25 (3 H, s, Me), 1.45 (3 H, s, Me), 1.5–2.5 (3 H, m), 2.7–3.25 (2 H, m), 3.75 (1 H, br s, 3-H), 4.05 (2 H, m, CH_2OH), 4.75 (2 H, m, 7- and 8-H), 5.20 (1 H, br s, 4-H) and 7.55–8.05 (5 H, m, Ph); *m/z* (EI) 331 ([M − CH_3], 16%), 149 (5), 121 (5), 105 (100) and 77 (34). Data for isomer **35b**: ν_{max}/cm^{-1} 3600–3200, 3050, 1710 and 1605; δ_H(90 MHz) 1.30 (3 H, s, Me), 1.45 (3 H, s, Me), 1.5–2.9 (4 H, m), 3.35 (1 H, m), 3.80 (1 H, br s, 3-H), 4.00 (2 H, m, CH_2OH), 4.80 (2 H, m, 7- and 8-H), 5.30 (1 H, dd, *J* 7.5 and 1.5, 4-H) and 7.50–8.05 (5 H, m, Ph); *m/z* (EI) 331 ([M − CH_3], 20%), 105 (100) and 77 (35).

(±)-cis-*Bicyclo*[3.3.0]*octa*-2,7-*diene*-2-*carbaldehyde* **24**.—The procedure for the reaction of ketone **5** (210 mg, 1.72 mmol) with (methoxymethylene)triphenylphosphorane was the same as described for the reaction of compound **12a** above. The crude enol ether was used without further purification in the singlet-oxygen ene reaction and the procedure was the same as described above for the reaction of enol ether **20**. Purification of the product by flash chromatography provided enal **24** (110 mg, 48%), ν_{max}/cm^{-1} 3050, 2710, 1680, 1625 and 1620; δ_H(60 MHz) 1.5–3.2 (5 H, m), 4.0 (1 H, m), 5.5–6.0 (2 H, m, 7- and 8-H), 6.7 (1 H, m, 3-H) and 9.8 (1 H, s, CHO); *m/z* (CH_4, CI) 135 ([M + H]$^+$, 100%) (Found: [M + H]$^+$, 135.0812. $C_9H_{11}O$ requires *m/z*, 135.0810).

(±)-exo,exo-7,8-*Bis*-(tert-*butyldimethylsiloxy*)-cis-*bicyclo*-[3.3.0]*oct*-2-*ene*-2-*carbaldehyde* **22b** *and* (±)-exo,exo-7,8-*Bis*-(tert-*butyldimethylsiloxy*)*bicyclo*[3.3.0]*oct*-1-*ene*-2-*carbaldehyde* **23b**.—The procedure for the reaction of the ketone **12b** (500 mg, 1.30 mmol) with (methoxymethylene)triphenylphosphorane was the same as that described above for reaction of the ketone **12a**. The crude enol ether was used without further purification in the next step; ν_{max}/cm^{-1} 3050, 1695 and 1260; δ_H(60 MHz; standard Me_2SiBu^t) 0.0 (6 H, s), 0.05 (6 H, s), 0.90 (18 H, s), 1.5–2.4 (7 H, m), 2.84 (1 H, m), 3.5 (3 H, s, MeO), 3.94 (2 H, m, 7- and 8-H) and 5.85 (1 H, m, CHO).

The procedure for the singlet-oxygen ene reaction was the same as described above for the reaction of enol ether **20**. Purification of the product by flash chromatography [light petroleum–ethyl acetate (100:1, then 50:1)] provided an inseparable mixture (245 mg, 48%) of the isomeric enals **22b** and **23b**; ν_{max}/cm^{-1} 3050, 2705, 1685 and 1610; δ_H(60 MHz; standard Me_2SiBu^t) 0.0 (6 H, s), 0.04 (6 H, s), 0.85 (18 H, s), 1.0–4.3 (8 H, m), 4.7 ($\frac{3}{8}$ H, d, *J* ~3.0), 6.85 ($\frac{5}{8}$ H, m), 9.75 ($\frac{5}{8}$ H, s) and 9.90 ($\frac{3}{8}$ H, s).

(±)-exo,exo-7,8-*Bis*(*benzyloxy*)-cis-*bicyclo*[3.3.0]*oct*-2-*ene*-2-*carbaldehyde* **22c** *and* (±)-exo,exo-7,8-*Bis*(*benzyloxy*)*bicyclo*-[3.3.0]*oct*-1-*ene*-2-*carbaldehyde* **23c**.—To a stirred suspension of (methoxymethyl)triphenylphosphonium chloride (1.64 g, 4.78 mmol), in dry THF (30 cm^3) at 0 °C was added sodium bis(trimethylsilyl)amide (1 mol dm^{-3} in THF; 4.5 cm^3, 4.50 mmol). After 10 min the mixture was warmed to room temperature and then left at room temperature for 10 min, then was re-cooled to 0 °C before a solution of the ketone **12c** (500 mg, 1.49 mmol) in THF (2 cm^3) was added dropwise to the deep red ylide solution. After 30 min at 0 °C, followed by 1.5 h at room temperature, the colour had changed to orange-red. The mixture was then diluted with dichloromethane (120 cm^3), washed with water (70 cm^3), dried, and evaporated. The enol ether produced was not fully characterised, but was used without purification in the next step; ν_{max}/cm^{-1} 3075, 3050, 1690 and 700; δ_H(60 MHz) 1.3–1.7 (3 H, m), 1.8–2.5 (3 H, m), 3.0 (1 H, m), 3.5 (3 H, s, OMe), 3.6–4.1 (2 H, m, 7- and 8-H), 4.4–4.75 (4 H, m, PhCH_2O × 2), 5.8 (1 H, m, 4-H) and 7.25 (10 H, m, Ph × 2).

A water-cooled suspension of the crude enol ether, MTPP (6 mg) and pyridine (1 drop) in dry benzene (15 cm^3) was irradiated with a tungsten filament lamp (150 W, 240 V), while oxygen was bubbled through. When no starting material remained (TLC), triphenylphosphine (390 mg, 1.49 mmol) was added and after 30 min the solvent was evaporated off. Purification by flash chromatography [light petroleum–ethyl acetate (30:1, 9:1, then 6:1)] provided *enal* **22c** (265 mg, 51% from ketone **12c**), ν_{max}/cm^{-1} 3075, 3050, 2750, 1680, 1620 and 700; δ_H(90 MHz) 1.5–2.0 (1 H, m), 2.6–2.0 (2 H, m), 2.7–3.2 (2 H, m), 3.40–3.85 (2 H, m), 3.96 (1 H, m, 7-H), 4.44 (2 H, br d, PhCH_2O), 4.78 (2 H, br s, PhCH_2O), 6.76 (1 H, m, 3-H), 7.30 (10 H, m, Ph × 2) and 9.75 (1 H, s, CHO); *m/z* (NH_3, CI) 366 ([M + NH_4], 25%) and 349 ([M + H]$^+$, 100) (Found: [M + H]$^+$, 349.1800. $C_{23}H_{25}O_3$ requires *m/z* 349.1804); and enal **23c** (200 mg, 39% from ketone **12e**), ν_{max}/cm^{-1} 3075, 3050, 2750, 1680 and 700; δ_H(90 MHz) 1.5–2.8 (6 H, m), 3.4–3.7 (1 H, m), 3.9–4.2 (1 H, m), 4.5–4.8 (5 H, m), 7.3 (10 H, m, Ph × 2) and 9.72 (1 H, s, CHO).

(±)-exo,exo-6,7-*Bis*(*benzyloxy*)-exo-4-(*hydroxymethyl*)-cis-*bicyclo*[3.3.0]*oct*-2-*ene* **28c**, (±)-exo,exo-6,7-*Bis*(*benzyloxy*)-endo-4-(*hydroxymethyl*)-cis-*bicyclo*[3.3.0]*oct*-2-*ene* **29c** *and* (±)-exo,exo-7,8-*Bis*(*benzylozy*)-2-(*hydroxymethyl*)-cis-*bicyclo*-[3.3.0]*oct*-2-*ene* **30c**.—To a stirred solution of the enal **22c** (1.2 g, 3.45 mmol) in dry THF (100 cm^3) at 0 °C was added dropwise potassium *tert*-butoxide (1.1 mol dm^{-3} in Bu^{t}OH; 7.8

cm^3, 8.58 mmol). After 30 min the mixture was allowed to reach room temperature and then left at room temperature for 2.5 h, then was cooled to 0 °C again before acetic anhydride (1.2 cm^3, 12.72 mmol) was added. After 15 min the mixture was allowed to warm to room temperature and most of the solvent was removed by evaporation. Dichloromethane (150 cm^3) was then added and the resultant solution was washed with saturated aq. $NaHCO_3$ (100 cm^3), dried, and evaporated. The crude enol acetate **26c** was not very stable and was used without further purification in the next step; ν_{max}/cm^{-1} 3075, 3050, 1760, 1660, 1200 and 700; δ_H(60 MHz) 1.5–2.3 (2 H, m), 2.05 (3 H, s, AcO), 3.2–4.0 (4 H, m), 4.5 (2 H, br s), 4.7 (2 H, br s), 5.9 (2 H, m, 3-and 4-H) and 7.3 (11 H, m).

To a stirred solution of the above crude enol acetate in ethanol (100 cm^3) was added portionwise sodium borohydride (500 mg, 13.21 mmol). When no starting material remained (TLC) the solvent was evaporated off and the residue was taken up in dichloromethane (100 cm^3). The resulting suspension was washed successively with 2 mol dm^{-3} HCl (75 cm^3) and saturated aq. $NaHCO_3$ (75 cm^3), dried, and evaporated. Purification by preparative HPLC {Dynamax column, 5μ-spherical silica [light petroleum–ethyl acetate (4:1)]} provided compound **28c** (256 mg, 21% from enal **22c**), ν_{max}/cm^{-1} 3600–3200, 3075, 3050, 1500 and 700; δ_H(300 MHz) 1.48 (1 H, dt, *J* 13.0, 5.0, 8α-H), 1.55 (1 H, br s, OH), 2.14 (1 H, ddd, *J* 13.0, 9.5 and 6.5, 8β-H), 2.55 (2 H, m, 4- and 5-H), 3.28 (1 H, m, 1-H), 3.45–3.60 (3 H, m, CH_2OH, 6-H), 3.80 (1 H, m, 7-H), 4.50–4.70 (4 H, m, $PhCH_2O$ × 2), 5.44 (1 H, ddd, *J* 5.5, 2.0, 2.0, 3-H), 5.69 (1 H, dt, *J* 5.6 and 1.0, 2-H) and 7.20–7.40 (10 H, m, Ph × 2); *m/z* (NH_3, CI) 368 ($[M + NH_4]^+$, 75%), 292 (20), 278 (100) and 188 (75) (Found: $[M + NH_4]^+$, 368.2215. $C_{23}H_{30}NO_3$ requires *m/z*, 368.2226); compound **29c** (254 mg, 21% from enal **22c**), ν_{max}/cm^{-1} 3600–3200, 3075, 3050, 1460 and 700; δ_H(300 MHz) 1.29 (1 H, ddd, *J* 14.5, 6.5 and 4.0, 8α-H), 2.23 (1 H, dd, *J* 14.5, 9.5, 8β-H), 3.12–3.40 (4 H, m, 1-H, 4-H, 5-H, OH), 3.50 (1 H, ~t, *J* 11, CH_2OH), 3.69 (2 H, m, 6-H and CH_2OH), 4.03 (1 H, ~t, *J* 3.5, 3.5, 7-H), 4.33 (1 H, d, *J* 11, CH_2Ph), 4.46 (1 H, d, *J* 12, CH_2Ph), 4.55 (1 H, d, *J* 11, CH_2Ph), 4.64 (1 H, d, *J* 12, CH_2Ph), 5.26 (1 H, ddd, *J* 5.5, 1.5, ~1, 3-H), 5.62 (1 H, ddd, *J* 5.5, 2.0, 2.0, 2-H) and 7.23–7.39 (10 H, m, Ph × 2); *m/z* (NH_3, CI), 368 ($[M + NH_4]^+$, 85%), 351 ($[M + H]^+$, 10), 292 (15), 278 (100) and 188 (50) (Found: $[M + NH_4]^+$, 368.2220. $C_{23}H_{30}NO_3$ requires *m/z*, 368.2226); and compound **30c** (170 mg, 14% from enal **22c**), ν_{max}/cm^{-1} 3600–3200, 3075, 3050 and 700; δ_H(60 MHz) 1.9–2.6 (4 H, m), 2.6–3.5 (3 H, m), 3.5–4.05 (2 H, m), 4.1 (2 H, br s), 4.5 (4 H, br s, $PhCH_2O$ × 2), 5.4 (1 H, m, 3-H) and 7.25 (10 H, m); *m/z* (NH_3, CI) 368 ($[M + NH_4]^+$, 55%), 351 ($[M + H]^+$, 15) and 278 (100) (Found: $[M + NH_4]^+$, 368.2228. $C_{23}H_{30}NO_3$ requires *m/z*, 368.2226).

(±)-exo-4-(*Acetoxymethyl*)-exo,exo-6,7-*bis*(*benzyloxy*)-cis-*bicyclo*[3.3.0]*oct*-2-*ene* **31**.—A solution of the alcohol **28c** (30 mg, 0.086 mmol), DMAP (65 mg, 0.53 mmol) and acetic anhydride (25 mm^3, 0.265 mmol) in dichloromethane (8 cm^3) was stirred at room temperature for 2 h. The reaction mixture was diluted with dichloromethane (25 cm^3), washed successively with 1 mol dm^{-3} HCl (15 cm^3) and saturated aq. $NaHCO_3$ (15 cm^3), dried, and evaporated. Purification by flash chromatography [light petroleum–ethyl acetate (9:1)] provided compound **31** (25 mg, 74%); ν_{max}/cm^{-1} 3075, 3050, 1730 and 1440; δ_H(300 MHz) 1.49 (1 H, m, 8α-H), 2.00 (3 H, s, Ac), 2.12 (1 H, m, 8β-H), 2.56 (1 H, m, 5-H), 2.65 (1 H, m, 4-H), 3.29 (1 H, m, 1-H), 3.56 (1 H, dd, *J* 4.5, 3.5, 6-H), 3.78 (1 H, m, 7-H), 3.92 (1 H, dd, *J* 11.0, 7.0, CH_2OAc), 4.01 (1 H, dd, *J* 11.0, 6.0, CH_2OAc), 4.50–4.65 (4 H, m, CH_2Ph), 5.43 (1 H, m, 3-H), 5.66 (1 H, m, 2-H) and 7.23–7.33 (10 H, m, 2 × Ph). Positive NOEs observed: at 5-H and 2-H when 1-H was irradiated; at 4-H when 6-H was irradiated; there was also a strong indirect negative effect at each of the CH_2OAc protons when 6-H was irradiated; *m/z* (NH_3, CI) 410 ($[M + NH_4]^+$, 100%), 393 ($[M + H]^+$, 35), 135 (55), 108 (35) and 91 (70) (Found: $[M + NH_4]^+$, 410.2340. $C_{25}H_{32}NO_4$ requires *m/z*, 410.2331).

(±)-endo-4-(*Acetoxymethyl*)-exo,exo-6,7-*bis*(*benzyloxy*)-cis-*bicyclo*[3.3.0]*oct*-2-*ene* **32**.—The procedure for the acetylation of the alcohol **29c** (43 mg, 0.12 mmol) was the same as that for the alcohol **28c** and provided compound **32** (44 mg, 91%), ν_{max}/cm^{-1} 3075, 3050, 1740, 1620, 1450 and 700; δ_H(300 MHz) 1.42 (1 H, ddd, $J_{8\alpha,8\beta}$ 13.5, $J_{1,8\alpha}$ 6.0, $J_{8\alpha,7}$ 4.5, 8α-H), 1.95 (3 H, s, Ac), 2.16 (1 H, ddd, $J_{8\alpha,8\beta}$ 13.5, $J_{1,8\beta}$ 9.5, $J_{8\beta,7}$ 4.0, 8β-H), 3.02 (1 H, ddd, $J_{1,5}$ 9.0, $J_{4,5}$ 8.5, $J_{5,6}$ 7.5, 5-H), 3.13 (1 H, m, 4-H), 3.27 (1 H, m, 1-H), 3.64 (1 H, dd, $J_{5,6}$ 7.5, $J_{7,6}$ 3.5, 6-H), 3.88 (1 H, ddd, $J_{8\alpha,7}$ 4.5, $J_{8\beta,7}$ 4.0, $J_{7,6}$ 3.5, 7-H), 4.00 (1 H, dd, *J* 11.0, 7.5, CH_2OAc), 4.28 (1 H, dd, *J* 11.0, 6.5, CH_2OAc), 4.45–4.60 (4 H, m, CH_2Ph), 5.46 (1 H, ~dt, $J_{3,2}$ 5.5, $J_{4,3}$ 2.0, $J_{3,1}$ 2.0, 3-H), 5.64 (1 H, ~dt, $J_{3,2}$ 5.5, $J_{1,2}$ 2.5, $J_{2,4}$ 2.5, 2-H) and 7.25–7.35 (10 H, m, 2 × Ph); positive NOEs observed: at 6-H and 3-H when each of the CH_2OAc protons was irradiated; at each of the CH_2OAc protons when 6-H was irradiated; *m/z* (NH_3, CI) 410 ($[M + NH_4]^+$, 100%), 393 ($[M + H]^+$, 25), 135 (45), 108 (40) and 91 (85) (Found: $[M + NH_4]^+$, 410.2335. $C_{25}H_{32}NO_4$ requires *m/z*, 410.2331).

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