Tetrahedron Vol. 47, No. 33, pp. 6813-6850, 1991
Printed in Great Britain

0040-4020/91 $3.00+.00

CHEMISTRY OF INSECT ANTIFEEDANTS FROM *AZADIRACHTA INDICA* (PART 8)[1]: SYNTHESIS OF HYDROXYDIHYDROFURAN ACETAL FRAGMENTS FOR BIOLOGICAL EVALUATION AND AZADIRACHTIN TOTAL SYNTHESIS STUDIES.

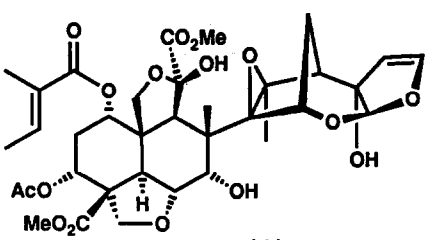
James C. Anderson, Steven V. Ley,* Dinos Santafianos and Richard N. Sheppard.

Department of Chemistry, Imperial College of Science, Technology and medicine, London. SW7 2AY, UK.

(*Received in UK* 17 *May* 1991)

Summary: The work describes a unified strategy towards the preparation of model hydroxydihydrofuran acetal fragments (**2**) (**3**) and (**45**) common to the potent insect antifeedant and growth disruption agent azadirachtin (**1**). These units, along with other analogues, were prepared for biological evaluation as antifeedants. Furthermore, several potential coupling fragments (**51**), (**52**), (**54**), (**55**), (**62**), (**63**) and (**56**) for azadirachtin synthesis were also prepared from common precursors. Methods were developed to prepare these materials in enantiomerically pure form and to conveniently protect the angular hydroxyl group and unmask the labile enol double bond at a late stage in the synthesis.

During the search for novel pest control agents which show environmentally acceptable biological profiles recent attention has focused on antifeedant materials[2] which can modify the behaviour of selected insect species. Furthermore compounds which, when ingested can cause additional effects, such as growth disruption, are even more attractive as lead compounds for study. In this regard the natural product azadirachtin (**1**) isolated from the neem tree *Azadirachta indica* A. Juss (Meliaceae) has stimulated considerable interest.[3,4]

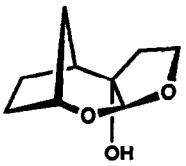


(**1**)

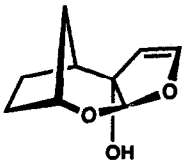
For some years we have been studying the synthesis of antifeedants[5] and in particular azadirachtin,[6] with the aim of determining the spatial and electronic requirements of functionality for biological activity. Additionally, we hope that the materials and natural product analogues that have been prepared will help in our understanding of the fundamental feeding and host plant recognition processes of insect pests. We have also shown that simpler fragments of the natural products can act as mimics and show some antifeedant activity.[7] These model studies[1,8] also facilitate the design of synthetic strategies towards more complex natural materials.

Here we describe in full, our efforts on the preparation of various simple hydroxy hydrofuran acetal units common to azadirachtin, for biological evaluation and ultimately for the total synthesis of (**1**).

In the first phase of this work the preparation of racemic model compounds (**2**) and (**3**) are described. This study showed these simple fragments displayed antifeedant activity and established some general synthetic sequences applicable to more substituted examples.



(**2**)



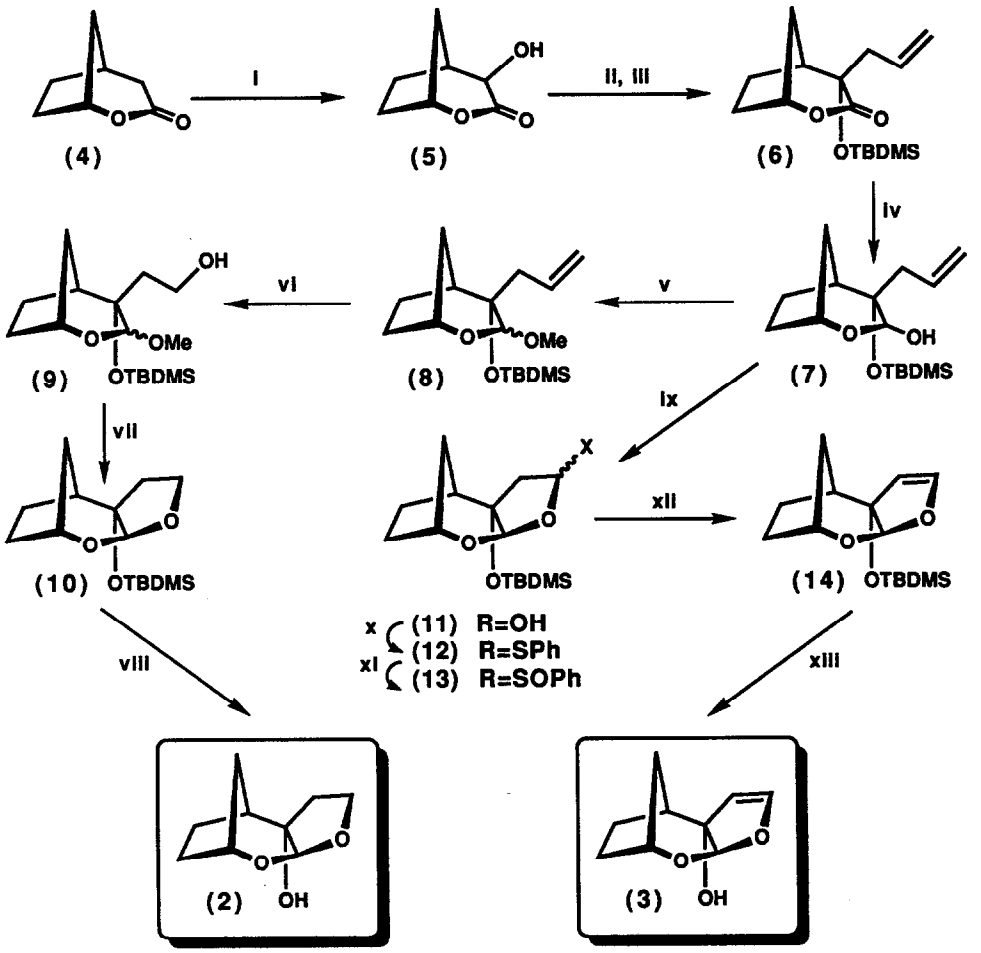
(**3**)

The synthesis proceeds from the known readily available lactone (**4**) which on oxidation of its enolate with MoO_5.Py.HMPA complex[9] (MoOPH) at -78° gave the alcohol (**5**) as a single isomer by oxidation from the least hindered face (Scheme 1). The stereochemistry of (**5**) was determined by nmr and x-ray crystallographic methods.[10] Following silylation of (**5**), enolate formation using potassium diisopropylamide (KDA)[11] and quenching with allylbromide, also from the least hindered face, we obtained the substituted lactone (**6**) as a single stereoisomer. No other isomer was detected during this allylation reaction and once again the relative stereochemistry was confirmed by x-ray crystallographic analysis. Conversion of (**6**) to the lactol (**7**) was achieved by the slow addition of di-isobutylaluminium hydride (DIBAL) *via* a syringe pump over several hours. This lactol (**7**) is the pivotal intermediate required for the preparation of both fragments (**2**) and (**3**) (Scheme 1). For the first of these syntheses, (**7**) was transformed to the methyl derivative as a mixture of anomers (**8**) in 60% yield by acetal exchange in methanol using a trace of concentrated sulphuric acid as a catalyst. Subsequent ozonolysis at -78°C in methanol followed by reductive work up with sodium borohydride gave the alcohols (**9**). These compounds were readily cyclized to (**10**) in acetonitrile as solvent using Amberlyst 15 sulphonic acid ion exchange resin to effect the transacetalization. Finally deprotection of (**10**) to give the first of the model compounds (**2**) was achieved using tetra-*n*-butylammonium fluoride (TBAF) in tetrahydrofuran (THF) at room temperature. (Scheme 1).

For the preparation of the second model compound (**3**) the key intermediate (**7**) was ozonolysed at -78°C and on work up at room temperature with triphenyl phospine[7] gave the lactols (**11**) in excellent yield. From nmr studies it was apparent that (**11**) existed in the closed form in solution. Attempted dehydration of (**11**) directly to an enol ether using a variety of reagents was unsuccessful. Treatment with thiophenol and Amberlyst 15 ion exchange resin in the presence of 4Å molecular sieves, gave the sulphides (**12**) in good yield. These upon oxidation with *m*-chloroperbenzoic acid (*m*-CPBA) afforded the corresponding sulphoxides (**13**) which underwent smooth *syn*-elimination to (**14**) on thermolysis in boiling toluene. Finally deprotection with TBAF, as above, gave compound (**3**) (Scheme 1). The biological assessment of these model compounds, which show considerable structural homology with azadirachtin (**1**) and its equally active dihydro analogue, have been reported elsewhere.[7] These data indicate that both are antifeedants and that, in a choice test, (**3**) is especially potent even at 1 ppm. This encouraging result suggests that, in future, it may be possible to design even simpler and more easily synthesised materials with antifeedant activity. It also implies that the hydroxy

furan acetal portion of azadirachtin may be important for binding to a potential antifeedant receptor in the insect.[12]

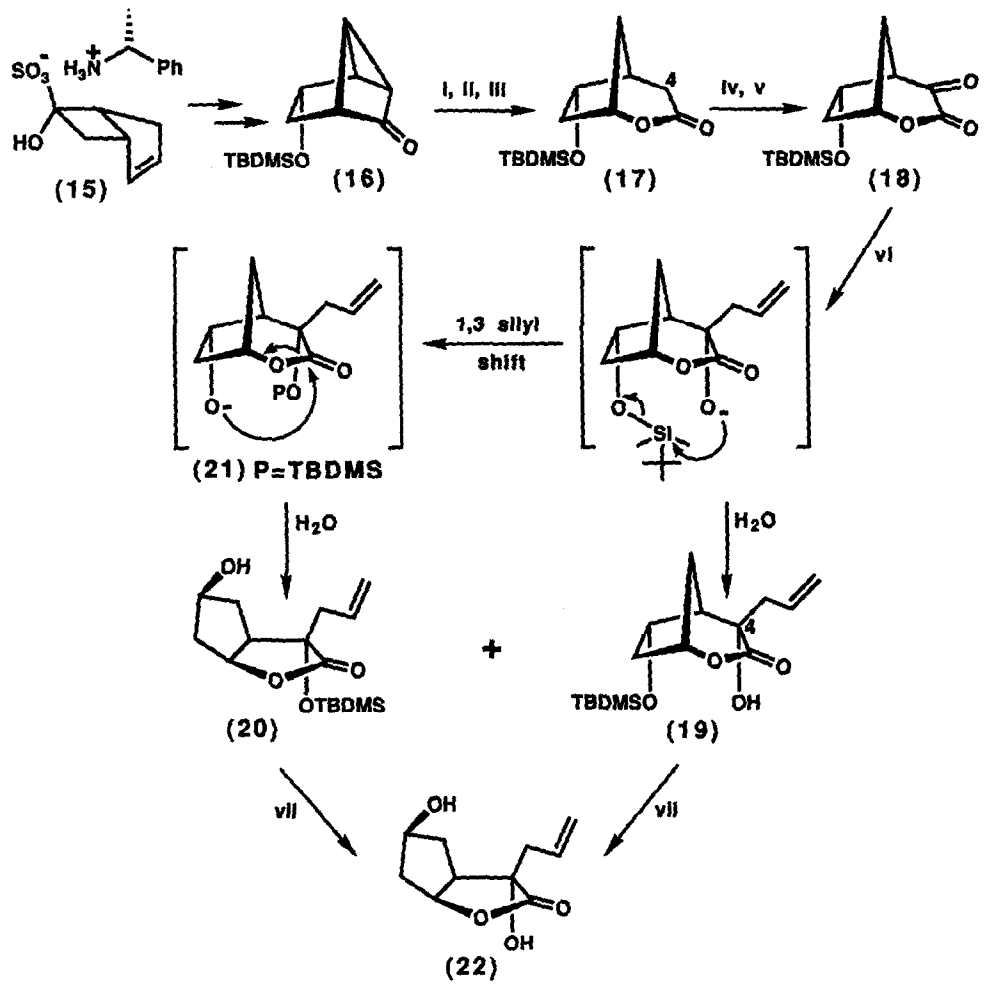
Scheme 1



Reagents: (i) LDA, THF, -78°C then MoOPH, -78°C to RT. 67%; (ii) $^{t}BuMe_2SiCl$, imidazole, DMF, RT, 1h. 94%; (iii) KDA, THF, -78°C; $CH_2{=}CHCH_2Br$, -78°C to RT. 83%; (iv) DIBAL, toluene, -78°C. 57%; (v) H_2SO_4, MeOH, RT. 60%; (vi) O_3, MeOH, -78°C then $NaBH_4$, RT. 88%; (vii) Amberlyst 15, MeCN, RT, 50 min. 64%; (viii) TBAF, THF, RT. 71%; (ix) O_3, CH_2Cl_2, -78°C then Ph_3P, RT, 4h. 93%; (x) Amberlyst 15, PhSH, 4Å sieves, MeCN, RT, 30 min. 85%; (xi) *m*-CPBA, CH_2Cl_2, 0°C. 72%; (xii) Et_3N, toluene, 110°C, 10 min. 99%; (xiii) TBAF, THF, RT, 1h. 76%.

Having established viable synthetic strategies to racemic materials we next addressed the issue of preparing compounds in an entiomerically pure fashion since these would be needed for total synthesis studies and to give a more accurate picture during the analogue screening programme.[13] To this end we converted

Scheme 2



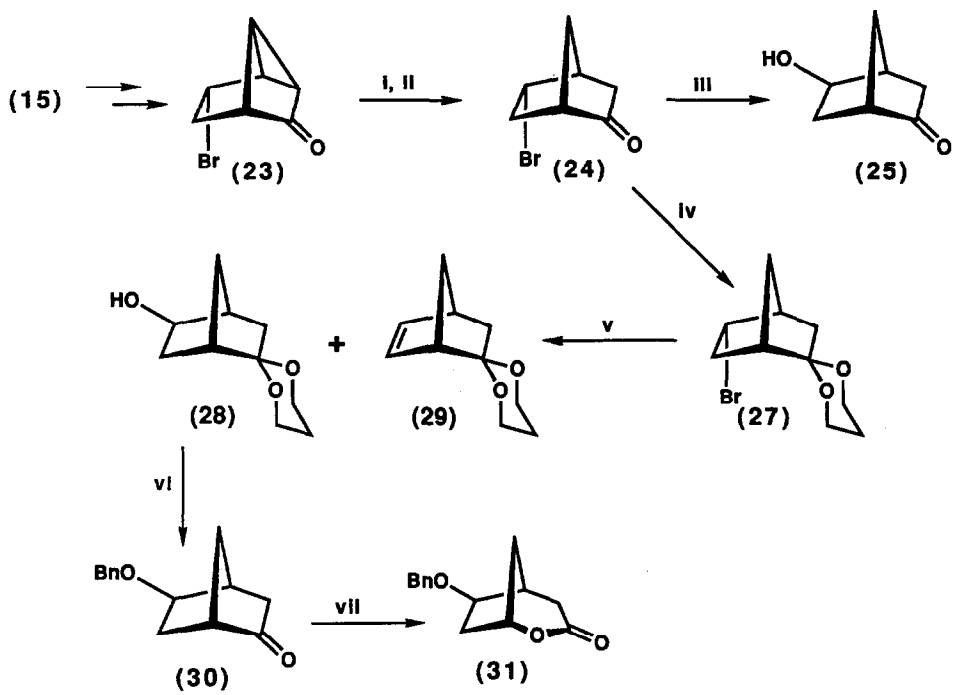
Reagents: (i) $NaBH_4$, MeOH, RT. 85%; (ii) DMSO, $(ClCO)_2$, -65°C; Et_3N, -65°C to RT. 93%; (iii) *m*-CPBA, TsOH.H_2O cat, CH_2Cl_2, RT. 87%; (iv) LDA, THF, -78°C then MoOPH, -78°C to RT. 76%; (v) DMSO, $(ClCO)_2$, -65°C; Et_3N, -65°C to RT. 77%; (vi) ^nBuLi, CH_2=$CHCH_2SnBu_3$, THF, -78°C to 15C. 84% (**19**:**20**, 3:2); (vii) TBAF, THF, RT. **20** to **22** 82%. **19** to **22** 92%.

(**15**)[14] to the known tricyclic ketone (**16**) using the literature procedure[15] (Scheme 2). This in turn was transformed to the lactone (**17**) *via* homoconjugate reduction with sodium borohydride in methanol, oxidation with the Swern conditions[16] and Baeyer-Villiger oxidation with *m*-CPBA. All these reactions proceeding in excellent yield. The lactone (**17**) is an optically pure *tert*-butyldimethylsilyloxy derivative of the lactone used previously in the racemic series. Oxidation of (**17**) (*via* the enolate generated by treatment with LDA) with the MoOPH complex gave the corresponding α-hydroxy lactone which appeared to be a single diastereoisomer by

^{1}H nmr. The C4-α-hydroxyl group was assumed to be in the β orientation by analogy with (**5**). Attempted deprotonation of its *tert*-butyldimethylsilyl (TBDMS) protected ether with a variety of bases and addition of allyl bromide yielded only starting material. Presumably this is due to a large 1,3 *pseudo* diaxial steric interaction between the C6-*tert*-butyldimethylsilyloxy group and the C4-H atom, thus hindering its abstraction. To overcome this problem the α-hydroxylactone was oxidised to the α-ketolactone (**18**) with the Swern reagent and treated with allyl lithium. This afforded the desired allyl hydroxylactone (**19**) along with the unwanted bicycle (**20**) (3:2 respectively) in 84% yield. These isomers (**19** and **20**) were partially separable by flash chromatography, however any attempt to protect the axial C4-hydroxyl group of (**19**) led to protected species of (**20**).

The formation of (**20**) occurs *via* an oxy-anion induced 1,3 silyl shift[17] to give an unstable intermediate (**21**). This spontaneously rearranges to the thermodynamically more stable [3.3.0] bicyclic framework *via* rapid intramolecular lactone transfer to the secondary hydroxyl group. This transfer and concurrent rearrangement can be exclusively induced by the addition of hexamethylphosphoramide (HMPA) at 0°C, after the addition of allyl lithium at -78°C, to give (**20**) in 67% yield. Separate treatment of (**19**) or (**20**) with TBAF gave the same *bis*-hydroxylactone product (**22**) (Scheme 2).

Scheme 3

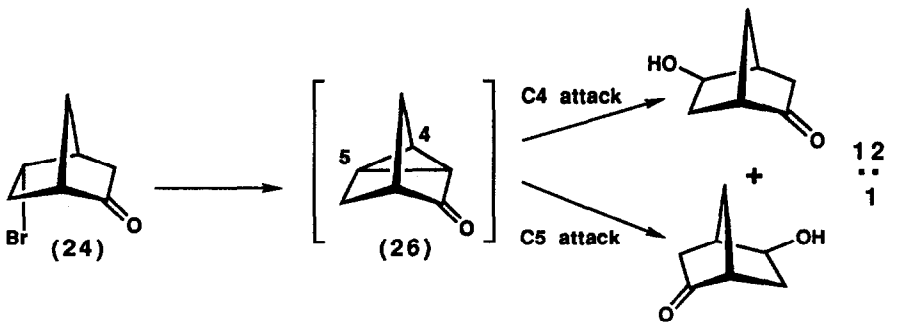


Reagents: (i) $NaBH_4$, MeOH, RT. 70% (2 steps); (ii) $^nPr_4NRuO_4$, 4Å sieves, NMO, MeCN, RT, 12 h. 83%; (iii) CF_3CO_2Ag, acetone/H_2O, 3:1, 60°C, dark, 40 h. 99%; (iv) $HO(CH_2)_3OH$, PPTS, PhH, 80°C, 3h. 92%; (v) KO_2, 18-C-6, DMSO-DME, 1:1, RT, 60 h. (**28**) 81%, (**29**) 7%; (vi) NaH, BnBr, $^nBu_4NI$, THF, 0°C to RT, 12h then 1M HCl, 50°C, 2h 45 min.73%; (vii) *m*-CPBA, TsOH.H_2O cat., CH_2Cl_2, RT, 3h. 91%.

Structural elucidation of these rearranged products follows from detailed nmr studies. It is apparent from these studies that placement of an *endo* C6-hydroxyl group in these structures is detrimental and leads to rapid rearrangement. We therefore had to revise our synthetic plan and believed that an *exo* C6-hydroxyl group would allow deprotonation of the α-*tert*-butyldimethylsilyloxy lactone and the resultant product, after the addition of allyl bromide, would not participate in the rearrangement described.

In this new approach the salt (**15**) was converted by known steps to the enantiomerically pure bromoketone (**23**)[18] (Scheme 3). Upon treatment with sodium borohydride (**23**) underwent homoconjugate reduction. Oxidation with tetra-*n*-propylammonium perruthenate (TPAP)[19] then gave the bicyclic bromoketone (**24**). Attempted displacement of bromide ion from (**24**) with an oxygen nucleophile caused partial racemisation during formation of the hydroxy ketone product (**25**). Even under the best conditions using silver trifluoracetate in aqueous acetone, (**25**) was obtained with only 85% ee (Scheme 3). This partial racemisation is undoubtedly due to a contribution from the tricyclic structure (**26**) (Scheme 4) which suffers ring opening at one of two enantiotopic sites. Attack of trifluoroacetate anion at C5 affords the major enantiomer while reaction at C4 gives the other enantiomer in the ratio ~12:1 as measured by the formation of the corresponding Mosher esters[20] (Scheme 4). This partial racemisation problem can be overcome by first protecting the carbonyl group as its 1,3-dioxane (**27**) using propanediol and *p*-toluenesulphonic acid (PTSA) as a catalyst. Displacement of the bromide in (**27**) using the Corey conditions[21] of potassium superoxide and 18-crown-6 in dimethylsulphoxide and dimethoxyethane, gave (**28**) in 81% yield together with a small amount of the eliminated product (**29**) (7%). For synthetic reasons, which will become apparent later, (**28**) was protected as its benzyl derivative and acidic work up released the carbonyl group to give (**30**) (Scheme 3). Compound (**30**) was debenzylated and

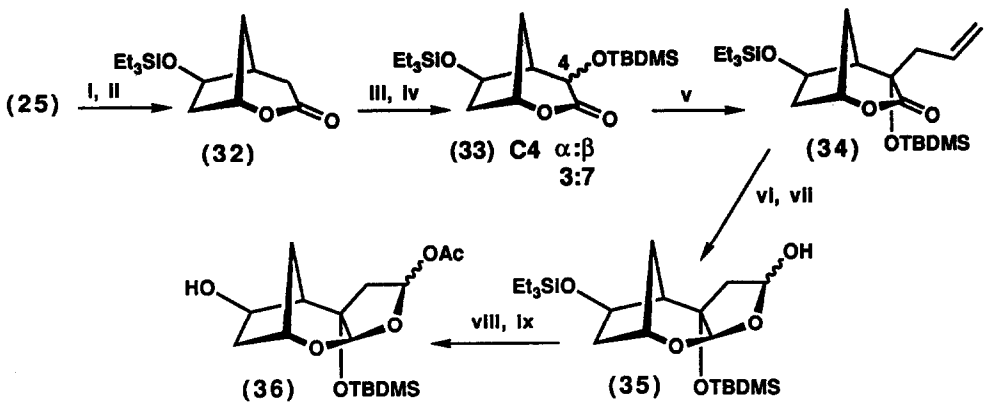
Scheme 4



shown to be enantiomerically pure following its conversion to its Mosher ester derivative and comparison with the racemic derivative. Compound (**30**) was then subjected to Baeyer-Villiger oxidation to give the protected lactone (**31**) which has since proved to be the preferred key intermediate for much of the remaining syntheses.

In the meantime further reactions of the 85% ee material (**25**) were progressed to determine the feasibility of the methodology established earlier in the model series and to provide materials for other synthetic studies. For example, (**25**) upon Baeyer-Villiger oxidation with *m*-CPBA and a trace of PTSA followed by protection of the secondary alcohol with triethylsilyl chloride gave the lactone (**32**) (Scheme 5). Following the

Scheme 5



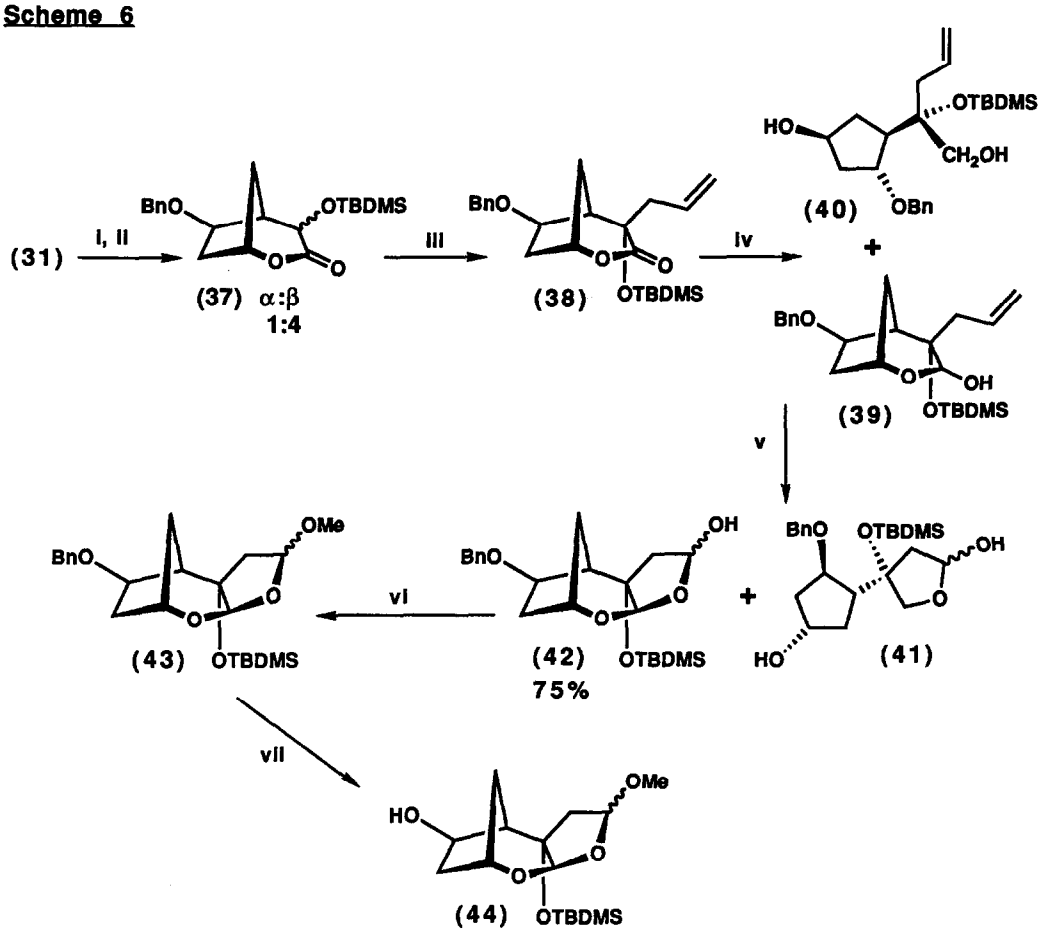
Reagents: (i) *m*-CPBA, TsOH.H_2O cat., CH_2Cl_2, RT, 30 min. 82%; (ii) Et_3SiCl, Et_3N, DMAP, CH_2Cl_2, RT, 1 h. 77%; (iii) LDA, THF, -78°C then MoOPH, -78°C to RT. 42%; (iv) $^tBuMe_2SiCl$, imidazole, DMF, RT, 4h. 89%; (v) KDA, THF, -78°C; HMPA; CH_2=$CHCH_2Br$, -78°C to RT. 42%; (vi) DIBAL, toluene, -78°C. 89%; (vii) O_3, CH_2Cl_2, -78°C then Ph_3P, RT, 12h. 90%; (viii) Ac_2O, Et_3N, DMAP, DCM, RT, 2h. 98%; (ix) AcOH/H_2O/THF, 3:3:1, RT, 1h. 85%.

previous route used in the model studies, deprotonation of (**32**) with LDA, oxidation with MoOPH complex and silylation with *tert*-butyldimethylsilyl chloride gave (**33**). As before this was deprotonated a second time using KDA and stereoselectively quenched with allylbromide to give (**34**) in a rather modest yield, presumably due to the lability of the triethylsilyl group during these anion reactions.[22] Compound (**34**) was further elaborated to the lactol (**35**) which was converted to the alcohol (**36**) by acetylation using acetic anhydride then selective removal of the triethylsilyl group with aqueous acetic acid (Scheme 5). The anomeric acetate was chosen in (**36**) since we anticipated this could be used to recover the sensitive enol ether double bond by pyrolysis at a later stage. We have shown the success of this process in other systems.[6b,d] The free hydroxyl group in (**36**) may be used to prepare further novel analogues or by oxidation may assist in coupling reactions to decalin fragments and therefore in the total synthesis of azadirachtin (**1**).

While this route was in progress we discovered the benefits of using a benzyl protecting group in the enantiomerically pure lactone (**31**) and the remaining syntheses all exploit this intermediate. In this case oxidation of (**31**) was achieved *via* the enolate using MoO_5 Py.DMPU (MoOPD), a new and safer alternative[23] to the conventional MoOPH reagent where hexamethylphosphoramide (HMPA) has been replaced by the much less toxic 1,3-dimethyl-3,4,5,6-tetrahydro-2-(1*H*)-pyrimidinone (DMPU)[24] (Scheme 6). The intermediate hydroxyl compound in this reaction was silylated in the normal way to give (**37**) in a 1:4 α:β ratio of isomers. Deprotonation of (**37**) with KDA and stereoselective allylation with allylbromide gave an excellent 80% yield of the desired lactone (**38**). The stereoselectivity in this reaction was confirmed by later x-ray crystallographic studies and by analogy with earlier reactions. DIBAL reduction of (**38**) in toluene at -78°C gave (**39**) together with a small amount (~15%) of the over reduced product (**40**) (Scheme 6). Once again ozonolysis of this mixture (**39** and **40**) in CH_2Cl_2 at -78° followed by standard work-up with Ph_3P afforded the isolable lactols (**41**) and (**42**). The tricyclic lactol (**42**) was further transformed to (**43**) (1:3 α:β) *via* anomeric exchange using

methanol, Amberlyst 15 ionic exchange resin and 3Å molecular sieves. Compound (**43**) was sufficiently crystalline for x-ray analysis,[10] allowing confident assignment of structures within this series. Finally the benzyl group in (**43**) was removed to give (**44**) using typical hydrogenolysis conditions in the presence of an essential trace amount of hydrochloric acid (Scheme 6). The alcohol (**44**) is the pivotal intermediate for the preparation of many further analogues and for the synthesis of key coupling fragments which should find application in the total synthesis of azadirachtin (**1**) itself. It is pertinent at this point to emphasise that (**44**) was prepared in enantiomerically pure form in 14 steps, from the known bromo tricycle (**23**) in 11% overall yield. This means that (**44**) may be readily obtained in useful gramme quantities for further synthesis.

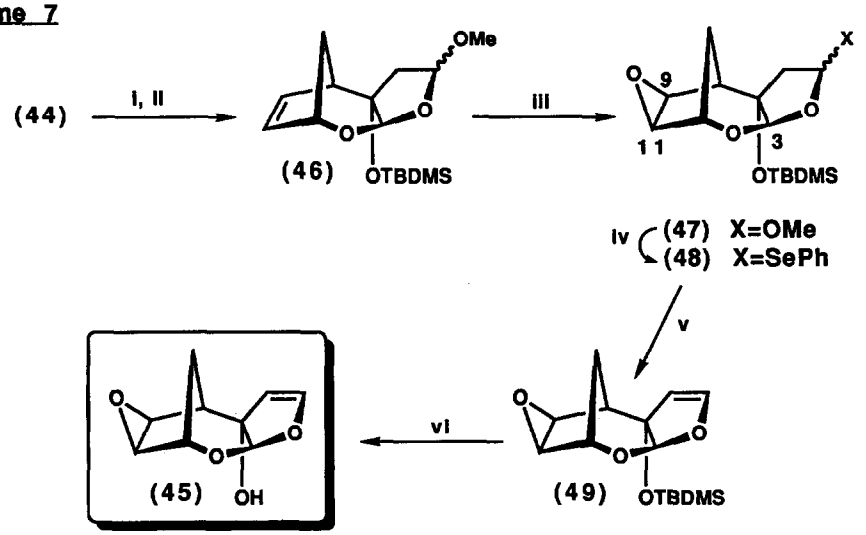
Scheme 6



Reagents: (i) LDA, THF, -78°C the MoOPD, -78°C to RT; (ii) $^{t}BuMe_2SiCl$, imidazole, DMF, RT, 14h. 81% overall; (iii) KDA, THF, -78°C; HMPA; CH_2=$CHCH_2Br$, -78°C to 0°C. 80%; (iv) DIBAL, toluene, -78°C; (v) O_3, CH_2Cl_2, -78°C then Ph_3P, RT, 14h. (**42**) 75% overall, α:β 1:4; (vi) Amberlyst 15, MeOH, 3Å sieves, MeCN, RT, 15 min. 83%, α:β 1:3; (vii) H_2, 10% Pd/C, HCl, MeOH, RT. 98%.

Indeed one of the important target model compounds for our studies incorporates the epoxide unit therefore we have also used (**44**) in the preparation of the epoxide model (**45**) (Scheme 7).

Scheme 7

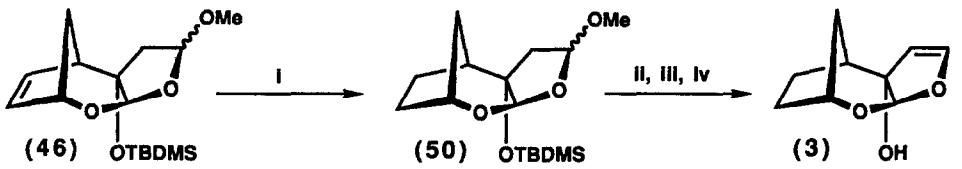


Reagents: (i) MsCl, Et_3N, CH_2Cl_2, RT, 10 min; (ii) DBU, toluene, 110°C, 38h. 95% overall; (iii) dimethyldioxirane, acetone/CH_2Cl_2, ~1:1, RT, 14h. 98%; (iv) Amberlyst 15, PhSeH, 4Å sieves, MeCN, RT. 44%; (v) 2-(phenylsulphonyl)-3-(*p*-nitrophenyl)oxaziridine, Py, CH_2Cl_2, RT, 10 min. 57%; (vi) TBAF, THF, RT, 5 min. 95%.

This was achieved by dehydrating (**44**) *via* its mesylate and elimination using 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in boiling toluene over 38 hours to give the strained alkene (**46**) (Scheme 7). These rather forcing conditions were necessary since attempts to use other reagents such as the Burgess salt[25] or Martins sulphurane[26] failed. Epoxidation of (**46**) to give the epoxide (**47**) was effected slowly in 60% yield by treatment with *m*-CPBA for 40 hours. However we found the use of dimethyldioxirane[27] in acetone/CH_2Cl_2 provided the desired epoxide in only 12 hours and in essentially quantitative yield. The stereochemical outcome of this oxidation was expected for steric reasons but was proved by high field nmr spectroscopy using selected n.O.e. difference experiments. For example a 3.1% enhancement, upon irradiation of H-3 (δ5.26, s), was observed to H-11 (δ3.50, br.d, J 2.5 Hz) together with a 1.9% enhancement of H-9 (δ3.80, d, J 2.9 Hz). The respective irradiation of H-9 and H-11 gave corresponding enhancements of H-3 (2.3% and 3.4% respectively). In order to introduce the enol ether double bond (**47**) was reacted with benzeneselenol, Amberlyst 15 ionic exchange resin and 4Å molecular sieves in anhydrous acetonitrile to give the selenides (**48**) in 44% yield, contaminated with an unknown by-product (2:3:1 C5 α:β:unknown). Attempts to improve this yield using alternative methods were unsuccessful owing to the lability of the epoxide ring to the acidic reaction conditions required for anomeric exchange. Nevertheless (**48**) *via* its selenoxide, generated by treatment with the Davis reagent[28] [2-(phenylsulphonyl)-3-(*p*-nitrophenyl)oxaziridine], underwent smooth *syn* elimination at room temperature to give (**49**). Final deprotection of the *endo*-hydroxyl group in (**49**) afforded the epoxide model compound (**45**) (Scheme 7). We find that use of the phenylselenoxide substituent to introduce the

sensitive enol ether double bond is superior to elimination of the corresponding sulphoxide as reported in our preliminary communications.[1,8] Additionally we have synthesised the enantiomerically pure model antifeedant (3) through hydrogenation of the alkene (46) (Scheme 8). Following similar methodology to that mentioned earlier;[7] selenide formation, treatment with Davis oxaziridine and deprotection of the hydroxyl group with TBAF (Scheme 8), compound (3) was furnished in good yield and was identical in all respects to the racemic material synthesised earlier.

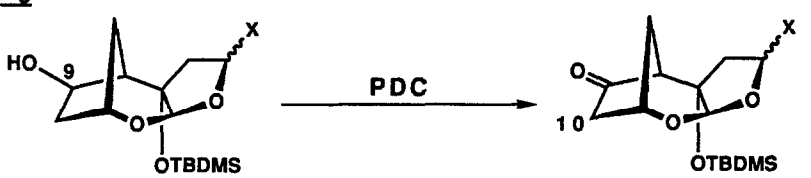
Scheme 8



Reagents: (i) H_2, 10% Pd/C, MeOH, RT. 97%; (ii) Amberlyst 15, PhSeH, 4Å sieves, MeCN, RT, 15 min. 58%; (iii) 2-(phenylsulphonyl)-3-(*p*-nitrophenyl)oxaziridine, Py, CH_2Cl_2, RT, 10 min. 82%; (iv) TBAF, THF, RT, 3h. 95%.

Other reactions which we studied for potential coupling fragments for azadirachtin synthesis were firstly to examine the oxidation of compounds (44) and (35).[29] In fact both these oxidations proceeded well using pyridinium dichromate (PDC)[30] in CH_2Cl_2 and 4Å molecular sieves to give (51) and (52) respectively (Scheme 9). In these compounds the C10 atom is activated for possible coupling strategies by the neighbouring carbonyl group.

Scheme 9

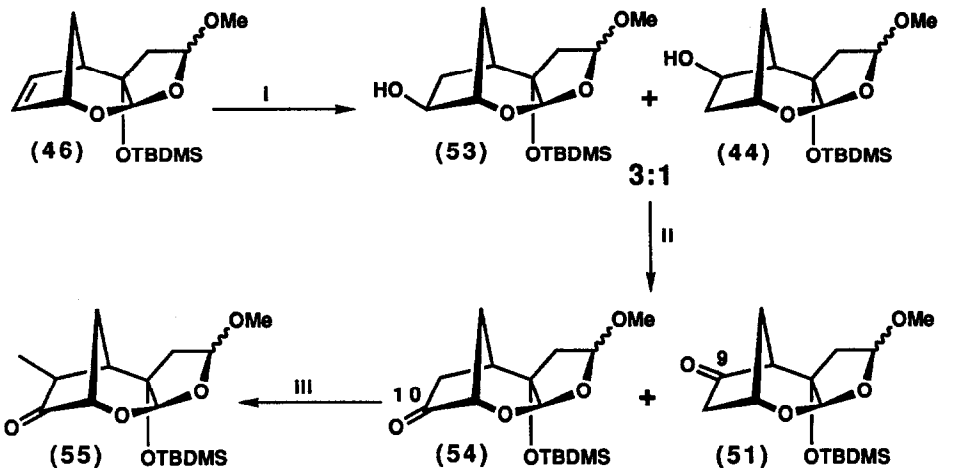


(44) X=OMe
(35) X=OAc

(51) X=OMe, 91%
(52) X=OAc, 76%

We have also investigated several oxygen transposition reactions whereby rather than have oxygen substitutents at C9, as in most of the above analogues or coupling species, the oxygen grouping is placed at C10. This gives a whole new series of compounds and coupling opportunities. The required substitution pattern is easily achieved by making use of the highly polarised double bond found in compounds such as (46).[31] Indeed hydroboration of (46), with 9-borabicyclo[3.3.1]nonane (9-BBN), occurs from the least hindered β face of the π bond to give an inseparable C10:C9 3:1 mixture of (53) and (44) in 95% yield. These were oxidised using PDC, as above, to produce the ketones (54) and (51) which were readily separated by flash chromatography (75% and 23% respectively). The C-10 ketone (54) can be converted to (55) by alkylation with methyl iodide of the intermediate enolate formed by treatment with LDA at -78°C, (Scheme 10).[32] Compound (55) constitutes a novel, suitably protected, coupling fragment for possible azadirachtin synthesis.

Scheme 10

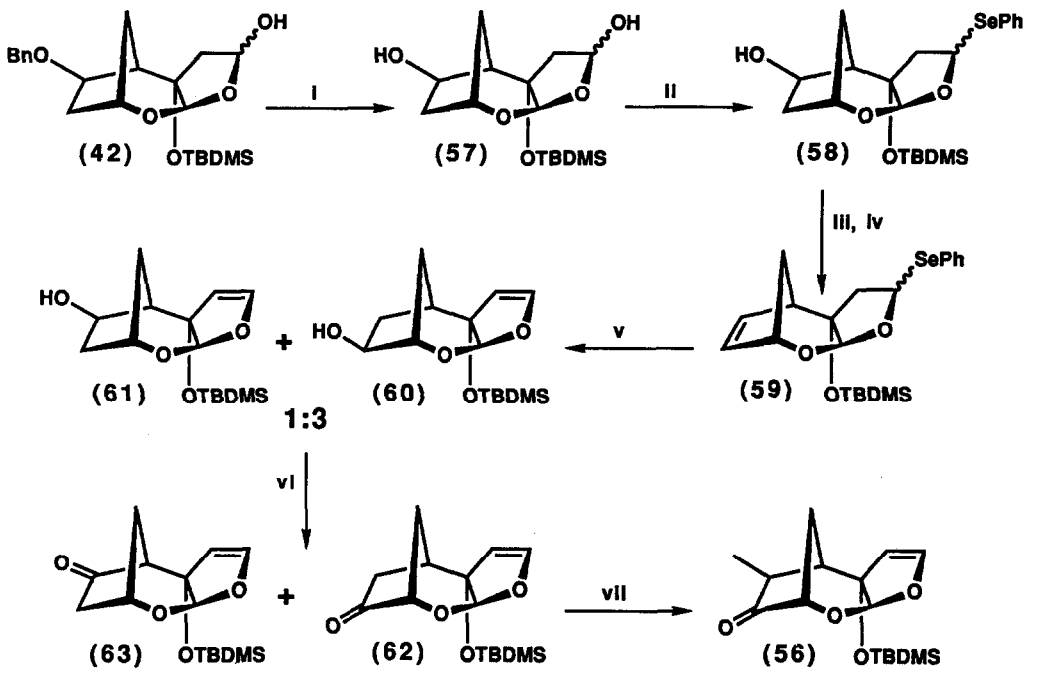


Reagents: (i) 9-BBN, THF, 67°C, 20 min then 3M NaOH, 27.5% aq. H_2O_2, 0°C to RT, 1h. 95%; (ii) PDC, 4Å sieves, CH_2Cl_2, RT, 16h. (**54**) 75%, (**51**) 23%; (iii) LDA, THF, -78°C then MeI, -78°C to RT. 69%.

In other studies towards potential coupling units we have also synthesised the Shibasaki intermediate[33] (**56**) (Scheme 11) from the readily prepared lactol (**42**) discussed earlier. This was achieved in the following sequence of reactions. Debenzylation of (**42**) by hydrogenolysis as in the above procedures gave the diol (**57**) which underwent borontrifluoride etherate induced anomeric exchange with benzeneselenol in CH_2Cl_2 at 0°C to produce the selenides (**58**) in 60% yield. Once again introduction of the double bond was straightforward and was accomplished *via* formation of the mesylate from (**58**) and elimination with DBU in boiling toluene to give (**59**). In a neat three step operation (**59**) was hydroborated with 9-BBN, basic hydrogen peroxide work-up was followed by selective selenoxide formation, with the Davis oxaziridine, and concomitant elimination to the alcohols (**60**) and (**61**). Although these were formed in an excellent 92% yield they were inseparable. Consequently they were subjected to PDC oxidation to give (**62**) and (**63**) which were readily separated in 76% and 20% yields respectively. Finally compound (**62**) could be deprotonated with lithium hexamethyl disilazide at -78°C and monoalkylated with methyliodide to produce (**56**). The spectral and physical data for which were identical to the previously reported material[32] (Scheme 11).

We believe the above syntheses display considerable scope for the preparation of many novel analogues of the hydroxy hydrofuran acetal fragment of azadirachtin and provides many useful units which may be exploited in total synthesis studies.

Scheme 11



Reagents: (i) H_2, 10% Pd/C, trace HCl, MeOH, RT. 87%; (ii) $BF_3.Et_2O$, PhSeH, CH_2Cl_2, 0°C, 10 min. 60%; (iii) MsCl, Et_3N, CH_2Cl_2, RT. 84%; (iv) DBU, PhMe, 110°C, 21 h. 78%; (v) 9-BBN, THF, 68°C, 5 min then 3M KOH, 27.5% aq. H_2O_2, 0°C to RT, 5 min then 2-(phenylsulphonyl)-3-(*p*-nitrophenyl)oxaziridine, RT, 10 min, 92%; (vi) PDC, 4Å sieves, CH_2Cl_2, RT, ~12h. (**62**) 76%, (**63**) 20%; (vii) LiHMDS, THF, -78°C then MeI, -78°C to RT. 93%.

Acknowledgements: *We thank Dr. R.F. Newton, Glaxo Group Research, for the generous gift of (-)-bicyclo[3.2.0]hept-2-en-6-one and the SERC, Rohm and Haas Co., Spring House, Pennsylvania, USA and the ICI strategic Research Fund for financial support. We also acknowledge support from The Royal Commission for the Exhibition of 1851 for a research fellowship to JCA.*

Experimental

^1H and ^{13}C nmr spectra were recorded in $CDCl_3$ unless otherwise stated, using a Bruker WM 250, WH 400 or AM-500 nmr spectrometer, using residual protic solvent $\underline{C}HCl_3$ (δ_H=7.26 ppm) or $\underline{C}DCl_3$ (δ_C=77.0 ppm, t) as internal reference. Infra-red spectra were recorded on a Perkin-Elmer 983G spectrometer. Mass spectra were recorded using VG-7070B, VG 12-253 and VG ZAB-E instruments in the Imperial College Chemistry Department Mass Spectroscopy laboratory and the SERC Mass Spectrometry Service in Swansea. Microanalyses were performed in the Imperial College Chemistry Department microanalytical laboratory. Melting points were determined on a Reichert hot stage apparatus. Optical rotations were measured using an Optical Activity AA-1000 polarimeter. Molecular modelling was performed using the MACROMODEL package,[34] on an Evans and Sutherland PS-390 graphics terminal. Flash column chromatography was

performed on Merck Kieselgel 60 (230-400 mesh) unless otherwise stated. Florisil refers to 200-300 U.S. mesh Florisil as supplied by BDH Ltd. Diethyl ether, tetrahydrofuran and dimethoxyethane solvents were distilled from sodium benzophenone ketyl; dichloromethane from phosphorus pentoxide; toluene from sodium; acetonitrile and dimethyl sulphoxide from calcium hydride; methanol from magnesium; triethylamine and diisopropylamine from potassium hydroxide. Petrol refers to petroleum ether b.p. 40-60°C which was distilled prior to use as was ethyl acetate. Other solvents and reagents were purified by standard procedures[35] as necessary.(R)-MTPA[20] (Aldrich) was converted to the acid chloride by refluxing in thionyl chloride with a trace of sodium chloride, followed by Kugelrohr distillation. Analytical thin layer chromatography was performed using pre-coated glass-backed plates (Merck Kieselgel 60 F_{254}) and visualised by acidic ammonium molybdate (IV). Numbering for ^1H nmr assignments follows the systematic (IUPAC) nomenclature. Coupling constants are measured in hertz.

Preparation of (1*R, 4*R**, 5*S**)-4-hydroxy-2-oxabicyclo[3.2.1]octan-3-one (5).**
n-Butyllithium (13.4 ml of a 2.6 M solution in hexane, 34.8 mmol, 1.1 eq) was added dropwise to stirred diisopropylamine (4.89 ml, 34.9 mmol, 1.1 eq) under argon at room temperature. After 1h anhydrous tetrahydrofuran (20 ml) was added and the mixture cooled to -78°C. A solution of the lactone (4) (4.00 g, 31.7 mmol) in anhydrous tetrahydrofuran (40 ml) was added slowly and stirred at -78°C for 2.5h. The solution was treated with solid MoOPH complex (16.5 g, 38.1 mmol, 1.2 eq); the cooling bath removed and the reaction mixture allowed to warm to room temperature giving a characteristic green colour. Saturated sodium sulphite (100 ml) was added cautiously, giving a blue solution which was treated with brine (100 ml) and solid sodium chloride until a suspension was formed. The brine suspension was extracted with ether (7x100 ml), the combined ethereal extracts were dried ($MgSO_4$), filtered through a pad of silica gel and evaporated *in vacuo* to give a brown oil. The oil was purified by flash chromatography (75% ether-petrol) to give the *exo* alcohol (5) (3.00 g, 67%) as a white solid; m.p. 74-76°C; υ_{max} (film) 3398, 2950 and 1725 cm^{-1}; ^1H δ(400 MHz) 1.61 (2H, m, H-8), 1.98 (3H, m), 2.24 (1H, d, J 13.5, H-8'), 2.63 (1H, m, H-5), 2.92 (1H, br.s, OH), 4.00 (1H, s, H-4) and 4.94 (1H, s, H-1); *m/z* (EI^+) 126 (M^+-H_2O), 98 (M^+-CO_2) and 80 (M^+-H_2O-CO_2); (Found; C, 58.93; H, 6.95. $C_7H_{10}O_3$ requires C, 59.14; H, 7.09%).

Preparation of (1*R, 4*R**, 5*S**)-4-(*tert*-butyldimethylsilyloxy)-2-oxabicyclo[3.2.1]octan-3-one.** A solution of the alcohol (5) (2.88 g, 20.3 mmol) and imidazole (5.51 g, 81.0 mmol, 4 eq) in dry dimethylformamide (20 ml) was treated with *tert*-butyldimethylsilyl chloride (3.05 g, 20.3 mmol, 1 eq) and stirred at room temperature for 1h. The reaction mixture was partitioned between water (60 ml) and diethyl ether (200 ml), the aqueous layer was discarded and the organic solution washed sequentially with water (3x60 ml) and brine (2x60 ml). The ethereal solution was dried ($MgSO_4$) and evaporated *in vacuo* to give a yellow oil which was purified by flash chromatography (35% ether-petrol) to give the silyl ether (4.90 g, 94%) as a white solid; m.p. 48-49°C; υ_{max} (film) 2952, 2886, 2856 and 1745 cm^{-1}; ^1H δ(250 MHz) 0.41 (6H, d, $SiMe_2$), 0.81 (9H, s, Si^tBu), 1.40-1.55 (5H, m, including H-8), 2.35-2.48 (2H, m, H-5 and H-8'), 4.13 (1H, dd, J 2.5, 1.5, H-4) and 4.82 (1H, br.s, H-1); *m/z* (EI^+) 241 (M^+-Me) and 199 (M^+-^{t}Bu); (Found; C, 60.67; H, 9.63. $C_{13}H_{24}O_3Si$ requires C, 60.89; H, 9.43%).

Preparation of (1*R, 4*S**, 5*S**)-4-(*tert*-butyldimethylsilyloxy)-4-(prop-2-enyl)-2-oxabicyclo[3.2.1]octan-3-one (6).** n-Butyllithium (5.36 ml of a 2.2 M solution in hexane, 11.8 mmol, 1.2 eq) was added dropwise to a stirred solution of diisopropylamine (1.65 ml, 11.8 mmol, 1.2 eq) and potassium *tert*-butoxide (1.32 g, 11.8 mmol, 1.2 eq) in dry tetrahydrofuran (24 ml) at -78°C. The resultant pale yellow solution was stirred for 0.5h before a solution of the lactone (prepared above) (2.52 g, 9.83 mmol) in tetrahydrofuran (24 ml) was added dropwise and the mixture stirred for 0.5h. The enolate was treated with allyl bromide (1.28 ml, 14.7 mmol, 1.5 eq) and allowed to warm to room temperature. The reaction mixture was quenched by the addition of a few drops of water, the solvent evaporated *in vacuo*. Brine (40 ml) was added to the residue and extracted with ether (3x80 ml). The combined ethereal extracts were dried ($MgSO_4$), the solvent

removed by evaporation to give an oil which was purified by flash chromatography (5% ether-petrol) to give the allyl lactone (**6**) (2.43 g, 83%) as a white solid; m.p. 50-51°C; υ_{max} (film) 3077, 2953, 2854, 1740 and 1636 cm^{-1}; ^1H δ(250 MHz) 0.32 (6H, s, $SiMe_2$), 0.88 (9H, s, Si^tBu), 1.59 (1H, ddd, J 13.0, 5.5, 2.5, H-8), 1.71 (1H, dd, J 12.5, 6.5), 1.77-2.04 (2H, m), 2.11-2.25 [2H, m, (includes d, J 14.0, H-8')], 2.47 (1H, dd, J 14.0, 9.0, H-9'), 2.52 (1H, t, J 5.5, H-5), 2.65 (1H, ddt, J 14.0, 5.0, 1.5, H-9), 4.77 (1H, br.s, H-1), 5.10 (1H, br.d, J 17.0, H-11), 5.16 (1H, br.d, J 10.5, H-11') and 5.88 (1H, dddd, J 17.0, 10.5, 9.0, 5.0, H-10); *m/z* (EI^+) 297 (MH^+), 255 (M^+-$CH_2CH{=}CH_2$) and 239 (M^+-^{t}Bu); (Found; C, 65.13; H, 9.62. $C_{16}H_{28}O_3Si$ requires C, 64.82; H, 9.52%).

Preparation of (1*R, 4*S**, 5*S**)-4-(*tert*-butyldimethylsilyloxy)-4-(prop-2-enyl)-2-oxabicyclo[3.2.1]octan-3-ol (7).** Diisobutylaluminium hydride (15.90 ml of a 0.56 M solution in toluene, 8.90 mmol, 1.1 eq) was added dropwise over 6h to a stirred solution of the lactone (**6**) (2.34 g, 7.89 mmol) in dry toluene (140 ml) under argon at -78°C. The reaction mixture was treated with water (4 ml) dropwise and allowed to warm to room temperature, to give a gel. The gel was treated with alternating portions of solid sodium bicarbonate and magnesium sulphate until a paste was formed. The paste was manipulated with ethyl acetate and filtered under vacuum, the resulting powder was washed with ethyl acetate (4x150 ml). The solvent was evaporated in vacuo to give an oil which was purified by flash chromatography (25% to 60% ether-petrol) to give, in order of elution, the lactol (**7**) (1.35 g, 57%) as a white solid; m.p. 66-68°C; υ_{max} (film) 3366, 3050, 2954, 2855, 1734 and 1631 cm^{-1}; ^1H δ(250 MHz) 0.15 (6H, s, $SiMe_2$), 0.90 (9H, s, Si^tBu), 1.19 (1H, ddd, J 12.0, 5.5, 2.0, H-8), 1.48-2.03 (5H, m, H-6, H-6', H-7, H-7' and H-8'), 2.27-2.57 (4H, m, OH, H-5, H-9 and H-9'), 4.31 (1H, br.s, H-1), 4.71 (1H, d, J 7.5, H-3), 5.12 (2H, br.d, J 11.5, H-11 and H-11'), and 5.73-5.99 (1H, m, H-10); *m/z* (EI^+) 298 (M^+), 269 (M^+-CHO), 241 (M^+-^{t}Bu) and 223 (M^+-H_2O-^{t}Bu); (Found; C, 64.67; H, 10.13. $C_{16}H_{30}O_3Si$ requires C, 64.38; H, 10.13%); and the diol (0.35 g, 23%) as a white solid; m.p. 91-92°C; υ_{max} (film) 3315, 3049, 2941 and 1640 cm^{-1}; ^1H δ(250 MHz) 0.16 (6H, s, $SiMe_2$), 0.90 (9H, s, Si^tBu), 1.50-2.00 (8H, m, $-CH_2-$), 2.10 (1H, q, J 9.0, H-2), 2.31 (1H, dd, J 13.5, 7.5, H-3"), 2.53 (1H, dd, J 13.5, 7.5, H-3'), 3.55 (2H, br.s, 2xOH), 4.24 (1H, br.quin. J 5.0, H-1), 5.07 (1H, br.d, J 11.0, H-5"), 5.12 (1H, br.d, J 17.5, H-5') and 5.82 (1H, ddt, J 17.5, 11.0, 7.5, H-4'); *m/z* (EI^+) 269 (M^+-CH_2OH), 241 and 225 (M^+-H_2O-^{t}Bu); (Found; C, 64.00; H, 10.93. $C_{16}H_{32}O_3Si$ requires C, 63.95; H, 10.74%).

Preparation of (1*R, 4*S**, 5*S**)-4-(*tert*-butyldimethylsilyloxy)-3-methoxy-4-(prop-2-enyl)-2-oxabicyclo[3.2.1]octane (8).** Concentrated sulphuric acid (4 drops) was added to a solution of the lactol (**7**) (51.3 mg, 0.17 mmol) in anhydrous methanol (5 ml) and stirred at room temperature until no more starting material was present by thin layer chromatographic analysis. Solid sodium bicarbonate (100 mg, 1.19 mmol) was added, the solvent removed by evaporation and the residue treated with saturated aqueous sodium bicarbonate (5 ml). The aqueous solution was extracted with ether (3x10 ml), the combined ethereal extracts were dried ($MgSO_4$), filtered and the solvent removed by evaporation *in vacuo* to give an oil which was purified by flash chromatography (35% ether-petrol) to give an epimeric mixture of the methoxy acetals (**8**) (31.7 mg, 60%) as a clear colourless oil; υ_{max} (film) 3074, 2954, 2854 and 1636 cm^{-1}; ^1H δ(250 MHz) for the major isomer only, 0.07 (6H, s, $SiMe_2$), 0.89 (9H, s, Si^tBu), 1.17 (1H, ddd, J 12.0, 5.5, 2.5, H-8), 1.40-2.06 (5H, m, H-6, H-6', H-7, H-7' and H-8'), 2.12-2.62 (3H, m, H-5, H-9 and H-9'), 3.43 (3H, s, OMe), 4.27 (1H, s, H-3), 4.33 (1H, br.s, H-1), 5.09 (2H, d, J 14.0, H-11 and H-11') and 5.89 (1H, m, H-10); *m/z* (EI^+) 312 (M^+), 297 (M^+-Me), 281 (M^+-$CH_2CH{=}CH_2$), 255 (M^+-^{t}Bu) and 252 (M^+-2Me); (Found; C, 65.37; H, 10.62. $C_{17}H_{32}O_3Si$ requires C, 65.33; H, 10.32%).

Preparation of (1*R, 4*S**, 5*S**)-4-(*tert*-butyldimethylsilyloxy)-4-(2-hydroxyethyl)-3-methoxy-2-oxabicyclo[3.2.1]octane (9).** Ozone was bubbled through a solution of the methoxy acetal (**8**) (29 mg, 93.0 μmol) in methanol (5 ml) at -78°C until the solution turned blue. The mixture was purged with oxygen to remove excess ozone, allowed to warm to room temperature and treated with small portions of sodium borohydride until the reaction was complete by thin layer chromatographic analysis. The solvent was removed by evaporation *in vacuo* and the residue purified by flash chromatography (50% ether-petrol) to give a mixture of the two alcohols (**9**) (25.9 mg, 88%) as a white solid; m.p. 85-87°C; υ_{max} (film) 3425, 2954 and

2854 cm^{-1}; ^1H δ(250 MHz) for the major isomer only, 0.08 (3H, s, $SiMe_2$), 0.15 (3H, s, $SiMe_2$), 0.89 (9H, s, Si^tBu), 1.27 (1H, ddd, J 12.5, 5.5, 2.5, H-8), 1.50-2.08 (8H, m), 2.29 (1H, br.t, J 5.5, H-5), 3.43 (3H, s, OMe), 3.69-3.91 (2H, m, H-10 and H-10'), 4.25 (1H, s, H-3) and 4.36 (1H, br.s, H-1); *m/z* (EI^+) 240 (M^+-CH_2CH_2OH-OMe), 228 (M^+-^{t}Bu-OMe), 214 (M^+-CH_2CH_2OH-^{t}Bu), 199 and 183 (M^+-CH_2CH_2OH-OMe-^{t}Bu); (Found; C, 60.65; H, 10.32. $C_{16}H_{32}O_4Si$ requires C, 60.71; H, 10.19%).

Preparation of (1*R, 3*S**, 7*S**, 8*S**)-7-(*tert*-butyldimethylsilyloxy)-2,4-dioxatricyclo-[6.2.1.0^{3,7}]undecane (10).** A few grains of Amberlyst 15 sulphonic acid ion exchange resin was added to a a solution of the alcohol (**9**) (179 mg, 0.57 mmol) in anhydrous acetonitrile (6 ml) at room temperature for 50 min. The mixture was filtered, the solvent removed by evaporation *in vacuo* and the residue purified by flash chromatography (25% ether-petrol) to give the silyl protected tricyclic furan acetal (**10**) (104 mg, 64%) as a white solid; m.p. 50-51°C; υ_{max} (film) 2954, 2929, 2894 and 2854 cm^{-1}; ^1H δ(250 MHz) 0.14 (6H, s, $SiMe_2$), 0.90 (9H, s, Si^tBu), 1.35 (1H, ddd, J 12.5, 5.0, 2.5, H-11), 1.55-2.01 (5H, m), 2.23 (1H, m), 2.37 (1H, ddd, J 13.5, 9.0, 8.0), 2.51 (1H, t, J 5.5, H-8), 4.12-4.23 (2H, m, H-5 and H-5'), 4.33 (1H, br.s, H-1) and 4.85 (1H, s, H-3); *m/z* (EI^+) 284 (M^+), 269 (M^+-Me), 239 and 227 (M^+-^{t}Bu); (Found; C, 63.58; H, 8.34. $C_{15}H_{28}O_3Si$ requires C, 63.57; H, 8.30%).

Preparation of (1*R, 3*S**, 7*S**, 8*S**)-7-hydroxy-2,4-dioxatricyclo-[6.2.1.0^{3,7}]undecane (2).** Tetra-n-butylammonium fluoride (486 μl of a 1 M solution in tetrahydrofuran, 0.486 mmol, 1.5 eq) was added to a solution of the silylether (**10**) (92 mg, 0.32 mmol) in tetrahydrofuran (5 ml) and stirred at room temperature until the reaction was complete by chromatographic analysis. The solvent was removed by evaporation *in vacuo* and the residue purified by flash chromatography (80% ether-petrol) to give the tricyclic furan acetal (**2**) (39 mg, 71%) as a white solid; m.p. 77-78°C; υ_{max} (film) 3434 and 2959 cm^{-1}; ^1H δ(250 MHz) 1.40 (1H, ddd, J 12.5, 5.0, 3.0, H-11), 1.81 (4H, m), 2.02 [2H, m, (includes ddd, J 9.0, 5.0, 3.0, H-6')], 2.17 (1H, m), 2.43 (1H, ddd, J 13.5, 8.0, 8.0, H-6), 2.58 (1H, t, J 5.5, H-8), 4.20 (1H, d, J 6.0, H-5'), 4.22 (1H, d, J 7.0, H-5), 4.38 (1H, br.s, H-1) and 4.58 (1H, s, H-3); ^{13}C δ(22.51 MHz) 103.9 (C3), 81.4 (C7), 76.1 (C1), 68.5 (C5), 41.8 (C8), 35.8, 37.1, 28.7 and 24.5; *m/z* (EI^+) 170 (M^+); (Found; C, 63.44; H, 9.95. $C_9H_{14}O_2$ requires C, 63.33; H, 9.92%).

Preparation of (1*R, 3*R**, 7*S**, 8*S**)-7-(*tert*-butyldimethylsilyloxy)-2,4-dioxatricyclo[6.2.1.0^{3,7}]undecan-5-ol (11).** Ozone was bubbled through a solution of the lactol (**7**) (100 mg, 0.34 mmol) in dichloromethane (10 ml) at -78°C until the solution turned pale blue. The mixture was purged with oxygen to remove excess ozone, allowed to warm to room temperature and treated with triphenylphosphine (98 mg, 0.37 mmol, 1.1eq), with stirring for 4h. The solvent was removed by evaporation *in vacuo* and the residue purified by flash chromatography (70% ether-petrol) to give the epimeric acetal lactols (**11**) (94 mg, 93%) as a white solid; m.p. 75-78°C; υ_{max} (film) 3418, 2954 and 2854 cm^{-1}; ^1H δ(250 MHz) for the major isomer only, 0.14 (6H, 2s $SiMe_2$), 0.86 (9H, s, Si^tBu), 1.35 (1H, ddd, J 13.0, 5.0, 2.5, H-11), 1.50-2.60 (8H, m), 3.22 (1H, br.s, OH), 4.37 (1H, br.s, H-1), 4.81 (1H, s, H-3) and 5.68 (1H, t, J 5.0, H-5); *m/z* (EI^+) 283 (M^+-OH), 271 (M^+-CHO), 267 (M^+-Me-H_2O), 243 (M^+-^{t}Bu) and 225 (M^+-H_2O-^{t}Bu); (Found; C, 59.77; H, 9.62. $C_{15}H_{28}O_4Si$ requires C, 59.96; H, 9.39%).

Preparation of (1*R, 3*R**, 7*S**, 8*S**)-7-(*tert*-butyldimethylsilyloxy)-5-phenylsulphide-2,4-dioxatricyclo[6.2.1.0^{3,7}]undecane (12).** Activated 4Å molecular sieves (2.00 g), Amberlyst 15 sulphonic acid ion exchange resin (0.71 g) and thiophenol (0.82 ml, 7.99 mmol, 3.0eq) were sequentially added to a stirred solution of the acetal lactols (**11**) (0.80 g, 2.66 mmol) in anhydrous acetonitrile (20 ml) at room temperature under argon. After 0.5h the mixture was filtered, the solvent removed by evaporation *in vacuo* and the residue purified by flash chromatography (5% ether-petrol) to give the epimeric sulphides (**12**) (884 mg, 85%) as a clear colourless oil; υ_{max} (film) 2952, 2928, 2854 and 1583 cm^{-1}; ^1H δ(250 MHz) for the least polar isomer only, 0.18 (6H, 2s, $SiMe_2$), 0.90 (9H, s, Si^tBu), 1.41 (1H, ddd, J 13.0, 5.0, 2.5, H-11), 1.51-2.55 [7H, m, (includes 2.29, dd, J 14.5, 6.5, H-6')], 2.78 (1H, dd, J 14.5, 8.5, H-6), 4.39 (1H, br.s, H-1), 5.04 (1H, s, H-3), 5.72 (1H, m, H-5), 7.27 (3H, m, *m*- and *p*-Ph) and 7.52 (2H, m, *o*-Ph); *m/z* (EI^+) 392 (M^+), 335 (M^+-^{t}Bu) and 283 (M^+-SPh); (Found; C, 64.26; H, 8.16. $C_{21}H_{32}O_3SSi$ requires C, 64.24; H, 8.22%).

Preparation of (1*R, 3*R**, 7*S**, 8*S**)-7-(*tert*-butyldimethylsilyloxy)-5-phenylsulphoxide-2,4-dioxatricyclo[6.2.1.0^{3,7}]undecane (13).** A solution of *m*-chloroperbenzoic acid (486 mg of 80%, 2.25 mmol, 1.0eq) in dichloromethane (45 ml) was added dropwise to a stirred solution of the sulphides (12) (884 mg, 2.25 mmol) in dichloromethane at 0°C in air. The organic solution was washed with saturated aqueous sodium bicarbonate (2x20 ml) and water (10 ml), dried ($MgSO_4$), filtered and the solvent evaporated *in vacuo*. The residue was purified by flash chromatography (60% ether-petrol) to give only three sulphoxides (13) (658 mg, 72%), the main diastereoisomer as a white solid; m.p. 102-103°C; υ_{max} (film) 3058, 2954 and 2857 cm^{-1}; ^{1}H δ(250 MHz) for the major diastereoisomer only, 0.07 (6H, 2s, $SiMe_2$), 0.82 (9H, s, Si^{t}Bu,),1.44 (1H, ddd, J 12.5, 5.0, 2.5 H-11), 1.56-2.00 (3H, m), 2.12-2.27 (2H, m), 2.32 (1H, dd, J 15.0, 8.0, H-6'), 2.56 (1H, t, J 5.5, H-8), 3.02 (1H, dd, J 15.0, 6.0, H-6), 4.46 (1H, br.s, H-1), 4.72 (1H, dd, J 8.0, 6.0, H-5), 4.91 (1H, s, H-3), 7.53 (3H, m, *m*- and *p*-Ph) and 7.71 (2H, m, *o*-Ph); *m/z* (EI$^+$) 392 (M$^+$-O), 283 (M$^+$-SOPh), 253 (M$^+$-SOPh-2Me) and 225 (M$^+$-SOPh-^{t}Bu); (Found; C, 61.58; H, 7.92. $C_{21}H_{32}O_4Si$ requires C, 61.72; H, 7.89%).

Preparation of (1*R, 3*S**, 7*R**, 8*S**)-7-(*tert*-butyldimethylsilyloxy)-2,4-dioxatricyclo[6.2.1.0^{3,7}]undec-5-ene (14).** Triethylamine (1.12 ml, 8.07 mmol, 5.0eq) and the sulphoxides (13) (658 mg, 1.61 mmol) were refluxed for 10 min in anhydrous toluene. The solvent was removed by evaporation *in vacuo* and the residue purified by flash chromatography (3% ether-petrol) to give the silyloxytricycle (14) (455 mg, 99%) as a clear colourless oil; υ_{max} (film) 2932, 2857 and 1611 cm^{-1}; ^{1}H δ(250 MHz) 0.03 (6H, 2s, $SiMe_2$), 0.84 (9H, s, Si^{t}Bu),1.34 (1H, ddd, J 16.0, 7.0, 5.3, H-11), 1.56 (1H, m, H-11'), 1.65-1.93 (3H, m, H-9, H-9' and H-10'), 2.22-2.38 (2H, t, J 7.5, H-8 and H-10), 4.25 (1H, m, H-1), 5.01 (1H, d, J 3.0, H-6), 5.15 (1H, s, H-3) and 6.42 (1H, d, J 3.0, H-5); *m/z* (EI$^+$) 282 (M$^+$), 267 (M$^+$-Me) and 225 (M$^+$-^{t}Bu); [Found (M$^+$) 282.1659. $C_{15}H_{26}O_3Si$ requires 282.1651].

Preparation of (1*R, 3*S**, 7*R**, 8*S**)2,4-dioxatricyclo[6.2.1.0^{3,7}]undec-5-ene (3).** Tetra-n-butylammonium fluoride (4.83 ml of a 1 M solution in tetrahydrofuran, 4.83 mmol, 3eq) was added to a solution of the silylether (14) (455 mg, 1.61 mmol) in tetrahydrofuran (10 ml) and stirred at room temperature for 1h. The solvent was removed by evaporation *in vacuo* and the residue purified by flash chromatography (60% ether-petrol) to give the tricycle (3) (207 mg, 76%) as a white solid; m.p. 66-67°C; υ_{max} (film) 3430, 3101, 2939 and 1611 cm^{-1}; ^{1}H δ(500 MHz) 1.42 (1H, ddd, J 12.6, 5.5, 2.9, H-11), 1.63-1.72 (2H, m, H-9eq and OH), 1.78-1.87 (2H, m, H-10eq and H-11'), 1.90-1.96 (1H, m, H-9ax), 2.25 (1H, dddd, J 13.5, 9.2, 4.4, 2.0, H-10ax), 2.47 (1H, t, J 5.8, H-8), 4.32 (1H, m, H-1), 5.12 (1H, d, J 2.7, H-6), 5.28 (1H, s, H-3) and 6.50 (1H, d, J 2.7, H-5); ^{13}C δ(22.51 MHz) 148.4 (C5), 107.5, 106.0 (C3 and C6), 82.6 (C7), 74.2 (C1), 40.6, 34.7, 30.1 and 23.5; *m/z* (EI$^+$) 168 (M$^+$), 139 (M$^+$-CHO) and 127 (M$^+$-CH=CHCH$_2$); (Found; C, 64.14; H, 6.93. $C_9H_{12}O_3$ requires C, 64.27; H, 7.19%).

For the enantiomerically pure material $[\alpha]_D^{20}$=-193.0 (c=1.13, chloroform).

Preparation of (1*S*, 2*S*, 4*S*, 5*S*)-5-(*tert*-butyldimethylsilyloxy)bicyclo[2.2.1]-heptan-2-ol. Sodium borohydride (5.4 g, 143 mmol, 1.5eq) was added portionwise to a stirred solution of the tricycle (16) (22.68 g, 95.1 mmol) in methanol. Water (10 ml) was added cautiously and the organic solvent removed by evaporation *in vacuo*. The residue was added to water (100 ml) and extracted with dichloromethane (4x200 ml). The combined organic extracts were dried ($MgSO_4$), filtered and the solvent removed by evaporation *in vacuo* to give an oil which was purified by flash chromatography (10% ether-petrol) to give the bicyclic alcohol (19.50 g, 85%) as a white amorphous solid; m.p. 36-37°C; $[\alpha]_D^{20}$=-10.5 (c=0.21, chloroform); υ_{max} (film) 3362, 2953, 2857, 1462, 1360, 1252, 1130, 1085 and 937 cm^{-1}; ^{1}H δ(500 MHz) 0.03 (3H, s, $SiMe_2$), 0.05 (3H, s, $SiMe_2$), 0.89 (9H, s, Si^{t}Bu), 1.40 (1H, br.s, OH), 1.53 (1H, dt, J 13.5, 2.8 Hz, H-7), 1.65-1.78 (5H, m, H-3, H-3', H-6, H-6' and H-7'), 2.14 (1H, dd, J~4.0 Hz, H-4), 2.22 (1H, dd, J~4.0 Hz, H-1) and 4.20-4.24 (2H, m, H-2 and H-5); *m/z* (EI$^+$) 227 (M$^+$-Me), 185 (M$^+$-^{t}Bu), 209 (M$^+$-Me-H_2O), 93 (C_7H_9) and 75 (C_2H_7OSi); (Found; C, 64.52; H, 10.84. $C_{13}H_{26}O_2Si$ requires C, 64.41; H, 10.81%).

Preparation of (1*S*, 4*S*, 5*S*)-5-(*tert*-butyldimethylsilyloxy)bicyclo[2.2.1]heptan-2-one. Dichloromethane (500 ml) was cooled, under argon with stirring, to between -60 and -70°C. Oxalyl chloride (8.37 ml, 96.0 mmol, 1.2eq) was added and treated with dimethylsulphoxide (13.6 ml, 192.0 mmol, 2.4eq)

added by syringe over 5 min. The resultant solution was stirred for 5 min and a solution of the bicyclic alcohol (prepared above) (19.39 g, 80.0 mmol) in dichloromethane (80 ml) added to give a white precipitate which was stirred for 20 min. Triethylamine (63 ml, 453 mmol, 5.7eq) was added and the reaction allowed to warm to room temperature. The mixture was concentrated by evaporation *in vacuo* to give a white sludge which was partitioned between ether (500 ml) and water (300 ml) and shaken vigorously. The aqueous layer was removed and the organic layer washed sequentially with dilute hydrochloric acid (200 ml) and brine (2x200 ml). The ethereal solution was dried ($MgSO_4$), filtered and the solvent removed by evaporation *in vacuo* to give an oil which was purified by flash chromatography (10% ether-petrol) to give the bicyclic ketone (17.84 g, 93%) as a clear colourless oil; $[\alpha]_D^{20}$=-13.5 (c=0.26, chloroform); υ_{max} (film) 2955, 2930, 2886, 2857, 1747, 1463, 1404, 1369, 1256, 1183, 1143, 1120, 1100, 1063, 1022, 1007 and 941 cm^{-1}; ^1H δ(500 MHz) 0.04 (6H, 2s, $SiMe_2$), 0.87 (9H, s, Si^tBu), 1.24 (1H, dt, J 13.5, 3.3, H-6ax), 1.64 (1H, br.d, J 10.8, H-7eq), 1.72 (1H, br.d, J 10.7, H-7ax), 1.91 (1H, ddd, J 17.9, 4.7, 0.8, H-3ax), 2.18 (1H, ddd, J 14.2, 8.9, 5.3, H-6eq), 2.50 (1H, br.d, J 5.1, H-1), 2.57-2.61 (1H, m, H-4), 2.59 (1H, dd, J 17.9, 4.2, H-3eq) and 4.38 (1H, m, H-5); *m/z* (EI^+) 240 (M^+), 225 (M^+-Me), 183 (M^+-^{t}Bu), 75 (C_2H_7OSi); (Found; C, 65.08; H, 10.22. $C_{13}H_{24}O_2Si$ requires C, 64.95; H, 10.06%).

Preparation of (1*R*, 5*S*, 6*S*)-6-(*tert*-butyldimethylsilyloxy)-2-oxabicyclo[3.2.1]octan-3-one (17). *p*-Toluenesulphonic acid monohydrate (141 mg, 0.74 mmol, 1mol%) and *m*-chloroperbenzoic acid (24.0 g of 80%, 111 mmol, 1.5eq) were added sequentially to a stirred solution of the bicyclic ketone (prepared above) (17.8 g, 74.0 mmol) in dichloromethane (400 ml). After 4h at room temperature the organic solution was washed sequentially with saturated aqueous sodium bicarbonate-10% sodium sulphite (1:2, 300 ml), water (100 ml) and brine (2x100 ml). The organic phase was then dried ($MgSO_4$), filtered and the solvent removed *in vacuo* to give a clear oil which was purified by flash chromatography (35% ether-petrol) to give the bicyclic lactone (**17**) (16.71 g, 87%) as a white amorphous solid; m.p. 149-151 °C; $[\alpha]_D^{20}$=-6.9 (c=0.31, chloroform); υ_{max} (film) 2954, 2856, 1727, 1462, 1377, 1260, 1188, 1114, 1091 and 1008 cm^{-1}; ^1H δ(500 MHz) 0.05 (6H, 2s, $SiMe_2$), 0.88 (9H, s, Si^tBu), 1.67 (1H, br.d, J 13.2, H-8eq), 1.81 (1H, dt, J 15.5, 4.0, H-7ax), 2.02 (1H, dd, J 13.1, 3.6, H-8ax), 2.30 (1H, ddd, J 15.3, 10.0, 5.3, H-7eq), 2.41 (1H, br.s, H-5), 2.51 (1H, ddd, J 18.6, 5.7, 0.8, H-4eq), 3.10 (1H, dt, J 18.5, 1.7, H-4ax), 4.38 (1H, dt, J 9.8, 4.9, H-6) and 4.69 (1H, m, H-1); *m/z* (EI^+) 256 (M^+), 241 (M^+-Me), 221, 199 (M^+-^{t}Bu), 169, 155, 125 and 75 (C_2H_7OSi); (Found; C, 61.12; H, 9.73. $C_{13}H_{24}O_3Si$ requires C, 60.89; H, 9.45%).

Preparation of (1*S*, 4*R*, 5*S*, 6*S*)-6-(*tert*-butyldimethylsilyloxy)-4-hydroxy-2-oxabicyclo[3.2.1]octan-3-one. n-Butyllithium (30.9 ml of a 2.5 M solution in hexane, 77.3 mmol, 1.2eq) was added dropwise, *via* syringe, to a stirred solution of diisopropylamine (10.82 ml, 77.2 mmol, 1.2eq) under argon at room temperature. After 1 h anhydrous tetrahydrofuran (150 ml) was added and the mixture cooled to -78°C. A solution of the lactone (**17**) (16.50 g, 64.4 mmol) in anhydrous tetrahydrofuran (150 ml) was added dropwise *via* cannula and the mixture stirred at -78°C for 2 h. MoOPH complex (33.53 g, 77.2 mmol, 1.2eq) was added giving a crimson/red colour; the cooling bath was removed, the reaction mixture allowed to warm to room temperature and stirred for 15 min to give a characteristic green colour. Sodium sulphite 10% aqueous (200 ml) was added cautiously with stirring followed by extraction with diethyl ether (3x300 ml). The combined ethereal extracts were washed sequentially with water (200 ml), 1M hydrochloric acid (200 ml) and brine (2x200 ml). The solution was dried ($MgSO_4$), filtered through a short pad of silica gel and the solvent removed *in vacuo*. The residue was purified by dissolving in dichloromethane (500 ml), stirring with activated charcoal for 0.5 h, filtering through florisil and removing the solvent *in vacuo* to give a clear oil which was purified by flash chromatography (35% ether-petrol) to give the α-hydroxylactone (13.30 g, 76%) as white plates; m.p. 90-91 °C; $[\alpha]_D^{20}$=+41.7 (c=0.52, chloroform); υ_{max} (film) 3465, 2950, 2930, 2858, 1724, 1463, 1378, 1303, 1252, 1239, 1211, 1181, 1137, 1110, 1078, 1051, 1006, 981, 959 and 902 cm^{-1}; ^1H δ(500 MHz) 0.66 (3H, s, $SiMe_2$), 0.85 (3H, s, $SiMe_2$), 0.89 (9H, s, Si^tBu), 1.57 (1H, br.d, J 13.5 Hz, H-8eq), 1.70 (1H, dt, J 15.6, 4.1 Hz, H-7ax), 2.16 (1H, dd, J 13.5, 3.5 Hz, H-8ax), 2.35 (1H, ddd, J 15.3, 10.1, 5.2 Hz, H-7eq), 2.56 (1H, br.t, J 5.0 Hz, H-5), 2.69 (1H, d, J 1.6, OH), 4.44 (1H, ddd, J 10.3, 5.8, 4.6 Hz, H-6), 4.62 (1H, d, J 1.3 Hz, H-4) and 4.77 (1H, m, H-1); *m/z* (EI^+) 272 (M^+), 257 (M^+-Me),

241, 223, 215 (M^+-^{t}Bu), 199, 187, 179, 171, 153, 131, 84 and 75 (C_2H_7OSi); (Found; C, 57.08; H, 9.15. $C_{13}H_{24}O_4Si$ requires C, 57.32; H, 8.88%).

Preparation of (1*S*, 5*R*, 6*S*)-6-(*tert*-butyldimethylsilyloxy)-2-oxabicyclo[3.2.1]octan-2,3-dione (18). Dimethylsulphoxide (4.48 ml, 63.1 mmol, 2.1eq) was added dropwise, *via* syringe, to a stirred solution of oxalyl chloride (2.75 ml, 31.6 mmol, 1.1eq) in anhydrous dichloromethane (250 ml) at between -60 and -65°C, under argon, over 5 min. The resultant solution was stirred for 5 min before the addition of the alcohol (prepared above) (8.00 g, 29.4 mmol), *via* cannular, as a solution in anhydrous dichloromethane (25 ml). The resultant white precipitate was stirred for 20 min, triethylamine (20.72 ml, 149 mmol, 5.1eq) was added and the reaction allowed to warm to room temperature. The mixture was concentrated by evaporation *in vacuo* to give a white sludge which was dissolved in ethyl acetate (600 ml) and washed sequentially with water (100 ml) and brine (2x100 ml). The organic phase was dried ($MgSO_4$), filtered and the solvent removed *in vacuo* to give an oil which was purified by flash chromatography (60% ether-petrol) to give the α-ketolactone (**18**) (6.11 g, 77%) as white plates; m.p. 108-109 °C; $[\alpha]_D^{20}$=+105.8 (c=0.66, chloroform); υ_{max} (film) 2949, 2855, 1737, 1461, 1366, 1310, 1260, 1196, 1154, 1111, 1069, 971 and 917 cm^{-1}; ^1H δ(500 MHz) 0.06 (6H, s, $SiMe_2$), 0.82 (9H, s, Si^{t}Bu), 2.10 (1H, ddd, J 14.3, 4.9, 2.7, H-8), 2.17 (1H, dt, J 15.6, 2.9, H-7), 2.44 (2H, m, H-7 and H-8), 3.52 (1H, ddd, J 6.5, 5.0, 1.6, H-5), 4.79 (1H, ddd, J 9.3, 6.8, 2.5, H-6), and 5.00 (1H, br.s, H-1); *m/z* (EI^+) 270 (M^+), 255 (M^+-Me), 237 (M^+-Me-H_2O), 227 (MH^+-CO_2), 214 (MH^+-^{t}Bu), 169, 75 (C_2H_7OSi); (Found; C, 57.90; H, 8.40. $C_{13}H_{22}O_4Si$ requires C, 57.75; H, 8.20%).

Preparation of (1*S*, 4*S*, 5*R*, 6*S*)-6-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(prop-2-enyl)-2-oxabicyclo[3.2.1]octan-3-one (19) and (1*S*, 4*S*, 5*R*, 7*S*)-4-(*tert*-butyldimethylsilyloxy)-7-hydroxy-4-(prop-2-enyl)-2-oxabicyclo[3.3.0]octan-3-one (20). n-Butyllithium [888 μl of a 2.5 M solution in hexane, 2.22 mmol, 1.1 eq wrt (**18**)] was added dropwise to a stirred solution of allyl tri-n-butyltin [689 μl, 2.22 mmol, 1.1 eq wrt (**18**)] at -78°C under argon over 5 min. This was then added dropwise, *via* cannular, to a stirred solution of the α-ketolactone (**18**) (546 mg, 2.02 mmol) in anhydrous tetrahydrofuran (8 ml + 1 ml washing) at -78°C under argon. The mixture was stirred for 5 min at -78°C then allowed to warm to 15°C over 10 min. The reaction was quenched by the addition of saturated aqueous sodium bicarbonate (5 ml), stirred for 5 min. and then extracted with ether (40 ml, 3x25 ml). The combined ethereal layers were washed sequentially with 10% aqueous sodium fluoride (20 ml) and brine (20 ml). The ethereal extract was then dried ($MgSO_4$), filtered and evaporated *in vacuo* to give a yellow oil which was purified by flash chromatography (gradient elution: 50% to 65% ether-petrol) to give the desired alcohol (**19**) and the *cis* fused 5.5-bicyclic alcohol (**20**) (3:2, 533 mg, 84%) as a clear oil. A small amount was purified by flash chromatography, as above, to give the two isomerically pure compounds.

Data for (1*S*, 4*S*, 5*R*, 6*S*)-6-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(prop-2-enyl)-2-oxabicyclo[3.2.1]octan-3-one (19). mp. 63-64.5°C; $[\alpha]_D^{20}$=+51.9 (c=0.42, chloroform); υ_{max} (film) 3432, 2929, 2857, 1742, 1463, 1368, 1254, 1121, 1063, 1017, 968 and 913 cm^{-1}; ^1H δ(500 MHz) 0.11 (3H, s, $SiMe_2$), 0.13 (3H, s, $SiMe_2$), 0.91 (9H, s, Si^{t}Bu), 1.62 (1H, ddd, J 13.8, 5.0, 2.5, H-8eq), 1.97 (1H, dt, J 15.4, 4.1, H-7ax), 2.29 (1H, dd, J 13.5, 3.0, H-8ax), 2.38 (1H, ddd, J 15.2, 10.2, 5.0, H-7eq), 2.47 (1H, ddt, J 14.5, 8.9, 1.0, H-9), 2.64 (1H, br.t, J 5.5, H-5), 2.68 (1H, dd, J 14.6, 5.6, H-9), 4.65-4.69 (2H, m, H-1 and H-6), 5.13 (1H, br.d, J 17.3, H-11), 5.19 (1H, br.d, J 10.1, H-11'), 5.72 (1H, dd, J 2.1, 0.7, OH) and 5.99 (1H, m, H-10); *m/z* (EI^+) 312 (M^+), 297 (M^+-Me), 285 (M^+-$CH{=}CH_2$), 279, 271 (M^+-$CH_2CH{=}CH_2$), 255 (M^+-^{t}Bu), 227 (M^+-CO_2-$CH_2CH{=}CH_2$), 211 (M^+-^{t}Bu-CO_2), 189 and 75 (Me_2SiOH); (Found; C, 61.33; H, 9.34. $C_{16}H_{28}O_4Si$ requires C, 61.50; H, 9.03%).

Data for (1*S*, 4*S*, 5*R*, 7*S*)-4-(*tert*-butyldimethylsilyloxy)-7-hydroxy-4-(prop-2-enyl)-2-oxabicyclo[3.3.0]octan-3-one (20) mp. 48-50°C; $[\alpha]_D^{20}$= -2.0 (c=0.64, chloroform), υ_{max} (film) 3422, 3078, 2954, 2929, 2856, 1769, 1639, 1462, 1432, 1359, 1254, 1194, 1143, 1081, 1026, 1005, 972 and 917 cm^{-1}; ^1H δ(500 MHz) 0.08 (3H, s, $SiMe_2$), 0.19 (3H, s, $SiMe_2$), 0.86 (9H, s, Si^{t}Bu), 1.57 (1H, br.s, OH), 1.62 (1H, dddd, J 14.3, 7.6, 5.4, 1.2, H-6*endo*), 2.03-2.11 (2H, m, H-6*exo* and H-8*endo*), 2.18 (1H, dtd, J 15.0, 6.0, 0.6, H-8*exo*), 2.34 (1H, ddt, J 15.6, 8.0, 1.1, H-9), 2.68 (1H, ddd, J 9.2, 8.1, 5.4, H-5), 2.76 (1H, ddt, J 15.6, 7.3, 1.7, H-9), 4.37 (1H, m, H-7), 4.98 (1H, td, J 5.6, 1.0, H-1), 5.16 (1H, t, J 1.4, H-

11'), 5.89 (1H, ddd, J 6.9, 3.1, 1.7, H-11) and 5.89 (1H, m, H-10); *m/z* (EI$^+$) 313 (MH$^+$), 297 (M$^+$-Me), 285, 271 (M$^+$-$CH_2CH{=}CH_2$), 255 (M$^+$-^{t}Bu), 237 (M$^+$-^{t}Bu-H_2O), 227 (M$^+$-CO_2-$CH_2CH{=}CH_2$), 211 (M$^+$-^{t}Bu-CO_2), 193 (M$^+$-^{t}Bu-CO_2-H_2O), 171, 127 and 75 (Me_2SiOH); (Found: C, 61.82; H, 9.18. $C_{16}H_{28}O_4Si$ requires C, 61.50; H, 9.03%).

Preparation of (1*S*, 4*S*, 5*R*, 7*S*)-4-(*tert*-butyldimethylsilyloxy)-7-hydroxy-4-(prop-2-enyl)-2-oxabicyclo[3.3.0]octan-3-one (20). n-Butyllithium [316 µl of a 2.5 M solution in hexane, 0.790 mmol, 1.2 eq wrt (**18**)] was added dropwise, *via* syringe, to a magnetically stirred solution of allyl tri-n-butyltin [245 µl, 0.790 mmol, 1.2 eq wrt (**18**)] in anhydrous tetrahydrofuran (2 ml) at -78°C under argon. After 5 min the lemon yellow allyl lithium was added dropwise, *via* cannular, to a stirred solution of the α-ketolactone (**18**) (178 mg, 0.658 mmol) in anhydrous tetrahydrofuran (2 ml) at -78°C, under argon. Five minutes after complete addition the golden yellow reaction mixture was warmed to 0°C (ice bath) over five minutes and anhydrous hexamethylphosphoramide (600 µl, ~15% vol. of tetrahydrofuran) added smoothly *via* syringe. After 5 min the now orange reaction mixture was quenched by the addition of saturated aqueous ammonium chloride (1 ml) with vigorous stirring for 15 min. Water (4 ml) was added and the mixture extracted with ether (30 ml, 3x20 ml), dried ($MgSO_4$), filtered and evaporated to dryness *in vacuo*. The resultant yellow oil was purified by flash chromatography (gradient elution: 50% to 70% ether-petrol) to give the *cis* fused 5.5-bicyclic alcohol (**20**) (138 mg, 67 %) as an amorphous white solid. The physical data of this compound was in exact agreement with that prepared earlier.

Preparation of (1*S*, 4*S*, 5*S*, 7*S*)-4,7-dihydroxy-4-(prop-2-enyl)-2-oxabicyclo[3.3.0]octan-3-one (22). Tetra-n-butylammonium fluoride (190 µl of a 1 M solution in tetrahydrofuran, 0.19 mmol, 1.5 eq) was added dropwise *via* syringe to a stirred solution of the silyl ether (**20**) (39.6 mg, 0.127 mmol) in tetrahydrofuran (3 ml) at room temperature, in air. After 5 min the reaction mixture was evaporated to dryness *in vacuo* and purified by flash chromatography (20% petrol-ethyl acetate) to give the diol (**22**) (20.7 mg, 82%) as a clear glass; $[\alpha]_D^{20}$=-62.5 (c=0.48, chloroform); υ_{max} (film) 3390, 3009, 2980, 1753, 1635, 1360, 1199, 1067 and 1014 cm^{-1}; ^{1}H δ(500 MHz) 1.76 (1H, br.s, C7-OH), 1.84 (1H, dddd, J 14.3, 5.6, 3.7, 1.9, H-6endo), 2.01 (1H, ddd, J 14.2, 9.7, 4.7, H-6exo), 2.05 (1H, dt, J 15.2, 5.5, H-8), 2.14 (1H, br.d, J 15.2, H-8), 2.48 (1H, dd, J 15.0, 8.0, H-9), 2.61 (1H, br.s, C4-OH), 2.72 (1H, ddt, J 14.9, 6.3, 1.3, H-9), 2.78 (1H, dt, J 9.9, 5.8, H-5), 4.41 (1H, br.quin, J 4.2, H-7), 5.13 (1H, t, J 5.7, H-1), 5.26 (1H, br.d, J 9.4, H-11), 5.29 (1H, m, H-11') and 6.00-6.08 (1H, m, H-10); *m/z* (EI$^+$) 199 (MH$^+$), 198 (M$^+$), 180 (M$^+$-H_2O), 170 (M$^+$-CO), 167, 157 (M$^+$-$CH_2CH{=}CH_2$)), 113, 95, 83, 69, 67, 55 and 41; (Found C, 60.48; H, 7.16. $C_{10}H_{14}O_4$ requires C, 60.60; H, 7.12%).

Treatment of (1*S*, 4*S*, 5*R*, 6*S*)-6-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(prop-2-enyl)-2-oxabicyclo[3.2.1]octan-3-one (19) with tetra-n-butylammonium fluoride. A solution of the silyl ether (**19**) (8.2 mg, 26.2 µmol) in tetrahydrofuran (1 ml) was treated with tetra-n-butylammonium fluoride (39 µl of a 1M solution in tetrahydrofuran, 39.3 µmol, 1.5 eq) at room temperature in air. After 5 min the reaction was worked up and purifed as above to yield the rearranged diol (**22**) (4.8 mg, 92%). The physical data of this compound was in exact agreement with that prepared earlier.

Preparation of (1*S*, 2*S*, 4*S*, 5*S*)-5-bromobicyclo[2.2.1]heptan-2-ol. The ketodibromide[36] (2.05 g, 7.65 mmol) in anhydrous tetrahydrofuran (25 ml) was added dropwise, via cannular, to a vigorously stirred suspension of potassium *tert*-butoxide (1.03 g, 9.18 mmol, 1.2 eq) in anhydrous tetrahydrofuran (25 ml) at -78°C, under argon, over 5 min. After stirring for 30 min at -78°C the solution was allowed to reach ambient temperature over 30 min. The reaction mixture was then filtered swiftly over a small plug of silica gel, copiously washing with tetrahydrofuran and the filtrate evaporated to dryness *in vacuo*. The resultant buff solid was partitioned between dichloromethane (100 ml) and saturated aqueous ammonium chloride (50 ml). Upon separation the organic phase was dried ($MgSO_4$), filtered and evaporated *in vacuo* to give the crude tricycle (**23**) (1.30 g). Sodium borohydride (0.31 g, 8.25 mmol, 1.2 eq) was added portionwise to a vigorously stirred suspension of the crude tricycle (**23**) (1.30 g, 6.88 mmol) in methanol (30 ml) at room temperature. Stirring was continued for 5 min after the initial effervescence and the reaction was then quenched by the cautious addition of water (2 ml) followed by removal of the methanol *in vacuo*. Water (15 ml) was added to the yellow

sludge-like residue and the mixture extracted with dichloromethane (75 ml, 3x50 ml). The combined organic residues were dried ($MgSO_4$), filtered and evaporated *in vacuo* to give a buff solid. Purification by flash chromatography (gradient elution: 35% to 45% ether-petrol) gave the bromobicyclic alcohol (0.92 g, 70%) as a white solid. mp. 61-63°C; $[\alpha]_D^{20}$=-21.7 (c=1.55, chloroform); υ_{max} (film) 3314, 2955, 2872, 1443, 1349, 1322, 1290, 1257, 1207, 1174, 1143, 1124, 1093, 1053, 1019 and 965 cm^{-1}; ^1H δ(500 MHz) 1.48-1.55 (2H, m, 2xH-7), 1.53 (1H, d, J 12.3, OH), 1.72 (1H, dt, J 13.8, 3.5, H-3ax), 1.95-2.01 (1H, m, H-3eq), 2.12-2.18 (2H, m, 2xH-6), 2.24 (1H, t, J 4.0, H-1), 2.40 (1H, t, J 3.8, H-4), 4.28 (1H, ddt, J 12.3, 10.3, 3.8, H-2) and 4.37-4.41 (1H, m, H-5); *m/z* (EI+) Br^{79}, 189 (M^+-H), 145 (M^+-H-C_2H_2-H_2O), 141, 111 (M^+-Br), 109, 81, 19, 67, 66 ($C_5H_6^+$), 41 and 39; [Found: (M^+-H) 188.9917. $C_7H_{10}BrO$ requires 188.9915].

Preparation of (1*S*, 4*S*, 5*S*)-5-bromobicyclo[2.2.1]heptan-2-one (24). Tetra-n-propylammonium perruthenate (549 mg, 2 mol%), was added in one portion to a prestirred (5 min) suspension of powdered 4Å activated molecular sieves (~3g) in a solution of the alcohol (prepared above) (14.92 g, 78.0 mmol) and N-methylmorpholine-N-oxide (13.72 g, 117 mmol, 1.5 eq) in anhydrous acetonitrile (250 ml) at room temperature, under argon. After stirring the reaction overnight it was filtered over a dichloromethane damp pad of silica gel, copiously washed with dichloromethane and the filtrate evaporated to dryness *in vacuo* to give a black oil. Purification by flash chromatography (gradient elution: 40% to 50% ether-petrol) gave the bromoketone (**24**) (12.32 g, 83%) as an amorphous white solid; mp. 42-43°C; $[\alpha]_D^{20}$=+1.4 (c=0.83, chloroform); υ_{max} (film) 2968, 1745, 1460, 1405, 1276, 1249, 1207, 1177, 1144, 1071 and 956 cm^{-1}; ^1H δ(500 MHz) 1.73-1.78 (2H, m, H-6 and H-7), 1.90 (1H, dquin, J 11.0, 1.6, H-7), 2.18 (1H, ddd, J 18.3, 4.7, 1.4, H-3eq), 2.55 (1H, dt, J 14.1, 5.1, H-6), 2.57 (1H, br.s, H-1), 2.69 (1H, dd, J 18.3, 4.5, H-3ax), 2.88 (1H, br.s, H-4) and 4.41-4.45 (1H, m, H-5); *m/z* (EI+) Br^{79}, 188 (M^+), 145 (M^+-H-CH_2=CO), 109 (M^+-Br), 108 (M^+-HBr), 79, 66 ($C_5H_6^+$), 65, 53 and 39; [Found (M^+) 187.9844. C_7H_9BrO requires 187.9837].

Preparation of (1*S*, 4*S*, 5*R*)-5-hydroxybicyclo[2.2.1]heptan-2-one (25). Bromoketone (**24**) (12.32 g, 65.0 mmol) and silver trifluoroacetate (33.00 g, 149 mmol, 2.3 eq) were dissolved in acetone-water (3:1, 220 ml) and heated to ~60°C in darkness. After 40 hr the reaction was worked up as above. Purification by flash chromatography (gradient elution: 75% to 80% ethyl acetate-petrol) yielded the hydroxyketone (**25**) (8.20 g, 99%) as an amorphous solid; mp. ~20°C; $[\alpha]_D^{20}$=-13.2 (~85% ee. c=2.81, chloroform); υ_{max} (film) 3413, 2968, 1745, 1405, 1341, 1304, 1183, 1142, 1093, 1060, 1002, 959, 927 and 908 cm^{-1}; ^1H δ(500 MHz) 1.63 (1H, ddt, J 13.9, 4.2, 2.1, H-6), 1.69 (1H, ddd, J 10.7, 2.2, 1.4, H-7), 1.73 (1H, dd, J 17.9, 4.3, H-3), 1.86 (1H, br.s, OH), 1.98 (1H, ddd, J 13.9, 6.7, 2.3, H-6), 2.02 (1H, dd, J 18.0, 5.9, H-3), 2.03-2.06 (1H, m, H-7), 2.57 (2H, m, H-1 and H-4) and 4.08 (1H, br.d, J 6.6, H-5); *m/z* (EI+) 126 (M^+), 108 (M^+-H_2O), 82, 79, 67, 66, 57, 55, 41, 39, 27 and 26; (Found: C, 66.44; H, 7.96. $C_7H_{10}O_2$ requires C, 66.65; H, 7.99%).

Preparation of (1*S*, 4*S*, 5*R*)-5-hydroxybicyclo[2.2.1]heptan-2-one R-(+)-α-methoxy-α-(trifluoromethyl)phenylacetate. S-(+)-α-Methoxy-α-(tri-fluoromethyl)phenylacetic acid chloride (100 μl, xs) was added dropwise *via* syringe to a stirred solution of the hydroxybicyclicketone (**25**) (23.5 mg, 0.186 mmol), triethylamine (130 ml, 0.931 mmol, 5 eq) and a trace of 4-dimethylaminopyridine in anhydrous dichloromethane (1 ml) at room temperature, under argon. After 4 hr the reaction was quenched by the addition of saturated aqueous sodium bicarbonate (2 ml) with vigorous stirring for 5 min. The mixture was then extracted with ether (3x5 ml), the combined ethereal layers washed with saturated brine (10 ml), dried ($MgSO_4$), filtered and evaporated *in vacuo* to give a yellow oil. Purification by flash chromatography (25% ethyl acetate-petrol) gave the Mosher's ester derivative (49.7 mg, 78%) as a clear oil; υ_{max} (film) 2950, 1748, 1448, 1409, 1270, 1169, 1121, 1081, 1022 and 997 cm^{-1}; ^1H δ(500 MHz) 1.74-1.79 (2H, m), 1.86-1.92 (2H, m), 2.10-2.17 (2H, m), 2.63 (1H, br.d, J 4.9, H-4), 2.80 (1H, br.d, J 5.4, ~15% H-1), 2.85 (1H, br.d, J 5.0, ~85% H-1), 3.55 (3H, s, OMe), 5.10 (1H, br.d, J 6.8, H-5), 7.40-7.44 (3H, m, *o*- and *p*-Ph) and 7.51-7.53 (2H, m, *m*-Ph); *m/z* (EI+) 342 (M^+), 312 (MH^+-MeO^-), 300 (M^+-CH_2CO), 278, 273 (M^+-CF_3), 268, 258, 224, 195, 189 ($C_9H_8F_3O^+$), 109 (M^+-$C_{10}H_8F_3O_3$), 81; (Found: C, 59.93; H, 5.10. $C_{16}H_{26}O_4Si$ requires C, 59.65; H, 5.01%).

Preparation of (1*S*, 4*S*, 5*S*)-5-bromospiro[bicyclo[2.2.1]heptan-2,2'-[1,3]dioxane] (27). The bromobicyclicketone (**24**) (13.27 g, 0.270 mol), 1,3-propanediol (25.36 ml, 0.351 mol, 5 eq) and pyridinium *para*-toluenesulphonate (353 mg, 1.4 mmol, 2 mol%) were heated to ~80°C in anhydrous benzene (270 ml) under argon for 3 hr with a Dean and Stark apparatus. Saturated sodium bicarbonate (100 ml) was added and the mixture extracted with ether (3x300 ml).The combined ethereal layers were washed with saturated sodium bicarbonate (250 ml), dried ($MgSO_4$), filtered and evaporated *in vacuo* to give a clear oil. Purification by flash chromatography (25% ether-petrol) gave the bromobicyclicacetal (**27**) (16.00 g, 92%) as an amorphous, white solid; $[\alpha]_D^{20}$=-35.7 (c=1.50, chloroform); υ_{max} (film) 2967, 2862, 2714, 1461, 1429, 1378, 1365, 1334, 1317, 1302, 1283, 1259, 1250, 1225, 1202, 1165, 1147, 1131, 1115, 1105, 1070, 1038, 983, 951 and 925 cm^{-1}; ^1H δ(500 MHz) 1.39 (1H, ddt, J 10.5, 3.3, 1.6, H-7), 1.64-1.78 [2H, m, CH_2-2(CH_2CO-)], 1.78-1.84 (2H, m, H-3eq and H-7), 1.92 (1H, ddd, J 14.0, 4.5, 3.4, H-6), 2.13 (1H, ddd, J 14.0, 10.8, 4.8, H-6), 2.23 (1H, dd, J 13.5, 3.3, H-3ax), 2.45 (1H, br.s, H-4), 2.57 (1H, br.d, J 4.6, H-1), 3.81 (1H, ddd, J 11.4, 7.3, 4.1, -O$CH_2CH_2CH_2O$-), 3.86-3.93 (3H, m, -O$CH_2CH_2CH_2O$-) and 4.28-4.32 (1H, m, H-5); *m/z* (EI^+) ^{79}Br 246 (M^+), 167 (M^+-Br), 140, 113, 100, 81, 67, 55 and 41; [Found (M^+) 246.0255. $C_{10}H_{16}BrO_2$ requires 246.0255].

Preparation of (1*S*, 4*S*, 5*R*)-spiro[bicyclo[2.2.1]heptan-2,2'-[1,3]dioxane]-5-ol (28) and (1*S*, 4*S*)-spiro[bicyclo[2.2.1]hept-5-en-2,2'-[1,3]dioxane] (29). Potassium superoxide (18.4 g, 258.8 mmol, 4 eq) was added to a solution of the bromobicyclicacetal (**27**) (16.00 g, 64.7 mmol) and 18-crown-6 (34.22 g, 129.4 mmol, 2 eq) in anhydrous dimethylsulphoxide-dimethoxyethane (1:1, 160 ml) at room temperature, under argon. A further 2 equivalents of potassium superoxide and 1 equivalent of 18-crown-6 were added after 12 and 41 hrs. After a further 18 hr the reaction was quenched by the cautious dropwise addition of saturated ammonium chloride (250 ml) at 0°C and extracted with dichloromethane (4x250 ml). The combined organic layers were dried ($MgSO_4$), filtered and evaporated *in vacuo* to give a yellow oil (~130 ml). Purification by flash chromatography (gradient elution: 60% to 70% ethyl acetate-petrol) gave, in order of elution, an inseparable mixture of the starting material (**27**) and the olefin (**29**) (1.73 g, 6% and 7% respectively by nmr); data for (**29**); υ_{max} (film) 3062, 2966, 2859, 2714, 1459, 1430, 1378, 1364, 1334, 1313, 1298, 1283, 1247, 1225, 1191, 1180, 1167, 1136, 1106, 1092, 1043, 998, 983, 971, 953 and 924 cm^{-1}; ^1H δ(500 MHz) 1.45 (1H, dd, J 11.8, 3.3, H-3ax), 1.59-1.62 (1H, m, H-7), 1.67-1.79 [3H, m, H-7 and CH_2-2(CH_2O-)], 1.85 (1H, dd, J 11.8, 3.9, H-3eq), 2.86 (1H, s, H-4), 3.14 (1H, dd, J 2.8, 1.4, H-1), 3.77-3.83 (1H, m, -O$CH_2CH_2CH_2O$-), 3.86-3.95 (2H, m, -O$CH_2CH_2CH_2O$-), 4.02-4.06 (1H, m, -O$CH_2CH_2CH_2O$-), 6.08 (1H, dd, J 5.6, 3.2, H-5 or H-6) and 6.31 (1H, dd, J 5.7, 2.9, H-5 or H-6); *m/z* (EI^+) 167 (M^+), 140, 100, 79, 66 and 42; [Found (M^+) 167.1072. $C_{10}H_{15}O_2$ requires 167.1072]; and the desired hydroxybicyclicacetal (**28**) (9.70 g, 81%) as a clear oil (R_f 0.17, 60% ether-petrol); $[\alpha]_D^{20}$=-26.4 (c=1.38, chloroform); υ_{max} (film) 3409, 2965, 2867, 1461, 1431, 1339, 1310, 1249, 1216, 1182, 1153, 1139, 1102, 1080, 1038, 1018, 976 and 929 cm^{-1}; ^1H δ(500MHz) 1.19 (1H, dddd, J 13.4, 4.6, 2.3, 1.0, H-6eq), 1.24 (1H, dd, J 13.3, 2.5, H-3ax), 1.50 (1H, br.s, OH), 1.57-1.65 [1H, m, CH_2-2(CH_2O-)], 1.62-1.63 (2H, m, 2xH-7), 1.75 (1H, dd, J 13.1, 6.0, H-3eq), 1.75-1.82 [1H, m, CH_2-2(CH_2O-)], 2.12 (1H, ddd, J 13.4, 6.8, 1.7, H-6ax), 2.15 (1H, br.d, J 5.3, H-4), 2.69 (1H, br.d, J 4.4, H-1), 3.78 (2H, t, J 5.6, -O$CH_2CH_2CH_2O$-), 3.83-3.87 (2H, m, H-5 and -O$CH_2CH_2CH_2O$-) and 3.93 (1H, ddd, J 11.9, 8.2, 3.7, -O$CH_2CH_2CH_2O$-); *m/z* (EI^+) 184 (M^+), 167 (M^+-OH), 140 (M^+-CH_2=CHOH), 113, 100, 82, 57 and 55; [Found (M^+) 184.1099. $C_{10}H_{16}O_3$ requires 184.1099].

Preparation of (1*S*, 4*S*, 5*R*)-5-benzyloxybicyclo[2.2.1]heptan-2-one (30). Sodium hydride (2.32 g of a 60% dispersion in mineral oil, 57.9 mmol, 1.1 eq) was washed with sodium dry petrol (30-40°C, 2x20 ml), dried with a stream of argon and then suspended in anhydrous tetrahydrofuran (30 ml). The mixture was cooled to 0°C and the alcohol (**28**) added dropwise, *via* cannular, as a solution in anhydrous tetrahydrofuran (35 ml + 10 ml washings) under argon over 5 min. The reaction was allowed to warm to room temperature and stirred for 30 min before the addition of benzyl bromide (6.89 ml, 57.9 mmol, 1.1 eq) dropwise, via syringe, over 5 min, followed by tetra-n-butylammonium iodide (19 mg, 0.53 mmol, 1 mol%). After stirring for 12 h the reaction was quenched by the cautious addition of 1 M hydrochloric acid (25 ml) at

0°C. After vigorously stirring for 5 min the reaction was warmed to ~50°C for 2 h 45 min. The reaction was then cooled added to saturated aqueous sodium bicarbonate and extracted with dichloromethane (3x250 ml). The combined organic layers were dried ($MgSO_4$), filtered and evaporated *in vacuo* to give a yellow oil that was purified by flash chromatography (gradient elution: 30% to 40% ether-petrol) to give the benzyloxybicyclicketone (**30**) (8.32 g, 73%) as a clear oil; $[\alpha]_D^{20}$=-32.6 (c=0.96, chloroform).; υ_{max} (film) 3028, 2972, 2879, 1745, 1604, 1494, 1450, 1406, 1354, 1309, 1201, 1235, 1183, 1144, 1097, 1073, 1028, 992, 962 and 911 cm^{-1}; ^1H δ(500MHz) 1.69 (1H, dt, J 9.2, 1.8, H-7), 1.70 (1H, dd, J 18.1, 4.1, H-3), 1.79 (1H, br.d, J 13.9, H-6), 1.92 (1H, ddd, J 13.9, 6.6, 2.2, H-6), 2.00-2.04 (1H, m, H-7), 2.07 (1H, ddd, J 19.0, 5.3, 0.9, H-3), 2.58 (1H, br.d, J 4.9, H-4), 2.79 (1H, br.d, J 5.0, H-1), 3.74 (1H, br.d, J 6.6, H-5), 4.51 (1H, d, J 11.8, PhC$\underline{H_2}$O-), 4.54 (1H, d, J 11.8, PhC$\underline{H_2}$O-) and 7.28-7.37 (5H, m, Ph); *m/z* (EI^+) 216 (M^+), 198 (M^+-H_2O), 172 (M^+-H_2O-C_2H_2), 156, 130, 125 (M^+-C_7H_7), 117, 107 ($C_7H_7O^+$), 104 and 91 ($C_7H_7^+$); (Found: C, 77.91; H, 7.74. $C_{14}H_{16}O_2$ requires C, 77.75; H, 7.46%).

Preparation of (1*S*, 4*S*, 5*R*)-5-hydroxybicyclo[2.2.1]heptan-2-one (25). 10% Palladium on carbon (trace) was added to a solution of the benzyloxybicyclicketone (**30**) (9.6 mg, 44.4 μmol) and 1M HCl (1 drop) in redistilled methanol (1 ml). The reaction was then degassed and filled with hydrogen (from a balloon) three times before finally being allowed to vigorously stir at room temperature, under an atmosphere of hydrogen. After 20 min the reaction was filtered over a small plug of celite, copiously washed with ethyl acetate and the filtrate evaporated to dryness *in vacuo* to give a pale yellow oil. Purification by flash chromatography (12x1 cm, 75% ethyl acetate-petrol) gave the desired hydroxy bicyclicketone (**25**) (4.8 mg, 86%) as a clear oil $[\alpha]_D^{20}$=-13.1 (c=0.35, chloroform).[37] All other physical data of this compound were identical to that prepared earlier.

Mosher ester formation proceeded in the same manner as described earlier, the physical data being in exact agreement; $[\alpha]_D^{20}$=+23.4 (c=1.25, chloroform).

Preparation of (1*S*, 5*S*, 6*R*)-6-benzyloxy-2-oxabicyclo[3.2.1]octan-3-one (31). The benzyloxyketone (**30**) (11.99 g, 55.4 mmol) was subjected to Baeyer-Villager oxidation with *m*-CPBA in a similar manner to that described earlier. Purification by flash chromatography (gradient elution: 70% to 80% ether-petrol) gave the benzyloxylactone (**31**) (11.66 g, 91%), containing ~5% of the regiolactone, as an amorphous white solid; mp. 51-54°C; υ_{max} (film) 2941, 1733, 1494, 1450, 1373, 1311, 1243, 1195, 1139, 1080, 1063, 1013, 974 and 906 cm^{-1}; ^1H δ(500 MHz) 1.94 (1H, br.d, J 13.0, H-8), 2.01 (1H, dddd, J 15.9, 5.0, 2.3, 1.1, H-7ax), 2.08 (1H, dquin, J 12.9, 2.5, H-8), 2.46 (1H, dt, J 18.9, 1.7, H-4ax), 2.55 (1H, ddd, J 15.9, 6.7, 2.6, H-7eq), 2.62 (1H, br.t, J 5.4, H-5), 2.79 (1H, dd, J 19.0, 6.1, H-4eq), 3.96 (1H, dt, J 6.4, 1.7, H-6), 4.47 (1H, d, J 11.8, PhC$\underline{H_2}$O-), 4.50 (1H, d, J 11.8, PhC$\underline{H_2}$O-), 4.89 (1H, m, H-1), 7.28-7.33 (3H, m, *o*-and *p*-Ph) and 7.34-7.37 (2H, m, *m*-Ph); *m/z* (EI^+) 232 (M^+), 214 (M^+-H_2O), 204 (M^+-CO), 186 (M^+-CO-H_2O), 162, 141 (M^+-$C_7H_7^+$), 126, 107 ($C_7H_7O^+$) and 91 ($C_7H_7^+$); (Found: C, 72.69; H, 6.93. $C_{14}H_{16}O_3$ requires C, 72.39; H, 6.94%).

Preparation of (1*S*, 5*S*, 6*R*)-6-hydroxy-2-oxabicyclo[3.2.1]octan-3-one. *meta*-Chloroperbenzoic acid (277 mg of 80%, 1.28 mmol, 1.5 eq) was added to a stirred solution of the hydroxyketone (**25**) (108 mg, 0.86 mmol) and *para*-toluenesulphonic acid (1.6 mg, 1 mol%) in dichloromethane (2 ml) in air at room temperature. After 30 min a dense white precipitate had developed and the reaction mixture was evaporated to dryness *in vacuo* to give a white solid. Purification by flash chromatography [neutral alumina (3% water, Act.III), gradient elution: 1% to 4% methanol-ethyl acetate] gave the hydroxylactone (99 mg, 82%) as a clear oil; $[\alpha]_D^{20}$=-16.3 (~85% ee. c=0.24, chloroform); υ_{max} (film) 3413, 2940, 2850, 1726, 1377, 1245, 1196, 1077, 1050 and 973 cm^{-1}; ^1H δ(500MHz) 1.67 (1H, br.d, J 1.7, OH), 1.89 (1H, ddt, J 16.0, 4.9, 1.6, H-7ax), 1.95 (1H, br.dd, J 13.0, 1.1, H-8), 2.14 (1H, dquin, J 13.0, 2.5, H-8'), 2.40-2.43 (1H, m, H-5), 2.50 (1H, ddd, J 19.0, 2.0, 1.6, H-4ax), 2.60 (1H, ddd, J 16.0, 6.7, 2.6, H-7eq), 2.78 (1H, dd, J 19.0, 6.1, H-4eq), 4.33 (1H, br.d, J 5.7, H-6) and 4.89 (1H, qd, J 3.1, 1.8, H-1); *m/z* (EI^+) 142 (M^+), 124 (M^+-H_2O), 114 (M^+-CO), 98 (M^+-CO_2), 94, 86, 83, 73, 70, 57 and 41; (Found: C, 59.02; H, 7.20. $C_7H_{10}O_3$ requires C, 59.15; H, 7.09%).

Preparation of (1*S*, 5*S*, 6*R*)-6-(triethylsilyloxy)-2-oxabicyclo[3.2.1]octan-3-one (32). Triethylsilyl chloride (386 µl, 2.30 mmol, 1.5 eq) was added dropwise, *via* syringe, to a stirred solution of the hydroxylactone (prepared above) (218 mg, 1.53 mmol), 4-dimethylaminopyridine (trace) and triethylamine (1.07 ml, 7.67 mmol, 5 eq) in anhydrous dichloromethane (3 ml) at room temperature, under argon. After 5 min a white precipitate appeared and the reaction mixture was stirred for 1 h. The reaction was quenched by the addition of saturated aqueous sodium bicarbonate (5 ml) and extracted with ether (25 ml, 3x15 ml). The combined organic phases were dried ($MgSO_4$), filtered and evaporated to dryness *in vacuo* to give a yellow oil. Purification by flash chromatography (35% ether-petrol) gave the triethylsilyl protected lactone (32) (302 mg, 77%) as a clear oil; $[\alpha]_D^{20}$=-27.0 (~85% ee. c=1.05, chloroform); υ_{max} (film) 2954, 2910, 2875, 1741, 1457, 1412, 1372, 1336, 1310, 1242, 1192, 1166, 1137, 1089, 1040, 1011, 976, 939 and 916 cm^{-1}; ^1H δ(500MHz) 0.58 [6H, q, J 7.9, Si-($C\underline{H}_2CH_3$)], 0.94 [9H, t, J 7.9, Si-($CH_2C\underline{H}_3$)3], 1.86 (1H, br.ddt, J 15.9, 5.1, 1.5, H-7ax), 1.89 (1H, br.dd, J 13.0, 1.1, H-8), 2.12 (1H, dquin, J 12.8, 2.5, H-8'), 2.33 (1H, br.t, J 5.2, H-5), 2.45 (1H, dt, J 19.0, 1.7, H-4ax), 2.53 (1H, ddd, J 15.8, 6.5, 2.5, H-7eq), 2.74 (1H, dd, J 19.0, 6.1, H-4eq), 4.18 (1H, br.d, J 6.5, H-5) and 4.86 (1H, dd, J 3.1, 2.0, H-1); *m/z* (EI^+) 256 (M^+), 240, 227 (M^+-Et), 183, 103, 87, 75, 59 and 47; (Found: C, 60.88; H, 9.45. $C_{13}H_{24}O_3Si$ requires C, 60.89; H, 9.43%).

Preparation (1*S*, 4*RS*, 5*S*, 6*R*)-4-hydroxy-6-(triethylsilyloxy)-2-oxabicyclo[3.2.1]octan-3-one. n-Butyllithium (562 µl of a 2.5 M solution in hexane, 1.40 mmol, 1.2 eq) was added dropwise, *via* syringe, to a stirred solution of diisopropylamine (197 µl, 1.40 mmol, 1.2 eq) in anhydrous tetrahydrofuran (1 ml) at 0°C, under argon. After stirring for 30 min at 0°C the lithium diisopropylamide was cooled to -78°C and the triethylsilyloxylactone (32) (300 mg, 1.17 mmol) added, *via* cannular, as a solution in anhydrous tetrahydrofuran (1 ml + 1 ml washings). After 1 hr at -78°C pre-dried oxodiperoxymolybdenum(pyridine)hexamethylphosphoramide (MoOPH, 610 mg, 1.40 mmol, 1.2 eq) was added swiftly in one portion to the vigorously stirred ketene acetal. The resultant yellow solution was allowed to warm to room temperature after 5 min to give a green solution. This was quenched by the addition of saturated aqueous sodium sulphite (2 ml) with stirring for 5 min before the addition of saturated brine (2 ml) and extraction with ethyl acetate (3x15 ml, 3x10 ml). The combined organic extracts were dried ($MgSO_4$), filtered and evaporated to dryness *in vacuo* to give a yellow oil. Purification by flash chromatography (gradient elution: 35% to 45% ether-petrol) gave, in order of elution, starting material (32) (57 mg, 19% recovery) and an inseparable 3:7, α:β epimeric mixture of hydroxylactones (135 mg, 42%) as a clear oil; υ_{max} (film) 3442, 2954, 2876, 1739, 1454, 1375, 1209, 1138, 1099, 1068, 1046, 1004, 962 and 943 cm^{-1}; ^1H δ(500MHz) for the major C4-β hydroxy epimer, 0.60 [6H, q, J 8.0, Si-($C\underline{H}_2CH_3$)3], 0.94 [9H, t, J 7.8, Si-($CH_2C\underline{H}_3$)3], 1.89 (1H, ddt, J 16.0, 5.2, 1.7, H-7eq), 2.07 (2H, br.s, 2xH-8), 2.36 (1H, dd, J 15.9, 6.5, H-7ax), 2.47 (1H, br.s, H-5), 2.81 (1H, br.s, OH), 3.95 (1H, s, H-4), 4.22 (1H, dd, J 6.5, 1.9, H-6) and 4.92-4.94 (1H, m, H-1); and for the minor C4-α hydroxy epimer, 0.60 [6H, q, J 7.9, Si-($C\underline{H}_2CH_3$)3], 0.94 [9H, t, J 7.8, Si-($CH_2C\underline{H}_3$)3], 1.84 (1H, ddd, J 15.7, 4.5, 2.9, H-7eq), 2.00 (1H, dt, J 13.4, 1.3, H-8), 2.23 (1H, ddd, J 13.4, 5.5, 2.8, H-8'), 2.54 (1H, ddd, J 15.6, 7.0, 2.7, H-7ax), 2.65 (1H, br.t, J 5.3, H-5), 3.00 (1H, br.s, OH), 4.20 (1H, d, J 5.1, H-4), 4.56 (1H, ddd, J 6.9, 2.1, 0.7, H-6) and 4.85-4.87 (1H, m, H-1); *m/z* (EI^+) 272 (M^+), 255 (M^+-OH), 243 (M^+-Et), 227, 215, 197, 181, 171, 157 (M^+-$SiEt_3$), 131, 123, 115, 103, 87, 75, 67, 59 and 47; [Found (M^+-Et) 243.1059. $C_{11}H_{19}O_4Si$ requires 243.1053].

Preparation of (1*S*, 4*RS*, 5*R*, 6*R*)-4-(*tert*-butyldimethylsilyloxy)-6-(triethylsilyloxy)-2-oxabicyclo[3.2.1]octan-3-one (33). The hydroxylactones (prepared above) (189 mg, 0.694 mmol) were protected as their TBDMS ethers in a similar manner to that described earlier. Purification by flash chromatography (gradient elution: 7% to 10% ether-petrol) gave the corresponding 3:7, α:β epimeric mixture of *tert*-butyldimethylsilyloxylactones (33) (239 mg, 89%) as a clear oil; υ_{max} (film) 2954, 2878, 2856, 1753, 1461, 1375, 1256, 1128, 1104, 1080, 1006 and 946 cm^{-1}; ^1H δ(500 MHz) for the major β *tert*-butyldimethylsilyloxy epimer, 0.15 (3H, s, SiMe), 0.16 (3H, s, SiMe), 0.59 [6H, q, J 8.0, Si-($C\underline{H}_2CH_3$)3], 0.90 (9H, s, Si^tBu), 0.95 [9H, t, J 8.0, Si-($CH_2C\underline{H}_3$)3],1.78 (1H, dt, J 15.4, 3.7, H-7eq), 1.93 (1H, br.d, J 13.0, H-8), 2.26 (1H, br.d, J 14.9, H-8'), 2.33 (1H, m, H-5), 2.42 (1H, ddd, J 15.4, 6.9, 2.5, H-7ax),

3.99 (1H, m, H-4), 4.11 (1H, dd, J 6.6, 2.5, H-6) and 4.84 (1H, br.d, J 1.3, H-1); and for the minor α *tert*-butyldimethylsilyloxy epimer, 0.14 (3H, s, SiMe), 0.19 (3H, s, SiMe), 0.59 [6H, q, J 7.9, Si-(CH_2CH_3)$_3$], 0.94 (9H, s, Si^{t}Bu), 0.99 [9H, t, J 7.9, Si-(CH_2CH_3)$_3$], 1.76-1.82 (1H, m, H-7eq), 1.92 (1H, br.ddd, J 13.2, 4.4, 1.2, H-8), 2.15-2.21 (1H, m, H-8'), 2.48-2.51 (1H, m, H-5), 2.52 (1H, ddt, J 15.5, 6.8, 2.4, H-7ax), 4.18 (1H, t, J 5.1, H-4), 4.59-4.62 (1H, m, H-6) and 4.76 (1H, br.dd, J 3.0, 1.6, H-1); *m/z* (EI$^+$) 385 (M$^+$-H), 371 (M$^+$-Me), 357 (M$^+$-Et), 329 (M$^+$-^{t}Bu), 301 (MH$^+$-^{t}Bu-Et), 225, 197 ($C_{11}H_{21}OSi$), 181, 153, 131, 75, 67 and 59; [Found (M$^+$-Et) 357.1922. $C_{17}H_{33}O_4Si_2$ requires 357.1917].

Preparation of (1*S*, 4*S*, 5*R*, 6*R*)-4,6-bis(*tert*-butyldimethylsilyloxy)-4-(prop-2-enyl)-2-oxabicyclo[3.2.1]octan-3-one and (1*S*, 4*S*, 5*R*, 6*R*)-4-(*tert*-butyldimethylsilyloxy)-4-(prop-2-enyl)-6-(triethylsilyloxy)-2-oxabicyclo[3.2.1]octan-3-one (34). Diisopropylamine (58.7 μl, 0.419 mmol, 1.2 eq) and n-butyllithium (168 μl of a 2.5 M solution in hexane, 0.419 mmol, 1.2 eq) were added sequentially to a stirred suspension of resublimed potassium *tert*-butoxide (47.0 mg, 0.419 mmol, 1.2 eq) in anhydrous tetrahydrofuran (1 ml) at -78°C, under argon. After 30 min the lactones (**33**) (135 mg, 0.349 mmol) were added to the faintly yellow solution at -78°C, *via* cannular, as a soluion in anhydrous tetrahydrofuran (1 ml + 0.5 ml washings), under argon. Hexamethylphosphoramide (375 μl, ~15% volume of tetrahydrofuran) was added, via syringe, to the yellow solution after stirring for 45 min at -78°C, under argon. After 15 min allyl bromide (45.3 μl, 0.524 mmol, 1.5 eq) was added swiftly, *via* syringe and the reaction mixture stirred at -78°C for 5 min before being allowed to gradually warm to room temperature. The reaction was quenched by the addition of saturated aqueous ammonium chloride (3 drops) and the tetrahydrofuran removed *in vacuo*. Ether (15 ml) was added to the yellow residue which was washed sequentially with water (2x2 ml) and saturated brine (2 ml). The ethereal layer was dried ($MgSO_4$), filtered and evaporated to dryness *in vacuo* to give a yellow oil. Purification by flash chromatography (gradient elution: 6% to 7% ether-petrol) gave, in order of elution, the bis(*tert*-butyldimethylsilyloxy)allyl lactone (6.6 mg, 4%) as a clear oil; $[\alpha]_D^{20}$=+28.2 (~85% ee. c=0.66, chloroform); υ_{max} (film) 2953, 2930, 2855, 1742, 1635, 1460, 1374, 1316, 1254, 1164, 1121, 1088, 1061, 1030, 996, 940 and 919 cm^{-1};^{1}H δ(500 MHz) 0.04 (3H, s, SiMe), 0.05 (3H, s, SiMe), 0.07 (3H, s, SiMe), 0.32 (3H, s, SiMe), 0.85 (9H, s, Si^{t}Bu), 0.92 (9H, s, Si^{t}Bu), 1.85 (1H, ddt, J 15.7, 5.2, 1.3, H-7eq), 1.97 (1H, br.dd, J 13.3, 1.0, H-8'), 2.06 (1H, ddd, J 13.4, 4.9, 2.9, H-8), 2.33 (1H, ddd, J 15.8, 6.3, 2.3, H-7ax), 2.45 (1H, dd, J 14.7, 8.8, H-9), 2.48 (1H, br.d, J 4.0, H-5), 2.68 (1H, ddt, J 14.8, 5.3, 1.6, H-9), 4.65 (1H, d, J 6.3, H-6), 4.75-4.77 (1H, m, H-1), 5.13 (1H, ddd, J 17.1, 2.8, 1.7, H-11), 5.21 (1H, dd, J 10.2, 1.3, H-11') and 5.84-5.92 (1H, m, H-10); *m/z* (EI$^+$) 427 (MH$^+$), 411 (M$^+$-Me), 397 (MH$^+$-2Me), 385 (M$^+$-$CH_2CH{=}CH_2$), 369 (M$^+$-^{t}Bu), 325 (M$^+$-^{t}Bu-CO_2), 279, 193, 171, 149, 127, 73, 57 and 41; [Found (M$^+$-^{t}Bu) 369.1921. $C_{18}H_{33}O_4Si_2$ requires 369.1917]; a mixed fraction containing the bis(*tert*-butyldimethylsilyloxy)allyl lactone (9.9 mg, 6%, therefore a total of 10%) and the desired allyl lactone (**34**) (3.3 mg, 2%); the pure desired allyl lactone (**34**) (44.0 mg, 32%) as a clear oil; $[\alpha]_D^{20}$=+33.1 (~85% ee. c=0.96, chloroform); υ_{max} (film) 2954, 2877, 2856, 1743, 1636, 1459, 1412, 1373, 1316, 1241, 1164, 1121, 1087, 1061, 1030, 996, 942 and 918 cm^{-1}; ^{1}H δ(500 MHz) 0.07 (3H, s, SiMe), 0.32 (3H, s, SiMe), 0.57 [6H, q, J 8.0, Si-(CH_2CH_3)$_3$], 0.92 (9H, s, Si^{t}Bu), 0.92 [9H, t, J 8.0, Si-(CH_2CH_3)$_3$], 1.87 (1H, dd, J 15.8, 5.2, H-7ax), 1.97 (1H, br.d, J 12.8, H-8'), 2.09 (1H, ddd, J 13.4, 4.9, 3.0, H-8), 2.34 (1H, ddd, J 15.8, 6.3, 2.4, H-7eq), 2.45 (1H, dd, J 14.6, 8.9, H-9), 2.49 (1H, d, J 4.7, H-5), 2.69 (1H, ddt, J 14.6, 5.3, 1.5, H-9), 4.50 (1H, d, J 6.3, H-6), 4.76 (1H, dd, J 3.1, 2.0, H-1), 5.12 (1H, dd, J 17.1, 1.0, H-11), 5.20 (1H, d, J 10.1, H-11') and 5.88 (1H, dddd, J 19.0, 9.3, 7.8, 5.3, H-10); *m/z* (EI$^+$) 426 (M$^+$), 411 (M$^+$-Me), 397 (M$^+$-Et), 385 (M$^+$-$CH_2CH{=}CH_2$), 369 (M$^+$-^{t}Bu), 341 (MH$^+$-^{t}Bu-Et), 325 (MH$^+$-^{t}Bu-CO_2), 237, 221, 193, 171, 127, 115, 87 and 75; [Found (M$^+$-^{t}Bu) 369.1921. $C_{18}H_{33}O_4Si_2$ requires 369.1917]; a mixed fraction of the desired allyl lactone (**34**) (12 mg, 8%, therefore a total of 42%) and what was possibly the bis(triethylsilyloxy)allyl lactone (12 mg, 8%); a mixed fraction of the β epimer of the starting material (**33**) (12.5 mg, 9% recovery) and an unknown compound (12.5 mg); and the α epimer of the starting material (**33**) (22.5 mg, 17%, therefore a total of 26% recovery).

Preparation of (1*S*, 3*RS*, 4*S*, 5*R*, 6*R*)-4-(*tert*-butyldimethylsilyloxy)-4-(prop-2-enyl)-6-(triethylsilyloxy)-2-oxabicyclo[3.2.1]octan-3-ol and (β*S*, 1*R*, 2*R*, 4*S*)-β-(*tert*-

butyldimethylsilyloxy)-4-hydroxy-β-(prop-2-enyl)-2-(triethylsilyloxy)cyclopentane ethanol. Diisobutylaluminium hydride (90.0 µl of a 1.5 M solution in toluene, 0.136 mmol, 1.8 eq) was added dropwise, *via* syringe, to a stirred solution of the allyl lactone (**34**) (32.2 mg, 75.5 µmol) in anhydrous toluene at -78°C, under argon. Five min after complete addition, water (90 µl) was added and the quenched reaction mixture gradually warmed to room temperature. Sodium bicarbonate (1 small spatula) and ethyl acetate (~2 ml) were added and the mixture vigorously stirred for 30 min. The resultant white solid was filtered off and the filtrate evaporated to dryness *in vacuo* to give a clear oil. Purification by flash chromatography (gradient elution: 25% to 45% ether-petrol) gave, in order of elution, the desired lactol (28.9 mg, 89%), 20% of which was in its open hydroxy-aldehyde form (^{1}H δ 9.48, s, CHO), as a clear oil; υ_{max} (film) 3381, 3074, 2954, 2933, 2877, 2855, 1739 (weak, aldehydic), 1636, 1459, 1435, 1412, 1359, 1345, 1306, 1285, 1248, 1174, 1144, 1122, 1086, 1060, 1004, 968, 936 and 912 cm^{-1}; ^{1}H δ(500 MHz) 0.14 (3H, s, SiMe), 0.17 (3H, s, SiMe), 0.58 [6H, q, J 7.9, Si-(C$\underline{H}_2$CH$_3$)$_3$], 0.92 (9H, s, Si^{t}Bu), 0.93 [9H, t, J 7.9, Si-(CH$_2$C$\underline{H}_3$)$_3$], 1.59-1.72 (3H, m, H-7 and 2xH-8), 2.21 (1H, d, J 4.8, H-5), 2.28-2.37 (2H, m, H-7 and H-9), 2.50 (1H, d, J 7.0, OH), 2.51-2.57 (1H, m, H-9), 4.37 (1H, m, H-1), 4.48 (1H, d, J 7.1, H-3), 5.12 (1H, dd, J 17.1, 0.9, H-11), 5.15 (1H, d, J 9.9, H-11') and 5.84-5.93 (1H, m, H-10); *m/z* (EI$^+$) 428 (M$^+$), 412 (MH$^+$-OH), 399 (M$^+$-Et), 381 (M$^+$-Et-H$_2$O), 371 (M$^+$-^{t}Bu), 353, 341 (M$^+$-CH$_2$CH=CH$_2$-Et-OH), 267, 239, 211, 169, 157, 115, 87, 73, 59 and 41; [Found (M$^+$-^{t}Bu) 371.2079. $C_{18}H_{35}O_4Si_2$ requires 371.2074]; and the over-reduced diol (3.1 mg, 10%) as a clear oil; $[\alpha]_D^{20}$=-31.7 (~85% ee. c=0.30, chloroform); υ_{max} (film) 3409, 2954, 2879, 2855, 1635, 1459, 1411, 1359, 1249, 1060, 1004 and 915 cm^{-1}; ^{1}H δ(500 MHz) 0.14 (3H, s, SiMe), 0.15 (3H, s, SiMe), 0.63 [6H, q, J 7.9, Si-(C$\underline{H}_2$CH$_3$)$_3$], 0.88 (9H, s, Si^{t}Bu), 0.97 [9H, t, J 7.9, Si-(CH$_2$C$\underline{H}_3$)$_3$], 1.44 (1H, br.d, J 4.1, C4-OH), 1.59 (1H, dddd, J 13.5, 9.8, 5.4, 1.0, H-5), 1.81 (1H, dtd, J 13.0, 6.6, 0.9, H-3), 1.93 (1H, dddd, J 12.8, 7.2, 5.6, 1.0, H-3), 2.15 (1H, m, H-5), 2.31-2.36 (2H, m, H-1 and H-1'), 2.42 (1H, ddt, J 13.6, 7.3, 1.2, H-1'), 2.59 (1H, dd, J 9.1, 5.4, α-OH), 3.47 (1H, dd, J 12.0, 9.2, H-α), 3.57 (1H, dd, J 12.1, 5.4, H-α), 4.32-4.36 (2H, m, H-2 and H-4), 5.06 (1H, br.d, J 10.2, H-3'c), 5.10 (1H, br.d, J 17.2, H-3't) and 5.92-6.00 (1H, m, H-2'); *m/z* (EI$^+$) 399 (M$^+$-CH$_2$OH), 383 (M$^+$-Et-H$_2$O), 371, 355(M$^+$-^{t}Bu-H$_2$O), 341, 301, 281, 267, 257, 251, 241, 223, 211, 199, 157, 149, 131, 123, 115, 103, 87 and 75; [Found (M$^+$-CH$_2$OH) 399.2754. $C_{21}H_{43}O_3Si_2$ requires 399.2751].

Preparation of (1*S*, 3*R*, 5*RS*, 7*S*, 8*R*, 9*R*)-7-(*tert*-butyldimethylsilyloxy)-9-(triethylsilyloxy)-2,4-dioxatricyclo[6.2.1.0^{3,7}]undecan-5-ol (35). The terminal alkene (prepared above) (28.9 mg, 67.4 µmol) was subjected to ozonolysis with triphenylphosphine work up in a similar manner to that described earlier. Purification by flash chromatography (gradient elution: 40% to 50% ether petrol) gave a C5 1:4, α:β epimeric mixture of the tricyclic lactols (**35**) (26.1 mg, 90%) as a clear oil; υ_{max} (film) 3428, 2953, 2877, 2856, 1726 (w), 1459, 1359, 1307, 1256, 1179, 1129, 1068, 1021, 970, 932 and 906 cm^{-1}; ^{1}H δ(500 MHz) for the major β epimer, 0.12 (3H, s, SiMe), 0.13 (3H, s, SiMe), 0.58 [6H, q, J 7.9, Si-(C$\underline{H}_2$CH$_3$)$_3$], 0.90 (9H, s, Si^{t}Bu), 0.93 [9H, t, J 7.9, Si-(CH$_2$C$\underline{H}_3$)$_3$], 1.69 (1H, ddt, J 15.6, 5.5, 1.5, H-10eq), 1.89 (1H, br.dd, J 13.0, 1.3, H-11'), 1.92 (1H, ddd, J 12.8, 4.6, 2.6, H-11), 2.27 (1H, dd, J 15.3, 3.7, H-6), 2.32 (1H, dd, J 15.3, 6.1, H-6), 2.36-2.40 (2H, m, H-8 and H-10ax), 3.10 (1H, d, J 9.0, OH), 4.42 (1H, br.dd, J 4.1, 1.5, H-1), 4.61 (1H, br.d, J 6.3, H-9), 4.75 (1H, s, H-3) and 5.65 (1H, ddd, J 9.1, 6.0, 3.6, H-5); and for the minor α epimer, 0.23 (3H, s, SiMe), 0.26 (3H, s, SiMe), 0.59 [6H, q, J 7.7, Si-(C$\underline{H}_2$CH$_3$)$_3$], 0.93 (9H, s, Si^{t}Bu), 0.94 [9H, t, J 8.6, Si-(CH$_2$C$\underline{H}_3$)$_3$], 1.66-1.71 (1H, m, H-10eq), 1.77 (1H, br.d, J 13.2, H-11'), 1.84 (1H, ddd, J 12.8, 5.0, 2.6, H-11), 1.87-1.94 (1H, m, H-6), 2.36-2.40 (1H, m, H-10ax), 2.47 (1H, br.d, J 4.6, H-8), 2.53 (1H, dd, J 14.5, 6.3, H-6), 2.91 (1H, d, J 9.3, OH), 4.35 (1H, br.s, H-1), 4.64 (1H, br.d, J 6.4, H-9), 4.85 (1H, s, H-3) and 5.62 (1H, ddd, J 9.4, 6.3, 2.1, H-5); *m/z* (EI$^+$) 401 (M$^+$-Et), 383 (M$^+$-Et-H$_2$O), 373 (M$^+$-^{t}Bu), 355 (M$^+$-^{t}Bu-H$_2$O), 343, 329 (M$^+$-^{t}Bu-CO$_2$), 301, 281, 269, 241, 223, 197, 185, 171, 157, 149, 129, 115, 87, 75 and 73; [Found (M$^+$-Et) 401.2187. $C_{19}H_{37}O_5Si_2$ requires 401.2180].

Preparation of (1*S*, 3*R*, 5*RS*, 7*S*, 8*R*, 9*R*)-5-acetoxy-7-(*tert*-butyldimethylsilyloxy)-9-(triethylsilyloxy)-2,4-dioxatricyclo[6.2.1.0^{3,7}]undecane. Acetic anhydride (11.4 µl, 0.121 mmol, 2 eq) was added dropwise, *via* syringe, to a stirred solution of the tricyclic alcohol (**35**) (26.1 mg, 60.6 µmol),

triethylamine (42.2 µl, 0.303 mmol, 5 eq) and a trace of 4-dimethylaminopyridine in anhydrous dichloromethane (1 ml) at room temperature, under argon. After 2 hr the reaction was evaporated to dryness *in vacuo* and purified by flash chromatography (gradient elution: 25% to 35% ether-petrol) to give the corresponding C5 1:4, α:β anomeric acetate mixture (28.7 mg, 98%) as a clear oil; υ_{max} (film) 2953, 2876, 1748, 1459, 1361, 1234, 1177, 1132, 1061, 1030, 968, 932 and 906 cm^{-1}; ^1H δ(500 MHz) for the major β epimer, 0.16 (3H, s, SiMe), 0.17 (3H, s, SiMe), 0.58 [6H, q, J 7.9, Si-($C\underline{H}_2CH_3)_3$], 0.91 (9H, s, Si^{t}Bu), 0.94 [9H, t, J 8.0, Si-($CH_2C\underline{H}_3)_3$], 1.69 (1H, ddt, J 15.5, 5.7, 1.5, H-10eq), 1.89 (2H, br.s, 2xH-11), 2.09 (3H, s, OAc), 2.38 (1H, d, J 6.4, H-6α), 2.39 (1H, d, J 4.8, H-6β), 2.40-2.43 (2H, m, H-8 and H-10ax), 4.43-4.44 (1H, m, H-1), 4.63 (1H, br.d, J 5.0, H-9), 4.78 (1H, s, H-3) and 6.44 (1H, dd, J 6.1, 4.7, H-5); and for the minor α epimer, 0.19 (3H, s, SiMe), 0.21 (3H, s, SiMe), 0.59 [6H, q, J 7.8, Si-($C\underline{H}_2CH_3)_3$], 0.93 (9H, s, Si^{t}Bu), 0.94 [9H, t, J 7.9, Si-($CH_2C\underline{H}_3)_3$], 1.65-1.70 (1H, m, H-10eq), 1.80 (1H, br.dd, J 14.2, 1.5, H-11'), 1.87 (1H, ddd, J 12.6, 5.1, 2.6, H-11), 2.03 (1H, dd, J 15.1, 1.4, H-6), 2.06 (3H, s, OAc), 2.40-2.43 (1H, m, H-10ax), 2.45 (1H, br.d, J 4.7, H-8), 2.66 (1H, dd, J 14.9, 6.8, H-6), 4.36-4.37 (1H, m, H-1), 4.66 (1H, br.d, J 6.3, H-9), 4.90 (1H, s, H-3) and 6.42 (1H, dd, J 6.8, 1.9, H-5); *m/z* (EI$^+$) 443 (M^+-Et), 431, 415 (M^+-^{t}Bu), 413 (M^+-AcO), 397 (M^+-AcOH-Me), 383 (M^+-Et-AcOH), 371, 355 (M^+-^{t}Bu-AcOH), 311, 281, 251, 223, 197, 169, 157, 149, 115, 103, 87, 75 and 73; [Found (M^+-^{t}Bu) 415.1973. $C_{19}H_{35}O_6Si_2$ requires 415.1972].

Preparation of (1*S*, 3*R*, 5*RS*, 7*S*, 8*R*, 9*R*)-5-acetoxy-7-(*tert*-butyldimethylsilyloxy)-2,4-dioxatricyclo[6.2.1.0^{3,7}]undecan-9-ol (36). The bis-silyl ether (prepared above) (26.6 mg, 56.3 µmol) was stirred in acetic acid-water-tetrahydrofuran (3:3:1, 1 ml) at room temperature in air for 1 hr. Evaporation to dryness *in vacuo*, azeotroping with anhydrous toluene followed by purification by flash chromatography (gradient elution: 50% to 60% ethyl acetate-petrol) gave the 9-hydroxytricyclic acetates, C5 1:4, α:β, (**36**) (16.5 mg, 82%) as a clear oil; υ_{max} (film) 3478, 2930, 2855, 1743, 1461, 1436, 1360, 1253, 1172, 1133, 1106, 1053, 1005, 965 and 927 cm^{-1}; ^1H δ(500 MHz) for the major β epimer, 0.17 (3H, s, SiMe), 0.19 (3H, s, SiMe), 0.90 (9H, s, Si^{t}Bu), 1.43 (1H, d, J 3.6, OH), 1.70 (1H, br.dd, J 14.5, 6.4, H-10eq), 1.82-1.86 (1H, m, H-11), 1.96 (1H, br.d, J 11.9, H-11'), 2.09 (3H, s, OAc), 2.35 (1H, dd, J 14.8, 6.2, H-6α), 2.40 (1H, dd, J 14.8, 5.0 Hz, H-6β), 2.44 (1H, d, J 4.9, H-8), 2.48 (1H, ddd, J 15.6, 6.9, 2.5, H-10ax), 4.48 (1H, br.s, H-1), 4.71 (1H, br.s, H-9), 4.74 (1H, s, H-3) and 6.44 (1H, dd, J 6.2, 5.0, H-5); and for the minor α epimer, 0.19 (3H, s, SiMe), 0.23 (3H, s, SiMe), 0.94 (9H, s, Si^{t}Bu), 1.41 (1H, d, J 3.7, OH), 1.86-1.72 (1H, m, H-10eq), 1.82-1.86 (2H, m, 2xH-11), 2.02 (1H, br.d, J 14.9, H-6), 2.06 (3H, s, OAc), 2.43-2.44 (1H, m, H-8), 2.45-2.50 (1H, m, H-10ax), 2.66 (1H, dd, J 14.8, 6.7, H-6), 4.40 (1H, br.d, J 3.6, H-1), 4.71 (1H, br.s, H-9), 4.90 (1H, s, H-3) and 6.43-6.45 (1H, m, H-5); *m/z* (CI, NH_3) 316 (MNH_4^+-AcOH), 299 (M^+-AcO), 281 (M^+-AcO-H_2O), 241 (M^+-AcOH-^{t}Bu), 223 (M^+-AcOH-^{t}Bu-H_2O), 195, 184, 167, 149, 123 and 91; [Found (MNH_4^+) 376.2155. $C_{17}H_{34}NO_6Si$ requires 376.2155].

Preparation of (1*S*, 4*RS*, 5*R*, 6*R*)-6-benzyloxy-4-(*tert*-butyldimethylsilyloxy)-2-oxabicyclo[3.2.1]octan-3-one (37). n-Butyllithium (21.1 ml of a 2.5 M solution in hexane, 52.7 mmol, 1.05 eq) was added dropwise, *via* syringe, to a stirred solution of diisopropylamine (7.39 ml, 52.7 mmol, 1.05 eq) in anhydrous tetrahydrofuran (100 ml) at 0°C, under argon. After stirring for 20 min at 0°C the lithium diisopropylamide was cooled to -78°C and the benzyloxylactone (**31**) (11.66 g, 50.2 mmol) added dropwise, *via* cannular, as a solution in anhydrous tetrahydrofuran (250 ml + 20 ml washings). The yellow solution was stirred at -78°C for 1 hr before the addition of oxodiperoxymolybdenum(pyridine)-1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone[23] (28.84 g, 75.3 mmol, 1.5 eq) smoothly in one portion. The yellow heterogeneous solution was stirred at -78°C for 15 min, then at -30 to -20°C for 30 min before being allowed to warm to room temperature. The reaction was quenched by the cautious addition of saturated aqueous sodium sulphate (100 ml) with stirring for 20 min. Water (150 ml) was added and the mixture extracted with ether (800 ml, 3x500 ml). The combined ethereals were then washed sequentially with 1N HCl (250 ml) and saturated brine (2x250 ml), dried ($MgSO_4$), filtered and evaporated *in vacuo* to give a yellow oil (14.1 g). The crude hydroxylactones were treated with *tert*-butyldimethylsilyl chloride [7.57 g, 50.2 mmol, 1 eq with respect to (**31**)] and imidazole [13.67 g, 200 mmol, 4 eq with respect to (**31**)] in anhydrous dimethylformamide (20 ml)

at room temperature, under argon. After stirring for 14 hr, the mixture was worked up in a similar manner to that described earlier. Purification by flash chromatography (gradient elution: 25% to 100% ether-petrol) gave, in order of elution, a C4 1:4, α:β epimeric mixture of the *tert*-butyldimethylsilyloxylactones (**37**) (14.7 g, 81%) as a clear oil; υ_{max} (film) 2929, 2855, 1745, 1461, 1360, 1308, 1252, 1215, 1188, 1088, 1055, 967 and 908 cm^{-1}; ^1H δ(500 MHz) for the major β epimer, 0.14 (3H, s, SiMe), 0.16 (3H, s, SiMe), 0.90 (9H, s, Si^{t}Bu), 1.87-1.89 (1H, m, H-8), 1.91 (1H, dt, J 15.3, 3.8, H-7eq), 2.31 (1H, br.d, J 13.3, H-8'), 2.44 (1H, ddd, J 15.5, 7.0, 2.6, H-7ax), 2.58 (1H, br.m, H-5), 3.87 (1H, dd, J 6.9, 3.0, H-6), 3.97 (1H, t, J 1.8, H-4), 4.49 (2H, s, PhC$\underline{H_2}$O-), 4.87 (1H, br.t, J 1.4, H-1), 7.30-7.38 (5H, m, Ph); and for the minor α epimer, 0.15 (3H, s, SiMe), 0.19 (3H, s, SiMe), 0.92 (9H, s, Si^{t}Bu), 1.93 (1H, dt, J 16.3, 4.0, H-7eq), 1.97 (1H, br.d, J 12.9, H-8'), 2.15 (1H, ddd, J 13.3, 5.5, 2.8, H-8), 2.56 (1H, ddd, J 15.6, 7.1, 2.6, H-7ax), 2.73 (1H, br.t, J 4.8, H-5), 4.23 (1H, d, J 5.3, H-4), 4.38 (1H, dd, J 7.1, 3.0, H-6), 4.47 (1H, d, J 11.8, PhC$\underline{H_2}$O-), 4.50 (1H, d, J 11.8, PhC$\underline{H_2}$O-), 4.80 (1H, br.dd, J 2.8, 1.5, H-1) and 7.27-7.36 (5H, m, Ph); *m/z* (EI$^+$) 305 (M$^+$-^{t}Bu), 243 (M$^+$-C_7H_7-CO), 197, 181, 153, 132, 91 ($C_7H_7^+$) and 75; (Found: C, 66.01; H, 8.45. $C_{20}H_{30}O_4Si$ requires C, 66.26; H, 8.34%); and the benzyloxylactone (**31**) (1.68g, 14% recovery).

Preparation of (1*S*, 4*S*, 5*R*, 6*R*)-6-benzyloxy-4-(*tert*-butyldimethylsilyloxy)-4-(prop-2-enyl)-2-oxabicyclo[3.2.1]octan-3-one (38). The *tert*-butyldimethylsilyloxylactones (**37**) (12.60 g, 34.8 mmol) were treated sequentially with KDA (1.1 eq), HMPA (50 ml, ~15% vol. of THF) and allyl bromide (2.0 eq), followed by work up, all in a similar manner to that described earlier. Purification by flash chromatography (gradient elution: 10% to 15% ether-petrol) gave the desired allyl lactone (**38**) (11.6 g, 80%) as a clear oil; $[\alpha]_D^{20}$=+45.2 (c=1.26, chloroform); υ_{max} (film) 2950, 2929, 2860, 1742, 1445, 1355, 1249, 1122, 1100 and 836 cm^{-1}; ^1H δ (500 MHz) 0.05 (3H, s, SiMe), 0.34 (3H, s, SiMe), 0.89 (9H, s, Si^{t}Bu), 1.98 (1H, br.d, J 14.9, H-7ax), 2.00 (1H, ddd, J 14.0, 5.0, 2.7, H-8), 2.07 (1H, br.d, J 14.1, H-8'), 2.45 (1H, ddd, J 15.7, 6.9, 2.3, H-7eq), 2.49 (1H, dd, J 14.6, 8.9, H-9), 2.66 (1H, ddt, J 14.6, 5.2, 1.5, H-9), 2.73 (1H, br.d, J 4.7, H-5), 4.40 (1H, br.d, J 5.8, H-6), 4.46 (2H, s, PhC$\underline{H_2}$O-), 4.80 (1H, br.s, H-1), 5.14 (1H, dd, J 17.2, 0.9, H-11), 5.21 (1H, d, J 10.1, H-11'), 5.91 (1H, dddd, J 17.1, 10.1, 9.0, 5.3, H-10) and 7.28-7.35 (5H, m, Ph); *m/z* (EI$^+$) 361 (M$^+$-$CH_2CH{=}CH_2$), 345 (M$^+$-^{t}Bu), 317 (M$^+$-^{t}Bu-CO), 283, 252, 237, 209, 193, 171, 149, 135, 127, 107, 91 ($C_7H_7^+$), 75, 57 and 43; (Found: C, 68.72; H, 8.60. $C_{23}H_{34}O_4Si$ requires C, 68.62; H, 8.51%).

Preparation of (1*S*, 3*S*, 4*S*, 5*R*, 6*R*)-6-benzyloxy-4-(*tert*-butyldimethylsilyloxy)-4-(prop-2-enyl)-2-oxabicyclo[3.2.1]octan-3-ol (39) and (β*S*, 1*R*, 2*R*, 4*S*)-2-benzyloxy-β-(*tert*-butyldimethylsilyloxy)-4-hydroxy-β-(prop-2-enyl) ethanol (40). The allyl lactone (**38**) (14.6 g, 36.3 mmol) was reduced with DIBAL (1.35 eq) and worked up in a similar manner to that described earlier. A small sample was purified by flash chromatography (gradient elution: 40% to 100% ether-petrol) to give, in order of elution, the desired lactol (**39**), ~17% of which was in its open hydroxy-aldehyde form (^1H δ 9.49, s, CHO), as a clear oil; υ_{max} (film) 3373, 2953, 2854, 1740, 1630, 1461, 1357, 1248, 1091, 1062, 1003 and 914 cm^{-1}; ^1H δ(500 MHz) 0.12 (3H, s, SiMe), 0.18 (3H, s, SiMe), 0.90 (9H, s, Si^{t}Bu), 1.61 (1H, ddd, J 12.6, 5.2, 2.3, H-8), 1.77 (1H, br.d, J 11.3, H-8'), 1.80 (1H, ddd, J 15.5, 4.0, 2.9, H-7ax), 2.32-2.36 (1H, m, H-7eq), 2.38 (1H, dd, J 15.4, 9.3, H-9), 2.47 (1H, d, J 5.0, H-5), 2.51 (1H, ddt, J 14.9, 5.0, 1.8, H-9), 2.69 (1H, m, OH), 4.25 (1H, dd, J 6.9, 1.5, H-1), 4.41 (1H, br.s, H-6), 4.45 (1H, d, J 11.5, PhC$\underline{H_2}$O-), 4.49 (1H, d, J 11.6, PhC$\underline{H_2}$O-), 4.51 (1H, d, J 6.9, H-3), 5.12-5.17 (2H, m, H-11 and H-11'), 5.86-5.95 (1H, m, H-10) and 7.25-7.38 (5H, m, Ph); *m/z* (EI$^+$) 375 (M$^+$-CHO), 347 (M$^+$-^{t}Bu), 329 (M$^+$-^{t}Bu-H_2O), 317, 269, 255, 239 (M$^+$-^{t}Bu-PhCH_2OH), 211, 181, 169, 157, 131, 117, 91 ($C_7H_7^+$), 84, 73 and 49; (Found: C, 68.14; H, 9.05. $C_{23}H_{36}O_4Si$ requires C, 68.27; H, 8.97%); and the over reduced diol (**40**) as a clear oil; $[\alpha]_D^{20}$=-60.3 (c=0.61, chloroform); υ_{max} (film) 3390, 2951, 2927, 2854, 1453, 1357, 1250, 1066 and 916 cm^{-1}; ^1H δ(500 MHz) 0.10 (3H, s, SiMe), 0.12 (3H, s, SiMe), 0.86 (9H, s, Si^{t}Bu), 1.60 (1H, ddd, J 12.6, 10.2, 7.0, H-5), 1.86 (1H, quin, J 6.7, H-3), 2.02 (1H, dddd, J 12.9, 6.5, 5.1, 1.4, H-3), 2.26 (1H, dddd, J 12.9, 7.3, 5.8, 1.2, H-5), 2.36-2.40 (1H, m, H-1), 2.40 (1H, dd, J 13.7, 7.3, H-1'), 2.44 (1H, br.t, J 6.6, α-OH), 3.45 (1H, br.dd, J 12.0, 7.8, α-H), 3.50 (1H, br.dd, J 11.9, 4.7, α-H), 4.07 (1H, td, J 7.0, 5.0, H-2), 4.37 (1H, m, H-4), 4.37 (1H, d, J 11.1, PhC$\underline{H_2}$O-), 4.54 (1H, d, J 11.2, PhC$\underline{H_2}$O-), 5.05 (1H,

br.d, J 10.2, H-3'c), 5.08 (1H, br.d, J 17.3, H-3't), 5.93 (1H, ddt, J 17.3, 10.1, 7.2, H-2') and 7.28-7.36 (5H, m, Ph); *m/z* (EI+) 375 (M^+-CH_2OH), 347 (M^+-$CH_2CH{=}CH_2$-H_2O), 285 (MH^+-CH_2OH-C_7H_7), 269 (MH^+-CH_2OH-C_7H_7O), 257, 241 (M^+-^{t}Bu-$PhCH_2OH$), 223, 199, 157, 131, 91 ($C_7H_7^+$) and 75; [Found (M^+-CH_2OH) 375.2363. $C_{22}H_{35}O_3Si$ requires 375.2355].

Preparation of (1*S*, 3*R*, 5*RS*, 7*S*, 8*R*, 9*R*)-9-benzyloxy-7-(*tert*-butyldimethylsilyloxy)-2,4-dioxatricyclo[6.2.1.0^{3,7}]undecan-5-ol (42) and (2*RS*, 4*S*, 1'*R*, 2'*S*, 4'*S*)-4-[*tert*-butyldimethylsilyloxy(2-benzyloxy-4-hydroxycyclopentyl)]tetrahydro-2-furan-2-ol (41). Ozone (140 V, 35 l hr^{-1}) was bubbled through a solution of the crude alkenelactol (**39** + **40**) (15.89 g, assumed 36.2 mmol) in dichloromethane (500 ml) at -78°C until a faint blue colour persisted (4 hr). The reaction mixture was purged with oxygen, triphenylphosphine (11.39 g, 43.4 mmol, 1.2 eq) was added at -78°C and the resultant clear solution slowly warmed to room temperature and stirred overnight. Evaporation to dryness *in vacuo*, followed by purification by flash chromatography (gradient elution: 30% to 60% ethyl acetate-petrol) gave, in order of elution, a C5 1:4, α:β epimeric mixture of the tricyclic lactols (**42**) (11.04 g, 75% over 2 steps) as a clear oil; υ_{max} (film) 3418, 2951, 2929, 2854, 1459, 1357, 1310, 1257, 1185, 1132, 1098, 1069, 1027 and 971 cm^{-1}; ^1H δ(500 MHz) for the major β isomer, 0.13 (3H, s, SiMe), 0.15 (3H, s, SiMe), 0.88 (9H, s, Si^{t}Bu), 1.83-1.90 (2H, m, H-10eq and H-11'), 1.96 (1H, br.d, J 13.1, H-11), 2.28 (1H, dd, J 15.1, 4.1, H-6), 2.33 (1H, dd, J 15.0, 6.1, H-6), 2.46 (1H, ddd, J 15.4, 6.7, 2.5, H-10ax), 2.64 (1H, d, J 4.9, H-8), 3.07 (1H, br.d, J 8.5, OH), 4.38-4.40 (1H, m, H-9), 4.44 (1H, d, J 11.3, $PhC\underline{H}_2O$-), 4.46 (1H, m, H-1), 4.48 (1H, d, J 11.3, $PhC\underline{H}_2O$-), 4.75 (1H, s, H-3), 5.66-5.70 (1H, m, H-5) and 7.27-7.37 (5H, m, Ph); and for the minor α isomer, 0.22 (3H, s, SiMe), 0.26 (3H, s, SiMe), 0.92 (9H, s, Si^{t}Bu), 1.83-1.90 (2H, m, H-10eq and H-11'), 1.93-1.95 (1H, m, H-11), 2.35-2.38 (1H, m, H-6), 2.38-2.43 (1H, m, H-10ax), 2.56 (1H, dd, J 14.4, 6.2, H-6), 2.68 (1H, br.s, H-8), 2.97 (1H, br.d, J 9.9, OH), 4.36-4.38 (1H, m, H-9), 4.45-4.49 (2H, m, $PhC\underline{H}_2O$-), 4.47 (1H, m, H-1), 4.88 (1H, s, H-3), 5.64 (1H, ddd, J 10.0, 6.4, 1.3, H-5) and 7.27-7.37 (5H, m, Ph); *m/z* (EI+) 377 (M^+-CHO), 359 (M^+-CHO-H_2O), 349 (M^+-^{t}Bu), 331 (M^+-^{t}Bu-H_2O), 319, 313, 269, 257, 241 (M^+-^{t}Bu-$PhCH_2OH$), 223 (M^+-^{t}Bu-$PhCH_2OH$-H_2O), 195, 183, 167, 157, 149, 129, 123, 111, 91 ($C_7H_7^+$) and 75; (Found: C, 64.70; H, 8.34. $C_{22}H_{34}O_5Si$ requires C, 64.99; H, 8.43%); and a mixed fraction containing the hydroxylactol (**41**) derived from the over reduced diol (**40**) and triphenylphosphine oxide (1.94 g). A small portion of this was purified to analytical purity by flash chromatography (gradient elution: 40% to 50% ethyl acetate-petrol) to give the C2 1:4, α:β epimeric mixture of hydroxylactols as a clear oil; υ_{max} (film) 3390, 3062, 3029, 2952, 2929, 2886, 2856, 1494, 1459, 1433, 1405, 1387, 1359, 1253, 1206, 1142, 1068, 1004, 938 and 912 cm^{-1}; ^1H δ(500 MHz) for the major isomer only, 0.07 (3H, s, SiMe), 0.09 (3H, s, SiMe), 0.85 (9H, s, Si^{t}Bu), 1.52 (1H, ddd, J 12.5, 9.9, 7.4, H-5'), 1.79-1.84 (2H, m, 2xH-3'), 1.98-2.08 (1H, m, H-5'), 2.15-2.22 (2H, m, 2xH-3), 3.03 (1H, br.d, J 3.5, OH), 3.33 (1H, br.d, J 5.8, OH), 3.70 (1H, d, J 9.6, H-5), 3.85 (1H, d, J 9.7, H-5), 4.08 (1H, dt, J 6.9, 5.2, H-2'), 4.32-4.38 (1H, m, H-4'), 4.38 (1H, d, J 11.5, $PhC\underline{H}_2O$-), 4.55 (1H, d, J 11.6, $PhC\underline{H}_2O$-), 5.62-5.64 (1H, m, H-2) and 7.27-7.36 (5H, m, Ph); *m/z* (EI+) 351 (M^+-^{t}Bu), 333 (M^+-^{t}Bu-H_2O), 307, 291, 258, 243, 225, 217, 199, 185, 170, 152, 120, 84 and 75; (Found: C, 64.55; H, 8.92. $C_{22}H_{36}O_5Si$ requires C, 64.67; H, 8.88%).

Preparation of (1*S*, 3*R*, 5*RS*, 7*S*, 8*R*, 9*R*)-9-benzyloxy-7-(*tert*-butyldimethylsilyloxy)-5-methoxy-2,4-dioxatricyclo[6.2.1.0^{3,7}]undecane (43). Methanol (0.79 ml, 33.0 mmol) and then anhydrous acetonitrile (~250 ml) were added swiftly to the tricyclic lactols (**42**) (2.68 g, 6.59 mmol), flame dried 3Å molecular sieves (2.1 g) and Amberlyst 15 sulphonic acid ion exchange resin (1.8 g), at room temperature under argon. After vigorously stirring for 15 min the reaction mixture was filtered over celite, washed copiously with ethyl acetate and the filtrate evaporated to dryness *in vacuo* to give a white solid. Purification by flash chromatography (gradient elution: 15% to 20% ethyl acetate-petrol) gave the desired tricyclic acetal (**43**) (2.30 g, 83%) as an amorphous white solid; mp. 78-88°C; υ_{max} (film) 2927, 2854, 1453, 1369, 1253, 1192, 1124, 1083, 1069, 1050, 1029, 1010, 967 and 948 cm^{-1}; ^1H δ(500 MHz) for the major β isomer only, 0.15 (3H, s, SiMe), 0.17 (3H, s, SiMe), 0.89 (9H, s, Si^{t}Bu), 1.80 (1H, ddd, J 12.8, 5.2, 2.6, H-11), 1.84 (1H, m, H-10eq), 1.98 (1H, br.d, J 12.8, H-11'), 2.22 (1H, dd, J 14.6, 6.0, H-6), 2.32 (1H,

dd, J 14.7, 5.1, H-6), 2.40 (1H, ddd, J 15.3, 6.6, 2.5, H-10ax), 2.62 (1H, d, J 4.9, H-8), 3.46 (3H, s, OMe), 4.42 (1H, d, J 11.0, PhC$\underline{H}_2$O-), 4.40-4.43 (1H, m, H-9), 4.47-4.48 (1H, m, H-1), 4.48 (1H, d, J 11.2, PhC$\underline{H}_2$O-), 4.73 (1H, s, H-3), 5.29 (1H, dd, J 5.9, 5.2, H-5) and 7.27-7.35 (5H, m, Ph); *m/z* (CI, NH_3) 438 (MNH_4^+), 406 (MNH_3-MeO), 389 (M^+-MeO), 281, 123, 108 and 91 ($C_7H_7^+$); (Found: C, 65.67; H, 8.60. $C_{23}H_{36}O_5Si$ requires C, 65.68; H, 8.63%). Crystals suitable for single crystal X-ray analysis were prepared by slow evaporation from diethyl ether at room temperature; white needles mp. 99-101°C.

Preparation of (1*S*, 3*R*, 5*RS*, 7*S*, 8*R*, 9*R*)-7-(*tert*-butyldimethylsilyloxy)-5-methoxy-2,4-dioxatricyclo[6.2.1.0^{3,7}]undecan-9-ol (44). 10% Palladium on carbon (230 mg, 10% wt.) was added, as a slurry in methanol, to a solution of the tricyclicacetals (**43**) (2.30 g, 5.47 mmol) and 1M HCl (15 drops) in redistilled methanol (200 ml). The reaction was then degassed and filled with hydrogen (from a balloon) three times before finally being stirred vigorously at room temperature, under an atmosphere of hydrogen. After 1 hr the reaction was filtered over a small plug of celite, copiously washed with ethyl acetate and the filtrate evaporated to dryness *in vacuo* to give a pale yellow solid. Purification by flash chromatography (gradient elution: 50% to 60% ethyl acetate-petrol) gave the desired 9-hydroxytricyclicacetals as a C5-methoxy 1:3, α:β epimeric mixture (**44**) (1.80 g, 98%) as a clear oil; υ_{max} (film) 3452, 2952, 2929, 2854, 1461, 1439, 1375, 1359, 1257, 1217, 1191, 1128, 1110, 1092, 1060, 1007, 967, 941 and 925 cm^{-1}; ^1H δ(500 MHz) for the major β isomer, 0.16 (3H, s, SiMe), 0.18 (3H, s, SiMe), 0.90 (9H, s, Si^{t}Bu), 1.43 (1H, br.s, OH), 1.67 (1H, dddd, J 15.5, 5.2, 2.2, 1.0, H-10eq), 1.79 (1H, ddd, J 12.8, 5.1, 2.6, H-11), 1.98 (1H, br.d, J 12.7, H-11'), 2.19 (1H, dd, J 14.6, 5.9, H-6), 2.29 (1H, dd, J 14.6, 5.3, H-6), 2.40 (1H, br.d, J 4.9, H-8), 2.45-2.50 (1H, m, H-10ax), 3.46 (3H, s, OMe), 4.46-4.48 (1H, m, H-1), 4.69 (1H, br.d, J 6.0, H-9), 4.69 (1H, s, H-3) and 5.28 (1H, t, J 5.6, H-5); and for the minor α isomer, 0.17 (3H, s, SiMe), 0.18 (3H, s, SiMe), 0.90 (9H, s, Si^{t}Bu), 1.43 (1H, br.s, OH), 1.64-1.69 (1H, m, H-10eq), 1.81 (2H, m, 2xH-11), 1.93 (1H, ddd, J 14.5, 2.6, 0.6, H-6), 2.40 (1H, m, H-8), 2.42-2.45 (1H, m, H-6), 2.44-2.49 (1H, m, H-10ax), 3.39 (3H, s, OMe), 4.35-4.37 (1H, m, H-1), 4.73 (1H, br.d, J 5.3, H-9), 4.82 (1H, s, H-3) and 5.26 (1H, dd, J 6.6, 2.5, H-5); *m/z* (CI, NH_3) 348 (MNH_4^+), 316 (MNH_3-MeO), 299 (M^+-MeO), 241 (MNH_3-^{t}Bu-MeO-H_2O), 201, 184, 167, 153, 123 and 91 ($C_7H_7^+$); (Found: C, 57.87; H, 9.36. $C_{16}H_{30}O_5Si$ requires C, 58.15; H, 9.15%).

Preparation of (1*S*, 3*R*, 5*RS*, 7*S*, 8*R*, 9*R*)-7-(*tert*-butyldimethylsilyloxy)-5-methoxy-2,4-dioxatricyclo[6.2.1.0^{3,7}]undecan-9-ol methanesulphonate. Methanesulphonyl chloride (422 μl, 5.45 mmol, 1.5 eq) was added dropwise to a stirred solution of the 9-hydroxytricyclicacetals (**44**) (1.20 g, 3.63 mmol) and triethylamine (1.31 ml, 18.2 mmol, 5 eq) in anhydrous dichloromethane (50 ml) at room temperature, under argon. The reaction mixture gradually turned yellow and after 10 min was quenched by the addition of saturated aqueous sodium bicarbonate (25 ml) with vigorous stirring for 5 min. Upon separation the aqueous phase was extracted with dichloromethane (3x30 ml). The combined organic layers were dried ($MgSO_4$), filtered and evaporated *in vacuo* to give a yellow oil. Purification by flash chromatography (gradient elution: 40% to 50% ethyl acetate-petrol) gave the 9-methanesulphonates as a C5-methoxy 1:3, α:β epimeric mixture (1.48 g, 99%) as a clear oil; υ_{max} (film) 2932, 2855, 1461, 1356, 1256, 1193, 1174, 1130, 1091, 1052, 967, 949 and 929 cm^{-1}; ^1H δ(500 MHz) for the major β isomer, 0.17 (3H, s, SiMe), 0.19 (3H, s, SiMe), 0.92 (9H, s, Si^{t}Bu), 1.79 (1H, ddd, J 13.1, 5.0, 2.8, H-11), 2.07-2.15 (2H, m, H-10eq and H-11'), 2.30 (2H, d, J 5.3, 2xH-6), 2.61 (1H, ddd, J 16.3, 6.8, 2.5, H-10ax), 2.75 (1H, br.d, J 4.8, H-8), 2.99 (3H, s, $MeSO_3$-), 3.44 (3H, s, OMe), 4.49-4.51 (1H, m, H-1), 4.76 (1H, s, H-3), 5.29 (1H, t, J 5.3, H-5) and 5.50 (1H, dt, J 6.8, 1.5, H-9); and for the minor α isomer, 0.20 (3H, s, SiMe), 0.21 (3H, s, SiMe), 0.92 (9H, s, Si^{t}Bu), 1.80-1.83 (1H, m, H-11), 1.92 (1H, br.d, J 13.0, H-11'), 2.03 (1H, dd, J 14.2, 3.2, H-6), 2.12-2.15 (1H, m, H-10eq), 2.48 (1H, dd, J 14.8, 6.6, H-6), 2.58 (1H, ddd, J 16.3, 6.9, 2.5, H-10ax), 2.72 (1H, br.d, J 5.0, H-8), 2.99 (3H, s, $MeSO_3$-), 3.41 (3H, s, OMe), 4.40-4.42 (1H, m, H-1), 4.87 (1H, s, H-3), 5.25 (1H, dd, J 6.6, 3.3, H-5) and 5.53 (1H, br.d, J 6.9, H-9); *m/z* (EI^+) 407 (M^+-H), 377 (M^+-MeO), 361, 351 (M^+-^{t}Bu), 335, 319 (M^+-^{t}Bu-MeOH), 223, 201, 153, 121, 93, 73, 67 and 41; (Found: C, 49.91; H, 8.02. $C_{17}H_{32}O_7SSi$ requires C, 49.97; H, 7.89%).

Preparation of (1*S*, 3*R*, 5*RS*, 7*S*, 8*R*)-7(*tert*-butyldimethylsilyloxy)-5-methoxy-2,4-dioxatricyclo[6.2.1.0^{3,7}]undec-9-ene (46). 1,8-Diazabicyclo[5.4.0]undec-7-ene (5.43 ml, 36.3 mmol, 10 eq) was added to a solution of the 9-methanesulphonates (prepared above) (1.48 g, 3.63 mmol) in anhydrous toluene (25 ml) and the mixture heated to ~120°C, under argon, for 38 hr. The cooled reaction mixture was then purified by flash chromatography, loaded in the reaction solvent (gradient elution: 25% to 30% ethyl acetate-petrol), to give the alkenes as a C5-methoxy 1:3, α:β epimeric mixture (**46**) (1.08 g, 95% over two steps) as a clear oil; υ_{max} (film) 2931, 2854, 1461, 1360, 1342, 1318, 1256, 1194, 1131, 1105, 1075, 1028, 967 and 938 cm^{-1}; ^{1}H δ(500 MHz) for the major β isomer, 0.12 (3H, s, SiMe), 0.15 (3H, s, SiMe), 0.87 (9H, s, Si^{t}Bu), 1.76 (1H, ddd, J 11.6, 5.0, 3.0, H-11), 2.06 (1H, br.d, J 11.6, H-11'), 2.28 (2H, d, J 6.3, 2xH-6), 2.97 (1H, dd, J 5.0, 2.9, H-8), 3.46 (3H, s, MeO), 4.57 (1H, br.s, H-1), 4.81 (1H, s, H-3), 5.30 (1H, t, J 5.3, H-5), 6.08 (1H, dd, J 5.7, 2.6, H-10), 6.46 (1H, dd, J 5.7, 2.8, H-9); and for the minor α isomer, 0.14 (3H, s, SiMe), 0.17 (3H, s, SiMe), 0.87 (9H, s, Si^{t}Bu), 1.81 (1H, ddd, J 11.7, 4.8, 2.9, H-11), 1.86 (1H, br.d, J 11.7, H-11'), 1.98 (1H, dd, J 14.5, 3.4, H-6), 2.46 (1H, dd, J 14.5, 6.4, H-6), 2.96 (1H, dd, J 4.7, 3.0, H-8), 3.42 (3H, s, OMe), 4.57 (1H, br.s, H-1), 4.96 (1H, s, H-3), 5.36 (1H, dd, J 6.4, 3.5, H-5), 6.10 (1H, dd, J 6.4, 3.5, H-10) and 6.46 (1H, m, H-9); *m/z* (CI, NH_3) 330 (MNH_4^+), 298 (MNH_4^+-MeOH), 281 (M^+-MeO), 267, 235, 223, 166, 149, 132 and 90; (Found: C, 61.38; H, 9.21. $C_{16}H_{28}O_4Si$ requires C, 61.50; H, 9.03%).

Preparation of (1*S*, 3*R*, 5*RS*, 7*S*, 8*R*, 9*S*, 11*S*)-7-(t-butyldimethylsilyloxy)-5-methoxy-2,4,10-tri-oxatetracyclo[6.3.1.0.^{3,7}0^{9,11}]dodecane (47). A chilled (-78°C) solution of dimethyldioxirane in acetone[27] (22.5 ml of a 0.1M solution, ~1.5 eq) was added in one portion to the alkenes (**46**) (480 mg, 1.54 mmol) in dichloromethane (25 ml) at room temperature in air and left to stir overnight. Evaporation of the solvents gave the epoxides as a C5-methoxy 1:3, α:β epimeric mixture (**47**) (516 mg, 99%) as a clear oil; υ_{max} (film) 2953, 2930, 2855, 1462, 1359, 1318, 1257, 1211, 1194, 1136, 1122, 1099, 1078, 1042, 1028, 970, 954 and 938 cm^{-1}; ^{1}H δ(500 MHz) for the major β isomer, 0.15 (3H, s, SiMe), 0.19 (3H, s, SiMe), 0.90 (9H, s, Si^{t}Bu), 1.45 (1H, ddd, J 13.1, 5.3, 3.2, H-12), 1.70 (1H, d, J 13.1, H-12'), 2.23 (1H, dd, J 15.0, 3.9, H-6), 2.31 (1H, dd, J 15.0, 6.2, H-6), 2.99 (1H, d, J 5.4, H-8), 3.42 (3H, s, OMe), 3.50 (1H, br.d, J 2.5, H-11), 3.80 (1H, d, J 2.9, H-9), 4.41 (1H, br.d, J 3.2, H-1), 5.26 (1H, s, H-3) and 5.27 (1H, dd, J 6.2, 3.9, H-5); and for the minor α isomer, 0.18 (3H, s, SiMe), 0.21 (3H, s, SiMe), 0.90 (9H, s, Si^{t}Bu), 1.47 (1H, ddd, J 13.2, 4.6, 2.9, H-12), 1.50 (1H, br.d, J 13.5, H-12'), 2.07 (1H, dd, J 14.7, 3.0, H-6), 2.37 (1H, dd, J 14.8, 3.0, H-6), 2.66 (1H, d, J 4.6, H-8), 3.40 (3H, s, OMe), 3.50 (1H, br.s, H-11), 3.77 (1H, d, J 3.0, H-9), 4.36 (1H, m, H-1), 5.21 (1H, dd, J 6.3, 3.1, H-5) and 5.29 (1H, s, H-3); *m/z* (CI, NH_3) 346 (MNH_4^+), 329 (MH^+), 314 (MNH_4^+-MeOH), 297 (M^+-MeOH) and 271 (M^+-^{t}Bu); (Found: C, 58.29; H, 8.50. $C_{16}H_{28}O_5Si$ requires C, 58.50; H, 8.59%).

Preparation of (1*S*, 3*R*, 5*RS*, 7*S*, 8*R*, 9*S*, 11*S*)-7-(*tert*-butyldimethylsilyloxy)-5-phenylseleno-2,4,10-tri-oxatetracyclo[6.3.1.0.^{3,7}0^{9,11}]dodecane (48). Amberlyst 15 sulphonic acid ion exchange resin (~500 beads) was added to a vigorously stirred suspension of activated 4Å molecular sieves (~500 beads) in a solution of the methoxy acetals (**47**) (377 mg, 1.15 mmol) and benzene selenol (609 μl, 5.74 mmol, 5 eq) in anhydrous acetonitrile (25 ml) at room temperature, under argon. After 1 hr the reaction mixture was filtered over a small plug of sodium bicarbonate and evaporated to dryness *in vacuo* to give a yellow oil. Purification by flash chromatography (gradient elution: 15% to 20% ether-petrol) gave the epoxides and a trace of an unknown by-product as a C5-phenylselenide 2:3:1, α:β epimeric mixture:unknown, (**48**) (227 mg, 44%) as a pale yellow oil; υ_{max} (film) 2970, 2960, 2945, 1570,1470, 1460, 1420, 1330, 1250, 1185, 1130, 1100, 1050 and 980 cm^{-1}; ^{1}H δ(500 MHz) for the β epimer only, 0.13 (3H, s, SiMe), 0.19 (3H, s, SiMe), 0.88 (9H, s, Si^{t}Bu), 1.41 (1H, ddd, J ~13, 4.5, 2.8 H-12), 1.43 (1H, br.d, J ~13, H-12'), 2.49 (2H, dd, J 7.3, 0.8, 2xH-6), 2.71 (1H, d, J 4.4, H-8), 3.50 (1H, dd, J 2.9, 1.0, H-11), 3.80 (1H, d, J 2.8, H-9), 4.39 (1H, t, J 1.3, H-1), 5.28 (1H, s, H-3), 5.88 (1H, t, J 7.4, H-5), 7.28-7.31 (3H, m, *o*- and *p*-Ph) and 7.64-7.65 (2H, m, *m*-Ph); *m/z* (CI, NH_3) 472 (MNH_4^+), 455 (MH^+), 391, 314 and 297 (M^+-PhSeH); [Found (MH^+) 455.1157. $C_{21}H_{31}O_4SeSi$ requires 455.1157].

Preparation of (1*S*, 3*R*, 5*RS*, 7*S*, 8*R*, 9*S*, 11*S*)-7-(*tert*-butyldimethylsilyloxy)-2,4,10-trioxatetracyclo[6.3.1.0.^{3,7}0^{9,11}]dodec-5-ene (49). 2-(Phenylsulphonyl)-3-(*p*-nitrophenyl)oxaziridine (169 mg, 0.551 mmol, 1.1 eq) was added to a solution of the selenides (**48**) (227 mg, assumed 0.551 mmol) and pyridine (44.5 µl, 0.551 mmol, 1.1 eq) in dichloromethane (10 ml) at room temperature in air. After 10 min saturated aqueous sodium bicarbonate (10 ml) was added with vigorous stirring for 10 min and the mixture extracted with dichloromethane (3x10 ml). The combined organic layers were dried ($MgSO_4$), filtered and evaporated to dryness *in vacuo* to give a pale yellow solid that was purified by flash chromatography (gradient elution: 15% to 20% ether-petrol) to give the epoxytetracyclic enol ether (**49**) (87 mg, 57%) as a clear oil; $[\alpha]_D^{20}$=-157.2 (c=0.93, chloroform); υ_{max} (film) 3061, 2953, 2887, 2855, 1612, 1469, 1439, 1387, 1360, 1327, 1253, 1230, 1209, 1138, 1104, 1074, 1023 and 947 cm^{-1}; ^{1}H δ(500 MHz) 0.06 (3H, s, SiMe), 0.12 (3H, s, SiMe), 0.88 (9H, s, Si^{t}Bu), 1.34 (1H, d, J 13.3, H-12'), 1.48 (1H, ddd, J 13.2, 5.5, 3.4, H-12), 2.59 (1H, d, J 5.5, H-8), 3.52 (1H, d, J 3.0, H-11), 3.79 (1H, d, J 2.9, H-9), 4.32 (1H, dt, J 3.4, 1.0, H-1), 5.04 (1H, d, J 2.9, H-6), 5.40 (1H, s, H-3) and 6.47 (1H, d, J 2.9, H-5); *m/z* (CI, NH_3) 297 (MH^+), 239 (M^+-^{t}Bu), 157, 129, 81 and 75; [Found (MH^+) 297.1522. $C_{15}H_{25}O_4Si$ requires 297.1522].

Preparation of (1*S*, 3*R*, 7*S*, 8*R*, 9*S*, 11*S*)-2,4,10-trioxatetracyclo[6.3.1.0.^{3,7}0^{9,11}]dodec-5-ene-7-ol (45). Tetra-n-butylammonium fluoride (526 µl of a 1M solution in tetrahydrofuran, 0.526 mmol, 1.5 eq) was added, *via* syringe, to a stirred solution of the silyl ether (**49**) (104 mg, 0.351 mmol) in tetrahydrofuran (5 ml) at room temperature, in air. After 30 min the reaction was evaporated to dryness *in vacuo* and the residue purified by flash chromatography (50% ethyl acetate-petrol) to give the desired alcohol (**45**) (61 mg, 95%) as an amorphous white solid; mp. 97-99°C; $[\alpha]_D^{20}$=-146.4 (c=0.80, chloroform); υ_{max} (film) 3465, 3109, 3057, 2935, 1617, 1449, 1382, 1328, 1298, 1275, 1225, 1213, 1176, 1143, 1101, 1088, 1059, 1004 and 934 cm^{-1}; ^{1}H δ(500 MHz) 1.36 (1H, d, J 13.1, H-12'), 1.54 (1H, ddd, J 13.2, 5.5, 3.4, H-12), 1.77 (1H, br.s, OH), 2.67 (1H, d, J 5.4, H-8), 3.53 (1H, d, J 2.9, H-11), 3.84 (1H, d, J 2.9, H-9), 4.36 (1H, dt, J 3.4, 0.9, H-1), 5.12 (1H, d, J 2.7, H-6), 5.50 (1H, s, H-3) and 6.53 (1H, d, J 2.7, H-5); *m/z* (CI, NH_3) 200 (MNH_4^+), 183 (MH^+), 165 (M^+-OH), 153, 147 (MH^+-2H_2O), 137, 119, 109, 99, 84 and 78; (Found: C, 59.48; H, 5.49. $C_9H_{10}O_4$ requires C, 59.34; H, 5.53%).

Preparation of (1*R*, 3*R*, 5*RS*, 7*S*, 8*S*)-7-(*tert*-butyldimethylsilyloxy)-5-methoxy-2,4-dioxatricyclo[6.2.1.0^{3,7}]undecane (50). 10% Palladium on carbon (15 mg, 10% wt) was added, as a slurry in methanol, to a solution of the alkenes (**46**) (148 mg, 0.474 mmol) in methanol (7 ml total). The reaction was then degassed and filled with hydrogen (from a balloon) three times before finally being vigorously stirred at room temperature, under an atmosphere of hydrogen. After 25 min the reaction was filtered over a small plug of celite, washed copiously with ethyl acetate and the filtrate evaporated to dryness *in vacuo* to give the saturated methoxy acetal (**50**) (144 mg, 97%) as a pure white, low melting point solid; υ_{max} (film) 2930, 2857 and 1055 cm^{-1}; ^{1}H δ(500 MHz) 0.13 (6H, s, $SiMe_2$), 0.88 (9H, s, Si^{t}Bu), 1.33 (1H, ddd, J 12.6, 5.0, 2.6, H-11), 1.56-1.63 (1H, H-9eq), 1.68-1.76 (1H, m, H-10eq), 1.91 (1H, dddd, J 14.6, 9.4, 5.2, 2.6, H-9ax), 2.07 (1H, d, J 12.6, H-11'), 2.15 (1H, dd, J 14.4, 5.9, H-6), 2.16-2.22 (1H, m, H-10ax), 2.30 (1H, dd, J 14.4, 5.4, H-6), 2.44 (1H, t, J 5.5, H-8), 3.46 (3H, s, OMe), 4.40 (1H, br.s, H-1), 4.84 (1H, s, H-3) and 5.30 (1H, t, J 5.6, H-5); *m/z* (EI^+) 314 (M^+), 283 (M^+-OMe), 257 (M^+-^{t}Bu) and 225 (M^+-^{t}Bu-Me); [Found (M^+) 314.1913. $C_{16}H_{30}O_4Si$ requires 314.1919].

Preparation of (1*R*, 3*R*, 5*RS*, 7*S*, 8*S*)-7-(*tert*-butyldimethylsilyloxy)-5-phenylseleno-2,4-dioxatricyclo[6.2.1.0^{3,7}]undecane. Amberlyst 15 sulphonic acid ion exchange resin (~120 beads) was added to a vigorously stirred suspension of activated 4Å molecular sieves (~120 beads) in a solution of the methoxy acetals (**50**) (144 mg, 0.4585 mmol) and benzene selenol (58 µl, 0.549 mmol, 51.2 eq) in anhydrous acetonitrile (14 ml) at room temperature, under argon. After 15 min the reaction mixture was filtered over a small plug of sodium bicarbonate and evaporated to dryness *in vacuo* to give a yellow oil. Purification by flash chromatography (gradient elution 10% to 15% ether-petrol) gave the phenylselenides as a C5 1:2, α:β epimeric mixture (109 mg, 58%) as a clear oil; υ_{max} (film) 2960, 2930, 2850, 1580, 1465, 1440, 1260, 1180, 1130, 1080, 1050, 1030 and 1000 cm^{-1}; ^{1}H δ(500 MHz) for the major β epimer, 0.11 (6H, s, $SiMe_2$), 0.86 (9H, s, Si^{t}Bu), 1.28 (1H, ddd, J 12.4, 5.1, 2.6, H-11), 1.57-1.65 (1H, H-9eq), 1.68-1.79 (1H, m, H-10eq), 1.87-

1.92 (2H, m, H-9ax and H-11'), 2.16-2.23 (1H, m, H-10ax), 2.33 (1H, dd, J 14.3, 6.9, H-6), 2.47 (1H, t, J 5.4, H-8), 2.56 (1H, dd, J 14.4, 8.2, H-6), 4.35 (1H, br.s, H-1), 4.89 (1H, s H-3), 5.92 (1H, dd, J 8.2, 7.0, H-5), 7.23-7.31 (3H, m, *o*- and *p*-Ph) and 7.60-7.66 (2H, m, *m*-Ph); and for the minor α epimer, 0.16 (3H, s, SiMe), 0.21 (3H, s, SiMe), 0.93 (9H, s, Si^{t}Bu), 1.40 (1H, ddd, J 12.5, 5.3, 2.6, H-11), 1.57-1.65 (1H, H-9eq), 1.68-1.79 (1H, m, H-10eq), 1.87-1.92 (2H, m, H-9ax and H-11'), 2.15 (1H, dd, J 14.8, 6.4, H-6), 2.16-2.23 (1H, m, H-10ax), 2.52 (1H, t, J 5.6, H-8), 2.83 (1H, dd, J 14.6, 8.3, H-6), 4.31 (1H, br.s, H-1), 5.04 (1H, s, H-3), 5.88 (1H, dd, J 8.3, 6.4, H-5), 7.23-7.31 (3H, m, *o*- and *p*-Ph) and 7.60-7.66 (2H, m, *m*-Ph); *m/z* (CI, NH_3) 458 (MNH_4^+), 300 (MNH_4^+-PhSeH), 283 (M^+-PhSe), 255, 241, 168, 151, 123 and 90; [Found (M^+-PhSe) 283.1729. $C_{15}H_{27}O_3Si$ requires 283.1729].

Preparation of (1*R*, 3*S*, 7*R*, 8*S*)-7-(*tert*-butyldimethylsilyloxy)-2,4-dioxatricyclo[6.2.1.0^{3,7}]undec-5-ene. The selenides (prepared above) (107 mg, 0.260 mmol) were treated with 2-(phenylsulphonyl)-3-(*p*-nitrophenyl)oxaziridine in a similar manner to that described earlier. Purification by flash chromatography yielded the enol ether (60 mg, 82%) with all physical data identical to the racemic material: $[\alpha]_D^{20}$=-194.1 (c=1.55, chloroform).

Preparation of (1*S*, 3*R*, 5*RS*, 7*S*, 8*S*)-7-(*tert*-butyldimethylsilyloxy)-5-methoxy-2,4-dioxatricyclo[6.2.1.0^{3,7}]undecan-9-one (51). Pyridinium dichromate (2.90 g, 8.33 mmol, 2.5 eq) was added in one portion to a vigorously prestirred (5 min) suspension of activated 4Å molecular sieves (~3.0 g) in a solution of the 9-hydroxytricyclicmethoxyacetals (**44**) (1.10 g, 3.33 mmol) in anhydrous dichloromethane (35 ml). The heterogeneous reaction mixture was left to stir at room temperature under argon. After 16 hr the reaction mixture was diluted with ethyl acetate (40 ml) and vigorously stirred for 10 min before filtering over a small plug of florisil, washed copiously with ethyl acetate and the filtrate evaporated to dryness *in vacuo*. The resulting clear oil was purified by flash chromatography (gradient elution: 25% to 30% ethyl acetate-petrol) to give the 9-ketone derivative as a C-5 methoxy 1:3, α:β epimeric mixture of acetals (**51**) (993 mg, 91%) as an amorphous, white solid; mp. 70-72°C; υ_{max} (film) 2928, 1747, 1459, 1402, 1387, 1360, 1327, 1302, 1217, 1189, 1159, 1133, 1093, 1066, 1048, 1020, 986, 965 and 942 cm^{-1}; ^{1}H δ(500 MHz) for the β isomer, 0.12 (3H, s, SiMe), 0.19 (3H, s, SiMe), 0.87 (9H, s, Si^{t}Bu), 1.83 (1H, ddd, J 13.3, 5.3, 2.7, H-11), 2.26 (1H, ddd, J 19.5, 5.4, 1.1, H-10eq), 2.33 (2H, t, J 5.3, 2xH-6), 2.35 (1H, br.d, J 13.2, H-11), 2.60 (1H, dd, J 19.5, 4.2, H-10ax), 2.74 (1H, br.d, J 5.1, H-8), 3.48 (3H, s, OMe), 4.72-4.74 (1H, m, H-1), 5.05 (1H, s, H-3) and 5.33 (1H, dd, J 5.8, 4.9, H-5); and for the α isomer, 0.15 (3H, s, SiMe), 0.20 (3H, s, SiMe), 0.86 (9H, s, Si^{t}Bu), 1.82-2.04 (1H, m, H-11), 2.13 (1H, dd, J 14.6, 2.7, H-6), 2.25 (1H, ddd, J 19.2, 6.7, 1.3, H-10eq), 2.31-2.34 (1H, m, H-11), 2.46 (1H, dd, J 14.7, 6.5, H-6), 2.54 (1H, dd, J 19.2, 4.1, H-10ax), 2.70 (1H, br.d, J 5.2, H-8), 3.42 (3H, s, OMe), 4.67 (1H, m, H-1), 5.19 (1H, s, H-3) and 5.25 (1H, dd, J 6.5, 2.7, H-5); *m/z* (CI, NH_3) 346 (MNH_4^+), 314 (MNH_4^+-MeO) and 297 (M^+-MeOH); (Found: C, 58.67; H, 8.85. $C_{16}H_{28}O_5Si$ requires C, 58.50; H, 8.59%).

Preparation of (1*S*, 3*R*, 5*RS*, 7*S*, 8*S*)-5-acetoxy-7-(*tert*-butyldimethylsilyloxy)-2,4-dioxatricyclo[6.2.1.0^{3,7}]undecan-9-one (52). The 9-hydroxytricyclicacetates (**35**) (80 mg, 0.223 mmol) were oxidised with PDC in a similar manner to that described above. Purification by flash chromatography (gradient elution: 40% to 50% ethyl acetate-petrol) gave the 9-ketotricyclicacetates as a C5 1:4, α:β epimeric mixture (**52**) (64 mg, 76%) as an amorphous, white solid; mp. 67-77°C; υ_{max} (film) 2952, 2928, 2888, 2855, 1752, 1470, 1461, 1431, 1361, 1301, 1237, 1184, 1157, 1134, 1078, 1053, 1030, 967 and 916 cm^{-1}; ^{1}H δ(500 MHz) for the β isomer only, 0.14 (3H, s, SiMe), 0.20 (3H, s, SiMe), 0.87 (9H, s, Si^{t}Bu), 1.89 (1H, ddd, J 13.4, 5.2, 2.6, H-11), 2.12 (3H, s, OAc), 2.29 (1H, dd, J 19.6, 5.4, H-10eq), 2.32 (1H, ddd, J 13.2, 4.2, 1.4, H-11'), 2.44 (1H, dd, J 15.4, 5.0, H-6), 2.48 (1H, dd, J 15.4, 6.4, H-6), 2.61 (1H, dd, J 19.5, 4.2, H-10ax), 2.78 (1H, br.d, J 5.1, H-8), 4.74 (1H, br.s, H-1), 5.09 (1H, s, H-3) and 6.50 (1H, dd, J 6.0, 4.8, H-5); *m/z* (CI, NH_3) 314 (MNH_4^+-AcOH), 297 (M^+-AcO), 239, 195, 182, 165, 123 and 91; (Found: C, 57.56; H, 8.13. $C_{17}H_{28}O_6Si$ requires C, 57.28; H, 7.92%).

Preparation of (1*S*, 3*R*, 5*RS*, 7*S*, 8*R*)-7-(*tert*-butyldimethylsilyloxy)-5-methoxy-2,4-dioxatricyclo[6.2.1.0^{3,7}]undecan-10-one (54) and (1*S*, 3*R*, 5*RS*, 7*S*, 8*S*)-7-(*tert*-butyldimethylsilyloxy)-5-methoxy-2,4-dioxatricyclo[6.2.1.]undecan-9-one (51). 9-

Borabicyclo[3.3.1]nonane (4.91 ml of a 0.5M solution in tetrahydrofuran, 2.45 mmol, 1.5 eq) was added dropwise, *via* syringe, to a stirred solution of the alkene (**46**) (511 mg, 1.64 mmol) in anhydrous tetrahydrofuran (5 ml) at room temperature, under argon. The reaction was immediately placed into a hot oil bath and heated at reflux for 20 min. The reaction mixture was then cooled to 0°C and quenched by the cautious, dropwise addition of water (5 ml) with vigorous stirring. After 5 min 3M sodium hydroxide (6 ml) and 27.5% aqueous hydrogen peroxide solution (5 ml) were added sequentially, the mixture warmed to room temperature and stirred for 1 h in air. The heterogeneous mixture was extracted with ether (4x50 ml), the combined ethereal layers were then washed with saturated brine (2x50 ml), dried ($MgSO_4$), filtered and evaporated to dryness, *in vacuo*, to give a clear oil. Purification by flash chromatography (50% ethyl acetate-petrol) gave an inseparable mixture of the C10-hydroxy:C9-hydroxy, 3:1, derivatives (**53**) and (**44**) respectively as a C5-methoxy 1:3, α:β epimeric mixture (515 mg, 95%) as an amorphous, white solid. The above mixture of alcohols (**53**) and (**44**) (510 mg, 1.54 mmol) were oxidised to their corresponding ketones by treatment with PDC as described earlier. Purification by flash chromatography (gradient elution 15% to 25% ethyl acetate-petrol) gave, in order of elution, the 10-ketone derivative as a C5-methoxy 1:3, α:β epimeric mixture (**54**) (380 mg, 75%) as an amorphous, white solid; mp. 107-110°C; υ_{max} (film) 2953, 2929, 2855, 1753, 1459, 1403, 1386, 1314, 1257, 1200, 1186, 1163, 1124, 1101, 1076, 1044, 1026, 958 and 923 cm^{-1}; ^1H δ(500 MHz) for the major β epimer, 0.12 (3H, s, SiMe), 0.14 (3H, s, SiMe), 0.87 (9H, s, Si^{t}Bu), 1.79 (1H, ddd, J 13.8, 4.9, 3.1, H-11), 2.23 (1H, dd, J 18.9, 6.5, H-9eq), 2.34 (1H, dd, J 14.7, 6.0, H-6), 2.40 (1H, dd, J 13.7, 4.2, H-11'), 2.41 (1H, dd, J 14.7, 4.8, H-6), 2.72 (1H, dd, J 18.9, 4.1, H-9ax), 2.79 (1H, br.dd, J 6.3, 5.3, H-8), 3.47 (3H, s, OMe), 3.92 (1H, br.s, H-1), 4.95 (1H, s, H-3) and 5.34 (1H, dd, J 6.0, 4.9, H-5); and for the minor α epimer, 0.13 (3H, s, SiMe), 0.17 (3H, s, SiMe), 0.88 (9H, s, Si^{t}Bu), 1.78-1.82 (1H, m, H-11), 2.15 (1H, dd, J 14.6, 2.3, H-6), 2.16-2.20 (1H, m, H-9eq), 2.25-2.28 (1H, m, H-11'), 2.53 (1H, dd, J 14.6, 6.4, H-6), 2.71-2.73 (1H, m, H-8), 2.83 (1H, dd, J 19.1, 3.8, H-9ax), 3.40 (3H, s, OMe), 3.87 (1H, br.s, H-1), 5.11 (1H, s, H-3) and 5.26 (1H, dd, J 6.4, 2.3, H-5); *m/z* (CI, NH_3) 346 (MNH_4^+), 314 (MNH_4^+-MeOH), 297 (M^+-MeO), 239 (M^+-MeOH-^{t}Bu), 214, 182, 165, 132, 106 and 91; (Found: C, 58.45; H, 8.74. $C_{16}H_{28}O_5Si$ requires C, 58.50; H, 8.59%); and the 9-ketone derivative as a C5-methoxy 1:3, α:β epimeric mixture (**51**) (116 mg, 23%) as an amorphous, white solid that had identical physical data to that previously prepared.

Preparation of (1*S*, 3*R*, 5*RS*, 7*S*, 8*R*, 9*S*)-7-(*tert*-butyldimethylsilyloxy)-5-methoxy-9-methyl-2,4-dioxatricyclo[6.2.1.0^{3,7}]undecan-10-one (55). n-Butyllithium (678 μl of a 1.6M solution in hexane, 1.08 mmol, 1.2 eq) was added dropwise, *via* syringe, to a stirred solution of diisopropylamine (152 μl, 1.08 mmol, 1.2 eq) in anhydrous tetrahydrofuran at 0°C. After stirring for 30 min at 0°C the lithium diisopropylamide was cooled to -78°C and the 10-ketone (**54**) (297 mg, 0.904 mmol) as a solution in anhydrous tetrahydrofuran (4 ml + 2 ml washing) was added dropwise, *via* cannular. After 5 min freshly redistilled methyl iodide (419 μl, 4.52 mmol, 5 eq) was swiftly added to the yellow anion. The reaction mixture turned bright lemon yellow and after 10 min at -78°C was allowed to warm to room temperature. During warming to room temperature the solution gradually turned golden brown and was quenched by the cautious addition of saturated aqueous ammonium chloride (10 ml) with vigorous stirring for 10 min. The mixture was extracted with ether (4x20 ml) and the combined ethereal layers washed with saturated brine (2x25 ml), dried ($MgSO_4$), filtered and evaporated to dryness, *in vacuo*, to give a yellow oil. Purification by flash chromatography (gradient elution: 15% to 20% ethyl acetate-petrol) gave, in order of elution, the pure C9*S*-methyl derivative as a C5-methoxy 1:3, α:β epimeric mixture (**55**) (215 mg, 69%) as an amorphous, white solid; mp. 75-77°C; υ_{max} (film) 2953, 2930, 2855, 1752, 1461, 1375, 1317, 1257, 1194, 1119, 1090, 1065, 1036, 970 and 942 cm^{-1}; ^1H δ(500 MHz) for the major β isomer, 0.13 (3H, s, SiMe), 0.15 (3H, s, SiMe), 0.87 (9H, s, Si^{t}Bu), 1.18 (3H, d, J 7.7, C-9Me), 1.89 (1H, ddd, J 14.1, 5.1, 3.1, H-11), 2.31 (1H, dd, J 13.1, 3.2, H-11'), 2.34 (1H, dd, J 15.0, 6.0, H-6), 2.41 (1H, dd, J 14.7, 4.9, H-6), 2.42 (1H, br.t, J 4.2, H-8), 2.75 (1H, qd, J 7.7, 3.2, H-9), 3.47 (3H, s, OMe), 3.91 (1H, br.s, H-1), 4.93 (1H, s, H-3) and 5.34 (1H, dd, J 6.0, 4.9, H-5); and for the minor α isomer, 0.14 (3H, s, SiMe), 0.17 (3H, s, SiMe), 0.88 (9H, s, Si^{t}Bu), 1.16 (3H, d, J 8.0, C-9Me), 1.86 (1H, ddd, J 13.8, 5.4, 2.8, H-11), 2.17 (1H, dd, J 14.6,

2.1, H-6), 2.16-2.19 (1H, m, H-11'), 2.31 (1H, m, H-8), 2.49 (1H, dd, J 14.6, 6.4, H-6), 2.88 (1H, qd, J 7.9, 2.9, H-9), 3.40 (3H, s, OMe), 3.89 (1H, s, H-1), 5.11 (1H, s, H-3) and 5.24 (1H, dd, J 6.4, 2.2, H-5); *m/z* (CI, NH_3) 360 (MNH_4^+), 328 (MNH_4^+-MeOH), 311 (M^+-MeO), 285 (M^+-^{t}Bu), 253 (M^+-^{t}Bu-MeOH), 239, 227, 201, 179, 151, 129, 89 and 73; (Found: C, 59.54; H, 9.02. $C_{17}H_{30}O_5Si$ requires C, 59.62; H, 8.83%); and some starting material (**54**) (13 mg, 4% recovery).

Data for (1*S*, 3*R*, 5*RS*, 7*S*, 8*S*, 9*S*)-7-(*tert*-butyldimethylsilyloxy)-9-iodo-5-methoxy-2,4-dioxatricyclo[6.2.1.0^{3,7}]undecan-10-one. Clear oil; υ_{max} (film) 2951, 2928, 2855, 1751, 1461, 1379, 1325, 1304, 1258, 1192, 1136, 1112, 1086, 1040, 1024, 966, 944 and 924 cm^{-1}; ^{1}H δ(500 MHz) for the major β isomer only, 0.16 (3H, s, SiMe), 0.20 (3H, s, SiMe), 0.90 (9H, s, Si^{t}Bu), 2.36-2.41 (4H, m, 2xH-6 and 2xH-11), 2.82-2.84 (1H, m, H-8), 3.46 (3H, s, OMe), 3.93 (1H, br.s, H-1), 4.90 (1H, s, H-3), 4.97 (1H, d, J 2.9, H-9) and 5.33 (1H, t, J 5.3, H-5); *m/z* (CI, NH_3) 472 (MNH_4^+), 440 (MNH_4^+-MeOH), 423 (M^+-MeO), 365 (M^+-^{t}Bu-MeOH), 346, 314 (MNH_4^+-I-MeO), 297 (MH^+-I-MeO), 239 (M^+-I-MeO-^{t}Bu), 213, 201, 165, 137, 106, 90, 73 and 49; [Found (MNH_4^+) 472.1016. $C_{16}H_{31}INO_5Si$ requires 472.1016].

Preparation of (1*S*, 3*R*, 5*RS*, 7*S*, 8*R*, 9*R*)-7-(*tert*-butyldimethylsilyloxy)-2,4-dioxatricyclo[6.2.1.0^{3,7}]undecan-5,9-diol (57). The benzyloxytricycliclactols (**42**) (194 mg, 0.477 mmol) were hydrogenated over 10% palladium on carbon in the prescence of a trace of hydrochloric acid in a manner similar to that described earlier. Purification by flash chromatography (10% petrol-ethyl acetate) gave the diol (**57**) (132 mg, 87%) as a white foam, ~20% of which was present as the hydroxy aldehyde form of the lactol (^{1}H δ 9.51, s, CHO). υ_{max} (film) 3394, 2952, 2930, 2855, 1733, 1460, 1439, 1387, 1359, 1257, 1192, 1132, 1101, 1057, 1005, 980, 942 and 924 cm^{-1}; ^{1}H δ(500 MHz) for the major lactol only, 0.14 (3H, s, SiMe), 0.16 (3H, s, SiMe), 0.88 (9H, s, Si^{t}Bu), 1.58-1.64 (1H, m, H-11), 1.69 (1H, br.dd, J 15.9, 3.4, H-10eq), 1.89-1.91 (2H, m, 2xOH), 1.96 (1H, d, J 13.1, H-11'), 2.24 (1H, dd, J 15.2, 4.2, H-6), 2.30 (1H, dd, J 15.5, 5.4, H-6), 2.41 (1H, d, J 4.9, H-8), 2.47 (1H, dd, J 15.6, 6.9, H-10ax), 4.45 (1H, br.s, H-1), 4.68 (1H, br.s, H-9), 4.70 (1H, s, H-3) and 5.66-5.70 (1H, m, H-5); *m/z* (EI$^+$) 299 (M^+-OH), 287, 273, 259 (M^+-^{t}Bu), 241 (M^+-^{t}Bu-H_2O), 223 (M^+-^{t}Bu-2H_2O), 213, 195, 167, 129, 84, 75 and 49; (Found: C, 56.96; H, 9.18. $C_{15}H_{28}O_5Si$ requires C, 56.93; H, 8.92%).

Preparation of (1*S*, 3*R*, 5*RS*, 7*S*, 8*R*, 9*R*)-7-(*tert*-butyldimethylsilyloxy)-5-phenylseleno-2,4-dioxatricyclo[6.2.1.0^{3,7}]undecan-9-ol (58). Benzeneselenol (45.8 μl, 0.431 mmol, 1.1 eq) was added smoothly, *via* syringe, to a prestirred (2 min) solution of the diols (**57**) (124 mg, 0.392 mmmol) and boron trifluoride etherate (96.4 μl, 0.784 mmol, 2.0 eq) in anhydrous dichloromethane (5 ml) at 0°C, under argon. After 10 min the reaction mixture was quenched by the addition of saturated aqueous sodium bicarbonate (5 ml) with vigorous stirring for 5 min. Water (1 ml) was added and the mixture extracted with dichloromethane (5 ml, 2x10 ml). The combined organic extracts were then washed with saturated brine (2x10 ml), dried ($MgSO_4$), filtered and evaporated to dryness, *in vacuo*, to give a yellow oil. Purification by flash chromatography (gradient elution: 25% to 40% ethyl acetate-petrol) gave the C9-hydroxytricyclicphenylselenides as a C-5 1:4, α:β epimeric mixture (**58**) (107 mg, 60%) as a clear oil; υ_{max} (film) 3443, 2929, 2854, 1577, 1470, 1435, 1387, 1256, 1187, 1127, 1100, 1052, 1005, 939 and 901 cm^{-1}; ^{1}H δ(500 MHz) for the major β epimer only, 0.08 (3H, s, SiMe), 0.19 (3H, s, SiMe), 0.82 (9H, s, Si^{t}Bu), 1.38 (1H, br.s, OH), 1.60 (1H, br.dd, J 15.5, 5.3, H-10eq), 1.68 (1H, ddd, J 12.8, 4.7, 2.5, H-11), 1.73 (1H, br.d, J 13.1, H-11'), 2.32 (1H, dd, J 14.5, 7.0, H-6), 2.37 (1H, br.d, J 5.0, H-8), 2.40 (1H, ddd, J 15.6, 6.9, 2.2, H-10ax), 2.49 (1H, dd, J 14.5, 8.1, H-6), 4.36 (1H, br.d, J 1.4, H-1), 4.63 (1H, br.d, J 6.7, H-9), 4.68 (1H, s, H-3), 5.83 (1H, dd, J 8.1, 7.0, H-5), 7.18-7.25 (3H, m, 2x*o*- and *p*-Ph) and 7.57-7.59 (2H, m, 2x*m*-Ph); *m/z* (EI$^+$) 427, 399 (M^+-^{t}Bu), 381 (M^+-^{t}Bu-H_2O), 355, 327, 314, 299 (M^+-PhSe), 281 (M^+-PhSe-H_2O), 269, 255, 241 (M^+-PhSeH-^{t}Bu), 167, 139, 123 and 73; (Found: C, 55.23; H, 7.33. $C_{21}H_{32}O_4SeSi$ requires C, 55.37; H, 7.08%).

Preparation of (1*S*, 3*R*, 5*RS*, 7*S*, 8*R*, 9*R*)-7-(*tert*-butyldimethylsilyloxy)-5-phenylseleno-2,4-dioxatricyclo[6.2.1.0^{3,7}]undecan-9-ol methanesulphonate. The 9-hydroxytricyclicphenylselenides (**58**) (100 mg, 0.220 mmol) were treated with methanesulphonyl chloride and triethylamine in a similar manner to that described earlier. Purification by flash chromatography (gradient

elution: 30% to 35% ethyl acetate-petrol) gave the methanesulphonate derivative as a C5 1:4, α:β epimeric mixture (98 mg, 84%) as a clear oil; υ_{max} (film) 3054, 2951, 2930, 2855, 1732, 1576, 1471, 1459, 1435, 1411, 1355, 1336, 1259, 1219, 1176, 1127, 1102, 1051, 1032, 1000, 973, 950 and 902 cm^{-1}; ^1H δ(500 MHz) for the major β epimer only, 0.14 (3H, s, SiMe), 0.18 (3H, s, SiMe), 0.90 (9H, s, Si^{t}Bu), 1.74 (1H, ddd, J 13.2, 4.9, 2.7, H-11), 1.88 (1H, br.d, J 13.5, H-11'), 2.09 (1H, br.dd, J 16.4, 5.5, H-10eq), 2.49 (1H, dd, J 14.9, 7.3, H-6), 2.59 (1H, dd, J 14.9, 7.5, H-6), 2.59-2.64 (1H, m, H-10ax), 2.76 (1H, br.d, J 4.6, H-8), 2.99 (3H, s, $MeSO_3$-), 4.47 (1H, br.d, J 5.3, H-1), 4.80 (1H, s, H-3), 5.49 (1H, d, J 6.6, H-9), 5.90 (1H, t, J 7.3, H-5), 7.27-7.31 (3H, m, 2x*o*- and *p*-Ph) and 7.62-7.64 (2H, m, 2x*m*-Ph); *m/z* (EI^+) 505, 480, 477 (M^+-^{t}Bu), 454 (M^+-$MeSO_2H$), 439 (M^+-$MeSO_3$), 409, 390, 361, 319, 281, 268, 236, 215, 157, 149, 121, 73 and 67; (Found: C, 49.42; H, 6.47. $C_{22}H_{34}O_6SSeSi$ requires C, 49.52; H, 6.42%).

Preparation of (1*S*, 3*R*, 5*RS*, 7*S*, 8*R*)-7(*tert*-butyldimethylsilyloxy)-5-phenylseleno-2,4-dioxatricyclo[6.2.1.0^{3,7}]undec-9-ene (59). The methanesulphonates (prepared above) (94 mg, 0.176 mmol) were heated in anhydrous toluene and 1,8-diazabicyclo[5.4.0]undec-7-ene for 21 hr in a similar manner to that described earlier. Purification by flash chromatography (gradient elution: 15% to 20% ethyl acetate-petrol) gave the corresponding alkene as a C5 1:4, α:β epimeric mixture (**59**) (60 mg, 78%) as a clear oil; υ_{max} (film) 3066, 2950, 2929, 2890, 2854, 1577 (w), 1470, 1435, 1387, 1334, 1256, 1188, 1124, 1104, 1089, 1022, 998, 940 and 901 cm^{-1}; ^1H δ, for the major β epimer, 0.11 (3H, s, SiMe), 0.15 (3H, s, SiMe), 0.85 (9H, s, Si^{t}Bu), 1.72 (1H, ddd, J 11.7, 4.9, 2.9, H-11), 1.87 (1H, br.d, J 11.7, H-11'), 2.47 (1H, dd, J 14.7, 7.2, H-6), 2.57 (1H, dd, J 14.7, 7.5, H-6), 2.99 (1H, dd, J 4.9, 2.8, H-8), 4.65 (1H, br.s, H-1), 4.89 (1H, s, H-3), 5.94 (1H, t, J 7.4, H-5), 6.09 (1H, dd, J 5.7, 2.6, H-10), 6.47 (1H, dd, J 5.7, 2.8, H-9), 7.24-7.30 (3H, m, 2x*o*- and *p*-Ph) and 7.64-7.68 (2H, m, 2x*m*-Ph); and for the minor α epimer, 0.17 (3H, s, SiMe), 0.20 (3H, s, SiMe), 0.89 (9H, s, Si^{t}Bu), 1.84-1.85 (2H, m, 2xH-11), 2.16 (1H, dd, J 14.5, 8.2, H-6), 2.72 (1H, dd, J 14.4, 7.5, H-6), 3.02 (1H, br.s, H-8), 4.59 (1H, br.s, H-1), 5.01 (1H, s, H-3), 5.87 (1H, dd, J 8.1, 7.6, H-5), 6.14 (1H, dd, J 5.8, 2.6, H-10), 6.45 (1H, dd, J 5.7, 2.7, H-9), 7.24-7.30 (3H, m, 2x*o*- and *p*-Ph) and 7.61-7.63 (2H, m, 2x*m*-Ph); *m/z* (EI^+) 390, 361 (M^+-C_6H_5), 281, 268, 236, 215, 204, 177, 149, 73 and 64; [Found (M^+-C_6H_5) 361.0742. $C_{15}H_{25}O_3SeSi$ requires 361.0742].

Preparation of (1*S*, 3*R*, 7*S*, 8*S*, 10*S*)-7(*tert*-butyldimethylsilyloxy)-10-hydroxy-2,4-dioxatricyclo[6.2.1.0^{3,7}]undec-5-ene (60) and (1*S*, 3*R*, 7*S*, 8*R*, 9*R*)-7(*tert*-butyldimethylsilyloxy)-9-hydroxy-2,4-dioxatricyclo[6.2.1.0^{3,7}]undec-5-ene (61). 9-Borabicyclo[3.3.1]nonane (3.84 ml of a 0.5M solution in tetrahydrofuran, 1.92 mmol, 1.5 eq) was added dropwise, *via* syringe, to a stirred solution of the alkene (**59**) (0.56 g, 1.28 mmol) in anhydrous tetrahydrofuran (25 ml) at room temperature, under argon. The reaction was immediately placed into a hot oil bath and heated at 70°C for 5 min. The reaction mixture was then cooled to 0°C and quenched by the cautious, dropwise addition of water (5 ml) with vigorous stirring. After 5 min 3M potassium hydroxide (6 ml) and 27.5% aqueous hydrogen peroxide solution (6 ml) were added sequentially, the mixture was warmed to room temperature and stirred for 5 min in air. 2-(Phenylsulphonyl)-3-(*p*-nitrophenyl)oxaziridine (0.47g, 1.54 mmol, 1.2 eq) was then added and the reaction mixture stirred for 10 min before being extracted with ether (3x50 ml). The combined ethereal layers were then washed with brine (50 ml), dried ($MgSO_4$), filtered and evaporated to dryness, *in vacuo*, to give a yellow oil. Purification by flash chromatography (gradient elution: 25% to 35% ethyl acetate-petrol) gave an inseparable mixture of the C10-hydroxy:C9-hydroxy, 3:1, enol ethers (**60**) and (**61**) (0.35 g, 92%) as an amorphous white solid; υ_{max} (film) 3413, 2950, 2930, 2855, 1611 (w), 1460, 1405, 1387, 1359, 1252, 1137, 1082, 1016, 980 and 953 cm^{-1}; ^1H δ(500 MHz) for the major C10 hydroxy enol ether, 0.04 (3H, s, SiMe), 0.07 (3H, s, SiMe), 0.87 (9H, s, Si^{t}Bu), 1.42 (1H, ddd, J 14.7, 7.1, 1.2, H-9eq), 1.53 (1H, br.d, J 2.1, OH), 1.75 (1H, br.d, J 13.9, H-11'), 1.83 (1H, ddd, J 13.2, 5.8, 2.9, H-11), 2.36 (1H, t, J 6.6, H-8), 2.76 (1H, ddd, J 14.7, 7.0, 1.7, H-9ax), 4.00 (1H, br.s, H-10), 4.30 (1H, br.d, J 6.6, H-1), 4.98 (1H, d, J 2.9, H-6), 5.18 (1H, s, H-3) and 6.42 (1H, d, J 2.9, H-5); and for the minor C9 hydroxy enol ether, 0.05 (3H, s, SiMe), 0.11 (3H, s, SiMe), 0.88 (9H, s, Si^{t}Bu), 1.41 (1H, br.s, OH), 1.69 (1H, br.d, J 13.3, H-11'), 1.68-1.72 (1H, m, H-10eq), 1.82-1.85 (1H, m, H-11), 2.36 (1H, t, J 6.6, H-8), 2.44 (1H, ddd, J 15.4, 6.9, 2.5, H-10ax), 4.34 (1H, br.s, H-1), 4.83 (1H, br.d, J 6.7, H-9), 5.05 (1H, d, J

2.8, H-6), 5.08 (1H, s, H-3) and 6.47 (1H, d, J 2.7, H-5); *m/z* (EI+) 298 (M^+), 283, 269 (M^+-HCO), 257, 253, 241 (M^+-^{t}Bu), 223 (M^+-^{t}Bu-H_2O), 214, 198, 179, 169, 157, 129, 121, 103, 83, 75 and 73; [Found (M^+-^{t}Bu) 241.0902. $C_{11}H_{17}O_4Si$ requires 241.0896].

Preparation of (1*R*, 3*S*, 7*R*, 8*R*)-7-(*tert*-butyldimethylsilyloxy)-2,4-dioxatricyclo[6.2.1.0^{3,7}]undec-5-ene-10-one (62) and (1*R*, 3*S*, 7*R*, 8*S*)-7-(*tert*-butyldimethylsilyloxy)-2,4-dioxatricyclo[6.2.1.0^{3,7}]undec-5-ene-9-one (63). The C9 and C10 hydroxy enol ethers (**61**) and (**60**) (0.35 g, 1.17 mmol) were oxidised with PDC in a manner similar to that described earlier. Purification by flash chromatography (gradient elution: 12% to 16% ethyl acetate-petrol) to give in order of elution, the C10-keto enol ether (**62**) (265 mg, 76%) as an amorphous, white solid; mp. 81-82°C; $[\alpha]_D^{20}$=-140.4 (c=1.36, chloroform); υ_{max} (film) 3098, 2927, 2854, 1748, 1619, 1459, 1402, 1358, 1251, 1200, 1180, 1137, 1113, 1080, 1022, 952 and 922 cm^{-1}; ^{1}H δ(500 MHz) 0.07 (3H, s, SiMe), 0.09 (3H, s, SiMe), 0.86 (9H, s, Si^{t}Bu), 1.84 (1H, ddd, J 14.0, 5.5, 3.1, H-11), 2.06 (1H, ddt, J 14.0, 3.5, 0.8, H-11'), 2.18 (1H, dd, J 19.5, 7.0, H-9eq), 2.62 (1H, br.t, J 6.3, H-8), 2.92 (1H, dd, J 19.4, 3.6, H-9ax), 3.84 (1H, br.d, J 1.4, H-1), 5.08 (1H, d, J 2.9, H-6), 5.39 (1H, s, H-3) and 6.51 (1H, d, J 2.9, H-5); *m/z* (EI+) 297 (MH^+), 281 (M^+-Me), 267, 253, 239 (M^+-^{t}Bu), 211, 193, 169, 157, 141, 129, 119, 101, 81, 75, 73 and 55; (Found: C, 61.04; H, 8.39. $C_{15}H_{24}O_4Si$ requires C, 60.78; H, 8.16%); and the C9-keto enol ether (**63**), contaminated with ~5% of the C10-keto isomer (**62**), (71 mg, 20%) as an amorphous, white solid. A small amount was purified, as above, to obtain an isomerically pure sample; mp. 57-59°C; $[\alpha]_D^{20}$=-223.7 (c=1.25, chloroform); υ_{max} (film) 3093, 2926, 2854, 1747, 1611, 1459, 1388, 1359, 1293, 1253, 1225, 1158, 1108, 1090, 1075, 1025 and 940 cm^{-1}; ^{1}H δ 0.05 (3H, s, SiMe), 0.13 (3H, s, SiMe), 0.85 (9H, s, Si^{t}Bu), 1.90 (1H, ddd, J 13.4, 5.6, 2.9, H-11), 2.08 (1H, ddd, J 13.3, 4.1, 1.5, H-11'), 2.28 (1H, ddd, J 19.2, 4.8, 1.4, H-10ax), 2.56 (1H, dd, J 19.2, 4.0, H-10eq), 2.63 (1H, br.d, J 5.6, H-8), 4.68 (1H, td, J 3.1, 1.5, H-1), 5.01 (1H, d, J 2.9, H-6), 5.42 (1H, s, H-3) and 6.56 (1H, d, J 2.9, H-5); *m/z* (EI+) 239 (M^+-^{t}Bu), 195 (M^+-^{t}Bu-C_2H_4O), 157, 129, 99, 75, 73 and 59; (Found: C, 60.86; H, 8.31. $C_{15}H_{24}O_4Si$ requires C, 60.78; H, 8.16%).

Preparation of (1*R*, 3*S*, 7*R*, 8*R*, 9*S*)-7-(*tert*-butyldimethylsilyloxy)-9-methyl-2,4-dioxatricyclo[6.2.1.0^{3,7}]undec-5-ene-10-one (56). Lithium hexamethyldisilazide (579 µl, 0.579 mmol, 1.2 eq) was added dropwise, *via* syringe, to a stirred solution of the 10-keto enol ether (**62**) (143 mg, 0.483 mmol) in anhydrous tetrahydrofuran (7.5 ml) at -78°C under argon (the solution goes bright yellow over 5 min). After 10 min methyl iodide (224 µl, 2.42 mmol, 5.0 eq) was swiftly added, *via* syringe and the mixture stirred for a further 5 min before being allowed to warm to room temperature at which time the solution was golden brown. The reaction was quenched by the addition of saturated aqueous sodium bicarbonate (6 ml) with vigorous stirring for 5 min before the addition of water (5 ml) and extracting with ether (4x25 ml). The combined ethereal layers were washed with saturated brine (2x25 ml), dried ($MgSO_4$), filtered and evaporated, *in vacuo*, to give a clear oil. Purification by flash chromatography (gradient elution: 20% to 25% ether-petrol) gave exclusively the C9*S*-methyl derivative (**56**) (140 mg, 93%) as an amorphous white solid; mp. 38-39°C; $[\alpha]_D^{20}$=-96.9 (~85% ee. c=0.45, chloroform); υ_{max} (film) 2952, 2930, 2885, 2855, 1755, 1613, 1459, 1405, 1388, 1359, 1283, 1252, 1174, 1149, 1106, 1081, 1023, 942 and 901 cm^{-1}; ^{1}H δ(500 MHz) 0.07 (3H, s, SiMe), 0.10 (3H, s, SiMe), 0.86 (9H, s, Si^{t}Bu), 1.16 (3H, d, J 7.8, C-9Me), 1.88 (1H, ddd, J 14.3, 5.6, 2.9, H-11), 1.96 (1H, ddt, J 14.3, 3.4, 1.1, H-11'), 2.21 (1H, br.d, J 5.6, H-8), 2.98 (1H, qd, J 7.8, 2.6, H-9), 3.86 (1H, br.t, J 1.3, H-1), 5.07 (1H, d, J 2.8, H-6), 5.39 (1H, s, H-3), 6.49 (1H, d, J 2.9, H-5); *m/z* (EI+) 295, 281, 253 (M^+-^{t}Bu), 213, 207, 169, 157, 141, 133, 129, 95, 75 and 55; (Found: C, 61.82; H, 8.58. $C_{16}H_{26}O_4Si$ requires C, 61.90; H, 8.44%).

References and footnotes

1 For part 7 see Anderson, J.C.; Ley, S.V. *Tetrahedron Lett.* **1990**, *31*, 3437-3440.

2 For recent reviews see a) van Beek, T.A.; de Groot, Ae. *Recl. Trav. Chim. Pays-Bas.* **1986**, *105*, 513-527. b) de Groot, Ae; van Beek, T.A. *ibid.* **1987**, *106*, 1-18.

3 a) Turner, C.J.; Tempesta, M.S.; Taylor, R.B.; Zagorski, M.G.; Termini, J.S.; Schroeder, D.R.; Nakanishi, K. *Tetrahedron* **1987**, *43*, 2789-2803. b) Bilton, J.N.; Broughton, H.B.; Jones, P.S.; Ley, S.V.; Lidert, Z.; Morgan, E.D.; Rzepa, H.S.; Sheppard, R.N.; Slawin, A.M.Z.; Williams, D.J. *ibid.* **1987**, *43*, 2805-2815. c) Kraus, W.; Bokel, M.; Bruhn, A.; Cramer, R.; Klaiber, I.; Klenk, A.; Nagl, G.; Pöhnl, H.; Sadlo, H.; Vogler, B. *ibid.* **1987**, *43*, 2817-2830.

4 '1988 Focus on Phytochemical Pesticides', Vol. 1, The Neem Tree, Jacobson, M. (Ed.), CRC Press Inc. **1989**.

5 a) Ley, S.V. 'Synthesis and Modification of Azadirachtin and Related Antifeedants' in 'Recent Advances in the Chemistry of Insect Control II', Crombie, L. (Ed.), Royal Society of Chemistry Special Publication No. 79, **1989**, 90-98. b) Ley, S.V. 'Synthesis of Antifeedants for Insects: Novel Behaviour-Modifying Chemicals from Plants' in 'Bioactive Compounds from Plants' Ciba Foundation Symposium 154, John Wiley and Sons, **1990**, 80-98.

6 a) Brasca, M.G.; Broughton, H.B.; Craig, D.; Ley, S.V.; Somovilla, A.A.; Toogood, P.L. *Tetrahedron Lett.* **1988**, *29*, 1853-1856. b) Ley, S.V.; Anderson, J.C.; Blaney, W.M.; Lidert, Z.; Morgan, E.D.; Robinson, N.G.; Simmonds, M.S.J. *ibid.* **1988**, *29*, 5433-5436. c) Ley, S.V.; Somovilla, A.A.; Broughton, H.B.; Craig, D.; Slawin, A.M.Z.; Toogood, P.L.; Williams, D.J. *Tetrahedron* **1989**, *45*, 2143-2164. d) Ley, S.V.; Anderson, J.C.; Blaney, W.M.; Jones, P.S.; Lidert, Z.; Morgan, E.D.; Robinson, N.G.; Santafianos, D.; Simmonds, M.S.J.; Toogood, P.L. *ibid* **1989**, *45*, 5175-5192.

7 Ley, S.V.; Santafianos, D.; Blaney, W.M.; Simmonds, M.S.J. *Tetrahedron Lett.* **1987**, *28*, 221-224.

8 Anderson, J.C.; Ley, S.V. *Tetrahedron Lett.* **1990**, *31*, 431-432.

9 a) Vedejs, E. *J. Am. Chem. Soc.* **1974**, *96*, 5944-5946. b) Vedejs, E.; Engler, D.A.; Telschow, J.E. *J. Org. Chem.* **1978**, *43*, 188-196.

10 We thank Dr. D.J. Williams and Ms. A.M.Z. Slawin of this department for this result.

11 Raucher, S.; Koolpe, G.A. *J. Org. Chem.* **1978**, *43*, 3794-3796.

12 Studies to verify this are underway in our laboratories and will be reported at a later date.

13 The biological evaluation of these compounds and similar models will be reported at a later date.

14 Obtained in enantiomerically pure form from either formation of the bisulphite addition complex of the bicyclic ketone and resolution of the adduct with R (+)-α-methylbenzylamine a) Collington, E.W.; Wallis, C.J.; Waterhouse, I. *Tetrahedron Lett.* **1983**, *24*, 3125-3128. b) Greuter, H.; Dingwall, J.; Martin, P.; Bellus, D. *Helv. Chim. Acta.* **1981**, *64*, 2812-2820; or via a chiral enzymatic reduction c) Butt, S.; Davies, H.G.; Dawson, M.J.; Lawrence, G.C.; Leaver, J.; Roberts, S.M.; Turner, M.K.; Wakefield, B.J.; Wall, W.F.; Winders, J.A. *Tetrahedron Lett.* **1985**, *26*, 5077-5080.

15 Lee, T.V.; Roberts, S.M.; Dimsdale, M.J.; Newton, R.F.; Rainey, D.K.; Webb, C.F. *J. Chem. Soc., Perkin Trans.* 1 **1978**, 1176-1178.

16 For a recent review see Tidwell, T.T. *Synthesis* **1990**, 857-870.

17 For other examples of this migration see a) Franke, F.; Guthrie, R.D. *Aust. J. Chem.* **1978**, *31*, 1285-1290. b) Torisawa, Y.; Shibasaki, M.; Ikegami, S. *Tetrahedron Lett.* **1979**, *19*, 1865-1868. c) Ogilvie, K.K.; Beaucage, S.L.; Schifman, A.L.; Theriault, N.Y.; Sadana, K.L. *Can. J. Chem.* **1978**, *56*, 2768-2780.

18 Mitch, E.; Dreiding, A.S. *Chimica (Switz)* **1960**, *14*, 424.

19 a) Griffith, W.P.; Ley, S.V.; Whitcombe, G.P.; White, A.D. *J. Chem. Soc., Chem. Commun.* **1987**, 1625-1627. b) Griffith, W.P.; Ley, S.V. *Aldrichimica Acta* **1990**, *23*, 13-19.

20 Dale, J.A.; Dull, D.L.; Mosher, H.S. *J. Org. Chem.* **1969**, *34*, 2543-2549.

21 Corey, E.J.; Nicolau, K.C.; Shibasaki, M.; Machida, Y.; Shiner, C.S. *Tetrahedron Lett.* **1975**, 3183-3186.

22 A small amount (~10%) of the *bis*(*tert*-butyldimethylsilyloxy) compound was formed during this anion reaction and provides support for the lability of the triethylsilyl group.

23 Anderson, J.C.; Smith, S.C. *Synlett* **1990**, 107-108.

24 For a leading reference see Seebach, D. *Chem. Br.* **1985**, *21*, 632- .

25 Burgess, E.M.; Penton, H.R.Jr.; Taylor, E.A. *J. Org. Chem.* **1973**, *38*, 26-31.

26 Arhart, R.J.; Martin, J.C. *J. Am. Chem. Soc.* **1972**, *94*, 5003-5010.

27 Adam, W.; Chan, Y.-Y.; Cremer, D.; Gauss, J.; Scheutzow, D.; Schindler, M. *J. Org. Chem.* **1987**, *52*, 2800-2803.

28 For a review of the chemistry of oxaziridine reagents see Davis, F.A.; Sheppard, A.S. *Tetrahedron* **1989**, *45*, 5703-5742.

29 Compound (**35**) can be prepared from (**42**) *via* standard acetylation followed by hydrogenolysis.

30 a) Coates, W.M.; Corrigan, J.R. *Chem. Ind. (London)* **1969**, 1594. b) Corey, E.J.; Schmidt, G. *Tetrahedron Lett.* **1979**, *19*, 399-402.

31 a) Pasto, D.J.; Hickman, J. *J. Am. Chem. Soc.* **1968**, *90*, 4445-4449. b) Schreiber, S.L.; Smith, D.B. *J. Org. Chem.* **1989**, *54*, 9-10. c) Linde, R.G.II; Egbertson, M.; Coleman, R.S.; Jones, A.B.; Danishefsky, S.J. *ibid.* **1990**, *55*, 2771-2776.

32 A small amount (~3%) of the (9*S*)-iodo derivative was always obtained in this reaction and could be isolated *via* flash chromatography.

33 Nishikimi, Y.; Iimori, T.; Sodeoka, M.; Shibasaki, M. *J. Org. Chem.* **1989**, *54*, 3354-3359.

34 Program and documentation available from W.C. Still, Columbia University, New York.

35 Perrin, D.D.; Armarego, W.L.F.; Perrin, D.R. 'Purification of Laboratory Chemicals, Second Edition', Pergamon Press Oxford.

36 Grudzinski Z.; Roberts, S.M. *J. Chem. Soc., Perkin Trans.* 1 **1975**, 1767-1773.

37 The absolute rotation of this alcohol was found to be concentration dependant.