Samarium(II)-mediated 4-*exo-trig* cyclisations of unsaturated aldehydes. A stereoselective approach to functionalised cyclobutanols

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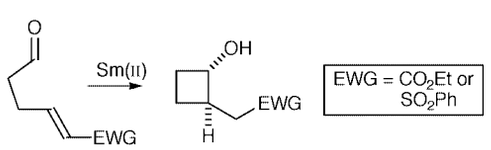
γ,δ-Unsaturated aldehydes having a fully substituted centre in either the α- or β-positions, have been prepared from substituted γ-butyrolactones and undergo efficient 4-*exo-trig* cyclisation on treatment with samarium(II) iodide to give functionalised cyclobutanols. In all cases cyclisation occurs with complete diastereocontrol to give *anti*-cyclobutanol products. The stereochemistry of the products has been confirmed by NOE and X-ray crystallographic studies. In the cyclisation of substrates having a third substituent on the double bond, α- to the ester, significant control is achieved at the third newly formed stereocentre lying outside the ring. The origin of the stereoselectivity at this third centre and its marked dependence on cosolvent are discussed.

Introduction

Samarium(II) iodide continues to prove an incredibly versatile reagent in organic synthesis.[1] Arguably the most important role for samarium(II) iodide lies in the mediation of radical or anionic cyclisations, or sequences that involve both types of process.[2] The samarium(II) mediated reductive coupling of unsaturated aldehydes or ketones is a particularly powerful cyclisation protocol which allows a variety of cyclic alcohols of varying ring size to be assembled under mild conditions with moderate to good diastereoselectivity.[3] Importantly, the functionality present in the starting material is retained in the product, albeit in a different oxidation state, and thus highly functionalised products with multiple stereocentres can often be prepared in an atom-efficient manner. Our interest in lanthanide-mediated transformations led us to consider new routes to small ring systems and in particular, to cyclobutanols, using cyclisations mediated by samarium(II) iodide (Scheme 1).



Scheme 1 General representation of the samarium(II)-mediated 4-*exo-trig* cyclisation of unsaturated aldehydes.

Radical cyclisations forming cyclobutane rings are reversible and hence few efficient reactions employing such processes have been reported.[4] We believed that the ability of samarium(II) iodide to not only generate carbon-centred radicals but to further reduce such radicals to the corresponding carbanions might provide a way of trapping the cyclic product and hence prevent the facile ring-opening process.[5] A radical cyclisation pathway, however, is not the only mechanistic possibility. The operation of an alternative anionic mechanism is also possible.[6]

There is only one previous example of a samarium(II) mediated 4-*exo-trig* 'ketyl-olefin' cyclisation,[7] prior to our preliminary report,[8] and this disclosure contained only a single example employing substrate **13** and using relatively harsh conditions. Despite limited precedent, we believed the reaction had considerable potential as a general route to cyclobutanols and that the nature of the reaction would result in a highly diastereoselective process.

Cyclobutane and cyclobutanol derivatives are important building blocks in organic synthesis and constitute a structural motif that is found extensively in natural products,[9] and non-natural, biologically important molecules.[10] Cyclobutanes are most often prepared using photochemical [2 + 2] cycloaddition processes.[11] Although these reactions are useful in synthesis, alternative processes which would allow more substituted cyclobutanes, and in particular cyclobutanols, to be prepared with good stereoselectivity, would be very useful. We felt that a samarium(II)-mediated approach to cyclobutanols would follow a well-defined stereochemical course, very different to those involved in conventional cyclobutane ring-forming reactions.

Here we report in full, the synthesis of aldehyde substrates and their cyclisation using samarium(II) iodide, and thus the development of a general, stereoselective approach to functionalised cyclobutanols.

Results and discussion

Preparation of cyclisation substrates

Simple cyclisation substrates were prepared by a general route from γ-butyrolactone or α-benzyloxy-γ-butyrolactone. The lactone starting materials were first mono- or dimethylated and then reduced to the corresponding lactols. Ring-opening with propane-1,3-dithiol under protic or Lewis acid conditions then gave alcohols **2a**–**c**. Modified Swern oxidation and subsequent Wittig reaction with (ethoxycarbonylmethylene)triphenylphosphorane, or (1-ethoxycarbonylethylidene)triphenylphosphorane, gave the protected unsaturated esters **3aa**–**c**. Finally, removal of the dithioacetal protection gave the required series of unsaturated aldehydes **4aa**, **4ab**, **4b**, and **4c** in good overall yield (Scheme 2).

Diallyl substrate **7a** and the related cyclopentene substrate **7b** were prepared from 3,3-diallyl-2,3,4,5-tetrahydrofuran-2-one **5a**. Conversion of **5a** to spirocyclic lactone **5b** was achieved using Grubb's catalyst in a facile ring-closing metathesis reaction. Reduction of **5a** and **5b** to the corresponding lactols

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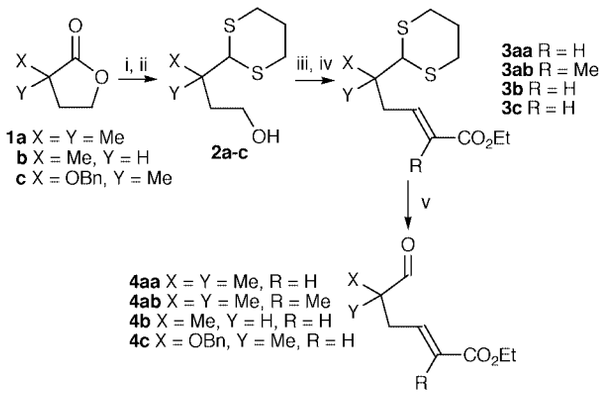
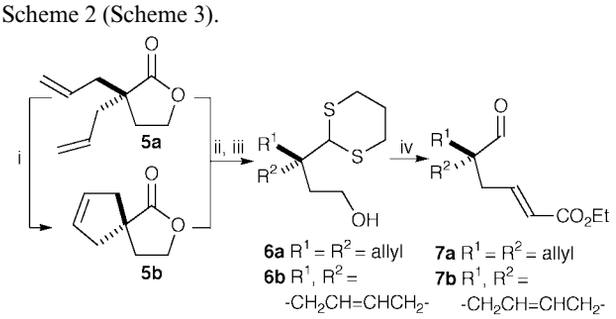


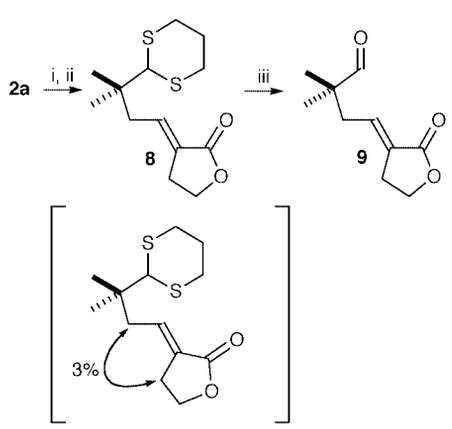
Scheme 2 *Reagents and conditions*: i, DIBAL-H, CH_2Cl_2, −78 °C; ii, propane-1,3-dithiol, CF_3SO_3H (or $BF_3{\cdot}Et_2O$), CH_2Cl_2, 4 Å MS, −15 °C–rt, 30–65% (for two steps); iii, py·SO_3, DMSO, NEt_3, CH_2Cl_2; iv, $PPh_3{=}CRCO_2Et$, CH_2Cl_2, rt, 71–86% (for two steps); v, $CaCO_3$, MeI, MeCN, H_2O, 60 °C, 85–98%.

followed by ring-opening with propane-1,3-dithiol under Lewis acid conditions gave **6a**,**b**. Cyclisation substrates **7a**,**b** were then prepared from **6a** and **6b** using the approach outlined in Scheme 2 (Scheme 3).



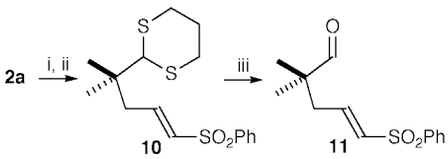
Scheme 3 *Reagents and conditions*: i, $(PCy)_3Ru(Cl)_2{=}CHPh$ 2.5 mol%, CH_2Cl_2, Δ, 99%; ii, DIBAL-H, CH_2Cl_2, −78 °C; iii, propane-1,3-dithiol, $BF_3{\cdot}OEt_2$, CH_2Cl_2, 4 Å MS, −15 °C–0 °C, 52–94% (for two steps); iv, see Scheme 2 (steps iii, iv (R=H), v), 62–64% (for three steps).

Substrate **9** was prepared from alcohol **2a** by oxidation and Wittig reaction with 1-(butyrolactonylidene)triphenylphosphorane.[12] Intermediate **8** was obtained as a 4:1 mixture of *E* and *Z*-isomers which were separated by chromatography. Removal of the dithioacetal protection then gave substrate **9** in excellent yield (Scheme 4).



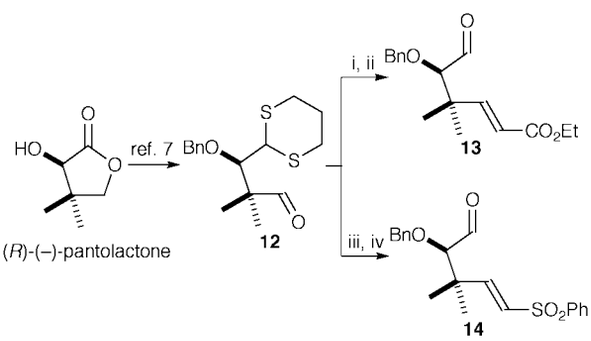
Scheme 4 *Reagents and conditions*: i, py·SO_3, DMSO, NEt_3, CH_2Cl_2; ii, (1-butyrolactonylidene)triphenylphosphorane, CH_2Cl_2, rt, 85% (for two steps); iii, $CaCO_3$, MeI, MeCN, H_2O, 60 °C, 99%.

In order to assess the feasibility of using other radical acceptors in the cyclisation, vinyl sulfone substrate **11** was prepared from alcohol **2a**. Oxidation followed by a stereoselective Wittig–Horner reaction with α-phosphorylated-α-lithio methyl phenyl sulfone gave **10**, which upon subsequent deprotection gave **11** in high yield (Scheme 5).[13]



Scheme 5 *Reagents and conditions*: i, py·SO_3, DMSO, NEt_3, CH_2Cl_2, 72%; ii, Bu^{n}Li, $MeSO_2Ph$, $(EtO)_2P(O)Cl$, THF, 0 °C then −78 °C–rt, 69%; iii, $CaCO_3$, MeI, MeCN, H_2O, 98%.

Enantiomerically pure aldehyde substrates **13** and **14** were prepared from aldehyde **12** by Wittig and Wittig–Horner reactions as outlined previously. Aldehyde **12** was prepared from (*R*)-(−)-pantolactone by adaptation of a literature route (Scheme 6).[7]



Scheme 6 *Reagents and conditions*: i, $PPh_3{=}CHCO_2Et$, CH_2Cl_2, rt, 65%; ii, $CaCO_3$, MeI, MeCN, H_2O, 60 °C, 95%; iii, Bu^{n}Li, $MeSO_2Ph$, $(EtO)_2P(O)Cl$, THF, 0 °C then −78 °C–rt, 79%; iv, $CaCO_3$, MeI, MeCN, H_2O, 60 °C, 95%.

Cyclisation reactions

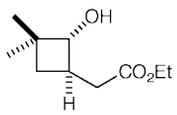
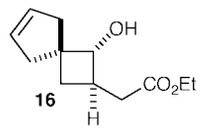
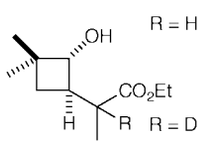
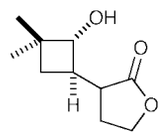
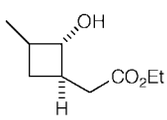
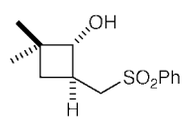
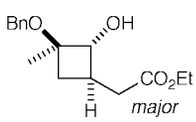
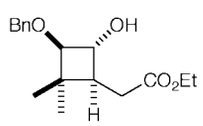
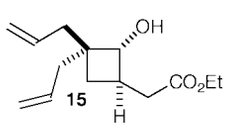
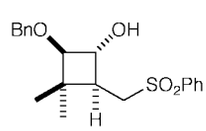
In the only previous example of a cyclisation of this kind, the substrate was treated with samarium(II) iodide using an excess of HMPA as cosolvent.[7] We wished to move away from the use of HMPA due to its toxicity and also due to the harshness of the samarium(II) iodide–HMPA reagent system. We therefore chose to investigate the use of alcohol cosolvents in the reaction.

After extensive studies, optimal conditions for almost all cyclisations were found to involve the addition of the substrate to a solution of samarium(II) iodide (inverse addition) in THF, in the presence of excess MeOH (ratio of THF to MeOH, 4:1) as cosolvent. The MeOH serves not only as a proton source but also appears to promote cyclisation by increasing the reduction potential of samarium(II) iodide, a phenomenon which has been suggested,[14] but has since received little attention. Cyclisations carried out using EtOH or Bu^{t}OH as cosolvent were found to be considerably slower, and were only successful using the inverse mode of addition. Results from the cyclisation reactions are shown in Table 1.

In all cases, *anti*-cyclobutanol products were obtained with no trace of the corresponding *syn*-products. The *anti*-selectivity in the cyclisations was initially confirmed by NOE studies on several cyclobutanol products (Fig. 1), and inferred by comparison of the ^1H NMR data for the remainder.

Early in our studies we observed that the presence of a quaternary centre facilitated cyclisation:[15] while substrates **4aa** and **4ab** underwent efficient, stereoselective cyclisation, the attempted cyclisation of **4b** simply led to the acyclic product in which both the aldehyde and double bond had been reduced (compare entries 1 and 2 with entry 4). However, substrate **4c**,

Table 1 4-*exo-trig* Cyclisations of aldehyde substrates using samarium(II) iodide

Entry	Substrate	Product (isolated yield %)		Entry	Substrate	Product (isolated yield %)	
1	**4aa**		(65)	7	**7b**		(62)
2	**4ab**		(66)[a]	8	**9**		(66)[a]
3	**4ab**		(66)[a,b]				
4	**4b**		(0)[c]	9	**11**		(21)[e]
5	**4c**		(57)[a,d]	10	**13**		(70)[f]
6	**7a**		(80)	11	**14**		(60)[g]

See Experimental section for reaction conditions. [a] 4:1 mixture of diastereoisomers. [b] CH_3OD used as cosolvent. [c] Ethyl 6-hydroxy-5-methylhexanoate was the major product (31%). [d] HMPA added. [e] (*E*)-2,2-Dimethyl-5-phenylsulfonylpent-4-enol was the major product (35%). [f] *Cf.* ref. 7. [g] (*E*)-3,3-Dimethyl-5-phenylsulfonylpent-4-enal (26%) was also obtained.

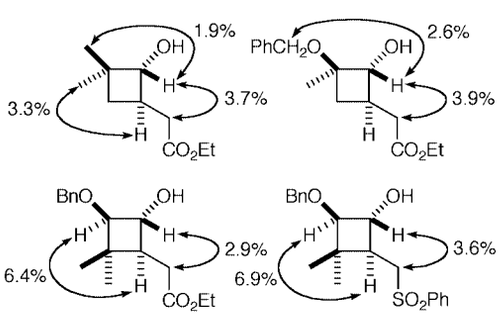
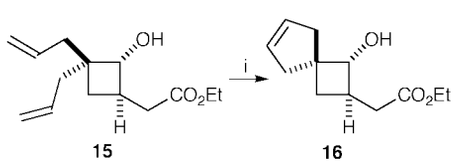


Fig. 1 NOE Studies on selected cyclobutanol products.

where a methyl group from **4aa** has been replaced by a benzyloxy group, was found to cyclise efficiently and with good diastereoselectivity to give the *anti*,*anti*-cyclobutanol as the major product (entry 5). This illustrates that dialkyl substitution is not the only means of promoting cyclisation.

Diallyl substrate **7a** underwent reaction to give the expected cyclobutanol product **15** resulting from cyclisation onto the electron-deficient olefin (entry 6). Similarly, related substrate **7b** underwent smooth spirocyclisation to generate the spiro[3.4]-octene skeleton in cyclobutanol **16** (entry 7). The conversion of **15** to **16** could readily be achieved by ring-closing metathesis using Grubb's catalyst (Scheme 7).



Scheme 7 *Reagents and conditions*: i, $(PCy)_3Ru(Cl)_2$=CHPh 20 mol%, CH_2Cl_2, Δ, 95%.

The cyclisation of lactone **9** proceeded as expected (entry 8), while enantiomerically pure substrates **13** and **14** cyclised under our mild conditions to give *anti*,*anti*-cyclobutanol products selectively and in good yield (entries 10 and 11).

In general, vinyl sulfone substrates were found to cyclise less efficiently than the corresponding unsaturated esters and as a result gave rise to acyclic by-products (entries 9 and 11): the attempted cyclisation of substrate **11** gave (*E*)-2,2-dimethyl-5-phenylsulfonylpent-4-enol as the major product presumably by competitive reduction of the intermediate ketyl-radical anion and protonation. In the cyclisation of **14**, further evidence for a slow cyclisation step is seen as reduction and elimination of the α-benzyloxy group competes to some extent with the 4-*exo-trig* cyclisation.

Stereochemistry α- to the ester in the 4-*exo-trig* cyclisation

When the cyclisation of **4ab** was carried out in MeOD (entry 3), complete deuterium incorporation was observed. This clearly illustrates that protonation rather than hydrogen atom capture terminates the reaction. This agrees with the accepted two electron mechanism for ketyl-olefin cyclisation reactions with samarium(II) iodide[16] although it does not rule out an anionic mechanism. In the cyclisation of **4ab** (and **9**) protonation of the intermediate samarium(III) enolate generates a third chiral centre. With MeOH as the cosolvent, we found that selectivities at this centre range from 4.5–3:1.

Little is known about the stereochemistry of processes in which prochiral enolates, generated by radical addition to an olefin, followed by further reduction, react with electrophiles.

Recently, an analogous stereochemical issue involving a 5-*exo-trig* ketyl-olefin cyclisation mediated by samarium(II) iodide was discussed and selectivities slightly lower than our own were observed.[17] In a vanadium(II)-mediated ketyl-olefin cyclisation, similar selectivities were again observed but not

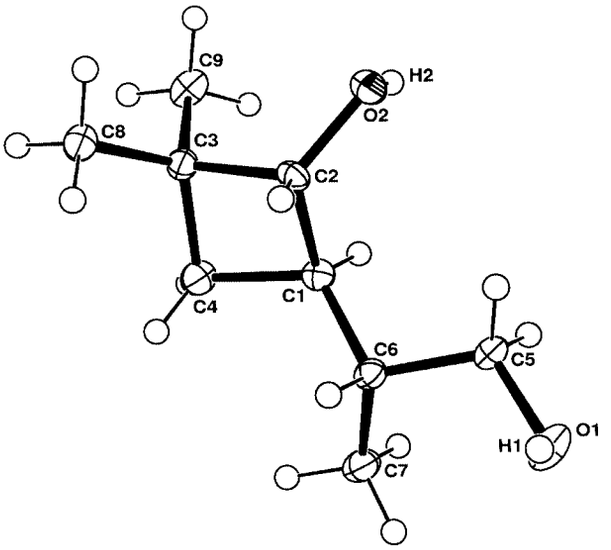
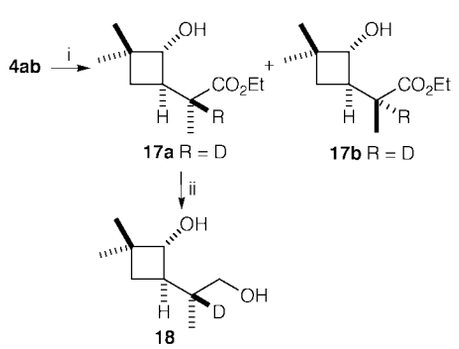


Fig. 2 Molecular drawing of **18** showing the atom numbering and 50% probability ellipsoids for non-hydrogen atoms.

discussed.[18] The intramolecular addition of alkyl radicals to α-substituted-α,β-unsaturated esters mediated by zinc metal or cobalt complexes has also been studied.[19] This study concluded that the 1,2-asymmetric induction in enolate protonation was comparable to that observed for hydrogen atom capture in the same system. It was also observed that the stereoselectivity of protonation could be influenced to a small degree by the addition of amines.[19]

In the cyclisation of **4ab**, we observed that the stereochemistry at the centre α- to the ester in the product cyclobutanols was highly dependent on the alcohol employed as the cosolvent in the cyclisation. In order to rationalise the observed stereoselectivity, we sought to determine the stereochemistry of diastereoisomer **17a**, the major diastereoisomer from the cyclisation in MeOH. Unfortunately, both the 3-nitrobenzoyl, and the 3,5-dinitrobenzoyl esters of **17a** were non-crystalline. However, reduction of **17a** gave diol **18**, and subsequent sublimation of the low-melting solid gave crystals suitable for low temperature X-ray crystallographic analysis (Scheme 8, Fig. 2 and Fig. 3).



Scheme 8 *Reagents and conditions*: i, SmI_2, THF, MeOR, 0 °C, 66%; ii, $LiAlH_4$, THF, 0 °C, 65%.

The cyclisation of **4ab** using a variety of cosolvents under otherwise identical conditions was then carried out and the stereoselectivity α- to the ester determined (Table 2). The use of water as an additive gave the highest selectivities under these specific conditions, and the fastest reaction, as indicated by the time taken for the samarium(II) iodide solution to decolourise. Unfortunately, additional products arising from over-reduction prior to cyclisation were formed. The use of EtOH gave a slower reaction and a 1:1 mixture of diastereoisomers **17a** and **17b** (R=H) was formed. When Bu^{t}OH was employed as a cosolvent, the reaction was extremely slow and showed a small, but reproducible, switch in selectivity in favour of **17b** (R=H).

Table 2 Cyclisation of **4ab** in the presence of different cosolvents

Cosolvent	Additive	Time/ min[a]	Ratio of **17a**:**17b** (R = H)[b]	Isolated yield of **17a** and **17b** (R = H) (%)
H_2O		<1	4.5:1	44
MeOH		5	4:1	66
MeOH	HMPA[c]	<1	4:1	35
EtOH		85	1:1	84
Bu^{t}OH		540	1:2	53

Reaction conditions: **4ab** in THF (0.25 M) was added to a solution of SmI_2 (0.1 M in THF, 2 eq. and cosolvent (123 eq.) (+additive) at 0 °C. [a] Time taken for SmI_2 to decolourise. [b] From crude ^{1}H NMR. [c] 12 eq. added.

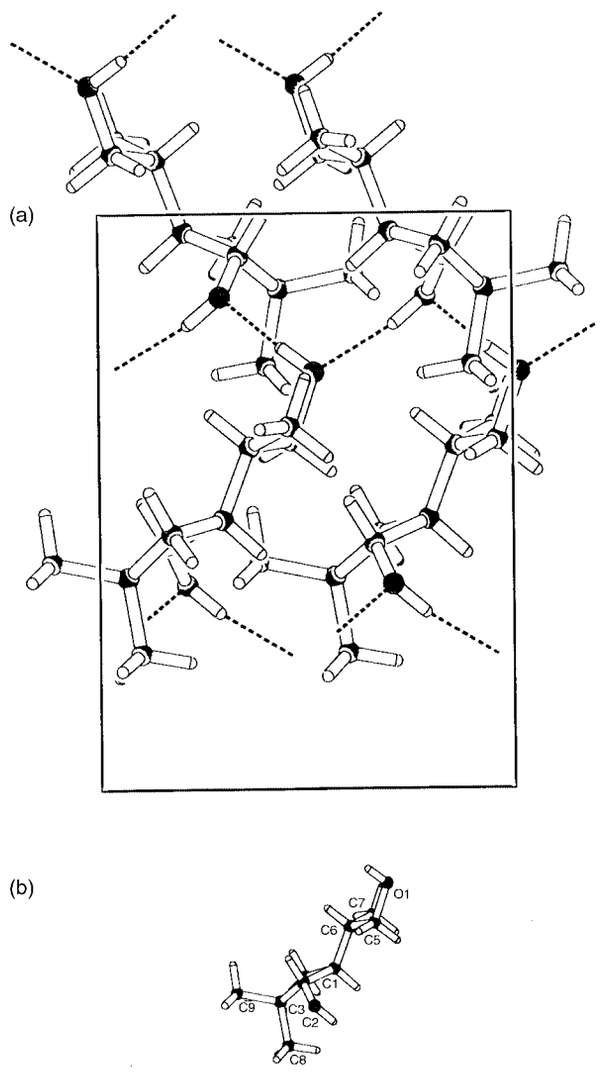


Fig. 3 (a) Packing in **18** viewed down the *c* axis; (b) a single molecule viewed down the *c* axis with the atom numbering scheme shown.

A similar switch in selectivity was also observed in the cyclisation of **9**. Cyclisation of **9** in MeOH gave a 4:1 mixture of diastereoisomers, while in Bu^{t}OH, a 1:1.6 ratio was obtained. (Although the relative stereochemistry of the major and minor products obtained from the cyclisations of **9** have not been determined, we presume the reactions show the same sense of selectivity in a particular cosolvent as those of **4ab**.)

We feel a possible explanation for the cosolvent dependency of the stereochemistry, lies in the degree of solvation about the

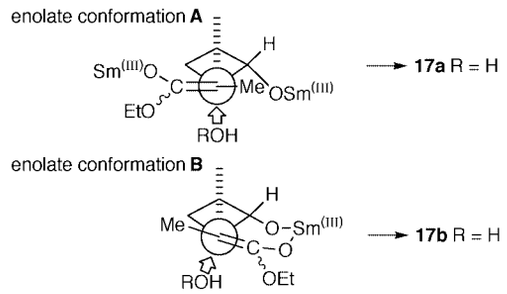


Fig. 4

samarium(III) centres in the key samarium(III) enolate intermediate. In Fig. 4 two possible conformations, **A** and **B**, of the intermediate samarium(III) enolate are shown. In the absence of strongly coordinating solvents, coordination of the lanthanide centre to both the alkoxide on the cyclobutane ring and the enolate would be expected to lock the system in conformation **B**. Protonation of the intermediate whilst in conformation **B** would lead to **17b** (R=H). In highly coordinating solvents, such as water and methanol, however, this chelation will be disrupted and conformation **A** will predominate, due to electronic and steric factors.[20] Protonation of the intermediate whilst in conformation **A** will lead to **17a** (R=H). Hence, the reactions in EtOH and Bu^{t}OH show a gradual swing towards enolate conformation **B** as chelation becomes more important.

The additional observation that cyclisation of **4ab** in the presence of only 4 equivalents of MeOH gave a low yield of **17a** and **17b** (R=H) as a 1 : 1 ratio, not only supports these ideas but also shows the importance of excess alcohol for activation of samarium(II) iodide and thus, efficient reaction. In the cyclisation of **9**, the intermediate samarium(III) enolate geometry is locked. As a similar cosolvent dependency is observed in this cyclisation when compared to that of **4ab**, it appears that enolate geometry is not an important factor in the variation of product stereochemistry with solvent. Epimerisation studies on the product cyclobutanols proved difficult, however, in the cyclisation of **4ab** in MeOH, quenching after 1, 4 and 18 h gave identical diastereoisomeric mixtures suggesting epimerisation under the reaction conditions was not occurring. As shown in Table 2, attempts to break down any chelation by the addition of HMPA led to very different cyclisation conditions and thus results that were not meaningful.

Conclusions

The scope and limitations of a samarium(II)-mediated, stereoselective approach to functionalised cyclobutanols have been established. In all cases the reaction shows complete *anti*-selectivity and a range of functionality in the substrates is tolerated. Preliminary investigations into the factors that influence the stereochemistry at a third newly formed chiral centre lying outside the ring have been carried out. Further studies into the mechanism and stereochemistry of cyclisation, and its application in synthesis are ongoing.

Experimental

General considerations

All reactions were performed under argon or nitrogen atmospheres with anhydrous solvents unless otherwise stated. THF was distilled from sodium and benzophenone. CH_2Cl_2 was distilled from CaH_2. Toluene was distilled from sodium wire. MeOH, EtOH and Bu^{t}OH were distilled from the corresponding magnesium alkoxide and stored under argon. HMPA was dried by refluxing with CaH_2 followed by fractional distillation under reduced pressure. Samarium(II) iodide was prepared by the method of Imamoto and Ono[21] with the modification that the samarium–iodine–THF solution was heated at 60 °C rather than at reflux.

Melting points were measured on a Kofler hot stage apparatus and are uncorrected. Optical rotations were measured on a polAAr 2000 polarimeter. $[\alpha]_D$ Values are given in units of 10^{-1} deg cm^2 g^{-1}.

^{1}H NMR and ^{13}C NMR were recorded on Bruker AM 360 or DPX 400 spectrometers with chemical shift values being reported in ppm relative to residual chloroform ($\delta_H = 7.27$ or $\delta_C = 77.2$) as internal standard unless otherwise stated. All coupling constants (J) are reported in hertz (Hz). Infrared spectra were recorded using JASCO FT/IR 410 and Impact 400 spectrometers and mass spectra were obtained using a JEOL JMS-700 spectrometer. Microanalyses were carried out at the University of Glasgow using an Elemental Analyser MOD 1106.

Column chromatography was carried out using Fisher Matrex silica 60. Macherey–Nagel aluminium backed plates pre-coated with silica gel 60 (UV_{254}) were used for thin layer chromatography and were visualised by UV or staining with iodine or alkali $KMnO_4$.

Preparation of cyclisation substrates

3-(1,3-Dithian-2-yl)-3-methylbutan-1-ol 2a. To a stirred solution of α,α-dimethyl-γ-butyrolactone[22] **1a** (3.59 g, 31.5 mmol, 1 eq.) in CH_2Cl_2 (80 ml) at −78 °C was added dropwise DIBAL-H (1.5 M in toluene, 29.4 ml, 44.0 mmol, 1.4 eq.) and the reaction stirred for 2 h. The mixture was then added dropwise to a stirred solution of K/Na tartrate (26.6 g, 94.3 mmol, 3 eq.) in H_2O (8 ml) and CH_2Cl_2 (80 ml). The aqueous layer was separated and extracted with CH_2Cl_2 (3 × 40 ml), and the combined organic extracts dried ($MgSO_4$) and concentrated *in vacuo* to give the lactol (2.55 g, 22.0 mmol, 70%) as a pale yellow oil which was used without further purification: δ_H (400 MHz, $CDCl_3$) 4.90 (1H, d, J 3.4, C*H*OH), 4.09 (1H, td, J 8.4, 3.4, 1H from CH_2O), 3.92 (1H, apparent q, J 8.4, 1H from CH_2O), 2.58 (1H, d, J 3.4, OH), 1.99–1.92 (1H, m, 1H from CH_2), 1.68–1.62 (1H, m, 1H from CH_2), 1.13 (3H, s, CH_3), and 1.03 (3H, s, CH_3).

To a stirred solution of the lactol (1.86 g, 16.0 mmol, 1 eq.) in CH_2Cl_2 (30 ml) at −20 °C was added activated 4 Å molecular sieves and propane-1,3-dithiol (1.93 ml, 19.2 mmol, 1.2 eq.) before the dropwise addition of $BF_3{\cdot}OEt_2$ (2.03 ml, 16.0 mmol, 1 eq.). The reaction was left for 1.5 h and then aqueous saturated $NaHCO_3$ (5 ml) was added. The aqueous layer was then separated and extracted with CH_2Cl_2 (4 × 50 ml). The organic layers were dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by column chromatography (eluting with 30% EtOAc in hexane) yielded **2a** (1.92 g, 9.28 mmol, 58%) as a clear pale yellow oil: ν_{max} (neat)/cm^{-1} 3369s (OH), 2961s, 2930s, 2899s, 1465m, 1388m, 1367m, 1277m, 1055m, and 1026m; δ_H (400 MHz, $CDCl_3$) 4.13 (1H, s, SCHS), 3.77 (2H, apparent q, J 6.9, CH_2OH), 2.91–2.89 (4H, m, 2 × SCH_2), 2.09 (1H, dquintets, J 14.0, 3.3, 1H from CH_2), 1.88–1.76 (1H, m, 1H from CH_2), 1.81 (2H, t, J 6.9, CH_2CH$_2$OH), and 1.15 (6H, s, 2 × CH_3); δ_C (100 MHz, $CDCl_3$) 60.9 (SCHS), 59.6 (CH_2OH), 43.0 (*C*H$_2$CH$_2$OH), 38.0 (C), 31.5 (2 × SCH_2), 26.2 (CH_2), and 26.1 (2 × CH_3); *m*/*z* (EI mode) 206 (82%), 119 (100), 99 (19), 85 (14), 69 (14), and 55 (17) (Found: M$^+$, 206.0797. $C_9H_{18}OS_2$ requires *M*, 206.0799).

General oxidation–olefination procedure A

Ethyl (*E*)-5-(1,3-dithian-2-yl)-5-methylhex-2-enoate 3aa. To a solution of 3-(1,3-dithian-2-yl)-3-methylbutan-1-ol **2a** (187 mg, 0.91 mmol, 1 eq.) in CH_2Cl_2 (10 ml) at room temperature was added DMSO (0.64 ml, 9.00 mmol, 10 eq.) and triethylamine (0.61 ml, 5.94 mmol, 6.6 eq.) and the resulting solution stirred at room temperature for 5 min before cooling to 0 °C. Pyridine–sulfur trioxide complex (544 mg, 3.42 mmol, 3.8 eq.) was then

added and the solution allowed to warm to room temperature. After 1 h, (ethoxycarbonylmethylene)triphenylphosphorane (627 mg, 1.80 mmol, 2 eq.) was added and the reaction mixture stirred for a further 16 h at room temperature. Aqueous saturated $NaHCO_3$ (6 ml) was then added and the aqueous layer separated and extracted with CH_2Cl_2 (3 × 5 ml). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by column chromatography (eluting with 20% EtOAc in hexane) gave **3aa** (187 mg, 0.68 mmol, 76%) as a colourless oil: ν_{max} (neat)/cm^{-1} 2978m, 2898m, 1720s (C=O), 1653s (C=C), 1367m, and 1175s; δ_H (400 MHz, $CDCl_3$) 6.97 (1H, dt, *J* 15.6, 7.9, C*H*=CHCO$_2$Et), 5.91 (1H, dt, *J* 15.6, 1.2, CH=C*H*CO$_2$Et), 4.20 (2H, q, *J* 7.1, C*H*$_2$CH$_3$), 3.98 (1H, s, SCHS), 2.90–2.87 (4H, m, 2 × CH$_2$S), 2.39 (2H, dd, *J* 7.9, 1.2, C*H*$_2$CH=), 2.11–2.04 (1H, m, 1H from CH$_2$), 1.87–1.77 (1H, m, 1H from CH$_2$), 1.29 (3H, t, *J* 7.1, CH$_2$C*H*$_3$), and 1.12 (6H, s, 2 × Me); δ_C (100 MHz, $CDCl_3$) 167.0 (C=O), 144.9 (*C*H=CHCO$_2$Et), 124.4 (CH=*C*HCO$_2$Et), 60.3 (CH$_2$O), 60.2 (CH), 42.8 (CH$_2$C=), 39.0 (C), 31.3 (2 × SCH$_2$), 26.0 (CH$_2$), 25.3 (2 × Me), and 14.3 (CH$_2$*C*H$_3$); *m*/*z* (EI mode) 274 (14%), 229 (6), 161 (12), 160 (7), 119 (100), and 85 (4) (Found: M$^+$, 274.1059. $C_{13}H_{22}O_2S_2$ requires *M*, 274.1061) (Found: C, 56.72; H, 8.19. $C_{13}H_{22}O_2S_2$ requires C, 56.89; H, 8.08%).

General deprotection procedure B

Ethyl (*E*)-5,5-dimethyl-6-oxohex-2-enoate 4aa. To a solution of **3aa** (160 mg, 0.58 mmol, 1 eq.) in MeCN (2 ml) and H_2O (0.5 ml) at room temperature was added $CaCO_3$ (174 mg, 1.74 mmol, 3 eq.) and iodomethane (0.36 ml, 5.80 mmol, 10 eq.). The resulting solution was then heated at 60 °C for 17 h. The reaction mixture was then passed down a short silica gel column (eluting with 20% EtOAc in hexane). Concentration *in vacuo* gave aldehyde **4aa** (102 mg, 0.55 mmol, 95%) as a pale yellow oil which was used without further purification: ν_{max} (neat)/cm^{-1} 2980s, 2719m, 1716s (C=O), 1655s, 1270s, 1179s, and 1044s; δ_H (400 MHz, $CDCl_3$) 9.48 (1H, s, CHO), 6.85 (1H, dt, *J* 15.6, 7.8, C*H*=CHCO$_2$Et), 5.87 (1H, dt, *J* 15.6, 1.3, CH=C*H*CO$_2$Et), 4.19 (2H, q, *J* 7.2, C*H*$_2$CH$_3$), 2.36 (2H, dd, *J* 7.8, 1.3, C*H*$_2$CH=), 1.29 (3H, t, *J* 7.2, CH$_2$C*H*$_3$), and 1.11 (6H, s, 2 × Me); δ_C (100 MHz, $CDCl_3$) 204.6 (CHO), 166.0 (*C*O$_2$Et), 143.4 (*C*H=CHCO$_2$Et), 124.8 (CH=*C*HCO$_2$Et), 60.4 (CH$_2$O), 45.8 (C), 39.3 (*C*H$_2$CH=), 21.4 (2 × Me), and 14.2 (CH$_2$*C*H$_3$); *m*/*z* (CI mode, isobutane) 185 (100%), 156 (4), and 139 (30) (Found: (M + H)$^+$, 185.1180. $C_{10}H_{17}O_3$ requires *M*, 185.1178).

Ethyl (*E*)-2,5-dimethyl-5-(1,3-dithian-2-yl)hex-2-enoate 3ab. As for general procedure A. 3-(1,3-Dithian-2-yl)-3-methylbutan-1-ol **2a** (500 mg, 2.42 mmol, 1 eq.), after oxidation, reaction with (1-ethoxycarbonylethylidene)triphenylphosphorane for 14 h, and purification by column chromatography (eluting with 10% EtOAc in hexane), gave **3ab** (684 mg, 2.37 mmol, 98%) as a clear colourless oil: ν_{max} (neat)/cm^{-1} 2964s, 2900s, 2828m, 1712s (C=O), 1647s (C=C), 1465s, 1422m, 1388s, 1367s, 1261s, 1177m, and 1101m; δ_H (400 MHz, $CDCl_3$) 6.84 (1H, t, *J* 7.8, CH$_2$C*H*=), 4.21 (2H, q, *J* 7.1, C*H*$_2$CH$_3$), 4.03 (1H, s, SCHS), 2.91–2.88 (4H, m, 2 × SCH$_2$), 2.38 (2H, d, *J* 7.8, C*H*$_2$CH=), 2.09 (1H, dquint., *J* 14.1, 3.3, 1H from CH$_2$), 1.87 (3H, s, =CCH$_3$), 1.87–1.76 (1H, m, 1H from CH$_2$), 1.31 (3H, t, *J* 7.1, CH$_2$C*H*$_3$), and 1.13 (6H, s, 2 × CH$_3$); δ_C (100 MHz, $CDCl_3$) 168.3 (C=O), 138.0 (CH=), 130.3 (=*C*CH$_3$), 60.8 (SCHS), 60.7 (*C*H$_2$CH$_3$), 39.7 (C), 39.1 (*C*H$_2$CH=), 31.5 (2 × SCH$_2$), 26.2 (CH$_2$), 25.5 (2 × CH$_3$), 14.5 (C*C*H$_3$), and 12.9 (CH$_2$*C*H$_3$); *m*/*z* (EI mode) 288 (26%), 243 (8), 162 (17), 123 (12), 119 (100), 99 (5), and 55 (5) (Found: M$^+$, 288.1220. $C_{14}H_{24}O_2S_2$ requires *M*, 288.1218).

Ethyl (*E*)-2,5,5-trimethyl-6-oxohex-2-enoate 4ab. As for general procedure B. Ethyl (*E*)-2,5-dimethyl-5-(1,3-dithian-2-yl)hex-2-enoate **3ab** (724 mg, 2.51 mmol, 1 eq.) gave aldehyde **4ab** (490 mg, 2.46 mmol, 98%) as a clear colourless oil which was used without further purification: ν_{max} (neat)/cm^{-1} 2976s, 2935s, 2809m, 2705m, 1716s (C=O), 1650s (C=C), 1390s, 1367s, 1255s, 1109s, and 1082s; δ_H (400 MHz, $CDCl_3$) 9.51 (1H, s, CHO), 6.70 (1H, t, *J* 7.8, CH$_2$C*H*=), 4.19 (2H, q, *J* 7.1, C*H*$_2$CH$_3$), 2.35 (2H, d, *J* 7.8, C*H*$_2$CH=), 1.85 (3H, s, CH$_3$C=), 1.29 (3H, t, *J* 7.1, CH$_2$C*H*$_3$), and 1.11 (6H, s, 2 × C*H*$_3$); δ_C (100 MHz, $CDCl_3$) 205.3 (C=O), 167.9 (*C*O$_2$Et), 136.3 (CH=), 130.7 (C=), 60.8 (*C*H$_2$CH$_3$), 46.5 (C), 35.7 (CH$_2$), 21.6 (2 × CH$_3$), 14.4 (CH$_2$*C*H$_3$), and 12.8 (=C*C*H$_3$); *m*/*z* (CI mode, NH$_3$) 216 (100%), 199 (8), 134 (7), 96 (6), and 79 (4) (Found: (M + H)$^+$, 199.1332. $C_{11}H_{19}O_3$ requires *M*, 199.1329).

3-(1,3-Dithian-2-yl)butan-1-ol 2b. To a stirred solution of α-methyl-γ-butyrolactone[23] **1b** (2.99 g, 29.9 mmol, 1 eq.) in CH_2Cl_2 (80 ml) at −78 °C was added DIBAL-H (1.5 M in toluene, 23.9 ml, 35.9 mmol, 1.2 eq.) and the reaction left for 1 h. The mixture was then added dropwise to a stirred solution of K/Na tartrate (25.8 g, 89.7 mmol, 3 eq.) in H_2O (8 ml) and CH_2Cl_2 (80 ml). The aqueous layer was then separated and extracted with CH_2Cl_2 (3 × 20 ml) and the combined organic extracts dried ($NaSO_4$). Concentration *in vacuo* gave the lactol (2.82 g, 27.61 mmol, 92%) as a pale yellow oil (2:1 mixture of diastereoisomers) which was used without further purification: δ_H (400 MHz, $CDCl_3$) 5.29 (1H, t, *J* 3.6, C*H*OH of one isomer), 5.13 (1H, dd, *J* 3.3, 1.3, C*H*OH of one isomer), 4.14–4.04 (2H, m, 1H from CH$_2$O for each isomer), 4.01–3.95 (1H, m, 1H from CH$_2$O for one isomer), 3.87–3.81 (1H, m, 1H from CH$_2$O for one isomer), 2.83 (1H, d, *J* 3.3, OH of one isomer), 2.64 (1H, d, *J* 3.6, OH of one isomer), 2.29–2.22 (2H, m, 1H from C*H*$_2$ for both isomers), 2.18–2.12 (1H, m, 1H from C*H*$_2$ for one isomer) and 2.05–1.97 (1H, m, 1H from C*H*$_2$ for one isomer), 1.81–1.71 (1H, m, C*H*CH$_3$ of one isomer), 1.58–1.52 (1H, m, C*H*CH$_3$ of one isomer), 1.12 (3H, d, *J* 6.8, C*H*$_3$CH of one isomer), and 1.05 (3H, d, *J* 7.1, C*H*$_3$CH of one isomer).

To a stirred solution of the lactol (2.82 g, 27.6 mmol, 1 eq.) in CH_2Cl_2 (3 ml) at 0 °C was added propane-1,3-dithiol (3.3 ml, 33.1 mmol, 1.2 eq.) and 4 Å molecular sieves. Trifluoromethanesulfonic acid (0.98 ml, 11.0 mmol, 0.4 eq.) was then added and the reaction mixture allowed to warm to room temperature and stirred for 19 h. Aqueous saturated $NaHCO_3$ (1 ml) was added and the aqueous layer separated and extracted with EtOAc (4 × 20 ml). The combined organic extracts were then dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography (eluting with 20% EtOAc in hexane) to give alcohol **2b** (3.32 g, 17.28 mmol, 63%) as a pale yellow oil: ν_{max} (neat)/cm^{-1} 3397br s (OH), 2930s, 1276s, 1185s, 1053s, 1011s, and 907s; δ_H (400 MHz, $CDCl_3$) 4.17 (1H, d, *J* 4.1, SCHS), 3.77–3.67 (2H, m, C*H*$_2$OH), 2.95–2.82 (4H, m, 2 × SCH$_2$), 2.14–2.06 (2H, m, 1H from CH$_2$ and C*H*CH$_3$), 1.95–1.80 (2H, m, 1H from C*H*$_2$CH and 1H from CH$_2$), 1.64–1.56 (1H, m, CHC*H*$_2$), 1.34 (1H, s, OH), and 1.12 (3H, d, *J* 6.9, C*H*$_3$CH); δ_C (100 MHz, $CDCl_3$) 60.8 (CH$_2$OH), 55.3 (SCHS), 36.9 (CH*C*H$_2$), 35.3 (*C*HCH$_3$), 31.0 (SCH$_2$), 30.8 (SCH$_2$), 26.3 (CH$_2$), and 17.1 (CH$_3$); *m*/*z* (EI mode) 192 (26%), 119 (100), 106 (4), 86 (10), 75 (6), and 74 (4) (Found: M$^+$, 192.0643. $C_8H_{16}OS_2$ requires *M*, 192.0639).

Ethyl (*E*)-5-(1,3-dithian-2-yl)hex-2-enoate 3b. As for general procedure A. 3-(1,3-Dithian-2-yl)butan-1-ol **2b** (500 mg, 2.60 mmol, 1 eq.), after oxidation and reaction with (ethoxycarbonylmethylene)triphenylphosphorane for 11 h, and purification by column chromatography (eluting with 10% EtOAc in hexane), gave **3b** (482 mg, 1.85 mmol, 71%) as a clear, yellow oil: ν_{max} (neat)/cm^{-1} 2978m, 2930m, 2898m, 1717s (C=O), 1653s (C=C), 1367m, 1175s, 1042s, and 983s; δ_H (400 MHz, $CDCl_3$) 6.90 (1H, dt, *J* 15.5, 7.5, C*H*=CHCO$_2$Et), 5.87 (1H, d, *J* 15.5, CH=C*H*CO$_2$Et), 4.19 (2H, q, *J* 7.1, C*H*$_2$CH$_3$), 4.09 (1H, d, *J* 4.6, SCHS), 2.94–2.82 (4H, m, 2 × SCH$_2$), 2.58–2.51 (1H,

dt, *J* 14.4, 7.5, 1H from C*H*$_2$CH=), 2.27–2.19 (1H, dt, *J* 14.4, 7.5, 1H from C*H*$_2$CH=), 2.15–2.02 (2H, m, 1H from CH_2 and C*H*CH_3), 1.86–1.80 (1H, m, 1H from CH_2), 1.29 (3H, t, *J* 7.1, CH_2CH_3), and 1.10 (3H, d, *J* 6.9, CH_3CH); δ_C (100 MHz, $CDCl_3$) 166.6 (C=O), 146.8 (*C*H=CHCO$_2$Et), 123.5 (CH=*C*HCO$_2$Et), 60.4 (*C*H$_2$CH$_3$), 54.5 (SCHS), 38.1 (*C*HCH$_3$), 36.8 (*C*H$_2$CH=), 31.1 (SCH$_2$), 30.8 (SCH$_2$), 26.4 (CH_2), 17.2 (CH*C*H$_3$), and 14.4 (CH$_2$*C*H$_3$); *m*/*z* (EI mode) 260 (14%), 215 (7), 147 (36), 119 (100), 114 (12), and 73 (10) (Found: M^+, 260.0905. $C_{12}H_{20}S_2O_2$ requires *M*, 260.0900).

Ethyl (*E*)-5-methyl-6-oxohex-2-enoate 4b. As for general procedure B. Ethyl (*E*)-5-(1,3-dithian-2-yl)hex-2-enoate **3b** (458 mg, 1.76 mmol, 1 eq.) gave the aldehyde **4b** (276 mg, 1.62 mmol, 92%) as a pale red oil which was used without further purification: ν_{max} (neat)/cm^{-1} 2980s, 2936s, 2816m, 2719m, 1716s (C=O), 1655s (C=C), 1270s, 1179s, and 1044s; δ_H (400 MHz, $CDCl_3$) 9.67 (1H, d, *J* 1.2, CHO), 6.90 (1H, dt, *J* 15.6, 7.0, C*H*=CHCO$_2$Et), 5.89 (1H, dt, *J* 15.6, 1.5, CH=C*H*CO$_2$Et), 4.20 (2H, q, *J* 7.1, C*H*$_2$CH$_3$), 2.73–2.59 (1H, m, 1H from C*H*$_2$CH=), 2.59–2.50 (1H, m, CH$_3$C*H*), 2.30–2.22 (1H, m, 1H from C*H*$_2$CH=), 1.30 (3H, t, *J* 7.1, CH$_2$C*H*$_3$), and 1.17 (3H, d, *J* 7.2, C*H*$_3$CH); δ_C (100 MHz, $CDCl_3$) 203.4 (CHO), 166.3 (C=O), 145.2 (CH$_2$*C*H=), 123.9 (CH=*C*HCO$_2$Et), 60.6 (*C*H$_2$CH$_3$), 45.4 (CH$_3$*C*H), 33.0 (CH_2), 14.4 (CH$_2$*C*H$_3$), and 13.4 (*C*H$_3$CH); *m*/*z* (CI mode, isobutane) 171 (100%), 169 (4), 125 (22), 111 (4), 95 (6), and 85 (19) (Found: $(M + H)^+$, 171.1021. $C_9H_{15}O_3$ requires *M*, 171.1017).

α-Benzyloxy-α-methyl-γ-butyrolactone[24] 1c. To a solution of diisopropylamine (3.06 ml, 21.8 mmol, 1.4 eq.) in THF (20 ml) at −78 °C was added *n*-butyllithium (1.6 M in hexanes, 13.7 ml, 21.8 mmol, 1.4 eq.) and the resulting solution stirred at −78 °C for 50 min. α-Benzyloxy-γ-butyrolactone (3.00 g, 15.6 mmol, 1 eq.) in THF (20 ml) was then added dropwise over 10 min. After a further 50 min at −78 °C, iodomethane (4.08 ml, 65.5 mmol, 3 eq.) was added dropwise and the reaction mixture allowed to warm to −20 °C. Aqueous saturated NH_4Cl (5 ml) and H_2O (5 ml) were then added and the aqueous layer separated and extracted with EtOAc (3 × 10 ml). The combined organic extracts were then dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the residue by column chromatography (eluting with 30% EtOAc in hexane) gave α-benzyloxy-α-methyl-γ-butyrolactone **1c** (2.20 g, 10.6 mmol, 68%): ν_{max} (neat)/cm^{-1} 2978m, 2908m, 2867m, 1780s (C=O), 1716m, 1492m, 1451m, 1381s, 1222s, and 1193s; δ_H (400 MHz, $CDCl_3$) 7.39–7.30 (5H, m, ArH), 4.62 (2H, apparent s, PhC*H*$_2$), 4.44 (1H, dt, *J* 8.9, 7.5, 1H from CH_2O), 4.28 (1H, td, *J* 8.9, 4.3, 1H from CH_2O), 2.57–2.50 (1H, m, 1H from CH_2), 2.26–2.19 (1H, m, 1H from CH_2), and 1.59 (3H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 175.8 (C=O), 137.8 (ArC), 128.4 (2 × ArCH), 127.7 (ArCH), 127.6 (2 × ArCH), 76.7 (C), 66.6 (Ph*C*H$_2$), 65.3 (CH_2O), 36.3 (CH_2), and 19.6 (CH_3); *m*/*z* (CI mode, isobutane) 207 (100%), 181 (8), 131 (3), 117 (5), and 91 (36) (Found: $(M + H)^+$, 207.1021. $C_{12}H_{15}O_3$ requires *M*, 207.1021).

3-(Benzyloxy)-3-(1,3-dithian-2-yl)butan-1-ol 2c. To a solution of α-benzyloxy-α-methyl-γ-butyrolactone **1c** (1.60 g, 7.72 mmol, 1 eq.) in CH_2Cl_2 (15 ml) at −78 °C was added DIBAL-H (1.5 M in toluene, 6.20 ml, 9.27 mmol, 1.2 eq.) and the solution stirred for 1 h. The reaction mixture was then poured into a solution of K/Na tartrate (5.84 g, 23.2 mol, 3 eq.) in CH_2Cl_2 (5 ml) and H_2O (3 ml). The resulting solution was stirred for 2 h and the aqueous layer then separated and extracted with CH_2Cl_2 (3 × 5 ml). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to give the corresponding lactol (1.29 g, 6.17 mmol, 80%) as a colourless oil which was used without further purification: (mixture of two diastereoisomers): δ_H (400 MHz, $CDCl_3$) 7.45–7.35 (10H, m, 5 × ArH for both isomers), 5.32 (1H, d, *J* 3.2, C*H*OH of one isomer), 5.09 (1H, d, *J* 7.8, C*H*OH of other isomer), 4.77 (1H, d, *J* 7.8, OH of one isomer), 4.60 (AB system, 1H, d, *J* 11.0, 1H from PhC*H*$_2$ of one isomer), 4.54 (AB system, 1H, d, *J* 11.0, 1H from PhC*H*$_2$ of one isomer), 4.58 (2H, s, PhC*H*$_2$ of other isomer), 4.21–4.09 (3H, m, C*H*$_2$O from one isomer and 1H from C*H*$_2$O of the other isomer), 3.84–3.79 (1H, m, 1H from C*H*$_2$O), 2.80 (1H, d, *J* 3.2, OH of one isomer), 2.38–2.32 (1H, m, 1H from CH_2), 2.28–2.23 (1H, m, 1H from CH_2), 2.12–2.02 (1H, m, 1H from CH_2), 2.00–1.93 (1H, m, 1H from CH_2), 1.55 (3H, s, Me of one isomer), and 1.53 (3H, s, Me of other isomer).

To a solution of the lactol (1.29 g, 6.17 mmol, 1 eq.) in CH_2Cl_2 (4 ml) was added propane-1,3-dithiol (0.74 ml, 7.40 mmol, 1.2 eq.) and powdered 4 Å molecular sieves, and the solution cooled to −15 °C. Trifluoromethanesulfonic acid (0.22 ml, 2.47 mmol, 0.4 eq.) was then added dropwise and the resulting solution allowed to warm gradually to room temperature and stirred for 48 h. Aqueous saturated $NaHCO_3$ (10 ml) and H_2O (10 ml) were then added and the aqueous layer separated and extracted with CH_2Cl_2 (3 × 20 ml). The combined organic layers were then dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the residue by column chromatography (eluting with 20% EtOAc in hexane) gave **2c** (789 mg, 2.64 mmol, 43%) as a colourless oil: ν_{max} (soln. in $CHCl_3$)/cm^{-1} 3513m, 3009m, 2903m, 1525m, 1419m, and 1100m; δ_H (400 MHz, $CDCl_3$) 7.40–7.25 (5H, m, ArH), 4.65 (1H, d, *J* 10.3, 1H from PhC*H*$_2$), 4.52 (1H, d, *J* 10.3, 1H from PhC*H*$_2$), 4.52 (1H, s, SCHS), 3.94–3.87 (1H, m, 1H from CH_2O), 3.80–3.75 (1H, m, 1H from CH_2O), 2.94–2.89 (4H, m, CH_2S × 2), 2.33–2.26 (1H, m, 1H from C*H*$_2$CH$_2$OH), 2.13 (1H, dt, *J* 14.0, 3.4, 1H from CH_2), 1.97–1.92 (1H, m, 1H from C*H*$_2$CH$_2$OH), 1.92–1.80 (1H, m, 1H from CH_2), and 1.46 (3H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 138.1 (ArC), 128.4 (2 × ArCH), 127.6 (2 × ArCH), 127.5 (ArCH), 80.3 (C), 64.1 (Ph*C*H$_2$), 59.1 (CH_2O), 57.5 (SCHS), 38.6 (*C*H$_2$CH$_2$OH), 31.2 (CH_2S), 31.1 (CH_2S), 26.0 (CH_2), and 21.6 (CH_3); *m*/*z* (CI mode, isobutane) 299 (11%), 281 (6), 191 (62), 161 (26), 119 (12), and 85 (100) (Found: $(M + H)^+$, 299.1138. $C_{15}H_{23}O_2S_2$ requires *M*, 299.1139).

Ethyl (*E*)-5-(benzyloxy)-5-(1,3-dithian-2-yl)hex-2-enoate 3c. As for general procedure A. 3-(Benzyloxy)-3-(1,3-dithian-2-yl)butan-1-ol **2c** (371 mg, 1.31 mmol, 1 eq.), after oxidation and reaction with (ethoxycarbonylmethylene)triphenylphosphorane for 22 h, and purification by column chromatography (eluting with 20% EtOAc in hexane), gave **3c** (359 mg, 0.98 mmol, 75%) as a colourless oil: ν_{max} (soln. in $CHCl_3$)/cm^{-1} 2987s, 2892s, 1699s (C=O), 1654s, 1453m, 1374s, 1273s, and 1178s; δ_H (400 MHz, $CDCl_3$) 7.42–7.28 (5H, m, ArH × 5), 7.06 (1H, dt, *J* 15.5, 8.0, CH$_2$C*H*=), 5.95 (1H, d, *J* 15.5, =C*H*CO$_2$Et), 4.60 (AB system, 1H, d, *J* 10.8, 1H from PhC*H*$_2$), 4.57 (AB system, 1H, d, *J* 10.8, 1H from PhC*H*$_2$), 4.43 (1H, s, SCHS), 4.21 (2H, q, *J* 7.2, C*H*$_2$CH$_3$), 2.96–2.78 (4H, m, CH_2S × 2), 2.81 (1H, dd, *J* 14.7, 8.0, 1H from C*H*$_2$CH=), 2.71 (1H, dd, *J* 14.7, 8.0, 1H from C*H*$_2$CH=), 2.11 (1H, dt, *J* 11.0, 4.0, 1H from CH_2), 1.92–1.81 (1H, m, 1H from CH_2), 1.46 (3H, s, CH_3), and 1.28 (3H, t, *J* 7.2, CH$_2$C*H*$_3$); δ_C (100 MHz, $CDCl_3$) 166.2 (C=O), 143.8 (CH$_2$*C*H=), 138.5 (ArC), 128.2 (2 × ArCH), 127.4 (2 × ArCH), 127.3 (ArCH), 124.5 (=*C*HCO$_2$Et), 79.0 (C), 64.1 (Ph*C*H$_2$), 60.2 (*C*H$_2$CH$_3$), 57.1 (SCHS), 39.6 (*C*H$_2$CH=), 31.0 (CH_2S), 30.9 (CH_2S), 25.9 (CH_2), 21.7 (CH_3), and 14.2 (CH$_2$*C*H$_3$); *m*/*z* (CI mode, isobutane) 367 (32%), 309 (9), 259 (100), 153 (4), 107 (6), and 91 (10) (Found: $(M + H)^+$, 367.1401. $C_{19}H_{27}O_3S_2$ requires *M*, 367.1402) (Found: C, 62.12; H, 7.04. $C_{19}H_{26}O_3S_2$ requires C, 62.26; H, 7.15%).

Ethyl (*E*)-5-(benzyloxy)-5-methyl-6-oxohex-2-enoate 4c. As for general procedure B. Ethyl (*E*)-5-(benzyloxy)-5-(1,3-dithian-2-yl)hex-2-enoate **3c** (171 mg, 0.49 mmol, 1 eq.) gave aldehyde **4c** (124 mg, 0.47 mmol, 96%) as a pale yellow oil which was used without further purification: ν_{max} (soln. in

$CDCl_3$)/cm^{-1} 3019s, 2984m, 1735s (C=O), 1716s (C=O), 1657m, 1421m, and 1269s; δ_H (400 MHz, $CDCl_3$) 9.67 (1H, s, CHO), 7.37–7.30 (5H, m, ArH × 5), 6.96 (1H, dt, *J* 15.6, 7.6, CH_2CH=), 5.93 (1H, d, *J* 15.6, =$CHCO_2Et$), 4.51 (2H, apparent s, $PhCH_2$), 4.20 (2H, q, *J* 7.2, CH_2CH_3), 2.70 (1H, dd, *J* 15.0, 7.6, 1H from CH_2CH=), 2.56 (1H, dd, *J* 15.0, 7.6, 1H from CH_2CH=), 1.37 (3H, s, CH_3), and 1.30 (3H, t, *J* 7.2, CH_2CH_3); δ_C (100 MHz, $CDCl_3$) 203.6 (CHO), 165.9 (CO_2Et), 141.7 (CH_2CH=), 137.7 (ArC), 128.5 (2 × ArCH), 127.9 (2 × ArCH), 127.5 (ArCH), 125.3 (=$CHCO_2Et$), 82.0 (C), 66.6 ($PhCH_2$), 60.4 (CH_2CH_3), 37.5 (CH_2CH=), 18.7 (CH_3), and 14.2 (CH_3CH_2); *m*/*z* (CI mode, isobutane) 277 (100%), 247 (6), 187 (5), 169 (32), 157 (6), and 91 (26) (Found: $(M + H)^+$, 277.1442. $C_{16}H_{21}O_4$ requires *M*, 277.1440).

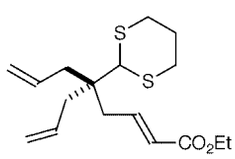
3,3-Diallyl-2,3,4,5-tetrahydrofuran-2-one[25] **5a.** To a solution of diisopropylamine (8.40 ml, 60.0 mmol, 1.2 eq.) in THF (70 ml) at −78 °C was added *n*-butyllithium (1.55 M in hexanes, 38.7 ml, 60.0 mmol, 1.2 eq.) dropwise. The solution was stirred at −78 °C for 40 min before the addition of γ-butyrolactone (3.84 ml, 50.0 mmol, 1 eq.) in THF (50 ml). The resulting solution was then stirred for 1 h. Neat allyl bromide (13.0 ml, 150 mmol, 3 eq.) was added and the solution allowed to warm gradually to −20 °C over 18 h. Aqueous saturated NH_4Cl (6 ml) and H_2O (2 ml) were then added and the aqueous layer separated and extracted with EtOAc (2 × 25 ml). The combined organic extracts were then dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by column chromatography (eluting with 40% EtOAc in hexane) gave 3-allyl-2,3,4,5-tetrahydrofuran-2-one (5.05 g, 40.0 mmol, 80%) as a pale yellow oil: δ_H (400 MHz, $CDCl_3$) 5.88–5.73 (1H, m, CH=), 5.20–5.11 (2H, m, $=CH_2$), 4.38–4.27 (1H, m, 1H from CH_2O), 4.24–4.19 (1H, m, 1H from CH_2), 2.69–2.60 (2H, m, CH_2CH=), 2.42–2.34 (1H, m, CH), 2.33–2.25 (1H, m, 1H from CH_2), and 2.07–1.96 (1H, m, 1H from CH_2).

To a solution of diisopropylamine (6.70 ml, 48.0 mmol, 1.2 eq.) in THF (50 ml) at −78 °C was added *n*-butyllithium (1.55 M in hexanes, 31.0 ml, 48.0 mmol, 1.2 eq.) dropwise. The solution was stirred at −78 °C for 1 h before the addition of 3-allyl-2,3,4,5-tetrahydrofuran-2-one (5.05 g, 40.0 mmol, 1 eq.) in THF (50 ml). The resulting solution was then stirred for 1 h. Neat allyl bromide (10.4 ml, 120 mmol, 3 eq.) was added dropwise and the solution allowed to warm gradually to −20 °C over 3 h. Aqueous saturated NH_4Cl (6 ml) and H_2O (3 ml) were then added and the aqueous layer separated and extracted with EtOAc (2 × 25 ml). The combined organic extracts were then dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by column chromatography (eluting with 10% EtOAc in hexane) gave 3,3-diallyl-2,3,4,5-tetrahydrofuran-2-one **5a** (5.05 g, 30.4 mmol, 76%) as a colourless oil: ν_{max} (film)/cm^{-1} 3078s, 2978s, 1768s (C=O), 1639m, 1439m, 1381m, 1186s, and 1028s; δ_H (400 MHz, $CDCl_3$) 5.82–5.71 (2H, m, 2 × -CH=), 5.19–5.14 (4H, m, 2 × CH_2=), 4.21 (2H, t, *J* 7.4, CH_2O), 2.43–2.38 (2H, m, 1H from each CH_2CH=), 2.35–2.27 (2H, m, 1H from each CH_2CH=), and 2.17 (2H, t, *J* 7.4, CH_2); δ_C (100 MHz, $CDCl_3$) 180.4 (C=O), 132.6 (2 × =CH), 119.6 (2 × CH_2=), 65.3 (CH_2O), 46.1 (C), 40.9 (2 × CH_2CH=), and 30.5 (CH_2); *m*/*z* (CI mode, isobutane) 167 (100%), 123 (5), and 81 (5) (Found: $(M + H)^+$, 167.1073. $C_{10}H_{15}O_2$ requires *M*, 167.1072).

3-Allyl-3-(1,3-dithian-2-yl)hex-5-en-1-ol 6a. To a solution of **5a** (1.18 g, 7.11 mmol, 1 eq.) in CH_2Cl_2 (18 ml) at −78 °C was added DIBAL-H (1.5 M in toluene, 5.68 ml, 8.53 mmol, 1.2 eq.) and the solution stirred at −78 °C for 1 h. The reaction mixture was then poured into a solution of K/Na tartrate (5.37 g, 21.3 mmol, 3 eq.) in CH_2Cl_2 (1.5 ml) and H_2O (1.5 ml), and the solution stirred for 1 h. The aqueous layer was then separated and extracted with CH_2Cl_2 (3 × 5 ml). The combined organic extracts were then dried (Na_2SO_4) and concentrated *in vacuo* to give the lactol (0.95 g, 5.66 mmol, 80%) as a colourless oil which was used without further purification: δ_H (400 MHz, $CDCl_3$) 5.91–5.77 (2H, m, 2 × =CH), 5.15–5.03 (5H, m, 2 × CH_2= and CHOH), 4.09 (1H, td, *J* 8.4, 3.5, 1H from CH_2O), 3.90 (1H, apparent q, *J* 8.4, 1H from CH_2O), 2.38–2.24 (3H, m, $=CHCH_2$ and OH), 2.16 (1H, dd, *J* 13.9, 7.3, 1H from $=CHCH_2$), 2.06 (1H, dd, *J* 13.9, 7.3, 1H from $=CHCH_2$), 1.91–1.84 (1H, m, 1H from CH_2), and 1.80–1.74 (1H, m, 1H from CH_2).

To a solution of the crude lactol (0.95 g, 5.66 mmol, 1 eq.) in CH_2Cl_2 (15 ml) was added propane-1,3-dithiol (0.68 ml, 6.79 mmol, 1.2 eq.) and powdered 4 Å molecular sieves. The resulting solution was then cooled to −15 °C before the dropwise addition of $BF_3{\cdot}Et_2O$ (0.72 ml, 5.66 mmol, 1 eq.) and gradual warming to 0 °C. Aqueous saturated $NaHCO_3$ (5 ml), H_2O (5 ml), and CH_2Cl_2 (15 ml) were then added and the aqueous layer separated and extracted with CH_2Cl_2 (2 × 10 ml). The combined organic extracts were then dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by column chromatography (eluting with 30% EtOAc in hexane) to give **6a** (0.76 g, 2.94 mmol, 52%) as a colourless oil: ν_{max} (neat)/cm^{-1} 3390br s, 2931s, 2892s, 1643m, 1419m, 1279m, 1033s, and 1005s; δ_H (400 MHz, $CDCl_3$) 5.95–5.84 (2H, m, 2 × CH=), 5.15–5.11 (4H, m, 2 × CH_2=), 4.13 (1H, s, SCHS), 3.82 (2H, t, *J* 7.0, CH_2OH), 2.92–2.85 (4H, m, 2 × CH_2S), 2.36–2.26 (4H, m, 2 × CH_2CH=), 2.14–2.07 (1H, m, 1H from SCH_2CH_2), 1.87–1.74 (1H, m, 1H from SCH_2CH_2), and 1.76 (2H, t, *J* 7.0, CH_2CH_2OH); δ_C (100 MHz, $CDCl_3$) 134.0 (2 × CH=), 118.5 (2 × CH_2=), 59.0 (SCHS), 58.8 (CH_2OH), 43.3 (C), 40.6 (2 × CH_2CH=), 38.9 (CH_2CH_2OH), 31.9 (2 × CH_2S), and 26.4 (CH_2); *m*/*z* (CI mode, isobutane) 259 (5%), 241 (10), 151 (100), and 119 (5) (Found: $(M + H)^+$, 259.1190. $C_{13}H_{23}OS_2$ requires *M*, 259.1190).

Ethyl (2*E*)-5-allyl-5-(1,3-dithian-2-yl)octa-2,7-dienoate.



As for general procedure A. 3-Allyl-3-(1,3-dithian-2-yl)hex-5-en-1-ol **6a** (438 mg, 1.70 mmol, 1 eq.), after oxidation and reaction with (ethoxycarbonylmethylene)triphenylphosphorane for 3 d, and purification by column chromatography (eluting with 15% EtOAc in hexane), gave ethyl (2*E*)-5-allyl-5-(1,3-dithian-2-yl)octa-2,7-dienoate (360 mg, 1.10 mmol, 65%) as a colourless oil: ν_{max} (neat)/cm^{-1} 2981m, 2931s, 2897s, 1721s, 1649m, 1436m, 1268s, and 1173m; δ_H (400 MHz, $CDCl_3$) 7.11 (1H, dt, *J* 15.5, 7.8, CH_2CH=), 5.97–5.88 (3H, m, =$CHCO_2Et$ and 2 × CH=), 5.18–5.11 (4H, m, 2 × $=CH_2$), 4.21 (2H, q, *J* 7.1, CH_2CH_3), 4.08 (1H, s, SCHS), 2.93–2.83 (4H, m, 2 × SCH_2), 2.44 (2H, dd, *J* 7.8, 1.3, CH_2CH=), 2.33 (4H, d, *J* 7.4, 2 × CH_2CH=), 2.14–2.07 (1H, m, 1H from CH_2), 1.90–1.80 (1H, m, 1H from CH_2), and 1.31 (3H, t, *J* 7.1, CH_3CH_2); δ_C (100 MHz, $CDCl_3$) 166.4 (C=O), 145.3 (CH_2CH=), 133.9 (2 × -CH=), 124.2 (=$CHCO_2Et$), 118.8 (2 × CH_2=), 60.2 (CH_2O), 59.1 (SCHS), 44.5 (C), 40.5 (2 × CH_2CH=), 38.7 (CH_2CH=), 32.0 (2 × SCH_2), 26.3 (CH_2), and 14.3 (CH_3); *m*/*z* (CI mode, isobutane) 327 (100%), 281 (19), 219 (7), 107 (5), and 81 (7) (Found: $(M + H)^+$, 327.1453. $C_{17}H_{27}O_2S_2$ requires *M*, 327.1452) (Found: C, 62.35; H, 8.13. $C_{17}H_{26}O_2S_2$ requires C, 62.53; H, 8.03%).

Ethyl (2*E*)-5-allyl-5-formylocta-2,7-dienoate 7a. As for general procedure B. Ethyl (2*E*)-5-allyl-5-(1,3-dithian-2-yl)-octa-2,7-dienoate (277 mg, 0.85 mmol, 1 eq.) gave aldehyde **7a** (192 mg, 0.81 mmol, 96%) as a pale yellow oil which was used without further purification: ν_{max} (neat)/cm^{-1} 3080m, 2984s,

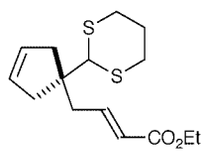
2903s, 2833m, 2727m, 1727s (C=O), 1652s, 1448s, 1363s, 1277s, 1224s, and 1170s; δ_H (400 MHz, $CDCl_3$) 9.54 (1H, s, CHO), 6.85 (1H, dt, *J* 15.6, 8.0, CH_2CH=), 5.89 (1H, dt, *J* 15.6, 1.2, =$CHCO_2Et$), 5.73–5.62 (2H, m, 2 × CH=), 5.16–5.11 (4H, m, 2 × CH_2=), 4.19 (2H, q, *J* 7.2, CH_2CH_3), 2.42 (2H, dd, *J* 8.0, 1.2, CH_2CH=), 2.37–2.26 (4H, m, 2 × CH_2CH=), and 1.29 (3H, t, *J* 7.2, CH_3CH_2); δ_C (100 MHz, $CDCl_3$) 204.5 (C=O), 165.9 (CO_2Et), 143.0 (CH_2CH=), 132.1 (2 × CH=), 125.1 (=$CHCO_2Et$), 119.5 (2 × CH_2=), 60.4 (CH_2CH_3), 52.0 (C), 37.2 (2 × CH_2CH=), 34.4 (CH_2CH=), and 14.2 (CH_3); *m*/*z* (CI mode, isobutane) 237 (100%), 191 (21), 163 (5), and 85 (12) (Found: $(M + H)^+$, 237.1490. $C_{14}H_{21}O_3$ requires *M*, 237.1491).

2-Oxaspiro[4.4]non-7-en-1-one 5b. To a solution of 3,3-diallyl-2,3,4,5-tetrahydrofuran-2-one **5a** (1.00 g, 6.02 mmol, 1 eq.) in $CHCl_2$ (40 ml) at room temperature was added $(PCy_3)_2Ru(Cl)_2$=CHPh (113 mg, 0.15 mmol, 0.025 eq.) and the solution heated under reflux for 5 h. After the reaction mixture had cooled, filtration through a short column of silica gel (eluting with 30% EtOAc in hexane), then through Celite, was followed by concentration *in vacuo*. Purification of the residue by column chromatography (eluting with 20% EtOAc in hexane) gave 2-oxaspiro[4.4]non-7-en-1-one **5b** (822 mg, 5.96 mmol, 99%) as a colourless oil: ν_{max} (soln. in $CHCl_3$)/cm^{-1} 3019s, 2919m, 1763s (C=O), 1440m, 1375m, 1228m, and 1181s; δ_H (400 MHz, $CDCl_3$) 5.69 (2H, br s, CH=CH), 4.29 (2H, t, *J* 6.8, CH_2O), 2.89 (2H, d, *J* 14.7, 1H from each CH_2CH=), 2.42 (2H, d, *J* 14.7, 1H from each CH_2CH=), and 2.24 (2H, t, *J* 6.8, CH_2); δ_C (100 MHz, $CDCl_3$) 182.3 (C=O), 128.1 (2 × CH=), 65.4 (CH_2O), 47.3 (C), 43.6 (2 × CH_2CH=), and 38.3 (CH_2); *m*/*z* (EI mode) 138 (24%), 110 (18), 94 (18), 83 (100), 79 (48), and 66 (36) (Found: M^+, 138.0678. $C_8H_{10}O_2$ requires *M*, 138.0681).

2-[1-(1,3-Dithian-2-yl)cyclopent-3-enyl]ethanol 6b. To a solution of **5b** (829 mg, 6.00 mmol, 1 eq.) in CH_2Cl_2 (12 ml) at −78 °C was added DIBAL-H (1.5 M in toluene, 4.80 ml, 7.20 mmol, 1.2 eq.) dropwise and the resulting solution stirred at −78 °C for 1 h. The reaction mixture was then poured into a solution of K/Na tartrate (4.54 g, 18.0 mmol, 3 eq.) in CH_2Cl_2 (2 ml) and H_2O (2 ml), and the mixture stirred for 1 h. The aqueous layer was separated and extracted with CH_2Cl_2 (2 × 5 ml). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to give 2-oxaspiro[4.4]non-7-en-1-ol (675 mg, 4.82 mmol, 80%) as a colourless oil which was used without further purification: δ_H (400 MHz, $CDCl_3$) 5.74–5.71 (1H, m, CH=), 5.66–5.62 (1H, m, CH=), 5.03 (1H, d, *J* 3.3, CHOH), 4.11 (1H, td, *J* 8.4, 2.3, 1H from CH_2O), 3.87 (1H, dt, *J* 8.4, 7.0, 1H from CH_2O), 2.79–2.74 (1H, m, 1H from CH_2CH), 2.58 (1H, d, *J* 3.3, OH), 2.36–2.21 (2H, m, 1H from each CH_2CH), 2.17–2.09 (2H, m, 1H from each CH_2), and 1.89 (1H, ddd, *J* 11.9, 7.0, 2.2, 1H from CH_2).

To a solution of the lactol (675 mg, 4.82 mmol, 1 eq.) in CH_2Cl_2 (10 ml) was added propane-1,3-dithiol (0.58 ml, 5.79 mmol, 1.2 eq.) and powdered 4 Å molecular sieves and the resulting solution cooled to −15 °C. $BF_3{\cdot}OEt_2$ (0.61 ml, 4.82 mmol, 1 eq.) was then added dropwise and the reaction mixture allowed to warm to 0 °C over 2 h. Aqueous saturated $NaHCO_3$ (6 ml) and H_2O (6 ml) were then added and the aqueous layer separated and extracted with CH_2Cl_2 (3 × 6 ml). The combined organic extracts were then dried (Na_2SO_4) and concentrated *in vacuo*. The residue was then purified by column chromatography (eluting with 30% EtOAc in hexane) to give **6b** (1.04 g, 4.52 mmol, 94%) as a colourless oil: ν_{max} (film)/cm^{-1} 3378br s (OH), 2896s, 2843m, 1416m, 1275m, and 1034s; δ_H (400 MHz, $CDCl_3$) 5.61 (2H, br s, CH=CH), 4.20 (1H, s, SCHS), 3.71 (2H, t, *J* 6.7, CH_2OH), 2.93–2.83 (4H, m, 2 × CH_2S), 2.75 (2H, d, *J* 14.3, 1H from each CH_2CH=), 2.24 (2H, d, *J* 14.3, 1H from each CH_2CH=), 2.14–2.07 (1H, m, 1H from CH_2), 1.93 (2H, t, *J* 6.7, CH_2CH_2OH), and 1.89–1.75 (1H, m, 1H from CH_2); δ_C (100 MHz, $CDCl_3$) 128.9 (2 × CH=), 60.0 (CH), 59.9 (CH_2OH), 48.0 (C), 42.9 (2 × CH_2CH=), 41.4 (CH_2), 31.2 (2 × CH_2S), and 26.0 (CH_2); *m*/*z* (CI mode, isobutane) 231 (5%), 213 (10), 123 (100), and 119 (8) (Found: $(M + H)^+$, 231.0876. $C_{11}H_{19}OS_2$ requires *M*, 231.0877) (Found: C, 57.50; H, 7.92. $C_{11}H_{18}OS_2$ requires C, 57.34; H, 7.87%).

Ethyl (*E*)-4-[1-(1,3-dithian-2-yl)cyclopent-3-enyl]but-2-enoate.



As for general procedure A. 2-[1-(1,3-Dithian-2-yl)cyclopent-3-enyl]ethanol **6b** (1.02 g, 4.43 mmol, 1 eq.), after oxidation and reaction with (ethoxycarbonylmethylene)triphenylphosphorane for 16 h, and purification by column chromatography (eluting with 15% EtOAc in hexane), gave ethyl (*E*)-4-[1-(1,3-dithian-2-yl)cyclopent-3-enyl]but-2-enoate (912 mg, 3.06 mmol, 69%) as a colourless oil: ν_{max} (film)/cm^{-1} 2984m, 2895s, 2849m, 1721s (C=O), 1651s, 1428m, 1269s, and 1169s; δ_H (400 MHz, $CDCl_3$) 6.94 (1H, dt, *J* 15.4, 7.7, CH_2CH=), 5.93 (1H, d, *J* 15.4, CH=), 5.60 (2H, br s, CH=CH), 4.20 (2H, q, *J* 7.2, CH_2CH_3), 4.13 (1H, s, SCHS), 2.94–2.85 (4H, m, 2 × CH_2S), 2.79 (2H, d, *J* 14.9, 1H from each CH_2CH=), 2.51 (2H, d, *J* 7.7, CH_2CH=$CHCO_2Et$), 2.20 (2H, d, *J* 14.9, 1H from each CH_2CH=), 2.10 (1H, dt, *J* 10.4, 3.4, 1H from CH_2), 1.88–1.77 (1H, m, 1H from CH_2), and 1.31 (3H, t, *J* 7.2, CH_2CH_3); δ_C (100 MHz, $CDCl_3$) 166.4 (C=O), 145.0 (CH_2CH=), 128.8 (2 × CH=), 124.0 (=CH), 60.2 (OCH_2), 59.2 (CH), 48.7 (C), 42.0 (2 × CH_2CH=), 41.1 (CH_2CH=), 31.1 (2 × CH_2S), 25.9 (CH_2), and 14.2 (CH_3); *m*/*z* (EI mode) 298 (12%), 253 (6), 185 (17), and 119 (100) (Found: M^+, 298.1060. $C_{15}H_{22}O_2S_2$ requires *M*, 298.1061) (Found: C, 60.12; H, 7.23. $C_{15}H_{22}O_2S_2$ requires C, 60.36; H, 7.43%).

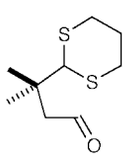
Ethyl (*E*)-4-(1-formylcyclopent-3-enyl)but-2-enoate 7b. As for general procedure B. Ethyl (*E*)-4-[1-(1,3-dithian-2-yl)cyclopent-3-enyl]but-2-enoate (300 mg, 1.01 mmol, 1 eq.) gave **7b** (195 mg, 0.94 mmol, 93%) which was used without further purification: ν_{max} (soln. in $CHCl_3$)/cm^{-1} 3019s, 1721s (C=O), 1657m, 1440m, 1275m, 1222s, and 1034m; δ_H (400 MHz, $CDCl_3$) 9.55 (1H, s, CHO), 6.83 (1H, dt, *J* 15.3, 7.5, CH_2CH=), 5.87 (1H, dt, *J* 15.3, 1.4, =$CHCO_2Et$), 5.66 (2H, br s, CH=CH), 4.18 (2H, q, *J* 7.1, CH_2CH_3), 2.74 (2H, d, *J* 14.4, 1H from each CH_2CH=), 2.55 (2H, dd, *J* 7.5, 1.4, CH_2CH=$CHCO_2Et$), 2.31 (2H, d, *J* 14.4, 1H from each CH_2CH=), and 1.29 (3H, q, *J* 7.1, CH_2CH_3); δ_C (100 MHz, $CDCl_3$) 202.6 (CHO), 166.0 (C=O), 143.9 (CH_2CH=$CHCO_2Et$), 128.6 (2 × CH=), 124.4 (=$CHCO_2Et$), 60.3 (OCH_2), 55.7 (C), 39.0 (2 × CH_2CH=), 37.5 (CH_2CH=), and 14.6 (CH_3); *m*/*z* (CI mode, isobutane) 209 (100%), 163 (12), 85 (5) and 69 (7) (Found: $(M + H)^+$, 209.1178. $C_{12}H_{17}O_3$ requires *M*, 209.1178).

2-[(*E*)-1,1-Dimethyl-3-(2-oxotetrahydrofuran-3-ylidene)-propyl]-1,3-dithiane 8. As for general procedure A. 3-(1,3-Dithian-2-yl)3-methylbutan-1-ol **2a** (481 mg, 2.33 mmol, 1 eq.), after oxidation and reaction with (1-butyrolactonylidene)-triphenylphosphorane[12] for 27 h, and purification by column chromatography (eluting with 30% EtOAc in hexane), gave **8** (603 mg, 2.21 mmol, 84%) as a 4:1 mixture of (*E*) and (*Z*) isomers: ν_{max} (neat)/cm^{-1} 2965s, 2929s, 2828m, 1755s (C=O), 1679s, 1483m, 1465s, 1422s, 1387s, 1368s, 1216s, and 1034s; *m*/*z* (EI mode) 272 (10%), 161 (35), 119 (100), 112 (5), 83 (5), and 41 (5) (Found: M^+, 272.0905. $C_{13}H_{20}S_2O_2$ requires *M*, 272.0900). The isomers were isolated by further chromatography (eluting with CH_2Cl_2): (*E*) isomer; δ_H (400 MHz, $CDCl_3$) 6.82 (1H, tt,

J 7.8, 2.9, CH_2CH=), 4.38 (2H, t, *J* 7.4, CH_2CH_2O), 4.03 (1H, s, SCHS), 2.96–2.88 (6H, m, 2H from CH_2CH_2O and 4H from 2 × SCH_2), 2.39 (2H, d, *J* 7.8, CH_2CH=), 2.13–2.06 (1H, m, 1H from SCH_2CH_2), 1.86–1.77 (1H, m, 1H from SCH_2CH_2), and 1.17 (6H, s, 2 × Me); δ_C (100 MHz, $CDCl_3$) 171.3 (C=O), 136.8 (CH_2CH=), 127.9 (CH=*C*), 65.7 (CH_2CH_2O), 60.2 (SCHS), 41.1 (CH_2CH=), 39.7 (C), 31.5 (2 × SCH_2), 26.1 (SCH_2CH_2), 25.7 (CH_2CH_2O), and 25.7 (2 × CH_3): (*Z*) isomer; δ_H (400 MHz, $CDCl_3$) 6.38–6.33 (1H, m, CH_2CH=), 4.32 (2H, t, *J* 7.4, CH_2O), 4.06 (1H, s, SCHS), 2.99–2.94 (4H, m, 2H from CH_2CH_2O and 2H from CH_2CH=), 2.91–2.88 (4H, m, 2 × SCH_2), 2.13–2.06 (1H, m, 1H from SCH_2CH_2), 1.88–1.77 (1H, m, 1H from SCH_2CH_2), and 1.13 (6H, s, 2 × Me); δ_C (100 MHz, $CDCl_3$) 170.0 (C=O), 140.0 (CH_2CH=), 125.9 (CH=*C*), 65.4 (CH_2O), 60.7 (SCHS), 39.6 (C), 37.4 (CH_2CH=), 31.6 (2 × SCH_2), 29.7 (CH_2CH_2O), 26.2 (SCH_2CH_2), and 25.3 (2 × Me).

(*E*)-2,2-Dimethyl-4-[2-oxotetrahydrofuran-3-ylidene]butanal 9. As for general procedure B. 2-[(*E*)-1,1-Dimethyl-3-(2-oxotetrahydrofuran-3-ylidene)propyl]-1,3-dithiane **8** (117 mg, 0.43 mmol, 1 eq.) gave the aldehyde **9** (80 mg, 0.43 mmol, 99%) as a clear yellow oil which was used without further purification: ν_{max} (neat)/cm^{-1} 2969s, 2930s, 2873s, 2816m, 2712m, 1752s, 1725s, 1681s, 1366m, 1354m, 1214s, and 1034s; δ_H (400 MHz, $CDCl_3$) 9.49 (1H, s, CHO), 6.71 (1H, tt, *J* 7.9, 3.0, CH_2CH=), 4.39 (2H, t, *J* 7.4, CH_2CH_2O), 2.92–2.87 (2H, m, CH_2CH_2O), 2.35 (2H, d, *J* 7.9, CH_2CH=), and 1.15 (6H, s, 2 × Me); δ_C (100 MHz, $CDCl_3$) 204.6 (CHO), 170.9 (C=O), 135.4 (CH_2CH=), 128.3 (CH=*C*), 65.6 (CH_2CH_2O), 46.5 (C), 37.2 (CH_2CH=), 25.4 (CH_2CH_2O), 21.7 (2 × Me); *m*/*z* (CI mode, isobutane) 183 (100%), 169 (3), 165 (2), 154 (2), 121 (1), and 99 (1) (Found: $(M + H)^+$, 183.1019. $C_{10}H_{15}O_3$ requires *M*, 183.1017).

3-(1,3-Dithian-2-yl)-3-methylbutan-1-al.

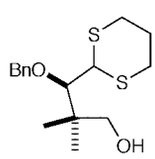


To a solution of 3-(1,3-dithian-2-yl)-3-methylbutan-1-ol **2a** (300 mg, 1.45 mmol, 1 eq.) in CH_2Cl_2 (15 ml) at 0 °C was added DMSO (1.03 ml, 14.5 mmol, 10 eq.) and triethylamine (0.99 ml, 9.59 mmol, 6.6 eq.). After 5 min, pyridine–sulfur trioxide complex (879 mg, 5.52 mmol, 3.8 eq.) was added and the reaction mixture stirred for 4.5 h. Aqueous saturated $NaHCO_3$ (2 ml) was then added and the aqueous layer separated and extracted with CH_2Cl_2 (3 × 25 ml). The combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo*. The residue was then purified by column chromatography (eluting with 20% EtOAc in hexane) to give 3-(1,3-dithian-2-yl)-3-methylbutan-1-al (218 mg, 1.06 mmol, 72%) as a clear colourless oil: ν_{max} (neat)/cm^{-1} 2963s, 2931s, 2900s, 2829m, 2734m, 1718s (C=O), 1389m, 1369m, 1046m, and 907m; δ_H (400 MHz, $CDCl_3$) 9.86 (1H, d, *J* 2.0, CHO), 4.24 (1H, s, SCHS), 2.94–2.89 (4H, m, 2 × SCH_2), 2.60 (2H, d, *J* 2.0, CH_2CHO), 2.13–2.08 (1H, m, 1H from SCH_2CH_2), 1.88–1.76 (1H, m, 1H from SCH_2CH_2), and 1.27 (6H, s, 2 × CH_3); δ_C (100 MHz, $CDCl_3$) 201.9 (CHO), 60.1 (SCHS), 53.1 (CH_2CHO), 38.7 (Me), 31.5 (2 × SCH_2), 26.1 (CH_2), and 26.0 (2 × CH_3); *m*/*z* (EI mode) 204 (11%), 160 (89), 145 (8), 119 (100), 85 (12), 59 (8), and 41 (23) (Found: M^+, 204.0643. $C_9H_{16}OS_2$ requires *M*, 204.0639).

2-[(*E*)-(1,1-Dimethyl-4-phenylsulfonylbut-3-enyl)]-1,3-dithiane 10. To a stirred solution of $MeSO_2Ph$ (321 mg, 2.05 mmol, 2 eq.) in THF (16 ml) at 0 °C was added *n*-butyllithium (1.55 M in hexane, 2.92 ml, 4.52 mmol, 4.4 eq.) and the mixture left for 30 min before the dropwise addition of a solution of diethylchlorophosphate (0.30 ml, 2.05 mmol, 2 eq.) in THF (4 ml). The reaction was stirred for a further 30 min before being cooled to −78 °C and a solution of the 3-(1,3-dithian-2-yl)-3-methylbutan-1-al (210 mg, 1.03 mmol, 1 eq.) in THF (4 ml) was added. After a further 1 h, the reaction mixture was allowed to warm to room temperature and stirred for 12 h. Aqueous saturated $NaHCO_3$ (1 ml) was added and the aqueous layer separated and extracted with CH_2Cl_2 (3 × 10 ml). The combined organic extracts were then dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by column chromatography (eluting with 20% EtOAc in hexane) to give vinyl sulfone **10** (244 mg, 0.71 mmol, 69%) as a pale yellow oil: ν_{max} (neat)/cm^{-1} 3023s, 2968m, 2903m, 1631m (C=C), 1526m, 1451m, 1426m, 1321s (SO_2), 1226s, 1201s, 1146s (SO_2), and 1086s; δ_H (400 MHz, $CDCl_3$) 7.91 (2H, d, *J* 7.7, 2 × ArH), 7.64–7.54 (3H, m, 3 × ArH), 7.00 (1H, dt, *J* 14.9, 8.0, CH=$CHSO_2Ph$), 6.45 (1H, d, *J* 14.9, =$CHSO_2Ph$), 3.85 (1H, s, SCHS), 2.87–2.72 (4H, m, 2 × SCH_2), 2.40 (2H, d, *J* 8.0, CH_2CH=), 2.07–2.01 (1H, m, 1H from CH_2), 1.81–1.71 (1H, m, 1H from CH_2), and 1.13 (6H, s, 2 × Me); δ_C (100 MHz, $CDCl_3$) 143.0 (*C*H=$CHSO_2Ph$), 141.1 (ArC), 133.6 (CH=*C*HSO_2Ph), 133.5 (ArCH), 129.5 (2 × ArCH), 127.8 (2 × ArCH), 60.1 (SCHS), 42.1 (CH_2CH=), 39.4 (C), 31.4 (2 × SCH_2), 26.0 (CH_2), and 25.7 (2 × Me); *m*/*z* (CI mode, isobutane) 343 (100%), 271 (9), 237 (15), 201 (12), and 119 (5) (Found: $(M + H)^+$, 343.0860. $C_{16}H_{23}O_2S_3$ requires *M*, 343.0855).

(*E*)-2,2-Dimethyl-5-phenylsulfonylpent-4-enal 11. As for general procedure B. (*E*)-2-(1,1-Dimethyl-4-phenylsulfonylbut-3-enyl)-1,3-dithiane **10** gave aldehyde **11** (181 mg, 0.72 mmol, 100%) as a clear pale yellow oil which was used without further purification: ν_{max} (neat)/cm^{-1} 3049w, 2968m, 2932m, 2873m, 2813w, 2713w, 1725s (C=O), 1632m (C=C), 1379w, 1368w, 1317s (SO_2), 1147s (SO_2), 1086s, and 750s; δ_H (400 MHz, $CDCl_3$) 9.46 (1H, s, CHO), 7.88 (2H, d, *J* 7.9, 2 × ArH), 7.65–7.62 (1H, m, ArH), 7.58–7.54 (2H, m, 2 × ArH), 6.91 (1H, dt, *J* 15.0, 7.8, CH_2CH=), 6.39 (1H, d, *J* 15.0, =$CHSO_2Ph$), 2.39 (2H, d, *J* 7.8, CH_2CH=), and 1.11 (6H, s, 2 × Me); δ_C (100 MHz, $CDCl_3$) 204.0 (CHO), 142.1 (CH_2CH=), 140.5 (ArC), 133.8 (=$CHSO_2Ph$), 133.6 (ArCH), 129.5 (2 × ArCH), 127.8 (2 × ArCH), 46.0 (C), 38.4 (CH_2), and 21.7 (2 × Me); *m*/*z* (CI mode, isobutane) 253 (100%), 183 (6), 111 (4), 81 (3), and 69 (3) (Found: $(M + H)^+$, 253.0898. $C_{13}H_{17}SO_3$ requires *M*, 253.0894).

(3*R*)-3-(Benzyloxy)-2,2-dimethyl-3-(1,3-dithian-2-yl)propan-1-ol.



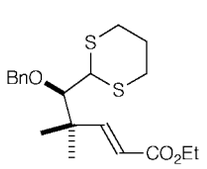
To a solution of (3*R*)-3-(benzyloxy)-4,5-dihydro-4,4-dimethylfuran-2(3*H*)-one[7] (800 mg, 3.62 mmol, 1 eq.) in CH_2Cl_2 (10 ml) at −78 °C was added DIBAL-H (1.5 M in toluene, 2.90 ml, 4.34 mmol, 1.2 eq.) and the solution stirred for 1 h. The reaction mixture was then poured into a solution of K/Na tartrate (2.74 g, 10.9 mmol, 3 eq.) in CH_2Cl_2 (3 ml) and H_2O (3 ml). After stirring for 1 h, the aqueous layer was separated and extracted with CH_2Cl_2 (3 × 5 ml). The combined organic extracts were then dried (Na_2SO_4) and concentrated *in vacuo* to give the crude lactol (646 mg, 2.90 mmol, 80%) as a crystalline solid which was used without further purification: δ_H (400 MHz, $CDCl_3$) 7.37–7.28 (5H, m, ArH), 5.38 (1H, dd, *J* 3.8, 2.9, $CHOH$), 4.71 (1H, d, *J* 12.0, 1H from $PhCH_2$), 4.59 (1H, d, *J* 12.0, 1H from $PhCH_2$), 3.82 (1H, d, *J* 8.4, 1H from CH_2O),

3.64 (1H, d, *J* 8.4, 1H from CH_2O), 3.52 (1H, d, *J* 2.9, C*H*OBn), 3.10 (1H, d, *J* 3.8, OH), 1.11 (3H, s, Me), and 1.10 (3H, s, Me).

To a solution of the crude lactol (646 mg, 2.90 mmol, 1 eq.) in CH_2Cl_2 (4 ml) at −10 °C was added 4 Å molecular sieves and propane-1,3-dithiol (0.40 ml, 3.98 mmol, 1.2 eq.). Trifluoromethanesulfonic acid (0.10 ml) was then added dropwise and the resulting solution allowed to warm to room temperature and stirred for 60 h. Aqueous saturated $NaHCO_3$ (4 ml) was then added and the aqueous layer separated and extracted with CH_2Cl_2 (3 × 5 ml). The combined organic extracts were then dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by column chromatography (eluting with 20% EtOAc in hexane) gave (3*R*)-3-(benzyloxy)-2,2-dimethyl-3-(1,3-dithian-2-yl)propan-1-ol (724 mg, 2.32 mmol, 80%) as a colourless oil: $[a]_D$ +34.9 (*c* 1.05, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3448br s, 2961s, 2890s, 1475m, 1451m, 1422m, 1269m, and 1099s; δ_H (400 MHz, $CDCl_3$) 7.36–7.26 (5H, m, 5 × ArH), 5.12 (1H, d, *J* 11.2, 1H from PhCH_2), 4.57 (1H, d, *J* 11.2, 1H from PhCH_2), 4.57 (1H, d, *J* 1.6, SCHS), 3.48–3.40 (2H, m, CH_2OH), 3.27 (1H, d, *J* 1.6, C*H*OBn), 3.04 (1H, td, *J* 12.8, 2.4, 1H from $^{A}CH_2S$), 2.96 (1H, td, *J* 12.0, 2.0, 1H from $^{B}CH_2S$), 2.86–2.80 (2H, m, 1H from each CH_2S), 2.46 (1H, t, *J* 6.4, OH), 2.15 (1H, dm, *J* 14.0, 1H from CH_2), 1.91 (1H, qm, *J* 14.0, 1H from CH_2), 1.00 (3H, s, Me), and 0.95 (3H, s, Me); δ_C (100 MHz, $CDCl_3$) 137.7 (ArC), 128.4 (ArCH × 2), 128.3 (ArCH × 2), 127.8 (ArCH), 87.9 (*C*HOBn), 74.5 (Ph*C*H_2), 69.4 (*C*H_2OH), 51.2 (SCHS), 40.6 (C), 32.9 ($S^{A}CH_2$), 30.7 ($S^{B}CH_2$), 26.3 (CH_2), 23.1 (Me), and 20.7 (Me); *m*/*z* (EI mode) 312 (5%), 193 (32), 119 (64), 91 (100), 83 (7), and 57 (8) (Found: C, 61.28; H, 7.63. $C_{16}H_{24}O_2S_2$ requires C, 61.50; H, 7.74%).

(3*R*)-3-(Benzyloxy)-2,2-dimethyl-3-(1,3-dithian-2-yl)propan-1-al[7] **12.** To a solution of (3*R*)-3-(benzyloxy)-2,2-dimethyl-3-(1,3-dithian-2-yl)propan-1-ol (477 mg, 1.53 mmol, 1 eq.) in CH_2Cl_2 (10 ml) at 0 °C was added DMSO (1.08 ml, 15.3 mmol, 10 eq.) and NEt_3 (1.04 ml, 10.1 mmol, 6.6 eq.) and the resulting solution stirred at 0 °C for 5 min. Pyridine–sulfur trioxide complex (922 mg, 5.80 mmol, 3.8 eq.) was then added and the solution stirred at 0 °C for 30 min, then at room temperature for 3 h. Aqueous saturated $NaHCO_3$ (5 ml) and H_2O (5 ml) were added and the aqueous layer separated and extracted with CH_2Cl_2 (3 × 5 ml). The combined organic extracts were then dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by column chromatography (eluting with 10% EtOAc in hexane) gave the aldehyde **12** (420 mg, 1.36 mmol, 89%) as a colourless oil: $[a]_D$ +31.7 (*c* 1.10, $CHCl_3$); ν_{max} (soln. in $CHCl_3$)/cm^{-1} 3025s, 2902m, 1721s, 1692m, 1528m, 1469m, and 1422m; δ_H (400 MHz, $CDCl_3$) 9.58 (1H, s, CHO), 7.41–7.27 (5H, m, 5 × ArH), 5.09 (1H, d, *J* 11.2, 1H from PhCH_2), 4.62 (1H, d, *J* 11.2, 1H from PhCH_2), 4.09 (1H, d, *J* 4.4, SCHS), 3.76 (1H, d, *J* 4.4, C*H*OBn), 2.88 (1H, ddd, *J* 14.0, 6.4, 2.8, 1H from SCH_2), 2.82–2.74 (3H, m, 1H from SCH_2 and SCH_2), 2.12–2.06 (1H, m, 1H from CH_2), 2.00–1.95 (1H, m, 1H from CH_2), 1.18 (3H, s, Me), and 1.14 (3H, s, Me); δ_C (100 MHz, $CDCl_3$) 203.2 (CHO), 137.7 (ArC), 128.3 (ArCH × 2), 128.0 (ArCH × 2), 127.7 (ArCH), 85.1 (*C*HOBn), 75.1 (*C*H_2Ph), 51.0 (C), 48.6 (SCHS), 30.2 (SCH_2), 28.8 (SCH_2), 25.6 (CH_2), 20.0 (Me), and 18.7 (Me); *m*/*z* (CI mode, isobutane) 311 (100%), 239 (11), 203 (9), 197 (8), 119 (6), and 91 (3) (Found: C, 61.93; H, 7.08. $C_{16}H_{22}O_2S_2$ requires C, 61.90; H, 7.14%).

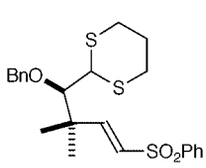
Ethyl (*E*,5*R*)-5-(benzyloxy)-4,4-dimethyl-5-(1,3-dithian-2-yl)-pent-2-enoate.[7]



To a solution of **12** (360 mg, 1.16 mmol, 1 eq.) in CH_2Cl_2 (8 ml) at room temperature was added (ethoxycarbonyl)triphenylphosphorane (1.21 g, 3.48 mmol, 3 eq.) and the solution stirred at room temperature for 4 days. Aqueous saturated $NaHCO_3$ (5 ml) was then added and the aqueous layer separated and extracted with CH_2Cl_2 (2 × 5 ml). The combined organic extracts were then dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by column chromatography (eluting with 10% EtOAc in hexane) gave recovered aldehyde **12** (72.0 mg, 0.23 mmol, 20%), and ethyl (*E*,5*R*)-5-(benzyloxy)-4,4-dimethyl-5-(1,3-dithian-2-yl)pent-2-enoate (287 mg, 0.75 mmol, 65%) as a colourless oil: $[a]_D$ +28.0 (*c* 1.00, $CHCl_3$); ν_{max} (soln. in $CHCl_3$)/cm^{-1} 3017s, 2899m, 1711s, 1648m, 1423m, and 1310s; δ_H (400 MHz, $CDCl_3$) 7.35–7.18 (5H, m, 5 × ArH), 6.97 (1H, d, *J* 16.0, C*H*=CHCO$_2$Et), 5.75 (1H, d, *J* 16.0, CH=C*H*CO$_2$Et), 5.00 (1H, d, *J* 11.4, 1H from PhCH_2), 4.50 (1H, d, *J* 11.4, 1H from PhCH_2), 4.25 (1H, d, *J* 2.1, SCHS), 4.12 (2H, q, *J* 7.1, CH_2CH$_3$), 3.14 (1H, d, *J* 2.1, C*H*OBn), 2.88 (1H, td, *J* 12.6, 2.4, 1H from SCH_2), 2.81–2.64 (3H, m, 1H from SCH_2 and SCH_2), 2.04–1.97 (1H, m, 1H from CH_2), 1.84–1.72 (1H, m, 1H from CH_2), 1.21 (3H, t, *J* 7.1, CH_2CH_3), 1.06 (3H, s, Me), and 1.03 (3H, s, Me); δ_C (100 MHz, $CDCl_3$) 166.6 (C=O), 154.4 (*C*H=CHCO$_2$Et), 137.6 (ArC), 128.1 (ArCH), 128.1 (ArCH), 128.0 (ArCH), 127.6 (ArCH), 127.5 (ArCH), 119.1 (CH=*C*HCO$_2$Et), 87.1 (*C*HOBn), 74.4 (Ph*C*H_2), 60.1 (*C*H_2CH$_3$), 51.2 (SCHS), 42.8 (C), 32.5 (CH_2S), 30.4 (CH_2S), 26.1 (CH_2), 24.1 (CH_3), 22.5 (CH_3), and 14.2 (CH_2*C*H_3); *m*/*z* (CI mode, isobutane) 381 (100%), 261 (12), 239 (5), 197 (32), 119 (12), and 91 (9) (Found: $(M + H)^+$, 381.1559. $C_{20}H_{29}O_3S_2$ requires *M*, 381.1558).

Ethyl (*E*,5*R*)-5-(benzyloxy)-4,4-dimethyl-6-oxohex-2-enoate[7] **13.** As for general procedure B. Ethyl (*E*,5*R*)-5-(benzyloxy)-4,4-dimethyl-5-(1,3-dithian-2-yl)pent-2-enoate (200 mg, 0.53 mmol, 1 eq.) gave aldehyde **13** (146 mg, 0.50 mmol, 95%) as a pale yellow oil which was used without further purification: $[a]_D$ +16.6 (*c* 1.00, $CHCl_3$); ν_{max} (soln. in $CHCl_3$)/cm^{-1} 3017s, 1726s, 1520m, 1310m, and 1100m; δ_H (400 MHz, $CDCl_3$) 9.61 (1H, d, *J* 3.4, CHO), 7.36–7.31 (5H, m, 5 × ArH), 7.07 (1H, d, *J* 16.0, C*H*=CHCO$_2$Et), 5.80 (1H, d, *J* 16.0, CH=C*H*CO$_2$Et), 4.68 (1H, d, *J* 11.6, 1H from PhCH_2), 4.46 (1H, d, *J* 11.6, 1H from PhCH_2), 4.20 (2H, q, *J* 7.2, CH_2CH$_3$), 3.44 (1H, d, *J* 3.4, C*H*OBn), 1.30 (3H, t, *J* 7.2, CH_2CH_3), and 1.16 (6H, s, 2 × Me); δ_C (100 MHz, $CDCl_3$) 203.2 (CHO), 166.5 (*C*O$_2$Et), 152.5 (*C*H=CHCO$_2$Et), 136.9 (ArC), 128.5 (2 × ArCH), 128.1 (ArCH), 128.0 (2 × ArCH), 120.1 (CH=*C*HCO$_2$Et), 88.5 (CHOBn), 73.1 (Ph*C*H_2), 60.4 (*C*H_2CH$_3$), 40.7 (C), 23.3 (Me), 22.7 (Me), and 14.2 (CH_2*C*H_3); *m*/*z* (CI mode, isobutane) 291 (100%), 261 (8), 245 (11), 171 (8), and 91 (42) (Found: $(M + H)^+$, 291.1596. $C_{17}H_{23}O_4$ requires *M*, 291.1596).

2-[(*E*,1*R*)-1-(Benzyloxy)-2,2-dimethyl-4-(phenylsulfonyl)but-3-enyl]-1,3-dithiane.



To a solution of methyl phenyl sulfone (24.0 mg, 0.15 mmol, 1 eq.) in THF (1 ml) at 0 °C was added *n*-butyllithium (1.55 M in hexanes, 0.22 ml, 0.33 mmol, 2.2 eq.) and the solution stirred at 0 °C for 30 min. A solution of diethylchlorophosphate (0.02 ml, 0.15 mmol, 1 eq.) in THF (1 ml) was then added dropwise and the resulting solution stirred for 30 min at 0 °C, then cooled to −78 °C. Aldehyde **12** (47.0 mg, 0.15 mmol, 1 eq.) was then added as a solution in THF (1 ml) and the reaction allowed to warm to room temperature over 12 h. Aqueous saturated $NaHCO_3$ (2 ml) and H_2O (2 ml) were then added and the aqueous layer separated and extracted with

CH_2Cl_2 (3 × 5 ml). The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by column chromatography (eluting with 30% EtOAc in hexane) to give recovered aldehyde **12** (7.4 mg, 0.02 mmol, 16%) and 2-[(*E*,1*R*)-1-(benzyloxy)-2,2-dimethyl-4-(phenylsulfonyl)-but-3-enyl]-1,3-dithiane (45 mg, 0.10 mmol, 67%) as a colourless oil: $[\alpha]_D$ +63.5 (*c* 0.6, $CHCl_3$); ν_{max} (soln. in $CHCl_3$)/cm^{-1} 3019s, 1522m, 1474w, 1416m, 1322w, and 1152m; δ_H (400 MHz, $CDCl_3$) 7.91 (2H, apparent d, *J* 7.9, 2 × ArH), 7.60–7.56 (1H, m, ArH), 7.50–7.46 (2H, m, 2 × ArH), 7.39–7.28 (5H, m, $C_6H_5CH_2$), 7.14 (1H, d, *J* 15.4, C*H*=CHSO$_2$Ph), 6.30 (1H, d, *J* 15.4, CH=C*H*SO$_2$Ph), 5.09 (1H, d, *J* 11.3, 1H from PhCH_2), 4.53 (1H, d, *J* 11.3, 1H from PhCH_2), 4.21 (1H, d, *J* 2.2, SCHS), 3.24 (1H, d, *J* 2.2, C*H*OBn), 2.88–2.61 (4H, m, CH_2S × 2), 2.10–1.95 (1H, m, 1H from CH_2), 1.89–1.82 (1H, m, 1H from CH_2), 1.14 (3H, s, Me), and 1.13 (3H, s, Me); δ_C (100 MHz, $CDCl_3$) 152.3 (*C*H=CHSO$_2$Ph), 140.6 (ArC), 137.5 (ArC), 133.1 (ArCH), 129.1 (2 × ArCH), 128.6 (CH=*C*HSO$_2$Ph), 128.2 (2 × ArCH), 128.0 (2 × ArCH), 127.7 (2 × ArCH), 127.7 (ArCH), 87.3 (*C*HOBn), 74.6 (Ph*C*H_2), 51.1 (SCHS), 43.1 (C), 32.5 (SCH_2), 30.48 (SCH_2), 26.0 (CH_2), 23.6 (CH_3), and 23.4 (CH_3); *m*/*z* (CI mode, isobutane) 449 (100%), 307 (9), 197 (34), 165 (8), 147 (4), and 119 (22) (Found: $(M + H)^+$, 449.1278. $C_{23}H_{29}O_3S_3$ requires *M*, 449.1279).

(*E*,2*R*)-2-(Benzyloxy)-3,3-dimethyl-5-(phenylsulfonyl)pent-4-enal 14. As for general procedure B. 2-[(*E*,1*R*)-1-(Benzyloxy)-2,2-dimethyl-4-(phenylsulfonyl)but-3-enyl]-1,3-dithiane (128 mg, 0.29 mmol, 1 eq.) gave aldehyde **14** (100 mg, 0.28 mmol, 98%) as a colourless oil which was used without further purification: $[\alpha]_D$ +39.7 (*c* 1.2, $CHCl_3$); ν_{max} (soln. in $CHCl_3$)/cm^{-1} 3010s, 1733s (C=O), 1516m, 1445m, 1422m, 1310m, and 1263s; δ_H (400 MHz, $CDCl_3$) 9.49 (1H, d, *J* 3.3, CHO), 7.78 (2H, d, *J* 8.3, 2 × ArH), 7.55–7.51 (1H, m, ArH), 7.45–7.42 (2H, m, 2 × ArH), 7.30–7.19 (5H, m, $C_6H_5CH_2$), 7.02 (1H, d, *J* 15.4, C*H*=CHSO$_2$Ph), 6.20 (1H, d, *J* 15.4, CH=C*H*SO$_2$Ph), 4.57 (1H, d, *J* 11.7, 1H from PhCH_2), 4.37 (1H, d, *J* 11.7, 1H from PhCH_2), 3.37 (1H, d, *J* 3.3, C*H*OBn), and 1.07 (6H, s, 2 × Me); δ_C (100 MHz, $CDCl_3$) 202.7 (CHO), 150.7 (*C*H=CHSO$_2$Ph), 140.3 (ArC), 136.5 (ArC), 133.3 (ArCH), 129.5 (CH=*C*H-SO$_2$Ph), 129.2 (2 × ArCH), 128.5 (2 × ArCH), 128.2 (ArCH), 128.0 (2 × ArCH), 127.5 (2 × ArCH), 87.9 (*C*HOBn), 73.2 (*C*H_2Ph), 41.1 (C), 23.0 (CH_3), and 22.1 (CH_3); *m*/*z* (CI mode, isobutane) 359 (100%), 329 (4), 269 (15), 239 (38), 211 (12), 209 (8), 181 (7), 143 (10), 91 (73), and 79 (7) (Found: $(M + H)^+$, 359.1319. $C_{20}H_{23}O_4S$ requires *M*, 359.1317).

Cyclisations: general cyclisation procedure C

Ethyl [*rel*-(1*R*,2*R*)-2-hydroxy-3,3-dimethylcyclobutyl]ethanoate (entry 1, Table 1). To a solution of samarium(II) iodide (0.1 M in THF, 2.80 ml, 0.28 mmol, 2 eq.) and MeOH (0.83 ml) at 0 °C, was added **4aa** (25.1 mg, 0.14 mmol, 1 eq.) in THF (0.5 ml). The reaction mixture was then stirred at 0 °C for 5 min. Aqueous saturated NaCl (1 ml) and citric acid (58.8 mg, 0.28 mmol, 2 eq.) were added and the reaction mixture allowed to warm to room temperature. The aqueous layer was separated and extracted with EtOAc (3 × 4 ml). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by column chromatography (eluting with 30% EtOAc in hexane) gave ethyl [*rel*-(1*R*,2*R*)-2-hydroxy-3,3-dimethylcyclobutyl]ethanoate (17.0 mg, 0.09 mmol, 65%) as a colourless oil: ν_{max} (soln. in $CHCl_3$)/cm^{-1} 3500br s (OH), 2954m, 2859w, 1714s (C=O), 1467m, 1377m, 1215m, and 1099m; δ_H (400 MHz, $CDCl_3$) 4.13 (2H, q, *J* 7.2, CH_2CH$_3$), 3.54 (1H, br d, *J* 7.4, C*H*OH), 2.53–2.40 (2H, m, CH_2CO$_2$Et), 2.33 (1H, apparent septet, *J* 7.4, C*H*CH$_2$CO$_2$Et), 1.73 (1H, apparent t, *J* 10.0, 1H from CH_2), 1.26 (3H, t, *J* 7.2, CH_2CH_3), 1.10 (3H, s, CH_3), 1.09 (3H, s, CH_3), and 1.04 (1H, apparent t, *J* 10.0, 1H from CH_2); δ_C (100 MHz, $CDCl_3$) 173.6 (C=O), 79.4 (CHOH), 60.5 (CH_2CH_3), 38.8 (*C*H_2CO$_2$Et), 38.5 (C), 36.9 (CH), 33.6 (CH_2), 28.6 (CH_3), 20.8 (CH_3), and 14.2 (CH_2CH_3); *m*/*z* (CI mode, isobutane) 187 (27%), 169 (100), and 130 (3) (Found: $(M + H)^+$, 187.1333. $C_{10}H_{19}O_3$ requires *M*, 187.1334).

Ethyl *rel*-(2*R*)-[*rel*-(1*R*,2*R*)-2-hydroxy-3,3-dimethylcyclobutyl]propionate 17a and ethyl *rel*-(2*S*)-[*rel*-(1*R*,2*R*)-2-hydroxy-3,3-dimethylcyclobutyl]propionate 17b (entry 2, Table 1). As for the general procedure C. Ethyl (*E*)-2,5,5-trimethyl-6-oxohex-2-enoate **4ab** (100 mg, 0.50 mmol, 1 eq.), after a reaction time of 2.5 h, gave cyclobutanols **17a** and **17b** (67.0 mg, 0.33 mmol, 66%) as a clear colourless oil. Careful chromatography (eluting with 10% EtOAc in CH_2Cl_2) allowed the two diastereoisomers to be separated (the major diastereoisomer eluting first): ν_{max} (neat)/cm^{-1} 3448s (OH), 2957s, 2867s, 1731s (C=O), 1461m, 1368m, 1272m, 1132m, 1096m, and 1025m; (major diastereoisomer **17a**) δ_H (400 MHz, $CDCl_3$) 4.13 (2H, q, *J* 7.1, CH_2CH$_3$), 3.60 (1H, dd, *J* 7.6, 3.5, C*H*OH), 2.49 (1H, d, *J* 3.5, OH), 2.42–2.34 (1H, m, C*H*CH$_3$), 2.18–2.08 (1H, m, CH), 1.71 (1H, apparent t, *J* 10.1, 1H from CH_2), 1.28 (3H, t, *J* 7.1, CH_2CH_3), 1.10 (3H, d, *J* 7.0, CHCH_3), 1.08 (3H, s, CH_3), 1.07 (3H, s, CH_3), and 1.00 (1H, apparent t, *J* 10.1, 1H from CH_2); δ_C (100 MHz, $CDCl_3$) 176.6 (*C*O$_2$Et), 78.4 (CHOH), 60.8 (*C*H_2CH$_3$), 44.2 (*C*HCH$_3$), 43.8 (CH), 37.6 (C), 32.9 (CH_2), 28.8 (CH_3), 21.1 (CH*C*H$_3$), 14.8 (CH_3), and 14.4 (CH_2CH_3); (minor diastereoisomer **17b**) mp 57–60 °C (hexane); δ_H (400 MHz, $CDCl_3$) 4.13 (2H, q, *J* 7.1, CH_2CH$_3$), 3.57 (1H, t, *J* 7.3, C*H*OH), 2.49–2.41 (1H, m, C*H*CH$_3$), 2.24–2.15 (1H, m, CH), 1.80 (1H, d, *J* 7.3, OH), 1.64 (1H, apparent t, *J* 10.2, 1H from CH_2), 1.26 (3H, t, *J* 7.1, CH_2CH_3), 1.21 (3H, d, *J* 7.0, CHCH_3), 1.13 (1H, apparent t, *J* 10.2, 1H from CH_2), 1.07 (3H, s, Me), and 1.06 (3H, s, Me); δ_C (100 MHz, $CDCl_3$) 176.1 (CO), 78.0 (CHOH), 60.4 (*C*H_2CH$_3$), 44.4 (CH), 43.9 (*C*HCH$_3$), 38.3 (C), 32.3 (CH_2), 28.5 (Me), 20.9 (Me), 15.0 (CH*C*H$_3$), and 14.5 (CH_2CH_3).

(Entry 3, Table 1). For deuterated **17a**: δ_H (400 MHz, $CDCl_3$) as for **17a** except 2.42–2.34 (1H, m, C*H*CH$_3$) missing; δ_C (100 MHz, $CDCl_3$) as for **17a** except 44.2 (*C*HCH$_3$) missing; *m*/*z* (CI mode, NH_3) 219 (100%), 184 (56), 96 (79), and 79 (34) (Found: $(M + H)^+$, 202.1553. $C_{11}H_{20}O_3D$ requires *M*, 202.1548).

For deuterated **17b**: δ_H (400 MHz, $CDCl_3$) as for **17b** except 2.49–2.41 (1H, m, C*H*CH$_3$) missing; δ_C (100 MHz, $CDCl_3$) as for **17b** except 43.9 (*C*HCH$_3$) missing (Found: C, 65.67; H, 9.61. $C_{11}H_{19}O_3D$ requires, C, 65.64; H, 9.51%).

Attempted cyclisation of ethyl 6-hydroxy-5-methylhexanoate 4b (entry 4, Table 1). As for the general procedure C. Ethyl (*E*)-5-methyl-6-oxohex-2-enoate **4b** (20.0 mg, 0.12 mmol, 1 eq.), after a reaction time of 20 min which involved the addition of further samarium(II) iodide (1 eq.), gave ethyl 6-hydroxy-5-methylhexanoate as the major product (11.0 mg, 0.07 mmol, 31%) after purification by column chromatography (eluting with 30% EtOAc in hexane): ν_{max} (soln. in $CHCl_3$)/cm^{-1} 3154m (OH), 3012s, 2983w, 1731m (C=O), 1467m, and 1217s; δ_H (400 MHz, $CDCl_3$) 4.13 (2H, q, *J* 7.1, CH_2CH$_3$), 3.53–3.43 (2H, m, CH_2OH), 2.32 (2H, m, CH_2CO$_2$Et), 1.73–1.57 (3H, m, 2H from CH_2 and 1H from CH_3CH), 1.49–1.40 (1H, m, 1H from CH_2), 1.26 (3H, t, *J* 7.1, CH_2CH_3), 1.21–1.09 (1H, m, 1H from CH_2), and 0.93 (3H, d, *J* 6.7, CH_3CH); δ_C (100 MHz, $CDCl_3$) 174.1 (C=O), 68.2 (CH_2OH), 60.5 (*C*H_2CH$_3$), 35.7 (CH), 34.7 (*C*H_2CO$_2$Et), 32.7 (CH_2), 22.4 (CH_2), 16.6 (*C*H_3CH), and 14.4 (CH_2CH_3); *m*/*z* (CI mode, NH_3) 192 (100%), 175 (18), 146 (10), and 52 (8) (Found: $(M + H)^+$, 175.1334. $C_9H_{19}O_3$ requires *M*, 175.1329).

Ethyl [*rel*-(1*R*,2*R*,3*R*)-3-(benzyloxy)-2-hydroxy-3-methylcyclobutyl]ethanoate (entry 5, Table 1). To samarium(II) iodide (0.1 M in THF, 1.60 ml, 0.16 mmol, 2 eq.) and HMPA (0.11 ml,

0.64 mmol, 8 eq.) at 0 °C, was added a solution of aldehyde **4c** (20.0 mg, 0.08 mmol, 1 eq.) and *tert*-butanol (0.01 ml, 0.10 mmol, 1.2 eq.) in THF (0.3 ml). The resulting solution was then stirred for 30 min at 0 °C before the addition of aqueous saturated NaCl (0.5 ml) and citric acid (33.5 mg, 0.16 mmol, 2 eq.). The aqueous layer was separated and extracted with EtOAc (3 × 1 ml), and the combined organic extracts dried (Na_2SO_4), and concentrated *in vacuo*. Purification by column chromatography (eluting with 30% EtOAc in hexane) gave ethyl [*rel*-(1*R*,2*R*,3*R*/*S*)-3-(benzyloxy)-2-hydroxy-3-methylcyclobutyl]ethanoate (12.6 mg, 0.05 mmol, 57%) as a 4 : 1 mixture of diastereoisomers (the major diastereoisomer being the most polar): for the major diastereoisomer; ν_{max} (soln. in $CDCl_3$)/cm^{-1} 3149br s, 2987s, 2914m, 1817m (C=O), 1789m, 1721m, 1637m, 1598m, 1570m, 1464s, and 1385s; δ_H (400 MHz, $CDCl_3$) 7.35–7.28 (5H, m, ArH × 5), 4.50 (AB system, 1H, d, *J* 11.4, 1H from PhCH_2), 4.46 (AB system, 1H, d, *J* 11.4, 1H from PhCH_2), 4.16 (2H, q, *J* 7.1, CH_2CH$_3$), 3.96 (1H, dd, *J* 6.8, 3.0, C*H*OH), 2.76 (1H, d, *J* 3.0, OH), 2.62 (1H, dd, *J* 16.7, 5.5, 1H from CH_2CO$_2$Et), 2.49 (1H, dd, *J* 16.7, 9.0, 1H from CH_2CO$_2$Et), 2.04 (1H, apparent t, *J* 9.0, 1H from CH_2), 2.06–1.96 (1H, m, CH), 1.47 (1H, obscured, 1H from CH_2), 1.43 (3H, s, CH_3), and 1.28 (3H, t, *J* 7.1, CH$_2$CH_3); δ_C (100 MHz, $CDCl_3$) 173.5 (C=O), 138.9 (ArC), 128.3 (2 × ArCH), 127.5 (2 × ArCH), 127.4 (ArCH), 79.0 (CHOH), 78.8 (C), 65.3 (Ph*C*H$_2$), 60.7 (*C*H$_2$CH$_3$), 38.7 (*C*H$_2$CO$_2$Et), 33.4 (CH_2), 32.7 (CH), 16.9 (CH_3), and 14.2 (CH$_2$*C*H$_3$); *m*/*z* (CI mode, isobutane) 279 (26%), 261 (35), 187 (6), 171 (100), 169 (6), and 91 (8) (Found: (M + H)$^+$, 279.1599. $C_{16}H_{23}O_4$ requires *M*, 279.1596).

Ethyl [*rel*-(1*R*,2*R*)-3,3-diallyl-2-hydroxycyclobutyl]ethanoate 15 (entry 6, Table 1). As for the general procedure C. Aldehyde **7a** (40.0 mg, 0.17 mmol, 1 eq.), after a reaction time of 10 min and subsequent purification by column chromatography (eluting with 20% EtOAc in hexane), gave **15** (32.2 mg, 0.14 mmol, 80%) as a colourless oil: ν_{max} (soln. in $CHCl_3$)/cm^{-1} 3451br s, 2970s, 2931s, 1727s, 1643m, 1441m, 1318m, and 1178s; δ_H (400 MHz, $CDCl_3$) 5.96–5.75 (2H, m, 2 × CH=), 5.13–5.02 (4H, m, 2 × CH_2=), 4.13 (2H, q, *J* 7.2, CH_2CH$_3$), 3.76 (1H, m, C*H*OH), 2.56 (1H, d, *J* 3.2, CHO*H*), 2.51–2.28 (5H, m, 2 × CH_2CH=, and C*H*CH$_2$CO$_2$Et), 2.20 (1H, dd, *J* 14.0, 7.6, 1H from CH_2CO$_2$Et), 2.09 (1H, dd, *J* 14.0, 7.2, 1H from CH_2CO$_2$Et), 1.87 (1H, apparent dd, *J* 11.6, 8.8, 1H from CH_2), 1.26 (3H, t, *J* 7.2, CH$_2$CH_3), and 1.03 (1H, apparent dd, *J* 11.6, 8.8, 1H from CH_2); δ_C (100 MHz, $CDCl_3$) 173.4 (C=O), 135.2 (CH=), 134.5 (CH=), 117.3 (2 × CH_2=), 77.9 (CHOH), 60.5 (*C*H$_2$CH$_3$), 44.3 (C), 43.4 (*C*H$_2$CO$_2$Et), 38.7 (*C*H$_2$CH=), 36.7 (CH), 36.0 (*C*H$_2$CH=), 29.2 (CH_2), and 14.2 (CH$_2$*C*H$_3$); *m*/*z* (CI mode, isobutane) 239 (21%), 221 (100), 193 (5), 175 (16), 147 (15), 133 (25), and 130 (14) (Found: (M + H)$^+$, 239.1648. $C_{14}H_{23}O_3$ requires *M*, 239.1647).

Ethyl [*rel*-(1*R*,2*R*)-1-hydroxyspiro[3.4]oct-6-en-2-yl]-ethanoate 16 and ethyl 4-[1-(hydroxymethyl)cyclopent-3-enyl]-butanoate (entry 7, Table 1). As for the general procedure C. Ethyl (*E*)-4-(1-formylcyclopent-3-enyl)but-2-enoate **7b** (50.0 mg, 0.24 mmol, 1 eq.), after a reaction time of 15 min and subsequent purification by column chromatography (eluting with 20% EtOAc in hexane), gave **16** (31.0 mg, 0.15 mmol, 62%) as a colourless oil; ν_{max} (soln. in $CHCl_3$)/cm^{-1} 3524br m (OH), 3013s, 2931m, 1721s (C=O), 1381m, 1216s, and 1093m; δ_H (400 MHz, $CDCl_3$) 5.71–5.68 (1H, m, CH=), 5.53–5.59 (1H, m, CH=), 4.14 (2H, q, *J* 7.2, CH_2CH$_3$), 3.75 (1H, d, *J* 7.9, C*H*OH), 2.98 (1H, dt, *J* 16.5, 2.2, 1H from ^{A}CH_2CH=), 2.72 (1H, br s, OH), 2.54–2.41 (3H, m, CH_2CO$_2$Et and 1H from ^{B}CH_2CH=), 2.34 (1H, dt, *J* 16.7, 1.8, 1H from ^{B}CH_2CH=), 2.25 (1H, apparent sextet, *J* 8.7, CH), 2.15 (1H, dt, *J* 16.5, 1.8, 1H from ^{A}CH_2CH=), 1.95 (1H, apparent t, *J* 10.3, 1H from CH_2), 1.26 (3H, t, *J* 7.2, CH$_2$CH_3), and 1.24 (1H, apparent t, *J* 10.3, 1H from CH_2); δ_C (100 MHz, $CDCl_3$) 173.5 (C=O), 129.5 (CH=), 128.8 (CH=), 78.6 (*C*HOH), 60.5 (OCH_2), 48.1 (C), 45.4 (^{B}*C*H$_2$CH=), 38.5 (*C*H$_2$CO$_2$Et), 37.7 (^{A}*C*H$_2$CH=), 37.7 (CH), 34.4 (CH_2), and 14.1 (CH_3); *m*/*z* (CI mode, isobutane) 211 (50%), 193 (100), 165 (4), 130 (40) and 80 (6) (Found: (M + H)$^+$, 211.1333. $C_{12}H_{19}O_3$ requires *M*, 211.1334).

Further elution then gave ethyl 4-[1-(hydroxymethyl)-cyclopent-3-enyl]butanoate (4.1 mg, 0.02 mmol, 8%) ν_{max} (soln. in $CHCl_3$)/cm^{-1} 3026s, 2919w, 2841w, 1727 (C=O), 1531m, 1469w, 1419m, 1217s, and 1038m; δ_H (400 MHz, $CDCl_3$) 5.61 (2H, s, 2 × CH=), 4.14 (2H, q, *J* 7.1, CH_2CH$_3$), 3.49 (2H, br s, CH_2OH), 2.32 (2H, t, *J* 6.8, CH_2CO$_2$Et), 2.25 (2H, apparent d, *J* 18.0, 1H from each CH_2CH=), 2.15 (2H, apparent d, *J* 18.0, 1H from each CH_2CH=), 1.64–1.56 (2H, m, CH_2CH$_2$CO$_2$Et), 1.54–1.47 (2H, m, CH_2), and 1.27 (3H, t, *J* 7.1 Hz, CH$_2$CH_3); δ_C (100 MHz, $CDCl_3$) 173.9 (C=O), 129.2 (2 × CH=), 68.9 (CH_2OH), 60.4 (*C*H$_2$CH$_3$), 46.1 (C), 41.3 (2 × *C*H$_2$CH=), 36.6 (CH_2), 34.6 (*C*H$_2$CO$_2$Et), 19.8 (*C*H$_2$CH$_2$CO$_2$Et), and 14.2 (CH_3); *m*/*z* (CI mode, isobutane) 213 (100%), 195 (46), 167 (6) and 149 (6) (Found: (M + H)$^+$, 213.1489. $C_{12}H_{21}O_3$ requires *M*, 213.1491).

***rel*-(3*R*)-3-[*rel*-(1*R*,2*R*)-2-Hydroxy-3,3-dimethylcyclobutyl]-4,5-dihydrofuran-2(3*H*)-one (entry 8, Table 1).** As for the general procedure C. Aldehyde **9** (42 mg, 0.23 mmol, 1 eq.), after a reaction time of 0.5 h and subsequent purification by column chromatography (eluting with 50% EtOAc in hexane) gave (3*R*/*S*)-3-[*rel*-(1*R*,2*R*)-2-hydroxy-3,3-dimethylcyclobutyl]-4,5-dihydrofuran-2(3*H*)-one (28 mg, 0.15 mmol, 66%) as a 4 : 1 mixture of diastereoisomers: for the major diastereoisomer; ν_{max} (soln. in $CHCl_3$)/cm^{-1} 3548m, 3025s, 2961s, 2925s, 2867s, 1762s, 1375s, 1216s, 1105s, and 1028s; δ_H (400 MHz, $CDCl_3$) 4.40 (1H, td, *J* 8.8, 2.6, 1H from CH$_2$CH_2O), 4.27–4.20 (1H, m, 1H from CH$_2$CH_2O), 3.76 (1H, d, *J* 7.7, C*H*OH), 2.81 (1H, br s, CHO*H*), 2.60 (1H, q, *J* 9.6, CHCO-O), 2.38–2.30 (1H, m, 1H from CH_2CH$_2$O), 2.23–2.14 (1H, m, CH), 1.99–1.88 (1H, m, 1H from CH_2CH$_2$O), 1.71 (1H, t, *J* 9.9, 1H from CH_2), 1.16 (1H, obscured, 1H from CH_2), 1.13 (3H, s, Me), and 1.12 (3H, s, Me); δ_C (100 MHz, $CDCl_3$) 180.0 (C=O), 78.1 (CHOH), 67.6 (CH$_2$*C*H$_2$O), 44.0 (*C*HCO$_2$), 41.6 (CH), 38.8 (C), 32.4 (CH_2), 28.8 (CH_3), 27.7 (*C*H$_2$CH$_2$O), 21.0 (CH_3); *m*/*z* (CI mode, isobutane) 185 (41%), 167 (100), 149 (1), 128 (3), and 113 (2) (Found: (M + H)$^+$, 185.1178. $C_{10}H_{17}O_3$ requires *M*, 185.1173).

***rel*-(1*R*,4*S*)-2,2-Dimethyl-4-(phenylsulfonylmethyl)cyclobutan-1-ol and (*E*)-2,2-dimethyl-5-(phenylsulfonyl)pent-4-en-1-ol (entry 9, Table 1).** As for the general procedure C. Aldehyde **11** (20.0 mg, 0.08 mmol, 1 eq.), after a reaction time of 2 h and subsequent purification by column chromatography (eluting with 30% EtOAc in hexane), gave *rel*-(1*R*,4*S*)-2,2-dimethyl-4-(phenylsulfonylmethyl)cyclobutan-1-ol (4.0 mg, 0.02 mmol, 21%) as a clear colourless oil: ν_{max} (soln. in $CDCl_3$)/cm^{-1} 3606m, 3159m, 3070m, 3033m, 2970s, 2928m, 2865m, 1709s, 1598s, 1451s, 1309s, and 1152s; δ_H (400 MHz, $CDCl_3$) 7.94 (2H, d, *J* 7.2, 2 × ArH), 7.71–7.67 (1H, m, ArH), 7.62–7.58 (2H, m, 2 × ArH), 3.71 (1H, d, *J* 7.7, C*H*OH), 3.26 (2H, apparent d, *J* 7.4, CH_2SO$_2$Ph), 2.69 (1H, br s, CHO*H*), 2.50–2.40 (1H, m, C*H*CH$_2$), 1.72 (1H, apparent t, *J* 10.1, 1H from CH_2), 1.11 (6H, s, 2 × CH_3), and 1.07 (1H, obscured 1H from CH_2); δ_C (100 MHz, $CDCl_3$) 139.4 (ArC), 134.0 (ArCH), 129.6 (2 × ArCH), 128.3 (2 × ArCH), 79.0 (CHOH), 60.8 (*C*H$_2$SO$_2$Ph), 39.6 (C), 35.1 (CH), 33.7 (CH_2), 28.7 (Me), and 20.8 (Me); *m*/*z* (CI mode, NH_3) 272 (100%), 254 (10), 237 (5), and 95 (2) (Found: M + NH_4^+, 272.1320. $C_{13}H_{22}NO_3S$ requires *M*, 272.1315). Further elution then gave (*E*)-2,2-dimethyl-5-(phenylsulfonyl)-pent-4-en-1-ol (7 mg, 0.03 mmol, 35%) as a colourless oil: ν_{max} (soln. in $CHCl_3$)/cm^{-1} 3627m, 3017s, 2965s, 2928m, 2875m, 1630m, 1519m (aromatic), 1446m, 1320s, 1309s, 1215s, and 1146s; δ_H (400 MHz, $CDCl_3$) 7.89 (2H, d, *J* 8.6, 2 × ArH),

7.64–7.60 (1H, m, ArH), 7.57–7.53 (2H, m, 2 × ArH), 7.03 (1H, dt, *J* 14.9, 8.0, CH_2CH=), 6.36 (1H, d, *J* 14.9, =$CHSO_2Ph$), 3.34 (2H, s, CH_2OH), 2.22 (2H, d, *J* 8.0, CH_2CH=), and 0.93 (6H, s, 2 × Me); δ_C (100 MHz, $CDCl_3$) 144.5 (CH_2CH=), 140.9 (ArC), 133.5 (ArCH), 132.6 (=$CHSO_2Ph$), 129.4 (2 × ArCH), 127.7 (2 × ArCH), 71.3 (CH_2OH), 40.7 (CH_2CH=), 36.5 (C), 24.1 (2 × Me); *m*/*z* (CI mode, isobutane) 255 (100%), 237 (73), 198 (2), 154 (2), 143 (2), 125 (3), 113 (4), 95 (14), and 81 (12) (Found: $(M + H)^+$, 255.1055. $C_{13}H_{19}O_3S$ requires *M*, 255.1050).

Ethyl [(1*S*,3*R*,4*R*)-3-(benzyloxy)-4-hydroxy-2,2-dimethylcyclobutyl]ethanoate[7] (entry 10, Table 1). As for the general procedure. Ethyl (*E*,5*R*)-5-(benzyloxy)-4,4-dimethyl-6-oxohex-2-enoate **13** (42 mg, 0.15 mmol, 1 eq.), after a reaction time of 20 min and subsequent purification by column chromatography (eluting with 20% EtOAc in hexane) gave ethyl [(1*S*,3*R*,4*R*)-3-(benzyloxy)-4-hydroxy-2,2-dimethylcyclobutyl]ethanoate (30 mg, 0.11 mmol, 70%) as a colourless oil: $[\alpha]_D$ −26.2 (*c* 0.91, $CHCl_3$); ν_{max} (soln. in $CHCl_3$)/cm^{-1} 3527br m, 3023s, 2959m, 2875m, 1719s, 1451w, and 1372m; δ_H (400 MHz, $CDCl_3$) 7.39–7.26 (5H, m, 5 × ArH), 4.61 (AB system, 1H, d, *J* 11.9, 1H from $PhCH_2$), 4.58 (AB system, 1H, d, *J* 11.9, 1H from $PhCH_2$), 4.15 (2H, q, *J* 7.1, CH_2CH_3), 3.81 (1H, apparent t, *J* 6.2, CHOH), 3.51 (1H, d, *J* 6.2, CHOBn), 2.92 (1H, br s, OH), 2.51–2.38 (2H, m, CH_2CO_2Et), 1.73–1.67 (1H, m, CH), 1.28 (3H, t, *J* 7.1, CH_2CH_3), 1.15 (3H, s, Me), and 0.96 (3H, s, Me); δ_C (100 MHz, $CDCl_3$) 173.9 (C=O), 138.5 (ArC), 128.3 (2 × ArCH), 127.6 (2 × ArCH), 127.5 (ArCH), 86.0 (CHOBn), 75.8 (CHOH), 71.5 ($PhCH_2$), 60.7 (CH_2CH_3), 42.4 (CH), 35.5 (C), 32.8 (CH_2), 29.2 (Me), 17.6 (Me), and 14.1 (CH_2CH_3); *m*/*z* (CI mode, isobutane) 293 (66%), 275 (100), 257 (11), 229 (10), 185 (34), 162 (22), and 91 (18) (Found: $(M + H)^+$, 293.1753. $C_{17}H_{25}O_4$ requires *M*, 293.1753).

(4*R*,2*S*,1*R*)-4-(Benzyloxy)-3,3-dimethyl-2-(phenylsulfonylmethyl)cyclobutanol and (*E*)-3,3-dimethyl-5-(phenylsulfonyl)-pent-4-enal (entry 11, Table 1). As for the general procedure. The aldehyde **14** (22 mg, 0.06 mmol, 1 eq.) in THF (0.3 ml), after a reaction time of 15 min and subsequent purification by column chromatography (eluting with 40% EtOAc in hexane), gave byproduct (*E*)-3,3-dimethyl-5-(phenylsulfonyl)pent-4-enal (4.0 mg, 0.016 mmol, 26%) as a colourless oil: ν_{max} (soln. in $CHCl_3$)/cm^{-1} 3013s, 1709s (C=O), 1522m, 1469m, 1422m, 1304s, and 1152s; δ_H (400 MHz, $CDCl_3$) 9.59 (1H, t, *J* 2.3, CHO), 7.89 (2H, d, *J* 7.8, 2 × ArH), 7.65–7.60 (1H, m, ArH), 7.58–7.54 (2H, m, 2 × ArH), 7.06 (1H, d, *J* 15.3, CH=CH-SO_2Ph), 6.28 (1H, d, *J* 15.3, CH=C*H*SO_2Ph), 2.50 (2H, d, *J* 2.3, CH_2CHO), and 1.23 (6H, s, Me × 2); δ_C (100 MHz, $CDCl_3$) 200.1 (CHO), 153.0 (*C*H=$CHSO_2Ph$), 140.3 (ArC), 133.4 (ArCH), 129.3 (2 × ArCH), 128.5 (CH=*C*HSO_2Ph), 127.6 (2 × ArCH), 54.1 (CH_2), 36.0 (C), and 26.5 (2 × CH_3); *m*/*z* (CI mode, isobutane) 253 (100%), 209 (19), 143 (4), 125 (4), 111 (2), and 79 (7) (Found: $(M + H)^+$, 253.0900. $C_{13}H_{17}O_3S$ requires *M*, 253.0898). Further elution then gave (4*R*,2*S*,1*R*)-4-(benzyloxy)-3,3-dimethyl-2-(phenylsulfonylmethyl)cyclobutanol (13.0 mg, 0.036 mmol, 60%) as a colourless oil: $[\alpha]_D$ −19.2 (*c* 0.9, $CHCl_3$); ν_{max} (soln. in $CHCl_3$)/cm^{-1} 3548br s, 2961s, 1604m, 1522s, 1463s, 1387m, and 1299s; δ_H (400 MHz, $CDCl_3$) 7.94 (2H, d, *J* 7.2, 2 × ArH), 7.71–7.66 (1H, m, ArH), 7.62–7.44 (2H, m, 2 × ArH), 7.38–7.27 (5H, m, $C_6H_5CH_2$), 4.63 (AB system, 1H, d, *J* 11.9, 1H from $PhCH_2$), 4.58 (AB system, 1H, d, *J* 11.9, 1H from $PhCH_2$), 4.03 (1H, apparent td, *J* 6.4, 2.8, CHOH), 3.58 (1H, d, *J* 6.4, CHOBn), 3.21 (1H, dd, *J* 13.9, 4.4, 1H from CH_2SO_2Ph), 3.14 (1H, dd, *J* 13.9, 10.8, 1H from CH_2SO_2Ph), 3.05 (1H, d, *J* 2.8, OH), 1.84–1.78 (1H, m, CH), 1.09 (3H, s, Me), and 0.96 (3H, s, Me); δ_C (100 MHz, $CDCl_3$) 139.0 (ArC), 138.3 (ArC), 138.1 (ArCH), 134.0 (2 × ArCH), 129.4 (2 × ArCH), 128.4 (2 × ArCH), 127.6 (3 × ArCH), 85.1 (CHOBn), 74.5 (CHOH), 71.7 (CH_2Ph), 55.9 (CH_2SO_2Ph), 40.3 (CH), 36.5 (C), 28.9 (CH_3), and 17.7 (CH_3); *m*/*z* (CI mode, isobutane) 361 (64%), 343 (100), 325 (17), 251 (19), 223 (12), 201 (37), 183 (57), 162 (18), 127 (10), and 91 (20) (Found: $(M + H)^+$, 361.1475. $C_{20}H_{25}O_4S$ requires *M*, 361.1474).

Ethyl (*rel*-(1*R*,2*R*)-1-hydroxyspiro[3.4]oct-6-en-2-yl)-ethanoate 16 (by ring-closing metathesis). To **15** (18.0 mg, 0.08 mmol, 1 eq.) in CH_2Cl_2 (0.3 ml) was added $(PCy_3)_2Ru(Cl)_2$=CHPh (11.3 mg, 0.02 mmol, 0.2 eq.) and the solution heated at reflux for 1 h. The reaction mixture was passed down a short silica gel column (eluting with 20% EtOAc in hexane). Concentration *in vacuo* then gave crude **16** as a dark oil. Purification by column chromatography (eluting with 20% EtOAc in hexane) then gave **16** (15.1 mg, 0.07 mmol, 95%) as a colourless oil.

***rel*-(1*R*,4*R*)-4-[(1*R*)-2-Hydroxy-1-deuteromethylethyl]-2,2-dimethylcyclobutanol 18.** To a stirred solution of deuterated cyclobutanol **17a** (30 mg, 0.15 mmol, 1 eq.) in THF (1 ml), at 0 °C was added $LiAlH_4$ (11.0 mg, 0.30 mmol, 2 eq.). After 1.5 h the reaction mixture was transferred to a solution of K/Na tartrate (421 mg, 1.49 mmol, 10 eq.) in H_2O (1 ml) and the resulting mixture stirred for 10 min. The aqueous layer was then separated and extracted with EtOAc (4 × 5 ml) and the combined organic extracts dried ($NaSO_4$). Concentration *in vacuo* gave crude **18** as a clear colourless oil. The residue was then purified by sublimation which gave **18** as a white crystalline solid (14.0 mg, 0.09 mmol, 59%), mp 61–63 °C: ν_{max} (neat)/cm^{-1} 3685m (OH), 3601w, 3017s, 2954s, 2933m, 1604w, 1525m, 1477m, 1420m, 1078m, and 1020m; δ_H (400 MHz, $CDCl_3$) 3.65 (1H, dd, *J* 11.0, 8.3, 1H from CH_2OH), 3.58 (1H, dd, *J* 7.6, 5.8, CHOH), 3.37 (1H, dd, *J* 11.0, 4.0, 1H from CH_2OH), 2.60 (1H, dd, *J* 8.3, 4.0, CH_2OH), 2.37 (1H, d, *J* 5.8, CHOH), 1.79–1.69 (1H, m, CH), 1.67 (1H, apparent t, *J* 9.9, 1H from CH_2), 1.09 (3H, s, Me), 1.08 (3H, s, Me), 1.01 (1H, apparent t, *J* 9.9, 1H from CH_2), and 0.73 (3H, s, $CDCH_3$); δ_C (100 MHz, $CDCl_3$) 79.3 (CHOH), 68.9 (CH_2OH), 46.3 (CH), 37.7 (C), 32.1 (CH_2), 28.6 (Me), 20.8 (Me), and 14.1 ($CDCH_3$) ['CD' signal not observed]; *m*/*z* (CI mode, NH_3) 177 (16%), 159 (10), 142 (4), 124 (1), 88 (1), and 77 (1) (Found: $(M + NH_4)^+$, 177.1713. $C_9H_{21}DNO_2$ requires *M*, 177.1708).

Crystal structure determination

The crystals sublime at room temperature but proved stable at 123 K when mounted in a Lindemann glass capillary. All measurements were made with Mo X-rays on a CAD4 diffractometer.

Crystal data for 18. $C_9H_{18}O_2$, $M = 158.23$, orthorhombic, $a = 8.254(2)$, $b = 11.229(2)$, $c = 20.088(2)$ Å, $U = 1861.8(5)$ Å^3, $T = 123$ K, space group *Pbna* (No. 60), $Z = 8$, μ(Mo-K_a) 0.08 mm^{-1}, 2044 reflections measured, 1454 unique F^2 values used in refinement ($R_{int} = 0.056$). R_1[933 with $I > 2\sigma(I)$] = 0.051, wR_2(all data) = 0.14.[26]

The parameters of the hydroxylic H atoms were freely refined since O(1) and O(2) act both as hydrogen bond donors and acceptors. Molecules of **18** are linked into chains through an O(2)–H···O(1)–H···O(2)–H hydrogen bond system [O···O 2.754(3) & 2.734(3) Å]. CCDC reference number 207/394. See http://www.rsc.org/suppdata/p1/a9/a909549g

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