

0040-4020(95)01029-7

Enantioselective Preparation of 2-Substituted-1,3-Dithiane 1-Oxides using Modified Sharpless Sulphoxidation Procedures

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Abstract: Enantioselective sulphoxidation of a wide range of 2-substituted-1,3-dithianes has been carried out using modified Sharpless conditions to furnish the corresponding sulphoxides in optically enriched form. Deacylation of 2-acyl-1,3-dithiane 1-oxide derivatives allows the preparation of 2-alkyl-1,3-dithiane 1-oxides and the parent 1,3-dithiane 1-oxide itself in high enantiomeric excesses.

Introduction

Over the last several years, we have developed the uses of 1,3-dithiane 1-oxides as stereocontrol elements for a wide variety of synthetic transformations, principally involving carbonyl group reactivity.¹ Reaction types subject to a high level of stereocontrol include inter and intramolecular enolate alkylation^{1a} and amination,^{1b} nucleophilic addition,^{1c} reduction,^{1d} conjugate addition,^{1e} cycloaddition,^{1f} and Mannich reaction.^{1g} All of these reaction types were initially investigated using racemic 2-acyl-1,3-dithiane 1-oxide substrates. The ever-increasing need for the preparation of chiral compounds in enantiomerically pure form, and the growing importance of enantiomerically pure sulphoxides as enantiocontrol elements for carbon-carbon bond formation,² encouraged us to investigate the preparation of optically enriched 2-substituted-1,3-dithiane 1-oxides.

Unfortunately, there is still a lack of general, efficient methods for the asymmetric synthesis of sulphoxides. Perhaps the most well known method for optically pure sulphoxide preparation is the Andersen procedure,³ in which an organometallic reagent induces nucleophilic displacement at an asymmetric sulphinate sulphur atom with inversion and without loss of stereochemical integrity. A more satisfactory and more general approach involves the enantioselective sulphoxidation of a prochiral sulphide substrate. Established methods of asymmetric sulphur oxidation however often suffer from a lack of generality and/or a low degree of asymmetric induction. For example, while enzymatic and microbial processes can give rise to sulphoxides with high optical purity,⁴ yields and ees are commonly highly substrate dependent. Of the known chemical methods of enantioselective sulphur oxidation, the oxaziridines of Davis,⁵ and the modified Sharpless protocols developed independently by Kagan⁶ and Modena⁷ have proved the most successful, and indeed it was the modified Sharpless procedures which we first chose to examine for the preparation of optically enriched dithiane oxides.



method A: Ti(OiPr)₄ (1 eq), (+)- or (-)-DET (2 eq), H₂O (1 eq), CHP or TBHP (\geq 1 eq) ⁶ **method B:** Ti(OiPr)₄ (1 eq), (+)- or (-)-DET (4 eq), CHP or TBHP (\geq 1 eq) ⁷ DET = diethyl tartrate; CHP = cumene hydroperoxide

Scheme 1. Modified Sharpless Conditions for Asymmetric Sulphoxidation

These methods can also be somewhat substrate dependent and so to some degree are unpredictable. In general, for efficient asymmetric induction to be achieved, either considerable steric differentiation is required around the sulphide sulphur atom, or a dipolar unit is required within the substrate molecule, presumably for some crucial interaction with the reagent system. The conditions involving stoicheiometric catalyst initially employed by us are indicated in scheme 1.

Kagan has proposed a rule of thumb for predicting absolute configurations in these oxidations: if the sulphide substrate is drawn as a two-dimensional representation with the larger or co-ordinating group pointing to the right and downwards, and the smaller alkyl group pointing to the left and downwards, then the use of (+)-tartrate results in oxygenation at the front face,⁶ as shown in Scheme 2, generally to furnish the *R*-sulphoxide. Our own work supports this rule of thumb in every case.



Scheme 2. Prediction of Absolute Configuration

We report here the results of asymmetric sulphur oxidation using modified Sharpless conditions of variously 2-substituted 1,3-dithianes, including 2-alkyl, acyl, carboxy and heteroatomic derivatives, and the application of this chemistry to the enantioselective preparation of 2-substituted 1,3-dithiane oxides with very high ees.

Asymmetric Oxidation of 2-Alkyl-, 2-Aryl-, and 2-Heterosubstituted-1,3-Dithianes

Initially we examined the oxidation of simple 2-substituted-1,3-dithianes, only to obtain rather poor enantioselectivies, in broad agreement with the reports of both Kagan⁶ and Modena⁷ (Table 1), due perhaps to the lack of a co-ordinating group in the substrate for interaction with the reagent system. High diastereoselectivity was however observed in the oxidation reactions, the *anti* diastereoisomer **3** being predominant, presumably due to preferential equatorial sulphur oxidation.⁸

2-Heterosubstituted-1,3-dithianes have received relatively little synthetic attention compared with their 2-alkyl- and 2-acyl counterparts. Such 2-heterosubstituted-1,3-dithiane 1-oxides have obvious importance as chiral carboxylic acid equivalents, and we were intrigued to determine the effect of the presence of various heteroatoms within the dithiane substrate upon the enantioselectivity of oxidation.



Table 1. Asymmetric Oxidation of 2-Alkyl and 2-Aryl-1,3-Dithianes

* syn minor isomer not detected using 200 MHz ¹H NMR spectroscopy ‡ TBHP used as oxidant § CHP used as oxidant

Several 2-heterosubstituted-1,3-dithianes were synthesized as shown in Scheme 3.9 2-Thiomethyl-1,3-dithiane 1a, 2-trimethylsilyl-1,3-dithiane 1b, 2-triisopropylsilyl-1,3-dithiane 1c, and 2-tributylstannyl-1,3-dithiane 1d, were all furnished in good to excellent yields by initial deprotonation followed by addition of a suitable electrophilic reagent. 2-Thiophenyl-1,3-dithiane 1e was prepared via the unisolable 2-chloro-1,3-dithiane, itself prepared by a PummereR-type rearrangement involving the use of N-chlorosuccinimide as a source of electrophilic chlorine.¹⁰ 2-Methoxy-1,3-dithiane 1f, was prepared in 70% yield by in situ alcoholysis of the sulphimine derived from the treatment of 1.3-dithiane with anhydrous chloramine-T.¹¹ The unstable 2-N.Ndimethylamino derivative was prepared by the method of Juaristi,¹² unfortunately in only ca. 10% yield, and decomposition had begun even before full analysis could be completed. Asymmetric oxidation of this derivative was therefore not performed. The 2-cyano derivative 1g a substrate containing a heteroatom which is not directly attached to the C2 position of the dithiane ring, was not synthesized by literature routes, ¹³ but instead in 92% yield by treatment of the tetrafluoroborate salt derived from 1,3-dithiane using trityl tetrafluoroborate, after isolation, with trimethylsilyl cyanide in dichloromethane at -20 °C.¹⁴ 2-Heterosubstituted-1,3-dithianes are particularly unstable, and of the seven substrates shown in Scheme 3, only 1e and 1g, both of which are solids, are stable at room temperature.

A conformational study by Juaristi based upon NMR data for a range of dithiane substrates has indicated that sizeable anomeric effects can operate in these systems.¹² The relative magnitudes of the anomeric effects observed for substrates used by us were in the order COPh > CO₂Me > SPh > SMe >>> NMe₂. Sizeable axial preferences were apparent for the thiomethyl (0.64 kcal/mol) and thiophenyl (0.92 kcal/mol) derivatives. Similar studies of 2-metallated-1,3-dithianes including the silyl substrate **1b** have indicated an equatorial preference.¹⁵

We have examined the asymmetric oxidation of the 2-heterosubstituted-1,3-dithianes **1a-g** using modified Sharpless conditions.¹⁶ Oxidation was achieved with yields ranging from fair to excellent, and with widely varying ees, as shown in Table 2.



i) n-BuLi, thf, -78 °C, 1.5 h; Me_2S_2 , thf, -78 °C to rt, overnight (100%); ii) NCS, toluene, rt, 15 min; PhSH, rt, 3 h (44%); iii) Chloramine-T, MeOH, 0 °C, 5 min; KOH, rt, overnight (70%); iv) n-BuLi, thf, -78 °C, 1.5 h; R₃SiCl, thf, -78 °C to rt, 1.5h (R = Me, 60%; R = iPr, 90%); v) n-BuLi, thf, -78 °C, 1 h; Bu₃SnCl, -78 °C to rt, overnight (68%); vi) Ph₃C⁺BF₄⁻, CH₂Cl₂, Δ , 45 min (94%); TMSCN, CH₂Cl₂, -20 °C (98%)

Scheme 3. Preparation of 2-Heterosubstituted-1,3-dithianes

It is particularly interesting that the *syn:anti* ratios found in the sulphoxide products do not parallel the magnitude of the anomeric effects in the starting materials; in several cases the minor diastereoisomers of the sulphoxide products were not observed, either because the oxidations are very highly diastereoselective or as a result of equilibration at the C2 position through enolization under the reaction conditions following sulphur oxidation, a known process for the carboxyethyl derivative.¹⁷ Where equilibration occurs, the ratios observed may reflect a balance between the anomeric effect, favouring axial C2 substituents; 1,3-diaxial interactions, favouring equatorial substituents; and dipole-dipole interactions; for example, exposure of the major, *anti*, isomer of 2-thiomethyl-1,3-dithiane 1-oxide to titanium tetraisopropoxide induces an equilibration process, reaching an *anti:syn* ratio of 10:1 after two days. Where equilibration does not occur, the ratios observed may reflect the operation of the anomeric effect in the starting materials coupled with preferential equatorial oxidation, or may merely reflect a late transition state. In the case of the 2-methoxy derivative **1f**, an inseparable 5:2 ratio of isomers was obtained, but the relative and absolute configurations of the products could not be determined. For 2-trimethylsilyl-1,3-dithiane

1b, the diastereoselection, in this case in favour of the *anti* 1-oxide isomer, may be assisted to a small extent by ready decomposition of any *syn* diastereoisomer through a sila-Pummerer rearrangement,¹⁸ a known process when a 2-trimethylsilyl group is situated *syn* to the sulphoxide oxygen in a 1,3-dithiane 1-oxide.¹⁹ A similar process may occur for the 2-tributylstannyl derivative **1d**; stannyl-Pummerer rearrangements have previously been observed.²⁰ The metal-carbon bond in both of these unusual 2-metallated-1,3-dithiane 1-oxides is prone to cleavage under mild conditions, and it is remarkable that we are able to achieve efficient oxidation. In the case of the stannyl derivative, the product is isolable, but the stannyl group is rapidly lost, and ee determination was carried out on the resulting 1,3-dithiane 1-oxide.

S R	S oxida	tion meth CH ₂ C	nod A or B I₂	S S R S S S S S S S S S S	_ +	S R	S [‡] O ⁻ anti	
1a-	g			2		3		
<u>R</u>	Temp/°C	Yield/%	ratio	major isomer	ee/%anti	[α]D ²⁰	ee/%syn	<u>[α]_D20</u>
SMe	-35	36	8:1	anti	16	+41.0°	16	+5.9°
SPh	-32	65	≥ 99 : 1 ‡	anti	10	+ 39 .1°		—
OMe	-31	63	5 : 2	t	†		†	_
SiMe ₃	-32	91	≥99:1‡	anti	65	+2.2°	_	
Si ⁱ Pr3	-32	67§	—	_	12§	_		
SnBu ₃	-35	43	≥99:1‡	anti	55§	_	_	
CN	-35	80	≥ 98 : 2 ‡	syn	_	_	37	+69. 8 °

Table 2. Asymmetric Oxidation of 2-Heterosubstituted-1,3-Dithianes

[†] could not be determined

[‡] minor diastereoisomer not detected using 400MHz ¹H NMR spectroscopy [§] measurements carried out on isolated 1,3-dithiane 1-oxide

Ready loss of the C2 substituent upon oxidation also occured for the 2-triisopropyl derivative **1c**, leading to isolation of 1,3-dithiane 1-oxide only, and, indeed, the poor ee obtained suggests that loss of the silyl-containing group may occur even before oxidation takes place. 2-Thiomethyl-1,3-dithiane **1a** and 2-thiophenyl-1,3-dithiane **1e** were oxidized with poor ee, comparable to that achieved with only an alkyl group at the C2 position (Table 1), although, significantly, exocyclic sulphur oxidation was not observed. Much higher ees were achieved with the trimethylsilyl **1b**, tributylstannyl **1d**, and cyano **1g** derivatives.

We have been able to prepare 2-alkyl-1,3-dithiane 1-oxides in high ees by sequential asymmetric oxidation and deacylation of 2-acyl-2-alkyl-1,3-dithianes (*vide infra*).²¹ This procedure is also applicable to certain 2-heterosubstituted substrates. For example, asymmetric oxidation and careful base mediated deacylation of 2-butanoyl-2-thiophenyl-1,3-dithiane **4** gave 2-thiophenyl-1,3-dithiane 1-oxide in 35% overall yield but with 77% ee. (1.6:1 *anti:syn*) (Scheme 4).



Scheme 4. 2-Thiophenyl-1,3-dithiane 1-oxide by oxidation/deacylation

Preparation of 2-Acyl-1,3-Dithiane 1-Oxides

Several methods exist for the preparation of simple 2-acyl-1,3-dithianes. These methods can be divided into two distinct categories: direct acylation of a dithiane anion with a carboxylic acid derivative²² or, alternatively, reaction of a dithiane anion with an aldehyde followed by subsequent oxidation.²³ Both of these routes are capricious, with side reactions such as deprotonation of the acid derivative or of the product presenting serious drawbacks. We have found however that use of a two-base combination,²⁴ as shown in Scheme 5, involving the use of sodium hexamethyl disilazide and butyllithium, prevents compromise of the yield of the desired 2-acyl-1,3-dithiane by driving the product entirely to the deprotonated form *in situ*. We have synthesized both 2-pivaloyl- **6a** and 2-benzoyl-1,3-dithiane **6b** in high yields by use of this protocol. 2-Ethoxycarbonyl-1,3-dithiane **6c** (R = OEt) was obtained commercially.



Scheme 5. Preparation of 2-Acyl-1,3-Dithianes using a two-base combination

2-Acyl-1,3-dithianes undergo asymmetric oxidation with widely differing degrees of success. While asymmetric sulphoxidation occurred readily for most 2-acyl-1,3-dithianes, the 2-acetyl-, 2-butanoyl-, and 2-naphthoyl- derivatives did not undergo oxidation to any appreciable extent using the conditions of Kagan.²⁵ As shown in Table 3, 2-pivaloyl-1,3-dithiane **6a**, 2-benzoyl-1,3-dithiane **6b** and the commercially available 2-ethoxycarbonyl-1,3-dithiane **6c** did undergo oxidation using modified Sharpless conditions to furnish the corresponding 1-oxide products as a mixture of *syn* and *anti* diastereoisomers in good yields and with good to excellent ees.

As expected, *anti* isomers were formed as the major products of the oxidations, presumably due to preferential equatorial oxidation,⁸ the acyl group adopting an equatorial orientation during the reaction. This pattern mirrors the results obtained in the corresponding racemic oxidations, where the expectation of preferential equatorial oxidation is supported by use of a 2-*t*-butyl group, which results in the *syn* isomer becoming the major product, the acyl group then adopting an axial orientation.^{1a} Stereochemical assignment to the *syn* or *anti* configuration was made by correlation of ¹H NMR spectra with those of racemic materials previously prepared in our laboratories,¹ the structures of which are supported by single crystal X-ray analyses.



Table 3. Asymmetric Oxidation of 2-Acyl-1,3-dithianes

[†] diastereoselectivities have been found to vary from 3 : 1 up to exclusively *anti* [‡] one recrystallization from EtOH or Et₂O leads to optical purity

Table 4. Preparation of 2-Acyl-2-Alkyl-1,3-Dithianes

S S R	i) BuLi, thf, -20 ii) R'CHO, thf, -7	°C 78 °C	$\begin{array}{c} OH \\ H \\ H \\ H \\ H \\ OH \\ O$	DMSO, TFAA, ► H ₂ Cl ₂ , -78 °C Et ₃ N	S R R
		9			10
	<u>R</u>	R'	vield of 9/%	<u>yield of 10/%</u>	
	Ph	Me	88	93	
	Ph	Et	87	90	
	Me	Me	73	83	
	Me	Ph	68	89	
	Et	Me	52	78	
	Et	Et	86	74	
	Et	Pr	85	62	
	Et	PhCH ₂	42 †	67	
	Et	PhCH ₂ CH ₂	37†	77	

[†] overall yield from 1,3-dithiane

Preparation of 2-Acyl-2-Alkyl-1,3-Dithiane 1-Oxides

2-Acyl-2-alkyl-1,3-dithiane substrates were prepared by one of our standard procedures, ^{1a-i} which entailed the deprotonation of an appropriate 2-alkyl-1,3-dithiane, reaction with an aldehyde to

furnish an alcohol **9** which was subsequently oxidized to the acyl compound by the method of Swern, using trifluoroacetic anhydride as an activator of DMSO.²⁶ The desired 2-acyl-2-alkyl-1,3- dithianes **10** were produced in high overall yields, as shown in Table 4.

The work of both the Kagan and Modena groups on the asymmetric sulphoxidation of 1,3dithianes suggests a tendency for 2-disubstituted-1,3-dithianes to undergo enantioselective oxidation under modified Sharpless conditions with a higher degree of asymmetric induction than the corresponding 2-monosubstituted-1,3-dithianes which contain an acidic proton at the C2 position. As we obtained up to *ca*. 90% ee in the asymmetric oxidation of monosubstituted 2-acyl-1,3-dithianes, we expected to obtain excellent ees from the oxidation of 2-acyl-2-alkyl-1,3-dithianes, and, indeed, this proved to be the case, as shown in Table 5.²⁷ Again, *anti* isomers were formed as the major products of the oxidations.

S R'	oxidation method A CH ₂ Cl ₂	S ⁺ B S ⁺ B S	+	S ⁻ R S ⁺ R'
		syn		anti
		11		12

Table J. Asymmetric Oxidation of 2-Acyr-2-Aikyr-1,5-Diunane.	Table	5.	Asymmetric	Oxidation	of	2-Acyl-2-	Alkyl-	1,3-Dh	thianes
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<u>R</u>	R'	Yield/%	<u>[α]</u> _D 20/°	<u>e.e./%</u>
Ph	Ме	anti 65	-111.6	99*
		syn 6	-314.3	99*
Ph	Et	anti 42	+137.6	97*
		syn 15	+182.3	57 [*]
Me	Me	anti 47	+255.0	78
		syn 43	-243.2	82
Me	Ph	anti 58	+116.9	86
		syn 0	_	
Et	Me	anti 61	+274.7	81
		syn 4	+77.4	+
Et	Et	anti 67	+236.8	87
		syn 6	+132.3	+
Et	Pr	anti 60	+217.2	90
		syn 6	+139.4	+
Et	PhCH ₂	anti 65	+243.6	82
	-	syn 0		_
Et	PhCH,CH,	anti 61	+143.5	81
	£ £	syn 2	+51.0	81

The oxathiane **13** was also oxidized with excellent ee using a modified Sharpless procedure, as shown in Scheme 6. The predominant 1-oxide diastereoisomer formed, however, was in this case the *syn* isomer, confirmed by X-ray analysis.



Scheme 6. Asymmetric Oxidation of 2-Phenyl-2-Propanoyl-1,3-Oxathiane

Enantioselective Preparation of 2-Substituted-1,3-Dithiane 1-Oxides

During the course of our study of the asymmetric oxidation of 2-acyl-2-alkyl-1,3-dithianes,²¹ it became apparent that considerable destruction of our desired 1-oxide products was taking place during work-up through a deacylation process. Interestingly, however, the deacylated compounds, simple 2-alkyl-1,3-dithiane 1-oxides, were formed with high ee, suggesting that sulphur oxidation had taken place before deacylation, the high ee of the products being imparted by the initial presence of a dipolar acyl grouping within the molecule and the configurational stability of the sulfoxide units.

O S S S S S S		10% NaOH R'	10% NaOH,DCM/H ₂ O, rt or 10% NaOH, acetone/H ₂ O, 60 °C			
11	+ 12			2 -	+ 3	
<u>R</u>	<u>R'</u>	_anti : syn (10/11)	Yield/%	<u>anti : syn (product)</u>	<u>ee/%</u>	
Me	Me	1.2 : 1	91	1 : 7.9	77	
Et	Et	11:1	78	1:11	86	
Pr	Et		46	1:6	92	
Bu	Et		43	1:8	94	
Ph	Me	11:1	62	1:30	93	
Bn	Me		95	1:4	94	
PhS	Pr	3:2	35	1.6 : 1	77	

Table 6. Deacylation of 2-Acyl-2-Alkyl-1,3-Dithiane 1-Oxides

The deacylation process proved to result from over-long exposure to the normal alkaline work-up procedure, and conditions were subsequently refined to allow complete deacylation of 2-acyl-2-alkyl-1,3-dithiane 1-oxides **11,12** and 1,3-dioxides, producing an efficient asymmetric synthesis of 2-alkyl-1,3-dithiane 1-oxides **2,3** and 2-alkyl-1,3-dithiane 1,3-dioxides in much higher ee than can be obtained directly from 2-alkyl-1,3-dithianes by modified Sharpless conditions (Table

1).²¹ 2-Acyl-2-alkyl-1,3-dithiane 1-oxide mixtures were treated with 10% sodium hydroxide in dichloromethane/water at room temperature over 1-3 days, to furnish 2-alkyl-1,3-dithiane 1-oxides in high ees (Table 6). In some cases, heating of the acyl compound to 60 °C in acetone/water was required for efficient deacylation, although this was sometimes accompanied by some product decomposition.

Stereochemical integrity at the C2 position of the acyl dithiane oxides tends to be preserved during the deacylation reaction, in that predominantly *anti* acyl dithiane oxides give predominantly *syn* products upon deacylation, as would be expected for retention of configuration at C2. *syn*-2-Alkyl-1,3-dithiane 1-oxides are otherwise difficult to prepare, even in racemic form, due to favourable equatorial sulphoxidation. Clearly, however, product equilibration occurs to a certain extent in some cases, and, indeed, Kagan has witnessed a similar phenomenon.¹⁷ The fairly high ee of the *syn* product in the case of the 2-methyl compound indicates that the same absolute configuration at the sulphoxide sulphur atom is produced in both the *syn* and *anti* 2-methyl systems (Scheme 7).



Scheme 7. Deacylation of 2-Acyl-2-Alkyl-1,3-Dithiane 1-Oxides



Table 7. Deacylation of 2-Acyl-1,3-Dithlane 1-Oxides

Attempts to deacylate the *anti/syn* mixture of 2-carboethoxy-1,3-dithiane 1-oxides could not be achieved without decomposition, however both the 2-benzoyl- and 2-pivaloyl-1,3-dithiane 1-oxide mixtures underwent deacylation using 5% aqueous sodium hydroxide solution to furnish non-racemic 1,3-dithiane 1-oxide **2/3**, **R** = **H** (Table 7). In this way, enantiomerically pure 2-pivaloyl-1,3-dithiane 1-oxide was readily converted into enantiomerically pure 1,3-dithiane 1-oxide,²⁵ which had only previously been prepared rather less efficiently, principally by resolution-based methods.²⁸ Using this method, either optical antipode of 1,3-dithiane 1-oxide is available by appropriate choice of the chiral tartrate co-factor used in the asymmetric sulphur oxidation reaction, use of the natural (+)-DET leading to isolation of R-(+)-1,3-dithiane 1-oxide stage; we have so far been unable to recrystallize 1,3-dithiane 1-oxide from high ee to optical purity. This preparation of enantiomerically pure 1,3-dithiane 1-oxide is successful in quantities of several grammes.²⁹

2-Substituted-1,3-dithiane 1,3-dioxides may also be prepared in high ee's by this acylation/oxidation/deacylation procedure (Scheme 8). The dioxides obtained are of the *anti* configuration; *syn* 1,3-dioxides are achiral.



Scheme 8. Preparation of 2-Substituted-1,3-Dithiane anti 1,3-Dioxides

Acknowledgments

This investigation has enjoyed the support of the EPSRC and Pfizer Central Research (CASE award to RDW). We are indebted to the EPSRC very high field NMR services at the Universities of Edinburgh and Warwick for their help and patience.

EXPERIMENTAL SECTION

General experimental details

Purification of Reagents

Commercially available reagents were used as supplied unless otherwise stated. Butyllithium was purchased from the Aldrich Chemical Company in 800 mL bottles as a 2.5 M solution in hexanes. The molarity was determined by titration against a solution of diphenyl acetic acid. Sodium bis(trimethylsilyl)amide was purchased from the Aldrich Chemical Company in 100 or 800 mL bottles as a 1 M solution in tetrahydrofuran. 1,3-Dithiane was recrystallized if necessary and stored in a desiccator over self-indicating silica gel. (+)- and (-)- Diethyl tartrate (Aldrich) and titanium (IV) isopropoxide (Aldrich) were distilled under vacuum, and stored under nitrogen in the presence of molecular sieves. Cumene hydroperoxide (80%) and *tert*-butyl hydroperoxide (80%) were purchased from the Aldrich Chemical Company and used as supplied.

Purification of Solvents

Tetrahydrofuran and diethyl ether were freshly distilled under nitrogen from the sodium/benzophenone ketyl radical immediately prior to use. Toluene and dichloromethane were allowed to stand over calcium hydride overnight prior to distillation under nitrogen. Ethyl acetate and petroleum ether were distilled prior to use. Petroleum ether refers to petroleum ether (bp 40-60 °C).

Preparation of glassware

All organometallic and oxidation reactions were carried out in round bottomed flasks which were either oven baked at 150 °C overnight or dried in a Bunsen burner flame. The flasks were allowed to cool in a dessicator over self-indicating silica gel, and were purged with nitrogen prior to being stoppered with septum caps. Syringes, needles, cannulas, and magnetic stirrer bars were also oven baked, and allowed to cool in a desiccator. Reactions were maintained under a slight static positive pressure of nitrogen, and reagents and solvents introduced *via* syringe or using cannula techniques, through a septum cap.

Purification of Products

Flash column chromatography was carried out using Merck 9385 Kieselgel 60 (230-400 mesh), using hand bellows or an air line to apply pressure to the column. Ethyl acetate was used as eluent for the purification of oxidation products unless otherwise stated. A Büchi GK*R*-50 Kugelrohr oven was used as the heat source for bulb to bulb distillations; boiling points quoted refer to the oven temperature. Thin layer chromatography was carried out using glass or aluminium backed plates coated with a 0.25 mm layer of silica gel 60H containing fluorescer, using ethyl acetate as eluent unless otherwise stated. UV inactive compounds were visualized by spraying with either dodecamolydophosphoric acid (15% w/v in ethanol), or an alkaline solution of potassium permanganate (1% w/v in water) followed in both cases by charring where appropriate.

Spectroscopy and other data

Infrared spectra were recorded in the range 4000-600 cm⁻¹ using Perkin-Elmer 883 and Pye-Unicam SP2000 spectrophotometers, and were calibrated against the 1602 cm⁻¹ absorption of polystyrene. Solid samples were run as Nujol mulls on sodium chloride plates, as thin potassium bromide discs or as solutions in chloroform, and liquids as thin films on sodium chloride plates. ¹H NMR spectra were recorded using Bruker AC200, Bruker WM250, or Bruker AMX400 instruments, using deuteriochloroform solutions except where stated, and tetramethylsilane as an internal reference. High field NMR spectra were also obtained by the 400 MHz service at the University of Warwick and the 500 MHz instrument at Imperial College, London. Mass spectra were obtained on VG Micromass 7070E and Fisons Trio 1000 mass spectrometers. Microanalyses were performed using a Carlo Erba elemental analyser at the University of Liverpool Department of Chemistry microanalytical laboratory or at Pfizer Central Research, Sandwich. Melting points were determined on a Reichert hot stage apparatus and are uncorrected. Optical rotations were measured on an Optical Activity AA-1000 polarimeter operating at λ =589 nm, corresponding to the sodium D line. Enantiomeric excesses were determined by ¹H NMR chiral shift reagent studies using (R)-(-)- or (S)-(+)-2, 2, 2-trifluoro-1-(9-anthryl)ethanol (Pirkle reagent), except where stated. In general, ten molar equivalents of Pirkle reagent were employed for each determination of optical purity.

Normal work-up procedure

Organometallic reactions were worked up by the addition of saturated aqueous ammonium chloride, followed by extraction of the aqueous phase into dichloromethane. The combined organic

extracts were washed with water and dried over anhydrous magnesium sulphate, which was subsequently removed by filtration. The solvents were removed under reduced pressure, and the crude products subjected to purification.

2-(4-Bromophenyl)-1,3-dithiane 1, $\mathbf{R} = \mathbf{p} - \mathbf{C_6} \mathbf{H_4} \mathbf{Br}$

1,3-Propane dithiol (6.00 g, 5.56 mL, 55 mmol) and a catalytic amount of *para* toluenesulphonic acid were added to 4-bromobenzaldehyde (11.30 g, 61 mmol) in toluene (70 mL). The mixture was heated under reflux in a Dean-Stark apparatus for 3 hours, allowed to cool to room temperature, and the solution poured onto water (50 mL). The organic layer was collected, and the aqueous layer extracted with diethyl ether (3 x 50 mL). The combined organic extracts were washed with water, dried over magnesium sulphate and the solvent removed *in vacuo* to yield 2-(4-bromophenyl)-1,3-dithiane as a beige solid which was recrystallized from methanol (14.20 g, 93%), mp 88-89 °C; v_{max} (KBr disc) 2900, 850 and 800 cm⁻¹; δ_{H} (250 MHz, CDCl₃) 1.85-2.06 (1H, m), 2.14-2.29 (1H, m), 2.85-3.18 (4H, m), 5.15 (1H, s), 7.37 (2H, d, *J* = 9.7 Hz) and 7.51 (2H, d, *J* = 9.7 Hz); *m/z* (El) 274/276 (M⁺). Found: C, 43.67; H, 3.96. C₁₀H₁₁S₂Br requires C, 43.64; H, 4.03%.

2-Thiomethyl-1,3-dithiane 1a

A solution of dimethyldisulphide (3.30 mL, 36.7 mmol) in thf (50 mL), precooled to -78 °C, was added to a solution of 2-lithio-1,3-dithiane (33.3 mmol) in thf (100 mL). The solution was allowed to reach room temperature overnight. Normal work-up procedure and flash column chromatography using 10% ethyl acetate/petroleum ether as eluent gave 2-thiomethyl-1,3-dithiane as a yellow oil (5.53 g, 100%); v_{max} (neat) 2910 cm⁻¹; δ_{H} (200 MHz, CDCl₃) 1.94-2.14 (2H, m), 2.24 (3H, s), 2.56-2.77 (2H, m), 3.11-3.37 (2H, m) and 4.80 (1H, s); *m/z* (El)166 (M⁺). Found: C, 36.54; H, 6.17. C₅H₁₀S₃ requires C, 36.11; H, 6.06%.

2-Trimethylsilyl-1 3-dithiane 1b

A 2.5 M solution of butyllithium in hexanes (13.97 mL, 34.9 mmol) was added to a solution of 1,3-dithiane (3.50 g, 29.1 mmol) in thf (50 mL) at -78 °C. The resulting pale yellow solution was stirred at -78 °C for 1.5 hours before addition by cannula to a solution of chlorotrimethylsilane (3.48 g, 4.06 mL, 32.0 mmol) in thf (50 mL) at -78 °C. The mixture was allowed to reach room temperature overnight. Normal work-up yielded a pale yellow oil. Bulb to bulb distillation gave 2-trimethylsilyl-1 3-dithiane as a colourless oil (3.4 g, 60%), bp 70–73 °C at 0.7 mmHg; v_{max} (neat) 2897, 1422, 1250 and 844 cm⁻¹; $\delta_{\rm H}$ (200 MHz, CDCl₃) 0.15 (9H, s), 1.85-2.20 (2H, m), 2.62-2.96 (4H, m) and 3.70 (1H, s); *m/z* (EI) 192.04597 (M⁺); C₇H₁₆S₂Si requires 192.04627. Found: C, 43.53; H, 8.37. C₇H₁₆S₂Si requires C, 43.70; H, 8.38%.

2-Triisopropylsilyl-1,3-dithiane 1c

A 2.5 M solution of butyllithium in hexanes (1.83 mL, 4.57 mmol) was added to a solution of 1,3-dithiane (0.50 g, 4.16 mmol) in thf (30 mL) at -35 °C. The resulting pale yellow solution was stirred at -35 °C for one hour before addition by cannula to a solution of chlorotriisopropylsilane (0.80 g, 0.89 mL, 4.16 mmol) in thf (10 mL) at -35 °C. The mixture was allowed to reach room temperature over 3 hours. Normal work-up yielded an orange oil. Bulb to bulb distillation gave 2-triisopropylsilyl-1,3-dithiane as a colourless solid (1.04 g, 90%), bp 130 °C at 0.2 mmHg; mp 43-45 °C; v_{max} (Nujol) 2852 and 762 cm⁻¹; δ_{H} (200 MHz, CDCl₃) 1.04-1.07 (3H, m), 1.05 (18H, s), 2.01-2.14 (2H, m), 2.76-2.90 (4H, m) and 3.78 (1H, s); *m/z* (GC/MS) 277 (M⁺ +1). Found: C, 56.27; H, 10.26. C₁₃H₂₈S₂Si requires C, 56.46; H, 10.20%.

2-Tributylstannyl-1,3-dithiane 1d

A 2.3 M solution of butyllithium in hexanes (11.93 mL, 27.5 mmol) was added to a solution of 1,3-dithiane (3.00 g, 25.0 mmol) in thf (50 mL) at -78 °C. The resulting pale yellow solution was stirred at -78 °C for one hour. Tributyltin chloride (8.93 g, 7.45 mL, 27.5 mmol) in thf (20 mL) was added and the mixture allowed to reach room temperature overnight. Water (20 mL) was added, and the aqueous phase extracted into petroleum ether (3 x 50 mL). The combined organic layers were washed with water (50 mL), dried over magnesium sulphate and the solvents removed *in vacuo* to yield a brown oil. Bulb to bulb distillation gave 2-tributylstannyl-1,3-dithiane as a colourless oil (6.96 g, 68%), bp 170-175 °C at 0.3 mmHg; v_{max} (neat) 2925 cm⁻¹; δ_{H} (200 MHz, CDCl₃) 0.74-1.75 (27H, m), 2.01-2.22 (2H, m), 2.49-2.68 (2H, m), 2.76-3.03 (2H, m) and 4.00 (1H, s); *m/z* (EI) 410/408 and 406.11198 (M⁺); C₁₆H₃₄S₂¹¹⁶Sn requires 406.11194.

2-Thiophenyl-1,3-dithiane 1e

N-Chlorosuccinimide (6.18 g, 46.3 mmol) in powder form was added to a solution of 1,3dithiane (5.06 g, 42.1 mmol) in toluene (100 mL) at room temperature over a period of 15 minutes. The mixture was stirred at room temperature for a further 15 minutes and filtered to remove solid residues. Thiophenol (12.96 g, 126.2 mmol) was added dropwise to the filtrate under a nitrogen atmosphere. After stirring for 3 hours, the solvents were removed *in vacuo* to yield a yellow oil. Trituration with cold hexane gave 2-thiophenyl-1,3-dithiane as a colourless solid (4.18 g, 44%), mp 59-60 °C; v_{max} (NuJol) 2926 cm⁻¹; δ_{H} (200 MHz, CDCl₃) 1.91-2.18 (2H, m), 2.62-2.80 (2H, m), 3.26-3.45 (2H, m), 5.14 (1H, s), 7.29-7.40 (3H, m) and 7.46-7.57 (2H, m); *m/z* (EI) 228 (M⁺). Found: C, 52.60; H, 5.28. C₁₀H₁₂S₃ requires C, 52.59; H, 5.30%.

2-Methoxy-1,3-dithiane 1f

Anhydrous chloramine-T (12.50 g, 55.0 mmol) was added to a solution of 1,3-dithiane (6.00 g, 50.0 mmol) in methanol (300 mL) at 0 °C. The mixture was stirred for 5 minutes, and potassium hydroxide (11.20 g, 200.0 mmol) added. The mixture was allowed to reach room temperature overnight. The resulting colourless suspension was reduced to *ca*. one quarter of its volume by removal of methanol *in vacuo*. The suspension was poured onto water (200 mL), and the resulting mixture extracted into diethyl ether (3 x 100 mL). The combined organic layers were dried over magnesium sulphate and the solvents removed *in vacuo* to yield a pale yellow oil. Flash column chromatography using 5% ethyl acetate/petroleum ether as eluent gave 2-methoxy-1,3-dithiane as a colourless oil (5.26 g, 70%); v_{max} (neat) 2932 and 1064 cm⁻¹; $\delta_{\rm H}$ (200 MHz, CDCl₃) 2.06-2.21 (2H, m), 2.54-2.68 (2H, m), 3.20-3.40 (2H, m), 3.50 (3H, s) and 5.14 (1H, s); *m/z* (EI) 150.01730 (M⁺); C₅H₁₀OS₂ requires 150.01731.

2-Cyano-1,3-dithiane 1g

Triphenylcarbenium tetrafluoroborate (1.51 g, 4.57 mmol) was added to a solution of 1,3dithiane (0.50 g, 4.16 mmol) in dichloromethane (30 mL). The mixture was heated under reflux for 45 minutes, allowed to cool to room temperature, and the solvents removed *in vacuo* to yield an orange solid. Trituration with cold, dry diethyl ether gave 1,3-dithienium tetrafluoroborate as a yellow solid (0.81 g, 94%). Trimethylsilyl cyanide (0.36 g, 0.48 mL, 3.64 mmol) was added to 1,3dithienium tetrafluoroborate (0.75 g, 3.64 mmol) In dichloromethane (50 mL) under a nitrogen atmosphere at -20 °C. The reaction mixture was stirred at -20 °C for one hour and quenched by the addition of 1N hydrochloric acid (1 mL). The resulting solution was washed with saturated aqueous ammonium chloride (50 mL), the aqueous layer extracted with dichloromethane (2 x 15 mL), the combined organic layers dried over magnesium sulphate and the solvents removed *in vacuo* to yield a brown solid, which was purified by flash column chromatography using 10% ethyl acetate/petroleum ether as eluent to give 2-cyano-1,3-dithiane as a pale brown solid (0.52 g, 98%) (92% over 2 steps), mp 87-88 °C; v_{max} (Nujol) 2926 and 2228 cm⁻¹; δ_H (200 MHz, CDCl₃) 1.92-2.32 (2H, m), 2.73-2.95 (2H, m), 3.26-3.46 (2H, m) and 4.41 (1H, s); *m/z* (EI) 145.00197 (M⁺); C₅H₇NS₂ requires 145.00199. Found: C, 41.32; H, 4.87; N, 9.61. C₅H₇NS₂ requires C, 41.35; H, 4.86; N, 9.64%.

2-(2,2-Dimethylpropanoyl) -1,3-dithiane 6a

A 1 M solution of sodium bis(trimethylsilyl)amide in thf (13.7 mL, 13.7 mmol) was added to a solution of 1,3-dithiane (1.5 g, 12.5 mmol) in thf (25 mL) at -78 °C. The resulting yellow solution was stirred at -78 °C for 15 minutes. A 2.5 M solution of butyllithium in hexanes (1.2 eq., 6.0 mL, 15 mmol) was added and the yellow solution stirred at -78 °C for a further 10 minutes. Ethyl 2,2-dimethylpropanoate (1.78 g, 2.10 mL, 13.7 mmol) was added and the mixture allowed to reach room temperature over 1 hour. Normal work-up procedure yielded a yellow solid. Repeated trituration with petroleum ether followed by filtration gave 2-(2,2-dimethylpropanoyl)-1,3-dithiane as colourless needles (1.99 g, 78%), mp 97-99 °C; v_{max} (Nujol) 2900 and 1673 cm⁻¹; δ_{H} (400 MHz, CDCl₃) 1.23 (9H, s), 1.89-2.07 (1H, m), 2.08-2.25 (1H, m), 2.50-2.59 (2H, m), 3.36-3.51 (2H, m) and 4.51 (1H, s); *m/z* (El) 204.06445 (M⁺); C₉H₁₆OS₂ requires 204.06426. Found: C, 52.73; H, 7.87. C₉H₁₆OS₂ requires C, 52.90; H, 7.89%.

2-Benzoyl-1,3-dithiane 6b

A 1 M solution of sodium bis(trimethylsilyl)amide in thf (13.7 mL, 13.7 mmol) was added to a solution of 1,3-dithiane (1.5 g, 12.5 mmol) in thf (35 mL) at -78 °C. The resulting yellow solution was stirred at -78 °C for 15 minutes. A 2.5 M solution of butyllithium in hexanes (1.2 eq., 6.0 mL, 15 mmol) was added and the yellow solution stirred at -78 °C for a further 10 minutes. Ethyl benzoate (2.06 g, 1.96 mL, 13.7 mmol) was added and the mixture allowed to reach room temperature over 1 hour. Normal work-up procedure yielded a pale yellow solid. Flash column chromatography using 100% dichloromethane as eluent gave 2-benzoyl-1,3-dithiane as an off-white solid (2.05 g, 73%), mp 100-101.5 °C; v_{max} (Nujol) 2924 and 1666 cm⁻¹; δ_{H} (200 MHz, CDCl₃) 1.95-2.28 (2H, m), 2.60-2.90 (2H, m), 3.27-3.48 (2H, m), 5.16 (1H, s), 7.36-7.64 (3H, m) and 7.90-8.10 (2H, m); *m/z* (El) 224.03303 (M⁺); C₁₁H₁₂OS₂ requires 224.03296. Found: C, 59.20; H, 5.42. C₁₁H₁₂OS₂ requires C, 58.89; H, 5.39%.

2-N,N-Dimethylamino-1,3-dithiane

1,3-Propanedithiol (3.00 g, 2.78 mL, 27.7 mmol) and *N*, *N*-dimethylformamide dimethyl acetal (3.68 mL, 27.7 mmol) were heated under reflux overnight in toluene (50 mL) under Dean-Stark conditions in the presence of 4Å molecular sieves and a catalytic amount of *para* toluenesulphonic acid. The reaction mixture was allowed to cool, water (30 mL) added, and the aqueous phase extracted into diethyl ether (2 x 50 mL). The combined organic layers were washed with water (30 mL), dried (MgSO₄) and the solvents removed *in vacuo* to yield a pale yellow oil. Bulb to bulb distillation gave 2-*N*,*N*-dimethylamino-1,3-dithiane as a colourless oil (0.45 g, 10%); v_{max} (neat) 2940 and 1043 cm⁻¹; δ_{H} (200 MHz, CDCl₃) 1.94-2.14 (2H, m), 2.49 (6H, s), 2.87-3.03 (4H, m), 5.30 (1H, s); *m/z* (EI) 163.04919 (M⁺); C₆H₁₃NS₂ requires 163.04894.

General method of asymmetric oxidation (Method A)

Titanium (IV) isopropoxide (1 eq.) was added to a solution of (+)-diethyl-(L)-tartrate (2 eq.) in dichloromethane under a nitrogen atmosphere. The resulting pale yellow solution was stirred at room temperature for 5 minutes. Water (1 eq.) was added carefully and the solution stirred at room temperature for a further 30 minutes. The 1,3-dithiane substrate was dissolved in dichloromethane and added by syringe to the mixture. The solution was stirred at room temperature for 5 minutes

and then at between -20 and -40 °C (actual temperature stated below for each substrate) for 30 minutes. Hydroperoxide oxidant (1-2 eq.) was added and the mixture stirred at between -20 and - 40 °C for 1-6 days.

General method of asymmetric oxidation (Method B)

Titanium (IV) isopropoxide (1 eq.) was added to a solution of (+)-diethyl-(L)-tartrate (4 eq.) in dichloromethane under a nitrogen atmosphere. The resulting pale yellow solution was stirred at room temperature for 5 minutes. The 1,3-dithiane substrate was dissolved in dichloromethane and added by syringe to the mixture. The solution was stirred at room temperature for a further 5 minutes and then at between -20 and -40 °C (actual temperature stated below for each substrate) for 30 minutes. Hydroperoxide oxidant (1 eq.) was added and the mixture stirred at between -20 and -40 °C (or 1-6 days.

Oxidation work-up procedure

Water (10 eq.) was added to the reaction mixture and the mixture stirred at -20 to -40 °C for one hour and allowed to reach room temperature over one hour further with stirring. Celite was added together with additional dichloromethane, and the mixture stirred for a further 5 minutes. The mixture was filtered under vacuum and the celite washed with several portions of dichloromethane. The filtrate was washed with 5% aqueous sodium thiosulphate solution saturated with brine, 5% aqueous sodium hydroxide solution saturated with brine, dried over magnesium sulphate, and the solvents removed *in vacuo* to give a crude oily reaction mixture. Flash column chromatography using, in most cases, 100% ethyl acetate as eluent, furnished the desired 1,3-dithiane 1-oxide products.

1,3-Dithiane 1*R*-oxide **2**, $\mathbf{R} = \mathbf{H}$ (method A)

Treatment of 1,3-dithiane (0.50 g, 4.16 mmol), under the conditions described above using (+)-diethyl-(L)-tartrate (1.72 g, 1.42 mL, 8.32 mmol), titanium (IV) isopropoxide (1.18 g, 1.24 mL, 4.16 mmol), water (75 μ L, 4.16 mmol) and cumene hydroperoxide (0.87 g, 0.85 mL, 5.72 mmol) at ~20 °C for 4 days, followed by flash column chromatography using gradient elution from 100% dichloromethane to 5% ethanol/dichloromethane as eluent, furnished 1.3-dithiane 1*R*-oxide as a colourless solid (0.405 g, 71%), mp 106-107 °C; ν_{max} (Nujol) 2950 and 1050 cm⁻¹; δ_{H} (250 MHz, CDCl₃) 2.19-2.32 (1H, m), 2.40-2.70 (4H, m), 3.25-3.38 (1H, m), 3.64 (1H, d, *J* = 12.8 Hz) and 3.98 (1H, dd, *J* = 2.8 and 12.7 Hz); ee = 7% (splitting signal at δ 3.64); *m/z* (El) 136 (M⁺). Found: C, 35.46; H, 5.89. C₄H₈OS₂ requires C, 35.27; H, 5.89%.

1,3-Dithiane 1*R*-oxide 2, R = H (method B)

Treatment of 1,3-dithiane (0.50 g, 4.16 mmol) under the conditions described above (method B) using (+)-diethyl-(L)-tartrate (3.43 g, 2.85 mL, 16.64 mmol), titanium (IV) isopropoxide (1.18 g, 1.24 mL, 4.16 mmol) and cumene hydroperoxide (0.87 g, 0.85 mL, 5.72 mmol) at ~20 °C for 4 days, followed by flash column chromatography using 5% ethanol/ dichloromethane as eluent, furnished 1,3-dithiane 1*R*-oxide as a colourless solid (0.31 g, 55%), ee = 17%.

anti-2-Methyl-1,3-dithiane 1*R*-oxide 3, **R** = Me (method A)

Treatment of 2-methyl-1,3-dithiane (0.45 g, 3.37 mmol) under the conditions described above (method A) using (+)-diethyl-(L)-tartrate (1.39 g, 1.16 mL, 6.75 mmol), titanium (IV) isopropoxide (0.96 g, 1.00 mL, 3.37 mmol), water (61 μ L, 3.37 mmol) and *tert*-butyl hydroperoxide (0.42 g, 0.45 mL, 4.63 mmol) at -20 °C for 3 days furnished *anti*-2-methyl-1,3-dithiane 1*R*-oxide as a colourless solid (0.350 g, 69%), mp 92-94 °C; v_{max} (Nujol) 2900 and 1010 cm⁻¹; δ_{H} (200 MHz,

CDCl₃) 1.62 (3H, d, J = 7.2 Hz), 2.20-2.85 (5H, m), 3.33-3.48 (1H, m) and 3.63 (1H, q, J = 7.2 Hz); ee = 10% (splitting signal at δ 1.62, determined using *R*-(-)-*N*-(3,5-dinitrobenzoyl)- α -methylbenzylamine (1 eq.)); m/z (Cl) 151 (M⁺ +1); $[\alpha]_D^{20} = +18.9^\circ$ (c = 1.37, CH₂Cl₂). Found: C, 39.85; H, 6.74. C₅H₁₀OS₂ requires C, 39.97; H, 6.71%.

anti-2-Phenyl-1,3-dithiane 1*R*-oxide 3, **R** = Ph (method A)

Treatment of 2-phenyl-1,3-dithiane (0.50 g, 2.55 mmol), under the conditions described above (method A) using (+)-diethyl-(L)-tartrate (1.05 g, 0.87 mL, 5.10 mmol), titanium (IV) isopropoxide (0.725 g, 0.76 mL, 2.55 mmol), water (61 μ L, 3.37 mmol) and *tert*-butyl hydroperoxide (0.53 g, 0.52 mL, 3.51 mmol) at -20 °C for 3 days furnished *anti*-2-phenyl-1,3-dithiane 1*R*-oxide as a colourless solid (0.450 g, 83%); mp 146-148 °C; v_{max} (Nujol) 2900 and 1040 cm⁻¹; $\delta_{\rm H}$ (200 MHz, CDCl₃) 2.20-2.50 (2H, m), 2.55-2.95 (3H, m), 3.45-3.60 (1H, m), 4.55 (1H, s) and 7.34-7.48 (5H, m); ee = 10% (splitting signal at δ 4.55, determined using tris[3-(trifluoromethylhydroxymethylene)-(+)-camphorato]europium (III) [(+)-Eu(tfc)₃], (0.2 eq.); *m/z* (EI) 212 (M⁺); [α]_D²⁰ = -6.9° (*c* = 1.44, CH₂Cl₂). Found: C, 56.47; H, 5.70. C₁₀H₁₂OS₂ requires C, 56.57; H, 5.70%.

syn- And anti-2- (4-bromophenyl)-1,3-dithiane 1*R*-oxides 2 and 3, $\mathbf{R} = \mathbf{pC_6H_4Br}$ (method A)

Treatment of 2-(4-bromophenyl)-1,3-dithiane (0.60 g, 2.18 mmol) under the conditions described above (method A) using (+)-diethyl-(L)-tartrate (0.89 g, 0.75 mL, 4.36 mmol), titanium (IV) isopropoxide (0.62 g, 0.65 mL, 2.18 mmol), water (39 μ L, 2.18 mmol) and cumene hydroperoxide (0.40 mL, 2.73 mmol) at -20 °C for 5 days, followed by reverse phase HPLC using gradient elution from 50% methanol/water to 100% methanol as eluent, furnished the *syn* sulphoxide as a colourless solid (21 mg, 7%) and the *anti* sulphoxide as a colourless solid (0.170 g, 54%).

syn- And anti-2-(4-bromophenyl)-1,3-dithiane 1*R*-oxides 2 and 3, $\mathbf{R} = \mathbf{pC_6H_4Br}$ (method B)

Treatment of 2-(4-bromophenyl)-1,3-dithiane (0.60 g, 2.18 mmol) under the conditions described above (method B) using (+)-diethyl-(L)-tartrate (1.80 g, 1.50 mL, 8.72 mmol), titanium (IV) isopropoxide (0.62 g, 0.65 mL, 2.18 mmol) and cumene hydroperoxide (0.40 mL, 2.73 mmol) at – 20 °C for 5 days, followed by reverse phase HPLC using gradient elution from 50% methanol/water to 100% methanol as eluent, furnished the *syn* sulphoxide as a colourless solid (20 mg, 6%) and the *anti* sulphoxide as a colourless solid (0.193 g, 61%).

For *syn*-2-(4-bromophenyl)-1,3-dithiane 1*R*-oxide **2**, **R** = pC_6H_4Br : mp 190-191 °C; v_{max} (Nujol) 2924 and 1040 cm⁻¹; δ_H (250 MHz, CDCl₃) 1.84-2.00 (1H, m), 2.63-2.85 (3H, m), 2.97-3.13 (1H, m), 3.21-3.32 (1H, m), 4.75 (1H, s), 7.36 (2H, d, *J* = 9 Hz) and 7.55 (2H, d, *J* = 9 Hz); ee = 13% (method A); 20% (method B) (splitting signal at δ 4.75); *m/z* (Cl) 291/293 (M⁺ + 1). Found: C, 41.25; H, 3.80. C₁₀H₁₁OS₂Br requires C, 41.24; H, 3.81%.

For *anti*-2-(4-bromophenyl)-1,3-dithiane 1*R*-oxide **3**, **R** = pC_6H_4Br : mp 161-162 °C; v_{max} (Nujol) 2924 and 1041 cm⁻¹; δ_H (250 MHz, CDCl₃) 2.27-2.63 (2H, m), 2.63-2.97 (3H, m), 3.55-3.63 (1H, m), 4.53 (1H, s), 7.29 (2H, d, *J* = 12 Hz) and 7.53 (2H, d, *J* = 12 Hz); ee = 22% (method A); 17% (method B) (splitting signal at δ 4.53); *m/z* (Cl) 291/293 (M⁺ + 1). Found: C, 41.13; H, 3.75. C₁₀H₁₁OS₂Br requires C, 41.24; H, 3.81%.

syn- And anti-2-thiomethyl-1,3-dithiane 1R-oxides 2 and 3, R = MeS (method A)

Treatment of 2-thiomethyl-1,3-dithiane (0.50 g, 3.01 mmol) under the conditions described above (method A) using (+)-diethyl-(L)-tartrate (1.24 g, 1.03 mL, 6.011 mmol), titanium (IV) isopropoxide (0.85 g, 0.895 mL, 3.01 mmol), water (54 μ L, 3.01 mmol) and cumene hydroperoxide (0.57 g, 0.56 mL, 3.76 mmol) at -35 °C for 1 day furnished the *syn* sulphoxide as a clear oil (20 mg, 4%) and the *anti* sulphoxide as a colourless crystalline solid (0.178 g, 32%).

syn- And anti-2-thiomethyl-1,3-dithiane 1*R*-oxides 2 and 3, R = MeS (method B)

Treatment of 2-thiomethyl-1,3-dithiane (0.50 g, 3.01 mmol) under the conditions described above (method B) using (+)-diethyl-(L)-tartrate (2.48 g, 2.06 mL, 12.04 mmol), titanium (IV) isopropoxide (0.85 g, 0.89 mL, 3.01 mmol) and cumene hydroperoxide (0.57 g, 0.56 mL, 3.76 mmol) at -30 °C for 4 days furnished the *syn* sulphoxide as a clear oil (31 mg, 6%) and the *anti* sulphoxide as a colourless crystalline solid (40 mg, 7%).

For *syn*-2-thiomethyl-1,3-dithiane 1*R*-oxide **2**, **R** = **MeS**: v_{max} (neat) 2925 and 1056 cm⁻¹; δ_{H} (200 MHz, CDCl₃) 2.11-2.49 (3H, m), 2.48 (3H, s), 2.79-3.11 (2H, m), 3.17-3.40 (1H, m) and 4.91 (1H, s); ee = 16% (splitting signal at δ 4.93); *m/z* (EI) 181.98933 (M⁺); C₅H₁₀OS₃ requires 181.98938; [α]_D²⁰ = +5.9° (c = 0.196, EtOH).

For *anti*-2-thiomethyl-1,3-dithiane 1*R*-oxide **3**, **R** = **MeS**: mp 76–78 °C; v_{max} (Nujol) 2950 and 1040 cm⁻¹; δ_{H} (200 MHz, CDCl₃) 1.95-2.18 (1H, m), 2.35 (3H, s), 2.43-2.95 (4H, m), 3.32-3.49 (1H, m) and 4.39 (1H, s); ee = 16% (splitting signal at δ 4.39); *m/z* (EI) 181.98951 (M⁺); C₅H₁₀OS₃ requires 181.98938; [α]_D²⁰ = +41.0° (c = 0.05, EtOH).

anti-2-Thiophenyl~1,3-dithiane 1*R*-oxide 3, R = PhS (method A)

Treatment of 2-thiophenyl-1,3-dithiane (96 mg, 0.42 mmol) under the conditions described above (method A) using (+)-diethyl-(L)-tartrate (0.17 g, 0.144 mL, 0.84 mmol), titanium (IV) isopropoxide (0.12 g, 0.125 mL, 0.42 mmol), water (8 μ L, 0.42 mmol) and cumene hydroperoxide (78 μ L, 0.525 mmol) at -32 °C for 5 days furnished the *anti* sulphoxide as a pale yellow crystalline solid (67 mg, 65%), mp 91-93 °C; v_{max} (Nujol) 2924 and 1023 cm⁻¹; δ_{H} (200 MHz, CDCl₃) 1.84-2.08 (1H, m), 2.39-3.01 (4H, m), 3.18-3.50 (1H, m), 4.67 (1H, s), 7.29-7.42 (3H, m) and 7.54-7.66 (2H, m); ee = 10% (splitting signal at δ 4.67); m/z (El) 244.00520 (M⁺); C₁₀H₁₂OS₃ requires 244.00503; [α]_D²⁰ = +39.1° (c = 0.046, EtOH). Found: C, 48.87; H, 5.25. C₁₀H₁₂OS₃ requires C, 49.15; H, 4.95%.

syn- And anti-2-methoxy-1,3-dithiane 1*R*-oxides 2 and 3, R = MeO (method A)

Treatment of 2-methoxy-1,3-dithiane (0.20 g, 1.33 mmol) under the conditions described above (method A) using (+)-diethyl-(L)-tartrate (0.55 g, 0.456 mL, 2.66 mmol), titanium (IV) isopropoxide (0.378 g, 0.396 mL, 1.33 mmol), water (24 μ L, 1.33 mmol) and cumene hydroperoxide (0.25 g, 0.246 mL, 1.66 mmol) at -31 °C for 5 days furnished an inseparable mixture of the *syn* and *anti* sulphoxides (5 : 2) as a colourless oil (0.138 g, 63%); v_{max} (neat) 2927, 1087 and 1030 cm⁻¹; $\delta_{\rm H}$ (400 MHz, CDCl₃) (major isomer) 1.72-1.77 (1H, m), 2.12-2.39 (1H, m), 2.59-2.64 (1H, m), 2.80-2.85 (1H, m), 2.92-3.04 (2H, m), 3.65 (3H, s) and 5.04 (1H, s); (minor isomer) distinct signals at 3.32-3.40 (1H, m), 3.76 (3H, s) and 5.34 (1H, s); *m/z* (EI) 166.01209 (M⁺); C₅H₁₀O₂S₂ requires 166.01222; ee could not be determined. Found: C, 35.83; H, 6.09. C₅H₁₀O₂S₂ requires C, 36.12; H, 6.06%.

anti-2-Trimethylsilyl-1,3-dithiane 1*R*-oxide 3, **R = Me₃Si** (method A)

Treatment of 2-trimethylsilyl-1,3-dithiane (0.316g, 1.64 mmol) under the conditions described above (method A) using (+)-diethyl-(L)-tartrate (0.68 g, 0.56 mL, 3.29 mmol), titanium (IV) isopropoxide (0.47 g, 0.49 mL, 1.64 mmol), water (29.6 μ L, 1.64 mmol) and cumene hydroperoxide (0.304 mL, 2.05 mmol) at -32 °C for 1 day, followed by usual work-up and flash column chromatography using 5% ethanol/dichloromethane as eluent, furnished the *anti* sulphoxide as a colourless oil (0.31 g, 91%); v_{max} (neat) 2909, 1253, 1020 and 848 cm⁻¹; δ_{H} (400 MHz, CDCl₃) 0.26 (9H, s), 2.20-2.70 (5H, m), 3.21 (1H, s) and 3.39-3.48 (1H, m) ; ee = 65% (splitting signal at δ 3.21); *m/z* (El) 208.04110 (M⁺); C₇H₁₆OS₂Si requires 208.04119; [α]_D²⁰ = +2.2° (c = 0.156, EtOH).

anti-2-Tributylstannyl-1,3-dithiane 1*R*-oxide **3**, **R** = **Bu₃Sn** (method A)

Treatment of 2-tributyIstannyl-1,3-dithiane (0.50g, 1.22 mmol) under the conditions described above (method A) using (+)-diethyl-(L)-tartrate (0.50 g, 0.42 mL, 2.44 mmol), titanium (IV) isopropoxide (0.35 g, 0.36 mL, 1.22 mmol), water (22 μ L, 1.22 mmol) and cumene hydroperoxide (0.23 mL, 1.53 mmol) at -35 °C for 3 days furnished the *anti* sulphoxide as a pale yellow oil (0.224 g, 43%); v_{max} (neat) 2923 and 1020 cm⁻¹; δ_{H} (200 MHz, CDCl₃) 0.90 (9H, t, *J* = 6.0 Hz), 1.04-1.70 (18H, m), 2.22-2.61 (5H, m), 3.39 (1H, s) and 3.30-3.48 (1H, m); *m/z* (EI) 425, 427 and 429 (M⁺).

syn-2-Cyano-1,3-dithiane 1*R*-oxide 2, R = CN (method A)

Treatment of 2-cyano-1,3-dithiane (0.30 g, 2.07 mmol) under the conditions described above (method A) using (+)-diethyl-(L)-tartrate (0.85 g, 0.71 mL, 4.13 mmol), titanium (IV) isopropoxide (0.59 g, 0.62 mL, 2.07 mmol), water (37 μ L, 2.07 mmol) and cumene hydroperoxide (0.38 mL, 2.58 mmol) at -35 °C for 3 days furnished the *syn* sulphoxide as a pale yellow crystalline solid (0.27 g, 80%), mp 94-95 °C; v_{max} (Nujol) 2924, 2233 and 1059 cm⁻¹; δ_{H} (200 MHz, CDCI₃) 2.28-2.41 (1H, m), 2.45-2.65 (2H, m), 2.92-3.25 (2H, m), 3.32-3.45 (1H, m) and 4.81 (1H, s); ee = 37% (splitting signal at δ 4.81); *m/z* (El) 160.99671 (M⁺); C₅H₇NOS₂ requires 160.99691; [α]_D²⁰ = +69.8° (c = 0.044, EtOH). Found: C, 37.24; H, 4.44; N, 8.34. C₅H₇NOS₂ requires C, 37.25; H, 4.38; N, 8.69%.

syn- And anti-2-(2,2,2-trimethylacetyl)-1,3-dithiane 1 R-oxides 7 and 8, R = tert-Bu (method A)

Treatment of 2-trimethylacetyl-1,3-dithiane (10.0 g, 48.9 mmol) under the conditions described above (method A) using (+)-dlethyl-(L)-tartrate (20.18 g, 16.76 mL, 97.9 mmol), titanium (IV) isopropoxide (13.91 g, 14.57 mL, 48.9 mmol), water (0.88 mL, 48.9 mmol) and cumene hydroperoxide (9.32 g, 9.05 mL, 61.2 mmol) at -35 °C for 2 days furnished an inseparable mixture of the *syn* and *anti* sulphoxides as a colourless crystalline solid (6.81 g, 63%). The diastereoselectivity was observed to vary from run to run up to exclusively *anti*.

syn- And anti-2-(2,2,2-trimethylacetyl)-1,3-dithiane 1*R*-oxides **7** and **8**, **R** = tert-Bu (method B)

Treatment of 2-trimethylacetyl-1,3-dithiane (0.10 g, 0.49 mmol) under the conditions described above (method B) using (+)-diethyl-(L)-tartrate (0.404 g, 0.34 mL, 1.96 mmol), titanium (IV) isopropoxide (139 mg, 0.146 mL, 0.49 mmol) and cumene hydroperoxide (93.2 mg, 91 μ L, 0.61 mmol) at -37 °C for 1 day furnished an inseparable mixture of the *syn* and *anti* sulphoxides as a colourless crystalline solid (69.4 mg, 64%), mp 103-105 °C; v_{max} (Nujol) 2923, 1707 and 1033 cm⁻¹; δ_{H} (400 MHz, CDCl₃) (*anti*) 1.26 (9H, s), 1.99-2.22 (1H, m), 2.41-2.70 (2H, m), 2.71-2.90 (2H, m), 3.42-3.58 (1H, m), and 4.71 (1H, m); (*syn*) distinct signals at 1.24 (9H, s), 2.20-2.38 (1H, m), 3.00-3.20 (1H, m), 3.90-4.10 (1H, m), 4.98 (1H, s), other signals masked by *anti* signals; ee = 90% (splitting signals at δ 4.71 (*anti*) and δ 4.98 (*syn*)); *m/z* (El) 220.05931 (M+). C9H₁₆O₂S₂ requires

220.05917; $[\alpha]_D^{20}$ (*anti*) = -20.5° (c = 0.10, EtOH). Found: C, 48.91; H, 7.35. C₉H₁₆O₂S₂ requires C, 49.06; H, 7.32%.

syn- And anti-2-benzoyl-1,3-dithiane 1*R*-oxides 7 and 8, R = Ph (method A)

Treatment of 2-benzoyl-1,3-dithiane (0.20 g, 0.89 mmol) under the conditions described above (method A) using (+)-diethyl-(L)-tartrate (367 mg, 0.305 mL, 1.78 mmol), titanium (IV) isopropoxide (235 mg, 0.265 mL, 0.89 mmol), water (16 μ L, 0.89 mmol) and cumene hydroperoxide (170 mg, 165 μ L, 1.11 mmol) at -37 °C for 2 days furnished an inseparable mixture of the *syn* and *anti* sulphoxides as a beige solid (0.129 g, 60%), mp 104-106 °C; v_{max} (Nujol) 2922, 1739, 1677 and 1039 cm⁻¹; δ_{H} (400 MHz, CDCl₃) (*anti*) 2.07-2.17 (1H, m), 2.55-2.72 (2H, m), 2.78-2.86 (1H, m), 2.92-3.03 (1H, m), 3.55-3.63 (1H, m), 5.27 (1H, s), 7.44–7.53 (2H, m), 7.62–7.72 (1H, m) and 7.95-8.06 (2H, m); (*syn*) 2.30-2.45 (2H, m), 2.55-2.72 (1H, m), 3.03-3.14 (1H, m), 3.21-3.30 (1H, m), 3.84-3.92 (1H, m), 5.57 (1H, s), 7.44–7.53 (2H, m), 7.62–7.72 (1H, m) and 7.95-8.06 (2H, m); ee = 60% (splitting signals at δ 5.27 (*anti*) and δ 5.57 (*syn*), determined using R-(-)-N-(3,5-dinitrobenzoyl)- α -methylbenzylamine (1 eq.)); *m/z* (Cl) 258.06295 (M⁺ + 18); C₁₁H₁₂O₂S₂ requires 258.06225. Diastereoisomeric ratios can vary from 3 : 1 to 7 : 1 (*anti* : *syn*).

syn- and anti-2-Carboethoxy-1,3-dithiane 1R-oxides 7 and 8, R = OEt (method A)

Treatment of commercially available 2-carboethoxy-1,3-dithiane (0.82 mL, 5.20 mmol) under the conditions described above (method A) using (+)-diethyl-(L)-tartrate (2.144 g, 1.78 mL, 10.40 mmol), titanium (IV) isopropoxide (1.48 g, 1.55 mL, 5.20 mmol), water (94 μ L, 5.20 mmol) and cumene hydroperoxide (0.99 g, 0.96 mL, 6.50 mmol) at -32 °C for 1 day furnished an inseparable mixture of the *syn* and *anti* sulphoxides as a yellow crystalline solid (0.763 g, 71%), mp 42-43 °C and 65-66 °C; v_{max} (Nujol) 2924, 1732 and 1023 cm⁻¹; δ_{H} (200 MHz, CDCl₃) (*anti*) 1.34 (3H, t, *J* = 7.2 Hz), 2.02-2.25 (1H, m), 2.43-2.72 (2H, m), 2.73-2.95 (2H, m), 3.34-3.47 (1H, m), 4.32 (2H, q, *J* = 7.2 Hz) and 4.33 (1H, s); (*syn*) distinct signals at 2.26-2.42 (1H, m), 2.98-3.13 (1H, m), 3.20-3.30 (1H, m). 3.53-3.68 (1H, m) and 4.60 (1H, s); *m/z* (EI) 208.02285 (M⁺); C₇H₁₂O₃S₂ requires 208.02279; ee = 88% (splitting signals at δ 4.33 (*anti*) and δ 4.60 (*syn*)). Found: C, 40.52; H, 5.84. C₇H₁₂O₃S₂ requires C, 40.37; H, 5.81%.

(+)-1,3-Dithiane 1*R*-oxide 2, R = H

To a stirred solution of *syn-* and *anti-*2-(2,2-dimethylpropanoyl)-1,3-dithiane 1*R*-oxides (6.00g, 27.2 mmol) in ethanol (120 mL) was added 5% aqueous sodium hydroxide solution (70 mL). The solution was heated under reflux overnight, and the organic layer separated. Further extraction of the aqueous layer with dichloromethane, followed by drying of the combined organic extracts over magnesium sulphate and removal of the solvent *in vacuo* gave a beige coloured solid, which was purified by repeated trituration with diethyl ether to yield (*R*)-(+)-1,3-dithiane 1*R*-oxide as a pale yellow crystalline solid (2.26 g, 61%), mp 106-107 °C; v_{max} (Nujol) 2927 and 1047 cm⁻¹; $\delta_{\rm H}$ (400 MHz, CDCl₃) 2.19-2.32 (1H, m), 2.40-2.70 (4H, m), 3.25-3.38 (1H, m), 3.64 (1H, d, *J* = 12.8Hz) and 3.98 (1H, dd, *J* = 2.8 and 12.7Hz); ee = 90% (splitting signal at δ 3.64); *m/z* (EI) 136.00151 (M⁺); C₄H₈OS₂ requires 136.00166; [α]_D²⁰ = +208.6° (c = 1.05, EtOH). Found: C, 35.18; H, 5.93. C₄H₈OS₂ requires C, 35.27; H, 5.89%.

2-(1-Hydroxy-2-phenylethyl)-2-ethyl-1,3-dithiane 9, R = Et, R' = PhCH₂

A 2.3 M solution of butyllithium in hexanes (11.83 mL, 27.45 mmol) was added to a stirring solution of 1,3-dithiane (3.00 g, 24.95 mmol) in thf (200 mL) at -78 °C. The solution was allowed to reach -20 °C and stirred at this temperature for 1 hour, before being cooled to -78 °C. Ethyl iodide

(2.20 mL, 27.45 mmol) was added and the reaction mixture allowed to reach room temperature over 2 hours before being recooled to -78 °C. A 2.3 M solution of butyllithium in hexanes (11.83 mL, 27.45 mmol) was added, and the mixture allowed to reach -20 °C. The reaction mixture was stirred at -20 °C for 1 hour before being cooled to -78 °C. Phenylacetaldehyde (3.21 mL, 27.45 mmol) was added, and the reaction mixture allowed to reach room temperature overnight. Normal work-up procedure followed by flash column chromatography using 10% ethyl acetate/petroleum ether as eluent furnished 2-(1-hydroxy-2-phenylethyl)-2-ethyl-1,3-dithiane as a viscous yellow oil (2.831 g, 42%); v_{max} (Nujol) 3600-3000 and 2931 cm⁻¹; $\delta_{\rm H}$ (200 MHz, CDCl₃) 1.16 (3H, t, *J* = 7.4 Hz), 1.66-2.16 (4H, m), 2.54-2.79 (4H, m), 2.84-3.15 (2H, m), 3.35 (1H, d, *J* = 13.8 Hz), 4.05-4.24 (1H, m) and 7.17-7.36 (5H, m); *m/z* (El) 268.09571 (M⁺); $C_{14}H_{20}OS_2$ requires 268.09555. Found: C, 62.64; H, 7.51 %.

2-(1-Hydroxy-3-phenylpropyl)-2-ethyl-1,3-dithiane 9, R = Et, R' = PhCH₂CH₂

A 2.5 M solution of butyllithium in hexanes (18.30 mL, 45.74 mmol) was added to a stirring solution of 1,3-dithiane (5.00 g, 41.58 mmol) in thf (200 mL) at –78 °C. The solution was stirred at this temperature for 2 hours. Ethyl iodide (3.66 mL, 45.74 mmol) was added and the reaction mixture allowed to reach room temperature over 1.5 hours, before being recooled to –78 °C. A 2.5 M solution of butyllithium in hexanes (18.30 mL, 45.74 mmol) was added, and the solution stirred at –78 °C for 2 hours. 2-Phenylpropanal (6.69 mL, 50.82 mmol) was added, and the reaction mixture allowed to reach room temperature overnight. Normal work-up procedure followed by flash column chromatography using 10% ethyl acetate/petroleum ether as eluent furnished 2-(1-hydroxy-3-phenylpropyl)-2-ethyl-1,3-dithiane as a viscous yellow oil (4.34 g, 37%); v_{max} (neat) 3600-3000 and 2930 cm⁻¹; $\delta_{\rm H}$ (200 MHz, CDCl₃) 1.06 (3H, t, *J* = 7.7 Hz), 1.62-2.04 (4H, m), 2.21-2.89 (8H, m), 2.91-3.10 (1H, m), 3.96 (1H, dt, *J* = 1.7 and 9.9 Hz) and 7.11-7.35 (5H, m); *m/z* (EI) 282.11111 (M⁺); C₁₅H₂₂OS₂ requires 282.11121.

2-(2-Phenylacetyl)-2-ethyl-1,3-dithiane 10, R = Et, R' = PhCH₂

A 2 M solution of oxalyl chloride (3.80 mL, 7.60 mmol) was added to a stirring solution of DMSO (1.08 mL, 15.21 mmol) in dichloromethane (75 mL) at –78 °C. After stirring at –78 °C for 30 minutes, a solution of 2-(1-hydroxy-2-phenylethyl)-2-ethyl-1,3-dithiane (1.856 g, 6.91 mmol) in dichloromethane (15 mL) was added dropwise *via* cannula, and stirring continued at –78 °C for 1 hour. Triethylamine (2.90 mL, 20.7 mmol) was added and the solution allowed to reach room temperature overnight. The solution was poured onto 5% aqueous hydrochloric acid (50 mL), and the organic phase collected, washed with aqueous sodium hydrogen carbonate solution (2 x 50 mL), dried over magnesium sulphate and concentrated *in vacuo* to give a brown oil. Trituration and recrystallization from petroleum ether gave 2-(2-phenylacetyl)-2-ethyl-1,3-dithiane as a pale yellow crystalline solid (1.232 g, 67%), mp 79-80 °C; v_{max} (neat) 2924 and 1710 cm⁻¹; δ_{H} (200 MHz, CDCl₃) 1.04 (3H, t, *J* = 7.4 Hz), 1.66-2.06 (2H, m), 2.14 (2H, q, *J* = 7.4 Hz), 2.50-2.68 (2H, m), 2.79-2.98 (2H, m), 3.97 (2H, s) and 7.20-7.39 (5H, m); *m/z* (EI) 266.07954 (M⁺); C₁₄H₁₈OS₂ requires 266.07990. Found: C, 63.17; H, 6.83. C₁₄H₁₈OS₂ requires C, 63.12; H, 6.81%.

2-(3-Phenylpropanoyl)~2-ethyl-1,3-dithiane 10, R = Et, R' = PhCH₂CH₂

A solution of trifluoroacetic anhydride (1.88 mL, 13.28 mmol) in dichloromethane (25 mL) was added to a stirring solution of DMSO (1.38 mL, 19.47 mmol) in dichloromethane (75 mL) at -78 °C via cannula. After stirring at -78 °C for 30 minutes, a solution of 2-(1-hydroxy-3-phenylpropyl)-2-ethyl-1,3-dithiane (2.50 g, 8.85 mmol) in dichloromethane (15 mL) was added dropwise via cannula, and stirring continued at -78 °C for 1 hour. Triethylamine (3.70 mL, 26.55 mmol) was added and the solution allowed to reach room temperature overnight. The solution was poured onto

5% aqueous hydrochloric acid (50 mL), and the organic phase collected, washed with aqueous sodium hydrogen carbonate solution (2 x 50 mL), dried over magnesium sulphate and concentrated *in vacuo* to give a yellow oil. Flash column chromatography using 10% ethyl acetate/petroleum ether as eluent gave 2-(3-phenylpropanoyl)-2-ethyl-1,3-dithiane as a colourless crystalline solid (1.917 g, 77%), mp 61-62 °C; v_{max} (Nujol) 2923 and 1706 cm⁻¹; δ_{H} (200 MHz, CDCl₃) 0.91 (3H, t, *J* = 7.4 Hz), 1.71-1.91 (1H, m), 1.92-2.13 (3H, m), 2.50-2.67 (2H, dt, *J* = 3.9 and 14.3 Hz), 2.77-3.11 (6H, m) and 7.12-7.36 (5H, m); *m/z* (EI, 280.09461 (M⁺); C₁₅H₂₀OS₂ requires 280.09555. Found: C, 64.34; H, 7.22. C₁₅H₂₀OS₂ requires C, 64.24; H, 7.19%.

syn- And anti-2-acetyl-2-phenyl-1,3-dithiane 1*R*-oxides 11 and 12, R = Ph, R' = Me (method A)

Treatment of 2-acetyl-2-phenyl-1,3-dithiane (0.55 g, 2.30 mmol) under the conditions described above (method A) using (+)-diethyl-(L)-tartrate (0.95 g, 0.79 mL, 4.61 mmol), titanium (IV) isopropoxide (0.65 g, 0.685 mL, 2.30 mmol), water (41.4 μ L, 2.30 mmol) and *tert*-butyl hydroperoxide (0.23 g, 0.25 mL, 2.55 mmol) at -20 °C for 2 days furnished the *syn* sulphoxide as a colourless crystalline solid (30 mg, 6%) and the *anti* sulphoxide as a colourless crystalline solid (0.340 g, 65%).

For *syn*-2-acetyl-2-phenyl-1,3-dithiane 1*R*-oxide 11, **R** = **Ph**, **R'** = **Me**: υ_{max} (CHCl₃) 2900, 1680 and 1055 cm⁻¹; δ_{H} (400 MHz, CDCl₃) 2.19 (3H, s), 2.65-2.77 (2H, m), 3.11-3.23 (2H, m), 3.46-3.52 (1H, m), 3.67-3.75 (1H, m) and 7.35-7.57 (5H, m); *m/z* (El) 254 (M+); $[\alpha]_{D}^{20} = -314.3^{\circ}$ (c = 0.07, CH₂Cl₂); ee = 99% (recrystallization gave 100% ee).

For *anti*-2-acetyl-2-phenyl-1,3-dithiane 1*R*-oxide **12**, **R** = **Ph**, **R'** = **Me**: v_{max} (CHCl₃) 2900, 1695 and 1060 cm⁻¹; δ_{H} (400 MHz, CDCl₃) 1.76-1.83 (1H, m), 2.26 (3H, s), 2.45-2.57 (1H, m), 2.70-2.73 (2H, m), 3.06-3.12 (1H, m), 3.32-3.39 (1H, m) and 7.41-7.48 (5H, m); *m/z* (El) 254 (M⁺); $[\alpha]_{D}^{20} = -111.6^{\circ}$ (c = 0.41, CH₂Cl₂); ee = 99% (recrystallization gave 100% ee). Found: C, 56.49; H, 5.54. C₁₂H₁₄O₂S₂ requires C, 56.66; H, 5.55%.

syn- And anti-2-propanoyl-2-phenyl-1,3-dithiane 1*R*-oxides 11 and 12, R = Ph, R' = Et (method A)

Treatment of 2-propanoyl-2-phenyl-1,3-dithiane (1.00 g, 3.97 mmol) under the conditions described above (method A) using (+)-diethyl-(L)-tartrate (1.64 g, 1.36 mL, 7.95 mmol), titanium (IV) isopropoxide (1.13 g, 1.18 mL, 3.97 mmol), water (71.5 μ L, 3.97 mmol) and *tert*-butyl hydroperoxide (0.72 g, 0.77 mL, 7.94 mmol) at -20 °C for 3 days furnished the *syn* sulphoxide as a colourless crystalline solid (0.143 g, 15%) and the *anti* sulphoxide as a colourless crystalline solid (0.409 g, 42%).

For *syn*-2-propanoyl-2-phenyl-1,3-dithiane 1*R*-oxide **11**, **R** = **Ph**, **R'** = **Et** mp 72–74 °C; v_{max} (Nujol) 2900, 1720 and 1070 cm⁻¹; δ_{H} (400 MHz, CDCl₃) 0.98 (3H, t, *J* = 7.16Hz), 1.92-2.00 (1H, m), 2.37-2.58 (3H, m), 2.65-2.73 (2H, m), 2.79-2.86 (1H, m), 3.13-3.20 (1H, m) and 7.38-7.48 (5H, m); *m/z* (El) 268.05925 (M⁺); C₁₃H₁₆O₂S₂ requires 268.05917; [α]_D²⁰ = +182.3° (c = 0.485, CH₂Cl₂); ee = 57%.

For *anti*-2-propanoyl-2-phenyl-1,3-dithiane 1*R*-oxide **12**, **R** = **Ph**, **R'** = **Et**: mp 125-126 °C; υ_{max} (CHCl₃) 2900, 1700 and 1060 cm⁻¹; δ_{H} (400 MHz, CDCl₃) 1.04 (3H, t, *J* = 7.30Hz), 1.75-1.83 (1H, m), 2.39-2.56 (2H, m), 2.63-2.81 (3H, m), 3.06-3.12 (1H, m), 3.32-3.40 (1H, m) and 7.38–7.46 (5H, m); *m/z* (El) 268.05899 (M⁺); C₁₃H₁₆O₂S₂ requires 268.05917; [α]_D²⁰ = +137.6° (c = 0.59, CH₂Cl₂); ee. = 97% (recrystallization gave 100% ee).

syn- And anti-2-acetyl-2-methyl-1,3-dithiane 1R-oxides 11 and 12, R = R' = Me

Treatment of 2-acetyl-2-methyl-1,3-dithiane (0.55 g, 3.12 mmol) under the conditions described above (method A) using (+)-diethyl-(L)-tartrate (1.29 g, 1.07 mL, 6.26 mmol), titanium (IV) isopropoxide (0.89 g, 0.93 mL, 3.13 mmol), water (56 μ L, 3.12 mmol) and *tert*-butyl hydroperoxide (0.31 g, 0.33 mL, 3.44 mmol) at -20 °C for 3 days, followed by flash column chromatography using 10% ethanol/ethyl acetate as eluent, furnished the *syn* sulphoxide as a colourless crystalline solid (0.260 g, 43%) and the *anti* sulphoxide as a colourless crystalline solid (0.280 g, 47%).

For *syn*-2-acetyl-2-methyl-1,3-dithiane 1*R*-oxide 11, **R** = **R'** = **Me**: mp 62-64 °C; υ_{max} (Nujol) 2900, 1710 and 1055 cm⁻¹; δ_{H} (400 MHz, CDCl₃) 1.88 (3H, s), 2.25-2.37 (2H, m), 2.38 (3H, s), 2.41-2.48 (1H, m) and 3.05-3.28 (3H, m); *m/z* (EI) 192 (M⁺); $[\alpha]_{D}^{20} = -243.2^{\circ}$ (c = 1.25, CH₂Cl₂); ee = 82%. Found: C, 43.55; H, 6.23. C₇H₁₂O₂S₂ requires C, 43.72; H, 6.29%.

For anti-2-acetyl-2-methyl-1,3-dithiane 1*R*-oxide **12**, **R** = **R**' = **Me**: mp 50-52 °C; υ_{max} (Nujol) 2900, 1695 and 1040 cm⁻¹; δ_{H} (400 MHz, CDCl₃) 1.67 (3H, s), 1.77-1.85 (1H, m), 2.38-2.45 (1H, m), 2.43 (3H, s), 2.45-2.64 (2H, m), 2.97-3.03 (1H, m) and 3.15-3.23 (1H, m); *m/z* (EI) 192 (M⁺); $[\alpha]_{D}^{20}$ = +255.0° (c = 1.60, CH₂Cl₂); ee = 78%. Found: C, 43.61; H, 6.22. C₇H₁₂O₂S₂ requires C, 43.72; H, 6.29%.

anti-2-Benzoyl-2-methyl-1,3-dithiane 1*R*-oxide 12, **R** = Me, **R'** = Ph (method A)

Treatment of 2-benzoyl-2-methyl-1,3-dithlane (1.00 g, 4.20 mmol) under the conditions described above (method A) using (+)-diethyl-(L)-tartrate (1.73 g, 1.44 mL, 8.40 mmol), titanium (IV) isopropoxide (1.19 g, 1.25 mL, 4.20 mmol), water (76 μ L, 4.20 mmol) and *tert*-butyl hydroperoxide (0.57 g, 0.61 mL, 6.32 mmol) at -20 °C for 3 days furnished the *anti* sulphoxide as a colourless crystalline solid (0.600 g, 58%); v_{max} (Nujol) 2900, 1665 and 1050 cm⁻¹; δ_{H} (200 MHz, CDCl₃) 1.84 (3H, s), 1.82-1.86 (1H, m), 2.48-2.73 (3H, m), 3.08-3.13 (1H, m), 3.35-3.47 (1H, m), 7.47-7.63 (3H, m) and 8.20-8.24 (2H, m); m/z (EI) 255 (M⁺); $[\alpha]_D^{20} = +116.9^\circ$ (c = 1.30, CH₂Cl₂); ee = 86%.

syn- And anti-2-acetyl-2-ethyl-1,3-dithiane 1*R*-oxides 11 and 12, R = Et, R' = Me (method A)

Treatment of 2-acetyl-2-ethyl-1,3-dithiane (1.02 g, 5.37 mmol) under the conditions described above (method A) using (+)-diethyl-(L)-tartrate (2.21 g, 1.84 mL, 10.74 mmol), titanium (IV) isopropoxide (1.53 g, 1.60 mL, 5.37 mmol), water (97 μ L, 5.37 mmol) and *tert*-butyl hydroperoxide (0.97 g, 1.03 mL, 10.74 mmol) at -20 °C for 6 days furnished the *syn* sulphoxide as a viscous colourless oil (42 mg, 4%) and the *anti* sulphoxide as a colourless crystalline solid (0.680 g, 61%).

For syn-2-acetyl-2-ethyl-1,3-dithiane 1*R*-oxide 11, **R** = **Et**, **R'** = **Me**: mp 57-58 °C; v_{max} (neat) 2900, 1700 and 1040 cm⁻¹; δ_{H} (250 MHz, CDCl₃) 1.08 (3H, t, *J* = 7.5 Hz), 2.03-2.25 (2H, m), 2.40 (3H, s) 2.29-2.52 (2H, m), 2.55-2.68 (2H, m), 2.72-2.97 (1H, m) and 3.04-3.33 (1H, m); *m/z* (EI) 206.04369 (M⁺); C₈H₁₄O₂S₂ requires 206.04352; $[\alpha]_D^{20} = +77.4^\circ$ (c = 0.775, CH₂Cl₂); ee could not be determined.

For *anti*-2-acetyl-2-ethyl-1,3-dithiane 1*R*-oxide **12**, **R** = **Et**, **R'** = **Me**: mp 40-41 °C; v_{max} (Nujol) 2900, 1695 and 1040 cm⁻¹; δ_{H} (250 MHz, CDCl₃) 1.05 (3H, t, *J* = 7.5 Hz), 1.72-1.89 (2H, m),

2.13-2.28 (2H, m), 2.44 (3H, s), 2.42-2.63 (2H, m) and 3.05-3.10 (2H, m); m/z (EI) 206.04390 (M⁺); C₈H₁₄O₂S₂ requires 206.04352; [α]_D²⁰ = +274.7° (c = 1.325, CH₂Cl₂); ee = 81%.

syn- And anti-2-propanoyl-2-ethyl-1,3-dithiane 1R-oxides 11 and 12, R = R' = Et (method A)

Treatment of 2-propanoyl-2-ethyl-1,3-dithiane (1.01 g, 4.95 mmol) under the conditions described above (method A) using (+)-diethyl-(L)-tartrate (2.04 g, 1.70 mL, 9.90 mmol), titanium (IV) isopropoxide (1.41 g, 1.47 mL, 4.95 mmol), water (89 μ L, 4.95 mmol) and *tert*-butyl hydroperoxide (0.89 g, 0.95 mL, 9.90 mmol) at -20 °C for 2 days furnished the *syn* sulphoxide as a colourless oil (65.4 mg, 6%) and the *anti* sulphoxide as a colourless oil (0.789 g, 67%).

For anti-2-propanoyl-2-ethyl-1,3-dithiane 1*R*-oxide **12**, **R** = **R'** = **Et**: mp 61-63 °C; v_{max} (neat) 2900, 1690 and 1060 cm⁻¹; δ_{H} (400 MHz, CDCl₃) 1.01 (3H, t, *J* = 7.5 Hz), 1.13 (3H, t, *J* = 7.3 Hz), 1.71-1.85 (2H, m), 2.13-2.23 (1H, m), 2.39-2.66 (4H, m) and 2.96-3.07 (3H, m); *m/z* (EI) 220.05932 (M⁺); C₉H₁₆O₂S₂ requires 220.05917; $[\alpha]_D^{20}$ = +236.8° (c = 1.875, CH₂Cl₂); ee = 87% (recrystallization gave 100% ee).

syn- And anti-2-butanoyl-2-ethyl-1,3-dithiane 1R-oxides 11 and 12, R = Et, R' = Pr

Treatment of 2-butanoyl-2-ethyl-1,3-dithiane (0.49 g, 2.29 mmol) under the conditions described above (method A) using (+)-diethyl-(L)-tartrate (0.95 g, 0.79 mL, 4.59 mmol), titanium (IV) isopropoxide (0.65 g, 0.67 mL, 2.29 mmol), water (41 μ L, 2.29 mmol) and *tert*-butyl hydroperoxide (0.41 g, 0.43 mL, 4.50 mmol) at ~20 °C for 2 days furnished the *syn* sulphoxide as a colourless oil (34 mg, 6%) and the *anti* sulphoxide as a colourless oil (0.313 g, 60%).

For syn-2-butanoyl-2-ethyl-1,3-dithiane 1*R*-oxide 11, **R** = **Et**, **R**' = **Pr**: v_{max} (neat) 2900, 1730 and 1090 cm⁻¹; δ_H (400 MHz, CDCl₃) 0.94 (3H, t, *J* = 7.4 Hz), 1.05 (3H, t, *J* = 7.5 Hz), 1.62-1.71 (2H, m), 2.04-2.14 (1H, m), 2.23-2.44 (3H, m), 2.53-2.65 (2H, m), 2.67-2.79 (1H, m), 2.86-2.93 (1H, m), 3.00-3.05 (1H, m) and 3.14-3.21 (1H, m); *m/z* (EI) 234 (M⁺); $[\alpha]_D^{20} = +139.4^\circ$ (c = 1.225, CH₂Cl₂); ee could not be determined.

For anti-2-butanoyl-2-ethyl-1,3-dithiane 1*R*-oxide **12**, **R** = **Et**, **R'** = **Pr**: v_{max} (neat) 2900, 1700 and 1060 cm⁻¹; δ_H (400 MHz, CDCl₃) 0.96 (3H, t, *J* = 7.4 Hz), 1.02 (3H, t, *J* = 7.5 Hz), 1.62-1.85 (4H, m), 2.12-2.21 (1H, m), 2.41-2.61 (4H, m), 2.94-3.02 (1H, m) and 3.04-3.08 (2H, m); *m/z* (EI) 234 (M⁺); [α]_D²⁰ = +217.2° (c = 1.455, CH₂Cl₂); ee = 90%.

anti-2-(2-Phenylacetyl)-2-ethyl-1,3-dithiane 1*R*-oxide 12, R = Et, R' = PhCH₂ (method A)

Treatment of 2-(2-phenylacetyl)-2-ethyl-1,3-dithiane (0.742 g, 2.79 mmol) as described above (method A) using (+)-diethyl-(L)-tartrate (1.149 g, 0.95 mL, 5.57 mmol), titanium (IV) isopropoxide (0.792 g, 0.83 mL, 2.79 mmol), water (50.2 μL, 2.79 mmol) and cumene hydroperoxide (1.03 mL, 6.97 mmol) at -20 °C for 2 days furnished the *anti* sulphoxide as a pale yellow crystalline solid (0.509 g, 65%), mp 110-112 °C; v_{max} (Nujol) 2924, 1698 and 1040 cm⁻¹; $\delta_{\rm H}$ (200 MHz, CDCl₃) 1.07 (3H, t, *J* = 7.4 Hz), 1.60-1.79 (1H, m), 1.81-2.07 (1H, m), 2.14-2.60 (4H, m), 2.95-3.12 (2H, m), 3.81 (1H, d, *J* = 16.0 Hz), 4.32 (1H, d, *J* = 15.4 Hz) and 7.25-7.42 (5H, m); ee = 82% (splitting signal at δ 3.81); *m/z* (EI) 282.07458 (M⁺); C₁₄H₁₈O₂S₂ requires 282.07483; [α]_D²⁰ = +243.6° (c = 0.335, CHCl₃). Found: C, 59.52; H, 6.43. C₁₄H₁₈O₂S₂ requires C, 59.54; H, 6.42%.

A by-product of the above reaction was *anti*-2-(2-phenylacetyl)-2-ethyl-1,3-dithiane *anti*-1,3-dioxide, which was isolated as a colourless crystalline solid (86.8 mg, 11%), mp 120-121 °C; v_{max} (Nujol) 2923, 1681, 1056 and 1044 cm⁻¹; δ_{H} (200 MHz, CDCl₃) 1.27 (3H, t, *J* = 7.4 Hz), 2.14-2.55 (1H, m), 2.66-3.27 (5H, m), 3.28-3.60 (2H, m), 3.92 (1H, d, *J* = 18.2 Hz), 4.27 (1H, d, *J* = 18.2 Hz) and 7.16-7.44 (5H, m); *m/z* (El) 298 (M⁺); $[\alpha]_D^{20} = +279.7^\circ$ (c = 0.383, CHCl₃). Found: C, 56.71; H, 6.21. C₁₄H₁₈O₃S₂ requires C, 56.35; H, 6.08%.

syn- And anti-2-(3-phenylpropanoyl)-2-ethyl-1,3-dithiane 1*R*-oxides 11 and 12, R = Et, $R' = PhCH_2CH_2$ (method A)

Treatment of 2-(3-phenylpropanoyl)-2-ethyl-1,3-dithiane (1.00 g, 3.566 mmol) as described above (method A) using (+)-diethyl-(L)-tartrate (1.47 g, 1.22 mL, 7.132 mmol), titanium (IV) isopropoxide (1.014 g, 1.06 mL, 3.566 mmol), water (64.2 μ L, 3.566 mmol) and cumene hydroperoxide (1.32 mL, 8.915 mmol) at -20 °C for 4 days furnished the *syn* sulphoxide as a yellow oil (23.5 mg, 2%) and the *anti* sulphoxide as a colourless oil (64.7 mg, 61%).

For *syn*-2-(3-phenylpropanoyl)-2-ethyl-1,3-dithiane 1*R*-oxide 11, **R** = Et, **R'** = PhCH₂CH₂: v_{max} (neat) 2932, 1703 and 1039 cm⁻¹; δ_{H} (200 MHz, CDCl₃) 0.97 (3H, t, *j* = 7.4 Hz), 1.96-2.20 (1H, m), 2.21-2.65 (3H, m), 2.66-2.84 (1H, m), 2.88-3.35 (7H, m) and 7.12-7.40 (5H, m); ee = 81% (splitting signal at δ 0.97); *m/z* (EI) 296.09007 (M⁺); C₁₅H₂₀O₂S₂ requires 296.09048; [α]_D²⁰ = +51.0° (c = 0.767, CHCl₃).

For *anti*-2-(3-phenylpropanoyl)-2-ethyl-1,3-dithiane 1*R*-oxide **12**, **R** = **Et**, **R'** = **PhCH₂CH₂**: υ_{max} (neat) 2922, 1692 and 1054 cm⁻¹; δ_{H} (200 MHz, CDCl₃) 0.92 (3H, t, *J* = 7.4 Hz), 1.60-1.98 (2H, m), 2.04-2.54 (4H, m), 2.77-3.13 (5H, m), 3.32-3.52 (1H, m) and 7.15-7.35 (5H, m); ee = 81% (splitting signal at δ 0.92); *m/z* (El) 296.09007 (M⁺); C₁₅H₂₀O₂S₂ requires 296.09048; [α]_D²⁰ = +143.5° (c = 0.767, CHCl₃). Found: C, 60.49; H, 6.83. C₁₅H₂₀O₂S₂ requires C, 60.78; H, 6 80%.

2-(1-Hydroxybutyl)-1,3-dithiane

To a stirring solution of 1,3-dithiane (6.00 g, 50.0 mmol) in thf (80 ml) at –78 °C was added a 2.32 M solution of butyllithium in hexanes (1.1 eq., 23.66 ml, 55.00 mmol). After stirring at –78 °C for 1.5 hours, the yellow solution of the anion was added by cannula to a solution of butyraldehyde (5.40 ml, 60.00 mmol) in thf (50 ml) and the solution allowed to reach room temperature over 4 hours. Normal work-up procedure followed by flash column chromatography using 10% ethyl acetate/petroleum ether as eluent gave 2-(1-hydroxybutyl)-1,3-dithiane as a colourless oil (8.44 g, 88%); v_{max} (neat) 3600-3000 and 2957 cm⁻¹; $\delta_{\rm H}$ (200 MHz, CDCl₃) 0.97 (3H, t, *J* = 7.4 Hz,), 1.30-1.68 (3H, m), 1.70-1.84 (1H, m), 1.90-2.20 (2H, m), 2.65 (1H, br s), 2.70-2.90 (2H, m), 2.90-3.04 (2H, m) and 3.90-4.00 (2H, m); *m/z* (El) 192.06461 (M⁺); C₈H₁₆OS₂ requires 192.06426. Found: C, 49.83; H, 8.41. C₈H₁₆OS₂ requires C, 49.96; H, 8.38%.

2-Butanoyl-1,3-dithiane

To a stirring solution of DMSO (5.69 ml, 80.2 mmol) in dichloromethane (60 ml) at -78 °C was added a 2 M solution of oxalyl chloride (17.29 ml, 40.1 mmol) in dichloromethane (50 ml). After stirring at -78 °C for 30 minutes, a solution of 2-(1-hydroxybutyl)-1,3-dithiane (7.00 g, 36.5 mmol) in dichloromethane (50 ml) was added dropwise by cannula, and stirring continued at -78 °C for 1 hour. Triethylamine (25.41 ml, 182.3 mmol) was added and the solution allowed to reach 0 °C overnight. The solution was poured onto 5% aqueous hydrochloric acid (75 ml), and the organic phase collected, washed with aqueous sodium hydrogen carbonate solution (2 x 50 ml), dried over magnesium sulphate and concentrated *in vacuo* to give an orange oil. Flash column chromatography

using 10% ethyl acetate/petroleum ether as eluent, gave 2-butanoyl-1,3-dithiane as a yellow oil (6.38 g, 92%); v_{max} (neat) 2962 and 1710 cm⁻¹; δ_{H} (200 MHz, CDCl₃) 0.95 (3H, t, *J* = 7.5 Hz,), 1.60-1.77 (2H, m), 1.92-2.20 (2H, m), 2.54-2.71 (4H, m), 3.20-3.34 (2H, m) and 4.26 (1H, s); *m/z* (Cl) 190.04887 (M⁺); $C_8H_{14}OS_2$ requires 190.04861. Found: C, 50.50; H, 7.44. $C_8H_{14}OS_2$ requires C, 50.49; H, 7.41%.

2-Butanoyl-2-thiophenyl-1,3-dithiane

To a stirring solution of 2-butanoyl-1,3-dithiane (0.249 g, 1.31 mmol) in thf (15 ml) at -78 °C was added a 1 M solution of lithium bis(trimethylsilyl)amide in thf (1.57 ml, 1.57 mmol). After stirring at -78 °C for 1 hour, a solution of phenyl benzenethiosulphonate (0.36 g, 1.44 mmol) in thf (6 ml) was added, and the solution allowed to reach room temperature over 1 hour. Normal work-up procedure followed by flash column chromatography using 10% ethyl acetate/petroleum ether as eluent, gave 2-butanoyl-2-thiophenyl-1,3-dithiane as a yellow oil (0.357 g, 91%); v_{max} (neat) 2962 and 1706 cm⁻¹; δ_{H} (200 MHz, CDCl₃) 0.85 (3H, t, *J* = 7.4 Hz), 1.45-2.15 (4H, m), 2.63-2.82 (4H, m), 3.12-3.30 (2H, m) and 7.13-7.31 (5H, m); *m/z* (ET) 298 (M⁺). Found: C, 56.33; H, 6.11. C₁₄H₁₈OS₃ requires C, 56.34; H, 6.08%.

(±)- syn- and anti-2-butanoyl-2-thiophenyl-1,3-dithiane 1-oxides 5

To a solution of 2-butanoyl-2-thiophenyl-1,3-dithiane (0.208 g, 0.696 mmol) in methanol (20 ml) at -10 °C was added dropwise a solution of socium meraperiodate (0.164 g, 0.766 mmol) in water (10 ml) over a period of 15 minutes. The resulting pale yellow suspension was stirred at -10 °C for 48 hours, after which time the solution was allowed to reach room temperature over 3 hours. The precipitate was removed by filtration, washed thoroughly with dichloromethane, and the filtrate concentrated *in vacuo* to give a viscous yellow mixture which was partitioned between dichloromethane and saturated aqueous sodium chloride. The aqueous layer was extracted with dichloromethane (2 x 25 ml), and the combined organic extracts dried over magnesium sulphate and concentrated *in vacuo* to give a pale yellow oil. Flash column chromatography using 5% ethanol/ethyl acetate as eluent, yielded an inseparable 2: 1 mixture of the *syn* and *anti* sulphoxides as a colourless oil (0.0482 g, 22%); v_{max} (neat) 2962, 1709,1066 and 1025 cm⁻¹; *m/z* (EI) 314.04710 (M⁺); $C_{14}H_{18}O_2S_3$ requires 314.04689.

syn- And anti-2-thiophenyl-1,3-dithiane 1*R*-oxides 2 and 3, R = PhS (method A) by deacylation of syn- and anti-2-butanoyl-2-thiophenyl-1,3-dithiane 1*R*-oxides 5

Treatment of 2-butanoyl-2-thiophenyl-1,3-dithiane **4** (0.129 g, 0.43 mmol) as described above (method A) using (+)-diethyl-(L)-tartrate (0.18 g, 0.149 ml, 0.87 mmol), titanium (IV) isopropoxide (0.12 g, 0.129 ml, 0.43 mmol), water (8 μ l, 0.43 mmol) and cumene hydroperoxide (80.2 μ l, 0.54 mmol) at -32 °C for 3 days furnished a 1.6:1 mixture of the *anti* and *syn* sulphoxides **5** as a colourless oil (36.3 mg, 27%). The mixture of sulphoxides (36 mg, 0.115 mmol) was dissolved in dichloromethane (3 ml) and stirred with 5% aqueous sodium hydroxide solution (3 ml) at room temperature for one day. The solution was saturated with sodium chloride and the organic layer separated. The aqueous layer was extracted with dichloromethane (3 x 20 ml), and the combined organic layers dried over magnesium sulphate and concentrated *in vacuo* to give a colourless solid. Flash column chromatography using 100% ethyl acetate as eluent gave a 1.6:1 mixture of the *syn*-and *anti*-2-thiophenyl-1,3-dithiane 1*R*-oxides as a colourless solid (10.0 mg, 35%), data as recorded above; ee = 77% (*anti*) (splitting signal at δ 4.67) and 77% (*syn*) (splitting signal at δ 5.10).

General method of deacylation of 2-acyl-2-alkyl-1,3-dithiane 1R-oxides 11 and 12

To a stirred solution of the mixture of *syn-* and *anti-* 2-acyl-2-alkyl-1,3-dithiane 1*R*-oxides (3 mmol) in dichloromethane was added 10% aqueous sodium hydroxide. The mixture was stirred at room temperature for 24 hours, saturated with sodium chloride, and the organic layer separated. Further extraction of the aqueous layer with dichloromethane, followed by drying of the combined organic extracts over magnesium sulphate and removal of the solvent *in vacuo* gave a mixture of *syn-* and *anti-* 2-alkyl-1,3-dithiane 1*R*-oxides which were purified by flash column chromatography. The data given below refers to the *syn* isomer, normally the major, except where stated.

syn- And anti-2-methyl-1,3-dithiane 1*R*-oxides 2 and 3, R = Me

Treatment of a mixture of *syn- and anti-2*-acetyl-2-methyl-1,3-dithiane 1*R*oxides (1 : 1.2) (1.45 g, 7.54 mmol) under the conditions described above gave a mixture of *syn- and anti-*2-methyl-1,3-dithiane 1*R*-oxides (7.9 : 1) as a colourless solid (1.03 g, 91%). For *syn-2*-methyl-1,3-dithiane 1*R*-oxide: $\delta_{\rm H}$ (500 MHz, CDCl₃) 1.62-1.63 (3H, d, *J* = 7.1 Hz), 1.99-2.07 (1H, m), 2.39-2.49 (1H, m), 2.51-2.62 (1H, m), 2.63-2.71 (1H, m), 2.73-2.78 (1H, m), 2.91-2.96 (1H, m) and 3.83-3.87 (1H, q, *J* = 14.2 Hz); [α]_D²⁰ = +136.6° (c = 1.03, CH₂Cl₂); ee = 77%.

syn- And anti-2-ethyl-1,3-dithiane 1 R-oxides 2 and 3, R = Et

Treatment of a mixture of *syn- and anti-*2-propanoyl-2-ethyl-1,3-dithiane 1*R*-oxides (1 : 11) (0.42 g, 2.83 mmol) under the conditions described above gave a mixture of *syn- and anti-*2-methyl-1,3-dithiane 1*R*-oxides (11 : 1) as a colourless oil (0.364 g, 78%). For *syn-*2-ethyl-1,3-dithiane 1*R*-oxide: v_{max} (neat) 2900 and 1040 cm⁻¹; δ_{H} (400 MHz, CDCl₃) 1.17 (3H, t, *J* = 7.4 Hz), 1.71-1.81 (1H, m), 1.98-2.09 (1H, m), 2.12-2.23 (1H, m), 2.41-2.75 (4H, m), 2.93-3.00 (1H, m) and 3.54-3.62 (1H, m); *m/z* (EI) 164.03265 (M⁺); C₆H₁₂OS₂ requires 164.03296; ee = 86% (determined using tris[3-(trifluoromethylhydroxymethylene)-(+)-camphorato]europium (III) (0.2 eq.)).

syn- And anti-2-propyl-1,3-dithiane 1*R*-oxides 2 and 3, R = Pr

An unpurified mixture of *syn-* and anti-2-propanoyl-2-propyl-1,3-dithiane 1*R*-oxides was treated as described above to give a mixture of *syn-* and anti-2-propyl-1,3-dithiane 1*R*-oxides (6 : 1) as a colourless solid (46%). For *syn-*2-propyl-1,3-dithiane 1*R*-oxide: v_{max} (CHCl₃) 2900 and 1030 cm⁻¹; $\delta_{\rm H}$ (500 MHz, CDCl₃) 0.99 (3H, t, *J* = 7.23 Hz), 1.45-1.59 (1H, m), 1.67-1.76 (2H, m), 1.99-2.13 (2H, m), 2.43-2.66 (3H, m), 2.68-2.75 (1H, m), 2.94-2.99 (1H, m) and 3.69-3.72 (1H, q, *J* = 8.9 Hz); *m/z* (EI) 178.04864 (M⁺); C₇H₁₄OS₂ requires 178.04861; ee = 92%.

syn- And anti-2-butyl-1,3-dithiane 1R-oxides 2 and 3, R = Bu

An unpurified mixture of *syn- and anti-2*-propanoyl-2-butyl-1,3-dithiane 1*R*-oxides was treated as described above to give a mixture of *syn- and anti-2*-butyl-1,3-dithiane 1*R*-oxides (8 : 1) as a colourless oil (43%). For *syn-2*-butyl-1,3-dithiane 1*R*-oxide: v_{max} (neat) 2900 and 1040 cm⁻¹; $\delta_{\rm H}$ (400 MHz, CDCl₃) 0.94 (3H, t, *J* = 7.3 Hz), 1.34-1.53 (3H, m), 1.59-1.76 (2H, m), 1.99-2.09 (1H, m), 2.10-2.16 (1H, m), 2.43-2.66 (3H, m), 2.68-2.75 (1H, m), 2.94-2.99 (1H, m) and 3.67-3.70 (1H, q, *J* = 9.3 Hz); *m/z* (EI) 192.06487 (M⁺); C₈H₁₆OS₂ requires 192.06426; ee = 94%.

syn- And anti-2-phenyl-1,3-dithiane 1R-oxides 2 and 3, R = Ph

Treatment of an unpurified mixture of *syn- and anti-* 2-acetyl-2-phenyl-1,3-dithiane 1*R*-oxides (20 mg, 0.08 mmol), (11 : 1), under the conditions described above gave a mixture of *syn- and anti-* 2-phenyl-1,3-dithiane 1*R*-oxides (30 : 1) as a colourless solid (10.5 mg, 63%). For *syn*-2-phenyl-1,3-dithiane 1*R*-oxide: mp 150-153 °C; v_{max} (CHCl₃ solution) 2900 and 1030 cm⁻¹; δ_{H} (400 MHz, CDCl₃) 1.75-1.98 (1H, m), 2.53-2.85 (3H, m), 2.93-3.15 (1H, m), 3.16-3.37 (1H, m), 4.78 (1H, s)

and 7.32-7.50 (5H, m); m/z (El) 212.03326 (M⁺); $C_{10}H_{12}OS_2$ requires 212.03296; $[\alpha]_D^{20} = -141.9^{\circ}$ (c = 0.97, CH_2Cl_2); ee = 93%. Found: C, 56.61; H, 5.73. $C_{10}H_{12}OS_2$ requires C, 56.57; H, 5.70%.

syn- And anti-2-benzyl-1,3-dithiane 1R-oxides 2 and 3, R = PHCH₂

Treatment of an unpurified mixture of *syn-* and anti-2-acetyl-2-benzyl-1,3-dithiane 1*R*-oxides under the conditions described above gave a mixture of *syn-* and anti-2-benzyl-1,3-dithiane 1*R*-oxides (4 : 1) as a colourless solid (95%). For *syn*-2-benzyl-1,3-dithiane 1*R*-oxide: v_{max} (CHCl₃) 2900 and 1050 cm⁻¹; $\delta_{\rm H}$ (400 MHz, CDCl₃) 2.00-2.07 (1H, m), 2.48-2.52 (1H, m), 2.58-2.65 (1H, m), 2.67-2.74 (1H, m), 2.94-3.05 (3H, m), 3.40-3.44 (1H, m), 3.86-3.89 (1H, m) and 7.26-7.36 (5H, m); ee = 94% (determined using *R*-(-)-N-(3,5-dinitrobenzoyl)- α -methylbenzylamine (1 eq.)).

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(Received in UK 13 October 1995; revised 17 November 1995; accepted 23 November 1995)