Diastereoselective Control of Enolate Alkylation in 2-Acyl-2-alkyl-1,3-dithiane 1-Oxides

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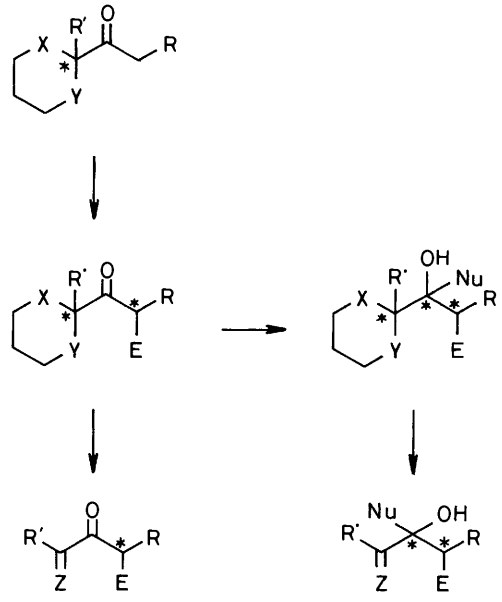
Stereochemical control of enolate alkylation in *syn* (**5**) and *anti* (**4**) acyl dithiane monosulphoxides has been investigated. The substrates were prepared in high yields from 2-substituted dithianes by acylation in two steps *via* the corresponding aldehydes followed by sulphoxidation. 2-Acyl-2-alkyl-1,3-dithiane 1-oxides were readily deprotonated using a variety of bases. The enolates so generated reacted with methyl iodide and other alkylating agents to give diastereoisomeric mixtures of the alkylated products, the ratios observed being dependent upon the relative stereochemistry of the acyl dithiane oxide, the 2-alkyl substituent, and the base, solvent, and temperature used for the reaction. Diastereoselectivities sufficiently high that the minor isomer could not be detected by ^{1}H n.m.r. spectroscopy at 250 MHz have been observed in some cases (Tables 2 and 3), the most selective system being the *anti* 2-acyl-2-ethyl derivative (**4c**). The data obtained fall into clear patterns which may be rationalized by proposing chelated chair-form transition states involving interaction of both the enolate and sulphoxide oxygen atoms with the metal counter-ions.

Diastereoselective and enantioselective control of enolate alkylation reactions are currently of great interest.[1] Those methods which do not rely upon asymmetric alkylating agents usually hinge upon a derivatisation of the ketonic substrate with an enantiomerically pure auxiliary which has no other function and which must subsequently be removed or destroyed. Such methods include the use of chiral oxazolines,[2] hydrazones,[3] acyl oxazolidinones,[4] and acyl iron complexes.[5] A rather different and pleasing approach involves enantioselective deprotonation using enantiomerically pure chiral bases.[6]

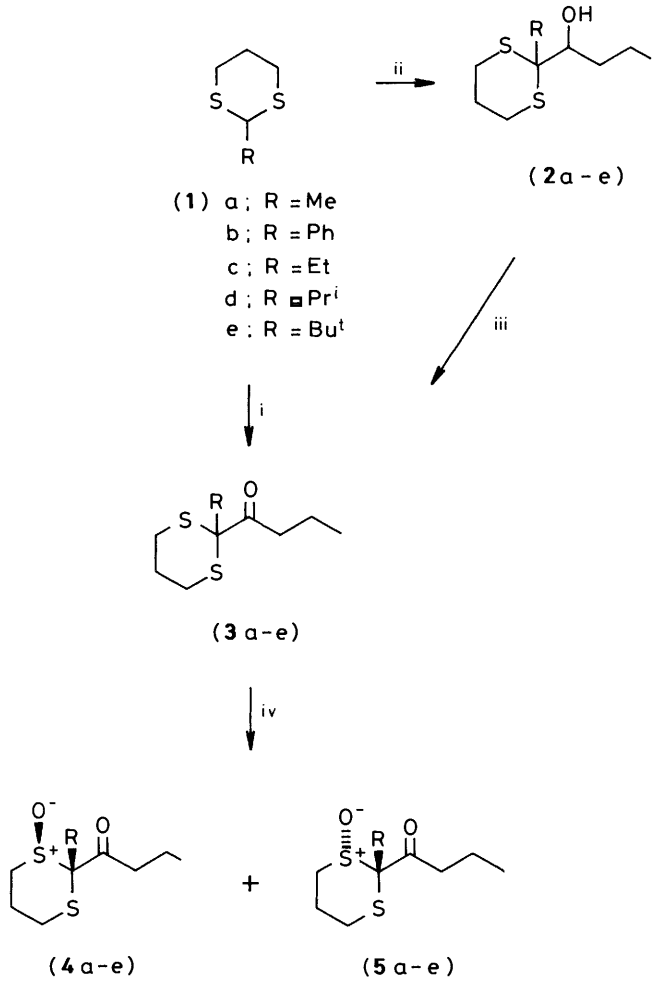
We are investigating a system which provides a method for diastereoselective and potentially enantioselective enolate alkylation reactions using a simple heterocyclic acyl derivative formed at the α′-carbon as the controlling element and source of chirality.[7] This method also has the potential for control of reactions subsequent to the alkylation, such as nucleophilic addition to the carbonyl group, and for removal or modification of the heterocycle to expose a second synthetically useful group (Scheme 1). This is possible in our system because the auxiliary/building block is bonded to the carbonyl group *via* a carbon atom rather than a heteroatom. An ideal system for our requirements should be inexpensive, stable, and easily prepared. Both enantiomers should be available, and unfamiliar or experimentally difficult chemistry should not be involved. All these requirements are fulfilled by the 2-acyl-1,3-dithiane 1-oxide grouping. This type of derivative has the additionally attractive property of excellent potential flexibility in terms of variability of ring size and heteroatom.

The 2-acyl-2-alkyl-1,3-dithiane 1-oxide systems are amenable to stereoselective preparation (Scheme 2). Direct acylation of the 2-lithio-2-alkyl-1,3-dithianes derived from (**1**) with ethyl butyrate[8] (5 equiv.) gave 2-alkyl-2-butyryl-1,3-dithianes (**3**) in up to 45% yield. The reaction was complicated by a double addition of the lithiodithianes derived from (**1**) to the ester, leading to formation of the tertiary alcohol species (**6**).[9] Attempts to circumvent this problem by acylating with carboxylates or *N*-methoxy tertiary amides[10] were unsuccessful, no reaction being observed under the conditions used for the ester acylation.

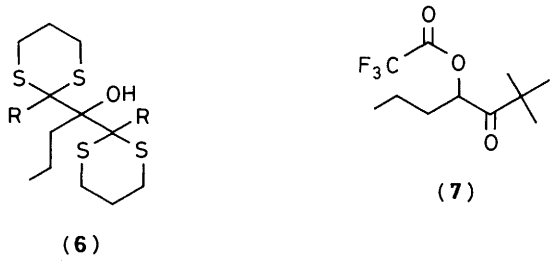


Scheme 1.

A more satisfactory route to the acyl dithianes (**3**) involved a two-step process *via* the alcohols (**2**). Thus, reaction of the lithiodithianes derived from (**1**) with butanal gave the alcohols (**2**) which were then converted into the ketones (**3**) by oxidation with dimethyl sulphoxide activated with trifluoroacetic anhydride[11] in up to quantitative yield. Exceptionally, for R = Bu^t, only a poor yield of the acyl derivative (**3e**) was obtained by either route, perhaps due to incomplete metallation of dithiane (**1e**). During the oxidation of the alcohol (**2e**) a by-product was obtained in 38% yield and identified as the trifluoroacetate (**7**). Such by-products are known to occur in the Swern oxidation reaction as a result of decomposition of the reagent.[11] Interestingly, however, the 1,3-dithiane ring had also been hydrolytically removed, presumably through action of the trifluoroacetic acid generated in the reaction medium; although



Scheme 2. *Reagents:* (i), BuLi, THF, −78 °C; ethyl butyrate; (ii), BuLi, THF, −78 °C; butanal; (iii), DMSO, $(CF_3CO)_2O$, CH_2Cl_2, −50 °C, Et_3N; (iv), $NaIO_4$

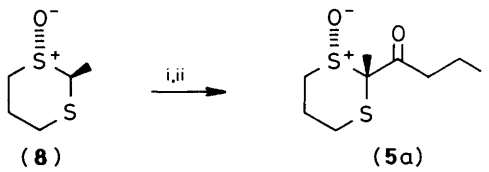


known to occur with dithioacetals, such a process is reported not to take place with 1,3-dithianes.[12]

Construction of the auxiliary was completed by chemoselective and stereoselective oxidation of the sulphides (**3**) to the mono-sulphoxides with sodium periodate or *m*-chloroperbenzoic acid[13] in excellent yields. The mixture of *anti* (**4**) and *syn* (**5**) 2-butyryl-2-alkyl-1,3-dithiane 1-oxides was readily separable in each case by flash column chromatography on silica gel. This route gave convenient access to both types of diastereoisomers (**4**) and (**5**) in up to 92% total yield and with diastereoselectivities ranging from *ca.* 1:2 (R = Bu^t) to *ca.* 3:1 (R = Pr^i). Simultaneous diastereoselective and enantioselective oxidations of 2-acyldithianes to the corresponding monosulphoxides are currently being investigated in our laboratories.[14,15]

The sulphoxide unit in our substrate was expected to influence the transition state geometry of the enolate by chelation to the metal counter ion,[16] and hence control the stereochemistry of the alkylation. Indeed this controlling group has recently been employed for the resolution of racemic ketones.[15]

Structural assignments of (**4a**) and (**5a**) were made by comparisons of their ^1H and ^{13}C n.m.r. spectra with those of the products arising from direct acylation of *anti* 2-methyl-1,3-dithiane 1-oxide (**8**)[13] and by analogy with compound (**11**), prepared from (**12**) by addition of a Grignard reagent, the structure of which was solved by *X*-ray analysis.[17,*] Treatment of (**8**) with lithium di-isopropylamide (1 equiv.) in tetrahydrofuran (THF) solution at −78 °C gave the anion[13] which reacted with ethyl buryrate stereospecifically to give (**5a**) in good yield (Scheme 3). Structural assignments of (**4b**) and (**5b**)



Scheme 3. *Reagents:* (i), LDA, THF; (ii), Ethyl butyrate

were made by comparisons of their ^1H and ^{13}C n.m.r. spectra with those of (**4a**) and (**5a**) and by inference from alkylated material (**13**) (the major product in Table 2, entry d), the structure of which was solved by *X*-ray analysis.[7,*] Structural assignments of (**4c—e**) and (**5c—e**) were made by comparisons of their ^1H and ^{13}C n.m.r. spectra and chromatographic behaviour with those of (**4a** and **b**) and (**5a** and **b**).

Deprotonation of systems (**4**) and (**5**) to give the corresponding enolates was carried out with a variety of bases, but typically by treatment with lithium (LHMDS) or potassium (KHMDS) hexamethyldisilazide (1.1 equiv.) in THF solution at −78 °C for 5—10 min or potassium t-butoxide (1.1 equiv.) in THF solution at 25 °C. The enolates were quenched at the reaction temperature with iodomethane or chlorotrimethylsilane, followed by aqueous work-up using saturated aqueous ammonium chloride or sodium hydrogen carbonate. The crude products were directly analysed by ^1H n.m.r. spectroscopy; reactions were generally very clean, simple rapid purification using a short silica gel column being necessary for some of the alkylated products. Separation of the diastereoisomeric products was not usually possible.

Ratios of the trimethylsilyl enol ether geometric isomers (**14**) and (**15**) were estimated by observation of the signals in the ^1H n.m.r. spectrum due to the vinylic protons and are shown in Table 1. Most importantly, essentially one enolate geometry is generated in the majority of cases irrespective of which base is used or its temperature of action. However, we have been unable to assign enolate stereochemistry by this method using the generalisation of House[18] with any degree of confidence.

Observed diastereoisomeric ratios for the alkylated products (**9**) and (**10**) are given in Tables 2 and 3. We have found that in all cases changing the counter ion from lithium to potassium results in a change in the sense of the preferred diastereoselection,[19] despite each reaction apparently proceeding through the same enolate geometry. We therefore propose that a change occurs from a chelated (closed) chair

* Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.

Table 1. Preparation of trimethylsilyl enol ethers of selected 2-acyl-2-alkyl-1,3-dithiane 1-oxides

Substrate	R	Base	Product	Ratio of isomers[a]
(**4a**)	Me	LHMDS	(**14a**)	Exclusive
(**4a**)	Me	KOBu^t	(**14a**)	>10:1
(**4b**)	Ph	LHMDS	(**14b**)	Exclusive
(**4b**)	Ph	KOBu^t	(**14b**)	10:1
(**5a**)	Me	LHMDS	(**15a**)	Exclusive
(**5a**)	Me	KOBu^t	(**15a**)	10:1
(**5b**)	Ph	LHMDS	(**15b**)	>10:1
(**5b**)	Ph	KOBu^t	(**15b**)	Exclusive

[a] Measured by 250 MHz ^{1}H n.m.r.

Table 2. Alkylation of enolates of *anti*-2-acyl-2-alkyl-1,3-dithiane 1-oxides (**4**)

Entry	Substrate	R	Base	Temp (°C)	Product type	Ratio of isomers[a]
a	(**4a**)	Me	LHMDS	−78	(**9a**)	2:1
b	(**4a**)	Me	LHMDS	−100	(**9a**)	2.6:1
c	(**4a**)	Me	KBuO^t	25	(**9a**)	1:1.9
d	(**4b**)	Ph	LHMDS	−78	(**9b**)	2:1
e	(**4b**)	Ph	KBuO^t	25	(**9b**)	1:1.4
f	(**4b**)	Ph	KHMDS	−78	(**9b**)	1:1.3
g	(**4c**)	Et	LHMDS	−100	(**9c**)	Exclusive
h	(**4d**)	Pr^i	LHMDS	−100	(**9d**)	*ca.* 25:1
i	(**4e**)	Bu^t	LHMDS	−78	(**17**)	—
j	(**4e**)	Bu^t	KBuO^t	25	(**17**)	—

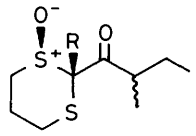
Table 3. Alkylation of enolates of *syn*-2-acyl-2-alkyl-1,3-dithiane 1-oxides (**5**)

Entry	Substrate	R	Base	Temp (°C)	Product type	Ratio of isomers[a]
a	(**5a**)	Me	LHMDS	−78	(**10a**)	*ca.* 25:1
b	(**5a**)	Me	KBuO^t	25	(**10a**)	1:1.2
c	(**5a**)	Me	KHMDS	−78	(**10a**)	1:1.1
d	(**5b**)	Ph	LHMDS	−78	(**10b**)	1:1
e	(**5b**)	Ph	LHMDS	−100	(**10b**)	1:1
f	(**5b**)	Ph	KBuO^t	25	(**10b**)	1:1.7
g	(**5c**)	Et	LHMDS	−100	(**10c**)	*ca.* 20:1
h	(**5d**)	Pr^i	LHMDS	−100	(**17**)	(3:1)[b]
i	(**5e**)	Bu^t	LHMDS	−78	(**17**)	—
j	(**5e**)	Bu^t	KBuO^t	25	(**17**)	—

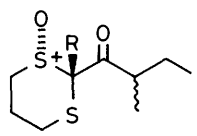
[a] Measured by 250 MHz ^{1}H n.m.r. [b] See text.

transition state[20] with the sulphoxide unit equatorial [necessary in the *anti* system (**4**) for chelation to take place] to another form, perhaps with an open chain[21] or a dipolar[22] (open) geometry.

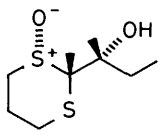
Thus, for the *anti* system (**4**) a chelated chair transition state, containing an equatorial sulphoxide, would require R to occupy an axial position and to provide the only steric bulk for any observed diastereoselectivity upon enolate alkylation [Scheme 4(i)]. Indeed, with LHMDS as base and when R is methyl, a selectivity of only *ca.* 2:1 is obtained (Table 2, entry a); however, as R becomes larger a very significant improvement in selectivity is observed and in one case the minor isomer was not detected in the product mixture (R = Et, entry g). A transition state where R occupies an equatorial position [Scheme 4(ii)], a situation which may become important for large R (entry d), would contain an axial sulphoxide and would eliminate any possibility of chelation control. With potassium as the counter-ion the ion-pairing in the transition state may be less tight than with lithium and the chelate model may not apply.[19] Thus the observed reversal of sense of diastereoselection (entries c, e, f)



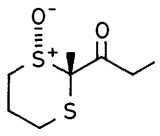
(**9**)



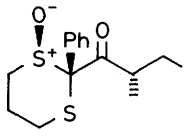
(**10**)



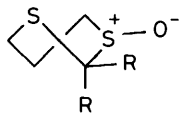
(**11**)



(**12**)



(**13**)



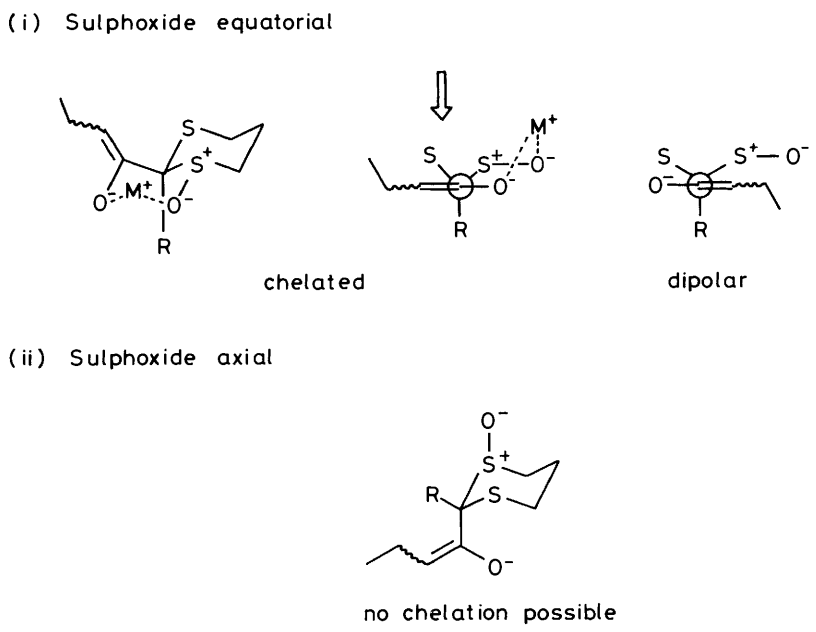
(**16**)

can be accounted for by the adoption of a non-chelated transition state or a dipolar system, which may or may not be the same [Scheme 4(i)]. In this instance the diastereoselection is rather poor and apparently independent of temperature, also consistent with an open, less rigid, transition state.[23]

For the *syn* system (**5**) when R is small (methyl, ethyl) the diastereoisomeric ratio is high (Table 3, entries a, g) when lithium is the counter ion. This is consistent with a chelated chair transition state in which both the sulphoxide and the R group occupy equatorial positions, the bulk of the dithiane ring then providing a steric restriction to the incoming electrophile greater than and opposing that of the R group [Scheme 5(i)]. In this case, as R increases in size (entries a, g, h, e) the diastereoselectivity obtained in the alkylation falls off, as should be expected from our model; when R is phenyl a more equally crowded transition state would be expected and indeed a ratio of 1:1 is observed (entries d, e). When R is isopropyl (entry h) the major product, of type (**17**), results from reaction at oxygen, although some starting material is recovered and some carbon alkylation can also be seen (diastereoisomeric ratio *ca.* 3:1). The alternative chelated chair conformation in which both the sulphoxide and the R group occupy axial positions [Scheme 5(ii)], which may contribute for small R groups, would not be expected to produce any diastereoselection from inspection of open or closed transition states.

For both *syn* and *anti* substrates, when R is t-butyl [(**4e**) and (**5e**)], no C-alkylation products (**9**) or (**10**) are obtained. These reactions are characterised by incomplete metallation and a recovery of starting material; however, products of type (**17**) are also isolated in up to 40% yield.

Conformational preferences among cyclic sulphoxides do not seem to be well-understood. For example, while 1,2-dithiane 1-oxide[24] and 1,2-oxathiane 2-oxide (ΔG^0 estimated >2.0 kcal mol^{-1} at −90 °C),[25] show a preference for axial sulphoxide, perhaps for reasons of minimisation of dipole-dipole interactions,[25] and thiane 1-oxide (ΔG^0 *ca.* 175 cal mol^{-1} at −90 °C),[26,27] selenane 1-oxide,[28] thiane-1-(*N*-tosyl)imide (ΔG *ca.* 145 cal mol^{-1} at −89 °C),[29] 1,4-dithiane 1-oxide,[24] 1,3-oxathiane 3-oxide (ΔG^0 *ca.* 570 cal mol^{-1} at −98 °C),[30,31] and 1,4-oxathiane 4-oxide (ΔG^0 *ca.* 680 cal mol^{-1} at −80 °C)[32] all show a preference for axial sulphoxide for less apparent



Scheme 4. *anti*-System (**4**)

reasons,[27,31,33,34] 1,3-dithiane 1-oxide and its derivatives show a preference for equatorial sulphoxide (ΔG^0 *ca.* 640 cal mol^{-1} at −80 °C, $\Delta G^{\ddagger}$ = 11.0 kcal mol^{-1} at coalescence).[24,31,33] Solvent effects were not observed in the case of 1,3-dithiane 1-oxide, suggesting that dipole-dipole interactions are not involved.[24]

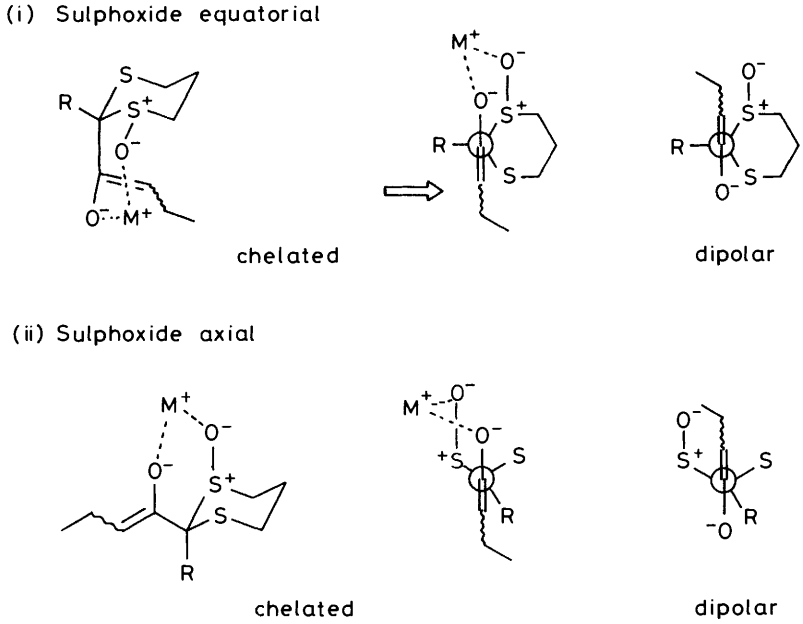
The structure of (**13**), the major component of (**9b**), was solved by single crystal *X*-ray analysis.[7] The crystal used was obtained by repeated recrystallisation of the product mixture (Table 2, entry d) and was shown to be the major product by ^{1}H n.m.r. analysis after the diffraction data had been obtained. Such a structure is consistent with a transition state as in Scheme 4(i), employing a *Z*-enolate. Earlier work by Carey[35] has suggested that 2,2-disubstituted 1,3-dithiane 1-oxides exist in solution with significant contributions from the twist conformations as in (**16**). In this situation, the sulphoxide oxygen atom occupies an isoclinal site and substituents become pseudo-axial and pseudo-equatorial. Such solution conformations could alleviate the energetic deficiencies of postulating a transition state containing an axial phenyl group while maintaining the stereochemistry of the reaction as observed.

The 1,3-dithiane 1-oxide group is readily removed under a variety of conditions.[36] Use of our systems as synthetic building blocks for stereocontrolled alkylation of ketones requires a clean removal or hydrolysis of the auxiliary, and we have investigated the method of Corey[37] with particular success. Hence, for example, treatment of substrates (**4b**) and (**5b**) with excess of *N*-bromosuccinimide leads after work-up to quantitative formation of the diketone (**18**).

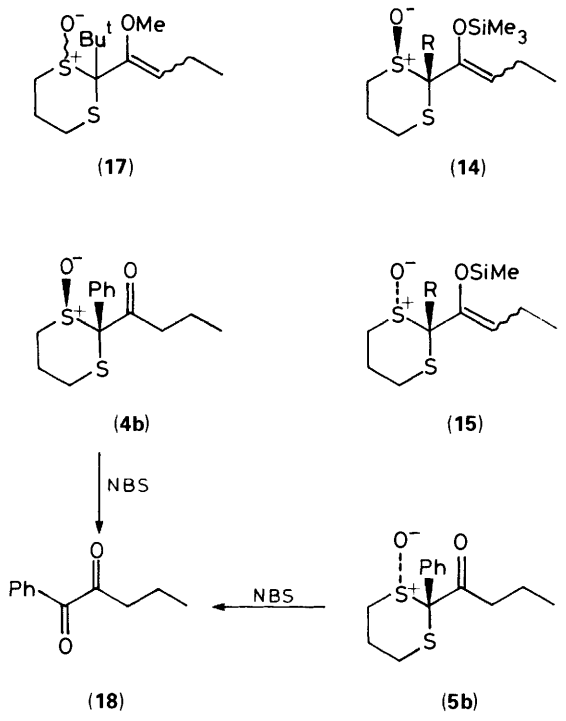
Experimental

General Experimental Details.—I.r. spectra were recorded in the range 4 000—600 cm^{-1} on Perkin-Elmer 298 and 1720FT spectrophotometers, and were calibrated against polystyrene. Solid samples were run as Nujol mulls or potassium bromide discs and liquids as thin films. ^{1}H N.m.r. spectra were recorded on Bruker WM 250, Bruker AC 200, Perkin-Elmer R34, and Jeol PMX60 instruments using deuteriochloroform solutions and tetramethylsilane as internal reference. Mass spectra were obtained on VG Micromass 7070E and AEI MS 902 mass spectrometers. Microanalyses were performed in the University of Liverpool Department of Chemistry microanalytical laboratory. M.p.s were determined on a Reichert hot stage apparatus and are uncorrected. Solvents used for recrystallisation are indicated in brackets after the m.p. Flash column chromatography was carried out using Merck 9385 silica gel, using hand-bellows or an air line to apply pressure to the column. Dry flash column chromatography was carried out using Merck 15111 silica gel with light petroleum (b.p. 40—60 °C) containing an increasing proportion of ethyl acetate as eluant. Medium pressure liquid chromatography was carried out using a Gilson 303 metering pump, a Gilson 804C pressure module, a Rheodyne 7125 injector fitted with a 5 ml loop, Omnifit and Buchi glass chromatography columns packed with Merck 15111 silica gel, a Waters R403 differential refractometer, a Chessell chart recorder, and a Gilson TDC80 fraction collector. High pressure liquid chromatography was carried out using a Waters Prep LC3000 pumping system, Waters R401 and R404 differential refractometers, Rainin Dynamax normal and reverse phase columns, a Waters 745 integrator, an ISCO 2150 peak separator, and an ISCO Foxy fraction collector. T.l.c. was carried out on glass or aluminium backed plates coated with a 0.25 mm layer of silica gel 60H. Compounds were visualised by u.v. irradiation or by spraying with dodecamolybdophosphoric acid (15% w/v in EtOH) followed by charring.

Purification of solvents and reagents. Tetrahydrofuran (THF) was freshly distilled under nitrogen from the sodium/-benzophenone ketyl radical immediately prior to use. Dichloromethane was freshly distilled from calcium hydride immediately prior to use. Butyl-lithium was purchased from the Lithium Corporation of Europe in one gallon quantities and decanted into 500 ml oven baked bottles stoppered with septa. The molarity of the butyl-lithium was determined by the Gilman double titration method[38] or by titration with diphenylacetic acid.[39] Chlorotrimethylsilane was distilled from calcium hydride under nitrogen and stored over type 4 Å molecular sieve. 1,3-Dithiane was stored in a desiccator over self-indicating silica gel; it was occasionally necessary to recrystallise the reagent from light petroleum (b.p. 40—60 °C). Triethylamine was distilled from potassium hydroxide pellets under nitrogen, and stored over type 4 Å molecular sieve.



Scheme 5. *syn*-System (**5**)



Preparation of glassware. All organometallic reactions were carried out in two- or three-necked round-bottom flasks which were baked at 150 °C for a minimum of 4 h. The flasks were allowed to cool in a desiccator over self-indicating silica gel, and were purged with nitrogen prior to being stoppered with septum caps. Syringes, needles, cannulas, and magnetic stirring bars used in organometallic reactions were also baked and allowed to cool in a desiccator. All organometallic reactions were carried out under a small static positive pressure of nitrogen.

Normal work-up procedure. Reactions were usually worked-up by addition of saturated aqueous ammonium chloride followed by extraction of the aqueous phase using several portions of chloroform or dichloromethane. The combined organic extracts were dried over anhydrous magnesium sulphate which was later removed by filtration. The filtrate was reduced in volume on a rotary evaporator to give the crude reaction mixture which was purified by chromatography or distillation.

2-(1-*Hydroxybutyl*)-2-*methyl*-1,3-*dithiane* (**2a**).—To a solution of 2-methyl-1,3-dithiane (1.02 g, 7.61 mmol) in THF (40 ml) at −30 °C was added a solution of butyl-lithium in hexane (1.1 equiv.). The resultant pale yellow anion was stirred for 2 h at −30 °C before cooling to −78 °C and quenching with butanal (0.66 g, 9.13 mmol). After warming to room temperature overnight the mixture was subjected to normal work-up to yield the alcohol (**2a**) as a pale yellow oil (1.56 g, 100%). This was distilled to give a colourless oil using a Kugelrohr bulb-to-bulb distillation apparatus, b.p. 140 °C at 1.25 mmHg (Found: C, 52.35; H, 8.8. $C_9H_{18}OS_2$ requires C, 52.38; H, 8.79%); $\nu_{max.}$(neat) 3 450 cm^{-1}; δ_H(220 MHz, CCl_4), 0.95 (3 H, t, *J* 7.3 Hz), 1.30—1.45 (2 H, m), 1.35 (3 H, s), 1.60—1.70 (1 H, m), 175—1.90 (2 H, m), 2.00—2.10 (1 H, m), 2.50—2.60 (3 H, m), 2.90—3.05 (2 H, m), and 3.80—3.90 (1 H, d, *J* 11 Hz); *m/z* (e.i.) 206 (M^+).

2-(1-*Hydroxybutyl*)-2-*phenyl*-1,3-*dithiane* (**2b**). 2-Phenyl-1,3-dithiane (5.32 g, 27.14) mmol) was treated as for (**2a**) using butyl-lithium (1.1 equiv.) and butanal (2.15 g, 29.86 mmol) in THF (180 ml) to yield the alcohol (**2b**) as a pale yellow oil. This was distilled to give a colourless oil (6.95 g, 96%), b.p. 225 °C at 0.5 mmHg (Found: C, 62.65; H, 7.65. $C_{14}H_{20}OS_2$ requires C, 62.64; H, 7.51%); $\nu_{max.}$(neat) 3 450 cm^{-1}; δ_H(220 MHz, CCl_4), 0.85 (3 H, t, *J* 8.0 Hz), 1.10—1.30 (2 H, m), 1.35—1.55 (2 H, m), 1.85—2.00 (3 H, m), 2.70—2.80 (4 H, m), 3.65—3.75 (1 H, m), 7.20—7.30 (1 H, m), 7.30—7.40 (2 H, m), and 7.85—7.95 (2 H, m); *m/z* (e.i.) 268 (M^+).

2-*Ethyl*-2-(1-*hydroxybutyl*)-1,3-*dithiane* (**2c**). 2-Ethyl-1,3-dithiane (5.20 g, 35.1 mmol) treated as for (**2a**) using butyl-lithium (1.1 equiv.) and butanal (3.54 g, 49.1 mmol) in THF (50 ml) yielded alcohol (**2c**) as a colourless oil (5.41 g, 70%) after flash chromatography over silica gel (Merck 9385) using 10% ethyl acetate–light petroleum (40—60 °C) as eluant (Found: C, 54.6; H, 9.2. $C_{10}H_{20}OS_2$ requires: C, 54.50; H, 9.15%); $\nu_{max.}$(neat) 3 500 cm^{-1}; δ_H(200 MHz, $CDCl_3$), 0.98 (3 H, t, *J* 7.1 Hz), 1.09 (3

H, t, *J* 7.4 Hz), 1.26—1.51 (2 H, m), 1.59—2.14 (6 H, m), 2.58—2.76 (3 H, m), 2.91—3.05 (2 H, m), and 3.97—4.02 (1 H, br d, *J* 9.4 Hz).

2-(1-*Hydroxybutyl*)-2-*isopropyl*-1,3-*dithiane* (**2d**). 2-Isopropyl-1,3-dithiane (5.60 g, 34.6 mmol) treated as for (**2a**) using butyl-lithium (1.1 equiv.) and butanal (3.54 g, 49.1 mmol) in THF (50 ml) yielded alcohol (**2d**) as a colourless oil (5.41 g, 67%) after flash chromatography over silica gel (Merck 9385) using 10% ethyl acetate–light petroleum (40—60 °C) as eluant (Found: C, 56.3; H, 9.5. $C_{11}H_{22}OS_2$ requires: C, 56.36; H, 9.46%); $\nu_{max.}$(neat) 3 500 cm^{-1}; δ_H(200 MHz, $CDCl_3$), 1.00 (3 H, t, *J* 7.2 Hz), 1.13 (3 H, d, *J* 6.7 Hz), 1.20 (3 H, d, *J* 6.7 Hz), 1.39—2.22 (7 H, m), 2.58—2.70 (2 H, m), 2.85—3.07 (3 H, m), and 4.06 (1 H, br, d, *J* 9.6 Hz).

2-(1-*Hydroxybutyl*-2-*t-butyl*-1,3-*dithiane* (**2e**). 2-t-Butyl-1,3-dithiane (16.66 g, 94.7 mmol) treated as for (**2a**) using butyl-lithium (1.1 equiv.) and butanal (7.50 g, 104 mmol) in THF (400 ml) yielded the alcohol (**2e**) as a colourless oil (15.55 g, 66%) after flash chromatography over silica gel (Merck 9385) using 10% ethyl acetate–light petroleum (40—60 °C) as eluant and distillation on a Kugelrohr apparatus, b.p. 160 °C at 0.7 mmHg (Found: C, 58.1; H, 9.9. $C_{12}H_{24}OS_2$ requires C, 58.01; H, 9.74%); $\nu_{max.}$(neat) 3 500 cm^{-1}; δ_H(220 MHz, $CDCl_3$), 0.95—1.00 (3 H, t, *J* 7.3 Hz), 1.20 (9 H, s), 1.30—1.45 (2 H, m), 1.60—1.90 (2 H, m), 2.00—2.20 (2 H, m), 2.60—2.70 (2 H, m), 2.90—3.10 (3 H, m), and 4.10—4.15 (1 H, d, *J* 10 Hz); *m/z* (c.i.) 249 ($M^+ + 1$).

2-*Butyryl*-2-*methyl*-1,3-*dithiane* (**3a**).—(i) *From* 2-*methyl*-1,3-*dithiane* (**1a**). To a solution of 2-methyl-1,3-dithiane (7.47 g, 55.75 mmol) in THF (200 ml) was added a solution of butyl-lithium in hexane (1.1 equiv.) at −20 °C for 1 h. The resultant anion was then added to a solution of ethyl butyrate (32.33 g, 278.8 mmol) in THF (50 ml) at −78 °C and allowed to warm to room temperature overnight. The reaction mixture was subjected to normal work-up to yield the ketone (**3a**) as a pale yellow oil which was distilled on a Kugelrohr apparatus to give a clear oil (5.10 g, 45%), b.p. 150 °C at 1 mmHg (Found: C, 53.15; H, 7.90. $C_9H_{16}OS_2$ requires C, 52.90; H, 7.89%); $\nu_{max.}$(neat) 1 700 cm^{-1}; δ_H(220 MHz, $CDCl_3$), 0.95 (3 H, t, *J* 8.0 Hz), 1.60—1.70 (2 H, m), 1.65 (3 H, s), 1.75—1.90 (1 H, m), 2.0—2.15 (1 H, m), 2.55—2.70 (4 H, m), and 3.05—3.20 (2 H, m); *m/z* (e.i.) 204 (M^+).

(ii) *From* 2-(1-*hydroxybutyl*)-2-*methyl*-1,3-*dithiane* (**2a**). To a solution of dimethyl sulphoxide (DMSO) (0.21 g, 2.71 mmol) in dry dichloromethane (5 ml) at −78 °C was added dropwise a solution of trifluoroacetic anhydride (0.57 g, 2.70 mmol) in dichloromethane (2 ml). After stirring for 30 min at −78 °C the alcohol (**2a**) (0.5 g, 2.43 mmol) in dichloromethane solution (5 ml) was added dropwise. Stirring was continued at −78 °C for 1 h, and triethylamine (0.60 g, 5.96 mmol) was added dropwise. The solution was allowed to warm to 0 °C before pouring onto 5% aqueous hydrochloric acid (30 ml) and shaking thoroughly. The organic phase was washed with aqueous sodium hydrogen carbonate (10 ml) and dried ($MgSO_4$) before evaporating to yield a pale yellow oil. Distillation furnished the ketone (**3a**) as a colourless oil (0.49 g, 100%).

2-*Butyryl*-2-*phenyl*-1,3-*dithiane* (**3b**).—(i) *From* 2-*phenyl*-1,3-*dithiane* (**1b**). 2-Phenyl-1,3-dithiane (8.27 g, 42.19 mmol), treated as described above using butyl-lithium (1.1 equiv.) and ethyl butyrate (24.0 g, 206 mmol) in THF (200 ml) gave the ketone (**3b**) after distillation as a pale yellow oil (4.71 g, 42%), b.p. 220 °C at 0.5 mmHg (Found: C, 63.05; H, 6.85. $C_{14}H_{18}OS_2$ requires C, 63.12; H, 6.81%); $\nu_{max.}$(neat) 1 710 cm^{-1}; δ_H(220 MHz, $CDCl_3$), 0.85 (3 H, t, *J* 9.0 Hz), 1.55—1.70 (2 H, m), 1.90—2.05 (1 H, m), 2.10—2.25 (1 H, m), 2.40—2.50 (2 H, t, *J* 9.0 Hz), 2.75—2.90 (2 H, m), 3.15—3:30 (2 H, m), 7.40—7.50 (3 H, m), and 7.60 (2 H, m); *m/z* (e.i.) 266 (M^+).

(ii) *From* 2-(1-*hydroxybutyl*)-2-*phenyl*-1,3-*dithiane* (**2b**). The alcohol (**2b**) (6.76 g, 25.22 mmol) treated as for the preparation of (**3a**) (ii) using DMSO (2.19 g, 28.10 mmol), trifluoroacetic anhydride (5.84 g, 27.80 mmol), and triethylamine (6.10 g, 60.42 mmol) in dichloromethane (100 ml) furnished the ketone (**3b**) as a pale yellow oil after distillation (6.03 g, 90%).

2-*Butyryl*-2-*ethyl*-1,3-*dithiane* (**3c**).—The alcohol (**2c**) (1.60 g, 7.27 mmol) treated as for the preparation of (**3a**) (ii) using DMSO (0.94 g, 14.54 mmol), trifluoroacetic anhydride (2.29 g, 10.91 mmol), and triethylamine (3.07 g, 16.00 mmol) in dichloromethane (25 ml) furnished the ketone (**3c**) as a pale yellow oil (0.95 g, 60%) after chromatography on silica gel (Merck 9385) using 10% ethyl acetate–light petroleum (40—60 °C) as eluant; $\nu_{max.}$(neat) 1 700 cm^{-1}; δ_H(200 MHz, $CDCl_3$), 0.97 (3 H, t, *J* 7.4 Hz), 1.00 (3 H, t, *J* 7.6 Hz), 1.56—1.73 (2 H, m), 1.77—1.95 (1 H, m), 2.00—2.25 (3 H, m), 2.53—2.70 (4 H, m), and 2.92—3.06 (2 H, m) (Found: C, 54.8; H, 8.35. $C_{10}H_{18}OS_2$ requires C, 55.00: H, 8.31%).

2-*Butyryl*-2-*isopropyl*-1,3-*dithiane* (**3d**).—The alcohol (**2d**) (1.55 g, 6.62 mmol) treated as for the preparation of (**3a**) (ii) using DMSO (0.85 g, 13.24 mmol), trifluoroacetic anhydride (2.09 g, 9.93 mmol), and triethylamine (2.80 g, 14.56 mmol) in dichloromethane (25 ml) furnished the ketone (**3d**) as a pale yellow oil (0.72 g, 47%) after chromatography on silica gel (Merck 9385) using 10% ethyl acetate–light petroleum (b.p. 40—60 °C) as eluant; $\nu_{max.}$(neat) 1 700 cm^{-1}; δ_H(200 MHz, $CDCl_3$), 0.96 (3 H, t, *J* 7.4 Hz), 1.12 (6 H, d, *J* 6.8 Hz), 1.60—1.75 (2 H, m), 1.78—1.90 (1 H, m), 1.97—2.07 (1 H, m), 2.25—2.39 (1 H, m), 2.59—2.75 (4 H, m), and 2.88—3.03 (2 H, m).

2-*Butyryl*-2-*t-butyl*-1,3-*dithiane* (**3e**).—(i) *From* 2-*t-butyl*-1,3-*dithiane* (**1e**).—2-t-Butyl-1,3-dithiane (**1e**) (0.82 g, 4.66 mmol) treated as for the preparation of (**3a**) (i) using butyl lithium (1.1 equiv.) and ethyl butyrate (2.90 g, 25.00 mmol) in THF (100 ml) yielded the ketone (**3e**) as a colourless oil (0.30 g, 26%) after distillation on Kugelrohr apparatus, b.p. 180 °C at 1.5 mmHg (Found: C, 58.45; H, 9.2. $C_{12}H_{22}OS_2$ requires C, 58.49; H, 9.00%); $\nu_{max.}$(neat) 1 700 cm^{-1}; δ_H(220 MHz, $CDCl_3$), 1.00 (3 H, t, *J* 8.0 Hz), 1.20 (9 H, s), 1.65—2.05 (4 H, m), 2.60—2.80 (4 H, m), and 2.90—3.00 (2 H, m); *m/z* (e.i.) 247 (M^+).

(ii) *From* 2-(1-*hydroxybutyl*)-2-*t-butyl*-1,3-*dithiane* (**2e**). The alcohol (**2e**) (14.67 g, 59.2 mmol) treated as for the preparation of (**3a**) (ii) using DMSO (5.17 g, 66.25 mmol), trifluoroacetic anhydride (13.86 g, 66.0 mmol), and triethylamine (14.65 g, 145.0 mmol) in dichloromethane (230 ml) furnished the ketone (**3e**) (6.00 g, 40%) after chromatography on silica gel (Merck 9385) using a gradient elution from light petroleum (b.p. 40—60 °C) to 10% ethyl acetate–light petroleum (b.p. 40–60 °C) and distillation.

General Procedure for Oxidation of 2-*Alkyl*-2-*butyryl*-1,3-*dithianes* (**3**) *to Sulphoxides* (**4**) *and* (**5**).—To a solution of(**3**) in methanol [*ca.* 50 ml/g of (**3**)] at 0 °C was added dropwise a solution of sodium metaperiodate (1.1 equiv.) in water [*ca.* 2 ml/g of (**3**)] over 30 min. The resulting white suspension was stirred for 24—28 h and allowed to reach room temperature. The precipitate was removed by filtration and washed thoroughly with chloroform. The filtrate was evaporated to a slush and partitioned between water and chloroform. The water was twice extracted with chloroform and the combined organic fractions were dried ($MgSO_4$) and the solvents removed to yield a crude mixture of the diastereoisomers (**4**) and (**5**). These were separated by flash chromatography (Merck 9385), high pressure

liquid chromatography, or medium pressure liquid chromatography (Merck 15111) using chloroform or ethyl acetate as eluant. The pure diastereoisomers were recrystallised or distilled as necessary.

anti-(**4a**) *and* syn-(**5a**) 2-*Butyryl*-2-*methyl*-1,3-*dithiane* 1-*oxides*. Treatment of 2-butyryl-2-methyl-1,3-dithiane (**3a**) (3.50 g, 17.16 mmol) as described above using sodium periodate (4.02 g, 18.78 mmol) in water (40 ml) and methanol (150 ml) furnished (**4a**) as a white crystalline solid (2.24 g, 60%) and (**5a**) as a colourless oil (0.90 g, 24%).

For (**4a**): m.p. 52—53 °C (diethyl ether–light petroleum) (Found: C, 49.0; H, 7.34. $C_9H_{16}O_2S_2$ requires C, 49.06; H, 7.32%); $\nu_{max.}$(neat) 1 695 and 1 050 cm^{-1}; δ_H(250 MHz, $CDCl_3$) 0.95 (3 H, t, *J* 7.5 Hz), 1.60—1.70 (2 H, m), 1.65 (3 H, s), 1.85—1.95 (1 H, m), 2.40—2.70 (4 H, m), 2.90—3.10 (2 H, m), and 3.20—3.35 (1 H, m); *m/z* (e.i.) 220 (M^+).

For (**5a**): (Found: C, 49.15; H, 7.45. $C_9H_{16}O_2S_2$ requires C, 49.06; H, 7.32%); $\nu_{max.}$(neat) 1 705 and 1 060 cm^{-1}; δ_H(250 MHz, $CDCl_3$) 0.95 (3 H, t, *J* 7.5 Hz), 1.60—1.70 (2 H, m), 1.90 (3 H, s), 2.35—2.40 (3 H, m), 2.60—2.70 (2 H, m), and 3.10—3.20 (3 H, m); *m/z* (e.i.) 220 (M^+).

anti-(**4b**) *and* syn-(**5b**) 2-*Butyryl*-2-*phenyl*-1,3-*dithiane* 1-*oxides*. Treatment of 2-butyryl-2-phenyl-1,3-dithiane (**3b**) (5.20 g, 19.55 mmol) as described above using sodium periodate (4.39 g, 20.53 mmol) in water (80 ml) and methanol (350 ml), furnished (**4b**) (3.11 g, 56%) and (**5b**) (1.96 g, 36%) as colourless crystalline solids.

For (**4b**): m.p. 66—67 °C (diethyl ether) (Found: C, 59.75; H, 6.45. $C_{14}H_{18}O_2S_2$ requires C, 59.54; H, 6.42%); $\nu_{max.}$(Nujol) 1 695 and 1 060 cm^{-1}; δ_H(250 MHz, $CDCl_3$) 0.85 (3 H, t, *J* 7.5 Hz), 1.50—1.65 (2 H, m), 1.75—1.85 (1 H, m), 2.30—2.80 (5 H, m), 3.05—3.10 (1 H, m), 3.30—3.40 (1 H, m), and 7.40—7.50 (5 H, m); *m/z* (e.i.) 282 (M^+).

For (**5b**): m.p. 84—85 °C (diethyl ether) (Found: C, 59.75; H, 6.45. $C_{14}H_{18}O_2S_2$ requires C, 59.54; H, 6.42%); $\nu_{max.}$(Nujol) 1 710 and 1 065 cm^{-1}; δ_H(250 MHz, $CDCl_3$) 0.75 (3 H, t, *J* 7.5 Hz), 1.45—1.60 (2 H, m), 1.85—2.00 (1 H, m), 2.30—2.85 (6 H, m), 3.15—3.25 (1 H, m), 7.40—7.50 (3 H, m), and 7.65—7.70 (2 H, m); *m/z* (e.i.) 282 (M^+).

anti-(**4c**) *and* syn-(**5c**) 2-*Butyryl*-2-*ethyl*-1,3-*dithiane* 1-*oxides*. A solution of *m*-chloroperbenzoic acid (4.59 mmol) in dichloromethane (50 ml) was added dropwise to a solution of 2-butyryl-2-ethyl-1,3-dithiane (**3c**) (1.00 g, 4.59 mmol) in dichloromethane (50 ml) at 0 °C with stirring. After being stirred at 0 °C for 18 h the solution was washed with saturated aqueous sodium carbonate (2 × 50 ml) and concentrated *in vacuo*. Separation by flash column chromatography using ethyl acetate as eluant furnished (**4c**) as a colourless crystalline solid (0.404 g, 33%) and (**5c**) as a pale yellow oil (0.247 g, 25%).

For (**4c**): m.p. 50—52 °C (light petroleum); $\nu_{max.}$(Nujol) 1 695 and 1 040 cm^{-1}; δ_H(200 MHz, $CDCl_3$), 0.88 (3 H, t, *J* 7.4 Hz), 1.03 (3 H, t, *J* 7.5 Hz), 1.59—1.91 (4 H, m), 2.09—2.28 (1 H, m), 2.41—2.67 (4 H, m), and 2.88—3.10 (2 H, m) (Found: C, 51.05; H, 7.80. $C_{10}H_{18}O_2S_2$ requires C, 51.25; H, 7.74%).

For (**5c**): $\nu_{max.}$(neat) 1 700 and 1 062 cm^{-1}; δ_H(200 MHz, $CDCl_3$) 0.95 (3 H, t, *J* 7.4 Hz), 1.07 (3 H, t, *J* 7.5 Hz), 1.59—1.77 (2 H, m), 2.01—2.20 (1 H, m), and 2.27—23.27 (9 H, m).

anti-(**4d**) *and* syn-(**5d**) 2-*Butyryl*-2-*isopropyl*-1,3-*dithiane* 1-*oxides*. Treatment of 2-butyryl-2-isopropyl-1,3-dithiane (**3d**) (0.72 g, 3.10 mmol) with *m*-chlorobenzoic acid (3.10 mmol) as described above for (**3c**) followed by separation with flash column chromatography using ethyl acetate as eluant furnished (**4d**) (0.528 g, 68%) and (**5d**) (0.183 g, 24%) as pale yellow oils.

For (**4d**): $\nu_{max.}$(neat) 1 686 and 1 053 cm^{-1}; δ_H(200 MHz, $CDCl_3$), 0.98 (3 H, t, *J* 7.1 Hz), 1.12 (3 H, d, *J* 6.7 Hz)), 1.21 (3 H, d, *J* 7.1 Hz), 1.59—1.77 (3 H, m), 2.28—2.49 (1 H, m), and 2.50—3.11 (7 H, m).

For (**5d**): $\nu_{max.}$(neat) 1 699 and 1 063 cm^{-1}; δ_H(200 MHz, $CDCl_3$) 0.97 (3 H, t, *J* 7.4 Hz), 1.00 (3 H, d, *J* 6.7 Hz), 1.26 (3 H, d, *J* 6.6 Hz), 1.61—1.86 (2 H, m), 2.27—2.41 (3 H, m), 2.56—2.87 (3 H, m), and 2.90—3.29 (3 H, m).

anti-(**4e**) *and* syn-(**5e**) 2-*Butyryl*-2-*t-butyl*-1,3-*dithiane* 1-*oxides*. Treatment of 2-butyryl-2-t-butyl-1,3-dithiane (**3e**) (4.00 g, 16.26 mmol) as described above using sodium periodate (3.48 g, 16.26 mmol) in water (50 ml) and methanol (200 ml) after separation by flash column chromatography using a gradient elution of 25—60% ethyl acetate–light petroleum (40—60 °C) as eluant furnished (**4e**) as a colourless crystalline solid (0.96 g, 23%) and (**5e**) as a pale yellow oil (1.82 g, 43%) after Kugelrohr distillation.

For (**4e**): m.p. 77—79 °C (light petroleum) (Found: C, 54.95; H, 8.55. $C_{12}H_{22}O_2S_2$ requires C, 54.92; H, 8.45%); $\nu_{max.}$(Nujol) 1 680 and 1 045 cm^{-1}; δ_H(220 MHz, $CDCl_3$), 1.00 (3 H, t, *J* 8.0 Hz), 1.20 (9 H, s), 1.65—2.80 (3 H, m), 2.45—2.95 (6 H, m), and 3.10—3.25 (1 H, m); *m/z* (e.i.) 262 (M^+).

For (**5e**): b.p. 180 °C at 1.5 mmHg (Found: C, 54.9; H, 8.7. $C_{12}H_{22}O_2S_2$ requires C, 54.92; H, 8.45%); $\nu_{max.}$(neat) 1 695 and 1 040 cm^{-1}; δ_H(220 MHz, $CDCl_3$) 1.00 (3 H, t, *J* 8.0 Hz), 1.3 (9 H, s), 1.70—1.85 (2 H, m), 2.30—2.40 (2 H, m), 2.45—2.50 (2 H, m), and 2.90—3.10 (4 H, m); *m/z* (e.i.) 263 (M^+).

General Procedure for Alkylation of Ketonic Substrates (**4**) *and* (**5**) *to give* (**9**) *and* (**10**) *respectively*.—(i) *Using lithium hexamethyldisilazide or potassium hexamethyldisilazide*. A solution of the ketone (**4**) or (**5**) in THF (*ca.* 25 ml/mmol of substrate) was added to a solution of freshly prepared lithium (or potassium) hexamethyldisilazide (1.1 equiv.) in THF (*ca.* 15 ml/mmol of substrate) at −78 °C. After being stirred for 5—10 min the reaction mixture was treated with neat methyl iodide (1.5 equiv.) and allowed to reach room temperature overnight. The mixture was poured into saturated aqueous ammonium chloride (*ca.* 60 ml/mmol substrate) and extracted with dichloromethane (2 × 30 ml). The combined organic extracts were dried and evaporated to yield solutions of the crude alkylated products which were analysed by 250 MHz ^1H n.m.r. spectroscopy either directly or after passage through a short column of silica gel (Merck 9385) using chloroform or ethyl acetate as eluant. Yields of the order of 70% were generally obtained.

For (**9a**) (major isomer): δ_H(250 MHz, $CDCl_3$), 0.95 (3 H, t, *J* 7.4 Hz), 1.22 (3 H, d, *J* 6.7 Hz), 1.34—1.55 (3 H, m), 1.68 (3 H, s), 1.70—1.85 (2 H, m), 2.27—2.71 (3 H, m), and 2.84—3.36 (1 H, m); *m/z* (e.i.) 234 (M^+).

For (**9b**) (major isomer): δ_H(250 MHz, $CDCl_3$), 0.85 (3 H, d, *J* 6.7 Hz), 0.87 (3 H, t, *J* 7.3 Hz), 1.21—1.52 (3 H, m), 1.67—1.87 (2 H, m), 2.44—2.78 (2 H, m), 3.05—3.14 (1 H, m), 7.38—7.50 (3 H, m), and 7.54—7.57 (2 H, m).

For (**9c**) (major isomer): δ_H(200 MHz, $CDCl_3$), 0.96 (3 H, t, *J* 7.4 Hz), 1.09 (3 H, t, *J* 7.5 Hz), 1.24 (3 H, d, *J* 6.6 Hz), 1.30—1.70 (1 H, m), 1.75—2.00 (2 H, m), 2.05—2.30 (2 H, m), 2.40—2.60 (3 H, m), and 3.00—3.20 (3 H, m).

For (**9d**) (major isomer): δ_H(200 MHz, $CDCl_3$), 1.08 (3 H, t, *J* 7.4 Hz), 1.33 (3 H, d, *J* 7.0 Hz), 1.35 (3 H, d, *J* 6.5 Hz), 1.38 (3 H, d, *J* 7.0 Hz), 1.50—1.90 (3 H, m), 2.45—2.90 (4 H, m), 3.00—3.25 (2 H, m), and 3.30—3.50 (1 H, m).

For (**10a**) (major isomer): δ_H(250 MHz, $CDCl_3$), 0.92 (3 H, t, *J* 7.5 Hz), 1.10 (3 H, d, *J* 6.5 Hz), 1.39—1.50 (1 H, m), 1.67—1.78 (1 H, m), 1.93 (3 H, s), 2.24—2.50 (3 H, m), 2.88—3.11 (3 H, m), and 3.56—3.62 (1 H, m); *m/z* (e.i.) 234 (M^+).

For (**10b**) (major isomer): δ_H(250 MHz, $CDCL_3$), 0.32 (3 H, t, *J* 7.4 Hz), 1.05 (3 H, d, *J* 6.7 Hz), 1.08—1.38 (3 H, m), 1.57—1.74 (2 H, m), 2.32—3.10 (4 H, m), 7.31—7.51 (3 H, m), and 7.74—7.77 (2 H, m).

For (**10c**) (major isomer): δ_H(200 MHz, $CDCl_3$), 0.93 (3 H, t, *J*

7.3 Hz), 1.10 (3 H, d, *J* 6.8 Hz), 1.14 (3 H, t, *J* 7.5 Hz), 1.33—1.55 (1 H, m), 1.60—1.81 (1 H, m), 2.10—2.53 (5 H, m), 2.83—3.12 (3 H, m), and 3.24—3.37 (1 H, m).

(ii) *With Potassium t-Butoxide.*—To a solution of the ketone (**4**) or (**5**) in THF (*ca.* 25 ml/mmol of substrate) at room temperature was added solid freshly sublimed potassium t-butoxide (1.1 equiv.) in one portion. After being stirred for 10—30 min the mixture was treated with methyl iodide (1.5 equiv.) and stirred for a further 16 h before work-up in the manner described above.

General Procedure for Preparation of Trimethylsilyl Enol Ethers (**14**) *and* (**15**).—Ketones (**4a** and **b**) and (**5a** and **b**) were deprotonated as described above and then treated with trimethylsilyl chloride (1.5 equiv.) over 4 h; work-up using saturated aqueous sodium hydrogen carbonate gave after removal of solvents, the enol ethers (**14**) and (**15**) respectively, solutions of which were analysed directly by 220 MHz ^{1}H n.m.r. spectroscopy.

For (**14a**) (major isomer): δ_H(250 MHz, $CDCl_3$), 0.10 (9 H, s), 0.75 (3 H, t, *J* 7.3 Hz), 1.40 (3 H, s), 1.60—1.95 (3 H, m), 2.10—2.85 (5 H, m), and 5.00 (1 H, t, *J* 9.0 Hz).

For (**14b**) (major isomer): δ_H(250 MHz, $CDCl_3$), 0.10 (9 H, s), 0.80 (3 H, t, *J* 7.3 Hz), 1.85—2.00 (3 H, m,), 2.10—2.30 (1 H, m), 2.30—2.85 (4 H, m), 4.85 (1 H, t, *J* 7.3 Hz), 7.25—7.35 (3 H, m), and 7.75—7.85 (2 H, m).

For (**15a**) (major isomer): δ_H(250 MHz, $CDCl_3$), 0.10 (9 H, s), 0.85 (3 H, t, *J* 7.3 Hz), 1.50 (3 H, s), 1.85—2.05 (3 H, m), 2.20—2.45 (2 H, m), 2.60—2.85 (3 H, m), and 5.00 (1 H, t, *J* 7.8 Hz).

For (**15b**) (major isomer): δ_H(250 MHz, $CDCl_3$), 0.10 (9 H, s), 1.05 (3 H, t, *J* 7.3 Hz), 1.80—1.95 (1 H, m), 2.05—2.25 (2 H, m), 2.40—2.80 (4 H, m), 3.00—3.25 (1 H, m), 5.50 (1 H, t, *J* 7.3 Hz), 7.20—7.50 (3 H, m), and 7.65—7.75 (2 H, m).

1-*Phenylpentane*-1,2-*dione* (**18**).—A solution of (**4b**) or (**5b**) (200 mg, 0.71 mmol) in acetone (1.5 ml) was added dropwise to a solution of *N*-bromosuccinimide (1.01 g, 5.68 mmol) in 3% water–acetone (12.0 ml) at 5 °C. The mixture was stirred and allowed to reach room temperature over 30 min, before being poured onto a mixture of saturated aqueous sodium sulphite (20 ml) and dichloromethane (20 ml). After the mixture had been stirred for 15 min, the organic layer was separated and washed sequentially with saturated aqueous sodium hydrogen carbonate (10 ml), water (10 ml), and brine (10 ml). The organic fraction was dried ($MgSO_4$) and the solvents removed to yield the diketone (**18**) as a pale yellow oil (125 mg, 100%); $\nu_{max.}$(neat) 1 675 and 1 710 cm^{-1}; δ_H(220 MHz, $CDCl_3$), 1.00 (3 H, t, *J* 8.8 Hz), 1.70—1.85 (2 H, m), 2.90 (2 H, t, *J* 7.3 Hz), 7.50—7.60 (2 H, m), 7.60—7.70 (1 H, m), and 8.00—8.05 (2 H, m); *m/z* (e.i.) 176 (M^+).

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