Synthesis of Some Thietanoprostanoids

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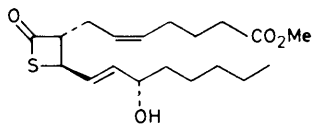
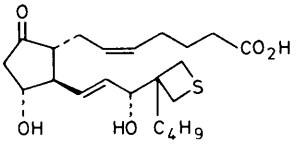
Four isomers of 2-(hydroxymethyl)-3-(6-methoxycarbonylhexyl)-4-methylthietan 1-oxide have been prepared by way of intramolecular sulphenic acid–olefin additions. The sulphenic acids were generated by thermolysis of *erythro*- and *threo*-(methyl 10-hydroxy-9-t-butylsulphinyl-8-vinyldecanoate), which were synthesized in eleven steps from 6-bromohexanol. Oxidation of the thietan 1-oxide derivatives to the corresponding 1,1-dioxides, followed by oxidation of the hydroxymethyl groups, furnished (±)-2β-formyl-3α-(6-methoxycarbonyl)-4β-methylthietan 1,1-dioxide and its 4α-isomer, which were converted into thietanoprostanoids by standard methods. Configurations were assigned throughout by comparison with analogous compounds derived from four isomers of 6-hexyl-2-(hydroxymethyl)-4-methylthietan 1-oxide of established stereochemistry.

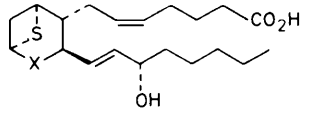
THE search for prostaglandin analogues of specific biological activity which may be exploited therapeutically has produced many synthetic heterocyclic prostanoids,[1] but among them thietan derivatives are represented only by the compounds (1)—(3).[2,3] Compound (1) in which the thietan ring takes the place of the



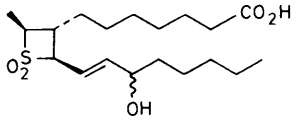
(1)



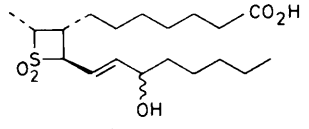
(2)



X = CH_2 or S
(3)

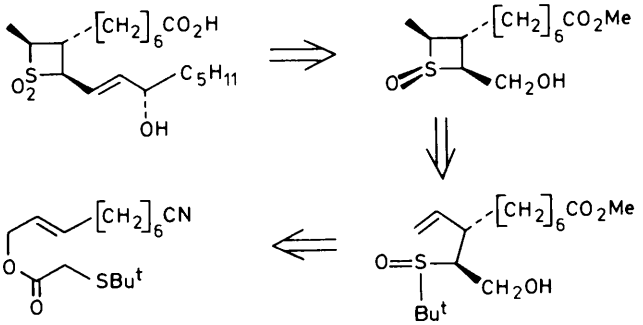


(4) a ; α - OH
b ; β - OH



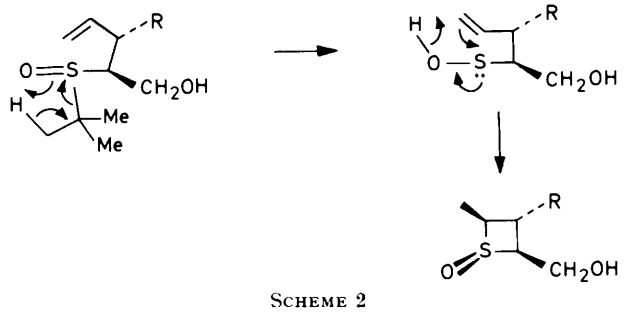
(5) a ; α - OH
b ; β - OH

cyclopentane ring of natural prostaglandins, showed transient hypotensive activity.[2] Interest in thietanoprostanoids of this type stems from the approximately isosteric relationship between thietan and cyclopentane rings, a phenomenon which might facilitate the accommodation of the unnatural compounds at an appropriate receptor site. This paper describes the synthesis of the thietanoprostanoids (4) and (5) guided by a retrosynthetic analysis, the salient features of which are outlined in Scheme 1. This exploits a new method of constructing thietan rings which involves the intramolecular addition of a sulphenic acid, itself generated by thermolysis of a t-butyl sulphoxide, to an olefin (Scheme 2). The stereochemical features of this cyclization had been elucidated previously.[4] We con-



SCHEME 1

sidered that the presence of a methyl group adjacent to the sulphur in the target molecules would not necessarily inhibit biological activity, since activity is retained in some prostaglandins bearing ring methyl substituents.[5] Furthermore, examples of the easy reduction of thietan

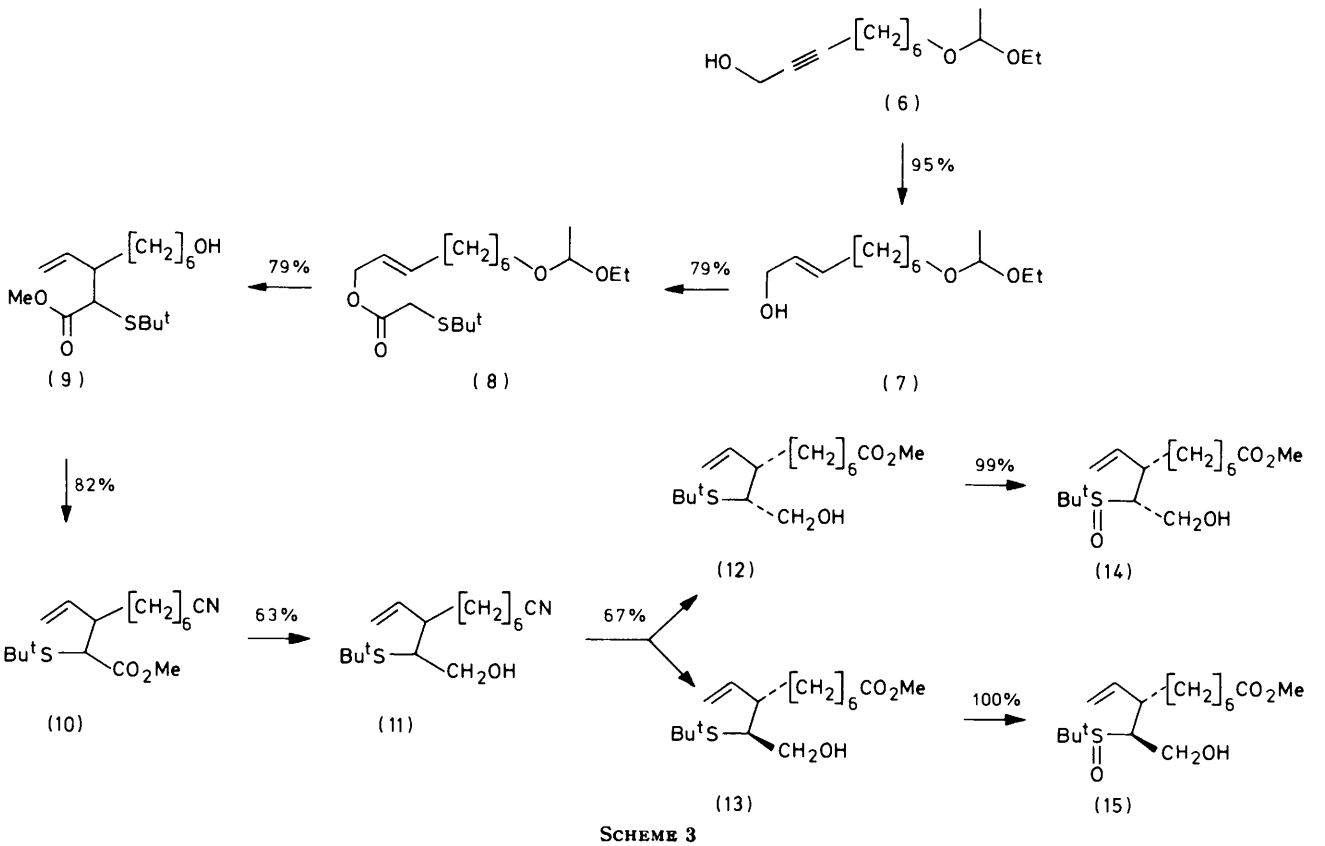


SCHEME 2

1-oxides and 1,1-dioxides to thietans (in marked contrast to the extreme difficulty in reducing most sulphones) and the oxidation of thietans to 1-oxides and 1,1-dioxides suggested that any necessary adjustment of the oxidation level at sulphur for synthetic purposes was feasible.[6]

RESULTS AND DISCUSSION

The key acyclic intermediates (14) and (15) were synthesized in the following manner (Scheme 3). Protection of the hydroxy-group of 6-bromohexanol by acetal formation using ethyl vinyl ether followed by reaction of the bromide with the dilithio-derivative of prop-2-yn-



SCHEME 3

1-ol gave the acetylenic hydroxy-acetal (6). Reduction with lithium aluminium hydride gave the expected[7] (*E*)-allylic alcohol (7), which was converted into the ester (8) on treatment with t-butylthioacetyl chloride. The silylketen acetals, derived from the ester (8) by treatment in sequence with lithium cyclohexylisopropylamide and chlorotrimethylsilane, underwent Claisen rearrangement[4,8] at 60 °C to give the hydroxy-ester (9), after hydrolysis of the silyl esters and re-esterification with acidic methanol, which concomitantly removed the acetal protecting group. The hydroxy-ester (9) was converted into its *p*-tolyl sulphonate and subsequently treated with potassium cyanide in dimethyl sulphoxide to furnish the cyano-ester (10).*

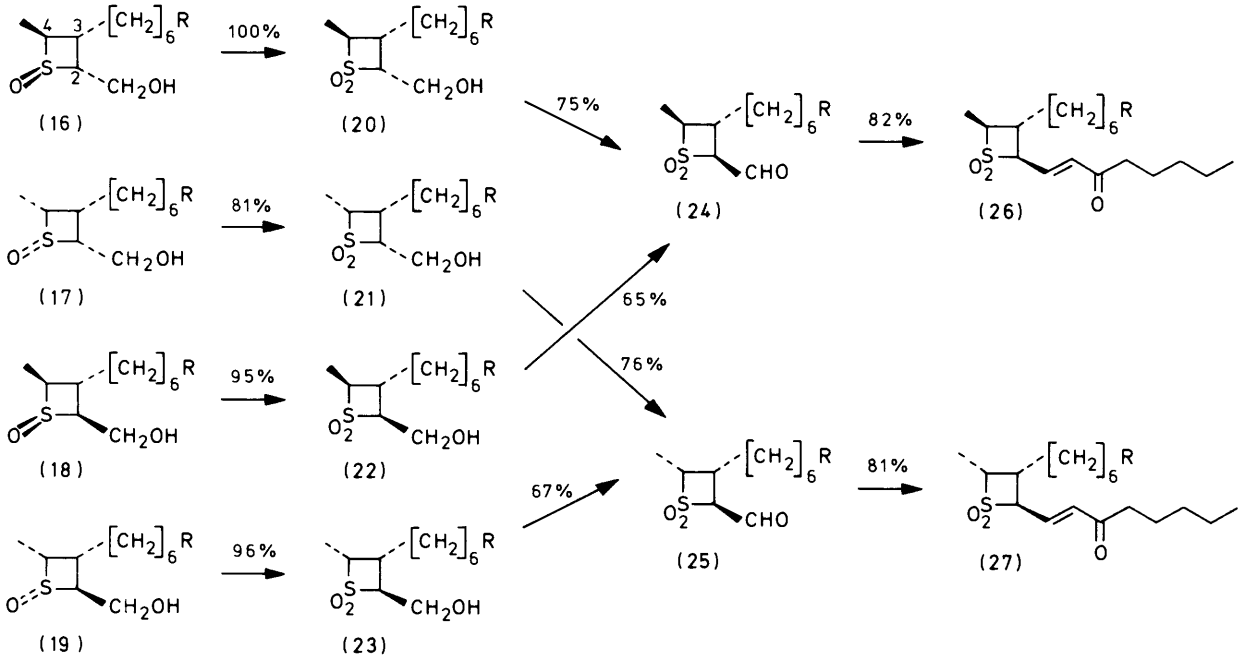
Selective reduction of the ester function in compound (10) by treatment with lithium borohydride in tetrahydrofuran (THF)[9] was complicated by the formation of several unidentified by-products, and by a moderate recovery (48%) of the required hydroxy-nitrile (11). We presumed that this was due to the formation of stable five-membered cyclic borate complexes involving the contiguous hydroxy and sulphide functions,[10] and yields were subsequently improved to 63% by decomposition of the complexes with boiling methanol. Selective reduction of the cyano-ester (10) by treatment with sodium bis(2-methoxyethoxy)aluminium hydride in boiling toluene or lithium aluminium hydride at −10 °C in diethyl ether proceeded much less efficiently. Base-catalysed hydrolysis of the nitrile (11) followed by treatment of the crude acid with diazomethane furnished the *erythro*- and *threo*-isomers of methyl 10-hydroxy-9-t-butylthio-8-vinyldecanoate, (12) and (13) respectively, in the ratio 8 : 5, which were separated by repeated chromatography on silica.† The assignment of *erythro*-configuration to the major isomer by analogy with previous studies[4] was confirmed by subsequent chemical transformations (see later). Oxidation of the *erythro*- and *threo*-sulphides (12) and (13) separately with peroxydodecanoic acid gave the sulphoxides (14) and (15).

With the acyclic precursors in hand the thietan rings were constructed in a manner similar to that described previously.[4] Thermolysis of the *erythro*-isomer (14) for 6 min in boiling xylene (140 °C) furnished a mixture of 2α-(hydroxymethyl)-3α-(6-methoxycarbonylhexyl)-4β-methylthietan 1β-oxide (16; R = CO_2Me) and the 1α,2α,3α,4α-isomer (17; R = CO_2Me) in the ratio *ca.* 3 : 1 (22% combined yield), whilst the *threo*-isomer (15) under the same conditions gave a mixture of the 1β,2β,3α,4β-

* Compounds (9)—(11) are mixtures of diastereoisomers by virtue of the generation of two chiral centres in the Claisen rearrangement. In each case the diastereoisomers were inseparable chromatographically, and for convenience stereochemical features are disregarded in the depiction of structures.

† For the convention used to describe the stereochemistry of compounds (12)—(15) see ref. 4. The compounds (4), (5), and (12)—(29) are racemic modifications and only one enantiomer is depicted in each case.

and 1α,2β,3α,4α-isomers (18; R = CO_2Me) and (19; R = CO_2Me), respectively, in the ratio *ca.* 3 : 1 (36% combined yield) (Scheme 4).* These cyclic products were readily separated by chromatography, and their configurations were assigned on the basis of the close similarity of their salient n.m.r. characteristics with those of the known thietan 1-oxide derivatives (16—19; R = H).[4] The relative chromatographic mobilities



SCHEME 4 Yields are for R = CO_2Me

(t.l.c.) of the compounds (16—19; R = CO_2Me) paralleled those for the known compounds (16—19; R = H), as did the relative yields in the cyclizations leading to compounds (16—19; R = CO_2Me) and (16—19; R = H). This strengthened our confidence in the assignments of configuration.

The elaboration of the β-side-chain of the thietanoprostanoids from the hydroxymethyl substituents in the thietan 1-oxide derivatives (16—19; R = CO_2Me) now remained. The first step in this transformation, the oxidation of the hydroxymethyl group to an aldehyde, proved to be troublesome. Initial experiments with the model compound (16; R = H) revealed that oxidation with chromium(VI) reagents (Jones,[11] Collins,[12] Corey-Kim,[13] pyridinium dichromate [14]) and with the Moffatt reagent (dimethyl sulphoxide–dicyclohexylcarbodiimide–trifluoroacetic acid) [15] gave unidentified mixtures of products and low recoveries of material. We ascribed this to the presence of the sulphoxide function, and consequently oxidised the hydroxy-sulphoxide (16; R = H) to the hydroxy-sulphone (20; R = H) with peroxydodecanoic acid before treatment with the aforementioned oxidants; with silver carbonate on Celite; [16] and with dimethyl sulphoxide–trifluoroacetic anhydride.[17] All gave unsatisfactory results except for the Moffatt reagent, which converted the hydroxy-sulphone (20; R = H) into the aldehyde (24; R = H) (65%). This was in equilibrium with its hydroxymethylene tautomer, present to the extent of *ca.* 80% in deuteriochloroform (n.m.r. spectroscopy). Oxidation of the hydroxy-sulphoxide (18; R = H) with peroxydodecanoic acid to give the hydroxy-sulphone (22; R = H) and then with Moffatt reagent gave the same aldehyde (24; R = H). That tautomerization led to complete isomerization in the thermodynamically more stable configuration at C-2 was indicated by the presence of only one signal (δ 9.74, d, *J* 1.5 Hz) due to an aldehydic proton in the n.m.r. spectrum of compound (24; R = H), and by the conversion of the tautomeric mixture into only one enone (26; R = H) on treatment with tri-n-butylphosphoranylideneheptan-2-one.[18] We allocated the *trans*-configuration to the substituents at C-2 and C-3 in the thietan derivatives (24; R = H) and (26; R = H) on the assumption that steric factors would render this arrangement thermodynamically the more stable.

Application of the same two-step oxidation procedure to the hydroxy-sulphoxides (17; R = H) and (19; R = H) furnished the same aldehyde (25; R = H) [epimeric at C-4 to the aldehyde (24; R = H)] which on treatment with tri-n-butylphosphoranylideneheptan-2-one gave the enone (27; R = H).

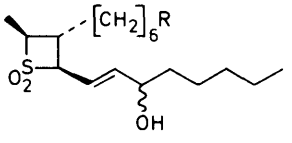
These transformations unambiguously established the configurations of the thietan 1-oxide derivatives (18; R = H) and (19; R = H) (which had previously been

* The α,β convention is used to describe the stereochemistry of these compounds in order to facilitate the correlation of their structures with those of the derived thietanoprostanoids. The side-chain at C-3 is arbitrarily assigned the α-configuration throughout.

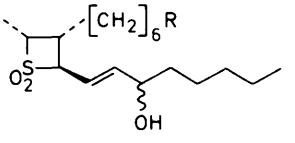
allocated on the basis of n.m.r. correlations and mechanistic considerations) since the configurations of compounds (16; R = H) and (17; R = H) are anchored by an *X*-ray analysis of the compound (16; R = H).[4] They also substantiated the configurations assigned to the analogous compounds (16—19; R = CO_2Me), and to the thiaprostanoids derived from them (see below). Furthermore, the easy and complete isomerization of the C-2 aldehyde function permitted the conversion of the isomers (16; R = CO_2Me) and (17; R = CO_2Me), with *cis*-related substituents at C-2 and C-3, into thietanoprostanoids with the required *trans*-disposition of side-chains.

The same sequence of reactions (peroxydodecanoic acid oxidation, Moffatt oxidation, and treatment with the Wittig reagent) when applied to the thietan 1-oxide derivatives (16; R = CO_2Me) and (18; R = CO_2Me) furnished the ester enone (26; R = CO_2Me), whilst compounds (17; R = CO_2Me) and (19; R = CO_2Me) were similarly converted into the enone (27; R = CO_2Me). The assumption that the *trans*-orientation of the C-2 aldehyde and C-3 side-chain pertained was validated by the sodium borohydride reduction of the aldehyde (24; R = CO_2Me), obtained by Moffatt oxidation of both compounds (20; R = CO_2Me) and (22; R = CO_2Me), to give only the *trans*-isomer (22; R = CO_2Me) (85%).

Reduction of the enones (26; R = H) and (27; R = H) separately with sodium borohydride gave the allylic alcohols (28; R = H) and (29; R = H) respectively,



(28) a ; α - OH
b ; β - OH



(29) a ; α - OH
b ; β - OH

which after chromatography gave the component epimeric alcohols (28a; R = H), (28b; R = H), (29a; R = H), and (29b; R = H). The relative α-configuration was allocated to the hydroxy-groups in the stereoisomers (28a; R = H) and (29a; R = H) only on the basis of their lesser chromatographic mobilities than their respective isomers (*cf.* ref. 18). Similarly, reduction of the enones (26; R = CO_2Me) and (27; R = CO_2Me) gave the allylic alcohols (28; R = CO_2Me) and (29; R = CO_2Me). Whereas compound (28; R = CO_2Me) could be separated (albeit inefficiently) into its constituent epimers (28a; R = CO_2Me) and (28b; R = CO_2Me) by preparative h.p.l.c., separation of compound (29; R = CO_2Me) into its constituents was possible only on an analytical scale. Hydrolysis of the alcohols (28a; R = CO_2Me) and (28b; R = CO_2Me) gave the thietanoprostaglandin E1 analogue (4a) and its epimer (4b) respectively, whilst hydrolysis of compound (29; R = CO_2Me) gave the thietanoprostanoid (5) as a mixture of alcohol epimers.

A brief investigation of the modification of the oxidation level at sulphur was not fruitful, because reduction of the model compound (28; R = H) with lithium aluminium hydride in diethyl ether at 20 °C gave a gross mixture of products. In contrast, the hydroxy-sulphone (20; R = H) was readily reduced in good yield to the corresponding hydroxy-sulphide under these conditions. However, the hydroxy-sulphide thus obtained rearranged on attempted oxidation to the corresponding aldehyde, so that it could not be used for elaboration into thietanoprostanoids. These reductions and rearrangements will be discussed in detail elsewhere.

The thietanoprostanoids (4a) and (4b) displayed potent thromboxane-like activity on smooth muscle preparations, and (4a) [but not (4b)] was a moderate PGE_2 agonist. The mixture of compounds (5a) and (5b) showed activity similar in nature to that of the stereoisomer (4a), but was only 1/10th as potent; this mixture also had weak thromboxane antagonist activity. None of the compounds affected blood platelet aggregation.

EXPERIMENTAL

High-resolution mass spectra were determined with a Kratos MS 30 double-beam instrument, and n.m.r. spectra with a Perkin-Elmer R34 or Bruker WH-400 spectrometer. High-performance liquid chromatography (h.p.l.c.) on Hypersil (5 μ) used 250 × 4-mm columns with ethyl acetate–light petroleum (3 : 17) as mobile phase at a flow rate of 3 ml min^{-1}, monitored by a differential refractometer, whilst h.p.l.c. on silica (14 μ) used 250 × 15-mm columns with ethanol–hexane (1 : 24) as mobile phase at a flow rate of 8 ml min^{-1}, monitored by u.v. absorption at 215 nm. Light petroleum refers to the fraction with b.p. 40—60 °C. Magnesium sulphate was used to dry ethereal and dichloromethane extracts. All reaction mixtures were stirred efficiently. Apparatus used for distillation of acetals was flushed with ammonia prior to use. For other directions see ref. 4.

11-*Methyl*-10,12-*dioxatetradec*-2-*yn*-1-*ol* (6).—Toluene-*p*-sulphonic acid (70 mg) and 6-bromohexan-1-ol (5 g) were added in sequence to freshly distilled ethyl vinyl ether (60.5 g, 0.84 mol) at 0 °C. After the initial reaction had subsided more 6-bromohexan-1-ol (70.6 g, 0.418 mol in total) was added dropwise during 20 min at 0—10 °C. After 1 h at room temperature the solution was treated with saturated aqueous potassium carbonate (5 ml) at 5 °C for 5 min and then with sufficient solid potassium carbonate to remove the water. The solids were filtered off, washed thoroughly with diethyl ether, and the combined filtrate and washings treated with gaseous ammonia introduced through a bubbler for 5 s. Evaporation of the solvent under reduced pressure gave 1-bromo-8-methyl-7,9-dioxaundecane (105.7 g) which was not purified further.

Prop-2-yn-1-ol (23.5 g, 0.42 mol) was added during 15 min to a suspension of lithium amide in liquid ammonia, prepared from lithium (5.88 g, 0.84 mol), ferric nitrate (100 mg), and liquid ammonia (750 ml). 1-Bromo-8-methyl-7,9-dioxaundecane (105.7 g, 0.428 mol) was added dropwise during 75 min, and after an additional 1.5 h the ammonia was allowed to evaporate. The residue was dissolved in ice–water (200 ml), extracted with diethyl ether, and the ethereal extract dried and evaporated. Distillation of the residue gave the *product* (6) (54.5 g, 57%), b.p. 125—135 °C

at 0.02 mmHg, $\nu_{max.}$ (liq. film) 3 420 (OH) and 2 220 cm^{-1} (C≡C); δ 4.68 [1 H, q, *J* 5 Hz, OC*H*(CH_3)O], 4.20 (2 H, t, *J* 1.5 Hz, ≡CCH_2OH), 3.72—3.3 [5 H, m, CH_2OCH(CH_3)O-CH_2 and OH], 2.20 (2 H, m, CH_2C≡), 1.65—1.2 [8 H, m, $(CH_2)_4$], 1.29 [3 H, d, *J* 5 Hz, OCH(CH_3)O], and 1.19 (3 H, t, *J* 7 Hz, C$H_3$$CH_2$O); *m/e* 228 (Found: C, 68.2; H, 10.3. $C_{13}H_{21}O_3$ requires C, 68.4; H, 10.6%).

(E)-11-*Methyl*-10,12-*dioxatetradec*-2-*en*-1-*ol* (7).—11-Methyl-10,12-dioxatetradec-2-yn-1-ol (54.4 g, 0.239 mol) in diethyl ether (150 ml) was added dropwise to lithium aluminium hydride (9.2 g, 0.24 mol) in diethyl ether (1 l) during 15 min. The solution was boiled for 20 h, then wet diethyl ether was cautiously added, followed by drops of water. Removal of the solids by filtration, evaporation of the filtrate, and distillation of the residue gave the *product* (7) (52.0 g, 95%), b.p. 118—122 °C at 0.1 mmHg, $\nu_{max.}$ (liq. film) 3 400 cm^{-1} (OH); δ 5.66 (2 H, m, CH=CH), 4.68 [1 H, q, *J* 5 Hz, OC*H*(CH_3)O], 4.06 (2 H, d, *J* 4 Hz, =CHCH_2OH), 3.75—3.35 [4 H, m, CH_2OCH(CH_3)OCH_2], 2.40br (1 H, OH), 2.04 (2 H, m, CH_2CH=), 1.65—1.2 [8 H, m, $(CH_2)_4$], 1.29 [3 H, d, *J* 5 Hz, OCH$_2$(CH_3)O], and 1.19 (3 H, t, *J* 7 Hz, C$H_3$$CH_2$O); *m/e* 230 (Found: C, 67.9; H, 11.45. $C_{13}H_{26}O_3$ requires C, 67.8; H, 11.4%).

(E)-11-*Methyl*-10,12-*dioxatetradec*-2-*en*-1-*yl* *t-Butylthioacetate* (8).—t-Butylthioacetyl chloride (37.6 g, 0.226 mol) was added dropwise to (*E*)-11-methyl-10,12-dioxatetradec-2-en-1-ol (7) (51.9 g, 0.226 mol) in pyridine (300 ml) at 0 °C under nitrogen. After 12 h at room temperature the mixture was worked up with diethyl ether in the usual way and the residue chromatographed on silica (550 g; diethyl ether–light petroleum–triethylamine, 5 : 94 : 1 as eluant) to give the *product* (8) (64.0 g, 79%) as an oil, $\nu_{max.}$ (liq. film) 1 736 (CO), 1 670, and 962 cm^{-1} (CH=CH); δ 5.80 (1 H, dt, *J* 15 and 7 Hz, =C*H*CH_2O), 5.58 (1 H, dt, *J* 15 and 7 Hz, =CH-CH_2), 4.68 [1 H, q, *J* 5 Hz, OC*H*(CH_3)O], 4.57 (2 H, d, *J* 7 Hz, =CHCH_2O), 3.72—3.32 [4 H, m, CH_2OCH(CH_3)OCH_2], 3.27 (2 H, s, CH_2S), 2.07 (2 H, m, CH_2CH=), 1.65—1.2 [8 H, m, $(CH_2)_4$], 1.32 (9 H, s, Bu^t), 1.29 [3 H, d, *J* 5 Hz, OCH$_2$-(CH_3)O], and 1.19 (3 H, t, *J* 7 Hz, C$H_3$$CH_2$O); *m/e* 345 ($M^+$ − 15) and 314 (M^+ − 46) (Found: C, 63.5; H, 9.8; S, 8.75. $C_{19}H_{36}O_4S$ requires C, 63.3; H, 10.1; S, 8.9%).

Methyl 9-*Hydroxy*-2-*t-butylthio*-3-*vinylnonanoate* (9).—n-Butyl-lithium (0.181 mol) in hexane (142 ml) was added to isopropylcyclohexylamine (29.7 ml, 0.181 mol) in THF (150 ml) at −10 °C under argon. The solution was cooled to −78 °C and (*E*)-11-methyl-10,12-dioxatetradec-2-en-1-yl t-butylthioacetate (61.8 g, 0.172 mol) in THF (170 ml) was added during 20 min. After 30 min at −78 °C, chlorotrimethylsilane (23 ml, 0.181 mol) was added dropwise, the mixture allowed to warm to room temperature, and then heated at 60 °C for 2 h. The solution was extracted with diethyl ether, the extract washed with 2N-hydrochloric acid, dried, and evaporated to give a residue which was dissolved in methanol (150 ml) and cooled in an ice-bath. Concentrated sulphuric acid (6 ml) in methanol (150 ml) was added slowly, and after 1 h at room temperature, and then 30 min at 50 °C, most of the methanol was removed under reduced pressure and a further 200 ml of methanol added. The solution was boiled for 20 h after which most of the methanol was removed under reduced pressure and the residue poured into water. The latter was extracted with diethyl ether and the extract dried and evaporated to give a residue which was chromatographed on silica (500 g; diethyl ether–light petroleum, 1 : 1 as eluant) to afford the *product* (9) (40.9 g, 79%), as an oil, $\nu_{max.}$ (liq. film) 3 390 (OH), 1 740 and 1 732 (CO), 1 638, 989, and 912 cm^{-1} (CH=CH_2); δ 5.58 (1 H, m, =CH), 5.07 (2 H, m, =CH_2), 3.71 (s, CO_2CH_3, minor diastereoisomer), 3.65 (s, CO_2CH_3, major diastereoisomer), 3.58 (2 H, t, *J* 7 Hz, CH_2OH), 3.14br (1 H, OH), 2.22 (1 H, m, =CHC*H*), 1.6—1.1 [10 H, m, $(CH_2)_5$], and 1.31 (9 H, s, Bu^t); *m/e* 302 (Found: C, 63.7; H, 10.1; S, 10.35. $C_{16}H_{30}O_3S$ requires C, 63.5; H, 10.0; S, 10.6%).

Methyl 9-*Cyano*-2-*t-butylthio*-3-*vinylnonanoate* (10).—Freshly machine-powdered potassium hydroxide (13 g, 0.23 mol) was added during 15 min to toluene-*p*-sulphonyl chloride (7.89 g, 41.4 mmol) and methyl 9-hydroxy-2-t-butylthio-3-vinylnonanoate (10.0 g, 33.1 mmol) in dry diethyl ether (55 ml) whilst the temperature was maintained between −5 and 0 °C. After 2.5 h at 0 °C the mixture was poured into ice–water, extracted with dichloromethane, and the extracts dried and evaporated. Dimethyl sulphoxide (20 ml) and potassium cyanide (2.8 g, 43 mmol) were added to the residue, and after 12 h at 20 °C and subsequently 1 h at 70 °C the mixture was poured into saturated aqueous sodium hydrogen carbonate and extracted with dichloromethane. The extract was dried and evaporated, and the residue chromatographed on silica (100 g; ethyl acetate–light petroleum, 1 : 9 as eluant) to give the *product* (10) (8.46 g, 82%), $\nu_{max.}$ (liq. film) 2 226 (CN), 1 737 (CO), 1 642, 995, and 918 cm^{-1} (CH=CH_2); δ 5.55 (1 H, =CH), 5.05 (2 H, m, =CH_2), 3.70 (s, CO_2CH_3, minor diastereoisomer), 3.64 (s, CO_2CH_3, major diastereoisomer), 3.27 (d, *J* 9 Hz, C*H*SBu^t, minor diastereoisomer), 3.21 (d, *J* 9 Hz, C*H*SBu^t, major diastereoisomer), 2.31 (2 H, t, *J* 7 Hz, CH_2CN), 1.90 (1 H, m, =CHC*H*), 1.61 (2 H, m, CH_2), 1.5—1.1 (8 H, m, $[CH_2]_4$), and 1.31 (9 H, s, Bu^t); *m/e* 311 (Found: C, 65.6; H, 9.4; N, 4.3; S, 10.4. $C_{17}H_{29}NO_2S$ requires C, 65.55; H, 9.4; N, 4.5; S, 10.3%).

9-*Cyano*-2-*t-butylthio*-3-*vinylnonan*-1-*ol* (11).—A solution of lithium borohydride (106 mg, 4.82 mmol) and methyl 9-cyano-2-t-butylthio-3-vinylnonanoate (500 mg, 1.61 mmol) in THF (5 ml) was boiled under nitrogen for 26 h, cooled, and methanol (5 ml) added carefully. After the mixture had been boiled for 1.5 h the solvent was removed under reduced pressure and the residue dissolved in water and worked up with diethyl ether in the usual way. Chromatography on silica (12 g; ethyl acetate–light petroleum, 1 : 4 as eluant) gave the *product* (11) (286 mg, 63%), as an oil, $\nu_{max.}$ (liq. film) 3 450 (OH), 2 221 (CN), 1 640, 998, and 912 cm^{-1} (CH=CH_2); δ 5.65 (1 H, m, =CH), 5.07 (2 H, m, =CH_2), 3.69 [1 H, m, C*H*(H)OH], 3.52 [1 H, m, CH(*H*)OH], 2.70 (1 H, m, =CHC*H*), 2.54 (1 H, s, OH), 2.32 (2 H, t, *J* 7 Hz, CH_2CN), 1.66 (2 H, m, CH_2), 1.55—1.15 [8 H, m, $(CH_2)_4$], and 1.31 (9 H, s, Bu^t); *m/e* 283 (Found: C, 68.1; H, 10.4; N, 5.0; S, 11.5. $C_{16}H_{29}NOS$ requires C, 67.8; H, 10.3; N, 4.9; S, 11.3%).

erythro- *and* threo-(*Methyl* 10-*Hydroxy*-9-*t-butylthio*-8-*vinyldecanoate*), (12) *and* (13).—A solution of potassium hydroxide (20 g, 0.34 mol) and 9-cyano-2-t-butylthio-3-vinylnonan-1-ol (11) (12.3 g, 43.5 mmol) in ethanol (1 l) and water (250 ml) was boiled under argon for 24 h after which it was evaporated to low volume, and acidified with 2N-hydrochloric acid. The usual work-up with diethyl ether gave an oil (12.64 g) which was dissolved in dry diethyl ether and treated with a slight excess of ethereal diazomethane at 0 °C. After 15 min the solvent was evaporated and the residue was chromatographed on silica (100 g). Elution with ethyl acetate–light petroleum (1 : 4) gave a mixture of the *products* (12) and (13) (9.18 g, 67%), $\nu_{max.}$ (liq. film) 3 440 (OH), 1 744 (CO), 1 638, 998, and 912 cm^{-1} (CH=CH_2); δ 5.64 (1 H, m,

=CH), 5.05 (2 H, m, $=CH_2$), 3.75—3.44 (2 H, m, CH_2OH), 3.65 (3 H, s, CO_2CH_3), 2.72 (1 H, m, CHSBu^t), 2.45br (1 H, OH), 2.28 (2 H, t, *J* 7 Hz, CH_2CO_2Me), 2.26 (1 H, m, =CH-CH), 1.75—1.1 [10 H, m, $(CH_2)_5$], and 1.32 (9 H, s, Bu^t); *m/e* 316 (Found: C, 64.5; H, 10.1; S, 10.3. $C_{17}H_{32}O_3S$ requires C, 64.5; H, 10.2; S, 10.1%). H.p.l.c. on Hypersil indicated that the *erythro*- (12) and *threo*- (13) isomers were present in the ratio 8 : 5. Repeated chromatography on silica gave 5.75 g of the *erythro*-isomer (12) and 3.63 g of the *threo*-isomer (13).

erythro-(*Methyl* 10-*Hydroxy*-9-*t-butylsulphinyl*-8-*vinyldecanoate*) (14).—Peroxydodecanoic acid (93% pure; 3.49 g, 15.03 mmol) was added during 30 min to *erythro*-(methyl 10-hydroxy-9-t-butylthio-8-vinyldecanoate) (12) (4.75 g, 15.03 mmol) in light petroleum (150 ml) at 0 °C. After a further 15 min the solvent was evaporated under reduced pressure and the residue chromatographed on alumina (85 g) prepared in diethyl ether. Elution with methanol–diethyl ether (1 : 9) gave the *product* (14) (4.94 g, 99%), m.p. 36—37 °C, $\nu_{max.}$ ($CHBr_3$) 3 440 (OH), 1 728 (CO), and 1 040 cm^{-1} (SO); δ 5.62 (1 H, m, =CH), 5.18 (2 H, m, $=CH_2$), 4.09 [1 H, m, CH(H)OH], 3.94 [1 H, m, CH(H)OH], 3.65 (3 H, s, CO_2CH_3), 3.65br (1 H, OH), 2.96 [1 H, m, CHS(O)Bu^t], 2.28 (2 H, t, *J* 7 Hz, CH_2CO_2Me), 2.27 (1 H, m, =CHCH), 1.7—1.2 [10 H, m, $(CH_2)_5$], and 1.28 (9 H, s, Bu^t); *m/e* 332 (Found: C, 61.2; H, 9.5; S, 9.6. $C_{17}H_{32}O_4S$ requires, C, 61.4; H, 9.7; S, 9.6%).

threo-(*Methyl* 10-*Hydroxy*-9-*t-butylsulphinyl*-8-*vinyldecanoate*) (15).—Oxidation of *threo*-10-hydroxy-9-t-butylthio-8-vinyldecanoate (13) (2.63 g, 8.32 mmol) as for the *erythro*-isomer (12) gave the *sulphoxide* (15) (2.80 g, 100%), as an oil, $\nu_{max.}$ ($CHCl_3$) 3 440 (OH), 1 728 (CO), and 1 040 cm^{-1} (SO); δ 5.64 (1 H, m, =CH), 5.13 (2 H, m, $=CH_2$), 4.12 [1 H, dd, *J* 12 and 8 Hz, CH(H)OH], 3.92 [1 H, dd, *J* 12 and 3 Hz, CH(H)OH], 3.65 (3 H, s, CO_2CH_3), 3.5br (1 H, OH), 2.97 [1 H, m, CHS(O)Bu^t], 2.28 (2 H, t, *J* 7 Hz, CH_2CO_2Me), 2.27 (1 H, m, =CHCH), 1.75—1.1 [10 H, m, $(CH_2)_5$], and 1.28 (9 H, s, Bu^t); *m/e* 332 (Found: C, 61.4; H, 9.7; S, 9.6%). $C_{17}H_{32}O_4S$ requires C, 61.4; H, 9.7; S, 9.6%).

2α-*Hydroxymethyl*-3α-(6-*methoxycarbonylhexyl*)-4β-*methylthietan* 1β-*Oxide* (16; R = CO_2Me) *and Its* 1α,2α,3α,4α-*Isomer* (17; R = CO_2Me).—*erythro*-(Methyl 10-hydroxy-9-t-butylsulphinyl-8-vinyldecanoate) (14) (5.63 g, 17.0 mmol) in xylene (10 ml) was added rapidly to boiling xylene (560 ml) under nitrogen. After 6 min the solution was poured onto solid xylene (100 ml), cooled in a bath of liquid nitrogen. The solvent was removed under reduced pressure at 40 °C and the residue was chromatographed on silica (110 g). Elution with diethyl ether gave starting material (3.22 g), and elution with diethyl ether–methanol (9 : 1) gave a mixture of the thietan 1-oxide derivatives (16; R = CO_2Me) and (17; R = CO_2Me) (410 mg, 9%, 21% from starting material consumed). After subjecting the recovered starting material to a further two cycles of thermolysis and chromatography the cyclized material from the three reactions were combined (839 mg) and chromatographed on silica (100 g). Elution with ethyl acetate–methanol (49 : 1) gave 2α-(*hydroxymethyl*)-3α-(6-*methoxycarbonylhexyl*)-4α-*methylthietan* 1α-*oxide* (17; R = CO_2Me) (215 mg), m.p. 38—43 °C, $\nu_{max.}$ ($CDCl_3$) 3 440 (OH), 1 728 (CO), and 1 040 cm^{-1} (SO); δ 4.46 [1 H, m, CH(H)OH], 3.97 [1 H, m, CH(H)OH], 3.77 (2 H, m, CHMe and $CHCH_2OH$), 3.66 (3 H, s, CO_2CH_3), 3.37br (1 H, OH), 2.88 [1 H, quin, *J* 8 Hz, CH-$(CH_2)_6$], 2.30 (2 H, t, *J* 7 Hz, $CH_2CO_2CH_3$), 1.7—1.1 [10 H, m, $(CH_2)_5$], and 1.38 (3 H, d, *J* 7 Hz, $CHCH_3$); δ ($CDCl_3$–D_2O) 4.44 [1 H, dd, *J* 12 and 9 Hz, CH(H)OH], and 3.95 [1 H, dd, *J* 12 and 4 Hz, CH(H)OH]; δ (C_6D_6) 4.42 [1 H, m, CH(H)OH], 4.29br (1 H, OH) 3.83 [1 H, m, CH(H)OH], 3.39 (4 H, m, $CHCH_2OH$ and CO_2CH_3), 2.99 (1 H, m, $CHCH_3$), 2.15 [1 H, m, $CH(CH_2)_6$], 2.10 (2 H, t, *J* 7 Hz, $CH_2CO_2CH_3$), 1.6—0.65 [10 H, m, $(CH_2)_5$], and 1.08 (3 H, d, *J* 7 Hz, $CHCH_3$) {Found: $[M + H]^+$ 277.1471 (ammonia chemical ionization). $C_{13}H_{24}O_4S$ + H requires *M* 277.1474} (Found: C, 56.45; H, 9.0. $C_{13}H_{24}O_4S$ requires C, 56.5; H, 8.75%). Further elution gave 2α-(*hydroxymethyl*)-3α-(6-*methoxycarbonylhexyl*)-4β-*methylthietan* 1β-*oxide* (16; R = CO_2Me) (571 mg), as an oil, $\nu_{max.}$ ($CDCl_3$) 3 400 (OH), 1 728 (CO), and 1 045 cm^{-1} (SO); δ 4.13br (1 H, OH), 3.98 (2 H, m, CH_2OH), 3.66 (3 H, s, CO_2CH_3), 3.57 [1 H, m, CH(H)-OH], 3.32 (1 H, m, $CHCH_3$), 2.70 [1 H, m, $CH(CH_2)_6$], 2.29 (2 H, t, *J* 7 Hz, $CH_2CO_2CH_3$), 1.7—1.1 [10 H, m, $(CH_2)_5$], and 1.43 (3 H, d, *J* 7 Hz, $CHCH_3$); δ (C_6D_6) 5.07 (1 H, t, *J* 6 Hz, OH), 3.95 (2 H, m, CH_2OH), 3.67 (1 H, m, $CHCH_2$-OH), 3.40 (3 H, s, CO_2CH_3), 2.77 (1 H, m, $CHCH_3$), 2.24 [1 H, m, $CH(CH_2)_6$], 2.11 (2 H, t, *J* 7 Hz, $CH_2CO_2CH_3$), 1.6—0.7 [10 H, m, $(CH_2)_5$], and 1.28 (3 H, d, *J* 7 Hz, $CHCH_3$); *m/e* 276 (Found: C, 56.4; H, 9.0; S, 11.5. $C_{13}H_{24}O_4S$ requires C, 56.5; H, 8.75; S, 11.6%).

2β-*Hydroxymethyl*-3α-(6-*methoxycarbonylhexyl*)-4β-*methylthietan* 1β-*Oxide* (18; R = CO_2Me) *and Its* 1α,2β,3α,4α-*Isomer* (19; R = CO_2Me).—Thermolysis of *threo*-(methyl 10-hydroxy-9-t-butylsulphinyl-8-vinyldecanoate) (15) (3.80 g, 11.45 mmol) as for the *erythro*-isomer (14) gave, after chromatography, starting material (1.94 g) and a mixture of the thietan 1-oxide derivatives (18; R = CO_2Me) and (19; R = CO_2Me) (547 mg, 17%, 35% from starting material consumed). The products from three reactions were combined (958 mg) and chromatographed on silica (110 g). Elution with ethyl acetate–methanol (49 : 1) gave 2β-*hydroxymethyl*-3α-(6-*methoxycarbonylhexyl*)-4β-*methylthietan* 1β-*oxide* (18; R = CO_2Me) (674 mg), m.p. 44—46 °C, $\nu_{max.}$ ($CDCl_3$) 3 440 (OH), 1 728 (CO), and 1 030 cm^{-1} (SO); δ 4.07 [2 H, m, CH(H)OH], 3.90 [1 H, m, CH(H)OH], 3.66 (3 H, s, CO_2CH_3), 3.00 [3 H, m, $CHCH_3$, $CH(CH_2)_6$, and $CHCH_2OH$], 2.29 (2 H, t, *J* 7 Hz, $CH_2CO_2CH_3$), 1.7—1.1 [10 H, m, $(CH_2)_5$], and 1.30 (3 H, d, *J* 7 Hz, $CHCH_3$); δ ($CDCl_3$–D_2O) 4.04 [1 H, dd, *J* 12 and 8 Hz, CH(H)OH], and 3.84 [1 H, dd, *J* 12 and 3 Hz, CH(H)OH]; δ (C_6D_6) 5.04br (1 H, t, *J* 5 Hz, OH), 4.25 [1 H, m, CH(H)H], 3.77 [1 H, m, CH(H)OH], 3.40 (3 H, s, CO_2CH_3), 2.74 (1 H, m, $CHCH_2OH$), 2.60 [1 H, m, $CH(CH_2)_6$], 2.26 (1 H, m, $CHCH_3$), 2.12 (2 H, t, *J* 7 Hz, $CH_2CO_2CH_3$), 1.5 (2 H, quin., *J* 7 Hz, CH_2CH_2-CO_2CH_3), 1.15—0.75 [8 H, m, $(CH_2)_4$], and 1.03 (3 H, d, *J* 7 Hz, $CHCH_3$); *m/e* 276 (Found: C, 56.5; H, 8.9; S, 11.6. $C_{13}H_{24}O_4S$ requires C, 56.5; H, 8.75; S, 11.6%). Further elution gave 2β-*hydroxymethyl*-3α-(6-*methoxycarbonylhexyl*)-4α-*methylthietan* 1α-*oxide* (19; R = CO_2Me) (207 mg), as an oil, $\nu_{max.}$ ($CDCl_3$) 3 400 (OH), 1 728 (CO), and 1 040 cm^{-1} (SO); δ 4.05 [2 H, m, CH(H)OH], 3.77 [1 H, m, CH(H)OH], 3.66 (1 H, m, $CHCH_3$), 3.66 (3 H, s, CO_2CH_3), 3.28 (1 H, m, $CHCH_2OH$), 2.29 (2 H, t, *J* 7 Hz, $CH_2CO_2CH_3$), 2.27 [1 H, m, $CH(CH_2)_6$], 1.7—1.1 [10 H, m, $(CH_2)_5$), and 1.37 (3 H, d, *J* 7 Hz, $CHCH_3$); δ ($CDCl_3$–D_2O) 4.00 [1 H, dd, *J* 12 and 4 Hz, CH(H)OH], and 3.77 [1 H, dd, *J* 12 and 6 Hz, CH(H)OH]; δ (C_6D_6) 5.08br (1 H, OH), 4.02 [1 H, m, CH(H)OH], 3.73 [1 H, m, CH(H)OH], 3.40 (3 H, s, CO_2CH_3), 3.30 (1 H, m, $CHCH_2OH$), 3.10 (1 H, quin, *J* 7 Hz, $CHCH_3$), 2.11 (2 H, t, *J* 7 Hz, $CH_2CO_2CH_3$), 1.85 [1 H, m, $CH(CH_2)_6$], 1.50 (2 H, quin, *J* 7 Hz, $CH_2CH_2CO_2CH_3$), 1.22 (3 H, d, *J* 7 Hz, $CHCH_3$), and 1.15—0.75 [8 H, m, $(CH_2)_4$]; *m/e* 276

(Found: C, 56.3; H, 8.9; S, 11.4. $C_{13}H_{24}O_4S$ requires C, 56.5; H, 8.75; S, 11.6%).

Oxidation of the Sulphoxides (16)—(19) (R = H) *to the Sulphones* (20)—(23) (R = H).—Peroxydodecanoic acid (95% pure; 516 mg, 2.28 mmol) was added slowly to 3α-hexyl-2α-hydroxymethyl-4β-methylthietan 1β-oxide (16; R = H) (496 mg, 2.28 mmol) in dichloromethane (75 ml) at 0 °C. After 15 min at 0 °C and 15 min at room temperature the solvent was evaporated under reduced pressure and the residue chromatographed on alumina (10 g). Elution with diethyl ether and evaporation of the eluate gave a residue which was chromatographed on silica (20 g). Elution with diethyl ether–light petroleum (1 : 1) gave 3α-*hexyl*-2α-(*hydroxymethyl*)-4β-*methylthietan* 1,1-*dioxide* (20; R = H) (534 mg, 98%), $\nu_{max.}$ 3 480 (OH), 1 298, and 1 124 cm^{-1} (SO_2); δ 4.22 (1 H, m, C*H*CH_2OH), 4.08 (3 H, m, C*H*CH_3 and C*H*$_2$OH), 2.81br (1 H, OH), 2.17 [1 H, m, C*H*$(CH_2)_6$], 1.62 (2 H, m, CH_2), 1.45 (3 H, d, *J* 7 Hz, CHC*H*$_3$), 1.28 [8 H, m, $(CH_2)_4$], and 0.87 (3 H, t, *J* 7 Hz, CH_2CH_3); *m/e* 234 (Found: C, 56.3; H, 9.3; S, 13.8. $C_{11}H_{22}O_3S$ requires C, 56.4; H, 9.5; S, 13.7%).

Oxidation of the sulphoxides (17)—(19) (R = H) as above gave, respectively, the *sulphone* (21; R = H) (79%), m.p. 54 °C, $\nu_{max.}$ ($CHCl_3$) 3 550 (OH), 1 305, and 1 130 cm^{-1} (SO_2); δ 4.55—4.30 (2 H, m, C*H*CH_3 and C*H*CH_2OH), 4.11 [1 H, m, C*H*(H)OH], 3.97 [1 H, m, CH(*H*)OH], 2.96 (1 H, t, *J* 5 Hz, OH), 2.65 [1 H, C*H*$(CH_2)_6$], 1.48 (2 H, m, CH_2), 1.37 (3 H, d, *J* 7 Hz, CHC*H*$_3$), 1.25 [8 H, m, $(CH_2)_4$], and 0.86 (3 H, t, *J* 7 Hz, CH_2CH_3); *m/e* 234 (Found: C, 56.6; H, 9.5; S, 13.5. $C_{11}H_{22}O_3S$ requires C, 56.4; H, 9.5; S, 13.7%); 3α-*hexyl*-2β-*hydroxymethyl*-4β-*methylthietan* 1,1-*dioxide* (22; R = H) (100%), $\nu_{max.}$ (liq. film) 3 490 (OH), 1 302, and 1 136 cm^{-1} (SO_2); δ 4.13—3.80 (4 H, m, C*H*CH_3 and C*H*CH_2OH), 2.69br (1 H, OH), 1.90 [1 H, quin, *J* 7 Hz, C*H*$(CH_2)_6$], 1.63 (2 H, m, CH_2), 1.43 (3 H, d, *J* 7 Hz, CHC*H*$_3$), 1.28 [8 H, m, $(CH_2)_4$], and 0.87 (3 H, t, *J* 7 Hz, CH_2CH_3); *m/e* 170 ($M^+ - 64$) (Found: C, 56.1; H, 9.7; S, 13.8. $C_{11}H_{22}O_3S$ requires C, 56.4; H, 9.5; S, 13.7%); and 3α-*hexyl*-2β-*hydroxymethyl*-4α-*methylthietan* 1,1-*dioxide* (23; R = H) (84%), $\nu_{max.}$ (liq. film) 3 990 (OH), 1 300, and 1 136 cm^{-1} (SO_2); δ 4.35 (1 H, m, C*H*CH_3), 4.0 (3 H, m, C*H*C*H*$_2$OH), 3.18br (1 H, OH), 2.39 [1 H, m, C*H*$(CH_2)_6$], 1.53 (2 H, m, CH_2), 1.37 (3 H, d, *J* 7 Hz, CHC*H*$_3$), 1.26 [8 H, m, $(CH_2)_4$], and 0.86 (3 H, t, *J* 7 Hz, CH_2CH_3); *m/e* 170 ($M^+ - 64$) (Found: C, 56.3; H, 9.6; S, 13.7. $C_{11}H_{22}O_3S$ requires C, 56.4; H, 9.5; S, 13.7%).

Oxidation of the Sulphoxides (16)—(19) (R = CO_2Me) *to the Sulphones* (20)—(23) (R = CO_2Me).—The oxidations were carried out as described above except that the sulphones were purified by chromatography on alumina (30 g per 1 g of starting sulphoxide; diethyl ether–methanol, 4 : 1 as eluant). The sulphoxides (16)—(19) (R = CO_2Me) gave, respectively, 2α-*hydroxymethyl*-3α-(6-*methoxycarbonylhexyl*)-4β-*methylthietan* 1,1-*dioxide* (20; R = CO_2Me) (100%), $\nu_{max.}$ ($CDCl_3$) 3 530 (OH), 1 728 (CO), 1 302, and 1 127 cm^{-1} (SO_2); δ 4.19 (1 H, m, C*H*CH_2OH), 4.10 (2 H, m, C*H*$_2$OH), 4.05 (1 H, m, C*H*CH_3), 3.67 (3 H, s, CO_2CH_3), 2.49br (1 H, OH), 2.31 (2 H, t, *J* 7 Hz, C*H*$_2CO_2CH_3$), 2.19 [1 H, m, C*H*$(CH_2)_6$], 1.6 (4 H, m, 2 × CH_2), 1.48 (3 H, d, *J* 7 Hz, CHC*H*$_3$), and 1.32 [6 H, m, $(CH_2)_3$] {Found: $[M + NH_4]^+$ 310.1670 (ammonia chemical ionization). $C_{13}H_{24}O_5S{\cdot}NH_4$ requires *M*, 310.1688}; 2α-*hydroxymethyl*-3α-(6-*methoxycarbonylhexyl*)-4α-*methylthietan* 1,1-*dioxide* (21; R = CO_2Me) (81%), $\nu_{max.}$ (liq. film) 3 510 (OH), 1 730 (CO), 1 305, and 1 140 cm^{-1} (SO_2); δ 4.40 (2 H, m, C*H*CH_3 and C*H*CH_2OH), 4.03 (2 H, m, C*H*$_2$OH), 3.66 (3 H, s, CO_2CH_3), 2.75 [2 H, m, OH and C*H*$(CH_2)_6$], 2.32 (2 H, t, *J* 7 Hz, C*H*$_2CO_2CH_3$), 1.75—1.15 [10 H, m, $(CH_2)_5$], and 1.42 (3 H, d, *J* 7 Hz, CHC*H*$_3$) (Found: $[M + NH_4]^+$ 310.1691); 2β-*hydroxymethyl*-3α-6-*methoxycarbonylhexyl*)-4β-*methylthietan* 1,1-*dioxide* (22; R = CO_2Me) (91%), $\nu_{max.}$ ($CDCl_3$), 3 560 (OH), 1 728 (CO), 1 305, and 1 130 cm^{-1} (SO_2); δ 4.13 [1 H, dd, *J* 12.5 and 3 Hz, C*H*(H)OH], 3.91 [3 H, m, C*H*CH_3 and C*H*CH(*H*)OH], 3.67 (3 H, s, CO_2CH_3), 2.47br (1 H, OH), 2.31 (2 H, t, *J* 7 Hz, C*H*$_2CO_2CH_3$), 1.99 [1 H, quin, *J* 8 Hz, C*H*$(CH_2)_6$], 1.64 [4 H, m, CHC*H*$_2(CH_2)_3CH_2CH_2CO_2$Me], 1.47 (3 H, d, *J* 7 Hz, CHC*H*$_3$), and 1.33 [6 H, m, $(CH_2)_3$] {Found: $[M + H]^+$ 293.1407 (ammonia chemical ionization). $C_{13}H_{24}O_5S + H$ requires *M*, 293.1423}; and 2β-*hydroxymethyl*-3α-(6-*methoxycarbonylhexyl*)-4α-*methylthietan* 1,1-*dioxide* (23; R = CO_2Me) (96%), $\nu_{max.}$ (liq. film) 3 500 (OH), 1 730 (CO), 1 300, and 1 135 cm^{-1} (SO_2); δ 4.33 (1 H, m, C*H*CH_3), 4.0 (2 H, m, CHC*H*$_2$OH), 3.63 (3 H, s, CO_2CH_3), 2.77br (1 H, OH), 2.33 [1 H, m, C*H*$(CH_2)_6$], 2.30 (2 H, t, *J* 7 Hz, C*H*$_2CO_2CH_3$), 1.75—1.15 [10 H, m, $(CH_2)_5$], and 1.36 (3 H, d, *J* 7 Hz, CHC*H*$_3$) (Found: $[M + NH_4]^+$ 310.1695).

3α-*Hexyl*-4β-*methyl*-2β-(3-*oxo*-*oct*-1-*enyl*)*thietan* 1,1-*Dioxide* (26; R = H).—Dimethyl sulphoxide (20 ml), pyridine (0.36 ml, 4.44 mmol), trifluoroacetic acid (0.170 ml, 2.22 mmol), and dicyclohexylcarbodi-imide (2.75 g, 13.33 mmol) were added in sequence to 3α-hexyl-2β-hydroxymethyl-4β-methylthietan 1,1-dioxide (22; R = H) (1.04 g, 4.44 mmol) in benzene (20 ml), and the solution was set aside at room temperature overnight. Diethyl ether (150 ml) was added, followed by a solution of oxalic acid (1.68 g, 13.33 mmol) in methanol (5 ml), and after 30 min the solution was poured into water (100 ml) and the solids filtered off. The filtrate was washed with aqueous sodium hydrogen carbonate and water and then dried and evaporated. Chromatography on silica (20 g; diethyl ether–light petroleum, 3 : 2 as eluant) gave 2β-formyl-3α-hexyl-4β-methylthietan 1,1-dioxide (24; R = H) (757 mg, 73%), as an oil, $\nu_{max.}$ (liq. film) 3 420 (OH), 1 718 (CO), 1 308, and 1 138 cm^{-1} (SO_2); δ 9.75 (*ca.* 0.25 H, d, *J* 1.5 Hz, CHO), 5.5—3.8 (*ca.* 3 H, m), 3.47 (*ca.* 1 H, m), 2.47 (*ca.* 0.7 H, m), and 0.88 (3 H, t, *J* 7 Hz, CH_2CH_3). A solution of the aldehyde (24; R = H) (63 mg, 0.27 mmol) and 1-(tri-n-butylphosphoranylidene)heptan-2-one (128 mg, 0.41 mmol) was kept at room temperature for 15 h after which time the solvent was removed under reduced pressure. Chromatography of the residue on silica (8 g, diethyl ether–light petroleum, 3 : 7 as eluant) gave 3α-*hexyl*-4β-*methyl*-2β-(3-*oxo*-*oct*-1-*enyl*)*thietan* 1,1-*dioxide* (26; R = H) (75 mg, 84%), m.p. 33 °C, $\nu_{max.}$ ($CHCl_3$) 1 695, 1 672, and 1 624 (CH=CHCO), 1 310, and 1 136 cm^{-1} (SO_2); δ 6.75 (1 H, dd, *J* 15.8 and 8.8 Hz, C*H*=CHCO), 6.28 (1 H, d, *J* 15.8 Hz, CH=C*H*CO), 4.46 (1 H, t, *J* 8.8 Hz, C*H*CH=CH), 3.96 (1 H, m, C*H*CH_3), 2.59 (2 H, t, *J* 7 Hz, $COCH_2$), 1.93 [1 H, m, C*H*$(CH_2)_6$], 1.63 (4 H, m, 2 × CH_2), 1.48 (3 H, d, *J* 7 Hz, CHC*H*$_3$), 1.27 (12 H, m, 6 × CH_2), and 0.87 (6 H, m, 2 × CH_2CH_3); *m/e* 264 ($M^+ - 64$) (Found: C, 65.7; H, 10.0; S, 9.9. $C_{18}H_{32}O_3S$ requires C, 65.8; H, 9.8; S, 9.8%).

Oxidation of 3α-hexyl-2α-hydroxymethyl-4β-methylthietan 1,1-dioxide (20; R = H) as above gave the aldehyde (24; R = H) (55%), identical, chromatographically and spectroscopically, with the sample prepared previously. Treatment of the aldehyde with 1-(tri-n-butylphosphoranylidene)heptan-2-one as before, but for 10 d, gave the enone (26; R = H) (35%).

3α-*Hexyl*-4α-*methyl*-2β-(3-*oxo*-*oct*-1-*enyl*)*thietan* 1,1-*Di*-

oxide (27; R = H).—Oxidation of 3α-hexyl-2α-hydroxymethyl-4α-methylthietan 1,1-dioxide (21; R = H) (510 mg) as above gave 2β-formyl-3α-hexyl-4α-methylthietan 1,1-dioxide (25; R = H) (366 mg, 72%), δ 9.80 (*ca.* 0.25 H, d, *J* 1.5 Hz, CHO), 5.5—3.8 (*ca.* 3 H, m), 3.47 (*ca.* 1 H, m), 2.97 and 2.52 (*ca.* 1 H, m), and 0.87 (3 H, t, *J* 7 Hz, CH_2CH_3), which was treated with 1-(tri-n-butylphosphoranylidene)-heptan-2-one (776 mg, 2.37 mmol) in diethyl ether (5 ml) for 15 h at room temperature. Evaporation of the solvent and chromatography of the residue on silica (15 g, diethyl ether–light petroleum, 3 : 7 as eluant) gave 3α *hexyl-4α-methyl-2β-(3-oxo-oct-1-enyl)thietan* 1,1-*dioxide* (27; R = H) (441 mg, 85%), $\nu_{max.}$ (liq. film) 1 695, 1 680, and 1 630 (CH=CHCO), 1 318, and 1 140 cm^{-1} (SO_2); δ 6.81 (1 H, dd, *J* 15.7 and 9.1 Hz, C*H*=CHCO), 6.30 (1 H, d, *J* 15.7 Hz, CH=C*H*CO), 4.56 (1 H, t, *J* 9 Hz, C*H*CH=CH), 4.35 (1 H, m, C*H*CH_3), 2.59 (2 H, t, *J* 7 Hz, $COCH_2$), 2.51 [1 H, m, C*H*$(CH_2)_6$], 1.60 (4 H, m, 2 × CH_2), 1.45 (3 H, d, *J* 7 Hz, CHCH_3), 1.26 (12 H, m, 6 × CH_2), and 0.87 (6 H, m, 2 × CH_2CH_3); *m/e* 264 (M^+ − 64) (Found: C, 66.0; H, 9.7; S, 10.0. $C_{18}H_{32}O_3S$ requires C, 65.8; H, 9.8; S, 9.8%).

Oxidation of 3α-hexyl-2β-hydroxymethyl-4α-methylthietan 1,1-dioxide (23; R = H) (211 mg) in the same way gave the aldehyde (25; R = H) (117 mg, 56%), which on treatment with 1-(tri-n-butylphosphoranylidene)heptan-2-one gave the enone (27; R = H) (139 mg, 85%). Both products were spectroscopically and chromatographically identical with the samples obtained previously.

2β-Formyl-3α-(6-methoxycarbonylhexyl)-4β-methylthietan 1,1-Dioxide (24; R = CO_2Me).—2α-Hydroxymethyl-3α-(6-methoxycarbonylhexyl)-4β-methylthietan 1,1-dioxide (20; R = CO_2Me) (398 mg, 1.36 mmol) in benzene (8 ml) was treated with dimethyl sulphoxide (8 ml,) pyridine (0.11 ml, 1.36 mmol), trifluoroacetic acid (0.052 ml, 0.68 mmol), and dicyclohexylcarbodi-imide (840 mg, 4.08 mmol) as described previously. Chromatography on silica (9 g, diethyl ether as eluant) furnished the *product* (24; R = CO_2Me) (297 mg, 75%), as an oil, $\nu_{max.}$ (liq. film) 3 420 (OH), 1 725 (CO), 1 305, and 1 140 cm^{-1} (SO_2); δ 9.74 (*ca.* 0.25 H, d, *J* 1.5 Hz, CHO), 5.7—3.75 (*ca.* 3 H, m), 3.66 (3 H, s, CO_2CH_3), 3.48 (*ca.* 1 H, m), 2.45 (*ca.* 0.7 H, m), and 2.31 (2 H, d, *J* 7 Hz, $CH_2CO_2CH_3$) {Found: $[M + H]^+$ 291.1273 (methane chemical ionization). $C_{13}H_{22}O_5S$ + H requires *M*, 291.1266}.

A solution of the aldehyde (24; R = CO_2Me) (24 mg) and an excess of sodium borohydride in ethanol (5 ml) was kept at room temperature for 30 min and then worked up with diethyl ether in the usual way to give, after chromatography [silica (2 g), diethyl ether], 2β-hydroxymethyl-3α-)(6-methoxycarbonylhexyl)-4β-methylthietan 1,1-dioxide (22; R = CO_2Me) (20.5 mg, 85%), which was identical spectroscopically (n.m.r. at 400 MHz) and chromatographically (t.l.c.) with an authentic sample.

Oxidation of 2β-hydroxymethyl-3α-(6-methoxycarbonylhexyl)-4β-methylthietan 1,1-dioxide (22; R = CO_2Me) (642 mg) as described previously gave the aldehyde (24; R = CO_2Me) (416 mg, 65%), identical with the sample obtained above.

3α-(6-Methoxycarbonylhexyl)-4β-methyl-2β-(3-oxo-oct-1-enyl)thietan 1,1-*Dioxide* (26; R = CO_2Me).—The aldehyde (24; R = CO_2Me) (416 mg, 1.43 mmol) and 1-(tri-n-butylphosphoranylidene)heptan-2-one (676 mg, 2.15 mmol) in diethyl ether (5 ml) was kept at room temperature for 15 h, the solvent evaporated, and the residue chromatographed on silica (20 g; diethyl ether–light petroleum, 3 : 2 as eluant) to give the *product* (26; R = CO_2Me) (451 mg, 82%), as an oil, $\nu_{max.}$ ($CDCl_3$) 1 728 (ester CO), 1 697, 1 673, and 1 620 (CH=CHCO), 1 315, and 1 138 cm^{-1} (SO_2); δ 6.74 (1 H, dd, *J* 15.5 and 8.5 Hz, CHC*H*=CH), 6.28 (1 H, d, *J* 15.5 Hz, CH=C*H*CO), 4.47 (1 H, t, *J* 8.5 Hz, C*H*CH=CH), 3.96 (1 H, m, C*H*CH_3), 3.65 (3 H, s, CO_2CH_3), 2.60 (2 H, t, *J* 7 Hz, $COCH_2$), 2.31 (2 H, t, *J* 7 Hz, $CH_2CO_2CH_3$), 1.93 [1 H, m, $CH(CH_2)_6$], 1.75—1.2 (16 H, m, 8 × CH_2), 1.48 (3 H, d, *J* 7 Hz, CHCH_3), and 0.87 (3 H, t, *J* 7 Hz, CH_2CH_3), *m/e* 322 (M^+ − SO_2) (Found: C, 62.1; H, 8.8; S, 8.3. $C_{20}H_{34}O_5S$ requires C, 62.1; H, 8.9; S, 8.3%).

3α-(6-Methoxycarbonylhexyl)-4α-methyl-2β-(3-oxo-oct-1-enyl)thietan 1,1-*Dioxide* (27; R = CO_2Me).—Oxidation of 2α-hydroxymethyl-3α-(6-methoxycarbonylhexyl)-4α-methylthietan 1,1-dioxide (21; R = CO_2Me) (146 mg) with the Moffat reagent, as before, gave the aldehyde (25; R = CO_2Me) (110 mg, 76%), which was treated with 1-(tri-n-butylphosphoranylidene)heptan-2-one (179 mg) as described to give the *product* (27; R = CO_2Me) (118 mg, 81%), $\nu_{max.}$ ($CDCl_3$) 1 728 (ester CO), 1 695, 1 672, and 1 625 (CH=CHCO), 1 318, and 1 132 cm^{-1} (SO_2); δ 6.81 (1 H, dd, *J* 15.6 and 8.5 Hz, CHC*H*=CH), 6.28 (1 H, d, *J* 15.6 Hz, CH=C*H*CO), 4.51 (1 H, t, *J* 8.5 Hz, C*H*CH=CH), 4.36 (1 H, m, C*H*CH_3), 3.65 (3 H, s, CO_2CH_3), 2.67 (2 H, t, *J* 7 Hz, $COCH_2$), 2.48 [1 H, m, C*H*$(CH_2)_6$], 2.28 (2 H, t, *J* 7 Hz, $CH_2CO_2CH_3$), 1.7—1.2 (16 H, m, 8 × CH_2), 1.43 (3 H, d, *J* 7 Hz, CHCH_3), and 0.88 (3 H, t, *J* 7 Hz, CH_2CH_3) (Found: C, 62.2; H, 8.9; S, 7.9. $C_{20}H_{34}O_5S$ requires C, 62.1; H, 8.9; S, 8.3%).

Treatment of 2β-hydroxymethyl-3α-(6-methoxycarbonylhexyl)-4α-methylthietan 1,1-dioxide (23; R = CO_2Me) (173 mg) in the same way gave first the aldehyde (25; R = CO_2Me) (115 mg, 67%) and then the enone (27; R = CO_2Me) (111 mg, 73%).

3α-Hexyl-2β-(3α-hydroxyoct-1-enyl)-4β-methylthietan 1,1-*Dioxide* (28a; R = H) *and 3α-Hexyl-2β-(3β-hydroxyoct-1-enyl)-4β-methylthietan* 1,1-*Dioxide* (28b; R = H).—A solution of sodium borohydride (139 mg, 3.68 mmol) and 3α-hexyl-4β-methyl-2β-(3-oxo-oct-1-enyl)thietan 1,1-dioxide (26; R = H) (604 mg, 1.84 mmol) in ethanol (25 ml) was kept at 20 °C for 30 min and then poured into water. The mixture was extracted with diethyl ether and the extract dried and evaporated to give a residue which was chromatographed on silica (15 g). Elution with diethyl ether–light petroleum (3 : 7) gave *3α-hexyl-2β-(3β-hydroxyoct-1-enyl)-4β-methylthietan* 1,1-*dioxide* (28b; R = H) (63 mg), $\nu_{max.}$ (liq. film) 3 460 (OH), 1 310, and 1 140 cm^{-1} (SO_2); δ 5.81 (2 H, m, CH=CH), 4.34 (1 H, t, *J* 8 Hz, C*H*CH=CH), 4.18 (1 H, m, C*H*OH), 3.83 (1 H, m, C*H*CH_3), 2.40br (1 H, OH), 1.84 [1 H, m, C*H*$(CH_2)_6$], 1.70—1.10 (18 H, m, 9 × CH_2), 1.46 (3 H, d, *J* 7 Hz, CHCH_3), and 0.87 (6 H, m, 2 × CH_2CH_3); *m/e* 312 (M^+ − H_2O), 266 (M^+ − SO_2), and 248 (M^+ − H_2O and SO_2) (Found: C, 65.3; H, 10.4; S, 10.0. $C_{18}H_{34}O_3S$ requires C, 65.4; H, 10.4; S, 9.7%). Further elution gave a mixture of isomers (403 mg) followed by *3α-hexyl-2β-(3α-hydroxyoct-1-enyl)-4β-methylthietan* 1,1-*dioxide* (28a; R = H) (141 mg), $\nu_{max.}$ (liq. film) 3 420 (OH), 1 308, and 1 138 cm^{-1} (SO_2); δ 5.80 (2 H, m, CH=CH), 4.36 (1 H, t, *J* 8 Hz, C*H*CH=CH), 4.13 (1 H, m, C*H*OH), 3.81 (1 H, m, C*H*CH_3), 2.76br (1 H, OH), 1.80 [1 H, m, C*H*$(CH_2)_6$], 1.70—1.10 (18 H, m, 9 × CH_2), 1.45 (3 H, d, *J* 7 Hz, CHCH_3), and 0.87 (6 H, m, 2 × CH_2CH_3); *m/e* 312 (M^+ − H_2O), 266 (M^+ − SO_2), and 248 (M^+ − H_2O and SO_2) (Found: C, 65.2; H, 10.6; S, 9.5. $C_{18}H_{34}O_3S$ requires C, 65.4; H, 10.4; S, 9.7%). Further chromatography (h.p.l.c., Hypersil) of the mixed fractions revealed that the isomers (28a;

R = H) and (28b; R = H) were formed in the ratio 45 : 55.

3α-Hexyl-2β-(3α-hydroxyoct-1-enyl)-4α-methylthietan 1,1-Dioxide (29a; R = H) *and 3α-Hexyl-2β-(3β-hydroxyoct-1-enyl)-4α-methylthietan 1,1-Dioxide* (29b; R = H).—Reduction of 3α-hexyl-4α-methyl-2β-(3-oxo-oct-1-enyl)thietan 1,1-dioxide (27; R = H) (408 mg) with sodium borohydride as above gave a mixture of the isomers (29a; R = H) and (29b; R = H) (382 mg, 93%), after chromatography on silica (30 g; diethyl ether–light petroleum, 2 : 3 as eluant). A portion of the mixture was subjected to h.p.l.c. on Hypersil. The first compound eluted was *3α-hexyl-2β-(3β-hydroxyoct-1-enyl)-4α-methylthietan 1,1-dioxide* (29b; R = H), $\nu_{max.}$ (liq. film) 3 490 (OH), 1 304, and 1 148 cm^{-1} (SO_2); δ 5.83 (2 H, m, CH=CH), 4.43 (1 H, m, C*H*CH=CH), 4.20 (2 H, m, C*H*CH_3 and C*H*OH), 2.68br (1 H, OH), 2.42 [1 H, m, C*H*$(CH_2)_6$], 1.6—1.1 (18 H, m, 9 × CH_2), 1.41 (3 H, d, *J* 7 Hz, CHC*H*$_3$), and 0.87 (6 H, m, 2 × CH_2CH_3); *m/e* 312 ($M^+ - H_2O$), 266 ($M^+ - SO_2$), and 248 ($M^+ - H_2O$ and SO_2) (Found: C, 65.6; H, 10.6; S, 9.5. $C_{18}H_{34}O_3S$ requires C, 65.4; H, 10.4; S, 9.7%), followed by *3α-hexyl-2β-(3α-hydroxyoct-1-enyl)-4α-methylthietan 1,1-dioxide* (29a; R = H), $\nu_{max.}$ (liq. film) 3 490 (OH), 1 298, and 1 135 cm^{-1} (SO_2); δ 5.82 (2 H, m, CH=CH), 4.42 (1 H, m, C*H*CH=CH), 4.20 (2 H, m, C*H*CH_3 and C*H*OH), 2.52br (1 H, OH), 2.41 [1 H, m, C*H*$(CH_2)_6$], 1.6—1.1 (18 H, m, 9 × CH_2), 1.40 (3 H, d, *J* 7 Hz, CHC*H*$_3$), and 0.87 (6 H, m, 2 × CH_2CH_3); *m/e* 312 ($M^+ - H_2O$), 2.66 ($M^+ - SO_2$), and 248 ($M^+ - H_2O$ and SO_2) (Found: C, 65.6; H, 10.3; S, 9.4. $C_{18}H_{34}O_3S$ requires C, 65.4; H, 10.4; S, 9.7%).

2β-(3-Hydroxyoct-1-enyl)-3α-(6-methoxycarbonylhexyl)-4β-methylthietan 1,1-Dioxide (28; R = CO_2Me).—Reduction of the enone (26; R = CO_2Me) (733 mg) with sodium borohydride as above gave, after chromatography on silica (20 g; diethyl ether–light petroleum, 7 : 3 as eluant), the *product* (28; R = CO_2Me) (688 mg, 93%), $\nu_{max.}$ ($CDCl_3$) 3 600 (OH), 1 728 (CO), 1 310, and 1 138 cm^{-1} (SO_2); δ 5.80 (2 H, m, CH=CH), 4.33 (1 H, t, *J* 8 Hz, C*H*CH=CH), 4.17 (1 H, m, C*H*OH), 3.83 (1 H, m, C*H*CH_3), 3.67 (3 H, s, CO_2CH_3), 2.30 (2 H, t, *J* 7 Hz, $CH_2CO_2CH_3$), 1.82br (1 H, OH), 1.7—1.25 (16 H, m, 8 × CH_2), 1.47 (3 H, d, *J* 7 Hz, CHC*H*$_3$), and 0.89 (3 H, t, *J* 7 Hz, CH_2CH_3); *m/e* 324 ($M^+ - SO_2$) and 306 ($M^+ - H_2O$ and SO_2) (Found: C, 61.8; H, 9.2; S, 8.2. $C_{20}H_{36}O_5S$ requires C, 61.8; H, 9.3; S, 8.25%). Rechromatography (h.p.l.c., Hypersil) of the product (160 mg) gave the pure *isomers* (28a; R = CO_2Me) (28.5 mg) and (28b; R = CO_2Me) (41 mg).

2β-(3-Hydroxyoct-1-enyl)-3α-(6-methoxycarbonylhexyl)-4α-methylthietan 1,1-Dioxide (29; R = CO_2Me).—Treatment of the enone (27; R = CO_2Me) (66.5 mg) with sodium borohydride as above gave the *product* (29; R = CO_2Me) (62.4 mg, 94%), $\nu_{max.}$ ($CDCl_3$) 3 605 (OH), 1 728 (CO), 1 310, and 1 130 cm^{-1} (SO_2); δ 5.83 (2 H, m, CH=CH), 4.43 (1 H, m, C*H*CH=CH), 4.20 (2 H, m, C*H*CH_3 and C*H*OH), 3.66 (3 H, s, CO_2CH_3), 2.40 [2 H, m, C*H*$(CH_2)_6$ and OH], 2.31 (2 H, t, *J* 7 Hz, $CH_2CO_2CH_3$), 1.7—1.2 (16 H, m, 8 × CH_2), 1.42 (3 H, d, *J* 7 Hz, CHC*H*$_3$), and 0.89 (3 H, t, *J* 7 Hz, CH_2CH_3); *m/e* 388 (M^+), 372 ($M^+ - H_2O$), 324 ($M^+ - SO_2$), and 306 ($M^+ - H_2O$ and SO_2) (Found: C, 61.8; H, 9.3; S, 8.1. $C_{20}H_{36}O_5S$ requires C, 61.8; H, 9.3; S, 8.25%).

3α-(6-Carboxyhexyl)-2β-(3-hydroxyoct-1-enyl)-(4β-methylthietan 1,1-Dioxide (4).—A solution of the ester (28; R = CO_2Me) (488 mg) in a mixture of methanol (6 ml) and 2N-aqueous sodium hydroxide (3 ml) was kept at room temperature for 1.5 h after which most of the solvent was evaporated under reduced pressure; the residue was then diluted with water and acidified with 2N-hydrochloric acid. An ethereal extract of the suspension was dried and evaporated, and the residue chromatographed on silica (8 g; diethyl ether–light petroleum, 4 : 1, containing 0.2% acetic acid as eluant) to give the *product* (4) (470 mg, 100%), as a waxy solid, $\nu_{max.}$ ($CDCl_3$) 3 600 (OH), 3 510 (CO_2H), 1 710 (CO), 1 310, and 1 135 cm^{-1} (SO_2); δ 5.80 (2 H, m, CH=CH), 4.33 (1 H, m, C*H*CH=CH), 4.17 (1 H, m, C*H*OH), 3.83 (1 H, m, C*H*CH_3), 2.34 (2 H, t, *J* 7 Hz, CH_2CO_2H), 1.82 (1 H, m, C*H*$(CH_2)_6$], 1.7—1.25 (16 H, m, 8 × CH_2), 1.47 (3 H, d, *J* 7 Hz, CHC*H*$_3$), and 0.89 (3 H, t, *J* 7 Hz, CH_2CH_3); *m/e* 310 ($M^+ - SO_2$) and 292 ($M^+ - SO_2$ and H_2O) (Found: C, 61.1; H, 9.0; S, 8.3. $C_{19}H_{34}O_5S$ requires C, 60.9; H, 9.15; S, 8.6%).

Hydrolysis of the pure esters (28a; R = CO_2Me) and (28b; R = CO_2Me) in the same way gave the acids (4a) and (4b) respectively, the n.m.r. spectra of which differed from each other and from that quoted above only in the line-shape of the various multiplets.

3α-(6-Carboxyhexyl)-2β-(3-hydroxyoct-1-enyl)-4α-methylthietan 1,1-Dioxide (5).—Hydrolysis of the ester (29; R = CO_2Me) (167 mg) as described above gave the *product* (5) (160 mg, 99%), as a waxy solid, $\nu_{max.}$ ($CDCl_3$) 3 600 (OH), 3 520 (CO_2H), 1 710 (CO), 1 300, 1 310, and 1 135 cm^{-1} (SO_2); δ 5.82 (2 H, m, CH=CH), 4.41 (1 H, m, C*H*CH=CH), 4.19 (2 H, m, C*H*CH_3 and C*H*OH), 2.41 (1 H, m, C*H*$[CH_2]_6$), 2.34 (2 H, t, *J* 7 Hz, CH_2CO_2H), 1.70—1.20 (16 H, m, 8 × CH_2), 1.42 (3 H, d, *J* 7 Hz, CHC*H*$_3$), and 0.89 (3 H, t, *J* 7 Hz, CH_2CH_3) {Found: $[M + NH_4]^+$ 392.2476 ammonia chemical ionization). $C_{19}H_{34}O_5S{\cdot}NH_4$ requires *M*, 392.2471} (Found: C, 61.1; H, 9.0. $C_{19}H_{34}O_5S$ requires C, 60.9; H, 9.15%).

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