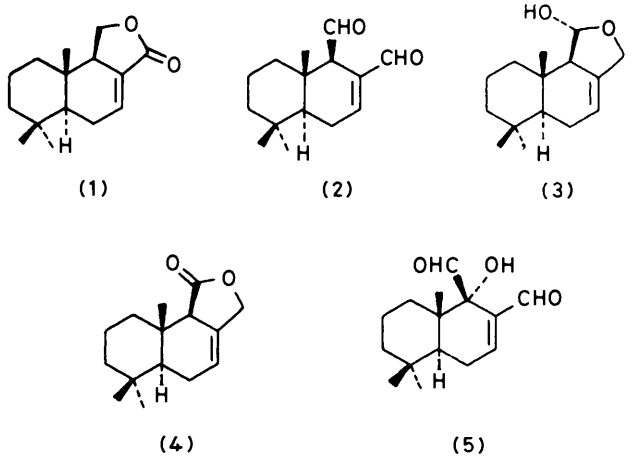
The Diels–Alder Route to Drimane related Sesquiterpenes; Synthesis of Cinnamolide, Polygodial, Isodrimeninol, Drimenin and Warburganal

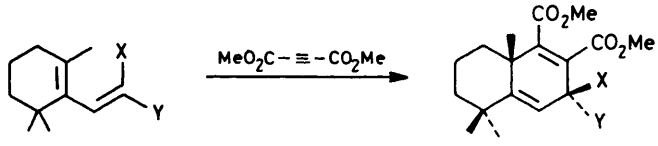
David M. Hollinshead, S. Christopher Howell, Steven V. Ley,* Michael Mahon, and Norman M. Ratcliffe
Department of Chemistry, Imperial College, London SW7 2AY
Paul A. Worthington
I.C.I. Plant Protection, Jealott's Hill, Bracknell, Berks RG12 6EY

The stereospecific preparation of various 1-vinyl-2,6,6-trimethylcyclohex-1-enes (6) as potential diene precursors in the Diels–Alder reaction with dimethyl acetylenedicarboxylate have been investigated. The reaction of the parent diene (6a) with dimethyl acetylenedicarboxylate affords an adduct (18) in 94% yield. This species was reductively isomerised using 10% Pd/C/H_2 and a mineral acid to give a *trans*-fused decalin diester (19). Reduction of (19) with lithium aluminium hydride afforded 1,4,4a,5,6,8,8a-octahydro-5,8,8a-trimethyl-1β,4aα,8aβ-naphthalene-1,2-dimethanol (24) a key starting material for the highly efficient syntheses of five drimane sesquiterpene natural products, cinnamolide (1), polygodial (2), isodrimeninol (3), drimenin (4), and warburganal (5). Microbial oxidation reactions using *C. elegans* or *A. niger* of (2), (24), and (1) gave good yields of the corresponding 3β-hydroxy derivatives, (30), (31), and (32). Several other unusually substituted drimane derivatives are reported.

Mainly as the result of diverse biological properties associated with many drimane sesquiterpenes, interest in their synthesis has increased noticeably in recent years. Although a number of different synthetic strategies to these molecules have been reported, the use of the Diels-Alder reaction to construct an appropriately functionalised decalin in a concise manner is especially attractive. The concept of using the Diels-Alder reaction in drimane natural product synthesis is not new and was first used by Brieger [1] in his synthesis of winterin. Improvements to the initial Diels-Alder process were later introduced by Campos [2] and Loperfido.[3] We [4,5] and others [6-8] have also exploited this approach to drimane sesquiterpene synthesis and here report in full on the preparation of five members of this group of compounds, namely cinnamolide (1), polygodial (2), isodrimeninol (3), drimenin (4), and warburganal (5).



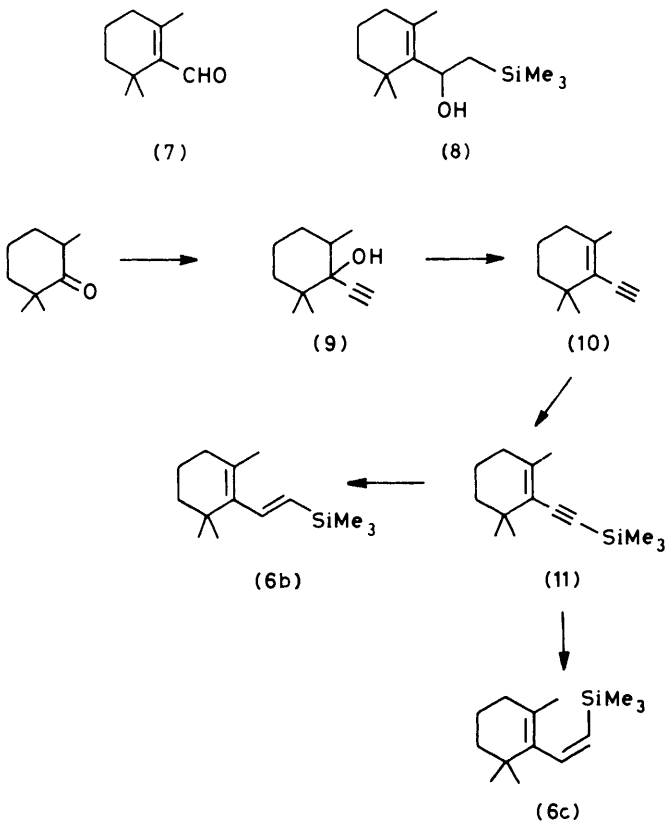
It was argued that dienes (6) might well react with dimethyl acetylenedicarboxylate to afford polyfunctionalised Diels-Alder products which would be amenable towards further elaboration to a range of natural products (Scheme 1). Consequently, a series of dienes (6) were prepared and their chemistry investigated. In the event, however, it was found that only the unsubstituted diene (6a) was a synthetically useful precursor species. The simple unsubstituted diene (6a) was prepared by reaction of β-cyclocitral (7) with methylenetriphenylphosphorane in 90% yield [6] or in even higher yield (95%) using a Peterson [9] olefination procedure. Thus (7), upon treatment with trimethylsilylmethylmagnesium chloride, gave the intermediate β-hydroxysilane (8), which on stirring with a mixture of toluene-*p* sulphonic acid and sulphuric acid gave the pure diene (6a) after distillation. By using sulphuric acid alone or potassium hydride in tetrahydrofuran, substantial quantities of the *E*-silylated diene (6b) were also formed from (8). In order to obtain the pure silylated diene (6b) free from (6a), it was necessary to treat (8) at low temperature (−78 °C) with potassium hydride and to follow this by acylation with trifluoroacetic anhydride and final elimination using pyridine. Alternatively, the *E*-silylated diene (6b) and the *Z*-silylated diene (6c) could be obtained selectively in four steps from 2,2,6-trimethylcyclohexanone *via* the intermediates (9), (10), and (11) (Scheme 2), the key step in these preparations being the stereocontrolled reduction of the silylenyne (11) was di-isobutylaluminium hydride (DIBAL). While stereoselective reductions of this type have been investigated before,[10] the use of trimethylsilylenynes have not previously been reported. Reaction of (11) with DIBAL in hexane at −78 °C followed by warming to room temperature and work-up gave (6b) in 98% yield. Correspondingly, reaction of (11)



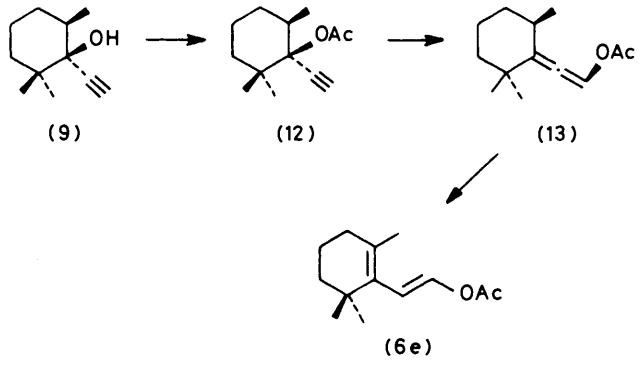
(6)

(a) X = Y = H
(b) X = H, Y = $SiMe_3$
(c) X = $SiMe_3$, Y = H
(d) X = H, Y = Br
(e) X = H, Y = OAc
(f) X = OMe, Y = H

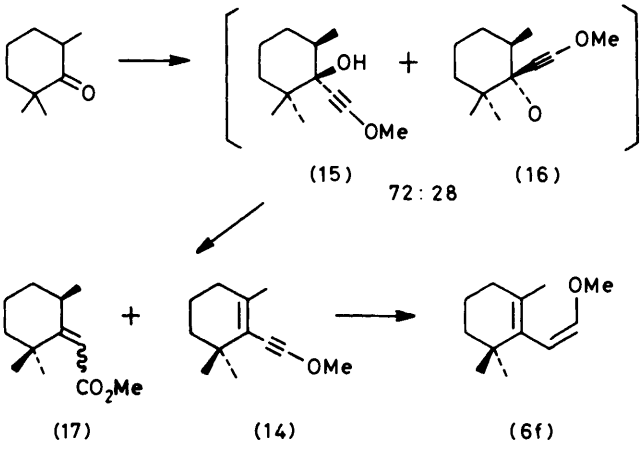
Scheme 1.



Scheme 2.



Scheme 3.

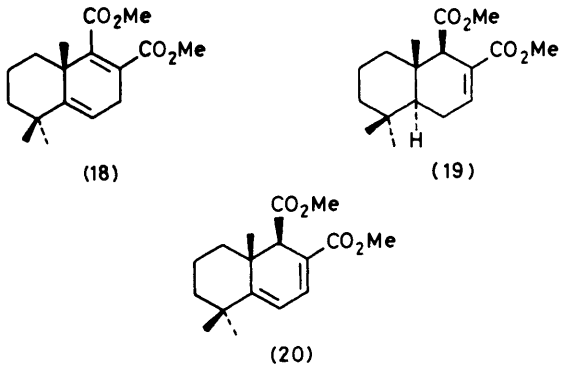


Scheme 4.

with DIBAL in tetrahydrofuran at 55—60 °C gave the *Z*-silylated diene (6c) (94%) together with a small amount of the *E*-isomer (6b) (5%). These were separable by silica gel chromatography.

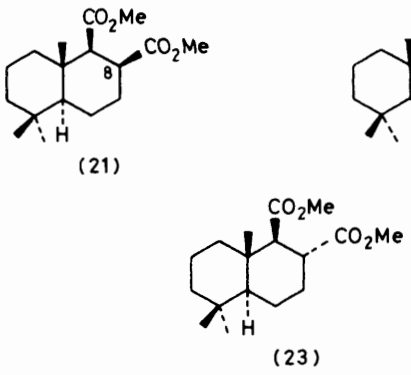
The bromine substituted diene (6d) was obtained from (6b), in 87% yield, in a straightforward manner,[11] by reaction with bromine in methylene chloride to give an unstable dibromide followed by rapid treatment with potassium fluoride in dimethyl sulphoxide. Two other less sterically bulky dienes (6e) and (6f) were also prepared in the additional hope that, being more electron rich, they might react well with dimethyl acetylenedicarboxylate. The first of these dienes (6e) was obtained from the propargylic acetate (12) by the reaction of silver hexafluoroantimonate. The first product to be formed in this reaction process was the allene (13) which rearranges further to (6e) upon extended (8 h under reflux) exposure to $AgSbF_6$ according to the literature precedented reaction [12] (Scheme 3). Finally, preparation of (6f) was accomplished, albeit in poor yield, by the sequence of reactions [13] shown in Scheme 4. The low yield (15% of the desired dehydrated product (14) from the carbinols (15) and (16) was due to the preferential formation (75%) of the conjugated ester (17) (Scheme 4). With a range of dienes (6b—f) now in hand, their reaction with dimethyl acetylenedicarboxylate was investigated. Under a variety of catalysed and uncatalysed reaction conditions, all failed to react. These failures are presumably due to the increased steric requirements for the necessary cisoid geometry in the transition state of the proposed Diels-Alder reaction together with the inherent instability of the dimethyl acetylenedicarboxylate at high temperatures. No attempt was made to react the diene precursors with the dimethyl acetylenedicarboxylate under high pressure reaction conditions.[14]

However, when the unsubstituted diene (6a) was heated



together with dimethyl acetylenedicarboxylate at 110 °C for 22 h, an excellent yield (94%) of the Diels-Alder adduct [3] (18) can be obtained. In order to obtain consistently high yields in this reaction we found it important always to use freshly distilled reagents.

It has been reported that (18), upon reduction with various catalysts, affords only *cis*-fused products.[6] A number of further steps were then necessary to convert this material into a synthetically useful precursor (19) to the natural *trans*-fused drimane derivatives. We regarded this as an inefficient process and therefore sought to achieve this conversion in one step. We speculated that hydrogenation of (18) could be carried out under conditions whereby prior double-bond isomerisation would occur, thus substantially altering the conformation of the ring system. Hydrogenation should then proceed in the desired fashion to give the *trans* fused product



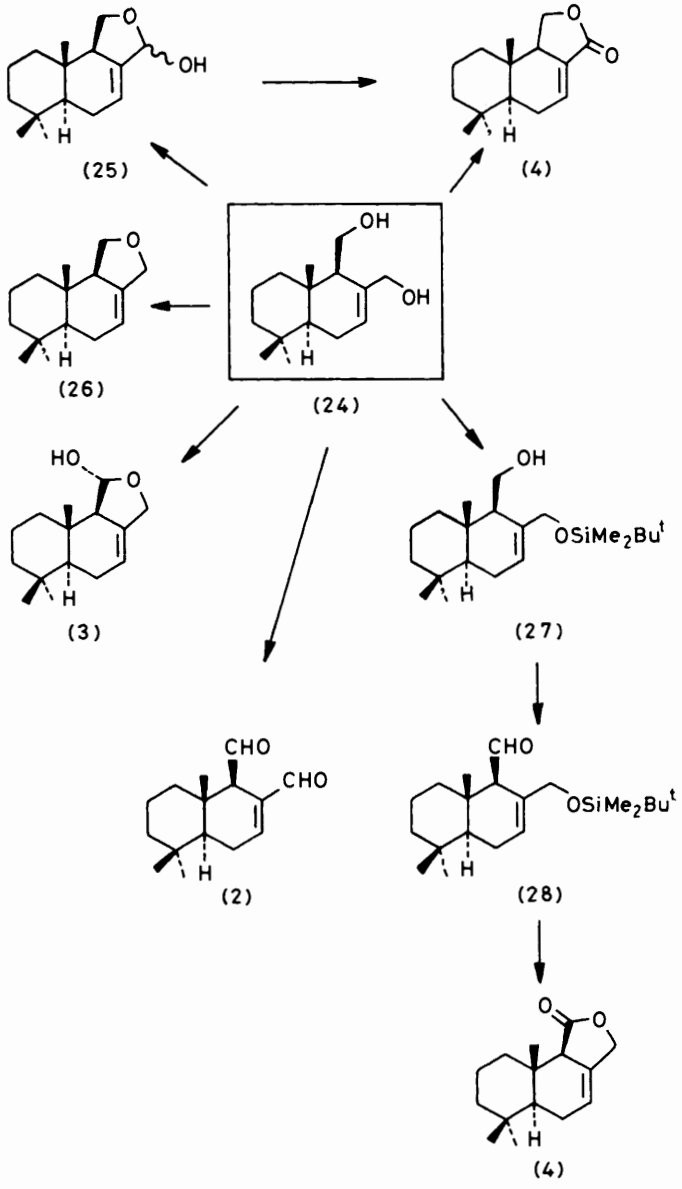
(19) directly. Thus, using typical reductive/isomerising conditions of 10% H_2–Pd–C in methanol in the presence of acid catalysts,[15] smooth conversion of (18) into the key building block (19) for drimane synthesis could be achieved in up to 80% yield.[4]

A related two-step conversion of (18) to (19) in 70% yield has recently been reported involving kinetically controlled stereospecific protonation of the enolate derived from (19) to afford (20) which on separate treatment with H_2–Pd–C gave (19).[7] We feel that this last interesting observation lends some credence to our earlier speculations.[4]

The role of the acid catalyst in prompting isomerisation of double bonds during hydrogenation is obviously important. Use of hydrochloric acid usually gives best yields although the reaction was fairly slow. The use of concentrated sulphuric acid permits a rapid reaction on a 50 g scale with yields of *ca.* 65%. Reduction of (18) in the absence of acid leads to a lower yield of (19) (50%) together with two other products, formed in 27 and 13% yields, to which we assign the structures (21) and (22) respectively.

The spectral properties of (19) are fully in accord with the assigned structure. Absolute proof of structure was obtained by an *X*-ray crystallographic determination.* Both (19) and (22) undergo further hydrogenation to give (21), as shown by 250 MHz ^{1}H n.m.r. spectroscopy. Furthermore, (21) can be epimerised at C-8 very readily by brief treatment with sodium methoxide in methanol at room temperature to give (23). In (23) the 9α-proton resonates as a doublet with a coupling constant of 12 Hz, typical of a *trans*-diaxial arrangement of the protons. Having established a highly efficient and very short route to multigramme quantities of (19), its true role as a precursor to drimane natural products was next investigated.

Reduction of (19) with lithium aluminium hydride gave the diol (24) in 90% yield. This key drimane diol [6] (24) is a pivotal compound for all the subsequent natural product syntheses. Oxidation of (24) using Collins reagents to afford cinnamolide (1) has been reported to proceed in 55% yield. We find that oxidation using the Fetizon reagent [16] affords (1) in essentially quantitative yield. The product was identical with previously synthesised material.[6,17,20] In an effort to find a cheaper alternative to the Ag_2CO_3/Celite oxidant, treatment with an excess of barium manganate [18] (10—20 equiv.) at room temperature in methylene chloride over 24 h, leads directly to (1) in 94% yield. However, if only 1—2 equiv. of barium manganate are used for shorter periods of time (4 h), the lactol (25) can be isolated (92%). This in turn can be oxidised to (1) with further reagent (Scheme 5). Polygodial [19] (2) is also an important synthetic target as it has been shown to possess antifeedant activity against army worms *Spodoptera littoralis* and *S. exempta*, both of which are common African crop pests.[20] In

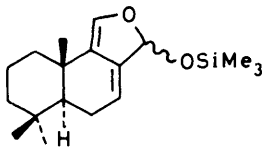


Scheme 5.

principle (2) should be readily available from the diol (24). Owing to the easy oxidation of the allylic hydroxyl relative to the other primary hydroxy-group, leading to rapid lactol/lactone formation, special oxidation conditions are therefore necessary if (24) is to be converted to polygodial (2). It was found that the use of the activated dimethyl sulphoxide (DMSO) complexes,[21] in particular oxalyl chloride–DMSO (the Swern oxidant) [22] at −50 °C, uniquely effected this transformation in excellent yields (95%). Once again the sample was identical with previously synthesised polygodial (2).[6,23] This route to polygodial (2), proceeding in 57% overall yield from (6a), is extremely short, very efficient and convenient, and is a vast improvement over previously reported procedures.[6,8,23] During the Swern oxidation it was noted that the quantity of triethylamine used to work up the intermediate sulphoxonium salts, was crucial. Omission of triethylamine in this process afforded the tricyclic compound (26) in 93% yield.

We next turned our attention to ways of selectively oxidising the primary hydroxy-group in (24) in the presence of the allylic hydroxy-group in the hope of preparing further natural

* We thank Dr. D. J. Williams, Imperial College for this determination.



(29)

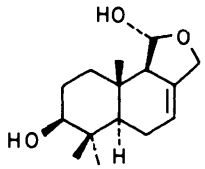
products. Partial success in this classically difficult transformation was achieved using tetraphenylphosphonium dioxoruthenium trichloride * in methylene chloride which gave the natural product isodrimeninol [24] (3) directly from (24) in 35% yield. The formation of only one lactol isomer from this reaction is not clear. Owing to the low yield above, we decided to use protecting groups to achieve the synthesis of drimenin (4). Thus, the diol (24) was treated with t-butyldimethylsilyl chloride (1—1.2 equiv.) to give the monoprotected species (27). Oxidation using the Swern conditions gave the aldehyde (28). Deprotection with tetra-n-butylammonium fluoride and oxidation with PCC gave pure drimenin (4) [6,25] in 36% overall yield from (24) (Scheme 5).

Finally, we investigated the synthesis of warburganal (5) which was the ultimate objective underlying this work. Warburganal has been shown to have insect antifeedant, plant growth regulation, cytotoxic, antimicrobial, molluscicidal, and anticomplemental properties.[20] For these reasons, intense interest has been stimulated in its preparation.[5,6,26] We have tried to design a concise and practically convenient route to this important molecule.

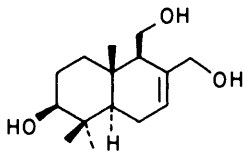
Several synthetic approaches were considered, although the most direct appeared to be the angular hydroxylation at the activated C-9 position of polygodial (2). Although this transformation appeared straightforward, in practice, none out of an extensive list of typical oxidants and reagent conditions were successful. Failure was probably due to the instability of both polygodial and especially warbuganal to the reaction conditions. Other problems which arose in this direct oxidation approach are illustrated by the reactions of the enolate of polygodial (2) with MoOPH [27] or O_2 which produced only recovered (2) on work-up. The lack of reactivity of the enolate must be due to it being present in a cyclised form, *i.e.* as the lactenolate. In accord with this proposal, work-up of the enolate by treatment with trimethylsilyl chloride gave (29) quantitatively. Attempts to convert (29) to warburganal by firstly reacting it with *m*-chloroperbenzoic acid followed by treatment with tetra-n-butylammonium fluoride also failed. This approach still seems reasonable but was not investigated fully owing to success in another strategy (see later).

As chemical methods apparently could not be used to oxidise polygodial (2) to warburganal (5), we decided to investigate microbiological methods. Hydroxylating organisms are well known and have been used extensively.[28] The chemical yields in these processes are often mediocre to poor, however, we felt that the potential reward more than justified their investigation. While these microbial oxidations also failed to provide warburganal (5) from (2) interesting and potentially very useful reactions were discovered which are discussed here.

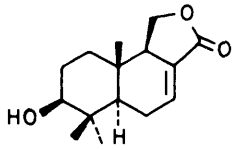
Hence incubation of polygodial together with *Cunninghamella elegans*, a known allylic hydroxylating organism,[29] for 10 days gave on work-up a single product in a remarkable 90% yield. That this product was not warburganal was shown by a molecular ion in the mass spectrum which corresponded to starting material plus 18 mass units. The high-field ^1H n.m.r. spectrum of the product showed the absence of signals



(30)



(31)



(32)

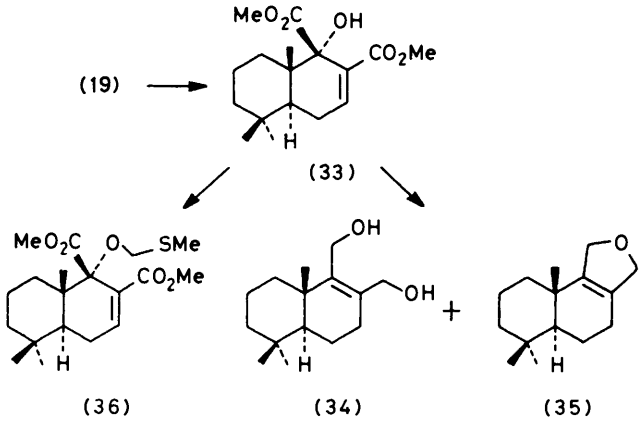
associated with the aldehydic protons and it also contained a signal at δ 3.3 which is suggestive of oxidation at C-3β. The other features of the spectrum are very similar to those obtained for the natural product isodrimeninol (3). We thus assign the structure of this product as 3β-hydroxyisodrimeninol (30). In this biological reaction of (2) therefore, several notable features arise. Firstly, stereospecific oxidation at C-3 occurs in high yield, and although the starting material is racemic no evidence for any optical activity in the product was observed nor was there any enantioselection when the product was worked up after a short incubation period. The yield of the product (30) was consistently high over several experimental runs. Another unusual feature of the biological reaction of (2) was the apparent concomitant selective reduction of the C-8 aldehyde group. In order to probe briefly these biological reactions in more detail, two other drimane substrates were also fed to the micro-organisms.

Hence when the diol (24) was incubated with either *Cunninghamella elegans* or *Aspergilla niger* [30] for *ca.* 3 days at 24 °C a major product was formed in 70—80% yield. By high-field ^1H n.m.r. spectroscopy this product was shown to be the triol (31), the characteristic feature of the spectrum being the resonance at δ 3.28 (1 H, dd, *J* 4.5 and 11 Hz) corresponding to the 3-hydrogen atom and the significant shifts in the neighbouring methyl resonances at C-4. In a similar fashion oxidation of cinnamolide (1) with *A. niger* at 26—27 °C for 4 days gave a product in 46% yield to which we assign the structure (32), again showing oxidation had taken place specifically at C-3. Oxidation of the triol (31) with Ag_2CO_3–Celite also gave (32) in essentially quantitative yield.

Although these biological oxidations were ineffective in producing warburganal (or suitable precursor molecules) they are of relevance for the possible synthesis of various 3-hydroxylated drimanes such as uvidin B [31] and 3β-hydroxywarburganal.† We hope to exploit these reactions at a later date. In a continued effort to introduce an angular hydroxy-substituent at C-9 in a suitable substrate and hence prepare warburganal (5), the oxidation of the diester (19) was investigated. It was proposed that after oxidation elaboration of the two ester groups to aldehyde moieties might be feasible. Oxidation of the enolate from (19) by MoOPH [27] in this example proceeds well to give a single isomer (33) as shown by high-field ^1H n.m.r. methods, in 95% yield. However, it was not possible to convert this hydroxy-diester species (33) into warburganal or a precursor under a variety of conditions. For example reduction using lithium aluminium hydride (or other reductants) gave a mixture of two products shown to be

* We thank Dr. W. P. Griffith and G. Green for developing and pointing out this reagent to us.

† Professor I. Kubo (University of California), personal communication.

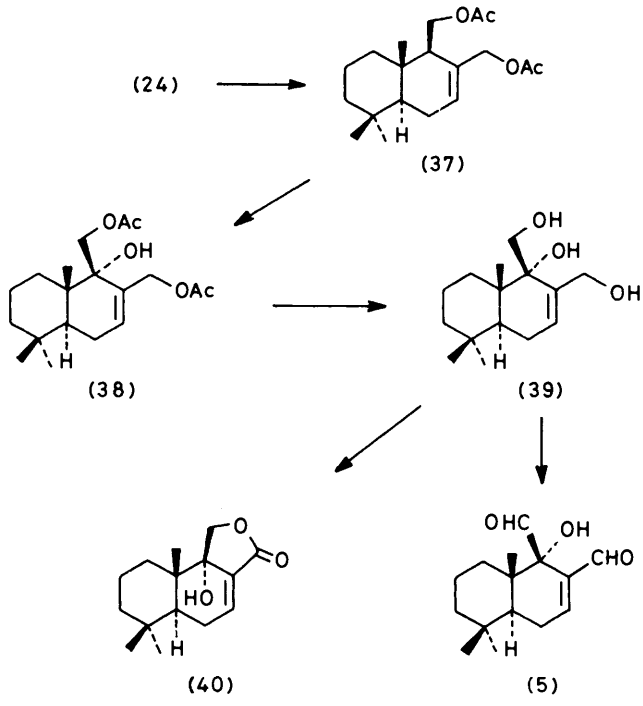


Scheme 6.

(34) [25a] and (35) in 47% and 20% yields respectively. It was clear from this experiment that the angular hydroxy-group in (33) was labile, therefore in order to improve its stability, it was protected as the thiomethyl methyl ether using DMSO–acetic anhydride [32] to give (36) again in good yield. Reduction of this compound with DIBAL (and other reducing agents) at −78 °C in toluene afforded (34) as the only isolable product (Scheme 6).

Finally, it was decided to introduce the 9-OH group into the key diol (24) as the starting material. Although direct oxidation methods failed on this substrate, after quantitative protection as the diacetate (37), oxidation with selenium dioxide gave (38) in 80% yield. The regio- and stereo-selectivity of this oxidation is entirely predictable by the Guillemonat rules [33] and is also in accord with the later conversion of (38) into the natural product. Deprotection of (38) with potassium carbonate in methanol gave the triol (39) in quantitative yield. Oxidation of (39) with the Fetizon reagent [16] in boiling benzene afforded the previously unknown compound 9α-hydroxycinnamolide (40). Oxidation of (39) with DMSO–trifluoroacetic anhydride [22] at −50 °C followed by treatment with triethylamine 9 equiv.) afforded the much sought after warburganal (5) in 45% yield. This product was identical on direct comparison with natural material.* Other oxidants (the Corey-Kim reagent) have been reported [26] to convert (39) into warburganal (5), although this method was less successful in our hands. Despite the disappointing final oxidation step the route described above constitutes an efficient 20% overall yield to warburganal from the diene (6a) (Scheme 7).

In summary, we believe we have described a versatile entry to the synthesis of a wide range of drimane natural products. It is conceivable that the route is also amenable to the preparation of congeners of the labdane series.



Scheme 7.

Experimental

M.p.s were determined on a Kofler hot-stage apparatus and are uncorrected. I.r. spectra were recorded on a Perkin-Elmer 298 spectrometer as neat oils or chloroform solutions. Mass spectra were obtained on an A.E.I. MS 9 or V.G. Micromass 7070 instruments at 70 eV. ^{1}H N.m.r. spectra were recorded on a Varian EM 360 A or a Bruker WH 250 instruments in deuteriochloroform with tetramethylsilane as internal standard. All solvents were purified and dried by standard techniques. Light petroleum refers to the fraction b.p. 60—80 °C.

All reactions were performed under a dry nitrogen atmosphere unless otherwise stated. Column chromatography was performed on silica gel 60 H, slurry packed, and run under low pressure (3—25 lb in^{-2}).

Preparation of 1-*Vinyl*-2,6,6-*trimethylcyclohexene* (6a).—2,3,4,5-Tetrahydro-2,2,6-trimethylbenzaldehyde (β-cyclocitral) (52 g, 0.34 mol) in ether (50 ml) was added to a solution of trimethylsilylmethylmagnesium chloride (1.05 equiv.), from magnesium (8.6 g), and chloromethyltrimethylsilane (52 ml, 0.36 mol) in ether (100 ml), and stirred for a further 1 h, at room temperature. The reaction mixture was transferred to ice–saturated ammonium chloride solution, and the layers separated. Drying and evaporation of the solvent from the organic fraction gave the alcohol (8) (80.8 g, 98.5%), $\nu_{max.}$ 3 630, 3 500, 1 460, 1 380, 1 245, and 1 030 cm^{-1}; δ (60 MHz) 0.95, 1.10 (6 H, 2 s), 1.20 (1 H, s, OH), 1.1—1.8 (8 H, m), 1.85 (3 H, s), and 4.50 (1 H, m); *m/z* 240, 223, 208, 190, 143, and 133 (Found: C, 69.9; H, 12.0. $C_{14}H_{28}OSi$ requires C, 69.93; H, 11.74%).

The crude alcohol (8) (80 g) in THF (200 ml) was added at once to a vigorously stirred solution of *p*-TSA (3 equiv.) and sulphuric acid (1 equiv.) in THF (1 l). After a further 5 min the mixture was transferred to saturated aqueous sodium hydrogen carbonate and extracted with light petroleum. Drying and removal of the solvent from the organic fraction, followed by distillation gave the diene (6a) (48 g, 96%), b.p. 54 °C (5 Torr), $\nu_{max.}$ 3 040, 1 620, 1 390, 1 370, 990, and 910 cm^{-1}; δ (250 MHz) 1.0 (6 H, s), 1.4—1.7 (4 H, m), 1.69 (3 H, m), 1.98 (2 H, m), 4.96 (1 H, dd, *J* 3, 18 Hz), 5.22 (1 H, dd, *J* 3, 12 Hz), and 6.21 (1 H, ddm, *J* 12, 18 Hz); *m/z* 150, 135, 119, and 107 (Found: C, 87.85; H, 12.2. $C_{11}H_{18}$ requires C, 87.93; H, 12.07%).

Preparation of 1-*Ethynyl*-2,6,6-*trimethylcyclohexanol* (9).—Purified acetylene was bubbled into a stirred suspension of sodamide (from 9.5 g sodium) in liquid ammonia (500 ml). After 1 h, 2,6,6-trimethylcyclohexanone (52 g, 0.37 mol)

* We thank Professor I. Kubo, University of California, for providing us with a sample of the natural product for comparison.

in ether (50 ml) was added during 30 min to the resulting grey suspension with mechanical stirring. After a further 2 h, ammonium chloride (25 g) and subsequently ether (20 ml) was added, and the ammonia evaporated with a warm water-bath. The mixture was filtered and the ethereal solution dried and evaporated. Distillation gave the carbinol (9) (59.3 g, 98%), b.p. 50 °C (0.5 Torr); $\nu_{max.}$ 3 450, 3 290, and 2 050 cm^{-1}; δ (60 MHz) 0.95, 1.0, 1.05 (9 H, 3s), 1.3—1.7 (7 H, m), 1.9 (1 H, s, OH), and 2.33 (1 H, s); *m/z* 166 (M^+) 151 140, 125, 123, 110, 95, and 92 (Found: C, 79.25; H, 10.95. $C_{11}H_{18}O$ requires C, 79.46; H, 10.91%).

Preparation of 1-*Trimethylsilylethynyl*-2,6,6,6-*trimethylcyclohexene* (11).—The carbinol (9) (20 g, 0.12 mol) was refluxed in xylene (200 ml) in the presence of copper sulphate trihydrate (2.2 g) for 6 h using a Dean-Stark trap. A fractionating column was attached, and xylene (180 ml) was distilled under nitrogen at atmospheric pressure. The residue, presumed to be compound (10), was decanted and dissolved in dry ether (60 ml) and cooled to −78 °C. Methyl-lithium (100 ml; 1.24M in ether) was added and the mixture stirred for 1 h. Trimethylsilyl chloride (16.5 ml, 0.13 mol) was added and the mixture stirred for a further 2 h at −78 °C, before being allowed to warm to room temperature. Addition of water (80 ml) with ice cooling was followed by extraction with light petroleum. Drying and removal of the solvents followed by distillation gave compound (11) (19.38 g, 70%), b.p. 70 °C (0.5 Torr); $\nu_{max.}$ 2 960, 2 930, 2 900, 2 860, 2 830, 2 130, 1 620, and 1 450 cm^{-1}; δ (60 MHz) 0.2 (9 H, s), 1.05 (6 H, s), 1.8 (3 H, s), and 1.0—2.0 (6 H, m); *m/z* 220 (M^+) 205, 177, 164, and 149 (Found: C, 76.3; H, 11.2. $C_{14}H_{24}Si$ requires C, 76.28; H, 10.97%).

Preparation of 1-(trans-*Trimethylsilylvinyl*)-2,6,6-*trimethylcyclohexene* (6b).—Compound (11) (3 g, 11.26 mmol) was treated with DIBAL (17 ml; 1M in hexane, 1.5 equiv.) at −78 °C under argon. The mixture was warmed to room temperature, stirred for 60 h, and water (0.4 ml, 2 equiv.) added. Filtration was followed by drying and evaporation of the solvents to give the *trans*-silylated diene (6b) (3.0 g, 98%), b.p. 64 °C (*ca.* 1 Torr); $\nu_{max.}$ 2 960, 2 930, 2 860, 2 130, 1 595, 1 460, and 1 250 cm^{-1}; δ (60 MHz) 0.1 (9 H, s), 0.9 (6 H, s), 1.5 (3 H, s), 0.9—2.0 (6 H, m), and 5.4, 6.25 (2 H, 2 d, *J* 19 Hz; 19 Hz); *m/z* 222 (M^+), 207, 148, 133, 124, 99, and 73 (Found: C, 75.55; H, 11.95. $C_{14}H_{26}Si$ requires C, 75.59; H, 11.78%).

Preparation of 1-(cis-*Trimethylsilylvinyl*)-2,6,6-*trimethylcyclohexene* (6c).—Compound (11) (3 g, 11.26 mmol) was heated to 55—60 °C under argon and treated with DIBAL (380 mg, 1.35 equiv.) in THF (0.215 ml, 1.35 equiv.) in one portion and stirred for 12 h. Addition of water (0.4 ml, 2 equiv.) to the cooled mixture followed by filtration and evaporation gave a clear liquid (480 mg) which was chromatographed on silica H (20 g) (light petroleum) to give (6b) (5%) and the *cis*-silylated diene (6c) (2.70 g, 94%); $\nu_{max.}$ 2 960, 2 920, 2 860, 2 130, and 1 600 cm^{-1}; δ (60 MHz) 0.05 (9 H, s), 0.95 (6 H, s), 1.65 (3 H, s), 0.9—2.0 (6 H, m), and 5.6 and 6.6 (2 H, 2 d, *J* 16 Hz, 16 Hz) (Found: C, 75.55; H, 11.95. $C_{14}H_{26}Si$ requires C, 75.59; H, 11.78%).

Preparation of 1-(trans-*Bromovinyl*)-2,6,6-*trimethylcyclohexene* (6d).—A solution of (6b) (1 g, 4.5 mmol) in methylene chloride (25 ml) at −78 °C was treated with a solution of bromine in methylene chloride (0.75M; 6 ml, 1 equiv.) during 10 min. After 2.5 h at −78 °C, the reaction mixture was quickly transferred to a cooled saturated solution of potassium fluoride in dimethyl sulphoxide (40 ml) with rapid stirring. After 4 h at room temperature, the reaction mixture was diluted with water and extracted with light petroleum. Drying and removal of solvent gave the bromide (6d) (0.89 g, 87%); $\nu_{max.}$ 1 600, 1 460, 990, 870, 840, and 740 cm^{-1}; δ (60 MHz) 1.03 (6 H, s), 1.6 (3 H, s), 0.9—2.0 (6 H, m), and 5.9 and 6.5 (2 H, 2 d, *J* 15 Hz, 15 Hz); *m/z* 228.0517 (M^+. $C_{11}H_{17}Br$ requires *M*, 228.0514, 213, 148, 135, 109.

Preparation of 1-(trans-*Acetoxyvinyl*)-2,6,6-*trimethylcyclohexene* (6e).—The acetate (12) (0.25 g, 4.8 mmol) was warmed in benzene (5 ml) in the presence of a catalytic amount of silver hexafluoroantimonate for 1—2 min to produce the allene (13) (100%); $\nu_{max.}$ 3 060, 1 920, and 1 750 cm^{-1}; δ (60 MHz) 0.97 (3 H, d, *J* 6 Hz), 1.07, 1.17 (6 H, 2 s), 1.0—1.7 (7 H, m), 2.06 (3 H, s), and 7.3 (1 H, d, *J* 2.5 Hz); *m/z* 208 (M^+), 193, 166, 151, and 133 (Found: C, 75.05; H, 9.95. $C_{13}H_{20}O_2$ requires C, 74.96; H, 9.68%).

Further heating of (13) for 8 h followed by filtration and evaporation of the solvent and filtration through Florisil gave the acetoxy diene (6e) (0.17 g, 68%), $\nu_{max.}$ 1 760, 1 690, 1 655, 1 450, 1 365, and 1 220 cm^{-1}; δ (60 MHz) 1.05 (6 H, s), 1.55 (3 H, s), 0.9—1.9 (6 H, m), and 5.70 and 6.85 (2 H, 2 d, *J* 13 Hz, 13 Hz); *m/z* 209.1467 (M^+. $C_{13}H_{20}O_2$ requires *M*, 208.1463), 193, 166, 148, and 133.

Preparation of 1-*Methoxyethynyl*-2,6,6-*trimethylcyclohexanol* (15) *and* (16).—To a solution of methoxyacetylene (0.875 g, 15.63 mmol) in ether (10 ml) at −78 °C under argon was added dropwise n-butyl-lithium (106 ml; 1.4M in hexane; 15 mmol). After 15 min the white suspension was warmed to −20 °C and 2,6,6-trimethylcyclohexanone (1.5 g, 7 mmol) in ether (5 ml) was added during 5 min. After a further 30 min, the reaction was warmed to 0 °C for 1 h and worked up as usual to provide a pale yellow oil which was chromatographed on silica H [45 g, ether–hexane (3 : 93)] to give (16) (550 mg, 28%), $\nu_{max.}$ 3 620, 3 500, 2 260, 1 450, and 1 240 cm^{-1}; δ (60 MHz) 0.92 (3 H, d, *J* 6 Hz), 0.95, 1.03 (6 H, 2 s), 1.57 (1 H, s, OH), 0.9—1.9 (7 H, m), and 3.85 (3 H, s); *m/z* 196.1461 (M^+. $C_{12}H_{20}O_2$ requires *M*, 196.1463), 181, 153, 139, 125, and 97; and (15) (1.42 g, 72%), $\nu_{max.}$ 3 620, 3 500, 2 255, 1 450, and 1 230 cm^{-1}; δ (60 MHz) 0.98 (3 H, d, *J* 6 Hz), 1.03 (6 H, s), 0.9—1.9 (7 H, m, and 3.82 (3 H, s); *m/z* 196.1461 (M^+. $C_{12}H_{20}O_2$ requires *M*, 196.1463), 181, 153, 139, 125, and 97.

Preparation of 1-*Methoxyethynyl*-2,6,6-*trimethylcyclohexene* (14).—Compound (15) (3.5 g, 17.8 mmol) in benzene (100 ml) with copper sulphate trihydrate was heated to reflux for 3 h. Filtration and evaporation of the solvent gave an oil which was chromatographed (silica H, 10 g, light petroleum and then ether–light petroleum) to afford (14) (475 mg, 15%), $\nu_{max.}$ 2 255, 1 455, 1 315, 1 250, 1 110, and 1 010 cm^{-1}; δ (60 MHz) 1.03 (6 H, s), 1.72 (3 H, s), 0.9—2.0 (6 H, m), and 3.82 (3 H, s); *m/z* 178.1360 (M^+. $C_{12}H_{28}O$ requires *M*, 178.1358), 163, and 151; and compound (17) as a mixture of isomers (1.85 g, 54%), $\nu_{max.}$ 1 720, 1 625, 1 430, and 1 265 cm^{-1}; δ (60 MHz) 1.15 (3 H, s), 1.15 (3 H, d, *J* 4 Hz), 1.28 (3 H, s), 0.9—1.9 (7 H, m), 3.60 (3 H, s), and 5.60 (1 H, s); *m/z* 196.1461 (M^+. $C_{12}H_{20}O_2$ requires *M*, 190.1463), 181, and 169; and (0.75 g, 21%), $\nu_{max.}$ 1 730, 1 640, 1 625, and 1 200 cm^{-1}; δ (60 MHz) 1.05 (3 H, d, *J* 6 Hz), 1.18 (6 H, s), 0.9—1.9 (7 H, m), 3.60 (3 H, s), and 5.35 (1 H, s); *m/z* 196.1461 (M^+. $C_{12}H_{20}O_2$ requires *M*, 196.1463), 181, and 169.

Preparation of 1-(cis-*Methoxyvinyl*)-2,6,6-*trimethylcyclohexene* (6f).—A solution of (14) (0.25 g, 1.4 mmol) in hexane (5 ml) at −78 °C under argon was treated with DIBAL (35 mg, 1.4 mmol, 1 equiv.) in THF (1 equiv.) and the solution then allowed to reach room temperature. Stirring for a

further 3 d was followed by addition of water (2 equiv.) and filtration through Florisil to give compound (6f) (175 mg, 69%); $\nu_{max.}$ 1 630, 1 450, 1 250, 1 055, and 1 010 cm^{-1}; δ (60 MHz) 1.10 (6 H, s), 1.5 (3 H, s), and 4.55 and 7.10 (2 H, 2 d, 18 Hz, 18 Hz); *m/z* 180.1511 (M^+. $C_{12}H_{20}O$ requires *M*, 180.1514) 165, and 153.

Preparation of Dimethyl 3,5,6,7,8,8a-*Hexahydro*-5,5,8a-*trimethylnaphthalene*-1,2-*dicarboxylate* (18).—The diene (6a) (35 g, 0.23 mol, distilled) together with freshly distilled dimethyl acetylenedicarboxylate (44 g, 1.4 equiv.) were heated together under argon in a sealed vessel at 110 °C for 22 h. The reaction mixture was then cooled, dissolved in hexane (80 ml), and filtered through silica gel (250 g) using ether–hexane (2 : 3), to provide an almost colourless oil. Seeding (if necessary) and trituration with a little methanol followed by cooling (< −50 °C) and filtering provided (18) (56.3 g) of white crystals, m.p. 53—54 °C (lit.,[6] 50—51 °C). Chromatography of the mother liquors provided a further 7.7 g of compound (18) (total yield 94%), $\nu_{max.}$ 1 720, 1 660, 1 620, and 1 250 cm^{-1}; δ (250 MHz) 1.14 (3 H, s), 1.19 (3 H, s), 1.43 (3 H, s), 1.2—1.9 (6 H, m), 2.78 (1 H, dd, *J* 3, 23 Hz), 3.16 (1 H, dd, *J* 6, 23 Hz), 3.72 (3 H, s), 4.01 (3 H, s), and 5.70 (1 H, dd, *J* 3, 6 Hz); *m/z* 292 (M^+) 261 and 245 (Found: C, 69.65; H, 8.35. $C_{17}H_{24}O_4$ requires C, 69.84; H, 8.27%).

Hydrogenation of Dimethyl 3,5,6,7,8,8a-*Hexahydro*-5,5,8a-*trimethylnaphthalene*-1,2-*dicarboxylate* (18) *in the Absence of Acid Catalysts*.—Compound (18) (1 g, 3.42 mmol) was dissolved in methanol (200 ml) and 10% Pd/C (150 mg) was added to it; the mixture was then stirred vigorously under an atmosphere of hydrogen. After 1 h, 1.2 equiv. of hydrogen had been absorbed and further uptake was very slow. The mixture was then filtered and the solvent removed to provide a crude product mixture (1.0 g) which was chromatographed on silica H (100 g, ether–hexane mixtures) to give compound (19) (507 mg, 50%), m.p. 82.5—83 °C; $\nu_{max.}$ 2 890, 1 730, 1 725, 1 650, 1 460, 1 280, and 1 245 cm^{-1}; δ (250 MHz) 0.89 (3 H, s), 0.92 (3 H, s), 0.96 (3 H, s), 1.24 (1 H, dd, *J* 5, 12 Hz), 1.0—1.7 (5 H, m), 1.85 (1 H, dm, *J* 13 Hz), 2.10 (1 H, dddd, *J* 3, 4, 12, 20 Hz), 2.29 (1 H, dddd, *J* 2.5, 5, 6, 20 Hz), 3.20 (1 H, ddd, *J* 2, 2.5, 4 Hz), 3.67 (3 H, s), 3.70 (3 H, s), and 7.06 (1 H, ddd, *J* 2, 3, 6 Hz); *m/z* 294 (M^+), 279, 262, and 234 (Found: C, 69.2; H, 8.8. $C_{17}H_{26}O_4$ requires C, 69.36; H, 8.90%); and compound (21) (270 mg, 27%), m.p. 68—70 °C, $\nu_{max.}$ 1 735, 1 465, 1 435, 1 210, 1 160, and 910 cm^{-1}; δ (250 MHz) 0.82 (3 H, s), 0.85 (3 H, s), 1.05 (3 H, s), 1.0—1.7 (9 H, m), 2.23 (1 H, ddd, *J* 2.5, 5, 13 Hz), 2.33 (1 H, m), 2.34 (1 H, d, *J* 5 Hz), 3.04 (1 H, ddd, *J* 2, 5, 5 Hz), 3.63 (3 H, s), and 3.65 (3 H, s); *m/z* 296 (M^+) 281, 264, 249, 208, and 1.45 (Found: C, 69.05; H, 9.2. $C_{17}H_{28}O_4$ requires C, 68.89; H, 9.52%); and compound (22) (127 mg, 12.6%), m.p. 78—79 °C; $\nu_{max.}$ 1 735, 1 430, 1 200, and 910 cm^{-1}; δ (250 MHz) 1.10 (6 H, s), 1.32 (3 H, s), 1.2—1 9 (6 H, m), 2.31 (1 H, ddd, *J* 5, 7, 18 Hz), 2.69 (1 H, ddd, *J* 3, 12, 18 Hz) 2.74 (1 H, d, *J* 4 Hz), 3.07 (1 H, ddd, *J* 4, 7, 12 Hz), 3.62 (1 H, d, *J* 4 Hz), 3.07 (1 H, ddd, *J* 4, 7, 12 Hz), 3.62 (3 H, s), 3.69 (3 H, s), and 5.59 (1 H, dd, *J* 3, 5 Hz); *m/z* 294 (M^+), 281, 279, 262, 235, 219, and 175 (Found: C, 69.2; H, 8.85. $C_{17}H_{26}O_4$ requires C, 69.36; H, 8.90%).

Preparation of Dimethyl 1,4,4a,5,6,7,8,8a-*Octahydro*-5,5,8a-*trimethylnaphthalene*-1,2-*dicarboxylate* (19); *Small Scale Experiment*.—Compound (18) (1 g, 3.4 mmol) was dissolved in methanol (500 ml) containing concentrated hydrochloric acid (0.25 ml); 10% Pd/C (100 mg) was added to the solution and the mixture then hydrogenated at atmospheric pressure in the usual way. The reaction was monitored by g.l.c. for formation of the desired product (19). The reaction products were worked up by firstly neutralising the mixture with sodium hydrogencarbonate followed by filtration to remove the catalyst. Solvents were removed under reduced pressure and the residue extracted with ether (2 × 50 ml). After drying (over magnesium sulphate) solvent was removed and the residue subjected to chromatography on silica gel H (100 g) to give compound (19) (0.805 mg, 80%) identical with the previously isolated sample.

Preparation of Dimethyl 1,4,4a,5,6,7,8,8a-*Octahydro*-5,5,8a-*trimethylnaphthalene*-1,2-*dicarboxylate* (19); *Large Scale Experiment*.—The adduct (18) (55 g, 0.19 mol) was dissolved in methanol (20 l) containing concentrated sulphuric acid (20 ml); 10% Pd/C (5 g) was added to the mixture and hydrogen then passed into the solution (*via* a sintered frit) with efficient mechanical stirring, at room temperature. After 30 min, g.l.c. indicated optimum yield of the desired product. Sodium hydrogencarbonate (2 equiv.) was added to the mixture which was then stirred for 5 min before filtration and removal of the solvent from the filtrate. The residue was taken up in ether (500 ml) and treated as usual to give a pale yellow oil. Seeding and trituration with a little methanol caused crystallisation of the desired product (19). The mixture was then cooled (< −60 °C) and filtered rapidly, small volumes of cold methanol being used for washing; this provided (19) (29.2 g). Chromatography of the mother liquor provided a further 7.3 g of (19) (combined yield 66%) which was shown to be identical with the previously isolated sample.

Preparation of 1,4,4a,5,6,7,8,8a-*Octahydro*-5,5,8a-*trimethyl*-1β,4aα,8aβ-*naphthalene*-1,2-*dimethanol* (24).—A solution of the diester (19) (2.05 g, 7 mmol) in ether (25 ml) was added dropwise to lithium aluminium hydride (0.27 g, 4 equiv.), in ether (100 ml) at 0 °C under argon. After a further 15 min at 0 °C, the mixture was transferred to ice–5% sulphuric acid (250 ml). The ethereal layer was washed with saturated aqueous sodium hydrogencarbonate and worked up to provide a colourless oil (1.7 g). Seeding and trituration with cold methanol (< −60 °C) followed by rapid filtration gave the diol (24) (1.2 g, 80%) as white crystals, m.p. 73—74 °C (lit.,[6] 73—74 °C). Chromatography (silica H, ethyl acetate–light petroleum mixtures) gave a further 0.29 g of (24) (combined yield 90%), $\nu_{max.}$ 3 620, 3 420, 1 665, 1 460, 1 440, 1 370, 1 040, and 990 cm^{-1}; δ(250 MHz, after D_2O exchange) 0.75 (3 H, s), 0.87 (3 H, s), 0.89 (3 H, s), 1.1—1.7 (7 H, m), 1.8—2.2 (3 H, m), 3.65 (1 H, dd, *J* 7.5, 10.5 Hz), 3.89 (1 H, dd, *J* 2, 10.5 Hz), 3.94 (1 H, d, *J* 12 Hz), 4.23 (1 H, d, *J* 12 Hz), and 5.79 (1 H, m); *m/z* 238 (M^+), 220, 207, 205, and 190 (Found: C, 75.75; H, 11.15. $C_{15}H_{26}O_2$ requires C, 75.58; H, 10.99%).

Preparation of 5,5,a,6,7,8,9,9a,9b-*Octahydro*-6,6,9a-*trimethyl*-5aα,9aβ,9bβ-*naphtho*[1,2-c]*furan*-3(1H)-*one* (*Cinnamolide* (1).—*Method* 1. The diol (24) (100 mg, 0.42 mmol) was stirred with barium manganate (1.06 g, 10 equiv.) with methylene chloride (4 ml) for 24 h at room temperature. Filtration through a Celite pad and removal of solvent gave crystals of cinnamolide (1) (92 mg, 94%), m.p. 83—84 °C (hexane) (lit.,[6] 85—85.5 °C); $\nu_{max.}$ 2 940, 2 900, 2 860, 2 840, 1 760, 1 705, and 1 360 cm^{-1}; δ (250 MHz) 0.82 (3 H, s), 0.93 (3 H, s), 0.95 (3 H, s), 1.40 (1 H, dd, *J* 5.5, 12 Hz), 1.10—1.70 (6 H, m), 2.12 (1 H, dddd, *J* 3.5, 5, 12, 19 Hz), 2.42 (1 H, dddd, *J* 4, 4, 5.5, 19 Hz), 2.82 (1 H, ddddd, *J* 3.5, 4, 5, 9.5, 9.5 Hz), 4.38 (1 H, dd, *J* 9.5, 9.5 Hz), and 6.88 (1 H, ddd, *J* 3.5, 3.5, 4 Hz); *m/z* 234 (M^+) 219, 201, 191, 124, and 109 (Found: C, 76.95; H, 9.5. $C_{15}H_{22}O_2$ requires C, 76.88; H, 9.46%) and was identical to previously prepared material.[17]

Method 2. The diol (24) (200 mg, 0.84 mmol) was heated to

reflux in benzene (25 ml) containing the Fetizon reagent (3.6 g) for 90 min. The cooled reaction mixture was filtered and solvent removed under reduced pressure to give cinnamolide (1) (200 mg, 100%) identical with the above sample.

Preparation of 1,3,5,5a,6,7,8,9,9a,9b-*Decahydro*-6,6,9a-*trimethyl*-5aα,9aβ,9b-1H-*naphtho*[1,2-c]*furan*-3-*ol* (25).—The diol (24) (100 mg, 0.42 mmol) was stirred with barium manganate (160 mg, 1.5 equiv.) in methylene chloride (4 ml) for 4 h. Filtration of the mixture through a Celite pad and removal of the solvent gave the lactol (25) (91 mg, 92%), m.p. 95—98 °C (lit.,[17] 95—97 °C); $\nu_{max.}$ 3 580, 3 390, 2 390, 2 860, 2 713, 1 670, and 1 630 cm^{-1}; δ (250 MHz) 0.72 (3 H, s), 0.91 (3 H, s), 0.93 (3 H, s), 1.0—1.7 (7 H, m), 1.9—2.5 (3 H, m), 3.46 (1 H, ddd, *J* 2.5, 7, 11.5 Hz), 3.79 (1 H, ddd, *J* 11.5, 11.5, 12 Hz), 4.70 (1 H, dd, OH, *J* 2.5, 12 Hz), 7.04 (1 H, ddd, *J* 2, 3, 5 Hz), and 9.38 (1 H, s); *m/z* 236.1770 (M^+. $C_{15}H_{24}O_2$ requires *M*, 236.1776), 221, 218, 206, 133, 124, and 109.

Preparation of 1,4,4a,5,6,7,8,8a-*Octahydro*-5,5,8a-*trimethyl*-1β,4aα,8a-*naphthalene*-1,2-*dicarbaldehyde* (*Polygodial*) (2).—A solution of the diol (24) (0.4 g, 1.7 mmol) in methylene chloride (5 ml) was added dropwise to the Swern reagent [6.8 mmol, 4 equiv., prepared by adding a solution of DMSO (1 g) in methylene chloride (2 ml) to a solution of oxalyl chloride (862 mg, 6.8 mmol) in methylene chloride (15 ml) at −50 °C] under argon at −50 °C, and stirred for 1 h at −50 °C. Addition of triethylamine (1.03 ml, 6 equiv.) and work-up by dilution with water and extraction, gave a crystalline product (0.4 g) which was recrystallised from hexane to give polygodial (2) (373 mg, 95%), m.p. 91—92.5 °C (lit.,[6] 93—94 °C); $\nu_{max.}$ 2 915, 2 870, 2 850, 2 710, 1 720, 1 680, and 1 645 cm^{-1}; δ (250 MHz) 0.93 (3 H, s), 0.96 (3 H, s), 0.97 (3 H, s), 1.27 (1 H, dd, *J* 5, 11.5 Hz), 1.15—1.65 (5 H, m), 1.85 (1 H, dm, *J* 12 Hz), 2.32 (1 H, dddd, *J* 3, 4, 11.5, 20 Hz), 2.52 (1 H, dddd, *J* 2, 5, 6, 20 Hz), 2.83 (1 H, dddd, *J* 2, 2.5, 4, 5 Hz), 7.14 (1 H, ddd, *J* 2.5, 3, 6 Hz), 9.47 (1 H, s), and 9.54 (1 H, d, *J* 5 Hz); *m/z* 234 (M^+), 219, 218, 217, 216, 206, 191, 121, and 109 (Found: C, 76.75; H, 9.55. $C_{15}H_{22}O_2$ requires C, 76.88; H, 9.46%) identical with previously prepared samples (23).[6] Omission of triethylamine before work-up using equivalent reaction conditions gave compound (26) (365 mg, 93%) as an oil, after chromatography (silica H, hexane); $\nu_{max.}$ 2 980—2 840, 1 660, 1 460, 1 460, 1 380, 1 365, 1 260, and 1 120 cm^{-1}; δ (250 MHz) 0.88 (3 H, s), 0.89 (3 H, s), 0.90 (3 H, s), 1.1—1.7 (7 H, m), 1.85—2.20 (3 H, m), 3.83 (1 H, dd, *J* 5, 11.5 Hz), 3.96 (1 H, dd, *J* 3, 11.5 Hz), 4.13 (1 H, d, *J* 10.5 Hz), 4.45 (1 H, ddd, *J* 1, 2, 10.5 Hz), and 5.98 (1 H, m); *m/z* 220.1825 (M^+. $C_{15}H_{24}O$ requires *M*, 220.1827), 205, 202, 190, 189, 187, 175, 124, and 109.

Preparation of 1,3,5,5a,6,7,8,9a,9b-*Decahydro*-6,6,9a-*trimethyl*-5aα,9aβ,9b-3H-*naphtho*[1,2-c]*furan*-1α-*ol* (3) (*Isodrimeninol*).—To a solution of (24) (69 mg, 0.29 mmol) dissolved in dry methylene chloride (2 ml) under an argon atmosphere, were added tetraphenylphosphonium ruthenium trichloride (101 mg, 0.3 mmol). T.l.c. indicated the reaction to be complete after 5 min. The brown solution was triturated by the addition of light petroleum (10 ml) and filtered through a pad of Celite. Removal of the solvent under reduced pressure gave an oil which was chromatographed on silica gel H to give (*a*) polygodial (2) (12.5 mg, 10%) identical with the previously prepared sample (by t.l.c. and ^1H n.m.r. 250 MHz) and (*b*) isodrimeninol (3) (22 mg, 35%); $\nu_{max.}$ 3 400, 1 390, 1 370, and 820 cm^{-1}; δ (250 MHz) 5.52 (1 H, m), 5.29br (1 H, d *J* 4 Hz), 4.49 (1 H, d, *J* 10.5 Hz), 4.18 (1 H, d, *J* 10.5 Hz), 2.86br (1 H, s, D_2O exch.), 1.15—2.2 (10 H, m), 0.93 (3 H, s), 0.89 (3 H, s), and 0.82 (3 H, s).

Preparation of 5,5a,6,7,8,9,9a,9b-*Octahydro*-6,6,9a-*trimethyl*-5aα,9aβ,9bβ-*naphtho*[1,2-c]*furan*-1(3H)-*one* (*Drimenin*) (4).—To a solution of the diol (24) (0.22 g, 0.92 mmol) in DMF (25 ml) at 0 °C under argon was added t-butyldimethylsilyl chloride (166 mg, 1.1 equiv.) and imidazole (125 mg, 2 equiv.) and the resulting mixture stirred for 24 h at room temperature. Dilution with water (100 ml) and work-up gave an oil (0.35 g) which was chromatographed (silica H 10 g, ether–hexane) to provide (27) (0.327 g, 100%) as an oil; $\nu_{max.}$ 3 350, 2 900, 1 660, 1 465, 1 255, and 1 045 cm^{-1}; δ (60 MHz) 0.1 (6 H, s), 0.89 (18 H, s), 0.9—2.4 (10 H, m), 3.7 (2 H, m), 4.15 (2 H, m), and 5.75 (1 H, m); *m/z* 352 (M^+), 321, 313, 277, 203, 191, 189, and 147.

Compound (27) (0.32 g, 0.9 mmol) in methylene chloride (5 ml) was added to the Swern reagent (2 equiv.) in methylene chloride (10 ml) at −50 °C under argon. After 30 min, triethylamine (0.37 ml, 3 equiv.) was added and the mixture worked up by dilution with water and extraction to provide the aldehyde (28) (0.285 g, 90%); $\nu_{max.}$ 3 920, 2 860, 1 720, 1 670, and 1 255 cm^{-1}; δ (60 MHz) 0.1 (6 H, s), 0.95 (15 H, s), 1.1 (3 H, s), 1.1—2.0 (7 H, m), 2.1 (1 H, m), 2.8 (1 H, m), 4.1 (2 H, m), 5.9 (1 H, m), and 9.7 (1 H, d, *J* 5 Hz).

To the above aldehyde (28) (0.28 g, 0.8 mmol) in THF (5 ml) at 0 °C under argon was added tetra-n-butylammonium fluoride (1.6 ml, 2 equiv.; 1M in THF), and stirred for 2 h at room temperature. Work-up provided an oil which was filtered through silica to provide the intermediate lactols (0.15 g, 80%); $\nu_{max.}$ 3 620, 3 450, 2 930, 2 870, 1 700, 1 460, and 1 260 cm^{-1}; δ (60 MHz) 0.85 (6 H, s), 0.9 (3 H, s), 1.05—2.2 (9 H, m), 4.05 (1 H, m), 4.4 (1 H, m), 5.15 (1 H, m), and 5.45 (1 H, m).

To a solution of these lactols (0.15 g, 0.64 mmol) in methylene chloride (10 ml) was added pyridinium chlorochromate (0.2 g, 1.5 equiv.) and the mixture stirred for 20 min at room temperature. Dilution with ether (100 ml) and filtration through a Celite pad gave a dark oil which was chromatographed [silica H (20 g), ether–hexane (1 : 9)] to provide drimenin (4) (75 mg, 50%) as colourless needles, m.p. 96—98 °C (lit.,[6] 95—96 °C) (hexane); $\nu_{max.}$ 2 920, 2 840, 1 780, 1 465, 1 455, and 1 130 cm^{-1}; δ (250 MHz) 0.88 (3 H, s), 0.90 (3 H, s), 0.92 (3 H, s), 1.36 (1 H, dd, *J* 5.5, 11.5 Hz), 1.1—1.7 (5 H, m), 1.98 (1 H, ddddm, *J* 3, 4.5, 11.5, 18 Hz), 2.20 (1 H, ddddm, *J* 3.5, 3.5, 5.5, 18 Hz), 2.49 (1 H, ddd, *J* 3, 6, 13 Hz), 2.78 (1 H, dddm, *J* 3, 3.5, 3.5 Hz), 4.68 (2 H, m), and 5.73 (1 H, dddm, *J* 3.5, 3.5, 4.5 Hz); *m/z* 234 (M^+) 219, 201, and 124 (Found: C, 76.9; H, 9.5. $C_{15}H_{22}O_2$ requires C, 76.88; H, 9.46%) and was identical with previously prepared material.[25]

Preparation of 3,5,6a,6,7,8,9,9a-*Octahydro*-6,6,9a-*trimethyl*-3-*trimethylsiloxy*-5aα,9aβ-*naphtho*[1,2-c]*furan* (29).—A solution of polygodial (2) (42 mg, 0.18 mmol) in THF (1.3 ml) was added dropwise to a solution of lithium diazopropylamide (LDA) (0.23 mmol, 1.3 equiv.) in THF (0.25 ml) at −78 °C under argon. After a further 5 min, trimethylsilyl chloride (0.11 ml, 5 equiv.) in triethylamine (1 : 1), after centrifugation of the hydroxide, was added and the mixture warmed to 0 °C; the solvent and excess reagents were then removed under reduced pressure to give a white gum (55 mg, 100%); $\nu_{max.}$ 2 980—2 840, 2 740, 2 600, 2 500, 1 480, 1 440, and 1 390 cm^{-1}; δ (60 MHz) 0.25 (9 H, s), 0.8—1.2 (9 H, 6 s), 1.0—2.5 (9 H, m), 5.20 (1 H, m), and 5.50 (2H, m); *m/z* 307.2094 (M + 1. $C_{18}H_{31}O_2Si$ requires 307.2093), 288, 278, 260, 218, 203, and 109.

Microbiological Oxidation Reactions: Preparation of Culture Medium.—Cultures of *C. elegans* (on Czapek Dox agar) were plated out on petri dishes, at 25 °C for 5—6 days before needed, to ensure healthy growth. The flasks containing the medium were then inoculated with approximately 1 cm^2 of

mycelial growth. The fungus was grown on a medium of glucose (5 g), sucrose (2 g), beef extract (1 g), malt extract (1 g), yeast extract (1 g), distilled water (to 1 l) and the pH adjusted to 5.5 with dilute hydrochloric acid. The flasks each containing 100 ml liquid culture medium were autoclaved at 120 °C for 15 min, before use. The cultures were then incubated for 3 days at 24 °C, using a rotary shaker (200 rev. min^{-1}) until a healthy growth had occurred.

Preparation of 1,3,5,5a,6,7,8,9,9a-*Decahydro*-6,6,9a-*trimethyl*-3β-*hydroxy*-5aα,9aβ,9bβ-*naphtho*[1,2-c]*furan*-1α-*ol* (30).—A solution of polygodial (2) (10 mg, 0.042 mmol) in hot ethanol (0.5 ml) was added to the culture medium (100 ml) containing a healthy growth of *C. elegans* as above, and incubated for 10 days at 24 °C. The fermentation broth was then saturated with sodium chloride and the mycelia filtered off. Thorough extraction with ethyl acetate (4 × 50 ml), followed by drying and removal of the solvent gave the crude product, which was purified by p.l.c. (ethyl acetate, 2 elutions) to provide compound (30) (9 mg, 90%), m.p. 126—128 °C; $\nu_{max.}$ 3 390, 2 970—2 840, 1 725, 1 670, 1 440, 1 365, 1 080, and 970 cm^{-1}; δ (250 MHz) 0.81 (3 H, s), 0.90 (3 H, s), 1.01 (3 H, s), 1.1—2.4 (8 H, m), 3.29 (1 H, dd, *J* 5.5, 10 Hz), 4.20 (1 H, dm, *J* 11 Hz), 4.50 (1 H, dm, *J* 11 Hz), 5.28 (1 H, d, *J* 4.5 Hz), and 5.54 (1 H, m); *m/z* 252.1719 (M^+. $C_{15}H_{24}O_3$ requires *M*, 252.1725), 234, 219, 217, 188, 173, 169, and 119.

Preparation of 1,4,4a,5,6,7,8,8a-*Octahydro*-5,5,8a-*trimethyl*-3β-*hydroxy*-1β,4aα,8aα-*naphthalene*-1,2-*dimethanol* (31).—The diol (24) [11] (10 mg, 0.042 mmol) in hot ethanol (0.5 ml) was added *via* a sterile syringe to culture medium (100 ml) as above. After 9 days, t.l.c. indicated complete conversion. Work-up as previously described gave compound (31) after p.l.c. (ethyl acetate, 2 elutions) (8 mg, 75%), m.p. 170—173 °C; $\nu_{max.}$ 3 300, 3 980—2 840, 1 650, 1 450, 1 380, and 1 090 cm^{-1}; δ (250 MHz), 0.78 (3 H, s), 0.87 (3 H, s), 1.00 (3 H, s), 1.2—2.2 (8 H, m), 2.83br (3 H, OH), 3.28 (1 H, dd, *J* 4.5, 11 Hz), 3.71 (1 H, dd, *J* 7.5, 10.5 Hz), 3.92 (1 H, dd, *J* 2, 10.5 Hz), 4.01 (1 H, d, *J* 12 Hz), 4.37 (1 H, d, *J* 12 Hz), and 5.82 (1 H, m); *m/z* 254.1875 (M^+. $C_{15}H_{26}O_3$ requires *M*, 254.1882), 236, 234, 223, 218, 188, 173, and 107. This reaction on a 2 g scale gave the product (31) in 62% yield.

Preparation of 3-β-*Hydroxycinnamolide* (32).—Cinnamolide (1) (50 mg) in hot ethanol (1 ml) was added to a culture medium (100 ml) of *A. niger*. After 4 days at 26.27 °C, the mixture was worked up as before to give compound (32) (23 mg, 46%); δ (250 MHz) 0.81 (3 H, s), 0.92 (3 H, s), 1.04 (3 H, s), 1.1—1.75 (4 H, m), 1.37 (1 H, dd, *J* 6, 12 Hz), 1.79br (1 H, s, D_2O exch.), 2.44 (1 H, dddd, *J* 4, 5, 6, 20 Hz), 2.21 (1 H, dddd, *J* 4, 5, 12, 20 Hz), 2.79 (1 H, ddddd *J*, 4, 4, 5, 9, 9 Hz), 3.31 (1 H, dd, *J* 5, 10 Hz), 4.05 (1 H, dd, *J* 9, 9 Hz), 4.39 (1 H, dd, *J* 9, 9 Hz), and 6.9 (1 H, ddd, *J* 4, 4, 5 Hz); *m/z* 251, 232, 217, and 189 (Found: C, 71.8; H, 8.85. $C_{15}H_{22}O_3$ requires C, 71.97; H, 8.86%).

Preparation of Dimethyl 1,4,4a,5,6,7,8,8a-*Octahydro*-1α-*hydroxy*-5,5,8a-*trimethyl*-4aα,8aβ-*naphthalene*-1,2-*dicarboxylate* (33).—A solution of the diester (19) (3 g, 10.2 mmol) in THF (50 ml) was added dropwise to a solution of LDA [1.1 equiv.; from di-isopropylamine (1.53 ml) and n-butyllithium (7.2 ml; 1.55M in hexane)] in THF (10 ml) at −78 °C under argon. To the resulting deep red enolate solution was added MoOPH [27] (5.75 g, 1.3 equiv.) and the mixture allowed to reach room temperature during 2—3 h. The resulting green solution was quenched with aqueous sodium thiosulphate (10%, 20 ml) and the mixture transferred to ether (100 ml). After separation of the organic layer and drying ($MgSO_4$) removal of solvent gave a crystalline product which was triturated with a little cold (< −60 °C) methanol and filtered to provide the hydroxy-diester (33) as a white solid (2.4 g, 80%). A further 0.6 g of (33) could be obtained after chromatography of the mother liquors (combined yield 95%), m.p. 138—140 °C (hexane); $\nu_{max.}$ 3 440, 2 920, 1 730, 1 435, 1 255, and 1 080 cm^{-1}; δ (250 MHz) 0.93 (3 H, s), 0.97 (3 H, s), 0.98 (3 H, s), 1.87 (1 H, dd, *J* 5, 12 Hz), 1.1—1.9 (6 H, m), 2.13 (1 H, ddd, *J* 2.5, 12, 19.5 Hz), 2.31 (1 H, ddd, *J* 5, 5.5, 19.5 Hz), 3.72 (3 H, s), 3.73 (3 H, s), 3.88 (1 H, s, OH), and 7.23 (1 H, dd, *J* 2.5, 5.5 Hz); *m/z* 310 (M^+), 278, 251, 219, 233, 186, 163, 124, and 109 (Found: C, 65.7; H, 8.65. $C_{17}H_{26}O_5$ requires C, 65.78; H, 8.44%).

Preparation of 3,4,4a,5,6,7,8,8a-*Octahydro*-5,5,8a-*trimethyl*-4aα,8aβ-*naphthalene*-1,2-*dimethanol* (34).—A solution of the hydroxy-diester (33) (0.266 g, 0.86 mmol) in ether (20 ml) was added dropwise to a suspension of LAH (0.2 g, 5 equiv.) in ether at 0 °C under argon. After a further 15 min the mixture was transferred to ice–5% sulphuric acid (100 ml) and ether (25 ml). The ethereal layer was washed with aqueous sodium hydrogencarbonate and worked up as usual to provide an oil (183 mg) which was chromatographed (silica H, 15 g, ether eluant) to provide (34) [25a] (96 mg, 47%), m.p. 123—124 °C (benzene); $\nu_{max.}$ 3 350, 1 460, 1 380, and 1 100 cm^{-1}; δ (250 MHz) 0.86 (3 H, s), 0.92 (3 H, s), 1.0 (3 H, s), 1.0—1.8 (9 H, m), 1.88 (1 H, dm, *J* 11.5 Hz), 2.34 (2 H, m), 4.04 (1 H, d, *J* 11.5 Hz), 4.17 (1 H, d, *J* 11.5 Hz), 4.13 (1 H, d, *J* 12 Hz), and 4.23 (1 H, d, *J* 12 Hz); *m/z* 238, 220, 205, 189, 139, 127, 124, and 109 (Found: C, 75.55; H, 11.05. $C_{15}H_{26}O_2$ requires C, 75.58; H, 10.99%); and compound (35) (37 mg, 20%) as an oil, $\nu_{max.}$ 2 980, 2 840, 1 660, 1 460, 1 440, and 1 260 cm^{-1}; δ (250 MHz) 0.92 (6 H, s), 0.98 (3 H, s), 1.1—1.85 (9 H, m), 1.9—2.25 (2 H, m), 4.17 (2 H, m), and 4.57 (2 H, m); *m/z* 220.1826 (M^+. $C_{15}H_{24}O$ requires *M*, 220.1827), 206, 205, 192, 177, 149, 123, and 109.

Preparation of Dimethyl 1,4,4a,5,6,7,8,8a-*Octahydro*-1α-*methylthiomethoxy*-5,5,8a-*trimethyl*-4aα,8aβ-*naphthalene*-1,2-*dicarboxylate* (36).—The hydroxy-diester (33) (1 g, 3.2 mmol) was stirred with DMSO (15 ml) and acetic anhydride (15 ml) for 120 h at room temperature. The solution was evaporated at 40 °C under reduced pressure and then high vacuum (2×10^{-3} Torr) to provide a crystalline product. Trituration with a little cold (< −50 °C) methanol and filtering afforded the protected tertiary alcohol (36) (1.0 g, 84%). A further 0.15 g of (36) was obtained by chromatography [silica H (15 g), ether] of the mother liquors (total yield 97%), m.p. 126—127 °C (hexane), $\nu_{max.}$ 2 950, 2 870, 1 760, 1 730, 1 655, 1 435, 1 250, and 1 070 cm^{-1}; δ (60 MHz) 0.95 (9 H, s), 1.0—2.4 (9 H, m), 2.20 (3 H, s), 3.69 (3 H, s), 3.74 (3 H, s), 4.5 (1 H, d, *J* 10.5 Hz), 4.85 (1 H, d, *J* 10.5 Hz), and 7.30; *m/z* 311, 295, 262, and 223 (Found: C 61.9; H, 7.95; S, 8.34. $C_{19}H_{30}O_5S$ requires C, 61.80; H, 8.16; S, 8.65%).

Preparation of 1,4,4a,5,6,7,8,8a-*Octahydro*-5,5,8a-*trimethyl*-1,2-*diacetoxymethylnaphthalen*-1α-*ol* (38).—The diol (24) (2.81 g, 11.8 mmol) was dissolved in pyridine (30 ml) and cooled to 0 °C. Acetic anhydride (3 ml) was added and the mixture allowed to warm to room temperature for 30 min. Excess of reagents were removed under reduced pressure and to the residue was added water (50 ml); the mixture was then extracted with ether (2 × 50 ml). The organic layers were separated, dried, and evaporated to afford the diacetate (37) (3.8 g, 100%); $\nu_{max.}$ 2 920, 1 740, 1 460, 1 385, 1 365, and 1 240 cm^{-1}; δ (60 MHz), 5.85 (1 H, m), 4.5br (2 H, s), 3.9—4.2 (2 H, m), 2.08 (3 H, s), 2.04 (3 H, s), 1.1—2,2 (10 H, m), 0,95 (6 H, s), and 0.85 (3 H, s).

The diacetate (37) (3.8 g, 11.8 mmol) was refluxed with selenium dioxide (1.63 g, 1.25 equiv.) in dioxan (100 ml) for 1 h. The reaction mixture was cooled, diluted with water (200 ml), and worked up as usual to provide the crude product. Chromatography [silica H (140 g), ether–hexane] gave compound (38) (2.60 g, 65%) as an oil; $\nu_{max.}$ 3 500, 2 970, 2 860, 1 740, 1 670, 1 460, 1 365, 1 240, and 1 080 cm^{-1}; δ (250 MHz) 0.92 (6 H, s), 0.95 (3 H, s), 1.82 (1 H, dd, *J* 5, 12 Hz), 1.0—1.7 (6 H, m), 2.06 (3 H, s), 2.07 (3 H, s), 1.97 (1 H, m), 2.16 (1 H, m), 4.21 (1 H, d, *J* 11.5 Hz), 4.29 (1 H, d, *J* 11.5 Hz), 4.60 (2 H, m), and 6.06 (1 H, m); *m/z* 338 (M^+) 322, 278, 265, 218, 214, and 154.

Preparation of 1,4,4a,5,6,**7**,8,8a-*Octahydro*-5,5,8a-*trimethyl*-1α-*hydroxy*-4aα,8aβ-*naphthalene*-1,2-*dimethanol* (39).—The hydroxy diacetate (38) prepared as described above (2 g, 5.9 mmol) was stirred with anhydrous potassium carbonate (5 g) in methanol (100 ml) at room temperature for 30 min. Filtration and evaporation of the solvent provided the triol (39) (1.49 g, 99%), m.p. 140—141 °C (ether); $\nu_{max.}$ 3 620, 3 500, 3 420, 1 664, 1 460, 1 440, 1 250, 1 040, and 990 cm^{-1}; δ (250 MHz) 0.82 (3 H, s), 0.91 (3 H, s), 0.93 (3 H, s), 1.73 (1 H, dd, *J* 5, 12 Hz), 1.1—1.9 (6 H, m), 1.91 (1 H, ddd *J* 2, 12, 18 Hz), 2.13 (1 H, ddd, *J* 5, 6, 18 Hz), 2.88 (1 H, s, OH), 2.99 (1 H, dd, *J* 6.5, 6.5 Hz, OH), 3.27 (1 H, dd, *J* 6.5, 6.5 Hz, OH), 3.72 (1 H, dd, *J* 6.5, −1.5 Hz), 3.77 (1 H, dd, *J* 6.5, 11.5 Hz), 4.11 (1 H, dd, *J* 6.5, 12 Hz), 4.31 (1 H, dd, *J* 6.5, 12 Hz), and 5.91 (1 H, dd, *J* 2, 5 Hz); *m/z* 254 (M^+) 237, 225, 218, and 205 (Found: C, 70.6; H, 10.35. $C_{15}H_{26}O_3$ requires C, 70.83; H, 10.30%).

Preparation of 1,4,4a,5,6,7,8,8a-*Octahydro*-5,5,8a-*trimethyl*-5aα,9aβ-1α-*hydroxynaphthalene*-1,2-*dicarbaldehyde* (*Warburganal*) (5).—A solution of the triol (39) (90 mg, 0.36 mmol) in DMSO–methylene chloride (1 : 1; 4 ml) was added to the Swern reagent (2.16 mmol, 6 equiv., prepared by the addition of trifluoroacetic anhydride (520 mg, 0.35 ml) in methylene chloride (4 ml) to DMSO (1.0 g) in methylene chloride (20 ml) at −50 °C under argon) dropwise under argon at −50 °C. After 30 min at −50 °C, triethylamine (0.43 ml, 9 equiv.) was added, and the reaction worked up as usual. Chromatography of the product mixture [silica H (3.0 g), ether–hexane] gave warburganal (5) (40 mg, 45%). Treatment with charcoal in ethanol and recrystallisation (hexane) gave m.p. 96—98 °C (lit.,[6] 98—99 °C); $\nu_{max.}$ 3 440, 3 420, 3 000—3 840, 1 715, 1 680, 1 645, 1 460, 1 120, and 1 040 cm^{-1}; δ (250 MHz) 0.94 (3 H, s), 0.99 (3 H, s), 1.09 (3 H, s), 1.15—1.75 (6 H, m), 1.89 (1 H, dd, *J* 5, 12 Hz), 2.34 (1 H, ddd, *J* 2.5, 12, 21 Hz), 2.58 (1 H, ddd, *J* 5, 6, 21 Hz), 4.09 (1 H, d, *J* 1 Hz, OH), 7.27 (1 H, dd, *J* 2.5, 6 Hz), 9.42 (1 H, s), and 9.74 (1 H, d, *J* 1 Hz); *m/z* 250 (M^+), 232, 221, 189, 161, 124, 109, and 105. These data were identical to an authentic sample.

Preparation of 5,5a,6,7,8,9a,9b-*Octahydro*-6,6,9a-*trimethyl*-1α-*hydroxy*-5aα,9aβ-*naphtho*[1,2-c]*furan*-3(1H)-*one* (40).—The triol (39) (50 mg, 0.2 mmol) was heated together with the Fetizon reagent (5 equiv.) in benzene (10 ml) for 20 min. Cooling and filtration through a Celite pad followed by evaporation of the solvent gave the compound (40) (48 mg, 98%) as white needles, m.p. 175—178 °C (ethyl acetate); $\nu_{max.}$ 3 440, 2 980, 2 840, 1 745, 1 720, 1 680, 1 460, 1 415, 1 230, and 1 100; δ (250 MHz) 0.91 (3 H, s), 0.97 (3 H, s), 0.99 (3 H, s), 1.86 (1 H, dd, *J* 5.5, 12 Hz), 1.20—2.05 (6 H, m), 2.15 (1 H, ddd, *J* 3.5, 12, 20.5 Hz), 2.45 (1 H, ddd, *J* 5, 5.5, 20.5 Hz), 2.17 (1 H, d, *J* 1 Hz, OH), 4.23 (1 H, d, *J* 10 Hz), 4.37 (1 H, dd, *J* 1, 10 Hz), and 7.04 (1 H, dd, *J* 3.5, 5.0 Hz); *m/z* 250.1571 (M^+), 233, 232, 217, and 114 (Found: C, 71.55; H, 8.85. $C_{15}H_{22}O_3$ requires C, 71.97; H, 8.86%).

Acknowledgements

We thank the S.E.R.C. for a research studentship (to M. M.), I.C.I. Plant Protection, Jealott's Hill, Bracknell (CASE award to S. C. H.), Johnson Matthey, Sonning Common, Reading (CASE award to D. M. H.), The Royal Society for an equipment grant, and the Royal Society of Chemistry for the Hickinbottom Research Fellowship (to S. V. L.).

References

1 G. Brieger, *Tetrahedron Lett.*, 1965, 4429.
2 J. A. Campos and F. G. Jimenez, *Rev. Soc. Quim. Mex.*, 1975, **19**, 93.
3 J. C. Loperfido, *J. Org. Chem.*, 1973, **38**, 399.
4 S. C. Howell, S. V. Ley, M. Mahon, and P. A. Worthington, *J. Chem. Soc., Chem. Commun.*, 1981, 507.
5 S. V. Ley and M. Mahon, *Tetrahedron Lett.*, 1981, **22**, 3909.
6 S. P. Tanis and K. Nakanishi, *J. Am. Chem. Soc.*, 1979, **101**, 4398.
7 L. P. J. Burton and J. D. White, *J. Am. Chem. Soc.*, 1981, **103**, 3226.
8 M. Jallali-Naini, G. Boussac, P. Lemaitre, M. Larcheveque, D. Guillerm, and J-Y. Lallemand, *Tetrahedron Lett.*, 1981, **22**, 2995.
9 D. J. Peterson, *J. Org. Chem.*, 1968, **33**, 780.
10 J. J. Eisch and M. W. Foxton, *J. Org. Chem.*, 1971, **36**, 3520.
11 R. B. Miller and G. McGarvey, *J. Org. Chem.*, 1978, **43**, 4424.
12 R. C. Cookson, M. C. Cramp, and P. J. Parsons, *J. Chem. Soc., Chem. Commun.*, 1980, 197.
13 For the use of lithium methoxyacetylide see I. Heilbron, E. R. H. Jones, M. Julia, and B. C. L. Weedon, *J. Chem. Soc.*, 1949, 1823.
14 W. G. Dauben and H. O. Krabbenhoft, *J. Am. Chem. Soc.*, 1976, 1992.
15 P. N. Rylander, *Aldrichimica Acta*, 1979, **12**, 53.
16 M. Fetizon and M. Golfier, *C.R. Acad. Sci. Ser. C*, 1968, **267**, 900.
17 (*a*) L. Canonica, A. Corbella, P. Gariboldi, G. Jommi, J. Křepinský, G. Ferrari, and C. Casagrande, *Tetrahedron*, 1969, **25**, 3895; (*b*) Y. Askawa, M. Toyota, and T. Takemoto, *Phytochem.*, 1978, **17**, 457; (*c*) H. Yanagawa, T. Kato, and Y. Kitahara, *Synthesis*, 1970, 257; (*d*) T. Suzuki, M. Tanemura, T. Kato, and Y. Kitahara, *Bull. Chem. Soc. Jpn.*, 1970, **43**, 1268.
18 H. Firouzabadi and E. Ghaderi, *Tetrahedron Lett.*, 1978, 839.
19 C. S. Barnes and J. W. Loder, *Aust. J. Chem.*, 1962, **15**, 322.
20 I. Kubo, Y-W. Lee, M. Pettei, F. Pilkiewicz, and K. Nakanishi, *J. Chem. Soc., Chem. Commun.*, 1976, 1013.
21 A. J. Mancuso and D. Swern, *Synthesis*, 1981, 165.
22 K. Omura and D. Swern, *Tetrahedron*, 1978, **34**, 1651.
23 T. Kato, T. Suzuki, M. Tanemura, A. S. Kumanireng, N. Otofani, and Y. Kitahara, *Tetrahedron Lett.*, 1971, 1961.
24 (*a*) Y. Asakawa and T. Takemoto, *Experientia*, 1979, **35**, 1420; (*b*) Y. Asakawa, S. Huneck, M. Toyota, T. Takemoto, and C. Swire, *J. Hattori Bot. Lab.*, 1979, **46**, 163.
25 (*a*) H. H. Appel, J. D. Connolly, K. H. Overton, and R. P. M. Bond, *J. Chem. Soc.*, 1960, 4685; (*b*) E. Wenkert and D. P. Strike, *J. Am. Chem. Soc.*, 1964, **86**, 2044; (*c*) Y. Kitahara, T. Kato, T. Suzuki, S. Kanno, and M. Tanemura, *Chem. Commun.*, 1969, 342.
26 For other warburganal syntheses see, (*a*) T. Nakata, H. Akita, T. Naito, and T. Oishi, *J. Am. Chem. Soc.*, 1979, **101**, 4401; (*b*) A. Ohsuka and A. Matsukawa, *Chem. Lett.*, 1979, 635; (*c*) A. Kimura and S. Isoe, 22nd ' Symposium on the Chemistry of Natural Products,' Fukuoka 1979, p. 198; (*d*) A. S. Kende, and T. J. Blacklock, *Tetrahedron Lett.*, 1980, 3119; (*e*) D. J. Goldsmith and H. S. Kezar III, *Tetrahedron Lett.*, 1980, 3543; (*f*) T. Nakata, H. Akita, T. Naito, and T. Oishi, *Chem. Pharm. Bull.*, 1980, **28**, 2172; (*g*) H. Okawara, H. Nakai, and M. Ohno, *Tetrahedron Lett.*, 1982, **23**, 1087; (*h*) P. A. Wender and S. L. Eck, *Tetrahedron Lett.*, 1982, **23**, 1871.
27 E. Vedejs, D. A. Engler, and J. E. Telschow, *J. Org. Chem.*, 1978, **43**, 188.
28 (*a*) L. L. Smith, in ' Terpenes and Steroids,' (*Specialist Periodical Reports*), Royal Society of Chemistry, London, 1974, vol. 4,

p. 394; (*b*) K. Kieslich, 'Microbial Transformations of Non-Steroid Cyclic Compounds,' Georg Thieme, Stuttgart, 1976; (*c*) R. A. Johnson, 'Oxygenations with Microorganisms,' in 'Oxidation in Organic Chemistry,' Academic Press, New York, 1978, vol. C, p. 131
29 T. A. Crabb, P. J. Dawson, and R. O. Williams, *J. Chem. Soc., Perkin Trans. 1*, 1980, 2535.
30 H. L. Holland and B. J. Auret, *Can. J. Chem.*, 1975, **53**, 845.
31 M. De Bernardi, G. Mellerio, G. Vidari, P. Vita-Finzi, and G. Fronza, *J. Chem. Soc., Perkin Trans. 1*, 1980, 221.
32 K. Yamada, K. Kato, H. Nagase, and Y. Hirata, *Tetrahedron Lett.*, 1976, 65.
33 A. Guillemonat, *Ann. Chim.*, 1939, **11**, 143.

Received 22*nd November* 1982; *Paper* 2/1945