Sulphone-based Elimination Reactions in Synthesis. Part 1. Moenocinol

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The fluoride-induced elimination of a β-phenylsulphonylsilane and the reductive elimination of a β-oxy sulphone are key olefin-forming reactions in a synthesis of moenocinol [(2*Z*, 6*E*, 13*E*)-3,8,8,14,18-pentamethyl-11-methylenenonadeca-2,6,13,17-tetraen-1-ol].

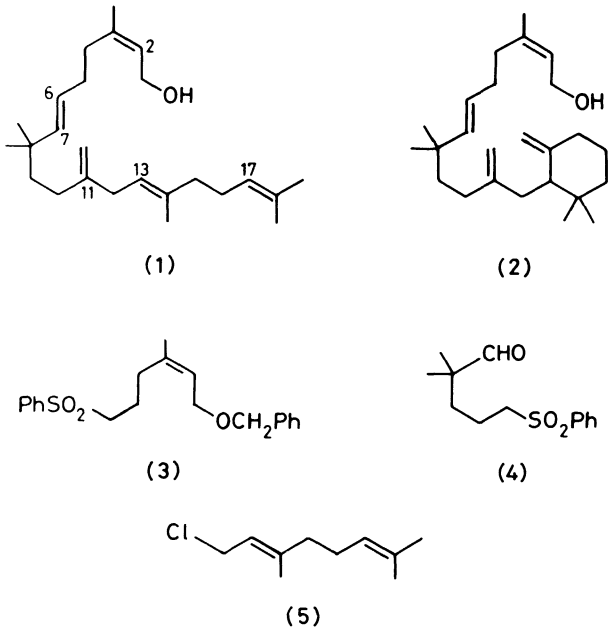
The moenomycins, prasinomycin, and the diumycins are members of a group of relatively non-toxic antibiotics which have long duration of action *in vivo* against Gram-positive bacteria. Interference in bacterial cell-wall biosynthesis is the mode of action.[1] The structures of these antibiotics have yet to be established in every detail; however, extensive degradative [2,3] and spectroscopic [4] studies have revealed some major fragments which include the C_{25} fragments moenocinol (1) and diumycinol (2). The structure of moenocinol has been proven by three total syntheses,[5–7] all of which have focused attention on the introduction of the hindered double bond at C(6)–C(7) and the methylene at C(11). We now give details of our approach [8] to (1) which uses sulphones to achieve similar objectives, and in the following paper we report the synthesis of diumycinol.

Our plan entailed the use of sulphone-stabilized carbanions to link the fragments (3), (4), and (5). By this highly convergent strategy, the entire skeleton of (1) except for the C(11) methylene was assembled. Since fragments (3) and (5) were prepared from commercial nerol and geraniol respectively, the stereochemistry of olefinic bonds at C(2) and C(13) was fixed.

Attempts to convert nerol benzyl ether (6) [6] into the sulphone (3) by a sequence of reactions beginning with the ozonolysis of (6) was abandoned owing to the poor selectivity for cleavage of the terminal three carbons—a problem which has been encountered by others.[7] By contrast, good selectivity was obtained in the epoxidation of (6) to give (7) in 82% yield (Scheme 2). Cleavage of the epoxide at the less substituted carbon was readily achieved with sodium thiophenoxide in refluxing EtOH. The resultant phenyl sulphide was then oxidised to the sulphone (8b) with *m*-chloroperbenzoic acid. Removal of the terminal three-carbon fragment occurred by a retro-aldol type reaction on warming (8b) with ethanolic KOH to give the desired fragment (3) in 60% overall yield from (7) without purification of intermediates.

The carbon skeleton of fragment (4) was assembled in one step by alkylation of 3-(phenylthio)-1-bromopropane (9) [9] with the lithio dianion of isobutyric acid to give the crystalline acid (10) in 85% yield (Scheme 2). Reduction of the carboxylic acid with lithium aluminium hydride followed by oxidation of the sulphide with H_2O_2 in acetic acid gave the sulphone (11) in 82% yield. Finally, oxidation of (11) with pyridinium chlorochromate gave the crystalline aldehyde (4) in 84% yield.

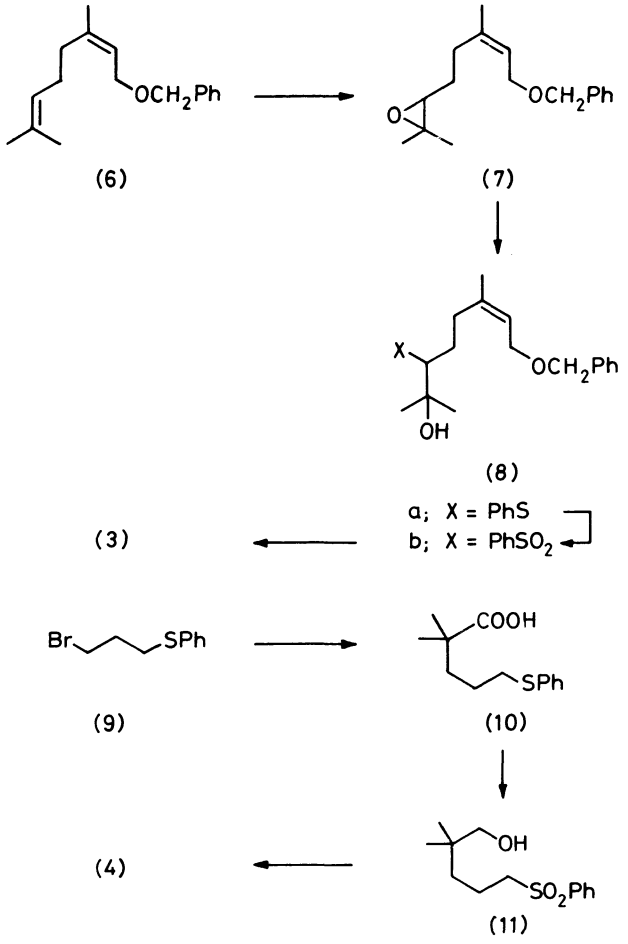
A key step in our synthetic plan, the union of fragments (3) and (4) with concomitant formation of a *trans*-double bond at C(6)–C(7), was accomplished by a procedure originally developed by Julia and Paris.[10] This involved reaction of the lithio derivative of (3) with the aldehyde (4) at −78 °C to give an adduct which was benzoylated (benzoyl chloride) to give a 1 : 1 diastereomeric mixture of the β-benzoyloxy sulphones (12) in 81% yield after chromatographic purification. Treatment of the mixture with sodium amalgam in methanol–tetrahydrofuran at −20 °C gave the desired olefin (13) in 54% yield. It was expected on the basis of earlier work that the stereochemistry of the olefin obtained in the reductive elimination would not depend on the stereochemistry of the β-benzoyloxy sulphone precursor [11] and that the presence of the *gem*-methyl groups at C(8) would enhance the *trans*-stereoselectivity of the reaction.[12] The product appeared to be a single isomer on t.l.c. and by ^{1}H n.m.r. analysis and ample precedent [12] would suggest that the double bond had *trans*-stereochemistry; proof however was obtained only at the end of the synthesis (*vide infra*). It is noteworthy that the isolated sulphone group in (13) was unchanged under the conditions of reductive elimination.



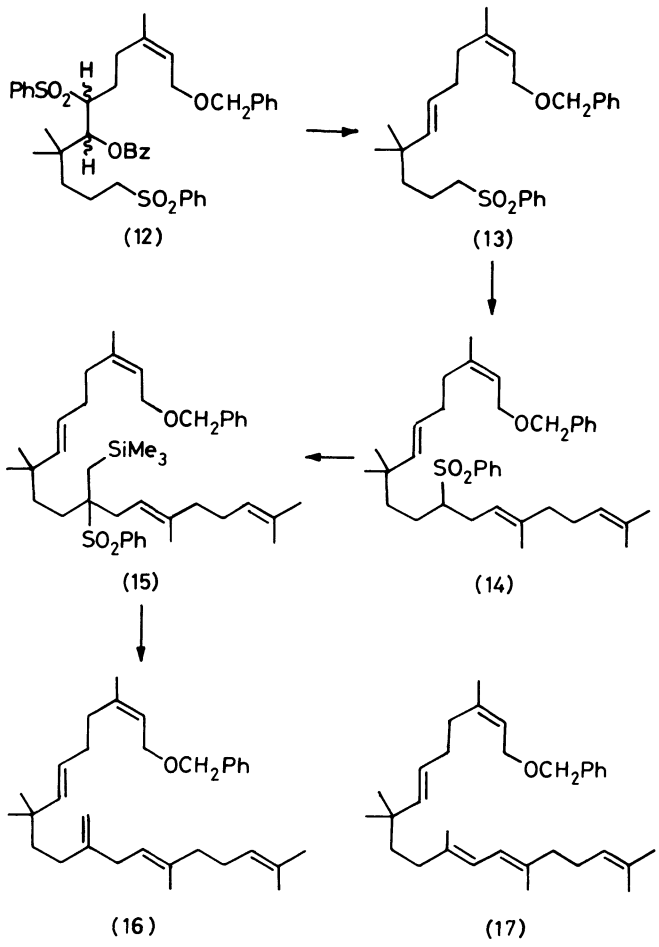
(1) (2) (3) (4) (5)

Scheme 1.

In order to complete the synthesis, fragment (5) and the methylene group at C(11) had to be incorporated. The synthesis of (14) was accomplished in 85% yield by reaction of (5) with the lithio derivative of sulphone (13). For the introduction of the C(11) methylene, however, a new reaction was developed [13] which used a fluoride-induced elimination of a fluorosilane and benzenesulphinate anion from a β-phenylsulphonylsilane to generate an olefin. Many related nucleophile-induced 1,2-eliminations of β-substituted silanes are known [14,15] but β-sulphonylsilanes had not been previously examined. The requisite β-phenylsulphonylsilane (15) was prepared by alkylation of the lithio derivative of the sulphone



Scheme 2.



Scheme 3.

(14) with Me_3SiCH_2I. Unfortunately, the alkylation could not be made to go to completion and attempts to recover unchanged (14) from (15) by chromatography failed owing to the chromatographic instability of (15). However, when the mixture of (14) and (15) was treated with $Bu^n_4NF{\cdot}3H_2O$ in refluxing tetrahydrofuran, (15) was cleanly converted into moenocinol benzyl ether (16) in 40% yield [92% based on recovered (14)]. Unchanged (14) was then recovered by chromatography and could be recycled.

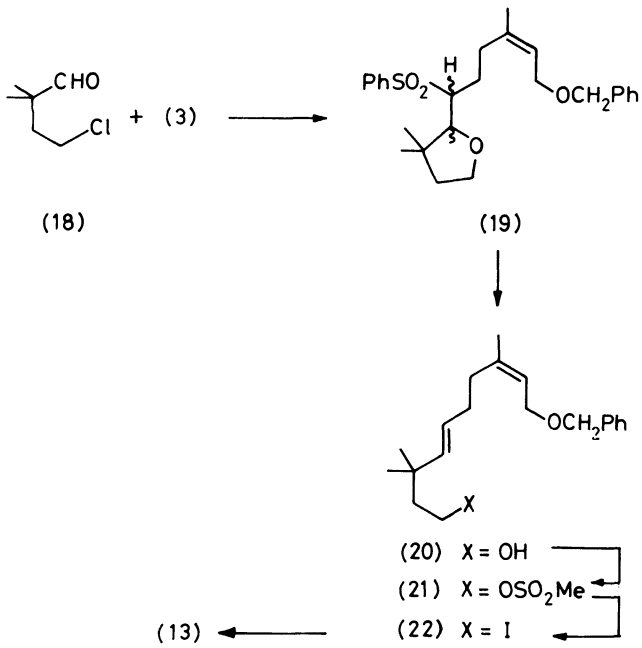
The chromatographic behaviour of a variety of β-sulphonylsilanes prepared in our laboratory gave no portent of the lability of (15) towards Kieselgel. Filtration of (15) through a plug of Kieselgel gave a variety of products among which were (16) and a conjugated diene tentatively assigned structure (17). Since control experiments showed that (16) was stable towards Kieselgel, it is likely that (17) was formed directly from the β-sulphonylsilane. The confluence of carbonium ion stabilizing features in (15) (the sulphone group occupies a position which is tertiary, homoallylic, and β to silicon) is probably responsible for the observed lability of (15).

Finally, brief treatment of the benzyl ether (16) with sodium in liquid ammonia gave moenocinol (1) which gave i.r. and ^1H and ^{13}C n.m.r. spectra which were identical with copies of the spectra of natural (1) derived from prasinomycin.* There was no evidence for the 6(*Z*) isomer of moenocinol which has characteristic signals in the ^1H n.m.r. spectrum.

An alternative synthesis of intermediate (13) was examined (Scheme 4) which was intended to address two aspects of the Julia olefin synthesis which hitherto have been neglected. First, conclusions previously drawn about the stereochemistry of the Julia reaction were based on the reductive elimination of β-acyloxy or β-methanesulphonyloxy sulphones; consequently little is known about the stereochemistry of the reaction as a function of the leaving group. Secondly, nothing is known about the effect that constraining the leaving group in a ring would have on stereochemistry.[16] Therefore, the tetrahydrofuran derivative (19) was prepared in 90% yield as a 1 : 1 mixture of diastereoisomers by reaction of the lithio derivative of (3) with the aldehyde (18).[5] The effect of the ether oxygen as a leaving group was apparent in the rate of reductive elimination which required 5 days at room temperature rather than 1—5 h at −20 °C which is typical of β-acyloxy or β-methanesulphonyloxy sulphones (*e.g.* 12). However, the stereochemistry of the product (20) was exclusively *trans*. The unstable iodide (22), prepared in *ca.* 98% overall yield from (20) *via* the methanesulphonate (21) using standard procedures, reacted with the lithio derivative of phenyl methyl sulphone to give (13) identical with the material prepared according to Scheme 3.

The sulphone group is conspicuous for its premier strategic role in our synthesis of moenocinol in which every C–C bond-forming reaction exploited the nucleophilic properties of sulphone-stabilised carbanions or the ability of a sulphone to

* We thank Dr. William Slusarchyk of the Squibb Institute for Medical Research for spectra of natural (1). The ^{13}C n.m.r. spectrum of natural moenocinol was recorded by Coates and Johnson.[7]



Scheme 4.

serve as a leaving group under specific and well-defined conditions. In particular, the virtues of the Julia reaction became apparent when compared with the unsuccessful attempts by Coates and Johnson [7] to use related reductive elimination methods for the introduction of the C(6)–C(7) double bond. The failure of the Wittig reaction and modifications thereto to give *trans*-stereoselectivity is noteworthy. Like the Julia reaction, the β-phenylsulphonyl silane route used to introduce the C(11) methylene was connective and effective under specific and mild conditions; however, extension of this method to more complex olefins is likely to be prevented by the inaccessibility of more complex α-halogenoalkylsilanes.

Experimental

Light petroleum refers to the fraction of b.p. 60—80 °C. T.l.c. was carried out using Kieselgel GF_{254} with 20% ethyl acetate in light petroleum as eluant. All compounds identified by accurate mass measurements were ascertained to be ≥95% pure by ^1H n.m.r. spectroscopy and t.l.c. Column chromatography was carried out using Kieselgel 60 with particle size 0.063—0.20 mm. Column dimensions refer to diameter and length of packed Kieselgel and unless otherwise stated the eluant was the same mixture used to pack the column. N.m.r. data refer to solutions in $CDCl_3$ at 90 MHz (^1H) or 22.6 MHz (^{13}C). Tetrahydrofuran (THF) was freshly distilled from sodium. Hexamethylphosphoric triamide (HMPA) was distilled from CaH_2. The drying agent used throughout was $MgSO_4$. Commercial *m*-chloroperbenzoic acid (MCPBA, *ca.* 85%) was used without further purification.

2,2-*Dimethyl*-3-[(Z)-5-*benzyloxy*-3-*methylpent*-3-*enyl*]*oxirane* (7).—To a stirred solution of nerol benzyl ether (6) (14.43 g, 59 mmol) in CH_2Cl_2 (150 cm³) cooled to 0 °C was added MCPBA (12.60 g, 63 mmol) portionwise during 30 min. After being stirred at 0 °C the mixture was diluted with ether (200 cm³) and washed successively with saturated aqueous $NaHCO_3$ and NaCl. The organic layer was dried and concentrated under reduced pressure to give an oil which was chromatographed on a 6.8 × 40 cm column of Kieselgel packed in 5% ethyl acetate in light petroleum to give recovered (6) (2.18 g). Elution with 20% ethyl acetate in light petroleum gave 10.70 g [70%, 82% based on recovered (6)] of the epoxide (7) [6] after short-path distillation; b.p. 130—132 °C/0.90 mmHg; $\nu_{max.}$ (film) 1 455, 1 375, 1 115, 1 050, 1 070, 735, and 695 (all s) cm⁻¹; δ 7.2—7.4 (4 H, m, ArH), 5.43 (1 H, t with further splitting, *J* 7 Hz, =CH–), 4.47 (2 H, s, PhCH_2O), 4.00 (2 H, d, *J* 7 Hz, =CH–CH_2–), 2.65 [1 H, t, *J* 6 Hz, –C(O)H–CH_2–], 1.75 (3 H, d, *J* 1 Hz, CH_3–C=C), 1.5—1.75 [2 H, m, –C(O)H–CH_2–], and 1.27 and 1.21 (3 H each, s).

(Z)-1-*Benzyloxy*-6-*phenylthio*-3,7-*dimethyloct*-2-*en*-7-*ol* (8a).—A solution of PhSNa in EtOH was prepared by adding sodium (0.63 g, 27.4 g-atom) to PhSH (2.42 g, 22 mmol) in absolute EtOH (25 cm³). The epoxide (7) (3.90 g, 15 mmol) in EtOH (5 cm³) was added in one portion and the mixture refluxed under N_2 for 3 h whereupon it was poured into 2M-NaOH (250 cm³) and the oily product extracted into Et_2O (150 cm³). The organic layer was washed with 2M-NaOH and saturated NH_4Cl and dried. Concentration under reduced pressure gave (8a) (5.56 g, *ca.* 100%) as a pale yellow oil which was used in the next step without further purification. Coloured impurities were removed from a small sample by filtration of an Et_2O solution through a plug of Kieselgel to give (8a) as a colourless oil, $\nu_{max.}$ (film) 3 450 cm⁻¹; δ 7.1—7.5 (5 H, m), 7.27 (5 H, s), 5.4br (1 H, t, *J* 7 Hz, =CH–CH_2), 4.41 (2 H, s, CH_2O), 3.90 (2 H, d with further splitting, *J* 7 Hz, =CH–CH_2), 3.00 (1 H, dd, *J* 11 and 3 Hz, PhS–CH), 1.5—2.1 (4 H, m), 1.75 (3 H, s with fine splitting, CH_3–C=), and 1.22 and 1.30 (3 H each, s) (Found: M^+, 370.194 42. Calc. for $C_{23}H_{30}O_2S$: *M*, 370.196 64).

(Z)-1-*Benzyloxy*-6-*phenylsulphonyl*-3-*methylhex*-2-*ene* (3).—To a stirred solution of the sulphide (8a) (5.55 g, 15 mmol) in CH_2Cl_2 (150 cm³) cooled to −30 °C was added portionwise MCPBA (6.0 g, 30 mmol) over 30 min. The mixture was allowed to warm slowly overnight. After being washed with saturated $NaHCO_3$ the organic layer was dried and evaporated to give crude (8b) which was dissolved in MeOH (75 cm³) to which was added KOH pellets (0.84 g, 15 mmol). After being refluxed for 1 h the mixture was poured into water (300 cm³) and the product extracted into ether (2 × 100 cm³). The combined organic layers were washed with water, dried, and evaporated to give an oil (5.54 g) which was chromatographed on a 4.5 × 10 cm column of Kieselgel packed in 20% ethyl acetate in light petroleum to give (3) as a viscous oil (3.10 g, 60%), $\nu_{max.}$ (film) 1 320, 1 305, and 1 150 cm⁻¹ (all s); δ 7.45—7.65 (2 H and 3 H, m, ArH–SO_2), 7.27 (5 H, s, ArH), 5.45 (1 H, t with further fine splitting, *J* 8 Hz, –CH–CH_2), 4.43 (s, 2 H, OCH_2), 3.9 (2 H, d, *J* 8 Hz, =CH–CH_2), 3.0 (2 H, m, SO_2CH_2), 2.12 (2 H, t with fine splitting, CH_2–C(Me)=), and 1.65 (3 H, s) (Found: C, 69.5; H, 7.05; S, 9.3. $C_{20}H_{24}O_3S$ requires C, 69.7; H, 7.0; S, 9.3%).

5-*Phenylthio*-2,2-*dimethylhexanoic Acid* (10).—To a mixture of 1.5M-n-BuLi (20 cm³) in hexane and THF (20 cm³) was added Pr^i_2NH (3.03 g, 30 mmol) at a rate sufficient to maintain the temperature below 10 °C. After addition was complete, isobutyric acid (1.32 g, 15 mmol) was added dropwise with ice-bath cooling. The mixture was heated at reflux for 1 h and then cooled to 0 °C whereupon 3-phenylthio-1-bromopropane (9) (2.31 g, 10 mmol) [9] was added in one portion. After being stirred at ambient temperature for 1 h and at reflux for 1 h the mixture was poured into M-HCl (100 cm³). The organic layer was washed with further M-HCl (50 cm³) followed by 2M-NaOH (2 × 20 cm³). The combined basic extracts were washed with Et_2O and then acidified with conc. HCl (10 cm³). The product was extracted into Et_2O and the extract washed

with water, dried, and evaporated. The product (1.87 g, 81%) crystallised from cold Et_2O–light petroleum: m.p. 40—41 °C, $\nu_{max.}$ (film) 3 500—2 500br, 1 700s cm^{-1}; δ 7.1—7.4 (5 H, m), 2.8—3.0 (2 H, m, CH_2S), 1.6—1.8 (4 H, m), and 1.18 (6 H, s, Me_2C) (Found: C, 65.2; H, 7.5; S, 13.4. $C_{13}H_{18}O_2S$ requires C, 65.5; H, 7.6; S, 13.4%).

5-Phenylsulphonyl-2,2-dimethylpentan-1-ol (11).—The acid (10) (3.00 g, 12.6 mmol) in Et_2O (10 cm^3) was added dropwise to a suspension of $LiAlH_4$ (0.48 g, 12.6 mmol) in Et_2O (20 cm^3). After being refluxed for 4 h the mixture was cooled to room temperature and $Na_2SO_4{\cdot}10H_2O$ (10 g) was added portionwise. After being stirred overnight, the mixture was filtered and evaporated to give 5-phenylthio-2,2-dimethylpentan-1-ol as a colourless oil (2.85 g, *ca.* 100%), $\nu_{max.}$ 3 380, 1 480, 1 440, 1 040, 1 025, 740, and 690 cm^{-1} (all s); δ 7.3—7.1 (5 H, m), 3.3 (2 H, s, CH_2O), 2.9 (2 H, t, *J* 7 Hz, SCH_2), 1.58 (1 H, s, D_2O exchange), and 0.85 (6 H, s, Me_2C). The phenylthio derivative and 30% H_2O_2 (5 cm^3) in acetic acid (35 cm^3) was heated on a steam-bath for 1 h. The mixture was poured into water and the product extracted into Et_2O. The organic layer was washed with M-NaOH and water, dried, and evaporated to give (11) (3.13 g) as a colourless oil, $\nu_{max.}$ (film) 3 500br, 1 315s, 1 305s, 1 290s, and 1 150s cm^{-1}; δ 8.0—7.5 (5 H, m), 3.27 (2 H, s, CH_2O), 3.0—3.2 (2 H, m, SO_2CH_2), 2.05br (1 H, D_2O exchange), 1.8—1.1 (4 H, m), and 0.82 (6 H, s, Me_2C). The crude sulphone (11) was used directly in the next step without further purification.

5-Phenylsulphonyl-2,2-dimethylpentan-1-al (4).—To a rapidly stirred solution of (11) (3.13 g, 12.2 mmol) in CH_2Cl_2 (100 cm^3) was added Celite (6.0 g) and pyridinium chlorochromate (4.07 g, 18.9 mmol). After being stirred at 20 °C for 2 h the mixture was diluted with ether (100 cm^3) and filtered through a 5 × 10 cm column of Florisil. Further Et_2O (200 cm^3) was used to elute the product from the column. Evaporation of the eluant gave a solid which was recrystallised from $CHCl_3$–light petroleum to give the aldehyde (4) (2.63 g, 89%) as white plates, m.p. 92—94 °C; $\nu_{max.}$ (CCl_4) 1 710, 1 310, and 1 145 cm^{-1} (all s); δ 9.39 (1 H, s, CHO), 7.97—7.55 (5 H, m), 3.0—3.2 (2 H, m, CH_2–SO_2), 1.57—1.85 (4 H, m), and 1.03 (6 H, s, Me_2C) (Found: C, 61.35; H, 7.2; S, 12.3. $C_{13}H_{18}O_3S$ requires C, 61.4; H, 7.1; S, 12.6%).

(2Z,6E)-1-*Benzyloxy*-11-*phenylsulphonyl*-3,8,8-*trimethylundeca*-2,6-*diene* (13).—To a stirred solution of (3) (0.884 g, 2.54 mmol) in THF (5 cm^3) was added dropwise at −78 °C 1.5M n-BuLi in hexane (1.7 cm^3, 2.57 mmol). After 15 min the aldehyde (4) (0.653 g, 2.57 mmol) in THF (3 cm^3) was added dropwise followed after 5 min by benzoyl chloride (0.5 cm^3). The cooling bath was removed and the mixture stirred at ambient temperature for 20 h. After the mixture had been cooled to 0 °C, 3-dimethylaminopropylamine (0.5 cm^3) was added dropwise. The mixture was poured into M-HCl (25 cm^3) and the product extracted into Et_2O. The Et_2O layer was dried and evaporated to give (12) as a viscous oil (1.61 g) which was used directly in the next step.

The crude product from above in THF–MeOH (3 : 1; 15 cm^3) was cooled to −20 °C and 6.5% Na(Hg) (2.50 g) added. After 3 h at −20 °C, M-HCl was added (15 cm^3). The mixture was extracted with Et_2O (2 × 40 cm^3). The combined organic layers were washed with saturated $NaHCO_3$ and NaCl, dried, and evaporated. Chromatography on a 3 × 10 cm column of Kieselgel with 20% ethyl acetate in light petroleum as eluant gave the pure sulphone (13) [0.525 g, 47% from (4)] as a viscous oil: $\nu_{max.}$ (film) 1 445, 1 320, 1 305, 1 150, 1 085, 735, and 690 cm^{-1} (all s); δ 7.8—8.0 and 7.5—7.7 (2 H and 3 H, m, ArH·SO_2), 7.3 (5 H, s, ArH), 5.4 (1 H, t with further fine splitting, *J* 7 Hz, =C*H*–CH_2), 5.15—5.30 (2 H, m, CH=CH), 4.50 (2 H, s, CH_2O), 4.00 (2 H, d, *J* 7 Hz, $^-$CH=CH_2), 3.03 (2 H, t, *J* 7 Hz, SO_2CH_2), 2.07 (4 H apparent doublet =CCH_2CH_2C=), 1.73 (3 H, d, *J* 1 Hz, CH_3C=), and 0.91 (6 H, s, Me_2C) (Found: M^+, 440.238 31. Calc. for $C_{27}H_{36}O_3S$: *M*, 440.238 503).

(2Z,6E,13E)-1-*Benzyloxy*-11-*phenylsulphonyl*-3,8,8,14,18-*pentamethylnonadeca*-2,6,13,17-*tetraene* (14).—To a stirred solution of the sulphone (13) (0.422 g, 0.96 mmol) in THF (3 cm^3) was added dropwise at −78 °C 1.5M-Bu^{n}Li (0.7 cm^3) in hexane. After 15 min at −78 °C geranyl chloride (0.410 g, 2.39 mmol) in THF (0.5 cm^3) was added. The mixture was allowed to warm slowly overnight whereupon Et_2O and brine were added. The organic layer was dried and evaporated to give an oil which was chromatographed on a 3 × 9 cm column of Kieselgel. Elution with 10% ethyl acetate in light petroleum gave (14) (470 mg, 85%) as a colourless, viscous oil: $\nu_{max.}$ (film) 1 450, 1 305, 1 150, 1 085, 1 070, 730, and 695 cm^{-1} (all s); δ 7.95—7.75 and 7.45—7.65 (2 H and 3 H, m, Ar*H*SO_2), 7.28 (5 H, s, ArH), 5.4 (1 H, t with further splitting, =C*H*–CH_2O), 5.25—5.1 (2 H, m, CH=CH), 5.0 (2 H, m, =C*H*=CH_2), 4.45 (2 H, s, $PhCH_2$), 3.97 (2 H, d, *J* 7 Hz, =CH–CH_2–O), 1.72, 1.65, 1.56, 1.50 (3 H each, s, Me–C=), and 0.86 (6 H, s, Me_2C). The product was homogeneous by t.l.c. but combustion analysis consistently gave high carbon figures and the mass spectrum (electron impact) gave no molecular ion. The product was used in the next step without further characterisation.

(2Z,6E,13E)-1-*Benzoyloxy*-11-*methylene*-3,8,8,14,18-*pentamethylnonadeca*-2,6,13,17-*tetraene* (16).—A solution of lithium di-isopropylamide was prepared at −78 °C by adding di-isopropylamine (101 mg, 1.00 mmol) to a mixture of 1.5M-Bu^{n}Li (0.67 cm^3) in hexane and THF (0.5 cm^3). The sulphone (14) (438 mg, 0.76 mmol) in THF (0.8 cm^3) was added dropwise and the mixture stirred at −78 °C for 1 h. Then ICH_2SiMe_3 (642 mg, 3.00 mmol) was added followed by HMPA (300 mg). The mixture was allowed to warm slowly over 3 h to −20 °C whereat the temperature was maintained for 2 h. The mixture was diluted with Et_2O (20 cm^3) and saturated aqueous $NaHCO_3$ added. The organic layer was dried and the residue obtained on evaporation dissolved in THF (3 cm^3) to which was added Bu$^n{}_4$NF·$3H_2O$ (540 mg, 1.71 mmol). After being refluxed for 1 h Et_2O (20 cm^3) was added and the mixture washed with water. The residue obtained on drying and evaporation of the organic layer was chromatographed on a 2 × 4 cm column of Kieselgel. Elution with 10% ethyl acetate in light petroleum gave moenocinol benzyl ether (16) as a colourless oil (143 mg, 42%): $\nu_{max.}$ (film) 1 655w, 1 695m, 1 455s, 1 485m, 1 465m, 1 070s, 970m, 890m, 760m, 735s, and 700s cm^{-1}; δ 7.2—7.4 (5 H, m), 5.0—5.5 (5 H, m), 4.68br (2 H, s, $=CH_2$), 4.48 (2 H, s, $PhCH_2$), 4.0 (2 H, d with fine splitting, *J* 7 Hz), 2.70 (2 H, d with fine splitting, *J* 7 Hz, =CH–CH_2–C=), 2.0—2.2 (8 H, m, =C–CH_2–C=), 1.75br and 1.69br (3 H, each, s), 1.61br (6 H, s), 0.95br (6 H, s, Me_2C) (Found: M^+, 448.370 57. Calc. for $C_{32}H_{48}O$: *M*, 448.370 497).

(2Z,6E,13E)-3,8,8,14,18-*Pentamethyl*-11-*methylenenonadeca*-2,6,13,17-*tetraen*-1-*ol* (*Moenocinol*) (1).—A solution of the benzyl ether (16) (102 mg, 0.227 mmol) in Et_2O (1 cm^3) was added to NH_3 (5 cm^3) at −78 °C. Lithium metal (*ca.* 10 mg) was added and the mixture stirred at −78 °C for 30 min. The dark blue colour was discharged by adding solid NH_4Cl (*ca.* 1 g) and the NH_3 evaporated. The residue was partitioned between water and Et_2O. The organic layer was washed with brine, dried, and evaporated. The residue (one component by t.l.c.) in Et_2O was filtered through a plug of Kieselgel and the filtrate concentrated to give moenocinol (1) as a colourless oil

(76.5 mg, 0.214 mmol, 94%), identical (i.r. and ^1H and ^{13}C n.m.r.) with the data reported * for natural (1).

2-[(Z)-1-*Phenylsulphonyl*-6-*benzyloxy*-4-*methylhex*-4-*enyl*]-3,3-*dimethyloxolane* (19).—To a stirred solution of the sulphone (3) (2.20 g, 6.42 mmol) in THF (10 cm^3) at −78 °C was added dropwise 1.43M-Bu^{n}Li in hexane (4.95 cm^3). After 20 min at −78 °C, the aldehyde (18) [5] (0.86 g, 6.42 mmol) in THF (5 cm^3) was added dropwise. After 20 min at −78 °C, the cooling bath was removed and the mixture stirred at ambient temperature for 2.5 h. The mixture was poured into brine and extracted with Et_2O. The organic layer was dried and evaporated to give a viscous oil (3.07 g) which was chromatographed on Kieselgel (150 g) (6 cm diameter column). Elution with 20% ethyl acetate in light petroleum gave (19) as a pale yellow oil (2.55 g, 90%): $\nu_{max.}$ (film) 1 300s, 1 295m, 1 145s, 1 090s, and 1 070s cm^{-1}; δ 7.25—8.05 (10 H, m), 5.30—5.50 (1 H, m, =C*H*−CH_2O), 4.50 and 4.53 (2 H, 2 singlets of equal area corresponding to two diastereoisomers), 3.93—4.15 (2 H, m, =CH−CH_2−O), 3.50—3.80 (3 H, m, CH_2−O−CH_2-$CHSO_2$), 2.80—3.20 (1 H, m, $CHSO_2$), 1.7 and 1.78 (3 H, s with fine splitting, =C−CH_3), 1.16, 0.95 and 0.90 (6 H, s, Me_2C, 2 diastereoisomers) (Found: M^+, 442.217 23. Calc. for $C_{26}H_{34}O_4S$: *M*, 442.217 768).

(2Z,6E)-1-*Benzyloxy*-3,8,8-*trimethyldeca*-2,6-*dien*-10-*ol* (20).—A mixture of the sulphone (19) (1.01 g, 2.28 mmol) and powdered 5.65% Na(Hg) (3 g) in THF (20 cm^3) and MeOH (5 cm^3) was stirred at 20 °C for 16 h after which further Na(Hg) (3 g) was added. After being stirred for 5 days at 20 °C, the mixture was decanted from unchanged Na(Hg) into water and the product extracted into Et_2O. The Et_2O extract was washed with water and brine, dried, and evaporated. The residual oil was chromatographed on Kieselgel (80 g) (6 cm diam.) with 5% Et_2O in benzene as eluant. The alcohol (20) (585 mg, 85%) was obtained as an oil, b.p. (bath) 190 °C/0.02 mmHg; $\nu_{max.}$ (film) 3 600—3 100s, 1 060s, 1 025s, and 970m cm^{-1}; δ_H 7.33 (5 H, s), 5.20—5.55 (3 H, m, 3 × =CH), 4.49 (2 H, s, OCH_2Ph), 4.00 (2 H, d, *J* 5 Hz, OCH_2CH=), 3.59 (2 H, t, *J* 5 Hz, CH_2OH), 2.00—2.20 (4 H, m, =C−CH_2CH_2−C=), 1.75 (3 H, s, MeC=), 1.55 (2 H, t, *J* 5 Hz, $HOCH_2CH_2$), and 0.97 (6 H, s, Me_2C); δ_C 23.40 (3-Me), 27.79 (2 × 8-Me), 31.15 (C-4 or C-5), 32.34 (C-4 or C-5), 34.84 (C-8), 45.56 (C-9), 60.08 (C-10), 66.36 (C-1), 92.16 (benzylic C), 122.11, 125.68, 127.53, 127.80, 128.34, 138.58, 140.09, and 140.37) (Found: M^+, 302.224 53. Calc. for $C_{20}H_{30}O_2$: *M*, 302.224 568).

(2Z,6E)-1-*Benzoyloxy*-10-*iodo*-3,8,8-*trimethyldeca*-2,6-*diene* (22).—To a stirred solution of the alcohol (0.47 g, 1.56 mmol) and Et_3N (0.33 cm^3) in CH_2Cl_2 (5 cm^3) was added dropwise at 0 °C methanesulphonyl chloride (0.13 cm^3). After 1 h at 0 °C the mixture was diluted with CH_2Cl_2 and washed with M-HCl and $NaHCO_3$, dried, and evaporated to give the methanesulphonate (21) (0.59 g, *ca.* 100%) (homogeneous by t.l.c.). The crude compound (21) and NaI (1.5 g) in acetone (15 cm^3) was refluxed for 16 h. Most of the acetone was removed under reduced pressure and the residue partitioned between Et_2O and aqueous $Na_2S_2O_3$. The organic layer was dried and concentrated under reduced pressure with protection from light to give the unstable iodide (22) as a pale yellow oil (0.63 g, 98%): $\nu_{max.}$ (film) 1 365, 1 065, 970, 740, 695 cm^{-1} (all s); δ 7.33 (5 H, s), 5.20—5.50 (3 H, m, 3 × =CH), 4.50 (2 H, s, $PhCH_2$), 4.00 (2 H, d, *J* 5 Hz, =CH−CH_2O), 3.05 (2 H, distorted t, *J* 7 Hz, CH_2I), 2.00—2.15 (4 H, m, =CCH_2CH_2C=), 1.7br (3 H, s, CH_3−C=), and 0.96 (s, 6 H, Me_2C). A satisfactory combustion analysis could not be obtained for this compound.

Conversion of (22) *into* (13).—To a stirred solution of phenyl methyl sulphone (0.312 g, 2.00 mmol) in THF (3 cm^3) was added at −78 °C 1.5M-Bu^{n}Li (1.35 cm^3). After 10 min, the iodide (22) (0.471 g, 1.14 mmol) in THF (1 cm^3) was added in one portion. The reaction mixture was allowed to warm slowly to room temperature over 3 h whereupon it was diluted with Et_2O (20 cm^3) and washed with brine. The residue obtained after drying and evaporation of solvent was chromatographed on a 2 × 4 cm column of Kieselgel. Elution with 20% Et_2O in light petroleum gave the sulphone (13) (0.417 g, 0.95 mmol, 83%) which was identical by ^1H n.m.r. spectroscopy with material prepared previously (*vide supra*).

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