Studies on the Synthesis of Aphidicolin. Preparation of Aromatic Precursors for Spirocyclic Dienone Formation.

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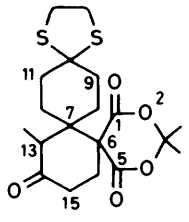
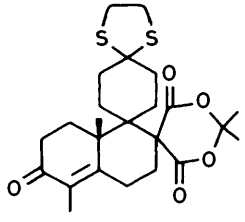
Novel syntheses of the alkenediones (**12**; R = Me, or CH_2Ph) and the corresponding epoxides (**13**) are described. Attempts to cyclise these compounds to the spirocyclic dienone (**4**) were unsuccessful. Model studies on the phenolic keto cyano toluene-*p*-sulphonate (**24**) showed that the cyclopropane (**25**) was formed preferentially. A variety of related model compounds (**29**), (**31**), (**32**), and (**37**) were prepared and studied, but none could be cyclised to spirocyclic dienones.

In the preceding paper,[1] it was reported that attempts to convert the spirocyclic ketone (**1**) into the enone (**2**) by Robinson annelation were largely unsuccessful, although there was some indication that the required specific enolate derived from compound (**1**) would undergo Michael addition with α-silylated ethyl vinyl ketone. The low reactivity of (**1**) is almost certainly associated with the severe steric congestion at C-13. An alternative approach is to have the requisite C-13 substituents intact on a suitable *seco*-precursor [*e.g.* compound (**3**)] and to make the C(6)–C(7) bond intramolecularly in a later step. The diketo phenol (**3**) or a suitable derivative could be expected to cyclise to the dienone (**4**) in the presence of base.


(1)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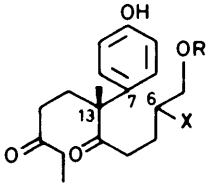
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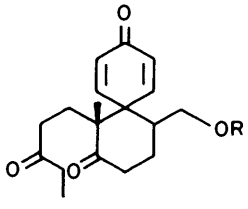
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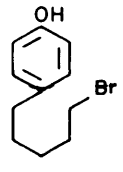
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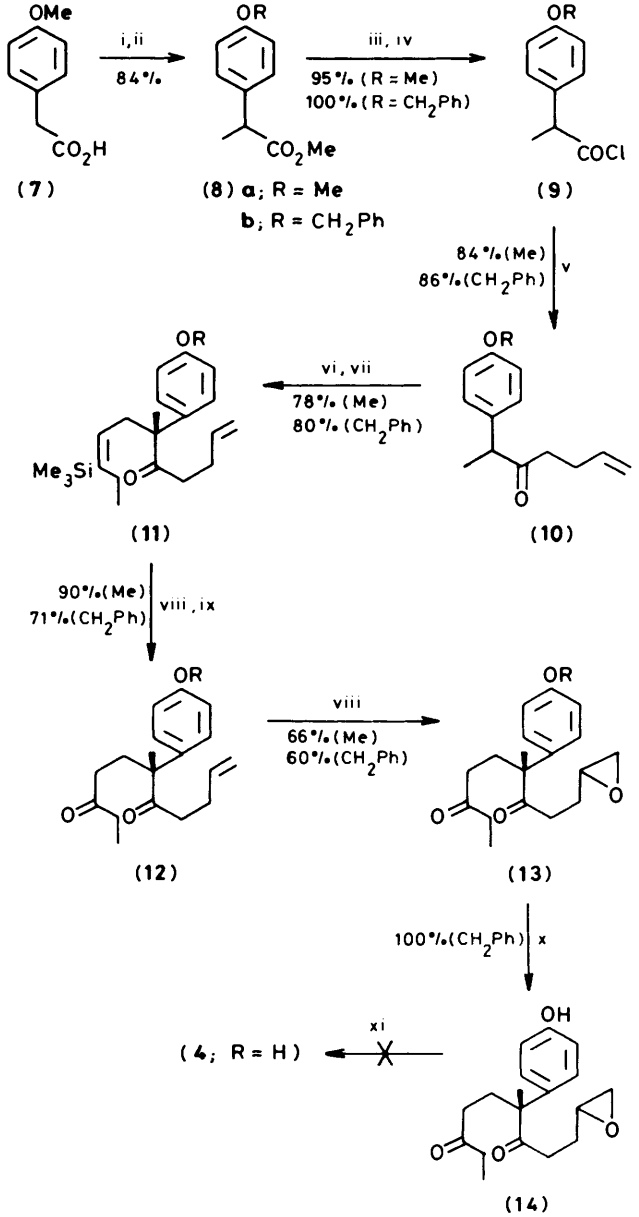
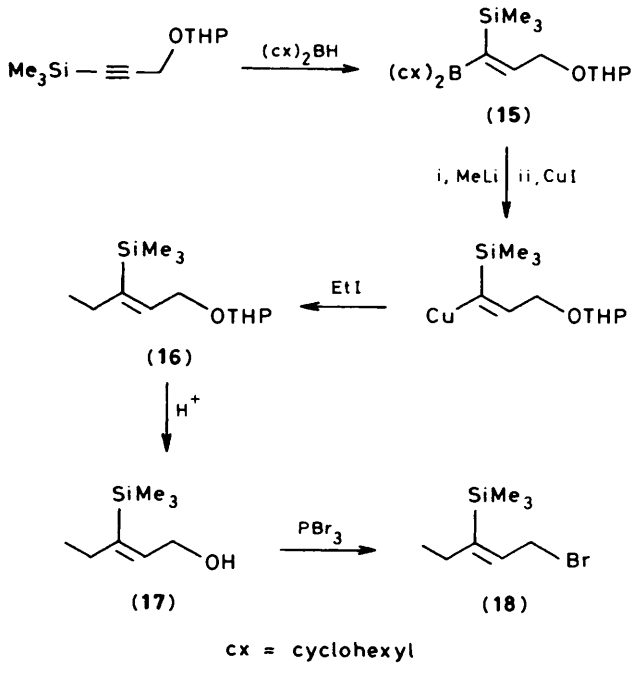
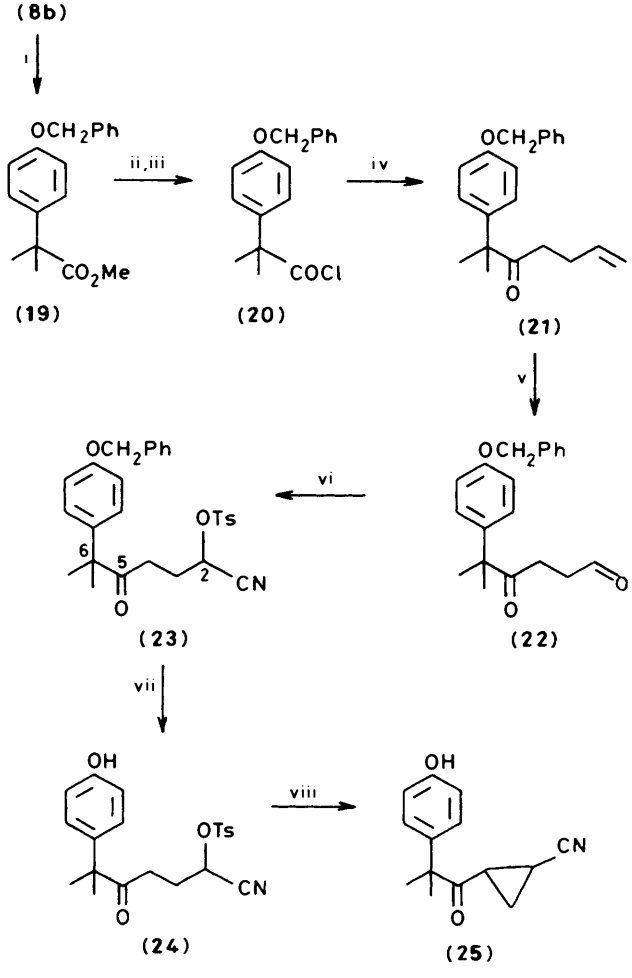
Intramolecular spirocyclisations of phenols to dienones have been well understood since the pioneering work of Winstein.[2] The subject has been reviewed,[3] and various applications to synthesis have been reported.[4] The most relevant example to the present proposal is from Dreiding's work in which the



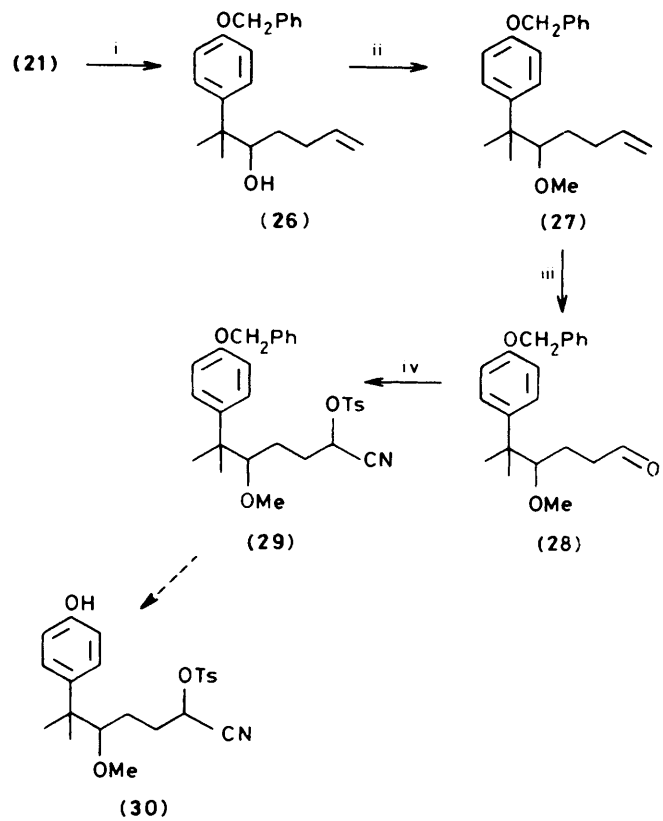
Scheme 1. *Reagents:* i, MeOH–H^+; ii, $NaNH_2$ MeI; iii, NaOH; iv, $SOCl_2$; v, $Cd(CH_2{=}CHCH_2CH_2)_2$; vi, NaH–HMPA–THF; vii, $EtC(SiMe_3){=}CHCH_2Br$; viii, MCPBA; ix, $BF_3{\cdot}OEt_2$; x, H_2–Pd; xi, KOBu^t



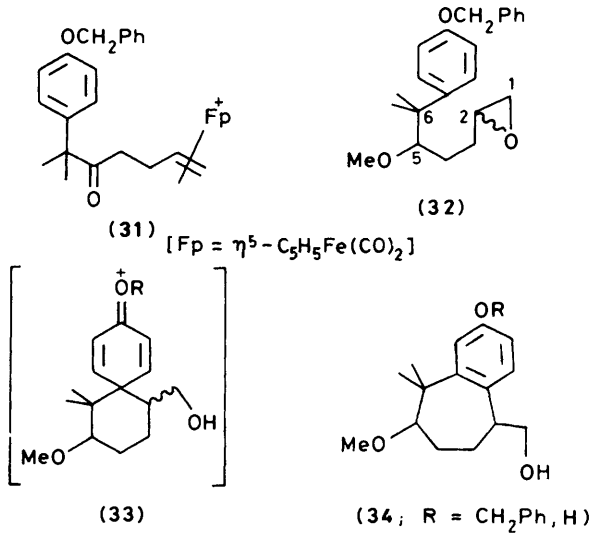
Scheme 2.



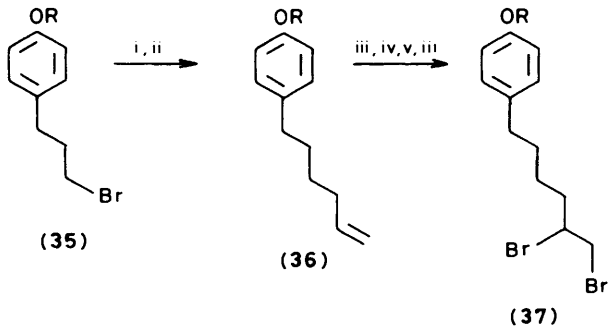
Scheme 3. *Reagents:* i, $NaNH_2$–MeI; ii, NaOH; iii, $SOCl_2$; iv, $Cd(CH_2{=}CHCH_2CH_2)_2$; v, O_3 then Me_2S; vi, NaCN–TsCl; vii, BCl_3; viii, KOBu^t



Scheme 4. *Reagents:* i, $NaBH_4$ (94%); ii, NaH–MeI (96%); iii, O_3 then Me_2S (60%); iv, NaCN–TsCl (65%)



ω-bromophenol (**5**) cyclised in the presence of KOBu^t in high yield to the spiro[5.5]undecadienone (**6**).[5] The alkenedione (**12**; R = Me or CH_2Ph) embodies all the carbon atoms present in aphidicolin except the two hydroxymethyl substituents in rings A and C and is in principle a precursor to the intermediate target (**3**). A variety of routes was investigated for the preparation of compound (**12**), and that illustrated in Scheme 1 proved the most efficient. Both the methyl (**12a**) and benzyl (**12b**) ethers were prepared, the ether transposition being carried out at the stage of the ester (**8**). Thus (**8a**) was converted into (**8b**) in two steps using $AlCl_3$ to cleave the methyl ether and then benzyl



Scheme 5. *Reagents:* R = H; i, Me_3SiCl; ii, Mg then CH_2=$CHCH_2Br$; iii, Na_2CO_3; iv, Ac_2O; v, Br_2

chloride and potassium carbonate to introduce the benzyloxy substituent. The pentanone side chain was added to compound (**10**) using the alkylative version of an ethyl vinyl ketone equivalent[6] in the form of the bromovinylsilane (**18**), which was prepared as shown in Scheme 2 according to the general procedure described by Uchida *et al.*[7] The epoxides (**13a**) and (**13b**) were prepared from the corresponding alkenes. Selective demethylation of the methyl ether (**13a**) without concomitant Lewis acid–catalysed epoxide opening reactions proved impossible. However, the benzyl ether (**13b**) could be hydrogenolysed to give the free phenol (**14**). This was treated with KOBu^t in Bu^{t}OH over a range of temperatures (60—170 °C) and reaction times (24—36 h) but could not be induced to cyclise to compound (**4**; R = H), starting material being recovered under all conditions.

The failure to induce cyclisation of compound (**14**) may have been due to the inadequacy of epoxide as a leaving group under basic conditions. More activated leaving groups have certainly been effective in such dienone closure reactions.[4] We therefore studied cyclisation of the model cyanotoluene-*p*-sulphonate (**24**) which was prepared according to the sequence shown in Scheme 3. Treatment of this with KOBu^t in Bu^{t}OH and other bases gave a good yield of the cyclopropane derivative (**25**), as may have been expected from the known kinetic preference for three-membered over six-membered rings in enolate cyclisations.[8] This could clearly be avoided by removal of the offending carbonyl group. The methoxy derivative (**29**), prepared as shown in Scheme 4, proved to be the best compound for this purpose, but selective debenzylation of compound (**29**) in the presence of the methoxy substituent using gaseous hydrogen (detoluene-*p*-sulphonylation), BCl_3, and Me_3SiI (demethylation) proved difficult. Transfer hydrogenolysis[9] in the presence of $Pd(OH)_2$ (20%) on carbon sometimes gave modest yields of the phenol (**30**), but insufficient quantities were obtained to enable the model cyclisation reaction to be studied.

A variety of alternative model compounds was prepared in order to study cyclisation reactions. Thus the $F_p{}^+$-complex (**31**) was expected to present an electrophilic alkene carbon to the electron rich aromatic ring,[10] but the complex could not be debenzylated despite a report in the literature that $F_p{}^+$-alkene complexes are stable to the conditions of catalytic reduction.[11] The cyclisation of the epoxide (**32**) in the presence of a variety of Lewis acids gave ring expanded products such as (**34**) arising almost certainly by dienone-phenol rearrangement of the required intermediate (**33**). Finally, the simple model dibromo compound (**37**), prepared as shown in Scheme 5, also failed to undergo butoxide-induced cyclisation to a dienone derivative.

Experimental

Apparatus and equipment have been described in the preceding paper.[1]

Methyl 2-(4-Methoxyphenyl)propionate (**8a**).—To a suspension of sodamide (5.6 g, 0.24 mol) in liquid ammonia (500 ml) was added dropwise from a syringe, a solution of methyl 2-(4-methoxyphenyl)acetate [40 g, 0.22 mol; prepared by esterification of the acid (**7**) in methanol saturated with dry HCl] in THF (30 ml). The grey reaction mixture was stirred at −33 °C (0.5 h), and then methyl iodide (15 ml, 34.7 g, 0.24 mol) was added dropwise by syringe. The mixture was stirred (1 h) at −33 °C, after which time solid NH_4Cl (13 g, 0.24 mol) was added, and the ammonia was allowed to evaporate overnight. The resulting yellow-brown residue was mixed with water (300 ml) which was then extracted with ether (3 × 500 ml). The organic extracts were washed with cold saturated aqueous NaCl solution, then combined and dried (Na_2SO_4). Evaporation of the solvent gave the *methyl compound* (**8a**) (41.6 g, 96.5%) as a colourless oil, b.p. 100 °C/0.4 mmHg; δ($CDCl_3$) 1.48 (3 H, d, *J* 7 Hz), 3.63 [4 H, m, including (3 H, s)], 3.77 (3 H, s), 6.8 (2 H, d, *J* 9 Hz), and 7.2 (2 H, d, *J* 9 Hz); $\nu_{max.}$($CHCl_3$) 1 730s, 1 610m, and 1 580w cm^{-1}; *m/z* 194 (M^+, 14%), 135 (100), 121 (4), and 91 (4) (Found: M^+, 194.0940. $C_{11}H_{14}O_3$ requires *M*, 194.0942). The compound was a single spot in a variety of silica t.l.c. analyses [R_F 0.57 in ether–light petroleum (b.p. 60—80 °C) (1:1)].

Methyl 2-(4-Benzyloxyphenyl)propionate (**8b**).—To a solution of the methyl ether (**8a**) (32 g, 0.165 mol) in benzene (500 ml) was added $AlCl_3$ (110 g, 0.825 mol). The reaction mixture was heated under reflux (7 h), then cooled to 0 °C, and **cautiously** added to ice. The aqueous layer was separated and extracted with ether (500 ml). The organic layers were washed with cold saturated aqueous $NaHCO_3$ (300 ml), saturated aqueous NaCl (300 ml), and they were then combined, dried (Na_2SO_4), and evaporated to give the *phenol* (**8**; R = H) as a red oil (32 g) which was used in the next step; $\nu_{max.}$($CHCl_3$) 3 600s, 3 420m, 1 725s, 1 620m, and 1 605m cm^{-1}. A mixture of the phenol (**8**; R = H) (32 g, 0.177 mol) benzyl chloride (24.8 g, 22.6 ml, 0.195 mol), anhydrous K_2CO_3 (48.9 g, 0.354 mol), KI (1 g, 6 mmol), and butanone (400 ml) was heated under reflux overnight. The solvent was evaporated, and the residue was mixed with water (400 ml). The aqueous layer was extracted with ether (2 × 500 ml) and the organic extracts were washed with saturated aqueous NaCl (400 ml), combined, and dried (Na_2SO_4). Evaporation of the solvent gave a red oil (52 g) which was chromatographed on a silica column (500 g). Elution of the column with ether–light petroleum (b.p. 60—80 °C) (5:95; 3 l), gave the *benzyl ether* (**8b**) (39.2 g, 82%) as a colourless oil, b.p. 150 °C/0.3 mmHg which solidified on cooling and was recrystallised from light petroleum, b.p. 30—40 °C at 0—5 °C to give prisms, m.p. 33—35 °C; δ($CDCl_3$) 1.49 (3 H, d, *J* 7 Hz), 3.63 (3 H, s), 3.7 (1 H, m), 5.02 (2 H, s,), 6.95 (2 H, d, *J* 9 Hz), 7.25 (2 H, d, *J* 9 Hz), and 7.37 (5 H, m); $\nu_{max.}$($CHCl_3$) 1 725s, 1 610s, and 1 585m cm^{-1}; *m/z* 270 (M^+, 39%), 244 (14), 135 (100), and 91 (80) (Found: C, 75.5; H, 7.0. $C_{17}H_{18}O_3$ requires C, 75.5; H, 6.7%).

2-(4-Methoxyphenyl)propionyl Chloride (**9a**).—A solution of the ester (**8a**) (41.6 g, 0.214 mol) in 2M-aqueous NaOH (150 ml) and ethanol (150 ml) was heated under reflux (1 h). Evaporation of the solvent gave an oil which was partitioned between water (200 ml) and ether (500 ml). The aqueous phase was acidified with conc. HCl (60 ml), and extracted with ether (2 × 500 ml). The organic extracts were washed with cold saturated aqueous NaCl solution (200 ml), combined, and dried (Na_2SO_4). Evaporation of the solvent gave 2-(4-methoxyphenyl)propionic acid (39 g, 100%), m.p. (cyclohexane) 56—57 °C (lit.,[12] 57 °C); δ($CDCl_3$) 1.4 (3 H, d, *J* 7 Hz), 3.65 (3 H, s), 3.65 (1 H, q, *J* 7 Hz), and 6.97 (4 H, dd, *J* 9 Hz). The carboxylic acid (39 g, 0.22 mol) and thionyl chloride (100 ml) were stirred overnight at room temperature. Evaporation of the excess thionyl chloride and

further azeotropic distillation with toluene gave the *acid chloride* (**9**) (42.5 g, 94%) as an oil which was used without further purification; δ($CDCl_3$) 1.4 (3 H, d, *J* 7 Hz), 3.65 (3 H, s), 3.89 (1 H, q, *J* 7 Hz), 6.9 (2 H, d, *J* 9 Hz), and 7.2 (2 H, d, *J* 9 Hz); $\nu_{max.}$($CHCl_3$) 1 780s cm^{-1}.

2-(4-*Methoxyphenyl*)*hept*-6-*en*-3-*one* (**10a**).—To a suspension of Mg turnings (7.3 g, 0.3 mol) in dry ether (250 ml) under nitrogen was added 4-bromobut-1-ene (1 ml, 1.33 g, 9.9 mmol). After formation of the Grignard reagent had been initiated (hot air blower) the remainder of the bromobutene (29.43 ml, 39.12 g, 0.29 mol) was added by syringe at a rate sufficient to maintain a gentle reflux. After the Grignard reagent had formed (1 h) anhydrous $CdCl_2$ (29.6 g, 0.3 mol) was added slowly at room temperature. The grey slurry was stirred (15 min), then most of the ether was distilled off, and was replaced by benzene (250 ml), a small volume of which was distilled off and replaced by an equal amount (50 ml) of fresh benzene. To this reaction mixture was added a solution of the acid chloride (**9a**) (30 g, 0.15 mol) in benzene (40 ml), and the mixture was heated under reflux. After 1 h, it was then cooled and poured into ether (500 ml) and 2M-HCl (200 ml) at 0 °C. The aqueous layer was separated and extracted with ether (500 ml). The ether extracts were washed with cold saturated aqueous $NaHCO_3$ (200 ml), and saturated aqueous NaCl (200 ml). They were then combined and dried (Na_2SO_4). Evaporation of the solvent and distillation of the residue gave the *keto alkene* (**10a**) (27.6 g, 84%) as a colourless oil, b.p. 110—112 °C/0.1 mmHg; δ($CDCl_3$) 1.33 (3 H, d, *J* 7 Hz), 2.12—2.52 (4 H, m), 3.7 (1 H, q, *J* 7 Hz), 3.74 (3 H, s), 4.8—4.94 (2 H, m), 5.48—5.88 (1 H, m), 6.8 (2 H, d, *J* 9 Hz), and 7.1 (2 H, d, *J* 9 Hz); $\nu_{max.}$($CHCl_3$) 1 710s, 1 640w, and 835s cm^{-1}; *m/z* 218 (M^+, 8%), 135 (93), 121 (8), 105 (11), and 83 (100) (Found: C, 76.8; H, 8.1. $C_{14}H_{18}O_2$ requires C, 77.1; H, 8.2%).

2-(4-*Benzyloxyphenyl*)*hept*-6-*en*-3-*one* (**10b**).—Hydrolysis of the ester (**8b**) gave in 84% yield 2-(4-*benzyloxyphenyl*)*propionic acid*, as prisms, m.p. (cyclohexane) 123—125 °C (Found: C, 74.6; H, 6.5. $C_{16}H_{16}O_3$ requires C, 74.9; H, 6.2%). The carboxylic acid was converted into the acid chloride (**9b**) which reacted with the cadmium reagent derived from 4-bromobut-1-ene in 86% yield to give the *keto alkene* (**10b**) as a colourless oil, b.p. 126 °C/0.2 mmHg; δ($CDCl_3$) 1.38 (3 H, d, *J* 7 Hz), 2.0—2.53 (4 H, m), 3.68 (1 H, q, *J* 7 Hz), 4.81—4.99 (2 H, m), 5.0 (2 H, s), 5.55—5.9 (1 H, m), 6.9 (2 H, d, *J* 9 Hz), 7.1 (2 H, d, *J* 9 Hz), and 7.37 (5 H, m); $\nu_{max.}$($CHCl_3$) 1 710s, 1 640w, and 835s cm^{-1}; *m/z* 294 (M^+, 8%), 213 (84.5), 121 (12.5), and 91 (100) (Found: C, 81.2; H, 7.9. $C_{20}H_{22}O_2$ requires C, 81.6; H, 7.5%).

6-(4-*Methoxyphenyl*)-6-*methyl*-9-*trimethylsilylundeca*-1,8-*dien*-5-*one* (**11a**).—To a solution of the keto alkene (**10a**) (1.2 g, 5.5 mmol) in THF (8 ml) and HMPA* (1 g, 5.5 mmol) was added NaH (0.317 g, 6.6 mmol; 50% dispersion). The suspension was stirred at room temperature (0.5 h), and was then cooled to 0 °C. The allyl bromide (**18**) (1.4 g, 6.3 mmol) (preparation to be described in succeeding papges) in THF (2 ml) was added dropwise by syringe. The reaction mixture was stirred at 0 °C (10 min) and then overnight at room temperature. Solid NH_4Cl (0.5 g, 11.5 mmol) was added, the THF was evaporated, and cold saturated aqueous NH_4Cl (15 ml) was added. The reaction mixture was extracted with ether (3 × 50 ml), and the ether extracts were washed with cold saturated aqueous NaCl (20 ml), and were then combined and dried (Na_2SO_4). Removal of the solvent gave a yellow-brown oil (2.8 g) which was chromatographed on a silica column (65 g). Elution with ether–light petroleum (b.p. 60—80 °C) (5:95; 425 ml) gave the *vinylsilane* (**11a**) as an oil, b.p. 110 °C/0.05 mmHg; δ(CCl_4) 0.23 (9 H, s), 0.97 (3 H, t, *J* 7 Hz), 1.5 (3 H, s), 1.89—2.32 (6 H, m), 2.65—2.82 (2 H, m), 3.88 (3 H, s), 4.78—5.0 (2 H, m), 5.3—5.88 (2 H, m), 6.85 (2 H, d, *J* 9 Hz), and 7.1 (2 H, d, *J* 9 Hz); $\nu_{max.}$($CHCl_3$) 1 710s, 1 640w, 1 620m, and 835s cm^{-1}; *m/z* 358 (M^+, 1%), 275 (74), 231 (7), 173 (28), and 85 (100) (Found: C, 73.3; H, 9.9. $C_{22}H_{34}O_2Si$ requires C, 73.5; H, 9.7%).

6-(4-*Benzyloxyphenyl*)-6-*methyl*-9-*trimethylsilylundeca*-1,8-*dien*-5-*one* (**11b**).—The keto alkene (**10b**) (3. 515 g, 11.8 mmol) was alkylated with NaH and the allyl bromide (**18**) to give the *vinylsilane* (**11b**) (4.2 g, 80%) as an oil, b.p. 185 °C/0.05 mmHg; δ(CCl_4) 0.18 (9 H, s), 0.89 (3 H, t, *J* 7 Hz), 1.4 (3 H, s), 1.88—2.38 (6 H, m), 2.6—2.8 (2 H, m), 4.78—5.16 (2 H, m), 5.2 (2 H, s), 5.38—5.85 (2 H, m), 6.8 (2 H, d, *J* 9 Hz), 7.1 (2 H, d, *J* 9 Hz), and 7.37 (5 H, m); $\nu_{max.}$($CHCl_3$) 1 700s, 1 640w, 1 620m, and 840s cm^{-1}; *m/z* 434 (M^+, 9%), 351 (100), 307 (44), 293 (77), 279 (73), 224 (83), and 91 (71) (Found: C, 77.7; H, 8.6. $C_{28}H_{38}O_2Si$ requires C, 77.4; H, 8.8%).

6-(4-*Methoxyphenyl*)-6-*methylundec*-10-*ene*-3,7-*dione* (**12a**).—The vinylsilane (**11a**) (1.55 g, 4.3 mmol) in CH_2Cl_2 (50 ml) containing Na_2CO_3 (0.911 g, 8.6 mmol) was treated with *m*-chloroperbenzoic acid (MCPBA) (85%, 1.75 g, 8.6 mmol) at 0 °C. The white suspension was stirred at room temperature (2 h) after which time it was poured into cold saturated aqueous Na_2SO_3 (25 ml). The organic layer was separated and the aqueous phase was further extracted with CH_2Cl_2 (2 × 50 ml). The organic layers were washed with cold saturated aqueous $NaHCO_3$ (25 ml), saturated aqueous NaCl (25 ml) and were then combined and dried (Na_2SO_4). Evaporation of the solvent gave the *epoxide* of (**11a**) (1.7 g) [R_F on silica t.l.c. 0.532; ether–light petroleum (b.p. 60—80 °C) (1:1)] which was used without further purification. The epoxide (1.7 g, 4.5 mmol) in dry ether (20 ml) at 0 °C was treated with BF_3·OEt_2 (0.643 g, 0.56 ml, 4.5 mmol) dropwise from a syringe, and the reaction mixture was stirred at 0 °C (0.5 h), followed by quenching with cold saturated aqueous Na_2CO_3 (20 ml). The aqueous phase was separated and extracted with ether (2 × 40 ml). The organic extracts were washed with cold saturated aqueous NaCl solution (20 ml), combined, and dried (Na_2SO_4). Evaporation of the solvent and distillation of the residue gave the *alkenedione* (**12a**) (1.23 g, 90%) as a colourless oil, b.p. 100 °C/0.05 mmHg; δ($CDCl_3$) 1.0 (3 H, t, *J* 7 Hz), 1.48 (3 H, s), 2.0—2.5 (10 H, m), 3.8 (3 H, s), 4.72—5.0 (2 H, m), 5.34—5.88 (1 H, m), 6.8 (2 H, d, *J* 9 Hz), and 7.1 (2 H, d, *J* 9 Hz); $\nu_{max.}$($CHCl_3$) 1 710s, 1 640w, and 835m cm^{-1}; *m/z* 302 (M^+, 1%), 219 (100), 148 (53), and 120 (8) (Found: C, 75.6; H, 8.9. $C_{19}H_{26}O_3$ requires C, 75.5; H, 8.6%).

6-(4-*Benzyloxyphenyl*)-6-*methylundec*-10-*ene*-3,7-*dione* (**12b**).—The vinylsilane (**11b**) (0.71 g, 1.62 mmol) was epoxidised with MCPBA in the presence of K_2CO_3 to give the *epoxide* of (**11b**) (0.77 g) [R_F on silica t.l.c., 0.59, ether–light petroleum (b.p. 60—80 °C) (1:1)] which was used without further purification. The epoxide (0.1 g, 0.22 mmol) was converted with BF_3·OEt_2 into the *alkenedione* (**12b**) (0.06 g, 71%) as a colourless oil, b.p. 200 °C/0.2 mmHg; δ($CDCl_3$) 1.0 (3 H, t, *J* 7 Hz), 1.47 (3 H, s), 2.0—2.5 (10 H, m), 4.68—5.15 (2 H, m), 5.0 (2 H, s), 5.34—5.8 (1 H, m), 6.85 (2 H, d, *J* 9 Hz), 7.1 (2 H, d, *J* 9 Hz), and 7.33 (5 H, br s); $\nu_{max.}$($CHCl_3$) 1 705s, 1 640w, and 840m cm^{-1}; *m/z* 378 (M^+, 3%), 295 (76), 226 (100), 211 (81), 157 (54), and 91 (83) (Found: C, 78.8; H, 8.4. $C_{25}H_{30}O_{30}$ requires C, 78.9; H, 8.4%).

10,11-*Epoxy*-6-(4-*methoxyphenyl*)-6-*methylundecane*-3,7-*dione* (**13a**).—To a solution of the alkene dione (**12a**) (0.1 g, 0.32 mmol) in CH_2Cl_2 (3 ml) containing $NaHCO_3$ (0.036 g, 0.45 mmol) was added MCPBA (85%, 0.08 g, 0.45 mmol). The reaction mixture was stirred (5 h) at room temperature and was

* HMPA = hexamethylphosphoric triamide.

then poured into cold saturated aqueous Na_2SO_3 (5 ml). The aqueous layer was separated and extracted with CH_2Cl_2 (3 × 20 ml). The organic extracts were washed with cold saturated aqueous $NaHCO_3$ (5 ml), saturated aqueous NaCl (5 ml), and were then combined and dried (Na_2SO_4). Evaporation of the solvent and distillation of the residue gave the *epoxide* (**13a**) (0.067 g, 66%) as a colourless oil, b.p. 90 °C/0.1 mmHg; δ($CDCl_3$) 1.01 (3 H, t, *J* 7 Hz), 1.42 (3 H, s), 1.8—2.52 (13 H, m), 3.8 (3 H, s), 6.85 (2 H, d, *J* 9 Hz), and 7.15 (2 H, d, *J* 9 Hz); $\nu_{max.}$($CHCl_3$) 1 710s cm^{-1}; *m/z* 219 (M^+ − 99, 100%), 201 (99), 135 (91), and 121 (74) (Found: C, 71.8; H, 8.3. $C_{19}H_{26}O_4$ requires C, 71.7; H, 8.2%).

6-(4-*Benzyloxyphenyl*)-10,11-*epoxy*-6-*methylundecane*-3,7-*dione* (**13b**).—The alkenedione (**12b**) (0.3 g, 0.79 mmol) was epoxidised with MCPBA to give the *epoxide* (**13b**) (0.188 g, 60%) as an oil, b.p. 185 °C/0.1 mmHg; δ($CDCl_3$) 1.01 (3 H, t, *J* 7 Hz), 1.47 (3 H, s), 1.8—2.6 (13 H, m), 5.08 (2 H, s), 6.95 (2 H, d, *J* 9 Hz), 7.15 (2 H, d, *J* 9 Hz), and 7.39 (5 H, br s); $\nu_{max.}$($CDCl_3$) 1 705s cm^{-1}; *m/z* 366 (M^+ − 28, 25%), 295 (100), 277 (83), 224 (92), and 91 (57).

10,11-*Epoxy*-6-(4-*hydroxyphenyl*)-6-*methylundecane*-3,7-*dione* (**14**).—A solution of the benzyl ether (**13b**) (0.04 g, 0.11 mmol) in 95% EtOH (3 ml) in the presence of 10% Pd–C catalyst (0.015 g) was stirred under H_2 (1 atm) for 45 min. The catalyst was removed by filtration through a Kieselguhr filter aid which was washed with 95% EtOH (10 × 3 ml). The ethanol extracts were combined and the solvent was evaporated to give the *phenol* (**14**) (0.03 g, 100%) as a colourless oil; δ($CDCl_3$) 1.01 (3 H, t, *J* 7 Hz), 1.47 (3 H, s), 1.8—2.6 (13 H, m), 6.8 (2 H, d, *J* 9 Hz), and 7.1 (2 H, d, *J* 9 Hz); $\nu_{max.}$($CDCl_3$) 3 580s, 3 500—3 140s, 1 705s, and 840m cm^{-1}; *m/z* 205 (M^+ − 99, 10%) and 134 (90); R_F [ether–light petroleum (b.p. 60—80 °C) (70:30), silica t.l.c. 0.25].

1-(*Tetrahydropyran*-2-*yloxy*)-3-*trimethylsilylpent*-2-*ene* (**16**).—Dicyclohexylborane was prepared by the addition of BH_3·THF (18.9 ml, 30 mmol, 1.58M) to cyclohexene (4.93 g, 6.08 ml, 60 mmol) in THF (10 ml) at 0 °C over 0.5 h. Stirring was maintained at 0 °C for 3 h, then 3-(tetrahydropyran-2-yloxy)-1-trimethylsilylprop-1-yne[7,13] (3 g, 15 mmol) in THF (10 ml) was added at 0 °C. After the reaction mixture had been stirred at room temperature (5 h) and remaining borane was quenched with but-1-ene (at 0 °C) for 5 min. The resulting clear solution was treated at 0 °C with methyl-lithium in ether (23.1 ml, 45 mmol; 1.95M) and it was then stirred at room temperature (20 min). This gave a yellow solution which was cooled to −30 °C. Cuprous iodide (2.87 g, 15 mmol) was added by spatula, and stirring was continued for 5 min at −30 °C. To the resulting dark suspension were added triethyl phosphite (3.12 ml 3 g, 18 mmol) and HMPA (9 ml), followed by ethyl iodide (3.5 g, 2.5 ml, 23 mmol) all whilst maintaining the temperature at −30 °C throughout. The reaction mixture was allowed to warm to room temperature overnight and was then treated at 0 °C with 3M-aqueous NaOH solution (22.5 ml) followed by 30% H_2O_2 (45 ml). The green-blue suspension was stirred at room temperature (1 h), then the bulk of the THF was removed, and the residue was partitioned between cold saturated aqueous NH_4Cl (50 ml) and ether (150 ml). The aqueous layer was separated and extracted with ether (2 × 150 ml). The separate organic extracts were washed with cold saturated aqueous NaCl (2 × 50 ml), combined, and dried (Na_2SO_4). Evaporation of the solvent gave a red-brown oil which was chromatographed on a silica column (210 g). Elution of the column with ether–light petroleum, b.p. 60—80 °C (5:95; 900 ml) gave the *vinylsilane* (**16**) (2 g, 55%) as a colourless oil; δ(CCl_4) 0.18 (9 H, s), 1.0 (3 H, t, *J* 7 Hz), 1.5—1.9 (6 H, m), 2.7 (2 H, q, *J* 7 Hz), 3.4—4.4 (4 H, m), 4.59 (1 H, m), and 6.2 (1 H, t, *J* 7 Hz); $\nu_{max.}$($CHCl_3$) 1 620w cm^{-1}; R_F 0.62 [silica t.l.c., ether–light petroleum (b.p. 60—80 °C) (1:1)].

3-*Trimethylsilylpent*-2-*en*-1-*ol* (**17**).—A solution of the THP ether (**16**) (1.34 g, 5.9 mmol) and toluene-*p*-sulphonic acid (a few crystals) in methanol (10 ml) was stirred at room temperature (1.5 h). Solid K_2CO_3 (1.6 g, 11.5 mmol) was added. The methanol was evaporated, and the residue was treated with cold saturated aqueous $NaHCO_3$ (10 ml); the aqueous layer was separated, and extracted with ether (2 × 60 ml). The ether extracts were washed with cold saturated aqueous NaCl (10 ml), combined, and dried (Na_2SO_4). Evaporation of the solvent gave the *alcohol* (**17**) (1.1 g, 100%) as a yellow oil, b.p. 58 °C/9 mmHg; δ(CCl_4) 0.2 (9 H, s), 1.03 (3 H, t, *J* 7 Hz), 2.19 (2 H, q, *J* 7 Hz), 2.92 (1 H, br s), 4.18 (2 H, br d, *J* 7 Hz), and 6.12 (1 H, t, *J* 7 Hz); $\nu_{max.}$($CHCl_3$) 3 650m, 3 420m, and 1 615w cm^{-1}; R_F 0.34 [silica t.l.c., ether–light petroleum (b.p. 60—80 °C) (1:1)].

1-*Bromo*-3-*trimethylsilylpent*-2-*ene* (**18**).—To a solution of the allyl alcohol (**17**) (1.1 g, 6.9 mmol) and pyridine (2 drops) in anhydrous ether (10 ml), was added PBr_3 (0.24 ml. 0.68 g, 2.5 mmol) dropwise by syringe. The reaction mixture was heated under reflux (1 h), cooled to 0 °C, and then poured into cold saturated aqueous Na_2CO_3 (10 ml). The aqueous layer was separated and extracted with ether (3 × 30 ml). The ether extracts were washed with cold saturated aqueous NaCl (10 ml), combined, and dried (Na_2SO_4). Evaporation of the solvent and distillation of the residue gave the *bromide* (**18**) (0.7 g, 54%) as a colourless oil, b.p. 38—40 °C/5.5 mmHg; δ(CCl_4) 0.29 (9 H, s), 1.09 (3 H, t, *J* 7 Hz), 2.22 (2 H, q, *J* 7 Hz), 4.12 (2 H, d, *J* 7 Hz), and 6.21 (1 H, t, *J* 7 Hz); $\nu_{max.}$($CHCl_3$) 1 610w cm^{-1} (Found: C, 46.6; H, 7.9. $C_8H_{17}BrSi$ requires C, 43.4; H, 7.6%). The poor analytical data are due to the instability of the allyl bromide (**18**) which had to be stored over anhydrous potassium carbonate. A freshly prepared sample was homogeneous on Kieselgel t.l.c. analysis [R_F 0.8; ether–light petroleum (30:70)].

Methyl 2-(4-*Benzyloxyphenyl*)-2-*methylpropionate* (**19**).—The ester (**8b**) (10 g, 0.037 mol) in dry THF (7.5 ml) was added to freshly prepared $NaNH_2$ [from Na (0.94 g, 0.041 mol)] in liquid ammonia (125 ml) by syringe. The reaction mixture was stirred at −33 °C (30 min) then MeI (5.82 g, 2.55 ml, 0.041 mol) was added, and stirring was continued (1 h) at −33 °C. Solid NH_4Cl (2.17 g, 0.041 mol) was added and the ammonia was allowed to evaporate overnight. Work-up as described for the preparation of (**8a,b**) gave the *dimethyl compound* (**19**) (8.47 g, 80%) as an oil; δ($CDCl_3$) 1.5 (6 H, s), 3.5 (3 H, s), 4.85 (2 H, s), 6.90 (2 H, d, *J* 9 Hz), 7.2 (2 H, d, *J* 9 Hz), and 7.25 (5 H, m).

2-(4-*Benzyloxyphenyl*)-2-*methylpropionyl Chloride* (**20**).—The ester (**19**) (8 g, 0.028 mol) was saponified in refluxing ethanol (120 ml) containing 2M-NaOH (120 ml) for 40 min. Work-up as described for the saponification of (**8a,b**) gave 2-(4-*benzyloxyphenyl*)-2-*methylpropionic acid* (6.34 g, 83%) as colourless crystals, m.p. 121.5—123 °C; δ($CDCl_3$) 1.55 (6 H, s), 5.0 (2 H, s), 6.9 (2 H, d, *J* 9 Hz), 7.25 (2 H, d, *J* 9 Hz), 7.35 (5 H, s), and 10.5 (1 H. br s); $\nu_{max.}$($CHCl_3$) 3 500—2 500m, and 1 710s cm^{-1}; *m/z* 270 (M^+, 10%), and 91 (100) (Found: C, 75.7; H, 7.0. $C_{17}H_{18}O_3$ requires C, 75.7; H, 6.7%). The carboxylic acid (5.13 g, 0.019 mol) was converted with thionyl chloride (40 ml) overnight at room temperature into the *acid chloride* (**20**) (5.36 g, 98%); δ($CDCl_3$) 1.65 (6 H, s), 5.05 (2 H, s). 6.95 (2 H, d, *J* 9 Hz), 7.25 (2 H, d, *J* 9 Hz), and 7.35 (5 H, s); $\nu_{max.}$($CHCl_3$) 1 790s cm^{-1}; *m/z* 290/288 (M^+), and 225 (100%) (Found: M^+, 288.0916. $C_{17}H_{17}{}^{35}ClO_2$ requires *M*, 288.0916; Found: C, 70.5; H, 6.0. $C_{17}H_{17}ClO_2$ requires C, 70.7; H, 5.9%).

2-(4-*Benzyloxyphenyl*)-2-*methylhept*-6-*en*-3-*one* (**21**).—4-Bromobut-1-ene was converted into the cadmium reagent (27

mmol) in benzene (30 ml) as described for the preparation of (**10a,b**). The acid chloride (**20**) (5.36 g, 18 mmol) in benzene (20 ml) was added to the cadmium reagent, and the mixture was heated under reflux (1 h). Work-up as described for the preparation of (**10a,b**) gave the *alkenone* (**21**) (5.21 g, 91%) as an oil which crystallised with time, and was purified by recrystallisation from light petroleum, b.p. 30—40 °C to give small prisms, m.p. 49—51 °C; δ($CDCl_3$) 1.44 (6 H, s), 2.15—2.4 (4 H, m), 4.88—5.0 (2 H, m), 5.02 (2 H, s), 5.2—6.0 (1 H, m), 6.94 (2 H, d, *J* 9 Hz), 7.15 (2 H, d, *J* 9 Hz), and 7.38 (5 H, s); $\nu_{max.}$($CHCl_3$) 1 710s, 1 640w, and 840s cm^{-1}; *m/z* 308 (M^+, 10%), 225 (100), 211 (83), and 135 (17) (Found: C, 81.5; H, 7.7. $C_{21}H_{24}O_2$ requires C, 81.8; H, 7.8%).

5-(4-*Benzyloxyphenyl*)-5-*methyl*-4-*oxohexanal* (**22**).—Ozone was bubbled (40 l h^{-1}) through a solution of the alkene (**21**) (0.265 g, 0.9 mmol) in CH_2Cl_2 (20 ml) at −78 °C, until the blue colour persisted (5 min). The solution was flushed with N_2 and then Me_2S (6 ml) was added. The solution was warmed to room temperature and then stirred overnight. Removal of the solvent gave a yellow brown oil (0.287 g) which was purified by silica preparative t.l.c. [ether–light petroleum (b.p. 60—80 °C) (1:1)] to give the *aldehyde* (**22**) (0.087 g, 32%) as an oil; δ($CDCl_3$) 1.5 (6 H, s), 2.59 (4 H, s), 5.06 (2 H, s), 6.95 (2 H, d, *J* 9 Hz); 7.2 (2 H, d, *J* 9 Hz), 7.39 (5 H, s), and 9.81 (1 H, s); $\nu_{max.}$($CHCl_3$) 1 725m and 1 710s cm^{-1}; *m/z* 310 (M^+, 5%), 225 (100) and 156 (58) (Found: $M^+ - C_4H_5O$, 225.1272. $C_{16}H_{17}O$ requires $M - C_4H_5O$, 225.1279).

6-(4-*Benzyloxyphenyl*)-6-*methyl*-5-*oxo*-2-(p-*tolylsulphonyloxy*)*heptanonitrile* (**23**).—To a solution of the aldehyde (**22**) (0.087 g, 0.28 mmol) and toluene-*p*-sulphonyl chloride (0.107 g, 0.56 mmol) in THF (4 ml) was added NaCN (0.055 g, 1.12 mmol), and the reaction mixture was stirred at room temperature (10 h). It was then poured into iced water (5 ml) and the aqueous layer was separated and extracted with $CHCl_3$ (2 × 20 ml). The organic extracts were washed with saturated aqueous NaCl (5 ml), combined, and dried (Na_2SO_4). Removal of the solvent and preparative silica t.l.c. [ether–light petroleum (b.p. 60—80 °C) (1:1)] gave the *cyano toluene*-p-*sulphonate* (**23**) (0.068 g, 50%) as an oil; δ($CDCl_3$) 1.49 (6 H, s), 1.7—2.4 (4 H, m), 2.48 (3 H, s), 5.08 (2 H, s), 5.12 (1 H, t, *J* 7 Hz), 6.95 (2 H, d, *J* 9 Hz), 7.25 (2 H, d, *J* 9 Hz), 7.4 (7 H, br s), and 7.79 (2 H, d, *J* 8 Hz); $\nu_{max.}$($CHCl_3$) 1 710s, and 1 610 cm^{-1}; R_F [silica t.l.c., ether–light petroleum (b.p. 60—80 °C) (1:1)] 0.29.

6-(4-*Hydroxyphenyl*)-6-*methyl*-5-*oxo*-2-(p-*tolylsulphonyloxy*)*heptanonitrile* (**24**).—To a solution of the benzyl ether (**23**) (0.015 g, 0.03 mmol) in CH_2Cl_2 at −78 °C was added BCl_3 solution (0.156 ml, 0.003 g, 0.03 mmol) in CH_2Cl_2. The red reaction mixture was warmed to room temperature and poured into cold saturated aqueous $NaHCO_3$ (5 ml). The aqueous layer was separated and extracted with CH_2Cl_2 (2 × 20 ml). The organic layers were washed with saturated aqueous NaCl, combined, and dried (Na_2SO_4). Evaporation of the solvent gave the *phenol* (**24**) (0.015 g, 100%) as an oil; δ($CDCl_3$) 1.48 (6 H, s), 1.7—2.4 (4 H, m), 2.48 (3 H, s), 4.12 (1 H, m), 5.11 (1 H, t, *J* 7 Hz), 6.8 (2 H, d, *J* 9 Hz), 7.1 (2 H, d, *J* 9 Hz), 7.36 (2 H, d, *J* 8 Hz), and 7.77 (2 H, d, *J* 8 Hz); $\nu_{max.}$($CHCl_3$) 3 580s and 1 705s cm^{-1}.

Butoxide Cyclisation of the Cyano Sulphonate (**24**).—A solution of the phenol (**24**) (0.01 g, 0.025 mmol) and potassium t-butoxide (0.003 g, 0.025 mmol) in t-butanol (30 ml) was heated in a sealed tube (170 °C) for 18 h. To the cooled reaction mixture was added solid NH_4Cl (0.01 g, 0.19 mmol), and the solvent was removed under reduced pressure. The residue was treated with cold saturated aqueous NH_4Cl (5 ml) and the aqueous layer was extracted with CH_2Cl_2 (2 × 15 ml). The organic extracts were washed with saturated aqueous NaCl (5 ml), combined, and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue on silica preparative t.l.c. [ether–light petroleum (b.p. 60—80 °C) (7:3)] gave the *cyclopropane* (**25**) (0.005 g, 87%) as an oil; δ($CDCl_3$) 1.18—1.4 (2 H, m), 1.55 (3 H, s), 1.6 (3 H, s), 1.8—2.0 (1 H, m), 2.22—2.54 (1 H, m), 6.95 (2 H, d, *J* 9 Hz), and 7.2 (2 H, d, *J* 9 Hz); $\nu_{max.}$($CHCl_3$) 3 580s, 2 075m, and 1 705s cm^{-1}; *m/z* 229 (M^+, 2%), 135 (100), 107 (5), and 91 (5).

6-(4-*Benzyloxyphenyl*)-6-*methylhept*-1-*en*-5-*ol* (**26**).—The ketone (**21**) (500 mg, 1.6 mmol) in methanol (25 ml) was reduced with sodium borohydride (30 mg, 0.8 mmol) at room temperature with stirring under N_2 (2 h). Ether was added, the phases were separated, and the organic layer was washed with water, then dried (Na_2SO_4). Evaporation of the solvent gave the *alcohol* (**26**) (472 mg, 94%) as a colourless oil; δ($CDCl_3$) 1.3 [3 H, m containing (1 H, s)], 1.3 (6 H, s), 2.2 (2 H, m), 3.5 (1 H, m), 4.8 (2 H, m), 4.95 (2 H, s), 5.5 (1 H, m), 6.95 (2 H, d, *J* 9 Hz), 7.3 (2 H, d, *J* 9 Hz), and 7.35 (5 H, s); $\nu_{max.}$($CHCl_3$) 3 550m, 1 620m, and 840s cm^{-1}; *m/z* 310 (M^+, 10%), 225, 135, and 91 (100) (Found: M^+, 310.1953. $C_{21}H_{26}O_2$ requires *M*, 310.1933).

6-(4-*Benzyloxyphenyl*)-5-*methoxy*-6-*methylhept*-1-*ene* (**27**).—Sodium hydride (50% dispersion in oil; 94 mg, 1.9 mmol) was freed of mineral oil by washing with light petroleum, b.p. 30—40 °C, and anhydrous THF (15 ml) was added. MeI (0.16 ml, 0.37 g, 2.6 mmol) was added, followed by the alcohol (**26**) (400 mg, 1.3 mmol) in THF (10 ml) and the reaction mixture was stirred overnight at 40—50 °C. Water (25 ml) was then added, and the reaction mixture was extracted with ether (3 × 50 ml). The organic phases were washed with saturated aqueous NaCl (25 ml), combined, and dried (Na_2SO_4). Evaporation of the ether gave the *methoxy compound* (**27**) (402 mg, 96%) as a colourless oil; δ($CDCl_3$) 1.3 (6 H, s), 1.30 (2 H, m), 2.0 (2 H, m), 3.1 (1 H, m), 3.3 (3 H, s), 4.85 (2 H, m), 4.95 (2 H, s), 5.5 (1 H, m), 6.95 (2 H, d, *J* 7 Hz), 7.25 (2 H, d, *J* 7 Hz), and 7.3 (5 H, s); $\nu_{max.}$($CHCl_3$) 1 635m and 855m cm^{-1} (Found: M^+, 324.2077. $C_{22}H_{28}O_2$ requires *M*, 324.2089).

5-(4-*Benzyloxyphenyl*)-4-*methoxy*-5-*methylhexanal* (**28**).—Ozonolysis of the alkene (**27**) (500 mg, 1.5 mmol) according to the procedure described for the preparation of compound (**22**) gave, after rapid column chromatography on Florisil [eluting with ether–light petroleum (b.p. 60—80 °C) (1:4)] the *aldehyde* (**28**) (320 mg, 60%) as a low-melting solid; δ($CDCl_3$) 1.3 (6 H, s), 1.6 (2 H, m), 2.2 (2 H, m), 3.2 [4 H, m including (3 H, s)], 5.0 (2 H, s), 6.7 (2 H, d, *J* 7 Hz), 7.1 (2 H, d, *J* 7 Hz), 7.3 (5 H, s), and 9.5 (1 H, s); $\nu_{max.}$($CHCl_3$) 1 720s cm^{-1}.

6-(4-*Benzyloxyphenyl*)-5-*methoxy*-6-*methyl*-2-(p-*tolylsulphonyloxy*)*heptanonitrile* (**29**).—The aldehyde (**28**) was treated with NaCN (102 mg, 2.08 mmol) and TsCl (198 mg, 1.04 mmol) according to the method for the preparation of compound (**23**) to give the *cyanosulphonate* (**29**) (164 mg, 62%) as a colourless oil; δ($CDCl_3$) 1.3 (2 H, m), 1.30 (6 H, s), 1.95 (2 H, m), 2.45 (3 H, s), 3.2 (1 H, m), 3.25 (3 H, s). 4.9 (1 H, m), 4.95 (2 H, s), 6.9 (2 H, d, *J* 7 Hz), 7.3 (2 H, d, *J* 7 Hz), 7.35 (2 H, d, *J* 8 Hz), 7.4 (5 H, m), and 7.7 (2 H, d, *J* 8 Hz); $\nu_{max.}$($CHCl_3$) 1 610m and 1 600m cm^{-1} (Found: $M^+ - TsOH$, 335.1885. $C_{22}H_{25}NO_2$ requires $M - TsOH$, 335.1885).

The F_p^+-*Complex* (**31**).*—The alkenone (**21**) (140 mg, 0.45 mmol) and F_p^+-isobutene tetrafluoroborate[14] (60 mg, 0.18 mmol) were heated at 60 °C in dry degassed $CHCl_3$ for 2 h. The resulting red-brown solution was cooled and diluted with ether. This gave a pale yellow precipitate which was filtered to give the

* $F_p = \eta^5$-$C_5H_5Fe(CO)_2$

complex (**31**) (39 mg, 68%) as a pale yellow solid; δ(CD_3CN) 1.42 (6 H, s), 2.0—3.0 (4 H, m), 3.3 (1 H, d, *J* 10 Hz), 3.65 (1 H, d, *J* 7 Hz), 5.1 (2 H, s), 5.55 (5 H, s), 5.8—6.2 (1 H, br s), 6.95 (2 H, d, *J* 7 Hz), 7.2 (2 H, d, *J* 7 Hz), and 7.4 (5 H, s).

6-(4-*Benzyloxyphenyl*)-1,2-*epoxy*-5-*methoxy*-6-*methylheptane* (**32**).—The alkene (**27**) (100 mg, 0.31 mmol) in CH_2Cl_2 (3 ml) was treated with MCPBA (85%, 86 mg, 0.5 mmol) and solid $NaHCO_3$ (36 mg, 0.5 mmol), and the reaction mixture was stirred at room temperature (5 h). The reaction mixture was then diluted with CH_2Cl_2 (15 ml) and washed with saturated aqueous $NaHCO_3$ (15 ml) and saturated aqueous NaCl (15 ml). The organic layer was dried (Na_2SO_4) and evaporated to give the *epoxide* (**32**) (100 mg, 96%) as a pale yellow oil; δ($CDCl_3$) 1.3 (6 H, s), 1.5 (4 H, m), 2.5 (3 H, m), 3.32 (1 H, m), 3.3 (3 H, s), 5.1 (2 H, s), 6.95 (2 H, d, *J* 7 Hz), 7.2 (2 H, d, *J* 7 Hz), and 7.4 (5 H, m); $\nu_{max.}$($CHCl_3$) 1 615w and 1 580m cm^{-1}; *m/z* 340 (M^+, 10%), 249, 226, 225 (100), 234, and 115 (Found: M^+, 340.2045. $C_{22}H_{28}O_3$ requires *M*, 340.2039).

4-(3-*Bromopropyl*)*phenol* (**35**; R = H).—3-(4-Hydroxyphenyl)propan-1-ol (5 g, 32.9 mmol) and conc. H_2SO_4 (2 ml) were added to HBr solution (48%; 30 ml) and the mixture was heated under reflux (6 h). The cooled reaction mixture was diluted with water (25 ml) and the organic layer was separated. The aqueous phase was extracted with ether (3 × 25 ml) and the combined organic layers were washed with a little cold conc. H_2SO_4, then with water (15 ml), and finally with saturated aqueous $NaHCO_3$ (15 ml). The organic layer was dried (Na_2SO_4) and evaporated to give a residue which was distilled (Kugelrohr), to yield the *bromide* (**35**; R = H) (5.3 g, 75%), b.p. (oven temp.) 145—150 °C/0.1 mmHg; δ($CDCl_3$) 1.97 (2 H, quintet, *J* 6.5 Hz), 2.6 (2 H, t, *J* 6.5 Hz), 3.25 (2 H, t, *J* 6.5 Hz), 6.68 (1 H, s), 6.9 (2 H, d, *J* 9 Hz), and 7.2 (2 H, d, *J* 9 Hz); $\nu_{max.}$($CHCl_3$) 3 600s, 3 400m, and 1 605s cm^{-1}; *m/z* 216/214 (M^+, 10%), and 107 (100) (Found: C, 50.0; H, 5.1. $C_9H_{11}BrO$ requires C, 50.2; H, 5.1%).

4-(3-*Bromopropyl*)-1-*trimethylsilyloxybenzene* (**35**; R = $SiMe_3$).—Chlorotrimethylsilane (9.74 ml) was added dropwise to a solution of the phenol (**35**; R = H) (5.2 g, 24.2 mmol) in pyridine (50 ml), and the reaction mixture was stirred at room temperature overnight. The pyridinium hydrochloride was filtered off, the filtrate was concentrated, and the residue was distilled (Kugelrohr) to give the *trimethylsilyl ether* (**35**; R = $SiMe_3$) (4.4 g, 63%) as an oil, b.p. (oven temp.) 125—135 °C/0.1 mmHg; δ($CDCl_3$) 0.25 (9 H, s), 1.8—2.3 (2 H, m), 2.7 (2 H, t, *J* 7 Hz), 3.45 (2 H, t, *J* 6 Hz), 6.6 (2 H, d, *J* 9 Hz), and 6.9 (2 H, d, *J* 9 Hz); $\nu_{max.}$($CHCl_3$) 1 605s and 1 580w cm^{-1}; *m/z* 288/286 (M^+, 10%), and 179 (100) (Found: M^+, 286.0378. $C_{12}H_{19}{}^{79}BrOSi$ requires *M*, 286.0389).

4-(*Hex*-5-*enyl*)-1-*trimethylsilyloxybenzene* (**36**; R = $SiMe_3$).—The bromo compound (**35**; R = $SiMe_3$) (6.85 g, 23.9 mmol) and magnesium turnings (0.63 g, 26.3 mmol) in dry ether (50 ml) were used to prepare a Grignard reagent which was added dropwise to a solution of allyl bromide (6.5 ml, 47.9 mmol) in ether (10 ml). The mixture was heated under reflux (1 h) and was subsequently stirred (24 h) at room temperature. Water (70 ml) was added carefully, and the aqueous layer was separated and extracted with ether (20 ml). The organic layers were washed with saturated aqueous NaCl, combined, and dried (Na_2SO_4). Evaporation of the solvent and distillation (Kugelrohr) of the residue gave the *alkene* (**36**; R = $SiMe_3$) (4.91 g, 83%) as an oil, b.p. (oven temp.) 105—115 °C/0.2 mmHg; δ($CDCl_3$) 0.2 (9 H, s), 1.1—2.7 (8 H, m), 4.6—5.1 (2 H, m), 5.15—6.1 (1 H, m), 6.6 (2 H, d, *J* 9 Hz), and 6.9 (2 H, d, *J* 9 Hz); *m/z* 248 (M^+, 8%), 179 (50), and 107 (100) (Found: M^+, 248.1597. $C_{15}H_{24}OSi$ requires *M*, 248.1597).

4-(*Hex*-5-*enyl*)*phenol* (**36**; R = H).—A solution of the trimethylsilyl ether (**36**; R = $SiMe_3$) (0.4 g, 1.61 mmol) in methanol (9 ml) was treated with a solution of Na_2CO_3 (0.5 g) and $NaHCO_3$ (0.6 g) in water (5 ml). The viscous mixture was stirred at room temperature (1 h) and was then shaken with ether (20 ml) and water (10 ml). The organic layer was separated, dried (Na_2SO_4), and evaporated. This gave a residue which was purified by silica preparative t.l.c. [ethyl acetate–light petroleum (b.p. 60—80 °C) (1:1)] to give the *phenol* (**36**; R = H) (0.22 g, 77%) as an oil; δ($CDCl_3$) 1.25—2.85 (8 H m), 4.7—5.15 (2 H, m), 5.55—6.05 (1 H, m), 6.1 (1 H, br s), 6.6 (2 H, d, *J* 9 Hz), and 6.9 (2 H, d, *J* 9 Hz); $\nu_{max.}$($CHCl_3$) 3 600s, 3 400m, and 1 640m cm^{-1}; *m/z* 176 (M^+, 25%), 133 (35), and 107 (100) (Found: M^+, 176.1201. $C_{12}H_{16}O$ requires *M*, 176.1201).

1-*Acetoxy*-4-(*hex*-5-*enyl*)*benzene* (**36**; R = Ac).—Acetic anhydride (1.58 ml, 16.75 mmol) was added to a solution of the phenol (**36**; R = H) (1.44 g, 8.18 mmol) in pyridine (24 ml), and the mixture was stirred at room temperature (24 h). It was then poured into ice–water, and the product was extracted into ether (3 × 50 ml). The organic extracts were washed with cold dilute HCl, saturated aqueous $NaHCO_3$, and saturated aqueous NaCl solution (each 20 ml), combined, and dried (Na_2SO_4). Removal of the solvent and distillation (Kugelrohr) of the residue gave the *acetate* (**36**; R = Ac) (1.69 g, 95%) as an oil, b.p. (oven temp.) 90—100 °C/0.2 mmHg; δ($CDCl_3$) 2.85—4.15 [11 H, m including (3 H, s) at 2.2], 4.8—5.1 (2 H, m), 5.3—6.0 (1 H, m), 6.95 (2 H, d, *J* 9 Hz), and 7.15 (2 H, d, *J* 9 Hz); $\nu_{max.}$($CHCl_3$) 1 750s and 1 635m cm^{-1}; *m/z* 218 (M^+, 3%), 175 (35), and 107 (100) (Found: M^+, 218.1310. $C_{14}H_{18}O_2$ requires *M*, 218.1307).

1-*Acetoxy*-4-(5,6-*dibromohexyl*)*benzene* (**37**; R = Ac).—A solution of bromine (0.12 ml; 2.33 mmol) in CCl_4 (3 ml) was added dropwise to a solution of the alkene (**36**; R = Ac) (0.5 g, 2.09 mmol) in CCl_4 (6 ml) at 0 °C. After 5 min the solvent was evaporated and the residue was distilled (Kugelrohr) to give the *dibromide* (**37**; R = Ac) (0.6 g, 69%) as an oil, b.p. (oven temp.) 150—180 °C/0.15 mmHg; δ($CDCl_3$) 1.3—2.8 [11 H, m including (3 H, s) at 2.1], 3.35—3.9 (2 H, m), 3.9—4.25 (1 H, m), 6.75 (2 H, d, *J* 9 Hz), and 7.15 (2 H, d, *J* 9 Hz); $\nu_{max.}$($CHCl_3$) 1 745s cm^{-1}; *m/z* 380/378/376 (M^+, 1%), 338/336/334 (20), and 107 (100) (Found: M^+, 375.9672. $C_{14}H_{18}{}^{79}Br_2O_2$ requires *M*, 375.9673).

4-(5,6-*Dibromohexyl*)*phenol* (**37**; R = H).—A solution of the acetate (**37**; R = Ac) (0.595 g, 1.57 mmol) in methanol (10 ml) was treated with a solution of Na_2CO_3 (0.47 g) and $NaHCO_3$ (0.55 g) in water (5 ml). The mixture was stirred at room temperature until t.l.c. indicated that all starting material had disappeared. The reaction mixture was then shaken with ether (20 ml) and water (10 ml). The organic layer was separated, dried (Na_2SO_4), and evaporated. The resulting residue was purified on silica preparative t.l.c. [ethyl acetate–light petroleum (b.p. 60—80 °C) (1:1)] to give the *phenol* (**37**; R = H) (0.52 g, 97%) as an oil; δ($CDCl_3$) 1.3—2.8 (8 H, m), 3.4—3.9 (2 H, m), 3.95—4.3 (1 H, m), 5.43 (1 H, br s), 6.75 (2 H, d, *J* 9 Hz), and 7.05 (2 H, d, *J* 9 Hz); $\nu_{max.}$($CHCl_3$) 3 600s and 3 300m cm^{-1}; *m/z* 338/336/334 (M^+, 7%), and 107 (100) (Found: M^+, 333.9570. $C_{12}H_{16}{}^{79}Br_2O$ requires *M*, 333.9568).

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